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RESPIRATORY

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INDICES

Other Online EBM Resources/Links:

EBM Portal Links (SK): http://web.mac.com/malees/Primary_Care_Portal/EBM.html; Evidence Updates service: http://plus.mcmaster.ca/EvidenceUpdates/Default.aspx

General: U of T: http://www.cebm.utoronto.ca/; Oxford: http://www.cebm.net/?o=1011; McMasters: How to teach evidence based clinical practice – Links: http://hsl.mcmaster.ca/ebcp/. Dynamed: *www.ebscohost.com/dynamed/*

User's Guide: UofA, Centre for Health Evidence: http://www.cche.net/usersguides/main.asp; UBC: http://www.ti.ubc.ca/; Grey Literature Searching: http://www.cadth.ca/index.php/en/cadth/products/grey-matters

ScHARR Intro to Evidence Based Practice (Sheffield, UK) http://www.shef.ac.uk/scharr/ir/netting/; BMJ – Clinical Evidence Links: http://clinicalevidence.bmj.com/ceweb/resources/useful_links.jsp; NNTs http://www.thennt.com/

Clinical significance CALCULATORS: UBC: http://spph.ubc.ca/sites/healthcare/files/calc/clinsig.html; Wisconsin: http://intsmain.is.mcw.edu/clincalc/bayes.html. Essential Evidence Plus: http://www.essentialevidenceplus.com/

Dalhousie Katie Clinical Significance Calculator*: http://ktcalc.cme.dal.ca/site/login.php Z-score: http://www.socscistatistics.com/pvalues/normaldistribution.aspx Teaching EBM Videos: McMaster Guyatt: http://ebm.mcmaster.ca/materials_videos.htm

RxFiles – Select Trial Summaries (more available online at www.RxFiles.ca)

Anemia: Trials Summary: http://www.rxfiles.ca/rxfiles/uploads/documents/CHT-Anemia-Key-Trials.pdf

Dementia: CATIE-AD: http://www.rxfiles.ca/rxfiles/uploads/documents/Psych-CATIE-AD-trial-summary.pdf

Diabetes: Landmark Trials Summary: Glucose: http://www.rxfiles.ca/rxfiles/uploads/documents/CHT-Diabetes-Landmark-Trials-Links.pdf

Landmark Trials Summary: NON-Glucose: http://www.rxfiles.ca/rxfiles/uploads/documents/members/CHT-DIABETES-Landmark-Trials-Non-Glucose.pdf

ACCORD-ADVANCE Comparison: http://www.rxfiles.ca/rxfiles/uploads/documents/Diabetes-A1C-ACCORD-vs-ADVANCE-COMPARISON.pdf

ACCORD-BP & LIPID: http://www.rxfiles.ca/rxfiles/uploads/documents/ACCORD-BP-Lipid-Trial-Overview.pdf

ACCORD: Glucose http://www.rxfiles.ca/rxfiles/uploads/documents/Diabetes-Targets-ACCORD-A1C.pdf

ADVANCE: http://www.rxfiles.ca/rxfiles/uploads/documents/Diabetes-ADVANCE-trial.pdf

AVANDIA & CV risk – Meta-analysis: http://www.rxfiles.ca/rxfiles/uploads/documents/Diabetes-Avandia-CV-Meta-Comments.pdf

DREAM: http://www.rxfiles.ca/rxfiles/uploads/documents/Dream-QandA.pdf

ELIXA: Lixisenatide : http://www.rxfiles.ca/rxfiles/uploads/documents/Lixisenatide-ELIXA%20Trial%20Summary.pdf 2016

EMPA-REG: http://www.rxfiles.ca/rxfiles/uploads/documents/EMPA-REG%20Trial%20Summary.pdf 2016

LEADER: Liraglutide: http://www.rxfiles.ca/rxfiles/uploads/documents/Leader-Liraglutide%20VICTOZA%20and%20Cardiovascular%20Outcomes%20in%20Type%202%20Diabetes.pdf 2016

RECORD:http://www.rxfiles.ca/rxfiles/uploads/documents/Diabetes-RECORD-Trial-Summary.pdf

SAVOR-TIMI 53: http://www.rxfiles.ca/rxfiles/uploads/documents/SAVOR-TIMI-53-Saxagliptin-CV-Outcomes-Trial-Summary.pdf

TECOS: Sitagliptin CV outcomes: http://www.rxfiles.ca/rxfiles/uploads/documents/TECOS-Trial-Summary.pdf 2016

Hypertension: Summary Table: http://www.rxfiles.ca/rxfiles/uploads/documents/HTNLandmarkHypertensionTrials.pdf

ACCOMPLISH: http://www.rxfiles.ca/rxfiles/uploads/documents/HTN-QandA-Accomplish.pdf

ALLHAT: http://www.rxfiles.ca/rxfiles/uploads/documents/HTN-Update-2003-Final.pdf

ANBP2: http://www.rxfiles.ca/rxfiles/uploads/documents/HTN-QandA-ANBP2.pdf

ASCOT-BPLA: http://www.rxfiles.ca/rxfiles/uploads/documents/HTN-QandA-ASCOT.pdf

SPRINT: http://www.rxfiles.ca/rxfiles/uploads/documents/SPRINT-BP-Trial-Overview.pdf 2015

Trial Summary table - abridged: http://www.rxfiles.ca/rxfiles/uploads/documents/members/cht-HTN-trial-summary.pdf

HF: CHARM: http://www.rxfiles.ca/rxfiles/uploads/documents/CHARM-Comments.pdf

PARADIGM-HF: http://www.rxfiles.ca/rxfiles/uploads/documents/PARADIGM-HF-Trial-Sacubitril.pdf 2015

Hirsutism: http://www.rxfiles.ca/rxfiles/uploads/documents/members/Hirsutism%20Trial%20Summary.pdf

HRT: WHI: http://www.rxfiles.ca/rxfiles/uploads/documents/HRT Post-WHI-2002-Header.pdf

WHI & Age: http://www.rxfiles.ca/rxfiles/uploads/documents/HRT-Age-and-the-WHI.pdf ;

WHI & Extras/Perspectives on NNTs, NNHs: http://www.rxfiles.ca/rxfiles/uploads/documents/HRT-WHI-Extras-Perspectives.pdf

Lipid: Summary Table: http://www.rxfiles.ca/rxfiles/uploads/documents/members/CHT-lipid agents-major trials.pdf

& Q&A 2004: http://www.rxfiles.ca/rxfiles/uploads/documents/Lipid-QandA-Update-Oct04.pdf

AIM-HIGH: http://www.rxfiles.ca/rxfiles/uploads/documents/Lipid-AIM-HIGH-nicotinic-acid-Niaspan-trial.pdf

ASCOT-LLA: http://www.rxfiles.ca/rxfiles/uploads/documents/Lipid-QandA-ASCOT.pdf

CARDS: http://www.rxfiles.ca/rxfiles/uploads/documents/Lipid-QandA-CARDS.pdf

ENHANCE: http://www.rxfiles.ca/rxfiles/uploads/documents/Lipid-ENHANCE trial overview.pdf

FIELD Substudy: http://www.rxfiles.ca/rxfiles/uploads/documents/FIELD-Sub-Analysis-Women-Trial-Summary.pdf 2015

IDEAL: http://www.rxfiles.ca/rxfiles/uploads/documents/Lipid-QandA-IDEAL.pdf

IMPROVE-IT: http://www.rxfiles.ca/rxfiles/uploads/documents/Lipid-IMPROVE-IT-Trial-Summary-QandA.pdf 2014

JUPITER: http://www.rxfiles.ca/rxfiles/uploads/documents/Lipid-Jupiter-trial-overview.pdf

PROVE-IT: http://www.rxfiles.ca/rxfiles/uploads/documents/Lipid-QandA-Prove-It.pdf

SHARP: http://www.rxfiles.ca/rxfiles/uploads/documents/Lipid-Sharp-CKD-trial.pdf

SPARCL: http://www.rxfiles.ca/rxfiles/uploads/documents/Lipid-QandA-SPARCL.pdf

Thrombotic (antithrombotics: ASA, clopidogrel, anticoagulants: warfarin) :

ACTIVE-A & ACTIVE-W trials http://www.rxfiles.ca/rxfiles/uploads/documents/ACTIVE-A-Trial-Summary.pdf

Antithrombotics Summary Chart:: http://www.rxfiles.ca/rxfiles/uploads/documents/members/cht-AntiThrombotics.pdf

ARISTOTLE: Apixaban vs warfarin in A Fib: http://www.rxfiles.ca/rxfiles/uploads/documents/ARISTOTLE-AF-Apixaban.pdf

CHARISMA: http://www.rxfiles.ca/rxfiles/uploads/documents/Charisma-QandA.pdf

Clopidogrel-PPI drug interaction: http://www.rxfiles.ca/rxfiles/uploads/documents/Clopidogrel-PPI-interaction-QandA.pdf

DAPT: 12 vs 30months http://www.rxfiles.ca/rxfiles/uploads/documents/DAPT-Trial-12vs30months.pdf

PCI-Clarity: http://www.rxfiles.ca/rxfiles/uploads/documents/PCI-CLARITY%20Trial%20Summary.pdf 2016

PCI-CURE: http://www.rxfiles.ca/rxfiles/uploads/documents/PCI-CURE%20Trial%20Summary.pdf 2016

PEGASUS-TIMI 54: Ticagrelor vs Pl, prior-MI: http://www.rxfiles.ca/rxfiles/uploads/documents/PEGASUS%20Trial%20Summary.pdf 2016

PLATO: Ticagrelor vs clopidogrel ACS: http://www.rxfiles.ca/rxfiles/uploads/documents/PLATO%20Trial%20Summary.pdf 2016

RE-LY: Dabigatran vs warfarin in Atrial Fibrillation http://www.rxfiles.ca/rxfiles/uploads/documents/RE-LY-Trial-Dabigatran.pdf

ROCKET-AF: Rivaroxaban vs warfarin in A Fib: http://www.rxfiles.ca/rxfiles/uploads/documents/ROCKET-AF-Rivaroxaban.pdf

TRITON-TIMI 38: Prasugrel vs clopidogrel, ACS: http://www.rxfiles.ca/rxfiles/uploads/documents/TRITON-TIMI%2038%20Trial%20Summary.pdf 2016

MISC.:

Catie-AD: Atypical Antipsychotics in Patients with Alzheimer's http://www.rxfiles.ca/rxfiles/uploads/documents/Psych-CATIE-AD-trial-summary.pdf

FLAME*: Indacaterol+Glycopyrronium vs Salmeterol+Fluticasone for COPD:http://www.rxfiles.ca/rxfiles/uploads/documents/FLAME-Trial-Summary.pdf* 2016

Meloxicam: SELECT, MELISSA; *celecoxib* CLASS, *rofecoxib* VIGOR,: http://www.rxfiles.ca/rxfiles/uploads/documents/QandA-Meloxicam-2.pdf

OAB: Darifenacin-Oxybutynin Memory Trial : http://www.rxfiles.ca/rxfiles/uploads/documents/UI-Darifenacin-Kay-Trial-QandA.pdf

SENIOR: http://www.rxfiles.ca/rxfiles/uploads/documents/Senior-Trial-Oxybutynin-Solifenacin-Elderly-Cognitive-Impairment.pdf

WARFASA: http://www.rxfiles.ca/rxfiles/uploads/documents/Aspirin-warfarin-trial-summary-WarfASA.pdf

RxFiles: Evidence Based Medicine (EBM) Overview - References

[1] Sackett D, Straus S, Richardson WS, Rosenberg, Haynes R. Evidence-Based Medicine: how to practice and teach EBM. Churchill Livinstone. 2000.

[2] Dawes M, Davies P, Gray A, Mant J, Seers K, Snowball. Evidence-based Practice; a primer for health care professionals. Elsevier, 2nd edition 2005.

[3] Allen J. Pharmacist's Letter / Prescriber's Letter. Applying Study Results to Patient Care. June 2005, 21;1-14.

[4] Jadad A, Enkin M. Randomized Controlled Trials: Questions, Answers and Musings 2nd edition. Blackwell Publishing 2007; BMJ Books

[5] Edited by: Geyman J, Deyo R, Ramsey S. Evidence-Based Clinical Practice: Concepts and Approaches. Butterworth Heinemann 2000.

[6] Centre for Evidence Based Medicine (CEBM) Oxford: EBM Tools accessed online 31Jul08 at: http://www.cebm.net/index.aspx?o=1157

[7] Centre for Evidence Based Medicine, University Health Network, Toronto. Critical Appraisal tools; accessed online 31Jul08: http://www.cebm.utoronto.ca/teach/materials/caworksheets.htm

[8] Schulz KF, Chalmers I, Hayes RJ, Altman DG. Empirical evidence of bias. Dimensions of methodological quality associated with estimates of treatment effects in controlled trials. JAMA. 1995 Feb 1;273(5):408-12. {Compared with trials in which authors reported adequately concealed treatment allocation, trials in which concealment was either inadequate or unclear (did not report or incompletely reported a concealment approach) yielded larger estimates of treatment effects (P < .001). Odds ratios were exaggerated by 41% for inadequately concealed trials and by 30% for unclearly concealed trials (adjusted for other aspects of quality). Trials in which participants had been excluded after randomization did not yield larger estimates of effects, but that lack of association may be due to incomplete reporting. Trials that were not double-blind also yielded larger estimates of effects (P = .01), with odds ratios being exaggerated by 17%.}

[9] Moher D, Pham B, Jones A, Cook DJ, Jadad AR, Moher M, Tugwell P, Klassen TP. Does quality of reports of randomised trials affect estimates of intervention efficacy reported in meta-analyses? Lancet. 1998 Aug 22;352(9128):609-13. {FINDINGS: The quality of trials was low. Masked assessments provided significantly higher scores than unmasked assessments (mean 2.74 [SD 1.10] vs 2.55 [1.20]). Low-quality trials (score < or = 2), compared with high-quality trials (score > 2), were associated with an increased estimate of benefit of 34% (ratio of odds ratios [ROR] 0.66 [95% CI 0.52-0.83]). Trials that used inadequate allocation concealment, compared with those that used adequate methods, were also associated with an increased estimate of benefit (37%; ROR=0.63 [0.45-0.88]). The average treatment benefit was 39% (odds ratio [OR] 0.61 [0.57-0.65]) for all trials, 52% (OR 0.48 [0.43-0.54]) for low-quality trials, and 29% (OR 0.71 [0.65-0.77]) for high-quality trials. Use of all the trial scores as quality weights reduced the effects to 35% (OR 0.65 [0.59-0.71]) and resulted in the least statistical heterogeneity. INTERPRETATION: Studies of low methodological quality in which the estimate of quality is incorporated into the meta-analyses can alter the interpretation of the benefit of intervention, whether a scale or component approach is used in the assessment of trial quality.}

[10] Fletcher J. Subgroup analyses: how to avoid being misled. BMJ. 2007 Jul 14;335(7610):96-7.

[11] Centre for Evidence Based Medicine (CEBM) Oxford: EBM Tools accessed online 31Jul08 at: http://www.cebm.net/index.aspx?o=1039

[12] Oleckno WA. Essential Epidemiology Principles and Applications. Long Grove IL: Waveland Press Inc, 2002. (page 108)

[13] http://www.cochrane.org/ ; http://www.cfp.ca/cgi/content/full/55/11/1155?etoc

[14] http://www.campbellcollaboration.org/ ; http://www.campbellcollaboration.org/library.php

[15] Centre for Evidence Based Medicine (CEBM) Oxford: EBM Tools accessed online 31Jul08 at: http://www.cebm.net/index.aspx?o=1025

[16] Barratt A, Wyer PC, Hatala R, McGinn T, Dans AL, Keitz S, Moyer V, For GG; Evidence-Based Medicine Teaching Tips Working Group. Tips for learners of evidence-based medicine: 1. Relative risk reduction, absolute risk reduction and number needed to treat. CMAJ. 2004 Aug 17;171(4):353-8.

[17] Bandolier; Number Needed to Treat. Accessed online 31Jul08 at: http://www.medicine.ox.ac.uk/bandolier/band59/NNT1.html

[18] Finlay A. McAlister. The "number needed to treat" turns 20 — and continues to be used and misused. CMAJ 2008; 179: 549-553. http://www.cmaj.ca/cgi/content/full/179/6/549

[19] James P McCormack. NNT misses the mark on baseline risks. Electronic Letter, CMAJ online. (17 September 2008) http://www.cmaj.ca/cgi/eletters/179/6/549#20357

[20] Centre for Evidence Based Medicine (CEBM) Oxford: NNT calculator tool. Accessed online 31Jul08 at http://www.cebm.net/index.aspx?o=1044 .

[21] Montori VM, Kleinbart J, Newman TB, Keitz S, Wyer PC, Moyer V, Guyatt G; Evidence-Based Medicine Teaching Tips Working Group. Tips for learners of evidence-based medicine: 2. Measures of precision (confidence intervals). CMAJ. 2004 Sep 14;171(6):611-5.

[22] Hatala R, Keitz S, Wyer P, Guyatt G; Evidence-Based Medicine Teaching Tips Working Group. Tips for learners of evidence-based medicine: 4. Assessing heterogeneity of primary studies in systematic reviews and whether to combine their results. CMAJ. 2005 Mar 1;172(5):661-5.

[23] Kaduszkiewicz H, Zimmermann T, Beck-Bornholdt HP, van den Bussche H. Cholinesterase inhibitors for patients with Alzheimer's disease: systematic review of randomised clinical trials. BMJ. 2005 Aug 6;331(7512):321-7. http://www.bmj.com/cgi/reprint/331/7512/321 {A systematic review by Kaduszkiewicz and colleagues (p 321) included 22 double blind randomised controlled trials with the follow-up ranging from six weeks to three years, but the trials scored poorly on a predefined checklist of criteria of methodological quality. Further, the outcomes measuring cognition did show beneficial effects of cholinesterase inhibitors, but these effects were minimal (ranging from 1.5 points to 3.9 points on a 70 point Alzheimer's disease assessment scale).}

[24] Regier L. RxFiles Trial Summary: Darifenacin (ENABLEX) vs Oxybutynin ER extended release (DITROPAN XL) vs Placebo: Effects On Memory / Cognitive Impairment. Accessed at: http://www.rxfiles.ca/rxfiles/uploads/documents/UI-Darifenacin-Kay-Trial-QandA.pdf

[25] Montori VM, Isley WL, Guyatt GH. Waking up from the DREAM of preventing diabetes with drugs. BMJ. 2007 Apr 28;334(7599):882-4.

[26] Montori VM. Treat the Target or Treat the Patient. Aust Prescr 2011;34:94-5. Accessed online Aug 2, 2011 http://www.australianprescriber.com/magazine/34/4/94/5.

[27] Halvorsen PA, Selmer R, Kristiansen IS. Different ways to describe the benefits of risk-reducing treatments: a randomized trial. Ann Intern Med. 2007 Jun 19;146(12):848-56. Summary for patients in: Ann Intern Med. 2007 Jun 19;146(12):I50.

[28] Anonymous. Intensive blood glucose control with sulphonylureas or insulin compared with conventional treatment and the risk of complications in patients with type 2 diabetes (UKPDS 33). Lancet 1998;352:837-53.

[29] Regier L. HRT in Light of the WHI – Data in Perspective. Sept 2002. Available online at: **http://www.rxfiles.ca/rxfiles/uploads/documents/HRT-WHI-Extras-Perspectives.pdf**

[30] Ross JS, Mulvey GK, Hines EM, et al. Trial publication after **registration** in ClinicalTrials.Gov: A cross-sectional analysis. PLoS Med 2009; DOI:10.1371/journal.pmed.1000144.

[31] Mathieu S, Boutron I, Moher D, et al. Comparison of registered and published **primary outcomes** in randomized controlled trials. JAMA 2009; 302: 977-984.

[32] McNutt Robert A.; Livingston Edward H. Evidence-Based Medicine Requires Appropriate **Clinical Context**.JAMA. 2010;303(5):454-455.

[33] Kent DM, Steyerberg E, van Klaveren D. Personalized evidence based medicine: predictive approaches to heterogeneous treatment effects. BMJ. 2018 Dec 10;363:k4245.

[34] Laffin LJ, Besser SA, Alenghat FJ. A data-zone scoring system to assess the generalizability of clinical trial results to individual patients. Eur J Prev Cardiol.2018:2047487318815967.

[35] Senn SJ, Lewis RJ. Treatment Effects in Multicenter Randomized Clinical Trials. JAMA. 2019 Mar 1.

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Additional References:

Aubin D, Hebert M, Eurich D. The importance of measuring the impact of **patient-oriented research**. CMAJ. 2019 Aug 6;191(31):E860-E864.

Dal-Ré R. **Analysis of retracted articles on medicines administered to humans**. Br J Clin Pharmacol. 2019 Jun 24.

Herrera-Perez D, Haslam A, Crain T, et al. A comprehensive review of **randomized clinical trials** in three medical journals reveals 396 medical reversals. Elife. 2019 Jun 11;8.

Khan MS, Lateef N, Siddiqi TJ, et al. Level and Prevalence of **Spin in Published Cardiovascular Randomized Clinical Trial Reports** With Statistically Nonsignificant Primary Outcomes: A Systematic Review. JAMA Netw Open. 2019 May 3;2(5):e192622.

Mostofsky E, Dunn JA, Hernández-Díaz S, Mittleman MA. Patient and Physician **Preferences for Reporting Research Findings**. Fam Med. 2019 Jun;51(6):502-508.

Murray SB, Heathers JA, Schauer RM, et al. Postpublication Metrics of Randomized Clinical Trials With and Without Null Findings. JAMA. 2019 May 14;321(18):1825-1826.

Niforatos JD, Weaver M, Johansen ME. Assessment of **Publication Trends of Systematic Reviews and Randomized Clinical Trials**, 1995 to 2017. JAMA Intern Med. 2019 Jul 29.

Nissen SE, Reed GW. Can we trust **observational data for clinical decision-making**? Eur Heart J. 2018 Dec 27.

Norton EC, Dowd BE, Maciejewski ML. Marginal Effects-Quantifying the Effect of Changes in Risk Factors in Logistic Regression Models. JAMA. 2019 Mar 8.

Reynolds-Vaughn V, Riddle J, Brown J, et al. Evaluation of **Spin in the Abstracts of Emergency Medicine Randomized Controlled Trials**. Ann Emerg Med. 2019 May 14.

Sanders GD, Maciejewski ML, Basu A. Overview of Cost-effectiveness Analysis. JAMA. 2019 Mar 11.

Trinquart L, Erlinger AL, Petersen JM, et al. Applying the E-value to Assess the Robustness of Epidemiologic Fields of Inquiry to Unmeasured Confounding. Am J Epidemiol. 2019 Mar 15.

REFERENCES:

Canadian Hypertension Society -**2017 Canadian** Hypertension **Recommendations** Working Group-downloadable Summary & Slides; www.hypertension.ca

Leung AA, Nerenberg K, Daskalopoulou SS, et al; CHEP Guidelines Task Force. Hypertension Canada's **2016 CHEP guidelines** for blood pressure measurement, diagnosis, assessment of risk, prevention and treatment of hypertension. Can J Cardiol 2016 (accepted manuscript) doi: 10.1016/j.cjca.2016.02.066 www.onlinecjc.ca/article/S0828-282X(16)00192-6/pdf (accessed April 11, 2016).

Hackam DG, Quinn RR, Ravani P, et al. Canadian Hypertension Education Program. The 2013 Canadian Hypertension Education Program (CHEP) Recommendations for Blood Pressure Measurement, Diagnosis, Assessment of Risk, Prevention, and Treatment of Hypertension. Can J Cardiol. 2013 Mar 28.

Canadian Hypertension Education Program. 2013 CHEP recommendations for the management of hypertension. http://hypertension.ca/chep/wp-content/uploads/2011/05/FullCHEPRecommendations_EN_2011.pdf

ACCF American College of Cardiology Foundation / AHA American Heart Association 2011 – Hypertension in the Elderly: http://circ.ahajournals.org/cgi/reprint/CIR.0b013e31821daaf6

Dasgupta K, Quinn RR, Zarnke KB, et al. Canadian Hypertension Education Program. The **2014 CHEP-Canadian Hypertension** Education Program Recommendations for Blood Pressure Measurement, Diagnosis, Assessment of Risk, Prevention, and Treatment of Hypertension. Can J Cardiol. 2014 May;30(5):485-501.

The 2016 Canadian Hypertension Education Program Recommendations www.hypertension.ca

Dionne JM, Harris KC, Benoit G, et al. **Hypertension Canada's 2017 Guidelines for the Diagnosis, Assessment, Prevention, and Treatment of Pediatric Hypertension**. Can J Cardiol. 2017 May;33(5):577-585

Leung AA, Daskalopoulou SS, Dasgupta K, et al. **Hypertension Canada's 2017 Guidelines for Diagnosis, Risk Assessment, Prevention, and Treatment of Hypertension in Adults**. Can J Cardiol. 2017 May;33(5):557-576

ACC/AHA 2017 Whelton PK, Carey RM, et al. **2017 ACC/AHA**/AAPA/ABC/ACPM/AGS/APhA/ASH/ASPC/NMA/PCNA **Guideline for the Prevention, Detection, Evaluation, and Management of High Blood Pressure** in Adults: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. Hypertension. 2017 Nov 13.

Nerenberg KA, Zarnke KB, Leung AA, et al. **Hypertension Canada's 2018 guidelines for diagnosis, risk assessment, prevention, and treatment of hypertension in adults and children**. Can J Cardiol 2018; February 20, 2018.

[1] Genest J, McPherson R, Frohlich J, et al. **2009 Canadian** Cardiovascular Society/Canadian guidelines for the diagnosis and treatment of dyslipidemia and prevention of cardiovascular disease in the adult - 2009 recommendations. Can J Cardiol. 2009 Oct;25(10):567-79.

McPherson R, Frohlich J, Fodor G, Genest J. **Canadian 2006** Cardiovascular Society position statement -- Recommendations for the diagnosis and treatment of dyslipidemia and prevention of cardiovascular disease. Can J Cardiol. 2006 Sep;22(11):913-27. (Genest J, Frohlich J, Fodor G, McPherson R; Working Group on Hypercholesterolemia and Other Dyslipidemias. Recommendations for the management of dyslipidemia and the prevention of cardiovascular disease: summary of the **Canadian 2003 update**. CMAJ. 2003 Oct 28;169(9):921-4. http://www.cmaj.ca/cgi/data/169/9/921/DC1/1 Full Report.)

Anderson TJ, Grégoire J, Hegele RA, et al. **2012 Update of the Canadian Cardiovascular Society Guidelines** for the diagnosis and treatment of dyslipidemia for the prevention of cardiovascular disease in the adult. Can J Cardiol 2013;29(2):151-67. www.onlinecjc.ca/article/S0828-282X(12)01510-3/fulltext (accessed February 5, 2013).

Anderson TJ, Grégoire J, Pearson GJ, et al. **2016** Canadian Cardiovascular Society guidelines for the management of **dyslipidemia** for the prevention of cardiovascular disease in the adult. Can J Cardiol 2016 [accepted manuscript published online], doi: 10.1016/j.cjca.2016.07.510.

[1] **Canadian 2008 Guidelines (Sept 2008)**: http://www.diabetes.ca/files/cpg2008/cpg-2008.pdf

Canadian 2003 Diabetes Guidelines http://www.diabetes.ca/cpg2003/download.aspx (Meltzer S, Leiter L, Daneman D, et al 1998. Clinical practice guidelines for the management of diabetes in Canada. CMAJ 1998;159 (8 Suppl).)

Canadian 2013 Guidelines (April 2013): http://guidelines.diabetes.ca/

Diabetes Canada Clinical Practice Guidelines Expert Committee, Lipscombe L, Booth G, Butalia S, et al. **Pharmacologic Glycemic Management of Type 2 Diabetes in Adults. Can J Diabetes. 2018** Apr;42 Suppl 1:S88-S103.

[1] Brown AF, Mangione CM, Saliba D, Sarkisian CA; California Healthcare Foundation/**American Geriatrics Society** Panel on Improving Care for Elders with Diabetes. Guidelines for improving the care of the older person with diabetes mellitus. J Am Geriatr Soc. **2003** May;51(5 Suppl Guidelines):S265-80.

[7] Stone NJ et al. **2013 ACC/AHA** guideline on the treatment of **blood cholesterol to reduce atherosclerotic cardiovascular risk in adults**: A report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. J Am Coll Cardiol 2013 Nov 12.

Grundy SM, Stone NJ, Bailey AL, et al. **2018 AHA/ACC**/AACVPR/AAPA/ABC/ACPM/ADA/AGS/APhA/ASPC/NLA/PCNA Guideline on the **Management of Blood Cholesterol**: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. J Am Coll Cardiol. 2018 Nov 8.

Grundy SM, Stone NJ, Bailey AL, et al. **2018 AHA/ACC**/AACVPR/AAPA/ABC/ACPM/ADA/AGS/APhA/ASPC/NLA/PCNA Guideline on the **Management of Blood Cholesterol: Executive Summary**: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. J Am Coll Cardiol. 2018 Nov 3.

Wilson PWF, Polonsky TS, Miedema MD, et al. **Systematic Review for the 2018 AHA/ACC**/AACVPR/AAPA/ABC/ACPM/ADA/AGS/APhA/ASPC/NLA/PCNA Guideline on the **Management of Blood Cholesterol**: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. J Am Coll Cardiol. 2018 Nov 3.

Additonal articles of interest for CV Risk:

Abdelhamid AS, Martin N, Bridges C, et al. **Polyunsaturated fatty acids for the primary and secondary prevention of cardiovascular disease**. Cochrane Database Syst Rev. 2018 Jul 18;7:CD012345. This is the most extensive systematic review of RCTs conducted to date to assess effects of increasing PUFA on cardiovascular disease, mortality, lipids or adiposity. Increasing PUFA intake probably slightly reduces risk of coronary heart disease and cardiovascular disease events, may slightly reduce risk of coronary heart disease mortality and stroke (though not ruling out harms), but has little or no effect on all-cause or cardiovascular disease mortality. The mechanism may be via lipid reduction, but increasing PUFA probably slightly increases weight.

Aburto NJ, Hanson S, Gutierrez H, Hooper L, Elliott P, Cappuccio FP. Effect of increased **potassium intake** on cardiovascular risk factors and disease: systematic review and meta-analyses. BMJ. 2013 Apr 3;346:f1378.

Aburto NJ, Ziolkovska A, Hooper L, et al. Effect of lower **sodium intake** on health: systematic review and meta-analyses. BMJ. 2013 Apr 3;346:f1326.

Abuzaid AS, Al Ashry HS, Elbadawi A, et al. Meta-Analysis of Cardiovascular Outcomes With **Continuous Positive Airway Pressure** Therapy in Patients With Obstructive Sleep Apnea. Am J Cardiol. 2017 Jun 1.

ACC/AHA 2017 Whelton PK, et al. **2017 ACC/AHA**/AAPA/ABC/ACPM/AGS/APhA/ASH/ASPC/NMA/PCNA **Guideline for the Prevention, Detection, Evaluation, and Management of High Blood Pressure** in Adults: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. Hypertension. 2017 Nov 13.

ADA 2013: American Diabetes Association. Clinical practice recommendations. Diabetes Care 2013; 36:S1-S110. http://care.diabetesjournals.org/content/36/Supplement_1.toc

Adabag S, Huxley RR, Lopez FL, et al. **Obesity-related risk of sudden cardiac death**: the Atherosclerosis Risk in Communities study (ARIC). Heart 2014;10.1136/heartjnl-2014-306238.

Agca R, Heslinga SC, Rollefstad S, et al.**EULAR** recommendations for **cardiovascular disease risk management in patients with rheumatoid arthritis and other forms of inflammatory joint disorders**: 2015/2016 update. Ann Rheum Dis. 2016 Oct 3.

AHA 2013 Risk Calculator: http://my.americanheart.org/professional/StatementsGuidelines/PreventionGuidelines/Prevention-Guidelines_UCM_457698_SubHomePage.jsp

ADA 2014: American Diabetes Association. Standards of **Medical Care in Diabetes**. Diabetes Care January 2014 37:S14-S80; doi:10.2337/dc14-S014. http://care.diabetesjournals.org/content/37/Supplement_1.toc

ADA 2015: Standards of medical care in diabetes--2015: summary of revisions. Diabetes Care. 2015 Jan;38 Suppl:S4.

ADA 2017: American Diabetes Association.. 8. Pharmacologic Approaches to Glycemic Treatment. Diabetes Care. 2017 Jan;40(Suppl 1):S64-S74.

ADA 2017: American Diabetes Association.. 13. Management of Diabetes in Pregnancy. Diabetes Care. 2017 Jan;40(Suppl 1):S114-S119.

Aengevaeren VL, Mosterd A, Braber TL, et al. Relationship between **lifelong exercise** volume and coronary atherosclerosis in athletes. Circulation. 2017;136;138–148.

Afshin A, Babalola D, Mclean M, et al. **Information Technology and Lifestyle**: A Systematic Evaluation of Internet and Mobile Interventions for Improving Diet, Physical Activity, Obesity, Tobacco, and Alcohol Use. J Am Heart Assoc. 2016 Aug 31;5(9).

Aggio D, Papacosta O, Lennon L, et al. Association between **physical activity levels in mid-life with physical activity in old age**: a 20-year tracking study in a prospective cohort. BMJ Open. 2017 Sep 21;7(8):e017378.

Ahmad FS, Ning H, Rich JD, et al. **Hypertension, Obesity, Diabetes, and Heart Failure-Free Survival**: The **Cardiovascular Disease Lifetime Risk Pooling Project**. JACC Heart Fail. 2016 Dec;4(12):911-919.

Ahmadi N, Hajsadeghi F, Mirshkarlo HB, et al. **Post-traumatic stress disorder**, **coronary atherosclerosis, and mortality**. Am J Cardiol. 2011 Jul 1;108(1):29-33.

Ahmed HM, Blaha MJ, Nasir K, et al. Effects of **Physical Activity** on Cardiovascular Disease. Am J Cardiol. 2011 Oct 17.

Ahmed HM, Blaha MJ, Nasir K, et al. **Low-risk lifestyle, coronary calcium**, cardiovascular events, and mortality: results from MESA.Am J Epidemiol 2013.

Ahmad S, Moorthy MV, Demler OV, et al. **Assessment of Risk Factors and Biomarkers Associated With Risk of Cardiovascular Disease Among Women Consuming a Mediterranean Diet**. JAMA Netw Open. 2018;1(8):e185708.

Akesson A, Larsson SC, Discacciati A, et al. **Low-Risk Diet and Lifestyle Habits** in the Primary Prevention of Myocardial Infarction in Men: A Population-Based Prospective Cohort Study. J Am Coll Cardiol. 2014 Sep 30;64(13):1299-306.

Aladin AI, Al Rifai M, Rasool SH, et al. Relation of **Coronary Artery Calcium and Extra-Coronary Aortic Calcium** to Incident Hypertension (from the Multi-Ethnic Study of Atherosclerosis). Am J Cardiol. 2018 Jan 15;121(2):210-216

Alageel S, Gulliford MC. **Health checks and cardiovascular risk** factor values over six years' follow-up: Matched cohort study using electronic health records in England. PLoS Med. 2019 Jul 30;16(7):e1002863.

Alcaraz KI, Eddens KS, Blase JL, et al. **Social Isolation and Mortality** in US Black and White Men and Women. Am J Epidemiol. 2018 Oct 16.

Allan, G. Michael, Mallery, Laurie, Ivers, Noah. Treating hypertension in the **very elderly**. Can Fam Physician 2010 56: 1141.

Allan GM, Nouri F, Korownyk C, et al. Agreement among **cardiovascular disease risk calculators**. Circulation. 2013;127:1948–195

Allen K, Pearson-Stuttard J, Hooton W, et al. Potential of **trans fats policies** to reduce socioeconomic inequalities in mortality from coronary heart disease in England: cost effectiveness modeling study. BMJ. 2015 Sep 15;351:h4583.

Allen N, Berry J, Ning H, et al. **Impact of blood pressure** and blood pressure change during middle age on the remaining lifetime risk for cardiovascular disease the cardiovascular lifetime risk pooling project. Circulation 2012;

Allen NB, Zhao L, Liu L, et al. **Favorable cardiovascular health**, compression of morbidity, and healthcare costs: **forty-year follow-up of the CHA study** (**Chicago** Heart Association Detection Project in Industry). Circulation. 2017;135:1693–1701.

Alhalabi L, Singleton MJ, Oseni AO, et al. Relation of Higher Resting Heart Rate to Risk of Cardiovascular Versus Noncardiovascular Death. Am J Cardiol. 2017 Jan 5.

Alimujiang A, Wiensch A, Boss J, Fleischer NL, Mondul AM, McLean K, Mukherjee B, Pearce CL**. Association Between Life Purpose and Mortality** Among US Adults Older Than 50 Years. JAMA Netw Open. 2019 May 3;2(5):e194270.

Alpert JS. Cardiology **patient page**. What you need to know if you have **coronary artery disease**. Circulation. 2011 Aug 9;124(6):e176-8.

Alvarez-Bueno C, Cavero-Redondo I, Martinez-Andres M, et al. Effectiveness of **multifactorial interventions** in **primary health care** settings for primary prevention of cardiovascular disease: A systematic review of systematic reviews. Prev Med. 2014 Dec 12.

Andersen K, Farahmand B, Ahlbom A, et al. Risk of arrhythmias in 52 755 **long-distance cross-country skiers**: a cohort study. Eur Heart J. 2013 Jun 11.

Andersen K, Rasmussen F, Held C, et al. **Exercise capacity and muscle strength** and risk of vascular disease and arrhythmia in 1.1 million young Swedish men: cohort study. BMJ. 2015 Sep 16;351:h4543.

Anderson JB, Grenier M, Edwards NM, et al. Usefulness of Combined History, Physical Examination, Electrocardiogram, and Limited Echocardiogram in Screening Adolescent Athletes for Risk for Sudden Cardiac Death. Am J Cardiol. 2014 Sep 17.

Anderson J, et al. **Calcium intake from Diet and Supplements** & the Risk of Coronary Atery Calcification and its Progression Among Older Adults : 10-Year Follow-Up of the Multi-Ethnic Study of Atherosclerosos (MESA). J Am Heart Assoc.2016 ;5 :e003815.

Angell SY, Cobb LK, Curtis CJ, et al. Change in **trans fatty acid** content of fast-food purchases associated with New York City's restaurant regulation. Ann Intern Med 2012

Ankle Brachial Index Collaboration, Fowkes FG, Murray GD, Butcher I, Heald CL, Et al. **Ankle brachial index combined with Framingham** Risk Score to predict cardiovascular events and mortality: a meta-analysis. JAMA. 2008 Jul 9;300(2):197-208. Measurement of the ABI may improve the accuracy of cardiovascular risk prediction beyond the FRS.

Antman EM, Appel LJ, Balentine D, et al. Stakeholder discussion to reduce population-wide sodium intake and decrease **sodium in the food supply**: a conference report from the american heart association sodium conference 2013 planning group. Circulation. 2014 Jun 24;129(25):e660-79.

Appel LJ. Reducing **Sodium** Intake to Prevent Stroke: Time for Action, Not Hesitation. Stroke. 2014 Jan 21.

Arbab-Zadeh A, Miller JM, Rochitte CE, et al. Diagnostic accuracy of **computed tomography coronary angiography** according to pre-test probability of coronary artery disease and severity of coronary arterial calcification: The CORE-64 (Coronary Artery Evaluation Using 64-Row Multidetector Computed Tomography Angiography) international multicenter

Arbab-Zadeh A, Perhonen M, Howden E, et al. Cardiac remodeling in response to 1 year of **intensive endurance training**. *Circulation* 2014.

Arcand J, Steckham K, Tzianetas R, et al. Evaluation of **sodium levels in hospital patient menus**. Arch Intern Med 2012.

Arcaya M, Glymour MM, Chakrabarti P, et al. Effects of proximate **foreclosed properties** on individuals' systolic blood pressure in Massachusetts, 1987 to 2008. Circulation. 2014;129:2262–2268.

Arem H, Moore SC, Patel A, et al. Leisure Time **Physical Activity and Mortality**: A Detailed Pooled Analysis of the Dose-Response Relationship. JAMA Intern Med. 2015 Apr 6.

Armenian SH, Sun CL, Vase T, Ness KK, et al. Cardiovascular risk factors in **hematopoietic cell transplantation** (HCT) survivors: Role in development of subsequent cardiovascular disease. Blood 2012

Armstrong AW, Harskamp CT, Ledo L et al. Coronary Artery Disease in Patients With **Psoriasis** Referred for Coronary Angiography. Am J Cardiol. 2012 Jan 3.

Armstrong ME, Green J, et al. **Million Women Study** Collaborators. **Frequent physical activity** may not reduce vascular disease risk as much as moderate activity: large prospective study of women in the United kingdom. Circulation. 2015 Feb24;131(8):721-9.

Armstrong S, Wong CA, Perrin E, et al. Association of **Physical Activity With Income, Race/Ethnicity, and Sex Among Adolescents and Young Adults** in the United States: Findings From the National Health and Nutrition Examination Survey, 2007-2016. JAMA Pediatr. 2018 Jun 11.

Andersen K et al. **Exercise capacity and muscle strength** and risk of vascular disease and arrhythmia in 1.1 million young Swedish men: Cohort study. BMJ 2015 Sep 16; 351:h4543.

Anderson JJ, Kruszka B, et al. **Calcium intake from diet and supplements** and the risk of coronary artery calcification and its progression among older adults: 10-year follow-up of the Multi-Ethnic Study of Atherosclerosis (MESA). *J Am Heart Assoc* 2016.

Anderson L, Taylor RS. Cardiac rehabilitation for people with heart disease: an overview of Cochrane systematic reviews. Cochrane Database of Systematic Reviews 2014, Issue 12. Art. No.: CD011273. DOI: 10.1002/14651858.CD011273.pub2. Exercise-based cardiac rehabilitation is an effective and safe therapy to be used in the management of clinically stable people following myocardial infarction or percutaneous coronary intervention or who have heart failure. Future RCTs of cardiac rehabilitation need to improve their reporting methods and reflect the real world practice better including the recruitment of higher risk people and consideration of contemporary models of cardiac rehabilitation delivery, and identify effective interventions for enhancing adherence to rehabilitation.

Anderson L, Oldridge N, Thompson DR, et al. **Exercise-Based Cardiac Rehabilitation** for Coronary Heart Disease: Cochrane Systematic Review and Meta-Analysis. J Am Coll Cardiol. 2016 Jan 5;67(1):1-12.

Antonisamy B, Vasan SK, Geethanjali FS, et al. **Weight Gain and Height Growth during Infancy**, Childhood, and Adolescence as Predictors of Adult Cardiovascular Risk. J Pediatr. 2016 Nov 4.

Arnett DK, Blumenthal RS, Albert MA, et al. 2019 ACC/AHA Guideline on the **Primary Prevention** of Cardiovascular Disease: Executive Summary. J Am Coll Cardiol. 2019 Mar 7.

Arnett DK, Khera A, Blumenthal RS. 2019 ACC/AHA **Guideline on the Primary Prevention** of Cardiovascular Disease: Part 1, Lifestyle and Behavioral Factors. JAMA Cardiol. 2019 Jul 31.

Arnson Y, Rozanski A, Gransar H, et al. Comparison of the **Coronary Artery Calcium Score and Number of Calcified Coronary Plaques** for Predicting Patient Mortality Risk. Am J Cardiol. 2017 Dec 15;120(12):2154-2159.

Aro AL, Rusinaru C, Uy-Evanado A, et al. **Sexual Activity** as a Trigger for Sudden Cardiac Arrest. J Am Coll Cardiol.2017 Oct 30.

Arsenault, Benoit J., Lemieux, Isabelle, Despres, Jean-Pierre, et al. The **hypertriglyceridemic-waist phenotype** and the risk of coronary artery disease: results from the EPIC-Norfolk Prospective Population Study. CMAJ 2010 182: 1427-1432.

Artinian NT, Fletcher G, Mozaffarian D, et al on behalf of the American Heart Association (AHA) Prevention Committee of the Council on Cardiovascular Nursing. Interventions to promote **physical activity and dietary lifestyle** changes for cardiovascular risk factor reduction in adults; a scientific statement from the American Heart Association. Circulation 2010; DOI: 10.1161/CIR.0b013e3181e8edf1.

Arts EE, Fransen J, den Broeder AA, et al. The effect of disease duration and disease activity on the **risk of cardiovascular disease** in rheumatoid arthritis patients. Ann Rheum Dis. 2014 Jan 23.

Arts EE, Popa C, Den Broeder AA, Semb et al. Performance of four current **risk algorithms in predicting cardiovascular events in patients with early rheumatoid arthritis**. Ann Rheum Dis. 2015 Apr; 74(4):668-74.

Ashley EA, Hershberger RE, Caleshu C, et al. **Genetics and cardiovascular disease**. A policy statement from the American Heart Association. Circulation 2012.

Aspry KE, Van Horn L, Carson JAS, et al. Medical Nutrition Education, Training, and Competencies **to Advance Guideline-Based Diet Counseling by Physicians**: A Science Advisory From the American Heart Association. Circulation. 2018 Jun 5;137(23):e821-e841.

Astrup A, Bertram HC, Bonjour JP, et al. **WHO draft guidelines on dietary saturated and trans fatty acids**: time for a new approach? BMJ. 2019 Jul 3;366:l4137.

Auer R, Bauer DC, Marques-Vidal P, et al. **Association of major and minor ECG abnormalities** with coronary heart disease events.JAMA 2012; 307:1497-1505.

Auger N et al. Long-term risk of cardiovascular disease in **women who have had infants with heart defects**. Circulation 2018. Apr 2

Aune D, Sen A, Prasad M, et al. **Body mass index** and all cause mortality: systematic review and non-linear dose-response meta-analysis of 230 prospective studies with 3.74 million deaths among 30.3 million participants. BMJ 2016;353:i1256.

Aune D, Chan DS, Lau R, et al. **Dietary fibre, whole grains**, and risk of colorectal cancer: systematic review and dose-response meta-analysis of prospective studies. BMJ 2011;343:d6617. doi:10.1136/bmj.d6617 pmid:22074852.

Aune D, Keum N, Giovannucci E, et al. **Nut consumption** and risk of cardiovascular disease, total cancer, all-cause and cause-specific mortality: a systematic review and dose-response meta-analysis of prospective studies. BMC Med. 2016 Dec 5;14(1):207

Aung T, Halsey J, Kromhout D, et al. Associations of **Omega-3 Fatty Acid Supplement Use** With Cardiovascular Disease Risks: Meta-analysis of 10 Trials Involving 77 917 Individuals. JAMA Cardiol. 2018 Jan 31.

Ayyavoo A, Savage T, Derraik JG, et al. **First-born Children** Have Reduced Insulin Sensitivity and Higher Daytime Blood Pressure Compared to Later-Born Children. J Clin Endocrinol Metab. 2013 Jan 30.

Azad MB, Abou-Setta AM, Chauhan BF, et al. **Nonnutritive sweeteners** and cardiometabolic health: a systematic review and meta-analysis of randomized controlled trials and prospective cohort studies. CMAJ. 2017 Jul 17;189(28):E929-E939

Bachmann JM, Willis BL, Ayers CR, et al. Association between **Family History and Coronary Heart Disease Death** across Long-Term Follow-Up in Men: The Cooper Center Longitudinal Study. Circulation. 2012 May 23.

Baggish, Aaron L. Hutter, Jr Adolph M.., Wang, Francis Et al. Cardiovascular Screening in College **Athletes** With and Without Electrocardiography: A Cross-sectional Study. Ann Intern Med March 2, 2010 152:269-275

Bairey Merz CN, Andersen H, Sprague E, et al. Knowledge, Attitudes, and Beliefs Regarding **Cardiovascular Disease in Women**: The Women's Heart Alliance. J Am Coll Cardiol. 2017 Jun 20.

Baker PRA, Francis DP, Soares J, Weightman AL, Foster C. **Community wide interventions for increasing physical activity**. Cochrane Database of Systematic Reviews 2011, Issue 4. Art. No.: CD008366. DOI: 10.1002/14651858.CD008366.pub2.

Bandosz P, O'Flaherty M, Drygas W, et al. **Decline in mortality from coronary heart disease in Poland** after socioeconomic transformation: modelling study. BMJ 2012;344:d8136.

Banerjee A, Newman DR, Van den Bruel A, Heneghan C. **Diagnostic accuracy of exercise stress testing** for coronary artery disease: a systematic review and meta-analysis of prospective studies. Int J Clin Pract. 2012 May;66(5):477-92.

Banerjee A. **Macroeconomics and cardiovascular risk factors**: the same view through a different lens? Circulation. 2013 Apr 9;127(14):1451-2.

Bangalore S, Kumar S, Lobach I, et al. **Blood pressure targets in subjects with type 2 diabetes mellitus/impaired fasting glucose**: Observations from traditional and Bayesian random-effects meta-analyses of randomized trials. Circulation 2011.

Bangalore S, Fayyad R, Laskey R, et al. **Body-Weight Fluctuations** and Outcomes in Coronary Disease. N Engl J Med. 2017 Apr 6;376(14):1332-1340.

Bansilal S, Castellano JM, Garrido E, et al. Assessing the impact of **medication adherence** on long-term cardiovascular outcomes. J Am Coll Cardiol 2016; 68:789-801.

Barbarawi M, Kheiri B, Zayed Y, et al. **Vitamin D supplementation** and cardiovascular disease risks in more than 83 000 individuals: meta-analysis of 21 randomized clinical trials [online June 19, 2019]. JAMA Cardiol. doi:10.1001/jamacardio.2019.1870

Baron SL, Hein MJ, Lehman E et al. **Body Mass Index, Playing Position, Race, and the Cardiovascular Mortality** of Retired **Professional Football Players**. (NFL) Am J Cardiol. 2012 Jan 13.

Barraclough K, Gale CP, Hall R. Assessment of **chest pain** in a low risk patient: is the **exercise tolerance test** obsolete? BMJ. 2015 May 6;350:h1905.

Barreto Pde S. Global health agenda on non-communicable diseases: has WHO set a smart goal for **physical activity**? BMJ. 2015 Jan 21;350:h23.

Barry AR, O'Neill DE, Graham MM. **Primary Prevention** of Cardiovascular Disease in Older Adults. Can J Cardiol. 2016 Apr 19.

Bartels SJ, Pratt SI, Aschbrenner KA, et al. Pragmatic replication trial of **health promotion coaching** for obesity in serious mental illness and maintenance of outcomes. Am J Psychiatry 2015;172:344–52.

Bartlett J, Predazzi IM, Williams SM, et al. Is isolated **low high-density lipoprotein cholesterol** a cardiovascular disease risk factor? New insights from the Framingham Offspring Study. *Circ Cardiovasc Qual Outcomes* 2016.

Barton P, Andronis L, Briggs A, et al. Effectiveness and cost effectiveness of **cardiovascular disease prevention in whole populations**: modelling study. BMJ. 2011 Jul 28;343:d4044.

Basterra-Gortari FJ, Bes-Rastrollo M, Gea A, et al. **Television Viewing, Computer Use, Time Driving** and All-Cause Mortality: The SUN Cohort. J Am Heart Assoc. 2014 Jun 25;3(3).

Batacan RB Jr, Duncan MJ, Dalbo VJ, et al. Effects of **high-intensity interval training** on cardiometabolic health: a systematic review and meta-analysis of intervention studies. Br J Sports Med. 2017 Mar;51(6):494-503.

Battes L, Barendse R, Steyerberg EW, et al. Development and Validation of a **Cardiovascular Risk Assessment Model** in Patients With Established Coronary Artery Disease. Am J Cardiol. 2013 Apr 1.

Bayturan Ozgur; Tuzcu E. Murat; Lavoie Andrea; et al. The **Metabolic Syndrome**, Its **Component Risk Factors**, and Progression of Coronary Atherosclerosis. *Arch Intern Med*. 2010;170(5):478-484.

Beatty AL, Schiller NB, Whooley MA. **Six-minute walk test** as a prognostic tool in stable coronary heart disease: data from the heart and soul study. Arch Intern Med. 2012 Jul 23;172(14):1096-102.

Beatty AL, Ku IA, Christensen RH, et al. **High-sensitivity cardiac troponin T levels** and secondary events in outpatients with coronary heart disease from the Heart and Soul study. JAMA Intern Med 2013 .

Beatty AL, Ku IA, Bibbins-Domingo K, et al. **Traditional Risk Factors Versus Biomarkers** for Prediction of Secondary Events in Patients With Stable Coronary Heart Disease: From the Heart and Soul Study. J Am Heart Assoc. 2015 Jul 6;4(7).

Beckett NS, Peters R, Fletcher AE, Staessen JA, Liu L, et al.; the **HYVET** Study Group. Treatment of Hypertension in Patients 80 Years of Age or Older.N Engl J Med. 2008 Mar 31; [Epub ahead of print].

Beelen R, Raaschou-Nielsen O, Stafoggia M, et al. Effects of long-term exposure to **air pollution** on natural-cause mortality: an analysis of 22 European cohorts within the multicentre ESCAPE project. Lancet 2013; online Dec 9.

Bell KJ, Hayen A, Irwig L, et al. When to **remeasure cardiovascular risk** in untreated people at low and intermediate risk: observational study. BMJ. 2013 Apr 3;346:f1895.

Bell GA, Kantor ED, Lampe JW, et al. Intake of **Long-Chain ω-3 Fatty Acids From Diet and Supplements** in Relation to Mortality. Am J Epidemiol. 2014 Feb 3.

Bell JA, Hamer M, Sabia S, et al. The natural course of **healthy obesity** over 20 years. J Am Coll Cardiol 2014; 65:101-102.

Beller GA, et al. 2010 ACCF/AHA Guideline: **Assessment of Cardiovascular Risk in Asymptomatic Adults.** A Report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines Developed in Collaboration With the American Society of Echocardiography, American Society of Nuclear Cardiology, Society of Atherosclerosis Imaging and Prevention, Society for Cardiovascular Angiography and Interventions, Society of Cardiovascular Computed Tomography, and Society for Cardiovascular Magnetic Resonance. J Am Coll Cardiol. 2010 Dec 14;56(25):e50-e103. http://content.onlinejacc.org/cgi/reprint/56/25/e50.pdf

Bellettiere J, LaMonte MJ, Evenson KR, et al. **Sedentary behavior and cardiovascular disease** in older women: The Objective Physical Activity and Cardiovascular Health (OPACH) Study. Circulation. 2019 Feb 19;139(8):1036-1046.

Benjamin EJ, Muntner P, Alonso A, et al. Heart Disease and Stroke **Statistics-2019 Update**: A Report From the American Heart Association. Circulation. 2019 Jan 31: CIR0000000000000659.

Bennett DA, Du H, et al; China Kadoorie Biobank Study Collaborative Group. Association of **physical activity** with risk of major cardiovascular diseases in Chinese men and women [online November 8, 2017].JAMA Cardiol. doi:10.1001/jamacardio.2017.4069

Bennett-Britton I, Teyhan A, et al. Changes in **marital quality** over 6 years and its association with cardiovascular disease risk factors in men: findings from the ALSPAC prospective cohort study. J Epidemiol Community Health. 2017 Nov;71(11):1094-1100.

Berge LI, Skogen JC, Sulo G, et al. **Health anxiety** and risk of ischaemic heart disease: a prospective cohort study linking the Hordaland Health Study (HUSK) with the Cardiovascular Diseases in Norway (CVDNOR) project. BMJ Open. 2016 Nov 3;6(11):e012914.

Bergeron N, Chiu S, Williams PT, et al. Effects of red meat, white meat, and nonmeat **protein sources on atherogenic lipoprotein measures** in the context of low compared with high saturated fat intake: a randomized controlled trial. Am J Clin Nutr. 2019Jun4.

Bergh C, Udumyan R, Fall K, et al. **Stress resilience and physical fitness** in adolescence and risk of coronary heart disease in middle age. Heart. 2015 Mar 4. pii: heartjnl-2014-306703.

Berkelmans GFN, Gudbjornsdottir S, Visseren FLJ, et al. Prediction of **individual life-years gained without cardiovascular events** from lipid, blood pressure, glucose, and aspirin treatment based on data of more than 500 000 patients with **Type 2 diabetes mellitus**. Eur Heart J. 2019 Jan 9.

Berra K, Rippe J, Manson JE. Making **physical activity counseling a priority** in clinical practice: the time for action is now. JAMA. 2015 Dec 10.

Berry JD et al. **Lifetime risks** of cardiovascular disease. N Engl J Med 2012 Jan 26; 366:321.

Bhaskaran K, dos-Santos-Silva I, Leon DA, et al. Association of **BMI with overall and cause-specific mortality**: a population-based cohort study of 3·6 million adults in the UK. Lancet Diabetes Endocrinol 2018; online Oct 30.

Bhaskaran K, Hajat S, Armstrong B, Haines A, Herrett E, Wilkinson P, et al. The effects of hourly differences in **air pollution** on the risk of myocardial infarction: case crossover analysis of the MINAP database. BMJ 2011;343:d5531.

Bhatia RS, Pendrith C, Ross H; Canadian Cardiovascular Society Choosing Wisely Canada Committee. **Cardiac testing in an asymptomatic** 42-year-old man. CMAJ. 2015 Jul 14;187(10):747-9.

Bhatia RS, Bouck Z, Ivers NM, et al. **Electrocardiograms** in Low-Risk Patients Undergoing An Annual Health Examination. JAMA Intern Med. 2017 Jul 10.

Bhatt Deepak L.; Eagle Kim A.; Ohman E. Magnus; et al. for the **REACH** Registry Investigators. Comparative Determinants of 4-Year Cardiovascular Event **Rates in Stable Outpatients** at Risk of or With Atherothrombosis. JAMA. 2010;0(2010):jama.2010.1322.

Bibbins-Domingo, Kirsten, Chertow, Glenn M., Coxson, Pamela G., et al. Projected Effect of Dietary **Salt Reductions** on Future Cardiovascular Disease. N Engl J Med 2010 0: NEJMoa0907355.

Bibbins-Domingo K. The **Institute of Medicine (IOM) Report Sodium Intake** in Populations: Assessment of Evidence: Summary of Primary Findings and Implications for Clinicians. JAMA Intern Med. 2013 Oct 28.

Bilhorn KR, Luo Y, Lee BT, Wong ND. High-Density Lipoprotein Cholesterol, **High-Sensitivity C-Reactive Protein**, and Cardiovascular Disease in United States Adults. Am J Cardiol. 2012 Aug 1.

Biswas A, Oh PI, Faulkner GE, et al. **Sedentary Time** and Its Association With Risk for Disease Incidence, Mortality, and Hospitalization in Adults: A Systematic Review and Meta-analysis. Ann Intern Med. 2015 Jan 20;162(2):123-32.

Bittner V, Bertolet M, Barraza R, et al. **Comprehensive cardiovascular risk factor control improves survival**. *J Am Coll Cardiol* 2015; 66:765-773.

Blaha M, Budoff M, DeFilippis A, et al. Association between **C-reactive protein, coronary artery calcium**, and cardiovascular events: implications for the JUPITER population from MESA, a population-based cohort study. Lancet 2011; 378: 684-692.

Blaha MJ, Hung RK, Dardari Z, Feldman et al. Age-dependent prognostic value of exercise capacity and derivation of **fitness-associated biologic age**. Heart. 2016 Mar;102(6):431-7.

Bloomfield HE, Koeller E, Greer N, et al. Effects on Health Outcomes of a **Mediterranean Diet** With No Restriction on Fat Intake: A Systematic Review and Meta-analysis. Ann Intern Med. 2016 Jul 19.

Blumenthal James A.; Babyak Michael A.; Hinderliter Alan; et al. Effects of the **DASH Diet** Alone and in Combination With Exercise and Weight Loss on Blood Pressure and Cardiovascular Biomarkers in Men and Women With High Blood Pressure: The **ENCORE** Study. *Arch Intern Med*. 2010;170(2):126-135.

Bluemke DA, Achenbach S, Budoff M, et al. Noninvasive Coronary Artery Imaging. **Magnetic Resonance Angiography and Multidetector Computed Tomography Angiography**. A Scientific Statement From the American Heart Association Committee on Cardiovascular Imaging and Intervention of the Council on Cardiovascular Radiology and Intervention, and the Councils on Clinical Cardiology and Cardiovascular Disease in the Young. Circulation. 2008 Jun 27. [Epub ahead of print]

Bonaccio M, Di Castelnuovo A, Costanzo S, et al. **Mediterranean diet and mortality in the elderly**: a prospective cohort study and a meta-analysis. Br J Nutr. 2018 Oct;120(8):841-854.

Boden WE, Franklin BA, Wenger NK. **Physical activity** and structured exercise for patients with stable ischemic heart disease.JAMA 2013; 309:143-144.

Bolla M, Van Tienhoven G, Warde P, et al. External irradiation with or without long-term **androgen suppression for prostate cancer** with high metastatic risk: 10-year results of an EORTC randomised study. Lancet Oncol 2010;11:1066-73.

Bonow, Robert O. Should **Coronary Calcium Screening** Be Used in Cardiovascular Prevention Strategies? N Engl J Med 2009 361: 990-997.

Bosner, Stefan, Haasenritter, Jorg, Becker, Annette, et al. Ruling out coronary artery disease in **primary care**: development and validation of a **simple prediction rule**. CMAJ 2010 0: cmaj.100212.

Bouchard C, Blair SN, Church TS, et al. **Adverse metabolic response to regular exercise**: Is it a rare or common occurrence? PLoS ONE 2012.

Bozeman W, Teacher E, Winslow J, et al. Transcardiac conducted electrical weapon (**Taser**) probe deployments: incidence and outcomes. J Emerg Med 2012.

Brander G, Isomura K, Chang Z, et al. Association of **Tourette Syndrome and Chronic Tic Disorder** With Metabolic and Cardiovascular Disorders. JAMA Neurol. 2019 Jan 14.

Brandt R J, Myerson R, Coca M, et al. Hospital admissions for myocardial infarction and stroke before and after the **trans-fatty acid restrictions** in New York. JAMA Cardiol 2017.

Bredin SS, Gledhill N, Jamnik VK, et al. **PAR-Q+ and ePARmed-X+:** New risk stratification and **physical activity** clearance strategy for physicians and patients alike. Can Fam Physician. 2013 Mar;59(3):273-7.

Brenner DJ, Shuryak I, Jozsef G, deWyngaert JK, Formenti SC. Risk and risk reduction of major coronary events associated with contemporary **breast radiotherapy** [online October 28, 2013]. JAMA Intern Med. doi:10.1001/jamainternmed.2013.11790.

Breton CV, Wang X, Mack WJ, et al. Childhood **air pollutant exposure (ozone)** and carotid artery intima-media thickness in young adults. Circulation. 2012;126:1614 –1620.

Brett T, Arnold-Reed D, Phan C, et al. The **Fremantle** Primary Prevention Study: a multicentre randomised trial of **absolute cardiovascular risk reduction**. Br J Gen Pract. 2012;e22-28.

Brewer N, Wright CS, Travier N, Cunningham CW, Hornell J, Pearce N, Jeffreys M. A New Zealand linkage study examining the associations between A1C concentration and mortality. Diabetes Care. 2008 Jun;31(6):1144-9. Epub 2008 Feb 25. This is the largest study to date of **A1C** levels and subsequent mortality risk. It confirms previous findings that A1C levels are strongly associated with subsequent mortality in both men and women without a prior diabetes diagnosis.

Brindle P, Beswick A, Fahey T, Ebrahim S. Accuracy and impact of risk assessment in the primary prevention of cardiovascular disease: a systematic review. Heart. 2006 Dec;92(12):1752-9. Epub 2006 Apr 18. For CHD, the predicted to observed ratios ranged from an underprediction of 0.43 (95% CI 0.27 to 0.67) in a high-risk population to an overprediction of 2.87 (95% CI 1.91 to 4.31) in a lower-risk population.

Brotons C, Calvo-Bonacho E, Moral I, et al. Comparison of application of **different methods to estimate lifetime cardiovascular risk**. Eur J Prev Cardiol. 2015 Mar 31.

Brown WJ, Pavey T, Bauman AE. Comparing **population attributable risks** for heart disease across the adult lifespan in **women**. Br J Sports Med. 2014 May 8.

Brown AF, Liang LJ, et al. **Trends in racial/ethnic and nativity disparities** in cardiovascular health among adults without prevalent cardiovascular disease in the United States, 1988 to 2014. Ann Intern Med. 2018. [Epub ahead of print]. doi:10.7326/M17-0996

Brown HL, Warner JJ, Gianos E, et al. Promoting Risk Identification and Reduction of Cardiovascular Disease in Women Through Collaboration With Obstetricians and Gynecologists: A Presidential Advisory From the American Heart Association and the American College of Obstetricians and Gynecologists. Circulation. 2018 May 10.

Brown TJ, Brainard J, Song F, et al. **Omega-3, omega-6, and total dietary polyunsaturated fat** for prevention and treatment of type 2 diabetes mellitus: systematic review and meta-analysis of randomised controlled trials. BMJ. 2019 Aug 21;366:l4697.

Buckley D. I., Fu R., Freeman M., et al. **C-Reactive Protein** as a Risk Factor for Coronary Heart Disease: A Systematic Review and Meta-analyses for the U.S. Preventive Services Task Force. *Ann Intern Med* 2009; 483-495.

Buckley JP, Hedge A, et al. The **sedentary office**: a growing case for change towards better health and productivity. Expert statement commissioned by Public Health England and the Active Working Community Interest Company. Br J Sports Med. 2015 Jun 1.

Budhathoki S, Sawada N, Iwasaki M, et al. Association of **Animal and Plant Protein Intake** With All-Cause and Cause-Specific Mortality. JAMA Intern Med. 2019 Aug 26.

Budoff MJ, Mayrhofer T, Ferencik M, et al; on behalf of the PROMISE Investigators. Prognostic value of **coronary artery calcium** in the **PROMISE** Study (Prospective Multicenter Imaging Study for Evaluation of Chest Pain). Circulation. 2017;136:1993–2005.

Buitrago-Lopez A, Sanderson J, Johnson L, et al. **Chocolate consumption** and cardiometabolic disorders: systematic review and meta-analysis. BMJ 2011; DOI:10.1136/bmj.d4488.

Bullo V, Bergamin M, Gobbo S, et al. The effects of **Pilates exercise** training on physical fitness and wellbeing in the elderly: A systematic review for future exercise prescription. Prev Med. 2015 Mar 12;75:1-11.

Bulugahapitiya U, Siyambalapitiya S, Sithole J, Idris I. Is **diabetes** a coronary risk equivalent? Systematic review and meta-analysis. Diabet Med. 2009;26:142-8. {InfoPOEMs Apr09: This meta-analysis found no evidence to support the contention that diabetes alone is a coronary heart disease (CHD) risk equivalent to a history of prior myocardial infarction (MI). The blanket use of aspirin and statins for patients with type 2 diabetes, regardless of their lipid levels, is not supported by the evidence. (LOE = 2a)}

Burke LE, Ma J, Azar KM et al. Current Science on **Consumer Use of Mobile Health** for Cardiovascular Disease Prevention: A Scientific Statement From the American Heart Association. Circulation. 2015 Aug 13.

Burzynska AZ, Wong CN, Voss MW, et al. **Physical Activity** Is Linked to Greater Moment-To-Moment Variability in Spontaneous Brain Activity in Older Adults. PLoS One. 2015 Aug 5;10(8):e0134819.

Byberg L, Melhus H, et al. Total mortality after changes in leisure time **physical activity** in 50 year old men: 35 year follow-up of population based cohort. BMJ. 2009 Mar 5;338:b688. doi: 10.1136/bmj.b688. Increased physical activity in middle age is eventually followed by a reduction in mortality to the same level as seen among men with constantly high physical activity. This reduction is comparable with that associated with smoking cessation.

Cadmus-Bertram LA, Marcus BH, Patterson RE, et al. Randomized Trial of a **Fitbit-Based Physical Activity Intervention** for Women. Am J Prev Med. 2015 Jun 10.

Cahill LE, Chiuve SE, Mekary RA, et al. Prospective Study of **Breakfast Eating** and Incident Coronary Heart Disease in a Cohort of Male US Health Professionals. Circulation. 2013 Jul 23;128(4):337-43.

Cai Y, Hansell AL, Blangiardo M, et al. Long-term exposure to **road traffic noise**, ambient air pollution, and cardiovascular risk factors in the HUNT and Lifelines cohorts. Eur Heart J 2017;38:2290–2296.

Caleyachetty R, Thomas GN, Toulis KA, et al. **Metabolically Healthy Obese** and Incident Cardiovascular Disease Events Among 3.5 Million Men and Women. JACC. 2017;70(12):1429-37

Calvin CM, Batty GD, Der G, et al. **Childhood intelligence** in relation to major causes of death in 68 year follow-up: prospective population study. BMJ 2017;357:j2708.

Campbell N, Lackland D, Chockalingam A, et al. The World Hypertension League and International Society of Hypertension call on governments, nongovernmental organizations, and the food industry to work to **reduce dietary sodium**. J Clin Hypertens (Greenwich). 2014;16:99-100.

Campos-Rodriguez F, Martinez-Garcia MA, de la Cruz-Moron I et al. Cardiovascular mortality in women with **obstructive sleep apnea** with or without continuous positive airway pressure treatment: a cohort study. Ann Intern Med. 2012 Jan 17;156(2):115-22.

Canoy D, Beral V, Balkwill A, et al. **Age at menarche** and risks of coronary heart and other vascular diseases in a large UK cohort. Circulation. 2015;131:237–244.

Canto JG, Kiefe CI, Roger WJ, et al; NRMI Investigators. **Number of coronary heart disease risk factors and mortality** in patients with first myocardial infarction. JAMA. 2011;306(19):2120-2127.

Capewell S, O'Flaherty M. Rapid **mortality falls after risk-factor changes** in populations. Lancet. 2011 Mar 15.

Cappuccio FP, Cooper D, D'Elia L, Strazzullo P, Miller MA. **Sleep duration predicts cardiovascular outcomes**: a systematic review and meta-analysis of prospective studies. Eur Heart J 2011; online 7 February.

Cappuccio FP, Capewell S, Lincoln P, McPherson K. Policy options to reduce population **salt** intake. BMJ 2011; DOI:10.1136/bmj.d4995.

Cardiovascular Disease Risk Calculator: http://bestsciencemedicine.com/chd/calc2.html

Cardoso R, Nasir K, Blumenthal RS, Blaha MJ. Selective Use of **Coronary Artery Calcium Testing** for Shared Decision Making: Guideline Endorsed and Ready for Prime Time. Ann Intern Med. 2019 Feb 12.

Carey IM, Shah SM, Dewilde S, et al. Increased Risk of Acute Cardiovascular Events After **Partner Bereavement**: A Matched Cohort Study. JAMA Intern Med. 2014 Feb 24.

Carr JJ, Jacobs DR Jr, Terry JG, et al. **Association of coronary artery calcium** in adults aged 32 to 46 years with incident coronary heart disease and death [online Feb 8, 2017].JAMA Cardiol. doi:10.1001/jamacardio.2016.5493

Case MA, Burwick HA, Volpp KG, Patel MS. Accuracy of **smartphone applications** and wearable devices for **tracking physical activity data**. JAMA. 2015 Feb 10; 313(6):625-6.

Casper M, Kramer MR, Quick H, et al. Changes in the **Geographic Patterns of Heart Disease** Mortality in the United States: 1973 to 2010. Circulation. 2016 Mar 22;133(12):1171-80.

Cassidy A, Mukamal KJ, Liu L, et al. High **anthocyanin intake (blueberries, strawberries)** is associated with a reduced risk of myocardial infarction in young and middle-aged women (NHS II). Circulation 2013.

CDC Sep/11 **Million Hearts**: Strategies to Reduce the Prevalence of Leading Cardiovascular Disease Risk Factors --- United States, 2011 http://www.cdc.gov/mmwr/preview/mmwrhtml/mm60e0913a1.htm?s_cid=mm60e0913a1_x

CDC. Feb 2012 Vital Signs: Food Categories Contributing the Most to **Sodium Consumption** — United States, 2007–2008. Early Release. February 7, 2012 / 61(Early Release);1-7. http://www.cdc.gov/mmwr/pdf/wk/mm61e0207.pdf Overall, the mean daily sodium consumption (excluding table salt) was 3266 mg, well above recommendations to keep intake below 2300 mg. The top 10 food categories contributing to sodium consumption were, in descending order: bread and rolls, cold cuts, pizza, poultry, soups, sandwiches, cheese, pasta mixed dishes, meat mixed dishes, and savory snacks.

Celis-Morales CA, Lyall DM, Steell L, et al. Associations of discretionary **screen time with mortality, cardiovascular disease and cancer** are attenuated by strength, fitness and physical activity: findings from the UK Biobank study. BMC Med. 2018 May 24;16(1):77.

Celis-Morales CA, Lyall DM, Welsh P, et al. Association between **active commuting** (**biking**) and incident cardiovascular disease, cancer, and mortality: prospective cohort study. BMJ 2017;357:j1456.

Celis-Morales CA, Welsh P, Lyall DM, et al. Associations of **grip strength** with cardiovascular, respiratory, and cancer outcomes and all cause mortality: prospective cohort study of half a million UK Biobank participants. BMJ. 2018 May 8;361:k1651.

Cerhan JR, Moore SC, Jacobs EJ, et al. A pooled analysis of **waist circumference and mortality** in 650 000 adults.Mayo Clin Proc 2014; 89: 335-345.

Cesa CC, Sbruzzi G, Ribeiro RA, et al. **Physical activity and cardiovascular risk factors in children**: meta-analysis of randomized clinical trials. Prev Med. 2014 Aug 29;69C:54-62.

Cesaroni G, Forastiere F, Stafoggia M, et al. Long term exposure to **ambient air pollution** and incidence of acute coronary events: prospective cohort study and meta-analysis in 11 European cohorts from the ESCAPE Project. BMJ. 2014 Jan 21;348:f7412

Chaddha A, Jackson EA, Richardson CR, Franklin BA. **Technology to Help Promote Physical Activity**. Am J Cardiol. 2017 Jan 1;119(1):149-152

Chaikriangkrai K, Palamaner Subash Shantha G, et al. Prognostic Value of **Coronary Artery Calcium Score** in Acute Chest Pain Patients Without Known Coronary Artery Disease: Systematic Review and Meta-analysis. Ann Emerg Med. 2016 Oct 10.
Chamnan Parinya, Simmons Rebecca K, Khaw Kay-Tee, et al. Estimating the population impact of **screening** strategies for identifying and treating people at high risk of cardiovascular disease: modelling study. BMJ 2010;340:c1693, (Pub 25 April 2010)
Chamnan P, Simmons RK, Hori H, Sharp S, Khaw KT, Wareham NJ, Griffin SJ. A **simple risk score** using routine data for predicting cardiovascular disease in primary care. Br J Gen Pract. 2010 Aug;60(577):e327-34.
Chan PS, Spertus JA, Krumholz HM, et al. Validated **prediction tool** for initial survivors of **in-hospital cardiac arrest**. Arch Intern Med2012; 172:947-953.
Chang AM, Litt HI, Snyder BS, et al. **Impact of Coronary Computed Tomography Angiography** Findings on Initiation of Cardioprotective Medications. Circulation. 2017 Nov 28;136(22):2195-2197.
Chang SM, Nabi F, Xu J, et al. **Values of CACS compared with ETT and myocardial perfusion imaging** for predicting long-term outcome in asymptomatic and symptomatic patients at low risk for coronary disease. *JACC Cardiovasc Imaging* 2015; 8:134-144.
Charchar FJ, Bloomer LDS, Barnes TA, et al. **Inheritance of coronary artery disease in men**: an analysis of the role of the **Y chromosome**. Lancet 2012; published online Feb 9.
Chatterjee A, Harris SB, Leiter LA, et al. Managing **cardiometabolic risk in primary care**: summary of the 2011 consensus statement. Can Fam Physician. 2012 Apr;58(4):389-93, e196-201.
Chen F, Du M, Blumberg JB, et al. Association Among **Dietary Supplement Use, Nutrient Intake, and Mortality Among U.S. Adults:** A Cohort Study. Ann Intern Med. 2019 Apr 9.
Chen GC, Arthur R, Iyengar NM, et al. Association between **regional body fat and cardiovascular disease risk among postmenopausal women** with normal body mass index. Eur Heart J. 2019 Jun 30.
Chen J, Budoff MJ, Reilly MP, et al. **Coronary artery calcification** and risk of cardiovascular disease and death among patients with chronic kidney disease. JAMA Cardiol 2017.
Chen L, Caballero B, Mitchell DC, et al. Reducing consumption of **sugar-sweetened beverages** is associated with reduced blood pressure. A prospective study among United States adults. Circulation 2010.
Chen R, Yin P, Wang L, et al. Association between **ambient temperature and mortality risk** and burden: time series study in 272 main Chinese cities. BMJ. 2018 Oct 31;363:k4306.
Chen ST, Maruthur NM, Appel LJ. The effect of **dietary patterns** on estimated coronary heart disease risk: results from the Dietary Approaches to Stop Hypertension (**DASH**) trial. Circ Cardiovasc Qual Outcomes. 2010;3:484 – 489.
Chen ZY, Chiang CH, Huang CC, et al. The Association of **Tooth Scaling** and Decreased Cardiovascular Disease: A Nationwide Population-based Study. Am J Med. 2012 Jun;125(6):568-75.
Cheng M, He H, Wang D, Xu L, Wang B, Ho KM, Chen W. **Shift work** and ischaemic heart disease: meta-analysis and dose-response relationship. Occup Med (Lond). 2019 May 25;69(3):182-188.
Cheng S, Claggett B, Correia AW, et al. **Temporal trends in the population attributable risk** for cardiovascular disease: the atherosclerosis risk in communities study. Circulation. 2014 Sep 2;130(10):820-8.
Cheng VY, Berman DS, Rozanski A, et al. Performance of the traditional age, sex, and angina typicality-based approach for estimating **pretest probability of angiographically significant coronary artery disease** in patients undergoing coronary computed tomographic angiography: results from the multinational coronary CT angiography evaluation for clinical outcomes: an international multicenter registry (CONFIRM). Circulation. 2011 Nov 29;124(22):2423-32, 1-8.
Chetty R, Stepner M, Abraham S, et al. The association between **income and life expectancy** in the United States, 2001-2014.JAMA. doi:10.1001/jama.2016.4226.
Chin MT. Basic mechanisms for adverse cardiovascular events associated with **air pollution**. Heart. 2015 Feb;101(4):253-6.
Chinthapalli K. Dethroning the king of condiments (**salt**). BMJ. 2013 Dec 4;347:f7192
Chirinos JA, Gurubhagavatula I, Teff K, et al. **CPAP, weight loss, or both for obstructive sleep apnea.** N Engl J Med 2014;370: 2265-75.
Chiu M, Rahman F, Vigod S, et al. **Mortality in single fathers compared with single mothers** and partnered parents: a population-based cohort study. Lancet Public Health 2018; online Feb 14
Chiuve SE, Fung TT, Rexrode KM, et al. Adherence to a low-risk, healthy **lifestyle** and risk of sudden cardiac death among women. JAMA 2011; 306:62-69.
Choi Y, Chang Y, Ryu S,et al. **Coffee consumption** and coronary artery calcium in young and middle-aged asymptomatic adults. Heart. 2015 Mar 2.
Chomistek AK, Manson JE, Stefanick, ML, et al. The relationship of **sedentary behavior and physical activity** to incident cardiovascular disease: Results from the Women's Health Initiative. J Am Coll Cardiol 2013.
Chomistek AK, Chiuve SE, Eliassen AH, Mukamal KJ, Willett WC, Rimm EB. **Healthy lifestyle** in the primordial prevention of cardiovascular disease among young **women** (**NHS**) . J Am Coll Cardiol 2015;65:43–51.
Chomistek AK, Henschel B, Eliassen AH, et al. Frequency, Type, and Volume of **Leisure-Time Physical Activity** and Risk of Coronary Heart Disease in Young Women. Circulation. 2016 Jul 26;134(4):290-9.
Chou R, Arora B, Dana T, Fu R, et al. **Screening asymptomatic adults with resting or exercise electrocardiography (ECG)**: a review of the evidence for the U.S. Preventive Services Task Force. (USPSTF) Ann Intern Med. 2011; 155:375-85.
Chou R; High Value Care Task Force of the American College of Physicians. **Cardiac screening** with electrocardiography, stress echocardiography, or myocardial perfusion imaging: advice for high-value care from the American college of physicians. Ann Intern Med. 2015 Mar 17;162(6):438-47.
Choudhry NK, Isaac T, Lauffenburger JC, et al. Effect of a **Remotely Delivered Tailored Multicomponent Approach to Enhance Medication Taking for Patients With Hyperlipidemia**, Hypertension, and Diabetes: The STIC2IT Cluster Randomized Clinical Trial. JAMA Intern Med. 2018 Aug 6.
Chow BJ, Freeman MR, Bowen JM, et al. Ontario Multidetector **Computed Tomographic Coronary Angiography** Study: Field Evaluation of Diagnostic Accuracy. Arch Intern Med. 2011 Mar 14.
Chow CK, Pell AC, Walker A, O'Dowd C, Dominiczak AF, Pell JP. **Families of patients with premature** coronary heart disease: an obvious but neglected target for primary prevention. BMJ. 2007 Sep 8;335(7618):481-5.
Chow CK, Jolly S, Rao-Melacini P, Fox KA, Anand SS, Yusuf S. Association of **diet, exercise, and smoking** modification with risk of early cardiovascular events after acute coronary syndromes. Circulation. 2010 Feb 16;121(6):750-8.
Chow CK, Islam S, Bautista L, et al. **Parental history** and myocardial infarction risk across the world: The INTERHEART study. J Am Coll Cardiol 2011; 57:619-627.
Chow CK, Redfern J, Hillis GS, et al. Effect of **lifestyle-focused text messaging** on risk factor modification in patients with coronary heart disease: a randomized clinical trial. JAMA. doi:10.1001/jama.2015.10945.
Chowdhury R, Ramond A, O'Keeffe LM, et al. **Environmental toxic metal contaminants and risk of cardiovascular disease**:systematic review and meta-analysis. BMJ. 2018 Aug 29;362:k3310.
Chowdhury R, Stevens S, Gorman D, Pan A, Warnakula S, Chowdhury S, et al. Association between **fish consumption, long chain omega 3 fatty acids**, and risk of cerebrovascular disease: systematic review and meta-analysis. BMJ 2012;345:e6698.
Chowdhury R, Warnakula S, Kunutsor S, et al. Association of **dietary, circulating, and supplement fatty acids** with coronary risk. A systematic review and meta-analysis. *Ann Intern Med* 2014; 160;398-406.
Christoffersen M, Frikke-Schmidt R, Schnohr P, Jensen GB, Nordestgaard BG, Tybjærg-Hansen A. **Xanthelasmata, arcus corneae**, and ischaemic vascular disease and death in general population: prospective cohort study. BMJ 2011;343:d5497
Christoffersen M, Frikke-Schmidt R, Schnohr P, et al. **Visible age-related signs** and risk of ischemic heart disease in the general population: a prospective cohort study. Circulation. 2014 Mar 4;129(9):990-8.
Chronic Kidney Disease Prognosis Consortium, Matsushita K, van der Velde M, Astor BC, Woodward M, et al. Association of **estimated glomerular filtration rate and albuminuria** with all-cause and cardiovascular mortality in general population cohorts: a Collaborative meta-analysis. Lancet. 2010 Jun 12;375(9731):2073-81.
Chrysant SG. **Coffee Consumption** and Cardiovascular Health. Am J Cardiol. 2015 Jun 4.
Chung M, Tang AM, Fu Z, et al. **Calcium Intake and Cardiovascular Disease Risk**: An Updated Systematic Review and Meta-analysis. Ann Intern Med. 2016 Oct 25.
Cirino AL, Harris S, Lakdawala NK, et al. Role of **Genetic Testing** in Inherited Cardiovascular Disease: A Review. JAMA Cardiol. 2017 Aug 9.
Cirino AL, Ho CY. **Genetic testing for inherited heart disease**. Circulation. 2013 Jul 2;128(1):e4-8.
Cirillo PM, Cohn BA. **Pregnancy Complications and Cardiovascular Disease Death**: 50-Year Follow-Up of the Child Health and Development Studies Pregnancy Cohort. Circulation. 2015 Sep 29;132(13):1234-42.
Clase CM, Gao P, Tobe SW, et al. on behalf of the ONTARGET (ONgoing Telmisartan Alone and in combination with Ramipril Global Endpoint Trial) and TRANSCEND (Telmisartan Randomized Assessment Study in Angiotensin-Converting-Enzyme-Inhibitor Intolerant Subjects with Cardiovascular Disease). **Estimated Glomerular Filtration Rate and Albuminuria** as Predictors of Outcomes in Patients With High Cardiovascular Risk: A Cohort Study. Ann Intern Med. 2011 Mar 1;154(5):310-318.
Clar C;Al-Khudairy L;Loveman E;Kelly SA;Hartley L;. **Low glycaemic index diets** for the prevention of cardiovascular disease. Cochrane Database Syst Rev. 2017 Jul 31;7:CD004467. T here is currently no evidence available regarding the effect of low GI diets on cardiovascular disease events. Moreover, there is currently no convincing evidence that low GI diets have a clear beneficial effect on blood lipids or blood pressure parameters.
Clarke R, Peden JF, Hopewell JC, et al. PROCARDIS Consortium. Genetic variants associated with **Lp(a) lipoprotein** level and coronary disease. N Engl J Med. 2009 Dec 24;361(26):2518-28.
Clarke R, Bennett DA, Parish S, et al. **Homocysteine** and coronary heart disease: meta-analysis of MTHFR case-control studies, avoiding publication bias. PLoS Med 2012
Clarke PM, Walter SJ, Hayen A, et al. **Survival** of the fittest: retrospective cohort study of the longevity of **Olympic medallists** in the modern era. BMJ. 2012 Dec 13;345:e8308.
Clausen JSR, Marott JL, Holtermann A, et al. **Midlife Cardiorespiratory Fitness and the Long-Term Risk of Mortality**: 46 Years of Follow-Up. J Am Coll Cardiol. 2018 Aug 28;72(9):987-995.
Cobb LK, Anderson CAM, Elliott P, et al. Methodological issues in cohort studies that relate **sodium intake** to cardiovascular disease outcomes: a science advisory from the American Heart Association. Circulation. 2014;129:1173–1186.
Cogswell ME, Mugavero K, Bowman BA, et al. **Dietary Sodium** and Cardiovascular Disease Risk - Measurement Matters. N Engl J Med. 2016 Jun 1.
Cohen AJ, Brauer M, Burnett R, et al. Estimates and **25-year trends of the global burden of disease attributable to ambient air pollution**: an analysis of data from the Global Burden of Diseases Study 2015. Lancet 2017; online April 10.
Cohen DA, Han B, Nagel CJ, et al. The First National Study of **Neighborhood Parks**: Implications for Physical Activity. Am J Prev Med. 2016 Oct;51(4):419-26.
Cohen HW, Zeig-Owens R, Joe C, et al. Long-term Cardiovascular Disease **Risk Among Firefighters After the World Trade Center Disaster**. JAMA Netw Open. 2019 Sep 4;2(9):e199775.
Cohen JC, Boerwinkle E, Mosley TH Jr, Hobbs HH. Sequence variations in PCSK9, low LDL, and protection against coronary heart disease. N Engl J Med. 2006 Mar 23;354(12):1264-72. These data indicate that moderate lifelong

reduction in the plasma level of LDL cholesterol is associated with a substantial reduction in the incidence of coronary events, even in populations with a high prevalence of non-lipid-related cardiovascular risk factors.
Cohen R, Budoff M, McClelland RL, et al. Significance of a **Positive Family History** for Coronary Heart Disease in Patients With a Zero Coronary Artery Calcium Score (from the Multi-Ethnic Study of Atherosclerosis). Am J Cardiol. 2014 Jul 30.
Cohen R, Bavishi C, Haider, et al. Meta-Analysis of **Relation of Vital Exhaustion** to Cardiovascular Disease Events. Am J Cardiol. 2017.
Colantonio LD, Richman JS, Carson AP, et al. Performance of the Atherosclerotic Cardiovascular Disease Pooled Cohort Risk Equations by **Social Deprivation Status**. J Am Heart Assoc. 2017 Mar 17;6(3).
Collins GS, Altman DG. An independent external validation and evaluation of **QRISK** cardiovascular risk prediction: a prospective open cohort study. BMJ. 2009 Jul 7;339:b2584. doi: 10.1136/bmj.b2584.
Collins GS, Altman DG. An independent and external validation of **QRISK2** cardiovascular disease risk score: a prospective open cohort study. BMJ. 2010 May 13;340:c2442. doi: 10.1136/bmj.c2442.
Collins GS, Altman DG. External validation of **QDSCORE**((R)) for predicting the 10-year risk of developing Type 2 diabetes. Diabet Med. 2011 May;28(5):599-607. doi: 10.1111/j.1464-5491.2011.03237.x
Collins GS, Altman DG. Predicting the 10 year risk of cardiovascular disease in the United Kingdom: independent and external validation of an updated version of **QRISK2**. BMJ 2012;344:e4181.
Conen David, Chae Claudia U., Glynn Robert J., et al. Risk of Death and Cardiovascular Events in Initially Healthy Women With **New-Onset Atrial Fibrillation**. JAMA. 2011;305(20):2080-2087.doi:10.1001/jama.2011.659
Cook NR, Obarzanek E, Cutler JA, Buring JE, Rexrode KM, Kumanyika SK, Appel LJ, Whelton PK; Trials of Hypertension Prevention Collaborative Research Group. Joint effects of **sodium and potassium intake** on subsequent Cardiovascular disease: the Trials of Hypertension Prevention follow-up study. Arch Intern Med. 2009 Jan 12;169(1):32-40. A higher sodium to potassium excretion ratio is associated with increased risk of subsequent CVD, with an effect stronger than that of sodium or potassium alone.
Cook NR, Paynter NP, Eaton CB, et al. Comparison of the **Framingham** and **Reynolds Risk Scores** for Global Cardiovascular Risk Prediction in the Multiethnic Women`s Health Initiative. Circulation. 2012 Mar 7.
Cook NR, Appel LJ, Whelton PK. Lower levels of **sodium** intake and reduced cardiovascular risk. Circulation. 2014 Mar 4;129(9):981-9.
Cook NR, Appel LJ, Whelton PK. **Sodium intake** and all-cause mortality over 20 years in the Trials of Hypertension Prevention. J Am Coll Cardiol 2016;68:1609–17.
Cook NR, Ridker PM. **Calibration of the Pooled Cohort Equations for Atherosclerotic Cardiovascular Disease**: An Update. Ann Intern Med. 2016 Oct 11.
Cooney Marie Therese, Dudina Alexandra, D'Agostino Ralph, et al. **Cardiovascular Risk-Estimation** Systems in Primary Prevention: Do They Differ? Do They Make a Difference? Can We See the Future? Circulation 122: 300-310.
Cooper Rachel, Kuh Diana, Hardy Rebecca, Mortality Review Group . Objectively measured **physical capability** levels and mortality: systematic review and meta-analysis. BMJ 341:doi:10.1136/bmj.c4467 (Published 9 September 2010).
Cooper R, Strand BH, Hardy R, et al. **Physical capability in mid-life and survival** over 13 years of follow-up: British birth cohort study. BMJ 2014;348:g2219.
Corrales-Medina VF, Alvarez KN, Weissfeld LA, et al. Association between **hospitalization for pneumonia** and subsequent risk of cardiovascular disease. *JAMA* 2015; 313:264-274.
Correia A, Peters JL, Levy JI, Melly S, Dominici F. **Residential exposure to aircraft noise** and hospital admissions for cardiovascular diseases: multi-airport retrospective study. BMJ 2013;347:f5561
Coutinho T, Goel K, Correa de Sá D, et al. **Combining body mass index with measures of central obesity** in the assessment of mortality in subjects with coronary heart disease. Role of "normal weight central obesity." J Am Coll Cardiol 2012; 61:553-560.
Coxson PG, Cook NR, Joffres M, et al. Mortality benefits from US population-wide reduction in **sodium consumption** projections from 3 modeling approaches. Hypertension 2013; 61:564-570.
Cragg JJ, Noonan VK, Krassioukov A, Borisoff J. Cardiovascular disease and **spinal cord injury**: results from a national population health survey. Neurology 2013;81:723–728.
Cremer PC, Wu Y, Ahmed HM, et al. Use of **sex-specific clinical and exercise risk scores** to identify patients at increased risk for all-cause mortality [online October 26, 2016]. JAMA Cardiol. doi:10.1001/jamacardio.2016.3720
Criqui MH, Denenberg JO, Ix JH, et al. **Calcium density of coronary artery plaque** and risk of incident cardiovascular events. (MESA) JAMA. 2014 Jan 15;311(3):271-8
Cromar KR, et al. American Thoracic Society & Marron Institute Report. Estimated Excess Morbidity and Mortality Caused by **Air Pollution** above American Thoracic Society-Recommended Standards, 2011-2013. Ann Am Thorac Soc. 2016 Aug;13(8):1195-2016
Crous-Bou M, Fung TT, Prescott J, Julin B, Du M, Sun Q, et al. **Mediterranean diet** and telomere length in Nurses Health Study (NHS): population based cohort study. BMJ 2014;349:g6674.
Crowson CS, Matteson EL, Roger VL, et al. Usefulness of Risk Scores to Estimate the Risk of **Cardiovascular Disease in Patients With Rheumatoid Arthritis**. Am J Cardiol. 2012 Apr 20.
Crum-Cianflone NF, Bagnell ME, Schaller E, et al. Impact of combat deployment and **posttraumatic stress disorder** on newly reported coronary heart disease among US active duty and reserve forces. Circulation. 2014;129:1813–1820.
Crump C, Howell EA, Stroustrup A, et al. Association of **Preterm Birth With Risk of Ischemic Heart Disease** in Adulthood. JAMA Pediatr. 2019 Jun 3.
Cruz M, Covinsky K, Widera EW, et al. **Predicting 10-year mortality** for older adults. JAMA. 2013 Mar 6;309(9):874-6.
Dagfinn Aune, Edward G, et al. **Fruit and vegetable intake** and the risk of cardiovascular disease, total cancer and all-cause mortality–a systematic review and dose-response meta-analysis of prospective studies. International Journal of Epidemiology, 2017.
Dalal HM, Doherty P, Taylor RS. **Cardiac rehabilitation**. BMJ. 2015 Sep 29;351:h5000.
Dall PM, et al The influence of **dog ownership** on objective measures of free-living physical activity and sedentary behaviour in community-dwelling older adults: a longitudinal case-controlled study. BMC Public Health. 2017 Jun 9;17(1):496
Dalton JE, Perzynski AT, Zidar DA, et al. Accuracy of cardiovascular risk prediction varies by **neighborhood socioeconomic position**. A retrospective cohort study. Ann Intern Med. 2017. [Epub ahead of print]. doi:10.7326 /M16-2543
Dalton JE;Perzynski AT;Zidar DA;Rothberg MB;Coulto Accuracy of Cardiovascular Risk Prediction Varies by **Neighborhood Socioeconomic Position**: A Retrospective Cohort Study. Ann Intern Med. 2017 Aug 29.
Dam MK, Hvidtfeldt UA, Tjønneland A, et al. Five Year change in **alcohol intake and risk of breast cancer** and coronary heart disease among postmenopausal women: prospective cohort study. BMJ. 2016 May 11;353:i2314.
Damen JAAG, Hooft L, Schuit E, et al. **Prediction models for cardiovascular disease risk in the general population**: systematic review. BMJ 2016;353:i2416.
Danaei G, Finucane MM, et al. **National, regional, and global trends in systolic blood pressure since 1980**: systematic analysis of health examination surveys and epidemiological studies with 786 country-years and 5.4 million participants. Lancet 2011.
Danaei G, Singh GM, Paciorek CJ, et al. Global Burden of Metabolic Risk Factors of Chronic Diseases Collaborating Group. The global cardiovascular risk transition: associations of **four metabolic risk factors** with national income, urbanization, and Western diet in 1980 and 2008. Circulation. 2013 Apr 9;127(14):1493-502.
Daniels SR, Pratt CA, Hayman LL. **Reduction** of risk for cardiovascular disease in **children and adolescents**. Circulation. 2011 Oct 11;124(15):1673-86.
Darby SD et al. Risk of ischemic heart disease in women after **radiotherapy for breast cancer**. N Engl J Med 2013 Mar 14; 368:987.
Daviglus ML, Talavera GA, Avilés-Santa ML, et al. Prevalence of major cardiovascular risk factors and cardiovascular diseases among **Hispanic/Latino** individuals of diverse backgrounds in the United States. JAMA 2012.
Day DB, Xiang J, Mo J, et al. Association of **Ozone Exposure** With Cardiorespiratory Pathophysiologic Mechanisms in Healthy Adults. JAMA Intern Med. 2017 Jul 17.
De Caterina Raffaele. **n–3 Fatty Acids** in Cardiovascular Disease. N Engl J Med 2011; 364:2439-2450.
de Gonzalez Amy Berrington, Hartge Patricia, Cerhan James R., et al. **Body-Mass Index** and Mortality among 1.46 Million White Adults. N Engl J Med 2010; 363:2211-2219.
de Koning L, Malik VS, Kellogg MD et al. **Sweetened beverage consumption**, incident coronary heart disease and biomarkers of risk in men. Circulation 2012; DOI: 10.1161/CIRCULATIONAHA.111.067017
de Lemos JA., Drazner MH., Omland T, et al. Association of **Troponin T** Detected With a Highly Sensitive Assay and Cardiac Structure and Mortality Risk in the General Population. JAMA. 2010;304(22):2503-2512.
de Lemos JA, Ayers CR, Levine BD, et al. A **Multimodality Strategy for Cardiovascular Risk Assessment**: Performance in Two Population-Based Cohorts. Circulation. 2017 Mar 30.
de Oliveira C, Watt R, Hamer M. **Toothbrushing**, inflammation, and risk of cardiovascular disease: results from Scottish Health Survey. BMJ. 2010 May 27;340:c2451. doi: 10.1136/bmj.c2451.
de Souza RJ, Mente A, et al. Intake of **saturated and trans unsaturated fatty acids** and risk of all cause mortality, cardiovascular disease, and type 2 diabetes: systematic review and meta-analysis of observational studies. BMJ. 2015 Aug 11;351:h3978.
DeFilippis AP, Young R, Carrubba CJ, et al. An analysis of **calibration and discrimination among multiple cardiovascular risk scores in a modern multiethnic cohort**. *Ann Intern Med* 2015; 162: 266-275.
DeFilippis AP, Young R, McEvoy JW, et al. **Risk score overestimation**: the impact of individual cardiovascular risk factors and preventive therapies on the performance of the American Heart Association-American College of Cardiology-Atherosclerotic Cardiovascular Disease risk score in a modern multi-ethnic cohort. Eur Heart J. 2016 Jul 19
DeFina LF, Radford NB, Barlow CE, et al. Association of **all-cause and cardiovascular mortality with high levels of physical activity** and concurrent coronary artery calcification [online Jan 30, 2019]. JAMA Cardiol. doi:10.1001/jamacardio.2018.4628
Deo Rajat; Vittinghoff Eric; Lin Feng; et al. **Risk Factor and Prediction Modeling for Sudden Cardiac Death** in Women With Coronary Artery Disease. Arch Intern Med. 2011;0(2011):archinternmed.2011.328.
De Lorgeril M, Renaud S, Mamelle N, Salen P, Martin JL, Monjaud I, et al. **Mediterranean alpha-linolenic acid-rich diet** in secondary prevention of coronary heart disease. *Lancet* 1994;343(8911):1454-59.
De Marchis GM, Dankowski T, König IR, et al. A novel **biomarker-based prognostic score in acute ischemic stroke**: The CoRisk score. Neurology. 2019 Mar 26;92(13):e1517-e1525.
De Ruijter W, et al. Use of Framingham risk score and new biomarkers (**homocysteine**) to predict cardiovascular mortality in older people: population-based observational cohort study. BMJ 2009; DOI: 10.1136/bmj.a3083.
Dehghan M, Mente A, Teo KK, et al. Relationship between **healthy diet and risk of CVD** among patients on drug therapies for secondary prevention. A prospective cohort study of 31536 high-risk individuals from 40 countries. Circulation 2012.
Dehghan M, Mente A, Zhang X, et al. Associations of **fats and carbohydrate intake** with cardiovascular disease and mortality in 18 countries from five continents (PURE): a prospective cohort study. Lancet. 2017 Aug 28.
Dehghan M, Mente A, Rangarajan S, et al; Prospective Urban Rural Epidemiology (PURE) study investigators. Association of **dairy intake with cardiovascular disease and mortality** in 21 countries from five continents (PURE): a prospective cohort study.

Lancet. 2018 Sep 11.
Deijle IA, Van Schaik SM, Van Wegen EE, et al. **Lifestyle Interventions** to Prevent Cardiovascular Events After Stroke and Transient Ischemic Attack: Systematic Review and Meta-Analysis. Stroke. 2017 Jan;48(1):174-179.
Del Gobbo LC, Imamura F, Aslibekyan S, et al; Cohorts for Heart and Aging Research in Genomic Epidemiology (CHARGE) **Fatty Acids** and Outcomes Research Consortium (FORCe). ω-3 Polyunsaturated Fatty Acid Biomarkers and Coronary Heart Disease: Pooling Project of 19 Cohort Studies. JAMA Intern Med. 2016 Jun 27.
Delp MD, Charvat JM, Limoli CL, et al. **Apollo lunar astronauts** show higher cardiovascular disease mortality: Possible deep space radiation effects on the vascular endothelium. *Sci Rep* 2016; 6:29901.
Den Ruijter HM, Peters SAE, Anderson TJ, et al. **Common carotid intima-media thickness** measurements in cardiovascular risk prediction: : A meta-analysis. JAMA 2012; 308:796-803.
Despréaux T, Saint-Lary O, Danzin F, et al. **Stress at work**. BMJ. 2017 Jun 15;357:j2489
Detrano R, Guerci AD, Carr JJ, et al. **Coronary calcium** as a predictor of coronary events in four racial or ethnic groups. N Engl J Med 2008; 358:1336-1345.
Devi R, Singh SJ, Powell J, et al. **Internet-based interventions for the secondary prevention** of coronary heart disease. Cochrane Database Syst Rev. 2015 Dec 22;12:CD009386.
Devlin RB, Duncan KE, Jardim M, et al. Controlled exposure of healthy young volunteers to **ozone** causes cardiovascular effects. Circulation. 2012 Jul 3;126(1):104-11.
Dhoble A, Lahr BD, Allison TG, et al. **Predicting Long-Term Cardiovascular Risk Using the Mayo Clinic Cardiovascular Risk Score** in a Referral Population. Am J Cardiol. 2014 Jun 19.
Dhurandhar NV, Thomas D. The link between **dietary sugar** intake and cardiovascular disease mortality: an unresolved question. JAMA. 2015 Mar 3; 313(9):959-60.
Di Angelantonio Emanuele, Chowdhury Rajiv, Sarwar Nadeem, et al. **Chronic kidney disease** and risk of major cardiovascular disease and non-vascular mortality: prospective population based cohort study. BMJ 341:doi:10.1136/bmj.c4986 (30 Sept 2010).
Di Q, Wang Y, Zanobetti A, et al. **Air pollution** and mortality in the Medicare population. N Engl J Med 2017;376:2513-22.
Di Q, Dai L, Wang Y, et al. Association of Short-term Exposure to **Air Pollution** With Mortality in Older Adults. JAMA. 2017 Dec 26;318(24):2446-2456.
Diaz KM, Duran AT, Colabianchi N, et al. Potential Effects of **Replacing Sedentary Time With Short Sedentary Bouts or Physical Activity** on Mortality: A National Cohort Study. Am J Epidemiol. 2018 Dec 14.
Diaz KM, Howard VJ, Hutto B, et al. Patterns of **sedentary behavior** and mortality in U.S. middle-aged and older adults. A national cohort study. Ann Intern Med. 2017. [Epub ahead of print]. doi:10.7326/M17-0212
Diaz KM, Goldsmith J, et al. **Prolonged, Uninterrupted Sedentary Behavior** and Glycemic Biomarkers Among US Hispanic/Latino Adults: The HCHS/SOL (Hispanic Community Health Study/Study of Latinos). Circulation. 2017 Oct 10;136(15):1362-1373.
Dibben GO, Dalal HM, Taylor RS, et al. **Cardiac rehabilitation and physical activity**: systematic review and meta-analysis. Heart. 2018 Apr 13.
Dimakopoulou K, Koutentakis K, Papageorgiou I, et al. Is **aircraft noise exposure** associated with cardiovascular disease and hypertension? Results from a cohort study in Athens, Greece. Occup Environ Med. 2017 Jun 13.
Ding M, Satija A, et al. Association of **Coffee Consumption** with Total and Cause-Specific Mortality in Three Large Prospective Cohorts. Circulation. 2015 Nov 16.
DiNicolantonio JJ, Lucan SC. The wrong white crystals: **not salt but sugar** as aetiological in hypertension and cardiometabolic disease. Open Heart. 2014 Nov 3;1(1)
Dietary Guidelines for Americans (DGA) 2010. Full Guideline: http://www.health.gov/dietaryguidelines/dga2010/DietaryGuidelines2010.pdf, Summary: http://www.cnpp.usda.gov/Publications/DietaryGuidelines/2010/PolicyDoc/ExecSumm.pdf
Ding M, Bhupathiraju SN, Satija A, et al. Long-term **coffee** consumption and risk of cardiovascular disease: a systematic review and a dose-response meta-analysis of prospective cohort studies. Circulation. 2014 Feb 11;129(6):643-59
Ding D, Rogers K, van der Ploeg H, et al. **Traditional and Emerging Lifestyle Risk Behaviors** and All-Cause Mortality in Middle-Aged and Older Adults: Evidence from a Large Population-Based Australian Cohort. PLoS Med. 2015 Dec 8;12(12):e1001917.
Do R, Xie C, Zhang X, et al. INTERHEART investigators. The Effect of **Chromosome 9p21 Variants** on Cardiovascular Disease May Be Modified by Dietary Intake: Evidence from a Case/Control and a Prospective Study. PLoS Med. 2011 Oct;9(10):e1001106.
Dong JY, Zhang YH, Wang P, Qin LQ. Meta-analysis of **dietary glycemic load and glycemic index** in relation to risk of coronary heart disease. Am J Cardiol. 2012 Jun 1;109(11):1608-13.
Dong C, Rundek T, Wright CB, et al. Ideal **Cardiovascular Health Predicts** Lower Risks of Myocardial Infarction, Stroke, and Vascular Death across Whites, Blacks and Hispanics: the Northern Manhattan Study. Circulation. 2012 May 22.
Drozda J. Jr., Messer JV, Spertus J, et al. **ACCF/AHA/AMA-PCPI 2011 performance measures** for adults with coronary artery disease and hypertension: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Performance Measures and the American Medical Association-Physician Consortium for Performance Improvement. J Am Coll Cardiol 2011;58:xxx–xxx. http://content.onlinejacc.org/cgi/reprint/j.jacc.2011.05.002v1.pdf
Du H, Li L, Bennett D, Guo et al; China Kadoorie Biobank Study. **Fresh Fruit Consumption** and Major Cardiovascular Disease in China. N Engl J Med. 2016 Apr 7;374(14):1332-43.
Du Y, Liu B, Sun Y, et al. Trends in Adherence to the **Physical Activity Guidelines for Americans** for Aerobic Activity and Time Spent on Sedentary Behavior Among US Adults, 2007 to 2016. JAMA Netw Open. 2019 Jul 3;2(7):e197597.
Dufouil C, Beiser A, McLure LA, et al. **Revised Framingham Stroke Risk Profile** to Reflect **Temporal Trends**. Circulation. 2017 Mar 21;135(12):1145-1159.
Dukes JW, Dewland TA, Vittinghoff E, et al. Access to **alcohol** and heart disease among patients in hospital: observational cohort study using differences in alcohol sales laws. BMJ. 2016 Jun14;353:i2714.
Dumurgier Julien, Elbaz Alexis, , et al. **Slow walking speed** and cardiovascular death in well functioning older adults: prospective cohort study. BMJ 2009;339:b4460, doi: 10.1136/bmj.b4460 (Published 10 November 2009).
Dunlop DD, Song J, Semek PA, et al. Relation of **physical activity time** to incident disability in community dwelling adults with or at risk of knee arthritis: prospective cohort study. BMJ 2014;348:g2472.
Duvivier BM, Schaper NC, Hesselink MK, et al. **Breaking sitting with light activities vs structured exercise**: a randomised crossover study demonstrating benefits for glycaemic control and insulin sensitivity in type 2 diabetes. Diabetologia. 2016 Dec 1.
Dwyer-Lindgren L, Bertozzi-Villa A, Stubbs RW, et al. **US county-level trends** in mortality rates for major causes of death, 1980-2014.JAMA. doi:10.1001/jama.2016.13645
Dyakova M, Shantikumar S, Colquitt JL, et al. **Systematic versus opportunistic risk assessment for the primary prevention of cardiovascular disease**. Cochrane Database Syst Rev. 2016 Jan 29;1:CD010411. The results are limited by the heterogeneity between trials in terms of participants recruited, interventions and duration of follow-up. Limited data suggest that systematic risk assessment for CVD has no statistically significant effects on clinical endpoints. There is limited evidence to suggest that CVD systematic risk assessment may have some favourable effects on cardiovascular risk factors. The completion of the five ongoing trials will add to the evidence base.
Ebrahim S, Taylor F, Ward K, Beswick A, Burke M, Davey Smith G. **Multiple risk factor interventions for primary prevention** of coronary heart disease. Cochrane Database of Systematic Reviews 2011, Issue 1. Art. No.: CD001561. DOI: 10.1002/14651858.CD001561.pub3. Interventions using counselling and education aimed at behaviour change do not reduce total or CHD mortality or clinical events in general populations but may be effective in reducing mortality in high-risk hypertensive and diabetic populations. Risk factor declines were modest but owing to marked unexplained heterogeneity between trials, the pooled estimates are of dubious validity. Evidence suggests that health promotion interventions have limited use in general populations.
Eckardt KU, Gillespie IA, Kronenberg F. High cardiovascular event rates occur within the **first weeks of starting hemodialysis**. Kidney Int. 2015;88:1117-1125.
Eckel RH et al. **2013 AHA/ACC guideline** on **lifestyle management** to **reduce cardiovascular risk**: A report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. J Am Coll Cardiol 2013 Nov.
Eder L, Chandran V, Gladman DD. The **Framingham** Risk Score underestimates the extent of subclinical atherosclerosis in patients with **psoriatic** disease. Ann Rheum Dis. 2014 Nov;73(11):1990-6.
Edwardson CL, Yates T, Biddle SJH, et al. Effectiveness of the **Stand More AT (SMArT) Work intervention**: cluster randomised controlled trial. BMJ. 2018 Oct 10;363:k3870.
Egan BM, Li J, White K, et al. **2013 ACC/AHA Cholesterol Guideline** and Implications for Healthy People 2020 Cardiovascular Disease Prevention Goals. J Am Heart Assoc. 2016 Aug 19;5(8)
Egeberg A, Skov L, Joshi AA, et al. The relationship between duration of **psoriasis**, vascular inflammation, and cardiovascular events. J Am Acad Dermatol. 2017 Oct;77(4):650-656.e3.
Eggers KM, Venge P, Lind L. Prognostic Usefulness of the Change in **N-terminal pro B-type Natriuretic Peptide Levels** to Predict Mortality in a Single Community Cohort Aged ≥70 Years. Am J Cardiol. 2012 Oct 2.
Ekelund U. Infographic: **Physical activity, sitting time and mortality**. Br J Sports Med. 2018 Sep;52(18):1164-1165.
Ekelund U, Luan J, Sherar LB, et al. **Moderate to vigorous physical activity** and sedentary time and cardiometabolic risk factors in children and adolescents. JAMA 2012; 307:704-712.
Ekelund U, Steene-Johannessen J, et al. **Does physical** activity attenuate, or even eliminate, the detrimental association of sitting time with mortality? A harmonised meta-analysis of data from more than 1 million men and women. Lancet. 2016 Jul 27.
Ekelund U, Tarp J, Steene-Johannessen J, et al. Dose-response associations between **accelerometry measured physical activity and sedentary time** and all cause mortality: systematic review and harmonised meta-analysis. BMJ. 2019 Aug 21;366:l4570.
Ekelund U, Ward HA, Norat T, et al. **Physical activity** and all-cause mortality across levels of overall and abdominal adiposity in European men and women: the European Prospective Investigation into Cancer and Nutrition Study (EPIC). Am J Clin Nutr. 2015 Mar;101(3):613-21.
Elfassy T, Swift SL, Glymour MM, et al. Associations **of Income Volatility With Incident Cardiovascular Disease** and All-Cause Mortality in a US Cohort: 1990 to 2015. Circulation. 2019 Jan 7.
Elkind MS, Luna JM, Moon YP, Liu KM, Spitalnik SL, Paik MC, Sacco RL. High-sensitivity **C-reactive protein** predicts mortality but not stroke: The Northern Manhattan Study. Neurology. 2009 Oct 20;73(16):1300-7.
Elizabeth Dunford MPH, Jacqueline Webster PhD, Mark Woodward PhD, et al. The **variability of reported salt levels in fast foods** across six countries: Opportunities for salt reduction. CMAJ 2012
Elliott P, Chambers JC, Zhang W, et al. Genetic Loci associated with **C-reactive protein** levels and risk of coronary heart disease. JAMA. 2009 Jul 1;302(1):37-48.
Elliott L, Cifu AS. **Healthy Lifestyle Counseling** in Persons With Cardiovascular Risk Factors. JAMA. 2015 Jul 28;314(4):398-9.
Elnabawi YA, Oikonomou EK, Dey AK, et al. Association of **Biologic Therapy With Coronary Inflammation in Patients With Psoriasis** as Assessed by Perivascular Fat Attenuation Index. JAMA Cardiol. 2019 Jul 31.
Elsayed EF, et al. Waist-to-hip ratio, body mass index, and subsequent kidney disease and death. Am J Kidney Dis. 2008 Jul;52(1):29-38. Epub 2008 May 29. WHR, but not BMI, is associated with incident CKD and mortality.

Assessment of CKD risk should use WHR rather than BMI as an anthropomorphic measure of obesity.
Emdin CA, Khera AV, Natarajan P, et al. **Evaluation of the Pooled Cohort Equations** for Prediction of Cardiovascular Risk in a Contemporary Prospective Cohort. Am J Cardio. 2017.
Emdin CA, Odutayo A, Wong CX, et al. Meta-Analysis of **Anxiety** as a Risk Factor for Cardiovascular Disease. Am J Cardiol. 2016 Aug 15;118(4):511-9
Emdin CA, Khera AV, Natarajan P, et al. **Genetic association of waist-to-hip ratio** with **cardiometabolic traits, type 2 diabetes**, and coronary heart disease.JAMA. doi:10.1001/jama .2016.21042
Emerging Risk Factors Collaboration. **C-reactive protein** concentration and risk of coronary heart disease, stroke and mortality: an individual participant meta-analysis. Lancet 2009; DOI:10.1016/S0140-6736(09)61717-7.
Emerging Risk Factors Collaboration, Diabetes mellitus, **fasting blood glucose** concentration, & risk of vascular disease: a collaborative meta-analysis of 102 prospective studies, Lancet, Volume 375, Issue 9733, 26 June 2010-2 July 2010, Pages 2215-2222.
Emerging Risk Factors Collaboration. Separate and combined associations of **body-mass index and abdominal adiposity** with cardiovascular disease: collaborative analysis of 58 prospective studies.Lancet 2011;online Mar11.DOI:10.1016/S0140-6736(11)60105-0.
Emerging Risk Factors Collaboration. Lipid-related markers and cardiovascular disease prediction. JAMA 2012; 307:2499-2506.
Emerging Risk Factors Collaboration. **C-reactive protein, fibrinogen**, and cardiovascular disease prediction. N Engl J Med2012 Oct 4; 367:1310.
Emerging Risk Factors Collaboration. **Glycated hemoglobin measurement** and prediction of cardiovascular disease. JAMA. 2014 Mar 26;311(12):1225-33.
Emerging Risk Factors Collaboration, Di Angelantonio E, Kaptoge S, Wormser D, et al. Association of **Cardiometabolic Multimorbidity** With Mortality. JAMA. 2015 Jul 7;314(1):52-60.
England BR, Thiele GM, Anderson DR, et al. Increased **cardiovascular risk in rheumatoid arthritis**: mechanisms and implications. BMJ. 2018 Apr 23;361:k1036.
Ensor KB, Raun LH, Persse D. A Case-Crossover Analysis of Out-of-Hospital Cardiac Arrest and **Air Pollution**. Circulation. 2013 Feb 13.
Esposito K, Maiorino MI, Ciotola M, Di Palo C, et al. Effects of a **Mediterranean-style diet** on the need for antihyperglycemic drug therapy in patients with newly diagnosed type 2 diabetes: a randomized trial. *Ann Intern Med* 2009;151(5):306-14.
Erickson J, Sadeghirad B, Lytvyn L, et al. The Scientific Basis of Guideline Recommendations on **Sugar Intake**: A Systematic Review. Ann Intern Med. 2016 Dec 20.
Eskild A. Mothers who give **birth to offspring with low birth weight may have increased risk for cardiovascular death**. BMJ Evid Based Med. 2019 Feb;24(1):39-40.
Estruch R, Ros E, Salas-Salvadó J, et al; the **PREDIMED** Study Investigators. Primary Prevention of Cardiovascular Disease with a **Mediterranean Diet**. N Engl J Med. 2013 Feb 25.
Estruch R, Ros E, Salas-Salvadó J, et al. Primary Prevention of Cardiovascular Disease with a **Mediterranean Diet Supplemented with Extra-Virgin Olive Oil or Nuts**. (**PREDIMED**) N Engl J Med. 2018 Jun 13.
Etemadi A, Sinha R, Ward MH, et al. Mortality from different causes associated with **meat, heme iron, nitrates, and nitrites in the NIH-AARP Diet and Health Study**: population cohort study. BMJ 2017;357:j1957.
Ezzati M, Riboli E. **Behavioral and dietary risk factors** for noncommunicable diseases. N Engl J Med. 2013 Sep 5;369(10):954-64.
Faeh D, Braun J, Bopp M. **Body mass index vs cholesterol** in cardiovascular disease risk prediction models. Arch Intern Med. 2012 Dec 10;172(22):1766-8.
Fanaroff AC, Califf RM, Windecker S, Smith SC Jr, Lopes RD**. Levels of evidence supporting** American College of Cardiology/American Heart Association and European Society of Cardiology **guidelines**, 2008-2018 [Mar 19, 2019]. JAMA. doi:10.1001/jama.2019.1122
Fang J, Shaw KM, Keenan NL, Centers for Disease Control and Prevention. **Prevalence of coronary heart disease**—United States, 2006-2010. MMWR Morb Mortal Wkly Rep 2011; 60:1377-1381.
Fang J, Yang Q, Hong Y, et al. **Status of cardiovascular health among adult Americans** in the 50 states and the District of Columbia, 2009. J Am Heart Assoc 2012; DOI:10.1161/jaha. 112.005371.
Fardet L, Petersen I, Nazareth I. Risk of cardiovascular events in people prescribed **glucocorticoids** with iatrogenic Cushing's syndrome: cohort study. BMJ. 2012 Jul 30;345:e4928.
Farquhar WB, Edwards DG, Jurkovitz CT, Weintraub WS. **Dietary Sodium** and Health: More Than Just Blood Pressure. J Am Coll Cardiol. 2015 Mar 17;65(10):1042-1050.
Farvid MS, Ding M, Pan A, et al. **Dietary Linoleic Acid** and Risk of Coronary Heart Disease: A Systematic Review and Meta-Analysis of Prospective Cohort Studies. Circulation. 2014 Aug 26.
Farzadfar F, Finucane MM, Danaei G, et al. **National, regional, and global trends in serum total cholesterol since 1980**: systematic analysis of health examination surveys and epidemiological studies with 321 country-years and 3.0 million participants. Lancet 2011.
Fearon WF, Achenbach S, Engstrom T, et al. **Accuracy of Fractional Flow Reserve** Derived From Coronary Angiography. Circulation. 2019 Jan 22;139(4):477-484.
Feinstein M, Ning H, Kang J, et al. **Racial Differences** in Risks for First Cardiovascular Events and Non-Cardiovascular Death: The Atherosclerosis Risk in Communities Study (ARIC), the Cardiovascular Health Study (CHS), and the Multi-Ethnic Study of Atherosclerosis (MESA). Circulation. 2012 Jun 12.
Feldman RD, Nattel S. Increasing appreciation for the role of single-pill combinations for the prevention of atherosclerotic disease: a pro-**polypill** polemic. Can J Cardiol. 2014 May;30(5):517-9.
Ference BA, Bhatt DL, Catapano AL, et al. Association of **Genetic Variants Related to Combined Exposure to Lower Low-Density Lipoproteins** and Lower Systolic Blood Pressure With Lifetime Risk of Cardiovascular Disease. JAMA. 2019 Sep 2.
Ferencik M, Mayrhofer T, Bittner DO, et al. Use of **high-risk coronary atherosclerotic plaque detection** for risk stratification of patients with stable chest pain [published online January 10, 2018].JAMA Cardiol. doi:10.1001/jamacardio.2017.4973.
Ferket Bart S.; Colkesen Ersen B.; Visser Jacob J.; et al. Systematic Review of Guidelines on **Cardiovascular Risk Assessment**: Which Recommendations Should Clinicians Follow for a Cardiovascular Health Check? *Arch Intern Med*. 2010;170(1):27-40.
Ferrie JE, Virtanen M, Jokela M, et al. **Job insecurity** and risk of diabetes: a meta-analysis of individual participant data. CMAJ. 2016 Oct 3.
Ferraro PM, Taylor EN, Eisner BH, et al. History of kidney stones and the risk of coronary heart disease. JAMA. 2013 Jul 24;310(4):408-15.
Fidler MM, Reulen RC, Henson K, et al. Population-Based Long-Term Cardiac-Specific Mortality Among 34 489 Five-Year **Survivors of Childhood Cancer** in Great Britain. Circulation. 2017 Mar 7;135(10):951-963.
Fihn SD, Bucher JB, McDonell M, et al. **Collaborative care intervention** for stable ischemic heart disease. Arch Intern Med. 2011 Sep 12;171(16):1471-9.
Finegold JA, Shun-Shin MJ, Cole GD, et al. Distribution of **lifespan gain from primary prevention intervention**. *Open Heart.* 2016.
Finkelstein EA, Haaland BA, Bilger M, et al. Eff ectiveness of **activity trackers** with and without incentives to increase physical activity (**TRIPPA**): a randomised controlled trial. Lancet Diabetes Endocrinol 2016; online Oct 4.
Finucane MM, Stevens GA, Cowan MJ. **National, regional, and global trends in body-mass index since 1980**: systematic analysis of health examination surveys and epidemiological studies with 960 country-years and 9.1 million participants. Lancet 2011.
Fitzgerald JD, Johnson L, Hire DG, et al. **LIFE** Study Research Group. Association of Objectively Measured **Physical Activity** With Cardiovascular Risk in Mobility-limited Older Adults. J Am Heart Assoc. 2015 Feb 18;4(2).
Fleg JL, Forman DE, Berra K, et al; on behalf of the American Heart Association Committees on Older Populations and Exercise Cardiac Rehabilitation and Prevention of the Council on Clinical Cardiology, Council on Cardiovascular and Stroke Nursing, Council on Lifestyle and Cardiometabolic He. **Secondary Prevention of Atherosclerotic Cardiovascular Disease in Older Adults**: A Scientific Statement From the American Heart Association. Circulation. 2013 Oct 28.
Flegal KM, Kit BK, Oprana H, Graubard BI. Association of **all-cause mortality with overweight and obesity** using standard body mass index categories: a systematic review and meta-analysis. JAMA. 2012;309(1):71-82.
Flueckiger P, Longstreth W, Herrington D, et al. **Revised Framingham Stroke Risk Score, Nontraditional Risk Markers**, and Incident Stroke in a Multiethnic Cohort. Stroke. 2018 Feb;49(2):363-369.
Ford MK, Beattie WS, Wijeysundera DN. Systematic review: prediction of **perioperative** cardiac complications and mortality by the revised cardiac risk index. Ann Intern Med. 2010 Jan 5;152(1):26-35.
Ford ES. Trends in **mortality from all causes and cardiovascular disease among hypertensive and nonhypertensive adults** in the United States. Circulation. 2011 Apr 26;123(16):1737-44.
Ford ES, Greenlund KJ, Hong Y. **Ideal cardiovascular health and mortality** from all causes and diseases of the circulatory system among adults in the United States. Circulation 2012
Forman JP, Scheven L, de Jong PE, et al. Association between **sodium intake and change in uric acid**, urine albumin excretion and risk of developing hypertension. Circulation 2012.
Forouhi NG, Krauss RM, Taubes G, et al. **Dietary fat and cardiometabolic health**: evidence, controversies, and consensus for guidance. BMJ. 2018 Jun 13;361:k2139.
Foster HME, Celis-Morales CA, Nicholl BI, et al. The **effect of socioeconomic deprivation** on the association between an extended measurement of unhealthy lifestyle factors and health outcomes: a prospective analysis of the UK Biobank cohort. Lancet Public Health. 2018 Nov 16.
Foy AJ, et al. **Coronary computed tomography angiography vs functional stress testing** for patients with suspected coronary artery disease: systematic review & meta-analysis [online Oct 2, 2017]. JAMA Intern Med. doi:10.1001/jamainternmed.2017.4772
Fox CS, Matsushita K, Woodward M, et al, for the Chronic Kidney Disease Prognosis Consortium. Associations of **kidney disease** measures with mortality and end-stage renal disease in individuals with and without diabetes: a meta-analysis. Lancet 2012.
Fradley MG, Larson MG, Cheng S, et al. Reference Limits for **N-Terminal-pro-B-Type Natriuretic Peptide** in Healthy Individuals (from the Framingham Heart Study). Am J Cardiol. 2011 Aug 23.
Franco M, Bilal U, Urduñez P, et al. **Population-wide weight loss and regain in relation to diabetes** burden and cardiovascular mortality in Cuba 1980-2010: repeated cross sectional surveys and ecological comparison of secular trends. BMJ 2013;346:f1515.
Franklin BA, Brinks J, Sacks R, et al. **Reduced Walking Speed** and Distance as Harbingers of the Approaching Grim Reaper. Am J Cardiol. 2015 Jul 15;116(2):313-7.
Freak-Poli RL, Cumpston M, Peeters A, et al. **Workplace pedometer** interventions for increasing physical activity. Cochrane Database Syst Rev. 2013 Apr 30;4:CD009209. There was limited and low quality data providing insufficient evidence to assess the effectiveness of pedometer interventions in the workplace for increasing physical activity and improving subsequent health outcomes.
Freedman ND, Park Y, Abnet CC, et al. Association of **coffee drinking with total and cause-specific mortality**. N Engl J Med. 2012 May 17;366(20):1891-904.

Frémont P, Fortier M, Frankovich RJ. **Exercise prescription** and referral tool to facilitate brief advice to adults in primary care. Can Fam Physician. 2014 Dec;60(12):1120-2.

Friedemann C, Heneghan C, Mahtani K, Thompson M, Perera R, Ward AM. Cardiovascular disease risk in healthy children and its association with **body mass index**: systematic review and meta-analysis. BMJ 2012;345:e4759

Frieden TR. **Sodium Reduction**-Saving Lives by Putting Choice Into Consumers' Hands. JAMA. 2016 Aug 9;316(6):579-80.

Fukuoka Y, Haskell W, Lin F, Vittinghoff E. Short- and Long-term **Effects of a Mobile Phone App in Conjunction With Brief In-Person Counseling on Physical Activity** Among Physically Inactive Women: The mPED Randomized Clinical Trial. JAMA Netw Open. 2019 May 3;2(5):e194281

Fulton Janet E.; Simons-Morton Denise G.; Galuka Deborah A. **Physical Activity**: An Investment That Pays Multiple Health Dividends: Comment on "Combined Effects of Cardiorespiratory Fitness, Not Smoking, and Normal Waist Girth on Morbidity and Mortality in Men," "Physical Activity and Survival in Male Colorectal Cancer Survival," "Effects of a Television Viewing Reduction on Energy Intake and Expenditure in Overweight and Obese Adults," and "Physical Activity and Rapid Decline in Kidney Function Among Older Adults". Arch Intern Med. 2009;169(22):2124-2127.

Fung Teresa T., van Dam Rob M., Hankinson, Susan E. **Low-Carbohydrate Diets** and All-Cause and Cause-Specific Mortality: Two Cohort Studies. *Ann Intern Med* September 7, 2010 153:289-298.

Galan P, Kesse-Guyot E, Czernichow S, et al. , for the SU.FOL.OM3 Collaborative Group. Effects of **B vitamins and omega 3 fatty acids** on cardiovascular diseases: a randomised placebo controlled trial. BMJ 341:doi:10.1136/bmj.c6273 (29 Nov 2010).

Gale CR, Batty GD, Osborn DP, et al. **Mental disorders** across the adult life course and future coronary heart disease: evidence for general susceptibility. Circulation. 2014 Jan 14;129(2):186-93.

Gami AS, Olson EJ, Shen WK, et al. **Obstructive sleep apnea** and the risk of sudden cardiac death: A longitudinal study. JACC 2013.

Gan WQ, Moline J, Kim H, et al. Exposure to **loud noise**, bilateral high-frequency hearing loss and coronary heart disease. Occup Environ Med. 2015 Sep 15.

Ganesan AN et al. International **mobile-health intervention on physical activity, sitting, and weight**: The Stepathlon cardiovascular health study. J Am Coll Cardiol 2016 Apr 3.

Ganz P, Heidecker B, Hveem K, et al. Development and validation of a **protein-based risk score** for cardiovascular outcomes among patients with stable coronary heart disase.JAMA. doi:10.1001/jama.2016.5951

Garcia JM, Duran AT, Schwartz JE, et al. **Types of Sedentary Behavior** and Risk of Cardiovascular Events and Mortality in Blacks: The Jackson Heart Study. J Am Heart Assoc. 2019 Jul 2;8(13):e010406.

García-Almagro FJ, Gimeno JR, Villegas M, et al. Prognostic value of the Thrombolysis in Myocardial Infarction risk score in a unselected population with chest pain. Construction of a new predictive model. Am J Emerg Med. 2008 May;26(4):439-45. In this developmental study, a **modified Thrombolysis in Myocardial Infarction (TIMI) risk score** was better at predicting coronary events 6 months after patients present with chest pain suspected to be ischemic in origin. Since models generally perform better in developmental studies than in subsequent testing, the new score needs independent validation. (LOE = 2b-)

Gardener H, Rundek T, Wright CB, Elkind MSV, Sacco RL. Dietary **sodium and risk of stroke** in the Northern Manhattan Study. Stroke. 2012;43:1200 –1205.

Gardener H, Rundek T, Wright CB, et al. A **Mediterranean-Style Diet** and Left Ventricular Mass (from the Northern Manhattan Study). Am J Cardiol. 2015 Feb 15;115(4):510-4.

Gardner C, Wylie-Rosett J, Gidding SS, et al. **Nonnutritive sweeteners**: Current use and health perspectives. A scientific statement from the American Heart Association and the American Diabetes Association. Circulation 2012; 126:509-519. (Aspartame, acesulfame-K, neotame, saccharin, and sucralose)

Garland A, Jeon SH, Stepner Met al. Effects of **cardiovascular and cerebrovascular health events on work and earnings**: a population-based retrospective cohort study. CMAJ. 2019 Jan 7;191(1):E3-E10.

Garovic VD, Bailey KR, Boerwinkle E, et al. Hypertension in **pregnancy** as a risk factor for cardiovascular disease later in life. J Hypertens. 2010 Jan 16. [Epub ahead of print]

Gaudreault V, Tizon-Marcos H, Poirier P, et al. Transient myocardial tissue and function changes during a **marathon in less fit marathon runners**. Can J Cardiol. 2013 Oct;29(10):1269-76.

Guasch-Ferré M, Liu X, Malik VS, et al. **Nut consumption** and risk of cardiovascular disease. J Am Coll Cardiol 2017;70:2519–32.

Gaye B, Canonico M, Perier MC, et al. **Ideal Cardiovascular Health**, Mortality, and Vascular Events in Elderly Subjects: The **Three-City Study**. J Am Coll Cardiol. 2017 Jun 27;69(25):3015-3026.

Gaziano TA, Young CR, Fitzmaurice G, et al. Laboratory-based versus **non-laboratory**-based method for assessment of cardiovascular disease risk: the NHANES I Follow-up Study cohort. Lancet. 2008 Mar 15;371(9616):923-31. Cardiovascular prediction models that do not require laboratory testing perform as well as models that use laboratory testing. (LOE = 2b)

GBD 2013 Mortality and Causes of Death Collaborators. **Global**, regional, and national age-sex specific **all-cause and cause-specific mortality** for 240 causes of death, 1990-2013: a systematic analysis for the Global Burden of Disease Study 2013. Lancet. 2014 Dec 17.

GBD 2017 Diet Collaborators. **Health effects of dietary risks** in 195 countries, 1990-2017: a systematic analysis for the Global Burden of Disease Study 2017. Lancet. 2019 Apr 3. doi:10.1016/S0140-6736(19)30041-8.

Gebel K, Ding D, Chey T, et al. Effect of **Moderate to Vigorous Physical Activity on All-Cause Mortality** in Middle-aged and Older Australians. JAMA Intern Med. 2015 Apr 6.

Geisel MH, Bauer M, Hennig F, et al. Comparison of **coronary artery calcification, carotid intima-media thickness and ankle-brachial index** for predicting 10-year incident cardiovascular events in the general population. Eur Heart J. 2017 Mar 30.

Genders TS, Steyerberg EW, Hunink MG, et al. Prediction **model to estimate presence of coronary artery disease**: retrospective pooled analysis of existing cohorts. BMJ. 2012 Jun 12;344:e3485.

George J, Majeed W, Mackenzie IS, et al. Association between cardiovascular events and **sodium-containing effervescent, dispersible, and soluble drugs**: nested case-control study. BMJ. 2013 Nov 26;347:f6954.

Gepner Y, Shelef I, Komy O, et al. The **beneficial effects of Mediterranean diet** over low-fat diet may be mediated by decreasing hepatic fat content. J Hepatol. 2019 May 8.

Gibbons RJ, Miller TD. Optimal Medical Therapy for Known Coronary Artery Disease: A Review. JAMA Cardiol. 2017 Jul 12.

Gidding SS, Rana JS, et al. **Pathobiological Determinants of Atherosclerosis in Youth (PDAY) Risk Score** in Young Adults Predicts Coronary Artery and Abdominal Aorta Calcium in Middle Age: The CARDIA Study. Circulation. 2016 Jan 12;133(2):139-46.

Gillen JB, et al. Twelve Weeks of **Sprint Interval Training** Improves Indices of Cardiometabolic Health Similar to Traditional Endurance Training despite a **Five-Fold Lower Exercise Volume** and Time Commitment. PLoS One. 2016 Apr 26;11(4):e0154075

Giuseppe M, Suzanne O, Paul KW et al. **Salt** intake and Cardiovascular Disease : Summary of the technical report on sodium intake and cardiovascular disease in low-and middle-income countries by the joint working group of the World Heart Federation, the European Society of Hypertension and the European Public Health Association. Euro J Heart. 2017 ;38 :697-704.

Glei DA, Goldman N, Risques RA, et al. **Predicting Survival from Telomere Length versus Conventional Predictors**: A Multinational Population-Based Cohort Study. PLoS One. 2016 Apr 6

Global Burden of Metabolic Risk Factors for Chronic Diseases Collaboration (BMI Mediated Effects). Metabolic mediators of the effects of **body-mass index, overweight, and obesity** on coronary heart disease and stroke: a pooled analysis of 97 prospective cohorts with 1·8 million participants. Lancet. 2013 Nov 21.

Go AS, Mozaffarian D, Roger VL, et al. **Heart and stroke statistics—2013 update**: A report from the American Heart Association.Circulation 2013;

Gogebakan O, Kohl A, Osterhoff MA, et al. Effects of weight loss and long-term weight maintenance with **diets varying in protein and glycemic index** on cardiovascular risk factors: the Diet, Obesity, and Genes (**DiOGenes**) study, a randomized controlled trial. Circulation. 2011;124:2829 –2838.

Goel K, Lennon RJ, Tilbury RT, et al. Impact of **cardiac rehabilitation** on mortality and cardiovascular events after percutaneous coronary intervention in the community. Circulation. 2011 May 31;123(21):2344-52.

Goff DC Jr et al. **2013 ACC/AHA guidelines** on the **assessment of cardiovascular risk**: A report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. J Am Coll Cardiol 2013 Nov 12.

Gold DR, Mittleman MA. New insights into **pollution** and the cardiovascular system: 2010 to 2012. Circulation. 2013 May 7;127(18):1903-13.

Gold DR, Samet JM. **Air pollution**, climate, and heart disease. Circulation. 2013 Nov 19;128(21):e411-4.

Goldberger JJ, Basu A, Boineau R, et al. **Risk stratification for sudden cardiac death**: a plan for the future. Circulation. 2014 Jan 28;129(4):516-26

Goldstein BI, Carnethon MR, et al. **Major Depressive Disorder and Bipolar Disorder** Predispose Youth to Accelerated Atherosclerosis and Early Cardiovascular Disease: A Scientific Statement From the American Heart Association. Circulation. 2015 Aug 10.

Goliasch G, Kleber ME, Richter B, et al. Routinely available **biomarkers** improve prediction of long-term mortality in stable coronary artery disease: the **Vienna and Ludwigshafen Coronary Artery Disease (VILCAD) risk score**.

Gómez E, Fernández-Alvira JM, Vilanova M, et al. A **Comprehensive Lifestyle Peer-Group-Based Intervention** on Cardiovascular Risk Factors: The Randomized Controlled Fifty-Fifty Program. J Am Coll Cardiol. 2015 Oct 30.

Gooding HC, Ning H, Gillman MW, et al. Application of a **Lifestyle-Based Tool** to Estimate Premature Cardiovascular Disease Events in Young Adults: The Coronary Artery Risk Development in Young Adults (CARDIA) Study. JAMA Intern Med. 2017 Jul 17.

Gooding HC, et al. Application of a **Lifestyle-Based Tool (HHS) to Estimate Premature Cardiovascular Disease Events in Young Adults**: Coronary Artery Risk Development in Young Adults (**CARDIA**)Study. JAMA Intern Med. 2017Sep 1;177(9):1354-1360.

Goodman J, Thomas S, Burr JF. Physical Activity Series: **Cardiovascular risks of physical activity** in apparently healthy individuals: Risk evaluation for exercise clearance and prescription. Can Fam Physician. 2013 Jan;59(1):46-9.

Gore FM, Bloem PJN, Patton GC, et al. **Global burden of disease in young people aged 10–24 years**: a systematic analysis. Lancet 2011; published online June 7. DOI:10.1016/S0140-6736(11)60512-6.

Gordon-Larsen P, Boone-Heinomen J, Sidney S, et al. **Active commuting** and cardiovascular disease risk. Arch Intern Med 2009; 169: 1216-1223.

Gottlieb DJ, Punjabi NM, Mehra R, et al. **CPAP versus oxygen in obstructive sleep apnea**. N Engl J Med 2014;370:2276-85.

Goulden R. **Moderate Alcohol Consumption** Is Not Associated with Reduced All-cause Mortality. Am J Med. 2016 Feb;129(2):180-186.e4.

Gozdzik A, Salehi R, O'Campo P, et al. Cardiovascular risk factors and 30-year cardiovascular risk in **homeless adults with mental illness**. BMC Public Health. 2015 Dec;15(1):1472.

Graciani A, León-Muòoz LM, Guallar-Castillón, et al. **Cardiovascular health in a southern Mediterranean European country**. A nationwide population-based study. Circulation: Cardiovascular Quality and Outcomes 2013.

Graudal NA, Hubeck-Graudal T, Jurgens G. Effects of low **sodium** diet versus high sodium diet on blood pressure, renin, aldosterone, catecholamines, cholesterol, and triglyceride. Cochrane Database of Systematic Reviews 2011, Issue 11. Art. No.: CD004022. DOI: 10.1002/14651858.CD004022.pub3. Sodium reduction resulted in a 1% decrease in blood pressure in normotensives, a 3.5% decrease in hypertensives, a significant increase in plasma renin, plasma aldosterone, plasma adrenaline and plasma noradrenaline, a 2.5% increase in cholesterol, and a 7% increase in triglyceride. In general, these effects were stable in studies lasting for 2 weeks or more.

Graudal N, Jürgens G, Baslund B, et al. Compared With Usual **Sodium** Intake, Low- and Excessive-Sodium Diets Are Associated With Increased Mortality: A Meta-Analysis. Am J Hypertens. 2014 Apr 1.

Gray L, Lee I-M, Sesso HD, Batty GD. **Blood pressure in early adulthood**, hypertension in middle age, and future cardiovascular disease mortality: HAHS (Harvard Alumni Health Study). J Am Coll Cardiol 2011; 58:2396-2403.

Green P, Newman JD, Shaffer JA, et al. Relation of **Patients Living Without a Partner or Spouse** to Being Physically Active After Acute Coronary Syndromes (from the PULSE Accelerometry Substudy). Am J Cardiol. 2013 Feb 11. Greenland P, Alpert JS,

Grøntved A, Koivula RW, Johansson I, et al. **Bicycling to Work** and Primordial Prevention of Cardiovascular Risk: A Cohort Study Among Swedish Men and Women. J Am Heart Assoc. 2016 Oct 31;5(11).

Grossman C, Ehrlich S, Shemesh J, et al. **Coronary Artery Calcium and Exercise Electrocardiogram** as Predictors of Coronary Events in Asymptomatic Adults. Am J Cardiol. 2015 Jan 6.

Gutiérrez OM, Khodneva YA, Muntner P, et al. Association Between **Urinary Albumin Excretion** and Coronary Heart Disease in Black vs White Adults. JAMA. 2013 Aug 21;310(7):706-14.

Greenberg JA, Manson JE, Neuhouser ML, et al. **Chocolate intake and heart disease and stroke in the Women's** Health Initiative: a prospective analysis. Am J Clin Nutr. 2018 Jul 1;108(1):41-48.

Greenwood JP, Maredia N, Younger JF, et al. **Cardiovascular magnetic resonance** and single-photon emission computed tomography for diagnosis of coronary heart disease (CE-MARC): a prospective trial. Lancet. 2011 Dec 22.

Gregg EW, Cheng YJ, Saydah S, et al. Trends in **death rates among US adults with and without diabetes** between 1997 and 2006. Diabetes Care 2012; 35:1252-1257.

Griffing G. Images in clinical medicine. **Frank's sign**. N Engl J Med. 2014 Mar 6;370(10):e15.

Grioni S, Agnoli C, Sieri S, Pala et al. **Espresso coffee consumption** and risk of coronary heart disease in a large italian cohort. PLoS One. 2015 May 6;10(5)

Grooms KN, Ommerborn MJ, Pham DQ, et al. **Dietary Fiber** Intake and Cardiometabolic Risks among US Adults, NHANES 1999-2010. Am J Med. 2013 Oct 9.

Grunwald JE, Ying GS, Maguire M, et al. Association Between **Retinopathy and Cardiovascular Disease** in Patients With Chronic Kidney Disease (from the Chronic Renal Insufficiency Cohort [CRIC] Study). Am J Cardiol. 2012 Apr 18.

Guallar-Castillón P, Rodriguez-Artalejo F, Lopez-Garcia E, et al. Consumption of **fried foods** and risk of coronary heart disease: Spanish cohort of the European Prospective Investigation into Cancer and Nutrition study. BMJ 2012;344;e363.

Gubbi S, Schwartz E, Crandall J, et al. Effect of **Exceptional Parental Longevity and Lifestyle Factors** on Prevalence of Cardiovascular Disease in Offspring. Am J Cardiol. 2017 Dec 15;120(12):2170-2175.

Gullikkson Mats; Burell Grundy SM, Barlow CE, Farrell SW, et al. **Cardiorespiratory Fitness** and Metabolic Risk. Am J Cardiol. 2012 Jan 3.

Gunilla; Vessby Bengt; et al. Randomized Controlled Trial of **Cognitive Behavioral Therapy** vs Standard Treatment to Prevent Recurrent Cardiovascular Events in Patients With Coronary Heart Disease: Secondary Prevention in Uppsala Primary Health Care Project (SUPRIM). *Arch Intern Med*. 2011;171(2):134-140.

Gunderson EP, Jacobs DR Jr, Chiang V, et al. Duration of **Lactation** and Incidence of the Metabolic Syndrome in Women of Reproductive Age According to Gestational Diabetes Mellitus Status: A 20-Year Prospective Study in CARDIA--The Coronary Artery Risk Development in Young Adults Study. Diabetes. 2009 Dec 3.

Gunderson EP, Chiang V, Pletcher MJ, et al. **History of Gestational Diabetes** Mellitus and Future Risk of Atherosclerosis in Mid-life: The Coronary Artery Risk Development in Young Adults Study. J Am Heart Assoc. 2014 Mar 12

Gunter MJ, Murphy N, Cross AJ, et al. **Coffee drinking** and mortality in 10 European countries. A multinational cohort study. Ann Intern Med. [Epub ahead of print]. doi:10.7326/M16-2945

Guo Y, Li S, Tian Z, et al. The burden of **air pollution** on years of life lost in Beijing, China, 2004-08: retrospective regression analysis of daily deaths. BMJ. 2013 Dec 9;347:f7139

Guthold R, Stevens GA, Riley LM, et al. **Worldwide trends in insufficient physical activity from 2001 to 2016**: a pooled analysis of 358 population-based surveys with 1·9 million participants. Lancet Glob Health. 2018 Oct;6(10):e1077-e1086.

Hackam DG, Shojania KG, Spence JD, et al. Influence of **Noninvasive Cardiovascular Imaging in Primary Prevention**: Systematic Review and Meta-analysis of Randomized Trials. Arch Intern Med. 2011 Mar 14.

Haddy N, Diallo S, El-Fayech C, et al. **Cardiac Diseases Following Childhood Cancer** Treatment: Cohort Study. Circulation. 2015 Oct 20.

Hadigan C, Paules CI, Fauci AS. Association Between **Human Immunodeficiency Virus** Infection and Cardiovascular Diseases: Finding a Solution to Double Jeopardy. JAMA Cardiol. 2016 Dec 21.

Hadley MB, Baumgartner J, Vedanthan R. Developing a Clinical Approach to **Air Pollution** and Cardiovascular Health. Circulation. 2018 Feb 13;137(7):725-742.

Hagger-Johnson G, Gow AJ, Burley V, et al. **Sitting Time, Fidgeting, and All-Cause Mortality** in the UK Women's Cohort Study. Am J Prev Med 2016;50:154–60.

Haikerwal A, Akram M, Del Monaco A, et al. Impact of **Fine Particulate Matter** (PM2.5) Exposure During **Wildfires** on Cardiovascular Health Outcomes. J Am Heart Assoc. 2015 Jul 15;4(7).

Hajifathalian K, Ueda P, Lu Y, et al. A novel **risk score** to predict cardiovascular disease risk in national populations (**Globorisk**): a pooled analysis of prospective cohorts and health examination surveys. Lancet Diabetes Endocrinol. 2015 Mar 25.

Halkin A, Steinvil A, Rosso, et al. **Preventing sudden death of athletes** with electrographic screening. J Am Coll Cardiol 2012; 60: 2271-2276.

Hallal PC, Anderson LB, Bull FC, et al. **Global physical activity** levels: Surveillance progress, pitfalls, and prospects. Lancet 2012.

Hallan SI, Matsushita K, et al; Chronic Kidney Disease Prognosis Consortium. Age and association of **kidney measures** with mortality and endstage renal disease [online October 30, 2012]. JAMA. (eGFR & albuminuria)

Halonen JI, Hansell AL, Gulliver J, et al. **Road traffic noise** is associated with increased cardiovascular morbidity and mortality and all-cause mortality in London. Eur Heart J. 2015 Jun 23.

Halonen JI, Stenholm S, Pentti J, et al. **Childhood Psychosocial Adversity** and Adult Neighborhood Disadvantage as Predictors of Cardiovascular Disease: A Cohort Study. Circulation. 2015 Aug 4;132(5):371-9.

Hamer M, Sabia S, Batty GD, et al. **Physical Activity and Inflammatory Markers** Over 10 Years: Follow-Up in Men and Women From the Whitehall II Cohort Study. Circulation. 2012 Aug 21;126(8):928-33.

Hammill BG, Curtis LH, Schulman KA, Whellan DJ. Relationship between **cardiac rehabilitation** and long-term risks of death and myocardial infarction among elderly Medicare beneficiaries. Circulation 2009; DOI: 10.1161/CIRCULATIONAHA.109.876383.

Hancock AT, Mallen CD, Muller S, et al. Risk of vascular events in patients with **polymyalgia rheumatica**. CMAJ. 2014 Jul 28.

Hankey GJ. **Nutrition** (salt, overeating etc…) and the risk of stroke. Lancet Neurol 2012; 11:66-81.

Hansel B, Roussel R, Elbez Y, et al; **REACH** Registry Investigators. Cardiovascular risk in relation to **body mass index** and use of evidence-based preventive medications in patients with or at risk of atherothrombosis. Eur Heart J. 2015 Aug 4.

Hansell AL, Blangiardo M, Fortunato L, Floud S, de Hoogh K, Fecht D, et al. **Aircraft noise** and cardiovascular disease near Heathrow airport in London: small area study. BMJ 2013;347:f5432.

Hansell A, Ghosh RE, Blangiardo M, et al. Historic **air pollution** exposure and long-term mortality risks in England and Wales: prospective longitudinal cohort study. Thorax. 2016 Feb 8.

Harcombe Z, Baker JS, Cooper SM, et al. Evidence from randomised controlled trials did **not support the introduction of dietary fat guidelines** in 1977and 1983: a systematic review and meta-analysis. Open Heart 2015;2:e000196.

Hardoon SL, Morris RW, Whincup PH, et al. Rising **adiposity** curbing decline in the incidence of myocardial infarction: 20-year follow-up of British men and women in the **Whitehall II cohort**. Eur Heart J 2011.

Haroon NN, Paterson JM, Li P, et al. Patients With **Ankylosing Spondylitis** Have Increased Cardiovascular and Cerebrovascular Mortality: A Population-based Study. Ann Intern Med. 2015 Aug 11.

Harmon KG, Asif IM, Klossner D, et al. Incidence of sudden cardiac death in **national collegiate athletic association athletes**. Circulation. 2011 Apr 19;123(15):1594-600.

Harmon KG, Drezner JA, Wilson MG, et al. Incidence of **sudden cardiac death in athletes**: a state-of-the-art review. Heart. 2014 Aug 15;100(16):1227-1234.

Harnack LJ, Cogswell ME, Shikany JM, et al. **Sources of sodium** in US adults from 3 geographic regions. Circulation. 2017;135:1775–1783.

Harrington JL, Ayers C, Berry JD, et al. **Sedentary Behavior** and Subclinical Cardiac Injury: Results From the Dallas Heart Study. Circulation. 2017 Oct10;136(15):1451-1453.

Harris CD, Watson KB, Carlson SA, et al. **Adult participation in aerobic and muscle-strengthening physical activities**—United States, 2011. MMWR Morb Mortal Wkly Rep 2013; 62:326-330.

Harris KM, Creswell LL, Haas TS, et al. Death and cardiac arrest in **U.S. triathlon participants**, 1985 to 2016. A case series. Ann Intern Med. 2017. [Epub ahead of print]. doi:10.7326/M17-0847

Harris T, et al. Effect of a Primary Care **Walking Intervention** with and without Nurse Support on Physical Activity Levels in 45- to 75-Year-Olds: **Pedometer** And Consultation Evaluation (**PACE-UP**) Cluster Randomised Trial. PLoS Med. 2017 Jan 3;14(1):e1002210.

Harris WS, Mozaffarian D, Rimm E, Kris-Etherton P, et al. **Omega-6 Fatty Acids** and Risk for Cardiovascular Disease. A Science Advisory From the American Heart Association Nutrition Subcommittee of the Council on Nutrition, Physical Activity, and Metabolism; Council on Cardiovascular Nursing; and Council on Epidemiology and Prevention. Circulation. 2009 Jan 26. [Epub ahead of print] In summary, the AHA supports an omega-6 PUFA intake of at least **5% to 10% of energy** in the context of other AHA lifestyle and dietary recommendations. To reduce omega-6 PUFA intakes from their current levels would be more likely to increase than to decrease risk for CHD.

Hart JE, Puett RC, Rexrode KM, Albert CM, Laden F. Effect Modification of Long-Term **Air Pollution** Exposures and the Risk of Incident Cardiovascular Disease in US Women. J Am Heart Assoc. 2015 Nov 25;4(12).

Hartley L, May MD, Loveman E, et al. **Dietary fibre** for the primary prevention of cardiovascular disease. Cochrane Database Syst Rev. 2016 Jan 7;1:CD011472. Studies were short term and therefore did not report on our primary outcomes, CVD clinical events. The pooled analyses for CVD risk factors suggest reductions in total cholesterol and LDL cholesterol with increased fibre intake, and reductions in diastolic blood pressure. There were no obvious effects of subgroup analyses by type of

intervention or fibre type but the number of studies included in each of these analyses were small. Risk of bias was unclear in the majority of studies and high for some quality domains so results need to be interpreted cautiously. There is a need for longer term, well-conducted RCTs to determine the effects of fibre type (soluble versus insoluble) and administration (supplements versus foods) on CVD events and risk factors for the primary prevention of CVD.

Hartley A, Marshall DC, Salciccioli JD, et al. **Trends in Mortality from Ischaemic Heart Disease** and Cerebrovascular Disease in **Europe**: 1980-2009. Circulation. 2016 Mar 22

Haseeb S, Alexander B, Baranchuk A. **Wine** and Cardiovascular Health: A Comprehensive Review. Circulation. 2017 Oct 10;136(15):1434-1448.

Hashem KM, He FJ, Jenner KH, et al. Cross-sectional survey of **salt content** in cheese: a major contributor to salt intake in the UK. BMJ Open. 2014 Jul 18;4(8):e005051.

Hartley L, Dyakova M, Holmes J, et al. **Yoga** for the primary prevention of cardiovascular disease. Cochrane Database Syst Rev. 2014 May 13;5:CD010072. The limited evidence comes from small, short-term, low-quality studies. There is some evidence that yoga has favourable effects on diastolic blood pressure,HDL cholesterol and triglycerides, and uncertain effects on LDL cholesterol.These results should be considered as exploratory and interpreted with caution.

Haufe S, Kerling A, Protte G, et al. **Telemonitoring-supported exercise training**, metabolic syndrome severity, and work ability in company employees: a randomised controlled trial. Lancet Public Health. 2019 Jun 13.

Hausenblas HA, Schreiber K, Smoliga JM. **Addiction to exercise**. BMJ. 2017 Apr 26;357:j1745.

Häusler N, Haba-Rubio J, Heinzer R, Marques-Vidal P. Association of **napping with incident cardiovascular events** in a prospective cohort study. Heart. 2019 Sep 9.

Haycock PC, Heydon EE, Kaptoge S, Butterworth AS, Thompson A, Willeit P. **Leucocyte telomere length** and risk of cardiovascular disease: systematic review and meta-analysis. BMJ 2014;349:g4227

He FJ, Marciniak M, Visagie E, et al. Effect of Modest **Salt Reduction** on Blood Pressure, Urinary Albumin, and Pulse Wave Velocity in White, Black, and Asian Mild Hypertensives. Hypertension. 2009 Jul 20. [Epub ahead of print]

He FJ, Li J, Macgregor GA. Effect of longer term **modest salt reduction** on blood pressure: Cochrane systematic review and meta-analysis of randomised trials. BMJ. 2013 Apr 3;346:f1325.

He FJ, Li J, Macgregor GA. Effect of **longer-term modest salt reduction on blood pressure**. Cochrane Database Syst Rev. 2013 Apr 30;4:CD004937. doi:10.1002/14651858.CD004937.pub2. A modest reduction in salt intake for 4 or more weeks causes significant and, from a population viewpoint, important falls in BP in both hypertensive and normotensive individuals, irrespective of sex and ethnic group.With salt reduction, there is a small physiological increase in plasma renin activity, aldosterone and noradrenaline. There is no significant change in lipid levels.

He FJ, Pombo-Rodrigues S, Macgregor GA. **Salt reduction** in England from 2003 to 2011: its relationship to blood pressure, stroke and ischaemic heart disease mortality. BMJ Open. 2014 Apr 14

He FJ, Wu Y, Feng XX, et al. School based education programme to **reduce salt** intake in children and their families (**School-EduSalt**): cluster randomised controlled trial. BMJ. 2015 Mar 18;350:h770.

He M, Wolpin B, Rexrode K, et al. **ABO blood group** and risk of coronary heart disease in two prospective cohort studies.Arterioscler Thromb Vasc Biol 2012; 32:2314-2320.

He Q, Zhang P, Li G, et al. The association between **insomnia symptoms** and risk of cardio-cerebral vascular events: A meta-analysis of prospective cohort studies. Eur J Prev Cardiol. 2017 Jan 1:2047487317702043.

Healy GN, Winkler EA, Owen N, et al. Replacing **sitting time with standing** or stepping: associations with cardio-metabolic risk biomarkers. Eur Heart J. 2015 Jul 30.

Health Canada Sep/11 **GnRH Agonists**: Heart-related Risk in Men Treated for Prostate Cancer. Health Canada is informing health professionals and patients about a possible increased risk of certain heart-related events in men being treated for prostate cancer with a type of prescription drug known as a Gonadotropin-Releasing Hormone (GnRH) agonist.

Health Canada Apr/13: TASIGNA (**nilotinib**) - Possible Risk of Developing Atherosclerosis-Related Conditions - Novartis Pharmaceuticals Canada Inc.

Heath GW, Parra DC, Sarimento OL, et al. Evidence-based intervention in **physical activity**: Lessons from around the world. Lancet 2012.

Heitmann Berit L, Frederiksen Peder. **Thigh circumference** and risk of heart disease and premature death: prospective cohort study. BMJ 2009;339:b3292, doi: 10.1136/bmj.b3292 (Published 3 September 2009)

Held C, Iqbal R, Lear SA, et al. **Physical activity levels**, ownership of goods promoting sedentary behavior and risk of myocardial infarction: results of the **INTERHEART** study. Eur Heart J 2012

Hemmelgarn Brenda R.; Manns Braden J.; Lloyd Anita; et al. for the Alberta Kidney Disease Network. Relation Between Kidney Function, **Proteinuria**, and Adverse Outcomes. JAMA. 2010;303(5):423-429.

Henney JE, Taylor CL, and Boon CS, eds. Institute of Medicine. **Strategies to Reduce Sodium Intake** in the United States; Washington, DC: National Academies Press, 2010. Available here.

Henson KE, Reulen RC, Winter DL, et al.Cardiac Mortality Among 200,000 Five-Year **Survivors of Cancer** Diagnosed Aged 15-39 Years: The Teenage and Young Adult Cancer Survivor Study. Circulation. 2016 Nov 7.

Hess EP, Agarwal D, Chandra S, et al. **Diagnostic accuracy of the TIMI risk score in patients with chest pain** in the emergency department: a meta-analysis. CMAJ. 2010 Jul 13;182(10):1039-44. Epub 2010 Jun 7.

Hinnouho GM, Czernichow S, Dugravot A, et al. **Metabolically healthy obesity** and the risk of cardiovascular disease and type 2 diabetes: the Whitehall II cohort study. Eur Heart J. 2014 Mar 26.

Hippisley-Cox J, et al. Performance of the QRISK cardiovascular risk prediction algorithm in an independent UK sample of patients from general practice: a validation study. Heart. 2008 Jan;94(1):34-9. Epub 2007 Oct 4.

This analysis demonstrated that **QRISK** is better calibrated to the UK population than Framingham and has better discrimination. www.qrisk.org

Hippisley-Cox J, Coupland C, Vinogradova Y, Robson J, Minhas R, Sheikh A, Brindle P. Predicting cardiovascular risk in England and Wales: prospective derivation and validation of QRISK2. BMJ. 2008 Jun 23. [Epub ahead of print]
Incorporating ethnicity, deprivation, and other clinical conditions into the **QRISK2** algorithm for risk of cardiovascular disease improves the accuracy of identification of those at high risk in a nationally representative population. At the 20% threshold, QRISK2 is likely to be a more efficient and equitable tool for treatment decisions for the primary prevention of cardiovascular disease. As the validation was performed in a similar population to the population from which the algorithm was derived, it potentially has a "home advantage." Further validation in other populations is therefore advised. www.qrisk.org

Hippisley-Cox J, Coupland C, Robson J, et al. Derivation, validation, and evaluation of a new **QRISK model to estimate lifetime** risk of cardiovascular disease: cohort study using QResearch database. BMJ 341:doi:10.1136/bmj.c6624 (Published 9 Dec 2010)

Hippisley-Cox J, Coupland C, Brindle P. **Development and validation** of **QRISK3** risk prediction algorithms to **estimate future risk of cardiovascular disease**: prospective cohort study. BMJ. 2017 May 23;357:j2099.

Hippisley-Cox J, Coupland C. Development and validation of **QMortality risk prediction algorithm** to estimate short term risk of death and assess frailty: cohort study. BMJ 2017;358:j4208. doi:10.1136/bmj.j4208 pmid:28931509.

Hippisley-Cox J, Coupland C. Development and validation of **QDiabetes-2018 risk prediction algorithm** to estimate future risk of type 2 diabetes: cohort study. BMJ. 2017 Nov 20;359:j5019.

Hizo-Abes P, Clark WF, Sontrop JM, et al. Cardiovascular disease after **Escherichia coli O157:H7 gastroenteritis**. CMAJ 2012; DOI:10.1503/cmaj.112161.

Hoffmann TC, Maher CG, Briffa T, et al. **Prescribing exercise interventions** for patients with chronic conditions. CMAJ. 2016 Mar 14.

Högström G, Nordström A, Nordström P. **High aerobic fitness** in late adolescence is associated with a reduced risk of myocardial infarction later in life: a nationwide cohort study in men. Eur Heart J. 2014 Jan 7

Högström G, Nordström A, Nordström P. **Aerobic fitness in late adolescence** and the risk of early death: a prospective cohort study of 1.3 million Swedish men. Int J Epidemiol. 2015 Dec 20.

Holmes MV, Dale CE, Zuccolo L, et al. Association between **alcohol and cardiovascular disease**: Mendelian randomization analysis based on individual participant data. *BMJ* 2014;

Holmes MV, Dale CE, Zuccolo L, et al; InterAct Consortium. Association between **alcohol and cardiovascular disease**: Mendelian randomisation analysis based on individual participant data. BMJ. 2014 Jul 10;349:g4164.

Hong KN, Fuster V, Rosenson RS, et al. **How Low to Go With Glucose, Cholesterol, and Blood Pressure in Primary Prevention of CVD**. J Am Coll Cardiol. 2017 Oct 24;70(17):2171-2185.

Honigberg MC, Givertz MM. **Peripartum cardiomyopathy**. BMJ. 2019 Jan 30;364:k5287.

Hoogwegt MT, Versteeg H, Hansen TB, et al. **Exercise** mediates the asscoation between **positive affect** and five-year mortality in patients with ischemic heart disease. Circ Cardiovasc Qual Outcomes 2013.

Hooper L, Summerbell CD, Thompson R, et al. **Reduced or modified dietary fat** for preventing cardiovascular disease. Cochrane Database of Systematic Reviews 2011, Issue 7. Art. No.: CD002137. DOI: 10.1002/14651858.CD002137.pub2. The findings are suggestive of a small but potentially important reduction in cardiovascular risk on modification of dietary fat, but not reduction of total fat, in longer trials. Lifestyle advice to all those at risk of cardiovascular disease and to lower risk population groups, should continue to include permanent reduction of dietary saturated fat and partial replacement by unsaturates. The ideal type of unsaturated fat is unclear.

Horne BD, May HT, Muhlestein JB, et al. Exceptional mortality prediction by risk scores from **common laboratory tests**. Am J Med. 2009 Jun;122(6):550-8.

Hotchkiss JW, Davies CA, Dundas R, et al. **Explaining trends in Scottish coronary heart disease mortality** between 2000 and 2010 using IMPACTSEC model: retrospective analysis using routine data. BMJ. 2014 Feb 6;348:g1088.

Howard G et al. **Racial Differences** in the Incidence of Cardiovascular Risk Factors in Older Black and White Adults. Journal of the American Geriatric Society. September 26, 2016.

Howden EJ, Leano R, Petchey W, et al. Effects of **exercise** and lifestyle intervention on cardiovascular function in **CKD**. Clin J Am Soc Nephrol. 2013 Sep;8(9):1494-501.

Howden EJ, Sarma S, Lawley JS, et al. Reversing the Cardiac Effects of **Sedentary Aging** in Middle Age-A Randomized Controlled Trial: Implications For Heart Failure Prevention. Circulation. 2018 Jan 8.

Howe KB, Suharlim C, Ueda P, et al. Gotta catch'em all! **Pokémon GO** and physical activity among young adults: difference in differences study. BMJ. 2016 Dec 13;355:i6270.

Hshieh TT, Petrone AB, Gaziano JM, Djoussé L. **Nut consumption** and risk of mortality in the Physicians' Health Study. Am J Clin Nutr. 2015 Feb;101(2):407-12.

Hsia J, Larson JC, Ockene JK, Sarto GE, Allison MA, et al.; Women's Health Initiative Research Group. Resting heart rate as a low tech predictor of coronary events in women: prospective cohort study. BMJ. 2009 Feb 3;338:b219. doi: 10.1136/bmj.b219. **Resting heart rate,** a low tech and inexpensive measure of autonomic tone, independently predicts myocardial infarction or coronary death, but not stroke, in women.

Hsu CY, Chen YT, Chen MH, et al. The association between **insomnia** and increased future cardiovascular events: a nationwide population-based study. Psychosom Med 2015;77:743–51.

Hsue PY, Waters DD. Time to Recognize **HIV Infection** as a Major Cardiovascular Risk Factor. Circulation. 2018 Sep 11;138(11):1113-1115.
Huang C, Barnett AG, Wang X, Tong S. Effects of **extreme temperatures** on years of life lost for cardiovascular deaths: a time series study in brisbane, australia. Circ Cardiovasc Qual Outcomes. 2012 Sep 1;5(5):609-14.
Huang C, Moran AE, Coxson PG, et al. Potential Cardiovascular and Total Mortality Benefits of **Air Pollution** Control in Urban China. Circulation. 2017 Sep 7.
Huang T, Xu M, Lee A, et al. **Consumption of whole grains** and cereal fiber and total and cause-specific mortality: prospective analysis of 367,442 individuals. BMC Med. 2015 Mar 24;13(1):59.
Huelsmann M, Neuhold S, Resl M, et al. PONTIAC (**NT-proBNP** selected prevention of cardiac events in a population of diabetic patients without a history of cardiac disease): a prospective randomized controlled trial. J Am Coll Cardiol. 2013 Oct 8;62(15):1365-72.
Huffman MD, Capewell S, Ning H, et al. **Cardiovascular health behavior and health factor changes (1988 –2008) and projections to 2020**: results from the National Health and Nutrition Examination Surveys. Circulation. 2012;125:2595–2602.
Hughes-Austin JM et al. Relationship of **coronary calcium** on standard chest CT scans with mortality. JACC Cardiovasc Imaging 2016 Feb; 9:152.
Hupin D, Roche F, Gremeaux V, et al. Even a **low-dose of moderate-to-vigorous physical activity** reduces mortality by 22% in adults aged ≥60 years: a systematic review and meta-analysis. Br J Sports Med. 2015 Aug 3.
Hurst RT, Nelson MR, Kendall CB, et al. **Carotid Intimal-Medial Thickness in Active Professional American Football Players** Aged 23 to 35 Years. Am J Cardiol. 2011 Dec 21.
Huxley RR, Woodward M. Cigarette **smoking as a risk factor for coronary heart disease in women** compared with men: a systematic review and meta-analysis of prospective cohort studies. Lancet 2011; DOI: DOI:10.1016/S0140-6736(11)60781-2.
ICSI: Institute for Clinical Systems Improvement. **Primary prevention** of chronic disease risk factors. Bloomington (MN): Institute for Clinical Systems Improvement (ICSI); 2010 May.
Iggman D, Arnlov J, Cederholm, et al. Association of **adipose tissue fatty acid** with cardiovascular and all-cause mortality in elderly men. *JAMA Cardiol* 2016.
Iglayreger HB, Peterson MD, Liu D, et al. **Sleep Duration** Predicts Cardiometabolic Risk in Obese Adolescents. J Pediatr. 2014 Feb 28.
Iina MV, Kepron CA, Taylor GP, et al. Undiagnosed Heart Disease Leading to **Sudden Unexpected Death in Childhood**: A Retrospective Study. Pediatrics. 2011 Aug 8.
Iliodromiti S, Celis-Morales CA, Lyall DM, et al. The impact of **confounding on the associations of different adiposity measures** with the incidence of cardiovascular disease: a cohort study of 296 535 adults of white European descent. Eur Heart J. 2018 May 1;39(17):1514-1520.
IL6R Genetics Consortium and Emerging Risk Factors Collaboration IL-6 (**Interleukin-6**) pathways in coronary heart disease: a collaborative meta-analysis of 82 studies. Lancet 2012.
Imboden MT, Harber MP, Whaley MH, et al. **Cardiorespiratory Fitness and Mortality** in Healthy Men and Women. J Am Coll Cardiol. 2018 Nov 6;72(19):2283-2292.
Ingelsson E, Schaefer EJ, Contois JH, et al. Clinical utility of different lipid measures for prediction of coronary heart disease in men and women. JAMA 2007; 298:776-785. In this large, population-based cohort, the overall performance of apo B:apo A-I ratio for prediction of CHD was comparable with that of traditional lipid ratios but did not offer incremental utility over total cholesterol:HDL-C. These data do not support measurement of apo B or apo A-I in clinical practice when total cholesterol and HDL-C measurements are available. Measurement of the apolipoprotein B:apolipoprotein A-I ratio is comparable with, but does not offer any incremental utility to, standard lipid level ratios in predicting coronary heart disease (CHD). Routine measurement of apolipoprotein levels in clinical practice should be discouraged. (LOE = 1b)
International Working Group on Chest Pain in Primary Care (**INTERCHEST**)., Aerts M, Minalu G, Bösner S, et al. Pooled individual patient data from five countries were used to derive a **clinical prediction rule for coronary artery disease in primary care**. J Clin Epidemiol. 2017 Jan;81:120-128.
Israel A, Kivity S, Sidi Y, et al. Use of **exercise capacity to improve SCORE risk prediction** model in asymptomatic adults. Eur Heart J. 2016 Feb 24.
Jabre P, Jouven X, Adnet F, et al. **Atrial Fibrillation** and Death After Myocardial Infarction: A Community Study. Circulation. 2011 May 2.
Jackson Andrew S.; Sui Xuemei; Hebert James R.; et al. Role of **Lifestyle and Aging** on the Longitudinal Change in Cardiorespiratory Fitness. *Arch Intern Med*. 2009;169(19):1781-1787.
Jackson R, Kerr A, Wells S. **Vascular risk calculators**: essential but flawed clinical tools? Circulation. 2013 May 14;127(19):1929-31.
Jacobs Eric J.; Newton Christina C.; Wang Yiting; et al. **Waist Circumference** and All-Cause Mortality in a Large US Cohort. Arch Intern Med. 2010;170(15):1293-1301.
Jacobson MF, Havas S, McCarter R. Changes in **sodium levels in processed and restaurant foods**, 2005 to 2011. JAMA Intern Med2013; online May 13, 2013.
Jacobson MF, Havas S, McCarter R. Changes in **sodium levels in processed and restaurant foods**, 2005 to 2011. JAMA Intern Med. 2013 Jul 22;173(14):1285-91.
Jaddoe VW, de Jonge L, Hofman A, Franco OH, et al. **First trimester fetal growth restriction** and cardiovascular risk factors in school age children: population based cohort study. BMJ 2014;348:g14.
Jaiswal S, Natarajan P, Silver AJ, et al. **Clonal hematopoiesis** (**CHIP**) and risk of atherosclerotic cardiovascular disease. N Engl J Med. DOI: 10.1056/NEJMoa1701719.
James Matthew T, Hemmelgarn Brenda R, Wiebe N. **Glomerular filtration rate, proteinuria**, and the incidence and consequences of acute kidney injury: a cohort study. The Lancet, Early Online, 22 November 2010 doi:10.1016/S0140-6736(10)61271-8.
Jarmul JA, Pignone M, Pletcher MJ. Interpreting **hemoglobin A1c** in combination with conventional risk factors for prediction of cardiovascular risk. *Circ Cardiovasc Qual Outcomes*. 2015; 8:501–507.
Jaspers NEM, Blaha MJ, Matsushita K, et al. **Prediction of individualized lifetime benefit** from cholesterol lowering, blood pressure lowering, antithrombotic therapy, and smoking cessation in apparently healthy people. Eur Heart J. 2019 May 18.
JATOS Study Group. Principal results of the Japanese trial to assess optimal systolic blood pressure in elderly hypertensive patients (JATOS). Hypertens Res 2008; 31:2115–2127. (n=4418 over 2yrs)
Javaheri S, Redline S. **Insomnia** and risk of cardiovascular disease. Chest. 2017 Jan 30.
JBS3 Board. **Joint British Societies' consensus recommendations** for the prevention of cardiovascular disease (JBS3). Heart 2014.
JBS3: Risk Calculator: Joint British Societies' Consensus Recommendations for the Prevention of Cardiovascular Disease (JBS3). http://www.jbs3risk.com/
Jeevarethinam A, Venuraju S, Dumo A, et al. Usefulness of **Carotid Plaques** as Predictors of Obstructive Coronary Artery Disease and Cardiovascular Events in Asymptomatic Individuals With Diabetes Mellitus. Am J Cardiol. 2018 Apr 15;121(8):910-916.
Jefferis BJ, Parsons TJ, Sartini C, et al. Objectively measured **physical activity, sedentary behaviour** and all-cause mortality in older men: does volume of activity matter more than pattern of accumulation? Br J Sports Med. 2018 Feb 12.
Jena AB, Prasad V, Goldman DP, Romley J. **Mortality** and treatment patterns among patients hospitalized with acute **cardiovascular conditions** during dates of **national cardiology meetings**. *JAMA Intern Med* 2014; DOI:10.1001/jamainternmed.2014.6781.
Jennings C, Kotseva K, De Bacquer D, et al; on behalf of **EUROACTION PLUS** Study Group. Effectiveness of a **preventive cardiology programme** for high CVD risk persistent smokers: the EUROACTION PLUS varenicline trial. Eur Heart J. 2014 Mar 9.
Jensen MT, Wod M, Galatius S, et al. **Heritability of resting heart rate** and association with mortality in middle-aged and elderly **twins**. Heart. 2017 Jun 21.
Jeong SW, Kim SH, Kang SH, et al. **Mortality reduction with physical activity** in patients with and without cardiovascular disease. Eur Heart J. 2019 Sep 1.
Jhamnani S, Patel D, Heimlich L, et al. Meta Analysis of the Effects of **Lifestyle Modifications** on Coronary and Carotid Atherosclerotic Burden. Am J Cardiol. 2015 Jan 15;115(2):268-275.
Ji J, Zöller B, Sundquist K, Sundquist J. Increased risks of coronary heart disease and stroke among **spousal caregivers of cancer patients**. Circulation. 2012 Apr 10;125(14):1742-7.
Jin J, Sugerman DT. JAMA **patient page. Salt** in the diet. JAMA. 2014 Mar 26;311(12):1265.
Jin J. **Counseling on Healthy Living** to Prevent Cardiovascular Disease in Adults Without Risk Factors. JAMA. 2017 Jul 11;318(2):210.
Jobs E, Ingelsson E, Risérus U, et al. Association Between Serum **Cathepsin S** and Mortality in Older Adults. JAMA. 2011 Aug 29.
Johnson KM, Dowe DA, Brink JA. Traditional clinical risk assessment tools do not accurately predict coronary atherosclerotic plaque burden: a **CT angiography study**. AJR Am J Roentgenol. 2009 Jan;192(1):235-43.
Johnson KM, Dowe DA. The detection of any **coronary calcium outperforms Framingham risk** score as a first step in screening for coronary atherosclerosis. AJR Am J Roentgenol 2010; 194:1235-1243.
Johnson CM, Angell SY, Lederer A, et al. **Sodium content** of **lunchtime fast food** purchases at major US chains. Arch Intern Med 2010; 170:732-734.
Joosten MM, Gansevoort RT, Mukamal KJ, et al; for the PREVEND Study Group. **Sodium** Excretion and Risk of Developing Coronary Heart Disease. Circulation. 2014 Jan 14.
Jordan KP, Timmis A, Croft P, et al. **Prognosis of undiagnosed chest pain**: linked electronic health record cohort study. BMJ 2017;357:j1194.
Jørgensen T, Jacobsen RK, Toft U, et al. Effect of **screening and lifestyle counselling** on incidence of ischaemic heart disease in general population: Inter99 randomised trial. BMJ 2014;348:g3617.
Jørstad HT, Colkesen EB, Boekholdt SM, et al. **Estimated 10-year cardiovascular mortality** seriously underestimates overallcardiovascular risk. Heart. 2016 Jan;102(1):63-8.
Jose PO, Frank ATH, Kapphahn KI, et al. Cardiovascular disease **mortality in Asian Americans**. *J Am Coll Cardiol*2014; 64:2486-94
Joshi NV, Vesey AT, Williams MC, et al. **18F-fluoride positron emission tomography** for identification of ruptured and high-risk coronary atherosclerotic plaques: a prospective clinical trial. Lancet 2013; published
Jousilahti P, Laatikainen T, et al. **Primary prevention** and **risk factor reduction** in coronary heart disease mortality among working aged men and women in eastern Finland over 40 years: population based observational study. BMJ. 2016 Mar 1;352:i721.
Juonala M, Magnussen CG, Venn A, et al. Influence of age and associations between **childhood risk factors and carotid IMT** in adulthood. The Cardiovascular Risk in Young Finns Study, the Childhood Determinants of Adult Health study, the Bogalusa Heart Study, and the Muscatine Study for the International Childhood Cardiovascular Cohort (i3C) Consortium. Circulation 2010; DOI:10.1161/CIRCULATIONAHA.110.966465.
Juonala M et al. **Childhood psychosocial factors** and coronary artery calcification in adulthood: The Cardiovascular Risk in Young Finns Study. JAMA Pediatr 2016 Mar 14.

Juraschek SP, Blaha MJ, Whelton SP, et al. **Physical fitness and hypertension** in a population at risk for cardiovascular disease: The Henry Ford ExercIse Testing (FIT) project. *J Am Heart Assoc* 2014.
Kaasenbrood L, Boekholdt SM, van der Graaf Y, et al. **Distribution of estimated 10-year risk of recurrent vascular events** and residual risk in a secondary prevention population. Circulation. 2016;134:1419– 1429.
Kaczorowski Janusz, Chambers LW, Dolovich Lisa, et al. Improving **cardiovascular health at population level**: 39 community cluster randomised trial of Cardiovascular Health Awareness Program (**CHAP**). BMJ 2011;342:doi:10.1136/bmj.d442 (7 Feb 2011)
Kahn HS, Cheng YJ, Thompson TJ, Imperatore G, Gregg EW. Two risk-scoring systems for **predicting incident diabetes mellitus** in U.S. adults age 45 to 64 years. Ann Intern Med. 2009 Jun 2;150(11):741-51. Basic information identified adults at high risk for diabetes. Additional data from fasting blood tests better identified those at extreme risk.
Khan SS, Ning H, Wilkins JT, et al. Association of **Body Mass Index With Lifetime Risk** of Cardiovascular Disease and Compression of Morbidity. JAMA Cardiol. 2018 Feb 28.
Kalogeropoulos AP, Georgiopoulou VV, Murphy RA, et al. **Dietary Sodium** Content, Mortality, and Risk for Cardiovascular Events in Older Adults: The Health, Aging, and Body Composition (Health ABC) Study. JAMA Intern Med. 2015 Jan 19.
Kaltman JR, Thompson PD, Lantos J, et al. **Screening for sudden cardiac death in the young**: report from a national heart, lung, and blood institute working group. Circulation. 2011 May 3;123(17):1911-8.
Kaluza J, Åkesson A, Wolk A. **Processed and unprocessed red meat** consumption and risk of heart failure: A prospective study of men. *Circ Heart Fail* 2014.
Kaminsky LA, Arena R, Beckie TM. The importance of **cardiorespiratory fitness** in the United States: the need for a national registry.Circulation 2013; DOI:10.1161/CIR0b013e31827ee100.
Kamiya K, Masuda T, Matsue Y, et al. Prognostic Usefulness of **Arm and Calf Circumference** in Patients >65 years of age with Cardiovascular Disease. The American Journal of Cardiology (2016).
Kaplan H, Thompson R, Trumble BC, et al. **Coronary atherosclerosis in indigenous South American Tsimane (Bolivian tribe):** a cross-sectional cohort study. Lancet 2017; online March 17.
Karmali KN, Lloyd-Jones DM, Berendsen MA, et al. **Drugs for Primary Prevention** of Atherosclerotic Cardiovascular Disease: An Overview of Systematic Reviews. JAMA Cardiol. 2016 Jun 1;1(3):341-9.
Karmali KN, Persell SD, Perel P, et al. **Risk scoring for the primary prevention of cardiovascular disease**. Cochrane Database Syst Rev. 2017 Mar 14;3:CD006887. : There is uncertainty whether current strategies for providing CVD risk scores affect CVD events. Providing CVD risk scores may slightly reduce CVD risk factor levels and may increase preventive medication prescribing in higher-risk people without evidence of harm. There were multiple study limitations in the identified studies and substantial heterogeneity in the interventions, outcomes, and analyses, so readers should interpret results with caution. New models for implementing and evaluating CVD risk scores in adequately powered studies are needed to define the role of applying CVD risk scores in primary CVD prevention.
Karthikeyan G, Moncur RA, Levine O, et al. Is a pre-operative brain natriuretic peptide or **N-terminal pro-B-type natriuretic peptide** measurement an independent predictor of adverse cardiovascular outcomes within 30 days of noncardiac surgery? A systematic review and meta-analysis of observational studies. J Am Coll Cardiol. 2009 Oct 20;54(17):1599-606.
Kasiman K, Lundholm C, Sandin S, et al. **Familial Effects on Ischemic Stroke**: The Role of Sibling Kinship, Sex and Age of Onset. Circ Cardiovasc Genet. 2012 Mar 9.
Katz D, Gavin MC. **Stable Ischemic Heart Disease**. Ann Intern Med. 2019 Aug 6;171(3):ITC17-ITC32.
Katz MH. Writing More **Specific Exercise Prescriptions**. Arch Intern Med. 2012 Aug 6:1-2.
Katzmarzyk PT, Lee IM. **Sedentary behaviour** and **life expectancy** in the USA: a cause-deleted life table analysis. BMJ Open. 2012 Jul 9;2(4).
Kaufman JD, Adar SD, Barr RG, et al. Association between **air pollution** and coronary artery calcification within six metropolitan areas in the USA (the Multi-Ethnic Study of Atherosclerosis and Air Pollution): A longitudinal cohort study. *Lancet* 2016.
Kavousi M, Elias-Smale S, Rutten JH, Leening MJ, Vliegenthart R, Verwoert GC, et al. Evaluation of **newer risk markers** for coronary heart disease risk classification. A cohort study. Ann Intern Med. 2012;156:438-44
Kavousi M, Desai CS, Ayers C, et al. Prevalence and Prognostic Implications of **Coronary Artery Calcification in Low-Risk Women**: A Meta-analysis. JAMA. 2016 Nov 22;316(20):2126-2134.
Kearns CE, Schmidt LA, Glantz SA. **Sugar industry and coronary heart disease research**: A historical analysis of internal industry documents. *JAMA Intern Med* 2016.
Kerns E, Masterson EA, Themann CL, et al. **Cardiovascular conditions, hearing difficulty, and occupational noise exposure** within US industries and occupations. Am J Ind Med. 2018 Mar 14.
Kerr AJ, Broad J, Wells S, et al. Should the first priority in cardiovascular risk management be those with **prior cardiovascular disease**?. Heart. 2009 Feb;95(2):125-9. Epub 2008 Apr 1. Patients with prior CVD have five-year CVD risks approximately 20% higher, in absolute terms than patients without prior CVD, after accounting for standard risk factors. Almost half the CVD events occurred in those with prior CVD. These patients should be the highest priority for intensive preventive management in primary care.
Kershaw KN, Osypuk TL, Do DP, et al. **Neighborhood-level racial/ethnic residential segregation** and incident cardiovascular disease: the multi-ethnic study of atherosclerosis. Circulation. 2015 Jan 13;131(2):141-8.
Khairy LT, Barin R, Demonière F, et al. **Heart rate response** in spectators of the **Montreal Canadiens hockey team**. Can J Cardiol, in press.
Khan H, Kunutsor SK, Rauramaa R, et al. **Long-Term Change in Cardiorespiratory Fitness** in Relation to Atrial Fibrillation and Heart Failure (from the Kuopio Ischemic Heart Disease Risk Factor Study). Am J Cardiol. 2018 Apr 15;121(8):956-960.
Khan KM, Weiler R, Blair SN. **Prescribing exercise** in primary care. BMJ. 2011 Jul 15;343:d4141. doi: 10.1136/bmj.d4141.
Khan SU, Khan MU, Riaz H, et al. Effects of **Nutritional Supplements and Dietary Interventions** on Cardiovascular Outcomes: An Umbrella Review and Evidence Map. Ann Intern Med. 2019 Jul 9.
Khanji MY, Bicalho VV, van Waardhuizen CN, et al. **Cardiovascular Risk Assessment**: A Systematic Review of Guidelines. Ann InternMed. 2016 Sep 13.
Khanna A, Pequeno P, Gupta S, et al. Increased **Risk of All Cardiovascular Disease Subtypes** Among Childhood Cancer Survivors: Population-Based Matched Cohort Study. Circulation. 2019 Aug 26.
Kharazmi E, Dossus L, Rohrmann S, Kaaks R. **Pregnancy loss and risk of cardiovascular disease**: a prospective population-based cohort study (EPIC-Heidelberg). Heart. 2010 Dec 1.
Khaw KT, Friesen MD, Riboli E, et al. Plasma **Phospholipid Fatty Acid** Concentration and Incident Coronary Heart Disease in Men and Women: The EPIC-Norfolk Prospective Study. PLoS Med. 2012 Jul;9(7):e1001255.
Khera A, Budoff MJ, O'Donnell CJ, et al. Astronaut Cardiovascular Health and Risk Modification (**Astro-CHARM**) Coronary Calcium Atherosclerotic Cardiovascular Disease Risk Calculator. Circulation. 2018 Oct 23;138(17):1819-1827.
Khera AV, Emdin CA, Drake I, et al. **Genetic Risk, Adherence to Healthy Lifestyle** a, and Coronary Disease. N Engl J Med. 2016 Dec 15;375(24):2349-2358.
Kieneker LM, Gansevoort RT, de Boer RA, et al. **Urinary potassium excretion** and risk of cardiovascular events. Am J Clin Nutr. 2016 May;103(5):1204-12
Kim ES, Hagan KA, Grodstein F, et al. **Optimism** and Cause-Specific Mortality: A Prospective Cohort Study. Am J Epidemiol. 2016 Dec 7.
Kim ES, VanderWeele TJ. Mediators of the Association Between **Religious Service Attendance and Mortality**. Am J Epidemiol. 2018 Sep 27.
Kim H, Caulfield LE, Garcia-Larsen V, et al. **Plant-Based Diets** Are Associated With a Lower Risk of Incident Cardiovascular Disease, Cardiovascular Disease Mortality, and All-Cause Mortality in a General Population of Middle-Aged Adults. J Am Heart Assoc. 2019 Aug 20;8(16):e012865.
Kim JH, Malhotra R, Chiampas G et al, Cardiac arrest during **long-distance running** races. N Engl J Med 2012; 366:130-140.
Kim S, Eliot M, Koestler DC, et al. Association of **Neutrophil-to-Lymphocyte Ratio With Mortality and Cardiovascular Disease** in the Jackson Heart Study and Modification by the Duffy Antigen Variant. JAMA Cardiol. 2018 May 2.
Kim SH, Reaven G. Sex Differences in **Insulin Resistance** and Cardiovascular Disease Risk. J Clin Endocrinol Metab. 2013 Sep 24.
Kinge JM, Modalsli JH, Øverland S, et al. Association of **household income with life expectancy and cause-specific mortality** in Norway, 2005-2015 [online May 13, 2019]. JAMA. doi:10.1001/jama.2019.4329
Kipping RR, Howe LD, Jago R, et al. Effect of intervention aimed at increasing **physical activity**, reducing sedentary behaviour, and increasing **fruit and vegetable** consumption in children: Active for Life Year 5 (AFLY5) school based cluster randomised controlled trial. BMJ. 2014 May 27;348:g3256.
Kit BK, Kuklina E, Carroll MD, et al. Prevalence of and Trends in **Dyslipidemia and Blood Pressure** Among US Children and Adolescents, 1999-2012. JAMA Pediatr. 2015 Jan 19.
Kivimäki Mika, Batty G. David, Hamer Mark, et al. Using Additional Information on **Working Hours** to Predict Coronary Heart Disease: A Cohort Study. *Ann Intern Med* April 5, 2011 154:457-463.
Kivimäki M, Nyberg ST, Batty GD, et al. **Job strain** as a risk factor for coronary heart disease: a collaborative meta-analysis of individual participant data. Lancet 2012; published online Sept 14.
Kivimäki M, Nyberg ST, Fransson EI, et al. Associations of **job strain and lifestyle** risk factors with risk of coronary artery disease: a meta-analysis of individual participant data. CMAJ. 2013 May 13.
Kivimäki M, Jokela M, et al, for the IPD-Work Consortium. **Long working hours** and risk of coronary heart disease and stroke: a systematic review and meta-analysis of published and unpublished data for 603 838 individuals. Lancet 2015; online Aug 20.
Kivimäki M, Pentti J, Ferrie JE, et al. **Work stress and risk of death in adults** with and without cardiometabolic disease: a multicohort study. Lancet Diabetes Endocrinol 2018; published online May 31.
Kluzek S, Sanchez-Santos MT, Leyland KM, et al. **Painful knee** but not hand osteoarthritis is an independent predictor of mortality over 23 years follow-up of a population-based cohort of middle-aged women. Ann Rheum Dis. 2015 Nov 5.
Knight J, Schilling C, Barnett A, et al. Revisiting the "**Christmas Holiday Effect**" in the Southern Hemisphere. J Am Heart Assoc. 2016 Dec 22;5(12).
Kobylecki CJ, Afzal S, Smith GD, Nordestgaard BG. Genetically high plasma **vitamin C, intake of fruit and vegetables**, and risk of ischemic heart disease and all-cause mortality: a Mendelian randomization study. *Am J Clin Nutr* 2015; 101:1135-1143.
Kodama S, Saito K, Tanaka S, et al. **Cardiorespiratory fitness** as a quantitative predictor of all-cause mortality and cardiovascular events in healthy men and women: a meta-analysis. JAMA. 2009 May 20;301(19):2024-35. Better CRF was associated with lower risk of all-cause mortality and CHD/CVD. Participants with a MAC of 7.9 METs or more had substantially lower rates of all-cause mortality and CHD/CVD events compared with those with a MAC of less 7.9 METs.

Kolber MR, Scrimshaw C. **Family history** of cardiovascular disease. Can Fam Physician. 2014 Nov;60(11):1016.

Koller MT, Leening MJ, Wolbers M, et al. Development and validation of a **coronary risk prediction model** for older US And European persons in the cardiovascular health study and the Rotterdam study. Ann Intern Med. 2012 Sep 18;157(6):389-97.

Kontis V, Bennett JE, Mathers CD, Li G, Foreman K, Ezzati M. **Future life expectancy in 35 industrialised countries**: projections with a Bayesian model ensemble. Lancet 2017; online Feb 21.

Kontis V, Cobb LK, Mathers CD, et al. **Three Public Health Interventions** Could Save 94 Million Lives in 25 Years Global Impact Assessment Analysis. Circulation. 2019 Jun 10.

Kontis V, Mathers CD, Rehm J, et al. Contribution of **six risk factors to achieving the 25×25 non-communicable disease mortality** reduction target: a modelling study. Lancet 2014; online May 3.

Kontro TK, Sarna S, Kaprio J, et al. Mortality and health-related habits in 900 Finnish **former elite athletes** and their brothers. Br J Sports Med. 2018 Jan;52(2):89-95.

Koolhaas CM, Dhana K, Schoufour JD, et al. Impact of **physical activity** on the association of overweight and obesity with cardiovascular disease: The Rotterdam Study. Eur J Prev Cardiol. 2017 Jan 1:2047487317693952

Koolhaas CM, Dhana K, Schoufour JD, et al. **Physical activity and cause-specific mortality**: the Rotterdam Study. Int J Epidemiol. 2018 Oct 1;47(5):1705-1713.

Kopecky SL, Bauer DC, Gulati M, et al. Lack of **Evidence Linking Calcium With or Without Vitamin D Supplementation to Cardiovascular Disease** in Generally Healthy Adults: A Clinical Guideline From the National Osteoporosis Foundation and the American Society for Preventive Cardiology. Ann Intern Med. 2016 Oct 25.

Korownyk C, Burgess E, Taylor I. Does **sodium reduction affect mortality**? Can Fam Physician. 2013 Jun;59(6):640.

Kotchen TA, Cowley AW Jr, Frohlich ED. **Salt in health and disease**--a delicate balance. N Engl J Med. 2013 Mar 28;368(13):1229-37.

Kottke T, Wilkinson J, Baechler C, Danner C, Erickson K, O'Connor P, Sanford M, Straub R. **Healthy lifestyles**. Bloomington (MN): Institute for Clinical Systems Improvement (**ICSI**); 2016 Jan.

Kovesdy CP, Norris KC, Boulware LE, et al. Association of **Race** With Mortality and Cardiovascular Events ina Large Cohort of **US Veterans**. Circulation. 2015 Oct 20;132(16):1538-48.

Kovtun KA, Chen MH, Braccioforte MH, et al. Race and mortality risk after **radiation** therapy in men treated with or without androgen-suppression therapy for favorable-risk prostate cancer. Cancer. 2016 Aug 4.

Kramer CK, Zinman B, Gross JL, et al. **Coronary artery calcium score** prediction of all cause mortality and cardiovascular events in people with type 2 diabetes: systematic review and meta-analysis. BMJ. 2013 Mar 25;346:f1654.

Kraus WE, Bhapkar M, Huffman KM, et al. **2 years of calorie restriction and cardiometabolic risk** (CALERIE): exploratory outcomes of a multicentre, phase 2, randomised controlled trial. Lancet Diabetes Endocrinol. 2019 Jul 11.

Kraus WE, Bittner V, Appel L, et al; **American Heart Association** (**AHA**) Physical Activity Committee of the Council on Lifestyle and Metabolic Health, Council on Clinical Cardiology, Council on Hypertension, and Council on Cardiovascular and Stroke Nursing. The **national physical activity plan:** a call to action from the american heart association: a science advisory from the american heart association. Circulation. 2015 May 26;131(21):1932-40.

Kshirsagar AV, Bang H, Bomback AS, et al. A simple algorithm to **predict incident kidney disease**. Arch Intern Med. 2008 Dec 8;168(22):2466-73. In the simplified model, age, anemia, female sex, hypertension, diabetes mellitus, peripheral vascular disease, and history of congestive heart failure or cardiovascular disease were associated with the development of a GFR less than 60 mL/min/1.73 m(2).

Ku PW, Chen LJ, Fox KR, et al. **Leisure-Time, Domestic, and Work-Related Physical Activity** and Their Prospective Associations With All-Cause Mortality in Patients With Cardiovascular Disease. Am J Cardiol. 2018 Jan 15;121(2):177-181

Kubesch NJ, Therming Jørgensen J, Hoffmann B, et al. Effects of **Leisure-Time and Transport-Related Physical Activities** on the Risk of Incident and Recurrent **Myocardial Infarction** and Interaction With Traffic-Related Air Pollution: A Cohort Study. J Am Heart Assoc. 2018 Jul 18;7(15).

Kubota Y, Heiss G, MacLehose RF, et al. Association of **educational attainment** with lifetime risk of cardiovascular disease: the Atherosclerosis Risk in Communities study [online June 12, 2017].JAMA Intern Med. doi:10.1001/jamainternmed.2017.1877

Kuh D, Cooper R, Sattar N, et al. **Systemic Inflammation** and **Cardio-Renal Organ Damage Biomarkers** in Middle Age Are Associated With Physical Capability Up to 9 Years Later Findings From a British Birth Cohort Study. Circulation. 2019 Jan 22.

Kujala UM, Makinen VP, Heinonen I, et al. **Long-term leisure-time physical activity** and serum **metabolome**. Circulation. 2013;127:340–348.

Kuk JL, Rotondi M, Sui X, et al. Individuals with **obesity but no other metabolic risk factors** are not at significantly elevated **all-cause mortality** risk in men and women. Clin Obes. 2018 Jul 12.

Kuller LH, Lopez OL, Mackey RH, et al. **Subclinical Cardiovascular Disease** and Death, Dementia, and Coronary Heart Disease in Patients 80+ Years. J Am Coll Cardiol. 2016 Mar 8;67(9):1013-22.

Kullo IJ, Jouni H, Austin EE, Brown et al. Incorporating a **Genetic Risk Score Into Coronary Heart Disease Risk Estimates**: Effect on Low-Density Lipoprotein Cholesterol Levels (the **MI-GENES** Clinical Trial). Circulation. 2016 Mar 22;133(12):1181-8.

Kuo H-K, Fujise K. **Human papillomavirus** and cardiovascular disease among US women in the National Health and Nutrition Examination Survey, 2003 to 2006. J Am Coll Cardiol 2011; 58: 2001-2006.

Kure CE, Chan YK, Ski CF, et al. **Gender-specific secondary prevention**? Differential psychosocial risk factors for major cardiovascular events. *OpenHeart* 2016.

Kurotani K, Akter S, Kashino I, et al; Japan Public Health Center based Prospective Study Group. **Quality of diet and mortality** among Japanese men and women: Japan Public Health Center based prospective study. BMJ. 2016 Mar 22;352:i1209.

Kurth T, Schürks M, Logroscino G, Gaziano JM, et al. **Migraine**, vascular risk, and cardiovascular events in women: prospective cohort study. BMJ. 2008 Aug 7;337:a636. doi: 10.1136/bmj.a636. The association between migraine with aura and cardiovascular disease varies by vascular risk status. Information on history of migraine and vascular risk status might help to identify women at increased risk for specific future cardiovascular disease events.

Kurth T, de Jong PE, Cook NR, Buring JE, Ridker PM. **Kidney function** and risk of cardiovascular disease and mortality in women: a prospective cohort study. BMJ. 2009 Jun 29;338:b2392. doi: 10.1136/bmj.b2392.

Kvaavik Elisabeth; Batty G. David; Ursin Giske; et al. Influence of Individual and Combined **Health Behaviors** on Total and Cause-Specific Mortality in Men and Women: The United Kingdom Health and Lifestyle Survey. Arch Intern Med. 2010;170(8):711-718.

Kypridemos C, Allen K, Hickey GL, et al. **Cardiovascular screening** to reduce the burden from cardiovascular disease: microsimulation study to quantify policy options. BMJ. 2016 Jun 8;353:i2793.

Kyu HH, et al. **Physical activity** and risk of breast cancer, colon cancer, diabetes, ischemic heart disease, and ischemic stroke events: systematic review and dose-response meta-analysis for the Global Burden of Disease Study 2013. BMJ. 2016 Aug9;354

Kwak SM, Myung SK, Lee YJ, et al. Efficacy of **Omega-3 Fatty Acid Supplements** (Eicosapentaenoic Acid and Docosahexaenoic Acid) in the Secondary Prevention of Cardiovascular Disease: A Meta-analysis of Randomized, Double-blind, Placebo-Controlled Trials. Arch Intern Med. 2012 Apr 9.

Kwok CS, Boekholdt SM, Lentjes MA, et al. **Habitual chocolate consumption** and risk of cardiovascular disease among healthy men and women. Heart. 2015 Jun 15.

Kytömaa S, Hegde S, Claggett B, et al**. Association of Influenza-like Illness Activity** With Hospitalizations for Heart Failure: The Atherosclerosis Risk in Communities Study. JAMA Cardiol. 2019 Mar 27

La Gerche A, Heidbuchel H. Can **intensive exercise** harm the heart? You can get too much of a good thing. Circulation. 2014 Sep 16;130(12):992-1002.

Labarthe DR, Dunbar SB. **Global cardiovascular health promotion** and disease prevention: 2011 and beyond. Circulation. 2012 May 29;125(21):2667-76.

Lachman S, Boekholdt SM, Luben RN, et al. Impact of **physical activity** on the risk of cardiovascular disease in middle-aged and older adults: EPIC Norfolk prospective population study. Eur J Prev Cardiol. 2017 Jan 1:2047487317737628.

Laclaustra M, Casasnovas JA, Fernandez-Ortiz A, et al. **Femoral and carotid subclinical atherosclerosis** association with risk factors and **coronary calcium**. *J Am Coll Cardiol* 2016; 67:1263-1274.

LaCroix AZ, Bellettiere J, Rillamas-Sun E, et al; Women's Health Initiative (WHI). **Association of Light Physical Activity** Measured by Accelerometry and Incidence of Coronary Heart Disease and Cardiovascular Disease in Older Women. JAMA Netw Open. 2019 Mar 1;2(3):e190419.

Ladabaum U, Mannalithara A, Myer PA, et al. **Obesity, Abdominal Obesity, Physical Activity, and Caloric Intake** in U.S. Adults: 1988-2010. Am J Med. 2014 Mar 10.

Laddu DR, et al. 25**-Year Physical Activity Trajectories** & Development of Subclinical Coronary Artery Disease as Measured by Coronary Artery Calcium: The Coronary Artery Risk Development in Young Adults (**CARDIA**) Study. Mayo Clin Proc. 2017 Oct 13.

Lahtinen M, Toukola T, Junttila MJ, et al. Effect of Changes in **Physical Activity** on Risk for Cardiac Death in Patients With Coronary Artery Disease. Am J Cardiol. 2018 Jan 15;121(2):143-148.

Lai HTM, de Oliveira Otto MC, Lemaitre RN, et al. Serial circulating **omega 3 polyunsaturated fatty acids** and healthy ageing among older adults in the Cardiovascular Health Study: prospective cohort study. BMJ2018;363:k4263.

Laitinen TT, Pahkala K, Magnussen CG, et al. **Ideal cardiovascular health in childhood and cardiometabolic outcomes in adulthood**: the Cardiovascular Risk in Young Finns Study. Circulation. 2012;125: 1971–1978.

Lamas GA, Goertz C, Boineau R, et al. Effect of **disodium EDTA chelation** regimen on cardiovascular events in patients with previous myocardial infarction. (**TACT**) JAMA 2013; 309: 1241-1250.

LaMonte MJ, Genco RJ, Hovey KM, et al. History of **Periodontitis** Diagnosis and Edentulism as Predictors of Cardiovascular Disease, Stroke, and Mortality in Postmenopausal Women. J Am Heart Assoc. 2017 Mar 29;6(4).

LaMonte MJ, Buchner DM, Rillamas-Sun E, et al.**Accelerometer-Measured Physical Activity** and Mortality in Women Aged 63 to 99. J Am Geriatr Soc. 2017 Nov 16.

Lanier JB, Bury DC, Richardson SW. **Diet and Physical Activity** for Cardiovascular Disease Prevention. Am Fam Physician. 2016;93(11):919-924.

Larsson SC, Virtamo J, Wolk A. **Chocolate consumption** and risk of stroke: A prospective cohort of men and meta-analysis. Neurology. 2012 Aug 29.

Larsson SC, Burgess S, Michaëlsson K. Association of Genetic Variants Related to **Serum Calcium Levels** With Coronary Artery Disease and Myocardial Infarction. JAMA. 2017 Jul 25;318(4):371-380.

Larsson SC, Drca N, Björck M, et al. **Nut consumption** and incidence of seven cardiovascular diseases. Heart. 2018 Apr 16.

Laukkanen T, Khan H, Zaccardi F, Laukkanen JA. Association between **sauna bathing** and fatal cardiovascular and all-cause mortality events [online February 23, 2015]. JAMA Intern Med. doi:10.1001/jamainternmed.2014.8187.

Laukkanen JA, Laukkanen T, Khan H, et al. Combined Effect of **Sauna Bathing and Cardiorespiratory Fitness on the Risk of Sudden Cardiac Deaths** in Caucasian Men: A Long-term Prospective Cohort Study. Prog Cardiovasc Dis. 2018 Mar 16.

Laukkanen JA, Laukkanen T, Kunutsor SK. **Cardiovascular and Other Health Benefits of Sauna Bathing**: A Review of the Evidence. Mayo Clin Proc. 2018 Aug;93(8):1111-1121.

Laureano-Phillips J, Robinson RD, Aryal S, et al. **HEART Score Risk Stratification** of Low-Risk Chest Pain Patients in the Emergency Department: A Systematic Review and Meta-Analysis. Ann Emerg Med. 2019 Feb 1.

Laverty AA, Kypridemos C, Seferidi P, et al. **Quantifying the impact of the Public Health responsibility deal** on salt intake, cardiovascular disease and gastric cancer burdens: interrupted time series and microsimulation study. J Epidemiol Comm Health 2019. 10.1136/jech2018-211749
Lavie CJ, Milani RV, Mehra MR, et al. **Omega-3 polyunsaturated fatty acids** and cardiovascular disease. J Am Coll Cardiol 2009; 54: 585-594.
Lawlor ER, Bradley DT, Cupples ME, Tully MA. The effect **of community-based interventions for cardiovascular disease secondary prevention on behavioural risk factors**. Prev Med. 2018 Sep;114:24-38.

Lawman HG, Troiano RP, Perna FM, et al. Associations of Relative **Handgrip Strength** and Cardiovascular Disease Biomarkers in U.S. Adults, 2011-2012. Am J Prev Med. 2016 Jun;50(6):677-83.
Lear SA, Hu W, Rangarajan S, et al. The effect of **physical activity on mortality and cardiovascular disease** in 130 000 people from 17 highincome, middle-income, and low-income countries: the **PURE** study. Lancet 2017; online Sept 21.
Lebwohl B, Cao Y, Zong G, et al. Long term **gluten consumption** in adults without celiac disease and risk of coronary heart disease: prospective cohort study. BMJ. 2017 May 2;357:j1892.
Lee Chong-Do; Sui Xuemei; Blair Steven N. Combined Effects of **Cardiorespiratory Fitness, Not Smoking, and Normal Waist** Girth on Morbidity and Mortality in Men. Arch Intern Med. 2009;169(22):2096-2101.
Lee DC, Sui X, Artero EG, et al. **Long-term effects of changes in cardiorespiratory fitness** and body mass index on all-cause and cardiovascular disease mortality in men. Circulation 2011
Lee DC et al. Long-term effects of changes in **cardiorespiratory fitness** and **body mass index** on all-cause and cardiovascular disease mortality in men: the aerobics center longitudinal study. Circulation. 2011 Dec 6;124(23):2483-90.
Lee DC, Sui X, Church TS, et al. Changes in **fitness and fatness** on the development of cardiovascular disease risk factors. J Am Coll Cardiol 2012; 59:665-672.
Lee DC, Pate RR, Lavie JR, et al. **Leisure-time running** reduces all-cause and cardiovascular mortality risk. *J Am Coll Cardiol* 2014; DOI: 10.1016./j.jacc.2014.04.058.
Lee DH, Keum N, Hu FB, et al. Predicted **lean body mass, fat mass, and all cause and cause specific mortality in men**: prospective US cohort study. BMJ. 2018 Jul 3;362:k2575.
Lee IM, Shiroma EJ, Lobela F, et al. Effect of **physical inactivity** on major non-communicable diseases worldwide: An analysis of burden of disease and life expectancy. Lancet 2012.
Lee IM, Shiroma EJ, Evenson KR, et al.**Accelerometer-Measured Physical Activity** and Sedentary Behavior in Relation to All-Cause Mortality: The Women's Health Study. Circulation. 2017 Nov 6.
Lee IM, Shiroma EJ, Kamada M, et al. **Association of Step Volume and Intensity With All-Cause Mortality** in Older Women. JAMA Intern Med. 2019 May 29.
Lee J, Pedley A, Hoffmann U, et al. Association of changes in **Abdominal Fat Quantity and Quality** With Incident Cardiovascular Disease Risk Factors. JACC. 2016 Oct 4;68(11):1509-21.
Lee MP, Desai RJ, Jin Y, et al. Association of **Ustekinumab vs TNF Inhibitor Therapy** With Risk of Atrial Fibrillation and Cardiovascular Events in Patients With Psoriasis or Psoriatic Arthritis. JAMA Dermatol. 2019 Mar 27.
Lee Meng, Saver Jeffrey L, Chang Kuo-Hsuan, et al. **Low glomerular filtration** rate and risk of stroke: meta-analysis. BMJ 341:doi:10.1136/bmj.c4249 (Published 30 September 2010). Leunissen RW, Kerkhof GF, Stijnen T, et al. Timing and tempo of **first-year rapid growth** in relation to cardiovascular and metabolic risk profile in early adulthood. JAMA. 2009 Jun 3;301(21):2234-42. Rapid weight gain in the first 3 months of life is associated with several determinants of cardiovascular disease and type 2 diabetes in early adulthood.
Lee Y, Berryman CE, West SG, et al. Effects of **Dark Chocolate and Almonds** on Cardiovascular Risk Factors in Overweight and Obese Individuals: A Randomized Controlled-Feeding Trial. J Am Heart Assoc. 2017 Nov 29;6(12).
Leening MJ, Ferket BS, Steyerberg EW, et al. **Sex differences in lifetime risk** and first manifestation of cardiovascular disease: prospective population based cohort study. BMJ. 2014 Nov 17;349:g5992.
LeFevre ML. **Behavioral Counseling** to Promote a Healthful **Diet and Physical Activity** for Cardiovascular Disease Prevention in Adults With Cardiovascular Risk Factors: U.S. Preventive Services Task Force Recommendation Statement. Ann Intern Med. 2014 Aug 26.
Legge A, Hanly JG. Managing **premature atherosclerosis in patients with chronic inflammatory diseases**. CMAJ. 2018 Apr 9;190(14):E430-E439.
Lehmann N, Erbel R, Mahabadi AA, et al. Value of **Progression of Coronary Artery Calcification** for Risk Prediction of Coronary and Cardiovascular Events: Result of the HNR Study (Heinz Nixdorf Recall). Circulation. 2018 Feb 13;137(7):665-679.
Lehmann N, et al; on behalf Heinz Nixdorf Recall Study Investigators. Value of progression of **coronary artery calcification** for risk prediction of coronary and cardiovascular events: result of the HNR study (Heinz Nixdorf Recall). Circulation. 2018;137:665–679.
Leong DP, Teo KT, Rangarajan S, et al. **Prognostic value of grip strength**: Findings from the Prospective Urban Rural Epidemiology (PURE) study.*Lancet* 2015.
Leppert MH, Poisson SN, Sillau SH, et al. Is Prevalence of **Atherosclerotic Risk Factors Increasing Among Young Adults**? It Depends on How You Ask. J Am Heart Assoc. 2019 Mar 19;8(6):e010883.
Leslie LK, Cohen JT, Newburger JW, et al. Costs and benefits of targeted **screening for causes of sudden cardiac death in children and adolescents**. Circulation. 2012;125:2621–2629.
Leung AA, McAlister FA, Rogers SO Jr, Pazo V, Wright A, Bates DW. **Preoperative hyponatremia** and perioperative complications [published online September 10, 2012]. Arch Intern Med. doi:10.1001/archinternmed.2012.3992.
Levine BD. Can **intensive exercise** harm the heart? The benefits of competitive endurance training for cardiovascular structure and function. Circulation. 2014 Sep 16;130(12):987-91.
Levine Glenn N., D'Amico Anthony V., Berger Peter, et al. and on behalf of the American Heart Association Council on Clinical Cardiology and Council on Epidemiology and Prevention, the American Cancer Society, and the American Urological Association. **Androgen-Deprivation Therapy in Prostate Cancer and Cardiovascular Risk**. A Science Advisory From the American Heart Association, American Cancer Society, and American Urological Association. Circulation published February 1, 2010, doi:10.1161/CIRCULATIONAHA.109.192695
Levine GN, Allen K, Braun LT, et al. **Pet ownership** and cardiovascular risk: a scientific statement from the American Heart Association. Circulation 2013;
Levine GN, Lange RA, Bairey-Merz CN, et al. **Meditation** and Cardiovascular Risk Reduction: A Scientific Statement From the American Heart Association. J Am Heart Assoc. 2017 Sep 28;6(10).
Lewis JR, Prince RL, Zhu K, Devine A, Thompson PL, Hodgson JM. Habitual **chocolate** intake and vascular disease: a prospective study of clinical outcomes in older women. Arch Intern Med. 2010 Nov 8;170(20):1857-8.
Lewis G. **Psychological distress** and death from cardiovascular disease. BMJ. 2012 Jul 31;345:e5177.
Li Chaoyang; Ford Earl S.; Zhao Guixiang; et al. **Serum {alpha}-Carotene** Concentrations and Risk of Death Among US Adults: The Third National Health and Nutrition Examination Survey Follow-up Study. *Arch Intern Med*. 2010;0(2010):archinternmed.2010.440. (**Higher fruit & vegetable consumption**)
Li S, Flint A, Pai JK, et al. **Dietary fiber** intake and mortality among survivors of myocardial infarction: prospective cohort study. BMJ. 2014 Apr 29;348:g2659.
Li S, Stampfer MJ, Williams DR, VanderWeele TJ. Association of **religious service attendance** with mortality among women [online May 15, 2016].JAMA Intern Med. doi:10.1001 /jamainternmed.2016.1615.
Li S, Stampfer MJ, Williams DR, et al. Association of **Religious Service Attendance** With Mortality Among Women. JAMA Intern Med. 2016 May 16.
Li W, Ruan W, Lu Z, Wang D. **Parity and risk of maternal cardiovascular disease**: A dose-response meta-analysis of cohort studies. Eur J Prev Cardiol. 2018 Dec 19:2047487318818265.
Li Y, Hruby A, Bernstein AM, et al. **Saturated Fats** Compared With Unsaturated Fats and Sources of Carbohydrates in Relation to Risk of Coronary Heart Disease: A Prospective Cohort Study. J Am Coll Cardiol. 2015 Oct 6;66(14):1538-48.
Li Y, Pan A, Wang DD, et al. Impact of **Healthy Lifestyle Factors on Life Expectancies** in the US Population. Circulation. 2018 Apr 30.
Lian XQ, Zhao D, Zhu M, et al. The influence of **regular walking** at different times of day on blood lipids and inflammatory markers in sedentary patients with coronary artery disease. Prev Med. 2014 Jan;58:64-9.
LIFE Study Investigators, Pahor M, Blair SN, Espeland M, et al. Effects of a **physical activity** intervention on measures of physical performance: Results of the lifestyle interventions and independence for Elders Pilot (**LIFE-P**) study. J Gerontol A Biol Sci Med Sci. 2006 Nov;61(11):1157-65.
Lim LS, Haq N, Mahmood S, Hoeksema L, **ACPM** Prevention Practice Committee, American College of Preventive Medicine. **Atherosclerotic cardiovascular disease screening in adults**: American College of Preventive Medicine position statement on preventive practice. Am J Prev Med 2011 Mar;40(3):381.e1-10.
Lima BB, Hammadah M, Kim JH, et al. Association of **Transient Endothelial Dysfunction Induced by Mental Stress** With Major Adverse Cardiovascular Events in Men and Women With Coronary Artery Disease. JAMA Cardiol. 2019 Sep 11.
Lin JS, Evans CV, Johnson E, Redmond N, Coppola EL, Smith N. **Nontraditional risk factors** in cardiovascular disease risk assessment: updated evidence report and systematic review for the US Preventive Services Task Force USPSTF [online July 10, 2018]. JAMA. doi:10.1001/jama.2018.4242
Lin JS, O'Connor E, Whitlock EP, Beil TL. **Behavioral counseling to promote physical activity** and a healthful diet to prevent cardiovascular disease in adults: a systematic review for the u.s. Preventive services task force. Ann Intern Med. 2010 Dec 7;153(11):736-50.
Lindberg S, Mogelvang R, Pedersen SH, et al. Relation of Serum **Adiponectin** Levels to Number of Traditional Atherosclerotic Risk Factors and All-Cause Mortality and Major Adverse Cardiovascular Events (from the Copenhagen City Heart Study). Am J Cardiol. 2013 Jan 31
Lindekleiv H, Løchen ML, Mathiesen EB, et al. **Echocardiographic Screening** of the General Population and Long-term Survival: A Randomized Clinical Study. JAMA Intern Med. 2013 Jul 22.
Lindhardsen J, Ahlehoff O, Gislason GH, et al. The **risk of myocardial infarction in rheumatoid arthritis** and diabetes mellitus: a Danish nationwide cohort study. Ann Rheum Dis. 2011 Mar 9.
Lindholm D;Lindback J;Armstrong PW;Budaj A;Cannon . **Biomarker-Based Risk Model** to Predict Cardiovascular Mortality in Patients With Stable Coronary Disease. J Am Coll Cardiol. 2017 Aug 15;70(7):813-826.
Ling CH, Taekema D, de Craen AJ, Gussekloo J, Westendorp RG, Maier AB. **Handgrip strength** and mortality in the oldest old population: the Leiden 85-plus study. CMAJ. 2010 Feb 8. [Epub ahead of print]

Link MS, Estes NA 3rd. Sudden cardiac death in the **athlete**: bridging the gaps between evidence, policy, and practice. Circulation. 2012 May 22;125(20):2511-6.

Lipshultz SE, Adams MJ, Colan SD, et al. Long-term Cardiovascular Toxicity in **Children, Adolescents, and Young Adults Who Receive Cancer Therapy**: Pathophysiology, Course, Monitoring, Management, Prevention, and Research Directions: A Scientific Statement From the American Heart Association. Circulation. 2013 Sep 30

Liu B, Luo Z, Pinto JM, et al. Relationship between **poor olfaction and mortality** among community-dwelling older adults. A cohort study. Ann Intern Med. 2019. [Epub ahead of print]. doi:10.7326/M18-0775

Liu G, Guasch-Ferre M, Hu Y, et al. **Nut Consumption** in Relation to Cardiovascular Disease Incidence and Mortality among Patients with Diabetes Mellitus. Circ Res. 2019 Feb 19.

Liu H, Tian Y, Xiang X, et al. **Air Pollution** and Hospitalization for **Acute Myocardial Infarction** in China. Am J Cardio. 2017.

Liu K, Daviglus ML, Loria CM, et al. **Healthy Lifestyle Through Young Adulthood** and the Presence of Low Cardiovascular Disease Risk Profile in Middle Age: The Coronary Artery Risk Development in (Young) Adults (CARDIA) Study. Circulation. 2012 Feb 28;125(8):996-1004.

Liu J, Sui X, Lavie CJ, et al. Association of **coffee consumption with all-cause** and cardiovascular disease mortality. Mayo Clin Proc 2013.

Liu S, Li Y, Zeng X, et al. **Burden of Cardiovascular Diseases in China, 1990-2016**: Findings From the 2016 Global Burden of Disease Study. JAMA Cardiol. 2019 Mar 13.

Lloyd-Jones D, Adams R, Carnethon M, et al. **Heart disease and stroke statistics—2009 update**. A report from the American Heart Association Statistics Committee and Stroke Statistics Subcommittee. Circulation 2008; DOI: 10.1161/CIRCULATIONAHA.108.191261. Available at: http://circ.ahajournals.org.

Lloyd-Jones DM, Huffman MD, Karmali KN, et al. **Estimating Longitudinal Risks and Benefits** From Cardiovascular Preventive Therapies Among Medicare Patients: The Million Hearts Longitudinal ASCVD Risk Assessment Tool: A Special Report From the American Heart Association and American College of Cardiology. Circulation. 2016 Nov 4.

Lobelo F, Rohm Young D, Sallis R, et al. Routine Assessment and **Promotion of Physical Activity in Healthcare Settings**: A Scientific Statement From the **American Heart Association (AHA).** Circulation. 2018 Apr 4.

Lockhart P B, Bolger AF, Papapanou PN, et al **Periodontal disease** and atherosclerotic vascular disease: Does the evidence support an independent association? A scientific statement from the American Heart Association. Circulation 2012

Loftfield E, Cornelis MC, Caporaso N, et al. **Association of Coffee Drinking With Mortality** by Genetic Variation in Caffeine Metabolism: Findings From the UK Biobank. JAMA Intern Med. 2018 Jul 2.

Longmuir PE, Brothers JA, de Ferranti SD, et al; American Heart Association Atherosclerosis, Hypertension and Obesity in Youth Committee of the Council on Cardiovascular Disease in the Young. **Promotion of physical activity** for children and adults with congenital heart disease: a scientific statement from the american heart association. Circulation. 2013 May 28;127(21):2147-59.

Loo CK, Greiver M, Aliarzadeh B, et al. Association between **neighbourhood walkability** and metabolic risk factors influenced by physical activity: a cross-sectional study of adults in Toronto, Canada. BMJ Open. 2017 Apr 8;7(4):e013889.

Look AHEAD Research Group. Long-term Effects of a **Lifestyle** Intervention on Weight and Cardiovascular Risk Factors in Individuals With Type 2 Diabetes Mellitus: Four-Year Results of the Look AHEAD Trial. Arch Intern Med. 2010;170(17):1566-1575.

Lorenz MW, Polak JF, Kavousi M, et al, on behalf of the **PROG-IMT** Study Group. **Carotid intima-media thickness** progression to predict cardiovascular events in the general population (the PROG-IMT collaborative project): a meta-analysis of individual participant data. Lancet 2012

Loria CM, Mussolino ME, Cogswell ME, et al. Usual **sodium intakes** (**salt**) compared with current dietary guidelines—United States, 2005-2008. MMWR Morb Mortal Wkly Rep 2011; 60:1413-1417.

Lozano R, Naghavi M, Lim SS, et al. **Global and regional mortality** from 235 causes of death for 20 age groups in 1990 and 2010: A systematic analysis for the **Global Burden of Disease Study** 2010. Lancet 2012; 380:2095-128.

Lp-PLA(2) Studies Collaboration, Thompson A, Gao P, Orfei L et al. **Lipoprotein-associated phospholipase A(2)** and risk of coronary disease, stroke, and mortality: collaborative analysis of 32 prospective studies. Lancet. 2010 May 1;375(9725):1536-44.

Lu J, Lu Y, Yang H, et al. **Characteristics of high cardiovascular risk** in 1.7 million Chinese adults. Ann Intern Med. 2019. [Epub ahead of print]. doi:10.7326 /M18-1932

Lu Y, Ezzati M, Rimm EB, Hajifathalian et al. Sick Populations and Sick Subpopulations: **Reducing Disparities** in Cardiovascular Disease Between Blacks and Whites in the United States. Circulation. 2016 Aug 9;134(6):472-85.

Ludvigsson JF, James S, Askling J, et al. Nationwide cohort study of risk of ischemic heart disease in patients with **celiac disease**. Circulation. 2011 Feb 8;123(5):483-90.

Ludwig DS, Willett WC, Volek JS, Neuhouser ML. **Dietary fat**: From foe to friend? Science. 2018 Nov 16;362(6416):764-770

Lui GK, Rogers IS, Ding VY et al. **Risk Estimates for Atherosclerotic Cardiovascular Disease** in Adults with Congenital Heart Disease. Am J Cardio.2017;119:112-118.

Luu HN, Blot WJ, Xiang YB, et al. Prospective Evaluation of the Association of **Nut/Peanut Consumption** With Total and Cause-Specific Mortality. JAMA Intern Med. 2015 Mar 2.

Lv J, Qi L, Yu C, et al; China Kadoorie Biobank collaborative group. **Consumption of spicy foods** and total and cause specific mortality: population based cohort study. BMJ. 2015 Aug 4;351:h3942.

Lyall DM, Celis-Morales C, Ward J, et al. Association of **body mass index** with cardiometabolic disease in the **UK Biobank**: a mendelian randomization study [online July 5, 2017].JAMA Cardiol. doi:10.1001 /jamacardio.2016.5804

Ma J, Ward EM, Siegel RL, et al. **Temporal Trends in Mortality** in the United States, 1969-2013. JAMA. 2015 Oct 27;314(16):1731-1739.

Ma Y, Olendzki BC, Wang J, et al. **Single-component versus multicomponent dietary goals for the metabolic syndrome**: a randomized trial. Ann Intern Med. 2015 Feb 17;162(4):248-57.

MacGregor GA, He FJ, Pombo-Rodrigues S. **Food and the responsibility deal**: how the salt reduction strategy was derailed. BMJ. 2015 Apr 28;350:h1936.

Macknin M, Kong T, Weier A, et al. **Plant-Based, No-Added-Fat or American Heart Association Diets**: Impact on Cardiovascular Risk in Obese Children with Hypercholesterolemia and Their Parents. J Pediatr. 2015 Apr;166(4):953-959.e3.

Maclagan LC, Park J, Sanmartin C, et al. The **CANHEART health index**: a tool for monitoring the cardiovascular health of the Canadian population. CMAJ. 2014 Feb 18;186(3):180-7.

MacLeod SM, Cairns JA. **Controversial sodium guidelines**: Scientific solution or perpetual debate? CMAJ. 2015 Feb 3;187(2):95-6.

Magnani JW, Mujahid MS, Aronow HD, et al. **Health Literacy** and Cardiovascular Disease: Fundamental Relevance to Primary and Secondary Prevention: A Scientific Statement From the American Heart Association. Circulation. 2018 Jul 10;138(2):e48-e74.

Magnus P, Bakke E, Hoff DA, et al. Controlling for high-density lipoprotein cholesterol does not affect the magnitude of the relationship between **alcohol** and coronary heart disease. Circulation. 2011;124:2296 –2302.

Mahase E. **Vegetarian and pescatarian diets** are linked to lower risk of ischaemic heart disease, study finds. BMJ. 2019 Sep 4;366:l5397.

Mahmoodi BK, Matsushita K, et al, for the Chronic Kidney Disease Prognosis Consortium. Associations of **kidney disease** measures with mortality and end-stage renal disease in individuals with and without hypertension: a meta-analysis. Lancet 2012.

Mahmood SS, Levy D, Vasan RS, et al. The **Framingham Heart Study** and the epidemiology of cardiovascular disease: a historical perspective. Lancet. 2013 Sep 27.

Mahle WT, Sable CA, Matherne PG, et al; on behalf of the American Heart Association Congenital Heart Defects Committee of the Council on Cardiovascular Disease in the Young. Key Concepts in the Evaluation of **Screening Approaches** for Heart Disease in **Children and Adolescents**: A Science Advisory From the American Heart Association (AHA). Circulation. 2012 Jun 5;125(22):2796-2801.

Majed B, Tafflet M, Kee F, et al. External validation of the **2008 Framingham cardiovascular risk equation** for CHD and stroke events in a European population of middle-aged men. The PRIME study. Prev Med. 2013 Jul;57(1):49-54.

Malhotra A, Redberg RF, Meier P. **Saturated fat does not clog the arteries**: coronary heart disease is a chronic inflammatory condition, the risk of which can be effectively reduced from healthy lifestyle interventions. Br J Sports Med. 2017 Apr 25.

Malik S, Zhao Y, Budoff M, et al. **Coronary Artery Calcium Score** for Long-term Risk Classification in Individuals With Type 2 Diabetes and Metabolic Syndrome From the Multi-Ethnic Study of Atherosclerosis. JAMA Cardiol. 2017 Nov 8.

Malik VS, Hu FB. **Fructose** and Cardiometabolic Health: What the Evidence From Sugar-Sweetened Beverages Tells Us. J Am Coll Cardiol. 2015 Oct 6;66(14):1615-24.

Malik VS, Li Y, Pan A, et al. Long-Term Consumption of Sugar-Sweetened and Artificially **Sweetened Beverages and Risk of Mortality** in US Adults. Circulation. 2019 Mar 18.

Malinowski B, Zalewska K, Węsierska A, et al. **Intermittent Fasting** in Cardiovascular Disorders-An Overview. Nutrients. 2019 Mar 20;11(3).

Mancia G, Schumacher H, Redon J, Verdecchia P, et al. **Blood pressure targets** recommended by guidelines and incidence of cardiovascular and renal events in the Ongoing Telmisartan Alone and in Combination With Ramipril Global Endpoint Trial (**ONTARGET**). Circulation. 2011;124:1727–1736.

Mandsager K, Harb S, Cremer P, et al. **Association of Cardiorespiratory Fitness With Long-term Mortality Among Adults Undergoing Exercise** Treadmill Testing. JAMA Netw Open. 2018;1(6):e183605.

Manenschijn L, Schaap L, van Schoor NM, et al. High Long-Term **Cortisol Levels, Measured in Scalp Hair**, Are Associated With a History of Cardiovascular Disease. J Clin Endocrinol Metab. 2013 Apr 17.

Manson JE, Cook NR, Lee I-M, et al. **Vitamin D supplements** and prevention of cancer and cardiovascular disease. (VITAL) N Engl J Med. DOI: 10.1056/NEJMoa1809944.

Manson JE, Cook NR, Lee I-M, et al. **Marine n−3 fatty acids** and prevention of cardiovascular disease and cancer. N Engl J Med. (VITAL) DOI: 10.1056/NEJMoa1811403.

Mansoor H, Elgendy IY, et al. **Duration of Reproductive Years** and the Risk of Cardiovascular and Cerebrovascular Events in Older Women: Insights from the National Health and Nutrition Examination Survey. J Womens Health (Larchmt). 2017 May 19.

Manuel DG, Tuna M, Hennessy D, et al; Simulation Technology for Applied Research Team and the Canadian Cardiovascular Outcome Research Team. **Projections of preventable risks for cardiovascular disease in Canada** to 2021: a microsimulation modeling approach. CMAJ Open. 2014 May 20;2(2):E94-E101.

Manuel DG, Perez R, Sanmartin C, et al. **Measuring Burden of Unhealthy Behaviours** Using a Multivariable Predictive Approach: Life Expectancy Lost in Canada Attributable to Smoking, Alcohol, Physical Inactivity, and Diet. PLoS Med. 2016 Aug 16;13(8)

Manuel DG, Tuna M, Bennett C, et al. Development and validation of a **cardiovascular disease risk-prediction model using population health surveys**: the Cardiovascular Disease Population Risk Tool (CVDPoRT). CMAJ. 2018 Jul 23;190(29):E871-E882.

Marijon E, Tafflet, Antero-Jacquemin J, et al. Mortality of French participants in the **Tour de France** (1947-2012). Eur Heart J 2013.

Marijon E, Uy-Evanado A, Reinier K, et al. **Sudden Cardiac Arrest During Sports** Activity in Middle Age. Circulation. 2015 Apr 6.

Maron BJ, Thompson PD, Ackerman MJ, et al. American Heart Association Council on Nutrition, Physical Activity, and Metabolism. Recommendations and considerations related to **preparticipation screening** for cardiovascular abnormalities in competitive athletes: 2007 update: a scientific statement from the AHA Council on Nutrition, Physical Activity, and Metabolism: endorsed by the American College of Cardiology Foundation. Circulation. 2007 Mar 27;115(12):1643-455. Epub 2007 Mar 12.

Maron BJ, Friedman RA, Kligfield P, et al; American Heart Association Council on Clinical Cardiology; Advocacy Coordinating Committee; Council on Cardiovascular Disease in the Young; Council on Cardiovascular Surgery and Anesthesia; Council on Epidemiology and Prevention; Council on Functional Genomics and Translational Biology; Council on Quality of Care and Outcomes Research, and American College of Cardiology. Assessment of the **12-Lead Electrocardiogram as a Screening Test for Detection of Cardiovascular Disease in Healthy General Populations of Young People** (12-25 Years of Age): A Scientific Statement From the American Heart Association and the American College of Cardiology. J Am Coll Cardiol. 2014 Sep 5.

Matsushita K, Sang Y, Ballew SH, et al. **Subclinical Atherosclerosis Measures** for Cardiovascular Prediction in **CKD**. J Am Soc Nephrol. 2014 Aug 21.

Matsushita K, Coresh J, et al; CKD Prognosis Consortium. **Estimated glomerular filtration rate and albuminuria** for prediction of cardiovascular outcomes: a collaborative meta-analysis of individual participant data. Lancet Diabetes Endocrinol. 2015 May 28.

May AL, Kuklina EV, Yoon PW. Prevalence of **Cardiovascular Disease Risk Factors Among US Adolescents**, 1999-2008. Pediatrics. 2012 May 21.

May HT, Horne BD, Knight S, et al. The association of **depression** at any time to the risk of death following **coronary artery disease diagnosis**. European Heart J. 2017;0:1-7

May RW, Sanchez-Gonzalez MA, Hawkins KA, et al. Effect of **Anger and Trait Forgiveness** on Cardiovascular Risk in Young Adult Females. Am J Cardiol. 2014 Apr 18.

Mazidi M, Mikhailidis DP, Sattar N, et al; Lipid and Blood Pressure Meta-analysis Collaboration (LBPMC) Group. Consumption of **dairy product and its association with total and cause specific mortality** – A population-based cohort study and meta-analysis. Clin Nutr. 2018 Dec 18.

Mazidi M, Katsiki N, Mikhailidis DP, et al. **Lower carbohydrate diets and all-cause and cause-specific mortality**: a population-based cohort study and pooling of prospective studies. Eur Heart J. 2019 Apr 19.

McClelland RL, Jorgensen NW, Budoff M, et al. 10-year coronary heart disease risk prediction using **coronary artery calcium and traditional risk factors**. J Am Coll Cardiol 2015; 66: 1643-1653.

McCullough Peter A.; Chinnaiyan Kavitha M. Annual Progression of Coronary Calcification (**CAC**) in Trials of Preventive Therapies: A Systematic Review. Arch Intern Med. 2009;169(22):2064-2070.

McCullough ML, Peterson JJ , Patel R, et al. **Flavonoid** (chocolate, wine) intake and cardiovascular disease mortality in a prospective cohort of US adults. Am J Clin Nutr 2012; 95:454-464.

McEvoy John W.; Blaha Michael J.; Nasir Khurram; et al. Impact of **Coronary Computed Tomographic Angiography** Results on Patient and Physician Behavior in a Low-Risk Population. Arch Intern Med. 2011;0(2011):archinternmed.2011.204.

McEvoy JW, Blaha M, Rivera JJ, et al. Mortality rates in smokers and nonsmokers in the presence or absence of **coronary artery calcification** (CAC). JACC Cardiovasc Imaging 2012; 5:1037-1045.

McGeechan K, Liew G, Macaskill P, et al. Meta-analysis: **retinal vessel caliber** and risk for coronary heart disease. Ann Intern Med. 2009 Sep 15;151(6):404-13.

McKee G, Kearney PM, Kenny RA. The factors associated with **self-reported physical activity** in older adults living in the community. Age Ageing. 2015 Apr 11.

McKee M, Exall S, Stuckler D, Wolff A. 'Normal' serum **sodium concentration** among inpatients over 65 admitted to hospital: an observational study. Postgrad Med J. 2015 Nov 11.

McKinlay CJ, Cutfield WS, Battin MR, et al. on behalf of the ACTORDS Study Group. Cardiovascular Risk Factors in Children After Repeat Doses of **Antenatal Glucocorticoids**: An RCT. Pediatrics. 2015 Jan 19.

McQueen MJ, Hawken S, Wang X, Ounpuu S, Sniderman A, Probstfield J, Steyn K, Sanderson JE, Hasani M, Volkova E, Kazmi K, Yusuf S; **INTERHEART** study investigators. Lipids, lipoproteins, and apolipoproteins as risk markers of myocardial infarction in 52 countries (the INTERHEART study): a case-control study. Lancet. 2008 Jul 19;372(9634):224-33. The **non-fasting ApoB/ApoA1 ratio** was superior to any of the cholesterol ratios for estimation of the risk of acute myocardial infarction in all ethnic groups, in both sexes, and at all ages, and it should be introduced into worldwide clinical practice.

Medina-Inojosa JR, Batsis JA, Supervia M, et al. Relation of **Waist-Hip Ratio** to Long-Term Cardiovascular Events in Patients With Coronary Artery Disease. Am J Cardiol. 2018 Apr 15;121(8):903-909.

Mega JL, Stitziel NO, Smith GJ, et al. **Genetic risk, coronary heart disease events, and the clinical benefi t of statin** therapy: an analysis of primary and secondary prevention trials. Lancet 2015; online March 4.

Mehta H, Sacrinty M, Johnson D, et al. Comparison of Usefulness of **Secondary Prevention of Coronary Disease in Patients <80 Versus ≥80 Years** of Age. Am J Cardiol. 2013 Jul 3.

Melander O, Newton-Cheh C, Almgren P, et al. **Novel and conventional biomarkers** for prediction of incident cardiovascular events in the community. JAMA. 2009 Jul 1;302(1):49-57.

Melander O, Maisel AS, Almgren P, et al. **Plasma proneurotensin** and incidence of diabetes, cardiovascular disease, breast cancer, and mortality. JAMA 2012; 308:1469-1475.

Mellerio H, Alberti C, Druet C, et al. **Novel modeling of reference values** of cardiovascular risk factors in **children aged 7 to 20 years**. Pediatrics. 2012 Apr;129(4):e1020-9.

Mellett LH, Bousquet G. **Heart-healthy exercise**. Circulation. 2013 Apr 30;127(17):e571-2.

Melzer D, Osborne NJ, Henley WE, et al. **Urinary bisphenol**: A concentration and risk of future coronary artery disease in apparently healthy men and women. Circulation 2012.

Melzer D, Gates P, Osborn NJ, et al. **Urinary bisphenol** a concentration and angiography-defined coronary artery stenosis. PLoS ONE 2012; 7: e43378.

Mente A, de Koning L, Shannon HS, et al. A systematic review of the evidence supporting a causal link between **dietary factors** and coronary heart disease. *Arch Intern Med 2009*; 169:659-669.

Mente A, Yusuf S, Islam S, et al. **Metabolic syndrome** and risk of acute myocardial infarction. A case-control study of 26 903 subjects from 52 countries. J Am Coll Cardiol 2010; 55:2390-2398.

Mente A, O'Donnell MJ, Yusuf S. The population risks of **dietary salt excess** are exaggerated. Can J Cardiol. 2014 May;30(5):507-12.

Mente A, O'Donnell MJ, Rangarajan S, et al. Association of **urinary sodium and potassium excretion** with blood pressure. (Pure) N Engl J Med 2014;371:601-11.

Mente A, O'Donnell M, Rangarajan S, et al, for the PURE, EPIDREAM, and ONTARGET/TRANSCEND Investigators. Associations of **urinary sodium excretion** with cardiovascular events in individuals with and without hypertension: a pooled analysis of data from four studies. Lancet 2016; online May 20.

Mente A, O'Donnell M, Rangarajan S, et al. **Urinary sodium excretion, blood pressure, cardiovascular disease, and mortality**: a community-level prospective epidemiological cohort study. Lancet. 2018 Aug 11;392(10146):496-506.

Merghani A, Maestrini V, Rosmini S, et al. Prevalence of subclinical coronary artery disease in masters **endurance athletes** with a low atherosclerotic risk profile. Circulation. 2017;136;126–137.

Metcalf BS, Hosking J, et al. **Physical activity attenuates the mid-adolescent peak in insulin resistance** but by late adolescence the effect is lost: a longitudinal study with annual measures from 9-16 years (EarlyBird 66). Diabetologia. 2015 Aug 12.

Meyers DG, Neuberger JS, He J et al. Cardiovascular effect of bans on **smoking in public places**. A systematic review and meta-analysis. J Am Coll Cardiol 2009; 54: 1249-1255.

Micha R, Peñalvo JL, Cudhea F, et al. Association between **dietary factors and mortality** from heart disease, stroke, and type 2 diabetes in the United States.JAMA. doi: 0.1001/jama.2017.0947

Michalsky MP, Inge TH, Simmons M, et al; for the Teen-LABS Consortium. Cardiovascular Risk Factors in Severely Obese Adolescents: The **Teen Longitudinal Assessment of Bariatric Surgery** (**Teen-LABS**) Study. JAMA Pediatr. 2015 Mar 2.

Michos ED, Blumenthal RS. How Accurate Are 3 **Risk Prediction Models in US Women**? Circulation. 2012 Apr 10;125(14):1723-6.

Miedema MD, Petrone A, Shikany JM, et al. The association of **fruit and vegetable consumption** during early adulthood with the prevalence of coronary artery calcium after 20 years of follow-up: The CARDIA study. *Circulation*2015.

Millard LA, Lawlor DA, Fraser A, Howe LD. **Physical activity during pregnancy** and offspring cardiovascular risk factors: findings from a prospective cohort study. BMJ Open. 2013 Sep 25;3(9):e003574.

Miller JM, Rochitte CE, Dewey M, et al. Diagnostic performance of coronary angiography by **64-row CT**. N Engl J Med. 2008 Nov 27;359(22):2324-36. December 3, 2008

Miller PE, Zhao D, Frazier-Wood AC, et al. Associations between **coffee, tea, and caffeine** intake with coronary artery calcification and cardiovascular events. *Am J Med* 2016.

Miller PE et al. Associations of **coffee, tea, and caffeine intake** with coronary artery calcification and cardiovascular events. Am J Med 2017 Feb; 130:188.

Miller V, Mente A, Dehghan M, et al. **Fruit, vegetable, and legume intake**, and cardiovascular disease and deaths in 18 countries (Prospective Urban Rural Epidemiology [**PURE**]): a prospective cohort study. Lancet 2017; online Aug 29.

Miller VM, Mankad R. **Sex Steroids and Incident Cardiovascular Disease** in **Post-Menopausal Women**: New Perspective on an Old Controversy. J Am Coll Cardiol. 2018 Jun 5;71(22):2567-2569.

Mills KT, Chen J, Yang W, et al. **Sodium excretion** and the risk of cardiovascular disease in patients with chronic kidney disease.JAMA. doi:10.1001 /jama.2016.4447.

Milojevic A, Wilknson P, Armstrong B, et al. Short-term effects of **air pollution** on a range of cardiovascular events in England and Wales: case-crossover analysis of the MINAP database, hospital admissions and mortality. Heart (2014): heartjnl-2013.

Min J, Lin F, Gidseg D, et al. Determinants of coronary calcium conversion among patients with a normal **coronary calcium scan**: What is the "warranty period" for remaining normal? J Am Coll Cardiol 2010 55:1110-1117.

Min JY, Min KB. **Serum C-peptide levels** and risk of death among adults without diabetes mellitus. CMAJ. 2013 Apr 15.

Min JY, Min KB. Serum **C-peptide levels** and risk of death among adults without diabetes mellitus. CMAJ. 2013 Jun 11;185(9):E402-8.

Minassian C, D'Aiuto F, Hingorani AD, Smeeth L. **Invasive dental treatment** and risk for vascular events: a self-controlled case series. Ann Intern Med. 2010 Oct 19;153(8):499-506.

Mincu RI, Mahabadi AA, Michel L, et al. Cardiovascular **Adverse Events Associated With BRAF and MEK Inhibitors**: A Systematic Review and Meta-analysis. JAMA Netw Open. 2019 Aug 2;2(8):e198890.

Minder CM, Shaya GE, Michos ED, et al. Relation Between Self-Reported **Physical Activity Level, Fitness, and Cardiometabolic Risk**. Am J Cardiol. 2013 Nov 23

Mitter SS, Vedanthan R, Islami F, et al. **Household fuel** use and cardiovascular disease mortality: Golestan Cohort Study. Circulation. 2016;133:2360–2369.

Möbius-Winkler S, et al. **Coronary collateral growth** induced by **physical exercise**: Impact of Intensive Exercise Training on Coronary Collateral Circulation in Patients With Stable Coronary Artery Disease (**EXCITE**) trial. Circulation. 2016;133:1438–1448.

Möhlenkamp S, Lehmann N, Moebus S, et al. Quantification of **coronary atherosclerosis and inflammation** (CRP) to predict coronary events and all-cause mortality. J Am Coll Cardiol 2011; 57:1455-1464

Mok A, Khaw KT, Luben R, et al. **Physical activity trajectories and mortality**: population based cohort study. BMJ. 2019 Jun 26;365:l2323.

Mongraw-Chaffin M, Foster MC, Anderson CAM, et al. **Metabolically Healthy Obesity, Transition to Metabolic Syndrome, and Cardiovascular Risk**. J Am Coll Cardiol. 2018 May 1;71(17):1857-1865.

Mongraw-Chaffin M, Foster MC, Anderson CAM, et al. **Metabolically Healthy Obesity**, Transition to Metabolic Syndrome, and Cardiovascular Risk. J Am Coll Cardiol. 2018 May 1;71(17):1857-1865.

Mons U, Hahmann H, Brenner H. A reverse J-shaped association of **leisure time physical activity** with prognosis in patients with stable coronary heart disease: evidence from a large cohort with repeated measurements. Heart. 2014 May 14.

Moon KA, Guallar E, Umans JG, Devereux RB, et al. Association between exposure to low to moderate **arsenic levels** and incident cardiovascular disease. A prospective cohort study. Ann Intern Med. 2013;159:649-59.

Moore SC, Patel AV, Matthews CE, et al. **Leisure time physical activity of moderate to vigorous intensity and mortality**: a large pooled cohort analysis. PLoS Med. 2012 Nov;9(11):e1001335.

Mora S, Wenger NK, Cook NR, et al. Evaluation of the **pooled cohort risk equations** for cardiovascular risk prediction in a multiethnic cohort of women: the Women's Health Initiative [online July 23, 2018]. JAMA Intern Med. doi:10.1001/jamainternmed.2018.2875

Morrison JA, Glueck CJ, Wang P. The Child as **Proband for Future Parental Cardiometabolic Disease**: The 26-Year Prospective Princeton Lipid Research Clinics Follow-Up Study. J Pediatr. 2012 Jan 12.

Morrow DA. **Cardiovascular risk prediction** in patients with stable and unstable coronary heart disease. Circulation. 2010 Jun 22;121(24):2681-91.

Mortensen MB, Fuster V, Muntendam P, et al. **Negative Risk Markers** for Cardiovascular Events in the Elderly. J Am Coll Cardiol. 2019 Jul 9;74(1):1-11.

Mosca Lori, Benjamin Emelia J., Berra Kathy, et al. Effectiveness-Based Guidelines for the **Prevention of Cardiovascular Disease in Women**—2011 Update: A Guideline From the American Heart Association. Circulation published Feb 14, 2011.

Mosca L, Aggarwal B, Mochari-Greenberger H, et al. Association Between Having a **Caregiver** and Clinical Outcomes 1 Year After Hospitalization for Cardiovascular Disease. Am J Cardiol. 2011 Sep 29.

Mossavar-Rahmani Y, Kamensky V, Manson JE, et al. **Artificially Sweetened Beverages and Stroke, Coronary Heart Disease, and All-Cause Mortality** in the Women's Health Initiative. Stroke. 2019 Mar;50(3):555-562.

Mostofsky E, Chahal HS, Mukamal KJ, et al. **Alcohol** and Immediate Risk of Cardiovascular Events: A Systematic Review and Dose-Response Meta-Analysis. Circulation. 2016 Mar 2.

Motoyama S, Ito H, Sarai M, et al. **Plaque Characterization by Coronary Computed Tomography Angiography** and the Likelihood of Acute Coronary Events in Mid-term Follow-up. *J Am Coll Cardiol* 2015; 66:337-346.

Moyer VA; on behalf of the U.S. Preventive Services Task Force*. Screening for Coronary Heart Disease With **Electrocardiography**: U.S. Preventive Services Task Force Recommendation Statement. Ann Intern Med. 2012 Jul 31.

Moyer VA; on behalf of the U.S. Preventive Services Task Force. Behavioral Counseling Interventions to Promote a **Healthful Diet and Physical Activity** for Cardiovascular Disease Prevention in Adults: U.S. Preventive Services Task Force Recommendation Statement. Ann Intern Med. 2012 Jun 26.

Mozaffarian D, Micha R, Wallace S. Effects on coronary heart disease of increasing **polyunsaturated fat** in place of saturated fat: a systematic review and meta-analysis of randomized controlled trials. PLoS Med 2010;**7**:e1000252.

Mozaffarian Dariush, Shi Peilin, Morris J. Steven, et al. **Mercury Exposure** and Risk of Cardiovascular Disease in Two U.S. Cohorts. N Engl J Med. 2011;364:1116-1125.

Mozaffarian D, Afshin A, Benowitz NL, et al; on behalf of the American Heart Association Council on Epidemiology and Prevention, Council on Nutrition, Physical Activity and Metabolism, Council on Clinical Cardiology, Council on Cardiovascular Disease in the Young, Council on the Kidney in Cardiovasc. Population Approaches to Improve Diet, Physical Activity, and Smoking Habits: A Scientific Statement From the American Heart Association. Circulation. 2012 Sep 18;126(12):1514-1563.

Mozaffarian D, Lemaitre RN, King IB, et al. Plasma **phospholipid long-chain omega-3 fatty acids** and total and cause-specific mortality in older adults. A cohort study. Ann Intern Med 2013; 158:515-525.

Mozaffarian D, Fahimi S, Singh GM, et al. **Global sodium consumption** and death from cardiovascular causes. (Nutricode) N Engl J Med 2014;371:624-34.

Mozaffarian D. **Dietary and Policy Priorities** for Cardiovascular Disease,Diabetes, and Obesity: A Comprehensive Review. Circulation. 2016 Jan 8.

Mu F, Rich-Edwards J, Rimm EB, et al. **Endometriosis** and risk of coronary heart disease. *Circ Cardiovasc Qual Outcomes* 2016. DOI:10.1161/CIRCOUTCOMES.115.002224.

Muhlestein JB, Lappé DL, Lima JA, et al. Effect of screening for coronary artery disease using **CT angiography on mortality** and cardiac events in high-risk patients with diabetes: the FACTOR-64 randomized clinical trial. JAMA. 2014 Dec 3;312(21):2234-43.

Muka T, Oliver-Williams C, Kunutsor S, et al. Association of age at **onset of menopause** and time since onset of menopause with cardiovascular outcomes, intermediate vascular traits, and all-cause mortality: a systematic review and meta-analysis [online Sept 14, 2016].JAMA Cardiol. doi:10.1001/jamacardio.2016.2415.

Mullee A, Romaguera D, Pearson-Stuttard J, et al. Association Between **Soft Drink Consumption and Mortality** in 10 European Countries. JAMA Intern Med. 2019 Sep 3.

Mulrooney Daniel A, Yeazel Mark W, Kawashima Toana, et al. Cardiac outcomes in a cohort of adult survivors of **childhood and adolescent cancer**: retrospective analysis of the Childhood Cancer Survivor Study cohort. BMJ 2009;339:b4606, doi: 10.1136/bmj.b4606 (Published 8 December 2009).

Mulrooney DA, Armstrong GT, Huang S, et al. Cardiac Outcomes in **Adult Survivors of Childhood Cancer Exposed to Cardiotoxic Therapy**: A Cross-sectional Study. Ann Intern Med. 2016 Jan 5.

Münzel T, Schmidt FP, Steven S, et al. **Environmental Noise** and the Cardiovascular System. J Am Coll Cardiol. 2018 Feb 13;71(6):688-697.

Murabito JM, Pencina MJ, Nam BH, et al. **Sibling cardiovascular disease** as a risk factor for cardiovascular disease in middle-aged adults. JAMA. 2005 Dec 28;294(24):3117-23.

Murphy A W, Cupples M E, Smith S M, et al., for the SPHERE study team. Effect of tailored practice and **patient care plans** on secondary prevention of heart disease in general practice: cluster randomised controlled trial. BMJ 2009;339:b4220, doi: 10.1136/bmj.b4220 (Published 29 October 2009)

Murphy E, Vellinga A, Byrne M, et al. **Primary care organisational interventions** for secondary prevention of ischaemic heart disease: a systematic review and meta-analysis. Br J Gen Pract. 2015 Jul;65(636):e460-8.

Murthy VL, Naya M, Taqueti VR, et al. Effects of **sex** on coronary microvascular dysfunction and cardiac outcomes. Circulation. 2014;129:2518–2527.

Mytton OT, Forouhi NG, Scarborough P, et al. Association between **intake of less-healthy foods** defined by the United Kingdom's nutrient profile model and cardiovascular disease: A population-based cohort study. PLoS Med. 2018 Jan 4;15(1):e1002484.

Naci H, Ioannidis JP. Comparative effectiveness of **exercise and drug interventions** on mortality outcomes: metaepidemiological study. BMJ. 2013 Oct 1.

Nadir MA, Rekhraj S, Wei L, et al. Improving the primary prevention of cardiovascular events by using **biomarkers** to identify individuals with silent heart disease. J Am Coll Cardiol. 2012 Sep 11;60(11):960-8.

Nafiu OO, Burke C, Lee J, Voepel-Lewis T, Malviya S, Tremper KK. **Neck Circumference** as a Screening Measure for Identifying Children With High Body Mass Index. Pediatrics. 2010 Jul 5.

Nanda A, Chen MH, et al. **Hormonal therapy** use for **prostate cancer** and mortality in men with coronary artery disease-induced congestive heart failure or myocardial infarction. JAMA. 2009 Aug 26;302(8):866-73.

Narang I, Manlhiot C, Davies-Shaw J. **Sleep disturbance** and cardiovascular risk in adolescents. CMAJ 2012.

Näslund U, Ng N, Lundgren A, et al. **Visualization of asymptomatic atherosclerotic disease for optimum cardiovascular prevention (VIPVIZA**): a pragmatic, open-label, randomised controlled trial. Lancet. 2018 Dec 3.

Natarajan P, Young R, Stitziel NO, et al. **Polygenic Risk Score** Identifies Subgroup with Higher Burden of Atherosclerosis and Greater Relative Benefit from Statin Therapy in the Primary Prevention Setting. Circulation. 2017 Feb 21.

Nawrot TS, Perez L, Künzli N, et al. Public health importance of triggers of myocardial infarction: A comparative risk assessment. Lancet 2011; DOI: 10.1016/S0140-6736(10)62296-9. A comparative risk assessment of various triggers for MI suggests that **cocaine** is most likely to trigger an event in an individual, but **traffic and exposure to air pollution** has the greatest effect on triggering an MI at the population level.

NaumanJ, Janszky I, Vatten LJ, Wisløff U. **Temporal changes in resting heart rate** and deaths from ischemic heart disease. JAMA2011; 306:2579-2587.

Navar AM, Peterson ED, Wojdyla D, Sanchez RJ, Sniderman AD, D'Agostino RB Sr, Pencina MJ. **Temporal Changes in the Association Between Modifiable Risk Factors** and Coronary Heart Disease Incidence. JAMA. 2016 Nov 15;316(19):2041-2043.

Navar AM, Wang TY, Mi X, et al.Influence of **Cardiovascular Risk Communication Tools and Presentation Formats** on Patient Perceptions and Preferences. JAMA Cardiol. 2018 Nov 7

Navar-Boggan AM, Peterson ED, D'Agostino RB, et al. **Hyperlipidemia in early adulthood** increases long-term risk of coronary heart disease. Circulation. 2015;131:451–458.

Neal B. **Dietary salt** is a public health hazard that requires vigorous attack. Can J Cardiol. 2014 May;30(5):502-6.

Nerenberg KA, Zarnke KB, Leung AA, et al. **Hypertension Canada's 2018 guidelines for diagnosis, risk assessment, prevention, and treatment of hypertension in adults and children**. Can J Cardiol 2018; February 20, 2018.

Newby D, Mannucci P, Tell G, et al. Expert position paper on **air pollution** and cardiovascular disease. *Eur Heart J*2014. DOI:10.1093/eurheart/ehu458.

Newell K, Kartsonaki C, Lam KBH, et al. Cardiorespiratory health effects of **gaseous ambient air pollution** exposure in low and middle income countries: a systematic review and meta-analysis. Environ Health. 2018 Apr 18;17(1):41.

Newman AB, Dodson JA, Church TS, et al. **LIFE** Study Group. Cardiovascular Events in a **Physical Activity Intervention** Compared With a Successful Aging Intervention: The LIFE Study Randomized Trial. JAMA Cardiol.2016 Jun 29.

Newman JD, Thurston GD, Cromar K, et al. Particulate **Air Pollution** and Carotid Artery Stenosis. J Am Coll Cardiol. 2015 Feb 18.

Nguyen XT, Quaden RM, Wolfrum S, et al. Prevalence of **Ideal Cardiovascular Health Metrics** in the Million Veteran Program. Am J Cardiol. 2018 Apr 12.

Nicklett EJ, Semba RD, Xue QL, et al. **Fruit and vegetable intake, physical activity, and mortality** in older community-dwelling women. J Am Geriatr Soc. 2012 May;60(5):862-8.

Nielsen LH, Bøtker HE, Sørensen HT, et al. Prognostic assessment of stable coronary artery disease as determined by **coronary computed tomography angiography**: a Danish multicentre cohort study. Eur Heart J. 2016 Dec 9.

Nilsson G, Holmberg L, Garmo H, et al. Distribution of Coronary Artery Stenosis **After Radiation for Breast Cancer**. J Clin Oncol. 2011 Dec 27.
Ning H, Van Horn L, et al. Associations of **Dietary Fiber** Intake With Long-Term Predicted Cardiovascular Disease Risk and C-Reactive Protein Levels (from the National Health and Nutrition Examination Survey Data [2005-2010]). Am J Cardiol. 2013 Oct 3
Ning H, Labarthe DR, Shay CM, et al. Status of **Cardiovascular Health in US Children** Up to 11 Years of Age: The National Health and Nutrition Examination Surveys 2003-2010. Circ Cardiovasc Qual Outcomes. 2015 Mar;8(2):164-71.
Niiranen TJ, Lyass A, Larson MG, et al. Prevalence, Correlates, and Prognosis of **Healthy Vascular Aging in a Western Community-Dwelling Cohort**: The Framingham Heart Study. Hypertension. 2017 May 30.
Nitsch D, Grams M, Sang Y, et al; for the Chronic Kidney Disease Prognosis Consortium. Associations of **estimated glomerular filtration rate and albuminuria** with mortality and renal failure by sex: a meta-analysis. BMJ. 2013 Jan 29;346:f324.
Noad RL, Rooney C, McCall D, et al. Beneficial effect of a **polyphenol-rich diet** on cardiovascular risk: a randomised control trial. Heart. 2016 Sep 1;102(17):1371-9.
Nordestgaard BG, Palmer TM, Benn M, et al. The effect of **elevated body mass index** on ischemic heart disease risk: causal estimates from a mendelian randomisation approach. PLoS Med. 2012 May;9(5):e1001212.
Nordmann AJ, Suter-Zimmermann K, Bucher HC, et al. Meta-analysis comparing **Mediterranean to low-fat diets** for modification of cardiovascular risk factors. Am J Med. 2011;124:841-51.
Norheim Ole Frithjof, Gjelsvik Bjørn, Klemsdal Tor Ole, et al. **Norway's new principles for primary prevention** of cardiovascular disease: age differentiated risk thresholds. BMJ 2011;343:doi:10.1136/bmj.d3626 (Published 13 July 2011)
Nupponen M, Pahkala K, Juonala M, et al. Metabolic syndrome from adolescence to early adulthood: Effect of **infancy-onset dietary counseling of low-saturated-fat**: The Special Turku Coronary Risk Factor Intervention Project (STRIP). *Circulation* 2015.
Nupponen M, Pahkala K, et al. **Metabolic syndrome from adolescence to early adulthood**: effect of infancy-onset dietary counseling of low saturated fat: The Special Turku Coronary Risk Factor Intervention Project (STRIP). Circulation. 2015;131:605–613.
O'Donovan G, Lee I-M, et al. Association of "**weekend warrior**" and other leisure time physical activity patterns with risks for all-cause, cardiovascular disease, and cancer mortality [online Jan 9, 2017].JAMA Intern Med. doi:10.1001/jamainternmed.2016.8014
O'Donnell M et al. Joint association of **urinary sodium and potassium excretion** with cardiovascular events and mortality: Prospective cohort study. BMJ 2019 Mar 13; 364:l772.
O'Donnell M, Mente A, Rangarajan S, et al; PURE Investigators. Joint **association of urinary sodium and potassium excretion** with cardiovascular events and mortality: prospective cohort study. BMJ. 2019 Mar 13;364:l772.
O'Donnell MJ, Xavier D, Liu Lisheng, et al; and on behalf of the **INTERSTROKE** investigators, Risk factors for ischaemic and intracerebral haemorrhagic stroke in 22 countries (the INTERSTROKE study): a case-control study, The Lancet, Online 17 June 2010
O'Donnell MJ, Yusuf S, Mente A, et al. **Urinary sodium and potassium excretion** and risk of cardiovascular events. JAMA 2011; 306:2229-2238.
O'Donnell MJ, Mente A, Rangarajan S, et al. **Urinary sodium and potassium excretion**, mortality, and cardiovascular events. (Pure) N Engl J Med 2014;371:612-23.
O'Hare Ann M.; Hailpern Susan M.; Pavkov Meda E.; et al. Prognostic Implications of the **Urinary Albumin to Creatinine Ratio** in Veterans of Different Ages With Diabetes. Arch Intern Med. 2010;170(11):930-936.
O'Hare C, Kuh D, Hardy R. Association of Early-Life Factors With Life-Course Trajectories of **Resting Heart Rate**: More Than 6 Decades of Follow-up. JAMA Pediatr. 2018 Feb 12:e175525.
O'Keefe JH, Patil HR, Lavie CJ, et al. Potential adverse cardiovascular effects from **excessive endurance exercise**. Mayo Clin Proc2012; 87:587-595.
O'Keefe JH, Bhatti SK, Patil HR, et al. Effects of Habitual **Coffee Consumption** on Cardiometabolic Disease, Cardiovascular Health, and All-cause Mortality. J Am Coll Cardiol. 2013 Jul 3.
O'Neil AE, Sanderson K. The use of **cognitive behavioral therapy** for secondary prevention in patients with coronary heart disease. Arch Intern Med. 2011 Sep 12;171(16):1506.
O'Neil A, Scovelle AJ, Milner AJ, et al. **Gender/Sex as a Social Determinant** of Cardiovascular Risk. Circulation. 2018 Feb 20;137(8):854-864.
Ochs-Balcom HM, Preus L, Nie J, et al. **Physical activity** modifies genetic **susceptibility to obesity** in postmenopausal women. Menopause. 2018 May 14.
Odegaard AO, Koh WP, Gross MD, Yuan JM, Pereira MA. Combined lifestyle factors and cardiovascular disease mortality in Chinese men and women: the Singapore Chinese health study. Circulation. 2011 Dec 20;124(25):2847-54.
Odegaard AO, Koh WP, Yuan JM, et al. **Western-style fast food** intake and cardiometabolic risk in an Eastern country. Circulation 2012.
Odutayo A, Gill P, Shepherd S, et al. **Income Disparities** in Absolute Cardiovascular Risk and Cardiovascular Risk Factors in the United States, 1999-2014. JAMA Cardiol. 2017 Jun 7.
Oikonomou EK, Marwan M, et al. Non-invasive detection of **coronary inflammation using computed tomography** and prediction of residual cardiovascular risk (the CRISP CT study): a post-hoc analysis of prospective outcome data. Lancet. 2018 Aug 24.
Oja P, Kelly P, Pedisic Z, et al. Associations of specific types of **sports**(**raquet sports, bike, swim, & aerobics**) and exercise with all-cause and cardiovascular-disease mortality: a cohort study of 80 306 British adults. Br J Sports Med. 2016 Nov 28.
Okamoto R, Ali Y, Hashizume R, et al. **BNP as a Major Player** in the Heart-Kidney Connection. Int J Mol Sci. 2019 Jul 22;20(14).
Okunrintemi V, Benson EA, Tibuakuu M, et al. Trends and Costs Associated With **Suboptimal Physical Activity Among US Women** With Cardiovascular Disease. JAMA Netw Open. 2019 Apr 5;2(4):e191977.
Olde Engberink RHG, van den Hoek TC, van Noordenne ND, et al. Use of a Single Baseline Versus Multi-Year 24-Hour Urine Collections for Estimation of Long-Term **Sodium Intake** and Associated Cardiovascular and Renal Risk. Circulation. 2017 Jun 27.
Olde Engberink RHG, van den Hoek TC, et al. Use of a **Single Baseline Versus Multi-Year 24-Hour Urine Collections for Estimation of Long Term Sodium** Intake and Associated Cardiovascular and Renal Risk. Circulation. 2017 Jun 27.
Omland T, de Lemos JA, et al. the Prevention of Events with Angiotensin Converting Enzyme Inhibition (PEACE) Trial. A Sensitive Cardiac **Troponin T Assay** in Stable Coronary Artery Disease. N Engl J Med. 2009 Nov 25.
ORIGIN trial investigators. **n-3 fatty acids** and cardiovascular outcomes in patients with dysglycemia. N Engl J Med 2012.
Orimoloye OA, Mirbolouk M, Uddin SMI, et al. Association Between **Self-rated Health, Coronary Artery Calcium Scores, and Atherosclerotic Cardiovascular Disease Risk**: The Multi-Ethnic Study of Atherosclerosis (MESA). JAMA Netw Open. 2019 Feb 1;2(2):e188023.
Orlich JM, Singh P, Sabate J, et al. **Vegetarian dietary patterns** and mortality in Adventist Health Study 2 [published online June 3, 2013]. JAMA Intern Med. doi:10.1001/jamainternmed.2013.6473.
Orrow G, Kinmonth AL, Sanderson S, Sutton S. Effectiveness of **physical activity** promotion based in primary care: systematic review and meta-analysis of randomised controlled trials. BMJ. 2012 Mar 26;344:e1389.
Ortega FB, Silventoinen K, Tynelius P, et al. **Muscular strength** in male adolescents and premature death: cohort study of one million participants. BMJ 2012;345:e7279
Osborn DP, Hardoon S, Omar RZ, et al. **Cardiovascular Risk** Prediction Models for People With Severe **Mental Illness**: Results From the Prediction and Management of Cardiovascular Risk in People With Severe Mental Illnesses (PRIMROSE) Research Program. JAMA Psychiatry. 2014 Dec 23.
O'Shaughnessy MM, Liu S, Montez-Rath ME, et al. Cause of **kidney disease and cardiovascular events in a national cohort of US patients with end-stage renal disease on dialysis**: a retrospective analysis. Eur Heart J 2019;40:887–898.
Otaki Y, Gransar H, Berman DS, et al. Impact of **Family History** of Coronary Artery Disease in Young Individuals (from the CONFIRM Registry). Am J Cardiol. 2013 Feb 11.
Otten Jennifer J.; Jones Katherine E.; et al. Effects of **Television Viewing** Reduction on Energy Intake and Expenditure in Overweight and Obese Adults: A Randomized Controlled Trial. Arch Intern Med. 2009;169(22):2109-2115.
Oyebode O, Gordon-Dseagu V, Walker A, et al. **Fruit and vegetable consumption** and all-cause, cancer and CVD mortality: analysis of Health Survey for England data. J Epidemiol Community Health. 2014 Mar 31.
Pack QR, Mansour M, Barboza JS, et al. An **early appointment to outpatient cardiac rehabilitation** at hospital discharge improves attendance at orientation: a randomized, single-blind, controlled trial. Circulation. 2013 Jan 22;127(3):349-55.
Pack QR, Goel K, Lahr BD et al. **Participation in cardiac rehabilitation** and survival after coronary artery bypass graft surgery: a community-based study. Circulation. 2013 Aug 6;128(6):590-7.
Pagan E, Chatenoud L, Rodriguez T, et al. Comparison of Trends in Mortality from Coronary Heart and Cerebrovascular Diseases in **North and South America**:1980-2013. Am J Cardio. 2017.
Page RL, Husain S, White LY, et al. **Cardiac arrest at exercise facilities**: Implications for placement of automated external defibrillators. J Am Coll Cardiol 2013.
Paik JM, Curhan GC, Sun Q, et al. **Calcium supplement** intake and risk of cardiovascular disease in women. Osteoporos Int. 2014 May 7.
Pahkala K, Heinonen OJ, Simell O, et al. Association of **physical activity with vascular endothelial function and intima-media thickness**. Circulation. 2011 Nov 1;124(18):1956-63.
Pahkala K, Hietalampi H, Laitinen TT, et al. Ideal Cardiovascular Health in Adolescence: Effect of **Lifestyle Intervention** and Association With Vascular Intima-Media Thickness and Elasticity (The Special Turku Coronary Risk Factor Intervention Project for Children [STRIP] Study). Circulation. 2013 May 28;127(21):2088-96.
Pänkäläinen M, Kerola T, Kampman O, et al. **Pessimism** and risk of death from coronary heart disease among middle-aged and older Finns: an eleven-year follow-up study. BMC Public Health. 2016 Nov 17;16(1):1124.
Pahor M, Guralnik JM, Ambrosius WT, et al; for the LIFE study investigators. Effect of Structured **Physical Activity** on Prevention of Major Mobility Disability in Older Adults: The LIFE Study Randomized Clinical Trial. JAMA. 2014 May 27.
Pandey A, Salahuddin U, Garg S, et al. Continuous dose-response association between **sedentary time** and risk for cardiovascular disease. A meta-analysis. *JAMA Cardio* 2016.
Papadakis M, Whyte G, Sharma S. **Preparticipation screening** for cardiovascular abnormalities in young competitive athletes. BMJ. 2008 Sep 29;337:a1596. doi: 10.1136/bmj.a1596.
Parikh KS, Greiner MA, Suzuki T, DeVore et al. **Resting Heart Rate** and Long-term Outcomes Among the African American Population: Insights From the Jackson Heart Study. JAMA Cardiol. 2016 Sep 28.
Park K. How low to go with glucose control? http://www.australianprescriber.com/magazine/32/2/30/1
Park SY, Freedman ND, Haiman CA, et al. Association of **coffee consumption** with total and cause-specific mortality among nonwhite populations. Ann Intern Med. [Epub ahead of print]. doi:10.7326/M16-2472
Park SY, Kim SH, Kang SH, et al. Improved **oral hygiene care attenuates the cardiovascular risk of oral health disease**: a population-based study from Korea. Eur Heart J. 2019 Apr 7;40(14):1138-1145.
Park Yikyung; Subar Amy F.; Hollenbeck Albert; et al. **Dietary Fiber** Intake and Mortality in the NIH-AARP Diet and Health Study. Arch Intern Med. 2011;171(12):1061-1068.
Parker BA, Augeri AL, Capizzi JA, et al. Effect of **Marathon Run and Air Travel** on Pre- and Post-Run Soluble D-Dimer, Microparticle Procoagulant Activity, and P-Selectin Levels. Am J Cardiol. 2012 Feb 17.
Parker DR, Lu B, Sands-Lincoln M, et al. Risk of Cardiovascular Disease Among **Postmenopausal Women with Prior Pregnancy Loss**: The Women's Health Initiative. Ann Fam Med. 2014 Jul;12(4):302-9.

Parker JD, et al. **Particulate Matter Air Pollution** Exposure and Heart Disease Mortality Risks by Race and Ethnicity in the United States: 1997 to 2009 National Health Interview Survey With Mortality Follow-Up Through 2011. Circulation. 2018 Apr 17;137(16):1688-1697.
Parmar D, Stavropoulou C, Ioannidis JPA. Health outcomes during the **financial crisis** in Europe: systematic literature review. BMJ 2016;354:i4588.
Patel AV, Hildebrand JS, Leach CR, et al. **Walking** in Relation to Mortality in a Large Prospective Cohort of Older U.S. Adults. Am J Prev Med. 2017 Oct 11.
Patel KK, Taksler GB, Hu B, Rothberg MB. Prevalence of **elevated cardiovascular risks in young adults**: a cross-sectional analysis of National Health and Nutrition Examination Surveys. Ann Intern Med. 2017. [Epub ahead of print]. doi:10.7326/M16-2052
Patel SA, Winkel M, Ali MK, et al. Cardiovascular Mortality Associated With **5 Leading Risk Factors**: National and State Preventable Fractions Estimated From Survey Data. Ann Intern Med. 2015 Jun 30
Patnode CD, Evans CV, Senger CA, Redmond N, Lin JS. **Behavioral counseling to promote a healthful diet and physical activity** for cardiovascular disease prevention in adults without known cardiovascular risk factors: updated evidence report and systematic review for the US Preventive Services Task Force.JAMA. doi:10.1001/jama.2017.3303
Pavey TG, Taylor AH, Fox KR, et al. Effect of **exercise referral schemes** in primary care on physical activity and improving health outcomes: systematic review and meta-analysis. BMJ 2011;343:d6462.
Paynter NP, Chasman DI, Paré G, Buring JE, Cook NR, Miletich JP, Ridker PM. Association between a literature-based **genetic risk score and cardiovascular events in women**. JAMA. 2010 Feb 17;303(7):631-7.
Paynter NP, Mazer NA, Pradhan AD, Gaziano JM, Ridker PM, Cook NR. Cardiovascular risk prediction in **diabetic** men and women using **haemoglobin A1c** vs diabetes as a high-risk equivalent. Arch Intern Med. 2011.
Pearson TA, Palaniappan LP, Artinian NT, et al. American heart association guide for **improving cardiovascular health at the community level, 2013 update**: a scientific statement for public health practitioners, healthcare providers, and health policy makers. Circulation. 2013 Apr 23;127(16):1730-53.
Pearson-Stuttard J, Guzman Castillo M, Penalvo JL, et al. Modelling Future Cardiovascular Disease Mortality in the United States: National Trends and **Racial and Ethnic Disparities**. Circulation. 2016 Feb 4.
Peker Y, et al. Effect of **Positive Airway Pressure** on Cardiovascular Outcomes in Coronary Artery Disease Patients with Nonsleepy Obstructive Sleep Apnea. RICCADSA Randomized Controlled Trial. Am J Respir Crit Care Med. 2016 Sep 1;194(5):613-20.
Peñalvo JL, Fernández-Friera L, López-Melgar B, et al. Association Between a **Social-Business Eating Pattern** and Early Asymptomatic Atherosclerosis. J Am Coll Cardiol. 2016 Aug 23;68(8):805-14.
Pencina MJ, D'Agostino RB Sr, Larson MG, Massaro JM, Vasan RS. Predicting the **30-year risk of cardiovascular disease**: the framingham heart study. Circulation. 2009 Jun 23;119(24):3078-84. Epub 2009 Jun 8.
Pennells L, Kaptoge S, Wood A, et al. **Equalization of four cardiovascular risk algorithms after systematic recalibration**: individual-participant meta-analysis of 86 prospective studies. Eur Heart J. 2018 Nov 22.
Péquignot R, Dufouil C, Prugger C, et al. High Level of **Depressive Symptoms** at Repeated Study Visits and Risk of Coronary Heart Disease and Stroke over 10 Years in Older Adults: The Three-City Study. J Am Geriatr Soc. 2016 Jan;64(1):118-25.
Perissinotto CM, Stijacic Cenzer I, Covinsky KE. **Loneliness** in older persons: a predictor of functional decline and death. Arch Intern Med. 2012 Jul 23;172(14):1078-84.
Persell SD.; Zei C; Cameron KA.; et al. Potential Use of 10-Year and Lifetime **Coronary Risk Information** for Preventive Cardiology Prescribing Decisions: A Primary Care Physician Survey. *Arch Intern Med*. 2010;170(5):470-477.
Peters MJ, Symmons DP, McCarey D, et al. EULAR evidence-based recommendations for cardiovascular risk management in patients with **rheumatoid arthritis** and other forms of inflammatory arthritis. Ann Rheum Dis. 2009 Sep 22.
Peters SA, Woodward M. **Women's reproductive factors** and incident cardiovascular disease in the UK Biobank. Heart. 2018 Jan 15.
Peterson JC, Charlson ME, Wells MT, Altemus M. **Depression, coronary artery disease, and physical activity**: how much exercise is enough? Clin Ther. 2014 Nov 1;36(11):1518-30.
Petr EJ, Ayers CR, Pandey A, et al. **Perceived Lifetime Risk** for Cardiovascular Disease (from the Dallas Heart Study). Am J Cardiol. 2014 Apr 18.
Pickett CA, et al. Carotid bruits as a prognostic indicator of cardiovascular death and myocardial infarction: a meta-analysis. Lancet. 2008 May 10;371(9624):1587-94. **Auscultation for carotid bruits** in patients at risk for heart disease could help select those who might benefit the most from an aggressive modification strategy for cardiovascular risk.
Piercy KL, Troiano RP, Ballard RM, et al. **The Physical Activity Guidelines for Americans**. JAMA. 2018 Nov 12.
Piette JD, List J, Rana GK, et al. **Mobile Health Devices** as Tools for Worldwide Cardiovascular Risk Reduction and Disease Management. Circulation. 2015 Nov 24;132(21):2012-27.
Pikula A, Beiser AS, Decarli C, et al. Multiple **biomarkers** and risk of clinical and subclinical vascular brain injury:the framingham offspring study. Circulation. 2012 May 1;125(17):2100-7.
Pimenta E, Gaddam KK, Oparil S, et al. Effects of **Dietary Sodium Reduction** on Blood Pressure in Subjects With Resistant Hypertension. Results From a Randomized Trial. Hypertension. 2009 Jul 20. [Epub ahead of print]
Pimpin L, Wu JH, Haskelberg H, Del Gobbo L, Mozaffarian D. Is butter back? A systematic review and meta-analysis of **butter consumption** and risk of cardiovascular disease, diabetes, and total mortality. PLoS One. 2016;11:e0158118.
Pischon T, Boeing H, Hoffmann K, et al. General and abdominal adiposity and risk of death in Europe. N Engl J Med. 2008 Nov 13;359(20):2105-20. These data suggest that both general adiposity and abdominal adiposity are associated with the risk of death and support the use of **waist circumference or waist-to-hip ratio** in addition to **BMI** in assessing the risk of death.
Pittaras AM, Faselis C, Doumas M, et al. **Heart Rate at Rest, Exercise Capacity, and Mortality** Risk in Veterans. Am J Cardiol. 2013 Sep 12.
Pletcher MJ, Sibley CT, Pignone M, et al. Interpretation of the **Coronary Artery Calcium Score** in Combination With Conventional Cardiovascular Risk Factors: The Multi-Ethnic Study of Atherosclerosis (MESA). Circulation. 2013 Sep 3;128(10):1076-84.
Poldervaart JM, Reitsma JB, Backus BE, et al. Effect of Using the **HEART Score** in Patients With Chest Pain in the Emergency Department: A Stepped-Wedge, Cluster Randomized Trial. Ann Intern Med. 2017 Apr 25.
Polonsky Tamar S.; McClelland Robyn L.; Jorgensen Neal W.; et al. **Coronary Artery Calcium Score** and Risk Classification for Coronary Heart Disease Prediction. JAMA. 2010;303(16):1610-1616.
Pool LR, Burgard SA, Needham BL, Elliott MR, Langa KM, Mendes de Leon CF. Association of a **negative wealth shock** with all-cause mortality in middle-aged and older adults in the United States [April 3, 2018].JAMA. doi:10.1001/jama .2018.2055
Poole R, Kennedy OJ, Roderick P, et al. **Coffee consumption** and health: umbrella review of meta-analyses of multiple health outcomes**.** BMJ. 2017 Nov 22;359:j5024.
Poornima IG, et al; WHI and WHI-CAC Study Investigators. **Coronary Artery Calcification(CAC)** and Post-Trial Cardiovascular Events and Mortality Within the Women's Health Initiative (WHI) Estrogen-Alone Trial. J Am Heart Assoc. 2017 Oct27;6(11).
Postley JE, Luo Y, Wong ND, et al. Identification by **Ultrasound Evaluation** of the Carotid and Femoral Arteries of High-Risk Subjects Missed by Three Validated Cardiovascular Disease Risk Algorithms. Am J Cardiol. 2015 Sep 5.
Poti JM, Dunford EK, Popkin BM. **Sodium reduction** in US households' packaged food and beverage purchases, 2000 to 2014 [online June 5, 2017].JAMA Intern Med. doi:10.1001 /jamainternmed.2017.1407
Poti JM, Dunford EK, Popkin BM. **Sodium reduction** in US households' packaged food and beverage purchases, 2000 to 2014 [online June 5, 2017].JAMA Intern Med. doi:10.1001 /jamainternmed.2017.1407
Prasad V, Vandross A. Cardiovascular **primary prevention**: **How high should we set the bar**? Arch Intern Med 2012; 172:656-659.
Preis SR, Massaro JM, Hoffmann U, et al. **Neck Circumference** as a Novel Measure of Cardiometabolic Risk: The Framingham Heart Study. J Clin Endocrinol Metab. 2010 May 19.
Prince SA, Blanchard CM, Grace SL, Reid RD. Objectively-measured **sedentary time** and its association with markers of cardiometabolic health and fitness among cardiac rehabilitation graduates. *Eur J Prev Cardiol* 2015.
Pulkki-Råbach L, Elovainio M, Hakulinen C, et al. **Cumulative effect of psychosocial factors** in youth on ideal cardiovascular health in adulthood: the Cardiovascular Risk in Young Finns Study. Circulation. 2015;131:245–253.
Pulsford RM, Stamatakis E, Britton AR, et al. Associations of **sitting behaviours** with all-cause mortality over a 16-year follow-up: the Whitehall II study. Int J Epidemiol. 2015 Oct 9.
Pussinen PJ, Paju S, Koponen J, et al. Association of **Childhood Oral Infections With Cardiovascular Risk Factors** and Subclinical Atherosclerosis in Adulthood. JAMA Netw Open. 2019 Apr 5;2(4):e192523.
Qaseem A, Wilt TJ, Rich R, et al. Pharmacologic treatment of **hypertension in adults aged 60 years or older to higher versus lower blood pressure targets**: a clinical practice guideline from the American College of Physicians (**ACP**) and the American Academy of Family Physicians (**AAFP**). Ann Intern Med. 2017. [Epub ahead of print]. doi:10.7326/M16-1785
Qi L, Qi Q, Prudente S, et al. Association between a genetic variant related to **glutamic acid** metabolism and coronary heart disease in individuals with type 2 diabetes. JAMA 2013.
Qin C, Lv J, Guo Y, et al. Associations of **egg consumption with cardiovascular disease** in a cohort study of 0.5 million Chinese adults. Heart. 2018 May 21.
Qureshi N, Armstrong S, Dhiman P, et al. Effect of adding **systematic family history enquiry** to cardiovascular disease risk assessment in primary care. Ann Intern Med 2012; 156:253-262.
Rådholm K, Chalmers J, Ohkuma T, et al. Use of the **waist-to-height-ratio** to predict cardiovascular risk in patients with diabetes: results from ADVANCE-ON. Diabetes Obes Metab. 2018 Mar 30.
Radford NB, DeFina LF, et al. **Cardiorespiratory fitness, coronary artery calcium, and cardiovascular disease events** in a cohort of generally healthy, middle-age men: results from the Cooper Center longitudinal study. Circulation. 2018;137:1888–1895.
Rai M, Baker WL, Parker MW, et al. Meta-analysis of optimal **risk stratification in patients >65 years of age**. Am J Cardiol. 2012 Oct 15;110(8):1092-9.
Ramsden CE, Zamora D, Leelarthaepin B, et al. Use of **dietary linoleic acid** for secondary prevention of coronary heart disease and death: evaluation of recovered data from the Sydney Diet Heart Study and updated meta-analysis. BMJ 2013;346:e8707.
Ramsden CE, Zamaora D, Majchrzak-Hong S, et al. Re-evaluation of the **traditional diet-heart hypothesis**: analysis of recovered data from Minnesota Coronary Experiment (1968-73). BMJ 2016;352:i1246.
Rana JS, Gransar H, Wong ND, et al. Comparative Value of **Coronary Artery Calcium and Multiple Blood Biomarkers** for Prognostication of Cardiovascular Events. Am J Cardiol. 2012 Mar 15.
Rana JS, Tabada GH, Solomon MD, et al. Accuracy of the Atherosclerotic Cardiovascular **Risk Equation** in a Large Contemporary, Multiethnic Population. J Am Coll Cardiol. 2016 May 10;67(18):2118-30.
Rana JS, Tabada GH, Solomon MD, et al. **Accuracy of the Atherosclerotic Cardiovascular Risk Equation** in a Large Contemporary, Multiethnic Population. J Am Coll Cardiol. 2016 May 10;67(18):2118-30.
Rankin P, Morton DP, Diehl H, et al. Effectiveness of a **Volunteer-Delivered Lifestyle Modification Program** for Reducing Cardiovascular Disease Risk Factors. Am J Cardiol. 2011 Sep 23.
Ranthe MV, Winkel BG, Andersen EW, et al. Risk of cardiovascular disease in **family members of young sudden cardiac death victims**. Eur Heart J 2012 .

Rao G, Powell-Wiley TM, Ancheta I, et al. Identification of **Obesity and Cardiovascular Risk in Ethnically and Racially Diverse Populations**: A Scientific Statement From the **American Heart Association**. Circulation. 2015 Jul 6.

Rasella D, Harhay MO, Pamponet ML, et al. **Impact of primary health care** on mortality from heart and cerebrovascular diseases in Brazil: a nationwide analysis of longitudinal data. BMJ. 2014 Jul 3;349:g4014.

Rasmussen-Torvik LJ, Shay CM, Abramson JG, et al. **Ideal cardiovascular health is inversely associated with incident cancer**: the Atherosclerosis Risk in Communities Study. Circulation. 2013;127:1270–1275.

Ratchford EV, Carson KA, Jones SR, et al. Usefulness of **coronary and carotid imaging** rather than traditional atherosclerotic risk factors to identify firefighters at increased risk for cardiovascular disease. Am J Cardiol. 2014 May 1;113(9):1499-504.

Ravi B, Croxford R, Austin PC, et al. The relation between **total joint arthroplasty and risk for serious cardiovascular events** in patients with moderate-severe osteoarthritis: propensity score matched landmark analysis. BMJ. 2013 Oct 30;347:f6187.

Record NB, Onion DK, Prior RE, et al. **Community-wide cardiovascular disease prevention programs** and health outcomes in a rural county, 1970-2010. JAMA. 2015 Jan 13;313(2):147-55.

Reddigan JI, Ardern CI, Riddell MC, Kuk JL. Relation of **Physical Activity** to Cardiovascular Disease Mortality and the Influence of Cardiometabolic Risk Factors. Am J Cardiol. 2011 Aug 17.

Rees K,Hartley L,DayC, FlowersN,ClarkeA, Stranges S. **Selenium supplementation** for the primary prevention of cardiovascular disease. CochraneDatabase of Systematic Reviews 2013, Issue 1. Art.No.: CD009671. DOI: 10.1002/14651858.CD009671.pub2. The limited trial evidence that is available to date does not support the use of selenium supplements in the primary prevention of CVD.

Rees K, Dyakova M, Ward K, et al. **Dietary advice** for reducing cardiovascular risk. Cochrane Database Syst Rev. 2013 Mar 28;3:CD002128. doi: 10.1002/14651858.CD002128.pub4. Dietary advice appears to be effective in bringing about modest beneficial changes in diet and cardiovascular risk factors over approximately 12 months, but longer-term effects are not known.

Rees K, Hartley L, Flowers N, Clarke A, Hooper L, Thorogood M, Stranges S. **'Mediterranean' dietary pattern** for the primary prevention of cardiovascular disease. Cochrane Database of Systematic Reviews 2013, Issue 8. Art. No.: CD009825. DOI:10.1002/14651858.CD009825.pub2. The limited evidence to date suggests some favourable effects on cardiovascular risk factors.

Rees K, Takeda A, Martin N, et al. **Mediterranean-style diet** for the primary and secondary prevention of cardiovascular disease. Cochrane Database Syst Rev. 2019 Mar 13;3:CD009825.

Rees-Punia E, Evans EM, Schmidt MD, et al. Mortality **Risk Reductions for Replacing Sedentary Time** With Physical Activities. Am J Prev Med. 2019 May;56(5):736-741.

Reichkendler MH, Rosenkilde M, Auerbach PL, et al. Only minor additional metabolic health benefits of **high as opposed to moderate dose physical exercise** in young, moderately overweight men. Obesity (Silver Spring). 2014 May;22(5):1220-32.

Reid RD, McDonnell LA, Riley DL, et al. Effect of an intervention to improve the cardiovascular health of **family members of patients with coronary artery disease**: a randomized trial. CMAJ. 2013 Nov 18.

Rein P, Saely CH, Vonbank A, et al. Impact of the **albumin to creatinine ratio** and the coronary artery state on vascular events. Am J Cardiol. 2014 May 15;113(10):1616-20.

Reinhart RA. Robert E. **Lee's Right Ear and the Relation of Earlobe Crease** to Coronary Artery Disease. Am J Cardio. 2017.

Restrepo BJ, Rieger M. Denmark's Policy on **Artificial Trans Fat** and Cardiovascular Disease. Am J Prev Med. 2015 Aug 26.

Retnakaran, Ravi, Shah, Baiju R. **Mild glucose intolerance in pregnancy** and risk of cardiovascular disease: a population-based cohort study. CMAJ 2009 0: cmaj.090569

Reynolds A, Mann J, Cummings J, et al. **Carbohydrate quality and human health**: a series of systematic reviews and meta-analyses. Lancet. 2019 Jan 10.

Rhee JJ, Kim E, Buring JE, Kurth T. **Fish consumption, omega-3 fatty acids**, and risk of cardiovascular disease. Am J Prev Med 2016.

Rich-Edwards JW, Mason S, Rexrode K, et al. **Physical and sexual abuse** in childhood as predictors of early-onset cardiovascular events in women. Circulation. 2012 Aug 21;126(8):920-7.

Richards SH, Anderson L, Jenkinson CE, et al. **Psychological interventions** for coronary heart disease. Cochrane Database of Systematic Reviews 2017, Issue 4. Art. No.: CD002902 This updated Cochrane Review found that for people with CHD, there was no evidence that psychological treatments had an effect on total mortality, the risk of revascularisation procedures, or on the rate of non-fatal MI, although the rate of cardiac mortality was reduced and psychological symptoms (depression, anxiety, or stress) were alleviated; however, the GRADE assessments suggest considerable uncertainty surrounding these effects. Considerable uncertainty also remains regarding the people who would benefit most from treatment (i.e. people with or without psychological disorders at baseline) and the specific components of successful interventions. Future large-scale trials testing the effectiveness of psychological therapies are required due to the uncertainty within the evidence. Future trials would benefit from testing the impact of specific (rather than multifactorial) psychological interventions for participants with CHD, and testing the targeting of interventions on different populations (i.e. people with CHD, with or without psychopathologies).

Richards SH, Anderson L, Jenkinson CE, et al. **Psychological interventions for coronary heart disease**. Cochrane Database Syst Rev. 2017 Apr 28;4:CD002902. This updated Cochrane Review found that for people with CHD, there was no evidence that psychological treatments had an effect on total mortality, the risk of revascularisation procedures, or on the rate of non-fatal MI, although the rate of cardiac mortality was reduced and psychological symptoms (depression, anxiety, or stress) were alleviated; however, the GRADE assessments suggest considerable uncertainty surrounding these effects. Considerable uncertainty also remains regarding the people who would benefit most from treatment (i.e. people with or without psychological disorders at baseline) and the specific components of successful interventions. Future large-scale trials testing the effectiveness of psychological therapies are required due to the uncertainty within the evidence. Future trials would benefit from testing the impact of specific (rather than multifactorial) psychological interventions for participants with CHD, and testing the targeting of interventions on different populations (i.e. people with CHD, with or without psychopathologies).

Richards SH, Anderson L, et al. **Psychological interventions** for coronary heart disease: Cochrane systematic review and meta-analysis. Eur J Prev Cardiol. 2018 Feb;25(3):247-259.

Richardson S, Shaffer JA, Falzon L, et al. Meta-Analysis of Perceived **Stress** and Its Association With Incident Coronary Heart Disease. Am J Cardiol. 2012 Sep 10.

Rico-CampàA, Martínez-GonzálezMA, Alvarez-Alvarezl, etal . Association between **consumption of ultra-processed foods and all cause mortality**: SUN prospective cohort study. BMJ 2019;365:l1949.

Ridker PM, Everett BM, Pradhan A, et al; CIRT Investigators. **Low-Dose Methotrexate for the Prevention of Atherosclerotic Events**. N Engl J Med. 2018 Nov 10.

Ridker PM, Paynter NP, Rifai N, et al. C-reactive protein and parental history improve global cardiovascular risk prediction: the **Reynolds risk score** for men. Circulation. 2008 Nov 25;118(22):2243-51. Epub 2008 Nov 9. As previously shown in women, a prediction model in men that incorporates high-sensitivity C-reactive protein and parental history significantly improves global cardiovascular risk prediction.

Rifkin DE, Shlipak MG, Katz R, et al. Rapid **kidney function** decline and mortality risk in older adults. Arch Intern Med. 2008 Nov 10;168(20):2212-8. Rapid decline in eGFR is associated with an increased risk of cardiovascular and all-cause mortality in older adults, independent of baseline eGFR and other demographic variables.

Rimm EB, Appel LJ, Chiuve SE, et al. Seafood Long-Chain **n-3 Polyunsaturated Fatty Acids and Cardiovascular Disease**: A Science Advisory From the American Heart Association. Circulation. 2018 May 17.

Ripatti S, Tikkanen E, Orho-Melander M, et al. A **multilocus genetic risk score** for coronary heart disease: case-control and prospective cohort analyses. Lancet. 2010 Oct 23;376(9750):1393-400.

Risk and Prevention Study Collaborative Group. **n-3 fatty acids** (omega) in patients with multiple cardiovascular risk factors. N Engl J Med 2013 May 9; 368:1800.

RitcheyMD, Loustalot F, Bowman BA, Hong Y. **Trends in mortality** rates by subtypes of **heart disease in the United States, 2000-2010**. JAMA.doi:10.1001/jama.2014.11344.

Rizos EC, Ntzani EE, Bika E, et al. Association between **omega-3 fatty acid supplementation** and risk of major cardiovascular disease events: a systematic review and meta-analysis. JAMA. 2012 Sep 12;308(10):1024-33.

Rizzuto D, Orsini N, Qiu C, et al. **Lifestyle, social factors**, and survival after age 75: population based study. BMJ. 2012 Aug 29;345:e5568.

Roberts R. Genetic Risk Stratification: **Tipping Point for Global Primary Prevention of Coronary Artery Disease**. Circulation. 2018 Jun 12;137(24):2554-2556.

Rocco PTP, Bensenor IM, Griep RH, et al. **Job Strain** and Cardiovascular Health Score (from the Brazilian Longitudinal Study of Adult Health [ELSA-Brasil] Baseline). Am J Cardiol. 2017 Jul 15;120(2):207-212.

Rockette-Wagner B, Storti KL, Dabelea D, et al. **Activity and Sedentary Time** 10 Years After a Successful **Lifestyle Intervention**: The Diabetes Prevention Program (**DPPOS**). Am J Prev Med. 2017 Mar;52(3):292-299.

Rockwood, Kenneth, Song, Xiaowei, Mitnitski, Arnold. Changes in relative **fitness and frailty** across the adult lifespan: evidence from the Canadian National Population Health Survey. CMAJ 2011 183: E487-494

Rodriguez CJ. **Disparities in ideal cardiovascular health**: a challenge or an opportunity? Circulation. 2012 Jun 19;125(24):2963-4.

Rodríguez-López C, Garlito-Díaz H, Madroñero-Mariscal R, et al. **Earlobe Crease** Shapes and Cardiovascular Events. Am J Cardiol. 2015 Jul 15;116(2):286-93.

Rognmo Ø, Moholdt T, Bakken H, Hole T, Mølstad P, Myhr NE, Grimsmo J, Wisløff U. Cardiovascular risk of **high- versus moderate intensity aerobic exercise** in coronary heart disease patients. Circulation. 2012;126:1436 –1440.

Rohrmann S, Overvad K, Bueno-de-Mesquita HB, et al. **Meat consumption** (processed meat) and mortality. Results from the European Prospective Investigation into Cancer and Nutrition. BMC Med 2013.

Rong S, Snetselaar LG, Xu G, et al. **Association of Skipping Breakfast With Cardiovascular and All-Cause Mortality**. J Am Coll Cardiol. 2019 Apr 30;73(16):2025-2032.

Rong Y, Chen L, Zhu T, et al. **Egg consumption** and risk of coronary heart disease and stroke: dose-response meta-analysis of prospective cohort studies. BMJ. 2013 Jan 7;346:e8539.

Ronksley PE, Brien SE, Turner BJ, et al. Association of alcohol consumption with selected cardiovascular disease outcomes: a systematic review and meta-analysis. BMJ 2011; DOI:10.1136/bmj.d671.

Rosenzweig JL, Bakris GL, Berglund LF, et al. **Primary Prevention of ASCVD and T2DM in Patients at Metabolic Risk**: An Endocrine Society* Clinical Practice Guideline. J Clin Endocrinol Metab. 2019 Jul 31.

Ross R, Hudson R, Stotz PJ, Lam M. Effects of **exercise amount and intensity** on abdominal obesity and glucose tolerance in obese adults. A randomized trial. Ann Intern Med. 2015;162:325-34.

Rostamian S, van Buchem MA, Westendorp RG, et al **Executive function, but not memory**, associates with incident coronary heart disease and stroke. Neurology. 2015 Aug 5.

Roth GA, Huffman MD, Moran AE, et al. **Global and Regional Patterns in Cardiovascular Mortality** From 1990 to 2013. Circulation. 2015 Oct 27;132(17):1667-78.

Roth GA, Dwyer-Lindgren L, Bertozzi-Villa A, et al. **Trends and patterns of geographic variation** in cardiovascular mortality among US counties, 1980-2014.JAMA. doi:10.1001/jama.2017.4150

Rovio SP, Pahkala K, Nevalainen J, et al. **Cardiovascular Risk Factors From Childhood and Midlife Cognitive Performance**: The Young Finns Study. J Am Coll Cardiol. 2017 May 9;69(18):2279-2289

Rozanski A, Gransar H, Shaw LJ, et al. Impact of **coronary artery calcium scanning** on coronary risk factors and downstream testing. J Am Coll Cardiol 2011; DOI:10.1016/j.jacc.2011.01.019.

Ruidavets Jean-Bernard, Ducimetière Pierre, Evans Alun, et al. Patterns of **alcohol consumption** and ischaemic heart disease in culturally divergent countries: the Prospective Epidemiological Study of Myocardial Infarction (PRIME) . BMJ 341:doi:10.1136/bmj.c6077 (Published 23 Nov 2010)

Ruiz JR, Sui X, Lobelo F, Morrow JR Jr, Jackson AW, Sjöström M, Blair SN. Association between **muscular strength** and mortality in men: prospective cohort study. BMJ. 2008 Jul 1;337:a439. doi: 10.1136/bmj.a439. Muscular strength is inversely and independently associated with death from all causes and cancer in men, even after adjusting for cardiorespiratory fitness and other potential confounders.

Rumsfeld JS, Alexander KP, Goff DC, et al. **Cardiovascular health**: the importance of measuring patient-reported health status.Circulation 2013.

Russ TC, Stamatakis E, Hamer M et al. Association between **psychological distress** and mortality: individual participant pooled analysis of 10 prospective cohort studies. BMJ. 2012 Jul 31;345:e4933.

Russell-Jones R. **Air pollution** in the UK: better ways to solve the problem. BMJ. 2017 Jun 14;357:j2713.

Ruwald MH, Numé AK, Lamberts M, et al. Incidence and influence of **hospitalization for recurrent syncope** and its effect on short- and long-term all-cause and cardiovascular mortality. Am J Cardiol. 2014 May 15;113(10):1744-50.

Ruzicka M, Hiremath S, Steiner S, et al. What is the feasibility of implementing effective **sodium reduction strategies** to treat hypertension in primary care settings? A systematic review. J Hypertens. 2014 Apr 2.

Rydén L, Buhlin K, Ekstrand E, et al. **Periodontitis** increases the risk of a first myocardial infarction: A report from the PAROKRANK study.*Circulation* 2016.

Sabanayagam C; Shankar A. **Sleep duration** and cardiovascular disease: Results from the National Health Interview Survey. Sleep 2010; 33:1037-1042.

Sacco Ralph L.. Achieving **Ideal Cardiovascular and Brain Health**: Opportunity Amid Crisis: Presidential Address at the American Heart Association (**AHA**)2010 Scientific Sessions. Circulation 123: 2653-2657, doi:10.1161/CIR.0b013e318220dec1

Sacks FM, Lichtenstein AH, Wu JHY, et al. Dietary **Fats and Cardiovascular Disease**: A Presidential Advisory From the American Heart Association. Circulation. 2017 Jun 15.

Saeidifard F, Medina-Inojosa JR, Supervia M, et al. Differences of energy expenditure while **sitting versus standing**: A systematic review and meta-analysis. Eur J Prev Cardiol. 2018 Jan 1:2047487317752186.

Safford MM, Brown TM, Muntner PM, et al; for the REGARDS Investigators. Association of **Race and Sex With Risk of Incident Acute Coronary Heart Disease** Events. JAMA. 2012 Nov 7;308(17):1768-1774.

Said MA, Verweij N, van der Harst P. Associations of Combined **Genetic and Lifestyle Risks** With Incident **Cardiovascular Disease and Diabetes** in the UK Biobank Study. JAMA Cardiol. 2018 Jun 27.

Saigal CS, Gore JL, Krupski TL, Hanley J, Schonlau M, Litwin MS; and the Urologic Diseases in America Project. **Androgen deprivation** therapy increases cardiovascular morbidity in men with prostate cancer. Cancer 2007;110:1493-500.

Saint-Maurice PF, Coughlan D, Kelly SP, et al. Association of **Leisure-Time Physical Activity** Across the Adult Life Course With All-Cause and Cause-Specific Mortality. JAMA Netw Open. 2019 Mar 1;2(3):e190355.

Sallis JF, Floyd MF, Rodríguez DA et al. Role of **built environments** in physical activity, obesity, and cardiovascular disease. Circulation. 2012 Feb 7;125(5):729-37.

Sallis JF, Cerin E, Conway TL, et al. **Physical activity** in relation to **urban environments** in 14 cities worldwide: a cross-sectional study. Lancet 2016; online April 1.

Samieri C, Sun Q, Townsend MK, et al. The association between **dietary patterns** at midlife and health in aging: an observational study. Ann Intern Med. 2013 Nov 5;159(9):584-91.

Sandbakk S, Nauman J, Zisko N, et al. **Sedentary time, cardiorespiratory fitness and cardiovascular risk factor** clustering in older adults—the **Generation 100 study**. *Mayo Clinic Proc* 2016.

Sands M, Loucks EB, Lu B, et al. Self-reported **Snoring** and Risk of Cardiovascular Disease Among Postmenopausal Women (from the Women's Health Initiative). Am J Cardiol. 2012 Dec 4.

Santschi V, Chiolero A, Burnand B, et al. Impact of **Pharmacist Care** in the Management of Cardiovascular Disease Risk Factors: A Systematic Review and Meta-analysis of Randomized Trials. Arch Intern Med. 2011 Sep 12;171(16):1441-53.

Satija A, Bhupathiraju SN, Spiegelman D, et al. Healthful and unhealthful **plant-based diets** and the risk of coronary heart disease in U.S. adults. J Am Coll Cardiol 2017;70:411–22.

Sattelmair JR, Kurth T, Buring JE, et al. **Physical activity** and risk of stroke in women. Stroke 2010; 41:1243-1250.

Sattelmair J, Pertman J, Ding EL, et al. **Dose response between physical activity and risk** of coronary heart disease. A meta-analysis. Circulation 2011; DOI: 10.1161/CIRCULATIONAHA.110.010710.

Schreier HM, Schonert-Reichl KA, Chen E. Effect of **Volunteering** on Risk Factors for Cardiovascular Disease in Adolescents: A Randomized Controlled Trial. JAMA Pediatr. 2013 Feb 25:1-6.

Scherrer U, Rimoldi SF, Rexhaj E, Stuber T, Duplain H, et al. Systemic and pulmonary vascular dysfunction in children conceived by **assisted reproductive technologies**. Circulation. 2012;125:1890 –1896.

Schmidt M, Jacobsen JB, et al. **25 year trends in first time hospitalisation** for acute myocardial infarction, subsequent short and long term mortality, and the prognostic impact of sex and comorbidity: a Danish nationwide cohort study. BMJ 2012;344:e356.

Schnabel L, Kesse-Guyot E, Allès B, et al. Association Between **Ultraprocessed Food Consumption and Risk of Mortality** Among Middle-aged Adults in France. JAMA Intern Med. 2019 Feb 11.

Schneider RH, Grim CE, Rainforth MV, et al. **Stress reduction** in the secondary prevention of cardiovascular disease (**Transcendental Meditation**). Circ Cardiovasc Qual Outcomes 2012.

Schnohr P, O'Keefe JH, Marott JL, Lange P, Jensen GB. **Dose of jogging and long-term mortality**: the copenhagen city heart study. J Am Coll Cardiol. 2015 Feb 10; 65(5):411-9.

Schoos MM, Sejersten M, Baber U, et al. Outcomes of **patients calling emergency medical services** for suspected acute cardiovascular disease. Am J Cardiol. 2015 Jan 1;115(1):13-20.

Schroeder EC, Welk GJ, Franke WD, et al. Associations of **Health Club Membership with Physical Activity** and Cardiovascular Health. PLoS One. 2017 Jan 20;12(1):e0170471.

Schultz SA, Boots EA, Darst BF, et al. **Cardiorespiratory fitness** alters the influence of a **polygenic risk score** on biomarkers of AD. Neurology. 2017 Mar 24.

Schultz WM, Hayek SS, Samman Tahhan A, et al. **Marital Status** and Outcomes in Patients With Cardiovascular Disease. J Am Heart Assoc. 2017 Dec 20;6(12).

Schulze MB, Martínez-González MA, Fung TT, et al. Food based **dietary patterns and chronic disease prevention**. BMJ. 2018 Jun 13;361:k2396.

Schuna JM Jr, Swift DL, Hendrick CA, et al. Evaluation of a **workplace treadmill desk intervention**: a randomized controlled trial. J Occup Environ Med. 2014 Dec;56(12):1266-76.

Schwalm JD, McKee M, Huffman MD, Yusuf S. **Resource Effective Strategies to Prevent** and Treat Cardiovascular Disease. Circulation. 2016 Feb 23;133(8):742-755.

Scirica BM, Bhatt DL, Braunwald E, et al. Prognostic Implications of **Biomarker Assessments** in Patients With Type 2 **Diabetes** at **High Cardiovascular Risk**: A Secondary Analysis of a Randomized Clinical Trial. JAMA Cardiol. 2016 Sep 28.

Scourboutakos MJ, Semnani-Azad Z, L'Abbe MR. **Restaurant meals**: almost a full day's worth of calories, fats, and sodium. JAMA Intern Med 2013; online May 13, 2013.

Sebastian RS, Wilkinson Enns C, et al. **Sandwiches Are Major Contributors of Sodium** in the Diets of American Adults: Results from What We Eat in America, National Health and Nutrition Examination Survey 2009-2010. J Acad Nutr Diet. 2014 Oct 6.

See VHL, Mori TA, Prescott SL, et al. **Cardiometabolic Risk Factors at 5 Years After Omega-3 Fatty Acid Supplementation in Infancy**. Pediatrics. 2018 Jun 8.

Seely D, Szczurko O, Cooley K, et a. **Naturopathic medicine** for the prevention of cardiovascular disease: a randomized clinical trial.CMAJ 2013; DOI:10.1503/cmaj.120567

Seferidi P, Laverty AA, Pearson-Stuttard J, et al. **Impacts of Brexit on fruit and vegetable intake and cardiovascular disease** in England: a modelling study. BMJ Open. 2019 Jan 28;9(1):e026966.

Seidelmann SB, Claggett B, Bravo PE, et al. **Retinal Vessel Calibers** in Predicting Long-term Cardiovascular Outcomes: The Atherosclerosis Risk in Communities Study. Circulation. 2016 Sep 28. pii: CIRCULATIONAHA.116.023425.

Seidelmann SB, Claggett B, Cheng S, et al. **Dietary carbohydrate intake and mortality**: a prospective cohort study and meta-analysis. Lancet Public Health 2018; online Aug 16.

Selvin E, Rawlings AM, Lutsey PL, et al. **Fructosamine and Glycated Albumin** and the Risk of Cardiovascular Outcomes and Death. Circulation. 2015 Jul 28;132(4):269-77.

Semba RD, Ferrucci L, Bartali B, et al. **Resveratrol** Levels and All-Cause Mortality in Older Community-Dwelling Adults. JAMA Intern Med. 2014 May 12.

Sénéchal M, Wicklow B, Wittmeier K, et al. **Cardiorespiratory Fitness and Adiposity** in Metabolically Healthy Overweight and Obese Youth. Pediatrics. 2013 Jun 24.

Seron P, Lanas F, Pardo Hernandez H, Bonfill Cosp X. **Exercise for people with high cardiovascular risk**. Cochrane Database of Systematic Reviews 2014, Issue 8. Art. No.: CD009387. DOI: 10.1002/14651858.CD009387.pub2. Evidence to date is entirely limited to small studies with regard to sample size, short-term follow-up, and high risk of methodological bias, which makes it difficult to derive any conclusions on the efficacy or safety of aerobic or resistance exercise on groups with increased cardiovascular risk or in individuals with two or more coexisting risk factors. Further randomized clinical trials assessing controlled exercise programmes on total cardiovascular risk in individuals are warranted.

Shah AJ, Ghasemzadeh N, Zaragoza-Macias E, et al. **Sex and age differences in the association of depression** with obstructive coronary artery disease and adverse cardiovascular events. J Am Heart Assoc. 2014 Jun 18;3(3).

Shah AJ, Vaccarino V, Janssens AC, et al. An **Electrocardiogram-Based** Risk Equation for Incident Cardiovascular Disease From the National Health and Nutrition Examination Survey. JAMA Cardiol. 2016 Aug 3

Shah AM, Claggett B, Folsom AR, et al. **Ideal cardiovascular health during adult life** and cardiovascular structure and function among the elderly. *Circulation* 2015.

Shah AS, Dolan LM, Gao Z, Kimball TR, Urbina EM. **Clustering of Risk Factors:** A Simple Method of Detecting Cardiovascular Disease in Youth. Pediatrics. 2011 Jan 17.

Shah NS, Lloyd-Jones DM, O'Flaherty M, et al. **Trends in Cardiometabolic Mortality** in the United States, 1999-2017. JAMA. 2019 Aug 27;322(8):780-782.

Shah RV, Murthy VL, Colangelo LA, et al. Association of **fitness in young** adulthood with survival and cardiovascular risk: the Coronary Artery Risk Development in Young Adults (CARDIA) Study [online November 30, 2015].JAMA Intern Med.

Shan Z, Li Y, Zong G, et al. Rotating **night shift work and adherence to unhealthy lifestyle** in predicting risk of type 2 diabetes: results from two large US cohorts of female nurses. BMJ. 2018 Nov 21;363:k4641.

Shankar A, Xiao J, Ducatman A. **Perfluorooctanoic acid** and cardiovascular disease in US adults [published online September 3, 2012]. Arch Intern Med. doi:10.1001/archinternmed.2012.3393.

Shaw LJ, Giambrone AE, Blaha MJ, et al. Long-Term Prognosis After **Coronary Artery Calcification Testing in Asymptomatic Patients**: A Cohort Study. Ann Intern Med. 2015 Jul 7;163(1):14-21.

Shaw LJ, Min JK, Nasir K, et al. **Sex differences in calcified plaque** and long-term cardiovascular mortality: observations from the CAC Consortium. Eur Heart J. 2018 Nov 1;39(41):3727-3735.

Shay CM, Ning H, Allen NB et al. Status of Cardiovascular Health in **US Adults: Prevalence Estimates** From the National Health and Nutrition Examination Surveys (NHANES) 2003-2008. Circulation. 2012 Jan 3;125(1):45-56.

Shay CM, Ning H, Daniels SR, et al. Status of Cardiovascular Health in **US Adolescents**: **Prevalence Estimates** From the National Health and Nutrition Examination Surveys (NHANES) 2005-2010. Circulation. 2013 Apr 2;127(13):1369-76.

Sheikh N, Papadakis M, Ghani S, et al. Comparison of **electrocardiographic criteria** for the detection of cardiac abnormalities in elite black and white athletes. Circulation. 2014 Apr 22;129(16):1637-49.

Shemesh J, Motro M, Morag-Koren N et al. Relation of **Coronary Artery Calcium** to Cardiovascular Risk in Patients With Combined Diabetes Mellitus and Systemic Hypertension. Am J Cardiol. 2011 Dec 21.

Shen J, Wong KT, Cheng IT, et al. Increased prevalence of coronary plaque in patients with **psoriatic arthritis** without prior diagnosis of coronary artery disease. Ann Rheum Dis. 2017 Jul;76(7):1237-1244

Sheppard JP, Singh S, Fletcher K, et al. Impact of **age and sex** on primary preventive treatment for cardiovascular disease in the West Midlands, UK:cross sectional study. BMJ. 2012 Jul 12;345:e4535.

Sheridan Stacey L.; Viera Anthony J.; Krantz Mori J.; et al. for the Cardiovascular Health Intervention Research and Translation Network Work Group on Global Coronary Heart Disease Risk. The Effect of **Giving Global Coronary Risk Information to Adults**: A Systematic Review. Arch Intern Med. 2010;170(3):230-239.

Sheridan SL. **Global risk** of coronary heart disease: assessment and application. Am Fam Physician. 2010 Aug 1;82(3):265-74.

Shibata S, Fujimoto N, Hastings JL, et al. The effect of **lifelong exercise frequency on arterial stiffness**. J Physiol. 2018 May 20.

Shikany JM, Safford MM, Newby PK, et al. **Southern Dietary Pattern** is Associated with Hazard of Acute Coronary Heart Disease in the Reasons for Geographic and Racial Differences in Stroke (REGARDS) Study. Circulation. 2015 Aug 10.

Shirakawa T, Iso H, Yamagishi K, et al. **Watching Television and Risk of Mortality From Pulmonary Embolism** Among Japanese Men and Women: The JACC Study (Japan Collaborative Cohort). Circulation. 2016 Jul 26;134(4):355-7.

Shiroma EJ, Lee IM, Schepps MA, et al. **Physical Activity Patterns and Mortality**: The Weekend Warrior and Activity Bouts. Med Sci Sports Exerc. 2019 Jan;51(1):35-40.

Shmilovich H, Cheng VY, Rajani R, et al. **Relation of diagonal ear lobe crease** to the presence, extent, and severity of coronary artery disease determined by coronary computed tomography angiography. Am J Cardiol. 2012 May 1;109(9):1283-7.

Shockey TM, Sussell AL, Odom EC. Cardiovascular Health Status by **Occupational** Group - 21 States, 2013. MMWR Morb Mortal Wkly Rep. 2016 Aug 12;65(31):793-798.

Shreibati JB, Baker LC, Hlatky MA. Association of **coronary CT angiography or stress testing** with subsequent utilization and spending among Medicare beneficiaries. JAMA. 2011;306(19):2128-2136

Shrestha N, Ijaz S, Kukkonen-Harjula KT, Kumar S, Nwankwo CP. **Workplace interventions for reducing sitting at work**. Cochrane Database of Systematic Reviews 2015, Issue 1. Art. No.: CD010912. DOI: 10.1002/14651858.CD010912.pub2.
At present there is very low quality evidence that sit-stand desks can reduce sitting time at work, but the effects of policy changes and information and counselling are inconsistent. There is a need for high quality cluster-randomised trials to assess the effects of different types of interventions on objectively measured sitting time. There are many ongoing trials that might change these conclusions in the near future.

Sidney S, Quesenberry CP Jr, Jaffe MG, Sorel M, et al. Recent **Trends** in Cardiovascular Mortality in the United States and Public Health Goals. JAMA Cardiol. 2016 Jun 29.

Siegel KR, McKeever Bullard K, Imperatore G, et al. Association of higher consumption of foods derived from **subsidized commodities** with adverse cardiometabolic risk among US adults [online July 5, 2016].JAMA Intern Med.

Sieri S, Krogh V, Berrino F, et al. **Dietary glycemic load** and index and risk of coronary heart disease in a large italian cohort: the EPICOR study. Arch Intern Med. 2010 Apr 12;170(7):640-7.

Sigurdardottir FD, Lyngbakken MN, Holmen OL, et al. Relative Prognostic Value of Cardiac **Troponin** I and **C-Reactive Protein** in the General Population (from the Nord-Trøndelag Health [HUNT] Study). Am J Cardiol. 2018 Apr 15;121(8):949-955.

Silverman MG, Blaha MJ, Krumholz HM, et al. Impact of **coronary artery calcium** on coronary heart disease events in individuals at the extremes of traditional risk factor burden: the Multi-Ethnic Study of Atherosclerosis. Eur Heart J. 2013 Dec 23.

Silverwood RJ, Forbes HJ, Abuabara K, et al . Severe and predominantly active **atopic eczema in adulthood and long-term risk of cardiovascular disease**: population based cohort study. BMJ 2018;361:k1786. 10.1136/bmj.k1786

Silvestre OM, Nadruz W Jr, Querejeta Roca G, et al. **Declining Lung Function** and Cardiovascular Risk: The ARIC Study. J Am Coll Cardiol. 2018 Sep 4;72(10):1109-1122.

Simes J, Robledo KP, White HD, et al; LIPID study investigators . **D-dimer** Predicts Long-Term Cause-Specific Mortality, Cardiovascular Events and Cancer in Stable Coronary Heart Disease Patients: The LIPID Study. Circulation. 2018 Jan 24.

Simmons RK, Sharp S, Boekholdt SM, et al. Evaluation of the Framingham risk score in the European Prospective Investigation of Cancer-Norfolk cohort: does adding glycated hemoglobin improve the prediction of coronary heart disease events? Arch Intern Med. 2008 Jun 9;168(11):1209-16. The Framingham risk score predicts CHD in this cohort. The addition of **HbA(1c)** made a small but statistically significant improvement to discrimination in men but not in women, without significant improvement in reclassification of risk category.

Singh RB, Dubnov G, Niaz MA, Ghosh S, et al. Effect of an **Indo-Mediterranean diet** on progression of coronary artery disease in high risk patients (Indo-Mediterranean Diet Heart Study): a randomised single-blind trial. *Lancet* 2002;360(9344):1455-61.

Singh-Manoux A, Shipley MJ, Bell JA, et al. Association between **inflammatory biomarkers** and all-cause, cardiovascular and cancer-related mortality. CMAJ. 2016 Nov 28.

Sinha R, Cross AJ, Graubard BI, Leitzmann MF, Schatzkin A. **Meat intake** and mortality: a prospective study of over half a million people. Arch Intern Med. 2009;169:562-71.

Sinharay R, Gong J, Barratt B, et al. Respiratory and cardiovascular responses to **walking down a traffic-polluted road** compared with walking in a traffic-free area in participants aged 60 years and older with chronic lung or heart disease and age-matched healthy controls: a randomised, crossover study. Lancet. 2017 Dec 5.

Siontis GCM, Tzoulaki I, Siontis KC, Ioannidis JPA. **Comparisons of established risk prediction models** for cardiovascular disease: systematic review. BMJ 2012;344:3318

Siontis GC, Mavridis D, Greenwood JP, et al. Outcomes of **non-invasive diagnostic modalities** for the detection of coronary artery disease: network meta-analysis of diagnostic randomised controlled trials. BMJ. 2018 Feb 21;360:k504.

Siscovick DS, Barringer TA, Fretts AM, et al. **Omega-3 Polyunsaturated Fatty Acid (Fish Oil) Supplementation** and the Prevention of Clinical Cardiovascular Disease: A Science Advisory From the American Heart Association. Circulation. 2017 Mar 13.

Sisti LG, Dajko M, Campanella P, et al. The effect of **multifactorial lifestyle interventions** on cardiovascular risk factors: A systematic review and meta-analysis of trials conducted in the general population and high risk groups. Prev Med. 2017 Dec 29.

Sjostrom L, Peltonen M, Jacobson P, et al. **Bariatric surgery** and long-term cardiovascular events. (**SOS**) JAMA. 2012;307(1):56-65.

Skalski J, Allison TG, Miller TD. The Safety of Cardiopulmonary **Exercise Testing** in a Population with High-Risk Cardiovascular Diseases. Circulation. 2012 Oct 22.

Skinner AC, Perrin EM, Moss LA, et al. **Cardiometabolic Risks and Severity of Obesity** in Children and Young Adults. N Engl J Med. 2015 Oct;373(14):1307-17.

Sliwa K, Acquah L, Gersh BJ, Mocumbi AO. Impact of **Socioeconomic Status, Ethnicity, and Urbanization** on Risk Factor Profiles of Cardiovascular Disease in Africa. Circulation. 2016 Mar 22;133(12):1199-208.

Slopen N, Glynn RJ, Buring JE, et al. **Job Strain, Job Insecurity**, and Incident Cardiovascular Disease in the Women's Health Study: Results from a 10-Year Prospective Study. PLoS One. 2012;7(7):e40512.

Smith P, Ma H, Glazier RH, et al. The Relationship Between **Occupational Standing and Sitting** and Incident Heart Disease Over a 12-Year Period in Ontario, Canada. Am J Epidemiol. 2018 Jan 1;187(1):27-33.

Smith S, Benjamin E, Bonow R, et al. **AHA/ACCF secondary prevention and risk reduction therapy** for patients with coronary and other atherosclerotic vascular disease: 2011 update: A guideline from the American Heart Association and American College of Cardiology Foundation. Circulation. 2011; DOI:10.1161/CIR.0b013e318235eb4d.

Smith TW, Baucom BRW. **Intimate relationships, individual adjustment**, and coronary heart disease: Implications of overlapping associations in psychosocial risk. Am Psychol. 2017 Sep;72(6):578-589.

Smyth A, O'Donnell MJ, Yusuf S, et al. **Sodium** Intake and Renal Outcomes: A Systematic Review. Am J Hypertens. 2014 Feb 7.

Sniderman AD, Toth PP, Thanassoulis G, et al. Taking a **longer term view** of cardiovascular risk: the causal exposure paradigm. BMJ. 2014 May 21;348:g3047.

Soares-Miranda L, Siscovick DS, Psaty BM, et al. **Physical Activity** and Risk of Coronary Heart Disease and Stroke in Older Adults: The Cardiovascular Health Study. Circulation. 2015 Nov 4.

Soedamah-Muthu SS, De Neve M, Shelton NJ, et al. Joint Associations of **Alcohol Consumption and Physical Activity** With All-Cause and Cardiovascular Mortality. Am J Cardiol. 2013 May 3.

Sofi F, Cesari F, Abbate R, Gensini GF, Casini A. Ad herence to **Mediterranean diet** and health status: meta-analysis. *BMJ* 2008;337:a1344.

Sofi F, Capalbo A, Pucci N, et al. Cardiovascular evaluation, including **resting and exercise electrocardiography**, before participation in competitive sports: cross sectional study. BMJ. 2008 Jul 3;337:a346. doi: 10.1136/bmj.a346.
Among people seeking to take part in competitive sports, exercise ECG can identify those with cardiac abnormalities. Follow-up studies would show if disqualification of such people would reduce the incidence of CV events among athletes.

Sofi F, Abbate R, Gensini GF, Casini A. Accruing evidence on benefits of adherence to the **Mediterranean diet** on health: an updated systematic review and meta-analysis. Am J Clin Nutr. 2010 Nov;92(5):1189-96.

Sofi F, Dinu M, Pagliai G, et al. Low-Calorie **Vegetarian Versus Mediterranean Diets** for Reducing Body Weight and Improving Cardiovascular Risk Profile: CARDIVEG Study (Cardiovascular Prevention With Vegetarian Diet). Circulation. 2018 Feb 26.

Soliman EZ, Zhang Z-M, Chen LY et al. Usefulness of **Maintaining a Normal Electrocardiogram** over Time for Predicting Cardiovascular Health. The American Journal of Cardiology (2016).

Song H, Fang F, Arnberg FK, et al. **Stress related disorders** and risk of cardiovascular disease: population based, sibling controlled cohort study. BMJ. 2019 Apr 10;365:l1255

Song M, Giovannucci E. Preventable Incidence and Mortality of Carcinoma Associated With **Lifestyle Factors** Among White Adults in the United States. JAMA Oncol. 2016 May 19.

Song M, Fung TT, Hu FB, et al. Association of **Animal and Plant Protein** Intake With All-Cause and Cause-Specific Mortality. JAMA Intern Med. 2016 Aug 1.

Smetana GW, Cutlip DE, Pinto DS. **Should We Screen for Coronary Heart Disease in Asymptomatic Persons**?: Grand Rounds Discussion From Beth Israel Deaconess Medical Center. Ann Intern Med. 2016 Apr 5

Smolina K, Wright FL, Rayner M, Goldacre MJ. Determinants of the **decline in mortality from acute myocardial infarction in England** between 2002 and 2010: linked national database study. BMJ 2012;344:d8059.

Sniderman AD, Thanassoulis G, Lawler PR, et al. Comparison of **Coronary Calcium Screening Versus Broad Statin** Therapy for Patients at Intermediate Cardiovascular Risk. Am J Cardiol. 2012 May 9.
Song H, Fang F, Arnberg FK, et al. **Stress related disorders and risk of cardiovascular disease**: population based, sibling controlled cohort study. BMJ. 2019 Apr 10;365:l1255.
Song M, Hu FB, Wu K, et al. **Trajectory of body shape** in early and middle life and all cause and cause specific mortality: results from two prospective US cohort studies. BMJ 2016;353:i2195.
Song YS, Koo BK, Cho NH, Moon MK. Effect of Low Serum Total **Bilirubin Levels** (≤0.32 mg/dl) on Risk of Coronary Artery Disease in Patients With Metabolic Syndrome. Am J Cardiol. 2014 Sep 16.
Sotos-Prieto M, Bhupathiraju SN, Mattei J, et al. Changes in **Diet Quality Scores** and Risk of Cardiovascular Disease Among US Men and Women. Circulation. 2015 Dec 8;132(23):2212-9.
Sotos-Prieto M, Bhupathiraju SN, Mattei J, et al. Association of Changes in **Diet Quality** with Total and Cause-Specific Mortality. N Engl J Med. 2017 Jul 13;377(2):143-153.
Sparling PB, Howard BJ, Dunstan DW, et al. Recommendations for **physical activity** in older adults. BMJ. 2015 Jan 21;350:h100.
Spence JD, Jenkins DJA, and Davignon J. **Egg yolk consumption** and carotid plaque. Atherosclerosis 2012.
Spence JD. A **single fixed-dose combination** (**polypill**) for all patients is bad medicine. Can J Cardiol. 2014 May;30(5):513-6.
Spring B, Ockene JK, Gidding SS, et al. Better Population Health Through **Behavior Change in Adults**: A Call to Action. Circulation. 2013 Oct 7.
Spring B, Moller AC, Colangelo LA, et al. Healthy **Lifestyle Change and Subclinical Atherosclerosis in Young Adults**: Coronary Artery Risk Development in Young Adults (CARDIA) Study. Circulation. 2014 Jul 1;130(1):10-7.
Srikanthan P and Karlamangla AS.**Muscle mass index** as a predictor of longevity in older adults. Am J Med 2014 Jun; 127:547.
Srikanthan P, Horwich TB, Tseng CH. Relation of **Muscle Mass and Fat Mass** to Cardiovascular Disease Mortality. Am J Cardiol. 2016 Apr 15;117(8):1355-60
Srivaratharajah K, Abramson BL. **Identifying and managing younger women at high risk** of cardiovascular disease. CMAJ. 2019 Feb 11;191(6):E159-E163.
Srour B, FezeuLK, Kesse-GuyotE, etal . **Ultra-processed food intake and risk of cardiovascular disease**: prospective cohort study (NutriNet-Santé). BMJ 2019;365:l1451.
St-Onge MP, Ard J, Baskin ML, et al. **Meal Timing and Frequency**: Implications for Cardiovascular Disease Prevention: A Scientific Statement From the American Heart Association. Circulation. 2017 Jan 30.
Stamatakis E, Gale J, Bauman A, et al. **Sitting Time, Physical Activity, and Risk of Mortality** in Adults. J Am Coll Cardiol. 2019 Apr 30;73(16):2062-2072.
Stamatakis E, Hamer M, Dunstan DW et al. **Screen based** entertainment time (TV etc), all-cause mortality, and cardiovascular events. Population based study with ongoing mortality and hospital events follow-up. J Am Coll Cardiol 2011; 57: 292-299.
Stamatakis E, Kelly P, Strain T, et al. Self-rated **walking pace and all-cause, cardiovascular disease and cancer mortality**: individual participant pooled analysis of 50 225 walkers from 11 population British cohorts. Br J Sports Med. 2018 Jun;52(12):761-768.
Stefler D, Pikhart H, Kubinova R, et al. **Fruit and vegetable consumption** and mortality in Eastern Europe: Longitudinal results from the Health, Alcohol and Psychosocial Factors in Eastern Europe study. Eur J Prev Cardiol. 2015 Apr 22.
Steinberger J, Daniels SR, Hagberg N, et al. **Cardiovascular Health Promotion in Children**: Challenges and Opportunities for 2020 and Beyond: A Scientific Statement From the American Heart Association. Circulation. 2016 Sep 20;134(12):e236-e255
Stenestrand U, Wijkman M, Fredrikson M, et al. Association between admission **supine systolic blood pressure** and 1-year mortality in patients admitted to the intensive care unit for acute chest pain. JAMA. 2010 Mar 24;303(12):1167-72.
Steriotis AK, Nava A, Rigato I, et al. **Noninvasive Cardiac Screening** in Young **Athletes** With Ventricular Arrhythmias. Am J Cardiol. 2012 Dec 6.
Stessman Jochanan; Hammerman-Rozenberg Robert; Cohen Aaron; et al. **Physical Activity**, Function, and Longevity Among the Very Old. Arch Intern Med. 2009;169(16):1476-1483.
Stewart IJ, Sosnov JA, Howard JT, Orman JA, Fang R, Morrow BD, Zonies DH, Bollinger M, Tuman C, Freedman BA, Chung KK. Retrospective analysis of long-term outcomes after **combat injury**: a hidden cost of war. Circulation. 2015;132:2126-2133.
Stewart RA, Wallentin L, Benatar J, et al. **Dietary patterns** and the risk of major adverse cardiovascular events in a global study of high-risk patients with stable coronary heart disease. *Eur Heart J* 2016.
Stewart RA, Colquhoun DM, Marschner SL, et al. **Persistent psychological distress** and mortality in patients with stable coronary artery disease. Heart;2017 10.1136/heartjnl-2016-311097.
Stewart RAH, Held C, Hadziosmanovic N, et al. **Physical Activity** and Mortality in Patients With Stable Coronary Heart Disease. J Am Coll Cardiol. 2017 Oct 3;70(14):1689-1700.
Stockwell T, Zhao J, Roemer A, et al. Do "**moderate" drinkers** have reduced mortality risk? A systematic review and meta–analysis of alcohol consumption and all–cause mortality. J Stud Alcohol Drugs 2016;77:185–98.
Stolarz-Skrzypek K, Kuznwtsova T, Thijs L et al. Fatal and nonfatal outcomes, incidence of hypertension, and BP changes in relation to urinary **sodium excretion**. JAMA 2011; 305: 1777-1785.
Stone GW et al. for the **PROSPECT** Investigators. A prospective **natural-history study of coronary atherosclerosis**. N Engl J Med 2011 Jan 20; 364:226.
Stone GW, Maehara A, Lansky AJ, et al. A prospective **natural-history study of coronary atherosclerosis**. N Engl J Med. 2011;364:226 –235.
Strath SJ, Kaminsky LA, Ainsworth BE, et al. Guide to the assessment of **physical activity**: clinical and research applications: a scientific statement from the american heart association. Circulation. 2013 Nov 12;128(20):2259-79.
Strazzullo Pasquale, D'Elia Lanfranco, et al. **Salt** intake, stroke, and cardiovascular disease: meta-analysis of prospective studies. BMJ 2009;339:b4567, doi: 10.1136/bmj.b4567 (24 November 2009).
Streed CG Jr, Harfouch O, Marvel F, et al. Cardiovascular Disease Among **Transgender** Adults Receiving **Hormone Therapy**: A Narrative Review. Ann Intern Med. 2017 Jul 25.
Stringhini S, Carmeli C, Jokela M, etal . **Socioeconomic status, non-communicable disease risk factors**, and **walking speed** in older adults: multi-cohort population based study. BMJ 2018;360:k1046.
Ström M, Halldorsson TI, Mortensen EL, et al. **Fish, n-3 fatty acids and cardiovascular diseases in women** of reproductive age. A prospective study in a large national cohort. Hypertension 2011
Strongman H, Gadd S, Matthews A, et al. Medium and long-term **risks of specific cardiovascular diseases in survivors of 20 adult cancers**: a population-based cohort study using multiple linked UK electronic health records databases. Lancet. 2019 Aug 20.
Suckling RJ, He FJ, MacGregor GA. Altered dietary salt intake for preventing and treating diabetic kidney disease. Cochrane Database of Systematic Reviews 2010, Issue 12. Art. No.: CD006763.
Suh Y, Lee CJ, Cho DK, et al. Impact of National Health Checkup Service on **Hard Atherosclerotic Cardiovascular Disease** Events and All-Cause Mortality in the General Population. Am J Cardio. 2017
Sukkar L, Hong D, Wong MG, et al. Effects of **ischaemic conditioning** on major clinical outcomes in people undergoing invasive procedures: systematic review and meta-analysis. BMJ. 2016 Nov 7;355:i5599.
Sumner JA, Kubzansky LD, Elkind MS, et al. **Trauma Exposure and Posttraumatic Stress Disorder Symptoms** Predict Onset of Cardiovascular Events in Women. Circulation. 2015 Jun 29.
Sun Qi; Townsend Mary K.; Okereke Olivia I.; et al. **Physical Activity** at Midlife in Relation to Successful Survival in Women at Age 70 Years or Older. (Nurses' Health Study) *Arch Intern Med*. 2010;170(2):194-201.
Sun Q, Townsend MK, Okereke OI, et al. **Alcohol consumption** at midlife and successful ageing in women: a prospective cohort analysis in the nurses' health study. PLoS Med. 2011 Sep;8(9)
Sun Q, Kiernan UA, Shi L, et al. Plasma **Retinol-Binding Protein 4 (RBP4)** Levels and Risk of Coronary Heart Disease: A Prospective Analysis Among Women in the Nurses' Health Study. Circulation. 2013 May 14;127(19):1938-47
Sun Y, Liu B, Snetselaar LG, et al. Association of **fried food consumption with all cause, cardiovascular, and cancer mortality**: prospective cohort study. BMJ. 2019 Jan 23;364:k5420.
Superko HR, Superko SM, Nasir K, et al. **Omega-3 Fatty Acid blood levels**: clinical significance and controversy. Circulation. 2013 Nov 5;128(19):2154-61.
Suri S, Topiwala A, Chappell MA, et al. Association of **Midlife Cardiovascular Risk Profiles With Cerebral Perfusion** at Older Ages. JAMA Netw Open. 2019 Jun 5;2(6):e195776.
Sverre E, Peersen K, Husebye E, et al. **Unfavourable risk factor control after coronary events** in routine clinical practice. BMC Cardiovasc Disord. 2017 Jan 21;17(1):40.
Swerdel JN, Janevic TM, Cosgrove NM, Kostis JB; Myocardial Infarction Data Acquisition System (MIDAS 24) Study Group. The effect of **hurricane sandy** on cardiovascular events in new jersey. J Am Heart Assoc. 2014 Dec 8;3(6).
Tang G, Wang D, Long J, et al. Meta-Analysis of the Association Between **Whole Grain Intake** and Coronary Heart Disease Risk. Am J Cardiol. 2015 Mar 1;115(5):625-629.
Tang L, Patao C, Chuang J, Wong ND. **Cardiovascular Risk Factor Control and Adherence to Recommended Lifestyle** and Medical Therapies in Persons With Coronary Heart Disease (from the National Health and Nutrition Examination Survey 2007-2010). Am J Cardiol. 2013 Jul 2.
Tang WHW, Wang Z, Levison BS, et al. Intestinal microbial metabolism of **phosphatidylcholine** (lecithin & metabolite TMAO) and cardiovascular risk. N Engl J Med 2013;368:1575-84.
Tanz L, Stuart J, Williams P, et al. **Preterm delivery and maternal cardiovascular disease** in young and middle aged adult women. Circulation 2017.
Tawakol A, Ishai A, Takx RAP, et al. Relation between resting **amygdalar activity** and cardiovascular events: a longitudinal and cohort study. Lancet 2017; online Jan 11.
Tawakol A, Osborne MT, Wang Y, et al. **Stress-Associated Neurobiological Pathway** Linking Socioeconomic Disparities to Cardiovascular Disease. J Am Coll Cardiol. 2019 Jul 2;73(25):3243-3255.
Taylor RS, Ashton KE, Moxham T, et al. **Reduced dietary salt** for the prevention of cardiovascular disease. Cochrane Database of Systematic Reviews 2011, Issue 7. Art. No.: CD009217. DOI: 10.1002/14651858.CD009217. Despite collating more event data than previous systematic reviews of randomised controlled trials (665 deaths in some 6,250 participants), there is still insufficient power to exclude clinically important effects of reduced dietary salt on mortality or cardiovascular morbidity in normotensive or hypertensive populations. Further RCT evidence is needed to confirm whether restriction of sodium is harmful for people with heart failure. Our estimates of benefits from dietary salt restriction are consistent with the predicted small effects on clinical events attributable to the small blood pressure reduction achieved.
Temple JL, Ziegler AM, Graczyk A, et al. Cardiovascular Responses to **Caffeine** by Gender and Pubertal Stage. Pediatrics. 2014 Jun 16.
Temporelli PL, Zito G, Faggiano P; **SOCRATES** Investigators. Cardiovascular Risk Profile and **Lifestyle Habits** in a Cohort of Italian Cardiologists (from the SOCRATES Survey). Am J Cardiol. 2013 Apr 12.

Teo K, Lear S, Islam S, et al. Prevalence of a **healthy lifestyle** among individuals with cardiovascular disease in high-, middle- and low-income countries. The Prospective Urban Rural Epidemiology (**PURE**) study. JAMA 2013; 309:1613-1621.

Thijssen DHJ, Redington A, George KP, et al. Association of **Exercise Preconditioning** With Immediate Cardioprotection: A Review. JAMA Cardiol. 2018 Feb 1;3(2):169-176.

Thomas B, Matsushita K, Abate KH, et al. **Global Cardiovascular and Renal Outcomes** of Reduced GFR. J Am Soc Nephrol. 2017 Apr 13.

Thomas Mathew, Haas Tammy S., Doerer Joseph J., et al. Epidemiology of Sudden Death in Young, **Competitive Athletes Due to Blunt Trauma**. Pediatrics 2011; 128:1 e1-e8; doi:10.1542/peds.2010-2743

Thomas RJ, Beatty AL, Beckie TM, et al. **Home-Based Cardiac Rehabilitation**: A Scientific Statement From the American Association of Cardiovascular and Pulmonary Rehabilitation, the American Heart Association, and the American College of Cardiology. J Am Coll Cardiol. 2019 May 7.

Thompson RC, Allam AH, Lombardi GP, et al. **Atherosclerosis across 4000 years of human history**: The **HORUS** study of four ancient populations. Lancet 2013.

Thorndike AN, Gelsomin ED, McCurley JL, Levy DE. **Calories Purchased by Hospital Employees** After Implementation of a Cafeteria Traffic Light-Labeling and Choice Architecture Program. JAMA Netw Open. 2019 Jul 3;2(7):e196789.

Thorsten Jensen M, Suadicani P, Ole Hein H, Gyntelberg F. **Elevated resting heart rate**, physical fitness and all-cause mortality: a 16-year follow-up in the Copenhagen Male Study. Heart doi:10.1136/heartjnl-2012-303375.

Threapleton DE, Greenwood DC, Evans CEL, et al. **Dietary fibre intake** and risk of cardiovascular disease: systematic review and meta-analysis. BMJ 2013;347:f6879.

Thurston GD, Burnett RT, Turner MC, et al. Ischemic Heart Disease Mortality and Long-Term Exposure to Source-Related Components of **U.S. Fine Particle Air Pollution**. Environ Health Perspect. 2015 Dec 2.

Tian M, Ajay V, Dunzhu D, et al. A Cluster-Randomized Controlled Trial of a **Simplified Multifaceted Management Program** for Individuals at High Cardiovascular Risk (**SimCard** Trial) in Rural Tibet, China, and Haryana, India. Circulation. 2015 Jul 17.

Tigbe WW, Granat MH, Sattar N, et al. **Time spent in sedentary posture** is associated with waist circumference and cardiovascular risk. Int J Obes (Lond). 2017 Mar 7.

Tikkanen E, Gustafsson S, Ingelsson E. Associations of **Fitness, Physical Activity, Strength, and Genetic Risk** With Cardiovascular Disease: Longitudinal Analyses in the UK Biobank Study. Circulation. 2018 Apr 9.

Tillmann T, Vaucher J, Okbay A, et al. **Education and coronary heart disease**: mendelian randomisation study. BMJ 2017;358:j3542.

Tillmann T, Pikhart H, Peasey A, et al. **Psychosocial and socioeconomic determinants** of cardiovascular mortality in Eastern Europe: A multicentre prospective cohort study. PLoS Med. 2017 Dec 6;14(12):e1002459.

Tirosh A et al. Adolescent **BMI trajectory and risk of diabetes versus coronary disease**. N Engl J Med 2011 Apr 7; 364:1315.

Tivesten A et al. **Dehydroepiandrosterone** (**DHEA**) and its sulfate predict the 5-year risk of coronary heart disease events in elderly men. J Am Coll Cardiol 2014 Oct 28; 64:1801.

Tobe SW, Stone JA, Brouwers M, et al. **Harmonization of guidelines** for the prevention and treatment of cardiovascular disease: the **C-CHANGE Initiative**. CMAJ. 2011 Sep 12.

Tobe SW, Stone JA, et al. Canadian Cardiovascular Harmonized National Guidelines Endeavour (**C-CHANGE**) guideline for the prevention and management of **cardiovascular disease in primary care: 2018 update**. CMAJ. 2018 Oct 9;190(40):E1192-E1206.

Tobías A, Armstrong B, Gasparrini A, et al. Effects of **high summer temperatures** on mortality in 50 Spanish cities. Environ Health. 2014 Jun 9;13(1):48.

Toews I, Lohner S, Küllenberg de Gaudry D, etal . Association between **intake of non-sugar sweeteners and health outcomes**: systematic review and meta-analyses of randomised and non-randomised controlled trials and observational studies. BMJ 2018;363:k4718.

Tofler GH, Spinaze M, Shaw E, Buckley T. **Therapy for Triggered Acute Risk Prevention** in Subjects at Increased Cardiovascular Risk. Am J Cardiol. 2013 Apr 3.

Tomdio A, Ritchie M, Miller AC. **Omega-3 Fatty Acids** and Cardiovascular Disease Prevention. Am Fam Physician. 2019 Aug 15;100(4):209-210.

Ton TG, Fogg TT, Fong CT, et al. Knowledge, perception, and **behaviors of relatives** of people with premature heart disease: a systematic literature review. Circulation. 2011 Aug 23;124(8):958-64.

Tonelli M, Muntner P, Lloyd A, et al. Risk of coronary events in people with **chronic kidney disease** compared with those with diabetes: a population-level cohort study. Lancet 2012

Tong TY, Wareham NJ, et al. Prospective association of the **Mediterranean diet** with cardiovascular disease incidence and mortality and its population impact in a non-Mediterranean population: the **EPIC-Norfolk** study. BMC Med. 2016 Sep 29;14(1):135.

Tong TYN, Appleby PN, Bradbury KE, et al. Risks of **ischaemic heart disease and stroke in meat eaters, fish eaters, and vegetarians** over 18 years of follow-up: results from the prospective EPIC-Oxford study. BMJ. 2019 Sep 4;366:l4897.

Traiperm N, Gatterer H, Wille M, Burtscher M. Cardiac Troponins in Young **Marathon Runners**. Am J Cardiol. 2012 May 9.

Tresserra-Rimbau A, Rimm EB, Medina-Remón A, et al; PREDIMED Study Investigators. **Polyphenol intake** and mortality risk: a re-analysis of the PREDIMED trial. BMC Med. 2014 May 13;12(1):77.

Trichopoulou A, Bamia C, Trichopoulos D. Anatomy of health effects of **Mediterranean diet**: Greek EPIC prospective cohort study. BMJ. 2009 Jun 23;338:b2337. doi: 10.1136/bmj.b2337. Some food groups in the Mediterranean diet are more important than others in promoting health and longer life, according to this prospective cohort study from the Greek segment of the European Prospective Investigation into Cancer and nutrition (EPIC). The researchers investigated the importance of individual components of the diet and found that eating more vegetables, fruits, nuts, pulses, and olive oil, and drinking moderate amounts of alcohol is linked to people living longer, whereas following a Mediterranean diet high in seafood and cereals and low in dairy products was not an indicator of longevity.

Trieu K, Neal B, Hawkes C, et al. **Salt Reduction Initiatives around the World** - A Systematic Review of Progress towards the Global Target. PLoS One. 2015 Jul 22;10(7):e0130247.

Triglyceride Coronary Disease Genetics Consortium and Emerging Risk Factors Collaboration, Sarwar N, Sandhu MS, Ricketts SL et al. **Triglyceride**-mediated pathways and coronary disease: collaborative analysis of 101 studies. Lancet. 2010 May 8;375(9726):1634-9.

Tsuyuki RT et al. Effectiveness of **community pharmacist prescribing** and care on **cardiovascular risk reduction**: Randomized controlled **RxEACH** trial. J Am Coll Cardiol 2016 Apr 4.

Tsuyuki RT, Al Hamarneh YN, Jones CA, et al. The Effectiveness of **Pharmacist Interventions on Cardiovascular Risk**: The Multicenter Randomized Controlled **RxEACH** Trial. J Am Coll Cardiol. 2016 Jun 21;67(24):2846-54.

Tu JV, Chu A, Donovan LR, et al. The Cardiovascular Health in Ambulatory Care Research Team (**CANHEART**): Using **Big Data to Measure and Improve Cardiovascular Health** and Healthcare Services. Circ Cardiovasc Qual Outcomes. 2015 Feb 3.

Tu JV, Chu A, Rezai MR et al. The Incidence of Major **Cardiovascular Events in Immigrants** to Ontario, Canada: The **CANHEART** Immigrant Study. Circulation. 2015 Aug 31.

Tu WJ, Ma GZ, Ni Y, et al. **Copeptin and NT-proBNP for prediction** of all-cause and cardiovascular death in ischemic stroke. Neurology. 2017 May 16;88(20):1899-1905.

Tucker Andrew M.; Vogel Robert A.; Lincoln Andrew E.; et al. Prevalence of Cardiovascular Disease Risk Factors Among **National Football League** Players. JAMA. 2009;301(20):2111-2119.

Turner MC, Jerrett M, Pope Iii CA, et al. Long-Term **Ozone Exposure** and Mortality in a Large Prospective Study. Am J Respir Crit Care Med. 2015 Dec 17.

Tzoulaki Ioanna; Liberopoulos George; A. Ioannidis John P.. **Assessment of Claims** of Improved Prediction **Beyond the Framingham** Risk Score. JAMA. 2009;302(21):2345-2352.

Tzoulaki I, Siontis KCM, Ioannidis JPA. Prognostic effect size of **cardiovascular biomarkers** in datasets from observational studies versus randomised trials: meta-epidemiology study. BMJ 2011;343:d6829.

Tzoulaki I, Elliott P, Kontis V, et al. **Worldwide Exposures** to **Cardiovascular Risk Factors** and Associated Health Effects: Current Knowledge and Data Gaps. Circulation. 2016 Jun 7;133(23):2314-33.

Uberoi A, Stein R, Freeman J, et al. Interpretation of the **electrocardiogram of young athletes**. Circulation. Circulation 2011; 124:746-757.

Udell JA, Steg PG, Scirica BM, et al. **Living alone** and cardiovascular risk in outpatients at risk or with atherothrombosis. Arch Intern Med 2012.

Udell JA, Lu H, Redelmeier DA. **Failure of fertility therapy** and subsequent adverse cardiovascular events. CMAJ. 2017 Mar 13;189(10):E391-E397.

Umpierre D, Ribeiro P. B., Kramer CK., et al. **Physical Activity Advice** Only or Structured **Exercise** Training and Association With HbA1c Levels in Type 2 Diabetes: A Systematic Review and Meta-analysis. JAMA. 2011;305(17):1790-1799.

Unverzagt FW, McClure LA, Wadley VG, et al. **Vascular risk factors** and cognitive impairment in a stroke-free cohort. Neurology. 2011 Nov 8;77(19):1729-36.

Usoro AO, Bradford N, Shah AJ, Soliman EZ. Risk of Mortality in Individuals With **Low QRS Voltage** and Free of Cardiovascular Disease. Am J Cardiol. 2014 May 1;113(9):1514-7.

USPSTF: U.S. Preventive Services Task Force. Using **nontraditional risk factors** in coronary heart disease risk assessment: U.S. Preventive Services Task Force recommendation statement. Ann Intern Med. 2009 Oct 6;151(7):474-82.

USPSTF: US Preventive Services Task Force. **Behavioral counseling to promote a healthful diet and physical activity** for cardiovascular disease prevention in adults without cardiovascular risk factors: US Preventive Services Task Force recommendation statement.JAMA. doi:10.1001/jama.2017.7171 7.

USPSTF: US Preventive Services Task Force. **Risk assessment** for cardiovascular disease with **nontraditional risk factors**: US Preventive Services Task Force Recommendation Statement [online July 10, 2018]. JAMA. 2018. doi:10.1001/jama.2018.8359

Ussery EN, Fulton JE, Galuska DA, et al. Joint **Prevalence of Sitting Time and Leisure-Time Physical Activity** Among US Adults, 2015-2016. JAMA. 2018 Nov 20;320(19):2036-2038.

Uzhova I, Fuster V, Fernández-Ortiz A, et al. The importance of **breakfast** in atherosclerosis disease: insights from the **PESA** study. J Am Coll Cardiol 2017;70:1833–42.

Vaduganathan M, De Palma G, Manerba A, et al. Risk of cardiovascular hospitalizations from exposure to **coarse particulate matter** (PM10) below the European Union safety threshold. *Am J Cardiol* 2016.

Vaidya D, Becker DM, Bittner V, et al. **Ageing, menopause, and ischaemic heart disease** mortality in England, Wales, and the United States: modeling study of national mortality data. BMJ 2011; 343: DOI:10.1136/bmj.d5170.

Väistö J, Haapala EA, Viitasalo A, et al. Longitudinal associations of **physical activity and sedentary time** with cardiometabolic risk factors in children. Scand J Med Sci Sports. 2018 Oct 1.

Valero-Elizondo J, Salami JA, Osondu CU, et al. **Economic Impact of Moderate-Vigorous Physical Activity** Among Those With and Without Established Cardiovascular Disease: 2012 Medical Expenditure Panel Survey. J Am Heart Assoc. 2016 Sep 7;5(9).

Valenti V, Hartaigh B, Heo R, et al. A 15-year warranty period for **asymptomatic individuals without coronary artery calcium**: A prospective follow-up of 9715 individuals. *J Am Coll Cardiol Img* 2015.

Valenti V, Hartaigh B, Cho I, et al. Absence of **coronary artery calcium** identifies asymptomatic diabetic individuals at low near-term but not long-term risk of mortality: A 15-year follow-up study of 9715 patients. *Circ Cardiovasc Imaging*2016.
Valenzuela-Alcaraz B, Crispi F, Bijnens B, et al. **Assisted Reproductive Technologies** Are Associated With Cardiovascular Remodeling In Utero That Persists Postnatally. Circulation. 2013 Sep 24;128(13):1442-1450.
Vallance JK, Gardiner PA, Lynch BM, et al. **Evaluating the Evidence on Sitting, Smoking, and Health**: Is **Sitting Really the New Smoking?** Am J Public Health. 2018 Nov;108(11):1478-1482
Valtorta NK, Kanaan M, Gilbody S, et al. **Loneliness and social isolation** as risk factors for coronary heart disease and stroke: systematic review and meta-analysis of longitudinal observational studies. Heart. 2016 Apr 18.
van den Berg MJ, Bhatt DL, Kappelle LJ, et al. Identification of **vascular patients** at very high risk for recurrent cardiovascular events: validation of the current **ACC/AHA very high risk criteria**. Eur Heart J. 2017 Mar 28.
van den Berg MJ, Westerink J, van der Graaf Y, et al. **Risk Factors for Recurrent Cardiovascular Events Before Age 65 Years or Within 2.5 Years of a Recent First Cardiovascular Event**. Am J Cardiol. 2017 Jul 15;120(2):167-173.
van der Heijden AA, Ortegon MM, Niessen LW, et al. Prediction of coronary heart disease risk in a general, pre-diabetic, and diabetic population during 10 years of follow-up: accuracy of the Framingham, SCORE, and UKPDS risk functions: The Hoorn Study. Diabetes Care. 2009 Nov;32(11):2094-8. The use of the Framingham function for prediction of the first CHD event is likely to overestimate an individual`s absolute CHD risk. In CHD prevention, application of the **SCORE and UKPDS functions** might be useful in the absence of a more valid tool.
van der Leeuw J, van Dieren S, Beulens JW, et al. The **validation of cardiovascular risk scores for patients with type 2 diabetes mellitus**. Heart. 2014 Sep 25.
van der Ploeg HP, Chey T, Korda RJ, Banks E, Bauman A. **Sitting time** and all-cause mortality risk in 222 497 Australian adults. Arch Intern Med. 2012; 172(6):494-500.
Van Hemelrijk M, Garmo H, Holmberg L, Ingelsson E, Bratt O, Bill-Axelson A, et al. Absolute and relative risk of cardiovascular disease in men with **prostate cancer**; results from the Population-based PCBaSe Sweden. J Clin Oncol 2010;28:3448-56.Viera AJ,
Van Kempen BJH, Spronk S, Koller M, et al. Comparative effectiveness and cost-effectiveness of **computed tomography screening** for coronary artery calcium in asymptomatic individuals. J Am Coll Cardiol 2011; 58:1690-701.
van Nimwegen FA, Schaapveld M, Janus CPM, et al. **Cardiovascular disease after Hodgkin lymphoma** treatment: 40-year disease risk [online April 27, 2015]. JAMA Intern Med. doi:10.1001/jamainternmed.2015.1180.
Van Vliet BN, Campbell NR; Canadian Hypertension Education Program. Efforts to **reduce sodium intake** in Canada: why, what, and when? Can J Cardiol. 2011 Jul-Aug;27(4):437-45.
Varma VR, Dey D, Leroux A, et al. Re-evaluating the effect of **age on physical activity over the lifespan**. Prev Med. 2017 Jun 1;101:102-108
Vaucher J, Marques-Vidal P, Preisig M, et al. Population and economic impact of the **2013 ACC/AHA guidelines compared with European guidelines** to prevent cardiovascular disease. *Eur Heart J* 2014.
Vaught AJ, Kovell LC, Szymanski LM, et al. Acute cardiac effects of **severe pre-eclampsia**. J Am Coll Cardiol 2018;72:1–11.
Vazir A, Claggett B, Cheng S, et al. Association of **Resting Heart Rate and Temporal Changes in Heart Rate** With Outcomes in Participants of the Atherosclerosis Risk in Communities Study. JAMA Cardiol. 2018 Jan 24.
Vedin O, Hagström E, Budaj A, et al. **Tooth loss** is independently associated with poor outcomes in stable coronary heart disease. *Eur J Prev Cardiol* 2015.
Veeranna V, Zalawadiya SK, Niraj A, et al. **Homocysteine** and reclassification of cardiovascular disease risk. J Am Coll Cardiol2011; 58:1025-1033.
Venkataramani AS, Gandhavadi M, Jena AB. Association Between **Playing American Football in the National Football League** and Long-term Mortality. JAMA. 2018 Feb 1.
Venkatesh S, O'Neal WT, Broughton ST, et al. Utility of Normal Findings on **Electrocardiogram** and Echocardiogram in Individuals >65 Years of Age. Am J Cardio. 2017.
Vernooij JWP, Kaasjager HAH, van der Graaf Y, et al. **Internet based vascular risk factor management** for patients with clinically manifest vascular disease: randomized controlled trial. BMJ 2012.
Veronese N, Trevisan C, De Rui M, et al. **Osteoarthritis** increases the risk of cardiovascular diseases in the elderly: The progetto Veneto anziano study. Arthritis Rheumatol. 2015 Dec 29.
Veronese N, Li Y, Manson JE, et al. Combined associations of **body weight and lifestyle factors** with all cause and cause specific mortality in men and women: prospective cohort study. BMJ. 2016 Nov 24;355:i5855.
Veronese N, Stubbs B, Noale M, et al. **Fried potato consumption** is associated with elevated mortality: an 8-y longitudinal cohort study. Am J Clin Nutr. 2017 Jul;106(1):162-167.
Vest AR, Heneghan HM, Agarwal S, et al. **Bariatric surgery** and cardiovascular outcomes: A systematic review. Heart 2012.
Vetter C, Devore EE, Wegrzyn LR, et al. Association between **rotating night shift work** and risk of coronary heart disease among women. JAMA 2016 Apr 26; 315:1726.
Villines TC, Hsu LL, Blackshear C, et al. **Relation of Carotid Intima-Media Thickness** to Cardiovascular Events in Black Americans (From the Jackson Heart Study). Am J Cardiol. 2017 Nov 1;120(9):1528-1532.
Viner RM, Coff ey C, Mathers C, et al. **50-year mortality trends** in children and young people: a study of 50 low-income, middle-income, and high-income countries. Lancet 2011; 377: 1162–74.
Virani SS, Brautbar A, Davis BC, et al. Associations between **lipoprotein (a) levels** and cardiovascular outcomes in African Americans and Caucasians: The atherosclerosis risk in communities (ARIC) study. Circulation 2011.
Virtanen M, Ferrie JE, Singh-Manoux A, Shipley MJ, Vahtera J, Marmot MG, Kivimäki M. **Overtime work** and incident coronary heart disease: the Whitehall II prospective cohort study. Eur Heart J. 2010 May 11.
Virtanen M, Nyberg ST, Batty GD, et al;PD-Work Consortium. Perceived **job insecurity** as a risk factor for incident coronary heart disease: systematic review and meta-analysis. BMJ. 2013 Aug 8;347:f4746.
Virtanen M, Elovainio M, Josefsson K, et al. Coronary heart disease and risk factors as predictors of trajectories of **psychological distress from midlife to old age**. Heart 2017;103:659–65.
Voelker R. **Vacationing More Often** May Reduce Metabolic Syndrome Risk. JAMA. 2019 Aug 14. doi: 10.1001/jama.2019.11134.
Volgman AS, Palaniappan LS, Aggarwal NT, et al. **Atherosclerotic Cardiovascular Disease** in South Asians in the United States: Epidemiology, Risk Factors, and Treatments: A Scientific Statement From the American Heart Association. Circulation. 2018 Jul 3;138(1):e1-e34.
Vos MB, Kaar JL, Welsh JA, et al. **Added Sugars** and Cardiovascular Disease Risk in Children: A Scientific Statement From the American Heart Association. Circulation. 2016 Aug 22.
Vyas MV, Garg AX, Iansavichus AV, et al. **Shift work** and vascular events: systematic review and meta-analysis. BMJ. 2012 Jul 26;345:e4800.
Wannamethee SG, Shaper AG, Lennon L, et al. Metabolic Syndrome vs **Framingham Risk Score** for Prediction of Coronary Heart Disease, Stroke, and Type 2 Diabetes Mellitus. Arch Intern Med. 2005 Dec 26;165(22):2644-50.
Wannamethee S. Goya; Shaper A. Gerald; Whincup Peter H.; et al. Impact of **Diabetes on Cardiovascular Disease Risk and All-Cause Mortality** in Older Men: Influence of Age at Onset, Diabetes Duration, and Established and Novel Risk Factors. Arch Intern Med. 2011;171(5):404-410.
Wald DS, Bestwick JP, Wald NJ. Child-parent screening for familial hypercholesterolaemia: screening strategy based on a meta-analysis. BMJ. 2007 Sep 22;335(7620):599. Epub 2007 Sep 13. The proposed strategy of screening children and parents for familial hypercholesterolaemia could have considerable impact in preventing the medical consequences of this disorder in two generations simultaneously.
Walldius G, Aastveit AH, Jungner I. Stroke mortality and the **apoB/apoA-I ratio**: results of the AMORIS prospective study. J Intern Med. 2006 Mar;259(3):259-66.
Wang DD, Toledo E, Hruby A, et al. **Plasma Ceramides, Mediterranean Diet, and Incident Cardiovascular Disease** in the **PREDIMED** Trial (Prevención con Dieta Mediterránea). Circulation. 2017 May 23;135(21):2028-2040.
Wang EY, Dixson J, Schiller NB, Whooley MA. **Causes and Predictors of Death** in Patients With Coronary Heart Disease (from the **Heart and Soul Study**). Am J Cardiol. 2016 Sep 29.
Wang H, Dwyer-Lindgren L, Lofgren KT, et al. Age-specific and sex-specific **mortality in 187 countries**, 1970-2010: A systematic analysis for the Global Burden of Disease Study 2010. Lancet 2012; 380:2071-94.
Wade KH, Chiesa ST, Hughes AD, et al. Assessing the **causal role of body mass index on cardiovascular health in young adults**: Mendelian randomization and recall-by-genotype analyses. Circulation. 2018 Nov 13;138(20):2187-2201.
Wang D, Jackson EA, Karvonen-Gutierrez CA, et al. **Healthy Lifestyle During the Midlife Is Prospectively Associated With Less Subclinical Carotid Atherosclerosis**: The Study of Women's Health Across the Nation. J Am Heart Assoc. 2018 Dec 4;7(23):e010405.
Wang F, Harel-Sterling L, Cohen S, et al. Heart failure **risk predictions in adult patients with congenital heart disease**: a systematic review. Heart. 2019 Jul 26.
Wang NY, Young JH, et al. Blood pressure change and risk of hypertension associated with **parental hypertension**: the johns hopkins precursors study. Arch Intern Med. 2008 Mar 24;168(6):643-8. Hypertension in both mothers and fathers has a strong independent association with elevated BP levels and incident hypertension over the course of adult life.
Wang Q, Afshin A, Yakoob MY, et al. Impact of **Nonoptimal Intakes of Saturated, Polyunsaturated, and Trans Fat** on Global Burdens of Coronary Heart Disease. J Am Heart Assoc. 2016 Jan 20;5(1).
Wang T, Lu J, Su Q, et al. Ideal Cardiovascular Health Metrics and Major Cardiovascular Events in **Patients With Prediabetes and Diabetes**. JAMA Cardiol. 2019 Jul 31.
Wang TJ et al. Multiple biomarkers for the prediction of first major cardiovascular events and death. N Engl J Med 2006 Dec 21; 355:2631-9. Ware JH. (The limitations of risk factors as prognostic tools. N Engl J Med 2006 Dec 21; 355:2615-7.) After adjustment for traditional cardiovascular risk factors, five biomarkers -- BNP, CRP, albumin/creatinine ratio, homocysteine, and renin -- were associated with higher risk of death from any cause, and two – BNP and albumin/creatinine ratio -- with risk of first major cardiovascular events. However, statistically, these biomarkers added only moderately to the predictive ability of conventional risk factors.
Wang X, Ouyang Y, Liu J, et al. **Fruit and vegetable consumption** and mortality from all causes, cardiovascular disease, and cancer: Systematic review and dose-response meta-analysis of prospective cohort studies. *BMJ* 2014
Wanigatunga AA, Ambrosius WT, Rejeski WJ, et al. Association Between Structured **Physical Activity and Sedentary Time** in Older Adults. JAMA. 2017 Jul 18;318(3):297-299.
Wannamethee SG, Welsh P, Lowe GD, et al**. N-terminal pro-brain natriuretic peptide** is a more useful predictor of cardiovascular disease risk than **C-reactive protein** in older men with and without preexisting cardiovascular disease. J Am Coll Cardiol 2011; 58:56-64.

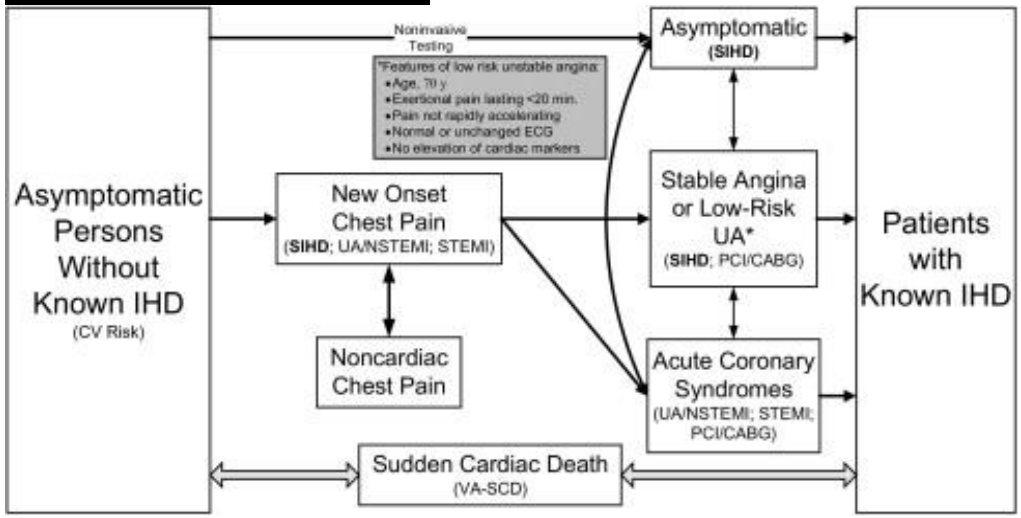
Waqar S, Mughal F, Rashid A, et al. Assessment of **cardiovascular risk in primary care**. BMJ. 2016 Jun 13;353:i3022.
Watkins LL, Koch GG, Sherwood A, et al. Association of **anxiety and depression** with all-cause mortality in individuals with coronary heart disease. J Am Heart Assoc. 2013 Mar 19;2(2):e000068.
Wattamwar K, Qian ZJ, Otter J, et al. Association of **Cardiovascular Comorbidities With Hearing Loss** in the Older Old. JAMA Otolaryngol Head Neck Surg. 2018 Jun 14.
Webb M, Fahimi S, Singh GM, et al. Cost effectiveness of a **government supported policy strategy to decrease sodium intake**: global analysis across 183 nations. BMJ. 2017 Jan 10;356:i6699.
Webber BJ, Seguin PG, Burnett DG, et al. Prevalence of and risk factors for **autopsy-determined atherosclerosis** among **US service members**, 2001-2011. JAMA 2012; 308:2577-2583.
Wei Y, Zhang JJ, Li Z, et al. Chronic exposure to **air pollution** particles increases the risk of obesity and metabolic syndrome: findings from a natural experiment in Beijing. FASEB J. 2016 Feb 18.
Weinstein AR, Sesso HD, Lee IM, Rexrode KM, et al. The joint effects of **physical activity** and body mass index on coronary heart disease risk in women. Arch Intern Med. 2008 Apr 28;168(8):884-90. The risk of CHD associated with elevated body mass index is considerably reduced by increased physical activity levels. However, the risk is not completely eliminated, reinforcing the importance of being lean and physically active.
Weinstock MB,Weingart S, Orth F, et al. **Risk for clinically relevant adverse cardiac events** in patients with chest pain at hospital admission [onlineMay 18, 2015]. JAMA Intern Med. doi:10.1001 /jamainternmed.2015.1674.
Weiss J, Freeman M, et al. **Benefits and harms of intensive blood pressure treatment in adults aged 60 years or older**: a systematic review and meta-analysis. Ann Intern Med. 2017. [Epub ahead of print]. doi:10.7326/M16-1754 3.
Welsh JA, Sharma A, Cunningham SA, Vos MB. **Consumption of Added Sugars** and Indicators of Cardiovascular Disease Risk Among US Adolescents. Circulation. 2011 Jan 25;123(3):249-57.
Weintraub WS, Daniels SR, Burke LE, et al. Value of **primordial and primary prevention** for cardiovascular disease: A policy statement from the American Heart Association (**AHA**). Circulation 2011. DOI: 10.1161/CIR.0b013e3182285a81.
Wen CP, Wai JPM, Tsai MK, et al. Minimum amount of **physical activity** for reduced mortality and extended life expectancy: a prospective cohort study. Lancet 2011. (15min a day or 90 min a week of moderate intensity exercise)
Wenger NK. Recognizing **Pregnancy-Associated Cardiovascular Risk Factors**. Am J Cardiol. 2013 Oct 6.
Wennberg P, Gustafsson PE, Dunstan DW, et al. **Television viewing and low leisure-time physical activity** in adolescence independently predict the metabolic syndrome in mid-adulthood. Diabetes Care 2013 .
Wettstein ZS, Hoshiko S, Fahimi J, et al. Cardiovascular and Cerebrovascular Emergency Department Visits Associated With **Wildfire Smoke Exposure** in California in 2015. J Am Heart Assoc. 2018 Apr 11;7(8).
Weustink AC, Mollet NR, Neefjes LA, et al. Diagnostic accuracy and clinical utility of **noninvasive testing** for coronary artery disease. Ann Intern Med. 2010 May 18;152(10):630-9.
Wheeler, Matthew T. Heidenreich, Paul A. Froelicher, Victor F. Et al. Cost-Effectiveness of **Preparticipation Screening** for Prevention of Sudden Cardiac Death in Young **Athletes**. Ann Intern Med March 2, 2010 152:276-286.
Whelton PK. **Urinary sodium** and cardiovascular disease risk. Informing guidelines for sodium consumption. JAMA 2011; 306:2262-2264.
White MP, Alcock I, Grellier J, et al. Spending at least 120 minutes a week in **nature is associated with good health and wellbeing**. Sci Rep. 2019 Jun 13;9(1):7730.
Whitman IR, Agarwal V, Nah G, et al. **Alcohol abuse** and cardiac disease. J Am Coll Cardiol 2017; 69:13–24.
Wickramasinghe CD, Ayers CR, Das S, et al. Prediction of **30-Year Risk** for Cardiovascular Mortality by **Fitness and Risk Factor Levels**. The Cooper Center Longitudinal Study. *Circ Cardiovasc Qual Outcomes* 2014.
Willeit P, Welsh P, Evans JDW, et al. High-Sensitivity **Cardiac Troponin** Concentration and Risk of First-Ever Cardiovascular Outcomes in 154,052 Participants. J Am Coll Cardiol. 2017 Aug 1;70(5):558-568.
Willey JZ, Moon YP, Kahn E, et al. **Population attributable risks of hypertension and diabetes** for cardiovascular disease and stroke in the northern Manhattan study. J Am Heart Assoc. 2014 Sep 16;3(5).
Wilkins JT et al. **Lifetime risk and years lived free** of total cardiovascular disease. JAMA 2012 Nov 7; 308:1795.
Williams MC, Hunter A, Shah AS, et al. Use of **Coronary Computed Tomographic Angiography** to Guide Management of Patients With Coronary Disease. J Am Coll Cardiol. 2016 Apr 19;67(15):1759-68
Williams PT, Thompson PD. **Walking versus running** for hypertension, cholesterol, and diabetes mellitus risk reduction. Arterioscler Thromb Vasc Biol. 2013 May;33(5):1085-91.
Williams PT, Thompson PD. Increased cardiovascular disease mortality associated with **excessive exercise** in heart attack survivors. *Mayo Clin Proc* 2014.
Willis BL, Gao A, Leonard D, et al. **Midlife Fitness** and the Development of Chronic Conditions in Later Life. Arch Intern Med. 2012 Aug 27:1-8.
Willis BL, DeFina LF, Bachmann JM, et al. Association of **Ideal Cardiovascular Health** and Long-term Healthcare Costs. Am J Prev Med. 2015 Nov;49(5):678-85.
Wilmot KA, O'Flaherty M, Capewell S, et al. Coronary Heart Disease **Mortality Declines in the United States From 1979 Through 2011**: Evidence for Stagnation in Young Adults, Especially Women. Circulation. 2015 Sep 15;132(11):997-1002.
Wilson PW, D`Agostino R Sr, Bhatt DL, et al. An **international model** to predict recurrent cardiovascular disease. Am J Med. 2012 Jul;125(7):695-703.e1.
Wilson PW, Pencina MJ. **Estimation of Risk** for Initial Atherosclerotic Cardiovascular Disease Events: Taking Stock and Moving Forward. Circulation. 2016 Dec 6;134(23):1792-1793.
Wijeysundera DN, Beattie WS, Austin PC, et al. **Non-invasive cardiac stress testing** before elective major non-cardiac surgery: population based cohort study. BMJ 2010;340:b5526, doi: 10.1136/bmj.b5526 (Published 28 Jan 2010)
Wijeysundera Harindra C.; Machado Marcio; Farahati Farah et al; Association of **Temporal Trends in Risk Factors** and Treatment Uptake With Coronary Heart Disease Mortality, 1994-2005. JAMA. 2010;303(18):1841-1847.
Wing JJ, August E, Adar SD, et al. Change in **Neighborhood** Characteristics and Change in Coronary Artery Calcium: A Longitudinal Investigation in the MESA (Multi-Ethnic Study of Atherosclerosis) Cohort. Circulation. 2016 Aug 16;134(7):504-13.
Winning A, Glymour MM, McCormick MC, et al. **Psychological Distress** Across the Life Course and Cardiometabolic Risk: Findings From the 1958 British Birth Cohort Study. J Am Coll Cardiol. 2015 Oct 6;66(14):1577-86.
Wong A, Figueroa A, Son WM, et al. The effects of **stair climbing** on arterial stiffness, blood pressure, and leg strength in postmenopausal women with stage 2 hypertension. Menopause. 2018 Feb 12.
Wong CW, Kwok CS, Narain A, et al. **Marital status and risk of cardiovascular diseases**: a systematic review and meta-analysis. Heart. 2018 Jun 19.
Wong ND, Patao C, Malik S, et al. Preventable Coronary Heart Disease Events from Control of Cardiovascular Risk Factors in US **Adults With Diabetes** (Projections from Utilizing the **UKPDS Risk Engine**). Am J Cardiol. 2014 Apr 15;113(8):1356-61.
Wong J, Rexrode K, Sandhu R, et al. Number of **pregnancies and atrial fibrillation risk**: the Women's Health Study. Circulation 2017.
World Health Organization. **Sodium** intake for adults and children. Geneva, Switzerland: 2012.
World Health Organization. **Potassium** intake for adults and children. Geneva, Switzerland: 2012.
Writing Group for the **AREDS2** Research Group. Effect of long-chain **ω-3 fatty acids and lutein + zeaxanthin** supplements on cardiovascular outcomes: results of the Age-Related Eye Disease Study 2 (AREDS2) randomized clinical trial [online March 17, 2014]. JAMA Intern Med. doi:10.1001/jamainternmed.2014.328.
Wu CJ, Kao TW, Chang YW, et al. Does the additional component of **calf-circumference** refine metabolic syndrome in Correlating with Cardiovascular Risk? J Clin Endocrinol Metab. 2018 Jan 15.
Wu H, Flint AJ, Qi Q, et al. Association Between Dietary **Whole Grain Intake** and Risk of Mortality: Two Large Prospective Studies in US Men and Women. JAMA Intern Med. 2015 Jan 5.
Wu P, Haththotuwa R, Kwok CS, et al. **Preeclampsia** and Future Cardiovascular Health: A Systematic Review and Meta-Analysis. Circ Cardiovasc Qual Outcomes. 2017 Feb;10(2).
Wu V-C, Wu C-H, Huang T-M, Wang C-Y, et al. NSARF Group: Long-term risk of **coronary events after AKI**. J Am Soc Nephrol 25: XXX–XXX, 2014
Wu W, Masri A, Popovic ZB, et al. Long-term survival of patients with **radiation heart disease** undergoing cardiac surgery: a cohort study. Circulation. 2013 Apr 9;127(14):1476-84.
Wu YT, Luben R, Jones A. **Dog ownership** supports the maintenance of physical activity during poor weather in older English adults: cross-sectional results from the EPIC Norfolk cohort. J Epidemiol Community Health. 2017 Jul 24.
Würtz P, Havulinna AS, Soininen P, et al. **Metabolite profiling** and cardiovascular event risk: a prospective study of 3 population-based cohorts. Circulation. 2015 Mar 3;131(9):774-85.
Xanthakis V, Enserro DM, Murabito JM, et al. **Ideal cardiovascular health**: associations with biomarkers and subclinical disease and impact on incidence of cardiovascular disease in the framingham offspring study. Circulation. 2014 Nov 4;130(19):1676-83.
Xie W, Li G, Zhao D, et al. Relationship between fine particulate **air pollution** and ischaemic heart disease morbidity and mortality. Heart. 2015 Feb;101(4):257-63.
Xu H, Cupples LA, Stokes A, et al. **Association of Obesity With Mortality Over 24 Years of Weight History Findings From the Framingham Heart Study**. JAMA Netw Open. 2018;1(7):e184587.
Xu T, Magnusson Hanson LL, Lange T, et al. Workplace bullying and workplace violence as risk factors for cardiovascular disease: a multi-cohort study. Eur Heart J. 2019 Apr 7;40(14):1124-1134.
Yadlowsky S, Hayward RA, Sussman JB, et al. Clinical implications of revised pooled cohort equations for **estimating atherosclerotic cardiovascular disease risk**. Ann Intern Med. 2018. [Epub ahead of print]. doi:10.7326/M17-3011
Yamada T, Hara K, Umematsu H, Kadowaki T. **Male pattern baldness** and its association with coronary heart disease: A meta-analysis. BMJ Open 2013.
Yancy William S Jr; Westman Eric C.; McDuffie Jennifer R.; et al. A Randomized Trial of a **Low-Carbohydrate Diet vs Orlistat Plus a Low-Fat Diet** for Weight Loss. Arch Intern Med. 2010;170(2):136-145.
Yanek LR, Kral BG, Moy TF, et al. Effect of **Positive Well-Being** on Incidence of Symptomatic Coronary Artery Disease. Am J Cardiol. 2013 Jun 28.
Yang BY, Guo Y, Markevych I, et al. Association of Long-term Exposure to Ambient Air Pollutants With Risk Factors for Cardiovascular Disease in China. JAMA Netw Open. 2019 Mar 1;2(3):e190318.
Yang J, Christophi CA, Farioli A, et al. Association Between **Push-up Exercise Capacity and Future Cardiovascular Events** Among Active Adult Men. JAMA Netw Open. 2019 Feb 1;2(2):e188341.
Yang J, Teehan D, Farioli A, et al. **Sudden Cardiac Death Among Firefighters** ≤45 Years of Age in the United States. Am J Cardiol. 2013 Sep 27.
Yang J, Farioli A, Korre M, Kales SN. Modified Mediterranean diet score and cardiovascular risk in a North American working population. *PLoS One* 2014.
Yang L, Cao C, Kantor ED, et al. **Trends in Sedentary Behavior** Among the US Population, 2001-2016. JAMA. 2019 Apr 23;321(16):1587-1597.

Yang Lin, Sahlqvist Shannon, McMinn Alison, et al. Interventions to promote **cycling**: systematic review. BMJ 341:doi:10.1136/bmj.c5293 (Published 18 October 2010)
Yang Q, Liu T, Kuklina EV, et al. **Sodium and potassium intake** and mortality among US adults: prospective data from the Third National Health and Examination Survey. Arch Intern Med. 2011;171(13):1183-1191.
Yang Q, Cogswell ME, Flanders WD, et al. **Trends in cardiovascular health metrics** and associations with **all-cause and CVD mortality** among US adults [published online March 16, 2012]. JAMA. doi:10.1001/jama.2012.339.
Yang Q, Zhang Z, Kuklina EV, et al. **Sodium Intake** and Blood Pressure Among US Children and Adolescents. Pediatrics. 2012 Sep 17.
Yang Q, Zhang Z, Gregg EW, et al. **Added sugar intake** and cardiovascular diseases mortality among US adults.*JAMA Intern Med* 2014.
Yang WY, Melgarejo JD, Thijs L, et al. Association of **Office and Ambulatory Blood Pressure With Mortality** and Cardiovascular Outcomes. JAMA. 2019 Aug 6;322(5):409-420.
Yang X, Li J, Hu D, et al. Predicting the **10- year risks of atherosclerotic cardiovascular disease in Chinese** population: the China-PAR project (Prediction for ASCVD Risk in China). Circulation. 2016;134:1430–1440.
Yankelson L, Sadeh B, Gershovitz L, et al. **Life-threatening events during endurance sports**: Is heat stroke more prevalent than arrhythmic death? *J Am Coll Cardiol* 2014; 64:463-469.
Yano Y, O'Donnell CJ, Kuller L, et al. Association of **Coronary Artery Calcium Score** vs Age With Cardiovascular Risk in Older Adults: An Analysis of Pooled Population-Based Studies. JAMA Cardiol. 2017 Jul 26.
Yarur AJ, Deshpande AR, Pechman DM, et al. **Inflammatory Bowel Disease** Is Associated With an Increased Incidence of Cardiovascular Events. Am J Gastroenterol. 2011 Mar 8.
Yates T, Haff ner SM, Schulte PJ, et al. Association between change in **daily ambulatory activity** and cardiovascular events in people with impaired glucose tolerance (NAVIGATOR trial): a cohort analysis. Lancet 2014; online Dec 20.
Yates T, Zaccardi F, Dhalwani NN, et al. Association of **walking pace and handgrip strength** with all-cause, cardiovascular, and cancer mortality: a UK Biobank observational study. Eur Heart J. 2017 Nov 14;38(43):3232-3240.
Ye S, Shaffer JA, Kang MS, et al. Relation Between **Leukocyte Telomere Length** and Incident Coronary Heart Disease Events (from the 1995 Canadian Nova Scotia Health Survey). Am J Cardiol. 2013 Jan 29.
Yeboah J, McClelland RL, Polonsky TS, et al. Comparison of **novel risk markers** for improvement in cardiovascular risk assessment in intermediate-risk individuals. JAMA. 2012 Aug 22;308(8):788-95.
Yin P, He G, Fan M, et al. **Particulate air pollution** and mortality in 38 of China's largest cities: time series analysis. BMJ. 2017 Mar 14;356:j667.
Yokoyama Y, Nishimura K, Barnard ND, et al. **Vegetarian diets** and blood pressure. A meta-analysis. *JAMA Intern Med* 2014; DOI:10.1001/jamainternmed.2013.14547.
Yoon SS, Dillon CF, Illoh K, et al. Trends in the **Prevalence of Coronary Heart Disease in the U.S.:** National Health and Nutrition Examination Survey, 2001-2012. Am J Prev Med. 2016 Oct;51(4):437-45.
Young DR, Hivert MF, Alhassan S, et al. **Sedentary Behavior** and Cardiovascular Morbidity and Mortality: A Science Advisory From the American Heart Association. Circulation. 2016 Aug 15
Young LH, Wackers FJ, et al. Cardiac outcomes after screening for asymptomatic coronary artery disease in patients with type 2 diabetes: the DIAD study: a randomized controlled trial. JAMA. 2009 Apr 15;301(15):1547-55.
Screening for coronary artery disease (CAD) in adults with type 2 diabetes and no indication of existing CAD does not improve outcomes more than standard care. This should come as no surprise -- screening for asymptomatic CAD with electron beam tomography (JAMA 2003; 289:2215-23.) and carotid intima-thickness (Stroke 2001;32:1532-8) also did not improve outcomes. Knowing with additional certainty that a patient is "at risk" for CAD does not result in different medication use nor improved compliance. (LOE = 1b-)
Young DR, Reynolds K, Sidell M, et al. Effects of **physical activity and sedentary time on the risk of heart failure.** Circ Heart Fail. 2014 Jan 1;7(1):21-7
Yu D, Sonderman J, Buchowski MS, McLaughlin JK, et al. **Healthy Eating and Risks of Total and Cause-Specific Death** among Low-Income Populations of African-Americans and Other Adults in the Southeastern United States: A Prospective Cohort Study. PLoS Med. 2015 May 26;12(5):e1001830
Yu E, Malik VS, Hu FB. **Cardiovascular Disease Prevention by Diet Modification**: JACC Health Promotion Series. J Am Coll Cardiol. 2018 Aug 21;72(8):914-926.
Yu J, Zhou Z, McEvoy RD, et al. Association of **positive airway pressure** with cardiovascular events and death in adults with **sleep apnea**: a systematic review and meta-analysis.JAMA. doi:10.1001/jama .2017.7967
Zacho J, Tybjaerg-Hansen A, Jensen JS, Grande P, Sillesen H, Nordestgaard BG. Genetically elevated C-reactive protein and ischemic vascular disease. N Engl J Med. 2008 Oct 30;359(18):1897-908.
Zaninotto P, Wardle J, Steptoe A. Sustained **enjoyment of life and mortality at older ages**: analysis of the English Longitudinal Study of Ageing. BMJ. 2016 Dec 13;355:i6267.
Zethelius B, Berglund L, Sundström J, et al. Use of **multiple biomarkers** to improve the prediction of death from cardiovascular causes. N Engl J Med. 2008 May 15;358(20):2107-16. (troponin I, N-terminal pro-brain natriuretic peptide, cystatin C, and C-reactive protein, respectively) Our data suggest that in elderly men with or without prevalent cardiovascular disease, the simultaneous addition of several biomarkers of cardiovascular and renal abnormalities substantially improves the risk stratification for death from cardiovascular causes beyond that of a model that is based only on established risk factors.
Zhang D, Shen X, Qi X. **Resting heart rate** and all-cause and cardiovascular mortality in the general population: a meta-analysis. CMAJ. 2015 Nov 23.
Zhang D, Wang W, Li F. Association between **resting heart rate** and coronary artery disease, stroke, sudden death and noncardiovascular diseases: a meta-analysis. CMAJ. 2016 Aug 22.
Zhang Y, Tuomilehto J, Jousilahti P, et al. **Lifestyle Factors on the Risks** of Ischemic and Hemorrhagic Stroke. Arch Intern Med. 2011 Sep 12.
Zhao D, Guallar E, Ouyang P, et al. **Endogenous Sex Hormones and Incident Cardiovascular Disease** in Post-Menopausal Women. J Am Coll Cardiol. 2018 Jun 5;71(22):2555-2566.
Zhao M, Veeranki SP, Li S, et al. **Beneficial associations of low and large doses of leisure time physical activity** with all-cause, cardiovascular disease and cancer mortality: a national cohort study of 88,140 US adults. Br J Sports Med. 2019 Mar 19.
Zheng G, Li S, Huang M, et al. The effect of **Tai Chi training on cardiorespiratory fitness in healthy adults**: a systematic review and meta-analysis. PLoS One. 2015 Feb 13;10(2):e0117360.
Zheng W, McLerran DF, and Rolland B. Association between BMI and risk of death in more than one million Asians. New Engl J Med 2011; 364:719-729.
Zheng Y, Li Y, Satija A, et al. Association of changes in **red meat consumption with total and cause specific mortality** among US women and men: two prospective cohort studies. BMJ. 2019 Jun 12;365:l2110.
Zhong VW, Van Horn L, Cornelis MC, et al. **Associations of Dietary Cholesterol or Egg Consumption** With Incident Cardiovascular Disease and Mortality. JAMA. 2019 Mar 19;321(11):1081-1095.
Zipes DP. Sudden Cardiac Arrest and Death Following Application of Shocks From a **TASER** Electronic Control Device. Circulation. 2012 May 22;125(20):2417-22.
Zomer E, Owen A, Magliano DJ, et al. The effectiveness and cost effectiveness of **dark chocolate consumption** as prevention therapy in people at high risk of cardiovascular disease: Best case scenario analysis using a Markov model. BMJ 2012.
Zong G, Gao A, Hu FB, et al. **Whole Grain Intake** and Mortality From All Causes, Cardiovascular Disease, and Cancer: A Meta-Analysis of Prospective Cohort Studies. Circulation. 2016 Jun 14;133(24):2370-80.
Zong G, Li Y, Wanders AJ, et al. Intake of individual **saturated fatty acids** and risk of coronary heart disease in US men and women: two prospective longitudinal cohort studies. BMJ. 2016 Nov 23;355:i5796.

Additional Links:

AHA: Beneficial & Harmful Fats 1 pager – Jan 2009: http://americanheart.mediaroom.com/file.php/290/Fats+--+beneficial+vs+harmful%282%29.pdf

SPECTRUM OF CORONARY ARTERY DISEASE AHA '12



References- ANGINA:

Canadian Guidelines

1. Mancini GB, Gosselin G, Chow B, et al. Canadian Cardiovascular Society. Canadian Cardiovascular Society guidelines for the diagnosis and management of **stable ischemic heart disease**. Can J Cardiol. 2014 Aug;30(8):837-49.
2. Parker JD, Parker JO. **Stable angina pectoris**: the medical management of symptomatic myocardial ischemia. Can J Cardiol. 2012 Mar-Apr;28(2 Suppl):S70-80.

USA Guidelines

3. Fihn SD, Blankenship JC, Alexander KP, et al. American College of Cardiology/America Heart Association Task Force on Practice Guidelines; American Association for Thoracic Surgery; Preventive Cardiovascular Nurses Association; Society for Cardiovascular Angiography and Interventions; Society of Thoracic Surgeons. 2014 ACC/AHA/AATS/PCNA/SCAI/STS focused update of the guideline for the diagnosis and management of patients with **stable ischemic heart disease**: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines, and the American Association for Thoracic Surgery, Preventive Cardiovascular Nurses Association, Society for Cardiovascular Angiography and Interventions, and Society of Thoracic Surgeons. J Thorac Cardiovasc Surg. 2015 Mar;149(3):e5-23.

4. Fihn SD, Gardin JM, Abrams J, et al. 2012 ACCF/AHA/ACP/AATS/PCNA/SCAI/ STS guideline for the diagnosis and management of patients with **stable ischemic heart disease**: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines, and the American College of Physicians, American Association for Thoracic Surgery, Preventive Cardiovascular Nurses Association, Society for Cardio- vascular Angiography and Interventions, and Society of Thoracic Surgeons. J Am Coll Cardiol 2012;60(24):e44-164.
5. Gibbons RJ, Abrams J, Chatterjee K, et al. ACC/AHA 2002 guideline update for the management of patients with **chronic stable angina**—summary article: a report of the American College of Cardiology/American Heart Association Task Force on practice guidelines (Committee on the Management of Patients with **Chronic Stable Angina**. J Am Coll Cardiol. 2003;41:159-68.
6. Amsterdam EA, Wenger NK, Ralph GB et al. 2014 AHA/ACC Guideline for the management of patients with **non-ST-elevation acute coronary syndromes**: A Report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. JACC 2014;64:e139-228.
7. Anderson JL, Adams CD, Antman EM. ACC/AGA 2007 Guidelines for the management of patients with **unstable angina/non-ST-elevation myocardial infarction**: A Report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Writing Committee to Revise the 2002 Guidelines for the Management of Patients With Unstable Angina/Non–ST-Elevation Myocardial Infarction). Circulation 2007;116:e148-e304.

<u>European Guidelines</u>

8. Montalescot G, Sechtem U, Achenbach S, et al. **2013 ESC guidelines** on the management of **stable coronary artery disease**: the Task Force on the management of stable coronary artery disease of the European Society of Cardiology. Eur Heart J. 2013 Oct;34(38):2949-3003.
   Knuuti J, Wijns W, Saraste A, et al. **2019 ESC Guidelines** for the diagnosis and management of chronic coronary syndromes. Eur Heart J. 2019 Aug 31.
9. Fox K, Garcia MA, Ardissino D, et al. Guidelines on the management of **stable angina** pectoris: executive summary: The Task Force on the Management of Stable Angina Pectoris of the European Society of Cardiology. Eur Heart J 2006;27:1341–1381.
10. Roffie M, PatronoC, Collet JP. 2015 ESC Guidelines for the management of **acute coronary syndromes in patients presenting without persistent ST-segment elevation**: Task Force for the Management of Acute Coronary Syndromes in Patients Presenting without Persistent ST-Segment Elevation of the European Society of Cardiology (ESC). European Heart Journal 2016;37:267-315.

<u>UK Guidelines</u>

11. Henderson RA, O'Flynn N; Guideline Development Group. **Management of stable angina**: summary of NICE guidance. Heart. 2012 Mar;98(6):500-7.

<u>Other Articles</u>

12. Steg PG, Bhatt DL, Wilson PW, et al. One-year cardiovascular event rates in outpatients with atherothrombosis. JAMA 2007;297:1197 – 1206. (**REACH registry**)
13. Boden WE, O'Rourke RA, Teo KK, et al. Optimal medical therapy with or without PCI for stable coronary disease. N Eng J Med 2007;356:1503 – 1516.
14. Chung SC, Hlatky MA, Faxon D, et al. The effect of age on clinical out- comes and health status BARI 2D (Bypass Angioplasty Revascularization Investigation in Type 2 Diabetes). J Am Coll Cardiol 2011;58:810 – 819.
15. Frye RL, August P, Brooks MM, et al. A randomized trial of therapies for type 2 diabetes and coronary artery disease. N Eng J Med 2009;360:2503 – 2515.
16. Henderson RA, Pocock SJ, Clayton TC, et al. Seven-year outcome in the RITA-2 trial: coronary angioplasty versus medical therapy. J Am Coll Cardiol 2003;42:1161–1170.
17. Poole-Wilson PA, Lubsen J, Kirwan BA, et al. Effect of long-acting nifedipine on mortality and cardiovascular morbidity in patients with stable angina requiring treatment (ACTION trial): randomised controlled trial. Lancet 2004;364:849 – 857.
18. Steg PG, Greenlaw N, Tardif JC, et al. Women and men with stable coronary artery disease have similar clinical outcomes: insights from the international prospective CLARIFY registry. Eur Heart J 2012;33:2831 – 2840.
19. Antman EM, Cohen M, Bernink PJ, et al. The TIMI risk score for unstable angina/non-ST elevation MI: A method for prognostication and therapeutic decision making. JAMA.2000 Aug 16;284(7):835-42.
20. Bairey Merz CN, Shaw LJ, Reis SE, et al. Insights from the NHLBI-Sponsored Women's Ischemia Syndrome Evaluation (WISE) Study: Part II: gender differences in presentation, diagnosis, and outcome with regard to gender-based pathophysiology of atherosclerosis and macrovascular and microvascular coronary disease. J Am CollCardiol. 2006 Feb 7;47(3 Suppl):S21-9.
21. Canto JG, Fincher C, Kiefe CI, et al. Atypical presentations among Medicare beneficiaries with unstable angina pectoris. Am J Cardiol 2002;90:248–253.

22. Mackay MH, Ratner PA, Johnson JL, Humphries KH, Buller CE. Gender differences in symptoms of myocardial ischaemia. Eur Heart J 2011;32:3107 – 3114.
23. Rubini Gimenez M, Reiter M, et al. Specific chest pain characteristics in the early diagnosis of acute myocardial infarction. JAMA Intern Med 2014;174:241 – 249.
24. Menees DS, Bates ER. Evaluation of patients with suspected coronary artery disease. Coron Artery Dis. 2010 Nov;21(7):386-90
25. George J, Rapsomaniki E, Pujades-Rodriguez M,et al. How Does Cardiovascular Disease First Present in Women and Men? Incidence of 12 Cardiovascular Diseases in a Contemporary Cohort of 1,937,360 People. Circulation. 2015 Oct 6;132(14):1320-8.
26. Go AS, Mozaffarian D, Roger VL, et al. Heart Disease and Stroke Statistics–2013 Update: a report from the American Heart Association. Circulation 2013;127: e6–245.
27. Rothwell PM, Coull AJ, Silver LE, et al. Population-based study of event-rate, incidence, case fatality, and mortality for all acute vascular events in all arterial territories (Oxford Vascular Study). Lancet. 2005 Nov 19;366(9499):1773-83.
28. Shroff GR, Heubner BM, Herzog CA. Incidence of acute coronary syndrome in the general Medicare population, 1992 to 2009: a real-world perspective. JAMA Intern Med. 2014 Oct;174(10):1689-90.
29. Braunwald E, Morrow DA. Unstable angina: is it time for a requiem? Circulation 2013;127:2452 – 2457.
30. Mueller C. Biomarkers and acute coronary syndromes: an update. Eur Heart J 2014;35:552 – 556.
31. Reichlin T, et al. Risk stratification in patients with unstable angina using ab- solute serial changes of 3 high-sensitive troponin assays. Am Heart J 2013;165: 371 – 378, e373.
32. Reichlin T, Twerenbold R, Reiter M, et al. Introduction of high-sensitivity troponin assays: impact on myocardial infarction incidence and prognosis. Am J Med 2012;125:1205 – 1213, e1201.
33. Weiss R, Ferry D, Pickering E, Smith LK, Dennish G 3rd, Krug-Gourley S, Lukas MA. Effectiveness of three different doses of carvedilol for exertional angina. Carvedilol-Angina Study Group. Am J Cardiol. 1998 Oct 15;82(8):927-31.
34. Ogawa H, Yasue H, Nakamura N, Fujii H, Miyagi H, Kikuta K. Comparison of efficacy of nisoldipine, metoprolol, and isosorbide dinitrate in patients with stable exertional angina: a randomized, cross-over, placebo-controlled study. Int J Cardiol. 1995 Feb;48(2):131-7.
35. van der Does R, Hauf-Zachariou U, Pfarr E, Holtbrügge W, König S, Griffiths M, Lahiri A. Comparison of safety and efficacy of carvedilol and metoprolol in stable angina pectoris. Am J Cardiol. 1999 Mar 1;83(5):643-9.
36. Heidenreich PA, McDonald KM, Hastie T, et al. Meta-analysis of trials comparing beta-blockers, calcium antagonists, and nitrates for stable angina. JAMA. 1999 May 26;281(20):1927-36.
36a. Shu de F, Dong BR, Lin XF, Wu TX, Liu GJ. Long-term beta blockers for stable angina: systematic review and meta-analysis. Eur J Prev Cardiol. 2012 Jun;19(3):330-41.
36b. Rehnqvist N, Hjemdahl P, Billing E, et al. Effects of metoprolol vs verapamil in patients with stable angina pectoris (**APSIS**). Eur Heart J. 1996;17:76-81.
36c. 'Fox KM, Mulcahy D, Findlay I, Ford I, Dargie HJ. The Total Ischaemic Burden European Trial (**TIBET**). Effects of atenolol, nifedipine SR and their combination on the exercise test and the total ischaemic burden in 608 patients with stable angina. Eur Heart J. 1996 Jan;17(1):96-103.
36d. Ardissino D, Savonitto S, Egstrup K, et al. Selection of medical treatment in stable angina pectoris: results of the International Multicenter Angina Exercise (**IMAGE**) Study. J Am Coll Cardiol. 1995 Jun;25(7):1516-21.
37. Chatterjee S, Chaudhuri D, Vedanthan R, Fuster V, Ibanez B, Bangalore S, Mukherjee D. Early intravenous beta-blockers in patients with acute coronary syndrome—a meta-analysis of randomized trials. Int J Cardiol 2013;168:915 – 921.
38. Miller CD, Roe MT, Mulgund J, et al. Impact of acute beta-blocker therapy for patients with non-ST-segment elevation myocardial infarction. Am J Med 2007;120:685–692.
39. de Peuter OR, Lussana F, Peters RJ, et al. A systematic review of selective and non-selective beta blockers for prevention of vascular events in patients with acute coronary syndrome or heart failure. Neth J Med 2009;67:284–94.
40. Kernis SJ, Harjai KJ, Stone GW, et al. Does beta-blocker therapy improve clinical outcomes of acute myocardial infarction after successful primary angioplasty? J Am Coll Cardiol. 2004;43:1773–9.
41. Freemantle N, Cleland J, Young P, et al. Beta blockade after myocardial infarction: systematic review and meta regression analysis. BMJ. 1999;318:1730 –7.
42. Chen ZM, Pan HC, Chen YP, Peto R, Collins R, Jiang LX, Xie JX, Liu LS; **COMMIT** (ClOpidogrel and Metoprolol in Myocardial Infarction Trial) collaborative group. Early intravenous then oral metoprolol in 45,852 patients with acute myocardial infarction: randomised placebo-controlled trial. Lancet. 2005 Nov 5;366(9497):1622-32.

43. Pepine CJ, Faich G, Makuch R. Verapamil use in patients with cardiovascular disease: an overview of randomized trials. Clin Cardiol 1998;21:633–41.
44. Smith NL, Reiber GE, Psaty BM, et al. Health outcomes associated with beta-blocker and diltiazem treatment of unstable angina. J Am Coll Cardiol 1998; 32:1305–11.
45. Collaborative overview of randomised trials of antiplatelet therapy: I: Prevention of death, myocardial infarction, and stroke by prolonged antiplatelet therapy in various categories of patients. Antiplatelet Trialists' Collaboration. BMJ 1994; 308:81 – 106.
46. Collaborative meta-analysis of randomised trials of antiplatelet therapy for prevention of death, myocardial infarction, and stroke in high risk patients. BMJ 2002;324: 71–86.
47. Juul-Moller S, Edvardsson N, Jahnmatz B, et al. Double-blind trial of aspirin in primary prevention of myocardial infarction in patients with stable chronic angina pectoris. The Swedish Angina Pectoris Aspirin Trial (SAPAT) Group. Lancet. 1992;340:1421–5.
48. A randomised, blinded, trial of clopidogrel versus aspirin in patients at risk of ischaemic events (**CAPRIE**). CAPRIE Steering Committee. Lancet 1996;348:1329 – 1339.
49. Randomised trial of intravenous streptokinase, oral aspirin, both, or neither among 17,187 cases of suspected acute myocardial infarction: **ISIS-2**. ISIS-2 (Second International Study of Infarct Survival) Collaborative Group. Lancet. 1988 Aug 13;2(8607):349-60.
50. Wallentin L, Becker RC, Budaj A, Cannon CP, et al. Ticagrelor versus clopidogrel in patients with acute coronary syndromes (**PLATO**). N Engl J Med. 2009 Sep 10;361(11):1045-57.
51. Wiviott SD, Braunwald E, McCabe CH et al.Prasugrel versus clopidogrel in patients with acute coronary syndromes (**TRITON-TIMI 38**). N Engl J Med. 2007 Nov 15;357(20):2001-15.
52. Yusuf S, Zhao F, Mehta SR, Chrolavicius S, Tognoni G, Fox KK; Clopidogrel in Unstable Angina to Prevent Recurrent Events Trial Investigators.. Effects of clopidogrel in addition to aspirin in patients with acute coronary syndromes without ST-segment elevation (**CURE**). N Engl J Med. 2001 Aug 16;345(7):494-502. Erratum in: N Engl J Med 2001 Nov 15;345(20):1506. N Engl J Med 2001 Dec 6;345(23):1716.
53. Goodman SG, Cohen M, Bigonzi F, et al. A Randomized trial of low molecular weight heparin (enoxaparin) versus unfractionated heparin for unstable coronary artery disease: one-year results of the **ESSENCE** Study. Efficacy and Safety of Subcutaneous Enoxaparin in Non-Q Wave Coronary Events. J Am CollCardiol. 2000 Sep;36(3):693-8.
54. Yusuf S, Mehta SR, Chrolavicius S, et al. Comparison of fondaparinux and enoxaparin in acute coronary syndromes (**OASIS 5**). N Engl J Med. 2006 Apr 6;354(14):1464-76.
55. LaRosa JC, Grundy SM, Waters DD, et al. Intensive lipid lowering with atorvastatin in patients with stable coronary disease (**TNT**). N Engl J Med. 2005;352:1425–35.
56. MRC-BHF Heart Protection Study of cholesterol lowering with simvastatin in 20,536 high-risk individuals: a randomised placebo- controlled trial (**HPS**). Lancet. 2002;360:7–22.
57. Pedersen TR, Faergeman O, Kastelein JJ, et al. High-dose atorvastatin vs usual-dose simvastatin for secondary prevention after myocardial infarction: the **IDEAL** study: a randomized controlled trial. JAMA. 2005;294:2437– 45.
58. de Lemos JA, Blazing MA, Wiviott SD, et al. Early intensive vs a delayed conservative simvastatin strategy in patients with acute coronary syndromes: phase Z of the **A to Z trial**. JAMA. 2004 Sep 15;292(11):1307-16.
59. Schwartz GG, Olsson AG, Ezekowitz MD, et al. Effects of atorvastatin on early recurrent ischemic events in acute coronary syndromes: the **MIRACL** study: a randomized controlled trial. JAMA 2001;285: 1711–8.
60. Cannon CP, Braunwald E, McCabe CH, et al. Intensive versus moderate lipid lowering with statins after acute coronary syndromes (**PROVE-IT**). N Engl J Med 2004;350:1495–1504.
61. Cannon CP, Blazing MA, Giugliano RP, et al. Ezetimibe added to statin therapy after acute coronary syndromes (**IMPROVE-IT**). N Engl J Med 2015;372:2387–97. see RxFiles Improve-It Trial Summary: http://www.rxfiles.ca.ezproxy.shirp.ca/rxfiles/uploads/documents/Lipid-IMPROVE-IT-Trial-Summary-QandA.pdf
62. Yusuf S, Sleight P, Pogue J, et al. Effects of an angiotensin- converting-enzyme inhibitor, ramipril, on cardiovascular events in high-risk patients. The Heart Outcomes Prevention Evaluation Study Investigators (**HOPE**). N Engl J Med. 2000;342:145–53.
63. Fox KM. Efficacy of perindopril in reduction of cardiovascular events among patients with stable coronary artery disease: randomised, double-blind, placebo-controlled, multicentre trial (**the EUROPA study**). Lancet. 2003;362:782–8.
64. Young JB, Dunlap ME, Pfeffer MA, et al. Mortality and morbidity reduction with Candesartan in patients with chronic heart failure and left ventricular systolic dysfunction: results of the **CHARM** low-left ventricular ejection fraction trials. Circulation. 2004 Oct 26;110(17):2618-26.
65. Braunwald E, Domanski MJ, Fowler SE, et al. Angiotensin- converting-enzyme inhibition in stable coronary artery disease. N Engl J Med. 2004;351:2058
66. Danchin N, Cucherat M, Thuillez C, et al. Angiotensin-converting enzyme inhibitors in patients with coronary artery disease and absence of heart failure or left ventricular systolic dysfunction: an overview of long-term randomized controlled trials. Arch Intern Med. 2006;166:787–96.

67. Al-Mallah MH, Tleyjeh IM, bdel-Latif AA, et al. Angiotensin- converting enzyme inhibitors in coronary artery disease and preserved left ventricular systolic function: a systematic review and meta-analysis of randomized controlled trials. J Am Coll Cardiol. 2006;47:1576 – 83.
68. Yusuf S, Teo KK, Pogue J, Dyal L, Copland I, Schumacher H, Dagenais G, Sleight P, Anderson C. Telmisartan, ramipril, or both in patients at high risk for vascular events. N Engl J Med 2008;358:1547 – 1559.
69. Garg R, Yusuf S. Overview of randomized trials of angiotensin-converting enzyme inhibitors on mortality and morbidity in patients with heart failure. Collaborative Group on ACE Inhibitor Trials. JAMA 1995;273: 1450–6.
70. Dagenais GR, Pogue J, Fox K, et al. Angiotensin- converting-enzyme inhibitors in stable vascular disease without left ventricular systolic dysfunction or heart failure: a combined analysis of three trials. Lancet 2006;368:581–8.
71. Hjalmarson A, Goldstein S, Fagerberg B, et al. Effects of controlled-release metoprolol on total mortality, hospitalizations, and well-being in patients with heart failure: the Metoprolol CR/XL Randomized Intervention Trial in congestive heart failure (**MERIT-HF**). MERIT-HF Study Group. JAMA 2000;283:1295 – 1302.
72. The Cardiac Insufficiency Bisoprolol Study II (**CIBIS-II**): a randomised trial. Lancet 1999;353:9 -13.
73. Packer M, Bristow MR, Cohn JN, et al. The effect of carvedilol on morbidity and mortality in. patients with chronic heart failure. U.S. Carvedilol Heart Failure Study Group (**COMET**). N Eng J Med 1996;334:1349 – 1355.
74. Bangalore S, Steg G, Deedwania P, Crowley K, et al. beta-Blocker use and clinical outcomes in stable outpatients with and without coronary artery disease. JAMA 2012;308:1340 – 1349.
75. de Peuter OR, Lussana F, Peters RJ, et al. A systematic review of selective and non-selective beta blockers for prevention of vascular events in patients with acute coronary syndrome or heart failure. Neth J Med. 2009;67:284 –94.
76. Wright JT Jr, Williamson JD, Whelton PK, et al. A Randomized Trial of Intensive versus Standard Blood-Pressure Control (**SPRINT**). N Engl J Med. 2015 Nov 26;373(22):2103-16.
77. Dahlof B, Sever PS, Poulter NR, et al. Prevention of cardiovascular events with an antihypertensive regimen of amlodipine adding perindopril as required versus atenolol adding bendroflumethiazide as required, in the Anglo-Scandinavian Cardiac Outcomes Trial- Blood Pressure Lowering Arm (**ASCOT**-BPLA): a multicentre randomised controlled trial. Lancet 2005;366:895–906.
78. Jamerson K, Weber MA, Bakris GL, Dahlof B, Pitt B, Shi V, Hester A, Gupte J, Gatlin M, Velazquez EJ. Benazepril plus amlodipine or hydrochlorothiazide for hypertension in high-risk patients (**ACCOMPLISH**). N Eng J Med 2008;359:2417–2428.
79. Weiss RJ, Hicks D, Bittar N, Bowers J, Shah A. A double-blind, placebo-controlled trial of sustained-release diltiazem in patients with angina. Sustained-Release Diltiazem Study Group. Clin Ther. 1993 Nov-Dec;15(6):1069-75.
80. Weiss R, Ferry D, Pickering E, Smith LK, Dennish G 3rd, Krug-Gourley S, Lukas MA. Effectiveness of three different doses of carvedilol for exertional angina. Carvedilol-Angina Study Group. Am J Cardiol. 1998 Oct 15;82(8):927-31.
81. Lubsen J, Tijssen JG. Efficacy of nifedipine and metoprolol in the early treatment of unstable angina in the coronary care unit: findings from the Holland Interuniversity Nifedipine/metoprolol Trial (**HINT**). Am J Cardiol 1987;60:18A–25A.
82. Furberg CD, Psaty BM, Meyer JV. Nifedipine. Dose-related increase in mortality in patients with coronary heart disease. Circulation 1995;92:1326–31.
83. Lubsen J, Wagener G, Kirwan BA, et al. Effect of long-acting nifedipine on mortality and cardiovascular morbidity in patients with symptomatic stable angina and hypertension: the **ACTION** trial. J Hypertens. 2005 Mar;23(3):641-8.
84. Ezekowitz MD, Hossack K, Mehta JL, et al. Amlodipine in chronic stable angina: results of a multicenter double-blind crossover trial. Am Heart J. 1995;129:527–35.
85. Boman K, Saetre H, Karlsson LG, et al. Antianginal effect of conventional and controlled release diltiazem in stable angina pectoris. Eur J Clin Pharmacol. 1995;49:27–30.
86. Brogden RN, Benfield P. Verapamil: a review of its pharmacological properties and therapeutic use in coronary artery disease. Drugs. 1996;51:792– 819.
87. Alderman MH, Cohen H, Roque R, et al. Effect of long-acting and short-acting calcium antagonists on cardiovascular outcomes in hypertensive patients. Lancet. 1997;349:594–8.
88. A randomised factorial trial assessing early oral captopril, oral mononitrate, and intravenous magnesium sulphate in 58,050 patients with suspected acute myocardial infarction. **ISIS-4** (Fourth International Study of Infarct Survival) Collaborative Group. Lancet. 1995 Mar 18;345(8951):669-85.
89. Effects of lisinopril and transdermal glyceryl trinitrate singly and together on 6-week mortality and ventricular function after acute myocardial infarction (**GISSI-3**). Lancet. 1994 May 7;343(8906):1115-22.

90. Same efficacy- Savonitto S, Motolese M, Agabiti-Rosei E. Antianginal effect of transdermal nitroglycerin and oral nitrates given for 24 hours a day in 2,456 patients with stable angina pectoris. The Italian Multicenter Study. Int J Clin Pharmacol Ther. 1995 Apr;33(4):194-203.
91. Meluzín J, Zeman K, Stětka F, Simek P. Effects of nifedipine and diltiazem on myocardial ischemia in patients with severe stable angina pectoris treated with nitrates and beta-blockers. J Cardiovasc Pharmacol. 1992 Dec;20(6):864-9.
92. Akhras F, Jackson G. Efficacy of nifedipine and isosorbide mononitrate in combination with atenolol in stable angina. Lancet. 1991 Oct 26;338(8774):1036-9.
93. Boden WE, Bough EW, Reichman MJ et al. Beneficial effects of high-dose diltiazem in patients with persistent effort angina on beta-blockers and nitrates: a randomized, double-blind, placebo-controlled cross-over study. Circulation 1985;71:11197-2015.
94. Tolins M, Weir K, Chesler E. Pierpont GL. "Maximal" drug therapy is not necessarily optimal in chronic angina pectoris. J Am Coll Cardiol 1984;3:1051-7.
95. Archbold RA. Comparison between National Institute for Health and Care Excellence (NICE) and European Society of Cardiology (ESC) guidelines for the diagnosis and management of stable angina: implications for clinical practice. Open Heart. 2016 Jun 10;3(1):e000406.
96. Arnold SV, Grodzinsky A, Gosch KL, et al. Predictors of physician under-recognition of angine in outpatients with stable coronary artery disease. *Circ Cardiovasc Qual Outcomes* 2016.
97. Cayla G, Cuisset T, Silvain J, et al. ANTARCTIC investigators.. Platelet function monitoring to adjust antiplatelet therapy in elderly patients stented for an acute coronary syndrome (ANTARCTIC): an open-label, blinded-endpoint, randomised controlled superiority trial. Lancet. 2016 Oct 22;388(10055):2015-2022.
98. Chew DP, Zeitz C, Worthley M, et al. Randomized comparison of high-sensitivity troponin reporting in undifferentiated chest pain assessment. *JAMA Cardiol* 2016.
99. Hsia RY, Hale Z, Tabas JA. A National Study of the Prevalence of Life-Threatening Diagnoses in Patients With Chest Pain. JAMA Intern Med. 2016 Jun 13.
100. Mitchell JD, Brown DL. Update on Percutaneous Coronary Intervention in Stable Coronary Artery Disease. JAMA Intern Med. 2016 Dec 1;176(12):1855-1856.
101. Sekhri N, Perel P, Clayton T, et al. A 10-year prognostic model for patients with suspected angina attending a chest pain clinic.Heart. 2016 Feb 29.
102. Sibbing D, Kastrati A, Berger PB. Pre-treatment with P2Y12 inhibitors in ACS patients: who, when, why, and which agent? Eur Heart J. 2016 Apr 21;37(16):1284-95.
103. Siller-Matula JM, Specht S, Kubica J, Alexopoulos D, et al. Abciximab as a bridging strategy to overcome morphine-prasugrel interaction in STEMI patients. Br J Clin Pharmacol. 2016 Jul 1.
104. Syed S et al. Prospective validation of a clinical decision rule to identify patients presenting to the emergency department with chest pain who can safely be removed from cardiac monitoring. CMAJ 2017Jan 30; 189:E139.
105. Patel MR, Calhoon JH, Dehmer GJ, et al. ACC/AATS/AHA/ASE/ASNC/SCAI/SCCT/STS 2017 Appropriate Use Criteria for Coronary Revascularization in Patients With Stable Ischemic Heart Disease: A Report of the American College of Cardiology Appropriate Use Criteria Task Force, American Association for Thoracic Surgery, American Heart Association, American Society of Echocardiography, American Society of Nuclear Cardiology, Society for Cardiovascular Angiography and Interventions, Society of Cardiovascular Computed Tomography, and Society of Thoracic Surgeons. J Am Coll Cardiol. 2017 Mar 9.
106. Salazar CA, Basilio Flores JE, Veramendi Espinoza LE, et al. Ranolazine for stable angina pectoris. Cochrane Database Syst Rev. 2017 Feb 8;2:CD011747. We found very low quality evidence showing that people with stable angina who received ranolazine as monotherapy had increased risk of presenting non-serious adverse events compared to those given placebo. We found low quality evidence indicating that people with stable angina who received ranolazine showed uncertain effect on the risk of cardiovascular death (for ranolazine given as monotherapy), all-cause death and non-fatal AMI, and the frequency of angina episodes (for ranolazine given as monotherapy) compared to those given placebo. Moderate quality evidence indicated that people with stable angina who received ranolazine showed uncertain effect on quality of life compared with people who received placebo. Moderate quality evidence also indicated that people with stable angina who received ranolazine as add-on therapy had fewer angina episodes but increased risk of presenting non-serious adverse events compared to those given placebo.
107. Switaj TL, Christensen SR, Brewer DM. Acute Coronary Syndrome: Current Treatment. Am Fam Physician. 2017;95(4):232-240.
108. Hoffmann U, Ferencik M, Udelson JE, et al. Prognostic Value of Noninvasive Cardiovascular Testing in Patients With Stable Chest Pain: Insights From the PROMISE Trial (Prospective Multicenter Imaging Study for Evaluation of Chest Pain). Circulation. 2017 Jun 13;135(24):2320-2332.
109. Jørgensen ME, Andersson C, Nørgaard BL, et al. Functional Testing or Coronary Computed Tomography Angiography in Patients With Stable Coronary Artery Disease. J Am Coll Cardiol. 2017 Apr 11;69(14):1761-1770.
110. Lanza GA, Filice M, De Vita A, et al. Primary Stable Microvascular Angina: A Long-Term Clinical Follow-Up Study. Circulation. 2017 May 16;135(20):1982-1984.
111. Fanaroff AC, James SK, Weisz G, et al. **Ranolazine** After Incomplete Percutaneous Coronary Revascularization in Patients With Versus Without Diabetes Mellitus: **RIVER-PCI** Trial. J Am Coll Cardiol. 2017 May 9;69(18):2304-2313.
112. Nejatian A, Omstedt Å, Höijer J, et al. Outcomes in Patients With Chest Pain Discharged After Evaluation Using a High-Sensitivity Troponin T Assay. J Am Coll Cardiol. 2017 May 30;69(21):2622-2630.

113. Sandhu AT, Heidenreich P, Bhattacharya J, Bundorf MK. Cardiovascular testing and clinical outcomes in emergency department patients with chest pain: an instrumental variable analysis [online June 26, 2017].JAMA Intern Med. doi:10.1001/jamainternmed.2017.2432
114. Timmis A, Roobottom CA. National Institute for Health and Care Excellence updates the stable chest pain guideline with radical changes to the diagnostic paradigm. Heart. 2017 Jul;103(13):982-986.
115. Crea F, Libby P. Acute Coronary Syndromes: The Way Forward From Mechanisms to Precision Treatment. Circulation. 2017 Sep 19;136(12):1155-1166.
116. Danad I, Raijmakers PG, Driessen RS, et al. Comparison of Coronary CT Angiography, SPECT, PET, and Hybrid Imaging for Diagnosis of Ischemic Heart Disease Determined by Fractional Flow Reserve. JAMA Cardiol. 2017 Aug 16.
117. Ford TJ, Corcoran D, Berry C. Stable coronary syndromes: pathophysiology, diagnostic advances and therapeutic need. Heart. 2017 Oct 13.
118. Beltrame JF, Crea F, Kaski JC, et al; Coronary Vasomotion Disorders International Study Group (COVADIS).International standardization of diagnostic criteria for vasospastic angina. Eur Heart J. 2017 Sep 1;38(33):2565-2568.
119. Fearon WF, Nishi T, De et al. Clinical Outcomes and Cost-Effectiveness of Fractional Flow Reserve-Guided Percutaneous CoronaryIntervention in Patients With Stable Coronary Artery Disease: Three-Year Follow-Up of the FAME 2 Trial (Fractional Flow Reserve Versus Angiography forMultivessel Evaluation). Circulation. 2017 Nov 2.
120. Reinhardt SW, Lin C-J, Novak E, et al. Noninvasive cardiac testing versus clinical evaluation alone in acute chest pain: a secondary analysis of the ROMICAT-II randomized clinical trial. [published online November 14, 2017].JAMA Intern Med. doi:10.1001/jamainternmed.2017.7360.
121. Chiu MH. A Case of Chest Pain and Transient Cardiac Arrest. JAMA Intern Med. 2017 Oct 30. (Vasospastic angina)
122. Degerud E, Nygård O, de Vogel S, et al. Plasma 25-hydroxyvitamin D and mortality in patients with suspected stable angina pectoris. J Clin Endocrinol Metab. 2018 Jan 9.
123. Long L, Anderson L, Dewhirst AM, et al. Exercise-based cardiac rehabilitation for adults with stable angina. Cochrane Database Syst Rev. 2018 Feb 2;2:CD012786. Due to the small number of trials and their small size, potential risk of bias and concerns about imprecision and lack of applicability, we are uncertain of the effects of exercise-based CR compared to control on mortality, morbidity, cardiovascular hospital admissions, adverse events, return to work and health-related quality of life in people with stable angina. Low-quality evidence indicates that exercise-based CR may result in a small increase in exercise capacity compared to usual care.
124. Braun MM,Stevens WA, Barstow CH. Stable Coronary Artery Disease: Treatment. Am Fam Physician. 2018;97(6):376-384.,
125. Giannini F, Baldetti L, Ponticelli F, et al. **Coronary Sinus Reducer Implantation** for the Treatment of Chronic Refractory Angina: A Single-Center Experience. JACC Cardiovasc Interv. 2018 Apr 23;11(8):784-792.
126. Xaplanteris P, Fournier S, Pijls NHJ, et al. Five-Year Outcomes with **PCI Guided by Fractional Flow Reserve**. (FAME 2) N Engl J Med. 2018 May 22.
127. Al-Lamee R, Howard JP, Shun-Shin MJ, et al**. Fractional Flow Reserve and Instantaneous Wave-Free Ratio as Predictors** of the Placebo-Controlled Response to Percutaneous Coronary Intervention in Stable Single-Vessel Coronary Artery Disease: Physiology-Stratified Analysis of ORBITA. Circulation. 2018 May 22.
128. Ferrari R, Pavasini R, Camici PG, et al. Anti-anginal drugs-beliefs and evidence: systematic review covering 50 years of medical treatment. Eur Heart J. 2019 Jan 7;40(2):190-194.
129. Ford TJ, Stanley B, Good R, et al. Stratified Medical Therapy Using Invasive Coronary Function Testing in Angina: The CorMicA Trial. J Am Coll Cardiol. 2018 Dec 11;72(23 Pt A):2841-2855.
130. Kaul S. Evaluating the Evidence for Coronary Computed Tomography Angiography as the Noninvasive Test of Choice for Patients With Stable Chest Pain. JAMA Cardiol. 2018 Dec 26.
131. Yoshikawa Y, Kimura T. Percutaneous coronary intervention in stable coronary artery disease: still in equipoise? Eur Heart J. 2019 Jan 7;40(2):187-189.
132. Fernando SM, Tran A, Cheng W, et al**. Prognostic Accuracy of the HEART Score** for Prediction of Major Adverse Cardiac Events in Patients Presenting With Chest Pain: A Systematic Review and Meta-analysis. Acad Emerg Med. 2019 Feb;26(2):140-151.
133. Januzzi JL Jr, Suchindran S, Hoffmann U, et al. **Single-Molecule hsTnI and Short-Term Risk** in Stable Patients With Chest Pain. J Am Coll Cardiol. 2019 Jan 29;73(3):251-260.
134. Cook CM, Ahmad Y, Howard JP, et al. Association Between **Physiological Stenosis Severity and Angina**-Limited Exercise Time in Patients With Stable Coronary Artery Disease. JAMA Cardiol. 2019 May 1.
135. Haase R, Schlattmann P, Gueret P, et al; COME-CCT Consortium. **Diagnosis of obstructive coronary artery disease** using computed tomography angiography in patients with stable chest pain depending on clinical probability and in clinically important subgroups: meta-analysis of individual patient data. BMJ. 2019 Jun 12;365:l1945.
136. Laureano-Phillips J, Robinson RD, Aryal S, et al. **HEART Score Risk Stratification of Low-Risk Chest Pain Patients** in the Emergency Department: A Systematic Review and Meta-Analysis. Ann Emerg Med. 2019 Feb 1.
137. Knuuti J, Wijns W, Saraste A, et al. **2019 ESC Guidelines** for the diagnosis and management of chronic coronary syndromes. Eur Heart J. 2019 Aug 31.
138. Rahman H, Corcoran D, Aetesam-Ur-Rahman M, et al. **Diagnosis of patients** with angina and non-obstructive coronary disease in the catheter laboratory. Heart.

2019Jul31.
139. Pdf Zhao L, Li D, Zheng H, et al. **Acupuncture as Adjunctive Therapy** for Chronic Stable Angina: A Randomized Clinical Trial. JAMA Intern Med. 2019 Jul 29.
140.

ACE INHIBITOR (ACEI) / ANGIOTENSIN II RECEPTOR BLOCKER (ARB): Comparison Chart

[1] Major Outcomes in High-Risk Hypertensive Patients Randomized to Angiotensin-Converting Enzyme Inhibitor or Calcium Channel Blocker vs Diuretic. The Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial (**ALLHAT**). The ALLHAT Officers and Coordinators for the ALLHAT Collaborative Research Group. JAMA. 2002;288:2981-2997.

[2] 2001 Canadian Hypertension Recommendations: What's New & What's Not so New but is Still Important. CJHP 2002;55:4651.

[3] FA McAlister, M Levine, KB Zarnke, et al. The 2000 recommendations for the management of hypertension. Can J Cardiol 2001; 17(5):543-559.

[4] 1999 Canadian recommendations for the management of hypertension. CMAJ 1999;161(Suppl):S1-S16.

[5] **1999 World Health Organization**–International Society of Hypertension Guidelines:Management of Hypertension. J Hypertens 1999;17:151-183.

[6] 6th Report-Joint National Committee-JNC on Prevention,Detection,Evaluation & Treatment of High Blood Pressure. Arch Intern Med 1997;157:2413-46.

[7] Drugs for hypertension. Med Lett Drugs Ther 2001;43:17-22.

[8] Drugs in Pregnancy & Lactation, 11th Ed. Briggs GE,et al. Wilkins; Baltimore, MD. 2017.

[9] Micromedex 2018 online

[10] Hansten & Horn's Drug Interactions: Analysis & Management-Facts & Comparisons 2008.

[11] Treatment Guidelines: Drugs for Hypertension from The Medical Letter Feb 2003, repeated June 2005, January 2009, January 2012, May 2014 & updated **March 2017**.

[12] The **2017** Canadian Hypertension Education Program **Recommendations** www.hypertension.ca
Leung AA, Nerenberg K, Daskalopoulou SS, et al; CHEP Guidelines Task Force. Hypertension Canada's **2016 CHEP guidelines** for blood pressure measurement, diagnosis, assessment of risk, prevention and treatment of hypertension. Can J Cardiol 2016 (accepted manuscript) doi: 10.1016/j.cjca.2016.02.066 www.onlinecjc.ca/article/S0828-282X(16)00192-6/pdf (accessed April 11, 2016).
Hackam DG, Quinn RR, Ravani P, et al. Canadian Hypertension Education Program. The 2013 Canadian Hypertension Education Program (CHEP) Recommendations for Blood Pressure Measurement, Diagnosis, Assessment of Risk, Prevention, and Treatment of Hypertension. Can J Cardiol. 2013 Mar 28.
Canadian Hypertension Education Program. **2011 CHEP recommendations** for the management of **hypertension**. http://hypertension.ca/chep/wp-content/uploads/2011/05/FullCHEPRecommendations_EN_2011.pdf .
Dionne JM, Harris KC, Benoit G, et al. **Hypertension Canada's 2017 Guidelines for the Diagnosis, Assessment, Prevention, & Treatment of Pediatric Hypertension**. Can J Cardiol. 2017 May;33(5):577-585
Leung AA, Daskalopoulou SS, Dasgupta K, et al. **Hypertension Canada's 2017 Guidelines for Diagnosis, Risk Assessment, Prevention, & Treatment of Hypertension in Adults**. Can J Cardiol. 2017 May;33(5):557-576
Nerenberg KA, Zarnke KB, Leung AA, et al; Hypertension Canada. **Hypertension Canada's 2018 Guidelines** for Diagnosis, Risk Assessment, Prevention, and Treatment of Hypertension in Adults and Children. Can J Cardiol. 2018 May;34(5):506-525.

[13] ALLHAT Working Group. Major cardiovascular events in hypertensive patients randomized to doxazosin vs chlorthalidone: the antihypertensive and lipid-lowering treatment to prevent heart attack trial (**ALLHAT**). JAMA 2000;283:1967-75.

[14] Liu P, Arnold JM, Belenkie I, et al. The 2002/3 Canadian Cardiovascular Society consensus guideline update for the diagnosis and management of **heart failure**. Can J Cardiol. **2003** Mar 31;19(4):347-56.

[15] **Treatment Guidelines**: Drugs for Treatment of **Heart Failure** from The Medical Letter April **2003** & Jan **2006.**

[16] Jessup M, Brozena S. Heart Failure. N Engl J Med 2003;348:2007-18.

[17] The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (The **JNC 7**); JAMA. **2003** May;289(19):2560-72.
James PA, Oparil S, Carter BL, et al. **2014** evidence-based guideline for the management of **high blood pressure in adults**: report from the panel members appointed to the Eighth Joint National Committee (**JNC 8**). JAMA. doi:10.1001/jama.2013.284427.

[18] Pfeffer Marc A, Swedberg Karl, Granger Christopher B. et al, Effects of candesartan on mortality and morbidity in patients with chronic heart failure: the **CHARM**-Overall programme. Lancet 2003 **362:** 759-66. (Granger BB, Swedberg K, Ekman I, et al.; for the CHARM investigators. Adherence to candesartan and placebo and outcomes in chronic heart failure in the CHARM programme: double-blind, randomised, controlled clinical trial. Lancet. 2005 Dec 10;366(9502):2005-2011.) (Hillege HL, et al. Candesartan in Heart Failure: Assessment of Reduction in Mortality and Morbidity (CHARM) Investigators. Renal function as a predictor of outcome in a broad spectrum of patients with heart failure. Circulation. 2006 Feb 7;113(5):671-8.)(Ducharme A, et al. Prevention of atrial fibrillation in patients with symptomatic chronic heart failure by candesartan in the Candesartan in Heart failure: assessment of Reduction in Mortality and morbidity (CHARM) program. Am Heart J. 2006 May;151(5):985-91.)

[19] The EURopean trial On reduction of cardiac events with Perindopril in stable coronary Artery disease Investigators. Efficacy of perindopril in reduction of cardiovascular events among patients with stable coronary artery disease: randomised, double-blind, placebo-controlled, multicentre trial (the **EUROPA** study). Lancet 2003; 362: 782-88.

[20] Pfeffer MA, McMurray JJ, Velazquez EJ, et al. Valsartan, Captopril, or Both in Myocardial Infarction Complicated by Heart Failure, Left Ventricular Dysfunction, or Both.(the **VALIANT** study). N Engl J Med. 2003 Nov 10
(McMurray J, et al. The effect of valsartan, captopril, or both on atherosclerotic events after acute myocardial infarction: an analysis of the Valsartan in Acute Myocardial Infarction Trial (VALIANT). J Am Coll Cardiol. 2006 Feb 21;47(4):726-33. Epub 2006 Jan 26.)

[21] Chobanian AV, Bakris GL, Black HR, et al.; Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure. National Heart, Lung, and Blood Institute; National High Blood Pressure Education Program Coordinating Committee. 7th report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure. Hypertension. 2003 Dec;42(6):1206-52. Epub 2003 Dec 01.

[22] Strippoli GF, et al. Effects of angiotensin converting enzyme inhibitors and angiotensin II receptor antagonists on mortality and renal outcomes in diabetic nephropathy: systematic review. BMJ. 2004 Oct 9;329(7470):828.

[23] Scheen AJ. Renin-angiotensin system inhibition prevents type 2 diabetes mellitus. Part 1. A meta-analysis of randomised clinical trials. Diabetes Metab. 2004 Dec;30(6):487-96.

[24] Diagnosis and Management of Chronic **Heart Failure** in the Adult: **ACC/AHA 2005 Guideline Update** for the (J Am Coll Cardiol 2005) http://www.acc.org/clinical/guidelines/failure/index.pdf

[25] **PROGRESS** Collaborative Group. Randomised trial of perindopril-based blood-pressure-lowering regimen among 6,105 individuals with previous stroke or transient ischaemic attack.Lancet 2001 Sep29;358(9287):1033-41.
(Arima H, et al.; for the PROGRESS Collaborative Group. Lower target blood pressures are safe and effective for the prevention of recurrent stroke: the PROGRESS trial. J Hypertens. 2006 Jun;24(6):1201-1208.)
Patel A; **ADVANCE** Collaborative Group, MacMahon S, Chalmers J, Neal B, Woodward et al. Effects of a fixed combination of perindopril and indapamide on macrovascular and microvascular outcomes in patients with type 2 diabetes mellitus (the ADVANCE trial): a randomised controlled trial. Lancet. 2007 Sep 8;370(9590):829-40.

[26] Yusuf S, Sleight P, et al. The Heart Outcomes Prevention Evaluation (**HOPE**) Study Investigators, Effects of an Angiotensin-Converting-Enzyme Inhibitor, Ramipril, on Cardiovascular Events in High-Risk Patients. N Engl J Med 2000 342: 145-153.

[27] Palmer, B. Managing Hyperkalemia Caused by Inhibitors of the Renin-Angiotensin-Aldosterone System. N Engl J Med 2004;351:585-92.

Additional references:

Abuissa H, Jones PG, Marso SP, et al. **ACE or ARB** for **prevention of type 2 diabetes** a meta-analysis of randomized clinical trials. J Am Coll Cardiol. 2005 Sep 6;46(5):821-6. CONCLUSIONS: The use of an ACE inhibitor or ARB should be considered in patients with pre-diabetic conditions such as metabolic syndrome, hypertension, impaired fasting glucose, family history of diabetes, obesity, congestive heart failure, or coronary heart disease.

ACCF/AHA 2011 Focused Update of the Guidelines for the Management of Patients With **Unstable Angina/Non-ST-Elevation Myocardial Infarction (Updating the 2007 Guideline):** A Report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. J Am Coll Cardiol 2011 0: j.jacc.2011.02.009. http://content.onlinejacc.org/cgi/reprint/j.jacc.2011.02.009v1.pdf

ACC/AHA 2017 Whelton PK, et al. **2017 ACC/AHA**/AAPA/ABC/ACPM/AGS/APhA/ASH/ASPC/NMA/PCNA **Guideline for the Prevention, Detection, Evaluation, and Management of High Blood Pressure** in Adults: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. Hypertension. 2017 Nov 13.

ACTIVE I Investigators. Irbesartan in Patients with Atrial Fibrillation. N Engl J Med 2011; 364:928-938. (Not reduce CV events)

Aguilar D, Solomon SD. ACE inhibitors and angiotensin receptor antagonists and the incidence of **new-onset diabetes mellitus** : an emerging theme. Drugs. 2006;66(9):1169-77.

Ahimastos AA, et al. Brief communication: ramipril markedly improves walking ability in patients with **peripheral arterial disease**: a randomized trial. Ann Intern Med. 2006 May 2;144(9):660-4.

Ahimastos AA, Aggarwal A, D'Orsa KM, et al. Effect of perindopril on large artery stiffness and aortic root diameter in patients with Marfan syndrome: a randomized controlled trial. JAMA. 2007 Oct 3;298(13):1539-47. Perindopril reduced both aortic stiffness and aortic root diameter in patients with **Marfan syndrome** taking standard beta-blocker therapy, possibly through attenuation of TGF-beta signaling. Large clinical trials are needed to assess the clinical benefit of angiotensin II blockade in Marfan syndrome.

Ahimastos AA, Walker PJ, Askew C, et al. Effect of **ramipril on walking times and quality of life among patients with peripheral artery disease** and intermittent claudication, a randomized controlled trial. JAMA. 2013;309(5):453-460. **RETRACTION**

Ahimastos AA, Askew C, Leicht A, et al. **RETRACTION: Effect of Ramipril on Walking Times and Quality of Life Among Patients with Peripheral Artery Disease** and Intermittent Claudication: A Randomized Controlled Trial. JAMA. 2013;309(5):453-460. JAMA. 2015 Sep 14.

Al-Kindi SG, Oliveira GH. Abrupt Increase in Reporting of **Neoplasms Associated with Valsartan** After Medication Recall. Circ Cardiovasc Qual Outcomes. 2019 Jul;12(7):e005536.

Al-Mallah MH, et al. Angiotensin-converting enzyme inhibitors in coronary artery disease and **preserved left ventricular** systolic function: a systematic review and meta-analysis of randomized controlled trials. J Am Coll Cardiol. 2006 Apr 18;47(8):1576-83. Epub 2006 Mar 29. Treatment of 100 patients for an average duration of 4.4 years prevents either of the adverse outcomes (one death, or one nonfatal myocardial infarction, or one cardiovascular death or one coronary revascularization procedure). CONCLUSIONS: The cumulative evidence provided by this meta-analysis shows a modest favorable effect of ACEIs on the outcome of patients with CAD and preserved LV systolic function.

Andersen NH, et al. Long-term dual blockade with candesartan and lisinopril in hypertensive patients with diabetes: the **CALM II** study. Diabetes Care. 2005 Feb;28(2):273-7.

Ambrosioni E, Borghi C, Magnani B. The effect of the angiotensin-converting-enzyme inhibitor **zofenopril** on mortality and morbidity after anterior myocardial infarction. The Survival of Myocardial Infarction Long-Term Evaluation (**SMILE**) Study Investigators. N Engl J Med. 1995 Jan 12;332(2):80-5.

American College of Cardiology Foundation, , American Heart Association Task Force on Practice Guidelines, , American Association for Thoracic Surgery, , Society of Cardiovascular Anesthesiologists, , Society of Thoracic Surgeons, Hillis, L. David, Smith, Peter K., Anderson, Jeffrey L., et al. **2011 ACCF/AHA Guideline for Coronary Artery Bypass Graft Surgery**: Executive Summary. J Am Coll Cardiol 2011 0: j.jacc.2011.08.008. http://content.onlinejacc.org/cgi/reprint/j.jacc.2011.08.008v1.pdf

American College of Obstetricians and Gynecologists (**ACOG**). **Chronic hypertension in pregnancy**. Washington (DC): American College of Obstetricians and Gynecologists (ACOG); 2012 Feb. 12.

Anand IS, Rector TS, et al. Effect of baseline blood pressure and changes in systolic blood pressure over time on the effectiveness of valsartan in the Valsartan Heart Failure Trial (**Val-HeFT**). Circ Heart Fail 2008; 1: 34-42.

Antoniou T, Camacho X, Yao Z, et al. Comparative effectiveness of **angiotensin-receptor blockers for preventing macrovascular disease in patients with diabetes**: a population-based cohort study. CMAJ. 2013 Jul 8.

Appel LJ, Wright JT Jr, Greene T, et al.; for the African American Study of Kidney Disease and Hypertension Collaborative Research Group. (**AASK** trial) Long-term Effects of Renin-Angiotensin System-Blocking Therapy and a Low Blood Pressure Goal on Progression of Hypertensive Chronic Kidney Disease in African Americans. Arch Intern Med. 2008 Apr 28;168(8):832-839. Despite the benefits of renin-angiotensin system-blocking therapy on CKD progression, most African Americans with hypertensive CKD who are treated with currently recommended BP therapy continue to progress during the long term.

ARB Trialists Collaboration. Effects of **telmisartan, irbesartan, valsartan, candesartan, and losartan on cancers** in 15 trials enrolling 138 769 individuals. J Hypertens 2011; 29:623-635.

Arnold JM, et al.; Canadian Cardiovascular Society. **Canadian** Cardiovascular Society consensus conference recommendations on **heart failure 2006**: diagnosis and management. Can J Cardiol. 2006 Jan;22(1):23-45. Erratum in: Can J Cardiol. 2006 Mar 1;22(3):271. http://www.ccs.ca/download/consensus_conference/consensus_conference_archives/Arnold_CCS_final.pdf (Arnold JM, Howlett JG, Dorian P, et al. Canadian Cardiovascular Society Consensus Conference recommendations on heart failure **update 2007**: Prevention, management during intercurrent illness or acute decompensation, and use of biomarkers. Can J Cardiol. 2007 Jan;23(1):21-45.)

Asselbergs FW, et al. Prevention of Renal and Vascular Endstage Disease Intervention Trial (PREVEND IT) Investigators. Effects of fosinopril and pravastatin on cardiovascular events in subjects with microalbuminuria. Circulation. 2004 Nov 2;110(18):2809-16. Epub 2004 Oct 18. In microalbuminuric subjects, treatment with fosinopril had a significant effect on urinary albumin excretion. In addition, fosinopril treatment was associated with a trend in reducing cardiovascular events. Treatment with pravastatin did not result in a significant reduction in urinary albumin excretion or cardiovascular events.

Axelsson A, Iversen K, Vejlstrup N, et al. Efficacy and safety of the angiotensin II receptor blocker **losartan for hypertrophic cardiomyopathy**: The **INHERIT** randomized, double-blind, placebo-controlled trial. Lancet Diabetes Endocrinol 2014; DOI:10.1016/S2213.8587(14)70241-4.

Baguet JP, et al. A placebo-controlled **comparison** of the efficacy and tolerability of **candesartan** cilexetil, 8 mg, and los**a**rtan, 50 mg, as monotherapy in patients with essential hypertension, using 36-h ambulatory blood pressure monitoring.Int J Clin Pract. 2006 Apr;60(4):391-8.

Bainey KR, Rahim S, Etherington K, et al;. Effects of **withdrawing vs continuing renin-angiotensin blockers on incidence of acute kidney injury** in patients with renal insufficiency undergoing cardiac catheterization: Angiotensin Converting Enzyme Inhibitor/Angiotensin Receptor Blocker and Contrast Induced Nephropathy in Patients Receiving Cardiac Catheterization (**CAPTAIN**) trial. Am Heart J. 2015 Jul;170(1):110-6.

Baker WL, Coleman CI, et al. Effectiveness of therapies for **stable ischemic heart** disease. Systematic review comparative effectiveness of **ACE inhibitors or ARBs** for ischemic heart disease. *Annals Internal Med* 2009

Bakris GL, Pitt B, Weir MR, et al. Effect of **patiromer** on serum **potassium** level in patients with hyperkalemia and diabetic kidney disease: the AMETHYST-DN randomized clinical trial.JAMA. doi: 10.1001/jama.2015.7446.

Ballout RA, Musharrafieh U, Khattar J. **Lisinopril-associated bullous pemphigoid in an elderly woman**: a case report of a rare adverse drug reaction. Br J Clin Pharmacol. 2018 Aug 29.

Bandeali SJ, Kayani WT, Lee VV, et al. Outcomes of Preoperative Angiotensin-Converting Enzyme Inhibitor Therapy in Patients Undergoing Isolated **Coronary Artery Bypass Grafting**. Am J Cardiol. 2012 Jun 20.

Bangalore Sripal, Kumar Sunil, Kjeldsen Sverre E et al. Antihypertensive drugs and **risk of cancer**: network meta-analyses and trial sequential analyses of 324,168 participants from randomised trials. *The Lancet Oncology* - 30 November 2010 DOI: 10.1016/S1470-2045(10)70260-6. (Combo of ACEI & ARB possible higher risk)

Bangalore Sripal, Kumar Sunil, Wetterslev Jørn, et al. **Angiotensin receptor blockers and risk of myocardial infarction**: meta-analyses and trial sequential analyses of 147 020 patients from randomised trials. BMJ 2011;342:doi:10.1136/bmj.d2234 (Published 26 April 2011). –no increase in MI.

Bangalore S, Ogedegbe G, Gyamfi J, et al. Outcomes with **Angiotensin-converting Enzyme Inhibitors vs Other Antihypertensive** Agents in Hypertensive **Blacks**. Am J Med. 2015 Nov;128(11):1195-203.

Bangalore S, Fakheri R, Toklu B, et al. **Angiotensin-Converting Enzyme Inhibitors or Angiotensin Receptor Blockers in Patients Without Heart Failure**? Insights From 254,301 Patients From Randomized Trials. Mayo Clin Proc. 2016 Jan;91(1):51-60.

Bangalore S, Fakheri R, et al. Renin angiotensin system inhibitors for patients **with stable coronary artery disease without heart failure**: systematic review and meta-analysis of randomized trials. BMJ. 2017 Jan 19;356:j4.

Barnett AH, Bain SC, Bouter P, ET AL. Angiotensin-Receptor Blockade versus Converting-Enzyme Inhibition in Type 2 Diabetes and Nephropathy (**DETAIL**). N Engl J Med. 2004 Oct 31

Barvaliya MJ, Naik VN, Shah AC, et al. Safety of **Olmesartan in a patient with telmisartan induced myotoxicity**: A case report. Br J Clin Pharmacol. 2014 Dec 11.

Baş M, Greve J, Stelter K, et al. A randomized trial of **icatibant in ACE-inhibitor-induced angioedema**. N Engl J Med. 2015 Jan 29;372(5):418-25.

Basson M, Mezzarobba M, Weill A, et al. **Severe intestinal malabsorption associated with olmesartan**: a French nationwide observational cohort study. Gut. 2015 Aug 6.

Bateman BT, Patorno E, Desai RJ, et al. Angiotensin-Converting Enzyme Inhibitors and the **Risk of Congenital Malformations**. Obstet Gynecol. 2017 Jan;129(1):174-184.

Bavishi C, Ahmed M, Trivedi V, et al. Meta-Analysis of Randomized Trials on the Efficacy and Safety of **Angiotensin-Converting Enzyme Inhibitors in Patients >/=65 Years of Age**. Am J Cardiol. 2016 Aug 22.

Beavers Craig James, Dunn Steven P, Macaulay Tracy E. The Role of Angiotensin Receptor Blockers in Patients with Angiotensin-Converting Enzyme Inhibitor–**Induced Angioedema**. Articles Ahead of Print published on 1 April 2011, DOI 10.1345/aph.1P630. Ann Pharmacother ;45:520-524.

Beckett NS, Peters R, Fletcher AE, et al. the **HYVET** Study Group. Treatment of Hypertension in Patients 80 Years of Age or Older. N Engl J Med. 2008 Mar 31; [Epub ahead of print] The results provide evidence that

antihypertensive treatment with indapamide (sustained release), with or without perindopril, in persons 80 years of age or older is beneficial.

Berger AK, Duval S, Manske C, et al. Angiotensin-converting enzyme inhibitors and angiotensin receptor blockers in patients with congestive heart failure and chronic kidney disease. Am Heart J. 2007 Jun;153(6):1064-73. ACE inhibitors & ARB are underused in patients with heart failure with chronic kidney disease. Given the reduction in 30-day & 1-year mortality, these medications should be considered in most patients with heart failure, independent of underlying renal function. Among patients on hemodialysis, further investigation is warranted.

Bhandari S, Ives N, Brettell EA, et al. Multicentre randomized controlled trial of **angiotensin-converting enzyme inhibitor/ angiotensin receptor blocker withdrawal** in advanced renal disease: the **STOP-ACEi** trial. Nephrol Dial Transplant. 2015 Sep 30.

Bhaskaran K, Douglas I, Evans S, et al. Angiotensin receptor blockers and **risk of cancer**: cohort study among people receiving antihypertensive drugs in UK General Practice Research Database. BMJ. 2012 Apr 24;344:e2697.

Bhatia RS, et al. Outcome of **heart failure with preserved ejection fraction** in a population-based study. N Engl J Med. 2006 Jul 20;355(3):260-9.

Bilous R, Chaturvedi N, Sjølie AK, et al. Effect of Candesartan on Microalbuminuria and Albumin Excretion Rate in Diabetes: Three Randomized Trials (**DIRECT**). Ann Intern Med. 2009 May 18. [Epub ahead of print]. Candesartan, 32 mg/d, for 4.7 years did not prevent microalbuminuria in mainly normotensive patients with type 1 or type 2 diabetes.

Boal AH, Smith DJ, McCallum L, et al. **Monotherapy** with Major Antihypertensive Drug Classes and Risk of **Hopsital Admissions for Mood Disorders**. Hypertension.2016 :68 :00-00. (Beta-blockers & CCBs may increase risk, ACEI & ARBs may decrease risk)

Bokma JP, Winter MM, van Dijk AP, et al. Effect of **Losartan on RV Dysfunction**: Results from the Double-Blind, Randomized **REDEFINE Trial** in Adults with Repaired Tetralogy of Fallot. Circulation. 2017 Dec 8.

Borghi C, et al. on behalf of the Survival of Myocardial Infarction Long-Term Evaluation (**SMILE**) Study. Effects of early angiotensin-converting enzyme inhibition in patients with non-ST-elevation acute anterior myocardial infarction. Am Heart J. 2006 Sep;152(3):470-7.

Bosch J, Lonn E, Pogue J, Arnold JM, Dagenais GR, Yusuf S; **HOPE/HOPE-TOO** Study Investigators. Long-term effects of ramipril on cardiovascular events and on diabetes: results of the HOPE study extension. Circulation. 2005 Aug 30;112(9):1339-46.

Bosch X, Rovira M, Sitges M, et al. **Enalapril and carvedilol** for preventing **chemotherapy-induced** left ventricular systolic dysfunction in patients with malignant hemopathies: OVERCOME trial. J Am Coll Cardiol 2013.

Brar S, Ye F, James MT, Hemmelgarn B, et al; Interdisciplinary Chronic Disease Collaboration. Association of angiotensin-converting enzyme inhibitor or angiotensin receptor blocker use with outcomes **after acute kidney injury**. JAMA Intern Med. online Oct 27, 2018. doi:10.1001/jamainternmed.2018.4749

Braunwald E, et al. Rosenberg YD, Rouleau JL; **PEACE** Trial Investigators. Angiotensin-converting-enzyme inhibition in stable coronary artery disease. N Engl J Med. 2004 Nov 11;351(20):2058-68. Epub 2004 Nov 7. In patients with stable coronary heart disease and preserved left ventricular function who are receiving "current standard" therapy and in whom the rate of cardiovascular events is lower than in previous trials of ACE inhibitors in patients with vascular disease, there is no evidence that the addition of an ACE inhibitor provides further benefit in terms of death from cardiovascular causes, myocardial infarction, or coronary revascularization. (Solomon SD, et al; Prevention of Events with ACE inhibition (PEACE) Investigators. **Renal function** and effectiveness of angiotensin-converting enzyme inhibitor therapy in patients with chronic stable coronary disease in the Prevention of Events with ACE inhibition (PEACE) trial. Circulation. 2006 Jul 4;114(1):26-31. Epub 2006 Jun 26.)

Brener SJ, Ivanc TB, Poliszczuk R, et al. Antihypertensive therapy and regression of coronary artery disease: insights from the Comparison of Amlodipine versus Enalapril to Limit Occurrences of Thrombosis (**CAMELOT**) and Norvasc for Regression of Manifest Atherosclerotic Lesions by Intravascular Sonographic Evaluation (NORMALISE) trials. Am Heart J. 2006 Dec;152(6):1059-63.

Brooke BS, Habashi JP, Judge DP, et al. Angiotensin II blockade (**losartan**) and aortic-root dilation in **Marfan's** syndrome. N Engl J Med. 2008 Jun 26;358(26):2787-95. In a small cohort study, the use of ARB therapy in patients with Marfan's syndrome significantly slowed the rate of progressive aortic-root dilation.

Brown MJ, McInnes GT, Papst CC, et al. **Aliskiren** and the calcium channel blocker **amlodipine combination** as an initial treatment strategy for hypertension control (**ACCELERATE**): a randomised, parallel-group trial. Lancet. 2011 Jan 12.

Burgess E, Muirhead N, de Cotret PR, Chiu A, Pichette V, Tobe S; the **SMART** (Supra Maximal Atacand Renal Trial) Investigators. Supramaximal Dose of Candesartan in Proteinuric Renal Disease. J Am Soc Nephrol. 2009 Feb 11. [Epub ahead of print] The authors randomly assigned 269 patients who had persistent proteinuria (>/=1 g/d) despite 7 wk of treatment with the highest approved dosage of candesartan (16 mg/d) to 16, 64, or 128 mg/d candesartan for 30 wk. In conclusion, proteinuria that persists despite treatment with the maximum recommended dosage of candesartan can be reduced by increasing the dosage of candesartan further, but serum potassium levels should be monitored during treatment.

Caldeira D, Alarcão J, et al. Risk of **pneumonia associated with** use of angiotensin converting enzyme inhibitors and angiotensin receptor blockers: systematic review and meta-analysis. BMJ 2012;345:e4260.

Caton AR, Bell EM, Druschel CM, Werler MM, Lin AE, Browne ML, et al. **Antihypertensive medication use during pregnancy** and the risk of cardiovascular malformations. Hypertension 2009;54:63-70.

Casas JP, et al. Effect of inhibitors of the **renin-angiotensin system** and other antihypertensive drugs on **renal outcomes**: systematic review and meta-analysis. Lancet. 2005 Dec 10;366(9502):2026-2033. INTERPRETATION: The benefits of ACE inhibitors or ARBs on renal outcomes in placebo-controlled trials probably result from a blood-pressure-lowering effect. In patients with diabetes, additional renoprotective actions of these substances beyond lowering blood pressure remain unproven, and there is uncertainty about the greater renoprotection seen in non-diabetic renal disease.

Chang CH, Lin JW, Wu LC, Lai MS. Angiotensin receptor blockade and risk of **cancer** in type 2 diabetes mellitus: A nationwide case-control study. J Clin Oncol 2011; DOI 10.1200/JCO.2011.35.1908. The results did not show an effect of ARBs as a class on increasing cancer incidence in patients with diabetes. However, there was a negative association of losartan but a positive one of candesartan and telmisartan with the overall occurrence of cancer.

Chang CH, Chang YC, Wu LC, et al. Different angiotensin receptor blockers and incidence of diabetes: a nationwide population-based cohort study. Cardiovasc Diabetol. 2014 May 14;13:91. Among all ARBs, **olmesartan** might be associated with a slightly increased risk of diabetes mellitus. Our data suggest differential diabetes risks associated with ARBs beyond a class effect.

Charles JA, et al. Prevention of migraine with **olmesartan** in patients with hypertension/prehypertension. Headache. 2006 Mar;46(3):503-7. Tronvik E, et al. Prophylactic treatment of migraine with an angiotensin II receptor blocker (**candesartan**): a randomized controlled trial. JAMA. 2003 Jan 1;289(1):65-9.

Chaturvedi N, Porta M, Klein R, et al. for the **DIRECT** Programme Study Group. Effect of candesartan on prevention (DIRECT-Prevent 1) and progression (**DIRECT-Protect 1**) of retinopathy in type 1 diabetes: randomised, placebo-controlled trials. Lancet. 2008 Sep 25. [Epub ahead of print]

Cheng J, Zhang W, Zhang X, et al. Effect of **Angiotensin-Converting Enzyme Inhibitors and Angiotensin II Receptor Blockers** on All-Cause Mortality, Cardiovascular Deaths, and Cardiovascular Events in Patients **With Diabetes** Mellitus: A Meta-analysis. JAMA Intern Med. 2014 Mar 31.

Cheung BM, Cheung GT, Lauder IJ, Lau CP, Kumana CR. Meta-analysis of large outcome trials of angiotensin receptor blockers in hypertension. J Hum Hypertens. 2005 Aug 25; [Epub ahead of print] In conclusion, the reduction in new-onset diabetes partly offsets any increase in the risk of myocardial infarction. Most hypertensive patients require more than one class of drugs. Small differences in treatment outcome should not over-ride the importance of good blood pressure control.

Choi HK, Soriano LC, Zhang Y, Rodríguez LAG. **Calcium channel blockers, losartan**, and the risk of **incident gout** among patients with hypertension: population based case-control study. BMJ 2012;344:d8190.

Chrysostomou A, Pedagogos E, MacGregor L.. Double-blind, placebo-controlled study on the effect of the aldosterone receptor antagonist **spironolactone** in patients who have persistedt proteinuria and are on long-term angiotension-converting enzyme inhibitor therapy, with or without an angiotensin II receptor blocker. Clin J Am Soc Nephrol. 2006 Jan 3;1:256-62.

Cice G, Di Benedetto A, D'Isa S, et al. Effects of **telmisartan** added to angiotensin-converting enzyme inhibitors on mortality and morbidity in **hemodialysis patients with chronic heart failure**: a double-blind, placebo-controlled trial. J Am Coll Cardiol. 2010;56:1701-8.

Cleland JG, et al. The perindopril 4mg od in elderly people ≥70yr with chronic heart failure (**PEP-CHF**) study. Eur Heart J. 2006 Oct;27(19):2338-45. Epub 2006 Sep 8.

Cohn JN, Tognoni G . A randomized trial of the angiotensin-receptor blocker valsartan in chronic heart failure (**Val-HeFT**); Valsartan Heart Failure Trial Investigators. N Engl J Med 2001 Dec 6;345(23):1667-75.

Cooper WO, et al. Major congenital malformations after **first-trimester exposure to ACE** inhibitors. (pregnancy) N Engl J Med. 2006 Jun 8;354(23):2443-51. (see also Pharmacist's Letter July 2006)

Cooperate: The Editors Of The Lancet. **Retraction**-Combination treatment of angiotensin-II receptor blocker and angiotensin-converting-enzyme inhibitor in non-diabetic renal disease (**COOPERATE**): a randomised controlled trial. Lancet. 2009 Oct 10;374(9697):1226.

Cragan JD, Young BA, Correa A. **Renin-Angiotensin System Blocker Fetopathy**. J Pediatr. 2015 Aug 5.

Cressman AM, Macdonald EM, Fernandes KA, et al; Canadian Drug Safety and Effectiveness Research Network (CDSERN). A population-based study of the drug **interaction between clopidogrel and angiotensin converting enzyme inhibitors**. Br J Clin Pharmacol. 2015 May 15.

Culley CM, DiBridge JN, et al. Off-Label Use of Agents for **Management of Serious or Life-threatening Angiotensin Converting Enzyme Inhibitor-Induced Angioedema**. Ann Pharmacother. 2016 Jan;50(1):47-59.

Dagenais GR, et al. Angiotensin-converting-enzyme inhibitors in **stable vascular disease without left ventricular** systolic dysfunction or heart failure:a combined analysis of three trials. Lancet. 2006 Aug 12;368(9535):581-8.

Dahlof B, et al. LIFE Study Group. Cardiovascular morbidity and mortality in the Losartan Intervention For Endpoint reduction in hypertension study (**LIFE**): a randomised trial against atenolol. Lancet. 2002 Mar 23;359(9311):995-1003. (Lindholm LH, et al.; LIFE Study Group. Cardiovascular morbidity and mortality in patients with diabetes in the Losartan Intervention For Endpoint reduction in hypertension study (LIFE): a randomised trial against atenolol. Lancet. 2002 Mar 23;359(9311):1004-10.)(Ibsen H, et al. Does albuminuria predict cardiovascular outcomes on treatment with losartan versus atenolol in patients with diabetes, hypertension, and left ventricular hypertrophy? The LIFE study. Diabetes Care. 2006 Mar;29(3):595-600.)

Damman K, Solomon SD, Pfeffer MA, et al. **Worsening renal function** and outcome in heart failure patients with reduced and preserved ejection fraction and the impact of angiotensin receptor blocker treatment: data from the **CHARM**-study programme. Eur J Heart Fail. 2016 Jul 18.

Danchin N, et al. Angiotensin-Converting Enzyme Inhibitors in Patients With Coronary Artery Disease and **Absence of Heart Failure** or Left Ventricular Systolic Dysfunction: An Overview of Long-term Randomized Controlled Trials. Arch Intern Med. 2006 Apr 10;166(7):787-96. Angiotensin-converting enzyme inhibitors reduce total mortality and major cardiovascular end points in patients who have CAD and no left ventricular systolic dysfunction or heart failure. (InfoPOEMs: Angiotensin-converting enzyme (ACE) inhibitors decrease overall mortality, cardiovascular mortality, myocardial infarction risk, and stroke risk in patients with coronary artery disease (CAD) but without signs or symptoms of heart failure. The benefit is not pronounced, with only 1 death prevented in more than **400** patients treated for 2 years. (LOE = 1a))

Davies NM, Kehoe PG, Ben-Shlomo T, Martin RM. Associations of anti-hypertensive treatments (**ARBS**) with **Alzheimer's disease**, vascular dementia, and other dementias. J Alzheimer's Dis 2011; 26:699-708.

Demers C, McMurray JJ, Swedberg K; **CHARM** Investigators. Impact of candesartan on nonfatal myocardial infarction and cardiovascular death in patients with heart failure. JAMA. 2005 Oct 12;294(14):1794-8.

de Man FS, Tu L, Handoko ML, Rain S, Ruiter G, Franc¸ois C, Schalij I, Dorfmüller P, Simonneau G, Fadel E, et al. Dysregulated renin– angiotensin–aldosterone system contributes to **pulmonary arterial hypertension**. Am J Respir Crit Care Med 2012;186:780–789.

Dial S, Nessim SJ, Kezouh A, et al. Antihypertensive agents acting on the **renin angiotensin system and the risk of sepsis**. Br J Clin Pharmacol. 2014 May 6.

Dicpinigaitis PV. **Angiotensin-converting enzyme inhibitor**-induced **cough**: ACCP evidence-based clinical practice guidelines. Chest. 2006 Jan;129(1 Suppl):169S-173S.

Drenger B, Fontes ML, Miao Y, et al. Patterns of use of **perioperative angiotensin-converting enzyme inhibitors** in coronary artery bypass graft surgery with cardiopulmonary bypass: effects on in-hospital morbidity and mortality. (fACE) Circulation. 2012;126:261–269.

Dufouil C, Chalmers J, Coskun O, et al. Effects of Blood Pressure Lowering on Cerebral White Matter Hyperintensities in Patients With Stroke. The PROGRESS (Perindopril Protection Against Recurrent Stroke Study) Magnetic Resonance Imaging Substudy. Circulation. 2005 Sep 6; [Epub ahead of print]

Effect of Ramipril on the Incidence of Diabetes. (**DREAM**) N Engl J Med. 2006 Sep 15; [Epub ahead of print]

Egiziano G et al. Improved outcomes in **heart failure** treated with **high-dose ACE inhibitors and ARBs**: a population-based study. Arch Intern Med [Epub ahead of print] 2 July 2012;

Eklind-Cervenka M, Benson L, Dahlstro¨m U, et al. Association of **candesartan vs losartan** with all-cause mortality in patients with **heart failure**. JAMA. 2011;305(2):175-182.

Elder DHJ, Wei L, Szwejkowski BR, et al. The impact of renin-angiotensin-aldosterone system blockade on heart failure outcomes and mortality in patients identified to have **aortic regurgitation**. A large population cohort study. J Am Coll Cardiol 2011; 58:2084-2091.

Elgendy IY, Huo T, Chik V, et al. Efficacy and safety of **Angiotensin receptor blockers in older patients**: a meta-analysis of randomized trials. Am J Hypertens. 2015 May;28(5):576-85.

EMA: European Medicines Agency. European Medicines Agency Oct/11 concludes that benefit-risk balance of **angiotensin II receptor antagonists remains positive** (**cancer** etc) [press release]. October 20, 2011.

Emdin CA, Callender T, Cao J, et al. Meta-Analysis of Large-Scale Randomized Trials to Determine the Effectiveness of Inhibition of the **Renin-Angiotensin Aldosterone System in Heart Failure**. Am J Cardiol. 2015 Apr 9

European Medicines Agency, 2011. Questions and answers on the review of **angiotensin II receptor antagonists and the risk of cancer** [online]. Available: http://www.ema.europa.eu/docs/en_GB/document_library/Medicine_QA/2011/10/WC500116862.pdf [Accessed 22 December 2011].

EXPERT PANEL ON INTEGRATED GUIDELINES FOR CARDIOVASCULAR HEALTH AND RISK REDUCTION IN CHILDREN AND ADOLESCENTS. Expert Panel on Integrated Guidelines for Cardiovascular Health and Risk Reduction in Children and Adolescents: Summary Report. Pediatrics. 2011 Nov 14. [Epub ahead of print]

Evangelista A, Tornos P, Sambola A, et al.. Long-term vasodilator therapy in patients with severe aortic regurgitation. N Engl J Med. 2005 Sep 29;353(13):1342-9. (InfoPOEMs: This small study does not find that vasodilators such as nifedipine (Procardia) or enalapril (Vasotec) delay the need for aortic valve replacement (AVR) in patients with asymptomatic but severe aortic regurgitation. The study was quite small, and although it is possible that a small but clinically important benefit was not detected, this seems unlikely since the trends actually run against active treatment. (LOE = 1b-))

Famularo G, Minisola G. Relapsing **Olmesartan-Associated Ileitis**. Ann Pharmacother. 2016 Dec;50(12):1070.

FDA June/10 June 14, 2010 (Washington, DC) — The FDA is conducting a safety review of the angiotensin receptor blocker **olmesartan** (Benicar, Daiichi Sankyo) after determining that diabetic patients taking the drug in two completed phase 3 trials may have had an excess risk of **cardiovascular death**, the regulatory body has announced [1].The safety announcement says that the FDA's review is "ongoing, and the agency has not concluded that Benicar increases the risk of death. FDA currently believes that the benefits of Benicar in patients with high blood pressure continue to outweigh its potential risks." The agency also notes that "other controlled clinical trials evaluating Benicar and other ARBs have not suggested an increased risk of cardiovascular-related death."The primary end points of the two trials were dominated by measures of renal function.In the Randomized Olmesartan and Diabetes Microalbuminuria Prevention (ROADMAP) study, conducted in Europe, 4447 patients with diabetes and at least one additional cardiovascular risk factor, but no evidence of renal dysfunction, were randomized to receive either olmesartan at 40 mg/day (n=2232) or placebo (n=2215). The trial, sponsored by Sankyo Pharma, ended in July 2009 [2]. In the Olmesartan Reducing Incidence of End Stage Renal Disease in Diabetic Nephropathy Trial (ORIENT), conduced in Japan and Hong Kong, 566 patients with diabetes and renal dysfunction were randomized to receive olmesartan at 10 mg/day to 40 mg/day (n=282) or placebo (n=284).

FDA June/11 Food and Drug Administration drug safety: **No increase in risk of cancer** with certain blood pressure drugs—**angiotensin receptor blockers (ARBs).** June 2, 2011. http://www.fda.gov/Drugs/DrugSafety/ucm257516.htm

FDA Apr/12 notified healthcare professionals of possible risks when using blood pressure medicines containing aliskiren with other drugs called angiotensin converting enzyme inhibitors (ACEIs) and angiotensin receptor blockers (ARBs) in patients with diabetes or kidney (renal) impairment. (Altitude study)

FDA July/13 is warning that the blood pressure drug **Olmesartan** Medoxomil (marketed as Benicar, Benicar HCTZ, Azor, Tribenzor, and generics) can cause intestinal problems known as sprue-like enteropathy. Symptoms of **sprue-like enteropathy** include severe, chronic diarrhea with substantial weight loss. FDA has approved changes to the labels of these drugs to include this concern. Sprue-like enteropathy has not been detected with ARB drugs other than olmesartan.

FDA Nov/18: Sandoz Inc. Issues Voluntary Nationwide Recall of One Lot of **Losartan Potassium and Hydrochlorothiazide** Due to the Detection of Trace Amounts of NDEA (N-Nitrosodiethylamine) Impurity Found in the Active Pharmaceutical Ingredient (API)

FDA Nov/18: All **Amlodipine/Valsartan** Combination Tablets and **Amlodipine/Valsartan/Hydrochlorothiazide** Combination Tablets by Teva Pharmaceuticals USA: Recall - Due to an Impurity Detected Above Specification Limits in an Active Pharmaceutical Ingredient (API)

FDA Nov/18: Sandoz Inc. Issues Voluntary Nationwide Recall of One Lot of **Losartan Potassium and Hydrochlorothiazide** Due to the Detection of Trace Amounts of NDEA (N-Nitrosodiethylamine) Impurity Found in the Active Pharmaceutical Ingredient (API)

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FDA Jan/19: **Losartan Potassium Tablets**, USP and **Losartan Potassium and Hydrochlorothiazide Tablets**, USP by Torrent Pharmaceuticals: Recall Due to the Detection of N-nitrosodiethylamine (NDEA)

FDA Dec/18: **Losartan Potassium Tablets**, USP by Torrent Pharmaceuticals Limited: Due to the detection of trace amounts of an unexpected impurity, N-nitrosodiethylamine (NDEA), found in the active pharmaceutical ingredient (API) was just added to the FDA Recalls webpage.

FDA Jan/19: **Irbesartan and Irbesartan/Hydrochlorothiazide** (HCTZ) Tablets by Prinston Pharmaceutical: Recall - Due to Detection of a Trace Amount of Unexpected Impurity, N-nitrosodiethylamine (NDEA)

Jan/19 Prinston Pharmaceutical Inc has recalled one consumer-level lot of irbesartan and seven lots of irbesartan hydrochlorothiazide (HCTZ) tablets because of the presence of the probable carcinogen N-nitrosodiethylamine (NDEA), marking the latest recall of tainted sartan products produced in the United States.

FDA Mar/19: **Valsartan Tablets USP, 160 mg** by American Health Packaging: Recall - Due to Detection of N-Nitrosodiethylamine (NDEA) Impurity

FDA Mar/19 on Friday announced that India's Hetero Labs was recalling 87 lots of **losartan potassium tablets** distributed by Camber Pharmaceuticals because they contain the impurity, N-Nitroso-N-methyl-4-aminobutyric Acid(NMBA).

FDA Mar/19: **Losartan Potassium** Tablets by Legacy Pharmaceutical Packaging: Recall - Due to The Detection of Trace Amounts Of N-Nitroso N-Methyl 4-Amino Butyric Acid Impurity Found in The Active Pharmaceutical Ingredient

Fernandez Juarez G, Luño J, Barrio V, et al. **PRONEDI** Study Group. Effect of **Dual Blockade** of the Renin-Angiotensin System on the Progression of Type 2 Diabetic Nephropathy: A Randomized Trial (N=133). Am J Kidney Dis. 2012 Aug 28. (lisinopril, irbesartan or both)

Ferrari R; Perindopril and Remodeling in Elderly with Acute Myocardial Infarction Investigators. Effects of angiotensin-converting enzyme inhibition with perindopril on left ventricular remodeling and clinical outcome: results of the randomized Perindopril and Remodeling in Elderly with Acute Myocardial Infarction (**PREAMI**) Study. Arch Intern Med. 2006 Mar 27;166(6):659-66.

Fitzharris P, Jordan A. Investigating **recurrent angio-oedema**. BMJ. 2011 Oct 24;343:d6607.

Forsmark CE, Swaroop Vege S, Wilcox CM. **Acute Pancreatitis**. N Engl J Med. 2016 Nov 17;375(20):1972-1981 (azathioprine, 6-mercaptopurine, didanosine, valproic acid,angiotensin-converting–enzyme inhibitors, and mesalamine)

Fralick M, Mandonald EM, Gomes T, et al. **Co-trimoxazole and sudden death in patients receiving inhibitors of renin-angiotensin system**: population based study. BMJ 2014;349:g6196.

Fried LF, Emanuele N, Zhang JH, et al. **Combined angiotensin inhibition** for the treatment of diabetic nephropathy. (**VA Nephron-D**) N Engl J Med 2013. DOI: 10.1056/NEJMoa1303154.

Gao Y, O'Caoimh R, Healy L, et al. Effects of **centrally acting ACE inhibitors on the rate of cognitive decline in dementia**. BMJ Open 2013.

Garlo KG, Bates DW, Seger DL, et al. Association of **Changes in Creatinine and Potassium Levels After Initiation of Renin Angiotensin Aldosterone System Inhibitors With Emergency Department Visits, Hospitalizations, and Mortality in Individuals With Chronic Kidney Disease**. JAMA Netw Open. 2018;1(7):e183874.

Geng DF, Jin DM, Wu W, Liang YD, Wang JF. Angiotensin converting enzyme inhibitors for **prevention of new-onset type 2 diabetes mellitus**: A meta-analysis of 72,128 patients. Int J Cardiol. 2012 Jul 16.

Giles TD, Weber MA, et al, for the NAC-MD-01 Study Investigators. Efficacy and safety of **nebivolol and valsartan** as fi xed-dose combination in hypertension: a randomised, multicentre study. Lancet 2014; 383: 1889–98.

Gillespie EL, White CM, Kardas M, et al. The impact of ACE inhibitors or angiotensin II type 1 receptor blockers on the development of new-onset type 2 diabetes. Diabetes Care. 2005 Sep;28(9):2261-6. CONCLUSIONS: ACEIs or ARBs may decrease patients' odds of developing new-onset type 2 diabetes but does not reduce the odds of mortality, cardiovascular, or cerebrovascular outcomes over the study follow-up periods among patients with hypertension.

GISSI-AF Investigators, Disertori M, Latini R, Barlera S, et al. Valsartan for prevention of recurrent **atrial fibrillation**. N Engl J Med. 2009 Apr 16;360(16):1606-17. Treatment with valsartan was not associated with a reduction in the incidence of recurrent atrial fibrillation.

Gliddon AE, Doré CJ, Black CM, et al. Prevention of vascular damage in **scleroderma** and autoimmune Raynaud's phenomenon: a multicenter, randomized, double-blind, placebo-controlled trial of the angiotensin-converting enzyme inhibitor quinapril. Arthritis Rheum. 2007 Nov;56(11):3837-46. Administration of quinapril for up to 3yrs had no demonstrable effects on the occurrence of upper limb digital ulcers or on other vascular manifestations of lcSSc in this pt population.

Goel SS, Aksoy O, Gupta S, et al. Renin-Angiotensin system blockade therapy after surgical **aortic valve replacement** for severe aortic stenosis: a cohort study. Ann Intern Med. 2014 Nov 18;161(10):699-710.

Goh KL, Bhaskaran K, Minassian C, et al. **Angiotensin receptor blockers and risk of dementia**: cohort study in UK Clinical Practice Research Datalink. Br J Clin Pharmacol. 2014 Sep 16.

Goh SS-N, Sia C-H, Ngiam NJ, et al. Effect of Renin-Angiotensin Blockers on Left Ventricular Remodeling in Severe **Aortic Stenosis**. Am J Cardio. 2017.

Goldenberg I, et al. **Polymorphism** in the angiotensinogen gene, hypertension, and ethnic differences in the risk of recurrent coronary events. Hypertension. 2006 Oct;48(4):693-9. Epub 2006 Aug 28.

Goundry B, Bell L, Langtree M, Moorthy A. Diagnosis and management of **Raynaud's phenomenon**. BMJ. 2012 Feb 7;344:e289.

Growdon ME, Sacks CA, Kesselheim AS, Avorn J. Potential Medicare **Savings From Generic Substitution** and Therapeutic Interchange of ACE Inhibitors and Angiotensin-II-Receptor Blockers.JAMA Intern Med.2019Aug5

Guertin JR, Jackevicius CA, Cox JL, et al. The potential economic impact of **restricted access to angiotensin-receptor blockers** (ARBs). *CMAJ* 2011; DOI: 10.1503/cmaj.100787ARBs.

Guglin M, Krischer J, Tamura R, et al. Randomized Trial of **Lisinopril Versus Carvedilol to Prevent Trastuzumab Cardiotoxicity** in Patients With Breast Cancer. J Am Coll Cardiol. 2019 Jun 11;73(22):2859-2868.

Hackam DG, Thiruchelvam D, Redelmeier DA. Angiotensin-converting enzyme inhibitors and **aortic rupture**: a population-based case-control study. Lancet. 2006 Aug 19;368(9536):659-665.

Hajjar I, Brown L, Mack WJ, Chui H. Impact of Angiotensin Receptor Blockers on **Alzheimer Disease Neuropathology** in a Large Brain Autopsy Series. Arch Neurol. 2012 Sep 10:1-7.

Haller H, Ito S, Izzo JL Jr, et al. **Olmesartan** for the delay or prevention of microalbuminuria in type 2 diabetes. (**ROADMAP**) N Engl J Med 2011;364:907-17. (n=4447 over 3.2yr. Improved microalbuminuria, but increased fatal CV events)

Harel Z et al. The effect of combination treatment with **aliskiren and blockers of the renin-angiotensin system** on hyperkalaemia and acute kidney injury: systematic review and meta-analysis. BMJ. 2012 Jan 9;344:e42.

Haymore BR, Yoon J, et al. Risk of **angioedema** with angiotensin receptor blockers in patients with prior angioedema associated with angiotensin-converting enzyme inhibitors: a meta-analysis. Ann Allergy Asthma Immunol. 2008 Nov;101(5):495-9. Limited evidence suggests that for patients who develop angioedema when taking an ACE-I, the risk of development of any subsequent angioedema when taking an ARB is between 2% and 17%; for confirmed angioedema, the risk is 0% to 9.2%.

Haynes R, Judge PK, Staplin N, et al. **Effects of Sacubitril/Valsartan Versus Irbesartan in Patients with Chronic Kidney Disease: A Randomised Double-Blind Trial.** Circulation. 2018 Jul 12.

Head GA. **Ambulatory blood pressure monitoring** is ready to replace clinic blood pressure in the diagnosis of hypertension: pro side of the argument. Hypertension. 2014 Dec;64(6):1175-81.

Heinze G, et al. Angiotensin-converting enzyme inhibitor or angiotensin II type 1 receptor antagonist therapy is associated with prolonged patient and graft survival after renal **transplantation**. J Am Soc Nephrol. 2006 Mar;17(3):889-99. Epub 2006 Feb 15.

Health Canada Jan/12 **RASILEZ** (aliskiren) and RASILEZ HCT (aliskiren/hydrochlorothiazide) - Potential Risks of Cardiovascular and Renal Adverse Events in Patients with Type 2 Diabetes - Novartis Pharmaceuticals Canada Inc. The combination of **aliskiren with ACE inhibitors and ARBs is now contraindicated in patients with type 2 diabetes**. The Product Monograph will be updated accordingly.

Health Canada Feb/14 wishes to inform healthcare professionals and patients of the risks associated with **combining more than one of the following blood pressure medicines**: aliskiren (renin inhibitor), angiotensin-converting enzyme inhibitors (ACEIs) or angiotensin receptor blockers (ARBs).

Health Canada Sep/18: is advising Canadians that a second impurity, called N-nitrosodiethylamine (NDEA) has been found in valsartan manufactured by Zhejiang Huahai Pharmaceuticals in China. All drugs containing valsartan manufactured by Zhejiang Huahai Pharmaceuticals have already been recalled in Canada after the first impurity, N-nitrosodimethylamine (NDMA), was identified earlier this summer.

Health Canada Nov/18: Mylan Pharmaceuticals ULC is voluntarily **recalling four lots of Mylan-Valsartan tablets** (40 mg, 80 mg, 160 mg and 320 mg strength) after testing found low levels of an impurity, N-nitrosodiethylamine (NDEA).

Health Canada Nov/18: Mylan **Pharmaceuticals ULC is voluntarily recalling four lots of Mylan-Valsartan tablets** (40 mg, 80 mg, 160 mg and 320 mg strength) after testing found low levels of an impurity, N-nitrosodiethylamine (NDEA).

Health Canada Dec/18 tested 48 samples (**certain sartan drugs**: **valsartan, candesartan, irbesartan, losartan, and olmesartan**) representing 43 different products and did not identify any new safety concerns. Of the 48 samples, six valsartan samples representing four products were found to contain levels of impurities that were, on average, higher than what is considered to be reasonably safe. All four of the products have already been recalled from the Canadian market.

Health Canada Mar/19 is advising Canadians that Pro Doc Limitée is voluntarily recalling two lots of **irbesartan** tablets because of a nitrosamine impurity, N-nitrosodiethylamine (NDEA).

Health Canada Mar/19 is advising Canadians that multiple lots of **Losartan-containing drugs** are being voluntarily recalled by Teva Canada, Apotex Inc., Pharmascience Inc., and Pro Doc Limitée because of the potential for a nitrosamine impurity, N-Nitroso-N-methyl-4-aminobutyric acid (NMBA). NMBA is potentially a human carcinogen, which means that long-term exposure could increase the potential risk of cancer.

Health Canada Apr/19 is advising Canadians that Auro Pharma Inc. is voluntarily recalling one lot of Auro-Irbesartan/hydrochlorothiazide (HCT) combination tablets because of a nitrosamine impurity, N-nitrosodiethylamine

(NDEA).
Heart Failure Society Of America. **HFSA 2006** Comprehensive Heart Failure Practice Guideline. J Card Fail. 2006 Feb;12(1):e1-2.
Heran BS, et al. Blood pressure lowering efficacy of angiotensin receptor blockers for primary hypertension. Cochrane Database Syst Rev. 2008 Oct 8;(4):CD003822. The evidence from this review suggests that there are no clinically meaningful BP lowering differences between available ARBs. The BP lowering effect of ARBs is modest and similar to ACE inhibitors as a class; the magnitude of average trough BP lowering for ARBs at maximum recommended doses and above is -8/-5 mmHg. Furthermore, 60 to 70% of this trough BP lowering effect occurs with recommended starting doses. The review did not provide a good estimate of the incidence of harms associated with ARBs because of the short duration of the trials and the lack of reporting of adverse effects in many of the trials.
Heran BS, Musini VM, Bassett K, et al. Angiotensin receptor blockers for heart failure. Cochrane Database Syst Rev. 2012 Apr 18;4:CD003040. In patients with symptomatic HF and systolic dysfunction or with preserved ejection fraction, ARBs compared to placebo or ACEIs do not reduce total mortality or morbidity. ARBs are better tolerated than ACEIs but do not appear to be as safe and well tolerated as placebo in terms of withdrawals due to adverse effects. Adding an ARB in combination with an ACEI does not reduce total mortality or total hospital admission but increases withdrawals due to adverse effects compared with ACEI alone.
HicksBM, FilionKB, YinH, SakrL, UdellJA, AzoulayL. Angiotensin converting enzyme inhibitors and **risk of lung cancer**: population based cohort study. BMJ 2018;636:k4209.
Hippisley-Cox J., Coupland C. Effect of combinations of drugs on all cause mortality in patients with ischaemic heart disease: nested case-control analysis. BMJ 2005;330:1059-1063 (7 May), doi:10.1136/bmj.330.7499.1059. Conclusions: Combo of statins, aspirins, & beta-blockers improve survival in high risk pts with cardiovascular dx, although the addition of an angiotensin converting enzyme inhibitor conferred no additional benefit despite the analysis being adjusted for congestive cardiac failure.
Hirsch S, Hirsch J, Bhatt U, et al. **Tolerating increases in the serum creatinine** following aggressive treatment of chronic kidney disease, hypertension and proteinuria: Pre-renal success. Am J Nephrol 2012; 36:430-437.
Ho JM, Juurlink DN. Considerations when prescribing **trimethoprim-sulfamethoxazole**. CMAJ. 2011 Oct 11.
Hofmann Bowman MA, Eagle KA, Milewicz DM. Update on Clinical Trials of **Losartan** With and Without β-Blockers to Block Aneurysm Growth in Patients **With Marfan Syndrome**: A Review. JAMA Cardiol.2019 May 8.
Hou FF, Zhang X, Zhang GH, et al. Efficacy & safety of **benazepril** for advanced chronic renal (**CKD pts**) insufficiency. N Engl J Med. 2006 Jan 12;354(2):131-40. (InfoPOEMs: In a group of nondiabetic patients with serum creatinine levels between 3.0 & 5.0 mg/dL, benazepril slows the progression of renal disease. These pts were carefully monitored for any changes in renal function during the first 8 weeks, and were carefully screened & monitored to detect any early adverse effects on renal function. (LOE = 1b))
Hsu T-W, Liu J-S, Hung S-C, et al. **Renoprotective effect** of renin-angiotensin-aldosterone system blockade in patients with **predialysis advanced chronic kidney disease, hypertension, and anemia** [online December 16, 2013]. JAMA Intern Med. doi:10.1001/jamainternmed.2013.12176.
Huang CC, Chan WL, Chen YC, Chen TJ, Lin SJ, Chen JW, Leu HB. Angiotensin II Receptor Blockers and **Risk of Cancer** in Patients With Systemic Hypertension. Am J Cardiol. 2011 Jan 20.
Ibrahim HN, Jackson S, Connaire J, et al M. **Angiotensin II Blockade (losartan) in Kidney Transplant Recipients**. J Am Soc Nephrol. 2013 Jan 10.
Inohara T, Manandhar P, Kosinski AS, et al. Association of Renin-Angiotensin Inhibitor Treatment With Mortality and Heart Failure Readmission in Patients With Transcatheter Aortic Valve Replacement. JAMA. 2018 Dec 4;320(21):2231-2241.
Inohara T, Manandhar P, Kosinski AS, et al. Association of **Renin-Angiotensin Inhibitor Treatment With Mortality and Heart Failure Readmission** in Patients With **Transcatheter Aortic Valve Replacement**. JAMA. 2018 Dec 4;320(21):2231-2241.
Jamerson K, Weber MA, Bakris GL, et al. Benazepril plus Amlodipine or Hydrochlorothiazide for Hypertension in High-Risk Patients. (**ACCOMPLISH**)N Engl J Med. 2008 Dec 4;359(23):2417-2428. The benazepril-amlodipine combination was superior to the benazepril-hydrochlorothiazide combination in reducing cardiovascular events in patients with hypertension who were at high risk for such events.
Johnston K, Stephens S. Effect of Angiotensin-converting enzyme inhibitors and Angiotensin receptor blockers on risk of **atrial fibrillation** before coronary artery bypass grafting. Ann Pharmacother. 2012 Sep;46(9):1239-44.
Julius S, et al.; VALUE trial group. Outcomes in hypertensive patients at high cardiovascular risk treated with regimens based on valsartan or amlodipine: the **VALUE** randomised trial. Lancet. 2004 Jun 19;363(9426):2022-31. (Kjeldsen SE, et al.; for the VALUE Trial. Effects of valsartan compared to amlodipine on preventing type 2 diabetes in high-risk hypertensive patients: the VALUE trial. J Hypertens. 2006 Jul;24(7):1405-1412.)(Julius S, et al. The Valsartan Antihypertensive Long-Term Use Evaluation (**VALUE**) trial: outcomes in patients receiving monotherapy. Hypertension. 2006 Sep;48(3):385-91. Epub 2006 Jul 24.)
Julius S, et al.; Trial of Preventing Hypertension (**TROPHY**) Study. Feasibility of treating prehypertension with an ARB.(candesartan) N Engl J Med. 2006 Apr 20;354(16):1685-97. Epub 2006 Mar 14. (see also PharmLetter May06.) (InfoPOEMs: This study tells us what we already know (that is, that blood pressure medications reduce blood pressure), but says nothing about what really matters: Does intervention in patients with prehypertension improve patient-oriented outcomes? The choice to study such an expensive drug is also disappointing, but not surprising. Given that the number needed to treat [NNT] to prevent 1 stroke, heart attack, or death in patients with mild hypertension is 140 for 5 years (http://www.jr2.ox.ac.uk/bandolier/index.html), it is likely that the actual clinical benefit of treating prehypertension is even smaller. (LOE = 1b))
Kalavrouziotis D, Buth KJ, Cox JL, and Baskett RJ. Should all patients be treated with an angiotensin converting enzyme inhibitor after **coronary artery bypass graft surgery**? The impact of angiotensin converting enzyme inhibitors, statins, and beta blockers after coronary artery bypass graft surgery. Am Heart J 2011.
Kim-Mitsuyama S, Ogawa H, Matsui K, et al. An angiotensin II receptor blocker (**olmesartan**) -calcium channel blocker combination prevents cardiovascular events in elderly high-risk hypertensive patients with chronic kidney disease better than high-dose angiotensin II receptor blockade alone. (**OSCAR**) Kidney Int. 2013 Jan;83(1):167-76.
Kjeldsen SE, et al. **VALUE** Trial Investigators. Effects of valsartan compared to amlodipine on preventing type 2 diabetes in high-risk hypertensive patients: the VALUE trial. J Hypertens. 2006 Jul;24(7):1405-12.
Knoll GA, Fergusson D, Chassé M, et al. **Ramipril versus placebo in kidney transplant patients with proteinuria**: a multicentre, double-blind, randomised controlled trial. Lancet Diabetes Endocrinol. 2015 Oct 21.
Kober L, Torp-Pedersen C, Carlsen JE, et al. A clinical trial of the angiotensin-converting-enzyme inhibitor trandolapril in patients with left ventricular dysfunction after myocardial infarction. Trandolapril Cardiac Evaluation (**TRACE**) Study Group. N Engl J Med. 1995 Dec 21;333(25):1670-6.
Kolber MR, Garrison S, Turgeon RD. **Electrolyte disturbance** with **diuretics** and **ACEIs**. Can Fam Physician. 2016 Jul;62(7):569.
Konstam MA, Neaton JD, Dickstein K, et al. Effects of high-dose versus low-dose losartan on clinical outcomes in patients with heart failure (**HEAAL** study): a randomised, double-blind trial. *Lancet* 2009; DOI:10.1016/S0140-6736(09)61913-9.
Korniyenko A, Alviar CL, Cordova JP, Messerli FH. **Visceral angioedema** due to angiotensin-converting enzyme inhibitor therapy. Cleve Clin J Med. 2011 May;78(5):297-304.
Kostis JB, Kim HJ, Rusnak J, et al. Incidence and characteristics of **angioedema** associated with enalapril. Arch Intern Med. 2005 Jul 25;165(14):1637-42. RESULTS: Angioedema occurred in 86 of 12 557 (0.68%) of the subjects.
Krause T, Lovibond K, Caulfield M, McCormack T, Williams B; on behalf of the Guideline Development Group. **Management of hypertension**: summary of **NICE** guidance. BMJ. 2011 Aug 25;343:d4891.
Ku E, Park J, Vidhun J, Campese V. The **hazards of dual renin-angiotensin blockade** in chronic kidney disease. Arch Intern Med. 2009 Jun 8;169(11):1015-8.
Kuenzli A, Bucher HC, Anand I, et al. **Meta-analysis** of combined therapy with angiotensin receptor antagonists versus ACE inhibitors alone in patients with **heart failure**. PLoS One. 2010 Apr 1;5(4):e9946.
Kunz R, Friedrich C, Wolbers M, Mann JF. Meta-analysis: Effect of **Monotherapy and Combination** Therapy with Inhibitors of the Renin Angiotensin System on Proteinuria in Renal Disease. Ann Intern Med. 2007 Nov 5; [Epub ahead of print] ARBs reduce **proteinuria**, independent of the degree of proteinuria and of underlying disease, to a similar degree as placebo or calcium-channel blocker. Reduction in proteinuria from ARB and ACE inhibitors is similar, but their combination is more effective than either drug alone.
Kurnik D, Vesterman-Landes J, Bialik M, et al. **Hyperkalemia and renal function during monotherapy and dual Renin-Angiotensin blockade** in the community setting. Clin Ther. 2011 Apr;33(4):456-64.
Lacourcière Y, Poirier L, Lefebvre J, et al. Increasing the doses of both **diuretics and angiotensin receptor blockers** is beneficial in subjects with uncontrolled systolic hypertension. Can J Cardiol. 2010 Oct;26(8):313-9.
Lacro RV, Dietz HC, Sleeper LA, et al. **Atenolol versus losartan** in children and young adults with **Marfan's syndrome**. N Engl J Med. DOI: 10.1056/NEJMoa1404731.
Lacro RV, Dietz HC, Sleeper LA, et al. Pediatric Heart Network Investigators. **Atenolol versus losartan** in children and young adults with **Marfan's syndrome**. N Engl J Med. 2014 Nov 27;371(22):2061-71.
Lammel-Lindemann JA, Flores-Villalba E, Martagón AJ, et al. **Non-cholestatic acute hepatitis following Candesartan** administration. Br J Clin Pharmacol. 2017 Aug 25
Lapi F, Azoulay L, Yin H, et al. Concurrent use of diuretics, angiotensin converting enzyme inhibitors, and angiotensin receptor blockers with **non-steroidal anti-inflammatory drugs** (NSAIDs) and risk of acute kidney injury: nested case-control study. BMJ 2013;346:e8525.

Latini R, Tognoni G, Maggioni AP, et al. Clinical effects of early angiotensin-converting enzyme inhibitor treatment for acute myocardial infarction are similar in the presence and absence of **aspirin**: systematic overview of individual data from 96,712 randomized patients. Angiotensin-converting Enzyme Inhibitor Myocardial Infarction Collaborative Group. J Am Coll Cardiol. 2000 Jun;35(7):1801-7.

Lee VC, Rhew DC, Dylan M, Badamgarav E, et al. Meta-Analysis: Angiotensin-Receptor Blockers in Chronic Heart Failure and High-Risk Acute Myocardial Infarction. Ann Intern Med. 2004 Nov 2;141(9):693-704.

Lee HY, Hong BK, Chung WJ, et al. Phase IV, 8-week, multicenter, randomized, active treatment-controlled, parallel group, efficacy, and tolerability study of **high-dose candesartan** cilexetil combined with hydrochlorothiazide in Korean adults with stage II hypertension. Clin Ther. 2011 Aug;33(8):1043-56.

Lennestal R, Olausson PO, Kallen B. **Maternal use of antihypertensive drugs in early pregnancy** and delivery outcome, notably the presence of heart defects in the infants. Eur J Clin Pharmacol 2 009;65:615-25.

Levin A, Hemmelgarn B, Culleton B, Tobe S, McFarlane P, Ruzicka M, Burns K, Manns B, White C, Madore F, Moist L, Klarenbach S, Barrett B, Foley R, Jindal K, Senior P, Pannu N, Shurraw S, Akbari A, Cohn A, Reslerova M, Deved V, Mendelssohn D, Nesrallah G, Kappel J, Tonelli M; Canadian Society of Nephrology. Guidelines for the management of **chronic kidney disease**. CMAJ. 2008 Nov 18;179(11):1154-62. http://www.cmaj.ca/cgi/data/179/11/1154/DC1/1

Li NC, Lee A, Whitmer RA, et al. Use of angiotensin receptor blockers and risk of **dementia** in a predominantly male population: prospective cohort analysis. BMJ. 2010 Jan 12;340:b5465. doi:10.1136/bmj.b5465.

Li DK, Yang C, Andrade S, et al. Maternal exposure to **angiotensin converting enzyme inhibitors** in the **first trimester and risk of malformations** in offspring: A retrospective cohort study. BMJ 2011.

Li EC, Heran BS, Wright JM. **Angiotensin converting enzyme (ACE) inhibitors versus angiotensin receptor blockers for primary hypertension.** Cochrane Database Syst Rev. 2014 Aug 23;8:CD009096. Our analyses found no evidence of a difference in total mortality or cardiovascular outcomes for ARBs as compared with ACE inhibitors, while ARBs caused slightly fewer WDAEs than ACE inhibitors. Although ACE inhibitors have shown efficacy in these outcomes over placebo, our results cannot be used to extrapolate the same conclusion for ARBs directly, which have not been studied in placebo-controlled trials for hypertension. Thus, the substitution of an ARB for an ACE inhibitor, while supported by evidence on grounds of tolerability, must be made in consideration of the weaker evidence for the efficacy of ARBs regarding mortality and morbidity outcomes compared with ACE inhibitors. Additionally, our data mostly derives from participants with existing clinical sequelae of hypertension, and it would be useful to have data from asymptomatic people to increase the generalizability of this review. Unpublished subgroup data of hypertensive participants in existing trials comparing ACE inhibitors and ARBs needs to be made available for this purpose.

Lin FC, Tsai CP, Kuang-Wu Lee J, et al. **Angiotensin-Converting Enzyme Inhibitors and Amyotrophic Lateral Sclerosis Risk**: A Total Population-Based Case-Control Study. JAMA Neurol. 2014 Nov 10.

Littman J, Halil R. Potential effects of **rational prescribing** on national health care **spending**: More than half a billion dollars in annual savings (escitalopram, esomeprazole, perindoril). Can Fam Physician. 2016 Mar;62(3):235-44.

Liu Y, Ma X, Zheng J, Jia J, Yan T. Effects of **angiotensin-converting enzyme inhibitors and angiotensin receptor blockers on cardiovascular events and residual renal function in dialysis** patients: a meta-analysis of randomized controlled trials. BMC Nephrol. 2017 Jun 30;18(1):206.

Lv J, Perkovic V, Foote CV, et al. **Antihypertensive agents for preventing diabetic kidney disease**. Cochrane Database Syst Rev. 2012 Dec 12;12:CD004136. doi: 10.1002/14651858.CD004136.pub3. ACEi were found to prevent new onset DKD and death in normoalbuminuric people with diabetes, and could therefore be used in this population. More data are needed to clarify the role of ARB and other drug classes in preventing DKD.

Madison JR, Spies C, Schatz IJ, Masaki K, Chen R, et al. **Proteinuria** and risk for stroke and coronary heart disease during 27 years of follow-up: the Honolulu Heart Program. Arch Intern Med. 2006 Apr 24;166(8):884-9.

Maggioni AP, Anand I, Gottlieb SO, Latini R, Tognoni G, Cohn JN. Effects of valsartan on morbidity and mortality in patients with heart failure not receiving angiotensin-converting enzyme inhibitors. **Val-HeFT** Investigators (Valsartan Heart Failure Trial). J Am Coll Cardiol 2002 Oct 16;40(8):1414-21.

Mahmoudpour SH, Asselbergs FW, Souverein PC, et al. Prescription Patterns of **Angiotensin-Converting Enzyme Inhibitors for Various Indications**: A UK Population-based Study. Br J Clin Pharmacol. 2018 Jun 26.

Mahmoudpour SH, Baranova EV, et al. Determinants of angiotensin converting enzyme-inhibitor **(ACEI) intolerance and angioedema** in the UK clinical practice research datalink. Br J Clin Pharmacol. 2016 Aug 15.

Makani H, Bangalore S, Romero J, et al. Effect of Renin-Angiotensin system blockade (ACEI/ARB) on calcium channel blocker-associated **peripheral edema**. Am J Med. 2011 Feb;124(2):128-35.

Makani H, Messerli FH, Romero J, et al. Meta-Analysis of Randomized Trials of **Angioedema** as an Adverse Event of Renin-Angiotensin System Inhibitors. Am J Cardiol. 2012 Apr 20.

Makani H, Bangalore S, Desouza KA, et al. Efficacy and safety of **dual blockade** of the renin-angiotensin system: meta-analysis of randomised trials. BMJ. 2013 Jan 28;346:f360.

Makani H, Bangalore S, Supariwala A, et al. Antihypertensive efficacy of **angiotensin receptor blockers as monotherapy** as evaluated by ambulatory blood pressure monitoring: a meta-analysis. Eur Heart J. 2013 Aug 21.

Manfrini O, Morrell C, Das R, et al; EMMACE-2 (Evaluation of Methods and Management of Acute Coronary Events) Study Group. Effects of **Angiotensin-Converting Enzyme Inhibitors and Beta Blockers** on Clinical Outcomes in Patients **With and Without Coronary Artery Obstructions** at Angiography (from a Register-Based Cohort Study on **Acute Coronary Syndromes**). Am J Cardiol. 2014 Mar 3.

Mansfield KE, Nitsch D, Smeeth L, et al. Prescription of renin-angiotensin system blockers and **risk of acute kidney injury**: a population-based cohort study. BMJ Open. 2016 Dec 21;6(12):e012690.

Marcovecchio ML et al. **ACE inhibitors and statins in adolescents with type 1 diabetes. (AdDit)** N Engl J Med2017 Nov 2; 377:1733.

Massie BM, Carson PE, McMurray JJ, et al.; the **I-PRESERVE** Investigators. Irbesartan in Patients with Heart Failure and Preserved Ejection Fraction. N Engl J Med. 2008 Nov 11. [Epub ahead of print]

Matchar DB, McCrory DC, Orlando LA, et al. **Systematic Review**: Comparative Effectiveness of Angiotensin-Converting Enzyme Inhibitors and Angiotensin II Receptor Blockers for Treating Essential Hypertension. Ann Intern Med. 2007 Nov 5; [Epub ahead of print] Available evidence shows that ACE inhibitors and ARBs have similar effects on blood pressure control, and that ACE inhibitors have higher rates of cough than ARBs. Data regarding other outcomes are limited.

Mauer M, Zinman B, Gardiner R, et al. Renal and retinal effects of **enalapril and losartan in type 1** diabetes. N Engl J Med. 2009 Jul 2;361(1):40-51. Early blockade of the renin-angiotensin system in patients with type 1 diabetes did not slow nephropathy progression but slowed the progression of retinopathy.

McAlister, Finlay A., Zhang, Jianguo, Tonelli, Marcello, et al. The safety of **combining angiotensin-converting-enzyme inhibitors with angiotensin-receptor blockers** in elderly patients: a population-based longitudinal analysis. CMAJ 2011 0: cmaj.101333.

McAlister FA; for the Renin Angiotension System Modulator Meta-Analysis Investigators. Angiotensin-converting enzyme inhibitors or angiotensin receptor blockers are beneficial in **normotensive atherosclerotic** patients: a collaborative meta-analysis of randomized trials. Eur Heart J. 2011 Oct 31.

McAlister FA. Angiotensin-converting enzyme inhibitors or angiotensin receptor blockers are beneficial in **normotensive** atherosclerotic patients: a collaborative meta-analysis of randomized trials. Eur Heart J. 2012 Feb;33(4):505-514.

McCall KL, Craddock D, Edwards K. Effect of Angiotensin-Converting Enzyme Inhibitors and Angiotensin II Type 1 Receptor Blockers on the Rate of **New-Onset Diabetes Mellitus**: A Review and Pooled Analysis. Pharmacotherapy. 2006 Sep;26(9):1297-306.

McDonald MA, Simpson SH, Ezekowitz JA, et al. Angiotensin receptor blockers and risk of **myocardial infarction**: systematic review. BMJ. 2005Oct 15;331(7521):873. Epub 2005 Sep 23. CONCLUSIONS: Treatment with angiotensin receptor blockers was not associated with a significantly increased risk of myocardial infarction. The 95% confidence intervals do, however, not exclude an increase of up to 16% in the risk of myocardial infarction or a reduction in risk of up to 25%. Until further information specifically dealing with this issue is available from large prospective trials, our findings may alleviate recent concerns over the safety of this class of medications.

McDowell SE, et al. Systematic review and meta-analysis of **ethnic differences** in risks of adverse reactions to drugs used in cardiovascular medicine. BMJ. 2006 May 20;332(7551):1177-81. Epub 2006 May 5.

McMurray JJ, Young JB, Dunlap ME, et al. Relationship of dose of background angiotensin-converting enzyme inhibitor to the benefits of candesartan in Candesartan in Heart failure: Assessment of reduction in Mortality and morbidity (**CHARM**)-added trial. American Heart Journal 2006;151: 992-998

McMurray JJV, Packer M, Desai AS, et al. **Angiotensin-neprilysin inhibition LCZ696 versus enalapril** in heart failure. (**Paradigm HF**) N Engl J Med. DOI: 10.1056/NEJMoa1409077.

Medical Letter. **Aliskiren (Tekturna)** for Hypertension. April 9,2007.

Mehdi UF, Adams-Huet B, Raskin P, Vega GL, Toto RD. Addition of angiotensin receptor blockade or mineralocorticoid antagonism to maximal angiotensin-converting enzyme inhibition in diabetic nephropathy. J Am Soc Nephrol. 2009 Dec;20(12):2641-50. Epub 2009 Nov 19.

Messerli FH, Bangalore S. Angiotensin Receptor Blockers **Reduce Cardiovascular Events, Including the Risk of Myocardial Infarction**. Circulation. 2017 May 30;135(22):2085-2087.

Mitchell AA. Fetal risk from **ACE inhibitors in the first trimester**. BMJ 2011; DOI:10.1136/bmj.d5931.

Mogensen CE, et al. Randomised controlled trial of dual blockade of renin-angiotensin system in patients with hypertension, microalbuminuria, and non-insulin dependent diabetes: the candesartan and lisinopril

microalbuminuria (**CALM**) study. BMJ. 2000 Dec 9;321(7274):1440-4.
Mujib M, Patel K, Fonarow GC, et al. Angiotensin-converting Enzyme Inhibitors and Outcomes in **Heart Failure and Preserved Ejection Fraction**. Am J Med. 2013 Mar 16.
Musini VM, Fortin PM, Bassett K, et al. Blood pressure lowering efficacy of **renin inhibitors** for primary hypertension: a Cochrane systematic review. J Hum Hypertens. 2009 Jan 22. We concluded that aliskiren has a dose-related blood pressure lowering effect better than placebo and magnitude of effect is similar to that determined for angiotensin-converting enzyme inhibitors and angiotensin receptor blockers.
Nadeem S, Hashmat S, Defreitas MJ, et al. **Renin Angiotensin System Blocker Fetopathy**: A Midwest Pediatric Nephrology Consortium Report. J Pediatr. 2015 Oct;167(4):881-5.
Nagashima K, Katsurada T, Sakamoto N. A Case of **Olmesartan-associated Sprue-like Enteropathy**. Clin Gastroenterol Hepatol. 2017 Dec 13.
Nia AM, Er F. **Angioedema** associated with the use of angiotensin-converting enzyme inhibitor (**image**). CMAJ. 2013 Jan 8;185(1):E80.
Nakamae H, et al. Notable effects of angiotensin II receptor blocker, **valsartan, on acute cardiotoxic changes** after cyclophosphamide, doxorubicin, vincristine, & prednisolone. Cancer. 2005 Dec 1;104(11):2492-8.
NAVIGATOR Study Group, Effect of **Valsartan** on the Incidence of Diabetes and Cardiovascular Events. N Engl J Med 2010 0: NEJMoa1001121.
NICE: National Institute for Health and Clinical Excellence. **Hypertension Guidelines**. Aug 2011. http://www.nice.org.uk/nicemedia/live/13561/56015/56015.pdf
Nicholls SJ, Bakris GL, Kastelein JJP, et al. Effect of **aliskiren** on progression of coronary disease in patients with **prehypertension: the AQUARIUS** randomized clinical trial. JAMA. doi:10.1001/jama.2013.277169.
Nielson E, Hennrikus E, Lehman E, Mets B. **Angiotensin axis blockade, hypotension, and acute kidney injury in elective major orthopedic surgery**. J Hosp Med. 2014 May;9(5):283-8.
Nishiwaki M, Hosoai H, Ikewaki K, et al; ABC Study Group. Efficacy and Effects on Lipid Metabolism of Combination Treatment With **Losartan + Hydrochlorothiazide** Versus **Losartan + Amlodipine**: A 48-Week Prospective, Multicenter, Randomized, Open-Label Trial. Clin Ther. 2013 Mar 12.
Nissen SE, Tuzcu EM, Libby P, et al. **CAMELOT** Investigators. Effect of antihypertensive agents on cardiovascular events in patients with coronary disease and normal blood pressure: the CAMELOT study: a randomized controlled trial. JAMA. 2004 Nov 10;292(18):2217-25.
Nyirenda MJ, Tang JI, Padfield PL, Seckl JR. **Hyperkalaemia**. BMJ. 2009 Oct 23;339:b4114. doi: 10.1136/bmj.b4114.
O'Hare AM, Kaufman JS, Covinsky KE, et al. Current guidelines for using angiotensin-converting enzyme inhibitors and angiotensin II-receptor antagonists in **chronic kidney disease**: is the evidence base relevant to **older** adults? Ann Intern Med. 2009 May 19;150(10):717-24.
Oertelt-Prigione Sabine, Crosignani Andrea, Gallieni Maurizio et al. Severe **hepatic encephalopathy** in a patient with liver cirrhosis after administration of angiotensin-converting enzyme inhibitor/angiotensin II receptor blocker combination therapy: a case report. Journal of Medical Case Reports 2010, 4:141doi:10.1186/1752-1947-4-141.
Ogawa H, Soejima H, Matsui K, et al. A trial of **telmisartan** prevention of cardiovascular diseases (**ATTEMPT-CVD**): Biomarker study.*Eur J Prev Cardiol* 2015.
Opelz G and Döhler B. Treatment of kidney transplant recipients with ACE inhibitor/ARB and risk of **respiratory tract cancer**: a collaborative transplant study report. Am J Transplant 2011; DOI: 10.1111/j.1600-6143.2011.03681.x. (Higher cancers in subgroup: ACEi/ARB & if smokers)
Oppermann M, Padberg S, Kayser A, et al. Angiotensin-II-receptor-1-antagonist **fetopathy** - Risk assessment, critical time period, and vena cava thrombosis as a possible new feature. Br J Clin Pharmacol. 2012 Jul 23.
Ouwerkerk W, Voors AA, Anker SD, et al. Determinants and clinical outcome of **uptitration of ACE-inhibitors and beta-blockers** in patients with **heart failure**: a prospective European study. Eur Heart J. 2017 Mar 11.
Owan TE, et al. Trends in prevalence and outcome of **heart failure with preserved ejection fraction**. N Engl J Med. 2006 Jul 20;355(3):251-9.
Packer M, Poole-Wilson PA, Armstrong PW, et al. Comparative effects of low and high doses of the angiotensin-converting enzyme inhibitor, lisinopril, on morbidity and mortality in chronic heart failure. **ATLAS** Study Group. Circulation. 1999;100:2312-8.
Padwal R, Lin M, Etminan M, Eurich DT. Comparative Effectiveness of **Olmesartan and Other Angiotensin Receptor Blockers in Diabetes** Mellitus: Retrospective Cohort Study. Hypertension. 2014 Feb 17.
Pantzaris ND, Karanikolas E, Tsiotsios K, Velissaris D. **Renin Inhibition with Aliskiren**: A Decade of Clinical Experience. J Clin Med. 2017 Jun 9;6(6).
Paoletti E, Bellino D, Marsano L, et al. Effects of **ACE inhibitors on long-term** outcome of **renal transplant recipients**: a randomized controlled trial. Transplantation. 2013 Mar 27;95(6):889-95.
Papademetriou V, Farsang C, Elmfeldt D, et al.; Study on Cognition and Prognosis in the Elderly study group. Stroke prevention with the angiotensin II type 1-receptor blocker candesartan in elderly patients with isolated systolic hypertension: the Study on Cognition and Prognosis in the Elderly (**SCOPE**). J Am Coll Cardiol. 2004 Sep 15;44(6):1175-80. (Zanchetti A, Elmfeldt D. Findings and implications of the Study on COgnition and Prognosis in the Elderly (SCOPE) - A review. Blood Press. 2006;15(2):71-9.)
Parati G, Bilo G, et al. Changes in 24 h ambulatory blood pressure and effects of angiotensin II receptor blockade during acute and prolonged **high-altitude exposure**: a randomized clinical trial. Eur Heart J. 2014 Aug 26.
Parving HH, Persson F, Lewis JB, Lewis EJ, Hollenberg NK; **AVOID** Study Investigators. **Aliskiren** 150→300mg od combined with losartan 100mg od in type 2 diabetes and nephropathy. N Engl J Med. 2008 Jun 5;358(23): 2433-46. (n=599 6months) Aliskiren may have renoprotective effects that are independent of its blood-pressure-lowering effect in patients with hypertension, type 2 diabetes, and nephropathy who are receiving the recommended renoprotective treatment.
Parving HH, Brenner BM, McMurray JJ, et al; the **ALTITUDE** Investigators. Cardiorenal End Points in a Trial of **Aliskiren for Type 2 Diabetes**. N Engl J Med. 2012 Nov 3.
Pasternak B, Svanström H, Callréus T, et al. Use of angiotensin receptor blockers and the risk of **cancer**. Circulation 2011; 123:1729-1736.
Patel A; ADVANCE Collaborative Group, MacMahon S, Chalmers J, Neal B, et al. Effects of a fixed combination of perindopril and indapamide on macrovascular and microvascular outcomes in patients with type 2 diabetes mellitus (the **ADVANCE** trial): a randomised controlled trial. Lancet. 2007 Sep 8;370(9590):829-40. Routine administration of a fixed combination of perindopril and indapamide to patients with type 2 diabetes was well tolerated and reduced the risks of major vascular events, including death. Although the confidence limits were wide, the results suggest that over 5 years, one death due to any cause would be averted among every 79 patients assigned active therapy. (InfoPOEMs: Perindopril (Aceon) plus indapamide (Lozol) is better than placebo in decreasing clinically relevant events in patients with type 2 diabetes who are at high risk of cardiovascular complications. Whether the combination is better than other medications -- like aspirin -- isn't addressed by this study. (LOE = 1b))
Pees C, Laccone F, Hagl M, et al. Usefulness of **Losartan on the Size of the Ascending Aorta** in an Unselected Cohort of Children, Adolescents, and Young Adults With Marfan Syndrome. Am J Cardiol. 2013 Jul 19.
Persson F, Lewis JB, Lewis EJ, Rossing P, Hollenberg NK, Parving HH; for the **AVOID** study investigators. Impact of Baseline Renal Function on the Efficacy and Safety of Aliskiren Added To Losartan in Patients with Type 2 Diabetes and Nephropathy. Diabetes Care. 2010 Aug 6.
Persson F, Rossing P, Parving HH. **Direct renin inhibition in chronic kidney disease**. Br J Clin Pharmacol. 2012 Dec 25.
Petrella R, Michailidis P. Retrospective Analysis of Real-World Efficacy of **Angiotensin Receptor Blockers Versus Other Classes** of Antihypertensive Agents in Blood Pressure Management. Clin Ther. 2011 Aug 31.
Pharmacist's Letter. Angiotensin Receptor Blockers (ARBS) and **Cancer Risk.** Aug 2010.
Phillips CO, Kashani A, Ko DK, Francis G, Krumholz HM. Adverse Effects of **Combination Angiotensin II Receptor Blockers Plus Angiotensin-Converting Enzyme Inhibitors** for Left Ventricular Dysfunction: A Quantitative Review of Data From Randomized Clinical Trials. Arch Intern Med. 2007 Oct 8;167(18):1930-6. Four studies (N = 17 337; mean follow-up, 25 months [range, 11-41 months]) were selected. Combination ARB plus ACE inhibitor vs control treatment that included ACE inhibitors was associated with significant increases in medication discontinuations because of adverse effects in patients with chronic heart failure (RR, 1.38 [95% CI, 1.22-1.55]) or in patients with acute myocardial infarction with symptomatic left ventricular dysfunction (RR, 1.17 [95% CI, 1.03-1.34]), and for both conditions there were significant increases in worsening renal function (RR, 2.17 [95% CI, 1.59-2.97] and RR, 1.61 [95% CI, 1.31-1.98], respectively), hyperkalemia (RR, 4.87 [95% CI, 2.39-9.94] and RR, 1.33 [95% CI, 0.90-1.98], respectively; the latter was not significant), and symptomatic hypotension (RR, 1.50 [95% CI, 1.09-2.07], and RR, 1.48 [95% CI, 1.33-3.18], respectively).Combination ARB plus ACE inhibitor therapy in subjects with symptomatic left ventricular dysfunction was accompanied by marked increases in adverse effects.
Phomakay V, Huett WG, Gossett JM, et al. **β-Blockers and Angiotensin Converting Enzyme Inhibitors**: Comparison of Effects on Aortic Growth in Pediatric Patients with **Marfan Syndrome**. J Pediatr. 2014 Aug 7.
Pierson-Marchandise M, Gras V, Moragny J, et al. The drugs that mostly frequently **induce acute kidney injury**: a case - non-case study of a pharmacovigilance database. Br J Clin Pharmacol. 2016 Dec 21. The most frequently implicated drug classes were antibacterials for systemic use (29.5%), diuretics (18.5%), agents acting on the renin-angiotensin system (16.3%), antineoplastic agents (10.2%) and anti-inflammatory agents (5.4%). Gentamicin, eplerenone, spironolactone, candesartan, cisplatin and acyclovir had the highest RORs (>10).
Pilote L, Abrahamowicz M, Eisenberg M, et al. Effect of **different angiotensin-converting-enzyme inhibitors** on mortality among elderly patients with congestive **heart failure**. CMAJ. 2008 May 6;178(10):1303-11. When prescribing ACE inhibitors to patients, physicians should consider a possible 10%-15% increase in mortality with captopril and enalapril compared with ramipril among patients with congestive heart failure.
Pitt B, et al.; QUIET Study Group. The QUinapril Ischemic Event Trial (**QUIET**): evaluation of chronic ACE inhibitor therapy in patients with ischemic heart disease and preserved left ventricular function. Am J Cardiol. 2001 May 1;87(9):1058-63.

Pohl MA, Blumenthal S, Cordonnier DJ, et al. Independent and Additive Impact of Blood Pressure Control and Angiotensin II Receptor Blockade on Renal Outcomes in the Irbesartan Diabetic Nephropathy Trial: Clinical Implications and Limitations. J Am Soc Nephrol. 2005 Oct;16(10):3027-37. Epub 2005 Aug 24.

Pottegård A, Kristensen KB, Ernst MT, et al. Use of **N-nitrosodimethylamine (NDMA) contaminated valsartan products and risk of cancer**: Danish nationwide cohort study. BMJ. 2018 Sep 12;362:k3851.

Potier L, Roussel R, Elbez Y, et al. **REACH** Registry Investigators. Angiotensin-converting enzyme inhibitors and angiotensin receptor blockers **in high vascular risk**. Heart2017;103:1310–2.

Qaseem A, Hopkins RH, Sweet DE, et al. **Screening, Monitoring, and Treatment of Stage 1 to 3 Chronic Kidney Disease**: A Clinical Practice Guideline From the Clinical Guidelines Committee of the American College of Physicians (**ACP**). Ann Intern Med. 2013 Oct 22.

Rahman M, Pressel S, Davis BR, et al. Renal outcomes in high-risk hypertensive patients treated with an angiotensin-converting enzyme inhibitor or a calcium channel blocker vs. a diuretic. A report from the antihypertensive and lipid-lowering treatment to prevent heart attack trial (**ALLHAT**). Arch Intern Med 2005; 165:936-46. (InfoPOEMs: It's blood pressure reduction, not the choice of drug, that prevents renal function decline in patients with hypertension, with or without diabetes. Neither the calcium channel blocker amlodipine (Norvasc) nor the angiotensin-converting enzyme inhibitor lisinopril (Prinivil) prevents the combined outcome of end-stage renal disease or a 50% decrease in renal function any better than the diuretic chlorthalidone (Hygroton). Results were the same in patients with already compromised renal function, as well as in patients with type 2 diabetes. (LOE = 1b))

Reboldi G, Angeli F, Cavallini C, Gentile G, Mancia G, Verdecchia P. Comparison between angiotensin-converting enzyme inhibitors and angiotensin receptor blockers on the risk of myocardial infarction, stroke and death: a meta-analysis. J Hypertens. 2008 Jul;26(7):1282-9. This overview suggests that angiotensin II receptor blockers are as effective as angiotensin-converting enzyme inhibitors on the risk of myocardial infarction, cardiovascular mortality and total mortality. Angiotensin II receptor blockers may be slightly more protective than angiotensin-converting enzyme inhibitors on the risk of stroke.

REIN-Randomised placebo-controlled trial of effect of ramipril on decline in glomerular filtration rate and risk of terminal renal failure in proteinuric, non-diabetic nephropathy. The GISEN Group (Gruppo Italiano di Studi Epidemiologici in Nefrologia)Lancet. 1997 Jun 28;349(9069):1857-63.

Ridker PM, et al. Valsartan, Blood Pressure Reduction, and **C-Reactive Protein**. Primary Report of the Val-MARC Trial. Hypertension. 2006 May 19; [Epub ahead of print]

Rim MY et al. The effect of renin-angiotensin-aldosterone system blockade **(ACEI,ARB) on contrast-induced acute kidney injury**: A propensity-matched study. Am J Kidney Dis 2012 Oct; 60:576.

Ritter J M. Therapeutics: **Angiotensin converting enzyme inhibitors and angiotensin receptor blockers in hypertension**. BMJ 2011;342:doi:10.1136/bmj.d1673 (Published 7 April 2011)

Rouleau JL, Warnica WJ, Baillot R, et al.; IMAGINE (Ischemia Management with Accupril post-bypass Graft via Inhibition of the converting Enzyme) Investigators. Effects of angiotensin-converting enzyme inhibition in low-risk patients early after coronary artery bypass surgery. Circulation. 2008 Jan 1;117(1):24-31. Epub 2007 Dec 10. In patients at low risk of cardiovascular events after CABG, routine early initiation of angiotensin-converting enzyme inhibitor therapy does not appear to improve clinical outcome up to 3 years after CABG; however, it increases the incidence of adverse events, particularly early after CABG. Thus, early after CABG, initiation of angiotensin-converting enzyme inhibitor therapy should be individualized and continually reassessed over time according to risk.

Ripamonti V, et al. Angiotensin-converting enzyme inhibitors slow recovery from **anemia** following cardiac surgery. Chest. 2006 Jul;130(1):79-84.

Robins GW, Scott LJ. **Eprosartan**: a review of its use in the management of hypertension. Drugs. 2005;65(16):2355-77.

Rodriguez-Gabella T, Catalá P, Muñoz-García AJ, et al. **Renin-Angiotensin System Inhibition** Following Transcatheter Aortic Valve Replacement. J Am Coll Cardiol. 2019 Aug 6;74(5):631-641.

Roshanov PS, Rochwerg B, Patel A, et al. **Withholding versus Continuing Angiotensin-converting Enzyme Inhibitors or Angiotensin II Receptor Blockers before Noncardiac Surgery**: An Analysis of the Vascular events In noncardiac Surgery patIents cOhort evaluatioN Prospective Cohort. Anesthesiology. 2016 Oct 24.

Rossing K, Schjoedt KJ, Jensen BR, et al. Enhanced renoprotective effects of **ultrahigh doses of irbesartan** in patients with type 2 diabetes and microalbuminuria. Kidney Int. 2005 Sep;68(3):1190-8.

Rubio-Tapia A, Herman M, Ludvigsson J, et al. Severe **spruelike enteropathy** associated with **olmesartan**. Mayo Clin Proc 2012.

Ruggenenti P, Perna A, Loriga G, et al.; **REIN-2** Study Group. Blood-pressure control for renoprotection in patients with non-diabetic chronic renal disease: multicentre, randomised controlled trial. Lancet. 2005 Mar 12;365(9463):939-46. (Interpretation: In pts with non-diabetic proteinuric nephropathies receiving background ACE-inhibitor therapy, no additional benefit from further blood-pressure reduction by felodipine could be shown.)

Ruggenenti P, Fassi A, Ilieva AP, ET AL. Preventing Microalbuminuria in Type 2 Diabetes (**BENEDICT**). N Engl J Med. 2004 Oct 31 (Ruggenenti P, et al. Impact of Blood Pressure Control and Angiotensin-Converting Enzyme Inhibitor Therapy on New-Onset **Microalbuminuria** in Type 2 Diabetes: A Post Hoc Analysis of the **BENEDICT** Trial. J Am Soc Nephrol. 2006 Nov 2; [Epub ahead of print]) Ruggenenti P, Iliev I, Costa GM, Parvanova A, Perna A, Giuliano GA, Motterlini N, Ene-Iordache B, Remuzzi G; Bergamo Nephrologic Diabetes Complications Trial Study Group. Preventing left ventricular hypertrophy by ACE inhibition in hypertensive patients with type 2 diabetes: a prespecified analysis of the Bergamo Nephrologic Diabetes Complications Trial (BENEDICT). Diabetes Care. 2008 Aug;31(8):1629-34. Epub 2008 Apr 28.

Sadat-Ebrahimi SR, Parnianfard N, Vahed N, et al. An Evidence-Based Systematic Review of the **Off-Label Uses of Lisinopril**. Br J Clin Pharmacol. 2018 Jul 3.

Sandset EC, Bath PMW, Boysen G et al. The angiotensin-receptor blocker **candesartan for treatment of acute stroke (SCAST):** A randomised, placebo-controlled, double-blind trial. *Lancet* 2011.

Sarrias A, Bayes-Genis A. Is **Sacubitril/Valsartan (Also) an Antiarrhythmic Drug**? Circulation. 2018 Aug 7;138(6):551-553

Sawano T, Ozaki A, Saito H, Shimada Y, Tanimoto T. Payments From Pharmaceutical Companies to Authors Involved in the **Valsartan Scandal** in Japan. JAMA Netw Open. 2019 May 3;2(5):e193817.

Schaer BA, Schneider C, Jick SS, et al. Risk for incident **AF** in patients who receive antihypertensive drugs. Ann Intern Med 2010; 152:78-84.

Schrader J, Luders S, Kulschewski A, et al.; Acute Candesartan Cilexetil Therapy in Stroke Survivors Study Group. The **ACCESS** Study: evaluation of Acute Candesartan Cilexetil Therapy in Stroke Survivors. Stroke. 2003 Jul;34(7):1699-703. Epub 2003 Jun 19.

Schrier RW, Abebe KZ, Perrone RD, et al. **Blood pressure** in early **autosomal dominant polycystic kidney disease**. N Engl J Med. DOI: 10.1056/NEJMoa1402685.

Schellenbaum GD, et al. **Weight loss, muscle strength**, and angiotensin-converting enzyme inhibitors in older adults with congestive heart failure or hypertension. J Am Geriatr Soc. 2005 Nov;53(11):1996-2000.

Schmidt M, Mansfield KE, Bhaskaran K, et al. **Serum creatinine elevation** after renin-angiotensin system blockade **and long term cardiorenal risks**: cohort study. BMJ 2017;356:j791.

Schmidt M, Mansfield KE, Bhaskaran K, et al. **Adherence to guidelines for creatinine and potassium monitoring and discontinuation** following renin-angiotensin system blockade: a UK general practice-based cohort study. BMJ Open. 2017 Jan 9;7(1):e012818.

Schrader J, Luders S, Kulschewski A, et al. **MOSES** Study Group. Morbidity and Mortality After Stroke, Eprosartan Compared with Nitrendipine for Secondary Prevention: principal results of a prospective randomized controlled study (MOSES). Stroke. 2005 Jun;36(6):1218-26. Epub 2005 May 5.

Schmieder RE, Philipp T, Guerediaga J, et al. Long-term antihypertensive efficacy and safety of the oral direct renin inhibitor **aliskiren**: a 12-month randomized, double-blind comparator trial with **hydrochlorothiazide**. Circulation. 2009;119:417– 445.

Sciarretta Sebastiano; Palano Francesca; Tocci Giuliano; et al. Antihypertensive Treatment and Development of Heart Failure in Hypertension: A Bayesian Network Meta-analysis of Studies in Patients With Hypertension and High Cardiovascular Risk. Arch Intern Med. 2010;0(2010):archinternmed.2010.427.

Shahinfar S, Simpson RL, Carides AD, et al. Safety of **losartan** in hypertensive patients with **thiazide-induced hyperuricemia**. Kidney Int 1999;56:1879-1885.

Sharma P, Nagarajan V. Q: Can an **ARB be given to patients who have had angioedema on an ACE inhibitor**? Cleve Clin J Med. 2013 Dec;80(12):755-7.

Shih CJ, Chen HT, Kuo SC, et al. Comparative effectiveness of **angiotensin-converting-enzyme inhibitors and angiotensin II receptor blockers** in patients with type 2 **diabetes** and **retinopathy**. CMAJ. 2016 Mar 21.

Shiraishi J, Sawada T, Koide M, et al; Kyoto Heart Study Group. Cardio-Cerebrovascular Protective Effects of **Valsartan** in High-Risk Hypertensive Patients With Coronary Artery Disease (from the Kyoto Heart Study). Am J Cardiol. 2012 May 1;109(9):1308-14.

Sipahi I, Debanne SM, Rowland DT et al. **Angiotensin-receptor blockade and risk of cancer**: Meta-analysis of randomised controlled trials. Lancet Oncol 2010; DOI:10.1016/S1470-2045(10)70106-6.

Sink KM, Leng X, et al. Angiotensin-converting enzyme inhibitors and **cognitive decline** in older adults with hypertension: results from the cardiovascular health study. Arch Intern Med. 2009 Jul 13;169(13):1195-202. Centrally active ACE inhibitors included **captopril** (Capoten, Bristol-Myers Squibb), **fosinopril** (Monopril, Bristol-Myers Squibb), **lisinopril**, **perindopril**, **ramipril** (Altace, King Pharmaceuticals), and **trandolapril** (Mavik, Abbott Laboratories). Non-centrally-active ACE inhibitors included **benazepril** (Lotensin, Novartis Pharmaceuticals), **enalapril** (Vasotec, Merck), **moexipril** (Univasc, Schwarz Pharma), and **quinapril** (Accupril, Pfizer).

Sjølie AK, Klein R, Porta M, et al. for the **DIRECT** Programme Study Group. Effect of candesartan on progression and regression of retinopathy in type 2 diabetes (**DIRECT-Protect 2**): a randomised placebo-controlled trial.

Lancet. 2008 Sep 25. [Epub ahead of print]
Slagman Maartje C J, Waanders Femke, Hemmelder Marc H, et al. for the HONEST (HOlland NEphrology STudy) Group. Moderate dietary **sodium restriction added to angiotensin converting enzyme inhibition** compared with dual blockade in lowering proteinuria and blood pressure: randomised controlled trial. BMJ 2011;343:doi:10.1136/bmj.d4366 (26 July 2011)
Solomon SD, Appelbaum E, Manning WJ, et al.; for the Aliskiren in Left Ventricular Hypertrophy (**ALLAY**) Trial Investigators. Effect of the Direct Renin Inhibitor Aliskiren, the Angiotensin Receptor Blocker Losartan, or Both on Left Ventricular Mass in Patients With Hypertension and Left Ventricular Hypertrophy. Circulation. 2009 Jan 19. [Epub ahead of print] Aliskiren was as effective as losartan in promoting LV mass regression. Reduction in LV mass with the combination of aliskiren plus losartan was not significantly different from that with losartan monotherapy, independent of blood pressure lowering. These findings suggest that aliskiren was as effective as an angiotensin receptor blocker in attenuating this measure of myocardial end-organ damage in hypertensive patients with LV hypertrophy.
Solomon SD, Hee Shin S, Shah A, et al. Effect of the direct rennin inhibitor aliskiren on left ventricular remodelling following myocardial infarction *with systolic dysfunction.(**ASPIRE**) Eur Heart J 2011; 32: 1227–34.*
Sorbets E, Labreuche J, Simon T, et al. Renin-angiotensin system antagonists and clinical outcomes in **stable coronary artery disease** without heart failure. Eur Heart J. 2014 Mar 9.
Sousa-Uva M, Head SJ, Milojevic M, et al; Document Reviewers. **2017 EACTS Guidelines on perioperative medication in adult cardiac surgery**. Eur J Cardiothorac Surg. 2017 Oct 6.
Strauss MH, Hall AS. The Divergent Cardiovascular Effects of Angiotensin Converting Enzyme Inhibitors and Angiotensin Receptor Blockers on **Myocardial Infarction** and Death. Prog Cardiovasc Dis. 2015 Nov 14.
Strauss MH, Hall AS. Angiotensin Receptor Blockers **Do Not Reduce Risk of Myocardial Infarction, Cardiovascular Death, or Total Mortality**: Further Evidence for the ARB-MI Paradox. Circulation. 2017 May 30;135(22):2088-2090.
Strippoli GF, Craig MC, Schena FP, Craig JC. Role of blood pressure targets and specific antihypertensive agents used to prevent **diabetic nephropathy** and delay its progression. J Am Soc Nephrol. 2006 Apr;17 Suppl 2:S153-5. On the basis of available RCT evidence, ACEi are the only agents with proven renal benefit in patients who have diabetes with no nephropathy and the only agents with proven survival benefit in patients who have diabetes with nephropathy.
Sumukadas D, Witham MD, Struthers AD, McMurdo ME. Effect of **perindopril on physical function** in elderly people with functional impairment: a randomized controlled trial. CMAJ. 2007 Oct 9;177(8):867-74. Use of the ACE inhibitor perindopril improved exercise capacity in functionally impaired elderly people who had no heart failure and maintained health-related quality of life. The degree of improvement was equivalent to that reported after 6 months of exercise training.
Susantitaphong P, Sewaralthahab K, Balk EM, Eiam-ong S, Madias NE, Jaber BL. Efficacy and safety of **combined vs. single renin-angiotensin-aldosterone system blockade in chronic kidney disease**: a meta-analysis. Am J Hypertens. 2013 Mar;26(3):424-41.
Suzuki T, Isselbacher EM, Nienaber CA, et al. Type-Selective Benefits of Medications in Treatment of **Acute Aortic Dissection** (from the International Registry of Acute Aortic Dissection [IRAD]). Am J Cardiol. 2011 Sep 23.
Tachjian A, Maria V, Jahangir A. Use of herbal products and potential interactions in patients with cardiovascular diseases. J Am Coll Cardiol. 2010 Feb 9;55(6):515-25.
Takahashi A, et al. Candesartan, an angiotensin II type-1 receptor blocker, reduces cardiovascular events in patients on **chronic haemodialysis**--a randomized study. Nephrol Dial Transplant. 2006 Sep;21(9):2507-12. Epub 2006 Jun 9.
Tapaninen T, Backman JT, et al. **Itraconazole**, a P-glycoprotein and CYP3A4 inhibitor, markedly raises the plasma concentrations and enhances the renin-inhibiting effect of **aliskiren**. Clin Pharmacol. 2011Mar;51(3):359-67.
Teo KK, Yusuf S, Pfeffer M, et al.; ACE Inhibitors Collaborative Group. Effects of long-term treatment with angiotensin-converting-enzyme inhibitors in the presence or absence of **aspirin**: a systematic review. Lancet. 2002 Oct 5;360(9339):1037-43. Review. Erratum in: Lancet 2003 Jan 4;361(9351):90.
Teo KK, Pfeffer M, Mancia G, et al; on behalf of the **Aliskiren** Prevention of Later Life Outcomes (**APOLLO**) trial Investigators. Aliskiren alone or with other antihypertensives in the **elderly** with borderline and stage 1 hypertension: the APOLLO trial. Eur Heart J. 2014 Mar 9.
Teun van der Bom MD, Winter MM, Bourna BJ, et al. Effect of **valsartan on systemic right ventricular function**: a double-blind, randomized, placebo-controlled pilot trial. Circulation. 2013;127:322–330.
Thind GS, Mahapatra RK, Johnson A, et al. **Low-dose captopril** titration in patients with moderate-to-severe hypertension treated with diuretics. *Circulation* 1983;67: 1340-6.
Thomas L. Managing **hypertensive emergencies** in the ED. Can Fam Physician. 2011 Oct;57(10):1137-97.
Thornley-Brown D, et al. Differing effects of antihypertensive drugs on the incidence of diabetes mellitus among patients with hypertensive kidney disease. (**AASK**) Arch Intern Med. 2006 Apr 10;166(7):797-805.
Tocci G, Paneni F, Palano F, et al. Angiotensin-Converting Enzyme Inhibitors, Angiotensin II Receptor Blockers and **Diabetes**: A Meta-Analysis of Placebo-Controlled Clinical Trials. Am J Hypertens. 2011 May;24(5):582-90.
Tofts RPH, Ferrer G, Oliveira E. How should one investigate a **chronic cough**? *Cleveland Clinic Journal of Medicine 2011; 78(2):84-85, 89; doi:10.3949/ccjm.77a.10033.*
Toh S, Reichman ME, Houstoun M, et al. Comparative Risk for **Angioedema** Associated With the Use of Drugs That Target the Renin-Angiotensin-Aldosterone System. Arch Intern Med. 2012 Oct 15:1-8.
Tomlinson LA, Abel GA, Chaudhry AN, et al. ACE Inhibitor and Angiotensin Receptor-II Antagonist Prescribing and Hospital Admissions with **Acute Kidney Injury**: A Longitudinal Ecological Study. PLoS One. 2013 Nov 6;8(11):e78465.
Torres VE, Abebe KZ, Chapman AB, et al. **Angiotensin blockade** in late **autosomal dominant polycystic kidney disease**. (**Halt-PKD**) N Engl J Med. DOI: 10.1056/NEJMoa1402686.
TRANSCEND: The Telmisartan Randomised AssessmeNt Study in ACE iNtolerant subjects with cardiovascular Disease (**TRANSCEND**) Investigators. Effects of the angiotensin-receptor blocker telmisartan on cardiovascular events in high-risk patients intolerant to angiotensin-converting enzyme inhibitors: a randomised controlled trial. Lancet. 2008 Aug 29. [Epub ahead of print] (Mann JF, Schmieder RE, Dyal L, McQueen MJ, Schumacher H, et al.; TRANSCEND (Telmisartan Randomised Assessment Study in ACE Intolerant Subjects with Cardiovascular Disease) Investigators. Effect of telmisartan on renal outcomes: a randomized trial. Ann Intern Med. 2009 Jul 7;151(1):1-10, W1-2. Epub 2009 May 18.)
Tu K, Gunraj N, Mamdani M. Is **ramipril** really better than other angiotensin-converting enzyme inhibitors after acute myocardial infarction? Am J Cardiol. 2006 Jul 1;98(1):6-9. Epub 2006 Apr 27.
Turnbull F; Blood Pressure Lowering Treatment Trialists' Collaboration. Effects of different blood-pressure-lowering regimens on major cardiovascular events: results of prospectively-designed overviews of randomised trials. Lancet. 2003 Nov 8;362(9395):1527-35.
Turner ST, Schwartz GL, Chapman AB, et al. **Plasma renin activity** predicts blood pressure responses to beta-blocker and thiazide diuretics as monotherapy and add-on for hypertension. Am J Hypertens 2010.
Twersky RS, Goel V, Narayan P, et al. The risk of **hypertension after preoperative discontinuation of angiotensin-converting enzyme inhibitors or angiotensin receptor antagonists** in ambulatory and same-day admission patients. Anesth Analg. 2014 May;118(5):938-44.
van der Sande NG, et al. Individualized prediction of the effect of **angiotensin receptor blockade** on **renal and cardiovascular outcomes** in patients with diabetic nephropathy. Diabetes Obes Metab. 2016 Jun 23.
van Vark LC, Bertrand M, Akkerhuis KM, et al. Angiotensin-converting enzyme inhibitors **reduce mortality in hypertension**: A meta-analysis of randomized clinical trials of renin-angiotensin-aldosterone system inhibitors involving 158 998 patients. Eur Heart J2012.
Vasilakis-Scaramozza C, Aschengrau A, Cabral HJ, Jick SS. Antihypertensive drugs and the risk of **congenital anomalies**. Pharmacotherapy. 2013 May;33(5):476-82. (ACEI)
Verdecchia P, et al. Do angiotensin II receptor blockers increase the risk of myocardial infarction? Eur Heart J. 2005 Nov;26(22):2381-6. Epub 2005 Aug 4.
Viana-Tejedor A, Nunez-Gil IJ. Images in clinical medicine. **Isolated uvular angioedema** (likely captopril-ACE inhibitor induced). N Engl J Med. 2014 Apr 10;370(15):e24
Viollet L, Thrush PT, Flanigan KM, et al. Effects of Angiotensin-Converting Enzyme Inhibitors and/or Beta Blockers on the **Cardiomyopathy in Duchenne Muscular Dystrophy**. Am J Cardiol. 2012 Mar 29.
Webb NJ, Shahinfar S, Wells TG, et al. **Losartan and enalapril** are comparable in reducing **proteinuria in children**. Kidney Int. 2012 Oct;82(7):819-26.
Webb NJ, Wells TG, Shahinfar S, et al. A Randomized, Open-Label, Dose-Response Study of **Losartan in Hypertensive Children**. Clin J Am Soc Nephrol. 2014 May 29.
Weber MA, Schiffrin EL, White WB, et al. **ASH/ISH**: Clinical practice guidelines for the **management of hypertension** in the community. A statement by the American Society of Hypertension and the International Society of Hypertension. *J Clin Hypertens* 2013; DOI:10.1111/jch.12237.
Weir MR, Hollenberg NK, Zappe DH, et al. Antihypertensive effects of double the maximum dose of **valsartan in African-American's** with type 2 diabetes mellitus and albuminuria. J Hypertens. 2010 Jan;28(1):186-93.
Wetmore JB, Tang F, Sharma A, et al. The association of **chronic kidney disease with the use of renin-angiotensin system inhibitors after acute myocardial infarction**. Am Heart J. 2015 Oct;170(4):735-43.
Winkelmayer WC, et al. Efficacy & Safety of Angiotensin II Receptor Blockade in **Elderly** Patients With Diabetes. Diabetes Care. 2006 Oct;29(10):2210-2217. Of 1,513 people, 421 (27.8%) were aged >65 yrs (max 74 yrs).

Wright JT Jr, et al. Effect of blood pressure lowering and antihypertensive drug class on progression of hypertensive kidney disease: results from the **AASK** trial.; African American Study of Kidney Disease and Hypertension Study Group. JAMA 2002 Nov 20;288(19):2421-31.

Wright JM, Musini VM. First-line drugs for hypertension. Cochrane Database Syst Rev. 2009 Jul 8;(3):CD001841. First-line low-dose thiazides reduce all morbidity and mortality outcomes. First-line ACE inhibitors and calcium channel blockers may be similarly effective but the evidence is less robust. First-line high-dose thiazides and first-line beta-blockers are inferior to first-line low-dose thiazides.

Wu HY, Huang JW, Lin HJ, et al. Comparative effectiveness of **renin-angiotensin system blockers and other antihypertensive drugs in patients with diabetes**: systematic review and bayesian network meta-analysis. BMJ. 2013 Oct 24;347:f6008.

Xie X, Liu Y, et al. **Renin-angiotensin system inhibitors and kidney and cardiovascular** outcomes in patients with CKD: a Bayesian network meta-analysis of randomized clinical trials. Am J Kidney Dis. 2016;67:728-741.

Yoon C, Yang HS, Jeon I, et al. Use of angiotensin-converting-enzyme inhibitors or angiotensin-receptor blockers and **cancer risk**: a meta-analysis of observational studies. CMAJ. 2011 Oct 4;183(14):E1073-84.

Yusuf S, Teo KK, Pogue J, et al for the **ONTARGET** investigators. Telmisartan, ramipril, or both in patients at high risk for vascular events. N Engl J Med 2008: 358:1547-1559. Telmisartan was equivalent to ramipril in patients with vascular disease or high-risk diabetes and was associated with less angioedema. The combination of the two drugs was associated with more adverse events without an increase in benefit.

Mann JF, Schmieder RE, McQueen M, et al. ONTARGET investigators. Renal outcomes with telmisartan, ramipril, or both, in people at high vascular risk (the ONTARGET study): a multicentre, randomised, double-blind, controlled trial. Lancet. 2008 Aug 16;372(9638):547-53. In people at high vascular risk, telmisartan's effects on major renal outcomes are similar to ramipril. Although **combination** therapy reduces proteinuria to a greater extent than monotherapy, overall it worsens major renal outcomes.

Yusuf S, Diener HC, Sacco RL, et al. **PRoFESS** Study Group. **Telmisartan** to Prevent Recurrent Stroke and Cardiovascular Events. N Engl J Med. 2008 Aug 27. [Epub ahead of print] Therapy with telmisartan initiated soon after an ischemic stroke and continued for 2.5 years did not significantly lower the rate of recurrent stroke, major cardiovascular events, or diabetes.

Zanchetti A, et al. Outcomes in subgroups of hypertensive patients treated with regimens based on valsartan and amlodipine: an analysis of findings from the **VALUE** trial. J Hypertens. 2006 Nov;24(11):2163-2168.

Zhang Y, Zhang P, Mu Y, et al. The role of renin-angiotensin system blockade therapy in the prevention of **atrial fibrillation**: a meta-analysis of randomized controlled trials. Clin Pharmacol Ther. 2010 Oct;88(4):521-31.

Zhang Y, Fonarow GC, Sanders PW, et al. A Propensity-Matched Study of the Comparative Effectiveness of **Angiotensin Receptor Blockers Versus Angiotensin-Converting Enzyme Inhibitors** in Heart Failure Patients Age ≥65 Years. Am J Cardiol. 2011 Sep 3.

BETA-BLOCKER (BB): Comparison Chart

[1] Major Outcomes in High-Risk Hypertensive Patients Randomized to Angiotensin-Converting Enzyme Inhibitor or Calcium Channel Blocker vs Diuretic. The Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial (**ALLHAT**). The ALLHAT Officers and Coordinators for the ALLHAT Collaborative Research Group. JAMA. 2002;288:2981-2997.

[2] 2001 Canadian Hypertension Recommendations: What's New & What's Not so New but is Still Important. CJHP 2002;55:4651.

[3] FA McAlister, M Levine, KB Zarnke, et al. The 2000 recommendations for the management of hypertension. Can J Cardiol 2001; 17(5):543-559.

[4] 1999 Canadian recommendations for the management of hypertension. CMAJ 1999;161(Suppl):S1-S16.

[5] **1999 World Health Organization**–International Society of Hypertension Guidelines:Management of Hypertension. J Hypertens 1999;17:151-183.

[6] 6th Report-Joint National Committee-JNC on Prevention,Detection,Evaluation & Treatment of High Blood Pressure. Arch Intern Med 1997;157:2413-46.

[7] Drugs for hypertension. Med Lett Drugs Ther 2001;43:17-22.
Webb AJS, Fischer U, Rothwell PM. Effects of **beta-blocker selectivity** on **blood pressure variability and stroke**: a systematic review. Neurology 2011;77:731–737.

[8] Drugs in Pregnancy & Lactation, 11th Ed. Briggs GE,et al. Wilkins;Baltimore, MD. 2017.

[9] Micromedex 2018 online

[10] Hansten & Horn's Drug Interactions: Analysis & Management-Facts & Comparisons 2008.

[11] Treatment Guidelines: **Drugs for Hypertension** from The Medical Letter Feb 2003, repeated June 2005, January 2009, January 2012, May 2014 & updated **March 2017**.

[12] The **2017** Canadian Hypertension Education Program **Recommendations** www.hypertension.ca
Leung AA, Nerenberg K, Daskalopoulou SS, et al; CHEP Guidelines Task Force. Hypertension Canada's **2016 CHEP guidelines** for blood pressure measurement, diagnosis, assessment of risk, prevention and treatment of hypertension. Can J Cardiol 2016 (accepted manuscript) doi: 10.1016/j.cjca.2016.02.066 www.onlinecjc.ca/article/S0828-282X(16)00192-6/pdf (accessed April 11, 2016).
Hackam DG, Quinn RR, Ravani P, et al. Canadian Hypertension Education Program. The 2013 Canadian Hypertension Education Program (CHEP) Recommendations for Blood Pressure Measurement, Diagnosis, Assessment of Risk, Prevention, and Treatment of Hypertension. Can J Cardiol. 2013 Mar 28.
Canadian Hypertension Education Program. **2011 CHEP recommendations** for the management of **hypertension**. http://hypertension.ca/chep/wp-content/uploads/2011/05/FullCHEPRecommendations_EN_2011.pdf .
Dionne JM, Harris KC, Benoit G, et al. **Hypertension Canada's 2017 Guidelines for the Diagnosis, Assessment, Prevention, and Treatment of Pediatric Hypertension**. Can J Cardiol. 2017 May;33(5):577-585
Leung AA, Daskalopoulou SS, Dasgupta K, et al. **Hypertension Canada's 2017 Guidelines for Diagnosis, Risk Assessment, Prevention, and Treatment of Hypertension in Adults**. Can J Cardiol. 2017 May;33(5):557-576
Nerenberg KA, Zarnke KB, Leung AA, et al; Hypertension Canada. **Hypertension Canada's 2018 Guidelines** for Diagnosis, Risk Assessment, Prevention, and Treatment of Hypertension in Adults and Children. Can J Cardiol. 2018 May;34(5):506-525.

[13] ALLHAT Working Group. Major cardiovascular events in hypertensive patients randomized to doxazosin vs chlorthalidone: the antihypertensive and lipid-lowering treatment to prevent heart attack trial (**ALLHAT**). JAMA 2000;283:1967-75.

[14] Liu P, Arnold JM, Belenkie I, et al. The 2002/3 Canadian Cardiovascular Society consensus guideline update for the diagnosis and management of **heart failure**. Can J Cardiol. **2003** Mar 31;19(4):347-56.

[15] **Treatment Guidelines**: Drugs for Treatment of **Heart Failure** from The Medical Letter April **003**& Jan **2006.**

[16] Jessup M, Brozena S. Heart Failure. N Engl J Med 2003;348:2007-18.

[17] The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (The **JNC 7**); JAMA. **2003** May;289(19):2560-72.
James PA, Oparil S, Carter BL, et al. **2014** evidence-based guideline for the management of **high blood pressure in adults**: report from the panel members appointed to the Eighth Joint National Committee (**JNC 8**). JAMA. doi:10.1001/jama.2013.284427.

[18] ACC/AHA Guidelines for the Management of Patients with ST-Elevation Myocardial Infarction **2004**. http://www.acc.org/clinical/guidelines/stemi/index.pdf

[19] Turnbull F; Blood Pressure Lowering Treatment Trialists' Collaboration. Effects of different blood-pressure-lowering regimens on major cardiovascular events: results of prospectively-designed overviews of randomised trials. Lancet. 2003 Nov 8;362(9395):1527-35.

[20] van der Woude HJ, Zaagsma J, Postma DS, Winter TH, van Hulst M, Aalbers R. Detrimental Effects of {beta}-Blockers in COPD: A Concern for Nonselective {beta}-Blockers. Chest. 2005 Mar;127(3):818-24.

[21] Dulin BR, Haas SJ, Abraham WT, Krum H. Do elderly systolic heart failure patients benefit from beta blockers to the same extent as the non-elderly? Meta-analysis of >12,000 patients in large-scale clinical trials. Am J Cardiol 2005; 95:896-898.

[22] Snow V, Barry P, Fihn SD, et al; American College of Physicians; American College of Cardiology Chronic Stable Angina Panel. Primary care management of chronic stable angina and asymptomatic suspected or known coronary artery disease: a clinical practice guideline from the American College of Physicians. Ann Intern Med. 2004 Oct 5;141(7):562-7. Erratum in: Ann Intern Med. 2005 Jan 4;142(1):79.

[23] Diagnosis and Management of Chronic **Heart Failure** in the Adult: **ACC/AHA 2005 Guideline Update** for the (J Am Coll Cardiol 2005) http://www.acc.org/clinical/guidelines/failure/index.pdf
(**European 2005** Chronic Heart failure guidelines http://www.escardio.org/NR/rdonlyres/8A2848B4-5DEB-41B9-9A0A-5B5A90494B64/0/CHFFullTextehi205FVFW170505.pdf)

[24] Carlberg B, Samuelsson O, Lindholm LH. Atenolol in hypertension: is it a wise choice? Lancet. 2004 Nov 6;364(9446):1684-9.
Kuyper LM, Khan NA. **Atenolol vs Nonatenolol** β-Blockers for the Treatment of Hypertension: A Meta-analysis. Can J Cardiol. 2014 May;30(5S):S47-S53.

[25] Cissoko H, Jonville-Bera AP, Swortfiguer D, Giraudeau B, Autret-Leca E. [Neonatal outcome after exposure to beta adrenergic blockers late in pregnancy.] Arch Pediatr. 2005 May;12(5):543-7.
Seely EW, Ecker J. Clinical practice. **Chronic hypertension in pregnancy**. N Engl J Med. 2011 Aug 4;365(5):439-46.

[26] Chen ZM, Pan HC, Chen YP, et al.; **COMMIT** (ClOpidogrel and Metoprolol in Myocardial Infarction Trial) collaborative group. Early intravenous then oral metoprolol in 45,852 patients with acute myocardial infarction: randomised placebo-controlled trial. Lancet. 2005 Nov 5;366(9497):1622-32. Second Chinese Cardiac Study COMMIT/CCS-2. Metoprolol 5mg IV over 2-3mins x 3 if HR & BP ok, then 15mins later 50mg po q6h Day 0-1, then 200mg controlled release od vs placebo x ~15days. ↓Reinfarction 2 vs 2.5%, ↓Ventricular fibrilation 2.5 vs 3 %, BUT ↑Cardiogenic shock 5 vs 3.9% (risk more with heart failure, systolic BP <120 & in the first 24hrs). INTERPRETATION: The use of early beta-blocker therapy in acute MI reduces the risks of reinfarction & ventricular fibrillation, but increases the risk of cardiogenic shock, esp. during the first day or so after admission. Consequently, it might generally be prudent to consider starting **beta-blocker therapy in hospital only when the haemodynamic condition after MI has stabilised**.

[27] Merkel C, Marin R, Angeli P, et al.. A placebo-controlled clinical trial of nadolol in the prophylaxis of growth of small esophageal varices in cirrhosis. Gastroenterology. 2004 Aug;127(2):476-84.
Mandorfer M, Bota S, Schwabl P, et al. Non-selective Beta-blockers increase risk for hepatorenal syndrome and death in patients with cirrhosis and spontaneous bacterial peritonitis. Gastroenterology 2014;146. 000–000.
Leithead JA, Rajoriya N, Tehami N, et al. Non-selective beta-blockers are associated with improved survival in patients with ascites listed for liver transplantation. Gut. 2014 Oct 3.
Ge PS and Runyon BA.The changing role of beta-blocker therapy in patients with cirrhosis. J Hepatol 2014 Mar; 60:643.
Ge PS, Runyon BA. Treatment of Patients with Cirrhosis. N Engl J Med. 2016 Aug 25;375(8):767-77.

[28] Jutabha R, Jensen DM, et al. Randomized study comparing banding and propranolol to prevent initial variceal hemorrhage in cirrhotics with high-risk esophageal varices. Gastroenterology. 2005 Apr;128(4):870-81.
Chalasani N, Boyer TD. Primary prophylaxis against variceal bleeding: beta-blockers, endoscopic ligation, or both? Am J Gastroenterol. 2005 Apr;100(4):805-7.
Mandorfer M, Bota S, Schwabl P, et al. **Non-selective Beta-blockers increase risk for hepatorenal syndrome** and death in patients with cirrhosis and spontaneous bacterial peritonitis. Gastroenterology 2014;146. 000–000.
Ge PS and Runyon BA.The changing role of beta-blocker therapy in patients with cirrhosis. J Hepatol 2014 Mar; 60:643.
Ge PS, Runyon BA. Treatment of Patients with Cirrhosis. N Engl J Med. 2016 Aug 25;375(8):767-77.

[29] Singh BN, Singh SN, Reda DJ, et al.; Sotalol Amiodarone Atrial Fibrillation Efficacy Trial (SAFE-T) Investigators. Amiodarone versus sotalol for atrial fibrillation. N Engl J Med. 2005 May 5;352(18):1861-72. Conclusion: Amiodarone and sotalol are equally efficacious in converting atrial fibrillation to sinus rhythm. Amiodarone is superior for maintaining sinus rhythm, but both drugs have similar efficacy in patients with ischemic heart disease. Sustained sinus rhythm is associated with an improved quality of life and improved exercise performance. (InfoPOEMs: Amiodarone was more effective than sotalol at maintaining normal sinus rhythm in patients with chronic atrial fibrillation. However, there was a worrisome trend toward increased mortality in the active treatment groups, and other studies have not found a benefit of rhythm therapy over rate control with anticoagulation. (LOE = 1b))

[30] Groszmann RJ. Beta-blockers to Prevent **Gastroesophageal Varices** in Patients with Cirrhosis. N Engl J Med 2005;353:2254-61. (Timolol is ineffective in preventing varices in unselected patients with cirrhosis & portal hypertension & are associated with an increased number of adverse events.) (InfoPOEMs: Beta-blockers do not prevent the development of varices in patients with cirrhosis and they increase the likelihood of serious adverse events. They are still appropriate for patients with established varices to prevent gastrointestinal hemorrhage. (LOE = 1b))

[31] Fleisher LA, et al.; American College of Cardiology/American Heart Association Task Force on Practice Guidelines Writing Committee to Update the 2002 Guidelines on Perioperative Cardiovascular Evaluation for Noncardiac Surgery; American Society of Echocardiography; American Society of Nuclear Cardiology; Heart Rhythm Society; Society of Cardiovascular Anesthesiologists; Society for Cardiovascular Angiography and Interventions; Society for Vascular Medicine and Biology. **ACC/AHA 2006** guideline update on perioperative cardiovascular evaluation for noncardiac surgery: focused update on perioperative **beta-blocker** therapy: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Writing Committee to Update the 2002 Guidelines on Perioperative Cardiovascular Evaluation for noncardiac Surgery): developed in collaboration with the American Society of Echocardiography, American Society of Nuclear Cardiology, Heart Rhythm Society, Society of Cardiovascular Anesthesiologists, Society for Cardiovascular Angiography and Interventions, and Society for Vascular Medicine and Biology. Circulation. 2006 Jun 6;113(22):2662-74.
http://www.americanheart.org/downloadable/heart/1142081026765PeriopFinal.pdf
Fleisher LA, Beckman JA, Brown KA, Calkins H, Chaikof E, Fleischmann KE, Freeman WK, Froehlich JB, Kasper EK, Kersten JR, Riegel B, Robb JF. ACC/AHA 2007 Guidelines on **Perioperative Cardiovascular** Evaluation and Care for **Noncardiac Surgery**. A Report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Writing Committee to Revise the 2002 Guidelines on Perioperative Cardiovascular Evaluation for Noncardiac Surgery). Circulation. 2007 Sep 27; [Epub ahead of print]

[32] Devereaux PJ, Beattie WS, et al.. How strong is the evidence for the use of perioperative {beta} blockers in non-cardiac surgery? Systematic review and meta-analysis of randomised controlled trials. BMJ. 2005 Jul 4; CONCLUSION: The evidence that perioperative beta blockers reduce major cardiovascular events is encouraging but too unreliable to allow definitive conclusions to be drawn.

[33] Perioperative Beta-Blockers. Pharmacist's Letter Aug, 2006.

POISE Study Group. Effects of extended-release metoprolol succinate (100mg SR x1 preop, then ~200mg SR od x 30 days if HR>45 & SBP>100) in patients undergoing non-cardiac surgery (POISE trial): a randomised controlled trial. Lancet. 2008 May 12. [Epub ahead of print] Our results highlight the risk in assuming a perioperative beta-blocker regimen has benefit without substantial harm, and the importance and need for large randomised trials in the perioperative setting. N=8,351.

Dunkelgrun M et al. Bisoprolol (Starting dose 2.5 mg daily, titrated to a perioperative heart rate of 50 to 70 beats per minute) and fluvastatin (fixed dose of 80 mg) for the reduction of perioperative cardiac mortality and myocardial infarction in intermediate-risk patients undergoing noncardiovascular surgery (before surgery, median: 34 days): A randomized controlled trial (**DECREASE-IV**). Ann Surg 2009 Jun; 249:921. (n=1066) Patients randomized to bisoprolol (N = 533) had a lower incidence of perioperative cardiac death and nonfatal MI than those randomized to bisoprolol-control (2.1% vs. 6.0% events; hazard ratios: 0.34; 95% confidence intervals: 0.17-0.67; P = 0.002). Patients randomized to fluvastatin experienced a lower incidence of the end point than those randomized to fluvastatin-control therapy (3.2% vs. 4.9% events; hazard ratios: 0.65; 95% confidence intervals: 0.35-1.10), but statistical significance was not reached (P = 0.17). Bisoprolol was associated with a significant reduction of 30-day cardiac death and nonfatal MI, while fluvastatin showed a trend for improved outcome.

Poldermans D, Bax JJ, Boersma E, et al. Guidelines for pre-operative cardiac risk assessment and perioperative cardiac management in non-cardiac surgery: The Task Force for Preoperative Cardiac Risk Assessment and Perioperative Cardiac Management in Non-cardiac Surgery of the European Society of Cardiology (**ESC**) and endorsed by the European Society of Anaesthesiology (ESA). Eur Heart J. 2009 Aug 27. [Epub ahead of print]

Fleischmann KE, Beckman JA, Buller CE, et al. **2009 ACCF/AHA** focused update on **perioperative beta blockade**. A report of the American College of Cardiology Foundation/American Heart Association task force on practice guidelines. *J Am Coll Cardiol* 2009; DOI:10.1016/j.jacc.2009.07.004. Available at: http://content.onlinejacc.org. *Circulation* 2009: DOI: 10.1161/CIRCULATIONAHA.109.192690. Available at: http://circ.ahajournals.org.. http://content.onlinejacc.org/cgi/reprint/j.jacc.2009.07.004v1.pdf

BrinkmanW, HerbertMA, O'Brien S, et al. Preoperative β-blocker use in **coronary artery bypass grafting** surgery: national database analysis [online June 16, 2014]. JAMA Intern Med. doi:10.1001/jamainternmed.2014.2356.

Fleisher LA, Fleischmann KE, Auerbach AD, et al. **2014 ACC/AHA Guideline on Perioperative Cardiovascular** Evaluation and Management of Patients Undergoing Noncardiac Surgery: A Report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. J Am Coll Cardiol. 2014 Jul 29.

Wijeysundera DN, Duncan D, Nkonde-Price C, et al. **Perioperative Beta Blockade in Noncardiac Surgery: A Systematic Review for the 2014 ACC/AHA Guideline** on Perioperative Cardiovascular Evaluation and Management of Patients Undergoing Noncardiac Surgery: A Report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. J Am Coll Cardiol. 2014 Dec 9;64(22):2406-25.

Urbach DR, Bell CM. A Revised Quality Measure for Surgical Care: More Alpha Testing for **Perioperative β-Blockers**? JAMA. 2015 Jun 16;313(23):2369-70.

Stern T, Cifu AS. Perioperative β-Blocker Therapy. JAMA. 2015 Jun 23-30;313(24):2486-7.

Additional sources:

Abalos E, Duley L, Steyn DW, Henderson-Smart DJ. Antihypertensive drug therapy for mild to moderate **hypertension during pregnancy**. Cochrane Database Syst Rev 2007;(1):CD002252.

Abbasi J. **Do All Patients Need β-Blockers After a Heart Attack**? JAMA. 2018 Mar 6;319(9):853-855.

ACCF/AHA 2011 Focused Update of the Guidelines for the Management of Patients With **Unstable Angina/Non-ST-Elevation Myocardial Infarction (Updating the 2007 Guideline):** A Report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. J Am Coll Cardiol 2011 0: j.jacc.2011.02.009. http://content.onlinejacc.org/cgi/reprint/j.jacc.2011.02.009v1.pdf

ACCF- AHA-HRS Atrial Fibrillation 2011 Focused Update. Circulation 2011. http://circ.ahajournals.org/cgi/reprint/CIR.0b013e3181fa3cf4v1 (Wann LS, Curtis AB, January CT, et al. 2011 ACCF/AHA/HRS focused update on the management of patients with atrial fibrillation (updating the 2006 guideline): A report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. Circulation 2010; DOI: 10.1161/CIR.0b013e3181fa3cf4.)
Wann L. Samuel, Curtis Anne B., Ellenbogen Kenneth A., et al. **2011 ACCF/AHA/HRS Focused Update on the Management of Patients With Atrial Fibrillation (Update on Dabigatran):** A Report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines Circulation published February 14, 2011, doi:10.1161/CIR.0b013e31820f14c0 http://circ.ahajournals.org/cgi/reprint/CIR.0b013e31820f14c0v1

ACC/AHA 2017 Whelton PK, et al. **2017 ACC/AHA**/AAPA/ABC/ACPM/AGS/APhA/ASH/ASPC/NMA/PCNA **Guideline for the Prevention, Detection, Evaluation, and Management of High Blood Pressure** in Adults: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. Hypertension. 2017 Nov 13.

Agarwal R, Sinha AD, Pappas MK, et al. Hypertension in **hemodialysis patients treated with atenolol or lisinopril**: a randomized controlled trial. Nephrol Dial Transplant. 2014;29:672-681.

Ahmed MI, Aban I, Lloyd SG, et al. A randomized controlled phase IIb trial of beta(1)-receptor blockade for chronic degenerative **mitral regurgitation**. J Am Coll Cardiol. 2012 Aug 28;60(9):833-8.

American College of Cardiology Foundation, , American Heart Association Task Force on Practice Guidelines, , American Association for Thoracic Surgery, , Society of Cardiovascular Anesthesiologists, , Society of Thoracic Surgeons, Hillis, L. David, Smith, Peter K., Anderson, Jeffrey L., et al. **2011 ACCF/AHA Guideline for Coronary Artery Bypass Graft Surgery**: Executive Summary. J Am Coll Cardiol 2011 0: j.jacc.2011.08.008. http://content.onlinejacc.org/cgi/reprint/j.jacc.2011.08.008v1.pdf

American College of Obstetricians and Gynecologists (**ACOG**). **Chronic hypertension in pregnancy**. Washington (DC): American College of Obstetricians and Gynecologists (ACOG); 2012 Feb. 12.

Andell P, Erlinge D, Smith JG, et al. **β-blocker use and mortality in COPD** patients after myocardial infarction: a Swedish nationwide observational study. J Am Heart Assoc. 2015 Apr 8;4(4).

Andersson C, Mérie C, Jørgensen MB, et al. Association of **β-blocker therapy with risks of adverse cardiovascular events and deaths in patients with ischemic heart disease undergoing** noncardiac surgery: a Danish nationwide Cohort study [online November 18, 2013]. JAMA Intern Med. doi:10.1001/jamainternmed.2013.11349.

Andersson C, Shilane D, Go AS, et al. **Beta-blocker therapy and cardiac events** among patients with newly diagnosed coronary heart disease.*J Am Coll Cardiol* 2014.

Anderson JL, Adams CD, Antman EM, et al. **2012 ACCF/AHA focused update** incorporated into the ACCF/AHA 2007 guidelines for the management of patients with unst**able angina/non-ST-elevation myocardial infarction**: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. Circulation. 2013;127:e663-828.

Argulian E, Messerli FH, Aziz EF, et al. Antihypertensive Therapy in **Hypertrophic Cardiomyopathy**. Am J Cardiol. 2013 Jan 19.

Arnold JM, et al.; Canadian Cardiovascular Society. **Canadian** Cardiovascular Society consensus conference recommendations on **heart failure 2006**: diagnosis and management. Can J Cardiol. 2006 Jan;22(1):23-45. Erratum in: Can J Cardiol. 2006 Mar 1;22(3):271. http://www.ccs.ca/download/consensus_conference/consensus_conference_archives/Arnold_CCS_final.pdf (Arnold JM, Howlett JG, Dorian P, et al. Canadian Cardiovascular Society Consensus Conference recommendations on heart failure **update 2007**: Prevention, management during intercurrent illness or acute decompensation, & use of biomarkers. Can J Cardiol. 2007 Jan;23(1):21-45.)

Arnold AC, Okamoto LE, Diedrich A, et al. Low-dose propranolol and exercise capacity in **postural tachycardia syndrome**: A randomized study. Neurology. 2013 May 21;80(21):1927-33.

Bahar MA, Kamp J, Borgsteede SD, et al. The impact of CYP2D6 mediated drug-drug interaction: a systematic review on a combination of **metoprolol and paroxetine/fluoxetine**. Br J Clin Pharmacol. 2018 Sep 24.

Bangalore S, Wetterslev J, Pranesh S, Sawhney S, Gluud C, Messerli FH. **Perioperative** beta blockers in patients having non-cardiac surgery: a meta-analysis. Lancet. 2008 Dec 6;372(9654):1962-76. Epub 2008 Nov 13. Noncardiac surgical patients given perioperative beta-blockers had the same rate of death from all causes, cardiovascular deaths, and congestive heart failure as patients given placebo. The rate of nonfatal myocardial infarctions was lower (number needed to treat [NNT] = 63) at the expense of a higher rate of nonfatal strokes (number needed to treat to harm [NNTH] = 275). In other words, for every 4 heart attacks averted, we would cause 1 stroke. (LOE = 1a-)

Bangalore S, Parkar S, Grossman E, Messerli FH. A meta-analysis of 94,492 patients with hypertension treated with beta blockers to determine the risk of **new-onset diabetes** mellitus. Am J Cardiol. 2007 Oct 15;100(8):1254-62. Epub 2007 Aug 10. In conclusion, beta blockers are associated with an increased risk for new-onset DM, with no benefit for the end point of death or myocardial infarction and with a 15% increased risk for stroke compared with other agents. This risk was greater in patients with higher baseline body mass indexes and higher baseline fasting glucose levels and in studies in which beta blockers were less efficacious antihypertensive agents compared with other treatments.

Bangalore S, et al. Relation of Beta-Blocker–Induced Heart Rate Lowering and Cardioprotection in Hypertension. J Am Coll Cardiol. 2008 October;52:1482–9. In contrast to patients with myocardial infarction and heart failure, beta-blocker–associated reduction in heart rate increased the risk of cardiovascular events and death for hypertensive patients.

Bangalore S, Steg PHG, Deedwania P, et al. Beta blocker use and clinical outcomes in **stable outpatients with and without coronary artery disease**. JAMA 2012; 308:1340-1349.

Bangalore S, Makani H, Radford M, et al. **Clinical Outcomes with β-blockers for Myocardial Infarction** A Meta-Analysis of Randomized Trials. Am J Med. 2014 Jun 10.

Bangalore S, Bhatt DL, Steg PG, et al. **ß-blockers and cardiovascular events in patients with and without myocardial infarction**: Post hoc analysis from the **CHARISMA** trial. *Circ Cardiovasc Qual Outcomes* 2014.

Barron TI et al. Beta blockers and **breast cancer mortality**: a population-based study. J Clin Oncol 2011; 29:2635.

Barron AJ, Zaman N, Cole GD, et al. Systematic review of **genuine versus spurious side-effects** of **beta-blockers** in heart failure using placebo control: Recommendations for patient information. Int J Cardiol 2013.

Barton AL, Moffett BS, Valdes SO, et al. Efficacy and safety of high-dose **propranolol** for the management of **infant supraventricular tachyarrhythmias**. J Pediatr. 2015 Jan;166(1):115-8.

Baselga E, Dembowska-Baginska B, Przewratil P, et al. Efficacy of **Propranolol Between 6 and 12 Months of Age in High-Risk Infantile Hemangioma**. Pediatrics. 2018 Aug 6.

Barsheshet A, Goldenberg I, O-Uchi J, et al. Mutations in cytoplasmic loops of the **KCNQ1 channel** and the risk of life-threatening events: implications for mutation-specific response to Beta-blocker therapy in type 1 **long-QT syndrome**. Circulation. 2012;125:1988 –1996.

Bateman BT, Patorno E, Desai RJ, et al. Late **Pregnancy β Blocker Exposure** and Risks of Neonatal Hypoglycemia and Bradycardia. Pediatrics. 2016 Sep;138(3).

Bateman BT, Heide-Jørgensen U, Einarsdottir K, et al. Beta-blocker **use in pregnancy** and the risk for congenital malformations. An international cohort study. Ann Intern Med. 2018. [Epub ahead of print]. doi:10.7326/M18-0338

Bateman BT, Ho E, et al. The risk of **congenital malformations** associated with exposure to β-blockers early in **pregnancy**: a meta-analysis. Hypertension. 2013;62:375-381.

Bauman NM, McCarter RJ, Guzzetta PC, et al. **Propranolol vs Prednisolone** for Symptomatic Proliferating **Infantile Hemangiomas**: A Randomized Clinical Trial. JAMA Otolaryngol Head Neck Surg. 2014 Feb 13.

Beta-Blocker Evaluation of Survival Trial Investigators. (**BEST** trial)A trial of the beta-blocker bucindolol in patients with advanced chronic heart failure. N Engl J Med. 2001 May 31;344(22):1659-67. In a demographically diverse group of patients with NYHA class III and IV heart failure, bucindolol resulted in no significant overall survival benefit.

Bhardwaj A, Kedarisetty CK, Vashishtha C, et al. **Carvedilol delays the progression of small oesophageal varices** in patients with cirrhosis: a randomised placebo-controlled trial. Gut. 2016 Jun 13.

Bhatia V, Bajaj NS, Sanam K, et al. Beta-blocker use and **30-day all-cause readmission** in Medicare beneficiaries with **systolic heart failure**. *Am J Med* 2015.

Blessberger H, Kammler J, Domanovits H, et al. **Perioperative beta-blockers** for preventing surgery-related mortality and morbidity. Cochrane Database of Systematic Reviews 2014, Issue 9. Art. No.: CD004476. DOI: 10.1002/14651858.CD004476.pub2. According to our findings, perioperative application of beta-blockers still plays a pivotal role in cardiac surgery , as they can substantially reduce the high burden of supraventricular and ventricular arrhythmias in the aftermath of surgery. Their influence on mortality, AMI, stroke, congestive heart failure, hypotension and bradycardia in this setting remains unclear. In non-cardiac surgery, evidence from low risk of bias trials shows an increase in all-cause mortality and stroke with the use of betablockers. As the quality of evidence is still low to moderate, more evidence is needed before a definitive conclusion can be drawn. The substantial reduction in supraventricular arrhythmias and AMI in this setting seems to be offset by the potential increase in mortality and stroke.

Blessberger H, Kammler J, Domanovits H, et al. **Perioperative beta-blockers for preventing surgery-related mortality and morbidity.** Cochrane Database Syst Rev. 2018 Mar 13;3:CD004476. According to our findings, perioperative application of beta-blockers still plays a pivotal role in cardiac surgery, as they can substantially reduce the high burden of supraventricular and ventricular arrhythmias in the aftermath of surgery. Their influence on mortality, AMI, stroke, congestive heart failure, hypotension and bradycardia in this setting remains unclear.In non-cardiac surgery, evidence shows an association of beta-blockers with increased all-cause mortality. Data from low risk of bias trials further suggests an increase in stroke rate with the use of beta-blockers.

Boal AH, Smith DJ, McCallum L, et al. Monotherapy with Major **Antihypertensive Drug Classes** and Risk of Hopsital Admissions for **Mood Disorders**. Hypertension.2016 :68 :00-00. (Beta-blockers & CCBs may increase risk, ACEI & ARBs may decrease risk)

Bolin EH, Lang SM, Tang X, et al. **Propranolol Versus Digoxin** in the Neonate for **Supraventricular Tachycardia** (from the Pediatric Health Information System). Am J Cardiol. 2017 Mar 1.

Bosch X, Rovira M, Sitges M, et al. **Enalapril and carvedilol** for preventing **chemotherapy-induced** left ventricular systolic dysfunction in patients with malignant hemopathies: OVERCOME trial. J Am Coll Cardiol 2013.

Botteri E, Munzone E, Rotmensz N, et al. Therapeutic **effect** of β-blockers in **triple-negative breast cancer** postmenopausal women. Breast Cancer Res Treat. 2013 Aug;140(3):567-75.

Bouri S, Shun-Shin MJ, Cole GD, Mayet J, Francis DP. Meta-analysis of secure randomized controlled trials of **beta-blockade to prevent perioperative death in noncardiac surgery**. *Heart* 2013.

Bradley D, et al.; American College of Chest Physicians. Pharmacologic prophylaxis: American College of Chest Physicians guidelines for the prevention and management of postoperative atrial fibrillation after cardiac surgery. Chest. 2005 Aug;128(2 Suppl):39S-47S.

BrinkmanW, HerbertMA, O'Brien S, et al. **Preoperative β-blocker use in coronary artery bypass grafting surgery**: national database analysis [online June 16, 2014]. JAMA Intern Med. doi:10.1001/jamainternmed.2014.2356.

Brodine WN, Tung RT, Lee JK, et al. MADIT-II Research Group. Effects of beta-blockers on implantable cardioverter defibrillator therapy and survival in the patients with ischemic cardiomyopathy (from the Multicenter Automatic Defibrillator Implantation Trial-II). Am J Cardiol. 2005 Sep 1;96(5):691-5.

Buckmiller L, Dyamenahalli U, Richter GT. Propranolol for airway **hemangiomas**: Case report of novel treatment. Laryngoscope. 2009 Jul 31. [Epub ahead of print]

Cadrin-Tourigny J, Shohoudi A, Roy D, et al. **Decreased mortality with beta-blockers in patients with heart failure and coexisting atrial fibrillation**. *JACC: Heart Fail* 2017.

Canney M, O'Connell MD, Murphy CM, et al. Single agent antihypertensive therapy and **orthostatic blood pressure** behaviour in older adults using beat-to-beat measurements: the Irish longitudinal study on ageing. PLoS One2016;11:e0146156. (Beta-blockers more orthostatic hypotension)

Chan H, McKay C, Adams S, Wargon O. RCT of **Timolol Maleate Gel** for Superficial Infantile **Hemangiomas** in 5- to 24-Week-Olds. Pediatrics. 2013 May 6.

Chatterjee S, Biondi-Zoccai G, Abbate A, D'Ascenzo F, Castagno D, Van Tassell B, et al. Benefits of β blockers in patients with **heart failure** and reduced ejection fraction: network meta-analysis. BMJ 2013;346:f55.

Chatzidou S, Kontogiannis C, Tsilimigras DI, et al. **Propranolol Versus Metoprolol** for Treatment of **Electrical Storm in Patients With Implantable Cardioverter-Defibrillator**. J Am Coll Cardiol. 2018 May 1;71(17):1897-1906.

Chen ZM, Pan HC, Chen YP, et al.; **COMMIT** (ClOpidogrel and Metoprolol in Myocardial Infarction Trial) collaborative group. Early intravenous then oral metoprolol in 45,852 patients with acute myocardial infarction: randomised placebo-controlled trial. Lancet. 2005 Nov 5;366(9497):1622-32. Second Chinese Cardiac Study COMMIT/CCS-2. Metoprolol 5mg IV over 2-3mins x 3 if HR & BP ok, then 15mins later 50mg po q6h Day 0-1, then 200mg controlled release od vs placebo x ~16days. ↓Reinfarction 2 vs 2.5%, ↓Ventricular fibrilation 2.5 vs 3 %, BUT ↑Cardiogenic shock 5 vs 3.9%. INTERPRETATION: The use of early beta-blocker therapy in acute MI reduces the risks of reinfarction & ventricular fibrillation, but increases the risk of cardiogenic shock, esp. during the first day or so after admission. Consequently, it might generally be prudent to consider starting **beta-blocker therapy in hospital only when the haemodynamic condition after MI has stabilised**.(InfoPOEMs: The early use of metoprolol in patients with acute myocardial infarction who are also receiving thrombolytics and aspirin provides no short-term benefit compared with placebo. Since the early use, however, increases the risk of cardiogenic shock, it may be wise to delay starting metoprolol until the patient is hemodynamically stable. (LOE = 1b))

Chen JM, Heran BS, Perez MI, Wright JM. Blood pressure lowering efficacy of **beta-blockers** as second-line therapy for primary hypertension. **Cochrane** Database Syst Rev. **2010** Jan 20;(1):CD007185. Addition of a beta-blocker to diuretics or calcium-channel blockers reduces BP by 6/4mmHg at 1 times the starting dose and by 8/6 mmHg at 2 times the starting dose. When the blood pressure lowering effect of beta-blockers from this review was compared to that of thiazide diuretics from our previous review (Chen 2009), second-line beta-blockers

reduce systolic BP to the same extent as second-line thiazide diuretics, but reduce diastolic BP to a greater degree. The different effect on diastolic BP means that beta-blockers have little or no effect on pulse pressure whereas thiazides cause a significant dose-related decrease in pulse pressure. This difference in the pattern of BP lowering with beta-blockers as compared to thiazides might be the explanation for the fact that beta-blockers appear to be less effective at reducing adverse cardiovascular outcomes than thiazide diuretics, particularly in older individuals.

Chen TS, Eichenfield LF, Friedlander SF. **Infantile hemangiomas**: an update on pathogenesis and therapy. Pediatrics. 2013 Jan;131(1):99-108. (propranolol)

Chinnadurai S, Snyder K, Sathe N, et al. Diagnosis and management of **infantile hemangioma**. Comparative Effectiveness Review No. 168. Rockville (MD): Agency for Healthcare Research and Quality (US); 2016 Jan. Report No.: 16-EHC002-EF

Chinnadurai S, Fonnesbeck C, Snyder KM, et al. Pharmacologic Interventions for **Infantile Hemangioma**: A Meta-analysis. Pediatrics. 2016 Jan 15.

Chirapongsathorn S, Valentin N, Alahdab F, et al. **Non-Selective Beta-Blockers** and Survival in Patients with **Cirrhosis and Ascites**: A Systematic Review and Meta-analysis. Clin Gastroenterol Hepatol. 2016 Jan 29.

Choi E, Pak G, Burket J. **Beta Blockers Compared with Other Drug Options for the Treatment of Hypertension**. Am Fam Physician. 2018 Feb 1;97(3):Online.

Chow W, Amaya CN, Rains S, et al. **Growth Attenuation of Cutaneous Angiosarcoma** With Propranolol-Mediated β-Blockade. JAMA Dermatol. 2015 Sep 16:1-4.

Ciarka A, Lund LH, Van Cleemput J, et al. Effect of **Heart Rate and Use of Beta Blockers on Mortality After Heart Transplantation**. Am J Cardiol. 2016 Dec 15;118(12):1916-1921.

Clayton B, Raju V, Roobottom C, et al. Safety of **intravenous beta-blockers for CT coronary angiography**. Br J Clin Pharmacol. 2014 Sep 16.

Cleland JG, et al. COMET Investigators. A comparison of the effects of carvedilol and metoprolol on well-being, morbidity, and mortality (the "patient journey") in patients with heart failure: a report from the Carvedilol Or Metoprolol European Trial (**COMET**). J Am Coll Cardiol. 2006 Apr 18;47(8):1603-11. Epub 2006 Mar 29. (InfoPOEMs: Carvedilol (Coreg) treatment of patients with New York Heart Association (NYHA) functional class II-IV heart failure decreases mortality over 4 years more than metoprolol (number needed to treat = 18). Hospitalization rates, length of stay, and patient reports of symptoms are not different between the 2 drugs. (LOE = 1b))

Cleland JGF, Bunting KV, Flather MD, et al. Beta-blockers **for heart failure with reduced, mid-range, and preserved ejection fraction**: an individual patient-level analysis of double-blind randomized trials. Eur Heart J. 2017 Oct 10.

Cohn SL. Updated guidelines on **cardiovascular evaluation before noncardiac surgery**: a view from the trenches. Cleve Clin J Med 2014; 81:742–751.

Cole GD, Francis DP. **Perioperative ß blockade**: guidelines do not reflect the problems with the evidence from the **DECREASE** trials. *BMJ* 2014.

Connolly SJ, et al. Optimal Pharmacological Therapy in Cardioverter Defibrillator Patients (OPTIC) Investigators. Comparison of beta-blockers, amiodarone plus beta-blockers, or sotalol for prevention of shocks from implantable cardioverter defibrillators: the OPTIC Study: a randomized trial. JAMA. 2006 Jan 11;295(2):165-71. Despite use of advanced ICD technology and treatment with a beta-blocker, shocks occur commonly in the first year after ICD implant. Amiodarone plus beta-blocker is effective for preventing these shocks and is more effective than sotalol but has an increased risk of drug-related adverse effects.

Cresci S, Kelly RJ, Cappola TP, et al. Clinical and **genetic** modifiers of long-term survival in heart failure. J Am Coll Cardiol 2009; 54:432-444). DOI:10.1016/j.jacc.2009.05.009.

Cubiró X, Planas-Ciudad S, Garcia-Muret MP, Puig L. **Topical Timolol for Paronychia and Pseudopyogenic Granuloma** in Patients Treated With Epidermal Growth Factor Receptor Inhibitors and Capecitabine. JAMA Dermatol. 2017 Nov 8.

Czarnecki A, Morrison LJ, Qiu F, et al. Association of **prior β-blocker use and the outcomes of patients with out-of-hospital cardiac arrest**. Am Heart J. 2015 Nov;170(5):1018-1024.e2.

Dahl Aarvik M, Sandven I, Dondo TB, et al. Effect of **Oral β-blocker Treatment on Mortality in Contemporary Post-myocardial Infarction Patients**. Eur Heart J Cardiovasc Pharmacother. 2018 Sep 6.

Dahlof B, Devereux RB, Kjeldsen SE, et al.; **LIFE** Study Group. Cardiovascular morbidity and mortality in the Losartan Intervention For Endpoint reduction in hypertension study (LIFE): a randomised trial against atenolol. Lancet. 2002 Mar 23;359(9311):995-1003.

Dahlof B, Sever PS, Poulter NR, Wedel H, et al. **ASCOT** Investigators. Prevention of cardiovascular events with an antihypertensive regimen of amlodipine adding perindopril as required versus atenolol adding bendroflumethiazide as required, in the Anglo-Scandinavian Cardiac Outcomes Trial-Blood Pressure Lowering Arm (ASCOT-BPLA): a multicentre RCT. Lancet. 2005 Sep 10;366(9489):895-906.

Darrow DH, Greene AK, et al; Section on Dermatology, Section on Otolarynology-Head and Neck Surgery and Section on Plastic Surgery, Diagnosis and Management of **Infantile Hemangioma**. Pediatrics. 2015 Sep 28.

Darrow DH, Greene AK, Mancini AJ, et al; S Section on Dermatology, Section on Otolarynology-Head and Neck Surgery and Section on Plastic Surgery. Diagnosis and Management of **Infantile Hemangioma**: Executive Summary. Pediatrics. 2015 Sep 28.

De Giorgi Vincenzo; Grazzini Marta; Gandini Sara; et al. Treatment With {beta}-Blockers and Reduced Disease Progression in Patients With **Thick Melanoma**. Arch Intern Med. 2011;171(8):779-781.

De Giorgi V, Grazzini M, Benemei S, et al. **Propranolol** for Off-Label Treatment of Patients With **Melanoma**: Results From a Cohort Study. JAMA Oncol. 2017 Sep 28.

Deepmala, Agrawal M. Use of **propranolol for hypersexual behavior** in an adolescent with autism. Ann Pharmacother. 2014 Oct;48(10):1385-8.

Desai VC, Kelton CM, Metzger AH, Cavanaugh TM, Guo JJ, Heaton PC. Comparative Persistence on **β-Blockers Versus Calcium Channel Blockers** for Ventricular Rate Control in Nonelderly Patients With Atrial Fibrillation. Ann Pharmacother. 2014 Dec;48(12):1570-9.

Devereaux PJ, Beattie WS, Choi PT, et al.. How strong is the evidence for the use of perioperative {beta} blockers in non-cardiac surgery? Systematic review and meta-analysis of randomised controlled trials. BMJ. 2005 Jul 4; CONCLUSION: The evidence that perioperative beta blockers reduce major cardiovascular events is encouraging but too unreliable to allow definitive conclusions to be drawn.

Dézsi CA, Szentes V. The **Real Role of β-Blockers in Daily Cardiovascular Therapy**. Am J Cardiovasc Drugs. 2017 Mar 29.

Dharmarajan K, Masoudi FA, Spertus JA, et al. **Contraindicated Initiation of β-Blocker** Therapy in Patients Hospitalized for **Heart Failure**. JAMA Intern Med. 2013 Jun 24:1-3

Dharod A, Soliman EZ, et al. Association of **asymptomatic bradycardia** with incident cardiovascular disease and mortality: The Multi-Ethnic Study of Atherosclerosis (**MESA**). *JAMA Intern Med* 2015.

Dib N, Oberti F, Cales P. Current management of the complications of **portal hypertension**: variceal bleeding and ascites. CMAJ. 2006 May 9;174(10):1433-43.

Dimmitt S, Stampfer H, Warren J. Beta blockers valuable but **higher doses not necessary**. Br J Clin Pharmacol. 2014 Jun 10.

Dinicolantonio JJ, Lavie CJ, Fares H, et al. Meta-Analysis of **Carvedilol Versus Beta 1 Selective Beta-Blockers (Atenolol, Bisoprolol, Metoprolol**, and **Nebivolol**). Am J Cardiol. 2013 Jan 3.

Dinicolantonio JJ, Beavers CJ, et al. Meta-Analysis Comparing **Carvedilol Versus Metoprolol** for the Prevention of **Postoperative Atrial Fibrillation** Following Coronary Artery Bypass Grafting. Am J Cardiol. 2013 Nov 8

Disse SC, Zemlin M, Mueller C, et al. **PHACE Syndrome-before and after Propranolol** Therapy. J Pediatr. 2017 Dec 6.

Dondo TB, Hall M, West RM, et al. **Beta-blockers and mortality after acute myocardial infarction** in patients **without heart failure or ventricular dysfunction**. J Am Coll Cardiol 2017;69: 2710–20.

Dorian P, Angaran P. **β-Blockers and atrial fibrillation**: hypertension and other medical conditions influencing their use. Can J Cardiol. 2014 May;30(5 Suppl):S38-41.

Dransfield MT, Rowe SM, Johnson JE, Bailey WC, Gerald LB. Use of beta blockers and the risk of death in hospitalised patients with acute exacerbations of **COPD**. Thorax. 2008 Apr;63(4):301-5. Epub 2007 Oct 19. The use of beta blockers by inpatients with exacerbations of COPD is well tolerated and may be associated with reduced mortality. The potential protective effect of beta blockers in this population warrants further study.

Droitcourt C, Kerbrat S, Rault C, et al. Safety of **Oral Propranolol for Infantile Hemangioma**. Pediatrics. 2018 Jun;141(6).

Drolet BA, Frommelt PC, Chamlin SL, et al. Initiation and use of **propranolol for infantile hemangioma**: report of a consensus conference. Pediatrics. 2013 Jan;131(1):128-40.

Duan L, Ng A, Chen W, et al. **β-Blocker Exposure in Pregnancy** and Risk of **Fetal Cardiac Anomalies**. JAMA Intern Med. 2017 Apr 17.

Duché M, Ducot B, Ackermann O, et al. Experience with **endoscopic management of high-risk gastroesophageal varices**, with and without bleeding, in children with biliary atresia. Gastroenterology 2013;145:801–807.

Duffin J. **Do practice guidelines cause drug shortages**? The historical example of β-blockers. CMAJ. 2019 Sep 16;191(37):E1029-E1031.

Effect of metoprolol CR/XL in chronic heart failure: Metoprolol CR/XL Randomised Intervention Trial in Congestive Heart Failure (**MERIT-HF**) Lancet. 1999 Jun 12;353(9169):2001-7.

Ellenberger C, Tait G, Beattie WS. **Chronic beta Blockade** Is Associated with a Better Outcome after **Elective Noncardiac Surgery** than Acute beta Blockade: A Single-center Propensity-matched Cohort Study. Anesthesiology. 2011 Apr;114(4):817-23.

Espinola-Klein C, Weisser G, Jagodzinski A, et al. {beta}-Blockers in Patients With Intermittent Claudication and Arterial Hypertension: Results From the **Nebivolol or Metoprolol in Arterial Occlusive Disease** Trial. Hypertension. 2011 Aug;58(2):148-54.

EXPERT PANEL ON INTEGRATED GUIDELINES FOR CARDIOVASCULAR HEALTH AND RISK REDUCTION IN CHILDREN AND ADOLESCENTS. Expert Panel on Integrated Guidelines for Cardiovascular Health and Risk Reduction in Children and Adolescents: Summary Report. Pediatrics. 2011 Nov 14. [Epub ahead of print]

Fanari Z, Kennedy KK, Lim MJ, et al. Comparison of in-hospital outcomes for beta-blocker use versus non-beta blocker use in patients presenting with **cocaine-associated chest pain**. Am J Cardiol. 2014 Jun 1;113(11):1802-6.

Farland MZ, Peters CJ, Williams JD, et al. β-Blocker Use an Incidence of **Chronic Obstructive Pulmonary Disease Exacerbations** (May). Ann Pharmacother. 2013 Apr 12.
Filippi L, Cavallaro G, Bagnoli P, et al. Oral **Propranolol for Retinopathy of Prematurity**: Risks, Safety Concerns, and Perspectives. J Pediatr. 2013 Sep 18.
Flather MD, Shibata MC, Coats AJ, et al. Randomized trial to determine the effect of **nebivolol** on mortality and cardiovascular hospital admission in elderly patients with heart failure (**SENIORS**). Eur Heart J 2005;26:215-25.
Fleisher LA, et al.; American College of Cardiology/American Heart Association Task Force on Practice Guidelines Writing Committee to Update the 2002 Guidelines on Perioperative Cardiovascular Evaluation for Noncardiac Surgery; American Society of Echocardiography; American Society of Nuclear Cardiology; Heart Rhythm Society; Society of Cardiovascular Anesthesiologists; Society for Cardiovascular Angiography and Interventions; Society for Vascular Medicine and Biology. **ACC/AHA 2006** guideline update on perioperative cardiovascular evaluation for noncardiac surgery: focused update on perioperative **beta-blocker** therapy: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Writing Committee to Update the 2002 Guidelines on Perioperative Cardiovascular Evaluation for noncardiac Surgery): developed in collaboration with the American Society of Echocardiography, American Society of Nuclear Cardiology, Heart Rhythm Society, Society of Cardiovascular Anesthesiologists, Society for Cardiovascular Angiography and Interventions, and Society for Vascular Medicine and Biology. Circulation. 2006 Jun 6;113(22):2662-74.
http://www.americanheart.org/downloadable/heart/1142081026765PeriopFinal.pdf
Fleisher LA, Fleischmann KE, Auerbach AD, et al. **2014 ACC/AHA Guideline on Perioperative Cardiovascular Evaluation** and Management of Patients Undergoing Noncardiac Surgery: A Report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. J Am Coll Cardiol. 2014 Jul 29.
Flynn NO, Timmis A, Henderson R, Rajesh S, Fenu E; on behalf of the Guideline Development Group. Management of **stable angina**: summary of **NICE** guidance. BMJ. 2011 Aug 5;343:d4147. doi: 10.1136/bmj.d4147.
Fonarow GC, Abraham WT, Albert NM, et al. OPTIMIZE-HF Investigators and Coordinators. Influence of beta-blocker continuation or withdrawal on outcomes in patients hospitalized with heart failure: findings from the **OPTIMIZE-HF** program. J Am Coll Cardiol. 2008 Jul 15;52(3):190-9. The continuation of beta-blocker therapy in patients hospitalized with decompensated HF is associated with lower post-discharge mortality risk & improved treatment rates. In contrast, withdrawal of beta-blocker therapy is associated with worse risk and propensity-adjusted mortality.
Fontana RJ, Sanyal AJ, Ghany MG, et al. HALT-C Trial Group. Factors that Determine the Development and Progression of **Gastroesophageal Varices** in Patients with Chronic **Hepatitis C**. Gastroenterology. 2010 Mar 5.
Fanari Z, Kennedy KK, et al. Comparison of in-hospital outcomes for **Beta-blocker use versus non-Beta blocker use** in patients presenting with **cocaine-associated chest pain**. Am J Cardiol. 2014 Jun 1;113(11):1802-6.
Friedell ML, Van Way CW 3rd, Freyberg RW, et al. **β-Blockade and Operative Mortality** in **Noncardiac Surgery**: Harmful or Helpful? JAMA Surg. 2015 May 27.
Frithsen IL, Simpson WM Jr. Recognition and management of acute medication poisoning. Am Fam Physician. 2010 Feb 1;81(3):316-23.
Garcia-Pagan JC, Villanueva C, Albillos A, et al. Nadolol plus isosorbide mononitrate alone or associated with band ligation in the prevention of **recurrent bleeding**: a multicentre randomised controlled trial. Gut. 2009 Aug;58(8):1144-50. Epub 2009 Feb 12. Adding EBL (endoscopic band ligation) to pharmacological treatment did not reduce recurrent bleeding, the need for rescue therapy, or mortality, and was associated with more adverse events. Furthermore, associating EBL to drug therapy did not reduce the high rebleeding risk of HVPG (hepatic venous pressure gradient) non-responders.
Garcia-Tsao G, Sanyal AJ, Grace ND, Carey W, Practice Guidelines Committee of the American Association for the Study of Liver Diseases, Practice Parameters Committee of the American College of Gastroenterology. Prevention and management of **gastroesophageal varices and variceal hemorrhage in cirrhosis**. Hepatology 2007;46(3):922-38.
https://www.aasld.org/eweb/docs/practiceguidelines/VariesinGuidelinesSept2007FT.pdf
Garcia-Tsao, Guadalupe, Bosch, Jaime. Management of **Varices and Variceal Hemorrhage** in Cirrhosis. N Engl J Med 2010 362: 823-832.
Ge PS and Runyon BA.The changing role of **beta-blocker therapy in** patients with **cirrhosis**. J Hepatol 2014 Mar; 60:643.
Ge PS, Runyon BA. **Treatment of Patients with Cirrhosis**. N Engl J Med. 2016 Aug 25;375(8):767-77.
Gelineau AM, et al. Intraoperative **Esmolol** as an Adjunct for Perioperative Opioid and Postoperative **Pain Reduction**: A Systematic Review, Meta-analysis, and Meta-regression. Anesth Analg. 2018 Mar;126(3):1035-1049.
Gersh BJ, Maron BJ, Bonow RO, et al. 2011 ACCF/AHA guideline for the diagnosis and treatment of **hypertrophic cardiomyopathy**: A report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines.Circulation 2011; DOI:10.1161/CIR.0b013e318223e2bd. http://content.onlinejacc.org/cgi/reprint/j.jacc.2011.06.011v1.pdf
Giles TD, Weber MA, et al, for the NAC-MD-01 Study Investigators. Efficacy and safety of **nebivolol and valsartan** as fi xed-dose combination in hypertension: a randomised, multicentre study. Lancet 2014; 383: 1889–98.
Gillis AM, Verma A, Talajic M, et al. **CCS** Atrial Fibrillation Guidelines. **Canadian cardiovascular society atrial fibrillation guidelines 2010: rate and rhythm management**. Can J Cardiol. 2011 Jan-Feb;27(1):47-59.
Gluud LL, Klingenberg S, Nikolova D, Gluud C. **Banding ligation versus beta-blockers** as primary prophylaxis in **esophageal varices**: systematic review of randomized trials. Am J Gastroenterol. 2007 Dec;102(12):2842-8; quiz 2841, 2849. Banding ligation and beta-blockers may be used as primary prophylaxis in high-risk esophageal varices. The estimated effect of banding ligation in some trials may be biased and was associated with the duration of follow-up. Further high-quality trials are still needed.
Goldberger JJ, Bonow RO, Cuffe M, Dyer A, et al. PACE-MI Investigators. beta-Blocker use following myocardial infarction: **Low prevalence of evidence-based dosing**. Am Heart J. 2010 Sep;160(3):435-442.e1.
Go AS, et al. Atherosclerotic Disease, Vascular Function & Genetic Epidemiology (ADVANCE) Study. Statin & beta-blockers & the initial presentation of coronary heart disease. Ann Intern Med. 2006 Feb 21;144(4):229-38.
Go AS, Yang J, Gurwitz JH, Hsu J, Lane K, Platt R. Comparative effectiveness of different beta-adrenergic antagonists on mortality among adults with **heart failure** in clinical practice. Arch Intern Med. 2008 Dec 8;168(22):2415-21. Compared with atenolol, the adjusted risks of death were slightly higher with shorter-acting metoprolol tartrate but did not significantly differ for carvedilol in adults with heart failure. Our results should be interpreted cautiously and they suggest the need for randomized trials within real-world settings comparing a broader spectrum of beta-blockers for heart failure.
Goundry B, Bell L, Langtree M, Moorthy A. Diagnosis and management of **Raynaud's phenomenon**. BMJ. 2012 Feb 7;344:e289.
Guglin M, Krischer J, Tamura R, et al. Randomized Trial of **Lisinopril Versus Carvedilol to Prevent Trastuzumab Cardiotoxicity** in Patients With Breast Cancer. J Am Coll Cardiol. 2019 Jun 11;73(22):2859-2868.
Gupta A, Das SR, Pandey A. **β-Blockers in myocardial infarction**: issues with standard admission orders sets [published online March 27, 2018].JAMA. doi:10.1001/jama.2018.0845
Halonen J, et al. **Intravenous** administration of **metoprolol** is more effective than oral administration in the prevention of **atrial fibrillation** after cardiac surgery. Circulation. 2006 Jul 4;114(1 Suppl):I1-4. The dosage was 1 to 3 mg/h in the intravenous group and from 25 mg twice per day to 50 mg 3 times per day in the oral group. The incidence of postoperative AF was significantly lower in the intravenous group than in the oral group (16.8% versus 28.1%, P=0.036). No serious adverse effects were associated with intravenous metoprolol therapy. CONCLUSIONS: Our study suggests that intravenous metoprolol is well-tolerated and more effective than oral metoprolol in the prevention of AF after cardiac surgery.
Halonen Jari, Loponen Pertti, Järvinen Otso, et al. **Metoprolol Versus Amiodarone** in the Prevention of **Atrial Fibrillation** After Cardiac Surgery: A Randomized Trial. *Ann Intern Med* Dec 7, 2010 153:703-709.
Ham AC, van Dijk SC, Swart KMA, et al. Beta-blocker use and **fall risk** in older individuals; original results from two studies with meta-analysis. Br J Clin Pharmacol. 2017 Jun 7.
Hamm CW, Bassand JP, Agewall S, et al. **ESC** Guidelines for the management of **acute coronary syndromes** in patients presenting without persistent ST-segment elevation: The Task Force for the management of acute coronary syndromes (ACS) in patients presenting without persistent ST-segment elevation of the European Society of Cardiology (ESC). Eur Heart J. 2011 Sep 21.
Hawkins NM, Petrie MC, MacDonald MR, et al. **Heart failure and chronic obstructive pulmonary disease**. The quandary of beta-blockers and beta-agonists. J Am Coll Cardiol 2011; 57:2127-2138.
Heart Failure Society Of America. **HFSA 2006** Comprehensive Heart Failure Practice Guideline. J Card Fail. 2006 Feb;12(1):e1-2.
Hedblad B, Wikstrand J, Janzon L, Wedel H, Berglund G. Low-dose metoprolol CR/XL and fluvastatin slow progression of carotid intima-media thickness: Main results from the Beta-Blocker Cholesterol-Lowering Asymptomatic Plaque Study (BCAPS). Circulation. 2001 Apr 3;103(13):1721-6.
Hernandez AF, Hammill BG, O'Connor CM, et al. Clinical effectiveness of beta-blockers in **heart failure**. Findings from the OPTIMIZE-HF (Organized Program to Initiate Lifesaving Treatment in Hospitalized Patients With Heart Failure) registry. J Am Coll Cardiol 2009; 53:184-192. In elderly patients hospitalized with heart failure and LVSD, incident beta-blocker use was clinically effective and independently associated with lower risks of death and rehospitalization. Patients with preserved systolic function had poor outcomes, and beta-blockers did not significantly influence the mortality and rehospitalization risks for these patients.
Hirst JA, Farmer AJ, Feakins BG, et al. Quantifying the effects of **diuretics and beta-blockers on glycaemic control** in diabetes mellitus - a systematic review and meta-analysis. Br J Clin Pharmacol. 2014 Nov 6.
Hogeling M, Adams S, Wargon O. A randomized controlled trial of **propranolol for infantile hemangiomas**. Pediatrics. 2011 Aug;128(2):e259-66.
Howlett JG. **Nebivolol**: vasodilator properties and evidence for relevance in treatment of cardiovascular disease. Can J Cardiol. 2014 May;30(5 Suppl):S29-37.

Huang BT, Huang FY, Zuo ZL, et al. Meta-Analysis of Relation Between **Oral β-Blocker Therapy and Outcomes in Patients With Acute Myocardial Infarction** Who Underwent **Percutaneous Coronary Intervention**. Am J Cardiol. 2015 Jun 1;115(11):1529-38.

Hung RK, et al. Effect of **Beta-Blocker Therapy, Maximal Heart Rate, and Exercise Capacity** During Stress Testing on Long-Term Survival (from The Henry Ford Exercise Testing Project). Am J Cardiol. 2016 Aug 31.

Huynh BC, Rovner A, Rich MW. Long-term survival in elderly patients hospitalized for **heart failure**: 14-year follow-up from a prospective randomized trial. Arch Intern Med. 2006 Sep 25;166(17):1892-8.

ICSI: Institute for Clinical Systems Improvement (ICSI). **Preoperative evaluation**. Bloomington (MN): Institute for Clinical Systems Improvement (ICSI); 2010 Jun.

Ishibashi K, Aiba T, Kamiya C, et al. **Arrhythmia risk and β-blocker therapy** in **pregnant women with long QT syndrome**. Heart. 2017 Mar 14.

Jabbour A, Macdonald PS, Keogh AM, et al. **Differences between beta-blockers** in patients with chronic **heart failure and chronic obstructive pulmonary disease**: a randomized crossover trial. J Am Coll Cardiol. 2010 Apr 27;55(17):1780-7.

Jansen L, Below J, Chang-Claude J, et al. Beta blocker use and **colorectal cancer risk**: Population-based case-control study. Cancer. 2012 May 14.

Jeon H, Jang IJ, Lee S, Ohashi K, Kotegawa T, Ieiri I, Cho JY, Yoon SH, Shin SG, Yu KS, Lim KS. **Apple Juice** Greatly Reduces Systemic Exposure to **Atenolol**. Br J Clin Pharmacol. 2012 May 11.

Jondeau Guillaume, Neuder Yannick, Eicher Jean-Christophe, et al. , and for the **B-CONVINCED** Investigators. B-CONVINCED: Beta-blocker CONtinuation Vs. INterruption in patients with Congestive heart failure hospitalizED for a decompensation episode. European Heart Journal Advance Access published on August 30, 2009, DOI 10.1093/eurheartj/ehp323.

Jørgensen ME, Hlatky MA, Køber L, et al, Andersson C**. β-Blocker-Associated Risks in Patients With Uncomplicated Hypertension Undergoing Noncardiac Surgery**. JAMA Intern Med. 2015 Oct 5:1-9.

Jorgensen ME, Sanders RD, Kober L, et al. **Beta-blocker subtype** and risks of **perioperative adverse events** following non-cardiac surgery: a nationwide cohort study. European Heart Journal. 2017;38,2421-2428.

Juul AB, et al. Effect of perioperative beta blockade in patients with diabetes undergoing major non-cardiac surgery: randomised placebo controlled, blinded multicentre trial. BMJ. 2006 Jun 24;332(7556):1482. Perioperative metoprolol did not significantly affect mortality and cardiac morbidity in these patients with diabetes.

Kaempfen S, Neumann RP, Jost K, Schulzke SM. **Beta-blockers for prevention and treatment of retinopathy of prematurity in preterm infants**. Cochrane Database Syst Rev. 2018 Mar 2;3:CD011893. Limited evidence of low-to-moderate quality suggests that prophylactic administration of oral beta-blockers might reduce progression towards stage 3 ROP and decrease the need for anti-VEGF agents or laser therapy. The clinical relevance of those findings is unclear as no data on long-term visual impairment were reported. Adverse events attributed to oral propranolol at a dose of 2 mg/kg/d raise concerns regarding systemic administration of this drug for prevention of ROP at the given dose.

Kanthan GL, Wang JJ, Rochtchina E, Mitchell P. Use of antihypertensive medications and topical beta-blockers and the long-term incidence of **cataract** and cataract surgery. Br J Ophthalmol. 2009 Jul 23. [Epub ahead of print]

Khan N, McAlister FA. Re-examining the efficacy of **beta-blockers** for the treatment of hypertension: a **meta-analysis**. CMAJ. 2006 Jun 6;174(12):1737-42. Beta-blockers should not be considered first-line therapy for older hypertensive patients without another indication for these agents; however, in younger patients beta-blockers are associated with a significant reduction in cardiovascular morbidity and mortality.

Khouri C, Blaise S, Carpentier P, et al. **Drug-induced Raynaud's phenomenon**: beyond beta-blockers. Br J Clin Pharmacol. 2016 Mar 7.

Khouri C, Jouve T, Blaise S, et al. **Peripheral vasoconstriction induced by beta-blockers**: a systematic review and a network meta-analysis. Br J Clin Pharmacol. 2016 Apr 16.

Kim SG, Kim TY, et al. A Randomized, Multi-Center, Open-Label Study to Evaluate the Efficacy of **Carvedilol vs. Propranolol** to Reduce Portal Pressure in Patients With **Liver Cirrhosis**. Am J Gastroenterol. 2016 Aug 30.

Komajda M, Lutiger B, Madeira H, et al.; CARMEN investigators and co-ordinators. Tolerability of carvedilol and ACE-Inhibition in mild heart failure. Results of CARMEN (Carvedilol ACE-Inhibitor Remodelling Mild CHF EvaluatioN). Eur J Heart Fail. 2004 Jun;6(4):467-75.

Korownyk C, Ross D, Fiorillo L. Novel treatment for **infantile hemangiomas**. Can Fam Physician. 2014 Dec;60(12):e590.

Kotecha D, Holmes J, Krum H, et al; on behalf of the Beta-Blockers in Heart Failure Collaborative Group. Efficacy of **β blockers** in patients with **heart failure plus atrial fibrillation**: an individual-patient data meta-analysis. Lancet. 2014 Sep 2.

Kotecha D, Flather MD, Altman DG, et al. **Heart** Rate and **Rhythm** and the Benefit of **Beta-Blockers** in Patients With **Heart Failure**. J Am Coll Cardiol. 2017 Jun 20;69(24):2885-2896.

Koyak Z, Kroon B, de Groot JR, et al. Efficacy of **Antiarrhythmic Drugs** in Adults With **Congenital Heart Disease and Supraventricular Tachycardias**. Am J Cardiol. 2013 Aug 29. (Options: sotalol)

Krakowski AC, Nguyen TA. **Inhibition of Angiofibromas** in a Tuberous Sclerosis Patient Using Topical Timolol 0.5% Gel. Pediatrics. 2015 Aug 24.

Ko DT, Hebert PR, Coffey CS, et al. Beta-blocker therapy and **symptoms of depression, fatigue, and sexual dysfunction**. JAMA. 2002;288:351-357.

Kotecha D, Manzano L, Krum H, et al. Effect of **age and sex** on efficacy and tolerability of **β blockers in patients with heart failure with reduced ejection fraction**: individual patient data meta-analysis. BMJ 2016;353:i1855.

Kotecha D, Flather MD, Altman DG, et al. Heart Rate, Heart Rhythm, and Prognostic Benefits of Beta-Blockers in **Heart Failure**: Individual Patient-Data Meta-Analysis. J Am Coll Cardiol. 2017 Apr 5.

Kramer JM, Curtis LH, Dupree CS, Pelter D, Hernandez A, Massing M, Anstrom KJ. Comparative effectiveness of beta-blockers in **elderly patients with heart failure**. Arch Intern Med. 2008 Dec 8;168(22):2422-8; discussion 2428-32. this elderly population, the comparative effectiveness of EBBBs vs non-EBBBs was similar for 1-year survival, whereas the rehospitalization rate was higher for patients receiving EBBBs.

Krause T, Lovibond K, Caulfield M, McCormack T, Williams B; on behalf of the Guideline Development Group. **Management of hypertension**: summary of **NICE** guidance. BMJ. 2011 Aug 25;343:d4891.

Krowchuk DP, Frieden IJ, Mancini AJ, et al. Clinical Practice Guideline for the Management of **Infantile Hemangiomas**. Pediatrics. 2018 Dec 24.

Kuyper LM, Khan NA. **Atenolol vs Nonatenolol** β-Blockers for the Treatment of Hypertension: A Meta-analysis. Can J Cardiol. 2014 May;30(5S):S47-S53.

Kwon S, Thompson R, Florence M, et al. **β-Blocker Continuation After Noncardiac Surgery**: A Report From the Surgical Care and Outcomes Assessment Program. Arch Surg. 2012 Jan 16.

Lacro RV, Dietz HC, Sleeper LA, et al. Pediatric Heart Network Investigators. **Atenolol versus losartan** in children and young adults with **Marfan's syndrome.** N Engl J Med. 2014 Nov 27;371(22):2061-71.

Lafuente-Lafuente C, et al. Antiarrhythmic drugs for maintaining sinus rhythm after cardioversion of **atrial fibrillation**: a systematic review of randomized controlled trials. Arch Intern Med. 2006 Apr 10;166(7):719-28.

Lafuente-Lafuente Carmelo, Isabelle Mahé, Fabrice Extramiana. Management of **atrial fibrillation**. BMJ 2009;339:b5216, doi: 10.1136/bmj.b5216

Lanfear DE, Jones PG, Marsh S, et al. Beta2-adrenergic receptor genotype and survival among patients receiving beta-blocker therapy after an acute coronary syndrome. JAMA. 2005 Sep 28;294(12):1526-33.

Lanfear DE, Hrobowski T, Peterson EL, et al. Association of **Beta Blocker Exposure** with Outcomes in Heart Failure Differs Between **African American** and White Patients. Circ Heart Fail. 2012 Jan 19.

Larochelle P, Tobe SW, Lacourcière Y. **β-Blockers in hypertension**: studies and meta-analyses over the years. Can J Cardiol. 2014 May;30(5 Suppl):S16-22.

Lawless CE, Tamlyn T, Shah R, Karim FM, Khan E, Creech S. **Titration of carvedilol in elderly** heart failure patients. Am J Geriatr Cardiol. 2005 Sep-Oct;14(5):230-5.

Léauté-Labrèze C, Hoeger P, Mazereeuw-Hautier J, et al. A randomized, controlled trial of oral **propranolol in infantile hemangioma**. N Engl J Med. 2015 Feb 19;372(8):735-46.

Léaute-Labrèze C, Boccara O, Degrugillier-Chopinet C, et al. Safety of Oral **Propranolol** for the Treatment of **Infantile Hemangioma**: A Systematic Review. Pediatrics. 2016 Sep 29.

Léauté-Labrèze C, Harper JI, Hoeger PH. **Infantile haemangioma**. Lancet. 2017 Jan 12.

Leithead JA, Rajoriya N, Tehami N, et al. **Non-selective beta-blockers** are associated with improved survival in patients with **ascites listed for liver transplantation**. Gut. 2014 Oct 3.

Li C, et al. Relationship **Between β-Blocker Therapy at Discharge** and Clinical Outcomes in Patients With **Acute Coronary Syndrome** Undergoing Percutaneous Coronary Intervention. J Am Heart Assoc. 2016 Nov 16;5(11).

Li X, Zhang Y, Liu H, et al. Efficacy of Intravenous **Sotalol** for Treatment of Incessant Tachyarrhythmias in Children. Am J Cardiol. 2017.

Lindholt JS, Vammen S, Juul S, Henneberg EW, Fasting H. The validity of ultrasonographic scanning as screening method for **abdominal aortic aneurysm**. Eur J Vasc Endovasc Surg. 1999;17:472– 475.

Lindholm LH, Carlberg B, Samuelsson O. Should beta blockers remain first choice in the treatment of primary hypertension? A meta-analysis. Lancet. 2005 Oct 29-Nov 4;366(9496):1545-53. (InfoPOEMs: If these authors have identified all the relevant research, it appears that in comparison with placebo, beta-blockers do not reduce cardiovascular morbidity or mortality but decrease the risk of strokes. However, in comparison with other antihypertensive medications, beta-blockers are associated with a significantly higher risk of stroke. Most of the included studies used atenolol and the data on other beta-blockers are inconclusive. Before throwing the baby out with the bathwater, remember that some patients with hypertension will need beta-blockers to treat their comorbid coronary artery disease, congestive heart failure, and so forth. (LOE = 1a-))

Lo GH, Chen WC, Wang HM, Lee CC. Controlled trial of ligation plus nadolol versus **nadolol alone** for the prevention of first **variceal bleeding**. Hepatology. 2010 Jul;52(1):230-7.

London MJ, Hur K, Schwartz GG, et al. Association of **perioperative Beta-blockade** with mortality and cardiovascular morbidity following major noncardiac surgery. JAMA 2013; 309:1704-1713.

Loth DW, Brusselle GG, Lahousse L, et al. **Beta-blockers and pulmonary function** in the general population: The Rotterdam Study. Br J Clin Pharmacol. 2013 Jun 17.

Lou Y, Peng WJ, Cao Y, et al. The effectiveness of **propranolol in treating infantile hemangiomas**: A Meta-analysis including 35 studies. Br J Clin Pharmacol. 2013 Sep 3.

Lund LH, Benson L, Dahlstrom U, Edner M, Friberg L. Association between use of **β-blockers and outcomes in patients with heart failure and preserved ejection fraction**. JAMA. doi:10.1001 /jama.2014.15241.

Maglie R, Caproni M. A case of blood sweating: **hematohidrosis syndrome. (propranolol)** CMAJ. 2017 Oct 23;189(42):E1314.

Mandorfer M, Bota S, Schwabl P, et al. **Non-selective Beta-blockers increase risk for hepatorenal syndrome** and death in patients with cirrhosis and spontaneous bacterial peritonitis. Gastroenterology 2014;146. 000–000.

Manfrini O, Morrell C, Das R, et al; EMMACE-2 (Evaluation of Methods and Management of Acute Coronary Events) Study Group. Effects of **Angiotensin-Converting Enzyme Inhibitors and Beta Blockers** on Clinical Outcomes in Patients **With and Without Coronary Artery Obstructions** at Angiography (from a Register-Based Cohort Study on **Acute Coronary Syndromes**). Am J Cardiol. 2014 Mar 3.

Mareev Y, Cleland JG. **Should β-Blockers** Be Used in Patients With **Heart Failure and Atrial Fibrillation**? Clin Ther. 2015 Sep 18.

McAlister FA, Wiebe N, Ezekowitz JA, Leung AA, Armstrong PW. Meta-analysis: **beta-blocker dose, heart rate** reduction, and death in patients with heart failure. Ann Intern Med. 2009 Jun 2;150(11):784-94. The magnitude of heart rate reduction is statistically significantly associated with the survival benefit of beta-blockers in heart failure, whereas the dose of beta-blocker is not.

Medical Letter- Treatment Guidelines. **Treatment of Atrial Fibrillation**. Sept 2010.

Melhem-Bertrandt A et al. Beta-blocker use is associated with improved relapse-free survival in patients with triple-negative **breast cancer**. J Clin Oncol 2011; 29:2645.

Mentz RJ, Wojdyla D, Fiuzat M, et al. Association of **Beta-Blocker Use and Selectivity** With Outcomes in Patients With Heart Failure and **Chronic Obstructive Pulmonary Disease** (from OPTIMIZE-HF). Am J Cardiol. 2013 Feb 15;111(4):582-7.

Messerli FH, Bell DS, Fonseca V, et al. GEMINI Investigators. Body weight changes with beta-blocker use: results from GEMINI. Am J Med. 2007 Jul;120(7):610-5. (n=1106 over 5months) Patients taking metoprolol had a significant mean (+/-SE) weight gain of 1.19 (+/-0.16) kg (P <.001); patients taking carvedilol did not (0.17 [+/-0.19] kg; P =.36). Metoprolol tartrate was associated with increased weight gain compared to carvedilol; weight gain was most pronounced in subjects with hypertension and diabetes who were not taking insulin therapy.

Messerli FH, Grossman E. **Beta-blocker therapy and depression**. JAMA. 2002;288:1845-1846.

Migliazzo CV, Hagan JC 3rd. **Beta blocker eye drops** for treatment of acute migraine. Mo Med. 2014 Jul-Aug;111(4):283-8.

Misaka S, Yatabe J, Müller F, et al. **Green tea** ingestion greatly reduces plasma concentrations of **nadolol** in healthy subjects. *Clin Pharmacol Ther* 2014.

Mitchell LB; **CCS** Atrial Fibrillation Guidelines Committee. Canadian cardiovascular society atrial fibrillation guidelines 2010: prevention and treatment of **atrial fibrillation following cardiac surgery**. Can J Cardiol. 2011 Jan-Feb;27(1):91-7.

Molvi SN, et al. Role of antihypertensive therapy in mild to moderate **pregnancy**-induced hypertension: a prospective randomized study comparing **labetalol with alpha methyldopa**. Arch Gyne Obstet. 2012 Jun;285(6):1553-62.

Morales DR, Jackson C, Lipworth BJ, et al. Adverse respiratory effect of acute **beta-blocker exposure in asthma**: a systematic review and meta-analysis of randomized controlled trials. Chest. 2013 Nov 7.

Morales DR, Dreischulte T, Lipworth BJ, et al. **Respiratory effect of beta-blocker eye drops** in asthma: population based study and meta-analysis of clinical trials. Br J Clin Pharmacol. 2016 May 10.

Morelli A, Ertmer C,Westphal M, et al. Effect of heart rate control with **esmolol** on hemodynamic and clinical outcomes in patients with **septic shock**: a randomized clinical trial. JAMA. doi10.1001/JAMA.2013.278477.

Motivala AA, Parikh V, Roe M, et al. Predictors, trends, and outcomes (among older patients >65 years of age) associated with beta-blocker use in patients with **stable angina undergoing elective percutaneous coronary intervention**: Insights from the NCDR Registry. *JACC Cardiovasc Interv* 2016.

Moyakine AV, Kerstjens JM, et al. **Propranolol** treatment of **infantile hemangioma (IH)** is not associated with developmental risk or growth impairment at age 4 years. J Am Acad Dermatol. 2016 Jul;75(1):59-63.e1.

Moyakine AV, Spillekom-van Koulil S, van der Vleuten CJ. **Propranolol** treatment of **infantile hemangioma** is not associated with psychological problems at 7 years of age. J Am Acad Dermatol. 2017 Feb 9.

Nakatani D, Sakata Y, Suna S, et al; Osaka Acute Coronary Insufficiency Study (OACIS). Impact of Beta Blockade Therapy on **Long-Term Mortality** After ST-Segment Elevation Acute Myocardial Infarction (**STEMI**) in the Percutaneous Coronary Intervention Era. Am J Cardiol. 2012 Dec 7.

NICE: National Institute for Health and Clinical Excellence. **Hypertension Guidelines**. Aug 2011. http://www.nice.org.uk/nicemedia/live/13561/56015/56015.pdf

Nistri S, Olivotto I, Maron MS, et al. β Blockers for Prevention of Exercise-Induced Left Ventricular Outflow Tract Obstruction in Patients With **Hypertrophic Cardiomyopathy**. Am J Cardiol. 2012 May 23.

Norberto L, Polese L, Cillo U, et al. A randomized study comparing ligation with propranolol for primary prophylaxis of **variceal bleeding** in candidates for liver transplantation. Liver Transpl. 2007 Sep;13(9):1272-8.
In conclusion, propranolol and banding are similarly effective in reducing the incidence of variceal bleeding in candidates for LT, but ligation can be complicated by fatal bleeding and is more expensive. Our results suggest that banding should not be utilized as primary prophylaxis in transplant candidates who can be treated with BB.

Nowbar AN, Cole GD, et al. International RCT-based guidelines for use of **preoperative stress testing and perioperative beta-blockers** and statins in non-cardiac surgery. Int J Cardiol. 2014 Mar 1;172(1):138-43.

O'Neal JB, Billings FT 4th, Liu X, et al. Effect of **Preoperative Beta-Blocker Use on Outcomes Following Cardiac Surgery**. Am J Cardiol. 2017 Oct 15;120(8):1293-1297.

October 28, 2010 (Chicago, Illinois) — Propranolol, an old drug being used off label, is an effective way to reduce vision-threatening **periocular infantile hemangiomas**, according to a study presented here at the American Academy of Ophthalmology and Middle East Africa Council of Ophthalmology 2010 Joint Meeting."[Oral] propranolol is not a common treatment used by ophthalmologists, but it may be now," said David Plager, MD, who presented the findings. "It gives impressive results." Dr. Plager is professor of ophthalmology and director of the Section of Pediatric Ophthalmology at Indiana University in Indianapolis. Propranolol, an oral beta blocker, "looks to be a very promising addition to our treatment armamentarium," Dr. Plager told Medscape Medical News. J AAPOS. 2010;14:251-256. Abstract

Ohman EM. Clinical Practice. **Chronic Stable Angina**. N Engl J Med. 2016 Mar 24;374(12):1167-76.

Ong HT. **Beta blockers in hypertension and cardiovascular disease**. BMJ. 2007 May 5;334(7600):946-9.

Oregon's Drug Effectiveness Review Project (DERP) **Beta Adrenergic Blockers: Comparative Drug Class Review** July 2009. **http://derp.ohsu.edu/final/BB_Final_Report_Update%204_09_JUL1.pdf**

Ouwerkerk W, Voors AA, Anker SD, et al. Determinants and clinical outcome of **uptitration of ACE-inhibitors and beta-blockers** in patients with **heart failure**: a prospective European study. Eur Heart J. 2017 Mar 11.

Packer M, et al. Carvedilol Prospective Randomized Cumulative Survival Study Group. (**COPERNICUS**) Effect of carvedilol on survival in severe chronic heart failure. N Engl J Med. 2001 May 31;344(22):1651-8. The previously reported benefits of carvedilol with regard to morbidity and mortality in patients with mild-to-moderate heart failure were also apparent in the patients with severe heart failure who were evaluated in this trial.

Paravastu SC, Mendonca D, Da Silva A. Beta blockers for **peripheral arterial disease**. Cochrane Database Syst Rev. 2008 Oct 8;(4):CD005508. There is currently no evidence that beta blockers adversely affect walking distance in people with intermittent claudication. However, due to the lack of large published trials beta blockers should be used with caution if clinically indicated.

Parikh SR, et al. **Propranolol** use for **infantile hemangiomas**: american society of pediatric otolaryngology vascular anomalies task force practice patterns. JAMA Otolaryngol Head Neck Surg. 2013 Feb 1;139(2):153-6.

Parker ED, Margolis KL, Trower NK, et al. Comparative Effectiveness of 2 β-Blockers (**atenolol vs metoprolol**) in Hypertensive Patients. Arch Intern Med. 2012 Aug 27:1-7.

Pasker-de Jong PC, Zielhuis GA, van Gelder MM, et al. Antihypertensive treatment during pregnancy and functional development at primary school age in a historical cohort study. BJOG. 2010 May 12. Conclusions In this hypothesis-generating study, **labetalol exposure** in utero seemed to increase the risk of **ADHD** among children of primary school age, whereas prenatal methyldopa exposure might influence sleep.

Pasternak B, Svanström H, Melbye M, et al. Association of Treatment With **Carvedilol vs Metoprolol Succinate and Mortality in Patients With Heart Failure**. JAMA Intern Med. 2014 Aug 31.

Pepine CJ, Handberg EM, Cooper-DeHoff RM, et al. **INVEST** Investigators. A calcium antagonist vs a non-calcium antagonist hypertension treatment strategy for patients with coronary artery disease. The International Verapamil-Trandolapril Study (INVEST): a randomized controlled trial. JAMA. 2003 Dec 3;290(21):2805-16.

Perioperative Beta-Blockers. Pharmacist's Letter Aug,2006.

Peter K. Lindenauer, M.D., Penelope Pekow, Ph.D., Kaijun Wang et al. **Perioperative Beta-Blocker** Therapy and Mortality after Major Noncardiac Surgery. NEJM 2005; 353:349-361. *Conclusions:* Perioperative beta-blocker therapy is associated with a reduced risk of in-hospital death among high-risk, but not low-risk, patients undergoing major noncardiac surgery. Patient safety may be enhanced by increasing the use of beta-blockers in high-risk patients (InfoPOEMs: Patients undergoing major surgery who are at high risk of complications -- those with heart disease, cerebrovascular disease, diabetes, or renal insufficiency -- benefit from perioperative beta-blockade. Low-risk patients (except perhaps those with hypertension and those undergoing high-risk surgery) do not. However, given the possible harms of suddenly discontinuing beta-blockers, those who are already taking them should continue doing so, even if they are at low-risk. (LOE = 2b))

Pham D, Addison D, Kayani W, et al. Outcomes of **beta blocker use in cocaine-associated chest pain**: a meta-analysis. Emerg Med J. 2018 Jun 19.

Phomakay V, Huett WG, Gossett JM, et al. **β-Blockers and Angiotensin Converting Enzyme Inhibitors**: Comparison of Effects on Aortic Growth in Pediatric Patients with **Marfan Syndrome**. J Pediatr. 2014 Aug 7.

Poldermans D, et al. Dutch Echocardiographic Cardiac Risk Evaluation Applying Stress Echo Study Group. Should major vascular surgery be delayed because of **preoperative cardiac testing** in intermediate-risk patients

receiving beta-blocker therapy with tight heart rate control? J Am Coll Cardiol. 2006 Sep 5;48(5):964-9. Epub 2006 Aug 17.
Poralla C, Specht S, Born M, et al. Treatment of **congenital generalized lymphangiectasia** with propranolol in a preterm infant. Pediatrics. 2014 Feb;133(2):e439-42.
Porcel Chacón R, Del Boz González J, et al. Delayed-Onset of Multiple Cutaneous **Infantile Hemangiomas Due to Propranolol**: A Case Report. Pediatrics. 2015 Mar 16.
Poulter NR, Dobson JE, et al. **Baseline heart rate**, antihypertensive treatment, and prevention of cardiovascular outcomes in ASCOT (Anglo-Scandinavian Cardiac Outcomes Trial). J Am Coll Cardiol 2009; 54:1154-1161.
Powe DG et al. Beta-blocker drug therapy reduces **secondary cancer formation in breast cancer** and improves cancer specific survival. Oncotarget 2010; 1:628.
Prey S, Voisard JJ, Delarue A, et al. Safety of **Propranolol** Therapy for Severe **Infantile Hemangioma**. JAMA. 2016 Jan 26;315(4):413-5
Price C et al. Propranolol vs corticosteroids for infantile hemangiomas. Arch Dermatol Dec 2011; 147(12):1371-76.
Propranolol for small abdominal aortic aneurysms: results of a randomized trial. J Vasc Surg. 2002;35:72–79.
Püttgen K, Lucky A, Adams D, et al. **Topical Timolol** Maleate Treatment of **Infantile Hemangiomas**. Pediatrics.2016 Aug 15.
Puymirat E, Riant E, Aissoui N, et al. **β blockers and mortality after myocardial infarction in patients without heart failure**: multicentre prospective cohort study. BMJ. 2016 Sep 20;354:i4801.
Qaseen A, Fihn SD, Dallas P, et al. Management of patients with **stable ischemic heart disease** (**SIHD**): Executive summary of a clinical practice guideline from the American College of Physicians, American College of Cardiology Foundation/American Heart Association (**AHA**)/American Association for Thoracic Surgery/Preventive Cardiovascular Nurses Association/Society of Thoracic Surgeons. Ann Intern Med 2012.
Quint JK, Herrett E, Bhaskaran K, et al. Effect of **β blockers on mortality after myocardial infarction in adults with COPD**: population based cohort study of UK electronic healthcare records. BMJ. 2013 Nov 22;347:f6650.
Rabinovich-Guilatt L, Steiner L, Hallak H, et al. **Metoprolol-pridopidine** drug-drug interaction and food effect assessments of pridopidine, a new drug for treatment of Huntington Disease. Br J Clin Pharmacol. 2017 Apr 27.
Raheem IA, Saaid R, Omar SZ, et al. **Oral nifedipine versus intravenous labetalol** for acute blood pressure control in **hypertensive emergencies of pregnancy**: a randomised trial. BJOG. 2012 Jan;119(1):78-85.
Rangel Carlos; Shu Richard G.; Lazar Lawrence D. et al; {beta}-Blockers for Chest Pain Associated With Recent **Cocaine Use** Arch Intern Med. 2010;170(10):874-879.
Redelmeier D, Scales D, Kopp A. {beta} blockers for **elective surgery** in elderly patients: population based, retrospective cohort study. BMJ. 2005 Oct 6; [Epub ahead of print] CONCLUSIONS: Patients receiving metoprolol do not have as low a perioperative cardiac risk as patients receiving atenolol, in accord with possible acute withdrawal after missed doses.
Reiberger T, Mandorfer M. **Beta adrenergic blockade and decompensated cirrhosis**. J Hepatol. 2016 Nov 15.
Richards TR, Tobe SW. **Combining Other Antihypertensive Drugs With β-Blockers** in Hypertension: A Focus on Safety and Tolerability. Can J Cardiol. 2014 Feb 8. pii: S0828-282X(13)01367-6.
Richman JS, Itani KM, Deierhoi RJ, et al. Improved Outcomes Associated With a Revised Quality Measure for Continuing **Perioperative β-Blockade**. JAMA Surg. 2014 Aug 20.
Rienstra M, Damman K, Mulder BA, et al. **Beta-blockers and outcome in heart failure and atrial fibrillation**. A meta-analysis. JACC:Heart Fail 2013; 1:21-28.
Ripley TL, Saseen JJ. **β-Blockers**: A Review of Their Pharmacological and Physiological Diversity in Hypertension. Ann Pharmacother. 2014 Jun;48(6):723-33.
Roden DM. Clinical practice. **Long-QT syndrome**. N Engl J Med. 2008 Jan 10;358(2):169-76.
Roy D, Talajic M, Nattel S, Wyse DG, et al. Atrial Fibrillation and Congestive Heart Failure Investigators. Rhythm control versus **rate control** for atrial fibrillation and heart failure. (**AF-CHF**) N Engl J Med. 2008 Jun 19;358(25):2667-77. In patients with atrial fibrillation and congestive heart failure, a routine strategy of rhythm control does not reduce the rate of death from cardiovascular causes, as compared with a rate-control strategy.
Rutten Frans H.; Zuithoff Nicolaas P. A.; et al; {beta}-Blockers May Reduce Mortality and Risk of Exacerbations in Patients With **Chronic Obstructive Pulmonary Disease**. Arch Intern Med. 2010;170(10):880-887.
Ruwald MH, Ruwald AC, Jons C, et al. Effect of **metoprolol** (~64mg) **versus carvedilol** (~18mg) on outcomes in **MADIT-CRT** (Multicenter Automatic Defibrillator Implantation Trial with Cardiac Resynchronization Therapy). J Am Coll Cardiol 2013; 61:1518-1526.
Salpeter S, Ormiston T, Salpeter E, Salpeter S Md. Cardioselective beta-blockers for chronic obstructive pulmonary disease. Cochrane Database Syst Rev. 2005 Oct 19;4:CD003566. AUTHORS' CONCLUSIONS: Cardioselective beta-blockers, given to patients with COPD in the identified studies did not produce adverse respiratory effects. Given their demonstrated benefit in conditions such as heart failure, coronary artery disease and hypertension, cardioselective beta-blockers should not be routinely withheld from patients with COPD.
Salpeter S, Ormiston T, Salpeter E. Cardioselective beta-blockers for reversible airway disease. Cochrane Database Syst Rev. 2002;(1):CD002992. CONCLUSIONS: Cardioselective beta1-blockers, given to patients with mild-moderate reversible airway disease, do not produce clinically significant adverse respiratory effects in the short term. It is not possible to comment on their effects in patient with more severe or less reversible disease, or on their effect on the frequency or severity of acute exacerbations. Given their demonstrated benefit in conditions such as heart failure, coronary artery disease and hypertension, cardioselective beta1-blockers should not be withheld from patients with mild-moderate reversible airway disease.
Sampat U, Varadarajan P, Turk R, et al. Effect of beta-blocker therapy on survival in patients with **severe aortic regurgitation**. Results from a cohort of 756 patients. J Am Coll Cardiol 2009; 54:452-457.
Sanghvi KP, Kabra NS, Padhi P, et al. **Prophylactic propranolol for prevention of ROP and visual** outcome at 1 year (**PreROP** trial). Arch Dis Child Fetal Neonatal Ed. 2017 Jan 13.
Sarafidis P, Bogojevic Z, Basta E, Kirstner E, Bakris GL. Comparative efficacy of two different beta-blockers on 24-hour blood pressure control. J Clin Hypertens (Greenwich). 2008 Feb;10(2):112-8. In conclusion, metoprolol succinate was more effective in sustaining 24-hour and early morning BP reductions compared with atenolol in a small group of hypertensive patients also treated with once-daily low-dose hydrochlorothiazide.
Schaer BA, Schneider C, Jick SS, et al. Risk for **incident AF** in patients who receive antihypertensive drugs. Ann Intern Med 2010; 152:78-84.
Scheer FA, Morris CJ, Garcia JI, et al. Repeated **melatonin supplementation** improves sleep in hypertensive patients treated with Beta-blockers: a randomized controlled trial. Sleep. 2012 Oct 1;35(10):1395-402.
Schwartz BG, Rezkalla S, Kloner RA. Cardiovascular effects of **cocaine**. Circulation. 2010 Dec 14;122(24):2558-69.
Seegobin K, Maharaj S, Deosaran A, Reddy P. **Severe beta blocker and calcium channel blocker overdose**: **Role of high dose insulin**. Am J Emerg Med. 2018 Jan 10.
Seely EW, Ecker J. Clinical practice. **Chronic hypertension in pregnancy**. N Engl J Med. 2011 Aug 4;365(5):439-46.
Senzolo M, Cholongitas E, Burra P, et al. beta-Blockers protect against **spontaneous bacterial peritonitis** in cirrhotic patients: a meta-analysis. Liver Int. 2009 Apr 28. [Epub ahead of print] This analysis suggests a role of beta-blockers in preventing SBP in ascitic cirrhotics, independent of haemodynamic response. Further formal RCTs are needed to confirm this finding.
Sersté T, Melot C, Francoz C, et al. **Deleterious effects of beta-blockers** on survival in patients with cirrhosis and **refractory ascites**. Hepatology. 2010 May 25.
Shaddy RE, Boucek MM, Hsu DT, et al. Pediatric Carvedilol Study Group. **Carvedilol for children** and adolescents with heart failure: a randomized controlled trial. JAMA. 2007 Sep 12;298(10):1171-9. These preliminary results suggest that carvedilol does not significantly improve clinical heart failure outcomes in children and adolescents with symptomatic systolic heart failure. However, given the lower than expected event rates, the trial may have been underpowered. There may be a differential effect of carvedilol in children and adolescents based on ventricular morphology.
Shah A, Moon-Grady A, Bhogal N, et al. Effectiveness of **sotalol as first-line therapy for fetal supraventricular tachyarrhythmias**. Am J Cardiol. 2012 Jun 1;109(11):1614-8.
Shah SD, Baselga E, McCuaig C. **Rebound growth of infantile hemangiomas** after **propranolol** therapy. Pediatrics. 2016;137(4):e20151754
Shahin MH, Conrado DJ, Gonzalez D, et al. **Genome-Wide Association Approach** Identified Novel Genetic **Predictors of Heart Rate Response to β-Blockers**. J Am Heart Assoc. 2018 Feb 24;7(5).
Shavadia JS, Holmes DN, Thomas L, et al. Comparative Effectiveness of **β-Blocker Use Beyond 3 Years After Myocardial Infarction** and Long-Term Outcomes Among Elderly Patients. Circ Cardiovasc Qual Outcomes. 2019 Jul;12(7):e005103.
Shayan, Yasaman R., Prendiville, Julie S., Goldman, Ran D. Use of **propranolol in treating hemangiomas**. Can Fam Physician 2011 57: 302-303.
Sheikh AS, Ali K, Mazhar S. **Acute aortic syndrome**. Circulation. 2013 Sep 3;128(10):1122-7. (First line IV beta-blockers)
Shores J, Berger KR, Murphy EA, Pyeritz RE. Progression of aortic dilatation and the benefit of long-term beta-adrenergic blockade (**propranolol**) in **Marfan's syndrome**. N Engl J Med. 1994;330:1335–1341
Short Philip M, Lipworth Samuel I W, Elder Douglas H J, et al. Effect of **β blockers in treatment of chronic obstructive pulmonary disease**: a retrospective cohort study. BMJ 2011;342:doi:10.1136/bmj.d2549 (10 May 2011)
Short PM, Anderson WJ, Williamson PA, et al. Effects of **intravenous and oral β-blockade in persistent asthmatics** controlled on inhaled corticosteroids. Heart. 2013 Nov 7.
Sipahi I, Tuzcu EM, Wolski KE, Nicholls SJ, Schoenhagen P, Hu B, Balog C, Shishehbor M, Magyar WA, Crowe TD, Kapadia S, Nissen SE. Beta-blockers and progression of coronary atherosclerosis: pooled analysis of 4 intravascular ultrasonography trials. Ann Intern Med. 2007 Jul 3;147(1):10-8. The analysis demonstrates that beta-blockers can slow progression of coronary atherosclerosis.
Sousa-Uva M, Head SJ, Milojevic M, et al; Document Reviewers. **2017 EACTS Guidelines on perioperative medication in adult cardiac surgery**. Eur J Cardiothorac Surg. 2017 Oct 6.
Stecker EC, et al. Prophylactic **pacemaker** use to allow beta-blocker therapy in patients with chronic heart failure with bradycardia. Am Heart J. 2006 Apr;151(4):820-8.

Steinman MA, Zullo AR, Lee Y, et al. Association of **β-blockers with functional outcomes, death, and rehospitalization in older nursing home residents after acute myocardial infarction** [online Dec 12, 2016]. JAMA Intern Med. doi:10.1001/jamainternmed.2016.7701

Stern T, Cifu AS. **Perioperative β-Blocker Therapy**. JAMA. 2015 Jun 23-30;313(24):2486-7.

Suzuki T, Isselbacher EM, Nienaber CA, et al. Type-Selective Benefits of Medications in Treatment of **Acute Aortic Dissection** (from the International Registry of Acute Aortic Dissection [IRAD]). Am J Cardiol. 2011 Sep 23.

Synnes A. Screening for **Neonatal Hypoglycemia** After Fetal Exposure to **β-Blockers**. Pediatrics. 2016 Sep;138(3).

Tachjian A, Maria V, Jahangir A. Use of herbal products and potential interactions in patients with cardiovascular diseases. J Am Coll Cardiol. 2010 Feb 9;55(6):515-25.

Talwalkar JA, Kamath PS. An evidence-based medicine approach to beta-blocker therapy in patients with **cirrhosis**. Am J Med. 2004 Jun 1;116(11):759-66.

Tan ST, Itinteang T, Leadbitter P. Low-dose propranolol for multiple **hepatic and cutaneous hemangiomas** with deranged liver function. Pediatrics. 2011 Mar;127(3):e772-6.

Tess AV, Smetana GW. Medical evaluation of patients undergoing **electroconvulsive** therapy. N Engl J Med. 2009 Apr 2;360(14):1437-44.

The Cardiac Insufficiency Bisoprolol Study II (**CIBIS-II**): a randomised trial. Lancet. 1999 Jan 2;353(9146):9-13.

Thomas L. Managing **hypertensive emergencies** in the ED. Can Fam Physician. 2011 Oct;57(10):1137-97.

Tobe SW. **β-adrenergic receptor blockers in hypertension**. Can J Cardiol. 2014 May;30(5 Suppl):S1-2.

Tripathi D, Ferguson JW, Kochar N, et al.. Randomized controlled trial of **carvedilol** versus variceal band ligation for the prevention of the first **variceal bleed**. Hepatology. 2009 Apr 24. [Epub ahead of print] Carvedilol is effective in preventing the first variceal bleed. Carvedilol is an option for primary prophylaxis in patients with high-risk esophageal varices.

Treatment Guidelines from the Medical Letter. Pharmaceutical Drug **Overdose**. Sept 2006. (Beta blockers/Calcium-channel blockers: Treatment glucagon, calcium chloride, calcium gluconate)

Tsujimoto T, Kajio H, Shapiro MF, et al. **Risk of All-Cause Mortality in Diabetic Patients Taking β-Blockers**. Mayo Clin Proc. 2018 Apr;93(4):409-418.

Turnes J, et al. Pharmacological reduction of portal pressure and long-term risk of first **variceal bleeding** in patients with cirrhosis. Am J Gastroenterol. 2006 Mar;101(3):506-12.

Urbach DR, Bell CM. A Revised Quality Measure for Surgical Care: More Alpha Testing for **Perioperative β-Blockers**? JAMA. 2015 Jun 16;313(23):2369-70.

UK Prospective Diabetes Study Group. Efficacy of atenolol and captopril in reducing risk of macrovascular and microvascular complications in type 2 diabetes: UKPDS 39. BMJ 1998;317:713-9.

Valle JA, Zhang M, Dixon S, et al. Impact of **Pre-Procedural Beta Blockade** on Inpatient Mortality in Patients Undergoing Primary Percutaneous Coronary Intervention for ST Elevation Myocardial Infarction. Am J Cardiol. 2013 Mar 22.

van Gelder IC, Groenveld HF, Crijns HJ, et al. **Lenient** versus strict **rate control** in patients with atrial fibrillation. (**RACE 2**) N Engl J Med 2010; DOI:10.1056/NEJMoa1001337.

van Gestel YR, Hoeks SE, Sin DD, et al. The Impact of **Cardioselective Beta-Blockers** on Mortality in Patients with **COPD and Atherosclerosis**. Am J Respir Crit Care Med. 2008 Jun 19. [Epub ahead of print] Cardioselective beta-blockers were associated with reduced mortality in COPD patients undergoing vascular surgery. In carefully selected patients with **COPD**, the use of cardioselective beta-blockers appears to be safe and associated with reduced mortality.

Veselka J, Anavekar NS, Charron P. **Hypertrophic obstructive cardiomyopathy**. Lancet. 2016 Nov 29.

Villanueva C, Albillos A, Genesca J, et al. beta blockers **to prevent decompensation of cirrhosis** in patients with clinically significant portal hypertension (PREDESCI): a randomised, double-blind, placebo-controlled, multicentre trial. Lancet. 2019 Mar 22.

Viollet L, Thrush PT, Flanigan KM, et al. Effects of Angiotensin-Converting Enzyme Inhibitors and/or Beta Blockers on the **Cardiomyopathy in Duchenne Muscular Dystrophy**. Am J Cardiol. 2012 Mar 29.

Waqar S, Sarkar PK. **Exacerbation of psoriasis** with beta-blocker therapy. CMAJ. 2009 Jul 7;181(1-2):60.

Wang HM, Liao ZX, Komaki R, et al. **Improved survival** outcomes with the incidental use of beta-blockers among patients with non-small-cell **lung cancer** treated with definitive radiation therapy. Ann Oncol, 9 Jan.

Wann L. Samuel, Curtis Anne B., Ellenbogen Kenneth A., et al. **2011 ACCF/AHA/HRS Focused Update on the Management of Patients With Atrial Fibrillation (Update on Dabigatran):** A Report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines Circulation published February 14, 2011, doi:10.1161/CIR.0b013e31820f14c0 http://circ.ahajournals.org/cgi/reprint/CIR.0b013e31820f14c0v1

Warmack TS, Estes MA, Heldenbrand S, Franks AM. {beta}-Adrenergic Antagonists in **Hypertension**: A Review of the Evidence (December). Ann Pharmacother. 2009 Nov 24.

Watkins JL, Thaker PH, Nick AM, et al. Clinical impact of selective and nonselective **beta-blockers** (eg. **propranolol**) on survival in patients with **ovarian cancer**. Cancer. 2015 Aug 24.

Wax PM, et al. **Beta-blocker ingestion**: an evidence-based consensus guideline for out-of-hospital management. Clin Toxicol (Phila). 2005;43(3):131-46. http://www.aapcc.org/FinalizedPMGdlns/beta-blocker%20guideline%20for%20AAPCC%202005-3-30.pdf

Webb AJS, Fischer U, Rothwell PM. Effects of **beta-blocker selectivity** on **blood pressure variability and stroke**: a systematic review. Neurology 2011;77:731–737.

Weber MA, Schiffrin EL, White WB, et al. **ASH/ISH**: Clinical practice guidelines for the **management of hypertension** in the community. A statement by the American Society of Hypertension and the International Society of Hypertension. *J Clin Hypertens* 2013; DOI:10.1111/jch.12237.

Wigley FM, Flavahan NA. **Raynaud's Phenomenon**. N Engl J Med. 2016 Aug 11;375(6):556-65

Wijeysundera DN, Mamdani M, Laupacis A, et al. Clinical Evidence, Practice Guidelines, and β-Blocker Utilization **Before Major Noncardiac Surgery**. Circ Cardiovasc Qual Outcomes. 2012 Jun 26

Wijeysundera DN, Duncan D, Nkonde-Price C, et al. **Perioperative Beta Blockade in Noncardiac Surgery: A Systematic Review for the 2014 ACC/AHA Guideline** on Perioperative Cardiovascular Evaluation and Management of Patients Undergoing Noncardiac Surgery: A Report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. J Am Coll Cardiol. 2014 Dec 9;64(22):2406-25.

Wikstrand J, Warnold I, Olsson G, Tuomilehto J, Elmfeldt D, Berglund G. Primary prevention with metoprolol in patients with hypertension. Mortalityresults from the **MAPHY** study. JAMA. 1988 Apr 1;259(13):1976-82.

Willenheimer R, van Veldhuisen DJ, Silke B, et al. Effect on Survival and Hospitalization of Initiating Treatment for Chronic Heart Failure With Bisoprolol Followed by Enalapril, as Compared With the Opposite Sequence. Results of the Randomized Cardiac Insufficiency Bisoprolol Study (CIBIS) III. Circulation. 2005 Sep 4; [Epub ahead of print] CONCLUSIONS: Although noninferiority of bisoprolol-first versus enalapril-first treatment was not proven in the per-protocol analysis, our results indicate that it may be as safe and efficacious to initiate treatment for CHF with bisoprolol as with enalapril. n=1010.

Willenheimer R. Effect on mode and cause of death of initiation of treatment for chronic heart failure with bisoprolol followed by additional enalapril compared to the opposite sequence: results of the randomized **CIBIS III** trial. World Congress of Cardiology 2006; September 6, 2006; Barcelona, Spain.

Winchester DE, Pepine CJ. Usefulness of **Beta Blockade in Contemporary Management** of Patients With Stable Coronary Heart Disease. Am J Cardiol. 2014 Aug 27.

Wiysonge C, et al. **Beta-blockers for hypertension**. Cochrane Database Syst Rev. 2007 Jan 24;(1):CD002003. The available evidence does not support the use of beta-blockers as first-line drugs in the treatment of hypertension. This conclusion is based on the relatively weak effect of beta-blockers to reduce stroke and the absence of an effect on coronary heart disease when compared to placebo or no treatment. More importantly, it is based on the trend towards worse outcomes in comparison with calcium-channel blockers, renin-angiotensin system inhibitors, and thiazide diuretics. Most of the evidence for these conclusions comes from trials where atenolol was the beta-blocker used (75% of beta-blocker participants in this review). However, it is not known at present whether beta-blockers have differential effects on younger and elderly patients or whether there are differences between the different sub-types of beta-blockers.

Wiysonge CS, Bradley HA, Volmink J, et al. **Beta-blockers for hypertension**. Cochrane Database Syst Rev. 2012 Aug 15;8:CD002003. Initiating treatment of hypertension with beta-blockers leads to modest reductions in cardiovascular disease and no significant effects on mortality. These effects of beta-blockers are inferior to those of other antihypertensive drugs.

Wiysonge CS, Opie LH. **β-Blockers as initial therapy for hypertension**. JAMA. 2013 Nov 6;310(17):1851-2.

Wiysonge CS, Bradley HA, Volmink J, et al. **Beta-blockers for hypertension**. Cochrane Database Syst Rev. 2017 Jan 20;1:CD002003. Most outcome RCTs on beta-blockers as initial therapy for hypertension have high risk of bias. Atenolol was the beta-blocker most used. Current evidence suggests that initiating treatment of hypertension with beta-blockers leads to modest CVD reductions and little or no effects on mortality. These beta-blocker effects are inferior to those of other antihypertensive drugs. Further research should be of high quality and should explore whether there are differences between different subtypes of beta-blockers or whether beta-blockers have differential effects on younger and older people.

Wong GW, Wright JM. Blood pressure lowering efficacy of **nonselective beta-blockers** for primary hypertension. Cochrane Database Syst Rev. 2014 Feb 28;2:CD007452. doi: 10.1002/14651858.CD007452.pub2. In people with mild-to-moderate hypertension, nonselective beta-blockers lowered peak BP by a mean of -10/-7 mmHg (systolic/diastolic) and reduced heart rate by 12 beats per minute. Propranolol and penbutolol were the two drugs that contributed to most of the data for nonselective beta-blockers. This estimate is likely exaggerated due to the presence of extreme outliers and other sources of bias. If we removed the extreme outliers from the analysis, the estimate for non-selective beta-blockers was lower (-8/-5 mmHg (systolic/diastolic)). Nonselective beta-blockers did not show a convincing graded dose-response in the recommended dose range for systolic BP and diastolic BP, while higher dose nonselective beta-blockers provided greater reduction of heart rate. Using higher dose nonselective beta-blockers might cause more side effects, such as bradycardia, without producing an additional BP lowering effect. The effect of nonselective beta-blockers on pulse pressure was likely small, at about 2 mmHg.

World Gastroenterology Organisation (WGO). **Esophageal varices**. Munich (Germany): WGO; 2008 Jun. 17 p. http://www.worldgastroenterology.org/assets/downloads/en/pdf/guidelines/18_treatment_e_varices_en.pdf

Wright JM, Musini VM. First-line drugs for hypertension. Cochrane Database Syst Rev. 2009 Jul 8;(3):CD001841. First-line low-dose thiazides reduce all morbidity and mortality outcomes. First-line ACE inhibitors and calcium channel blockers may be similarly effective but the evidence is less robust. First-line high-dose thiazides and first-line beta-blockers are inferior to first-line low-dose thiazides.

Wu S, Han J, Li WQ, et al. Hypertension, Antihypertensive Medication Use, and **Risk of Psoriasis**. JAMA Dermatol. 2014 Jul 2.

Wyse DG, Waldo AL, DiMarco JP, et al. Atrial Fibrillation Follow-up Investigation of Rhythm Management (**AFFIRM**) Investigators. A comparison of rate control and rhythm control in patients with atrial fibrillation. N Engl J Med. 2002 Dec 5;347(23):1825-33. Management of atrial fibrillation with the rhythm-control strategy offers no survival advantage over the **rate-control** strategy, and there are potential advantages, such as a lower risk of adverse drug effects, with the rate-control strategy. Anticoagulation should be continued in this group of high-risk patients.

Zhang H, Yuan X, Zhang H, et al. Efficacy of **Long-Term β-Blocker Therapy for Secondary Prevention** of Long-Term Outcomes After Coronary Artery Bypass Grafting Surgery. Circulation. 2015 Jun 23;131(25):2194-201.

Zimetbaum Peter. **In the Clinic: Atrial Fibrillation**. *Ann Intern Med* December 7, 2010 153:ITC6-1; doi:10.1059/0003-4819-153-11-201012070-01006

CALCIUM CHANNEL BLOCKER (CCB): Comparison Chart

[1] Major Outcomes in High-Risk Hypertensive Patients Randomized to Angiotensin-Converting Enzyme Inhibitor or Calcium Channel Blocker vs Diuretic. The Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial (**ALLHAT**). The ALLHAT Officers and Coordinators for the ALLHAT Collaborative Research Group. JAMA. 2002;288:2981-2997.

[2] 2001 Canadian Hypertension Recommendations: What's New & What's Not so New but is Still Important. CJHP 2002;55:4651.

[3] FA McAlister, M Levine, KB Zarnke, et al. The 2000 recommendations for the management of hypertension. Can J Cardiol 2001; 17(5):543-559.

[4] 1999 Canadian recommendations for the management of hypertension. CMAJ 1999;161(Suppl):S1-S16.

[5] **1999 World Health Organization**–International Society of Hypertension Guidelines:Management of Hypertension. J Hypertens 1999;17:151-183.

[6] 6th Report-Joint National Committee on Prevention,Detection,Evaluation & Treatment of High Blood Pressure. Arch Intern Med 1997;157:2413-46.

[7] Drugs for hypertension. Med Lett Drugs Ther 2001;43:17-22.

[8] Drugs in Pregnancy & Lactation, 11th Ed. Briggs GE,et al. Wilkins;Baltimore, MD.2017.

[9] Micromedex 2018 online

[10] Hansten & Horn's Drug Interactions: Analysis & Management-Facts & Comparisons 2008.

[11] Treatment Guidelines: **Drugs for Hypertension** from The Medical Letter Feb 2003, repeated June 2005, January 2009, January 2012, May 2014 & updated **March 2017**.

[12] The **2017 Canadian** Hypertension Education Program **Recommendations** www.hypertension.ca
Leung AA, Nerenberg K, Daskalopoulou SS, et al; CHEP Guidelines Task Force. Hypertension Canada's **2016 CHEP guidelines** for blood pressure measurement, diagnosis, assessment of risk, prevention and treatment of hypertension. Can J Cardiol 2016 (accepted manuscript) doi: 10.1016/j.cjca.2016.02.066 www.onlinecjc.ca/article/S0828-282X(16)00192-6/pdf (accessed April 11, 2016).
Hackam DG, Quinn RR, Ravani P, et al. Canadian Hypertension Education Program. The 2013 Canadian Hypertension Education Program (CHEP) Recommendations for Blood Pressure Measurement, Diagnosis, Assessment of Risk, Prevention, and Treatment of Hypertension. Can J Cardiol. 2013 Mar 28.
Canadian Hypertension Education Program. **2011 CHEP recommendations** for the management of **hypertension**. http://hypertension.ca/chep/wp-content/uploads/2011/05/FullCHEPRecommendations_EN_2011.pdf .
Dionne JM, Harris KC, Benoit G, et al. **Hypertension Canada's 2017 Guidelines for the Diagnosis, Assessment, Prevention, & Treatment of Pediatric Hypertension**. Can J Cardiol. 2017 May;33(5):577-585
Leung AA, Daskalopoulou SS, Dasgupta K, et al. **Hypertension Canada's 2017 Guidelines for Diagnosis, Risk Assessment, Prevention, & Treatment of Hypertension in Adults**. Can J Cardiol. 2017 May;33(5):557-576
Nerenberg KA, Zarnke KB, Leung AA, et al; Hypertension Canada. **Hypertension Canada's 2018 Guidelines** for Diagnosis, Risk Assessment, Prevention, and Treatment of Hypertension in Adults and Children. Can J Cardiol. 2018 May;34(5):506-525.

[13] ALLHAT Working Group. Major cardiovascular events in hypertensive patients randomized to doxazosin vs chlorthalidone: the antihypertensive and lipid-lowering treatment to prevent heart attack trial (**ALLHAT**). JAMA 2000;283:1967-75.

[14] The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (The **JNC 7**); JAMA. **2003** May;289(19):2560-72.
James PA, Oparil S, Carter BL, et al. **2014** evidence-based guideline for the management of **high blood pressure in adults**: report from the panel members appointed to the Eighth Joint National Committee (**JNC 8**). JAMA. doi:10.1001/jama.2013.284427.

[15] Black HR, Elliott WJ, et al. Principal results of the Controlled Onset Verapamil Investigation of Cardiovascular End Points (**CONVINCE**) trial. JAMA. 2003 Apr 23-30;289(16):2073-82. The CONVINCE trial did not demonstrate equivalence of a COER verapamil-based antihypertensive regimen compared with a regimen beginning with a diuretic or beta-blocker. When considered in the context of other trials of calcium antagonists, these data indicate that the effectiveness of calcium-channel therapy in reducing cardiovascular disease is similar but not better than diuretic or beta-blocker treatment.

[16] Ruggenenti P, Fassi A, Ilieva AP, ET AL. Preventing Microalbuminuria in Type 2 Diabetes (**BENEDICT**). N Engl J Med. 2004 Oct 31
Ruggenenti P, Fassi A, Ilieva AP, et al. BENEDICT-B Study Investigators. Effects of verapamil added-on trandolapril therapy in hypertensive type 2 diabetes patients with microalbuminuria: the BENEDICT-B randomized trial. J Hypertens. 2011 Feb;29(2):207-16.

[17] Turnbull F; Blood Pressure Lowering Treatment Trialists' Collaboration. Effects of different blood-pressure-lowering regimens on major cardiovascular events: results of prospectively-designed overviews of randomised trials. Lancet. 2003 Nov 8;362(9395):1527-35.

[18] Wassertheil-Smoller S, Psaty B, Greenland P, et al. Association between cardiovascular outcomes and antihypertensive drug treatment in older women. JAMA 2004; 292:2849-59.

[19] Ruggenenti P, Perna A, Loriga G, et al.; **REIN-2** Study Group. Blood-pressure control for renoprotection in patients with non-diabetic chronic renal disease: multicentre, randomised controlled trial. Lancet. 2005 Mar 12;365(9463):939-46. (Interpretation: In pts with non-diabetic proteinuric nephropathies receiving background ACE-inhibitor therapy, no additional benefit from further blood-pressure reduction by felodipine could be shown.)

Additional articles:

ACCF- AHA-HRS Atrial Fibrillation 2011 Focused Update. Circulation 2011. http://circ.ahajournals.org/cgi/reprint/CIR.0b013e3181fa3cf4v1 (Wann LS, Curtis AB, January CT, et al. 2011 ACCF/AHA/HRS focused update on the management of patients with atrial fibrillation (updating the 2006 guideline): A report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. Circulation 2010; DOI: 10.1161/CIR.0b013e3181fa3cf4.)

ACC/AHA 2017 Whelton PK, et al. **2017 ACC/AHA**/AAPA/ABC/ACPM/AGS/APhA/ASH/ASPC/NMA/PCNA **Guideline for the Prevention, Detection, Evaluation, and Management of High Blood Pressure** in Adults: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. Hypertension. 2017 Nov 13.

Alabdulrazzaq F, Koren G. **Fetal safety** of calcium channel blockers. Can Fam Physician. 2012 Jul;58(7):746-7.

Allan GM, Ivers N, Kolber M. **Medical management of renal stones**: More than analgesia? Can Fam Physician. 2011 Feb;57(2):198.

American College of Obstetricians and Gynecologists (**ACOG**). **Chronic hypertension in pregnancy**. Washington (DC): American College of Obstetricians and Gynecologists (ACOG); 2012 Feb. 12.

Argulian E, Messerli FH, Aziz EF, et al. Antihypertensive Therapy in **Hypertrophic Cardiomyopathy**. Am J Cardiol. 2013 Jan 19.

Bakris GL, Sarafidis PA, Weir MR, et al. Renal outcomes with different fixed-dose combination therapies in patients with hypertension at high risk for cardiovascular events (**ACCOMPLISH**): a prespecified secondary analysis of a randomised controlled trial. Lancet. 2010 Feb 17.

Bärtsch P, Swenson ER. Clinical practice: **Acute high-altitude illnesses**. N Engl J Med. 2013 Jun 13;368(24):2294-302. (nifedipine option)

Bateman B, Hernandez-Diaz S, Huybrechts K, et al. Outpatient calcium-channel blockers and the **risk of postpartum haemorrhage**: a cohort study. BJOG. 2013 Sep 11.

Bergman GJ, Khan S, Danielsson B, et al. **Breast cancer risk and use** of calcium channel blockers using Swedish population registries. JAMA Intern Med. 2014 Oct 1;174(10):1700-1.

Bernard E, Goutelle S, Bertrand Y, et al. Pharmacokinetic **drug-drug interaction of calcium channel blockers with cyclosporine** in hematopoietic stem cell transplant children. Ann Pharmacother. 2014 Dec;48(12):1580-4.

Boal AH, Smith DJ, McCallum L, et al. Monotherapy with Major **Antihypertensive Drug Classes** and Risk of Hopsital Admissions for **Mood Disorders**. Hypertension.2016 :68 :00-00. (Beta-blockers & CCBs may increase risk, ACEI & ARBs may decrease risk)

Boeckxstaens GE, Zaninotto G, Richter JE. **Achalasia**. Lancet. 2013 Jul 16.(nitrates & calcium channel blockers, botulinum toxin A)

Busby J, Mills K, Zhang SD, et al. **Postdiagnostic Calcium Channel Blocker Use and Breast Cancer Mortality**: A Population-based Cohort Study. Epidemiology. 2018 May;29(3):407-413.

Chen N, Zhou M, Yang M, et al. Calcium channel blockers versus other classes of drugs for hypertension. Cochrane Database Syst Rev. 2010 Aug 4;8:CD003654. Diuretics are preferred first-line over CCBs to optimize reduction of cardiovascular events. The review does not distinguish between CCBs, ACE inhibitors or ARBs, but does provide evidence supporting the use of CCBs over beta-blockers.

Cho SK, Kim CO, Park ES, et al. **Verapamil decreases** the glucose-lowering effect of **metformin** in healthy volunteers. Br J Clin Pharmacol. 2014 Jul 24.

Choi HK, Soriano LC, Zhang Y, Rodríguez LAG. **Calcium channel blockers, losartan**, and the risk of **incident gout** among patients with hypertension: population based case-control study. BMJ 2012;344:d8190.

Conde-Agudelo A, Romero R, Kusanovic JP. **Nifedipine in the management of preterm labor**: a systematic review and metaanalysis. Am J Obstet Gynecol. 2011 Feb;204(2):134.e1-20.

Dahlof B, Sever PS, Poulter NR, Wedel H, et al. ASCOT Investigators. Prevention of cardiovascular events with an antihypertensive regimen of amlodipine adding perindopril as required versus atenolol adding bendroflumethiazide as required, in the Anglo-Scandinavian Cardiac Outcomes Trial-Blood Pressure Lowering Arm (ASCOT-BPLA): a multicentre RCT. Lancet. 2005 Sep 10;366(9489):895-906. (InfoPOEMs: In this study, patients with hypertension and at least 3 additional cardiac risk factors have slightly fewer deaths from all causes, slightly fewer strokes, and were slightly less likely to develop diabetes if they were treated with amlodipine plus perindopril than if they were treated with atenolol and bendroflumethiazide. One would need to treat between 60 and 1000 high-risk patients for a median of 5.5 years with amlodipine instead of atenolol to prevent one additional death. (LOE = 2b))

Evangelista A, Tornos P, Sambola A, et al.. Long-term vasodilator therapy in patients with severe aortic regurgitation. N Engl J Med. 2005 Sep 29;353(13):1342-9. (InfoPOEMs: This small study does not find that vasodilators such as nifedipine (Procardia) or enalapril (Vasotec) delay the need for aortic valve replacement (AVR) in patients with asymptomatic but severe aortic regurgitation. The study was quite small, and although it is possible that a small but clinically important benefit was not detected, this seems unlikely since the trends actually run against active treatment. (LOE = 1b-))

EXPERT PANEL ON INTEGRATED GUIDELINES FOR CARDIOVASCULAR HEALTH AND RISK REDUCTION IN CHILDREN AND ADOLESCENTS. Expert Panel on Integrated Guidelines for Cardiovascular Health and Risk Reduction in Children and Adolescents: Summary Report. Pediatrics. 2011 Nov 14. [Epub ahead of print]

Flenady V, Wojcieszek AM, Papatsonis DN, et al. Calcium channel blockers for **inhibiting preterm birth**. Cochrane Database Syst Rev 2014;6:CD002255. Calcium channel blockers (mainly nifedipine) for women in preterm labour have benefits over placebo or no treatment in terms of postponement of birth thus, theoretically, allowing time for administration of antenatal corticosteroids and transfer to higher level care. Calcium channel blockers were shown to have benefits over betamimetics with respect to prolongation of pregnancy, serious neonatal morbidity, and maternal adverse effects. Calcium channel blockers may also have some benefits over ORAs and magnesium sulphate, although ORAs results in fewer maternal adverse effects. However, it must be noted that no difference was shown in perinatal mortality, and data on longer-term outcomes were limited. Further, the lack of blinding of the intervention diminishes the strength of this body of evidence. Further well-designed tocolytic trials are required to determine short- and longer-term infant benefit of CCBs over placebo or no treatment and other tocolytics, particularly ORAs. Another important focus for future trials is identifying optimal dosage regimens of different types of CCBs (high versus low, particularly addressing speed of onset of uterine quiescence) and formulation (capsules versus tablets). All future trials on tocolytics for women in preterm labour should employ blinding of the intervention and outcome assessment, include measurement of longer-term effects into early childhood, and also costs.

Flynn NO, Timmis A, Henderson R, Rajesh S, Fenu E; on behalf of the Guideline Development Group. Management of **stable angina**: summary of **NICE** guidance. BMJ. 2011 Aug 5;343:d4147. doi: 10.1136/bmj.d4147.

Fraser LA, Shariff SZ, McArthur E, et al. **Calcium channel blocker-clarithromycin drug interaction** did not increase the risk of nonvertebral fracture: a population-based study. Ann Pharmacother. 2015 Feb;49(2):185-8.

Friedman GD, Asgari MM, Warton EM, et al. Antihypertensive Drugs (hydrochlorothiazide, nifedipine) and **Lip Cancer** in Non-Hispanic Whites. Arch Intern Med. 2012 Aug 6:1-6.

Frithsen IL, Simpson WM Jr. Recognition and management of acute medication **poisoning**. Am Fam Physician. 2010 Feb 1;81(3):316-23.

Gandhi S, Fleet JL, Bailey DG, et al. **Calcium-channel blocker-clarithromycin** drug interactions and acute kidney injury. JAMA. 2013 Dec 18;310(23):2544-53.

Gersh BJ, Maron BJ, Bonow RO, et al. 2011 ACCF/AHA guideline for the diagnosis and treatment of **hypertrophic cardiomyopathy**: A report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines.Circulation 2011; DOI:10.1161/CIR.0b013e318223e2bd. http://content.onlinejacc.org/cgi/reprint/j.jacc.2011.06.011v1.pdf

Gillis AM, Verma A, Talajic M, et al. CCS Atrial Fibrillation Guidelines. **Canadian cardiovascular society atrial fibrillation guidelines 2010: rate and rhythm management**. Can J Cardiol. 2011 Jan-Feb;27(1):47-59.

Goundry B, Bell L, Langtree M, Moorthy A. Diagnosis and management of **Raynaud's phenomenon**. BMJ. 2012 Feb 7;344:e289.

Graudins A, Lee HM, Druda D. **Calcium channel and beta-blocker antagonist antidotes** and adjunct therapies. Br J Clin Pharmacol. 2015 Sep 7.

Haas DM, Caldwell DM, Kirkpatrick P, McIntosh JJ, Welton NJ. **Tocolytic therapy** for preterm delivery: systematic review and network meta-analysis. BMJ. 2012 Oct 9;345:e6226.

Hambly N, Alawfi F, Mehta S. **Pulmonary hypertension**: diagnostic approach and optimal management. CMAJ. 2016 Aug 9;188(11):804-12

Hamm CW, Bassand JP, Agewall S, et al. **ESC** Guidelines for the management of **acute coronary syndromes** in patients presenting without persistent ST-segment elevation: The Task Force for the management of acute coronary syndromes (ACS) in patients presenting without persistent ST-segment elevation of the European Society of Cardiology (ESC). Eur Heart J. 2011 Sep 21.

Hammerstrom AE. Possible **amlodipine-induced hepatotoxicity** after stem cell transplant. Ann Pharmacother. 2015 Jan;49(1):135-9.

Hollingsworth JM, et al. Medical therapy to **facilitate urinary stone passage**: a meta-analysis. Lancet. 2006 Sep 30;368(9542):1171-9. Patients given calcium-channel blockers or alpha blockers had a 65% (absolute risk reduction=0.31 95% CI 0.25-0.38) greater likelihood of stone passage than those not given such treatment (pooled risk ratio 1.65; 95% CI 1.45-1.88). The pooled risk ratio for alpha blockers was 1.54 (1.29-1.85) and for calcium-channel blockers with steroids was 1.90 (1.51-2.40). (InfoPOEMs: The limited amount of available data suggest that alpha blockers and calcium channel blockers appear to speed the passage of kidney stones. Furthermore, it appears that combining these medications with steroids provides additional benefit. (LOE = 1a-))

Jamerson K, Weber MA, Bakris GL, et al. Benazepril plus Amlodipine or Hydrochlorothiazide for Hypertension in High-Risk Patients. (**ACCOMPLISH**) N Engl J Med. 2008 Dec 4;359(23):2417-2428.
The benazepril-amlodipine combination was superior to the benazepril-hydrochlorothiazide combination in reducing cardiovascular events in patients with hypertension who were at high risk for such events.
(Bakris GL, Sarafidis PA, Weir MR, et al. Renal outcomes with different fixed-dose combination therapies in patients with hypertension at high risk for cardiovascular events (ACCOMPLISH): a prespecified secondary analysis of a randomized, controlled trial. Lancet 2010; DOI:10.1016/S0140-6736(09)62100-0.)

Julius S, Kjeldsen SE, Weber M, Brunner HR, Ekman S, Hansson L, Hua T, Laragh J, McInnes GT, Mitchell L, Plat F, Schork A, Smith B, Zanchetti A; VALUE trial group. Outcomes in hypertensive patients at high cardiovascular risk treated with regimens based on valsartan or amlodipine: the **VALUE** randomised trial. Lancet. 2004 Jun 19;363(9426):2022-31.

Jung S-Y, Choi N-K, Kim J-Y, et al. **Short-acting nifedipine and risk of stroke** in elderly hypertensive patients. Neurology 2011;77:1229 –1234.

Kulakov E, and Baron S. **Nicorandil induced perianal ulceration**. BMJ: British Medical Journal 346 (2013).

Krause T, Lovibond K, Caulfield M, McCormack T, Williams B; on behalf of the Guideline Development Group. **Management of hypertension**: summary of **NICE** guidance. BMJ. 2011 Aug 25;343:d4891.

Lafuente-Lafuente Carmelo, Isabelle Mahé, Fabrice Extramiana. Management of **atrial fibrillation**. BMJ 2009;339:b5216, doi: 10.1136/bmj.b5216

Leenen FH, et al. Clinical Events in High-Risk Hypertensive Patients Randomly Assigned to **Calcium Channel Blocker Versus Angiotensin-Converting Enzyme Inhibitor** in the Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial. Hypertension. 2006 Jul 24; [Epub ahead of print]

Li CI, Daling JR, Tang JC, Haugen KL, et al.. Use of **antihypertensive medications and breast cancer (calcium channel blockers)** risk among women aged 55 to 74 years [online August 5, 2013]. JAMA Intern Med.

Liu L, Zhang Y, Liu G, Li W, Zhang X, Zanchetti A. The **Felodipine Event Reduction (FEVER)** Study: a randomized long-term placebo controlled trial in Chinese hypertensive patients. *J Hypertens*. 2005;23:2157–2172.

López-Pintor RM, et al. Amlodipine and **nifedipine** used with cyclosporine induce different effects on **gingival enlargement**. Transplant Proc. 2009 Jul-Aug;41(6):2351-3.

Lyell DJ, Pullen KM, Mannan J, et al. Maintenance **nifedipine tocolysis** compared with placebo: a randomized controlled trial. Obstet Gynecol. 2008 Dec;112(6):1221-6. When compared with placebo, maintenance nifedipine tocolysis did not confer a large reduction in preterm birth or improvement in neonatal outcomes.

Maher MA, Sayyed TM, El-Khadry SW. **Nifedipine alone or combined with sildenafil citrate for management of threatened preterm labour**: a randomised trial. BJOG. 2018 Oct 13.

Makani H, Bangalore S, Romero J, et al. Effect of Renin-Angiotensin system blockade (ACEI/ARB) on calcium channel blocker-associated **peripheral edema**. Am J Med. 2011 Feb;124(2):128-35.

Medical Letter- Treatment Guidelines. **Treatment of Atrial Fibrillation**. Sept 2010.

Melmed S, Casanueva FF, Hoffman AR, et al. **Diagnosis and treatment of hyperprolactinemia**: an endocrine society clinical practice guideline. J Clin Endocrinol Metab. 2011 Feb;96(2):273-88.

Morgan MS, Pearle MS. Medical management of **renal stones**. BMJ. 2016 Mar 14;352:i52.

NICE: National Institute for Health and Clinical Excellence. **Hypertension Guidelines**. Aug 2011. http://www.nice.org.uk/nicemedia/live/13561/56015/56015.pdf

Non-surgical treatments for **anal fissure** in adults. Drug Ther Bull. 2013Sep;51(9):102-4.

O'Connor CM, et al. Effect of amlodipine on mode of death among patients with advanced heart failure in the **PRAISE** trial. Prospective Randomized Amlodipine Survival Evaluation. Am J Cardiol. 1998 Oct 1;82(7):881-7.

Ohman EM. Clinical Practice. **Chronic Stable Angina**. N Engl J Med. 2016 Mar 24;374(12):1167-76.

Olson KR, et al. **Calcium channel blocker ingestion**: an evidence-based consensus guideline for out-of-hospital management. Washington (DC): American Association of Poison Control Centers; 2005.
http://www.aapcc.org/DiscGuidelines/CCB%20guidelinefinal.pdf

Ovalle F, Grimes T, Xu G, et al. **Verapamil and beta cell function in adults with recent-onset type 1 diabetes**. Nat Med. 2018 Jul 9.
Pepine CJ, et al.; **INVEST** Investigators. A calcium antagonist vs a non-calcium antagonist hypertension treatment strategy for patients with coronary artery disease. The International Verapamil-Trandolapril Study (INVEST): a randomized controlled trial. JAMA. 2003 Dec 3;290(21):2805-16.
Pickard R, Starr K, MacLennan G, et al. **Medical expulsive therapy in adults with ureteric colic**: a multicentre, randomised, placebo-controlled trial. Lancet 2015; online May 19.
Pickard R, Starr K, MacLennan G, et al. Use of drug therapy in the management of symptomatic **ureteric stones** in hospitalised adults: a multicentre, placebo-controlled, randomised controlled trial and cost-effectiveness analysis of a calcium channel blocker (**nifedipine**) and an alpha-blocker (**tamsulosin**) (the **SUSPEND** trial). Health Technol Assess 2015;19:1–172.
Raebel MA, et al. **Risk of Breast Cancer** With Long-Term Use of Calcium Channel Blockers or Angiotensin-Converting Enzyme Inhibitors Among Older Women. Am J Epidemiol. 2017 Feb 15;185(4):264-273.
Raheem IA, Saaid R, Omar SZ, et al. **Oral nifedipine versus intravenous labetalol** for acute blood pressure control in **hypertensive emergencies of pregnancy**: a randomised trial. BJOG. 2012 Jan;119(1):78-85.
Roos C, Spaanderman ME, et al; APOSTEL-II Study Group. Effect of maintenance **tocolysis with nifedipine** in threatened preterm labor on perinatal outcomes: a randomized controlled trial. JAMA. 2013 Jan 2;309(1):41-7.
Rothwell PM, Howard SC, Dolan E, et al. on behalf of the ASCOT-BPLA and MRC Trial Investigators. Effects of **beta blockers and calcium-channel blockers** on within-**individual variability** in blood pressure and risk of stroke. Lancet Neurol. 2010 Mar 11.
Sanaee F, Clements JD, Waugh AW, et al. Drug-disease interaction: **Crohn's disease elevates verapamil** plasma concentrations but reduces response to the drug proportional to disease activity. Br J Clin Pharmacol. 2011 Nov;72(5):787-97. doi: 10.1111/j.1365-2125.2011.04019.x.
Saseen JJ, et al. Comparison of **nifedipine alone and with diltiazem or verapamil** in hypertension. Hypertension. 1996 Jul;28(1):109-14.
Schetz D, Kocić I. A new adverse drug reaction - **Schamberg's disease caused by amlodipine** administration - a case report. Br J Clin Pharmacol. 2015 Aug 10. Pdf Rivkees SA. Evaluating the Rare and Predicting the Worst: Lessons for Thyroid Nodules. J Pediatr. 2015 Aug 11.
Seegobin K, Maharaj S, Deosaran A, Reddy P. Severe **beta blocker and calcium channel blocker overdose**: Role of high dose **insulin**. Am J Emerg Med. 2018 Jan 10.
Shah SJ. **Pulmonary hypertension**. JAMA. 2012 Oct 3;308(13):1366-74.
Shen SC, House RA. **Hand-arm vibration syndrome**: What family physicians should know. (calcium channel blocker) Can Fam Physician. 2017 Mar;63(3):206-210.
Shibata MC, Leon H, Chatterley T, et al. Do calcium channel blockers increase the diagnosis of **heart failure** in patients with hypertension? Am J Cardiol. 2010 Jul 15;106(2):228-35.
Singh A, Alter HJ, Littlepage A. A systematic review of medical therapy to facilitate passage of **ureteral calculi**. Ann Emerg Med. 2007 Nov;50(5):552-63. Epub 2007 Aug 3. Our results suggest that "medical expulsive therapy," using either alpha-antagonists or calcium channel blockers, augments the stone expulsion rate compared to standard therapy for moderately sized distal ureteral stones. This meta-analysis of low-quality studies shows that ureteral stone passage can be enhanced by treating patients with an alpha-blocker such as tamsulosin (Flomax) or the calcium channel blocker nifedipine (Procardia). Better studies may refute these findings, but for now either approach is an option. (LOE = 1a-)
Souwer IH, Bor JH, Smits P, et al. **Nifedipine vs Placebo** for Treatment of **Chronic Chilblains**: A Randomized Controlled Trial. Ann Fam Med. 2016 Sep;14(5):453-9
St-Onge M et al. Experts consensus recommendations for the **management of calcium channel blocker poisoning** in adults. Crit Care Med 2016 Oct 3.
Stavropoulos SN, Friedel D, Modayil R, et al. Diagnosis and management of **esophageal achalasia**. BMJ. 2016 Sep 13;354:i2785.
Stone PH, et al.; Antianginal efficacy of **ranolazine** when added to treatment with amlodipine: the **ERICA** (Efficacy of Ranolazine in Chronic Angina) trial. J Am Coll Cardiol. 2006 Aug 1;48(3):566-75. Epub 2006 Jun 15.
Sucu Murat, Yuce Murat, Davutoglu Vedat. **Amlodipine-induced massive gingival** hypertrophy *Can Fam Physician* April 2011 57: 436-437.
Suzuki T, Isselbacher EM, Nienaber CA, et al. Type-Selective Benefits of Medications in Treatment of **Acute Aortic Dissection** (from the International Registry of Acute Aortic Dissection [IRAD]). Am J Cardiol. 2011Sep 23.
Tachjian A, Maria V, Jahangir A. Use of herbal products and potential interactions in patients with cardiovascular diseases. J Am Coll Cardiol. 2010 Feb 9;55(6):515-25.
Thomas L. Managing **hypertensive emergencies** in the ED. Can Fam Physician. 2011 Oct;57(10):1137-97.
Tran KC, Leung AA, et al. Efficacy of Calcium Channel Blockers on Major Cardiovascular Outcomes for the **Treatment of Hypertension in Asian Populations**: A Meta-analysis. Can J Cardiol. 2017 May;33(5):635-643.
Treatment Guidelines from the Medical Letter. Pharmaceutical Drug **Overdose**. Sept 2006. (Beta blockers/Calcium-channel blockers: Treatment glucagon, calcium chloride, calcium gluconate)
Tully PJ, Dartigues JF, Debette S, Helmer C, Artero S, Tzourio C. **Dementia risk** with antihypertensive use and blood pressure variability: A cohort study.Neurology. 2016 Aug 9;87(6):601-8.
Uniyal R, Paliwal VK, Kumar N, et al. Teaching NeuroImages: **Amlodipine-responsive trigeminal neuralgia**: An alibi for vascular compression theory. Neurology. 2017 Jul 18;89(3):e20
van Gelder IC, Groenveld HF, Crijns HJ, et al. **Lenient** versus strict **rate control** in patients with atrial fibrillation. (**RACE 2**) N Engl J Med 2010; DOI:10.1056/NEJMoa1001337.
Vaezi MF et al. ACG clinical guideline: Diagnosis and management of **achalasia**. Am J Gastroenterol 2013 Aug; 108:1238. (Options include calcium channel blockers)
Veselka J, Anavekar NS, Charron P. **Hypertrophic obstructive cardiomyopathy**. Lancet. 2016 Nov 29.
Wang L, Li YM, Li L. Meta-analysis of randomized and controlled treatment trials for achalasia. Dig Dis Sci. 2009 Nov;54(11):2303-11. Epub 2008 Dec 24. Sublingual nifedipine results in excellent or good clinical results in approximately 75% of adults with mild to moderate achalasia. For those patients not responding to pharmacotherapy, laparoscopic or thoracic myotomy is more effective than either botulinum toxin injection or pneumatic dilation. (LOE = 1a-)
Wang RC. **Managing Urolithiasis**. Ann Emerg Med. 2015 Nov 23.
Webb AJ, Rothwell PM. Effect of **dose and combination of antihypertensives on interindividual blood pressure variability**: a systematic review. Stroke. 2011 Oct;42(10):2860-5.
Weber MA, Schiffrin EL, White WB, et al. **ASH/ISH**: Clinical practice guidelines for the **management of hypertension** in the community. A statement by the American Society of Hypertension and the International Society of Hypertension. *J Clin Hypertens* 2013; DOI:10.1111/jch.12237.
Wigley FM, Flavahan NA. **Raynaud's Phenomenon**. N Engl J Med. 2016 Aug 11;375(6):556-65
Wilcox CB, Nassar N, Roberts CL. Effectiveness of **nifedipine tocolysis** to facilitate external cephalic version: a systematic review. BJOG. 2011 Mar;118(4):423-8. doi: 10.1111/j.1471-0528.2010.02824.x.
Wilson LE, D'Aloisio AA, et al. Long-term use of calcium channel blocking drugs and **breast cancer risk** in a prospective cohort of US and Puerto Rican women. Breast Cancer Res 2016. doi:10.1186/s13058-016-0720-6.
Worcester EM, Coe FL. Clinical practice. **Calcium kidney stones**. N Engl J Med. 2010 Sep 2;363(10):954-63.
Wright JM, Musini VM. First-line drugs for hypertension. Cochrane Database Syst Rev. 2009 Jul 8;(3):CD001841. First-line low-dose thiazides reduce all morbidity and mortality outcomes. First-line ACE inhibitors and calcium channel blockers may be similarly effective but the evidence is less robust. First-line high-dose thiazides and first-line beta-blockers are inferior to first-line low-dose thiazides.
Wright AJ, Gomes T, Mamdani MM, et al. The risk of **hypotension following co-prescription of macrolide antibiotics and calcium-channel blockers**. CMAJ. 2011 Feb 22;183(3):303-7.
Zimetbaum Peter. In the Clinic: **Atrial Fibrillation**. *Ann Intern Med* December 7, 2010 153:ITC6-1; doi:10.1059/0003-4819-153-11-201012070-01006

Diuretics and Miscellaneous Antihypertensives- References

1. Nerenberg KA, Zarnke KB, Leung AA, et al; Hypertension Canada. Hypertension Canada's 2018 Guidelines for Diagnosis, Risk Assessment, Prevention, and Treatment of Hypertension in Adults and Children. Can J Cardiol. 2018 May;34(5):506-525. doi: 10.1016/j.cjca.2018.02.022. Epub 2018 Mar 1. PubMed PMID: 29731013.
2. Williams B, Mancia G, Spiering W, et al; ESC Scientific Document Group . 2018 ESC/ESH Guidelines for the management of arterial hypertension. Eur Heart J. 2018 Sep 1;39(33):3021-3104.doi: 10.1093/eurheartj/ehy339. PubMed PMID: 30165516.
3. Whelton PK, Carey RM, Aronow WS, et al. ACC/AHA/AAPA/ABC/ACPM/AGS/APhA/ASH/ASPC/NMA/PCNA Guideline for the Prevention, Detection, Evaluation, and Management of High Blood Pressure in Adults: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. Hypertension. 2018 Jun;71(6):e13-e115. doi: 10.1161/HYP.0000000000000065. Epub 2017 Nov 13. Review. Erratum in: Hypertension. 2018 Jun;71(6):e140-e144. PubMed PMID: 29133356.
4. National Institute for Health Care Excellence [NICE]. Hypertension in adults: diagnosis and management. NICE. 2011 Aug 24.
5. National High Blood Pressure Education Program. The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure. Bethesda (MD): National Heart, Lung, and Blood Institute (US); 2004 Aug. PubMed PMID: 20821851.
6. James PA, Oparil S, Carter BL, et al. 2014 evidence-based guideline for the management of high blood pressure in adults: report from the panel members appointed to the Eighth Joint National Committee (JNC 8). JAMA. 2014 Feb 5;311(5):507-20. doi: 10.1001/jama.2013.284427. Erratum in: JAMA. 2014 May 7;311(17):1809. PubMed PMID: 24352797.
7. Weber MA, Schiffrin EL, White WB, et al. Clinical practice guidelines for the management of hypertension in the community: a statement by the American Society of Hypertension and the International Society of Hypertension. J Clin Hypertens (Greenwich). 2014 Jan;16(1):14-26. doi: 10.1111/jch.12237. Epub 2013 Dec 17. PubMed PMID: 24341872.
8. ACOG Practice Bulletin No. 203: Chronic Hypertension in Pregnancy. Obstet Gynecol. 2019 Jan;133(1):e26-e50.
9. Wright JM, Musini VM, Gill R. First-line drugs for hypertension. Cochrane Database Syst Rev. 2018 Apr 18;4:CD001841.
10. MHRA drug safety update: hydrochlorothiazide and non-melanoma skin cancer.Drug Ther Bull. 2019 May;57(5):70.
11. Major Outcomes in High-Risk Hypertensive Patients Randomized to Angiotensin-Converting Enzyme Inhibitor or Calcium Channel Blocker vs Diuretic. The Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial (ALLHAT). The ALLHAT Officers and Coordinators for the ALLHAT Collaborative Research Group. JAMA. 2002;288:2981-2997.
12. Veterans Cooperative Study Group on Antihypertensive Agents. Effects of treatment on morbidity in hypertension: results in patients with diastolic blood pressures averaging 115 through 129 mm Hg. JAMA. 1967;202(11):1028-1034.
13. Hypertension Detection and Follow-up Program Cooperative Group (HDFP). Five-year findings of the Hypertension Detection and Follow-up Program, I: reduction in mortality of persons with high blood pressure, including mild hypertension. JAMA. 1979;242(23):2562-2571.
14. Multiple Risk Factor Intervention Trial Research Group (MRFIT) . Multiple Risk Factor Intervention Trial: risk factor changes and mortality results. JAMA. 1982;248(12):1465-1477.
15. 2001 Canadian Hypertension Recommendations: What's New & What's Not so New but is Still Important. CJHP 2002;55:4651.
16. FA McAlister, M Levine, KB Zarnke, et al. The 2000 recommendations for the management of hypertension. Can J Cardiol 2001; 17(5):543-559.
17. 1999 Canadian recommendations for the management of hypertension. CMAJ 1999;161(Suppl):S1-S16.
18. 1999 World Health Organization–International Society of Hypertension Guidelines:Management of Hypertension. J Hypertens 1999;17:151-183.
19. 6th Report-Joint National Committee on Prevention,Detection,Evaluation & Treatment of High Blood Pressure. Arch Intern Med 1997;157:2413-46.
20. Drugs for hypertension. Med Lett Drugs Ther 2001;43:17-22.
21. Drugs in Pregnancy & Lactation, 11th Ed. Briggs GE,et al. Wilkins;Baltimore, MD.2017.
22. Micromedex 2018 online
23. Hansten & Horn's Drug Interactions: Analysis & Management-Facts & Comparisons 2008.
24. Treatment Guidelines: Drugs for Hypertension from The Medical Letter Feb 2003, repeated June 2005, January 2009, January 2012, May 2014 & updated March 2017.
25. The 2017 Canadian Hypertension Education Program Recommendations www.hypertension.ca
26. Leung AA, Nerenberg K, Daskalopoulou SS, et al; CHEP Guidelines Task Force. Hypertension Canada's 2016 CHEP guidelines for blood pressure measurement, diagnosis, assessment of risk, prevention and treatment of hypertension. Can J Cardiol 2016 (accepted manuscript) doi: 10.1016/j.cjca.2016.02.066 www.onlinecjc.ca/article/S0828-282X(16)00192-6/pdf (accessed April 11, 2016).
    Hackam DG, Quinn RR, Ravani P, et al. Canadian Hypertension Education Program. The 2013 Canadian Hypertension Education Program (CHEP) Recommendations for Blood Pressure Measurement, Diagnosis, Assessment of Risk, Prevention, and Treatment of Hypertension. Can J Cardiol. 2013 Mar 28.
    Canadian Hypertension Education Program. 2011 CHEP recommendations for the management of hypertension. http://hypertension.ca/chep/wp-content/uploads/2011/05/FullCHEPRecommendations_EN_2011.pdf .
    Dionne JM, Harris KC, Benoit G, et al. Hypertension Canada's 2017 Guidelines for the Diagnosis, Assessment, Prevention, & Treatment of Pediatric Hypertension. Can J Cardiol. 2017 May;33(5):577-585
    Leung AA, Daskalopoulou SS, Dasgupta K, et al. Hypertension Canada's 2017 Guidelines for Diagnosis, Risk Assessment, Prevention, & Treatment of Hypertension in Adults. Can J Cardiol. 2017 May;33(5):557-576
    Nerenberg KA, Zarnke KB, Leung AA, et al; Hypertension Canada. Hypertension Canada's 2018 Guidelines for Diagnosis, Risk Assessment, Prevention, and Treatment of Hypertension in Adults and Children. Can J Cardiol. 2018 May;34(5):506-525.
27. ALLHAT Working Group. Major cardiovascular events in hypertensive patients randomized to doxazosin vs chlorthalidone: the antihypertensive and lipid-lowering treatment to prevent heart attack trial (ALLHAT). JAMA 2000;283:1967-75.
28. Liu P, Arnold JM, et al. The 2002/3 Canadian Cardiovascular Society consensus guideline update for the diagnosis and management of heart failure. Can J Cardiol. 2003 Mar 31;19(4):347-56. [Arnold JM, et al.; Canadian
29. Cardiovascular Society. Canadian Cardiovascular Society consensus conference recommendations on heart failure 2006: diagnosis and management. Can J Cardiol. 2006 Jan;22(1):23-45. Erratum in: Can J Cardiol. 2006 Mar 1;22(3):271. (Arnold JM, Howlett JG, Dorian P, et al. Canadian Cardiovascular Society Consensus Conference recommendations on heart failure update 2007: Prevention, management during intercurrent illness or acute decompensation, and use of biomarkers. Can J Cardiol. 2007 Jan;23(1):21-45.)
30. Treatment Guidelines: Drugs for Treatment of Heart Failure from The Medical Letter April 2003
31. The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (The JNC 7); JAMA. 2003 May;289(19):2560-72.
32. James PA, Oparil S, Carter BL, et al. 2014 evidence-based guideline for the management of high blood pressure in adults: report from the panel members appointed to the Eighth Joint National Committee (JNC 8). JAMA. doi:10.1001/jama.2013.284427.
33. Messerli FH, Grossman E, Lever AF. Do thiazide diuretics confer specific protection against strokes? Arch Intern Med. 2003 Nov 24;163(21):2557-60.
34. Carter BL, Ernst ME, Cohen JD. Hydrochlorothiazide versus chlorthalidone: evidence supporting their interchangeability. Hypertension. 2004 Jan;43(1):4-9. Epub 2003 Nov 24.
35. Davis BR, Furberg CD, Wright JT Jr, Cutler JA, Whelton P; ALLHAT Collaborative Research Group. Setting the record straight. Ann Intern Med. 2004 Jul 6;141(1):39-46.
36. Turnbull F; Blood Pressure Lowering Treatment Trialists' Collaboration. Effects of different blood-pressure-lowering regimens on major cardiovascular events: results of prospectively-designed overviews of randomised trials. Lancet. 2003 Nov 8;362(9395):1527-35.

37. Davis BR, Furberg CD, Wright JT Jr, Cutler JA, Whelton P; ALLHAT Collaborative Research Group. ALLHAT: setting the record straight. Ann Intern Med. 2004 Jul 6;141(1):39-46.
38. Dickerson LM, Gibson MV. Management of hypertension in older persons. Am Fam Physician. 2005 Feb 1;71(3):469-76.
39. Jackson T. Wright, Jr, MD, PhD; J. Kay Dunn, PhD; et al.; for the ALLHAT Collaborative Research Group. Outcomes in Hypertensive Black and Nonblack Patients Treated With Chlorthalidone, Amlodipine, and Lisinopril. JAMA. 2005;293:1595-1608.
40. Mahboob Rahman, MD, MS; Sara Pressel, MS; Barry R. Davis, MD, PhD; et al.; for the ALLHAT Collaborative Research Group Renal Outcomes in High-Risk Hypertensive Patients Treated With an Angiotensin-Converting Enzyme Inhibitor or a Calcium Channel Blocker vs a Diuretic. A Report From the Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial (ALLHAT)
41. Arch Intern Med. 2005;165:936-946.
42. Diagnosis and Management of Chronic Heart Failure in the Adult: ACC/AHA 2005 Guideline Update for the (J Am Coll Cardiol 2005) http://www.acc.org/clinical/guidelines/failure/index.pdf
43. Pitt B, Remme W, Zannad F, et al.; Eplerenone Post-Acute Myocardial Infarction Heart Failure Efficacy and Survival Study Investigators. (EPHESUS) Eplerenone, a selective aldosterone blocker, in patients with left ventricular dysfunction after myocardial infarction. N Engl J Med. 2003 Apr 3;348(14):1309-21.
44. Yilmaz E, Batislam E, Basar MM, Tuglu D, Ferhat M, Basar H. The comparison and efficacy of 3 different a1-adrenergic blockers for distal ureteral stones. J Urology 2005; 173:2010-12. (InfoPOEMs: Alpha1-adrenergic blockers increase the frequency of spontaneous passage of distal ureteral renal stones. All 3 agents -- tamsulosin (Flomax), terazosin (Hytrin), and doxazosin (Cardura) -- were equally effective. (LOE = 2b))
45. McConnell JD, et al. The Long-Term Effect of Doxazosin, Finasteride, and Combination Therapy on the Clinical Progression of Benign Prostatic Hyperplasia. N Engl J Med. 2003 Dec 18;349(25):2387-2398. Anothaisintawee T, Attia J, Nickel JC, et al.. Management of chronic prostatitis/chronic pelvic pain syndrome: a systematic review and network meta-analysis. JAMA. 2011 Jan 5;305(1):78-86.
46. Taylor AL, Ziesche S, Yancy C, Carson P, D'Agostino R Jr, Ferdinand K, Taylor M, Adams K, Sabolinski M, Worcel M, Cohn JN; African-American Heart Failure Trial Investigators. Combination of isosorbide dinitrate (20-40mg tid) and hydralazine (37.5-75mg tid) in blacks with heart failure (A-HeFT). N Engl J Med. 2004 Nov 11;351(20):2049-57.

29. Wright JT, JA, et al, for the ALLHAT Collaborative Research Group. Outcomes in hypertensive black and nonblack patients treated with chlorthalidone, amlodipine, and lisinopril. JAMA 2005;293:1595- 608 & ACP Journal Club . (InfoPOEMs: Thiazide-type diuretics are the best initial agents for the treatment of hypertension for most patients, including both blacks and nonblacks. (LOE = 1b-))
30. Whelton PK, Barzilay J, Cushman WC, et al.; ALLHAT Collaborative Research Group. Clinical outcomes in antihypertensive treatment of type 2 diabetes, impaired fasting glucose concentration, and normoglycemia: Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial (ALLHAT). Arch Intern Med. 2005 Jun 27;165(12):1401-9.
31. Rahman M, Pressel S, Davis BR, et al. Renal outcomes in high-risk hypertensive patients treated with an angiotensin-converting enzyme inhibitor or a calcium channel blocker vs. a diuretic. A report from the antihypertensive and lipid-lowering treatment to prevent heart attack trial (ALLHAT). Arch Intern Med 2005; 165:936-46. (InfoPOEMs: It's blood pressure reduction, not the choice of drug, that prevents renal function decline in patients with hypertension, with or without diabetes. Neither the calcium channel blocker amlodipine (Norvasc) nor the angiotensin-converting enzyme inhibitor lisinopril (Prinivil) prevents the combined outcome of end-stage renal disease or a 50% decrease in renal function any better than the diuretic chlorthalidone (Hygroton). Results were the same in patients with already compromised renal function, as well as in patients with type 2 diabetes. (LOE = 1b))
32. Turnbull F, Neal B, Algert C, et al.; Blood Pressure Lowering Treatment Trialists' Collaboration. Effects of different blood pressure-lowering regimens on major cardiovascular events in individuals with and without diabetes mellitus: results of prospectively designed overviews of randomized trials. Arch Intern Med. 2005 Jun 27;165(12):1410-9.
33. Kaplan SA, et al; Medical Therapy of Prostatic Symptoms (MTOPS) Research Group. Combination therapy with doxazosin & finasteride for benign prostatic hyperplasia in patients with lower urinary tract symptoms and a baseline total prostate volume of 25 ml or greater. J Urol. 2006 Jan;175(1):217-20; discussion 220-1.
34. Rahman M, et al.; ALLHAT Collaborative Research Group. Cardiovascular outcomes in high-risk hypertensive patients stratified by baseline glomerular filtration rate. Ann Intern Med. 2006 Feb 7;144(3):172-80.
35. Khachaturian et al. Antihypertensive Medication Use and Incident Alzheimer Disease: The Cache County Study. Arch Neurol. 2006 Mar 13; [Epub ahead of print] CONCLUSIONS: These data suggest that AH medications, and specifically potassium-sparing diuretics, are associated with reduced incidence of AD. Because the latter association is a new finding, it requires confirmation in further study.
36. Pitt B, White H, Nicolau J, et al. Eplerenone reduces mortality 30 days after randomization following acute myocardial infarction in patients with left ventricular systolic dysfunction and heart failure. J Am Coll Cardiol. 2005;46:425-31.
37. Chrysostomou A, Pedagogos E, MacGregor L.. Double-blind, placebo-controlled study on the effect of the aldosterone receptor antagonist spironolactone in patients who have persistednt proteinuria and are on long-term angiotension-converting enzyme inhibitor therapy, with or without an angiotensin II receptor blocker. Clin J Am Soc Nephrol. 2006 Jan 3;1:256-62.
38. Davis BR, et al.; Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial Collaborative Research Group. Role of diuretics in the prevention of heart failure: the Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial. Circulation. 2006 May 9;113(18):2201-10. Epub 2006 May 1. HF risk decreased with chlorthalidone versus amlodipine or lisinopril use during year 1. Subsequently, risk for those individuals taking chlorthalidone versus amlodipine remained decreased but less so, whereas it was equivalent to those given lisinopril. Prior medication use, follow-up blood pressures, and concomitant medications are unlikely to explain most of the HF differences. Diuretics are superior to calcium channel blockers and, at least in the short term, angiotensin-converting enzyme inhibitors in preventing HF in hypertensive individuals.
39. Ahmed A, et al. Heart failure, chronic diuretic use, and increase in mortality and hospitalization: an observational study using propensity score methods. Eur Heart J. 2006 Jun;27(12):1431-1439. Epub 2006 May 18.
40. Hunter DJ, York M, Chaisson CE, Woods R, Niu J, Zhang Y. Recent diuretic use and the risk of recurrent gout attacks: the online case-crossover gout study. J Rheumatol. 2006 Jul;33(7):1341-5. Epub 2006 Jun 1.
41. Eshaghian S, Horwich TB, Fonarow GC. Relation of loop diuretic dose to mortality in advanced heart failure. Am J Cardiol. 2006 Jun 15;97(12):1759-64. Epub 2006 Apr 27.
42. Verhamme K, Mosis et al. Spironolactone and risk of upper gastrointestinal events: population based case-control study. BMJ. 2006 Aug 12;333(7563):330. Epub 2006 Jul 13.
43. Ho KM, Sheridan DJ. Meta-analysis of frusemide to prevent or treat acute renal failure. BMJ. 2006 Jul 21; [Epub ahead of print] (InfoPOEMs: In-hospital mortality is not affected by the use of high-dose furosemide to treat or prevent acute renal failure, and furosemide increases the hospital length of stay. (LOE = 1a))
44. Zhang W, et al. EULAR Standing Committee for International Clinical Studies Including Therapeutics. EULAR evidence based recommendations for gout. Part I: Diagnosis. Report of a task force of the Standing Committee for International Clinical Studies Including Therapeutics (ESCISIT). Ann Rheum Dis. 2006 Oct;65(10):1301-11. Epub 2006 May 17.
45. Esptein M, et al. Selective Aldosterone Blockade with Eplerenone Reduces Albuminuria in Patients with Type 2 Diabetes. Clin J Am Soc Nephrol. 2006 Sep;1(5):940-51.
46. Janssens HJ, et al. Gout, not induced by diuretics? A case-control study from primary care. Ann Rheum Dis. 2006 Aug;65(8):1080-3. Epub 2005 Nov 16.
47. Eshaghian S, Horwich TB, Fonarow GC. Relation of loop diuretic dose to mortality in advanced heart failure. Am J Cardiol. 2006 Jun 15;97(12):1759-64. Epub 2006 Apr 27.
48. Barzilay JI, Davis BR, Cutler JA, et al. Fasting Glucose Levels and Incident Diabetes Mellitus in Older NondiabeticAdults Randomized to Receive 3 Different Classes of Antihypertensive Treatment: A Report From the Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial (ALLHAT). Arch Intern Med. 2006 Nov 13;166(20):2191-201. Fasting glucose levels increase in older adults with hypertension regardless of treatment type. For those taking chlorthalidone vs other

medications, the risk of developing FG levels higher than 125 mg/dL (6.9 mmol/L) is modestly greater, but there is no conclusive or consistent evidence that this diuretic-associated increase in DM risk increases the risk of clinical events.
49. Hollingsworth JM, et al. Medical therapy to facilitate urinary stone passage: a meta-analysis. Lancet. 2006 Sep 30;368(9542):1171-9. Patients given calcium-channel blockers or alpha blockers had a 65% (absolute risk reduction=0.31 95% CI 0.25-0.38) greater likelihood of stone passage than those not given such treatment (pooled risk ratio 1.65; 95% CI 1.45-1.88). The pooled risk ratio for alpha blockers was 1.54 (1.29-1.85) and for calcium-channel blockers with steroids was 1.90 (1.51-2.40). (InfoPOEMs: The limited amount of available data suggest that alpha blockers and calcium channel blockers appear to speed the passage of kidney stones. Furthermore, it appears that combining these medications with steroids provides additional benefit. (LOE = 1a-))
50. Chobanian AV. Clinical practice. Isolated systolic hypertension in the elderly. N Engl J Med. 2007 Aug 23;357(8):789-96.
51. Black HR, Davis B, Barzilay J, Nwachuku C, et al. Metabolic and Clinical Outcomes in Non-Diabetic Individuals with the Metabolic Syndrome Assigned to Chlorthalidone, Amlodipine, or Lisinopril as Initial Treatment for Hypertension: A Report from the ALLHAT Study. Diabetes Care. 2007 Nov 13; [Epub ahead of print] Despite a less favorable metabolic profile, thiazide-like diuretic initial therapy for hypertension offers similar, and in some instances possibly superior, CV disease outcomes in older hypertensive adults with MetS, as compared to treatment with CCBs and ACEI.
52. Wright JT, Harris-Haywood S, Pressel S, et al. Clinical outcomes by race in hypertensive patients with and without the metabolic syndrome. ALLHAT. Arch Intern Med 2008; 168:207-217. The ALLHAT findings fail to support the preference for calcium channel blockers, alpha-blockers, or angiotensin-converting enzyme inhibitors compared with thiazide-type diuretics in patients with the MetS, despite their more favorable metabolic profiles.
53. Bomback AS, et al. Change in proteinuria after adding aldosterone blockers to ACE inhibitors or angiotensin receptor blockers in CKD: a systematic review. Am J Kidney Dis. 2008 Feb;51(2):199-211. Although data suggest that adding MRBs to ACE-inhibitor and/or ARB therapy yields significant decreases in proteinuria without adverse effects of hyperkalemia and impaired renal function, routine use of MRBs as additive therapy in patients with chronic kidney disease cannot be recommended yet.
54. Lim LS, Fink HA, Kuskowski MA, Taylor BC, Schousboe JT, Ensrud KE; for the Osteoporotic Fractures in Men (MrOS) Study Group. Loop Diuretic Use and Increased Rates of Hip Bone Loss in Older Men: The Osteoporotic Fractures in Men Study. Arch Intern Med. 2008 Apr 14;168(7):735-740. We conclude that loop diuretic use in older men is associated with increased rates of hip bone loss. These results suggest that the potential for bone loss should be considered when loop diuretics are prescribed to older patients in clinical practice.
55. Arroll B, Kenealy T, Elley CR. Should we prescribe diuretics for patients with prediabetes and hypertension? BMJ. 2008 Aug 21;337:a679. doi: 10.1136/bmj.a679.
56. Davis BR, Kostis JB, Simpson LM, et al. for the ALLHAT Collaborative Research Group. Heart Failure With Preserved and Reduced Left Ventricular Ejection Fraction in the Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial. Circulation. 2008 Nov 10. [Epub ahead of print] In ALLHAT, with adjudicated outcomes, chlorthalidone significantly reduced the occurrence of new-onset hospitalized HFPEF and HFREF compared with amlodipine and doxazosin. Chlorthalidone also reduced the incidence of new-onset HFPEF compared with lisinopril. Among high-risk hypertensive men and women, HFPEF has a better prognosis than HFREF.
57. FDA Nov/08 Balanced Health Products, Inc. announced a recall of STARCAPS due to the presence of an undeclared drug ingredient, Bumetanide. Bumetanide is a diuretic indicated for the treatment of edema associated with congestive heart failure, hepatic and renal disease including nephrotic syndrome.
58. Jamerson K, Weber MA, Bakris GL, et al. Benazepril plus Amlodipine or Hydrochlorothiazide for Hypertension in High-Risk Patients. (ACCOMPLISH)N Engl J Med. 2008 Dec 4;359(23):2417-2428.
The benazepril-amlodipine combination was superior to the benazepril-hydrochlorothiazide combination in reducing cardiovascular events in patients with hypertension who were at high risk for such events.
59. Escribano J, Balaguer A, Pagone F, Feliu A, Roqué I Figuls M. Pharmacological interventions for preventing complications in idiopathic hypercalciuria. Cochrane Database Syst Rev. 2009 Jan 21;(1):CD004754. There is some evidence that in patients with idiopathic hypercalciuria and recurrent stones, the addition of thiazides to a normal or modified diet for short to long periods (five months to three years) reduced the number of stone recurrences and decreased the stone formation rate. Thiazides and neutral potassium phosphate decreased calciuria in symptomatic patients with idiopathic hypercalciuria. There were no studies investigating the effect of pharmacological treatment on other clinical complications or asymptomatic idiopathic hypercalciuria.
60. Carbone LD, Johnson KC, Bush AJ, Robbins J, Larson JC, Thomas A, LaCroix AZ. Loop diuretic use and fracture in postmenopausal women: findings from the Women's Health Initiative. Arch Intern Med. 2009 Jan 26;169(2):132-40. After adjustment for confounding variables, no significant association was found between ever use of loop diuretics and changes in BMD, falls, and fractures. Loop diuretics were used by women in poor health who were already at risk for fractures. However, prolonged use of loop diuretics was associated with higher fracture risk in postmenopausal women.
61. Al-Balas M, Bozzo P, Einarson A. Use of diuretics during pregnancy. Can Fam Physician. 2009 Jan;55(1):44-5. Many studies--including a meta-analysis of almost 7000 neonates exposed to diuretics during pregnancy—did not find an increased risk of adverse effects, such as birth defects, fetal growth restriction, thrombocytopenia, or diabetes, among neonates exposed to diuretics in utero.
62. Funder JW, Carey RM, Fardella C, Gomez-Sanchez CE, Mantero F, Stowasser M, Young WF Jr, Montori VM, Endocrine Society. Case detection, diagnosis, and treatment of patients with primary aldosteronism: an endocrine society clinical practice guideline. J Clin Endocrinol Metab 2008 Sep;93(9):3266-81.
63. Pitt B, et al. The effect of spironolactone on morbidity and mortality in patients with severe heart failure. Randomized Aldactone Evaluation Study Investigators. (RALES) N Engl J Med. 1999 Sep 2;341(10):709-17.
64. Juurlink DN, Mamdani MM, Lee DS, Kopp A, Austin PC, Laupacis A, Redelmeier DA. Rates of hyperkalemia after publication of the Randomized Aldactone Evaluation Study. N Engl J Med. 2004 Aug 5;351(6):543-51.
65. Krum H, Skiba M, Gilbert RE. Comparative metabolic effects of hydrochlorothiazide and indapamide in hypertensive diabetic patients receiving ACE inhibitor therapy. Diabet Med. 2003 Sep;20(9):708-12. Hydrochlorothiazide 12.5 mg/day, when added to background ACE inhibitor therapy with fosinopril in hypertensive diabetic patients, resulted in a metabolic profile that was similar, if not superior on certain parameters, in comparison with indapamide 2.5 mg/day.
66. Spence JD, Huff M, Barnett PA. Effects of indapamide versus hydrochlorothiazide on plasma lipids and lipoproteins in hypertensive patients: a direct comparison. Can J Clin Pharmacol. 2000 Spring;7(1):32-7. Triglyceride levels increased significantly more with indapamide than with HCTZ (P=0.02). The two drugs had similar effects on blood pressure and serum potassium; neither drug affected plasma glucose. Claims that indapamide is superior to HCTZ appear unwarranted; in view of the substantial cost difference, this finding, if confirmed in larger studies, has important policy implications.
67. Shafi T, Appel LJ, Miller ER 3rd, Klag MJ, Parekh RS. Changes in serum potassium mediate thiazide-induced diabetes. Hypertension. 2008 Dec;52(6):1022-9. Epub 2008 Nov 3. Erratum in: Hypertension. 2009 Feb;53(2):e19. After year 1, chlorthalidone use was not associated with increased diabetes risk. In conclusion, thiazide-induced diabetes occurs early after initiating treatment and appears to be mediated by changes in serum potassium. Potassium supplementation might prevent thiazide-induced diabetes. This hypothesis can and should be tested in a randomized trial.
68. Grimm RH Jr, Grandits GA, Prineas RJ, et al. Long-term effects on sexual function of five antihypertensive drugs and nutritional hygienic treatment in hypertensive men and women. Treatment of Mild Hypertension Study (TOMHS) Hypertension. 1997 Jan;29(1 Pt 1):8-14. In conclusion, long-term incidence of erection problems in treated hypertensive men is relatively low but is higher with chlorthalidone treatment. Effects of erection dysfunction with chlorthalidone appear relatively early and are often tolerable, and new occurrences after 2 years are unlikely. The rate of reported sexual problems in hypertensive women is low and does not appear to differ by type of drug. Similar incidence rates of erection dysfunction in placebo and most active drug groups caution against routine attribution of erection problems to antihypertensive medication.
69. Jackson T. Wright, Jr; Jeffrey L. et al; ALLHAT Collaborative Research Group ALLHAT Findings Revisited in the Context of Subsequent Analyses, Other Trials, & Meta-analyses Arch Intern Med. 2009;169(9):832-842.
70. Sowers JR, Whaley-Connell A, Epstein M. Narrative review: the emerging clinical implications of the role of aldosterone in the metabolic syndrome and resistant hypertension. Ann Intern Med. 2009 Jun 2;150(11):776-83.
71. Guerrera M. et al. Therapeutic Uses of Magnesium. Am Fam Physician. 2009; 80(1):157-162.
72. Wright JM, Musini VM. First-line drugs for hypertension. Cochrane Database Syst Rev. 2009 Jul 8;(3):CD001841. First-line low-dose thiazides reduce all morbidity and mortality outcomes. First-line ACE inhibitors and calcium channel blockers may be similarly effective but the evidence is less robust. First-line high-dose thiazides and first-line beta-blockers are inferior to first-line low-dose thiazides.
73. Chen JM, Heran BS, Wright JM. Blood pressure lowering efficacy of diuretics as second-line therapy for primary hypertension. Cochrane Database Syst Rev. 2009 Oct 7;(4):CD007187.
74. Moser Marvin; Feig Peter U. Fifty Years of Thiazide Diuretic Therapy for Hypertension. Arch Intern Med. 2009;169(20):1851-1856.
75. Ernst ME, Moser M. Use of diuretics in patients with hypertension. N Engl J Med. 2009 Nov 26;361(22):2153-64.

76. Nyirenda MJ, Tang JI, Padfield PL, Seckl JR. Hyperkalaemia. BMJ. 2009 Oct 23;339:b4114. doi: 10.1136/bmj.b4114.
77. Boger-Megiddo I, Heckbert SR, Weiss NS, et al. Myocardial infarction and stroke associated with diuretic based two drug antihypertensive regimens: population based case-control study. BMJ 2010;340: 25 Jan 2010.
78. Pharmacist's Letter. Clonidine abuse. Mar, 2010.
79. Thomson MR, Nappi JM, Dunn SP, Hollis IB, Rodgers JE, Van Bakel AB. Continuous versus intermittent infusion of furosemide in acute decompensated heart failure. J Card Fail. 2010 Mar;16(3):188-93.
80. Wei Li, Struthers Allan D, Fahey Tom, et al. Spironolactone use and renal toxicity: population based longitudinal analysis. BMJ 2010;340:c1768
81. Stafford RS.; Bartholomew L. Kay; et al; the ALLHAT Collaborative Research Group Impact of the ALLHAT/JNC7 Dissemination Project on Thiazide-Type Diuretic Use. Arch Intern Med. 2010;170(10):851-858.
82. European Association for the Study of the Liver. EASL clinical practice guidelines on the management of ascites, spontaneous bacterial peritonitis, and hepatorenal syndrome in cirrhosis. J Hepatol. 2010 Jun 1.
83. Abdel-Qadir HM, Tu JV, Yun L, Austin PC, Newton GE, Lee DS. Diuretic dose and long-term outcomes in elderly patients with heart failure after hospitalization. Am Heart J. 2010 Aug;160(2):264-271.e1.
84. Worcester EM, Coe FL. Clinical practice. Calcium kidney stones. N Engl J Med. 2010 Sep 2;363(10):954-63.
85. Lacourcière Y, Poirier L, Lefebvre J, et al. Increasing the doses of both diuretics and angiotensin receptor blockers is beneficial in subjects with uncontrolled systolic hypertension. Can J Cardiol. 2010 Oct;26(8):313-9.
86. Sciarretta Sebastiano; Palano Francesca; Tocci Giuliano; et al. Antihypertensive Treatment and Development of Heart Failure in Hypertension: A Bayesian Network Meta-analysis of Studies in Patients With Hypertension and High Cardiovascular Risk. Arch Intern Med. 2010;0(2010):archinternmed.2010.427.
87. Health Canada Nov/10: Beijing 101 Hair Consultants: Hair Growth Formula D-2653-Band Hair Growth Tonic E-0583-D: The Singapore Health Sciences Authority advised consumers to stop using one batch of these products (Beijing 101 Hair Consultants Hair Growth Formula D-2653-B batch# 20091201, and Hair Growth Tonic E-0583-D batch# 20091201) after testing of these batches revealed the presence of undeclared minoxidil. 101 Zhangguang: Gold 101 Super Effective Hair Growth Agentand Fabao 101D Doctor Zhao's Chinese Traditional Herbal Hair Care Formula: The Hong Kong Department of Health warned consumers not to buy or use these two products after they were found to contain undeclared minoxidil.
88. Medical Letter. Drugs for Kidney Stones. Nov 29, 2010. (Tamsulosin or long aciting nifedipine +/- corticosteroid) Medical Letter. Drugs for Kidney Stones. Nov 29, 2010. (Tamsulosin or nifedipine +/- ocrticosteroid)
89. CAU (Canadian Urological Association) 2010 Update: Guidelines for the management of benign prostatic hyperplasia http://www.cua.org/guidelines/bph_2009_en__v2a.pdf Nickel JC, Méndez-Probst CE, Whelan TF, Paterson RF, Razvi H. 2010 Update: Guidelines for the management of benign prostatic hyperplasia. Can Urol Assoc J. 2010 Oct;4(5):310-6.
90. Rossitto G, Kamath G, Messerli FH. Should alpha-blockers ever be used as antihypertensive drugs? Cleveland Clinic Journal of Medicine 2010; 77(12):884-888; doi:10.3949/ccjm.77a.10058
91. Kurlan R. Clinical practice. Tourette's Syndrome. N Engl J Med. 2010 Dec 9;363(24):2332-8.
92. Messerli F, Makani H, Benjo A, et al. Antihypertensive efficacy of HCTZ (hydrochlorothiazide) as evaluated by ABPM. A meta-analysis of randomized trials. J Am Coll Cardiol 2011; 57:590-600.
93. Anothaisintawee T, Attia J, Nickel JC, et al.. Management of chronic prostatitis/chronic pelvic pain syndrome: a systematic review and network meta-analysis. JAMA. 2011 Jan 5;305(1):78-86.
94. Benign prostatic hyperplasia (BPH): American Urological Association (AUA) Guidelines 2011. http://www.auanet.org/content/guidelines-and-quality-care/clinical-guidelines/main-reports/bph-management/chap_1_GuidelineManagementof(BPH).pdf
95. Allan GM, Ivers N, Kolber M. Medical management of renal stones: More than analgesia? Can Fam Physician. 2011 Feb;57(2):198.
96. Aurora RN, Zak RS, Auerbach SH, et al. Standards of Practice Committee, American Academy of Sleep Medicine. Best practice guide for the treatment of nightmare disorder in adults. J Clin Sleep Med 2010 Aug 15;6(4):389-401. (prazosin, ? clonidine etc)
97. FDA Mar/11 : USA Far Ocean Group, Inc. issues voluntary nationwide recall of U-Prosta, a product marketed as a dietary supplement that contains undeclared terazosin.
98. Psaty BM, Lumley T, Furberg CD. Meta-analysis of health outcomes of chlorthalidone-based vs nonchlorthalidone-based low-dose diuretic therapies. JAMA 2004;292:43-44.
99. Shahinfar S, Simpson RL, Carides AD, et al. Safety of losartan in hypertensive patients with thiazide-induced hyperuricemia. Kidney Int 1999;56:1879-1885.
100. Dorsch MP, Gillespie BW, Erickson SR, et al. Chlorthalidone reduces cardiovascular events compared with hydrochlorothiazide: a retrospective cohort analysis. Hypertension. 2011 Apr;57(4):689-94.
101. Pacak K. Preoperative management of the pheochromocytoma patient. J Clin Endocrinol Metab 2007;92:4069-4079.
102. Václavík Jan, Sedlák Richard, Plachy Martin, et al. Addition of Spironolactone in Patients With Resistant Arterial Hypertension (ASPIRANT): A Randomized, Double-Blind, Placebo-Controlled Trial. Hypertension 57: 1069-1075;.
103. NICE: National Institute for Health and Clinical Excellence. Hypertension Guidelines. Aug 2011. http://www.nice.org.uk/nicemedia/live/13561/56015/56015.pdf
104. Falk RH. Cardiac amyloidosis: a treatable disease, often overlooked. Circulation. 2011 Aug 30;124(9):1079-85.
105. Cockburn J, Moar VA, et al. Final report of study on hypertension during pregnancy: the effects of specific treatment on the growth (eg. methyldopa) and development of the children. Lancet 1982;1:647-9.
106. Collins R, Yusuf S, Peto R. Overview of randomised trials of diuretics in pregnancy. Br Med J (Clin Res Ed) 1985;290:17-23.
107. Krause T, Lovibond K, Caulfield M, McCormack T, Williams B; on behalf of the Guideline Development Group. Management of hypertension: summary of NICE guidance. BMJ. 2011 Aug 25;343:d4891.
108. Antoniou T, Gomes T, Mamdani MM, et al. Trimethoprim-sulfamethoxazole induced hyperkalaemia in elderly patients receiving spironolactone: nested case-control study. BMJ. 2011 Sep 12;343:d5228.
109. Sica DA, Carter B, Cushman W, Hamm L. Thiazide and Loop Diuretics. J Clin Hypertens (Greenwich). 2011 Sep;13(9):639-643. doi:10.1111/j.1751-7176.2011.00512.x.
110. Health Canada Oct/11: Huo Li Bao and Ren Sem Tu Chon Chin Kuo Pill - The Singapore Health Sciences Authority warned that these Chinese pain-relief products contain prescription and/or over-the-counter drugs (furosemide, piroxicam, chlorpheniramine, and/or dexamethasone).
111. Thomas L. Managing hypertensive emergencies in the ED. Can Fam Physician. 2011 Oct;57(10):1137-97.
112. Ho JM, Juurlink DN. Considerations when prescribing trimethoprim-sulfamethoxazole. CMAJ. 2011 Oct 11.
113. Piller LB, Baraniuk S, Simpson LM, et al. Long-term follow-up of participants with heart failure in the Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial (ALLHAT). Circulation. 2011;124:1811–1818.
114. Health Canada Nov/11 Slimming Kapsul The Hong Kong Department of Health warned that this weight-loss product contains an unauthorized drug (sibutramine) and a prescription drug (spironolactone).
115. EXPERT PANEL ON INTEGRATED GUIDELINES FOR CARDIOVASCULAR HEALTH AND RISK REDUCTION IN CHILDREN AND ADOLESCENTS. Expert Panel on Integrated Guidelines for Cardiovascular Health and Risk Reduction in Children and Adolescents: Summary Report. Pediatrics. 2011 Nov 14. [Epub ahead of print]
116. Leung AA, Wright A, Pazo V, et al. Risk of thiazide-induced hyponatremia in patients with hypertension. Am J Med. 2011 Nov;124(11):1064-72.
117. Kostis JB, Cabrera J, Cheng JQ, et al. Association between chlorthalidone treatment of systolic hypertension and long-term survival (SHEP). JAMA. 2011 Dec 21;306(23):2588-93. In the SHEP trial, treatment of isolated systolic hypertension with chlorthalidone stepped-care therapy for 4.5 years was associated with longer life expectancy at 22 years of follow-up.
118. Choi HK, Soriano LC, Zhang Y, Rodríguez LAG. Calcium channel blockers, losartan, and the risk of incident gout among patients with hypertension: population based case-control study. BMJ 2012;344:d8190.
119. Garrison SR, Dormuth CR, Morrow RL, et al. Nocturnal leg cramps and prescription use that precedes them: a sequence symmetry analysis. Arch Intern Med. 2012 Jan 23;172(2):120-6. (common with LABA's, diuretics)
120. Jones AG, Evans PH, Vaidya B. Phaeochromocytoma. BMJ. 2012 Feb 20;344:e1042.
121. Worster AS, Bhanich Supapol W. Fluids and diuretics for acute ureteric colic. Cochrane Database Syst Rev. 2012 Feb 15;2:CD004926. We found no reliable evidence in the literature to support the use of diuretics and high volume fluid therapy for people with acute ureteric colic.
122. Ernst ME, Neaton JD, Grimm RH Jr, et al. Multiple Risk Factor Intervention Trial Research Group. Long-term effects of chlorthalidone versus hydrochlorothiazide on electrocardiographic left ventricular hypertrophy in

the multiple risk factor intervention trial. (MRFIT) Hypertension. 2011 Dec;58(6):1001-7.
123. Frassetto L, Kohlstadt I. Treatment and prevention of kidney stones: an update. Am Fam Physician. 2011 Dec 1;84(11):1234-42.
124. Dickson G. Gynescomastia. Am Fam Physician. 2012 Apr 1;85(7):716-722. (spironolactone SE)
125. Baker WL, White WB. Safety of mineralocorticoid receptor antagonists (spironolactone) in patients receiving hemodialysis. Ann Pharmacother. 2012 Jun;46(6):889-94.
126. Strom BL, Schinnar R, et al. Absence of cross-reactivity between sulfonamide antibiotics and sulfonamide nonantibiotics. N Engl J Med. 2003 Oct 23;349(17):1628-35.
127. Mackenzie IS, Macdonald TM, Thompson A, et al. Spironolactone and risk of incident breast cancer in women older than 55 years: retrospective, matched cohort study. BMJ. 2012 Jul 13;345:e4447.
128. van Zuuren EJ et al. Interventions for female pattern hair loss. Cochrane Database Syst Rev 2012; 5: CD007528. DOI:10.1002/14651858.CD007628.pub3
129. Musini VM, Rezapour P, Wright JM, et al. Blood pressure lowering efficacy of loop diuretics for primary hypertension. Cochrane Database Syst Rev. 2012 Aug 15;8:CD003825. Based on the limited number of published RCTs, the systolic/diastolic blood pressure lowering effect of loop diuretics is modest (-8/-4 mmHg) and is likely an overestimate due to the high risk of bias in the included studies. There are no clinically meaningful BP lowering differences between different drugs within the loop diuretic class.
130. Nagarajan V, Chamsi-Pasha M, Tang WH. The role of aldosterone receptor antagonists (spironolactone, eplerenone) in the management of heart failure: An update. Cleve Clin J Med. 2012 Sep;79(9):631-9.
131. Friedman GD, Asgari MM, Warton EM, et al. Antihypertensive Drugs (hydrochlorothiazide, nifedipine) and Lip Cancer in Non-Hispanic Whites. Arch Intern Med. 2012 Aug 6:1-6.
132. Chan CY, Peterson EJ, Ng TM. Thiazide diuretics as chronic antihypertensive therapy in patients with severe renal disease--is there a role in the absence of diuresis? Ann Pharmacother. 2012 Nov;46(11):1554-8.
133. Bakris GL, Sica D, White WB, et al. Antihypertensive Efficacy of Hydrochlorothiazide vs Chlorthalidone Combined with Azilsartan Medoxomil. Am J Med. 2012 Dec;125(12):1229.e1-1229.e10.
134. Tachjian A, Maria V, Jahangir A. Use of herbal products and potential interactions in patients with cardiovascular diseases. J Am Coll Cardiol. 2010 Feb 9;55(6):515-25.
135. Heran BS, Chen JM, Wang JJ, et al. Blood pressure lowering efficacy of potassium-sparing diuretics (amiloride, triamterene: that block the epithelial sodium channel) for primary hypertension. Cochrane Database Syst Rev. 2012 Nov 14;11:CD008167. doi: 10.1002/14651858.CD008167.pub3. ENaC blockers do not have a statistically or clinically significant BP lowering effect at low doses but trials at higher doses are not available.
136. Lapi F, Azoulay L, Yin H, et al. Concurrent use of diuretics, angiotensin converting enzyme inhibitors, and angiotensin receptor blockers with non-steroidal anti-inflammatory drugs (NSAIDs) and risk of acute kidney injury: nested case-control study. BMJ 2013;346:e8525.
137. Kung S, Espinel Z, Lapid MI. Treatment of nightmares with prazosin: a systematic review. Mayo Clin Proc. 2012 Sep;87(9):890-900.
138. Weber MA, Jamerson K, Bakris GL et al. Effects of body size and hypertension treatments on cardiovascular event rates: subanalysis of the ACCOMPLISH randomized controlled trial. Lancet 2012.
139. American College of Obstetricians and Gynecologists (ACOG). Chronic hypertension in pregnancy. Washington (DC): American College of Obstetricians and Gynecologists (ACOG); 2012 Feb. 12.
140. Edelmann F, Wachter R, Schmidt AG, et al for the Aldo-DHF Investigators. Effect of spironolactone on diastolic function and exercise capacity in patients with heart failure with preserved ejection fraction: The Aldo-DHF randomized controlled trial. JAMA2013; 309:781-791.
141. Slaughter JL, Stenger MR, Reagan PB. Variation in the Use of Diuretic (eg. Furosemide) Therapy for Infants With Bronchopulmonary Dysplasia. Pediatrics. 2013 Mar 11.
142. Nishiwaki M, Hosoai H, Ikewaki K, et al; ABC Study Group. Efficacy and Effects on Lipid Metabolism of Combination Treatment With Losartan + Hydrochlorothiazide Versus Losartan + Amlodipine: A 48-Week Prospective, Multicenter, Randomized, Open-Label Trial. Clin Ther. 2013 Mar 12.
143. Dhalla IA, Gomes T, Yao Z, et al. Chlorthalidone versus hydrochlorothiazide for the treatment of hypertension in older adults: a population-based cohort study. Ann Intern Med. 2013 Mar 19;158(6):447-55.
144. Fink HA, Wilt TJ, Eidman KE, et al. Medical management to prevent recurrent nephrolithiasis in adults: a systematic review for an american college of physicians clinical guideline. Ann Intern Med. 2013 Apr 2;158(7):535-43. (Thiazide, citrate or allopurinol reduced risk)
145. Maron BA, Waxman AB, Opotowsky AR, et al. Effectiveness of Spironolactone Plus Ambrisentan for Treatment of Pulmonary Arterial Hypertension (from the [ARIES] Study 1 and 2 Trials). Am J Cardiol. 2013 Jun 7.
146. Raskind MA, Peterson K, Williams T, et al. A Trial of Prazosin for Combat Trauma PTSD With Nightmares in Active-Duty Soldiers Returned From Iraq and Afghanistan. Am J Psychiatry. 2013 Jul 12.
147. Roush GC, Holford TR, Guddati AK. Chlorthalidone compared with hydrochlorothiazide in reducing cardiovascular events: systematic review and network meta-analyses. Hypertension. 2012;59:1110–1117.
148. Runyon BA. Management of adult patients with ascites due to cirrhosis: update 2012. Alexandria (VA): American Association for the Study of Liver Diseases-AASLD; 2013 Feb.
149. Spoendlin J et al. Spironolactone may reduce the risk of incident rosacea. J Invest Dermatol 2013 Oct; 133:2480.
150. Türk C, Knoll T, Petrik A, Sarica K, Skolarikos A, Straub M, Seitz C. Guidelines on urolithiasis. Arnhem (The Netherlands): European Association of Urology (EAU); 2013 Mar.
151. FDA Dec/13 IQ Formulations, of Sunrise, Florida is initiating a recall of all lots of its 45-capsule bottles of Hydravax due to potential inclusion of an unlisted ingredient. The FDA has advised IQ Formulations that an analysis of a sample from one lot of Hydravax (Lot # 2458, Exp # 07/16) revealed the presence of an undeclared ingredient – a diuretic.
152. Ganie MA, Khurana ML, Nisar S, et al. Improved Efficacy of Low-Dose Spironolactone and Metformin Combination Than Either Drug Alone in the Management of Women With Polycystic Ovary Syndrome (PCOS): A Six-Month, Open-Label Randomized Study. J Clin Endocrinol Metab. 2013 Sep;98(9):3599-607.
153. Bruderer S, Jick SS, Bodmer M, Meier CR. Use of diuretics and risk of incident gout: Population-based case-control study. Arthritis Rheum. 2013 Oct 21.
154. Weber MA, Schiffrin EL, White WB, et al. ASH/ISH: Clinical practice guidelines for the management of hypertension in the community. A statement by the American Society of Hypertension and the International Society of Hypertension. J Clin Hypertens 2013; DOI:10.1111/jch.12237.
155. Wang GS, Le Lait MC, Heard K. Unintentional pediatric exposures to central alpha-2 agonists (clonidine, guanfacine, tizanidine) reported to the national poison data system. J Pediatr. 2014 Jan;164(1):149-52.
156. Devereaux PJ, Sessler DI, Leslie K, et al. Clonidine in patients undergoing noncardiac surgery. (Poise-2 trial) N Engl J Med. DOI: 10.1056/NEJMoa1401106.
157. Su JA, Tang W, Rivero N, et al. Prenatal Exposure to Methyldopa Leading to Hypertensive Crisis and Cardiac Failure in a Neonate. Pediatrics. 2014 Apr 28.
158. Makam AN, John Boscardin W, Miao Y, et al. Risk of Thiazide-Induced Metabolic Adverse Events in Older Adults. J Am Geriatr Soc. 2014 May 13.
159. Mandell BF. Q: Should patients with gout avoid thiazides for hypertension? Cleve Clin J Med. 2014 Feb;81(2):83-6.
160. Leonard CE, Razzaghi H, Freeman CP, et al. Empiric potassium supplementation and increased survival in users of loop diuretics. PLoS One. 2014 Jul 16;9(7)
161. Makam AN, John Boscardin W, Miao Y, et al. Risk of Thiazide-Induced Metabolic Adverse Events in Older Adults. J Am Geriatr Soc. 2014 May 13.
162. Ueda S, Morimoto T, Ando S, et al; DIME Investigators. A randomised controlled trial for the evaluation of risk for type 2 diabetes in hypertensive patients receiving thiazide diuretics: Diuretics In the Management of Essential hypertension (DIME) study. BMJ Open. 2014 Jul 16;4(7):e004576.
163. Maisel A, Xue Y, van Veldhuisen DJ, et al. Effect of Spironolactone on 30-Day Death and Heart Failure Rehospitalization (from the COACH Study). Am J Cardiol. 2014 Sep 1;114(5):737-42.
164. Barber J, McKeever TM, et al. A systematic review and meta-analysis of thiazide-induced hyponatraemia: time to reconsider electrolyte monitoring regimens after thiazide initiation? Br J Clin Pharmacol. 2014 Aug 19.
165. Lovegrove MC, Mathew J, Hampp C, et al. Emergency Hospitalizations for Unsupervised Prescription Medication Ingestions by Young Children. Pediatrics. 2014 Sep 15. (buprenorphine & clonidine concerning)
166. Pearle MS, Goldfarb DS, Assimos DG, et al; American Urological Assocation. Medical management of kidney stones: AUA guideline. J Urol. 2014 Aug;192(2):316-24.
167. Garg AX, Kurz A, Sessler DI, et al; POISE-2 Investigators. Effect of perioperative aspirin and clonidine on acute kidney injury: a randomized clinical trial. JAMA. doi:10.1001/jama.2014.15284.
168. Hirst JA, Farmer AJ, Feakins BG, et al. Quantifying the effects of diuretics and beta-blockers on glycaemic control in diabetes mellitus - a systematic review and meta-analysis. Br J Clin Pharmacol. 2014 Nov 6.
169. Shen L, Shah BR, Reyes EM, et al. Role of diuretics, beta blockers, and statins in increasing the risk of diabetes in patients with impaired glucose tolerance: reanalysis of data from the NAVIGATOR study. BMJ. 2013 Dec 9;347:f6745.
170. Jakes AD, Bhandari S. Investigating polyuria. BMJ. 2013 Dec 2;347:f6772
171. Qaseem A, Dallas P, Forciea MA, et al; Clinical Guidelines Committee of the American College of Physicians. Dietary and pharmacologic management to prevent recurrent nephrolithiasis in adults: a clinical practice

guideline from the american college of physicians. Ann Intern Med. 2014 Nov 4;161(9):659-67.
172. van Blijderveen JC, Straus SM, Rodenburg EM, et al. Risk of hyponatremia with diuretics: chlorthalidone versus hydrochlorothiazide. Am J Med. 2014 Aug;127(8):763-71.
173. Raman SV, Hor KN, Mazur W, et al. Eplerenone for early cardiomyopathy in Duchenne muscular dystrophy: a randomised, placebo-controlled trial. Lancet Neurol 2014; online Dec 30.
174. Matsumoto Y, Mori Y, Kageyama S, et al. Spironolactone reduces cardiovascular and cerebrovascular morbidity and mortality in hemodialysis patients. J Am Coll Cardiol. 2014;63:528-536
175. Campschroer T, Zhu Y, Duijvesz D, Grobbee DE, Lock MT. Alpha-blockers as medical expulsive therapy for ureteral stones. Cochrane Database Syst Rev. 2014;(4):CD008509.
The use of alpha-blockers in patients with ureteral stones results in a higher stone-free rate and a shorter time to stone expulsion. Alphablockers should therefore be offered as part of medical expulsive therapy as one of the primary treatment modalities.
176. Antoniou T, Hollands S, et al; the Canadian Drug Safety and Effectiveness Research Network. Trimethoprim-sulfamethoxazole and risk of sudden death among patients taking spironolactone. CMAJ. 2015 Feb 2.
177. Plovanich M,Weng QY, Mostaghimi A. Low usefulness of potassium monitoring among healthy young women taking spironolactone for acne [Mar 23, 2015]. JAMA Dermatol. doi:10.1001/jamadermatol.2015.34.
178. FDA May/15 laboratory analysis confirmed that Jianbu Huqian Wan contains dexamethasone, a corticosteroid, chlorpheniramine, and furosemide.
179. Dahal K, Kunwar S, Rijal J, et al. The Effects of Aldosterone Antagonists in Patients With Resistant Hypertension: A Meta-Analysis of Randomized and Nonrandomized Studies. Am J Hypertens. 2015 Mar 23.
180. Lai CL, Kuo RN, Chen HM, et al. Risk of hip/femur fractures during the initiation period of alpha-blocker therapy among elderly males: a self-controlled case series study. Br J Clin Pharmacol. 2015 Apr 28.
182. Bakris GL, Agarwal R, Chan JC, et al; Mineralocorticoid Receptor Antagonist Tolerability Study–Diabetic Nephropathy (ARTS-DN) Study Group. Effect of Finerenone on Albuminuria in Patients With Diabetic Nephropathy: A Randomized Clinical Trial. JAMA. 2015 Sep 1;314(9):884-94.
183. Bao Y, Curhan G, Merriman T, et al. Lack of gene-diuretic interactions on the risk of incident gout: the Nurses' Health Study and Health Professionals Follow-up Study. Ann Rheum Dis. 2015 Feb 9.
184. Hou J, Xiong W, Cao L, et al. Spironolactone Add-On for Preventing or Slowing the Progression of Diabetic Nephropathy: A Meta-Analysis. Clin Ther. 2015 Aug 4. pii: S0149-2918(15)00847-4.
185. Viera AJ, Wouk N. Potassium Disorders: Hypokalemia and Hyperkalemia. Am Fam Physician. 2015 Sep 15;92(6):487-95.
186. Williams B, MacDonald TM, Morant S, et al, for The British Hypertension Society's PATHWAY Studies Group. Spironolactone versus placebo, bisoprolol, and doxazosin to determine the optimal treatment for drug-resistant hypertension (PATHWAY-2): a randomised, double-blind, crossover trial. Lancet 2015; online Sept 21.
187. Kowalczyk WJ, Phillips KA, Jobes ML, et al. Clonidine Maintenance Prolongs Opioid Abstinence and Decouples Stress From Craving in Daily Life: A Randomized Controlled Trial With Ecological Momentary Assessment. Am J Psychiatry. 2015 Aug 1;172(8):760-7. Clonidine is a promising drug when used as adjuvant treatment to buprenorphine for maintaining abstinence from opioids. These authors documented longer duration of abstinence with clonidine as compared with placebo.
They also credibly documented that patients in the clonidine-treated group experienced less craving when confronted with life stresses. (LOE = 1b)
188. Brown MJ, Williams B, Morant SV, et al; British Hypertension Society's Prevention; Treatment of Hypertension with Algorithm-based Therapy (PATHWAY) Studies Group. Effect of amiloride, or amiloride plus hydrochlorothiazide, versus hydrochlorothiazide on glucose tolerance and blood pressure (PATHWAY-3): a parallel-group, double-blind randomised phase 4 trial. Lancet Diabetes Endocrinol. 2015 Oct 16.
189. Cooper LB, Hammill BG, et al. Consistency of Laboratory Monitoring During Initiation of Mineralocorticoid Receptor Antagonist Therapy in Patients With Heart Failure. JAMA. 2015 Nov 10;314(18):1973-5.
190. Lai CL, Kuo RN, Chen HM, et al. Risk of ischemic stroke during the initiation period of α-blocker therapy among older men. CMAJ. 2015 Dec 7.
191. Wang RC. Managing Urolithiasis. Ann Emerg Med. 2015 Nov 23.
192. Chang TI, Evans G, et al; SPRINT Study Research. Patterns and Correlates of Baseline Thiazide-Type Diuretic Prescription in the Systolic Blood Pressure Intervention Trial. Hypertension. 2016 Mar;67(3):550-5.
193. Streetz VN, Gildon BL, Thompson DF. Role of Clonidine in Neonatal Abstinence Syndrome: A Systematic Review. Ann Pharmacother. 2016 Apr;50(4):301-10.
194. Tu W et al. Triamterene enhances the blood pressure lowering effect of hydrochlorothiazide in patients with hypertension. J Gen Intern Med 2016 Jan; 31:30.
195. Elsaman AM, Radwan AR, Mohammed WI, et al. Low-dose Spironolactone: Treatment for Osteoarthritis-related Knee Effusion. A Prospective Clinical and Sonographic-based Study. J Rheumatol. 2016 Apr 1.
196. Solomon SD, et al; TOPCAT Investigators. Influence of ejection fraction on outcomes and efficacy of spironolactone in patients with heart failure with preserved ejection fraction. Eur Heart J. 2016 Feb 1;37(5):455-62.
197. Woodruff AE, Kelley AM, Hempel CA, et al. Discharge Diuretic Dose and 30-Day Readmission Rate in Acute Decompensated Heart Failure. Ann Pharmacother. 2016 Mar 8.
198. Funder JW, Carey RM, et al. The Management of Primary Aldosteronism: Case Detection, Diagnosis & Treatment: Endocrine Society Clinical Practice Guideline. J Clin Endocrinol Metab. 2016 May;101(5):1889-916.
199. Versmissen J, Koch BC, Roofthooft DW, et al. Doxazosin treatment of phaeochromocytoma during pregnancy: placental transfer and disposition in breast milk. Br J Clin Pharmacol. 2016 May 19.
200. Morgan MS, Pearle MS. Medical management of renal stones. BMJ. 2016 Mar 14;352:i52.
201. Kolber MR, Garrison S, Turgeon RD. Electrolyte disturbance with diuretics and ACEIs. Can Fam Physician. 2016 Jul;62(7):569. PubMed PMID: 27412211.
202. Mackenzie IS, Morant SV, Wei L, et al. Spironolactone use and risk of incident cancers: a retrospective, matched cohort study. Br J Clin Pharmacol. 2016 Oct 13.
203. Tully PJ, Dartigues JF, Debette S, Helmer C, Artero S, Tzourio C. Dementia risk with antihypertensive use and blood pressure variability: A cohort study. Neurology. 2016 Aug 9;87(6):601-8.
204. Dion M, Ankawi G, Chew B, et al. CUA (Canadian) guideline on the evaluation and medical management of the kidney stone patient – 2016 update.
www.cua.org/themes/web/assets/files/cua_guideline_on_the_evaluation_and_medical_management_of_the_kidney_stone_patient.pdf (accessed November 18, 2016).
205. Hollingsworth JM, Canales BK, Rogers MA, et al. Alpha blockers for treatment of ureteric stones: systematic review and meta-analysis. BMJ. 2016 Dec 1;355:i6112.
206. Hoorn EJ, Ellison DH. Diuretic Resistance. Am J Kidney Dis. 2016 Nov 1. pii: S0272-6386(16)30511-X.
207. Kosmala W, Rojek A, Przewlocka-Kosmala M, et al. Effect of aldosterone antagonism on exercise tolerance in heart failure with preserved ejection fraction. J Am Coll Cardiol 2016; 68:1823-34.
208. Fuchs SC, Poli-de-Figueiredo CE, et al. Effectiveness of Chlorthalidone Plus Amiloride for the Prevention of Hypertension: The PREVER-Prevention Randomized Clinical Trial. J Am Heart Assoc. 2016 Dec 13;5(12).
208. Muncie HL, Sirmans SM, James LE. Dizziness: Approach to Evaluation and Management. Am Fam Physician. 2017;95(3):154-162.
208. Pierson-Marchandise M, Gras V, Moragny J, et al. The drugs that mostly frequently induce acute kidney injury: a case - non-case study of a pharmacovigilance database. Br J Clin Pharmacol. 2016 Dec 21.
The most frequently implicated drug classes were antibacterials for systemic use (29.5%), diuretics (18.5%), agents acting on the renin-angiotensin system (16.3%), antineoplastic agents (10.2%) and anti-inflammatory agents (5.4%). Gentamicin, eplerenone, spironolactone, candesartan, cisplatin and acyclovir had the highest RORs (>10).
208. Raison N, Ahmed K, Brunckhorst O, et al. Alpha blockers in the management of ureteric lithiasis: A meta-analysis. Int J Clin Pract. 2017 Jan;71(1).
209. Molvi SN, Mir S, Rana VS, Jabeen F, Malik AR. Role of antihypertensive therapy in mild to moderate pregnancy-induced hypertension: a prospective randomized study comparing labetalol with alpha methyldopa. Arch Gynecol Obstet. 2012 Jun;285(6):1553-62.
210. ACC/AHA 2017 Whelton PK, et al. 2017 ACC/AHA/AAPA/ABC/ACPM/AGS/APhA/ASH/ASPC/NMA/ Guideline for the Prevention, Detection, Evaluation, and Management of High Blood Pressure in Adults: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. Hypertension. 2017 Nov 13.
211. de Denus S, O'Meara E, Desai AS, et al. Spironolactone Metabolites in TOPCAT - New Insights into Regional Variation. N Engl J Med. 2017 Apr 27;376(17):1690-1692.
212. Roush GC, Sica DA. Diuretics for Hypertension: A Review and Update. Am J Hypertens. 2016 Oct;29(10):1130-7.
213. Vozoris NT, Wang X, Austin PC, et al. Incident diuretic drug use and adverse respiratory events among older adults with COPD. Br J Clin Pharmacol. 2017 Nov 15.
214. Arnspang S, Gaist D, Johannesdottir Schmidt SA, et al. Hydrochlorothiazide use and risk of non-melanoma skin cancer: A nationwide case-control study from Denmark. J Am Acad Dermatol. 2017 Nov 30.
215. Duncan D, Sankar A, Beattie WS, et al. Alpha-2 adrenergic agonists (eg. Clonidine) for the prevention of cardiac complications among adults undergoing surgery. Cochrane Database Syst Rev. 2018 Mar 6;3:CD004126. Our review concludes that prophylactic-2 adrenergic agonists generally do not prevent perioperative death or major cardiac complications. For non-cardiac surgery, there is moderate-to-high quality evidence that these agents do not prevent death, myocardial infarction or stroke. Conversely, there is moderate quality evidence that these agents have important adverse effects, namely increased risks of hypotension and

bradycardia. For cardiac surgery, there is moderate quality evidence that alpha-2 adrenergic agonists have no effect on the risk of mortality or myocardial infarction, and that they increase the risk of bradycardia. The quality of evidence was inadequate to draw conclusions regarding the effects of alpha-2 agonists on stroke or hypotension during cardiac surgery.
216. Srivastava T, Jafri S, Truog WE, et al. Successful Reversal of Furosemide-Induced Secondary Hyperparathyroidism With Cinacalcet. Pediatrics. 2017 Dec;140(6).
217. Williams TA, Reincke M. Management of Endocrine Disease: Diagnosis and Management of Primary Aldosteronism: the Endocrine Society guideline 2016 revisited. Eur J Endocrinol. 2018 Apr 19.
218. Wright JM, Musini VM, Gill R First-line drugs for hypertension. Cochrane Database Syst Rev. 2018 Apr 18;4:CD001841. First-line low-dose thiazides reduced all morbidity and mortality outcomes in adult patients with moderate to severe primary hypertension. First-line ACE inhibitors and calcium channel blockers may be similarly effective, but the evidence was of lower quality. First-line high-dose thiazides and first-line beta-blockers were inferior to first-line low-dose thiazides.
219. Hundemer GL, Curhan GC, et al. Incidence of Atrial Fibrillation and Mineralocorticoid Receptor Activity in Patients With Medically and Surgically Treated Primary Aldosteronism. JAMA Cardiol. 2018 Jul 18.
220. Macfarlane TV, Pigazzani F, Flynn RWV, Macdonald TM. The effect of indapamide versus bendroflumethiazide for primary hypertension: a systematic review. Br J Clin Pharmacol. 2018 Oct 12.
221. Pottegård A, Pedersen SA, Schmidt SAJ, et al. Association of Hydrochlorothiazide Use and Risk of Malignant Melanoma. JAMA Intern Med. 2018 May 29.
222. Simpson TL, Saxon AJ, Stappenbeck C, et al. Double-Blind Randomized Clinical Trial of Prazosin for Alcohol Use Disorder. Am J Psychiatry. 2018 Aug 29:appiajp201817080913.
223. Anisman SD, Erickson SB, Morden NE. How to prescribe loop diuretics in oedema. BMJ. 2019 Feb 21;364:l359.
224. Fontenelle LF, Sarti TD. Kidney Stones: Treatment and Prevention. Am Fam Physician. 2019;99(8):490-496.
225. Health Canada Jan/19: has completed a safety review of hydrochlorothiazide and has found that prolonged use of the drug could increase a person's risk for non-melanoma skin cancer.
226. Musini VM, Rezapour P, Wright JM, Bassett K, Jauca CD. Blood pressure-lowering efficacy of loop diuretics for primary hypertension. Cochrane Database Syst Rev. 2015 May 22;(5):CD003825.
227 Cheng L, Zhang K, Zhang Z. Effectiveness of thiazides on serum and urinary calcium levels and bone mineral density in patients with osteoporosis: a systematic review and meta-analysis. Drug Des Devel Ther. 2018 Nov 14;12:3929 3935.
228. Kaplan NM. Indapamide: is it the better diuretic for hypertension? Hypertension. 2015 May;65(5):983-4. doi: 10.1161/HYPERTENSIONAHA.115.05138. Epub 2015 Mar 2.
229. Springer K. Chlorthalidone vs. Hydrochlorothiazide for Treatment of Hypertension. Am Fam Physician. 2015 Dec 1;92(11):1015-6.
230. Roush GC, Ernst ME, Kostis JB, Tandon S, Sica DA. Head-to-head comparisons of hydrochlorothiazide with indapamide and chlorthalidone: antihypertensive and metabolic effects. Hypertension. 2015 May;65(5):1041-6.
231. MHRA drug safety update: hydrochlorothiazide and non-melanoma skin cancer. Drug Ther Bull. 2019 May;57(5):70.
232. Shin D, Lee ES, Kim J, Guerra L, Naik D, Prida X. Association Between the Use of Thiazide Diuretics and the Risk of Skin Cancers: A Meta-Analysis of Observational Studies. J Clin Med Res. 2019 Apr;11(4):247-255.
233. Malha L, Mann SJ. Loop Diuretics in the Treatment of Hypertension. Curr Hypertens Rep. 2016 Apr;18(4):27.
234. Lader E. ACP Journal Club. Review: eplerenone is not more effective for reducing mortality than other aldosterone antagonists. Ann Intern Med. 2012 Dec 18;157(12):JC6-10.
235. Garcá Puig J, Miranda ME, Mateos F, Herrero E, Lavilla P, Gil A. Hydrochlorothiazide versus spironolactone: long-term metabolic modifications in patients with essential hypertension. J Clin Pharmacol. 1991 May;31(5):455-61.
236. Tam TS, Wu MH, Masson SC, Tsang MP, Stabler SN, Kinkade A, Tung A, Tejani AM. Eplerenone for hypertension. Cochrane Database Syst Rev. 2017 Feb 28;2:CD008996.
237. Sternlicht H, Bakris GL. Spironolactone for resistant hypertension--hard to resist? Lancet. 2015 Nov 21;386(10008):2032-2034.
238. Reid JL, Campbell BC, Hamilton CA. Withdrawal reactions following cessation of central alpha-adrenergic receptor agonists. Hypertension. 1984 Sep-Oct;6(5 Pt 2):II71-5.
239. Krieger EM, Drager LF, Giorgi DMA, et al; ReHOT Investigators. Spironolactone Versus Clonidine as a Fourth-Drug Therapy for Resistant Hypertension: The ReHOT Randomized Study (Resistant Hypertension Optimal Treatment). Hypertension. 2018 Apr;71(4):681-690.
240. Rossitto G, Kamath G, Messerli FH. Q: Should alpha-blockers ever be used as antihypertensive drugs? Cleve Clin J Med. 2010 Dec;77(12):884-8.
241. Rosenberg M, Stephens E. ACP Journal Club. In resistant hypertension, add-on spironolactone reduced SBP more than placebo, doxazosin, or bisoprolol over 12 wk. Ann Intern Med. 2016 Feb 16;164(4):JC16.
242. Sharma C, Soni A, Gupta A, Verma A, Verma S. Hydralazine vs nifedipine for acute hypertensive emergency in pregnancy: a randomized controlled trial. Am J Obstet Gynecol. 2017 Dec;217(6):687.e1-687.e6.
243. Mundt HM, Matenaer M, Lammert A, Göttmann U, Krämer BK, Birck R, Benck U. Minoxidil for Treatment of Resistant Hypertension in Chronic Kidney Disease—A Retrospective Cohort Analysis. J Clin Hypertens (Greenwich). 2016 Nov;18(11):1162-1167.
244. Pettinger WA. Hypertension's 3 Dilemmas and 3 Solutions: Pharmacology of the Kidney in Hypertension. J Cardiovasc Pharmacol. 2017 Mar;69(3):129-139.
245. Slim HB, Black HR, Thompson PD. Older blood pressure medications-do they still have a place? Am J Cardiol. 2011 Jul 15;108(2):308-16.
246. ACOG Practice Bulletin No. 202: Gestational Hypertension and Preeclampsia. Obstet Gynecol. 2019 Jan;133(1):e1-e25.
247. Pedersen SA, Johannesdottir Schmidt SA, et al. Hydrochlorothiazide use and risk for Merkel cell carcinoma and malignant adnexal skin tumors: A nationwide case-control study. J Am Acad Dermatol. 2019 Feb;80(2):460-465.e9.
248. Pedersen SA, Gaist D, Schmidt SAJ, et al. Hydrochlorothiazide use and risk of nonmelanoma skin cancer: A nationwide case-control study from Denmark. J Am Acad Dermatol. 2018 Apr;78(4):673-681.e9.
249. Hiremath S, Ruzicka M, Petrcich W, et al. **Alpha-Blocker Use and the Risk of Hypotension** and Hypotension-Related Clinical Events in Women of Advanced Age. Hypertension. 2019 Sep;74(3):645-651.
250. Millington K, Liu E, Chan YM. The Utility of **Potassium Monitoring in Gender-Diverse Adolescents** Taking Spironolactone. J Endocr Soc. 2019 Apr 4;3(5):1031-1038.
251. Shin D, Lee ES, Kim J, et al. Association Between the Use of Thiazide Diuretics and the **Risk of Skin Cancers**: A Meta-Analysis of Observational Studies. J Clin Med Res. 2019 Apr;11(4):247-255.

ONLINE RxFILES EXTRAS

CI: **DIURETICS**: symptomatic gout, allergy sulpha: cross reactivity not proven, anuria, hyponatremia. **β-BLOCKERS**: asthma, 2nd or 3rd degree heart block, severe bradycardia, uncompensated HF, severe PAD. **ACEI / ARB**: bilateral artery stenosis (or kidney solitary stenosis if only 1 kidney), angioedema hx, (ACEI/ARB + aliskiren) diabetes, pre-contrast concern coronary angio, pregnancy (2nd & 3rd trimester; ? 1st trimester – appears safe). Less effective/safe in black people? **CCB**:systolic BP<90, recent MI with pulmonary edema Non-LA-DHP, sick sinus sx or 2nd/3rd degree AV block, systolic dysfx/HF especially diltiazem & verapamil.

Aliskiren **RASILEZ**ˣ ⊗150,300mg tab daily $55; **RASILEZ-HCTZ**ˣ ⊗ 150,300//12.5,25mg tab. Direct renin inhibitor (DRI) **AE**: diarrhea, HA, ↑K+, rash, allergy & pharyngitis.Rare: cough ~1%, angioedema, gout 0.2%. (rats: colonic mucosal hyperplasia). **CI**: Pregnancy. **DI**: cyclosporine, furosemide, grapefruit juice, irbesartan, juices, keto- & itra -conazole, + ACEi or ARB(↑CV events ALTITUDE; prehypertension NS AQUARIUS). High-fat meals reduce absorption.

	Generic/ TRADE / Strength	Comments/ Drug Interactions [11] DI	Adverse Events [8,10] AE	Indications ✓, Contraindication CI	Initial Dose (Max)	Usual Dose; $🇨🇦/30d
OTHER	**CloNIDine** CATAPRES, g 0.1ᶜ, 0.2ᶜ mg tab; (0.025mg tab) ▼	**CENTRAL ALPHA AGONIST** (3rd line): use if others CI/ refractory HTN **Clonidine**: •Used for acute ↓BP •**DI**: cyclosporine,mirtazapine,TCA's **Methyldopa**: • **DI**: levodopa↓BP,TCAs↑BP	•**Sedation,dry mouth**,↓HR,depression & **rebound HTN** on withdrawal,impotence	•On the Beers Criteria for older patients list •**CI**:HF/heart block,diabetes autonomic neuropathy	0.1mg BID (0.2mg TID)	0.1-0.2mg BID $19-27
	Methyldopa ALDOMET, g 125, 250, 500mg tab		•Sedation, dry mouth, impotence, depression, **hepatotoxic**, lupus like sx & ↓ platelets/RBC	•Used in pregnancy; •An option for pheochromocytoma	125mg BID (500mg QID)	250mg BID $21
	Prazosin MINIPRESS, g 1ᶜ, 2ᶜ, 5ᶜ mg tab	**ALPHA BLOCKERS** (3rd line): use if others CI / refractory HTN **Doxoazosin** • removed from **ALLHAT** due to ↑ **HF/stroke** •**First dose syncope**: minimize by gradual dose titration & give @HS	•Sedation, dizziness, vertigo,headache, palpitations, ↑HR, fluid retention, weakness, nasal congestion & priapism.	•Useful for lower urinary tract symptoms (LUTS) e.g. poor stream, hesitancy, dribbling, incomplete voiding, prostatism [8,19] •An option for pheochromocytoma	0.5mg BID (5mg TID)	2mg BID $34
	Terazosin HYTRIN, g 1,2,5,10mg tab				1mg HS (10mg BID)	5mg HS $21
	Doxazosin CARDURA, g 1,2ᶜ,4ᶜmg tab				1mg HS (16mg daily)	4mg HS $28
	HydrALAZINE APRESOLINE, g 10ᶜ, 25, 50mg tab	**VASODILATOR** •Reflex ↑HR, edema&renin sx activation; often add β-blocker/diuretic	•↑↑HR, aggravate angina,headache,dizzy, fluid retention,lupus like>200mg/d & hepatitis	•**Alt:** HFrEF hydralazine with isosorbide A-HeFT •**CI:** LVH. •IV 1st line HTN emergency in pregnancy	10mg QID (50mg QID)	25mg QID $18
	Labetalol TRANDATE, g 100ᶜ, 200ᶜ mg tab	**ALPHA & BETA BLOCKADE** •↓ BP more than other β-blockers	•Postural hypotension & **hepatotoxicity** more than other Beta-Blockers 7	•Used in pregnancy; •**CI:** as per β-Blockers above	100mg BID (400mg TID)	200mg BID $44

ORAL ANTIHYPERTENSIVES Summary/Guidelines Comparison Chart

[1] Palmer, B. Managing Hyperkalemia Caused by Inhibitors of the Renin-Angiotensin-Aldosterone System. N Engl J Med 2004;351:585-92.

[1] Major Outcomes in High-Risk Hypertensive Patients Randomized to Angiotensin-Converting Enzyme Inhibitor or Calcium Channel Blocker vs Diuretic. The Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial (**ALLHAT**). The ALLHAT Officers and Coordinators for the ALLHAT Collaborative Research Group. JAMA. 2002;288:2981-2997.

[1] 2001 Canadian Hypertension Recommendations: What's New & What's Not so New but is Still Important. CJHP 2002;55:4651.

[1] FA McAlister, M Levine, KB Zarnke, et al. The 2000 recommendations for the management of hypertension. Can J Cardiol 2001; 17(5):543-559.

[1] 1999 Canadian recommendations for the management of hypertension. CMAJ 1999;161(Suppl):S1-S16.

[1] **1999 World Health Organization**–International Society of Hypertension Guidelines:Management of Hypertension. J Hypertens 1999;17:151-183.

[1] 6th Report-Joint National Committee-JNC on Prevention,Detection,Evaluation & Treatment of High Blood Pressure. Arch Intern Med 1997;157:2413-46.

[1] Drugs for hypertension. Med Lett Drugs Ther 2001;43:17-22. & Initial Therapy of Hypertension Med Lett Drugs Ther **2004**;46:53-55.

[1] Drugs in Pregnancy & Lactation, 11th Ed. Briggs GE,et al. Wilkins;Baltimore, MD. 2017.

[1] Micromedex 2018 online

[1] Hansten & Horn's Drug Interactions: Analysis & Management-Facts & Comparisons 2008.

[1] Treatment Guidelines: Drugs for Hypertension from The Medical Letter Feb 2003, repeated June 2005, January 2009, January 2012, May 2014 & updated **March 2017**.

[1] The **2017 Canadian** Hypertension Education Program **Recommendations** www.hypertension.ca

Hackam DG, Quinn RR, Ravani P, et al. Canadian Hypertension Education Program. The 2013 Canadian Hypertension Education Program (CHEP) Recommendations for Blood Pressure Measurement, Diagnosis, Assessment of Risk, Prevention, and Treatment of Hypertension. Can J Cardiol. 2013 Mar 28.

(Patient instructions for purchasing & using home blood pressure measurements can be found at www.hypertension.ca/tools & at www.heartandstroke.ca/bp)

Hackam DG, Khan NA, Hemmelgarn BR, et al. Canadian Hypertension Education Program. The 2010 Canadian Hypertension Education Program recommendations for the management of hypertension: part 2 - **therapy**. Can J Cardiol. 2010 May;26(5):249-58.

Quinn RR, Hemmelgarn BR, Padwal RS, et al. Canadian Hypertension Education Program. The 2010 Canadian Hypertension Education Program recommendations for the management of hypertension: part I - blood pressure measurement, **diagnosis and assessment of risk**. Can J Cardiol. 2010 May;26(5):241-8.

Canadian Hypertension Education Program. **2011 CHEP recommendations** for the management of **hypertension**. http://hypertension.ca/chep/wp-content/uploads/2011/05/FullCHEPRecommendations_EN_2011.pdf .

Dasgupta K, Quinn RR, Zarnke KB, et al. Canadian Hypertension Education Program. The **2014 CHEP-Canadian Hypertension** Education Program Recommendations for Blood Pressure Measurement, Diagnosis, Assessment of Risk, Prevention, and Treatment of Hypertension. Can J Cardiol. 2014 May;30(5):485-501.

Leung AA, Nerenberg K, Daskalopoulou SS, et al; CHEP Guidelines Task Force. Hypertension Canada's **2016 CHEP guidelines** for blood pressure measurement, diagnosis, assessment of risk, prevention and treatment of hypertension. Can J Cardiol 2016 (accepted manuscript) doi: 10.1016/j.cjca.2016.02.066 www.onlinecjc.ca/article/S0828-282X(16)00192-6/pdf (accessed April 11, 2016).

Harris KC, Benoit G, Dionne J, et al; **CHEP** Guidelines Task Force. Hypertension Canada's **2016 Canadian Hypertension** Education Program Guidelines for Blood Pressure Measurement,Diagnosis, and Assessment of Risk of **Pediatric Hypertension**. Can J Cardiol. 2016 May;32(5):589-97.

Dionne JM, Harris KC, Benoit G, et al. **Hypertension Canada's 2017 Guidelines for the Diagnosis, Assessment, Prevention, and Treatment of Pediatric Hypertension**. Can J Cardiol. 2017 May;33(5):577-585

Leung AA, Daskalopoulou SS, Dasgupta K, et al. **Hypertension Canada's 2017 Guidelines for Diagnosis, Risk Assessment, Prevention, and Treatment of Hypertension in Adults**. Can J Cardiol. 2017 May;33(5):557-576

Nerenberg KA, Zarnke KB, Leung AA, et al. **Hypertension Canada's 2018 guidelines for diagnosis, risk assessment, prevention, and treatment of hypertension in adults and children**. Can J Cardiol 2018; February 20, 2018.

Diabetes Canada Clinical Practice Guidelines Expert Committee, Tobe SW, Gilbert RE, Jones C, et al. **Treatment of Hypertension**. Can J Diabetes. 2018 Apr;42 Suppl 1:S186-S189.

Butalia S, Audibert F, Côté AM, et al. **Hypertension Canada's 2018 Guidelines for the Management of Hypertension in Pregnancy**. Can J Cardiol. 2018 May;34(5):526-531.

Nerenberg KA, Zarnke KB, et al. **Hypertension Canada's 2018 Guidelines for Diagnosis, Risk Assessment, Prevention, and Treatment of Hypertension in Adults and Children**. Can J Cardiol. 2018 May;34(5):506-525.

[1] ALLHAT Working Group. Major cardiovascular events in hypertensive patients randomized to doxazosin vs chlorthalidone: the antihypertensive and lipid-lowering treatment to prevent heart attack trial (**ALLHAT**). JAMA 2000;283:1967-75.

[1] The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, & Treatment of High Blood Pressure (The **JNC 7**); JAMA. **2003** May;289(19):2560-72. (Complete report in Hypertension 2003;42:1206-1252)

James PA, Oparil S, Carter BL, et al. **2014** evidence-based guideline for the management of **high blood pressure in adults**: report from the panel members appointed to the Eighth Joint National Committee (**JNC 8**). JAMA. doi:10.1001/jama.2013.284427.

[1] Black HR, Elliott WJ, Grandits G, et al. Principal results of the Controlled Onset Verapamil Investigation of Cardiovascular End Points (**CONVINCE**) trial. JAMA. 2003 Apr 23-30;289(16):2073-82.

[1] August P. Initial treatment of hypertension. N Engl J Med. 2003 Feb 13;348(7):610-7.
[1] Blood Pressure Lowering Treatment Trialists' Collaboration. Effects of different blood-pressure regimens on major cardiovascular events: results of prospectively-designed overviews of randomised trials. Lancet 2003; 362: 1527-35
[1] McConnell JD, Roehrborn CG, et al. The Long-Term Effect of Doxazosin, Finasteride, and Combination Therapy on the Clinical Progression of Benign Prostatic Hyperplasia. N Engl J Med. 2003 Dec 18;349(25):2387-2398.
[1] NICE Guidelines Aug,2004 Management of Hypertension in Adults in Primary Care http://www.nice.org.uk/pdf/CG018fullguideline.pdf
NICE: National Institute for Health and Clinical Excellence. **Hypertension Guidelines**. Aug 2011. http://www.nice.org.uk/nicemedia/live/13561/56015/56015.pdf
[1] Davis BR, Furberg CD, Wright JT Jr, Cutler JA, Whelton P; ALLHAT Collaborative Research Group. ALLHAT: setting the record straight. Ann Intern Med. 2004 Jul 6;141(1):39-46.
[1] Taylor AL, Ziesche S, Yancy C, Carson P, D'Agostino R Jr, Ferdinand K, Taylor M, Adams K, Sabolinski M, Worcel M, Cohn JN; African-American Heart Failure Trial Investigators. Combination of isosorbide dinitrate (20-40mg tid) and hydralazine (37.5-75mg tid) in blacks with heart failure (**A-HeFT**). N Engl J Med. 2004 Nov 11;351(20):2049-57.
[1] Diagnosis and Management of Chronic **Heart Failure** in the Adult: **ACC/AHA 2005 Guideline Update** for the (J Am Coll Cardiol 2005) http://www.acc.org/clinical/guidelines/failure/index.pdf
(**European 2005** Chronic Heart failure guidelines http://www.escardio.org/NR/rdonlyres/8A2848B4-5DEB-41B9-9A0A-5B5A90494B64/0/CHFFullTextehi205FVFW170505.pdf)
[1] Yusuf S., Effect of potentially modifiable risk factors associated with myocardial infarction in 52 countries (the INTERHEART study): case-control study. Lancet 2004 (online version published Sept 3,2004) Yusuf S, et al. INTERHEART Study Investigators. Effect of potentially modifiable risk factors associated with myocardial infarction in 52 countries (the INTERHEART study): case-control study. Lancet. 2004 Sep 11-17;364(9438):937-52.

Additional sources:
AACE Hypertension Task Force. American Association of Clinical **Endocrinologists** Medical Guidelines for Clinical Practice for the diagnosis and treatment of hypertension. Endocr Pract. **2006** Mar-Apr;12(2):193-222.
Abalos E, et al. Antihypertensive drug therapy for mild to moderate **hypertension during pregnancy**. Cochrane Database Syst Rev. 2007 Jan 24;(1):CD002252. It remains unclear whether antihypertensive drug therapy for mild to moderate hypertension during pregnancy is worthwhile.
Abalos E, Duley L, Steyn DW. Antihypertensive drug therapy for **mild to moderate hypertension during pregnancy**. Cochrane Database Syst Rev. 2014 Feb 6;2:CD002252. It remains unclear whether antihypertensive drug therapy for mild to moderate hypertension during pregnancy is worthwhile.

Abalos E, Duley L, Steyn DW, et al. Antihypertensive drug therapy for mild to moderate **hypertension during pregnancy**. Cochrane Database Syst Rev. 2018 Oct 1;10:CD002252. Antihypertensive drug therapy for mild to moderate hypertension during pregnancy reduces the risk of severe hypertension. The effect on other clinically important outcomes remains unclear. If antihypertensive drugs are used, beta blockers and calcium channel blockers appear to be more effective than the alternatives for preventing severe hypertension. High-quality large sample-sized randomised controlled trials are required in order to provide reliable estimates of the benefits and adverse effects of antihypertensive treatment for mild to moderate hypertension for both mother and baby, as well as costs to the health services, women and their families.
Abdalla M, Booth JN 3rd, Seals SR, et al. **Masked Hypertension** and Incident Clinic Hypertension Among Blacks in the Jackson Heart Study. Hypertension. 2016 May 16.
Abell JG, Kivimäki M, Dugravot A, et al. Association between **systolic blood pressure and dementia** in the Whitehall II cohort study: role of age, duration, and threshold used to define hypertension. Eur Heart J. 2018 Jun 12.
Abidov A, Rozanski A, Hachamovitch R, et al. Prognostic significance of **dyspnea** in patients referred for cardiac stress testing. N Engl J Med. 2005 Nov 3;353(18):1889-98.
ACCF/AHA 2011 Focused Update of the Guidelines for the Management of Patients With **Unstable Angina/Non-ST-Elevation Myocardial Infarction (Updating the 2007 Guideline):** A Report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines**.** J Am Coll Cardiol 2011 0: j.jacc.2011.02.009. http://content.onlinejacc.org/cgi/reprint/j.jacc.2011.02.009v1.pdf
ACCF/AHA 2011 American College of Cardiology Foundation Task Force on Clinical Expert Consensus Documents, , American Academy of Neurology, , American Geriatrics Society, , American Society for Preventive Cardiology, American Society of Hypertension, American Society of Nephrology, , Association ofBlack Cardiologists, , European Society of Hypertension, , Aronow, Wilbert S., Fleg, Jerome L., Pepine, Carl J., et al.
ACCF/AHA 2011 Expert Consensus Document on **Hypertension in the Elderly.** J Am Coll Cardiol 2011 0: j.jacc.2011.01.008. http://content.onlinejacc.org/cgi/reprint/j.jacc.2011.01.008v1.pdf
ACC/AHA 2017 Whelton PK, Carey RM, et al. **2017 ACC/AHA**/AAPA/ABC/ACPM/AGS/APhA/ASH/ASPC/NMA/PCNA **Guideline for the Prevention, Detection, Evaluation, and Management of High Blood Pressure** in Adults: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. Hypertension. 2017 Nov 13.
ACCORD Study Group, Effects of Intensive Blood-Pressure Control in Type 2 Diabetes Mellitus. N Engl J Med 2010 0: NEJMoa1001286
ACOG Committee on Obstetric Practice. Committee Opinion No. 623: **Emergent therapy for acute-onset, severe hypertension during pregnancy** and the postpartum period. Obstet Gynecol. 2015 Feb;125(2):521-5.
ACOG Committee Opinion No. 767 Summary: Emergent Therapy for Acute-Onset, **Severe Hypertension During Pregnancy and the Postpartum Period**. Obstet Gynecol. 2019 Feb;133(2):409-412.
ACOG Practice Bulletin No. 203: **Chronic Hypertension in Pregnancy**. Obstet Gynecol. 2019 Jan;133(1):e26-e50.
Acosta AA et al. Prevalence of Persistent **Prehypertension in Adolescents**. J Pediatr. 2011 Dec 6.
ACTIVE I Investigators. Irbesartan in Patients with Atrial Fibrillation. N Engl J Med 2011; 364:928-938. (Not reduce CV events)
ADA 2015: Standards of medical care in diabetes--2015: summary of revisions. Diabetes Care. 2015 Jan;38 Suppl:S4.
ADA 2017: American Diabetes Association.. 8. Pharmacologic Approaches to Glycemic Treatment. Diabetes Care. 2017 Jan;40(Suppl 1):S64-S74.
ADA 2017: American Diabetes Association.. 13. Management of Diabetes in Pregnancy. Diabetes Care. 2017 Jan;40(Suppl 1):S114-S119.
Adams AS, Uratsu C, Dyer W, et al. Health system factors and antihypertensive **adherence** in a racially and ethnically diverse cohort of new users. Arch Intern Med 2012.
Adamsson Eryd S, Gudbjörnsdottir S, et al. Blood pressure and complications in individuals with type 2 **diabetes** and no previous cardiovascular disease: national population based cohort study. BMJ. 2016 Aug 4;354:i4070.
Adderley NJ, Subramanian A, Nirantharakumar K, et al. Association Between **Idiopathic Intracranial Hypertension and Risk of Cardiovascular Diseases** in Women in the United Kingdom. JAMA Neurol. 2019 Jul 8
Agarwal R, Rossignol P, Romero A, et al. **Patiromer versus placebo** to enable spironolactone use in patients with resistant hypertension and chronic kidney disease (AMBER): a phase 2, randomised, double-blind, placebo-controlled trial. Lancet. 2019 Sep 13. doi: 10.1016/S0140-6736(19)32135-X.
Agarwal R, Sinha AD, Pappas MK, et al. Hypertension in **hemodialysis patients treated with atenolol or lisinopril**: a randomized controlled trial. Nephrol Dial Transplant. 2014;29:672-681.
Aggarwal B, Makarem N, Shah R, et al. Effects of **Inadequate Sleep on Blood Pressure and Endothelial Inflammation** in Women: Findings From the American Heart Association Go Red for Women Strategically Focused Research Network. J Am Heart Assoc. 2018 Jun 9;7(12).
AHA Writing Group Members, Roger VL, Go AS, Lloyd-Jones DM, et al; on behalf of the American Heart Association Statistics Committee and Stroke Statistics Subcommittee, Roger VL, Turner MB; On behalf of the American Heart Association Heart Disease and Stroke Statistics Writing Group. Executive Summary: **Heart Disease and Stroke Statistics—2011 Update**: A Report From the American Heart Association. Circulation. 2011 Feb 1;123(4):459-463.
AHA/ACC/ASH 2015 Rosendorff C, Lackland DT, Allison M, et al. **Treatment of Hypertension in Patients With Coronary Artery Disease**: A Scientific Statement From the American Heart Association (**AHA**), American College of Cardiology (**ACC**) , and American Society of Hypertension (**ASH**). Circulation. 2015 Mar 31.
AHA: Muntner P, Shimbo D, Carey RM, et al; American Heart Association Council on Hypertension; Council on Cardiovascular Disease in the Young; Council on Cardiovascular and Stroke Nursing; Council on Cardiovascular Radiology and Intervention; Council on Clinical Cardiology; and Council on Quality of Care and Outcomes Research. Measurement of Blood Pressure in Humans: A Scientific Statement From the American Heart Association. Hypertension. 2019 Mar 4:HYP0000000000000087.
Ahmadizar F, et al. **Undertreatment of hypertension and hypercholesterolaemia in children and adolescents with type 1 diabetes**: long-term follow-up on time trends in the occurrence of cardiovascular disease, risk factors and medications use. Br J Clin Pharmacol. 2018 Apr;84(4):776-785.
Ahmed SH, Ewins DL, Nair S, et al. **Spontaneous hypokalaemia** in a man with treated hypertension. BMJ. 2015 Apr 30;350:h2154.
Akkerman D, Cleland L, Croft G, et al. **Routine prenatal care**. Bloomington (MN): Institute for Clinical Systems Improvement (ICSI); 2012 Jul.
Al Hamarneh YN, Houle SK, Padwal R, Tsuyuki RT. **Hypertension Canada's 2016 Canadian Hypertension Education Program guidelines for pharmacists**: An update. Can Pharm J (Ott). 2016 Nov;149(6):337-344.
Al-Kindi SG, Oliveira GH. Abrupt Increase in Reporting of **Neoplasms Associated with Valsartan** After Medication Recall. Circ Cardiovasc Qual Outcomes. 2019 Jul;12(7):e005536.
Al-Mallah MH, et al. Angiotensin-converting enzyme inhibitors in coronary artery disease and **preserved left ventricular** systolic function: a systematic review and meta-analysis of randomized controlled trials. J Am Coll

Cardiol. 2006 Apr 18;47(8):1576-83. Epub 2006 Mar 29. Treatment of 100 patients for an average duration of 4.4 years prevents either of the adverse outcomes (one death, or one nonfatal myocardial infarction, or one cardiovascular death or one coronary revascularization procedure). CONCLUSIONS: The cumulative evidence provided by this meta-analysis shows a modest favorable effect of ACEIs on the outcome of patients with CAD and preserved LV systolic function.

Aladin AI, Al Rifai M, et al. Relation of **Coronary Artery Calcium and Extra-Coronary Aortic Calcium** to Incident Hypertension (from the Multi-Ethnic Study of Atherosclerosis). Am J Cardiol. 2018 Jan 15;121(2):210-216

Albanese E, Lombardo FL, Prince MJ, Stewart R. **Dementia and lower blood pressure** in Latin America, India, and China: A 10/66 cross-cohort study. Neurology. 2013 Jul 16;81(3):228-35.

Alexander D, Northcross A, Wilson N, et al. Randomized Controlled **Ethanol Cookstove Intervention** and Blood Pressure in Pregnant Nigerian Women. Am J Respir Crit Care Med. 2017 Jun 15;195(12):1629-1639.

Alharbi FF, Souverein PC, de Groot MCH, et al. The Impact of **Serum Potassium**-Influencing Antihypertensive Drugs on the Risk of Out-of-Hospital Cardiac Arrest: A Case Control Study. Br J Clin Pharmacol. 2017 Jun 29.

Allan, G. Michael, Mallery, Laurie, Ivers, Noah. Treating hypertension in the **very elderly**. Can Fam Physician 2010 56: 1141.

Allen N, Berry J, Ning H, et al. Impact of blood pressure and **blood pressure change during middle age** on the remaining lifetime risk for cardiovascular disease the cardiovascular lifetime risk pooling project. Circulation 2012;

Allen M, Kelly K, Fleming I. **Hypertension in elderly patients**: Recommended systolic targets are **not evidence based**. Can Fam Physician. 2013 Jan;59(1):19-21.

Allen NB, Siddique J, Wilkins JT, et al. Blood pressure trajectories in **early adulthood and subclinical atherosclerosis in middle age. (CARDIA**) JAMA 2014; 311:490-497.

Allesøe K, Søgaard K, Aadahl M, Boyle E, Holtermann A. Are **hypertensive women at additional risk** of ischaemic heart disease from **physically demanding work**? Eur J Prev Cardiol. 2016 Feb 14.

Alsabbagh MH, Lemstra M, Eurich D, et al. **Socioeconomic status and nonadherence** to antihypertensive drugs: a systematic review and meta-analysis. Value Health. 2014 Mar;17(2):288-96.

American College of Physicians. **In the clinic. Hypertension**. Ann Intern Med. Dec 2,2008;149:ITC6(1-15; quiz 16).

American Heart Association Nutrition Committee, Lichtenstein AH, Appel LJ, Brands M, et al. **Diet and lifestyle recommendations revision 2006**: a scientific statement from the American Heart Association Nutrition Committee. Circulation 2006 Jul 4;114(1):82-96.

American College of Obstetricians and Gynecologists (**ACOG**). **Chronic hypertension in pregnancy**. Washington (DC): American College of Obstetricians and Gynecologists (ACOG); 2012 Feb. 12.

Anderson AH, Yang W, et al. Chronic Renal Insufficiency Cohort Study Investigators. **Time-updated systolic blood pressure** and the progression of chronic kidney disease: a cohort study. Ann Intern Med. 2015 Feb 17;162(4):258-65.

Anderson JL, Adams CD, Antman EM, et al. **ACC/AHA 2007** guidelines for the management of patients with **unstable angina/non-ST-elevation myocardial infarction**. A report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. *J Am Coll Cardiol* 2007; DOI:10.1016/j.jacc.2007.02.028. Available at: http://content.onlinejacc.org/cgi/content/full/50/7/e1. *Circulation* 2007; DOI:10.1161/CIRCULATIONAHA.107.185752. Available at: http://circ.ahajournals.org/cgi/reprint/CIRCULATIONAHA.107.185752. (**2011 ACCF/AHA Focused Update** of the Guidelines for the Management of Patients With **Unstable Angina/Non-ST-Elevation Myocardial Infarction (Updating the 2007 Guideline):** A Report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. J Am Coll Cardiol 2011 0: j.jacc.2011.02.009. http://content.onlinejacc.org/cgi/reprint/j.jacc.2011.02.009v1.pdf)

Anderson RJ, Bahn GD, Moritz TE, et al.; for the **VADT** Study Group. Blood Pressure and Cardiovascular Disease risk in the Veterans Affairs Diabetes Trial (VADT) Diabetes Care. 2010 Nov 8. DBP <70 mmHg elevated CVD risk.

Anderson CS, Huang Y, Arima H, et al. Effects of early intensive blood pressure-lowering treatment on the growth of hematoma and perihematomal edema in **acute intracerebral hemorrhage**: the Intensive Blood Pressure Reduction in Acute Cerebral Haemorrhage Trial (**INTERACT**). Stroke 2010;41:307-12.

Anderson CS, Heeley E, Huang Y, et al. **Rapid blood-pressure lowering in patients with acute intracerebral hemorrhage**. (**Interact 2**) N Engl J Med 2013. DOI: 10.1056/NEJMoa1214609.

Anderson TS, Jing B, Auerbach A, et al. Clinical **Outcomes After Intensifying Antihypertensive Medication Regimens** Among Older Adults at Hospital Discharge. JAMA Intern Med. 2019 Aug 19.

Anderson TS, Wray CM, Jing B, et al. **Intensification of older adults' outpatient blood pressure treatment at hospital discharge**: national retrospective cohort study. BMJ. 2018 Sep 12;362:k3503.

Anderson CS, Huang Y, Lindley RI,et al. Intensive blood pressure reduction with **intravenous thrombolysis therapy for acute ischaemic stroke** (ENCHANTED): an international, randomised, open-label, blinded-endpoint, phase 3 trial. Lancet. 2019 Feb 6.

Andrews PJ, Sinclair HL, Rodriguez A, et al; Eurotherm3235 Trial Collaborators. **Hypothermia for Intracranial Hypertension** after Traumatic Brain Injury. N Engl J Med. 2015 Oct 7.

Andrew NE, Kim J, Thrift AG, et al. **Prescription of antihypertensive medication at discharge influences survival following stroke**. Neurology. 2018 Feb 27;90(9):e745-e753.

Anker D, Santos-Eggimann B, Santschi V, et al. **Screening and treatment of hypertension in older adults:** less is more? Public Health Rev. 2018 Sep 3;39:26.

Antoniou T, Camacho X, Yao Z, et al. Comparative effectiveness of **angiotensin-receptor blockers for preventing macrovascular disease in patients with diabetes**: a population-based cohort study. CMAJ. 2013 Jul 8.

Anthonisen NR, Skeans MA, Wise RA, Manfreda J, Kanner RE, Connett JE, for the Lung Health Study Research Group. The effects of a smoking cessation intervention on 14.5-year mortality. A randomized clinical trial. Ann Intern Med 2005; 142:233-39. (InfoPOEMs: A smoking cessation program resulted in fewer deaths over the next 15 years than usual care, even though only 1 in 5 (21.7%) of the participants actually quit smoking. More important, though, is the good evidence that smoking cessation decreases the risk of dying by heart disease, cardiovascular disease, or lung cancer. Yes, it's what we expected, but it's good to know for sure. (LOE = 1b-))

Antonia Trichopoulou, Philippos Orfanos, Teresa Norat, et al. Modified Mediterranean diet and survival: EPIC-elderly prospective cohort study. BMJ, Apr 2005; 10.1136/bmj.38415.644155.8F.

Appel LJ, et al. American Heart Association. **Dietary approaches** to prevent and treat hypertension: a scientific statement from the American Heart Association. Hypertension. 2006 Feb;47(2):296-308.

Appel LJ, Wright JT Jr, Greene T, et al. Intensive bloodpressure control in hypertensive chronic kidney disease. (**AASK**) N Engl J Med 2010;363:918-29.

Arcand J, Wong MMY, Santos JA, et al. More evidence that **salt increases blood pressure** and risk of kidney disease from the Science of Salt: A regularly updated systematic review of salt and health outcomes (April-July 2016). J Clin Hypertens (Greenwich). 2017 Aug;19(8):813-823.

Archbold KH, Vasquez MM, Goodwin J et al. Effects of **Sleep Patterns** and Obesity on Increases in **Blood Pressure** in a 5-Year Period: Report from the Tucson Children's Assessment of Sleep Apnea Study. J Pediatr. 2012 Jan 25.

Arguedas JA, Perez MI, Wright JM. **Treatment blood pressure targets** for hypertension. Cochrane Database Syst Rev 2009; 3:CD004349. Treating patients to lower than standard BP targets, </=140-160/90-100 mmHg, does not reduce mortality or morbidity.

Arguedas JA, Leiva V, Wright JM. **Blood pressure targets for hypertension in people with diabetes** mellitus. Cochrane Database Syst Rev. 2013 Oct 30;10:CD008277. doi: 10.1002/14651858.CD008277.pub2. At the present time, evidence from randomized trials does not support blood pressure targets lower than the standard targets in people with elevated blood pressure and diabetes. More randomized controlled trials are needed, with future trials reporting total mortality, total serious adverse events as well as cardiovascular and renal events.

Argulian E, Messerli FH, Aziz EF, et al. **Antihypertensive Therapy in Hypertrophic Cardiomyopathy**. Am J Cardiol. 2013 Jan 19.

Arima H, Anderson C, Omae T, et al; for the Perindopril Protection Against Recurrent Stroke Study (**PROGRESS**) Collaborative Group. Effects of Blood Pressure Lowering on Intracranial and Extracranial Bleeding in Patients on Antithrombotic Therapy: The PROGRESS Trial. Stroke. 2012 Jun;43(6):1675-1677.

Arima H, Heeley E, Delcourt C, et al. INTERACT2 Investigators; **INTERACT2** Investigators. **Optimal achieved blood pressure in acute intracerebral hemorrhage**: INTERACT2. Neurology. 2015 Feb 3;84(5):464-71.

Arnlov J, et al. Low-grade albuminuria and incidence of cardiovascular disease events in nonhypertensive and nondiabetic individuals: the Framingham Heart Study. Circulation. 2005 Aug 16;112(7):969-75.

Arnold JM, et al.; Canadian Cardiovascular Society. **Canadian** Cardiovascular Society consensus conference recommendations on **heart failure 2006**: diagnosis and management. Can J Cardiol. 2006 Jan;22(1):23-45. Erratum in: Can J Cardiol. 2006 Mar 1;22(3):271. (Arnold JM, Howlett JG, Dorian P, et al. Canadian Cardiovascular Society Consensus Conference recommendations on heart failure **update 2007**: Prevention, management during intercurrent illness or acute decompensation, and use of biomarkers. Can J Cardiol. 2007 Jan;23(1):21-45.)

Arnspang S, Gaist D, Johannesdottir Schmidt SA, et al. **Hydrochlorothiazide** use and **risk of non-melanoma skin cancer**: A nationwide case-control study from Denmark. J Am Acad Dermatol. 2017 Nov 30.

Arora P, Song Y, Dusek J, et al. **Vitamin D** Therapy in Individuals With Prehypertension or Hypertension: The **DAYLIGHT** Trial. Circulation. 2015 Jan 20;131(3):254-62.

Arvanitakis Z, Capuano AW, Lamar M, et al. **Late-life blood pressure association with cerebrovascular and Alzheimer disease** pathology. Neurology. 2018 Jul 11.

Askie LM, Duley L, Henderson-Smart DJ, Stewart LA. **Antiplatelet agents for prevention of pre-eclampsia**: a meta-analysis of individual patient data. Lancet 2007;369:1791-8.

Atasoy S, Johar H, Peters A, Ladwig KH. Association of **hypertension cut-off values with 10-year cardiovascular mortality and clinical consequences**: a real-world perspective from the prospective MONICA/KORA study. Eur Heart J. 2018 Nov 21.

Atsma F, Veldhuizen I, de Kort W, et al. **Hemoglobin level** is positively associated with blood pressure in a large cohort of healthy individuals. Hypertension. 2012 Oct;60(4):936-41.

Attaei MW, Khatib R, McKee M, et al, for the **PURE** study investigators. Availability and **affordability of blood pressure-lowering medicines** and the effect on blood pressure control in high-income, middle-income, and low-income countries: an analysis of the PURE study data. Lancet Public Health 2017; 2: e411–419.

Atzema CL, Wong A, et al. The Characteristics and Outcomes of Patients Who Make an **Emergency Department Visit for Hypertension After Use of a Home or Pharmacy Blood Pressure Device**. Ann Emerg Med. 2018 Jul 18.

Au CT, Ho CK, Wing YK, et al. Acute and Chronic Effects of **Sleep Duration on Blood Pressure**. Pediatrics. 2013 Dec 16

August P, Malha L. **Post Partum Hypertension**: "It Ain't Over 'til It's Over". Circulation. 2015 Sep 28.

Avataneo V, De Nicolò A, Rabbia F, et al. Therapeutic drug monitoring guided definition of adherence profiles in **resistant hypertension and identification of predictors of poor adherence**. Br J Clin Pharmacol. 2018 Jul 3.

Azizi M, Sapoval M, Gosse P, et al, and the Renal Denervation for Hypertension (**DENERHTN**) investigators. Optimum and stepped care **standardised antihypertensive treatment with or without renal denervation** for resistant hypertension (DENERHTN): a multicentre, open-label, randomised controlled trial. Lancet 2015; online Jan 26.

Azizi M, Schmieder RE, Mahfoud F, et al. Endovascular ultrasound renal denervation to treat hypertension (**RADIANCE-HTN SOLO**): a multicentre, international, single-blind, randomised, sham-controlled trial. Lancet 2018; online May 23. http://dx.doi.org/10.1016/S01406736(18)31082-1.

Azizi M, Schmieder RE, Mahfoud F, et al. Six-Month Results of Treatment-Blinded Medication Titration for Hypertension Control Following Randomization to **Endovascular Ultrasound Renal Denervation or a Sham Procedure** in the RADIANCE-HTN SOLO Trial. Circulation. 2019 Mar 17.

Azizi M, Pereira H, Hamdidouche I, et al, and the DENERHTN investigators. Adherence to antihypertensive treatment and the blood pressure-lowering effects of **renal denervation** in the Renal Denervation for Hypertension (**DENERHTN**) trial. Circulation. 2016;134:847–857.

Bae S, Hong YC. Exposure to **Bisphenol A** From Drinking Canned Beverage Increases Blood Pressure: Randomized Crossover Trial. Hypertension. 2014 Dec 8.

Bae S, Kim JH, Lim YH, Park HY, Hong YC. Associations of **bisphenol A** exposure with heart rate variability and blood pressure. Hypertension. 2012 Sep;60(3):786-93.

Bahiru E, de Cates AN, Farr MRB, et al. **Fixed-dose combination therapy** for the prevention of atherosclerotic cardiovascular diseases. Cochrane Database of Systematic Reviews 2017, Issue 3. Art. No.: CD009868. The effects of fixed-dose combination therapy on all-cause mortality or ASCVD events are uncertain. A limited number of trials reported these outcomes, and the included trials were primarily designed to observe changes in ASCVD risk factor levels rather than clinical events, which may partially explain the observed differences in risk factors that were not translated into differences in clinical outcomes among the included trials. Fixed-dose combination therapy is associated with modest increases in adverse events compared with placebo, active comparator, or usual care but may be associated with improved adherence to a multidrug regimen. Ongoing, longerterm trials of fixed-dose combination therapy will help demonstrate whether short-term changes in risk factors might be maintained and lead to expected differences in clinical events based on these changes.

Bailey DG, Dresser GK, Urquhart BL, et al. **Coffee-Antihypertensive Drug Interaction**: A Hemodynamic and Pharmacokinetic Study With Felodipine. Am J Hypertens. 2016 Aug 1.

Bainey KR, Rahim S, Etherington K, et al; Effects of **withdrawing vs continuing renin-angiotensin blockers on incidence of acute kidney** injury in patients with renal insufficiency undergoing cardiac catheterization: Results from the Angiotensin Converting Enzyme Inhibitor/Angiotensin Receptor Blocker and Contrast Induced Nephropathy in Patients Receiving Cardiac Catheterization (**CAPTAIN**) trial. Am Heart J. 2015 Jul;170(1):110-6.

Baker-Smith CM, Flinn SK, Flynn JT, et al. Diagnosis, Evaluation, and Management of **High Blood Pressure in Children and Adolescents**. Pediatrics. 2018 Aug 20.

Bakris GL, Townsend RR, Liu M, et al. Impact of **renal denervation** on 24-hour **ambulatory blood pressure**: Results from **SYMPLICITY HTN-3.** *J Am Coll Cardiol* 2014; DOI:10.1016/j.jacc.2014.05.012.

Bakris GL. The Implications of **Blood Pressure Measurement** Methods on Treatment Targets for Blood Pressure. Circulation. 2016 Aug 30.

Bakris G, Ali W, Parati G. **ACC/AHA Versus ESC/ESH on Hypertension Guidelines**: JACC Guideline Comparison. J Am Coll Cardiol. 2019 Jun 18;73(23):3018-3026.

Bakris G, Sorrentino M. **Redefining Hypertension - Assessing the New Blood-Pressure Guidelines**. N Engl J Med. 2018 Jan 17.

Bandeali SJ, Kayani WT, Lee VV, et al. Outcomes of Preoperative Angiotensin-Converting Enzyme Inhibitor Therapy in Patients Undergoing Isolated **Coronary Artery Bypass Grafting**. Am J Cardiol. 2012 Jun 20.

Banegas JR, Ruilope LM, de la Sierra A, et al. High prevalence of **masked uncontrolled hypertension** in people with treated hypertension. Eur Heart J. 2014 Dec 7;35(46):3304-12.

Banegas JR, Ruilope LM, de la Sierra A, et al. Relationship between **clinic and ambulatory blood-pressure measurements and mortality**. N Engl J Med 2018; 378: 1509-20.

Bangalore S, Qin J, Sloan S, Murphy SA, Cannon CP; for the PROVE IT-TIMI 22 Trial Investigators. What Is the **Optimal Blood Pressure in Patients After Acute Coronary Syndromes**?: Relationship of Blood Pressure and Cardiovascular Events in the Pravastatin or Atorvastatin Evaluation and Infection Therapy-Thrombolysis in Myocardial Infarction (**PROVE IT-TIMI**) 22 Trial. Circulation. 2010 Nov 8.

Bangalore Sripal, Kumar Sunil, Kjeldsen Sverre E et al. Antihypertensive drugs and **risk of cancer**: network meta-analyses and trial sequential analyses of 324,168 participants from randomised trials. *The Lancet Oncology* - 30 November 2010 DOI: 10.1016/S1470-2045(10)70260-6. (Combo of ACEI & ARB possible higher risk)

Bangalore Sripal, Kumar Sunil, Wetterslev Jørn, et al. **Angiotensin receptor blockers and risk of myocardial infarction**: meta-analyses and trial sequential analyses of 147 020 patients from randomised trials. BMJ 2011;342:doi:10.1136/bmj.d2234 (Published 26 April 2011). –no increase in MI.

Bangalore S, Kumar S, Lobach I, et al. **Blood pressure targets in subjects with type 2 diabetes mellitus/impaired fasting glucose**: Observations from traditional and Bayesian random-effects meta-analyses of randomized trials. Circulation 2011. DOI: 10.1161/CIRCULATIONAHA.110.016337.

Bangalore S, Kumar S, Fusaro M et al. Outcomes with various **drug eluting** or bare metal stents in patients with diabetes mellitus: mixed treatment comparison analysis of 22 844 patient years of follow-up from randomised trials. BMJ. 2012 Aug 10;345:e5170.

Bangalore S, Steg PHG, Deedwania P, et al. **Beta blocker use** and clinical outcomes in **stable outpatients with and without coronary artery disease**. JAMA 2012; 308:1340-1349.

Bangalore S, Gong Y, Cooper-DeHoff RM, et al. **2014 Eighth Joint National Committee-JNC** Panel recommendations for **blood pressure targets** revisited: Results from the **INVEST** study. *J Am Coll Cardiol* 2014; 64:784-793.

Bangalore S, Bhatt DL, Steg PG, et al. **ß-blockers and cardiovascular events in patients with and without myocardial infarction**: Post hoc analysis from the **CHARISMA** trial. *Circ Cardiovasc Qual Outcomes* 2014.

Bangalore S, Ogedegbe G, Gyamfi J, et al. Outcomes with **Angiotensin-converting Enzyme Inhibitors vs Other Antihypertensive Agents in Hypertensive Blacks**. Am J Med. 2015 Nov;128(11):1195-203.

Bangalore S, Fakheri R, et al. **Angiotensin-Converting Enzyme Inhibitors or Angiotensin Receptor Blockers in Patients Without Heart Failure**? Insights From 254,301 Patients From Randomized Trials. Mayo Clin Proc. 2016 Jan;91(1):51-60.

Bangalore S, Fakheri R, Toklu B, Messerli FH. **Diabetes** mellitus as a **compelling indication for using renin angiotensin system blockers**: systematic review and meta-analysis of randomized trials. BMJ 2016;352:i438.

Bangalore S, Fakheri R, Wandel S, et al. **Renin angiotensin system inhibitors** for patients with stable coronary artery disease without heart failure: systematic review and meta-analysis of randomized trials. BMJ. 2017 Jan 19;356:j4.

Bangalore S, Toklu B, Gianos E, et al. **Optimal Systolic Blood Pressure Target After SPRINT**: Insights from a Network Meta-Analysis of Randomized Trials. Am J Med. 2017 Jan 19.

Barakat R, Pelaez M, Cordero Y, et al. Exercise during pregnancy protects against hypertension and macrosomia: randomized clinical trial. Am J Obstet Gynecol. 2016 May;214(5):649.e1-8.

Barbe´ F, Dura´ n-Cantolla J, Sa´ nchez-de-la-Torre M, et al. Effect of continuous positive airway pressure on the incidence of hypertension and cardiovascular events in nonsleepy patients with obstructive sleep apnea: a randomized controlled trial. JAMA. 2012;307(20):2161-2168.

Baron RB. Treating Blood Pressure Correctly by Measuring It Correctly. JAMA Intern Med. 2018 Apr 16.

Barzilay JI, Davis BR, Cutler JA, et al. Fasting Glucose Levels and Incident **Diabetes Mellitus** in Older NondiabeticAdults Randomized to Receive 3 Different Classes of Antihypertensive Treatment: A Report From the Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial (**ALLHAT**). Arch Intern Med. 2006 Nov 13;166(20):2191-201. Fasting glucose levels increase in older adults with hypertension regardless of treatment type. For those taking chlorthalidone vs other medications, the risk of developing FG levels higher than 125 mg/dL (6.9 mmol/L) is modestly greater, but there is no conclusive or consistent evidence that this diuretic-associated increase in DM risk increases the risk of clinical events.

Baş M, Greve J, Stelter K, et al. A randomized trial of **icatibant in ACE-inhibitor-induced angioedema**. N Engl J Med. 2015 Jan 29;372(5):418-25.

Basson M, Mezzarobba M, Weill A, et al. **Severe intestinal malabsorption associated with olmesartan**: a French nationwide observational cohort study. Gut. 2015 Aug 6.

Basu S, Sussman JB, Hayward RA. Detecting **Heterogeneous Treatment Effects to Guide Personalized Blood Pressure Treatment**: A Modeling Study of Randomized Clinical Trials. Ann Intern Med. 2017 Jan 3.

Bateman BT, Hernandez-Diaz S, Huybrechts KF, et al. Patterns of Outpatient **Antihypertensive Medication Use During Pregnancy** in a Medicaid Population. Hypertension. 2012 Sep 10.

Bateman BT, Huybrechts KF, Fischer MA, et al. **Chronic Hypertension in Pregnancy** and the Risk of Congenital Malformations: A Cohort Study. Am J Obstet Gynecol. 2014 Sep 26.

Bath PMW, Krishnan K. Interventions for deliberately **altering blood pressure in acute stroke**. Cochrane Database of Systematic Reviews 2014, Issue 10. Art. No.: CD000039. DOI: 10.1002/14651858.CD000039.pub3. There is insufficient evidence that lowering blood pressure during the acute phase of stroke improves functional outcome. It is reasonable to withhold blood pressure-lowering drugs until patients are medically and neurologically stable, and have suitable oral or enteral access, after which drugs can than be reintroduced. In people with acute stroke, CCBs, ACEI, ARA, beta blockers and NO donors each lower blood pressure while phenylephrine probably increases blood pressure. Further trials are needed to identify which people are most likely to benefit from early treatment, in particular whether treatment started very early is beneficial.

Batool-Anwar S, Malhotra A, Forman J, Winkelman J, Li Y, Gao X. **Restless legs syndrome and hypertension** in middle-aged women. Hypertension. 2011;58:791–796.

Bavishi C, Ahmed M, Trivedi V, et al. Meta-Analysis of Randomized Trials on the Efficacy and Safety of **Angiotensin-Converting Enzyme Inhibitors in Patients >/=65 Years of Age**. Am J Cardiol. 2016 Aug 22.

Bavishi C, Bangalore S, Messerli FH. Outcomes of **intensive blood pressure lowering in older hypertensive patients**. J Am Coll Cardiol 2017;69: 486–93.

Bavry AA, Kumbhani DJ, Gong Y et al.**Simple integer risk score** to determine prognosis of patients with hypertension and chronic stable coronary artery disease. J Am Heart Assoc. 2013 Aug 15;2(4):e000205.

Beardmore KS, Morris JM, Gallery ED. Excretion of **antihypertensive medication into human breast milk**: a systematic review. Hypertens Pregnancy 2002;21:85-95.

Beckett NS, Peters R, Fletcher AE, et al. the **HYVET** Study Group. Treatment of Hypertension in Patients 80 Years of Age or Older. N Engl J Med. 2008 Mar 31; [Epub ahead of print] The results provide evidence that antihypertensive treatment with indapamide (sustained release), with or without perindopril, in persons 80 years of age or older is beneficial.

Beckett N, Peters R, Tuomilehto J, et al. for the **HYVET** Study Group. **Immediate and late benefits** of treating very elderly people with hypertension: results from active treatment extension to Hypertension in the Very Elderly randomised controlled trial. BMJ. 2011 Jan 4;344:d7541. doi: 10.1136/bmj.d7541.

Beddhu S, et al. Effects of **Intensive Systolic Blood Pressure Control on Kidney and Cardiovascular Outcomes in Persons Without Kidney Disease**: A Secondary Analysis of a Randomized Trial. Ann Intern Med. 2017 Sep 5.

Beddhu S, Chertow GM, Cheung AK, et al; for the **SPRINT** Research Group. Influence of **baseline diastolic blood pressure** on effects of intensive compared with standard blood pressure control. Circulation. 2018;137:134–143.

Beddhu S, Greene T, Boucher R, et al. Intensive **systolic blood pressure control** and incident **chronic kidney disease** in people with and without diabetes mellitus: secondary analyses of two randomised controlled trials. Lancet Diabetes Endocrinol 2018; online April 20.

Beeftink MM, van der Sande NG, Bots ML, et al. **Safety of Temporary Discontinuation of Antihypertensive Medication** in Patients With Difficult-to-Control Hypertension. Hypertension. 2017 May;69(5):927-932.

Behrens I, Basit S, Lykke JA, et al. Association Between **Hypertensive Disorders of Pregnancy** and Later Risk of **Cardiomyopathy**. JAMA. 2016 Mar 8;315(10):1026-33.

Behrens I, Basit S, Melbye M, et al. Risk of **post-pregnancy hypertension** in women with a history of hypertensive disorders of pregnancy: nationwide cohort study. BMJ 2017;358:j3078.

Bell KJL, Doust J, Glasziou P. Incremental Benefits and Harms of the **2017American College of Cardiology/American Heart Association High Blood Pressure Guideline**. JAMA Intern Med. 2018 Apr 16.

Bello NA, Woolley JJ, Cleary KL, et al. **Accuracy of Blood Pressure Measurement Devices in Pregnancy**: A Systematic Review of Validation Studies. Hypertension. 2018 Feb;71(2):326-335.

Benetos A, Labat C, Rossignol P, et al. Treatment With Multiple Blood Pressure Medications, Achieved Blood Pressure, and Mortality in **Older Nursing Home Residents**: The **PARTAGE** Study. JAMA Intern Med. 2015 Feb 16.

Benetos A, Rossignol P, Cherubini A, et al. Polypharmacy in the Aging Patient: **Management of Hypertension in Octogenarians**. JAMA. 2015 Jul 14;314(2):170-180.

Benetos A, et al. An Expert Opinion From the European Society of Hypertension-European Union Geriatric Medicine Society Working Group on the Management of Hypertension in **Very Old, Frail Subjects**. Hypertension. 2016 May;67(5):820-5.

Benjamin EJ, Blaha MJ, et al; **Heart Disease and Stroke Statistics-2017** Update: A Report From the American Heart Association. Circulation. 2017 Jan 25.

Bennett A, Chow CK, Chou M, et al. Efficacy and safety of **quarter dose blood pressure lowering agents**: a systematic review and meta-analysis of randomized controlled trials. Hypertension. 2017;70:85–93.

Benschop L, Duvekot JJ, Versmissen J, et al. **Blood Pressure Profile 1 Year After Severe Preeclampsia**. Hypertension. 2018 Feb 5.

Bergersen BM. Cardiovascular Risk in Patients with **HIV Infection** : Impact of Antiretroviral Therapy. Drugs. 2006;66(15):1971-87.

Bergman GJ, Khan S, Danielsson B, et al. **Breast cancer risk and use of calcium channel blockers** using Swedish population registries. JAMA Intern Med. 2014 Oct 1;174(10):1700-1.

Berlowitz DR, CG Foy, Kazis LE, et al. Effect of **intensive blood-pressure treatment** on patient-recorded outcomes. (**SPRINT**) N Engl J Med 2017; DOI:10.1056/NEJMoa1611179.

Bernstein PS et al. National Partnership for Maternal Safety: Consensus bundle on **severe hypertension** during **pregnancy** and the **postpartum** period. Obstet Gynecol 2017 Aug; 130:347.

Beveridge LA, Struthers AD, Khan F, et al.; D-PRESSURE Collaboration. Effect of **Vitamin D** Supplementation on Blood Pressure: A Systematic Review and Meta-analysis Incorporating Individual Patient Data. JAMA Intern Med. 2015 Mar 16.

Beyer F, Dickinson H, Nicolson Dj, Ford G, Mason J. Combined **calcium, magnesium and potassium** supplementation for the management of primary hypertension in adults. Cochrane Database Syst Rev. 2006 Jul 19;3:CD004805.

Bhandari S, et al. Multicentre randomized controlled trial of **angiotensin-converting enzyme inhibitor/ angiotensin receptor blocker withdrawal** in advanced renal disease: the **STOP-ACEi** trial. Nephrol Dial Transplant. 2015 Sep 30.

Bhaskaran K, Douglas I, Evans S, et al. Angiotensin receptor blockers and **risk of cancer**: cohort study among people receiving antihypertensive drugs in UK General Practice Research Database. BMJ. 2012 Apr 24;344:e2697.

Bhatt DL, et al. **REACH** Registry Investigators. International prevalence, recognition, and treatment of **cardiovascular risk factors** in outpatients with atherothrombosis. JAMA. 2006 Jan 11;295(2):180-9.

Bhatt DL, Kandzari DE, O'Neill WW, et al. A controlled trial of **renal denervation** for resistant hypertension. (**Symplicity HTN 3**) N Engl J Med. DOI: 10.1056/NEJMoa1402670.

Bhatia RS, et al. Outcome of **heart failure** with **preserved ejection fraction** in a population-based study. N Engl J Med. 2006 Jul 20;355(3):260-9.

Bibbins-Domingo, Kirsten, Chertow, Glenn M., Coxson, Pamela G., et al. Projected Effect of Dietary **Salt Reductions** on Future Cardiovascular Disease. N Engl J Med 2010 0: NEJMoa0907355.

Biffi A, Anderson CD, Battey TW, et al. Association Between Blood Pressure Control and **Risk of Recurrent Intracerebral Hemorrhage**. JAMA. 2015 Sep 1;314(9):904-12.

Billington CK, Appleton JP, Berge E, et al. Impact of **hydration status on haemodynamics, effects of acute blood pressure lowering treatment, and prognosis after stroke**. Br J Clin Pharmacol. 2018 Sep 8.

Birks EJ, et al. **Left ventricular assist device** and drug therapy for the reversal of heart failure. N Engl J Med. 2006 Nov 2;355(18):1873-84.

Bis JC et al. **Drug-Gene Interactions** of Antihypertensive Medications and Risk of Incident Cardiovascular Disease: A Pharmacogenomics Study from the CHARGE Consortium. PLoS One. 2015 Oct 30;10(10):e0140496.

Bisognano JD, Bakris G, Nadim MK, et al. **Baroreflex activation therapy** lowers blood pressure in patients with resistant hypertension. Results from the double-blind, randomized, placebo-controlled **Rheos Pivotal Trial**. J Am Coll Cardiol 2011; DOI:10.1016/j.jacc.2011.06.008.

Blom K, Baker B, How M, Dai M, et al. Hypertension Analysis of Stress Reduction Using **Mindfulness Meditation and Yoga**: Results From the Harmony Randomized Controlled Trial. Am J Hypertens. 2013 Sep 14.

Blood Pressure Lowering Treatment Trialists' Collaboration. (BPLTTC) Effects of different regimens to lower blood pressure on major cardiovascular events in **older & younger adults**: meta-analysis of randomised trials. BMJ. 2008 May 17;336(7653):1121-1123. Epub 2008 May 14. Reduction of blood pressure produces benefits in younger (<65 years) and older (>/=65 years) adults, with no strong evidence that protection against major vascular events afforded by different drug classes varies substantially with age.

Blood Pressure Lowering Treatment Trialists' Collaboration (BPLTTC). Blood pressure lowering and major cardiovascular events in people **with and without chronic kidney disease**: meta-analysis of randomised controlled trials. BMJ. 2013 Oct 3;347:f5680.

Blood Pressure Lowering Treatment Trialists' Collaboration. Blood pressure-lowering treatment **based on cardiovascular risk**: a meta-analysis of individual patient data. Lancet 2014; 384: 591–98.

Blood Pressure Lowering Treatment Trialists' Collaboration. Effects of blood pressure lowering on **cardiovascular risk** according to **baseline body-mass index**: a meta-analysis of randomised trials. Lancet. 2014 Nov 4.

Blumenthal James A.; Babyak Michael A.; Hinderliter Alan; et al. Effects of the **DASH Diet** Alone and in Combination With Exercise and Weight Loss on Blood Pressure and Cardiovascular Biomarkers in Men and Women With High Blood Pressure: The **ENCORE** Study. *Arch Intern Med*. 2010;170(2):126-135.

Boal AH, Smith DJ, McCallum L, et al. Monotherapy with Major Antihypertensive Drug Classes and Risk of **Hopsital Admissions** for **Mood Disorders**. Hypertension.2016 :68 :00-00.

Bobrow K, Farmer AJ, Springer D, et al. **Mobile Phone Text Messages** to Support Treatment Adherence in Adults With High Blood Pressure (**StAR**): A Single-Blind, Randomized Trial. Circulation. 2016 Jan 14.

Bobrie G, et al. Cardiovascular prognosis of "masked hypertension" detected by blood pressure **self-measurement** in elderly treated hypertensive patients. JAMA. 2004 Mar 17;291(11):1342-9. (Bobrie G, et al. Is "isolated home" hypertension as opposed to "isolated office" hypertension a sign of greater cardiovascular risk? Arch Intern Med. 2001 Oct 8;161(18):2205-11.) (Fagard RH, et al.Prognostic significance of blood pressure measured in the office, at home and during ambulatory monitoring in older patients in general practice. J Hum Hypertens. 2005 Oct;19(10):801-7.) (Hozawa A, et al. Prognostic value of **home heart rate** for cardiovascular mortality in the general population: the Ohasama study. Am J Hypertens. 2004 Nov;17(11 Pt 1):1005-10.)

Boden WE, O'rourke RA, Teo KK, Hartigan PM, et al. Optimal Medical Therapy with or without PCI for Stable Coronary Disease. **COURAGE** Trial Research Group. N Engl J Med. 2007 Mar 26; [Epub ahead of print] As an initial management strategy in patients with stable coronary artery disease, PCI did not reduce the risk of death, myocardial infarction, or other major cardiovascular events when added to optimal medical therapy. PCI does not lower the rates of myocardial infarction or death in patients with stable coronary artery disease who receive optimal medical treatment, a large trial concluded. The study, released early online by NEJM, randomized nearly 2300 patients either to PCI with optimal medical therapy (intensive pharmacologic treatment plus lifestyle intervention) or to optimal medical therapy alone. After a median follow-up of almost 5 years, 19% in the PCI group died or had MIs, compared with 18.5% who received medical therapy alone. PCI patients were more likely to be free of angina after 1 and 3 years, but there was no significant difference after 5 years. One-third of patients in the medical therapy group ultimately required revascularization, while 21% in the PCI group needed additional revascularization. An editorialist concludes: "Patients whose condition is clinically unstable, who have left main coronary artery disease, or in whom medical therapy has failed to control symptoms remain candidates for revascularization, but PCI should not play a major role as part of a secondary prevention strategy."
Weintraub WS, Spertus JA, Kolm P, Maron DJ, Zhang Z, Jurkovitz C, Zhang W,et al.; COURAGE Trial Research Group, Mancini GB. Effect of PCI on quality of life in patients with stable coronary disease. N Engl J Med. 2008 Aug 14;359(7):677-87. Among patients with stable angina, both those treated with PCI and those treated with optimal medical therapy alone had marked improvements in health status during follow-up. The PCI group had small,

but significant, incremental benefits that disappeared by 36 months.
Borden WB, Redberg RF, Mushlin AI, et al. **Patterns and intensity of medical therapy** in patients undergoing percutaneous coronary intervention. JAMA 2011; 305:1882-1889. (after Courage study publication)
Böhm M, Schumacher H, Leong D, et al. Systolic blood pressure variation and mean heart rate is associated with **cognitive dysfunction** in patients with high cardiovascular risk. Hypertension 2015.
Böhm M, Schumacher H, Teo KK, et al. **Achieved blood pressure** and cardiovascular outcomes in high-risk patients: results from **ONTARGET** and **TRANSCEND** trials. Lancet 2107; online Apr 5.
Böhm M, Mahfoud F. **High blood pressure in coronary artery disease: when to start treating and what to target**? Eur Heart J. 2018 Nov 14;39(43):3864-3866.
Bokma JP, Winter MM, van Dijk AP, et al. Effect of **Losartan on RV Dysfunction**: Results from the Double-Blind, Randomized **REDEFINE** Trial in **Adults with Repaired Tetralogy of Fallot**. Circulation. 2017 Dec 8.
Bonow RO, Maurer G, Lee KL, et al. Myocardial viability and survival in ischemic left ventricular dysfunction (**STICH**). N Engl J Med 2011. DOI: 10.1056/NEJMoa1100358. (CABG vs medical therapy)
Booth JN 3rd, Abdalla M, Tanner RM, et al. Cardiovascular Health and Incident Hypertension in **Blacks**: **JHS** (**The Jackson Heart Study**). Hypertension. 2017 Aug;70(2):285-292.
Borghi C, Cicero AF. **Nutraceuticals** with clinically detectable blood pressure lowering effect: a review of available randomized clinical trials and their meta-analyses. Br J Clin Pharmacol. 2016 Feb 6.
Borgi L, Muraki I, Satija A, et al. **Fruit and Vegetable Consumption** and the Incidence of Hypertension in Three Prospective Cohort Studies. Hypertension. 2016 Feb;67(2):288-93.
Borgi L, Rimm E, Willett WC, Forman JP. **Potato intake** and incidence of hypertension: results from three prospective US cohort studies. BMJ 2016;353:i2351.
Bos MJ, Buis S. Thirty-Minute **Office Blood Pressure Monitoring** in Primary Care. Ann Fam Med. 2017 Mar;15(2):120-123.
Bosch J, O'Donnell M, Swaminathan B, et al; HOPE-3 Investigators. **Effects of blood pressure and lipid lowering on cognition**: Results from the HOPE-3 study. Neurology. 2019 Mar 26;92(13):e1435-e1446.
Bosworth, HB. Olsen, Maren K. et al. Two **Self-management** Interventions to Improve Hypertension Control: A Randomized Trial. Ann Intern Med November 17, 2009 151:687-695; doi:10.1059/0003-4819-151-10-200911170-00148.
Bosworth HB, Powers BJ, Olsen MK, et al. **Home blood pressure management** and improved blood pressure control: results from a randomized controlled trial. Arch Intern Med. 2011;171(13):1173-1180.
Boyd HA, Basit S, Behrens I, et al. Association between **fetal congenital heart defects and maternal risk of hypertensive disorders of pregnancy** in the same pregnancy and across pregnancies. Circulation 2017.
Bradley TD, Logan AG, Kimoff RJ, et al.; CANPAP Investigators. **Continuous positive airway pressure** for central sleep apnea & heart failure. N Engl J Med. 2005 Nov 10;353(19):2025-33. (InfoPOEMs: There is no evidence that continuous positive airway pressure (CPAP) improves mortality or reduces the need for transplantation in patients with heart failure and central sleep apnea. (LOE = 1b))
Brady TM, Stefani-Glücksberg A, Simonetti GD. **Management of high blood pressure in children**: similarities and differences between US and European guidelines. Pediatr Nephrol. 2018 Mar 28.
Bramham K, Nelson-Piercy C, Brown MJ, Chappell LC. **Postpartum management of hypertension**. BMJ. 2013 Feb 25;346:f894.
Bramham K, Parnell B, Nelson-Piercy C, et al. **Chronic hypertension and pregnancy** outcomes: systematic review and meta-analysis. BMJ 2014;348:g2301.
Brandt MC, Mahfoud F, Reda S, et al. **Renal sympathetic denervation** reduces left ventricular hypertrophy and improves cardiac function in patients with resistant hypertension J Am Coll Cardiol 2012; 59:901-909.
Brar S, Ye F, James MT, Hemmelgarn B, Klarenbach S, Pannu N; Interdisciplinary Chronic Disease Collaboration. Association of **angiotensin-converting enzyme inhibitor or angiotensin receptor blocker use** with outcomes after acute **kidney injury**. JAMA Intern Med. online Oct 27, 2018.
Bratton DJ, Stradling JR, Barbe F, et al. Effect of **CPAP on blood pressure** in patients with minimally symptomatic obstructive sleep apnoea: a meta-analysis using individual patient data from four randomised controlled trials. Thorax. 2014 Jun 19. pii: thoraxjnl-2013-204993.
Bratton DJ, Gaisl T, Wons AM, Kohler M. **CPAP vs Mandibular Advancement Devices** and Blood Pressure in Patients With **Obstructive Sleep Apnea**: A Systematic Review and Meta-analysis. JAMA. 2015 Dec 1;314(21):2280-2293.
Braunwald E, et al. Rosenberg YD, Rouleau JL; **PEACE** Trial Investigators. Angiotensin-converting-enzyme inhibition in stable coronary artery disease. N Engl J Med. 2004 Nov 11;351(20):2058-68. Epub 2004 Nov 7.
Bravo E. **Resistant hypertension**: Diagnostic strategies and management. CleveClin J Med. 2013 Feb;80(2):91-6.
Bress AP, Bellows BK, King JB, et al. **Cost-effectiveness** of **intensive** versus **standard** blood pressure control. (**SPRINT**) N Engl J Med 2017; DOI:10.1056/NEJMsa1616035.
Bress AP, Colantonio LD, Cooper RS, et al. Potential Cardiovascular Disease **Events Prevented with Adoption of the 2017 American College of Cardiology/American Heart Association Blood Pressure Guideline**. Circulation. 2019 Jan 2;139(1):24-36.
Bress AP, Tanner RM, Hess R, et al. **Generalizability of results from the Systolic Blood Pressure Intervention Trial** (**SPRINT**) to the US adult population. J Am Coll Cardiol. 2015 Oct 31.
Bress AP, Kramer H, et al. **Potential Deaths Averted** and **Serious Adverse Events Incurred** from Adoption of the **SPRINT** Intensive Blood Pressure Regimen in the U.S.: Projections from NHANES. Circulation. 2017 Feb 13.
Brguljan-Hitij J, Thijs L, Li Y, et al; on behalf of the International Database on Ambulatory blood pressure in relation to Cardiovascular Outcome Investigators. Risk Stratification by **Ambulatory Blood Pressure Monitoring** Across JNC Classes of Conventional Blood Pressure. Am J Hypertens. 2014 Feb 26.
Briasoulis A, Agarwal V, Tousoulis D, et al. Effects of antihypertensive treatment in **patients over 65 years of age**: a meta-analysis of randomised controlled studies. Heart. 2013 Jun 27.
Brindle P, et al. Accuracy and impact of **risk assessment in the primary prevention** of cardiovascular disease: a systematic review. Heart. 2006 Dec;92(12):1752-9. Epub 2006 Apr 18.
Bromfield SG, Ngameni CA, et al. **Blood Pressure, Antihypertensive Polypharmacy, Frailty, and Risk for Serious Fall Injuries** Among Older Treated Adults With Hypertension. Hypertension. 2017 Aug;70(2):259-266.
Brook RD, Appel LJ, Rubenfire M, et al. Beyond Medications and Diet: **Alternative Approaches** to Lowering Blood Pressure: A Scientific Statement From the American Heart Association. Hypertension. 2013 Apr 22.
Brouwer IA, et al. SOFA Study Group. Effect of **fish oil on ventricular tachyarrhythmia** and death in patients with implantable cardioverter defibrillators: the Study on Omega-3 Fatty Acids and Ventricular Arrhythmia (SOFA) randomized trial. JAMA. 2006 Jun 14;295(22):2613-9. Our findings do not indicate evidence of a strong protective effect of intake of omega-3 PUFAs from fish oil against ventricular arrhythmia in patients with ICDs.
Brown IJ, Stamler J, Van Horn L, et al. **Sugar-sweetened beverage**, sugar intake of individuals and their blood pressure: INTERMAP study. Hypertension 2011.
Brown MJ, McInnes GT, Papst CC, et al. **Aliskiren** and the calcium channel blocker **amlodipine combination** as an initial treatment strategy for hypertension control (**ACCELERATE**): a randomised, parallel-group trial. Lancet. 2011 Jan 12.
Brown MJ, Williams B, Morant SV, et al; British Hypertension Society's Prevention; Treatment of Hypertension with Algorithm-based Therapy (PATHWAY) Studies Group. Effect of **amiloride, or amiloride plus hydrochlorothiazide**, **versus hydrochlorothiazide** on glucose tolerance & blood pressure (**PATHWAY-3**): a parallel-group, double-blind randomised phase 4 trial. Lancet Diabetes Endocrinol. 2015 Oct 16.
Brown JM, Robinson-Cohen C, Luque-Fernandez MA, et al. The spectrum of **subclinical primary aldosteronism** and incident hypertension. A cohort study. Ann Intern Med. 2017. [Epub ahead of print]. doi:10.7326/M17-0882
Bruno RM, Taddei S. **Asleep blood pressure: a target for cardiovascular event reduction**? Eur Heart J. 2018 Sep 5.
Brunström M, Carlberg B. Effect of **antihypertensive treatment at different blood pressure levels in patients with diabetes mellitus**: systematic review and meta-analyses. BMJ. 2016 Feb 24;352:i717.
Brush LN, Monagle PT, Mackay MT, et al. **Hypertension at time of diagnosis and long-term outcome after childhood ischemic stroke**. Neurology. 2013 Mar 26;80(13):1225-30.
Budoff MJ, et al. Assessment of Coronary Artery Disease by **Cardiac Computed Tomography**, A Scientific Statement From the American Heart Association Committee on Cardiovascular Imaging and Intervention, Council on Cardiovascular Radiology and Intervention, and Committee on Cardiac Imaging, Council on Clinical Cardiology. Circulation. 2006 Oct 2; [Epub ahead of print]
Buckley LF, Dixon DL, Wohlford GF 4th, et al. **Intensive Versus Standard Blood Pressure** Control in **SPRINT**-Eligible Participants of the **ACCORD-BP** Trial. Diabetes Care. 2017 Sep 25.
Buendia JR, Bradlee ML, Daniels SR, et al. **Longitudinal Effects of Dietary Sodium and Potassium** on Blood Pressure in Adolescent Girls. JAMA Pediatr. 2015 Apr 27.
Buijsse B, Feskens EJ, Kok FJ, Kromhout D. **Cocoa intake**, blood pressure, and cardiovascular mortality: the Zutphen Elderly Study. Arch Intern Med. 2006 Feb 27;166(4):411-7.
Buijsse, B, Weikert C, Drogan D et al. **Chocolate consumption** in relation to blood pressure and risk of CV disease in German adults. Eur Heart J 2010: DOI:10.1093/eurheartj/ehq068.
Bundy JD, Li C, et al. **Systolic blood pressure reduction and risk of cardiovascular disease and mortality**: a systematic review and network meta-analysis [online May 31, 2017].JAMA Cardiol. doi:10.1001/jamacardio.2017 .1421 9.
Bundy JD, Li C, Stuchlik P, Bu X, et al. **Systolic Blood Pressure Reduction** and Risk of Cardiovascular Disease and **Mortality**: A Systematic Review and Network Meta-analysis. JAMA Cardiol. 2017 May 31.
Bundy JD, Mills KT, Chen J, Li C, Greenland P, He J. Estimating the association of the **2017 and 2014 hypertension guidelines** with cardiovascular events and deaths in US adults: an analysis of national data [online May 23, 2018]. JAMA Cardiol. doi:10.1001/jamacardio.2018.1240
Busby J, Mills K, Zhang SD, et al. Postdiagnostic **Calcium Channel Blocker Use and Breast Cancer** Mortality: A Population-based Cohort Study. Epidemiology. 2018 May;29(3):407-413.
Brunstrom M;Carlberg B. Association of **Blood Pressure Lowering With Mortality and Cardiovascular Disease Across Blood Pressure Levels**: A Systematic Review and Meta-analysis. JAMA Intern Med. 2017 Nov 13.
Buletko AB, Thacker T, Cho SM, et al**. Cerebral ischemia and deterioration with lower blood pressure target in intracerebral hemorrhage**. Neurology. 2018 Sep 11;91(11):e1058-e1066.
Burkard T, Mayr M, Winterhalder C, et al. Reliability of **single office blood pressure measurements**. Heart. 2018 Jul;104(14):1173-1179.
Burns NS, Miller PW. **Learning What We Didn't Know** - The **SPRINT** Data Analysis Challenge. N Engl J Med. 2017 Apr 26.

Bursi F, et al. **Systolic and diastolic heart failure** in the community. JAMA. 2006 Nov 8;296(18):2209-16.

Butalia S, Audibert F, Côté AM, et al. **Hypertension Canada's 2018 guidelines for the management of hypertension in pregnancy**. Can J Cardiol 2018.

Butt DA, Mamdani M, Austin PC et al. The risk of **hip fracture after initiating antihypertensive** drugs in the elderly. Arch Intern Med; DOI:10.1001/2013.

Butt DA, Harvey PJ. **Benefits and risks of antihypertensive medications in the elderly**. J Intern Med. 2015 Oct 26.

Byrd JB, Chertow GM, Bhalla V. Hypertension Hot Potato - Anatomy of the **Angiotensin-Receptor Blocker Recalls**. N Engl J Med. 2019 Apr 25;380(17):1589-1591.

Byrd JB, Brook RD. **In the Clinic: Hypertension**. Ann Intern Med. 2019 May 7;170(9):ITC65-ITC80.

Byun JI;Moon J;Kim DY;Shin H;Sunwoo JS;Lim JA;Kim . Efficacy of single or combined **midodrine** and **pyridostigmine** in **orthostatic** hypotension. Neurology. 2017 Aug 9.

Cai A, Calhoun DA. **Resistant Hypertension**: An Update of Experimental and Clinical Findings. Hypertension. 2017 Jul;70(1):5-9.

Cai L, Wu Y, Wilson RF, et al. Effect of **Childhood Obesity** Prevention Programs on Blood Pressure: A Systematic Review and Meta-Analysis. Circulation. 2014 Feb 19.

Cai Y, Zhang B, Ke W, et al. Associations of Short-Term and Long-Term Exposure to **Ambient Air Pollutants** With Hypertension: A Systematic Review and Meta-Analysis. Hypertension. 2016 May 31.

Caldeira D, Alarcão J, et al. Risk of **pneumonia associated with** use of angiotensin converting enzyme inhibitors and angiotensin receptor blockers: systematic review and meta-analysis. BMJ 2012;345:e4260.

Calhoun DA, Jones D, Textor S, et al. **Resistant Hypertension**: Diagnosis, Evaluation, and Treatment. A Scientific Statement From the American Heart Association Professional Education Committee of the Council for High Blood Pressure Research. Hypertension. 2008 Apr 7; [Epub ahead of print] (Tobe SW, Lewanczuk R. Resistant hypertension. Can J Cardiol. 2009 May;25(5):315-7.)

Campbell DJ, Ronksley PE, Manns BJ, et al. Interdisciplinary Chronic Disease Collaboration. The Association of **Income with Health Behavior** Change and Disease Monitoring among Patients with Chronic Disease. PLoS One. 2014 Apr 10;9(4):e94007.

Campbell NR, Brant R, Johansen H, et al.; Canadian Hypertension Education Program Outcomes Research Task Force. Increases in antihypertensive prescriptions and reductions in cardiovascular events in Canada. Hypertension. 2009 Feb;53(2):128-34. Epub 2008 Dec 29. This study demonstrates that the reduction in cardiovascular death and hospitalization rates is associated with an increase in antihypertensive prescriptions and that it coincides with the introduction of the Canadian Hypertension Education Program.

Campbell NR, Hemmelgarn BR. New recommendations for the use of **ambulatory blood pressure monitoring** in the diagnosis of hypertension. CMAJ. 2012 Apr 3;184(6):633-4.

Campbell N, Ordunez P, Jaffe MG, et al. Implementing **standardized performance indicators** to improve hypertension control at both the population and healthcare organization levels. J Clin Hypertens (Greenwich). 2017 Feb 13.

Campschroer T, Zhu Y, Duijvesz D, Grobbee DE, Lock MT. **Alpha-blockers as medical expulsive therapy for ureteral stones**. Cochrane Database Syst Rev. 2014;(4):CD008509.
The use of alpha-blockers in patients with ureteral stones results in a higher stone-free rate and a shorter time to stone expulsion. Alphablockers should therefore be offered as part of medical expulsive therapy as one of the primary treatment modalities.

Canadian Physical Activity Guidelines-Jan 2011. Clinical Practice Guideline Development Report. Canadian Society for Exercise Physiology. http://www.csep.ca/CMFiles/Guidelines/CPAGuideline_Report_JAN2011.pdf

Canney M, O'Connell MD, Murphy CM, et al. Single agent antihypertensive therapy and **orthostatic blood pressure** behaviour in older adults using **beat-to-beat measurements**: the Irish longitudinal study on ageing. PLoS One2016;11:e0146156.

Carey RM, Calhoun DA, Bakris GL, et al; **American Heart Association** Professional/Public Education and Publications Committee of the Council on Hypertension; Council on Cardiovascular and Stroke Nursing; Council on Clinical Cardiology; Council on Genomic and Precision Medicine; Council on Peripheral Vascular Disease; Council on Quality of Care and Outcomes Research; and Stroke Council. Resistant Hypertension: Detection, Evaluation, and Management: A Scientific Statement From the American Heart Association. Hypertension. 2018 Nov;72(5):e53-e90.

Carey RM, Whelton PK; **2017 ACC/AHA** Hypertension Guideline Writing Committee. Prevention, detection, evaluation, and management of high blood pressure in adults: **synopsis of the 2017 American College of Cardiology/American Heart Association hypertension guideline**. Ann Intern Med. [Epub ahead of print]. doi:10.7326/M17- 3203

Caritis S, Sibai B, Hauth J, et al. Lowdose **aspirin to prevent preeclampsia** in women at high risk. N Engl J Med 1998; 338:701-5.

Carlson DJ, Dieberg G, Hess NC, Millar PJ, Smart NA. **Isometric exercise training** for blood pressure management: a systematic review and meta-analysis. Mayo Clin Proc. 2014 Mar;89(3):327-34.

Carson MP, Chen KK. **Hypertension in a woman planning pregnancy**. CMAJ. 2014 Feb 4;186(2):129-30

Carter Barry L.; Rogers Meaghan; Daly Jeanette; et al. The Potency of **Team-Based** Care Interventions for Hypertension: A Meta-analysis. *Arch Intern Med*. 2009;169(19):1748-1755.

Carter Barry L.; Ardery Gail; Dawson Jeffrey D.;et al. **Physician and Pharmacist Collaboration** to Improve Blood Pressure Control. Arch Intern Med. 2009;169(21):1996-2002.

Casas JP, et al. Effect of inhibitors of the **renin-angiotensin system** and other antihypertensive drugs on **renal outcomes**: systematic review and meta-analysis. Lancet. 2005 Dec 10;366(9502):2026-2033. INTERPRETATION: The benefits of ACE inhibitors or ARBs on renal outcomes in placebo-controlled trials probably result from a blood-pressure-lowering effect. In patients with diabetes, additional renoprotective actions of these substances beyond lowering blood pressure remain unproven, and there is uncertainty about the greater renoprotection seen in non-diabetic renal disease.

Castellano JM, Sanz G, Ortiz AF, et al. A **polypill** strategy to improve global secondary cardiovascular prevention. *J Am Coll Cardiol* 2014; 64: 613-621.

Castellano JM, Sanz G, Peñalvo JL, et al. A **polypill** strategy to improve adherence: results from **FOCUS** (Fixed-dose Combination Drug for Secondary Cardiovascular Prevention) Project. J Am Coll Cardiol. 2014 Aug 29.

Caton AR, Bell EM, Druschel CM, Werler MM, Lin AE, Browne ML, et al. **Antihypertensive medication use during pregnancy** and the risk of cardiovascular malformations. Hypertension 2009;54:63-70.

CDC: Centers for Disease Control and Prevention. Vital signs: **Prevalence, treatment, and control of hypertension—United States**, 1999-2002 and 2005-2008. MMWR Morb Mortal Wkly Rep 2011; 60:1-6.

CDC: Centers for Disease Control and Prevention. **Self-reported hypertension and use of antihypertensive medication** among adults-United States 2005-2009. MMWR Morb Mortal Wkly Rep 2013; 62:237-243.

Chan AWK, Chair SY, et al. **Tai Chi exercise is more effective than brisk walking** in reducing cardiovascular disease risk factors among adults with hypertension: A randomised controlled trial. Int J Nurs Stud. 2018 Aug 24;88:44-52.

Chang CH, Lin JW, Wu LC, Lai MS. Angiotensin receptor blockade and risk of **cancer** in type 2 diabetes mellitus: A nationwide case-control study. J Clin Oncol 2011; DOI 10.1200/JCO.2011.35.1908. The results did not show an effect of ARBs as a class on increasing cancer incidence in patients with diabetes. However, there was a negative association of losartan but a positive one of candesartan and telmisartan with the overall occurrence of cancer.

Chang CH, Chang YC, Wu LC, et al. Different **angiotensin receptor blockers and incidence of diabetes**: a nationwide population-based cohort study. Cardiovasc Diabetol. 2014 May 14;13:91. (**olmesartan**)

Chang TI, Evans G, Cheung AK, et al; **SPRINT** Study Research Group. Patterns and Correlates of Baseline **Thiazide-Type Diuretic Prescription** in the Systolic Blood Pressure Intervention Trial. Hypertension. 2016 Mar;67(3):550-5.

Chappell LC, Brocklehurst P, Green ME, et al. Planned early delivery or expectant management for **late preterm pre-eclampsia** (PHOENIX): a randomised controlled trial. Lancet. 2019 Aug 28.

Charles L, Triscott J, Dobbs B. **Secondary Hypertension**: Discovering the Underlying Cause. Am Fam Physician. 2017;96(7):453-461.

Charles R, Swales C, Bonnett T, et al. **Hypertensive disorder of pregnancy**. BMJ. 2017 Feb 2;356:j285

Charpentier MM, Bundeff A. Treating hypertension in the **very elderly**. Ann Pharmacother. 2011 Sep;45(9):1138-43.

Chaudhry KN, Chavez P, Gasowski J, et al. Hypertension in the **elderly**: Some practical considerations. Cleve Clin J Med. 2012 Oct;79(10):694-704.

Cheema E, Sutcliffe P, et al. The impact of **interventions by pharmacists** in community pharmacies on control of hypertension: a systematic review and meta-analysis of randomised controlled trials. Br J Clin Pharmacol. 2014 Jun 26.

Chen C, Anderson CS. Does reducing blood pressure and cholesterol provide any **HOPE for preventing cognitive decline and dementia**? Neurology. 2019 Mar 26;92(13):593-594

Chen H, Burnett RT, Kwong JC, et al. Spatial association between **ambient fine particulate matter** and incident hypertension. Circulation. 2014 Feb 4;129(5):562-9.

Chen JM, Heran BS, Perez MI, Wright JM. Blood pressure lowering efficacy of **beta-blockers** as second-line therapy for primary hypertension. **Cochrane** Database Syst Rev. 2010 Jan 20;(1):CD007185.

Chen ST, Maruthur NM, Appel LJ. The effect of **dietary patterns** on estimated coronary heart disease risk: results from the Dietary Approaches to Stop Hypertension (**DASH**) trial. Circ Cardiovasc Qual Outcomes. 2010;3:484 – 489.

Chen L, Caballero B, Mitchell DC, et al. Reducing consumption of **sugar-sweetened beverages** is associated with reduced blood pressure. A prospective study among United States adults. Circulation 2010.

Chen N, Zhou M, Yang M, et al. **Calcium channel blockers versus** other classes of drugs for hypertension. Cochrane Database Syst Rev. 2010 Aug 4;8:CD003654. Diuretics are preferred first-line over CCBs to optimize reduction of cardiovascular events. The review does not distinguish between CCBs, ACE inhibitors or ARBs, but does provide evidence supporting the use of CCBs over beta-blockers.

Chen S, Sudharsanan N, Huang F, et al. Impact of community based screening for hypertension on blood pressure after two years: regression discontinuity analysis in a national cohort of older adults in China. BMJ. 2019 Jul 11;366:l4064.

Chen V, Ning H, Allen N, et al. Lifetime Risks for Hypertension by **Contemporary Guidelines in African American and White Men and Women**. JAMA Cardiol. 2019 Mar 27.

Chen YJ, Li LJ, Tang WL, et al. **First-line drugs inhibiting the renin angiotensin system** versus other first-line antihypertensive drug classes for hypertension. Cochrane Database Syst Rev. 2018 Nov 14;11:CD008170. All-cause death is similar for first-line RAS inhibitors and first-line CCBs, thiazides and beta-blockers. There are, however, differences for some morbidity outcomes. First-line thiazides caused less HF and stroke than first-line RAS inhibitors. First-line CCBs increased HF but decreased stroke compared to first-line RAS inhibitors. The magnitude of the increase in HF exceeded the decrease in stroke. Low-quality evidence suggests that first-line RAS inhibitors reduced stroke and total CV events compared to first-line beta-blockers. The small differences in effect on blood pressure between the different classes of drugs did not correlate with the differences in the morbidity outcomes.

Cheng J, Zhang W, Zhang X, et al. Effect of **Angiotensin-Converting Enzyme Inhibitors and Angiotensin II Receptor Blockers** on All-Cause Mortality, Cardiovascular Deaths, and Cardiovascular Events in Patients

With Diabetes Mellitus: A Meta-analysis. JAMA Intern Med. 2014 Mar 31.
Cheung AK, Chang TI, Cushman WC, et al; Conference Participants. **Blood pressure in chronic kidney disease**: conclusions from a Kidney Disease: Improving Global Outcomes (KDIGO) Controversies Conference. Kidney Int. 2019 May;95(5):1027-1036.
Cheung AK, Rahman M, Reboussin DM, et al. Effects of **Intensive BP** Control in **CKD**. J Am Soc Nephrol. 2017 Jun 22
Cheung EL, Bell CS, Samuel JP, et al. **Race and Obesity in Adolescent Hypertension**. Pediatrics. 2017;139(5):e20161433
Chim C, Dimitropoulos E, Ginzburg R. Implementing a Policy and Protocol on Managing Patients With **Hypertensive Urgencies**. Ann Pharmacother. 2016 Jul;50(7):548-54.
Chiolero A, Bovet P, Paradis G, et al. **Screening** for elevated blood pressure in **children and adolescents**. A critical appraisal. JAMA Pediatr 2013. DOI:10.1001/jamapediatrics.2013.438.
Chiu CL, Lujic S, Thornton C, et al. **Menopausal hormone therapy** is associated with having high blood pressure in postmenopausal women: observational cohort study. PLoS ONE 2012;7:e40260.
Chobanian AV. Clinical practice. **Isolated systolic hypertension in the elderly**. N Engl J Med. 2007 Aug 23;357(8):789-96.
Chobanian, Aram V.The **Hypertension Paradox** -- More Uncontrolled Disease despite Improved Therapy. N Engl J Med 2009 361: 878-887.
Choi E, Pak G, Burket J. Beta **Blockers Compared with Other Drug Options for the Treatment of Hypertension**. Am Fam Physician. 2018 Feb 1;97(3):Online.
Choi HK, Soriano LC, Zhang Y, Rodríguez LAG. **Calcium channel blockers, losartan**, and the risk of **incident gout** among patients with hypertension: population based case-control study. BMJ 2012;344:d8190.
Chow CK, Pell AC, Walker A, O'Dowd C, Dominiczak AF, Pell JP. **Families of patients with premature** coronary heart disease: an obvious but neglected target for primary prevention. BMJ. 2007 Sep 8;335(7618):481-5.
Chow CK, Teo KK, Rangarajan S, et al; **PURE** (Prospective Urban Rural Epidemiology) Study investigators. **Prevalence, awareness, treatment, and control of hypertension** in rural and urban communities in high-, middle-, and low-income countries. JAMA. 2013 Sep 4;310(9):959-68.
Chow CK, Thakkar J, Bennett A, et al. **Quarter-dose quadruple combination therapy** for initial treatment of hypertension: placebo-controlled, crossover, randomised trial and systematic review. Lancet 2017; published online Feb 9.
Christiansen SC, Zuraw BL. Treatment of **Hypertension in Patients with Asthma**. N Engl J Med. 2019 Sep 12;381(11):1046-1057.
Chrysant SG, and Chrysant GS. **Future of the Polypill** Use for the Prevention of Cardiovascular Disease and Strokes. The American Journal of Cardiology (2014).
Chun S, Qiu F, Austin PC, et al. Predictors and Outcomes of **Routine Versus Optimal Medical Therapy in Stable Coronary Heart Disease**. Am J Cardiol. 2015 Jun 3.
Cicolini G, Simonetti V, Comparcini D, et al. Efficacy of a **nurse-led email reminder program** for cardiovascular prevention risk reduction in hypertensive patients: A randomized controlled trial. Int J Nurs Stud. 2013 Oct 25.
Cifu AS, Davis AM. **Prevention, detection, evaluation, and management of high blood pressure in adults**. JAMA. doi:10.1001/jama.2017.18706
Cissoko H, Jonville-Bera AP, Swortfiguer D, Giraudeau B, Autret-Leca E. [Neonatal outcome after exposure to beta adrenergic blockers late in pregnancy.] Arch Pediatr. 2005 May;12(5):543-7.
Clark C. E., Smith L. F. P., Taylor R. S., Campbell J. L. **Nurse led interventions** to improve control of blood pressure in people with hypertension: systematic review and meta-analysis BMJ 2010;341:c3995
Clark CE, Taylor RS, Shore AC, Ukoumunne OC, Campbell JL. Association of a difference in systolic **blood pressure between arms** with vascular disease and mortality: a systematic review and meta-analysis. Lancet 2012
Clark CE, Taylor RS, Shore AC, Campbell JL. The difference in blood pressure readings **between arms** and survival: primary care cohort study. BMJ 2012;344:e1327.
Clark CE, Horvath IA, Taylor RS, et al. **Doctors record higher blood pressures than nurses**: systematic review and meta-analysis. Br J Gen Pract. 2014 Apr
Clark CE, Taylor RS, Butcher I, et al. **Inter-arm blood pressure difference and mortality**: a cohort study in an asymptomatic primary care population at elevated cardiovascular risk. Br J Gen Pract 2016;66:e297-308.
Clark CE, Boddy K, Warren FC, et al. Associations between **interarm differences in blood pressure and cardiovascular disease outcomes**: protocol for an individual patient data meta-analysis and development of a prognostic algorithm. BMJ Open. 2017 Jul 2;7(6):e016844.
Clark D 3rd, Nicholls SJ, St John J, et al. Visit-to-Visit **Blood Pressure Variability**, **Coronary Atheroma Progression**, and Clinical Outcomes. JAMA Cardiol. 2019 Apr 10.
Clayton TC, Lubsen J, et al. **Risk score** for predicting death, myocardial infarction, and stroke in patients with stable angina, based on a large randomised trial cohort of patients. BMJ. 2005 Oct 15;331(7521):869. Epub 2005 Oct 6.
Cleary KL, Siddiq Z, Ananth CV, et al. Use of **Antihypertensive Medications During Delivery Hospitalizations Complicated by Preeclampsia**. Obstet Gynecol. 2018 Feb 5.
Cleland JG, et al.; Cardiac **Resynchronization**-Heart Failure (CARE-HF) Study. The effect of cardiac resynchronization on morbidity and mortality in heart failure. N Engl J Med. 2005 Apr 14;352(15):1539-49. Epub 2005 Mar 7.
Cloutier L, Daskalopoulou SS, Padwal RS, et al. A New **Algorithm for the Diagnosis of Hypertension in Canada**. Can J Cardiol. 2015 May;31(5):620-630.
Cloutier L, Lamarre-Cliche M. Hypertension in Adults With **Type 2 Diabetes**: A Review of Blood Pressure Measurement Methods, Targets and Therapy. Can J Diabetes. 2018 Apr;42(2):188-195.
Cnossen JS, Vollebregt KC, Vrieze N, et al. Accuracy of mean arterial pressure and blood pressure measurements in predicting **pre-eclampsia**: systematic review and meta-analysis. BMJ. 2008 May 17;336(7653):1117-20. Epub 2008 May 14. When blood pressure is measured in the first or second trimester of pregnancy, the mean arterial pressure is a better predictor for pre-eclampsia than systolic blood pressure, diastolic blood pressure, or an increase of blood pressure.
Cohen HW, Hailpern SM, Fang J, Alderman MH. **Sodium intake** and mortality in the NHANES II follow-up study. Am J Med. 2006 Mar;119(3):275.e7-14.
Cohen JB, Lotito MJ, Trivedi UK, et al. **Cardiovascular events and mortality in white coat hypertension**. A systematic review and meta-analysis. Ann Intern Med.2019. [Epub ahead of print]. doi:10.7326/M19-0223
Cohen JB, Townsend RR. The **ACC/AHA 2017 Hypertension Guidelines**: Both Too Much and Not Enough of a Good Thing? Ann Intern Med. 2017 Dec 5.
Cohen L, Curhan G, Forman J. Association of **sweetened beverage** intake with incident hypertension. J Gen Intern Med. 2012 Sep;27(9):1127-34.
Conen D, et al. Usefulness of B-type **natriuretic peptide and C-reactive protein** in predicting the presence or absence of left ventricular hypertrophy in patients with systemic hypertension. Am J Cardiol. 2006 Jan 15;97(2):249-52.
Conen D, Aeschbacher S, Thijs L, et al. Age-specific differences between **conventional and ambulatory daytime blood pressure values**. Hypertension. 2014 Nov;64(5):1073-9.
Conroy SP, Harrison JK, Van Der Wardt V, et al. **Ambulatory blood pressure monitoring** in **older people with dementia**: a systematic review of tolerability. Age Ageing. 2016 Apr 7.
Cook NR, Cutler JA, Obarzanek E, et al. Long term effects of dietary **sodium reduction on cardiovascular disease** outcomes: observational follow-up of the trials of hypertension prevention (TOHP). BMJ. 2007 Apr 20; [Epub ahead of print] Sodium reduction, previously shown to lower blood pressure, may also reduce long term risk of cardiovascular events.
Cook R, Lamont T, Martin R; NIHR Dissemination Centre. **Lifestyle changes may be more important than drugs for mild hypertension**. BMJ. 2019 Feb 15;364:l571.
Cooper WO, et al. Major congenital malformations after **first-trimester exposure to ACE** inhibitors. N Engl J Med. 2006 Jun 8;354(23):2443-51. (see also Pharmacist's Letter July 2006)
Cooper-DeHoff RM, Gong Y, Handberg EM, et al. **Tight blood pressure control and cardiovascular outcomes among hypertensive patients with diabetes and coronary artery disease**. (**INVEST**) JAMA. 2010 Jul 7;304(1):61-8.
Corrada MM, Hayden KM, Paganini-Hill A, et al. Age of onset of hypertension and **risk of dementia** in the oldest-old: The 90+ Study. Alzheimers Dement. 2017 Jan 6.
Corrao G, Rea F, Ghirardi A, et al. **Adherence with antihypertensive drug therapy and the risk of heart failure** in clinical practice. *Hypertension* 2015.
Cosselman KE, Krishnan RM, Oron AP, et al. Blood pressure response to controlled **diesel exhaust** exposure in human subjects. Hypertension. 2012 May;59(5):943-8.
Council on Cardiovascular Disease in the Young, Council on Cardiovascul. **Genetics and genomics** for the prevention and treatment of cardiovascular disease: update: a scientific statement from the american heart association. Circulation. 2013 Dec 24;128(25):2813-51.
Cragan JD, Young BA, Correa A. **Renin-Angiotensin System Blocker Fetopathy**. J Pediatr. 2015 Aug 5.
Cragg J, Krassioukov A. **Autonomic dysreflexia**. CMAJ. 2011 Oct 11.
Croall ID, et al; PRESERVE Study Team. Effect of **Standard vs Intensive Blood Pressure Control on Cerebral Blood Flow in Small Vessel Disease**: The **PRESERVE** Randomized Clinical Trial. JAMA Neurol. 2018 Mar 5.
Crump C, Sundquist J, Winkleby MA, et al. Interactive Effects of **Physical Fitness and Body Mass Index** on the Risk of Hypertension. JAMA Intern Med. 2016 Jan 19:1-7.
Crump C, Sundquist J, Winkleby MA, et al. **Low stress resilience in late adolescence** and risk of hypertension in adulthood. Heart. 2016 Feb 1.
Cruz MO et al. What is the optimal time for delivery in women with **gestational hypertension**? Am J Obstet Gynecol 2012 Sep; 207:214.e1.
CTFPHC-Canadian Task Force on Preventive Health Care. Recommendations on **screening for high blood pressure** in Canadian Adults. Ottawa (ON): Canadian Task Force on Preventive Health Care; 2012.
Culley CM, DiBridge JN, Wilson GL Jr. Off-Label Use of Agents for Management of Serious or Life-threatening **Angiotensin Converting Enzyme Inhibitor-Induced Angioedema**. Ann Pharmacother. 2016 Jan;50(1):47-59.
Curreri C, Giantin V, Veronese N, et al. **Orthostatic Changes** in Blood Pressure and Cognitive Status in the **Elderly**: The Progetto Veneto Anziani Study. Hypertension. 2016 Jun 20.
Cuspidi C, Facchetti R, Bombellia M, et al. **High normal blood pressure and left ventricular hypertrophy echocardiographic findings** from the PAMELA population. Hypertension.2019;73:xxx–xxx.
Dahal K, Kunwar S, Rijal J, et al. The Effects of **Aldosterone Antagonists in Patients With Resistant Hypertension**: A Meta-Analysis of Randomized and Nonrandomized Studies. Am J Hypertens. 2015 Mar 23.

Dahlof B, Sever PS, Poulter NR, Wedel H, et al. ASCOT Investigators. Prevention of cardiovascular events with an antihypertensive regimen of amlodipine adding perindopril as required versus atenolol adding bendroflumethiazide as required, in the Anglo-Scandinavian Cardiac Outcomes Trial-Blood Pressure Lowering Arm (**ASCOT-BPLA**): a multicentre RCT. Lancet. 2005 Sep 10;366(9489):895-906. (InfoPOEMs: In this study, patients with hypertension and at least 3 additional cardiac risk factors have slightly fewer deaths from all causes, slightly fewer strokes, and were slightly less likely to develop diabetes if they were treated with amlodipine plus perindopril than if they were treated with atenolol and bendroflumethiazide. One would need to treat between 60 and 1000 high-risk patients for a median of 5.5 years with amlodipine instead of atenolol to prevent one additional death. (LOE = 2b)) (Sever P, Dahlof B, Poulter N, et al. Potential synergy between lipid-lowering and blood-pressure-lowering in the Anglo-Scandinavian Cardiac Outcomes Trial. Eur Heart J 2006; 27:2982-2988.)

Dahlof B, et al. LIFE Study Group. Cardiovascular morbidity and mortality in the Losartan Intervention For Endpoint reduction in hypertension study (**LIFE**): a randomised trial against atenolol. Lancet. 2002 Mar 23;359(9311):995-1003. (Lindholm LH, et al.; LIFE Study Group. Cardiovascular morbidity and mortality in patients with diabetes in the Losartan Intervention For Endpoint reduction in hypertension study (LIFE): a randomised trial against atenolol. Lancet. 2002 Mar 23;359(9311):1004-10.)(Ibsen H, et al. Does albuminuria predict cardiovascular outcomes on treatment with losartan versus atenolol in patients with diabetes, hypertension, and left ventricular hypertrophy? The LIFE study. Diabetes Care. 2006 Mar;29(3):595-600.)

Dalton AR, Vamos EP, Harris MJ, et al. Impact of **universal health insurance coverage** on hypertension management: a cross-national study in the United States and England. *PLoS One* 2014

Danaei G, Finucane MM, Kin JK, et al. **National, regional, and global trends in systolic blood pressure since 1980**: systematic analysis of health examination surveys and epidemiological studies with 786 country-years and 5.4 million participants. Lancet 2011.

Dagenais GR, Jung H, Lonn E, et al. Effects of **Lipid-Lowering and Antihypertensive Treatments in Addition to Healthy Lifestyles** in Primary Prevention: An Analysis of the HOPE-3 Trial. J Am Heart Assoc. 2018 Jul 22;7(15).

Dagenais GR, Lu J, Faxon DP, et al. Effects of Optimal Medical Treatment With or Without Coronary Revascularization on Angina and Subsequent Revascularizations in Patients With Type 2 Diabetes Mellitus and Stable Ischemic Heart Disease. Circulation. 2011 Mar 28. (**BARI 2D**)

Daley MF, Sinaiko AR, Reifler LM et al. **Patterns of care and persistence** after incident elevated blood pressure. Pediatrics. 2013 Aug;132(2):e349-55.

Dasgupta K, Padwal R, Poirier L, Quinn RR; on behalf of the Canadian Hypertension Education Program Scientific Summary Writing Group. Managing hypertension: **evidence supporting the 2013/2014 recommendations of the Canadian Hypertension Education Program**. CMAJ. 2015 Feb 3;187(2):116-119.

Daskalopoulou SS, Rabi DM, Schiffrin EL, et al; Hypertension Canada. **Hypertension Guidelines** in the United States and Canada: Are We Getting Closer? Hypertension. 2018 Jun;71(6):976-978.

Daskalopoulou SS, Rabi DM, Zarnke KB, et al. The **2015 Canadian Hypertension Education Program (CHEP)** recommendations for blood pressure measurement, diagnosis, assessment of risk, prevention, and treatment of hypertension. Can J Cardiol. 2015 May;31(5):549-68.

Davis BR, et al.; Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial Collaborative Research Group. Role of diuretics in the prevention of **heart failure**: the ALLHAT. Circulation. 2006 May 9;113(18):2201-10. Epub 2006 May 1. HF risk decreased with chlorthalidone versus amlodipine or lisinopril use during year 1. Subsequently, risk for those individuals taking chlorthalidone versus amlodipine remained decreased but less so, whereas it was equivalent to those given lisinopril. Prior medication use, follow-up blood pressures, and concomitant medications are unlikely to explain most of the HF differences. Diuretics are superior to calcium channel blockers and, at least in the short term, angiotensin-converting enzyme inhibitors in preventing HF in hypertensive individuals.

Davis MI, Filion KB, Zhang D, et al. Effectiveness of **renal denervation therapy for resistant hypertension**: a systematic review and meta-analysis. J Am Coll Cardiol. 2013 Jul 16;62(3):231-41.

de Beus E, et al. Prevalence and clinical characteristics of **apparent therapy-resistant hypertension** in patients with cardiovascular disease: a cross-sectional cohort study in secondary care. BMJ Open. 2017 Sep 6;7(9):e016692.

de Boer IH, Bangalore S, Benetos A, et al. **Diabetes and Hypertension**: A Position Statement by the American Diabetes Association. Diabetes Care. 2017 Sep;40(9):1273-1284

de Boer IH, et al. Individualizing Blood Pressure Targets for People With **Diabetes and Hypertension**: **Comparing the ADA** and the **ACC/AHA Recommendations**. JAMA. 2018 Mar 15.

De Bruyne B, Pijls NHJ, Kalesan B, et al. **Fractional flow reserve**–guided PCI versus medical therapy in stable coronary disease. (**FAME 2**) N Engl J Med 2012.

de Jager RL, de Beus E, Beeftink MM, et al. Impact of **Medication Adherence** on the Effect of **Renal Denervation**: The **SYMPATHY** Trial. Hypertension. 2017 Apr;69(4):678-684.

de Jong DLK, de Heus RAA, Rijpma A, et al. Effects of **Nilvadipine** on Cerebral Blood Flow in Patients With Alzheimer Disease. Hypertension. 2019 Jun 17:HYPERTENSIONAHA11912892.

de la Sierra A, Banegas JR, Vinyoles E, et al. Prevalence of **Masked Hypertension in Untreated and Treated Patients** With Office Blood Pressure Below 130/80 mm Hg. Circulation. 2018 Apr 30.

de la Sierra A, Segura J, et al. Oliveras A, Ruilope LM. Clinical features of 8295 patients with resistant hypertension classified on the basis of **ambulatory blood pressure monitoring**. Hypertension. 2011 May;57(5):898-902.

de Oliveira Filgueira GC, Silva Filgueira OA, Carvalho DM, et al. Effect of type 2 diabetes mellitus on the pharmacokinetics and **transplacental transfer of nifedipine** in hypertensive pregnant women. Br J Clin Pharmacol. 2017 Jan 2.

DeCarli C. **Blood pressure control and cognitive performance**: something to think about with aging. JAMA. 2015 May 19;313(19):1963-4.

Delgado J, Masoli JA, Bowman K, et al; As part of the Ageing Well Programme of the NIHR School for Public Health Research, England.. Outcomes of **Treated Hypertension at Age 80 and Older**: Cohort Analysis of 79,376 Individuals. J Am Geriatr Soc. 2016 Dec 30.

Delgado J, Bowman K, Ble A, et al. **Blood pressure trajectories in the 20 years before death** [published online December 4, 2017].JAMA Intern Med. doi:10.1001/jamainternmed.2017.7023

Derakhshan A, Bagherzadeh-Khiabani F, et al. Different Combinations of **Glucose Tolerance** and Blood Pressure Status and Incident Diabetes, Hypertension, and Chronic Kidney Disease. J Am Heart Assoc. 2016 Aug 20;5(8).

Desch S, Schmidt J, Kobler D, et al. Effect of **cocoa products** (chocolate) on blood pressure: systematic review and meta-analysis. Am J Hypertens. 2010 Jan;23(1):97-103.

Deshmukh A, Kumar G, Kumar N, et al. Effect of Joint National Committee VII Report on Hospitalizations for **Hypertensive Emergencies** in the United States. Am J Cardiol. 2011 Sep3

Dewland TA, Soliman EZ, Davis BR, et al. Effect of the Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial (**ALLHAT**) on conduction system disease [online June 27, 2016].JAMA Intern Med (**lisinopril**)

Dhalla IA, Gomes T, Yao Z, et al. **Chlorthalidone versus hydrochlorothiazide** for the treatment of hypertension in older adults: a population-based cohort study. Ann Intern Med. 2013 Mar 19;158(6):447-55.

Dhruva SS, Huang C, Spatz ES, et al. Heterogeneity in Early Responses in **ALLHAT** (Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial). Hypertension. 2017 Jul;70(1):94-102. (**chlorthalidone is best**)

Diabetes Canada Clinical Practice Guidelines Expert Committee, Tobe SW, Gilbert RE, Jones C, et al. **Treatment of Hypertension**. Can J Diabetes. 2018 Apr;42 Suppl 1:S186-S189.

Diao D, Wright JM, Cundiff DK, Gueyffier F. **Pharmacotherapy for mild hypertension**. Cochrane Database of SystematicReviews 2012, Issue 8. Art. No.: CD006742. DOI: 10.1002/14651858.CD006742.pub2. Antihypertensive drugs used in the treatment of adults (primary prevention) with mild hypertension (systolic BP 140-159 mmHg and/or diastolic BP 90-99 mmHg) have not been shown to reduce mortality or morbidity in RCTs. Treatment caused 9% of patients to discontinue treatment due to adverse effects. More RCTs are needed in this prevalent population to know whether the benefits of treatment exceed the harms.

Diaz KM, Booth JN 3rd, Seals SR, et al. **Physical Activity** and Incident Hypertension in African Americans: The Jackson Heart Study. Hypertension. 2017 Jan 30.

Dibaba DT, Xun P, Song Y, et al. The effect of **magnesium supplementation** on blood pressure in individuals with **insulin resistance**, **prediabetes**, or noncommunicable chronic diseases: a meta-analysis of randomized controlled trials. Am J Clin Nutr. 2017 Jul 19.

Dietary Guidelines for Americans (DGA) 2010. Full Guideline: http://www.health.gov/dietaryguidelines/dga2010/DietaryGuidelines2010.pdf, Summary: http://www.cnpp.usda.gov/Publications/DietaryGuidelines/2010/PolicyDoc/ExecSumm.pdf

Dickerson T, Wiczer T, Waller A, et al. Hypertension and Incident Cardiovascular **Events Following Ibrutinib Initiation**. Blood. 2019 Oct 3. doi: 10.1182/blood.2019000840.

Dickinson BD, Havas S for the Council on Science and Public Health. Reducing the population burden of cardiovascular disease by reducing **sodium intake**. Arch Intern Med 2007; 167:1460-1468.

Dicpinigaitis PV. **Angiotensin-converting enzyme inhibitor**-induced **cough**: ACCP evidence-based clinical practice guidelines. *Chest* 2006;129(suppl):169-73S.

Digoxin (Ahmed A, et al. Digoxin and reduction in mortality and hospitalization in heart failure: a comprehensive post hoc analysis of the **DIG** trial. Eur Heart J. 2006 Jan;27(2):178-86. Epub 2005 Dec 8. & Adams KF Jr, et al. Relationship of serum digoxin concentration to mortality and morbidity in women in the digitalis investigation group trial: a retrospective analysis. J Am Coll Cardiol. 2005 Aug 2;46(3):497-504).

Ding M, Huang T, Bergholdt HK, et al. **Dairy consumption**, systolic blood pressure, and risk of hypertension: Mendelian randomization study. BMJ. 2017 Mar 16;356:j1000.

Dionne JM, Harris KC, Benoit G, et al. **Hypertension Canada's 2017 Guidelines for the Diagnosis, Assessment, Prevention, and Treatment of Pediatric Hypertension**. Can J Cardiol. 2017 May;33(5):577-585

Ditisheim A, Wuerzner G, Ponte B, et al. Prevalence of **Hypertensive Phenotypes After Preeclampsia**: A Prospective Cohort Study. Hypertension. 2018 Jan;71(1):103-109.

Do DV, Wang X, Vedula SS, et al. **Blood pressure control for diabetic retinopathy**. Cochrane Database Syst Rev. 2015 Jan 31;1:CD006127. Hypertension is a well-known risk factor for several chronic conditions in which lowering blood pressure has proven to be beneficial. The available evidence supports a beneficial effect of intervention to reduce blood pressure with respect to preventing diabetic retinopathy for up to 4 to 5 years. However, the lack of evidence to support such intervention to slow progression of diabetic retinopathy or to prevent other outcomes considered in this review, along with the relatively modest support for the beneficial effect on incidence, weakens the conclusion regarding an overall benefit of intervening on blood pressure solely to prevent diabetic retinopathy.

Dobrosielski DA, Gibbs BB, Ouyang P, et al. Effect of **Exercise** on Blood Pressure in Type 2 Diabetes: A Randomized Controlled Trial. J Gen Intern Med. 2012 May 19.

Dobson CP, Eide M, Nylund CM. Hypertension Prevalence, Cardiac Complications, and Antihypertensive **Medication Use in Children**. J Pediatr. 2015 May 6.

Dong C, Della-Morte D, Rundek T, et al. Evidence to Maintain the **Systolic Blood Pressure** Treatment Threshold at **140 mm Hg** for **Stroke Prevention**: The **Northern Manhattan Study**. Hypertension. 2016 Feb 1.

Dong YH, Chang CH, Wu LC, et al. Comparative **cardiovascular safety of non-steroidal anti-inflammatory drugs** in patients with hypertension: a population-based cohort study. Br J Clin Pharmacol. 2018 Feb 22.

Dorsch MP, Gillespie BW, Erickson SR, et al. **Chlorthalidone reduces cardiovascular events compared with hydrochlorothiazide**: a retrospective cohort analysis. Hypertension. 2011 Apr;57(4):689-94.

Douma S, Petidis K, Doumas M, et al. Prevalence of **primary hyperaldosteronism** in resistant hypertension: a retrospective observational study. Lancet. 2008 Jun 7;371(9628):1921-6. Although the prevalence of primary hyperaldosteronism in patients with resistant hypertension was high, it was substantially lower than previously reported.

Doust JA, Pietrzak E, Dobson A, Glasziou P. How well does **B-type natriuretic peptide** predict death and cardiac events in patients with **heart failure**: systematic review. BMJ. 2005 Mar 19;330(7492):625.

Dregan A, Ravindrarajah R, Hazra N, et al. **Longitudinal Trends** in Hypertension Management and Mortality Among **Octogenarians**:Prospective Cohort Study. Hypertension. 2016 May 9.

Drozda J. Jr., Messer JV, Spertus J, et al. **ACCF/AHA/AMA-PCPI 2011 performance measures for adults with coronary artery disease and hypertension**: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Performance Measures and the American Medical Association-Physician Consortium for Performance Improvement. J Am Coll Cardiol 2011;58:xxx–xxx. http://content.onlinejacc.org/cgi/reprint/j.jacc.2011.05.002v1.pdf

Du T, Fernandez C, Barshop R, et al. **2017 Pediatric Hypertension Guidelines** Improve Prediction of **Adult Cardiovascular Outcomes**. Hypertension. 2019 Apr 22:HYPERTENSIONAHA11812469.

Duceppe E et al. **Preoperative antihypertensive medication intake and acute kidney injury** after major vascular surgery J Vasc Surg 2018 Jun; 67:1872.

Duggan ST, Chwieduk CM, Curran MP. **Aliskiren**: a review of its use as monotherapy and as combination therapy in the management of hypertension. Drugs. 2010 Oct 22;70(15):2011-49. Dusing R. Sexual dysfunction in male patients with hypertension: influence of antihypertensive drugs. Drugs. 2005;65(6):773-86.

Duley L, Meher S, Jones L. Drugs for treatment of **very high blood pressure during pregnancy**. Cochrane Database Syst Rev. 2013 Jul 31;7:CD001449. doi: 10.1002/14651858.CD001449.pub3. Until better evidence is available the choice of antihypertensive should depend on the clinician`s experience and familiarity with a particular drug; on what is known about adverse effects; and on women`s preferences. Exceptions are nimodipine, magnesium sulphate (although this is indicated for women who require an anticonvulsant for prevention or treatment of eclampsia), diazoxide and ketanserin, which are probably best avoided.

Duncan D, Sankar A, Beattie WS, et al. **Alpha-2 adrenergic agonists (eg. Clonidine) for the prevention of cardiac complications** among adults undergoing surgery. Cochrane Database Syst Rev. 2018 Mar 6;3:CD004126. Our review concludes that prophylactic-2 adrenergic agonists generally do not prevent perioperative death or major cardiac complications. For non-cardiac surgery, there is moderate-to-high quality evidence that these agents do not prevent death, myocardial infarction or stroke. Conversely, there is moderate quality evidence that these agents have important adverse effects, namely increased risks of hypotension and bradycardia. For cardiac surgery, there is moderate quality evidence that alpha-2 adrenergic agonists have no effect on the risk of mortality or myocardial infarction, and that they increase the risk of bradycardia. The quality of evidence was inadequate to draw conclusions regarding the effects of alpha-2 agonists on stroke or hypotension during cardiac surgery.

Dyke CM, Benz CL, Taggart CM, et al. **Systolic and Diastolic Blood Pressure Variability as Risk Factors** for Adverse Events After **Coronary Artery Bypass Grafting**. JAMA Surg. 2018 Oct 3.

Easterling T, Mundle S, Bracken H, et al. Oral antihypertensive regimens (nifedipine retard, labetalol, and methyldopa) for management of severe **hypertension in pregnancy**: an open-label, randomised controlled trial. Lancet. 2019Aug1

Ebrahim S, Beswick A, Burke M, Davey Smith G. **Multiple risk factor interventions** for **primary** prevention of coronary heart disease. Cochrane Database Syst Rev. 2006 Oct 18;(4):CD001561.

Edwards C, Hiremath S, Gupta A, McCormick BB, Ruzicka M. **BpTRUth**: Do **automated blood pressure monitors outperform mercury**? J Am Soc Hypertens. 2013 Aug 19.

Egan Brent M.; Zhao Yumin; Axon R. Neal. **US Trends in Prevalence, Awareness, Treatment, and Control** of Hypertension, 1988-2008. JAMA. 2010;303(20):2043-2050.

Egan BM, Zhao Y, Axon RN, Brzezinski WA, Ferdinand KC. Uncontrolled and Apparent Treatment **Resistant Hypertension in the United States, 1988 to 2008**. Circulation. 2011 Aug 8.

Egan BM, Li J, Qanungo S, Wolfman TE. Blood pressure and **cholesterol control in hypertensive** hypercholesterolemic patients **1988-2010**. Circulation 2013.

Egan BM, Zhao Y, Li J, et al. Prevalence of optimal treatment regimens in patients with apparent **treatment-resistant hypertension** based on office blood pressure in a community-based practice network. Hypertension 2013.

Egan BM, Li J, Shatat IF, et al. Closing the Gap in Hypertension **Control Between Younger and Older** Adults: National Health and Nutrition Examination Survey (**NHANES**) 1988 to 2010. Circulation. 2014 May 20;129(20):2052-61.

Egan BM, Li J, Hutchison FN, et al. **Hypertension in the United States**, 1999 to 2012: progress toward healthy people 2020 goals. Circulation. 2014 Nov 4;130(19):1692-9.

Einstadter D, Bolen SD, Misak JE, et al. Association of Repeated Measurements With Blood Pressure Control in Primary Care. JAMA Intern Med. 2018 Apr 16.

Eleid MF, Nishimura RA, Sorajja P,et al. Systemic **hypertension in low-gradient severe aortic stenosis** with preserved ejection fraction. Circulation. 2013 Sep 17;128(12):1349-53.

Ellison DH. **Clinical Pharmacology** in Diuretic Use. Clin J Am Soc Nephrol. 2019 Apr 1.

Elmer PJ, et al. **PREMIER** Collaborative Research Group. Effects of comprehensive **lifestyle** modification on diet, weight, physical fitness, and blood pressure control: 18-month results of a randomized trial. Ann Intern Med. 2006 Apr 4;144(7):485-95. Summary for patients in: Ann Intern Med. 2006 Apr 4;144(7):I27.

Emdin CA, Rahimi K, Neal B, et al. **Blood pressure lowering in type 2 diabetes**: a systematic review and meta-analysis. JAMA. doi:10.1001/jama.2014.18574.

ENOS Trial Investigators. Efficacy of **nitric oxide**, with or without continuing antihypertensive treatment, for management of **high blood pressure in acute stroke** (**ENOS**): a partial-factorial randomised controlled trial. Lancet 2014; online Oct 22. http://dx.doi.org/10.1016/S0140-6736(14)61121-1.

Erbel R, Lehmann N, Möhlenkamp S, et al. **Subclinical coronary atherosclerosis** predicts cardiovascular risk in different stages of hypertension: result of the Heinz Nixdorf Recall Study. Hypertension 2012; 59:44-53.

Ernst ME, Neaton JD, Grimm RH Jr, et al. Multiple Risk Factor Intervention Trial Research Group. Long-term effects of **chlorthalidone versus hydrochlorothiazide** on electrocardiographic left ventricular hypertrophy in the multiple risk factor intervention trial. (**MRFIT**) Hypertension. 2011 Dec;58(6):1001-7.

Etyang AO, et al. Clinical and Epidemiological Implications of **24-Hour Ambulatory Blood Pressure Monitoring** for the Diagnosis of Hypertension in Kenyan Adults: A Population-Based Study. J Am Heart Assoc. 2016 Dec 15;5(12).

ESC: Williams B, Mancia G, Spiering W, et al. 2018 ESC/ESH Guidelines for the management of arterial hypertension: The Task Force for the management of arterial hypertension of the European Society of Cardiology and the European Society of Hypertension: The Task Force for the management of arterial hypertension of the European Society of Cardiology and the European Society of Hypertension. J Hypertens. 2018 Oct;36(10):1953-2041.

ESH/ESC: Mancia G, De Backer G, Dominiczak A, et al. Management of Arterial Hypertension of the ESH; European Society of Cardiology. 2007 Guidelines for the Management of Arterial Hypertension: The Task Force for the Management of Arterial Hypertension of the European Society of Hypertension (**ESH**) and of the European Society of Cardiology (**ESC**). J Hypertens. **2007** Jun;25(6):1105-87. Erratum: J Hypertens. 2007 Aug;25(8):1749.

ESH/ESC: Mancia G, Fagard R, Narkiewicz K, et al. **2013 ESH/ESC guidelines** for the management of arterial **hypertension**. Eur Heart J 2013; DOI: 10.1093/eurheartj/eht.151.

ESH/ESC: Williams B, Mancia G, Spiering W, et al. **2018 ESC/ESH Guidelines** for the management of arterial **hypertension**: The Task Force for the management of arterial hypertension of the European Society of Cardiology and the European Society of Hypertension: The Task Force for the management of arterial hypertension of the European Society of Cardiology and the European Society of Hypertension. J Hypertens. 2018 Oct;36(10):1953-2041.

ESCAPE Trial Group. Strict blood-pressure control and progression of renal failure in children. *N Engl J Med* 2009 Oct 22; 361:1639.

Esler MD, Krum H, Schlaich M, et al; for the **Symplicity HTN-2** Investigators. **Renal Sympathetic Denervation** for Treatment of Drug-Resistant Hypertension: One-Year Results From the Symplicity HTN-2 Randomized, Controlled Trial. Circulation. 2012 Dec 18;126(25):2976-2982.

Esler M. **SPRINT**, or false start, towards a lower universal treated blood pressure target in hypertension. *Hypertension*2015; DOI:10.1161/HYPERTENSIONAHA.115.06735.

Espinola-Klein C, Weisser G, Jagodzinski A, et al. {beta}-Blockers in Patients With Intermittent Claudication and Arterial Hypertension: Results From the **Nebivolol or Metoprolol in Arterial Occlusive Disease** Trial. Hypertension. 2011 Aug;58(2):148-54.

Estruch R, Martinez-González MA, Corella D et al. Effects of a **Mediterranean-style diet** on cardiovascular risk factors. A randomized trial. Ann Intern Med 2006; 145:1-11.

Ettehad D, Emdin CA, Kiran A, et al. **Blood pressure lowering for prevention of cardiovascular disease and death**: a systematic review and meta-analysis Lancet 2015; online Dec 23.

Evrard AS, Lefèvre M, Champelovier P, et al. Does **aircraft noise** exposure increase the risk of hypertension in the population living near airports in France? Occup Environ Med. 2016 Aug 1.

Expert Panel on Integrated Guidelines for Cardiovascular Health and Risk Reduction in Children and Adolescents. Expert Panel on **Integrated Guidelines for Cardiovascular Health and Risk Reduction in Children and Adolescents**: Summary Report. Pediatrics. 2011 Nov 14.

Fagard RH, Celis H, Thijs L, Wouters S. **Regression of left ventricular mass** by antihypertensive treatment: a meta-analysis of randomized comparative studies. Hypertension. 2009 Nov;54(5):1084-91.

Falaschetti E, Mindell J, Knott C, Poulter N. **Hypertension management in England**: a serial cross-sectional study from 1994 to 2011. Lancet 2014; 383: 1912–19.

Falet JP, Elkrief A, Green L. **Hypertensive emergency induced by licorice tea**. CMAJ. 2019 May 27;191(21):E581-E583.

Falkner B, Gidding SS. Is the **SPRINT** Blood Pressure Treatment Target of 120/80 mm Hg **Relevant for Children**? Hypertension. 2016 May;67(5):826-8.

Famularo G, Minisola G. Relapsing **Olmesartan-Associated Ileitis**. Ann Pharmacother. 2016 Dec;50(12):1070.

Farkouh ME et al. for the **FREEDOM** Trial Investigators. Strategies for multivessel revascularization in patients with diabetes. N Engl J Med 2012 Nov 4; [e-pub ahead of print]. (**CABG** vs PCI)
Farrell B, Monahan A, Dore N, et al. **Blood pressure targets in the very old**: Development of a tool in a geriatric day hospital. Can Fam Physician. 2014 Jul;60(7):e350-5.
Faselis C, Doumas M, Pittaras A, et al. **Exercise Capacity and All-Cause Mortality** in Male Veterans With Hypertension Aged >=70 Years. Hypertension. 2014 May 12.
Fava C, Dorigoni S, Dalle Vedove F, et al. Effect of **CPAP on blood pressure** in patients with OSA/hypopnea a systematic review and meta-analysis. Chest. 2014 Apr;145(4):762-71.
FDA June/11 Food and Drug Administration drug safety: **No increase in risk of cancer** with certain blood pressure drugs—**angiotensin receptor blockers (ARBs).** June 2, 2011. http://www.fda.gov/Drugs/DrugSafety/ucm257516.htm
FDA July/13 is warning that the blood pressure drug **Olmesartan** Medoxomil (marketed as Benicar, Benicar HCT, Azor, Tribenzor, and generics) can cause intestinal problems known as sprue-like enteropathy. Symptoms of **sprue-like enteropathy** include severe, chronic diarrhea with substantial weight loss. FDA has approved changes to the labels of these drugs to include this concern. Sprue-like enteropathy has not been detected with ARB drugs other than olmesartan.
Feldman RD. Down the Rabbit Hole: Hypertension Guidelines, Goals and Gulfs Across the 49th Parallel. Can J Cardiol. 2018 May;34(5):543-545.
Fengler K, Rommel KP, Blazek S, et al. A Three-Arm Randomized Trial of **Different Renal Denervation Devices and Techniques** in Patients With Resistant Hypertension (RADIOSOUND-HTN). Circulation. 2019 Jan 29;139(5): 590-600.
Ferdinand KC, Bakris GL, Cushman WC, et al. **Comparison of Effectiveness of Azilsartan Medoxomil and Olmesartan in Blacks Versus Whites With Systemic Hypertension**. Am J Cardiol. 2018 Aug 4.
Fernstrom JD, et al. Long-term Changes in Blood Pressure in Extremely Obese Patients Who Have Undergone **Bariatric** Surgery. Arch Surg. 2006 Mar;141(3):276-83.
Feringa HH, et al. Cardioprotective medication is associated with improved survival in patients with **peripheral arterial disease**. J Am Coll Cardiol. 2006 Mar 21;47(6):1182-7. Epub 2006 Feb 23.
Fihn SD, Gardin JM, Abrams J, et al. 2012 ACCF/AHA/ACP/AATS/PCNA/SCAI/STS Guideline for the **Diagnosis and Management of Patients With Stable Ischemic Heart Disease**: A Report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines, and the American College of Physicians, American Association for Thoracic Surgery, Preventive Cardiovascular Nurses Association, Society for Cardiovascular Angiography and Interventions, and Society of Thoracic Surgeons. Circulation. 2012 Nov 19.
Fihn SD, Blankenship JC, Alexander KP, et al. **2014 ACC/AHA**/AATS/PCNA/SCAI/STS Focused Update of the Guideline for the **Diagnosis and Management of Patients With Stable Ischemic Heart Disease**: A Report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines, and the American Association for Thoracic Surgery, Preventive Cardiovascular Nurses Association, Society for Cardiovascular Angiography and Interventions, and Society of Thoracic Surgeons. J Am Coll Cardiol. 2014 Jul 18. pii: S0735-1097(14)04510-0.
Finucane C, O'Connell MDL, et al. Age-related normative changes in phasic **orthostatic blood pressure** in a large population study: findings from The Irish Longitudinal Study on Ageing (TILDA). Circulation. 2014;130:1780–1789.
Fisayo A, Bruce BB, Newman NJ, Biousse V. **Overdiagnosis of idiopathic intracranial hypertension**. Neurology 2016;86: 341–350.
Fischer U, Cooney MT, Bull LM, et al. **Acute post-stroke blood pressure** relative to pre-morbid levels in intracerebral haemorrhage versus major ischaemic stroke: population-based study. Lancet Neurol 2014; online Feb 28.
Fisher NDL, Fera LE, Dunning JR, et al. Development of an **entirely remote, non-physician led hypertension management program**. Clin Cardiol 2019;1-7.
Fitzharris P, Jordan A. Investigating **recurrent angio-oedema**. BMJ. 2011 Oct 24;343:d6607.
Flack JM, Sica DA, Bakris G, et al. **Management of high blood pressure in blacks**. An update of the International Society on Hypertension in Blacks consensus statement. *Hypertension* 2010; DOI: 10.1161/HYPERTENSIONAHA.110.152892. Available at: http://hyper.ahajournals.org
Fletcher RD, Amdur RL, et al. **Blood Pressure Control Among US Veterans**: A Large Multiyear Analysis of Blood Pressure Data From the Veterans Administration Health Data Repository. Circulation. 2012 May 22;125(20):2462-8.
Flint AC, Conell C, Ren X, et al. Effect of Systolic and Diastolic Blood Pressure on **Cardiovascular Outcomes**. N Engl J Med. 2019 Jul 18;381(3):243-251.
Flynn NO, Timmis A, Henderson R, Rajesh S, Fenu E; on behalf of the Guideline Development Group. Management of **stable angina**: summary of **NICE** guidance. BMJ. 2011 Aug 5;343:d4147. doi: 10.1136/bmj.d4147.
Flynn JT et al. Clinical practice guideline for screening and management of **high blood pressure in children and adolescents**. *Pediatrics* 2017 Aug 21.
Flynn JT, Pierce CB, Miller ER 3rd, Charleston J, et al. Reliability of **resting blood pressure measurement** and classification using an **oscillometric device** in **children** with chronic kidney disease. J Pediatr 2011.
Flynn JT, Daniels SR, Hayman LL, et al; American Heart Association **Atherosclerosis**, **Hypertension** and **Obesity** in **Youth** Committee of the Council on Cardiovascular Disease in the Young. Update: **ambulatory blood pressure monitoring in children and adolescents**: a scientific statement from the american heart association. (AHA) Hypertension. 2014 May;63(5):1116-35.
Flynn JT, Falkner BE. New Clinical Practice Guideline for the Management of **High Blood Pressure in Children and Adolescents**. Hypertension. 2017 Oct;70(4):683-686.
Folsom AR, et al. An assessment of incremental coronary risk prediction using **C-reactive protein** and other novel risk markers: the atherosclerosis risk in communities study. Arch Intern Med. 2006 Jul 10;166(13):1368-73.
Ford ES. Trends in **mortality from all causes and cardiovascular disease among hypertensive and nonhypertensive adults** in the United States. Circulation. 2011 Apr 26;123(16):1737-44.
Forman JP, Stampfer MJ, Curhan GC. **Diet and lifestyle** risk factors associated with incident hypertension in women. JAMA. 2009 Jul 22;302(4):401-11.
Forouzanfar MH, Liu P, Roth GA, et al. **Global burden of hypertension** and systolic blood pressure of at least 110 to 115 mm Hg, 1990-2015.JAMA. doi:10.1001/jama.2016.19043
Fouque D, Laville M, Boissel JP. **Low protein diets for chronic kidney disease** in non diabetic adults. Cochrane Database Syst Rev. 2006 Apr 19;(2):CD001892.
Fox K, Ford I, Steg PG, et al. **Ivabradine** in stable coronary artery disease without clinical heart failure. (Signify) N Engl J Med. DOI:10.1056/NEJMoa1406430.
Fralick M, Kesselheim AS, Avorn J, et al. Use of **health care databases to support supplemental indications** of approved medications (**Ontarget**) [online Nov 20, 2017]. JAMA Intern Med. doi:10.1001/jamainternmed.2017.3919
Fralick M, Mandonald EM, Gomes T, et al. **Co-trimoxazole and sudden death in patients receiving inhibitors of renin-angiotensin system**: population based study. BMJ 2014;349:g6196.
Franco OH, de Laet C, Peeters A, Jonker J, Mackenbach J, Nusselder W. Effects of **physical activity** on life expectancy with cardiovascular disease. Arch Intern Med. 2005 Nov 14;165(20):2355-60.
Franklin SS, Thijs L, Hansen TW, et al. Significance of **White-Coat Hypertension in Older Persons** With Isolated Systolic Hypertension: A Meta-Analysis Using the International Database on Ambulatory Blood Pressure Monitoring in Relation to Cardiovascular Outcomes Population. Hypertension. 2012 Jan 17.
Franklin SS, Thijs L, Hansen TW, et al. **White-coat hypertension**: new insights from recent studies. Hypertension. 2013 Dec;62(6):982-7
Franklin SS, Gokhale SS, Chow VH, et al. Does **low diastolic blood pressure** contribute to the risk of recurrent hypertensive **cardiovascular** disease **events**? The framingham heart study. Hypertension. 2015 Feb;65(2):299-305.
Franklin SS, Thijs L, Asayama K, et al; IDACO Investigators.. The Cardiovascular Risk of **White-Coat Hypertension**. J Am Coll Cardiol. 2016 Nov 8;68(19):2033-2043.
Fraser LA, Shariff SZ, McArthur E, et al. **Calcium channel blocker-clarithromycin drug interaction** did not increase the risk of nonvertebral fracture: a population-based study. Ann Pharmacother. 2015 Feb;49(2):185-8.
Fried LF, Emanuele N, Zhang JH, et al. **Combined angiotensin inhibition** for the treatment of diabetic nephropathy. (**VA Nephron-D**) N Engl J Med 2013. DOI: 10.1056/NEJMoa1303154.
Frieden TR, King SM, Wright JS. **Protocol-Based Treatment of Hypertension**: A Critical Step on the Pathway to Progress. JAMA. 2013 Nov 14.
Friedman GD, Asgari MM, Warton EM, et al. Antihypertensive Drugs (hydrochlorothiazide, nifedipine) and **Lip Cancer** in Non-Hispanic Whites. Arch Intern Med. 2012 Aug 6:1-6.
Fuchs SC, Poli-de-Figueiredo CE, et al. Effectiveness of **Chlorthalidone Plus Amiloride** for the Prevention of Hypertension: The **PREVER**-Prevention Randomized Clinical Trial. J Am Heart Assoc. 2016 Dec 13;5(12).
Fujiwara T, Yano Y, Hoshide S, et al. Association of **Cardiovascular Outcomes With Masked Hypertension** Defined by **Home Blood Pressure Monitoring** in a Japanese General Practice Population. JAMA Cardiol. 2018 May 23.
Fung TT, Chiuve SE, McCullough ML, Rexrode KM, Logroscino G, Hu FB. Adherence to a DASH-style diet and risk of coronary heart disease and stroke in women. Arch Intern Med. 2008 Apr 14;168(7):713-20. Adherence to the **DASH-style diet** is associated with a lower risk of CHD and stroke among middle-aged women during 24 years of follow-up.
Fung MM, Peters K, Redline S, et al. for the Osteoporotic Fractures in Men Research Group. **Decreased Slow Wave Sleep** Increases Risk of Developing Hypertension in Elderly Men. Hypertension. 2011 Aug 29.
Futier E, Lefrant JY, et al.Effect of **Individualized vs Standard Blood Pressure Management Strategies on Postoperative Organ Dysfunction** Among High-Risk Patients Undergoing Major Surgery: A Randomized Clinical Trial. JAMA. 2017 Oct 10;318(14):1346-1357.
Ganesh SK, Arnett DK, Assimes TL, et al. American Heart Association Council on Functional Genomics and Translational Biology, Council on Epidemiology and Prevention, Council on Basic Cardiovascular Sciences, Council on Cardiovascular Disease in the Young, Council on Cardiovascul. **Genetics and genomics for the prevention and treatment of cardiovascular disease**: update: a scientific statement from the american heart association. Circulation. 2013 Dec 24;128(25):2813-51.
Gangwisch JE. A Review of Evidence for the Link Between **Sleep Duration and Hypertension**. Am J Hypertens. 2014 Apr 28.

Ganguli M, Fu B, Snitz BE, et al. **Mild cognitive impairment**: Incidence and vascular risk factors in a population-based cohort. Neurology. 2013 May 8.

Garcia MJ, Lessick J, Hoffmann MH; CATSCAN Study Investigators. Accuracy of 16-row multidetector computed tomography for the assessment of coronary artery stenosis. JAMA. 2006 Jul 26;296(4):403-11. The results of this study indicate that MDCT coronary angiography performed with **16-row scanners** is limited by a high number of nonevaluable cases and a high false-positive rate. Thus, its routine implementation in clinical practice is not justified. Nevertheless, given its high sensitivity & negative predictive value, 16-row MDCT may be useful in excluding coronary disease in selected patients in whom a false-positive or inconclusive stress test result is suspected.

Garies S, Hao S, McBrien K, et al. **Prevalence of Hypertension, Treatment, and Blood Pressure Targets** in Canada Associated With the 2017 American College of Cardiology and American Heart Association Blood Pressure Guidelines. JAMA Netw Open. 2019 Mar 1;2(3):e190406.

Garjon J, Saiz LC, Azparren A, et al. **First-line combination therapy versus first-line monotherapy for primary hypertension**. Cochrane Database Syst Rev. 2017 Jan 13;1:CD010316. The numbers of included participants and, hence the number of events, were too small to draw any conclusion about the relative efficacy of monotherapy versus combination therapy as initial treatment for primary hypertension. There is a need for large clinical trials that address the question and report clinically relevant endpoints.

Garlo KG, Bates DW, Seger DL, et al. Association of Changes in **Creatinine and Potassium Levels After Initiation of Renin Angiotensin Aldosterone System Inhibitors** With Emergency Department Visits, Hospitalizations, and Mortality in Individuals With Chronic Kidney Disease. JAMA Netw Open. 2018;1(7):e183874.

Garrison SR;Kolber MR;Korownyk CS;McCracken RK;Her. **Blood pressure targets for hypertension in older adults.** Cochrane Database Syst Rev. 2017 Aug 8;8:CD011575. At the present time there is insufficient evidence to know whether a higher BP target (less than150 to 160/95 to 105 mmHg) or a lower BP target (less than 140/90 mmHg) is better for older adults with high BP. Additional good-quality trials assessing BP targets in this population are needed.

Gauer R. **Severe Asymptomatic Hypertension**: Evaluation and Treatment. Am Fam Physician. 2017;95(8):492-500

Gee ME, et al. Outcomes Research Task Force of the Canadian Hypertension Education Program. **Antihypertensive Medication Use**, Adherence, Stops, & Starts in Canadians With Hypertension. Can J Cardiol. 2012Apr 20.

Gee ME, Pickett W, Janssen I, Campbell NR, Birtwhistle R. **Validity of self-reported blood pressure control** in people with hypertension attending a primary care center. Blood Press Monit. 2014 Feb;19(1):19-25.

Geisler B, Egan B, Cohen J, et al. Cost-effectiveness and clinical effectiveness of catheter-based **renal denervation** for resistant hypertension. J Am Coll Cardiol 2012.

Gelber RP, Ross GW, Petrovitch H, et al. Antihypertensive medication use and risk of **cognitive impairment: The Honolulu-Asia Aging Study**. Neurology. 2013 Sep 3;81(10):888-95.

Geldsetzer P, Manne-Goehler J, Theilmann M, et al. **Diabetes and hypertension in India**: a nationally representative study of 1.3 million adults [online Jan 29, 2018].JAMA Intern Med. doi:10.1001/jamainternmed.2017.8094

Gelfer M, Dawes M, Kaczorowski J, et al. **Diagnosing hypertension**: Evidence supporting the **2015 recommendations of the Canadian Hypertension Education Program**. Can Fam Physician. 2015 Nov;61(11):957-61.Review.

Gelfer M, Dawes M, Kaczorowski J, Padwal R, et al. **Diagnosing hypertension**: Evidence supporting the **2015 recommendations of the Canadian Hypertension Education Program**. Can Fam Physician. 2015 Nov;61(11):957-61.

Gennari-Moser C, Escher G, Kramer S, et al. **Normotensive Blood Pressure in Pregnancy**: The Role of Salt and Aldosterone. Hypertension. 2013 Dec 2

George J, Majeed W, Mackenzie IS, et al. Association between cardiovascular events and **sodium-containing effervescent, dispersible, and soluble drugs**: nested case-control study. *BMJ* 2013;347:f6954.

Georgianos PI, Agarwal R **Ambulatory Blood Pressure Reduction With SGLT-2 Inhibitors**: Dose-Response Meta-analysis and Comparative Evaluation With Low-Dose Hydrochlorothiazide. Diabetes Care. 2019 Apr;42(4):693-700.

Ghadieh AS, Saab B. Evidence for **exercise training** in the management of hypertension in adults. Can Fam Physician. 2015 Mar;61(3):233-9.

Ghadri JR, Wittstein IS, Prasad A, et al. International Expert Consensus Document on **Takotsubo Syndrome** (Part II): Diagnostic Workup, Outcome, and Management. Eur Heart J. 2018 Jun 7;39(22):2047-2062.

Gheorghiade M, et al. **OPTIMIZE-HF** Investigators and Coordinators. **Systolic blood pressure** at admission, clinical characteristics, and outcomes in patients hospitalized with acute heart failure. JAMA. 2006 Nov 8;296(18):2217-26.

Ghossein-Doha C, Peeters L, van Heijster S, et al. **Hypertension after preeclampsia** is preceded by changes in cardiac structure and function. Hypertension 2013.

Gibbons CH, Schmidt P, Biaggioni I, et al. The recommendations of a consensus panel for the **screening, diagnosis, and treatment of neurogenic orthostatic hypotension** and associated supine hypertension. J Neurol. 2017 Jan 3.

Giles TD, Weber MA, Basile J, et al, for the NAC-MD-01 Study Investigators. Efficacy and safety of **nebivolol and valsartan** as fixed-dose combination in hypertension: a randomised, multicentre study. Lancet 2014; 383: 1889–98.

Gill P, Haque MS, Martin U, et al. **Measurement of blood pressure** for the diagnosis and management of hypertension in **different ethnic groups**: one size fits all. BMC Cardiovasc Disord. 2017 Feb 8;17(1):55.

Gilsanz P, Mayeda ER, Glymour MM, et al. **Female sex, early-onset hypertension, and risk of dementia**. Neurology. 2017 Oct 31;89(18):1886-1893

Gioia LC, Zewude RT, Kate MP, et al. **Prehospital systolic blood pressure is higher in acute stroke** compared with stroke mimics. Neurology. 2016 May 18.

Gladstone RA, Pudwell J, Nerenberg KA, et al. **Cardiovascular Risk Assessment and Follow-Up of Women** After Hypertensive Disorders of Pregnancy: A Prospective Cohort Study. J Obstet Gynaecol Can. 2019 Jan 14.

Glynn LG, Murphy AW, Smith SM, Schroeder K, Fahey T. **Self-monitoring and other non-pharmacological interventions** to improve the management of hypertension in primary care: a systematic review. Br J Gen Pract. 2010 Dec;60(581):e476-88.

Go AS, Mozaffarian D, Roger VL, et al. on behalf of the American Heart Association Statistics Committee and Stroke Statistics Subcommittee. Executive Summary: **Heart Disease and Stroke Statistics--2013 Update**: A Report From the American Heart Association. Circulation. 2013 Jan 1;127(1):143-152.

Go AS, Bauman M, et al. An Effective Approach to **High Blood Pressure Control**: A Science Advisory From the American Heart Association (AHA), the American College of Cardiology (ACC), and the Centers for Disease Control and Prevention. Hypertension. 2013 Nov 15.

Go AS, Mozaffarian D, Roger VL, et al. **Heart disease and stroke statistics--2014** update: a report from the American heart association. Circulation. 2014 Jan 21;129(3):e28-e292

Goel A, Maski MR, Bajracharya S, et al. Epidemiology and Mechanisms of **De Novo and Persistent Hypertension** in the **Postpartum Period**. Circulation. 2015 Sep 28.

Goh KL, Bhaskaran K, Minassian C, et al. **Angiotensin receptor blockers and risk of dementia**: cohort study in UK Clinical Practice Research Datalink. Br J Clin Pharmacol. 2014 Sep 16.

Gottesman RF, Schneider AL, Albert M, et al. **Midlife Hypertension and 20-Year Cognitive Change**: The Atherosclerosis Risk in Communities Neurocognitive Study. JAMA Neurol. 2014 Aug 4.

Godtfredsen NS, Prescott E, Osler M. Effect of **smoking** reduction on lung cancer risk. JAMA. 2005 Sep 28;294(12):1505-10.

Gottlieb DJ, Punjabi NM, Mehra R, et al. **CPAP** versus oxygen in obstructive **sleep apnea**. N Engl J Med 2014;370:2276-85.

Goyal N, Tsivgoulis G, Pandhi A, et al. Blood pressure levels post **mechanical thrombectomy** and outcomes in **large vessel occlusion strokes**. Neurology. 2017 Aug 8;89(6):540-547.

Gradman AH, Parisé H, Lefebvre P, Falvey H, Lafeuille MH, Duh MS. **Initial combination therapy** reduces the risk of cardiovascular events in hypertensive patients: a matched cohort study. Hypertension. 2013;61:309-318.

Grandi SM, Vallée-Pouliot K, Reynier P, et al. Hypertensive Disorders in **Pregnancy** and the **Risk** of **Subsequent Cardiovascular Disease**. Paediatr Perinat Epidemiol. 2017 Aug 17.

Gray L, Lee I-M, Sesso HD, Batty GD. **Blood pressure in early adulthood**, hypertension in middle age, and future cardiovascular disease mortality: HAHS (Harvard Alumni Health Study). J Am Coll Cardiol 2011; 58:2396-2403.

Green BB, Cook AJ, Ralston JD, et al. Effectiveness of home blood pressure monitoring, **Web communication, and pharmacist** care on hypertension control: a randomized controlled trial. JAMA. 2008 Jun 25;299(24):2857-67. Pharmacist care management delivered through secure patient Web communications improved BP control in patients with hypertension.

Gritter M, Rotmans JI, Hoorn EJ. Role of **Dietary K(+) in Natriuresis, Blood Pressure Reduction, Cardiovascular Protection, and Renoprotection**. Hypertension. 2019 Jan;73(1):15-23.

Grotta JC. Clinical practice. **Carotid stenosis**. N Engl J Med. 2013 Sep 19;369(12):1143-50.

Grundvold I, Skretteberg PT, Liestøl K, et al. **Upper normal blood pressures** predict **incident atrial fibrillation** in healthy middle-aged men: a 35-year follow-up study. Hypertension. 2012;59:198 –204.

Gu A, Yue Y, Desai RP, et al. **Racial and Ethnic Differences** in Antihypertensive Medication Use and Blood Pressure Control Among **US Adults** With Hypertension: The National Health and Nutrition Examination Survey, 2003 to 2012. Circ Cardiovasc Qual Outcomes. 2017 Jan;10(1).

Gu Q, Burt VL, Dillon CF, and Yoon S. Trends in **antihypertensive medication** use and blood pressure control among **United States** adults with hypertension. The National Health and Nutrition Examination Survey, 2001 to 2010. Circulation 2012.

Gueyffier F, et al. Antihypertensive drugs in **very old people**: a subgroup meta-analysis of randomised controlled trials. INDANA Group. Lancet. 1999 Mar 6;353(9155):793-6.

Guimont C, et al. Effects of **job strain** on blood pressure: a prospective study of male and female white-collar workers. Am J Public Health. 2006 Aug;96(8):1436-43. Epub 2006 Jun 29. (InfoPOEMs: Work stress has no meaningful effect on blood pressure. (LOE = 1b))

Guo F, Di H, Zhang W, Walton RG. Trends in prevalence, awareness, management and control of **hypertension among United States** adults 1999 to 2010. J Am Coll Cardiol 2012.

Gupta AK, Dahlof B, Dobson J, Sever PS, Wedel H, Poulter NR; Anglo-Scandinavian Cardiac Outcomes Trial Investigators. (**Ascot**) Determinants of new-onset diabetes among 19,257 hypertensive patients randomized in the Anglo-Scandinavian Cardiac Outcomes Trial--Blood Pressure Lowering Arm and the relative influence of antihypertensive medication. Diabetes Care. 2008 May;31(5):982-8. Epub 2008 Jan 30. Baseline FPG >5 mmol/l, BMI, and use of an atenolol +/- diuretic regimen were among the major determinants of NOD in hypertensive patients. The model developed from these data allows accurate prediction of NOD among hypertensive subjects.

Gupta P, Patel P, Štrauch B, et al. Risk Factors for **Nonadherence to Antihypertensive Treatment**. Hypertension. 2017 Jun;69(6):1113-1120.
Gupta A, Mackay J, Whitehouse A, et al. Long-term mortality after blood pressure-lowering and lipid-lowering treatment in patients with hypertension in the **Anglo-Scandinavian Cardiac Outcomes Trial (ASCOT)** Legacy study: 16-year follow-up results of a randomised factorial trial. Lancet. 2018 Aug 24.
Hackett C, Garrison S, Kolber MR. What is **urgent about hypertensive urgency**? Can Fam Physician. 2017 Jul;63(7):543.
Hajjar I, Goldstein FC, Martin GS, et al. Roles of **Arterial Stiffness** and Blood Pressure in Hypertension-Associated **Cognitive Decline** in Healthy Adults. Hypertension. 2016 Jan;67(1):171-5.
Hajjar I, Rosenberger KJ, Kulshreshtha A, et al. Association of **JNC**-8 and **SPRINT** systolic blood pressure levels with **cognitive function** and related **racial disparity** [online August 21, 2017]. JAMA Neurol. doi:10.1001/jamaneurol.2017.1863
Hallan S, Astor B, Romundstad S, Aasarød K, Kvenild K, Coresh J. Association of Kidney Function and Albuminuria With Cardiovascular Mortality in Older vs Younger Individuals: The HUNT II Study. Arch Intern Med. 2007 Dec 10;167(22):2490-6. Reduced kidney function and microalbuminuria are risk factors for cardiovascular death, independent of each other and traditional risk factors. The combined variable improved cardiovascular risk stratification at all age levels, but particularly in elderly persons where the predictive power of traditional risk factors is attenuated.
Haller H, Ito S, Izzo JL Jr, et al. **Olmesartan** for the delay or prevention of microalbuminuria in type 2 diabetes. (**ROADMAP**) N Engl J Med 2011;364:907-17. (n=4447 over 3.2yr. Improved microalbuminuria, but increased fatal CV events)
Halton TL, Willett WC, Liu S et al. **Low-carbohydrate-diet** score and the risk of coronary heart disease in **women**. N Engl J Med 2006; 355:1991-2002.
Hameed MA, Dasgupta I, Gill P. Poor **adherence** to antihypertensive drugs. BMJ. 2016 Jul 21;354:i3268.
Hamrahian SM. Management of **Hypertension in Patients with Chronic Kidney Disease**. Curr Hypertens Rep. 2017 May;19(5):43.
Hanevold CD. **White Coat Hypertension in Children and Adolescents**. Hypertension. 2019 Jan;73(1):24-30.
Hankey GJ, Norman PE, Eikelboom JW. Medical treatment of **peripheral arterial disease**. JAMA. 2006 Feb 1;295(5):547-53.
Hara A, Tanaka K, Ohkubo T, et al. **Ambulatory Versus Home Versus Clinic Blood Pressure**: The Association With Subclinical Cerebrovascular Diseases: The Ohasama Study. Hypertension. 2011 Nov 14.
Harel Z et al. The effect of combination treatment with **aliskiren and blockers of the renin-angiotensin system** on hyperkalaemia and acute kidney injury: systematic review and meta-analysis. BMJ. 2012 Jan 9;344:e42.
Haring B, Liu J, Salmoirago-Blotcher E, et al. Blood pressure **variability and brain morphology** in elderly women without cardiovascular disease. Neurology. 2019 Mar 19;92(12):e1284-e1297.
Harris KC, Benoit G, Dionne J, et al; **CHEP** Guidelines Task Force. Hypertension Canada's **2016 Canadian Hypertension** Education Program Guidelines for Blood Pressure Measurement,Diagnosis, and Assessment of Risk of **Pediatric Hypertension**. Can J Cardiol. 2016 May;32(5):589-97.
Harris WS, Mozaffarian D, Rimm E, Kris-Etherton P, et al. **Omega-6 Fatty Acids** and Risk for Cardiovascular Disease. A Science Advisory From the American Heart Association Nutrition Subcommittee of the Council on Nutrition, Physical Activity, and Metabolism; Council on Cardiovascular Nursing; and Council on Epidemiology and Prevention. Circulation. 2009 Jan 26. [Epub ahead of print] In summary, the AHA supports an omega-6 PUFA intake of at least **5% to 10% of energy** in the context of other AHA lifestyle and dietary recommendations. To reduce omega-6 PUFA intakes from their current levels would be more likely to increase than to decrease risk for CHD.
Haskell WL, Lee IM, Pate RR, Powell KE, Blair SN, Franklin BA, Macera CA, Heath GW, Thompson PD, Bauman A. **Physical Activity** and Public Health. Updated Recommendation for Adults From the American College of Sports Medicine and the American Heart Association. (**AHA**) Circulation. 2007 Aug 1; [Epub ahead of print] To promote and maintain health, all healthy adults aged 18 to 65 yr need moderate-intensity aerobic (endurance) physical activity for a minimum of 30 min on five days each week or vigorous-intensity aerobic physical activity for a minimum of 20 min on three days each week. [I (A)] Combinations of moderate- and vigorous-intensity activity can be performed to meet this recommendation. [IIa (B)] For example, a person can meet the recommendation by walking briskly for 30 min twice during the week and then jogging for 20 min on two other days. Moderate-intensity aerobic activity, which is generally equivalent to a brisk walk and noticeably accelerates the heart rate, can be accumulated toward the 30-min minimum by performing bouts each lasting 10 or more minutes.
Hata J, Arima H, Rothwell PM,et al. Effects of **Visit-to-Visit Variability in Systolic Blood Pressure** on Macrovascular and Microvascular Complications in Patients With Type 2 Diabetes Mellitus: The **ADVANCE** Trial. Circulation. 2013 Sep 17;128(12):1325-1334.
Haug EB, Horn J, Markovitz AR, et al. Association of Conventional Cardiovascular Risk Factors With **Cardiovascular Disease After Hypertensive Disorders of Pregnancy**: Analysis of the Nord-Trøndelag Health Study. JAMA Cardiol. 2019 Jun 12.
Hauspurg A, Lemon LS, Quinn BA, et al. A **Postpartum Remote Hypertension Monitoring Protocol** Implemented at the Hospital Level. Obstet Gynecol. 2019 Oct;134(4):685-691.
Havas S, Dickinson BD, Wilson M. The urgent need to **reduce sodium (salt) consumption**. JAMA. 2007 Sep 26;298(12):1439-41.
Hayes JF, Lundin A, Wicks S, et al. Association of **Hydroxylmethyl Glutaryl Coenzyme A Reductase Inhibitors, L-Type Calcium Channel Antagonists, and Biguanides With Rates of Psychiatric Hospitalization and Self-Harm** in Individuals With Serious Mental Illness. JAMA Psychiatry. 2019 Jan 9.
Haynes R, Judge PK, Staplin N, et al. Effects of **Sacubitril/Valsartan Versus Irbesartan in Patients with Chronic Kidney Disease**: A Randomised Double-Blind Trial. Circulation. 2018 Jul 12.
He FJ, Marciniak M, Visagie E, et al. Effect of Modest **Salt Reduction** on Blood Pressure, Urinary Albumin, and Pulse Wave Velocity in White, Black, and Asian Mild Hypertensives. Hypertension. 2009 Jul 20. [Epub ahead of print]
He FJ, Li J, Macgregor GA. Effect of longer term **modest salt reduction** on blood pressure: Cochrane systematic review and meta-analysis of randomised trials. BMJ. 2013 Apr 3;346:f1325.
He J, Wofford MR, Reynolds K, et al. Effect of **dietary protein** (40g/day: soy & milk) supplementation on blood pressure. A randomized controlled trial. Circulation 2011; doi:10.1161/circulationaha.110.009159.
He J, Zhang Y, Xu T, et al; CATIS Investigators. Effects of **Immediate Blood Pressure Reduction** on Death and Major Disability in Patients With Acute **Ischemic Stroke**: The **CATIS** Randomized Clinical Trial. JAMA. 2013 Nov 17.
He J, Irazola V, Mills KT, et al. Effect of a **community health worker–led multicomponent intervention** on blood pressure control in low-income patients in Argentina: a randomized clinical trial.JAMA. doi:10.1001/jama.2017.11358
Head Geoffrey A, Mihailidou Anastasia S, Duggan Karen A, et al. **Ambulatory Blood Pressure** Working Group of the High Blood Pressure Research Council of Australia. Definition of ambulatory blood pressure targets for diagnosis and treatment of hypertension in relation to clinic blood pressure: prospective cohort study. BMJ 2010;340:c1104, doi: 10.1136/bmj.c1104
Head GA. **Ambulatory blood pressure monitoring is ready to replace clinic blood pressure** in the diagnosis of hypertension: pro side of the argument. Hypertension. 2014 Dec;64(6):1175-81.
Health Canada Jan/12 **RASILEZ** (aliskiren) and RASILEZ HCT (aliskiren/hydrochlorothiazide) - Potential Risks of Cardiovascular and Renal Adverse Events in Patients with Type 2 Diabetes - Novartis Pharmaceuticals Canada Inc. The combination of **aliskiren with ACE inhibitors and ARBs is now contraindicated in patients with type 2 diabetes**. The Product Monograph will be updated accordingly.
Health Canada Feb/14 wishes to inform healthcare professionals and patients of the risks associated with **combining more than one of the following blood pressure medicines**: aliskiren (renin inhibitor), angiotensin-converting enzyme inhibitors (ACEIs) or angiotensin receptor blockers (ARBs).
Health Canada Jan/17 is advising Canadians that it has seized the unauthorized health product "**Blow**", by Limitless Pharma, from Atomik Nutrition at 450 Boulevard de Mortagne, Boucherville, QC. "Blow" is promoted as a pre-workout supplement and is labelled to contain the unauthorized drug 1,3 Dimethylamylamine (DMAA), which may pose serious health risks such as high blood pressure and stroke.
Health Canada Jul/18: Several drugs containing the ingredient **valsartan are being recalled by their manufacturers**. An impurity, **N-nitrosodimethylamine (NDMA), was found in the valsartan** used in these products. NDMA is a **potential human carcinogen**.
Health Canada Jan/19: has completed a safety review of **hydrochlorothiazide** and has found that prolonged use of the drug **could increase a person's risk for non-melanoma skin cancer**.
Heath I. **Waste and harm in the treatment of mild hypertension**. JAMA Intern Med. 2013 Jun 10;173(11):956-7.
Heart Failure Society Of America. **HFSA 2006** Comprehensive Heart Failure Practice Guideline. J Card Fail. 2006 Feb;12(1):e1-2.
Heisler M, Hofer TP, Schmittdiel JA, et al. Improving blood pressure control through a **clinical pharmacist outreach program** in patients with diabetes mellitus in 2 high-performing health systems: the adherence and intensification of medications cluster randomized, controlled pragmatic clinical trial. *Circulation.* 2012;125:2863–2872.
Heran BS, Musini VM, Bassett K, et al. **Angiotensin receptor blockers for heart failure**. Cochrane Database Syst Rev. 2012 Apr 18;4:CD003040. In patients with symptomatic HF and systolic dysfunction or with preserved ejection fraction, ARBs compared to placebo or ACEIs do not reduce total mortality or morbidity. ARBs are better tolerated than ACEIs but do not appear to be as safe and well tolerated as placebo in terms of withdrawals due to adverse effects. Adding an ARB in combination with an ACEI does not reduce total mortality or total hospital admission but increases withdrawals due to adverse effects compared with ACEI alone.
Hermida RC, Ayala DE, Mojón A, Fernández JR. **Bedtime Dosing of Antihypertensive Medications** Reduces Cardiovascular Risk in CKD. J Am Soc Nephrol. 2011 Oct 24.
Hermida RC, Ayala DE, Mojón A, et al. **Bedtime ingestion of hypertension medications** reduces the risk of new-onset type 2 diabetes: a randomized controlled trial. Diabetologia. 2015 Sep 23.
Hermida RC, Ayala DE, Mojón A, et al. **Sleep-time BP**: prognostic marker of type 2 diabetes and therapeutic target for prevention. Diabetologia. 2015 Sep 23.
Hernandez AV, Emonds EE, Chen BA, et al. **Effect of low-sodium salt substitutes** on blood pressure, detected hypertension, stroke and mortality. Heart. 2019 Jan 19.

Hernández-Aceituno A, Guallar-Castillón P, García-Esquinas E, et al. Association between **sleep characteristics and cummingantihypertensive treatment** in older adults. Geriatr Gerontol Int. 2019 Mar 25.
Herrett E, Gadd S, Jackson R, et al. Eligibility and subsequent burden of cardiovascular disease of **four strategies for blood pressure-lowering treatment**: a retrospective cohort study. Lancet. 2019 Aug 24;394(10199):663-671.
Herttua K, Tabák AG, Martikainen P, et al. **Adherence to antihypertensive** therapy prior to the first presentation of stroke in hypertensive adults: population-based study. Eur Heart J. 2013 Jul 16.
Herttua K, Martikainen P, Batty GD, et al. **Poor Adherence to Statin and Antihypertensive** Therapies as Risk Factors for Fatal **Stroke**. J Am Coll Cardiol. 2016 Apr 5;67(13):1507-15.
Heys M, Lin SL, Lam TH, et al. Lifetime Growth and Blood Pressure in Adolescence: Hong Kong's "Children of 1997" Birth Cohort. Pediatrics. 2013 Jan;131(1):e62-72.
Hicks BM, FilionKB, YinH, SakrL, UdellJA, AzoulayL. **Angiotensin converting enzyme inhibitors and risk of lung cancer**: population based cohort study. BMJ 2018;636:k4209.
Hilkens NA, Greving JP, Algra A, et al. **Blood pressure levels and the risk of intracerebral hemorrhage** after ischemic stroke. Neurology. 2017 Jan 10;88(2):177-181
Hill MD, Muir KW. **INTERACT-2**: Should Blood Pressure Be Aggressively **Lowered Acutely After Intracerebral Hemorrhage**? Stroke. 2013 Aug 29.
Hippisley-Cox J., Coupland C. Effect of combinations of drugs on all cause mortality in patients with ischaemic heart disease: nested case-control analysis. BMJ 2005;330:1059-1063 (7 May), doi:10.1136/bmj.330.7499.1059.
Conclusions: Combo of statins, aspirins, & beta-blockers improve survival in high risk pts with cardiovascular dx, although the addition of an angiotensin converting enzyme inhibitor conferred no additional benefit despite the analysis being adjusted for congestive cardiac failure.
Hippisley-Cox J, Coupland C, Vinogradova Y, Robson J, May M, Brindle P. Derivation and validation of **QRISK**, a new cardiovascular disease risk score for the United Kingdom: prospective open cohort study. BMJ. 2007 Jul 5; [Epub ahead of print] Using QRISK 8.5% of patients aged 35-74 are at high risk (20% risk or higher over 10 years) compared with 13% when using the Framingham algorithm and 14% when using ASSIGN. Using QRISK 34% of women and 73% of men aged 64-75 would be at high risk compared with 24% and 86% according to the Framingham algorithm. UK estimates for 2005 based on QRISK give 3.2 million patients aged 35-74 at high risk, with the Framingham algorithm predicting 4.7 million and ASSIGN 5.1 million.
Hirakawa Y, Arima H, Webster R, et al. Risks associated with **permanent discontinuation of blood pressure-lowering medications** in patients with type 2 **diabetes**. J Hypertens. 2016 Apr;34(4):781-7.
Hiremath S, Ruzicka M, Petrcich W, et al. **Alpha-Blocker Use and the Risk** of Hypotension and Hypotension-Related Clinical Events in Women of Advanced Age. Hypertension. 2019 Sep;74(3):645-651.
Hirsch S, Hirsch J, Bhatt U, et al. **Tolerating increases in the serum creatinine** following aggressive treatment of chronic kidney disease, hypertension and proteinuria: Pre-renal success. Am J Nephrol 2012; 36:430-437.
Hirsch JD, Steers N, Adler DS, et al. Primary Care-Based, **Pharmacist-Physician Collaborative** Medication-Therapy Management of Hypertension: A Randomized, Pragmatic Trial. Clin Ther. 2014 Jul 29.
Ho CLB, Breslin M, Doust J, et al. Effectiveness of **blood pressure-lowering drug treatment by levels of absolute risk**: post hoc analysis of the Australian National Blood Pressure Study. BMJ Open. 2018 Mar 19;8(3):e017723.
Hodgkinson J, Mant J, Martin U, et al. Relative effectiveness of **clinic and home blood pressure monitoring compared with ambulatory** blood pressure monitoring in diagnosis of hypertension: systematic review. BMJ 2011;342:doi:10.1136/bmj.d3621 (Published 24 June 2011).
Hodgkinson JA, Tucker KL, Crawford C, et al. Is **self monitoring of blood pressure in pregnancy** safe and effective? BMJ. 2014 Nov 18;349:g6616.
Hodgson JM, Puddey IB, Woodman RJ, et al. Effects of **black tea** on blood pressure: A randomized controlled trial. Arch Intern Med2012; 172:186-188.
Hofmann Bowman MA, Eagle KA, Milewicz DM. Update on **Clinical Trials of Losartan** With and Without β-Blockers to Block Aneurysm Growth in **Patients With Marfan Syndrome**: A Review. JAMA Cardiol. 2019 May 8
Hofmeyr GJ, Lawrie TA, Atallah AN, et al. **Calcium supplementation during pregnancy** for preventing hypertensive disorders and related problems. Cochrane Database Syst Rev. 2010 Aug 4;8:CD001059.
Hofmeyr GJ, Lawrie TA, Atallah ÁN, Duley L, Torloni MR. **Calcium supplementation during pregnancy for preventing hypertensive disorders and related problems**. Cochrane Database of Systematic Reviews 2014, Issue 6. Art. No.: CD001059. DOI: 10.1002/14651858.CD001059.pub4. Calcium supplementation (_ 1 g/day) is associated with a significant reduction in the risk of pre-eclampsia, particularly for women with low calcium diets. The treatment effectmay be overestimated due to small-study effects or publication bias. It also reduces preterm birth and the occurrence of the composite outcome 'maternal death or serious morbidity'. We considered these benefits to outweigh the increased risk of HELLP syndrome, which was small in absolute numbers. The World Health Organization recommends calcium 1.5 g to 2 g daily for pregnant women with low dietary calcium intake. The limited evidence on low-dose calcium supplementation suggests a reduction in pre-eclampsia, but needs to be confirmed by larger, high-quality trials. Pending such results, in settings of low dietary calcium where high-dose supplementation is not feasible, the option of lower-dose supplements (500 to 600 mg/day) might be considered in preference to no supplementation.
Hollingsworth JM, et al. Medical therapy to **facilitate urinary stone passage**: a meta-analysis. Lancet. 2006 Sep 30;368(9542):1171-9. Patients given calcium-channel blockers or alpha blockers had a 65% (absolute risk reduction=0.31 95% CI 0.25-0.38) greater likelihood of stone passage than those not given such treatment (pooled risk ratio 1.65; 95% CI 1.45-1.88). The pooled risk ratio for alpha blockers was 1.54 (1.29-1.85) and for calcium-channel blockers with steroids was 1.90 (1.51-2.40). (InfoPOEMs: The limited amount of available data suggest that alpha blockers and calcium channel blockers appear to speed the passage of kidney stones. Furthermore, it appears that combining these medications with steroids provides additional benefit. (LOE = 1a-))
Holman RR, Paul SK, Bethel MA, Neil HA, Matthews DR. Long-Term Follow-up after Tight Control of Blood Pressure in Type 2 Diabetes. N Engl J Med. 2008 Sep 10. [Epub ahead of print] (**UKPDS 81**) The benefits of previously improved blood-pressure control were not sustained when between-group differences in blood pressure were lost. Early improvement in blood-pressure control in patients with both type 2 diabetes and hypertension was associated with a reduced risk of complications, but it appears that good blood-pressure control must be continued if the benefits are to be maintained.
Hong KN, Fuster V, Rosenson RS, et al. **How Low to Go With Glucose, Cholesterol, and Blood Pressure in Primary Prevention of CVD**. J Am Coll Cardiol. 2017 Oct 24;70(17):2171-2185.
Hong L, Cheng X, Lin L, et al; INSPIRE Study Group. The Blood Pressure **Paradox in Acute Ischemic Stroke**. Ann Neurol. 2019 Feb 5
Hong SJ, Jeong HS, Han SH, et al. Comparison of Fixed-Dose Combinations of **Amlodipine/Losartan Potassium/Chlorthalidone and Amlodipine/Losartan Potassium** in Patients With Stage 2 Hypertension Inadequately Controlled With Amlodipine/Losartan Potassium: A Randomized, Double-blind, Multicenter, Phase III Study. Clin Ther. 2017 Sep 19.
Hooper L, et al. Risks and benefits of **omega 3 fats** for mortality, cardiovascular disease, and cancer: systematic review. BMJ. 2006 Mar 24; [Epub ahead of print] (Wang C, et al. n-3 Fatty acids from fish or fish-oil supplements, but not alpha-linolenic acid, benefit cardiovascular disease outcomes in primary- and secondary-prevention studies: a systematic review. Am J Clin Nutr. 2006 Jul;84(1):5-17.)
Hooper L, Summerbell CD, Thompson R, et al. **Reduced or modified dietary fat** for preventing cardiovascular disease. Cochrane Database of Systematic Reviews 2011, Issue 7. Art. No.: CD002137. DOI: 10.1002/14651858.CD002137.pub2. The findings are suggestive of a small but potentially important reduction in cardiovascular risk on modification of dietary fat, but not reduction of total fat, in longer trials. Lifestyle advice to all those at risk of cardiovascular disease and to lower risk population groups, should continue to include permanent reduction of dietary saturated fat and partial replacement by unsaturates. The ideal type of unsaturated fat is unclear.
Hoorn EJ, Ellison DH. **Diuretic Resistance**. Am J Kidney Dis. 2016 Nov 1. pii: S0272-6386(16)30511-X.
Horne Rosemary S. C., Yang Joel S. C., Walter Lisa M., et al. **Elevated Blood Pressure During Sleep** and Wake in Children With Sleep-Disordered Breathing. Pediatrics 2011; 128:1 e85-e92; doi:10.1542/peds.2010-3431
Horwitz A, Klemp M, Jeppesen J, et al. **Antihypertensive Medication Postpones the Onset of Glaucoma**: Evidence From a Nationwide Study. Hypertension. 2017 Feb;69(2):202-210.
Howard BV, et al. **Low-fat dietary pattern** and risk of cardiovascular disease: the Women's Health Initiative Randomized Controlled Dietary Modification Trial. JAMA. 2006 Feb 8;295(6):655-66.
Howard G, Cushman M, Moy CS, et al. Association of **Clinical and Social Factors With Excess Hypertension Risk in Black Compared With White** US Adults. JAMA. 2018 Oct 2;320(13):1338-1348.
Howard JP, Nowbar AN, Francis DP. Size of blood pressure reduction from **renal denervation**: Insights from meta-analysis of antihypertensive drug trials of 4121 patients with focus on trial design: The CONVERGE report. Heart 2013.
Hou FF, Zhang X, Zhang GH, et al. Efficacy & safety of **benazepril** for advanced chronic renal (CKD pts) insufficiency. N Engl J Med. 2006 Jan 12;354(2):131-40. (InfoPOEMs: In a group of nondiabetic patients with serum creatinine levels between 3.0 & 5.0 mg/dL, benazepril slows the progression of renal disease. These pts were carefully monitored for any changes in renal function during the first 8 weeks, and were carefully screened & monitored to detect any early adverse effects on renal function. (LOE = 1b))
Houle SK, Padwal R, Poirier L, Tsuyuki RT. The **2015 Canadian Hypertension Education Program** (**CHEP**) guidelines for pharmacists: An update. Can Pharm J (Ott). 2015 Jul;148(4):180-6.
Houle SK, Charrois TL, McAlister FA, et al. **Pay-for-performance remuneration for pharmacist prescribers'** management of hypertension: A substudy of the RxACTION trial. Can Pharm J (Ott). 2016 Nov;149(6):345-351.
Houston TK, Allison JJ, Sussman M, et al. Culturally appropriate **storytelling** to improve blood pressure. A randomized trial. *Ann Intern Med* 2011; 154:77-84.
Howard JT, Sosnov JA, Janak JC, et al. Associations of **Initial Injury Severity and Posttraumatic Stress Disorder Diagnoses With Long-Term Hypertension Risk** After Combat Injury. Hypertension. 2018 May;71(5):824-832.
Huai P, Xun H, Reilly KH, et al. **Physical Activity** and Risk of Hypertension: A Meta-Analysis of Prospective Cohort Studies. Hypertension. 2013 Sep 30.
Huang C, Dhruva SS, Coppi AC, et al. Systolic Blood Pressure Response in **SPRINT** (Systolic Blood Pressure Intervention Trial) and **ACCORD** (Action to Control Cardiovascular Risk in Diabetes): A Possible Explanation for **Discordant Trial Results**. J Am Heart Assoc. 2017 Nov 13;6(11).
Huang Y, Su L, Cai X, Mai W, et al. Association of all-cause and cardiovascular **mortality with prehypertension**: A meta-analysis. Am Heart J. 2014 Feb;167(2):160-168.e1.
Huang Y, Cai X, Li Y, et al. **Prehypertension and the risk of stroke**: A meta-analysis. Neurology. 2014 Apr 1;82(13):1153-61.
Hueb Whady, Lopes Neuza, Gersh Bernard J., et al. Ten-Year Follow-Up Survival of the Medicine, Angioplasty, or Surgery Study (**MASS II**): A Randomized Controlled Clinical Trial of 3 Therapeutic Strategies for Multivessel Coronary Artery Disease. Circulation 122: 949-957.
Huesch MD. Association of Baseline **Statin Use Among Older Adults Without Clinical Cardiovascular Disease in the SPRINT** Trial. JAMA Intern Med. 2018 Jan 22.
Huffman MD, de Cates AN, Ebrahim S. Fixed-dose combination therapy (**polypill**) for the prevention of cardiovascular disease. JAMA. 2014 Nov 19;312(19):2030-1.
Hung RK, et al. Effect of **Beta-Blocker Therapy**, Maximal Heart Rate, and **Exercise Capacity During Stress Testing** on Long-Term Survival (from The Henry Ford Exercise Testing Project). Am J Cardiol. 2016 Aug 31.
Husted SE, Ohman EM. Pharmacological and emerging therapies in the **treatment of chronic angina**. Lancet. 2015 Aug 15;386(9994):691-701.

Hutchinson PJ, Kolias AG, Timofeev IS, et al. Trial of **decompressive craniectomy** for **traumatic intracranial hypertension**. N Engl J Med. DOI: 10.1056/NEJMoa1605215.
Iadecola C, Yaffe K, Biller J, et al. Impact of **Hypertension on Cognitive Function** : A Scientific Statement From the American Heart Association. (**AHA**) Hypertension. 2016 ;68 :000-000.
Ibrahim MM, Damasceno A. Hypertension in **developing countries**. Lancet. 2012 Aug 11;380(9841):611-9.
ICSI Health Care Guideline: Hypertension Diagnosis and Treatment. Nov 2010.
In the Clinic: Stable Ischemic Heart Disease. ITC1-2 Annals of Internal Medicine 7 January 2014
Ingelfinger JR. Clinical practice. The **child or adolescent with elevated blood pressure**. N Engl J Med. 2014 Jun 12;370(24):2316-25.
Inzucchi SE. Clinical practice. **Diagnosis** of diabetes. N Engl J Med. 2012 Aug 9;367(6):542-50.
Ismail-Beigi F, Craven TE, O`Connor PJ, et al. Combined intensive **blood pressure and glycemic** control does not produce an additive benefit on microvascular outcomes in type 2 diabetic patients. (**ACCORD**) Kidney Int. 2012 Mar;81(6):586-94.
Izcovich A, González Malla C, Manzotti M, et al. **Midodrine** for orthostatic hypotension and recurrent reflex syncope: A systematic review. Neurology. 2014 Aug 22.
Jackson SL, et al. Association Between **Urinary Sodium & Potassium Excretion** & Blood Pressure Among Adults in the United States: National Health and Nutrition Examination Survey, 2014. Circulation. 2018 Jan 16;137(3):237-246.
Jackson R, Broad J, Connor J, Wells S. **Alcohol** and ischaemic heart disease: probably no free lunch. Lancet. 2005 Dec 3;366(9501):1911-2.
Jacob V, Chattopadhyay SK, et al; Community Preventive Services Task Force. Economics of **Self-Measured Blood Pressure Monitoring**: A Community Guide Systematic Review. Am J Prev Med. 2017 Sep;53(3):e105-e113.
Jae SY, Babu AS, Yoon ES, et al. Impact of **Cardiorespiratory Fitness** and **Risk** of Systemic Hypertension in **Nonobese** Versus **Obese** Men Who Are Metabolically Healthy or Unhealthy. Am J Cardiol. 2017 Jun 15.
Jae SY, Kurl S, Laukkanen JA, et al. Usefulness of **blood pressure rise prior to exercise stress testing** to predict the risk of future hypertension in normotensive korean men. Am J Cardiol. 2014 Oct 15;114(8):1238-42.
Jaffe MG, Lee GA, Young JD, et al. Improved blood pressure control associated with a large-scale **hypertension program**. JAMA2013; 310:699-705.
Jamerson KA. Should Certain **Antihyperglycemic Medications Be Preferred Over Antihypertensive Medications** for Blood Pressure Control in Special Populations With Diabetes Mellitus? Circulation. 2019 Apr 30;139(18):2110-2112.
Janke EA, Richardson C, Schneider KL; Society of **Behavioral Medicine**. Beyond Pharmacotherapy: Lifestyle Counseling Guidance Needed for Hypertension. Ann Intern Med. 2019 Jan 8.
Jansen L, Below J, Chang-Claude J, et al. **Beta blocker use and colorectal cancer risk**: Population-based case-control study. Cancer. 2012 May 14.
Jaspers NEM, Blaha MJ, Matsushita K, et al. Prediction of individualized lifetime benefit from **cholesterol lowering, blood pressure lowering, antithrombotic therapy, and smoking cessation** in apparently healthy people. Eur Heart J. 2019 May 18.
Jayalath VH, de Souza RJ, Ha V, Mirrahimi A, et al. **Sugar-sweetened beverage consumption** and incident hypertension: a systematic review and meta-analysis of prospective cohorts. Am J Clin Nutr. 2015 Aug 12.
JBS3 Board. **Joint British Societies' consensus recommendations** for the prevention of cardiovascular disease (JBS3). Heart 2014.
Janke AT, McNaughton CD, Brody AM, et al. Trends in the Incidence of **Hypertensive Emergencies in US Emergency Departments** From 2006 to 2013. J Am Heart Assoc. 2016 Dec 5;5(12).
Jegatheswaran J, Ruzicka M, Hiremath S, Edwards C. Are **Automated Blood Pressure Monitors Comparable to Ambulatory Blood Pressure Monitors**? Systematic Review and Meta-analysis. Can J Cardiol. 2017 May;33(5):644-652.
Jerschow E, Lin RY, Scaperotti MM, et al. **Fatal anaphylaxis** in the United States, 1999-2010: Temporal patterns and demographic associations. J Allergy Clin Immunol. 2014 Sep 26.
Jin J. **Checking Blood Pressure at Home**. JAMA. 2017 Jul 18;318(3):310.
Joaquín Durán-Cantolla, Felipe Aizpuru, Jose María Montserrat, et al. , Spanish Sleep and Breathing Group. **Continuous positive airway pressure (CPAP) as** treatment for systemic hypertension in people with obstructive **sleep apnoea**: randomised controlled trial. BMJ 341:doi:10.1136/bmj.c5991 (Published 24 Nov 2010).
Jochemsen HM, Muller M, Visseren FL, et al; for the SMART Study Group. Blood Pressure and **Progression of Brain Atrophy**: The SMART-MR Study. JAMA Neurol. 2013 Jun 10:1-7.
Joffres M, Falaschetti E, Gillespie C, et al. **Hypertension prevalence, awareness, treatment** and control in national surveys from England, the USA and Canada, and correlation with stroke and ischaemic heart disease mortality: a cross-sectional study. BMJ Open. 2013 Aug 30;3(8):e003423.
Johnson DA, Thomas SJ, Abdalla M, et al. Association Between **Sleep Apnea and Blood Pressure Control** Among Blacks: Jackson Heart Sleep Study. Circulation. 2018 Dec 10.
Johnson HM, Thorpe CT, Bartels CM, et al. Antihypertensive **medication initiation** among young adults with regular primary care use. J Gen Intern Med. 2014 May;29(5):723-31.
Jones AG, Evans PH, Vaidya B. **Phaeochromocytoma**. BMJ. 2012 Feb 20;344:e1042.
Jørgensen ME, Hlatky MA, Køber L, et al, Andersson C. **β-Blocker-Associated Risks** in Patients With Uncomplicated Hypertension Undergoing **Noncardiac Surgery**. JAMA Intern Med. 2015 Oct 5:1-9.
Joseph P, Lonn E, Bosch J, et al; **HOPE-3** Investigators. **Long-term Effects of Statins, Blood Pressure-Lowering, and Both on Erectile Function** in Persons at Intermediate Risk for Cardiovascular Disease: A Substudy of the Heart Outcomes Prevention Evaluation-3 (HOPE-3) Randomized Controlled Trial. Can J Cardiol. 2018 Jan;34(1):38-44.
Joung KI, Cho SI. Association of **low blood pressure with suicidal ideation**: a cross-sectional study of 10,708 adults with normal or low blood pressure in Korea. BMC Public Health. 2018 Mar 1;18(1):200.
Judy AE, McCain CL, Lawton ES, et al. Systolic **Hypertension, Preeclampsia-Related Mortality, and Stroke** in California. Obstet Gynecol. 2019 Jun;133(6):1151-1159.
Juhola J, Oikonen M, Magnussen CG, et al. **Childhood physical, environmental, and genetic** predictors of adult hypertension: the cardiovascular risk in young Finns study. Circulation. 2012 Jul 24;126(4):402-9.
Juhola J, Magnussen CG, et al. Combined effects of **child and adult elevated blood pressure on subclinical atherosclerosis**: the International Childhood Cardiovascular Cohort Consortium (**iC3**). Circulation. 2013;128:217–224.
Jung HH. Association of Optimal Blood Pressure With **Critical Cardiorenal Events** and Mortality in High-Risk and Low-Risk Patients Treated With Antihypertension Medications. JAMA Netw Open. 2019 Aug 2;2(8):e199307.
Jung S-Y, Choi N-K, Kim J-Y, et al. **Short-acting nifedipine and risk of stroke** in elderly hypertensive patients. Neurology 2011;77:1229 –1234.
Juraschek SP, Guallar E, Appel LJ, Miller ER 3rd. Effects of **vitamin C supplementation** on blood pressure: a meta-analysis of randomized controlled trials. Am J Clin Nutr. 2012 May;95(5):1079-88.
Juraschek SP, Gelber AC, Choi HK, et al. Effects of the Dietary Approaches To Stop Hypertension (**DASH**) **Diet** and Sodium Intake on Serum Uric Acid. Arthritis Rheumatol. 2016 Aug 14.
Juraschek SP, Daya N, et al. Association of History of **Dizziness** and Long-term Adverse Outcomes With **Early vs Later Orthostatic Hypotension** Assessment Times in Middle-aged Adults. JAMA Intern Med. 2017 Jul 24.
Juraschek SP, Miller ER 3rd, Weaver CM, et al. Effects of **Sodium Reduction and the DASH Diet** in Relation to Baseline Blood Pressure. J Am Coll Cardiol. 2017 Dec 12;70(23):2841-2848.
Kaboli PJ, Howren MB, Ishani A, et al. Efficacy of patient activation interventions with or without financial incentives to **promote prescribing of thiazides and hypertension control**: a randomized clinical trial. JAMA Netw Open. 2018;1(8):e185017. doi:10.1001/jamanetworkopen.2018.5017
Kaddumukasa MN, Katabira E, Sajatovic M, et al. Influence of **sodium consumption** and associated knowledge on poststroke hypertension in Uganda. Neurology 2016;87:1198–1205.
Kaczorowski J, Myers MG, Gelfer M, et al. How do **family physicians measure blood pressure in routine clinical practice**? National survey of Canadian family physicians. Can Fam Physician. 2017 Mar;63(3):e193-e199
Kaelber DC, et al; Comparative Effectiveness Research Through Collaborative Electronic Reporting. **Diagnosis and medication treatment of pediatric hypertension**: a retrospective cohort study. Pediatrics. 2016;138(6):e20162195
Kaess BM, Rong J, Larson MG, et al. **Aortic stiffness**, blood pressure progression, and incident hypertension. JAMA 2012; 308: 875-881.
Kaikkonen KS, et al. **Family history** and the risk of sudden cardiac death as a manifestation of an acute coronary event. Circulation. 2006 Oct 3;114(14):1462-7. Epub 2006 Sep 25.
Kalkman DN, Brouer TF, Vehmeijer JT, et al. **J curve in patients randomly assigned to different systolic blood pressure targets**: an experimental approach to an observational paradigm. Circulation. 2017;136:2220–2229.
Kandzari DE, Böhm M, Mahfoud F, et al. Effect of **renal denervation on blood pressure** in the presence of antihypertensive drugs: 6-month efficacy and safety results from the **SPYRAL HTN-ON MED** proof-of-concept randomised trial. Lancet 2018; online May 23.
Kang J, Ko Y, Park JH, et al. Effect of blood pressure (**variability & not average**) on 3-month functional outcome in the **subacute stage of ischemic stroke**. Neurology. 2012 Nov 13;79(20):2018-2024.
Kario K, Saito I, Kushiro T, et al. LB01.02: **Monitoring Home Blood Pressure** is a strong predictor of coronary artery disease events as well as stroke events In hypertensive patients on antihypertensive treatment. The Honest Study. J Hypertens. 2015 Jun.
Karmali KN, Ning H, Goff DC, et al. Identifying Individuals at **Risk for Cardiovascular Events Across the Spectrum of Blood Pressure Levels**. J Am Heart Assoc. 2015 Sep 21;4(9).
Karmali KN, Lloyd-Jones DM. **Global Risk Assessment to Guide Blood Pressure Management** in Cardiovascular Disease Prevention. Hypertension. 2017 Mar;69(3):e2-e9.
Karmali KN, Lloyd-Jones DM, et al. **Blood pressure-lowering treatment strategies based on cardiovascular risk versus blood pressure**: A meta-analysis of individual participant data. PLoS Med. 2018 Mar 20;15(3):e1002538.

Katritsis DG, Ioannidis JP. Percutaneous coronary intervention versus conservative therapy in nonacute coronary artery disease: a meta-analysis. Circulation. 2005 Jun 7;111(22):2906-12. Epub 2005 May 31. (InfoPOEMs: There is no evidence from randomized trials that percutaneous coronary intervention (PCI) improves important clinical outcomes better than careful medical management for patients with chronic stable coronary artery disease (CAD). Although this is the largest study to date, it's still limited by a relatively small number of outcomes of interest. (LOE = 1a))

Kaul S. How Strong Is the **Evidence to Support Blood Pressure Treatment Goal of 130/80 mm Hg**? Circulation. 2018 Dec 4;138(23):2594-2596.

Käyser SC, Deinum J, de Grauw WJ, et al. **Prevalence of primary aldosteronism** in primary care: a cross-sectional study. Br J Gen Pract. 2018 Feb;68(667):e114-e122.

KDIGO clinical practice guideline for the management of **blood pressure in chronic kidney disease**. Kidney Int Suppl. 2012 Dec;2(5):337-414.

Kerr E, Lucatorto MA, Holleman R, et al. **Monitoring performance for blood pressure** management among patients with **diabetes** mellitus. Arch Intern Med 2012.

Kerry SM, Markus HS, Khong TK, et al. **Home blood pressure monitoring with nurse-led telephone support** among patients with hypertension and a history of stroke: a community-based randomized controlled trial. CMAJ. 2013 Jan 8;185(1):23-31.

Kelly RK, Thomson R, Smith KJ, et al. Factors Affecting Tracking of **Blood Pressure from Childhood to Adulthood**: The Childhood Determinants of Adult Health Study. J Pediatr. 2015 Sep 2.

Kennard L, O'Shaughnessy KM. **Treating hypertension in patients with medical** comorbidities. BMJ. 2016 Feb 16;352:i101.

Kessler CS, Joudeh Y. Evaluation and treatment of **severe asymptomatic hypertension**. Am Fam Physician. 2010 Feb 15;81(4):470-6.

Khachaturian et al. Antihypertensive Medication Use and Incident **Alzheimer** Disease: The Cache County Study. Arch Neurol. 2006 Mar 13; [Epub ahead of print]

Khalesi S, Sun J, Buys N, Jayasinghe R. Effect of **Probiotics on Blood Pressure** : A Systematic Review and Meta-Analysis of Randomized, Controlled Trials. Hypertension. 2014 Jul 21.

Khan NA, et al. Canadian Hypertension Education Program. The **2006 Canadian Hypertension Education Program** recommendations for the management of hypertension: Part II - Therapy. Can J Cardiol. 2006 May 15;22(7):583-93.

Khan NA, Herman RJ, Quinn RR, et al. **Canadian** Hypertension Education Program. **Renal Denervation** Therapy for the Treatment of Resistant Hypertension: A Position Statement by the Canadian Hypertension Education Program. Can J Cardiol. 2013 Oct 23. doi:pii: S0828-282X(13)00450-9.

Khan N, Bacon SL, Khan S, et al; Hypertension Canada Priority Setting Partnership Group. **Hypertension management research priorities from patients, caregivers, and healthcare providers**: A report from the **Hypertension Canada** Priority Setting Partnership Group. J Clin Hypertens (Greenwich). 2017 Sep 25.

Khan NA, Rabkin SW, et al. Effect of Lowering Diastolic Pressure in Patients With and Without Cardiovascular Disease: Analysis of the **SPRINT** (Systolic Blood Pressure Intervention Trial). Hypertension. 2018 May;71(5):840-847.

Khanna RR, Victor R, Bibbins-Domingo K, et al. Research Letter: **Missed opportunities for treatment of uncontrolled hypertension** at physician office visits in the United States, 2005 to 2009. Arch Intern Med 2012; 172:1344-1345.

Kharbanda EO, Asche SE, Sinaiko AR, et al. **Clinical decision support** for recognition and management of **hypertension**: a randomized trial. **Pediatrics**. 2018;141(2):e20172954

Khashan AS, Evans M, Kublickas M, et al. **Preeclampsia and risk of end stage kidney disease**: A Swedish nationwide cohort study. PLoS Med. 2019 Jul 30;16(7):e1002875.

Khatib R, et al; **PURE** study. **Availability and affordability of cardiovascular disease medicines** and their effect on use in high-income, middle-income, and low-**income** countries: analysis of the PURE study data. Lancet. 2015 Oct 20.

Khera R, Lu Y, Lu J, et al. Impact of **2017 ACC/AHA guidelines on prevalence of hypertension** and eligibility for antihypertensive treatment in United States and China: nationally representative cross sectional study. BMJ. 2018 Jul 11;362:k2357.

Khouri C, Jouve T, Blaise S, et al. **Peripheral vasoconstriction induced by beta-blockers**: a systematic review and a network meta-analysis. Br J Clin Pharmacol. 2016 Apr 16.

Khoury M, Khoury PR, Dolan LM, et al Clinical Implications of the **Revised AAP Pediatric Hypertension Guidelines**. Pediatrics. 2018 Jul 5.

Kibria GMA, Swasey K, KC A, et al. Estimated **change in prevalence of hypertension in Nepal** following application of the **2017 ACC/AHA guideline**. JAMA Netw Open. 2018;1(3):e180606.

Kim JW, et al. How well do clinic-based **blood pressure measurements** agree with the mercury standard? J Gen Intern Med. 2005 Jul;20(7):647-9. (InfoPOEMs: In this study, usual blood pressure readings in an office were frequently higher a standardized measurement, leading to incorrect labeling of blood pressure control in 1 of 5 patients. Several conclusions can be drawn from this study, which replicates the findings in other studies: First, retrain yourself to take an accurate blood pressure reading (see: http://www.theberries.ns.ca/SPRING2005a/taking_BP_technique.html). Second, train your office nurses how to do it correctly. Third, retrain them often, since other research has shown high recidivism. Fourth, check any patients with high blood pressure readings yourself, using good technique. (LOE = 1b))

Kim J, Song TJ, Song D, et al. **Interarm blood pressure difference** and mortality in patients with acute ischemic stroke. Neurology. 2013 Apr 16;80(16):1457-64.

Kirwa K, Eliot MN, et al. **Residential Proximity to Major Roadways** and Prevalent Hypertension Among Postmenopausal Women: Results From the Women's Health Initiative San Diego Cohort. J Am Heart Assoc. 2014 Oct 1;3(5).

Kit BK, Kuklina E, Carroll MD, et al. Prevalence of and Trends in **Dyslipidemia and Blood Pressure** Among **US Children and Adolescents**, 1999-2012. JAMA Pediatr. 2015 Jan 19.

Kitagawa K, Yamamoto Y, Arima H: (RESPECT) Study Group. Effect of **Standard vs Intensive Blood Pressure Control** on the Risk of Recurrent Stroke: A Randomized Clinical Trial and Meta-analysis. JAMA Neurol. 2019 Jul 29.

Kivimäki M, Batty D, Hamer M, et al. Influence of **retirement on nonadherence** to medication for hypertension and diabetes. CMAJ. 2013 Sep 30.

Klein R, Myers CE, Klein BE. Vasodilators, Blood Pressure-Lowering Medications, and **Age-related Macular Degeneration**: The Beaver Dam Eye Study. Ophthalmology. 2014 Apr 11.

Kline GA, Prebtani APH, Leung AA, et al. **Primary aldosteronism**: a common cause of resistant hypertension. CMAJ. 2017 Jun 5;189(22):E773-E778

Klinger JR, Elliott CG, Levine DJ, et al. **Therapy for Pulmonary Arterial Hypertension** in Adults: Update of the CHEST Guideline and Expert Panel Report. Chest. 2019 Mar;155(3):565-586.

Knoll GA, Fergusson D, Chassé M, et al. **Ramipril** versus placebo in **kidney transplant patients with proteinuria**: a multicentre, double-blind, randomised controlled trial. Lancet Diabetes Endocrinol. 2015 Oct 21.

Ko MJ et al. Level of blood pressure control and cardiovascular events: **SPRINT** criteria **versus the 2014 hypertension recommendations**. J Am Coll Cardiol 2016 Jun 21; 67:2821.

Koebnick C, Mohan Y, Li X, et al. **Failure to confirm high blood pressures in pediatric** care-quantifying the risks of misclassification. J Clin Hypertens (Greenwich). 2018 Jan;20(1):174-182.

Kokkinos P, Myers J, Kokkinos JP, et al. **Exercise Capacity and Mortality** in Black and White Men. Circulation. 2008 Jan 22; [Epub ahead of print] Exercise capacity is a strong predictor of all-cause mortality in blacks and whites. The relationship was inverse and graded, with a similar impact on mortality outcomes for both blacks and whites.

Kolber MR, Garrison S, Turgeon RD. **Electrolyte disturbance** with **diuretics** and **ACEIs**. Can Fam Physician. 2016 Jul;62(7):569. PubMed PMID: 27412211.

Korniyenko A, Alviar CL, Cordova JP, Messerli FH. **Visceral angioedema** due to angiotensin-converting enzyme inhibitor therapy. Cleve Clin J Med. 2011 May;78(5):297-304.

Kostis WJ, Cabrera J, Messerli FH, et al. Competing **Cardiovascular and Noncardiovascular Risks and Longevity** in the Systolic Hypertension in the Elderly Program (SHEP). Am J Cardiol. 2013 Nov 23

Kotchen TA, Cowley AW Jr, Liang M. Ushering Hypertension Into a New Era of **Precision Medicine**. JAMA. 2016 Jan 14:1-2.

Kovesdy CP, Bleyer AJ, Molnar MZ, Ma JZ, Sim JJ, Cushman WC, et al. **Blood pressure and mortality in U.S. veterans with chronic kidney disease**. A cohort study. Ann Intern Med. 2013;159:233-42.

Kovesdy CP, Lu JL, Molnar MZ, et al. Observational Modeling of **Strict vs Conventional Blood Pressure Control** in Patients With **Chronic Kidney Disease**. JAMA Intern Med. 2014 Aug 4.

Krause T, Lovibond K, Caulfield M, McCormack T, Williams B; on behalf of the Guideline Development Group. **Management of hypertension**: summary of **NICE** guidance. BMJ. 2011 Aug 25;343:d4891.

Krieger EM et al. **Spironolactone versus clonidine** as a fourth-drug therapy for **resistant hypertension**: The **ReHOT** randomized study (Resistant Hypertension Optimal Treatment). Hypertension 2018 Apr; 71:681.

Krishnaswami A, Kim DH, McCulloch CE, et al. Individual and **Joint Effects of Pulse Pressure and Blood Pressure Treatment Intensity on Serious Adverse Events in the SPRINT Trial**. Am J Med. 2018 Jun 27.

Krogager ML, Torp-Pedersen C, Mortensen RN, et al. **Short-term mortality risk of serum potassium levels** in hypertension: a retrospective analysis of nationwide registry data. Eur Heart J. 2017 Jan 7;38(2):104-112.

Kronish IM, Woodward M, Sergie Z, et al. Meta-analysis: impact of drug class on **adherence to antihypertensives**. Circulation. 2011 Apr 19;123(15):1611-21.

Kronish IM, et al. Electronic **Adherence** Measurement Intervention to Reduce Clinical Inertia in the Treatment of Uncontrolled Hypertension: **MATCH** Cluster Randomized Clinical Trial. J Gen Intern Med. 2016 Nov;31(11):1294-1300.

Krum H, Schlaich MP, Böhm M, et al. **Percutaneous renal denervation** in patients with treatment-resistant hypertension: final 3-year report of the **Symplicity HTN-1** study. Lancet 2013; online Nov 7.

Krumholz HM, Normand SL, Wang Y. **Trends in hospitalizations** and outcomes for **acute cardiovascular disease and stroke,** 1999-2011. Circulation. 2014 Sep 16;130(12):966-75.

Ku E, Lee BJ, Wei J, Weir MR. Hypertension in CKD: Core Curriculum 2019. Am J Kidney Dis. 2019 Mar 19.

Ku E, McCulloch CE, Vittinghoff E, Lin F, Johansen KL. Use of **Antihypertensive Agents** and Association With Risk of Adverse Outcomes **in Chronic Kidney Disease**: Focus on Angiotensin-Converting Enzyme Inhibitors and Angiotensin Receptor Blockers. J Am Heart Assoc. 2018 Oct 2;7(19):e009992.

Ku E, Park J, Vidhun J, Campese V. The **hazards of dual renin-angiotensin blockade** in chronic kidney disease. Arch Intern Med. 2009 Jun 8;169(11):1015-8.

Ku E, Glidden DV, Johansen KL, et al. Association between strict blood pressure control during **chronic kidney disease** and lower mortality after onset of end-stage renal disease. Kidney Int. 2014 Dec 10.

Kumar B, Swee M. **Aldosterone-renin ratio** in the assessment of primary aldosteronism. JAMA. 2014 Jul;312(2):184-5.

Kumar N, Khunger M, Gupta A, Garg. A content analysis of **smartphone-based applications** for hypertension management. J Am Soc Hypertens 2014

Kurnik D, Vesterman-Landes J, Bialik M, et al. **Hyperkalemia and renal function during monotherapy and dual Renin-Angiotensin blockade** in the community setting. Clin Ther. 2011 Apr;33(4):456-64.
Kuyper LM, Khan NA. **Atenolol vs Nonatenolol** β-Blockers for the Treatment of Hypertension: A Meta-analysis. Can J Cardiol. 2014 May;30(5S):S47-S53.
LactMed 2011. http://www.toxnet.nlm.nih.gov/cgi-bin/sis/htmlgen?LACT
Lacourcière Y, Taddei S, Konis G, et al. Clinic and ambulatory blood pressure-lowering effect of aliskiren/amlodipine/hydrochlorothiazide combination in patients with moderate-to-severe hypertension: a randomized active-controlled trial. J Hypertens. 2012 Jul 22.
Lacey B, Lewington S, Clarke R, et al**. Age-specific association between blood pressure and vascular and non-vascular chronic diseases** in 0·5 million adults in China: a prospective cohort study. Lancet Glob Health. 2018 Jun;6(6):e641-e649.
Laffin LJ, Besser SA, Alenghat FJ. A data-zone scoring system to assess the **generalizability of clinical trial results to individual patients**. (**Sprint, Accord-BP**) Eur J Prev Cardiol. 2018 Nov 26:2047487318815967.
Lai CL, Kuo RN, Chen HM, et al. Risk of **hip/femur fractures during the initiation period of alpha-blocker therapy** among elderly males: a self-controlled case series study. Br J Clin Pharmacol. 2015 Apr 28.
Lakoski SG, Greenland P, Wong ND, et al. **Coronary Artery Calcium Scores** and Risk for Cardiovascular Events in Women Classified as "Low Risk" Based on Framingham Risk Score: The Multi-Ethnic Study of Atherosclerosis (MESA).Arch Intern Med. 2007 Dec 10;167(22):2437-42. The presence of CAC in women considered to be at low risk based on FRS was predictive of future CHD and CVD events. Advanced CAC identified a subset of low-risk women at higher risk based on current risk stratification strategies.
Lamas GA, Boineau R, Goertz C, et al. **EDTA chelation** therapy alone and in combination with oral high-dose multivitamins and minerals for coronary disease: The factorial group results of the Trial to Assess Chelation Therapy. Am Heart J. 2014 Jul;168(1):37-44.e5.
Lamas GA, Boineau R, Goertz C, et al. **EDTA chelation** therapy alone and in combination with oral high-dose multivitamins and minerals for coronary disease: The factorial group results of the Trial to Assess Chelation Therapy. Am Heart J. 2014 Jul;168(1):37-44.e5.
Lamb SA, et al. **Hypertension Canada's 2017 guidelines for diagnosis, risk assessment, prevention and treatment of hypertension in adults for pharmacists**: An update. Can Pharm J (Ott). 2017 Nov 29;151(1):33-42.
Lammel-Lindemann JA, Flores-Villalba E, Martagón AJ, et al. **Non-cholestatic acute hepatitis** following **Candesartan** administration. Br J Clin Pharmacol. 2017 Aug 25
Lande MB, Batisky DL, Kupferman JC, et al. **Neurocognitive Function** in Children with Primary Hypertension. J Pediatr. 2016 Sep 27.
Landman GW, Drion I, et al. **Device-Guided Breathing** as Treatment for Hypertension in Type 2 Diabetes Mellitus: A Randomized, Double-blind, Sham-Controlled Trial. JAMA Intern Med. 2013 Jul 22;173(14):1346-50.
Landman GW, van Hateren KJ, van Dijk PR, et al. Efficacy of **Device-Guided Breathing** for Hypertension in Blinded, Randomized, Active-Controlled Trials: A Meta-analysis of Individual Patient Data. JAMA Intern Med. 2014 Sep 15.
Lane CA, Barnes J, Nicholas JM, et al. Associations between blood pressure across adulthood and late-life **brain structure and pathology** in the neuroscience substudy of the 1946 British birth cohort (Insight 46): an epidemiological study. Lancet Neurol. 2019 Aug 20.
Langan R, Jones K. Common Questions About the **Initial Management of Hypertension**. Am Fam Physician. 2015;91(3):172-177.
Lapi F, Azoulay L, Yin H, et al. Concurrent use of diuretics, angiotensin converting enzyme inhibitors, and angiotensin receptor blockers with **non-steroidal anti-inflammatory drugs** (NSAIDs) and risk of acute kidney injury: nested case-control study. BMJ 2013;346:e8525.
Larochelle P, Tobe SW, Lacourcière Y**. β-Blockers in hypertension**: studies and meta-analyses over the years. Can J Cardiol. 2014 May;30(5 Suppl):S16-22.
Laurent S, Schlaich M, Esler M. New **drugs, procedures, and devices** for hypertension. Lancet. 2012 Aug 11;380(9841):591-600.
Laurent S, Boutouyrie P. Visit-to-visit blood pressure variability: added 'VALUE' as a risk marker in low- and high-risk patients. Eur Heart J. 2018 Jun 21;39(24):2252-2254.
Lavie CJ, Milani RV, Ventura HO. **Blood pressure measurements for treating hypertension**: which method counts the most? Heart. 2018 Jul;104(14):1142-1143.
Law M R, Morris J K, Wald N J et al. Use of blood pressure lowering drugs in the prevention of cardiovascular disease: meta-analysis of 147 randomised trials in the context of expectations from prospective epidemiological studies. BMJ 2009;338:b1665, doi: 10.1136/bmj.b1665 (Published 19 May 2009) With the exception of the extra protective effect of β blockers given shortly after a myocardial infarction and the minor additional effect of calcium channel blockers in preventing stroke, all the classes of blood pressure lowering drugs have a similar effect in reducing CHD events and stroke for a given reduction in blood pressure so excluding material pleiotropic effects.
Lawrence Gould A, Unniachan S, Wu D. Indirect treatment comparison between fixed-dose-combinations of **amlodipine/losartan and amlodipine/valsartan** in blood pressure control. Int J Clin Pract. 2014 Feb;68(2):163-72.
Leaf A, et al.; Fatty Acid Antiarrhythmia Trial Investigators. Prevention of fatal arrhythmias in high-risk subjects by **fish oil n-3** fatty acid intake. Circulation. 2005 Nov 1;112(18):2762-8.
Leasure AC, Qureshi AI, Murthy SB, et al. Association of Intensive Blood Pressure Reduction With **Risk of Hematoma Expansion in Patients With Deep Intracerebral Hemorrhage**. JAMA Neurol. 2019 May 13.
Leclerc J, Blais C, Rochette L, Hamel D, Guénette L, Poirier P. Impact of the **commercialization of three generic angiotensin II receptor blockers on adverse events** in Quebec, Canada: a population-based time series analysis. (candesartan) Circulation: Cardiovascular Quality and Outcomes. 2017;10:e003891.
Lee CJ, Hwang J, Lee YH, et al. **Blood pressure level** associated with lowest **cardiovascular event in hypertensive diabetic patients**. J Hypertens. 2018 Jul 13.
Lee CH, Kang KT, Chiu SN, et al. Association of **Adenotonsillectomy With Blood Pressure** Among Hypertensive and Nonhypertensive Children With Obstructive Sleep Apnea. JAMA Otolaryngol Head Neck Surg. 2018 Feb 15.
Lee HY, Kim SY, Choi KJ, et al. A Randomized, Multicenter, Double-blind, Placebo-controlled Study to Evaluate the Efficacy and the Tolerability of a Triple Combination of **Amlodipine/Losartan/Rosuvastatin** in Patients With Comorbid Essential Hypertension and Hyperlipidemia. Clin Ther. 2017 Nov 14.
Lee JK, Grace KA, Taylor AJ. Effect of a pharmacy care program on **medication adherence** and persistence, blood pressure, and low-density lipoprotein cholesterol. *JAMA* 2006; DOI:10.1001/jama.296.21.joc60162.
Lee M, Saver JL, Chang B, Chang K-H, Hao Q, Ovbiagele B. Presence of baseline **prehypertension and risk of incident stroke**: a meta-analysis. Neurology 2011;77:1330 –1337.
Lee M, Ovbiagele B, Hong KS, et al. Effect of **Blood Pressure Lowering in Early Ischemic Stroke**: Meta-Analysis. Stroke. 2015 May 28.
Leeman L, Dresang LT, Fontaine P. **Hypertensive Disorders of Pregnancy**. Am Fam Physician. 2016;93(2):121-127.
Leenen FH, et al. Clinical Events in High-Risk Hypertensive Patients Randomly Assigned to **Calcium Channel Blocker Versus Angiotensin-Converting Enzyme Inhibitor** in the Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial. Hypertension. 2006 Jul 24; [Epub ahead of print]
Lei Q, Zhou X, Zhou YH, et al. **Prehypertension During Normotensive Pregnancy** and Postpartum Clustering of Cardiometabolic Risk Factors: A Prospective Cohort Study. Hypertension. 2016 Jun 27.
Leiba A, Fishman B, Twig G,et al. Association of **Adolescent Hypertension With Future End-Stage Renal Disease**. JAMA Intern Med. 2019 Feb 25.
Leithead JA, Rajoriya N, Tehami N, et al. **Non-selective beta-blockers** are associated with improved survival in patients with **ascites listed for liver transplantation**. Gut. 2014 Oct 3.
Lennestal R, Olausson PO, Kallen B. **Maternal use of antihypertensive drugs in early pregnancy** and delivery outcome, notably the presence of heart defects in the infants. Eur J Clin Pharmacol 2 009;65:615-25.
Leonard CE, Razzaghi H, Freeman CP, et al. Empiric **potassium supplementation** and increased survival in users of loop diuretics. PLoS One. 2014 Jul 16;9(7)
Leung AA, Nerenberg K, Daskalopoulou SS, et al; CHEP Guidelines Task Force. **Hypertension Canada's 2016 CHEP** guidelines for **blood pressure measurement, diagnosis, assessment of risk, prevention and treatment of hypertension**. Can J Cardiol 2016 (accepted manuscript) doi: 10.1016/j.cjca.2016.02.066 www.onlinecjc.ca/article/S0828-282X(16)00192-6/pdf (accessed April 11, 2016).
Leung AA, Daskalopoulou SS, Dasgupta K, et al. **Hypertension Canada's 2017 Guidelines for Diagnosis, Risk Assessment, Prevention, and Treatment of Hypertension in Adults**. Can J Cardiol. 2017 May;33(5):557-576
Leung AA, Chang HJ, McAlister FA, et al. Applicability of the Systolic Blood Pressure Intervention Trial (**SPRINT**) to the **Canadian Population**. Can J Cardiol. 2018 May;34(5):670-675.
Levine RJ, Hauth JC, Curet LB, et al. Trial of **calcium to prevent preeclampsia**. N Engl J Med 1997;337:69-76.
Lewington S, Lacey B, Clarke R, et al; China Kadoorie Biobank Consortium. The Burden of **Hypertension and Associated Risk for Cardiovascular Mortality in China**. JAMA Intern Med. 2016 Mar 14.
Lewis JE, Boyle E, Magharious L, Myers MG. Evaluation of a **community-based automated blood pressure measuring device**. CMAJ. 2002 Apr 30;166(9):1145-8.
Li CI, Daling JR, Tang JC, Haugen KL, Parter PL, Malone KE. Use of **antihypertensive medications and breast cancer** (calcium channel blockers) risk among women aged 55 to 74 years [online August 5, 2013]. *JAMA Intern Med*.
Li DK, Yang C, Andrade S, et al. Maternal exposure to **angiotensin converting enzyme inhibitors** in the **first trimester and risk of malformations** in offspring: A retrospective cohort study. BMJ 2011; DOI: 10.1136/bmj.d5931.
Li EC, Heran BS, Wright JM. **Angiotensin converting enzyme (ACE) inhibitors versus angiotensin receptor blockers for primary hypertension.** Cochrane Database Syst Rev. 2014 Aug 23;8:CD009096. Our analyses found no evidence of a difference in total mortality or cardiovascular outcomes for ARBs as compared with ACE inhibitors, while ARBs caused slightly fewer WDAEs than ACE inhibitors. Although ACE inhibitors have shown efficacy in these outcomes over placebo, our results cannot be used to extrapolate the same conclusion for ARBs directly, which have not been studied in placebo-controlled trials for hypertension. Thus, the substitution of an ARB for an ACE inhibitor, while supported by evidence on grounds of tolerability, must be made in consideration of the weaker evidence for the efficacy of ARBs regarding mortality and morbidity outcomes compared with ACE inhibitors. Additionally, our data mostly derives from participants with existing clinical sequelae of hypertension, and it would be useful to have data from asymptomatic people to increase the generalizability of this review.

Unpublished subgroup data of hypertensive participants in existing trials comparing ACE inhibitors and ARBs needs to be made available for this purpose.
Li L, Welch SJV, Gutnikov SA, et al. Time course of **blood pressure control prior to lacunar TIA and stroke**: Population-based study. Neurology. 2018 May 15;90(20):e1732-e1741.
Li P, McElligott S, Bergquist H, et al. Effect of the **medicare part d coverage** gap on medication use among patients with hypertension and hyperlipidemia. Ann Intern Med. 2012 Jun 5;156(11):776-84.
Li Q, Cui Y, Jin R, et al. Enjoyment of **Spicy Flavor** Enhances Central Salty-Taste Perception and Reduces Salt Intake and Blood Pressure. Hypertension. 2017 Oct 31
Li S, Zhu Y, Chavarro JE, et al. **Healthful Dietary Patterns** and the Risk of Hypertension Among Women With a History of Gestational Diabetes Mellitus: A Prospective Cohort Study. Hypertension. 2016 Apr 18.
Li X, Wang J, Shen X, et al. Higher blood pressure **predicts diabetes and enhances long-term risk of cardiovascular disease** events in individuals with impaired glucose tolerance: Twenty-three-year follow-up of the Daqing diabetes prevention study. J Diabetes. 2018 Dec 16.
Li Y, Wei FF, Thijs L, et al. **Ambulatory Hypertension Subtypes** and 24-hour Systolic and Diastolic Blood Pressure as Distinct Outcome Predictors in 8341 Untreated People Recruited from 12 Populations. Circulation. 2014 Jun 6.
Li Y, Vgontzas AN, Fernandez-Mendoza J, et al. **Insomnia With Physiological Hyperarousal** Is Associated With Hypertension. Hypertension. 2015 Jan 26.
Lin MP, Ovbiagele B, Markovic D, et al. **Systolic Blood Pressure and Mortality After Stroke**: Too Low, No Go? Stroke. 2015 Mar 12.
Linderman GC, Lu J, Lu Y, et al. **Association of Body Mass Index With Blood Pressure** Among 1.7 Million Chinese Adults. JAMA Netw Open. 2018;1(4):e181271. doi:10.1001/jamanetworkopen.2018.1271
Lindholm LH, Carlberg B, Samuelsson O. Should beta blockers remain first choice in the treatment of primary hypertension? A meta-analysis. Lancet. 2005 Oct 29-Nov 4;366(9496):1545-53. (InfoPOEMs: If these authors have identified all the relevant research, it appears that in comparison with placebo, beta-blockers do not reduce cardiovascular morbidity or mortality but decrease the risk of strokes. However, in comparison with other antihypertensive medications, beta-blockers are associated with a significantly higher risk of stroke. Most of the included studies used atenolol and the data on other beta-blockers are inconclusive. Before throwing the baby out with the bathwater, remember that some patients with hypertension will need beta-blockers to treat their comorbid coronary artery disease, congestive heart failure, and so forth. (LOE = 1a-))
Lindsay P, Connor Gorber S, Joffres M, et al. Recommendations on **screening for high blood pressure in Canadian adults**. Can Fam Physician. 2013 Sep;59(9):927-33.
Lip GY, Felmeden DC, Dwivedi G. **Antiplatelet agents and anticoagulants** for hypertension. Cochrane Database Syst Rev. 2011 Dec 7;12:CD003186. Antiplatelet therapy with ASA for primary prevention in patients with elevated blood pressure provides a benefit, reduction in myocardial infarction, which is negated by a harm of similar magnitude, increase in major haemorrhage.The benefit of antiplatelet therapy for secondary prevention in patients with elevated blood pressure is many times greater than the harm.Benefit has not been demonstrated for warfarin therapy alone or in combination with aspirin in patients with elevated blood pressure.
Lipsitz LA. **A 91-year-old woman** with difficult-to-control hypertension: a clinical review. JAMA. 2013 Sep 25;310(12):1274-80.
Lipsitz LA, Habtemariam D, Gagnon M, et al. Reexamining the Effect of **Antihypertensive Medications On Falls in Old Age**. Hypertension. 2015 May 4.
Liu G, Mi XN, Zheng XX, et al. Effects of **tea intake** on blood pressure: a meta-analysis of randomised controlled trials. Br J Nutr. 2014 Oct;112(7):1043-54.
Liu L, An Y, Chen M, et al. Trends in the Prevalence of **Hospitalization Attributable to Hypertensive** Diseases Among **United States** Adults Aged 35 and Older from 1980 to 2007. Am J Cardiol. 2013 May 28.
Liu J, Sui X, Lavie CJ, et al. Effects of **Cardiorespiratory Fitness** on Blood Pressure Trajectory With Aging in a Cohort of Healthy Men. J Am Coll Cardiol. 2014 Sep 23;64(12):1245-53.
Liu S, Brooks D, Thomas SG, et al. Effectiveness of **User- and Expert-Driven Web-based Hypertension** Programs: an RCT. Am J Prev Med. 2018 Feb 15.
Liu Y, Ma X, J, et al. Effects of **angiotensin-converting enzyme inhibitors and angiotensin receptor blockers** on cardiovascular events and residual renal function in **dialysis patients**: a meta-analysis of randomized controlled trials. BMC Nephrol. 2017 Jun 30;18(1):206.
Lobo MD, Sobotka PA, Stanton A, et al, for the **ROX CONTROL HTN** Investigators. **Central arteriovenous anastomosis** for the treatment of patients with uncontrolled hypertension (the ROX CONTROL HTN study): a randomized controlled trial. Lancet 2015; online Jan 23.
Lonn EM, Bosch J, Lopez-Jaramillo P, et al. **Blood-pressure lowering in intermediate-risk persons** without cardiovascular disease. (**Hope-3**) N Engl J Med. DOI: 10.1056/NEJMoa1600175.
Lopez-Garcia E, et al. **Coffee** consumption and coronary heart disease in men and women: a prospective cohort study. Circulation. 2006 May 2;113(17):2045-53. Epub 2006 Apr 24. (InfoPOEMs: There is no evidence that coffee consumption increases the likelihood that someone will develop heart disease. (LOE = 2b))
Lovibond K, Jowett S, Barton P, et al. **Cost-effectiveness of options for the diagnosis** of high blood pressure in primary care: a modelling study. Lancet 2011; DOI:10.1016/S0140-6736(11)61184-7.
Low PA, Tomalia VA. **Orthostatic Hypotension**: Mechanisms, Causes, Management. J Clin Neurol. 2015 Jul;11(3):220-6.
Lu J, Lu Y, et al. Prevalence, awareness, treatment, and control of **hypertension in China**: data from 1·7 million adults in a population-based screening study (China PEACE Million Persons Project). Lancet 2017; online Oct 25.
Lüscher TF. **What is a normal blood pressure**? Eur Heart J. 2018 Jun 21;39(24):2233-2240.
Luthra S, Leiva-Juarez MM, Taggart DP. Systematic Review of **Therapies for Stable Coronary Artery Disease in Diabetic Patients**. Ann Thorac Surg. 2015 Oct 31.
Lv J, Perkovic V, Foote CV, et al. **Antihypertensive agents for preventing diabetic kidney disease**. Cochrane Database Syst Rev. 2012 Dec 12;12:CD004136. doi: 10.1002/14651858.CD004136.pub3.
ACEi were found to prevent new onset DKD and death in normoalbuminuric people with diabetes, and could therefore be used in this population. More data are needed to clarify the role of ARB and other drug classes in preventing DKD.
Lv J, Ehteshami P, Sarnak MJ, et al. Effects of **intensive blood pressure lowering on the progression of chronic kidney disease**: a systematic review and meta-analysis. *CMAJ* 2013;185:949-57.
Lv YB, Gao X, Yin ZX, et al. Revisiting the **association of blood pressure with mortality in oldest old people in China**: community based, longitudinal prospective study. BMJ. 2018 Jun 5;361:k2158.
Lyon C, Utter B, DeSanto K. How effective is **spironolactone** for treating resistant hypertension? J Fam Pract. 2019 Jun;68(5):E11-E13.
Ma Y, Cheng HY, Cheng L, et al. The effectiveness of **electronic health interventions on blood pressure control, self-care behavioural outcomes and psychosocial well-being** in patients with hypertension: A systematic review and meta-analysis. Int J Nurs Stud. 2018 Dec 31;92:27-46.
MacDonald T, Williams B, Webb DJ, et al; for The British Hypertension Society Programme of Prevention And Treatment of Hypertension With Algorithm-based Therapy (**PATHWAY**). **Combination therapy is superior to sequential monotherapy for the initial treatment of hypertension**: a double-blind randomised controlled trial. J Am Heart Assoc. 2017;6:e006986.
Macfarlane TV, Pigazzani F, Flynn RWV, Macdonald TM. The effect of **indapamide versus bendroflumethiazide** for primary hypertension: a systematic review. Br J Clin Pharmacol. 2018 Oct 12.
Magee LA, Helewa M, Moutquin JM, von Dadelszen P, Hypertension Guideline Committee, Society of Obstetricians and Gynaecologists of Canada. Diagnosis and classification. In: Diagnosis, evaluation, and management of the **hypertensive disorders of pregnancy**. J Obstet Gynaecol Can 2008 Mar;30(3 Suppl 1):S9-15. http://www.sogc.org/guidelines/documents/gui206CPG0803_001.pdf
Magee LA, Pels A, Helewa M, et al; **Canadian Hypertensive Disorders of Pregnancy (HDP)** Working Group. Diagnosis, evaluation, and management of the **hypertensive disorders of pregnancy**.http://download.journals.elsevierhealth.com/pdfs/journals/2210-7789/PIIS221077891400004X.pdf (accessed June 25, 2014).
Magee LA, Pels A, Helewa M, Rey E, et al. **Diagnosis, evaluation, and management of the hypertensive disorders of pregnancy**: (**HDP**) executive summary. J Obstet Gynaecol Can. 2014 May;36(5):416-38.
Magee LA, von Dadelszen P, Rey E, et al. **Less-tight versus tight control of hypertension in pregnancy**. N Engl J Med 2015; 372:407-17.
Magee LA, Pels A, Helewa M, Rey E, von Dadelszen P; **Canadian Hypertensive Disorders of Pregnancy (HDP)** Working Group; Canadian Hypertensive Disorders of Pregnancy HDP Working Group. The **hypertensive disorders of pregnancy** (29.3). Best Pract Res Clin Obstet Gynaecol. 2015 Jul;29(5):643-57.
Magee LA, von Dadelszen P, Singer J, et al. **Can adverse maternal and perinatal outcomes** be predicted when blood pressure becomes elevated? Secondary analyses from the **CHIPS** (Control of Hypertension In Pregnancy Study) randomized controlled trial. Acta Obstet Gynecol Scand. 2016 Feb 24.
Magnus MC, Miliku K, Bauer A, et al. **Vitamin D and risk of pregnancy related hypertensive disorders**: mendelian randomisation study. BMJ. 2018 Jun 20;361:k2167.
Magriço R, Bigotte Vieira M, Viegas Dias C, et al. BP **Reduction, Kidney Function Decline, and Cardiovascular Events** in Patients without CKD. Clin J Am Soc Nephrol. 2018 Jan 6;13(1):73-80.
Maher GM, O'Keeffe GW, Kearney PM, et al. Association of **Hypertensive Disorders of Pregnancy With Risk of Neurodevelopmental Disorders in Offspring**: A Systematic Review and Meta-analysis. JAMA Psychiatry. 2018 Jun 6.
Mahfoud F, Lüscher TF, Andersson B, et al. Expert consensus document from the European Society of Cardiology (ESC) on **catheter-based renal denervation**. Eur Heart J 2013.
Mahfoud F, Ukena C, Schmieder RE, et al. **Ambulatory blood pressure changes** after **renal sympathetic denervation** in patients with resistant hypertension. Circulation. 2013 Jul 9;128(2):132-40.
Mahfoud F, Schlaich M, Böhm M, Esler M, Lüscher TF. **Catheter-based renal denervation:** the next chapter begins. Eur Heart J. 2018 Dec 14;39(47):4144-4149.
Mahmoudpour SH, Asselbergs FW, Souverein PC, et al. Prescription Patterns of **Angiotensin-Converting Enzyme Inhibitors for Various Indications**: A UK Population-based Study. Br J Clin Pharmacol. 2018 Jun 26.
Maillard P, Seshadri S, Beiser A, et al. Effects of **systolic blood pressure on white-matter integrity** in young adults in the Framingham Heart Study: a cross-sectional study. Lancet Neurol 2012.
Maitland ML, Bakris GL, Black HR et al. Initial assessment, surveillance, and management of blood pressure in patients receiving **vascular endothelial growth factor signaling pathway inhibitors**. J Natl Cancer Inst 2010;102:596-604.

Makam AN, John Boscardin W, Miao Y, et al. Risk of **Thiazide-Induced Metabolic Adverse Events** in Older Adults. J Am Geriatr Soc. 2014 May 13.

Makani H, Messerli FH, Romero J, et al. Meta-Analysis of Randomized Trials of **Angioedema** as an Adverse Event of Renin-Angiotensin System Inhibitors. Am J Cardiol. 2012 Apr 20.

Makani H, Bangalore S, Supariwala A, et al. Antihypertensive efficacy of **angiotensin receptor blockers as monotherapy** as evaluated by ambulatory blood pressure monitoring: a meta-analysis. Eur Heart J. 2013 Aug 21.

Makin S, Stott DJ. Managing blood pressure in **older adults**. BMJ. 2018 Jul 6;362:k2912.

Makridakis S, DiNicolantonio JJ. **Hypertension: empirical evidence** and implications in 2014. Open Heart. 2014 Jul 10;1(1):e000048.

Malem A, Farnworth D. Headache, flashing lights, and blurred vision (**hypertensive retinopathy**). BMJ. 2015 Feb 2;350:h446.

Malhotra R, Nguyen HA, Benavente O, et al. Association between more **intensive** vs less intensive blood pressure lowering and risk of mortality in **chronic kidney disease** stages 3 to 5: a systematic review and meta-analysis [online September 5, 2017].JAMA Intern Med. doi:10.1001/jamainternmed.2017.4377

Mallery LH, Allen M, Fleming I, et al. Promoting higher **blood pressure targets for frail older adults**: A **consensus** guideline from **Canada**. Cleve Clin J Med. 2014 Jul;81(7):427-437.

Malik AH, Akram Y, Shetty S, et al. Impact of **Sugar-Sweetened Beverages** on Blood Pressure. Am J Cardiol. 2014 May 1;113(9):1574-1580.

Mancia G, De Backer G, Dominiczak A, et al. Management of Arterial Hypertension of the ESH; European Society of Cardiology. 2007 Guidelines for the Management of Arterial Hypertension: The Task Force for the Management of Arterial Hypertension of the European Society of Hypertension (**ESH**) and of the European Society of Cardiology (ESC). J Hypertens. **2007** Jun;25(6):1105-87. Erratum: J Hypertens. 2007 Aug;25(8):1749.

Mancia G, Fagard R, Narkiewicz K, et al. **2013 ESH/ESC guidelines** for the management of arterial **hypertension**. Eur Heart J 2013; DOI: 10.1093/eurheartj/eht.151.

Mancia G, De Backer G, Dominiczak A, et al. **2007** Guidelines for the management of arterial hypertension: The Task Force for the Management of Arterial Hypertension of the European Society of Hypertension (ESH) and of the European Society of Cardiology (**ESC**). Eur Heart J 2007 Jun;28(12):1462-536.

Mancia Giuseppe, Parati Gianfranco, Revera Miriam, et al. **Statins**, antihypertensive treatment, and blood pressure control in clinic and over 24 hours: evidence from PHYLLIS randomised double blind trial. BMJ 2010

Mancia G, Agabiti-Rosei E, Ambrosioni E, et al. **Hypertension and migraine** comorbidity: Prevalence and risk of **cerebrovascular** events. Evidence from a large, multicenter, cross-sectional survey in Italy (MIRACLES study). J Hypertens 2011; 29:309-318.

Mancia G. Antihypertensives in **octogenarians**. BMJ. 2012 Jan 4;344:d7293.

Mancia G, Facchetti R, Parati G, Zanchetti A. **Visit-to-Visit Blood Pressure Variability**, Carotid Atherosclerosis, and Cardiovascular Events in the European Lacidipine Study on Atherosclerosis. Circulation. 2012 Jul 31;126(5):569-78.

Mancia G, Bombelli M, Brambilla G, et al. Long-term prognostic value of **white coat hypertension**: an insight from diagnostic use of **both ambulatory and home blood pressure measurements**. Hypertension. 2013 Jul;62(1):168-74.

Mancia G, Cannon CP, Tikkanen I, et al. Impact of **Empagliflozin on Blood Pressure** in Patients With Type 2 Diabetes Mellitus and Hypertension by Background Antihypertensive Medication. Hypertension.2016 ;68 :000-000.

Manning L, Hirakawa Y, Arima H, et al. Blood pressure variability and outcome in acute **intracerebral haemorrhage**: post-hoc analysis of the INTERACT2 randomised controlled trial. Lancet Neurol 2014; online Feb 13.

Mansfield KE, Nitsch D, Smeeth L, et al. Prescription of **renin-angiotensin system blockers and risk of acute kidney injury**: a population-based cohort study. BMJ Open. 2016 Dec 21;6(12):e012690.

Mant J, McManus RJ, et al. Different **systolic blood pressure targets for people with history of stroke or transient ischaemic attack**: **PAST-BP** (Prevention After Stroke-Blood Pressure) randomised controlled trial. BMJ 2016;352:i708.

Marczak L, Williams J, Loeffler M; For the Institute for Health Metrics and Evaluation. **Global Deaths Attributable to High Systolic Blood Pressure**, 1990-2016. JAMA. 2018 Jun 5;319(21):2163.

Marott SC, Nielsen SF, Benn M, et al. **Antihypertensive treatment and risk of atrial fibrillation**: a nationwide study. Eur Heart J. 2014 May;35(18):1205-14.

Margolis KL, Asche SE, Bergdall AR, et al. Effect of **home blood pressure telemonitoring** and **pharmacist management** on blood pressure control: a cluster randomized clinical trial. JAMA. 2013 Jul 3;310(1):46-56.

Margolis KL, Asche SE, Dehmer SP, et al. Long-term Outcomes of the Effects of **Home Blood Pressure Telemonitoring and Pharmacist Management** on Blood Pressure Among Adults With Uncontrolled Hypertension- Follow-up of a Cluster Randomized Clinical Trial. JAMA Netw Open. 2018;1(5):e181617.

Markovitz AA, Mack JA, Nallamothu BK, et al. **Incremental effects of antihypertensive drugs**: instrumental variable analysis. BMJ. 2017 Dec 22;359:j5542.

Marin JM, Agusti A, Villar I, et al. Association between treated and untreated **obstructive sleep apnea and risk of hypertension**. JAMA. 2012;307(20):2169-2176.

Marra C, Johnston K, Santschi V, et al. **Cost-effectiveness** of **pharmacist care for managing hypertension in Canada**. Can Pharm J (Ott). 2017 Mar 21;150(3):184-197

Marshall IJ, Wolfe CD, McKevitt C. Lay perspectives on hypertension and **drug adherence**: systematic review of qualitative research. BMJ. 2012 Jul 9;345:e3953.

Martin SA, Boucher M, Wright JM, et al. **Mild hypertension in people at low risk. BMJ**. 2014 Sep 14;349:g5432.

Martin U, Coleman JJ. Monitoring **renal function** in hypertension. BMJ. 2006 Oct 28;333(7574):896-9.

Martinez-Garcia MA, Capote F, Campos-Rodriguez F, et al. Effect of **CPAP** on blood pressure in patients with obstructive sleep apnea and resistant hypertension: the HIPARCO randomized clinical trial. JAMA. 2013 Dec 11;310(22):2407-15.

Martins D, Agodoa L, Norris KC. Hypertensive **chronic kidney disease in African Americans**: Strategies for improving care. Cleve Clin J Med. 2012 Oct;79(10):726-734.

Masood S, Austin PC, Atzema CL. A population-based analysis of outcomes in patients with a primary diagnosis of hypertension in the **emergency department**. Ann Emerg Med 2016.

Matthews KA, Brenner MJ, Brenner AC. Evaluation of the Efficacy and Safety of a **Hydrochlorothiazide to Chlorthalidone** Medication Change in Veterans With Hypertension. Clin Ther. 2013 Aug 28.

Mayor S. **Renal denervation** achieves sustained blood pressure reduction, finds trial. BMJ. 2019 Mar 19;364:l1274.

Mazzaglia G et al. **Adherence** to antihypertensive medications and cardiovascular morbidity among newly diagnosed hypertensive patients. *Circulation* 2009 Oct 20; 120:1598.

McAlister, Finlay A., Zhang, Jianguo, Tonelli, Marcello, et al. The safety of **combining angiotensin-converting-enzyme inhibitors with angiotensin-receptor blockers** in elderly patients: a population-based longitudinal analysis. CMAJ 2011 0: cmaj.101333.

McAlister FA, Wilkins K, Joffres M, et al. Changes in the rage of awareness, treatment and control of hypertension in **Canada over the past two decades.** CMAJ 2011; DOI:10.1503/cmaJ.101767.

McAlister FA; for the Renin Angiotension System Modulator Meta-Analysis Investigators. **Angiotensin-converting enzyme inhibitors or angiotensin receptor blockers** are beneficial in **normotensive atherosclerotic** patients: a collaborative meta-analysis of randomized trials. Eur Heart J. 2011 Oct 31.

McAlister FA; for the Renin Angiotension System Modulator Meta-Analysis Investigators. Angiotensin-converting enzyme inhibitors or angiotensin receptor blockers are beneficial in **normotensive atherosclerotic** patients: a collaborative meta-analysis of randomized trials. Eur Heart J. 2011 Oct 31.

McAlister FA, Majumdar SR, Padwal RS, et al. Case management for blood pressure and lipid level control **after minor stroke**: **PREVENTION** randomized controlled trial. CMAJ 2014. DOI:10.1503/cmaj.140053.

McBrien K, Rabi DM, Campbell N, et al. **Intensive and Standard Blood Pressure** Targets in Patients With Type 2 **Diabetes** Mellitus: Systematic Review and Meta-analysis. Arch Intern Med. 2012 Aug 6:1-8.

McCall DO, McGartland CP, McKinley MC, et al. **Dietary intake of fruits and vegetables** improves microvascular function in hypertensive subjects in a dose-dependent manner. Circulation. 2009;119:2153–2160.

McDonald MA, Simpson SH, Ezekowitz JA, et al. Angiotensin receptor blockers and risk of **myocardial infarction**: systematic review. BMJ. 2005Oct 15;331(7521):873. Epub 2005 Sep 23. CONCLUSIONS: Treatment with angiotensin receptor blockers was not associated with a significantly increased risk of myocardial infarction. The 95% confidence intervals do, however, not exclude an increase of up to 16% in the risk of myocardial infarction or a reduction in risk of up to 25%. Until further information specifically dealing with this issue is available from large prospective trials, our findings may alleviate recent concerns over the safety of this class of medications.

McDowell SE, Coleman JJ, Ferner RE. Systematic review and meta-analysis of **ethnic differences** in risks of adverse reactions to drugs used in cardiovascular medicine. BMJ. 2006 May 20;332(7551):1177-81. Epub 2006 May 5.

McEvoy JW, Chen Y, Nambi V, et al. **High-Sensitivity Cardiac Troponin T and** Risk of Hypertension. Circulation. 2015 Jul 7.

McEvoy JW, Chen Y, Rawlings A, et al. **Diastolic blood pressure, subclinical myocardial damage, and cardiac events**: Implications for blood pressure control. *J Am Coll Cardiol* 2016; 68:1713–1722.

McEvoy JW, Martin SS, Dardari ZA, et al. **Coronary Artery Calcium** to **Guide a Personalized Risk-Based Approach** to Initiation and Intensification of **Antihypertensive Therapy**. Circulation. 2017 Jan 10;135(2):153-165.

McGrath ER, Beiser AS, DeCarli C, et al. **Blood pressure from mid- to late life and risk of incident dementia**. Neurology. 2017 Dec 12;89(24):2447-2454.

McGuinness B, Todd S, Passmore P, Bullock R. The effects of blood pressure lowering on development of cognitive impairment & **dementia** in patients without apparent prior cerebrovascular disease. Cochrane Database Syst Rev. 2006 Apr 19;(2):CD004034. There was no convincing evidence from the trials identified that blood pressure lowering prevents the development of dementia or cognitive impairment in hypertensive patients with no apparent prior cerebrovascular disease. There were significant problems identified with analysing the data, however, due to the number of patients lost to follow-up and the number of placebo patients given active treatment. This introduced bias. More robust results may be obtained by analysing one year data to reduce differential drop-out or by conducting a meta-analysis using individual patient data.

Mackenzie IS, MacDonald TM. **Identifying poor adherence** to antihypertensive medications in patients with resistant hypertension. Br J Clin Pharmacol. 2018 Nov 26.

McKinstry B, Hanley J, Wild S, et al. **Telemonitoring** based service redesign for the management of uncontrolled hypertension: multicentre randomised controlled trial. BMJ. 2013 May 24;346:f3030.

McManus RJ, Glasziou P, Hayen A, Mant J, Padfield P, Potter J, Bray EP, Mant D. **Blood pressure self monitoring**: questions and answers from a national conference. BMJ. 2008 Dec 22;337:a2732. doi: 10.1136/bmj.a2732.

McManus RJ, Mant J, Bray EP, et al. Telemonitoring and **self-management in the control of hypertension (TASMINH2):** A randomised controlled trial. Lancet 2010; DOI:10.1016/S0140-6736(10)60964-6.

McManus RJ, Mant J, et al. Efficacy of **self-monitored blood pressure**, **with or without telemonitoring**, for titration of antihypertensive medication (**TASMINH4**): an unmasked randomised controlled trial. Lancet. 2018 Feb 27.

McNally RJ, Morselli F, Farukh B, et al. A REVIEW OF THE **PRESCRIBING TREND** OF THIAZIDE-TYPE AND THIAZIDE-LIKE DIURETICS IN HYPERTENSION: A UK PERSPECTIVE. Br J Clin Pharmacol. 2019 Aug 31.

McSweeney JC, Rosenfeld AG, Abel WM, et al. Preventing and Experiencing **Ischemic Heart Disease as a Woman**: State of the Science: A Scientific Statement From the American Heart Association. Circulation. 2016 Mar 29

Medical Letter. **Aliskiren (Tekturna)** for Hypertension. April 9,2007.

Mehrabadi A, Liu S, Bartholomew S, et al; **Canadian Perinatal Surveillance System** (Public Health Agency of Canada). **Hypertensive disorders of pregnancy** and the recent increase in obstetric acute renal failure in Canada: population based retrospective cohort study. BMJ. 2014 Jul 30

Mehlum MH, Liestøl K, Kjeldsen SE, et al. **Blood pressure variability and risk of cardiovascular events and death** in patients with hypertension and different baseline risks. Eur Heart J. 2018 Jun 21;39(24):2243-2251.

Mehta SJ, Volpp KG, Troxel AB, et al. **Electronic Pill Bottles or Bidirectional Text Messaging** to Improve Hypertension Medication Adherence (Way 2 Text): a Randomized Clinical Trial. J Gen Intern Med. 2019 Aug 8.

Meister TA, Rimoldi SF, Soria R, et al. Association of **Assisted Reproductive Technologies With Arterial Hypertension** During Adolescence. J Am Coll Cardiol. 2018 Sep 11;72(11):1267-1274.

Melgarejo JD, Maestre GE, Thijs L, et al. Prevalence, Treatment, and Control Rates of **Conventional and Ambulatory Hypertension Across 10 Populations** in 3 Continents. Hypertension. 2017 Jul;70(1):50-58.

Melville S, Byrd JB. **Monitoring Blood Pressure** Outside of the Doctor's Office. JAMA. 2018 Nov 6;320(17):1830.

Melville S, Byrd JB. **Out-of-Office** Blood Pressure Monitoring in 2018. JAMA. 2018 Nov 6;320(17):1805-1806.

Mente A, O'Donnell M, Rangarajan S, et al. **Urinary sodium excretion, blood pressure, cardiovascular disease, and mortality**: a community-level prospective epidemiological cohort study. Lancet. 2018 Aug 11;392(10146):496-506.

Messerli FH, Bangalore S, Bavishi C, et al. **Angiotensin-Converting Enzyme Inhibitors** in Hypertension: To Use or Not to Use? J Am Coll Cardiol. 2018 Apr 3;71(13):1474-1482.

Messerli FH, Bangalore S, Messerli AW. **Age, Blood Pressure Targets, and Guidelines**: Rift Between Those Who Preach, Those Who Teach, and Those Who Treat? Circulation. 2018 Jul 10;138(2):128-130.

Messerli FH, et al. Dogma disputed: can aggressively **lowering diastolic blood pressure** in hypertensive patients with coronary artery disease be **dangerous**? Ann Intern Med. 2006 Jun 20;144(12):884-93. (InfoPOEMs: Lower is not always better. Despite a push toward lower blood pressure in many populations, bad outcomes (mortality, myocardial infarction, and stroke) are increased in patients with coronary artery disease (CAD) if their blood pressure consistently remains lower than 70 mmHg diastolic. (LOE = 1b))

Messerli FH, Williams B, Ritz E. **Essential hypertension**. Lancet. 2007 Aug 18;370(9587):591-603.

Messerli FH, Rimoldi SF, Bangalore S. **Changing definition of hypertension in guidelines**: how innocent a number game? Eur Heart J. 2018 Jun 21;39(24):2241-2242.

Meyers RS, Siu A. Pharmacotherapy Review of Chronic **Pediatric Hypertension**. Clin Ther. 2011 Oct 7.

Micieli A, Micieli JA. **Recovery of vision in fulminant idiopathic intracranial hypertension**. CMAJ. 2019 Jun 10;191(23):E639.

Millington K, Liu E, Chan YM. The Utility of **Potassium Monitoring in Gender-Diverse Adolescents Taking Spironolactone**. J Endocr Soc. 2019 Apr 4;3(5):1031-1038.

Mills KT, Bundy JD, Kelly TN, et al. **Global Disparities** of Hypertension Prevalence and Control: A Systematic Analysis of Population-Based Studies From 90 Countries. Circulation. 2016 Aug 9;134(6):441-50.

Mills KT, Obst KM, Shen W, et al. **Comparative Effectiveness of Implementation Strategies** for Blood Pressure Control in Hypertensive Patients: A Systematic Review and Meta-analysis. Ann Intern Med. 2017 Dec 26.

Minutolo R, Agarwal R, Borrelli S, et al. Prognostic role of **ambulatory blood pressure measurement** in patients with **nondialysis chronic kidney disease.** *Arch Intern Med*. 2011;171(12):1090-1098.

Mitchell AA. Fetal risk from **ACE inhibitors in the first trimester**. BMJ 2011; DOI:10.1136/bmj.d5931.

Mohan A, Fazel R, Huang PH, Shen YC, Howard D. Changes in **geographic variation** in percutaneous coronary intervention for stable ischemic heart disease after publication of the clinical outcomes utilizing revascularization and aggressive drug evaluation (**COURAGE**) trial. *Circ Cardiovasc Qual Outcomes* 2014.

Mohammad J, Scanni R, Bestmann L, et al. A Controlled Increase in **Dietary Phosphate Elevates BP in Healthy Human Subjects**. J Am Soc Nephrol. 2018 Aug;29(8):2089-2098.

Mollan SP, Ali F, Hassan-Smith G, et al. Evolving evidence in **adult idiopathic intracranial hypertension**: pathophysiology and management. J Neurol Neurosurg Psychiatry. 2016 Feb 17.

Molnar F, Frank CC. Determining the **causes of postural hypotension**. Can Fam Physician. 2018 Jan;64(1):40.

Molvi SN, et al. Role of antihypertensive therapy in mild to moderate **pregnancy-induced hypertension**: a prospective randomized study comparing **labetalol** with alpha **methyldopa**. Arch Gynecol Obstet. 2012 Jun;285(6):1553-62.

Moolchan ET, Robinson ML, Ernst M, et al. Safety and efficacy of the nicotine patch and gum for the treatment of adolescent tobacco addiction. Pediatrics 2005;115:407-14. (InfoPOEMs: Approximately 1 in 5 adolescents (20%) given weekly therapy sessions and a nicotine patch will not be smoking 6 months after their quit date. (LOE = 1b-))

Moncada LV. Management of falls in older persons: a prescription for prevention. Am Fam Physician. 2011 Dec 1;84(11):1267-76.

Montalescot G, Sechtem U, Achenbach S, et al. 2013 **ESC guidelines on the management of stable coronary artery disease**. Eur Heart J 2013

Montani D, Bergot E, Gunther S, et al. **Pulmonary arterial hypertension** in patients treated by **dasatinib**. Circulation. 2012;125:2128–2137.

Montazeri K, Unitt C, Foody JM, et al. **ABCDE** steps to prevent heart disease in breast cancer survivors. Circulation. 2014 Oct 28;130(18):e157-9.

Moonen JE, Foster-Dingley JC, et al. Effect of **Discontinuation of Antihypertensive Treatment in Elderly People** on **Cognitive Functioning**-the **DANTE Study Leiden**: A Randomized Clinical Trial. JAMA Intern Med. 2015 Aug 24.

Moonen JE, Foster-Dingley JC, et al. Effect of **discontinuation of antihypertensive medication on orthostatic hypotension** in older persons with mild cognitive impairment: the **DANTE Study Leiden**. Age Ageing. 2016 Jan 11.

Morawski K, et al. Association of a **smartphone application** with medication **adherence**&**blood pressure control**: **MedISAFE-BP** randomized clinical trial [online Apr 16'18].JAMA Intern Med. doi:10.1001/jamainternmed.2018.0447

Moran AE, Odden MC, Thanataveerat A, et al. **Cost-effectiveness** of hypertension therapy according to **2014 guidelines**. N Engl J Med. 2015 Jan 29;372(5):447-55.

Moran AE. Still on the Road to **Worldwide Hypertension Control**. Circulation. 2016 Aug 9;134(6):451-4.

Moran AE, Pletcher MJ, Bibbins-Domingo K. **Whom to Treat for High Blood Pressure**-Time for a Precision Approach. JAMA Intern Med. 2018 Jan 1;178(1):37-38.

Morishita M, Adar SD, D'Souza J, et al. Effect of Portable **Air Filtration Systems on Personal Exposure to Fine Particulate Matter and Blood Pressure** Among Residents in a Low-Income Senior Facility: A Randomized Clinical Trial. JAMA Intern Med. 2018 Sep 10.

Morotti A, Boulouis G, Romero JM, et al. Blood pressure reduction and noncontrast CT markers of **intracerebral hemorrhage** expansion. Neurology. 2017 Aug 8;89(6):548-554.

Morrissey Y, Bedford M, Irving J, et al. **Older people** remain on blood pressure agents despite being **hypotensive** resulting in increased mortality and hospital admission. Age Ageing. 2016 Jun 30.

Morrow DA, de Lemos JA, Blazing MA, et al.; A to Z Investigators. Prognostic value of serial **B-type natriuretic peptide** testing during follow-up of patients with unstable coronary artery disease. JAMA. 2005 Dec 14;294(22):2866-71. (InfoPOEMs: Serial determination of B-type natriuretic peptide (BNP) during follow-up of patients after an acute coronary syndrome (ACS) helps predict the risk of subsequent death or congestive heart failure (CHF). It remains uncertain whether having this information will lead to a change in clinical management that improves patient-oriented outcomes or simply increases costs without any added benefit. (LOE = 1b))

Mosca L, Hammond G, Mochari-Greenberger, et al. Fifteen-year trends in awareness of heart disease in **women**. Results of a 2012 American Heart Association National Survey. Circulation 2012.

Moser M, Setaro JF. Clinical practice. **Resistant** or difficult-to-control **hypertension**. N Engl J Med. 2006 Jul 27;355(4):385-92.

Mossello E, Pieraccioli M, Nesti N, et al. Effects of **Low Blood Pressure in Cognitively Impaired Elderly Patients** Treated With Antihypertensive Drugs. JAMA Intern Med. 2015 Mar 2.

Moyer VA; U.S. Preventive Services Task Force. **Screening for primary hypertension in children and adolescents**: U.S. Preventive services task force recommendation statement. (USPSTF) Pediatrics. 2013 Nov;132(5):907-14.

Moynihan RN, Clark J, Albarqouni L. Media Coverage of the **Benefits and Harms of the 2017 Expanded Definition** of High Blood Pressure. JAMA Intern Med. 2018 Dec 28.

Mozaffarian D, Rimm EB. **Fish intake**, contaminants, and human health: evaluating the risks and the benefits. JAMA. 2006 Oct 18;296(15):1885-99.

Mozaffarian D, et al. **Trans fatty acids** and cardiovascular disease. N Engl J Med. 2006 Apr 13;354(15):1601-13.

Mozaffarian D, Benjamin EJ, Go AS, et al. **Heart disease and stroke statistics**—2015 update: A report from the American Heart Association. *Circulation* 2015; 131: DOI:10.1161/CIR.0000000000000152.

Mozaffarian D, Benjamin EJ, Go AS, et al. **Heart disease and stroke statistics—2016 update**: A report from the American Heart Association (AHA).*Circulation* 2015.

Mu L, Mukamal KJ. **Treatment Intensification for Hypertension in US Ambulatory Medical Care**. J Am Heart Assoc. 2016 Oct 22;5(10).
Mueller C, Laule-Kilian K, Frana B, Rodriguez D, Scholer A, Schindler C, Perruchoud AP. Use of **B-type natriuretic peptide** in the management of acute dyspnea in patients with pulmonary disease. Am Heart J. 2006 Feb;151(2):471-7. (InfoPOEMs: In patients with pre-existing pulmonary disease, B-type natriuretic peptide (BNP) testing in the emergency department is effective at distinguishing an exacerbation due to heart failure (HF) from that caused by pulmonary disease. As a result, hospitalizations are fewer, probably because of initiation of more appropriate therapy in the emergency department. Also, the duration of the hospital stay is shorter and the cost is less. (LOE = 1b))
Mueller NT, Noya-Alarcon O, Contreras M, et al. **Association of Age With Blood Pressure** Across the Lifespan in Isolated Yanomami and Yekwana Villages. JAMA Cardiol. 2018 Nov 14.
Mukamal KJ, Chiuve SE, Rimm EB. **Alcohol consumption** and risk for coronary heart disease in men with healthy lifestyles. Arch Intern Med. 2006 Oct 23;166(19):2145-50.
Muller M, Sigurdsson S, Kjartansson O, et al; Age, Gene/Environment Susceptibility-Reykjavik Study Investigators. Joint effect of **mid- and late-life blood pressure on the brain**: The AGES-Reykjavik Study. Neurology. 2014 Jun 17;82(24):2187-95.
Muñoz D, Uzoije P, Reynolds C, et al. **Polypill for Cardiovascular Disease Prevention** in an Underserved Population. N Engl J Med. 2019 Sep 19;381(12):1114-1123.
Muntner P, Whittle J, Lynch AI, et al. **Visit-to-Visit Variability of Blood Pressure** and Coronary Heart Disease, Stroke, Heart Failure, and Mortality: A Cohort Study. Ann Intern Med. 2015 Jul 28.
Muntner P, Carey RM, Gidding S, et al. **Potential U.S. Population Impact** of the 2017 American College of Cardiology (ACC) /American Heart Association (AHA) High Blood Pressure Guideline. Circulation. 2017 Nov 13.
Murabito JM, Pencina MJ, Nam BH, et al. **Sibling cardiovascular disease** as a risk factor for cardiovascular disease in middle-aged adults. JAMA. 2005 Dec 28;294(24):3117-23.
Murad MH, Larrea-Mantilla L, Haddad A, et al. Antihypertensive **Agents in Older Adults**: A Systematic Review and Meta-Analysis of Randomized Clinical Trials. J Clin Endocrinol Metab. 2019 May 1;104(5):1575-1584.
Murthy VL, Shah RV, Rubenfire M, et al. Comparison of the Treatment Implications of **American Society of Hypertension and International Society of Hypertension 2013 and Eighth Joint National Committee Guidelines**: An Analysis of National Health and Nutrition Examination Survey. Hypertension. 2014 May 12.
Musini VM;Gueyffier F;Puil L;Salzwedel DM;Wright J. **Pharmacotherapy** for **hypertension** in adults aged 18 to 59 years. Cochrane Database Syst Rev. 2017 Aug 16;8:CD008276. Antihypertensive drugs used to treat predominantly healthy adults aged 18 to 59 years with mild to moderate primary hypertension have a small absolute effect to reduce cardiovascular mortality and morbidity primarily due to reduction in cerebrovascular mortality and morbidity. All-cause mortality and coronary heart disease were not reduced. There is lack of good evidence on withdrawal due to adverse events. Future trials in this age group should be at least 10 years in duration and should compare different first-line drug classes and strategies.
Musini VM, Lawrence KA, Fortin PM, et al. Blood pressure lowering efficacy of **renin inhibitors for primary hypertension**. Cochrane Database Syst Rev. 2017 Apr 5;4:CD007066. Compared to placebo, aliskiren lowered BP and this effect is dose-dependent. This magnitude of BP lowering effect is similar to that for angiotensin-converting enzyme (ACE) inhibitors and angiotensin receptor blockers (ARBs). There is no difference in mortality, nonfatal serious adverse events or withdrawal due to adverse effects with short term aliskiren monotherapy. Diarrhoea was considerably increased with **aliskiren** 600 mg.
Musini VM, Nazer M, Bassett K, Wright JM. Blood pressure-lowering efficacy of **monotherapy with thiazide diuretics for primary hypertension**. Cochrane Database of Systematic Reviews 2014, Issue 5. Art. No.: CD003824. DOI: 10.1002/14651858.CD003824.pub2. This systematic review shows that hydrochlorothiazide has a dose-related blood pressure-lowering effect. The mean blood pressure-lowering effect over the dose range 6.25 mg, 12.5 mg, 25 mg and 50 mg/day is 4/2 mmHg, 6/3 mmHg, 8/3 mmHg and 11/5 mmHg, respectively. For other thiazide drugs, the lowest doses studied lowered blood pressure maximally and higher doses did not lower it more. Due to the greater effect on systolic than on diastolic blood pressure, thiazides lower pulse pressure by 4 mmHg to 6 mmHg. This exceeds the mean 3 mmHg pulse pressure reduction achieved by ACE inhibitors, ARBs and renin inhibitors, and the 2 mmHg pulse pressure reduction with non-selective beta-blockers as shown in other Cochrane reviews, which compared these antihypertensive drug classes with placebo and used similar inclusion/exclusion criteria. Thiazides did not increase withdrawals due to adverse effects in these short-term trials but there is a high risk of bias for that outcome. Thiazides reduced potassium, increased uric acid and increased total cholesterol and triglycerides.
Musini VM, Rezapour P, Wright JM, et al. Blood pressure lowering efficacy of **loop diuretics** for primary hypertension. Cochrane Database Syst Rev. 2012 Aug 15;8:CD003825. Based on the limited number of published RCTs, the systolic/diastolic blood pressure lowering effect of loop diuretics is modest (-8/-4 mmHg) and is likely an overestimate due to the high risk of bias in the included studies. There are no clinically meaningful BP lowering differences between different drugs within the loop diuretic class.
Musini VM, Tejani AM, Bassett K, et al. **Pharmacotherapy for hypertension in adults 60 years or older**. Cochrane Database Syst Rev. 2019 Jun 5;6:CD000028. Treating healthy adults 60 years or older with moderate to severe systolic and/or diastolic hypertension with antihypertensive drug therapy reduced all-cause mortality, cardiovascular mortality and morbidity, cerebrovascular mortality and morbidity, and coronary heart disease mortality and morbidity. Most evidence of benefit pertains to a primary prevention population using a thiazide as first-line treatment.
Musini VM, Tejani AM, Bassett K, Wright JM. Pharmacotherapy for **hypertension in the elderly**. Cochrane Database Syst Rev. 2009 Oct 7;(4):CD000028.
Myat A, Redwood SR, Qureshi AC, et al. **Resistant hypertension**. BMJ. 2012 Nov 20;345:e7473.
Myers Martin G, Godwin Marshall, Dawes Martin, et al. **Conventional versus automated measurement of blood pressure** in primary care patients with systolic hypertension: randomised parallel design controlled trial. BMJ 342:doi:10.1136/bmj.d286 (Published 7 Feb 2011).
Myers MG, Kaczorowski J, Dawes M, Godwin M. **Automated office blood pressure measurement** in primary care. Can Fam Physician. 2014 Feb;60(2):127-32.
Myers MG, Tobe SW. A **Canadian Perspective** on the Eighth Joint National Committee (**JNC 8**) Hypertension Guidelines. J Clin Hypertens (Greenwich). 2014 Apr;16(4):246-8.
Myers MG, Kaczorowski J, Paterson JM, et al. Thresholds for Diagnosing Hypertension Based on **Automated Office Blood Pressure Measurements** and Cardiovascular Risk. Hypertension. 2015 Sep;66(3):489-95.
Myers MG, Kaczorowski J. **Office blood pressure is lower than awake ambulatory blood pressure** at lower targets for treatment. J Clin Hypertens (Greenwich). 2017 Sep 24.
blood pressure in 2 trials. Acupuncture reduced blood pressure in 3 trials; in 1 of these it was no better than an invasive placebo. Melatonin was effective in 2 small trials, but caution is warranted in patients taking pharmacotherapy.
Myers MG, Asmar R, Staessen JA. Office blood pressure measurement in the 21st century. J Clin Hypertens (Greenwich). 2018 Jul;20(7):1104-1107.
Myers MG, Matangi M, Kaczorowski J. Comparison of **awake ambulatory blood pressure** and automated **office blood pressure** using linear regression analysis in untreated patients in routine clinical practice. J Clin Hypertens (Greenwich). 2018 Oct 16.
Naci H, Salcher-Konrad M, Dias S, et al. How does **exercise treatment compare with antihypertensive medications**? A network meta-analysis of 391 randomised controlled trials assessing exercise and medication effects on systolic blood pressure. Br J Sports Med. 2018 Dec 18.
Nagashima K, Katsurada T, Sakamoto N. A Case of **Olmesartan-associated Sprue-like Enteropathy**. Clin Gastroenterol Hepatol. 2017 Dec 13.
Naghavi M, Falk E, Hecht HS, et al. From vulnerable plaque to vulnerable patient: Part III. Introducing a new paradigm for the prevention of heart attack; identification and treatment of the asymptomatic vulnerable patient. Screening for Heart Attack Prevention and Education (SHAPE) task force report. Executive summary. *Am J Cardiol* 2006; DOI: 10.1016/j.amjcard.2006.03.002. Available at http://www.ajconline.org.
Nahas R. **Complementary and alternative** medicine approaches to blood pressure reduction: An evidence-based review. Can Fam Physician. 2008 Nov;54(11):1529-33. Evidence from systematic reviews supports the blood pressure–lowering effects of coenzyme Q10, polyphenol-rich dark chocolate, Qigong, slow breathing, and transcendental meditation. Vitamin D deficiency is associated with hypertension and cardiovascular risk; supplementation lowered
Narayan O, Davies JE, Hughes AD, et al. **Central Aortic Reservoir-Wave Analysis** Improves Prediction of Cardiovascular Events in Elderly Hypertensives. Hypertension. 2014 Dec 22.
Nerenberg KA, Zarnke KB, Leung AA, et al. **Hypertension Canada's 2018 guidelines for diagnosis, risk assessment, prevention, and treatment of hypertension in adults and children**. Can J Cardiol 2018; February 20, 2018.
Nathan HL,Duhig K, Hezelgrave NL, et al. **Blood pressure measurement in pregnancy**. The Obstetrician and Gynaecologist. 2015.
Nation DA, Edmonds EC, Bangen KJ, et al; Alzheimer's Disease Neuroimaging Initiative Investigators. **Pulse Pressure** in Relation to Tau-Mediated Neurodegeneration, Cerebral Amyloidosis, and Progression to **Dementia** in Very Old Adults. JAMA Neurol. 2015 Mar 30.
National High Blood Pressure Education Program Working Group on High Blood Pressure in **Children and Adolescents**. The fourth report on the diagnosis, evaluation, and treatment of high blood pressure in children and adolescents. Pediatrics. 2004 Aug;114(2 Suppl 4th Report):555-76.
Navar AM, Pencina MJ, Peterson ED. Assessing **Cardiovascular Risk** to Guide Hypertension Diagnosis and Treatment. JAMA Cardiol. 2016 Sep 7.
Navar-Boggan AM, Pencina MJ, Williams K, et al. Proportion of **US Adults Potentially Affected by the 2014 Hypertension Guideline**. JAMA. 2014 Mar 29.
Nazarzadeh M, Pinho-Gomes AC, Smith Byrne K, et al. Systolic Blood Pressure and **Risk of Valvular Heart Disease**: A Mendelian Randomization Study. JAMA Cardiol. 2019 Jul 10
Nazer B, Humphreys BD, Moslehi J. Effects of novel **angiogenesis inhibitors** for the treatment of cancer on the cardiovascular system: focus on hypertension. Circulation. 2011 Oct 11;124(15):1687-91.
NCD Risk Factor Collaboration (**NCD-RisC**). **Worldwide trends in blood pressure from 1975 to 2015**: a pooled analysis of 1479 population-based measurement studies with 19·1 million participants. Lancet 2016; online Nov 15.
Newton JL, Frith J. The **efficacy of nonpharmacologic intervention for orthostatic hypotension** associated with aging. Neurology. 2018 Jul 13.
NICE: Hypertensive disorders during pregnancy Aug/10 http://guidance.nice.org.uk/CG/Wave15/10 (Visintin C, Mugglestone MA, Almerie MQ, et al. Guideline Development Group. Management of hypertensive disorders during pregnancy: summary of NICE guidance. BMJ. 2010 Aug 25;341:c2207. doi: 10.1136/bmj.c2207).
NICE: National Institute for Health and Clinical Excellence. **Hypertension Guidelines**. Aug 2011. http://www.nice.org.uk/nicemedia/live/13561/56015/56015.pdf

Nicholls SJ, Bakris GL, Kastelein JJP, et al. Effect of **aliskiren** on progression of coronary disease in patients with **prehypertension: the AQUARIUS** randomized clinical trial. JAMA. doi:10.1001/jama.2013.277169.
Nielsen OW, Sajadieh A, Sabbah M, et al. Assessing Optimal Blood Pressure in Patients With **Asymptomatic Aortic Valve Stenosis**: The Simvastatin Ezetimibe in Aortic Stenosis Study (SEAS). Circulation. 2016 Aug 9;134(6):455-68.
Niiranen TJ, et al. A comparison of **home measurement** and **ambulatory monitoring** of blood pressure in the adjustment of antihypertensive treatment. Am J Hypertens. 2006 May;19(5):468-74.
Niiranen TJ, Asayama K, Thijs L, et al; **IDHOCO** Investigators. **Optimal number of days for home blood pressure measurement**. Am J Hypertens. 2015 May;28(5):595-603.
Niiranen TJ, McCabe EL, Larson MG, et al. **Heritability and risks associated with early onset hypertension**: multigenerational, prospective analysis in the Framingham Heart Study. BMJ. 2017 May 12;357:j1949.
Niiranen TJ, Larson MG, McCabe EL, et al. Prognosis of **Prehypertension Without Progression to Hypertension**. Circulation. 2017 Sep 26;136(13):1262-1264.
Niiranen TJ, Henglin M, Claggett Bet al. **Trajectories of Blood Pressure Elevation Preceding Hypertension Onset**: An Analysis of the Framingham Heart Study Original Cohort. JAMA Cardiol. 2018 Mar 21.
Nishiwaki M, Hosoai H, Ikewaki K, et al; ABC Study Group. Efficacy and Effects on Lipid Metabolism of Combination Treatment With **Losartan + Hydrochlorothiazide** Versus **Losartan + Amlodipine**: A 48-Week Prospective, Multicenter, Randomized, Open-Label Trial. Clin Ther. 2013 Mar 12.
Nobles CJ, Mendola P, Mumford SL, et al. **Preconception Blood Pressure Levels** and Reproductive Outcomes in a Prospective Cohort of Women Attempting Pregnancy. Hypertension. 2018 Apr 2.
O'Brien E, Parati G, Stergiou G. **Ambulatory blood pressure measurement**: what is the international consensus? Hypertension. 2013 Dec;62(6):988-94
O'Gara PT. Management of Hypertension in Patients With **Mild to Moderate Aortic Stenosis**: Navigating the SEAS. Circulation. 2016 Aug 9;134(6):469-71.
Oakeshott P, Chappell LC. Management of a **new pregnancy** in a woman with chronic hypertension. BMJ. 2016 Jun 6;353:i1497.
Odden MC, Peralta CA, Haan MH, Covinsky KE. Rethinking the association of high **blood pressure with mortality in elderly** adults. The impact of frailty. Arch Intern Med 2012.
Odden MC, Peralta CA, Berlowitz DR,et al. Effect of **Intensive Blood Pressure Control on Gait Speed** and Mobility Limitation in Adults 75 Years or Older: A Randomized Clinical Trial. (Sprint) JAMA Intern Med. 2017 Feb 6.
Ogedegbe GO, Boutin-Foster C, Wells MT, et al. A randomized controlled trial of **positive affect intervention** and medication adherence in hypertensive African-Americans. *Arch Intern Med*. doi:10.1001/archinternmed.2011.1307.
Ogedegbe G, Plange-Rhule J, Gyamfi J, et al. Health insurance coverage with or without a nurse-led task shifting **strategy for hypertension control**: A pragmatic cluster randomized trial in Ghana. PLoS Med. 2018 May 1;15(5):e1002561.
Ogedegbe G, Tobin JN, Fernandez S, et al. **Counseling African Americans to Control Hypertension**: cluster randomized clinical trial main effects. (CAATCH) Circulation. 2014;129:2044–2051.
Ogliari G, Westendorp RG, Muller M, et al. **Blood pressure and 10-year mortality risk in the Milan Geriatrics 75+ Cohort** Study: role of **functional and cognitive status**. Age Ageing 2015;44:932-7.
Oh GC, Han JK, Han KH, et alS. Efficacy and Safety of Fixed-dose Combination Therapy With **Telmisartan and Rosuvastatin** in Korean Patients With Hypertension and Dyslipidemia: TELSTA-YU (TELmisartan-rosuvaSTAtin from YUhan), a Multicenter, Randomized, 4-Arm, Double-blind, Placebo-controlled, Phase III Study. Clin Ther. 2018 Apr 16.
Ohkubo T, Kikuya M, Metoki H, et al. Prognosis of "masked" hypertension & "white-coat" hypertension detected by 24-h **ambulatory blood pressure monitoring** 10-year follow-up from the Ohasama study. J Am Coll Cardiol.2005 Aug 2;46(3):508-15. (InfoPOEMs: Using 24-hour ambulatory blood pressure monitoring as the standard, some patients will have white-coat hypertension (that is, higher blood pressures in the office than at home) and some will also have masked hypertension as a result of lower blood pressure measurements in the office. White-coat hypertension does not confer added risk, but masked hypertension underestimates a patient's risk. Evidence is accumulating that blood pressure should be measured at home, either with a 24-hour monitor or via self-monitoring (J Am Coll Cardiol 2005;46:743-51), before labeling someone as hypertensive and treating them accordingly. (LOE = 2b))
Oishi E, Ohara T, Sakata S, et al. Day-to-Day **Blood Pressure Variability** and Risk of **Dementia** in a General Japanese Elderly Population: The **Hisayama** Study. Circulation. 2017 Aug 8;136(6):516-525
Ojji DB, Mayosi B, Francis V, et al; CREOLE Study Investigators. **Comparison of Dual Therapies** for Lowering Blood Pressure in Black Africans. N Engl J Med. 2019 Mar 18.
Okin PM, et al. Regression of electrocardiographic left ventricular hypertrophy and decreased incidence of **new-onset atrial fibrillation** in patients with hypertension. (**LIFE** trial)JAMA. 2006 Sep 13;296(10):1242-8.
Okin PM, et al.; LIFE Study Investigators. **Electrocardiographic strain** pattern and prediction of new-onset congestive heart failure in hypertensive patients: the Losartan Intervention for Endpoint Reduction in Hypertension (LIFE) study. Circulation. 2006 Jan 3;113(1):67-73. Epub 2005 Dec 19.
Okin PM, et al. Impact of Diabetes Mellitus on Regression of Electrocardiographic Left Ventricular Hypertrophy and the Prediction of Outcome During Antihypertensive Therapy. The Losartan Intervention For Endpoint (LIFE) eduction in Hypertension Study. Circulation. 2006 Mar 13; [Epub ahead of print]
Okin PM, Hille DA, Larstorp AC, et al. Effect of **Lower On-Treatment Systolic Blood Pressure on the Risk of Atrial Fibrillation** in Hypertensive Patients. Hypertension. 2015 Aug;66(2):368-73.
Olde Engberink RH, et al. Blood pressure lowering effects of **sulodexide** depend on albuminuria severity: Post hoc analysis of the sulodexide microalbuminuria and macroalbuminuria studies. Br J Clin Pharmacol. 2016 Jul 14.
Omran D, Majumdar SR, Johnson JA, et al. **Pharmacists on primary care teams**: Effect on antihypertensive **medication management** in patients with type 2 diabetes. J Am Pharm Assoc (2003). 2015 May 1;55(3):265-8.
Oparil S, Lewis CE. Should Patients With Cardiovascular Risk Factors Receive **Intensive Treatment** of Hypertension to < 120/80 mmHg Target?: A Protagonist View from **SPRINT**. Circulation. 2016 Sep 12.
Orbach H, Matok I, Gorodischer R, et al. **Hypertension and antihypertensive drugs in pregnancy** and perinatal outcomes. Am J Obstet Gynecol. 2012 Nov 15.
Ortiz E, James PA. Let's Not **SPRINT** to Judgment About **New Blood Pressure** Goals. Ann Intern Med. 2016 Feb 23.
Østergaard Pedersen J, Heitmann B L, Schnohr P, and Grønbæk M. The combined influence of leisure-time **physical activity and weekly alcohol** intake on fatal ischaemic heart disease and all-cause mortality. Eur Heart J 2008; DOI:10.1093/eurheartj/ehm574.
Osranek M, Bursi F, Bailey KR, et al. **Left atrial volume** predicts cardiovascular events in patients originally diagnosed with lone atrial fibrillation: three-decade follow-up. Eur Heart J. 2005 Dec;26(23):2556-61. Epub 2005 Sep 1.
Ott C, Mahfoud F, Schmid A, et al. **Renal denervation** in moderate treatment-resistant hypertension. J Am Coll Cardiol. 2013 Nov 12;62(20):1880-6.
Owan TE, et al. Trends in prevalence and outcome of **heart failure** with **preserved ejection fraction**. N Engl J Med. 2006 Jul 20;355(3):251-9.
Ovbiagele B, Diener H-C, Yusuf S, et al; **PROFESS** Investigators. Level of **systolic blood pressure** within the normal range and risk of recurrent **stroke**. JAMA. 2011;306(19):2137-2144.
Oveisgharan S, Hachinski V. **Hypertension**, executive dysfunction, and progression to **dementia**: the Canadian study of health and aging. Arch Neurol 2010; 67:187-192.
Oza R, Garcellano M. **Nonpharmacologic management of hypertension**: what works? Am Fam Physician. 2015 Jun 1;91(11):772-6.
Ozone S, Shaku F, Sato M, et al. **Comparison of blood pressure measurements on the bare arm**, over a sleeve and over a rolled-up sleeve in the elderly. Fam Pract. 2016 Oct;33(5):517-22.
Pacak K. Preoperative management of the **pheochromocytoma** patient. J Clin Endocrinol Metab 2007;92:4069-4079.
Padwal RS, Rabkin S, Khan N. Assessment and management of **resistant hypertension**. CMAJ. 2014 Dec 9;186(18):E689-E697.
Padwal R, Hackam D, Khan N, Tobe S. **Primary prevention of CVD**: modification of **diet** in people with hypertension. BMJ Clin Evid. 2016 Jan 5;2016.
Padwal R, Rabi DM, Schiffrin EL. Recommendations for **Intensive Blood Pressure Lowering in High-Risk Patients**, the **Canadian Viewpoint**. Hypertension. 2016 May 9.
Palmer SC, Mavridis D, Navarese E, et al. Comparative efficacy and safety of **blood pressure-lowering agents in adults with diabetes and kidney disease**: a network meta-analysis. Lancet 2015; 385: 2047–56.
Paoletti E, Bellino D, Marsano L, et al. Effects of **ACE inhibitors on long-term** outcome of **renal transplant recipients**: a randomized controlled trial. Transplantation. 2013 Mar 27;95(6):889-95.
Panagiotakos DB, et al. The Relation Between Pulse Pressure & Cardiovascular Mortality in 12 763 Middle-aged Men From Various Parts of the World: A 25-Year Follow-up of the Seven Countries Study. Arch Intern Med. 2005 Oct 10;165(18):2142-7. CONCLUSIONS: Pulse pressure followed by diastolic and systolic blood pressures were the best predictors for CVD mortality among other blood pressures, as well as age, physical activity, total serum cholesterol level, anthropometric indexes, and smoking habits. No significant differences were observed among the different populations studied.
Pancholy SB, Shantha GP, Patel TM, et al. Meta analysis of the effect of **renal denervation** on blood pressure and pulse pressure in patients with resistant systemic hypertension. Am J Cardiol. 2014 Sep 15;114(6):856-61.
Pantell MS, Prather AA, Downing JM, et al. Association of **Social and Behavioral Risk Factors** With Earlier Onset of Adult Hypertension and Diabetes. JAMA Netw Open. 2019 May 3;2(5):e193933.
Pappaccogli M, Di Monaco S, Perlo E, et al. **Comparison of Automated Office Blood Pressure With Office and Out-Off-Office Measurement Techniques**. Hypertension. 2019 Feb;73(2):481-490.
Parati G, Ochoa JE, Bilo G. **Renal sympathetic denervation** and daily life blood pressure in resistant hypertension: simplicity or complexity? Circulation. 2013 Jul 23;128(4):315-7.
Parikh NI, Norberg M, Ingelsson E, et al. Association of **Pregnancy Complications** and Characteristics With Future Risk of Elevated Blood Pressure: The Västerbotten Intervention Program. Hypertension. 2017 Jan 30.
Park B, Lee HA, Lee SH, et al. Association Between Serum Levels of **Uric Acid and Blood Pressure** Tracking in Childhood. Am J Hypertens. 2017 Mar 14.
Park S, Choi NK. **Breastfeeding and Maternal Hypertension**. Am J Hypertens. 2018 Jan 25.
Parker ED, Margolis KL, Trower NK, et al. Comparative Effectiveness of 2 β-Blockers (**atenolol vs metoprolol**) in Hypertensive Patients. Arch Intern Med. 2012 Aug 27:1-7.
Parker ED, Sinaiko AR, Kharbanda EO, et al. Change in **Weight Status** and Development of Hypertension. Pediatrics. 2016 Feb 19.

Parving HH, Brenner BM, McMurray JJ, et al; the **ALTITUDE** Investigators. Cardiorenal End Points in a Trial of **Aliskiren for Type 2 Diabetes**. N Engl J Med. 2012 Nov 3.
Pase MP, Grima N, Cockerell R, et al. Habitual intake of **fruit juice** predicts central blood pressure. Appetite. 2014 Sep 30.
Patel A; ADVANCE Collaborative Group, MacMahon S, Chalmers J, Neal B, et al. Effects of a fixed combination of perindopril and indapamide on macrovascular and microvascular outcomes in patients with type 2 diabetes mellitus (the **ADVANCE** trial): a randomised controlled trial. Lancet. 2007 Sep 8;370(9590):829-40. Routine administration of a fixed combination of perindopril and indapamide to patients with type 2 diabetes was well tolerated and reduced the risks of major vascular events, including death. Although the confidence limits were wide, the results suggest that over 5 years, one death due to any cause would be averted among every 79 patients assigned active therapy. (InfoPOEMs: Perindopril (Aceon) plus indapamide (Lozol) is better than placebo in decreasing clinically relevant events in patients with type 2 diabetes who are at high risk of cardiovascular complications. Whether the combination is better than other medications -- like aspirin -- isn't addressed by this study. (LOE = 1b))
Patel KK, Young L, Howell EH, et al. Characteristics and outcomes of patients presenting with **hypertensive urgency** in the office setting [published online June 13, 2016].JAMA Intern Med. doi:10.1001/jamainternmed.2016.1509
Patel KK, et al. **Personalizing the Intensity of Blood Pressure Control**: Modeling the Heterogeneity of Risks and Benefits From **SPRINT** (Systolic Blood Pressure Intervention Trial). Circ Cardiovasc Qual Outcomes. 2017 Apr;10(4).
Paulose-Ram R, Gu Q, Kit B. **Characteristics of US adults with hypertension** who are unaware of their hypertension, 2011–2014. NCHS Data Brief 278, April 2017.
Pavy B, et al. Safety of **Exercise Training** for Cardiac Patients: Results of the French Registry of Complications During Cardiac Rehabilitation. Arch Intern Med. 2006 Nov 27;166(21):2329-2334.
Pazoki R, Dehghan A, Evangelou E, et al. **Genetic predisposition** to high blood pressure **and lifestyle factors**: associations with midlife blood pressure levels and cardiovascular events. Circulation. 2018;137:653–661.
Pearce LA, McClure LA, Anderson DC, et al, for the SPS3 Investigators. Effects of **long-term blood pressure** lowering and **dual antiplatelet** treatment on **cognitive function** in patients with recent **lacunar stroke**: a secondary analysis from the **SPS3** randomised trial. Lancet Neurol 2014; online Oct 24. http://dx.doi.org/10.1016/S1474-4422(14)70224-8.
Pedrosa RP, Drager LF, de Paula LK, et al. Effects of **OSA treatment** on BP in patients with resistant hypertension: a randomized trial. Chest. 2013 Nov;144(5):1487-94.
Peila R, et al. Reducing the risk of **dementia**: efficacy of long-term treatment of hypertension. Stroke. 2006 May;37(5):1165-70. Epub 2006 Apr 6.
Pels A, Mol BWJ, Singer J, et al; **CHIPS** Study Group. Influence of Gestational Age at Initiation of Antihypertensive Therapy: Secondary Analysis of CHIPS Trial Data (Control of Hypertension in Pregnancy Study). Hypertension. 2018 Jun;71(6):1170-1177.
Peng AW, Juraschek SP, Appel LJ, et al. Effects of the **DASH Diet and Sodium Intake on Bloating**: Results From the DASH-Sodium Trial. Am J Gastroenterol. 2019 Jun 17.
Peng M, Chen G, Tang KL, et al. **Blood pressure at age 60-65 versus age 70-75 and vascular dementia**: a population based observational study. BMC Geriatr. 2017 Oct 27;17(1):252.
Peralta CA, Norris KC, Li S, et al. Blood Pressure Components **and End-stage Renal Disease** in Persons With Chronic Kidney Disease: The Kidney Early Evaluation Program (**KEEP**). Arch Intern Med. 2012 Jan 9;172(1):41-47.
Peralta CA, McClure LA, Scherzer R, et al. Effect of **intensive versus usual blood pressure** control on kidney function among individuals with **prior lacunar stroke**: a post hoc analysis of the secondary prevention of small subcortical strokes (**SPS3**) randomized trial. Circulation. 2016;133:584–591.
Percutaneous Coronary Intervention: ACC/AHA/SCAI 2005 Guideline Update for (Update of the 2001 PCI Guidelines) (J Am Coll Cardiol, January 3, 2006 issue; Vol/Page Numbers pending) http://www.acc.org/clinical/guidelines/percutaneous/update/index.pdf
Perez M, Musini V. Pharmacological interventions for **hypertensive emergencies**. Cochrane Database Syst Rev. 2008 Jan 23;(1):CD003653. There is no RCT evidence demonstrating that anti-hypertensive drugs reduce mortality or morbidity in patients with hypertensive emergencies. Furthermore, there is insufficient RCT evidence to determine which drug or drug class is most effective in reducing mortality and morbidity. There were some minor differences in the degree of blood pressure lowering when one class of antihypertensive drug is compared to another. However, the clinical significance is unknown.
Perez MI, Musini VM, Wright JM. Effect of early treatment with **anti-hypertensive drugs on short and long-term mortality in patients with an acute cardiovascular event.** Cochrane Database Syst Rev. 2009 Oct 7;(4):CD006743. Nitrates reduce mortality (4-8 deaths prevented per 1000) at 2 days when administered within 24 hours of symptom onset of an acute myocardial infarction. No mortality benefit was seen when treatment continued beyond 48 hours. Mortality benefit of immediate treatment with ACE inhibitors post MI at 2 days did not reach statistical significance but the effect was significant at 10 days (2-4 deaths prevented per 1000). There is good evidence for lack of a mortality benefit with immediate or short-term treatment with beta-blockers and calcium channel blockers for acute myocardial infarction.
Peripheral Arterial Disease: ACC/AHA Guidelines for the Management of Patients With (Lower Extremity, Renal, Mesenteric, and Abdominal Aortic); A Collaborative Report From the AAVS/SVS, SCAI, SIR, SVMB, and the ACC/AHA Task Force on Practice Guidelines http://www.acc.org/clinical/guidelines/pad/summary.pdf (Abramson BL, et al.; **Canadian Cardiovascular Society**. Canadian Cardiovascular Society Consensus Conference: peripheral arterial disease - executive summary. Can J Cardiol. 2005 Oct;21(12):997-1006.)
Perk J, De Backer G, Gohlke H, et al. **European guidelines (ESC) on cardiovascular disease** in clinical practice (version 2012). Eur Heart J2012; DOI:10.1093/eurheartj/ehs092.
Perk J, De Backer G, Gohlke H, Graham I, et al. **European (ESC) guidelines on cardiovascular disease prevention** in clinical practice (version 2012). Eur Heart J. 2012 Jul;33(13):1635-701.
Perreault S, Yu AY, Côté R, et al. **Adherence to antihypertensive** agents after ischemic stroke and risk of cardiovascular outcomes. Neurology. 2012 Nov 13;79(20):2037-43.
Persaud N, Bedard M, Boozary AS, et al;(CLEAN Meds) Study Team. Effect on Treatment **Adherence of Distributing Essential Medicines at No Charge**: The CLEAN Meds Randomized Clinical Trial. JAMA Intern Med. 2019 Oct 7. doi: 10.1001/jamainternmed.2019.4472.
Persell SD, Karmali KN, Lazar D, et al. Effect of Electronic Health Record-Based Medication Support and Nurse-Led **Medication Therapy Management on Hypertension and Medication Self-management**: A Randomized Clinical Trial. JAMA Intern Med. 2018 Jul 9.
Peters SA, Huxley RR, Woodward M. Comparison of the **Sex-Specific Associations Between Systolic Blood Pressure** and the Risk of Cardiovascular Disease: A Systematic Review and Meta-Analysis of 124 Cohort Studies, Including 1.2 Million Individuals. Stroke. 2013 Jul 2.
Petersen LA, Simpson K, Pietz K, et al. Effects of individual physician-level and practice-level **financial incentives** on hypertension care. A randomized trial. JAMA 2013.
Petersen NH, Silverman A, Wang A, et al. Association of **Personalized Blood Pressure Targets With Hemorrhagic Transformation** and Functional Outcome After Endovascular Stroke Therapy. JAMA Neurol. 2019 Jul 29.
Pfeffer MA, McMurray JJ. Lessons in **Uncertainty and Humility - Clinical Trials Involving Hypertension**. N Engl J Med. 2016 Nov 3;375(18):1756-1766.
Pharmacists Letter. **New Blood Pressure Goal for Coronary Artery Disesease**. Aug 2007.
Phillips RA. Hypertension **Treatment and Outcomes in the Era of Population Health**, Coordinated Care, and Medicare Access and CHIP Reauthorization Act (MACRA). Circulation. 2017 Apr 25;135(17):1629-1631. (**Sprint**)
Phillips RA, Xu J, Peterson LE, et al. Impact of Cardiovascular Risk on the **Relative Benefit and Harm of Intensive Treatment of Hypertension**. J Am Coll Cardiol. 2018 Mar 2.
Pickering TG, Shimbo D, Haas D. **Ambulatory blood-pressure monitoring**. N Engl J Med. 2006 Jun 1;354(22):2368-74.
Pickering TG, Houston-Miller N, Ogedegbe G, et al. Call to action on use and reimbursement for **home blood pressure monitoring**. Hypertension 2008; DOI: 10.1161/hypertensionaha.107.189010.
Picone DS, Schultz MG, Otahal P, et al. Accuracy of **Cuff-Measured Blood Pressure**: Systematic Reviews and Meta-Analyses. J Am Coll Cardiol. 2017 Aug 1;70(5):572-586
Picone DS, Schultz MG, Peng X, et al. Discovery of New Blood Pressure Phenotypes and Relation to Accuracy of **Cuff Devices** Used in Daily Clinical Practice. Hypertension. 2018 Apr 9.
Piepoli MF, Hoes AW, Agewall S, et al. **2016 European Guidelines on cardiovascular disease prevention in clinical practice**: The Sixth Joint Task Force of the European Society of Cardiology and Other Societies on Cardiovascular Disease Prevention in Clinical Practice(constituted by representatives of 10 societies and by invited experts)Developed with the special contribution of the European Association for Cardiovascular Prevention & Rehabilitation (EACPR). Eur Heart J. 2016 Aug 1;37(29):2315-81.
Pierdomenico SD, Pierdomenico AM, Coccina F, et al. **Ambulatory Blood Pressure Parameters and Heart Failure** With Reduced or Preserved Ejection Fraction in Elderly Treated Hypertensive Patients. Am J Hypertens. 2016 Mar 18.
Piller LB, Baraniuk S, Simpson LM, et al. Long-term follow-up of participants with **heart failure** in the Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial (**ALLHAT**). Circulation. 2011;124:1811–1818.
PILL Collaborative Group (2011) An International Randomised Placebo-Controlled Trial of a Four-Component Combination Pill (‘‘**Polypill’’**) in People with Raised Cardiovascular Risk. PLoS ONE 6(5): e19857. doi:10.1371/journal.pone.0019857.
Pimenta E, Gaddam KK, Oparil S, et al. Effects of **Dietary Sodium Reduction** on Blood Pressure in Subjects With Resistant Hypertension. Results From a Randomized Trial. Hypertension. 2009 Jul 20. [Epub ahead of print]
Pimenta E and Calhoun DA. **Resistant hypertension**: Incidence, prevalence and prognosis. Circulation 2012; DOI:10.1161/_CIRCULATIONAHA.112.097345.
Pinho-Gomes AC, Rahimi K**. Management of blood pressure in heart failure**. Heart. 2019 Jan 23.
Piper MA, Evans CV, Burda BU, et al. **Diagnostic and Predictive Accuracy of Blood Pressure Screening** Methods With Consideration of **Rescreening Intervals**: An Updated Systematic Review for the U.S. Preventive Services Task Force (**USPSTF**). Ann Intern Med. 2014 Dec 23.
Piper RJ, Kalyvas AV, Young AM, et al. Interventions for **idiopathic intracranial hypertension**. Cochrane Database Syst Rev. 2015 Aug 7;8:CD003434. Although the two included RCTs showed modest benefits for acetazolamide for some outcomes, there is insufficient evidence to recommend or reject the efficacy of this intervention, or any other treatments currently available, for treating people with IIH. Further high-quality RCTs are required in order to adequately assess the effect of acetazolamide therapy in people with IIH.
PK, Barzilay J, Cushman WC; ALLHAT Collaborative Research Group. Clinical outcomes in antihypertensive treatment of type 2 diabetes, impaired fasting glucose concentration, and normoglycemia: Antihypertensive and

Lipid-Lowering Treatment to Prevent Heart Attack Trial (ALLHAT). Arch Intern Med. 2005 Jun 27;165(12):1401-9.
Plante TB, Urrea B, MacFarlane ZT, et al. Validation of the Instant **Blood Pressure Smartphone App**. JAMA Intern Med. 2016 Mar 2.
Platek AE, Szymanski FM, Filipiak KJ, et al. Prevalence of **Hypertension** in **Professional Drivers** (From the **RACER-ABPM** Study). Am J Cardio. 2017.
Pocock SJ, Stone GW. The **Primary Outcome Is Positive - Is That Good Enough**? N Engl J Med. 2016 Sep 8;375(10):971-9. (Sprint results)
Polonsky TS, Bakris GL. **Ambulatory Blood Pressure** Monitoring. JAMA. 2018 Nov 6;320(17):1807-1808
Pool LR, Ning H, Wilkins J, et al. Use of **Long-term Cumulative Blood Pressure in Cardiovascular Risk Prediction Models**. JAMA Cardiol. 2018 Sep 5.
Poti JM, Dunford EK, Popkin BM. **Sodium reduction in US households' packaged food and beverage purchases**, 2000 to 2014 [online June 5, 2017].JAMA Intern Med. doi:10.1001 /jamainternmed.2017.1407
Potier L, Roussel R, Elbez Y, *et al*. **REACH Registry** Investigators. **Angiotensin-converting enzyme inhibitors and angiotensin receptor blockers in high vascular risk**. Heart2017;103:1310–2.
Pottegård A, Pedersen SA, Schmidt SAJ, et al. Association of **Hydrochlorothiazide Use and Risk of Malignant Melanoma**. JAMA Intern Med. 2018 May 29.
Pottegård A, Kristensen KB, Ernst MT, et al. Use of **N-nitrosodimethylamine (NDMA) contaminated valsartan products and risk of cancer**: Danish nationwide cohort study. BMJ. 2018 Sep 12;362:k3851.
Portegies ML, Mirza SS, Verlinden VJ, et al. **Mid- to Late-Life Trajectories** of Blood Pressure and the Risk of Stroke: The **Rotterdam** Study. Hypertension. 2016 Jun;67(6):1126-32.
Powers BJ, Olsen MK, Smith VA, et al. **Measuring blood pressure** for decision making and quality reporting: where and how many measures? Ann Intern Med. 2011;154:781-8.
Powers WJ, Clarke WR, Grubb RL Jr, et al., for the **COSS** Investigators. **Lower stroke risk** with lower blood pressure in hemodynamic cerebral ischemia. Neurology 2014;82:1027–1032.
Powles K, Gandhi S. **Postpartum hypertension**. CMAJ. 2017 Jul 10;189(27):E913.
Poulter NR, Prabhakaran D, Caulfield M. **Hypertension**. Lancet. 2015 Mar 27.
P**rospective Studies Collaboration**, Lewington S, Whitlock G, Clarke R, et al. Blood cholesterol and vascular mortality by age, sex, and blood pressure: a meta-analysis of individual data from 61 prospective studies with 55,000 vascular deaths. Lancet 2007;370(9602):1829-1839. This study reinforces what we already know: Higher cholesterol levels and blood pressure are each associated with an increased risk of vascular mortality. Be careful with these results; this kind of study doesn't tell us that lowering cholesterol levels and blood pressure will prevent deaths. For that, we'd need an intervention trial. (LOE = 1a)
Psaty BM, Weiss NS, Furberg CD. Recent trials in hypertension: compelling science or **commercial speech**? JAMA. 2006 Apr 12;295(14):1704-6.
Pursnani S, Korley F, Gopaul R, et al. **Percutaneous coronary intervention versus optimal medical therapy** in stable coronary artery disease: a systematic review and meta-analysis of randomized clinical trials. Circ Cardiovasc Interv. 2012 Aug 1;5(4):476-90.
Puttnam R, Davis BR, Pressel SL, et al; Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial (**ALLHAT**) Collaborative Research Group. Association of 3 different **antihypertensive medications with hip and pelvic fracture risk** in older adults: secondary analysis of a randomized clinical trial [online Nov 21, 2016].JAMA Intern Med. doi:10.1001 /jamainternmed.2016.6821 (**chlorthalidone** useful)
Qi WX, Shen Z, Lin F et al. Incidence and Risk of Hypertension with **Vandetanib** in Cancer Patients: A Systematic review and Meta-analysis of clinical trials. Br J Clin Pharmacol. 2012 Aug 10.
Qi WX, He AN, Shen Z, Yao Y. Incidence and Risk of hypertension with a novel multitargeted kinase inhibitor **axitinib** in cancer patients: a systematic review and meta-analysis. Br J Clin Pharmacol. 2013 Apr 25.
Qin B, Viera AJ, Muntner P, et al. **Visit-to-Visit Variability in Blood Pressure** Is Related to Late-Life **Cognitive Decline**. Hypertension. 2016 May 23.
Qaseen A, Fihn SD, Dallas P, et al. **Management of patients with stable ischemic heart disease**: Executive summary of a clinical practice guideline from the American College of Physicians, American College of Cardiology Foundation/American Heart Association/American Association for Thoracic Surgery/Preventive Cardiovascular Nurses Association/Society of Thoracic Surgeons. Ann Intern Med 2012; available at: http://annals.org.
Qaseem A, Wilt TJ, Rich R, et al. Pharmacologic treatment of **hypertension in adults aged 60 years or older to higher versus lower blood pressure targets**: a clinical practice guideline from the American College of Physicians (**ACP**) and the American Academy of Family Physicians (**AAFP**). Ann Intern Med. 2017. [Epub ahead of print]. doi:10.7326/M16-1785
Quan H, Chen G, Walker RL, et al. for Hypertension Outcome and Surveillance Team. Incidence, **cardiovascular complications and mortality** of hypertension by **sex and ethnicity**. Heart. 2013 Feb 12.
Qaseem A, Hopkins RH, Sweet DE, et al. **Screening, Monitoring, and Treatment of Stage 1 to 3 Chronic Kidney Disease**: A Clinical Practice Guideline From the Clinical Guidelines Committee of the American College of Physicians (**ACP**). Ann Intern Med. 2013 Oct 22.
Qureshi AI, Palesch YY, et al; **ATACH-2** Trial Investigators and the Neurological Emergency Treatment Trials Network. **Intensive Blood-Pressure Lowering in Patients with Acute Cerebral Hemorrhage**. N Engl J Med. 2016 Jun 8.
Rabi DM, Padwal R, Tobe SW, et al. Canadian Hypertensive Education Program and Canadian Diabetes Association. Risks and benefits of **intensive blood pressure lowering in patients with type 2 diabetes**. CMAJ. 2013 Aug 6;185(11):963-7.
Rabi DM, Padwal R. **Intensive lowering** of blood pressure: Should we **SPRINT**? CMAJ. 2016 Jul 4.
Raebel MA, Zeng C, et al. Risk of **Breast Cancer With Long-Term Use of Calcium Channel Blockers or Angiotensin-Converting Enzyme Inhibitors** Among Older Women. Am J Epidemiol. 2017 Feb 15;185(4):264-273.
Raheem IA, Saaid R, Omar SZ, et al. **Oral nifedipine versus intravenous labetalol** for acute blood pressure control in **hypertensive emergencies of pregnancy**: a randomised trial. BJOG. 2012 Jan;119(1):78-85.
Rahman M, et al. ALLHAT Collaborative Research Group. Cardiovascular outcomes in high-risk hypertensive patients stratified by baseline **glomerular filtration rate**. Ann Intern Med. 2006 Feb 7;144(3):172-80.
Rahman F, Al Rifai M, Blaha MJ, et al. Relation of **Diastolic Blood Pressure** and **Coronary** Artery **Calcium** to Coronary Events and Outcomes (From the Multi-Ethnic Study of Atherosclerosis). Am J Cardio. 2017.
Rahman F, McEvoy JW, Ohkuma T, et al. Effects of **Blood Pressure Lowering on Clinical Outcomes According to Baseline Blood Pressure** and Cardiovascular Risk in Patients With **Type 2 Diabetes Mellitus**. Hypertension. 2019 Apr 29:HYPERTENSIONAHA11812414.
Rajan KB, Barnes LL, Wilson RS, et al. **Blood pressure and risk of incident Alzheimer's disease dementia by antihypertensive medications and APOE ε4 allele**. Ann Neurol. 2018 Apr 10.
Rakotz MK, Townsend RR, Yang J, et al. **Medical students and measuring blood pressure**: Results from the American Medical Association Blood Pressure Check Challenge. J Clin Hypertens (Greenwich). 2017 Jun;19(6):614-619
Rapsomaniki E, Timmis A, et al. **Blood pressure and incidence of twelve cardiovascular diseases**: lifetime risks, healthy life-years lost, and age-specifi c associations in 1.25 million people. Lancet 2014; 383: 1899–911.
Rastas S, et al. Association Between Blood Pressure and Survival over 9 Years in a General Population **Aged 85 elderly and Older**. J Am Geriatr Soc. 2006 Jun;54(6):912-8.
Rao G. Diagnosis, Epidemiology, and Management of Hypertension in **Children**. Pediatrics. 2016 Aug;138(2).
Ravenell J, Shimbo D, Booth JN 3rd, et al. **Thresholds for ambulatory blood pressure among African Americans** in the **Jackson Heart Study**. Circulation. 2017;135:2470–2480.
Ravindrarajah R, Hazra NC, Hamada S, et al. **Systolic Blood Pressure Trajectory, Frailty, and All-Cause Mortality >80 Years of Age**: Cohort Study Using Electronic Health Records. Circulation. 2017 Jun 13;135(24):2357-2368.
Rawlings AM, Juraschek SP, Heiss G, et al. Association of **orthostatic hypotension with incident dementia, stroke, and cognitive decline**. Neurology. 2018 Jul 25.
Ray JG, Vermeulen MJ, Schull MJ, Redelmeier DA. Cardiovascular health after **maternal placental syndromes** (CHAMPS): population-based retrospective cohort study. Lancet. 2005 Nov 19;366(9499):1797-803.
Reboldi G, Gentile G, Angeli F, et al. Effects of **intensive blood pressure reduction on myocardial infarction and stroke in diabetes**: a meta-analysis in 73 913 patients. J Hypertens 2011; 29:1253-1269.
Reboussin DM, Allen NB, Griswold ME, et al. **Systematic Review** for the **2017 ACC/AHA**/AAPA/ABC/ACPM/AGS/APhA/ASH/ASPC/NMA/PCNA Guideline for the Prevention, Detection, Evaluation, and **Management of High Blood Pressure** in Adults: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. J Am Coll Cardiol. 2017 Nov 7
Redon J, Lurbe E. **Ambulatory blood pressure monitoring** is ready to replace clinic blood pressure in the diagnosis of hypertension: con side of the argument. Hypertension. 2014 Dec;64(6):1169-74.
Redwine KM AA, Poffenbarger T, Portman RJ, Samuels J. Development of hypertension among **adolescents with pre-hypertension**. J Pediatr 2011.
Retnakaran R, Wen SW, et al. **Maternal Blood Pressure** Before Pregnancy and Sex of the Baby: A Prospective Preconception Cohort Study. Am J Hypertens. 2017 Jan 5.
Richards TR, Tobe SW. **Combining Other Antihypertensive Drugs With β-Blockers** in Hypertension: A Focus on Safety and Tolerability. Can J Cardiol. 2014 Feb 8. pii: S0828-282X(13)01367-6.
Richey M, Chang A, Powers C, et al. Vital signs: disparities in antihypertensive medication **nonadherence** among Medicare Part D beneficiaries—United States, 2014. *MMWR Morb Mortal Wkly Rep* 2016;.
Richman IB, Fairley M, Jørgensen ME, et al. **Cost-effectiveness of Intensive Blood Pressure Management**. JAMA Cardiol. 2016 Sep 14.
Ried K, Sullivan T, Fakler P, Frank OR, Stocks NP. Does **chocolate** reduce blood pressure? A meta-analysis. BMC Med 2010;8:39.
Ried K, Sullivan TR, Fakler P et al. Effect of **cocoa** on blood pressure. Cochrane Database of Systematic Reviews 2012, Issue 8. Art. No.: CD008893. DOI: 10.1002/14651858.CD008893.pub2. Flavanol-rich chocolate and cocoa products may have a small but statistically significant effect in lowering blood pressure by 2-3 mm Hg in the short term.
Riegel G, Moreira LB, Fuchs SC, et al. Long-term effectiveness of non-drug recommendations to treat hypertension in a clinical setting. Am J Hypertens 2012; 11:1202-1208. (low salt & calorie)
Riis J, Nordestgaard BG, Jensen GB, Afzal S. **Secular trends in risk of stroke** according to body mass index and blood pressure, 1976-2017. Neurology. 2019 Oct 1;93(14):e1397-e1407.

Riley M. **High Blood Pressure in Children and Adolescents**. Am Fam Physician. 2012 Apr 1;85(7):693-700.
Riley M, Hernandez AK. Kuznia AL. High Blood Pressure in **Children and Adolescents**. Am Fam Physician. 2018; 98(8):486-494.
Rim MY et al. The effect of renin-angiotensin-aldosterone system blockade **(ACEI,ARB) on contrast-induced acute kidney injury**: A propensity-matched study. Am J Kidney Dis 2012 Oct; 60:576.
Rimoldi SF, Messerli FH, Bangalore S, et al. **Resistant hypertension**: what the cardiologist needs to know. Eur Heart J. 2015 Aug 10.
Rinfret F, Cloutier L, Wistaff R, et al. **Comparison of Different Automated Office Blood Pressure Measurement Devices**: Evidence of Nonequivalence and Clinical Implications. Can J Cardiol. 2017 Dec;33(12):1639-1644.
Ringrose JS, Polley G, McLean D, et al An Assessment of the Accuracy of **Home Blood Pressure Monitors** When Used in Device Owners. Am J Hypertens. 2017 Apr 19.
Ringrose JS, Cena J, Ip S, et al. Comparability of **Automated Office Blood Pressure to Daytime 24-Hour Ambulatory Blood Pressure**. Can J Cardiol. 2018 Jan;34(1):61-65.
Ripley TL, Saseen JJ**. β-Blockers**: A Review of Their Pharmacological and Physiological Diversity in Hypertension. Ann Pharmacother. 2014 Jun;48(6):723-33.
Ritchey MD, Loustalot F, Bowman BA, Hong Y. **Trends in mortality** rates by subtypes of heart disease in the United States, 2000-2010. JAMA. 2014 Nov 19;312(19):2037-9.
Ritter J M. Therapeutics: **Angiotensin converting enzyme inhibitors and angiotensin receptor blockers in hypertension**. BMJ 2011;342:doi:10.1136/bmj.d1673 (Published 7 April 2011)
Robinson TG, Potter JF, Ford GA, et al. Effects of antihypertensive treatment after acute stroke in the Continue or Stop **Post-Stroke** Antihypertensives Collaborative Study (**COSSACS**): a prospective, randomised, open, blinded-endpoint trial. Lancet Neurol. 2010 Aug;9(8):767-75.
Robitaille C, Dai S, Waters C, et al. **Diagnosed hypertension in Canada**: incidence, prevalence and associated mortality. CMAJ. 2011 Nov 21.
Rocco MV, Sink KM, et al; SPRINT Research Group. Effects of **Intensive Blood Pressure Treatment on Acute Kidney Injury Events** in the Systolic Blood Pressure Intervention Trial (**SPRINT**). Am J Kidney Dis. 2017 Nov 18.
Rodriguez-Leyva D, Weighell W, Edel AL, et al. Potent antihypertensive action of **dietary flaxseed** in hypertensive patients. Hypertension. 2013 Dec;62(6):1081-9
Rodriguez-Mateos A, Istas G, Boschek L, et al. **Circulating anthocyanin metabolites mediate vascular benefits of blueberries**: insights from randomized controlled trials, metabolomics, and nutrigenomics. J Gerontol A Biol Sci Med Sci. 2019 Feb 16.
Rodriguez-Torres A, Murphy M, Kourkoulis C, et al. **Hypertension and intracerebral hemorrhage** recurrence among white, black, and Hispanic individuals. Neurology. 2018 Jul 3;91(1):e37-e44.
Rodriguez CJ, Swett K, Agarwal SK, et al. **Systolic blood pressure levels** and incident cardiovascular events in patients with hypertension: the Atherosclerosis Risk in Communities Study [online June 16, 2014]. JAMA Intern Med. doi:10.1001/jamainternmed.2014.2482.
Roerecke M, Kaczorowski J, Myers MG. Comparing Automated Office Blood Pressure Readings With Other Methods of Blood Pressure Measurement for **Identifying Patients With Possible Hypertension**: A Systematic Review and Meta-analysis. JAMA Intern Med. 2019 Feb 4.
Roerecke M, Kaczorowski J, Tobe SW, et al. The effect of a **reduction in alcohol consumption on blood pressure**: a systematic review and meta-analysis. *Lancet Public Health* 2017.
Roger VL, Go AS, Lloyd-Jones DM, et al. American Heart Association Statistics Committee and Stroke Statistics Subcommittee. **Heart disease and stroke statistics**—2011 update: a report from the American Heart Association. Circulation. 2011;123:e18 – e209.
Roger V, Go A, Lloyd-Jones DM, et al. **Heart disease and stroke statistics**—**2012 update**. A report from the American Heart Association. Circulation 2012; DOI: 10.1161/CIR.0b013e31823ac046.
Romero-Ortuno R, Cogan L, et al. Continuous noninvasive **orthostatic blood pressure** measurements and their relationship with orthostatic intolerance, falls, and frailty in **older** people. J Am Geriatr Soc. 2011 Apr;59(4):655-65.
Rosendorff C, Black HR, Cannon CP, et al. Treatment of hypertension in the prevention and management of ischemic heart disease: A scientific statement from the **American Heart Association Council for High Blood Pressure** Research and the Councils on Clinical Cardiology and Epidemiology and Prevention. *Circulation* 2007; 2007; 115:2761-2788.
Rosendorff C, Lackland DT, Allison M, et al. **Treatment of Hypertension in Patients With Coronary Artery Disease**: A Scientific Statement From the American Heart Association (**AHA**), American College of Cardiology (**ACC**) , and American Society of Hypertension (**ASH**). Circulation. 2015 Mar 31.
Roshandel G, Khoshnia M, Poustchi H, et al. Effectiveness of **polypill for primary and secondary prevention** of cardiovascular diseases (PolyIran): a pragmatic, cluster-randomised trial. Lancet. 2019 Aug 24;394(10199):672-683.
Roshanov PS, Rochwerg B, Patel A, et al. **Withholding versus Continuing Angiotensin-converting Enzyme Inhibitors or Angiotensin II Receptor Blockers before Noncardiac Surgery**: An Analysis of the Vascular events In noncardiac Surgery patIents cOhort evaluatioN Prospective Cohort. Anesthesiology. 2016 Oct 24.
Rosner B, Cook NR, Daniels S, Falkner B. **Childhood Blood Pressure Trends and Risk Factors** for High Blood Pressure: The **NHANES** Experience 1988-2008. Hypertension. 2013 Aug;62(2):247-54.
Ross KL, Bhasin S, Wilson MP, Stewart SA, Wilson TW. Accuracy of **drug store blood pressure monitors**: an observational study. Blood Press Monit. 2013 Dec;18(6):339-41.
Rossi GP, Seccia TM, Maniero C, Pessina AC. **Drug-related hypertension** and resistance to antihypertensive treatment: a call for action. J Hypertens. 2011 Oct 13.
Rossignol P, Massy ZA, Azizi M, et al; ERA-EDTA EURECA-m working group; Red de Investigación Renal (REDINREN) network; Cardiovascular and Renal Clinical Trialists (F-CRIN INI-CRCT) network. The double challenge of **resistant hypertension and chronic kidney disease.** Lancet. 2015 Oct 17;386(10003):1588-98.
Rothenbacher D, Koenig W, Brenner H. Life Time **Physical Activity** Patterns and Risk of Coronary Heart Disease. Heart. 2006 Jul 19; [Epub ahead of print]
Rothwell PM, Howard SC, Dolan E, et al. Prognostic significance of **visit-to-visit variability**, maximum **systolic blood pressure**, and episodic hypertension. Lancet 2010; 375: 895-905.
Rothwell PM. Limitations of the usual blood-pressure hypothesis and importance of **variability, instability, and episodic**. Lancet 2010; 375:938-948.
Rothwell PM, Howard SC, Dolan E, et al. on behalf of the ASCOT-BPLA and MRC Trial Investigators. Effects of **beta blockers and calcium-channel blockers** on within-**individual variability** in blood pressure and risk of stroke. Lancet Neurol. 2010 Mar 11.
Roush GC, Holford TR, Guddati AK. **Chlorthalidone compared with hydrochlorothiazide** in reducing cardiovascular events: systematic review and network meta-analyses. Hypertension. 2012;59:1110–1117.
Roush G, Fagard R, Salles G, et al. Prognostic impact of **clinic, daytime, and nighttime systolic blood pressure** in 9 cohorts of 13,843 patients with hypertension: systematic review and meta-analysis. *J Am Soc Hypertens* 2014; 8:e59.
Roush GC, Fagard RH, Salles GF, et al. The ABC-H Investigators. Prognostic impact from clinic, **daytime, and night- time systolic blood pressure** in nine cohorts of 13844 patients with hypertension. J Hypertens. 2014 Oct 18.
Roush GC, Fapohunda J, Kostis JB. **Evening dosing of** antihypertensive therapy to reduce cardiovascular events: a third type of evidence based on a systematic review and meta-analysis of randomized trials. J Clin Hypertens (Greenwich). 2014;16:561-568.
Roush GC, Sica DA. **Diuretics for Hypertension**: A Review and Update. Am J Hypertens. 2016 Oct;29(10):1130-7.
Ruggenenti P, Perna A, Loriga G, et al.; **REIN-2** Study Group. Blood-pressure control for renoprotection in patients with non-diabetic chronic renal disease: multicentre, randomised controlled trial. Lancet. 2005 Mar 12;365(9463):939-46. (Interpretation: In pts with non-diabetic proteinuric nephropathies receiving background ACE-inhibitor therapy, no additional benefit from further blood-pressure reduction by felodipine could be shown.)
Ruschitzka F, Borer JS, Krum H, et al; **PRECISION-ABPM** Investigators. Differential blood pressure effects of **ibuprofen, naproxen, and celecoxib** in patients with arthritis: the PRECISION-ABPM (Prospective Randomized Evaluation of Celecoxib Integrated Safety Versus Ibuprofen or Naproxen Ambulatory Blood Pressure Measurement) Trial. Eur Heart J. 2017 Aug 28.
Ruzicka M, Burns KD, et al. Precision Medicine for Hypertension Management in **Chronic Kidney Disease: Relevance of SPRINT** for Therapeutic Targets in **Nondiabetic Renal Disease**. Can J Cardiol. 2017 May;33(5):611-618.
Ruzicka M, Hiremath S, Steiner S, et al. What is the feasibility of implementing effective **sodium reduction strategies** to treat hypertension in primary care settings? A systematic review. J Hypertens. 2014 Apr 2.
Ruzicka M, Leenen FHH, Ramsay T, et al. Use of **Directly Observed Therapy to Assess Treatment Adherence** in Patients With Apparent Treatment-Resistant Hypertension. JAMA Intern Med. 2019 Jun 17.
Ruzicka M, McCormick B, et al. Adherence to Blood Pressure-Lowering Drugs and Resistant Hypertension: Should Trial of **Direct Observation Therapy Be Part of Preassessment for Renal Denervation**? Can J Cardiol. 2013 Oct 16.
Sabayan B et al. **High blood pressure** and resilience to physical and cognitive decline in the **oldest old**: The **Leiden 85-Plus** Study.J Am Geriatr Soc 2012 Nov; 60:2014.
Sabayan B, Wijsman LW, Foster-Dingley JC, et al. Association of **visit-to-visit variability** in blood pressure with **cognitive function** in old age: prospective cohort study. BMJ. 2013 Jul 29;347:f4600.
Sacks, Frank M., Campos, Hannia. **Dietary Therapy** in Hypertension. N Engl J Med 2010 362: 2102-2112.
Sacco Ralph L.. Achieving **Ideal Cardiovascular and Brain Health**: Opportunity Amid Crisis: Presidential Address at the American Heart Association (**AHA**) 2010 Scientific Sessions. Circulation 123: 2653-2657.
Sadat-Ebrahimi SR, Parnianfard N, Vahed N, et al. An Evidence-Based Systematic Review of the **Off-Label Uses of Lisinopril**. Br J Clin Pharmacol. 2018 Jul 3.
Saiz LC;Gorricho J;Garjon J;Celaya MC;Muruzabal L;. **Blood pressure targets for the treatment of people with hypertension and cardiovascular disease**. Cochrane Database Syst Rev. 2017 Oct 11;10:CD010315.
No evidence of a difference in total mortality and serious adverse events was found between treating to a lower or to a standard blood pressure target in people with hypertension and cardiovascular disease. This suggests no net health benefit from a lower systolic blood pressure target despite the small absolute reduction in total cardiovascular serious adverse events. There was very limited evidence on adverse events, which lead to high uncertainty. At present there is insufficient evidence to justify lower blood pressure targets (</= 135/85 mmHg) in people with

hypertension and established cardiovascular disease. More trials are needed to answer this question.

Salt Info: www.saltinstitute.org;

China Salt Substitute Study Collaborative Group. Salt substitution: a low-cost strategy for blood pressure control among rural Chinese. A randomized, controlled trial. J Hypertens. 2007 Oct;25(10):2011-8.

Cohen HW, Hailpern SM, Fang J, Alderman MH. Sodium intake and mortality in the NHANES II follow-up study. Am J Med. 2006 Mar;119(3):275.e7-14.

Parikh NI, Gona P, Larson MG, et al. Plasma renin and risk of cardiovascular disease and mortality: the Framingham Heart Study. Eur Heart J. 2007 Nov;28(21):2644-52. Epub 2007 Sep 25.

Sodium, potassium, body mass, alcohol and blood pressure: the INTERSALT Study. The INTERSALT Co-operative Research Group.J Hypertens Suppl. 1988 Dec;6(4):S584-6.

Sahu R, Pannu H, Yu R, et al. Systemic Hypertension Requiring Treatment in the **Neonatal Intensive Care Unit**. J Pediatr. 2013 Feb 6.

Saiz LC, Gorricho J, Garjón J, et al. **Blood pressure targets for the treatment of people with hypertension and cardiovascular disease**. Cochrane Database of Systematic Reviews 2018, Issue 7. Art. No.: CD010315. We found no evidence of a difference in total mortality, serious adverse events, or total cardiovascular events between people with hypertension and cardiovascular disease treated to a lower or to a standard blood pressure target. This suggests that no net health benefit is derived from a lower systolic blood pressure target. We found very limited evidence on adverse events, which led to high uncertainty. At present, evidence is insufficient to justify lower blood pressure targets (≤ 135/85 mmHg) in people with hypertension and established cardiovascular disease. More trials are needed to examine this topic.

Salles GF, Reboldi G, et al. Prognostic effect of the **nocturnal blood pressure** fall in hypertensive patients: The **ambulatory** blood pressure collaboration in patients with hypertension (ABC-H) meta-analysis.*Hypertension* 2016.

Samuel JP, Tyson JE, Green C, et al. **Treating Hypertension in Children With n-of-1 Trials**. Pediatrics. 2019 Mar 6.

Samuels, Martin A., Pomerantz, Benjamin J., Sadow, Peter M. Case 14-2010 -- A 54-Year-Old Woman with Dizziness and Falls. (**Pheochromocytoma**) N Engl J Med 2010 362: 1815-1823.

Sandset EC, Bath PMW, Boysen G et al. The angiotensin-receptor blocker **candesartan for treatment of acute stroke (SCAST):** A randomised, placebo-controlled, double-blind trial. *Lancet* 2011;DOI:10.1016/S0140-6736(11)60104-9. Am J Hypertens. 2013 Mar;26(3):424-41.

Sapiña-Beltrán E, Torres G, Benitez I, et al. Prevalence, Characteristics and Association of **Obstructive Sleep Apnea with Blood Pressure Control** in Patients with Resistant Hypertension. Ann Am Thorac Soc. 2019 Sep 13.

Sarafidis PA, Persu A, Agarwal R, et al. **Hypertension in dialysis patients**: a consensus document by the European Renal and Cardiovascular Medicine (**EURECA-m**) working group of the European Renal Association-European Dialysis and Transplant Association (**ERA-EDTA**) and the Hypertension and the Kidney working group of the European Society of Hypertension (**ESH**). Nephrol Dial Transplant. 2017 Mar 13.

Sardar P, Bhatt DL, Kirtane AJ, et al. Sham-Controlled Randomized Trials of **Catheter-Based Renal Denervation** in Patients With Hypertension. J Am Coll Cardiol. 2019 Apr 9;73(13):1633-1642.

Satoh M, Ohkubo T, Asayama K, et al. Evidence for Cardiovascular Prevention From Observational Cohorts in Japan (**EPOCH–JAPAN**) Research Group*. Combined effect of **blood pressure and total cholesterol** levels on long-term risks of subtypes of cardiovascular death: evidence for cardiovascular prevention from observational cohorts in Japan. Hypertension. 2015 Mar;65(3):517-24.

Satoru Kishi A, Teixido-Tura G, Ning H, et al. **Cumulative blood pressure in early adulthood and cardiac dysfunction in middle age**. (Cardia) *J Am Coll Cardiol*.2015; 65:2679-2687.

Sawano T, Ozaki A, Saito H, Shimada Y, Tanimoto T. Payments From Pharmaceutical Companies to **Authors Involved in the Valsartan Scandal** in Japan. JAMA Netw Open. 2019 May 3;2(5):e193817.

Scarpa J, Bruzelius E, Doupe P, et al. Assessment of risk of harm associated with intensive blood pressure management among **patients with hypertension who smoke**: a secondary analysis of the Systolic Blood Pressure Intervention Trial (SPRINT). JAMA Netw Open. 2019;2(3):e190005. doi:10.1001/jamanetworkopen.2019.0005

Schaare HL, Kharabian Masouleh S, Beyer F, et al. **Association of peripheral blood pressure with gray matter volume in 19- to 40-year-old adults**. Neurology. 2019 Jan 23.

Schaare HL, Masouleh SK, Beyer R. Association of **peripheral blood pressure with gray matter volume** in 19- to 40-year-old adults. Neurology. 2019 Mar 5;92(10):495.

Scheer FA, Morris CJ, Garcia JI, et al. Repeated **melatonin supplementation** improves sleep in **hypertensive** patients treated with Beta-blockers: a randomized controlled trial. Sleep. 2012 Oct 1;35(10):1395-402.

Scherpbier-de Haan ND, Vervoort GM, van Weel C, et al. Effect of **shared care on blood pressure** in patients with chronic kidney disease: a cluster randomised controlled trial.

Schiavon CA, et al. Effects of **Bariatric Surgery in Obese Patients** With **Hypertension**: **GATEWAY** Randomized Trial (Gastric Bypass to Treat Obese Patients With Steady Hypertension). Circulation. 2018 Mar 13;137(11):1132-1142.

Schiffrin EL, Calhoun DA, Flack JM. **SPRINT** Proves that Lower Is Better for Nondiabetic High-Risk Patients, but at a Price. Am J Hypertens. 2016 Jan;29(1):2-4.

Schiffrin EL, Calhoun DA, Flack JM. Do We Need a New Definition of Hypertension After **SPRINT**? Am J Hypertens. 2016 Jun 22.

Schiffrin EL. Global Impact of the **2017 American College of Cardiology/American Heart Association Hypertension Guidelines**: A **Perspective From Canada**. Circulation. 2018 Feb 27;137(9):883-885.

Schirmer SH, Sayed M, Reil J-C, et al. Improvements of left-ventricular hypertrophy and diastolic function following **renal denervation** – Effects beyond blood pressure and heart rate reduction. *J Am Coll Cardiol* 2013.

Schlaich MP, Sobotka PA, Krum H, Lambert E, Esler MD. **Renal sympathetic-nerve ablation** for uncontrolled hypertension. N Engl J Med. 2009 Aug 27;361(9):932-4.

Schmidt M, Mansfield KE, Bhaskaran K, et al. **Serum creatinine elevation after renin-angiotensin system blockade** and **long term cardiorenal risks**: cohort study. BMJ 2017;356:j791.

Schmidt M, et al. **Adherence to guidelines for creatinine & potassium monitoring and discontinuation following renin-angiotensin system blockade**: a UK general practice-based cohort study. BMJ Open. 2017 Jan 9;7(1):e012818.

Schmieder RE, Philipp T, Guerediaga J, et al. Long-term antihypertensive efficacy and safety of the oral direct renin inhibitor **aliskiren**: a 12-month randomized, double-blind comparator trial with hydrochlorothiazide. Circulation. 2009;119:417– 445.

Schoenthaler AM, Lancaster KJ, Chaplin W, et al. Cluster Randomized **Clinical Trial of FAITH** (Faith-Based Approaches in the Treatment of Hypertension) in Blacks. Circ Cardiovasc Qual Outcomes. 2018 Oct;11(10):e004691.

Schrier RW, Abebe KZ, Perrone RD, et al. **Blood pressure** in early **autosomal dominant polycystic kidney disease**. N Engl J Med. DOI: 10.1056/NEJMoa1402685.

Schuijf JD, et al. Diagnostic accuracy of **64-slice multislice computed tomography** in the noninvasive evaluation of significant coronary artery disease. Am J Cardiol. 2006 Jul 15;98(2):145-8. Epub 2006 May 19.

Schulman SP, et al. **L-arginine** therapy in acute myocardial infarction: the Vascular Interaction With Age in Myocardial Infarction (VINTAGE MI) randomized clinical trial. JAMA. 2006 Jan 4;295(1):58-64.

Schwalm JD, McCready T, Lopez-Jaramillo P, et al. A **community-based comprehensive intervention** to reduce cardiovascular risk in hypertension (HOPE 4): a cluster-randomised controlled trial. Lancet. 2019 Aug 30.

Schwarz EI, Schlatzer C, Rossi VA, et al. Effect of **CPAP Withdrawal on BP in OSA**: Data from Three Randomized Controlled Trials. Chest. 2016 Dec;150(6):1202-1210.

Schwartz JE, Burg MM, et al. **Clinic blood pressure underestimates ambulatory blood pressure** in an untreated employer-based US population: results from the Masked Hypertension Study. Circulation. 2016;134:1794–1807.

Schwimmer JB, Zepeda A, Newton KP, et al. **Nonalcoholic Steatohepatitis** Clinical Research Network. Longitudinal assessment of high blood pressure in children with nonalcoholic Fatty liver disease. PLoS One. 2014 Nov 24;9(11):e112569.

Sciarretta Sebastiano; Palano Francesca; Tocci Giuliano; et al. Antihypertensive Treatment and Development of Heart Failure in Hypertension: A Bayesian Network Meta-analysis of Studies in Patients With Hypertension and High Cardiovascular Risk. Arch Intern Med. 2010;0(2010):archinternmed.2010.427.

Sedlis SP, Jurkovitz CT, Hartigan PM, et al; **COURAGE** Study Investigators. Health Status and Quality of Life in Patients With Stable Coronary Artery Disease and Chronic Kidney Disease Treated With Optimal Medical Therapy or Percutaneous Coronary Intervention (Post Hoc Findings from the COURAGE Trial). Am J Cardiol. 2013 Aug 31.

Sedlis SP, Hartigan PM, Teo KK, et al; **COURAGE** Trial Investigators. Effect of **PCI on Long-Term Survival in Patients with Stable Ischemic Heart Disease**. N Engl J Med. 2015 Nov 12;373(20):1937-46.

Seely EW, Ecker J. Clinical practice. **Chronic hypertension in pregnancy**. N Engl J Med. 2011 Aug 4;365(5):439-46.

Seely EW, Ecker J. **Chronic hypertension in pregnancy**. Circulation. 2014 Mar 18;129(11):1254-61.

Selak V, Elley CR, Bullen C, et al. Effect of **fixed dose combination** treatment on adherence and risk factor control among patients at high risk of cardiovascular disease: randomised controlled trial in primary care. BMJ 2014;348:g3318.

Selak V, Webster R, Stepien S, et al. Reaching **cardiovascular prevention guideline targets** with a polypill-based approach: a meta-analysis of randomised clinical trials. Heart. 2018 Jun 28.

Selvaraj S, Claggett B, Shah SJ, et al. **Systolic blood pressure and cardiovascular outcomes in heart failure** with **preserved ejection fraction**: an analysis of the **TOPCAT** trial. Eur J Heart Fail. 2017 Nov 16.

Serinel Y, Yee BJ, Grunstein RR, et al. **Chronotherapy for hypertension** in **obstructive sleep apnoea** (**CHOSA**): a randomised, double-blind, placebo-controlled crossover trial. Thorax. 2016 Dec 14.

Serumaga B, Ross-Degnan D, Avery AJ, et al. Effect of **pay for performance** on the management and outcomes of hypertension in the United Kingdom: interrupted time series study. An interrupted time-series study. BMJ 2011.

Sexton DJ, Canney M, O'Connell MDL, Moore et al. **Injurious Falls** and **Syncope** in Older Community-Dwelling Adults Meeting Inclusion Criteria for **SPRINT**. JAMA Intern Med. 2017 Jul 17.

Shahi N, Tobe SW. Thresholds and **Targets** for Hypertension Management of Type 2 **Diabetes Mellitus Remain at 130/80 mmHg**: What's the Evidence? Can J Diabetes. 2017 Dec 20.

Shahu A, Herrin J, Dhruva SS, et al. **Disparities in Socioeconomic Context and Association** With Blood Pressure Control and Cardiovascular Outcomes in ALLHAT. J Am Heart Assoc. 2019 Aug 6;8(15):e012277.

Sharma AK, et al. Prevalence and severity of **high blood pressure among children based on the 2017 American Academy of Pediatrics guidelines** [online Apr 23, 2018].JAMA Pediatr. doi:10.1001/jamapediatrics.2018.0223

Sharma C, Soni A, Gupta A, et al. **Hydralazine vs nifedipine** for **acute hypertensive emergency in pregnancy**: a randomized controlled trial. Am J Obstet Gynecol. 2017 Dec;217(6):687.e1-687.e6.

Sharma P, Nagarajan V. Q: Can an **ARB be given to patients who have had angioedema on an ACE inhibitor**? Cleve Clin J Med. 2013 Dec;80(12):755-7.

Sharma SK et al. **CPAP** for the metabolic syndrome in patients with obstructive sleep apnea. N Engl J Med. 2011 Dec 15;365(24):2277-86.

Shen L, Ma H, Xiang MX, et al. Meta-Analysis of Cohort Studies of Baseline **Prehypertension** and Risk of Coronary Heart Disease. Am J Cardiol. 2013 Apr 19.

Shen WK, Sheldon RS, Benditt DG, et al. 2017 **ACC/AHA/HRS Guideline** for the Evaluation and Management of Patients With **Syncope**: A Report of the American College of Cardiology/ American Heart Association Task Force on Clinical Practice Guidelines, and the Heart Rhythm Society. Circulation. 2017 Mar 9

Sheppard JP, Fletcher B, Gill P, et al. Predictors of the **Home-Clinic Blood Pressure Difference**: A Systematic Review and Meta-Analysis. Am J Hypertens. 2015 Sep 22.

Sheppard JP, Stevens R, Gill P, et al. **Predicting Out-of-Office Blood Pressure in the Clinic** (**PROOF-BP**): Derivation and Validation of a Tool to Improve the Accuracy of Blood Pressure Measurement in Clinical Practice. Hypertension. 2016 May;67(5):941-50.

Sheppard JP, Martin U, McManus RJ. **Diagnosis and management of resistant hypertension**. Heart. 2017 Jun 29.

Sheppard JP, Martin U, Gill P, et al. Prospective external validation of the **Predicting Out-of-OFfice Blood Pressure (PROOF-BP**) strategy for triaging ambulatory monitoring in the diagnosis and management of hypertension: observational cohort study. BMJ. 2018 Jun 27;361:k2478.

Sheppard JP, Stevens S, Stevens R, et al. Benefits and Harms of Antihypertensive Treatment in **Low-Risk Patients With Mild Hypertension**. JAMA Intern Med. 2018 Oct 29.

Shimbo D, Kuruvilla S, Haas D, Pickering TG, Schwartz JE, Gerin W. Preventing misdiagnosis of ambulatory hypertension: **algorithm using office and home blood pressures**. J Hypertens. 2009 Sep;27(9):1775-83.

Shimbo D, Abdalla M, Falzon L, et al. Role of **Ambulatory and Home Blood Pressure Monitoring** in Clinical Practice: A Narrative Review. Ann Intern Med. 2015 Oct 13.

Shimbo D, Bowling CE, Levitan EB, et al. Short-term risk of serious **fall injuries** in older adults initiating and intensifying treatment with antihypertensive medication. *Circ Cardiovasc Qual Outcomes* 2016.

Shimbo D, Barrett Bowling C, Levitan EB, et al. Short-Term Risk of **Serious Fall Injuries** in Older Adults Initiating and Intensifying Treatment With Antihypertensive Medication. Circ Cardiovasc Qual Outcomes. 2016 May;9(3):222-9.

Shin D, Lee ES, Kim J, Guerra L, Naik D, Prida X. Association Between the Use of **Thiazide Diuretics and the Risk of Skin Cancers**: A Meta-Analysis of Observational Studies. J Clin Med Res. 2019 Apr;11(4):247-255.

Shlipak MG, et al. **Cystatin C** and prognosis for cardiovascular and kidney outcomes in elderly persons without chronic kidney disease. Ann Intern Med. 2006 Aug 15;145(4):237-46.

Shook RP, Lee DC, Sui X, et al. **Cardiorespiratory fitness** reduces the risk of incident hypertension associated with a parental history of hypertension. Hypertension. 2012 Jun;59(6):1220-4.

Sim JJ, Shi J, Kovesdy CP, Kalantar-Zadeh K, Jacobsen SJ. Impact of **achieved blood pressures on mortality risk and end-stage renal disease** among a large, diverse hypertension population. *J Am Coll Cardiol* 2014; 64:588-597.

Sim JJ, Zhou H, Bhandari S, et al. **Low Systolic Blood Pressure From Treatment and Association With Serious Falls/Syncope**. Am J Prev Med. 2018 Aug 17.

Singer W, et al. **Pyridostigmine** treatment trial in **neurogenic orthostatic hypotension**. Arch Neurol. 2006 Apr;63(4):513-8. Epub 2006 Feb 13.

Sink KM, Evans GW, Shorr RI, et al. **Syncope, Hypotension, and Falls in the Treatment of Hypertension**: Results from the Randomized Clinical Systolic Blood Pressure Intervention Trial. J Am Geriatr Soc. 2018 Mar 30.

Sinnott SJ, Smeeth L, Williamson E, Douglas IJ. Trends for prevalence and incidence of **resistant hypertension**: population based cohort study in the UK 1995-2015. BMJ. 2017 Sep 22;358:j3984.

Sipahi I, Debanne SM, Rowland DT et al. **Angiotensin-receptor blockade** and risk of **cancer**: Meta-analysis of randomised controlled trials. Lancet Oncol 2010; DOI:10.1016/S1470-2045(10)70106-6.

Sipahi I, Swaminathan A, Natesan V, et al. Effect of antihypertensive therapy on incident **stroke in cohorts with prehypertensive** blood pressure levels: A meta-analysis of randomized controlled trials. Stroke 2011

Siu AL. Screening for **High Blood Pressure in Adults**: U.S. Preventive Services Task Force Recommendation Statement (**USPSTF**). Ann Intern Med. 2015 Oct 13.

Skilton MR, et al. High Intake of Dietary **Long-Chain ω-3 Fatty Acids** Is Associated With Lower Blood Pressure in Children Born With Low Birth Weight: NHANES 2003-2008. Hypertension. 2013 May;61(5):972-976.

Skolnik N. Icarus, Blood Pressure, and the Dangers of Flying Too Close to the Sun. Circulation. 2018 Mar 13;137(11):1097-1099.

Slagman Maartje C J, Waanders Femke, Hemmelder Marc H, et al. for the **HONEST** (HOlland NEphrology STudy) Group. Moderate dietary **sodium restriction added to angiotensin converting enzyme inhibition** compared with dual blockade in lowering proteinuria and blood pressure: randomised controlled trial. BMJ 2011;343:doi:10.1136/bmj.d4366 (26 July 2011)

Small HY, Montezano AC, et al. Hypertension Due to **Antiangiogenic Cancer Therapy With Vascular Endothelial Growth Factor Inhibitors**: Understanding and Managing a New Syndrome. Can J Cardiol. 2014 May;30(5):534-543.

Smith PK, et al. Selection of **surgical or percutaneous coronary intervention** provides differential longevity benefit. Ann Thorac Surg. 2006 Oct;82(4):1420-8; discussion 1428-9.

Smith S, Benjamin E, Bonow R, et al. **AHA/ACCF secondary prevention and risk reduction therapy** for patients with coronary and other atherosclerotic vascular disease: 2011 update: A guideline from the American Heart Association and American College of Cardiology Foundation. Circulation. 2011; DOI:10.1161/CIR.0b013e318235eb4d.

Smith SC Jr, et al. **AHA/ACC** guidelines for **secondary prevention** for patients with coronary and other atherosclerotic vascular disease: 2006 update: endorsed by the National Heart, Lung, and Blood Institute. Circulation. **2006** May 16;113(19):2363-72. http://circ.ahajournals.org/cgi/reprint/113/19/2363

Smith SM, Gurka MJ, Calhoun DA, et al. Optimal **Systolic Blood Pressure Target** in Apparent Resistant and Non-Resistant Hypertension: A Pooled Analysis of Patient-Level Data from Sprint and ACCORD. Am J Med. 2018 Aug 21.

Smolen JR, Wang JJ, Anane SP. **Challenges and strategies for hypertension management**: qualitative analysis of small primary care practices with varying blood pressure control. Fam Pract. 2019 Feb 8.

Smyth A, Dehghan M, O'Donnell M, et al; **ONTARGET** and **TRANSCEND** Investigators. **Healthy eating and reduced risk of cognitive decline**: A cohort from 40 countries. Neurology. 2015 Jun 2;84(22):2258-65.

Society of Obstetricians and Gynaecologists of Canada. **Diagnosis, evaluation, and management of the hypertensive disorders of pregnancy**. J Obstet Gynaecol Can 2008;30:S1-S48.

Society of Obstetricians and Gynaecologists of Canada. **SOGC: Diagnosis, evaluation, and management of the hypertensive disorders of pregnancy**: executive summary. J Obstet Gynaecol Can 2014;36:416-38. http://sogc.org/wp-content/uploads/2014/05/gui307CPG1405E1.pdf?1668a1(accessed June 25, 2014).

Soedamah-Muthu SS, Verberne LD, Ding EL, et al. **Dairy consumption** and incidence of hypertension: a dose-response meta-analysis of prospective cohort studies. Hypertension. 2012 Nov;60(5):1131-7.

Sohn IS, Kim CJ, Ahn T, et al. Efficacy and Tolerability of Combination Therapy Versus Monotherapy with **Candesartan and/or Amlodipine** for Dose Finding in Essential Hypertension: A Phase II Multicenter, Randomized, Double-blind Clinical Trial. Clin Ther. 2017 Aug;39(8):1628-1638.

Solberg LI, Miller WL. The **new hypertension guideline: logical but unwise**. Fam Pract. 2018 Apr 5.

Soliman EZ, et al; Effect of **Intensive Blood Pressure Lowering on Left Ventricular Hypertrophy** in Patients with Hypertension: The Systolic Blood Pressure Intervention (**SPRINT**) Trial. Circulation. 2017 May 16.

Solomon SD, Hee Shin S, Shah A, et al. Effect of the direct rennin inhibitor aliskiren on left ventricular remodelling following myocardial infarction *with systolic dysfunction.(**ASPIRE**) Eur Heart J 2011; 32: 1227–34.*

Solomon SD, Appelbaum E, Manning WJ, et al; Aliskiren in Left Ventricular Hypertrophy (ALLAY) Trial Investigators. Effect of the direct Renin inhibitor **aliskiren**, the Angiotensin receptor blocker **losartan**, or both on left ventricular mass in patients with hypertension and left ventricular hypertrophy. Circulation. 2009 Feb 3;119(4):530-7.

Solomon SD, Appelbaum E, Manning WJ, et al.; for the Aliskiren in Left Ventricular Hypertrophy (**ALLAY**) Trial Investigators. Effect of the Direct Renin Inhibitor Aliskiren, the Angiotensin Receptor Blocker Losartan, or Both on Left Ventricular Mass in Patients With Hypertension and Left Ventricular Hypertrophy. Circulation. 2009 Jan 19.

Son JS, Choi S, Kim K, et al. Association of **blood pressure classification in Korean young adults** according to the 2017 American College of Cardiology/American Heart Association Guidelines with subsequent cardiovascular disease events [online Nov 6, 2018]. JAMA.

Sonawane KB, Qian J, Hansen RA. Utilization Patterns of Antihypertensive Drugs Among the **Chronic Kidney Disease** Population in the United States: A Cross-Sectional Analysis of the National Health and Nutrition Examination Survey. Clin Ther. 2014 Dec 15.

Song P, Zhang Y, Yu J, et al. Global Prevalence of **Hypertension in Children**: A Systematic Review and Meta-analysis. JAMA Pediatr. 2019 Oct 7:1-10. doi: 10.1001/jamapediatrics.2019.3310

Sood MM, et al. **Longitudinal Blood Pressure in Late-Stage Chronic Kidney Disease and the Risk of End-Stage Kidney Disease or Mortality** (Best Blood Pressure in Chronic Kidney Disease Study). Hypertension. 2017 Dec;70(6):1210-1218.

Sorbets E, Labreuche J, Simon T, et al. Renin-angiotensin system antagonists and clinical outcomes in **stable coronary artery disease** without heart failure. Eur Heart J. 2014 Mar 9.

Sowers JR, Whaley-Connell A, Epstein M. Narrative review: the emerging clinical implications of the role of **aldosterone** in the metabolic syndrome and **resistant hypertension**. Ann Intern Med. 2009 Jun 2;150(11):776-83.

Spaan JJ, Brown MA. Can we **protect the kidneys after hypertensive pregnancy**? CMAJ. 2013 Feb 19;185(3):199-200.

Spahr A, et al. **Periodontal infections** & coronary heart disease: role of periodontal bacteria & total pathogen burden in the Coronary Event & Periodontal Disease (CORODONT) study. Arch Intern Med. 2006 Mar 13;166(5):554-9.

Spiering W, Williams B, Van der Heyden J, et al, for the CALM-FIM_EUR investigators. Endovascular **baroreflex amplification** for **resistant hypertension**: a safety and proof-of-principle clinical study. Lancet 2017; online Sept 1

SPRINT Research Group. A randomized trial of **intensive versus standard blood-pressure control**. N Engl J Med. DOI: 10.1056/NEJMoa1511939. (Bress AP, Tanner RM, Hess R, et al. Generalizability of results from the Systolic Blood Pressure Intervention Trial (SPRINT) to the US adult population. J Am Coll Cardiol. 2015 Oct 31. Esler M. SPRINT, or false start, towards a lower universal treated blood pressure target in hypertension. *Hypertension*2015; DOI:10.1161/HYPERTENSIONAHA.115.06735.)

SPRINT: Williamson JD, Supiano MA, Applegate WB, et al. **Intensive vs standard blood pressure** control and cardiovascular disease outcomes in **adults aged 75 years**: a randomized clinical trial. JAMA. doi:10.1001/jama.2016.7050.

SPRINT MIND Investigators for the SPRINT Research Group. Effect of **intensive vs standard blood pressure control on probable dementia**: a randomized clinical trial [online Jan 28, 2019]. JAMA. doi:10.1001/jama.2018.21442

SPRINT MIND Investigators: Nasrallah IM, Pajewski NM, Auchus AP, et al. Association of **Intensive vs Standard Blood Pressure Control** With Cerebral White Matter Lesions. JAMA. 2019 Aug 13;322(6):524-534.

SPS3 Study Group. Blood-pressure targets in patients with recent **lacunar stroke: the SPS3** randomised trial. Lancet 2013; published online May 29. http://dx.doi.org/10.1016/S0140-6736(13)60852-1.

Squair JW, Phillips AA, Harmon M, et al. Emergency management of **autonomic dysreflexia** with neurologic complications. CMAJ. 2016 Oct 18;188(15):1100-1103

Sridharan K, Sequeira RP. Drugs for treating **severe hypertension in pregnancy**:A network meta-analysis and trial sequential analysis of randomized clinical trials. Br J Clin Pharmacol. 2018 Jul 4.

Stabler SN, Tejani AM,Huynh F, Fowkes C. **Garlic** for the prevention of cardiovascular morbidity and mortality in hypertensive patients. *Cochrane Database of Systematic Reviews* 2012, Issue 8. Art.No.: CD007653. DOI: 10.1002/14651858.CD007653.pub2. There is insufficient evidence to determine if garlic provides a therapeutic advantage versus placebo in terms of reducing the risk of mortality and cardiovascular morbidity in patients diagnosed with hypertension. There is also insufficient evidence to determine the difference in withdrawals due to adverse events between patients treated with garlic or placebo.

Staessen JA, et al. Risks of untreated and treated isolated systolic hypertension in the **elderly**: meta-analysis of outcome trials. Lancet. 2000 Mar 11;355(9207):865-72. Erratum in: Lancet 2001 Mar3;357(9257):724.

Staessen JA, Li Y, Richart T. Oral renin inhibitors. Lancet. 2006 Oct 21;368(9545):1449-56.

Staff AC, Redman CW, et al; Global Pregnancy Collaboration (CoLab)*. **Pregnancy and Long-Term Maternal Cardiovascular Health**: Progress Through Harmonization of Research Cohorts and Biobanks. Hypertension. 2016 Feb;67(2):251-60.

Steinke EE, Jaarsma T, Barnason SA, et al. on behalf of the Council on Cardiovascular and Stroke Nursing of the American Heart Association and the ESC Council on Cardiovascular Nursing and Allied Professions (CCNAP). **Sexual Counseling for Individuals With Cardiovascular Disease and Their Partners**: A Consensus Document From the American Heart Association and the ESC Council on Cardiovascular Nursing and Allied Professions (CCNAP). Circulation. 2013 Jul 29.

Stergiopoulos K, Brown DL. Initial coronary stent implantation with medical therapy vs **medical therapy alone for stable coronary artery disease**. Arch Intern Med 2012; 172:312-319.

Stergiopoulos K, Boden WE, Hartigan P, et al. **Percutaneous Coronary Intervention** Outcomes in Patients With Stable Obstructive Coronary Artery Disease and Myocardial Ischemia: A Collaborative Meta-analysis of Contemporary Randomized Clinical Trials. JAMA Intern Med. 2013 Dec 2.

Stergiou G, Palatini P, Asmar R, et al. **Blood Pressure Measurement and Hypertension Diagnosis** in the 2017 US Guidelines: First Things First. Hypertension. 2018 Jun;71(6):963-965.

Stergiou GS, Boubouchairopoulou N, Kollias A. **Accuracy of Automated Blood Pressure Measurement in Children**: Evidence, Issues, and Perspectives. Hypertension. 2017 Jun;69(6):1000-1006.

Stevens SL, Wood S, Koshiaris C, Law et al.**Blood pressure variability** and cardiovascular disease: systematic review and meta-analysis. BMJ. 2016 Aug 9;354:i4098.

Stewart S, Carrington MJ, et al. the VIPER-BP study investigators. Effect of **intensive structured care** on individual blood pressure targets in primary care: multicentre randomised controlled trial. BMJ. 2012 Nov 20;345:e7156.

Stocchetti N, Maas AI. **Traumatic intracranial hypertension**. N Engl J Med. 2014 May 29;370(22):2121-30.

Stone PH, Gratsiansky et al. **ERICA** Investigators. Antianginal efficacy of **ranolazine** when added to treatment with amlodipine: the ERICA (Efficacy of Ranolazine in Chronic Angina) trial. J Am Coll Cardiol. 2006 Aug 1;48(3):566-75. Epub 2006 Jun 15. (InfoPOEMs: Ranolazine (Ranexa), added to maximum dosing of amlodipine, decreases angina episodes and nitroglycerin doses slightly more than placebo does; patients taking ranolazine experienced approximately 1 fewer episode, on average, every 2 weeks. These results occurred in patients with frequent symptoms -- at least 4 anginal episodes per week -- and its effect is likely to be less pronounced in patients with less frequent symptoms. (LOE = 1b)

Strandberg TE, et al. **Multifactorial intervention** to prevent recurrent cardiovascular events in patients **75 years or older**: the Drugs and Evidence-Based Medicine in the Elderly (**DEBATE**) study: a randomized, controlled trial. Am Heart J. 2006 Sep;152(3):585-92. (InfoPOEMs: First, the good news: Researchers were able, without unusual effort, to apply evidence-based guidelines to older elderly patients with cardiovascular disease (CVD) and achieve goal blood pressure and cholesterol levels in the majority. Now, the bad news: These interventions did not decrease the likelihood of the patients experiencing a cardiovascular problem over the next 3.4 years. The treated patients did not live any longer over this period, and the treatment did not delay deaths. (LOE = 1b))

Stranges PM, Drew AM, Rafferty P, et al. Treatment of hypertension with **chronotherapy**: is it time of drug administration? Ann Pharmacother. 2015 Mar;49(3):323-34.

Strauss MH, Hall AS. The **Divergent Cardiovascular Effects of Angiotensin Converting Enzyme Inhibitors and Angiotensin Receptor Blockers** on **Myocardial Infarction** and Death. Prog Cardiovasc Dis. 2015 Nov 14.

Strazzullo Pasquale, D'Elia Lanfranco, et al. **Salt** intake, stroke, and cardiovascular disease: meta-analysis of prospective studies. BMJ 2009;339:b4567, doi: 10.1136/bmj.b4567 (24 November 2009).

Streit S, Poortvliet RKE, Elzen WPJD, et al. **Systolic Blood Pressure and Cognitive Decline** in Older Adults With Hypertension. Ann Fam Med. 2019 Mar;17(2):100-107.

Streit S, Poortvliet RKE, Gussekloo J. **Lower blood pressure during antihypertensive treatment is associated with higher all-cause mortality** and accelerated cognitive decline in the oldest-old-data from the Leiden 85-plus Study. Age Ageing. 2018 May 8.

Strippoli GF, Craig MC, Schena FP, Craig JC. Role of blood pressure targets and specific antihypertensive agents used to prevent **diabetic nephropathy** and delay its progression. J Am Soc Nephrol. 2006 Apr;17 Suppl 2:S153-5. On the basis of available RCT evidence, ACEi are the only agents with proven renal benefit in patients who have diabetes with no nephropathy and the only agents with proven survival benefit in patients who have diabetes with nephropathy.

Stuart JJ, Tanz LJ, Missmer SA, et al. **Hypertensive disorders of pregnancy** and maternal cardiovascular disease risk factor development. An observational cohort study. Ann Intern Med. 2018. [Epub ahead of print]. doi:10 .7326/M17-2740

Stuart JJ, Tanz LJ, Missmer SA. **High Blood Pressure During Pregnancy** and Development of Risk Factors for **Cardiovascular Disease**. Ann Intern Med. [Epub ahead of print 3 July 2018].

Su JA, Tang W, Rivero N, et al. **Prenatal Exposure to Methyldopa** Leading to Hypertensive Crisis and Cardiac Failure in a Neonate. Pediatrics. 2014 Apr 28.

Su M, Zhang Q, Bai X, et al. **Availability, cost, and prescription patterns** of antihypertensive medications in primary health care in **China**: a nationwide cross-sectional survey. Lancet 2017; online Oct 25.

Su S, Wang X, Pollock JS, et al. **Adverse Childhood Experiences and Blood Pressure Trajectories** from Childhood to Young Adulthood: The Georgia Stress and Heart Study. Circulation. 2015 Apr 9.

Sudano I, Flammer AJ, Périat D, et al. **Acetaminophen increases blood pressure** in patients with coronary artery disease. Circulation. 2010 Nov 2;122(18):1789-96.

Sun J, Buys N. **Community-Based Mind-Body Meditative Tai Chi Program** and Its Effects on Improvement of Blood Pressure, Weight, Renal Function, Serum Lipoprotein, and Quality of Life in Chinese Adults With Hypertension. Am J Cardiol. 2015 Jul 16.

Sundbøll J, Adelborg K, Mansfield KE, et al. **Seventeen-Year Nationwide Trends** in Antihypertensive Drug Use in **Denmark**. Am J Cardiol. 2017 Dec 15;120(12):2193-2200.

Sundquist K, Li X. Differences in maternal (**mother**) and paternal transmission of coronary heart disease. Am J Prev Med. 2006 Jun;30(6):480-6. Epub 2006 Apr 25.

Sundström J, Neovius M, Tynelius P, Rasmussen F. Association of **blood pressure ^{DBP} in late adolescence** with subsequent mortality: cohort study of Swedish male conscripts. BMJ. 2011 Feb 22;342:d643. doi: 10.1136/bmj.d643.

Sundström J, Arima H, Jackson R, et al; on behalf of the Blood Pressure Lowering Treatment Trialists' Collaboration*. Effects of Blood Pressure Reduction in **Mild Hypertension**: A Systematic Review and Meta-analysis. Ann Intern Med. 2014 Dec 23.

Sundstrom J, Arima H, et al. et al; **Blood Pressure Lowering Treatment Trialists' Collaboration**. Effects of **blood pressure reduction in mild hypertension**. A systematic review and meta-analysis. Ann Intern Med. 2015;162:184-91.

Sung KC, Oh YS, Cha DH, et al. Efficacy and Tolerability of **Telmisartan/Amlodipine + Hydrochlorothiazide** Versus Telmisartan/Amlodipine Combination Therapy for Essential Hypertension Uncontrolled With Telmisartan/Amlodipine: The Phase III, Multicenter, Randomized, Double-Blind TAHYTI Study. Clin Ther. 2017 Dec 13.

Sunwoo YE, Nguyen PTT, Chin MC, et al. Effect of **rifampin on enantioselective disposition and anti-hypertensive effect of benidipine**. Br J Clin Pharmacol. 2018 Dec 27.

Susantitaphong P, Sewaralthahab K, Balk EM, Eiam-ong S, Madias NE, Jaber BL. Efficacy and safety of **combined vs. single renin-angiotensin-aldosterone system blockade in chronic kidney disease**: a meta-analysis.

Sussman J, Vijan S, Hayward R. Using **benefit-based tailored treatment** to improve the use of antihypertensive medications. Circulation. 2013 Nov 19;128(21):2309-17.

Sutaria S, Katbamna R, Underwood M. Effectiveness of interventions for the **treatment of acute and prevention of recurrent gout**--a systematic review. Rheumatology (Oxford). 2006 Nov;45(11):1422-31. Epub 2006 Apr 21.

Suttipongkaset P, Chaikittisilpa N, Vavilala MS, et al. **Blood Pressure Thresholds and Mortality in Pediatric Traumatic Brain Injury**. Pediatrics. 2018 Aug;142(2).

Suzuki T, Isselbacher EM, Nienaber CA, et al. Type-Selective Benefits of Medications in Treatment of **Acute Aortic Dissection** (from the International Registry of Acute Aortic Dissection [IRAD]). Am J Cardiol. 2011 Sep 23.

Symplicity HTN-2 Investigators. **Renal sympathetic denervation** in patients with treatment-resistant hypertension (The Symplicity HTN-2 Trial): a randomised controlled trial. Lancet 2010; DOI:10.1016/S0140-6736(10)62039-9.
Tachjian A, Maria V, Jahangir A. Use of herbal products and potential interactions in patients with cardiovascular diseases. J Am Coll Cardiol. 2010 Feb 9;55(6):515-25.
Taipale H, Rysä J, Hukkanen J, et al. Long-term thiazide use and **risk of low-energy fractures among persons with Alzheimer's** disease-nested case-control study. Osteoporos Int. 2019 Apr 16
Tajeu GS, Booth JN, Colantonio LD, et al. Incident cardiovascular disease among adults with blood pressure <140/90 mm Hg. Circulation. 2017;136:798–812.
Takeshita J, Wang S, Shin DB, et al. Effect of **Psoriasis Severity on Hypertension Control**: A Population-Based Study in the United Kingdom. JAMA Dermatol. 2014 Oct 15.
Taler SJ. How Does **SPRINT** (Systolic Blood Pressure Intervention Trial) Direct Hypertension Treatment **Targets for CKD**? Am J Kidney Dis. 2016 Mar 22
Taler SJ. **Initial Treatment of Hypertension**. N Engl J Med. 2018 Feb 15;378(7):636-644.
Tan JE, Wu D, Stowasser M. A **young man with severe hypertension**. BMJ. 2018 Aug 3;362:k2935.
Taylor RS, Ashton KE, Moxham T, et al. **Reduced dietary salt** for the prevention of cardiovascular disease. Cochrane Database of Systematic Reviews 2011, Issue 7. Art. No.: CD009217. DOI: 10.1002/14651858.CD009217. Despite collating more event data than previous systematic reviews of randomised controlled trials (665 deaths in some 6,250 participants), there is still insufficient power to exclude clinically important effects of reduced dietary salt on mortality or cardiovascular morbidity in normotensive or hypertensive populations. Further RCT evidence is needed to confirm whether restriction of sodium is harmful for people with heart failure. Our estimates of benefits from dietary salt restriction are consistent with the predicted small effects on clinical events attributable to the small blood pressure reduction achieved.
Taverny G, Mimouni Y, LeDigarcher A, et al. **Antihypertensive pharmacotherapy for prevention of sudden cardiac death** in hypertensive individuals. Cochrane Database Syst Rev. 2016 Mar 10;3:CD011745.
Although antihypertensive drugs reduce the incidence of fatal and non-fatal myocardial infarction, they do not appear to reduce the incidence of sudden death. This suggests that sudden cardiac death may not be caused primarily by acute myocardial infarction. Continued research is needed to determine causes of sudden cardiac death.
Tennant IA, Barnett AT, Thompson DS, et al. Impaired cardiovascular structure and function in adult survivors of **severe acute malnutrition**. *Hypertension* 2014.
The "**Triple Whammy**". Pharmaicst's Letter Dec/06 (Impaired renal function while involving an ACE &/or ARB, an NSAID &/or a diuretic)
Theilen LH et al. All-cause and cause-specific mortality after **hypertensive disease of pregnancy**. Obstet Gynecol 2016 Aug; 128:238.
Theodore RF, Broadbent J, Nagin D, et al. **Childhood to Early-Midlife Systolic Blood Pressure Trajectories**: Early-Life Predictors, Effect Modifiers, and Adult Cardiovascular Outcomes. Hypertension. 2015 Dec;66(6):1108-15.
Thijs L, Richart T, de Leeuw PW, et al. Morbidity and mortality on **combination** versus monotherapy: a posthoc analysis of the Systolic Hypertension in Europe trial. J Hypertens. 2010 Jan 5. [Epub ahead of print]
Thom S, Poulter N, Field J, et al; **UMPIRE** Collaborative Group. Effects of a **fixed-dose combination** on medication adherence and risk factors in patients with or at risk of CVD: the UMPIRE randomized clinical trial. JAMA. doi:10.1001/jama.2013.277064. (pollypill contained aspirin, simvastatin, lisinopril, and either atenolol or hydrochlorothiazide)
Thomas G, Shishehbor MH, Bravo EL, Nally JV. **Renal denervation** to treat resistant hypertension: Guarded optimism. Cleve Clin J Med. 2012 Jul;79(7):501-10.
Thomas G, Shishehbor M, Brill D, et al. **New hypertension guidelines**: One size fits most? Cleve Clin J Med. 2014 Mar;81(3):178-88.
Thomas, KL, Shah, BR, Elliot-Bynum S, et al. **Check it, change it**: a community-based, multifaceted intervention to improve blood pressure control.*Circ Cardiovasc Qual Outcomes* 2014.
Thomas L. Managing **hypertensive emergencies** in the ED. Can Fam Physician. 2011 Oct;57(10):1137-97.
Thomas SJ, Booth JN 3rd, Dai C, et al. Cumulative **Incidence of Hypertension by 55 Years of Age** in Blacks and Whites: The CARDIA Study. J Am Heart Assoc. 2018 Jul 11;7(14).
Thompson AM, Hu T, Eshelbrenner CL, et al. Antihypertensive treatment and secondary prevention of cardiovascular disease events among persons **without hypertension**: a meta-analysis. JAMA 2011; 305:913-922.
Thompson M, Dana T, Bougatsos C, et al. **Screening** for Hypertension in **Children and Adolescents** to Prevent Cardiovascular Disease. Pediatrics. 2013 Feb 25.
Thompson S, Wiebe N, Padwal RS, et al. The effect of **exercise on blood pressure in chronic kidney disease**: A systematic review and meta-analysis of randomized controlled trials. PLoS One. 2019 Feb 6;14(2):e0211032.
Thornley-Brown D, et al. Differing effects of antihypertensive drugs on the incidence of diabetes mellitus among patients with hypertensive kidney disease. (**AASK**) Arch Intern Med. 2006 Apr 10;166(7):797-805.
Thukkani AK, Bhatt DL. **Renal denervation** therapy for hypertension. Circulation. 2013 Nov 12;128(20):2251-4.
Timpka S, Stuart JJ, Tanz LJ, et al. **Lifestyle** in progression from hypertensive disorders of pregnancy to chronic hypertension in **Nurses' Health Study II**: observational cohort study. BMJ 2017;358:j3024.
Tinetti ME, Han L, Lee DSH, et al. **Antihypertensive medications and serious fall injuries** in a nationally representative sample of older adults [online February 24, 2014]. JAMA Intern Med. doi:10.1001/jamainternmed.2013.14764.
Tinetti ME, McAvay G, Trentalange M, et al. Association between **guideline recommended drugs and death in older adults with multiple chronic conditions**: population based cohort study. BMJ 2015;351:h4984
Tissot AC, et al. Effect of **immunisation against angiotensin II** with CYT006-AngQb on ambulatory blood pressure: a double-blind, randomised, placebo-controlled phase IIa study. Lancet. 2008 Mar 8;371(9615):821-7.
Tobe SW, Stone JA, Brouwers M, et al. **Harmonization of guidelines** for the prevention and treatment of cardiovascular disease: the **C-CHANGE Initiative**. CMAJ. 2011 Sep 12.
Tobe SW. **β-adrenergic receptor blockers in hypertension**. Can J Cardiol. 2014 May;30(5 Suppl):S1-2.
Tobe SW, Izzo JL Jr. Controversies in hypertension: is **lower blood pressure always better**? J Am Soc Hypertens. 2016 Aug;10(8):618-20.
Tobe SW, Stone JA, Anderson T, et al. **Canadian Cardiovascular Harmonized National Guidelines Endeavour (C-CHANGE) guideline** for the prevention and management of cardiovascular disease in primary care: 2018 update. CMAJ. 2018 Oct 9;190(40):E1192-E1206.
Tocci G, Paneni F, Palano F, et al. **Angiotensin-Converting Enzyme Inhibitors, Angiotensin II Receptor Blockers** and **Diabetes**: A Meta-Analysis of Placebo-Controlled Clinical Trials. Am J Hypertens. 2011 May;24(5):582-90.
Toh S, Reichman ME, Houstoun M, et al. Comparative Risk for **Angioedema** Associated With the Use of Drugs That Target the Renin-Angiotensin-Aldosterone System. Arch Intern Med. 2012 Oct 15:1-8.
Tomaszewski M, White C, et al. High rates of **non-adherence** to antihypertensive treatment revealed by **high-performance liquid chromatography-tandem mass spectrometry** (HP LC-MS/MS) urine analysis. Heart. 2014 Apr 2.
Tonelli M, et al. Proteinuria, impaired kidney function, and adverse outcomes in people with coronary disease: analysis of a previously conducted randomised trial (**CARE**). BMJ. 2006 May 19; [Epub ahead of print] The presence or absence of proteinuria on dipstick urinalysis may be used to refine estimates of risk based on kidney function alone.
Torres VE, Abebe KZ, Chapman AB, et al. **Angiotensin blockade** in late **autosomal dominant polycystic kidney disease**. N Engl J Med. DOI: 10.1056/NEJMoa1402686.
Touyz RM, Dominiczak AF. Hypertension Guidelines: Is It Time to **Reappraise Blood Pressure Thresholds and Targets**? Hypertension. 2016 Apr;67(4):688-9. (**SPRINT**)
Touyz RM, Lang NN, Herrmann J, et al. Recent Advances in **Hypertension and Cardiovascular Toxicities With Vascular Endothelial Growth Factor Inhibition**. Hypertension. 2017 Aug;70(2):220-226.
Towfighi A, Markovic D, Ovbiagele B. Consistency of **Blood Pressure Control After Ischemic Stroke**: Prevalence and Prognosis. Stroke. 2014 Mar 27.
Townsend RR, Mahfoud F, Kandzari DE, et al, on behalf of the SPYRAL HTNOFF MED trial investigators. Catheter-based **renal denervation** in patients with **uncontrolled hypertension** in the absence of antihypertensive medications (**SPYRAL HTN-OFF MED**): a randomised, sham-controlled, proof-of-concept trial. Lancet 2017; online Aug 28.
Toyoda K, Koga M, Yamamoto H, et al; ATACH-2 Trial Investigators. **Clinical outcomes depending on acute blood pressure after cerebral hemorrhage**. Ann Neurol. 2018 Nov 12.
Trans CL, Ehrmann BJ, Messer KL, et al. Recent trends in healthcare utilization among **children and adolescents with hypertension** in the United States. Hypertension 2012.
Trasande L, Sathyanarayana S, Spanier AJ, et al. **Urinary phthalates** are associated with higher blood pressure in childhood. J Pediatr. 2013 Sep;163(3):747-753.
Treatment Guidelines: Drugs for Treatment of **Heart Failure** from The Medical Letter April **2003** & Jan **2006.**
Tsai WC, et al. Association of **Intensive Blood Pressure Control and Kidney Disease Progression** in Nondiabetic Patients With Chronic Kidney Disease: A Systematic Review and Meta-analysis. JAMA Intern Med. 2017 Mar 13.
Tsimploulis A, Lam PH, Arundel C, et al. **Systolic Blood Pressure and Outcomes in Patients With Heart Failure With Preserved Ejection Fraction**. JAMA Cardiol. 2018 Feb 14.
Tsuyuki RT, Houle SK, Charrois TL, et al. A Randomized Trial of the Effect of **Pharmacist Prescribing on Improving Blood Pressure in the Community**: The Alberta Clinical Trial in Optimizing Hypertension (**RxACTION**). Circulation. 2015 Jun 10.
Tu W et al. **Triamterene enhances** the blood pressure lowering effect of **hydrochlorothiazide** in patients with hypertension. J Gen Intern Med 2016 Jan; 31:30.
Tucker KL, Sheppard JP, Stevens R, et al. **Self-monitoring of blood pressure** in hypertension: A systematic review and individual patient data meta-analysis. PLoS Med. 2017 Sep 19;14(9):e1002389.
Tung EL, Besser SA, Chua RFM, et al. **Association of Rising Violent Crime** with Blood Pressure and Cardiovascular Risk: Longitudinal Evidence from Chicago, 2014-2016. Am J Hypertens. 2019 Aug 15. doi: 10.1093/ajh/hpz134.
Turgeon R, Allan GM. Taking blood pressure-lowering medications **at night**. Can Fam Physician. 2012 Sep;58(9):965.
Turgeon RD, Koshman SL, Seubert JM, Thompson AE. **Pharmacy student-led blood pressure clinic** as part of a comprehensive approach to teaching blood pressure assessment. Curr Pharm Teach Learn. 2019 Jun;11(6):609-613.
Turnbull F, Neal B, Algert C, et al.; Blood Pressure Lowering Treatment Trialists' Collaboration. Effects of different blood pressure-lowering regimens on major cardiovascular events in individuals with and without diabetes mellitus: results of prospectively designed overviews of randomized trials. Arch Intern Med. 2005 Jun 27;165(12):1410-9.
Turner JM, Peixoto AJ. **Blood pressure targets for hemodialysis patients**. Kidney Int. 2017 Oct;92(4):816-823.

Turner ST, Schwartz GL, Chapman AB, et al. **Plasma renin activity** predicts blood pressure responses to beta-blocker and thiazide diuretics as monotherapy and add-on for hypertension. Am J Hypertens 2010.
Turtle EJ, Dear JW, Webb DJ. A systematic review of the effect of **paracetamol** (acetaminophen) on blood pressure in hypertensive and non-hypertensive subjects. Br J Clin Pharmacol. 2012 Nov 12.
Twersky RS, Goel V, Narayan P, et al. The risk of hypertension after **preoperative discontinuation of angiotensin-converting enzyme inhibitors or angiotensin receptor antagonists** in ambulatory and same-day admission patients. Anesth Analg. 2014 May;118(5):938-44.
Tsuyuki RT, Houle SK, et al. A randomized trial of the effect of **pharmacist prescribing** on improving blood pressure in the community: the Alberta Clinical Trial in Optimizing Hypertension (**RxACTION**). *Circulation* 2015.
Ueda S, Morimoto T, Ando S, et al; **DIME** Investigators. A randomised controlled trial for the evaluation of risk for type 2 diabetes in hypertensive patients receiving **thiazide diuretics**: Diuretics In the Management of Essential hypertension (DIME) study. BMJ Open. 2014 Jul 16;4(7):e004576.
Uhlig K, Patel K, Ip S, Kitsios GD, Balk EM. **Self-Measured Blood Pressure Monitoring** in the Management of Hypertension: A Systematic Review and Meta-analysis. Ann Intern Med. 2013 Aug 6;159(3):185-94.
UK Prospective Diabetes Study Group. Efficacy of **atenolol and captopril** in reducing risk of macrovascular and microvascular complications in type 2 diabetes: **UKPDS 39**. BMJ 1998;317:713-9.
Upadhyay Ashish, Earley Amy, Haynes Shana M., et al. Systematic Review: Blood Pressure Target in **Chronic Kidney Disease and Proteinuria** as an Effect Modifier. *Ann Intern Med* April 19, 2011 154:541-548.
USPSTF U.S. Preventive Services Task Force (USPSTF). **Screening for high blood pressure**. U.S. Preventive Services Task Force reaffirmation recommendation statement. Rockville MD: Agency for Healthcare Research and Quality (AHRQ); 2007. 10 p. The USPSTF recommends screening for high blood pressure in adults aged 18 and older.
USPSTF US Preventive Services Task Force. **Screening for preeclampsia**: US Preventive Services Task Force recommendation statement.JAMA. doi:10.1001 /jama.2017.3439
Václavík Jan, Sedlák Richard, Plachy Martin, et al. Addition of **Spironolactone** in Patients With **Resistant Arterial Hypertension (ASPIRANT)**: A Randomized, Double-Blind, Placebo-Controlled Trial. Hypertension 57: 1069-1075;
Vamos EP, Harris M, Millett C, et al. Association of **systolic and diastolic** blood pressure and all cause mortality in people with newly diagnosed type 2 **diabetes**: retrospective cohort study. BMJ. 2012 Aug 30;345:e5567.
van Bemmel T, et al. In a population-based prospective study, no association between high blood pressure and mortality **after older age 85 years**. J Hypertens. 2006 Feb;24(2):287-92.
van Blijderveen JC, Straus SM, Rodenburg EM, et al. Risk of **hyponatremia** with diuretics: **chlorthalidone** versus **hydrochlorothiazide**. Am J Med. 2014 Aug;127(8):763-71.
van Breukelen-van der Stoep DF, van Zeben D, Klop B, et al. Marked underdiagnosis and **undertreatment** of **hypertension and hypercholesterolaemia in rheumatoid arthritis**. Rheumatology (Oxford). 2016 Mar 23
van Bussel E, Reurich L, Pols J, et al. **Hypertension management**: experiences, wishes and concerns among older people-a qualitative study. BMJ Open. 2019 Aug 18;9(8):e030742.
Van den Born BJ, Hulsman CA, Hoekstra JB, et al. Value of routine funduscopy in patients with hypertension: systematic review. BMJ 2005; 331:73-6. (InfoPOEMs: It is uncommon to see retinal changes by funduscopic examination in patients with hypertension, although when retinal changes occur they are almost always associated with hypertension. Though no studies have been performed to check the reliability of an actual funduscopic examination, there was only moderate agreement between 2 clinicians evaluating photographs of the retina of hypertensive patients for early changes. (LOE = 4))Whelton
van der Hoeven N, Visser I, Schene A, et al. Severe hypertension related to **caffeinated coffee and tranylcypromine**: a case report. Ann Intern Med. 2014 May 6;160(9):657-8.
van der Leeuw J, Visseren FL, Woodward M, et al. Predicting the Effects of Blood Pressure-Lowering Treatment on Major **Cardiovascular Events** for Individual Patients With Type 2 **Diabetes** Mellitus: Results From Action in Diabetes and Vascular Disease: Preterax and Diamicron MR Controlled Evaluation. Hypertension. 2015 Jan;65(1):115-21.
van der Wardt V, Harrison JK, Welsh T, et al. **Withdrawal of antihypertensive medication**: a systematic review. J Hypertens. 2017 May 9.
van Dongen MME, Aarnio K, Martinez-Majander N, et al. Use of **Antihypertensive Medication after Ischemic Stroke in Young Adults and its Association with Long-term Outcome**. Ann Med. 2018 Dec 28:1-29.
van Middelaar T, Ivens SD, van Peet PG, et al. Prescribing and **deprescribing antihypertensive** medication in older people by Dutch general practitioners: a qualitative study. BMJ Open. 2018 Apr 20;8(4):e020871.
van Vark LC, Bertrand M, Akkerhuis KM, et al. Angiotensin-converting enzyme inhibitors **reduce mortality in hypertension**: A meta-analysis of randomized clinical trials of renin-angiotensin-aldosterone system inhibitors involving 158 998 patients. Eur Heart J2012.
Van Vliet BN, Campbell NR; Canadian Hypertension Education Program. Efforts to **reduce sodium intake** in Canada: why, what, and when? Can J Cardiol. 2011 Jul-Aug;27(4):437-45.
Vasilakis-Scaramozza C, Aschengrau A, Cabral HJ, Jick SS. Antihypertensive drugs and the risk of **congenital anomalies**. Pharmacotherapy. 2013 May;33(5):476-82.
Verberk WJ, Kroon AA, Kessels AG, de Leeuw PW. **Home blood pressure measurement**: a systematic review. J Am Coll Cardiol. 2005 Sep 6;46(5):743-51. (InfoPOEMs: Blood pressure measurements taken at home with validated automatic monitors average lower than readings obtained in the office. They are also better prognostic indicators of the detrimental effects of hypertension. Before consigning patients to a diagnosis and treatment of hypertension, or before changing drug therapy, try a few days of at-home monitoring; it might avoid overdiagnosis and overtreatment. (LOE = 1a))
Verdecchia P, Staessen JA, Angeli F, et al. Usual versus tight control of systolic blood pressure in nondiabetic patients with hypertension (**CARDIO-SIS**): an open-label randomised trial. *Lancet* 2009; 374: 525-33.
Verdecchia P, Angeli F, Mazzotta G, et al. **Day-night dip and early-morning surge** in blood pressure in hypertension: prognostic implications. Hypertension. 2012 Jul;60(1):34-42.
Verdecchia P, Angeli F, Reboldi G. **Intensive Blood Pressure** Lowering and Regression of **Left Ventricular Hypertrophy**. Circulation. 2017 Aug 1;136(5):451-453
Verhamme K, Mosis et al. **Spironolactone** and risk of upper gastrointestinal events: population based case-control study. BMJ. 2006 Aug 12;333(7563):330. Epub 2006 Jul 13.
Verma AA, Khuu W, Tadrous M, et al. **Fixed-dose combination antihypertensive medications**, adherence, and clinical outcomes: A population-based retrospective cohort study. PLoS Med. 2018 Jun 11;15(6):e1002584.
Versmissen J, Koch BC, Roofthooft DW, et al. **Doxazosin** treatment of **phaeochromocytoma during pregnancy**: placental transfer and disposition in breast milk. Br J Clin Pharmacol. 2016 May 19.
Victor RG, Blyler, CA, Li, N, et al **Sustainability of Blood Pressure Reduction in Black Barbershops**. Circulation. Accepted. In press. doi: 10.1161/CIRCULATIONAHA. 118.038165.
Victor RG, Lynch K, Li N, et al. A Cluster-Randomized Trial of **Blood-Pressure Reduction in Black Barbershops**. N Engl J Med. 2018 Mar 12.
Vidal-Petiot E, Ford I, et al. **Cardiovascular event rates and mortality** according to achieved systolic and diastolic blood pressure in patients with **stable coronary artery disease**: an international cohort study. Lancet. 2016 Aug 26.
Vidal-Petiot E, et al; **CLARIFY** Investigators. **Relationships Between Components of Blood Pressure and Cardiovascular Events in Patients with Stable Coronary Artery Disease and Hypertension**. Hypertension. 2017 Oct 30.
Viera Anthony J., Hinderliter Alan L., Evaluation and Management of the Patient with Difficult-to-Control or **Resistant Hypertension** Am Fam Physician. 2009;79(10):863-869.
Viera AJ, Neutze DM. Diagnosis of **secondary hypertension**: an age-based approach. Am Fam Physician. 2010 Dec 15;82(12):1471-8.
Viera AJ, Hawes EM. **Management of mild hypertension in adults**. BMJ. 2016 Nov21;355:i5719
Vimaleswaran KS, Cavadino A, Berry DJ, et al.; LifeLines Cohort Study investigators; International Consortium for Blood Pressure (ICBP); Cohorts for Heart and Aging Research in Genomic Epidemiology (CHARGE) consortium; Global Blood Pressure Genetics (Global BPGen) consortium. Association of **vitamin D status** with arterial blood pressure and hypertension risk: a mendelian randomisation study. Lancet Diabetes Endocrinol. 2014 Jun 25.
Virani SS, Maddox TM, Chan PS, et al. **Provider Type and Quality of Outpatient Cardiovascular Disease Care**: Insights From the NCDR PINNACLE Registry. J Am Coll Cardiol. 2015 Oct 20;66(16):1803-12.
Viteri OA, England JA, Alrais MA, et al. Association of **Nonsteroidal Antiinflammatory Drugs and Postpartum Hypertension in Women With Preeclampsia** With Severe Features. Obstet Gynecol. 2017 Sep 5.
Vlachopoulos C, Terentes-Printzios D, Laurent S, et al. Association of **Estimated Pulse Wave Velocity With Survival**: A Secondary Analysis of SPRINT. JAMA Netw Open. 2019 Oct 2;2(10):e1912831.
Vohr BR, Heyne R, Bann C, et al. **High Blood Pressure at Early School Age** Among **Extreme Preterms**. Pediatrics. 2018 Aug;142(2).
von Dadelszen P, Ornstein MP, Bull SB, Logan AG, Koren G, Magee LA. Fall in mean **arterial pressure and fetal growth restriction in pregnancy** hypertension: a meta-analysis. Lancet 2000;355:87-92.
Vongpatanasin W. **Resistant hypertension**: a review of diagnosis and management. JAMA. 2014 Jun 4;311(21):2216-24.
Wald DS, Bestwick JP, Wald NJ. **Child-parent screening for familial hypercholesterolaemia**: screening strategy based on a meta-analysis. BMJ. 2007 Sep 22;335(7620):599. Epub 2007 Sep 13. The proposed strategy of screening children and parents for familial hypercholesterolaemia could have considerable impact in preventing the medical consequences of this disorder in two generations simultaneously.
Wald DS, Law M, Morris JK, Bestwick JP, Wald NJ. **Combination therapy** versus monotherapy in reducing blood pressure: meta-analysis on 11,000 participants from 42 trials. Am J Med. 2009 Mar;122(3):290-300.
Wald DS, Morris JK, Wald NJ. Randomized **polypill** crossover trial in people aged 50 and over. PLoS One. 2012;7(7):e41297.
Walker KA, Sharrett AR, Wu A, et al. Association of Midlife to Late-Life Blood Pressure Patterns With **Incident Dementia**. JAMA. 2019 Aug 13;322(6):535-545.
Wall HK, Hannan JA, Wright JS. Patients with **undiagnosed hypertension**: hiding in plain sight. JAMA. 2014 Nov 19;312(19):1973-4.
Walsh JM, et al. **Quality improvement strategies** for hypertension management: a systematic review.Med Care. 2006 Jul;44(7):646-57.
Walsh KB, Woo D, Sekar P, et al. **Untreated hypertension**: a powerful risk factor for lobar and nonlobar **intracerebral hemorrhage** in whites, blacks, and Hispanics. Circulation. 2016;134:1444–1453.
Wan Y, Heneghan C, Stevens R, McManus RJ, Ward A, Perera R, et al. Determining which **automatic digital blood pressure device** performs adequately: a systematic review. J Hum Hypertens. 2010 Jul;24(7):431-8.
Wang G, Liu X, Bartell TR, et al. **Vitamin D Trajectories** From Birth to Early Childhood **and Elevated Systolic Blood Pressure** During Childhood and Adolescence. Hypertension. 2019 Jul 1:HYPERTENSIONAHA11913120.
Wang JG, Liu L. **Global impact** of 2017 American College of Cardiology/American Heart Association **Hypertension guidelines**: a perspective from China. Circulation. 2018;137:546–548.
Wang L, Sharifi BG, Pan T, et al. Bone marrow transplantation shows superior atheroprotective effects of gene therapy with **apolipoprotein A-1 Milano** compared with wild-type apolipoprotein A-1 in hyperlipidemic mice. J Am Coll

Cardiol 2006; 48:1459-68.
Wang IK, Muo CH, Chang YC, et al. Association between **hypertensive disorders during pregnancy and end-stage renal disease**: a population-based study. CMAJ. 2013 Jan 21.
Wang S, Khera R, Das SR, et al. Usefulness of a Simple **Algorithm to Identify Hypertensive Patients** Who Benefit from Intensive Blood Pressure Lowering. Am J Cardiol. 2018 Apr 11.
Wang YC, Shimbo D, Muntner P, et al. **Prevalence of Masked Hypertension Among US Adults** With Nonelevated Clinic Blood Pressure. Am J Epidemiol. 2017 Jan 18.
Wang Z, Chen Z, Zhang L, et al; on behalf of the China Hypertension Survey Investigators. **Status of hypertension in China**: results from the China Hypertension Survey, 2012–2015. Circulation. 2018;137:2344–2356.
Wannamethee SG, Shaper AG, Lennon L, Morris RW. Metabolic Syndrome vs **Framingham Risk Score** for Prediction of Coronary Heart Disease, Stroke, and Type 2 Diabetes Mellitus. Arch Intern Med. 2005 Dec 26;165(22):2644-50.
Ward, Alison M.; Takahashi, Osamu; Stevens, Richard; Heneghan, Carl. **Home measurement of blood pressure** and cardiovascular disease: systematic review and meta-analysis of prospective studies. Journal of Hypertension Jan 11,12.
Warembourg C, Maitre L, Tamayo-Uria I, et al. Early-Life **Environmental Exposures and Blood Pressure in Children**. J Am Coll Cardiol. 2019 Sep 10;74(10):1317-1328.
Wartenberg KE, Mayer SA. Determining the **optimal target blood** pressure after **thrombectomy**: High or low? Neurology. 2017 Aug 8;89(6):528-529.
Watanabe N, Bando YK, Kawachi T, et al. Development and Validation of a Novel **Cuff-Less Blood Pressure Monitoring Device**. JACC: Basic to Translational Science. 2017 Dec; 2(6): 631-642.
Watkins JL, Thaker PH, Nick AM, et al. Clinical impact of selective and nonselective **beta-blockers** (eg. **propranolol**) on survival in patients with **ovarian cancer**. Cancer. 2015 Aug 24.
Weaver CG, Clement FM, et al. Alberta Kidney Disease Network and the Interdisciplinary Chronic Disease Collaboration. **Healthcare Costs Attributable to Hypertension: Canadian** Population-Based Cohort Study. Hypertension. 2015 Sep;66(3):502-8.
Webb AJS, Fischer U, Mehta Z, et al. Effects of antihypertensive-drug class on **interindividual variation** in blood pressure and risk of stroke: a systematic review and meta-analysis. Lancet 2010; 375:906-915.
Webb AJS, Fischer U, Rothwell PM. Effects of **beta-blocker selectivity** on **blood pressure variability and stroke**: a systematic review. Neurology 2011;77:731–737.
Webb AJ, Rothwell PM. Effect of **dose and combination of antihypertensives on interindividual blood pressure variability**: a systematic review. Stroke. 2011 Oct;42(10):2860-5.
Webb NJ, Wells TG, Shahinfar S, et al. A Randomized, Open-Label, Dose-Response Study of **Losartan in Hypertensive Children**. Clin J Am Soc Nephrol. 2014 May 29.
Weber Cynthia A.; Ernst Michael E.; Sezate Genesis S.; et al. Pharmacist-Physician Comanagement of Hypertension and Reduction in 24-Hour Ambulatory Blood Pressures. *Arch Intern Med*. 2010;170(18):1634-1639.
Weber KA, Mayo JA, Carmichael SL, et al. Occurrence of Selected **Structural Birth Defects Among Women With Preeclampsia and Other Hypertensive Disorders**. Am J Epidemiol. 2018 Apr 1;187(4):668-676.
Weber MA, Jamerson K, Bakris GL et al. Effects of **body size and hypertension treatments** on cardiovascular event rates: subanalysis of the **ACCOMPLISH** randomized controlled trial. Lancet 2012.
Weber MA, Schiffrin EL, White WB, et al. **ASH/ISH**: Clinical practice guidelines for the **management of hypertension** in the community. A statement by the American Society of Hypertension and the International Society of Hypertension. J Clin Hypertens 2013; DOI:10.1111/jch.12237.
Weber MA. **Blood pressure variability** and cardiovascular prognosis: implications for clinical practice. Eur Heart J. 2017 Oct 1;38(37):2823-2826.
Webster K, Fishburn S, Maresh M, et al. Diagnosis and management of **hypertension in pregnancy**: summary of updated NICE guidance. BMJ. 2019 Sep 9;366:l5119.
Webster LM, et al. Impact of **Antihypertensive Treatment on Maternal and Perinatal Outcomes in Pregnancy** Complicated by Chronic Hypertension: A Systematic Review and Meta-Analysis. J Am Heart Assoc. 2017 May 17;6(5).
Webster LM, Myers JE, Nelson-Piercy C, et al. **Labetalol Versus Nifedipine** as Antihypertensive Treatment for **Chronic Hypertension in Pregnancy**: A Randomized Controlled Trial. Hypertension. 2017 Nov;70(5):915-922.
Webster R, Salam A, Asita de Silva H, et al; TRIUMPH Study Group. **Fixed low-dose triple combination antihypertensive medication vs usual care for blood pressure control in patients with mild to moderate hypertension** in Sri Lanka: a randomized clinical trial. JAMA. doi:10.1001/jama.2018.10359
Weinberg I, Gona P, O'Donnell CJ, et al. The **systolic blood pressure difference between arms** and cardiovascular disease in the Framingham heart study. Am J Med. 2014 Mar;127(3):209-15.
Weiner RB, Wang F, Isaacs SK, et al. Blood pressure and left ventricular hypertrophy **during american-style football** participation. Circulation. 2013 Jul 30;128(5):524-31.
Weir MR. **Hypertension- In the Clinic**. Ann Intern Med. 2014 Dec 2;161(11).
Weiss A, Beloosesky Y, Kenett RS, Grossman E. **Systolic Blood Pressure During Acute Stroke** Is Associated With Functional Status and Long-term Mortality in the Elderly. Stroke. 2013 Sep;44(9):2434-40.
Weiss J, Freeman M, et al. **Benefits and harms of intensive blood pressure treatment in adults aged 60 years or older**: a systematic review and meta-analysis. Ann Intern Med. 2017. [Epub ahead of print]. doi:10.7326/M16-1754 3.
Weissgerber TL, Turner ST, Mosley TH Jr, et al. **Hypertension in Pregnancy** and **Future Cardiovascular Event Risk in Siblings**. J Am Soc Nephrol. 2015 Aug 27.
Wen CP, Wai JPM, Tsai MK, et al. Minimum amount of **physical activity** for reduced mortality and extended life expectancy: a prospective cohort study. Lancet 2011. (15min a day or 90 min a week of moderate intensity exercise)
Werumeus Buning J et al. Effects of **hydrocortisone** on the **regulation of blood pressure**: Results from a randomized controlled trial. J Clin Endocrinol Metab 2016 Oct; 101:3691.
Wheeler MJ, Dunstan DW, Ellis KA, et al. Effect of **Morning Exercise With or Without Breaks in Prolonged Sitting on Blood Pressure in** Older Overweight/Obese Adults. Hypertension. 2019 Feb 20:HYPERTENSIONAHA11812373.
Whelton PK, Appel LJ, Sacco RL, et al. **Sodium**, blood pressure, and cardiovascular disease: further evidence supporting the american heart association sodium reduction recommendations. Circulation. 2012 Dec 11;126(24):2880-9.
Whelton PK and Muntner P.Potential implications of the **systolic blood pressure intervention** trial in **Korea**. J Am Coll Cardiol 2016 Jun 21; 67:2832.
Whelton PK, Reboussin DM, Fine LJ. Comparing the **SPRINT** and the **HOPE-3** Blood Pressure Trial. JAMA Cardiol. 2016 Sep 7.
Whelton PK, Carey RM, Aronow WS, et al. **2017 ACC/AHA**/AAPA/ABC/ACPM/AGS/APhA/ASH/ASPC/NMA/PCNA **Guideline for the Prevention, Detection, Evaluation, and Management of High Blood Pressure** in Adults: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. Hypertension. 2017 Nov 13.
Whelton PK, Carey RM. The **2017 Clinical Practice Guideline for High Blood Pressure**. JAMA. 2017 Nov 20.
Whelton PK, Williams B. The 2018 European Society of Cardiology/European Society of Hypertension and 2017 American College of Cardiology/American Heart Association **Blood Pressure Guidelines**: More Similar Than Different. JAMA. 2018 Nov 6;320(17):1749-1750.
Whelton SP, Blumenthal RS. Beyond Headlines: Insights on **Potassium Supplementation** for the Treatment of Hypertension From the Canadian Hypertension Education Program Guidelines (CHEP). Circulation. 2017 Jan 3;135(1):3-4.
White WB et al. **Average daily blood pressure**, not office blood pressure, is associated with progression of cerebrovascular disease and cognitive decline in older people. Circulation. 2011 Nov 22;124(21):2312-9.
Whittle J. **Blood pressure variability** and cardiovascular risk. BMJ. 2016 Aug 10;354:i4190
Wiesel J, et al. Comparison of the **microlife blood pressure monitor with the omron blood pressure monitor** for detecting atrial fibrillation. Am J Cardiol. 2014 Oct 1;114(7):1046-8.
Wein T, Lindsay MP, Côté R, Foley N, Berlingieri J, Bhogal S, et al; Heart and Stroke Foundation **Canadian Stroke Best Practice Committees**. Canadian stroke best practice recommendations (**CSBPR**): Secondary prevention of stroke, sixth edition practice guidelines, update 2017. Int J Stroke. 2018 Jun;13(4):420-443.
Which drugs are best for treating severe hypertension in pregnancy? Drug Ther Bull. 2019 Apr;57(4):53.
Wijeysundera HC, Nallamothu BK, Krumholz HM, Tu JV, Ko DT. Meta-analysis: Effects of **Percutaneous Coronary Intervention Versus Medical Therapy** on Angina Relief. Ann Intern Med. 2010 Mar 16;152(6):370-9.
Wilhelm SM, Young J, Kale-Pradhan PB. Effect of **Bariatric Surgery** on Hypertension: A Meta-analysis. Ann Pharmacother. 2014 Jun;48(6):674-82.
Wikström AK, Gunnarsdottir J, Nelander M, et al. **Prehypertension in Pregnancy** and Risks of Small for Gestational Age Infant and Stillbirth. Hypertension. 2016 Feb 1.
Will JC, Zhang Z, Ritchey MD, et al. **Medication Adherence** and Incident Preventable Hospitalizations for Hypertension. Am J Prev Med. 2015 Oct 30.
Williams MA, Haskell WL, Ades PA, Amsterdam EA, Bittner V, Franklin BA, Gulanick M, Laing ST, Stewart KJ. **Resistance Exercise** in Individuals With and Without Cardiovascular Disease: 2007 Update. A Scientific Statement From the American Heart Association Council on Clinical Cardiology and Council on Nutrition, Physical Activity, and Metabolism. Circulation. 2007 Jul 16; [Epub ahead of print]
Williams B, MacDonald TM, Morant S, et al, for The British Hypertension Society's PATHWAY Studies Group. **Spironolactone** versus **placebo, bisoprolol, and doxazosin** to determine the optimal treatment for **drug-resistant hypertension (PATHWAY-2)**: a randomised, double-blind, crossover trial. Lancet 2015; online Sept 21.
Williamson JD, Supiano MA, Applegate WB, et al. **Intensive vs standard blood pressure** control and cardiovascular disease outcomes in **adults aged 75 years**: a randomized clinical trial (**SPRINT**).JAMA. doi:10.1001/jama.2016.7050.
Wilson JF. In the clinic. **Stable ischemic heart disease**. Ann Intern Med. 2014 Jan 7;160(1)
Winchester DE, Pepine CJ. Usefulness of **Beta Blockade in Contemporary Management** of Patients With Stable Coronary Heart Disease. Am J Cardiol. 2014 Aug 27.
Windecker S, Stortecky S, Stefanini GG, da Costa BR, Rutjes AW, di Nisio M, et al. **Revascularisation versus medical treatment** in patients with **stable coronary artery disease**: network meta-analysis. BMJ 2014;348:g3859.

Winkelmayer WC, Stampfer MJ, Willett WC, Curhan GC. Habitual **caffeine** intake and the risk of hypertension in women. JAMA. 2005 Nov 9;294(18):2330-5. (InfoPOEMs: Habitual caffeine consumption does not appear to increase the risk of hypertension in women. In particular, coffee and tea are not associated with increased risk. The development of hypertension is, however, significantly associated with the intake of cola drinks, including both sugared and diet versions. (LOE = 2b))

Wiysonge CS, Bradley HA, Volmink J, et al. **Beta-blockers for hypertension**. Cochrane Database Syst Rev. 2012 Aug 15;8:CD002003. Initiating treatment of hypertension with beta-blockers leads to modest reductions in cardiovascular disease and no significant effects on mortality. These effects of beta-blockers are inferior to those of other antihypertensive drugs.

Wiysonge CS, Opie LH. **β-Blockers as initial therapy for hypertension**. JAMA. 2013 Nov 6;310(17):1851-2.

Wiysonge CS, Bradley HA, Volmink J, et al. **Beta-blockers for hypertension**. Cochrane Database Syst Rev. 2017 Jan 20;1:CD002003. Most outcome RCTs on beta-blockers as initial therapy for hypertension have high risk of bias. Atenolol was the beta-blocker most used. Current evidence suggests that initiating treatment of hypertension with beta-blockers leads to modest CVD reductions and little or no effects on mortality. These beta-blocker effects are inferior to those of other antihypertensive drugs. Further research should be of high quality and should explore whether there are differences between different subtypes of beta-blockers or whether beta-blockers have differential effects on younger and older people.

Wolf SJ, Lo B, Shih RD, Smith MD, Fesmire FM, American College of Emergency Physicians Clinical Policies Committee. Clinical policy: critical issues in the evaluation and management of adult patients in the **emergency department with asymptomatic elevated blood pressure**. Ann Emerg Med. 2013 Jul;62(1):59-68.

Wolters FJ, Mattace-Raso FU, et al. **Orthostatic Hypotension** and the **Long-Term Risk of Dementia**: A Population-Based Study. PLoS Med. 2016 Oct 11;13(10):e1002143.

Wong A, Figueroa A, Son WM, et al. The effects of **stair climbing** on arterial stiffness, blood pressure, and leg strength in postmenopausal women with stage 2 hypertension. Menopause. 2018 Feb 12.

Wong ND, Lopez VA, L'italien G, Chen R, Kline SE, Franklin SS. **Inadequate Control of Hypertension** in US Adults With Cardiovascular Disease Comorbidities in 2003-2004. Arch Intern Med. 2007 Dec 10;167(22):2431-6.

Wong MC, Liu KQ, Wang HH, et al. Effectiveness of a **pharmacist-led drug counseling** on enhancing antihypertensive adherence and blood pressure control: a randomized controlled trial. J Clin Pharmacol. 2013 Jul;53(7):753-61.

Wong GW, Wright JM. Blood pressure lowering efficacy of **nonselective beta-blockers** for primary hypertension. Cochrane Database Syst Rev. 2014 Feb 28;2:CD007452. doi: 10.1002/14651858.CD007452.pub2. In people with mild-to-moderate hypertension, nonselective beta-blockers lowered peak BP by a mean of -10/-7 mmHg (systolic/diastolic) and reduced heart rate by 12 beats per minute. Propranolol and penbutolol were the two drugs that contributed to most of the data for nonselective beta-blockers. This estimate is likely exaggerated due to the presence of extreme outliers and other sources of bias. If we removed the extreme outliers from the analysis, the estimate for non-selective beta-blockers was lower (-8/-5 mmHg (systolic/diastolic)). Nonselective beta-blockers did not show a convincing graded dose-response in the recommended dose range for systolic BP and diastolic BP, while higher dose nonselective beta-blockers provided greater reduction of heart rate. Using higher dose nonselective beta-blockers might cause more side effects, such as bradycardia, without producing an additional BP lowering effect. The effect of nonselective beta-blockers on pulse pressure was likely small, at about 2 mmHg.

Wright JT, JA, et al, for the **ALLHAT** Collaborative Research Group. Outcomes in hypertensive black and nonblack patients treated with chlorthalidone, amlodipine, and lisinopril. JAMA 2005;293:1595- 608 & ACP Journal Club . (InfoPOEMs: Thiazide-type diuretics are the best initial agents for the treatment of hypertension for most patients, including both blacks and nonblacks. (LOE = 1b-))

Wright JM, Musini VM. **First-line drugs** for hypertension. Cochrane Database Syst Rev. 2009 Jul 8;(3):CD001841. First-line low-dose thiazides reduce all morbidity and mortality outcomes. First-line ACE inhibitors and calcium channel blockers may be similarly effective but the evidence is less robust. First-line high-dose thiazides and first-line beta-blockers are inferior to first-line low-dose thiazides.

Wright JM, Musini VM, Gill R First-line drugs for hypertension. Cochrane Database Syst Rev. 2018 Apr 18;4:CD001841. First-line low-dose thiazides reduced all morbidity and mortality outcomes in adult patients with moderate to severe primary hypertension. First-line ACE inhibitors and calcium channel blockers may be similarly effective, but the evidence was of lower quality. First-line high-dose thiazides and first-line beta-blockers were inferior to first-line low-dose thiazides.

Wright JT, Fine LJ, Lackland DT, et al. Evidence supporting a systolic blood pressure **goal of less than 150 mm Hg in patients aged 60 years or older**: The minority view. *Ann Intern Med* 2014.

Writing Group Members, Mozaffarian D, Benjamin EJ, et al; American Heart Association Statistics Committee; Stroke Statistics Subcommittee. **Heart Disease and Stroke Statistics-2016 Update**: A Report From the American Heart Association. Circulation. 2016 Jan 26;133(4):e38-60.

Wu HY, Huang JW, Lin HJ, et al. Comparative effectiveness of **renin-angiotensin system blockers** and other antihypertensive drugs in patients with **diabetes**: systematic review and bayesian network meta-analysis. BMJ. 2013 Oct 24;347:f6008. (ACEI treatment of choice)

Wu S, Chen JJ, Kudelka A, Lu J, Zhu X. Incidence and risk of hypertension with **sorafenib** in patients with cancer: a systematic review and meta-analysis. Lancet Oncol. 2008 Feb;9(2):117-23. Epub 2008 Jan 24.

Wu S, Han J, Li WQ, et al. Hypertension, Antihypertensive Medication Use, and **Risk of Psoriasis**. JAMA Dermatol. 2014 Jul 2.

Xi B, Zhang M, Zhang T, et al. Hypertension **Screening Using Blood Pressure to Height Ratio**. Pediatrics. 2014 Jun 9.

Xi B, Zong X, Kelishadi R, et al; on behalf of the International Child Blood Pressure References Establishment Consortium. Establishing **international blood pressure references among nonoverweight children and adolescents aged 6 to 17** years. Circulation. 2016;133:398–408.

Xie W, Zheng F, Evangelou E, et al. **Blood pressure-lowering drugs and secondary prevention of cardiovascular disease**: systematic review and meta-analysis. J Hypertens. 2018 Mar 14.

Xie X, Atkins E, Lv J, et al. Effects of **intensive blood pressure lowering on cardiovascular and renal outcomes**: updated systematic review and meta-analysis. Lancet 2015; online Nov 6.

Xie X, Wang Y, Yang Y, et al. Long-Term Effects of **Ambient Particulate Matter** (With an Aerodynamic Diameter ≤2.5 μm) on Hypertension and Blood Pressure and Attributable Risk Among Reproductive-Age Adults in China. J Am Heart Assoc. 2018 Apr 26;7(9).

Xu W, Goldberg SI, Shubina M, Turchin A. **Intensification and time to follow-up in treatment of hypertension**: A population-based retrospective study. *BMJ* 2015.

Xu W, Goldberg SI, Shubina M, Turchin A. **Optimal systolic blood pressure target, time to intensification, and time to follow-up** in treatment of hypertension: population based retrospective cohort study. BMJ 2015;350:h158.

Xue H, Lu Z, Tang WL, et al. **First-line drugs inhibiting the renin angiotensin system versus other first-line antihypertensive drug classes** for hypertension. Cochrane Database Syst Rev. 2015 Jan 11;1:CD008170. We found predominantly moderate quality evidence that all-cause mortality is similar when first-line RAS inhibitors are compared to other first-line antihypertensive agents. First-line thiazides caused less HF and stroke than first-line RAS inhibitors. The quality of the evidence comparing first-line beta-blockers and first-line RAS inhibitors was low and the lower risk of total CV events and stroke seen with RAS inhibitors may change with the publication of additional trials. Compared with first-line CCBs, first-line RAS inhibitors reduced HF but increased stroke. The magnitude of the reduction in HF exceeded the increase in stroke. The small differences in effect on blood pressure between the different classes of drugs did not correlate with the differences in the primary outcomes.

Yancy William S Jr; Westman Eric C.; McDuffie Jennifer R.; et al. A Randomized Trial of a **Low-Carbohydrate** Diet vs **Orlistat Plus a Low-Fat** Diet for Weight Loss. Arch Intern Med. 2010;170(2):136-145.

Yang J, Shen J, Fuller PJ. A practical approach to **diagnosing endocrine hypertension**. Nephrology (Carlton). 2017 May 27.

Yang Q, Liu T, Kuklina EV, et al. **Sodium and potassium intake and mortality** among US adults: prospective data from the Third National Health and Examination Survey. Arch Intern Med. 2011;171(13):1183-1191.

Yang Q, Zhang Z, Kuklina EV, et al. **Sodium Intake** and Blood Pressure Among US Children and Adolescents. Pediatrics. 2012 Sep 17.

Yang Q, Chang A, Ritchey MD, et al. Antihypertensive Medication **Adherence** and Risk of Cardiovascular Disease Among Older Adults: A Population-Based Cohort Study. J Am Heart Assoc. 2017 Jun 24;6(6).

Yang WY, Melgarejo JD, Thijs L, et al. Association of **Office and Ambulatory Blood Pressure** With Mortality and Cardiovascular Outcomes. JAMA. 2019 Aug 6;322(5):409-420.

Yano Y, Reis JP, Colangelo LA, et al. Association of blood pressure classification in young adults using the 2017 American College of Cardiology/American Heart Association blood pressure guideline with cardiovascular events later in life [online Nov 6, 2018]. JAMA.

Yano Y, Reis JP, Tedia Y, et al. **Racial differences** in associations of blood pressure components in **young adulthood with incident cardiovascular disease by middle age**. *JAMA Cardiol* 2017.

Yano Y, Rakugi H, Bakris GL, et al. **On-Treatment Blood Pressure** and Cardiovascular Outcomes in Older Adults With **Isolated Systolic Hypertension**. (**Valish**) Hypertension. 2017 Feb;69(2):220-227.

Yano Y, Stamler J, Garside DB, et al. **Isolated Systolic Hypertension in Young and Middle-Aged Adults** and 31-Year Risk for **Cardiovascular Mortality**: The Chicago Heart Association Detection Project in Industry Study. J Am Coll Cardiol. 2015 Feb 3;65(4):327-35.

Yano Y, Tanner RM, Sakhuja S, et al. Association of **Daytime and Nighttime Blood Pressure** With Cardiovascular Disease Events Among African American Individuals. JAMA Cardiol. 2019 Aug 14.

Yasar S, Xia J, Yao W, et al. **Antihypertensive drugs decrease risk of Alzheimer's disease**: Ginkgo Evaluation of Memory Study. Neurology 2013;81:896–903.

Yi SW, Mok Y, Ohrr H, et al. **Low Systolic Blood Pressure** and Vascular **Mortality** Among More Than 1 Million Korean Adults. Circulation. 2016 Jun 14;133(24):2381-90

Yokoyama Y, Nishimura K, Barnard ND, et al. **Vegetarian Diets** and Blood Pressure: A Meta-analysis. JAMA Intern Med. 2014 Feb 24.

Yoon C, Yang HS, Jeon I, et al. Use of angiotensin-converting-enzyme inhibitors or angiotensin-receptor blockers and **cancer risk**: a meta-analysis of observational studies. CMAJ. 2011 Oct 4;183(14):E1073-84.

Yoon EY, Cohn L, Rocchini A, et al. Use of **Diagnostic Tests in Adolescents** With Essential Hypertension. Arch Pediatr Adolesc Med. 2012 Jul 23:1-6.

Yoon SS, Gu Q, Nwankwo T, et al. **Trends in blood pressure** among adults with hypertension: United States, 2003 to 2012. Hypertension. 2015 Jan;65(1):54-61.

Young WF, Calhoun DA, Lenders JWM, et al. **Screening for Endocrine Hypertension**: An Endocrine Society Scientific Statement. Endocrine Reviews. 2017;38(2):103-122

Youngstrom M, Tita A, Grant J, et al. **Perinatal Outcomes** in Women With a **History of Chronic Hypertension but Normal Blood Pressures Before 20 Weeks of Gestation**. Obstet Gynecol. 2018 Apr 6.

Yusuf S, Islam S, Chow CK, et al. Use of **secondary prevention drugs** for cardiovascular disease in the community in high-income, middle-income, and low-income countries (the PURE Study): a prospective epidemiological survey. Lancet 2011; DOI:10.1016/ S0140-6736(11)61215-4.

Yusuf S, Rangarajan S, Teo K, et al. **Cardiovascular risk and events in 17 low-, middle-, and high-income countries**.N Engl J Med 2014; 371: 818-27.
Yusuf S, Lonn E, Pais P, et al. **Blood-pressure and cholesterol lowering** in persons **without cardiovascular disease**. (**Hope-3**) N Engl J Med. DOI: 10.1056/NEJMoa1600177.
Yusuf S, Lonn E. The **SPRINT** and the **HOPE-3** Trial in the Context of Other Blood Pressure-Lowering Trials. JAMA Cardiol. 2016 Sep 7.
Zaccardi F, Laukkanen T, Willeit P, et al. **Sauna Bathing** and Incident Hypertension: A Prospective Cohort Study. Am J Hypertens. 2017 Jun 13.
Zamorano JL, Lancellotti P, Rodriguez Muñoz D, et al. **2016 ESC** position paper on cancer treatments and cardiovascular toxicity developed under the auspices of the ESC Committee for Practice Guidelines: The Task Force for **cancer treatments and cardiovascular tox**icity of the European Society of Cardiology (ESC). Eur Heart J. 2016 Aug 26. [Epub ahead of print]
Zatonski W, Willett W. Changes in dietary fat and declining coronary heart disease in Poland: population based study. BMJ. July 23, 2005;331:187-88.
Zhang D, Wang G, Joo H. A Systematic Review of Economic Evidence on **Community Hypertension Interventions**. Am J Prev Med. 2017 Dec;53(6S2):S121-S130.
Zhang R, Zhong C, Zhang Y, et al. Immediate **Antihypertensive Treatment for Patients With Acute Ischemic Stroke** With or Without History of Hypertension: A Secondary Analysis of the CATIS Randomized Clinical Trial. JAMA Netw Open. 2019 Jul 3;2(7):e198103.
Zhang WR et al. **Kidney damage biomarkers** and incident chronic kidney disease **during blood pressure reduction**: A case–control study. Ann Intern Med 2018 Oct 23.
Zhang WR, Craven TE, Malhotra R, et al; SPRINT Research Group. **Kidney Damage Biomarkers** and Incident Chronic Kidney Disease During Blood Pressure Reduction: A Case-Control Study. Ann Intern Med. 2018 Oct 23.
Zhang X, Li Y, Del Gobbo LC, et al. Effects of **Magnesium Supplementation** on Blood Pressure: A Meta-Analysis of Randomized Double-Blind Placebo-Controlled Trials. Hypertension. 2016 Aug;68(2):324-33.
Zhang Y, Moran AE. Trends in the Prevalence, Awareness, Treatment, and Control of **Hypertension Among Young Adults in the United States**, 1999 to 2014. Hypertension. 2017 Aug 28.
Zhang Y, Vittinghoff E, Pletcher MJ, et al. Associations of **Blood Pressure and Cholesterol Levels During Young Adulthood** With Later Cardiovascular Events. J Am Coll Cardiol. 2019 Jul 23;74(3):330-341
Zhang Y, Yang L, Hou Y,et al. Performance of the **Simplified American Academy of Pediatrics Table to Screen Elevated Blood Pressure in Children**. JAMA Pediatr. 2018 Aug 13.
Zhao P, Xu P, Wan C, Wang Z. **Evening versus morning dosing regimen** drug therapy for hypertension. Cochrane Database of Systematic Reviews 2011, Issue 10. Art. No.: CD004184. DOI: 10.1002/14651858.CD004184.pub2. No RCT reported on clinically relevant outcome measures - all cause mortality, cardiovascular morbidity and morbidity. There were no significant differences in overall adverse events and withdrawals due to adverse events among the evening versus morning dosing regimens. In terms of BP lowering efficacy, for 24-hour SBP and DBP, the data suggests that better blood pressure control was achieved with bedtime dosing than morning administration of antihypertensive medication, the clinical significance of which is not known.
Zhao W, Katzmarzyk PT, Horswell R, et al. **Aggressive blood pressure control increases coronary heart disease risk among diabetic** patients. Diabetes Care 2013.
Zhu X, Wong FKY, Wu CLH. Development and evaluation of a **nurse-led hypertension management** model: A randomized controlled trial. Int J Nurs Stud. 2018 Jan;77:171-178.
Zillich AJ, Sutherland JM, Kumbera PA, Carter BL. Hypertension outcomes through blood pressure monitoring and evaluation by pharmacists (HOME study). J Gen Intern Med. 2005 Dec;20(12):1091-6.
Zonneveld TP, Richard E, Vergouwen MD, et al. **Blood pressure-lowering treatment for preventing recurrent stroke, major vascular events, and dementia in patients with a history of stroke or transient ischaemic attack.** Cochrane Database Syst Rev. 2018 Jul 19;7:CD007858. Our results support the use of BPLDs in people with stroke or TIA for reducing the risk of recurrent stroke. Current evidence is primarily derived from trials studying an ACE inhibitor or a diuretic. No definite conclusions can be drawn from current evidence regarding an optimal systolic blood pressure target after stroke or TIA.
Zou Y, Zhao X, Hou YY, et al. Meta-Analysis of Effects of Voluntary **Slow Breathing Exercises** for Control of Heart Rate and Blood Pressure in Patients With Cardiovascular Diseases. Am J Cardiol. 2017 Apr 12.

Web Sties:
American College of Physicians: ACP Special Report: Living with Hypertension www.doctorsforadults.com/images/healthpdfs/hypertension_report.pdf
American Heart Association: High Blood Pressure www.americanheart.org/presenter.jhtml?identifier=2114
National Heart, Lung, and Blood Institute: Your Guide to Lowering Blood Pressure www.nhlbi.nih.gov/health/public/heart/hbp/hbp_low/hbp_low.pdf
National Kidney Foundation: High Blood Pressure (Hypertension) www.kidney.org/atoz/atozTopic.cfm?topic=1

ORAL ANTIHYPERTENSIVES Summary/Guidelines Comparison Chart

[1] Palmer, B. Managing Hyperkalemia Caused by Inhibitors of the Renin-Angiotensin-Aldosterone System. N Engl J Med 2004;351:585-92.

[2] Major Outcomes in High-Risk Hypertensive Patients Randomized to Angiotensin-Converting Enzyme Inhibitor or Calcium Channel Blocker vs Diuretic. The Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial (**ALLHAT**). The ALLHAT Officers and Coordinators for the ALLHAT Collaborative Research Group. JAMA. 2002;288:2981-2997.

[3] 2001 Canadian Hypertension Recommendations: What's New & What's Not so New but is Still Important. CJHP 2002;55:4651.

[4] FA McAlister, M Levine, KB Zarnke, et al. The 2000 recommendations for the management of hypertension. Can J Cardiol 2001; 17(5):543-559.

[5] 1999 Canadian recommendations for the management of hypertension. CMAJ 1999;161(Suppl):S1-S16.

[6] **1999 World Health Organization**–International Society of Hypertension Guidelines:Management of Hypertension. J Hypertens 1999;17:151-183.

[7] 6th Report-Joint National Committee-JNC on Prevention,Detection,Evaluation & Treatment of High Blood Pressure. Arch Intern Med 1997;157:2413-46.

[8] Drugs for hypertension. Med Lett Drugs Ther 2001;43:17-22. & Initial Therapy of Hypertension Med Lett Drugs Ther **2004**;46:53-55.

[9] Drugs in Pregnancy & Lactation, 11th Ed. Briggs GE,et al. Wilkins;Baltimore, MD. 2017.

[10] Micromedex 2018 online

[11] Hansten & Horn's Drug Interactions: Analysis & Management-Facts & Comparisons 2008.

[12] Treatment Guidelines: Drugs for Hypertension from The Medical Letter Feb 2003, repeated June 2005, January 2009, January 2012, May 2014 & updated **March 2017**.

[13] The **2017 Canadian** Hypertension Education Program **Recommendations** www.hypertension.ca

Hackam DG, Quinn RR, Ravani P, et al. Canadian Hypertension Education Program. The 2013 Canadian Hypertension Education Program (CHEP) Recommendations for Blood Pressure Measurement, Diagnosis, Assessment of Risk, Prevention, and Treatment of Hypertension. Can J Cardiol. 2013 Mar 28.

(Patient instructions for purchasing & using home blood pressure measurements can be found at www.hypertension.ca/tools & at www.heartandstroke.ca/bp)

Hackam DG, Khan NA, Hemmelgarn BR, et al. Canadian Hypertension Education Program. The 2010 Canadian Hypertension Education Program recommendations for the management of hypertension: part 2 - **therapy**. Can J Cardiol. 2010 May;26(5):249-58.

Quinn RR, Hemmelgarn BR, Padwal RS, et al. Canadian Hypertension Education Program. The 2010 Canadian Hypertension Education Program recommendations for the management of hypertension: part I - blood pressure measurement, **diagnosis and assessment of risk**. Can J Cardiol. 2010 May;26(5):241-8.

Canadian Hypertension Education Program. **2011 CHEP recommendations** for the management of **hypertension**. http://hypertension.ca/chep/wp-content/uploads/2011/05/FullCHEPRecommendations_EN_2011.pdf .

Dasgupta K, Quinn RR, Zarnke KB, et al. Canadian Hypertension Education Program. The **2014 CHEP-Canadian Hypertension** Education Program Recommendations for Blood Pressure Measurement, Diagnosis, Assessment of Risk, Prevention, and Treatment of Hypertension. Can J Cardiol. 2014 May;30(5):485-501.

Leung AA, Nerenberg K, Daskalopoulou SS, et al; CHEP Guidelines Task Force. Hypertension Canada's **2016 CHEP guidelines** for blood pressure measurement, diagnosis, assessment of risk, prevention and treatment of hypertension. Can J Cardiol 2016 (accepted manuscript) doi: 10.1016/j.cjca.2016.02.066 www.onlinecjc.ca/article/S0828-282X(16)00192-6/pdf (accessed April 11, 2016).

Harris KC, Benoit G, Dionne J, et al; **CHEP** Guidelines Task Force. Hypertension Canada's **2016 Canadian Hypertension** Education Program Guidelines for Blood Pressure Measurement,Diagnosis, and Assessment of Risk of

Pediatric Hypertension. Can J Cardiol. 2016 May;32(5):589-97.
Dionne JM, Harris KC, Benoit G, et al. **Hypertension Canada's 2017 Guidelines for the Diagnosis, Assessment, Prevention, and Treatment of Pediatric Hypertension**. Can J Cardiol. 2017 May;33(5):577-585
Leung AA, Daskalopoulou SS, Dasgupta K, et al. **Hypertension Canada's 2017 Guidelines for Diagnosis, Risk Assessment, Prevention, and Treatment of Hypertension in Adults**. Can J Cardiol. 2017 May;33(5):557-576
Nerenberg KA, Zarnke KB, Leung AA, et al. **Hypertension Canada's 2018 guidelines for diagnosis, risk assessment, prevention, and treatment of hypertension in adults and children**. Can J Cardiol 2018; February 20, 2018.
Diabetes Canada Clinical Practice Guidelines Expert Committee, Tobe SW, Gilbert RE, Jones C, et al. **Treatment of Hypertension**. Can J Diabetes. 2018 Apr;42 Suppl 1:S186-S189.
Butalia S, Audibert F, Côté AM, et al. **Hypertension Canada's 2018 Guidelines for the Management of Hypertension in Pregnancy**. Can J Cardiol. 2018 May;34(5):526-531.
Nerenberg KA, Zarnke KB, et al. **Hypertension Canada's 2018 Guidelines for Diagnosis, Risk Assessment, Prevention, and Treatment of Hypertension in Adults and Children**. Can J Cardiol. 2018 May;34(5):506-525.

[14] ALLHAT Working Group. Major cardiovascular events in hypertensive patients randomized to doxazosin vs chlorthalidone: the antihypertensive and lipid-lowering treatment to prevent heart attack trial (**ALLHAT**). JAMA 2000;283:1967-75.
[15] The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, & Treatment of High Blood Pressure (The **JNC 7**); JAMA. **2003** May;289(19):2560-72. (Complete report in Hypertension 2003;42:1206-1252)
James PA, Oparil S, Carter BL, et al. **2014** evidence-based guideline for the management of **high blood pressure in adults**: report from the panel members appointed to the Eighth Joint National Committee (**JNC 8**). JAMA. doi:10.1001/jama.2013.284427.
[16] Black HR, Elliott WJ, Grandits G, et al. Principal results of the Controlled Onset Verapamil Investigation of Cardiovascular End Points (**CONVINCE**) trial. JAMA. 2003 Apr 23-30;289(16):2073-82.
[17] August P. Initial treatment of hypertension. N Engl J Med. 2003 Feb 13;348(7):610-7.
[18] Blood Pressure Lowering Treatment Trialists' Collaboration. Effects of different blood-pressure regimens on major cardiovascular events: results of prospectively-designed overviews of randomised trials. Lancet 2003; 362: 1527-35
[19] McConnell JD, Roehrborn CG, et al. The Long-Term Effect of Doxazosin, Finasteride, and Combination Therapy on the Clinical Progression of Benign Prostatic Hyperplasia. N Engl J Med. 2003 Dec 18;349(25):2387-2398.
[20] NICE Guidelines Aug,2004 Management of Hypertension in Adults in Primary Care http://www.nice.org.uk/pdf/CG018fullguideline.pdf
NICE: National Institute for Health and Clinical Excellence. **Hypertension Guidelines**. Aug 2011. http://www.nice.org.uk/nicemedia/live/13561/56015/56015.pdf
[21] Davis BR, Furberg CD, Wright JT Jr, Cutler JA, Whelton P; ALLHAT Collaborative Research Group. ALLHAT: setting the record straight. Ann Intern Med. 2004 Jul 6;141(1):39-46.

Antihypertensives: Landmark & Recent Trials – Summary

[1] Wright JT Jr, Bakris G, Greene T, Agodoa LY, et al. Effect of blood pressure lowering and antihypertensive drug class on progression of hypertensive kidney disease: results from the **AASK trial**.; African American Study of Kidney Disease and Hypertension Study Group. JAMA 2002;288:2421-31.

Appel LJ, Wright JT Jr, Greene T, Kusek JW, et al. for the African American Study of Kidney Disease and Hypertension Collaborative Research Group. (AASK trial) Long-term Effects of Renin-Angiotensin System-Blocking Therapy and a Low Blood Pressure Goal on Progression of Hypertensive Chronic Kidney Disease in African Americans. Arch Intern Med. 2008 Apr 28;168(8):832-839. Despite the benefits of renin-angiotensin system-blocking therapy on CKD progression, most African Americans with hypertensive CKD who are treated with currently recommended BP therapy continue to progress during the long term.

Weinberg Joy M.; Appel Lawrence J.; Bakris George; et al.; for the African American Study of Hypertension and Kidney Disease Collaborative Research Group. Risk of Hyperkalemia in Nondiabetic Patients With Chronic Kidney Disease Receiving Antihypertensive Therapy. Arch Intern Med. 2009;169(17):1587-1594.

Appel LJ, Wright JT Jr, Greene T, et al. Intensive bloodpressure control in hypertensive chronic kidney disease. (**AASK**) N Engl J Med 2010;363:918-29.

[2] ALLHAT Officers and Coordinators for the **ALLHAT** Collaborative Research Group. Major outcomes in high-risk hypertensive patients randomized to angiotensin-converting enzyme inhibitor or calcium channel block vs. diuretic. JAMA. 2002;288:2981–2997.

ALLHAT Working Group. Major outcomes in moderately hypercholesterolemic, hypertensive patients randomized to pravastatin vs usual care. The Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial (**ALLHAT-LLT**). JAMA. 2002;288:2998- 3007.

Piller LB, Baraniuk S, Simpson LM, et al. Long-term follow-up (8.9yr) of participants with heart failure in the Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial (ALLHAT). Circulation. 2011;124:1811–1818.

Alderman MH, Piller LB, Ford CE, et al. for the Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial Collaborative Research Group. Clinical Significance of Incident Hypokalemia and Hyperkalemia in Treated Hypertensive Patients in the Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial. Hypertension. 2012 May;59(5):926-933.

[3] Dahlof B, Sever PS, Poulter NR, et al. ASCOT investigators. Prevention of cardiovascular events with an antihypertensive regimen of amlodipine adding perindopril as required versus atenolol adding bendroflumethiazide as required, in the Anglo-Scandinavian Cardiac Outcomes Trial-Blood Pressure Lowering Arm (**ASCOT-BPLA**): a multicentre randomised controlled trial. Lancet. 2005 Sep 10;366(9489):895-906. Web: http://www.ascotstudy.co.uk (see also **Q&A Ascot-BPLA** http://www.rxfiles.ca/acrobat/HTN-Q&A-ASCOT.pdf)

[4] Poulter NR, Wedel H, Dahlof B, Sever PS, et al.; for the ASCOT investigators. Role of blood pressure and other variables in the differential cardiovascular event rates noted in the **ASCOT-BPLA**. Lancet. 2005 Sep 10;366(9489):907-13.

Ostergren J, Poulter NR, Sever PS, et al. for the ASCOT investigators. The Anglo-Scandinavian Cardiac Outcomes Trial: blood pressure-lowering limb: effects in patients with type II diabetes. J Hypertens. 2008 Nov;26(11):2103-2111. In the large diabetic subgroup in the blood pressure-lowering arm of the Anglo-Scandinavian Cardiac Outcomes Trial, the benefits of amlodipine-based treatment, compared with atenolol-based treatment, on the incidence of total cardiovascular events and procedures was significant (14% reduction) and similar to that observed in the total trial population (16% reduction).

Sever PS, Poulter NR, et al. on behalf of the ASCOT Investigators. Evaluation of C-reactive protein prior to and on-treatment as a predictor of benefit from atorvastatin: observations from the Anglo-Scandinavian Cardiac Outcomes Trial. Eur Heart J. 2011 Jul 28.

Sever PS, Chang CL, Prescott MF, Gupta A, Poulter NR, Whitehouse A, Scanlon M. Is plasma renin activity a biomarker for the prediction of renal and cardiovascular outcomes in treated hypertensive patients? Observations from the Anglo-Scandinavian Cardiac Outcomes Trial (ASCOT). Eur Heart J. 2012 Aug 31.

Gupta A, Mackay J, Whitehouse A, et al. Long-term mortality after blood pressure-lowering and lipid-lowering treatment in patients with hypertension in the Anglo-Scandinavian Cardiac Outcomes Trial (ASCOT) Legacy study: 16-year follow-up results of a randomised factorial trial. Lancet. 2018 Aug 24.

[5] Mogensen CE, Neldam S, Tikkanen I, Oren S, et al. Randomised controlled trial of dual blockade of renin-angiotensin system in patients with hypertension, microalbuminuria, and non-insulin dependent diabetes: the candesartan and lisinopril microalbuminuria (**CALM**) study. BMJ 2000;321:1440-4.

[6] Nakao N, Yoshimura A, Morita H et al. Combination treatment of angiotensin-II receptor blocker and angiotensin-converting enzyme inhibitor in non-diabetic renal disease (**COOPERATE**): a randomised controlled trial. Lancet 2003;361:117-24.

Kunz R, Wolbers M, Glass T, Mann JF. The COOPERATE trial: a letter of concern. Lancet. 2008 May 10;371(9624):1575-6.

The Editors Of The Lancet. **Retraction**-Combination treatment of angiotensin-II receptor blocker and angiotensin-converting-enzyme inhibitor in non-diabetic renal disease (COOPERATE): a randomised controlled trial. Lancet. 2009 Oct 10;374(9697):1226.

Fernandez Juarez G, Luño J, Barrio V, et al. **PRONEDI** Study Group. Effect of **Dual Blockade** of the Renin-Angiotensin System on the Progression of Type 2 Diabetic Nephropathy: A Randomized Trial (N=133).

Am J Kidney Dis. 2012 Aug 28. (lisinopril, irbesartan or both, unable to show benefit of the combo)

[7] Hansson L, Lindholm LH, Niskanen L, Lanke J et al. Effect of angiotensin-converting-enzyme inhibition compared with conventional therapy on cardiovascular morbidity and mortality in hypertension: the Captopril Prevention Project (**CAPPP**) randomised trial. Lancet 1999;353:611-6.

[8] Pitt B, Poole-Wilson PA, Segal R, Martinez FA et al. Effect of losartan compared with captopril on mortality in patients with symptomatic heart failure: randomised trial-the Losartan Heart Failure Survival Study **ELITE II**. Lancet 2000;355:1582-7.

[9] Tatti P, Pahor M, Byington RP, Di Mauro P et al. Outcome results of the Fosinopril Versus Amlodipine Cardiovascular Events Randomized Trial (**FACET**) in patients with hypertension and NIDDM. Diabetes Care 1998;21:597-603.

[10] Yusuf S, Sleight P, Pogue J, Bosch J, et al. The Heart Outcomes Prevention Evaluation (**HOPE**) Study. Effects of an angiotensin-converting-enzyme inhibitor, ramipril, on cardiovascular events in high-risk patients. N Engl J Med 2000;342:145-153.

[11] Heart Outcomes Prevention Evaluation Study Investigators. Effects of ramipril on cardiovascular & microvascular outcomes in people with diabetes mellitus: results of the HOPE study and **MICRO-HOPE** substudy. Lancet 2000;355:253-9.

[12] Bosch J, Yusuf S, Pogue J, Sleight P et al . Use of ramipril in preventing stroke: double blind randomised trial.; **HOPE** Investigators. Heart outcomes prevention evaluation. BMJ 2002;324:699-702.

[13] Sleight P, Yusuf S, Pogue J, Tsuyuki R, Diaz R, Probstfield J. Blood-pressure reduction and cardiovascular risk in HOPE study. Lancet. 2001;358:2130-1.

[14] Svensson P, de Faire U, Sleight P, Yusuf S, Ostergren J. Hypertension 2001;38:E28-32 Comparative effects of ramipril on ambulatory and office blood pressures: a **HOPE** Substudy.

[15] Hansson L, Zanchetti A, Carruthers SG, et al. Effects of intensive blood-pressure lowering and low-dose aspirin in patients with hypertension: principal results of the Hypertension Optimal Treatment randomised trial. **HOT** Study Group. Lancet 1998;351:1755-62.

Jardine, Meg J., Ninomiya, Toshiharu, Perkovic, Vlado, et al. Aspirin Is Beneficial in Hypertensive Patients With **Chronic Kidney Disease**: A Post-Hoc Subgroup Analysis of a Randomized Controlled Trial (**HOT**). J Am Coll Cardiol 2010 56: 956-965.

[16] Lewis EJ, Hunsicker LG, Clarke WR, Berl T et al. Renoprotective effect of the angiotensin-receptor antagonist irbesartan in patients with nephropathy due to type 2 diabetes (**IDNT**); Collaborative Study Group. N Engl J Med 2001 Sep 20;345(12):851-60.

[17] Brown MJ, Palmer CR, Castaigne A, de Leeuw PW et al. Morbidity and mortality in patients randomised to double-blind treatment with a long-acting calcium-channel blocker or diuretic in the International Nifedipine GITS study: Intervention as a Goal in Hypertension Treatment (**INSIGHT**). Lancet 2000;356:366-72.

[18] Parving HH, Lehnert H, Brochner-Mortensen J, Gomis R et al. The effect of irbesartan on the development of diabetic nephropathy in patients with type 2 diabetes (**IRMA II**). N Engl J Med 2001;345:870-8.

[19] Dahlof B, Devereux RB, Kjeldsen SE, Julius S et al. Cardiovascular morbidity and mortality in the Losartan Intervention For Endpoint reduction in hypertension study (**LIFE**): a randomised trial against atenolol. Lancet 2002;359:995-1003.

[20] Lindholm LH, Ibsen H, Dahlof B, Devereux RB et al. Cardiovascular morbidity and mortality in patients with diabetes in the Losartan Intervention For Endpoint reduction in hypertension study (**LIFE**): a randomised trial against atenolol. Lancet 2002;359:1004-10. (Note: in patients with left ventricular hypertrophy)

[21] Kjeldsen SE, Dahlof B, Devereux RB, Julius S et al. Effects of losartan on cardiovascular morbidity and mortality in patients with isolated systolic hypertension and left ventricular hypertrophy: a Losartan Intervention for Endpoint Reduction (**LIFE**) substudy. JAMA 2002;288:1491-8.

Fitzgerald JD, Johnson L, Hire DG, et al. **LIFE** Study Research Group. Association of Objectively Measured **Physical Activity** With Cardiovascular Risk in Mobility-limited Older Adults. J Am Heart Assoc. 2015 Feb 18;4(2).

[22] Hansson L, Hedner T, Lund-Johansen P, Kjeldsen SE et al. Randomised trial of effects of calcium antagonists compared with diuretics and beta-blockers on cardiovascular morbidity and mortality in hypertension: the Nordic Diltiazem (**NORDIL**) study. Lancet 2000;356:359-65.

[23] Dickstein K, Kjekshus J. Effects of losartan and captopril on mortality and morbidity in high-risk patients after acute myocardial infarction: the **OPTIMAAL** randomised trial. Optimal Trial in Myocardial Infarction with Angiotensin II Antagonist Losartan. Lancet 2002;360:752-60.

[24] **PROGRESS** Collaborative Group. Randomised trial of a perindopril-based blood-pressure-lowering regimen among 6,105 individuals with previous stroke or transient ischaemic attack. Lancet 2001;358:1033-41.

Arima H, Anderson C, Omae T, et al; for the Perindopril Protection Against Recurrent Stroke Study (PROGRESS) Collaborative Group. Effects of Blood Pressure Lowering on Intracranial and Extracranial Bleeding in Patients on Antithrombotic Therapy: The PROGRESS Trial. Stroke. 2012 Jun;43(6):1675-1677.

[25] Pitt B, O'Neill B, Feldman R, et al. The QUinapril Ischemic Event Trial (**QUIET**): evaluation of chronic ACE inhibitor therapy in patients with ischemic heart disease and preserved left ventricular function. The QUIET Study Group. Am J Cardiol 2001;87:1058-63.

[26] Brenner BM, Cooper ME, de Zeeuw D, Keane et al. Effects of losartan on renal and cardiovascular outcomes in patients with type 2 diabetes and nephropathy; **RENAAL** Study Investigators. N Engl J Med 2001;345:861-9.

[27] SHEP Cooperative Research Group. Prevention of stroke by antihypertensive drug treatment in older persons with isolated systolic hypertension. Final results of the Systolic Hypertension in the Elderly Program (**SHEP**). JAMA 1991 Jun 26;265(24):3255-64.

[28] Curb JD, Pressel SL, Cutler JA, Savage PJ et al. Effect of diuretic-based antihypertensive treatment on cardiovascular disease risk in older diabetic patients with isolated systolic hypertension (**SHEP**). JAMA 1996;276:1886-92.

Kostis JB, Wilson AC, et al.; **SHEP** Collaborative Research Group. Long-term effect (14.3 yrs) of diuretic-based therapy on fatal outcomes in subjects with isolated systolic hypertension with and without diabetes. Am J Cardiol. 2005 Jan 1;95(1):29-35.

Kostis JB, Cabrera J, Cheng JQ, et al. Association between chlorthalidone treatment of systolic hypertension and long-term survival (SHEP). JAMA. 2011 Dec 21;306(23):2588-93. In the SHEP trial, treatment of isolated systolic hypertension with chlorthalidone stepped-care therapy for 4.5 years was associated with longer life expectancy at 22 years of follow-up.

Kostis WJ, Cabrera J, Messerli FH, et al. Competing Cardiovascular and Noncardiovascular Risks and Longevity in the Systolic Hypertension in the Elderly Program (SHEP). Am J Cardiol. 2013 Nov 23

[29] Somes GW, Pahor M, Shorr RI, Cushman WC, Applegate WB. The role of diastolic blood pressure when treating isolated systolic hypertension (**SHEP program**). Arch Intern Med 1999;159:2004-9.

[30] Hansson L, Lindholm LH, Ekbom T, Dahlof B et al. Randomised trial of old and new antihypertensive drugs in elderly patients: cardiovascular mortality and morbidity the Swedish Trial in Old Patients with Hypertension-2 study (**STOP Hypertension-2**). Lancet 1999;354:1751-6.

[31] Staessen JA, Fagard R, Thijs L, Celis H et al. Randomised double-blind comparison of placebo and active treatment for older patients with isolated systolic hypertension. The Systolic Hypertension in Europe (**Syst-Eur**) Trial Investigators. Lancet 1997;350:757-64.

[32] Tuomilehto J, Rastenyte D, Birkenhager WH, Thijs L et al. Effects of calcium-channel blockade in older patients with diabetes and systolic hypertension. Systolic Hypertension in Europe Trial Investigators (**Syst-Eur**). N Engl J Med 1999;340:677-84.
Thijs L, Richart T, de Leeuw PW, et al. Morbidity and mortality on **combination** versus monotherapy: a posthoc analysis of the Systolic Hypertension in Europe trial. (**Syst-Eur**). J Hypertens. 2010 Jan 5. [Epub ahead of print]

[33] Forette F, Seux ML, Staessen JA, Thijs L et al. The prevention of dementia with antihypertensive treatment: new evidence from the Systolic Hypertension in Europe (**Syst-Eur**) study. Arch Intern Med 2002;162:2046-52.

[34] UK Prospective Diabetes Study Group. Tight blood pressure control and risk of macrovascular and microvascular complications in type 2 diabetes: **UKPDS 38**. BMJ 1998;317:703-13.

[35] UK Prospective Diabetes Study Group. Efficacy of atenolol and captopril in reducing risk of macrovascular and microvascular complications in type 2 diabetes: **UKPDS 39**. BMJ 1998;317:713-20.

[36] Cohn JN, Tognoni G . A randomized trial of the angiotensin-receptor blocker valsartan in chronic heart failure (**Val-HeFT**); Valsartan Heart Failure Trial Investigators. N Engl J Med 2001;345:1667-75.

[37] Maggioni AP, Anand I, Gottlieb SO, et al. Effects of valsartan on morbidity and mortality in patients with heart failure not receiving angiotensin-converting enzyme inhibitors. **Val-HeFT** Investigators (Valsartan Heart Failure Trial). J Am Coll Cardiol 2002;40:1414-21.
Anand IS, Bishu K, Rector TS, et al. Proteinuria, Chronic Kidney Disease, and the Effect of an Angiotensin Receptor Blocker in Addition to an Angiotensin-Converting Enzyme Inhibitor in Patients With Moderate to Severe Heart Failure. Circulation. 2009 Oct 5.

[38] Jamerson KA, Weber MA, Bakris GL, et al. Avoiding cardiovascular events through combination therapy in patients living with systolic hypertension, the early termination of the **ACCOMPLISH** trial for efficacy. Session 407; ACC 57th Annual Scientific Session; March 29-April 1, 2008. Jamerson K, Weber MA, Bakris GL, et al. Benazepril plus Amlodipine or Hydrochlorothiazide for Hypertension in High-Risk Patients. (**ACCOMPLISH**)N Engl J Med. 2008 Dec 4;359(23):2417-2428.
The benazepril-amlodipine combination was superior to the benazepril-hydrochlorothiazide combination in reducing cardiovascular events in patients with hypertension who were at high risk for such events.
Bakris GL, Sarafidis PA, Weir MR, et al. Renal outcomes with different fixed-dose combination therapies in patients with hypertension at high risk for cardiovascular events (ACCOMPLISH): a prespecified secondary analysis of a randomized, controlled trial. Lancet 2010; DOI:10.1016/S0140-6736(09)62100-0.
Jamerson KA, Bakris GL, Weber MA. 24-hour ambulatory blood pressure in the ACCOMPLISH trial. N Engl J Med. 2010 Jul 1;363(1):98.
Weber MA, Bakris GL, Jamerson K, et al. Cardiovascular events during differing hypertension therapies in patients with **diabetes**. (**Accomplish**) J Am Coll Cardiol. 2010 June 29;56(1):77-85.
Jamerson KA, Devereux R, Bakris GL, et al. Efficacy and Duration of Benazepril Plus Amlodipine or Hydrochlorthiazide on **24-Hour Ambulatory** Systolic Blood Pressure Control. (Accomplish) Hypertension. 2010 Dec 28.
Weber MA, Jamerson K, Bakris GL et al. Effects of **body size and hypertension treatments** on cardiovascular event rates: subanalysis of the **ACCOMPLISH** randomized controlled trial. Lancet 2012.
Bakris G, Briasoulis A, Dahlof B, et al; ACCOMPLISH Investigators. Comparison of Benazepril Plus Amlodipine or Hydrochlorothiazide in **High-Risk Patients** With Hypertension and Coronary Artery Disease. Am J Cardiol. 2013 Apr 11.

[39] **ACCORD** Study Group, Effects of Intensive Blood-Pressure Control in Type 2 Diabetes Mellitus. N Engl J Med 2010 0: NEJMoa1001286.
Williamson JD, Launer LJ, Bryan RN, et al. Cognitive Function and Brain Structure in Persons With Type 2 Diabetes Mellitus After Intensive Lowering of Blood Pressure and Lipid Levels: A Randomized Clinical Trial. JAMA Intern Med. 2014 Feb 3.

[40] Patel A; **ADVANCE** Collaborative Group, MacMahon S, Chalmers J, Neal B, et al. Effects of a fixed combination of perindopril and indapamide on macrovascular and microvascular outcomes in patients with type 2 diabetes mellitus (the ADVANCE trial): a randomised controlled trial. Lancet. 2007 Sep 8;370(9590):829-40.
Heerspink HJ, Ninomiya T, Perkovic V, et al. ADVANCE Collaborative Group. Effects of a fixed combination of perindopril and indapamide in patients with type 2 diabetes and chronic kidney disease. Eur Heart J. 2010 Dec;31(23):2888-96.
van der Leeuw J, Visseren FL, Woodward M, et al. Predicting the Effects of Blood Pressure-Lowering Treatment on Major Cardiovascular Events for Individual Patients With Type 2 Diabetes Mellitus: Results From Action in Diabetes and Vascular Disease: Preterax and Diamicron MR Controlled Evaluation. Hypertension. 2015 Jan;65(1):115-21.

[41] Beckett NS, Peters R, Fletcher AE, Staessen JA, Liu L, et al.; the **HYVET** Study Group. Treatment of Hypertension in Patients 80 Years of Age or Older.N Engl J Med. 2008 Mar 31; [Epub ahead of print].
Allan, G. Michael, Mallery, Laurie, Ivers, Noah. Treating hypertension in the very elderly. Can Fam Physician 2010 56: 1141.
Beckett N, Peters R, Tuomilehto J, et al. for the HYVET Study Group. Immediate and late benefits of treating very elderly people with hypertension: results from active treatment extension to Hypertension in the Very Elderly randomised controlled trial. BMJ. 2011 Jan 4;344:d7541. doi: 10.1136/bmj.d7541.
Mukhtar O, Jackson SH. The Hypertension in the Very Elderly Trial – Latest Data. Br J Clin Pharmacol. 2012 Aug 17.
JATOS Study Group. Principal results of the Japanese trial to assess optimal systolic blood pressure in elderly hypertensive patients (**JATOS**). Hypertens Res 2008; 31:2115–2127. (n=4418 over 2yrs)
Ogihara T, Saruta T, Rakugi H, et al. Valsartan in Elderly Isolated Systolic Hypertension Study Group. Target blood pressure for treatment of isolated systolic hypertension in the elderly: valsartan in elderly isolated systolic hypertension study. (**VALISH**) Hypertension. 2010 Aug;56(2):196-202.
Yano Y, Rakugi H, Bakris GL, et al. **On-Treatment Blood Pressure** and Cardiovascular Outcomes in Older Adults With **Isolated Systolic Hypertension**. (**Valish**) Hypertension. 2017 Feb;69(2):220-227.

[42] Schrader J, Lüders S, Kulschewski A, Hammersen F, Plate K, Berger J, Zidek W, Dominiak P, Diener HC; MOSES Study Group. Morbidity and Mortality After Stroke, Eprosartan Compared with Nitrendipine for Secondary Prevention: principal results of a prospective randomized controlled study (MOSES). Stroke. 2005 Jun;36(6):1218-26. Epub 2005 May 5. (Yusuf S, Diener HC, Sacco RL, et al. the **PRoFESS** Study Group. Telmisartan to Prevent Recurrent Stroke and Cardiovascular Events. N Engl J Med. 2008 Aug 27. [Epub ahead of print] (20,332 patients) Therapy with telmisartan initiated soon after an ischemic stroke and continued for 2.5 years did not significantly lower the rate of recurrent stroke, major cardiovascular events, or diabetes.)
Ovbiagele B, Diener H-C, Yusuf S, et al; **PROFESS** Investigators. Level of **systolic blood pressure** within the normal range and risk of recurrent **stroke**. JAMA. 2011;306(19):2137-2144.
Böhm M, Cotton D, Foster L et al. Impact of resting heart rate on mortality, disability and cognitive decline in patients after ischaemic stroke. (Profess) Eur Heart J 2012.

[43] Yusuf S, Teo KK, Pogue J, et al for the **ONTARGET** investigators. Telmisartan, ramipril, or both in patients at high risk for vascular events. N Engl J Med 2008: 358:1547-1559. The angiotensin-converting enzyme inhibitor (ACEI) ramipril and the angiotensin receptor blocker (ARB) telmisartan are equally effective for secondary cardiovascular prevention. The combination of both drugs is no more effective and causes more adverse effects at greater cost. ACEIs should remain the drug of choice for secondary prevention in high risk cardiovascular patients unless the drug is not tolerated because of angioedema or cough, in which case ARBs provide an effective alternative. (LOE = 1b). Mann JF, Schmieder RE, McQueen M, Dyal L, Schumacher H, Pogue J, Wang X, et al.; ONTARGET investigators. Renal outcomes with telmisartan, ramipril, or both, in people at high vascular risk (the ONTARGET study): a multicentre, randomised, double-blind, controlled trial. Lancet. 2008 Aug 16;372(9638):547-53. In people at high vascular risk, telmisartan's effects on major renal outcomes are similar to ramipril. Although combination therapy reduces proteinuria to a greater extent than monotherapy, overall it worsens major renal outcomes. The Telmisartan Randomised AssessmeNt Study in ACE iNtolerant subjects with cardiovascular Disease (TRANSCEND) Investigators. Effects of the angiotensin-receptor blocker telmisartan on cardiovascular events in high-risk patients intolerant to angiotensin-converting enzyme inhibitors: a randomised controlled trial. Lancet. 2008 Aug 29.
Sleight P, Redon J, Verdecchia P, et al.; on behalf of the ONTARGET investigators. Prognostic value of blood pressure in patients with high vascular risk in the Ongoing Telmisartan Alone and in combination with Ramipril Global Endpoint Trial study. J Hypertens. 2009 Jun 5. [Epub ahead of print] In high-risk patients, the benefits from SBP lowering below 130 mmHg are driven mostly by a reduction of stroke; myocardial infarction is unaffected and cardiovascular mortality is unchanged or increased. Future trials should be designed to test the value of SBP lowering in high-risk patients with SBP in the range of 130-150 mmHg. { FDA July/09: After carefully weighing the evidence, a US Food and Drug Administration advisory panel voted unanimously against expanding the indication for the angiotensin receptor blocker (ARB) telmisartan (Micardis, Boehringer Ingelheim Pharmaceuticals) for the reduction of cardiovascular events in high-risk patients. The decision, however, does provide physicians with an alternative first-line treatment in patients 55 years or older intolerant to ACE inhibitors but who are at high risk for cardiovascular events. In these patients, the Cardiovascular and Renal Drugs Advisory Committee voted 5 to 2 in favor of approving telmisartan to reduce the risk of MI, stroke, death from cardiovascular causes, or hospitalization for congestive heart failure. Complicating the whole affair was the fact that Boehringer Ingelheim and the FDA failed to come to an agreement in 2001 regarding the statistical plan for the noninferiority end point to determine efficacy. The sponsor chose a margin of 13%, or a hazard ratio of 1.13, which the FDA considered too liberal. Instead, the agency wanted a more conservative margin of 8%, or a hazard ratio of 1.08. Dr Salim Yusuf (McMaster University, Hamilton, ON), the lead investigator of the ONTARGET study, defended the decision to adopt the liberal noninferiority margin, noting that while his approach to clinical trials is to conduct the largest study possible, the margin requested by the FDA would have doubled ONTARGET to more than 50 000 patients, something that just wasn't feasible}
Mann JF, Schmieder RE, Dyal L, et al.; TRANSCEND (Telmisartan Randomised Assessment Study in ACE Intolerant Subjects with Cardiovascular Disease) Investigators. Effect of telmisartan on renal outcomes: a randomized trial. Ann Intern Med. 2009 Jul 7;151(1):1-10, W1-2. Epub 2009 May 18.
Cowan BR, Young AA, Anderson C, et al.; ONTARGET Investigators. Left ventricular mass and volume with telmisartan, ramipril, or combination in patients with previous atherosclerotic events or with diabetes mellitus (from the ONgoing Telmisartan Alone and in Combination With Ramipril Global Endpoint Trial [ONTARGET]). Am J Cardiol. 2009 Dec 1;104(11):1484-9. Epub 2009 Oct 14.
Anderson Craig, Teo Koon, Gao Peggy, et al. and for the ONTARGET and TRANSCEND Investigators, Renin-angiotensin system blockade and cognitive function in patients at high risk of cardiovascular disease: analysis of data from the ONTARGET and TRANSCEND studies, The Lancet Neurology, Volume 10, Issue 1, January 2011, Pages 43-53, ISSN 1474-4422, DOI: 10.1016/S1474-4422(10)70250-7.
Barzilay Joshua I.; Gao Peggy; O'Donnell Martin; et al. for the ONTARGET and TRANSCEND Investigators. Albuminuria and Decline in Cognitive Function: The ONTARGET/TRANSCEND Studies. Arch Intern Med. 2011;171(2):142-150.
Clase CM, Gao P, Tobe SW, et al. on behalf of the ONTARGET (ONgoing Telmisartan Alone and in combination with Ramipril Global Endpoint Trial) and TRANSCEND (Telmisartan Randomized Assessment Study in Angiotensin-Converting-Enzyme-Inhibitor Intolerant Subjects with Cardiovascular Disease). **Estimated Glomerular Filtration Rate and Albuminuria** as Predictors of Outcomes in Patients With High Cardiovascular Risk: A Cohort Study. Ann Intern Med. 2011 Mar 1;154(5):310-318.
Tobe SW, Clase CM, Gao P, et al; on behalf of the ONTARGET and TRANSCEND Investigators. **Cardiovascular and Renal Outcomes** With Telmisartan, Ramipril, or Both in People at High **Renal Risk**: Results From the ONTARGET and TRANSCEND Studies. Circulation. 2011 Mar 15;123(10):1098-1107.
Redon J, Sleight P, Mancia G, Gao O, Verdecchia P, Fagard R, Schumacher H, Weber M, Boehm M, Williams B, et al. Safety and efficacy of aggressive blood pressure lowering among patients with **diabetes**: subgroup analyses from the ONTARGET trial. J Hypertens. 2009;27(Suppl. 4):S16.
Redon J, Mancia G, Sleight P, Schumacher H, Gao P, Pogue J, Fagard R, Verdecchia P, Weber M, Böhm M, et al. Safety and efficacy of low blood pressure among patients with **diabetes**: sub-group analyses from the ONTARGET trial. J Hypertens. 2011;29(e-Suppl. A):e113.
Mancia G, Schumacher H, Redon J, et al. **Blood pressure targets** recommended by guidelines and incidence of cardiovascular and renal events in the Ongoing Telmisartan Alone and in Combination With Ramipril Global Endpoint Trial (**ONTARGET**). Circulation. 2011;124:1727–1736.
Kappert K, Böhm M, Schmieder R, et al; ONTARGET/TRANSCEND Investigators. Impact of **Sex** on Cardiovascular Outcome in Patients at High Cardiovascular Risk: Analysis of the Telmisartan Randomized Assessment Study in ACE-Intolerant Subjects With Cardiovascular Disease (TRANSCEND) and the Ongoing Telmisartan Alone and in Combination With Ramipril Global End Point Trial (ONTARGET). Circulation. 2012 Aug 21;126(8):934-41.
Mancia G, Parati G, Bilo G, Gao P, et al. Ambulatory Blood Pressure Values in the Ongoing Telmisartan Alone and in Combination with Ramipril Global Endpoint Trial (ONTARGET). Hypertension. 2012 Oct 15.

Additional trials:

ACTIVE I Investigators. Irbesartan in Patients with Atrial Fibrillation. N Engl J Med 2011; 364:928-938. (Not reduce CV events)

Bangalore S, Qin J, Sloan S, Murphy SA, Cannon CP; for the PROVE IT-TIMI 22 Trial Investigators. What Is the **Optimal Blood Pressure in Patients After Acute Coronary Syndromes**?: Relationship of Blood Pressure and Cardiovascular Events in the Pravastatin or Atorvastatin Evaluation and Infection Therapy-Thrombolysis in Myocardial Infarction (PROVE IT-TIMI) 22 Trial. Circulation. 2010 Nov 8.

Bangalore S, Gong Y, Cooper-DeHoff RM, et al. 2014 **Eighth Joint National Committee** Panel recommendations for **blood pressure targets revisited**: Results from the **INVEST** study. *J Am Coll Cardiol* 2014; 64:784-793.

Benetos A, Labat C, Rossignol P, et al. Treatment With Multiple Blood Pressure Medications, Achieved Blood Pressure, and Mortality in **Older Nursing Home Residents**: The PARTAGE Study. JAMA Intern Med. 2015 Feb 16.

Cheng J, Zhang W, Zhang X, et al. Effect of **Angiotensin-Converting Enzyme Inhibitors and Angiotensin II Receptor Blockers** on All-Cause Mortality, Cardiovascular Deaths, and Cardiovascular Events in Patients **With Diabetes** Mellitus: A Meta-analysis. JAMA Intern Med. 2014 Mar 31.

Cooper-DeHoff Rhonda M.; Gong Yan; Handberg Eileen M.; et al. Tight Blood Pressure Control and Cardiovascular Outcomes Among Hypertensive Patients With Diabetes and Coronary Artery Disease. (**INVEST**) JAMA. 2010;304(1):61-68.
Tight control of systolic BP among patients with diabetes and CAD was not associated with improved cardiovascular outcomes compared with usual control.

Filippone EJ. Foy A, Newman E. Goal-directed antihypertensive therapy: **Lower may not always be better.** *Cleveland Clinic Journal of Medicine* 2011; 78(2):123-133; doi:10.3949/ccjm.78a.10101.

Fried LF, Emanuele N, Zhang JH, et al. **Combined angiotensin inhibition** for the treatment of diabetic nephropathy. (**VA Nephron-D**) N Engl J Med 2013. DOI: 10.1056/NEJMoa1303154.

Haller H, Ito S, Izzo JL Jr, et al. **Olmesartan** for the delay or prevention of microalbuminuria in type 2 diabetes. (**ROADMAP**) N Engl J Med 2011;364:907-17. (n=4447 over 3.2yr. Improved microalbuminuria, but increased fatal CV events)

HOPE-3 Investigators. **Blood-Pressure Lowering** in Intermediate-Risk Persons without Cardiovascular Disease. N Engl J Med. 2016;374:2009-20.

HOPE-3 Investigators. **Cholesterol Lowering** in Intermediate-Risk Persons without Cardiovascular Disease. N Engl J Med. 2016;374:2021-31.

HOPE-3 Investigators. **Blood-Pressure and Cholesterol Lowering** in Intermediate-Risk Persons without Cardiovascular Disease. N Engl J Med. 2016;374:2032-43.Hypertension Detection and Follow-up Program Cooperative Group (**HDFP**). Five-year findings of the Hypertension Detection and Follow-up Program, I: reduction in mortality of persons with high blood pressure, including mild hypertension. JAMA. 1979;242(23):2562-2571.

JATOS Study Group. Principal results of the Japanese trial to assess optimal systolic blood pressure in elderly hypertensive patients (JATOS). Hypertens Res 2008; 31:2115–2127. (n=4418 over 2yrs)

Kim-Mitsuyama S, Ogawa H, Matsui K, et al. An angiotensin II receptor blocker (**olmesartan**) -calcium channel blocker combination prevents cardiovascular events in elderly high-risk hypertensive patients with chronic kidney disease better than high-dose angiotensin II receptor blockade alone. (**OSCAR**) Kidney Int. 2013 Jan;83(1):167-76.

Lancet editors. **Retraction**—Valsartan in a Japanese population with hypertension and other cardiovascular disease (**Jikei Heart Study**): A randomised, open-label, blinded endpoint morbidity-mortality study. Lancet 2013.

Multiple Risk Factor Intervention Trial Research Group (**MRFIT**) . Multiple Risk Factor Intervention Trial: risk factor changes and mortality results. JAMA. 1982;248(12):1465-1477.

Sabayan B et al. **High blood pressure** and resilience to physical and cognitive decline in the **oldest old**: The **Leiden 85-Plus** Study.J Am Geriatr Soc 2012 Nov; 60:2014.

Sandset EC, Bath PMW, Boysen G et al. The angiotensin-receptor blocker **candesartan for treatment of acute stroke** (**SCAST**): A randomised, placebo-controlled, double-blind trial. Lancet 2011;DOI:10.1016/S0140-6736(11)60104-9.

SPRINT Research Group. A randomized trial of intensive versus standard blood-pressure control. N Engl J Med. DOI: 10.1056/NEJMoa1511939

SPRINT: Williamson JD, Supiano MA, Applegate WB, et al. **Intensive vs standard blood pressure** control and cardiovascular disease outcomes in **adults aged 75 years**: a randomized clinical trial. JAMA. doi:10.1001/jama.2016.7050.

SPRINT: Bress AP, Kramer H, Khatib R, et al. Potential **Deaths Averted** and Serious Adverse Events Incurred from Adoption of the SPRINT Intensive Blood Pressure Regimen in the U.S.: Projections from NHANES. Circulation. 2017 Feb 13.

SPRINT: Phillips RA, Xu J, Peterson LE, et al. Impact of Cardiovascular Risk on the Relative Benefit and Harm of Intensive Treatment of Hypertension. J Am Coll Cardiol. 2018 Mar 2.

SPRINT: Scarpa J, Bruzelius E, Doupe P, et al. Assessment of risk of harm associated with intensive blood pressure management among patients with hypertension who **smoke**: a secondary analysis of the Systolic Blood Pressure Intervention Trial (SPRINT). JAMA Netw Open. 2019;2(3):e190005.

Upadhyay Ashish, Earley Amy, Haynes Shana M., et al. Systematic Review: **Blood Pressure Target in Chronic Kidney Disease and Proteinuria** as an Effect Modifier. Ann Intern Med E-335published ahead of print March 14, 2011, doi:10.1059/0003-4819-154-8-201104190-00335

VALSIH: Ogihara T, Saruta T, Rakugi H, et al. Valsartan in Elderly Isolated Systolic Hypertension Study Group. Target blood pressure for treatment of isolated systolic hypertension in the elderly: valsartan in elderly isolated systolic hypertension study. Hypertension. 2010 Aug;56(2):196-202.

Veterans Cooperative Study Group on Antihypertensive Agents. Effects of treatment on morbidity in hypertension: results in patients with diastolic blood pressures averaging 115 through 129 mm Hg. JAMA. 1967;202(11):1028-1034.

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REFERENCES FOR WARFARIN TIPS & DOSING NOMOGRAMS

1) Canadian Agency for Drugs and Technologies in Health. Optimal warfarin management for the prevention of thromboembolic events in patients with atrial fibrillation: a systematic review of the clinical evidence [Internet]. Ottawa: The Agency; 2011 Nov [cited 2011 Nov 21]. (Optimal use report; vol. 1 iss. 2a). Available from: http://www.cadth.ca/media/pdf/OP0508_warfarin-science-report-1_clinical_e.pdf.

2) Holbrook A, Schulman S, Witt D, Vandvik P, et al.,. Evidence Based Management of Anticoagulant Therapy: Antithrombotic Therapy and Prevention of Thrombosis, American College of Chest Physicians Evidence-Based Clinical Practice Guidelines (9th Edition). Chest. 2012; 141:152s-184s.
Kearon C, Akl EA, Ornelas J, Blaivas A, et al. Antithrombotic Therapy for VTE Disease: CHEST Guideline and Expert Panel Report. Chest. 2016 Feb;149(2):315-352.

3) Kim YK, Nieulaat R, Connolly SJ, et al. Effect of a simple two-step warfarin dosing algorithm on anticoagulant control as measured by time in therapeutic range: a pilot study. Journal of Thrombosis and Haemostasis. October 2009. 8: 101-106.

4) Ageno W, Gallus AS, Wittkowsky A, et al.,. Oral Anticoagulant Therapy**,** American College of Chest Physicians Evidence-Based Clinical Practice Guidelines (9th Edition). Chest. 2012; 141:44s-88s.

5) Harrison L, Johnston M, Massicotte MP, et al. Comparison of 5-mg and 10-mg Loading Doses in Initiation of Warfarin Therapy. Ann Intern Med. 1997;126:133-136.

6) Crowther MA, Harrison L, Hirsh J. Warfarin: less may be better [Letter]. Ann Intern Med. 1997;127:333.

7) Kovacs MJ, Rodger M, Anderson DR, et al. Comparison of 10-mg and 5-mg Warfarin Initiation Nomograms Together with Low-Molecular-Weight Heparin for Outpatient Treatment of Acute Venous Thromboembolism. Ann Intern Med. 2003;138:714-719.

8) Ageno W, Gallus A, Wittkowsky A, Crowther M, et al. Oral Anticoagulant Therapy: Antithrombotic Therapy and Prevention of Thrombosis American College of Chest Physicians Evidence-Based Clinical Practice Guidelines (9th Edition). Chest. 2012; 141:44s-88s.

9) University of Wisconsin Anticoagulation Services: Ambulatory Warfarin Management; Warfarin Dosing Algorithm. May 31, 2012. www.uwhealth.org.

10) Levine M, Gent M, Hirsh J, Leclerc J, Anderson D, Weitz J, et al. A comparison of low-molecular-weight heparin administered primarily at home with unfractionated heparin administered in the hospital for proximal deep-vein thrombosis. N Engl J Med. 1996;334:677-81. [PMID: 8594425]

11) Low-molecular-weight heparin in the treatment of patients with venous thromboembolism. The Columbus Investigators. N Engl J Med. 1997;337:657- 62. [PMID: 9280815]

12) Horton JD, Bushwick BM. Warfarin Therapy: Evolving Strategies in Anticoagulation. Am Fam Physician. 1999 Feb 1;59(3):635-646.

13) Le Gal G, Carrier M, Tierney S, et al. Prediction of the warfarin maintenance dose after completion of the 10 mg initiation nomogram: do we really need genotyping? Journal of Thrombosis & Haemostasis. Jan 2010;8(1):90-4.

14) Anthony M, Romero K, Malone DC, et al. Warfarin interactions with substances listed in drug information compendia and in the FDA-approved label for warfarin sodium. Clin Pharmacol Ther. 2009;86(4): 425-429.

15) Siegal D, Yudin J, Kaatz S, et al. Periprocedural heparin bridging in patients receiving vitamin K antagonists: systematic review and meta-analysis of bleeding and thromboembolic rates. Circulation 2012:126(13):1630-1639.

16) Douketis JD, Spyropoulos AC, Spencer FA, et al. Perioperative Management of Antithrombotic Therapy Antithrombotic Therapy and Prevention of Thrombosis, 9th ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines. Chest. 2012; 141:326s-350s.

17) Garcia P, Ruiz W, Loza Munarriz C. Warfarin initiation nomograms for venous thromboembolism. Cochrane Database Syst Rev. 2013 Jul 10;7:CD007699. In patients with acute thromboembolism (DVT or PE) aged 18 years or older, considerable uncertainty surrounds the use of a 10-mg or a 5-mg loading dose for initiation of warfarin to achieve an INR of 2.0 to 3.0 on the fifth day of therapy. Heterogeneity among analyzed studies limits certainty surrounding optimal warfarin initiation nomograms.

18) Kuramatsu JB, Gerner ST, Schellinger PD, et al. Anticoagulant reversal, blood pressure levels, and anticoagulant resumption in patients with anticoagulation-related intracerebral hemorrhage. JAMA. 2015 Feb 24; 313(8):824-36.

19) Boonyawat K, Wang L, Lazo-Langner A, et al. The effect of low-dose oral vitamin K supplementation on INR stability in patients receiving warfarin. A randomised trial. Thromb Haemost.2016 Aug 30;116(3):480-5.

20) Gage BF, Bass AR, Lin H, et al. Effect of **genotype-guided warfarin dosing** on clinical events and anticoagulation control among patients undergoing hip or knee arthroplasty: the **GIFT** randomized clinical trial. JAMA. doi:10.1001/jama.2017.11469

21) Verhoef TI, Ragia G, de Boer A, et al. A randomized trial of **genotype-guided dosing of acenocoumarol and phenprocoumon**. (**EU-PACT**) N Engl J Med 2013. DOI: 10.1056/NEJMoa1311388.

22) Pirmohamed M, Burnside G, Eriksson N, et al. A randomized trial of **genotype-guided dosing of warfarin**. (**EU-PACT**) N Engl J Med 2013. DOI: 10.1056/NEJMoa1311386.

23) Kimmel SE, French B, Kasner SE, et al. A **pharmacogenetic versus a clinical algorithm for warfarin** dosing. (**COAG**) N Engl J Med 2013. DOI: 10.1056/NEJMoa1310669

24) Stergiopoulos K, Brown DL. **Genotype-guided vs clinical dosing** of warfarin and its analogues: meta-analysis of randomized clinical trials [online June 16, 2014]. JAMA Intern Med. doi:10.1001/jamainternmed.2014.2368.

25) Writing Committee, Tomaselli GF, Mahaffey KW, et al. **2017 ACC Expert Consensus Decision Pathway on Management of Bleeding in Patients on Oral Anticoagulants**: A Report of the American College of Cardiology Task Force on Expert Consensus Decision Pathways. J Am Coll Cardiol. 2017 Nov 10.

26) Behera SK, Xavier AS, Selvarajan S, et al. **Acenocoumarol** As An Alternative Anticoagulant In A Patient With Warfarin Related Nephropathy. Br J Clin Pharmacol. 2018 Feb 8.

27) Biffi A, et al. Oral Anticoagulation and Functional Outcome after Intracerebral Hemorrhage. Ann Neurol. 2017 Nov;82(5):755-765. doi: 10.1002/ana.25079.

28) Steffel J, et al; ESC Scientific Document Group . The **2018 European Heart Rhythm Association Practical Guide on the use of non-vitamin K antagonist oral anticoagulants in patients with atrial fibrillation**. Eur Heart J. 2018 Apr 21;39(16):1330-1393.

What is bridging? What does it attempt to do?

"Bridging anticoagulation refers to giving a short-acting anticoagulant, typically low-molecular-weight heparin (LMWH), before and after surgery to minimize the time that patients are not anticoagulated, and thereby minimize the risk for thromboembolism."[2]

Additional references:

Armstrong MJ, Gronseth G, Anderson DC, et al. Summary of evidence-based guideline: **Periprocedural management** of **antithrombotic medications** in patients with ischemic cerebrovascular disease. Neurology 2013; 80:2065-2069.

Arnold MJ, Keung JJ, McCarragher B. **Interventional Radiology**: Indications and Best Practices. Am Fam Physician. 2019 May 1;99(9):547-556.

Biccard BM, Sigamani A, Chan MTV, et al. Effect of **aspirin in vascular surgery** in patients from a randomized clinical trial (**POISE-2**). Br J Surg. 2018 Jul 18.

Birnie DH, Healey JS, Wells GA, et al; **BRUISE-CONTROL** Investigators. Pacemaker or defibrillator surgery without interruption of anticoagulation. NEngl J Med. 2013 May 30;368(22):2084-93.

Chan FKL, Kyaw MH, Hsiang JC, et al. Risk of **Postpolypectomy Bleeding With Uninterrupted Clopidogrel** Therapy in an Industry-Independent, Double-Blind, Randomized Trial. Gastroenterology. 2019 Mar;156(4):918-925.e1.

Childers CP, Maggard-Gibbons M, Shekelle PG. **Antiplatelet Therapy** in Patients With **Coronary Stents** Undergoing Elective Noncardiac Surgery: Continue, Stop, or Something in Between? JAMA. 2017 Jul 11;318(2):120-121.

Clark NP, Witt DM, Davies LE, Saito EM, McCool KH, Douketis JD, Metz KR, Delate T. Bleeding, Recurrent Venous Thromboembolism, and Mortality Risks During Warfarin Interruption for Invasive Procedures. JAMA Intern Med. 2015 Jul;175(7):1163-8.

Cohn SL. **In the Clinic: Preoperative Evaluation for Noncardiac Surgery**. Ann Intern Med. 2016 Dec 6;165(11):ITC81-ITC96.

Cohn SL. Updated guidelines on **cardiovascular evaluation before noncardiac surgery**: a view from the trenches. Cleve Clin J Med 2014; 81:742–751.

Daniels PR. Peri-procedural management of patients taking **oral anticoagulants**. BMJ. 2015 Jul 14;351:h2391.

Devereaux PJ, Mrkobrada M, Sessler DI, et al; **POISE-2** Investigators. **Aspirin in patients undergoing noncardiac surgery**. N Engl J Med. 2014 Apr 17;370(16):1494-503.

Doherty JU, Gluckman TJ, Hucker WJ, et al. **2017 ACC Expert Consensus** Decision Pathway for **Periprocedural Management of Anticoagulation in Patients With Nonvalvular Atrial Fibrillation**: A Report of the American College of Cardiology Clinical Expert Consensus Document Task Force. J Am Coll Cardiol. 2017 Jan 5.

Douketis JD, Spyropoulos AC, Kaatz S, et al; **BRIDGE** Investigators. Perioperative Bridging Anticoagulation in Patients with Atrial Fibrillation. N Engl J Med. 2015 Aug 27;373(9):823-33.

Dunn AS, Turpie AG. **Perioperative management of patients receiving oral anticoagulants**: a systematic review. Arch Intern Med. 2003 Apr 28;163(8):901-8.

Eagle KA, Vaishnava P, Froehlich JB. **Perioperative cardiovascular care** for patients undergoing noncardiac surgical intervention. JAMA Intern Med. 2015 May 1;175(5):835-9.

Flaker GC, Theriot P, Binder LG, Dobesh et al. Management of **Periprocedural Anticoagulation**: A Survey of Contemporary Practice. J Am Coll Cardiol. 2016 Jul 12;68(2):217-26.

Flanders SA, Greene MT, Grant P, et al. Hospital performance for pharmacologic venous thromboembolism prophylaxis and rate of venous thromboembolism: a cohort study [online August 18, 2014]. JAMA Intern Med.

Fleisher LA, Fleischmann KE, Auerbach AD, et al. 2014 ACC/AHA Guideline on Perioperative Cardiovascular Evaluation and Management of Patients Undergoing Noncardiac Surgery: A Report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. J Am Coll Cardiol. 2014 Jul 29.

Godier A, Dincq AS, Martin AC, et al. **Predictors** of **pre-procedural c**oncentrations of **direct oral anticoagulants**: a prospective multicentre study. European Heart Journal. 2017;38:2431-2439

Goodman SM, Springer B, Guyatt G, et al. 2017 American College of Rheumatology/American Association of Hip and Knee Surgeons Guideline for the **Perioperative Management of Antirheumatic Medication in Patients With Rheumatic Diseases** Undergoing Elective Total Hip or Total Knee Arthroplasty. Arthritis Rheumatol. 2017 Jun 16.

Graham MM, Sessler DI, Parlow JL, et al. **Aspirin in patients with previous percutaneous coronary intervention** undergoing noncardiac surgery (**Poise-2**). Ann Intern Med. 2018;168: 237-44.

Grant PJ, Eagle KA. Annals for Hospitalists Inpatient Notes – **Perioperative Medicine**-The Past, Present, and Future of Cardiovascular Risk Assessment and Risk Reduction Strategies. Ann Intern Med. 2018 Feb 20;168(4):HO2-HO3.

Holcomb CN, Graham LA, Richman JS, et al. The incremental **risk of noncardiac surgery on adverse cardiac events following coronary stenting**. J Am Coll Cardiol. 2014 Dec 30;64(25):2730-9.

Hornor MA, Duane TM, Ehlers AP, et al. **American College of Surgeons' Guidelines for the Perioperative Management of Antithrombotic Medication**. J Am Coll Surg. 2018 Aug 23.

Keay L, Lindsley K, Tielsch J, et al. Routine **preoperative medical testing for cataract surgery**. Cochrane Database Syst Rev. 2019 Jan 8;1:CD007293. This review has shown that routine preoperative testing does not increase the safety of cataract surgery. Alternatives to routine preoperative medical testing have been proposed, including self administered health questionnaires, which could substitute for health provider histories and physical examinations. Such avenues may lead to cost-effective means of identifying those at increased risk of medical adverse events due to cataract surgery.

Koenig-Oberhuber V, Filipovic M. **New antiplatelet drugs and new oral anticoagulants**. Br J Anaesth. 2016 Sep;117 Suppl 2:ii74-ii84.

Ljungqvist O, Scott M, Fearon KC. **Enhanced Recovery After Surgery**: A Review. JAMA Surg. 2017 Jan 11.

Martin SK, Cifu AS. **Routine Preoperative Laboratory Tests** for Elective Surgery. JAMA. 2017 Aug 8;318(6):567-568.

Mikhail MA, Mohabbat AB, Ghosh AK. **Perioperative Cardiovascular Medication Management in Noncardiac surgery**: Common Questions. Am Fam Phys. 2017;95(10):645-650.

Mohanty S, Rosenthal RA, Russell MM, et al. **Optimal Perioperative Management of the Geriatric Patient**: A Best Practices Guideline from the American College of Surgeons NSQIP and the American Geriatrics Society. J Am Coll Surg. 2016 Jan 4

Myles PS, Smith JA, Forbes A, et al; **ATACAS** Investigators of the ANZCA Clinical Trials Network. Stopping vs. Continuing Aspirin before Coronary Artery Surgery. N Engl J Med. 2016 Feb 25;374(8):728-37.

NICE: National Institute for Health and Care Excellence. **Routine preoperative tests for elective surgery**. London (UK): National Institute for Health and Care Excellence (NICE); 2016 Apr 5.

Northup PG, Friedman LS, Kamath PS. AGA Clinical Practice Update: **Surgical Risk Assessment and Perioperative Management in Cirrhosis**. Clin Gastroenterol Hepatol. 2018 Sep 28.

Raval AN, Cigarroa JE, Chung MK, et al. Management of Patients on **Non-Vitamin K Antagonist Oral Anticoagulants in the Acute Care and Periprocedural Setting**: A Scientific Statement From the American Heart Association. Circulation. 2017 Feb 6.

Schulman S, Carrier M, Lee AY, et al; Periop Dabigatran Study Group. **Perioperative Management of Dabigatran**: A Prospective Cohort Study. Circulation. 2015 May 12.
Selby LV, Sovel M, Sjoberg DD, McSweeney M, et al; MSKCC VTE Task Force. **Preoperative Chemoprophylaxis Is Safe in Major Oncology** Operations and Effective at Preventing Venous Thromboembolism. J Am Coll Surg. 2015 Dec 15.
Smilowitz NR, Berger JS. **Perioperative Management** to Reduce Cardiovascular Events. Circulation. 2016 Mar 15;133(11):1125-30.
Smilowitz NR, Gupta N, Ramakrishna H, et al. **Perioperative major adverse cardiovascular and cerebrovascular events** associated with noncardiac surgery [online Dec 28, 2016]. JAMA Cardiol. doi:10 .1001/jamacardio.2016.4792
Steffel J, et al; ESC Scientific Document Group . The **2018 European Heart Rhythm Association Practical Guide on the use of non-vitamin K antagonist oral anticoagulants in patients with atrial fibrillation**. Eur Heart J. 2018 Apr 21;39(16):1330-1393.
Steinberg BA, Peterson ED, Kim S, et al. Use and **outcomes associated with bridging during anticoagulation interruptions** in patients with atrial fibrillation: findings from the Outcomes Registry for Better Informed Treatment of Atrial Fibrillation (**ORBIT-AF**). Circulation. 2015;131:488–494.
Verma A, Cairns JA, Mitchell LB, et al. CCS Atrial Fibrillation Guidelines Committee. 2014 focused update of the Canadian cardiovascular society (CCS) guidelines for the management of atrial fibrillation. Can J Cardiol. 2014 Oct;30(10):1114-30.
Wysokinski WE, McBane RD 2nd. **Periprocedural bridging management of anticoagulation**. Circulation. 2012 Jul 24;126(4):486-90.

References - Perioperative Management – Before & After an Invasive Procedure

[1] Douketis J, Spyropoulos A, Spencer F et al. Perioperative Management of Antithrombotic Therapy. Antithrombotic Therapy and Prevention of Thrombosis, 9th Ed: ACCP Guidelines. Chest 2012;141(2)(Suppl):e326S-e350S http://journal.publications.chestnet.org/article.aspx?articleid=1159479 accessed August 28, 2012
[2] Perioperative Management of Patients who are receiving warfarin. Thrombosis Canada. http://thrombosiscanada.ca/guides/pdfs/Warfarin_perioperative_management.pdf, accessed August 16, 2013
[3] Peri-operative Managements of Patients who are receiving a new oral anticoagulant (dabigatran, rivaroxaban, apixaban). Thrombosis Canada. http://thrombosiscanada.ca/guides/pdfs/NOACs_Perioperative_Managment.pdf, accessed August 16, 2013
[4] Mehta SR, et al. 2018 Canadian Cardiovascular Society/Canadian Association of Interventional Cardiology Focused Update of the Guidelines for the Use of Antiplatelet Therapy. Can J Cardiol. 2018Mar;34(3):214-233.
[5] Garcia DA, Regan S, Henault LE, et al. Risk of thromboembolism with short-term interruption of warfarin therapy. Arch Intern Med 2008;168:63-9
[6] Blacker DJ, Wijdicks EF, McClelland RL. Stroke risk in anticoagulated patients with atrial fibrillation undergoing endoscopy. Neurology. 2003;61:964-8
[7] Ansell JE. The perioperative management of warfarin therapy. Arch Intern Med. 2003;163(8):881-3
[8] Douketis JD, Spyropoulos AC. Vitamin K to reverse the anticoagulant effect of vitamin K antagonists: can you teach an old dog new tricks? J Thromb Haemost. 2010;8(3):496-8
[9] Douketis JD, Berger PB, Dunn AS, et al. American College of Chest Physicians. The perioperative management of antithrombotic therapy: American College of Chest Physicians evidence-based clinical practice guidelines (8th edition). Chest. 2008;133(suppl 6):299S-339S.
[10] Eckman MH. "Bridging on the river Kwai": the perioperative management of anticoagulation therapy. Med Decis Making. 2005;25(4):370-3
[11] Ickx BE, Steib A. Perioperative management of patients receiving vitamin K antagonists. Can J Anaesth. 2006;53(suppl 6):S113-S122
[12] Acetyl Salicylic Acid. Thrombosis Canada. http://thrombosiscanada.ca/?page_id=18&search=aspirin#, accessed September 9, 2013
[13] Clopidogrel. Thrombosis Canada. http://thrombosiscanada.ca/?page_id=18&search=clopidogrel# accessed September 9, 2013
[14] Prasugrel. Thrombosis Canada. http://thrombosiscanada.ca/?page_id=18&search=prasugrel# accessed September 9, 2013
[15] Ticagrelor. Thrombosis Canada. http://thrombosiscanada.ca/?page_id=18&search=ticagrelor# accessed September 9, 2013
[16] Pass ST, Simpson RW. Discontinuation and reinstitution of medications during perioperative period. Am J Health Syst Pharm. 2004;61(9). http://www.medscape.com/viewarticle/477683_4 accessed August 21, 2013
[17] Levine, Glenn N., et al. "2016 ACC/AHA Guideline Focused Update on Duration of Dual Antiplatelet Therapy in Patients With Coronary Artery Disease: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines." *Journal of the American College of Cardiology* (2016).

RxFiles On-Line Extras: Oral Antiplatelet & Antithrombotic Agents

Landmark Trials	Intervention	Population	Contribution to Current Knowledge
AAASPS [18] ≤2 yrs, n=1,809	Ticlopidine TICLID 250mg po BID vs ASA 325mg po BID	African Americans with stroke hx	Recurrent MI, stroke or vascular death: TICLID 14.7% vs ASA 12.3%, p=0.12
CLASSICS [4] 28 days, n=1,020	Clopidogrel PLAVIX $_{(\pm 300mg)\ 75mg}$ + ASA $_{325mg\ po\ daily}$ vs Ticlopidine TICLID $_{250mg\ po\ BID}$ + ASA $_{325mg\ po\ daily}$	Post-stent	NS in safety/efficacy for PLAVIX (either regimen) or TICLID in 1st 28 day post-stenting.

ORAL ANTIPLATELET & ANTITHROMBOTIC AGENTS

1. Micromedex 2018; Drugs in Pregnancy and Lactation, 11th ed. Briggs GE, Freeman RK, Yaffe SJ, editors. Williams and Wilkins; Baltimore, MD: 2017.; Hansten & Horn-Drug Interactions 2016.
2. Antithrombotic Trialists' Collaboration. (ATT) Collaborative meta-analysis of randomised trials of antiplatelet therapy for prevention of death, myocardial infarction, and stroke in high risk patients. BMJ. 2002 Jan 12;324(7329):71-86.
   Collins R et al. for the Antithrombotic Trialists' (**ATT**) Collaboration. **Aspirin in the primary and secondary prevention** of vascular disease: Collaborative meta-analysis of individual participant data from randomised trials. Lancet 2009 May 30; 373:1849.
3. CAPRIE Steering Committee. A randomized, blinded trial of clopidogrel vs aspirin in patients at risk of ischemic events (**CAPRIE**). Lancet 1996; 348:1329-39.
4. Bertrand ME et al. Double blind study of the safety of clopidogrel with and without loading dose in combination with aspirin compared with ticlopidine in combination with aspirin after coronary stenting. (**CLASSICS**). Circulation 2000; 102: 624-29.
5. Yusuf S et al. Effects of clopidogrel in addition to aspirin in patients with acute coronary syndromes without ST segment elevation (Clopidogrel in unstable angina to prevent recurrent events (**CURE**). N Engl J Med 2001; 345: 494-502.
6. Diener HC et al. European Stroke Prevention Study 2 (**ESPS2**). Dipyridamole and acetylsalicylic acid in the secondary prevention of stroke. J Neurol Sci 1996; 143: 1-13.
7. Hirsh J, Dalen J Guyatt G. The **sixth (2000) ACCP Guidelines** for antithrombotic therapy for prevention & treatment of thrombosis. **CHEST** 2001;119:1s-370s. The **Seventh ACCP** Evidence-Based Guidelines. **Chest 2004 September 2004** (**see also CHEST ACCP-AT9 Antithrombotic and Thrombolytic 9th Edition 2012**).
   Ansell J, Hirsh J, Hylek E, et al. Pharmacology and management of the vitamin K antagonists: American college of chest physicians evidence-based clinical practice guidelines (8th edition). Chest 2008;133:160-98.
   Douketis JD, Berger PB, Dunn AS, et al. The perioperative management of antithrombotic therapy: American college of chest physicians evidence-based clinical practice guidelines (8th edition). Chest 2008;133:299S-339S.
   Bell AD, Cartier R, Chan WS. Canadian Cardiovascular Society (**CCS**) Anti-Platelet Guideline 2010.
   Bell Alan D., Roussin André, Cartier Raymond, et al. The Use of **Antiplatelet Therapy in the Outpatient Setting**: Canadian Cardiovascular Society (**CCS**) Guidelines. Can J Cardiol. 2011 May-Jun;27 Suppl A:S1-59.
   Tanguay JF, Bell AD, Ackman ML et al. **Focused 2012 Update of the Canadian Cardiovascular Society Guidelines for the Use of Antiplatelet Therapy**. Can J Cardiol. 2013 Aug 23.
   Chassot PG, Marcucci C, Delabays A, Spahn DR. Perioperative antiplatelet therapy. Am Fam Physician. 2010 Dec 15;82(12):1484-9.
   Bartolucci AA, Tendera M, and Howard G. Meta-analysis of multiple primary prevention trials of cardiovascular events using aspirin. Am J Cardiol 2011; DOI:10.1016/j.amjcard.2011.02.325.
   Seshasai SRK, Wijesuriya S, Sivakumaran R, et al. Effect of **aspirin** on **vascular and nonvascular outcomes**: meta-analysis of randomized controlled trials [online Jan 9, 2012]. Archives Intern Med. doi:10.1001/archinternmed.2011.628.
   Lip GY, Felmeden DC, Dwivedi G. **Antiplatelet agents and anticoagulants** for **hypertension**. Cochrane Database Syst Rev. 2011 Dec7;12:CD003186. Antiplatelet therapy with ASA for primary prevention in patients with elevated blood pressure provides a benefit, reduction in myocardial infarction, which is negated by a harm of similar magnitude, increase in major haemorrhage.The benefit of antiplatelet therapy for secondary prevention in patients with elevated blood pressure is many times greater than the harm.Benefit has not been demonstrated for warfarin therapy alone or in combination with aspirin in patients with elevated blood pressure.
   Guyatt Gordon H., Akl EA., Crowther M. **Executive Summary**: Antithrombotic Therapy and Prevention of Thrombosis,**9th ed**: American College of Chest Physicians (**ACCP-AT9**). Evidence-Based Clinical Practice Guidelines. Chest 2012; 141(2)(Suppl):7S–47S.
   Lansberg MG, et al. Antithrombotic & thrombolytic therapy for **ischemic stroke**: antithrombotic therapy & prevention of thrombosis, 9th ed: American College of Chest Physicians (**ACCP-AT9**) evidence-based guidelines. Chest. 2012;141(2)(supp):e601S-e636S.
   You JJ, Singer DE, et al. Antithrombotic therapy for **atrial fibrillation**: antithrombotic therapy and prevention of thrombosis, 9th ed: American College of Chest Physicians evidence(**ACCP-AT9**) -based clinical guidelines. Chest. 2012;141(2)(suppl):e531S-575S.
   Vandvik PO, Lincoff AM, Gore JM, et al. American College of Chest Physicians. **Primary and secondary prevention of cardiovascular disease**: Antithrombotic Therapy and Prevention of Thrombosis, 9th ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines. Chest. 2012 Feb;141(2 Suppl):e637S-68S.
   Zheng SL, Roddick AJ. Association of aspirin use for primary prevention with cardiovascular events and bleeding events: a systematic review and meta-analysis [Jan 22, 2019]. JAMA. doi:10.1001/jama.2018.20578
8. Gent M, Blakely JA, Easton JD, et al. The Canadian American Ticlopidine Study (CATS) in thromboembolic stroke. Lancet 1989;2:1215-1220.
9. Hass WK, Easton JD, Adams HP, et al. A randomized trial comparing ticlopidine with aspirin for the prevention of stroke in high risk patients (**TASS**). N Engl J Med 1989;321:501-507.
10. Steering Committee of the Physicians Health Study Research Group. Final report on the aspirin component of the ongoing Physicians Health Study (**PHS**). N Eng J Med 1989;321:129-135.
11. Hansson L Zanchetti A, Carruthers SG, et al. Effects of intensive blood pressure lowering & low dose aspirin in patients with hypertension: principal results of the Hypertension Optimal Treatment (**HOT**) randomized trial. Lancet 1998;351:1755-1762.
    Jardine, Meg J., Ninomiya, Toshiharu, Perkovic, Vlado, et al. Aspirin Is Beneficial in Hypertensive Patients With **Chronic Kidney Disease**: A Post-Hoc Subgroup Analysis of a Randomized Controlled Trial (HOT). J Am Coll Cardiol 2010 56: 956-965.
12. Progress Collaborative Group. Randomized trial of a perindopril based blood pressure lowering regimen among 6105 individuals with previous stroke or transient ischaemic attack. (**PROGRESS**) Lancet 2001;358:1033-1041.
    (Arima H, et al.; for the PROGRESS Collaborative Group. Lower target blood pressures are safe and effective for the prevention of recurrent stroke: the PROGRESS trial. J Hypertens. 2006 Jun;24(6):1201-1208.)
13. Heart Outcomes Prevention Evaluation Study Investigators. Effects of an angiotensin converting enzyme inhibitor, ramipril on cardiovascular events in high risk patients (**HOPE**). N Engl J Med 2000;342:145-153.
14. The SALT Collaborators Group. Swedish Aspirin Low-dose Trial (**SALT**) of 75mg aspirin as secondary prophylaxis after cerebrovascular eschemic events. Lancet 1991;338:1345-9.
15. SPIRIT Study Group. A randomized trial of **anticoagulants versus aspirin** after cerebral ischemia presumed arterial origin. The Stroke Prevention in Reversible Ischemia Trial (**SPIRIT**) Study Group. Ann Neuro 1997;42:857-65.
16. Kovacs MJ, Rodger M, et al. Comparison of 10-mg and 5-mg Warfarin Initiation Nomograms Together with Low-Molecular-Weight Heparin for Outpatient Treatment of Acute Venous Thromboembolism. Ann Intern Med. 2003 May 6;138(9):714-9.
17. Ridker PM, Goldhaber SZ, et al. Long-term, low-intensity warfarin therapy for the prevention of recurrent venous thromboembolism (**PREVENT**). N Engl J Med. 2003 Apr 10;348(15):1425-34.
18. Gorelick PB, Richardson D, Kelly M, Ruland S, Hung E, Harris Y, Kittner S, Leurgans S. Aspirin and ticlopidine for prevention of recurrent stroke in black patients: a randomized trial. (**AAASPS**) JAMA. 2003 Jun 11;289(22):2947-57.
19. Pearson TA, et al. **AHA Guidelines** for Primary Prevention of Cardiovascular Disease and Stroke: **2002** Update. Circulation. 2002 Jul 16;106(3):388-91. (Pharmacists Letter. Using Aspirin in Hypertensive patients. Oct 2007.)
    Pignone Michael, Alberts Mark J., Colwell John A., et al. **Aspirin for Primary Prevention of Cardiovascular Events in People With Diabetes**. A Position Statement of the American Diabetes Association (**ADA**), a Scientific Statement of the American Heart Association (**AHA**), and an Expert Consensus Document of the American College of Cardiology Foundation (ACCF). Circulation published May 27, 2010, doi:10.1161/CIR.0b013e3181e3b133 http://circ.ahajournals.org/cgi/reprint/CIR.0b013e3181e3b133v1
    Furie Karen L., Kasner Scott E., Adams Robert J., et al., and on behalf of the American Heart Association Stroke Council, Council on Cardiovascular Nursing, Council on Clinical Cardiology, and Interdisciplinary Council on Quality of Care and Outcomes Research. Guidelines for the **Prevention of Stroke in Patients With Stroke or Transient Ischemic Attack** (Secondary Prevention). A Guideline for Healthcare Professionals From the American Heart Association (**AHA**) /American Stroke Association (**ASA**). Stroke published October 21, 2010, doi:10.1161/STR.0b013e3181f7d043 http://stroke.ahajournals.org/cgi/reprint/STR.0b013e3181f7d043v1
    Goldstein Larry B., Bushnell Cheryl D., Adams Robert J., et al., and on behalf of the American Heart Association Stroke Council, Council on Cardiovascular Nursing, Council on Epidemiology and Prevention, Council for High Blood Pressure Research, Council on Peripheral Vascular Disease, and Interdisciplinary Council on Quali Guidelines for the **Primary Prevention of Stroke**. A Guideline for Healthcare Professionals From the American Heart Association (**AHA**) /American Stroke Association (**ASA**). Stroke published December 2, 2010, doi:10.1161/STR.0b013e3181fcb238
    ADA- American Diabetes Association. Standards of Medical Care in Diabetes—**2011 Diabetes Care.** January 2011 34:S11-S61; doi:10.2337/dc11-S011. http://care.diabetesjournals.org/content/34/Supplement_1/S11.full.pdf+html
    ADA 2014: American Diabetes Association. **Standards of Medical Care in Diabetes**. Diabetes Care January 2014 37:S14-S80; doi:10.2337/dc14-S014. http://care.diabetesjournals.org/content/37/Supplement_1.toc
    ADA 2016: Standards of Medical Care in Diabetes-2016: Summary of Revisions. Diabetes Care. (American Diabetes Association) 2016 Jan;39 Suppl 1:S4-5.
20. Hurlen M, Abdelnoor M, Smith P, Erikssen J, Arnesen H. Warfarin, aspirin, or both after myocardial infarction. (**WARIS-II**) N Engl J Med. 2002 Sep 26;347(13):969-74.
21. Kearon C, et al. (**ELATE** Investigators). Comparison of low-intensity warfarin therapy with conventional-intensity warfarin therapy for long-term prevention of recurrent venous thromboembolism. N Engl J Med. 2003 Aug 14;349(7):631-9.
22. Crowther MA, Ginsberg JS, Julian J, et al. A comparison of two intensities of warfarin for the prevention of recurrent thrombosis in patients with the antiphospholipid antibody syndrome. N Engl J Med 2003;349:1133-1138.
23. **U.S. Preventive Services** Task Force: **Aspirin** for the **Primary Prevention** of Cardiovascular Events: Recommendation and Rationale Ann Intern Med. 2002;136:157–160
24. Rachel S. Eidelman et al. An Update on Aspirin in the Primary Prevention of Cardiovascular Disease**.** Arch Intern Med. 2003;163:2006-2010.
25. Peters RJ, Mehta SR, Fox KA, Zhao F, Lewis BS, Kopecky SL, Diaz R, Commerford PJ, Valentin V, Yusuf S. Effects of Aspirin Dose When Used Alone or in Combination With Clopidogrel in Patients With Acute Coronary Syndromes. Observations From the Clopidogrel in Unstable angina to prevent Recurrent Events (**CURE**) Study. Circulation. 2003 Sep 22 . (Budaj A, Yusuf S, Mehta SR, Fox KA, Tognoni G, Zhao F, Chrolavicius S, Hunt D, Keltai M, Franzosi MG; Clopidogrel in Unstable angina to prevent Recurrent Events (CURE) Trial Investigators. Benefit of clopidogrel in patients with acute coronary syndromes without ST-segment elevation in various risk groups. Circulation. 2002 Sep 24;106(13):1622-6.)
26. Steinhubl SR, Berger PB, Mann JT 3rd, Fry ET, DeLago A, Wilmer C, Topol EJ; **CREDO** Investigators. Clopidogrel for the Reduction of Events During Observation. Early and sustained dual oral antiplatelet therapy following percutaneous coronary intervention: a randomized controlled trial. JAMA. 2002 Nov 20;288(19):2411-20.
27. Crowther MA, Douketis JD, Schnurr T, Steidl L, Mera V, Ultori C, Venco A, Ageno W. Oral vitamin K lowers the international normalized ratio more rapidly than subcutaneous vitamin K in the treatment of warfarin-associated coagulopathy. A randomized, controlled trial. Ann Intern Med. 2002 Aug 20;137(4):251-4.
28. Possidente CJ, Howe JG, Cushman M. Evaluation of very low-dose subcutaneous vitamin K during postoperative warfarin therapy. Pharmacotherapy. 2001 Mar;21(3):295-300.
29. Crowther MA, Julian J, McCarty D, Douketis J, Kovacs M, Biagoni L, Schnurr T, McGinnis J, Gent M, Hirsh J, Ginsberg J. Treatment of warfarin-associated coagulopathy with oral vitamin K: a randomised controlled trial. Lancet. 2000 Nov 4;356(9241):1551-3.
30. Nee R, Doppenschmidt D, Donovan DJ, Andrews TC. Intravenous versus subcutaneous vitamin K1 in reversing excessive oral anticoagulation. Am J Cardiol. 1999 Jan 15;83(2):286-8, A6-7.

31. Lubetsky A, Yonath H, Olchovsky D, Loebstein R, et al.. Comparison of Oral vs Intravenous Phytonadione (Vitamin K1) in Patients With Excessive Anticoagulation: A Prospective Randomized Controlled Study. Arch Intern Med. 2003 Nov 10;163(20):2469-73.
32. Weibert RT, Le DT, Kayser SR, Rapaport SI. Correction of excessive anticoagulation with low-dose oral vitamin K1. Ann Intern Med. 1997 Jun 15;126(12):959-62.
33 Wilson SE, et al. Low-dose oral vitamin K therapy for the management of asymptomatic patients with elevated international normalized ratios: a brief review. CMAJ. 2004 Mar 2;170(5):821-4. (Dezee KJ, et al.Treatment of excessive anticoagulation with phytonadione (vitamin K): a meta-analysis. Arch Intern Med. 2006 Feb 27;166(4):391-7.)
34. Eidelman RS, Hebert PR, Weisman SM, Hennekens CH. An update on aspirin in the primary prevention of cardiovascular disease. Arch Intern Med. 2003 Sep 22;163(17):2006-10.
35. Lauer MS. Clinical practice. Aspirin for primary prevention of coronary events. N Engl J Med. 2002 May 9;346(19):1468-74.
36. Messerli FH, Grossman E, Lever AF. Do thiazide diuretics confer specific protection against strokes? Arch Intern Med. 2003 Nov 24;163(21):2557-60.
37. Lip GY, Kamath S, Hart RG. ABC of antithrombotic therapy: Antithrombotic therapy for cerebrovascular disorders. BMJ. 2002 Nov 16;325(7373):1161-3.
38. Straus SE, Majumdar SR, McAlister FA. New evidence for stroke prevention: scientific review. JAMA. 2002 Sep 18; 288(11): 1388-95.
39. Diabetes Care 27:S72-S73, 2004. Aspirin Therapy in Diabetes -American Diabetes Association. (American Diabetes Association (ADA). Standards of medical care in diabetes. VI. **Prevention and management of diabetes complications. Diabetes Care 2007** Jan;30(Suppl 1): S15-24. http://care.diabetesjournals.org/cgi/content/full/30/suppl_1/S4#SEC14)
American Diabetes Association (ADA). Standards of medical care in diabetes--2008. Diabetes Care. 2008 Jan;31 Suppl 1:S12-54. http://care.diabetesjournals.org/cgi/content/full/31/Supplement_1/S12
American Diabetes Assoc. Standards of Medical Care in Diabetes—**2009** Diabetes Care January 2009 32:S13-S61; doi:10.2337/dc09-S013. http://care.diabetesjournals.org/content/32/Supplement_1/S13.full http://care.diabetesjournals.org/content/32/Supplement_1/S13.full
American Diabetes Assoc-ADA. Standards of Medical Care in Diabetes—2010 Diabetes Care Diabetes Care January 2010 33:S11-S61; doi:10.2337/dc10-S011 http://care.diabetesjournals.org/content/33/Supplement_1/S11.full.pdf+html
40. Ringleb PA, Bhatt DL, Hirsch AT, Topol EJ, Hacke W. Benefit of Clopidogrel Over Aspirin Is Amplified in Patients With a History of Ischemic Events. Stroke. 2004 Jan 22.
41. Toole J.F., et al. Lowering Homocysteine in Patients With Ischemic Stroke to Prevent Recurrent Stroke, Myocardial Infarction, and Death. The Vitamin Intervention for Stroke Prevention (**VISP**) Randomized Controlled Trial. JAMA. 2004;291:565-575. (Spence JD, Bang H, Chambless LE, Stampfer MJ. Vitamin Intervention For Stroke Prevention trial: an efficacy analysis. Stroke. 2005 Nov;36(11):2404-9. Epub 2005 Oct 20.)
(Jamison RL, Hartigan P, Kaufman JS, Goldfarb DS, Warren SR, Guarino PD, Gaziano JM; Veterans Affairs Site Investigators. Effect of homocysteine lowering on mortality & vascular disease in **advanced chronic kidney disease** & end-stage renal disease: a randomized controlled trial. JAMA. 2007 Sep 12;298(10):1163-70.Treatment with high doses of folic acid and B vitamins did not improve survival or reduce the incidence of vascular disease in patients with advanced chronic kidney disease or end-stage renal disease.)
42. VITATOPS Trial Study Group. The **VITATOPS** (Vitamins to Prevent Stroke) Trial: rationale and design of an international, large, simple, randomised trial of homocysteine-lowering multivitamin therapy in patients with recent transient ischaemic attack or stroke. Cerebrovasc Dis. 2002;13(2):120-6. (McMahon JA, Green TJ, Skeaff CM, Knight RG, Mann JI, Williams SM. A controlled trial of homocysteine lowering and cognitive performance.
N Engl J Med. 2006 Jun 29;354(26):2764-72. (InfoPOEMs: There is no evidence from this well-designed study that vitamin supplementation to lower homocysteine levels has any beneficial effect on cognition. Although cognition actually appeared to worsen with the use of vitamins in one of the tests, this may be a spurious finding given the large number of comparisons made by the researchers. (LOE = 1b)))
VITATOPS Trial Study Group. B vitamins in patients with recent transient ischaemic attack or stroke in the VITAmins TO Prevent Stroke (VITATOPS) trial: a randomised, double-blind, parallel, placebo-controlled trial. Lancet Neurol. 2010 Aug 3.
Hankey GJ, Eikelboom JW, Yi Q, et al. Antiplatelet therapy and the effects of B vitamins in patients with previous stroke or transient ischaemic attack: a post-hoc subanalysis of VITATOPS, a randomised, placebo-controlled trial. Lancet Neurol 2012; online May 2.
Hankey GJ, Ford AH, Yi Q, et al. Effect of **B vitamins and lowering homocysteine** on cognitive impairment in patients with previous stroke or transient ischemic attack: a prespecified secondary analysis of a randomized, placebo-controlled trial (VITATOPS) and meta-analysis. Stroke. 2013 Aug;44(8):2232-9.
43. Linkins LA, Choi PT, Douketis JD. Clinical **impact of bleeding in patients taking oral anticoagulant** therapy for venous thromboembolism: a meta-analysis. Ann Intern Med. 2003 Dec 2;139(11):893-900.
44. Koennecke HC. Secondary prevention of stroke: a practical guide to drug treatment. CNS Drugs. 2004;18(4):221-41.
45. ACC/AHA Guidelines for the Management of Patients with ST-Elevation Myocardial Infarction **2004**. http://www.acc.org/clinical/guidelines/stemi/index.pdf
Antman EM, Hand M, Armstrong PW, et al. 2007 focused update of the ACC/AHA 2004 guidelines for the management of patients with ST-elevation myocardial infarction: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Writing Group to Review New Evidence and Update the ACC/AHA 2004 Guidelines for the Management of Patients With ST-Elevation Myocardial Infarction). ***Circulation* 2007**: DOI: 10.1161/CIRCULATIONAHA.107.188209. Available at: http://circ.ahajournals.org. *J Am Coll Cardiol* 2007: DOI:10.1016/j.jacc.2007.10.001. Available at: http://content.onlinejacc.org. http://content.onlinejacc.org/cgi/content/full/j.jacc.2007.10.001v1
Kushner, Frederick G., Hand, Mary, Smith, Sidney C., et al. **2009 Focused Updates**: ACC/AHA Guidelines for the Management of Patients With ST-Elevation Myocardial Infarction (Updating the 2004 Guideline and 2007 Focused Update) and ACC/AHA/SCAI Guidelines on Percutaneous Coronary Intervention (Updating the 2005 Guideline and 2007 Focused Update): A Report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. J Am Coll Cardiol 2009 0: j.jacc.2009.10.015
http://content.onlinejacc.org/cgi/reprint/j.jacc.2009.10.015v1.pdf
46. Bates SM, Ginsberg JS. Clinical practice. Treatment of deep-vein thrombosis. N Engl J Med. **2004** Jul 15;351(3):268-77.
47. Ramzi DW, Leeper KV. DVT & pulmonary embolism: **Part I**. Diagnosis. Am Fam Physician. 2004 Jun 15;69(12):2829-36 & DVT and pulmonary embolism: **Part II**. Treatment and prevention. Am Fam Physician. 2004 Jun 15;69(12):2841-8
48. Diener HC, Bogousslavsky J, Brass LM, et al.; MATCH investigators. Aspirin and clopidogrel compared with clopidogrel alone after recent ischaemic stroke or transient ischaemic attack in high-risk patients (MATCH): randomised, double-blind, placebo-controlled trial. Lancet. 2004 Jul 24;364(9431):331-7.
49. Hirsh J, Guyatt G, Albers G, Schunemann HJ. The **seventh ACCP** conference on antithrombotic and thrombolytic therapy. Evidence-Based Guidelines. **Chest 2004 September 2004** Supplement; 126:172S-696S.
(**see also ACCP Antithrombotic and Thrombolytic 8th Edition 2008**).
50. Tran H, Anand SS. Oral antiplatelet therapy in cerebrovascular disease, coronary artery disease, and peripheral arterial disease. JAMA. 2004 Oct 20;292(15):1867-74.
51. Hirsh J, Bhatt DL. Comparative benefits of clopidogrel and aspirin in high-risk patient populations: lessons from the CAPRIE and CURE studies. Arch Intern Med. 2004 Oct 25;164(19):2106-10.
52. Chan FKL, et al Clopidogrel versus Aspirin and Esomeprazole to Prevent Recurrent Ulcer Bleeding. N Engl J Med 2005;352:238-44. n=320 1yr (InfoPOEMs: For patients with a history of bleeding peptic ulcer, **aspirin and a proton pump inhibitor** twice a day was safer in terms of bleeding side effects than clopidogrel. While esomeprazole was used in this study, generic omeprazole 20 mg give twice a day provides nearly the same degree of acid suppression at a much lower cost. This study calls into question the overall safety of clopidogrel, which has been promoted as not increasing the risk of bleeding significantly. (LOE = 1b)) (Lai KC, et al. **Esomeprazole 20mg/d + ASA (100mg/d)** vs clopidogrel 75mg od for prevention of recurrent gastrointestinal ulcer complications. Clin Gastroenterol Hepatol. 2006 Jul;4(7):860-5. Epub 2006 Jun 22. n=170 1yr 0 esomeprazole + ASA vs 13.6% clopidogrel recurrent ulcer complications)
Bhatt DL, Scheiman J, Abraham NS, et al. **ACCF/ACG/AHA 2008 expert consensus document on reducing the gastrointestinal risks of antiplatelet therapy and NSAID** use: a report of the American College of Cardiology Foundation Task Force on Clinical Expert Consensus Documents. *J Am Coll Cardiol*. 2008; *Circulation*. 2008; DOI: DOI: 10.1161/CIRCULATIONAHA.108.191087. Available at: http://circ.ahajournals.org
American College of Cardiology Foundation Task Force on Expert Consensus Documents, , Abraham, Neena S., Hlatky, Mark A., Antman, Elliott M., Bhatt, Deepak L., et al. **ACCF/ACG/AHA 2010** Expert Consensus Document on the Concomitant Use of Proton **Pump Inhibitors and Thienopyridines**: A Focused Update of the ACCF/ACG/AHA 2008 Expert Consensus Document on Reducing the Gastrointestinal Risks of Antiplatelet Therapy and NSAID Use J Am Coll Cardiol 2010 0: j.jacc.2010.09.010 http://content.onlinejacc.org/cgi/reprint/j.jacc.2010.09.010v1.pdf
American College of Cardiology Foundation Task Force on Expert Consensus Documents, , Abraham, Neena S., Hlatky, Mark A., Antman, Elliott M., Bhatt, Deepak L., et al. ACCF/ACG/AHA **2010** Expert Consensus Document on the Concomitant Use of Proton Pump Inhibitors and Thienopyridines: A Focused Update of the ACCF/ACG/AHA 2008 Expert Consensus Document on Reducing the Gastrointestinal Risks of Antiplatelet Therapy and NSAID Use J Am Coll Cardiol 2010 0: j.jacc.2010.09.010
Hsu PI, Lai KH, Liu CP. Esomeprazole with Clopidogrel Reduces Peptic Ulcer Recurrence, Compared to Clopidogrel Alone, in Patients with Atherosclerosis. Gastroenterology. 2010 Dec 6. (n=165, 6months).
Luo JC, Huang KW, Leu HB, et al. Randomised clinical trial: **rabeprazole plus aspirin is not inferior to rabeprazole plus clopidogrel** for the healing of aspirin-related peptic ulcer. Aliment Pharmacol Ther. 2011 Sep;34(5):519-25.
53. Ridker PM, et al. A Randomized Trial of Low-Dose Aspirin in the Primary Prevention of Cardiovascular Disease in Women (**WHS**). N Engl J Med. 2005 Mar 7 pre release electronic;352. N Engl J Med 2005;352:1293-304.
(InfoPOEMs: Aspirin reduces the risk of stroke and transient ischemic attack in women but does not reduce the risk of myocardial infarction or cardiovascular death. The reduction in strokes over 10 years (number needed to treat = 444) must be balanced against an increase in serious gastrointestinal bleeds (number needed to treat to harm = 553). No change was seen in this large, long study regarding all-cause mortality. (LOE = 1b)) {Low dose Aspirin in the Primary Prevention of Cancer WHS study JAMA. 2005;294:47-55. Conclusions: Results from this large scale, long-term trial suggest that alternate day use of 100mg every other day for an average of 10yrs does not lower the risk of total, breast, colorectal, or other site-specific cancers. A protective effect on lung cancer or a benefit of higher doses of aspirin cannot be ruled out}
Kurth T, Barr RG, Gaziano JM, Buring J. Randomised Aspirin Assignment And Risk Of Adult-Onset Asthma In The Women's Health Study. (**WHS**) Thorax. 2008 Mar 13; [Epub ahead of print] In this large, randomised clinical trial of apparently healthy adult women, assignment of 100 mg of aspirin on alternate days reduced the relative risk of newly reported diagnosis of **asthma**.
54. Gage BF, van Walraven C, Pearce L, et al. Selecting patients with atrial fibrillation for anticoagulation: Stroke risk stratification in patients taking aspirin. Circulation 2004; 110:2287-92. (InfoPOEMs: Clinical decision rules, especially the well-validated Stroke Prevention in Atrial Fibrillation (SPAF) score, can help identify which groups of patients with atrial fibrillation are likely and unlikely to benefit from anticoagulation. (LOE = 1a).If the risk of stroke is low (< 2%), the harms of anticoagulation generally outweigh the benefits. If the risk of stroke is high (> 4%), the benefits of anticoagulation outweigh the risks for most pts. If the patient's stroke risk is in between both extremes, we have to look carefully at his or her risk for hemorrhage.)
55. Sabatine MS, et al. Addition of Clopidogrel to Aspirin and Fibrinolytic Therapy for Myocardial Infarction with ST-Segment Elevation (**CLARITY-TIMI 28**). N Engl J Med. 2005 Mar 9; [Epub] (N=3491,Groups: Plavix 300mg x1 then 75mg od (median **4 doses** given) until angiography vs placebo had 30 day mortality of less than 5%, age <75yr, excluded high bleeding risk pts, few CABG performed, thus select pts were studied, mechanism may be to prevent reocclusion) (InfoPOEMs: Adding clopidogrel to aspirin and fibrinolytic therapy during the first week in patients with ST-segment elevation myocardial infarction reduces the likelihood of recurrent myocardial infarction and ischemia leading to revascularization over a 30-day period (number needed to treat = 15). The short-term risk of major bleeding was low. This trial does not address how long patients should continue to take clopidogrel after the first week of treatment. (LOE = 1b)) {Sabatine MS, Cannon CP, Gibson CM, et al.; Clopidogrel as Adjunctive Reperfusion Therapy (CLARITY)-Thrombolysis in Myocardial Infarction (TIMI) 28 Investigators. Effect of clopidogrel pretreatment before percutaneous coronary intervention in patients with ST-elevation myocardial infarction treated with fibrinolytics: the **PCI-CLARITY** study. JAMA. 2005 Sep 14;294(10):1224-32. Epub 2005 Sep 4. CONCLUSIONS: Clopidogrel pretreatment significantly reduces the incidence of cardiovascular death or ischemic complications both before and after PCI and without a significant increase in major or minor bleeding. These data add further support to the early use of clopidogrel in STEMI and the strategy of routine clopidogrel pretreatment in patients undergoing PCI. (InfoPOEMs: Pretreatment with clopidogrel before percutaneous coronary intervention (PCI) reduces the risk of cardiovascular disease complications without increasing the risk of bleeding complications. This study only followed patients for 30 days after the intervention, so further long-term studies are needed before a general recommendation can be made. (LOE = 1b-)) } (Scirica BM, et al. The role of clopidogrel in early & sustained arterial patency after fibrinolysis for ST-segment elevation MI: the ECG CLARITY-TIMI 28 Study. J Am Coll Cardiol. 2006 Jul 4;48(1):37-42. Epub 2006Jun 12.)
56. Chen ZM, Jiang LX, Chen YP, et al. **COMMIT** (ClOpidogrel and Metoprolol in Myocardial Infarction Trial) collaborative group. Addition of clopidogrel to aspirin in 45,852 patients with acute myocardial infarction: randomised placebo-controlled trial. Lancet. 2005 Nov 5;366(9497):1607-21. COMMIT/CCS-2 trial (Mean age 61, n=45,852, <24hr since MI symptom onset, primary PCI or high risk bleeding were excluded, 54% rec'd thrombolysis, Plavix 75mg od + ASA162mg od vs ASA 162mg od for a mean of **15 days**, Death/MI/stroke 9.2 vs 10.1%, Death 7.5 vs 8.1%, Major Bleeding both equal ~0.6%, Minor bleeds 3.6 vs 3.1%) INTERPRETATION: In a wide range of patients with acute MI, adding clopidogrel 75 mg daily to aspirin and other standard treatments (such as fibrinolytic therapy) safely reduces mortality and major vascular events in hospital, and should be considered routinely.(InfoPOEMs: Patients with acute myocardial infarction treated with aspirin plus clopidogrel have better in-hospital or 28-day survival and fewer deaths, reinfarctions, or strokes than patients treated with aspirin alone. This study doesn't tell us if patients are better off 6 months to 1 year after their myocardial infarction. (LOE = 1b))
57. Chimowitz MI, Lynn MJ, Howlett-Smith H, et al.; Warfarin-Aspirin Symptomatic Intracranial Disease Trial Investigators. Comparison of warfarin and **aspirin** for symptomatic intracranial arterial stenosis. (**WASID**). N Engl J Med. 2005 Mar 31;352(13):1305-16.
(InfoPOEMs: Warfarin instead of aspirin causes 1 extra death every 2 years for patients with **intracranial arterial stenosis** and a recent stroke or transient ischemic attack. Given the risk and cost of the imaging studies done to diagnose intracranial arterial stenosis, one has to wonder whether we should just prescribe 650 mg aspirin twice a day for these patients and leave it at that. (LOE = 1b))
58. Dobkin BH. Rehabilitation after Stroke. N Engl J Med 2005;352:1677-85. (Langhorne P, Taylor G, Murray G, Dennis M, Anderson C, Bautz-Holter E, Dey P, Indredavik B, Mayo N, Power M, Rodgers H, Ronning OM, Rudd A, Suwanwela N, Widen-Holmqvist L,

Wolfe C. **Early supported discharge** services for stroke patients: a meta-analysis of individual patients' data. Lancet. 2005 Feb 5-11;365(9458):501-6.)

59. Siguret V, Gouin I, et al. Initiation of warfarin therapy in elderly medical inpatients: A safe and accurate regimen. Am J Med 2005; 118:137-42. ((InfoPOEMS: This algorithm, which starts with a lower dose than other algorithms, is effective in predicting the final dose of warfarin required by patients older than 70 years. (LOE = 2b) Here is the nomogram: Days 1, 2, 3 -- Give warfarin 4 mg Day 4 -- Check INR in the morning; according to the result, give the following dose (daily): 1.0 to < 1.3 = 5 mg, 1.3 to < 1.5 = 4 mg, 1.5 to < 1.7 = 3 mg, 1.7 to < 1.9 = 2 mg, 1.9 to < 2.5 =1mg, 2.5 or higher = Measure INR daily and hold warfarin until INR drops to < 2.5, then resume at 1 mg.)
60. Ergin A, Ergin N. Is thrombolytic therapy associated with increased mortality? Meta-analysis of randomized controlled trials. Arch Neurol 2005; 62:362-66. (InfoPOEMs: This meta-analysis suggests there is a small, but statistically insignificant, risk of death in patients with acute ischemic stroke receiving thrombolytics within either 3 or 6 hours, which is consistent with other meta-analyses. The available data are too limited to know if important differences exist between agents. (LOE = 1a-))
61. Zimarino M, Renda G, De Caterina R. Optimal duration of antiplatelet therapy in recipients of coronary drug-eluting stents. Drugs. 2005;65(6):725-32.
62. Weinberger J. Adverse effects and drug interactions of antithrombotic agents used in prevention of ischaemic stroke. Drugs. 2005;65(4):461-71.
63. Kyrle PA, Eichinger S. **Deep vein thrombosis**. Lancet. 2005 Mar 26;365(9465):1163-74. & Bates SM, Ginsberg JS. Clinical practice. Treatment of **deep-vein thrombosis**. N Engl J Med. 2004 Jul 15;351(3):268-77.
64. Nelson MR, Liew D, Bertram M, Vos T. Epidemiological modelling of routine use of low dose aspirin for the primary prevention of coronary heart disease and stroke in those aged >=70. BMJ. 2005 May 20; [Epub ahead of print]
65. Kerr CR, Humphries KH, Talajic M, et al. Progression to chronic atrial fibrillation after the initial diagnosis of paroxysmal atrial fibrillation: Results from the Canadian Registry of Atrial Fibrillation. Am Heart J 2005;149:489-96. (InfoPOEMs: After the first episode of paroxysmal atrial fibrillation, most patients (84.5%) will have at least one more episode of atrial fibrillation over the next 5 years. In this same period 24.7% of patients will develop chronic atrial fibrillation. (LOE = 1b))
66. Holbrook AM, Pereira JA, Labiris R, McDonald H, Douketis JD, Crowther M, Wells PS. Systematic overview of **warfarin and its drug and food interactions**. Arch Intern Med. 2005 May 23;165(10):1095-106.
67. Sherman DG, Kim SG, Boop BS, et al.; NHLBI AFFIRM Investigators. Occurrence & characteristics of stroke events in the Atrial Fibrillation Follow-up Investigation of Sinus Rhythm Management (**AFFIRM**). Arch Intern Med. 2005 May 23;165(10):1185-91.
68. Quiroz R, Kucher N, Zou KH, et al. Clinical validity of a negative computed tomography scan in patients with suspected pulmonary embolism. A systematic review. JAMA 2005; 293:2012-17. (InfoPOEMs: A negative computed tomography (CT) scan is as accurate as pulmonary angiography in ruling out suspected pulmonary embolism (PE). Clinicians should strongly consider using clinical decision rules to accurately assess the pretest probability of PE in a individual patient, and then interpret diagnostic tests in light of this probability. For example, a negative CT in a low-risk patient rules out PE, while a negative CT in a high-risk patient may require further confirmation. (LOE = 2a-))
69. Christiansen SC, Cannegieter SC, et al. Thrombophilia, clinical factors, and recurrent venous thrombotic events. JAMA 2005; 293:2352-61. (InfoPOEMs: The risk of recurrence after a first venous thrombotic event (VTE) is increased in men, patients whose initial event is idiopathic, and women using oral contraceptives after the initial VTE. This study found no increased risk for recurrence in patients with prothrombotic abnormalities. Testing for prothrombotic abnormalities should be considered only in patients with a recurrent VTE. (LOE = 1b-))
70. Perrier A, Roy PM, Sanchez O, et al. **Multidetector-row computed tomography** in suspected pulmonary embolism. N Engl J Med 2005; 352:1760-68. (InfoPOEMs: An algorithm that includes a careful, structured clinical assessment (D-dimer, lower extremity ultrasound, and multidetector-row computed tomography depending on risk status, and other testing as needed based on this initial assessment) provides a safe, and presumably cost-effective, evaluation for patients with suspected pulmonary embolism (PE). The authors argue that omitting the lower extremity ultrasound is a reasonable option given its low yield in this study, although further evaluation of that step is needed in subsequent studies. (LOE = 1a))
71. Witt DM, Sadler MA, Shanahan RL, Mazzoli G, Tillman DJ. Effect of a centralized clinical **pharmacy anticoagulation service** on the outcomes of anticoagulation therapy. Chest. 2005 May;127(5):1515-22.
72. Ost D, Tepper J, Mihara H, Lander O, Heinzer R, Fein A. **Duration of anticoagulation** following venous thromboembolism: a meta-analysis. JAMA. 2005 Aug 10;294(6):706-15. CONCLUSIONS: Patients who receive extended anticoagulation are protected from recurrent VTE while receiving long-term therapy. The clinical benefit is maintained after anticoagulation is discontinued, but the magnitude of the benefit is less pronounced. (InfoPOEMs: The optimal duration of anticoagulation following an initial venous thromboembolism (VTE) event is 6 months or more. The risk of a major bleeding event is most pronounced in the first month of treatment and the rate is similar to short-term (3 months or less) treatment. Since the magnitude of benefit appears to lessen beyond 6 months, physicians and patients should reassess individual risk/benefit profiles beyond this timeframe. (LOE = 1a))

Matchar David B., Jacobson Alan, Dolor Rowena, et al. for the **THINRS** Executive Committee and Site Investigators. Effect of **Home Testing of International Normalized Ratio** on Clinical Events**.** N Engl J Med 2010; 363:1608-1620.

73. Roy PM, Colombet I, Durieux P, Chatellier G, Sors H, Meyer G. Systematic review and meta-analysis of strategies for the **diagnosis of suspected pulmonary embolism**. BMJ. 2005 Jul 30;331(7511):259. (InfoPOEMs: Some tests are better at diagnosing pulmonary embolism (PE) and some are better at excluding it. To exclude PE in patients with a low likelihood of disease, use a lung scan, spiral computed tomography (CT) plus leg ultrasound, or D-dimer by ELISA. To diagnose PE in patients with a high likelihood of disease, use a ventilation perfusion scan, spiral CT, or leg ultrasound. (LOE = 1a))
74. Drummond AE, Pearson B, Lincoln NB, Berman P. Ten year follow-up of a randomised controlled trial of care in a stroke **rehabilitation unit**. BMJ. 2005 Aug 10; [Epub ahead of print]
75. Cook NR, Lee IM, Gaziano JM, Gordon D, Ridker PM, Manson JE, Hennekens CH, Buring JE. Low-dose **aspirin** in the primary prevention of **cancer**: the Women's Health Study (WHS) : a randomized controlled trial. JAMA. 2005 Jul 6;294(1):47-55. Results from this large-scale, long-term trial suggest that alternate day use of low-dose aspirin (100 mg) for an average 10 years of treatment does not lower risk of total, breast, colorectal, or other site-specific cancers. A protective effect on lung cancer or a benefit of higher doses of aspirin cannot be ruled out. (InfoPOEMs: Low-dose aspirin does not reduce the risk of lung, breast, colorectal, or other site cancer in healthy women 45 years and older. There may be a protective effect on reducing lung cancer mortality, but overall mortality is not reduced. (LOE = 1b))
76. Andrew T. Chan, MD, MPH; Edward L. et al. Long-term Use of Aspirin and Nonsteroidal Anti-inflammatory Drugs and Risk of Colorectal Cancer JAMA. 2005;294:914-923. CONCLUSIONS: Regular, long-term aspirin use reduces risk of colorectal cancer. Nonaspirin NSAIDs appear to have a similar effect. However, a significant benefit of aspirin is not apparent until more than a decade of use, with maximal risk reduction at doses greater than 14 tablets per week. These results suggest that optimal chemoprevention for colorectal cancer requires long-term use of aspirin doses substantially higher than those recommended for prevention of cardiovascular disease, but the dose-related risk of gastrointestinal bleeding must also be considered. (InfoPOEMs: Regular use of aspirin and other nonsteroidal anti-inflammatory drugs (NSAIDs), especially more than 14 doses per week for at least 10 years, reduces the risk of colon cancer while also increasing the risk of a major gastrointestinal bleeding event. All-cause mortality is not affected by regular use. We need additional methods (gene testing?) to determine who is at high risk of colorectal cancer before making specific recommendations for prevention. (LOE = 2b))
77. Goodacre S, Sutton AJ, Sampson FC. Meta-analysis: The value of clinical assessment in the diagnosis of deep venous thrombosis. Ann Intern Med. 2005 Jul 19;143(2):129-39. CONCLUSION: Individual clinical features are of limited value in diagnosing DVT. Overall assessment of clinical probability by using the Wells score is more useful. (InfoPOEMs: With the exception of either a previous deep vein thrombosis (DVT) or a previous malignancy, no other clinical feature effectively increases or decreases the odds of having a DVT. The Wells Clinical Probability Score, which combines several clinical features, is much more effective. (LOE = 1a))
78. Torn M, Bollen WL, van der Meer FJ, van der Wall EE, Rosendaal FR. **Risks** of **oral anticoagulant** therapy with increasing **age**. Arch Intern Med. 2005 Jul 11;165(13):1527-32.
79. Tapson VF, Hyers TM, Waldo AL, et al.; NABOR (National Anticoagulation Benchmark and Outcomes Report) Steering Committee. Antithrombotic therapy practices in US hospitals in an era of practice guidelines. Arch Intern Med. 2005 Jul 11;165(13):1458-64.
80. Rothwell PM, Giles MF, Flossmann E, Lovelock CE, Redgrave JN, Warlow CP, Mehta Z. A simple score (ABCD) to identify individuals at high early risk of stroke after transient ischaemic attack. Lancet. 2005 Jul 2;366(9479):29-36. (InfoPOEMs: Easy-to-assess clinical and demographic variables can be used to predict which patients with transient ischemic attacks (TIAs) are at greatest risk of stroke in the subsequent week. (LOE = 1b-))
Sciolla R, Melis F; SINPAC Group. Rapid identification of high-risk transient ischemic attacks: prospective validation of the ABCD score. Stroke. 2008 Feb;39(2):297-302. Epub 2008 Jan 3.
81. van Wijk I, Kappelle LJ, van Gijn J, et al.; LiLAC study gp. Long-term survival and vascular event risk after transient ischaemic attack or minor ischaemic stroke: a cohort study. Lancet. 2005 Jul 7;365(9477):2098-104. (48% survive 10yrs free of another vaxcular event)
82. Hankey GJ. Redefining risks after TIA and minor ischaemic stroke. Lancet. 2005 Jul 7;365(9477):2065-6. (Looking forward from the time of a TIA, the risk of a stroke is as high as 5% within the first 48hr and 12% within the first 30 days.)
Shah KH, Metz HA, Edlow JA. Clinical prediction rules to stratify short-term risk of stroke among patients diagnosed in the emergency department with a transient ischemic attack. Ann Emerg Med. 2009 May;53(5):662-73.
83. Schrader J, Luders S, et al; **MOSES** Study Group. Morbidity and Mortality After Stroke, **Eprosartan** Compared with Nitrendipine for Secondary Prevention: principal results of a prospective randomized controlled study (MOSES). Stroke. 2005 Jun;36(6):1218-26.
84. Drummond AE, Pearson B, Lincoln NB, Berman P. Ten year follow-up of a randomised controlled trial of care in a stroke rehabilitation unit. BMJ. 2005 Sep 3;331(7515):491-2. Epub 2005 Aug 10.
85. Rothwell PM, Warlow CP. Timing of **TIAs** preceding stroke: time window for prevention is very short. Neurology. 2005 Mar 8;64(5):817-20.
86. Duncan PW, Zorowitz R, Bates B, Choi JY, Glasberg JJ, Graham GD, Katz RC, Lamberty K, Reker D. Management of Adult Stroke **Rehabilitation Care**: a clinical practice guideline. Stroke. 2005 Sep;36(9):e100-43.
87. Wolak A, Amit G, Cafri C, Gilutz H, Ilia R, Zahger D. Increased long term rates of stent thrombosis and mortality in patients given clopidogrel as compared to **ticlopidine** following coronary stent implantation. Int J Cardiol. 2005 Sep 1;103(3):293-7.
88. Hermida RC, Ayala DE, Calvo C, Lopez JE. Aspirin administered at bedtime, but not on awakening, has an effect on ambulatory blood pressure in hypertensive patients. J Am Coll Cardiol. 2005 Sep 20;46(6):975-83.
89. Andreotti F, Testa L, Biondi-Zoccai G, Crea F. Aspirin plus warfarin compared to aspirin alone after acute coronary syndromes: an updated and comprehensive meta-analysis of 25 307 patients. Eur Heart J. 2005 Sep 5; [Epub ahead of print] CONCLUSION: For patients recovering from ACS, a combined strategy of A + W at INR values of 2-3 doubles the risk of MB, but is nonetheless superior to aspirin alone in preventing MAE. Whether this combined regimen is also superior to a 'double' anti-platelet strategy or to newer evolving treatments warrants further investigation.
90. Bonaa KH for the NORVIT Study Group. **NORVIT**: Randomised trial of homocysteine-lowering with B vitamins for secondary prevention of cardiovascular disease after acute myocardial infarction. European Society of Cardiology, Sept 3-7, 2005, Abstract 1334.
91. Rothberg MB, Celestin C, Fiore LD, Lawler E, Cook JR. **Warfarin plus aspirin after myocardial infarction** or the acute coronary syndrome: meta-analysis with estimates of risk and benefit. Ann Intern Med. 2005 Aug 16;143(4):241-50. Summary for patients in: Ann Intern Med. 2005 Aug 16;143(4):I14. (InfoPOEMs: Adding warfarin to aspirin prophylaxis does not affect overall death rates, though the combination decreases subsequent myocardial infarction risk (number needed to treat [NNT] = 56) and, to a lesser degree, ischemic stroke risk (NNT = 221). As one might expect, major bleeding episodes occur more often with the added warfarin, though only in a small number of patients (1.5% vs 0.56%). (LOE = 1a))
92. Fitzmaurice DA, Murray ET, McCahon D, et al. **Self management of oral anticoagulation**: randomised trial. BMJ. 2005 Nov 5;331(7524):1057. Epub 2005 Oct 10. (Menendez-Jandula B, Souto JC, et al. Comparing **self-management** of oral anticoagulant therapy with clinic management: a randomized trial. Ann Intern Med. 2005 Jan 4;142(1):1-10. (InfoPOEMs: Although many patients will not wish to do so, home monitoring of anticoagulation status and subsequent self-adjustment of dosing is safe and effective. Self-monitoring of anticoagulation is a bit trickier than home blood glucose monitoring, and approximately 30% of patients dropped out during the training period. The testing equipment is expensive ($1300 US), a cost-effectiveness analysis has not been done, and there is no evidence that it leads to better clinical outcomes (ie, less bleeding and less recurrent embolic events) . (LOE = 1b))
Garcia-Alamino JM, Ward AM, Alonso-Coello P, Perera R, Bankhead C, Fitzmaurice D, Heneghan CJ. Self-monitoring and self-management of oral anticoagulation. Cochrane Database of Systematic Reviews 2010, Issue 4. Art. No.: CD003839.
Stafford Leanne, Peterson Gregory M, Bereznicki Luke RE, et al..Clinical Outcomes of a Collaborative, Home-Based Postdischarge **Warfarin Management Service** (March). Articles Ahead of Print published 8 March 2011, DOI 10.1345/aph.1P617.
Bloomfield HE, Krause A, Greer N, Taylor BC, MacDonald R, Rutks I, et al. Meta-analysis: effect of patient **self-testing and self-management of longterm anticoagulation** on major clinical outcomes. Ann Intern Med. 2011;154: 472-82.
Grunau BE, Wiens MO, Harder KK. Patient **self-management of warfarin** therapy: Pragmatic feasibility study in Canadian primary care. Can Fam Physician. 2011 Aug;57(8):e292-8.
Cho HJ, On YK, Bang OY, et al. Development and Comparison of a Warfarin-Dosing **Algorithm** for Korean Patients With Atrial Fibrillation. Clin Ther. 2011 Oct 5.
Heneghan C, Ward, A, Perera R, and The Self-Monitoring Trialist Collaboration. **Self-monitoring** of oral anticoagulation: systematic review and meta-analysis of individual patient data. Lancet 2011; published online Dec 1.
Carlquist JF, Anderson JL. Using **pharmacogenetics in real time to guide warfarin** initiation: a clinician update. Circulation. 2011 Dec 6;124(23):2554-9.
Valentin II, Vazquez J, Rivera-Miranda G, et al. Prediction of Warfarin Dose Reductions in Puerto Rican Patients, Based on Combinatorial **CYP2C9 and VKORC1 Genotypes** (February). Ann Pharmacother. 2012 Jan 24.
Horne BD, Lenzini PA, Wadelius M, et al. **Pharmacogenetic warfarin** dose refinements remain significantly influenced by genetic factors after one week of therapy. Thromb Haemost 2012; 107:232-240.
Anderson JL, Horne BD, Stevens SM, et al. A randomized and clinical effectiveness trial comparing two **pharmacogenetic algorithms** and standard care for individualizing warfarin dosing (**Coumagen-II**). Circulation. 2012;125:1997–2005.
Bussey HI, Bussey M. Warfarin management: international normalized ratio self-testing and warfarin self-dosing. Circulation. 2012 Jul 31;126(5):e52-4.
Tse G, Gong M, Li G, et al. Genotype-guided warfarin dosing vs. conventional dosing strategies: a systematic review and meta-analysis of randomized controlled trials. Br J Clin Pharmacol. 2018 Apr 28.
93. ACTIVE Writing Group on behalf of the ACTIVE Investigators; Connolly S, Pogue J, Hart R, Pfeffer M, Hohnloser S, Chrolavicius S, Pfeffer M, Hohnloser S, Yusuf S. Clopidogrel plus aspirin versus oral anticoagulation for atrial fibrillation in the Atrial fibrillation Clopidogrel Trial with Irbesartan for prevention of Vascular Events (**ACTIVE W**): a randomised controlled trial. Lancet. 2006 Jun 10;367(9526):1903-12. There were 165 primary events in patients on oral anticoagulation therapy (**annual risk 3.93%**) and 234 in those on clopidogrel plus aspirin (**annual risk 5.60%**; relative risk 1.44 (1.18-1.76; p=0.0003). Patients on oral anticoagulation therapy who were already receiving this treatment at study entry had a trend towards a greater reduction in vascular events (relative risk 1.50, 95% CI 1.19-1.89) and a significantly (p=0.03 for interaction) **lower risk of major bleeding with oral anticoagulation** therapy (**2.2 vs 2.4% per year**) (1.30; 0.94-1.79) than patients not on this treatment at study entry (1.27, 0.85-1.89 and 0.59, 0.32-1.08, respectively). (InfoPOEMs: Warfarin is superior to the combination of clopidogrel (Plavix) plus aspirin in

preventing strokes and systemic emboli in high-risk patients with atrial fibrillation. (LOE = 2b)) Healey JS, Hart RG, Pogue J, et al. Risks and Benefits of Oral Anticoagulation Compared With Clopidogrel Plus Aspirin in Patients With Atrial Fibrillation According to Stroke Risk. The Atrial Fibrillation Clopidogrel Trial With Irbesartan for Prevention of Vascular Events (ACTIVE-W). Stroke. 2008 Mar 6. In this clinical trial, patients with a CHADS2=1 had a low risk of stroke, yet still derived a modest (<1% per year) but statistically significant absolute reduction in stroke with OAC and had low rates of major hemorrhage on OAC.
De Caterina R, Connolly SJ, Pogue J, Chrolavicius S, Budaj A, Morais J, Renda G, Yusuf S; on behalf of the ACTIVE Investigators. Mortality predictors and effects of antithrombotic therapies in atrial fibrillation: insights from ACTIVE-W. Eur Heart J. 2010 Aug 4. Non-fatal strokes increased mortality in ACTIVE-W, but non-disabling strokes did not. Among major bleeding events, only those also classified as severe increased mortality. Future research should emphasize the prevention of disabling strokes and severe bleeds and place less emphasis on non-disabling stroke or major bleeds that are not severe.
EAFT (European Atrial Fibrillation Trial) Study Group. Secondary prevention in non-rheumatic atrial fi brillation after transient ischaemic attack or minor stroke. Lancet 1993; 342: 1255–62.
Stroke Prevention in Atrial Fibrillation (**SPAF**) Investigators. Adjusted-dose warfarin versus low-intensity, fi xed-dose warfarin plus aspirin for high-risk patients with atrial fi brillation: Stroke Prevention in Atrial Fibrillation III randomised clinical trial. Lancet 1996; 348: 633–38.
94. von Beckerath N, Taubert D, et al.. Absorption, metabolization, and antiplatelet effects of 300-, 600-, and 900-mg loading doses of clopidogrel: results of the **ISAR-CHOICE** (Intracoronary Stenting and Antithrombotic Regimen: Choose Between 3 High Oral Doses for Immediate Clopidogrel Effect) Trial. Circulation. 2005 Nov 8;112(19):2946-50. Epub 2005 Oct 31. (Montalescot G, et al.; **ALBION** Trial Investigators. A randomized comparison of high clopidogrel loading doses in patients with non-ST-segment elevation acute coronary syndromes: the ALBION (Assessment of the Best Loading Dose of Clopidogrel to Blunt Platelet Activation, Inflammation and Ongoing Necrosis) trial. J Am Coll Cardiol. 2006 Sep 5;48(5):931-8. Epub 2006 Aug 17.)
King SB, Smith SC, Hirshfeld JW, et al. **2007** focused update of the ACC/AHA/SCAI 2005 Guideline Update for **Percutaneous Coronary Intervention**: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines: (2007 Writing Group to Review New Evidence and Update the 2005 ACC/AHA/SCAI Guideline Update for Percutaneous Coronary Intervention). Circulation 2007; DOI: 10.1161/CIRCULATIONAHA.107.188208. http://circ.ahajournals.org.
American College of Cardiology Foundation, , American Heart Association Task Force on Practice Guidelines, , Society for Cardiovascular Angiography and Interventions, , Levine, Glenn N., Bates, Eric R., et al.
2011 ACCF/AHA/SCAI Guideline for Percutaneous Coronary Intervention: Executive Summary. J Am Coll Cardiol 2011 0: j.jacc.2011.08.006. http://content.onlinejacc.org/cgi/reprint/j.jacc.2011.08.006v1.pdf
American College of Cardiology Foundation, , American Heart Association Task Force on Practice Guidelines, , American Association for Thoracic Surgery, , Society of Cardiovascular Anesthesiologists, , Society of Thoracic Surgeons, Hillis, L. David, Smith, Peter K., Anderson, Jeffrey L., et al. **2011 ACCF/AHA Guideline for Coronary Artery Bypass Graft Surgery**: Executive Summary. J Am Coll Cardiol 2011 0: j.jacc.2011.08.008. http://content.onlinejacc.org/cgi/reprint/j.jacc.2011.08.008v1.pdf
95. Aujesky D, Smith KJ, Cornuz J, Roberts MS. **Cost-effectiveness of low-molecular-weight heparin** for treatment of pulmonary embolism. Chest. 2005 Sep;128(3):1601-10.
95. Foerster V, et al. **CT and MRI** for selected clinical disorders: A systematic review of clinical systematic reviews Oct/05 https://www.ccohta.ca/publications/pdf/322_ctmri_tr_e.pdf
96. James AH, et al. Incidence & risk factors for stroke in **pregnancy** and the puerperium. Obstet Gynecol. 2005 Sep;106(3):509-16. (InfoPOEMs: Hospitalization with a diagnosis of stroke in pregnancy or puerperium occurs in 34 per 100,000 deliveries in the United States. It occurs in more that 50 per 100,000 in African American women and women older than 35 years. The most common comorbid conditions associated with increased risk are migraine headache and hypertension (including gestational hypertension). (LOE = 2c))
97. Doukas G, Samani NJ, Alexiou C, Oc M, Chin DT, Stafford PG, Ng LL, Spyt TJ. Left **atrial radiofrequency ablation during mitral valve surgery** for continuous atrial fibrillation: a randomized controlled trial. JAMA. 2005 Nov 9;294(18):2323-9.
98. Heit JA, Kobbervig CE, James AH, Petterson TM, Bailey KR, Melton LJ 3rd. Trends in the incidence of venous **thromboembolism during pregnancy** or postpartum: a 30-year population-based study. Ann Intern Med. 2005 Nov 15;143(10):697-706.
99. Ballantyne CM, Hoogeveen RC, Bang H, et al. **Lipoprotein-Associated Phospholipase A2**, High-Sensitivity **C-Reactive Protein**, and Risk for Incident Ischemic Stroke in Middle-aged Men and Women in the Atherosclerosis Risk in Communities (ARIC) Study. Arch Intern Med. 2005 Nov 28;165(21):2479-84.
101. Patrono C et al. Low-Dose **Aspirin** for the Prevention of Atherothrombosis. N Engl J Med 2005;353:2373-83.
102. Capone ML, Sciulli MG, Tacconelli S, Grana M, Ricciotti E, Renda G, Di Gregorio P, Merciaro G, Patrignani P. Pharmacodynamic interaction of **naproxen with low-dose aspirin** in healthy subjects. J Am Coll Cardiol. 2005 Apr 19;45(8):1295-301.
103. Catella-Lawson F, Reilly MP, Kapoor SC, Cucchiara AJ, DeMarco S, Tournier B, Vyas SN, FitzGerald GA. **Cyclooxygenase inhibitors** and the antiplatelet effects of **aspirin**. N Engl J Med. 2001 Dec 20;345(25):1809-17.
104. Corman SL, Fedutes BA, Ansani NT. Impact of **nonsteroidal antiinflammatory drugs** on the cardioprotective effects of **aspirin**. Ann Pharmacother. 2005 Jun;39(6):1073-9. Epub 2005 May 3.
105. Teo KK, Yusuf S, Pfeffer M, et al.; ACE Inhibitors Collaborative Group. Effects of long-term treatment with angiotensin-converting-enzyme inhibitors (**ACEI**) in the presence or absence of **aspirin**: a systematic review. Lancet. 2002 Oct 5;360(9339):1037-43. Erratum in: Lancet 2003 Jan 4;361(9351):90.
106. Latini R, Tognoni G, Maggioni AP, et al. Clinical effects of early angiotensin-converting enzyme inhibitor (**ACEI**) treatment for acute myocardial infarction are similar in the presence and absence of **aspirin**: systematic overview of individual data from 96,712 randomized patients. Angiotensin-converting Enzyme Inhibitor Myocardial Infarction Collaborative Group. J Am Coll Cardiol. 2000 Jun;35(7):1801-7.
107. PREPIC Study Group. Eight-year follow-up of patients with **permanent vena cava filters** in the prevention of pulmonary embolism: the PREPIC (Prevention du Risque d'Embolie Pulmonaire par Interruption Cave) randomized study. Circulation.2005Jul 19;112(3): 416-22. Epub 2005 Jul 11. (InfoPOEMs: In a fairly high-risk group of patients with venous thromboembolism (VTE), vena cava filters reduce the risk of pulmonary embolism (PE), increase the risk of deep vein thrombosis (DVT), and do not alter the risk of death.
However, this group was not typical of the group that is usually given these filters in clinical practice. (LOE = 1b))
108. Poole KE, Loveridge N, Barker PJ, et al. Reduced **Vitamin D** in Acute Stroke. Stroke. 2005 Dec 1; [Epub ahead of print]
109. Chambers B, Donnan G, Chambers B. **Carotid endarterectomy** for asymptomatic carotid stenosis. Cochrane Database Syst Rev. 2005 Oct 19;(4):CD001923. AUTHORS' CONCLUSIONS: Despite about a 3% perioperative stroke or death rate, CEA for asymptomatic carotid stenosis reduces the risk of ipsilateral stroke, and any stroke, by approximately 30% over three years. However, the absolute risk reduction is small (approximately 1% per annum over the first few years of follow up in the two largest and most recent trials) but it could be higher with longer follow up.
110. Mahaffey KW, et al. **SYNERGY** Trial Investigators. High-risk patients with acute coronary syndromes treated with low-molecular-weight or unfractionated heparin: outcomes at 6 months and 1 year in the SYNERGY trial. JAMA. 2005 Nov 23;294(20):2594-600. (InfoPOEMs: Low-molecular-weight heparin (enoxaparin) is no more effective than unfractionated heparin in the treatment of patients with acute coronary syndromes (ACS). (LOE = 1b-)) (Ferguson JJ, et al. SYNERGY Trial Investigators. Enoxaparin vs unfractionated heparin in high-risk patients with non-ST-segment elevation acute coronary syndromes managed with an intended early invasive strategy: primary results of the SYNERGY randomized trial. JAMA. 2004 Jul 7;292(1):45-54.)
111. Martel N, Lee J, Wells PS. Risk for **heparin-induced thrombocytopenia** with unfractionated and low-molecular-weight heparin thromboprophylaxis: a meta-analysis. Blood. 2005 Oct 15;106(8):2710-5. Epub 2005 Jun 28. The inverse variance-weighted average that determined the absolute risk for HIT with LMWH was 0.2%, and with UFH the risk was 2.6%. Most studies were of patients after orthopedic surgery.
112. Fang MC, Chang Y, Hylek EM, Rosand J, Greenberg SM, Go AS, Singer DE. Advanced age, anticoagulation intensity, and risk for intracranial hemorrhage among patients taking warfarin for atrial fibrillation. Ann Intern Med. 2004 Nov 16;141(10):745-52.
113. Witt BJ, Brown RD Jr, Jacobsen SJ, et al. A community-based study of stroke incidence after myocardial infarction. Ann Intern Med. 2005 Dec 6;143(11):785-92.
114. Albers GW, Diener HC, Frison L, et al.; SPORTIF Executive Steering Committee for the SPORTIF V Investigators. **Ximelagatran** vs warfarin for stroke prevention in patients with nonvalvular atrial fibrillation: a randomized trial. JAMA. 2005 Feb 9;293(6):690-8.
115. McKeown PP, et al.; American College of Chest Physicians. Executive summary: American College of Chest Physicians guidelines for the prevention and management of postoperative atrial fibrillation after cardiac surgery. Chest. 2005 Aug;128(2 Suppl):1S-5S.
116. Alexander KP, Chen AY, Roe MT, et al.; CRUSADE Investigators. **Excess dosing of antiplatelet and antithrombin agents** in the treatment of non-ST-segment elevation acute coronary syndromes. JAMA. 2005 Dec 28;294(24):3108-16.
117. Eikelboom JW, et al. Unfractionated & low-molecular-weight heparin as adjuncts to thrombolysis in aspirin-treated patients with ST-elevation acute MI: a meta-analysis of the randomized trials. Circulation. 2005 Dec 20;112(25):3855-67. Epub 2005 Dec 12.
118. Hayashino Y, Goto M, Noguchi Y, Fukui T. Ventilation-perfusion scanning and helical CT in suspected pulmonary embolism: meta-analysis of diagnostic performance. Radiology. 2005 Mar;234(3):740-8.
119. van Belle A, et al. Writing Group for the Christopher Study Investigators. Effectiveness of managing suspected **pulmonary embolism** using an **algorithm** combining clinical probability, D-dimer testing, & computed tomography. JAMA. 2006 Jan 11;295(2):172-9.
120. Roderick P, et al. Towards **evidence-based guidelines** for the prevention of venous thromboembolism: systematic reviews of mechanical, oral anticoagulation, dextran & regional anaesthesia as thromboprophylaxis. Health Technol Assess. 2005 Dec;9(49):1-94.
121. Choudhry NK, Anderson GM, Laupacis A, Ross-Degnan D, Normand SL, Soumerai SB. Impact of **adverse events on prescribing warfarin** in patients with atrial fibrillation: matched pair analysis. BMJ. 2006 Jan 10; [Epub ahead of print]
122. Berger JS, et al. **Aspirin for the primary** prevention of cardiovascular events in women and men: a sex-specific meta-analysis of randomized controlled trials. JAMA. 2006 Jan 18;295(3):306-13. CONCLUSIONS: For women and men, aspirin therapy reduced the risk of a composite of cardiovascular events due to its effect on reducing the risk of ischemic stroke in women and MI in men. Aspirin significantly increased the risk of bleeding to a similar degree among women and men. (InfoPOEMs: Primary prevention with aspirin reduces the risk of adverse cardiovascular events in both women and men. In particular, aspirin reduces the risk of stroke in women and the risk of myocardial infarction (MI) in men. The risk of major bleeding is significantly increased with regular aspirin therapy in both sexes and overall mortality is unchanged. Patients and their clinicians should weigh their independent risks and benefits before deciding on regular aspirin use. (LOE = 1a))
123. Gage BF, Birman-Deych E, Radford MJ, Nilasena DS, Binder EF. Risk of osteoporotic **fracture** in elderly patients taking warfarin: results from the National Registry of Atrial Fibrillation 2. Arch Intern Med. 2006 Jan 23;166(2):241-6.
124. Aujesky D, Obrosky DS, Stone RA, Auble TE, Perrier A, Cornuz J, Roy PM, Fine MJ. A **prediction rule** to identify low-risk patients with pulmonary embolism. Arch Intern Med. 2006 Jan 23;166(2):169-75.
125. Blann AD, Lip GY. Venous thromboembolism. BMJ. 2006 Jan 28;332(7535):215-9.
126. Sacco RL, et al. Guidelines for **Prevention of Stroke in Patients With Ischemic Stroke or Transient Ischemic Attack**: A Statement for Healthcare Professionals From the **American Heart Association/American Stroke Association** Council on Stroke: Co-Sponsored by the Council on Cardiovascular Radiology and Intervention: The American Academy of Neurology affirms the value of this guideline. Stroke. 2006 Feb;37(2):577-617. http://stroke.ahajournals.org/cgi/reprint/37/2/577
Adams RJ, Albers G, Alberts MJ, Benavente O, Furie K, Goldstein LB, Gorelick P, Halperin J, Harbaugh R, Johnston SC, Katzan I, Kelly-Hayes M, Kenton EJ, Marks M, Sacco RL, Schwamm LH, American Heart Association, American Stroke Association. Update to the AHA/ASA recommendations for the prevention of stroke in patients with stroke and transient ischemic attack. Stroke 2008 May;39(5):1647-52. http://stroke.ahajournals.org/cgi/reprint/39/5/1647
127. Touze E, Varenne O, Chatellier G, et al. Risk of myocardial infarction and vascular death after transient ischemic attack and ischemic stroke: a systematic review and meta-analysis. Stroke. 2005 Dec;36(12):2748-55. Epub 2005 Oct 27. (InfoPOEMs: Following a stroke or transient ischemic attack (TIA), the annual rate of nonstroke vascular **death and myocardial infarction (MI) is approximately 2% per year**. This information can be used to inform patients about the clinical course of their disease. (LOE = 1a-))
128. **Dalhousie** University Academic Detailing Service: Acute Coronary SyndromeJan 2006 http://cme.medicine.dal.ca/files/clop%20handout.pdf
129. Rodger MA, et al. The bedside investigation of pulmonary embolism diagnosis study: a double-blind randomized controlled trial comparing combinations of 3 bedside tests vs ventilation-perfusion scan for the initial investigation of suspected pulmonary embolism. Arch Intern Med. 2006 Jan 23;166(2):181-7.
130. Lim W, Crowther MA, et al. Management of antiphospholipid antibody syndrome: a systematic review. JAMA. 2006 Mar 1;295(9):1050-7. (InfoPOEMs: Patients who test positive for antiphospholipid antibodies are at an increased risk of thrombotic events. Similarly afflicted pregnant women are at an increased risk of fetal loss. Moderate-intensity anticoagulation with warfarin (target international normalized ratio (INR) = 2.0 - 3.0) prevents recurrent venous thrombosis. The optimal management of other thrombotic aspects of patients with antiphospholipid antibodies remains uncertain. (LOE = 1a-))
Cohen Danielle, Berger Stefan P, Steup-Beekman Gerda M et al., Diagnosis and management of the **antiphospholipid syndrome**. BMJ 2010;340
Ruiz-Irastorza Guillermo, Crowther Mark, Branch Ware, et al. **Antiphospholipid syndrome**, The Lancet, In Press, Corrected Proof, Available online 6 September 2010, ISSN 0140-6736, DOI: 10.1016/S0140-6736(10)60709-X.
131 Bhatt DL, Fox KA, Hacke W, et al. Clopidogrel and Aspirin versus Aspirin Alone for the Prevention of Atherothrombotic Events. N Engl J Med. 2006 Mar 12; (**Charisma**) [Epub ahead of print] (InfoPOEMs: The use of the combination of clopidogrel (Plavix) and aspirin should be limited to carefully defined groups of patients with acute coronary syndromes. It is not recommended for the broader group of patients with coronary disease, cerebrovascular disease, or multiple risk factors such as diabetes, hyperlipidemia, and hypertension. (LOE = 1b)) Wang TH, Bhatt DL, Fox KA, Steinhubl SR, Brennan DM, Hacke W, Mak KH, Pearson TA, Boden WE, Steg PG, Flather MD, Montalescot G, Topol EJ; on behalf of the CHARISMA Investigators. An analysis of mortality rates with dual-antiplatelet therapy in the primary prevention population of the CHARISMA trial. Eur Heart J. 2007 Aug 2; [Epub ahead of print] These findings do not support the use of dual-antiplatelet therapy with clopidogrel and aspirin in a primary prevention population. In this subgroup analysis, CV death occurred more frequently than anticipated.
Steinhubl SR, Bhatt DL, Brennan DM, et al. Aspirin to prevent cardiovascular disease: the association of aspirin dose and clopidogrel with thrombosis and bleeding. (Charisma) Ann Intern Med 2009; 150:379-386.
Dasgupta A, Steinhubl SR, Bhatt DL, et al.; CHARISMA Investigators. Clinical outcomes of patients with diabetic nephropathy randomized to clopidogrel plus aspirin versus aspirin alone (a post hoc analysis of the clopidogrel for high atherothrombotic risk and ischemic stabilization, management, and avoidance [CHARISMA] trial). Am J Cardiol. 2009 May 15;103(10):1359-63. Epub 2009 Apr 1
Berger PB, Bhatt DL, Fuster V, et al. for the CHARISMA Investigators. Bleeding Complications With Dual Antiplatelet Therapy Among Patients With Stable Vascular Disease or Risk Factors for Vascular Disease: Results From the Clopidogrel for High Atherothrombotic Risk and Ischemic Stabilization, Management, and

Avoidance (CHARISMA) Trial. Circulation. 2010 Jun 15;121(23):2575-2583.
Hankey GJ, Hacke W, Easton JD, et al. on behalf of the CHARISMA Trial Investigators. Effect of Clopidogrel on the Rate and Functional Severity of Stroke Among High Vascular Risk Patients. A Prespecified Substudy of the Clopidogrel for High Atherothrombotic Risk and Ischemic Stabilization, Management and Avoidance (CHARISMA) Trial. Stroke. 2010 Jul 1.

132. Bonaa KH, Njolstad I, Ueland PM, et al. Homocysteine Lowering and Cardiovascular Events after Acute Myocardial Infarction. (**NORVIT**) N Engl J Med. 2006 Mar 12; [Epub ahead of print]
Ebbing Marta; Bonaa Kaare Harald; Nygard Ottar; et al. Cancer Incidence and Mortality After Treatment With Folic Acid and Vitamin B12 (Norvit & Wenbit). JAMA. 2009;302(19):2119-2126.
Langan RC, Zawistoski KJ. Update on **Vitamin B12 Deficiency**. Am Fam Physician. 2011 Jun 15;83(12):1425-1430.
133. Lonn E, Yusuf S, Arnold MJ, et al.; Heart Outcomes Prevention Evaluation **(HOPE) 2** Investigators. **Homocysteine** lowering with folic acid and B vitamins in vascular disease. N Engl J Med. 2006 Apr 13;354(15):1567-77. Epub 2006 Mar 12. (InfoPOEMs: Supplementation with folic acid and B vitamins is ineffective for adults 55 years and older with known cardiovascular disease (CVD) or diabetes. A second report in the same issue found that similar supplementation in patients with a recent acute myocardial infarction was not helpful and may actually increase the risk of a bad cardiovascular outcome (relative risk = 1.22; 95% CI, 1.0 - 1.5). (LOE = 1b))
134. Choi-Kwon S, Han SW, Kwon SU, Kang DW, Choi JM, Kim JS. Fluoxetine treatment in poststroke depression, emotional incontinence, and anger proneness: a double-blind, placebo-controlled study.Stroke. 2006 Jan;37(1):156-61. Epub 2005 Nov 23.
135. Yusuf S, et al.; Fifth Organization to Assess Strategies in Acute Ischemic Syndromes Investigators. Comparison of fondaparinux and enoxaparin in acute coronary syndromes. N Engl J Med. 2006 Apr 6;354(14):1464-76. Epub 2006 Mar 14.
Comparison of Fondaparinux and Enoxaparin in Acute Coronary Syndromes. (OASIS-5) N Engl J Med. 2006 Mar 14; [Epub ahead of print] Conclusions Fondaparinux is similar to enoxaparin in reducing the risk of ischemic events at nine days, but it substantially reduces major bleeding and improves long term mortality and morbidity. (InfoPOEMs: **Fondaparinux** is a safer alternative to enoxaparin in patients with acute coronary syndrome (ACS), and has slightly better long-term efficacy, as well. (LOE = 1b))
136. Effects of Fondaparinux on Mortality and Reinfarction in Patients With Acute ST-Segment Elevation Myocardial Infarction: The **OASIS-6** Randomized Trial. JAMA. 2006 Mar 14; [Epub ahead of print] CONCLUSION: In patients with STEMI, particularly those not undergoing primary percutaneous coronary intervention, **fondaparinux** significantly reduces mortality & reinfarction without increasing bleeding and strokes. (InfoPOEMs: Fondaparinux (Arixtra) reduces the risk of mortality and reinfarction without increasing the risk of severe bleeding events in patients with acute ST-segment elevation myocardial infarction. Patients undergoing primary percutaneous coronary intervention (PCI) received no additional benefit from fondaparinux compared with unfractionated heparin (UFH). (LOE = 1b-)) Mehta SR, et al.; ASPIRE Investigators. Randomized, blinded trial comparing fondaparinux with unfractionated heparin in patients undergoing contemporary percutaneous coronary intervention: Arixtra Study in Percutaneous Coronary Intervention: a Randomized Evaluation (ASPIRE) Pilot Trial. Circulation. 2005 Mar 22;111(11):1390-7.
137. Mohr JP, et al. Warfarin-Aspirin Recurrent Stroke Study Group. A comparison of warfarin and aspirin for the prevention of recurrent ischemic stroke. (WARSS) N Engl J Med. 2001 Nov 15;345(20):1444-51.
138. Kastrati A, et al. **Abciximab** in Patients With Acute Coronary Syndromes Undergoing Percutaneous Coronary Intervention After Clopidogrel Pretreatment: The **ISAR-REACT 2** Randomized Trial. JAMA. 2006 Mar 13; [Epub ahead of print] CONCLUSIONS: Abciximab reduces the risk of adverse events in patients with non-ST-segment elevation ACS undergoing PCI after pretreatment with 600 mg of clopidogrel. The benefits provided by abciximab appear to be confined to patients presenting with an elevated troponin level.
139. Sacco RL et al **American Heart Association**/American Stroke Association Council on Stroke; Council on Cardiovascular Radiology and Intervention; American Academy of Neurology. Guidelines for **prevention of stroke** in patients with ischemic stroke or transient ischemic attack: a statement for healthcare professionals from the American Heart Association/American Stroke Association Council on Stroke: co-sponsored by the Council on Cardiovascular Radiology and Intervention: the American Academy of Neurology affirms the value of this guideline. Circulation. **2006** Mar 14;113(10):e409-49. http://circ.ahajournals.org/cgi/content/full/113/10/e409
140. Becker DM, et al. Sex differences in platelet reactivity and response to low-dose aspirin therapy. JAMA. 2006 Mar 22;295(12):1420-7.
141 **Peripheral Arterial Disease**: ACC/AHA 2005 Guideline for Management of Patients With (Lower Extremity, Renal, Mesenteric, and Abdominal Aortic); A Collaborative Report From the AAVS/SVS, SCAI, SIR, SVMB, and the ACC/AHA Task Force on Practice Guidelines http://content.onlinejacc.org/cgi/content/full/47/6/e1 (Abramson BL, et al.; Canadian Cardiovascular Society. Canadian Cardiovascular Society Consensus Conference: peripheral arterial disease - executive summary. Can J Cardiol. 2005 Oct;21(12):997-1006.)
142. Antman EM, et al. Enoxaparin versus Unfractionated Heparin with Fibrinolysis for ST-Elevation Myocardial Infarction. (**EXTRACT-TIMI 25**)N Engl J Med. 2006 Mar 20; [Epub ahead of print] Conclusions In patients receiving fibrinolysis for ST-elevation myocardial infarction, treatment with enoxaparin throughout the index hospitalization is superior to treatment with unfractionated heparin for 48 hours but is associated with an increase in major bleeding episodes. (InfoPOEMs: For every 1000 patients treated with enoxaparin instead of unfractionated heparin there were 15 fewer nonfatal myocardial infarctions (MIs), 7 fewer urgent revascularizations, and 6 fewer deaths, but there were 4 additional episodes of nonfatal major bleeding. (LOE = 1b))
143. Morice MC, et al. REALITY Trial Investigators. **Sirolimus- vs paclitaxel**-eluting stents in de novo coronary artery lesions: the REALITY trial: a randomized controlled trial. JAMA. 2006 Feb 22;295(8):895-904.
144. Kaplan RC, et al. Vascular events, mortality, and preventive therapy following ischemic stroke in the elderly. Neurology. 2005 Sep 27;65(6):835-42. Erratum in: Neurology. 2006 Feb 28;66(4):493.
145. Ernst A, Eberhardt R, Wahidi M, Becker HD, Herth FJ. Effect of routine clopidogrel use on bleeding complications after **transbronchial** biopsy in humans. Chest. 2006 Mar;129(3):734-7.
146. Purkayastha S, et al. Does clopidogrel affect outcome after coronary artery bypass grafting? A meta-analysis. Heart. 2006 Apr;92(4):531-2. (More blood lost & transfusions)
147. Stabile G, et al. Catheter ablation treatment in pts with drug-refractory atrial fibrillation: a prospective, multi-centre, randomized, controlled study (**Catheter Ablation For The Cure Of Atrial Fibrillation Study**). Eur Heart J.2006Jan;27(2):216-21.Epub 2005Oct 7.
148. Cohen AT, et al.; ARTEMIS Investigators. Efficacy and safety of **fondaparinux** for the prevention of venous thromboembolism in older acute medical patients: randomised placebo controlled trial. BMJ. 2006 Feb 11;332(7537):325-9. Epub 2006 Jan 26.
149. Wolfram RM, et al. Clopidogrel Loading Dose (**300** Versus 600 mg) Strategies for Patients With Stable Angina Pectoris Subjected to Percutaneous Coronary Intervention. Am J Cardiol. 2006 Apr 1;97(7):984-9. Epub 2006 Feb 13.
150. Heneghan C, Alonso-Coello P, Garcia-Alamino JM, Perera R, Meats E, Glasziou P. Self-monitoring of oral anticoagulation: a systematic review and meta-analysis. Lancet. 2006 Feb 4;367(9508):404-11. (InfoPOEMs: Patients who self-monitor oral anticoagulation had fewer thromboembolic events than those using standard approaches to monitoring. However, self-monitoring should only be offered to literate and motivated patients. Additionally, the machines are costly and not universally covered by insurance. (LOE = 1a))
151. Glueck CJ, Khalil Q, Winiarska M, Wang P. Interaction of **duloxetine and warfarin** causing severe elevation of international normalized ratio. JAMA. 2006 Apr 5;295(13):1517-8.
152. Ho WK, Hankey GJ, Quinlan DJ, Eikelboom JW. Risk of recurrent venous thromboembolism in patients with common **thrombophilia**: a systematic review. Arch Intern Med. 2006 Apr 10;166(7):729-36.
153. Tricoci P, Roe MT, Mulgund J, et al. Clopidogrel to treat patients with non-ST-segment elevation acute coronary syndromes after hospital discharge. Arch Intern Med 2006; 166:806-811.
154. Pignone M, Aspirin, statins, or both drugs for the primary prevention of coronary heart disease events in men: a cost-utility analysis. Ann Intern Med. 2006 Mar 7;144(5):326-36. Summary for patients in: Ann Intern Med. 2006 Mar 7;144(5):I29. (InfoPOEMs: From the viewpoint of cost to a third-party payer, the costs of aspirin alone are reasonable in men at low-risk for coronary heart disease (CHD); the addition of a statin to aspirin therapy in these men is above what is considered to be reasonable cost for prevention. However, the combination of aspirin and a statin is cost-effective when men are at high risk (10% or above). (LOE = 2a))
155. Lim W, Dentali F, Eikelboom JW, Crowther MA. Meta-analysis: **low-molecular-weight heparin** and **bleeding** in patients with severe **renal** insufficiency. Ann Intern Med. 2006 May 2;144(9):673-84.
156. Smith SC Jr, et al. **AHA/ACC guidelines for secondary prevention** for patients with coronary and other atherosclerotic vascular disease: 2006 update: endorsed by the National Heart, Lung, and Blood Institute. Circulation. 2006 May 16;113(19):2363-72. http://circ.ahajournals.org/cgi/reprint/113/19/2363
Furie Karen L., Kasner Scott E., Adams Robert J., et al., and on behalf of the American Heart Association Stroke Council, Council on Cardiovascular Nursing, Council on Clinical Cardiology, and Interdisciplinary Council on Quality of Care and Outcomes Research. Guidelines for the **Prevention of Stroke in Patients With Stroke or Transient Ischemic Attack**. (Secondary Prevention) A Guideline for Healthcare Professionals From the American Heart Association (AHA)/American Stroke Association (ASA). Stroke published October 21, 2010, doi:10.1161/STR.0b013e3181f7d043. http://stroke.ahajournals.org/cgi/reprint/STR.0b013e3181f7d043v1
157. Hand PJ, Kwan J, Lindley RI, Dennis MS, Wardlaw JM. Distinguishing between stroke and mimic at the bedside: the brain attack study. Stroke. 2006 Mar;37(3):769-75. Epub 2006 Feb 16. (InfoPOEMs: In this study, 31% of patients with suspected stroke actually had a stroke mimic. Eight clinical factors helped distinguish these patients from those with stroke. (LOE = 2b))
158. Rasoul S, et al. A comparison of dual vs. **triple antiplatelet** therapy in patients with non-ST-segment elevation acute coronary syndrome: results of the ELISA-2 trial. Eur Heart J. 2006 May 8; [Epub ahead of print]
159. Toff WD, et al. Effect of hypobaric hypoxia, simulating conditions during long-haul **air travel**, on coagulation, fibrinolysis, platelet function, and endothelial activation. JAMA. 2006 May 17;295(19):2251-61. (but up 5min/hr, not alcohol/narcotics)
160. ESPRIT Study Group; et al. Aspirin plus dipyridamole versus aspirin alone after cerebral ischaemia of arterial origin (**ESPRIT**): randomised controlled trial. Lancet. 2006 May 20;367(9523):1665-73. Norrving B. Dipyridamole with aspirin for secondary stroke prevention. Lancet. 2006 May 20;367(9523):1638-9. (InfoPOEMs: In this unblinded study, the combination of aspirin plus dipyridamole is more effective than aspirin alone in preventing death from all vascular causes, nonfatal stroke, nonfatal myocardial infarction, or major bleeding complications. However, patients taking dipyridamole are much more likely to experience headaches sufficient to stop taking it. (LOE = 2b)) (The ESPRIT Study Group; Algra A. Medium intensity oral **anticoagulants versus aspirin** after cerebral ischaemia of arterial origin (ESPRIT): a randomised controlled trial. Lancet Neurol. 2007 Feb;6(2):115-24. Oral anticoagulants (target INR range 2.0-3.0) are not more effective than aspirin for secondary prevention after transient ischaemic attack or minor stroke of arterial origin. A possible protective effect against ischaemic events is offset by increased bleeding complications.) (Sudlow C. Dipyridamole with aspirin is better than aspirin alone in preventing vascular events after ischaemic stroke or TIA. BMJ. 2007 Apr 28;334(7599):901.)
161. Bhatt DL, et al; REACH Registry Investigators. International prevalence, recognition, and treatment of cardiovascular risk factors in outpatients with atherothrombosis. JAMA. 2006 Jan 11;295(2):180-9.
162. Kumar S, Savitz S, Schlaug G, Caplan L, Selim M. **Antiplatelets, ACE inhibitors, and statins** combination reduces stroke severity and tissue at risk. Neurology. 2006 Apr 25;66(8):1153-8; discussion 1135.
163. Stein PD, et al.; PIOPED II Investigators. Multidetector computed tomography for acute pulmonary embolism. N Engl J Med. 2006 Jun 1;354(22):2317-27. (InfoPOEMs: Patients with high or intermediate probability of pulmonary embolism (PE) and an abnormal result on computed tomographic angiography (CTA) or CTA combined with venous-phase imaging (CTA-CTV) are very likely to have PE. Those with low or intermediate probability and a negative CTA or CTA-CTV result are unlikely to have PE. All other patients -- that is, those with discordant findings between the clinical examination and CTA or CTA-CTV -- need either further testing or close clinical follow-up to confirm or exclude the diagnosis. Clinical evaluation using a validated decision rule remains an important part of the evaluation. (LOE = 2b))
164. Kearon C, et al.; Canadian Pulmonary Embolism Diagnosis Study (CANPEDS) Group. An evaluation of D-dimer in the diagnosis of pulmonary embolism: a randomized trial.Ann Intern Med. 2006 Jun 6;144(11):812-21.
165. Khurram Z, et al. Combination therapy with **aspirin, clopidogrel and warfarin** following coronary stenting is associated with a significant risk of bleeding. J Invasive Cardiol. 2006 Apr;18(4):162-4. In patients requiring warfarin therapy, the addition of dual antiplatelet therapy is associated with an approximately 7% major bleeding risk. Thus, novel regimens are needed to reduce the bleeding risk.
166. Staresinic AG, Sorkness CA, Goodman BM, Pigarelli DW. Comparison of outcomes using 2 delivery models of anticoagulation care. Arch Intern Med. 2006 May 8;166(9):997-1002.
167. Regier DA, et al. Cost-effectiveness of **self-managed versus physician**-managed oral anticoagulation therapy. CMAJ. 2006 Jun 20;174(13):1847-52.
168. Cokkinos DV, et al. Efficacy of antithrombotic therapy in chronic **heart failure**: The **HELAS** study. Eur J Heart Fail. 2006 Jun;8(4):428-32. Epub 2006 Jun 5. Overall embolic events are rare in heart failure regardless of treatment & treatment does not seem to affect outcome.(Massie BM, et al. The Warfarin and Antiplatelet Therapy in Heart Failure trial (**WATCH**): rationale, design, and baseline patient characteristics. J Card Fail. 2004 Apr;10(2):101-12.) (Cleland JG, The Warfarin/Aspirin Study in Heart failure (**WASH**): a randomized trial comparing antithrombotic strategies for patients with heart failure. Am Heart J. 2004 Jul;148(1):157-64.)
169. Gage BF, van Walraven C, Pearce L, et al. Selecting patients with atrial fibrillation for anticoagulation: Stroke risk stratification in patients taking aspirin. Circulation 2004; 110:2287-92. (InfoPOEMs: Clinical decision rules, especially the well-validated Stroke Prevention in Atrial Fibrillation (SPAF) score, can help identify which groups of patients with atrial fibrillation are likely and unlikely to benefit from anticoagulation. (LOE = 1a).If the risk of stroke is low (< 2%), the harms of anticoagulation generally outweigh the benefits. If the risk of stroke is high (> 4%), the benefits of anticoagulation outweigh the risks for most pts. If the patient's stroke risk is in between both extremes, we have to look carefully at his or her risk for hemorrhage.)
Cooper NJ, Sutton AJ, Lu G, Khunti K. Mixed comparison of stroke prevention treatments in individuals with **nonrheumatic atrial fibrillation**. Arch Intern Med. 2006 Jun 26;166(12):1269-75. A lower rate of ischemic stroke and a higher rate of major bleeding episodes were found to be associated with oral anticoagulants compared with aspirin, and both anticoagulants and aspirin were found to be associated with a reduction in the rate of stroke compared with placebo. Assuming a baseline risk of 51 ischemic stroke

events per 1000 person-years, it can be estimated that adjusted standard-dose warfarin could prevent 28 (95% CrI, -37 to -19) ischemic strokes at the expense of 11 (95% CrI, -1 to +39) major or fatal bleeding episodes. In comparison, aspirin could prevent 16 (95% CrI, -26 to -5) ischemic strokes at the expense of 6 (95% CrI, -3 to +27) major or fatal bleeding episodes. (Fuster V, et al.; American College of Cardiology/American Heart Association Task Force on Practice Guidelines; European Society of Cardiology Committee for Practice Guidelines; European Heart Rhythm Association; Heart Rhythm Society. **ACC/AHA/ESC 2006 Guidelines for the Management of Patients with Atrial Fibrillation**: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines and the European Society of Cardiology Committee for Practice Guidelines (Writing Committee to Revise the 2001 Guidelines for the Management of Patients With Atrial Fibrillation) http://www.acc.org/qualityandscience/clinical/guidelines/atrial_fib/pdfs/AF_Full_Text.pdf developed in collaboration with the European Heart Rhythm Association and the Heart Rhythm Society. Circulation. 2006 Aug 15;114(7):e257-354.)

Hart RG, Pearce LA, Aguilar MI. Meta-analysis: Antithrombotic therapy to prevent stroke in patients who have nonvalvular atrial fibrillation. Ann Intern Med 2007;146:857-867.

Estes NAM, Halperin JL, Calkins H, et al. ACC/AHA physician consortium 2008 clinical performance measures for adults with nonvalvular atrial fibrillation or atrial flutter. J Am Coll Cardiol 2008; 51:865-884.

Singer DE, Albers GW, Dalen JE, Fang MC, Go AS, Halperin JL, Lip GY, Manning WJ; American College of Chest Physicians. Antithrombotic therapy in atrial fibrillation: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines (8th Edition). **Chest. 2008** Jun;133(6 Suppl):546S-592S.

Lip GYH, Nieuwlaat R, et al. Refi ning clinical risk stratifi cation for predicting stroke and thromboembolism in atrial fi brillation using a novel risk factor-based approach: the Euro Heart Survey on atrial fi brillation. Chest 2010; 137: 263–72. (**CHA_2DS_2-VASc**)

ACCF- AHA-HRS Atrial Fibrillation 2011 Focused Update. Circulation 2011. http://circ.ahajournals.org/cgi/reprint/CIR.0b013e3181fa3cf4v1

Wann L. Samuel, Curtis Anne B., Ellenbogen Kenneth A., et al. **2011 ACCF/AHA/HRS Focused Update on the Management of Patients With Atrial Fibrillation (Update on Dabigatran):** A Report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines Circulation published February 14, 2011, doi:10.1161/CIR.0b013e31820f14c0 http://circ.ahajournals.org/cgi/reprint/CIR.0b013e31820f14c0v1

Olesen JB, Lip G, Hansen ML, et al. Validation of risk stratification schemes for predicting stroke and thromboembolism in patients with atrial fibrillation: nationwide cohort study. BMJ 2011;342:doi:10.1136/bmj.d124 (31 Jan 11). CHADS2 vs **CHA2DS2-VASc**

Cairns JA, Connolly S, McMurtry S, et al. CCS Atrial Fibrillation Guidelines Committee. **Canadian cardiovascular society atrial fibrillation guidelines 2010**: prevention of stroke and systemic thromboembolism in atrial fibrillation and flutter. Can J Cardiol. 2011 Jan-Feb;27(1):74-90.

Hobbs F D R, Roalfe A K, Lip G Y H, et al. on behalf of Birmingham Atrial Fibrillation in the Aged (BAFTA) investigators and Midland Research Practices Consortium (MidReC) network. **Performance of stroke risk scores** in older people with atrial fibrillation not taking warfarin: comparative cohort study from BAFTA trial. BMJ 2011;342:doi:10.1136/bmj.d3653 (23 June 2011)

Klein D, Levine M. Are family physicians using the CHADS2 score?: is it useful for assessing risk of stroke in patients with atrial fibrillation? Can Fam Physician. 2011 Aug;57(8):e305-9.

Lip GYH, Banerjee A, Boriani G, et al. **Antithrombotic Therapy for Atrial Fibrillation: CHEST Guideline** and Expert Panel Report. Chest. 2018 Aug 21.

Lip GYH, Collet JP, Haude M, Huber K. Management of **antithrombotic therapy in AF patients presenting with ACS and/or undergoing PCI**: A Summary of the Joint Consensus Document of the European Heart Rhythm Association (EHRA), **European** Society of Cardiology (**ESC**) Working Group on Thrombosis, European Association of Percutaneous Cardiovascular Interventions (EAPCI) and European Association of Acute Cardiac Care (ACCA) endorsed by the Heart Rhythm Society (HRS), Asia-Pacific Heart Rhythm Society (APHRS), Latin America Heart Rhythm Society (LAHRS), and Cardiac Arrhythmia Society of Southern Africa (CASSA). Eur Heart J. 2018 Aug 14;39(31):2847-2850.

170. Tung R, Kaul S, Diamond GA, Shah PK. Narrative review: **drug-eluting stents** for the management of restenosis: a critical appraisal of the evidence. Ann Intern Med. 2006 Jun 20;144(12):913-9.
171. Ricci S, Lewis S, Sandercock P; IST Collaborative Group. **Previous use of aspirin** and baseline stroke severity: an analysis of 17,850 patients in the International Stroke Trial. Stroke. 2006 Jul;37(7):1737-40. Epub 2006 Jun 1.
172. Goldstein LB, et al. American Heart Association; American Stroke Association Stroke Council. **Primary prevention of ischemic stroke**: a guideline from the American Heart Association/American Stroke Association Stroke Council: cosponsored by the Atherosclerotic Peripheral Vascular Disease Interdisciplinary Working Group; Cardiovascular Nursing Council; Clinical Cardiology Council; Nutrition, Physical Activity, and Metabolism Council; and the Quality of Care and Outcomes Research Interdisciplinary Working Group. Circulation. 2006 Jun 20;113(24):e873-923. http://circ.ahajournals.org/cgi/reprint/113/24/e873
173. McRae S, Tran H, Schulman S, Ginsberg J, Kearon C. Effect of patient's **sex** on risk of recurrent venous thromboembolism: a meta-analysis. Lancet. 2006 Jul 29;368(9533):371-8.
174. Hron G, Kollars M, Binder BR, Eichinger S, Kyrle PA. Identification of patients at low risk for recurrent venous thromboembolism by measuring **thrombin generation**. JAMA. 2006 Jul 26;296(4):397-402.
175. Munoz R, Duran-Cantolla J, Martinez-Vila E, et al. Severe **sleep apnea** and risk of ischemic stroke in the elderly. Stroke 2006; DOI: 10.1161/01.STR.0000236560.15735.0f. Available at: http://stroke.ahajournals.org
176. Goodacre S, et al. How should we **diagnose suspected deep-vein thrombosis**? QJM. 2006 Jun;99(6):377-88. (InfoPOEMs: The most cost-effective algorithm for managing patients with suspected deep vein thrombosis (DVT) was identified, although several are nearly as good. The main message is that the best approach uses a combination of a validated clinical decision rule, D-dimer test, and venous ultrasound. (LOE = 1b))
177. McQuaid KR, Laine L. Systematic review and meta-analysis of adverse events of **low-dose aspirin** and clopidogrel in randomized controlled trials. Am J Med. 2006 Aug;119(8):624-38.
178. Park DW, Park SW, Park KH, Lee BK, Kim YH, Lee CW, Hong MK, Kim JJ, Park SJ. Frequency of and risk factors for **stent thrombosis** after drug-eluting stent implantation during long-term follow-up. Am J Cardiol. 2006 Aug 1;98(3):352-6. Epub 2006 Jun 12.
179. Almeida OP, Waterreus A, Hankey GJ. Preventing depression after stroke: Results from a randomized (**sertaline NS**) placebo-controlled trial. J Clin Psychiatry. 2006 Jul;67(7):1104-9.
180. Amarenco P, et al. Stroke Prevention by Aggressive Reduction in Cholesterol Levels (**SPARCL**) Investigators. High-dose **atorvastatin** after stroke or transient ischemic attack. N Engl J Med. 2006 Aug 10;355(6):549-59. (InfoPOEMs: High-dose atorvastatin reduces the risk of recurrent stroke, but does not improve mortality rates. A reduction in the risk of transient ischemic attack (TIA) or unclassified stroke was partially offset by an increase in the risk of hemorrhagic stroke. (LOE = 1b)) Amarenco P, Goldstein LB, Szarek M, Sillesen H, Rudolph AE, Callahan A 3rd, Hennerici M, Simunovic L, Zivin JA, Welch KM; SPARCL Investigators. Effects of Intense Low-Density Lipoprotein Cholesterol Reduction in Patients With Stroke or Transient Ischemic Attack. The Stroke Prevention by Aggressive Reduction in Cholesterol Levels (SPARCL) Trial. Stroke. 2007 Oct 25; [Epub ahead of print] As compared with having no change or an increase in LDL-C, achieving a >/=50% lowering was associated with a greater reduction in the risk of stroke and major coronary events with no increase in brain hemorrhages. Goldstein LB, Amarenco P, Szarek M, Callahan A 3rd, Hennerici M, Sillesen H, Zivin JA, Welch KM; On behalf of the SPARCL Investigators. Hemorrhagic stroke in the Stroke Prevention by Aggressive Reduction in Cholesterol Levels study. Neurology. 2007 Dec 12; [Epub ahead of print] Hemorrhagic stroke was more frequent in those treated with atorvastatin, in those with a hemorrhagic stroke as an entry event, in men, and increased with age. Those with Stage 2 hypertension at the last visit prior to the hemorrhagic stroke were also at increased risk. Treatment did not disproportionately affect the hemorrhagic stroke risk associated with these other factors. There were no relationships between hemorrhage risk and baseline low-density lipoprotein (LDL) cholesterol level or recent LDL cholesterol level in treated patients.
Sillesen H, Amarenco P, Hennerici MG, et al. on Behalf of the SPARCL Investigators. Atorvastatin Reduces the Risk of Cardiovascular Events in Patients With Carotid Atherosclerosis. A Secondary Analysis of the Stroke Prevention by Aggressive Reduction in Cholesterol Levels (SPARCL) Trial. Stroke. 2008 Oct 9. [Epub ahead of print]
Consistent with the overall results of the SPARCL intention to treat population, intense lipid lowering with atorvastatin reduced the risk of cerebro- and cardiovascular events in patients with and without carotid stenosis. The carotid stenosis group may have greater benefit.
Amarenco P, Benavente O, Goldstein LB, et al.; on behalf of the SPARCL Investigators. Results of the Stroke Prevention by Aggressive Reduction in Cholesterol Levels (SPARCL) Trial by Stroke Subtypes. Stroke. 2009 Feb 19. [Epub ahead of print] Atorvastatin 80 mg/d is similarly efficacious in preventing strokes and other cardiovascular events, irrespective of baseline ischemic stroke subtype.
Goldstein LB, Amarenco P, Zivin J, Messig M, Altafullah I, Callahan A, Hennerici M, Macleod MJ, Sillesen H, Zweifler R, Welch KM; on behalf of the SPARCL Investigators. Statin Treatment and Stroke Outcome in the Stroke Prevention by Aggressive Reduction in Cholesterol Levels (SPARCL) Trial. Stroke. 2009 Sep 10.
Amarenco P, Goldstein LB, Sillesen H, Benavente O, Zweifler RM, Callahan A 3rd, Hennerici MG, Zivin JA, Welch KM; on behalf of the SPARCL Investigators. Coronary Heart Disease Risk in Patients With Stroke or Transient Ischemic Attack and No Known Coronary Heart Disease. Findings From the Stroke Prevention by Aggressive Reduction in Cholesterol Levels (SPARCL) Trial. Stroke. 2010 Jan 28.
181. Eisenstein EL, Anstrom KJ, Kong DF, et al. Clopidogrel use and long-term clinical outcomes after drug-eluting stent implantation. JAMA 2006; 297:DOI:10.1001/jama.297.2.joc60179. Available at: http://jama.ama-assn.org. The extended use of clopidogrel in patients with DES may be associated with a reduced risk for death and death or MI. However, the appropriate duration for clopidogrel administration can only be determined within the context of a large-scale randomized clinical trial.
182. Pfisterer M, Brunner-La Rocca HP, Buser PT, et al. Late clinical events after **clopidogrel discontinuation** may limit the benefit of **drug-eluting stents**. J Am Coll Cardiol 2006; 48:2584-2591. The primary focus of this observation was cardiac death/MI. Rates of 18-month cardiac death/MI were not different between DES and BMS patients. However, after the discontinuation of clopidogrel (between months 7 and 18), these events occurred in 4.9% after DES vs 1.3% after BMS implantation. Target vessel revascularization remained lower after DES, resulting in similar rates of all clinical events for this time period (DES 9.3%, BMS 7.9%). Documented late stent thrombosis & related death/target vessel MI were twice as frequent after DES versus BMS (2.6% vs. 1.3%).
183. Harrington, RA, Califf RM, et al. Late ischemic events after **clopidogrel cessation** following drug-eluting stenting. Should we be worried? J Am Coll Cardiol 2006; 48:2592-2594.
184 Zeymer U, et al. Acute COronary Syndromes (**ACOS**) registry investigators. Effect of clopidogrel on 1-year mortality in hospital survivors of acute ST-segment elevation myocardial infarction in clinical practice. Eur Heart J. 2006 Nov;27(22):2661-6.
185. Shuchman M. Trading **restenosis for thrombosis**? New questions about **drug-eluting stents**. N Engl J Med. 2006 Nov 9;355(19):1949-52.
186. Shireman TI, et al. Development of a contemporary **bleeding risk model** for **elderly warfarin** recipients. Chest. 2006 Nov;130(5):1390-6.
187. Wald DS, Wald NJ, Morris JK, Law M. **Folic acid, homocysteine**, and cardiovascular disease: judging causality in the face of inconclusive trial evidence. BMJ. 2006 Nov 25;333(7578):1114-7.
188. Stone GW, et al. Bivalirudin for Patients with Acute Coronary Syndromes. (**ACUITY**)N Engl J Med. 2006 Nov 23;355(21):2203-2216. .
189. Hennerici M, Kay R, Bogousslavsky J, et al. Intravenous **ancrod** for acute ischaemic stroke in the European Stroke Treatment with Ancrod Trial: A randomised controlled trial. Lancet 2006; 368:1871-1878.
190 Bos MJ, et al. High serum **C-reactive protein** level is not an independent predictor for stroke: the Rotterdam Study. Circulation. 2006 Oct 10;114(15):1591-8. Epub 2006 Oct 2.
191 Albert C. A randomized trial of **folic acid and B-vitamins** in the secondary prevention of cardiovascular events in women: Results from the Women's Antioxidant and Folic Acid Cardiovascular Study (WAFACS). American Heart Association 2006 Scientific Sessions; November 13, 2006; Chicago, IL. PS.03.Late-Breaking Clinical Trials I. The Women's Antioxidant and Folic Acid Cardiovascular Study (**WAFACS**) enrolled 5,442 women at least 40 years of age, with established cardiovascular disease or at least 3 cardiovascular risk factors, who were already participating in a randomized study of antioxidant supplementation. Women who had been randomized to receive vitamins C and E plus beta-carotene were further randomized to receive either placebo or daily doses of 2.5 mg folic acid, 50 mg vitamin B6, and 1 mg vitamin B12. Albert CM, Cook NR, et al. Effect of folic acid and B vitamins on risk of cardiovascular events and total mortality among women at high risk for cardiovascular disease: a randomized trial. (**WAFACS**) JAMA. 2008 May 7;299(17):2027-36. After 7.3 years of treatment and follow-up, a combination pill of folic acid, vitamin B6, and vitamin B12 did not reduce a combined end point of total cardiovascular events among high-risk women, despite significant homocysteine lowering.
Cook NR, Albert CM, et al.. A randomized factorial trial of vitamins C and E and beta carotene in the secondary prevention of cardiovascular events in women: results from the Women's Antioxidant Cardiovascular Study (**WACS**). Arch Intern Med. 2007 Aug 13-27;167(15):1610-8. There were no overall effects of ascorbic acid, vitamin E, or beta carotene on cardiovascular events among women at high risk for CVD.
192. Marcucci R, et al. Usefulness of **Aspirin Resistance** After Percutaneous Coronary Intervention for Acute Myocardial Infarction in Predicting One-Year Major Adverse Coronary Events. Am J Cardiol. 2006 Nov 1;98(9):1156-1159. Epub 2006 Aug 31. A

significantly higher percentage of patients with MACEs had aspirin resistance (39.1% vs 23.2%, p <0.05).
193. Elkind MS, Tai W, Coates K, Paik MC, Sacco RL. High-sensitivity **C-reactive protein**, **lipoprotein-associated phospholipase A2**, and outcome after ischemic stroke. Arch Intern Med. 2006 Oct 23;166(19):2073-80.
194. Wolf SL, et al. **EXCITE** Investigators. Effect of **constraint-induced movement therapy** on upper extremity function 3 to 9 months after stroke: the EXCITE randomized clinical trial. JAMA. 2006 Nov 1;296(17):2095-104. Among patients who had a stroke within the previous 3 to 9 months, CIMT produced statistically significant and clinically relevant improvements in arm motor function that persisted for at least 1 year.
Langhorne P, Bernhardt J, Kwakkel G. **Stroke rehabilitation**. Lancet. 2011 May 14;377(9778):1693-702.
Laver KE, George S, Thomas S, Deutsch JE, Crotty M. **Virtual reality** for stroke rehabilitation. Cochrane Database of Systematic Reviews 2011, Issue 9. Art. No.: CD008349. DOI: 10.1002/14651858.CD008349.pub2. We found limited evidence that the use of virtual reality and interactive video gaming may be beneficial in improving arm function and ADL function when compared with the same dose of conventional therapy.
195. Paterson JM, Mamdani M, Juurlink DN, et al. Clinical consequences of **generic warfarin substitution**: an ecological study. JAMA. 2006 Oct 25;296(16):1969-72.
196. Dolitzky M, et al. A randomized study of **thromboprophylaxis** in women with unexplained consecutive recurrent miscarriages. Fertil Steril. 2006 Aug;86(2):362-6. Epub 2006 Jun 12. (InfoPOEMs: Daily treatment with aspirin or enoxaparin (Lovenox) each results in a high live birth rate for women with history of unexplained recurrent miscarriages. The lack of a control group is an important limitation of this study. (LOE = 1b-))
197. Budnitz DS, et al. National surveillance of emergency department visits for outpatient **adverse drug events**. JAMA. 2006 Oct 18;296(15):1858-66. In an analysis of routine surveillance data from 63 US hospitals, adverse drug events accounted for an estimated 2.5% of emergency department visits for unintentional injury and 0.6% of visits for all causes. About a third were allergic reactions and another third were unintentional overdoses, particularly of drugs that need regular monitoring such as digoxin and warfarin. Insulin and warfarin were implicated in over a quarter of all serious events. Insulin, warfarin, and digoxin accounted for more than 40% of serious events among people aged over 65.
198. Palareti G et al. for the **PROLONG** Investigators. **D-dimer** testing to determine the duration of anticoagulation therapy. N Engl J Med 2006 Oct 26; 355:1780-9.
199. Sellier E, et al. Effectiveness of a guideline for venous **thromboembolism prophylaxis** in **elderly post-acute care** patients: a multicenter study with systematic ultrasonographic examination. Arch Intern Med. 2006 Oct 23;166(19):2065-71.
200. Mas JL, et al.; **EVA-3S** Investigators. **Endarterectomy versus stenting** in patients with symptomatic severe carotid stenosis. N Engl J Med. 2006 Oct 19;355(16):1660-71. In this study of patients with symptomatic carotid stenosis of 60% or more, the rates of death and stroke at 1 and 6 months were lower with endarterectomy than with stenting. (But await NIH **CREST** trial) (InfoPOEMs: Carotid stenting as currently practiced should be abandoned. It significantly increases the risk of stroke in patients with symptomatic carotid stenosis. (LOE = 1b))
201. Blann AD, Lip GY. **Venous thromboembolism**. BMJ. 2006 Jan 28;332(7535):215-9.
202. SPACE Collaborative Group; Ringleb PA, et al. 30 day results from the **SPACE** trial of **stent-protected angioplasty versus carotid endarterectomy** in symptomatic patients: a randomised non-inferiority trial. Lancet. 2006 Oct 7;368(9543):1239-47.
203. Howard VJ, et al. High **Prevalence of Stroke** Symptoms Among Persons Without a Diagnosis of Stroke or Transient Ischemic Attack in a General Population: The REasons for Geographic And Racial Differences in Stroke (**REGARDS**) Study. Arch Intern Med. 2006 Oct 9;166(18):1952-8.
204. Hernandez-Diaz S, Garcia Rodriguez LA. Cardioprotective **aspirin** users and their excess **risk of upper gastrointestinal complications**. BMC Med. 2006 Sep 20;4:22.
205. Fairhead JF, Rothwell PM. **Underinvestigation and undertreatment** of carotid disease in **elderly** patients with transient ischaemic attack and stroke: comparative population based study. BMJ. 2006 Sep 9;333(7567):525-7. Epub 2006 Jul 18.
206 Spertus JA, et al. Prevalence, predictors, and outcomes of **premature discontinuation** of **thienopyridine therapy** after **drug-eluting stent** placement: results from the **PREMIER** registry. Circulation. 2006 Jun 20;113(24):2803-9. Epub 2006 Jun 12.
207. Morice MC, et al. **REALITY** Trial Investigators. **Sirolimus- vs paclitaxel-eluting stents** in de novo coronary artery lesions: the REALITY trial: a randomized controlled trial. JAMA. 2006 Feb 22;295(8):895-904.
208. Montalescot G, et al. **STEEPLE** Investigators. **Enoxaparin versus unfractionated heparin** in elective percutaneous coronary intervention. N Engl J Med. 2006 Sep 7;355(10):1006-17.
209. Lagerqvist B, et al. Fast Revascularisation during InStability in Coronary artery disease (**FRISC-II**) Investigators. 5-year outcomes in the FRISC-II randomised trial of an **invasive versus a non-invasive** strategy in non-ST-elevation acute coronary syndrome: a follow-up study. Lancet. 2006 Sep 16;368(9540):998-1004. (InfoPOEMs: In this study of patients with non-ST-elevation acute coronary syndromes, patients treated invasively had fewer subsequent myocardial infarctions after 5 years than patients treated medically. The benefits are seen mainly in men, nonsmokers, and patients with at least 2 risk factors. (LOE = 1b))
210. George-Phillips KL, Bungard TJ. Use of **low-molecular-weight heparin** to bridge therapy in **obese** patients and in patients with **renal dysfunction**. Pharmacotherapy. 2006 Oct;26(10):1479-90.
211. Mirkhel A, et al. Frequency of **aspirin resistance** in a community hospital. Am J Cardiol. 2006 Sep 1;98(5):577-9. Epub 2006 Jun 30. In conclusion, this study estimates aspirin resistance prevalence and shows a strong association of **smoking** with platelet hyperactivity in a diverse community hospital population. Nonresponders to 81 mg/day frequently responded to 325 mg/day or to the addition of clopidogrel.
212. Casele H, et al. **Bone density changes** in women who receive **thromboprophylaxis** in pregnancy. Am J Obstet Gynecol. 2006 Oct;195(4):1109-13. In this study, the incidence of clinically significant bone loss (> or = 10%) in the femur in women who received thromboprophylaxis in pregnancy is approximately 2% to 2.5% and appears to be similar, regardless of whether the patient receives low molecular weight heparin therapy or unfractionated heparin therapy.
213. Alexander KP, Chen AY, Newby K, et al. **Sex** differences in major **bleeding with glycoprotein IIb/IIIa inhibitors.** Circulation 2006; 114: 1380-1387.
214. Levine RL, McCollum D, Hursting MJ. How frequently is venous thromboembolism in heparin-treated patients associated with **heparin-induced thrombocytopenia**? Chest. 2006 Sep;130(3):681-7. VTE is associated with HIT infrequently (< 1%) in LMWH-treated patients, yet often (approximately one in eight cases) in unfractionated heparin-treated patients. Physicians should suspect the possibility of HIT if VTE develops during or soon after unfractionated heparin use; if thrombocytopenia is present, alternative anticoagulation should be used until HIT is excluded.
215. Suk Danik J, Rifai N, Buring JE, Ridker PM. **Lipoprotein(a)**, measured with an assay independent of apolipoprotein(a) isoform size, and risk of future cardiovascular events among initially healthy women. JAMA. 2006 Sep 20;296(11):1363-70.
216. Hallas J, et al. Use of **single and combined antithrombotic therapy and risk of serious upper gastrointestinal bleeding**: population based case-control study. BMJ. 2006 Sep 19; [Epub ahead of print] Adjusted odds ratios associating drug use with upper gastrointestinal bleeding were 1.8 (95% confidence interval 1.5 to 2.1) for low dose aspirin, 1.1 (0.6 to 2.1) for clopidogrel, 1.9 (1.3 to 2.8) for dipyridamole, and 1.8 (1.3 to 2.4) for vitamin K antagonists. Corresponding figures for combined use were 7.4 (3.5 to 15) for clopidogrel and aspirin, 5.3 (2.9 to 9.5) for vitamin K antagonists and aspirin, and 2.3 (1.7 to 3.3) for dipyridamole and aspirin.
217. Gibson CM, et al.; **TIMI** Study Group. Usefulness of **Clopidogrel** in Abolishing the Increased Risk of Reinfarction Associated With **Higher Platelet Counts** in Patients With ST-Elevation Myocardial Infarction (Results from **CLARITY-TIMI 28**). Am J Cardiol. 2006 Sep 15;98(6):761-763. Epub 2006 Aug 2.
218. Laarman GJ, et al. **Paclitaxel-eluting versus uncoated stents** in primary percutaneous coronary intervention.N Engl J Med. 2006 Sep 14;355(11):1105-13.
219. Spaulding C, et al.; **TYPHOON** Investigators. **Sirolimus-eluting versus uncoated stents** in acute myocardial infarction. N Engl J Med. 2006 Sep 14;355(11):1093-104.
220. McQuaid KR, et al. Systematic review and meta-analysis of **adverse events of low-dose aspirin and clopidogrel** in randomized controlled trials. Am J Med. 2006 Aug;119(8):624-38. Aspirin increased the risk of major bleeding (RR=1.71; 95% confidence interval [CI], 1.41-2.08), major gastrointestinal (GI) bleeding (RR=2.07; 95% CI, 1.61-2.66), and intracranial bleeding (RR=1.65; 95% CI, 1.06-5.99) versus placebo. No difference between 75-162.5 mg/day and >162.5-325 mg/day aspirin versus placebo was seen. The absolute annual increases attributable to aspirin were major bleeding: 0.13% (95% CI, 0.08-0.20); major GI bleeding: 0.12% (95% CI, 0.07-0.19), intracranial bleeding: 0.03% (95% CI, 0.01-0.08). No study compared clopidogrel with placebo. One study showed increased major GI bleeding (but not non-GI bleeding endpoints) with aspirin versus clopidogrel (RR=1.45; 95% CI, 1.00-2.10). The absolute annual increase was 0.12% (95% CI, 0.00-0.28). CONCLUSIONS: Low-dose aspirin increases the risk of major bleeding by approximately 70%, but the absolute increase is modest: 769 patients (95% CI, 500-1250) need to be treated with aspirin to cause one additional major bleeding episode annually. Compared with clopidogrel, aspirin increases the risk of GI bleeding but not other bleeding; however, 883 patients (95% CI, 357-infinity) would need to be treated with clopidogrel versus aspirin to prevent one major GI bleeding episode annually at a cost of over 1 million dollars.
221. Laine L. Review article: **gastrointestinal bleeding with low-dose aspirin** - what's the risk? Aliment Pharmacol Ther. 2006 Sep 15;24(6):897-908. The single endoscopic trial assessing ulcers showed no significant difference in 12-week ulcer incidence: 6% of 381 given placebo vs. 7% of 387 given 81 mg enteric-coated aspirin. The relative risk of major gastrointestinal bleeding with low-dose aspirin in a meta-analysis of placebo-controlled trials of vascular protection was 2.07 (95% CI: 1.61-2.66). The absolute rate increase with aspirin above placebo was 0.12% per year (95% CI: 0.07-0.19%) with a number-needed-to-harm of 833 patients (95% CI: 526-1429). A meta-analysis of aspirin 50-1500 mg daily reported an odds ratio for any gastrointestinal bleeding of 1.68 (95% CI: 1.51-1.88) with an number-needed-to-harm at 1 year of 247. The relative risk of hospitalization for upper gastrointestinal bleeding with low-dose aspirin in a large Danish cohort study was 2.6 (95% CI: 2.2-2.9) with an absolute annual incidence of 0.6%. Factors that may increase the risk of gastrointestinal bleeding include prior history of ulcers or gastrointestinal bleeding, corticosteroid use, anticoagulant therapy and addition of a non-aspirin non-steroidal anti-inflammatory drug.
222. Algra A, et al. Oral **anticoagulants versus antiplatelet** therapy for preventing further vascular events after transient ischaemic attack or minor **stroke** of presumed arterial origin. Cochrane Database Syst Rev. 2006 Jul 19;3:CD001342.
223. Brophy JM, et al. A pharmacoepidemiology study of the interaction between **atorvastatin and clopidogrel** after percutaneous coronary intervention. Am Heart J. 2006 Aug;152(2):263-9.
224.Eikelboom JW, Mehta SR, Anand SS, et al. Adverse impact of **bleeding** on prognosis in patients with acute coronary syndromes. Circulation 2006; 114: 774 - 782.
225.Montalescot G, Sideris G, Meuleman C, et al. A randomized comparison of **high clopidogrel loading doses** in patients with non-ST-segment elevation acute coronary syndromes. The **ALBION** (Assessment of the Best Loading Dose of Clopidogrel to Blunt Platelet Activation, Inflammation and Ongoing Necrosis) trial. J Am Coll Cardiol 2006; 48:931-938.
226. Kearon C, et al., Gent M; Fixed-Dose Heparin (**FIDO**) Investigators. Comparison of fixed-dose weight-adjusted unfractionated **heparin and low-molecular-weight heparin** for acute treatment of venous thromboembolism. JAMA. 2006 Aug 23;296(8):935-42. (InfoPOEMs: In this study, fixed-dose weight-adjusted unfractionated heparin (UFH) administered subcutaneously was as safe and effective as low-molecular-weight heparin (LMWH) in the treatment of venous thromboembolism (VTE). Estimated drug costs for a 6-day course are $712 for LMWH and $37 for UFH. Most clinicians will want to see similar results from at least 1 additional well-done clinical trial, including more patients with symptomatic pulmonary embolism, before routinely treating VTE with subcutaneous UFH. (LOE = 1b))
227. Turrentine MA. Single-dose **fluconazole** for vulvovaginal candidiasis: impact on **prothrombin** time in women taking **warfarin**. Obstet Gynecol. 2006 Feb;107(2 Pt 1):310-3.
228. Mehta RH, et al. Acute **clopidogrel** use and outcomes in patients with non-ST-segment elevation acute coronary syndromes undergoing coronary artery bypass surgery. J Am Coll Cardiol. 2006 Jul 18;48(2):281-6. Epub 2006 Jun 21.
229. Quiroz R, et al. Comparison of a Single End Point to Determine Optimal Initial **Warfarin Dosing** (5 mg Versus 10 mg) for Venous Thromboembolism. Am J Cardiol. 2006 Aug 15;98(4):535-537. Epub 2006 Jun 28.
230. Meune C, et al. Effects of **aspirin and clopidogrel** on plasma brain **natriuretic peptide** in patients with heart failure receiving ACE inhibitors. Eur J Heart Fail. 2006 Aug 14; [Epub ahead of print]
231. O'donnell M, et al.; on behalf of the Investigators of the Registry of the Canadian Stroke Network. **Preadmission antithrombotic treatment** and **stroke severity** in patients with atrial fibrillation and acute ischaemic stroke: an observational study. Lancet Neurol. 2006 Sep;5(9):749-54.
232. Cox D, Maree AO, Dooley M, Conroy R, Byrne MF, Fitzgerald DJ. Effect of **enteric coating** on antiplatelet activity of low-dose **aspirin** in healthy volunteers. Stroke. 2006 Aug;37(8):2153-8. Epub 2006 Jun 22.
233. Dec/06 Health Canada: Association of increased mortality and risk of serious adverse events when prophylactic low-dose heparin is abruptly discontinued in patients to be started on Xigris [drotrecogin alfa (activated)] therapy for severe sepsis.
234. Aguilar M, Hart R. **Antiplatelet therapy** for preventing stroke in patients with non-valvular **atrial fibrillation** and no previous history of stroke or transient ischemic attacks. Cochrane Database Syst Rev. 2005 Oct 19;(4):CD001925. Aspirin appears to reduce stroke and major vascular events in patients with non-valvular AF similar to its effect in other high-risk patients (ie by about 25%). For primary prevention among AF patients with an average stroke rate of 4% per year, about 10 strokes would likely be prevented yearly for every 1000 AF patients given aspirin.
235. Aguilar MI, Hart R. **Oral anticoagulants** for preventing stroke in patients with non-valvular **atrial fibrillation** and no previous history of stroke or transient ischemic attacks. Cochrane Database Syst Rev. 2005 Jul 20;(3):CD001927. Treatment with adjusted-dose

warfarin to achieved INRs of 2 to 3 reduces stroke, disabling or fatal stroke, and death for patients with non-valvular AF. The benefits were not substantially offset by increased bleeding among these participants in randomized clinical trials. Limitations include relatively short follow up and imprecise estimates of bleeding risks from the selected participants enrolled in the trials. For primary prevention of stroke in AF patients, about 25 strokes and about 12 disabling or fatal strokes would be prevented yearly for every 1000 atrial fibrillation patients given OACs.

236. Grines CL, Bonow RO, Casey DE. Prevention of premature **discontinuation of dual antiplatelet** therapy in patients with coronary artery **stents**. Circulation 2007; DOI: 10.1161/CIRCULATIONAHA.106.180944. Available at: http://www.circulationaha.org.
237. Pharmacist's Letter: FDA Statement of Coronary **Drug-Eluting Stents** Jan 07
238. Sarkiss MG, Yusuf SW, Warneke CL, et al. Impact of **aspirin** therapy in cancer patients with **thrombocytopenia** and acute coronary syndromes. Cancer. 2006 Dec 13;109(3):621-627 [Epub ahead of print] Therapy with ASA was associated with a significantly improved 7-day survival after ACS in cancer patients, with or without thrombocytopenia, and not associated with more severe bleeding.
239. Dentali F, Douketis JD, Lim W, Crowther M. Combined **Aspirin-Oral Anticoagulant Therapy Compared With Oral Anticoagulant Therapy Alone** Among Patients at Risk for Cardiovascular Disease: A Meta-analysis of Randomized Trials. Arch Intern Med. 2007 Jan 22;167(2):117-24. Our findings question the current practice of using combined aspirin-OAC therapy except in patients with a mechanical heart valve, given the questionable benefits in reducing thromboembolic events and the increased risk of major bleeding. (InfoPOEMs: **Except for patients with mechanical heart valves, the addition of aspirin to therapeutic warfarin doses does not decrease** the risk of death or of thromboembolism and does not increase the risk of a major bleed. (LOE = 1a))
240. The **ESPRIT** Study Group; Algra A. Medium **intensity oral anticoagulants versus aspirin** after cerebral ischaemia of arterial origin (ESPRIT): a randomised controlled trial. Lancet Neurol. 2007 Feb;6(2):115-24.
241. Hull RD, et al. **Self-managed long-term low-molecular-weight heparin** therapy: the balance of benefits and harms. Am J Med. 2007 Jan;120(1):72-82.
242. Durga J, van Boxtel MPJ, Schouten EG, et al. Effect of 3-year **folic acid** supplementation on **cognitive function** in older adults in the FACIT trial: a randomised, double blind, controlled trial. Lancet 2007; 369:208-216. Folic acid supplementation for 3 years significantly improved domains of cognitive function that tend to decline with age.
243. Biondi-Zoccai GG, et al. A systematic review and meta-analysis on the hazards of **discontinuing or not adhering to aspirin** among 50,279 patients at risk for coronary artery disease. Eur Heart J. 2006 Nov;27(22):2667-74. Epub 2006 Oct 19. Overall, aspirin non-adherence/withdrawal was associated with three-fold higher risk of major adverse cardiac events (OR=3.14 [1.75-5.61], P=0.0001). This risk was magnified in patients with intracoronary stents, as discontinuation of antiplatelet treatment was associated with an even higher risk of adverse events (OR=89.78 [29.90-269.60]).
244. Hodgson JM, et al. **Late stent thrombosis**: Considerations and practical advice for the use of drug-eluting stents: A report from the society for cardiovascular angiography and interventions drug-eluting stent task force. Catheter Cardiovasc Interv. 2007 Jan 11; [Epub ahead of print]
245. Serebruany VL, Atar D. **Assessment of bleeding events** in clinical trials-proposal of a new classification. Am J Cardiol. 2007 Jan 15;99(2):288-90. Epub 2006 Nov 27.
246. Nordmann AJ, Briel M, Bucher HC. Mortality in randomized controlled trials comparing **drug-eluting vs. bare metal stents** in coronary artery disease: a meta-analysis. Eur Heart J. 2006 Dec;27(23):2784-814. Epub 2006 Oct 4. Drug-eluting stents for the treatment of coronary artery disease do not reduce total mortality when compared with bare metal stents. Preliminary evidence suggests that sirolimus- but not paclitaxel-eluting stents may lead to increased non-cardiac mortality.
247. Dubinsky RM, Lai SM. Mortality from combined **carotid endarterectomy and coronary artery bypass** surgery in the US. Neurology. 2007 Jan 16;68(3):195-7.
248. Burton JR, Burton I, Pearson GJ. **Clopidogrel-precipitated rhabdomyolysis** in a stable heart transplant patient. Ann Pharmacother. 2007 Jan;41(1):133-7. Epub 2007 Jan 2.
249. Millan M, et al. Increased body **iron stores** are associated with **poor** outcome after **thrombolytic treatment** in acute stroke. Stroke. 2007 Jan;38(1):90-5. Epub 2006 Nov 30.
250. Subramaniam RM, et al. **Diagnosis** of lower limb **deep venous thrombosis** in emergency department patients: performance of Hamilton and modified Wells scores. Ann Emerg Med. 2006 Dec;48(6):678-85. Epub 2006 Jun 9.
251. Ferretti G, et al. Is recurrent venous thromboembolism after therapy reduced by **low-molecular-weight heparin** compared with **oral anticoagulants**? Chest. 2006 Dec;130(6):1808-16.
252. Steffen LM, Folsom AR, Cushman M, et al. Greater **fish, fruit, and vegetable** intakes are related to lower incidence of venous thromboembolism. The Longitudinal Investigation of Thromboembolism Etiology. Circulation 2006; DOI:10.1161/CIRCULATIONAHA.106.641688.
253. Carandang R, Seshadri S, Beiser A, et al. Trends in incidence, lifetime risk, severity, and 30-day mortality of **stroke** over the past 50 years. JAMA 2006; 296:2939-2946.
254. Health Canada Dec /06 Increased mortality and risk of serious adverse events when prophylactic **heparin is abruptly discontinued** in patients to be started on Xigris [drotrecogin alfa (activated)] for severe sepsis. Patients who had low dose heparin treatment abruptly discontinued when starting **Xigris** treatment had increased mortality and risk of serious adverse, including cardiac, gastrointestinal and venous thrombotic events. http://www.hc-sc.gc.ca/dhp-mps/medeff/advisories-avis/prof/index_e.html
255. Hoppener MR, et al. Low incidence of deep vein thrombosis after **knee arthroscopy** without thromboprophylaxis: a prospective cohort study of 335 patients. Acta Orthop. 2006 Oct;77(5):767-71. (InfoPOEMs:In patients undergoing knee arthroscopy, approximately 6% will develop a deep vein thrombosis (**DVT**) or symptomatic pulmonary embolism (PE). If these data are translatable to other settings, thromboprophylaxis would appear to be unnecessary. (LOE = 1b-))
256. Clarke P, et al. **Vitamin K prophylaxis for preterm** infants: a randomized, controlled trial of 3 regimens. Pediatrics. 2006 Dec;118(6):e1657-66. Epub 2006 Nov 13.
257. Bazzano LA, Reynolds K, Holder KN, He J. Effect of **folic acid** supplementation on risk of **cardiovascular diseases**: a meta-analysis of randomized controlled trials. JAMA. 2006 Dec 13;296(22):2720-6. Folic acid supplementation has not been shown to reduce risk of cardiovascular diseases or all-cause mortality among participants with prior history of vascular disease.
258. Campbell IA, Bentley DP, Prescott RJ, Routledge PA, Shetty HG, Williamson IJ. Anticoagulation for **three** versus six months in patients with **deep vein thrombosis or pulmonary embolism**, or both: randomised trial. BMJ. 2007 Feb 8; [Epub ahead of print] For patients in the UK with deep vein thrombosis or pulmonary embolism and no known risk factors for recurrence, there seems to be little, if any, advantage in increasing the duration of anticoagulation from three to six months. Any possible advantage would be small and would need to be judged against the increased risk of haemorrhage associated with the longer duration of treatment with warfarin.
259. Qaseem A, Snow V, Barry P, et al.; Joint American Academy of Family Physicians/American College of Physicians Panel on Deep Venous Thrombosis/Pulmonary Embolism. Current **diagnosis of venous thromboembolism** in primary care: a clinical practice guideline from the American Academy of Family Physicians and the American College of Physicians. Ann Fam Med. 2007 Jan-Feb;5(1):57-62.
260. King CS, Holley AB, Jackson JL, Shorr AF, Moores LK. **Twice vs three times daily heparin** dosing for thromboembolism prophylaxis in the general medical population: A metaanalysis. Chest. 2007 Feb;131(2):507-16. BID heparin dosing causes fewer major bleeding episodes, while TID dosing appears to offer somewhat better efficacy in preventing clinically relevant VTE events. (InfoPOEMs: Until a direct comparison study is performed, the best information available suggests that although 3-times-daily dosing of 5000 units unfractionated heparin (UH) is more effective then twice-daily dosing (approximately 1 fewer pulmonary embolism (PE) and 2 fewer deep vein thromboses (DVTs) per 1000 patient days), it is associated with more major bleeds (1 per 2500 patient days). Remember that both regimens are better than doing nothing for high-risk hospitalized medical patients. (LOE = 1a-))
261. Eshaghian S, Kaul S, Amin S, Shah PK, Diamond GA. **Role of clopidogrel in managing atherothrombotic cardiovascular disease**. Ann Intern Med. 2007 Mar 20;146(6):434-41.
262. Francis CW. Clinical practice. **Prophylaxis for thromboembolism in hospitalized medical patients**. N Engl J Med. 2007 Apr 5;356(14):1438-44.
263. Adams HP Jr, Del Zoppo G, et al. Guidelines for the **Early Management of Adults With Ischemic Stroke**. A Guideline From the American Heart Association/American Stroke Association Stroke Council, Clinical Cardiology Council, Cardiovascular Radiology and Intervention Council, and the Atherosclerotic Peripheral Vascular Disease and Quality of Care Outcomes in Research Interdisciplinary Working Groups. The American Academy of Neurology affirms the value of this guideline as an educational tool for neurologists. Stroke. 2007 Apr 12; [Epub ahead of print]
264. Segal JB, Streiff MB, Hoffman LV, Thornton K, Bass EB. **Management of venous thromboembolism: a systematic review** for a practice guideline. Ann Intern Med. 2007 Feb 6;146(3):211-22. Epub 2007 Jan 29. Review. Summary for patients in: Ann Intern Med. 2007 Feb 6;146(3):I43. (InfoPOEMs: Low-molecular-weight heparin (**LMWH**) is superior to unfractionated heparin (UFH) for deep venous thrombosis (DVT) and as effective as UFH for pulmonary embolism (PE). Outpatient DVT treatment is safe and cost effective for selected patients. Compression stockings should be provided to patients with DVT at discharge. (LOE = 1a))
Snow V, Qaseem A, Barry P, et al; American College of Physicians;American Academy of Family Physicians Panel on Deep Venous Thrombosis/Pulmonary Embolism. **Management** of venous thromboembolism: a clinical practice **guideline** from the American College of Physicians and the American Academy of Family Physicians. Ann Intern Med. 2007 Feb 6;146(3):204-10. Epub 2007 Jan 29.
Douketis James, Tosetto Alberto, Marcucci Maura, et al. Patient-Level Meta-analysis: Effect of Measurement Timing, Threshold, and Patient Age on Ability of **D-Dimer Testing** to Assess Recurrence Risk After Unprovoked Venous Thromboembolism. *Ann Intern Med* October 19, 2010 153:523-531.
van der Velde EF, Toll DB, Ten Cate-Hoek AJ, et al. Comparing the diagnostic performance of 2 clinical decision rules (**Well's or Primary care**) to rule out deep vein thrombosis in primary care patients. Ann Fam Med. 2011 Jan-Feb;9(1):31-6.
265. McFadden EP, et al. **Late thrombosis** in drug-eluting coronary stents after discontinuation of antiplatelet therapy. Lancet. 2004 Oct 23-29;364(9444):1519-21.
266. Beohar N, Davidson CJ, Kip KE, et al. Outcomes and complications associated with **off-label** and **untested** use of **drug-eluting stents**. JAMA 2007; 297:1992-2000. In contemporary US practice, off-label and untested use of drug-eluting stents is common. Compared with standard use, relative early safety is lower with off-label use, and the long-term effectiveness is lower with both off-label and untested use. However, the absolute event rates remain low.
267. Win HK, Caldera AE, Maresh K, et al. Clinical outcomes and stent thrombosis following **off-label** use of **drug-eluting stents**. Event Registry. JAMA 2007; 297:2001-2009. Compared with on-label use, off-label use of drug-eluting stents is associated with a higher rate of adverse outcomes during the index admission and at 1 year. Stent thrombosis occurred predominantly in patients who underwent off-label drug-eluting stent implantation. Clinicians should be cautious about extrapolating the benefits of drug-eluting stents over bare-metal stents observed in randomized clinical trials to higher-risk clinical settings that have not been assessed.
268. Harrington RA, Ohman EM. The enigma of **drug-eluting stents**: Hope, hype, humility, and advancing patient care. JAMA 2007; 297:2028-2030.
269 Deeugenio D, Kolman L, Decaro M, et al. Risk of major bleeding with concomitant **dual antiplatelet** therapy after percutaneous coronary intervention in patients receiving long-term **warfarin** therapy. Pharmacotherapy. 2007 May;27(5):691-6. There were 14/97 (14 %) major bleeds in the active group (including 1 death) and 3/97 (3 %) major bleeds in the control group during the study period. Mean international normalized ratio at the time of bleeding was 3.4. **Hazard ratio for major bleeding was 5.0** in patients receiving warfarin therapy (95% confidence interval 1.4-17.8, p=0.012). Warfarin was an independent predictor of major bleeding after PCI in patients receiving dual antiplatelet therapy. Prospective data to further characterize the safety of concomitant warfarin and dual antiplatelet therapy after PCI are needed.
270 **NICE** April 2007: **Venous thromboembolism**: reducing the risk of venous thromboembolism (deep vein thrombosis and pulmonary embolism) in **inpatients** undergoing surgery http://guidance.nice.org.uk/CG46
271 Johnston SC, Rothwell PM, Nguyen-Huynh MN, Giles MF, Elkins JS, Bernstein AL, Sidney S. Validation and refinement of scores to predict very early stroke risk after transient ischaemic attack. Lancet. 2007 Jan 27;369(9558):283-92. Existing prognostic scores for stroke risk after TIA validate well on multiple independent cohorts, but the unified **ABCD(2) score** is likely to be most predictive. Patients at high risk need immediate evaluation to optimise stroke prevention.
ABCD2 score http://www.ganfyd.org/index.php?title=ABCD2_score
272. **NICE Guidelines May 2007** Secondary prevention in primary and secondary care for patients following a **myocardial infarction.** http://guidance.nice.org.uk/CG48
273. Pharmacists Letter. Does a cranberry juice-warfarin interaction really exist? June 2007.
274. Campbell CL, Smyth S, Montalescot G, and Steinhubl SR. Aspirin dose for the prevention of cardiovascular disease. A systematic review. JAMA 2007; 297:2018-2024. Currently available clinical data do not support the routine, long-term use of aspirin dosages greater than 75 to 81 mg/d in the setting of cardiovascular disease prevention. Higher dosages, which may be commonly prescribed, do not better prevent events but are associated with increased risks of gastrointestinal bleeding.
275 Hylek EM, Evans-Molina C, Shea C, Henault LE, Regan S. **Major hemorrhage** and tolerability of **warfarin** in the first year of therapy among **elderly** patients with atrial fibrillation. Circulation. 2007 May 29;115(21):2689-96. Epub 2007 May 21. {InfoPOEMs: The

risk of major hemorrhage among older patients taking warfarin is higher than commonly reported (13.7% during the first year for patients aged 80 and older) and particularly in the first 3 months of treatment. If the decision is made to use anticoagulation, patients should be aware of the risks, the early warning signs of bleeding, and should be followed up closely during the first 3 months in particular to assure that the international normalized ratio (INR) does not exceed 3.0. (LOE = 2b)}
Abraham NS, Hartman C, Richardson P, et al. Risk of Lower and Upper Gastrointestinal Bleeding, Transfusions, and Hospitalizations with Complex Antithrombotic Therapy in Elderly Patients. Circulation. 2013 Sep 11.

276. Aguilar M, Hart R, Pearce L. Oral anticoagulants versus antiplatelet therapy for preventing stroke in patients with non-valvular atrial fibrillation and no history of stroke or transient ischemic attacks. Cochrane Database Syst Rev. 2007 Jul 18;3:CD006186. Adjusted-dose warfarin and related oral anticoagulants reduce stroke, disabling stroke and other major vascular events for those with non-valvular AF by about one third when compared with antiplatelet therapy.
277. Spencer FA, Lessard D, Emery C, et al. **Venous thromboembolism in the outpatient setting**. Arch Intern Med. 2007 Jul 23;167(14):1471-5. In all, 73.7% of patients developed VTE in the outpatient setting; a substantial proportion of these patients had undergone surgery (23.1%) or hospitalization (36.8%) in the preceding 3 months. More VTEs were diagnosed in the 3 months following hospitalization than during hospitalization. Efforts to improve in-hospital use of VTE prophylaxis may help decrease the incidence of outpatient VTE.
278. Wein L, Wein S, Haas SJ, Shaw J, et al. Pharmacological Venous **Thromboembolism Prophylaxis** in **Hospitalized Medical Patients**: A **Meta-analysis** of Randomized Controlled Trials. Arch Intern Med. 2007 Jul 23;167(14):1476-1486. A UFH dosage of 5000 U 3 times daily was more effective in preventing DVT than a UFH dosage of 5000 U twice daily when compared with the control (RR, 0.27; 95% CI, 0.20-0.36; vs RR, 0.52; 95% CI, 0.28-0.96). Both UFH and LMWH reduce venous thromboembolic risk in hospitalized medical patients, but neither agent alters mortality. When directly compared, LMWH is more effective in preventing DVT.
279. Warfarin Antiplatelet Vascular Evaluation Trial Investigators (**WAVE**), Anand S, Yusuf S, Xie C, Pogue J, Eikelboom J, Budaj A, Sussex B, Liu L, Guzman R, Cina C, Crowell R, Keltai M, Gosselin G. Oral anticoagulant and antiplatelet therapy and peripheral arterial disease. N Engl J Med. 2007 Jul 19;357(3):217-27. In patients with **peripheral arterial disease**, the combination of an **oral anticoagulant** and antiplatelet therapy was not more effective than antiplatelet therapy alone in preventing major cardiovascular complications and was associated with an increase in life-threatening bleeding.
280. Philbrick JT, Shumate R, Siadaty MS, Becker DM. **Air travel** and venous thromboembolism: a systematic review. J Gen Intern Med. 2007 Jan;22(1):107-14. All travelers, regardless of VTE risk, should avoid dehydration and frequently exercise leg muscles. Travelers on a flight of less than 6 hours and those with no known risk factors for VTE, regardless of the duration of the flight, do not need DVT prophylaxis. Travelers with 1 or more risk factors for VTE should consider graduated compression stockings and/or LMWH for flights longer than 6 hours.
Chandra D, Parisini E, and Mozaffarian D. **Travel** and risk for venous thromboembolism. Ann Intern Med 2009.
281. Paciaroni M, et al. Efficacy and safety of anticoagulant treatment in **acute cardioembolic stroke**: a meta-analysis of randomized controlled trials. Stroke. 2007Feb;38(2):423-30. Epub 2007 Jan4. Our findings indicate that in patients with acute cardioembolic stroke, early anticoagulation is associated with a nonsignificant reduction in recurrence of ischemic stroke, no substantial reduction in death and disability, and an increased intracranial bleeding.
282. Arepally GM, Ortel TL. Clinical practice. **Heparin-induced thrombocytopenia**. N Engl J Med. 2006 Aug 24;355(8):809-17.
283. Aster RH, Bougie DW. **Drug-induced immune thrombocytopenia**. N Engl J Med. 2007 Aug 9;357(6):580-7.
284. Chen ZM, Sandercock P, Pan HC, Counsell C, et al. Indications for early aspirin use in acute ischemic stroke : A combined analysis of 40 000 randomized patients from the chinese acute stroke trial and the international stroke trial. On behalf of the CAST and IST collaborative groups. Stroke. 2000 Jun;31(6):1240-9. CAST: randomised placebo-controlled trial of early aspirin use in 20,000 patients with acute ischaemic stroke. CAST (Chinese Acute Stroke Trial) Collaborative Group. Lancet. 1997 Jun 7;349(9066):1641-9. The International Stroke Trial (IST): a randomised trial of aspirin, subcutaneous heparin, both, or neither among 19435 patients with acute ischaemic stroke. International Stroke Trial Collaborative Group. Lancet. 1997 May 31;349(9065):1569-81.
van der Worp HB, van Gijn J. Clinical practice. **Acute ischemic stroke**. N Engl J Med. 2007 Aug 9;357(6):572-9.
285. Mant J, Hobbs FD, Fletcher K, et al. **Warfarin versus aspirin for stroke prevention in an elderly** community population with atrial fibrillation (the Birmingham Atrial Fibrillation Treatment of the Aged Study, **BAFTA**): a randomised controlled trial. Lancet. 2007; 370:493-503.
286. Anderson JL, Adams CD, Antman EM, et al. **ACC/AHA 2007** guidelines for the management of patients with **unstable angina/non-ST-elevation myocardial infarction**. A report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. *J Am Coll Cardiol* 2007; DOI:10.1016/j.jacc.2007.02.028. http://content.onlinejacc.org/cgi/content/full/50/7/e1. *Circulation* 2007; DOI:10.1161/CIRCULATIONAHA.107.185752. http://circ.ahajournals.org/cgi/reprint/CIRCULATIONAHA.107.185752.
American Academy of Family Physicians, American College of Emergency Physicians, Society for Cardiovascular Angiography and Interventions, and Society of Thoracic Surgeons, , Wright, R. Scott, Anderson, Jeffrey L., Adams, Cynthia D., et al. **2011 ACCF/AHA Focused Update** of the Guidelines for the Management of Patients With **Unstable Angina/Non-ST-Elevation Myocardial Infarction (Updating the 2007 Guideline):** A Report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. **J Am Coll Cardiol 2011 0: j.jacc.2011.02.009.** http://content.onlinejacc.org/cgi/reprint/j.jacc.2011.02.009v1.pdf
287. Cayley WE Jr. **Preventing deep vein thrombosis in hospital inpatients**. BMJ. 2007 Jul 21;335(7611):147-51.
288. Keller T, et al. Clopidogrel plus aspirin versus aspirin alone for preventing cardiovascular disease. Cochrane Database Syst Rev. 2007 Jul 18;(3):CD005158. The available evidence demonstrates that the use of clopidogrel plus aspirin is associated with a reduction in the risk of cardiovascular events compared with aspirin alone in patients with acute non-ST coronary syndrome. In patients at high risk of cardiovascular disease but not presenting acutely, there is only weak evidence of benefit and hazards of treatment almost match any benefit obtained.
289. Delaney JA, Opatrny L, Brophy JM, & Suissa S. **Drug-drug interactions between antithrombotic** medications and the risk of gastrointestinal bleeding. Can Med Assoc J 2007; 177:347-351. The prescribing of acetylsalicylic acid with either clopidogrel (adjusted rate ratio [RR] 3.90, 95% confidence interval [CI] 2.78-5.47) or warfarin (adjusted RR 6.48, 95% CI 4.25-9.87) was associated with a greater risk of gastrointestinal bleeding than that observed with each drug alone. The same was true when a nonsteroidal anti-inflammatory drug was combined with either clopidogrel (adjusted RR 2.93, 95% CI 1.74-4.93) or warfarin (RR 4.60, 95% CI 2.77-7.64). Drug combinations involving antiplatelets and anticoagulants are associated with a high risk of gastrointestinal bleeding beyond that associated with each drug used alone.
Shehab Nadine; Sperling Laurence S.; Kegler Scott R.; et al. National Estimates of Emergency Department Visits for Hemorrhage-Related Adverse Events From Clopidogrel Plus Aspirin and From Warfarin. Arch Intern Med. 2010;170(21):1926-1933.
Rodríguez Luis A. García, Lin Kueiyu Joshua, Hernández-Díaz Sonia, et al. **Risk of Upper Gastrointestinal Bleeding** With Low-Dose Acetylsalicylic Acid Alone and in Combination With Clopidogrel and Other Medications. Circulation 123: 1108-1115; online doi:10.1161/CIRCULATIONAHA.110.973008
Labos C, Dasgupta K, Nedjar H, et al. Risk of bleeding associated with combined use of **selective serotonin reuptake inhibitors** and antiplatelet therapy following acute myocardial infarction. CMAJ 2011; DOI:10.1503/cmaj.100912.
290. Pharmacists Letter. Genetic testing to aid warfarin dosing. Oct 2007.
291. Fleisher LA, Beckman JA, Brown KA, Calkins H, Chaikof E, Fleischmann KE, Freeman WK, Froehlich JB, Kasper EK, et al. ACC/AHA 2007 Guidelines on **Perioperative Cardiovascular Evaluation** and Care for **Noncardiac Surgery**. A Report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Writing Committee to Revise the 2002 Guidelines on Perioperative Cardiovascular Evaluation for Noncardiac Surgery). Circulation. 2007 Sep 27; [Epub ahead of print] http://content.onlinejacc.org/cgi/reprint/50/17/e159
292. De Schryver E, Algra A, van Gijn J. **Dipyridamole** for preventing stroke and other vascular events in patients with vascular disease. Cochrane Database Syst Rev. 2007 Jul 18;(3):CD001820. For patients who presented with arterial vascular disease, there was no evidence that dipyridamole, in the presence or absence of another antiplatelet drug reduced the risk of vascular death, though it reduces the risk of further vascular events. This benefit was found only in patients presenting after cerebral ischaemia. There was no evidence that dipyridamole alone was more efficacious than aspirin.
293. Kennedy J, Hill MD, Ryckborst KJ, Eliasziw M, Demchuk AM, Buchan AM; for the **FASTER** Investigators. Fast assessment of stroke and transient ischaemic attack to prevent early recurrence (FASTER): a randomised controlled pilot trial. Lancet Neurol. 2007 Oct 9; [Epub ahead of print] Immediately after TIA or minor stroke, patients are at high risk of stroke, were followed for 90 days, which might be reduced by using clopidogrel in addition to aspirin. The haemorrhagic risks of the combination of aspirin (162mg load then 81mg od) and clopidogrel (300mg load then 75mg od) do not seem to offset this potential benefit. We were unable to provide evidence of benefit of simvastatin (40mg od in evening) in this setting. This aggressive prevention approach merits further study.
294. Rothwell PM, Giles MF, Chandratheva A, et al; on behalf of the Early use of Existing Preventive Strategies for Stroke (**EXPRESS**) study. Effect of urgent treatment of transient ischaemic attack and minor stroke on early recurrent stroke (EXPRESS study): a prospective population-based sequential comparison. Lancet. 2007 Oct 8; [Epub ahead of print] (Drugs used:ASA 300mg x1 then 75mg od, clopidogrel 300mg x1 then 75mg od x 30 days, simvastatin 40mg od, perindopril 4mg od +/- indapamide 1.25mg od) Early initiation of existing treatments after TIA or minor stroke was associated with an 80% reduction in the risk of early recurrent stroke. Further follow-up is required to determine long-term outcome, but these results have immediate implications for service provision and public education about TIA and minor stroke.[300-mg loading dose and subsequent 75-mg daily dose of aspirin. This was combined with a 300-mg loading dose followed by a 75-mg daily dose of **clopidogrel for 30 days**.90-day stroke risk was 10.3% in phase 1 and 2.1% in phase 2 (adjusted hazard ratio, 0.20; P = .0001).]
295. Lavallee PC, Meseguer E, Abboud H, Cabrejo L, Olivot JM, Simon O, Mazighi M, Nifle C, Niclot P, Lapergue B, Klein IF, Brochet E, Steg PG, Leseche G, Labreuche J, Touboul PJ, Amarenco P. A transient ischaemic attack clinic with round-the-clock access (**SOS-TIA**): feasibility and effects. Lancet Neurol. 2007 Oct 8; [Epub ahead of print]
296. Wiviott SD, Braunwald E, McCabe CH, et al.; the **TRITON-TIMI 38** Investigators. **Prasugrel** versus Clopidogrel in atients with Acute Coronary Syndromes. N Engl J Med. 2007 Nov 4; [Epub ahead of print] In patients with acute coronary syndromes with scheduled percutaneous coronary intervention, prasugrel therapy was associated with significantly reduced rates of ischemic events, including stent thrombosis, but with an increased risk of major bleeding, including fatal bleeding. Overall mortality did not differ significantly between treatment groups.
297. Anderson JL, Horne BD, Stevens SM, Grove AS, Barton S, Nicholas ZP, Kahn SF, May HT, Samuelson KM, Muhlestein JB, Carlquist JF; Couma-Gen Investigators. Randomized trial of **genotype-guided** versus standard warfarin dosing in patients initiating oral anticoagulation. Circulation. 2007 Nov 27;116(22):2563-70. Epub 2007 Nov 7. An algorithm guided by pharmacogenetic and clinical factors improved the accuracy and efficiency of warfarin dose initiation. Despite this, the primary end point of a reduction in out-of-range INRs was not achieved. In subset analyses, pharmacogenetic guidance showed promise for wild-type and multiple variant genotypes.(**CYP2C9 *2 and CYP2C9 *3 and VKORC1C1173T**)
298. Ad2000 Collaborative Group. **Aspirin 75mg/d in Alzheimer's disease** (AD2000): a randomised open-label trial. Lancet Neurol. 2007 Dec 6; [Epub ahead of print] n=310. Although aspirin is commonly used in dementia, in patients with typical AD 2 years of treatment with low-dose aspirin has no worthwhile benefit and increases the risk of serious bleeds.
299. Garcia DA, Regan S, Henault LE, et al. Risk of thromboembolism with **short-term interruption** of warfarin therapy. Arch Intern Med. 2008;168 63-69. Current guidelines from several European and US cardiology groups allow for the cessation of warfarin for up to 1 week in patients at risk for bleeding because of an invasive procedure such as dental surgery or colonoscopy. Although we still need more research to provide a definitive answer, this study does not refute these recommendations, finding that 0.59% of patients who stop treatment develop a thromboembolism within the subsequent 30 days. (LOE = 2b)
300. Krasopoulos G, Brister SJ, Beattie WS, Buchanan MR. **Aspirin "resistance**" and risk of cardiovascular morbidity: systematic review and meta-analysis. BMJ. 2008 Jan 17; [Epub ahead of print] Patients who are resistant to aspirin are at a greater risk of clinically important cardiovascular morbidity long term than patients who are sensitive to aspirin.
301. van Stralen KJ, Rosendaal FR, Doggen CJ. **Minor injuries** as a risk factor for venous thrombosis. Arch Intern Med. 2008 Jan 14;168(1):21-6.
302. Oliveira GBF, Crespo EM, Becker RC, et al. Incidence and prognostic significance of **thrombocytopenia** in patients treated with **prolonged heparin** therapy. Arch Intern Med. 2008;168:94-102.
303. Cohen AT, Tapson VF, Bergmann JF, et al. Venous thromboembolism risk and prophylaxis in the **acute hospital care** setting (**ENDORSE** study): a multinational cross-sectional study. Lancet. 2008;371:387-394.
304. Ho PM, Peterson ED, Wang L, et al. Incidence of death and acute myocardial infarction associated with **stopping clopidogrel after acute coronary syndrome**. JAMA. 2008 Feb 6;299(5):532-9.

305. Sconce E, Avery P, Wynne H, et al. **Vitamin K supplementation can improve stability** of anticoagulation for patients with unexplained variability in response to warfarin. Blood. 2007 Mar 15;109(6):2419-23. Epub 2006 Nov 16. Vitamin K supplementation can help achieve control of anticoagulation in adults with unexplained instability of response to warfarin. This may be a welcome relief to frustrated patients, clinicians, and staff. (LOE = 1b)
306. Schwarz UI, Ritchie MD, Bradford Y, Li C, Dudek SM, Frye-Anderson A, Kim RB, Roden DM, Stein CM. Genetic determinants of response to warfarin during initial anticoagulation. N Engl J Med. 2008 Mar 6;358(10):999-1008. Initial variability in the INR response to warfarin was more strongly associated with genetic variability in the pharmacologic target of warfarin, **VKORC1**, than with CYP2C9.
307. Tapson VF. **Acute pulmonary embolism**. N Engl J Med. 2008 Mar 6;358(10):1037-52.
Douma Renée A., Mos Inge C.M., Erkens Petra M.G., et al. , for the Prometheus Study Group. Performance **of 4 Clinical Decision Rules in the Diagnostic Management of Acute Pulmonary Embolism**: A Prospective Cohort Study. Ann Intern Med June 7, 2011 154:709-718.
Lucassen W, Geersing GJ, Erkens PM, et al. **Clinical Decision Rules** for **Excluding Pulmonary Embolism**: A Meta-analysis. Ann Intern Med. 2011 Oct 4;155(7):448-60.
Geersing GJ, Erkens PM, Lucassen WA, et al. Safe exclusion of pulmonary embolism using the **Wells rule and qualitative D-dimer** testing in primary care: prospective cohort study. BMJ. 2012 Oct 4;345:e6564.
van Es N, van der Hulle T, van Es J, et al. Wells Rule and d-Dimer Testing to Rule Out Pulmonary Embolism: A Systematic Review and Individual-Patient Data Meta-analysis. Ann Intern Med. 2016 May 17.
308. Bennett CL, Silver SM, Djulbegovic B, et al. Venous thromboembolism and mortality associated with recombinant **erythropoietin and darbepoetin** administration for the treatment of cancer-associated anemia. JAMA. 2008 Feb 27;299(8):914-24.
309. L'Allier PL, et al. PREPAIR Study Investigators. **Clopidogrel 600-mg double loading** dose achieves stronger platelet inhibition than conventional regimens: results from the PREPAIR randomized study. J Am Coll Cardiol. 2008 Mar 18;51(11):1066-72.
310. Douketis JD, et al. The **risk for fatal pulmonary embolism after discontinuing anticoagulant** therapy for venous thromboembolism. Ann Intern Med. 2007 Dec 4;147(11):766-74. The risk for fatal PE is 0.19 to 0.49 events per 100 person-years for patients who have finished a course of anticoagulant therapy for a first episode of symptomatic VTE. The case-fatality rate for death from recurrent PE is 4% to 9%.
311. Thijs V, Lemmens R, Fieuws S. **Network meta-analysis**: simultaneous meta-analysis of common antiplatelet regimens after transient ischaemic attack or stroke. Eur Heart J. 2008 Mar 17; [Epub ahead of print] In the network meta-analysis, all antiplatelet regimens (aspirin, aspirin plus dipyridamole, thienopyridines, and combination of aspirin and thienopyridines) were significantly more effective than placebo. The combination of aspirin and dipyridamole was more effective than thienopyridines (OR, 0.84; 95% CI, 0.73-0.97) and more effective than aspirin (OR, 0.78; 95% CI, 0.70-0.87). Our analysis suggests that the most powerful antiplatelet regimen in the prevention of serious vascular events after TIA or stroke is the **combination of aspirin and dipyridamole**.
312. O'Donnell MJ, Hankey GJ, Eikelboom JW. Antiplatelet Therapy for **Secondary Prevention** of Noncardioembolic Ischemic Stroke. A Critical Review. Stroke. 2008 Mar 27; [Epub ahead of print] For patients with ischemic stroke or transient ischemic attack caused by atherothromboembolism, immediate & long-term aspirin reduces the relative risk of recurrent stroke, MI, & death attributable to vascular causes. Oral anticoagulation is not more effective than aspirin. Long-term clopidogrel reduces the relative risk of stroke, MI, or vascular death by about 9% (0.3% to 16.5%) compared with aspirin. Any long-term benefits of clopidogrel combined with aspirin, compared with aspirin or clopidogrel alone, appear to be offset by increased major bleeding. The combination of aspirin and extended-release dipyridamole reduces the relative odds of stroke, MI, or vascular death by about 18% (odds ratio 0.82, 0.74 to 0.91) compared with aspirin alone without causing more bleeding. Cilostazole reduces the risk of stroke, MI, or vascular death by 39% compared to placebo. A large clinical trial comparing clopidogrel with the combination of aspirin and dipyridamole, in >20 000 patients with recent (<120 days) atherothrombotic ischemic stroke, is expected to report in 2008. Emerging antiplatelet therapies presently being evaluated for secondary prevention of atherothromboembolism include other P2Y12 ADP receptor antagonists (prasugrel, cangrelor, AZD 6140), thromboxane receptor antagonists (eg, S18886 - terutroban), and thrombin receptor (PAR-1) antagonists (eg, SCH530348).
313. Verro P, Gorelick PB, Nguyen D. **Aspirin plus dipyridamole** versus aspirin for prevention of vascular events after stroke or TIA: a meta-analysis. Stroke. 2008 Apr;39(4):1358-63. Epub 2008 Mar 6. The combination of aspirin plus dipyridamole is more effective than aspirin alone in preventing stroke and other serious vascular events in patients with minor stroke and TIAs.
314. Perry DJ, Nokes TJ, Heliwell PS. Guidelines for the management of patients on **oral anticoagulants requiring dental surgery**. London (UK): British Committee for Standards in Haematology; 2007.
315. Dember LM, Beck GJ, Allon M, et al. Dialysis Access Consortium Study Group. Effect of **clopidogrel** on early failure of arteriovenous **fistulas for hemodialysis**: a randomized controlled trial. JAMA. 2008 May 14;299(18):2164-71. Clopidogrel reduces the frequency of early thrombosis of new arteriovenous fistulas but does not increase the proportion of fistulas that become suitable for dialysis.
316. Medical Letter. Treatment Guidelines: **Antiplatelet and Anticoagulant Drugs** May 2008 & **Antithrombotic Drugs Oct 2011 & updated Oct 2014**.
Medical Letter. **Drugs for Treatment and Prevention of Venous Thromboembolism**. Mar 2018.
317. Lubitz SA, Fischer A, Fuster V. **Catheter ablation** for atrial fibrillation. BMJ. 2008 Apr 12;336(7648):819-26.
318. Ovbiagele B, Cruz-Flores S, Lynn MJ, Chimowitz MI; Warfarin-Aspirin Symptomatic Intracranial Disease (**WASID**) Study Group. Early stroke risk after transient ischemic attack among individuals with symptomatic intracranial artery stenosis. Arch Neurol. 2008 Jun;65(6):733-7. Among individuals having intracranial atherosclerotic disease with TIA, most subsequent strokes in the territory of a stenotic intracranial artery occur early (ie, < or =90 days). Prompt management of TIA in patients having intracranial stenosis, particularly those demonstrating cerebral infarction on brain imaging, is indicated.
319. Rahme E, Dasgupta K, Burman M, et al. **Postdischarge thromboprophylaxis** and mortality risk after hip-or knee-replacement surgery. CMAJ. 2008 Jun 3;178(12):1545-54. Fewer than 1 in 5 elderly patients discharged home after a hip-or knee-replacement surgery received postdischarge thromboprophylaxis. Those prescribed these medications had a lower risk of short-term mortality.
320. Eriksson BI, Dahl OE, Rosencher N, et al..; RE-NOVATE Study Group. **Dabigatran** etexilate versus enoxaparin for prevention of venous thromboembolism after total hip replacement: a randomised, double-blind, non-inferiority trial. Lancet. 2007 Sep 15;370(9591):949-56. Erratum in: Lancet. 2007 Dec 15;370(9604):2004. Oral dabigatran etexilate was as effective as enoxaparin in reducing the risk of venous thromboembolism after total hip replacement surgery, with a similar safety profile.
321. Eriksson BI, et al. **Rivaroxaban** versus enoxaparin for thromboprophylaxis after hip arthroplasty. **RECORD1** N Engl J Med. 2008 Jun 26;358(26):2765-75. A once-daily, 10-mg oral dose of rivaroxaban was significantly more effective for extended thromboprophylaxis than a once-daily, 40-mg subcutaneous dose of enoxaparin in patients undergoing elective total hip arthroplasty. The two drugs had similar safety profiles.
322. Kakkar AK, Brenner B, Dahl OE, Eriksson BI, Mouret P, Muntz J, Soglian AG, Pap AF, Misselwitz F, Haas S; the **RECORD2** Investigators. Extended duration **rivaroxaban** versus short-term enoxaparin for the prevention of venous thromboembolism after total hip arthroplasty: a double-blind, randomised controlled trial. Lancet. 2008 Jul 5;372(9632):31-39. Epub 2008 Jun 24.
323. Lassen MR, Ageno W, Borris LC, Lieberman JR, Rosencher N, Bandel TJ, Misselwitz F, Turpie AG; **RECORD3** Investigators. **Rivaroxaban** versus enoxaparin for thromboprophylaxis after total knee arthroplasty. N Engl J Med. 2008 Jun 26;358(26):2776-86. **Rivaroxaban** was superior to enoxaparin for thromboprophylaxis after total knee arthroplasty, with similar rates of bleeding.
Turpie AG, Lassen MR, Davidson BL, et al.; for the **RECORD4** Investigators. Rivaroxaban versus enoxaparin for thromboprophylaxis after total knee arthroplasty (RECORD4): a randomised trial. Lancet. 2009 May 1. Oral rivaroxaban 10 mg once daily for 10-14 days was significantly superior to subcutaneous enoxaparin 30 mg given every 12 h for the prevention of venous thromboembolism after total knee arthroplasty.
324. Rietbrock S, Heeley E, Plumb J, van Staa T. Chronic atrial fibrillation: Incidence, prevalence, and prediction of stroke using the Congestive heart failure, Hypertension, Age >75, Diabetes mellitus, and prior Stroke or transient ischemic attack (**CHADS2**) risk stratification scheme. Am Heart J. 2008 Jul;156(1):57-64. (Increased with age & in men)
325. Ebbing M, Bleie Ø, Ueland PM, Nordrehaug JE, Nilsen DW, et al. Mortality and cardiovascular events in patients treated with homocysteine-lowering B vitamins after coronary angiography: a randomized controlled trial. (**WENBIT**) JAMA. 2008 Aug 20;300(7): 795-804. This trial did not find an effect of treatment with folic acid/vitamin B(12) or vitamin B(6) on total mortality or cardiovascular events. Our findings do not support the use of B vitamins as secondary prevention in patients with coronary artery disease.
326. Yusuf S, Diener HC, Sacco RL, et al. the **PRoFESS** Study Group. **Telmisartan** to Prevent Recurrent Stroke and Cardiovascular Events. N Engl J Med. 2008 Aug 27. [Epub ahead of print] Therapy with telmisartan initiated soon after an ischemic stroke & continued for 2.5 years did not significantly lower the rate of recurrent stroke, major cardiovascular events, or diabetes.
Diener HC, et al. Effects of aspirin plus extended-release dipyridamole versus clopidogrel and telmisartan on disability and cognitive function after recurrent stroke in patients with ischaemic stroke in the Prevention Regimen for Effectively Avoiding Second Strokes (PRoFESS) trial: a double-blind, active and placebo-controlled study. Lancet Neurol. 2008 Oct;7(10):875-84. Epub 2008 Aug 29. Disability due to recurrent stroke and cognitive decline in patients with ischaemic stroke were not different between the two antiplatelet regimens and were not affected by the preventive use of telmisartan.
327. Sacco RL, Diener HC, Yusuf S, et al. the PRoFESS Study Group. Aspirin and Extended-Release Dipyridamole versus Clopidogrel for Recurrent Stroke. N Engl J Med. 2008 Aug 27. [Epub ahead of print] There were more major hemorrhagic events among ASA-ERDP recipients (419 [4.1%]) than among clopidogrel recipients (365 [3.6%]) (hazard ratio, 1.15; 95% CI, 1.00 to 1.32), including intracranial hemorrhage (hazard ratio, 1.42; 95% CI, 1.11 to 1.83). The trial did not meet the predefined criteria for noninferiority but showed similar rates of recurrent stroke with ASA-ERDP and with clopidogrel. There is no evidence that either of the two treatments was superior to the other in the prevention of recurrent stroke.
328. Flaherty ML, Tao H, Haverbusch M, Sekar P, Kleindorfer D, Kissela B, Khatri P, Stettler B, Adeoye O, Moomaw CJ, Broderick JP, Woo D. **Warfarin** use leads to larger **intracerebral hematomas**. Neurology. 2008 Sep 30;71(14):1084-9.
329. Bhatt DL, Scheiman J, Abraham NS, et al. **ACCF/ACG/AHA 2008 expert consensus document on reducing the gastrointestinal risks of antiplatelet therapy and NSAID** use: a report of the American College of Cardiology Foundation Task Force on Clinical Expert Consensus Documents. *J Am Coll Cardiol***.** 2008; *Circulation*. 2008; DOI: DOI: 10.1161/CIRCULATIONAHA.108.191087. Available at: http://circ.ahajournals.org
330. Verhovsek M, et al. Systematic review: **D-dimer** to predict recurrent disease after stopping anticoagulant therapy for unprovoked venous thromboembolism. Ann Intern Med. 2008 Oct 7;149(7):481-90, W94.
331. Belch J, MacCuish A, Campbell I, et al. Prevention of Progression of Arterial Disease and Diabetes Study Group; Diabetes Registry Group; Royal College of Physicians Edinburgh. The prevention of progression of arterial disease and diabetes (**POPADAD**) trial: factorial randomised placebo controlled trial of aspirin and antioxidants in patients with diabetes and asymptomatic peripheral arterial disease. BMJ. 2008 Oct 16;337:a1840. doi: 10.1136/bmj.a1840. N=1276. (awaiting Ascend trial results)
This trial does not provide evidence to support the use of aspirin or antioxidants in primary prevention of cardiovascular events and mortality in the population with diabetes studied.
332. Aisen PS, Schneider LS, Sano M, et al. Alzheimer Disease Cooperative Study (ADCS). High-dose **B vitamin supplementation** and cognitive decline in Alzheimer disease: a randomized controlled trial. JAMA. 2008 Oct 15;300(15):1774-83.
This regimen of high-dose B vitamin supplements does not slow cognitive decline in individuals with mild to moderate AD.
333. Yeomans N, Lanas A, Labenz J, van Zanten SV, et al. Efficacy of esomeprazole (20 mg once daily) for reducing the risk of gastroduodenal ulcers associated with continuous use of low-dose aspirin. Am J Gastroenterol. 2008 Oct;103(10):2465-73. Epub 2008 Jul 12. Twenty-seven patients (5.4%) in the placebo group developed a gastric or duodenal ulcer during 26 weeks' treatment compared with eight patients (1.6%) in the esomeprazole group (life-table estimates: 6.2%vs 1.8%; P= 0.0007).
Esomeprazole 20 mg once daily reduces the risk of developing gastric and/or duodenal ulcers and symptoms associated with the continuous use of low-dose aspirin in patients aged > or =60 yr without preexisting gastroduodenal ulcers.
334. Xarelto (**Rivaroxaban**). Pharmacist's Letter Nov,2008.
335. Jackevicius CA, Tu JV, Demers V, et al. Cardiovascular outcomes after a change in **prescription policy for clopidogrel**. N Engl J Med. 2008 Oct 23;359(17):1802-10. The removal of a prior-authorization program led to improvement in timely access to clopidogrel for coronary stenting and improved cardiovascular outcomes.
336. Kearon C, Julian JA, Kovacs MJ, et al. Influence of thrombophilia on risk of recurrent venous thromboembolism while on warfarin: Results from a randomized trial. Blood. 2008 Sep 12. [Epub ahead of print]
We conclude that single or multiple thrombophilic defects are not associated with a higher risk of recurrent VTE during warfarin therapy.
337. Rodger MA, Kahn SR, Wells PS, et al. Identifying unprovoked thromboembolism patients at low risk for recurrence who can discontinue anticoagulant therapy. CMAJ. 2008 Aug 26;179(5):417-26.
338. Ogawa H, Nakayama M, Morimoto T, et al. for the Japanese Primary Prevention of Atherosclerosis With Aspirin for Diabetes (**JPAD**) Trial Investigators. Low-Dose Aspirin for Primary Prevention of Atherosclerotic Events in Patients With Type 2 Diabetes: A Randomized Controlled Trial. JAMA. 2008 Nov 9. [Epub ahead of print] In this study of patients with type 2 diabetes, low-dose aspirin as primary prevention did not reduce the risk of cardiovascular events.
339. Kahn SR, Shrier I, Julian JA, et al. Determinants and time course of the **postthrombotic syndrome** after acute deep venous thrombosis. Ann Intern Med. 2008 Nov 18;149(10):698-707. The postthrombotic syndrome occurs frequently after DVT. Patients with extensive DVT and those with more severe postthrombotic manifestations 1 month after DVT have poorer long-term outcomes.

340. Oake N, Jennings A, Forster AJ, Fergusson D, Doucette S, van Walraven C. Anticoagulation intensity and outcomes among patients prescribed oral anticoagulant therapy: a systematic review and meta-analysis. CMAJ. 2008 Jul 29;179(3):235-44. The risks of hemorrhage and thromboemboli are minimized at **international normalized ratios of 2-3**. Ratios that are moderately higher than this therapeutic range appear safe and more effective than subtherapeutic ratios.
341. Adams RJ, Albers G, Alberts MJ, Benavente O, Furie K, Goldstein LB, Gorelick P, Halperin J, Harbaugh R, Johnston SC, Katzan I, Kelly-Hayes M, Kenton EJ, Marks M, Sacco RL, Schwamm LH, American Heart Association, American Stroke Association. Update to the **AHA/ASA recommendations for the prevention of stroke** in patients with stroke and transient ischemic attack. Stroke 2008 May;39(5):1647-52. http://stroke.ahajournals.org/cgi/reprint/STROKEAHA.107.189063
342. Sacco RL, Adams R, Albers G, Alberts MJ, Benavente O, Furie K, Goldstein LB, Gorelick P, Halperin J, Harbaugh R, Johnston SC, Katzan I, Kelly-Hayes M, Kenton EJ, Marks M, Schwamm LH, Tomsick T. Guidelines for prevention of stroke in patients with ischemic stroke or transient ischemic attack: a statement for healthcare professionals from the American Heart Association/American Stroke Association Council on Stroke [trunc]. Stroke 2006 Feb;37(2):577-617.
343. Surgical management of the primary care **dental patient on warfarin** NHS Mar 2007: http://www.nelm.nhs.uk/en/NeLM-Area/Evidence/Medicines-Q--A/Surgical-management-of-the-primary-care-dental-patient-on-warfarin/
Warfarin Therapy - Management During Invasive Procedures and Surgery Oct 2010. http://www.bcguidelines.ca/pdf/warfarin_invasive.pdf
Lillis T, Ziakas A, Koskinas K, et al. Safety of Dental Extractions During Uninterrupted Single or Dual Antiplatelet Treatment. Am J Cardiol. 2011 Jul 22.
Ahmed I, Gertner E. Safety of arthrocentesis and joint injection in patients receiving anticoagulation at therapeutic levels. Am J Med. 2012 Mar;125(3):265-9.
344. Marik PE, Plante LA. **Venous thromboembolic disease and pregnancy**. N Engl J Med. 2008 Nov 6;359(19):2025-33.
345. Roy P, Bonello L, Torguson R, et al. Impact of nuisance **bleeding on clopidogrel** compliance in patients undergoing intracoronary drug-eluting stent implantation. Am J Cardiol 2008; 102:1614-1617. Overall, 11.1% of patients with nuisance bleeding discontinued clopidogrel. Greater education and follow-up in this patient subset may lead to improved compliance with clopidogrel therapy
346. Claassen DO, Kazemi N, Zubkov AY, Wijdicks EF, Rabinstein AA. **Restarting anticoagulation** therapy after warfarin-associated **intracerebral hemorrhage**. Arch Neurol. 2008 Oct;65(10):1313-8. In patients who resume warfarin after an intracranial hemorrhage (ICH) associated with warfarin, 22% will have serious rebleeding. However, in those who don't resume warfarin, 20% will have venous thromboembolic events. This study demonstrates that it is not easy to care for patients who take warfarin. (LOE = 2b-)
347. Collet JP, Hulot JS, Pena A, Villard E, Esteve JB, Silvain J, Payot L, Brugier D, Cayla G, Beygui F, Bensimon G, Funck-Brentano C, Montalescot G. Cytochrome P450 2C19 polymorphism in young patients treated with **clopidogrel after myocardial infarction**: a cohort study. Lancet. 2008 Dec 22. [Epub ahead of print] The **CYP2C19*2** genetic variant is a major determinant of prognosis in young patients who are receiving clopidogrel treatment after myocardial infarction.
348. Simon T, Verstuyft C, Mary-Krause M, Quteineh L, Drouet E, Méneveau N, Steg PG, Ferrières J, Danchin N, Becquemont L; the French Registry of Acute ST-Elevation and Non–ST-Elevation Myocardial Infarction (FAST-MI) Investigators. Genetic Determinants of Response to Clopidogrel and Cardiovascular Events. N Engl J Med. 2008 Dec 22. [Epub ahead of print] Among patients with an acute myocardial infarction who were receiving clopidogrel, those carrying **CYP2C19** loss-of-function alleles had a higher rate of subsequent cardiovascular events than those who were not. This effect was particularly marked among the patients undergoing percutaneous coronary intervention.
349. Mega JL, Close SL, Wiviott SD, Shen L, Hockett RD, Brandt JT, Walker JR, Antman EM, Macias W, et al. Cytochrome P-450 Polymorphisms and Response to Clopidogrel. N Engl J Med. 2008 Dec 22. [Epub ahead of print] Among persons treated with clopidogrel, carriers of a reduced-function **CYP2C19 allele** had significantly lower level of the active metabolite of clopidogrel, diminished platelet inhibition, and a higher rate of major adverse cardiovascular events, including stent thrombosis, than did noncarriers.
350. Andersen LV, Vestergaard P, Deichgraeber P, Lindholt JS, Mortensen LS, Frost L. Warfarin for the prevention of systemic embolism in patients with **non-valvular atrial fibrillation**: a meta-analysis. Heart. 2008 Dec;94(12):1607-13. Epub 2008 Jan 20. **Warfarin** not only reduces the risk of stroke but is better than placebo and antiplatelet agents in prevention of systemic embolism in patients with non-valvular AF. Warfarin increases the risk of major bleeding compared with placebo but not compared with antiplatelet agents.
351. Pradhan AD, Cook NR, Manson JE, Ridker PM, Buring JE. A randomized trial (WHS) of low-dose **aspirin in the prevention of clinical type 2 diabetes** in women. Diabetes Care. 2009 Jan;32(1):3-8. Epub 2008 Oct 3. These data suggest that long-term low-dose aspirin does not prevent the development of clinical type 2 diabetes in initially healthy women. These data suggest that long-term low-dose aspirin does not prevent the development of clinical type 2 diabetes in initially healthy women.
352. Gladstone DJ, Bui E, Fang J, et al. Potentially preventable strokes in high-risk patients with atrial fibrillation who are **not adequately anticoagulated**. Stroke. 2009 Jan;40(1):235-40. Epub 2008 Aug 28.
353. Lindsay P Bscn Phd, Bayley M Md, Hellings C Bsch, Hill M Msc Md, Woodbury E Bcom Mha, Phillips S Mbbs; (Canadian Stroke Strategy Best Practices and Standards Writing Group on behalf of the Canadian Stroke Strategy, a joint initiative of the Canadian Stroke Network and the Heart and Stroke Foundation of Canada*). **Canadian best practice recommendations for stroke care** (updated 2008). CMAJ. 2008 Dec 2;179(12):S1-S25. http://www.cmaj.ca/cgi/reprint/179/12/S1
354. Chassot PG, Delabays A, Spahn DR. **Perioperative** use of anti-platelet drugs. Best Pract Res Clin Anaesthesiol. 2007 Jun;21(2):241-56.
355. Juurlink DN, Gomes T, Ko D, et al. A population-based study of the drug interaction between proton pump inhibitors and clopidogrel. CMAJ 2009;180(7). DOI:10.1503/cmaj.082001. (RxFiles Jan/09 PPIs May Reduce Effectiveness Of Clopidogrel)
356. Eckman MH, Rosand J, Greenberg SM, Gage BF. Cost-effectiveness of using pharmacogenetic information in warfarin dosing for patients with nonvalvular atrial fibrillation. Ann Intern Med. 2009 Jan 20;150(2):73-83.
Warfarin-related **genotyping** is unlikely to be cost-effective for typical patients with nonvalvular atrial fibrillation, but may be cost-effective in patients at high risk for hemorrhage who are starting warfarin therapy.
357. Hacke W, et al. Thrombolysis with alteplase 3 to 4.5 hours after acute ischemic stroke. N Engl J Med. 2008 Sep 25;359(13):1317-29. As compared with placebo, intravenous **alteplase administered between 3 and 4.5 hours after** the onset of symptoms significantly improved clinical outcomes in patients with acute ischemic stroke; alteplase was more frequently associated with symptomatic intracranial hemorrhage.
358. Sibbing D, Stegherr J, Latz W, et al. Cytochrome P450 2C19 loss-of-function polymorphism and stent thrombosis following percutaneous coronary intervention. Eur Heart J 2009; DOIi:10.1093/eurheartj/ehp041. Available at: http://eurheartj.oxfordjournals.org.
359. Young AM, Billingham LJ, Begum G, et al. WARP Collaborative Group, UK. **Warfarin** thromboprophylaxis in cancer patients with central venous catheters (**WARP**): an open-label randomised trial. Lancet. 2009 Feb 14;373(9663):567-74. The findings show that prophylactic warfarin compared with no warfarin is not associated with a reduction in symptomatic catheter-related or other thromboses in patients with **cancer** and therefore we should consider newer treatments.
360. Crowther MA, Ageno W, Garcia D, et al. Oral **Vitamin K** Versus Placebo to Correct Excessive Anticoagulation in Patients Receiving Warfarin: A Randomized Trial. Ann Intern Med. 2009 Mar 3;150(5):293-300. Low-dose oral vitamin K did not reduce bleeding in warfarin recipients with INRs of 4.5 to 10.0.
361. **International Warfarin Pharmacogenetics Consortium**, Klein TE, Altman RB, Eriksson N, Gage BF, et al. Estimation of the **warfarin dose with clinical and pharmacogenetic data**. N Engl J Med. 2009 Feb 19;360(8):753-64.
362. Schnabel RB, Sullivan LM, Levy D, Pencina MJ, et al. Development of a **risk score for atrial fibrillation** (Framingham Heart Study): a community-based cohort study. Lancet. 2009 Feb 28;373(9665):739-45. From clinical factors readily accessible in primary care, our risk score could help to identify risk of atrial fibrillation for individuals in the community, assess technologies or markers for improvement of risk prediction, and target high-risk individuals for preventive measures.
363. Berger JS, Brown DL, et al. **Aspirin use, dose**, and clinical outcomes in postmenopausal women with stable cardiovascular disease--the Women's Health Initiative Observational Study. (WHI Observational Study) *Circ Cardiovasc Qual Outcomes* 2009; 2:78-87.
364. US Preventive Services Task Force. **Aspirin for the prevention** of cardiovascular disease: US Preventive Services Task Force recommendation statement. *Ann Intern Med* 2009; 150:396-404. http://www.ahrq.gov/clinic/uspstf/uspsasmi.htm
Wolff T, Miller T, Ko S. USPSTF. Aspirin for the primary prevention of cardiovascular events: an update of the **evidence** for the U.S. Preventive Services Task Force. Ann Intern Med. 2009 Mar 17;150(6):405-10.
365. Amarenco P, Labreuche J. Lipid management in the prevention of stroke: Review and updated meta-analysis of **statins** for stroke prevention. Lancet Neurol 2009; 8:453-463.
366. van Walraven C, Hart RG, Connolly S, et al. Effect of **age** on stroke prevention therapy in patients with atrial fibrillation: the atrial fibrillation investigators. Stroke. 2009 Apr;40(4):1410-6. Epub 2009 Jan 29.
367. Desai NR, Mega JL, Jiang S, et al. Interaction between cigarette **smoking** and clinical benefit of **clopidogrel**. J Am Coll Cardiol 2009; 53:1273-1278.
368. Chua D, Ignaszewski A. **Clopidogrel in acute coronary syndromes**. BMJ. 2009 Apr 14;338:b1180. doi: 10.1136/bmj.b1180.
369. Mahmoodi BK et al. **Microalbuminuria** and the risk of venous thromboembolism. JAMA 2009 May 6; 301:1790.
370. Sansing LH, Messe SR, Cucchiara BL, Cohen SN, Lyden PD, Kasner SE; CHANT Investigators. Prior antiplatelet use does not affect **hemorrhage growth** or outcome after **ICH**. Neurology. 2009 Apr 21;72(16):1397-402. Epub 2009 Jan 7.
371. Prandoni P, Prins MH, Lensing AW, et al. AESOPUS Investigators. Residual thrombosis on **ultrasonography to guide the duration** of anticoagulation in patients with deep venous thrombosis: a randomized trial. Ann Intern Med. 2009 May 5;150(9):577-85.
372. Berger JS, Krantz MJ, Kittelson JM, Hiatt WR. **Aspirin** for the prevention of cardiovascular events in patients with **peripheral artery disease (PAD)**: a meta-analysis of randomized trials. JAMA. 2009;301(18):1909-1919.
373. The ACTIVE Investigators. Effect of Clopidogrel Added to Aspirin in Patients with Atrial Fibrillation. (**Active A**) N Engl J Med. 2009 Apr 3. [Epub ahead of print] In patients with atrial fibrillation for whom vitamin K-antagonist therapy was unsuitable, the addition of clopidogrel to aspirin reduced the risk of major vascular events, especially stroke, and increased the risk of major hemorrhage. That in 1000 of AF patients treated for 3 years, 28 strokes would be prevented, 17 of which would be fatal or disabling, and 6 myocardial infarctions (MIs), at the cost of 20 nonstroke major bleeds, 3 of which would be fatal.
Connolly SJ, Eikelboom JW, Ng J, Hirsh J, Yusuf S, Pogue J, et al; on behalf of the **ACTIVE** Steering Committee and Investigators. Net clinical benefit of adding **clopidogrel to aspirin** therapy in patients with atrial fibrillation for whom **vitamin K antagonists are unsuitable**. Ann Intern Med. 2011;155:579-86.
374. Toyoda K. Pharmacotherapy for the **secondary prevention of stroke**. Drugs. 2009;69(6):633-47. doi: 10.2165/00003495-200969060-00001.
375. Massie BM, Collins JF, Ammon SE, et al. **WATCH** Trial Investigators. Randomized trial of warfarin, aspirin, and clopidogrel in patients with chronic heart failure: the Warfarin and Antiplatelet Therapy in Chronic Heart Failure (WATCH) trial. Circulation. 2009 Mar 31;119(12):1616-24. Epub 2009 Mar 16. n=1587. The primary outcome measure and the mortality data do not support the primary hypotheses that warfarin is superior to aspirin and that clopidogrel is superior to aspirin.
376. Dixon BS, Beck GJ, Vazquez MA, et al.; the DAC Study Group. Effect of **Dipyridamole plus Aspirin** on **Hemodialysis Graft Patency**. N Engl J Med. 2009 May 21;360(21):2191-2201. Treatment with dipyridamole plus aspirin had a significant but modest effect in reducing the risk of stenosis and improving the duration of primary unassisted patency of newly created grafts.
Haskal ZJ, Trerotola S, Dolmatch B, Schuman E, Altman S, Mietling S, Berman S, McLennan G, Trimmer C, Ross J, Vesely T. **Stent Graft** versus Balloon Angioplasty for Failing Dialysis-Access Grafts. N Engl J Med. 2010 Feb 11;362(6):494-503.
377. Adhiyaman V, Adhiyaman S. **Transient ischaemic attack**. BMJ. 2009 Mar 23;338:a2343. doi: 10.1136/bmj.a2343.
378. Friedland S, et al. **Colonoscopic polypectomy** in anticoagulated patients. World J Gastroenterol. 2009 Apr 28;15(16):1973-6. Polypectomy can be performed in therapeutically anticoagulated patients with lesions up to 1 cm in size with an acceptable bleeding rate.
379. Milionis HJ, Giannopoulos S, Kosmidou M, et al. **Statin therapy after first stroke** reduces 10-year stroke recurrence and improves survival. Neurology 2009; 72:1816-1822.
380. Collins R et al. for the Antithrombotic Trialists' (ATT) Collaboration. **Aspirin in the primary and secondary prevention** of vascular disease: Collaborative meta-analysis of individual participant data from randomised trials. Lancet 2009 May 30; 373:1849.
381. Montalescot G et al. **Prasugrel** compared with clopidogrel in patients undergoing percutaneous coronary intervention for ST-elevation myocardial infarction (TRITON-TIMI 38): Double-blind, randomised controlled trial. Lancet 2009 Feb 28; 373:723.
382. Wiviott SD, Trenk D, Frelinger AL, O'Donoghue M, et al.; PRINCIPLE-TIMI 44 Investigators. Prasugrel compared with high loading- and maintenance-dose clopidogrel in patients with planned percutaneous coronary intervention: the Prasugrel in Comparison to Clopidogrel for Inhibition of Platelet Activation and Aggregation-Thrombolysis in Myocardial Infarction 44 trial. Circulation. 2007 Dec 18;116(25):2923-32. Epub 2007 Dec 3.
383. Chandratheva A, Mehta Z, Geraghty OC, et al. Oxford Vascular Study. Population-based study of risk and predictors of **stroke in the first few hours after a TIA**. Neurology. 2009 Jun 2;72(22):1941-7. 384. Bousser MG. Antithrombotic agents in the prevention of ischemic stroke. Cerebrovasc Dis. 2009;27 Suppl 3:12-9. Epub 2009 May 14.
384. Usman MH, Notaro LA, Nagarakanti R, et al. Combination antiplatelet therapy for secondary stroke prevention: enhanced efficacy or double trouble?. Am J Cardiol. 2009 Apr 15;103(8):1107-12. Epub 2009 Mar 4. In conclusion, the combination of aspirin and clopidogrel is associated with significantly **greater bleeding than** either aspirin (< or =325 mg/day) or clopidogrel alone. Aspirin plus ER-DP has a greater bleeding rate than clopidogrel but a lower rate than aspirin (< or =325 mg/day) alone.
385. Subherwal S, Bach RG, Chen AY, et al. Baseline risk of major bleeding in non-ST-segment-elevation myocardial infarction: the **CRUSADE** (Can Rapid risk stratification of Unstable

angina patients Suppress Adverse outcomes with Early implementation of the ACC/AHA Guidelines) **Bleeding Score**. Circulation. 2009 Apr 14;119(14):1873-82. Epub 2009 Mar 30.
386. Cohen M. Expanding the recognition and assessment of **bleeding events** associated with antiplatelet therapy in primary care. Mayo Clin Proc. 2009 Feb;84(2):149-60.
387. Del Zoppo GJ, Saver JL, Jauch EC, Adams HP Jr; on behalf of the American Heart Association Stroke Council. Expansion of the Time Window for Treatment of Acute Ischemic Stroke With Intravenous **Tissue Plasminogen Activator**. A Science Advisory From the American Heart Association/American Stroke Association. Stroke. 2009 May 28. [Epub ahead of print]
388. Holmes DR, Kereiakes DJ, Kleiman NS, et al. **Combining antiplatelet and anticoagulant therapies**. J Am Coll Cardiol 2009; 54:95-109.
389. Mega JL, Braunwald E, et al.; **ATLAS ACS-TIMI 46** study group. **Rivaroxaban** versus placebo in patients with acute coronary syndromes (ATLAS ACS-TIMI 46): a randomised, double-blind, phase II trial. Lancet. 2009 Jul 4;374(9683):29-38. Epub 2009 Jun 17.
390. CLOTS Trials Collaboration, Dennis M, Sandercock PA, et al. Effectiveness of thigh-length graduated **compression stockings** to reduce the risk of deep vein thrombosis after stroke (CLOTS trial 1): a multicentre, randomised controlled trial. Lancet. 2009 Jun 6;373(9679):1958-65. Epub 2009 May 26. These data do not lend support to the use of thigh-length GCS in patients admitted to hospital with **acute stroke**. National guidelines for stroke might need to be revised on the basis of these results.
391. Lind M, Boman K, Johansson L, et al. **Thrombomodulin** as a marker for bleeding complications during warfarin treatment. Arch Intern Med. 2009 Jul 13;169(13):1210-5.
392. Tischenko A, Gula LJ, Yee R, et al. **Implantation of cardiac rhythm devices** without interruption of oral anticoagulation compared with perioperative bridging with low-molecular weight heparin. Am Heart J 2009; 158:252-256.
393. Hermida RC, Ayala DE, Mojón A, Fernández JR. Ambulatory blood pressure control with **bedtime aspirin** administration in subjects with prehypertension. Am J Hypertens. 2009 Aug;22(8):896-903. Epub 2009 Apr 30.
394. Geersing GJ, Janssen KJ, Oudega R, Bax L, Hoes AW, Reitsma JB, Moons KG. Excluding venous thromboembolism using point of care **D-dimer** tests in outpatients: a diagnostic meta-analysis. BMJ. 2009 Aug 14;339:b2990.
395. Chan AT, Ogino S, Fuchs CS. Aspirin use and survival after diagnosis of **colorectal cancer**. JAMA. 2009 Aug 12;302(6):649-58. Regular aspirin use after the diagnosis of colorectal cancer is associated with lower risk of colorectal cancer-specific and overall mortality, especially among individuals with tumors that overexpress COX-2.
396. Shuldiner AR, O'Connell JR, Bliden KP, et al. Association of cytochrome P450 2C19 genotype with the antiplatelet effect and clinical efficacy of clopidogrel therapy (**PAPI**). JAMA 2009; 302: 849-858.
397. O'Donoghue ML, et al. Pharmacodynamic effect and clinical efficacy of clopidogrel and prasugrel with or without a proton-pump inhibitor: An analysis of two randomised trials. (**TRITON-TIMI 38 & PRINCIPLE-TIMI 44)** Lancet 2009; DOI:10.1016/S0140-6736(09)61525-7.
398. Connolly, Stuart J., Ezekowitz, Michael D., Yusuf, Salim, et al., the **RE-LY** Steering Committee and Investigators, Dabigatran versus Warfarin in Patients with Atrial Fibrillation**.** N Engl J Med 2009 0: NEJMoa0905561. In patients with atrial fibrillation, dabigatran given at a dose of 110 mg was associated with rates of stroke and systemic embolism that were similar to those associated with warfarin, as well as lower rates of major hemorrhage. Dabigatran administered at a dose of 150 mg, as compared with warfarin, was associated with lower rates of stroke and systemic embolism but similar rates of major hemorrhage.
Wallentin L et al. Efficacy and safety of dabigatran compared with warfarin at different levels of international normalised ratio control for stroke prevention in atrial fibrillation: An analysis of the RE-LY trial. Lancet 2010 Aug 29; [e-pub ahead of print].
Diener HC, Connolly SJ, Ezekowitz MD, et al. Dabigatran compared with warfarin in patients with atrial fibrillation and previous transient ischaemic attack or stroke: a subgroup analysis of the RE-LY trial. Lancet Neurol. 2010 Nov 6.
Hohnloser SH, Oldgren J, Yang S, et al. Myocardial ischemic events in patients with atrial fibrillation treated with dabigatran or warfarin in the RE-LY trial. Circulation 2012.
399. Chan KE, Lazarus JM, Thadhani R, Hakim RM. Anticoagulant and antiplatelet usage associates with mortality among **hemodialysis** patients. J Am Soc Nephrol. 2009 Apr;20(4):872-81. Epub 2009 Mar 18.
400. Wallentin L, Becker RC, Budaj A, et al. **PLATO** Investigators. **Ticagrelor** versus Clopidogrel in Patients with **Acute Coronary Syndromes**. N Engl J Med. 2009 Aug 30. (1º NNT=53/1yr, Major bleed non-CABG:including fatal intracranial NNH=143/1yr)
401. Holmes DR Jr, Kereiakes DJ, Kleiman NS, Moliterno DJ, Patti G, Grines CL. **Combining antiplatelet and anticoagulant** therapies. J Am Coll Cardiol. 2009 Jul 7;54(2):95-109.
402. Singer DE, Chang Y, Fang MC, et al. The **net clinical benefit of warfarin** anticoagulation in atrial fibrillation. Ann Intern Med 2009; 151: 297-305.
403. Bezemer ID, van der Meer FJ, Eikenboom JC, et al. The value of **family history** as a risk indicator for venous thrombosis. Arch Intern Med. 2009 Mar 23;169(6):610-5.
404. Oake N, van Walraven C, Rodger MA, Forster AJ. Effect of an **interactive voice** response system on oral **anticoagulant management**. CMAJ. 2009 Apr 28;180(9):927-33.
405. De Berardis G, Sacco M, Strippoli GF, et al. **Aspirin for primary prevention** of cardiovascular events in people with diabetes: meta-analysis of randomised controlled trials. BMJ. 2009 Nov 6;339:b4531. doi: 10.1136/bmj.b4531.
Calvin AD, Aggarwal NR, Murad MH, et al. **Aspirin** for the Primary Prevention of Cardiovascular Events: A systematic review and meta-analysis comparing patients with and without **diabetes**. Diabetes Care December 2009 32:2300-2306; doi:10.2337/dc09-1297.
Canadian 2008 Guidelines (Sept 2008): http://www.diabetes.ca/files/cpg2008/cpg-2008.pdf
ADA- American Diabetes Association. Standards of Medical Care in Diabetes—**2011 Diabetes Care.** January 2011 34:S11-S61; doi:10.2337/dc11-S011. http://care.diabetesjournals.org/content/34/Supplement_1/S11.full.pdf+html
406. Berger JS, Bhatt DL, Cannon CP, et al. The relative efficacy and safety of **clopidogrel in women and men**. A sex-specific collaborative meta-analysis. J Am Coll Cardiol 2009; 54:1935-1945.
407. Tanzilli G, Greco C, et al. Effectiveness of two-year clopidogrel + aspirin in abolishing the risk of very late thrombosis after drug-eluting stent implantation (from the **TYCOON** [two-year ClOpidOgrel need] study). Am J Cardiol. 2009 Nov 15;104(10):1357-61.
408. Holmes DR, Reddy VY, Turi ZG, et al. Percutaneous closure of the **left atrial appendage** versus warfarin therapy for prevention of stroke in patients with atrial fibrillation: A randomised non-inferiority trial. Lancet 2009; 374:534-542.
409. Yinon Y, Siu SC, Warshafsky C, et al. Use of **low molecular weight Heparin in pregnant** women with mechanical heart valves. Am J Cardiol. 2009 Nov 1;104(9):1259-63. Epub 2009 Sep 16.
410. Strazzullo Pasquale, D'Elia Lanfranco, et al. **Salt** intake, stroke, and cardiovascular disease: meta-analysis of prospective studies. BMJ 2009;339:b4567, doi: 10.1136/bmj.b4567 (24 November 2009).
411. Sweetland Siân, Green Jane, Liu Bette, et al., on behalf of the **Million Women Study** collaborators. Duration and magnitude of the **postoperative risk** of venous thromboembolism in middle aged women: prospective cohort study. BMJ 2009;339:b4583, doi: 10.1136/bmj.b4583 (Published 3 December 2009)
412. **Thrombophillia testing**: may consider if neonatal thrombosis, recurrent thrombosis, first episode <40yr, family history esp if young first degree relative; Unusual presentation: cerebral, hepatic, mesenteric, or renal; or if warfarin skin necrosis; unexplained high PTT; or recurrent fetal loss, ITP, or SLE. Test may include: Antithrombin III measurement, Protein C antigen, Protein C activity, Protein S, Activated protein C resistance, antiphospholipid antibodies & lupus anticoagulant.
(Said JM et al. Inherited thrombophilia polymorphisms and pregnancy outcomes in nulliparous women. Obstet Gynecol 2010 Jan; 115:5.)
Shaheen K, Alraies MC, Alraiyes AH, et al. Factor V Leiden: How great is the risk of venous thromboembolism? Cleve Clin J Med. 2012 Apr;79(4):265-72.
Chong LY, Fenu E, Stansby G, Hodgkinson S; on behalf of the Guideline Development Group. Management of venous thromboembolic diseases and the role of thrombophilia testing: summary of NICE guidance. BMJ. 2012 Jun 27;344:e3979.
Cohoon KP, Heit JA. Inherited and secondary thrombophilia. Circulation. 2014 Jan 14;129(2):254-7.
MacCallum P, Bowles L, Keeling D. Diagnosis and management of **heritable thrombophilias**. BMJ. 2014 Jul 17;349:g4387.
Piazza G. **Thrombophilia Testing**, Recurrent Thrombosis, and Women's Health. Circulation. 2014 Jul 15;130(3):283-7.
Tseng E, Selby R. Testing for heritable thrombophilia in acute venous thromboembolism. CMAJ. 2017 Jul 4;189(26):E891.
Gupta A, Johnson DH, Nagalla S. **Antiphospholipid Antibodies**. JAMA. 2017 Sep 12;318(10):959-960.
Connors JM. **Thrombophilia Testing and Venous Thrombosis**. N Engl J Med. 2017 Sep 21;377(12):1177-1187.
413. Schulman, Sam, Kearon, Clive, Kakkar, Ajay K., et al. the **RE-COVER** Study Group, Dabigatran versus Warfarin in the Treatment of Acute Venous Thromboembolism. N Engl J Med 2009 0: NEJMoa0906598 (Online Dec/09)
414. Sung JJ, Lau JY, Ching JY, et al. **Continuation of Low-Dose Aspirin in Peptic Ulcer Bleeding**: A Randomized Trial. Ann Intern Med. 2009 Nov 30. [Epub ahead of print]
Chan FK, Leung Ki EL, Wong GL, Ching et al. Risks of **Bleeding Recurrence and Cardiovascular Events With Continued Aspirin Use After Lower Gastrointestinal Hemorrhage**. Gastroenterology. 2016 Aug;151(2):271-7.
415. Ay, H., Gungor, L., Arsava, E. M., et al. A **score** to predict **early risk of recurrence after ischemic stroke**. Neurology 2009 0: WNL.0b013e3181ca9cff.
A new tool to assess 90-day risk for ischemic stroke recurrence, the RRE-90 might help clinicians identify patients most in need of prompt follow-up. **RRE-90** (http://www.nmr.mgh.harvard.edu/RRE/
Tsivgoulis G et al. Multicenter external validation of the **ABCD2** score in triaging TIA patients. Neurology 2010 Apr 27; 74:1351.
Sheehan OC, Kyne L, Kelly LA, et al. Population-based study of **ABCD2** score, carotid stenosis, and atrial fibrillation for early stroke prediction after transient ischemic attack: the North Dublin TIA study. Stroke. 2010 May;41(5):844-50. Epub 2010 Mar 18.
Chandratheva A, Geraghty OC, Luengo-Fernandez R, et al. **ABCD2** score predicts severity rather than risk of early recurrent events after transient ischemic attack. Stroke. 2010 May;41(5):851-6.
Wijnhoud AD, Maasland L, Lingsma HF, et al. Prediction of major vascular events in patients with transient ischemic attack or ischemic stroke: a **comparison of 7 models**. Stroke. 2010 Oct;41(10):2178-85.
Merwick A, Albers GW, Amarenco P, et al. Addition of **brain and carotid imaging to the ABCD² score** to identify patients at early risk of stroke after transient ischaemic attack: a multicentre observational study. Lancet Neurol. 2010 Nov;9(11):1060-9.
Saposnik G, Kapral MK, Liu Y, et al; on behalf of the Investigators of the Registry of the Canadian Stroke Network and the Stroke Outcomes Research Canada (SORCan) Working Group. **IScore**: A Risk Score to Predict Death Early After Hospitalization for an Acute Ischemic Stroke. Circulation. 2011 Feb 22;123(7):739-749.
Perry JJ, Sharma M, Sivilotti ML, et al. Prospective validation of the **ABCD2 score** for patients in the emergency department with transient ischemic attack. CMAJ. 2011 Jul 12;183(10):1137-45.
Galvin R, Geraghty C, Motterlini N, et al. Prognostic value of the **ABCD(2)** clinical prediction rule: a systematic review and meta-analysis. Fam Pract. 2011 Aug;28(4):366-76.
Giles MF, Albers GW, Amarenco P, et al. Early stroke risk and **ABCD2 score** performance in tissue- vs time-defined TIA: A multicenter study. Neurology. 2011 Sep 27;77(13):1222-8.
Cancelli I, Janes F, Gigli GL, et al. Incidence of transient ischemic attack and early stroke risk: validation of the **ABCD2 score** in an Italian population-based study. Stroke. 2011 Oct;42(10):2751-7.
Sanders LM, Srikanth VK, Blacker DJ, et al. Performance of the **ABCD2** score for stroke risk post TIA: Meta-analysis and probability modeling. Neurology. 2012 Sep 4;79(10):971-80.
Hippisley-Cox J, Coupland C, Brindle P. Derivation and validation of **Qstroke score** for predicting risk of ischaemic stroke in primary care and comparison with other risk scores: a prospective open cohort study. BMJ. 2013 May 2;346:f2573.
416. Banerjee S, Brown A, Hutton B, McGahan L, Asakawa K, Clark M, Severn M, Cox JL, Sharma M. Clopidogrel versus Other Antiplatelet Agents in the Secondary Prevention of Vascular Events in Adults with Cerebrovascular Disease: Clinical and Cost-Effectiveness Analyses. [Technology report number 123]. Ottawa: Canadian Agency for Drugs and Technologies in Health; 2009.
417. Wardlaw JM, Murray V, Berge E, et al. **Thrombolysis** for acute ischaemic stroke. Cochrane Database Syst Rev. 2009 Oct 7;(4):CD000213.
418. Sørensen R, Hansen ML, Abildstrom SZ, et al. Risk of **bleeding** in patients with acute myocardial infarction treated with different combinations of aspirin, clopidogrel, and vitamin K antagonists in Denmark: a retrospective analysis of nationwide registry data. Lancet. 2009 Dec 12;374(9706):1967-74.
Hansen Morten L.; Sorensen Rikke; Clausen Mette T.; et al. Risk of Bleeding With Single, Dual, or Triple Therapy With Warfarin, Aspirin, and Clopidogrel in Patients With Atrial Fibrillation. Arch Intern Med. 2010;170(16):1433-1441. In patients with AF, all combinations of warfarin, aspirin, and clopidogrel are associated with increased risk of nonfatal and fatal bleeding. Dual warfarin and clopidogrel therapy and triple therapy carried a more than 3-fold higher risk than did warfarin monotherapy. In patients with atrial fibrillation, adding multiple-drug therapy to prevent thromboembolism can greatly increase the risk for major bleeding, according to an *Archives of Internal Medicine* study. Investigators used Danish national databases to follow bleeding outcomes in some 80,000 patients with a discharge diagnosis of first-time atrial fibrillation. All patients had at least one postdischarge prescription for warfarin, aspirin, or clopidogrel. After a follow-up averaging 3.3 years, the relative risks associated with various regimens for fatal and nonfatal bleeding, relative to warfarin monotherapy, were as follows: Aspirin, 0.96 , Clopidogrel, 1.45, Clopidogrel + aspirin, 1.91, Warfarin + aspirin= 1.75, Warfarin + clopidogrel= 3.57, Warfarin + clopidogrel + aspirin= 4.03.
Lamberts M, Olesen JB, Ruwald MH, et al. **Bleeding** after Initiation of Multiple Antithrombotic Drugs, Including **Triple Therapy**, in Atrial Fibrillation Patients Following Myocardial Infarction and Coronary Intervention: A Nationwide Cohort Study.

Circulation. 2012 Aug 6. (Compared with an anticoagulant plus antiplatelet monotherapy, triple antithrombotic therapy increased bleeding risk by ~ 40% without reducing risk for thrombotic events.)
419. Cheetham TC, Levy G, Niu F, Bixler F. Gastrointestinal safety of nonsteroidal antiinflammatory drugs and selective **cyclooxygenase-2** inhibitors in patients on warfarin. Ann Pharmacother. 2009 Nov;43(11):1765-73. Epub 2009 Oct 6.
420. Lewis HD Jr, Davis JW, Archibald DG, et al. Protective effects of **aspirin** against acute myocardial infarction and death in men with unstable angina. Results of a Veterans Administration Cooperative Study. N Engl J Med. 1983 Aug 18;309(7):396-403.
421. Bourjeily G, Paidas M, Khalil H, Rosene-Montella K, Rodger M. **Pulmonary embolism in pregnancy**. Lancet. 2009 Nov 2. [Epub ahead of print]
422. a) Barkun AN, Bardou M, Kuipers EJ, et al. and for the **International Consensus** Upper Gastrointestinal Bleeding Conference Group. Management of Patients With **Nonvariceal Upper Gastrointestinal Bleeding**. Ann Intern Med January 19, 2010 152:101-113.
b) Laine L, Jensen DM. ACG: Management of patients with ulcer bleeding. Am J Gastroenterol 2012 Mar;107(3):345-60.
Gralnek IM, Dumonceau JM, Kuipers EJ, et al. Diagnosis and management of nonvariceal upper gastrointestinal hemorrhage: European Society of Gastrointestinal Endoscopy (ESGE) Guideline. Endoscopy. 2015 Oct;47(10):a1-a46. (? **Restart ASA 1-3 days after**)
Strate LL and Gralnek IM.**ACG (American)** clinical guideline: **Management of patients with acute lower gastrointestinal bleeding**. *Am J Gastroenterol* 2016 Apr; 111:459
Li L,Geraghty OC, Mehta Z, Rothwell PM, on behalf of the Oxford Vascular Study. Age-specific risks, severity, time course, and outcome of bleeding on long-term antiplatelet (ASA) treatment after vascular events: a population-based cohort study. Lancet 2017; online June 5. (consider using PPI in older secondary CV prevention patients on aspirin)
Oakland K, Chadwick G, East JE, et al. Diagnosis and **management of acute lower Gastrointestinal bleeding: guidelines from the British Society of Gastroenterology (BSG)**. Gut. 2019 Feb 12.

423. Glader EL, Sjölander M, Eriksson M, Lundberg M. Persistent use of **secondary preventive drugs declines** rapidly during the first 2 years after stroke. Stroke 2010; DOI: 10.1161/STROKEAHA.109.566950.
424. Madhwal S, Lincoff AM, Rolston DDK. Should patients on long-term **warfarin take aspirin** for heart disease? Cleveland Clin J Med 2008;75:206-08.
425. National Institute for Health and Clinical Excellence (NICE). **Rivaroxaban** for the prevention of venous thromboembolism after total hip or total knee replacement in adults. London (UK): NICE; 2009 Apr. 23 p. (Technology appraisal guidance; no. 170).
426. Johnson Stacy A.; Stevens Scott M.; Woller Scott C.; et al. Risk of Deep Vein Thrombosis Following a Single Negative **Whole-Leg Compression Ultrasound**: A Systematic Review and Meta-analysis. JAMA. 2010;303(5):438-445.
427. Pai M, Douketis JD. **Preventing venous thromboembolism in long-term** care residents: Cautious advice based on limited data. Cleve Clin J Med. 2010 Feb;77(2):123-30.
428. Holmes, Michelle D., Chen, Wendy Y., Li, Lisa, et al. **Aspirin** Intake and Survival **After Breast Cancer**. J Clin Oncol 2010 0: JCO.2009.22.7918.
429. Breet NJ, van Werkum JW, Bouman HJ et al. Comparison of **platelet function tests** in predicting clinical outcome in patients undergoing coronary stent implantation. JAMA 2010; 303:754-762.
430. Hill J, Treasure T; National Clinical Guideline Centre for Acute and Chronic Conditions. **Reducing the risk of venous thromboembolism in patients admitted to hospital**: summary of **NICE** guidance. BMJ. 2010 Jan 27;340:c95. doi: 10.1136/bmj.c95.
NICE Jan 2010: Venous thromboembolism: reducing the risk Reducing the risk of venous thromboembolism (deep vein thrombosis and pulmonary embolism) in patients admitted to hospital. http://www.nice.org.uk/nicemedia/live/12695/47195/47195.pdf
431. Cannon CP, Harrington RA, James S, et al. Comparison of **ticagrelor** with clopidogrel in patients with a planned **invasive strategy** for acute coronary syndromes (PLATO): A randomised double-blind study Lancet 2009; DOI:10.1016/S0140-6736(09)62191-7.
432. Decousus H, Quéré I, Presles E, et al; POST (Prospective Observational Superficial Thrombophlebitis) Study Group. **Superficial** venous thrombosis and venous thromboembolism: a large, prospective epidemiologic study. Ann Intern Med. 2010Feb16;152(4):218-24.
433. Fowkes FGR, Price JF, Steward MCW, et al. **Aspirin** for prevention of cardiovascular events in a general population screened for a low **ankle brachial index**. A randomized controlled trial. (**AAA**) JAMA 2010; 303:841-848.
434. Prabhakaran Shyam; Rivolta Juan; Vieira Julio R.; et al. Symptomatic **Intracerebral Hemorrhage** Among Eligible **Warfarin**-Treated Patients Receiving Intravenous **Tissue Plasminogen Activator** for Acute Ischemic Stroke. Arch Neurol. 2010;0(2010):2010.25.
435. Mak A, Cheung MW, Cheak AA, Ho RC. Combination of **heparin and aspirin** is superior to aspirin alone in enhancing live births in patients with **recurrent pregnancy loss and positive anti-phospholipid antibodies**: a meta-analysis of randomized controlled trials and meta-regression. Rheumatology (Oxford). 2010 Feb;49(2):281-8. Epub 2009 Dec 4.
436. Gurbel PA, Bliden KP, Butler K, et al. Response to **Ticagrelor in Clopidogrel** Nonresponders and Responders and Effect of Switching Therapies. The **RESPOND** Study. Circulation. 2010 Mar 1.
437. Würtz M, Grove EL, Kristensen SD, Hvas AM. The antiplatelet effect of **aspirin is reduced by proton pump inhibitors** in patients with coronary artery disease. Heart. 2010 Mar;96(5):368-71. Epub 2009 Nov 11.
438. Snoep JD, Hovens MM, Pasha SM, Frölich M, Pijl H, Tamsma JT, Huisman MV. **Time-dependent** effects of low-dose **aspirin** on plasma renin activity, aldosterone, cortisol, and catecholamines. Hypertension. 2009 Nov;54(5):1136-42.
439. Sawhney MS, McDougall H, Nelson DB, Bond JH. Fecal **Occult Blood Test** in Patients on Low-Dose Aspirin, Warfarin, Clopidogrel, or Non-steroidal Anti-inflammatory Drugs. Dig Dis Sci. 2010 Mar 3. [Epub ahead of print] Anticoagulants and antiplatelet medications lower the positive-predictive-value of FOBT for advance colonic neoplasia and should be stopped if clinically feasible prior to stool collection.
440. Park SJ, Park DW, Kim YH, et al. Duration of **Dual Antiplatelet** Therapy after Implantation of Drug-Eluting Stents. (**Real-Late, Zest-Late-RCT**) N Engl J Med. 2010 Mar 15. n=2701, 19.2 months, Primary: clopidogrel + ASA 1.8% vs ASA 1.2% NS.
441. Kirtane AJ, Gupta A, Iyengar S, et al. Safety and efficacy of **drug-eluting and bare metal stents**: comprehensive meta-analysis of randomized trials and observational studies. Circulation. 2009 Jun 30;119(25):3198-206.
442. Hankey GJ, Eikelboom JW. **Antithrombotic** drugs for patients with **ischaemic stroke and transient ischaemic attack** to prevent recurrent major vascular events. Lancet Neurol. 2010 Mar;9(3):273-84.
443. International Carotid Stenting Study. Carotid artery **stenting** compared with **endarterectomy** in patients with symptomatic carotid stenosis (International Carotid Stenting Study-**ICSS**): an interim analysis of a randomised controlled trial. Lancet. 2010 Feb 25.
444. Diedler J, Ahmed N, Sykora M, et al. Safety of intravenous **thrombolysis for acute ischemic stroke** in patients receiving antiplatelet therapy at stroke onset. Stroke. 2010 Feb;41(2):288-94. Epub 2010 Jan 7.
445. Kaandorp, Stef P., Goddijn, Mariette, van der Post, Joris A.M., et al. Aspirin plus Heparin or Aspirin Alone in Women with **Recurrent Miscarriage**. N Engl J Med 2010 0: NEJMoa1000641.
Neither aspirin combined with nadroparin nor aspirin alone improved the live-birth rate, as compared with **placebo**, among women with unexplained recurrent miscarriage.
446. Chan, Wee-Shian, Spencer, Frederick A, Ginsberg, Jeffrey S. **Anatomic distribution of deep vein thrombosis in pregnancy**. CMAJ 2010 0: cmaj.091692.
447. Seshadri S, Beiser A, Pikula A, et al. **Parental occurrence of stroke** and risk of stroke in their **children**: the Framingham study. Circulation 2010; 121:1304-1312.
448. Fischer HD, Juurlink DN, Mamdani MM, et al. **Hemorrhage during warfarin therapy associated with cotrimoxazole** and other urinary tract anti-infective agents: A population-based study. Arch Intern Med 2010; 170:617-621.
449. American College of Obstetricians and Gynecologists Committee on Practice Bulletins-Obstetrics. ACOG Practice Bulletin No. 111: **Inherited thrombophilias in pregnancy**. Obstet Gynecol. 2010 Apr;115(4):877-87. (& **2011 Sep**.)
450. Stockl Karen M.; Le Lisa; Zakharyan Armen; et al. Risk of Rehospitalization for Patients Using **Clopidogrel With a Proton Pump Inhibitor**. Arch Intern Med. 2010;170(8):704-710.
451. Ho PM, Tsai TT, Maddox TM, et al. **Delays in filling clopidogrel** prescription after hospital discharge and adverse outcomes after drug-eluting stent implantation. Implications for transitions of care. Circ Cardiovasc Qual Outcomes 2010.
452. Schelleman H, Bilker WB, Brensinger CM, et al. **Fibrate/statin initiation in warfarin** users and gastrointestinal bleeding risk. Am J Med. 2010 Feb;123(2):151-7.
453. Di Sciascio G, Patti G, Pasceri V, et al. **Clopidogrel** reloading in patients undergoing percutaneous coronary intervention on chronic clopidogrel therapy: results of the **ARMYDA-4 RELOAD** (Antiplatelet Therapy for Reduction of Myocardial Damage During Angioplasty) randomized trial. Eur Heart J 2010
454. Salazar CA, Malaga G, Malasquez G. **Direct thrombin inhibitors versus vitamin K antagonists or low molecular weight heparins** for prevention of venous thromboembolism following total hip or knee replacement. Cochrane Database Syst Rev. 2010 Apr 14;4:CD005981.
455. Søgaard KK, Horváth-Puhó E, Grønbaek H, Jepsen P, Vilstrup H, Sørensen HT. Risk of **venous thromboembolism in patients with liver disease**: a nationwide population-based case-control study. Am J Gastroenterol. 2009 Jan;104(1):96-101.
456. Garcia-Alamino JM, Ward AM, Alonso-Coello P, et al. **Self-monitoring** and self-management of oral anticoagulation. Cochrane Database Syst Rev. 2010 Apr 14;4:CD003839.
457. Meyer G, Roy PM, Gilberg S, Perrier A. **Pulmonary embolism**. BMJ. 2010 Apr 13;340:c1421. doi: 10.1136/bmj.c1421.
Agnelli, Giancarlo, Becattini, Cecilia. **Acute Pulmonary Embolism**. N Engl J Med 2010 363: 266-274.
458. Brott, Thomas G., Hobson, Robert W., II, Howard, George, et al. the **CREST** Investigators, **Stenting versus Endarterectomy** for Treatment of Carotid-Artery Stenosis. N Engl J Med 2010 0: NEJMoa0912321.
459. Cohen Danielle, Berger Stefan P, Steup-Beekman Gerda M et al., Diagnosis and management of the **antiphospholipid syndrome**. BMJ 2010;340
460. Lovelock CE, Cordonnier C, Naka H, et al. Antithrombotic Drug Use, **Cerebral Microbleeds**, and **Intracerebral Hemorrhage**: A Systematic Review of Published and Unpublished Studies. Stroke. 2010 Jun;41(6):1222-1228. Epub 2010 Apr 29
461. Gutierrez A, Rao SV. Incidence, outcomes, and management of **bleeding** in non-ST-elevation acute coronary syndromes Cleveland Clinic Journal of Medicine 2010; 77(6):369-379; doi:10.3949/ccjm.77a.09142.
462. ASGE Standards of Practice Committee, Anderson MA, Ben-Menachem T, Gan SI, et al. Management of antithrombotic agents for **endoscopic procedures**. Gastrointest Endosc 2009 Dec;70(6):1060-70.
463. Paikin Jeremy S., Wright Douglas S., Crowther Mark A. et al; **Triple Antithrombotic Therapy in Patients With Atrial Fibrillation and Coronary Artery Stents** Circulation 121: 2067-2070, doi:10.1161/CIRCULATIONAHA.109.924944
464. Varis J, Kuusniemi K, Järveläinen H. **Cholesterol microembolization syndrome**: a complication of anticoagulant therapy. CMAJ. 2010 Jun 15;182(9):931-3.
465. O'Donnell MJ, Xavier D, Liu Lisheng, et al; and on behalf of the **INTERSTROKE** investigators, Risk factors for ischaemic and intracerebral haemorrhagic stroke in 22 countries (the INTERSTROKE study): a case-control study, The Lancet, Online 17 June 2010
466. Mehran R, Pocock SJ, Nikolsky E et al. A **risk score to predict bleeding** in patients with acute coronary syndromes (**ACS**). J Am Coll Cardiol. 2010 Jun 8;55(23):2556-66.
Ducrocq G, Wallace JS, Baron G, et al; REACH Investigators. **Risk score to predict serious bleeding** in stable outpatients with or at risk of atherothrombosis. Eur Heart J. 2010;31:1257-65.
Pisters R, Lane DA, Nieuwlaat R, et al. A novel userfriendly score (**HAS-BLED**) to assess one-year risk of major bleeding in atrial fi brillation patients: The Euro Heart Survey. Chest 2010; published online March 18. DOI:10.1378/chest.10-013 4.
467. Runchey S, McGee S. Does this patient have a hemorrhagic stroke?: clinical findings distinguishing **hemorrhagic stroke from ischemic stroke**. JAMA. 2010 Jun 9;303(22):2280-6.
468. Crowther MA, Garcia D, Ageno W, et al. **Oral vitamin K** effectively treats international normalised ratio (**INR**) values in **excess of 10**. Results of a prospective cohort study. Thromb Haemost. 2010 May 10;104(1).
469. Garcia D, Crowther MA, Ageno W. **Practical management of coagulopathy associated with warfarin**. BMJ. 2010 Apr 19;340:c1813. doi: 10.1136/bmj.c1813.
470. Collins L, Seraj S. Diagnosis and treatment of **venous ulcers**. Am Fam Physician. 2010 Apr 15;81(8):989-96.
471. Floyd JS, Serebruany VL. **Prasugrel as a potential cancer** promoter: Review of unpublished data. Arch Intern Med 2010; 170:1078-1080.
472. Dodd JM, McLeod A, Windrim RC, et al. Antithrombotic therapy for improving maternal or infant health outcomes in women considered at **risk of placental dysfunction**. Cochrane Database Syst Rev. 2010 Jun 16;6:CD006780.
473. Hull Russell D., Schellong, Sebastian M. Tapson, Victor F. Et al.and for the EXCLAIM (Extended Prophylaxis for Venous ThromboEmbolism in Acutely Ill Medical Patients With Prolonged Immobilization) study. **Extended-Duration Venous Thromboembolism** Prophylaxis in Acutely Ill Medical Patients With Recently Reduced Mobility: A Randomized Trial. Ann Intern Med July 6, 2010 153:8-18. (see also ACPJC AnnIntMed Nov,2010)
474. Hulot JS, Collet JP, Silvain J, et al. Cardiovascular risk in **clopidogrel**-treated patients according to cytochrome **P450 2C19*2** loss-of-function allele or proton pump inhibitor co-administration. A systematic meta-analysis. J Am Coll Cardiol 2010; 56:134-143.
475. Carrier M, Le Gal G, Wells PS, Rodger MA. Systematic review: **case-fatality rates of recurrent venous thromboembolism and major bleeding events** among patients treated for venous thromboembolism. Ann Intern Med. 2010 May 4;152(9):578-89.
476. Iorio A, Basileo M, Marcucci M, et al. **Influenza vaccination and vitamin K antagonist** treatment: a placebo-controlled, randomized, double-blind crossover study. Arch Intern Med. 2010 Apr 12;170(7):609-16.
477. Lee M, Hong KS, Chang SC, et al. Efficacy of homocysteine-lowering therapy with **folic Acid in stroke prevention**: a meta-analysis. Stroke. 2010 Jun;41(6):1205-12. Epub 2010 Apr 22.
478. Bushnell CD.; Zimmer LO.; Pan W; et al. for the **Adherence** Evaluation After Ischemic Stroke-Longitudinal Investigators. Persistence With Stroke Prevention Medications 3 Months After Hospitalization. Arch Neurol. 2010;0(2010):archneurol.2010.190.

479. Holmes David R., Jr, Dehmer Gregory J., Kaul Sanjay, et al. **ACCF/AHA Clopidogrel** Clinical Alert: Approaches to the FDA "Boxed Warning" **Genetic variability**: A Report of the American College of Cardiology Foundation Task Force on Clinical Expert Consensus Documents and the American Heart Association. Circulation 122: 537-557.
480. Iles-Shih L, Collins JF, Holub JL, Lieberman DA. Prevalence of Significant **Neoplasia in FOBT-Positive Patients** on Warfarin Compared With Those Not on Warfarin. Am J Gastroenterol. 2010 Aug 3.
481. Kobayashi H. Evaluation of the need to discontinue antiplatelet and anticoagulant medications before **cataract surgery**. J Cataract Refract Surg. 2010. Jul;36(7):1115-9.
482. Bujold E, Roberge S, Lacasse Y, et al. Prevention of **preeclampsia and intrauterine growth restriction with aspirin** started in early pregnancy: a meta-analysis. Obstet Gynecol. 2010 Aug;116(2 Pt 1):402-14. Low-dose aspirin initiated in early pregnancy is an efficient method of reducing the incidence of preeclampsia and IUGR.
483. Sachdeva A, Dalton M, Amaragiri SV, et al. **Elastic compression stockings** for prevention of deep vein thrombosis. Cochrane Database Syst Rev. 2010 Jul 7;7:CD001484. GCS are effective in diminishing the risk of DVT in hospitalised patients. Data examination also suggests that GCS on a background of another method of prophylaxis is more effective than GCS on its own.
484. Wallentin L et al. Efficacy and safety of **dabigatran** compared with warfarin at different levels of international normalised ratio control for stroke prevention in atrial fibrillation: An analysis of the RE-LY trial. Lancet 2010 Aug 29; [e-pub ahead of print].
485. Bellemain-Appaix A, Brieger D, Beygui F. **New P2Y12 inhibitors versus clopidogrel** in percutaneous coronary intervention. J Am Coll Cardiol 2010; DOI:10.1016/j.jacc.2010.07.012.
486. Paré G, Mehta SR, Yusuf S, et al. Effects of **CYP2C19 genotype** on clopidogrel treatment in CURE and ACTIVE. N Eng J Med 2010; DOI: 10.1056/NEJMoal008410.
487. Smith SB, Geske JB, Maguire JM, Zane NA, Carter RE, Morgenthaler TI. **Early anticoagulation** is associated with reduced mortality for acute pulmonary embolism. Chest. 2010 Jun;137(6):1382-90.
488. **CURRENT–OASIS 7** Investigators. 1. Dose comparisons of clopidogrel and aspirin in acute coronary syndromes. N Engl J Med 2010;363:930-42.
489. Cooper K, Squires H, Carroll C, et al. **Chemoprevention of colorectal cancer**: systematic review and economic evaluation. Health Technol Assess. 2010 Jun;14(32):1-206. (Especially aspirin & celecoxib reviewed)
490. Medical Letter- Treatment Guidelines. **Treatment of Atrial Fibrillation**. Sept 2010. Updated July 2014.
491. Din FVN et al. Effect of **aspirin and NSAIDs on risk and survival from colorectal cancer**. Gut 2010 Sep 15; [e-pub ahead of print].
492. Routine **Aspirin or Nonsteroidal Anti-inflammatory Drugs for the Primary Prevention of Colorectal Cancer**, Topic Page. March 2007. U.S. Preventive Services Task Force. http://www.uspreventiveservicestaskforce.org/uspstf/uspsasco.htm
USPSTF recommends against the routine use of aspirin and nonsteroidal anti-inflammatory drugs (NSAIDs) to prevent colorectal cancer in individuals at average risk for colorectal cancer.
493. Bushnell CD, Zimmer LO, Pan W, et al.; for the **Adherence** Evaluation After Ischemic Stroke–Longitudinal Investigators. Persistence With Stroke Prevention Medications 3 Months After Hospitalization. Arch Neurol. 2010 Aug 9.
494. **CLOTS** (Clots in Legs Or sTockings after Stroke) Trial Collaboration. **Thigh-Length** Versus Below-Knee **Stockings** for Deep Venous Thrombosis Prophylaxis After Stroke: A Randomized Trial. *Ann Intern Med* ahead of print Sept 20, 2010.
495. Parker Chris, Coupland Carol, Hippisley-Cox Julia. **Antipsychotic drugs and risk of venous thromboembolism**: nested case-control study. BMJ 341:doi:10.1136/bmj.c4245 (especially if new user or atypical antipsychotic)
496. Bhatt DL et al. for the **COGENT** Investigators. **Clopidogrel with or without omeprazole** in coronary artery disease. N Engl J Med 2010 Oct 6; [e-pub ahead of print]. (http://www.nejm.org/doi/full/10.1056/NEJMoa1007964)
497. Smith EE, Shobha N, Dai D, et al. **Risk Score** for In-Hospital Ischemic Stroke Mortality Derived and Validated Within the Get With The Guidelines-Stroke Program. Circulation. 2010 Sep 27.
498. Clarke R. Halsey J, Lewington S, et al. Effects of lowering **homocystein levels with B vitamins** on cardiovascular disease, cancer, and cause-specific mortality. Meta-analysis of 8 randomized trials involving 37 485. Arch Intern Med 2010; 170:1622-1631.
499. Coutinho JM., Ferro JM., Canhão P, et al., and for the ISCVT Investigators. **Unfractionated or Low–Molecular** Weight Heparin for the Treatment of **Cerebral Venous Thrombosis**. Stroke published October 7, 2010, doi:10.1161/STROKEAHA.110.588822
500. Schellinger PD et al. Evidence-based guideline: Role of diffusion & perfusion **MRI** for the diagnosis of acute ischemic stroke. Report of the Therapeutics & Technology Assessment Subcommittee of American Academy of Neurology. Neurology 2010Jul 13; 75:177.
501. Furie Karen L., Kasner Scott E., Adams Robert J., et al., and on behalf of the American Heart Association Stroke Council, Council on Cardiovascular Nursing, Council on Clinical Cardiology, and Interdisciplinary Council on Quality of Care and Outcomes Research. Guidelines for the **Prevention of Stroke in Patients With Stroke or Transient Ischemic Attack** (Secondary Prevention). A Guideline for Healthcare Professionals From the American Heart Association (**AHA**) /American Stroke Association (**ASA**).
Stroke published October 21, 2010, doi:10.1161/STR.0b013e3181f7d043 http://stroke.ahajournals.org/cgi/reprint/STR.0b013e3181f7d043v1
502. Iorio Alfonso; Kearon Clive; Filippucci Esmeralda; et al. **Risk of Recurrence** After a First Episode of Symptomatic **Venous Thromboembolism** Provoked by a Transient Risk Factor: A Systematic Review. Arch Intern Med. 2010;170(19):1710-1716.
503. Ruiz-Irastorza Guillermo, Crowther Mark, Branch Ware, et al. **Antiphospholipid syndrome**, The Lancet, In Press, Corrected Proof, Available online 6 September 2010, ISSN 0140-6736, DOI: 10.1016/S0140-6736(10)60709-X.
504. Shinohara Yukito, Katayama Yasuo, Uchiyama Shinichiro, et al. and for the CSPS 2 group, **Cilostazol** for prevention of secondary stroke (**CSPS 2**): an aspirin-controlled, double-blind, randomised non-inferiority trial, The Lancet Neurology, Volume 9, Issue 10, October 2010, Pages 959-968, ISSN 1474-4422
505. Wiviott SD, Antman EM, Braunwald E. **Prasugrel**. Circulation. 2010 Jul 27;122(4):394-403.
506. Mega JL, Simon T, Collet JP, et al. **Reduced-function CYP2C19 genotype** and risk of adverse clinical outcomes among patients treated with **clopidogrel** predominantly for PCI. (Meta-analysis) JAMA 2010; 304:1821-1830.
507. Branch DW, Gibson M, Silver RM. Clinical practice. **Recurrent miscarriage**. N Engl J Med. 2010 Oct 28;363(18):1740-7.
508. Goldstein JN, Greenberg SM. **Should anticoagulation be resumed after intracerebral hemorrhage**? Cleveland Clinic Journal of Medicine 2010; 77(11):791-799; doi:10.3949/ccjm.77a.10018
509. Institute for Clinical Systems Improvement (**ICSI**). **Venous thromboembolism diagnosis and treatment**. Bloomington (MN): Institute for Clinical Systems Improvement (ICSI); 2010 Feb. 81 p.
510. Kong, Jae Cheol, Lee, Myeong Soo, Shin, Byung-Cheul, et al. **Acupuncture** for functional recovery after stroke: a systematic review of sham-controlled randomized clinical trials. CMAJ 2010 182: 1723-1729.
511. Rothwell PM, Wilson M, Elwin CE, et al. Long-term effect of **aspirin on colorectal cancer** incidence and mortality: 20-year follow-up of five randomised trials. Lancet. 2010 Oct 21.
Rothwell PM, Fowkes FG, Belch JF, Ogawa H, Warlow CP, Meade TW. Effect of daily **aspirin on long-term risk of death due to cancer**: analysis of individual patient data from randomised trials. Lancet. 2011 Jan 1;377(9759):31-41.
512. Kahn, Susan R., Shrier, Ian, Shapiro, Stan, et al. Six-month **exercise training** program to treat **post-thrombotic syndrome**: a randomized controlled two-centre trial. CMAJ 2010 0: cmaj.100248
Enden T, Haig Y, Kløw NE, et al. Long-term outcome after additional **catheter-directed thrombolysis versus standard treatment for acute iliofemoral deep vein thrombosis** (the **CaVenT** study): a randomized controlled trial. Lancet 2011
Prandoni P, Noventa F, Quintavalla R, et al. Thigh-length versus **below-knee** compression elastic stockings for prevention of the postthrombotic syndrome in patients with proximal-venous thrombosis: a randomized trial. Blood. 2012 Feb 9;119(6):1561-1565
513. Nishant K Mishra, Niaz Ahmed, Grethe Andersen, et al. , for the VISTA and SITS collaborators. **Thrombolysis in very elderly** people: controlled comparison of SITS International Stroke Thrombolysis Registry and Virtual International Stroke Trials Archive. BMJ 341:doi:10.1136/bmj.c6046 (Published 23 November 2010)
514. Toyoda K, Yasaka M, Uchiyama S, et al .; Bleeding with Antithrombotic Therapy (BAT) Study Group. **Blood pressure levels and bleeding** events during antithrombotic therapy: the Bleeding with Antithrombotic Therapy (BAT) Study. Stroke 2010;41:1440–4.
515. Carotid Stenting Trialists' Collaboration, Bonati LH, Dobson J, Algra A; et al. Short-term outcome after **stenting versus endarterectomy** for symptomatic carotid stenosis: a preplanned meta-analysis of individual patient data.Lancet.2010Sep 25;376(9746):1062-73.
516. Alshekhlee A, Mohammadi A, Mehta S, et al. Is **thrombolysis safe in the elderly**?: analysis of a national database. Stroke. 2010 Oct;41(10):2259-64. Epub 2010 Sep 9.
517. **EINSTEIN DVT** investigators. Oral **rivaroxaban** for symptomatic venous thromboembolism. N Engl J Med 2010; DOI:10.1056/NEJMoa1007903.
518. Kyrle Paul Alexander, Rosendaal Frits R, Eichinger Sabine. **Risk assessment for recurrent venous thrombosis**. The Lancet 04 December 2010(Article in Press DOI: 10.1016/S0140-6736(10)60962-2)
519. Brenner Hermann, Tao Sha, Haug Ulrike. Low-Dose **Aspirin Use** and Performance of Immunochemical **Fecal Occult Blood Tests**. JAMA. 2010;304(22):2513-2520.doi:10.1001/jama.2010.1773.
520. Thompson BB, Béjot Y, Caso V, et al. **Prior antiplatelet therapy** and outcome following **intracerebral hemorrhage**: a systematic review. Neurology. 2010 Oct 12;75(15):1333-42.
521. **ACCF- AHA-HRS Atrial Fibrillation 2011 Focused Update**. Circulation 2011. http://circ.ahajournals.org/cgi/reprint/CIR.0b013e3181fa3cf4v1
522. Banerjee S, Brown A, McGahan L, et al. **Clopidogrel** versus other antiplatelet agents for secondary prevention of vascular events in adults with **acute coronary syndrome or peripheral vascular disease**: clinical and cost-effectiveness analyses. Canadian Agency for Drugs and Technologies in Health. 2010 Nov;133:1-213.
523. Nahab F, Le A, Judd S, Frankel MR, Ard J, Newby PK, Howard VJ. Racial and geographic differences in fish consumption: The REGARDS Study. Neurology. 2010 Dec 22.
524. Sattelmair JR, Kurth T, Buring JE, et al. **Physical activity** and risk of stroke in women. Stroke 2010; 41:1243-1250.
525. Smith EE, Shobha N, Dai D, et al. **Risk score** for **in-hospital ischemic stroke mortality** derived and validated within the Get With the Guidelines-Stroke Program. Circulation 2010; 122:1496-1504.
526. Cucchiara Brett, Kasner Scott E.. **In the Clinic: Transient Ischemic Attack**. *Ann Intern Med* Jan 4, 2011 154:ITC1-1; doi:10.1059/0003-4819-154-1-201101040-01001.
527. Freeman JV, Zhu RP, Owens DK., et al. **Cost-Effectiveness of Dabigatran Compared With Warfarin** for Stroke Prevention in Atrial Fibrillation. *Ann Intern Med* January 4, 2011 154:1-11; ahead of print Nov 1, 2010, doi:10.1059/0003-4819-154-1-201101040-00289.
528. Miesner Andrew R, Sullivan Timothy S. Elevated International Normalized Ratio from **Vitamin K Supplement Discontinuation**. Articles Ahead of Print published on 1 January 2011, DOI 10.1345/aph.1P461. Ann Pharmacother ;45:e2.
529. Dossett LA, Riesel JN, Griffin MR, Cotton BA. Prevalence and Implications of **Preinjury Warfarin Use**: An Analysis of the National **Trauma** Databank. Arch Surg. 2011 Jan 17.
530. Limdi NA, Limdi MA, Cavallari L, Anderson AM, Crowley MR, Baird MF, Allon M, Beasley TM. **Warfarin** dosing in patients with **impaired kidney function**. Am J Kdney Dis. 2010 Nov;56(5):823-31.
531. Ying Xian, Robert G. Holloway, Paul S. Chan, et al. Association Between **Stroke Center Hospitalization** for Acute Ischemic Stroke and Mortality. *JAMA*. 2011;305(4):373-380.doi:10.1001/jama.2011.22.
532. Olesen JB, Lip G, Hansen ML, et al. Validation of risk stratification schemes for predicting stroke and thromboembolism in patients with atrial fibrillation: nationwide cohort study. BMJ 2011;342:doi:10.1136/bmj.d124 (31 Jan 11). CHADS2 vs **CHA2DS2-VASc**
533. Chassot PG, Marcucci C, Delabays A, Spahn DR. **Perioperative** antiplatelet therapy. Am Fam Physician. 2010 Dec 15;82(12):1484-9.
534. Gutierrez C. Blanchard DG. **Atrial Fibrillation**: Diagnosis and Treatment. Am Fam Physician. 2011 Jan 1;83(1):61-68.
535. Brott TG, Halperin JL, Abbara S, et al. JASA/ACCF/AHA/AANN/AANS/ACR/ASNR/CNS/SAIP/SCAI/SIR/SNIS/SVM/SVS guideline on the management of patients with **extracranial carotid and vertebral artery disease**: Executive summary. Circulation 2011: DOI:10.1161/CIR.0b013e31820d8d78. http://content.onlinejacc.org/cgi/reprint/j.jacc.2010.11.006v1.pdf
536. Chollet F et al. **Fluoxetine for motor recovery after acute ischaemic stroke** (**FLAME**): A randomised placebo-controlled trial. Lancet Neurol 2011 Feb; 10:123.
537. Kulik A, Le May MR, Voisine P, et al. Aspirin plus clopidogrel versus aspirin alone after coronary artery bypass grafting (CABG): the clopidogrel after surgery for coronary artery disease (**CASCADE**) Trial. Circulation. 2010 Dec 21;122(25):2680-7.
538. Baerlocher, Mark O., Myers, Andy, Asch, Murray. Managing **anticoagulation and antiplatelet therapy before interventional radiology procedures**. CMAJ 2011 183: 223.
539. Bungard TJ, Yakiwchuk E, Foisy M. **Drug interactions involving warfarin**: Practice tool and practical management tips. CJP. Jan/Feb Vol 144. No 1. 2011.
Clark NP, Delate T, Riggs CS, et al. **Warfarin Interactions With Antibiotics** in the Ambulatory Care Setting. JAMA Intern Med. 2014 Jan 20
540. Connolly SJ., Eikelboom J, Joyner C, et al. **AVERROES** Steering Committee & Investigators. **Apixaban in Patients with Atrial Fibrillation**. February 10, 2011. (n=5599 over 1.1yr; apixaban 5mg bid vs ASA 81-324mg od; Stroke or systemic embolism 1.6 vs 3.7% NNT= 48/year)
541. Eikelboom JW, Weitz JI. New oral anticoagulants (**dabigatran, rivaroxaban**) for **thromboprophylaxis in patients having hip or knee arthroplasty**. BMJ. 2011 Jan 18;342:c7270. doi: 10.1136/bmj.c7270.
542. Chollet F, Tardy J, Albucher J-F, et al. **Fluoxetine** for motor recovery after acute ischaemic stroke (**FLAME**): a randomised placebo-controlled trial, The Lancet Neurology, Vol 10, Issue 2, Feb 2011, Pages 123-130, ISSN 1474-4422.
543. Baker William L., Colby Jennifer A., Tongbram Vanita, et al. **Neurothrombectomy** Devices for the Treatment of Acute Ischemic Stroke: State of the Evidence. *Ann Intern Med* E-306published ahead of print January 17, 2011.

544. Galioto NJ, Danley DL, Van Maanen RJ. **Recurrent venous thromboembolism**. Am Fam Physician. 2011 Feb 1;83(3):293-300.
545. Earnshaw Stephanie R.; Scheiman James; Fendrick A. Mark; et al. **Cost-Utility of Aspirin and Proton Pump Inhibitors for Primary Prevention**. Arch Intern Med. 2011;171(3):218-225.
546. Balami Joyce S, Chen Ruo-Li, Grunwald Iris Q, et al. **Neurological complications of acute ischaemic stroke**, The Lancet Neurology, In Press, Corrected Proof, Available online 17 January 2011, ISSN 1474-4422, DOI: 10.1016/S1474-4422(10)70313-6.
547. Sandset EC, Bath PMW, Boysen G et al. The angiotensin-receptor blocker **candesartan for treatment of acute stroke (SCAST):** A randomised, placebo-controlled, double-blind trial. *Lancet* 2011;DOI:10.1016/S0140-6736(11)60104-9.
548. Bartholomew JR, Schaffer JL, McCormick GF. **Air travel and venous thromboembolism**: Minimizing the risk *Cleveland Clinic Journal of Medicine* 2011; 78(2):111-120; doi:10.3949/ccjm.78a.10138
549. Lin, Yulia, Callum, Jeannie. **Emergency reversal of warfarin** anticoagulation. CMAJ 2010 182: 2004
550. Douketis J, Tosetto A, Marcucci M, et al. **Risk of recurrence after venous thromboembolism in men** and women: patient level meta-analysis. BMJ. 2011 Feb 24;342:d813. doi: 10.1136/bmj.d813.
551. Devos H, Akinwuntan AE, Nieuwboer A, et al. Screening for fitness to **drive after stroke**: A systematic review and meta-analysis. Neurology. 2011 Feb 22;76(8):747-56.
552. García Rodríguez LA, Cea Soriano L, Hill C, et al. Increased risk of **stroke after discontinuation of acetylsalicylic acid**: A UK primary care study. Neurology. 2011 Feb 22;76(8):740-6.
553. Rodríguez Luis A. García, Lin Kueiyu Joshua, Hernández-Díaz Sonia, et al. **Risk of Upper Gastrointestinal Bleeding** With Low-Dose Acetylsalicylic Acid Alone and in Combination With Clopidogrel and Other Medications. Circulation 123: 1108-1115; online doi:10.1161/CIRCULATIONAHA.110.973008
554. Cairns JA, Connolly S, McMurtry S, et al. CCS Atrial Fibrillation Guidelines Committee. **Canadian cardiovascular society atrial fibrillation guidelines 2010**: prevention of stroke and systemic thromboembolism in atrial fibrillation and flutter. Can J Cardiol. 2011 Jan-Feb;27(1):74-90.
555. Zhao HJ, Zheng ZT, Wang ZH, et al. ``**Triple therapy**`` rather than ``triple threat``: a meta-analysis of the two antithrombotic regimens **after stent implantation** in patients receiving long-term oral anticoagulant treatment. Chest. 2011 Feb;139(2):260-70.
556. AHA Writing Group Members, Roger VL, Go AS, Lloyd-Jones DM, et al; on behalf of the American Heart Association Statistics Committee and Stroke Statistics Subcommittee, Roger VL, Turner MB; On behalf of the American Heart Association Heart Disease and Stroke Statistics Writing Group. Executive Summary: **Heart Disease and Stroke Statistics**—2011 Update: A Report From the American Heart Association. Circulation. 2011 Feb 1;123(4):459-463.
557. Jacob M, Smedira N, Blackstone E, Williams S, Cho L. Effect of timing of chronic preoperative **aspirin discontinuation** on morbidity and mortality in **coronary artery bypass surgery**. Circulation. 2011 Feb 15;123(6):577-83.
558. Saposnik G, Kapral MK, Liu Y, et al; on behalf of the Investigators of the Registry of the Canadian Stroke Network and the Stroke Outcomes Research Canada (SORCan) Working Group. **IScore**: A Risk Score to Predict Death Early After Hospitalization for an Acute Ischemic Stroke. Circulation. 2011 Feb 22;123(7):739-749.
559. Kamal AK, Naqvi I, Husain MR, et al. **Cilostazol versus aspirin** for secondary prevention of vascular events after stroke of arterial origin. Cochrane Database of Systematic Reviews 2011, Issue 1. Art. No.: CD008076. DOI: 10.1002/14651858.CD008076.pub2.
560. Hamann Gale L, Campbell Jennifer D, George Christa M. **Warfarin-Cranberry Juice** Interaction. Articles Ahead of Print published on 1 March 2011, DOI 10.1345/aph.1P451. Ann Pharmacother ;45:e17.
561. Price MJ, Berger PB, Teirstein PS, et al. **Standard- vs high-dose clopidogrel** based on platelet function testing after percutaneous coronary intervention: The **GRAVITAS** randomized trial. JAMA 2011; 305:1097-1105. (high dose not reduce 1^0 events vs std dose)
562. **PROTECT** Investigators for the Canadian Critical Care Trials Group and the Australian and New Zealand Intensive Care Society Clinical Trials Group. **Dalteparin versus Unfractionated Heparin in Critically Ill Patients**. Mar 22, 11 (10.1056/NEJMoa1014475)
563. Leizorovicz A, Cohen AT, Turpie AGG, Olsson CG, Vaitkus PT, Goldhaber SZ. Randomized, Placebo-Controlled Trial of **Dalteparin** for the Prevention of Venous Thromboembolism in **Acutely Ill Medical Patients** (**PREVENT**). Circulation 2004; 110:874-9.
564. Samama MM, Cohen AT, Darmon JY, Desjardins L, et al. A comparison of **enoxaparin** with placebo for the prevention of venous thromboembolism in **acutely ill medical patients** (**MEDENOX**). N Engl J Med 1999; 341:793-800.
565. Jaff Michael R., McMurtry M. Sean, Archer Stephen L., et al. and on behalf of the American Heart Association (AHA) Council on Cardiopulmonary, Critical Care, Perioperative and Resuscitation, Council on Peripheral Vascular Disease, and Council on Arteriosclerosis, Thrombosis and Vascular Biology. Management of **Massive and Submassive Pulmonary Embolism, Iliofemoral Deep Vein Thrombosis, and Chronic Thromboembolic Pulmonary Hypertension:** A Scientific Statement From the American Heart Association. Circulation published March 21, 2011, doi:10.1161/CIR.0b013e318214914f
566. Rodriguez LAG et al. **Increased risk for stroke after discontinuation of acetylsalicylic acid**: a UK primary care study. Neurology. 2011;76:740.
567. Nils Kucher. **Deep-Vein Thrombosis of the Upper Extremities**. N Engl J Med 2011; 364:861-869.
568. Larsson SC et al. **Coffee consumption** and risk of stroke in women. Stroke 2011 Mar 10.
569. Silber S, Windecker S, Vranckx P, Serruys PW, on behalf of the **RESOLUTE All Comers** investigators. Unrestricted randomised use of two new generation drug-eluting coronary stents: 2-year patient-related versus stent-related outcomes from the RESOLUTE All Comers trial. Lancet 2011; published online Arpil 3. DOI:10.1016/S0140-6736(11)60395-4. (2yr data; Dual antiplate therapy was @ 1yr=~84%, 2yr= ~18% but >1yr stent thrombosis was only ~0.3%)
570. Bauer Kenneth A. **Long-term Management of Venous Thromboembolism**: A 61-Year-Old Woman With Unprovoked Venous Thromboembolism. JAMA. 2011;305(13):1336-1345.Published online March 8, 2011. doi:10.1001/jama.2011.361
571. McArthur K S, Quinn T J, Dawson J, et al. **Diagnosis and management of transient ischaemic attack and ischaemic stroke in the acute phase.** BMJ 2011;342:doi:10.1136/bmj.d1938 (Published 31 March 2011)
571. McArthur K S, Quinn T J, Higgins P, et al. **Post-acute care and secondary prevention** after ischaemic stroke. BMJ 2011;342:doi:10.1136/bmj.d2083 (Published 8 April 2011)
572. Bloomfield HE, Krause A, Greer N, Taylor BC, MacDonald R, Rutks I, et al. Meta-analysis: effect of patient **self-testing and self-management of longterm anticoagulation** on major clinical outcomes. Ann Intern Med. 2011;154: 472-82.
573. Callahan T, Baranowski B. Managing newly diagnosed atrial fibrillation: Rate, rhythm, and risk. Cleve Clin J Med. 2011 Apr;78(4):258-64.
574. Varbo A, Nordestgaard BG, Tybjaerg-Hansen A, et al. Nonfasting **triglycerides, cholesterol**, and ischemic stroke in the general population. Ann Neurol. 2011 Feb 18. doi: 10.1002/ana.22384.
575. Bigi S, Fischer U, Wehrli E, et al. Acute Ischemic **Stroke In Children Versus Young Adults**. Annals of Neurology. Accepted manuscript online: 21 MAR 2011: 1-30.
576. Akl EA, Vasireddi SR, Gunukula S, Barba M, Sperati F, Terrenato I, Muti P, Schünemann H. Anticoagulation for the initial treatment of venous **thromboembolism in patients with cancer**. Cochrane Database Syst Rev. 2011 Feb 16;2:CD006649
577. Morgenstern LB, Hemphill JC III, Anderson C, on behalf of the American Heart Association Stroke Council and endorsed by the American Academy of Neurology, American Association of Neurological Surgeons, and the Congress of Neurological Surgeons. Guidelines for the management of **spontaneous intracerebral hemorrhage**: a guideline for healthcare professionals from the American Heart Association/American Stroke Association. Stroke 2010; 41: 2108–29. http://stroke.ahajournals.org/cgi/reprint/41/9/2108
578. Hankey GJ, Eikelboom JW. **Dabigatran** etexilate: a new oral thrombin inhibitor. Circulation. 2011 Apr 5;123(13):1436-50.
579. Murad MH, Shahrour A, Shah ND, et al. A systematic review and meta-analysis of randomized trials of **carotid endarterectomy vs stenting**. J Vasc Surg. 2011 Mar;53(3):792-7.
580. Bartolucci AA, Tendera M, and Howard G. Meta-analysis of multiple **primary prevention** trials of cardiovascular events using **aspirin**. Am J Cardiol 2011; DOI:10.1016/j.amjcard.2011.02.325.
581. Nathisuwan S, Dilokthornsakul P, Chaiyakunapruk N, et al. Assessing Evidence of **Interaction Between Smoking and Warfarin**: A Systematic Review and Meta-analysis. Chest. 2011 May;139(5):1130-9.
582. Hong Keun-Sik, Yegiaian Sharon, Lee Meng, et al. **Declining Stroke and Vascular Event Recurrence Rates in Secondary Prevention Trials Over the Past 50 Years** and Consequences for Current Trial Design. Circulation 123: 2111-2119.
583. Langhorne P, Bernhardt J, Kwakkel G. **Stroke rehabilitation**. Lancet. 2011 May 14;377(9778):1693-702.
584. McArthur KS, Quinn TJ, Higgins P, Langhorne P. **Post-acute care and secondary prevention** after ischaemic stroke. BMJ. 2011 Apr 8;342:d2083. doi:10.1136/bmj.d2083.
585. Rothwell PM, Algra A, Amarenco P. **Medical treatment** in **acute and long-term secondary prevention** after transient ischaemic attack and ischaemic stroke. Lancet. 2011 May 14;377(9778):1681-92.
586. Saposnik G, Levin M; for the Stroke Outcome Research Canada (SORCan) Working Group. **Virtual Reality in Stroke Rehabilitation**: A Meta-Analysis and Implications for Clinicians. Stroke. 2011 May;42(5):1380-1386.
587. The Stroke Prevention in Reversible Ischemia Trial (**SPIRIT**) Study Group. A randomized trial of **anticoagulants versus aspirin** after cerebral ischemia of presumed arterial origin. Ann Neurol 1997;42: 857–65.
Mohr JP, Thompson JL, Lazar RM, et al. A comparison of **warfarin and aspirin** for the prevention of recurrent ischemic stroke. N Engl J Med 2001; 345: 1444–51.
The ESPRIT Study Group. Medium intensity oral **anticoagulants versus aspirin** after cerebral ischaemia of arterial origin (**ESPRIT**): a randomised controlled trial. Lancet Neurol 2007; 6: 115–24.
588. Martinsson L, Hårdemark H, Eksborg S. **Amphetamines** for improving recovery after stroke. Cochrane Database Syst Rev 2007; 1: CD002090.
589. Boutitie F, Pinede L, Schulman S, et al. Influence of preceding **length of anticoagulant treatmen**t and initial presentation of venous thromboembolism on risk of recurrence after stopping treatment: analysis of individual participants' data from seven trials. BMJ 2011;342:d3036.
590. Yingying Tang, Barbara Sampson, Stephanie Pack, et al. **Ethnic Differences** in Out-of-Hospital Fatal Pulmonary Embolism. Circulation 123: 2219-2225; published online before print as doi:10.1161/CIRCULATIONAHA.110.976134.
591. Cook-Norris RH et al. **Complications of cutaneous surgery in patients taking clopidogrel**-containing anticoagulation. J Am Acad Dermatol 2011 Apr 22.
592. Hoffman JT, Hartig C, Sonbol E, Lang M. Probable interaction between **warfarin and rifaximin** in a patient treated for small intestine bacterial overgrowth. Ann Pharmacother. 2011 May;45(5):e25.
593. Bovio JA, Smith SM, Gums JG. **Dabigatran** etexilate: a novel oral thrombin inhibitor for thromboembolic disease. Ann Pharmacother. 2011 May;45(5):603-14.
594. Rubboli A, Kovacic JC, Mehran R, Lip GY. **Coronary Stent Implantation** in Patients Committed to Long-term Oral Anticoagulation Therapy: Successfully Navigating the Treatment Options. Chest. 2011 May;139(5):981-7. (Triple therapy)
595. Charlot M, Grove EL, Hansen PR, et al. **Proton pump inhibitor use and risk of adverse cardiovascular events in aspirin treated patients** with first time myocardial infarction: nationwide propensity score matched study. BMJ. 2011 May 11;342:d2690. doi: 10.1136/bmj.d2690.
596. Bousser M-G, Amarenco P, Chamorro A, et al, the **PERFORM** Study Investigators. **Terutroban versus aspirin** in patients with cerebral ischaemic events (PERFORM): a randomised, double-blind, parallel-group trial. Lancet 2011; online May 25. DOI:10.1016/S0140-6736(11)60600-4.
597. PILL Collaborative Group (2011) An International Randomised Placebo-Controlled Trial of a Four-Component Combination Pill (``**Polypill**'') in People with Raised Cardiovascular Risk. PLoS ONE 6(5): e19857. doi:10.1371/journal.pone.0019857.
598. Wechsler Lawrence R. Intravenous **Thrombolytic Therapy (rt-PA)** for Acute Ischemic Stroke. N Engl J Med 2011; 364:2138-2146.
599. Eikelboom JW, Wallentin L, Connolly SJ, et al. Risk of **bleeding with 2 doses of dabigatran** compared with warfarin in older and younger patients with atrial fibrillation. Circulation 2011; 123:2363-2372.
600. Douma Renée A., Mos Inge C.M., Erkens Petra M.G., et al. , for the Prometheus Study Group. Performance **of 4 Clinical Decision Rules in the Diagnostic Management of Acute Pulmonary Embolism**: A Prospective Cohort Study. Ann Intern Med June 7, 2011 154:709-718.
601. Avorn Jerry. The Relative **Cost-Effectiveness of Anticoagulants**: Obvious, Except for the Cost and the Effectiveness. Circulation 123: 2519-2521; published online before print as doi:10.1161/CIRCULATIONAHA.111.030148
602. Shah Shimoli V., Gage Brian F.. **Cost-Effectiveness of Dabigatran** for Stroke Prophylaxis in Atrial Fibrillation. Circulation 123: 2562-2570; published online before print as doi:10.1161/CIRCULATIONAHA.110.985655
603. Callahan Alfred; Amarenco Pierre; Goldstein Larry B.; et al. for the **SPARCL** Investigators. Risk of Stroke and Cardiovascular Events After Ischemic Stroke or Transient Ischemic Attack in Patients With **Type 2 Diabetes or Metabolic Syndrome**: Secondary Analysis of the Stroke Prevention by Aggressive Reduction in Cholesterol Levels (SPARCL) Trial Arch Neurol. 2011;0(2011):archneurol.2011.146.
604. Ghate Sameer R, Biskupiak JE, Ye X, et al. Hemorrhagic and Thrombotic Events Associated with **Generic Substitution of Warfarin** in Patients with Atrial Fibrillation: A Retrospective Analysis. Ahead of Print on 1 June 2011, DOI 10.1345/aph.1P593. Ann Pharmacother ;45:701-712.
605. James SK, Roe MT, Cannon CP, et al. **Ticagrelor versus clopidogrel** in patients with **acute coronary syndromes intended for non-invasive management**: substudy from the Prospective Randomised PLATelet inhibition and patient Outcomes (**PLATO**) trial. BMJ 2011;342:d3527.
606. Callahan A, Amarenco P, Goldstein LB, et al. for the **SPARCL** Investigators. Risk of Stroke and Cardiovascular Events After Ischemic Stroke or Transient Ischemic Attack in Patients With **Type 2 Diabetes or Metabolic Syndrome**: Secondary Analysis of the Stroke Prevention by Aggressive Reduction in Cholesterol Levels (SPARCL) Trial. Arch Neurol. 2011 Jun 13.
607. Passacquale Gabriella, Ferro Albert. Therapeutics: Oral antiplatelet agents **clopidogrel and prasugrel** for the prevention of cardiovascular events. BMJ 2011;342:doi:10.1136/bmj.d3488 (Published 17 June 2011)
608. Aujesky D, Roy P-M, Verschuren F, et al. **Outpatient versus inpatient treatment for patients with acute pulmonary embolism**: an international, open-label, randomised, non-inferiority trial. Lancet 2011; published online June 23. DOI:10.1016/S0140-6736(11)60824-6.
609. Hobbs F D R, Roalfe A K, Lip G Y H, et al. on behalf of the Birmingham Atrial Fibrillation in the Aged (**BAFTA**) investigators and Midland Research Practices Consortium (MidReC) network. **Performance of stroke risk scores** in older people with atrial fibrillation not taking warfarin: comparative cohort study from BAFTA trial. BMJ 2011;342:doi:10.1136/bmj.d3653 (23 June 2011)
610. Geraghty AJ, Welch K. Antithrombotic agents for preventing thrombosis after **infrainguinal arterial bypass surgery**. Cochrane Database Syst Rev. 2011 Jun 15;6:CD000536. Patients undergoing infrainguinal venous graft are more likely to benefit from treatment with VKA than platelet inhibitors. Patients receiving an artificial graft benefit from platelet inhibitors (aspirin). However, the evidence is not conclusive.

611. Mehran R, Rao SV, Bhatt DL, et al. Standardized bleeding definitions for cardiovascular clinical trials: a consensus report from the bleeding academic research consortium. Circulation. 2011 Jun 14;123(23):2736-47.
Hicks KA, Stockbridge NL, Targum SL, Temple RJ. Bleeding academic research consortium (**BARC**) consensus report: the food and drug administration perspective. Circulation. 2011 Jun 14;123(23):2664-5.
612. Hochholzer W, Wiviott SD, Antman EM, et al. **Predictors of Bleeding** and Time Dependence of Association of Bleeding With Mortality: Insights From the Trial to Assess Improvement in Therapeutic Outcomes by Optimizing Platelet Inhibition With Prasugrel--Thrombolysis in Myocardial Infarction 38 (**TRITON-TIMI 38**). Circulation. 2011 Jun 14;123(23):2681-9. Conclusions— The major predictors of serious bleeding were a combination of patient and procedural characteristics and antiplatelet therapies. Although serious bleeding was strongly associated with mortality within the first month of the bleeding event, this association was not significant beyond 40 days.
613. Kawut SM, Bagiella E, Lederer DJ, et al; on behalf of the **ASA-STAT Study** Group. Randomized Clinical Trial of **Aspirin and Simvastatin for Pulmonary Arterial Hypertension**: ASA-STAT. Circulation. 2011 Jun 28;123(25):2985-2993.
614. García Rodriguez LA, Cea-Soriano L, Martín-Merino E, Johansson S. **Discontinuation of low dose aspirin and risk of myocardial infarction**: case-control study in UK primary care. BMJ 2011;343:d4094.
615. Raju N, Sobieraj-Teague M, Hirsh J, et al. Effect of **aspirin on mortality in the primary prevention** of cardiovascular disease. Am J Med. 2011 Jul;124(7):621-9.
616. Stanley AJ, Dalton HR, Blatchford O, et al. Multicentre comparison of the **Glasgow Blatchford and Rockall scores** in the prediction of clinical end-points after upper gastrointestinal haemorrhage. Aliment Pharmacol Ther. 2011 Aug;34(4):470-5. doi: 10.1111/j.1365-2036.2011.04747.x.
617. Marmo R, Koch M, Cipolletta L, et al. Italian registry on upper gastrointestinal bleeding (Progetto Nazionale Emorragie Digestive--**PNED 2**). Predicting mortality in non-variceal upper gastrointestinal bleeders: validation of the Italian PNED Score and Prospective Comparison with the **Rockall Score**. Am J Gastroenterol. 2010 Jun;105(6):1284-91.
618. Bhala Neeraj, Taggar Jaspal S, Rajasekhar Praveen, et al. Anticipating and **managing bleeding complications in patients with coronary stents** who are receiving dual antiplatelet treatment. BMJ 2011;343:doi:10.1136/bmj.d4264 (21 July 2011)
619. Alexander JH, Lopes RD, James S, et al. Apixaban with antiplatelet therapy after acute coronary syndrome (**Appraise-2**). N Engl J Med 2011 (5mg po bid: increased the number of **major bleeding** events without a significant reduction in recurrent ischemic events)
620. Hughes GJ, Patel PN, Saxena N.. Effect of **acetaminophen on international normalized ratio** in patients receiving warfarin therapy. Pharmacotherapy 2011 June;31(6):591–597.
621. Hippisley-Cox J, Coupland C. Development and validation of risk prediction algorithm (**QThrombosis**) to estimate **future risk of venous thromboembolism**: prospective cohort study. BMJ. 2011 Aug 16;343:d4656. doi: 10.1136/bmj.d4656.
622. Luo J-C et al. Randomised clinical trial: **Rabeprazole plus aspirin is not inferior to rabeprazole plus clopidogrel** for the healing of aspirin-related peptic ulcer. Aliment Pharmacol Ther 2011 Sep; 34:519.
623. Patel MR, Mahaffey KW, Garg J, et al. **Rivaroxaban** versus warfarin in nonvalvular atrial fibrillation. (**Rocket-AF**) N Engl J Med 2011.
Fox KA, Piccini JP, Wojdyla D, et al. Prevention of stroke and systemic embolism with **rivaroxaban** compared with warfarin in patients with non-valvular atrial fibrillation and moderate **renal impairment**. Eur Heart J. 2011 Aug 28.
Patel MR, Hellkamp AS, et al. Outcomes of **Discontinuing Rivaroxaban** Compared With Warfarin in Patients With Nonvalvular Atrial Fibrillation: Analysis From the **ROCKET AF** Trial (Rivaroxaban Once-Daily, Oral, Direct Factor Xa Inhibition Compared With Vitamin K Antagonism for Prevention of Stroke and Embolism Trial in Atrial Fibrillation). J Am Coll Cardiol. 2013 Feb 12;61(6):651-8.
Goodman SG, Wojdyla DM, Piccini JP, MD; et al. Factors associated with **major bleeding events**: insights from the rivaroxaban once-daily oral direct factor Xa inhibition compared with vitamin K antagonism for prevention of stroke and embolism trial in atrial fibrillation (**ROCKET AF**). J Am Coll Cardiol 2013.
624. Kuklina EV, Tong X, Bansil P, et al. Trends in **pregnancy hospitalizations that included a stroke** in the United States from 1994 to 2007. Stroke 2011; DOI: 10.1161/STROKEAHA.110.610592.
625. Faxon D, Eikelboom J, Berger P, et al. **Consensus document: Antithrombotic therapy in patients with atrial fibrillation undergoing coronary stenting**. Thromb Haemost 2011: DOI:10.1160/TH11-04-0262. (North American consensus)
626. Huhtakangas J, Tetri S, Juvela S, et al. Effect of Increased Warfarin Use on **Warfarin-Related Cerebral Hemorrhage**: A Longitudinal Population-Based Study. Stroke. 2011 Jul 28.
627. Rose AJ, Ozonoff A, Berlowitz DR, et al. Reexamining the Recommended **Follow-up Interval After Obtaining an In-Range International Normalized Ratio** Value: Results from the Veterans Affairs Study to Improve Anticoagulation. Chest. 2011 Aug;140(2):359-65.
628. Schultz Karen T, Bungard Tammy J, Dosing Options for **Decreasing the Time to Achieve Therapeutic Anticoagulation When Reinitiating Warfarin**:A Case Series. Pharmacotherapy 2011;31(8):793–805). In select patients, the option of administering a warfarin loading dose of approximately 40% greater than the previous daily maintenance dose for 2 or 3 days shortens the time to achieving therapeutic anticoagulation.
629. Jowett S, Bryan S, Mant J, et al. Cost effectiveness of **warfarin versus aspirin in patients older than 75 years** with atrial fibrillation. Stroke. 2011 Jun;42(6):1717-21
630. Granger CB et al. Apixaban versus warfarin in patients with atrial fibrillation (**ARISTOTLE**). N Engl J Med . 2011 Aug 28.
Easton JD, Lopes RD, Bahit MC, et al, for ARISTOTLE Committees and Investigators. Apixaban compared with warfarin in patients with atrial fibrillation and **previous stroke or transient ischaemic attack**: subgroup analysis of ARISTOTLE trial. Lancet Neurol 2012; online May 8.
631. Fang MC, Go AS, Chang Y, et al. A New Risk Scheme to **Predict Warfarin-Associated Hemorrhage The ATRIA** (Anticoagulation and Risk Factors in Atrial Fibrillation) Study. J Am Coll Cardiol. 2011 Jul 19;58(4):395-401.
632. Engelter ST, Soinne L, Ringleb P, et al. **IV thrombolysis and statins**. Neurology. 2011 Aug 17.
633. Zöller B, Li X, Sundquist J, Sundquist K. **Age- and Gender-Specific Familial Risks** for Venous Thromboembolism: A Nationwide Epidemiological Study Based on Hospitalizations in Sweden. Circulation. 2011 Aug 8.
634. Mahaffey KW, Wojdyla DM, Carroll K, et al. **Ticagrelor compared with clopidogrel** by geographic region in the Platelet Inhibition and Patient Outcomes (PLATO) Trial. Circulation 2011
635. Hill MD, Coutts SB. **Preventing stroke** after transient ischemic attack. CMAJ. 2011 Jul 12;183(10):1127-8.
636. Lillis T, Ziakas A, Koskinas K, et al. Safety of **Dental Extractions** During Uninterrupted Single or Dual Antiplatelet Treatment. Am J Cardiol. 2011 Jul 22.
637. Siristatidis CS, Dodd SR, Drakeley AJ. **Aspirin for in vitro fertilisation**. Cochrane Database of Systematic Reviews 2011, Issue 8. Art. No.: CD004832. DOI: 10.1002/14651858.CD004832.pub3
638. Broderick JP, Bonomo JB, Kissela BM, et al. **Withdrawal of antithrombotic agents** and its impact on ischemic stroke occurrence.Stroke 2011.
639. Fjaertoft H, Rohweder G, Indredavik B. Stroke unit care combined with early supported discharge improves 5-year outcome: a randomized controlled trial. Stroke. 2011 Jun;42(6):1707-11.
640. Institute for Clinical Systems Improvement (**ICSI**). Venous thromboembolism diagnosis and treatment. Bloomington (MN): Institute for Clinical Systems Improvement (ICSI); 2011 Mar.
641. Boggon R, van Staa TP, Timmis A, et al. **Clopidogrel discontinuation** after acute coronary syndromes: frequency, predictors and associations with death and myocardial infarction--a hospital registry-primary care linked cohort (MINAP-GPRD). Eur Heart J. 2011 Aug 29.
642. Samieri C., Féart C., Proust-Lima C., et al. **Olive oil consumption**, plasma oleic acid, and stroke incidence: The Three-City Study Neurology June 15, 2011
643. Grunau BE, Wiens MO, Harder KK. Patient **self-management of warfarin** therapy: Pragmatic feasibility study in Canadian primary care. Can Fam Physician. 2011 Aug;57(8):e292-8.
644. Alberts MJ, Latchaw RE, Jagoda A, et al. Revised and updated recommendations for the **establishment of primary stroke centers**: A summary statement from the Brain Attack Coalition. Stroke 2011; 42:2651-2665.
645. Davies R, Galloway JB, Watson KD, Lunt M, Symmons DP, Hyrich KL; ; BSRBR Control Centre Consortium, British Society for Rheumatology Biologics Register. Venous thrombotic events are not increased in patients with rheumatoid arthritis treated with anti-TNF therapy: results from the British Society for Rheumatology Biologics Register. Ann Rheum Dis. 2011 Jul 22.
646. Laver KE, George S, Thomas S, Deutsch JE, Crotty M. **Virtual reality for stroke rehabilitation**. Cochrane Database of Systematic Reviews 2011, Issue 9. Art. No.: CD008349. DOI: 10.1002/14651858.CD008349.pub2. We found limited evidence that the use of virtual reality and interactive video gaming may be beneficial in improving arm function and ADL function when compared with the same dose of conventional therapy.
647. Spyropoulos AC, Anderson FA Jr, et al. for the IMPROVE (International Medical Prevention Registry on Venous Thromboembolism) Investigators. Predictive and Associative Models to Identify Hospitalized Medical Patients at Risk for Venous Thromboembolism. Chest. 2011 Mar 24.
648. Hackam DG, Austin PC, Huang A, et al. **Statins and intracerebral hemorrhage**: a retrospective cohort study. Arch Neurol. doi:10.1001/archneurol.2011.228.
649. Griep LMO, Verschuren WM, Kromhout D, Ocke MC, Geleijnse JM. Colors of **fruit and vegetables** and 10-year incidence of stroke. Stroke. 2011.
650. Larsson SC, Orsini N. **Fish Consumption** and the Risk of Stroke: A Dose-Response Meta-Analysis. Stroke. 2011 Sep 8.
651. McKinney JS, Deng Y, Kasner SE, Kostis JB; for the Myocardial Infarction Data Acquisition System (MIDAS 15) Study Group. **Comprehensive Stroke Centers** Overcome the Weekend Versus Weekday Gap in Stroke Treatment and Mortality. Stroke. 2011 Sep;42(9):2403-2409.
652. Rerkasem K, Rothwell PM. **Carotid endarterectomy for symptomatic carotid stenosis**. Cochrane Database Syst Rev. 2011 Apr 13;(4):CD001081.
653. Zhang Y, Tuomilehto J, Jousilahti P, et al. **Lifestyle Factors on the Risks** of Ischemic and Hemorrhagic Stroke. Arch Intern Med. 2011 Sep 12.
654. Chimowitz MI, Lynn MJ, Derdeyn CP, et al. **Stenting versus aggressive medical therapy** for intracranial arterial stenosis. (**Sammpris**) N Engl J Med 2011. DOI: 10.1056/NEJMoa1105335.
655. Bushnell CD, Olson DM, Zhao X, et al. For the AVAIL Investigators. Secondary preventive medication **persistence and adherence** 1 year after stroke. Neurology. 2011 Sep 7.
656. Kaatz S, Qureshi W, Lavender RC. **Venous thromboembolism**: What to do after anticoagulation is started. Cleve Clin J Med. 2011 Sep;78(9):609-18.
657. Parodi G, Marcucci R, Valenti R, et al. **High residual platelet reactivity after clopidogrel** loading and long-term cardiovascular events among patients with acute coronary syndromes undergoing PCI (**RECLOSE-2 ACS**). JAMA. 2011;306(11):1215-1223.
658. Caritis S, Sibai B, Hauth J, et al. Lowdose **aspirin to prevent preeclampsia** in women at high risk. N Engl J Med 1998; 338:701-5.
659. Askie LM, Duley L, Henderson-Smart DJ, Stewart LA. **Antiplatelet agents for prevention of pre-eclampsia**: a meta-analysis of individual patient data. Lancet 2007;369:1791-8.
660. Health Canada Sep/11 is informing health professionals and patients of updated recommendations involving the use of Plavix (**clopidogrel**) in combination with a class of drugs known as proton pump inhibitors (PPIs). New evidence has shown that while **PPIs** do interact with Plavix, not all reduce the effectiveness of Plavix to the same degree. (Omeprazole interacts, but pantoprazole not interact as strongly)
661. Pluta RM, Lynm C, Golub RM. JAMA **patient page**. **Stroke imaging**. JAMA. 2011 Sep 21;306(11):1277.
662. Pan A, Sun Q, Okereke OI, Rexrode KM, Hu FB. **Depression and risk of stroke** morbidity and mortality: a meta-analysis and systematic review. JAMA. 2011 Sep 21;306(11):1241-9.
663. Spinler SA, Willey VJ. A **Patient's Guide** to Taking **Dabigatran** Etexilate. Circulation. 2011 Aug 23;124(8):e209-11.
664. Chen YL, Chang CL, et al. **Major Adverse Upper Gastrointestinal Events** in Patients with ST-Segment Elevation Myocardial Infarction Undergoing Primary Coronary Intervention and **Dual Antiplatelet Therapy**. Am J Cardiol. 2011 Sep 14. (Major GI 10.4% over 4yrs)
665. Squizzato A, Romualdi E, Dentali F, et al. **Statins for acute ischemic stroke**. Cochrane Database Syst Rev. 2011 Aug 10;(8):CD007551. **Insufficient data** were available from randomized trials to establish if statins are safe and effective in cases of acute ischemic stroke and TIA.
666. Albaladejo P, Marret E, Samama CM, et al. **Non-cardiac surgery in patients with coronary stents**: the RECO study. Heart. 2011 Oct;97(19):1566-72. **Interruption** of antiplatelet therapy **more than 5days prior** to invasive procedure is a key player for major CV events.
667. Holmes MV, Newcombe P, Hubacek JA, et al. Effect modification by population **dietary folate on the association between MTHFR genotype**, **homocysteine**, and stroke risk: a meta-analysis of genetic studies and randomised trials. Lancet 2011; published online Aug 1.
668. Poli D, Antonucci E, Testa S, et al. for the Italian Federation of Anticoagulation Clinics (FCSA). **Bleeding Risk in Very Old Patients on Vitamin K Antagonist** Treatment: Results of a Prospective Collaborative Study on Elderly Patients Followed by Italian Centres for Anticoagulation. Circulation. 2011 Aug 16;124(7):824-829.
669. Patti G, Bárczi G, Orlic D, et al. Outcome comparison of **600- and 300-mg loading doses of clopidogrel** in patients undergoing primary PCI for STEMI. Results from the **ARMYDA-6 MI** (Antiplatelet Therapy for Reduction of Myocardial Damage During Angioplasty—Myocardial Infarction) randomized study. J Am Coll Cardiol 2011; 58:1592-1599.
670. Labos C, Dasgupta K, Nedjar H, et al. Risk of **bleeding** associated with combined use of **selective serotonin reuptake inhibitors** and antiplatelet therapy following acute myocardial infarction. CMAJ 2011; DOI:10.1503/cmaj.100912.
671. Nallamothu BK, Gurm HS, Ting HH, et al . **Operator exper** ience and **carotid stenting outcomes (CAS)** in Medicare beneficiaries. JAMA. 2011;306(12): 1338-1343.
672. Jacob M, Smedira N, Blackstone E, et al. Effect of timing of chronic **preoperative aspirin discontinuation** on morbidity and mortality in **coronary artery bypass surgery**. Circulation 2011;DOI:10.1161/CIRCULATIONAHA.110.957373.
It is therefore acceptable to continue aspirin to within 3 days to 5 days of surgery for patients at higher risk of cardiovascular events preoperatively, while discontinuing aspirin a bit earlier for those who may be at higher risk of bleeding complications.
673. Cheema AN, Mohammad A, Hong T, et al. Characterization of **clopidogrel hypersensitivity** reactions and management with oral steroids (**prednisone** x 3 weeks) without clopidogrel discontinuation. J Am Coll Cardiol 2011; 58:1445-1454.
674. Jung S-Y, Choi N-K, Kim J-Y, et al. **Short-acting nifedipine and risk of stroke** in elderly hypertensive patients. Neurology 2011;77:1229 –1234.
675. Giles MF, Albers GW, Amarenco P, et al. Early stroke risk and **ABCD2 score** performance in tissue- vs time-defined TIA: A multicenter study. Neurology. 2011 Sep 27;77(13):1222-8.
676. Easton JD, Saver JL, Albers GW, et al. **Definition and evaluation of transient ischemic attack**: a scientific statement for healthcare professionals from the American Heart Association (AHA)/American Stroke Association (ASA) Stroke Council; Council on Cardiovascular Surgery and Anesthesia; Council on Cardiovascular Radiology and Intervention; Council on Cardiovascular Nursing; and the Interdisciplinary Council on Peripheral Vascular Disease: the American Academy of Neurology affirms the value of this statement as an educational tool for neurologists. Stroke 2009;40: 2276–2293.
677. Rooke TW, Hirsch AT, Misra S, et al. 2011 **ACCF/AHA** focused update of the guideline for the management of patients with **peripheral artery disease** (updating the 2005 guideline): a report of the American College of Cardiology Foundation/American Heart Association Task Force on

Practice Guidelines. Circulation. 2011;124.
678. Lee M, Saver JL, Chang B, Chang K-H, Hao Q, Ovbiagele B. Presence of baseline **prehypertension and risk of incident stroke**: a meta-analysis. Neurology 2011;77:1330 –1337.
679. Wiviott SD, Desai N, Murphy SA, et al. Efficacy and Safety of Intensive Antiplatelet Therapy With **Prasugrel** from **TRITON-TIMI 38** in a Core Clinical Cohort Defined by Worldwide Regulatory Agencies. Am J Cardiol. 2011 Oct 1;108(7):905-11.
680. George MG, Tong X, Kuklina EV, Labarthe DR. Trends in **stroke hospitalizations** and associated risk factors among **children and young adults**, 1995-2008. Ann Neurol. 2011 Sep 2. doi: 10.1002/ana.22539.
681. Amin AN, Lin J, Thompson S, Wiederkehr D. Inpatient and outpatient occurrence of deep vein thrombosis and pulmonary embolism and thromboprophylaxis following **selected at-risk surgeries**. Ann Pharmacother. 2011 Sep;45(9):1045-52.
682. Crouch MA, Colucci VJ, Howard PA, Spinler SA. P2Y12 Receptor Inhibitors: Integrating **Ticagrelor** into the Management of Acute Coronary Syndrome. Ann Pharmacother. 2011 Sep;45(9):1151-6.
683. Koennecke HC, Belz W, Berfelde D, et al. For the Berlin Stroke Register Investigators. Factors influencing in-hospital **mortality** and morbidity in patients treated on a **stroke unit**. Neurology. 2011 Sep 6;77(10):965-972.
684. Ussia GP, Scarabelli M, Mulè M, et al. **Dual Antiplatelet Therapy Versus Aspirin** Alone in Patients Undergoing **Transcatheter Aortic Valve Implantation**. Am J Cardiol. 2011 Sep 10.
685. Holmes MV, Newcombe P, Hubacek JA, et al. Effect modification by population **dietary folate** on the association between MTHFR genotype, homocysteine, and stroke risk: a meta-analysis of genetic studies and randomised trials. Lancet. 2011 Aug 13;378(9791):584-94.
686. Moores LK, King CS, Holley AB. Current approach to the diagnosis of acute nonmassive pulmonary embolism. Chest. 2011 Aug;140(2):509-18.
687. Bauer T, Bouman HJ, van Werkum JW, Ford NF, ten Berg JM, Taubert D. Impact of **CYP2C19 variant genotypes** on clinical efficacy of antiplatelet treatment with **clopidogrel**: systematic review and meta-analysis. BMJ. 2011 Aug 4;343:d4588.
688. Cuisset T, Quilici J, Cohen W, et al. Usefulness of **High Clopidogrel Maintenance Dose** According to **CYP2C19 Genotypes** in Clopidogrel Low Responders Undergoing Coronary Stenting for Non ST Elevation Acute Coronary Syndrome. Am J Cardiol. 2011Sep5;108(6):760-5.
689. Vargas-Hitos JA, Ateka-Barrutia O, Sangle S, Khamashta MA. Efficacy and safety of long-term **low molecular weight heparin in patients with antiphospholipid syndrome**. Ann Rheum Dis. 2011 Sep;70(9):1652-4.
690. Lucassen W, Geersing GJ, Erkens PM, et al. **Clinical Decision Rules** for **Excluding Pulmonary Embolism**: A Meta-analysis. Ann Intern Med. 2011 Oct 4;155(7):448-60.
691. Olesen JB, Lip GYH, Lindhardsen J, et al. Risks of thromboembolism and bleeding with thromboprophylaxis in patients with **atrial fibrillation**: A net clinical benefit analysis using a 'real world' nationwide cohort study. Thromb Haemost 2011; 106: 739-749. (**not ASA**)
692. Hamm CW, Bassand JP, Agewall S, et al. **ESC** Guidelines for the management of **acute coronary syndromes** in patients presenting without persistent ST-segment elevation: The Task Force for the management of acute coronary syndromes (ACS) in patients presenting without persistent ST-segment elevation of the European Society of Cardiology (ESC). Eur Heart J. 2011 Sep 21.
693. Warkentin TE, Davidson BL, Büller HR, et al. Prevalence and risk of pre-existing **heparin-induced thrombocytopenia antibodies** in patients with acute VTE. Chest. 2011 Aug;140(2):366-73.
694. Nagarakanti R, Ezekowitz MD, Oldgren J, et al. **Dabigatran** versus warfarin in patients with atrial fibrillation: an analysis of patients undergoing **cardioversion**. Circulation. 2011;123:131–136.
695. Greenhalgh J, Bagust A, Boland A, et al. Clopidogrel and modified-release dipyridamole for the prevention of **occlusive vascular events** (review of Technology Appraisal No. 90): systematic review and economic analysis. Health Technol Assess. 2011 Sep;15(31):1-178. The evidence suggests that the most cost-effective treatment for patients with ischaemic stroke/TIA is clopidogrel followed by MRD + ASA followed by ASA; for patients with MI, ASA followed by clopidogrel; and for patients with established peripheral arterial disease or multivascular disease, clopidogrel followed by ASA.
696. Rodríguez LA, Cea-Soriano L, Martín-Merino E, Johansson S. **Discontinuation of low dose aspirin and risk** of **myocardial infarction**: case-control study in UK primary care. BMJ. 2011 Jul 19;343:d4094.
697. Thomalla G, Cheng B, Ebinger M, et al. **DWI-FLAIR mismatch** for the identifi cation of patients with acute ischaemic stroke within 4·5 h of symptom onset (**PRE-FLAIR**): a multicentre observational study. Lancet Neurol 2011. DOI:10.1016/S1474-4422(11)70192-2.
698. Kim ES, Park N, Peterson C. Dispositional **optimism** protects older adults from stroke: the health and retirement study. Stroke. 2011 Oct;42(10):2855-9.
699. Cadavid JC, DiVietro ML, Torres EA, et al. **Warfarin-induced pulmonary metastatic calcification** and calciphylaxis in a patient with end-stage renal disease. Chest. 2011 Jun;139(6):1503-6.
700. Tarnutzer AA, Berkowitz AL, Robinson KA, et al. Does my **dizzy patient have a stroke**? A systematic review of bedside diagnosis in acute vestibular syndrome. CMAJ. 2011 Jun 14;183(9):E571-92.
701. Kabrhel C, Varraso R, Goldhaber SZ, et al. **Physical inactivity** and idiopathic pulmonary embolism in women: prospective study. BMJ. 2011 Jul 4;343:d3867.
702. Anthony CJ, Karim S, Ackroyd-Stolarz S, et al. **Intensity of anticoagulation** with warfarin and risk of **adverse events** in patients presenting to the emergency department. Ann Pharmacother. 2011 Jul;45(7-8):881-7.
703. Patanwala AE, Acquisto NM, Erstad BL. **Prothrombin complex concentrate** for critical bleeding. Ann Pharmacother. 2011 Jul;45(7-8):990-9.
704. Broderick JP, Bonomo JB, Kissela BM, et al. **Withdrawal of antithrombotic agents** and its impact on ischemic stroke occurrence. Stroke. 2011 Sep;42(9):2509-14.
705. Lillis T, Ziakas A, Koskinas K, et al. Safety of **dental extractions** during uninterrupted single or dual antiplatelet treatment. Am J Cardiol. 2011 Oct 1;108(7):964-7.
706. Loewen P, Dahri K. **Risk of bleeding** with oral anticoagulants: an updated systematic review and performance analysis of clinical prediction rules. Ann Hematol. 2011 Oct;90(10):1191-200.
707. Burn J, Gerdes A-M, Macrae F, et al, on behalf of the **CAPP2** Investigators. Long-term effect of **aspirin on cancer risk** (Lynch syndrome) in carriers of hereditary colorectal cancer: an analysis from the CAPP2 randomised controlled trial. Lancet 2011.
708. Strijkers R H W, Cate-Hoek A J ten, Bukkems S F F W, et al. Management of **deep vein thrombosis and prevention of post-thrombotic syndrome**. BMJ 2011;343:doi:10.1136/bmj.d5916 (Published 31 October 2011)
709. Pink J, Lane S, Pirmohamed M, Hughes DA. **Dabigatran** etexilate versus warfarin in management of non-valvular atrial fibrillation in UK context: quantitative benefit-harm and economic analyses. BMJ 2011;343:d6333.
710. Roger VL, Go AS, Lloyd-Jones DM, et al. American Heart Association Statistics Committee and Stroke Statistics Subcommittee. **Heart disease and stroke statistics**—2011 update: a report from the American Heart Association. Circulation. 2011;123:e18 – e209.
711. Connolly SJ, Eikelboom JW, Ng J, Hirsh J, Yusuf S, Pogue J, et al; on behalf of the **ACTIVE** Steering Committee and Investigators. Net clinical benefit of adding **clopidogrel to aspirin** therapy in patients with atrial fibrillation for whom **vitamin K antagonists are unsuitable**. Ann Intern Med. 2011;155:579-86.
712. Powers WP, Clarke WR, Grubb RL, Videen TO, Adams HP, Derdeyn CP; Carotid Occlusion Surgery Study (**COSS**) Investigators. **Extracranial-intracranial bypass surgery** for stroke prevention in hemodynamic cerebral ischemia: the Carotid Occlusion Surgery Study Randomized trial. JAMA 2011; 306 (18) : 1983-1992.
713. Goldhaber SZ, Leizorovicz A, Kakkar AK, et al. **Apixaban versus enoxaparin** for thromboprophylaxis in medically ill patients. (**ADOPT**) NewEngl J Med 2011; DOI:10.1056/NEJM0a1110899.
714. Mega JL et al. for the **ATLAS ACS 2–TIMI 51** Investigators. **Rivaroxaban** in patients with a recent acute coronary syndrome.N Engl J Med 2011 Nov 13. (but at baseline only 66% on BB, & 39% on ACEI)
715. American College of Obstetricians and Gynecologists (**ACOG**). **Thromboembolism in pregnancy**. Washington (DC): American College of Obstetricians and Gynecologists (ACOG); 2011 Sep. 12 p. (ACOG practice bulletin; no. 123).
716. Schulman S, Parpia S, Stewart C, Rudd-Scott L, Julian JA, Levine M. **Warfarin dose assessment every 4 weeks versus every 12 weeks** in patients with stable international normalized ratios. A randomized trial. Ann Intern Med. 2011;155:653-9.
717. Oldgren J, Alings M, Darius H, et al. Risks for stroke, bleeding, and death in patients with atrial fibrillation receiving dabigatran or warfarin in relation to the CHADS2 score: a subgroup analysis of the **RE-LY** trial. Ann Intern Med. 2011;155:660-7.
718. Lederle FA, Zylla D, Macdonald R, Wilt TJ. **Venous thromboembolism prophylaxis** in **hospitalized medical patients** and those with stroke: a background review for an american college of physicians clinical practice guideline. Ann Intern Med. 2011 Nov 1;155(9):602-15.
719. Qaseem A, Chou R, Humphrey LL, et al. for the Clinical Guidelines Committee of the American College of Physicians. **Venous Thromboembolism Prophylaxis in Hospitalized Patients**: A Clinical Practice Guideline From the American College of Physicians. Ann Intern Med. 2011 Nov 1;155(9):625-632.
720. Wong PF, Chong LY, Mikhailidis DP, et al. **Antiplatelet agents for intermittent claudication**. Cochrane Database Syst Rev. 2011 Nov 9;11:CD001272. Antiplatelet agents have a beneficial effect in reducing all cause mortality and fatal cardiovascular events in patients with IC. Treatment with antiplatelet agents in this patient group however is associated with an increase in adverse effects, including GI symptoms, and healthcare professionals and patients need to be aware of the potential harm as well as the benefit of therapy; more data are required on the effect of antiplatelets on major bleeding.
721. Biffi A, Battey TW, Ayres AM, et al. **Warfarin-related intraventricular hemorrhage**: Imaging and outcome. Neurology. 2011 Nov 15;77(20):1840-6.
722. Canadian Agency for Drugs and Technologies in Health (**CADTH**). **Optimal warfarin** management for the prevention of thromboembolic events in patients with atrial fibrillation: review of Canadian **economic studies** [Internet]. Ottawa: The Agency; 2011 Nov [cited 2011 Nov 21]. (Optimal use report; vol. 1 iss. 2b). Available from http://www.cadth.ca/media/pdf/OP0508_warfarin_science-report-2_cost_e.pdf
Canadian Agency for Drugs and Technologies in Health (**CADTH**). **Optimal warfarin** management for the prevention of thromboembolic events in patients with atrial fibrillation: a **systematic review** of the clinical evidence [Internet]. Ottawa: The Agency; 2011 Nov [2011 Nov 21]. (Optimal use report; vol. 1 iss. 2a). Available from http://www.cadth.ca/media/pdf/OP0508_warfarin-science-report-1_clinical_e.pdf
Canadian Agency for Drugs and Technologies in Health (**CADTH**). Recommendations for **Optimal Warfarin** Management for Prevention of Thromboembolic Events in Patients with Atrial Fibrillation.
http://www.cadth.ca/media/pdf/OP0508_warfarin_rec-report_e.pdf
CERC recommends that patients with NVAF requiring **warfarin** be managed by a **well-coordinated**, **structured approach** dedicated to their anticoagulation therapy. CERC does **not recommend self-management** for most patients with NVAF requiring warfarin.
723. Stone DH, Goodney PP, Schanzer A, et al. Vascular Study Group of New England. **Clopidogrel is not associated with major bleeding** complications during peripheral arterial surgery. J Vasc Surg. 2011 Sep;54(3):779-84.
724. Berger JS, Lala A, Krantz MJ, et al. **Aspirin for the prevention of cardiovascular events in patients without clinical cardiovascular disease**: a meta-analysis of randomized trials. Am Heart J. 2011 Jul;162(1):115-24.e2.
725. Zöller B, Li X, Sundquist J, Sundquist K. Risk of **pulmonary embolism in patients with autoimmune disorders**: a nationwide follow-up study from Sweden. Lancet 2011; published online Nov 26. DOI:10.1016/S0140-6736(11)61306-8.
726. Chapman SA, Irwin ED, Beal AL, et al. **Prothrombin complex concentrate** versus standard therapies for INR reversal in trauma patients receiving **warfarin**. Ann Pharmacother. 2011 Jul;45(7-8):869-75.
727. Teichert M, Visser LE, Uitterlinden AG, et al. **Selective serotonin re-uptake inhibiting antidepressants** and the risk of **overanticoagulation** during acenocoumarol maintenance treatment. Br J Clin Pharmacol. 2011 Nov;72(5):798-805.
728. Becker RC, Bassand JP, Budaj A, et al. Bleeding complications with the P2Y12 receptorantagonists **clopidogrel and ticagrelor** in the PLATelet inhibition and patient Outcomes (**PLATO**) trial. Eur Heart J. 2011 Nov 16.
729. Büller HR, Gallus AS, Pillion G, et al. on behalf of the Cassiopea Investigators. Enoxaparin followed by once-weekly **idrabiotaparinux** versus enoxaparin plus warfarin for patients with acute symptomatic pulmonary embolism: a randomised, double-blind, double-dummy, non-inferiority trial. Lancet 2011; published online Nov 28.
730. Rautiainen S, Larsson S, Virtamo J, Wolk A. **Total antioxidant capacity of diet and risk of stroke**: A population-based prospective cohort of women. Stroke 2012; DOI:10.1161/STROKEAHA.111.635557.
731. Heneghan C, Ward, A, Perera R, and The Self-Monitoring Trialist Collaboration. **Self-monitoring of oral anticoagulation**: systematic review and meta-analysis of individual patient data. Lancet 2011; published online Dec 1.
732. Simpson SH, Gamble JM, Mereu L, et al. Effect of **aspirin** dose on mortality and cardiovascular events in people with **diabetes**: a meta-analysis. J Gen Intern Med. 2011 Nov;26(11):1336-44.
733. Ho KM, Chavan S, Pilcher D. **Omission of early thromboprophylaxis and mortality in critically ill patients**: a multicenter registry study. Chest. 2011;140(6):1436-1446.
734. Lip GYH, Andreotti F, Fauchier L, et al. **Bleeding risk assessment and management in atrial fibrillation** patients. Executive summary of a position document from the European Heart Rhythm Association [EHRA], endorsed by the European Society of Cardiology [**ESC**] Working Group on Thrombosis. Thromb Haemost 2011; 106:997-1011.
735. Biondi-Zoccai G, Landoni G. **Discontinuation of aspirin** for secondary prevention. BMJ. 2011 Jul 19;343:d3942. doi: 10.1136/bmj.d3942.
736. Douketis JD, Iorio A. The association between **venous thromboembolism and physical inactivity** in everyday life. BMJ. 2011 Jul 4;343:d3865.
737. Sipahi I, Swaminathan A, Natesan V, et al. Effect of antihypertensive therapy on incident **stroke in cohorts with prehypertensive** blood pressure levels: A meta-analysis of randomized controlled trials. Stroke 2011
738. Enden T, Haig Y, Kløw NE, et al. Long-term outcome after additional **catheter-directed thrombolysis versus standard treatment for acute iliofemoral deep vein thrombosis** (the **CaVenT** study): a randomized controlled trial. Lancet 2011
739. Canadian Agency for Drugs and Technologies in Health. Optimal **warfarin management** for the prevention of thromboembolic events in patients with atrial fibrillation: review of Canadian economic studies. (CADTH). 2011 Nov; 1: 1-27.
740. Kakkar AK, Cimminiello C, Goldhaber SZ, et al. Low-molecular-weight heparin (**enoxaparin**) and mortality in acutely ill medical patients (**LIFENOX**). N Engl J Med 2011; 365: 2463-2472.
Kakkar VV, Corrigan TP, Fossard DP, et al. Prevention of **fatal postoperative pulmonary embolism by low doses of heparin**. An international multicentre trial. Lancet 1975; 2:45-51.
741. Holmes MV, Perel P, Shah T, et al. **CYP2C19 genotype, clopidogrel** metabolism, platelet function and cardiovascular events. A systematic review and meta-analysis. JAMA 2011; 306:2704-2714.
742. Uchino K, Hernandez AV. **Dabigatran** association with **higher risk of acute coronary events**: meta-analysis of noninferiority randomized controlled trials. Arch Intern Med. doi:10.1001/archinternmed.2011.1666.
743. Seshasai SRK, Wijesuriya S, Sivakumaran R, et al. Effect of **aspirin** on **vascular and nonvascular outcomes**: meta-analysis of randomized controlled trials [online Jan 9, 2012]. Archives Intern Med. doi:10.1001/archinternmed.2011.628.
744. Flinterman LE, van Hylckama Vlieg A, Cannegieter S, Rosendaal FR. **Long-term survival** in a large cohort of patients with venous thrombosis: Incidence and predictors. PLoS Med 2012; DOI:10.1371/journal.pmed.1001155.
745. Lip GY, Felmeden DC, Dwivedi G. **Antiplatelet agents and anticoagulants** for hypertension. Cochrane Database Syst Rev. 2011 Dec 7;12:CD003186. Antiplatelet therapy with ASA for primary prevention in patients with elevated blood pressure provides a benefit, reduction in

myocardial infarction, which is negated by a harm of similar magnitude, increase in major haemorrhage.The benefit of antiplatelet therapy for secondary prevention in patients with elevated blood pressure is many times greater than the harm.Benefit has not been demonstrated for warfarin therapy alone or in combination with aspirin in patients with elevated blood pressure.

746. Leung AN, Bull TM, Jaeschke R, et al. **ATS/STR** Committee on Pulmonary Embolism in Pregnancy. An official American Thoracic Society/Society of Thoracic Radiology clinical practice guideline: **evaluation of suspected pulmonary embolism in pregnancy**. Am J Respir Crit Care Med. 2011 Nov 15;184(10):1200-8.
747. Angiolillo DJ, Firstenberg MS, Price MJ, et al. Bridging antiplatelet therapy with **cangrelor** in patients undergoing cardiac surgery. A randomized controlled trial. (**BRIDGE**) JAMA 2012; 307:265-274.
748. Januel J-M, Chen G, Ruffieux C, et al. Symptomatic **in-hospital deep vein thrombus and pulmonary embolism** following **hip and knee arthroplasty** among patients receiving recommended prophylaxis. A systematic review. JAMA 2012; 307:294-303.
749. Roy B et al. Effect of **Warfarin on Outcomes in Septuagenarian** Patients With Atrial Fibrillation. (**AFFIRM**) Am J Cardiol. 2011 Nov 23.
750. Gwon HC, Hahn JY, et al. **Six-month versus 12-month dual antiplatelet** therapy after implantation of drug-eluting stents: the Efficacy of Xience/Promus Versus Cypher to Reduce Late Loss After Stenting (**EXCELLENT**) randomized, multicenter study.Circulation. 2012;125:505–513.
751. Menditto VG, Lucci M, Polonara S et al. Management of **Minor Head Injury in Patients Receiving Oral Anticoagulant Therapy (warfarin)**: A Prospective Study of a 24-Hour Observation Protocol. Ann Emerg Med. 2012 Jan 13. (Second CT scan to detect delayed bleeding)
752. Kappelman MD, Horvath-Puho E, Sandler RS, et al. **Thromboembolic risk among Danish children and adults with inflammatory bowel diseases**: a populationbased nationwide study. Gut 2011;60:937–943.
753. Cayla G, Hulot JS, O'Connor SA et al. Clinical, angiographic, and genetic factors associated with early coronary stent thrombosis. JAMA. 2011 Oct 26;306(16):1765-74. (3 genes and 2 clopidogrel related factors-loading dose & PPIs))
754. Carlquist JF, Anderson JL. Using **pharmacogenetics in real time to guide warfarin** initiation: a clinician update. Circulation. 2011 Dec 6;124(23):2554-9.
755. Lakkireddy D, Reddy YM, Di Biase L, et al. Feasibility and safety of **dabigatran versus warfarin** for periprocedural anticoagulation in patients undergoing **radiofrequency ablation** for atrial fibrillation. J Am Coll Cardiol 2012.
756. Diener HC, Eikelboom J, Connolly SJ, et al. **Apixaban versus aspirin** in patients with atrial fibrillation and **previous stroke** or transient ischaemic attack: a predefined subgroup analysis from **AVERROES**, a randomised trial. Lancet Neurol 2012.
Flaker GC, Eikelboom JW, Shestakovska O, et al. Bleeding During Treatment With Aspirin Versus Apixaban in Patients With Atrial Fibrillation Unsuitable for Warfarin: The Apixaban Versus Acetylsalicylic Acid to Prevent Stroke in Atrial Fibrillation Patients Who Have Failed or Are **Unsuitable for Vitamin k Antagonist** Treatment (**AVERROES**) Trial. Stroke. 2012 Oct 2.
757. Seshasai SRK, Wijesuriya S, Sivakumaran R, et al. Effect of **aspirin** on vascular and nonvascular outcomes: meta-analysis of randomized controlled trials [online January 9, 2012]. Arch Intern Med. 2012;172(3):209-216.
758. Wellenius GA, Burger MR, Coull BA, et al. Ambient **air pollution** and the risk of acute ischemic stroke. Arch Intern Med. 2012;172(3):229-23.
759. Agnelli G, George DJ, Kakkar AK, et al. **Semuloparin** for thromboprophylaxis in patients receiving chemotherapy for cancer. (**SAVE-ONCO**) N Engl J Med 2012;366:601-9.
760. Jaturapatporn D, Isaac MG, McCleery J, et al. **Aspirin, steroidal and non-steroidal anti-inflammatory drugs** for the treatment of **Alzheimer`s disease**. Cochrane Database Syst Rev. 2012 Feb 15;2:CD006378. Based on the studies carried out so far, the efficacy of aspirin, steroid and NSAIDs (traditional NSAIDs and COX-2 inhibitors) is not proven. Therefore, these drugs cannot be recommended for the treatment of AD.
761. Prandoni P, Noventa F, Quintavalla R, et al. Thigh-length versus below-knee compression elastic stockings for prevention of the postthrombotic syndrome in patients with proximal-venous thrombosis: a randomized trial. Blood. 2012 Feb 9;119(6):1561-1565
762. Cohen JM, Akl EA, Kahn SR. Pharmacologic and compression therapies for **postthrombotic syndrome** (PTS): a systematic review of randomized controlled trials. Chest. 2012 Feb;141(2):308-20. (supports **intermittent compression**)
763. Poli D, Antonucci E, Testa S, et al. Italian Federation of Anticoagulation Clinics. Bleeding risk in **very old patients** on vitamin K antagonist (**warfarin**) treatment: results of a prospective collaborative study on elderly patients followed by Italian Centres for Anticoagulation. Circulation. 2011 Aug 16;124(7):824-9.
764. Paikin J, Eikelboom, J. **Aspirin (patient page).** Circulation. 2012;125:e439-e442.
765. Furlan AJ, Reisman M, Massaro J, et al. **Closure** or medical therapy for cryptogenic stroke with **patent foramen ovale**. **(Closure I)** N Engl J Med 2012;366:991-9. (closure with a device did not benefit)
766. **Aspirin for cancer**: Rothwell PM, Price JF, Fowkes FGR, et al. Short-term eff ects of daily aspirin on cancer incidence, mortality, and non-vascular death: analysis of the time course of risks and benefi ts in 51 randomised controlled trials. Lancet 2012; online March 21.
Rothwell PM, Wilson M, Price JF, Belch JFF, Meade TW, Mehta Z. Eff ect of daily aspirin on risk of cancer metastasis: a study of incident cancers during randomised controlled trials. Lancet 2012; online March 21. DOI:10.1016/S0140-6736(12)60209-8.
Algra AM, Rothwell PM. Eff ects of regular aspirin on long-term cancer incidence and metastasis: a systematic comparison of evidence from observational studies versus randomised trials. Lancet Oncology 2012; online March 21. DOI:10.1016/S1470-2045(12)70112-2.
Rothwell PM, Wilson M, Elwin CE, et al. Long-term effect of **aspirin on colorectal cancer** incidence and mortality: 20-year follow-up of five randomised trials. Lancet. 2010 Oct 21.
Rothwell PM, Fowkes FG, Belch JF, Ogawa H, Warlow CP, Meade TW. Effect of daily **aspirin on long-term risk of death due to cancer**: analysis of individualpatient data from randomised trials. Lancet. 2011 Jan 1;377(9759):31-41.
Cook NR, Lee IM, Gaziano JM, et al. Low-dose aspirin in the primary prevention of cancer: the Women's Health Study (**WHS**): a randomized controlled trial. JAMA 2005; 294: 47–55. (no effect)
Sturmer T, Glynn RJ, Lee IM, Manson JE, Buring JE, Hennekens CH. Aspirin use and colorectal cancer: post-trial follow-up data from the Physicians' Health Study (**PHS**). Ann Intern Med 1998; 128: 713–20. (no effect)
767. Health Canada Mar/12 The Pradax (**dabigatran** etexilate) product monograph has been updated to include in elderly to assess **renal function** initially & at least once a year.
Use of Pradax® in patients with hemodynamically significant rheumatic valvular heart disease, especially mitral stenosis, or in patients with prosthetic heart valves is not recommended.
768. Palmer SC, Micco LD, Razavian M, et al. Effects of **antiplatelet therapy** on mortality and cardiovascular and bleeding outcomes in persons with **chronic kidney disease**. A systematic review and meta-analysis. Ann Intern Med 2012; 156:445-459.
769. Skanes AC, Healey JS, Cairns JA, et al. Focused **2012 update of the Canadian Cardiovascular Society (CCS) atrial fibrillation guidelines**: Recommendations for stroke prevention and rate/rhythm control. Can J Cardiol 2012; 28:125-136.
770. Schulman S. Resumption of oral anticoagulation after warfarin-associated intracerebral hemorrhage: no. Stroke. 2011 Dec;42(12):3663-4.
Steiner T. Resumption of oral anticoagulation after warfarin-associated intracerebral hemorrhage: yes. Stroke. 2011 Dec;42(12):3661-2.
771. Büller HR et al. for the **EINSTEIN–PE** Investigators. Oral **rivaroxaban** (15mg po bid x 3 wk, then 20mg od) for the treatment of symptomatic pulmonary embolism. N Engl J Med 2012 Mar 26.
772. Agarwal S, Hachamovitch R, Menon V. Current **trial-associated outcomes with warfarin** in prevention of stroke in patients with nonvalvular atrial fibrillation: a meta-analysis [published online March 26, 2012]. Arch Intern Med. doi10.1001/archinternmed.2012.121
773. Morrow DA et al. for the **TRA 2P–TIMI 50** Steering Committee and Investigators. **Vorapaxar** in the secondary prevention of atherothrombotic events. N Engl J Med 2012 Mar 24.
774. Roberts JD, Wells GA, Le May MR, et al. Point-of-care genetic testing for personalisation of antiplatelet treatment (**RAPID GENE**): a prospective, randomised, proof-of-concept trial. Lancet 2012; online March 29. (clopidogrel or prasugrel given)
775. Walter S, Kostopoulos P, Haass A, et al. Diagnosis and treatment of patients with stroke in a **mobile stroke unit** versus in hospital: A randomised controlled trial. Lancet Neurol 2012.
776. Ahmed I, Gertner E. Safety of **arthrocentesis and joint injection in patients receiving anticoagulation** at therapeutic levels. Am J Med. 2012 Mar;125(3):265-9.
777. Kasiman K, Lundholm C, Sandin S, et al. **Familial Effects on Ischemic Stroke**: The Role of Sibling Kinship, Sex and Age of Onset. Circ Cardiovasc Genet. 2012 Mar 9.
778. Piazza G. **Cerebral venous thrombosis**. Circulation. 2012 Apr 3;125(13):1704-9.
779. Shaheen K, Alraies MC, Alraiyes AH, et al. **Factor V Leiden**: How great is the risk of venous thromboembolism? Cleve Clin J Med. 2012 Apr;79(4):265-72.
780. Voore NK, Rahman A, Sanna S, Bahrain H. **Purpuric lesion** on the elbow. Cleve Clin J Med. 2012 Apr;79(4):253-4. (**warfarin induced necrosis**)
781. De Caterina R, Husted S, Wallentin L, et al. **New oral anticoagulants** in **atrial fibrillation** and acute coronary syndromes. **ESC** Working Group on Thrombosis—Task Force on Anticoagulants in Heart Disease position paper. J Am Coll Cardiol 2012; 59:1413-25.
782. Liu CP, Chen WC, Lai KH, et al. **Esomeprazole Alone Compared with Esomeprazole Plus Aspirin** for the Treatment of Aspirin-Related Peptic Ulcers. Am J Gastroenterol. 2012 Apr 17.
783. Hsu PI, Lai KH, Liu CP. **Esomeprazole with clopidogrel reduces peptic ulcer recurrence, compared with clopidogrel alone**, in patients with atherosclerosis. Gastroenterology. 2011 Mar;140(3):791-8.
784. Lin KJ, Hernández-Díaz S, García Rodríguez LA. **Acid suppressants reduce risk of gastrointestinal bleeding in patients on antithrombotic** or anti-inflammatory therapy. Gastroenterology. 2011 Jul;141(1):71-9.
785. Anderson JL, Horne BD, Stevens SM, et al. A randomized and clinical effectiveness trial comparing two **pharmacogenetic algorithms** and standard care for individualizing warfarin dosing (**Coumagen-II**). Circulation. 2012;125:1997–2005.
786. Valgimigli M, Campo G, Monti M, et al. **Short- versus long-term duration (6 vs 24 months)** of dual-antiplatelet therapy after coronary stenting: a randomized multicenter trial (**Prodigy**). Circulation. 2012;125:2015–2026.
787. Bastiaannet E, Sampieri K, Dekkers OM, et al. Use of **Aspirin** postdiagnosis improves survival for **colon cancer** patients. Br J Cancer. 2012 Mar 27.
788. Hart RG, Diener HC, Yang S, et al. **Intracranial hemorrhage** in atrial fibrillation patients during anticoagulation with warfarin or **dabigatran**: The **RE-LY** trial. Stroke 2012.
789. Baillargeon J, Holmes HM, Lin YL, et al. Concurrent use of **warfarin and antibiotics** (eg azoles, macrolides, quinolones etc..) and the risk of **bleeding** in older adults. Am J Med. 2012 Feb;125(2):183-9.
790. Olesen JB, Torp-Pedersen C, Hansen ML, and Lip GYH. The value of the **CHA2DS2-VASc score** for refining stroke risk stratification in patients with atrial fibrillation with a CHADS2 score 0-1: A nationwide cohort study. Thromb Haemost 2012.
791. Homma S, Thompson JLP, Pullicino PM, et al. **Warfarin and aspirin** in patients with **heart failure** and sinus rhythm. (**WARCEF**) N Engl J Med 2012. DOI: 10.1056/NEJMoa1202299.
792. Rogers MAM, Levine DA, Blumberg N, et al. **Triggers of hospitalization for venous thromboembolism**. Circulation. 2012;125:2092–2099.
793. Prasad V, Rho J, Cifu A. The Diagnosis and **Treatment of Pulmonary Embolism**: A Metaphor for Medicine in the Evidence-Based Medicine Era. Arch Intern Med. 2012 Apr 2.
794. Tsai J, Grosse SD, Grant AM, et al. Trends in In-Hospital **Deaths** Among Hospitalizations With **Pulmonary Embolism**. Arch Intern Med. 2012 Apr 2.
795. Goldhaber SZ, Bounameaux H. **Pulmonary embolism and deep vein thrombosis**. Lancet. 2012 Apr 5.
796. Larsson SC, Virtamo J, Wolk A. **Dairy** Consumption and Risk of **Stroke** in Swedish Women and Men. Stroke. 2012 Apr 19.
797. Lee SJ, Shin DH, Hwang HJ et al. **Bleeding Risk** and Major Adverse Events in Patients With **Previous Ulcer on Oral Anticoagulation** Therapy. Am J Cardiol. 2012 Apr 18.
798. Rubboli A, Magnavacchi P, Guastaroba P, et al.Antithrombotic Management and 1-Year Outcome of Patients on **Oral Anticoagulation Undergoing Coronary Stent** Implantation (from the Registro Regionale Angioplastiche Emilia-Romagna Registry). Am J Cardiol. 2012 Feb 17.
799. Di Nisio M, Wichers IM, Middeldorp S. **Treatment for superficial thrombophlebitis of the leg.** Cochrane Database Syst Rev. 2012 Mar 14;3:CD004982. Prophylactic dose fondaparinux given for six weeks appears to be a valid therapeutic option for ST of the legs. Further research is needed to assess the role of new oral direct thrombin and activated factor-X inhibitors, LMWH, NSAIDs; the optimal doses and duration of treatment; and whether a combination therapy may be more effective than single treatment. Adequately designed and conducted studies are required to clarify the role of topical and surgical treatments.
800. Frelinger AL 3rd, Lee RD, Mulford DJ, et al. A randomized, 2-period, crossover design study to assess the effects of **dexlansoprazole, lansoprazole, esomeprazole, and omeprazole** on the steady-state pharmacokinetics and pharmacodynamics of **clopidogrel** in healthy volunteers. J Am Coll Cardiol. 2012 Apr 3;59(14):1304-11.
801. Ng FH, Tunggal P, Chu WM, et al. **Esomeprazole compared with famotidine** in the prevention of upper gastrointestinal bleeding in patients with acute coronary syndrome or myocardial infarction. Am J Gastroenterol. 2012 Mar;107(3):389-96.
802. Derry S, Moore RA. Single dose oral **aspirin for acute postoperative pain** in adults. Cochrane Database Syst Rev. 2012 Apr 18;4:CD002067. Aspirin is an effective analgesic for acute pain of moderate to severe intensity. High doses are more effective, but are associated with increased adverse events, including drowsiness and gastric irritation. The pain relief achieved with aspirin was very similar milligram for milligram to that seen with paracetamol.
803. Perk J, De Backer G, Gohlke H, et al. **European guidelines (ESC) on cardiovascular disease** in clinical practice (version 2012). Eur Heart J2012; DOI:10.1093/eurheartj/ehs092.
804. Sobieraj DM, Lee S, Coleman CI et al. **Prolonged versus standard-duration** venous thromboprophylaxis in major orthopedic surgery. A systematic review. Ann Intern Med. 2012;156:720-7.
805. Neumann I, Rada G, Claro JC et al. **Oral direct factor Xa inhibitors versus low-molecular-weight heparin** to prevent thromboembolism in patients undergoing total hip or knee replacement. A systematic review and meta-analysis. Ann Intern Med. 2012;156:710-9.
806. Del Río Solá ML, Antonio J, Fajardo G, Vaquero Puerta C. Influence of **Aspirin** Therapy in the Ulcer Associated With **Chronic Venous Insufficiency**. Ann Vasc Surg. 2012 Mar 19.
807. Davis SM, Donnan GA. **Secondary Prevention after Ischemic Stroke or Transient Ischemic Attack**. N Engl J Med 2012; 366:1914-1922.
808. Maletis GB, Inacio MC, Reynolds S, Funahashi TT. Incidence of symptomatic **venous thromboembolism** after **elective knee arthroscopy**. J Bone Joint Surg Am. 2012 Apr 18;94(8):714-20. The ninety-day incidence of symptomatic venous thromboembolism after elective knee arthroscopy was relatively low, with a 0.25% incidence of deep venous thrombosis and a 0.17% incidence of pulmonary embolism.
809. Parkin L, Sweetland S, Balkwill A, et al. the **Million Women Study Collaborators**. **Body Mass Index, Surgery, and Risk of Venous Thromboembolism** in Middle-Aged Women: A Cohort Study. Circulation. 2012 Apr 17;125(15):1897-1904.
810. IST-3 collaborative group. The benefits and harms of **intravenous thrombolysis** with recombinant tissue plasminogen activator within 6 h of acute ischaemic stroke (the third international stroke trial [IST-3]): a randomised controlled trial. Lancet 2012; online May 23.
811. Wardlaw J, Murray V, Berge E, et al. **Recombinant tissue plasminogen activator** for acute ischaemic stroke: an updated systematic review and meta-analysis. Lancet 2012; published online May 23.

812. Becattini C, Agnelli G, Schenone A, et al. **Aspirin for preventing the recurrence of venous thromboembolism**. (**WARFASA**) N Engl J Med 2012;366:1959-67.
Brighton TA et al. **Low-dose aspirin for preventing recurrent venous thromboembolism**. (**Aspire**) N Engl J Med 2012 Nov 4; [e-pub ahead of print].
813. Park Y, Jeong YH, Tantry US, et al. Accelerated platelet inhibition (with **clopidogrel**) by switching from **atorvastatin to a non-CYP3A4-metabolized statin** in patients with high platelet reactivity (ACCEL-STATIN) study. Eur Heart J 2012.
814. Medical Letter. Choice of drugs for **Heparin-Induced Thrombocytopenia** (HIT). May 28, 2012. (argatroban, fondaparinux, danaparoid)
815. Lackland DT, Elkind MSV, D'Agostino R, et al. Inclusion of **stroke in cardiovascular risk prediction** instruments: A statement for healthcare professionals from the American Heart Association/American Stroke Association. Stroke 2012;
816. Feske SK. **Thrombolytic therapy of acute stroke**. Circulation. 2012 May 29;125(21):2662-6.
817. Schindewolf M, Lindhoff-Last E, Ludwig RJ, Boehncke WH. **Heparin-induced skin lesions**. Lancet. 2012 May 25.
818. Cappuccio FP, Ji C. **Less salt** and less risk of stroke: further support to action. Stroke. 2012 May;43(5):1195-6.
819. Banerjee C, Moon YP, Paik MC, et al. Duration of **diabetes and risk of ischemic stroke**: the northern Manhattan study. Stroke. 2012 May;43(5):1212-7.
820. Mazighi M, Meseguer E, Labreuche J, Amarenco P. **Bridging therapy in acute ischemic stroke**: a systematic review and meta-analysis. Stroke. 2012 May;43(5):1302-8.
821. Lee M, Saver JL, Hong K-S, Song S, Chang K-H, Ovbiagele B. Effect of **pre-diabetes on future risk of stroke**: meta-analysis. BMJ 2012;344:e3564.
822. Schouten HJ, Koek HL, Oudega R, et al. **Validation of two age dependent D-dimer cut-off values** for exclusion of deep vein thrombosis in suspected elderly patients in primary care: retrospective, cross sectional, diagnostic analysis. BMJ. 2012 Jun 6;344:e2985.
823. Dávalos A, Alvarez-Sabín J, Castillo J, et al, International Citicoline Trial on acUte Stroke (**ICTUS**) trial investigators. **Citicoline** in the treatment of acute ischaemic stroke: an international, randomised, multicentre, placebo-controlled study (ICTUS trial). Lancet 2012; online June 11.
824. Price MJ, Walder JS, Baker BA et al. Recovery of platelet function after **discontinuation of prasugrel or clopidogrel** maintenance dosing in aspirin-treated patients with stable coronary disease. The RECOVERY trial. J Am Coll Cardiol 2012.
825. Gómez-Outes A, et al. **Dabigatran, rivaroxaban, or apixaban versus enoxaparin** for thromboprophylaxis after total **hip or knee replacement**: systematic review, meta-analysis, and indirect treatment comparisons. BMJ 2012;344:e3675.
826. Garcia DA, Crowther MA. **Reversal of warfarin**: case-based practice recommendations. Circulation. 2012 Jun 12;125(23):2944-7.
827. Mills EJ, Wu P, Alberton M, et al. **Low-dose Aspirin** and **Cancer** Mortality: A Meta-analysis of Randomized Trials. Am J Med. 2012 Jun;125(6):560-7.
828. James SK, Storey RF, Khurmi NS, et al.. **Ticagrelor versus clopidogrel** in patients with acute coronary syndromes and a history of stroke or transient ischemic attack. (**Plato**) *Circulation.* 2012;125:2914 –2921.
829. Jardine MJ, Kang A, Zoungas S, et al. The effect of **folic acid based homocysteine lowering** on cardiovascular events in people with **kidney disease**: systematic review and meta-analysis. BMJ 2012;344:e3533.
830. Kiviniemi T, Karjalainen P, Pietilä M, et al. Comparison of **Additional Versus No Additional Heparin During Therapeutic Oral Anticoagulation** (warfarin) in Patients Undergoing Percutaneous Coronary Intervention. Am J Cardiol. 2012 Mar 29.
831. Kumai Y, Kamouchi M, Hata J, et al; For the FSR Investigators. **Proteinuria and clinical outcomes after ischemic stroke**. Neurology. 2012 Jun 12;78(24):1909-1915.
832. **BRIDGE** Study Investigators. Bridging **anticoagulation**: is it needed when warfarin is interrupted around the time of a surgery or procedure? Circulation. 2012 Mar 27;125(12):e496-8.
833. Geeganage CM, Diener HC, Algra A, et al. **Dual or mono antiplatelet therapy for patients with acute ischemic stroke** or transient ischemic attack: systematic review and meta-analysis of randomized controlled trials. Stroke. 2012 Apr;43(4):1058-66.
834. Gurbel PA, Nolin TD, Tantry US. **Clopidogrel efficacy and cigarette smoking** status. JAMA 2012; 307:2495-2496.
835. Hamer M, Kivimaki M, Stamatakis E, Batty GD. **Psychological distress** as a risk factor for death from cerebrovascular disease. CMAJ. 2012 Jun 18.
836. Streiff MB, Carolan HT, Hobson DB, et al. Lessons from the Johns Hopkins Multi-Disciplinary **Venous Thromboembolism (VTE) Prevention Collaborative**. BMJ. 2012 Jun 19;344:e3935.
837. Costa GL, Lamego RM, Colosimo EA, et al. Identifying Potential Predictors of **High-Quality Oral Anticoagulation** Assessed by Time in Therapeutic International Normalized Ratio Range: A Prospective, Long-Term, Single-Center, Observational Study. Clin Ther. 2012 Jun 18.
838. Suh DC, Nelson WW, Choi JC, Choi I. Risk of **Hemorrhage and Treatment Costs Associated With Warfarin Drug Interactions** in Patients With Atrial Fibrillation. Clin Ther. 2012 Jun 19.
839. Ndrepepa G, Schuster T, Hadamitzky M et al. Validation of the bleeding academic research consortium definition of bleeding (**BARC**) in patients with coronary artery disease undergoing percutaneous coronary intervention. Circulation. 2012 Mar 20;125(11):1424-31.
840. Subherwal S, Peterson ED, Chen AY, et al. Admission International Normalized Ratio Levels, Early Treatment Strategies, and Major Bleeding Risk Among **Non-ST-Segment-Elevation Myocardial Infarction** Patients on Home **Warfarin** Therapy: Insights From the National Cardiovascular Data Registry. Circulation. 2012 Mar 20;125(11):1414-23.
841. Capodanno D, Angiolillo DJ. **Antithrombotic therapy in patients with chronic kidney disease**. Circulation. 2012 May 29;125(21):2649-61.
842. De Berardis G, Lucisano G, D'Ettorre A, et al. Association of **aspirin use** with major **bleeding** in patients with and without **diabetes**. JAMA. 2012;307(21): 2286-2294.
843. Reny JL, Berdagué P, Poncet A, et al. **Antiplatelet Drug Response Status Does Not** Predict Recurrent Ischemic Events in Stable Cardiovascular Patients: Results of the ADRIE Study. Circulation. 2012 May 21.
844. Xian Y, Liang L, Smith EE, et al. Risks of intracranial hemorrhage among patients with acute ischemic stroke receiving **warfarin and treated with intravenous tissue plasminogen activator**. JAMA 2012; 307:2600-2608. (warfarin INR ≤ 1.7 seems safe)
845. Chong LY, Fenu E, Stansby G, Hodgkinson S; on behalf of the Guideline Development Group. Management of venous thromboembolic diseases and the role of **thrombophilia testing**: summary of **NICE** guidance. BMJ. 2012 Jun 27;344:e3979.
846. Noth I, Anstrom KJ, Calvert SB, et al; The Idiopathic Pulmonary Fibrosis Clinical Research Network (IPFnet). A Placebo-Controlled Randomized Trial of **Warfarin in Idiopathic Pulmonary Fibrosis.** Am J Respir Crit Care Med. 2012 May 3.
847. Ruecker M, Matosevic B, Willeit P, et al. **Subtherapeutic warfarin** therapy entails an increased bleeding risk after stroke **thrombolysis**. Neurology 2012;79:31–38.
848. Frost C, Wang J, Nepal S, et al. **Apixaban**, an oral, direct factor Xa inhibitor: single-dose safety, pharmacokinetics, pharmacodynamics and food effect in healthy subjects. Br J Clin Pharmacol. 2012 Jul 3.
849. Sanders LM, Srikanth VK, Blacker DJ, et al. Performance of the **ABCD2 score** for stroke risk post TIA: Meta-analysis and probability modelling. Neurology. 2012 Jun 13.
850. Zinkstok SM, Roos YB, on behalf of the ARTIS investigators. Early administration of IV **aspirin** in patients treated with **alteplase for acute ischaemic stroke**: a randomised controlled trial. Lancet 2012; online June 28. (not improve outcome at 3 months & more SICH)
851. Palmerini T, Biondi-Zoccai G, Della Riva D, et al. Stent thrombosis with drug-eluting and bare-metal stents: evidence from a comprehensive network meta-analysis. Lancet. 2012 Apr 14;379(9824):1393-402. (CoCr-EES **everolimus** least stent thrombosis)
852. Kostopoulos P, Walter S, Haass A, et al. **Mobile stroke** unit for diagnosis-based triage of persons with suspected stroke. Neurology. 2012 Jun 5;78(23):1849-52.
853. Kamel H, Johnston SC, Kirkham JC, et al. Association Between **Major Perioperative Hemorrhage and Stroke or Q-Wave Myocardial Infarction**. Circulation. 2012 Jun 7.
854. McKinney JS, Kostis WJ. **Statin Therapy and the Risk of Intracerebral Hemorrhage**: A Meta-Analysis of 31 Randomized Controlled Trials. Stroke. 2012 May 15.
855. Douglas IJ, Evans SJW, Hingorani A, et al. **Clopidogrel and interaction with proton pump inhibitors**: comparison between cohort and within person study designs. BMJ 2012;345:e4388.
856. Katsnelson M, Sacco RL, Moscucci M. Progress for stroke prevention with atrial fibrillation: emergence of alternative oral anticoagulants. Stroke. 2012 Apr;43(4):1179-85.
857. Palmer WL, Bottle A, Davie C, et al. **Dying for the weekend**: A retrospective cohort study on the association between day of hospital presentation and the quality and safety of **stroke care**. Arch Neurol 2012.
858. Schneeweiss S, Gagne JJ, Patrick AR, et al. Comparative Efficacy and Safety of **New Oral Anticoagulants** in Patients With Atrial Fibrillation. Circ Cardiovasc Qual Outcomes. 2012 Jul 10.
859. Staats MC, Ernst ME. Pharmacodynamic response to **warfarin after conversion of atrial fibrillation or flutter to sinus rhythm**. Am J Health Syst Pharm. 2012 Jul 1;69(13):1158-61.
860. Jneid H, Anderson JL, Wright SR, et al. **2012 ACCF/AHA** focused update on the guideline for the management of patients with **unstable angina/non-ST elevation myocardial infarction** (Updating the 2007 guideline and replacing the 2011 focused update): A report of the ACCF/AHA. Circulation 2012.
Amsterdam EA, Wenger NK, Brindis RG, et al. **2014 AHA/ACC Guideline for the Management of Patients With Non-ST-Elevation Acute Coronary Syndromes**: Executive Summary: A Report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. Circulation. 2014 Sep 23.
861. Lip GY, Larsen TB, Skjøth F, Rasmussen LH. **Indirect comparisons** of new oral **anticoagulant** drugs for efficacy and safety when used for stroke prevention in atrial fibrillation. J Am Coll Cardiol 2012; 60:738-46.
862. Levine MA, Shao W, Klein D. **Monitoring** of **international normalized ratios**: Comparison of community **nurses** with family **physicians**. Can Fam Physician. 2012 Aug;58(8):e465-71.
863. Kennedy F, Lanfranconi S, Hicks C et al; On behalf of the CADISS Investigators. **Antiplatelets vs anticoagulation** for dissection: CADISS nonrandomized arm and meta-analysis. Neurology. 2012 Aug 14;79(7):686-689.
864. Engelberger RP, Kucher N. Management of **deep vein thrombosis of the upper extremity**. Circulation. 2012 Aug 7;126(6):768-73.
865. Jacobs EJ, Newton CC, Gapstur SM, Thun MJ. Daily **aspirin use and cancer** mortality in a large US cohort. *J Natl Cancer Inst* 2012.
866. Furie KL, Goldstein LB, AlbersGW, et al. Oral **antithrombotic** agents for the prevention of stroke in nonvalvular atrial fibrillation: A science advisory for healthcare professionals from the American Heart Association-**AHA**/American Stroke Association-ASA. Stroke 2012.
867. Wysokinski WE, McBane RD 2nd. **Periprocedural bridging** management of anticoagulation. Circulation. 2012 Jul 24;126(4):486-90.
868. Roe MT et al. **Prasugrel versus clopidogrel** for acute coronary syndromes without revascularization. (**Trilogy ACS**) N Engl J Med 2012 Aug 26.
869. Robertson L, Ghouri MA, Kovacs F. Antiplatelet and anticoagulant drugs for prevention of **restenosis/reocclusion** following peripheral endovascular treatment. Cochrane Database Syst Rev. 2012 Aug 15;8:CD002071. There is limited evidence suggesting that restenosis/reocclusion at six months following peripheral endovascular treatment is reduced by use of antiplatelet drugs compared with placebo/control, but associated information on bleeding and gastrointestinal side effects is lacking. There is also some evidence of variation in effect according to different drugs with cilostazol reducing reocclusion/restenosis at 12 months compared with ticlopidine and both LMWH and batroxobin combined with aspirin appearing beneficial compared with aspirin alone.
870. Choe KS, Cowan JE, Chan JM, et al. **Aspirin** Use and the Risk of **Prostate Cancer** Mortality in Men Treated With Prostatectomy or Radiotherapy. J Clin Oncol. 2012 Aug 27.
871. Härtter S, Sennewald R, Nehmiz G, Reilly P. Oral bioavailability of **dabigatran** etexilate (Pradaxa) after co-medication with **verapamil** in healthy subjects. Br J Clin Pharmacol. 2012 Sep 5.
872. Sanders LM, Srikanth VK, Blacker DJ, et al. Performance of the **ABCD2 score** for stroke risk post TIA: Meta-analysis and probability modeling. Neurology. 2012 Sep 4;79(10):971-80.
873. **SPS3** Investigators, Benavente OR, Hart RG, McClure LA, et al. Effects of **clopidogrel added to aspirin** in patients with recent **lacunar stroke**. N Engl J Med. 2012 Aug 30;367(9):817-25.
874. Kurella Tamura M, Meyer JB, Saxena AB, et al. Prevalence and significance of stroke symptoms among patients receiving maintenance **dialysis**. Neurology. 2012 Sep 4;79(10):981-7.
875. Sobieraj DM, White CM, Alikhanov S, et al. The Impact of Antiplatelet and Anticoagulant Therapies on **Gastrointestinal Symptoms** in Patients with Atrial Fibrillation: A Systematic Review (September). Ann Pharmacother. 2012 Aug 28.
876. Kwong LM, Tong LM. Drug Interactions with **Rivaroxaban** Following Total Joint Replacement Surgery (September). Ann Pharmacother. 2012 Aug 28.
877. Lamberts M, Olesen JB, Ruwald MH, et al. **Bleeding** after Initiation of Multiple Antithrombotic Drugs, Including **Triple Therapy**, in Atrial Fibrillation Patients Following Myocardial Infarction and Coronary Intervention: A Nationwide Cohort Study. Circulation. 2012 Aug 6.
878. Ghanbari H, Phard WS, Al-Ameri H, et al. Meta-Analysis of Safety and Efficacy of **Uninterrupted Warfarin** Compared to Heparin-Based **Bridging** Therapy During Implantation of Cardiac Rhythm Devices. Am J Cardiol. 2012 Aug 17.
879. Camm AJ, Lip GY, De Caterina R, et al. **2012 focused update of the ESC** Guidelines for the management of atrial fibrillation: An update of the 2010 ESC Guidelines for the management of atrial fibrillation * Developed with the special contribution of the European Heart Rhythm Association. Europace. 2012 Aug 24. ESC Updated 2012 Management of Atrial Fibrillation Guidelines. http://www.escardio.org/guidelines-surveys/esc-guidelines/GuidelinesDocuments/Guidelines_Focused_Update_Atrial_Fib_FT.pdf
880. Adam SS, McDuffie JR, Ortel TL, et al. **Comparative Effectiveness of Warfarin and New Oral Anticoagulants** for the Management of Atrial Fibrillation and Venous Thromboembolism: A Systematic Review. Ann Intern Med. 2012 Aug 28.
881. Wijeysundera DN, Wijeysundera HC, Yun L, et al. Risk of **elective major noncardiac surgery after coronary stent insertion**: a population-based study. Circulation. 2012 Sep 11;126(11):1355-62.
882. Coleman CI, Straznitskas AD, Sobieraj DM, Kluger J, Anglade MW. Cost-effectiveness of clopidogrel plus aspirin for stroke prevention in patients with atrial fibrillation in whom warfarin is unsuitable. Am J Cardiol. 2012 Apr 1;109(7):1020-5.
883. Horsted F, West J, Grainge MJ. Risk of **venous thromboembolism** in patients with **cancer**: a systematic review and meta-analysis. PLoS Med. 2012 Jul;9(7):e1001275 (Highest: pancreas, brain, lung)
884. Witt DM, Delate T, Garcia DA, et al. Risk of thromboembolism, recurrent hemorrhage, and death after **warfarin therapy interruption for gastrointestinal tract bleeding** [online September 17, 2012]. Arch Intern Med.
885. Gioia LC, Tollard E, Dubuc V, et al. **Silent ischemic lesions** in young adults with first stroke are associated with recurrent stroke. Neurology. 2012 Sep 18;79(12):1208-14.
886. Tachjian A, Maria V, Jahangir A. Use of **herbal products** and potential interactions in patients with cardiovascular diseases. J Am Coll Cardiol. 2010 Feb 9;55(6):515-25.
887. Boulet SL, Grosse SD, Thornburg CD, et al. **Trends** in Venous **Thromboembolism**-Related Hospitalizations, 1994-2009. Pediatrics. 2012 Sep 17.
888. Coutts SB, Modi J, Patel SK, et al. What Causes **Disability** After **Transient Ischemic Attack and Minor Stroke**?: Results From the CT And MRI in the Triage of TIA and Minor Cerebrovascular Events to Identify High Risk Patients (CATCH) Study. Stroke. 2012 Sep 13.
889. Simmons B, Cirignano B, Gadegbeku a. **Transcient Ischemic Attack** Parts 1 (Diagnosis & Evaluation) and 2 (Risk Factor Modification & Treatment). Am Fam Physician. 2012;86(6): 521-32.

890. Casado Arroyo R, Polo-Tomas M, Roncalés MP, et al. **Lower GI bleeding** is more common than upper among patients on **dual antiplatelet** therapy: long-term follow-up of a cohort of patients commonly using PPI co-therapy. Heart. 2012 May;98(9):718-23.8
891. Komocsi A, Vorobcsuk A, Kehl D, Aradi D. Use of new-generation oral anticoagulant agents in patients receiving antiplatelet therapy after an **acute coronary syndrome**: systematic review and meta-analysis of randomized controlled trials [online Sept 24, 2012]. Arch Intern Med.
892. Kim BK, Hong MK, Shin DH, et al. A new strategy for discontinuation of dual antiplatelet therapy: Real Safety and Efficacy of **3-month Dual Antiplatelet Therapy** following Endeavor **Zotarolimus**-Eluting Stent Implantation (RESET) trial. J Am Coll Cardiol 2012.
893. Ferreira-Gonzales I, Marsal JR, Rivera A, et al. **Double antiplatelet therapy after drug-eluting stent implantation**: risk associated with **discontinuation within the first year**. J Am Coll Cardiol 2012 .
894. Konrad G, Katz A. Are medication restrictions before **FOBT** necessary?:Practical advice based on a systematic review of the literature. Can Fam Physician. 2012 Sep;58(9):939-48.
895. Price J, Hynes M, Labinaz M et al. **Mechanical valve thrombosis with dabigatran**. J Am Coll Cardiol 2012.
896. Palacio S, Hart RG, Pearce LA, et al. Effect of addition of **clopidogrel to aspirin on mortality**: systematic review of randomized trials. Stroke. 2012 Aug;43(8):2157-62.
897. Maddali S, Morton C, Biring T, Bluhm J, Hanson M, et al. **Antithrombotic therapy supplement**. Bloomington (MN): Institute for Clinical Systems Improvement (**ICSI**); 2012 May.
898. Kirley K, Qato DM, Kornfield R, et al. **National trends in oral anticoagulant use in the United States**, 2007 to 2011. Circ Cardiovasc Qual Outcomes 2012; 5:615-621.
899. Poulsen BK, Grove EL, Husted SE. New oral anticoagulants: a review of the literature with particular emphasis on patients with **impaired renal function**. Drugs. 2012 Sep 10;72(13):1739-53.
900. Van Spall HG, Wallentin L, Yusuf S, et al. Variation in warfarin dose adjustment practice is responsible for differences in the quality of anticoagulation control between centers and countries: an analysis of patients receiving warfarin in the **RE-LY** trial. Circulation2012.
901. Kern S, Skoog I, Östling S, et al. Does low-dose **acetylsalicylic acid prevent cognitive decline** in women with high cardiovascular risk? A 5-year follow-up of a non-demented population-based cohort of Swedish elderly women. BMJ Open 2012.
902. Tosetto A, Iorio A, Marcucci M, et al. **Predicting disease recurrence in patients with previous unprovoked venous thromboembolism**: a proposed prediction score (**DASH**). J Thromb Haemost. 2012 Jun;10(6):1019-25.
903. Dentali F, Riva N, Crowther M, et al. Efficacy and safety of the **novel oral anticoagulants in atrial fibrillation**: a systematic review and meta-analysis of the literature. Circulation 2012.
904. Mahmoodi BK, Gansevoort RT, Næss IA, et al. Association of **mild to moderate chronic kidney disease** with venous thromboembolism: pooled analysis of five prospective general population cohorts. Circulation. 2012 Oct 16;126(16):1964-71.
905. Siegal D, Yudin J, Kaatz S, et al. **Periprocedural heparin bridging** in patients receiving vitamin k antagonists: systematic review and meta-analysis of bleeding and thromboembolic rates. Circulation. 2012 Sep 25;126(13):1630-9.
906. Harskamp RE, Beijk MA, Damman P, et al. Prehospitalization Antiplatelet Therapy and Outcomes After **Saphenous Vein Graft** Intervention. Am J Cardiol. 2012 Oct 24.
907. Gomes T, Mamdani MM, Holbrook AM, et al. **Persistence** with therapy among patients treated with **warfarin** for atrial fibrillation. Arch Intern Med 2012.
908. Collet J-P et al. for the **ARCTIC** Investigators. **Bedside monitoring to adjust antiplatelet** therapy for coronary stenting. N Engl J Med. 2012 Nov 4; [e-pub ahead of print].
909. Gurbel PA et al. **Platelet function** during extended prasugrel and clopidogrel therapy for patients with ACS treated without revascularization: The **TRILOGY ACS** Platelet Function Substudy.JAMA 2012 Nov 5; [e-pub ahead of print].
910. Brighton TA et al. **Low-dose aspirin for preventing recurrent venous thromboembolism**. (**Aspire**) N Engl J Med 2012 Nov 4; [e-pub ahead of print].
911. Fox BD, Kahn SR, Langleben D, Eisenberg MJ, Shimony A. Efficacy and safety of **novel oral anticoagulants for treatment of acute venous thromboembolism**: direct and adjusted indirect meta-analysis of randomised controlled trials. BMJ. 2012 Nov 13;345:e7498.
912. Baker WL, Phung OJ. **Systematic review and adjusted indirect comparison meta-analysis of oral anticoagulants in atrial fibrillation**. Circ Cardiovasc Qual Outcomes. 2012 Sep 1;5(5):711-9.
913. Villa P, Kajantie E, Raikkonen K, et al. **Aspirin** in the prevention of **pre-eclampsia in high-risk women**: a randomised placebo-controlled PREDO Trial and a meta-analysis of randomised trials. BJOG. 2012 Nov 6.
914. Donzé J, Clair C, Hug B, Rodondi N, Waeber G, Cornuz J, Aujesky D. **Risk of falls** and major bleeds in patients on oral **anticoagulation** therapy. Am J Med. 2012 Aug;125(8):773-8.
915. Zheng ASY, Churilov L, Colley RE, et al. Association of **aspirin resistance** with increased stroke severity and infarct size. Arch Neurol 2012.
916. Weitz JI, Quinlan DJ, Eikelboom JW. **Periprocedural** management and approach to bleeding in patients taking **dabigatran**. Circulation. 2012 Nov 13;126(20):2428-32.
917. Valentine N, Van de Laar FA, van Driel ML. Adenosine-diphosphate (ADP) receptor antagonists (**clopidogrel, dipyridamole**) for the prevention of cardiovascular disease in type 2 **diabetes** mellitus. Cochrane Database Syst Rev. 2012 Nov 14;11:CD005449. doi: 10.1002/14651858.CD005449.pub2. The available evidence for ADP receptor antagonists in patients with diabetes mellitus is limited and most trials do not report outcomes for patients with diabetes separately.
918. Merie C, Køber L, Skov Olsen P, et al. Association of warfarin therapy duration after **bioprosthetic aortic valve replacement** with risk of mortality, thromboembolic complications, and bleeding. JAMA. 2012;308(20):2118-2125.
919. Gomes T, Mamdani MM, Holbrook AM, et al. Rates of **hemorrhage during warfarin** therapy for atrial fibrillation. CMAJ 2012.
920. Zheng AS, Churilov L, Colley RE, et al. Association of **Aspirin Resistanc**e With Increased **Stroke Severity and Infarct Size**. Arch Neurol. 2012 Nov 19:1-6.
921. Boden WE, Lansky A, Angiolillo DJ. Refining the Role of **Antiplatelet Therapy** in Medically Managed Patients With **Acute Coronary Syndrome**. Am J Cardiol. 2012 Nov 17.
922. FDA Dec/12: Pradaxa (**dabigatran** etexilate mesylate) should **not** be used to prevent stroke or blood clots (major thromboembolic events) in patients with **mechanical heart valves**, also known as mechanical prosthetic heart valves. A clinical trial in Europe (the RE-ALIGN trial) was recently stopped because Pradaxa was more likely to experience strokes, heart attacks, and blood clots forming on the mechanical heart valves than were users of the anticoagulant warfarin. There was also more bleeding after valve surgery in the Pradaxa users than in the warfarin users. Health Canada Dec/12 is advising health care professionals and the public that, based on new information, the blood-thinning drug Pradaxa is not to be used in patients with artificial heart valves (also known as prosthetic heart valves) due to the risk of strokes, bleeding, heart attacks, and blood clots forming on the artificial heart valves.
Eikelboom JW, Connolly SJ, Brueckmann M, et al. **Dabigatran versus warfarin in patients with mechanical heart valves**. (**RE-ALIGN**) N Engl J Med 2013; DOI: 10.1056/NEJMoa1300615.
923. Agnelli G, Buller HR, Cohen A, et al. **Apixaban for extended treatment of venous thromboembolism**. (**AMPLIFY-EXT**) N Engl J Med 2012.
924. Grosser T, Fries S, Lawson JA, et al. **Drug resistance** and pseudoresistance: An unintended consequence of **enteric coating aspirin**. Circulation 2012.
925. Radecki RP. **Dabigatran**: **uncharted waters** and potential harms. Ann Intern Med. 2012 Jul 3;157(1):66-8.
926. Vinson DR et al. Can selected patients with newly diagnosed **pulmonary embolism be safely treated without hospitalization**? A systematic review. Ann Emerg Med 2012 Nov; 60:651.
927. Donze J, Rodondi N, Waeber G, et al. **Scores to predict major bleeding** risk during oral anticoagulation therapy: a prospective validation study. Am J Med. 2012 Nov;125(11):1095-102.
928. Bellemain-Appaix A, O'Connor SA, Silvain J, et al. Association of **clopidogrel pretreatment** with mortality, CV events, and major bleeding among patients **undergoing PCI**. A systematic review and meta-analysis. JAMA 2012;308:2507-2517.
929. Klein BE, Howard KP, Gangnon RE, et al. Long-term Use of **Aspirin and Age-Related Macular Degeneration**. JAMA. 2012 Dec 19;308(23):2469-78.
930. Bauer KA. **Reversal of antithrombotic agents**. Am J Hematol. 2012 May;87 Suppl 1:S119-26.
931. Holmberg MT, Tornio A, Joutsi-Korhonen L, et al. **Grapefruit** juice markedly increases the plasma concentrations and antiplatelet effects of **ticagrelor** in healthy subjects. Br J Clin Pharmacol. 2012 Nov 6.
932. Mulukutla SR, Marroquin OC, Vlachos HA, et al. Benefit of Long-Term Dual Anti-Platelet Therapy in Patients Treated With Drug-Eluting Stents: From the NHLBI Dynamic Registry. Am J Cardiol. 2012 Dec 1.
933. Cohen AT, Spiro TE, Büller HR, et al. **Rivaroxaban for thromboprophylaxis in acutely ill medical** patients. (**Magellan**) N Engl J Med 2013; 368:513-523.
934. Ferraris VA, Saha SP, Oestreich JH, Song HK, Rosengart T, Reece TB, Mazer CD, et al. 2012 update to the Society of Thoracic Surgeons guideline on use of **antiplatelet drugs in patients having cardiac and noncardiac operations**. Ann Thorac Surg 2012 Nov;94(5):1761-81.
935. Jauch EC, Saver JL, Adams HP, et al. Guidelines for the early management of patients with **acute ischemic stroke**: A guideline for healthcare professionals from the American Heart Association (**AHA**) /American Stroke Association (**ASA**) 2013.
936. Sode BF, Allin KH, Dahl M, et al. Risk of venous thromboembolism and myocardial infarction associated with **factor V Leiden** and prothrombin mutations and blood type. CMAJ. 2013 Feb 4.
937. Lee S, Shafe AC, Cowie MR. **UK stroke incidence**, mortality and cardiovascular risk management 1999-2008: time-trend analysis from the General Practice Research Database. BMJ Open. 2011 Jan 1;1(2):e000269.
938. Bird ST, Hartzema AG, Brophy JM, et al. Risk of venous **thromboembolism** in women with **polycystic ovary syndrome**: a population-based matched cohort analysis. CMAJ. 2013 Feb 5;185(2):E115-20.
939. Kohli P, Wallentin L, Reyes E, et al. Reduction in First and Recurrent Cardiovascular Events With **Ticagrelor Compared With Clopidogrel** in the **PLATO** Study. Circulation. 2013 Feb 12;127(6):673-80.
940. Dans AL, Connolly SJ, Wallentin L, et al. **Concomitant use of antiplatelet therapy with dabigatran or warfarin** in the Randomized Evaluation of Long-term Anticoagulation Therapy (**RE-LY**) trial. Circulation. 2013;127:634–640.
941. Dewilde WJM, Oirbans T, Verheught FWA, et al, **WOEST** study. Use of **clopidogrel with or without aspirin in patients taking oral anticoagulant** therapy and undergoing percutaneous coronary intervention: an open-label, randomised, controlled trial. Lancet 2013; online Feb 13.
942. Kelton JG, Arnold DM, Bates SM. Nonheparin anticoagulants for **heparin-induced thrombocytopenia (HIT)** . N Engl J Med. 2013 Feb 21;368(8):737-44.
943. Schulman S, Kearon C, Kakkar AK, et al. Extended use of **dabigatran, warfarin**, or placebo in venous **thromboembolism**. (**RE-MEDY, RE-SONATE**) N Engl J Med 2013; 368:709-718.
944. Mergenhagen KA, Olbrych PM, Mattappallil A, et al. Effect of **Azithromycin** on Anticoagulation-Related Outcomes in Geriatric Patients Receiving **Warfarin**. Clin Ther. 2013 Feb 28.
945. Palmer SC, Di Micco L, Razavian M, et al. **Antiplatelet agents for chronic kidney disease**. Cochrane Database Syst Rev. 2013 Feb 28;2:CD008834. doi: 10.1002/14651858.CD008834.pub2. Antiplatelet agents reduce myocardial infarction but increase major bleeding. Risks may outweigh harms among people with low annual risks of cardiovascular events, including those with early stages of CKD who do not have clinically-evident occlusive cardiovascular disease.
946. Gamba CA, Swetter SM, Stefanick ML, et al. **Aspirin** is associated with **lower melanoma risk** among postmenopausal Caucasian women: The Women's Health Initiative. Cancer. 2013 Mar 11.
947. Ross Southworth M, Reichman ME, Unger EF. **Dabigatran** and **Postmarketing Reports of Bleeding**. N Engl J Med. 2013 Mar 13.
948. Chan WS, Spencer FA, Lee AY, et al. Safety of **withholding anticoagulation** in **pregnant** women with suspected deep vein thrombosis following negative serial compression ultrasound and iliac vein imaging. CMAJ. 2013 Mar 5;185(4):E194-200.
949. Sun D, Lazo-Langner A. **New oral anticoagulants**. CMAJ. 2013 Mar 5;185(4):E212.
950. Wangge G, Roes KC, de Boer A, Hoes AW, Knol MJ. The challenges of determining **noninferiority margins**: a case study of noninferiority randomized controlled trials of **novel oral anticoagulants.** CMAJ. 2013 Feb 19;185(3):222-7.
951. Bhatt DL et al. Effect of platelet inhibition with **cangrelor** during PCI on ischemic events. (**CHAMPION PHOENIX**) N Engl J Med 2013 Mar 10.
952. Wong PF, Chong LY, Stansby G. **Antiplatelet therapy** to prevent cardiovascular events and mortality in patients with **intermittent claudication**. JAMA. 2013 Mar 6;309(9):926-7.
953. Sun D, Lazo-Langner A. **New oral anticoagulants**-Five things to know about. CMAJ. 2013 Mar 5;185(4):E212.
954. Kolber M, Sharif N, Marceau R, Szafran O. Family practice patients' use of **acetylsalicylic acid for CVD prevention (primary or secondary**). Can Fam Physician 2013; 59:55-61.
955. Larsen TB, Rasmussen LH, Skjøth F, et al. Efficacy and safety of **dabigatran etexilate and warfarin in "real world"** patients with atrial fibrillation: A prospective nationwide cohort study. J Am Coll Cardiol 2013.
956. Harrington AR, Armstrong EP, Nolan PE Jr, Malone DC. **Cost-Effectiveness of Apixaban, Dabigatran, Rivaroxaban, and Warfarin** for Stroke Prevention in Atrial Fibrillation. Stroke. 2013 Apr 2.
957. Makris M, Van Veen JJ, Tait CR, Mumford AD, Laffan M; **British** Committee for Standards in Haematology. Guideline on the **management of bleeding in patients on antithrombotic agents**. Br J Haematol. 2013 Jan;160(1):35-46.
958. Johannesdottir SA, Horváth-Puhó E, Dekkers OM, et al. Use of **Glucocorticoids** and Risk of Venous **Thromboembolism**: A Nationwide Population-Based Case-Control Study. JAMA Intern Med. 2013 Apr 1:1-10.
959. Abdul Sultan A, Tata LJ, West J, Fiaschi L, Fleming KM, Nelson-Piercy C,Grainge MJ. Risk factors for first venous **thromboembolism around pregnancy**: a population based cohort study from the United Kingdom. Blood. 2013 Apr 2.
960. Paré G, Eriksson N, Lehr T, et al. **Genetic** determinants of **dabigatran** plasma levels and their relation to bleeding. Circulation. 2013 Apr 2;127(13):1404-12.
961. Wigle P, Bloomfield HE, Tubb M et al. **Updated Guidelines on Outpatient Anticoagulation**. Am Fam Physician. 2013 Apr 15;87(8):556-566.
962. Canadian Agency for Drugs and Technologies in Health (CADTH). Antithrombotic agents for the prevention of stroke and systemic embolism in patients with atrial fibrillation. CADTH. 2013 Mar: 1(1B); 1-142.
963. Torpy JM, Livingston EH. JAMA **patient page. Aspirin** therapy. JAMA. 2013 Apr 17;309(15):1645.
964. Diamantouros A, Bartle W, Geerts W. **Patient information about warfarin**: an assessment of accuracy and readability. JAMA 2013;173(7):582-3.
965. Vaturi M, Vaduganathan M, Bental T, et al. Relation of **Aspirin Response to Age** in Patients With Stable Coronary Artery Disease. Am J Cardiol. 2013 Apr 5.
966. Heidbuchel H, Verhamme P, Alings M, et al. **EHRA practical guide on the use of new oral anticoagulants** in patients with non-valvular atrial fibrillation: Executive summary. Eur Heart J 2013.
967. Patti G, Pasceri V, Mangiacapra F, et al. Efficacy of **Clopidogrel Reloading** in Patients With Acute Coronary Syndrome Undergoing Percutaneous Coronary Intervention During Chronic Clopidogrel Therapy (from the Antiplatelet therapy for Reduction of MYocardial Damage during Angioplasty [**ARMYDA-8 RELOAD-ACS**] Trial). Am J Cardiol. 2013 Apr 18.
968. Sweetland S, Parkin L, Balkwill A, et al; Million Women Study Collaborators. **Smoking, surgery, and venous thromboembolism risk** in women: United kingdom cohort study. Circulation. 2013 Mar 26;127(12):1276-82.

969. Birnie DH, Healey JH, Wells GA, et al. Pacemaker or defibrillator surgery without interruption of anticoagulation. (Bruise Control) N Engl J Med 2013.
970. Atay JK, Fanikos J, Barnes GD, et al. Effect of **Dabigatran on Referrals to and Switching from Warfarin** in Two Academic Anticoagulation Management Services. Am J Cardiol. 2013 May 3.
971. Park K, Bavry AA. **Aspirin**: Its risks, benefits, and optimal use in **preventing cardiovascular events**. Cleve Clin J Med. 2013 May;80(5):318-26.
972. Hippisley-Cox J, Coupland C, Brindle P. Derivation and validation of **Qstroke score** for predicting risk of ischaemic stroke in primary care and comparison with other risk scores: a prospective open cohort study. BMJ. 2013 May 2;346:f2573.
973. Rist PM, Buring JE, Kase CS, et al. Effect of **low-dose aspirin** on functional outcome from cerebral vascular events in **women**. Stroke. 2013 Feb;44(2):432-6.
974. Bates D, Dalton B, Gilmour J, Kapler J. Venous thromboembolism due to suspected interaction between **rivaroxaban and nevirapine**. Can J Hosp Pharm. 2013 Mar;66(2):125-9.
975. Reaves AB, Clarke CJ, Tillman EM. Supratherapeutic international normalized ratio due to reduced **vitamin k intake secondary to prolonged vomiting** in a patient on warfarin. Ann Pharmacother. 2013 Jun;47(6):e28.
976. Baron TH, Kamath PS, McBane RD. Management of **antithrombotic therapy in patients undergoing invasive procedures**. N Engl J Med. 2013 May 30;368(22):2113-24.
977. CLOTS (Clots in Legs Or sTockings after Stroke) collaboration. Effectiveness of **intermittent pneumatic compression** (IPC)in reduction of risk of deep vein thrombosis in patients who have had a stroke (**CLOTS 3**): multicentre randomised controlled trial. Lancet 2013; online May 31.
978. Mega JL, Braunwald E, Wiviott SD, et al. Comparison of the Efficacy and Safety of Two **Rivaroxaban** Doses in **Acute Coronary Syndrome** (from ATLAS ACS 2-TIMI 51). Am J Cardiol. 2013 May 24.
979. Chopra V, Anand S, Hickner A, et al. Risk of venous **thromboembolism** associated with **peripherally inserted central catheters**: a systematic review and meta-analysis. Lancet. 2013 May 17.
980. Armstrong MJ, Gronseth G, Anderson DC, et al. Summary of evidence-based guideline: **Periprocedural management** of **antithrombotic medications** in patients with ischemic cerebrovascular disease. Neurology 2013; 80:2065-2069.
981. Schouten HJ, Geersing GJ, Koek HL, et al. Diagnostic accuracy of conventional or age adjusted **D-dimer cut-off values** in **older patients** with suspected venous thromboembolism: systematic review and meta-analysis. BMJ. 2013 May 3;346:f2492.
982. Sarafoff N, Martischnig A, Wealer J, et al. **Triple therapy with aspirin, prasugrel and vitamin K antagonists** in patients with drug eluting stent implantation and an indication for oral anticoagulation. J Am Coll Cardiol. 2013 Mar 21.
983. Lam J, Gomes T, Juurlink DN, et al. Hospitalization for Hemorrhage Among **Warfarin** Recipients Prescribed **Amiodarone**. Am J Cardiol. 2013 May 8.
984. Sørensen R, Gislason G, Torp-Pedersen C, et al. **Dabigatran use in Danish** atrial fibrillation patients in 2011: a nationwide study. BMJ Open. 2013 May 3;3(5).
985. Wallentin L, Lopes RD, Hanna M, et al. Efficacy and safety of **apixaban compared with warfarin at different levels of predicted INR** control for stroke prevention in atrial fibrillation. Circulation 2013.
986. Perera MA, Cavallari LH, Limdi NA, et al. **Genetic variants associated with warfarin dose in African-American** individuals: a genome-wide association study. Lancet 2013; online June 5. http://dx.doi.org/10.1016/S0140-6736(13)60681-9.
987. Mazya MV, Lees KR, Markus R, et al; for the SITS investigators. Safety of **IV thrombolysis for ischemic stroke** in patients treated with **warfarin**. Ann Neurol. 2013 Jun 6.
988. Lamberts M, Gislason GH, Olesen JB, et al. Oral **anticoagulation and antiplatelets in atrial fibrillation patients after myocardial infarction and coronary intervention**. J Am Coll Cardiol 2013.
989. Tandjung K, Sen H, Kai Lam M, et al. Clinical Outcome Following Stringent Discontinuation of **Dual Anti-Platelet Therapy After 12 Months** in Real-World Patients Treated With Second-Generation Zotarolimus-Eluting Resolute and Everolimus-Eluting Xience V Stents: Two-Year Follow-up of the Randomized **TWENTE** Trial. J Am Coll Cardiol. 2013 Apr 16.
990. Connolly SJ, Wallentin L, Ezekowitz MD, et al. The Long Term Multi-Center Observational Study of **Dabigatran** Treatment in Patients with Atrial Fibrillation (**RELY-ABLE**) study. Circulation 2013.
991. Nishihara R, Lochhead P, Kuchiba A, et al. **Aspirin** use and risk of **colorectal cancer** according to **BRAF** mutation status. JAMA. 2013;309(24):2563-2571.
992. Mahaffey KW, Wojdyla D, Hankey GJ, et al. Clinical outcomes with **rivaroxaban** in patients **transitioned from vitamin k antagonist** therapy: a subgroup analysis of a randomized trial. (Rocket AF) Ann Intern Med. 2013 Jun 18;158(12):861-8.
993. Wang Y, Wang Y, Zhao X, et al. **Clopidogrel with aspirin** in acute minor stroke or transient ischemic attack. (**Chance**) N Engl J Med 2013;369:11-19.

Wang Y, Pan Y, Zhao X, et al; **CHANCE** Investigators†. **Clopidogrel With Aspirin** in Acute Minor Stroke or Transient Ischemic Attack (CHANCE) Trial: **One-Year Outcomes**. Circulation. 2015 Jul 7;132(1):40-6.

Wang X, Zhao X, Johnston SC, et al. Effect of **clopidogrel with aspirin on functional outcome** in TIA or minor stroke: **CHANCE** substudy. Neurology 2015;85:573–579.

Pan Y, Jing J, Chen W, et al. Risks and benefits of **clopidogrel-aspirin in minor stroke or TIA**: Time course analysis of **CHANCE**. Neurology. 2017 May 16;88(20):1906-1911.

Jing J, et al. **Dual Antiplatelet Therapy in Transient Ischemic Attack & Minor Stroke** With Different Infarction Patterns: Subgroup Analysis CHANCE Randomized Clinical Trial. JAMA Neurol. 2018 Mar 26.

994. The **IST-3** collaborative group. Eff ect of **thrombolysis with alteplase within 6 h** of acute ischaemic stroke on long-term outcomes (the third International Stroke Trial [IST-3]): 18-month follow-up of a randomised controlled trial. Lancet Neurol 2013; online June 21.
995. Holster L, Valkhoff VE, Kuipers EJ, et al. **New oral anticoagulants increase risk for gastrointestinal bleeding**: a systematic review and meta-analysis. Gastroenterology 2013;145:105-12.
996. Agnelli G, Buller HR, Cohen A, et al. Oral **apixaban for the treatment of acute venous thromboembolism**. (**Amplify**) N Engl J Med 2013. DOI: 10.1056/NEJMoa1302507.
997. Rao N, Crail S. Images in clinical medicine. **Metastatic calcification** and long-term hemodialysis. N Engl J Med. 2013 Jun 20;368(25):2415. (**Warfarin association with high calcium-phosphorus product**)
998. Brilakis ES, Patel VG, Banerjee S. Medical management after **coronary stent implantation**: a review. JAMA. 2013 Jul 10;310(2):189-98.
999. Fawole A, Daw HA, Crowther MA. Practical management of **bleeding due to the anticoagulants dabigatran, rivaroxaban, and apixaban**. Cleve Clin J Med. 2013 Jul;80(7):443-51.
1000. Cook NR, Lee IM, Zhang SM, Moorthy MV, Buring JE. **Alternate-day, low-dose aspirin (100mg EOD) and cancer (colon)** risk: long-term observational follow-up of a randomized trial. Ann Intern Med. 2013;159:77-85.
1001. Oldgren J, Wallentin L, Alexander JH, James S, Jönelid B, Steg G, Sundström J. **New oral anticoagulants in addition to single or dual antiplatelet therapy after an acute coronary syndrome**: a systematic review **and meta-analysis. Eur Heart J. 2013 Jun;34(22):1670-80.**
1002. Greig MF, Rochow SB, Crilly MA, Mangoni AA. Routine pharmacological **venous thromboembolism prophylaxis in frail older hospitalised patients**: where is the evidence? Age Ageing. 2013 Jul;42(4):428-34.
1003. Dinicolantonio JJ, Lavie CJ, Fares H, et al. Meta-Analysis of **Cilostazol Versus Aspirin** for the Secondary Prevention of Stroke. Am J Cardiol. 2013 Jul 2.
1004. Bruins Slot KMH, Berge E. **Factor Xa inhibitors versus vitamin K antagonists** for preventing cerebral or systemic embolism in patients with atrial fibrillation. *Cochrane Database of Systematic Reviews* 2013, Issue 8. Art. No.: CD008980. DOI:10.1002/14651858.CD008980.pub2. Factor Xa inhibitors significantly reduced the number of strokes and systemic embolic events compared with warfarin in patients with AF. Factor Xa inhibitors also seem to reduce the number of major bleedings and ICHs compared with warfarin, though the evidence for a reduction of major bleedings is somewhat less robust. There is currently no conclusive evidence to determine which factor Xa inhibitor is more effective and safer for long-term anticoagulant treatment of patients with AF as head-to-head studies of the different factor Xa inhibitors have not yet been performed.
1005. Rouse M, Cristiani C, Teng KA. Q: Should we use **pharmacogenetic testing when prescribing warfarin**? Cleve Clin J Med. 2013 Aug;80(8):483-6.
1006. García-Rodríguez LA, Gaist D, Morton J, et al. **Antithrombotic drugs and risk of hemorrhagic stroke** in the general population. Neurology. 2013 Aug 6;81(6):566-74.
1007. Piazza G, Anderson FA, Ortel TL, et al. Randomized trial of **physician alerts** for **thromboprophylaxis** after discharge. Am J Med. 2013 May;126(5):435-42.
1008. Verhoef TI, Redekop WK, Daly AK et al. **Pharmacogenetic-guided dosing of coumarin** anticoagulants: algorithms for warfarin, acenocoumarol and phenprocoumon. Br J Clin Pharmacol. 2013 Aug 7.
1009. Garcia P, Ruiz W, Loza Munarriz C. **Warfarin initiation nomograms** for venous thromboembolism. Cochrane Database Syst Rev. 2013 Jul 10;7:CD007699. In patients with acute thromboembolism (DVT or PE) aged 18 years or older, considerable uncertainty surrounds the use of a 10-mg or a 5-mg loading dose for initiation of warfarin to achieve an INR of 2.0 to 3.0 on the fifth day of therapy. Heterogeneity among analyzed studies limits certainty surrounding optimal warfarin initiation nomograms.
1010. Stone GW, Witzenbichler B, Weisz G, et al, for the **ADAPT-DES** Investigators. **Platelet reactivity** and clinical outcomes after coronary artery implantation of drug-eluting stents (ADAPT-DES): a prospective multicentre registry study. Lancet 2013; online July 26.
1011. Hickey M, Gatien M, Taljaard M, et al. Outcomes of urgent **warfarin reversal** with **frozen plasma versus prothrombin complex concentrate** in the emergency department. Circulation. 2013 Jul 23;128(4):360-4.
1012. Killu AM, Wright RS, Kopecky SL. Questions and Answers on Proper **Peri-Operative Management** of Antiplatelet Therapy After Coronary Stent Implantation to Prevent Stent Thrombosis. Am J Cardiol. 2013 Jul 25.
1013. Wasserlauf G, Grandi SM, Filion KB, Eisenberg MJ. Meta-Analysis of **Rivaroxaban and Bleeding** Risk. Am J Cardiol. 2013 May 1.
1014. Schulman S et al. **Adherence to anticoagulant** treatment with **dabigatran** in a real-world setting. J Thromb Haemost 2013 Jul; 11:1295.
1015. Dodd JM, McLeod A, Windrim RC, et al. **Antithrombotic therapy for improving maternal or infant health outcomes in women considered at risk of placental dysfunction.** Cochrane Database Syst Rev. 2013 Jul 24;7:CD006780. While treatment with heparin for women considered to be at particularly high risk of adverse pregnancy complications secondary to placental insufficiency was associated with a statistically significant reduction in risk of perinatal mortality, preterm birth before 34 and 37 weeks` gestation, and infant birthweight below the 10th centile for gestational age when compared with no treatment for women considered at increased risk of placental dysfunction, to date, important information about serious adverse infant and long-term childhood outcomes is unavailable.
1015. Hohnloser SH, Shestakovska O, Eikelboom J, et al. The effects of **apixaban on hospitalizations** in patients with different types of atrial fibrillation: insights from the **AVERROES** trial. Eur Heart J. 2013 Jul 25.
1016. Dennis M, Sandercock P, Reid J, et al. The effect of **graduated compression stockings** on long-term outcomes after stroke: the **CLOTS** trials 1 and 2. Stroke. 2013 Apr;44(4):1075-9.
1017. Lyman GH, Khorana AA, Kuderer NM, et al. Venous **thromboembolism prophylaxis** and treatment in patients with cancer: **American Society of Clinical Oncology-ASCO**-clinical practice guideline update. J Clin Oncol. 2013 Jun 10;31(17):2189-204.
1018. Bhutia S, Wong PF. **Once versus twice daily low molecular weight heparin for the initial treatment of venous thromboembolism.** Cochrane Database Syst Rev. 2013 Jul 16;7:CD003074. Once daily treatment with LMWH is as effective & safe as twice daily treatment with LMWH.
1019. Hokusai-VTE investigators. **Edoxaban** versus warfarin for the treatment of symptomatic venous thromboembolism. New Engl J Med 2013.
1020. Mehran R, Baber U, Steg PG, et al. **Cessation of dual antiplatelet treatment** and cardiac events after percutaneous coronary intervention (PARIS): 2 year results from a prospective observational study. Lancet 2013.
1021. Montalescot G, Bolognese L, Dudek D, et al. Pretreatment with **prasugrel** in non-ST-segment elevation **acute coronary syndromes. (Accoast)** N Engl J Med 2013.
1022. Castellucci LA, Cameron C, Le Gal G, et al. Efficacy and safety outcomes of **oral anticoagulants and antiplatelet drugs in the secondary prevention of venous thromboembolism**: systematic review and network meta-analysis. BMJ. 2013 Aug 30;347:f5133.
1023. Sarode R, Milling TJ Jr, Refaai MA, et al. Efficacy and safety of a **4-factor prothrombin complex concentrate** in patients on vitamin K antagonists presenting with major bleeding: a randomized, plasma-controlled, phase IIIb study. Circulation. 2013;128:1234–1243.
1024. Ho KM, Tan JA. Stratified meta-analysis of **intermittent pneumatic compression** of the lower limbs to prevent venous thromboembolism in hospitalized patients.Circulation. 2013 Aug 27;128(9):1003-20.
1025. Adam SS, McDuffie JR, Lachiewicz PF, et al. Comparative effectiveness of **new oral anticoagulants and standard thromboprophylaxis in patients having total hip or knee replacement**: a systematic review. Ann Intern Med. 2013 Aug 20;159(4):275-84.
1026. Roe MT, et al. Elderly Patients With Acute Coronary Syndromes Managed Without Revascularization: Insights Into the Safety of Long-Term Dual Antiplatelet Therapy With Reduced-Dose Prasugrel Versus Standard-Dose Clopidogrel. Circulation. 2013 Aug 20;128(8):823-833.
1027. Majeed A, Hwang HG, Connolly SJ, et al. Management and outcomes of major bleeding during treatment with dabigatran or warfarin. *Circulation* 2013.
1028. Artang R, Rome E, Nielsen JD, Vidaillet HJ. Meta-Analysis of Randomized Controlled Trials on Risk of **Myocardial Infarction** from the Use of Oral Direct **Thrombin Inhibitors (dabigatran)**. Am J Cardiol. 2013 Sep 25.
1029. Gagne JJ, Bykov K, Choudhry NK, et al. Effect of **smoking on comparative efficacy of antiplatelet agents**: systematic review, meta-analysis, and indirect comparison. BMJ. 2013 Sep 17;347:f5307. (**clopidogrel benefit in smokers**)
1030. Lee M, Saver JL, Hong KS, et al. **Risk-Benefit Profile of Long-Term Dual- Versus Single**-Antiplatelet Therapy Among Patients With **Ischemic Stroke**: A Systematic Review and Meta-analysis. Ann Intern Med. 2013 Oct 1;159(7):463-470.
1031. HawnMT, Graham LA, Richman JS, Itani KMF, HendersonWG, Maddox TM. Risk of major adverse **cardiac events following noncardiac surgery in patients with coronary stents**. JAMA.doi:10.1001/jama.2013.278787.
1032. Murphy MF, Waters JH, Wood EM, Yazer MH. **Transfusing blood safely and appropriately**. BMJ. 2013 Jul 16;347:f4303.
1033. Zondag W, Kooiman J, Klok FA, et al. **Outpatient versus inpatient treatment** in patients with **pulmonary embolism**: a meta-analysis. Eur Respir J. 2013 Jul;42(1):134-44.
1034. Wong KS, Wang Y, Leng X, et al. Early **Dual versus Mono Antiplatelet Therapy** for Acute Non-Cardioembolic **Ischemic Stroke** or Transient Ischemic Attack: An Updated Systematic Review and Meta-Analysis. Circulation. 2013 Sep 12.
1035. Bilimoria KY, Chung J, Ju MH, et al. Evaluation of surveillance bias and the validity of the **venous thromboembolism quality measure**. JAMA. doi:10.1001/jama.2013.280048.
1036. Varenhorst C, Jensevik K, Jernberg T, et al. Duration of **dual** antiplatelet treatment with **clopidogrel and aspirin in patients with actue coronary syndrome**. *Eur Heart J* 2013.
1037. Hankey GJ, Ford AH, Yi Q, et al. Effect of **B vitamins and lowering homocysteine** on cognitive impairment in patients with previous stroke or transient ischemic attack: a prespecified secondary analysis of a randomized, placebo-controlled trial (VITATOPS) and meta-analysis. Stroke. 2013 Aug;44(8):2232-9.
1038. Xu Y, Holbrook AM, Simpson CS, et al. Prescribing patterns of **novel oral anticoagulants following regulatory approval for atrial fibrillation in Ontario**, Canada: A population-based descriptive analysis. *CMAJ*2013;DOI:10.9778/cmajo.20130032.
1039. Jones SB, Sen S, Lakshminarayan K, et al. **Poststroke outcomes vary by pathogenic stroke subtype** in the Atherosclerosis Risk in Communities Study. Stroke. 2013 Aug;44(8):2307-10.
1040. Carrier M et al. Management of challenging cases of patients with **cancer-associated thrombosis** including recurrent thrombosis and bleeding: Guidance from the **SSC of the ISTH**. J Thromb Haemost 2013 Sep; 11:1760.

1041. Patel AA, Reardon G, Nelson WW, Philpot T, Neidecker MV. **Persistence of Warfarin** Therapy for Residents in Long-term Care Who Have Atrial Fibrillation. Clin Ther. 2013 Oct 15.
1042. Malloy RJ, Kanaan AO, Silva MA, Donovan JL. Evaluation of **Antiplatelet Agents for Secondary Prevention of Stroke** Using Mixed Treatment Comparison Meta-analysis. Clin Ther. 2013 Oct;35(10):1490-1500.e7.
1043. Abraham NS, Hartman C, Richardson P, et al. Risk of Lower and Upper Gastrointestinal **Bleeding**, Transfusions, and Hospitalizations with **Complex Antithrombotic Therapy in Elderly** Patients. Circulation. 2013 Sep 11.
1044. Derdeyn CP, Chimowitz MI, Lynn MJ, et al. Aggressive **medical treatment with or without stenting** in high-risk patients with intracranial artery stenosis (SAMMPRIS): the fi nal results of a randomised trial. Lancet 2013; online Oct 26.
1045. Feigin VL, Forouzanfar MH, Krishnamurthi R, et al, on behalf of the Global Burden of Diseases, Injuries, and Risk Factors Study 2010 (GBD 2010) and the GBD Stroke Experts Group. **Global and regional burden of stroke** during 1990–2010: findings from the Global Burden of Diseases Study 2010. Lancet 2013; published online Oct 24.
1046. Krishnamurthi R, Feigin VL, Forouzanfar MH, et al, on behalf of the Global Burden of Diseases, Injuries, and Risk Factors Study 2010 (GBD 2010) and the GBD Stroke Experts Group. **Global and regional burden of first-ever** ischaemic and haemorrhagic **stroke** during 1990–2010: findings from the Global Burden of Diseases Study 2010. Lancet Glob Health 2013; 1: e259–81.
1047. Baglin T. Clinical use of **new oral anticoagulant drugs**: dabigatran and rivaroxaban. Br J Haematol. 2013 Oct;163(2):160-7.
1048. Meyer S, Frei CR, Daniels KR, et al. Impact of a New Method of **Warfarin Management** (**STORM2:** self testing) on Patient Satisfaction, Time, and Cost. Pharmacotherapy. 2013 Aug 22.
1049. Lin C-C et al. Risk factors of **gastrointestinal bleeding in clopidogrel** (150mg) users: A nationwide population-based study. Aliment Pharmacol Ther 2013 Nov; 38:1119.
1050. Antoniou GA, Georgiadis GS, Georgakarakos EI, et al.Meta-analysis and meta-regression analysis of outcomes of **carotid endarterectomy (CEA) and stenting (CAS)** in the elderly [published online October 23, 2013]. JAMA Surg. doi:10.1001/jamasurg.2013.4135.
1051. Abdul Sultan A, West J, Tata LJ, et al. Risk of **first venous thromboembolism in pregnant women** in hospital: population based cohort study from England. BMJ. 2013 Nov 7;347:f6099.
1052. Verhoef TI, Ragia G, de Boer A, et al. A randomized trial of **genotype-guided dosing of acenocoumarol and phenprocoumon**. (**EU-PACT**) N Engl J Med 2013. DOI: 10.1056/NEJMoa1311388.
1053. Pirmohamed M, Burnside G, Eriksson N, et al. A randomized trial of **genotype-guided dosing of warfarin**. (**EU-PACT**) N Engl J Med 2013. DOI: 10.1056/NEJMoa1311386.
1054. Kimmel SE, French B, Kasner SE, et al. A **pharmacogenetic versus a clinical algorithm for warfarin** dosing. (**COAG**) N Engl J Med 2013. DOI: 10.1056/NEJMoa1310669
1055. Feres F, Costa RA, Abizaid A, et al; for the **OPTIMIZE** Trial Investigators. **Three vs Twelve Months of Dual Antiplatelet** Therapy After **Zotarolimus-Eluting Stents**: The OPTIMIZE Randomized Trial. JAMA. 2013 Oct 31.
1056, Lee SW, Lee JY, Ahn JM, et al. Comparison of **Dual Versus Triple** Antiplatelet Therapy After **Drug-Eluting Stent** According to **Stent Length** (from the Pooled Analysis of DECLARE Trials). Am J Cardiol. 2013 Sep 21.
1057. Migliorini A, Valenti R, Parodi G, et al. Comparison of the Degree of Platelet Aggregation Inhibition With **Prasugrel Versus Clopidogrel** and Clinical Outcomes in Patients With **Unprotected Left Main Disease** Treated With Everolimus-Eluting Stents. Am J Cardiol. 2013 Sep 21.
1058 Grotta JC. Clinical practice. **Carotid stenosis**. N Engl J Med. 2013 Sep 19;369(12):1143-50.
1059. Giugliano RP, Ruff CT, Braunwald E, et al. **Edoxaban versus Warfarin** in Patients with Atrial Fibrillation. (**ENGAGE AF-TIMI 48**) N Engl J Med. 2013 Nov 19. Goldstein BA, Arce CM,
1060. Lee CW, Ahn JM, Park DW et al. **Optimal Duration of Dual Antiplatelet Therapy (12 vs 36months)** after **Drug-Eluting Stent** (DES) Implantation: A Randomized Controlled Trial. Circulation. 2013 Oct 4.
1061. Ji Y, Tan S, Xu Y, Chandra A, et al. **Vitamin B supplementation, homocysteine levels, and the risk of cerebrovascular disease**: a meta-analysis. Neurology. 2013 Oct 8;81(15):1298-307.
Marti-Carvajal AJ, Sola I, Lathyris D. **Homocysteine-lowering** interventions for preventing cardiovascular events. Cochrane Database Syst Rev. 2015 Jan 15;1:CD006612. This second update of this Cochrane Review found no evidence to suggest that homocysteine-lowering interventions in the form of supplements of vitamins B6, B9 or B12 given alone or in combination should be used for preventing cardiovascular events. Furthermore, there is no evidence to suggest that homocysteine-lowering interventions are associated with an increased risk of cancer.
1062. Baruch L, Sherman O. **Inaccuracy of Point-of-Care International Normalized Ratio in Rivaroxaban**-Treated Patients. Ann Pharmacother. 2013 Sep;47(9):1210-2.
1063. Chua D, Nishi C. **New antiplatelet agents** for cardiovascular disease. CMAJ. 2013 Nov 5;185(16):1405-11.
1064. Sipahi I, Celik S, Tozun N. A Comparison of Results of the US Food and Drug Administration's Mini-Sentinel Program With Randomized Clinical Trials: The Case of **Gastrointestinal Tract Bleeding With Dabigatran**. JAMA Intern Med. 2013 Nov 18.
1065. Maki ED, Miesner AR, Grady SE, et al. Effects of **depressive and other psychiatric disorders on anticoagulation control** in a pharmacist-managed anticoagulation clinic. Ann Pharmacother. 2013 Oct;47(10):1292-300.
1066. Bartle WR, Presse N, Ferland G. Quality **Concerns of Over-the-Counter Vitamin K Supplements**: Implications for Warfarin Therapy. Ann Pharmacother. 2013 Oct;47(10):1372-3.
1067. Hellwig T, Gulseth M. Pharmacokinetic and pharmacodynamic **drug interactions with new oral anticoagulants**: what do they mean for patients with atrial fibrillation? Ann Pharmacother. 2013 Nov;47(11):1478-87.
1068. Sutcliffe P, Connock M, Gurung T, et al. **Aspirin for prophylactic use in the primary prevention** of cardiovascular disease and cancer: a systematic review and overview of reviews. Health Technol Assess. 2013 Sep;17(43):1-253.
1069. Jefferis BJ, Whincup PH, Papacosta O, Wannamethee SG. Protective Effect of **Time Spent Walking** on Risk of Stroke in Older Men. Stroke. 2013 Nov 14.
1070. Ashby RL, Gabe R, Ali S, et al. Clinical and cost-eff ectiveness of **compression hosiery versus compression bandages** in treatment of venous leg ulcers (Venous leg Ulcer Study IV, VenUS IV): a randomised controlled trial. Lancet 2013; online Dec 6.
1071. Kahn SR, Shapiro S, Wells PS, et al, for the SOX trial investigators. **Compression stockings to prevent post-thrombotic syndrome**: a randomised placebo-controlled trial. Lancet 2013; online Dec 6.
1072. Ruff CT, Giugliano RP, Braunwald E. Comparison of the **efficacy and safety of new oral anticoagulants with warfarin** in patients with atrial fibrillation: a meta-analysis of randomised trials. *Lancet* 2013; DOI: 10.1016/S0140-6736(13)62343-0.
1073. Apostolakis S, Sullivan RM, Olshansky B, Lip GY. Factors Affecting Quality of Anticoagulation Control Among Patients With Atrial Fibrillation on Warfarin: The **SAMe-TT2R2 Score**. Chest. 2013 Nov 1;144(5):1555-63.
1074. Qureshi W, Mittal C, Patsias I, et al. **Restarting Anticoagulation** and Outcomes After Major **Gastrointestinal Bleeding** in Atrial Fibrillation. Am J Cardiol. 2013 Nov 23
1075. Kayssi A, Roche-Nagle G. **Postthrombotic syndrome**. CMAJ. 2014 Jan 7;186(1):62
1076. Capodanno D, Angiolillo DJ. Management of **antiplatelet therapy** in patients with coronary artery disease requiring **cardiac and noncardiac surgery**. Circulation. 2013 Dec 24;128(25):2785-98.
1077. Cuadrado MJ, Bertolaccini ML, Seed PT, et al. **Low-dose aspirin vs low-dose aspirin plus low-intensity warfarin in thromboprophylaxis**: a prospective, multicentre, randomized, open, controlled trial in patients positive for antiphospholipid antibodies (ALIWAPAS). Rheumatology (Oxford). 2013 Oct 4.
1078. Damman P, Varenhorst C, Koul S, et al. Treatment Patterns and Outcomes in Patients Undergoing Percutaneous Coronary Intervention Treated With **Prasugrel or Clopidogrel** (from the Swedish Coronary Angiography and Angioplasty Registry [SCAAR]). Am J Cardiol. 2014 Jan 1;113(1):64-9
1079. DiNicolantonio JJ, Tomek A. Inactivations, deletions, non-adjudications, and downgrades of clinical endpoints on **ticagrelor: Serious concerns** over the reliability of the **PLATO** trial. *Int J Cardiol* 2013; 168:4076-4080.
1080. Fosbol EL, Wang TY, Li S, et al. **Warfarin** use among **older atrial fibrillation** patients with **non-ST-segment elevation myocardial infarction** managed with coronary stenting and dual antiplatelet therapy. Am Heart J. 2013 Nov;166(5):864-70.
1081. Hankey GJ. **Secondary stroke prevention**. Lancet Neurol. 2013 Dec 19
1082. Hobl EL, Stimpfl T, Ebner J, et al. **Morphine Decreases Clopidogrel** Concentrations and Effects: A Randomized, Double Blind, Placebo-Controlled Trial. J Am Coll Cardiol. 2013 Nov 21
1083. Larsson SC. **Coffee, tea, and cocoa and risk of stroke**. Stroke. 2014 Jan;45(1):309-14.
1084. Lambiase MJ, Kubzansky LD, Thurston RC. Prospective Study of **Anxiety and Incident Stroke**. Stroke. 2013 Dec 19.
1085. Matteau A, Yeh RW, Kereiakes D, et al. Frequency of the Use of **Low- Versus High-Dose Aspirin in Dual Antiplatelet Therapy** After Percutaneous Coronary Intervention (from the Dual Antiplatelet Therapy Study). Am J Cardiol. 2013 Nov 8
1086. Piazza G. **Venous thromboembolism and cancer**. Circulation. 2013 Dec 17;128(24):2614-8
1087. Sarraj A, Grotta JC. **Stroke**: new horizons in treatment. Lancet Neurol. 2014 Jan;13(1):2-3
1088. Sugerman DT. JAMA **patient page. Blood thinners**. JAMA. 2013 Dec 18;310(23):2579.
1089. Lee CW, Ahn JM, Park DW, et al. Optimal duration of **dual antiplatelet therapy after drug-eluting stent** implantation: a randomized, controlled trial. Circulation. 2014 Jan 21;129(3):304-12. (**12** vs additional 24 months no different)
1090. Bloom BJ, Filion KB, Atallah R, et al. Meta-Analysis of Randomized Controlled Trials on the Risk of **Bleeding With Dabigatran**. Am J Cardiol. 2013 Dec 24
1091. Clark NP, Delate T, Riggs CS, et al. **Warfarin Interactions With Antibiotics** in the Ambulatory Care Setting. JAMA Intern Med. 2014 Jan 20
1092 National Institute for Health and Care Excellence (**NICE**). **Rivaroxaban** for treating pulmonary embolism and preventing recurrent venous thromboembolism. London (UK): National Institute for Health and Care Excellence (NICE); 2013 Jun.
1093. Wallentin L, Lindholm D, Siegbahn A, et al. for the PLATO study group. Biomarkers (**elevated troponin: hs-TnT**) in relation to the effects of **ticagrelor in comparison with clopidogrel** in non-ST-elevation acute coronary syndrome patients managed with or without in-hospital revascularization: a substudy from the Prospective Randomized Platelet Inhibition and Patient Outcomes (PLATO) trial. Circulation. 2014;129:293–303.
1094. Olsson KM, Delcroix M, Ghofrani HA, et al. **Anticoagulation and Survival in Pulmonary Arterial Hypertension**: Results From the Comparative, Prospective Registry of Newly Initiated Therapies for Pulmonary Hypertension (COMPERA). Circulation. 2014 Jan 7;129(1):57-65
1095. McCully SP, Fabricant LJ, Kunio NR, et al. The **International Normalized Ratio overestimates coagulopathy** in stable trauma and surgical patients. J Trauma Acute Care Surg. 2013 Dec;75(6):947-53
1096. Di Minno MN, Dentali F, Lupoli R, et al. **Mild Antithrombin Deficiency** and the Risk of Recurrent Venous **Thromboembolism**: A Prospective Cohort Study. Circulation. 2013 Oct 21
1097. Mansoor AH, Mujtaba MT, Silver B. **Antiplatelet therapy to prevent recurrent stroke: Three good options**. Cleve Clin J Med. 2013 Dec;80(12):787-95.
1098. Singh D, Gupta K, Vacek JL. Anticoagulation and antiplatelet therapy in **acute coronary syndromes**. Cleve Clin J Med. 2014 Feb;81(2):103-14.
1099. Kiyohara T, Kamouchi M, Kumai Y, Ninomiya T, Hata J, et al. **ABCD3 and ABCD3-I Scores** Are Superior to **ABCD2** Score in the Prediction of Short- and Long-Term Risks of Stroke After Transient Ischemic Attack. Stroke. 2014 Feb;45(2):418-25.
1100. Bushnell C, McCullough LD, Awad IA, et al. Guidelines for the Prevention of **Stroke in Women**: A Statement for Healthcare Professionals From the American Heart Association (**AHA**)/American Stroke Association (ASA). Stroke. 2014 Feb 6.
1101. Reilly PA, Lehr T, Haertter S, et al. The effect of dabigatran plasma concentrations and patient characteristics on the frequency of ischemic stroke and major bleeding in atrial fibrillation patients. J Am Coll Cardiol 2014; 63:321-328.
1102. Watson L, Broderick C, Armon MP. **Thrombolysis** for acute deep vein thrombosis. Cochrane Database Syst Rev. 2014 Jan 23;1:CD002783.
1103. Shah M, Avgil Tsadok M, Jackevicius CA, et al. **Warfarin** Use and the Risk for Stroke and Bleeding in Patients with **Atrial Fibrillation** Undergoing **Dialysis**. Circulation. 2014 Jan 22.
1104. Côté R, Zhang Y, Hart RG, et al. **ASA failure**: does the combination ASA/clopidogrel confer better long-term vascular protection? Neurology 2014;82:382–389.
1105. Tai WA, Albers GW. **Secondary prevention** of atherothrombotic or **cryptogenic stroke**. Circulation. 2014 Jan 28;129(4):527-31
1106. Nishimura RA, Otto CM, Bonow RO, et al. **2014 AHA/ACC Guideline** for the Management of Patients With **Valvular Heart Disease**: Executive Summary: A Report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. J Am Coll Cardiol. 2014 Feb 27.
1107. Hijazi Z, Hohnloser SH, Oldgren J, et al. Efficacy and Safety of **Dabigatran Compared With Warfarin** in Relation to Baseline **Renal Function** in Patients With Atrial Fibrillation: A RE-LY (Randomized Evaluation of Long-term Anticoagulation Therapy) Trial Analysis. Circulation. 2014 Mar 4;129(9):961-70.
1108. Muriel A, Jiménez D, Aujesky D, et al. Survival Effects of **Inferior Vena Cava Filter** in Patients with Acute Symptomatic Venous Thromboembolism and a Significant Bleeding Risk. J Am Coll Cardiol. 2014 Feb 24.
1109. Caldeira D, Barra M, Santos AT, et al. Risk of drug-induced **liver injury** with the **new oral anticoagulants**: systematic review and meta-analysis. Heart. 2014 Jan 29.
1110. Wells PS, Forgie MA, Rodger MA. Treatment of **venous thromboembolism**. JAMA. 2014 Feb 19;311(7):717-28.
1111. Cardwell CR, Kunzmann AT, Cantwell MM, et al. **Low-dose aspirin** use after diagnosis of **colorectal cancer** does not increase survival: a case-control analysis of a population-based cohort. Gastroenterology. 2014 Mar;146(3):700-708.
1112. Pdf Pezzini A, Grassi M, Paciaroni M, et al; Multicenter Study on Cerebral Hemorrhage in Italy (MUCH-Italy) Investigators. **Antithrombotic** medications and the etiology of **intracerebral hemorrhage**: MUCH-Italy. Neurology. 2014 Feb 11;82(6):529-35
1113. Bruins Slot KM, Berge E. **Factor Xa Inhibitors vs Warfarin** for Preventing Stroke and Thromboembolism in Patients With Atrial Fibrillation. JAMA. 2014 Mar 19;311(11):1150-1151.
1114. Ishikawa H, Mutoh M, Suzuki S, et al. The preventive effects of low-dose enteric-coated **aspirin** tablets on the development of **colorectal** tumours in Asian patients: a randomised trial. Gut. 2014 Jan 31.
1115. Righini M et al. **Age-adjusted D-dimer** cutoff levels to rule out pulmonary embolism: The ADJUST-PE Study. JAMA 2014 Mar 19; 311:1117.
1116. Cetin M, Cakici M, Zencir C, et al. Prediction of Coronary Artery Disease Severity Using **CHADS2** and **CHA2DS2-VASc** Scores and a Newly Defined **CHA2DS2-VASc-HS** Score. Am J Cardiol. 2014 Mar 15;113(6):950-6.
1117. Halvorsen S, Atar D, Yang H, et al. Efficacy and safety of **apixaban compared with warfarin** according to age for **stroke** prevention in atrial fibrillation: observations from the ARISTOTLE trial. Eur Heart J. 2014 Feb 20.

1118. Peters SA, Huxley RR, Woodward M. **Diabetes** as a risk factor for stroke in women compared with men: a systematic review and meta-analysis of 64 cohorts, including 775 385 individuals and 12 539 strokes. Lancet. 2014 Mar 6.
1119. Sun CH, Bhatt DL, Nogueira RG, et al. **Endovascular therapy** for stroke: getting to the "heart" of the matter. Circulation. 2014 Mar 11;129(10):1152-60.
1120. Geersing GJ, Zuithoff NP, Kearon C, et al. Exclusion of deep vein thrombosis using the **Wells rule** in clinically important subgroups: individual patient data meta-analysis. BMJ. 2014 Mar 10;348:g1340.
1121. Loke YK, Pradhan S, Yeong JK, et al. Comparative **coronary risks of apixaban, rivaroxaban and dabigatran**: a meta-analysis and adjusted indirect comparison. Br J Clin Pharmacol. 2014 Mar 11.
1122. Fortinsky KJ, Stall NM, Barkun AN. A 77-year-old man with nonvariceal **upper gastrointestinal bleeding. (on warfarin)** CMAJ. 2014 Mar 18;186(5):363-5.
1123. Gorelick PB, Goldstein LB, Ovbiagele B. **New guidelines** to reduce risk of **atherosclerotic cardiovascular disease**: implications for stroke prevention in 2014. Stroke. 2014 Apr;45(4):945-7.
1124. Lane MA, Zeringue A, McDonald JR. Serious **Bleeding** Events due to **Warfarin and Antibiotic Co-prescription** In a Cohort of Veterans. Am J Med. 2014 Mar 19.
1125. Pannucci CJ, Laird S, Dimick JB, et al. A Validated Risk Model to **Predict 90-Day VTE Events in Postsurgica**l Patients. Chest. 2014 Mar 1;145(3):567-73.
1126. Poli D, Antonucci E, Dentali F, et al. Recurrence of **ICH** after **resumption of anticoagulation with VK antagonists**: **CHIRONE** Study. Neurology 2014;82:1020–1026.
1127. Reimers MS, Bastiaannet E, Langley RE, et al. Expression of HLA Class I Antigen, **Aspirin** Use, and Survival After a Diagnosis of **Colon Cancer**. JAMA Intern Med. 2014 Mar 31.
1128. Schisterman EF, Silver RM, Lesher LL, et al. Preconception low-**dose aspirin and pregnancy outcomes**: results from the **EAGeR** randomised trial. Lancet 2014; online April 2. http://dx.doi.org/10.1016/S0140-6736(14)60157-4.
1129. Towfighi A, Markovic D, Ovbiagele B. Consistency of **Blood Pressure Control After Ischemic Stroke**: Prevalence and Prognosis. Stroke. 2014 Mar 27.
1130. Yadlapati A, Groh C, Passman R. Safety of short-term use of **dabigatran or rivaroxaban** for **direct-current cardioversion** in patients with atrial fibrillation and atrial flutter. Am J Cardiol. 2014 Apr 15;113(8):1362-3.
1131. Lip GY, Shantsila E. **Anticoagulation versus placebo for heart failure** in sinus rhythm. Cochrane Database Syst Rev. 2014 Mar 28;3:CD003336. Based on the two major randomised trials (HELAS 2006; WASH 2004), there is no convincing evidence that oral anticoagulant therapy modifies mortality or vascular events in patients with heart failure and sinus rhythm
1132. Devereaux PJ, Mrkobrada M, Sessler DI, et al. **Aspirin** in patients **undergoing noncardiac surgery**. (**Poise-2** trial) N Engl J Med. DOI:10.1056/NEJMoa1401105.
1133. Hunt BJ. **Bleeding and coagulopathies** in critical care. N Engl J Med. 2014 Feb 27;370(9):847-59.
1134. Gouya G, Arrich J, Wolzt M, et al. **Antiplatelet treatment for prevention of cerebrovascular events** in patients with vascular diseases: a systematic review and meta-analysis. Stroke. 2014 Feb;45(2):492-503.
1135. Kumar R, Smith RE, Henry BL. A review of and recommendations for the **management** of patients with **life-threatening dabigatran-associated hemorrhage**: a single-center university hospital experience. *J Intensive Care Med*2014.
1136. Vidale S. **Antithrombotic drugs and risk of hemorrhagic stroke** in the general population. Neurology. 2014 Apr 1;82(13):1193.
1137. Kleinjan A, Di Nisio M, Beyer-Westendorf J, et al. Safety and Feasibility of a **Diagnostic Algorithm** Combining Clinical Probability, d-Dimer Testing, and Ultrasonography for **Suspected Upper Extremity Deep Venous Thrombosis**: A Prospective Management Study. Ann Intern Med. 2014 Apr 1;160(7):451-7.
1138. Harel Z, Sholzberg M, Shah PS, et al. Comparisons between **novel oral anticoagulants and vitamin K antagonists in patients with CKD.** J Am Soc Nephrol. 2014 Mar;25(3):431-42.
1139. Steinberg BA, Piccini JP. **Anticoagulation in atrial fibrillation**. BMJ 2014;348:g2116 doi: 10.1136/bmj.g2116
1140. Henderson JT, Whitlock EP, O'Connor E, et al. **Low-Dose Aspirin** for Prevention of Morbidity and Mortality From **Preeclampsia**: A Systematic Evidence Review for the U.S. Preventive Services Task Force. (**USPSTF**) Ann Intern Med. 2014 Apr 8.
1141. Kernan WN, Ovbiagele B, Black HR, et al; on behalf of the American Heart Association Stroke Council, Council on Cardiovascular and Stroke Nursing, Council on Clinical Cardiology, and Council on Peripheral Vascular Disease. Guidelines for the **Prevention of Stroke** in Patients With Stroke and Transient Ischemic Attack: A Guideline for Healthcare Professionals From the American Heart Association (**AHA**)/American Stroke Association (**ASA**). Stroke. 2014 May 1.
1142. Faye E, Drouet L, De Raucourt E, et al. Absorption and efficacy of **acetylsalicylic Acid (aspirin/ASA) in patients with short bowel syndrome**. Ann Pharmacother. 2014 Jun;48(6):705-10.
1143. Egan G, Hughes CA, Ackman ML. Drug interactions between **antiplatelet or novel oral anticoagulant medications and antiretroviral** medications. Ann Pharmacother. 2014 Jun;48(6):734-40.
1144. Waldron B, Moll S. A **Patient's Guide** to Recovery After **Deep Vein Thrombosis or Pulmonary Embolism**. Circulation. 2014 Apr 29;129(17):e477-9.
1145. Davidson BL, Verheijen S, Lensing AW, et al. Bleeding Risk of Patients With Acute Venous Thromboembolism (**on warfarin**) Taking **Nonsteroidal Anti-Inflammatory Drugs or Aspirin**. JAMA Intern Med. 2014 Apr 14.
1146. Mueller JA, Patel T, Halawa A, et al. **Warfarin** dosing and **body mass index**. Ann Pharmacother. 2014 May;48(5):584-8.
1147. Chee CE, Ashrani AA, Marks RS, Petterson TM, Bailey KR, Melton LJ 3rd, Heit JA. **Predictors of venous thromboembolism recurrence and bleeding** among active cancer patients: a population-based cohort study. Blood. 2014 Apr 29.
1148. Siepmann T, Heinke D, Kepplinger J, et al. **Interaction of clopidogrel and statins** in secondary prevention after cerebral ischemia – a randomized, double-blind, double-dummy crossover-study. Br J Clin Pharmacol. 2014 May 6.
1149. Miedema MD, Duprez DA, Misialek JR, et al. Use of **coronary artery calcium testing to guide aspirin utilization** for primary prevention: Estimates from the Multi-Ethnic Study of Atherosclerosis (**MESA**). *Circ Cardiovasc Qual Outcomes* 2014.
1150. Beyer-Westendorf J, Gelbricht V, Förster K, et al. Safety of switching from **Vitamin-K antagonists to dabigatran or rivaroxaban** in daily care - results from the Dresden NOAC registry. Br J Clin Pharmacol. 2014 Apr 2
1151. Dlott JS, George RA, Huang X, et al. **National assessment** of **warfarin anticoagulation** therapy for stroke prevention in atrial fibrillation. Circulation. 2014 Apr 1;129(13):1407-14.
1152. Frost C, Shenker A, Gandhi MD, et al. Evaluation of the effect of **naproxen** on the pharmacokinetics and pharmacodynamics of **apixaban**. Br J Clin Pharmacol. 2014 Apr 2.
1153. **FDA** May/14 recently completed a new study in Medicare patients comparing **Pradaxa to warfarin**, for risk of ischemic or clot-related stroke, bleeding in the brain, major gastrointestinal (GI) bleeding, myocardial infarction (MI), and death. The new study included information from more than 134,000 Medicare patients, 65 years or older, and found that among new users of blood-thinning drugs, Pradaxa was associated with a lower risk of clot-related strokes, bleeding in the brain, and death, than warfarin. The study also found an increased risk of major gastrointestinal bleeding with use of Pradaxa as compared to warfarin. The MI risk was similar for the two drugs.
1154. Skjøth F, Larsen TB, Rasmussen LH, et al. Efficacy and safety of **edoxaban in comparison with dabigatran, rivaroxaban and apixaban** for stroke prevention in atrial fibrillation: An indirect comparison analysis. *Thromb Haemost* 2014; 111:981-988.
1155. El-Hayek, Messerli, Bangalore, et al. Meta-analysis of Randomized Clinical Trials Comparing **Short term-vs-Long term Dual Antiplatelet Therapy Following Drug Eluting Stents**. The American Journal of Cardiology. 2014.
1156. Matteau A, Bhatt DL. Recent advances in **antithrombotic therapy after acute coronary syndrome**. CMAJ. 2014 May 13;186(8):589-96.
1157. Gladman M, DeHaan M, Pinto H, et al. **Venous thromboembolism in amyotrophic lateral sclerosis**: a prospective study. Neurology 2014;82:1674–1677.
1158. Birnie DH, Healey JS, Essebag V. Management of **anticoagulation around pacemaker and defibrillator surgery**. Circulation. 2014 May 20;129(20):2062-5.
1159. Carreras ET, Mega JL. **Dual antiplatelet therapy** for heart disease. Circulation. 2014 May 27;129(21):e506-8.
1160. Cruden NL, Din JN, Janssen C, et al. **Delay** in **filling first clopidogrel prescription** after coronary stenting is associated with an increased risk of death and myocardial infarction. J Am Heart Assoc. 2014 May 28;3(3).
1161. Loh JP, Torguson R, Pendyala LK, et al. Impact of **Early Versus Late Clopidogrel Discontinuation** on Stent Thrombosis Following Percutaneous Coronary Intervention With First- and Second-Generation Drug-Eluting Stents. Am J Cardiol. 2014 Apr 1.
1162. Sardar P, Chatterjee S, Chaudhari S, et al. **New oral anticoagulants** in **elderly** adults: evidence from a meta-analysis of randomized trials. J Am Geriatr Soc. 2014 May;62(5):857-64.
1163. Selby R et al. Symptomatic venous **thromboembolism uncommon without thromboprophylaxis after isolated lower-limb fracture**: The Knee-to-Ankle Fracture (KAF) cohort study. J Bone Joint Surg Am 2014 May 21; 96:e83.
1164. Taglieri N, Bacchi Reggiani ML, Palmerini T, et al. Risk of **stroke in patients with high on-clopidogrel platelet reactivity** to adenosine diphosphate after percutaneous coronary intervention. Am J Cardiol. 2014 Jun 1;113(11):1807-14.
1165. Voora D, Becker RC. A **freeze on tailored antiplatelet therapy**? Circulation. 2014 May 27;129(21):2088-90.
1166. **NICE**: National Institute for Health and Care Excellence. The **management of atrial fibrillation (update). Clinical guidelines CG180. June 2014**.
1167. Stergiopoulos K, Brown DL. **Genotype-guided vs clinical dosing of warfarin** and its analogues: meta-analysis of randomized clinical trials [online June 16, 2014]. JAMA Intern Med. doi:10.1001/jamainternmed.2014.2368.
1168. Hylek EM, Held C, Alexander JH, et al. **Major Bleeding** in Patients With Atrial Fibrillation Receiving **Apixaban** or Warfarin: The **ARISTOTLE** Trial (Apixaban for Reduction in Stroke and Other Thromboembolic Events in Atrial Fibrillation): Predictors, Characteristics, and Clinical Outcomes. J Am Coll Cardiol. 2014 May 27;63(20):2141-7.
1169. Halperin JL, Hankey GJ, et al; on behalf of the **ROCKET AF** Steering Committee and Investigators. Efficacy and Safety of **Rivaroxaban** Compared with Warfarin among **Elderly** Patients with Nonvalvular Atrial Fibrillation in the ROCKET AF Trial. Circulation. 2014 Jun 3.
1170. Albrecht JS, Liu X, Baumgarten M, et al. Benefits and Risks of **Anticoagulation Resumption Following Traumatic Brain Injury**. JAMA Intern Med. 2014 Jun 10.
1171. Hira RS, Kennedy K, Jneid H, et al. Frequency and practice level variation in inappropriate and non-recommended **prasugrel** prescribing: Insights from the NCDR PINNACLE registry. J Am Coll Cardiol 2014.
1172. Douxfils J, Buckinx F, Mullier F, et al. **Dabigatran Etexilate and Risk of Myocardial Infarction**, Other Cardiovascular Events, Major Bleeding, and All-Cause Mortality: A Systematic Review and Meta-analysis of Randomized Controlled Trials. J Am Heart Assoc. 2014 Jun 6;3(3).
1173. Gladstone DJ et al. Atrial fibrillation in patients with **cryptogenic stroke**. (EMBRACE) N Engl J Med 2014 Jun 26; 370:2467.
1174. Sanna T et al. **Cryptogenic stroke** and underlying atrial fibrillation. (CRYSTAL AF) N Engl J Med 2014 Jun 26; 370:2478.
1175. Holmes DR, Kar S, Price MJ, et al. Prospective randomized evaluation of the **Watchman left atrial appendage** closure device in patients with atrial fibrillation versus long-term warfarin therapy. *J Am Coll Cardiol* 2014.
1176. Al-Khatib SM, Allen LaPointe NM, Chatterjee R, et al. **Rate- and rhythm**-control therapies in patients with atrial fibrillation: a systematic review. Ann Intern Med. 2014 Jun 3;160(11):760-73.
1177. Marott SC, Nielsen SF, Benn M, et al. **Antihypertensive treatment** and risk of atrial fibrillation: a nationwide study. Eur Heart J. 2014 May;35(18):1205-14.
1178. Jones C, Pollit V, Fitzmaurice D, et al; Guideline Development Group. The **management of atrial fibrillation**: summary of updated **NICE** guidance. BMJ. 2014 Jun 19;348:g3655.
1179. Mavaddat N, Roalfe A, Fletcher K, et al. **Warfarin versus aspirin for prevention of cognitive** decline in atrial fibrillation: randomized controlled trial (Birmingham Atrial Fibrillation Treatment of the Aged Study-**BAFTA**). Stroke. 2014 May;45(5):1381-6.
1180. Akl EA, Kahale L, Terrenato I, et al. **Oral anticoagulation in patients with cancer** who have no therapeutic or prophylactic indication for anticoagulation. Cochrane Database Syst Rev. 2014 Jul 1;7:CD006466. Existing evidence does not suggest a mortality benefit from oral anticoagulation in patients with cancer while the risk for bleeding is increased.
1181. Connors JM. **Prophylaxis against venous thromboembolism in ambulatory patients with cancer**. N Engl J Med. 2014 Jun 26;370(26):2515-9.
1182. Navi BB, Singer S, Merkler AE, et al. **Recurrent thromboembolic events after ischemic stroke in patients with cancer**. Neurology 2014;83:26–33.
1183. Zhang Z, Xu G, Yang F, Zhu W, Liu X. Quantitative analysis of **dietary protein intake and stroke risk**. Neurology 2014;83:19–25.
1184. Collet JP, Silvain J, Barthelemy O, et al, for the **ARCTIC** Investigators. **Dual-antiplatelet** treatment **beyond 1 year** after **drug-eluting stentimplantation** (ARCTIC-Interruption): the second phase of a randomised trial. Lancet 2014; online July 16.
1185. Koton S. Schneider ALC, Rosamond WD, et al.. **Stroke incidence and mortality** trends in US communities, 1987 to 2011. JAMA. doi:10.1001/jama.2014.7692.
1186. **CADTH**. **Point-of-care testing of International Normalized Ratio (INR)** for patients on oral anticoagulant therapy: Systemic review and economic analysis.. Canadian Agency for Drugs and Technologies in Health (CADTH). 2014 Jul:1-161.
1187. Akl EA, Kahale L, Sperati F, et al. **Low molecular weight heparin versus unfractionated heparin for perioperative thromboprophylaxis in patients with cancer**. Cochrane Database of Systematic Reviews 2014, Issue 6. Art. No.: CD009447. DOI: 10.1002/14651858.CD009447.pub2. We found no difference between perioperative thromboprophylaxis with LMWH versus UFH in their effects on mortality, thromboembolic outcomes, major bleeding, or minor bleeding in patients with cancer. Further trials are needed to evaluate the benefits and harms of different heparin thromboprophylaxis strategies in this population more thoroughly.
1188. Tsang K, Hartmark-Hill JR. **Ticagrelor** (Brilinta) for secondary prevention of thrombotic events following acute coronary syndrome. Am Fam Physician. 2013 Dec 15;88(12):821-2.
1189. Hippisley-Cox J, Coupland C. Predicting risk of upper gastrointestinal bleed and intracranial bleed with anticoagulants: cohort study to derive and validate the QBleed scores. BMJ 2014;349:g4606.
1190. Larsen TB, Gorst-Rasmussen A, Rasmussen LH, et al. **Bleeding events among new starters** and switchers to **dabigatran compared with warfarin** in atrial fibrillation. Am J Med. 2014 Jul;127(7):650-656.e5.
1191. Moore TJ, Cohen MR, Mattison DR. **Dabigatran, bleeding, and the regulators**. BMJ 2014;349:g4517.
1192. Cohen D. **Dabigitran**: how the drug **company withheld** important analyses. BMJ 2014;349:g4670.
1193. Lim CS, Davies AH. **Graduated compression stockings**. CMAJ. 2014 Jul 8;186(10):E391-E398. Epub 2014 Mar 3.
1194. López-Valdés HE, Clarkson AN, Ao Y, et al. **Memantine** enhances recovery from stroke. Stroke. 2014 Jul;45(7):2093-100.

1195. Piazza G. **Thrombophilia Testing**, Recurrent Thrombosis, and Women's Health. Circulation. 2014 Jul 15;130(3):283-7.
1196. Akl EA, Kahale L, Barba M, et al. **Anticoagulation** for the long-term treatment of **venous thromboembolism** in patients with **cancer**. Cochrane Database Syst Rev. 2014 Jul 8;7:CD006650. For the long-term treatment of VTE in patients with cancer, LMWH compared with VKA reduces venous thromboembolic events but not mortality. The decision for a patient with cancer and VTE to start long-term LMWH versus oral anticoagulation should balance the benefits and harms and integrate the patient`s values and preferences for the important outcomes and alternative management strategies.
1197. Fiscella K, Winters PC, Mendoza M, et al. Do clinicians recommend **aspirin to patients for primary prevention** of cardiovascular disease? *J Gen Intern Med* 2014; DOI:10.1007/s11606-014-2985-8.
1198. Tilton R, Michalets EL, Delk B, et al. Outcomes Associated With **Prothrombin Complex Concentrate** for **International Normalized Ratio Reversal** in Patients on Oral Anticoagulants With Acute Bleeding. Ann Pharmacother. 2014 Jun 4;48(9):1106-1119.
1199. Harris JR, Coons JC. **Ticagrelor** Use in a Patient With a Documented **Clopidogrel Hypersensitivity**. Ann Pharmacother. 2014 Jun 23;48(9):1230-1233.
1200.Geisbüsch C, Richter D, Herweh C, et al. Novel **factor xa inhibitor** for the treatment of **cerebral venous and sinus thrombosis**: first experience in 7 patients. Stroke. 2014 Aug;45(8):2469-71.
1201.MacCallum P, Bowles L, Keeling D. Diagnosis and management of **heritable thrombophilias**. BMJ. 2014 Jul 17;349:g4387.
1202. Cook RM, Rondina MT, Horton DJ. **Rivaroxaban** for the Long-term Treatment of **Spontaneous Ovarian Vein Thrombosis** Caused by Factor V Leiden Homozygosity. Ann Pharmacother. 2014 May 5;48(8):1055-1060.
1203. Denetclaw TH, Nguyen MT. Patient **Failure** to Seek Care for Non-ST-Elevated **Myocardial Infarction** Because of Symptoms Being Attributed to **Dyspepsia From Dabigatran**. Ann Pharmacother. 2014 May 8;48(8):1093-1094.
1204. Chatterjee S, Sardar P, Giri JS, et al. **Treatment Discontinuations** With **New Oral Agents** for Long-term Anticoagulation: Insights From a Meta-analysis of 18 Randomized Trials Including 101,801 Patients. Mayo Clin Proc. 2014 Jul;89(7):896-907.
1205. Cuzick J, Thorat MA, Bosetti C, et al. Estimates of benefits and harms of **prophylactic use of aspirin** in the general population. Ann Oncol. 2014 Aug 5.
1206. Clemens A, Peng S, Brand S, et al. Efficacy and Cost-Effectiveness of **Dabigatran Etexilate Versus Warfarin** in Atrial Fibrillation in Different Age Subgroups. Am J Cardiol. 2014 Jul 2.
1207. Cohen D. Concerns over data in key dabigatran trial. BMJ. 2014 Jul 23;349:g4747.
1208. Cappato R, Ezekowitz MD, Klein AL, et al. **Rivaroxaban vs. vitamin K antagonists** for **cardioversion** in atrial fibrillation.Eur Heart J 2014.
1209. Cotté FE, Benhaddi H, Duprat-Lomon I, et al. **Vitamin K Antagonist** Treatment in Patients With Atrial Fibrillation and **Time in Therapeutic Range in Four European Countries**. Clin Ther. 2014 Aug 20.
1210. Larock AS, Mullier F, Sennesael AL, et al. **Appropriateness of prescribing dabigatran** etexilate and **rivaroxaban** in patients with **nonvalvular atrial fibrillation**: a prospective study. Ann Pharmacother. 2014 Oct;48(10):1258-68.
1211. Seth A, Mossavar-Rahmani Y, Kamensky V, et al. **Potassium** Intake and Risk of **Stroke** in Women With Hypertension and Nonhypertension in the Women's Health Initiative. Stroke. 2014 Sep 4.
1212. Søgaard KK, Schmidt M, Pedersen L, et al. **30-year mortality after venous thromboembolism**: a population-based cohort study. Circulation. 2014 Sep 2;130(10):829-36.
1213. Poidvin A, Touzé E, Ecosse E, et al. **Growth hormone** treatment for childhood short stature and risk of **stroke** in early adulthood. Neurology. 2014 Aug 26;83(9):780-6.
1214. Berkowitz AL, Westover MB, Bianchi MT, et al. **Aspirin** for **secondary prevention after stroke** of unknown etiology in resource-limited settings. Neurology. 2014 Aug 13.
1215. Lee M, Saver JL, Hong KS, et al. **Cognitive impairment** and risk of future **stroke**: a systematic review and meta-analysis. CMAJ. 2014 Aug 25.
1216. Simes J, Becattini C, Agnelli G, et al; **INSPIRE** (International Collaboration of Aspirin Trials for Recurrent Venous Thromboembolism) Study Investigators. **Aspirin** for the **Prevention** of **Recurrent Venous Thromboembolism**: The INSPIRE Collaboration. Circulation. 2014 Aug 25.
1217. Liakoni E, Rätz Bravo AE, et al. Symptomatic **Hepatocellular Liver Injury With Hyperbilirubinemia** in Two Patients Treated With **Rivaroxaban**. JAMA Intern Med. 2014 Aug 25.
1218. Dang LT, Shavit JA, Singh RK, et al. **Subdural hemorrhages** associated with **antithrombotic therapy** in infants with cerebral atrophy. Pediatrics. 2014 Sep;134(3):e889-93.
1219. Connolly BJ, Pearce LA, Hart RG. **Vitamin K antagonists** and risk of subdural **hematoma**: meta-analysis of randomized clinical trials. Stroke. 2014 Jun;45(6):1672-8.
1220. Lip GYH, Windecker S, Huber K, et al. Management of antithrombotic therapy in **atrial fibrillation patients presenting with acute coronary syndrome and/or undergoing percutaneous coronary or valve interventions**: A joint consensus document of the European Society of Cardiology Working Group on Thrombosis, European Heart Rhythm Association [**EHRA**], European Association of Percutaneous Cardiovascular Interventions [**EAPCI**] and European Association of Acute Cardiac Care [**ACCA**]. August 25, 2014. *Eur Heart J* 2014;
1221. Hall HM, de Lemos JA, Enriquez JR, et al. Contemporary Patterns of **Discharge Aspirin Dosing After Acute Myocardial Infarction** in the United States: Results From the National Cardiovascular Data Registry (NCDR). Circ Cardiovasc Qual Outcomes. 2014 Aug 12.
1222. Montalescot G, Hof AW, Lapostolle F, et al; the **ATLANTIC** Investigators. **Prehospital Ticagrelor** in ST-Segment Elevation Myocardial Infarction. N Engl J Med. 2014 Sep 1.
1223. Zareba P, Wu C, Agzarian J, Rodriguez D, Kearon C. Meta-analysis of randomized trials comparing combined **compression and anticoagulation** with either modality alone for **prevention of venous thromboembolism** after surgery. Br J Surg. 2014 Aug;101(9):1053-62.
1224. Lip GY, Haguenoer K, Saint-Etienne C, et al. Relationship of the **SAMe-TT2R2 Score** to Poor-Quality Anticoagulation, Stroke, Clinically Relevant Bleeding, and Mortality in Patients With Atrial **Fibrillation**. Chest. 2014 Sep 1;146(3):719-26.
1225. Carruthers EC, Choi HK, Sayre EC, et al. Risk of **deep venous thrombosis and pulmonary embolism** in individuals with **polymyositis and dermatomyositis**: a general population-based study. Ann Rheum Dis. 2014 Sep 5. pii: annrheumdis-2014-205800.
1226. Castellucci LA, Cameron C, Le Gal G, et al. Clinical and safety outcomes associated with **treatment of acute venous thromboembolism**: a systematic review and meta-analysis. JAMA. 2014 Sep 17;312(11):1122-35.
1227. Connolly SJ, Wallentin L, Yusuf S. **Additional Events** in the **RE-LY** Trial. N Engl J Med. 2014 Sep 24.
1228. Amsterdam EA, Wenger NK, Brindis RG, et al. **2014 AHA/ACC Guideline for the Management of Patients With Non-ST-Elevation Acute Coronary Syndromes**: Executive Summary: A Report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. Circulation. 2014 Sep 23.
1229. De Caterina R, Ammentorp B, Darius H, et al. PREFER in AF Registry. Frequent and possibly **inappropriate use of combination therapy with an oral anticoagulant and antiplatelet** agents in patients with atrial fibrillation in Europe. Heart. 2014 Oct 15;100(20):1625-35.
1230. **NICE**; National Institute for Health and Care Excellence. **Prasugrel with percutaneous coronary intervention** for treating acute coronary syndromes (review of technology appraisal guidance 182). London (UK): National Institute for Health and Care Excellence (NICE); 2014 Jul.
1231. Windecker S, Kolh P, Alfonso F, et al. **2014 ESC/EACTS Guidelines on myocardial revascularization**. Eur Heart J 2014.
1232. Ungprasert P, Srivali N, Wijarnpreecha K, et al. **Non-steroidal anti-inflammatory drugs** and risk of venous thromboembolism: a systematic review and meta-analysis. Rheumatology (Oxford). 2014 Sep 24.
1233. Seo KW, Tahk SJ, Yang HM, et al. Point-of-Care Measurements of Platelet Inhibition After Clopidogrel Loading in Patients With Acute Coronary Syndrome: Comparison of **Generic and Branded Clopidogrel** Bisulfate. Clin Ther. 2014 Sep 10.
1234. Simes J, Becattini C, Agnelli G, et al; **INSPIRE** Study Investigators* (International Collaboration of Aspirin Trials for Recurrent Venous Thromboembolism). **Aspirin for the Prevention of Recurrent Venous Thromboembolism**: The INSPIRE Collaboration. Circulation. 2014 Sep 23;130(13):1062-71.
1235. Wakefield TW, Obi AT, Henke PK. An **aspirin a day to keep the clots away**: can aspirin prevent recurrent thrombosis in extended treatment for venous thromboembolism? Circulation. 2014 Sep 23;130(13):1031-3.
1236. Atchison CM, Arlikar S, Amankwah E, et al. Development of a new **risk score for hospital-associated venous thromboembolism in noncritically ill children** findings from a large single-institutional case-control study. J Pediatr. 2014 Oct;165(4):793-8.
1237. Larsson SC, Akesson A, Wolk A. **Healthy diet and lifestyle** and **risk of stroke** in a prospective cohort of women. Neurology. 2014 Oct 8.
1238. Schulz S, Richardt G, Laugwitz KL, et al; Bavarian Reperfusion Alternatives Evaluation (**BRAVE**) **4** Investigators; Bavarian Reperfusion Alternatives Evaluation BRAVE 4 Investigators. **Prasugrel plus bivalirudin vs.clopidogrel plus heparin** in patients with ST-segment elevation myocardial infarction. Eur Heart J. 2014 Sep 7;35(34):2285-94.
1239. Kahn SR, Comerota AJ, Cushman M, et al; on behalf of the **American Heart Association** (AHA) Council on Peripheral Vascular Disease, Council on Clinical Cardiology, and Council on Cardiovascular and Stroke Nursing. The **Postthrombotic Syndrome**: Evidence-Based Prevention, Diagnosis, and Treatment Strategies: A Scientific Statement From the American Heart Association. Circulation. 2014 Sep 22.
1240. Maaijwee NA, Rutten-Jacobs LC, Arntz RM, et al. Long-term increased **risk of unemployment after young stroke**: A long-term follow-up study. Neurology. 2014 Sep 23;83(13):1132-8.
1241. Falcone GJ, Radmanesh F, Brouwers HB, et al; International Stroke Genetics Consortium. **APOE ε variants increase risk of warfarin-related intracerebral hemorrhage**. Neurology. 2014 Sep 23;83(13):1139-46.
1242. Anderson M, Hassell KL, Trujillo TC, et al. When patients on **target-specific oral anticoagulants need surgery**. Cleve Clin J Med. 2014 Oct;81(10):629-639.
1243. Hamon M, Lemesle G, Tricot O, et al. **Incidence, source, determinants, and prognostic impact of major bleeding** in outpatients with stable coronary artery disease. *J Am Coll Cardiol* 2104.
1244. Crowl A, Schullo-Feulner A, Moon JY. **Warfarin Monitoring in Antiphospholipid Syndrome and Lupus Anticoagulant**. Ann Pharmacother. 2014 Nov;48(11):1479-1483. Epub 2014 Aug 7.
1245. Whisenant B, Kar S, Bunch TJ. **Left atrial appendage occlusion** addresses the tremendous unmet needs of stroke prevention in **atrial fibrillation** that persist despite recent advances in anticoagulation therapy. Circulation. 2014 Oct 21;130(17):1516-23.
1246. Kounis NG, Davlouros P. **Bleeding complication with dual antiplatelet therapy**: spontaneous uvula hematoma. CMAJ. 2014 Oct 21;186(15):1168.
1247. Ezekowitz MD, Kent AP. **Novel anticoagulants eliminate** the need for **left atrial appendage exclusion devices**. Circulation. 2014 Oct 21;130(17):1505-14.
1248. ENOS Trial Investigators. Efficacy of **nitric oxide**, **with or without continuing antihypertensive treatment**, for management of high **blood pressure in acute stroke** (**ENOS**): a partial-factorial randomised controlled trial. Lancet 2014; online Oct 22.
1249. Bellemain-Appaix A, Kerneis M, O'Connor SA, Silvain J, Cucherat M, Beygui F, et al. Reappraisal of **thienopyridine pretreatment** in patients with non-ST elevation **acute coronary syndrome**: a systematic review and meta-analysis. BMJ 2014;349:g6269.
1250. Ikeda Y et al. **Low-dose aspirin for primary prevention** of cardiovascular events in Japanese patients 60 years or older with atherosclerotic risk factors: A randomized clinical trial. (**JPPP**) JAMA 2014 Nov 17. In this large cohort study, 100 mg aspirin daily did not reduce the risk for cardiovascular events among older Japanese patients with atherosclerotic risk factors. The findings add to a growing body of evidence that helps refine our decision-making: Patients at very low risk for vascular events or high risk for bleeding should not take aspirin for primary prevention of vascular events, even at low doses. Ongoing studies (ARRIVE, ASCEND, ASPREE) will assess the role of aspirin in moderate- to high-risk individuals without vascular disease. For now, clinicians must individualize decision-making based on potential benefits (including non-cardiovascular benefits) as well as bleeding risk.

Uchiyama S, Ishizuka N, Shimada K, et al. **Aspirin for Stroke Prevention in Elderly Patients With Vascular Risk Factors: Japanese Primary Prevention Project (JPPP) .** Stroke. 2016 Jun;47(6):1605-11.

1251. Najafzadeh M, Gagne JJ, Choudhry NK, et al. **Patients' preferences in anticoagulant therapy**. *Circulation Cardiovasc Qual Outcomes* 2014; 7:912-919.
1252. Mauri L, Kereiakes DJ, Yeh RW, et al. **Twelve or 30 months** of dual antiplatelet therapy after drug-eluting stents. (**DAPT**) N Engl J Med. DOI: 10.1056/NEJMoa1409312.
1253. Elmariah S, Mauri L, Doros G, et al. **Extended duration dual antiplatelet therapy and mortality**: a systematic review and meta-analysis. Lancet 2014: online Nov 16. http://dx.doi.org/10.1016/S0140-6736(14)62052-3.
1254. Sundararajan V, Thrift AG, Phan TG, et al. **Trends** over time in the risk of stroke **after an incident transient ischemic attack**. Stroke. 2014 Nov;45(11):3214-8.
1255. Meschia JF, Bushnell C, Boden-Albala B, et al. **Guidelines for the Primary Prevention of Stroke**: A Statement for Healthcare Professionals From the American Heart Association (**AHA**) /American Stroke Association (**ASA**). Stroke. 2014 Oct 28.
1256. Fowler RA, Mittmann N, Geerts W, et al; for the Canadian Critical Care Trials Group and the Australia and New Zealand Intensive Care Society Clinical Trials Group. Cost-effectiveness of **Dalteparin vs Unfractionated Heparin** for the Prevention of Venous Thromboembolism in Critically Ill Patients. JAMA. 2014 Nov 1.
1257. Ansell JE, Bakhru SH, Laulicht BE, et al. Use of **PER977** to Reverse the Anticoagulant Effect of Edoxaban. N Engl J Med. 2014 Nov 5.
1258 Frost CE, Byon W, Song Y, et al. Effect of ketoconazole and diltiazem on the pharmacokinetics of **apixaban**, an oral direct factor Xa inhibitor. Br J Clin Pharmacol. 2014 Nov 6.
1259. Hernandez I, Baik SH, Pinera A, Zhang Y. **Risk of bleeding with dabigatran** in atrial fibrillation. *JAMA Intern Med*2014; published online November 3, 2014.
1260. Graham DJ, Reichman ME, Wernecke M, al. Cardiovascular, **bleeding**, and mortality risks in elderly Medicare patients treated with **dabigatran** or warfarin for nonvalvular atrial fibrillation. *Circulation* 2014; published online October 30, 2014.
1261. Garg AX, Kurz A, Sessler DI, et al; **POISE-2** Investigators. Effect of perioperative aspi**rin and clonidine on acute kidney injury**: a randomized clinical trial. JAMA. doi:10.1001/jama.2014.15284.
1262. **CLOTS** (Clots in Legs Or sTockings after Stroke) Trials. Effect of **intermittent pneumatic compression** on disability, living circumstances, quality of life, and hospital costs after stroke: secondary analyses from CLOTS 3, a randomised trial. Lancet Neurology 2014; online Oct 31
1263. Bushnell C, McCullough LD, Awad IA, et al. on behalf of the American Heart Association Stroke Council, Council on Cardiovascular and Stroke Nursing, Council on Clinical Cardiology, Council on Epidemiology and Prevention, Council for High Blood Pressure Research. Guidelines for the **prevention of stroke in women**: a statement for healthcare professionals from the American Heart Association (AHA)/American Stroke Association (ASA). Stroke. 2014 May;45(5):1545-88.
1264. Gasparovic H, Petricevic M, Kopjar T, et al. Impact of **dual antiplatelet therapy on outcomes among aspirin-resistant patients following coronary artery bypass grafting**. Am J Cardiol. 2014 May 15;113(10):1660-7.
1265. Schmidt M, Hovath-Puho E, Christiansen CF, et al. **Preadmission use of nonaspirin nonsteroidal anti-inflammatory drugs** and 30-day **stroke mortality**. Neurology. 2014 Nov 5.
1266. Cohn SL. Updated guidelines on **cardiovascular evaluation before noncardiac surgery**: a view from the trenches. Cleve Clin J Med 2014; 81:742–751.
1267. van Kruijsdijk R, Visseren F, Ridker P, et al. Individualized prediction of **alternate-day aspirin** treatment effects on the combined risk of cancer, cardiovascular disease and gastro-intestinal bleeding in healthy women. (**WHS**) Heart 2014, 10.1136/heartjnl-2014-306342

1268. Ayerbe L, Ayis S, Crichton SL, et al. Explanatory factors for the increased **mortality of stroke patients with depression**. Neurology. 2014 Nov 25;83(22):2007-12.
1269. Chai-Adisaksopha C, Crowther M, Isayama T, Lim W. The impact of **bleeding complications in patients receiving target-specific oral anticoagulants**: a systematic review and meta-analysis. Blood. 2014;124:2450-2458.
1270. Douketis J, Bell AD, Eikelboom J, Liew A. Approach to the **new oral anticoagulants** in family practice: Part 1: **comparing the options**. Can Fam Physician. 2014 Nov;60(11):989-995.
1271. Douketis J, Bell AD, Eikelboom J, Liew A. Approach to the **new oral anticoagulants** in family practice: Part 2: **addressing frequently asked questions**. Can Fam Physician. 2014 Nov;60(11):997-1001.
1272. Dupree LH, Reddy P. Use of **rivaroxaban** in a patient with history of nephrotic syndrome and hypercoagulability. Ann Pharmacother. 2014 Dec;48(12):1655-8.
1273. Park JH, Ovbiagele B. **Optimal combination secondary prevention** drug treatment and **stroke** outcomes. Neurology. 2015 Jan 6;84(1):50-6.
1274. Kim JY, Khavanin N, Rambachan A, et al. **Surgical Duration** and Risk of Venous Thromboembolism. JAMA Surg. 2014 Dec 3.
1275. Lee M, Wu YL, Saver JL, et al. Is **clopidogrel better than aspirin following breakthrough strokes while on aspirin**? A retrospective cohort study. BMJ Open. 2014 Dec 2;4(12):e006672.
1276. Moore KT, Byra W, Vaidyanathan S, et al. Switching from **rivaroxaban to warfarin**: an open-label pharmacodynamic study in healthy subjects. Br J Clin Pharmacol. 2014 Dec 5.
1277. Najafzadeh M, Gagne JJ, Choudhry NK, et al. **Patients' preferences in anticoagulant therapy**: discrete choice experiment. Circ Cardiovasc Qual Outcomes. 2014 Nov;7(6):912-9.
1278. Ntsiea M, Van Aswegen H, Lord S, Olorunju S S. The effect of a workplace intervention programme on return to work after stroke: A randomised controlled trial. Clin Rehabil. 2014 Oct 16.
1279. Siegmund HU, Burghaus R, Kubitza D, et al. Contribution of **rivaroxaban** to the **international normalized ratio** when switching to **warfarin** for anticoagulation as determined by simulation studies. Br J Clin Pharmacol. 2014 Dec 16.
1280. Smilowitz NR, Mega JL, Berger JS. **Duration of anticoagulation for venous thromboembolic events**. Circulation. 2014 Dec 23;130(25):2343-8.
1281. Thaler DE, Ruthazer R, Weimar C, et al. Determinants of **antithrombotic choice for patent foramen ovale** in cryptogenic stroke. Neurology. 2014 Nov 18;83(21):1954-7.
1282. Wadhera RK, Russell CE, Piazza G. **Warfarin versus novel oral anticoagulants**: how to choose? Circulation. 2014 Nov 25;130(22):e191-3.
1283. Garratt KN, Weaver WD, Jenkins RG, et al. **Prasugrel plus aspirin beyond 12 months** is associated with improved outcomes after **TAXUS Liberté paclitaxel-eluting coronary stent** placement. Circulation. 2015;131: 62–73.
1284. Hira RS, Kennedy K, Nambi V, et al. Frequency and practice-level variation in **inappropriate aspirin use for the primary prevention** of cardiovascular disease: insights from the National Cardiovascular Disease Registry's Practice Innovation and Clinical Excellence Registry. J Am Coll Cardiol 2015; 65:111–21.
1285. Liu N, Cadilhac DA, Andrew NE, et al. Randomized controlled trial of **early rehabilitation after intracerebral hemorrhage stroke**: difference in outcomes within 6 months of stroke. Stroke. 2014 Dec;45(12):3502-7.
1286. Holmberg MT, Tornio A, Hyvärinen H, et al. Effect of **grapefruit juice** on the bioactivation of **prasugrel**. Br J Clin Pharmacol. 2014 Dec 31.
1287. Kearon C, Spencer FA, O'Keeffe D, et al; d-Dimer Optimal Duration Study Investigators. **d-Dimer Testing** to Select Patients With a First Unprovoked Venous Thromboembolism Who Can **Stop Anticoagulant Therapy**: A Cohort Study. Ann Intern Med. 2015 Jan 6;162(1):27-34.
1288. Sridhar VS, Leung P, Seymour N, Nagge J. Evaluation of an initiation **protocol of 4 mg of warfarin** for atrial fibrillation in the outpatient setting. Can Fam Physician. 2014 Nov;60(11):e535-40.
1289. Touma L, Filion KB, Atallah R, et al. A Meta-Analysis of Randomized Controlled Trials of the Risk of **Bleeding With Apixaban Versus Vitamin K Antagonists**. Am J Cardiol. 2014 Dec 2.
1290. Zahir H, Brown KS, Vandell AG, et al. **Edoxaban** effects on bleeding following punch biopsy and reversal by a **4-factor prothrombin complex concentrate**. Circulation. 2015 Jan 6;131(1):82-90.
1291. Zylla MM, Pohlmeier M, Hess A, et al. Prevalence of **Intracardiac Thrombi** Under **Phenprocoumon, Direct Oral Anticoagulants (Dabigatran and Rivaroxaban), and Bridging** Therapy in Patients With Atrial Fibrillation and Flutter. Am J Cardiol. 2014 Dec 18.
1292. Held C, Hylek EM, Alexander JH, et al. Clinical outcomes and management associated with major bleeding in patients with atrial fibrillation treated with **apixaban or warfarin: insights from the ARISTOTLE** trial. Eur Heart J. 2014 Dec 12.
1293. Granger CB, Lopes RD, et al. Clinical events after **transitioning from apixaban versus warfarin to warfarin** at the end of the Apixaban for Reduction in Stroke and Other Thromboembolic Events in Atrial Fibrillation (**ARISTOTLE**) trial. Am Heart J. 2015 Jan;169(1):25-30.
1294. Åsberg S, Eriksson M, Henriksson KM, Terént A. **Warfarin-associated intracerebral hemorrhage** after ischemic stroke. Stroke. 2014 Jul;45(7):2118-20.
1295. Sengupta N et al. The risks of **thromboembolism vs. recurrent gastrointestinal bleeding** after interruption of systemic anticoagulation in hospitalized **inpatients with gastrointestinal bleeding**: A prospective study. Am J Gastroenterol 2014 Dec 16.
1296. Holcomb CN, Graham LA, Richman JS, et al. The incremental **risk of noncardiac surgery on adverse cardiac events following coronary stenting**. J Am Coll Cardiol. 2014 Dec 30;64(25):2730-9.
1297. Chan KE, Edelman ER, Wenger JB, et al. **Dabigatran and Rivaroxaban** Use in Atrial Fibrillation Patients on **Hemodialysis**. Circulation. 2015 Jan 16.
1298. Ma W, Liang Y, Zhu J, et al. Meta-Analysis Appraising High Maintenance Dose Clopidogrel in Patients Who Underwent Percutaneous Coronary Intervention With and Without **High On-Clopidogrel Platelet Reactivity**. Am J Cardiol. 2014 Dec 18.
1299. Marti-Carvajal AJ, Sola I, Lathyris D. **Homocysteine-lowering interventions** for preventing cardiovascular events. Cochrane Database Syst Rev. 2015 Jan 15;1:CD006612. This second update of this Cochrane Review found no evidence to suggest that homocysteine-lowering interventions in the form of supplements of vitamins B6, B9 or B12 given alone or in combination should be used for preventing cardiovascular events. Furthermore, there is no evidence to suggest that homocysteine-lowering interventions are associated with an increased risk of cancer.
1300. Messori A. **Cardiovascular safety of new oral anticoagulants**: re-analysis of 27 randomized trials based on Bayesian network meta-analysis. Br J Clin Pharmacol. 2015 Jan 22.
1301. Barrett TW, Storrow AB, Jenkins CA, et al. The **AFFORD Clinical Decision** Aid to Identify Emergency Department Patients With Atrial Fibrillation at **Low Risk for 30-Day Adverse Events**. Am J Cardiol. 2015 Jan 6.
1302. Friberg L, Skeppholm M, Terént A. **Benefit of Anticoagulation Unlikely** in Patients With Atrial Fibrillation and a **CHA2DS2-VASc Score of 1**. J Am Coll Cardiol. 2015 Jan 27;65(3):225-32.
1303. Peguero JG, Issa O, Podesta C, et al. Usefulness of the **CHA(2)DS(2)VASc** Score to Predict Postoperative Stroke in Patients Having **Cardiac Surgery** Independent of Atrial Fibrillation. Am J Cardiol. 2015 Jan 6.
1304. Melloni C, Washam JB, Jones WS, et al. Conflicting results between randomized trials and observational studies on the impact of **proton pump inhibitors on cardiovascular events when coadministered with dual antiplatelet** therapy. Circ Cardiovasc Qual Outcomes 2015; 8: 47-55.
1305. Vaughan Sarrazin MS, Jones M, Mazur A, et al. **Bleeding rates in Veterans Affairs** patients with atrial fibrillation who **switch from warfarin to dabigatran.** Am J Med. 2014 Dec;127(12):1179-85.
1306. Gilard M, Barragan P, Noryani AA, et al. **Six-month versus 24-month dual antiplatelet therapy after implantation of drug eluting stents** in patients non-resistant to aspirin: **ITALIC**, a randomized multicenter trial. J Am Coll Cardiol. 2014 Nov 16.
1307. Prabhakaran S, Herbers P, Khoury J, et al. Is **prophylactic anticoagulation** for deep venous thrombosis common practice **after intracerebral hemorrhage**? Stroke. 2015 Feb;46(2):369-75.
1308. Saver JL, Starkman S, Eckstein M, et al; **FAST-MAG** Investigators and Coordinators. Prehospital use of **magnesium** sulfate as **neuroprotection in acute stroke**. N Engl J Med. 2015 Feb 5;372(6):528-36.
1309. Tsivgoulis G, Psaltopoulou T, Wadley VG, et al. Adherence to a **Mediterranean Diet** and Prediction of Incident Stroke. Stroke. 2015 Jan 27.
1310. Jun M, James MT, Manns BJ, et al. Alberta Kidney Disease Network. The association between **kidney function and major bleeding** in older adults with atrial fibrillation starting warfarin treatment: population based observational study. BMJ. 2015 Feb 3;350:h246.
1311. Carrier M, Lazo–Langner A, Shivakumar S, et al. Clinical challenges in patients with **cancer-associated thrombosis**: Canadian expert consensus recommendations. Curr Oncol 2015;22:49-59. http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4324343/pdf/conc-22-49.pdf (accessed February 23, 2015).
1312. Razouki Z, Ozonoff A, Zhao S, et al. Improving quality measurement for anticoagulation: adding **international normalized ratio variability** to percent time in therapeutic range. Circ Cardiovasc Qual Outcomes. 2014;7:664-669.
1313. Wang EHZ, BVolt JL, Decarie D, et al. Stability of **Dabigatran Etexilate in Manufacturer's Blister Pack, Unit-Dose Packaging, and Community Pharmacy Blister Pack**. Can J Hosp Pharm 2015;68 (1):16-21.
1314. Chao TF, Liu CJ, Wang KL, et al. Should atrial fibrillation patients **with 1 additional risk factor of the CHA2DS2-VASc score (beyond sex) receive oral anticoagulation**? *J Am Coll Cardiol* 2015; 65: 635-642.
1315. Goldstein JN, Refaai MA, Milling TJ Jr, et al. **Four-factor prothrombin complex concentrate versus plasma for rapid vitamin K antagonist reversal** in patients needing urgent surgical or invasive interventions: a phase 3b, open-label, non-inferiority, randomised trial. Lancet.2015 Feb 26.
1316. Vanni S, Jimenez D, Nazerian P, et al. Short-term clinical outcome of normotensive patients with **acute PE and high plasma lactate**. Thorax. 2015 Feb 6. pii: thoraxjnl-2014-206300.
1317. Armbruster HL, Lindsley JP, Moranville MP, et al. Safety of **novel oral anticoagulants compared with uninterrupted warfarin for catheter ablation** of atrial fibrillation. Ann Pharmacother. 2015 Mar;49(3):278-84.
1318. Kuramatsu JB, Gerner ST, Schellinger PD, et al. **Anticoagulant reversal, blood pressure levels, and anticoagulant resumption in patients with anticoagulation-related intracerebral hemorrhage**. JAMA. 2015 Feb 24;313(8):824-36.
1319. Raschi E, Poluzzi E, Koci A, Salvo F, et al. **Liver injury with novel oral anticoagulants**: assessing post-marketing reports in the US Food and Drug Administration Adverse Event Reporting System. Br J Clin Pharmacol. 2015 Feb 16.
1320. Fang J, George MG, Gindi RM, et al. Use of **Low-Dose Aspirin as Secondary Prevention** of Atherosclerotic Cardiovascular Disease in US Adults (from the National Health Interview Survey, 2012). Am J Cardiol. 2015 Apr 1;115(7):895-900.
1321. Haley WE, Roth DL, Hovater M, et al. Long-term **impact of stroke on family caregiver well-being**: A population-based case-control study. Neurology. 2015 Mar 31;84(13):1323-9.
1322. Huo Y, Li J, Qin X, et al. Efficacy of **Folic Acid** Therapy in Primary Prevention of Stroke Among Adults With Hypertension in China: The **CSPPT** Randomized Clinical Trial. JAMA. 2015 Mar 15.
1323. Jung JM, Choi J, Eun MY, et al. **Prestroke antiplatelet agents** in first-ever ischemic stroke: Clinical effects. Neurology. 2015 Mar 17;84(11):1080-9.
1324. Kereiakes DJ, Yeh RW, Massaro JM, et al. Dual Antiplatelet Therapy (**DAPT**) Study Investigators. **Antiplatelet therapy duration following bare metal or drug-eluting coronary stents**: the dual antiplatelet therapy randomized clinical trial. JAMA. 2015 Mar 17;313(11):1113-21.
1325. Li J, Wang Y, Wang D, et al. **Glycated albumin** predicts the effect of dual and single antiplatelet therapy on recurrent stroke. Neurology 2015;84:1330–1336.
1326. Palmerini T, Benedetto U, Bacchi-Reggiani L, et al. Mortality in patients treated with extended duration **dual antiplatelet therapy after drug-eluting stent implantation**: a pairwise and Bayesian network meta-analysis of randomised rials. Lancet. 2015 Mar 13.
1327. Lhermusier T, Baker NC, Waksman R. Overview of the 2014 Food and Drug Administration Cardiovascular and Renal Drugs Advisory Committee Meeting Regarding **Cangrelor**. Am J Cardiol. 2015 Feb 3.
1328. Robertson L, Yeoh SE, Stansby G, Agarwal R. Effect of testing for **cancer on cancer- and venous thromboembolism (VTE)-** related mortality and morbidity in patients with unprovoked VTE. Cochrane Database of Systematic Reviews 2015, Issue 3. Art. No.: CD010837. DOI: 10.1002/14651858.CD010837.pub2. Testing for cancer in patients with idiopathic VTE leads to earlier diagnosis of cancer at an earlier stage of the disease. However, there is currently insufficient evidence to draw definitive conclusions concerning the effectiveness of testing for undiagnosed cancer in patients with a first episode of unprovoked VTE (DVT or PE) in reducing cancer and VTE-related morbidity and mortality. The results are imprecise and could be consistent with either harmor benefit. Further good-quality large-scale randomised controlled trials are required before firm conclusions can be made.
1329. Sandercock PAG, Counsell C, Kane EJ. **Anticoagulants for acute ischaemic stroke**. Cochrane Database of Systematic Reviews 2015, Issue 3. Art. No.: CD000024. DOI: 10.1002/14651858.CD000024.pub4. Since the last version of the review, no new relevant studies have been published and so there is no additional information to change the conclusions. Early anticoagulant therapy is not associated with net short- or long-term benefit in people with acute ischaemic stroke. Treatment with anticoagulants reduced recurrent stroke, deep vein thrombosis and pulmonary embolism, but increased bleeding risk. The data do not support the routine use of any of the currently available anticoagulants in acute ischaemic stroke.
1330. Shah ASV, Lee KK, McAllister DA, et al. Short term exposure to **air pollution and stroke**: a systematic review and meta-analysis. BMJ 2015;350:h1295.
1331. Yeh RW, Kereiakes D, Steg PG, et al. Benefits and risks of **extended duration dual antiplatelet therapy after PCI** in patients with and without acute myocardial infarction. *J Am Coll Cardiol* 2015.
1332. Zaidat OO, Fitzsimmons BF,Woodward BK, et al; **VISSIT** Trial Investigators. Effect of a balloon-expandable intracranial **stent vs medical therapy on risk of stroke in patients with symptomatic intracranial stenosis**: the VISSIT Randomized Clinical Trial. JAMA. doi:10.1001/jama.2015.1693.
1333. D'Ascenzo F, Taha S, Moretti C, et al. Meta-analysis of randomized controlled trials and adjusted observational results of use of clopidogrel, aspirin, and oral anticoagulants in patients undergoing percutaneous coronary intervention. Am J Cardiol. 2015 May 1;115(9):1185-93.

1334. White DC, Grines CL, Grines LL, et al. Comparison of usefulness of **enoxaparin versus warfarin** for prevention of left ventricular mural thrombus after **anterior wall acute myocardial infarction**. Am J Cardiol. 2015 May 1;115(9):1200-3.
1335. CADISS trial investigators. Antiplatelet treatment compared with anticoagulation treatment for **cervical artery dissection** (**CADISS**): a randomized trial. Lancet Neurol. 2015 Apr;14(4):361-7.
1336. Dai Q, Sun W, Xiong Y, et al. From clinical to tissue-based dual TIA: Validation and refinement of **ABCD3-I score**. Neurology. 2015 Apr 7;84(14):1426-32.
1337. Jallow T, D'Cruz D, Lempp H. **Antiphospholipid syndrome**. BMJ. 2015 Apr 2;350:h1426.
1338. Kwok CS, Shoamanesh A, Copley HC, et al. Efficacy of **antiplatelet therapy in secondary prevention** following **lacunar stroke**: pooled analysis of randomized trials. Stroke. 2015 Apr;46(4):1014-23
1339. Parry-Jones AR, Di Napoli M, Goldstein JN, et al. **Reversal strategies for vitamin K antagonists in acute intracerebral hemorrhage**. Ann Neurol. 2015 Apr 8.
1340. Reddy U, Mallepaddi NR, Chevassut TJ. **High INR on warfarin**. BMJ. 2015 Apr 9;350:h1282.
1341. Shore S, Ho PM, Lambert-Kerzner A, et al. Site-level variation in and practices associated with **dabigatran adherence**. JAMA. 2015 Apr 14;313(14):1443-50.
1342. Bonaca MP, Bhatt DL, Cohen M, et al; **PEGASUS-TIMI 54** Steering Committee and Investigators. Long-Term Use of **Ticagrelor** in Patients with Prior **Myocardial Infarction**. N Engl J Med. 2015 Mar 14.
1343. Cornel JH, Lopes RD, James S, et al; **APPRAISE-2** Study Group. Anticoagulant therapy and outcomes in patients with prior or acute heart failure and acute coronary syndromes: Insights from the **APixaban** for PRevention of Acute ISchemic Events 2 trial. Am Heart J. 2015 Apr;169(4):531-8.
1344. Ranta A, Dovey S, Weatherall M, et al. Cluster randomized controlled trial of **TIA electronic decision support** in primary care. Neurology 2015; 84:1545–1551.
1345. Compter AE, van der Worp HB, et al; **VAST** investigators. **Stenting versus medical treatment in patients with symptomatic vertebral artery stenosis**: a randomised open-label phase 2 trial. Lancet Neurol 2015; online April 21.
1346. Navarese EP, Andreotti F, Schulze V, et al. **Optimal duration of dual antiplatelet therapy** after percutaneous coronary intervention with **drug eluting stents**: meta-analysis of randomised controlled trials. BMJ. 2015 Apr 16;350:h1618.
1347. Williams CD, Chan AT, Elman MR, et al. **Aspirin** use among **adults in the u.s.:** results of a national survey. Am J Prev Med. 2015 May;48(5):501-8.
1348. Lane DA, Wood K. **Patient guide** for taking the non-vitamin k antagonist oral anticoagulants for atrial fibrillation. Circulation. 2015 Apr 21;131(16):e412-5.
1349. Abraham NS, Singh S, Alexander GC, et al. **Comparative risk of gastrointestinal bleeding with dabigatran, rivaroxaban, and warfarin**: population based cohort study. BMJ 2015;350:h1857.
1350. Chang H, Zhou M, Tang W, et al. Risk of **gastrointestinal bleeding associated with oral anticoagulants**: population based retrospective cohort study. BMJ 2015;350:h1585.
1351. Mismetti P, Laporte S, Pellerin O, et al; **PREPIC2** Study Group. Effect of a **retrievable inferior vena cava filter plus anticoagulation** vs anticoagulation alone on risk of recurrent pulmonary embolism: a randomized clinical trial. JAMA. 2015 Apr 28;313(16):1627-35.
1352. Wagner J, Abdel-Rahman SM. **Oseltamivir-warfarin interaction** in hypoplastic left heart syndrome: case report and review. Pediatrics. 2015 May;135(5):e1333-6.
1353. Gupta A, Chui P, et al. Frequency and Effects of **Excess Dosing of Anticoagulants** in Patients **≤55 Years** With **Acute Myocardial Infarction** Who Underwent **Percutaneous Coronary Intervention** (VIRGO Study). Am J Cardiol. 2015 Apr 6.
1354. Varenhorst C, Eriksson N, Johansson Å, et al. Effect of **genetic variations on ticagrelor** plasma levels and clinical outcomes. Eur Heart J. 2015 May 2.
1355. Wagner J, Abdel-Rahman SM. **Oseltamivir-warfarin interaction** in hypoplastic left heart syndrome: case report and review. Pediatrics. 2015 May;135(5):e1333-6.
1356. Colantino A, Jaffer AK, Brotman DJ. **Resuming anticoagulation after hemorrhage**: A practical approach. Cleve Clin J Med. 2015 Apr;82(4):245-256.
1357. Cressman AM, Macdonald EM, Fernandes KA, et al; Canadian Drug Safety and Effectiveness Research Network (CDSERN). A population-based study of the drug interaction between **clopidogrel and angiotensin converting enzyme inhibitors**. Br J Clin Pharmacol. 2015 May 15.
1358. Kitchen S, Gray E, Mackie I, Baglin T, Makris M; BCSH committee. Measurement of **non-coumarin anticoagulants and their effects on tests of Haemostasis**: Guidance from the British Committee for Standards in Haematology. Br J Haematol. 2014 Sep;166(6):830-41.
1359. Larsen TB, Rasmussen LH, Gorst-Rasmussen A, et al. **Dabigatran and warfarin** for secondary prevention of stroke in atrial fibrillation patients: a nationwide cohort study. Am J Med 2014;127:1172–8.
1360. Miyares MA, Davis KA. **Direct-Acting Oral Anticoagulants** as Emerging Treatment Options for **Heparin-Induced Thrombocytopenia**. Ann Pharmacother. 2015 Jun;49(6):735-739. Epub 2015 Apr 8.
1361. Moore SJ, Blair EA, Steeb DR, et al. Impact of **video technology** on efficiency of pharmacist-provided **anticoagulation counseling** and patient comprehension. Ann Pharmacother. 2015 Jun;49(6):631-8.
1362. O'Gorman J, Russell HK, Li J, Phillips G, Kurukulasuriya NC, Viglietta V. Effect of **Aspirin Pretreatment or Slow Dose Titration on Flushing and Gastrointestinal Events** in Healthy Volunteers Receiving Delayed-Release Dimethyl Fumarate. Clin Ther. 2015 May 18.
1363. Okubo K, Kuwahara T, Takagi K, et al. Relation between **dabigatran concentration**, as assessed using the direct thrombin inhibitor assay, and activated clotting time/activated partial thromboplastin time in patients with atrial fibrillation. Am J Cardiol. 2015 Jun 15
1364. Palareti G, Cosmi B, Legnani C, et al. DULCIS (D-dimer and Ultrasonography in Combination Italian Study) Investigators. **D-dimer to guide the duration of anticoagulation** in patients with venous thromboembolism: a management study. Blood. 2014 Jul 10;124(2):196-203.
1365. Schulman S, Carrier M, Lee AY, et al; **Periop Dabigatran** Study Group. Perioperative Management of Dabigatran: A Prospective Cohort Study. Circulation. 2015 May 12.
1366. Spandorfer J, Galanis T. In the Clinic: **Deep venous thrombosis**. Ann Intern Med. 2015 May 5;162(9):ITC1.
1367. Spencer FA, Prasad M, Vandvik PO, et al. **Longer Versus Shorter Duration Dual-Antiplatelet Therapy After Drug-Eluting Stent Placement**: A Systematic Review and Meta-analysis. Ann Intern Med. 2015 May 26.
1368. Brener SJ. Are at least **12 months** of dual antiplatelet therapy needed for all patients with **drug-eluting stents**? All patients with drug-eluting stents need at least 12 months of dual antiplatelet therapy. Circulation. 2015 Jun 2;131(22):2001-9.
1369. Caldeira D, Rodrigues FB, et al. **Non-vitamin K antagonist oral anticoagulants and major bleeding**-related fatality in patients with atrial fibrillation and venous thromboembolism: a systematic review and meta-analysis. Heart. 2015 Jun 2.
1370. Clark NP, Witt DM, Davies LE, et al. Bleeding, Recurrent Venous Thromboembolism, and Mortality Risks During **Warfarin Interruption** for Invasive Procedures. JAMA Intern Med. 2015 May 26.
1371. Di Marca S, Cilia C, Campagna A, et al. Comparison of **Wells and Revised Geneva Rule** to Assess Pretest Probability of Pulmonary Embolism in High-Risk Hospitalized Elderly Adults. J Am Geriatr Soc. 2015 Jun 1.
1372. Mega JL, Walker JR, Ruff CT, et al. **Genetics** and the clinical response to warfarin and **edoxaban**: fi ndings from the randomised, double-blind **ENGAGE AF-TIMI 48** trial. Lancet 2014; online March 11.
1373. Nighoghossian N, Berthezène Y, Mechtouff L, et al. **Cyclosporine** in acute ischemic stroke. Neurology. 2015 Jun 2;84(22):2216-23.
1374. Ruff CT, Giugliano RP, et al. Association between **edoxaban** dose, **concentration**, anti-Factor Xa activity, and outcomes: an analysis of data from the randomised, double-blind **ENGAGE AF-TIMI 48** trial. Lancet 2015; online March 11.
1375. Sharma M, Cornelius VR, Patel JP, et al. **Efficacy and Harms of Direct Oral Anticoagulants** in the **Elderly** for Stroke Prevention in Atrial Fibrillation and Secondary Prevention of Venous Thromboembolism: Systematic Review and Meta-Analysis. Circulation. 2015 May 20.
1376. Silveira PC, Ip IK, Goldhaber SZ, et al. Performance of **Wells Score** for Deep Vein Thrombosis in the Inpatient Setting. JAMA Intern Med. 2015 May 18.
1377. Glund S, Stangier J, Schmohl M, et al. Safety, tolerability, and efficacy of **idarucizumab** for the reversal of the anticoagulant effect of **dabigatran** in healthy male volunteers: a randomised, placebo-controlled, double-blind phase 1 trial. Lancet 2015; online June 16.
1378. Shah S, Luby M, Poole K, et al. **Screening with MRI for Accurate and Rapid Stroke Treatment: SMART**. Neurology 2015;84:2438–2444.
1379. Chen HB, Zhang XL, Liang HB, et al. Meta-Analysis of Randomized Controlled Trials Comparing Risk of Major Adverse Cardiac Events and Bleeding in Patients With **Prasugrel Versus Clopidogrel**. Am J Cardiol. 2015 May 12. pii: S0002-9149(15)01252-7.
1380. Pollack CV Jr, Reilly PA, Eikelboom J, et al. **Idarucizumab for dabigatran reversal**. N Engl J Med. June 2015. DOI: 10.1056/NEJMoa1502000.
1381. Denetclaw TH, Wang PK, Wong G, et al. **Pulmonary Embolism After Early Change From Rivaroxaban** to Aspirin Following Total Knee Replacement in an Obese Patient. Ann Pharmacother. 2015 Jul;49(7):851-2.
1382. Douketis JD, Spyropoulos AC, Kaatz S, et al; **BRIDGE** Investigators. **Perioperative Bridging Anticoagulation** in Patients with Atrial Fibrillation. N Engl J Med. 2015 Jun 22.
1384. Greinacher A, Thiele T, Selleng K. **Reversal of anticoagulants**: an overview of current developments. Thromb Haemost. 2015 Apr 29;113(5):931-42.
1385. Gladstone DJ et al. Clinical **tool facilitates careful monitoring of patients receiving direct oral anticoagulants**. Ann Intern Med 2015 Jun 30.
1386. Nasr H, Scriven JM. **Superficial thrombophlebitis** (superficial venous thrombosis). BMJ. 2015 Jun 22;350:h2039.
1387. Avezum A, Lopes RD, Schulte PJ, et al. **Apixaban** compared with warfarin in patients with atrial fibrillation and **valvular heart disease**: Findings from the **ARISTOTLE** trial. *Circulation* 2015.
1388. Eskes GA, Lanctôt KL, Herrmann N, et al; Heart Stroke Foundation Canada **Canadian Stroke Best Practices Committees**. Canadian stroke best practice recommendations: **mood, cognition and fatigue following stroke** practice guidelines, update 2015. Int J Stroke 2015 Jun 29.
1389. Robertson L, Kesteven P, McCaslin JE. **Oral direct thrombin inhibitors or oral factor Xa inhibitors for the treatment of deep vein thrombosis**. Cochrane Database Syst Rev. 2015 Jun 30;6: CD010956. doi: 10.1002/14651858.CD010956.pub2. NOACs such as DTIs and factor Xa inhibitors may be an effective and safe alternative to conventional anticoagulation treatment for acute DVT.
1390. Couturaud F, Sanchez O, Pernod G, et al. **Six Months vs Extended Oral Anticoagulation After a First Episode of Pulmonary Embolism**: The **PADIS-PE** Randomized Clinical Trial. JAMA. 2015 Jul 7;314(1):31-40.
1391. Middeldorp S, Hutten BA. **Long-term vs Short-term Therapy With Vitamin K Antagonists for Symptomatic Venous Thromboembolism**. JAMA. 2015 Jul 7;314(1):72-3.
1392. Sharma P, Scotland G, Cruickshank M, et al. The clinical effectiveness and cost-effectiveness of **point-of-care tests (CoaguChek system, INRatio2 PT/INR monitor and ProTime Microcoagulation system)** for the self-monitoring of the coagulation status of people receiving long-term vitamin K antagonist therapy, compared with standard UK practice: systematic review and economic evaluation. Health Technol Assess. 2015 Jun;19(48):1-172.
1393. Wang Y, Pan Y, Zhao X, et al; **CHANCE** Investigators†. **Clopidogrel With Aspirin** in Acute Minor Stroke or Transient Ischemic Attack (CHANCE) Trial: **One-Year Outcomes**. Circulation. 2015 Jul 7;132(1):40-6.
1394. Yazji K, Kakhi S, Ossei-Gerning N, et al. Complex Disease, Partial Revascularization, and Adverse Outcomes in Patients Treated With Long-Term **Warfarin** Therapy Who Underwent **Percutaneous Coronary Intervention**. Am J Cardiol. 2015 Aug 1;116(3):350-4.

1395. Gladstone DJ, Geerts WH, Douketis J, et al. How to **Monitor Patients Receiving Direct Oral Anticoagulants for Stroke Prevention in Atrial Fibrillation**: A Practice Tool Endorsed by **Thrombosis Canada**, the Canadian Stroke Consortium, the Canadian Cardiovascular Pharmacists Network, and the Canadian Cardiovascular Society. Ann Intern Med. 2015 Jun 30.
1396. Berian JR, Livingston EH. JAMA **PATIENT PAGE**. Preventing Stroke in People With **Atrial Fibrillation**. JAMA. 2015 Jul 21;314(3):310.
1397. Moss JD, Cifu AS. **Management of Anticoagulation in Patients With Atrial Fibrillation**. JAMA. 2015 Jul 21;314(3):291-2.
1398. Prystowsky EN, Padanilam BJ, Fogel RI. **Treatment of Atrial Fibrillation**. JAMA. 2015 Jul 21;314(3):278-88.
1399. Daniels PR. **Peri-procedural management of patients taking oral anticoagulants**. BMJ. 2015 Jul 14;351:h2391.
1400. Pottegård A, Henriksen DP, Madsen KG, et al. Change in **International Normalized Ratio** Among Patients Treated With **Dicloxacillin** and Vitamin K Antagonists. JAMA. 2015 Jul 21;314(3):296-7.
1401. Xian Y, Wang TY, McCoy LA, et al. Association of **Discharge Aspirin Dose** With Outcomes **After Acute Myocardial Infarction**: Insights From the Treatment with ADP Receptor Inhibitors: Longitudinal Assessment of Treatment Patterns and Events after Acute Coronary Syndrome (**TRANSLATE-ACS**) Study. Circulation. 2015 Jul 21;132(3):174-81.
1402. Cardoso RN, Benjo AM, et al. Incidence of cardiovascular events and gastrointestinal bleeding in patients receiving **clopidogrel with and without proton pump inhibitors**: an updated meta-analysis. Open Heart. 2015 Jun 30;2(1):e000248.
1403. FDA July/15 is warning health care professionals and patients that reports of confusion between the antidepressant **Brintellix** and anti-blood clotting medication **Brilinta** have resulted in the **wrong medication** being prescribed or dispensed.
1404. Li L, Yiin GS, et al, the Oxford Vascular Study. Incidence, outcome, risk factors, and long-term prognosis of **cryptogenic transient ischaemic attack and ischaemic stroke**: a population-based study. Lancet Neurol 2015; online July 28.
1405. Brønnum *Nielsen P, Larsen TB, Gorst-Rasmussen A, et al. **Intracranial hemorrhage** and subsequent ischemic stroke in patients with atrial fibrillation: a nationwide cohort study. Chest. 2015 Jun;147(6):1651-8.
1406. Health Canada Aug/15: Co-administration of **repaglinide and clopidogrel** (a CYP2C8 inhibitor) may lead to a significant decrease in blood glucose levels due to a drug-drug interaction, concomitant use is now contraindicated.
1407. Hess CN, Peterson ED, Peng SA, et al. Use and outcomes of **triple therapy among older patients with acute myocardial infarction and atrial fibrillation**. J Am Coll Cardiol 2015;66:616–27.
1408. Maura G, Blotière PO, Bouillon K, et al. Comparison of the Short-Term Risk of Bleeding and Arterial Thromboembolic Events in Nonvalvular Atrial Fibrillation Patients **Newly Treated With Dabigatran or Rivaroxaban versus Vitamin K Antagonists**: A French Nationwide Propensity-Matched Cohort Study. Circulation. 2015 Jul 21.
1409. **NICE**: National Institute for Health and Care Excellence. **Rivaroxaban** for preventing adverse outcomes after acute management of **acute coronary syndrome**. London (UK): National Institute for Health and Care Excellence 2015 Mar.
1410. Nielsen PB, Larsen TB, Skjøth F, et al. **Restarting Anticoagulant Treatment After Intracranial Hemorrhage** in Patients With Atrial Fibrillation and the Impact on Recurrent Stroke, Mortality, and Bleeding: A Nationwide Cohort Study. Circulation. 2015 Aug 11;132(6):517-25.
1411. Wardlaw JM, Brazzelli M, Chappell FM, et al. **ABCD2 score and secondary stroke prevention**: Meta-analysis and effect per 1,000 patients triaged. Neurology. 2015 Jul 28;85(4):373-80.
1412. Wang X, Zhao X, Johnston SC, et al. Effect of **clopidogrel with aspirin on functional outcome** in TIA or minor stroke: **CHANCE** substudy. Neurology 2015;85:573–579.
1413. Andreotti F, Rocca B, Husted S, et al; **ESC** Thrombosis Working Group. **Antithrombotic therapy in the elderly**: expert position paper of the European Society of Cardiology Working Group on Thrombosis. Eur Heart J. 2015 Jul 9.
1414. Barry KA, Somerville NJ. **Vorapaxar** (Zontivity) for the Prevention of Thrombotic Cardiovascular Events. Am Fam Physician. 2015 Aug 15;92(4):304-5.
1415. Dakik HA. Successful Treatment of **Clopidogrel Hypersensitivity** With a Seven-Day Taper of Oral Corticosteroid. Ann Pharmacother. 2015 Sep;49(9):1077-8.
1416. Del Campo M, Roberts G. Changes in **Warfarin Sensitivity During Decompensated Heart Failure and Chronic Obstructive Pulmonary** Disease. Ann Pharmacother. 2015Sep;49(9):962-8.
1417. Friis S, Riis AH, Erichsen R, et al. **Low-Dose Aspirin or Nonsteroidal Anti-inflammatory Drug Use and Colorectal Cancer Risk**: A Population-Based, Case-Control Study. Ann Intern Med. 2015 Aug 25.
1418. Hassell ME, Hildick-Smith D, Durand E, et al. **Antiplatelet therapy following transcatheter aortic valve implantation**. Heart. 2015 Jul 15;101(14):1118-25.
1419. Hess CN, James S, Lopes RD, et al. **Apixaban Plus Mono Versus Dual Antiplatelet Therapy in Acute Coronary Syndromes:** Insights From the **APPRAISE-2** Trial. J Am Coll Cardiol. 2015 Aug 18;66(7):777-87.
1420. Lee AY, Kamphuisen PW, Meyer G, et al; **CATCH** Investigators. **Tinzaparin vs Warfarin** for Treatment of Acute Venous Thromboembolism in Patients With Active Cancer: A Randomized Clinical Trial. JAMA. 2015 Aug 18;314(7):677-86.
1421. Morrill AM, Ge D, Willett KC. **Dosing of Target-Specific Oral Anticoagulants in Special Populations**. Ann Pharmacother. 2015 Sep;49(9):1031-45.
1422. Serebruany VL, Tomek A, Kim MH. **Survival After Solid Cancers in Antithrombotic Trials**. Am J Cardiol. 2015 Jun 25.
1423. Xian Y, Wu J, O'Brien EC, et al. **Real world effectiveness of warfarin** among ischemic stroke patients with atrial fibrillation: observational analysis from Patient-Centered Research into Outcomes Stroke Patients Prefer and Effectiveness Research (PROSPER) study. BMJ. 2015 Jul 31;351:h3786.
1424. Ye S, Cheng B, et al; **WARCEF** Investigators. **Bleeding Risk and Antithrombotic Strategy** in Patients With Sinus Rhythm and **Heart Failure** With Reduced Ejection Fraction Treated With Warfarin or Aspirin. Am J Cardiol. 2015 Jun 24.
1425. Hendriksen JM, Geersing G, Lucassen WA, et al. **Diagnostic prediction models** for suspected **pulmonary embolism**: systematic review and independent external validation in primary care. BMJ 2015;351:h4438.
1426. Kalra L, et al. **Prophylactic antibiotics after stroke** for reducing pneumonia in patients with dysphagia (**STROKE-INF**): a prospective, cluster-randomised, open-label, masked endpoint, controlled clinical trial. Lancet 2015; online Sept 4.
1427. Roldán V, Cancio S, Gálvez J, et al. The **SAMe-TT(2)R(2) Score** Predicts Poor Anticoagulation Control in AF Patients: A Prospective "Real-World" Inception Cohort Study. Am J Med. 2015 Jun 15.
1428. Song Y, Wang X, Perlstein I, et al. Relative **Bioavailability** of **Apixaban** Solution or Crushed Tablet Formulations Administered by Mouth or Nasogastric Tube in Healthy Subjects. Clin Ther. 2015 Aug 1;37(8):1703-12.
1429. Udell JA, et al. **Long-term dual antiplatelet therapy** for secondary prevention of cardiovascular events in subgroup of patients with previous myocardial infarction: a collaborative meta-analysis of randomized trials. Eur Heart J. 2015 Aug 31.
1430. Fullerton HJ, Stratton K, Mueller S, et al. **Recurrent stroke in childhood cancer survivors**. Neurology. 2015 Aug 26.
1431. Li J, Liu J, Liu M, et al. **Closure versus medical therapy for preventing recurrent stroke in patients with patent foramen ovale and a history of cryptogenic stroke or transient ischemic attack**. Cochrane Database Syst Rev. 2015 Sep 8;9:CD009938. The combined data from recent RCTs have shown no statistically significant differences between TDC and medical therapy in the prevention of recurrent ischemic stroke. TDC closure was associated with an increased risk of atrial fibrillation but not with serious adverse events.
1432. Yaghi S, Kamel H, Elkind MS. Potential new uses of **non-vitamin K antagonist oral anticoagulants to treat and prevent stroke**. Neurology. 2015 Jul 17.
1433. Spiller HA, Mowry JB, Aleguas A, et al. An observational study of the **factor XA inhibitors rivaroxaban and apixaban as reported to eight poison centers**. *Ann Emerg Med* 2015.
1434. Liu L, Wong KS, Leng X, et al; **CHANCE** Investigators. **Dual antiplatelet therapy** in stroke and **ICAS**: Subgroup analysis of CHANCE. Neurology. 2015 Aug 28.
1435. Nagarakanti R, Wallentin L, Noack H, et al. Comparison of Characteristics and Outcomes of **Dabigatran Versus Warfarin** in **Hypertensive Patients** With Atrial Fibrillation (from the **RE-LY** Trial). Am J Cardiol. 2015 Oct 15;116(8):1204-9.
1436. Raja AS, Greenberg JO, et al. Evaluation of Patients With **Suspected Acute Pulmonary Embolism: Best Practice** Advice From the Clinical Guidelines Committee of the American College of Physicians. Ann Intern Med. 2015 Sep 29.
1437. Seiffge DJ, et al; NOACISP Group. **Recanalization Therapies** in **Acute Ischemic Stroke** Patients: Impact of Prior Treatment With Novel Oral Anticoagulants on Bleeding Complications and Outcome. Circulation. 2015 Sep 29;132(13):1261-9.
1438. Dennis M, Sandercock P, Graham C, et al. The Clots in Legs Or sTockings after Stroke (**CLOTS**) 3 trial: a randomised controlled trial to determine whether or not **intermittent pneumatic compression** reduces the risk of post-stroke deep vein thrombosis and to estimate its cost-effectiveness. Health Technol Assess. 2015 Sep;19(76):1-90.
1439. Gralnek IM, Dumonceau JM, Kuipers EJ, et al. Diagnosis and management of **nonvariceal upper gastrointestinal hemorrhage**: **European** Society of Gastrointestinal Endoscopy (ESGE) Guideline. Endoscopy. 2015 Oct;47(10):a1-a46.
1440. Hermiller JB, Krucoff MW, Kereiakes DJ, et al. Benefits and risks of **extended dual antiplatelet therapy after everolimus-eluting stents.** *JACC Cardiovasc Interv* 2015; DOI:10.1016/j.jcin.2015.10.001.
1441. Yarrington CD, Valente AM, Economy KE. **Cardiovascular Management in Pregnancy**: **Antithrombotic Agents and Antiplatelet Agents**. Circulation. 2015 Oct 6;132(14):1354-64.
1442. Blin P, Dureau-Pournin C, Lassalle R, et al. A population database study of outcomes associated with **vitamin K antagonists in atrial fibrillation**. Br J Clin Pharmacol. 2015 Oct 22.
1443. Steffel J, Giugliano RP, Braunwald E, et al. **Edoxaban vs. warfarin** in patients with atrial fibrillation on **amiodarone**: a subgroup analysis of the **ENGAGE AF-TIMI 48** trial. Eur Heart J. 2015 Sep 1;36(33):2239-45.
1444. Urban P, Meredith IT, Abizaid A, et al; **LEADERS FREE** Investigators. **Polymer-free Drug-Coated Coronary Stents** in Patients at High Bleeding Risk. N Engl J Med. 2015 Oct 14. (**only 1month course of DAPT therapy**)
1445. Avgil Tsadok M, Jackevicius CA, Rahme E, et al. **Sex Differences in Dabigatran** Use, Safety, And Effectiveness In a Population-Based Cohort of Patients With Atrial Fibrillation. Circ Cardiovasc Qual Outcomes. 2015 Oct 27.
1446. **NICE**: National Clinical Guideline Centre for Acute and Chronic Conditions. **Venous thromboembolism in adults admitted to hospital**: reducing the risk. London (UK): National Institute for Health and Care Excellence (NICE); 2015 Jun.
1447. Christensen TD, Skjøth F, Nielsen PB, et al. **Self-Management of Anticoagulant Therapy** in **Mechanical Heart Valve Patients**: A Matched Cohort Study. Ann Thorac Surg. 2015 Nov 3.
1448. Giacoppo D, Gargiulo G, Aruta P, et al. Treatment strategies for **coronary in-stent restenosis**: systematic review and hierarchical Bayesian network meta-analysis of 24 randomised trials and 4880 patients. BMJ. 2015 Nov 4;351:h5392.
1449. Huang Y, Xu S, Hua J, et al. Association between **job strain and risk of incident stroke**: a meta-analysis. Neurology 2015;85:1648–1654.
1450. Kreutz R, Haas S, Holberg G, et al. **Rivaroxaban compared with standard thromboprophylaxis** after major **orthopaedic surgery**: co-medication interactions. Br J Clin Pharmacol. 2015 Nov 18.
1451. Rodés-Cabau J, Horlick E, Ibrahim R, et al. Effect of **Clopidogrel and Aspirin vs Aspirin Alone** on **Migraine Headaches** After **Transcatheter Atrial Septal Defect Closure**: The **CANOA** Randomized Clinical Trial. JAMA. 2015 Nov 9:1-8.
1452. Siegal DM, Curnutte JT, Connolly SJ, et al. **Andexanet alfa** for the reversal of factor Xa inhibitor activity. N Engl J Med. (**Annexa-A, Annexa-R**) DOI: 10.1056/NEJMoa1510991.
1453. Toner P, McAuley DF, Shyamsundar M. **Aspirin** as a potential treatment in **sepsis or acute respiratory distress syndrome**. Crit Care. 2015 Oct 23;19(1):374.
1454. Truong C. **Low-dose acetylsalicylic acid for primary prevention** of cardiovascular disease: Do not misinterpret the recommendations. Can Fam Physician. 2015 Nov;61(11):971-2.
1455. Xian Y, Federspiel JJ, et al. Risks and Benefits Associated With **Prestroke Antiplatelet Therapy** Among Patients With Acute Ischemic Stroke Treated With Intravenous **Tissue Plasminogen Activator**. JAMA Neurol. 2015 Nov 9:1-10.
1456. Egbe AC, Pislaru SV, Pellikka PA, et al. **Bioprosthetic valve thrombosis** versus structural failure: Clinical and echocardiographic predictors. *J Am Coll Cardiol* 2015; 66:2285–94.
1457. Liu D, Peterson E, et al. Interdisciplinary Expert Panel on **Iliofemoral Deep Vein Thrombosis** (InterEPID). Diagnosis and management of iliofemoral deep vein thrombosis: clinical practice guideline. CMAJ. 2015 Nov 17;187(17):1288-96.
1458. NICE: National Institute for Health and Care Excellence (**NICE**). **Edoxaban** for treating and for **preventing deep vein thrombosis and pulmonary embolism**. London (UK): National Institute for Health and Care Excellence; 2015 Aug.
1459. Sherwood M, Nessel C, Hellkamp A, et al. **Gastrointestinal bleeding** in patients with atrial fibrillation treated with rivaroxaban or warfarin. (**Rocket-AF**) *J Am Coll Cardiol* 2015; 66:2271-2281.
1460. Werner EF, Hauspurg AK, Rouse DJ. A Cost-Benefit Analysis of **Low-Dose Aspirin Prophylaxis** for the Prevention of **Preeclampsia** in the United States. Obstet Gynecol. 2015 Dec;126(6):1242-50.

1461. Mauri L, Elmariah S, Yeh RW, et al. Causes of late **mortality with dual antiplatelet therapy** after coronary stents. Eur Heart J. 2015 Nov 18.
1462. Parry-Jones AR, Di Napoli M, Goldstein JN, et al. **Reversal strategies for vitamin K antagonists in acute intracerebral hemorrhage**. Ann Neurol. 2015 Jul;78(1):54-62.
1463. Cohen D. Data on trial of anticoagulant is to be reanalyzed after discovery that investigators used **faulty device**. (**Rocket-AF**) BMJ. 2015 Dec 3;351:h6431.
1464. Liu X, Johnson M, Mardekian J, et al. **Apixaban** Reduces Hospitalizations in Patients With Venous Thromboembolism: An Analysis of the Apixaban for the Initial Management of Pulmonary Embolism and Deep-Vein Thrombosis as First-Line Therapy (**AMPLIFY**) Trial. J Am Heart Assoc. 2015 Dec 1;4(12).
1465. Rao MP, Halvorsen S, Wojdyla D, et al; **Apixaban** for Reduction in Stroke and Other Thromboembolic Events in Atrial Fibrillation (**ARISTOTLE**) Steering Committee and Investigators. Blood Pressure Control and Risk of Stroke or Systemic Embolism in Patients With Atrial Fibrillation: Results From the Apixaban for Reduction in Stroke and Other Thromboembolic Events in Atrial Fibrillation (ARISTOTLE) Trial. J Am Heart Assoc. 2015 Dec 1;4(12).
1466. Jacobs V, Woller SC, et al. Percent Time With a **Supratherapeutic INR** in Atrial Fibrillation Patients Also Using an Antiplatelet Agent Is Associated With **Long-Term Risk of Dementia**. J Cardiovasc Electrophysiol. 2015 Aug 13.
1467. Robertson L, Kesteven P, McCaslin JE. **Oral direct thrombin inhibitors or oral factor Xa inhibitors** for the **treatment of pulmonary embolism**. Cochrane Database Syst Rev. 2015 Dec 4;12:CD010957. Moderate to high quality evidence suggests that there are no differences between DOACs and standard anticoagulation for the long-term treatment of pulmonary embolism, for the outcomes recurrent pulmonary embolism, recurrent venous thromboembolism, DVT, all-cause mortality and major bleeding.
1468. Fisher M, Moores L, Alsharif MN, et al. Definition and Implications of the **Preventable Stroke**. JAMA Neurol. 2015 Dec 7:1-4.
1469. Heeney MM, Hoppe CC, Abboud MR, et al; **DOVE** Investigators. A Multinational Trial of **Prasugrel** for **Sickle Cell Vaso-Occlusive Events**. N Engl J Med. 2015 Dec 8.
1470. Jacobs V, Woller SC, et al. Percent Time With a **Supratherapeutic INR in** Atrial Fibrillation Patients Also Using an Antiplatelet Agent Is Associated With **Long-Term Risk of Dementia**. J Cardiovasc Electrophysiol. 2015 Aug 13.
1471. Lai CL, Kuo RN, Chen HM, Chen MF, Chan KA, Lai MS. Risk of **ischemic stroke** during the initiation period of **α-blocker therapy** among older men. CMAJ. 2015 Dec 7.
1472. Lip GY, Lanitis T, Kongnakorn T, et al. **Cost-effectiveness** of **Apixaban Compared With Edoxaban** for Stroke Prevention in Nonvalvular Atrial Fibrillation. Clin Ther. 2015 Nov 1;37(11):2476-2488.e27.
1473. Purrucker JC, Haas K, Rizos T, et al. Early Clinical and Radiological Course, Management, and Outcome of **Intracerebral Hemorrhage Related to New Oral Anticoagulants**. JAMA Neurol. 2015 Dec 14:1-10.
1474. Romley JA, Gong C, Jena AB, et al. Association between use of **warfarin with common sulfonylureas** and serious hypoglycemic events: retrospective cohort analysis. BMJ. 2015 Dec 7;351:h6223.
1475. Weitz JI, Semchuk W, Turpie AG, et al. Trends in **Prescribing Oral Anticoagulants in Canada**, 2008-2014. Clin Ther. 2015 Nov 1;37(11):2506-2514.e4.
1476. Chai-Adisaksopha C, Hillis C, Isayama T, et al. **Mortality outcomes in patients receiving direct oral anticoagulants: a systematic review and meta-analysis of randomized controlled trials.** J Thromb Haemost. 2015 Nov;13(11):2012-20.
1477. Eikelboom JW, Quinlan DJ, van Ryn J, et al. **Idarucizumab**: The Antidote for Reversal of Dabigatran. Circulation. 2015 Dec 22;132(25):2412-22.
1478. Jackson L, Ju C, et al. Outcomes of patients with **acute myocardial infarction** undergoing **percutaneous coronary intervention** receiving an **oral anticoagulant and dual antiplatelet therapy**. *JACC Cardiovasc Interv* 2015; 8:1880-1889.
1479. Marshall A, Levine M, Howell ML, et al. Dose-associated Pulmonary Complication Rates after **Fresh Frozen Plasma Administration for Warfarin Reversal**. J Thromb Haemost. 2015 Dec 8.
1480. Martinelli I, Lensing AW, Middeldorp S, et al. Recurrent venous **thromboembolism and abnormal uterine bleeding with anticoagulant and hormone therapy use**. Blood. 2015 Dec 22.
1481. Preston IR, et al. Effect of **Warfarin** Treatment on Survival of Patients With **Pulmonary Arterial Hypertension (PAH):** Registry to Evaluate Early and Long-Term PAH Disease Management (REVEAL). Circ. 2015 Dec 22;132(25):2403-11.
1482. Roe MT, Cyr DD, Eckart D, et al. Ascertainment, classification, and impact of **neoplasm detection** during prolonged treatment with dual antiplatelet therapy with **prasugrel vs clopidogrel** following acute coronary syndrome. *Eur Heart J*2015.
1483. Selby LV, Sovel M, Sjoberg DD, et al; MSKCC VTE Task Force. **Preoperative Chemoprophylaxis** Is Safe in Major **Oncology** Operations and Effective at **Preventing Venous Thromboembolism**. J Am Coll Surg. 2015 Dec 15.
1484. Staerk L, Lip GYH, Olesen JB, et al. **Stroke and recurrent haemorrhage** associated with **antithrombotic treatment after gastrointestinal bleeding in patients with atrial fibrillation**: nationwide cohort study. *BMJ* 2015.
1485. Wysokinski WE, McBane RD 2nd. **Periprocedural bridging** management of anticoagulation. Circulation. 2012 Jul 24;126(4):486-90.
1486. Meyer AV, Green M, Pautler HM, et al. Impact of Vitamin K Administration on **INR Changes** and Bleeding Events Among Patients With **Cirrhosis**. Ann Pharmacother. 2015 Nov 18.
1487. Park JM, Kang K, Cho YJ, et al; on the behalf of CRCS-5 investigators. Comparative Effectiveness of **Pre-stroke Aspirin on Stroke Severity and Outcome**. Ann Neurol. 2016 Jan 11.
1488. Piccini JP, Hellkamp AS, Washam JB, et al. **Polypharmacy** and the Efficacy and Safety of **Rivaroxaban versus Warfarin** in the Prevention of Stroke in Patients With Nonvalvular Atrial Fibrillation. (**Rocket-AF**) Circulation. 2015 Dec 16.
1489. Cannon CP, Husted S, Harrington RA, et al; **DISPERSE-2** Investigators. Safety, tolerability, and initial efficacy of AZD6140 (**ticagrelor**), the first reversible oral adenosine diphosphate receptor antagonist, compared with clopidogrel, in patients with non-ST-segment elevation acute coronary syndrome: primary results of the DISPERSE-2 trial. J Am Coll Cardiol. 2007 Nov 6;50(19):1844-51.
1490. Del-Carpio Munoz F, Gharacholou SM, Munger TM, et al. Meta-Analysis of **Renal Function** on the Safety and Efficacy of **Novel Oral Anticoagulants for Atrial Fibrillation**. Am J Cardiol. 2016 Jan 1;117(1):69-75.
1491. Casaubon1 LK, Boulanger JM, Glasser E, et al; Heart and Stroke Foundation of Canada **Canadian Stroke Best Practices** Advisory Committee. Canadian stroke best practice recommendations: acute inpatient stroke care guidelines, update 2015. Int J Stroke 2016;11:239-52.
1492. Feng W, Wu K, Liu Z, et al. **Oral direct factor Xa inhibitor versus enoxaparin** for **thromboprophylaxis after hip or knee arthroplasty**: Systemic review, traditional meta-analysis, dose-response meta-analysis and network meta-analysis. Thromb Res. 2015 Dec;136(6):1133-44.
1493. Hermiller JB, Krucoff MW, Kereiakes DJ, et al; **DAPT** Study Investigators. Benefits and Risks of **Extended Dual Antiplatelet Therapy After Everolimus-Eluting Stents**. JACC Cardiovasc Interv. 2016 Jan 25;9(2):138-47.
1494. Kim JT, Park MS, Choi KH, et al. Different Antiplatelet Strategies in Patients With **New Ischemic Stroke While Taking Aspirin**. Stroke. 2016 Jan;47(1):128-34.
1495. Majeed A, Goldhaber SZ, Kakkar A, et al. **Bleeding events** with **dabigatran or warfarin** in patients with venous thromboembolism. Thromb Haemost. 2015 Sep 24;115(2).
1496. Montalescot G, Crea F. The year in cardiology 2015: **acute coronary syndromes**. Eur Heart J. 2016 Jan 14;37(3):221-8.
1497. Wilson D, Charidimou A, Shakeshaft C, et al; **CROMIS-2** collaborators. Volume and functional outcome of **intracerebral hemorrhage according to oral anticoagulant type**. Neurology. 2016 Jan 26;86(4):360-6.
1498. Casaubon LK, Boulanger JM, Glasser E, et al. Heart and Stroke Foundation of Canada Canadian Stroke Best Practices Advisory Committee. **Canadian Stroke Best Practice** Recommendations: Acute Inpatient Stroke Care Guidelines, Update 2015. Int J Stroke. 2016 Feb;11(2):239-52.
1499. Di Nisio M, Ageno W, Rutjes AW, et al. Risk of major **bleeding** in patients with **venous thromboembolism** treated with **rivaroxaban or with heparin and vitamin K antagonists**. Thromb Haemost. 2015 Oct 29;115(2).
1500. Liu X, Thompson J, Phatak H, et al. Extended anticoagulation with **apixaban** reduces hospitalisations in patients with **venous thromboembolism**. An analysis of the **AMPLIFY-EXT** trial. Thromb Haemost. 2015 Dec 22;115(1):161-8.
1501. Palmerini T, Stone GW. **Optimal duration of dual antiplatelet** therapy **after drug-eluting stent implantation**: conceptual evolution based on emerging evidence. Eur Heart J. 2016 Jan 21;37(4):353-64.
1502. Raccah BH, Perlman A, Danenberg HD, et al. Major **Bleeding** and Hemorrhagic **Stroke** with **Direct Oral Anticoagulants** in Patients with **Renal Failure**: Systematic Review and Meta-Analysis of Randomized Trials. Chest. 2016 Jan 18.
1503. Raskob GE, Gallus AS, Sanders P, et al. Early time courses of recurrent **thromboembolism** and **bleeding** during **apixaban** or **enoxaparin/warfarin** therapy. A sub-analysis of the **AMPLIFY** trial. Thromb Haemost. 2015 Dec 10;115(4).
1504. Camm AJ, Amarenco P, Haas S, et al. **XANTUS**: A **real-world**, prospective, observational study of patients treated with **rivaroxaban** for stroke prevention in atrial fibrillation. *Eur Heart J* 2015.
1505. Cohen D. **Rivaroxaban**: **Can we trust the evidence**? *BMJ* 2015.
1506. Berntsen CF, Kristiansen A, Akl EA, et al. **Compression Stockings** for Preventing the Postthrombotic Syndrome in Patients with Deep Vein Thrombosis. Am J Med. 2015 Dec 31.
1507. Brott TG, Howard G, Roubin GS, et al. Long-term results of **stenting versus endarterectomy for carotid-artery stenosis**. N Engl J Med. (**CREST**) DOI: 10.1056/NEJMoa1505215.
1508. Burnett AE, Mahan CE, Vazquez SR, et al. Guidance for the **practical management** of the direct oral anticoagulants (**DOACs**) in VTE treatment. J Thromb Thrombolysis. 2016 Jan;41(1):206-32.
1509. Entezari-Maleki T, Dousti S, Hamishehkar H, et al. A systematic review on comparing 2 common models for management of **warfarin** therapy; **pharmacist-led service versus usual medical care**. J Clin Pharmacol. 2016 Jan;56(1):24-38.
1510. He Y, Wong IC, Li X, et al. The association between **Non-vitamin K antagonist** oral anticoagulants and **gastrointestinal bleeding**: a meta-analysis of observational studies. Br J Clin Pharmacol. 2016 Feb 17.
1511. Kearon C, Akl EA, Ornelas J, et al. **Antithrombotic Therapy for VTE Disease**: **CHEST Guideline** and Expert Panel Report. Chest. 2016 Feb;149(2):315-52.
Lip GYH, Banerjee A, Boriani G, et al. **Antithrombotic Therapy for Atrial Fibrillation: CHEST** Guideline and Expert Panel Report. Chest. **2018** Aug 21.

1512. Kline JA, Jimenez D, Courtney DM, et al. Comparison of **Four Bleeding Risk Scores** to Identify **Rivaroxaban**-treated Patients With Venous Thromboembolism at Low Risk for Major Bleeding. Acad Emerg Med. 2016 Feb;23(2):144-50.
1513. Laidlaw TM, Boyce JA. **Aspirin-Exacerbated Respiratory Disease**--New Prime Suspects. N Engl J Med. 2016 Feb 4;374(5):484-8.
1514. Marciniak TA, Cherepanov V, Golukhova E, et al. **Drug Discontinuation** and Follow-up Rates in **Oral Antithrombotic Trials**. JAMA Intern Med. 2016 Feb 1;176(2):257-9.
1515. Ng KH, Shestakovska O, Connolly SJ, et al. Efficacy and safety of **apixaban** compared with **aspirin** in the **elderly**: a subgroup analysis from the **AVERROES** trial. Age Ageing. 2016 Jan;45(1):77-83.
1516. Patel MR, Hellkamp AS, Fox KA; ROCKET AF Executive Committee and Investigators. **Point-of-Care Warfarin Monitoring** in the **ROCKET AF Tria**l. N Engl J Med. 2016 Feb 3.
1517. Romanelli RJ, Nolting L, Dolginsky M, et al. **Dabigatran Versus Warfarin** for Atrial Fibrillation in **Real-World** Clinical Practice: A Systematic Review and Meta-Analysis. Circ Cardiovasc Qual Outcomes. 2016 Jan 26.
1518. Rosenfield K, Matsumura JS, Chaturvedi S, et al. Randomized trial of **stent versus surgery for asymptomatic carotid stenosis**. N Engl J Med. (**ACT 1**) DOI: 10.1056/NEJMoa1515706. 2.
1519. Wood B, Sholzberg M, Ackery A. **Direct oral anticoagulants and the bleeding patient**. CMAJ. 2016 Feb 16;188(3):215.
1520. Ying GS, Maguire MG, Daniel E, et al. Comparison of Age-Related Macular Degeneration Treatments Trials Research Group. Association between **Antiplatelet or Anticoagulant Drugs** and **Retinal or Subretinal Hemorrhage** in the Comparison of Age-Related Macular Degeneration Treatments Trials. Ophthalmology. 2016 Feb;123(2):352-60.
1521. Alotaibi GS, Wu C, Senthilselvan A, et al. Secular trends in incidence and **mortality of acute venous thromboembolism**: The AB-VTE population based sudy. Am J Med. 2016 Feb 26.
1522. Andrade JG, Deyell MW, Khoo C, et al. Risk of **bleeding on triple antithrombotic therapy** after percutaneous coronary intervention/stenting: a systematic review and meta-analysis. Can J Cardiol. 2013 Feb;29(2):204-12.
1523. Bonaca MP, Bhatt DL, Steg PG, et al. Ischaemic risk and efficacy of **ticagrelor in relation to time from P2Y12 inhibitor withdrawal** in patients with prior myocardial infarction: insights from **PEGASUS-TIMI 54.** *Eur Heart J* 2015;

doi:10.1093/eurheartj/ehv531. Published online ahead of print 21 October 2015.

1524. Braun OÖ, Bico B, Chaudhry U, et al. Concomitant use of **warfarin and ticagrelor** as an alternative to triple antithrombotic therapy after an acute coronary syndrome. Thromb Res. 2015 Jan;135(1):26-30.
1525. de Oliveira Carvalho PE, Magolbo NG, De Aquino RF, et al. **Oral aspirin for treating venous leg ulcers**. Cochrane Database Syst Rev. 2016 Feb 18;2:CD009432. Low quality evidence from two trials indicate that there is currently insufficient evidence for us to draw definitive conclusions about the benefits and harms of oral aspirin on the healing and recurrence of venous leg ulcers. We downgraded the evidence to low quality due to potential selection bias and imprecision due to the small sample size. The small number of participants may have a hidden real benefit, or an increase in harm. Due to the lack of reliable evidence, we are unable to draw conclusions about the benefits and harms of oral daily aspirin as an adjunct to compression in VLU healing or recurrence. Further high quality studies are needed in this area.
1526. Kubica J, Adamski P, Ostrowska M, et al. **Morphine delays and attenuates ticagrelor** exposure and action in patients with myocardial infarction: the randomized, double-blind, placebo-controlled IMPRESSION trial. Eur Heart J. 2016 Jan 14;37(3):245-52.
1527. Myles PS, Smith JA, Forbes A, et al. **Stopping vs continuing aspirin before coronary artery surgery**. (**ATACAS**) *N Engl J Med*2016; 374:728-737.
1528. Sambola A, Mutuberría M, García Del Blanco B, et al. Impact of **Triple Therapy in Elderly Patients with Atrial Fibrillation Undergoing Percutaneous Coronary Intervention**. PLoS One. 2016 Jan 25;11(1):e0147245.
1529. Vazquez FJ, Gonzalez JP, LeGal G, et al. Risk of major **bleeding** in patients receiving **vitamin K antagonists or low doses of aspirin**. A systematic review and meta-analysis. Thromb Res. 2016 Feb;138:1-6.
1530. Veitch AM, Vanbiervliet G, Gershlick AH, et al. **Endoscopy** in patients **on antiplatelet or anticoagulant therapy**, including direct oral anticoagulants: **British** Society of Gastroenterology (BSG) and **European** Society of Gastrointestinal Endoscopy (ESGE) guidelines. Endoscopy. 2016 Feb 18.
1531. Cao Y, Nishihara R, Wu K, et al. Population-wide Impact of **Long-term** Use of **Aspirin** and the **Risk for Cancer**. JAMA Oncol. 2016 Mar 3.
1532. Gajic-Veljanoski O, Phua CW, Shah PS, et al. Effects of Long-Term **Low-Molecular-Weight Heparin on Fractures and Bone Density** in Non-Pregnant Adults: A Systematic Review With Meta-Analysis. J Gen Intern Med. 2016 Feb 19.
1533. Hostler DC, Marx ES, Moores LK, et al. Validation of the International Medical Prevention Registry on **Venous Thromboembolism Bleeding Risk Score** (**IMPROVE BRS**). Chest. 2016 Feb;149(2):372-9.
1534. Myles PS, Smith JA, Forbes A, et al; ATACAS Investigators of the ANZCA Clinical Trials Network. **Stopping vs. Continuing Aspirin before Coronary Artery Surgery**. N Engl J Med. 2016 Feb 25;374(8):728-37.
1535. Palareti G, Antonucci E, Lip GY, et al. The **SAME-TT2R2 score** predicts the quality of **anticoagulation** control in patients with **acute VTE**. A real-life inception cohort study. Thromb Haemost. 2016 Jan 28;115(6).
1536. Rillig A, Lin T, Plesman J, et al. **Apixaban, Rivaroxaban, and Dabigatran** in Patients Undergoing **Atrial Fibrillation Ablation**. J Cardiovasc Electrophysiol. 2016 Feb;27(2):147-53.
1537. Levy JH, Ageno W, et al. Subcommittee on Control of Anticoagulation. When and how to use **antidotes for the reversal of direct oral anticoagulants: guidance from the SSC of the ISTH**. J Thromb Haemost. 2016 Mar;14(3):623-7.
1538. Vasan S, Rostgaard K, Majeed A, et al. **ABO blood group** and risk of thromboembolic and arterial disease: A study of 1.5 million blood donors.*Circulation* 2016.
1539. Yao X, Abraham N, Alexander C, et al. Effect of **adherence** to oral anticoagulants on risk of stroke and major bleeding among patients with atrial fibrillation. *J Am Heart Assoc* 2016.
1540. Pdf Aminian A, Andalib A, Khorgami Z, et al. Who Should Get **Extended Thromboprophylaxis After Bariatric Surgery**?: A Risk Assessment Tool to Guide Indications for Post-discharge Pharmacoprophylaxis. Ann Surg. 2016 Mar 8.
1541. Dodson JA, Petrone A, Gagnon DR, et al. Incidence and determinants of **traumatic intracranial bleeding** among older veterans receiving **warfarin** for atrial fibrillation. *JAMA Cardiol* 2016.
1542. Diener HC, Selim MH, Molina CA, Greenberg SM. **Embolic Stroke, Atrial Fibrillation, and Microbleeds**: Is There a Role for Anticoagulation? Stroke. 2016 Mar;47(3):904-7.
1543. Fralick M, Juurlink DN, Marras T. Bleeding associated with coadministration of **rivaroxaban and clarithromycin**. CMAJ 2016. [Epub ahead of print 2016 Jan. 25.]
1544. Kullo IJ, Rooke TW. Clinical Practice. **Peripheral Artery Disease**. N Engl J Med. 2016 Mar 3;374(9):861-71.
1545. Ricket AL, Stewart DW, Wood RC, et al. Comparison of **Postoperative Bleeding** in Total Hip and Knee **Arthroplasty** Patients Receiving Rivaroxaban or Enoxaparin. Ann Pharmacother. 2016 Apr;50(4):270-5.
1546. Vasan SK, Rostgaard K, Majeed A, et al. **ABO Blood Group** and Risk of Thromboembolic and Arterial Disease: A Study of 1.5 Million Blood Donors. Circulation. 2016 Mar 3.
1547. Yao X, Abraham NS, Alexander GC, et al. Effect of **Adherence** to Oral Anticoagulants on Risk of Stroke and Major Bleeding Among Patients With Atrial Fibrillation. J Am Heart Assoc. 2016 Feb 23;5(2).
1548. Ahrens KA, Silver RM, Mumford SL, et al. Complications and Safety of Preconception **Low-Dose Aspirin Among Women With Prior Pregnancy Losses**. Obstet Gynecol. 2016 Apr;127(4):689-98.
1549. Bibbins-Domingo K; US Preventive Services Task Force. **Aspirin Use for the Primary Prevention of Cardiovascular Disease and Colorectal Cancer**: US Preventive Services Task Force Recommendation Statement. (**USPSTF**) Ann Intern Med. 2016 Apr 12
1550. Cao Y, Nishihara R, Wu K, et al. Population-wide Impact of **Long-term Use of Aspirin and the Risk for Cancer**. JAMA Oncol. 2016 Mar 3.
1551. Choi M, Mintz M, Bates D. Interaction between **Warfarin and Apple Juice**. Can J Hosp Pharm. 2016 Jan-Feb;69(1):42-4.
1552. Chubak J, Whitlock EP, Williams SB, et al. **Aspirin** for the Prevention of **Cancer Incidence and Mortality**: Systematic Evidence Reviews for the U.S. Preventive Services Task Force. (**USPSTF**) Ann Intern Med. 2016 Apr 12.
1553. Dreischulte T, Donnan P, Grant A, et al. Prescribing--A Trial of **Education, Informatics, and Financial Incentives**. (antiplatelets & NSAIDS) N Engl J Med. 2016 Mar 17;374(11):1053-64.
1554. Fan W, Plent S, Prats J, Deliargyris EN. **Trends in P2Y12 Inhibitor** Use in Patients Referred for Invasive Evaluation of Coronary Artery Disease in Contemporary US Practice. Am J Cardiol. 2016 May 1;117(9):1439-43.
1555. Fralick M, Juurlink DN, Marras T. Bleeding associated with coadministration of **rivaroxaban and clarithromycin**. CMAJ. 2016 Jan 25.
1556. Forster R, Stewart M. **Anticoagulants (extended duration) for prevention of venous thromboembolism following total hip or knee replacement or hip fracture repair**. Cochrane Database Syst Rev. 2016 Mar 30;3:CD004179. Moderate quality evidence suggests extended-duration anticoagulants to prevent VTE should be considered for people undergoing hip replacement surgery, although the benefit should be weighed against the increased risk of minor bleeding. Further studies are needed to better understand the association between VTE and extended-duration oral anticoagulants in relation to knee replacement and hip fracture repair, as well as outcomes such as distal and proximal DVT, reoperation, wound infection and healing.
1557. Gage BF, Birman-Deych E, Kerzner R, et al. Incidence of **intracranial hemorrhage in patients with atrial fibrillation** who are prone to fall. Am J Med. 2005 Jun;118(6):612-7.
1558. Guirguis-Blake JM, Evans CV, Senger CA, et al. **Aspirin for the Primary Prevention** of **Cardiovascular Events**: A Systematic Evidence Review for the U.S. Preventive Services Task Force. (**USPSTF**) Ann Intern Med. 2016 Apr 12.
1559. Hsu JC, Chan PS, Tang F, Maddox TM, et al. **Oral Anticoagulant Prescription in Patients With Atrial Fibrillation** and a Low Risk of Thromboembolism: Insights From the **NCDR PINNACLE Registry**. JAMA Intern Med. 2015 Jun
1560. Jain A, Cifu AS. Prevention, Diagnosis, and Treatment of **Postthrombotic Syndrome**. JAMA. 2016 Mar 8;315(10):1048-9.
1561. Levine GN, Bates ER, Bittl JA, et al; Focused Update Writing Group. 2016 ACC/AHA Guideline Focused Update on **Duration of Dual Antiplatelet Therapy in Patients With Coronary Artery Disease**: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. J Am Coll Cardiol. 2016 Mar 23.
1562. Lip GY, Nielsen PB. Should Patients With Atrial Fibrillation & 1 Stroke Risk Factor **(CHA2DS2-VASc Score 1 in Men, 2 in Women) Be Anticoagulated**? Yes: Even 1 Stroke Risk Factor Confers Real Risk of Stroke. Circulation. 2016 Apr 12
1563. Mastoris I, Maria Mathias P, Dangas GD. Dual **Antiplatelet Therapy Duration**: A Review of Current Available Evidence. Clin Ther. 2016 Mar 15. pii: S0149-2918(16)30076-5.
1564. Orvin K, Bental T, Assali A, et al. Usefulness of the **CHA2DS2-VASC Score to Predict Adverse Outcomes** in Patients Having Percutaneous Coronary Intervention. Am J Cardiol. 2016 May 1;117(9):1433-8.
1565. Pollack CV Jr. **Antidotes for Bleeding Caused by Novel Oral Anticoagulants**. Circulation. 2016 Jan 12;133(2):e18-9.
1566. Savino JA 3rd, Halperin JL. Should Patients With Atrial Fibrillation and 1 Stroke Risk Factor (**CHA2DS2-VASc Score 1 in Men, 2 in Women) Be Anticoagulated**? The CHA2 DS2-VASc 1 Conundrum: Decision Making at the Lower End of the Risk Spectrum. Circulation. 2016 Apr 12
1567. Senoo K, Proietti M, Lane DA, et al. Evaluation of the **HAS-BLED, ATRIA and ORBIT bleeding risk scores** in atrial fibrillation patients on warfarin. Am J Med. 2015 Oct 16.
1568. Vaduganathan M, Bhatt DL, Cryer BL, et al. **Proton-pump inhibitors reduce gastrointestinal events** regardless of aspirin dose in patients requiring dual antiplatelet therapy. *J Am Coll Cardiol* 2016.
1569. Whitlock EP, Burda BU, Williams SB, et al. **Bleeding Risks With Aspirin** Use for Primary Prevention in Adults: A Systematic Review for the U.S. Preventive Services Task Force. (**USPSTF**) Ann Intern Med. 2016 Apr 12.
1570. Yeh RW, Secemsky EA, et al; **DAPT** Study Investigators. Development and Validation of a **Prediction Rule for Benefit and Harm** of Dual Antiplatelet Therapy Beyond 1 Year After Percutaneous Coronary Intervention. JAMA. 2016 Mar 29.
1571. Amarenco P, Lavallée PC, Labreuche J, et al. **One-year risk of stroke after transient ischemic attack or minor stroke**. (**TIAregistry.org**) N Engl J Med 2016;374:1533-42.
1572. Cao Y, Nishihara R, Wu K, et al. Population-wide Impact of Long-term Use of **Aspirin** and the **Risk for Cancer**. JAMA Oncol. 2016 Mar 3.
1573. Rodrigues FB, Neves JB, Caldeira D, Ferro JM, Ferreira JJ, Costa J. **Endovascular treatment versus medical** care alone for **ischaemic stroke**: systematic review and meta-analysis. BMJ 2016;353:i1754.
1574. Basaraba JE, Barry AR. What is the **optimal duration of dual antiplatelet** therapy **after percutaneous coronary intervention** with drug-eluting stent implantation? Am J Health Syst Pharm. 2016 May 1;73(9):e229-37
1575. Berntsen CF, Kristiansen A, Akl EA, et al. **Compression Stockings** for **Preventing the Postthrombotic Syndrome** in Patients with Deep Vein Thrombosis. Am J Med. 2016 Apr;129(4):447.e1-447.e20. Elastic compression stockings do not relieve pain or prevent postthrombotic syndrome or its recurrence in patients who have experienced venous thromboembolism. They will, however, give you that "I've just been in the hospital" look. (LOE = 1a-)
1576. Elwood PC, Morgan G, Pickering JE, et al. **Aspirin** in the Treatment of Cancer: Reductions in **Metastatic Spread and in Mortality**: A Systematic Review and Meta-Analyses of Published Studies. PLoS One. 2016 Apr 20
1577. Martinelli I, et al. Recurrent venous thromboembolism and **abnormal uterine bleeding with anticoagulant and hormone therapy use**. Blood. 2016 Mar 17;127(11):1417-25.
1578. Martin K, Key NS. How I treat patients with **inherited bleeding disorders** who need anticoagulant therapy. Blood. 2016 Apr 22.
1579. Meredith IT, Tanguay JF, et al. **DAPT** Study Investigators. **Diabetes Mellitus and Prevention of Late Myocardial Infarction** After Coronary Stenting in the Randomized Dual Antiplatelet Therapy Study. Circulation. 2016 Mar 18.
1580. Schwann TA, Habib RH, Suri RM, et al. Variation in **Warfarin Use at Hospital Discharge After Isolated Bioprosthetic Mitral Valve Replacement** – An Analysis of the Society of Thoracic Surgeons Adult Cardiac Surgery Database. Chest. 2016 Apr 28. pii: S0012-3692(16)48651-4.
1581. Giugliano RP, Ruff CT, Wiviott SD, et al. **Mortality** in Patients with Atrial Fibrillation Randomized to **Edoxaban or Warfarin**: Insights from the **ENGAGE AF-TIMI 48** Trial. Am J Med. 2016 Mar 17.
1582. Johnston SC, Amarenco P, Albers GW, et al; **SOCRATES** Steering Committee and Investigators. **Ticagrelor versus Aspirin** in Acute **Stroke** or Transient Ischemic Attack. N Engl J Med. 2016 May 10.
1583. Kor DJ, Carter RE, Park PK, et al. Effect of **aspirin** on development of **ARDS** in at-risk patients presenting to the emergency department: the **LIPS-A** randomized clinical trial.JAMA. doi:10.1001 /jama.2016.6330.

1584. Winstein CJ, Stein J, Arena R, et al; **American** Heart Association Stroke Council, Council on Cardiovascular and Stroke Nursing, Council on Clinical Cardiology, and Council on Quality of Care and Outcomes Research. **Guidelines** for **Adult Stroke Rehabilitation and Recovery**: A Guideline for Healthcare Professionals From the American Heart Association/American Stroke Association. Stroke. 2016 May 4.
1585. Bagai A, Bhatt DL, Eikelboom JW, et al. **Individualizing Duration of Dual Antiplatelet Therapy After Acute Coronary Syndrome or Percutaneous Coronary Intervention**. Circulation. 2016 May 24;133(21):2094-8.
1586. Baharoglu MI, et al. **Platelet transfusion versus standard care after acute stroke** due to spontaneous cerebral haemorrhage associated with antiplatelet therapy (PATCH): a randomised, open-label, phase 3 trial. Lancet. 2016 May 9.
1587. Oh MS, Yu KH, Lee JH, et al. **Aspirin resistance** is associated with **increased stroke severity and infarct volume**. Neurology. 2016 May 10;86(19):1808-17.
1588. van Es N, van der Hulle T, van Es J, et al. **Wells Rule and d-Dimer Testing** to Rule Out **Pulmonary Embolism**: A Systematic Review and Individual-Patient Data Meta-analysis. Ann Intern Med. 2016 May 17.
1589. White RH, Brunson A, Romano PS, Li Z, Wun T. Outcomes after **vena cava filter use in noncancer patients with acute venous thromboembolism**: a population-based study. Circulation. 2016;133:2018–2029.
1590. Aminian A, Andalib A, Khorgami Z, et al. Who Should Get Extended **Thromboprophylaxis After Bariatric Surgery**?: A Risk Assessment Tool to Guide Indications for Post-discharge Pharmacoprophylaxis. Ann Surg. 2016 Mar 8.
1591. Becattini C, Agnelli G. Treatment of Venous **Thromboembolism With New Anticoagulant Agents**. J Am Coll Cardiol. 2016 Apr 26;67(16):1941-55.
1592. Cadilhac DA, Kim J, Lannin NA, et al. Better outcomes for hospitalized patients with TIA when in **stroke units**: an observational study. Neurology 2016;86:2042–2048.
1593. Cohen AT, Harrington RA, Goldhaber SZ, et al; APEX Investigators. **Extended Thromboprophylaxis with Betrixaban** in Acutely Ill Medical Patients. N Engl J Med. 2016 May 27.
1594. Crijnen YS, Nouwens F, de Lau LM, et al; MR CLEAN investigators. Early effect of **intra-arterial treatment** in ischemic stroke on aphasia recovery in **MR CLEAN**. Neurology. 2016 May 31;86(22):2049-55.
1595. Mol GC, van de Ree MA, Klok FA, et al. One versus two years of elastic **compression stockings** for prevention of post-thrombotic syndrome (**OCTAVIA** study): randomized controlled trial. BMJ 2016;353:i2691.
1596. Rothwell PM, Algra A, Chen Z, et al. Effects of **aspirin on risk and severity of early recurrent stroke** after transient ischaemic attack and ischaemic stroke: time-course analysis of randomised trials. Lancet. 2016 May 18.
1597. Saver JL. Clinical Practice. **Cryptogenic Stroke**. N Engl J Med. 2016 May 26;374(21):2065-74.
1598. Steiner T, Poli S, Griebe M, et al. **Fresh frozen plasma versus prothrombin complex concentrate** in patients with **intracranial haemorrhage** related to **vitamin K antagonists** (**INCH**): a randomised trial. Lancet Neurol 2016; 15: 566–73.
1599. Wang SV, Franklin JM, Glynn RJ, et al. Prediction of rates of thromboembolic and major bleeding outcomes with **dabigatran or warfarin** among patients with atrial fibrillation: new initiator cohort study. BMJ. 2016 May 24;353:i2607.
1600. Yoo AJ, Berkhemer OA, Fransen PS, et al, for the **MR CLEAN** Investigators. Effect of baseline Alberta Stroke Program Early CT Score on safety and efficacy of **intra-arterial treatment**: a subgroup analysis of a randomised phase 3 trial (MR CLEAN). Lancet Neurol 2016; 15: 685–94.
1601. Bains SJ, Mahic M, Myklebust TÅ, Småstuen et al. **Aspirin As Secondary Prevention in Patients With Colorectal Cancer**: An Unselected Population-Based Study. J Clin Oncol. 2016 May 31.
1602. FDA Jun/16 FDA is warning consumers about the risk of **serious bleeding** when using nonprescription, also known as over-the-counter or OTC, aspirin-containing antacid products to treat heartburn, sour stomach, acid indigestion, or upset stomach. **OTC aspirin-antacid products** are sold under various trade names, including Alka-Seltzer Original, Bromo Seltzer, Medique Medi Seltzer, Picot Plus Effervescent, Vida Mia Pain Relief, Winco Foods Effervescent Antacid and Pain Relief, and Zee-Seltzer Antacid and Pain Reliever. They are also available as generic products.
1603. Bonaca MP, Bhatt DL, Oude Ophuis T, et al. Long-term tolerability of **ticagrelor** for the secondary prevention of major adverse cardiovascular events: a secondary analysis of the **PEGASUS-TIMI 54** trial [online June 15, 2016]. JAMA Cardiol. doi:10.1001/jamacardio.2016 .1017.
1604. Chan FK, Leung Ki EL, Wong GL, et al. Risks of Bleeding Recurrence and Cardiovascular Events With Continued **Aspirin Use After Lower Gastrointestinal Hemorrhage**. Gastroenterology. 2016 Apr 26.
1605. Feigin VL, Roth GA, et al, and Risk Factors Study 2013 and Stroke Experts Writing Group. **Global burden of stroke and risk factors in 188 countries**, 1990–2013: a systematic analysis for the Global Burden of Disease Study 2013. Lancet Neurol 2016; online June 9.
1606. Ferreira JP, Girerd N, Alshalash S, et al. **Antithrombotic therapy in heart failure patients with and without atrial fibrillation**: update and future challenges. Eur Heart J. 2016 Jun 1.
1607. Matsuo K, Cahoon SS, Yoshihara K, et al. Association of **Low-Dose Aspirin and Survival of Women With Endometrial Cancer**. Obstet Gynecol. 2016 Jun 6.
1608. Saliba W, Gronich N, Barnett-Griness O, et al. The role of **CHADS and CHA DS -VASc scores** in the prediction of stroke in individuals **without atrial fibrillation**: a population-based study. J Thromb Haemost. 2016 Apr 1.
1609. Song Y, Chang M, Suzuki A, et al. Evaluation of **Crushed Tablet for Oral Administration and the Effect of Food on Apixaban** Pharmacokinetics in Healthy Adults. Clin Ther. 2016 Jun 9.
1610. Giustino G, Kirtane AJ, et al. Impact of **Anemia** on **Platelet Reactivity** and Ischemic and **Bleeding** Risk:From the Assessment of **Dual Antiplatelet Therapy** With Drug-Eluting Stents Study. Am J Cardiol. 2016 Jun 15;117(12):1877-83
1611. Mora S, Manson JE. **Aspirin for Primary Prevention** of Atherosclerotic Cardiovascular Disease: Advances in Diagnosis and Treatment. JAMA Intern Med. 2016 Jun 20.
1612. Bhatt DL, Bonaca MP, Bansilal S, et al. Reduction in Ischemic Events With **Ticagrelor in Diabetic Patients** With Prior Myocardial Infarction in **PEGASUS-TIMI 54**. J Am Coll Cardiol. 2016 Jun 14;67(23):2732-40.
1613. Bonaca M, Bhatt D, Ophuis TO, et al. **Long-term tolerability of ticagrelor** for the secondary prevention of major adverse cardiovascular events: A secondary analysis of the **PEGASUS TIMI 54** trial. *JAMA Cardiol* 2016.
1614. Mol GC et al. One versus two years of **elastic compression stockings for prevention of post-thrombotic syndrome** (**OCTAVIA** study): Randomised controlled trial. BMJ 2016 May 31; 353:i2691.
1615. Barra ME, Fanikos J, Connors JM, Sylvester et al.Evaluation of **Dose-Reduced Direct Oral Anticoagulant Therapy**. Am J Med. 2016 Jun 21.
1616. Bartsch E, Medcalf KE, Park AL, et al. High Risk of Pre-eclampsia Identification Group. Clinical **risk factors for pre-eclampsia** determined in early pregnancy: systematic review and meta-analysis of large cohort studies. BMJ2016;353:i1753.
1617. Bohula EA, Giugliano RP, Ruff CT, et al. Impact of renal function on outcomes with **edoxaban** in the **ENGAGE AF-TIMI 48** trial. Circulation. 2016;134:24-36.
1618. Fett N. Management of **Antiplatelet Allergy** (**clopidogrel**) After Cardiac Stenting. JAMA Dermatol. 2016 Jun 22.
1619. Jaspers Focks J, Brouwer MA, Wojdyla DM, et al. **Polypharmacy** and effects of **apixaban** versus warfarin in patients with atrial fibrillation: post hoc analysis of the **ARISTOTLE** trial. BMJ. 2016 Jun 15;353:i2868.
1620. Mora S, Ames JM, Manson JE. **Low-Dose Aspirin in the Primary Prevention** of Cardiovascular Disease: Shared Decision Making in Clinical Practice. JAMA. 2016 Jun 20.
1621.Timmis A, Rapsomaniki E, Chung SC, et al. **Prolonged dual antiplatelet therapy in stable coronary disease**: comparative observational study of benefits and harms in unselected versus trial populations. BMJ. 2016 Jun 22;353:i3163.
1622. Barber EL, Clarke-Pearson DL. The limited utility of currently available venous **thromboembolism risk assessment tools in gynecological oncology patients**. Am J Obstet Gynecol. 2016 Apr 27.
1623. Becattini C, et al. **Risk Stratification** of Patients With Acute Symptomatic **Pulmonary Embolism Based on Presence or Absence of Lower Extremity DVT**: Systematic Review and Meta-analysis. Chest. 2016 Jan;149(1):192-200.
1624. Boonyawat K, Wang L, Lazo-Langner A, et al. The effect of **low-dose oral vitamin K supplementation on INR stability** in patients receiving warfarin. A randomised trial. Thromb Haemost.2016 Jun 23;116(3).
1625. Byrd JB, et al. **Clopidogrel prescription filling delays** and cardiovascular outcomes in a pharmacy system integrating inpatient and outpatient care: insights from the Veterans Affairs CART Program. Am Heart J. 2014 Sep;168(3):340-5.
1626. Chowdhry U, Jacques A, Karovitch A, et al. Appropriateness of **Dabigatran and Rivaroxaban Prescribing** for Hospital Inpatients. Can J Hosp Pharm. 2016 May-Jun;69(3):194-201.
1627. Crawford F, Andras A, Welch K, et al. **D-dimer test** for excluding the diagnosis of **pulmonary embolism**. Cochrane Database Syst Rev. 2016 Aug 5;8
1628. Di Nisio M, van Es N, Büller HR. **Deep vein thrombosis and pulmonary embolism**. Lancet. 2016 Jun 30. pii: S0140-6736(16)30514-1.
1629. FDA July/16: **INRatio and INRatio2 PT/INR Monitor System by Alere: Recall** - Potentially Inaccurate INR Results.
1630. Fordyce CB, Hellkamp AS, Lokhnygina Y, et al; On-Treatment Outcomes in Patients With **Worsening Renal Function** With **Rivaroxaban** Compared With Warfarin: Insights From **ROCKET AF**. Circulation. 2016 Jul 5;134(1):37-47.
1631. Freedman B, Martinez C, Katholing A, et al. **Residual Risk of Stroke and Death in Anticoagulant-Treated Patients With Atrial Fibrillation**. JAMA Cardiol. 2016 Jun 1;1(3):366-8.
1632. Goldhaber SZ, Schellong S, Kakkar A, et al. Treatment of acute pulmonary embolism with **dabigatran versus warfarin**. A pooled analysis of data from **RE-COVER and RE-COVER II**. Thromb Haemost. 2016 Jul 14;116(4).
1633. Ha NB, Yang K, Hanigan S, et al. Impact of a Guideline for the Management of **Antimicrobial/Warfarin Interactions** in the Inpatient Setting and Across Transition of Care. Ann Pharmacother. 2016 Jun 16
1634. Health Canada July/16: Alere Inc. initiating **voluntary withdrawal** of **Alere INRatio® and INRatio® 2 PT/INR Monitoring System** that may pose serious health risks.
1635. Heneghan CJ, Garcia-Alamino JM, Spencer EA, et al. **Self-monitoring and self-management of oral anticoagulation**. Cochrane Database Syst Rev. 2016 Jul 5;7:CD003839. Participants who self-monitor or self-manage can improve the quality of their oral anticoagulation therapy. Thromboembolic events were reduced, for both those self-monitoring or self-managing oral anticoagulation therapy. A reduction in all-cause mortality was observed in trials of self-management but not in self-monitoring, with no effects on major haemorrhage.
1636. Hijazi, Z, Hohnloser SH, et al. Efficacy and safety of **apixaban compared with warfarin** in patients with atrial fibrillation in relation to **renal function** over time: Insights from the **ARISTOTLE** randomized trial. *JAMA Cardiol* 2016.
1637. Martin K, Beyer-Westendorf J, Davidson BL, et al. Use of the **direct oral anticoagulants in obese patients**: guidance from the SSC of the ISTH. J Thromb Haemost. 2016 Jun;14(6):1308-13.
1638. Masri A, Gillinov AM, Johnston DM, et al. **Anticoagulation versus antiplatelet** or no therapy in patients undergoing **bioprosthetic valve implantation**: a systematic review and meta-analysis. Heart. 2016 Aug 3.
1639. Mora S, Ames JM, Manson JE. Low-Dose **Aspirin in the Primary Prevention** of Cardiovascular Disease: Shared Decision Making in Clinical Practice. JAMA. 2016 Aug 16;316(7):709-10.
1640. Nochaiwong S, Ruengorn C, Awiphan R, et al. Efficacy and safety of **warfarin in dialysis patients with atrial fibrillation**: a systematic review and meta-analysis. Open Heart. 2016 Jun 16;3(1)
1641. O'Donnell MJ, Chin SL, Rangarajan S, et al. Global and regional effects of potentially **modifiable risk factors associated with acute stroke** in 32 countries (**INTERSTROKE**): a case-control study. Lancet. 2016 Jul 15.
1642. Parasrampuria DA, Mendell J, Shi M, et al. **Edoxaban drug-drug interactions with ketoconazole, erythromycin, and cyclosporine**. Br J Clin Pharmacol. 2016 Aug 16.
1643. Pokorney SD, Simon DN, Thomas L, et al. **Stability of International Normalized Ratios** in Patients Taking **Long-term Warfarin** Therapy. JAMA. 2016 Aug 9;316(6):661-3.
1644. Raccah BH, Perlman A, et al. Major **Bleeding and Hemorrhagic Stroke With Direct Oral Anticoagulants** in Patients With **Renal Failure**: Systematic Review and Meta-Analysis of Randomized Trials. Chest. 2016 Jun;149(6):1516-24.
1645. Rost NS, Giugliano RP, Ruff CT, Murphy et al. Outcomes With **Edoxaban Versus Warfarin** in Patients **With Previous Cerebrovascular Events**: Findings From **ENGAGE AF-TIMI 48.** Stroke. 2016 Aug;47(8):2075-82.
1646. Ruff CT, Giugliano RP, Antman EM. Management of **Bleeding With Non-Vitamin K Antagonist Oral Anticoagulants in the Era of Specific Reversal Agents**. Circulation. 2016 Jul 19;134(3):248-61.
1647. Sibbing D, Kastrati A, Berger PB. **Pre-treatment with P2Y12 inhibitors in ACS** patients: who, when, why, and which agent? Eur Heart J. 2016 Apr 21;37(16):1284-95.
1648. Staerk L, Lip GY, Olesen JB, et al. **Stroke and recurrent haemorrhage associated with antithrombotic treatment after gastrointestinal bleeding** in patients with atrial fibrillation: nationwide cohort study. BMJ. 2015 Nov 16;351:h5876.
1649. Steiger N, Cifu AS. **Primary Prevention of Stroke**. JAMA. 2016 Aug 9;316(6):658-9.

1650. van Es N, van der Hulle T, van Es J, et al. **Wells Rule and d-Dimer Testing to Rule Out Pulmonary Embolism**: A Systematic Review and Individual-Patient Data Meta-analysis. Ann Intern Med. 2016 Aug 16;165(4):253-61.
1651. Wang Y, et al; **CHANCE**. Association Between **CYP2C19 Loss-of-Function Allele Status and Efficacy of Clopidogrel** for Risk Reduction Among Patients With Minor Stroke or Transient Ischemic Attack. JAMA. 2016 Jul 5;316(1):70-78.
1652. Cayla G et al. **Platelet function monitoring** to adjust antiplatelet therapy in elderly patients stented for an acute coronary syndrome (ANTARCTIC): An open-label, blinded-endpoint, randomised controlled superiority trial. Lancet 2016 Aug 28.
1653. Ezekowitz MD, Nagarakanti R, Noack H, et al. Comparison of **Dabigatran and Warfarin** in Patients With Atrial Fibrillation and Valvular Heart Disease: The **RE-LY** Trial (Randomized Evaluation of Long-Term Anticoagulant Therapy). Circulation. 2016 Aug 23;134(8):589-98
1654. Passman R. **Time in Therapeutic Range in Warfarin**-Treated Patients: Is Very Good Good Enough? JAMA. 2016 Aug 23-30;316(8):872-3.
1655. Jia H, Dai J, Hou J, et al. Effective **antithrombotic therapy without stenting**: Intravascular optical coherence tomography-based management in plaque erosion (the **EROSION** study). *Eur Heart J* 2016.
1656. Kunutsor SK, Seidu S, Khunti K. **Aspirin for primary prevention** of cardiovascular and all-cause mortality events in diabetes: updated meta-analysis of randomized controlled trials. Diabet Med. 2016 Apr 17.
1657. Lip GY, Pan X, et al. Major bleeding risk among non-valvular atrial fibrillation patients initiated on **apixaban, dabigatran, rivaroxaban or warfarin**: a ``**real-world**`` observational study in the United States. Int J Clin Pract. 2016 Aug 23.
1658. Motovska Z, Hlinomaz O, Miklik R, et al. **Prasugrel versus ticagrelor** in patients with **acute myocardial infarction** treated with primary percutaneous coronary intervention: Multicenter randomized **PRAGUE-18** study. *Circulation*2016.
1659. Franchi F, Rollini F, Aggarwal N, et al. Pharmacodynamic comparison of **prasugrel versus ticagrelor** in patients with type 2 **diabetes** mellitus and **coronary artery disease**: the **OPTIMUS** (Optimizing Antiplatelet Therapy in Diabetes Mellitus)-4 study. Circulation. 2016;134:780–792.
1660. Frontera JA, Lewin JJ III, Rabinstein AA, et al. Guideline for reversal of **antithrombotics in intracranial hemorrhage**: a statement for healthcare professionals from the Neurocritical Care Society and Society of Critical Care Medicine. Neurocrit Care. 2016 Feb;24(1):6-46.
1661. Hansson NC, Grove El, Andersen HR, et al. **Transcatheter aortic valve thrombosis**: predisposing factors and clinical implications. *J Am Coll Cardiol* 2016.
1662. Sharma A, Lavie CJ, Sharma SK, et al. **Duration of Dual Antiplatelet Therapy After Drug-Eluting Stent Implantation** in Patients **With and Without Acute Coronary Syndrome**: A Systematic Review of Randomized Controlled Trials. Mayo Clin Proc. 2016 Aug;91(8):1084-93.
1663. Basaraba JE, Barry AR. **Short- versus standard-term dual antiplatelet** therapy **after percutaneous coronary intervention** with drug-eluting stent implantation: A meta-analysis. J Cardiol. 2016 Aug 30.
1664. Cameron JI, O'Connell C, Foley N, et al; Heart and Stroke Foundation Canadian Stroke Best Practice Committees. Canadian Stroke Best Practice Recommendations: **Managing transitions of care following Stroke**,Guidelines Update 2016. Int J Stroke. 2016 Oct;11(7):807-22.
1665. Cavender MA, Bhatt DL, Stone GW, et al. Consistent Reduction in Periprocedural Myocardial Infarction With **Cangrelor** as Assessed by Multiple Definitions: Findings From CHAMPION PHOENIX (Cangrelor Versus Standard Therapy to Achieve Optimal Management of Platelet Inhibition). Circulation. 2016 Sep 6;134(10):723-33.
1666. Clarke MJ, Broderick C, Hopewell S, Juszczak E, Eisinga A. **Compression stockings** for preventing deep vein thrombosis in airline passengers. Cochrane Database of Systematic Reviews 2016, Issue 9. Art. No.: CD004002. There is high-quality evidence that airline passengers similar to those in this review can expect a substantial reduction in the incidence of symptomless DVT and low-quality evidence that leg oedema is reduced if they wear compression stockings. Quality was limited by the way that oedema was measured. There is moderate-quality evidence that superficial vein thrombosis may be reduced if passengers wear compression stockings. We cannot assess the effect of wearing stockings on death, pulmonary embolism or symptomatic DVT because no such events occurred in these trials. Randomised trials to assess these outcomes would need to include a very large number of people.
1667. Connolly SJ, Milling TJ Jr, Eikelboom JW, et al. **Andexanet Alfa** for Acute Major Bleeding Associated with Factor Xa Inhibitors. N Engl J Med. 2016 Aug 30.
1668. Franzone A, Piccolo R, Gargiulo G, et al. **Prolonged vs short duration of dual antiplatelet therapy after percutaneous coronary intervention** in patients with or without **peripheral arterial disease**: a subgroup analysis of the **PRODIGY** randomized clinical trial [online August 30, 2016].JAMA Cardiol. doi: 10.1001/jamacardio .2016.2811.
1669. Giannoni A, Emdin M, Passino C. Cheyne-Stokes Respiration, Chemoreflex, and **Ticagrelor-Related Dyspnea**. N Engl J Med. 2016 Sep 8;375(10):1004-6
1670. Goette A, Merino JL, Ezekowitz MD, Zamoryakhin et al. **Edoxaban versus enoxaparin-warfarin** in patients undergoing cardioversion of atrial fibrillation (**ENSURE-AF**): a randomised, open-label, phase 3b trial. Lancet. 2016 Aug 26.
1671. Samuelson BT, Cuker A, Siegal DM, Crowther M, Garcia DA. **Laboratory Assessment** of the Anticoagulant Activity of Direct Oral Anticoagulants (**DOACs**): A Systematic Review. Chest. 2016 Sep 13.
1672. Yogaratnam D, Ditch K, Medeiros K, et al. **Idarucizumab** for Reversal of Dabigatran-Associated Anticoagulation. Ann Pharmacother. 2016 Oct;50(10):847-54.
1673. Woods EA, Ackman ML, Graham MM, et al. **Anticoagulant and Antiplatelet Prescribing Patterns** for Patients with Atrial Fibrillation after Percutaneous Coronary Intervention. Can J Hosp Pharm. 2016 Jul-Aug;69(4):280-5.
1674. Bonaca MP, Goto S, Bhatt DL, et al. **Prevention of Stroke with Ticagrelor** in Patients with Prior Myocardial Infarction: Insights from **PEGASUS-TIMI 54**. Circulation. 2016 Sep 20;134(12):861-871.
1675. Bonaca MP, Bhatt DL, Storey RF, et al. Efficacy and safety of **ticagrelor** as long-term secondary prevention in patients **with peripheral artery disease** and priormyocardial infarction. (**PEGASUS-TIMI 54**) J AmColl Cardiol. 2016.
1676. Foley TR, Armstrong EJ, Waldo SW. Contemporary evaluation and **management of lower extremity peripheral artery disease**. Heart. 2016 Sep 15;102(18):1436-41.
1677. Koenig-Oberhuber V, Filipovic M. **New antiplatelet drugs and new oral anticoagulants**. Br J Anaesth. 2016 Sep;117 Suppl 2:ii74-ii84.
1678. Yasmina A, de Boer A, Deneer VH, et al. Patterns of **antiplatelet drug use after a first myocardial infarction during a 10-years period**. Br J Clin Pharmacol. 2016 Sep 23.
1679. Gherli R, et al. Safety of **Preoperative Use of Ticagrelor** With or Without **Aspirin** Compared With Aspirin Alone in Patients With Acute Coronary Syndromes Undergoing **Coronary Artery Bypass Grafting**. JAMA Cardiol. 2016 Sep 21.
1680. Graham DJ, Reichman ME, Wernecke M, et al. Stroke, bleeding, and mortality risks in **elderly Medicare beneficiaries** treated with **dabigatran or rivaroxaban** for nonvalvular atrial fibrillation [online Oct 3, 2016].JAMA Intern Med.
1681. Shantsila E, Lip GYH. **Antiplatelet versus anticoagulation treatment for patients with heart failure in sinus rhythm**. Cochrane Database of Systematic Reviews 2016, Issue 9. Art. No.: CD003333. There is evidence from RCTs to suggest that neither oral anticoagulation with warfarin or platelet inhibition with aspirin is better for mortality in systolic heart failure with sinus rhythm (high quality of the evidence for all-cause mortality and moderate quality of the evidence for non-fatal cardiovascular events and major bleeding events). Treatment with warfarin was associated with a 20% reduction in non-fatal cardiovascular events but a twofold higher risk of major bleeding complications (high quality of the evidence). We saw a similar pattern of results for the warfarin versus clopidogrel comparison (low quality of the evidence). At present, there are no data on the role of oral anticoagulation versus antiplatelet agents in heart failure with preserved ejection fraction with sinus rhythm. Also, there were no data from RCTs on the utility of non-vitamin K antagonist oral anticoagulants compared to antiplatelet agents in heart failure with sinus rhythm.
1682. Lip GY, et al. **Real-world comparison** of major bleeding risk among non-valvular atrial fibrillation patients initiated on **apixaban, dabigatran, rivaroxaban, or warfarin**. A propensity score matched analysis. Thromb Haemost. 2016 Aug 19;116(5).
1683. Mahtani KR, Heneghan C. **Novel oral anticoagulants for atrial fibrillation**. BMJ. 2016 Sep 28;354:i5187.
1684. Rathi VK, Krumholz HM, Ross JS. Commentary: **Diagnostic devices** in clinical trials have high stakes for patient care. BMJ. 2016 Sep 28;354:i5197
1685. Shah R, Hellkamp A, Lokhnygina Y, et al. Use of **concomitant aspirin** in patients with atrial fibrillation: Findings from the **ROCKET AF** trial. (**rivaroxaban**) Am Heart J. 2016 Sep;179:77-86.
1686. FDA Oct/16: In July 2016, the **Alere INRatio device** was recalled due to the potential to generate inaccurate results. This device was used to monitor warfarin therapy in the control group of the ROCKET-AF clinical trial, which provided the primary data to support the 2011 approval of the blood thinner drug Xarelto (rivaroxaban). Xarelto is indicated to reduce the rates of stroke and blood clots in patients with non-valvular atrial fibrillation. Because of the concern about the Alere INRatio device, the FDA has completed a variety of analyses to assess the impact that this faulty monitoring device had on the ROCKET-AF study results. The Agency has determined that effects on strokes or bleeding, including bleeding in the head, were minimal. The FDA concludes that Xarelto is a safe and effective alternative to warfarin in patients with atrial fibrillation.
1687. Knoflach M, Lang W, Seyfang L, et al. Predictive value of **ABCD2 and ABCD3-I scores in TIA and minor stroke** in the stroke unit setting. Neurology. 2016 Aug 30;87(9):861-9.
1688. Pokorney SD, Shrader P, et al. Influence of **Kidney Function** Estimation Methods on Eligibility of **Edoxaban** Population Impact of the US Food and Drug Administration's Approach for its Product Labeling. Circulation ;134 :1122-1124.
1689. Resor CD, Nathan A, Kereiakes DJ, Yeh et al. Impact of **Optimal Medical Therapy in the Dual Antiplatelet Therapy Study**. Circulation. 2016 Oct 4;134(14):989-998.
1690. Kelly PJ, Albers GW, Chatzikonstantinou A, et al. Validation and comparison of **imaging-based scores for prediction of early stroke risk** after transient ischaemic attack: pooled analysis of individual-patient data from prospective cohort studies. Lancet Neurol 2016; 15: 1238–47.
1691. Komen J, Forslund T, Hjemdahl P, et al. Effects of **policy interventions** on the introduction of **novel oral anticoagulants in Stockholm**: an interrupted time series analysis. Br J Clin Pharmacol. 2016 Oct 11.
1692. Margolis JM, Deitelzweig S, Kline J, et al. **Pulmonary Embolism Inpatients** Treated With **Rivaroxaban** Had Shorter Hospital Stays and Lower Costs Compared With Warfarin. Clin Ther. 2016 Oct 14.
1693. Cucchiara B. How long should we **wait to start oral anticoagulation after cardioembolic stroke**? Neurology. 2016 Sep 30.
1694. Hellyer JA, et al. Impact of **Baseline Stroke Risk and Bleeding Risk on Warfarin International Normalized Ratio Control** in Atrial Fibrillation (TREAT-AF Study). American Journal of Cardiology (2016).
1695. Seiffge DJ, Traenka C, Polymeris A, et al. **Early start of DOAC after ischemic stroke**: risk of intracranial hemorrhage and recurrent events. Neurology 2016;87:1856–1862.
1696. Carnicelli AP, O'Gara PT, Giugliano RP. **Anticoagulation After Heart Valve Replacement or Transcatheter Valve Implantation**. Am J Cardiol. 2016 Nov 1;118(9):1419-1426.
1697. Gargiulo G, Windecker S, da Costa BR, et al. **Short term versus long term dual antiplatelet therapy after implantation of drug eluting stent in patients with or without diabetes**: systematic review and meta-analysis of individual participant data from randomised trials. BMJ 2016;355:i5483.
1698. Pan Y, Chen W, Xu Y, et al. **Genetic Polymorphisms and Clopidogrel Efficacy** for Acute Ischemic Stroke or Transient Ischemic Attack: A Systematic Review and Meta-analysis. Circulation. 2016 Nov 2.
1699. Björck F, Renlund H, Lip GY, et al. Outcomes in a Warfarin-Treated Population With Atrial Fibrillation. JAMA Cardiol. 2016 May 1;1(2):172-80.
1700. Dong K, Song Y, Li X, et al. Pentasaccharides for the prevention of **venous thromboembolism. (fondaparinux, idraparinux, idrabiotaparinux**) Cochrane Database Syst Rev. 2016 Oct 31;10:CD005134. Moderate to high quality evidence shows that fondaparinux iseffective for short-term prevention of VTE when compared with placebo. It can reduce total VTE, DVT, total PE and symptomatic VTE, and does not

demonstrate a reduction in deaths compared with placebo. Low to moderate quality evidence shows that fondaparinux is more effective for short-term VTE prevention when compared with LMWH. It can reduce total VTE and total DVT and does not demonstrate a reduction in deaths when compared with LMWH.

1701. Gerhard-Herman MD, Gornik HL, Barrett C, et al. **2016 AHA/ACC Guideline** on the Management of Patients With **Lower Extremity Peripheral Artery Disease**: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. Circulation. 2016 Nov 13.
1702. Gibson CM, Pinto DS, Chi G, et al. **Recurrent hospitalization** among patients with atrial fibrillation undergoing intracoronary stenting **treated with two treatment strategies of rivaroxaban or** a dose-adjusted oral **vitamin k antagonist** treatment strategy. Circulation. 2016;134:xx– xx.doi: xxxxxxxx.
1703. Gibson CM, Mehran R, Bode C, et al. An open-label, randomized, controlled, multicenter study exploring two treatment strategies of **rivaroxaban and a doseadjusted oral vitamin K** antagonist treatment strategy in subjects with **atrial fibrillation who undergo percutaneous coronary intervention**: **PIONEER AF-PCI**. N Engl J Med. 2016. doi: 10.1056/ NEJMoa1611594.
1704. Halvorsen S, Storey RF, Rocca B, et al. **ESC** Working Group on Thrombosis. Management of **antithrombotic therapy after bleeding** in patients with **coronary artery disease and/or atrial fibrillation**: expert consensus paper of the European Society of Cardiology Working Group on Thrombosis. Eur Heart J. 2016 Oct 27.
1705. Jones WS, Baumgartner I, Hiatt WR, et al; International Steering Committee and Investigators of the **EUCLID** Trial (Examining Use of tiCagreLor In paD) .. **Ticagrelor Compared With Clopidogrel** in Patients with Prior Lower Extremity Revascularization for **Peripheral Artery Disease**. Circulation. 2016 Nov 13.
1706. McDowell TY, Blank M, Lawrence J, et al. **Food and Drug Administration Analysis of Ticagrelor**: Using Data From an Enriched Trial to Evaluate Benefit-Risk Difference in an Unstudied Population. Circulation. 2016 Nov 8;134(19):1500-1502
1707. Patti G, Cavallari I. **Extended duration dual antiplatelet therapy in patients with myocardial infarction**: A study-level meta-analysis of controlled randomized trials. Am Heart J. 2016 Jun;176:36-43.
1708. Shirakawa T, et al. **Watching television** and risk of mortality from **pulmonary embolism** among Japanese men and women: the **JACC** Study (Japan Collaborative Cohort). Circulation. 2016;134:355-35
1709. Capodanno D, Angiolillo DJ. **Aspirin for Primary Cardiovascular Risk Prevention** and Beyond in **Diabetes** Mellitus. Circulation. 2016 Oct 11.
1710. Guo L, Li S, Wang P, et al. Comparative Efficacy of Clinical Events **Prevention of Five Anticoagulants** in Patients with **Atrial Fibrillation** (A Network Meta-Analysis). American Journal of Cardiology. 2016.
1711. Lip GY, Waldo AL, Ip J, et al. Determinants of **Time in Therapeutic Range** in Patients Receiving Oral Anticoagulants (A Substudy of **IMPACT**). Am J Cardiol. 2016 Dec 1;118(11):1680-1684
1712. Turner GM, et al. **Under-prescribing of Prevention Drugs and Primary Prevention of Stroke and Transient Ischaemic Attack in UK** General Practice: A Retrospective Analysis. PLoS Med. 2016 Nov 15;13(11):e1002169.
1713. Bykov K, Schneeweiss S, Donneyong MM, et al. Impact of an **Interaction Between Clopidogrel and Selective Serotonin Reuptake Inhibitors**.Am J Cardio (2016)
1714. Rodger MA, Gris JC, de Vries JIP, et al, for the Low-Molecular-Weight Herapin for Placenta-Medicated Pregnancy Complications Study Group. **Low-molecular-weight heparin and recurrent placenta mediated pregnancy complications**: a meta-analysis of individualised patient data from randomised controlled trials. Lancet 2016; online Oct 6.
1715. Saito Y, et al. **Low-Dose Aspirin for Primary Prevention** of Cardiovascular Events in Patients with Type 2 **Diabetes:10-year Follow-up (JPAD)** of a Randomized Controlled Trial. Circulation. 2016 Nov 15.
1716. Vilahur G, Gutiérrez M, Casani L, et al. Protective effects of **ticagrelor on myocardial injury** after infarction. Circulation. 2016;134:1708–1719.
1717. Yang M, et al. Evaluation of 16 Genotype-Guided **Warfarin Dosing Algorithms** in 310 Korean Patients Receiving Warfarin Treatment: Poor Prediction Performance in VKORC1 1173C Carriers. Clin Ther. 2016 Nov 22.
1718. Di Nisio M, Porreca E, Candeloro M, De Tursi M, Russi I, Rutjes AWS. **Primary prophylaxis for venous thromboembolism in ambulatory cancer patients receiving chemotherapy**. Cochrane Database of Systematic Reviews 2016, Issue 12. Art. No.: CD008500. In this second update, we confirmed that primary thromboprophylaxis with LMWH significantly reduced the incidence of symptomatic VTE in ambulatory cancer patients treated with chemotherapy. In addition, the uLMWH semuloparin, which is not commercially available, significantly reduced the incidence of symptomatic VTE. The risk of major bleeding associated with LMWH, while not reaching statistical significance, suggest caution and mandate additional studies to determine the risk-to-benefit ratio of LMWH in this setting. Despite the encouraging results of this review, routine prophylaxis in ambulatory cancer patients cannot be recommended before safety issues are adequately addressed. We need additional studies investigating targeted primary prophylaxis in people with specific types or stages of cancer associated with a higher risk of VTE.
1719. Gargiulo G, Windecker S, Vranckx P, et al. A Critical Appraisal of **Aspirin in Secondary Prevention**: Is Less More? Circulation. 2016 Dec 6;134(23):1881-1906.
1720. Gordon LA, Kumar P, Brooks KM, et al. Antiretroviral Boosting Agent **Cobicistat Increases the Pharmacokinetic Exposure and Anticoagulant Effect of Dabigatran** in HIV-Negative Healthy Volunteers. Circulation. 2016 Dec 6;134(23):1909-1911.
1721. Hernandez I, Zhang Y, Brooks MM, et al. **Anticoagulation Use** and Clinical Outcomes **After Major Bleeding on Dabigatran or Warfarin** in Atrial Fibrillation. Stroke. 2016 Dec 1.
1722. Vaduganathan M, Harrington RA, Stone GW, et al. Evaluation of Ischemic and Bleeding Risks Associated With 2 Parenteral Antiplatelet Strategies Comparing **Cangrelor** With **Glycoprotein** IIb/IIIa Inhibitors: An Exploratory Analysis From the **CHAMPION** Trials. JAMA Cardiol. 2016 Nov 30.
1723. Venker BT, Ganti BR, Lin H, et al. Safety and Efficacy of New **Anticoagulants** for the Prevention of Venous Thromboembolism **After Hip and Knee Arthroplasty**: A Meta-Analysis. J Arthroplasty. 2016 Oct 5.
1724. Agus DB, Gaudette É, Goldman DP, Messali A. The **Long-Term Benefits of Increased Aspirin Use** by At-Risk Americans Aged 50 and Older. PLoS One. 2016 Nov 30;11(11):e0166103.
1725. Chan YH, Yeh YH, See LC, et al. **Acute Kidney Injury in Asians** With Atrial Fibrillation Treated With **Dabigatran or Warfarin**. J Am Coll Cardiol. 2016 Nov 29;68(21):2272-2283.
1726. Vaduganathan M, Harrington RA, Stone GW, et al. Evaluation of Ischemic and Bleeding Risks Associated With 2 Parenteral Antiplatelet Strategies Comparing **Cangrelor** With **Glycoprotein IIb/IIIa Inhibitors**: An Exploratory Analysis From the **CHAMPION** Trials. JAMA Cardiol. 2016 Nov 30.
1727. Chai-Adisaksopha C, et al. **Prothrombin complex concentrates versus fresh frozen plasma** for **warfarin reversal**. A systematic review and meta-analysis. Thromb Haemost. 2016 Oct 28;116(5):879-890.
1728. Chan FK, Leung Ki EL, et al. Risks of Bleeding Recurrence and Cardiovascular Events With **Continued Aspirin Use After Lower Gastrointestinal Hemorrhage**. Gastroenterology. 2016 Aug;151(2):271-7.
1729. Gómez-Outes A, Lagunar-Ruíz J, Terleira-Fernández AI, et al. **Causes of Death** in Anticoagulated Patients With **Atrial Fibrillation**. J Am Coll Cardiol. 2016 Dec 13;68(23):2508-2521.
1730. Guo Q, Huang B, Zhao J, et al. Perioperative Pharmacological **Thromboprophylaxis in Patients With Cancer**: A Systematic Review and Meta-analysis. Ann Surg. 2016 Nov 15.
1731. Hiatt WR, Fowkes FG, Heizer G, et al. **Ticagrelor versus Clopidogrel** in Symptomatic **Peripheral Artery Disease**. (**EUCLID**) N Engl J Med. 2016 Nov 13.
1732. Jolly SS, Natarajan MK. **Atrial Fibrillation and PCI - Do We Still Need Aspirin**? N Engl J Med. 2016 Dec 22;375(25):2490-2492.
1733. Kurtul A, Yarlioglues M, et al. Predictive Value of **CHA2DS2-VASC Score** for **Contrast- Induced Nephropathy** after **Percutaneous Coronary Intervention** for Acute Coronary Syndrome. Am J Cardio. 2017.
1734. Lu D-Y, Huang C-C, Huang P-H et al. Usefulness of the **CHADS2 Score** for Prognostic Stratification in Patients with Coronary Artery Disease Having **Coronary Artery Bypass Grafting**. Am J Cardio. 2017.
1735. Mahmoodi BK, Cushman M, Naess IA, et al. Association of traditional cardiovascular risk factors with **venous thromboembolism**: an individual participant data meta-analysis of prospective studies. Circulation. 2017;135:7–16. doi: 10.1161/CIRCULATIONAHA.116.024507. (smoking)
1736. Pan Y, Chen W, Xu Y, et al. **Genetic polymorphisms and clopidogrel** efficacy for acute ischemic stroke or transient ischemic attack: a systematic review and meta-analysis. Circulation. 2017;135:21–33. doi: 10.1161/ CIRCULATIONAHA.116.024913.
1737. Peacock WF, Tamayo S, Patel M, et al. **CHA(2)DS(2)-VASc Scores** and Major **Bleeding** in Patients With Nonvalvular Atrial Fibrillation Who Are Receiving **Rivaroxaban**. Ann Emerg Med. 2016 Nov 29.
1738. Peacock WF, et al. Comparison of the Incidence of Major **Bleeding** with **Rivaroxaban** Use among Nonvalvular Atrial Fibrillation Patients With versus Without **Diabetes** Mellitus. Am J Cardio. 2017.
1739. Steblovnik K, Blinc A, Mijovski MB, et al. **Ticagrelor Versus Clopidogrel** in Comatose **Survivors of Out-of-Hospital Cardiac** Arrest Undergoing Percutaneous Coronary Intervention and Hypothermia: A Randomized Study. Circulation. 2016 Dec 20;134(25):2128-2130.
1740. van Adrichem RA, Nemeth B, Algra A, et al. **Thromboprophylaxis after Knee Arthroscopy and Lower-Leg Casting**. N Engl J Med. 2016 Dec 3.
1741. Achilles A, Mohring A, Dannenberg L, et al. **Dabigatran enhances platelet reactivity** and platelet thrombin receptor expression in patients with atrial fibrillation. J Thromb Haemost. 2016 Dec 19.
1742. Barnes GD, Kaatz S, et al. **Discontinuation of Warfarin** Therapy for Patients With Atrial Fibrillation: The Michigan Anticoagulation **Quality Improvement** Initiative Experience. JAMA Cardiol. 2017 Jan 4.

1743. Monaco L, Biagi C, Conti V, et al. **Safety profile of the direct oral anticoagulants**: an analysis of the **WHO database** of adverse drug reactions. Br J Clin Pharmacol. 2017 Jan 10.
1744. Stanley AJ, Laine L, Dalton HR, et al. Comparison of **risk scoring systems for patients presenting with upper gastrointestinal bleeding**: international multicentre prospective study. BMJ. 2017 Jan 4;356:i6432.
1745. Abraham NS et al. **Gastrointestinal safety of direct oral anticoagulants**: A large population-based study.Gastroenterology 2016 Dec 31.
1746. Antoniou T, Macdonald EM, Yao Z, et al. Association between **statin use and ischemic stroke or major hemorrhage in patients taking dabigatran** for atrial fibrillation. CMAJ. Online. Nov 21, 2016.
1747. Ovbiagele B, Wang J, Johnston SC, et al. Effect of **Clopidogrel by Smoking Status** on Secondary Stroke Prevention. Circulation. 2017 Jan 17;135(3):315-316.
1748. Bassand J-P., et al. Two-year outcomes of patients with **newly diagnosed atrial fibrillation**: results from **GARFIELD-AF.** Eur Heart J. 2016; 37: 2882–2889. doi:10.1093/eurheartj/ehw233.
1749. Benjamin EJ, et al; **Heart Disease and Stroke Statistics-2017** Update: A Report From the American Heart Association. Circulation. 2017 Jan 25.
1750. Camm A.J., Amarenco P., et al. **XANTUS**: a real-world, prospective, observational study of patients treated with **rivaroxaban** for **stroke prevention in atrial fibrillation**. Eur Heart J. 2016; 37: 1145–1153.
1751. Chaturvedi S, Ofner S, Baye F, et al. Have clinicians adopted the **use of brain MRI for patients with TIA and minor stroke**? Neurology. 2017 Jan 17;88(3):237-244.
1752. Coleman C.I., Antz M., et al. **Real-world evidence** of stroke prevention in patients with nonvalvular atrial fibrillation in the United States: the **REVISIT-US** study. Curr Med Res Opin. 2016;32: 2047–2053.
1753. Coleman C.I., Antz M., Ehlken B., Evers T. **REal-LIfe** Evidence of stroke prevention in patients with atrial Fibrillation — The **RELIEF** study. Int J Cardiol. 2016; 203: 882–884.
1754. Kröll D, Stirnimann G, Vogt A, et al. Pharmacokinetics and pharmacodynamics of single doses of **Rivaroxaban** in **obese** patients before and after bariatric surgery. Br J Clin Pharmacol. 2017 Jan 25.
1755. Link MS, Giugliano RP, Ruff CR, et al. **Stroke and mortality** risk in patients with various **patterns of atrial fibrillation**. Results from the **ENGAGE AF-TIMI 48** Trial (Effective Anticoagulation With Factor Xa Next Generation in Atrial Fibrillation–Thrombolysis in Myocardial Infarction 48). *Circ Arrhythmia Electrophysiol* 2017.
1756. Yu WY, Bhutani T, Kornik R, et al. **Warfarin-Associated Nonuremic Calciphylaxis**. JAMA Dermatol. 2017 Jan 11.
1757. Irish AB, et al. Effect of **Fish Oil Supplementation and Aspirin** Use on **Arteriovenous Fistula Failure** in Patients Requiring Hemodialysis: A Randomized Clinical Trial. JAMA Intern Med. 2017 Feb 1;177(2):184-193.
1758. Link MS, Giugliano RP, Ruff CT, et al. Stroke and Mortality Risk in Patients With **Various Patterns of Atrial Fibrillation**: Results From the **ENGAGE AF-TIMI 48** Trial (Effective Anticoagulation With Factor Xa Next Generation in Atrial Fibrillation-Thrombolysis in Myocardial Infarction 48). Circ Arrhythm Electrophysiol. 2017 Jan;10(1).
1759. Palmerini T, Della Riva D, Benedetto U, et al. **Three, six, or twelve months of dual antiplatelet therapy after DES implantation** in patients with or without acute coronary syndromes: an individual patient data pairwise and network meta-analysis of six randomized trials and 11 473 patients. Eur Heart J. 2017 Jan 21
1760. Plitt A, McGuire DK, Giugliano RP. **Atrial Fibrillation, Type 2 Diabetes, and Non-Vitamin K Antagonist Oral Anticoagulants**: A Review. JAMA Cardiol. 2017 Jan 25.
1761. Aggarwal A. **Rivaraoxaban** dosing is based on more than just pharmacokinetic properties. BMJ. 2017 Feb 6;356:j608.
1762. Dasenbrock HH, Robertson FC, Vaitkevicius H, et al. Timing of **Decompressive Hemicraniectomy for Stroke**: A Nationwide Inpatient Sample Analysis. Stroke. 2017 Jan 20.
1763. Gaglia Jr MA, Lipinski MJ, Lhermusier T, et al. Comparison Platelet Reactivity in **Black versus White** Patients With Acute Coronary Syndromes Following Treatment with **Ticagrelor**. Am J Cardiol. 2017.
1764. Huffman MD, Malaisrie SC, Karmali KN. **Concomitant Atrial Fibrillation Surgery for People Undergoing Cardiac Surgery**. JAMA Cardiol. 2017 Feb 8.
1765. Lip GY. **Stroke prevention in Atrial Fibrillation**. Eur Heart J. 2017 Jan 1;38(1):4-5.
1766. Poli D, Antonucci E, Pengo V, et al. Comparison of **HAS-BLED versus CHADS2 and CHA2DS2VASC** Stroke and Bleeding Scores in Patients with Atrial Fibrillation. AM J Cardiol. 2017.
1767. Raffel KE, Goldschlager N. Abnormal Electrocardiogram in a Woman With **Atrial Fibrillation** and Recent Care Transition. JAMA Intern Med. 2017 Feb 13.
1768. Raval AN, Cigarroa JE, Chung MK, et al. Management of Patients on **Non-Vitamin K Antagonist Oral Anticoagulants** in the Acute Care and **Periprocedural** Setting: A Scientific Statement From the American Heart Association. Circulation. 2017 Feb 6.
1769. Siontis KC, Yao X, Gersh BJ, et al. **Direct Oral Anticoagulants** in Patients With **Atrial Fibrillation and Valvular Heart Disease Other Than Significant Mitral Stenosis and Mechanical Valves**: A Meta-Analysis. Circulation. 2017 Feb 14;135(7):714-716.
1770. Carnicelli AP, et al; **ENGAGE AF-TIMI 48** Investigators.. **Edoxaban** for the Prevention of Thromboembolism in Patients with **AtrialFibrillation** and **Bioprosthetic Valves**. Circulation. 2017 Feb 16.
1771. Gieling E, van den Ham HA, et al. Risk of **major bleeding and stroke associated with the use of VKAs, NOACs and aspirin** in patients with atrial fibrillation: a cohort study. Br J Clin Pharmacol. 2017 Feb 16.
1772. Nene RV, Coyne CJ. Management of **Cancer-Associated Venous Thromboembolism** in the Emergency Department. Ann Emerg Med. 2017 Feb 3.
1773. Norris S, Ramael S, Ikushima I, et al. Evaluation of the immunogenicity of the **dabigatran reversal agent idarucizumab** during phase I studies. Br J Clin Pharmacol. 2017 Feb 23.
1774. Sjaarda LA, et al. **Preconception low-dose aspirin** restores diminished **pregnancy** and live birth rates in women with low grade inflammation: a secondary analysis of a randomized trial. J Clin Endocrinol. Metab. 2017. Online.
1775. Xu Y, Schulman S, Dowlatshahi D, et al; Bleeding Effected by Direct Oral Anticoagulants (**BLED-AC**) Study Group.. **Direct oral anticoagulant- or warfarin-related major bleeding**: characteristics, reversal strategies and outcomes from a multi-center observational study. Chest. 2017 Feb 17.
1776. Amarenco P, Albers GW, Denison H, et al. Efficacy and safety of ticagrelor versus aspirin in acute stroke or transient ischaemic attack of atherosclerotic origin: a subgroup analysis of SOCRATES, a randomised, double-blind, controlled trial. Lancet Neurol. 2017 Feb 23.
1777. Gaist D, García Rodríguez LA, Hellfritzsch M, et al. Association of **Antithrombotic Drug Use With Subdural Hematoma Risk**. JAMA. 2017 Feb 28;317(8):836-846.
1778. Lang C, Seyfang L, Ferrari J, et al. Do **Women** With Atrial Fibrillation Experience More Severe **Strokes**? Results From the Austrian Stroke Unit Registry. Stroke. 2017 Mar;48(3):778-780.
1779. Lauw MN, Eikelboom JW, Coppens M, et al. Effects of **dabigatran** according to **age** in atrial fibrillation. Heart. 2017 Feb 17.
1780. Moffitt P, Lane DA, Park H, et al. **Thromboprophylaxis** in atrial fibrillation and association with **cognitive decline**: systematic review. Age Ageing. 2016 Nov;45(6):767-775.
1781. Nielsen PB, Skjøth F, Søgaard M, et al. Effectiveness and safety of reduced dose non-**vitamin K antagonist** oral anticoagulants and **warfarin** in patients with atrial fibrillation: propensity weighted nationwide cohort study. BMJ. 2017 Feb 10;356:j510.
1782. Wilbur J, Shian B. **Deep Venous Thrombosis and Pulmonary Embolism**: Current Therapy. Am Fam Physician. 2017;95(5):295-302.
1783. Bhatt DL, Grosser T, Dong JF, Logan D, et al. **Enteric Coating and Aspirin Nonresponsiveness in Patients With Type 2 Diabetes** Mellitus. J Am Coll Cardiol. 2017 Feb 14;69(6):603-612.
1784. Nielsen PB, Larsen TB, Skjoth F, et al. Outcomes Associated With **Resuming Warfarin Treatment After Hemorrhagic Stroke or Traumatic Intracranial Hemorrhage** in Patients With Atrial Fibrillation. JAMA Intern Med. 2017 Feb 20.
1785. Roquer J, Vivanco Hidalgo RM, Ois A, et al. **Antithrombotic pretreatment increases very-early mortality in primary intracerebral hemorrhage**. Neurology. 2017 Feb 28;88(9):885-891.
1786. Costa F, van Klaveren D, James S, et al, for the PRECISE-DAPT Study Investigators. Derivation and validation of the predicting **bleeding** complications in patients **undergoing stent implantation** and **subsequent dual antiplatelet therapy** (**PRECISE-DAPT**) **score**: a pooled analysis of individual-patient datasets from clinical trials. Lancet 2017; 389: 1025–34.
1787. Elalamy I, Mahé I, Ageno W, Meyer G. Long-term treatment of **cancer-associated thrombosis**: the choice of the optimal anticoagulant. J Thromb Haemost. 2017 Feb 21.
1788. Lee MS, Shlofmitz E, Haag E, et al. **Optimal Same-Day Platelet Inhibition** in Patients Receiving **Drug-Eluting Stents With or Without Previous Maintenance Thienopyridine** Therapy: from the Evaluation of Platelet Inhibition in Patients Having A VerifyNow Assay (**EPIPHANY**) Trial. Am J Cardiol. 2017 Jan 5.
1789. Lindner SM, Fordyce CB, Hellkamp AS, et al. Treatment Consistency Across Levels of **Baseline Renal Function** With **Rivaroxaban** or Warfarin: A **ROCKET AF** (Rivaroxaban Once-Daily, Oral, Direct Factor Xa Inhibition Compared With Vitamin K Antagonism for Prevention of Stroke and Embolism Trial in Atrial Fibrillation) Analysis. Circulation. 2017 Mar 7;135(10):1001-1003
1790. Malagù M, Trevisan F, Scalone A, et al. Frequency of "Pocket" **Hematoma** in Patients Receiving **Vitamin K Antagonist and Antiplatelet Therapy** at the Time of **Pacemaker or Cardioverter Defibrillator Implantation** (from the **POCKET** Study). Am J Cardiol. 2017 Jan 6
1791. Mangieri A, Jabbour RJ, et al. **Single-Antiplatelet Therapy** in Patients with **Contraindication to Dual-Antiplatelet Therapy** After **Transcatheter Aortic Valve Implantation**. Am J Cardiol. 2017 Jan 6.

1792. Roberge S, Nicolaides K, et al. The role of **aspirin dose** on the prevention of **preeclampsia and fetal growth restriction**: systematic review and meta-analysis. Am J Obstet Gynecol. 2017 Feb;216(2):110-120.e6.
1793. Brekelmans MP, Scheres LJ, Bleker SM, et al. **Abnormal vaginal bleeding** in women with venous thromboembolism treated with **apixaban or warfarin**. Thromb Haemost. 2017 Feb 9.
1794. Cangemi DJ et al. A comparison of the rate of **gastrointestinal bleeding** in patients taking **non-vitamin K antagonist oral anticoagulants or warfarin**. Am J Gastroenterol 2017 Feb 28;
1795. Chakravarty T, Søndergaard L, Friedman J, et al, on behalf of the **RESOLVE** and **SAVORY** Investigators. **Subclinical leaflet thrombosis** in surgical and **transcatheter bioprosthetic aortic valves**: an observational study. Lancet 2017; online Mar 19.
1796. Meher S, et al. **Antiplatelet therapy before or after 16 weeks` gestation for preventing preeclampsia**: an individual participant data meta-analysis. Am J Obstet Gynecol. 2017 Feb;216(2):121-128.e2.
1797. Ohman EM, Roe MT, Steg PG, et al. Clinically **significant bleeding with low-dose rivaroxaban versus aspirin**, in addition to P2Y12 inhibition, in acute coronary syndromes (**GEMINI-ACS-1**): a double-blind, multicentre, randomised trial. Lancet 2017; online Mar 18.
1798. Sterne JA, Bodalia PN, Bryden PA, et al. **Oral anticoagulants for primary prevention, treatment and secondary prevention of venous thromboembolic disease, and for prevention of stroke in atrial fibrillation**: systematic review, network meta-analysis and cost-effectiveness analysis. Health Technol Assess. 2017 Mar;21(9):1-386. NOACs have advantages over warfarin in patients with AF, but we found no strong evidence that they should replace warfarin or LMWH in primary prevention, treatment or secondary prevention of VTE.
1799. Weitz JI, Lensing AWA, Prins MH, et al. **Rivaroxaban or aspirin for extended treatment of venous thromboembolism**. (**Einstein Choice**) N Eng J Med 2017; DOI:10.1056/NEJMoa1700518.
1800. Wilson SJ, Newby DE, Dawson D, Irving J, Berry C. **Duration of dual antiplatelet therapy in acute coronary syndrome**. Heart. 2017 Mar 1.
1801. Blin P, et al. Outcomes in **Post-Myocardial Infarction patients** similar to those of the **PEGASUS-TIMI 54** trial: a cohort study in the French national claims database. Br J Clin Pharmacol. 2017 Mar 26.
1802. Calkins H, Willems S, Gerstenfeld EP, et al. **Uninterrupted Dabigatran versus Warfarin** for **Ablation** in Atrial Fibrillation. N Engl J Med. 2017 Mar 19.
1803. Cowper PA, Sheng S, Lopes RD, et al. **Economic analysis** of **apixaban** therapy for patients with atrial fibrillation from a US perspective. *JAMA Cardiol* 2017; DOI:10.1001/jamacardio.2017.0065.
1804. De Caterina R, Renda G, Carnicelli AP, et al. **Valvular Heart Disease** Patients on **Edoxaban or Warfarin** in the **ENGAGE AF-TIMI 48 Trial**. J Am Coll Cardiol. 2017 Mar 21;69(11):1372-1382.
1805. Dehmer SP, et al. Aspirin for Primary **Prevention of Cardiovascular Disease and Colorectal Cancer**: A Decision Analysis- U.S. Preventive Services Task Force. Ann Intern Med. 2016 Jun 21;164(12):777-86.
1806. Jackevicius CA, Tsadok MA, Essebag V, et al. Early **non-persistence with dabigatran and rivaroxaban** in patients with atrial fibrillation. Heart. 2017 Mar 12.
1807. Korn D, Sean McMurtry M, George-Phillips K, et al. **Critical international normalized ratio results after hours**: To call or not to call? Can Fam Physician. 2017 Mar;63(3):e170-e176
1808. Kottmaier M, Bourier F, et al. Safety and Feasibility of **Subcutaneous Purse-String Suture** of the Femoral Vein after electrophysiological procedures on Uninterrupted Oral Anticoagulation. Am J Cardio. 2017.
1809. Lau WC, Chan EW, et al. Association Between **Dabigatran vs Warfarin** and **Risk of Osteoporotic Fractures** Among Patients With Nonvalvular Atrial Fibrillation. JAMA. 2017 Mar 21;317(11):1151-1158.
1810. Nishimura RA, Otto CM, Bonow RO, et al. 2017 **AHA/ACC Focused Update** of the 2014 AHA/ACC Guideline for the Management of Patients With **Valvular Heart Disease**: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. Circulation. 2017 Mar 15.
1811. Renda G, Ricci F, Giugliano RP, et al. **Non-Vitamin K Antagonist Oral Anticoagulants in Patients With Atrial Fibrillation and Valvular Heart Disease**. J Am Coll Cardiol. 2017 Mar 21;69(11):1363-1371.
1812. Scott MJ, Veitch A, Thachil J. **Reintroduction of anti-thrombotic therapy after a gastrointestinal haemorrhage**: if and when? Br J Haematol. 2017 Mar 8.
1813. Stolk LM, de Vries F, et al. **Risk of myocardial infarction** in patients with atrial fibrillation using **vitamin K antagonists, aspirin or direct acting oral anticoagulants**. Br J Clin Pharmacol. 2017 Mar 22.
1814. Xian Y, et al. Association **Preceding Antithrombotic Treatment With Acute Ischemic Stroke Severity** & In-Hospital Outcomes Among Patients With Atrial Fibrillation. JAMA. 2017Mar14;317(10):1057-1067.
1815. Xian Y, et al. Use of **Intravenous Recombinant Tissue Plasminogen Activator** in Patients With Acute Ischemic Stroke Who Take Non-Vitamin K Antagonist Oral Anticoagulants Before Stroke. Circulation. 2017 Mar 14;135(11):1024-1035.
1816. Chan W, Drummond A, Kelly M. Deep vein thrombosis in a transgender woman. CMAJ. 2017 Apr 3;189(13):E502-E504.
1817. De Luca L, D'Ascenzo F, Musumeci G, et al. Incidence and Outcome of **Switching of Oral Platelet P2Y12 Receptor Inhibitors in Patients with Acute Coronary Syndromes** Undergoing Percutaneous Coronary Intervention: The **SCOPE** Registry. EuroIntervention. 2017 Apr 4.
1818. Eikelboom JW, Quinlan DJ, Hirsh J, et al. **Laboratory Monitoring of Non-Vitamin K Antagonist Oral Anticoagulant Use** in Patients With Atrial Fibrillation: A Review. JAMA Cardiol. 2017 Mar 29.
1819. Larsen TB, Skjøth F, Kjældgaard JN, et al. Effectiveness and safety of **rivaroxaban** and **warfarin** in patients with **unprovoked venous thromboembolism**: a propensity-matched nationwide cohort study Lancet Haematol 2017; online April 11.
1820. Lau ES, Braunwald E, Murphy SA, et al. **Potent P2Y12 Inhibitors in Men Versus Women**: A Collaborative Meta-Analysis of Randomized Trials. J Am Coll Cardiol. 2017 Mar 28;69(12):1549-1559.
1821. Rodger MA, et al. Validating **HERDOO2 rule to guide treatment duration for women with unprovoked venous thrombosis**: multinational prospective cohort management study. BMJ. 2017 Mar 17;356:j1065.
1822. Loo SY, Dell'Aniello S, Huiart L, et al. **Trends in the prescription of novel oral anticoagulants in UK** primary care. Br J Clin Pharmacol. 2017 Apr 7.
1823. Murthy SB, Gupta A, Merkler AE, et al. **Restarting Anticoagulant Therapy After Intracranial Hemorrhage**: A Systematic Review and Meta-Analysis. Stroke. 2017 Apr 17
1824. Reiffel JA. **Time in the Therapeutic Range** for Patients Taking Warfarin in Clinical Trials: Useful, but Also Misleading, Misused, and Overinterpreted. Circulation. 2017 Apr 18;135(16):1475-1477.
1825. Shah R, Rashid A, Hwang I, et al. Meta-Analysis of the Relative Efficacy and Safety of Oral **P2Y12 Inhibitors in Patients With Acute Coronary Syndrome**. Am J Cardiol. 2017 Mar 16.
1826. Waljee AK, Rogers MA, Lin P, et al. Short term use of **oral corticosteroids and related harms** (eg. VTE) among adults in the United States: population based cohort study. BMJ. 2017 Apr 12;357:j1415.
1827. Klok FA, Barco S, Konstantinides SV. External validation of the **VTE-BLEED score** for predicting major bleeding in stable anticoagulated patients with venous thromboembolism. Thromb Haemost. 2017 Mar 9.
1828. Leader A, Zelikson-Saporta R, Pereg D, et al. The Effect of **Combined Aspirin and Clopidogrel** Treatment on **Cancer** Incidence. Am J Med. 2017 Feb 14.
1829. Steinberg BA, Simon DN, Thomas L, et al. Management of Major **Bleeding in Patients With Atrial Fibrillation** Treated With Non-Vitamin K Antagonist Oral Anticoagulants Compared With Warfarin in Clinical Practice (from Phase II of the Outcomes Registry for Better Informed Treatment of Atrial Fibrillation [**ORBIT-AF II**]). Am J Cardiol. 2017 Mar 28.
1830. Alfredsson J, Neely B, Neely ML, et al. Predicting the **risk of bleeding during dual antiplatelet therapy after acute coronary syndromes**. Heart. 2017 Apr 5.
1831. Bahit MC, Lopes RD, Wojdyla DM, et al. **Non-major bleeding with apixaban versus warfarin** in patients with atrial fibrillation. (**Aristotle**) Heart. 2017 Apr;103(8):623-628.
1832. Wilson D, Seiffge DJ, Traenka C, et al. Outcome of **intracerebral hemorrhage** associated **with different oral anticoagulants**. Neurology 2017;88:1693–1700.
1833. Dallaire F, Fortier-Morissette Z, Blais S, et al. **Aspririn Dose** and Prevention of Coronary Abnormalities in **Kawasaki** Disease. Pediatrics. 2017;139(6):e20170098
1834. Nathan S, Goodarzi Z, Jette N, Gallagher C, Holroyd-Leduc J. **Anticoagulant and antiplatelet** use in seniors with **chronic subdural hematoma**: systematic review. Neurology 2017;88:1889–1893.
1835. Ofek F, Bar Chaim S, Kronenfeld N, et al. **International Normalized Ratio** Is Significantly Elevated With **Rivaroxaban** and **Apixaban** DrugTherapies: A Retrospective Study. Clin Ther. 2017 May 2
1836. Pelletier-Galarneau M, et al. Randomized Trial Comparing the Effects of **Ticagrelor Versus Clopidogrel** on Myocardial Perfusion in Patients With Coronary Artery Disease. J Am Heart Assoc. 2017 May 2;6(5).
1837. Phan K, Moore JM, Griessenauer CJ, et al. **Aspirin and Risk of Subarachnoid Hemorrhage**: Systematic Review and Meta-Analysis. Stroke. 2017 May;48(5):1210-1217.
1838. Schulman S. How I **treat recurrent venous thromboembolism** in patients on anticoagulant therapy. Blood. 2017 May 8.
1839. Secemsky EA, Yeh RW, et al. **Mortality** Following Cardiovascular and Bleeding Events Occurring **Beyond 1 Year After Coronary Stenting**: A Secondary Analysis of the Dual Antiplatelet Therapy (**DAPT**) Study. JAMA Cardiol. 2017 Mar 15.
1840. Valgimigli M, Gargiulo G. Deciding on the **Duration of Dual Antiplatelet Therapy**-When the Choice Between 2 Evils Is Still Evil. JAMA Cardiol. 2017 Mar 15.
1841. Zhao M, Wu G, Li Y, et al. Meta-analysis of **folic acid** efficacy trials in **stroke prevention**: Insight into effect modifiers. Neurology. 2017 May 9;88(19):1830-1838.
1842. Cuisset T, et al. Benefit of **switching dual antiplatelet therapy after acute coronary syndrome: TOPIC** (timing of platelet inhibition after acute coronary syndrome) randomized. Eur Heart J. 2017 May 16.
1843. Emilsson L, Holme Ø, et al. Systematic review with meta-analysis: the **comparative effectiveness of aspirin vs. screening for colorectal cancer** prevention. Aliment Pharmacol Ther. 2017 Jan;45(2):193-204.
1844. Pan Y, Jing J, Chen W, et al. Risks and benefits of **clopidogrel-aspirin in minor stroke or TIA**: Time course analysis of **CHANCE**. Neurology. 2017 May 16;88(20):1906-1911.

1845. Stefanescu Schmidt AC, et al; **DAPT** Investigators. **Myocardial Infarction Risk After Discontinuation of Thienopyridine Therapy** in the Randomized DAPT Study (Dual Antiplatelet Therapy). Circulation. 2017 May 2;135(18):1720-1732.
1842. van der Hulle T, Cheung WY, Kooij S, et al. **Simplified diagnostic management of suspected pulmonary embolism** (the **YEARS** study): a prospective, multicentre, cohort study. Lancet 2017; online May 23.
1843. FDA May/17 AstraZeneca is notifying physicians and consumers that it is **voluntarily recalling** one lot of professional (physician) sample bottles containing eight tablets of **Brilinta (ticagrelor)** 90mg tablets as a precautionary measure. This voluntary recall follows a report that a professional sample bottle containing eight tablets of Brilinta 90mg also contained another medicine called Zurampic (lesinurad) 200 mg tablets which is also manufactured by AstraZeneca.
1844. Jain A, Cifu AS. **Antithrombotic Therapy for Venous Thromboembolic Disease**. JAMA. 2017 May 16;317(19):2008-2009.
1845. Marzec LN, Wang J, Shah ND, et al. Influence of **Direct Oral Anticoagulants on Rates of Oral Anticoagulation for Atrial Fibrillation**. J Am Coll Cardiol. 2017 May 23;69(20):2475-2484.
1846. Miller EO, Krishnamoorthy VK, Ling FSK, et al. A man with chest pain and acute ST elevations on electrocardiogram. (**Coronary artery aneurysms**) BMJ. 2017 May 18;357:j2198
1847. Bhatt DL, Bonaca MP, et al. Reduction in Ischemic Events With **Ticagrelor** in **Diabetic** Patients With Prior Myocardial Infarction in **PEGASUS-TIMI 54.** J Am Coll Cardiol. 2016 Jun 14;67(23):2732-40.
1848. Burnett A, Siegal D, Crowther M. **Specific antidotes for bleeding associated with direct oral anticoagulants**. BMJ. 2017 May 25;357:j2216.
1849. Columbo JA, Lambour AJ, et al. A Meta-analysis of the Impact of **Aspirin, Clopidogrel, and Dual Antiplatelet Therapy on Bleeding Complications** in **Noncardiac Surgery**. Ann Surg. 2017 May 1.
1850. Khan F, Vaillancourt C, Bourjeily G. **Diagnosis and management of deep vein thrombosis in pregnancy**. BMJ. 2017 May 31;357:j2344.
1851. Steinberg ZL, Dominguez-Islas CP, Otto CM, et al. Maternal and fetal outcomes of **anticoagulation in pregnant women with mechanical heart valves**. J Am Coll Cardio 2017;69: 2681–91.
1852. Cuisset T, et al. Benefit of **switching dual antiplatelet therapy after acute coronary syndrome**: **TOPIC** (timing of platelet inhibition after acute coronary syndrome) randomized study. Eur Heart J. 2017 May 16.
1853. Golive A, May HT, et al. The Population-Based Long-Term Impact of **Anticoagulant and Antiplatelet Therapies in Low-Risk Patients With Atrial Fibrillation**. Am J Cardiol. 2017 Jul 1;120(1):75-82.
1854. Leentjens J, Peters M, et al. **Initial anticoagulation in patients with pulmonary embolism**: thrombolysis, unfractionated heparin, LMWH, fondaparinux, or DOACs? Br J Clin Pharmacol. 2017 Jun 7
1855. Melkonian M, et al. **Bleeding risk of antiplatelet drugs compared with oral anticoagulants** in older patients with atrial fibrillation: a systematic review and meta-analysis. J Thromb Haemost. 2017 Apr 10.
1856. Pennlert J, Overholser R, Asplund K, et al. **Optimal Timing of Anticoagulant Treatment After Intracerebral Hemorrhage** in Patients With Atrial Fibrillation. Stroke. 2017 Feb;48(2):314-320.
1857. Piccolo R, et al. Use of the **dual-antiplatelet therapy score** to guide treatment duration after percutaneous coronary intervention. Ann Intern Med. [Epub ahead of print 13 June 2017]. doi:10.7326/M16-2389
1858. Yao X, Shah ND, et al. **Non-Vitamin K Antagonist Oral Anticoagulant Dosing** in Patients With Atrial Fibrillation and **Renal Dysfunction**. J Am Coll Cardiol. 2017 Jun 13;69(23):2779-2790.
1859. Alonso A, MacLehose RF, Chen LY, Bet al. Prospective study of **oral anticoagulants and risk of liver injury** in patients with atrial fibrillation. Heart. 2017 Jun;103(11):834-839.
1860. Choi KN, Jin HY, Shin HC, et al. Comparison of the **Antiplatelet Effects of Once and Twice Daily Low-Dose Ticagrelor and Clopidogrel** After Percutaneous Coronary Intervention. Am J Cardiol. 2017 Jul 15;120(2):201-206.
1861. Li L,Geraghty OC, Mehta Z, Rothwell PM, on behalf of the Oxford Vascular Study. Age-specific risks, severity, time course, and outcome of **bleeding on long-term antiplatelet (ASA)** treatment after vascular events: a population-based cohort study. Lancet 2017; online June 5. (consider using PPI in older secondary CV prevention patients on aspirin)
1862. Hess CN, Norgren L, Ansel GM, et al. A Structured Review of **Antithrombotic Therapy in Peripheral Artery Disease** With a Focus on Revascularization: A TASC (InterSociety Consensus for the Management of Peripheral Artery Disease) Initiative. Circulation. 2017 Jun 20;135(25):2534-2555.
1863. Sun Q, et al. The Efficacy and Safety of **3 Types ofInterventions for Stroke Prevention** in Patients With Cardiovascular and Cerebrovascular Diseases: A Network Meta-analysis. Clin Ther. 2017 Jun 10.
1864. Chu DK, et al. Benefits and risks of **antithrombotic therapy in essential thrombocythemia**. A systematic review. Ann Intern Med. [Epub ahead of print 27 June 2017] doi:10.7326/M17-0284
1865. Lip GYH, Skjøth F, Nielsen PB, et al. Effectiveness and Safety of Standard-Dose **Nonvitamin K Antagonist Oral Anticoagulants and Warfarin** Among Patients With Atrial Fibrillation With a **Single Stroke Risk Factor:** A Nationwide Cohort Study. JAMA Cardiol. 2017 Jun 14.
1866. Rolnik DL, Wright D, Poon LC, et al. **Aspirin versus Placebo in Pregnancies** at High Risk for **Preterm Preeclampsia**. N Engl J Med. 2017 Jun 28.
1867. Warkentin TE, Pai M, Linkins LA. **Direct oral anticoagulants for treatment of HIT**: update of Hamilton experience and literature review. Blood. 2017 Jun 23.
1868. Badreldin HA, et al. Safety and Tolerability of **Transitioning from Cangrelor to Ticagrelor** in Patients Who Underwent Percutaneous Coronary Intervention. Am J Cardiol. 2017 Aug 1;120(3):359-361
1869. Baker AL, Vanderpluym C, Gauvreau KA, et al. Safety and Efficacy of **Warfarin Therapy in Kawasaki Disease**. J Pediatr. 2017 May 25.
1870. Black-Maier E, Piccini JP. Oral **anticoagulation in end-stage renal disease and atrial fibrillation**: is it time to just say no to drugs? Heart. 2017 Jun;103(11):807-808
1871. Childers CP, et al **Antiplatelet Therapy in Patients With Coronary Stents Undergoing Elective Noncardiac Surgery**: **Continue, Stop, or Something in Between**? JAMA. 2017 Jul 11;318(2):120-121.
1872. Gibson CM, Korjian S, Chi G, et al; **APEX** Investigators. Comparison of Fatal or Irreversible Events With Extended-Duration **Betrixaban** Versus Standard Dose Enoxaparin in Acutely Ill Medical Patients: An APEX Trial Substudy. J Am Heart Assoc. 2017 Jul 11;6(7).
1873. Lettino M, Leonardi S, De Maria E, et al. **Antiplatelet and antithrombotic treatment for secondary prevention** in ischaemic heart disease. Eur J Prev Cardiol. 2017 Jun;24(3_suppl):61-70.
1874. Pollack CV Jr, Reilly PA, van Ryn J, et al. **Idarucizumab for Dabigatran Reversal** - Full Cohort Analysis. N Engl J Med. 2017 Jul 11.
1875. Pottie K, Premji K, Cheskey SL. **Critical elevation of international normalized ratio** in an elderly woman using a **natural health product**. Can Fam Physician. 2017 Jul;63(7):536-537.
1876. Scott MJ, Veitch A, Thachil J. **Reintroduction of anti-thrombotic therapy after a gastrointestinal haemorrhage**: if and when? Br J Haematol. 2017 Mar 8.
1877. Shah RR, Pillai A, Schafer P, et al. Safety and Efficacy of **Uninterrupted Apixaban Therapy Versus Warfarin During Atrial Fibrillation Ablation**. Am J Cardiol. 2017 Aug 1;120(3):404-407
1878. Sun MT, Wood MK, Chan W, et al. Risk of **Intraocular Bleeding With Novel Oral Anticoagulants Compared With Warfarin**: A Systematic Review and Meta-analysis. JAMA Ophthalmol. 2017 Jul 6.
1879. Tai C, Wu H, San C, et al. Management of **Supratherapeutic International Normalized Ratio** without Bleeding after Warfarin Use: An Evaluation of **Vitamin K Administration** (**SUPRA-WAR-K Study**). Can J Hosp Pharm. 2017 May-Jun;70(3):207-214.
1880. Tseng E, Selby R. **Testing for heritable thrombophilia** in acute venous thromboembolism. CMAJ. 2017 Jul 4;189(26):E891.
1881. Ardoino I, Rossio R, et al. Appropriateness of **antiplatelet therapy for primary and secondary cardio- and cerebrovascular prevention** in acutely hospitalized older people. Br J Clin Pharmacol. 2017 Jul 19.
1882. Loffredo L, Pastori D, et al. Effects of **Anticoagulants in Patients With Cirrhosis and Portal Vein Thrombosis**: A Systematic Review and Meta-analysis. Gastroenterology. 2017 Aug;153(2):480-487.e1.
1883. Moñux G, Zamorano-León JJ, Marqués P, et al. Fxa inhibition by **Rivaroxaban** modifies mechanisms associated with the pathogenesis of human **abdominal aortic aneurysms**. Br J Clin Pharmacol. 2017 Jul 23.
1884. Patel JP, Woolcombe SA, Patel RK, et al. **Managing direct oral anticoagulants in patients undergoing dentoalveolar surgery**. Br Dent J. 2017 Feb 24;222(4):245-249.
1885. Ashburner JM, Singer DE, Lubitz SA, et al. Changes in **Use of Anticoagulation in Patients With Atrial Fibrillation Within a Primary Care** Network Associated With the Introduction of Direct Oral Anticoagulants. Am J Cardiol. 2017 Jun 15
1886. Bavishi C, Trivedi V, Singh M, et al. Duration of Dual Antiplatelet Therapy in Patients with an Acute Coronary Syndrome Undergoing Percutaneous Coronary Intervention. Am J Med. 2017 Jun 13.
1887. Chu DK, Hillis CM, Leong DP, et al. Benefits and Risks of **Antithrombotic Therapy** in **Essential Thrombocythemia**: A Systematic Review. Ann Intern Med. 2017 Aug 1;167(3):170-180.
1888. D'Souza R, Ostro J, Shah PS, et al. **Anticoagulation for pregnant women** with **mechanical heart valves**: a systematic review and meta-analysis. European Heart J. 2017;38:1509-1516.
1889. Hilkens NA;Algra A;Diener HC;et al. Predicting major bleeding in patients with noncardioembolic stroke on antiplatelets: **S2TOP-BLEED**. Neurology. 2017 Aug 2.
1890. Korompoki E, Filippidis FT, Nielsen PB, et al. Long-term antithrombotic treatment in **intracranial hemorrhage survivors** with atrial fibrillation. Neurology. 2017 Jul 19.
1891. Lavi S, Alemayehu M, Puka K, et al. Association Between Administration of **Ticagrelor and Microvascular Endothelial Function**. JAMA Cardiol. 2017 Jul 26
1892. Lip GYH, Al-Saady N, Jin J, et al. Anticoagulation Control in Warfarin-Treated Patients Undergoing **Cardioversion of Atrial Fibrillation** (from the **Edoxaban** Versus Enoxaparin-Warfarin in Patients Undergoing Cardioversion of Atrial Fibrillation Trial). Am J Cardiol. 2017 Jun 15.
1893. Sakulchit T, Benseler SM, Goldman RD. **Acetylsalicylic acid** for children with **Kawasaki disease**. Canadian Family Physician. 2017 August;63:607-609.

1894. Teerlink JR, Qian M, Bello NA, et al. **Aspirin** Does Not Increase **Heart Failure** Events in Heart Failure Patients: From the WARCEF Trial. JACC Heart Fail. 2017 Aug;5(8):603-610.
1895. van Es N, Le Gal G, et al. **Screening for occult cancer in patients** with unprovoked **venous thromboembolism**. A systematic review and meta-analysis of individual patient data. Ann Intern Med. 2017.
1896. Cannon CP et al. **Dual antithrombotic therapy with dabigatran** after PCI in atrial fibrillation. (**RE-DUAL**) *N Engl J Med*2017 Aug 27.
1897. Cuisset T, Verheugt FWA, Mauri L. Update on antithrombotic therapy **after percutaneous coronary revascularisation**. Lancet. 2017 Aug 19;390(10096):810-820.
1898. Eikelboom JW et al. **Rivaroxaban with or without aspirin** in **stable cardiovascular disease**. (**COMPASS**) *N Engl J Med*2017 Aug 27.
1899. Fan F, Zou Y, Zhang S, Zhang et al. **Rivaroxaban in the Treatment of PICC-Associated Upper Extremity Venous Thrombosis**. Clin Ther. 2017 Aug 17
1900. Godier A, Dincq AS, Martin AC, et al. Predictors of **pre-procedural concentrations of direct oral anticoagulants**: a prospective multicentre study. European Heart Journal. 2017;38:2431-2439
1901. Harada Y;Michel J;Lohaus R;et al. **Validation of the DAPT score** in patients randomized to 6 or 12 months clopidogrel after predominantly second-generation drug-eluting stents. Thromb Haemost. 2017 Jul 27;117(10).
1902. Hilkens NA, Algra A, Diener HC, et al. **Predicting major bleeding** in patients with noncardioembolic stroke on **antiplatelets**: **S2TOP-BLEED**. Neurology 2017;89:936–943.
1903. Sibbing D, Aradi D, Jacobshagen C, et al, on behalf of the TROPICAL-ACS Investigators. Guided **De-Escalation of Antiplatelet Treatment** in **Acute Coronary Syndrome** Patients Undergoing percutaneous coronary intervention (**TROPICAL-ACS**): a randomised, open-label, multicentre trial. Lancet 2017; published online Aug 27.
1904. Brass EP, Hiatt WR. **Aspirin Monotherapy Should Not** Be Recommended for Cardioprotection in Patients With Symptomatic **Peripheral Artery Disease**. Circulation. 2017 Aug 29;136(9):785-786.
1905. Easton JD, Aunes M, et al. Risk for Major **Bleeding in Patients Receiving Ticagrelor Compared with Aspirin** After TIA or Acute Ischemic Stroke in the SOCRATES Study. Circulation. 2017 Jun 27.
1906. Gulilat M, Tang A, Gryn SE, et al. Interpatient Variation in **Rivaroxaban and Apixaban Plasma Concentrations** in Routine Care. Can J Cardiol. 2017 Aug;33(8):1036-1043.
1907. Hu L, Chang L, Zhang Y, et al. **Platelets Express Activated P2Y(12) Receptor in Patients With Diabetes Mellitus**. Circulation. 2017 Aug 29;136(9):817-833.
1908. Niessner A, Tamargo J, Morais J, et al. **Reversal strategies for non-vitamin K antagonist oral anticoagulants**: a critical appraisal of available evidence and recommendations for clinical management-a joint position paper of the **European** Society of Cardiology Working Group on Cardiovascular Pharmacotherapy and European Society of Cardiology Working Group on Thrombosis. Eur Heart J. 2017 Jun 7;38(22):1710-1716.
1909. Vinereanu D, Lopes RD, et al. A **multifaceted intervention** to improve treatment with oral anticoagulants in atrial fibrillation (**IMPACT-AF**): an international, cluster-randomised trial. Lancet. 2017 Aug 25.
1910. Aboyans V, Ricco JB, Bartelink MEL, et al. **2017 ESC Guidelines on the Diagnosis and Treatment of Peripheral Arterial Diseases**, in collaboration with the European Society for Vascular Surgery (ESVS): Document covering atherosclerotic disease of extracranial carotid and vertebral, mesenteric, renal, upper and lower extremity arteriesEndorsed by: the European Stroke Organization (ESO)The Task Force for the Diagnosis and Treatment of Peripheral Arterial Diseases of the European Society of Cardiology (ESC) and of the European Society for Vascular Surgery (ESVS). Eur Heart J. 2017 Aug 26.
1911. Akl EA, Kahale LA, Hakoum MB, et al. **Parenteral anticoagulation in ambulatory patients with cancer**. Cochrane Database of Systematic Reviews 2017, Issue 9. Art. No.: CD006652.
Heparin appears to have no effect on mortality at 12 months and 24 months. It reduces symptomatic VTE and likely increases major and minor bleeding. Future research should further investigate the survival benefit of different types of anticoagulants in patients with different types and stages of cancer. The decision for a patient with cancer to start heparin therapy should balance the benefits and downsides, and should integrate the patient's values and preferences.
1912. Hong K-S, Kwon SU, Lee SH, et al; Phase 2 Exploratory Clinical Study to Assess the Effects of **Xarelto (Rivaroxaban) Versus Warfarin** on Ischemia, Bleeding, and Hospital Stay in **Acute Cerebral Infarction Patients With Non-valvular Atrial Fibrillation** (**Triple AXEL**) study group. Rivaroxaban vs warfarin sodium in the ultra-early period after atrial fibrillation–related mild ischemic stroke: a randomized clinical trial [online September 11, 2017].JAMA Neurol. doi:10.1001/jamaneurol.2017.2161
1913. Gupta A, Johnson DH, Nagalla S. **Antiphospholipid Antibodies**. JAMA. 2017 Sep 12;318(10):959-960.
1914. Horinaka S, Sugawara R, Yonezawa Y, et al. Factor Xa inhibition by **rivaroxaban in the trough steady state** can significantly reduce thrombin generation. Br J Clin Pharmacol. 2017 Sep 9.
1915. Khan F, Le Gal G, Rodger MA. **Stopping anticoagulation in a woman with unprovoked venous thromboembolism**. CMAJ. 2017 Sep 5;189(35):E1112-E1114.
1916. Lobos-Bejarano JM, et al. Influence of **renal function on anticoagulation** control in patients with non-valvular **atrial fibrillation** taking vitamin K antagonists. Int J Clin Pract. 2017 Jul 19
1917. Mas J-L et al. **Patent foramen ovale closure** or anticoagulation vs. antiplatelets after stroke. (**CLOSE**) N Engl J Med 2017 Sep 14; 377:1011.
1918. Ntaios G, Papavasileiou V, Makaritsis K, et al. **Real-World** Setting Comparison of **Nonvitamin-K Antagonist Oral Anticoagulants Versus Vitamin-K Antagonists** for Stroke Prevention in **Atrial Fibrillation**: A Systematic Review and Meta-Analysis. Stroke. 2017 Sep;48(9):2494-2503.
1919. Ropper AH.Tipping point for **patent foramen ovale closure**. N Engl J Med 2017 Sep 14; 377:1093.
1920. Saver JL et al. Long-term outcomes of **patent foramen ovale closure** or medical therapy after stroke. (**RESPECT**) N Engl J Med 2017 Sep 14; 377:1022.
1921. Søndergaard L et al. Patent **foramen ovale closure** or antiplatelet therapy for cryptogenic stroke. (**Gore REDUCE**) N Engl J Med 2017 Sep 14; 377:1033.
1922. Tsivgoulis G, Lioutas VA, Varelas P, et al. **Direct oral anticoagulant- vs vitamin K antagonist-related nontraumatic intracerebral hemorrhage**. Neurology. 2017 Sep 12;89(11):1142-1151
1923. van Sloten TT, de Klaver PAG, et al. Co-administration of **cyclosporine and ticagrelor** may lead to a higher exposure to cyclosporine: a case report of a 49-year old man. Br J Clin Pharmacol. 2017 Sep 11.
1924. Bungard TJ, Semchuk W. The management of venous thromboembolism: A practical tool for the front-line clinician. Can Pharm J (Ott). 2017 Feb 9;150(2):81-89.
1925. Valgimigli M, Bueno H, Byrne RA, et al. **2017 ESC focused update on dual antiplatelet therapy** in **coronary artery disease** developed in collaboration with EACTS: The Task Force for dual antiplatelet therapy in coronary artery disease of the European Society of Cardiology ESC) and of the European Association for Cardio-Thoracic Surgery (EACTS). Eur Heart J. 2017 Aug 26.
1926. Collet JP, Roffi M, Byrne RA, Costa F, Valgimigli M; Task Force for the Management of Dual Antiplatelet Therapy in Coronary Artery Disease of the European Society of Cardiology (ESC) ; ESC Scientific Document Group ; Task Force for the **Management of Dual Antiplatelet Therapy in Coronary Artery Disease of the European Society of Cardiology (ESC) . Case-based implementation** of the **2017 ESC Focused Update on Dual Antiplatelet Therapy in Coronary Artery Disease**. Eur Heart J. 2018 Jan 14;39(3):e1-e33.
1927. Wang H, Qi J, et al. Pharmacodynamics and Pharmacokinetics of **Ticagrelor Versus Clopidogrel in Patients with Acute Coronary Syndromes** and Chronic Kidney Disease. Br J Clin Pharmacol. 2017 Sep 15.
1928. Connors JM. **Thrombophilia Testing and Venous Thrombosis**. N Engl J Med. 2017 Sep 21;377(12):1177-1187.
1929. Nagata N, Yasunaga H, Matsui H, et al. **Therapeutic endoscopy-related GI bleeding** and thromboembolic events in patients using **warfarin or direct oral anticoagulants**: results from a large nationwide database analysis. Gut. 2017 Sep 5.
1930. Bleker SM, et al. Clinical impact of **major bleeding in patients with venous thromboembolism treated with factor Xa inhibitors or vitamin K antagonists**. An individual patient data meta-analysis. Thromb Haemost. 2017 Aug 17;117(10).
1931. Oza R, Rundell K, Garcellano M. **Recurrent Ischemic Stroke: Strategies for Prevention**. Am Fam Physician. 2017;96(7):436-440.
1932. Sundström J, Hedberg J, et al. **Low-Dose Aspirin Discontinuation and Risk of Cardiovascular Events**: A Swedish Nationwide, Population-Based Cohort Study. Circulation. 2017 Sep26;136(13):1183-1192
1933. Chang SH, Chou IJ, Yeh YH, et al. Association Between Use of **Non-Vitamin K Oral Anticoagulants With and Without Concurrent Medications and Risk of Major Bleeding** in Nonvalvular Atrial Fibrillation. JAMA. 2017 Oct 3;318(13):1250-1259.
1934. Lau WCY, Li X, Wong ICK, et al. **Bleeding-related hospital admissions** and 30-day readmissions in patients with non-valvular atrial fibrillation treated with **dabigatran versus warfarin**. J Thromb Haemost. 2017 Oct;15(10):1923-1933.
1935. Wallis CJD, Juvet T, Lee Y, et al. Association Between Use of **Antithrombotic Medication and Hematuria-Related Complications**. JAMA. 2017 Oct 3;318(13):1260-1271.
1936. Bala MM;Celinska-Lowenhoff M;Szot W;et al. **Antiplatelet and anticoagulant agents for secondary prevention of stroke and other thromboembolic events in people with antiphospholipid syndrome**. Cochrane Database Syst Rev. 2017 Oct 2;10:CD012169. There is not enough evidence for or against NOACs or for high-intensity VKA compared to the standard VKA therapy in the secondary prevention of thrombosis in people with APS. There is some evidence of harm for high-intensity VKA regarding minor and any bleeding. The evidence was also not sufficient to show benefit or harm for VKA plus

antiplatelet agent or dual antiplatelet therapy compared to a single antiplatelet drug

1937. Banerjee K, Poddar K, Mick S, et al. Meta-Analysis of Usefulness of **Anticoagulation After Transcatheter Aortic Valve Implantation**. Am J Cardiol. 2017 Nov 1;120(9):1612-1617.
1938. Biffi A, Kuramatsu JB, Leasure A, et al. **Oral Anticoagulation and Functional Outcome after Intracerebral Hemorrhage**. Ann Neurol. 2017 Oct 13.
1939. Gateman D, Trojnar ME, Agarwal G. **Time in therapeutic range: Warfarin anticoagulation** for atrial fibrillation in a community-based practice. Can Fam Physician. 2017 Oct;63(10):e425-e431.
1940. Jun M, Lix LM, Durand M, et al. Comparative safety of **direct oral anticoagulants and warfarin in venous thromboembolism**: multicentre, population based, observational study. BMJ. 2017 Oct 17;359:j4323.
1941. Patrono C, Morais J, Baigent C, et al. **Antiplatelet Agents for the Treatment and Prevention of Coronary Atherothrombosis**. J Am Coll Cardiol. 2017 Oct 3;70(14):1760-1776.
1942. Asher E, Tal S, et al. Effect of **Chewing vs Swallowing Ticagrelor** on Platelet Inhibition in Patients With ST-Segment Elevation Myocardial Infarction: A Randomized Clinical Trial. JAMA Cardiol. 2017 Oct 25.
1943. Bai Y, Shi XB, Ma CS, et al. Meta-Analysis of **Effectiveness and Safety** of Oral Anticoagulants in Atrial Fibrillation With Focus on **Apixaban**. Am J Cardiol. 2017 Nov 1;120(9):1689-1695.
1944. D'Ascenzo F, Iannaccone M, Saint-Hilary G, et al. Impact of design of **coronary stents and length of dual antiplatelet therapies on ischaemic and bleeding events**: a network meta-analysis of 64 randomized controlled trials and 102 735 patients. Eur Heart J. 2017 Aug 11.
1945. Floyd CN, Ferro A. **Indications for anticoagulant and antiplatelet combined therapy**. BMJ. 2017 Oct 5;359:j3782.
1946. Friberg L, Rosenqvist M. **Less dementia with oral anticoagulation in atrial fibrillation**. Eur Heart J. 2017 Oct 24.
1947. Karcutskie CA, Dharmaraja A, Patel J, et al. Association of **Anti-Factor Xa-Guided Dosing of Enoxaparin** With Venous Thromboembolism After Trauma. JAMA Surg. 2017 Oct 25.
1948. Maniwa N, Fujino M, Nakai M, et al. **Anticoagulation combined with antiplatelet therapy** in patients with **left ventricular thrombus after first acute myocardial infarction**. Eur Heart J. 2017 Oct 3.
1949. Quon MJ, et al. **Anticoagulant Use and Risk of Ischemic Stroke and Bleeding in Patients With Secondary Atrial Fibrillation** Associated With Acute Coronary Syndromes, Acute Pulmonary Disease, or Sepsis. J Am Coll Cardiol EP. 2017.
1950. Croles FN, Nasserinejad K, Duvekot JJ, et al. **Pregnancy, thrombophilia, and the risk of a first venous thrombosis**: systematic review and bayesian meta-analysis. BMJ. 2017 Oct 26;359:j4452.
1951. Patell R;Gutierrez A;Rybicki L;Khorana AA Usefulness of **CHADS2 and CHA2DS2-VASc Scores for Stroke Prediction in Patients With Cancer and Atrial Fibrillation.** Am J Cardiol. 2017 Sep 20.
1952. Turpie AGG, Purdham D, Ciaccia A. **Nonvitamin K antagonist oral anticoagulant use** in patients with **renal impairment**. Ther Adv Cardiovasc Dis. 2017 Sep;11(9):243-256.
1953. Anand SS, Bosch J, Eikelboom JW, et al on behalf of the **COMPASS** Investigators. **Rivaroxaban with or without aspirin in patients with stable peripheral or carotid artery disease**: an international, randomised, double-blind, placebo-controlled trial. Lancet 2017; online Nov 10.
1954. Angiolillo DJ, Rollini F, Storey RF, et al. International Expert Consensus on Switching Platelet P2Y(12) Receptor-Inhibiting Therapies. Circulation. 2017 Nov 14;136(20):1955-1975.
1955. Boonyawat K, O'Brien SH, Bates SM. How we treat heavy menstrual bleedingassociated with anticoagulants. Blood. 2017 Nov 1.
1956. Cea Soriano L;Gaist D;Soriano-Gabarro M;Bromley S; **Low-dose aspirin and risk of intracranial bleeds: An observational study in UK general practice.** Neurology. 2017 Nov 1.
1957. Connolly SJ, Eikelboom JW, 1953. Bosch J, et al. **Rivaroxaban with or without aspirin in patients with stable coronary artery disease**: an international, randomised, double-blind, placebo-controlled trial. (**Compass**) Lancet 2017; online Nov 10.
1958. Graham MM, et al. **Aspirin** in patients with **previous percutaneous coronary intervention undergoing noncardiac surgery**. Ann Intern Med. 2017. [Epub ahead of print]. doi:10.7326/M17-2341
1959. Haaland GS, Falk RS, Straume O, et al. Association of **Warfarin Use With Lower Overall Cancer Incidence** Among Patients Older Than 50 Years. JAMA Intern Med. 2017 Nov 6.
1960. Kimachi M;Furukawa TA;Kimachi K;et al. **Direct oral anticoagulants versus warfarin for preventing stroke and systemic embolic events among atrial fibrillation patients with chronic kidney disease**. Cochrane Database Syst Rev. 2017 Nov 6;11:CD011373. Our findings indicate that DOAC are as likely as warfarin to prevent all strokes and systemic embolic events without increasing risk of major bleeding events among AF patients with kidney impairment. These findings should encourage physicians to prescribe DOAC in AF patients with CKD without fear of bleeding. The major limitation is that the results of this study chiefly reflect CKD stage G3. Application of the results to CKD stage G4 patients requires additional investigation. Furthermore, we could not assess CKD stage G5 patients. Future reviews should assess participants at more advanced CKD stages. Additionally, we could not conduct detailed analyses of subgroups and sensitivity analyses due to lack of data.
1961. Sousa-Uva M, Head SJ, Milojevic M, et al; Document Reviewers. **2017 EACTS Guidelines on perioperative medication in adult cardiac surgery**. Eur J Cardiothorac Surg. 2017 Oct 6.
1962. Agarwal N;Mahmoud AN;Patel NK;Jain A;Garg J;Mojadi. Meta-Analysis of **Aspirin Versus Dual Antiplatelet Therapy Following Coronary Artery Bypass Grafting.** Am J Cardiol. 2017 Oct 26.
1963. Go AS, Singer DE, Toh S, et al. Outcomes of **Dabigatran and Warfarin for Atrial Fibrillation in Contemporary Practice**: A Retrospective Cohort Study. Ann Intern Med. 2017 Nov 14.
1964. Jobski K, Hoffmann F, Herget-Rosenthal S, Dörks M. **Oral Anticoagulants in German nursing home residents** - Drug use patterns and predictors for treatment choice. Br J Clin Pharmacol. 2017 Nov 17.
1965. Cea Soriano L, Gaist D, Soriano-Gabarró M, et al. **Low-dose aspirin and risk of intracranial bleeds**: An observational study in UK general practice. Neurology. 2017 Nov 28;89(22):2280-2287.
1966. Goldhaber SZ;Schulman S;Eriksson H;et al. **Dabigatran versus Warfarin for Acute Venous Thromboembolism** in Elderly or Impaired Renal Function Patients: Pooled Analysis of RE-COVER and RE-COVER II. Pooled analysis of **RE-COVER** and **RE-COVER II**. Thromb Haemost. 2017 Oct 4;117(11).
1967. Shafran DM, Wu C. Treatment of **venous thromboembolism in a 22-year-old woman taking an oral contraceptive pill**. CMAJ. 2017 Nov 27;189(47):E1459-E1460.
1968. Burns RB, Graham K, Sawhney MS, et al. **Should This Patient Receive Aspirin**?: Grand Rounds Discussion From Beth Israel Deaconess Medical Center. Ann Intern Med. 2017 Dec 5;167(11):786-793.
1969. Jull A, Wadham A, et al. **Low dose aspirin as adjuvant treatment for venous leg ulceration:** pragmatic, randomised, double blind, placebo controlled trial (**Aspirin4VLU**). BMJ. 2017 Nov 24;359:j5157.
1970. Sasor SE, Evans TA, Cook JA, et al. Assessing the **Necessity of Stopping Antithrombotic Agents Before Wide-Awake Hand Surgery**. JAMA Surg. 2017 Nov 29.
1971. Writing Committee, Tomaselli GF, Mahaffey KW, et al. **2017 ACC Expert Consensus Decision Pathway on Management of Bleeding in Patients on Oral Anticoagulants**: A Report of the American College of Cardiology Task Force on Expert Consensus Decision Pathways. J Am Coll Cardiol. 2017 Nov 10.
1972. Zahed R, Mousavi Jazayeri MH, et al. **Topical Tranexamic Acid Compared With Anterior Nasal Packing for Treatment of Epistaxis** in Patients **Taking Antiplatelet Drugs**: Randomized Controlled Trial. Acad Emerg Med. 2017 Nov 10.
1973. Dunn AS, Turpie AG. **Perioperative management of patients receiving oral anticoagulants**: a systematic review. Arch Intern Med. 2003 Apr 28;163(8):901-8.
1974. Bath PM, Woodhouse LJ, Appleton JP, et al. Antiplatelet therapy with **aspirin, clopidogrel, and dipyridamole** versus clopidogrel alone or aspirin and dipyridamole in patients with acute cerebral ischaemia (**TARDIS**): a randomised, open-label, phase 3 superiority trial. Lancet. 2017 Dec 20
1975. Charidimou A, Karayiannis C, Song TJ, et al. **Brain microbleeds, anticoagulation, and hemorrhage risk**: Meta-analysis in stroke patients with AF. Neurology. 2017 Dec 5;89(23):2317-2326
1976. Chi G, Yee MK, Amin AN, et al. Extended-Duration **Betrixaban** Reduces the Risk of Rehospitalization Associated With Venous Thromboembolism Among Acutely Ill Hospitalized Medical Patients: Findings From the **APEX** Trial (Acute Medically Ill Venous Thromboembolism Prevention With Extended Duration Betrixaban Trial). Circulation. 2018 Jan 2;137(1):91-94
1977. Jones NR, Hobbs FDR, Taylor CJ. **Underuse of anticoagulation therapy for atrial fibrillation**: Are we failing our patients? Can Fam Physician. 2017 Dec;63(12):943-944.
1978. Kawai T, Oda K, Funao N, et al. **Vonoprazan** prevents low-dose aspirin-associated ulcer recurrence: randomised phase 3 study. Gut. 2017 Dec 1.
1979. Lee AYY. **When can we stop anticoagulation in patients with cancer-associated thrombosis**? Blood. 2017 Dec 6.
1980. Nishimura M, Hsu JC. **Non-Vitamin K Antagonist Oral Anticoagulants** in Patients **With Atrial Fibrillation** and End-Stage **Renal Disease**. Am J Cardiol. 2018 Jan 1;121(1):131-140.
1981. Pascale P, Rosset S, Müller O, Pruvot E. **Prolonged Asystole After a Loading Dose of Ticagrelor**. Ann Intern Med. 2017 Dec 19.
1982. Raskob GE, van Es N, Verhamme P, et al. **Edoxaban** for the Treatment of Cancer-Associated Venous Thromboembolism. (**HOKUSAI VTE CANCER**) N Engl J Med. 2017 Dec 12.
1983. Rivera-Caravaca JM, Roldán V, Esteve-Pastor MA, et al. Reduced Time in Therapeutic Range and Higher Mortality in Atrial Fibrillation Patients Taking **Acenocoumarol**. Clin Ther. 2017 Dec 20.
1984. Robertson L, Yeoh SE, Stansby G, Agarwal R. Effect of **testing for cancer on cancer- and venous thromboembolism (VTE)-related mortality** and morbidity in people with unprovoked VTE. Cochrane Database Syst Rev. 2017 Aug 23;8:CD010837. Testing for cancer in people with unprovoked VTE may lead to earlier diagnosis of cancer at an earlier stage of the disease. However, there is currently insufficient evidence to draw definitive conclusions concerning the effectiveness of testing for undiagnosed cancer in people with a first episode of unprovoked VTE (DVT or PE) in reducing cancer and VTE-related morbidity

and mortality. The results could be consistent with either benefit or no benefit. Further good-quality large-scale randomised controlled trials are required before firm conclusions can be made.

1985. Swartz RH, Ladhani NNN, Foley N, et al; Heart and Stroke Foundation Canadian Stroke Best Practice Committees. **Canadian stroke best practice consensus sta**tement: **secondary stroke** prevention during **pregnancy**. Int J Stroke 2017 (accessed December 12, 2017).
1986. Uyhazi KE, Miano T, Pan W, et al Association of **novel oral antithrombotics with the risk of intraocular bleeding** [online Dec 14, 2017].JAMA Ophthalmol. doi:10.1001 /jamaophthalmol.2017.5677
1987. Wein T, Lindsay MP, Cote R, et al; Heart and Stroke Foundation Canadian Stroke Best Practice Committees. **Canadian stroke best practice recommendations: secondary prevention of stroke**, sixth edition practice guidelines, update 2017. Int J Stroke 2017 (accessed December 12, 2017).
1988. Ando T, Holmes AA, Pahuja M, et al. Meta-Analysis Comparing **Patent Foramen Ovale Closure** Versus Medical Therapy to Prevent Recurrent Cryptogenic Stroke. Am J Cardiol. 2017 Dec 11.
1989. Gerner ST, Kuramatsu JB, et al. Association of **prothrombin complex concentrates administration and hematoma enlargement in NOAC-related intracerebral hemorrhage**. Ann Neurol. 2018 Jan 3.
1990. Hunt BJ, Levi M. **Urgent reversal of vitamin K antagonists.** BMJ. 2018 Jan 4;360:j5424.
1991. Khan SU, et al. Meta-Analysis of the Safety and Efficacy of the Oral Anticoagulant Agents **(Apixaban, Rivaroxaban, Dabigatran) With Acute Coronary Syndrome**. Am J Cardiol. 2018 Feb 1;121(3):301-307.
1992. Sinnaeve PR, Van de Werf F. **Clopidogrel instead of prasugrel or ticagrelor after 1 month in stabilized ACS patients**: back to square one for **DAPT**? Eur Heart J. 2017 Nov 1;38(41):3079-3081.
1993. Squizzato A, Bellesini M, Takeda A, et al. **Clopidogrel plus aspirin versus aspirin alone for preventing cardiovascular events.** Cochrane Database of Systematic Reviews 2017, Issue 12. Art. No.: CD005158. The available evidence demonstrates that the use of clopidogrel plus aspirin in people at high risk of cardiovascular disease and people with established cardiovascular disease without a coronary stent is associated with a reduction in the risk of myocardial infarction and ischaemic stroke, and an increased risk of major and minor bleeding compared with aspirin alone. According to GRADE criteria, the quality of evidence was moderate for all outcomes except all-cause mortality (low quality evidence) and adverse events (very low quality evidence).
1994. De Rosa S, Sievert H, et al. **Percutaneous Closure Versus Medical Treatment in Stroke Patients With Patent Foramen Ovale**: A Systematic Review and Meta-analysis. Ann Intern Med. 2018 Jan 9.
1995. Goldhaber SZ, Schulman S, Eriksson H, et al. **Dabigatran versus Warfarin for Acute Venous Thromboembolism in Elderly or Impaired Renal Function** Patients: Pooled Analysis of RE-COVER and RE-COVER II. Thromb Haemost. 2017 Nov;117(11):2045-2052.
1996. McEvoy JW, Ibrahim K, Kickler TS, et al. Effect of Intravenous **Fentanyl on Ticagrelor Absorption and Platelet Inhibition** Among Patients Undergoing Percutaneous Coronary Intervention: The **PACIFY** Randomized Clinical Trial (Platelet Aggregation With Ticagrelor Inhibition and Fentanyl). Circulation. 2018 Jan 16;137(3):307-309.
1997. Powers WJ, Rabinstein AA, Ackerson T, et al. **2018 guidelines** for the early management of patients with **acute ischemic stroke**: a guideline for healthcare professionals from the **American Heart Association (AHA)/American Stroke Association (ASA)**. Stroke. 2018;49:xxx–xxx. doi: 10.1161/STR.0000000000000158.
1998. Robertson L, Yeoh SE, Ramli A. **Secondary prevention of recurrent venous thromboembolism after initial oral anticoagulation therapy in patients with unprovoked venous thromboembolism**. Cochrane Database Syst Rev. 2017 Dec 15;12:CD011088. Evidence is currently insufficient to permit definitive conclusions concerning the effectiveness and safety of extended thromboprophylaxis in prevention of recurrent VTE after initial oral anticoagulation therapy among participants with unprovoked VTE.
1999. Inohara T, et al. Association of **Intracerebral Hemorrhage Among Patients Taking Non-Vitamin K Antagonist vs Vitamin K Antagonist** Oral Anticoagulants With In-Hospital Mortality. JAMA. 2018 Jan 25.
2000. Levy JH, Moore KT, Neal MD, et al.**Rivaroxaban reversal with prothrombin complex concentrate or tranexamic acid** in healthy volunteers. J Thromb Haemost. 2018 Jan;16(1):54-64.
2001. Lüscher TF. **Dual antiplatelet therapy**: how, how long, and in which patients? Eur Heart J. 2018 Jan 14;39(3):181-183.
2002. Oakland K, Desborough MJ, et al. **Re-bleeding and Mortality After Lower Gastrointestinal Bleeding in Patients Taking Anti-platelets or Anti-coagulants**. Clin Gastroenterol Hepatol. 2017 Dec 22.
2003. Shore-Lesserson L, Baker RA, et al. The Society of Thoracic Surgeons, The Society of Cardiovascular Anesthesiologists, and The American Society of ExtraCorporeal Technology: Clinical Practice Guidelines-**Anticoagulation During Cardiopulmonary Bypass**. Ann Thorac Surg. 2018 Feb;105(2):650-662.
2004. Collet JP, Roffi M, Byrne RA, Costa F, Valgimigli M; Task Force for the Management of Dual Antiplatelet Therapy in Coronary Artery Disease of the European Society of Cardiology (ESC) ; ESC Scientific Document Group ; Task Force for the **Management of Dual Antiplatelet Therapy in Coronary Artery Disease of the European Society of Cardiology (ESC) . Case-based implementation** of the 2017 ESC Focused Update on Dual Antiplatelet Therapy in Coronary Artery Disease. Eur Heart J. 2018 Jan 14;39(3):e1-e33.
2005. Doll JA, Li S, Chiswell K, et al. **Clopidogrel reloading** for patients **with acute myocardial infarction** already on clopidogrel therapy. Eur Heart J. 2018 Jan 14;39(3):193-200.
2006. Ng PY, Ng AK-Y, Subramaniam B, et al. Association of **preoperatively diagnosed patent foramen ovale with perioperative ischemic stroke**. JAMA. doi:10.1001/jama.2017.21899
2007. Gage BF, Bass AR, Lin H, et al. Effect of **genotypeguided warfarin dosing** on clinical events and anticoagulation control among patients undergoing hip or knee arthroplasty: the **GIFT** randomized clinical trial. JAMA. doi:10.1001/jama.2017.11469
2008. Anderson DR, Dunbar M, Murnaghan J, et al. **Aspirin or Rivaroxaban for VTE Prophylaxis after Hip or Knee Arthroplasty**. N Engl J Med. 2018 Feb 22;378(8):699-707.
2009. Bansilal S, et al. **Ticagrelor** for Secondary Prevention of Atherothrombotic Events in Patients With **Multivessel Coronary Disease. (Pegasus Timi 54)** J Am Coll Cardiol. 2018 Feb 6;71(5):489-496.
2010. Behera SK, Xavier AS, Selvarajan S, et al. **Acenocoumarol As An Alternative** Anticoagulant In A Patient **With Warfarin Related Nephropathy**. Br J Clin Pharmacol. 2018 Feb 8.
2011. Cavallari I, et al. Frequency, Predictors, and Impact of **Combined Antiplatelet Therapy** on Venous Thromboembolism in Patients With **Symptomatic Atherosclerosis**. Circulation. 2018 Feb 13;137(7):684-692.
2012. Chiarito M, et al. **Direct Oral Anticoagulants in Addition to Antiplatelet Therapy** for Secondary Prevention After Acute Coronary Syndromes: Systematic Review & Meta-analysis. JAMA Cardiol. 2018 Feb 7.
2013. Ebrahimi R, Gupta S, Carr BM, et al. Comparison of Outcomes and Costs Associated With **Aspirin ± Clopidogrel After Coronary Artery Bypass Grafting**. Am J Cardiol. 2018 Jan 2.
2014. Graham MM, Sessler DI, Parlow JL, Biccard BM, et al. **Aspirin in patients with previous percutaneous coronary intervention undergoing noncardiac surgery**. Ann Intern Med. 2018;168: 237-44.
2015. Hilkens NA, Algra A, Kappelle LJ, et al. **Early time course of major bleeding on antiplatelet therapy after TIA or ischemic stroke**. Neurology. 2018 Jan 26.
2016. Johnson JA, et al. Clinical Pharmacogenetics Implementation Consortium (**CPIC**) guideline for **pharmacogenetics-guided warfarin dosing**: 2017 update. Clin Pharmacol Ther. 2017 Sep;102(3):397-404.
2017. Kheiri B, Abdalla A, Haykal T, et al. Meta-Analysis of **Genotype-Guided Versus Standard Dosing of Vitamin K Antagonists**. Am J Cardiol. 2018 Jan 12.
2018. Lee SY, Hong MK, et al. **Short-Term Versus Long-Term Dual Antiplatelet Therapy After Drug-Eluting Stent Implantation in Elderly** Patients: A Meta-Analysis of Individual Participant Data From 6 Randomized Trials. JACC Cardiovasc Interv. 2018 Feb 8.
2019. Li J, Wang A, Zhao X, et al. **High-sensitive C-reactive protein and dual antiplatelet** in **intracranial arterial stenosis**. Neurology 2018;90:e447–e454.
2020. Malhotra K, Katsanos AH, Bilal M, et al.**Cerebrovascular Outcomes** With **Proton Pump Inhibitors and Thienopyridines**: A Systematic Review and Meta-Analysis. Stroke. 2018 Feb;49(2):312-318.
2021. Mehta SR, et al. **2018 Canadian Cardiovascular Society**/Canadian Association of Interventional Cardiology Focused Update of the Guidelines for the **Use of Antiplatelet Therapy**. Can J Cardiol. 2018 Mar;34(3):214-233.
2022. Morley RL, Sharma A, Horsch AD, Hinchliffe RJ. **Peripheral artery disease**. BMJ.2018 Feb 1;360:j5842.
2023. Raggio BS, Barton BM, et al. Association of Continued **Preoperative Aspirin Use** and Bleeding Complications in Patients Undergoing Thyroid Surgery. JAMA Otolaryngol Head Neck Surg. 2018 Mar 1.
2024. Sandhu RK, Guirguis LM, Bungard TJ, et al. Evaluating the potential for **pharmacists to prescribe oral anticoagulants for atrial fibrillation.** Can Pharm J (Ott). 2017 Nov 29;151(1):51-61.
2025. Seiffge DJ, Kägi G, Michel P, et al. **Rivaroxaban plasma levels** in acute ischemic stroke and intracerebral hemorrhage. Ann Neurol. 2018 Feb 2.
2026. Stubbs MJ, Mouyis M, Thomas M. **Deep vein thrombosis**. BMJ. 2018 Feb 22;360:k351.
2027. Tang YD, Wang W, Yang M, et al; **CREATIVE** investigators. Randomized Comparisons of **Double-Dose Clopidogrel or Adjunctive Cilostazol** versus Standard Dual Anti-platelet in Patients with High Post-Treatment **Platelet Reactivity**: Results of the CREATIVE Trial (Clopidogrel Response Evaluation and AnTi-platelet InterVEntion in High Thrombotic Risk PCI Patients). Circulation. 2018 Feb 2.
2028. Tornkvist M, Smith JG, Labaf A. Current evidence of **oral anticoagulant reversal**: A systematic review. Thromb Res. 2018 Feb;162:22-31.
2029. Ueshima S, Hira D, Kimura Y, et al. Population pharmacokinetics and pharmacogenomics of **apixaban** in **Japanese** adult patients with atrial fibrillation. Br J Clin Pharmacol. 2018 Feb 19.
2030. van Es N, Louzada M, Carrier M, et al. Predicting the risk of recurrent **venous thromboembolism in patients with cancer**: A prospective cohort study. Thromb Res. 2018 Jan 9;163:41-46.

2031. Yoshikawa Y, Shiomi H, et al. **Validating utility of dual antiplatelet therapy score** in a large pooled cohort from 3 Japanese percutaneous coronary intervention studies. Circulation. 2018;137:551–562.
2032. Anand SS, Caron F, Eikelboom JW, et al. Major Adverse Limb Events in Lower Extremity Peripheral Artery Disease: COMPASS Trial. J Am Coll Cardiol. 2018 Mar 7.
2033. Bruins Slot KM, Berge E. **Factor Xa inhibitors versus vitamin K antagonists for preventing cerebral or systemic embolism in patients with atrial fibrillation**. Cochrane Database Syst Rev. 2018 Mar 6;3:CD008980. Treatment with factor Xa inhibitors significantly reduced the number of strokes and systemic embolic events compared with warfarin in people with AF. The absolute effect of factor Xa inhibitors compared with warfarin treatment was, however, rather small. Factor Xa inhibitors also reduced the number of ICHs, all-cause deaths and major bleedings compared with warfarin, although the evidence for a reduction in the latter is less robust.
2034. Notarangelo FM, Maglietta G, Bevilacqua P, et al. Pharmacogenomic Approach to **Selecting Antiplatelet Therapy in Acute Coronary Syndromes**: **PHARMCLO** trial. J Am Coll Cardiol. 2018 Feb 24.
2035. Sennesael AL, Larock AS, Devalet Bet al. **Preventability of serious thromboembolic and bleeding events related to the use of oral anticoagulants**: a prospective study. Br J Clin Pharmacol. 2018 Mar 9.
2036. Berwanger O, Nicolau JC, et al. **Ticagrelor vs Clopidogrel After Fibrinolytic** Therapy in Patients With ST-Elevation **Myocardial Infarction**: Randomized Clinical Trial. (**TREAT**) JAMA Cardiol. 2018 Mar 11.
2037. Douros A, Azoulay L, Yin H, et al. **Non-Vitamin K Antagonist Oral Anticoagulants** and **Risk of Serious Liver Injury**. J Am Coll Cardiol. 2018 Mar 13;71(10):1105-1113.
2038. Hahn JY, et al. **6-month versus 12-month or longer** dual antiplatelet therapy after **percutaneous coronary intervention** in patients with **acute coronary syndrome** (**SMART-DATE**): a randomised, open-label, non-inferiority trial. Lancet. 2018 Mar 9.
2039. McCarthy CP, Steg G, Bhatt DL. The management of **antiplatelet therapy in acute coronary syndrome patients with thrombocytopenia**: a clinical conundrum. Eur Heart J. 2017 Dec 14;38(47):3488-3492.
2040. Cavallari I, et al. Frequency, Predictors, & Impact of **Combined Antiplatelet Therapy on Venous Thromboembolism** in Patients With **Symptomatic Atherosclerosis**. Circulation. 2018 Feb 13;137(7):684-692.
2041. Jing J, et al. **Dual Antiplatelet Therapy in Transient Ischemic Attack & Minor Stroke** With Different Infarction Patterns: Subgroup Analysis-**CHANCE** Randomized Trial. JAMA Neurol. 2018 Mar 26.
2042. Khalaf N, et al. **Regular Use of Aspirin or Non-Aspirin** Nonsteroidal Anti-Inflammatory Drugs Is Not Associated With Risk of **Incident Pancreatic Cancer** in Two Large Cohorts. Gastroenterology. 2018
2043. Kirchhof P, Haeusler KG, Blank B, et al. **Apixaban** in patients at **risk of stroke undergoing atrial fibrillation ablation**. Eur Heart J. 2018 Mar 20.
2044. Cavallari I, et al. Frequency, Predictors, and Impact of **Combined Antiplatelet Therapy on Venous Thromboembolism** in Patients With **Symptomatic Atherosclerosis**. Circulation. 2018 Feb 13;137(7):684-692.
2045. Kurogi R, Nishimura K, Nakai Met al. **Comparing intracerebral hemorrhages associated with direct oral anticoagulants or warfarin**. Neurology. 2018 Mar 27;90(13):e1143-e1149.
2046. Ezekowitz MD, et al. **Apixaban** compared to heparin/vitamin K antagonist in patients with atrial fibrillation scheduled for **cardioversion**: the **EMANATE** trial. Eur Heart J. 2018 Apr 6.
2047. Lutsey PL, Norby FL, et al. **Atrial fibrillation and venous thromboembolism**: evidence of bidirectionality in the Atherosclerosis Risk in Communities Study. J Thromb Haemost. 2018 Apr;16(4):670-679.
2048. Ten Cate-Hoek AJ, Amin EE, et al; **IDEAL DVT** investigators. **Individualised versus standard duration of elastic compression therapy** for prevention of post-thrombotic syndrome (IDEAL DVT): a multicentre, randomised, single-blind, allocation-concealed, non-inferiority trial. Lancet Haematol. 2018 Jan;5(1):e25-e33.
2049. Zhao Q, Zhu Y, Xu Z, et al. Effect of **ticagrelor plus aspirin, ticagrelor alone, or aspirin alone on saphenous vein graft patency** 1 year after coronary artery bypass grafting: a randomized clinical trial. (DACAB) JAMA. doi:10.1001/jama.2018.3197
2050. Capodanno D. Triple antithrombotic therapy after ACS and PCI in patients on chronic oral anticoagulation: update. Heart. 2018 Apr 25.
2051. Cohen H, Efthymiou M, Isenberg D. Use of direct oral anticoagulants in antiphospholipid syndrome. J Thromb Haemost. 2018 Apr 6.
2052. Roberge S, Bujold E, Nicolaides KH. Meta-analysis on the effect of aspirin use for prevention of preeclampsia on placental abruption and antepartum hemorrhage. Am J Obstet Gynecol. 2018 May;218(5):483-489.
2053. Verma A, Ha ACT, Rutka JT, Verma S. What Surgeons Should Know About Non-Vitamin K Oral Anticoagulants: A Review. JAMA Surg. 2018 Apr 18.
2054. Steffel J, et al; ESC Scientific Document Group . The 2018 European Heart Rhythm Association Practical Guide on the use of non-vitamin K antagonist oral anticoagulants in patients with atrial fibrillation. Eur Heart J. 2018 Mar 17.
2055. Man-Son-Hing M, et al. Choosing **antithrombotic** therapy for elderly patients with atrial fibrillation who are at **risk for falls**. Arch Intern Med. 1999 Apr 12;159(7):677-85.
2056. Burr N, Lummis K, Sood R, et al. Risk of **gastrointestinal bleeding with direct oral anticoagulants**: a systematic review and network meta-analysis. Lancet Gastroenterol Hepatol. 2017 Feb;2(2):85-93.
2057. Johnston SC, Easton JD, Farrant M, et al. **Clopidogrel and aspirin in acute ischemic stroke and high-risk TIA. (POINT)** N Engl J Med. DOI: 10.1056/NEJMoa1800410.
2058. Quon M, Behlouli H, Pilote L. **Anticoagulant Use and Risk of Ischemic Stroke and Bleeding in Patients With Secondary Atrial Fibrillation Associated With Acute Coronary Syndromes, Acute Pulmonary Disease, or Sepsis**. JACC: Clinical Electrophysiology. 2017 Sep 27.
2059. Madelaire C, Gislason G, Kristensen SL, et al. **Low-Dose Aspirin in Heart Failure Not Complicated by Atrial Fibrillation**: A Nationwide Propensity-Matched Study. JACC Heart Fail. 2018 Feb;6(2):156-167.
2060. Amarenco P, Lavallée PC, Monteiro Tavares L, et al. **Five-Year Risk of Stroke after TIA or Minor Ischemic Stroke**. N Engl J Med. 2018 May 16.
2061. Gupta S, Belley-Cote EP, Sarkaria A, et al. **International Normalized Ratio Targets for Left-Sided Mechanical Valve Replacement**. Thromb Haemost. 2018 Apr 3.
2062. Hart RG, Sharma M, Mundl H, et al. **Rivaroxaban for Stroke Prevention after Embolic Stroke** of Undetermined Source. N Engl J Med. 2018 May 16.
2063. Nigwekar SU, Thadhani R, Brandenburg VM. Calciphylaxis. N Engl J Med. 2018 May 3;378(18):1704-1714. (eg. warfarin induced)
2064. Anderson I, Cifu AS. **Management of Bleeding in Patients Taking Oral Anticoagulants**. JAMA. 2018 May 15;319(19):2032-2033.
2065. Carabenciov ID, Hawkes MA, Hocker S. **Safety of Lumbar Puncture Performed on Dual Antiplatelet Therapy**. Mayo Clin Proc. 2018 May;93(5):627-629.
2066. Dayoub EJ, Seigerman M, Tuteja S, et al. Trends in **Platelet Adenosine Diphosphate P2Y12 Receptor Inhibitor Use** and Adherence Among Antiplatelet-Naive Patients After Percutaneous Coronary Intervention, 2008-2016. JAMA Intern Med. 2018 May 21.
2067. Garcia D, Erkan D. Diagnosis and Management of the **Antiphospholipid Syndrome**. N Engl J Med. 2018 May 24;378(21):2010-2021.
2068. Kim MH, Chang J, Kim WJ, Banerjee S, Park SM. Cumulative Dose Threshold for the **Chemopreventive Effect of Aspirin Against Gastric Cancer**. Am J Gastroenterol. 2018 Jun 1.
2069. Tang YD, Wang W, Yang M, et al. Randomized Comparisons of **Double-Dose Clopidogrel or Adjunctive Cilostazol Versus Standard Dual Antiplatelet** in Patients With High Posttreatment Platelet Reactivity: Results of the CREATIVE Trial. Circulation. 2018 May 22;137(21):2231-2245.
2070. Young AM, Marshall A, Thirlwall J, et al. Comparison of an **Oral Factor Xa Inhibitor With Low Molecular Weight Heparin** in Patients With Cancer With Venous Thromboembolism: Results of a Randomized Trial (SELECT-D). J Clin Oncol. 2018 May 10.
2071. Al Halabi S, Newman J, Farkouh ME, et al. Meta-Analysis of Studies **Comparing Dual- Versus Mono-Antiplatelet Therapy Following Transcatheter Aortic Valve Implantation**. Am J Cardiol. 2018 Mar 28.
2072. Bruins Slot KM, Berge E. **Factor Xa inhibitors versus vitamin K antagonists for preventing cerebral or systemic embolism** in patients with atrial fibrillation. Cochrane Database Syst Rev. 2018 Mar 6;3:CD008980. Treatment with factor Xa inhibitors significantly reduced the number of strokes and systemic embolic events compared with warfarin in people with AF. The absolute effect of factor Xa inhibitors compared with warfarin treatment was, however, rather small. Factor Xa inhibitors also reduced the number of ICHs, all-cause deaths and major bleedings compared with warfarin, although the evidence for a reduction in the latter is less robust.
2073. Franchi F, Rollini F, Rivas Rios J, et al. **Pharmacodynamic Effects of Switching From Ticagrelor to Clopidogrel** in Patients With Coronary Artery Disease: Results of the SWAP-4 Study. Circulation. 2018 Jun 5;137(23):2450-2462.
2074. Savonitto S, Ferri LA, Piatti L, et al. Comparison of **Reduced-Dose Prasugrel and Standard-Dose Clopidogrel in Elderly Patients** With Acute Coronary Syndromes Undergoing Early Percutaneous Revascularization. Circulation. 2018 Jun 5;137(23):2435-2445.
2075. Bernhardt J, Zorowitz RD, Becker KJ, et al. Advances in Stroke 2017. Stroke. 2018 May;49(5):e174-e199.
2076. Hess CN, Hiatt WR. Antithrombotic Therapy for **Peripheral Artery Disease** in 2018. JAMA. 2018 Jun 12;319(22):2329-2330.
2077. Wright D, Rolnik DL, Syngelaki A, et al. **Aspirin for Evidence-Based Preeclampsia Prevention** trial: effect of aspirin on length of stay in the neonatal intensive care unit. Am J Obstet Gynecol. 2018 Jun;218(6):612.e1-612.e6.

2078. Wilson D, Ambler G, Shakeshaft C, et al; CROMIS-2 collaborators. **Cerebral microbleeds and intracranial haemorrhage risk** in patients anticoagulated **for atrial fibrillation after acute ischaemic stroke** or transient ischaemic attack (CROMIS-2): a multicentre observational cohort study. Lancet Neurol. 2018 Jun;17(6):539-547.
2079. Yamashita Y, Morimoto T, Toyota T, et al. Asian patients versus non-Asian patients in the **efficacy and safety of direct oral anticoagulants** relative to vitamin K antagonist for venous thromboembolism: A systemic review and meta-analysis. Thromb Res. 2018 Jun;166:37-42.
2080. Devereaux PJ, Duceppe E, Guyatt G, et al; MANAGE Investigators. **Dabigatran in patients with myocardial injury** after non-cardiac surgery (**MANAGE**): an international, randomised, placebo-controlled trial. Lancet. 2018 Jun 9;391(10137):2325-2334.
2081. Franchi C, Antoniazzi S, Proietti M, et al. **Appropriateness of oral anticoagulant therapy prescription** and its associated factors in hospitalized older people with atrial fibrillation. Br J Clin Pharmacol. 2018 May 10.
2082. Kim JT et al. Clinical significance of acute and serial platelet function testing in acute ischemic stroke. J Am Heart Assoc 2018 Jun 1; 7:e008313.
2083. Puskas JD, Gerdisch M, Nichols D, et al; PROACT Investigators. Anticoagulation and Antiplatelet Strategies After On-X Mechanical Aortic Valve Replacement. J Am Coll Cardiol. 2018 Jun 19;71(24):2717-2726.
2084. Sibbing D, Gross L, Trenk D, et al; TROPICAL-ACS Investigators. Age and outcomes following guided de- scalation of antiplatelet treatment in acute coronary syndrome patients undergoing percutaneous coronary intervention: results from the randomized TROPICAL-ACS trial. Eur Heart J. 2018 Jun 14.
2085. Chen CJ, Ding D, Buell TJ, et al. **Restarting antiplatelet therapy after spontaneous intracerebral hemorrhage**: Functional outcomes. Neurology. 2018 Jul 3;91(1):e26-e36.
2086. Saber H, Palla M, Kazemlou S, et al. Network meta-analysis of patent **foramen ovale management strategies in cryptogenic stroke**. Neurology. 2018 Jun 6.
2087. Selak V, Kerr A, Poppe K, et al. Annual Risk of **Major Bleeding Among Persons Without Cardiovascular Disease** Not Receiving Antiplatelet Therapy. JAMA. 2018 Jun 26;319(24):2507-2520.
2088. Seviiri M, Lynch BM, Hodge AM, et al. Resting heart rate, temporal changes in resting heart rate, and overall and cause-specific mortality. Heart. 2018 Jul;104(13):1076-1085.
2089. Tse G, Gong M, Li G, et al. Genotype-guided **warfarin dosing vs. conventional dosing strategies**: a systematic review and meta-analysis of randomized controlled trials. Br J Clin Pharmacol. 2018 Apr 28.
2090. Tsivgoulis G, Katsanos AH, Mavridis D, et al. Percutaneous **patent foramen ovale closure for secondary stroke prevention**: Network meta-analysis. Neurology. 2018 Jun 6.
2091. Vinogradova Y, Coupland C, Hill T, et al. Risks and benefits of **direct oral anticoagulants versus warfarin in a real world setting**: cohort study in primary care. BMJ. 2018 Jul 4;362:k2505.
2092. Kirchhof P, Radaideh G, Kim YH, et al. Global **XANTUS** program Investigators. Global Prospective **Safety Analysis of Rivaroxaban**. J Am Coll Cardiol. 2018 Jul 10;72(2):141-153.
2093. Lee CJ, Gerds TA, Carlson N, et al. Risk of **Myocardial Infarction in Anticoagulated Patients With Atrial Fibrillation**. J Am Coll Cardiol. 2018 Jul 3;72(1):17-26.
2094. Lyon TD, Frank I, Shah PH, et al. The Association of **Aspirin Use with Survival Following Radical Cystectomy**. J Urol. 2018 May 29.
2095. Kent AP, Brueckmann M, Fraessdorf M, et al. Concomitant **oral anticoagulant and nonsteroidal anti-inflammatory drug therapy in patients with atrial fibrillation**. (RE-LY) J Am Coll Cardiol 2018;72:255–67.
2096. Jung YJ, Seo HS, Park CH, et al. **Venous thromboembolism incidence and prophylaxis** use after gastrectomy among Korean patients with gastric adenocarcinoma: the **PROTECTOR randomized clinical trial** [online July 18, 2018]. JAMA Surg. doi:10.1001/jamasurg.2018.2081
2097. Liu N, Vigod SN, Farrugia MM, et al. **Venous thromboembolism after induced abortion**: a population-based, propensity-score-matched cohort study in Canada. Lancet Haematol 2018; published online June 8.
2098. Rothwell PM, Cook NR, Gaziano JM, et al. Effects of **aspirin on risks of vascular events and cancer** according to bodyweight and dose: analysis of individual patient data from randomised trials. Lancet 2018; online July 12.
2099. Siontis KC, Zhang X, Eckard A, et al. Outcomes Associated with **Apixaban Use in End-Stage Kidney Disease Patients with Atrial Fibrillation** in the United States. Circulation. 2018 Jun 28.
2100. Turner TE, Saeed MJ, Novak E, Brown DL. Association of **inferior vena cava filter placement for venous thromboembolic disease** and a contraindication to anticoagulation with 30-day mortality. JAMA Netw Open. 2018; 1(3):e180452.
2101. Wolfe Z, Khan SU, Nasir F, et al. A systematic review and Bayesian network meta-analysis of **risk of intracranial hemorrhage with direct oral anticoagulants**. J Thromb Haemost. 2018 Jul;16(7):1296-1306.
2102. Bala MM, Paszek E, Lesniak W, et al. **Antiplatelet and anticoagulant agents for primary prevention of thrombosis** in individuals with antiphospholipid antibodies. Cochrane Database Syst Rev. 2018 Jul 13;7:CD012534. There is insufficient evidence to demonstrate benefit or harm of using anticoagulants with or without ASA versus ASA alone in people with aPL antibodies and a history of recurrent pregnancy loss and with no such history; AA versus placebo in people with aPL antibodies; and ASA with LMWH versus placebo or IVIG, and ASA with high-dose LMWH versus ASA with low-dose LMWH or UFH, in women with aPL antibodies and a history of recurrent pregnancy loss, for the primary prevention of thrombotic events. In a mixed population of people with a history of previous pregnancy loss and without such a history treated with anticoagulant combined with ASA, the incidence of minor bleeding (nasal bleeding, menorrhagia) was increased when compared with ASA alone. Studies that are adequately powered and that focus mainly on thrombotic events are needed to draw any firm conclusions on the primary prevention of thrombotic events in people with antiphospholipid antibodies.
2103. Beiswenger AC, Jo A, Harth K, et al. A systematic review of the efficacy of **aspirin monotherapy versus other antiplatelet therapy regimens** in peripheral arterial disease. J Vasc Surg. 2018 Jun;67(6):1922-1932.e6.
2104. Donadini MP, Bellesini M, Squizzato A. **Aspirin Plus Clopidogrel vs Aspirin Alone** for Preventing Cardiovascular Events Among Patients at High Risk for Cardiovascular Events. JAMA. 2018 Jul 26.
2105. Kuijpers T, Spencer FA, Siemieniuk RAC, et al. **Patent foramen ovale closure, antiplatelet therapy or anticoagulation therapy** alone for management of cryptogenic stroke? A clinical practice guideline. BMJ. 2018 Jul 25;362:k2515.
2106. Kuramatsu JB, Sembill JA, Gerner ST, et al. Management of **therapeutic anticoagulation in patients with intracerebral haemorrhage** and mechanical heart valves. Eur Heart J. 2018 May 14;39(19):1709-1723.
2107. Pengo V, Denas G, Zoppellaro G, et al. **Rivaroxaban vs warfarin** in high-risk patients with antiphospholipid syndrome. Blood. 2018 Jul 12.
2108. Tsivgoulis G, Katsanos AH, Mavridis D, et al. **Intravenous Thrombolysis for Ischemic Stroke Patients on Dual Antiplatelets**. Ann Neurol. 2018 Jul 26.
2109. Vasanthamohan L, Boonyawat K, Chai-Adisaksopha C, et al. **Reduced-dose direct oral anticoagulants in the extended treatment of venous thromboembolism**: a systematic review and meta-analysis. J Thromb Haemost. 2018 Jul;16(7):1288-1295.
2110. Biccard BM, Sigamani A, Chan MTV, et al. **Effect of aspirin in vascular surgery in patients from a randomized clinical trial (POISE-2).** Br J Surg. 2018 Jul 18.
2111. Boulanger JM, Lindsay MP, Gubitz G, et al; Acute Stroke Management Best Practice Writing Group, pdf and the Canadian Stroke Best Practices and Quality Advisory Committees; in collaboration with the Canadian Stroke Consortium and the Canadian Association of Emergency Physicians. Canadian Stroke Best Practice recommendations for acute stroke management: prehospital, emergency department, and acute inpatient stroke care, 6th edition, update 2018. Int J Stroke 2018. http://www.strokebestpractices.ca/wp-content/uploads/2018/07/Acute-Stroke-Management-EN.pdf
2112. Huang WY, Singer DE, Wu YL, et al. Association of Intracranial Hemorrhage Risk With Non-Vitamin K Antagonist Oral Anticoagulant Use vs Aspirin Use: A Systematic Review and Meta-Analysis. JAMA Neurol. 2018 Aug 13.
2113. Ladhani NNN, Swartz RH, Foley N, et al; Heart and Stroke Foundation Canadian Stroke Best Practice and Quality Advisory Committees; Canadian Stroke Consortium. Canadian Stroke Best Practice consensus statement: acute stroke management during pregnancy. Int J Stroke 2018 http://www.strokebestpractices.ca/wp-content/uploads/2018/07/Acute-Stroke-Management-during-Pregnancy-EN.pdf (accessed August 7, 2018).
2114. Mujaj B, Bos D, Muka T, et al. **Antithrombotic treatment is associated with intraplaque haemorrhage in the atherosclerotic carotid artery: a cross-sectional analysis of The Rotterdam Study.** Eur Heart J. 2018 Jul 27.
2115. Wong KSL, Amarenco P, Albers GW, et al. Efficacy and Safety of Ticagrelor in Relation to Aspirin Use Within the Week Before Randomization in the SOCRATES Trial. Stroke. 2018 Jul;49(7):1678-1685.
2116. ACOG Committee Opinion No. 743: **Low-Dose Aspirin Use During Pregnancy**. Obstet Gynecol. 2018 Jul;132(1):e44-e52.
2117. ASCEND Study Collaborative Group. **Effects of Aspirin for Primary Prevention in Persons with Diabetes Mellitus**. N Engl J Med. 2018 Aug 26.

2118. Bath PM, Woodhouse LJ, Appleton JP, et al. **Triple versus guideline antiplatelet therapy to prevent recurrence after acute ischaemic stroke or transient ischaemic attack**: the TARDIS RCT. Health Technol Assess. 2018 Aug;22(48):1-76.
2119. Bhalla V, Abdel-Latif A, Bhalla M, et al. Meta-Analysis Comparing the Efficacy, Safety, and Cost-Benefit of Direct Acting **Oral Anticoagulants Versus Enoxaparin Thromboprophylaxis to Prevent Venous Thromboembolism** Among Hospitalized Patients. Am J Cardiol. 2018 Jul 5.
2120. Can A, Rudy RF, Castro VM, et al. Association between **aspirin dose and subarachnoid hemorrhage from saccular aneurysms**: A case-control study. Neurology. 2018 Sep 18;91(12):e1175-e1181.
2121. Donadini MP, Bellesini M, Squizzato A. **Aspirin Plus Clopidogrel vs Aspirin Alone for Preventing Cardiovascular Events** Among Patients at High Risk for Cardiovascular Events. JAMA. 2018 Aug 14;320(6):593-594.
2122. Generalova D, Cunningham S, Leslie SJ, et al. A systematic review of clinicians' views and experiences of **direct-acting oral anticoagulants in the management of non-valvular atrial fibrillation**. Br J Clin Pharmacol. 2018 Aug 15.
2123. Hornor MA, Duane TM, Ehlers AP, et al. **American College of Surgeons' Guidelines for the Perioperative Management of Antithrombotic Medication**. J Am Coll Surg. 2018 Aug 23.
2124. Huppertz A, Werntz L, Meid AD, et al. **Rivaroxaban and macitentan can be co-administered without dose adjustment but the combination of rivaroxaban and St. John´s Wort should be avoided**. Br J Clin Pharmacol. 2018 Sep 7.
2125. Kido K, Ngorsuraches S. Comparing the Efficacy and Safety **of Direct Oral Anticoagulants With Warfarin in the Morbidly Obese Population With Atrial Fibrillation**. Ann Pharmacother. 2018 Aug 22:1060028018796604.
2126. Levy JH, Douketis J, Steiner T, et al. **Prothrombin Complex Concentrates for Perioperative Vitamin K Antagonist and Non-vitamin K Anticoagulant Reversal**. Anesthesiology. 2018 Aug 29.
2127. Lip GYH, Banerjee A, Boriani G, et al. **Antithrombotic Therapy for Atrial Fibrillation**: CHEST Guideline and Expert Panel Report. Chest. 2018 Aug 21.
2128. Lip GYH, Collet JP, Haude M, Huber K. **Management of antithrombotic therapy in AF patients presenting with ACS and/or undergoing PCI**: A Summary of the Joint Consensus Document of the European Heart Rhythm Association (EHRA), European Society of Cardiology Working Group on Thrombosis, European Association of Percutaneous Cardiovascular Interventions (EAPCI) and European Association of Acute Cardiac Care (ACCA) endorsed by the Heart Rhythm Society (HRS), Asia-Pacific Heart Rhythm Society (APHRS), Latin America Heart Rhythm Society (LAHRS), and Cardiac Arrhythmia Society of Southern Africa (CASSA). Eur Heart J. 2018 Aug 14;39(31):2847-2850.
2129. McNeil JJ, Woods RL, Nelson MR, et al**. Effect of Aspirin on Disability-free Survival in the Healthy Elderly**. (ASPREE) N Engl J Med. 2018 Sep 16.
2130. McNeil JJ, Wolfe R, Woods RL, et al. **Effect of Aspirin on Cardiovascular Events and Bleeding in the Healthy Elderly**. (ASPREE) N Engl J Med. 2018 Sep 16.
2131. McNeil JJ, Nelson MR, Woods RL, et al. **Effect of Aspirin on All-Cause Mortality in the Healthy Elderly**. (ASPREE) N Engl J Med. 2018 Sep 16.
2132. Sengupta N, Marshall AL, et al. **Rebleeding vs Thromboembolism** After Hospitalization for Gastrointestinal Bleeding in Patients on Direct Oral Anticoagulants. Clin Gastroenterol Hepatol. 2018 May 15.
2133. Spyropoulos AC, Ageno W, Albers GW, et al. **Rivaroxaban for Thromboprophylaxis after Hospitalization for Medical Illness**. (Mariner) N Engl J Med. 2018 Aug 26.
2134. Tsivgoulis G, Goyal N, Kerro A, et al. **Dual antiplatelet therapy pretreatment in IV thrombolysis for acute ischemic stroke**. Neurology. 2018 Sep 11;91(11):e1067-e1076.
2135. Zannad F, Anker SD, Byra WM, et al. **Rivaroxaban in Patients with Heart Failure, Sinus Rhythm, and Coronary Disease**. (Commander HF) N Engl J Med. 2018 Aug 27.
2136. Andrikopoulou M, Purisch SE, Handal-Orefice R, et al. **Low-dose aspirin is associated with reduced spontaneous preterm birth in nulliparous women**. Am J Obstet Gynecol. 2018 Oct;219(4):399.e1-399.e6.
2137. ASCEND Study Collaborative Group. Effects of **Aspirin for Primary Prevention in Persons with Diabetes Mellitus**. N Engl J Med. 2018 Aug 26.
2138. Barnard ME, Poole EM, Curhan GC, et al. Association of **analgesic use with risk of ovarian cancer** in the Nurses' Health Studies [online Oct 4, 2018]. JAMA Oncol.
2139. Gaziano JM, Brotons C, Coppolecchia R, et al. Use of **aspirin to reduce risk of initial vascular events** in patients at moderate risk of cardiovascular disease (ARRIVE): a randomised, double-blind, placebo-controlled trial. Lancet. 2018 Sep 22;392(10152):1036-1046.
2140. MHRA Oct/18**: Rivaroxaban (Xarelto▼) after transcatheter aortic valve replacement**: increase in all-cause mortality, thromboembolic and bleeding events in a clinical trial.
2141. Simon TG, Ma Y, Ludvigsson JF, et al. Association between aspirin use and risk of hepatocellular carcinoma [online Oct 4, 2018]. JAMA Oncol.
2142. Spyropoulos AC, Ageno W, Albers GW, et al; **MARINER** Investigators. **Rivaroxaban** for **Thromboprophylaxis** after **Hospitalization for Medical Illness**. N Engl J Med. 2018 Sep 20;379(12):1118-1127.
2143. Zannad F, Anker SD, Byra WM, et al; **COMMANDER** HF. **Rivaroxaban** in Patients with **Heart Failure**, Sinus Rhythm, and Coronary Disease. N Engl J Med. 2018 Aug 27.
2144. Fuller GW, Evans R, Preston L, et al. Should Adults With Mild **Head Injury** Who Are Receiving Direct Oral Anticoagulants Undergo **Computed Tomography** Scanning? A Systematic Review. Ann Emerg Med 2018 Sep 17.
2145. Hood BR, Cowen ME, Zheng HT, et al. Association of **aspirin** with prevention of **venous thromboembolism** in patients **after total knee arthroplasty** compared with other anticoagulants: a non-inferiority analysis [online Oct 17, 2018]. JAMA Surg. doi:10.1001/jamasurg.2018.3858
2146. Kedhi E, Fabris E, van der Ent M, et al. **Six months versus 12 months dual antiplatelet therapy** after drug-eluting stent implantation in ST-elevation myocardial infarction (DAPT-STEMI): randomised, multicentre, non-inferiority trial. BMJ. 2018 Oct 2;363:k3793.
2147. Kyaw MH, Otani K, Ching JYL, et al. **Misoprostol Heals Small Bowel Ulcers in Aspirin Users** With Small Bowel Bleeding. Gastroenterology. 2018 Oct;155(4):1090-1097.e1.
2148. Nazha B, Pandya B, Cohen J, et al. **Periprocedural Outcomes** of Direct Oral Anticoagulants vs. Warfarin in Non-Valvular Atrial Fibrillation: A Meta-analysis of Phase III Trials. Circulation. 2018 May 24
2149. Tsivgoulis G, Wilson D, Katsanos AH, et al. **Neuroimaging and clinical outcomes of** oral anticoagulant associated **ICH.** Ann Neurol. 2018 Sep 26.
2150. Tritschler T, Kraaijpoel N, Le Gal G, Wells PS. **Venous Thromboembolism: Advances** in Diagnosis and Treatment. JAMA. 2018 Oct 16;320(15):1583-1594.
2151. Aimo A, Giugliano RP, De Caterina R. **Non-Vitamin K Antagonist Oral Anticoagulants** for Mechanical Heart Valves. Circulation. 2018 Sep 25;138(13):1356-1365.
2152. Bonello L, Laine M, Lemesle G, et al. Meta-Analysis of **Potent P2Y12-ADP Receptor Antagonist** Therapy Compared to **Clopidogrel Therapy** in Acute Coronary Syndrome Patients with Chronic Kidney Disease. Thromb Haemost. 2018 Oct;118(10):1839-1846.
2153. Chang TY, Liao JN, Chao TF, et al. **Oral anticoagulant use** for **stroke prevention** in atrial fibrillation patients with difficult scenarios. Int J Cardiol Heart Vasc. 2018 Aug 31;20:56-62.
2154. De T, Alarcon C, Hernandez W, et al. Association of **Genetic Variants With Warfarin-Associated Bleeding** Among Patients of African Descent. JAMA. 2018 Oct 23;320(16):1670-1677.
2155. Hylek EM. **Apixaban** for End-Stage Kidney Disease. Circulation. 2018 Oct 9;138(15):1534-1536.
2156. Pristipino C, Sievert H, D'Ascenzo F, et al; Evidence Synthesis Team ; Eapci Scientific Documents and Initiatives Committee ; International Experts . European position paper on the management of patients with **patent foramen ovale**. General approach and left circulation thromboembolism. Eur Heart J. 2018 Oct 25.
2157. Shah R, Rao SV, Latham SB, Kandzari DE. **Efficacy and safety of drug-eluting stents** optimized for biocompatibility vs bare-metal stents with a single month of dual antiplatelet therapy: a meta-analysis [online Oct 31, 2018]. JAMA Cardiol.
2158. Åstrand M, Amilon C, Röshammar D, et al. Pharmacokinetic-pharmacodynamic modelling **of platelet response to ticagrelor** in stable coronary artery disease and prior myocardial infarction patients. Br J Clin Pharmacol. 2018 Nov 10.
2159. Bawa H, Weick JW, Dirschl DR, Luu HH. Trends in Deep Vein Thrombosis Prophylaxis and Deep Vein Thrombosis **Rates After Total Hip and Knee Arthroplasty**. J Am Acad Orthop Surg. 2018 Oct 1;26(19):698-705.
2160. Blin P, Dureau-Pournin C, Cottin Y, et al. Effectiveness and safety of **110 or 150 mg dabigatran versus vitamin K** antagonists in non-valvular atrial fibrillation. Br J Clin Pharmacol. 2018 Nov 13.
2161. Franck B, Dulaurent S, El Balkhi S, et al. **Self-poisoning with 60 tablets of Apixaban**, a pharmacokinetics case report. Br J Clin Pharmacol. 2018 Nov 12.
2162. Hull MA, Sprange K, Hepburn T, et al; seAFOod Collaborative Group. **Eicosapentaenoic acid and aspirin**, alone and in combination, for the **prevention of colorectal adenomas** (seAFOod Polyp Prevention trial): a multicentre, randomised, double-blind, placebo-controlled, 2 × 2 factorial trial. Lancet. 2018 Nov 19.

2163. Mueller T, Alvarez-Madrazo S, Robertson C, et al. Comparative **safety and effectiveness of direct oral anticoagulants** in patients with atrial fibrillation in clinical practice in Scotland. Br J Clin Pharmacol. 2018 Nov 13.
2164. Ruiz Ortiz M, Muñiz J, Raña Míguez P, et al; FANTASIIA study investigators . **Inappropriate doses** of direct oral anticoagulants in real-world clinical practice: prevalence and associated factors. A subanalysis of the FANTASIIA Registry. Europace. 2018 Oct 1;20(10):1577-1583.
2165. Essien UR, Holmes DN, Jackson LR 2nd, et al. Association of **Race/Ethnicity With Oral Anticoagulant Use in Patients With Atrial Fibrillation**: Findings From the Outcomes Registry for Better Informed Treatment of Atrial Fibrillation II. JAMA Cardiol. 2018 Nov 28.
2166. Grant PJ. Web Exclusive. Annals for Hospitalists Inpatient Notes - How I Changed My Practice-**Perioperative Bridging Anticoagulation**. Ann Intern Med. 2018 Nov 20;169(10):HO2-HO3
2167. Pignone M, DeWalt DA. More Evidence to Help Guide **Decision Making About Aspirin for Primary Prevention**. Ann Intern Med. 2018 Nov 27.
2168. Reisman AM, Robbins BT, Chou DE, et al. Ticagrelor for Refractory Migraine/Patent Foramen Ovale (**TRACTOR)**: An open-label pilot study. Neurology. 2018 Nov 27;91(22):1010-1017.
2169. Seiffge DJ, Werring DJ, Paciaroni M, et al. **Timing of anticoagulation after recent ischaemic stroke** in patients with atrial fibrillation. Lancet Neurol. 2018 Nov 8.
2170. Sommer RJ, Nazif T, Privitera L, Robbins BT. Retrospective review of **thienopyridine therapy in migraineurs with patent foramen ovale**. Neurology. 2018 Nov 27;91(22):1002-1009.
2171. Borre ED, Goode A, Raitz G, et al. Predicting Thromboembolic and Bleeding Event Risk in Patients with **Non-Valvular Atrial Fibrillation**: A Systematic Review. Thromb Haemost. 2018 Oct 30.
2172. Carrier M, Abou-Nassar K, Mallick R, et al; AVERT Investigators. **Apixaban to Prevent Venous Thromboembolism** in Patients with Cancer. N Engl J Med. 2018 Dec 4.
2173. Schunemann HJ, Cushman M, Burnett AE, et al. American Society of Hematology 2018 guidelines for management of venous thromboembolism: **prophylaxis for hospitalized and nonhospitalized medical patients.** Blood Adv. 2018 Nov 27;2(22):3198-3225.
2174. Bikdeli B, Wang Y, Jimenez D, et al. Association of **Inferior Vena Cava Filter Use With Mortality Rates in Older Adults With Acute Pulmonary Embolism**. JAMA Intern Med. 2018 Dec 10.
2175. Haut ER, Aboagye JK, Shaffer DL, et al. **Effect of Real-time Patient-Centered Education Bundle on Administration of Venous Thromboembolism Prevention in Hospitalized Patients**. JAMA Netw Open. 2018;1(7):e184741.
2176. Mentias A, Shantha G, Chaudhury P, et al. Assessment of Outcomes of Treatment With **Oral Anticoagulants in Patients With Atrial Fibrillation and Multiple Chronic Conditions** A Comparative Effectiveness Analysis. JAMA Netw Open. 2018;1(5):e182870.
2177. O'Neal WT, Claxton JS, Sandesara PB, et al. **Provider Specialty, Anticoagulation, and Stroke Risk in Patients With Atrial Fibrillation and Cancer**.J Am Coll Cardiol. 2018 Oct 16;72(16):1913-1922.
2178. Pettinari I, Vukotic R, Stefanescu H, et al; **VALDIG-BO** (Vascular Liver Disease Interest study Group-Bologna) members Collaborators in this study:. Clinical Impact and Safety of Antic**oagulants for Portal Vein Thrombosis in Cirrhosis**. Am J Gastroenterol. 2018 Dec 11.
2179. Ray WA, Chung CP, Murray KT, et al. Association of **Oral Anticoagulants and Proton Pump Inhibitor Cotherapy With Hospitalization for Upper Gastrointestinal Tract Bleeding**. JAMA. 2018 Dec 4;320(21):2221-2230.
2180. Sholzberg M, Xu Y. **Coagulation Test Interpretation in a Patient Taking Direct Oral Anticoagulant Therapy**. JAMA. 2018 Oct 9;320(14):1485-1486.
2181. Åstrand M, Amilon C, Röshammar D, et al. **Pharmacokinetic-pharmacodynamic modelling of platelet response to ticagrelor** in stable coronary artery disease and prior myocardial infarction patients. Br J Clin Pharmacol. 2018 Nov 10.
2182. Blin P, Dureau-Pournin C, Cottin Y, et al. **Effectiveness and safety of 110 or 150 mg dabigatran vs. vitamin K antagonists i**n nonvalvular atrial fibrillation. Br J Clin Pharmacol. 2018 Nov 13.
2183. FDA Dec/18: CoaguChek XS PT Test Strips by Roche Diagnostics: **Found to Inaccurately Report High INR (International Normalized Ratio**) Test Results was just added to the FDA Recalls webpage.
2184. Hao Q, Tampi M, O'Donnell M, et al. **Clopidogrel plus aspirin versus aspirin alone for acute minor ischaemic stroke** or high risk transient ischaemic attack: systematic review and meta-analysis. BMJ. 2018 Dec 18;363:k5108.
2195. Health Canada Dec/18: Important Safety Information – **XARELTO (rivaroxaban**) - **Increase in all-cause mortality, thromboembolic and bleeding events in patients** after transcatheter aortic valve replacement - Bayer Inc.
2186. Prasad K, Siemieniuk R, Hao Q, et al. **Dual antiplatelet therapy with aspirin and clopidogrel for acute high risk transient ischaemic attack and minor ischaemic** stroke: a clinical practice guideline. BMJ. 2018 Dec 18;363:k5130.
2187. Ruiz Vargas E, Sposato LA, Lee SAW, et al. **Anticoagulation Therapy for Atrial Fibrillation in Patients With Alzheimer's Disease**. Stroke. 2018 Dec;49(12):2844-2850.
2188. Wang CL, Wu VC, Kuo CF, et al. **Efficacy and Safety of Non-Vitamin K Antagonist Oral Anticoagulants in Atrial Fibrillation** Patients With Impaired Liver Function: A Retrospective Cohort Study. J Am Heart Assoc. 2018 Aug 7;7(15):e009263.
2189. Bravata DM, Coffing JM, Kansagara D, et al. Association Between Antithrombotic Medication Use After **Bioprosthetic Aortic Valve Replacement** and Outcomes in the Veterans Health Administration System. JAMA Surg. 2018 Dec 26:e184679.
2190. Chen J-Y, He P-C, Liu Y-H, et al. Association of parenteral anticoagulation therapy with outcomes in Chinese patients undergoing **percutaneous coronary intervention for non–ST-segment elevation acute coronary syndrome** [online Dec 28, 2018]. JAMA Intern Med.
2191. Janion-Sadowska A, Chrapek M, Konieczyńska M, Undas A. **Altered Fibrin Clot Properties Predict Stroke and Bleedings** in Patients With Atrial Fibrillation on Rivaroxaban. Stroke. 2018 Nov 21 :STROKEAHA118023712.
2192. Matsumura-Nakano Y, Shizuta S, Komasa A, et al. An Open-Label Randomized Trial **Comparing Oral Anticoagulation with and without Single Antiplatelet Therapy** in Patients with Atrial Fibrillation and Stable Coronary Artery Disease Beyond One Year after Coronary Stent Implantation: The OAC-ALONE Study. Circulation. 2018 Sep 24.
2193. Hackam DG, Spence JD. Antiplatelet Therapy in **Ischemic Stroke and Transient Ischemic Attack**. Stroke. 2019 Jan 10:STROKEAHA118023954.
2194. Mahmoud AN, Gad MM, Elgendy AY, et al. Efficacy and safety of **aspirin for primary prevention of cardiovascular events**: a meta-analysis and trial sequential analysis of randomized controlled trials. Eur Heart J. 2018 Dec 17.
2195. Miller EC, Boehme AK, Chung NT, et al. **Aspirin** reduces long-term risk in women **with prior hypertensive disorders of pregnancy**. Neurology. 2018 Dec 26.
2196. Wang KL, Lopes RD, Patel MR, et al. Efficacy and safety of reduced-dose **non-vitamin K antagonist oral anticoagulants in patients with atrial fibrillation**: a meta-analysis of randomized controlled trials. Eur Heart J. 2018 Dec 22
2197. Wang TY, Kaltenbach LA, Cannon CP, et al. Effect of **medication co-payment vouchers on P2Y12 inhibitor use and major adverse cardiovascular events** among patients with myocardial infarction: the ARTEMIS randomized clinical trial [Jan 8, 2018]. JAMA. doi:10.1001/jama.2018.19791
2198. Bhattarai M, Hudali T, Robinson R, et al. Impact of **oral anticoagulants on 30-day readmissio**n: a study from a single academic centre. BMJ Evid Based Med. 2019 Feb;24(1):10-14.
2199. Leclerc J, Blais C, Rochette L, et al. Trends in Hospital Visits for **Generic and Brand-Name Warfarin Users** in Québec, Canada: A Population-Based Time Series Analysis. Am J Cardiovasc Drugs. 2018 Nov 24.
2200. Lüscher TF. **Myocardial revascularization**: guideline-based therapy today. Eur Heart J. 2019 Jan 7;40(2):75-78.
2201. Massicotte-Azarniouch D, Sood MM. Uncertainty surrounds **anticoagulation risks and benefits in patients with chronic kidney disease with atrial fibrillation**. BMJ Evid Based Med. 2019 Feb;24(1):35-36.
2202. Miller EC, Boehme AK, Chung NT, et al. **Aspirin reduces long-term stroke risk in women** with prior **hypertensive disorders of pregnancy**. Neurology 2019;92:e305–e316.
2203. Shin JI, Secora A, Alexander GC, et al. Risks and Benefits of **Direct Oral Anticoagulants across the Spectrum of GFR among** Incident and Prevalent Patients with Atrial Fibrillation. Clin J Am Soc Nephrol. 2018 Aug 7;13(8):1144-1152.

2204. Young A.M., Marshall A., Thirlwall J. et al. Comparison of an **oral factor Xa inhibitor with low molecular weight heparin in patients with cancer** with venous thromboembolism: results of a randomized trial (**SELECT-D**). J Clin Oncol. 2018.
2205. Zhang C, Gu ZC, Ding Z, et al. Decreased risk of **renal impairment in atrial fibrillation patients receiving non-vitamin K antagonist oral anticoagulants**: A pooled analysis of randomized controlled trials and real-world studies. Thromb Res. 2018 Dec 6;174:16-23.
2206. Zheng SL, Roddick AJ. Association of **aspirin use for primary prevention with cardiovascular events and bleeding events**: a systematic review and meta-analysis [Jan 22, 2019]. JAMA. doi:10.1001/jama.2018.20578
2207. Al-Sofiani ME, Yanek LR, Faraday N, et al. Diabetes and Platelet Response to Low-Dose Aspirin. J Clin Endocrinol Metab. 2018 Dec 1;103(12):4599-4608.
2208. Arabi YM, Al-Hameed F, Burns KEA, et al; Saudi Critical Care Trials Group. Adjunctive Intermittent **Pneumatic Compression for Venous Thromboprophylaxis**. N Engl J Med. 2019 Feb 18
2209. Connolly SJ, Crowther M, Eikelboom JW, et al; ANNEXA-4 Investigators. Full Study Report of Andexanet Alfa for **Bleeding Associated with Factor Xa Inhibitors**. N Engl J Med. 2019 Feb 7.
2210. Douros A, Renoux C, Yin H, et al. Concomitant Use of Direct Oral Anticoagulants with Antiplatelet Agents and the Risk of Major **Bleeding in Patients with Nonvalvular Atrial Fibrillation**. Am J Med. 2019 Feb;132(2):191-199.e12.
2211. Guo CG, Chen L, Chan EW, et al. Systematic review with meta-analysis: the risk of gastrointestinal bleeding in patients taking **third-generation P2Y(12) inhibitors compared with clopidogrel**. Aliment Pharmacol Ther. 2019 Jan;49(1):7-19.
2212. Hong L, Cheng X, Lin L, et al; INSPIRE Study Group. The **Blood Pressure Paradox** in Acute Ischemic Stroke. Ann Neurol. 2019 Feb 5
2213. Khorana AA, Soff GA, Kakkar AK, et al; CASSINI Investigators. **Rivaroxaban** for Thromboprophylaxis in High-Risk Ambulatory Patients with Cancer. N Engl J Med. 2019 Feb 21;380(8):720-728.
2214. Lin AM, Lin MP, Markovic D, et al. Less Than Ideal. Stroke. 2018 Dec 7:STROKEAHA118022644.
2215. Nastasi DR, Smith JR, Moxon JV, et al. Prescription of Pharmacotherapy and the Incidence of Stroke in Patients With Symptoms of **Peripheral Artery Disease**. Stroke. 2018 Dec;49(12):2953-2960.
2216. Pan Y, Chen W, Wang Y, et al;(CHANCE) Investigators. Association Between **ABCB1 Polymorphisms and Outcomes of Clopidogrel Treatment** in Patients With Minor Stroke or Transient Ischemic Attack: Secondary Analysis of a Randomized Clinical Trial. JAMA Neurol. 2019 Feb 11.
2217. van Rein N, Heide-Jørgensen U, Lijfering WM, et al. Major **Bleeding Rates in Atrial Fibrillation Patients** on Single, Dual, or Triple Antithrombotic Therapy. Circulation. 2019 Feb 5;139(6):775-786
2218. Varbo A, Nordestgaard BG. **Remnant cholesterol and risk of ischemic stroke** in 112,512 individuals from the general population. Ann Neurol. 2019 Feb 5.
2219. Arabi YM, Al-Hameed F, Burns KEA, et al. **Adjunctive Intermittent Pneumatic Compression for Venous Thromboprophylaxis**. N Engl J Med. 2019 Feb 18.
2220. Baumgartner C, de Kouchkovsky I, Whitaker E, Fang MC. **Periprocedural Bridging in Patients with Venous Thromboembolism**: A Systematic Review. Am J Med. 2019 Jan 16.
2221. Lamy A, Eikelboom J, Sheth T, et al. **Rivaroxaban, Aspirin, or Both to Prevent Early Coronary Bypass Graft Occlusion**: The COMPASS-CABG Study. J Am Coll Cardiol. 2019 Jan 22;73(2):121-130.
2222. Selak V, Jackson R, Poppe K, et al. **Predicting bleeding risk to guide aspirin use for the primary prevention of cardiovascular disease**. A cohort study. Ann Intern Med. 2019. [Epub ahead of print].
2223. Baumgartner C, de Kouchkovsky I, Whitaker E, Fang MC. **Periprocedural Bridging** in Patients with Venous Thromboembolism: A Systematic Review. Am J Med. 2019 Jan 16.
2224. Kang J, Park KW, Palmerini T, et al. **Racial Differences in Ischaemia/Bleeding** Risk Trade-Off during Anti-Platelet Therapy: Individual Patient Level Landmark Meta-Analysis from Seven RCTs. Thromb Haemost. 2019 Jan;119(1):149-162.
2225. Markus HS, Levi C, King A, et al. Antiplatelet Therapy vs Anticoagulation Therapy in **Cervical Artery Dissection**: The Cervical Artery Dissection in Stroke Study (CADISS) Randomized Clinical Trial Final Results. JAMA Neurol. 2019 Feb 25.
2226. Nishtala PS, Jamieson HA, Hanger HC, et al. Examining the **Risks of Major Bleeding Events in Older People** Using Antithrombotics. Cardiovasc Drugs Ther. 2019 Mar 2.
2227. Dawwas GK, Brown J, Dietrich E, Park H. Effectiveness and safety of **apixaban versus rivaroxaban for prevention of recurrent venous thromboembolism** and adverse bleeding events in patients with venous thromboembolism: a retrospective population-based cohort analysis. Lancet Haematol. 2019 Jan;6(1):e20-e28.
2228. Oakland K, Chadwick G, East JE, et al. Diagnosis and management of **acute lower Gastrointestinal bleeding**: guidelines from the British Society of Gastroenterology. Gut. 2019 Feb 12.
2229. Oldgren J, Steg PG, Hohnloser SH, et al. **Dabigatran dual therapy with ticagrelor or clopidogrel after percutaneous coronary intervention in atrial fibrillation** patients with or without acute coronary syndrome: a subgroup analysis from the RE-DUAL PCI trial. Eur Heart J. 2019 Feb 21.
2230. Schaefer JK, Li Y, Gu X, et al. Association of **Adding Aspirin to Warfarin Therapy** Without an Apparent Indication With Bleeding and Other Adverse Events. JAMA Intern Med. 2019 Mar 4.
2231. Seiffge DJ, Curtze S, Dequatre-Ponchelle N, et al. Hematoma location and morphology of **anticoagulation-associated intracerebral hemorrhage**. Neurology. 2019 Feb 19;92(8):e782-e791.
2232. Sharma M, Hart RG, Connolly SJ, et al. **Stroke Outcomes in the COMPASS Trial**. Circulation. 2019 Feb 26;139(9):1134-1145.
2233. Skriver C, Dehlendorff C, Borre M, et al. Use of **low-dose aspirin and mortality after prostate cancer diagnosis**: a nationwide cohort study. Ann Intern Med. 2019. [Epub ahead of print]. doi:10.7326/M17-3085
2234. Ye S, Lee M, Lee D, Ha EH, Chun EM. Association of Long-term Use of Low**-Dose Aspirin as Chemoprevention With Risk of Lung Cancer**. JAMA Netw Open. 2019 Mar 1;2(3):e190185.
2235. Arnett DK, Blumenthal RS, Albert MA, et al. **2019 ACC/AHA Guideline** on the Primary Prevention of Cardiovascular Disease: Executive Summary. J Am Coll Cardiol. 2019 Mar 7.
2236. Berwanger O, Lopes RD, Moia DDF, et al. **Ticagrelor versus Clopidogrel in Patients with STEMI Treated with Fibrinolytic Therapy**: TREAT Trial. J Am Coll Cardiol. 2019 Mar 12.
2237. Bhatt DL, Pollack CV, Weitz JI, et al. **Antibody-Based Ticagrelor Reversal Agent** in Healthy Volunteers. N Engl J Med. 2019 Mar 17.
2237. Chan FKL, Kyaw MH, Hsiang JC, et al. **Risk of Postpolypectomy Bleeding With Uninterrupted Clopidogrel Therapy** in an Industry-Independent, Double-Blind, Randomized Trial. Gastroenterology. 2019 Mar;156(4):918-925.e1.
2238. Elsebaie MAT, van Es N, Langston A, et al. Direct **oral anticoagulants in patients with venous thromboembolism and thrombophilia**: a systematic review and meta-analysis. J Thromb Haemost. 2019 Feb 25.
2239. Franchi F, James SK, Ghukasyan Lakic T, et al. Impact of **Diabetes Mellitus and Chronic Kidney Disease** on Cardiovascular Outcomes and Platelet P2Y(12) Receptor Antagonist Effects in Patients With Acute Coronary Syndromes: Insights From the PLATO Trial. J Am Heart Assoc. 2019 Mar 19;8(6):e011139.
2240. Lopes RD, Heizer G, Aronson R, et al. Antithrombotic therapy after **acute coronary syndrome or PCI in atrial fibrillation**. (AUGUSTUS-apixaban, warfarin) N Engl J Med. DOI: 10.1056/NEJMoa1817083.
2241. Firnhaber JM, Powell CS. **Lower Extremity Peripheral Artery Disease**: Diagnosis and Treatment. Am Fam Physician. 2019; 99(6): 362-369.
2242. Barow E, Boutitie F, Cheng B, et al. Functional **Outcome of Intravenous Thrombolysis** in Patients With Lacunar Infarcts in the **WAKE-UP Trial**. JAMA Neurol. 2019 Mar 25.
2243. Brings A, Lehmann ML, Foerster KI, et al. Perpetrator effects of **ciclosporin (P-glycoprotein inhibitor) and its combination with fluconazole (CYP3A inhibitor) on the pharmacokinetics of rivaroxaban** in healthy volunteers. Br J Clin Pharmacol. 2019 Mar 25.
2244. Erskine D. **DOAC dosing in renal impairment**. Drug Ther Bull. 2019 Apr;57(4):50.
2245. Georgakis MK, Duering M, Wardlaw JM, Dichgans M. **WMH and long-term outcomes in ischemic stroke**: A systematic review and meta-analysis. Neurology. 2019 Mar 19;92(12):e1298-e1308.
2246. Helin TA, Joutsi-Korhonen L, Asmundela H, et al. Warfarin dose **requirement in patients having severe thrombosis or thrombophilia**. Br J Clin Pharmacol. 2019 Apr 1.
2247. Jickling GC, Kittner SJ. **A SNP-it of stroke outcome**. Neurology. 2019 Mar 19;92(12):549-550.
2248. Little D, Chai-Adisaksopha C, Hillis C, et al. Resumption of anticoagulant **therapy after anticoagulant-related gastrointestinal bleeding**: A systematic review and meta-analysis. Thromb Res. 2019 Mar;175:102-109.
2249. Söderholm M, Pedersen A, Lorentzen E, et al. Genome-wide association meta-analysis of **functional outcome after ischemic stroke**. Neurology. 2019 Mar 19;92(12):e1271-e1283.

2250. Chan FKL, Kyaw MH, Hsiang JC, et al. Risk of **Postpolypectomy Bleeding With Uninterrupted Clopidogrel** Therapy in an Industry-Independent, Double-Blind, Randomized Trial. Gastroenterology. 2019 Mar;156(4):918-925.e1.

2251. Chan NC, Eikelboom JW. How I manage **anticoagulant therapy** in older individuals with **atrial fibrillation or venous thromboembolism**. Blood. 2019 Mar 29.
2252. Healey JS, Gladstone DJ, Swaminathan B, et al. **Recurrent Stroke With Rivaroxaban Compared With Aspirin According to Predictors of Atrial Fibrillation**: Secondary Analysis of the NAVIGATE ESUS Randomized Clinical Trial. JAMA Neurol. 2019 Apr 8.
2253. Khatib R, Ludwikowska M, Witt DM, et al. **Vitamin K for reversal of excessive vitamin K antagonist anticoagulation**: a systematic review and meta-analysis. Blood Adv. 2019 Mar 12;3(5):789-796.
2254. Lee TY, Hsu YC, Tseng HC, et al. Association of **Daily Aspirin Therapy With Risk of Hepatocellular Carcinoma in Patients With Chronic Hepatitis B**. JAMA Intern Med. 2019 Mar 18.
2255. Seiffge DJ, Paciaroni M, Wilson D, et al. **DOAC vs. VKA after recent ischemic stroke in patients with atrial fibrillation**. Ann Neurol. 2019 Apr 13.
2256. Sharma M, Hart RG, Connolly SJ, et al. **Stroke Outcomes in the COMPASS Trial**. Circulation. 2019 Feb 26;139(9):1134-1145.
2257. Valgimigli M. The remarkable story of a wonder drug, which now comes to an end in the primary prevention setting: **say bye-bye to aspirin**! Eur Heart J. 2019 Feb 14;40(7):618-620.
2258. Burlacu A, Genovesi S, Ortiz A, et al. Pros and cons of **antithrombotic therapy in end-stage kidney disease**: a 2019 update. Nephrol Dial Transplant. 2019 Mar 16.
2259. Lokhorst B, Rolfes L, Jessurun NT. **Interaction of OTC drug noscapine and acenocoumarol and phenprocoumon**. Br J Clin Pharmacol. 2019 May;85(5):1041-1043.
2260. Mahmoud AN, Gad MM, Elgendy AY, et al. **Efficacy and safety of aspirin for primary prevention of cardiovascular events**: a meta-analysis and trial sequential analysis of randomized controlled trials. Eur Heart J. 2019 Feb 14;40(7):607-617.
2261. Oakland K, Chadwick G, East JE, et al. **Diagnosis and management of acute lower Gastrointestinal bleeding**: guidelines from the British Society of Gastroenterology. Gut. 2019 Feb 12.
2262. Wright D, Nicolaides KH. **Aspirin delays the development of preeclampsia**. Am J Obstet Gynecol. 2019 Feb 21.
2263. Cuker A, Burnett A, Triller D, et al. **Reversal of direct oral anticoagulants**: Guidance from the Anticoagulation Forum. Am J Hematol. 2019 Mar 27.
2264. Greenberg B, Neaton JD, Anker SD, et al. Association of **Rivaroxaban With Thromboembolic Events** in Patients With Heart Failure, Coronary Disease, and Sinus Rhythm: A Post Hoc Analysis of the COMMANDER HF Trial. JAMA Cardiol. 2019 Apr 24.
2265. Komosa A, Lesiak M, Krasiński Z, et al. **Optimal Timing of P2Y12 Inhibitor Loading in Patients Undergoing PCI**: A Meta-Analysis. Thromb Haemost. 2019 Mar 27.
2266. Nogami A, Harada T, Sekiguchi Y, et al; ABRIDGE-J Investigators. Safety and Efficacy of **Minimally Interrupted Dabigatran vs Uninterrupted Warfarin** Therapy in Adults Undergoing Atrial Fibrillation Catheter Ablation: A Randomized Clinical Trial. JAMA Netw Open. 2019 Apr 5;2(4):e191994.
2267. Rahman H, Khan SU, Nasir F, et al. Optimal **Duration of Aspirin Plus Clopidogrel** After Ischemic Stroke or Transient Ischemic Attack. Stroke. 2019 Apr;50(4):947-953.
2267. Rossel A, Robert-Ebadi H, Combescure C, et al. Anticoagulant therapy for acute **venous thrombo-embolism in cancer patients**: A systematic review and network meta-analysis. PLoS One. 2019 Mar 21;14(3):e0213940.
2268. Almarshad F, Alaklabi A, Bakhsh E, et al. **Use of direct oral anticoagulants in daily practice**. Am J Blood Res. 2018 Dec 10;8(4):57-72.
2269. Arnold MJ, Keung JJ, McCarragher B**. Interventional Radiology**: Indications and Best Practices. Am Fam Physician. 2019 May 1;99(9):547-556.
2270. Hohnloser SH, Camm J, Cappato R, et al. Uninterrupted **edoxaban vs. vitamin K antagonists** for ablation of atrial fibrillation: the ELIMINATE-AF trial. Eur Heart J. 2019 Apr 11.
2271. Serenelli M, Pavasini R, Vitali F, et al. Efficacy and safety of alternative oral administrations of **P2Y12-receptor inhibitors**: Systematic review and meta-analysis. J Thromb Haemost. 2019 Mar 18.
2272. Stam-Slob MC, Connolly SJ, van der Graaf Y, et al. Individual Treatment Effect Estimation of 2 Doses of **Dabigatran on Stroke and Major Bleeding** in Atrial Fibrillation: Results from the RE-LY Trial. Circulation. 2019 May 3.
2273. Tillman H, Johnston SC, Farrant M, et al. Risk for Major Hemorrhages in Patients Receiving **Clopidogrel and Aspirin Compared With Aspirin Alone** After Transient Ischemic Attack or Minor Ischemic Stroke: A Secondary Analysis of the POINT Randomized Clinical Trial. JAMA Neurol. 2019 Apr 29.
2274. Afzal SK, Hasan SS, Babar ZU. A Systematic Review of **Patient Reported Outcomes Associated with the Use of Direct-acting Oral Anticoagulants**. Br J Clin Pharmacol. 2019 May 11.
2275. Bajaj NS, Vaduganathan M, Qamar A, et al. **Extended prophylaxis for venous thromboembolism** after hospitalization for medical illness: A trial sequential and cumulative meta-analysis. PLoS Med. 2019 Apr 29;16(4):e1002797.
2276. Brenner H, Calderazzo S, Seufferlein T, et al. Effect of a **Single Aspirin Dose Prior to Fecal Immunochemical Testing** on Test Sensitivity for Detecting Advanced Colorectal Neoplasms: A Randomized Clinical Trial. JAMA. 2019 May 7;321(17):1686-1692.
2277. Brings A, Lehmann ML, Foerster KI, et al. **Perpetrator effects of ciclosporin (P-glycoprotein inhibitor) and its combination with fluconazole** (CYP3A inhibitor) on the pharmacokinetics of rivaroxaban in healthy volunteers. Br J Clin Pharmacol. 2019 Mar 25.
2278. Dimmitt SB, Floyd CN, Ferner RE. **Antithrombotic dose**: some observations from published clinical trials. Br J Clin Pharmacol. 2019 May 3.
2279. Lancellotti P, Musumeci L, Jacques N, et al. **Antibacterial Activity of Ticagrelor** in Conventional Antiplatelet Dosages Against Antibiotic-Resistant Gram-Positive Bacteria. JAMA Cardiol. 2019 May 8.
2280. Malik AH, Yandrapalli S, Aronow WS, et al. Meta-Analysis of **Direct-Acting Oral Anticoagulants Compared With Warfarin** in Patients >75 Years of Age. Am J Cardiol. 2019 Mar 18.
2281. O'Leary JG et al. **Coagulation in cirrhosis**. Gastroenterology 2019 Apr 12.
2282. Diener HC, Sacco RL, Easton JD, et al. **Dabigatran for Prevention of Stroke after Embolic Stroke of Undetermined** Source. N Engl J Med. 2019 May 16;380(20):1906-1917.
2283. Fernandes A, McEvoy JW, Halvorsen S. "**Doctor, Should I Keep Taking an Aspirin a Day?"** N Engl J Med. 2019 May 16;380(20):1967-1970.
2284. Gurbel PA, Fox KAA, Tantry US, et al. Combination **Antiplatelet and Oral Anticoagulant Therapy in Patients With Coronary and Peripheral Artery Disease**. Circulation. 2019 Apr 30;139(18):2170-2185.
2285. Huang WY, Saver JL, Wu YL, et al. Frequency of **Intracranial Hemorrhage With Low-Dose Aspirin in Individuals Without Symptomatic Cardiovascular Disease**: A Systematic Review and Meta-analysis. JAMA Neurol. 2019 May 13.
2286. Kearon C, Parpia S, Spencer FA, et al. Long-**term risk of recurrence in patients with a first unprovoked venous thromboembolism** managed according to D-dimer results; a cohort study. J Thromb Haemost. 2019 Apr 29.
2287. Kahale LA, Hakoum MB, Tsolakian IG, et al. **Anticoagulation for the long-term treatment of venous thromboembolism** in people with cancer. Cochrane Database Syst Rev. 2018 Jun 19;6:CD006650. For the long-term treatment of VTE in people with cancer, evidence shows that LMWHs compared to VKAs probably produces an important reduction in VTE and DOACs compared to LMWH, may likely reduce VTE but may increase risk of major bleeding. Decisions for a person with cancer and VTE to start long-term LMWHs versus oral anticoagulation should balance benefits and harms and integrate the person's values and preferences for the important outcomes and alternative management strategies.
2288. Matar CF, Kahale LA, Hakoum MB, et al. **Anticoagulation for perioperative thromboprophylaxis in people with cancer**. Cochrane Database Syst Rev. 2018 Jul 11;7:CD009447. Low molecular weight heparin versus unfractionated heparin for perioperative thromboprophylaxis in patients with cancer.
2289. Simon TG, Henson J, Osganian S, et al. **Daily aspirin use associated with reduced risk for fibrosis progression** in patients with nonalcoholic fatty liver disease. Clin Gastroenterol Hepatol. 2019 May 8.
2290. Berberich A, Schneider C, Reiff T, et al. Dual Antiplatelet Therapy Improves Functional Outcome in Patients With **Progressive Lacunar Strokes**. Stroke. 2019 Apr;50(4):1007-1009.
2291. Cuker A, Burnett A, Triller D, et al. **Reversal of direct oral anticoagulants**: Guidance from the Anticoagulation Forum. Am J Hematol. 2019 Jun;94(6):697-709.
2292. Povsic TJ, Ohman EM, Roe MT, et al. **P2Y12 Inhibitor Switching in Response to Routine Notification of CYP2C19 Clopidogrel Metabolizer Status** Following Acute Coronary Syndromes. JAMA Cardiol. 2019 May 29.
2293. RESTART Collaboration. Effects of antiplatelet therapy after stroke due to intracerebral haemorrhage (**RESTART**): a randomised, open-label trial. Lancet. 2019 May 21.
2294. Tektonidou MG, Andreoli L, Limper M, et al. **EULAR recommendations for the management of antiphospholipid syndrome** in adults. Ann Rheum Dis. 2019 May 15.
2295. Urban P, Mehran R, Colleran R, et al. Defining **high bleeding risk in patients undergoing percutaneous coronary intervention**: a consensus document from the Academic Research Consortium for High

Bleeding Risk. Eur Heart J. 2019 May 22.

2296. Al-Shahi Salman R, Minks DP, et al. **Effects of antiplatelet therapy on stroke risk** by brain imaging features of intracerebral haemorrhage and cerebral small vessel diseases: subgroup analyses of the RESTART randomised, open-label trial. Lancet Neurol. 2019 May 21
2297. Malhotra K, Ishfaq MF, Goyal N, et al. **Oral anticoagulation in patients with chronic kidney disease**: A systematic review and meta-analysis. Neurology. 2019 May 21;92(21):e2421-e2431.
2298. Mart´õ-F`abregas J, Medrano-Martorell S, Merino E, et al. **MRI predicts intracranial hemorrhage** in patients who receive long-term oral anticoagulation. Neurology 2019 92:e2432–e2443.
2299. Povsic TJ, Ohman EM, Roe MT, et al. P2Y12 Inhibitor Switching in Response to Routine Notification of **CYP2C19 Clopidogrel Metabolizer Status Following Acute Coronary Syndromes**. JAMA Cardiol. 2019 May 29.
2300. Abdelaziz HK, Saad M, Pothineni NVK, et al. **Aspirin for Primary Prevention of Cardiovascular Events**. J Am Coll Cardiol. 2019 Jun 18;73(23):2915-2929.
2301. Aursulesei V, Costache II. **Anticoagulation in chronic kidney disease**: from guidelines to clinical practice. Clin Cardiol. 2019 May 17.
2302. Berwanger O, Lopes RD, Moia DDF, et al. **Ticagrelor Versus Clopidogrel in Patients With STEMI Treated With Fibrinolysis**: **TREAT** Trial. J Am Coll Cardiol. 2019 Jun 11;73(22):2819-2828.
2303. Mendel A, Bernatsky SB, Hanly JG, et al. **Low aspirin use and high prevalence of pre-eclampsia** risk factors among pregnant women in a multinational SLE inception cohort. Ann Rheum Dis. 2019 Jul;78(7):1010-1012.
2304. Moayyedi P, Eikelboom JW, Bosch J, et al; COMPASS investigators. **Safety of Proton Pump Inhibitors** Based on a Large, Multi-year, Randomized Trial of Patients Receiving Rivaroxaban or Aspirin. Gastroenterology. 2019 May 29.
2305. Sciascia S, Yazdany J, Dall'Era M, et al. Anticoagulation in **patients with concomitant lupus nephritis and thrombotic microangiopathy**: a multicentre cohort study. Ann Rheum Dis. 2019 Jul;78(7):1004-1006.
2306. Puel V, Théophile H, Godard I, et al. **Ticagrelor and central sleep apnoea**: Impact of withdrawal and reintroduction. Br J Clin Pharmacol. 2019 Jun 17.
2307. Raber I, McCarthy CP, Vaduganathan M, et al. The rise and fall of **aspirin in the primary prevention of cardiovascular disease**. Lancet. 2019 May 25;393(10186):2155-2167.
2308. Toyoda K, Uchiyama S, Yamaguchi T, et al; CSPS.com Trial Investigators. Dual antiplatelet therapy using **cilostazol for secondary prevention** in patients with high-risk ischaemic stroke in Japan: a multicentre, open-label, randomised controlled trial. Lancet Neurol. 2019 Jun;18(6):539-548.
2309. Hahn J-Y, Song YB, Oh J-H, et al; SMART-CHOICE Investigators. Effect of **P2Y12 inhibitor monotherapy vs dual antiplatelet therapy** on cardiovascular events in patients undergoing percutaneous coronary intervention: the SMART-CHOICE randomized clinical trial [June 25, 2019]. JAMA. doi:10.1001/jama.2019.8146
2310. Langlois E, Cusson-Dufour C, Moumneh T, et al. Could the **YEARS algorithm be used to exclude pulmonary embolism during pregnancy**? Data from the CT-PE-pregnancy study. J Thromb Haemost. 2019 May 20
2311. Mai V, Guay CA, Perreault L, et al. **Extended Anticoagulation for VTE**: A Systematic Review and Meta-Analysis. Chest. 2019 Jun;155(6):1199-1216.
2312. Watanabe H, Domei T, Morimoto T, et al; STOPDAPT-2 Investigators. Effect of **1-month dual antiplatelet therapy followed by clopidogrel vs 12-month dual antiplatelet therapy** on cardiovascular and bleeding events among patients receiving PCI: the STOPDAPT-2 randomized clinical trial [June 25, 2019]. JAMA. doi:10.1001/jama.2019.8145
2313. Xu J, Wang A, Wangqin R, et al; CHANCE investigators. Efficacy of **Clopidogrel for Stroke Depends on CYP2C19 Genotype and Risk Profile**. Ann Neurol. 2019 Jun 25.
2314. Yin SH, Xu P, Wang B, et al. Duration of dual antiplatelet therapy after percutaneous coronary **intervention with drug-eluting stent**: systematic review and network meta-analysis. BMJ. 2019 Jun 28;365:l2222
2315. Hall KT, Kessler T, Buring JE, et al. Genetic variation at the coronary artery disease risk **locus GUCY1A3 modifies cardiovascular disease prevention effects of aspirin**. Eur Heart J. 2019 Jun 22.
2316. Ho KM, Rao S, Honeybul S, et al. A Multicenter Trial of **Vena Cava Filters in Severely Injured Patients**. N Engl J Med. 2019 Jul 7.
2317. Leclerc J, Blais C, Rochette L, et al. Did **Generic Clopidogrel Commercialization** Affect Trends of ER Consultations and Hospitalizations in the Population Treated with Clopidogrel? Drugs Aging. 2019 May 10.
2318. Malik AH, Yandrapalli S, Aronow WS, et al. Oral anticoagulants in **atrial fibrillation with valvular heart disease and bioprosthetic heart valves**. Heart. 2019 Jun 14.
2319. Rali P, Gangemi A, Moores A, Mohrien K, Moores L. Direct acting oral anticoagulants **(DOACs) in critically ill patients**. Chest. 2019 Jun 25.
2320. Sukumar S, Gulilat M, Linton B, et al. **Apixaban Concentrations** with Lower than Recommended Dosing in Older Adults with Atrial Fibrillation. J Am Geriatr Soc. 2019 May 21.
2321. Greving JP, Diener HC, Reitsma JB, et al. Antiplatelet Therapy **After Noncardioembolic Stroke**. Stroke. 2019 Jul;50(7):1812-1818.
2322. Ha JT, Neuen BL, Cheng LP, et al. Benefits and harms of oral anticoagulant **therapy in chronic kidney disease**. A systematic review and meta-analysis. Ann Intern Med. 2019. [Epub ahead of print]. doi:10.7326/M19-0087
2323. O'Brien CW, Juraschek SP, Wee CC. Prevalence of **Aspirin Use for Primary Prevention of Cardiovascular Disease** in the United States: Results From the 2017 National Health Interview Survey. Ann Intern Med. 2019 Jul 23.
2324. Patti G, Sticchi A, Bisignani A, et al. Meta-**Regression to Identify Patients Deriving the Greatest Benefit** from Dual Antiplatelet Therapy after Stroke or Transient Ischemic Attack Without Thrombolytic or Thrombectomy Treatment. Am J Cardiol. 2019.
2325. Takeuchi Y, Mabe K, Shimodate Y, etal. Continuous **anticoagulation and cold snare polypectomy versus heparin bridging and hot snare polypectomy** in patients on anticoagulants with subcentimeter polyps. A randomized controlled trial. Ann Intern Med. 2019. [Epub ahead of print]. doi:10.7326/M19-0026
2326. Trevisan C, Piovesan F, Lucato P, et al. **Parathormone, vitamin D and the risk of atrial fibrillation** in older adults: A prospective study. Nutr Metab Cardiovasc Dis. 2019 May 29.
2327. Wang Y, Chen W, Lin Y, et al; PRINCE Protocol Steering Group. **Ticagrelor plus aspirin versus clopidogrel plus aspirin** for platelet reactivity in patients with minor stroke or transient ischaemic attack: open label, blinded endpoint, randomised controlled phase II trial. BMJ. 2019 Jun 6;365:l2211.
2328. Watanabe H, Domei T, Morimoto T, et al. Effect of **1-Month Dual Antiplatelet Therapy Followed by Clopidogrel vs 12-Month Dual Antiplatelet Therapy** on Cardiovascular and Bleeding Events in Patients Receiving PCI: The STOPDAPT-2 Randomized Clinical Trial. JAMA. 2019 Jun 25;321(24):2414-2427.
2329. Khan F, Rahman A, Carrier M, et al; MARVELOUS Collaborators. Long term **risk of symptomatic recurrent venous thromboembolism** after discontinuation of anticoagulant treatment for first unprovoked venous thromboembolism event: systematic review and meta-analysis. BMJ. 2019 Jul 24;366:l4363.
2330. Moayyedi P, Eikelboom JW, Bosch J, et al. **Pantoprazole to Prevent Gastroduodenal Events** in Patients Receiving Rivaroxaban and/or Aspirin in a Randomized, Double-Blind, Placebo-Controlled Trial. Gastroenterology. 2019 May 2.
2331. Xian Y, Xu H, O'Brien EC, et al. Clinical Effectiveness of **Direct Oral Anticoagulants vs Warfarin in Older Patients With Atrial Fibrillation and Ischemic Stroke**: Findings From the Patient-Centered Research Into Outcomes Stroke Patients Prefer and Effectiveness Research (PROSPER) Study. JAMA Neurol. 2019 Jul 22.
2332. Khan F, Rahman A, Carrier M, et al; MARVELOUS Collaborators. Long term risk of **symptomatic recurrent venous thromboembolism after discontinuation of anticoagulant** treatment for first unprovoked venous thromboembolism event: systematic review and meta-analysis. BMJ. 2019 Jul 24;366:l4363.
2333. Lee SR, Rhee TM, Kang DY, et al. Meta-Analysis of Oral Anticoagulant Monotherapy as an Antithrombotic **Strategy in Patients With Stable Coronary Artery Disease** and Nonvalvular Atrial Fibrillation. Am J Cardiol. 2019 Jun 25.
2334. Moayyedi P, Eikelboom JW, Bosch J, et al; COMPASS Investigators. Safety of **Proton Pump Inhibitors** Based on a Large, Multi-Year, Randomized Trial of Patients Receiving **Rivaroxaban or Aspirin**. Gastroenterology. 2019 May 29.
2335. Brouwers JRBJ, Roeters van Lennep JE, Beinema MJ. Biosimilars of **Low Molecular Weight Heparins**- Relevant Background Information for your Drug Formulary. Br J Clin Pharmacol. 2019 Aug 4.
2336. Douketis JD, Spyropoulos AC, Duncan J, et al. **Perioperative Management of Patients With Atrial Fibrillation** Receiving a Direct Oral Anticoagulant. JAMA Intern Med. 2019 Aug 5
2337. Fralick M, Goldberg N, Rohailla S, et al. Value of routine **echocardiography in the management of stroke**. CMAJ. 2019 Aug 6;191(31):E853-E859.
2338. Shah R, Khan B, Latham SB, et al. A Meta-Analysis of **Aspirin for the Primary Prevention of Cardiovascular Diseases** in the Context of Contemporary Preventive Strategies. Am J Med. 2019 May 31.

2339. Barbarawi M, Zayed Y, Kheiri B, et al. The role of anticoagulation in venous thromboembolism primary **prophylaxis in patients with malignancy**: A systematic review and meta-analysis of randomized controlled trials. Thromb Res. 2019 Jul 16;181:36-45.
2340. Cucchiara B, George DK, Kasner SE, et al. **Disability after minor stroke** and TIA: A secondary analysis of the **SOCRATES** trial. Neurology. 2019 Aug 13;93(7):e708-e716.
2341. Knijnik L, Rivera M, Blumer V, et al. **Prevention of Stroke** in Atrial Fibrillation After **Coronary Stenting**. Stroke. 2019 Aug;50(8):2125-2132.
2342. Li A, Kuderer NM, Garcia DA, et al. Direct Oral Anticoagulant for the Prevention of Thrombosis in **Ambulatory Patients with Cancer**: A Systematic Review and Meta-Analysis. J Thromb Haemost. 2019Aug 17.
2343. Lewis S, Glen J, Dawoud D, et al. Venous thromboembolism **prophylaxis strategies for people undergoing elective total knee replacement**: a systematic review and network meta-analysis. Lancet Haematol 2019; published online Aug 20.
2344. Johnston SC, Elm JJ, Easton JD, et al. Time Course for Benefit and Risk of **Clopidogrel and Aspirin After Acute Transient Ischemic Attack** and Minor Ischemic Stroke. Circulation. 2019 Aug 20;140(8):658-664. (Point)
2345. Pan Y, Elm JJ, Li H, et al. Outcomes Associated With **Clopidogrel-Aspirin Use in Minor Stroke or Transient Ischemic Attack**: A Pooled Analysis of Clopidogrel in High-Risk Patients With Acute Non-Disabling Cerebrovascular Events (CHANCE) and Platelet-Oriented Inhibition in New TIA and Minor Ischemic Stroke (POINT) Trials. JAMA Neurol. 2019 Aug 19.
2346. Steg PG, Bhatt DL, Simon T, et al. **Ticagrelor** in patients with stable coronary disease and diabetes. (THEMIS) N Engl J Med. DOI: 10.1056/NEJMoa1908077.
2347. Bhatt DL, Steg PG, Mehta SR, et al. **Ticagrelor** in patients with diabetes and stable coronary artery disease with a history of previous percutaneous coronary intervention (THEMIS-PCI): a phase 3, placebo-controlled, randomised trial. Lancet. 2019 Aug 30.
2348. Chakravarty T, Patel A, Kapadia S, et al. Anticoagulation **After Surgical or Transcatheter Bioprosthetic Aortic Valve Replacement**. J Am Coll Cardiol. 2019 Sep 3;74(9):1190-1200.
2349. Claassens DMF, Vos GJA, Bergmeijer TO, et al. A Genotype-Guided Strategy for **Oral P2Y(12) Inhibitors in Primary PCI**. N Engl J Med. 2019 Sep 3.
2350. Ferro JM, Coutinho JM, Dentali F, et al. Safety and Efficacy of **Dabigatran Etexilate vs Dose-Adjusted Warfarin** in Patients With Cerebral Venous Thrombosis: A Randomized Clinical Trial. JAMA Neurol. 2019 Sep 3.
2351. Gage BF, Bass AR, Lin H, et al. Effect of Low-Intensity vs Standard-Intensity **Warfarin Prophylaxis on Venous Thromboembolism** or Death Among Patients Undergoing Hip or Knee Arthroplasty: A Randomized Clinical Trial. JAMA. 2019 Sep 3;322(9):834-842.
2352. Konstantinides SV, Meyer G, Becattini C, et al. **2019 ESC Guidelines** for the diagnosis and management of acute pulmonary embolism developed in collaboration with the European Respiratory Society (ERS): The Task Force for the diagnosis and management of acute pulmonary embolism of the European Society of Cardiology (ESC). Eur Respir J. 2019 Aug 31.
2353. Liu S, Singer A, McAlister FA, et al. Quality of **warfarin management in primary care**: Determining the stability of international normalized ratios using a nationally representative prospective cohort. Can Fam Physician. 2019 Jun;65(6):416-425.
2354. Schüpke S, Neumann FJ, Menichelli M, et al. **Ticagrelor or Prasugrel** in Patients with Acute Coronary Syndromes. N Engl J Med. 2019 Sep 1.
2355. Xie J, Jiang M, Lin Y, et al. **Rivaroxaban versus Aspirin** in Prevention of Venous Thromboembolism: A Meta-Analysis of 9 Randomized Controlled Trials comprising 7,656 Patients. Thromb Haemost. 2019 Sep;119(9):1517-1526.
2356. de Vries TI, Eikelboom JW, Bosch J, et al. Estimating individual lifetime benefit and bleeding risk of adding rivaroxaban to aspirin for patients with stable cardiovascular disease: results from the COMPASS trial. Eur Heart J. 2019 Sep 1.
2357. Farrant M, Easton JD, Adelman EE, et al. Assessment of the End Point Adjudication Process on the Results of the Platelet-Oriented Inhibition in New TIA and Minor Ischemic Stroke (POINT) Trial: A Secondary Analysis. JAMA Netw Open. 2019 Sep 4;2(9):e1910769.
2358. Tektonidou MG, Andreoli L, Limper M, et al. EULAR recommendations for the management of antiphospholipid syndrome in adults. Ann Rheum Dis. 2019 Oct;78(10):1296-1304.
2359. Vranckx P, Valgimigli M, Eckardt L, et al. Edoxaban-based versus vitamin K antagonist-based antithrombotic regimen after successful coronary stenting in patients with atrial fibrillation (ENTRUST-AF PCI): a randomised, open-label, phase 3b trial. Lancet. 2019 Sep 2.
2360. Farge D, Frere C, Connors JM, et al; International Initiative on Thrombosis and Cancer (ITAC) advisory panel. **2019 international clinical practice guidelines** for the treatment and prophylaxis of venous thromboembolism in patients with cancer. Lancet Oncol. 2019 Sep 3.
2361. Perera KS, Ng KKH, Nayar S, et al. Association Between Low-Dose **Rivaroxaban With or Without Aspirin and Ischemic Stroke Subtypes**: A Secondary Analysis of the COMPASS Trial. JAMA Neurol. 2019 Sep 16.
2362. Tsushima T, Sahadevan J, Intini A. **Syncope After Percutaneous Coronary Intervention**. JAMA Cardiol. 2019 Sep 18.
2363. Yasuda S, Kaikita K, Akao M, et al. Antithrombotic **therapy for atrial fibrillation with stable coronary disease**. N Engl J Med. (AFIRE) DOI: 10.1056/NEJMoa1904143.
2364. Xue Z, Zhang H. **Non-Vitamin K Antagonist Oral Anticoagulants Versus Warfarin** in Asians With Atrial Fibrillation: Meta-Analysis of Randomized Trials and Real-World Studies. Stroke. 2019 Oct;50(10):2819-2828.
2365. Farge D, Debourdeau P, Beckers M, et al. International **clinical practice guidelines for the treatment and prophylaxis of venous thromboembolism** in patients with cancer. J Thromb Haemost. 2013 Jan;11(1):56-70.
2366. Mehran R, Baber U, Sharma SK, et al. **Ticagrelor with or without Aspirin in High-Risk Patients after PCI**. N Engl J Med. 2019 Sep 26.
2367. Paul JD, Cifu AS. **Prevention and Management of Venous Thromboembolism**. JAMA. 2019 Sep 23.
2368. Schreiber K, Hunt BJ. **Managing antiphospholipid syndrome in pregnancy**. Thromb Res. 2019 Sep;181 Suppl 1:S41-S46.
2369. Selak V, Jackson R, Poppe K, et al. Personalized prediction of **cardiovascular benefits and bleeding harms from aspirin for primary prevention**. A benefit–harm analysis. Ann Intern Med. 17 September 2019 [Epub ahead of print]. doi:10.7326/M19-1132

RxFiles Duration of DAPT, Dual & TT Online Extras:

SUMMARY OF ISCHEMIC STROKE DAPT TRIALS (NON-CARDIOEMBOLIC): SECONDARY PREVENTION					
Study	**Regimen ***	**Start of Treatment in Relation to Event**	**DAPT Duration**	**Benefit**	**Harm**
POINT (2018)	- DAPT vs ASA 50-325mg (62% on ASA 81mg daily)	Randomized within 12 hours, 1st dose given ASAP	90 days	- ↓ risk of ischemic stroke, MI or death from ischemic vascular cause NNT=67 (↓ driven by ischemic stroke) - Benefit was greater in the 1st 7 days (p=0.04), & 1st 30 days (p=0.02), versus at 90 days	- ↑ risk of major bleeding NNH=200 - The risk of bleeding between the two treatment arms was not statistically significant during the first 7 days (p=0.34), versus Day 8-90 (p=0.04)
CHANCE (2013, in China)	- Days 1-22: DAPT vs ASA - Days 22-90: clopidogrel vs ASA 75mg daily	within 24 hours	21 days	- ↓ risk of stroke NNT=29/90 days	- NS for bleeding & all-cause mortality
SPS3 (2012)	DAPT vs ASA 325mg	within 2 weeks to 180 days (mean 62 days)	3.4 years	NS for primary endpoint (stroke/MI)	- ↑ risk of all-cause mortality NNH=44 (or 143/year) - ↑ risk of major bleeding NNH=32 (or 100/year) - discontinuation rates NNH=34
FASTER (2007)	DAPT vs ASA 81mg	within 24 hours	90 days	NS for primary endpoint (stroke)	- ↑ risk of symptomatic bleeding NNH=34 & bruising NNH=6
MATCH (2004)	DAPT vs clopidogrel	within 3 months (mean 26 days)	18 months	NS for primary endpoint (stroke, MI, vascular death or rehospitalization for acute ischemic event)	- ↑ risk of bleeding (life-threatening NNH=50, major NNH=100) - GI bleeds were the most common location for life-threatening (53%) & major (58%) bleeds. - Kaplan-Meier curve for intracranial hemorrhage suggests no difference in risk for the first 90 days; ↑ risk with DAPT beyond 90 days.

* All DAPT regimens with clopidogrel 75mg daily

REFERENCES: DURATION OF DAPT & TT

CARDIOVASCULAR GUIDELINES:

CANADIAN CARDIOVASCULAR GUIDELINES

Ackman ML, Bucci C, Callaghan M, et al. A pharmacist's guide to the 2012 update of the Canadian Cardiovascular Society Guidelines for the Use of Antiplatelet Therapy. Can Pharm J (Ott).2015 Mar;148(2):71-81.

Tanguay JF, Bell AD, Ackman ML et al; **Canadian Cardiovascular Society**. Focused **2012** update of the Canadian Cardiovascular Society guidelines for the use of antiplatelet therapy. Can J Cardiol. 2013 Nov;29(11):1334-45.

Skanes AC, Healey JS, Cairns JA, et al; **Canadian Cardiovascular Society Atrial Fibrillation Guidelines** Committee. Focused **2012** update of the Canadian Cardiovascular Society atrial fibrillation guidelines: recommendations for stroke prevention and rate/rhythm control. Can J Cardiol. 2012 Mar-Apr;28(2):125-36.

Bell AD, Roussin A, Cartier R, et al; **Canadian Cardiovascular Society**. The use of antiplatelet therapy in the outpatient setting: Canadian Cardiovascular Society guidelines. Can J Cardiol. **2011** May-Jun;27 Suppl A:S1-59.

Mehta SR, Bainey KR, Cantor WJ, et al. **2018 Canadian Cardiovascular Society/Canadian Association of Interventional Cardiology Focused Update of the Guidelines for the Use of Antiplatelet Therapy**. Can J Cardiol. 2018 Mar;34(3):214-233.

EUROPEAN CARDIOVASCULAR GUIDELINES

Roffi M, Patrono C, Collet JP, et al. **2015 ESC Guidelines for the Management of Acute Coronary Syndromes in Patients Presenting Without Persistent ST-segment Elevation**. Rev Esp Cardiol (Engl Ed). 2015 Dec;68(12):1125.

Authors/Task Force members, Windecker S, Kolh P, Alfonso F, et al. **2014 ESC/EACTS Guidelines on myocardial revascularization**: The Task Force on Myocardial Revascularization of the European Society of Cardiology (ESC) and the European Association for Cardio-Thoracic Surgery (EACTS)Developed with the special contribution of the European Association of Percutaneous Cardiovascular Interventions (EAPCI). Eur Heart J. 2014 Oct 1;35(37):2541-619.

Lip GY, Windecker S, Huber K, et al. **Management of antithrombotic therapy in atrial fibrillation patients presenting with acute coronary syndrome and/or undergoing percutaneous coronary or valve interventions**: a joint consensus document of the **European Society of Cardiology Working Group on Thrombosis**, European Heart Rhythm Association (EHRA), European Association of Percutaneous Cardiovascular Interventions (EAPCI) and European Association of Acute Cardiac Care (ACCA) endorsed by the Heart Rhythm Society (HRS) and Asia-Pacific Heart Rhythm Society (APHRS). Eur Heart J. **2014** Dec 1;35(45):3155-79.

Montalescot G, Sechtem U, Achenbach S, et al. **2013 ESC guidelines on the management of stable coronary artery disease: the Task Force on the management of stable coronary artery disease of the European Society of Cardiology**. Eur Heart J. 2013 Oct;34(38):2949-3003.

European Stroke Organisation, Tendera M, Aboyans V, Bartelink ML, et al; ESC Committee for Practice Guidelines. ESC Guidelines on the diagnosis and treatment of **peripheral artery diseases**: Document covering atherosclerotic disease of extracranial carotid and vertebral,mesenteric, renal, upper and lower extremity arteries: the Task Force on the Diagnosis and Treatment of Peripheral Artery Diseases of the European Society of Cardiology (ESC). Eur Heart J. 2011 Nov;32(22):2851-906.

Aboyans V, Ricco JB, Bartelink MEL, et al. **2017 ESC Guidelines on the Diagnosis and Treatment of Peripheral Arterial Diseases**, in collaboration with the European Society for Vascular Surgery (ESVS): Document covering atherosclerotic disease of extracranial carotid and vertebral, mesenteric, renal, upper and lower extremity arteriesEndorsed by: the European Stroke Organization (ESO)The Task Force for the Diagnosis and Treatment of Peripheral Arterial Diseases of the European Society of Cardiology (ESC) and of the European Society for Vascular Surgery (ESVS). Eur Heart J. 2017 Aug 26.

Valgimigli M, Bueno H, Byrne RA, et al. **2017 ESC focused update on dual antiplatelet therapy in coronary artery disease** developed in collaboration with EACTS: The Task Force for dual antiplatelet therapy in coronary artery disease of the European Society of Cardiology ESC) and of the European Association for Cardio-Thoracic Surgery (EACTS). Eur Heart J. 2017 Aug 26.

Collet JP, Roffi M, Byrne RA, Costa F, Valgimigli M; Task Force for the Management of Dual Antiplatelet Therapy in Coronary Artery Disease of the European Society of Cardiology (ESC) ; ESC Scientific Document Group ; Task Force for the Management of Dual Antiplatelet Therapy in Coronary Artery Disease of the European Society of Cardiology (ESC) . Case-based implementation of the **2017 ESC Focused Update on Dual Antiplatelet Therapy** in Coronary Artery Disease. Eur Heart J. 2018 Jan 14;39(3):e1-e33.

USA CARDIOVASCULAR GUIDELINES

Levine GN, Bates ER, Bittl JA, et al. **2016 ACC/AHA Guideline Focused Update on Duration of Dual Antiplatelet Therapy in Patients With Coronary Artery Disease**: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines: An Update of the 2011 ACCF/AHA/SCAI Guideline for Percutaneous Coronary Intervention, 2011 ACCF/AHA Guideline for Coronary Artery Bypass Graft Surgery, 2012 ACC/AHA/ACP/AATS/PCNA/SCAI/STS Guideline for the Diagnosis and Management of Patients With Stable Ischemic Heart Disease, 2013 ACCF/AHA Guideline for the Management of ST-Elevation Myocardial Infarction, 2014 AHA/ACC Guideline for the Management of Patients With Non-ST-Elevation Acute Coronary Syndromes, and 2014 ACC/AHA Guideline on Perioperative Cardiovascular Evaluation and Management of Patients Undergoing Noncardiac Surgery. Circulation. 2016 Mar 29. pii: CIR.0000000000000404. [Epub ahead of print] PubMed PMID: 27026020.

Bittl JA, Baber U, Bradley SM, Wijeysundera DN. Duration of Dual Antiplatelet Therapy: A **Systematic Review for the 2016 ACC/AHA Guideline** Focused Update on Duration of Dual Antiplatelet Therapy in Patients With Coronary Artery Disease: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. Circulation. 2016 Mar 29. pii: CIR.0000000000000405. [Epub ahead of print] PubMed PMID: 27026019.

Kulik A, Ruel M, Jneid H et al; **American Heart Association** Council on Cardiovascular Surgery and Anesthesia. Secondary prevention after **coronary artery bypass graft** surgery: a scientific statement from the American Heart Association. Circulation. **2015** Mar 10;131(10):927-64.

Amsterdam EA, Wenger NK, Brindis RG, et al; American College of Cardiology; American Heart Association Task Force on Practice Guidelines; Society for Cardiovascular Angiography and Interventions; Society of Thoracic Surgeons; American Association for Clinical Chemistry. **2014 AHA/ACC Guideline for the Management of Patients with Non-ST-Elevation Acute Coronary Syndromes:** a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. J Am Coll Cardiol. 2014 Dec 23;64(24):e139-228.

January CT, Wann LS, Alpert JS, et al; ACC/AHA Task Force Members. **2014 AHA/ACC/HRS guideline for the management of patients with atrial fibrillation**: a report of the American College of Cardiology/American Heart Association Task Force on practice guidelines and the Heart Rhythm Society. Circulation. 2014 Dec 2;130(23):e199-267.

O'Gara PT, Kushner FG, Ascheim DD, et al; American College of Cardiology Foundation; American Heart Association Task Force on Practice Guidelines; American College of Emergency Physicians; Society for Cardiovascular Angiography and Interventions. **2013 ACCF/AHA guideline for the management of ST-elevation myocardial infarction**: executive summary: a

report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines: developed in collaboration with the American College of Emergency Physicians and Society for Cardiovascular Angiography and Interventions. Catheter Cardiovasc Interv. 2013 Jul 1;82(1):E1-27.

Vandvik PO, Lincoff AM, Gore JM, et al; American College of Chest Physicians. Primary and secondary prevention of cardiovascular disease: Antithrombotic Therapy and Prevention of Thrombosis, 9th ed: **American College of Chest Physicians Evidence-Based Clinical Practice Guidelines**. Chest. 2012 Feb;141(2 Suppl):e637S-68S. doi: 10.1378/chest.11-2306. Erratum in: Chest. 2012 Apr;141(4):1129.

Alonso-Coello P, Bellmunt S, McGorrian C, et al; American College of Chest Physicians. Antithrombotic therapy in **peripheral artery disease**: Antithrombotic Therapy and Prevention of Thrombosis, 9th ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines. Chest. 2012 Feb;141(2Suppl):e669S-90S.

Hillis LD, Smith PK, Anderson JL, et al; American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. **2011 ACCF/AHA guideline for coronary artery bypass graft surgery: executive summary**: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. J Thorac Cardiovasc Surg. 2012 Jan; 143(1):4-34.

Levine GN, Bates ER, Blankenship JC et al; ACCF; AHA; SCAI. **2011 ACCF/AHA/SCAI Guideline for Percutaneous Coronary Intervention**: executive summary: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines and the Society for Cardiovascular Angiography and Interventions. Catheter Cardiovasc Interv. 2012 Feb 15;79(3):453-95.

American College of Cardiology Foundation; American Heart Association Task Force; Society for Cardiovascular Angiography and Interventions; Society of Interventional Radiology; Society for Vascular Medicine; Society for Vascular Surgery, Rooke TW, Hirsch AT, Misra S, et al. 2011 ACCF/AHA focused update of the guideline for the management of patients with **peripheral artery disease** (updating the 2005 guideline). Vasc Med. 2011 Dec;16(6):452-76.

Grines CL, Bonow RO, Casey DE Jr, et al; American Heart Association; American College of Cardiology; Society for Cardiovascular Angiography and Interventions; American College of Surgeons; American Dental Association; American College of Physicians. **Prevention of premature discontinuation of dual antiplatelet therapy in patients with coronary artery stents**: a science advisory from the American Heart Association, American College of Cardiology, Society for Cardiovascular Angiography and Interventions, American College of Surgeons, and American Dental Association, with representation from the American College of Physicians. J Am Dent Assoc. **2007** May;138(5):652-5.

Laskey WK, Yancy CW, Maisel WH. Thrombosis in coronary drug-eluting stents: report from the meeting of the Circulatory System Medical Devices Advisory Panel of the Food and Drug Administration Center for Devices and Radiologic Health, December 7-8, 2006. Circulation. **2007** May 1;115(17):2352-7.

Smith SC Jr, Feldman TE, Hirshfeld JW Jr, et al; American College of Cardiology/American Heart Association Task Force on Practice Guidelines; ACC/AHA/SCAI Writing Committee to Update 2001 Guidelines for Percutaneous Coronary Intervention. **ACC/AHA/SCAI 2005 guideline update for percutaneous coronary intervention**: a report of the AmericanCollege of Cardiology/American Heart Association Task Force on Practice Guidelines (ACC/AHA/SCAI Writing Committee to Update 2001 Guidelines for Percutaneous Coronary Intervention). Circulation. 2006 Feb 21;113(7):e166-286.

Powers WJ, Rabinstein AA, Ackerson T, et al. **2018 guidelines for the early management of patients with acute ischemic stroke**: a guideline for healthcare professionals from the **American Heart Association/American Stroke Associatio**n. Stroke. 2018;49:xxx–xxx. doi: 10.1161/STR.0000000000000158.

Shore-Lesserson L, Baker RA, Ferraris VA, et al. The Society of Thoracic Surgeons, The Society of Cardiovascular Anesthesiologists, and The American Society of ExtraCorporeal Technology: Clinical Practice Guidelines-**Anticoagulation During Cardiopulmonary Bypass**. Ann Thorac Surg. 2018 Feb;105(2):650-662.

DAPT POST-PCI META-ANALYSES

Abo-Salem E, Alsidawi S, Jamali H, et al. Optimal Duration of Dual Antiplatelet Therapy after Drug-Eluting Stents: Meta-Analysis of Randomized Trials. Cardiovasc Ther. 2015 Oct;33(5):253-63.

Basaraba J, Barry A. Short- versus standard-term dual antiplatelet therapy after percutaneous coronary intervention with drug-eluting stent implantation: a meta-analysis. Abstract CSHP PPC 2016. CJHP 2016; 69(1).

Basaraba JE, Barry AR. Short- versus standard-term dual antiplatelet therapy after percutaneous coronary intervention with drug-eluting stent implantation: A meta-analysis. J Cardiol. 2016 Aug 30.

Cassese S, Byrne RA, Ndrepepa G, et al. Prolonged dual antiplatelet therapy after drug-eluting stenting: meta-analysis of randomized trials. Clin Res Cardiol. 2015 Oct;104(10):887-901.

Gargiulo G, Windecker S, da Costa BR, et al. Short term versus long term dual antiplatelet therapy after implantation of drug eluting stent in patients with or without diabetes: systematic review and meta-analysis of individual participant data from randomised trials. BMJ 2016;355:i5483.

Giustino G, Baber U, Sartori S, et al. Duration of dual antiplatelet therapy after drug-eluting stent implantation: a systematic review and meta-analysis of randomized controlled trials. J Am Coll Cardiol. 2015 Apr 7;65(13):1298-310.

Golwala HB, Cannon CP, Steg PG, et al. Safety and efficacy of **dual vs. triple antithrombotic therapy** in patients with **atrial fibrillation following percutaneous coronary intervention**: a systematic review and meta-analysis of randomized clinical trials. Eur Heart J. 2018 Apr 13.

Lou B, Liang X, Wu Y, et al. Meta-Analysis Comparing **Dual Versus Single** Antiplatelet Therapy in Combination With **Antithrombotic Therapy in Patients With Atrial Fibrillation** Who Underwent **Percutaneous Coronary Intervention** With Stent Implantation. Am J Cardiol. 2018 Aug 15;122(4):604-611.

Navarese EP, Andreotti F, Schulze V, et al. Optimal duration of dual antiplatelet therapy after percutaneous coronary intervention with drug eluting stents: meta-analysis of randomised controlled trials. BMJ. 2015 Apr 16;350:h1618.

Palmerini T, Benedetto U, Bacchi-Reggiani L, et al. Mortality in patients treated with extended duration dual antiplatelet therapy after drug-eluting stent implantation: a pairwise and Bayesian network meta-analysis of randomised trials. Lancet. 2015 Jun 13;385(9985):2371-82.

Palmerini T, Della Riva D, Benedetto U, et al. **Three, six, or twelve months of dual antiplatelet therapy after DES implantation** in patients with or without acute coronary syndromes: an individual patient data pairwise and network meta-analysis of six randomized trials and 11 473 patients. Eur Heart J. 2017 Jan 21

Sharma A, Lavie CJ, Sharma SK, et al. Duration of Dual Antiplatelet Therapy After Drug-Eluting Stent Implantation in Patients With and Without Acute Coronary Syndrome: A Systematic Review of Randomized Controlled Trials. Mayo Clin Proc. 2016 Aug;91(8):1084-93.

Spencer FA, Prasad M, Vandvik PO, et al. Longer- Versus Shorter-Duration Dual-Antiplatelet Therapy After Drug-Eluting Stent Placement: A Systematic Review and Meta-analysis. Ann Intern Med. 2015 Jul 21;163(2):118-26.

Tsoi MF, Cheung CL, Cheung TT, et al. Duration of dual antiplatelet therapy after drug-eluting stent implantation: Meta-analysis of large randomised controlled trials. Sci Rep. 2015 Aug 17;5:13204.

Valgimigli M, Gargiulo G. Deciding on the **Duration of Dual Antiplatelet Therapy**-When the Choice Between 2 Evils Is Still Evil. JAMA Cardiol. 2017 Mar 15.

Verdoia M, Schaffer A, Barbieri L, et al. Optimal Duration of Dual Antiplatelet Therapy After DES Implantation: A Meta-Analysis of 11 Randomized Trials. Angiology. 2015 Jun 11.

Wells GA, Elliott J, Kelly S, et al. **Dual antiplatelet therapy following percutaneous coronary intervention**: a review of the clinical impact of treatment duration. Ottawa (ON): Canadian Agency for Drugs and Technologies in Health; 2017 Aug.

Lee SY, Hong MK, Palmerini T, et al. **Short-Term Versus Long-Term Dual Antiplatelet Therapy After Drug-Eluting Stent Implantation in Elderly** Patients: A Meta-Analysis of Individual Participant Data From 6 Randomized Trials. JACC Cardiovasc Interv. 2018 Feb 8.

DAPT-POST PCI TRIALS (>1 year)

Collet JP, Silvain J, Barthélémy O, et al; **ARCTIC** investigators. Dual-antiplatelet treatment beyond 1 year after drug-eluting stent implantation (ARCTIC-Interruption): a randomised trial. Lancet. 2014 Nov 1;384(9954):1577-85.

Helft G, Steg PG, Le Feuvre C, et al; OPTImal DUAL Antiplatelet Therapy Trial Investigators. Stopping or continuing clopidogrel 12 months after drug-eluting stent placement: the **OPTIDUAL** randomized trial. Eur Heart J. 2016 Jan 21;37(4):365-74.

Lee CW, Ahn JM, Park DW, et al. Optimal duration of dual antiplatelet therapy after drug-eluting stent implantation: a randomized, controlled trial (**DES-LATE**). Circulation. 2014 Jan 21;129(3):304-12.

Mauri L, Kereiakes DJ, Yeh RW, et al; **DAPT Study Investigators**. Twelve or 30 months of dual antiplatelet therapy after drug-eluting stents. N Engl J Med. 2014 Dec 4; 371(23):2155-66.

Stefanescu Schmidt AC, Kereiakes DJ, Cutlip DE, et al; DAPT Investigators. **Myocardial Infarction Risk after Discontinuation of Thienopyridine Therapy in the Randomized DAPT** Study. Circulation. 2017 Feb 22.

Wallace EL, Abdel-Latif A, Charnigo R,et al. Meta-analysis of long-term outcomes for drug-eluting stents versus bare-metal stents in primary percutaneous coronary interventions for ST-segment elevation myocardial infarction. Am J Cardiol. 2012 Apr 1;109(7):932-40.

Yeh R, Secemsky E, Kereiakes J, et al. Individualizing treatment duration of dual antiplatelet therapy after percutaneous coronary intervention: an analysis from the DAPT study (**DAPT Score Calculator**). Available at: http://www.daptstudy.org/for-media/DAPT_Score_AHA_Slides.pdf. Accessed January 2016.

Yeh RW, Secemsky EA, Kereiakes DJ, et al; DAPT Study Investigators. Development and Validation of a Prediction Rule for Benefit and Harm of Dual Antiplatelet Therapy Beyond 1 Year After Percutaneous Coronary Intervention. JAMA. 2016 Mar 29.

DAPT-POST PCI TRIALS

Colombo A, Chieffo A, Frasheri A, Garbo R, Masotti-Centol M, Salvatella N, et al. Second-generation drug-eluting stent implantation followed by 6- versus 12-month dual antiplatelet therapy: the **SECURITY** randomized clinical trial. J Am Coll Cardiol. 2014;64: 2086-97.

Feres F, Costa RA, Abizaid A, et al; **OPTIMIZE** Trial Investigators. Three vs twelve months of dual antiplatelet therapy after zotarolimus-eluting stents: the OPTIMIZE randomized trial. JAMA. 2013;310:2510-22.

Franzone A, Piccolo R, Gargiulo G, et al. Prolonged vs Short Duration of Dual Antiplatelet Therapy After Percutaneous Coronary Intervention in Patients With or Without Peripheral Arterial Disease: A Subgroup Analysis of the **PRODIGY** Randomized Clinical Trial. JAMA Cardiol. 2016 Oct 1;1(7):795-803.

Gilard M, Barragan P, Noryani AA, et al. 6- versus 24-month dual antiplatelet therapy after implantation of drug-eluting stents in patients nonresistant to aspirin: the randomized, multicenter **ITALIC** trial. J Am Coll Cardiol. 2015;65:777-86.

Gwon HC, Hahn JY, Park KW, et al. Six-month versus 12-month dual antiplatelet therapy after implantation of drug-eluting stents: the Efficacy of Xience/Promus Versus Cypher to Reduce Late Loss After Stenting (**EXCELLENT**) randomized, multicenter study. Circulation. 2012;125:505-13.

Kedhi E, Fabris E, van der Ent M, et al. Six months versus 12 months **dual antiplatelet therapy after drug-eluting stent implantation in ST-elevation myocardial infarction** (DAPT-STEMI): randomised, multicentre, non-inferiority trial. BMJ. 2018 Oct 2;363:k3793.

Kim BK, Hong MK, Shin DH, et al; **RESET** Investigators. A new strategy for discontinuation of dual antiplatelet therapy: the RESET Trial (REal Safety and Efficacy of 3-month dual antiplatelet Therapy following Endeavor zotarolimus-eluting stent implantation). J Am Coll Cardiol. 2012;60:1340-8.

Schulz-Schupke S, Byrne RA, Ten Berg JM, et al; on behalf of the Intracoronary Stenting and Antithrombotic Regimen: Safety And EFficacy of 6 Months Dual Antiplatelet Therapy After Drug-Eluting Stenting (**ISAR-SAFE**) trial investigators. ISAR-SAFE: a randomized, double-blind, placebo controlled trial of 6 versus 12 months of clopidogrel therapy after drug-eluting stenting. Eur Heart J. 2015.

Secemsky EA, Yeh RW, Kereiakes DJ, et al. **Mortality** Following Cardiovascular and Bleeding Events Occurring **Beyond 1 Year After Coronary Stenting**: A Secondary Analysis of the Dual Antiplatelet Therapy (**DAPT**) Study. JAMA Cardiol. 2017 Mar 15.

Tsivgoulis G, Goyal N, Kerro A, et al. **Dual antiplatelet therapy** pretreatment in IV thrombolysis for acute **ischemic stroke**. Neurology. 2018 Sep 11;91(11):e1067-e1076.

Valgimigli M, Borghesi M, Tebaldi M, et al; PROlonging Dual antiplatelet treatment after Grading stent-induced Intimal hyperplasia studY Investigators. Should duration of dual antiplatelet therapy depend on the type and/or potency of implanted stent? A pre-specified analysis from the PROlonging Dual antiplatelet treatment after Grading stent-induced Intimal hyperplasia studY (**PRODIGY**). Eur Heart J. 2013;34:909-19.

BARE-METAL STENTS

Kereiakes DJ, Yeh RW, Massaro JM, et al; Dual Antiplatelet Therapy (**DAPT)** Study Investigators. Antiplatelet therapy duration following **bare metal** or drug-eluting coronary stents: the dual antiplatelet therapy randomized clinical trial. JAMA. 2015 Mar 17;313(11):1113-21.

Shah R, Rao SV, Latham SB, Kandzari DE. Efficacy and **safety of drug-eluting stents optimized for biocompatibility vs bare-metal stents with a single month of dual antiplatelet therapy**: a meta-analysis [online Oct 31, 2018]. JAMA Cardiol. doi:10.1001/jamacardio.2018.3551

Steinhubl SR, Berger PB, Mann JT et al; **CREDO** Investigators. Clopidogrel for the Reduction of Events During Observation. Early and sustained dual oral antiplatelet therapy following percutaneous coronary intervention: a randomized controlled trial. JAMA. 2002 Nov 20; 288(19):2411-20.

Yamaji K, Shiomi H, Morimoto T, et al. Influence of Sex on Long-Term Outcomes After Implantation of Bare-Metal Stent: A Multicenter Report From the Coronary Revascularization Demonstrating Outcome Study-Kyoto (CREDO-Kyoto) Registry Cohort-1. Circulation. 2015 Dec 15;132(24):2323-33.

DISCONTINUATION OF THERAPY

Eisenstein EL, Anstrom KJ, Kong DF, et al. Clopidogrel use and long-term clinical outcomes after drug-eluting stent implantation. JAMA. 2007 Jan 10;297(2):159-68.

Loh JP, Torguson R, Pendyala LK, et al. Impact of early versus late clopidogrel discontinuation on stent thrombosis following percutaneous coronary intervention with first- and second-generation drug-eluting stents. Am J Cardiol. 2014 Jun 15;113(12):1968-76.

Mehran R, Baber U, Steg PG, et al. Cessation of dual antiplatelet treatment and cardiac events after percutaneous coronary intervention (**PARIS**): 2 year results from a prospective observational study. Lancet. 2013 Nov 23;382(9906):1714-22.

Moussa ID, Colombo A. Antiplatelet therapy discontinuation following drug-eluting stent placement: dangers, reasons, and management recommendations. Catheter Cardiovasc Interv. 2009 Dec 1;74(7):1047-54.

Naidu SS, Krucoff MW, Rutledge DR, et al. Contemporary incidence and predictors of stent thrombosis and other major adverse cardiac events in the year after XIENCE V implantation: results from the 8,061-patient XIENCE V United States study. JACC Cardiovasc Interv. 2012 Jun;5(6):626-35.

Pfisterer M, Brunner-La Rocca HP, Buser PT, et al; BASKET-LATE Investigators. Late clinical events after clopidogrel discontinuation may limit the benefit of drug-eluting stents: an observational study of drug-eluting versus bare-metal stents. J Am Coll Cardiol. 2006 Dec 19;48(12):2584-91.

Schulz S, Schuster T, Mehilli J, et al. Stent thrombosis after drug-eluting stent implantation: incidence, timing, and relation to discontinuation of clopidogrel therapy over a 4-year period. Eur Heart J. 2009 Nov;30(22):2714-21.

Silber S, Kirtane AJ, Belardi JA, et al. Lack of association between dual antiplatelet therapy use and stent thrombosis between 1 and 12 months following resolute zotarolimus-eluting stent implantation. Eur Heart J. 2014 Aug 1;35(29):1949-56.

Stefanescu Schmidt AC, Kereiakes DJ, Cutlip DE, et al; **DAPT** Investigators. **Myocardial Infarction Risk After Discontinuation of Thienopyridine** Therapy in the Randomized DAPT Study (Dual Antiplatelet Therapy). Circulation. 2017 May 2;135(18):1720-1732.

Yano M, Natsuaki M, Morimoto T, Nakagawa Y, et al; j-Cypher Registry Investigators. Antiplatelet therapy discontinuation and stent thrombosis after sirolimus-eluting stent implantation: five-year outcome of the j-Cypher Registry. Int J Cardiol. 2015 Nov 15;199:296-301.

STENT THROMBOSIS

Byrne RA, Joner M, Kastrati A. Stent thrombosis and restenosis: what have we learned and where are we going? The Andreas Grüntzig Lecture ESC 2014. Eur Heart J. 2015 Dec 14;36(47):3320-31.

Eisen A, Bhatt DL. Antiplatelet therapy: Defining the optimal duration of DAPT after PCI with DES. Nat Rev Cardiol. 2015 Aug;12(8):445-6.

Daemen J, Wenaweser P, Tsuchida K, et al. Early and late coronary stent thrombosis of sirolimus-eluting and paclitaxel-eluting stents in routine clinical practice: data from a large two-institutional cohort study. Lancet. 2007 Feb 24;369(9562):667-78.

Dangas GD, Claessen BE, Mehran R, et al. Development and validation of a stent thrombosis risk score in patients with acute coronary syndromes. JACC Cardiovasc Interv. 2012 Nov;5(11):1097-105.

Jeger RV, Pfisterer ME, Sørensen R, et al; BASKET and BASKET-PROVE investigators. Tradeoff between bleeding and stent thrombosis in different dual antiplatelet therapy regimes: Importance of case fatality rates and effective treatment durations. Am Heart J. 2014 Nov;168(5):698-705.

Holmes DR Jr, Kereiakes DJ, Garg S et al. Stent thrombosis. J Am Coll Cardiol. 2010 Oct 19;56(17):1357-65.

Kaul U, Bangalore S, Seth A, et al; **TUXEDO**–India Investigators. Paclitaxel-Eluting versus Everolimus-Eluting Coronary Stents in Diabetes. N Engl J Med. 2015 Oct 29;373(18):1709-19.

Naidu SS, Krucoff MW, Rutledge DR, et al. Contemporary incidence and predictors of stent thrombosis and other major adverse cardiac events in the year after XIENCE V implantation: results from the 8,061-patient XIENCE V United States study. JACC Cardiovasc Interv. 2012 Jun;5(6):626-35.

Sarno G, Lagerqvist B, Fröbert O, et al. Lower risk of stent thrombosis and restenosis with unrestricted use of 'new-generation' drug-eluting stents: a report from the nationwide Swedish Coronary Angiography and Angioplasty Registry (SCAAR). Eur Heart J. 2012 Mar;33(5):606-13.

Serruys PW, Farooq V, Kalesan B, et al. Improved safety and reduction in stent thrombosis associated with biodegradable polymer-based biolimus-eluting stents versus durable polymer-based sirolimus-eluting stents in patients with coronary artery disease: final 5-year report of the LEADERS (Limus Eluted From A Durable Versus ERodable Stent Coating)randomized, noninferiority trial. JACC Cardiovasc Interv. 2013 Aug;6(8):777-89.

Tada T, Byrne RA, Simunovic I, et al. Risk of stent thrombosis among bare-metal stents, first-generation drug-eluting stents, and second-generation drug-eluting stents: results from a registry of 18,334 patients. JACC Cardiovasc Interv. 2013 Dec;6(12):1267-74.

van Werkum JW, Heestermans AA, Zomer AC, et al. Predictors of coronary stent thrombosis: the Dutch Stent Thrombosis Registry. J Am Coll Cardiol. 2009 Apr 21;53(16):1399-409.

REVIEWS ON THE DURATION OF DAPT AFTER CORONARY STENTING

Bavishi C, Trivedi V, Singh M, et al. Duration of **Dual Antiplatelet Therapy in Patients with an Acute Coronary Syndrome** Undergoing Percutaneous Coronary Intervention. Am J Med. 2017 Jun 13.

Binder R, Luscher T. Duration of DAPT after coronary artery stenting: where is the sweet spot between ischemia and bleeding? European Heart Jouranl. 2015; (36)1207-1211.

Kedhi E, Fabris E, van der Ent M, et al. **Six months versus 12 months dual antiplatelet therapy after drug-eluting stent implantation in ST-elevation myocardial infarction (DAPT-STEMI**): randomised, multicentre, non-inferiority trial. BMJ. 2018 Oct 2;363:k3793.

Mehran R, Giustino G, Baber U. DAPT duration after DES: what is the "mandatory" duration? J Am Coll Cardiol. 2015 Mar 24;65(11):1103-6.

Montalescot G, Brieger D, Dalby AJ, et al. Duration of Dual Antiplatelet Therapy After Coronary Stenting: A Review of the Evidence. J Am Coll Cardiol. 2015 Aug 18;66(7):832-47.

Park SJ, Kang SM, Park DW. Dual antiplatelet therapy after drug-eluting stents: defining the proper duration. Coron Artery Dis. 2014 Jan;25(1):83-9.

Sibbing D, Aradi D, Jacobshagen C, et al, on behalf of the **TROPICAL-ACS** Investigators. Guided **De-Escalation of Antiplatelet Treatment in Acute Coronary Syndrome** Patients Undergoing percutaneous coronary intervention (TROPICAL-ACS): a randomised, open-label, multicentre trial. Lancet 2017; published online Aug 27.

ASA

Antithrombotic Trialists' Collaboration. Collaborative meta-analysis of randomised trials of antiplatelet therapy for prevention of death, myocardial infarction, and stroke in high risk patients. BMJ. 2002 Jan 12;324(7329):71-86.

Antithrombotic Trialists' (ATT) Collaboration. Aspirin in the primary and secondary prevention of vascular disease: collaborative meta-analysis of individual participant data from randomised trials. Lancet. 2009 May 30;373(9678):1849-60.

CLOPIDOGREL

Belch JJ, Dormandy J et al; CASPAR Writing Committee. Results of the randomized, placebo-controlled clopidogrel and acetylsalicylic acid in bypass surgery for peripheral arterial disease (**CASPAR**) trial. J Vasc Surg. 2010 Oct;52(4):825-33, 833.e1-2.

Bhatt DL, Fox KA, Hacke W, et al; **CHARISMA** Investigators. Clopidogrel and aspirin versus aspirin alone for the prevention of atherothrombotic events. N Engl J Med. 2006 Apr 20;354(16):1706-17.

Chen ZM, Jiang LX, Chen YP, et al; **COMMIT** (ClOpidogrel and Metoprolol in Myocardial Infarction Trial) collaborative group. Addition of clopidogrel to aspirin in 45,852 patients with acute myocardial infarction: randomised placebo-controlled trial. Lancet. 2005 Nov 5; 366(9497):1607-21.

CURE Study Investigators. The Clopidogrel in Unstable angina to prevent Recurrent Events (**CURE**) trial programme. Eur Heart J 2000, 21:2033-2041.

Hao Q, Tampi M, O'Donnell M, et al. **Clopidogrel plus aspirin versus aspirin alone for acute minor ischaemic stroke or high risk transient ischaemic attack**: systematic review and meta-analysis. BMJ. 2018 Dec 18;363:k5108.

Ho PM, Tsai TT, Maddox TM, et al. Delays in filling clopidogrel prescription after hospital discharge and adverse outcomes after drug-eluting stent implantation: implications for transitions of care. Circ Cardiovasc Qual Outcomes. 2010 May;3(3):261-6.

Kulik A, Le May MR, Voisine P, et al. Aspirin plus clopidogrel versus aspirin alone after coronary artery bypass grafting: the clopidogrel after surgery for coronary artery disease (**CASCADE**) Trial. Circulation. 2010 Dec 21; 122(25):2680-7.

Mehta SR, Tanguay JF, Eikelboom JW, et al; CURRENT-OASIS 7 trial investigators. Double-dose versus standard-dose clopidogrel and high-dose versus low-dose aspirin in individuals undergoing percutaneous coronary intervention for acute coronary syndromes (**CURRENT-OASIS 7**): a randomised factorial trial. Lancet. 2010 Oct 9; 376(9748):1233-43.

Mehta SR, Bassand JP, Chrolavicius S, et al. **CURRENT-OASIS 7** Investigators. Dose comparisons of clopidogrel and aspirin in acute coronary syndromes. N Engl J Med. 2010 Sep 2;363(10):930-42.

Mehta SR, Yusuf S, Peter RJG, Bertrand ME, et al. Effects of pretreatment with clopidogrel and aspirin followed by long-term therapy in patients undergoing percutaneous coronary intervention: the **PCI-CURE** study. Lancet 2001. 358:527-533.

Mehta SR, Yusuf S; Clopidogrel in Unstable angina to prevent Recurrent Events (**CURE**) Study Investigators. The Clopidogrel in Unstable angina to prevent Recurrent Events (CURE) trial programme; rationale, design and baseline characteristics including a meta-analysis of the effects of thienopyridines in vascular disease. Eur Heart J. 2000 Dec; 21(24):2033-41.

Mega JL, Close SL, Wiviott SD, et al. Cytochrome p-450 polymorphisms and response to clopidogrel. N Engl J Med. 2009 Jan 22;360(4):354-62.

Notarangelo FM, et al. **Pharmacogenomic Approach to Selecting Antiplatelet Therapy in Acute Coronary Syndromes**: **PHARMCLO** trial. J Am Coll Cardiol. 2018 Feb 24.

Prasad K, Siemieniuk R, Hao Q, et al. **Dual antiplatelet therapy with aspirin and clopidogrel** for acute high risk transient ischaemic attack and minor ischaemic stroke: a clinical practice guideline. BMJ. 2018 Dec 18;363:k5130.

Sabatine MS, Cannon CP, Gibson CM, et al. Effect of Clopidogrel Pretreatment Before Percutaneous Coronary Intervention in Patients with ST-Elevation Myocardial Infarction Treated with Fibrinolytics: The **PCI-CLARITY** Study. JAMA. 2005 Sept 14; 29=4 (10): 1224-1232.

Sabatine MS, Cannon CP, Gibson CM, et al; **CLARITY-TIMI** 28 Investigators. Addition of clopidogrel to aspirin and fibrinolytic therapy for myocardial infarction with ST-segment elevation. N Engl J Med. 2005 Mar 24; 352(12):1179-89.

Sabatine MS, McCabe CH, Gibson CH & Cannon CP. Design and rationale of Clopidogrel as Adjunctive Reperfusion Therapy- Thrombolysis in Myocardial Infarction (CLARITY-TIMI) 28 trial. Am Heart J 2005 149: 227-233.

Simon T, Verstuyft C, Mary-Krause M, Quteineh L, Drouet E, Méneveau N, Steg PG, Ferrières J, Danchin N, Becquemont L; French Registry of Acute ST-Elevation and Non-ST-Elevation Myocardial Infarction (FAST-MI) Investigators. Genetic determinants of response to clopidogrel and cardiovascular events. N Engl J Med. 2009 Jan 22; 360(4):363-75.

Steinhubl SR, Berger PB, Mann JT et al; **CREDO** Investigators. Clopidogrel for the Reduction of Events During Observation. Early and sustained dual oral antiplatelet therapy following percutaneous coronary intervention: a randomized controlled trial. JAMA. 2002 Nov 20; 288(19):2411-20.

CLOPIDOGREL: MORTALITY

Elmariah S, Mauri L, Doros G et al Extended duration dual antiplatelet therapy and mortality: a systematic review and meta-analysis. Lancet. 2015 Feb 28;385(9970):792-8. FDA Drug Safety Communication: FDA review finds long-term treatment with blood-thinning medicine Plavix (clopidogrel) does not change risk of death. Available at: http://www.fda.gov/downloads/Drugs/DrugSafety/UCM471586.pdf. Accessed February 2016.

Mauri L, Elmariah S, Yeh RW et al; DAPT Study Investigators. Causes of late mortality with dual antiplatelet therapy after coronary stents. Eur Heart J. 2016 Jan 21;37(4):378-85.

TICAGRELOR

Bonaca MP, Bhatt DL, Cohen M, et al; **PEGASUS-TIMI** 54 Steering Committee and Investigators. Long-term use of ticagrelor in patients with prior myocardial infarction. N Engl J Med. 2015 May 7;372(19):1791-800.

Grima DT, Brown ST, Kamboj L, et al. Cost-effectiveness of ticagrelor versus clopidogrel in patients with acute coronary syndromes in Canada. Clinicoecon Outcomes Res. 2014 Jan 24;6:49-62.

Mahaffey KW, Wojdyla DM, Carroll K, et al; **PLATO** Investigators. Ticagrelor compared with clopidogrel by **geographic region** in the Platelet Inhibition and Patient Outcomes (PLATO) trial. Circulation. 2011 Aug 2;124(5):544-54.

Wallentin L, Becker RC, Budaj A, et al; **PLATO** Investigators, Freij A, Thorsén M. Ticagrelor versus clopidogrel in patients with acute coronary syndromes. N Engl J Med. 2009 Sep10;361(11):1045-57.

PRASUGREL

Montalescot G, Wiviott SD, Braunwald E, et al; **TRITON-TIMI** 38 investigators. Prasugrel compared with clopidogrel in patients undergoing percutaneous coronary intervention for **ST-elevation myocardial infarction** (TRITON-TIMI 38): double-blind, randomised controlled trial. Lancet. 2009 Feb 28;373(9665):723-31.

Roe MT, Armstrong PW, Fox KA, et al; **TRILOGY** ACS Investigators. Prasugrel versus clopidogrel for acute coronary syndromes without revascularization. N Engl J Med. 2012 Oct 4;367(14):1297-309.

Wiviott SD, Braunwald E, McCabe CH, et al; **TRITON-TIMI** 38 Investigators. Prasugrel versus clopidogrel in patients with acute coronary syndromes. N Engl J Med. 2007 Nov 15; 357(20):2001-15.

SWITCHING P2Y12 INHIBITORS

Angiolillo DJ, Rollini F, Storey RF, et al. **International Expert Consensus** on **Switching Platelet P2Y(12) Receptor-Inhibiting** Therapies. Circulation. 2017 Nov 14;136(20):1955-1975.

Bagai A, Chua D, Cohen EA, et al. Pharmacodynamic and clinical implications of switching between P2Y12 receptor antagonists: considerations for practice. Crit Pathw Cardiol. 2014 Dec;13(4):156-8.

Cuisset T, Deharo P, Quilici J, et al. Benefit of **switching dual antiplatelet therapy after acute coronary syndrome**: the **TOPIC** (timing of platelet inhibition after acute coronary syndrome) randomized study. Eur Heart J. 2017 May 16.

De Luca L, D'Ascenzo F, Musumeci G, et al. Incidence and Outcome of Switching of Oral Platelet P2Y12 Receptor Inhibitors in Patients with Acute Coronary Syndromes Undergoing Percutaneous Coronary Intervention: The SCOPE Registry. EuroIntervention. 2017 Apr 4.

Rollini F, Franchi F, Angiolillo DJ. Switching P2Y12-receptor inhibitors in patients with coronary artery disease. Nat Rev Cardiol. 2016 Jan;13(1):11-27.

Wallentin L, Becker RC, Budaj A, et al; **PLATO** Investigators. Ticagrelor versus clopidogrel in patients with acute coronary syndromes. N Engl J Med. 2009 Sep10; 361(11):1045-57.

BLEEDING RISK

Alfredsson J, Neely B, Neely ML, et al. Predicting the risk of bleeding during dual antiplatelet therapy after acute coronary syndromes. Heart. 2017 Apr 5.

Costa F, van Klaveren D, James S, et al, for the PRECISE-DAPT Study Investigators. Derivation and validation of the **predicting bleeding complications** in patients undergoing stent implantation and subsequent dual antiplatelet therapy (**PRECISE-DAPT**) **score**: a pooled analysis of individual-patient datasets from clinical trials. Lancet 2017; 389: 1025–34.

Ducrocq G, Wallace JS, Baron G, et al; **REACH Investigators**. Risk score to predict serious bleeding in stable outpatients with or at risk of atherothrombosis. Eur Heart J. 2010 May;31(10):1257-65.

Généreux P, Giustino G, Witzenbichler B, et al. Incidence, Predictors, and Impact of Post-Discharge Bleeding After Percutaneous Coronary Intervention. J Am Coll Cardiol. 2015 Sep 1;66(9):1036-45.

Harada Y;Michel J;Lohaus R;et al. **Validation of the DAPT score** in patients randomized to 6 or 12 months clopidogrel after predominantly second-generation drug-eluting stents. Thromb Haemost. 2017 Jul 27;117(10).

Ko DT, Yun L, Wijeysundera HC, et al. Incidence, predictors, and prognostic implications of hospitalization for late bleeding after percutaneous coronary intervention for patients older than 65 years. Circ Cardiovasc Interv. 2010 Apr;3(2):140-7.

Konishi H, Miyauchi K, Tsuboi S, et al. Impact of the **HAS-BLED Score** on Long-Term Outcomes **After Percutaneous Coronary Intervention**. Am J Cardiol. 2015 Aug 15;116(4):527-31.

Vries MJ, van der Meijden PE, Henskens YM, et al. Assessment of bleeding risk in patients with coronary artery disease on dual antiplatelet therapy. A systematic review. Thromb Haemost. 2015 Dec 22;115(1):7-24.

Palmerini T, Bacchi Reggiani L, Della Riva D, et al. **Bleeding-Related Deaths** in Relation to the Duration of Dual-Antiplatelet Therapy After Coronary Stenting. J Am Coll Cardiol. 2017 Apr 25;69(16):2011-2022.

Piccolo R, Gargiulo G, Franzone A, et al. Use of the **dual-antiplatelet therapy score** to guide treatment duration **after percutaneous coronary intervention**. Ann Intern Med. [Epub ahead of print 13 June 2017]. doi:10.7326/M16-2389

GASTROINTESTINAL BLEEDING & GASTROPROTECTION

Abraham NS, Hlatky MA, Antman EM, et al; ACCF/ACG/AHA. **ACCF/ACG/AHA 2010 expert consensus document on the concomitant use of proton pump inhibitors and thienopyridines**: a focused update of the ACCF/ACG/AHA 2008 expert consensus document on reducing the gastrointestinal risks of antiplatelet therapy and NSAID use. A Report of the American College of Cardiology Foundation Task Force on Expert Consensus Documents. J Am Coll Cardiol. 2010 Dec 7;56(24):2051-66.

Bhatt DL, Cryer BL, Contant CF, et al; **COGENT** Investigators. Clopidogrel with or without omeprazole in coronary artery disease. N Engl J Med. 2010 Nov 11;363(20):1909-17.
Cardoso RN, Benjo AM, DiNicolantonio JJ, et al. Incidence of cardiovascular events and gastrointestinal bleeding in patients receiving clopidogrel with and without proton pump inhibitors: an updated meta-analysis. Open Heart. 2015 Jun 30;2(1):e000248.
Moukarbel GV, Signorovitch JE, Pfeffer MA, et al. Gastrointestinal bleeding in high risk survivors of myocardial infarction: the **VALIANT** Trial. Eur Heart J. 2009 Sep;30(18):2226-32.
Roffi M, Patrono C, Collet JP, et al. **2015 ESC Guidelines for the Management of Acute Coronary Syndromes in Patients Presenting Without Persistent ST-segment Elevation**. Rev Esp Cardiol (Engl Ed). 2015 Dec;68(12):1125.
Schjerning Olsen AM, Lindhardsen J, Gislason GH, et al. Impact of proton pump inhibitor treatment on gastrointestinal bleeding associated with non-steroidal anti-inflammatory drug use among post-myocardial infarction patients taking antithrombotics: nationwide study. BMJ. 2015 Oct 19;351:h5096.
Vardi M, Cryer BL, Cohen M, et al. The effects of proton pump inhibition on patient-reported severity of dyspepsia when receiving dual anti-platelet therapy with clopidogrel and low-dose aspirin: analysis from the **Clopidogrel and the Optimization of Gastrointestinal Events Trial**. Aliment Pharmacol Ther. 2015 Aug;42(3):365-74.
Wilson S, Newby DE. **Predicting long-term bleeding risk after acute coronary syndrome**: a step closer to optimising dual antiplatelet therapy duration? Heart. 2017 May 20.

DAPT + CABG

Agarwal N, Mahmoud AN, Patel NK, et al. Meta-Analysis of **Aspirin Versus Dual Antiplatelet** Therapy **Following Coronary Artery Bypass Grafting**. Am J Cardiol. 2017 Oct 26.
Bomb R, Oliphant CS, Khouzam RN. Dual Antiplatelet Therapy After Coronary Artery Bypass Grafting in the Setting of Acute Coronary Syndrome. Am J Cardiol. 2015 Jul 1;116(1):148-54.
Gurbuz AT, Zia AA, Vuran AC, Cui H, Aytac A. Postoperative clopidogrel improves mid-term outcome after off-pump coronary artery bypass graft surgery: a prospective study. Eur J Cardiothorac Surg. 2006 Feb;29(2):190-5.
Patel JH, Stoner JA, Owora A, Mathew ST, Thadani U. Evidence for using clopidogrel alone or in addition to aspirin in post coronary artery bypass surgery patients. Am J Cardiol. 2009 Jun 15; 103(12):1687-93. doi: 10.1016/j.amjcard.2009.02.021. Epub 2009 May 4. Review.

TRIPLE THERAPY

Alexander JH, Lopes RD, James S, et al; **APPRAISE-2** Investigators. Apixaban with antiplatelet therapy after acute coronary syndrome. N Engl J Med. 2011 Aug 25;365(8):699-708.
Andrade JG, Deyell MW, Khoo C, et al. Risk of bleeding on triple antithrombotic therapy after percutaneous coronary intervention/stenting: a systematic review and meta-analysis. Can J Cardiol. 2013 Feb;29(2):204-12.
Barry AR, Ackman ML. Triple antithrombotic therapy in patients with atrial fibrillation who have undergone percutaneous coronary intervention with stent implantation. Am J Health Syst Pharm. 2012 Sep 1;69(17):1485-93.
Bavishi C, Koulova A, Bangalore S, et al. Evaluation of the efficacy and safety of dual antiplatelet therapy with or without warfarin in patients with a clinical indication for DAPT and chronic anticoagulation: A meta-analysis of observational studies. Catheter Cardiovasc Interv. 2015 Sep 10.
Briasoulis A, Papageorgiou N, Zacharia E, et al. Meta-Analysis of Oral Anticoagulants with Dual versus Single Antiplatelet Therapy in Patients after Percutaneous Coronary Intervention. Am J Cardiovasc Drugs. 2015 Dec 9.
Braun OÖ, Bico B, Chaudhry U, et al. Concomitant use of warfarin and **ticagrelor** as an alternative to triple antithrombotic therapy after an acute coronary syndrome. Thromb Res. 2015 Jan;135(1):26-30.
Cannon CP et al. Dual antithrombotic therapy with dabigatran after PCI in atrial fibrillation. (**RE-DUAL**) N Engl J Med2017 Aug 27.
Chamberlain AM, Gersh BJ, Mills RM, et al. Antithrombotic strategies and outcomes in acute coronary syndrome with atrial fibrillation. Am J Cardiol. 2015 Apr 15;115(8):1042-8.
Chen CF, Chen B, Zhu J, Xu YZ. Antithrombotic therapy after percutaneous coronary intervention in patients requiring oral anticoagulant treatment: A meta-analysis. Herz. 2015 Dec;40(8):1070-83.
Capodanno D. Triple antithrombotic therapy after **ACS and PCI** in patients on chronic oral anticoagulation: update. Heart. 2018 Apr 25.
Dans AL, Connolly SJ, Wallentin L, et al. Concomitant use of antiplatelet therapy with dabigatran or warfarin in the Randomized Evaluation of Long-Term Anticoagulation Therapy (**RE-LY**) trial. Circulation. 2013 Feb 5;127(5):634-40.
D'Ascenzo F, Taha S, Moretti C, et al. Meta-analysis of randomized controlled trials and adjusted observational results of use of clopidogrel, aspirin, and oral anticoagulants in patients undergoing percutaneous coronary intervention. Am J Cardiol. 2015 May 1;115(9):1185-93.

Dewilde WJ, Oirbans T, Verheugt FW, et al; **WOEST** study investigators. Use of clopidogrel with or without aspirin in patients taking oral anticoagulant therapy and undergoing percutaneous coronary intervention: an open-label, randomised, controlled trial. Lancet. 2013 Mar 30; 381(9872):1107-15.

Faxon DP, Eikelboom JW, Berger PB, et al. Antithrombotic therapy in patients with atrial fibrillation undergoing coronary stenting: a North American perspective: executive summary. Circ Cardiovasc Interv. 2011 Oct 1;4(5):522-34.

Fiedler KA, Maeng M, Mehilli J, et al. Duration of Triple Therapy inPatients Requiring Oral Anticoagulation After Drug-Eluting Stent Implantation:The **ISAR-TRIPLE** Trial. J Am Coll Cardiol. 2015 Apr 28; 65 (16):1619-29.

Fu A, Singh K, Abunassar J, et al; **CAPITAL** Investigators. **Ticagrelor** in Triple Antithrombotic Therapy: Predictors of Ischemic and Bleeding Complications. Clin Cardiol. 2016 Jan;39(1):19-23.

Gibson CM, Mehran R, Bode C, et al. An open-label, **atrial fibrillation who undergo percutaneous coronary intervention** randomized, controlled, multicenter study exploring two treatment strategies of **rivaroxaban** and a doseadjusted oral **vitamin K antagonist** treatment strategy in subjects with: **PIONEER AF-PCI**. N Engl J Med. 2016. doi: 10.1056/ NEJMoa1611594.

Hansen ML, Sørensen R, Clausen MT, Fog-Petersen ML, Raunsø J, Gadsbøll N, Gislason GH, Folke F, Andersen SS, Schramm TK, Abildstrøm SZ, Poulsen HE, Køber L, Torp-Pedersen C. Risk of bleeding with single, dual, or triple therapy with warfarin, aspirin, and clopidogrel in patients with atrial fibrillation. Arch Intern Med. 2010 Sep 13;170(16):1433-41

Hess CN, Peterson ED, Peng SA, et al. Use and Outcomes of Triple Therapy Among Older Patients With Acute Myocardial Infarction and Atrial Fibrillation. J Am Coll Cardiol. 2015 Aug 11;66(6):616-27.

Jackson LR 2nd, Ju C, Zettler M, et al. Outcomes of Patients With Acute Myocardial Infarction Undergoing Percutaneous Coronary Intervention Receiving an Oral Anticoagulant and Dual Antiplatelet Therapy: A Comparison of Clopidogrel Versus **Prasugrel** From the **TRANSLATE-ACS** Study. JACC Cardiovasc Interv. 2015 Dec 21;8(14):1880-9.

Lamberts M, Olesen JB, Ruwald MH, Hansen CM, Karasoy D, Kristensen SL, KøberL, Torp-Pedersen C, Gislason GH, Hansen ML. Bleeding after initiation of multiple antithrombotic drugs, including triple therapy, in atrial fibrillation patients following myocardial infarction & coronary intervention: a nationwide cohort study. Circulation. 2012 Sep 4;126(10):1185-93.
Mega JL, Braunwald E, Wiviott SD, et al; **ATLAS ACS 2**–TIMI 51 Investigators. Rivaroxaban in patients with a recent acute coronary syndrome. N Engl J Med. 2012 Jan 5;366(1):9-19.

Lamberts M, Gislason GH, Olesen JB, Kristensen SL, Schjerning Olsen AM, Mikkelsen A, Christensen CB, Lip GY, Køber L, Torp-Pedersen C, Hansen ML. Oral anticoagulation & antiplatelets in atrial fibrillation patients after myocardial infarction & coronary intervention. J Am Coll Cardiol. 2013 Sep 10;62(11):981-9.

Mennuni MG, Halperin JL, Bansilal S, et al. Balancing the Risk of Bleeding and Stroke in Patients With Atrial Fibrillation After Percutaneous Coronary Intervention (from the AVIATOR Registry). Am J Cardiol. 2015 Jul 1;116(1):37-42.

Oldgren J, Budaj A, Granger CB, et al; **RE-DEEM** Investigators. Dabigatran vs. placebo in patients with acute coronary syndromes on dual antiplatelet therapy: a randomized, double-blind, phase II trial. Eur Heart J. 2011 Nov;32(22):2781-9.

Sambola A, Mutuberría M, García Del Blanco B, et al. Impact of Triple Therapy in Elderly Patients with Atrial Fibrillation Undergoing Percutaneous Coronary Intervention. PLoS One. 2016 Jan 25;11(1):e0147245.

Sambola A, Mutuberría M, García Del Blanco B, et al. Effects of Triple Therapy in Patients With Non-Valvular Atrial Fibrillation Undergoing Percutaneous Coronary Intervention Regarding Thromboembolic Risk Stratification. Circ J. 2016 Jan 25;80(2):354-62.

Sarafoff N, Martischnig A, Wealer J, et al. Triple therapy with aspirin, **prasugrel**, and vitamin K antagonists in patients with drug-eluting stent implantation and an indication for oral anticoagulation. J Am Coll Cardiol. 2013 May 21;61(20):2060-6.

Sibbing D, Aradi D, Jacobshagen C, et al, on behalf of the **TROPICAL-ACS** Investigators. Guided **De-Escalation of Antiplatelet Treatment in Acute Coronary Syndrome** Patients Undergoing percutaneous coronary intervention (TROPICAL-ACS): a randomised, open-label, multicentre trial. Lancet 2017; published online Aug 27.

Valgimigli M, Patialiakas A, Thury A, et; **ZEUS** Investigators. Zotarolimus-eluting versus bare-metal stents in uncertain drug-eluting stent candidates. J Am Coll Cardiol. 2015 Mar 3;65(8):805-15.

Zhao HJ, Zheng ZT, Wang ZH, et al. "Triple therapy" rather than "triple threat": a meta-analysis of the two antithrombotic regimens after stent implantation in patients receiving long-term oral anticoagulant treatment. Chest. 2011 Feb;139(2):260-70.

OTHERS

Al Halabi S, Newman J, Farkouh ME, et al. Meta-Analysis of Studies Comparing **Dual- Versus Mono-Antiplatelet Therapy** Following Transcatheter **Aortic Valve Implantation**. Am J Cardiol. 2018 Mar 28.

Anand SS, Caron F, Eikelboom JW, et al. Major Adverse Limb Events in Lower Extremity **Peripheral Artery Disease: COMPASS** Trial. J Am Coll Cardiol. 2018 Mar 7.

CADTH **Dual antiplatelet therapy following percutaneous coronary intervention**: clinical and economic impact of standard versus extended duration. Canadian Coordinating Office for Health Technology Assessment (CCOHTA) 2019 Mar.

Carabenciov ID, Hawkes MA, Hocker S. Safety of **Lumbar Puncture Performed on Dual Antiplatelet Therapy**. Mayo Clin Proc. 2018 May;93(5):627-629.

Costa F, Van Klaveren D, Feres F, et al; PRECISE-DAPT Study Investigators. Dual Antiplatelet Therapy **Duration Based on Ischemic and Bleeding Risks After Coronary Stenting**. J Am Coll Cardiol. 2019 Feb 26;73(7):741-754.

Costa F, van Klaveren D, James S, et al, for the PRECISE-DAPT Study Investigators. Derivation and validation of the **predicting bleeding complications** in patients undergoing stent implantation and subsequent dual antiplatelet therapy (**PRECISE-DAPT**) **score**: a pooled analysis of individual-patient datasets from clinical trials. Lancet 2017; 389: 1025–34.

Cutlip DE, Windecker S, Mehran R, et al; **Academic Research Consortium**. Clinical end points in coronary stent trials: a case for standardized definitions. Circulation. 2007 May 1;115(17):2344-51.

D'Ascenzo F, Iannaccone M, Saint-Hilary G, et al. Impact of design of **coronary stents** and length of dual antiplatelet therapies on ischaemic and bleeding events: a network meta-analysis of 64 randomized controlled trials and 102 735 patients. Eur Heart J. 2017 Aug 11.

Eikelboom JW et al. Rivaroxaban with or without aspirin in stable cardiovascular disease. (**COMPASS**) N Engl J Med2017 Aug 27.

Floyd CN, Ferro A. Indications for **anticoagulant and antiplatelet combined therapy**. BMJ. 2017 Oct 5;359:j3782.

Gurbel PA, Fox KAA, Tantry US, et al. **Combination Antiplatelet and Oral Anticoagulant Therapy** in Patients With Coronary and Peripheral Artery Disease. Circulation. 2019 Apr 30;139(18):2170-2185.

Hess CN, Hiatt WR. Antithrombotic Therapy for **Peripheral Artery Disease** in 2018. JAMA. 2018 Jun 12;319(22):2329-2330.

Hilkens NA, Algra A, Kappelle LJ, et al. Early time course of major bleeding on antiplatelet therapy **after TIA or ischemic stroke**. Neurology. 2018 Jan 26.

Lee MS, Shlofmitz E, Haag E, et al. **Optimal Same-Day Platelet Inhibition** in Patients Receiving Drug-Eluting Stents With or Without Previous Maintenance Thienopyridine Therapy: from the Evaluation of Platelet Inhibition in Patients Having A VerifyNow Assay (**EPIPHANY**) Trial. Am J Cardiol. 2017 Jan 5.

Li J, Wang A, Zhao X, et al. High-sensitive C-reactive protein and dual antiplatelet in **intracranial arterial stenosis**. Neurology. 2018 Feb 6;90(6):e447-e454.

Lopes RD, Heizer G, Aronson R, et al. **Antithrombotic therapy after acute coronary syndrome or PCI in atrial fibrillation**. (AUGUSTUS-apixaban, warfarin) N Engl J Med. DOI: 10.1056/NEJMoa1817083.

Lüscher TF. **Dual antiplatelet therapy**: how, how long, and in which patients? Eur Heart J. 2018 Jan 14;39(3):181-183.

Mangieri A, Jabbour RJ, Montalto C, et al. **Single-Antiplatelet Therapy in Patients with Contraindication to Dual-Antiplatelet Therapy** After Transcatheter Aortic Valve Implantation. Am J Cardiol. 2017 Jan 6.

Morley RL, Sharma A, Horsch AD, Hinchliffe RJ. **Peripheral artery disease**. BMJ.2018 Feb 1;360:j5842.

Oldgren J, Steg PG, Hohnloser SH, et al. **Dabigatran dual therapy with ticagrelor or clopidogrel** after percutaneous coronary intervention in atrial fibrillation patients with or without acute coronary syndrome: a subgroup analysis from the RE-DUAL PCI trial. Eur Heart J. 2019 Feb 21.

Patti G, Cavallari I. **Extended duration dual antiplatelet therapy in patients with myocardial infarction**: A study-level meta-analysis of controlled randomized trials. Am Heart J. 2016 Jun;176:36-43.

Sibbing D, Gross L, Trenk D, et al; TROPICAL-ACS Investigators. Age and outcomes following guided **de-escalation of antiplatelet treatment in acute coronary syndrome** patients undergoing percutaneous coronary intervention: results from the randomized **TROPICAL-ACS** trial. Eur Heart J. 2018 Jun 14.

Siddamsetti S, Balasubramanian S, Yandrapalli S, et al. Meta-Analysis Comparing **Dual Antiplatelet Therapy Versus Single Antiplatelet Therapy Following Transcatheter Aortic Valve Implantation.** Am J Cardiol. 2018 Oct 15;122(8):1401-1408.

Sinnaeve PR, et al. Clopidogrel instead of **prasugrel or ticagrelor after 1 month in stabilized ACS patients**: back to square one for **DAPT**? Eur Heart J. 2017 Nov 1;38(41):3079-3081.

Squizzato A, Bellesini M, Takeda A, et al. **Clopidogrel plus aspirin versus aspirin alone for preventing cardiovascular events**. Cochrane Database of Systematic Reviews 2017, Issue 12. Art. No.: CD005158. The available evidence demonstrates that the use of clopidogrel plus aspirin in people at high risk of cardiovascular disease and people with established cardiovascular disease without a coronary stent is associated with a reduction in the risk of myocardial infarction and ischaemic stroke, and an increased risk of major and minor bleeding compared with aspirin alone. According to GRADE criteria, the quality of evidence was moderate for all outcomes except all-cause mortality (low quality evidence) and adverse events (very low quality evidence).

Udell JA, Bonaca MP, Collet JP, et al. Long-term dual antiplatelet therapy for secondary prevention of cardiovascular events in the subgroup of patients with **previous myocardial infarction**: a collaborative meta-analysis of randomized trials. Eur Heart J. 2016 Jan 21;37(4):390-9.

Van de Werf F. Prevention of Cardiovascular Events in Patients With **Diabetes**: How Beneficial Is Dual Antiplatelet Therapy? Circulation. 2017 May 2;135(18):1675-1676.

van Rein N, Heide-Jorgensen U, Lijfering WM, et al. **Major Bleeding Rates in Atrial Fibrillation Patients** on Single, Dual, or Triple Antithrombotic Therapy. Circulation. 2019 Feb 5;139(6):775-786. doi: 10.1161/CIRCULATIONAHA.118.036248. (Original)

Yoshikawa Y, Shiomi H, Watanabe H, et al. Validating Utility of **DAPT Score** in a Large Pooled Cohort from Three Japanese PCI Studies. Circulation. 2017 Oct 5.

Yoshikawa Y, Shiomi H, Watanabe H, et al. **Validating utility of dual antiplatelet therapy score** in a large pooled cohort from 3 Japanese percutaneous coronary intervention studies. Circulation. 2018;137:551–562.

CEREBROVASCULAR INDICATIONS

GUIDELINES

Wein T, Lindsay MP, Côté R, Foley N, Berlingieri J, Bhogal S, et al; Heart and Stroke Foundation **Canadian Stroke Best Practice Committees**. Canadian stroke best practice recommendations (**CSBPR**): Secondary prevention of stroke, sixth edition practice guidelines, update 2017. Int J Stroke. 2018 Jun;13(4):420-443.

Bell AD, Roussin A, Cartier R, Chan WS, Douketis JD, Gupta A, Kraw ME, Lindsay TF, Love MP, Pannu N, Rabasa-Lhoret R, Shuaib A, Teal P, Théroux P, Turpie AG,Welsh RC, Tanguay JF; **Canadian Cardiovascular Society**. The use of antiplatelet therapy in the outpatient setting: Canadian Cardiovascular Society Guidelines. Can J Cardiol. 2011 May-Jun;27 Suppl A:S1-59

Coutts SB, Wein TH, Lindsay MP, et al; Heart, and Stroke Foundation Canada Canadian Stroke Best Practices Advisory Committee. **Canadian Stroke Best Practice Recommendations**: **(CSBPR)** secondary prevention of stroke guidelines, update 2014. Int J Stroke. 2015 Apr;10(3):282-91.

Guyatt GH, Akl EA, Crowther M, Gutterman DD, Schuünemann HJ; American College of Chest Physicians Antithrombotic Therapy and Prevention of Thrombosis Panel. Executive summary: Antithrombotic Therapy and Prevention of Thrombosis, 9th ed: **American College of Chest Physicians Evidence-Based Clinical Practice Guidelines**. Chest. 2012 Feb;141(2 Suppl):7S-47S.

Kernan WN, Ovbiagele B, Black HR, et al; American Heart Association Stroke Council, Council on Cardiovascular and Stroke Nursing, Council on Clinical Cardiology, and Council on Peripheral Vascular Disease. Guidelines for the prevention of stroke in patients with stroke and transient ischemic attack: a guideline for healthcare professionals from the **American Heart Association/American Stroke Association**. Stroke. 2014 Jul;45(7):2160-236.

Skanes AC, Healey JS, Cairns JA, Dorian P, Gillis AM, McMurtry MS, Mitchell, LB, Verma A, Nattel S; Canadian Cardiovascular Society Atrial FibrillationGuidelines Committee. Focused 2012 update of the **Canadian Cardiovascular Society Atrial fibrillation** guidelines: recommendations for stroke prevention and rate/rhythm control. Can J Cardiol. 2012 Mar-Apr;28(2):125-36.

TRIALS

ACTIVE Investigators, Connolly SJ, Pogue J, Hart RG, Hohnloser SH, Pfeffer M, Chrolavicius S, Yusuf S. Effect of clopidogrel added to aspirin in patients with atrial fibrillation **(ACTIVE A)**. N Engl J Med. 2009 May 14;360(20):2066-78.

ACTIVE Writing Group of the ACTIVE Investigators, Connolly S, Pogue J, Hart R, Pfeffer M, Hohnloser S, Chrolavicius S, Pfeffer M, Hohnloser S, Yusuf S. Clopidogrel plus aspirin versus oral anticoagulation for atrial fibrillation in the Atrial fibrillation Clopidogrel Trial with Irbesartan for prevention of Vascular Events **(ACTIVE W)**: a randomised controlled trial. Lancet. 2006 Jun 10;367(9526):1903-12.

Bhatt DL, Fox KA, Hacke W, et al; **CHARISMA** Investigators. Clopidogrel and aspirin versus aspirin alone for the prevention of atherothrombotic events. N Engl J Med. 2006 Apr 20;354(16):1706-17.

Chimowitz MI, Lynn MJ, Derdeyn CP, et al; **SAMMPRIS** Trial Investigators. Stenting versus aggressive medical therapy for intracranial arterial stenosis. NEngl J Med. 2011 Sep 15;365(11):993-1003.

Chiu D, Klucznik RP, Turan TN, et al. Enrollment volume effect on risk factor control and outcomes in the **SAMMPRIS** trial. Neurology. 2015 Dec 15;85(24):2090-7.

Derdeyn CP, Chimowitz MI, Lynn MJ, et al; Stenting and Aggressive Medical Management for Preventing Recurrent Stroke in Intracranial Stenosis Trial Investigators. Aggressive medical treatment with or without stenting in high-risk patients with intracranial artery stenosis **(SAMMPRIS): the final results of a randomised trial**. Lancet. 2014 Jan 25;383(9914):333-41.

Diener HC, Bogousslavsky J, Brass LM, et al; **MATCH** investigators. Aspirin and clopidogrel compared with clopidogrel alone after recent ischaemic stroke or transient ischaemic attack in high-risk patients (MATCH): randomised, double-blind, placebo-controlled trial. Lancet. 2004 Jul 24-30;364(9431):331-7.

Hahn JY, et al. **6-month versus 12-month** or longer dual antiplatelet therapy after percutaneous coronary intervention in patients with **acute coronary syndrome (SMART-DATE):** a randomised, open-label, non-inferiority trial. Lancet. 2018 Mar 9.

Jing J, Meng X, Zhao X, et al. **Dual Antiplatelet Therapy in Transient Ischemic Attack and Minor Stroke With Different Infarction Patterns**: Subgroup Analysis of **CHANCE** Randomized Clinical Trial. JAMA Neurol. 2018 Mar 26.

Johnston SC, Easton JD, Farrant M, Barsan W, Conwit RA, Elm JJ, et al; Clinical Research Collaboration, Neurological Emergencies Treatment Trials Network, and the **POINT** Investigators. Clopidogrel and Aspirin in Acute Ischemic Stroke and High-Risk TIA. N Engl J Med. 2018 May 16. doi: 10.1056/NEJMoa1800410. [Epub ahead of print] PubMed PMID: 29766750.

Kennedy J, Hill MD, Ryckborst KJ, et al; **FASTER** Investigators. Fast assessment of stroke and transient ischaemic attack to prevent early recurrence (FASTER): a randomised controlled pilot trial. Lancet Neurol. 2007 Nov;6(11):961-9.

Kim JT, Park MS, Choi KH, et al. Different Antiplatelet Strategies in Patients With New Ischemic Stroke While Taking Aspirin. Stroke. 2016 Jan;47(1):128-34.

SPS3 Investigators, Benavente OR, Hart RG, McClure LA, et al. Effects of clopidogrel added to aspirin in patients with recent lacunar stroke. N Engl J Med. 2012 Aug 30;367(9):817-25.

Wang Y, Wang Y, Zhao X, et al; **CHANCE** Investigators. Clopidogrel with aspirin in acute minor stroke or transient ischemic attack. N Engl J Med. 2013 Jul 4;369(1):11-9.

Wang Y, Pan Y, Zhao X, et al; CHANCE Investigators. Clopidogrel With Aspirin in Acute Minor Stroke or Transient Ischemic Attack **(CHANCE) Trial: One-Year Outcomes**. Circulation. 2015 Jul 7;132(1):40-6.

Wiviott SD, Braunwald E, McCabe CH, et al; **TRITON-TIMI** 38 Investigators. Prasugrel versus clopidogrel in patients with acute coronary syndromes. N Engl J Med. 2007 Nov 15; 357(20):2001-15.

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References: RxFiles Atrial Fibrillation

Additional references:

Aakre CA, McLeod CJ, Cha SS, et al. **Comparison of clinical risk stratification** for predicting stroke and thromboembolism in atrial fibrillation. Stroke. 2014 Feb;45(2):426-31. (Cha2DS2-Vasc)

Abed HS, Wittert GA, et al. Effect of **weight reduction and cardiometabolic risk factor management** on symptom burden and severity in patients with atrial fibrillation: a randomized clinical trial. JAMA. 2013 Nov 20;310(19):2050-60.

Abed HS, Nelson AJ, Richardson JD, et al. Impact of weight reduction on pericardial adipose tissue and cardiac structure in patients with atrial fibrillation. Am Heart J 2015.

Abdel-Qadir H, Thavendiranathan P, Fung K, et al. Association of **Early-Stage Breast Cancer and Subsequent Chemotherapy With Risk** of Atrial Fibrillation. JAMA Netw Open. 2019 Sep 4;2(9):e1911838.

Abdul-Aziz AA, Altawil M, Lyon A, et al. Lifestyle Therapy for the Management of Atrial Fibrillation. Am J Cardiol. 2018 Feb 7.

Abdul-Aziz AA, Altawil M, Lyon A, et al. Lifestyle Therapy for the Management of Atrial Fibrillation. Am J Cardiol. 2018 May 1;121(9):1112-1117.

Abdul-Rahim AH, Wong J, McAlpine C, et al. Associations with **anticoagulation**: cross-sectional registry-based analysis of **stroke survivors** with atrial fibrillation. Heart. 2014Apr;100(7):557-62.

Abraham JM, Larson J, Chung MK, et al. Does **CHA2DS2-VASc** improve stroke risk stratification in **postmenopausal** women with atrial fibrillation?. Am J Med. 2013 Dec;126(12):1143.e1-8.

Abraham NS, Singh S, Alexander GC, et al. **Comparative risk of gastrointestinal bleeding with dabigatran, rivaroxaban, and warfarin**: population based cohort study. BMJ 2015;350:h1857.

Abraham NS et al. **Gastrointestinal safety of direct oral anticoagulants**: A large population-based study.Gastroenterology 2016 Dec 31.

Acharya T, Tringali S, Bhullar M, et al. **Frequent Atrial Premature Complexes** and Their Association With Risk of Atrial Fibrillation. Am J Cardiol. 2015 Dec 15;116(12):1852-7.

Adam SS, McDuffie JR, Ortel TL, et al. **Comparative Effectiveness** of **Warfarin and New Oral Anticoagulants** for the Management of Atrial Fibrillation and Venous Thromboembolism: A Systematic Review. Ann Intern Med. 2012 Aug 28.

Adderley NJ, Nirantharakumar K, Marshall T. Risk of **stroke and transient ischaemic attack** in patients with a diagnosis of resolved atrial fibrillation: retrospective cohort studies. BMJ. 2018 May 9;361:k1717.

Adlan AM, Lip GY. Role of the **CHADS2 Score in Acute Coronary Syndromes**: With or Without Atrial Fibrillation. Chest. 2012 Jun;141(6):1375-6.

Afzal SK, Hasan SS, Babar ZU. A Systematic Review of **Patient Reported Outcomes Associated with the Use of Direct-acting Oral Anticoagulants**. Br J Clin Pharmacol. 2019 May 11.

Agarwal S, Hachamovitch R, Menon V. Current **trial-associated outcomes with warfarin** in prevention of stroke in patients with nonvalvular atrial fibrillation: a meta-analysis [published online March 26, 2012]. Arch Intern Med. doi10.1001/archinternmed.2012.121

Agarwal M, Apostolakis S, Lane DA, et al. The Impact of **Heart Failure and Left Ventricular Dysfunction** in Predicting Stroke, Thromboembolism, and Mortality in Atrial Fibrillation Patients: A Systematic Review. Clin Ther. 2014 Aug 18.

Aggarwal A. **Rivaraoxaban** dosing is based on more than just pharmacokinetic properties. BMJ. 2017 Feb 6;356:j608.

Ahlehoff O, Gislason GH, Jørgensen CH, et al. **Psoriasis** and risk of atrial fibrillation and ischaemic stroke: a Danish Nationwide Cohort Study. Eur Heart J. 2012 Aug;33(16):2054-64.

Ahn MS, Yoo BS, Yoon J, et al. **Guideline-directed therapy at discharge** in patients with heart failure and atrial fibrillation. Heart. 2019 Sep 6.

Al-Khatib SM, Thomas L, Wallentin L, et al. Outcomes of **apixaban** vs. warfarin by type and duration of atrial fibrillation: results from the **ARISTOTLE** trial. Eur Heart J. 2013 Apr 17.

Al-Khatib SM, Allen Lapointe N, Chatterjee R, et al. Treatment of **Atrial Fibrillation. Comparative Effectiveness Review** 119. AHRQ Comparative Effectiveness Reviews. Rockville (MD): Agency for Healthcare Research and Quality (US); 2013 Jun. Report No.: 13-EHC095-EF.

Al-Khatib SM, Allen LaPointe NM, Chatterjee R, et al. **Rate- and rhythm-control therapies** in patients with atrial fibrillation: a systematic review. Ann Intern Med. 2014 Jun 3;160(11):760-73.

Aladin AI, et al. Relation of **Resting Heart Rate** to Incident Atrial Fibrillation (From the Hendry Ford Hospital Exercise Testing [FIT] Project). The American Journal of Cardiology (2016).

Alberts MJ, Bernstein RA, Naccarelli GV, Garcia DA. Using Dabigatran in Patients With Stroke: A Practical Guide for Clinicians. Stroke. 2011 Dec 8. [Epub ahead of print]

Alberts MJ, Eikelboom JW, Hankey GJ. **Antithrombotic therapy** for stroke prevention in non-valvular atrial fibrillation. Lancet Neurol. 2012 Dec;11(12):1066-81.

Albrecht JS, Liu X, Baumgarten M, et al. Benefits and Risks of **Anticoagulation Resumption Following Traumatic Brain Injury**. JAMA Intern Med. 2014 Jun 10.

Alexander JH, et al. **Apixaban** 5 mg twice daily and clinical outcomes in patients with atrial fibrillation and advanced **age, low body weight, or high creatinine**. JAMA Cardiol 2016.

Allan GM, Korownyk C, Kolber MR. **Rate versus rhythm** in atrial fibrillation: And how slow do you go? Can Fam Physician. 2011 Dec;57(12):1411.

Allan V, Banerjee A, Shah AD, et al. **Net clinical benefit of warfarin** in individuals with atrial fibrillation across stroke risk and across primary and secondary care. Heart. 2016 Aug 31.

Allen LaPointe NM, Dai D, Thomas L, Piccini JP, et al. **Antiarrhythmic drug use in patients <65 years** with atrial fibrillation and **without structural heart disease**. Am J Cardiol. 2015 Feb 1;115(3):316-22.

Alli O, Doshi S, Kar S, et al. Quality of life assessment in the randomized **PROTECT AF** trial of patients at risk for stroke with non-valvular atrial fibrillation. J Am Coll Cardiol 2013.

Alonso A, Lopez FL, Matsushita K, et al. **Chronic Kidney Disease** Is Associated With the Incidence of Atrial Fibrillation: The Atherosclerosis Risk in Communities (ARIC) Study. Circulation. 2011 Jun 28;123(25):2946-53.

Alonso A, MacLehose RF, Lutsey PL, et al. Association of **Amiodarone** Use With **Acute Pancreatitis** in Patients With Atrial Fibrillation: A Nested Case-Control Study. JAMA Intern Med. 2015 Jan 19.

Alonso A, MacLehose RF, Chen LY, Bet al. Prospective study of **oral anticoagulants and risk of liver injury** in patients with atrial fibrillation. Heart. 2017 Jun;103(11):834-839.

Amit G, Nyong J, Morillo CA. Efficacy of **Catheter Ablation** for Nonparoxysmal Atrial Fibrillation. JAMA Cardiol. 2017 Apr 19.

Anderson I, Cifu AS. Management of **Bleeding in Patients Taking Oral Anticoagulants**. JAMA. 2018 May 15;319(19):2032-2033.

Ando T, Holmes AA, Pahuja M, et al. Meta-Analysis Comparing **Patent Foramen Ovale Closure** Versus Medical Therapy to Prevent Recurrent Cryptogenic Stroke. Am J Cardiol. 2017 Dec 11.

Andrade JG, Verma A, Mitchell LB, et al; CCS Atrial Fibrillation Guidelines Committee. **2018 Focused Update** of the Canadian Cardiovascular Society Guidelines for the Management of Atrial Fibrillation. Can J Cardiol. 2018 Nov;34(11):1371-1392

Angel Y, Zeltser D, Berliner S, et al. **Hospitalization As An Opportunity To Correct Errors** In Anticoagulant Treatment In Patients With Atrial Fibrillation. Br J Clin Pharmacol. 2019 Sep 4.

Angraal S, Nuti SV, Masoudi FA, et al. **Digoxin Use and Associated Adverse Events** Among Older Adults. Am J Med. 2019 May 8.

Ansell J. **New oral anticoagulants** should not be used as first-line agents to prevent thromboembolism in patients with atrial fibrillation. Circulation. 2012 Jan 3;125(1):165-70; discussion 170. Review.

Ansell JE, Bakhru SH, Laulicht BE, et al. Use of **PER977** to Reverse the Anticoagulant Effect of Edoxaban. N Engl J Med. 2014 Nov 5.

Antoniou T, Macdonald EM, Yao Z, et al. Association between statin use and ischemic stroke or major hemorrhage in patients taking dabigatran for atrial fibrillation. CMAJ. Online. Nov 21, 2016.

Apostolakis S, Lane DA, Guo Y, et al. Performance of the HEMORR$_2$HAGES, ATRIA, and **HAS-BLED** bleeding risk-prediction scores in patients with atrial fibrillation undergoing anticoagulation. *J Am Coll Cardiol* 2012.

Apostolakis S, Guo Y, Lane DA, et al. **Renal function** and outcomes in anticoagulated patients with non-valvular atrial fibrillation: the AMADEUS trial. Eur Heart J. 2013 Aug 21.

Apostolakis S, Sullivan RM, Olshansky B, Lip GY. Factors Affecting Quality of Anticoagulation Control Among Patients With Atrial Fibrillation on Warfarin: The **SAMe-TT2R2 Score**. Chest. 2013 Nov 1;144(5):1555-63.

Apostolakis S, Sullivan RM, Olshansky B, et al. **Hormone replacement therapy** and adverse outcomes in women with atrial fibrillation: an analysis from the atrial fibrillation follow-up investigation of rhythm management trial. Stroke. 2014 Oct;45(10):3076-9.

Armbruster HL, Lindsley JP, Moranville MP, et al. Safety of **novel oral anticoagulants compared with uninterrupted warfarin for catheter ablation** of atrial fibrillation. Ann Pharmacother. 2015 Mar;49(3):278-84.

Arbelo E, Brugada J, Lundqvist CB, et al. Contemporary management of patients undergoing atrial fibrillation **ablation**: in-hospital and 1-year follow-up findings from the **ESC-EHRA** atrial fibrillation ablation long-term registry. Eur Heart J. 2017 Jan 18.

Artang R, Rome E, et al. Meta-Analysis of Randomized Controlled Trials on Risk of **Myocardial Infarction from the Use of Oral Direct Thrombin Inhibitors**. Am J Cardiol. 2013 Sep 25.

Aryal MJ, Ukaigwe A, Pandit A, et al. Meta-Analysis of Efficacy and Safety of **Rivaroxaban Compared with Warfarin or Dabigatran in Patients Undergoing Catheter Ablation** for Atrial Fibrillation. The American Journal of Cardiology (2014).

Åsberg S, Eriksson M, Henriksson KM, Terént A. **Warfarin-associated intracerebral hemorrhage** after ischemic stroke. Stroke. 2014 Jul;45(7):2118-20.

Ashburner JM, Go AS, Reynolds K, et al. Comparison of Frequency and Outcome of Major **Gastrointestinal Hemorrhage** in Patients With Atrial Fibrillation **on Versus Not Receiving Warfarin** Therapy (from the ATRIA and ATRIA-CVRN Cohorts). Am J Cardiol. 2015 Jan 1;115(1):40-6.

Ashburner JM, Singer DE, Lubitz SA, et al. Changes in Use of **Anticoagulation** in Patients With **Atrial Fibrillation** Within a Primary Care Network Associated With the Introduction of **Direct Oral Anticoagulants**. Am J Cardiol. 2017 Jun 15

Aspberg S, Chang Y, Atterman A, et al. Comparison of the **ATRIA, CHADS2, and CHA2DS2-VASc stroke risk scores** in predicting ischaemic stroke in a large Swedish cohort of patients with atrial fibrillation. Eur Heart J. 2016 Mar 3.

Assiri A, Al-Majzoub O, Kanaan AO, et al. **Mixed treatment comparison** meta-analysis of **aspirin, warfarin, and new anticoagulants** for stroke prevention in patients with nonvalvular atrial fibrillation. Clin Ther. 2013 Jul;35(7):967-984.e2.

Asuncion Esteve-Pastor M, Miguel Rivera-Caravaca J, Roldan V, et al. **Long-term bleeding risk prediction** in 'real world' patients with atrial fibrillation: Comparison of the HAS-BLED and ABC-Bleeding risk scores. Thromb Haemost. 2017 Oct;117(10):1848-1858.

Atrial Fibrillation Investigators. **Risk factors** for stroke and efficacy of antithrombotic therapy in atrial fibrillation: analysis of pooled data from 5 randomized controlled

trials. *Arch Intern Med.* 1994;154:1449–1457.
Attia ZI, Noseworthy PA, Lopez-Jimenez F, et al. An artificial intelligence-enabled **ECG algorithm for the identification of patients** with atrial fibrillation during sinus rhythm: a retrospective analysis of outcome prediction. Lancet. 2019 Aug 1.
Atzema CL, Lam K, Young C, Greene-Kester N. Patients with **atrial fibrillation and an alternative primary diagnosis in the emergency** department: a description of their characteristics and outcomes. Acad Emerg Med 2013; 20:193-199.
Atzema CL, Dorian P, Fang J, et al. A **Clinical Decision Instrument for 30-Day Death After an Emergency Department Visit** for Atrial Fibrillation: The Atrial Fibrillation in the Emergency Room (**AFTER**) Study. Ann Emerg Med. 2015 Sep 18
Atzema CL, Barrett TW. **Managing atrial fibrillation**. Ann Emerg Med. 2015 May;65(5):532-9.
Avezum A, Lopes RD, Schulte PJ, et al. **Apixaban** compared with warfarin in patients with atrial fibrillation and **valvular heart disease**: Findings from the **ARISTOTLE** trial. *Circulation* 2015.
Avgil Tsadok M, Jackevicius CA, Rahme E, et al. **Sex Differences** in **Dabigatran** Use, Safety, And Effectiveness In a Population-Based Cohort of Patients With Atrial Fibrillation. Circ Cardiovasc Qual Outcomes. 2015 Oct 27.
Azarbal F, Stefanick ML, Salmoirago-Blotcher E, et al. **Obesity, physical activity,** and their interaction in incident atrial fibrillation in postmenopausal women. J Am Heart Assoc. 2014 Aug 20;3(4).
Azoulay L, Dell'aniello S, Simon TA, et al. **Initiation of warfarin** in patients with atrial fibrillation: early effects on ischaemic strokes. Eur Heart J. 2013 Dec 18
Bäck M, Yin L, Ingelsson E. **Cyclooxygenase-2 inhibitors** and cardiovascular risk in a nationwide cohort study after the withdrawal of rofecoxib. Eur Heart J 2011.
Badheka AO, Marzouka GR, Rathod AD, et al. Comparison of **Rate Versus Rhythm Control in Patients With Atrial Fibrillation and a Pacemaker**. Am J Cardiol. 2013 Mar 27.
Badheka AO, Shah N, Grover PM, et al. Outcomes in Atrial Fibrillation Patients **With and Without Left Ventricular Hypertrophy** When Treated With a Lenient Rate-Control or Rhythm-Control Strategy. Am J Cardiol. 2014 Jan 14.
Bahit MC, Lopes RD, Wojdyla DM, et al. Non-major bleeding with **apixaban versus warfarin** in patients with atrial fibrillation. (**Aristotle**) Heart. 2017 Apr;103(8):623-628.
Bai Y, Wang YL, et al. The **Global Burden of Atrial Fibrillation and Stroke**: A Systematic Review of the Clinical Epidemiology of Atrial Fibrillation in Asia. Chest. 2017 Apr 17.
Bai Y, Shi XB, Ma CS, et al. Meta-Analysis of Effectiveness and Safety of Oral Anticoagulants in **Atrial Fibrillation With Focus on Apixaban**. Am J Cardiol. 2017 Nov 1;120(9):1689-1695.
Bajaj NS, Bhatia V, Sanam K, et al. Impact of **atrial fibrillation and heart failure**, independent of each other and in combination, on mortality in community-dwelling older adults. Am J Cardiol. 2014 Sep 15;114(6):909-13.
Baker WL, Phung OJ. **Systematic review and adjusted indirect comparison meta-analysis** of oral anticoagulants in atrial fibrillation. Circ Cardiovasc Qual Outcomes. 2012 Sep 1;5(5):711-9.
Baker WL, Jennings DL. **Pre-Cardiac Transplant Amiodarone Use Increases Postoperative Mortality**: A Meta-analysis. Ann Pharmacother. 2016 Apr 15.
Ball J et al. **Mild cognitive impairment** in high-risk patients with chronic atrial fibrillation: A forgotten component of clinical management? Heart 2013 Jan 12.
Balla SR, Cyr DD, Lokhnygina Y, et al. Relation of Risk of Stroke in Patients With Atrial Fibrillation to **Body Mass Index** (from Patients Treated With **Rivaroxaban and Warfarin** in the Rivaroxaban Once Daily Oral Direct Factor Xa Inhibition Compared with Vitamin K Antagonism for Prevention of Stroke and Embolism Trial in Atrial Fibrillation Trial-**Rocket AF**). Am J Cardiol. 2017 Jun 15;119(12):1989-1996.
Bansal N, Fan D, Hsu CY, et al. Incident atrial fibrillation and risk of **end-stage renal disease** in adults with chronic kidney disease. Circulation. 2013 Feb 5;127(5):569-74.
Bansal VK, et al. Oral Anticoagulants to Prevent Stroke in Nonvalvular Atrial Fibrillation in Patients With **CKD Stage 5D**: An NKF-KDOQI Controversies Report. Am J Kidney Dis. 2017 Sep 20.
Bansilal S, Bloomgarden Z, Halperin JL, et al. Efficacy and safety of **rivaroxaban** in patients with **diabetes** and nonvalvular atrial fibrillation: the **ROCKET AF** trial. Am Heart J. 2015.
Bapat A, Zhang Y, Post WS, et al. Relation of **Physical Activity** and Incident Atrial Fibrillation (from the Multi-Ethnic Study of Atherosclerosis). Am J Cardiol. 2015 Jun 24.
Barnes GD, et al. **Discontinuation of Warfarin** Therapy for Patients With Atrial Fibrillation: Michigan Anticoagulation Quality Improvement Initiative Experience. JAMA Cardiol. 2017 Jan 4.
Barra ME, Fanikos J, Connors JM, Sylvester et al.Evaluation of **Dose-Reduced Direct Oral Anticoagulant Therapy**. Am J Med. 2016 Jun 21.
Barrett TW, Abraham RL, et al. **Risk Factors for Bradycardia** Requiring Pacemaker Implantation in Patients With Atrial Fibrillation. Am J Cardiol. 2012 Jul 25.
Barrett TW, Abraham RL, Self WH. Usefulness of a Low **CHADS2 or CHA2DS2-VASc Score to Predict Normal Diagnostic Testing in Emergency Department** Patients With an Acute Exacerbation of Previously Diagnosed Atrial Fibrillation. Am J Cardiol. 2014 May 15;113(10):1668-73.
Barrett TW, Jenkins CA, Self WH. Validation of the **Risk Estimator Decision Aid for Atrial Fibrillation (RED-AF**) for Predicting 30-Day Adverse Events in Emergency Department Patients With Atrial Fibrillation. Ann Emerg Med. 2014 Sep 20.
Barrett TW, Martin AR, et al. A clinical prediction model to estimate risk **for 30-day adverse events in emergency department** patients with symptomatic atrial fibrillation. Ann Emerg Med. 2011 Jan;57(1):1-12.
Barrett TW, Storrow AB, Jenkins CA, et al. The **AFFORD Clinical Decision Aid** to Identify Emergency Department Patients With Atrial Fibrillation at **Low Risk for 30-Day Adverse Events**. Am J Cardiol. 2015 Jan 6.
Bassand J-P., et al. Two-year outcomes of patients with **newly diagnosed atrial fibrillation**: results from **GARFIELD-AF**. Eur Heart J. 2016; 37: 2882–2889. doi:10.1093/eurheartj/ehw233.
Bassiouny M, Saliba W, Rickard J, et al. Use of **dabigatran for peri-procedural** anticoagulation in patients undergoing **catheter ablation** for atrial fibrillation. Circ Arrhythm Electrophysiol 2013.
Batra G, Svennblad B, Held C, et al. **All types of atrial fibrillation in the setting of myocardial infarction** are associated with impaired outcome. Heart. 2016 Jun 15;102(12):926-33.
Baumgartner C, et al; for the Thyroid Studies Collaboration. **Thyroid function within the normal range, subclinical hypothyroidism**, and the risk of atrial fibrillation. Circulation. 2017;136:2100–2116.
Bauer KA. **Reversal of antithrombotic agents**. Am J Hematol. 2012 May;87 Suppl 1:S119-26.
Bavendiek U, Aguirre Davila L, Koch A, Bauersachs J. **Assumption versus evidence: the case of digoxin** in atrial fibrillation and heart failure. Eur Heart J. 2017 Jan 8.
Bekwelem W, Connolly SJ, Halperin JL, et al. **Extracranial systemic embolic events** in patients with nonvalvular atrial fibrillation: incidence, risk factors, and outcomes. Circulation 2015.
Bengtson LG, Chen LY, Chamberlain AM, et al. **Temporal Trends** in the Occurrence and Outcomes of Atrial Fibrillation in Patients With Acute Myocardial Infarction (from the Atherosclerosis Risk in Communities Surveillance Study). Am J Cardiol. 2014 Jun 18.
Benjamin MM, et al. Comparison of Outcomes of Atrial Fibrillation in Patients with **Reduced versus Preserved Left Ventricular Ejection Fraction**. The American Journal of Cardiology (2016).
Benjamin EJ, Blaha MJ, Chiuve SE, et al; **Heart Disease and Stroke Statistics-2017** Update: A Report From the American Heart Association. Circulation. 2017 Jan 25.
Bennaghmouch N, de Veer AJWM, Bode K, et al. The Efficacy and Safety of the Use of **Non-Vitamin-K Antagonist Oral Anticoagulants in Patients with Non-Valvular Atrial Fibrillation and Concomitant Aspirin** Therapy: A Meta-Analysis of Randomized Trials. Circulation. 2017 Nov 3.
Bennaghmouch N, de Veer AJWM, Bode K, et al. Efficacy and safety of the use of **non–vitamin K antagonist oral anticoagulants in patients with nonvalvular atrial fibrillation** and **concomitant aspirin therapy**: a meta-analysis of randomized trials. Circulation. 2018;137:1117–1129.
Berg DD, Ruff CT, Jarolim P, et al. **Performance of the ABC Scores** for Assessing the Risk of Stroke or Systemic Embolism and Bleeding in Patients With Atrial Fibrillation in ENGAGE AF-TIMI 48. Circulation. 2019 Feb 5;139(6):760-771.
Berian JR, Livingston EH. JAMA **PATIENT PAGE**. Preventing Stroke in People With **Atrial Fibrillation**. JAMA. 2015 Jul 21;314(3):310.
Berman JP, Norby FL, Mosley T, et al. Atrial **Fibrillation and Brain Magnetic Resonance Imaging Abnormalities**. Stroke. 2019 Apr;50(4):783-788.
Best JG, Bell R, Haque M, et al. Atrial fibrillation and stroke: **a practical guide**. Pract Neurol. 2019 Mar 2.
Bhave P, Lu X, Girotra S, et al. **Race and gender** related differences in care for patients newly diagnosed with atrial fibrillation. *Heart Rhythm* 2015
Bhave PD, Lu X, Girotra S, et al. **Race- and sex-related differences** in care for patients newly diagnosed with atrial fibrillation. Heart Rhythm. 2015 Jul;12(7):1406-12.
Biagi C, et al. **Dronedarone**-Associated Acute **Renal Failure**: Evidence Coming from the Italian Spontaneous ADR Reporting Database. Br J Clin Pharmacol. 2012 Oct17.
Birnie DH, Healey JS, Essebag V. Management of **anticoagulation around pacemaker and defibrillator surgery**. Circulation. 2014 May 20;129(20):2062-5.
Björck S, Palaszewski B, Friberg L, Bergfeldt L. **Atrial Fibrillation, Stroke Risk, and Warfarin** Therapy Revisited: A Population-Based Study. Stroke. 2013 Aug 27.
Björck F, Renlund H, Lip GY, et al. Outcomes in a **Warfarin-Treated Population With Atrial Fibrillation**. JAMA Cardiol. 2016 May 1;1(2):172-80.
Black-Maier E, Piccini JP. **Oral anticoagulation in end-stage renal disease** and atrial fibrillation: is it time to just say no to drugs? Heart. 2017 Jun;103(11):807-808
Blin P, Dureau-Pournin C, Cottin Y, et al. Effectiveness and safety of 110 or 150 mg dabigatran versus vitamin K antagonists in non-valvular atrial fibrillation. Br J Clin Pharmacol. 2018 Nov 13.
Butt JH et al. Risk of thromboembolism associated with atrial fibrillation following noncardiac surgery. J Am Coll Cardiol 2018 Oct 23; 72:2027.
Blin P, Dureau-Pournin C, Lassalle R, et al. A population database study of **outcomes associated with vitamin K antagonists in atrial fibrillation**. Br J Clin Pharmacol. 2015 Oct 22.
Blin P, Dureau-Pournin C, Cottin Y, et al. **Effectiveness and safety of 110 or 150 mg dabigatran vs. vitamin K antagonists** in nonvalvular atrial fibrillation. Br J Clin Pharmacol. 2018 Nov 13.
Blin P, Fauchier L, Dureau-Pournin C, et al. Effectiveness and Safety of **Rivaroxaban 15 or 20 mg Versus Vitamin K Antagonists** in Nonvalvular Atrial Fibrillation. Stroke. 2019 Aug 8:STROKEAHA119025824.
Blomström-Lundqvist C, Gizurarson S, Schwieler J, et al. **Effect of Catheter Ablation vs Antiarrhythmic Medication** on Quality of Life in Patients With Atrial Fibrillation: The CAPTAF Randomized Clinical Trial. JAMA. 2019 Mar 19;321(11):1059-1068.
Boersma LV, Castella M, van Boven WJ, et al. Atrial fibrillation **catheter ablation versus surgical ablation treatment (FAST):** A two-year randomized clinical trial. Circulation 2012
Bohula EA, Giugliano RP, Ruff CT, et al. Impact of **renal function on outcomes with edoxaban** in the **ENGAGE AF-TIMI 48** trial. Circulation. 2016;134:24-36.
Bouida W, Beltaief K, Msolli MA, et al. **Low-dose Magnesium Sulfate Versus High Dose** in the Early Management of Rapid Atrial Fibrillation: Randomized Controlled Double-blind Study (**LOMAGHI Study**). Acad Emerg Med. 2018 Jul 19.
Bonde AN, Lip GYH, Kamper AL, MD, et al. Net clinical benefit of antithrombotic therapy in patients with **atrial fibrillation and chronic kidney disease**: A nationwide observational cohort study. J Am Coll Cardiol 2014: 64:2471-2482.
Boraita A, Santos-Lozano A, Heras ME, et al. Incidence of Atrial Fibrillation in **Elite Athletes**. JAMA Cardiol. 2018 Oct 31.
Boriani G, Cervi E, Diemberger I, et al. Clinical management of atrial fibrillation: need for a comprehensive **patient-centered approach**. Chest. 2011 Oct;140(4):843-5.
Bosch NA, Cimini J, Walkey AJ. Contemporary Reviews in Critical Care Medicine: **Atrial Fibrillation in the Intensive Care Unit**. Chest. 2018 Apr 5.
Bosomworth NJ. **Atrial fibrillation and physical activity**: Should we exercise caution? Can Fam Physician. 2015 Dec;61(12):1061-70.
Bradley A, Sheridan P. **Atrial fibrillation**. BMJ. 2013 Jun 17;346:f3719.
Brambatti M, Connolly SJ, Gold MR, et al; ASSERT Investigators. Temporal relationship between **subclinical atrial fibrillation and embolic events**. Circulation. 2014 May 27;129(21):2094-9.

Brenyo A, Aktas MK. Review of Complementary and Alternative Medical Treatment of Arrhythmias. Am J Cardiol. 2014 Mar 1;113(5):897-903.

Brings A, Lehmann ML, Foerster KI, et al. **Perpetrator effects of ciclosporin (P-glycoprotein inhibitor) and its combination with fluconazole (CYP3A inhibitor**) on the pharmacokinetics of **rivaroxaban in healthy volunteers**. Br J Clin Pharmacol. 2019 Mar 25.

Bronnum Nielsen P, Larsen TB, Gorst-Rasmussen A, et al. **Intracranial hemorrhage** and subsequent ischemic stroke in patients with atrial fibrillation: a nationwide cohort study. Chest. 2015 Jun 1;147(6):1651-8.

Bruins Slot KM, Berge E. **Factor Xa Inhibitors vs Warfarin** for Preventing Stroke and Thromboembolism in Patients With Atrial Fibrillation. JAMA. 2014 Mar 19;311(11):1150-1151.

Bruins Slot KM, Berge E. **Factor Xa inhibitors versus vitamin K antagonists for preventing cerebral or systemic embolism in patients with atrial fibrillation**. Cochrane Database Syst Rev. 2018 Mar 6;3:CD008980. Treatment with factor Xa inhibitors significantly reduced the number of strokes and systemic embolic events compared with warfarin in people with AF. The absolute effect of factor Xa inhibitors compared with warfarin treatment was, however, rather small. Factor Xa inhibitors also reduced the number of ICHs, all-cause deaths and major bleedings compared with warfarin, although the evidence for a reduction in the latter is less robust.

Brumberg G, Gera N, Pray C, et al. Frequency of Toxicity With Chemical Conversion of Atrial Fibrillation With **Dofetilide**. Am J Cardiol. 2013 May 22.

Bucklew EA, Reis SE, Kancharla K. **Wide QRS Tachycardia** in a Man With a Medical History of Atrial Fibrillation. JAMA Intern Med. 2019 Feb 18.

Büller HR et al. for the **EINSTEIN–PE** Investigators. Oral **rivaroxaban** (15mg po bid x 3 wk, then 20mg od) for the treatment of symptomatic pulmonary embolism. N Engl J Med 2012 Mar 26.

Bunch TJ, May HT, Bair TL, et al. **Atrial fibrillation ablation** patients have long-term stroke rates similar to patients without atrial fibrillation regardless of CHADS2 score, Heart Rhythm 2013.

Bum Kim J, Suk Moon J, Yun SC, et al. Long-term outcomes of **mechanical valve replacement** in patients with atrial fibrillation: impact of the maze procedure. Circulation. 2012 May 1;125(17):2071-80.

Burnett AE, Mahan CE, et al. Guidance for the **practical management** of the **direct oral anticoagulants (DOACs)** in VTE treatment. J Thromb Thrombolysis. 2016 Jan;41(1):206-32.

Burnett A, Siegal D, Crowther M. **Specific antidotes for bleeding associated with direct oral anticoagulants**. BMJ. 2017 May 25;357:j2216.

Burr N, Lummis K, et al. Risk of **gastrointestinal bleeding with direct oral anticoagulants**: a systematic review and network meta-analysis. Lancet Gastroenterol Hepatol. 2017 Feb;2(2):85-93.

Butt JH, et al. **Long-term thromboembolic risk** in patients with **postoperative atrial fibrillation after coronary artery bypass graft surgery** and patients with nonvalvular atrial fibrillation [online Mar 28, 2018]. JAMA Cardiol. doi:10.1001/jamacardio.2018.0405

Butt JH, Olesen JB, Gundlund A, et al. Long-term **Thromboembolic Risk** in Patients With Postoperative Atrial Fibrillation After Left-Sided Heart Valve Surgery. JAMA Cardiol. 2019 Oct 9. doi:10.1001/jamacardio.2019.3649

Butt JH, Olesen JB, Havers-Borgersen E, et al. **Risk of Thromboembolism** Associated With Atrial Fibrillation Following Noncardiac Surgery. J Am Coll Cardiol. 2018 Oct 23;72(17):2027-2036.

Byatt K. **Overenthusiastic stroke risk factor modification in the over-80s**: Are we being disingenuous to ourselves, and to our oldest patients? Evid Based Med. 2014 Feb 26.

Caldeira D, Barra M, Santos AT, et al. Risk of **drug-induced liver injury** with the **new oral anticoagulants**: systematic review and meta-analysis. Heart. 2014 Jan 29.

Caldeira D, Rodrigues FB, Barra M, et al. **Non-vitamin K antagonist oral anticoagulants and major bleeding**-related fatality in patients with atrial fibrillation and venous thromboembolism: a systematic review and meta-analysis. Heart. 2015 Jun 2.

Caliskan E, Emmert MY. **Surgical occlusion of the left atrial appendage**: it is time to adopt newer techniques! Eur Heart J. 2018 Dec 1;39(45):3987-3998.

Calkins H, Kuck KH, Cappato R, et al. Heart Rhythm Society Task Force on Catheter and Surgical Ablation of Atrial Fibrillation. **2012 HRS/EHRA/ECAS** expert consensus statement on **catheter and surgical ablation** of atrial fibrillation: recommendations for patient selection, procedural techniques, patient management and follow-up, definitions, endpoints, and research trial design. Heart Rhythm 2012 Apr;9(4):632-696.e21.

Calkins H, Willems S, Gerstenfeld EP, et al. **Uninterrupted Dabigatran versus Warfarin for Ablation in Atrial Fibrillation**. (**RE-CIRCUIT**) N Engl J Med. 2017 Mar 19.

Camm AJ. **Left atrial ablation for management of atrial fibrillation**: CABANA vs. real-world data. Apples and oranges? Eur Heart J. 2019 Apr 21;40(16):1265-1267.

Camm A.J., et al. **XANTUS**: a **real-world**, prospective, observational study of patients treated with **rivaroxaban** for **stroke** prevention in atrial fibrillation. Eur Heart J. 2016; 37: 1145–1153.

Camm AJ, Amarenco P, Haas S, et al. **XANTUS**: A **real-world**, prospective, observational study of patients treated with **rivaroxaban** for stroke prevention in atrial fibrillation. *Eur Heart J* 2015.

Camm AJ, Corbucci G, Padeletti L. Usefulness of **Continuous Electrocardiographic Monitoring** for Atrial Fibrillation. Am J Cardiol. 2012 Apr 12.

Camm AJ, Lip GY, De Caterina R, et al. **2012 focused update of the ESC** Guidelines for the management of atrial fibrillation: An update of the 2010 ESC Guidelines for the management of atrial fibrillation * Developed with the special contribution of the European Heart Rhythm Association. Europace. 2012 Aug 24.
ESC Updated 2012 Management of Atrial Fibrillation Guidelines.
http://www.escardio.org/guidelines-surveys/esc-guidelines/GuidelinesDocuments/Guidelines_Focused_Update_Atrial_Fib_FT.pdf

Canadian Agency for Drugs and Technologies in Health (CADTH). **Dabigatran for stroke prevention in atrial fibrillation**: a review of the evidence on safety. March 6, 2012.

Cannon CP;Bhatt DL;Oldgren J;Lip GYH;Ellis SG;Kimu. **Dual Antithrombotic Therapy with Dabigatran after PCI** in Atrial Fibrillation. (**RE-DUAL PCI**) N Engl J Med. 2017 Aug 27.

Capodanno D, Capranzano P, Giacchi G, et al. **Novel oral anticoagulants versus warfarin** in non-valvular atrial fibrillation: A meta-analysis of 50,578 patients. Int J Cardiol. 2012 Apr 9.

Cappato R, Ezekowitz MD, Klein AL, et al. **Rivaroxaban vs. vitamin K antagonists for cardioversion** in atrial fibrillation.*Eur Heart J* 2014.

Cappato R, Marchlinski FE, Hohnloser SE, et al. **Uninterrupted rivaroxaban vs uninterrupted vitamin K antagonists for catheter ablation** in non-valvular atrial fibrillation. *Eur Heart J* 2015.

Cardoso R, et al. An updated meta-analysis of **novel oral anticoagulants versus vitamin K antagonists for uninterrupted anticoagulation in atrial fibrillation catheter ablation**. Heart Rhythm. 2018 Jan;15(1):107-115.

Carlberg B, Samuelsson O, Lindholm LH. **Atenolol in hypertension**: is it a wise choice? Lancet. 2004 Nov 6;364(9446):1684-9.

Carlsson J, Miketic S, Windeler J, et al. for the **STAF** Investigators. Randomized trial of rate-control versus rhythm-control in persistent atrial fibrillation: the Strategies of Treatment of Atrial Fibrillation (STAF) study. *J Am Coll Cardiol.* 2003;41:1690–1696.

Carley B, Griesbach S, et al. Assessment of **dabigatran utilization** and prescribing patterns for atrial fibrillation in a physician group practice setting. Am J Cardiol. 2014 Feb 15;113(4):650-4.

Carnicelli AP, et al; **ENGAGE AF-TIMI 48** Investigators.. **Edoxaban** for the Prevention of Thromboembolism in Patients with **AtrialFibrillation** and **Bioprosthetic Valves**. Circulation. 2017 Feb 16.

Carrero JJ, Evans M, Szummer K, et al. Warfarin, **kidney dysfunction**, and outcomes following **acute myocardial infarction** in patients with atrial fibrillation. (**SWEDEHEART**) JAMA. doi:10.1001/jama.2014.1334.

Carrier M, Lazo–Langner A, Shivakumar S, et al. Clinical challenges in patients with **cancer-associated thrombosis**: Canadian expert consensus recommendations. Curr Oncol 2015;22:49-59. http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4324343/pdf/conc-22-49.pdf (accessed February 23, 2015).

Cepelis A, Brumpton BM, Malmo V, et al. **Associations of Asthma** and Asthma Control **With Atrial Fibrillation Risk**: Results From the Nord-Trøndelag Health Study (HUNT). JAMA Cardiol. 2018 Jul 11.

Cetin M, Cakici M, Zencir C, et al. Prediction of Coronary Artery Disease Severity Using **CHADS2** and **CHA2DS2-VASc** Scores and a Newly Defined **CHA2DS2-VASc-HS** Score. Am J Cardiol. 2014 Mar 15;113(6):950-6.

Cha MJ, Park H, Lee MH, et al. Prevalence of and Risk Factors for **Silent Ischemic Stroke** in Patients With Atrial Fibrillation as Determined by Brain Magnetic Resonance Imaging. Am J Cardiol. 2013 Nov 23.

Chai-Adisaksopha C, Crowther M, Isayama T, Lim W. The impact of **bleeding complications in patients receiving target-specific oral anticoagulants**: a systematic review and meta-analysis. Blood. 2014;124:2450-2458.

Chaker L, Heeringa J, Dehghan A, et al. **Normal Thyroid Function** and the Risk of Atrial Fibrillation: the Rotterdam Study. J Clin Endocrinol Metab. 2015 Aug 11:jc20152480.

Chamberlain AM, Gersh BJ, Mills RM, et al. Antithrombotic strategies and outcomes in **acute coronary syndrome** with atrial fibrillation. Am J Cardiol. 2015 Apr 15;115(8):1042-8.

Chan KE, Edelman ER, Wenger JB, et al. **Dabigatran and rivaroxaban** use in atrial fibrillation patients on **hemodialysis**. Circulation. 2015 Mar 17;131(11):972-9.

Chan NC, Eikelboom JW. How I manage **anticoagulant therapy in older individuals** with atrial fibrillation or venous thromboembolism. Blood. 2019 Mar 29.

Chan PH et al. Head-to-Head Comparison of the **AliveCor Heart Monitor and Microlife WatchBP Office AFIB** for Atrial Fibrillation Screening in a Primary Care Setting. Circulation. 2017 Jan 3;135(1):110-112.

Chan PS, Maddox TM, Tang F, et al. **Practice-Level Variation in Warfarin** Use Among Outpatients With Atrial Fibrillation (from the NCDR PINNACLE Program). Am J Cardiol. 2011 Oct 15;108(8):1136-40.

Chan TC, Jhanji V. Images in clinical medicine. **Amiodarone-induced vortex keratopathy**. N Engl J Med. 2015 Apr 23;372(17):1656.

Chan TY, Chao TF, Liu CJ, et al. The association between **influenza infection, vaccination and atrial fibrillation**: A nationwide case-control study.*Heart Rhythm* 2016.

Chan W et al. Melbourne Interventional Group Investigators. Impact of **Periprocedural Atrial Fibrillation** on Short-Term Clinical Outcomes Following Percutaneous Coronary Intervention. Am J Cardiol. 2011 Dec 15.

Chan YH, Lee HF, See LC, et al**. Effectiveness and Safety of Four Direct Oral Anticoagulants** in Asians with Non-valvular Atrial Fibrillation. Chest. 2019 May 16.

Chan YH, Yeh YH, See LC, et al. **Acute Kidney Injury** in **Asians** With Atrial Fibrillation Treated With **Dabigatran or Warfarin**. J Am Coll Cardiol. 2016 Nov 29;68(21):2272-2283.

Chang H, Zhou M, Tang W, et al. Risk of **gastrointestinal bleeding associated with oral anticoagulants**: population based retrospective cohort study. BMJ 2015;350:h1585.

Chang S-H, Kuo C-F, Chou I-J, et al. **Association of a family history** of atrial fibrillation with incidence and outcomes of atrial fibrillation: a population-based family cohort study [published online July 5, 2017].JAMA Cardiol. doi:10.1001 /jamacardio.2017.1855

Chang TY, Liao JN, Chao TF, et al. **Oral anticoagulant use** for stroke prevention in atrial fibrillation patients with difficult scenarios. Int J Cardiol Heart Vasc. 2018 Aug 31;20:56-62.

Chao TF, Tsao HM, Lin YJ, Tsai CF, et al. Clinical Outcome of **Catheter Ablation** in Patients with Non-Paroxysmal Atrial Fibrillation:The Results of 3-Year Follow Up. Circ Arrhythm Electrophysiol. 2012 May 1.

Chao TF, Chiang CE, Chen TJ, et al. Reassessment of **Risk for Stroke During Follow-up of Patients With Atrial Fibrillation**. Ann Intern Med. 2019 Jan 1.

Chao TF, Liu CJ, Wang KL, et al. Using the **CHA2DS2-VASc Score** for Refining Stroke Risk Stratification in **`Low-Risk` Asian Patients** With Atrial Fibrillation. J Am Coll Cardiol. 2014 Oct 21;64(16):1658-65.

Chao TF, Liu CJ, Wang KL, et al. Should atrial fibrillation patients **with 1 additional risk factor of the CHA2DS2-VASc score (beyond sex) receive oral anticoagulation**? *J Am Coll Cardiol* 2015; 65: 635-642.

Chao TF, Liu CJ, Tuan TC, et al.. **Rate-control treatment and mortality** in atrial fibrillation. Circulation. 2015;132:1604–1612.

Chao TF, Liu CJ, Liao JN, et al. The Use of Oral Anticoagulants for Stroke Prevention in Atrial Fibrillation Patients with **History of Intra-Cranial Hemorrhage**. Circulation. 2016 Mar 11.

Chao TF, Lip GY, Liu CJ, et al. Validation of a **Modified CHA2DS2-VASc Score** for Stroke Risk Stratification in Asian Patients With Atrial Fibrillation: A Nationwide Cohort Study. Stroke. 2016 Oct;47(10):2462-9.

Chao TF, Liu CJ, Lin YJ, et al. Oral **Anticoagulation in Very Elderly Patients** With Atrial Fibrillation: A Nationwide Cohort Study. Circulation. 2018 Jul 3;138(1):37-47.

Chao TF, et al. Lifetime Risks, Projected Numbers and Adverse Outcomes in **Asian Patients** with Atrial Fibrillation: A Report from the Taiwan Nationwide AF Cohort Study. Chest. 2017 Oct 7.

Chao TF, Liu CJ, Lin YJ, et al. **Oral Anticoagulation in Very Elderly** Patients with Atrial Fibrillation – A Nationwide Cohort Study. Circulation. 2018 Feb 28.

Chao TF, Lip GYH, Lin YJ, et al. **Incident Risk Factors and Major Bleeding** in Patients with Atrial Fibrillation Treated with Oral Anticoagulants: A Comparison of Baseline, Follow-up and **Delta HAS-BLED** Scores with an Approach Focused on Modifiable Bleeding Risk Factors. Thromb Haemost. 2018 Apr;118(4):768-777.

Charidimou A, Karayiannis C, Song TJ, et al. **Brain microbleeds, anticoagulation, and hemorrhage risk**: Meta-analysis in stroke patients with AF. Neurology. 2017 Dec 5;89(23):2317-2326

Charitos EI, Stierle U, Ziegler P et al. A comprehensive evaluation of **rhythm monitoring** strategies for the detection of atrial fibrillation recurrence: insights from 647 continuously monitored patients and implications for monitoring after therapeutic interventions. Circulation. 2012 Aug 14;126(7):806-14.

Chatterjee S, Ghosh J, Lichstein E, et al. Meta-Analysis of Cardiovascular Outcomes With **Dronedarone** in Patients With Atrial Fibrillation or Heart Failure. Am J Cardiol. 2012 May 18.

Chatterjee S, Sardar P, Biondi-Zoccai G, Kumbhani DJ. **New oral anticoagulants and the risk of intracranial hemorrhage**: traditional and Bayesian meta-analysis and mixed treatment comparison of randomized trials of new oral anticoagulants in atrial fibrillation. JAMA Neurol. 2013 Dec;70(12):1486-90.

Chatterjee S, Herrmann HC, Wilensky RL, et al. Safety and Procedural Success of **Left Atrial Appendage Exclusion With the Lariat Device**: A Systematic Review of Published Reports and Analytic Review of the FDA MAUDE Database. JAMA Intern Med. 2015 May 4.

Chatterjee NA, Giulianini F, Geelhoed B, et al. **Genetic Obesity** and the Risk of Atrial Fibrillation- Causal Estimates from Mendelian Randomization. Circulation. 2016 Dec 14.

Chatterjee NA, Giulianini F, Geelhoed B, et al. **Genetic Obesity** and the Risk of Atrial Fibrillation- Causal Estimates from Mendelian Randomization. Circulation. 2016 Dec 14.

Chaturvedi S, Ofner S, Baye F, et al. Have clinicians adopted the **use of brain MRI for patients with TIA and minor stroke**? Neurology. 2017 Jan 17;88(3):237-244.

Chen JA, Ptaszek LM, Celano CM, Beach SR. Case 9-2019: A **62-Year-Old Man with Atrial Fibrillation, Depression, and Worsening Anxiety**. N Engl J Med. 2019 Mar 21;380(12):1167-1174.

Chen LY, Sotoodehnia N, Bůžková P, et al. Atrial fibrillation and the **risk of sudden cardiac death**: the atherosclerosis risk in communities study and cardiovascular health study. (**ARIC**) JAMA Intern Med. 2013 Jan 14;173(1):29-35.

Chen LY, Lopez FL, Gottesman RF, et al. Atrial Fibrillation and **Cognitive Decline**-The Role of Subclinical Cerebral Infarcts: The Atherosclerosis Risk in Communities Study. Stroke. 2014 Jul 22.

Chen LY, Norby FL, Chamberlain AM, et al. **CHA2DS2-VASc Score and Stroke Prediction in Atrial Fibrillation in Whites, Blacks, and Hispanics.** Stroke. 2018 Nov 29:STROKEAHA118021453.

Chen LY, Chung MK, Allen LA, et al. **Atrial Fibrillation Burden**: Moving Beyond Atrial Fibrillation as a Binary Entity: A Scientific Statement From the American Heart Association. Circulation. 2018 May 15;137(20):e623-e644.

Chen S, Purerfellner H, Meyer C, et al. **Rhythm control for patients** with atrial fibrillation complicated with heart failure in the contemporary era of catheter ablation: a stratified pooled analysis of randomized data. Eur Heart J. 2019 Jul 11.

Chen YL, Lin YS, Wang HT, et al. **Clinical outcomes of solitary atrial flutter patients using anticoagulation therapy**: a national cohort study. Europace. 2019 Feb 1;21(2):313-321.

Cheng M, Hu Z, Lu X, et al. **Caffeine intake** and atrial fibrillation incidence: Dose response meta-analysis of prospective cohort studies. *Canadian J Cardiol* 2014.

Cheng HC, Yeh HJ, Huang N, et al. **Amiodarone-Associated Optic Neuropathy**: A Nationwide Study. Ophthalmology. 2015 Sep 18.

Cheung JW, Cheng EP, Wu X, et al. **Sex-based differences in outcomes**, 30-day readmissions, and costs following catheter ablation of atrial fibrillation: the United States Nationwide Readmissions Database 2010-14. Eur Heart J. 2019 Sep 21;40(36):3035-3043

Chin PK, Patterson DM, et al. **Coagulation assays and plasma fibrinogen** concentrations in real-world patients with atrial fibrillation treated with **dabigatran**. Br J Clin Pharmacol. 2014 Mar 5.

Chin PK, Wright DF, Patterson DM, et al. A proposal for dose-adjustment of **dabigatran** etexilate in atrial fibrillation guided by **thrombin time**. Br J Clin Pharmacol. 2014 Mar 5.

Chinitz JS, Vaishnava P, Narayan RL, et al. **Atrial fibrillation through the years**: contemporary evaluation and management. Circulation. 2013 Jan 22;127(3):408-16.

Choe WC, Passman RS, Brachmann J, et al; **CRYSTAL AF** Investigators. A Comparison of Atrial Fibrillation **Monitoring Strategies After Cryptogenic Stroke** (from the Cryptogenic Stroke and Underlying AF Trial). Am J Cardiol. 2015 Jun 24.

Choi JY, Jung JM, Kwon DY, et al. **Free fatty acid** as an outcome predictor of atrial fibrillation-associated stroke. Ann Neurol. 2015 Nov 25.

Chowdhry U, Jacques A, Karovitch A, et al. **Appropriateness** of **Dabigatran and Rivaroxaban** Prescribing for Hospital Inpatients. Can J Hosp Pharm. 2016 May-Jun;69(3):194-201.

Chuang SY, et al. Association between **nonsteroidal anti-inflammatory drugs and atrial fibrillation** among a middle-aged population: a nationwide population-based cohort. Br J Clin Pharmacol. 2018 Mar 20.

Chugh SS, Havmoeller R, Narayana K, Singh D, et al. **Worldwide epidemiology** of atrial fibrillation: a Global Burden of Disease 2010 Study. Circulation. 2014;129:837–847.

Chun KJ, Byeon K, Il Im S, et al. Efficacy of **Dronedarone Versus Propafenone** in the Maintenance of Sinus Rhythm in Patients With Atrial Fibrillation After Electrical Cardioversion. Clin Ther. 2014 Aug 15.

Clarkesmith DE, Pattison HM, Khaing PH, et al. **Educational and behavioural interventions for anticoagulant therapy** in patients with atrial fibrillation. Cochrane Database Syst Rev. 2017 Apr 5;4:CD008600. This review demonstrates that there is insufficient evidence to draw definitive conclusions regarding the impact of educational or behavioural interventions on TTR in AF patients receiving OAT. Thus, more trials are needed to examine the impact of interventions on anticoagulation control in AF patients and the mechanisms by which they are successful. It is also important to explore the psychological implications for patients suffering from this long-term chronic condition.

Claro JC, Candia R, Rada G, et al. **Amiodarone** versus other pharmacological interventions for prevention of sudden cardiac death. Cochrane Database Syst Rev. 2015 Dec 8;12:CD008093.

Cohen D. **Dabigitran**: how the drug **company withheld** important analyses. BMJ 2014;349:g4670.

Cohen D. Data on trial of anticoagulant is to be reanalyzed after discovery that investigators used **faulty device**. (**Rocket-AF**) BMJ. 2015 Dec 3;351:h6431.

Cohen D. Manufacturer failed to disclose **faulty device** in **rivaroxaban** trial. BMJ 2016;354:i5131.

Cohen D. **Rivaroxaban**: **can we trust the evidence**?BMJ 2016;352:i575. doi:10.1136/bmj. i575 pmid:26843102.

Coleman C.I., et al. **Real-world** evidence of stroke prevention in patients with nonvalvular atrial fibrillation in the United States: the **REVISIT-US** study. Curr Med Res Opin. 2016;32: 2047–2053.

Coleman C.I., Antz M., Ehlken B., Evers T. **REal-LIfe** Evidence of stroke prevention in patients with atrial Fibrillation — The **RELIEF** study. Int J Cardiol. 2016; 203: 882–884.

Colilla S, Crow A, Petkun W, et al. Estimates of **Current and Future Incidence and Prevalence of Atrial Fibrillation in the U.S**. Adult Population. Am J Cardiol. 2013 Jul 4.

Conen D. **Epidemiology of atrial fibrillation**. Eur Heart J. 2018 Apr 21;39(16):1323-1324.

Conen D, Alonso-Coello P, Douketis J, et al. **Risk of stroke and other adverse outcomes** in patients with perioperative atrial fibrillation 1 year after non-cardiac surgery. Eur Heart J. 2019 Jun 25.

Conen D, Chae CU, Glynn RJ, et al. Risk of death & cardiovascular events in initially **healthy women with new-onset atrial fibrillation**. (WHS) JAMA. 2011;305:2080-7.

Conen D, Rodondi N, Müller A, et al; Swiss-AF Study Investigators. **Relationships of Overt and Silent Brain Lesions** With Cognitive Function in Patients With Atrial Fibrillation. J Am Coll Cardiol. 2019 Mar 12;73(9):989-999.

Conen D, Tedrow UB, Koplan BA, et al. Influence of **systolic and diastolic blood pressure** on the risk of incident atrial fibrillation in women. Circulation. 2009;119:2146 –2152.

Conen D, Wong JA, Sandhu RK, et al. **Risk of malignant cancer** among women with new-onset atrial fibrillation [online May 25, 2016]. JAMA Cardiol. doi:10.1001/jamacardio.2016.0280.

Connolly SJ, Wallentin L, Ezekowitz MD, et al. The Long Term Multi-Center Observational Study of **Dabigatran** Treatment in Patients with Atrial Fibrillation (**RELY-ABLE**) study. Circulation 2013.

Connolly SJ, Wallentin L, Yusuf S. **Additional Events in the RE-LY** Trial. N Engl J Med. 2014 Sep 24.

Connolly SJ, Milling TJ Jr, Eikelboom JW, et al. **Andexanet Alfa** for Acute Major Bleeding Associated with Factor Xa Inhibitors. N Engl J Med. 2016 Aug 30.

Coppens M, Eikelboom JW, Hart RG, et al. The **CHA2DS2-VASc** score identifies those patients with atrial fibrillation and a **CHADS2 score of 1** who are unlikely to benefit from oral anticoagulant therapy. Eur Heart J. 2012 Sep 27.

Coppens M, Hart RG, Eikelboom JW. **Stroke prevention** in older adults with atrial fibrillation. CMAJ. 2013 Oct 16.

Coppens M, Synhorst D, Eikelboom JW, et al. Efficacy and safety of **apixaban** compared with **aspirin** in patients who previously tried but failed treatment with vitamin K antagonists: results from the **AVERROES** trial. Eur Heart J. 2014 Feb 25.

Corbalan R, Bassand JP, Illingworth L, et al; GARFIELD-AF Investigators. Analysis of **Outcomes in Ischemic vs Nonischemic Cardiomyopathy in Patients With Atrial Fibrillation**: A Report From the GARFIELD-AF Registry. JAMA Cardiol. 2019 May 8.

Cornel JH, Lopes RD, James S, et al; **APPRAISE-2** Study Group. Anticoagulant therapy and outcomes in patients with prior or acute heart failure and acute coronary syndromes: Insights from the **APixaban** for PRevention of Acute ISchemic Events 2 trial. Am Heart J. 2015 Apr;169(4):531-8.

Cotté FE, Benhaddi H, et al. **Vitamin K Antagonist** Treatment in Patients With Atrial Fibrillation and Time in **Therapeutic Range in Four European Countries**. Clin Ther. 2014 Aug 20.

Cotter PE, Martin PJ, Ring L, Warburton EA, Belham M, Pugh PJ. Incidence of **atrial fibrillation detected by implantable loop recorders** in unexplained stroke. Neurology 2013;80:1546–1550.

Cowper PA, et al. **Economic analysis of apixaban therapy** for patients with atrial fibrillation from a US perspective. *JAMA Cardiol* 2017; DOI:10.1001/jamacardio.2017.0065.

Cremer PC, Mentias A, Newton D, et al. **Low Yield of Myocardial Perfusion Imaging** in Asymptomatic Patients With Atrial Fibrillation. JAMA Intern Med. 2015 Nov 1;175(11):1854-5.

Culebras A, Messé SR, Chaturvedi S, et al. **ANN**-Summary of evidence-based guideline update: **Prevention of stroke in nonvalvular atrial fibrillation**: Report of the Guideline Development Subcommittee of the American Academy of Neurology. Neurology. 2014 Feb 25;82(8):716-24.

Curley M, Berger M, Roth, J, et al.Predictors of mortality and major in-hospital **adverse events associated with electrophysiology catheter ablation**. JAMA Intern Med 2014.

Curtis AB. Practice Implications of the Atrial Fibrillation **Guidelines**. (ACCF, ESC, ACCP/AHA/HRS, CCS) Am J Cardiol. 2013 Mar 16.

Curtis AB and Khan HA. Should all atrial fibrillation be considered a **life-long problem requiring prophylaxis against thromboembolism**? J Am Coll Cardiol 2018 Oct 23; 72:2037.

Cuker A, Burnett A, Triller D, et al. Reversal of direct oral anticoagulants: Guidance from the Anticoagulation Forum. Am J Hematol. 2019 Mar 27.

Dadekian G, Kaplan AV, Chang CH, et al. Atrial Fibrillation and Stent Selection (Bare Metal vs Drug Eluting) (from Medicare Claims). Am J Cardiol. 2017Nov 1;120(9):1557-1561.

Dager WE, Gosselin RC, Kitchen S, Dwyre D. **Dabigatran effects on the international normalized ratio, activated partial thromboplastin time, thrombin time, and fibrinogen**: a multicenter, in vitro study. Ann Pharmacother. 2012 Dec;46(12):1627-36.

Dahlqvist S, Rosengren S, Gudbjörnsdottir S, et al. **Risk of atrial fibrillation in people with type 1 diabetes** compared with matched controls from the general population: a prospective case-control study. Lancet Diabetes Endocrinol 2017; online August 21.

Dalgaard F, Pallisgaard JL, Numé AK, et al. **Rate or Rhythm Control** in Older Atrial Fibrillation Patients: **Risk of Fall-Related Injuries and Syncope**. J Am Geriatr Soc. 2019 Jul 24.

Daniels PR. **Peri-procedural management of patients taking oral anticoagulants**. BMJ. 2015 Jul 14;351:h2391.

Dans AL, Connolly SJ, Wallentin L, et al. **Concomitant use of antiplatelet therapy with dabigatran or warfarin** in the Randomized Evaluation of Long-term Anticoagulation Therapy (**RE-LY**) trial. Circulation. 2013;127:634–640.

Darby AE, Dimarco JP. Management of atrial fibrillation in patients **with structural heart disease**. Circulation. 2012 Feb 21;125(7):945-57.

Darghosian L, Free M, et al. Effect of **omega-three polyunsaturated Fatty acids** on inflammation, oxidative stress, and recurrence of atrial fibrillation. Am J Cardiol. 2015 Jan 15;115(2):196-201.

Darkner S, Chen X, Hansen J, et al. Recurrence of arrhythmia following short- term oral **AMIOdarone after CATheter ablation** for atrial fibrillation: a double-blind, randomized, placebo-controlled study (AMIO-CAT trial). Eur Heart J. 2014 Sep 2.

Darkner S, Goetze JP, Chen X, et al. **Natriuretic Propeptides** as Markers of Atrial Fibrillation Burden and Recurrence (from the AMIO-CAT Trial). Am J Cardiol. 2017 Oct 15;120(8):1309-1315.

Darrat YH, Shah J, Elayi CS, et al. **Regional Lack of Consistency** in the Management of Atrial Fibrillation (from the **RECORD-AF** Trial). Am J Cardiol. 2016 Sep 30.

Davis SM, Donnan GA. **Secondary Prevention after Ischemic Stroke or Transient Ischemic Attack**. N Engl J Med 2012; 366:1914-1922.

De T, Alarcon C, Hernandez W, et al. Association of **Genetic Variants With Warfarin-Associated Bleeding** Among Patients of African Descent. JAMA. 2018 Oct 23;320(16):1670-1677.

De Angelis G, Cimon K, Cipriano L, et al. **Monitoring for Atrial Fibrillation in Discharged Stroke and Transient Ischemic Attack Patients**: A Clinical and Cost-Effectiveness Analysis and Review of Patient Preferences [Internet]. Ottawa (ON): Canadian Agency for Drugs and Technologies in Health; 2015 Sep

de Bruijn RF, Heeringa J, Wolters FJ, et al. Association Between **Atrial Fibrillation and Dementia** in the General Population. JAMA Neurol. 2015 Sep 21:1-7.

De Caterina Raffaele; Ruigomez Ana; Rodriguez Luis Alberto Garcia. Long-term Use of Anti-inflammatory Drugs (**NSAIDS**) and Risk of Atrial Fibrillation. Arch Intern Med. 2010;170(16):1450-1455.

De Caterina R, Ammentorp B, Darius H, et al. PREFER in AF Registry Investigators. Frequent and possibly **inappropriate use of combination therapy with an oral anticoagulant and antiplatelet** agents in patients with atrial fibrillation in Europe. Heart. 2014 Oct 15;100(20):1625-35.

De Caterina R, Renda G, et al. **Valvular Heart Disease** Patients on **Edoxaban or Warfarin** in the **ENGAGE AF-TIMI 48 Trial**. J Am Coll Cardiol. 2017 Mar 21;69(11):1372-1382.

DeCicco AE, Finkel JB, Greenspon AJ, Frisch DR. Clinical significance of atrial fibrillation **detected by cardiac implantable electronic devices**. *Heart Rhythm* 2014.

Deftereos S, Giannopoulos G, Kossyvakis C, et al. **Colchicine** for prevention of early atrial fibrillation recurrence after pulmonary vein isolation. J Am Coll Cardiol 2012.

Deftereos S, Giannopoulos G, Efremidis M, et al. **Colchicine** for prevention of atrial fibrillation recurrence after pulmonary vein isolation: Mid-term efficacy and effect on quality of life. Heart Rhythm 2014.

Deitelzweig SB, Buysman E, Pinsky B, et al. **Warfarin** Use and Stroke Risk Among Patients With Nonvalvular Atrial Fibrillation in a Large Managed Care Population. Clin Ther. 2013 Jul 15.

Deitelzweig SB, Pinsky B, Buysman E, et al. **Bleeding as an Outcome** Among Patients With Nonvalvular Atrial Fibrillation in a Large Managed Care Population. Clin Ther. 2013 Sep 25.

Deitelzweig SB, Jing Y, Swindle JP, Makenbaeva D. Reviewing a Clinical **Decision Aid** for the Selection of Anticoagulation Treatment in Patients With Nonvalvular Atrial Fibrillation: Applications in a US Managed Care Health Plan Database. Clin Ther. 2014 Nov 1;36(11):1566-1573.e3.

Del-Carpio Munoz F, et al. Meta-Analysis of **Renal Function** on the Safety and Efficacy of **Novel Oral Anticoagulants** for Atrial Fibrillation. Am J Cardiol. 2016 Jan 1;117(1):69-75.

Delgado V, Di Biase L, Leung M, et al. Structure and Function of the **Left Atrium and Left Atrial Appendage**: AF and Stroke Implications. J Am Coll Cardiol. 2017 Dec 26;70(25):3157-3172.

Dentali F, Riva N, Crowther M, et al. Efficacy and safety of the **novel oral anticoagulants** in atrial fibrillation: a systematic review and meta-analysis of the literature. Circulation 2012.

Desai NR, Krumme AA, Schneeweiss S, et al. **Patterns of initiation of oral anticoagulants** in patients with atrial fibrillation—quality and cost implications. *Am J Med* 2014.

Desmukh A, Pant S, Gagan K, et al. Comparison of outcomes of **weekend versus weekday admission** for atrial fibrillation. Am J Cardiol 2012.

Deshmukh A, Patel NJ, Pant S, et al. **Inhospital Complications Associated with Catheter Ablation** of Atrial Fibrillation in the United States between 2000-2010: Analysis of 93,801 Procedures. Circulation. 2013 Sep 23.

Dewland TA, Olgin JE, Vittinghoff E, et al. **Incident** Atrial Fibrillation Among **Asians, Hispanics, Blacks, and Whites**. Circulation. 2013 Oct 8.

Dewland TA, Vittinghoff E, Mandyam MC, et al. **Atrial ectopy** as a predictor of incident atrial fibrillation: a cohort study. Ann Intern Med. 2013 Dec 3;159(11):721-8.

Di Biase L, Burkhardt D, Santangeli P, et al. **Periprocedural** stroke and bleeding complications in patients undergoing **catheter ablation** of atrial fibrillation with different anticoagulation management: Results from the "COMPARE" randomized trial. *Circulation* 2014;

Di Biase, L, Briceno, DF, Trivedi C, et al. Is **transesophageal echocardiogram** mandatory in patients undergoing ablation of atrial fibrillation with uninterrupted novel oral anticoagulants? Results from a prospective multicenter registry. *Heart Rhythm* 2016.

Di Biase L, Mohanty P, Mohanty S, et al. **Ablation vs. Amiodarone** for Treatment of Persistent Atrial Fibrillation in Patients With Congestive Heart Failure and an Implanted Device: Results From the AATAC Multicenter Randomized Trial. Circulation. 2016 Mar 30.

Di Biase L, Mohanty S, Trivedi C, et al. **Stroke risk** in patients with atrial fibrillation undergoing electrical isolation of the left atrial appendage. J Am Coll Cardiol 2019;74:1019–28.

Di Biase L, Natale A, Romero J. **Thrombogenic and Arrhythmogenic Roles of the Left Atrial Appendage** in Atrial Fibrillation. Circulation. 2018 Oct 30;138(18):2036-2050.

Diener HC, Selim MH, Molina CA, Greenberg SM. **Embolic Stroke, Atrial Fibrillation, and Microbleeds**: Is There a Role for Anticoagulation? Stroke. 2016 Mar;47(3):904-7.

Diener HC. **Does atrial fibrillation lead to cognitive decline** and dementia? Eur Heart J. 2017 Sep 7;38(34):2619-2620.

Dimmitt SB, Floyd CN, Ferner RE. **Antithrombotic dose: some observations from published clinical trials**. Br J Clin Pharmacol. 2019 May 3.

Ding M, Fratiglioni L, Johnell K, et al. **Atrial fibrillation, antithrombotic treatment, and cognitive aging**: A population-based study. Neurology. 2018 Oct 10.

Dinh T, Baur LH, Pisters R, et al. **Aspirin versus vitamin K antagonist** treatment guided by transoesophageal echocardiography in patients with atrial fibrillation: a pilot study. Heart. 2014 Jan 31.

Dinicolantonio JJ, Beavers CJ, Menezes AR, et al. Meta-Analysis Comparing **Carvedilol Versus Metoprolol** for the Prevention of **Postoperative** Atrial Fibrillation Following Coronary Artery Bypass Grafting. Am J Cardiol. 2013 Nov 8

Dlott JS, George RA, Huang X, et al. **National assessment of warfarin anticoagulation therapy** for stroke prevention in atrial fibrillation. Circulation. 2014 Apr 1;129(13):1407-14.

Dogliotti A, Paolasso E, Giugliano RP. Current and **new oral antithrombotics** in non-valvular atrial fibrillation: a **network meta-analysis** of 79 808 patients. Heart. 2013 Sep 5.

Doherty JU, Gluckman TJ, et al. **2017 ACC Expert Consensus** Decision Pathway for **Periprocedural Management** of Anticoagulation in Patients With Nonvalvular Atrial Fibrillation: A Report of the American College of Cardiology Clinical Expert Consensus Document Task Force. J Am Coll Cardiol. 2017 Jan 5.

Dorian P, Angaran P. **β-Blockers and atrial fibrillation**: hypertension and other medical conditions influencing their use. Can J Cardiol. 2014 May;30(5 Suppl):S38-41.

Desai VC, Kelton CM, Metzger AH, Cavanaugh TM, Guo JJ, Heaton PC. Comparative Persistence on **β-Blockers Versus Calcium Channel Blockers** for Ventricular Rate Control in Nonelderly Patients With Atrial Fibrillation. Ann Pharmacother. 2014 Dec;48(12):1570-9.

Dodson JA, Petrone A, Gagnon DR, et al. Incidence and determinants of **traumatic intracranial bleeding** among older veterans receiving **warfarin** for atrial fibrillation. *JAMA Cardiol* 2016.

Donnellan E, Wazni OM, Kanj M, et al. Association between **pre-ablation bariatric surgery** and atrial fibrillation recurrence in morbidly obese patients undergoing atrial fibrillation ablation. Europace. 2019 Jul 15.

Douketis J, Bell AD, Eikelboom J, Liew A. Approach to the **new oral anticoagulants** in family practice: Part 1: **comparing the options**. Can Fam Physician. 2014 Nov;60(11):989-995.

Douketis J, Bell AD, Eikelboom J, Approach to the **new oral anticoagulants** in family practice: Part 2: addressing **frequently asked questions**. Can Fam Physician. 2014 Nov;60(11):997-1001.

Douketis JD, Spyropoulos AC, Duncan J, et al. Perioperative Management of Patients With Atrial Fibrillation **Receiving a Direct Oral Anticoagulant**. JAMA Intern Med. 2019 Aug 5

Douketis JD, Spyropoulos AC, Kaatz S, et al; **BRIDGE** Investigators. **Perioperative Bridging Anticoagulation** in Patients with Atrial Fibrillation. N Engl J Med. 2015 Jun 22.

Douros A, Azoulay L, Yin H, et al. **Non-Vitamin K Antagonist** Oral Anticoagulants and Risk of **Serious Liver Injury**. J Am Coll Cardiol. 2018 Mar 13;71(10):1105-1113.

Douros A, Renoux C, Yin H, et al. Concomitant Use of Direct **Oral Anticoagulants with Antiplatelet Agents** and the Risk of Major Bleeding in Patients with Nonvalvular Atrial Fibrillation. Am J Med. 2019 Feb;132(2):191-199.e12.

Drca N, Wolk A, Jensen-Urstad M, et al. Atrial fibrillation is associated with **different levels of physical activity** levels at different ages in men. Heart. 2014 May 14.

D'Souza M, Smedegaard L, Madelaire C, et al. Incidence of **atrial fibrillation in conjunction with breast cancer**. Heart Rhythm. 2019 Jan 24.

Dublin S, Anderson ML, Haneuse SJ, et al. Atrial fibrillation and risk of **dementia**: a prospective cohort study. J Am Geriatr Soc. 2011 Aug;59(8):1369-75.

Easton JD, Lopes RD, Bahit MC, et al, for the **ARISTOTLE** Committees and Investigators. Apixaban compared with warfarin in patients with atrial fibrillation and previous stroke or transient ischaemic attack: a subgroup analysis of the ARISTOTLE trial. Lancet Neurol 2012; online May 8.

Eckman MH, et al. Using an Atrial Fibrillation **Decision Support Tool** for Thromboprophylaxis in Atrial Fibrillation: Effect of Sex and Age. J Am Geriatr Soc. 2016 May;64(5):1054-60.

Eerenberg ES, Kamphuisen PW, Sijpkens MK, et al. **Reversal of Rivaroxaban** and Dabigatran by Prothrombin Complex Concentrate: A Randomized, Placebo-Controlled, Crossover Study in Healthy Subjects. Circulation.2011 Sep 6.

Egan G, Hughes CA, Ackman ML. **Drug interactions** between **antiplatelet or novel oral anticoagulant medications and antiretroviral medications**. Ann Pharmacother. 2014 Jun;48(6):734-40.

Eikelboom JW, Connolly SJ, Brueckmann M, et al. **Dabigatran versus warfarin in patients with mechanical heart valves**. (**RE-ALIGN**) N Engl J Med 2013; DOI: 10.1056/NEJMoa1300615.

Eikelboom JW, Quinlan DJ, et al. **Laboratory Monitoring** of **Non-Vitamin K Antagonist** Oral Anticoagulant Use in Patients With Atrial Fibrillation: A Review. JAMA Cardiol. 2017 Mar 29.

Eikelboom JW, van Ryn J, Reilly P, et al. **Dabigatran Reversal With Idarucizumab** in Patients With Renal Impairment. J Am Coll Cardiol. 2019 Oct 8;74(14):1760-1768.

El-Chami MF, Kilgo PD, Elfstrom KM, et al. Prediction of New Onset Atrial Fibrillation **After Cardiac Revascularization Surgery**. Am J Cardiol. 2012 May 21.

Elbadawi A, Olorunfemi O, Ogunbayo GO, et al. Cardiovascular Outcomes With **Surgical Left Atrial Appendage Exclusion** in Patients With Atrial Fibrillation Who Underwent **Valvular Heart Surgery** (from the National Inpatient Sample Database). Am J Cardiol. 2017 Jun 15;119(12):2056-2060.

Elbadawi A, Elgendy IY, et al. **In-Hospital Cerebrovascular Outcomes** of Patients with Atrial Fibrillation and **Cancer** (From the National Inpatient Sample Database). Am J Cardio. 2017.

Elgendy AY, Mahhta D, Barakat AF, et al. Meta-Analysis of Safety and Efficacy of Uninterrupted **Non-Vitamin K Antagonist** Oral Anticoagulants Versus Vitamin K Antagonists for **Catheter Ablation** of Atrial Fibrillation. Am J Cardio. 2017

Elgendy IY, Mahmoud A, et al. Meta-Analysis of 12 Trials Evaluating the Effects of **Statins** on Decreasing **Atrial Fibrillation** After Coronary Artery Bypass Grafting. Am J Cardiol. 2015 Mar12.

Elgendy IY, et al. Meta-analysis of 12 trials evaluating the effects of **statins on decreasing atrial fibrillation** after coronary artery bypass grafting. Am J Cardiol. 2015 Jun 1;115(11):1523-8.

Ellervik C, Roselli C, Christopherson IE, et al. Assessment of the relationship between **genetic determinants of thyroid function and atrial fibrillation**: a mendelian randomization study [online Jan 23, 2019]. JAMA Cardiol. doi:10.1001/jamacardio.2018.4635

EMA: European Medicines Agency. European Medicines Agency recommends restricting use of dronedarone- Multaq [press release]. September 22, 2011.

Emdin CA, et al. Atrial fibrillation as risk factor for cardiovascular disease & death in **women compared with men**: systematic review & meta-analysis of cohort studies. BMJ. 2016 Jan 19;532:h7013.

Engdahl J, Andersson L, Mirskaya M, Rosenqvist M. **Stepwise screening** of atrial fibrillation in a 75-year-old population: implications for stroke prevention. Circulation. 2013 Feb 26;127(8):930-7.

Essien UR, Holmes DN, Jackson LR 2nd, et al. Association of **Race/Ethnicity With Oral Anticoagulant Use in Patients With Atrial Fibrillation**: Findings From the Outcomes Registry for Better Informed Treatment of Atrial Fibrillation II. JAMA Cardiol. 2018 Nov 28.

Ezekowitz MD, et al. **Apixaban** compared to heparin/vitamin K antagonist in patients with **atrial fibrillation scheduled for cardioversion**: the **EMANATE** trial. Eur Heart J. 2018 Apr 6.

Ezekowitz MD, Aikens TH, Nagarakanti R, Shapiro T. Atrial fibrillation: **outpatient presentation and management**. Circulation. 2011 Jul 5;124(1):95-9.

Ezekowitz MD, Nagarakanti R, Noack H, et al. Comparison of **dabigatran versus warfarin** in patients with atrial fibrillation and **valvular heart disease**: The **RE-LY** trial. Circulation 2016.

Fang WT, Li HJ, Zhang H et al. The Role of **Statin** Therapy in the Prevention of Atrial Fibrillation: A Meta-Analysis of Randomized Controlled Trials. Br J Clin Pharmacol. 2012 Feb 29.

Fang MC, Go AS, Chang Y, et al. **Long-term survival** after ischemic stroke in patients with atrial fibrillation. Neurology. 2014 Mar 25;82(12):1033-7.

Fanola CL, Giugliano RP, et al. A novel **risk prediction score** in atrial fibrillation for a net clinical outcome from the **ENGAGE AF-TIMI** 48 randomized clinical trial. Eur Heart J. 2017 Jan 6.

Farkowski MM, Maciag A, Kowalik I, et al**. Intravenous antazoline**, a first generation antihistaminic drug with antiarrhythmic properties, is a suitable agent for pharmacological cardioversion of atrial fibrillation induced during pulmonary vein isolation due to the lack of influence on atrio-venous conduction and high clinical effectiveness (AntaEP Study). Br J Clin Pharmacol. 2019 Mar 28.

Farmakis D, Davlouros P, Giamouzis G, et al. **Direct Oral Anticoagulants in Nonvalvular Atrial Fibrillation**: Practical Considerations on the Choice of Agent and Dosing. Cardiology. 2018;140(2):126-132.

Fatemi O, Yuriditsky E, Tsioufis C, et al. Impact of **Intensive Glycemic Control** on the Incidence of Atrial Fibrillation and Associated Cardiovascular Outcomes in Patients With Type 2 Diabetes Mellitus (from the Action to Control Cardiovascular Risk in Diabetes Study). Am J Cardiol. 2014 Jul 30.

Fauchier L, Pellegrin C, Bernard A, et al. Comparison of Frequency of Major Adverse Events in Patients With Atrial Fibrillation Receiving **Bare-Metal Versus Drug-Eluting Stents** in Their Coronary Arteries. Am J Cardiol. 2012 Mar 29.

Fauchier L, Clementy N, et al. **Should Atrial Fibrillation Patients With Only 1 Nongender-Related CHA2DS2-VASc Risk Factor Be Anticoagulated**? Stroke. 2016 Jul;47(7):1831-6.

Fauchier L et al. Device-related thrombosis after percutaneous left atrial appendage occlusion for atrial fibrillation. J Am Coll Cardiol 2018 Apr 10; 71:1528.

Faxon DP, Eikelboom JW, Berger PB, et al. Consensus Document: Antithrombotic therapy in patients with atrial fibrillation undergoing **coronary stenting**. A North-American perspective. Thromb Haemost. 2011 Sep 27;106(4):572-84.

FDA Dec/11 Has revised the label of the antiarrhythmic drug **dronedarone** (Multaq) to caution against prescribing it to patients with permanent atrial fibrillation. Dronedarone doubles their risk for cardiovascular **death, stroke, and heart failure**, the agency announced after reviewing data from the **PALLAS** trial.

FDA Dec/12: Pradaxa (**dabigatran** etexilate mesylate) should **not** be used to prevent stroke or blood clots (major thromboembolic events) in patients with **mechanical heart valves**, also known as mechanical prosthetic heart valves. A clinical trial in Europe (the RE-ALIGN trial) was recently stopped because Pradaxa was more likely to experience strokes, heart attacks, and blood clots forming on the mechanical heart valves than were users of the anticoagulant warfarin. There was also more bleeding after valve surgery in the Pradaxa users than in the warfarin users.

FDA Mar/15 is warning that serious slowing of the heart rate can occur when the antiarrhythmic drug **amiodarone** is taken together with either the hepatitis C drug Harvoni (ledipasvir/**sofosbuvir**) or with Sovaldi (**sofosbuvir**) taken in combination with another direct acting antiviral for the treatment of hepatitis C infection.

Fender EA, et al. Severe **Pulmonary Vein Stenosis** Resulting From **Ablation** for Atrial Fibrillation: Presentation, Management, & Clinical Outcomes. Circulation. 2016 Dec 6;134(23):1812-1821.

Fenger-Grøn M, Vestergaard M, Pedersen HS, Frost L, et al. **Depression, antidepressants**, and the risk of non-valvular atrial fibrillation: A nationwide Danish matched cohort study. Eur J Prev Cardiol. 2018 Nov 19:2047487318811184.

Field TS, Weijs B, Curcio A, et al. Incident Atrial Fibrillation, **Dementia and the Role of Anticoagulation**: A Population-Based Cohort Study. Thromb Haemost. 2019 Mar 27.

Flaker G, Lopes RD, Al-Khatib SM, et al. ARISTOTLE Committees and Investigators. Efficacy and Safety of **Apixaban in Patients After Cardioversion** for Atrial Fibrillation: Insights From the ARISTOTLE Trial (Apixaban for Reduction in Stroke and Other Thromboembolic Events in Atrial Fibrillation). J Am Coll Cardiol. 2014 Mar 25;63(11):1082-7.

Flaker G, Lopes RD, Hylek E, et al. **ARISTOTLE** Committees and Investigators. **Amiodarone**, Anticoagulation, and Clinical Events in Patients With Atrial Fibrillation: Insights From the ARISTOTLE Trial. J Am Coll Cardiol. 2014 Oct 14;64(15):1541-50.

Fordyce CB, Hellkamp AS, Lokhnygina Y, et al; On-Treatment Outcomes in Patients With Worsening **Renal Function** With **Rivaroxaban Compared With Warfarin**: Insights From **ROCKET AF**. Circulation. 2016 Jul 5;134(1):37-47.

Foy AJ, Mandrola J, Liu G, et al. Relation of **Obesity to New-Onset Atrial Fibrillation** and Atrial Flutter in Adults. Am J Cardiol. 2018 Feb 6.

Frendl G, Sodickson AC, Chung MK, et al. 2014 **AATS guidelines** for the prevention and management of **perioperative atrial fibrillation and flutter** for thoracic surgical procedures. J Thorac Cardiovasc Surg 2014; 148:772-791

Fragakis N, Koskinas KC, Katritsis DG, et al. Comparison of Effectiveness of **Ranolazine Plus Amiodarone** Versus Amiodarone Alone for Conversion of Recent-Onset Atrial Fibrillation. Am J Cardiol. 2012 May 21.

Fralick M, Juurlink DN, Marras T. Bleeding associated with coadministration of **rivaroxaban and clarithromycin**. CMAJ 2016. [Epub ahead of print 2016 Jan. 25.]

Franchi C, Antoniazzi S, Proietti M, et al. Appropriateness of **oral anticoagulant therapy** prescription and its associated factors **in hospitalized older people** with atrial fibrillation. Br J Clin Pharmacol. 2018 May 10.

Freedman B, Martinez C, Kotholing A, et al. **Residual risk of stroke** and death in anticoagulant-treated patients with atrial fibrillation. *JAMA Cardiol* 2016.

Freedman B, Martinez C, Katholing A, et al. **Residual Risk of Stroke** and Death in Anticoagulant-Treated Patients With Atrial Fibrillation. JAMA Cardiol. 2016 Jun 1;1(3):366-8.

Freedman B, Camm J, Calkins H, et al. **Screening for Atrial Fibrillation**: A Report of the **AF-SCREEN International Collaboration**. Circulation. 2017 May 9;135(19):1851-1867.

Freedman B, Schnabel R, Calkins H. **Opportunistic Electrocardiogram Screening for Atrial Fibrillation** to Prevent Stroke. JAMA Cardiol. 2018 Dec 26.

Freeman JV, Reynolds K, Fang M, et al. **Digoxin and Risk of Death** in Adults with Atrial Fibrillation: The **ATRIA-CVRN** Study. Circ Arrhythm Electrophysiol. 2014 Nov 20.

Freeman JV, Wang Y, Akar JG, et al. **National Trends** in Atrial Fibrillation Hospitalization, Readmission, and Mortality for Medicare Beneficiaries, 1999-2013. Circulation. 2017 Feb 1.

Freeman JV, Wang Y, Akar JG, et al. **National Trends** in Atrial Fibrillation Hospitalization, Readmission,and Mortality for **Medicare Beneficiaries**, 1999-2013. Circulation. 2017 Feb 1.

Friberg Leif, Rosenqvist Mårten, Lip Gregory Y.H.. Evaluation of **risk stratification schemes** for ischaemic stroke and bleeding in 182 678 patients with atrial fibrillation: the Swedish Atrial Fibrillation cohort study. Eur Heart J first published online January 13, 2012 doi:10.1093/eurheartj/ehr488. (CHA2DS2-VASc, HAS-BLED)

Friberg L, Rosenqvist M, Lip GYH. **Net clinical benefit of warfar**in in patients with atrial fibrillation: a report from the Swedish Atrial Fibrillation Cohort Study. Circulation. 2012;125:2298 –2307.

Friberg L, Benson L, Rosenqvist M, Lip GY. Assessment of **female sex as a risk factor** in atrial fibrillation in Sweden: nationwide retrospective cohort study. BMJ. 2012 May 30;344:e3522.

Friberg L, Benson L, Lip GY. Balancing stroke and bleeding risks in patients with **atrial fibrillation** and **renal failure**: the Swedish Atrial Fibrillation Cohort study. Eur Heart J. 2014 Apr 9.

Friberg L, Skeppholm M, Terént A. **Benefit of Anticoagulation Unlikely** in Patients With Atrial Fibrillation and a **CHA2DS2-VASc Score of 1.** J Am Coll Cardiol. 2015 Jan 27;65(3):225-32.

Friberg L, et al. **Catheter ablation** for atrial fibrillation is associated with lower incidence of stroke and death: data from Swedish health registries. Eur Heart J. 2016 Aug;37(31):2478-87.

Friedman DJ, Piccini JP, Wang T, et al. Association between **left atrial appendage occlusion** and readmission for thromboembolism among patients with atrial fibrillation undergoing concomitant cardiac surgery.JAMA. doi:10.1001 /jama.2017.20125

Frost C, Shenker A, Gandhi MD, et al. Evaluation of the effect of **naproxen** on the pharmacokinetics and pharmacodynamics of **apixaban**. Br J Clin Pharmacol. 2014 Apr 2.

Frost CE, Byon W, Song Y, et al. Effect of ketoconazole and diltiazem on the pharmacokinetics of **apixaban**, an oral direct factor Xa inhibitor. Br J Clin Pharmacol. 2014 Nov 6.

Frost JL, Campos-Outcalt D, Hoelting D, et al. **Atrial Fibrillation Guideline** Summary **AAFP**. Ann Fam Med. 2017 Sep;15(5):490-491.

Furie KL, Goldstein LB, AlbersGW, et al. **Oral antithrombotic agents** for the prevention of stroke in nonvalvular atrial fibrillation: A science advisory for healthcare professionals from the American Heart Association-**AHA**/American Stroke Association-ASA. Stroke 2012.

Fuller GW, Evans R, Preston L, et al. Should Adults With **Mild Head Injury Who Are Receiving Direct Oral Anticoagulants Undergo Computed Tomography Scanning**? A Systematic Review. Ann Emerg Med. 2018 Sep 17.

Fuster V, Chinitz JS. Net clinical benefit of warfarin: extending the reach of antithrombotic therapy for atrial fibrillation. Circulation. 2012 May 15;125(19):2285-7. Epub 2012 Apr 18.

Fuster V, Ryde´n LE, Cannom DS, et al.**2011 ACCF/AHA/HRS** focused updates incorporated into the ACC/AHA/ESC 2006 guidelines for the management of patients with atrial fibrillation: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. *Circulation.* 2011;123:e269–e367.

Gaist D, García Rodríguez LA, Hellfritzsch M, et al. Association of **Antithrombotic Drug Use With Subdural Hematoma Risk**. JAMA. 2017 Feb 28;317(8):836-846.

Gallagher C, Elliott AD, Wong CX, et al. **Integrated care in atrial fibrillation**: a systematic review and meta-analysis. Heart. 2017 May 10.

Ganesan AN, Shipp NJ, Brooks AG, et al. Long-term Outcomes of **Catheter Ablation** of Atrial Fibrillation: Systematic Review and Meta-analysis. J Am Heart Assoc. 2013 Mar 18;2(2):e004549.

Ganesan AN, Chew DP, et al. The impact of **atrial fibrillation type** on the risk of thromboembolism, mortality, and bleeding: A systematic review and meta-analysis. *Eur Heart J* 2016.

Gao S, Juhaeri J, Schiappacasse HA, et al. Evaluation of **Dronedarone** Use in the US Patient Population Between 2009 and 2010: A Descriptive Study Using a Claims Database. Clin Ther. 2011 Sep 27.

Gage BF, Waterman AD, Shannon W, Boechler M, Rich MW, Radford MJ. **Validation of clinical classification schemes for predicting stroke**: results from the National Registry of Atrial Fibrillation. ($CHADS_2$) *JAMA.* 2001; 285:2864 –2870.

Gaita F, Scaglione M, Battaglia A, et al. Very long-term outcome following transcatheter ablation of atrial fibrillation. Are results maintained after 10 years of follow up? Europace. 2018 Mar 1;20(3):443-450.

Gale CP, Camm AJ. **Assessment of palpitations**. BMJ. 2016 Jan 6;352:h5649.

Ganesan AN, Brooks AG, Roberts-Thomson KC, et al. Role of **AV nodal ablation** in cardiac resynchronization therapy in patients with coexistent atrial fibrillation and **heart failure**: a systematic review. J Am Coll Cardiol 2012; 59:719-726.

Ganesan AN, et al. The impact of atrial fibrillation **type on the risk of thromboembolism, mortality, & bleeding**: systematic review and meta-analysis. Eur Heart J. 2016 May 21;37(20):1591-602.

Garg PK, O'Neal WT, Ogunsua A, et al. Usefulness of the American Heart Association's **Life Simple 7 to Predict the Risk** of Atrial Fibrillation (from the REasons for Geographic And Racial

Differences in Stroke [**REGARDS**] Study). Am J Cardiol. 2018 Jan 15;121(2):199-204
Garg L, Agrawal S, Agarwal M, et al. Influence of Atrial Fibrillation on Outcomes in Patients Undergoing **Primary Percutaneous Coronary Intervention** for St-Segment Elevation Myocardial Infarction. Am J Cardio. 2017
Garimella RS, Chung EH, Mounsey JP, et al. Accuracy of **patient perception of their prevailing rhythm**: A comparative analysis of monitor data and questionnaire responses in patients with atrial fibrillation. *Heart Rhythm* 2015.
Gateman D, Trojnar ME, Agarwal G. **Time in therapeutic range: Warfarin anticoagulation** for atrial fibrillation in a community-based practice. Can Fam Physician. 2017 Oct;63(10):e425-e431.
Gehi AK, O'Brien E, Pathak RK et al. **Frequency of Obesity** among Patients with Atrial Fibrillation (from the PINNACLE Registry). The American Journal of Cardiology. 2016.
Generalova D, Cunningham S, Leslie SJ, et al. A systematic review of **clinicians' views and experiences of direct-acting oral anticoagulants in the management of non-valvular atrial fibrillation**. Br J Clin Pharmacol. 2018 Aug 15.
Generalova D, Cunningham S, Leslie SJ, et al. Prescribers' views and experiences of using direct acting **oral anticoagulants in the management of non-valvular atrial fibrillation**: a survey in remote and rural Scotland. Br J Clin Pharmacol. 2019 Jul 17.
Genuardi MV, Ogilvie RP, Saand AR, et al. **Association of short sleep duration** and atrial fibrillation. Chest. 2019 Feb 27.
Gerner ST, et al. Association of **prothrombin complex concentrates administration and hematoma enlargement in NOAC-related intracerebral hemorrhage**. Ann Neurol. 2018 Jan 3.
Gheorghiade M, Fonarow GC, van Veldhuisen DJ, et al. **Lack** of evidence of increased **mortality among patients with atrial fibrillation taking digoxin**: findings from post hoc propensity-matched analysis of the AFFIRM trial. Eur Heart J 2013.
Gialdini G, Nearing K, Bhave PD, et al. **Perioperative atrial fibrillation** and the long-term risk of ischemic **stroke**. JAMA. 2014 Aug 13;312(6):616-22
Gibson CM, Pinto DS, Chi G, et al. **Recurrent hospitalization** among patients with atrial fibrillation undergoing intracoronary stenting **treated with two treatment strategies of rivaroxaban or** a dose-adjusted oral **vitamin k antagonist** treatment strategy. Circulation. 2016;134:xx– xx.doi: xxxxxxxx.
Gibson CM, Mehran R, Bode C, et al. An open-label, randomized, controlled, multicenter study exploring two treatment strategies of **rivaroxaban and a doseadjusted oral vitamin K** antagonist treatment strategy in subjects with **atrial fibrillation who undergo percutaneous coronary intervention**: **PIONEER AF-PCI**. N Engl J Med. 2016. doi: 10.1056/ NEJMoa1611594.
Gibson CM, Pinto DS, Chi G, et al. **Recurrent Hospitalization** Among Patients With Atrial Fibrillation Undergoing Intracoronary Stenting Treated With 2 Treatment Strategies of **Rivaroxaban** or a Dose-Adjusted Oral Vitamin K Antagonist Treatment Strategy. Circulation. 2017 Jan 24;135(4):323-333. (**Pioneer**)
Gieling E, van den Ham HA, et al. Risk of **major bleeding and stroke associated with the use of VKAs, NOACs and aspirin** in patients with atrial fibrillation: a cohort study. Br J Clin Pharmacol. 2017 Feb 16.
Gillinov AM, Gelijns AC, Parides MK, et al. **Surgical ablation** of atrial fibrillation **during mitral-valve surgery**. (**CTSN**) N Engl J Med. DOI: 10.1056/NEJMoa1500528.
Gillinov AM, Bagiella E, Moskowitz AJ, et al; **CTSN**. **Rate Control versus Rhythm Control** for Atrial Fibrillation **after Cardiac Surgery**. N Engl J Med. 2016 Apr 4.
Gillis AM. Atrial Fibrillation and **Ventricular Arrhythmias**: Sex Differences in Electrophysiology, Epidemiology, Clinical Presentation, & Clinical Outcomes. Circ 2017 Feb 7;135(6):593-608
Giannoni A, Emdin M, Passino C. Cheyne-Stokes Respiration, Chemoreflex, and **Ticagrelor-Related Dyspnea**. N Engl J Med. 2016 Sep 8;375(10):1004-6
Giugliano RP, Ruff CT, et al. **Mortality** in Patients with Atrial Fibrillation Randomized to **Edoxaban or Warfarin**: Insights from the **ENGAGE AF-TIMI 48** Trial. Am J Med. 2016 Mar 17.
Glassy MS, Wung W, Westcott S, et al. **Watchman Occlusion** in Long-Standing Persistent Atrial Fibrillation: Larger Left Atrial Appendages With Greater Residual Leak. JACC Cardiovasc Interv. 2019 Jun 10;12(11):1018-1026
Golive A, et al. The Population-Based **Long-Term Impact of Anticoagulant and Antiplatelet Therapies in Low-Risk** Patients With Atrial Fibrillation. Am J Cardiol. 2017 Jul 1;120(1):75-82.
Graham DJ, Reichman ME, Wernecke M, et al. Cardiovascular, bleeding, and mortality risks in **elderly medicare patients treated with dabigatran or warfarin** for nonvalvular atrial fibrillation. Circulation. 2015 Jan 13;131(2):157-64.
Griffiths HR, Lip GY. New **biomarkers and risk stratification** in atrial fibrillation: simplicity and practicality matter. Circulation. 2014 Nov 18;130(21):1837-9.
Giugliano RP, Ruff CT, Braunwald E, et al. **Edoxaban versus Warfarin** in Patients with Atrial Fibrillation. (**ENGAGE AF-TIMI 48**) N Engl J Med. 2013 Nov 19.
Gladstone DJ et al. Atrial fibrillation in patients with cryptogenic stroke. (EMBRACE) N Engl J Med 2014 Jun 26; 370:2467.
Gladstone DJ, Geerts WH, Douketis J, et al. How to **Monitor Patients Receiving Direct Oral Anticoagulants for Stroke Prevention in Atrial Fibrillation**: A Practice Tool Endorsed by **Thrombosis Canada**, the Canadian Stroke Consortium, the Canadian Cardiovascular Pharmacists Network, and the Canadian Cardiovascular Society. Ann Intern Med. 2015 Jun 30.
Gladstone DJ, Geerts WH, Douketis J, et al. **Anticoagulant monitoring checklist and quick-reference tables** for managing patients on direct oral anticoagulants (DOACs) for stroke prevention in atrial fibrillation. http://thrombosiscanada.ca/wp-content/uploads/2015/06/DOAC_Monitoring-Checklist-Reference-Tables.pdf (accessed July 30, 2015).
Go AS, Singer DE, Toh S, et al. Outcomes of **Dabigatran and Warfarin for Atrial Fibrillation in Contemporary Practice**: A Retrospective Cohort Study. Ann Intern Med. 2017 Nov 14.
Go AS, Reynolds K, Yang J, et al. Association **of burden of atrial fibrillation with risk of ischemic stroke in adults with paroxysmal atrial fibrillation**: the KP-RHYTHM study [online May 16, 2018]. JAMA Cardiol.
Goette A, et al. **Edoxaban versus enoxaparin-warfarin** in patients undergoing cardioversion of atrial fibrillation (**ENSURE-AF**): a randomised, open-label, phase 3b trial. Lancet. 2016 Aug 26.
Golwala HB, Cannon CP, Steg PG, et al. Safety and efficacy of **dual vs. triple antithrombotic therapy in patients with atrial fibrillation following percutaneous coronary intervention**: a systematic review and meta-analysis of randomized clinical trials. Eur Heart J. 2018 Apr 13.
Goldstein BA, Arce CM, Hlatky MA, et al. Trends in the incidence of atrial fibrillation in older patients initiating **dialysis** in the United States. Circulation. 2012 Nov 6;126(19):2293-301.
Goldstein JN, Refaai MA, Milling TJ Jr, et al. **Four-factor prothrombin complex concentrate versus plasma for rapid vitamin K antagonist reversal** in patients needing urgent surgical or invasive interventions: a phase 3b, open-label, non-inferiority, randomised trial. Lancet.2015 Feb 26.
Gomes T, Mamdani MM, Holbrook AM, et al. Rates of **hemorrhage during warfarin** therapy for atrial fibrillation. CMAJ 2012.
Gómez-Outes AA, et al. **Direct oral anticoagulants for stroke prevention** in patients with atrial fibrillation: meta-analysis by geographic region with a focus on **European** patients. Br J Clin Pharmacol. 2016 May 10.
Gómez-Outes A, Lagunar-Ruíz J, Terleira-Fernández AI, et al. **Causes of Death** in Anticoagulated Patients With Atrial Fibrillation. J Am Coll Cardiol. 2016 Dec 13;68(23):2508-2521.
Gorin L, Fauchier L, Nonin E, et al. Prognosis and Guideline-Adherent **Antithrombotic Treatment** in Patients With Atrial Fibrillation and Atrial Flutter: Implications of Undertreatment and Overtreatment in Real-life Clinical Practice; the Loire Valley Atrial Fibrillation Project. Chest. 2011 Oct;140(4):911-7.
Goto K, Nakai K, Shizuta S, et al; CREDO-Kyoto Registry Cohort-2 Investigators. Anticoagulant and antiplatelet therapy in patients with atrial fibrillation undergoing **percutaneous coronary intervention**. Am J Cardiol. 2014 Jul 1;114(1):70-8.
Graff S, Fenger-Grøn M, Christensen Bet al. Long-term risk of **atrial fibrillation after the death of a partner**. Open Heart. 2016 Mar 14
Graham DJ, Reichman ME, Wernecke M, al. Cardiovascular, **bleeding**, and mortality risks in elderly Medicare patients treated with **dabigatran** or warfarin for nonvalvular atrial fibrillation. Circulation 2014; published online October 30, 2014.
Graham DJ, Reichman ME, Wernecke M, et al. Stroke, bleeding, and mortality risks in **elderly Medicare beneficiaries** treated with **dabigatran or rivaroxaban** for nonvalvular atrial fibrillation [online Oct 3, 2016].JAMA Intern Med. doi:10.1001/jamainternmed.2016.5954.
Granger CB, Armaganijan LV. Newer oral anticoagulants should be used as first-line agents to prevent thromboembolism in patients with atrial fibrillation and risk factors for stroke or thromboembolism. Circulation. 2012 Jan 3;125(1):159-64; discussion 164. Review.
Greinacher A, Thiele T, Selleng K. **Reversal of anticoagulants**: an overview of current developments. Thromb Haemost. 2015 Apr 29;113(5):931-42.
Groenveld HF, Crijns HJGM, Van den Berg MP, et al., for the RACE II Investigators. The effect of **rate control on quality of life** in patients with permanent atrial fibrillation: data of the RACE II (Rate Control Efficacy in Permanent Atrial Fibrillation) study. J Am Coll Cardiol 2011;58:1795– 803.
Groh CA, Faulkner M, Getabecha S, et al. Patient-reported **triggers of paroxysmal atrial fibrillation**. Heart Rhythm. 2019 Feb 14.
Groh CA, Vittinghoff E, Benjamin EJ, et al. **Childhood Tobacco Smoke Exposure and Risk** of Atrial Fibrillation in Adulthood. J Am Coll Cardiol. 2019 Oct 1;74(13):1658-1664.
Grundvold I, Skretteberg PT, Liestøl K, et al. **Upper normal blood pressures** predict incident atrial fibrillation in healthy middle-aged men: a 35-year follow-up study. Hypertension. 2012;59:198 –204.
Grundvold I, Skretteberg PT, Liestøl K, et al. Importance of **Physical Fitness** on Predictive Effect of Body Mass Index and Weight Gain on Incident Atrial Fibrillation in Healthy Middle-Age Men. Am J Cardiol. 2012 May 9.
Gutierrez C, Blanchard DG. **Diagnosis and Treatment of Atrial Fibrillation**. Am Fam Physician. 2016;94(6):442-452.
Gundlund A, Xian Y, Peterson ED, et al. Prestroke and Poststroke **Antithrombotic Therapy in Patients With Atrial Fibrillation** Results From a Nationwide Cohort. JAMA Network Open. 2018;1(1):e180171.
Guo Y, Wang H, Tian Y, et al. Multiple risk factors and **ischaemic stroke in the elderly** Asian population with and without atrial fibrillation. An analysis of 425,600 Chinese individuals without prior stroke. Thromb Haemost. 2015 Dec 22;115(1):184-92.
Guo L, et al. Comparative Efficacy of Clinical Events **Prevention of Five Anticoagulants** in Patients with Atrial Fibrillation (A Network Meta-Analysis). American Journal of Cardiology. 2016.
Guyatt Gordon H., Akl Elie A., Crowther Mark. **Executive Summary**: Antithrombotic Therapy and Prevention of Thrombosis,**9th ed**: American College of Chest Physicians. (ACCP-AT9)Evidence-Based Clinical Practice Guidelines. Chest 2012; 141(2)(Suppl):7S–47S.
Haaland GS, Falk RS, Straume O, et al. Association of **Warfarin Use With Lower Overall Cancer Incidence** Among Patients Older Than 50 Years. JAMA Intern Med. 2017 Nov 6.
Haissaguerre M, Hocini M, Denis A, et al. **Driver domains** in persistent atrial fibrillation. Circulation. 2014 Aug 12;130(7):530-8.
Halcox JPJ;Wareham K;Cardew A;Gilmore M;Barry JP;P. Assessment of **Remote Heart Rhythm Sampling Using the AliveCor Heart Monitor** to Screen for Atrial Fibrillation: The **REHEARSE-AF** Study. Circulation. 2017 Aug 28.
Halperin JL, Hankey GJ, Wojdyla DM, et al; on behalf of the **ROCKET AF** Steering Committee and Investigators. Efficacy and Safety of **Rivaroxaban** Compared with Warfarin among **Elderly** Patients with Nonvalvular Atrial Fibrillation in the ROCKET AF Trial. Circulation. 2014 Jun 3.
Halvorsen S, Atar D, Yang H, et al. Efficacy and safety of **apixaban compared with warfarin** according to age for **stroke** prevention in atrial fibrillation: observations from the ARISTOTLE trial. Eur Heart J. 2014 Feb 20.
Halvorsen S, Storey RF, Rocca B, et al. ESC Working Group on Thrombosis. Management of **antithrombotic therapy after bleeding** in patients with **coronary artery disease and/or atrial fibrillation**: expert consensus paper of the European Society of Cardiology Working Group on Thrombosis. Eur Heart J. 2016 Oct 27.
Hammann F, Gotta V, Conen K, et al. Pharmacokinetic interaction between **taxanes and amiodarone** leading to severe toxicity. Br J Clin Pharmacol. 2016 Nov 20.

Hankey GJ, Stevens SR, Piccini JP, et al; **ROCKET AF** Steering Committee and Investigators. **Intracranial hemorrhage** among patients with atrial fibrillation anticoagulated with **warfarin or rivaroxaban**: the rivaroxaban once daily, oral, direct factor xa inhibition compared with vitamin k antagonism for prevention of stroke and embolism trial in atrial fibrillation. Stroke. 2014 May;45(5):1304-12.

Harel Z, Sholzberg M, Shah PS, et al. Comparisons between **novel oral anticoagulants and vitamin K antagonists in patients with CKD**. J Am Soc Nephrol. 2014 Mar;25(3):431-42.

Harrington AR, Armstrong EP, Nolan PE Jr, Malone DC. Cost-Effectiveness of Apixaban, Dabigatran, Rivaroxaban, and Warfarin for Stroke Prevention in Atrial Fibrillation. Stroke. 2013 Apr 2.

Hart RG, Diener HC, Yang S et al. Intracranial Hemorrhage in Atrial Fibrillation Patients During Anticoagulation With Warfarin or Dabigatran: The RE-LY Trial. Stroke. 2012 Jun;43(6):1511-7.

Härtter S, Sennewald R, Nehmiz G, Reilly P. Oral bioavailability of **dabigatran** etexilate (Pradaxa) after co-medication with **verapamil** in healthy subjects. Br J Clin Pharmacol. 2012 Sep 5.

He Y, et al. The association between **Non-vitamin K antagonist** oral anticoagulants and **gastrointestinal bleeding**: a meta-analysis of observational studies. Br J Clin Pharmacol. 2016 Feb 17.

Healey JS, Connolly SJ, Gold MR, et al. **Subclinical atrial fibrillation** and the risk of stroke. N Engl J Med 2012; 366:120-129.

Healey JS, Eikelboom J, Douketis J, et al. of the RE-LY investigators. **Periprocedural bleeding** and thromboembolic events with **dabigatran** compared with **warfarin**: results from the Randomized Evaluation of Long-Term Anticoagulation Therapy (RE-LY) randomized trial. Circulation. 2012;126:343–348.

Healey JS, Alings M, Ha A, et al.; **ASSERT-II** Investigators. **Subclinical** atrial fibrillation in older patients. Circulation. 2017;136:1276–1283.

Healey JS, Gladstone DJ, Swaminathan B, et al. Recurrent Stroke With **Rivaroxaban Compared With Aspirin** According to Predictors of Atrial Fibrillation: Secondary Analysis of the NAVIGATE ESUS Randomized Clinical Trial. JAMA Neurol. 2019 Apr 8.

Health Canada Mar/12 The Pradax (**dabigatran** etexilate) product monograph has been updated to include in elderly to assess **renal function** initially & at least once a year**.** Use of Pradax® in patients with hemodynamically significant rheumatic valvular heart disease, especially mitral stenosis, or in patients with prosthetic heart valves is not recommended.

Health Canada Dec/18: Important Safety Information – **XARELTO (rivaroxaban) - Increase in all-cause mortality, thromboembolic and bleeding events** in patients after transcatheter aortic valve replacement - Bayer Inc.

Heidbuchel H, Verhamme P, Alings M, et al. **EHRA practical guide on the use of new oral anticoagulants** in patients with non-valvular atrial fibrillation: Executive summary. Eur Heart J 2013.

Heidbuchel H, Verhamme P, Alings M, et al; Advisors:. Updated **European** Heart Rhythm Association practical guide on the use of **non-vitamin-K antagonist** anticoagulants in patients with **non-valvular atrial fibrillation**: Executive summary. Eur Heart J. 2016 Jun 9.

Heidenreich PA, Solis P, Mark Estes NA 3rd, et al. **2016 ACC/AHA** Clinical **Performance and Quality Measures for Adults With Atrial Fibrillation or Atrial Flutter**: A Report of the American College of Cardiology/American Heart Association Task Force on Performance Measures. Circ Cardiovasc Qual Outcomes. 2016 Jun 27.

Heist EK, Mansour M, Ruskin JN. Rate control in atrial fibrillation: targets, methods, resynchronization considerations. Circulation. 2011 Dec13;124(24):2746-55.

Heitz C, Morgenstern J, Bond C, Milne WK. Hot off the Press**: LOw dose MAGnesium sulfate versus HIgh dose i**n the early management of rapid atrial fibrillation: randomised controlled double-blind study. Acad Emerg Med. 2019 Feb 27.

Helgeson SA, Mwakyanjala EJ, Parikh PP, et al. **Hyoscyamine** for a Slow Ventricular Response **During Atrial Fibrillation**. Ann Intern Med. 2018 May 15.

Hellyer JA, , et al. Impact of Baseline Stroke Risk and Bleeding Risk on **Warfarin International Normalized Ratio Control** in Atrial Fibrillation (**TREAT-AF**). Amer J Cardio 2016.

Hendriks JM, de Wit R, Crijns HJ, et al. **Nurse-led care vs. usual care** for patients with atrial fibrillation: results of a randomized trial of integrated chronic care vs. routine clinical care in ambulatory patients with atrial fibrillation. Eur Heart J. 2012 Mar 27.

Heneghan CJ, Garcia-Alamino JM, Spencer EA, et al. **Self-monitoring and self-management of oral anticoagulation**. Cochrane Database Syst Rev. 2016 Jul 5;7:CD003839. Participants who self-monitor or self-manage can improve the quality of their oral anticoagulation therapy. Thromboembolic events were reduced, for both those self-monitoring or self-managing oral anticoagulation therapy. A reduction in all-cause mortality was observed in trials of self-management but not in self-monitoring, with no effects on major haemorrhage.

Hermida J, Lopez FL, Montes R, et al. Usefulness of **High-Sensitivity C-Reactive Protein** to Predict Mortality in Patients With Atrial Fibrillation (from the Atherosclerosis Risk In Communities [**ARIC**] Study). Am J Cardiol. 2011 Sep 29.

Hernandez I, Zhang Y, Saba S, et al. Comparison of the Effectiveness and Safety of **Apixaban**, **Dabigatran**, **Rivaroxaban** and **Warfarin** in Newly Diagnosed Atrial Fibrillation. Am J Cardio. 2017

Hernández Voth AR, Catalán JS, Benavides Mañas PD, et al. A 73-year-old man with **interstitial lung disease due to dronedarone**. Am J Respir Crit Care Med. 2012 Jul 15;186(2):201-2.

Hernandez I, Baik SH, Pinera A, Zhang Y. Risk of **bleeding** with **dabigatran** in atrial fibrillation. JAMA Intern Med2014; published online November 3, 2014. 1260.

Hernandez I, Zhang Y, Brooks MM, et al. Anticoagulation Use and Clinical Outcomes **After Major Bleeding on Dabigatran or Warfarin** in Atrial Fibrillation. Stroke. 2016 Dec 1.

Hess CN, Peterson ED, Peng SA, et al. Use and outcomes of **triple therapy among older patients with acute myocardial infarction** and atrial fibrillation. J Am Coll Cardiol 2015;66:616–27.

Hess CN, James S, Lopes RD, et al. **Apixaban Plus Mono Versus Dual Antiplatelet Therapy in Acute Coronary Syndromes**: Insights From the **APPRAISE-2** Trial. J Am Coll Cardiol. 2015 Aug 18;66(7):777-87.

Higgins P, MacFarlane PW, et al. **Noninvasive cardiac event monitoring** to detect atrial fibrillation after ischemic stroke: a randomized, controlled trial. Stroke. 2013 Sep;44(9):2525-31.

Hijazi Z, Wallentin L, Siegbahn A, et al. **N-terminal pro-B-type natriuretic peptide** for risk assessment in patients with atrial fibrillation: insights from the ARISTOTLE Trial (Apixaban for the Prevention of Stroke in Subjects With Atrial Fibrillation). J Am Coll Cardiol. 2013 Jun 4;61(22):2274-84.

Hijazi Z, Oldgren J, Andersson U, et al. **Cardiac Biomarkers** Are Associated With an Increased Risk of Stroke and Death in Patients With Atrial Fibrillation: A Randomized Evaluation of Long-Term Anticoagulation Therapy (RE-LY) Substudy. Circulation. 2012 Apr 3;125(13):1605-16. (troponin I, NT-proBNP)

Hijazi Z, Siegbahn A, Andersson U, et al. **High-Sensitivity Troponin I** for Risk Assessment in Patients With Atrial Fibrillation: Insights From the Apixaban for Reduction in Stroke and Other Thromboembolic Events in Atrial Fibrillation(ARISTOTLE) Trial. Circulation. 2014 Feb 11;129(6):625-34.

Hijazi Z, Hohnloser SH, Oldgren J, et al. Efficacy and Safety of **Dabigatran Compared With Warfarin** in Relation to Baseline **Renal Function** in Patients With Atrial Fibrillation: A RE-LY (Randomized Evaluation of Long-term Anticoagulation Therapy) Trial Analysis. Circulation. 2014 Mar 4;129(9):961-70.

Hijazi Z, Lindback J, et al. The **ABC (age, biomarkers, clinical history) stroke risk score**: a biomarker-based risk score for predicting stroke in atrial fibrillation. Eur Heart J. 2016 Feb 25.

Hijazi Z, Oldgren J, Lindbäck J, et al. The novel **biomarker-based ABC** (age, biomarkers, clinical history)-bleeding risk score for patients with atrial fibrillation: a derivation and validation study. *Lancet* 2016; 387:2302–2311.

Hijazi, Z, Hohnloser SH, Andersson U, et al. Efficacy and safety of **apixaban** compared with warfarin in patients with atrial fibrillation in relation to **renal function** over time: Insights from the **ARISTOTLE** randomized clinical trial. JAMA Cardiol 2016.

Hilkens NA;Algra A;Diener HC;et al. Predicting major bleeding in patients with noncardioembolic stroke on antiplatelets: **S2TOP-BLEED**. Neurology. 2017 Aug 2.

Hippisley-Cox J, Coupland C. Predicting risk of upper gastrointestinal bleed and intracranial bleed with anticoagulants: cohort study to derive and validate the QBleed scores. BMJ 2014;349:g4606.

Hohnloser SH, Kuck KH, Lilienthal J for the PIAF Investigators. Rhythm or rate control in atrial fibrillation: Pharmacological Intervention in Atrial Fibrillation (**PIAF**): a randomised trial. *Lancet.* 2000;356:1789 –1794.

Hohnloser SH, Camm J, Cappato R, et al. Uninterrupted **edoxaban vs. vitamin K antagonists** for ablation of atrial fibrillation: the ELIMINATE-AF trial. Eur Heart J. 2019 Apr 11.

Hohnloser SH, Crijns HJ, van Eickels M, et al. Effect of **dronedarone** on cardiovascular events in atrial fibrillation. (**ATHENA**) N Engl J Med 2009;360:668-78.

Hohnloser SH, Hijazi Z, Thomas L et al. Efficacy of apixaban when compared with warfarin in relation to **renal function** in patients with atrial fibrillation: insights from the ARISTOTLE trial. Eur Heart J 2012.

Holmes DR Jr, Kar S, Price MJ, et al. Prospective randomized evaluation of the **Watchman Left Atrial Appendage Closure device** in patients with atrial fibrillation versus long-term warfarin therapy: the PREVAIL trial. J Am Coll Cardiol. 2014 Jul 8;64(1):1-12.

Holmes DR Jr, Doshi SK, Kar S, et al. **Left Atrial Appendage Closure** as an **Alternative** to **Warfarin** for Stroke Prevention in Atrial Fibrillation: A Patient-Level Meta-Analysis. J Am Coll Cardiol. 2015 Jun 23;65(24):2614-23.

Holmqvist F, Kim S, Steinberg BA, et al. **Heart rate** is associated with progression of atrial fibrillation, independent of rhythm. Heart. 2015 Mar 2.

Holster L, Valkhoff VE, Kuipers EJ, et al. **New oral anticoagulants increase risk for gastrointestinal bleeding**: a systematic review and meta-analysis. Gastroenterology 2013;145:105-12.

Hong C, Alluri K, Shariff N, et al. Usefulness of the **CHA(2)DS(2)-VASc Score** to Predict **Mortality in Defibrillator Recipients**. Am J Cardiol. 2017 Jul 1;120(1):83-86.

Hong K-S, Kwon SU, Lee SH, et al; Phase 2 Exploratory Clinical Study to Assess the Effects of **Xarelto (Rivaroxaban) Versus Warfarin** on Ischemia, Bleeding, and Hospital Stay in **Acute Cerebral Infarction** Patients With Non-valvular Atrial Fibrillation (**Triple AXEL**) study group. Rivaroxaban vs warfarin sodium in the ultra-early period after atrial fibrillation–related mild ischemic stroke: a randomized clinical trial [online September 11, 2017].JAMA Neurol. doi:10.1001/jamaneurol.2017.2161

Horstmann S, Zugck C, Krumsdorf U, et al. **Left atrial appendage occlusion** in atrial fibrillation after intracranial hemorrhage. Neurology. 2014 Jan 14;82(2):135-8

Hsieh MJ, Wang CC, et al. **HAS-BLED** score predicts risk of in-hospital major bleeding in patients with acute **non-ST segment elevation myocardial infarction**. Thromb Res. 2015 Oct;136(4):775-80.

Hsu J, Maddox T, Kennedy T, et al. **Oral anticoagulant therapy prescription** in patients with atrial fibrillation across the **spectrum of stroke risk**. Insights from the NCDR RINNACLE registry. *JAMA Cardiol* 2016.

Hsu JC, Chan PS, Tang F, et al. **Oral Anticoagulant Prescription** in Patients With Atrial Fibrillation and a **Low Risk of Thromboembolism**: Insights From the NCDR PINNACLE Registry. JAMA Intern Med. 2015 Jun

Hsu JC, Maddox TM, Kennedy K, et al. **Aspirin instead of oral anticoagulant prescription** in atrial fibrillation patients at risk for stroke. J Am Coll Cardiol 2016;67:2913–23.

Huang G, Parikh PB, Malhotra A, et al. Relation of **Body Mass Index and Gender** to Left Atrial Size and Atrial Fibrillation. Am J Cardiol. 2017 Jul 15;120(2):218-222.

Huang WA, Dunipace EA, Sorg JM, Vaseghi M. **Liver Disease as a Predictor** of New-Onset Atrial Fibrillation. J Am Heart Assoc. 2018 Aug 7;7(15):e008703.

Huang WY, Singer DE, Wu YL, et al. **Association of Intracranial Hemorrhage Risk With Non-Vitamin K Antagonist Oral Anticoagulant Use vs Aspirin Use**: A Systematic Review and Meta-Analysis. JAMA Neurol. 2018 Aug 13.

Hudzik B, Polonski L. **Amiodarone-induced pulmonary toxicity**. CMAJ. 2012 May 7.

Huffman MD, Malaisrie SC, Karmali KN. **Concomitant Atrial Fibrillation Surgery for People Undergoing Cardiac Surgery**. JAMA Cardiol. 2017 Feb 8.

Hui DS, Morley JE, Mikolajczak PC, et al. Atrial fibrillation: A major risk factor for **cognitive decline**. Am Heart J. 2015 Apr;169(4):448-456.

Huisman MV, Rothman KJ, Paquette M, et al. The **changing landscape** for stroke prevention in AF: findings from the **GLORIA-AF Registry** phase 2. *J Am Coll Cardiol* 2017.

Hundemer GL, Curhan GC, Yozamp N, et al. Incidence of Atrial Fibrillation and **Mineralocorticoid Receptor Activity** in Patients With Medically and Surgically Treated Primary **Aldosteronism**. JAMA Cardiol. 2018 Jul 18.

Hunt BJ, Levi M. **Urgent reversal of vitamin K antagonists**. BMJ. 2018 Jan 4;360:j5424.

Hussain N, Gersh BJ, Gonzalez Carta K, et al. Impact of **Cardiorespiratory Fitness** on Frequency of Atrial Fibrillation, Stroke, and All-Cause Mortality. Am J Cardiol. 2018 Jan 1;121(1):41-49.

Hussein A, Bartz T, Gottdiener J, et al. **Serial measures of cardiac troponin-T levels** by a highly sensitive assay and incident atrial fibrillation in a prospective cohort of ambulatory older adults. *Heart Rhythm* 2015.

Hussein A, et al. **Radiofrequency ablation** of persistent atrial fibrillation diagnosis-to-ablation time, markers of pathways of atrial remodeling and outcomes. *Circ Arrhythm Electrophysiol* 2016.

Hylek EM. **Apixaban** for End-Stage Kidney Disease. Circulation. 2018 Oct 9;138(15):1534-1536.

Hylek EM, Held C, Alexander JH, et al. **Major Bleeding** in Patients With Atrial Fibrillation Receiving **Apixaban** or Warfarin: The **ARISTOTLE** Trial (Apixaban for Reduction in Stroke and Other Thromboembolic Events in Atrial Fibrillation): Predictors, Characteristics, and Clinical Outcomes. J Am Coll Cardiol. 2014 May 27;63(20):2141-7.

Hyman MC and Callans DJ.Mental exit block: **Escaping the pulmonary veins** in search of new approaches to atrial fibrillation management. Circulation 2016 Oct 11; 134:1082.

Iannone P, Haupt E, Flego G, et al. **Dronedarone** for atrial fibrillation: The limited reliability of clinical practice guidelines. JAMA Intern Med 2014; DOI:10.1001/jamainternmed.2013.14485.

Ibáñez L, Sabaté M, Vidal X, et al. Incidence of Direct Oral **Anticoagulant use in patients with non-valvular atrial fibrillation** and characteristics of users in six European countries (2008-2015): A cross-national drug utilization study. Br J Clin Pharmacol. 2019 Jul 18.

Ice DS, Shapiro TA, Gnall EM, et al. Unanswered Questions in Patients With Concurrent Atrial Fibrillation and **Acute Coronary Syndrome**. Am J Cardiol. 2014 Mar 1;113(5):888-896.

Imazio M, Brucato A, Ferrazzi P, et al. **Colchicine** reduces postoperative atrial fibrillation. Results of the colchicine for the prevention of **postperiocardiotomy symdrome** (**COPPS**) atrial fibrillation substudy. Circulation 2011; 124:2290-2295.

Inohara T, Kimura T, Ueda I, et al. Effect of Compliance to Updated AHA/ACC Performance and Quality Measures Among Patients With Atrial Fibrillation on Outcome (from Japanese Multicenter Registry). Am J Cardiol. 2017 Aug 15;120(4):595-600.

Inohara T, Shrader P, Pieper K, et al. Association of Atrial Fibrillation **Clinical Phenotypes** with Treatment Patterns and Outcomes: A Multicenter Registry Study. JAMA Cardiol. 2017 Nov 12.

Inohara T, Xian Y, Liang L, et al. Association of **Intracerebral Hemorrhage Among Patients Taking Non-Vitamin K Antagonist vs Vitamin K Antagonist** Oral Anticoagulants With In-Hospital Mortality. JAMA. 2018 Jan 25.

Inoue H, Atarashi H, Okumura K, et al. Impact of **gender** on the prognosis of patients with nonvalvular atrial fibrillation. Am J Cardiol. 2014 Mar 15;113(6):957-62.

Inoue YY, Alissa A, Khurram IM, et al. Quantitative Tissue-Tracking Cardiac **Magnetic Resonance** (CMR) of Left Atrial Deformation and the Risk of Stroke in Patients With Atrial Fibrillation. J Am Heart Assoc. 2015 Apr 27;4(4).

Ionescu-Ittu R, Abrahamowicz M, Jackevicius CA, et al. **Comparative effectiveness of rhythm control vs rate control** drug treatment effect on mortality in patients with atrial fibrillation [published online June 4, 2012]. *Arch Int Med*.

Isaew A, Adderley NJ, Ryan R, Fitzmaurice D, Marshall T. The **treatment of paroxysmal atrial fibrillation in UK primary care**. Heart. 2017 Jun 1.

Ito Y, Yamasaki H, et al. Effect of **Eplerenone** on Maintenance of Sinus Rhythm After Catheter Ablation in Patients With Long-Standing Persistent Atrial Fibrillation. Am J Cardiol. 2013 Jan 19.

Iwasaki YK, Nishida K, Kato T, Nattel S. **Atrial fibrillation** pathophysiology: implications for management. Circulation. 2011 Nov 15;124(20):2264-74.

Jaakkola J, et al. **Mobile Phone Detection** of Atrial Fibrillation With Mechanocardiography: The **MODE-AF** Study (Mobile Phone Detection of Atrial Fibrillation). Circulation. 2018 Mar 11.

Jabre P, Jouven X, Adnet F, et al. Atrial fibrillation and death **after myocardial infarction**: a community study. Circulation. 2011;123:2094-100.

Jackevicius CA, Tsadok MA, Essebag V, et al. Early **non-persistence with dabigatran and rivaroxaban** in patients with atrial fibrillation. Heart. 2017 Mar 12.

Jacobs V, Woller SC, Stevens S, et al. **Time outside of therapeutic** range in atrial fibrillation patients is associated with long-term risk of **dementia**. Heart Rhythm. 2014 Aug 9.

Jacobs V, Woller SC, Stevens SM, et al. Percent Time With a **Supratherapeutic INR** in Atrial Fibrillation Patients Also Using an Antiplatelet Agent Is Associated With **Long-Term Risk of Dementia.** J Cardiovasc Electrophysiol. 2015 Aug 13.

Jalini S, Rajalingam R, Nisenbaum R, Javier AD, Woo A, Pikula A. **Atrial cardiopathy** in patients with **embolic strokes of unknown source** and other stroke etiologies. Neurology 2019;92:e288–e294.

Janion-Sadowska A, Chrapek M, Konieczyńska M, Undas A. **Altered Fibrin Clot Properties Predict Stroke** and Bleedings in Patients With Atrial Fibrillation **on Rivaroxaban**. Stroke. 2018 Nov 21:STROKEAHA118023712.

January CT, Wann ST, Alpert JS, et al. **2014 AHA/ACC/HRS guideline** for the management of patients with **atrial fibrillation**. A report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines and the Heart Rhythm Society: Executive summary. *J Am Coll Cardio;* 2014.

January CT, Wann LS, Calkins H, et al. **2019 AHA/ACC/HRS Focused Update of the 2014 AHA/ACC/HRS Guideline for the Management of Patients With Atrial Fibrillation**. Circulation. 2019 Jan 28:CIR0000000000000665.

Jaspers Focks J, et al. **Polypharmacy and effects of apixaban versus warfarin** in patients with atrial fibrillation: post hoc analysis of the **ARISTOTLE** trial. BMJ. 2016 Jun 15;353:i2868.

Johnson JA, Caudle KE, Gong L, et al. Clinical Pharmacogenetics Implementation Consortium (**CPIC**) guideline for **pharmacogenetics-guided warfarin dosing**: 2017 update. Clin Pharmacol Ther. 2017 Sep;102(3):397-404.

Jolly U, Klein G. **Blue man syndrome** (**amiodarone**). CMAJ. 2016 May 17;188(8):604.

Jolly SS, Natarajan MK. **Atrial Fibrillation and PCI - Do We Still Need Aspirin**? N Engl J Med. 2016 Dec 22;375(25):2490-2492.

Jones C, Pollit V, Fitzmaurice D, et al; Guideline Development Group. The **management of atrial fibrillation**: summary of updated **NICE** guidance. BMJ. 2014 Jun 19;348:g3655.

Jones NR, Hobbs FDR, Taylor CJ. **Underuse of anticoagulation** therapy for atrial fibrillation: Are we failing our patients? Can Fam Physician. 2017 Dec;63(12):943-944.

Jones DG, Haldar SK, et al. A randomized trial to assess **catheter ablation versus rate control** in the management of persistent atrial fibrillation in heart failure (ARC-HF). J AmColl Cardiol 2013.

Joy PS, Gopinathannair R, Olshansky B. Effect of **Ablation for Atrial Fibrillation on Heart Failure** Readmission Rates. Am J Cardiol. 2017 Nov 1;120(9):1572-1577.

Jun M, James MT, Manns BJ, et al. Alberta Kidney Disease Network. The association between **kidney function and major bleeding** in older adults with atrial fibrillation starting warfarin treatment: population based observational study. BMJ. 2015 Feb 3;350:h246.

Jung H, Yang PS, Jang E, et al. Effectiveness and Safety of **Non-Vitamin K Antagonist Oral Anticoagulants in** Atrial Fibrillation Patients with **Hypertrophic Cardiomyopathy**: A Nationwide Cohort Study. Chest. 2018 Nov 22.

Kaakeh Y, Overholser BR, Lopshire JC, Tisdale JE. **Drug-induced atrial fibrillation**. Drugs. 2012 Aug 20;72(12):1617-30.

Kaiser DW, Fan J, Schmitt S, et al. **Gender differences** in clinical outcomes after **catheter ablation** of atrial fibrillation.JACC: Clinical Electrophysiol 2016.

Kaitani K, Inoue K, Kobori A, et al. Efficacy of **Antiarrhythmic Drugs Short-Term Use After Catheter Ablation** for Atrial Fibrillation (**EAST-AF**) trial. Eur Heart J. 2016 Feb 14

Kalantarian S, Stern TA, Mansour M, Ruskin JN. **Cognitive Impairment** Associated With Atrial Fibrillation: A Meta-analysis. Ann Intern Med. 2013 Mar 5;158(5 Pt 1):338-46.

Kalantarian S, Ay H, Gollub RL, et al. Association Between Atrial Fibrillation and **Silent Cerebral Infarctions**: Systematic Review and Meta-analysis. Ann Intern Med. 2014 Nov 4;161(9):650-8.

Kalman JM, Sanders P, Rosso R, et al. Should We Perform **Catheter Ablation** for **Asymptomatic** Atrial Fibrillation? Circulation. 2017 Aug 1;136(5):490-499.

Kalra R, Patel N, Doshi R, et al. Evaluation of the Incidence of New-Onset Atrial Fibrillation **After Aortic Valve Replacement**. JAMA Intern Med. 2019 Jun 3.

Kaplon-Cieslicka A, Budnik M, Gawalko M, et al. **Atrial fibrillation type and renal dysfunction as important predictors of left atrial thrombus**. Heart. 2019 Apr 30.

Kapur S, Barbhaiya C, Deneke T, et al. **Esophageal Injury and Atrioesophageal Fistula** Caused by **Ablation** for Atrial Fibrillation. Circulation. 2017 Sep 26;136(13):1247-1255.

Karamchandani K, Khanna AK, Bose S, et al. Atrial Fibrillation: **Current Evidence and Management Strategies** During the Perioperative Period. Anesth Analg. 2019 Sep 27.

Karasoy D, Gislason GH, Hansen J, et al. **Oral anticoagulation therapy after radiofrequency ablation** of atrial fibrillation and the risk of thromboembolism and serious bleeding: long-term follow-up in nationwide cohort of Denmark. Eur Heart J. 2015 Feb 1;36(5):307-14a.

Karlsson LO, Nilsson S, Bang M, et al. A **clinical decision support tool** for improving **adherence** to guidelines on anticoagulant therapy in patients with atrial fibrillation at risk of stroke: A cluster-randomized trial in a Swedish primary care setting (the **CDS-AF** study). PLoS Med. 2018 Mar 13;15(3):e1002528.

Karunanithi Z, Nyboe C, Hjortdal VE. **Long-term risk** of Atrial Fibrillation and Stroke in Patients with **Atrial Septal Defect Diagnosed in Childhood**. The American Journal of Cardiology (2016)

Katsnelson M, Sacco RL, Moscucci M. Progress for stroke prevention with atrial fibrillation: emergence of **alternative oral anticoagulants**. Circulation. 2012 Mar 27;125(12):1577-83.

Kaufman BG, Kim S, Pieper K, et al. **Disease understanding** in patients newly diagnosed with atrial fibrillation. Heart. 2017 Aug 8.

Kelly PJ. **Preventing the rise of atrial fibrillation-related stroke** in populations: a call to action. Circulation. 2014 Oct 7;130(15):1221-2.

Kendzerska T, Gershon A, Atzema C, et al. **Sleep Apnea Increases the Risk of New Hospitalized Atrial Fibrillation**: A Historical Cohort Study. Chest. 2018 Sep 19.

Kent AP, Brueckmann M, Fraessdorf M, et al. Concomitant **oral anticoagulant and nonsteroidal anti-inflammatory drug therapy** in patients with atrial fibrillation. (RE-LY) J Am Coll Cardiol 2018;72:255–67.

Khalil CA, Haddad F, Al Suwaidi J. Investigating palpitations: the role of **Holter monitoring** and loop recorders. BMJ. 2017 Jul 27;358:j3123.

Khan AM, Lubitz SA, Sullivan LM, et al. Low serum **magnesium** and the development of atrial fibrillation in the community: The Framingham Heart Study. Circulation 2012.

Khan F, Ramirez FD, Hibbert B. **Percutaneous left atrial appendage closure for managing thromboembolic risk in atrial fibrillation**. CMAJ. 2018 Oct 15;190(41):E1227-E1230.

Nazha B, Pandya B, et al. Periprocedural Outcomes of **Direct Oral Anticoagulants vs. Warfarin** in Non-Valvular Atrial Fibrillation: A Meta-analysis of Phase III Trials. Circulation. 2018 May 24

Khan H, Kella D, Rauramaa R, et al. **Cardiorespiratory fitness** and atrial fibrillation: A population-based follow-up study. *Heart Rhythm* 2015;

Khan SU, Arshad A, Riaz IB, et al. Meta-Analysis of the Safety and Efficacy of the Oral Anticoagulant Agents (**Apixaban, Rivaroxaban, Dabigatran**) in Patients **With Acute Coronary Syndrome**. Am J Cardiol. 2018 Feb 1;121(3):301-307.

Khan SU, Khan MU, Ghani AR, et al. Meta-Analysis of **Antithrombotic Therapy in Atrial Fibrillation After Percutaneous Coronary Intervention**. Am J Cardiol. 2018 Feb 14.

Khawaja O, Sarwar A, Albert CM, et al. **Sleep Duration** and Risk of Atrial Fibrillation (from the Physicians' Health Study). Am J Cardiol. 2012 Dec 6.

Khawaja O, Petrone AB, Kanjwal Y, et al. **Chocolate Consumption** and Risk of Atrial Fibrillation (from the Physicians' Health Study). Am J Cardiol. 2015 May 21.

Khormaee S, Do HT, Mayr Y, et al. Risk of **Ischemic Stroke After Perioperative Atrial Fibrillation** in Total Knee and Hip Arthroplasty Patients. J Arthroplasty. 2018 Apr 16.

Khurshid S, Weng LC, Hulme OL, et al. **Factors Associated with Anticoagulation Delay** Following New-Onset Atrial Fibrillation. Am J Cardiol. 2017 Oct 15;120(8):1316-1321.

Kido K, Ngorsuraches S. Comparing the Efficacy and Safety of in the **Morbidly Obese Population With Atrial Fibrillation**. Ann Pharmacother. 2018 Aug 22:1060028018796604.

Killu AM, Granger CB, Gersh BJ. **Risk stratification for stroke** in atrial fibrillation: a critique. Eur Heart J. 2019 Apr 21;40(16):1294-1302.

Kim JS, Jongnarangsin K, Chugh A, et al. **Dabigatran vs warfarin for radiofrequency catheter ablation** of atrial fibrillation. Heart Rhythm 2012.

Kim SC, Liu J, Solomon DH. The risk of atrial fibrillation in patients with **rheumatoid arthritis**. Ann Rheum Dis. 2014 Jun 1;73(6):1091-5.

Kim SC, Liu J, Solomon DH. Risk of **incident atrial fibrillation in gout**: a cohort study. Ann Rheum Dis. 2016 Aug;75(8):1473-8.

Kim TH, Yang PS, Uhm JS, et al. **CHA2DS2-VASc Score** (Congestive Heart Failure, Hypertension, Age >/=75 [Doubled], Diabetes Mellitus, Prior Stroke or Transient Ischemic Attack [Doubled], Vascular Disease, Age 65-74, Female) for **Stroke in Asian Patients** With Atrial Fibrillation: A Korean Nationwide Sample Cohort Study. Stroke. 2017 Jun;48(6):1524-1530.

Kim TH, Yang PS, Kim D, et al. **CHA2DS2-VASc Score** for Identifying Truly Low-Risk Atrial Fibrillation for Stroke: A **Korean** Nationwide Cohort Study. Stroke. 2017 Nov;48(11):2984-2990.

Kimura T, Takatsuki S, Inagawa K, et al. **Anatomical characteristics (cauliflower) of the left atrial appendage** in cardiogenic stroke with low CHADS(2) scores. Heart Rhythm 2013 Feb 2.

Kirchhof P, Andresen D, Bosch R et al. Short-term versus long-term antiarrhythmic drug (flecainide) treatment after cardioversion of atrial fibrillation (Flec-SL): a prospective, randomised, open-label, blinded endpoint assessment trial. Lancet. 2012 Jun 15.

Kirchhof P, Haeusler KG, Blank B, et al. **Apixaban** in patients at **risk of stroke undergoing atrial fibrillation ablation**. Eur Heart J. 2018 Mar 20.

Kiviniemi T, Karjalainen P, et al. **Thrombocytopenia** in Patients With Atrial Fibrillation on Oral Anticoagulation Undergoing Percutaneous Coronary Intervention. Am J Cardiol. 2013 May 11.

Kiviniemi T, Puurunen M, et al. Performance of **Bleeding Risk**-Prediction Scores in Patients With Atrial Fibrillation Undergoing **Percutaneous Coronary Intervention**. Am J Cardiol. 2014 Apr 1.

Kirchhof P, Curtis AB, Skanes AC, et al. **Atrial fibrillation guidelines across the Atlantic**: a comparison of the current recommendations of the European Society of Cardiology (ESC) /European Heart Rhythm Association/European Association of Cardiothoracic Surgeons, the American College of Cardiology Foundation (ACCF) /American Heart Association (AHA)/Heart Rhythm Society, and the Canadian Cardiovascular Society (CCS). Eur Heart J. 2013 May;34(20):1471-4.

Kirchhof P, Benussi S, Kotecha D, et al; Authors/Task Force Members; Document Reviewers:. **2016 ESC Guidelines** for the management of **atrial fibrillation** developed in collaboration with EACTS: The Task Force for the management of atrial fibrillation of the European Society of Cardiology (ESC)Developed with the special contribution of the European Heart Rhythm Association (EHRA) of the ESCEndorsed by the European Stroke Organisation (ESO). Eur Heart J. 2016 Aug 27.

Kirchhof P. The future of atrial fibrillation management: **integrated care and stratified therapy**. Lancet. 2017 Apr 28.

Kirchhof P, Radaideh G, Kim YH, et al. Global **XANTUS** program Investigators. Global Prospective **Safety Analysis of Rivaroxaban**. J Am Coll Cardiol. 2018 Jul 10;72(2):141-153.

Kivimaki M, Nyberg ST, Batty GD, et al. Long working hours as a risk factor for atrial fibrillation: a multi-cohort study. Euro Heart J. 2017;0:1-8

Klein Klouwenberg PM, et al. Incidence, Predictors and Outcomes of New-onset Atrial Fibrillation in **Critically Ill Patients with Sepsis**: a Cohort Study. Am J Respir Crit Care Med. 2016 Jul 28.

Knijnik L, Rivera M, Blumer V, et al. **Prevention of Stroke** in Atrial Fibrillation After Coronary Stenting. Stroke. 2019 Aug;50(8):2125-2132.

Køber L, Torp-Pedersen C, McMurray JJ, et al. Increased mortality after **dronedarone** therapy for severe heart failure. (**ANDROMEDA**) N Engl J Med 2008;358:2678-87.

Kochhäuser S, Khaykin Y, Beardsall J, et al. Comparison of outcomes after **cardioversion or atrial fibrillation ablation** in patients with **differing periprocedural anticoagulation** regimens. Can J Cardiol. 2014 Dec;30(12):1541-6.

Koci, Forbes, Mansour, et al. New **Classification Scheme** for Atrial Fibrillation Symptom **Severity and Burden**. The American Journal of Cardiology. 2014.

Koene RJ, Alraies MC, Norby FL, et al. Relation of the **CHA2DS2-VASc Score to Risk of Thrombotic and Embolic Stroke** in Community-Dwelling Individuals Without Atrial Fibrillation (From The Atherosclerosis Risk in Communities [ARIC] Study). Am J Cardiol. 2018 Nov 6.

Koenig-Oberhuber V, Filipovic M. **New antiplatelet drugs and new oral anticoagulants**. Br J Anaesth. 2016 Sep;117 Suppl 2:ii74-ii84.

Kolek MJ, et al. Evaluation of **prediction model** for development of atrial fibrillation in a repository of electronic medical records [online Oct 12,16].JAMA Cardiol. doi:10.1001/jamacardio.2016.3366

Komen J, Forslund T, et al. Effects of **policy interventions** on the introduction of **novel oral anticoagulants in Stockholm**: an interrupted time series analysis. Br J Clin Pharmacol. 2016 Oct 11.

Konishi H, Miyauchi K, Tsuboi S, et al. Impact of the **HAS-BLED** Score on Long-Term Outcomes **After Percutaneous Coronary Intervention**. Am J Cardiol. 2015 May 21.

Kooistra HAM, Piersma-Wichers M, Kluin-Nelemans HC, et al. Impact of **vitamin K antagonists on quality of life** in a prospective cohort of 807 atrial fibrillation patients. *Circ Cardiovasc Qual Outcomes* 2016.

Koplan BA, Stevenson WG. **Atrial Fibrillation in Heart Failure**: Should Catheter Ablation Play a Larger Role? Circulation. 2016 Mar 30.

Korantzopoulos P, Liu T, Papaioannides D, et al. Atrial fibrillation and **marijuana** smoking. Int J Clin Pract. 2008 Feb;62(2):308-13.

Korompoki E, Filippidis FT, Nielsen PB, et al. Long-term antithrombotic treatment in **intracranial hemorrhage** survivors with atrial fibrillation. Neurology. 2017 Jul 19.

Kosmidou I, Chen S, Kappetein AP, et al. **New-Onset Atrial Fibrillation After PCI or CABG for Left Main Disease**: The **EXCEL** Trial. J Am Coll Cardiol. 2018 Feb 20;71(7):739-748.

Kotecha D, Holmes J, Krum H, et al; on behalf of the Beta-Blockers in Heart Failure Collaborative Group. Efficacy of **β blockers** in patients with **heart failure plus atrial fibrillation**: an individual-patient data meta-analysis. Lancet. 2014 Sep 2.

Krijthe BP, Heeringa J, Hofman A, et al. **Non-steroidal anti-inflammatory drugs** (NSAIDS) and the risk of atrial fibrillation: a population-based follow-up study. BMJ Open. 2014 Apr 8

Kröll D, Stirnimann G, et al. Pharmacokinetics and pharmacodynamics of single doses of **Rivaroxaban in obese patients** before and after bariatric surgery. Br J Clin Pharmacol. 2017 Jan 25.

Kuck KH, Wissner E. Why **amiodarone failed** to lower the rate of recurrence six months after catheter ablation for atrial fibrillation. Eur Heart J. 2014 Sep 2.

Kuck KH, Brugada J, Fürnkranz A, et al; **FIRE AND ICE** Investigators. **Cryoballoon or Radiofrequency Ablation** for Paroxysmal Atrial Fibrillation. N Engl J Med. 2016 Apr 4.

Kuck KH, Fürnkranz A, Chun KR, et al. **Cryoballoon or radiofrequency** ablation for symptomatic paroxysmal atrial fibrillation: reintervention, rehospitalization, and quality-of-life outcomes in the **FIRE AND ICE** trial. Eur Heart J. 2016 Jul 5.

Kumagai N, Nusser JA, Inoue H, et al. Effect of Addition of a **Statin to Warfarin** on **Thromboembolic Events** in Japanese Patients With Nonvalvular Atrial Fibrillation and Diabetes Mellitus. Am J Cardiol. 2017 Jul 15;120(2):230-235.

Kumar P, Patel A, Mounsey JP, et al. Effect of Left Ventricular Diastolic Dysfunction on Outcomes of **Atrial Fibrillation Ablation**. Am J Cardiol. 2014 May 17.

Kumar S, de Lusignan S, McGovern A, et al. Ischaemic stroke, haemorrhage, and mortality in older patients with **chronic kidney disease** newly started on **anticoagulation** for atrial fibrillation: a population based study from UK primary care. BMJ. 2018 Feb 14;360:k342.

Kuramatsu JB, Gerner ST, Schellinger PD, et al. **Anticoagulant reversal, blood pressure levels, and anticoagulant resumption in patients with anticoagulation-related intracerebral hemorrhage**. JAMA. 2015 Feb 24;313(8):824-36.

Kurogi R, Nishimura K, Nakai Met al. **Comparing intracerebral hemorrhages associated with direct oral anticoagulants or warfarin**. Neurology. 2018 Mar 27;90(13):e1143-e1149.

Kurtul A, Acikgoz SK. Validation of the **CHA2DS2-VASc Score** in Predicting Coronary Atherosclerotic Burden and In-Hospital Mortality in Patients With **Acute Coronary Syndrome**. Am J Cardiol. 2017 Apr 12.

Lacoin L, et al. **Evolving landscape of stroke prevention** in atrial fibrillation within the UK between 2012 and 2016: a cross-sectional analysis study using CPRD. BMJ Open 2017;358:e015363.

LaHaye SA, Gibbens SL, et al. A **clinical decision aid** for the selection of antithrombotic therapy for the prevention of stroke due to atrial fibrillation. Eur Heart J. 2012 Sep;33(17):2163-71.

Lakkireddy D, Reddy YM, Di Biase L, et al. Feasibility and safety of **dabigatran versus warfarin** for periprocedural anticoagulation in patients undergoing **radiofrequency ablation** for atrial fibrillation. J Am Coll Cardiol 2012.

Laliberté F, Cloutier M, Crivera C, et al. Effects of **Rivaroxaban Versus Warfarin on Hospitalization Days** and Other Health Care Resource Utilization in Patients With Nonvalvular Atrial Fibrillation: An Observational Study From a Cohort of Matched Users. Clin Ther. 2015 Mar 3.

Lamberts M, Olesen JB, Ruwald MH, et al. **Bleeding** after Initiation of Multiple Antithrombotic Drugs, Including **Triple Therapy**, in Atrial Fibrillation Patients Following Myocardial Infarction and Coronary Intervention: A Nationwide Cohort Study. Circulation. 2012 Aug 6. Compared with an anticoagulant plus antiplatelet monotherapy, triple antithrombotic therapy increased bleeding risk by ~40% without reducing risk for thrombotic events.

Lamberts M, Gislason GH, et al. Oral **anticoagulation and antiplatelets in atrial fibrillation patients after myocardial infarction and coronary intervention**. J Am Coll Cardiol 2013.

Lamberts M, Gislason GH, Lip GY, et al. **Antiplatelet therapy for stable coronary artery disease** in atrial fibrillation patients taking an oral anticoagulant: a nationwide cohort study. Circulation. 2014 Apr 15;129(15):1577-85.

Lamberts M, Lip GY, Hansen ML, et al. Relation of **Nonsteroidal Anti-inflammatory Drugs** to Serious Bleeding and Thromboembolism Risk in Patients With Atrial Fibrillation Receiving Antithrombotic Therapy: A Nationwide Cohort Study. Ann Intern Med. 2014 Nov 18;161(10):690-8.

Lane DA, Dagres N, Dan GA, et al. **Antithrombotic treatment** in patients with atrial fibrillation and acute coronary syndromes: results of the European Heart Rhythm Association survey. Europace. 2019 Mar 14.

Lane DA, Lip GY. Use of the **CHA2DS2-VASc and HAS-BLED** Scores to Aid Decision Making for Thromboprophylaxis in Nonvalvular Atrial Fibrillation. Circulation. 2012 Aug 14;126(7):860-5.

Lane DA, Wood K. **Patient guide** for taking the non-vitamin k antagonist oral anticoagulants for atrial fibrillation. Circulation. 2015 Apr 21;131(16):e412-5.

Lang C, Seyfang L, Ferrari J, et al. Do **Women** With Atrial Fibrillation Experience More Severe **Strokes**? Results From the Austrian Stroke Unit Registry. Stroke. 2017 Mar;48(3):778-780.

Lansberg MG, et al. Antithrombotic and thrombolytic therapy for **ischemic stroke**: antithrombotic therapy & prevention of thrombosis, **9th ed:** American College of Chest Physicians (ACCP-AT9) evidence-based clinical practice guidelines. Chest. 2012;141(2)(supp):e601S-e636S.

Larock AS, Mullier F, Sennesael AL, et al. **Appropriateness of prescribing dabigatran** etexilate and **rivaroxaban** in patients with nonvalvular atrial fibrillation: a prospective study. Ann Pharmacother. 2014 Oct;48(10):1258-68.

Larsen TB, Rasmussen LH, Skjøth F, et al. Efficacy and safety of **dabigatran etexilate and warfarin in "real world" patients** with atrial fibrillation: A prospective nationwide cohort study. J Am Coll Cardiol 2013.

Larsen TB, Gorst-Rasmussen A, Rasmussen LH, et al. **Bleeding events among new starters** and switchers to **dabigatran compared with warfarin** in atrial fibrillation. Am J Med. 2014 Jul;127(7):650-656.e5.

Larsen TB, Rasmussen LH, et al. **Dabigatran and warfarin for secondary prevention** of stroke in atrial fibrillation patients: a nationwide cohort study. Am J Med 2014;127:1172–8.

Larsen TB, Skjøth F, et al. Comparative **effectiveness and safety of non-vitamin K antagonist oral anticoagulants and warfarin** in patients with atrial fibrillation: propensity weighted nationwide cohort study. BMJ. 2016 Jun 16;353:i3189.

Larsson SC, Drca N, Wolk A. **Alcohol consumption** and risk of atrial fibrillation: prospective study and dose-dependent meta-analysis.*J Am Coll Cardiol* 2014;

Larsson SC, et al. **Coffee consumption** is not associated with increased risk of atrial fibrillation: results from two prospective cohorts and a meta-analysis. BMC Med. 2015 Sep 23;13(1):207.

Larsson SC, Drca N, Björck M, et al. **Nut consumption** and incidence of seven cardiovascular diseases. Heart. 2018 Apr 16.

Lau CP, Tachapong N, Wang CC, et al. Prospective randomized study to assess the efficacy of **site and rate of atrial pacing** on long-term progression of atrial fibrillation in sick sinus syndrome: Septal Pacing for Atrial Fibrillation Suppression Evaluation (**SAFE**) study. *Circulation*. 2013;128:687–693.

Lau DH, Kalman J, Sanders P. Management of **Recent-onset** Sustained Atrial Fibrillation: **Pharmacologic and Nonpharmacologic Strategies**. Clin Ther. 2014 Sep 1;36(9):1151-1159.

Lau DH, Nattel S, Kalman JM, et al. **Modifiable Risk Factors** and Atrial Fibrillation. Circulation. 2017 Aug 8;136(6):583-596.

Lau WC, et al. Association Between **Dabigatran vs Warfarin** and **Risk of Osteoporotic Fractures** Among Patients With Nonvalvular Atrial Fibrillation. JAMA. 2017 Mar 21;317(11):1151-1158.

Lau WCY, et al. **Bleeding-related hospital admissions** and 30-day readmissions in patients with non-valvular atrial fibrillation treated with **dabigatran versus warfarin**. J Thromb Haemost. 2017 Oct;15(10):1923-1933.

Lau YC, Lane DA, Lip GY. Atrial Fibrillation and **Heart Failure**: A Bad Combination. Am J Cardiol. 2014 Jan 16.

Laube ES, Yu A, Gupta D, et al. **Rivaroxaban** for Stroke Prevention in Patients With Nonvalvular Atrial Fibrillation **and Active Cancer**. Am J Cardiol. 2017 Jul 15;120(2):213-217.

Lauffenburger JC, Farley JF, Gehi AK, et al. Factors Driving **Anticoagulant Selection** in Patients With Atrial Fibrillation in the United States. Am J Cardiol. 2015 Feb 2.

Lauw MN, Eikelboom JW, Coppens M, et al. Effects of **dabigatran** according to **age** in atrial fibrillation. Heart. 2017 Feb 17.

Law SWY, Lau WCY, Wong ICK, et al. **Sex-based differences in outcomes of oral anticoagulation** in patients with **atrial fibrillation**. J Am Coll Cardiol 2018;72:271–82.

Lee G, Sanders P, Kalman JM. **Catheter ablation** of atrial arrhythmias: state of the art. Lancet. 2012 Oct 27;380(9852):1509-19.

Lee MP, Desai RJ, Jin Y, et al. Association of **Ustekinumab vs TNF Inhibitor Therapy** With Risk of Atrial Fibrillation and Cardiovascular Events in Patients With Psoriasis or Psoriatic Arthritis. JAMA Dermatol. 2019 Mar 27.

Lee PH, Song JK, Kim JS, et al. **Cryptogenic Stroke and High-Risk Patent Foramen Ovale**: The **DEFENSE-PFO** Trial. J Am Coll Cardiol. 2018 Feb 28.

Lee S, Anglade MW, Meng J, et al. **Cost-Effectiveness of Apixaban Compared With Aspirin** for Stroke Prevention in Atrial Fibrillation Among Patients Unsuitable for Warfarin. Circ Cardiovasc Qual Outcomes. 2012 Jun 26.

Lee SR, Rhee TM, Kang DY, et al. Meta-Analysis of **Oral Anticoagulant Monotherapy as an Antithrombotic Strategy** in Patients With Stable Coronary Artery Disease and Nonvalvular Atrial Fibrillation. Am J Cardiol. 2019 Jun 25.

Lempereur M, Aminian A, Freixa X, et al. Left **Atrial Appendage Occlusion** in Patients With Atrial Fibrillation and Previous Major Gastrointestinal Bleeding (from the Amplatzer Cardiac Plug Multicenter Registry). Am J Cardiol. 2017 Aug 1;120(3):414-420

Levy JH, Ageno W, Chan NC, et al. Subcommittee on Control of Anticoagulation. When and how to use **antidotes for the reversal of direct oral anticoagulants: guidance from the SSC of the ISTH**. J Thromb Haemost. 2016 Mar;14(3):623-7.

Levy JH, Moore KT, Neal MD, et al.**Rivaroxaban reversal with prothrombin complex concentrate or tranexamic acid** in healthy volunteers. J Thromb Haemost. 2018 Jan;16(1):54-64.

Li J, Becker R, Rauch B, et al; OMEGA Study Group. Usefulness of **Heart Rate** to Predict One-Year Mortality in Patients With Atrial Fibrillation and Acute Myocardial Infarction (from the OMEGA Trial). Am J Cardiol. 2012 Dec 28.

Li TJ, Zang WD, Chen YL, et al. **Renin-angiotensin system inhibitors for prevention** of recurrent atrial fibrillation: a meta-analysis. Int J Clin Pract. 2013 Jun;67(6):536-43.

Li J, Agarwal SK, Alonso A, et al. **Airflow Obstruction, Lung Function**, and Incidence of Atrial Fibrillation: The Atherosclerosis Risk in Communities (ARIC) Study. Circulation. 2014 Mar 4;129(9):971-80.

Li YG, Pastori D, Farcomeni A, et al. A Simple Clinical Risk Score **(C2HEST) for Predicting Incident Atrial Fibrillation in Asian Subjects**: Derivation in 471,446 Chinese Subjects, With Internal Validation and External Application in 451,199 Korean Subjects. Chest. 2019 Mar;155(3):510-518.

Liakopoulos OJ, Kuhn EW, Slottosch I, et al. **Preoperative statin** therapy for patients undergoing cardiac surgery. Cochrane Database Syst Rev. 2012 Apr 18;4:CD008493.
Preoperative statin therapy reduces the odds of post-operative AF and shortens the stay on the ICU and in the hospital. Statin pretreatment had no influence on perioperative mortality, stroke, myocardial infarction or renal failure. Since analysed studies included mainly patients undergoing myocardial revascularizations the results cannot be extrapolated to patients undergoing other cardiac procedures such as heart valve or aortic surgery.

Liang Y, Mente A, Yusuf S, et al. **Alcohol consumption** and the risk of incident atrial fibrillation among people with cardiovascular disease. CMAJ. 2012 Oct 1.

Liao JN, Te ALD, Chang YT, et al. **Risk of Stroke in Patients With Short-Run Atrial Tachyarrhythmia**. Stroke. 2017 Dec;48(12):3232-3238.

Lindner SM, Fordyce CB, et al. Treatment Consistency Across Levels of **Baseline Renal Function With Rivaroxaban** or Warfarin: A **ROCKET AF** (Rivaroxaban Once-Daily, Oral, Direct Factor Xa Inhibition Compared With Vitamin K Antagonism for Prevention of Stroke and Embolism Trial in Atrial Fibrillation) Analysis. Circulation. 2017 Mar 7;135(10):1001-1003

Lindhardsen J, Ahlehoff O, Gislason GH, et al. Risk of atrial fibrillation and stroke **in rheumatoid arthritis**: Danish nationwide cohort study. BMJ. 2012 Mar 8;344:e1257.

Lindsay BD. Atrial fibrillation: New drugs, devices, and procedures. Cleve Clin J Med. 2012 Aug;79(8):553-9.

Lindquist DE, et al. Evaluation of the **Hemodynamic Effects of Intravenous Amiodarone** Formulations During the Maintenance Phase Infusion. Ann Pharmacother. 2015 Dec;49(12):1317-21.

Link MS, Haïssaguerre M, Natale A. **Ablation of Atrial Fibrillation**: Patient Selection, Periprocedural Anticoagulation, Techniques, and Preventive Measures After Ablation. Circulation. 2016 Jul 26;134(4):339-52.

Link MS, Giugliano RP, Ruff CR, et al. Stroke and mortality risk in patients with various **patterns of atrial fibrillation**. Results from the **ENGAGE AF-TIMI 48** Trial (Effective Anticoagulation With Factor Xa Next Generation in Atrial Fibrillation–Thrombolysis in Myocardial Infarction 48). *Circ Arrhythmia Electrophysiol* 2017.

Link MS, Giugliano RP, Ruff CT, et al. Stroke and Mortality Risk in Patients With Various **Patterns of Atrial Fibrillation**: Results From the **ENGAGE AF-TIMI 48** Trial (Effective Anticoagulation With Factor Xa Next Generation in Atrial Fibrillation-Thrombolysis in Myocardial Infarction 48). Circ Arrhythm Electrophysiol. 2017 Jan;10(1).

Linker DT, Murphy TB, Mokdad AH. **Selective screening** for atrial fibrillation using multivariable risk models. Heart. 2018 Mar 28.

Lip GYH et al. Predicting Stroke and Thromboembolism in Atrial Fibrillation Using a Novel **Risk Factor-Based Approach**: The Euro Heart Survey on Atrial Fibrillation. **(CHA_2DS_2VASc)** Chest 2010;137;263-272.

Lip GYH et al. **Comparative Validation** of a Novel Risk Score for Predicting Bleeding Risk in Anticoagulated Patients With Atrial Fibrillation The **HAS-BLED** Score. J Am Coll Cardiol 2011;57:173?80.

Lip GYH, Andreotti F, Fauchier L, et al. Bleeding risk assessment and management in atrial fibrillation patients. Executive summary of a position document from the European Heart Rhythm Association [EHRA], endorsed by the European Society of Cardiology [ESC] Working Group on Thrombosis. Thromb Haemost 2011; 106:997-1011.

Lip GYH, Al-Saady N, Jin J, et al. Anticoagulation Control in Warfarin-Treated Patients Undergoing **Cardioversio**n of Atrial Fibrillation (from the **Edoxaban** Versus **Enoxaparin-Warfarin** in Patients Undergoing Cardioversion of Atrial Fibrillation Trial). Am J Cardiol. 2017 Jun 15.

Lip GY, Tse HF, Lane DA. Atrial fibrillation. Lancet. 2011 Dec 9. [Epub ahead of print]

Lip GY, Larsen TB, Skjøth F, Rasmussen LH. **Indirect comparisons** of new oral **anticoagulant drugs** for efficacy and safety when used for stroke prevention in atrial fibrillation. J Am Coll Cardiol 2012; 60:738-46.

Lip GY, Kongnakorn T, Phatak H, et al. **Cost-Effectiveness of Apixaban** Versus Other New Oral Anticoagulants for Stroke Prevention in Atrial Fibrillation. Clin Ther. 2014 Feb 5.

Lip GY, Laroche C, Dan GA, Santini et al. '**Real-world' antithrombotic** treatment in atrial fibrillation: the **EURObservational** Research Programme Atrial Fibrillation General Pilot survey. Am J Med. 2014 Jan 28.

Lip GY, Haguenoer K, Saint-Etienne C, et al. Relationship of the **SAMe-TT2R2 Score** to Poor-Quality Anticoagulation, Stroke, Clinically Relevant Bleeding, and Mortality in Patients With Atrial Fibrillation. Chest. 2014 Sep 1;146(3):719-26.

Lip GY, Nielsen PB, Skjoth F, et al. The value of the **European society of cardiology guidelines for refining stroke risk stratification** in patients with atrial fibrillation categorized as low risk using the anticoagulation and risk factors in **atrial fibrillation stroke score (ATRIA)** : a nationwide cohort study. Chest. 2014 Nov 1;146(5):1337-46.

Lip GY, Skjøth F, Rasmussen LH, et al. Oral Anticoagulation, Aspirin, or No Therapy in Patients With Nonvalvular AF **With 0 or 1 Stroke Risk Factor Based on the CHA2DS2-VASc Score**. J Am Coll Cardiol. 2015 Apr 14;65(14):1385-94.

Lip GY, Lane DA. **Stroke prevention in atrial fibrillation**: a systematic review. JAMA. 2015 May 19;313(19):1950-62.

Lip GY, Lanitis T, et al. **Cost-effectiveness** of **Apixaban Compared With Edoxaban** for Stroke Prevention in Nonvalvular Atrial Fibrillation. Clin Ther. 2015 Nov 1;37(11):2476-2488.e27.

Lip GY. How to Manage Occult Atrial Fibrillation Detected on Long-Term Monitoring. Circulation. 2016 Mar 29;133(13):1290-5.

Lip GY, Nielsen PB. Should Patients With Atrial Fibrillation and 1 Stroke Risk Factor (**CHA2DS2-VASc Score 1 in Men, 2 in Women) Be Anticoagulated**? Yes: Even 1 Stroke Risk Factor Confers a Real Risk of Stroke. Circulation. 2016 Apr 12

Lip GY, Pan X, Kamble S, et al. Major bleeding risk among non-valvular atrial fibrillation patients initiated on **apixaban, dabigatran, rivaroxaban or warfarin: a ``real-world`` observational** Study in the United States. Int J Clin Pract. 2016 Aug 23.

Lip GY, Keshishian A, Kamble S, et al. **Real-world comparison** of major bleeding risk among non-valvular atrial fibrillation patients initiated on **apixaban, dabigatran, rivaroxaban, or warfarin**. A propensity score matched analysis. Thromb Haemost. 2016 Aug 19;116(5).

Lip GY, Waldo AL, Ip J, et al. Determinants of **Time in Therapeutic Range** in Patients Receiving Oral Anticoagulants (A Substudy of **IMPACT**). Am J Cardiol. 2016 Dec 1;118(11):1680-1684

Lip GY. **Stroke prevention in Atrial Fibrillation**. Eur Heart J. 2017 Jan 1;38(1):4-5.

Lip GYH, Skjøth F, Nielsen PB, et al. Effectiveness and Safety of **Standard-Dose Nonvitamin K Antagonist Oral Anticoagulants and Warfarin Among Patients With Atrial Fibrillation With a Single Stroke Risk Factor**: A Nationwide Cohort Study. JAMA Cardiol. 2017 Jun 14.

Lip GYH, Merino JL, Dan GA, et al. Relation of **Stroke and Bleeding Risk** Profiles to Efficacy and Safety of Edoxaban for Cardioversion of Atrial Fibrillation (from the **Edoxaban** versus warfarin in subjectS UndeRgoing cardiovErsion of Atrial Fibrillation [**ENSURE-AF**] Study). Am J Cardiol. 2018 Jan 15;121(2):193-198.

Lip GYH, Skjøth F, Nielsen PB, Kjældgaard JN, Larsen TB. The **HAS-BLED**, ATRIA, and ORBIT Bleeding Scores in Atrial Fibrillation Patients Using **Non-Vitamin K Antagonist Oral Anticoagulants**. Am J Med. 2018 May;131(5):574.e13-574.e27.

Lip GYH, Banerjee A, Boriani G, et al. **Antithrombotic Therapy for Atrial Fibrillation: CHEST Guideline** and Expert Panel Report. Chest. 2018 Aug 21.

Lip GYH, Banerjee A, Boriani G, et al. **Antithrombotic Therapy for Atrial Fibrillation: CHEST Guideline** and Expert Panel Report. Chest. 2018 Aug 21.

Lip GYH, Collet JP, Haude M, Huber K. Management of **antithrombotic therapy in AF patients presenting with ACS and/or undergoing PCI**: A Summary of the Joint Consensus Document of the European Heart Rhythm Association (EHRA), European Society of Cardiology Working Group on Thrombosis, European Association of Percutaneous Cardiovascular Interventions (EAPCI) and European Association of Acute Cardiac Care (ACCA) endorsed by the Heart Rhythm Society (HRS), Asia-Pacific Heart Rhythm Society (APHRS), Latin America Heart Rhythm Society (LAHRS), and Cardiac Arrhythmia Society of Southern Africa (CASSA). Eur Heart J. 2018 Aug 14;39(31):2847-2850.

Liu G, Yan YP, Zheng XX,et al. Meta-analysis of **nonsteroidal anti-inflammatory drug** use and risk of atrial fibrillation. Am J Cardiol. 2014 Nov 15;114(10):1523-9.

Liu T;Hui J;;et al. Meta-Analysis of Efficacy and Safety of **Low-Intensity Warfarin Therapy for East Asian Patients** With Nonvalvular Atrial Fibrillation. Am J Cardiol. 2017 Jul 31.

Löbe S, Salmáš J, John S, et al. Usefulness of **Dronedarone** in Patients With Atrial Arrhythmias. Am J Cardiol. 2013 Feb 25.

Lobo R, Jaffe AS, Cahill C, et al. Significance of **High-Sensitivity Troponin T After Elective External Direct Current Cardioversion** for Atrial Fibrillation or Atrial Flutter. Am J Cardiol. 2018 Jan 15;121(2):188-192

Lobos-Bejarano JM, Castellanos Rodríguez A, Barrios V, et al; **PAULA** Study Team. Influence of **renal function on anticoagulation control** in patients with non-valvular **atrial fibrillation** taking vitamin K antagonists. Int J Clin Pract. 2017 Jul 19.

Loewen P, Dahri K. Risk of **bleeding with oral anticoagulants**: an updated systematic review and performance analysis of clinical prediction rules. Ann Hematol. 2011 Oct;90(10):1191-200.

Loffredo L, Pastori D, Farcomeni A, et al. Effects of Anticoagulants in Patients With **Cirrhosis** and **Portal Vein Thrombosis**: A Systematic Review and Meta-analysis. Gastroenterology. 2017 Aug;153(2):480-487.e1.

Loikas D, Forslund T, Wettermark B, et al. **Sex and Gender Differences** in Thromboprophylactic Treatment of Patients With Atrial Fibrillation After the Introduction of Non-Vitamin K Oral Anticoagulants. Am J Cardiol. 2017 Oct 15;120(8):1302-1308.

Loke YK, Pradhan S, et al. Comparative **coronary risks of apixaban, rivaroxaban and dabigatran**: a meta-analysis and adjusted indirect comparison. Br J Clin Pharmacol. 2014 Mar 11.

Loo SY, Dell'Aniello S, Huiart L, et al. **Trends in the prescription of novel oral anticoagulants in UK** primary care. Br J Clin Pharmacol. 2017 Apr 7.

Lopes RD, Al-Khatib SM, Wallentin L, et al. efficacy and safety of apixaban compared with warfarin according to patient **risk of stroke and bleeding** in atrial fibrillation: a secondary analysis of a randomized controlled trial (**Aristotle**). Lancet 2012.

Lopes RD, Heizer G, Aronson R, et al. **Antithrombotic therapy** after acute coronary syndrome or PCI in atrial fibrillation. (AUGUSTUS-apixaban, warfarin) N Engl J Med. DOI: 10.1056/NEJMoa1817083.

Lopes RD, Hong H, Harskamp RE, et al. **Safety and Efficacy of Antithrombotic Strategies in Patients** With Atrial Fibrillation Undergoing Percutaneous Coronary Intervention: A Network Meta analysis of Randomized Controlled Trials. JAMA Cardiol. 2019 Jun 19.

Lopes RD, Rordorf R, De Ferrari GM, et al. **Digoxin and mortality** in patients with atrial fibrillation. (**Aristotle**) J Am Coll Cardiol 2018;71:1063–74.

Lopez FL, Agarwal SK, et al. Relation of Serum **Phosphorus Levels** to the Incidence of Atrial Fibrillation (the Atherosclerosis Risk In Communities [ARIC] Study). Am J Cardiol. 2012 Dec 27.

López-López J, et al. **Oral anticoagulants for prevention of stroke in atrial fibrillation**: systematic review, network meta-analysis, and cost-effectiveness analysis. BMJ 2017;359:j5399.

Lou B, Liang X, Wu Y, et al. Meta-Analysis Comparing **Dual Versus Single Antiplatelet Therapy in Combination With Antithrombotic Therapy** in Patients With Atrial Fibrillation Who Underwent Percutaneous Coronary Intervention With Stent Implantation. Am J Cardiol. 2018 Aug 15;122(4):604-611.

Lowenstern A, Al-Khatib SM, Sharan L, et al. Interventions for **Preventing Thromboembolic Events** in Patients With Atrial Fibrillation: A Systematic Review. Ann Intern Med. 2018 Oct 30.

Lown M, Moran P. **Should we screen** for atrial fibrillation? BMJ. 2019 Feb 13;364:l43.

Lubitz SA, Yin X, Rienstra M, et al. **Long-term outcomes** of secondary atrial fibrillation in the community: the **framingham** heart study. Circulation. 2015 May 12;131(19):1648-55.

Lubitz SA, Yin X, Lin H, et al. **Genetic Risk Prediction** of Atrial Fibrillation. Circulation. 2016 Oct 28.

Luik A, Radzewitz A, Kieser M, et al. **Cryoballoon versus Open Irrigated Radiofrequency Ablation** in Patients With Paroxysmal Atrial Fibrillation: The Prospective, Randomised, Controlled, Non-Inferiority FreezeAF Study. Circulation. 2015 Aug 17.

Luik A, Radzewitz A, Kieser M, et al. **Cryoballoon Versus Open Irrigated Radiofrequency Ablation** in Patients With Paroxysmal Atrial Fibrillation: The Prospective, Randomized, Controlled, Noninferiority FreezeAF Study. Circulation. 2015 Oct 6;132(14):1311-9.

Luo N, Merrill P, Parikh KS, et al. **Exercise Training** in Patients With Chronic Heart Failure and Atrial Fibrillation. J Am Coll Cardiol. 2017 Apr 4;69(13):1683-1691.

Lüscher TF. **Dual antiplatelet therapy**: how, how long, and in which patients? Eur Heart J. 2018 Jan 14;39(3):181-183.

Lüscher TF. **Atrial fibrillation and arrhythmias**: novel risk assessment, proper anticoagulation, and ablation. Eur Heart J. 2018 Apr 21;39(16):1317-1321.

Lutsey PL, et al. **Atrial fibrillation and venous thromboembolism**: evidence of bidirectionality in the Atherosclerosis Risk in Communities Study. J Thromb Haemost. 2018 Apr;16(4):670-679.

Maan A, Heist EK, Passeri J, Inglessis et al. Impact of atrial fibrillation on outcomes in patients who underwent **transcatheter aortic valve replacement**. Am J Cardiol. 2015 Jan 15;115(2):220-6.

Macchia A, Grancelli H, Varini S, et al. **Omega-3 fatty acids** for the prevention of recurrent symptomatic atrial fibrillation: results of the FORWARD (Randomized Trial to Assess Efficacy of PUFA for the Maintenance of Sinus Rhythm in Persistent Atrial Fibrillation) trial. J Am Coll Cardiol. 2013 Jan 29;61(4):463-8.

MacIntyre C, Lakdawala NK. **Management of Atrial Fibrillation in Hypertrophic Cardiomyopathy**. Circulation. 2016 May 10;133(19):1901-5.

Mackenzie C, Syed J, Pollak PT, Koren G. Falling between the cracks: a case of **amiodarone toxicity**. CMAJ. 2011 Sep 6;183(12):1393-7.

Macle L, Khairy P, Weerasooriya R, et al, for the ADVICE trial investigators. **Adenosine-guided pulmonary vein isolation** for the treatment of paroxysmal atrial fi brillation: an international, multicentre, randomised superiority trial. Lancet 2015; published online July 24.

Macle L, Cairns J, Leblanc K, et al. **CCS Atrial Fibrillation Guidelines** Committee. **2016 Focused Update** of the Canadian Cardiovascular Society Guidelines for the Management of Atrial Fibrillation. Can J Cardiol. 2016 Oct;32(10):1170-1185.

Magnani JW, Hylek EM, Apovian CM. **Obesity begets atrial fibrillation**: a contemporary summary. Circulation. 2013 Jul 23;128(4):401-5.

Magnani JW, Norby FL, Agarwal SK, et al. **Racial Differences** in Atrial Fibrillation-Related Cardiovascular Disease and Mortality: The Atherosclerosis Risk in Communities (**ARIC**) Study. JAMA Cardiol. 2016 Jul 1;1(4):433-41.

Magnussen C, Niiranen TJ, Ojeda FM, et al. **Sex Differences** and Similarities in Atrial Fibrillation Epidemiology, Risk Factors, and Mortality in Community Cohorts: Results From the BiomarCaRE Consortium (Biomarker for Cardiovascular Risk Assessment in Europe). Circulation. 2017 Oct 24;136(17):1588-1597

Mahaffey KW, Califf RM. Atrial fibrillation: a spectrum of risk with a uniform treatment effect of **novel anticoagulants**? Eur Heart J. 2013 Jun 13.

Maheshwari A, Norby FL, Roetker NS, et al. Refining **Prediction of Atrial Fibrillation-Related Stroke Using the P2-CHA2DS2-VASc Score**. Circulation. 2019 Jan 8;139(2):180-191.

Mahtani KR, Heneghan C. **Novel oral anticoagulants for atrial fibrillation**. BMJ. 2016 Sep 28;354:i5187.

Majeed A, Hwang HG, Connolly SJ, et al. Management and outcomes of **major bleeding during treatment with dabigatran or warfarin**. *Circulation* 2013.

Malagù M, Trevisan F, Scalone A, et al. Frequency of **"Pocket" Hematoma** in Patients Receiving Vitamin K Antagonist and Antiplatelet Therapy at the Time of Pacemaker or Cardioverter Defibrillator Implantation (from the **POCKET** Study). Am J Cardiol. 2017 Jan 6

Malhotra R, Bilchick KC, Dimarco JP. Usefulness of **Pharmacologic Conversion** of Atrial Fibrillation During **Dofetilide** Loading Without the Need for Electrical Cardioversion to Predict Durable Response to Therapy. Am J Cardiol. 2013 Nov 9

Malik AH, Yandrapalli S, Aronow WS, et al. Meta-Analysis of **Direct-Acting Oral Anticoagulants Compared With Warfarin in Patients** >75 Years of Age. Am J Cardiol. 2019 Mar 18.

Malik AH, Yandrapalli S, Aronow WS, et al. **Oral anticoagulants** in atrial fibrillation with valvular heart disease and bioprosthetic heart valves. Heart. 2019 Jun 14.

Malmo V, Nes BM, Amundsen BH, et al. **Aerobic interval training** reduces the burden of atrial fibrillation in the short term: a randomized trial.*Circulation* 2015.

Mandalenakis Z, Rosengren A, Lappas G, et al. Atrial Fibrillation **Burden in Young Patients** With Congenital Heart Disease. Circulation. 2018 Feb 27;137(9):928-937.

Mandyam MC, Vedantham V, Scheinman MM, et al. **Alcohol and Vagal Tone as Triggers** for Paroxysmal Atrial Fibrillation. Am J Cardiol. 2012 Apr 20.

Man-Son-Hing M, et al. Choosing **antithrombotic** therapy for elderly patients with atrial fibrillation who are at **risk for falls**. Arch Intern Med. 1999 Apr 12;159(7):677-85.

Marciniak TA, Cherepanov V, Golukhova E, et al. **Drug Discontinuation** and Follow-up Rates in **Oral Antithrombotic Trials**. JAMA Intern Med. 2016 Feb 1;176(2):257-9.

Mareev Y, Cleland JG. Should **β-Blockers Be Used in Patients With Heart Failure and Atrial Fibrillation**? Clin Ther. 2015 Sep 18.

Marijon E, Le Heuzey JY, Connolly S, et al. **Causes of death** and influencing factors in patients with atrial fibrillation: a competing-risk analysis from the randomized evaluation of long-term anticoagulant therapy study. Circulation. 2013 Nov 12;128(20):2192-201.

Mark DB, Anstrom KJ, Sheng S, et al; CABANA Investigators. Effect of **catheter ablation vs medical therapy** on quality of life among patients with atrial fibrillation: the CABANA randomized clinical trial [Mar 15, 2019]. JAMA. doi:10.1001/jama.2019.0692

Marlu R, Hodaj E, Paris A, et al. Effect of non-specific reversal agents on anticoagulant activity of dabigatran and rivaroxaban. A randomised crossover ex vivo study in healthy volunteers. *Thromb Haemost* 2012; 108:217-224.

Marott SC, Nielsen SF, Benn M, et al. **Antihypertensive treatment** and risk of atrial fibrillation: a nationwide study. Eur Heart J. 2014 May;35(18):1205-14.

Marriott C, George C. **New onset atrial fibrillation, prominent chest wall veins, and dyspnoea**. BMJ. 2018 Oct 11;363:k3779. (hyperthyroidism)

Marrouche NF, Wilber D, et al. Association of **atrial tissue fibrosis** identified by delayed-enhancement MRI and atrial fibrillation **catheter ablation**: the **DECAAF** study. *JAMA* 2014;311:498-506.

Marrouche NF, Brachmann J, Andresen D, et al. **Catheter ablation for atrial fibrillation with heart failure**. (**Castle-AF**) N Engl J Med 2018;378:417-27.

Martin RC, Burgin WS, Schabath MB, et al. **Sex-specific Differences** for Risk of Disability and Death in Atrial Fibrillation-related Stroke. The American Journal of Cardiology (2016).

Martin RI, Pogoryelova O, Koref MS, et al. **Atrial fibrillation associated** with **ivabradine** treatment: meta-analysis of randomized controlled trials. Heart. 2014 Oct 1;100(19):1506-10.

Martinez C, Katholing A, Freedman SB, et al. Adverse prognosis of incidentally detected **ambulatory atrial fibrillation**.*Thromb Haemost* 2014; 112:276-286.

Martínez-González MÁ, Toledo E, Arós F, et al; **PREDIMED** Investigators*. **Extravirgin Olive Oil Consumption** Reduces Risk of Atrial Fibrillation: The PREDIMED (Prevención con Dieta Mediterránea) Trial. Circulation. 2014 Jul 1;130(1):18-26.

Marzec LN, Wang J, Shah ND, et al. Influence of **Direct Oral Anticoagulants on Rates of Oral Anticoagulation for Atrial Fibrillation**. J Am Coll Cardiol. 2017 May 23;69(20):2475-2484.

Marzona I, O'Donnell M, Teo K, et al. Increased risk of **cognitive and functional decline** in patients with atrial fibrillation: results of the **ONTARGET** and **TRANSCEND** studies. CMAJ 2012

Mason PK, Lake DE, Dimarco JP et al. Impact of the CHA(2)DS(2)-VASc Score on Anticoagulation Recommendations for Atrial Fibrillation. Am J Med. 2012 Jun;125(6):603.e1-6. Epub 2012 Apr 11.

Masoudi FA, Calkins H, Kavinsky CJ, et al. 2015 ACC/HRS/SCAI **left atrial appendage occlusion device** societal overview. *Heart Rhythm* 2015.

Massicotte-Azarniouch D, Sood MM. Uncertainty surrounds **anticoagulation risks and benefits in patients with chronic kidney disease** with atrial fibrillation. BMJ Evid Based Med. 2019 Feb;24(1):35-36.

Massumi A, Chelu MG, Nazeri A, et al. Initial Experience With a Novel Percutaneous **Left Atrial Appendage Exclusion Device** in Patients With Atrial Fibrillation, Increased Stroke Risk, and Contraindications to Anticoagulation. Am J Cardiol. 2013 Jan 9.

Mastoris I, Maria Mathias P, Dangas GD. **Dual Antiplatelet Therapy Duration**: A Review of Current Available Evidence. Clin Ther. 2016 Mar 15. pii: S0149-2918(16)30076-5.

Mathew JS, Sachs MC, Katz R, et al. **Fibroblast Growth Factor-23** and Incident Atrial Fibrillation: The Multi-Ethnic Study of Atherosclerosis (MESA) and the Cardiovascular Health Study (CHS). Circulation. 2014 Jul 22;130(4):298-307.

Matsumura-Nakano Y, Shizuta S, Komasa A, et al. An Open-Label Randomized Trial Comparing **Oral Anticoagulation with and without Single Antiplatelet Therapy in Patients with Atrial Fibrillation** and Stable Coronary Artery Disease Beyond One Year after Coronary Stent Implantation: The OAC-ALONE Study. Circulation. 2018 Sep 24.

Mattison MLP, Muse VV, Simmons LH, et al. Case 15-2018: An 83-Year-Old Woman with Nausea, Vomiting, and Confusion. N Engl J Med. 2018 May 17;378(20):1931-1938. (digoxin toxicity)

Maura G, Blotière PO, Bouillon K, et al. Comparison of the Short-Term Risk of Bleeding and Arterial Thromboembolic Events in Nonvalvular Atrial Fibrillation Patients Newly **Treated With Dabigatran or Rivaroxaban versus Vitamin K Antagonists**: A French Nationwide Propensity-Matched Cohort Study. Circulation. 2015 Jul 21.

Mavaddat N, Roalfe A, Fletcher K, et al. **Warfarin versus aspirin for prevention of cognitive decline** in atrial fibrillation: randomized controlled trial (Birmingham Atrial Fibrillation Treatment of the Aged Study-**BAFTA**). Stroke. 2014 May;45(5):1381-6.

McAlister FA, Jacka M, et al. The **prediction of postoperative stroke or death** in patients with preoperative atrial fibrillation **undergoing non-cardiac surgery**: a **VISION** sub-study. J Thromb Haemost. 2015 Oct;13(10):1768-75.

McDowell TY, Blank M, Lawrence J, et al. **Food and Drug Administration Analysis of Ticagrelor**: Using Data From an Enriched Trial to Evaluate Benefit-Risk Difference in an Unstudied Population. Circulation. 2016 Nov 8;134(19):1500-1502

McGrath ER, Kapral MK, Fang J, et al; Investigators of the Ontario Stroke Registry. Association of atrial fibrillation with **mortality and disability after ischemic stroke**. Neurology. 2013 Aug 27;81(9):825-32.

McHorney CA, Peterson ED, Laliberté F, et al. Comparison of **Adherence to Rivaroxaban Versus Apixaban** Among Patients With Atrial Fibrillation. Clin Ther. 2016 Oct 24.

McIntyre WF, Um KJ, Alhazzani W, et al. Association of **Vasopressin Plus Catecholamine Vasopressors vs Catecholamines Alone** With Atrial Fibrillation in Patients With Distributive Shock: A Systematic Review and Meta-analysis. JAMA. 2018 May 8;319(18):1889-1900.

McManus DD, Rienstra M, Benjamin EJ. An update on the **prognosis** of patients with atrial fibrillation.Circulation.2012 Sep4;126(10):e143-6.

McManus DD, Huang W, et al. Trends in atrial fibrillation in patients **hospitalized with an acute coronary syndrome**. Am J Med. 2012 Nov;125(11):1076-84.

McManus DD, Lee J, Maitas O, et al. A novel application for the detection of an irregular pulse **using an iPhone 4S** in patients with atrial fibrillation. Heart Rhythm 2012.

McManus DD, Yin X, Gladstone R, et al. **Alcohol Consumption**, Left Atrial Diameter, and Atrial Fibrillation. J Am Heart Assoc. 2016 Sep 14;5(9)

Medical Letter- **Treatment Guidelines. Treatment of Atrial Fibrillation**. Sept 2010. July 2014. **Updated Sept 2019**.

Medical Letter. Treatment Guidelines: **Antithrombotic Drugs**. Oct 2011 and updated **Oct 2014.**

Melduni RM, Schaff HV, Lee HC, et al. Impact of **Left Atrial Appendage Closure** During Cardiac Surgery on the Occurrence of Early Postoperative Atrial Fibrillation, Stroke, and Mortality: A Propensity Score-Matched Analysis of 10 633 Patients. Circulation. 2017 Jan 24;135(4):366-378

Melgaard L, Rasmussen LH, Skjøth F, et al. **Age dependence of risk factors** for stroke and death in young patients with atrial fibrillation: a nationwide study. Stroke. 2014 May;45(5):1331-7.

Melgaard L, Gorst-Rasmussen A, Lane DA, et al. Assessment of the **CHA2DS2-VASc Score** in Predicting Ischemic Stroke, Thromboembolism, and Death in Patients With **Heart Failure** With and Without Atrial Fibrillation. JAMA. 2015 Aug 30:1-9.

Melkonian M, Jarzebowski W, Pautas E, et al. **Bleeding risk of antiplatelet drugs compared with oral anticoagulants** in older patients with atrial fibrillation: a systematic review and meta-analysis. J Thromb Haemost. 2017 Apr 10.

Messé SR, Gronseth G, Kent DM, Kizer et al. Practice advisory: Recurrent stroke with **patent foramen ovale** (update of practice parameter): Report of the Guideline Development, Dissemination, and Implementation Subcommittee of the American Academy of Neurology. Neurology. 2016 Jul 27

Meyer AV, Green M, Pautler HM, et al. Impact of Vitamin K Administration on **INR Changes** and Bleeding Events Among Patients With **Cirrhosis**. Ann Pharmacother. 2015 Nov 18.

Middeldorp ME, Pathak RK, Meredith M, et al. **PREVEntion and regReSsive Effect of weight-loss** and risk factor modification on Atrial Fibrillation: the **REVERSE-AF study**. Europace. 2018 Jun 14.

Miesbach W, Seifried E. New direct oral anticoagulants - current therapeutic options and treatment recommendations for bleeding complications. Thromb Haemost. 2012 Jul 10;108(4).

Miller CS, Grandi SM, Shimony A, et al. Meta-Analysis of Efficacy and Safety of New Oral Anticoagulants (**Dabigatran, Rivaroxaban, Apixaban) Versus Warfarin** in Patients With Atrial Fibrillation. Am J Cardiol. 2012 Apr 24.

Mir H, Siemieniuk RAC, Ge LC, et al. **Patent foramen ovale closure, antiplatelet therapy or anticoagulation in patients with patent foramen ovale and cryptogenic stroke**: a systematic review and network meta-analysis incorporating complementary external evidence. BMJ Open. 2018 Jul 25;8(7):e023761.

Miyares MA, Davis KA. **Direct-Acting Oral Anticoagulants** as Emerging Treatment Options for **Heparin-Induced Thrombocytopenia**. Ann Pharmacother. 2015 Jun;49(6):735-739.

Moayedi Y, Abdel-Qadir HM, Dorian P. Evaluation and care of a patient with **new-onset atrial fibrillation**. CMAJ. 2014 Feb 18;186(3):204-5.

Moffitt P, Lane DA, Park H, et al. **Thromboprophylaxis** in atrial fibrillation and association with **cognitive decline**: systematic review. Age Ageing. 2016 Nov;45(6):767-775.

Monahan K, Brewster J, Wang L, et al. Relation of the **Severity of Obstructive Sleep Apnea** in Response to Anti-Arrhythmic Drugs in Patients With Atrial Fibrillation or Atrial Flutter. Am J Cardiol. 2012 Apr 18.

Mohanty S, Mohanty P, Di Biase L, et al. Results From a Single-Blinded Randomized Study (APPROVAL)Comparing The Impact of Different **Ablation Strategies** on Long Term Procedure Outcome in Coexistent Atrial Fibrillation and Flutter. Circulation. 2013 Apr 9.

Mohanty S, Gianni C, Mohanty P, et al. Impact of **rotor ablati**on in non-paroxysmal AF patients: Results from a randomized trial (**OASIS**). *J Am Coll Cardiol* 2016.

Monaco L, Biagi C, Conti V, et al. Safety profile of the **direct oral anticoagulants**: an analysis of the **WHO database of adverse drug reactions**. Br J Clin Pharmacol. 2017 Jan 10.

Mont L, Bisbal F, Hernandez-Madrid A, et al. **Catheter ablation vs. antiarrhythmic** drug treatment of persistent atrial fibrillation: a multicentre, randomized, controlled trial (**SARA** study). Eur Heart J. 2013 Oct 17.

Moore KT, Byra W, Vaidyanathan S, et al. Switching from **rivaroxaban to warfarin**: an open-label pharmacodynamic study in healthy subjects. Br J Clin Pharmacol. 2014 Dec 5.

Moore SJ, Blair EA, et al. Impact of **video technology** on efficiency of pharmacist-provided **anticoagulation counseling** and patient comprehension. Ann Pharmacother. 2015 Jun;49(6):631-8.

Moore TJ, Cohen MR, Mattison DR. **Dabigatran, bleeding, and the regulators**. BMJ 2014;349:g4517.

Moran PS, Flattery MJ, Teljeur C, et al. Effectiveness of **systematic screening** for the detection of atrial fibrillation. Cochrane Database Syst Rev. 2013 Apr 30;4:CD009586. doi: 10.1002/14651858.CD009586.pub2. Systematic and opportunistic screening for AF increase the rate of detection of new cases compared with routine practice. While both approaches have a comparable effect on the overall AF diagnosis rate, the cost of systematic screening is significantly more than that of opportunistic screening from the perspective of the health service provider.

Morrill AM, Ge D, Willett KC. **Dosing of Target-Specific Oral Anticoagulants in Special Populations**. Ann Pharmacother. 2015 Sep;49(9):1031-45.

Morillo CA, Verma A, Connolly SJ; **RAAFT-2** Investigators, et al. **Radiofrequency ablation vs antiarrhythmic drugs** as first-line treatment of paroxysmal atrial fibrillation(RAAFT-2): a randomized trial. JAMA. 2014 Feb 19;311(7):692-700.

Morris DA, Parwani A, Huemer M, et al. Clinical Significance of the Assessment of the Systolic and Diastolic Myocardial Function of the Left Atrium in Patients With Paroxysmal Atrial Fibrillation and Low CHADS(2) Index Treated With **Catheter Ablation** Therapy. Am J Cardiol. 2013 Jan 18.

Moss JD, Cifu AS. **Management of Anticoagulation in Patients With Atrial Fibrillation**. JAMA. 2015 Jul 21;314(3):291-2.

Mostofsky E, BergJohansen E, Tjønneland E, et al. **Chocolate intake** and risk of clinically apparent atrialfibrillation: the danish diet, Cancer, and HealthStudy. Heart 2017.

Mozaffarian D, Marchioli R, Macchia A, et al. Fish oil and postoperative atrial fibrillation: The **Omega-3 Fatty Acids** for Prevention of Postoperative Atrial Fibrillation (**OPERA**) Randomized Trial. JAMA 2012 .

Mueller T, Alvarez-Madrazo S, Robertson C, et al. Comparative safety and effectiveness of **direct oral anticoagulants** in patients with atrial fibrillation in clinical practice in Scotland. Br J Clin Pharmacol. 2018 Nov 13.

Mugnai G, Chierchia GB, de Asmundis C, et al. Comparison of **pulmonary vein isolation using cryoballoon versus conventional radiofrequency** for paroxysmal atrial fibrillation. Am J Cardiol. 2014 May 1;113(9):1509-13.

Mugnai G, de Asmundis C, Iacopino S, et al. Comparison of the Incidences of **Complications After Second-Generation Cryoballoon Ablation** of Atrial Fibrillation Using Vitamin K Antagonists Versus Novel Oral Anticoagulants. Am J Cardiol. 2017 Jul 15;120(2):223-229

Müller P, Dietrich JW, Halbfass P, et al. Higher incidence of **esophageal lesions after AF ablation** related to the use of esophageal temperature probes. Heart Rhythm. 2015 Apr 3.

Munir MB, Sharbaugh MS, Ahmad S, et al. **Causes and Predictors of 30-Day Readmissions** in Atrial Fibrillation (from the Nationwide Readmissions Database). Am J Cardiol. 2017 Aug 1;120(3):399-403.

Murthy SB, Gupta A, Merkler AE, et al. **Restarting Anticoagulant Therapy After Intracranial Hemorrhage**: A Systematic Review and Meta-Analysis. Stroke. 2017 Apr 17

Musat DL, Adhaduk M, Preminger MW, et al. Correlation of **QT Interval** Correction Methods During Atrial Fibrillation and Sinus Rhythm. Am J Cardiol. 2013 Aug 22.

Muscari A, Bonfiglioli A, et al. Usefulness of the **MrWALLETS Scoring System** to Predict First **Diagnosed Atrial Fibrillation** in Patients With Ischemic Stroke. Am J Cardiol. 2017 Jan 5.

Myrstad M, Nystad W, Graff-Iversen S, et al. Effect of Years of **Endurance Exercise** on Risk of Atrial Fibrillation and Atrial Flutter. Am J Cardiol. 2014 Jul 30.

Naccarelli GV, Panaccio MP, Cummins G et al. **CHADS(2) and CHA(2)DS(2)-VASc** Risk Factors to Predict First Cardiovascular Hospitalization Among Atrial Fibrillation/Atrial Flutter Patients. Am J Cardiol. 2012 Feb 21.

Nagarakanti R, Ezekowitz MD, Oldgren J, et al. **Dabigatran** versus warfarin in patients with atrial fibrillation: an analysis of patients undergoing **cardioversion**. *Circulation.* 2011;123:131–136.

Nagarakanti R, Ellis CR. **Dabigatran** in Clinical Practice. Clin Ther. 2012 Sep 29.

Nagarakanti R, et al. Comparison of Characteristics and Outcomes of **Dabigatran Versus Warfarin** in **Hypertensive Patients** With Atrial Fibrillation (from the **RE-LY** Trial). Am J Cardiol. 2015 Oct 15;116(8):1204-9.

Nagata N, Yasunaga H, Matsui H, et al. **Therapeutic endoscopy-related GI bleeding** and thromboembolic events in patients using **warfarin or direct oral anticoagulants**: results from a large nationwide database analysis. Gut. 2017 Sep 5.

Najafzadeh M, Gagne JJ, Choudhry NK, et al. **Patients' preferences** in anticoagulant therapy: discrete choice experiment. Circ Cardiovasc Qual Outcomes. 2014 Nov;7(6):912-9.

Narayan SM, Krummen DE, Shivkumar K, et al. Treatment of atrial fibrillation by the **ablation** of localized sources. [**CONFIRM**] J Am Coll Cardiol 2012.

Naruse Y, Tada H, Satoh M, et al. Concomitant obstructive **sleep apnea** increases the recurrence of atrial fibrillation following radiofrequency catheter ablation of atrial fibrillation: clinical impact of continuous positive airway pressure therapy. Heart Rhythm2012.

Nattel S. Atrial Fibrillation and **Body Composition**: Is it Fat or Lean That Ultimately Determines the Risk? J Am Coll Cardiol. 2017 May 23;69(20):2498-2501.

Nazha B, Pandya B, Cohen J, et al. **Periprocedural Outcomes of Direct Oral Anticoagulants vs. Warfarin** in Non-Valvular Atrial Fibrillation: A Meta-analysis of Phase III Trials. Circulation.

2018 May 24.
Nedeltchev K. Critique of **apixaban versus warfarin** in patients with atrial fibrillation. Stroke. 2012 Mar;43(3):922-3.
Nelson WW, Choi JC, Vanderpoel J, et al. Impact of **Co-morbidities and Patient Characteristics** on International Normalized Ratio Control Over Time in Patients With Nonvalvular Atrial Fibrillation. Am J Cardiol. 2013 Jun 22.
Nessel C, Mahaffey K, Piccini J, et al. Incidence and Outcomes of **Gastrointestinal Hemorrhage in Patients With Atrial Fibrillation** Treated With **Rivaroxaban or Warfarin**: Results From the ROCKET AF Trial. Chest 142.4_MeetingAbstracts (2012): 84A-84A.
Neumann I, Rada G, Claro JC et al. **Oral direct factor Xa inhibitors versus low-molecular-weight heparin** to prevent thromboembolism in patients undergoing total hip or knee replacement. A systematic review and meta-analysis. Ann Intern Med. 2012;156:710-9.
Newell A, Haynes J, Smith R. **Evaluation of asymptomatic atrial fibrillation**. Am Fam Physician. 2012 Sep 15;86(6):Online.
NICE: National Institute for Health and Clinical Excellence (NICE). **Dabigatran** etexilate for the prevention of stroke and systemic embolism in atrial fibrillation. London (UK): National Institute for Health and Clinical Excellence; 2012 Mar. http://www.nice.org.uk/nicemedia/live/13677/58470/58470.pdf
NICE: National Institute for Health and Clinical Excellence. **Atrial fibrillation**: the management of atrial fibrillation. NICE guideline (draft for consultation). Jan 2014
NICE: National Institute for Health and Care Excellence. The **management of atrial fibrillation (update). Clinical guidelines CG180. June 2014**.
NICE: National Clinical Guideline Centre. **Atrial fibrillation**: the management of atrial fibrillation. London (UK): National Institute for Health and Care Excellence (NICE); 2014 Jun.
NICE: National Institute for Health and Care Excellence. Atrial fibrillation and heart valve disease: **self-monitoring coagulation status using point-of-care coagulometers** (the CoaguChek XS system and the INRatio2 PT/INR monitor). London (UK): National Institute for Health and Care Excellence (NICE); 2014 Sep.
Nielsen JC et al. **Radiofrequency ablation** as initial therapy in paroxysmal atrial fibrillation. (**MANTRA-PAF**) *N Engl J Med* 2012 Oct 25; 367:1587.
Nielsen PB, Larsen TB, Skjøth F, et al. **Restarting Anticoagulant Treatment After Intracranial Hemorrhage** in Patients With Atrial Fibrillation and the Impact on Recurrent Stroke, Mortality, and Bleeding: A Nationwide Cohort Study. Circulation. 2015 Aug 11;132(6):517-25.
Nielsen PB, Larsen TB, Lip GY. **Recalibration** of the **HAS-BLED score** – should haemorrhagic stroke account for 1 or 2 points? Chest. 2015 Sep 10.
Nielsen PB, Skjøth F, Søgaard M, et al. Effectiveness and safety of reduced dose **non-vitamin K antagonist** oral anticoagulants and **warfarin** in patients with atrial fibrillation: propensity weighted nationwide cohort study. BMJ. 2017 Feb 10;356:j510.
Nielsen PB, Larsen TB, Skjoth F, et al. Outcomes Associated With **Resuming Warfarin Treatment After Hemorrhagic Stroke or Traumatic Intracranial Hemorrhage** in Patients With Atrial Fibrillation. JAMA Intern Med. 2017 Feb 20.
Nielsen PB, Skjøth F, Overvad TF, et al. **Female Sex Is a Risk Modifier Rather Than a Risk Factor** for Stroke in Atrial Fibrillation: Should We Use a **CHA(2)DS(2)-VA** Score **Rather Than CHA(2)DS(2)-VASc**? Circulation. 2018 Feb 20;137(8):832-840.
Niessner A, Tamargo J, Morais J, et al. **Reversal strategies for non-vitamin K antagonist** oral anticoagulants: a critical appraisal of available evidence and recommendations for clinical management-a joint position paper of the **European** Society of Cardiology Working Group on Cardiovascular Pharmacotherapy and European Society of Cardiology Working Group on Thrombosis. Eur Heart J. 2017 Jun 7;38(22):1710-1716.
Nigam A, Talajic M, Roy D, et al; AFFORD Investigators. **Fish Oil** for the Reduction of Atrial Fibrillation Recurrence, Inflammation, and Oxidative Stress. J Am Coll Cardiol. 2014 Oct 7;64(14):1441-8.
Nishimura M, Hsu JC. **Non-Vitamin K Antagonist Oral Anticoagulants** in Patients With Atrial Fibrillation and End-Stage **Renal Disease**. Am J Cardiol. 2018 Jan 1;121(1):131-140.
Nishtala PS, Jamieson HA, Hanger HC, Chyou TY, Hilmer SN. Examining the **Risks of Major Bleeding Events** in Older People Using Antithrombotics. Cardiovasc Drugs Ther. 2019 Mar 2.
Ng KH, Shestakovska O, et al. Efficacy and safety of **apixaban** compared with **aspirin** in the **elderly**: a subgroup analysis from the **AVERROES** trial. Age Ageing. 2016 Jan;45(1):77-83.
Nochaiwong S, Ruengorn C, Awiphan R, et al. Efficacy and safety of **warfarin in dialysis patients** with atrial fibrillation: a systematic review and meta-analysis. Open Heart. 2016 Jun 16;3(1)
Nogami A, Harada T, Sekiguchi Y, et al; ABRIDGE-J Investigators. Safety and Efficacy of Minimally Interrupted **Dabigatran vs Uninterrupted Warfarin Therapy** in Adults Undergoing Atrial Fibrillation Catheter Ablation: A Randomized Clinical Trial. JAMA Netw Open. 2019 Apr 5;2(4):e191994
Norby FL, Soliman EZ, Chen LY, Bengtson et al. **Trajectories of Cardiovascular Risk Factors** and Incidence of Atrial Fibrillation Over a 25-Year Follow-Up: The ARIC Study (Atherosclerosis Risk in Communities).Circulation. 2016 Aug 23;134(8):599-610
Norris S, Ramael S, Ikushima I, et al. Evaluation of the immunogenicity of the **dabigatran reversal agent idarucizumab** during phase I studies. Br J Clin Pharmacol. 2017 Feb 23.
Ntaios G, Lip GY, Makaritsis K, et al. **CHADS2, CHA2DS2-VASc**, and long-term stroke outcome in patients **without atrial fibrillation**. Neurology. 2013 Mar 12;80(11):1009-17.
Ntaios G, Papavasileiou V, Makaritsis K, et al. **Real-World** Setting Comparison of Nonvitamin-K Antagonist **Oral Anticoagulants Versus Vitamin-K Antagonists** for Stroke Prevention in **Atrial Fibrillation**: A Systematic Review and Meta-Analysis. Stroke. 2017 Sep;48(9):2494-2503.
Nuotio I, Hartikainen JE, Grönberg T, et al. **Time to cardioversion** for acute atrial fibrillation and **thromboembolic complications**. JAMA. 2014 Aug 13;312(6):647-9.
O'Brien EC, Kim S, et al. Effect of the **2014 Atrial Fibrillation Guideline Revisions** on the Proportion of Patients Recommended for Oral Anticoagulation. JAMA Intern Med. 2015 Mar 2.
O`Brien EC, Simon DN, Thomas LE, et al. The **ORBIT bleeding score**: a simple bedside score to assess bleeding risk in atrial fibrillation. Eur Heart J. 2015 Sep 29.
O`Donoghue ML, Ruff CT, Giugliano RP, et al. **Edoxaban vs. warfarin** in vitamin K antagonist experienced and naive patients with atrial fibrillation. Eur Heart J. 2015 Feb 16.
O'Donoghue ML, Ruff CT, Giugliano RP, et al. **Edoxaban vs. warfarin in vitamin K antagonist experienced and naive** patients with atrial fibrillation†. Eur Heart J. 2015 Feb 16.
O'Neal WT, Efird JT, Dawood FZ, et al. **Coronary Artery Calcium** and Risk of Atrial Fibrillation (from the Multi-Ethnic Study of Atherosclerosis). Am J Cardiol. 2014 Sep 16.
O'Neal WT, Lakoski SG, Qureshi W, et al. Relation Between **Cancer** and Atrial Fibrillation (from the REasons for Geographic And Racial Differences in Stroke Study). Am J Cardiol. 2015 Jan 31.
O'Neal WT, et al. Effect of **Falls on Frequency of Atrial Fibrillation** and Mortality Risk (from the REasons for Geographic And Racial Differences in Stroke Study). Am J Cardiol. 2015 Oct 15;116(8):1213-8.
O'Neal WT, Efird JT, Qureshi WT, et al. **Coronary artery calcium progression** and atrial fibrillation: The Multi-Ethnic Study of Atherosclerosis. *Circ Cardiovasc Imaging* 2015; 8:e003786.
O'Neal WT, Sandesara P, et al. **Gender Differences** in the Risk of Adverse Outcomes in Patients with Atrial Fibrillation and Heart Failure with Preserved Ejection Fraction. Am J Cardio. 2017.
O'Neal WT, Sandesara PB, Kelli HM, et al. **Urban-rural differences in mortality** for atrial fibrillation hospitalizations in the United States. Heart Rhythm. 2017 Dec 1.
O'Neal WT, Claxton JS, et al. **Provider Specialty,Anticoagulation, and Stroke Risk** in Patients With Atrial Fibrillation and Cancer. J Am Coll Cardiol. 2018 Oct 16;72(16):1913-1922
Odutayo A, Wong CX, Hsiao AJ, et al. **Atrial fibrillation and risks of cardiovascular disease, renal disease, and death**: systematic review and meta-analysis. BMJ. 2016 Sep 6;354:i4482
Oesterle A, Weber B, Tung R, et al. **Preventing Postoperative Atrial Fibrillation After Noncardiac Surgery**: A Meta-analysis. Am J Med. 2018 Feb 21.
Ofek F, Bar Chaim S, et al. **International Normalized Ratio Is Significantly Elevated With Rivaroxaban and Apixaban** DrugTherapies: A Retrospective Study. Clin Ther. 2017 May 2
Ofman P, Petrone AB, Peralta A, et al. **Aspirin use** and risk of atrial fibrillation in the physicians' health study. J Am Heart Assoc. 2014 Jun 30;3(4).
Okin PM, Hille DA, Larstorp AC, et al. Effect of **Lower On-Treatment Systolic Blood Pressure** on the Risk of Atrial Fibrillation in Hypertensive Patients. Hypertension. 2015 Aug;66(2):368-73.
Oldgren J, Healey JS, Ezekowitz M, et al. **Variations in Cause and Management** of Atrial Fibrillation in a Prospective Registry of 15 400 Emergency Department Patients in 46 Countries: The RE-LY Atrial Fibrillation Registry. Circulation. 2014 Apr 15;129(15):1568-76.
O'Leary JG et al. **Coagulation in cirrhosis.** Gastroenterology 2019 Apr 12.
Olesen JB, Lip GYH, Lindhardsen J, et al. Risks of thromboembolism and bleeding with thromboprophylaxis in patients with **atrial fibrillation**: A net clinical benefit analysis using a 'real world' nationwide cohort study. Thromb Haemost 2011; 106: 739-749. (**not ASA**)
Oleson BJ et al. **Validation** of **risk stratification schemes** for predicting stroke and thromboembolism in patients with atrial fibrillation: nationwide cohort study. BMJ 2011;342:d124. **CHA2DS2-VASc performed better than CHADS2** in predicting patients at high risk, and those categorised as low risk by CHA2DS2-VASc were truly at low risk for thromboembolism.
Olesen JB, Fauchier L, Lane DA, et al. **Risk factors for stroke and thromboembolism in relation to age** among patients with atrial fibrillation: the Loire Valley Atrial Fibrillation Project. Chest. 2012 Jan;141(1):147-53.
Ogilvie IM, Weiner SA, Cowell W, Lip GY. Characterization of the proportion of **untreated** and antiplatelet therapy treated patients with atrial fibrillation. Am J Cardiol 2011;108:151–161.
Ogilvie IM, Newton N, Welner SA, Cowell W, Lip GY. **Underuse** of oral anticoagulants in atrial fibrillation: a systematic review. Am J Med 2010;123:638 – 645.
Okubo K, Kuwahara T, Takagi K, et al. Relation between **dabigatran concentration**, as assessed using the direct thrombin inhibitor assay, and activated clotting time/activated partial thromboplastin time in patients with atrial fibrillation. Am J Cardiol. 2015 Jun 15
Oldgren J, Alings M, Darius H, et al. Risks for stroke, bleeding, and death in patients with atrial fibrillation receiving **dabigatran or warfarin** in relation to the **CHADS2** score: a subgroup analysis of the **RE-LY** trial. Ann Intern Med. 2011;155:660-7.
Oldgren J, Hijazi Z, Lindbäck Jet al. **Performance and Validation of a Novel Biomarker**-Based Stroke Risk Score for Atrial Fibrillation. Circulation. 2016 Nov 29;134(22):1697-1707
Olesen JB, Torp-Pedersen C, Hansen ML, and Lip GYH. The value of the **CHA2DS2-VASc score** for refining stroke risk stratification in patients with atrial fibrillation with a CHADS2 score 0-1: A nationwide cohort study. Thromb Haemost 2012.
Olesen JB, Lip GYH, Kamper AL, et al. Stroke and bleeding in atrial fibrillation with **chronic kidney disease**. N Engl J Med 2012; 367:625-635.
Opolski G, Torbicki A, Kosior DA, et al. for the Investigators of the Polish HOT CAFÉ Trial. Rate control vs rhythm control in patients with nonvalvular persistent atrial fibrillation: the results of the Polish How to Treat Chronic Atrial Fibrillation (**HOT CAFE**) study. *Chest.* 2004;126:476–486.
Ording AG, Horvath-Puho E, Prandoni P, et al. Usefulness of **CHA2DS2-VASc Score to Predict Stroke Risk** Independent of Atrial Fibrillation. Am J Cardiol. 2019 Jul 15.
Orvin K, et al. Usefulness of the **CHA2DS2-VASC Score to Predict Adverse Outcomes** in Patients Having **Percutaneous Coronary Intervention**. Am J Cardiol. 2016 May 1;117(9):1433-8.
Orvin K, Levi A, Landes U, et al. Usefulness of the **CHA(2)DS(2)-VASc Score** to Predict Outcome in Patients Who Underwent **Transcatheter Aortic Valve Implantation**. Am J Cardiol. 2018 Jan 15;121(2):241-248
Osmanagic A, Moller S, et al. Effect of **Early Direct Current Cardioversion** on the Recurrence of Atrial Fibrillation in Patients With Persistent Atrial Fibrillation. Am J Cardiol. 2015 Apr 18.
Otite FO, Khandelwal P, Chaturvedi S, et al. **Increasing atrial fibrillation prevalence in acute ischemic stroke and TIA**. Neurology. 2016 Nov 8;87(19):2034-2042.
Ouyang AJ, Lv YN, Zhong HL, et al. Meta-analysis of **digoxin** use and risk of **mortality** in patients with atrial fibrillation. Am J Cardiol. 2015 Apr 1;115(7):901-6.
Packer DL, Kowal RC, Wheelan KR, et al. **STOP AF Cryoablation** Investigators. Cryoballoon Ablation of Pulmonary Veins for Paroxysmal Atrial Fibrillation: First Results of the North American Arctic Front (STOP AF) Pivotal Trial. J Am Coll Cardiol. 2013 Apr 23;61(16):1713-23.
Packer DL, Mark DB, Robb RA, et al; CABANA Investigators. Effect of **catheter ablation vs antiarrhythmic drug therapy** on mortality, stroke, bleeding, and cardiac arrest among patients with

atrial fibrillation: the CABANA randomized clinical trial [Mar 15, 2019]. JAMA. doi:10.1001/jama.2019.0693
Padfield GP, Steinberg C, Swampillai J, et al. **Progression of paroxysmal to persistent atrial fibrillation**: Canadian registry of atrial fibrillation 10-year follow up. *Heart Rhythm* 2017.
Parasrampuria DA, Mendell J, Shi M, et al. **Edoxaban** drug-**drug interactions** with ketoconazole, erythromycin, and cyclosporine. Br J Clin Pharmacol. 2016 Aug 16.
Park CS, Choi EK, Kim HM, et al. Increased risk of major **bleeding** in **underweight patients** with atrial fibrillation who were prescribed novel oral anticoagulants. Heart Rhythm. 2016 Dec 29.
Parikh MG et al. Usefulness of **Transesophageal Echocardiography** to Confirm Clinical Utility of **CHA(2)DS(2)-VASc and CHADS(2) Scores** in Atrial Flutter. Am J Cardiol. 2011 Nov 29.
Parkash R, Wells GA, Sapp JL, et al. Effect of **aggressive blood pressure control** on the recurrence of atrial fibrillation **after catheter ablation**: a randomized open label clinical trial (**SMAC-AF** [Substrate Modification With Aggressive Blood Pressure Control]). Circulation. 2017;135:1788–1798.
Parry-Jones AR, Di Napoli M, Goldstein JN, et al. **Reversal strategies for vitamin K antagonists in acute intracerebral hemorrhage**. Ann Neurol. 2015 Jul;78(1):54-62.
Parsons C, Cha S, Shen WK, et al. Usefulness of the **Addition of Renal Function to the CHA2DS2-VASc Score as a Predictor of Thromboembolism** and Mortality in Patients **Without Atrial Fibrillation**. Am J Cardiol. 2018 May 15.
Pastori D, Mezzaroma I, Pignatelli P, et al. **Atrial fibrillation and Human Immunodeficiency Virus type-1 infection**: a systematic review. Implications for anticoagulant and antiarrhythmic therapy. Br J Clin Pharmacol. 2018 Dec 21.
Patel AD, Tan MK, Angaran P, et al. Risk Stratification and Stroke Prevention **Therapy Care Gaps** in Canadian Atrial Fibrillation Patients (from the Co-ordinated National Network to Engage Physicians in the Care and Treatment of Patients With Atrial Fibrillation Chart Audit). Am J Cardiol. 2015 Mar 1;115(5):641-6.
Patel MR, Hellkamp AS, Fox KA; ROCKET AF Executive Committee and Investigators. **Point-of-Care Warfarin Monitoring in the ROCKET AF** Trial. N Engl J Med. 2016 Feb 3.
Patel N, Chung EH, Mounsey JP, et al. Effectiveness of **atrial fibrillation monitor characteristics** to predict severity of symptoms of atrial fibrillation. Am J Cardiol. 2014 May15;113(10):1674-8.
Patel NJ, Deshmukh A, Pant S, et al. Contemporary **Trends of Hospitalization** for Atrial Fibrillation in the United States, 2000 through 2010: Implications for Healthcare Planning. Circulation. 2014;129:XX-XXX.
Patel NJ, Deshmukh A, Pant S, et al. Contemporary **trends of hospitalization** for atrial fibrillation in the United States, 2000 through 2010: implications for healthcare planning. Circulation. 2014 Jun 10;129(23):2371-9.
Pathak R, Pandit A, Karmacharya P, et al. Meta-Analysis on **Risk of Bleeding With Apixaban in Patients With Renal Impairment**. Am J Cardiol. 2014 Nov 13.
Pathak RK, Middeldorp ME, Meredith M, et al. Long-Term Effect of **Goal Directed Weight Management** in an Atrial Fibrillation Cohort: A Long-term Follow-Up StudY (**LEGACY** Study). J Am Coll Cardiol. 2015 Mar 5.
Pathak RK, Elliott A, Middeldorp ME, et al. Impact of **Cardiorespiratory Fitness** on Arrhythmia Recurrence in Obese Individuals With Atrial Fibrillation: The **CARDIO-FIT** study. J Am Coll Cardiol 2015.
Pathak RK, Evans M, , et al. Cost-Effectiveness and clinical effectiveness of **The risk factor management** clinic in Atrial Fibrillation: The **CENT** study. *JACC Clin Electrophysiol* 2017.
Patrono C, Andreotti F. **Antithrombotic Therapy** for Patients with Atrial Fibrillation and Atherothrombotic Vascular Disease: Striking the Right Balance between Efficacy and Safety. Circulation. 2013 Jul 16.
Peacock WF, Tamayo S, et al. **CHA(2)DS(2)-VASc Scores** and Major **Bleeding** in Patients With Nonvalvular Atrial Fibrillation Who Are Receiving **Rivaroxaban**. Ann Emerg Med. 2016 Nov 29.
Peguero JG, Issa O, Podesta C, et al. Usefulness of the **CHA(2)DS(2)VASc Score to Predict Postoperative Stroke** in Patients Having **Cardiac Surgery** Independent of Atrial Fibrillation. Am J Cardiol. 2015 Jan 6.
Pena JM, Macfadyen J, Glynn RJ, et al. High-sensitivity C-reactive protein, **statin** therapy, and risks of atrial fibrillation: an exploratory analysis of the JUPITER trial. Eur Heart J. 2012 Feb;33(4):531-7.
Peng H, Sun Z, Chen H, et al. Usefulness of the **CHA2DS2-VASc Score to Predict Adverse Outcomes** in Acute Coronary Syndrome Patients Without Atrial Fibrillation Undergoing Percutaneous Coronary Intervention. Am J Cardiol. 2019 May 29.
Pennlert J, Overholser R, Asplund K, et al. **Optimal Timing of Anticoagulant Treatment After Intracerebral Hemorrhage** in Patients With Atrial Fibrillation. Stroke. 2017 Feb;48(2):314-320.
Perez MV, Wang PJ, Larson JC, et al. Effects of **postmenopausal hormone therapy** on incident atrial fibrillation: The Women's Health Initiative randomized controlled trials. Circ Arrhythm Electrophysiol 2012.
Perino AC, Fan J, Schmitt SK, et al. **Treating Specialty and Outcomes** in Newly Diagnosed Atrial Fibrillation: From the **TREAT-AF** Study. J Am Coll Cardiol. 2017 Jul 4;70(1):78-86
Personett HA, Smoot DL, Stollings JL, et al. Intravenous **metoprolol versus diltiazem** for rate control in noncardiac, nonthoracic postoperative atrial fibrillation. Ann Pharmacother. 2014 Mar;48(3):314-9.
Peterson ED, Ashton V, Chen YW, et al. Comparative effectiveness, safety, and costs of **rivaroxaban and warfarin among morbidly obese patients** with atrial fibrillation. Am Heart J. 2019 Jun;212:113-119.
Piccini JP, Sinner MF, Greiner MA, et al. Outcomes of **medicare** beneficiaries undergoing **catheter ablation** for atrial fibrillation. Circulation.2012 Oct 30;126(18):2200-7.
Piccini JP, Stevens SR, Chang Y, et al. **Renal Dysfunction** as a Predictor of Stroke and Systemic Embolism in Patients with Nonvalvular Atrial Fibrillation: Validation of the **R2CHADS2 Index** in the ROCKET AF and ATRIA Study Cohorts. Circulation. 2012 Dec 3.
Piccini, JP, Al-Khatib, SM., Wojdyla, DM., et al. Comparison of Safety of **Sotalol versus Amiodarone** in Patients with Atrial Fibrillation and Coronary Artery Disease. The American Journal of Cardiology. 2014.
Piccini JP, Hellkamp AS, Washam JB, et al. **Polypharmacy** and the Efficacy and Safety of **Rivaroxaban versus Warfarin** in the Prevention of Stroke in Patients With Nonvalvular Atrial Fibrillation. (**Rocket-AF**) Circulation. 2015 Dec 16.
Piccini JP, Simon DN, Steinberg BA, et al. Differences in Clinical and Functional Outcomes of Atrial Fibrillation in **Women and Men**: Two-Year Results From the ORBIT-AF Registry. JAMA Cardiol. 2016 Jun 1;1(3):282-91.
Piers RJ, Nishtala A, Preis SR, et al. Association between atrial fibrillation and **volumetric MRI brain measures**: Framingham Offspring Study. Heart Rhythm 2016.
Pison L, La Meir M, van Opstal J, et al. **Hybrid thoracopic surgical and transvenous catheter ablation** of atrial fibrillation. J Am Coll Cardiol 2012; 60:54-61.
Pisters R et al. A Novel User Friendly Score (**HAS-BLED**) to Assess 1-Year Risk of Major Bleeding in Patients With Atrial Fibrillation: The Euro Heart Survey. Chest 2010;138;1093-1100.
Plitt DC, Chung EH, Mounsey JP, et al. Relation of Atrial Fibrillation Burden and **N-Terminal Pro-Brain Natriuretic Peptide**. Am J Cardiol. 2013 Feb 14.
Plitt A, McGuire DK, Giugliano RP. Atrial Fibrillation, **Type 2 Diabetes, and Non-Vitamin K Antagonist Oral Anticoagulants**: A Review. JAMA Cardiol. 2017 Jan 25.
Pluymaekers NAHA, Dudink EAMP, Luermans JGLM, et al. **Early or delayed cardioversion** in recent-onset atrial fibrillation. (RACE 7 ACWAS) N Engl J Med. DOI:0.1056/NEJMoa1900353.
Pluymaekers NAHA, Dudink EAMP, Luermans JGLM, et al. Early or Delayed **Cardioversion in Recent-Onset Atrial Fibrillation**. N Engl J Med. 2019 Mar 18
Poçi D, Hartford M, Karlsson T, et al. Effect of **New Versus Known Versus No Atrial Fibrillation** on 30-Day and 10-Year Mortality in Patients With **Acute Coronary Syndrome**. Am J Cardiol. 2012 Apr 20. (especially AF with ACS)
Poçi D, Hartford M, Karlsson T, et al. Role of the **CHADS2 score in acute coronary syndromes** - risk of subsequent death or stroke in patients with and without atrial fibrillation. Chest. 2011 Oct 20.
Podolecki T, Lenarczyk R, et al. Effect of **Type of Atrial Fibrillation** on Prognosis in **Acute Myocardial Infarction** Treated Invasively. Am J Cardiol. 2012 Mar 20.
Podolecki T, Lenarczyk R, Kowalczyk J, et al. Significance of Atrial Fibrillation Complicating ST-Segment Elevation **Myocardial Infarction**. Am J Cardiol. 2017 Aug 15;120(4):517-521.
Pogge EK, Haber SL. Elevated international normalized ratio associated with use of **dronedarone and warfarin**. Ann Pharmacother. 2011 Sep;45(9):e46.
Pokorney, Hammill, Qualls, et al. Cost Analysis of **Peri-procedural Imaging** in Patients Undergoing **Catheter Ablation** for Atrial Fibrillation. The American Journal of Cardiology. 2014.
Pokorney SD, Holmes DN, Thomas L, et al; (ORBIT-AF) Investigators. Association Between **Warfarin Control Metrics and Atrial Fibrillation Outcomes** in the Outcomes Registry for Better Informed Treatment of Atrial Fibrillation. JAMA Cardiol. 2019 Jul 3.
Pokorney SD, Simon DN, Thomas L, et al; Outcomes Registry for Better Informed Treatment of Atrial Fibrillation (ORBIT-AF) Investigators. **Patients' time in therapeutic range on warfarin among US patients** with atrial fibrillation: Results from **ORBIT-AF** registry. Am Heart J. 2015 Jul;170(1):141-148.e1.
Pokorney SD, Simon DN, Thomas L, et al. **Stability of International Normalized Ratios** in Patients Taking Long-term **Warfarin** Therapy. JAMA. 2016 Aug 9;316(6):661-3.
Pokorney SD, et al. Influence of **Kidney Function** Estimation Methods on Eligibility of **Edoxaban** Population Impact of the US Food and Drug Administration's Approach for its Product Labeling. Circulation ;134 :1122-1124.
Pokushalov E, Kozlov B, Romanov A, et al. Long-Term Suppression of Atrial Fibrillation by **Botulinum Toxin Injection** into Epicardial Fat Pads in Patients Undergoing Cardiac Surgery: One Year Follow Up of a Randomized Pilot Study. Circ Arrhythm Electrophysiol. 2015 Oct 20.
Poli D, Antonucci E, Pengo V, et al. Comparison of **HAS-BLED versus CHADS2 and CHA2DS2VASC** Stroke and Bleeding Scores in Patients with Atrial Fibrillation. AM J Cardiol. 2017.
Pollack CV Jr, Reilly PA, Eikelboom J, et al. **Idarucizumab for dabigatran reversal**. N Engl J Med. June 2015. DOI: 10.1056/NEJMoa1502000.
Poli D, Testa S, Antonucci E, et al. **Bleeding and Stroke Risk** in a Real-world Prospective Primary Prevention Cohort of Patients With Atrial Fibrillation. Chest. 2011 Oct;140(4):918-24.
Pollack CV Jr, Reilly PA, Eikelboom J, et al. **Idarucizumab for dabigatran reversal**. N Engl J Med. June 2015. DOI: 10.1056/NEJMoa1502000.
Pollack CV Jr. **Antidotes for Bleeding Caused by Novel Oral Anticoagulants**. Circulation. 2016 Jan 12;133(2):e18-9.
Pollack CV Jr, Reilly PA, van Ryn J, et al. **Idarucizumab for Dabigatran Reversal** - Full Cohort Analysis. N Engl J Med. 2017 Jul 11.
Polovina M, Hindricks G, Maggioni A, et al. Association of **metabolic syndrome with non-thromboembolic** adverse **cardiac outcomes** in patients with atrial fibrillation. Eur Heart J. 2018 Aug 7.
Potpara TS , Vasiljevic ZM , Vujisic-Tesic BD , et al . **Mitral annular calcification** predicts cardiovascular morbidity and mortality in middle-aged patients with atrial fibrillation: the Belgrade Atrial Fibrillation Study. Chest . 2011 ; 140 (4): 902 - 910 .
Potpara TS, Stankovic GR, Beleslin BD, et al. A 12-year follow-up study of patients with newly-diagnosed **lone atrial fibrillation**: implications of arrhythmia progression on prognosis: The Belgrade Atrial Fibrillation Study. Chest. 2012;141(2):339-347.
Pottie K, Premji K, Cheskey SL. **Critical elevation** of **international normalized ratio** in an elderly woman using a **natural health product**. Can Fam Physician. 2017 Jul;63(7):536-537.
Poulsen BK, Grove EL, Husted SE. New oral anticoagulants: a review of the literature with particular emphasis on patients with **impaired renal function**. Drugs. 2012 Sep 10;72(13):1739-53.

Price J, Hynes M, Labinaz M et al. **Mechanical valve thrombosis with dabigatran**. J Am Coll Cardiol 2012.

Price MJ, Valderrábano M. **Left atrial appendage closure** to prevent stroke in patients with atrial fibrillation. Circulation. 2014 Jul 8;130(2):202-12.

Price MJ, Reddy VY, Valderrábano M, et al. **Bleeding** outcomes after **left atrial appendage closure** compared with long-term **warfarin**: A pooled, patient level analysis of the **WATCHMAN** randomized trial experience. *JACC Cardiovasc Interv* 2015.

Pritchett RV, Bem D, Turner GM, et al. Improving the **Prescription of Oral Anticoagulants** in Atrial Fibrillation: A Systematic Review. Thromb Haemost. 2019 Feb;119(2):294-307.

Proietti R, AlTurki A, Di Biase L, et al. **Anticoagulation after catheter ablation of atrial fibrillation**: An unnecessary evil? A systematic review and meta-analysis. J Cardiovasc Electrophysiol. 2019 Apr;30(4):468-478.

Proietti M, Lane DA, Lip GY. Relation of **Nonvalvular Atrial Fibrillation to Body Mass Index** (from the **SPORTIF** Trials). Am J Cardiol. 2016 Jul 1;118(1):72-8.

Providência R, Marijon E, Boveda S, et al. Meta-analysis of the **Influence of Chronic Kidney Disease on the Risk of Thromboembolism** Among Patients with Non-valvular Atrial Fibrillation. The American Journal of Cardiology (2014).

Prystowsky EN, Padanilam BJ, Fogel RI. **Treatment of Atrial Fibrillation**. JAMA. 2015 Jul 21;314(3):278-88.

Ptaszek LM, White B, Lubitz SA et al. Effect of a **Multidisciplinary Approach for the Management of Patients With Atrial Fibrillation** in the **Emergency Department** on Hospital Admission Rate and Length of Stay. Am J Cardiol. 2016 Jul 1;118(1):64-71.

Qamar A, Bhatt DL. Stroke Prevention in Atrial Fibrillation in Patients With **Chronic Kidney Disease**. Circulation. 2016 Apr 12

Quinn GR, Singer DE, et al. Effect of **selective serotonin reuptake inhibitors** on bleeding risk in patients with atrial fibrillation taking warfarin. Am J Cardiol. 2014 Aug 15;114(4):583-6.

Quinn GR, Severdija ON, Chang Y, et al. **Wide Variation in Reported Rates of Stroke Across Cohorts of Patients with Atrial Fibrillation**. Circulation. 2016 Oct 31.

Quon MJ, Behlouli H, Pilote L. **Anticoagulant Use and Risk of Ischemic Stroke and Bleeding in Patients With Secondary Atrial Fibrillation** Associated With Acute Coronary Syndromes, Acute Pulmonary Disease, or Sepsis. J Am Coll Cardiol EP. 2017.

Qureshi W, Mittal C, Patsias I, et al. **Restarting Anticoagulation** and Outcomes After Major Gastrointestinal **Bleeding** in Atrial Fibrillation. Am J Cardiol. 2013 Nov 23

Qureshi WT, O'Neal WT, Khodneva Y, et al. Association Between **Opioid Use** and Atrial Fibrillation: The Reasons for Geographic and Racial Differences in Stroke (REGARDS) Study. JAMA Intern Med. 2015 Apr 27.

Qureshi WT, Alirhayim Z, et al. **Cardiorespiratory Fitness** and Risk of Incident Atrial Fibrillation: Results from the Henry Ford ExercIse Tesing (FIT) Project. Circulation. 2015 Apr 22.

Qureshi WT, Nasir UB, Alqalyoobi S, et al. Meta-Analysis of **Continuous Positive Airway Pressure** as a Therapy of Atrial Fibrillation in Obstructive Sleep Apnea. Am J Cardiol. 2015 Sep 12.

Raccah BH, Perlman A, Danenberg HD, et al. Major **Bleeding and Hemorrhagic Stroke with Direct Oral Anticoagulants** in Patients with **Renal Failure**: Systematic Review and Meta-Analysis of Randomized Trials. Chest. 2016 Jan 18.

Radecki RP. Dabigatran--Uncharted Waters and Potential Harms. Ann Intern Med. 2012 May 28.

Raffel KE, Goldschlager N. Abnormal Electrocardiogram in a Woman With **Atrial Fibrillation** and Recent Care Transition. (digoxin toxicity) JAMA Intern Med. 2017 Feb 13.

Rahimi Kazem, Emberson Jonathan, McGale Paul, et al., PWM is acting on behalf of the PROSPER Executive. Effect of **statins** on atrial fibrillation: collaborative meta-analysis of published and unpublished evidence from randomised controlled trials. BMJ 342:doi:10.1136/bmj.d1250

Rao MP, Halvorsen S, Wojdyla D, et al; **Apixaban** for Reduction in Stroke and Other Thromboembolic Events in Atrial Fibrillation (**ARISTOTLE**) Steering Committee and Investigators. Blood Pressure Control and Risk of Stroke or Systemic Embolism in Patients With Atrial Fibrillation: Results From the Apixaban for Reduction in Stroke and Other Thromboembolic Events in Atrial Fibrillation (ARISTOTLE) Trial. J Am Heart Assoc. 2015 Dec 1;4(12).

Raposeiras Roubín S, Abellas-Sequeiros RA, et al. **Relation of Contrast Induced Nephropathy** to New Onset Atrial Fibrillation in **Acute Coronary Syndrome**. Am J Cardiol. 2014 Dec 18.

Raschi E, Poluzzi E, Koci A, Salvo F, et al. **Liver injury with novel oral anticoagulants**: assessing post-marketing reports in the US Food and Drug Administration Adverse Event Reporting System. Br J Clin Pharmacol. 2015 Feb 16.

Rasmussen LH, Larsen TB, Graungaard T, et al. **Primary and secondary prevention** with **new oral anticoagulant** drugs for stroke prevention in atrial fibrillation: indirect comparison analysis. BMJ. 2012 Nov 5;345:e7097.

Rathi VK, Krumholz HM, Ross JS. Commentary: **Diagnostic devices** in clinical trials have high stakes for patient care. BMJ. 2016 Sep 28;354:i5197

Raval AN, Cigarroa JE, Chung MK, et al. Management of Patients on **Non-Vitamin K Antagonist Oral Anticoagulants** in the Acute Care and **Periprocedural** Setting: A Scientific Statement From the American Heart Association. Circulation. 2017 Feb 6.

Razouki Z, Ozonoff A, Zhao S, et al. Improving quality measurement for anticoagulation: adding **international normalized ratio variability** to percent time in therapeutic range. Circ Cardiovasc Qual Outcomes. 2014;7:664-669.

Reddy VY, Doshi SK, Sievert H, et al; PROTECT AF Investigators. **Percutaneous Left Atrial Appendage Closure** for Stroke Prophylaxis in Patients With Atrial Fibrillation: 2.3-Year Follow-up of the PROTECT AF (Watchman Left Atrial Appendage System for Embolic Protection in Patients With Atrial Fibrillation) Trial. Circulation. 2013 Feb 12;127(6):720-9.

Reddy VY, Sievert H, Halperin J, et al; for the **PROTECT AF** Steering Committee and Investigators. Percutaneous left atrial **appendage closure vs warfarin** for atrial fibrillation: a randomized clinical trial. JAMA. doi:10.1001/jama.2014.15192.

Reddy YM, Gunda S, Vallakati A, et al. Impact of **Tricuspid Regurgitation** on the Success of **Atrioventricular Node Ablation** for Rate Control in Patients With Atrial Fibrillation: The Node Blast Study. Am J Cardiol. 2015 Jun 24.

Reddy VY, Dukkipati SR, Neuzil P, et al. A Randomized Controlled Trial of the Safety and Effectiveness of a **Contact Force Sensing Irrigated Catheter for Ablation** of Paroxysmal Atrial Fibrillation: Results of the **TOCCAST**AR Study. Circulation. 2015 Aug 10.

Reddy VY, Gibson DN, Kar S, et al. Post-FDA approval US experience with **left atrial appendage closure** for stroke prevention in atrial fibrillation. *J Am Coll Cardiol* 2016.

Reddy VY, Doshi SK, Kar S, et al.**5-Year Outcomes After Left Atrial Appendage Closure**: From the **PREVAIL** and **PROTECT** Trials. J Am CollCardiol. 2017 Oct 26.

Reed JL, Birnie DH, Pipe AL. **Exercise training** in patients with paroxysmal, persistent or permanent atrial fibrillation. CMAJ. 2014 Oct 7;186(14):E558.

Reiffel JA. **Time in the Therapeutic Range** for Patients Taking Warfarin in Clinical Trials: Useful, but Also Misleading, Misused, & Overinterpreted. Circulation. 2017 Apr 18;135(16):1475-1477.

Reiffel JA, Verma A, Kowey PR, et al; **REVEAL AF** Investigators. Incidence of Previously Undiagnosed Atrial Fibrillation Using **Insertable Cardiac Monitors** in a High-Risk Population: The REVEAL AF Study. JAMA Cardiol. 2017 Aug 26.

Reilly PA, Lehr T, Haertter S, et al. The effect of **dabigatran plasma concentrations** and patient characteristics on the frequency of ischemic **stroke and major bleeding** in atrial fibrillation patients. J Am Coll Cardiol 2014; 63:321-328.

Renda G, Ricci F, et al. **Non-Vitamin K Antagonist Oral Anticoagulants** in Patients With Atrial Fibrillation and Valvular Heart Disease. J Am Coll Cardiol. 2017 Mar 21;69(11):1363-1371.

Rene AG, Généreux P, Ezekowitz M, et al. Impact of Atrial Fibrillation in Patients With **ST-Elevation Myocardial Infarction Treated With Percutaneous Coronary Intervention** (from the **HORIZONS-AMI** [Harmonizing Outcomes With Revascularization and Stents in Acute Myocardial Infarction] Trial). Am J Cardiol. 2013 Oct 3.

Richter S, Di Biase L, Hindricks G. Atrial fibrillation **ablation in heart failure**. Eur Heart J. 2019 Feb 21;40(8):663-671.

Riccio PM, Klein FR, Pagani Cassará F, et al. Newly diagnosed atrial fibrillation linked to **wake-up stroke and TIA**: Hypothetical implications. Neurology. 2013 May 14;80(20):1834-40.

Rienstra M, Sun JX, Magnani JW, et al. **White Blood Cell Count** and Risk of Incident Atrial Fibrillation (From the Framingham Heart Study). Am J Cardiol. 2011 Nov 17.

Rienstra M, McManus DD, Benjamin EJ. **Novel risk factors** for atrial fibrillation: useful for risk prediction and clinical decision making? Circulation. 2012 May 22;125(20):e941-6.

Rienstra M, Lubitz SA, Mahida S, et al. **Symptoms and functional status** of patients with atrial fibrillation: state of the art and future research opportunities. Circulation. 2012 Jun 12;125(23):2933-43.

Rienstra M, Damman K, Mulder BA, et al. **Beta-blockers and outcome in heart failure and atrial fibrillation**. A meta-analysis. JACC:Heart Fail 2013; 1:21-28.

Rienstra M, et al. **Targeted therapy** of underlying conditions improves sinus rhythm maintenance in patients with persistent atrial fibrillation: results of the RACE 3 trial. Eur Heart J. 2018 Feb 1.

Rillig A, Lin T, Plesman J, et al. **Apixaban, Rivaroxaban, and Dabigatran** in Patients Undergoing Atrial Fibrillation **Ablation**. J Cardiovasc Electrophysiol. 2016 Feb;27(2):147-53.

Rivera-Caravaca JM, Marín F, et al. Usefulness of the **2MACE** Score to Predicts Adverse Cardiovascular Events in Patients With Atrial Fibrillation. Am J Cardiol. 2017 Dec 15;120(12):2176-2181

Rivera-Caravaca JM, Roldán V, et al. Reduced Time in Therapeutic Range and Higher Mortality in Atrial Fibrillation Patients Taking **Acenocoumarol**. Clin Ther. 2017 Dec 20.

Rodger MA, Scarvelis D, et al. **Long-term risk of venous thrombosis after stopping anticoagulants** for a first unprovoked event: A multi-national cohort. Thromb Res. 2016 Jul;143:152-8.

Rodríguez-Yáñez M, Arias-Rivas S, Santamaría-Cadavid M, et al. **High pro-BNP** levels predict the occurrence of atrial fibrillation after cryptogenic stroke. Neurology. 2013 Jul 30;81(5):444-7.

Roldán V, Marín F, Fernández H, et al. **Renal Impairment** in a "Real-Life" Cohort of Anticoagulated Patients With Atrial Fibrillation (Implications for Thromboembolism and Bleeding). Am J Cardiol. 2013 Jan 18.

Roldan V, Marin F, Fernandez H, et al. Predictive value of the **HAS-BLED** and ATRIA bleeding scores for the risk of serious bleeding in a ``real-world`` population with atrial fibrillation receiving anticoagulant therapy. Chest. 2013 Jan;143(1):179-84.

Roldan V, Marin F, Manzano-Fernandez S, et al. The **HAS-BLED** score has better prediction accuracy for major bleeding than CHADS2 or CHA2DS2-VASc scores in anticoagulated patients with atrial fibrillation. J Am Coll Cardiol. 2013 Dec 10;62(23):2199-204.

Roldan V, Vilchez JA, Manzano-Fernandez S, et al. Usefulness of **N-terminal pro-B-type natriuretic Peptide** levels for stroke risk prediction in anticoagulated patients with atrial fibrillation. Stroke. 2014 Mar;45(3):696-701.

Roldan V, Cancio S, Galvez J, et al. The **SAMe-TTR** Score Predicts Poor Anticoagulation Control in AF Patients: A Prospective ``Real-World`` Inception Cohort Study. Am J Med. 2015 Jun 15.

Roldán V, Cancio S, et al. The **SAMe-TT(2)R(2) Score** Predicts Poor Anticoagulation Control in AF Patients: A Prospective "Real-World" Inception Cohort Study. Am J Med. 2015 Jun 15.

Roetker NS. Chen LY, Heckbert SR, et al. Relation of **Systolic, Diastolic, and Pulse Pressures and Aortic Distensibility** with Atrial Fibrillation (From the Multi-Ethnic Study of Atherosclerosis). The American Journal of Cardiology (2014).

Rolf L, Muris AH, Damoiseaux J, et al. Paroxysmal atrial fibrillation after initiation of **fingolimod** for multiple sclerosis treatment. Neurology. 2014 Mar 18;82(11):1008-9.

Romanelli RJ, et al. **Dabigatran Versus Warfarin** for Atrial Fibrillation in **Real-World** Clinical Practice: A Systematic Review and Meta-Analysis. Circ Cardiovasc Qual Outcomes. 2016 Jan 26.

Romley JA, Gong C, et al. Association between use of **warfarin with common sulfonylureas** and serious hypoglycemic events: retrospective cohort analysis. BMJ. 2015 Dec 7;351:h6223.

Rommel J, Simpson R, Mounsey JP, et al. Effect of **Body Mass Index**, Physical Activity, Depression, and Educational Attainment on High-Sensitivity C-Reactive Protein in Patients With Atrial Fibrillation. Am J Cardiol. 2012 Nov 2.

Rosenberg MA, Manning WJ. **Diastolic dysfunction** and risk of atrial fibrillation: a mechanistic appraisal. Circulation. 2012 Nov 6;126(19):2353-62.

Rost NS, Giugliano RP, et al; With **Edoxaban** Versus Warfarin in Patients With Previous Cerebrovascular Events: Findings From **ENGAGE** AF-TIMI 48. Stroke. 2016 Aug;47(8):2075-82.

Rowin EJ, Ofranos A, Estes M, et al. Occurrence and Natural History of Clinically **Silent Episodes** of Atrial Fibrillation in Hypertrophic Cardiomyopathy. Am J Cardio. 2017.

Rowin EJ, et al. Clinical profile and consequences of atrial fibrillation **in hypertrophic cardiomyopathy**. Circulation. 2017;136:2420–2436. doi: 10.1161/CIRCULATIONAHA.117.029267.

Rowley CP, Bernard ML, Brabham WW, et al. Safety of Continuous Anticoagulation With **Dabigatran During Implantation of Cardiac Rhythm Devices**. Am J Cardiol. 2013 Jan 26.

Roy D, Talajic M, Nattel S, et al. Atrial Fibrillation and Congestive Heart Failure Investigators. (**AF CHF**) Rhythm control versus rate control for atrial fibrillation and heart failure. *N Engl J Med*. 2008;358:2667–2677.

Roy B et al. Effect of **Warfarin on Outcomes in Septuagenarian** Patients With Atrial Fibrillation. (AFFIRM) Am J Cardiol. 2011 Nov 23.

Ruff CT, Giugliano RP, Braunwald E. Comparison of the **efficacy and safety of new oral anticoagulants with warfarin** in patients with atrial fibrillation: a meta-analysis of randomised trials. Lancet 2013; DOI: 10.1016/S0140-6736(13)62343-0.

Ruff CT, Giugliano RP, et al. Management of **Bleeding** With **Non-Vitamin K Antagonist** Oral Anticoagulants in the Era of Specific Reversal Agents.Circulation. 2016 Jul 19;134(3):248-61.

Ruff CT, Giugliano RP, Braunwald E, et al. **Cardiovascular biomarker score** and clinical outcomes in patients with atrial fibrillation. *JAMA Cardiol* 2016;

Ruiz Vargas E, Sposato LA, Lee SAW, et al. **Anticoagulation Therapy for Atrial Fibrillation in Patients With Alzheimer's** Disease. Stroke. 2018 Dec;49(12):2844-2850.

Ruiz-Nodar JM, Marín F, Manzano-Fernández S, et al. An evaluation of the **CHADS2** stroke risk score in patients with atrial fibrillation who undergo **percutaneous coronary revascularization**. Chest. 2011 Jun;139(6):1402-9.

Ruiz-Nodar JM, Marín F, Roldán V, et al. Should We Recommend Oral Anticoagulation Therapy in Patients With **Atrial Fibrillation Undergoing Coronary Artery Stenting** With a High HAS-BLED Bleeding Risk Score? Circ Cardiovasc Interv. 2012 Aug 1;5(4):459-66.

Ruiz Ortiz M, Muñiz J, Raña Míguez P, et al; FANTASIIA study investigators . **Inappropriate doses** of direct oral anticoagulants in real-world clinical practice**: prevalence and associated factors**. A subanalysis of the FANTASIIA Registry. Europace. 2018 Oct 1;20(10):1577-1583.

Salehi Omran S, Chatterjee A, Chen ML, et al. National Trends in Hospitalizations for **Stroke Associated With Infective Endocarditis and Opioid Use** Between 1993 and 2015. Stroke. 2019 Jan 30:STROKEAHA118024436.

Salem J-E, Shoemaker MB, Bastarache L, et al. Association **of thyroid function genetic predictors** with atrial fibrillation: a phenome-wide association study and inverse-variance weighted average meta-analysis [online Jan 23, 2019]. JAMA Cardiol. doi:10.1001/jamacardio.2018.4615

Saliba W, Rennert G. **CHA2DS2-VASc** score is directly associated with the risk of pulmonary embolism in patients with atrial fibrillation. Am J Med. 2014 Jan;127(1):45-52.

Saliba W, Gronich N, et al. Usefulness of **CHADS** and **CHADS-VASc Scores** in the Prediction of **New-Onset Atrial Fibrillation**: A Population-Based Study. Am J Med. 2016 Mar 21.

Saliba W, Gronich N, Barnett-Griness O, et al. The role of **CHADS and CHA DS -VASc s**cores in the prediction of stroke in individuals **without atrial fibrillation**: a population-based study. J Thromb Haemost. 2016 Apr 1.

Sambola A, Mutuberría M, et al. Impact of **Triple Therapy** in Elderly Patients with Atrial Fibrillation Undergoing **Percutaneous Coronary Intervention**. PLoS One. 2016 Jan 25;11(1):e0147245.

Samuelson BT, Cuker A, Siegal DM, et al. **Laboratory Assessment** of the Anticoagulant Activity of Direct Oral Anticoagulants (**DOACs**): A Systematic Review. Chest. 2016 Sep 13.

Sandhu RK, Kurth T, Conen D, et al. Relation of **Renal Function** to Risk for Incident Atrial Fibrillation in Women. Am J Cardiol. 2011 Nov 17.

Sandhu RK, Guirguis LM, Bungard TJ, et al. Evaluating the potential for **pharmacists to prescribe oral anticoagulants** for atrial fibrillation. Can Pharm J (Ott). 2017 Nov 29;151(1):51-61.

Sanchis-Gomar F, Lucia A. Pathophysiology of atrial fibrillation in **endurance athletes**: an overview of recent findings. CMAJ. 2016 Dec 6;188(17-18):E433-E435.

Sanhoury M, Fassini G, Dello Russo A, et al. Early **Dislodgment** and **Migration** of a **Left Atrial Appendage Closure Device**. Am J Cardio. 2017.

Sanna T et al. **Cryptogenic stroke** and underlying atrial fibrillation. (**CRYSTAL AF**) N Engl J Med 2014 Jun 26; 370:2478.

Sapp JL, Wells GA, Parkash R, et al. **Ventricular tachycardia ablation versus escalation of antiarrhythmic drugs**. *New Engl J Med* 2016; (**VANISH**) DOI: 10.1056/NEJMoa1513614.

Sardar P, Chatterjee S, Chaudhari S, et al. **New oral anticoagulants** in **elderly** adults: evidence from a meta-analysis of randomized trials. J Am Geriatr Soc. 2014 May;62(5):857-64.

Sardar P, Nairooz R, Chatterjee S, et al. Meta-Analysis of Risk of Stroke or Transient Ischemic Attack With **Dabigatran** for Atrial Fibrillation **Ablation**. Am J Cardiol. 2014 Jan 15.

Sauer AJ, Kaplan R, et al. Electrocardiographic Markers of Repolarization Heterogeneity During **Dofetilide or Sotalol** Initiation for Paroxysmal Atrial Fibrillation. Am J Cardiol. 2014 Apr 1.

Savelieva I, Kakouros N, Kourliouros A, Camm AJ. **Upstream therapies** for management of **atrial fibrillation**: review of clinical evidence and implications for **European** Society of Cardiology guidelines: II, secondary prevention. Europace. 2011; 13(5):610-625.

Savino JA 3rd, Halperin JL. Should Patients With Atrial Fibrillation and 1 Stroke Risk Factor (**CHA2DS2-VASc Score 1 in Men, 2 in Women) Be Anticoagulated**? The CHA2 DS2-VASc 1 Conundrum: Decision Making at the Lower End of the Risk Spectrum. Circulation. 2016 Apr 12

Schmidt AS, Lauridsen KG, Torp P, et al. **Maximum-fixed energy shocks** for cardioverting atrial fibrillation. Eur Heart J. 2019 Aug 31.

Schmidt M et al. **Non-Steroidal anti-inflammatory drug** (NSAID) use and risk of atrial fibrillation or flutter: population based case-control study. BMJ 2011;343:d3450 doi: 10.1136/bmj.d3450

Schmidt M, Bøtker HE, Pedersen L, et al. Comparison of the Frequency of Atrial Fibrillation in **Young Obese Versus Young Nonobese** Men Undergoing Examination for Fitness for Military Service. Am J Cardiol. 2013 Dec 12

Schnabel RB, Yin X, et al. **50 year trends in atrial fibrillation prevalence, incidence, risk factors, and mortality** in the Framingham Heart Study: a cohort study. Lancet 2015; online May 8.

Schoen T, Pradhan AD, Albert CM, Conen D. **Type 2 diabetes mellitus** and risk of incident atrial fibrillation in women. J Am Coll Cardiol. 2012 Oct 9;60(15):1421-8.

Schneeweiss S, Gagne JJ, Patrick AR, et al. Comparative Efficacy and Safety of **New Oral Anticoagulants** in Patients With Atrial Fibrillation. Circ Cardiovasc Qual Outcomes. 2012 Jul 10.

Schulman S, Parpia S, Stewart C, Rudd-Scott L, Julian JA, Levine M. **Warfarin dose assessment every 4 weeks versus every 12 weeks** in patients with stable international normalized ratios. A randomized trial. Ann Intern Med. 2011;155:653-9.

Schulman S. Resumption of oral anticoagulation after warfarin-associated **intracerebral hemorrhage: no.** Stroke. 2011 Dec;42(12):3663-4.

Scott MJ, Veitch A, Thachil J. **Reintroduction of anti-thrombotic therapy after a gastrointestinal haemorrhage**: if and when? Br J Haematol. 2017 Mar 8.

Seaburg L, Hess EP, Coylewright M, et al. **Shared decision** making in atrial fibrillation: where we are and where we should be going. Circulation. 2014 Feb 11;129(6):704-10

Seccia TM, Calò LA. Is **exercise** becoming a danger for our health? The complex relationship between exercise and atrial fibrillation. Eur J Prev Cardiol. 2018 Apr;25(6):621-623.

Seet RC, Zhang Y, Wijdicks EF, et al. Relationship between chronic atrial fibrillation and **worse outcomes in stroke patients after intravenous thrombolysis**. Arch Neurol. 2011 Nov;68(11):1454-8.

Seiffge DJ, Kägi G, Michel P, et al. **Rivaroxaban plasma levels** in acute ischemic stroke and intracerebral hemorrhage. Ann Neurol. 2018 Feb 2.

Seiffge DJ, Paciaroni M, Wilson D, et al. **DOAC vs. VKA after recent ischemic stroke** in patients with atrial fibrillation. Ann Neurol. 2019 Apr 13.

Seiffge DJ, Werring DJ, Paciaroni M, et al. **Timing of anticoagulation after recent ischaemic stroke** in patients with atrial fibrillation. Lancet Neurol. 2018 Nov 8.

Selmer C, Olesen JB, et al. The spectrum of **thyroid disease** and risk of new onset atrial fibrillation: a large population cohort study. BMJ. 2012 Nov 27;345:e7895.

Sen S, Androulakis XM, Duda V, et al**. Migraine with visual aura** a risk factor for incident atrial fibrillation: A cohort study. Neurology. 2018 Nov 14.

Sengupta N et al. The risks of **thromboembolism vs. recurrent gastrointestinal bleeding** after interruption of systemic anticoagulation in hospitalized **inpatients with gastrointestinal bleeding**: A prospective study. Am J Gastroenterol 2014 Dec 16.

Sengupta N, Marshall AL, Jones BA, et al. **Rebleeding vs Thromboembolism After Hospitalization for Gastrointestinal Bleeding** in Patients on Direct Oral Anticoagulants. Clin Gastroenterol Hepatol. 2018 May 15.

Senoo K, Proietti M, Lane DA, Lip GY. Evaluation of the **HAS-BLED, ATRIA, and ORBIT Bleeding Risk Scores** in Patients with Atrial Fibrillation Taking Warfarin. Am J Med. 2015 Oct 22.

Shah R, Freeman J, Shilane D, et al. Procedural complications, rehospitalizations, and repeat procedures **after catheter ablation** for atrial fibrillation. J Am Coll Cardiol 2012; 59:143-149.

Shah M, Avgil Tsadok M, Jackevicius CA, et al. **Warfarin** Use and the Risk for Stroke and Bleeding in Patients With Atrial Fibrillation Undergoing **Dialysis**. Circulation. 2014 Jan 22.

Shah M, Avgil Tsadok M, Jackevicius CA, et al. Relation of **Digoxin Use in Atrial Fibrillation and the Risk of All-Cause Mortality** in Patients ≥65 Years of Age With Versus Without Heart Failure. Am J Cardiol. 2014 May 16.

Shah R, Hellkamp A, Lokhnygina Y, et al. Use of **concomitant aspirin** in patients with atrial fibrillation: Findings from the **ROCKET AF trial**. (rivaroxaban**)** Am Heart J. 2016 Sep;179:77-86.

Shah RR, Pillai A, Schafer P, et al. Safety and Efficacy of **Uninterrupted Apixaban Therapy Versus Warfarin** During Atrial Fibrillation Ablation. Am J Cardiol. 2017 Aug 1;120(3):404-407

Shah, SJ, Eckman MH, Aspberg S, Go AS, Singer DE. Effect of variation in published stroke rates on the net clinical benefit of anticoagulation for atrial fibrillation. Ann Intern Med. 2018.

Shantha GPS, Mentias A, Bhise V, et al. **Gender Differences** in the Trends of **Hospitalizations** for Acute Stroke Among Patients With Atrial Fibrillation in the United States: 2005 to 2014. Am J Cardiol. 2017 Nov 1;120(9):1541-1548.

Shantsila E, Shantsila A, Blann AD, Lip GY. **Left Ventricular Fibrosis** in Atrial Fibrillation. Am J Cardiol. 2013 Jan 16.

Sharma A, Einstein AJ, Vallakati A, et al. Risk of atrial fibrillation with use of oral and intravenous **bisphosphonates**.*Am J Cardiol* 2014; DOI: 10.1016/j.amjcard.2014.03.008.

Sharma M, Cornelius VR, Patel JP, et al. **Efficacy and Harms of Direct Oral Anticoagulants** in the Elderly for Stroke Prevention in Atrial Fibrillation and Secondary Prevention of Venous Thromboembolism: Systematic Review and Meta-Analysis. Circulation. 2015 May 20.

Sharma P, Scotland G, Cruickshank M, et al. The clinical effectiveness and cost-effectiveness of p**oint-of-care tests (CoaguChek system, INRatio2 PT/INR monitor and ProTime Microcoagulation system**) for the self-monitoring of the coagulation status of people receiving long-term vitamin K antagonist therapy, compared with standard UK practice: systematic review and economic evaluation. Health Technol Assess. 2015 Jun;19(48):1-172.

Shehata M, Yeow WL, Kar S. **Device interventions** for stroke prevention in atrial fibrillation. Circulation. 2014 Mar 4;129(9):e360-2.

Sherwood MW, Douketis JD, Patel MR, et al; on behalf of the ROCKET AF Investigators. Outcomes of **Temporary Interruption of Rivaroxaban Compared with Warfarin** in Patients with Nonvalvular Atrial Fibrillation: Results from ROCKET AF. Circulation. 2014 Feb 19.

Sherwood M, Nessel C, Hellkamp A, et al. **Gastrointestinal bleeding** in patients with atrial fibrillation treated with **rivaroxaban or warfarin**. *J Am Coll Cardiol* 2015; 66:2271-2281.

Shibazaki K, Kimura K, Fujii S et al. **Brain Natriuretic Peptide** Levels as a Predictor for New Atrial Fibrillation During Hospitalization in Patients With Acute Ischemic Stroke. Am J Cardiol. 2012 Feb 14.

Shih CJ, Ou SM, et al. Risks of death & stroke in patients undergoing **hemodialysis** with new-onset atrial fibrillation: competing-risk analysis of nationwide cohort. Circulation. 2016;133:265–272.

Shin JI, Secora A, Alexander GC, et al. Risks and Benefits of **Direct Oral Anticoagulants across the Spectrum of GFR** among Incident and Prevalent Patients with Atrial Fibrillation. Clin J Am Soc Nephrol. 2018 Aug 7;13(8):1144-1152.

Shoemaker MB, Muhammad R, Farrell M, et al. Relation of Morbid **Obesity and Female Gender** to Risk of Procedural Complications in Patients Undergoing

Atrial Fibrillation Ablation. Am J Cardiol. 2012 Nov 17.
Shore S, Ho PM, Lambert-Kerzner A, et al. Site-level variation in and practices associated with **dabigatran adherence**. JAMA. 2015 Apr 14;313(14):1443-50.
Shroff GR, Solid CA, Herzog CA. Temporal **Trends in Ischemic Stroke and Anticoagulation Therapy** Among Medicare Patients With Atrial Fibrillation: A 15-Year Perspective (1992-2007). Arch Intern Med. 2012 Dec 24:1-2.
Shroff GR, Stoecker R, Hart A. **Non-Vitamin K-Dependent Oral Anticoagulants for Nonvalvular Atrial Fibrillation in Patients With CKD**: Pragmatic Considerations for the Clinician. Am J Kidney Dis. 2018 May 2.
Siegal D, Yudin J, Kaatz S, et al. **Periprocedural heparin bridging** in patients receiving vitamin k antagonists: systematic review and meta-analysis of bleeding and thromboembolic rates. Circulation. 2012 Sep 25;126(13):1630-9.
Silberberg A, Tan MK, Yan AT, et al. Use of Evidence-Based Therapy for Cardiovascular Risk Factors in Canadian Outpatients With Atrial Fibrillation: From the Facilitating Review and Education to Optimize Stroke Prevention in Atrial Fibrillation (**FREEDOM AF**) and Co-ordinated National Network to Engage Physicians in the Care and Treatment of Patients With Atrial Fibrillation (**CONNECT AF**). Am J Cardiol. 2017 Aug 15;120(4):582-587.
Singh D, Huntwork M, Shetty V, et al. Prolonged **Atrial Fibrillatio**n Precipitated by New-Onset **Seizures** and **Marijuana** Abuse. Pediatrics. 2014 Jan 13
Singh SM, Nault I. Left **atrial-esophageal fistula after atrial fibrillation ablation**. CMAJ. 2013 Sep 17;185(13):1158.
Singh SM, Qiu F, et al. The Relationship Between **Cardiologist Care and Clinical Outcomes in Patients With New-Onset Atrial Fibrillation**. Can J Cardiol. 2017 Dec;33(12):1693-1700.
Sinner MF, Wang N, Fox CS, et al. Relation of Circulating **Liver Transaminase** Concentrations to Risk of New-Onset Atrial Fibrillation. Am J Cardiol. 2012 Nov 2.
Siontis KC, Zhang X, Eckard A, et al. Outcomes Associated with **Apixaban Use in End-Stage Kidney Disease Patients with Atrial Fibrillation** in the United States. Circulation. 2018 Jun 28.
Siu CW, Wong MP, Ho CM, et al. **Fatal lung toxic effects related to dronedarone** use. Arch Intern Med. 2012 Mar 26;172(6):516-7.
Singer DE, Chang Y, Fang MC, Borowsky et al. The net clinical benefit of warfarin anticoagulation in atrial fibrillation. Ann Intern Med. 2009 Sep 1;151(5):297-305.
Siontis KC, Yao X, Gersh BJ, et al. **Direct Oral Anticoagulants** in Patients With **Atrial Fibrillation and Valvular Heart Disease Other Than Significant Mitral Stenosis and Mechanical Valves**: A Meta-Analysis. Circulation. 2017 Feb 14;135(7):714-716.
Själander S, et al. Assessment of **Use vs Discontinuation of Oral Anticoagulation After Pulmonary Vein Isolation** in Patients With Atrial Fibrillation. JAMA Cardiol. 2016 Nov 23.
Skielboe AK, Marott JL, et al. **Occupational physical activity**, but not leisure-time physical activity increases the risk of atrial fibrillation: The Copenhagen City Heart Study. Eur J Prev Cardiol 2016.
Smer A, Salih M, Mahfood Haddad T, et al. Meta-analysis of Randomized Controlled Trials on Patent **Foramen Ovale Closure Versus Medical Therapy for Secondary Prevention of Cryptogenic Stroke.** Am J Cardiol. 2018 Mar 2.
Smigorowsky MJ, Norris CM, McMurtry MS, Tsuyuki RT. Measuring the effect of **nurse practitioner (NP)-led care** on health-related quality of life in adult patients with atrial fibrillation: study protocol for a randomized controlled trial. Trials. 2017 Aug 3;18(1):364.
Smith H, Battjes E, Yan S, et al. Chronic **Digoxin Toxicity Precipitated by Dronedarone**. Ann Pharmacother. 2014 Mar 31;48(7):923-927.
Sohara H, Ohe T, et al. **HotBalloon Ablation** of the Pulmonary Veins for Paroxysmal AF: A Multicenter Randomized Trial in Japan. J Am Coll Cardiol. 2016 Dec 27;68(25):2747-2757.
Soliman EZ, Safford MM, Muntner P, et al. Atrial Fibrillation and the **Risk of Myocardial Infarction**. JAMA Intern Med. 2013 Nov 4.
Soliman EZ, Lopez F, O'Neal WT, et al. Atrial fibrillation and **risk of ST-segment-elevation** versus non-ST-segment-elevation **myocardial infarction**. The atherosclerosis risk in communities (ARIC) study. *Circulation* 2015; DOI:10.1161/CIRCULATIONAHA.114.014145.
Soliman EZ, Zhang ZM, Judd S, et al. Comparison of Risk of Atrial Fibrillation Among **Employed Versus Unemployed** (from the REasons for Geographic and Racial Differences in Stroke Study). Am J Cardiol. 2017 Oct 15;120(8):1298-1301.
Song TJ, Kim J, Song D, et al. Association of **cerebral microbleeds** with mortality in stroke patients having atrial fibrillation. Neurology. 2014 Oct 7;83(15):1308-15.
Song Y, et al. Relative Bioavailability of **Apixaban** Solution or Crushed Tablet Formulations Administered by Mouth or Nasogastric Tube in Healthy Subjects. Clin Ther. 2015 Aug 1;37(8):1703-12.
Song Y, Chang M, Suzuki A, et al. Evaluation of **Crushed Tablet for Oral Administration and the Effect of Food on Apixaban** Pharmacokinetics in Healthy Adults. Clin Ther. 2016 Jun 9.
Sørensen R, Gislason G, Torp-Pedersen C, et al. **Dabigatran use in Danish** atrial fibrillation patients in 2011: a nationwide study. BMJ Open. 2013 May 3;3(5).
Sotomi Y, Inoue K, Ito N, et al. Cause of **Very Late Recurrence** of Atrial Fibrillation or Flutter After Catheter Ablation for Atrial Fibrillation. Am J Cardiol. 2012 Dec 1.
Sousa-Uva M, Head SJ, Milojevic M, et al; Document Reviewers. **2017 EACTS Guidelines on perioperative medication in adult cardiac surgery**. Eur J Cardiothorac Surg. 2017 Oct 6.
Spiller HA, Mowry JB, Aleguas A, et al. An observational study of the **factor XA inhibitors rivaroxaban and apixaban as reported to eight poison centers**. *Ann Emerg Med* 2015.
Spinler SA, Shafir V. **New oral anticoagulants** for atrial fibrillation. Circulation. 2012 Jul 3;126(1):133-7.
Sposato LA, Riccio PM, Hachinski V. **Poststroke atrial fibrillation**: Cause or consequence?: Critical review of current views. Neurology. 2014 Apr 1;82(13):1180-6.
Sposato LA, Cipriano LE, Saposnik G, et al. Diagnosis of atrial fibrillation **after stroke and transient ischaemic attack**: a systematic review and meta-analysis. Lancet Neurol. 2015 Mar 3.
Sposato LA, Cipriano LE, et al. **Diagnosis of atrial fibrillation after stroke and transient ischaemic attack**: a systematic review and meta-analysis. Lancet Neurol. 2015 Apr;14(4):377-87.
Sposato LA, Cerasuolo JO, Cipriano LE, et al. **Atrial fibrillation detected after stroke** is related to a low risk of ischemic stroke recurrence. Neurology. 2018 Mar 13;90(11):e924-e931.
Sposato LA et al. **Atrial fibrillation detected after stroke** is related to a low risk of ischemic stroke recurrence. Neurology 2018 Mar 13; 90:e924.
Sposato LA, Lopes RD. **Oral anticoagulation**: a step toward solving the **puzzle of dementia** related to atrial fibrillation? Eur Heart J. 2018 Feb 7;39(6):461-463.
Staerk L, Lip GYH, Olesen JB, et al. **Stroke and recurrent haemorrhage associated with antithrombotic treatment after gastrointestinal bleeding** in patients with atrial fibrillation: nationwide cohort study. BMJ 2015;351:h5876.
Staerk L, Lip GY, et al. **Stroke and recurrent haemorrhage** associated with **antithrombotic treatment after gastrointestinal bleeding** in patients with atrial fibrillation: nationwide cohort study. BMJ. 2015 Nov 16;351:h5876.
Staerk L, Sherer JA, Ko D, et al. **Atrial Fibrillation: Epidemiology, Pathophysiology, and Clinical Outcomes**. Circ Res. 2017 Apr 28;120(9):1501-1517.
Staerk L, Wang B, Preis SR, et al. **Lifetime risk of atrial fibrillation** according to optimal, borderline, or elevated levels of risk factors: cohort study based on longitudinal data from the Framingham Heart Study. BMJ. 2018 Apr 26;361:k1453.
Stam-Slob MC, Connolly SJ, van der Graaf Y, et al. Individual Treatment Effect Estimation of 2 Doses of **Dabigatran** on Stroke and Major Bleeding in Atrial Fibrillation: Results from the RE-LY Trial. Circulation. 2019 May 3.
Stangier J, Stähle H, Rathgen K, Fuhr R. Pharmacokinetics and pharmacodynamics of the direct oral thrombin inhibitor dabigatran in healthy elderly subjects. Clin Pharmacokinet. 2008;47(1):47-59. The effects of pantoprazole coadministration on the bioavailability of dabigatran were considered acceptable, and dose adjustment is not considered necessary.
Stanton RJ, Roesch MJ, Kanter D. **Neurologic Abnormalities After Atrial Fibrillation Ablative Procedure**. JAMA Neurol. 2018 Jun 11.
Stazi A, Scalone G, Laurito M, et al. Effect of **remote ischemic preconditioning** on platelet activation and reactivity induced by ablation for atrial fibrillation. Circulation. 2014 Jan 7;129(1):11-7
Steffel J, Giugliano RP, et al. **Edoxaban vs warfarin in patients with atrial fibrillation on amiodarone**: subgroup ENGAGE AF-TIMI 48 trial. Eur Heart J. 2015 Sep 1;36(33):2239-45.
Steffel J, Giugliano RP, et al. **Edoxaban Versus Warfarin** in Atrial Fibrillation Patients at Risk of Falling: E**NGAGE AF-TIMI 48** Analysis. J Am Coll Cardiol. 2016 Sep 13;68(11):1169-78.
Steffel J, et al; ESC Scientific Document Group . The **2018 European Heart Rhythm Association Practical Guide** on the use of **non-vitamin K antagonist oral anticoagulants in patients with atrial fibrillation**. Eur Heart J. 2018 Mar 17.
Steinbeck G, Sinner MF, Lutz M, et al. Incidence of complications related to **catheter ablation of atrial fibrillation and atrial flutter**: a nationwide in-hospital analysis of administrative data for Germany in 2014. Eur Heart J. 2018 Aug 1.
Steinberg BA, Kim S, Piccini JP, et al; on behalf of the Outcomes Registry for Better Informed Treatment of Atrial Fibrillation (**ORBIT-AF**) Investigators and Patients. Use and Associated Risks of **Concomitant Aspirin Therapy with Oral Anticoagulation** in Patients with Atrial Fibrillation: Insights from the ORBIT-AF Registry. Circulation. 2013 Jul 16.
Steinberg BA, Kim S, Thomas L, et al; Outcomes Registry for Better Informed Treatment of Atrial Fibrillation (**ORBIT-AF**) Investigators and Patients. Lack of Concordance Between Empirical Scores and Physician Assessments of Stroke and Bleeding Risk in Atrial Fibrillation: Results From the Outcomes Registry for Better Informed Treatment of Atrial Fibrillation (ORBIT-AF) Registry. Circulation. 2014 May 20;129(20):2005-12.
Steinberg BA, Piccini JP. **Anticoagulation in atrial fibrillation**. BMJ 2014;348:g2116 doi: 10.1136/bmj.g2116
Steinberg JS, Romanov A, Musat D, et al. **Prophylactic pulmonary vein isolation** during isthmus ablation for atrial flutter: The PREVENT AF Study I. Heart Rhythm 2014.
Steinberg BA, Peterson ED, Kim S, et al. **Use and outcomes associated with bridging during anticoagulation interruptions** in patients with atrial fibrillation: findings from the Outcomes Registry for Better Informed Treatment of Atrial Fibrillation (**ORBIT-AF**). Circulation. 2015;131:488–494.
Steinberg BA, Hellkamp AS, Lokhnygina Y, et al; **ROCKET-AF** Steering Committee and Investigators. Higher risk of death and stroke in patients with **persistent vs. paroxysmal** atrial fibrillation: results from the ROCKET-AF Trial. Eur Heart J. 2015 Feb 1;36(5):288-96.
Steinberg BA, Simon DN, Thomas L, et al. Management of **Major Bleeding** in Patients With **Atrial Fibrillation** Treated With Non-Vitamin K Antagonist Oral Anticoagulants Compared With Warfarin in Clinical Practice (from Phase II of the Outcomes Registry for Better Informed Treatment of Atrial Fibrillation [**ORBIT-AF II**]). Am J Cardiol. 2017 Mar 28.
Steinhubl SR, Waalen J, Edwards AM, et al. Effect of a home-based **wearable continuous ECG monitoring patch on detection of undiagnosed atrial fibrillation**: the **mSToPS** randomized clinical trial. JAMA. doi:10.1001/jama.2018.8102
Steiner T. Resumption of oral anticoagulation after warfarin-associated **intracerebral hemorrhage: yes**. Stroke. 2011 Dec;42(12):3661-2.
Stergiopoulos K, Brown DL. **Genotype-guided vs clinical dosing of warfarin** and its analogues: meta-analysis of randomized clinical trials [online June 16, 2014]. JAMA Intern Med. doi:10.1001/jamainternmed.2014.2368.
Stewart S, Ball J, Horowitz JD, et al. **Standard versus atrial fibrillation-specific management strategy (SAFETY)** to reduce recurrent admission and prolong survival: pragmatic, multicentre, randomised controlled trial. Lancet. 2014 Nov 17.
Stolk LM, et al. **Risk of myocardial infarction** in patients with atrial fibrillation using **vitamin K antagonists, aspirin or direct acting oral anticoagulants**. Br J Clin Pharmacol. 2017 Mar 22.
Strohecker J. Dabigatran for Prevention of Stroke in Atrial Fibrillation. Am Fam Physician. 2011 Dec 15;84(12):1397-1398.
Sukumar S, Gulilat M, Linton B, et al. **Apixaban Concentrations with Lower than Recommended Dosing** in Older Adults with Atrial Fibrillation. J Am Geriatr Soc. 2019 May 21.
Sun D, Lazo-Langner A. **New oral anticoagulants**. CMAJ. 2013 Mar 5;185(4):E212.
Suzuki S, Sagara K, Otsuka T, et al. A New Scoring System for Evaluating the Risk of **Heart Failure** Events in Japanese Patients With Atrial Fibrillation (**H_2ARDD**). Am J Cardiol. 2012 May 21.
Suzuki S, Sagara K, Otsuka T, et al. Usefulness of Frequent **Supraventricular Extrasystoles and a High CHADS(2)** Score to Predict First-Time Appearance of Atrial Fibrillation.

Am J Cardiol. 2013 Mar 14.
Swartz MF, Fink GW, Sarwar MF, et al. Elevated pre-operative serum **peptides for collagen I and III** synthesis result in post-surgical atrial fibrillation. J Am Coll Cardiol 2012.
Swiryn S, Orlov MV, Benditt DG, et al. Clinical Implications of **Brief Device-Detected Atrial Tachyarrhythmias** in a Cardiac Rhythm Management Device Population: Results from the Registry of Atrial Tachycardia and Atrial Fibrillation Episodes. Circulation. 2016 Oct 18;134(16):1130-1140
Su C, Liu Z, Gao Y, et al. Study on the relationship between **telomere length changes and recurrence of atrial fibrillation** after radiofrequency catheter ablation. J Cardiovasc Electrophysiol. 2019 Jul;30(7):1117-1124.
Su VY, Hu YW, Chou KT, et al. **Amiodarone and the risk of cancer**: A nationwide population-based study. Cancer 2013.
Sulzgruber P, Wassmann S, Semb AG, et al. **Oral Anticoagulation in patients** with non-valvular atrial fibrillation and a CHA2DS2-VASc score of 1. Eur Heart J. 2019 Sep 21;40(36):3010-3012.
Sun MT, Wood MK, et al. Risk of **Intraocular Bleeding** With **Novel Oral Anticoagulants Compared With Warfarin**: A Systematic Review and Meta-analysis. JAMA Ophthalmol. 2017 Jul 6.
Svennberg E, Engdahl J, Al-Khalili F, Friberg L, Frykman V, Rosenqvist M. **Mass screening** for untreated atrial fibrillation: the **STROKESTOP** study. 2015;131:2176–2184.
Tai C, Wu H, San C, et al. Management of **Supratherapeutic International Normalized Ratio without Bleeding after Warfarin Use**: An Evaluation of **Vitamin K Administration** (**SUPRA-WAR-K** Study). Can J Hosp Pharm. 2017 May-Jun;70(3):207-214. Epub 2017 Jun 30.
Taillandier S, Brunet Bernard A, Lallemand B, et al. Prognosis in Patients Hospitalized With Permanent and Nonpermanent Atrial Fibrillation in **Heart Failure**. Am J Cardiol. 2014 Jan 14.
Takahashi Y et al. **Renal function** after catheter ablation of atrial fibrillation. Circulation. 2011 Nov 29;124(22):2380-7. (improves kidney function over 1yr)
Tanaka-Esposito C, Chung MK. **Selecting antithrombotic therapy** for patients with atrial fibrillation. Cleve Clin J Med. 2015 Jan;82(1):49-63.
Thacker EL, McKnight B, Psaty BM, et al. Atrial fibrillation and **cognitive decline**: A longitudinal cohort study. Neurology. 2013 Jul 9;81(2):119-125.
Thijs VN, Brachmann J, Morillo CA, et al. Predictors for atrial fibrillation detection after **cryptogenic stroke: Results from CRYSTAL AF**. Neurology. 2016 Jan 19;86(3):261-9.
Thompson AE. JAMA **patient page**. **Atrial fibrillation**. JAMA. 2015 Mar 10;313(10):1070.
Thompson PL, Verheugt FW. Managing **antithrombotic therapy** in patients with both **atrial fibrillation and coronary heart disease**. Clin Ther. 2014 Sep 1;36(9):1176-81.
Tison GH et al. **Passive detection** of atrial fibrillation using a commercially available **smartwatch**. JAMA Cardiol 2018 Mar 21.
Touma L, Filion KB, et al. A Meta-Analysis of Randomized Controlled Trials of the Risk of **Bleeding With Apixaban Versus Vitamin K Antagonists**. Am J Cardiol. 2014 Dec 2. 1290.
Trevisan C, Piovesan F, Lucato P, et al. **Parathormone, vitamin D and the risk** of atrial fibrillation in older adults: A prospective study. Nutr Metab Cardiovasc Dis. 2019 May 29.
Tsadok MA, Jackevicius CA, Rahme E, et al. **Sex differences** in stroke risk among older patients with recently diagnosed atrial fibrillation. JAMA 2012; 307:1952-1958.
Tsadok MA, Jackevicius CA, et al. **Rhythm versus rate** control therapy and subsequent stroke or transient ischemic attack in patients with atrial fibrillation. Circulation.2012 Dec4;126(23):2680-7.
Tsivgoulis G, Katsanos AH, Mavridis D, et al. **Intravenous Thrombolysis for Ischemic Stroke** Patients on **Dual Antiplatelets**. Ann Neurol. 2018 Jul 26.
Tsivgoulis G, Lioutas VA, Varelas P, et al. **Direct oral anticoagulant- vs vitamin K antagonist-related nontraumatic intracerebral hemorrhage**. Neurology. 2017 Sep 12;89(11):1142-1151
Tsivgoulis G, Wilson D, Katsanos AH, et al. **Neuroimaging and clinical outcomes of oral anticoagulant associated ICH**. Ann Neurol. 2018 Sep 26.
Tung R, Buch E, Shivkumar K. **Catheter ablation** of atrial fibrillation. Circulation. 2012 Jul 10;126(2):223-9.
Turagam MK, Garg J, Whang W, et al**. Catheter Ablation of Atrial Fibrillation in Patients With Heart Failure**: A Meta-analysis of Randomized Controlled Trials. Ann Intern Med.2018 Dec 25.
Turagam MK, Velagapudi P, Kocheril AG. **Atrial fibrillation in athletes**. Am J Cardiol. 2012 Jan 15;109(2):296-302.
Turakhia MP, Santangeli P, Winkelmayer WC, et al. **Increased mortality associated with digoxin** in contemporary patients with atrial fibrillation: findings from the **TREAT-AF** study. *J Am Coll Cardiol* 2014; 64:660–668.
Uchino K, Hernandez AV. **Dabigatran** association with **higher risk of acute coronary events**: meta-analysis of noninferiority randomized controlled trials. Arch Intern Med. doi:10.1001/archinternmed.2011.1666.
Ueberham L, Bollmann A. Same-day discharge following atrial fibrillation **catheter ablation**: the perfect blend? Europace. 2019 Mar 1;21(3):363-365.
Ueshima S, Hira D, Kimura Y, et al. Population pharmacokinetics and pharmacogenomics of **apixaban** in **Japanese** adult patients with atrial fibrillation. Br J Clin Pharmacol. 2018 Feb 19.
Ulimoen SR, Enger S, et al. Comparison of **Four Single-Drug Regimens** on Ventricular Rate and Arrhythmia-Related Symptoms in Patients With Permanent Atrial Fibrillation. Am J Cardiol. 2012 Oct 27.
Uphaus T, Weber-Kr¨ uger M, Grond M, et al. Development and validation of **a score to detect paroxysmal atrial fibrillation after stroke**. Neurology 2019;92:e115–e124.
USPSTF: US Preventive Services Task Force. **Screening for atrial fibrillation with electrocardiography**: US Preventive Services Task Force recommendation statement [August 7, 2018]. JAMA. doi:10.1001/jama.2018.10321
USPSTF: Jonas DE, Kahwati LC, Yun JDY, Middleton JC, Coker-Schwimmer M, Asher GN. **Screening for atrial fibrillation with electrocardiography**: evidence report and systematic review for the US Preventive Services Task Force [August 7, 2018]. JAMA.doi:10.1001/jama.2018.4190
Valbusa F, Bertolini L, Bonapace S, et al. Relation of Elevated Serum **Uric Acid** Levels to Incidence of Atrial Fibrillation in Patients With Type 2 Diabetes Mellitus. Am J Cardiol. 2013 May 11.
Valembois L, Audureau E, Takeda A, et al. **Antiarrhythmics for maintaining sinus rhythm** after cardioversion of atrial fibrillation. Cochrane Database Syst Rev. 2019 Sep 4;9:CD005049. There is high-certainty evidence of increased mortality associated with sotalol treatment, and low-certainty evidence suggesting increased mortality with quinidine, when used for maintaining sinus rhythm in people with atrial fibrillation. We found few data on mortality in people taking disopyramide, flecainide and propafenone, so it was not possible to make a reliable estimation of the mortality risk for these drugs. However, we did find moderate-certainty evidence of marked increases in proarrhythmia and adverse effects with flecainide.Overall, there is evidence showing that antiarrhythmic drugs increase adverse events, increase proarrhythmic events and some antiarrhythmics may increase mortality. Conversely, although they reduce recurrences of atrial fibrillation, there is no evidence of any benefit on other clinical outcomes, compared with placebo or no treatment.
Valentinis A, Ivers N, Bhatia S, et al. Atrial fibrillation **anticoagulation care** in a large urban family medicine practice. Can Fam Physician. 2014 Mar;60(3):e173-9.
Vamos M, Erath JW, Hohnloser SH. **Digoxin-associated mortality**: a systematic review and meta-analysis of the literature. Eur Heart J. 2015 May 4.
Van Brabandt H, Neyt M, Devos C. **Caution over use of catheter ablation** for atrial fibrillation. BMJ. 2013 Sep 6;347:f5277.
van den Ham HA, Klungel OH, Singer DE, et al. **Comparative Performance of ATRIA, CHADS2, and CHA2DS2-VASc** Risk Scores Predicting Stroke in Patients With Atrial Fibrillation: Results From a National Primary Care Database. J Am Coll Cardiol. 2015 Oct 27;66(17):1851-9.
van Diepen S, Bakal JA, McAlister FA, Ezekowitz JA. Mortality and readmission of patients with heart failure, atrial fibrillation, or coronary artery disease **undergoing noncardiac surgery**: an analysis of 38 047 patients. Circulation. 2011 Jul 19;124(3):289-96.
van Doorn S, Debray TPA, et al. Predictive performance of the **CHA2DS2-VASc rule in atrial fibrillation**: a systematic review and meta-analysis. J Thromb Haemost. 2017 Apr 4.
Van Gelder IC, Hagens VE, Bosker HA, et al. for the Rate Control versus Electrical Cardioversion for Persistent Atrial Fibrillation Study Group. A comparison of rate control and rhythm control in patients with recurrent persistent atrial fibrillation. (**RACE)** *N Engl J Med.* 2002; 347:1834 –1840.
Van Gelder IC, Groenveld HF, Crijns HJ, et al.; **RACE II** Investigators. Lenient versus strict rate control in patients with atrial fibrillation. N Engl J Med. 2010 Apr 15;362(15):1363-73.
van Rein N, Heide-Jorgensen U, Lijfering WM, et al. **Major Bleeding Rates** in Atrial Fibrillation Patients on Single, Dual, or Triple Antithrombotic Therapy. Circulation. 2019 Feb 5;139(6):775-786. doi: 10.1161/CIRCULATIONAHA.118.036248. (Original)
Van Spall HG, Wallentin L, Yusuf S, et al. Variation in warfarin dose adjustment practice is responsible for differences in the quality of anticoagulation control between centers and countries: an analysis of patients receiving warfarin in the **RE-LY** trial. Circulation2012.
van Velzen HG, et al. Incidence of Device-Detected Atrial Fibrillation and Long-Term Outcomes in Patients with **Hypertrophic Cardiomyopathy**. Am J Cardiol. 2017;119:100-105.
Valbusa F, Bertolini L, Bonapace S, et al. Relation of **elevated serum uric Acid** levels to incidence of atrial fibrillation in patients with type 2 diabetes mellitus. Am J Cardiol. 2013 Aug 15;112(4):499-504.
Vaughan-Sarrazin MS, Mazur A, Chrischilles E, et al. **Trends in the pharmacologic management** of atrial fibrillation: Data from the Veterans Affairs health system. Am Heart J. 2014 Jul;168(1):53-9.e1.
Vaughan Sarrazin MS, Jones M, et al. **Bleeding rates in Veterans Affairs** patients with atrial fibrillation who **switch from warfarin to dabigatran.** Am J Med. 2014 Dec;127(12):1179-85.
Verdecchia P, Reboldi G, Di Pasquale G, et al; the RE-LY Study Investigators. Prognostic Usefulness of **Left Ventricular Hypertrophy** by Electrocardiography in Patients With Atrial Fibrillation (from the Randomized Evaluation of Long-Term Anticoagulant Therapy Study). Am J Cardiol. 2013 Nov 23
Verheugt FW. **Antithrombotic** therapy during and after **percutaneous coronary intervention** in patients with atrial fibrillation. Circulation. 2013 Oct 29;128(18):2058-61.
Verheugt FWA, Ten Berg JM, Storey RF, et al. Antithrombotic Agents: From **Aspirin to DOACs** in Coronary Artery Disease and in Atrial Fibrillation (Part I). J Am Coll Cardiol. 2019 Jun 7
Verma A, Champagne J, Sapp J, et al. Discerning the Incidence of Symptomatic and Asymptomatic Episodes of Atrial Fibrillation Before and After **Catheter Ablation** (DISCERN AF): A Prospective, Multicenter Study. Arch Intern Med. 2012 Dec 24:1-8.
Verma A, Cairns JA, Mitchell LB, et al. **CCS Atrial Fibrillation** Guidelines Committee. **2014 focused update of the Canadian cardiovascular society** guidelines for the management of atrial fibrillation. Can J Cardiol. 2014 Oct;30(10):1114-30.
Verma A, Ha ACT, Rutka JT, Verma S. What Surgeons Should Know About **Non-Vitamin K Oral Anticoagulants**: A Review. JAMA Surg. 2018 Apr 18.
Verma A, Ha ACT, Kirchhof P, et al. The Optimal Anti-Coagulation for Enhanced-Risk Patients Post-Catheter Ablation for Atrial Fibrillation (**OCEAN**) trial. Am Heart J. 2018 Mar;197:124-132.
Verma A, Jiang CY, Betts TR, et al; **STAR AF II** Investigators. Approaches to **catheter ablation for persistent atrial fibrillation**. (STAR AF 2) N Engl J Med. 2015 May 7;372(19):1812-22.
Verma A, Kalman JM, Callans DJ. Treatment of Patients With **Atrial Fibrillation and Heart Failure** With Reduced Ejection Fraction. Circulation. 2017 Apr 18;135(16):1547-1563.
Vidale S. **Antithrombotic drugs and risk of hemorrhagic stroke** in the general population. Neurology. 2014 Apr 1;82(13):1193.
Violi F, Pignatelli P. **Platelet activation** after **radiofrequency ablation** in atrial fibrillation: is there any clinical implication? Circulation. 2014 Jan 7;129(1):5-7
Vinereanu D, Lopes RD, Bahit MC, et al. A **multifaceted intervention** to improve treatment with oral anticoagulants in atrial fibrillation (**IMPACT-AF**): an international, cluster-randomised trial. Lancet. 2017 Aug 25.
Voskoboinik A, Wong G, Lee G, et al. **Moderate alcohol consumption** is associated with atrial electrical and structural changes: Insights from high-density left atrial electroanatomic mapping. Heart Rhythm. 2018 Dec 24.
Vranckx P, Valgimigli M, Eckardt L, et al. **Edoxaban-based versus vitamin K antagonist-based antithrombotic regimen** after successful coronary stenting in patients with atrial fibrillation (ENTRUST-AF PCI): a randomised, open-label, phase 3b trial. Lancet. 2019 Sep 2.
Wachter R, et al. **Holter-electrocardiogram-monitoring** in patients with acute ischaemic stroke (**FIND-AF RANDOMISED**): open-label randomised trial. Lancet Neurol 2017; online Feb 7.

Wadhera RK, Russell CE, Piazza G. **Warfarin versus novel oral anticoagulants**: how to choose? Circulation. 2014 Nov 25;130(22):e191-3.

Wahlstrom M, Karlsson MR, Medin J, et al. Effects of **yoga** in patients with paroxysmal atrial fibrillation—a randomized controlled study. *European J Cardiovasc Nursing* 2016.

Walkey AJ, Wiener RS, Ghobrial JM, Curtis LH, Benjamin EJ. Incident stroke and mortality associated with new-onset atrial fibrillation in patients hospitalized with **severe sepsis** [published online November 13, 2011]. JAMA. doi:10.1001 /jama.2011.1615.

Walkey AJ, Evans SR, Winter MR, Benjamin EJ. Practice patterns and outcomes of treatments for atrial **fibrillation during sepsis**: A propensity-matched cohort study. Chest. 2015 Aug 13.

Walkey AJ, Quinn EK, Winter MR, et al. Practice patterns and outcomes associated with use of anticoagulation among patients with atrial fibrillation during **sepsis**. JAMA Cardiol 2016.

Wallentin L, Yusuf S, Ezekowitz MD et al. Efficacy and safety of dabigatran compared with warfarin at different levels of international normalised ratio control for stroke prevention in atrial fibrillation: an analysis of the RE-LY trial. Lancet. 2010 Sep18;376(9745):975-83.

Wang CL, Wu VC, Lee CH, et al. **Effectiveness and safety of non-vitamin-K antagonist oral anticoagulants versus warfarin in atrial fibrillation patients with thrombocytopenia**. J Thromb Thrombolysis. 2018 Dec 18.

Wang CL, Wu VC, Kuo CF, et al. Efficacy and Safety of **Non-Vitamin K Antagonist Oral Anticoagulants in Atrial Fibrillation Patients With Impaired Liver Function**: A Retrospective Cohort Study. J Am Heart Assoc. 2018 Aug 7;7(15):e009263.

Wang EHZ, BVolt JL, Decarie D, et al. Stability of **Dabigatran Etexilate in Manufacturer's Blister Pack, Unit-Dose Packaging, and Community Pharmacy Blister Pack**. Can J Hosp Pharm 2015;68 (1):16-21.

Wang KL, Lopes RD, Patel MR, et al. Efficacy and safety of **reduced-dose non-vitamin K antagonist oral anticoagulants** in patients with atrial fibrillation: a meta-analysis of randomized controlled trials. Eur Heart J. 2018 Dec 22.

Wang M, Zhao Q, Ding W, et al. Comparison of **Direct Current Synchronized Cardioversion to Ibutilide-Guided Catheter Ablation** for Long-Term Sinus Rhythm Maintenance After Isolated Pulmonary Vein Isolation of Persistent Atrial Fibrillation. Am J Cardiol. 2017 Jun 15;119(12):1997-2002.

Wang SV, Franklin JM, Glynn RJ, et al. Prediction of rates of thromboembolic and major bleeding outcomes with **dabigatran or warfarin** among patients with atrial fibrillation: **new initiator cohort** study. BMJ. 2016 May 24;353:i2607.

Wang Z, Zhang Y, Gao M, et al. **Statin Therapy** for the Prevention of Atrial Fibrillation: A Meta-analysis of Randomized Controlled Trials. Pharmacotherapy. 2011 Nov;31(11):1051-62.

Wangge G, Roes KC, de Boer A, et al. The challenges of determining **noninferiority margins**: a case study of noninferiority randomized controlled trials of **novel oral anticoagulants**. CMAJ. 2013 Feb 19;185(3):222-7.

Warkentin TE, Margetts P, Connolly SJ, et al. Recombinant factor VIIa (rFVIIa) and hemodialysis to manage massive **dabigatran**-associated postcardiac surgery **bleeding**. Blood. 2012 Mar 1;119(9):2172-4.

Washam JB, Hellkamp AS, Lokhnygina Y, et al. Efficacy and Safety of **Rivaroxaban** Versus **Warfarin** in Patients Taking **Nondihydropyridine Calcium Channel Blockers** for Atrial Fibrillation (from the **ROCKET AF** Trial). Am J Cardiol. 2017 Aug 15;120(4):588-594

Washam JB, Stevens SR, Lokhnygina Y, et al; for the **ROCKET AF** Steering Committee and Investigators. **Digoxin** use in patients with atrial fibrillation and adverse cardiovascular outcomes: a retrospective analysis of the Rivaroxaban Once Daily Oral Direct Factor Xa Inhibition Compared with Vitamin K Antagonism for Prevention of Stroke and Embolism Trial in Atrial Fibrillation (ROCKET AF). Lancet. 2015 Mar 5.

Wazni OM, Marrouche NF, Martin DO, et al. **Radiofrequency ablation vs antiarrhythmic** drugs as first-line treatment of symptomatic atrial fibrillation: a randomized trial. JAMA. 2005 Jun 1;293(21):2634-40.

Weber-Krüger M, Lutz C, Zapf A, et al. **Relevance of supraventricular runs** detected after cerebral ischemia. Neurology 2017;89:1545–1552.

Weerasooriya R, Shah AJ, Hocini M, et al. Contemporary Challenges of **Catheter Ablation** for Atrial Fibrillation. Clin Ther. 2014 Sep 1.

Weitz JI, Quinlan DJ, Eikelboom JW. **Periprocedural management** and approach to bleeding in patients taking **dabigatran**. Circulation. 2012 Nov 13;126(20):2428-32.

Weitz JI, Healey JS, Skanes AC, et al. **Periprocedural management** of new oral anticoagulants in patients undergoing atrial fibrillation **ablation**. Circulation. 2014 Apr 22;129(16):1688-94.

Weitz JI, Semchuk W, Turpie AG, et al. **Trends in Prescribing Oral Anticoagulants in Canada**, 2008-2014. Clin Ther. 2015 Nov 1;37(11):2506-2514.e4.

Welton NJ, McAleenan A, Thom HH, et al. **Screening strategies** for atrial fibrillation: a systematic review and cost-effectiveness analysis. Health Technol Assess. 2017 May;21(29):1-236.

Weng LC, Preis SR, Hulme OL, et al. **Genetic Predisposition**, Clinical Risk Factor Burden, and Lifetime Risk of Atrial Fibrillation. Circulation. 2018 Mar 6;137(10):1027-1038.

Whitbeck MG, Charnigo RJ, Khairy P, et al. **Increased mortality among patients taking digoxin**—analysis from the **AFFIRM** study. Eur Heart J 2012:

Wickramasinghe SR, Patel VV. **Local Innervation** and Atrial Fibrillation.Circulation. 2013 Oct 1;128(14):1566-1575.

Wein T, Lindsay MP, Côté R, Foley N, Berlingieri J, Bhogal S, et al; Heart and Stroke Foundation **Canadian Stroke Best Practice Committees**. Canadian stroke best practice recommendations (**CSBPR**): Secondary prevention of stroke, sixth edition practice guidelines, update 2017. Int J Stroke. 2018 Jun;13(4):420-443.

Wiesel J, Abraham S, Messineo FC. **Screening for Asymptomatic** Atrial Fibrillation While Monitoring the Blood Pressure at Home: Trial of Regular Versus Irregular Pulse for Prevention of Stroke (TRIPPS 2.0). Am J Cardiol. 2013 Mar 14.

Wiesel J, et al. Comparison of the **microlife blood pressure monitor with the omron blood pressure monitor** for detecting atrial fibrillation. Am J Cardiol. 2014 Oct 1;114(7):1046-8.

Wiesel J, Salomone TJ. **Screening** for Atrial Fibrillation in Patients ≥65 Years Using an **Automatic Blood Pressure Monitor in a Skilled Nursing Facility**. Am J Cardiol. 2017 Oct 15;120(8):1322-1324.

Wijesurendra RS, Casadei B. **Mechanisms of atrial fibrillation**. Heart. 2019 Aug 23.

Wijesurendra RS, Liu A, et al. **Lone atrial fibrillation** is associated with impaired left ventricular energetics that persists despite successful catheter ablation. Circulation. 2016;134:1068– 1081.

Wilkinson GS, Baillargeon J, Kuo YF, et al. **Atrial fibrillation** and stroke associated with intravenous bisphosphonate therapy in older patients with cancer. J Clin Oncol. 2010 Nov 20;28(33):4898-905.

Wilson D, Ambler G, Shakeshaft C, et al; CROMIS-2 collaborators. **Cerebral microbleeds and intracranial haemorrhage risk in patients anticoagulated for atrial fibrillation** after acute ischaemic stroke or transient ischaemic attack (CROMIS-2): a multicentre observational cohort study. Lancet Neurol. 2018 Jun;17(6):539-547.

Windecker S, Lopes RD, Massaro T, et al; AUGUSTUS Investigators. Antithrombotic Therapy in Patients with **Atrial Fibrillation and Acute Coronary Syndrome** Treated Medically or with Percutaneous Coronary Intervention or Undergoing Elective Percutaneous Coronary Intervention: Insights from the AUGUSTUS Trial. Circulation. 2019 Sep 26. doi:10.1161/CIRCULATIONAHA.119.043308.

Winkle RA, Mead RH, Engel G, et al. The impact of **obesity** on atrial fibrillation: Patient characteristics, long-term outcomes and complications. *Heart Rhythm* 2017;

Wiysonge C, et al. **Beta-blockers for hypertension**. Cochrane Database Syst Rev. 2007 Jan 24;(1):CD002003.

Wolfe Z, Khan SU, Nasir F, et al. A systematic review and Bayesian network meta-analysis of risk of **intracranial hemorrhage with direct oral anticoagulants**. J Thromb Haemost. 2018 Jul;16(7):1296-1306.

Wolff A, Shantsila E, et al. Impact of **advanced age on management and prognosis in atrial fibrillation**: insights from a population-based study in general practice. Age Ageing. 2015 Jun 16.

Wong CX, Brooks AG, Lau DH et al. Factors Associated With the Epidemic of **Hospitalizations** Due to Atrial Fibrillation. Am J Cardiol. 2012 Aug 7.

Wong CX, et al. Meta-Analysis of Anticoagulation Use, Stroke, Thromboembolism, Bleeding, and Mortality in Atrial Fibrillation on **Dialysis**. Am J Cardiol. 2016 Jun 15;117(12):1934-41.

Wood B, Sholzberg M, Ackery A. **Direct oral anticoagulants and the bleeding patient**. CMAJ. 2016 Feb 16;188(3):215.

Woods EA, et al. **Anticoagulant and Antiplatelet Prescribing Patterns** for Patients with Atrial Fibrillation after Percutaneous Coronary Intervention. Can J Hosp Pharm. 2016 Jul-Aug;69(4):280-5.

Writing Committee, Tomaselli GF, Mahaffey KW, et al. **2017 ACC Expert Consensus** Decision Pathway on **Management of Bleeding in Patients on Oral Anticoagulants**: A Report of the American College of Cardiology Task Force on Expert Consensus Decision Pathways. J Am Coll Cardiol. 2017 Nov 10.

Wu C, Tcherny-Lessenot S, et al. Assessing the Risk for **Peripheral Neuropathy in Patients Treated With Dronedarone** Compared With That in Other Antiarrhythmics. Clin Ther. 2018 Feb 27.

Wu JH, Lemaitre RN, King IB, et al. Association of plasma phospholipid long-chain **omega-3 Fatty acids** with incident atrial fibrillation in older adults: the cardiovascular health study. Circulation. 2012 Mar 6;125(9):1084-93.

Wynn GJ, El-Kadri M, Haq I, et al. **Long-term Outcomes After Ablation** of Persistent Atrial Fibrillation: An Observational Study Over 6 Years. Open Heart.2016:3:e000394

Wyrembak J, Campbell KB, Steinberg BA, et al. **Incidence and Predictors of Left Atrial Appendage Thrombus** in Patients Treated With **Nonvitamin K Oral Anticoagulants Versus Warfarin** Before Catheter Ablation for Atrial Fibrillation. Am J Cardiol. 2017 Apr 1;119(7):1017-1022.

Wyse DG, Waldo AL, DiMarco JP, et al. Atrial Fibrillation Follow-up Investigation of Rhythm Management (**AFFIRM**) Investigators. A comparison of rate control and rhythm control in patients with atrial fibrillation. *N Engl J Med.* 2002;347:1825–1833.

Xian Y, Wu J, O'Brien EC, et al. **Real world effectiveness of warfarin** among ischemic stroke patients with atrial fibrillation: observational analysis from Patient-Centered Research into Outcomes Stroke Patients Prefer and Effectiveness Research (**PROSPER**) study. BMJ. 2015 Jul 31;351:h3786.

Xian Y, Xu H, O'Brien EC, et al. Clinical Effectiveness of **Direct Oral Anticoagulants vs Warfarin** in Older Patients With Atrial Fibrillation and Ischemic Stroke: Findings From the Patient-Centered Research Into Outcomes Stroke Patients Prefer and Effectiveness Research (PROSPER) Study. JAMA Neurol. 2019 Jul 22.

Xiao X, Han H, Wu C, et al. Prevalence of **atrial fibrillation in hospital encounters with end-stage chronic obstructive pulmonary disease** on home oxygen: National trends in the United States. Chest. 2019 Jan 23.

Xu B, Peng F, et al. Short-term **Antiarrhythmic Drugs After Catheter Ablation** for Atrial Fibrillation: A Meta-analysis of Randomize Controlled Trials. Ann Pharmacother. 2016 Jun 16.

Xu D, Murakoshi N, Sairenchi T, et al. **Anemia** and **Reduced Kidney Function as Risk Factors** for New Onset of Atrial Fibrillation (from the Ibaraki Prefectural Health Study). Am J Cardiol. 2015 Feb 1;115(3):328-33.

Xu Y, Holbrook AM, Simpson CS, et al. Prescribing patterns of **novel oral anticoagulants following regulatory approval for atrial fibrillation in Ontario**, Canada: A population-based descriptive analysis. CMAJ2013;DOI:10.9778/cmajo.20130032.

Xu Y, Schulman S, Dowlatshahi D, et al; Bleeding Effected by Direct Oral Anticoagulants (**BLED-AC**) Study Group.. **Direct oral anticoagulant- or warfarin-related major bleeding**: characteristics, reversal strategies and outcomes from a multi-center observational study. Chest. 2017 Feb 17

Xue Z, Zhang H. **Non-Vitamin K Antagonist Oral Anticoagulants Versus Warfarin** in Asians With Atrial Fibrillation: Meta-Analysis of Randomized Trials and Real-World Studies. Stroke. 2019 Oct;50(10):2819-2828.

Yaghi S, Kamel H, Elkind MS. Potential new uses of **non-vitamin K antagonist oral anticoagulants to treat and prevent stroke**. Neurology. 2015 Jul 17.

Yang M, Choi R, Kim JS, et al. Evaluation of 16 **Genotype-Guided Warfarin Dosing Algorithms** in 310 Korean Patients Receiving Warfarin Treatment: Poor Prediction Performance in VKORC1 1173C Carriers. Clin Ther. 2016 Nov 22.
Yang Y, Zhang Z, Ng CY, Li G, et al. **Meta-analysis of CHADS(2) Score** in Predicting Atrial Fibrillation. Am J Cardiol. 2015 May 21.
Yankelson L, Steinvil A, Gershovitz L, et al. Atrial fibrillation, stroke, and mortality rates after **transcatheter aortic valve implantation**. Am J Cardiol. 2014 Dec 15;114(12):1861-6.
Yao X, Abraham NS, et al. Effect of **Adherence** to Oral Anticoagulants on Risk of Stroke and Major Bleeding Among Patients With Atrial Fibrillation. J Am Heart Assoc. 2016 Feb 23;5(2).
Yao X, Shah ND, et al. **Non-Vitamin K Antagonist Oral Anticoagulant Dosing** in Patients With Atrial Fibrillation and **Renal Dysfunction**. J Am Coll Cardiol. 2017 Jun 13;69(23):2779-2790.
Yao X;Gersh BJ;Sangaralingham LR;Kent DM;Shah ND;A Comparison of the **CHA2DS2-VASc, CHADS2, HAS-BLED, ORBIT, and ATRIA Risk Scores** in Predicting Non-Vitamin K Antagonist Oral Anticoagulants-Associated Bleeding in Patients With Atrial Fibrillation. Am J Cardiol. 2017 Jul 31.
Yao X, Gersh BJ, Holmes DR Jr, et al. Association of Surgical **Left Atrial Appendage Occlusion With Subsequent Stroke** and Mortality Among Patients Undergoing Cardiac Surgery JAMA. 2018 May 22;319(20):2116-2126.
Yao X, Tangri N, Gersh BJ, et al. **Renal Outcomes in Anticoagulated Patients With Atrial Fibrillation**. J Am Coll Cardiol. 2017 Nov 28;70(21):2621-2632.
Yaranov DM, Smyrlis A, Usatii N, et al. Effect of **obstructive sleep apnea** on frequency of stroke in patients with atrial fibrillation. Am J Cardiol. 2015 Feb 15;115(4):461-5.
Yasuda S, Kaikita K, Akao M, et al. **Antithrombotic therapy** for atrial fibrillation with stable coronary disease. N Engl J Med. (AFIRE) DOI: 10.1056/NEJMoa1904143.
Yiin GS, Howard DP, Paul NL, et al; Oxford Vascular Study. **Age-specific incidence, outcome, cost, and projected future burden** of atrial fibrillation related embolic vascular events: a population-based study. Circulation. 2014 Oct 7;130(15):1236-44.
Yogaratnam D, Ditch K, Medeiros K, et al. **Idarucizumab** for Reversal of Dabigatran-Associated Anticoagulation. Ann Pharmacother. 2016 Oct;50(10):847-54.
You JJ, Singer DE, Howard PA, et al. Antithrombotic therapy for atrial fibrillation: antithrombotic therapy and prevention of thrombosis, 9th ed: American College of Chest Physicians evidence-based clinical practice guidelines. *Chest*. 2012;141(2)(suppl):e531S-e575S.
Yu AYX, Malo S, Svenson LW, et al. Temporal Trends in the Use and **Comparative Effectiveness of Direct Oral Anticoagulant Agents Versus Warfarin** for Nonvalvular Atrial Fibrillation: A Canadian Population-Based Study. J Am Heart Assoc. 2017 Oct 28;6(11).
Yu WY, Bhutani T, Kornik R, et al. **Warfarin-Associated Nonuremic Calciphylaxis**. JAMA Dermatol. 2017 Jan 11.
Zafrir B, Lund LH, Laroche C, et al; ESC-HFA HF Long-Term Registry Investigators. **Prognostic implications of atrial fibrillation in heart failure** with reduced, mid-range, and preserved **ejection fraction**: a report from 14 964 patients in the European Society of Cardiology Heart Failure Long-Term Registry. Eur Heart J. 2018 Oct 15.
Zahir H, Brown KS, Vandell AG, et al. **Edoxaban** effects on bleeding following punch biopsy and reversal by a **4-factor prothrombin complex concentrate**. Circulation. 2015 Jan 6;131(1):82-90.
Zakeri R, Chamberlain AM, Roger VL, Redfield MM. Temporal relationship and prognostic significance of atrial fibrillation in **heart failure** patients with preserved ejection fraction: a community-based study. Circulation. 2013 Sep 3;128(10):1085-93.
Zalesak M, Siu K, Francis K, et al. Higher **persistence** in newly diagnosed nonvalvular atrial fibrillation patients treated with **dabigatran versus warfarin**. Circ Cardiovasc Qual Outcomes 2103.
Zeng Z, Wang L, Hua L, et al. Population Pharmacokinetic/Pharmacodynamics Modeling of **Ibutilide** in Chinese Healthy Volunteers and Patients With Atrial Fibrillation (AF) and/or Atrial Flutter(AFL). Clin Ther. 2017 Jun 14.
Zhang C, Gu ZC, Ding Z, et al. **Decreased risk of renal impairment in atrial fibrillation patients receiving non-vitamin K antagonist oral anticoagulants**: A pooled analysis of randomized controlled trials and real-world studies. Thromb Res. 2018 Dec 6;174:16-23.
Zhang YY, Qiu C, Davis PJ, et al. Predictors of **Progression of Recently Diagnosed** Atrial Fibrillation in Registry on Cardiac Rhythm DisORDers Assessing the Control of Atrial Fibrillation(RecordAF)-United States Cohort. Am J Cardiol. 2013 Apr 2.
Ziegler PD, Glotzer TV, Daoud EG, et al. Detection of Previously Undiagnosed Atrial Fibrillation in Patients With Stroke Risk Factors and Usefulness of **Continuous Monitoring** in Primary Stroke Prevention. Am J Cardiol. 2012 Jul 20.
Ziff OJ, Lane DA, Samra M, et al. **Safety and efficacy of digoxin**: systematic review and meta-analysis of observational and controlled trial data. BMJ. 2015 Aug 30;351:h4451.
Zimetbaum P. **In the Clinic: Atrial Fibrillation**. Ann Intern Med. 2017 Mar 7;166(5):ITC33-ITC48.
Zipursky JS, Shadowitz S. **Severe gastroparesis after catheter ablation** for atrial fibrillation. CMAJ. 2017 Mar 6;189(9):E368
Zou R, et al. Meta-analysis of safety and efficacy for **direct oral anticoagulation treatment of non-valvular atrial fibrillation in relation to renal function**. Thromb Res. 2017 Dec;160:41-50.
Zungsontiporn N, Link MS. **Newer technologies for detection of atrial fibrillation**. BMJ. 2018 Oct 17;363:k3946.

[1] Healey JS, Parkash R, Pollak, T. et al. Society Guidelines. Canadian Cardiovascular Society Atrial Fibrillation Guidelines 2010: Etiology and Initial Investigations. Can J Cardiol 2011;27:31-7.
[2] Kannel WB, Wolf PA, Benjamin EJ. Prevalence, incidence, prognosis, and predisposing conditions for atrial fibrillation: population-based estimates. Am J Cardiol 1998;82:2N-9N
[3] Canadian Agency for Drugs and Technologies in Health. Therapeutic Review Report: Recommendations for New Oral Anticoagulants for the Prevention of Thromboembolic Events in Patients with Atrial Fibrillation. DRAFT April 9th, 2012. Final Mar 2013. http://www.cadth.ca/media/pdf/TR0003_AntithromboticAgents-AF_ScienceReport_e.pdf

Canadian Agency for Drugs and Technologies in Health (CADTH). Antithrombotic agents for the prevention of stroke and systemic embolism in patients with atrial fibrillation. CADTH. 2013 Mar: 1(1B); 1-142.
[4] Dorian P, Guerra PG, Kerr CR, et al. Validation of a new simple scale to measure symptoms in atrial fibrillation: the Canadian Cardiovascular Society Severity in Atrial Fibrillation scale. Circ Arrhythm Electrophysiol 2009;2:213-4.
[5] Callahan T, Baranowski B. Managing newly diagnosed atrial fibrillation: Rate, rhythm, and risk. Cleveland Clinic Journal of Medicine. 2011;78(4):258-64.
[6] http://www.theheart.org/documents/sitestructure/en/content/programs/1230553/1230553.html, accessed July 25, 2011
[7] Alboni P, Tomasi C, Menozzi C, et al. Efficacy and safety of out-of-hospital self-administered single-dose oral drug treatment in the management of infrequent, well-tolerated paroxysmal supraventricular tachycardia. J Am Coll Cardiol 2001;37:548-53
[8] Capucci A, Villani GQ, Piepoli MF. Reproducible efficacy of loading oral propafenone in restoring sinus rhythm in patients with paroxysmal atrial fibrillation. Am J Cardiol 2003;92:1345-7
[9] Khan IA. Single oral loading dose of propafenone for pharmacological cardioversion of recent-onset atrial fibrillation. J Am Coll Cardiol 2001;37:542-7.
[10] Gillis AM, Verma A, Talajic M, Nattel S, et al. and the **CCS** Atrial Fibrillation Guidelines Committee. Society Guidelines Canadian Cardiovascular Society Atrial Fibrillation Guidelines 2010: **Rate and Rhythm Management**. Can J Cardio 2011;27:47-59.
Verma A, Cairns JA, Mitchell LB, et al. CCS Atrial Fibrillation Guidelines Committee. **2014 focused update of the Canadian cardiovascular society (CCS) guidelines** for the management of atrial fibrillation. Can J Cardiol. 2014 Oct;30(10):1114-30.
Macle L, Cairns J, Leblanc K, et al. **CCS Atrial Fibrillation Guidelines** Committee. **2016 Focused Update** of the Canadian Cardiovascular Society Guidelines for the Management of Atrial Fibrillation. Can J Cardiol. 2016 Oct;32(10):1170-1185.

[11] Wyse DG, Waldo AL, DiMarco JP, et al. Atrial fibrillation follow-up investigation of rhythm management (**AFFIRM**) Investigators. A comparison of rate control and rhythm control in patients with atrial fibrillation. N Engl J Med 2002;347:1825-33.
Gillinov AM, Gelijns AC, Parides MK, et al. **Surgical ablation** of atrial fibrillation **during mitral-valve surgery**. (**CTSN**) N Engl J Med. DOI: 10.1056/NEJMoa1500528.
[12] Roy D, Talajic M, Nattel S, et al. Rhythm control versus rate control for atrial fibrillation and heart failure. N Engl J Med 2008;358:2667-77.
[13] Van Gelder IC, Hagens VE, Bosker HA, et al. A comparison of rate control and rhythm control in patietns with recurrent persistent atrial fibrillation. N Engl J Med 2002;347:1834-40.
[14] Testa L, Biondi-Zoccai GG, Dello Russo A, et al. Rate-control vs. rhythm-control in patients with atrial fibrillation: a meta-analysis. Eur Heart J 2005;26:2000-6.
[15] Ogawa S. Yamashita T, Yamazaki T, et al. Optimal treatment strategy for patients with paroxysmal atrial fibrillation. **J-RHYTHM** study. Circ J 2009;73:242-8.
[16] van der Hooft CS, Heeringa J, van Herpen G, et al. Drug-Induced Atrial Fibrillation. J Am Coll Cardiol 2004;44:2117-24
Kaakeh Y, Overholser BR, Lopshire JC, Tisdale JE. Drug-induced atrial fibrillation. Drugs. 2012 Aug 20;72(12):1617-30.
[17] Verma A, Macle L, Cox J, Skanes AC; CCS Atrial Fibrillation Guidelines Committee. Canadian Cardiovascular Society atrial fibrillation guidelines 2010:catheter ablation for atrial fibrillation/atrial flutter. Can J Cardiol. 2011 Jan-Feb;27(1):60-6.
[18] Wazni O, Wilkoff B, Saliba W. Catheter ablation for atrial fibrillation. N Engl J Med. 2011 Dec 15;365(24):2296-304.
[19] Rordorf R, Savastano S, Gandolfi E, Vicentini A, Petracci B, Landolina M. Pharmacological therapy following catheter ablation of atrial fibrillation. J Cardiovasc Med (Hagerstown). 2012 Jan;13(1):9-15.
Tung R, Buch E, Shivkumar K. Catheter ablation of atrial fibrillation. Circulation. 2012 Jul 10;126(2):223-9.
Calkins H, Kuck KH, Cappato R, et al. Heart Rhythm Society Task Force on Catheter and Surgical Ablation of Atrial Fibrillation. **2012 HRS/EHRA/ECAS** expert consensus statement on **catheter and surgical ablation** of atrial fibrillation: recommendations for patient selection, procedural techniques, patient management and follow-up, definitions, endpoints, and research trial design. Heart Rhythm 2012 Apr;9(4):632-696.e21.
Packer DL, et al; STOP AF Cryoablation Investigators. **Cryoballoon ablation** of pulmonary veins for paroxysmal atrial fibrillation: first results of the North American Arctic Front (STOP AF) pivotal trial. J Am Coll Cardiol. 2013 Apr 23;61(16):1713-23.
Deshmukh A, Patel NJ, Pant S, et al. Inhospital **Complications Associated with Catheter Ablation** of Atrial Fibrillation in the United States between 2000-2010: Analysis of 93,801 Procedures. Circulation. 2013 Sep 23.
January CT, Wann ST, Alpert JS, et al. **2014 AHA/ACC/HRS guideline** for the management of patients with atrial fibrillation. A report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines and the Heart Rhythm Society: Executive summary. *J Am Coll Cardio;* 2014.
Curley M, Berger M, Roth, J, et al.Predictors of mortality and major in-hospital adverse events associated with electrophysiology catheter ablation. *JAMA Intern Med* 2014.
Kuck KH, Brugada J, Fürnkranz A, et al; **FIRE AND ICE** Investigators. **Cryoballoon or Radiofrequency Ablation** for Paroxysmal Atrial Fibrillation. N Engl J Med. 2016 Apr 4.
Calkins H, Willems S, Gerstenfeld EP, et al. **Uninterrupted Dabigatran versus Warfarin for Ablation in Atrial Fibrillation**. (**RE-CIRCUIT**) N Engl J Med. 2017 Mar 19.

[20] Cairns JA, Connolly S, McMurtry S, Stepenson M, Talajic M, and the CCS Atrial Fibrillation Guidelines Committee. Society Guidelines Canadian Cardiovascular Society Atrial Fibrillation Guidelines 2010: Prevention of Stroke and Systemic Thromboembolism in Atrial Fibrillation and Flutter. Can J Cardiol 2011;27:74-90.
[21] Skanes A, Healey J, Cairns J, et al. Focused **2012 Update of the CCS Atrial Fibrillation Guidelines**: Recommendations for Stroke Prevention and Rate/Rhythm Control. Can J Cardiol 2012; 28:125-136.
Verma A, Cairns JA, Mitchell LB, et al. CCS Atrial Fibrillation Guidelines Committee. **2014 focused update of the Canadian cardiovascular society (CCS) guidelines** for the management of atrial fibrillation. Can J Cardiol. 2014 Oct;30(10):1114-30.
Macle L, Cairns J, Leblanc K, et al. **CCS Atrial Fibrillation Guidelines** Committee. **2016 Focused Update** of the Canadian Cardiovascular Society Guidelines for the Management of Atrial Fibrillation. Can J Cardiol. 2016 Oct;32(10):1170-1185.

[22] Camm AJ, Kirchhof P, Lip GY, et al; European Heart Rhythm Association; European Association for Cario-Thoracic Surgery. Guidelines for the management of atrial fibrillation: the Task Force for the Management of Atrial Fibrillation of the European Society of Cardiology (**ESC**). Eur Heart J. **2010**;31:2369-429.
De Caterina R, Husted S, Wallentin L, et al. New oral anticoagulants in atrial fibrillation and acute coronary syndromes. ESC Working Group on Thrombosis—Task Force on Anticoagulants in Heart Disease position paper. J Am Coll Cardiol 2012; 59:1413-25.
Camm AJ, Lip GY, De Caterina R, et al. **2012 focused update of the ESC** Guidelines for the management of atrial fibrillation: An update of the 2010 ESC Guidelines for the management of atrial fibrillation * Developed with the special contribution of the European Heart Rhythm Association. Europace. 2012 Aug 24. ESC Updated 2012 Management of Atrial Fibrillation Guidelines.
http://www.escardio.org/guidelines-surveys/esc-guidelines/GuidelinesDocuments/Guidelines_Focused_Update_Atrial_Fib_FT.pdf
Kirchhof P, Benussi S, Kotecha D, Ahlsson A, et al. **2016 ESC Guidelines for the management of atrial fibrillation** developed in collaboration with EACTS. Europace. 2016 Nov;18(11):1609-1678.
Lip GYH, Collet JP, Haude M, Huber K. Management of antithrombotic therapy in AF patients presenting with ACS and/or undergoing PCI: A Summary of the Joint Consensus Document of the **European** Heart Rhythm Association (EHRA), **European Society of Cardiology** (**ESC**) Working Group on Thrombosis, European Association of Percutaneous Cardiovascular Interventions (EAPCI) and European Association of Acute Cardiac Care (ACCA) endorsed by the Heart Rhythm Society (HRS), Asia-Pacific Heart Rhythm Society (APHRS), Latin America Heart Rhythm Society (LAHRS), and Cardiac Arrhythmia Society of Southern Africa (CASSA). Eur Heart J. **2018** Aug 14;39(31):2847-2850.

[23] Fang MC, Go AS, Chang Y, et al. A New Risk Scheme to Predict Warfarin-Associated Hemorrhage. The **ATRIA** (Anticoagulation and Risk Factors in Atrial Fibrillation Study). J Am Coll Cardiol 2011;58:395-401.
[24] Ruiz-Gimenez N, Suarez C, Gonzalez R, et al. Predictive variables for major bleeding events in patients presenting with documented acute venous thromboembolism. Findings from the **RIETE** Registry. Thrombos Haemostas 2008;100:26-31.
[25] Gage BF, Yan Y, Milligan PE, et al. Clinical classification schemes for predicting hemorrhage: results from the National Registry of Atrial Fibrillation (NRAF). Am Heart J 2006;151:713-9.
[26] You JJ, Singer DE, et al. **Antithrombotic therapy for atrial fibrillation**: antithrombotic therapy and prevention of thrombosis, 9th ed: American College of Chest Physicians (**ACCP-AT9**)evidence -based clinical practice guidelines. Chest. 2012;141(2)(suppl):e531S-575S.
[27] E-cps, accessed 2017
[28] Micromedex, accessed on-line, 2017
[29] Giorgi MA, Arazi Hc, Gonzalez CD et al. Changing anticoagulant paradigms for atrial fibrillation: dabigatran, apixaban and rivaroxaban. Expert Opin. Pharmacother. 2001;12(4):567-77.
[30] ISMP Quarter Watch: January 9, 2013. Update on anticoagulants dabigatran and rivaroxaban. Available at: http://www.ismp.org/quarterwatch/pdfs/2012Q2.pdf. Accessed January 14, 2013.
[31] Connolly SJ, Ezekowitz MD, Yusuf S, Eikelboom PJ, Oldgren J, Parekh A, et al. Dabigatran versus Warfarin in Patients with Atrial Fibrillation. N Engl J Med 2009;361:1139-51. **{RE-LY}** RxFiles Trial Summary: http://www.rxfiles.ca/rxfiles/uploads/documents/RE-LY-Trial-Dabigatran.pdf
[32] Patel MR, Mahaffey KW, Garg J, et al. Rivaroxaban versus warfarin in nonvalvular atrial fibrillation. N Engl J Med. August 10, 2011. http://www.nejm.org/doi/full/10.1056/NEJMoa1009638 {**ROCKET-AF**} RxFiles Trial Summary: http://www.rxfiles.ca/rxfiles/uploads/documents/ROCKET-AF-Rivaroxaban.pdf
Goodman SG, Wojdyla DM, Piccini JP, MD; et al. Factors associated with major bleeding events: insights from the rivaroxaban once-daily oral direct factor Xa inhibition compared with vitamin K antagonism for prevention of stroke and embolism trial in atrial fibrillation (ROCKET AF). J Am Coll Cardiol 2013.
[33] FDA Advisory Committee Briefing Document: Rivaroxaban for the Prevention of Stroke and Non-Central Nervous System (CNS) Systemic Embolism in Patients With Atrial Fibrillation. August 2011. http://www.fda.gov/downloads/AdvisoryCommittees/CommitteesMeetingMaterials/Drugs/CardiovascularandRenalDrugsAdvisoryCommittee/UCM270797.pdf
[34] Granger CB, Alexander JH, McMurray JJV et al. Apixaban versus Warfarin in Patients with Atrial Fibrillation. (**ARISTOTLE**) N Engl J Med August 28, 2011 http://www.nejm.org/doi/pdf/10.1056/NEJMoa1107039
Alexander JH, Lopes RD, James S, et al. Apixaban with antiplatelet therapy after acute coronary syndrome (**Appraise-2**). N Engl J Med 2011 (5mg po bid: increased **major bleeding** without a significant reduction in recurrent ischemic events) {**ARISTOTLE**} (RxFiles Trial Summary: http://www.rxfiles.ca/rxfiles/uploads/documents/ARISTOTLE-AF-Apixaban.pdf)
Connolly SJ, Eikelboom J, Joyner C, et al. Apixaban in patients with atrial fibrillation. (**AVERROES**) N Engl J Med 2011;364:806–17.
Diener HC, Eikelboom J, Connolly SJ, et al. **Apixaban versus aspirin** in patients with atrial fibrillation and **previous stroke** or transient ischaemic attack: a predefined subgroup analysis from **AVERROES**, a randomised trial. Lancet Neurol 2012.
[35] e-cps, 2012
[36] Micromedex, 2012
[37] Dorian P, Connors P. Pharmacological and non pharmacological methods for rate control. Can J Cardiol 2005;21(suppl B):11B-14B.
[38] Borrello F, Beahan M, Klein L, et al. Reappraisal of beta-blocker therapy in the acute and chronic post-myocardial infarction period. Rev Cardiovasc Med. 2003;4 Suppl 3:S13-24.
[39] Vittorio TJ, Zolty R, Kasper ME, et al. Differential effects of carvedilol and metoprolol succinate on plasma norepinephrine release and peak exercise heart rate in subjects with chronic heart failure. J Cardiovasc Pharmacol Ther 2008;13:51-7
[40] Ulimoen SR, Enger S, et al. Comparison of Four Single-Drug Regimens on Ventricular Rate and Arrhythmia-Related Symptoms in Patients With Permanent Atrial Fibrillation. Am J Cardiol. 2012 Oct 27.
Personett HA, Smoot DL, Stollings JL, et al. Intravenous metoprolol versus diltiazem for rate control in noncardiac, nonthoracic postoperative atrial fibrillation. Ann Pharmacother. 2014 Mar;48(3):314-9.
[41] Doyle JF, Ho KM. Benefits and risks of long-term amiodarone therapy for persistent atrial fibrillation: a meta-analysis. Mayo Clinic Proceedings 2009 84(3):234-242
[42] Connolly SJ, Camm AJ, Halperin JL, et al. Dronedarone in high-risk permanent atrial fibrillation. (**PALLAS**) N Engl J Med 2011. DOI: 10.1056/NEJMoa1109867. http://www.theheart.org/article/1252319.do, Heartwire, July 12, 2011
[43] Permanent Atrial fibrillation Outcome Study Using Dronedarone on Top of Standard Therapy (**PALLAS**), http://clinicaltrials.gov/ct2/show/NCT01151137?term=pallas&rank=1, July 15, 2011
Hohnloser SH, Crijns HJ, van Eickels M, et al. Effect of **dronedarone** on cardiovascular events in atrial fibrillation. (**ATHENA**) N Engl J Med 2009;360:668-78.
Køber L, Torp-Pedersen C, McMurray JJ, et al. Increased mortality after **dronedarone** therapy for severe heart failure. (**ANDROMEDA**) N Engl J Med 2008;358:2678-87.
[44] Heuzey JY, De Ferrari GM, Radzik D, et al. A Short-Term, Randomized, Double-Blind, Parallel-Group Study to Evaluate the Efficacy and Safety of Dronedarone versus Amiodarone in Patients with Persistent Atrial Fibrillation: The **DIONYSOS** Study. J Cardiovasc Electrophysiol 2010;21:597-605.
[45] Fetsch T, Bauer P, Engberding R, et al. Prevention of atrial fibrillation after cardioversion: results of the PAFAC trial. Eur Heart J 2004;25:1385-94.
[46] Singh BN, Singh SN, Reda DJ et al. Amiodarone versus sotalol for atrial fibrillation. N Engl J Med 2005;352:1861-72.
[47] The Cardiac Arrhythmia Suppression Trial (**CAST**) Investigators, Preliminary Report: Effect of Encainide and Flecainide on Mortality in a Randomized Trial of Arrhythmia Suppression after Myocardial Infarction. N Engl J Med 1989; 321:406-412
[48] Shireman T, Mahnken J, Howard P, et al. Development of a contemporary bleeding risk model for elderly warfarin recipients. Chest 2006;130:1390-6.
[49] Kearon C, Ginsberg JS, Kovacs MJ, et al. Comparison of low-intensity warfarin therapy with conventional-intensity warfarin therapy for long-term prevention of recurrent venous thromboembolism. N Engl J Med 2003;349:631-9
[50] Kuijer P, Hutten B, Prins M et al. **Prediction of the risk of bleeding** during anticoagulant treatment for venous thromboembolism. Arch Intern Med. 1999;159:457-60.
[51] Beyth R, Quinn L, Landefeld C. Prospective evaluation of an index for **predicting the risk of major bleeding** in outpatients treated with warfarin. Am J Med 1998;105-91-9.
[52] Stiell IG, Macle L, and **CCS** Atrial Fibrillation Guidelines Committee. Society Guidelines Canadian Cardiovascular Society Atrial Fibrillation Guidelines 2010: Management of Recent-Onset Atrial Fibrillation and Flutter in the Emergency Depeartment. Can J Cardiol 2011;27:38-46.

Anticoagulation/Atrial Fibrillation (AFib): Notes on Outcome Comparison

Warf vs DOACs (NOACs): pros & cons for each - Loren Regier, Zack Dumont - www.RxFiles.ca – Revised Nov 2019

Note, the RE-LY trial data for Canada found warfarin had a time in therapeutic range (TTR) >70%.

1) **Stroke/Embolism**: absolute differences minimal when INR control with warfarin reasonable **(TTR=>65%)**.
2) Stroke/Embolism: Dabi 150mg BID vs Warf; NNT=88/~2yr; ITT (no difference with 110mg BID dose, but less bleeding); open label RCT. (Study pop: renal fx 30+, adherence likely better than normal conditions, etc.)
3) Stroke/Embolism: Riva 20mg daily vs Warf; non-inferiority trial design (ITT analysis favoured Riva but did not achieve superiority); double-blind RCT. (Study pop: limitations similar to RE-LY.)
4) Stroke/Embolism: Apix 5mg BID vs Warf; NNT=167/~2yrs; ITT; double-blind RCT. Also ↓ death NNT=132/~2yr. (Study pop: limitations similar to RE-LY.)
5) Stroke/Embolism: Edox 60mg daily vs Warf was noninferior (ITT analysis); superior NNT=141/~2.8yr (mITT analysis) (no difference with 30mg daily dose, but less bleeding); open label RCT. (Study pop: limitations similar to RE-LY)
6) **ICH**: Dabi vs Warf; NNT=116/~2yr
7) ICH: Riva vs Warf; NNT=250/~2yr
8) ICH: Apix vs Warf; NNT=128/~2yr
9) ICH: Edox 60mg vs Warf; NNT=99/~2.8yr; 30mg vs Warf; NNT=77/~2.8yr

Note: Rate of ICH in AFib less in Canada than in trials. Gomes T, CMAJ 2012. Thus significance of this would be less in CDN context (ie. NNT would be much higher).

10) **GI Bleed**: Dabi vs Warf; NNH=100/~2yr
11) GI Bleed: Riva vs Warf; NNH=100/~2yrs
12) GI Bleed: Apix vs Warf; no difference
13) GI Bleed: Edox 60mg vs Warf; NNH=166/~2.8yr; 30mg vs Warf; NNT=115/~2.8yr
14) **Major Bleed**: Dabi 150mg BID vs Warfarin; no difference; however 110mg BID had reduced major bleeding (NNT=77/~2yr) but also less benefit.
15) Major Bleed: Riva vs Warf; no difference
16) Major Bleed: Apix vs Warf; NNT=67/~2yr
17) Major Bleed: Edox 60mg daily vs Warf; NNT=67/~2.8yr; 30mg daily; NNT=26/~2.8yr (but also less benefit).
18) **Manage Bleeding**: Warfarin - real world experience, & options include PCC & Vitamin K for reversal. New agents have less experience. Dabi has an antidote (Idarucizumab **PRAXBIND CDN'16, FDA'15**). Factor Xa inhibitors also have an antidote (Andexanet alfa **ANDEXXA FDA'18**). Shorter half life of new agents means less time until anti-coagulation status returns to normal. Life-threatening/ fatal bleed was less in dabi / riva trials. However, ISMP Jan 2013 found that bleeds with Dabi 5x more fatal than bleeds with warfarin. Peri-procedural: less experience in managing DOACs.
19) **MI Risk**: Dabi vs Warf; initial ↑ risk of borderline significance (p=0.048); reanalysis slightly different & non-significant (p=0.06 both doses). {↑ rates of bleeding & thrombotic AE in AFib with mechanical valves RE-ALIGN} Concerns. Controversial. [Warf considered protective.]
20) **Discontinuation** rates vs Warf: lower with Apix (NNT=45/~2yrs); higher with Dabi (NNH=25/~2yr); also more dyspepsia with Dabi (NNH=18/2yr).
21) All new agents lack study & experience in patients with decreased **renal Fx**. Dabi is contraindicated (CI) if CrCl <30ml/min. Warfarin can be used. Since AFib patients often older, impaired renal Fx an issue. Edoxaban & CrCl >95mL/min: ↑ risk of ischemic stroke[FDA], therefore avoid.
22) **Economic** review found new anticoagulants more costly than warfarin even after consideration for cost of INR monitoring was built in. However, "soft" indirect costs (e.g. time/travel to the patient) not included & may be assessed individually. Direct cost/month: Warf ~**$15**, Dabi **$120** (but generic g is $85 ✗⊗), Riva **$105**, Apix **$118**. Edoxaban **$104**, but is the newest in Canada.
23) **Half life** of new agents is shorter. "**Cons**" of this are that Dabi & Apix require BID dose; **poor compliance** (missed doses) will result in earlier loss of anticoagulation status; "**Pros**" are earlier achievement of anticoagulation after starting & return to normal after holding if over-coagulated.
24) **INR** "Con" -inconvenience factor; "Pro" -ability to assess anticoagulation status balance risk of stroke vs bleed. ? Dabi level.
25) Warfarin has **60yrs "real world" experience**; new agents have about 10yrs & in limited populations. This factor will gradually change over the next few yrs.
26) **If Valvular AFib**: Warf OK, DOACs (NOACs) not indicated; Dabi CI

(This editorial synthesis based on interpretation of data from RCTs (RELY, ROCKET-AF, ARISTOTLE, ENGAGE-AF), CADTH reports, product monographs & clinical consultation. Only direct comparisons of individual DOACs (NOACs) with warfarin have been studied. Trials designed for non-inferiority, with option for superiority analysis. Comparisons between DOACs (NOACs) have the inherent limitations of indirect comparisons. However, indirect comparisons are often required when decisions need to be made & direct comparisons are not available, nor likely to be done in the near future.)

☎ = Exception Drug Status in SK ✗ = Non-formulary in SK ✆ =prior approval by NIHB ⊗=not covered NIHB ▼= covered NIHB ç=scored tab **AHF**=acute heart failure **AMI**=acute myocardial infarction **ARNI**=angiotensin receptor-neprilysin inhibitor **BUN**=blood urea nitrogen **CA**=cancer **CCB**=calcium channel blocker **CV**=cardiovascular **ED**=erectile dysfunction **eGFR**=estimated glomerular filtration rate **HA**=headache **HCTZ**=hydrochlorothiazide **HR**=heart rate **K^+**=potassium **JVP**=jugular venous pressure **LBW**=lean body weight **LD**=loading dose **MD**=maintenance dose **NNT**=number needed to treat **NP**=natriuretic peptide **NS**=not significant **PAD**=peripheral arterial disease **PI**=Placebo **rxn**=reaction **SSS**=sick sinus syndrome **S&Sx**=signs & symptoms **SCr**= serum creatinine **TG**=triglycerides

Brain Natriuretic Peptide (BNP)/amioterminal fragment of propeptide BNP (NT-proBNP) has diagnostic value for both types of HF and is recommended where available, when diagnosis in unclear; may also be used in patients with established HF for prognostic stratification. The use of BNP or NT-BNP in ambulatory HF patients with systolic dysfunction may be considered to decrease HF-related hospitalizations & potentially reduce mortality (benefit uncertain in those >75 years of age).[2, 3]

Table: Brain natriuretic peptide (BNP mainly secreted by ventricular myocardium**) & prohormone of BNP (NT-proBNP** longer half life, affected by renal fx**) assay cut-off points for the diagnosis of HF** [3]

	Age	HF unlikely	HF possible but consider alternative diagnoses	HF very likely
BNP (pg/mL)	**All**	**<100**	**100-500**	**>500**
NT-proBNP (pg/mL)	**<50**	**<300**	**300-450**	**>450**
	50-75	**<300**	**450-900**	**>900**
	>75	**<300**	**900-1800**	**>1800**

Recent Heart Failure Trials

Trial	Design	Treatment Arms	Population	Contribution to Current Knowledge
TRED-HF (2018)	Open-label, randomized, single-arm crossover phase, single UK centre	1) HF treatment withdrawal arm (n=25) 2) Continued HF treatment x 6 months, then HF treatment withdrawal (n=26)	Recovered dilated cardiomyopathy	- 40% of patients relapsed within 8 weeks of discontinuing their HR medications - Additional 10% required re-initiation of HF medications for other indications (e.g. HTN, AF) - No difference in safety between treatment arms - HF treatment should continue indefinitely in patients who have recovered HF due to the risk of relapse
PIONEER-HF (2018)	Multicentre (USA), double-blind, randomized, active-controlled trial	1) Entresto 97mg / 103mg po BID (target dose) (n=440) 2) Enalapril 10mg BID (target dose) (n=441)	HF-rEF hospitalized for acute decompensated HF	- Entresto treatment arm had a greater reduction in NTproBNP at weeks 4 & 8 compared to baseline, vs enalapril: -46.7% vs -25.3% (95% CI 0.63 to 0.81, p<0.001) - No difference in safety between treatment arms - Exploratory secondary analysis: Entresto treatment arm had a lower rate of HF rehospitalizations versus enalapril (8% vs 13.8%, ARR 5.8% - but underpowered for this endpoint)
PARAGON-HF (2019)	Randomized, double-blind, active comparator multisite trial	3) Entresto 97mg / 103mg po BID (target dose) (n=2419) 4) Valsartan 103mg po BID (target dose) (n=2403)	HFpEF (≥45%), NYHA II-IV on diuretics	- Entresto did not significantly reduce the risk of HF hospitalizations & CV death, compared to valsartan.

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References: RxFiles Heart Failure

[1] Arnold JMO, Liu P, Demers C, et al. Canadian Cardiovascular Society consensus conference recommendations on heart failure 2006: Diagnosis & management. Can J Cardiol 2006;22(1):23-45.

[2] Arnold JMO, Howlett JG, Dorian P, et al. **Canadian Cardiovascular Society-CCS** Consensus Conference recommendations on heart failure update 2007: Prevention, management during intercurrent illness or acute decompensation, and use of biomarkers. Can J Cardiol 2007;23(1):21-45.

Malcom J, Arnold O, Howlett JG, Ducharme A, Ezekowitz JA, Gardner MJ, Giannetti N, Haddad H, Heckman GA, Isaac D, Jong P, Liu P, Mann E, McKelvie RS, Moe GW, Svendsen AM, Tsuyuki RT, O'Halloran K, Ross HJ, Sequeira EJ, White M; Canadian Cardiovascular Society. Canadian Cardiovascular Society Consensus Conference guidelines on heart failure--2008 update: best practices for the transition of care of heart failure patients, and the recognition, investigation and treatment of cardiomyopathies. Can J Cardiol. 2008 Jan;24(1):21-40.

Howlett JG, McKelvie RS, Arnold JM, et al. Canadian Cardiovascular Society. Canadian Cardiovascular Society Consensus Conference guidelines on heart failure, update 2009: diagnosis and management of right-sided heart failure, myocarditis, device therapy and recent important clinical trials. Can J Cardiol. 2009 Feb;25(2):85-105.
HFSA: Heart Failure Society of America, Lindenfeld J, Albert NM, Boehmer JP, et al. Evaluation of patients for ventricular dysfunction & heart failure: **HFSA 2010 comprehensive heart failure** practice guideline. J Card Fail **2010** Jun;16(6):e44-56. http://www.heartfailureguideline.org/home/3
McKelvie RS, Moe GW, Cheung A, et al. The 2011 Canadian cardiovascular society heart failure management guidelines update: focus on **sleep apnea, renal dysfunction, mechanical circulatory support, and palliative care**. Can J Cardiol. 2011 May-Jun;27(3):319-38.
Howlett JG, McKelvie RS, Costigan J, et al; Canadian Cardiovascular Society. The 2010 Canadian Cardiovascular Society guidelines for the diagnosis and management of heart failure update: Heart failure in **ethnic minority populations, heart failure and pregnancy, disease management, and quality improvement/assurance programs**. Can J Cardiol. 2010 Apr;26(4):185-202.
McMurray JJV, Adamopoulos S, Anker SD, et al. **ESC guidelines** for the diagnosis and treatment of acute and chronic heart failure **2012**: The Task Force for the Diagnosis and Treatment of Acute and Chronic Heart Failure 2012 of the European Society of Cardiology. Developed in collaboration with the Heart Failure Association (HFA) of the ESC. Eur Heart J 2012; DOI:10.1093/eurheartj/ehs104.
Tracy CM, Epstein AE, Darbar D, et al. 2012 **ACCF/AHA/HRS** Focused Update of the 2008 guidelines for **device-based therapy of cardiac rhythm abnormalities**. A report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. Developed in collaboration with the American Association for Thoracic Surgery, Heart Failure Society of America, and Society of Thoracic Surgeons. J Am Coll Cardiol 2012.
McKelvie RS, Moe GW, Ezekowitz JA, et al. The **2012 Canadian Cardiovascular Society (CCS) heart failure management guidelines** update: focus on **acute and chronic heart failure**. Can J Cardiol. 2013 Feb;29(2):168-81. http://www.onlinecjc.ca/article/S0828-282X(12)01379-7/fulltext
Yancy CW, Jessup M, Bozkurt B, et al. **2013 ACCF/AHA Guideline for the Management of Heart Failure**: A Report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. J Am Coll Cardiol. 2013 Jun 3.
Moe G, Ezekowitz J, O'Meara E, et al. **The 2014 Canadian Cardiovascular Society Heart Failure Management Guidelines Focus Update: Anemia, Biomarkers & Recent Therapeutic Trial Implications**. Canadian Journal of Cardiology 2015; 31:3-16.
Ponikowski P, Voors AA, Anker SD, et al. **2016 ESC guidelines for the diagnosis and treatment of acute and chronic heart failure**: The Task Force for the diagnosis and treatment of acute and chronic heart failure of the European Society of Cardiology (ESC). Developed with the special contribution of the Heart Failure Association (HFA) of the ESC. Eur Heart J 2016.
Yancy CW, Jessup M, Bozkurt B, et al. 2016 **ACC/AHA/HFSA focused update on new pharmacological therapy for heart failure: an update of the 2013 ACCF/AHA guideline** for the management of heart failure: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Clinical Practice Guidelines and the Heart Failure Society of America. Circulation. 2016.
Yancy CW, Jessup M, Bozkurt B, et al. **2017 ACC/AHA/HFSA Focused Update** of the 2013 ACCF/AHA Guideline for the **Management of Heart Failure**: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines and the Heart Failure Society of America. Circulation. 2017 Apr 28.
Ezekowitz JA, O'Meara E, McDonald M, et al. **2017 Comprehensive Update of the Canadian Cardiovascular Society** (**CCS**) Guidelines for the Management of Heart Failure. Canadian Journal of Cardiology. 2017.

[3] Guidelines & Protocols Advisory Committee, Heart Failure Care, February 15, 2008; accessed online www.OntarioMD.ca on June 15, 2008.
Gheorghiade Mihai, Braunwald Eugene. A Proposed Model for **Initial Assessment and Management of Acute Heart Failure** Syndromes. JAMA. 2011;305(16):1702-1703.doi:10.1001/jama.2011.515
Long B, Koyfman A, Gottlieb M. Management of Heart Failure in the Emergency Department Setting: An Evidence-Based Review of the Literature. J Emerg Med. 2018 Sep 26.

[4] http://www.saltinstitute.org/teaspoon.html, accessed April 30, 2008
[5] http://www.thecaregroup.com/Education/Education%20CD/PDF%20Files/Average%20Sodium%20Content%20of%20Foods.pdf, accessed April 30, 2008
[6] http://www.geocities.com/Heartland/4269/nutrition.html, accessed April 30, 2008
[7] http://www.mcdonalds.ca/en/food/calculator.aspx, accessed April 30, 2008
Strazzullo Pasquale, D'Elia Lanfranco, et al. **Salt** intake, stroke, and cardiovascular disease: meta-analysis of prospective studies. BMJ 2009;339:b4567, doi: 10.1136/bmj.b4567 (24 November 2009).
[8] Garg R. Yusuf S. Overview of randomized trials of angiotensin-converting enzyme inhibitors on mortality and morbidity in patients with heart failure. Collaborative Group on ACE Inhibitor Trials.[see comment][erratum appears in JAMA 1995 Aug 9;274(6):462]. [Journal Article. Meta-Analysis] JAMA. 273(18):1450-6, 1995 May 10.
[9] Clelan JGF, Tendera M, Adamus J et al. The perindopril in elderly people with chronic heart failure (PeP-CHF) study. Eur Heart J 2006;27:2338-45.
[10] Borrello F, Beahan M, Klein L, et al. Reappraisal of beta-blocker therapy in the acute and chronic post-myocardial infarction period. Rev Cardiovasc Med. 2003;4 Suppl 3:S13-24.
[11] Chen ZM, Pan HC, Chen YP, et al.; **COMMIT** (ClOpidogrel and Metoprolol in Myocardial Infarction Trial) collaborative group. Early intravenous then oral metoprolol in 45,852 patients with acute myocardial infarction: randomised placebo-controlled trial. Lancet. 2005 Nov 5;366(9497):1622-32. Second Chinese Cardiac Study COMMIT/CCS-2. Mean age 61, Fibrinolytic therapy 54%, Metoprolol 5mg IV over 2-3mins x 3 if HR & BP ok, then 15mins later 50mg po q6h Day 0-1, then 200mg controlled release od vs placebo x ~15days. ↓Reinfarction 2 vs 2.5%, ↓Ventricular fibrilation 2.5 vs 3 %, BUT ↑Cardiogenic shock 5 vs 3.9% (risk more with heart failure, systolic BP <120 & in the first 24hrs). INTERPRETATION: The use of early beta-blocker therapy in acute MI reduces the risks of reinfarction & ventricular fibrillation, but increases the risk of cardiogenic shock, esp. during the first day or so after admission. Consequently, it might generally be prudent to consider starting **beta-blocker therapy in hospital only when the haemodynamic condition after MI has stabilised**. (InfoPOEMs: The early use of metoprolol in patients with acute myocardial infarction who are also receiving thrombolytics and aspirin provides no short-term benefit compared with placebo. Since the early use, however, increases the risk of cardiogenic shock, it may be wise to delay starting metoprolol until the patient is hemodynamically stable. (LOE = 1b)).
[12] Packer M. Coats AJ. Fowler MB. Katus HA. Krum H. Mohacsi P. Rouleau JL. Tendera M. Castaigne A. Roecker EB. Schultz MK. DeMets DL. Carvedilol Prospective Randomized Cumulative Survival Study Group. Effect of carvedilol on survival in severe chronic heart failure.[see comment]. [Clinical Trial. Journal Article. Multicenter Study. Randomized Controlled Trial. Research Support, Non-U.S. Gov't] New England Journal of Medicine. 344(22):1651-8, 2001 May 31.
[13] Anonymous. The Cardiac Insufficiency Bisoprolol Study II (CIBIS-II): a randomised trial.[see comment]. [Clinical Trial. Comparative Study. Journal Article. Multicenter Study. Randomized Controlled Trial. Research Support, Non-U.S. Gov't] Lancet. 353(9146):9-13, 1999 Jan 2.
[14] Poole-Wilson PA. Swedberg K. Cleland JG. Di Lenarda A. Hanrath P. Komajda M. Lubsen J. Lutiger B. Metra M. Remme WJ. Torp-Pedersen C. Scherhag A. Skene A. Carvedilol Or Metoprolol European Trial Investigators. Comparison of carvedilol and metoprolol on clinical outcomes in patients with chronic heart failure in the Carvedilol Or Metoprolol European Trial (**COMET**): randomised controlled trial.[see comment]. [Clinical Trial. Comparative Study. Journal Article. Randomized Controlled Trial. Research Support, Non-U.S. Gov't] Lancet. 362(9377):7-13, 2003 Jul 5
[15] **MERIT-HF** Study Group. Effect of metoprolol CR/XL in chronic heart failure: Metoprolol CR/XL Randomised Intervention Trial in Congestive Heart Failure (MERIT-HF). Lancet 1999;353:2001-07
[16] Cohn JN. Tognoni G. Valsartan Heart Failure Trial Investigators. A randomized trial of the angiotensin-receptor blocker valsartan in chronic heart failure.[see comment][summary for patients in J Card Fail. 2002 Apr;8(2):56-8.Clinical Trial. Journal Article. Multicenter Study. Randomized Controlled Trial. Research Support, Non-U.S. Gov't.New England Journal of Medicine. 345(23):1667-75, 2001 Dec 6.
Anand IS, Bishu K, Rector TS, et al. Proteinuria, Chronic Kidney Disease, and the Effect of an Angiotensin Receptor Blocker in Addition to an Angiotensin-Converting Enzyme Inhibitor in Patients With Moderate to Severe Heart Failure. Circulation. 2009 Oct 5.
[17] Granger CB. McMurray JJ. Yusuf S. Held P. Michelson EL. Olofsson B. Ostergren J. Pfeffer MA. Swedberg K. **CHARM** Investigators and Committees. Effects of candesartan in patients with chronic heart failure and reduced left-ventricular systolic function intolerant to angiotensin-converting-enzyme inhibitors: the CHARM-Alternative trial.[see comment]. [Clinical Trial. Comparative Study. Journal Article. Randomized Controlled Trial. Research Support, Non-U.S. Gov't] Lancet. 362(9386):772-6, 2003 Sep 6
Eklind-Cervenka M, Benson L, Dahlström U, et al. Association of **candesartan vs losartan** with all-cause mortality in patients with heart failure. JAMA 2011; 305:175-182.
[18] McMurray JJ. Ostergren J. Swedberg K. Granger CB. Held P. Michelson EL. Olofsson B. Yusuf S. Pfeffer MA. CHARM Investigators and Committees. Effects of candesartan in patients with chronic heart failure and reduced left-ventricular systolic function taking angiotensin-converting-enzyme inhibitors: the CHARM-Added trial.[see comment]. [Clinical Trial. Comparative Study. Journal Article. Multicenter Study. Randomized Controlled Trial. Research Support, Non-U.S. Gov't] Lancet. 362(9386):767-71, 2003 Sep 6.
[19] Pitt B. Poole-Wilson PA. Segal R. Martinez FA. Dickstein K. Camm AJ. Konstam MA. Riegger G. Klinger GH. Neaton J. Sharma D. Thiyagarajan B. Effect of losartan compared with captopril on mortality in patients with symptomatic heart failure: randomised trial--the Losartan Heart Failure Survival Study **ELITE II**.[see comment]. [Clinical Trial. Comparative Study. Journal Article. Multicenter Study. Randomized Controlled Trial. Research Support, Non-U.S. Gov't] Lancet. 355(9215):1582-7, 2000 May 6.
[20] Massie BM, Carson PE, McMurray JJ, Komajda M, McKelvie R, Zile MR, Anderson S, Donovan M, Iverson E, Staiger C, Ptaszynska A; the **I-PRESERVE** Investigators. Irbesartan in Patients with Heart Failure and Preserved Ejection Fraction. N Engl J Med. 2008 Nov 11. [Epub ahead of print]
Zile MR, Gaasch WH, Anand IS, et al. Mode of Death in Patients With Heart Failure and a Preserved Ejection Fraction. Results From the Irbesartan in Heart Failure With Preserved Ejection Fraction Study (I-Preserve) Trial. Circulation. 2010 Mar 15.
[21] Granger CB, McMurray JJ, Yusuf S, et al. CHARM Investigators and Committees. Effects of candesartan in patients with chronic heart failure and reduced left-ventricular systolic function intolerant to angiotensin-converting-enzyme inhibitors: the **CHARM-Alternative** trial. Lancet. 2003 Sep 6;362(9386):772-6. (Granger BB, et al.; for the CHARM investigators. Adherence to candesartan and placebo and outcomes in chronic heart failure in the CHARM programme: double-blind, randomised, controlled clinical trial. Lancet. 2005 Dec 10;366(9502):2005-2011.)
[22] Effectiveness of spironolactone added to an angiotensin-converting enzyme inhibitor and a loop diuretic for severe chronic congestive heart failure (the Randomized Aldactone Evaluation Study [**RALES**]). Am J Cardiol. 1996 Oct 15;78(8):902-7. Pitt B, Zannad F, Remme WJ, Cody R, Castaigne A, Perez A, Palensky J, Wittes J. The effect of spironolactone on morbidity and mortality in patients with severe heart failure. Randomized Aldactone Evaluation Study Investigators. N Engl J Med. 1999 Sep 2;341(10):709-17. Juurlink DN, Mamdani MM, Lee DS, Kopp A, Austin PC, Laupacis A, Redelmeier DA. Rates of hyperkalemia after publication of the Randomized Aldactone Evaluation Study. N Engl J Med. 2004 Aug 5;351(6):543-51.

[23] Taylor AL. Ziesche S. Yancy C. Carson P. D'Agostino R Jr. Ferdinand K. Taylor M. Adams K. Sabolinski M. Worcel M. Cohn JN. African-American Heart Failure Trial Investigators. Combination of isosorbide dinitrate and hydralazine in blacks with heart failure.[see comment][erratum appears in N Engl J Med. 2005 Mar 24;352(12):1276]. [Clinical Trial. Journal Article. Multicenter Study. Randomized Controlled Trial. Research Support, Non-U.S. Gov't] New England Journal of Medicine. 351(20):2049-57, 2004 Nov 11.

[24] Anonymous. The effect of digoxin on mortality and morbidity in patients with heart failure. The Digitalis Investigation Group.[see comment]. [Clinical Trial. Journal Article. Multicenter Study. Randomized Controlled Trial] New England Journal of Medicine. 336(8):525-33, 1997 Feb 20.

[25] Rathore SS, Curtis JP, Wang Y, Bristow MR, Krumholz HM. Association of serum digoxin concentration and outcomes in patients with heart failure. **DIG study**. JAMA. 2003 Feb 19;289(7):871-8.

[26] Adams KF Jr, Patterson JH, Gattis WA, O'Connor CM, Lee CR, Schwartz TA, Gheorghiade M. Relationship of serum digoxin concentration to mortality and morbidity in **women** in the digitalis investigation group trial: a retrospective analysis. **DIG study.** J Am Coll Cardiol. 2005 Aug 2;46(3):497-504.

Rathore SS, Wang Y, Krumholz HM. Sex-based differences in the effect of digoxin for the treatment of heart failure. N Engl J Med. 2002 Oct 31;347(18):1403-11.

Gheorghiade M, Braunwald E. Reconsidering the Role for Digoxin in the Management of Acute Heart Failure Syndromes. JAMA. 2009 Nov 18;302(19):2146-2147.

Chan, Kevin E., Lazarus, J. Michael, Hakim, Raymond M. Digoxin Associates with Mortality in **ESRD**. J Am Soc Nephrol 2010 21: 1550-1559.

Georgiopoulou VV, Kalogeropoulos AP, Giamouzis G, et al. Digoxin therapy does not improve outcomes in patients with advanced heart failure on contemporary medical therapy. Circ Heart Fail. 2009;2:90 –97.

Additional references:

Abdelhamid AS, Brown TJ, Brainard JS, et al. **Omega-3 fatty acids for the primary and secondary prevention of cardiovascular disease**. Cochrane Database of Systematic Reviews 2018, Issue 7. Art. No.: CD003177. This is the most extensive systematic assessment of effects of omega-3 fats on cardiovascular health to date. Moderate- and high-quality evidence suggests that increasing EPA and DHA has little or no effect on mortality or cardiovascular health (evidence mainly from supplement trials). Previous suggestions of benefits from EPA and DHA supplements appear to spring from trials with higher risk of bias. Low-quality evidence suggests ALA may slightly reduce CVD event risk, CHD mortality and arrhythmia.

Abdelrahman M, Subzposh FA, Beer D, et al. Clinical Outcomes of **His Bundle Pacing Compared to Right Ventricular Pacing**. J Am Coll Cardiol. 2018 Mar 5.

Abdel-Qadir HM, Tu JV, Yun L, Austin PC, Newton GE, Lee DS. Diuretic dose and long-term outcomes in elderly patients with **heart failure** after hospitalization. Am Heart J. 2010 Aug;160(2):264-271.e1.

Abdul-Rahim AH, Perez A-C, Fulton RL, et al. **Risk of stroke** in chronic heart failure patients without atrial fibrillation: analysis of the CORONA and GISSI-HF trials. Circulation. 2015;131:1486–1494.

Abdul-Rahim AH, Perez AC, MacIsaac RL, et al. **Risk of stroke in chronic heart failure patients with preserved ejection fraction**, but without atrial fibrillation: analysis of the **CHARM-Preserved** and **I-Preserve** trials. Eur Heart J. 2017 Mar 7;38(10):742-750.

Abraham WT, Fonarow GC, Albert NM, Stough WG, Gheorghiade M, Greenberg BH, O'Connor CM, Sun JL, Yancy CW, Young JB; **OPTIMIZE-HF** Investigators and Coordinators. Predictors of in-hospital mortality in patients hospitalized for heart failure: insights from the Organized Program to Initiate Lifesaving Treatment in Hospitalized Patients with Heart Failure (OPTIMIZE-HF). J Am Coll Cardiol. 2008 Jul 29;52(5):347-56.

Abraham WT, Adamson PB, Bourge RC, et al, for the **CHAMPION** Trial Study Group. **Wireless pulmonary artery haemodynamic monitoring** (CardioMEMS) in chronic heart failure: a randomised controlled trial. Lancet 2011; published online Feb 10. DOI:10.1016/S0140-6736(11)60101-3.

Abraham WT, Stevenson LW, Bourge RC, et al. for the **CHAMPION** Trial Study Group. Sustained efficacy of **pulmonary artery pressure** to guide adjustment of chronic heart failure therapy: complete follow-up results from the CHAMPION randomised trial. Lancet 2015; published online Nov 8.

Adelstein E, Schwartzman D, Jain S, et al. Effect of **Digoxin on Shocks in Cardiac Resynchronization Therapy-Defibrillator Patients** With Coronary Artery Disease. Am J Cardiol. 2013 Dec 25

Afonso L, Arora NP, Mahajan N, et al. Comparison of Patients With **Peripartum Heart Failure** and Normal (≥55%) Versus Low (<45%) Left Ventricular Ejection Fractions. Am J Cardiol. 2014 May 2.

Agarwal M, Apostolakis S, Lane DA, et al. The Impact of Heart Failure and Left Ventricular Dysfunction in Predicting **Stroke, Thromboembolism, and Mortality in Atrial Fibrillation** Patients: A Systematic Review. Clin Ther. 2014 Aug 18.

Agarwal A, Bahiru E, Yoo SGK, et al. **Hospital-based quality improvement interventions** for patients with heart failure: a systematic review. Heart. 2019 Mar;105(6):431-438.

Agarwal V, Vittinghoff E, Whitman IR, et al. Relation Between **Ventricular Premature Complexes** and Incident Heart Failure. Am J Cardiol. 2017 Apr 15;119(8):1238-1242.

Agha G, Loucks EB, Tinker LF, et al. **Healthy lifestyle** and decreasing risk of heart failure in women: The Women's Health Initiative (WHI) Observational Study. *J Am Coll Cardiol* 2014; 64:1777–1785.

Aguirre Dávila L, Weber K, Bavendiek U, et al. **Digoxin-mortality**: randomized vs. observational comparison in the DIG trial. Eur Heart J. 2019 Jun 18.

AHA Writing Group Members, Roger VL, Go AS, Lloyd-Jones DM, et al; on behalf of the American Heart Association Statistics Committee and Stroke Statistics Subcommittee, Roger VL, Turner MB; On behalf of the American Heart Association Heart Disease and Stroke Statistics Writing Group. Executive Summary: **Heart Disease and Stroke Statistics**—2011 Update: A Report From the American Heart Association. Circulation. 2011 Feb 1;123(4):459-463.

Ahmad K, Chen EW, Nazir U, et al. Regional Variation in the **Association of Poverty and Heart Failure Mortality** in the 3135 Counties of the United States. J Am Heart Assoc. 2019 Sep 17;8(18):e012422.

Ahmad T, Fiuzat M, Pencina MJ, et al. Charting a **roadmap for heart failure biomarker** studies. JACC Heart Fail. 2014 Jun 5.

Ahmad T, Jackson K, Rao VS, et al. **Worsening Renal Function** in Acute Heart Failure Patients **Undergoing Aggressive Diuresis** is Not Associated with Tubular Injury. Circulation. 2018 Jan 19.

Ahmad T, Patel CB, Milano CA, Rogers JG. When the heart runs out of heartbeats: treatment **options for refractory end-stage heart failure**. Circulation. 2012 Jun 12;125(23):2948-55.

Ahmed, A, Bourge RC, Fonarow GC, et al. **Digoxin use and lower 30-day all-cause readmission** for Medicare beneficiaries hospitalised for heart failure. Am J Med 2014;127:61–70.

Ahn MS, Yoo BS, Yoon J, et al. **Guideline-directed therapy at discharge** in patients with heart failure and atrial fibrillation. Heart. 2019 Sep 6.

Aimo A, Januzzi JL Jr, Vergaro G, et al. **Prognostic Value of High-Sensitivity Troponin T** in Chronic Heart Failure: An Individual Patient Data Meta-Analysis. Circulation.2018 Jan 16;137(3):286-297.

Al-Damluji MS, Dzara K, Hodshon B, et al. Hospital variation in quality of **discharge summaries** for patients hospitalized with heart failure exacerbation. Circ Cardiovasc Qual Outcomes 2015.

Al-Damluji MS, Dzara K, Hodshon B, et al. Association of **discharge summary quality with readmission** risk for patients hospitalized with heart failure exacerbation: Data report. Circ Cardiovasc Qual Outcomes 2015.

Al-Khatib SM, Hellkamp AS, Fonarow GC, et al. Association between **prophylactic implantable cardioverter-defibrillators** and survival in patients with left ventricular ejection fraction between 30% and 35%. JAMA. 2014 Jun 4;311(21):2209-15.

Al-Khatib SM, Friedman P, Ellenbogen KA. **Defibrillators: Selecting the Right Device** for the Right Patient. Circulation. 2016 Nov 1;134(18):1390-1404

Al-Khatib SM, Fonarow GC, Joglar JA, et al. **Primary Prevention Implantable Cardioverter Defibillators** in Patients With Nonischemic Cardiomyopathy: A Meta-analysis. JAMA Cardiol. 2017 Mar 29.

Al-Mohammad A, Mant J, Laramee P, et al.; Chronic Heart Failure Guideline Development Group. **Diagnosis and management** of adults with chronic heart failure: summary of updated **NICE guidance**. BMJ. 2010 Aug 25;341:c4130. doi: 10.1136/bmj.c4130.

Al Suwaidi J, Al-Qahtani A, Asaad N et al. Comparison of **women versus men** hospitalized with heart failure (from a 20-year registry in a middle-eastern country 1991-2010). Am J Cardiol. 2012 Feb 1;109(3):395-400.

Akinkuolie AO, Aleardi M, Ashaye AO, et al. **Height** and Risk of Heart Failure in the Physicians' Health Study. Am J Cardiol. 2012 Jan 3.

Akintoye E, Briasoulis A, Egbe A, et al. Effect of **Hospital Ownership** on **Outcomes** of Heart Failure Hospitalization. Am J Cardiol. 2017 Jun 15.

Akintoye E, Briasoulis A, Egbe A, et al. Regional Variation in Mortality, Length of Stay, Cost, and Discharge Disposition Among Patients Admitted for Heart Failure in the United States. Am J Cardiol. 2017 Jun 15.

Akoudad S, Abkenari L, Schaer BA, et al. Comparison of Multivariate Risk Estimation Models to Predict **Prognosis in Patients with Implantable Cardioverter-Defibrillators** with or without Cardiac Resynchronization Therapy. Am J Cardiol. 2017.

Al-Naher A, Wright DJ, Devonald MAJ, et al. **Renal function monitoring** in heart failure - what is the optimal frequency? A narrative review. Br J Clin Pharmacol. 2017 Sep 13

Alba GA et al. Diagnostic and prognostic utility of **procalcitonin** in patients presenting to the emergency department with dyspnea. Am J Med 2016 Jan; 129:96.

Albert Nancy M.; Yancy Clyde W.; Liang Li; et al.Use of Aldosterone Antagonists (**spironolactone**) in Heart Failure. JAMA. 2009;302(15):1658-1665.

Aldahl M, Jensen ASC, Davidsen L, et al. Associations of serum **potassium** levels with **mortality** in chronic heart failure patients. European Heart Journal. 2017;0,1-7

Alexandre J, Foucault A, Coutance G et al. **Digitalis intoxication** induced by an acute accidental poisoning by **lily of the valley**. Circulation. 2012 Feb 28;125(8):1053-5.

Alehagen Urban, Dahlström Ulf, Rehfeld Jens F., et al. Association of **Copeptin and N-Terminal proBNP** Concentrations With Risk of Cardiovascular Death in Older Patients With Symptoms of Heart Failure. JAMA. 2011;305(20):2088-2095.doi:10.1001/jama.2011.666

AlJaroudi WA, Refaat MM, Habib RH, et al. Genetic Risk Assessment of Defibrillator Events Investigators. Effect of Angiotensin-Converting Enzyme Inhibitors and Receptor Blockers on Appropriate **Implantable Cardiac Defibrillator Shock** in Patients With Severe Systolic Heart Failure (from the GRADE Multicenter Study). Am J Cardiol. 2015 Apr 1;115(7):924-31.

AlJaroudi W, Alraies MC, Halley C, et al. Impact of progression of **diastolic dysfunction on mortality** in patients with normal ejection fraction. Circulation. 2012;125:782–788.

Allida SM, Inglis SC, Davidson PM, et al. **Thirst in chronic heart failure**: a review. J Clin Nurs. 2014 Nov 28.

Allen LA, Turer AT, Dewald T, et al. **Continuous versus bolus dosing of Furosemide** for patients hospitalized for heart failure. Am J Cardiol. 2010 Jun 15;105(12):1794-7.

Allen LA, Stevenson LW, Grady KL, et al. **Decision making (shared)** in advanced heart failure. Circulation 2012; DOI: 10.1161/cir.0b013e31824f2173.

Allen LA, McIlvennan CK, Thompson JSet al. Effectiveness of an Intervention Supporting **Shared Decision Making for Destination Therapy Left Ventricular Assist Device**: The **DECIDE-LVAD** Randomized Clinical Trial. JAMA Intern Med. 2018 Feb 26.

Almeida O P, Garrido G J, Beer C, et al. **Cognitive and brain changes** associated with ischemic heart disease and heart failure. Eur Heart J 2012

Altay H, Zorlu A, Binici S, et al. Relation of **Serum Parathyroid Hormone** Level to Severity of Heart Failure. Am J Cardiol. 2011 Oct 12.

Aliti GB, Rabelo ER, Clausell N, et al. **Aggressive Fluid and Sodium Restriction** in Acute Decompensated Heart Failure: A Randomized Clinical Trial. JAMA Intern Med. 2013 May 20:1-7.

Alvi RM, Neilan AM, Tariq N, et al. **Protease Inhibitors and Cardiovascular Outcomes in Patients With HIV and Heart Failure**. J Am Coll Cardiol. 2018 Jul 31;72(5):518-530.

Alvi RM, Neilan AM, Tariq N, et al. The **Risk for Sudden Cardiac Death** Among Patients Living With Heart Failure and Human Immunodeficiency Virus. JACC Heart Fail. 2019 Sep;7(9):759-767.

Ambesh P, Zivari K, Obiagwu C, et al. Rapidly developing heart failure from **capecitabine cardiotoxicity**: a case study. Br J Clin Pharmacol. 2018 Apr;84(4):800-802.

Ambrosy AP, Bhatt AS, et al. **Trajectory of Congestion Metrics by Ejection Fraction** in Patients With Acute Heart Failure (from the Heart Failure Network). Am J Cardiol. 2017 Jul 1;120(1):98-105.

Anand IS, Gupta P. **Anemia and Iron Deficiency in Heart Failure**: Current Concepts and Emerging Therapies. Circulation. 2018 Jul 3;138(1):80-98.

Andersen K, Mariosa D, Adami HO, et al. Dose-Response Relations of **Total and Leisure-Time Physical Activity** to Risk of Heart Failure: A Prospective Cohort Study. Circ Heart Fail. 2014 Sep 2.

Anderson L, Taylor RS. **Cardiac rehabilitation** for people with heart disease: an overview of Cochrane systematic reviews. Cochrane Database of Systematic Reviews 2014, Issue 12. Art. No.: CD011273. DOI: 10.1002/14651858.CD011273.pub2. Exercise-based cardiac rehabilitation is an effective and safe therapy to be used in the management of clinically stable people following myocardial infarction or percutaneous coronary intervention or who have heart failure. Future RCTs of cardiac rehabilitation need to improve their reporting methods and reflect the real world practice better including the recruitment of higher risk people and consideration of contemporary models of cardiac rehabilitation delivery, and identify effective interventions for enhancing adherence to rehabilitation.

Andriole, Gerald L., Bostwick, David G., Brawley, Otis W., et al. the REDUCE Study Group, Effect of **Dutasteride** on the Risk of Prostate Cancer. N Engl J Med 2010 362: 1192-1202.

Angermann CE, Gelbrich G, Störk S, et al; MOOD-HF Study Investigators and Committee Members. Effect of **Escitalopram** on All-Cause Mortality and Hospitalization in Patients With Heart Failure and Depression: The **MOOD-HF** Randomized Clinical trial. JAMA. 2016 Jun 28;315(24):2683-2693.

Angraal S, Nuti SV, Masoudi FA, et al. **Digoxin Use and Associated Adverse Events Among Older Adults**. Am J Med. 2019 May 8.

Anjan VY, et al. Prevalence, Clinical Phenotype, and Outcomes Associated With **Normal B-Type Natriuretic Peptide** Levels in Heart Failure With **Preserved** Ejection Fraction. Am J Cardiol. 2012 Jun 6.

Anker SD, Comin Colet J, Filippatos G, et al. the **FAIR-HF** Trial Investigators. **Ferric Carboxymaltose** in Patients with Heart Failure and Iron Deficiency. N Engl J Med. 2009 Nov 17. [Epub ahead of print]

Anker SD, Colet JC, Filippatos G, et al. Rationale and design of **Ferinject** assessment in patients with iron deficiency and chronic **heart failure** (**FAIR-HF**) study: a randomized, placebo-controlled study of intravenous iron supplementation in patients with and without anaemia. Eur J Heart Fail 2009;11:1084e1091.

Anker SD, Koehler F, Abraham WT. **Telemedicine** and remote management of patients with heart failure. Lancet. 2011 Aug 20;378(9792):731-9.

Anker SD, Coats AJS, Cristian G, et al. A prospective comparison of **alginate-hydrogel** with standard medical therapy to determine impact on functional capacity and clinical outcomes in patients with advanced heart failure (AUGMENT-HF trial). *Eur Heart J* 2015; 36:2297-309.

Antoniou T, Gomes T, Mamdani MM, et al. **Trimethoprim-sulfamethoxazole induced hyperkalaemia** in elderly patients receiving **spironolactone**: nested case-control study. BMJ. 2011 Sep 12;343:d5228.

Antoniou T, Hollands S, et al; the Canadian Drug Safety and Effectiveness Research Network. **Trimethoprim-sulfamethoxazole and risk of sudden death among patients taking spironolactone**. CMAJ. 2015 Feb 2.

Aoki S, et al. Usefulness of the Combination of **In-Hospital Poor Diuretic Response and Systemic Congestion** to Predict Future Cardiac Events in Patients With Acute Decompensated Heart Failure. Am J Cardiol. 2017 Jun 15;119(12):2010-2016.

Arif Sally A, Mergenhagen KA, et al. Treatment of Systolic Heart Failure in the **Elderly**: An Evidence-Based Review. Ahead of Print 1Oct 2010, DOI 10.1345/aph.1P128. Ann Pharmacother ;44:1604-1614.

Arfè A, Scotti L, Varas-Lorenzo C, et al. **Non-steroidal anti-inflammatory drugs** and risk of heart failure in four European countries: nested case-control study. BMJ 2016;354:i4857.

Armenian SH, et al. Prevention and monitoring of cardiac dysfunction in **survivors of adult cancers: American Society of Clinical Oncology (ASCO)** clinical practice guideline. J Clin Oncol. 2017 Mar 10;35(8):893-911.

Arora S, Lahewala S, Hassan Virk HU, et al. Etiologies, Trends, and Predictors of **30-Day Readmissions** in Patients With **Diastolic Heart Failure**. Am J Cardiol. 2017 Aug 15;120(4):616-624

Arora S, Patel P, Lahewala S, et al. Etiologies, **Trends, and Predictors of 30-Day Readmission** in Patients With Heart Failure. Am J Cardiol. 2016 Dec 14.

Arroll B, Doughty R, Andersen V. **Investigation and management of congestive heart failure**. BMJ. 2010 Jul 14;341:c3657. doi: 10.1136/bmj.c3657.

Ashrafian H, Pal N, Sivaswamy N, et al. The Effect of Selective Heart Rate Slowing (**ivabradine**) in Heart Failure with Preserved ejection Fraction. Circulation. 2015 Sep 2.

Aspry KE, Van Horn L, Carson JAS, et al. **Medical Nutrition Education, Training, and Competencies to Advance Guideline-Based Diet** Counseling by Physicians: A Science Advisory From the American Heart Association. Circulation. 2018 Jun 5;137(23):e821-e841.

Assmus B, Walter DH, Seeger FH, et al. Effect of **shock wave-facilitated intracoronary cell therapy on LVEF** in patients with chronic heart failure: the CELLWAVE randomized clinical trial. JAMA. 2013 Apr 17;309(15):1622-31.

Atzema CL, Austin PC, Yu B, et al. Effect of **early physician follow-up on mortality and subsequent hospital admissions after emergency care for heart failure**: a retrospective cohort study. CMAJ. 2018 Dec 17;190(50):E1468-E1477.

Aune D, Sen A, Norat T, et al. **Body Mass Index, Abdominal Fatness** and Heart Failure Incidence and Mortality: A Systematic Review and Dose-Response Meta-Analysis of Prospective Studies. Circulation. 2016 Jan 8.

Aurigemma GP, Gaasch WH. Clinical practice. **Diastolic heart failure**. N Engl J Med. 2004 Sep 9;351(11):1097-105.

Avery CL, Loehr LR, Baggett C, et al. The population burden of heart failure attributable to **modifiable risk factors**. The ARIC (Atherosclerosis Risk in Communities) study. J Am Coll Cardiol 2012.

Avila MS, Ayub-Ferreira SM, de Barros Wanderley Junior MR, et al. **Carvedilol for Prevention of Chemotherapy Related Cardiotoxicity**. J Am Coll Cardiol. 2018 Mar 3.

Avni T, Leibovici L, Gafter-Gvili A. Iron supplementation for the treatment of chronic **heart failure and iron deficiency**: systematic review and meta-analysis. Eur J Heart Fail 2012;14:423e429.

Badheka AO, Rathod A, Kizilbash MA, et al. Comparison of Mortality and Morbidity in Patients With **Atrial Fibrillation and Heart Failure With Preserved Versus Decreased Left Ventricular Ejection** Fraction. Am J Cardiol. 2011 Aug 18.

Bagur R, Chamula M, Brouillard E, et al. **Radiotherapy-induced Cardiac Implantable Electronic Device Dysfucntion** in Patients with Cancer. The American Journal of Cardiology (2016).

Bajaj NS, et al. Impact of **atrial fibrillation and heart failure**, independent of each other and in combination, on mortality in community-dwelling older adults. Am J Cardiol. 2014 Sep 15;114(6):909-13.

Bajaj NS, Gutiérrez OM, Arora G, et al. **Racial differences in plasma levels of N-terminal pro–B-type natriuretic peptide and outcomes**: the Reasons for Geographic and Racial Differences in Stroke (**REGARDS**) study [online Nov 22, 2017].JAMA Cardiol. doi:10.1001 /jamacardio.2017.4207

Baker WL, White WB. Safety of mineralocorticoid receptor antagonists (**spironolactone**) in patients receiving **hemodialysis**. Ann Pharmacother. 2012 Jun;46(6):889-94.

Bakris GL, Pitt B, Weir MR, et al. Effect of **patiromer** on serum potassium level in patients with hyperkalemia and diabetic kidney disease: the **AMETHYST-DN** randomized clinical trial. JAMA. doi: 10.1001/jama.2015.7446.

Balion C, Don-Wauchope A, Hill S, et al. Use of **Natriuretic Peptide Measurement** in the Management of Heart Failure. Comparative Effectiveness Review No. 126. AHRQ Comparative Effectiveness Reviews. Rockville (MD): Agency for Healthcare Research and Quality (US); 2013 Nov. Report No.: No. 13(14)-EHC118-EF.

Balmforth C, Simpson J, Shen L, et al. Outcomes and Effect of Treatment According to **Etiology in HFrEF: An Analysis of PARADIGM-HF**. JACC Heart Fail. 2019 Jun;7(6):457-465

Bangalore S, Kumar S, Messerli FH. When conventional heart failure therapy is not enough: Angiotensin receptor blocker, direct renin inhibitor, or **aldosterone antagonist**? Congest Heart Fail 2012.

Bansal N, Hailpern SM, Katz R, et al. Outcomes associated with **left ventricular assist devices among recipients with and without end-stage renal disease** [online Dec 18, 2017]. JAMA Intern Med. doi:10.1001/jamainternmed.2017 .4831

Bansal N, Szpiro A, Reynolds K, et al. Long-term Outcomes Associated With **Implantable Cardioverter Defibrillator** in Adults **With Chronic Kidney Disease**. JAMA Intern Med. 2018 Feb 5.

Bansal S, Munoz K, Brune S, et al. **High-Dose Spironolactone** When Patients With Acute Decompensated Heart Failure Are Resistant to Loop Diuretics: A Pilot Study. Ann Intern Med. 2019 Jul 16.

Bart BA et al. **Ultrafiltration in decompensated heart failure** with cardiorenal syndrome. N Engl J Med 2012 Nov 6.

Baskett R, Crowell R, Freed D, Giannetti N, Simpson CS; Canadian Cardiovascular Society. Canadian Cardiovascular Society focused position statement update on assessment of the cardiac patient for **fitness to drive: fitness following left ventricular assist device implantation**. Can J Cardiol. 2012 Mar-Apr;28(2):137-40.

Basuray A, French B, Ky B, et al. **Heart failure with recovered ejection fraction**: clinical description, biomarkers, and outcomes. Circulation. 2014 Jun 10;129(23):2380-7.

Basset A, et al. Development of a **clinical prediction score** for congestive heart failure diagnosis in the emergency care setting: The **Brest score**. Am J Emerg Med. 2016 Dec;34(12):2277-2283.

Bavendiek U, Aguirre Davila L, Koch A, Bauersachs J. **Assumption versus evidence: the case of digoxin** in atrial fibrillation and heart failure. Eur Heart J. 2017 Jan 8.

Bavishi C, Ather S, Bambhroliya A, et al. Prognostic significance of **hyponatremia** among ambulatory patients with heart failure and preserved and reduced ejection fractions. Am J Cardiol. 2014 Jun 1;113(11):1834-8.

Bax JJ, Di Carli M, Narula J, Delgado V**. Multimodality imaging** in ischaemic heart failure. Lancet. 2019 Mar 9;393(10175):1056-1070.

Beale AL, Meyer P, Marwick TH, et al. **Sex Differences in Cardiovascular Pathophysiology**: Why Women Are Overrepresented in Heart Failure With Preserved Ejection Fraction. Circulation. 2018 Jul 10;138(2):198-205.

Beavers Craig James, Dunn Steven P, Macaulay Tracy E. The Role of Angiotensin Receptor Blockers in Patients with Angiotensin-Converting Enzyme Inhibitor–**Induced Angioedema**. Articles Ahead of Print published on 1 April 2011, DOI 10.1345/aph.1P630. Ann Pharmacother ;45:520-524.

Beck-da-Silva L, Piardi D, Soder S, et al. **IRON-HF** study: a randomized trial to assess the effects of **iron in heart failure** patients with anemia. Int J Cardiol. 2013 Oct 9;168(4):3439-42.

Beggs SAS;Jhund PS;Jackson CE;et al. **Non-ischaemic cardiomyopathy, sudden death and implantable defibrillators**: a review and meta-analysis. Heart. 2017 Oct 6.

Bejan-Angoulvant T, Genet T, Vrignaud L, et al. Three case reports of involuntary **muscular movements as adverse reactions to sacubitril/valsartan**. Br J Clin Pharmacol. 2018 Mar 6.

Bekelman DB, Plomondon ME, et al. Primary Results of the **Patient-Centered Disease Management (PCDM) for Heart Failure** Study: A Randomized Clinical Trial. JAMA Intern Med. 2015 Mar 30.

Bekelman DB, Allen LA, McBryde CF, et al. Effect of a **Collaborative Care Intervention vs Usual Care** on Health Status of Patients With Chronic Heart Failure: The CASA Randomized Clinical Trial. JAMA Intern Med. 2018 Feb 26.

Belardinelli R, Georgiou D, Cianci G, et al. 10-year **exercise training in chronic heart failure**: a randomized controlled trial. J Am Coll Cardiol. 2012 Oct 16;60(16):1521-8.

Benites-Zapata VA, Hernandez AV, et al. Usefulness of **Neutrophil-to-Lymphocyte Ratio** in Risk Stratification of Patients With Advanced Heart Failure. Am J Cardiol. 2015 Jan 1;115(1):57-61.

Belin RJ, Greenland P, Martin L, et al. **Fish intake** and the risk of incident heart failure: The Women's Health Initiative. Circ Heart Fail 2011; DOI:10.1161/CIRCHEARTFAILURE.110.960450.
Benbarkat H, Addetia K, Eisenberg MJ, et al. Application of the **Seattle Heart Failure Model** in Patients >80 Years of Age Enrolled in a Tertiary Care Heart Failure Clinic. Am J Cardiol. 2012 Aug 21.
Bermingham M, Shanahan MK, O'Connell E, et al. **Aspirin use in heart failure**: Is low-dose therapy associated with mortality and morbidity benefits in a large community population? *Circ Heart Fail* 2014.
Bernocchi P; et a;. **Home-based telerehabilitation** in older patients with chronic obstructive pulmonary disease and heart failure: a randomized controlled trial. Age Ageing. 2017 Aug 30:1-7.
Beta-Blocker Evaluation of Survival Trial (**BEST**) Investigators. A trial of the beta-blocker **bucindolol** in patients with advanced chronic heart failure. N Engl J Med 2001;344:1659-67.
Betz JK, Katz DF, et al. Outcomes among **older patients** receiving **implantable cardioverter-defibrillators** for secondary prevention: from the NCDR ICD Registry. J Am Coll Cardiol 2017; 69:265–74.
Bhagat AA, Greene SJ, Vaduganathan M, Fonarow GC, Butler J. Initiation, continuation, switching, and withdrawal of heart failure **medical therapies during hospitalization**. JACC Heart Fail. 2019;7:1-12.
Bhatia RS, Austin PC, Stukel TA, et al. Outcomes in patients with heart failure treated in hospitals with **varying admission rates**: population-based cohort study. BMJ Qual Saf. 2014 Jul 30.
Bhatia V, Bajaj NS, Sanam K, et al. **Beta-blocker** use and **30-day all-cause readmission** in Medicare beneficiaries with **systolic heart failure**. Am J Med 2015.
Bhatt AS, DeVore AD, Hernandez AF, et al. Can **Vaccinations** Improve Heart Failure Outcomes?: Contemporary Data and Future Directions. JACC Heart Fail. 2017 Jan 28.
Biggar RJ, Wohlfahrt J, Oudin A, et al. **Digoxin use and the risk of breast cancer** in women. J Clin Oncol. 2011 Jun 1;29(16):2165-70.
Bikdeli B, Strait KM, Dharmarajan K, et. al. **Intravenous fluids in acute decompensated heart failure**. JACC Heart Fail. 2015 Feb; 3(2):127-33.
Bilchick KC, Stukenborg GJ. Comparative Effectiveness of Cardiac Resynchronization Therapy in Combination With **Implantable Defibrillator in Patients With Heart Failure and Wide QRS Duration**. Am J Cardiol. 2014 Aug 27.
Birks EJ, George RS, Hedger M, et al. Reversal of severe heart failure with a **continuous-flow left ventricular assist device** (LVAD) and pharmacological therapy: a prospective study. Circulation. 2011 Feb 1;123(4):381-90.
Blais C, Dai S, Waters C, Robitaille C, et al. Assessing the **burden of hospitalized and community-care** heart failure in Canada. Can J Cardiol. 2014 Mar;30(3):352-8.
Blecker S, Katz SD, Horwitz LI, et al. **Comparison of Approaches** for Heart Failure Case Identification From **Electronic Health Record Data**. JAMA Cardiol. 2016 Oct 5.
Blecker S, Herrin J, Li L, et al. Trends in **Hospital Readmission of Medicare-Covered Patients With Heart Failure**. J Am Coll Cardiol. 2019 Mar 12;73(9):1004-1012.
Block RC, Liu L, Herrington DM, et al. **Predicting Risk** for Incident Heart Failure With Omega-3 Fatty Acids: From MESA. JACC Heart Fail. 2019 Jul 3.
Blum A. Treating heart failure with **sildenafil**. Congest Heart Fail. 2009 Jul-Aug;15(4):181-5.
Böhm M, Swedberg K, Komajda M.; et al. **SHIFT** Investigators. **Heart rate** as a risk factor in chronic heart failure (SHIFT): the association between heart rate and outcomes in a randomised placebo-controlled trial. Lancet. 2010 Sep 11;376(9744):886-94.
Bonow RO, Maurer G, Lee KL, et al. Myocardial viability and survival in ischemic left ventricular dysfunction (**STICH**). N Engl J Med 2011. DOI: 10.1056/NEJMoa1100358. (CABG vs medical therapy)
Bonow RO et al. **ACCF/AHA/AMA**-PCPI 2011 **Performance Measures for Adults With Heart Failure**: A Report of the American College of Cardiology Foundation/American Heart Association Task Force on Performance Measures and the American Medical Association-Physician Consortium for Performance Improvement. J Am Coll Cardiol. 2012 May 5;59(20):1812-32.
Borer JS, Deedwania PC, et al. Benefits of **Heart Rate Slowing With Ivabradine** in Patients With Systolic Heart Failure and Coronary Artery Disease.Am J Cardiol. 2016 Dec 15;118(12):1948-1953.
Borlaug BA, Anstrom KJ, Lewis GD, et al; Blood Institute Heart Failure Clinical Research Network. Effect of **Inorganic Nitrite vs Placebo on Exercise Capacity** Among Patients With Heart Failure With Preserved Ejection Fraction: The INDIE-HFpEF Randomized Clinical Trial. JAMA 2018 Nov 6;320(17):1764-1773.
Borlaug BA, Obokata M. Is it time to recognize a **new phenotype**? **Heart failure with preserved ejection fraction with pulmonary vascular disease**. Eur Heart J. 2017 Oct 7;38(38):2874-2878.
Bosch X, et al. **Enalapril and carvedilol** for preventing **chemotherapy-induced** left ventricular systolic dysfunction in patients with malignant hemopathies: OVERCOME trial. J Am Coll Cardiol 2013.
Bowen GS, Diop MS, Jiang L, et al. A Multivariable **Prediction Model for Mortality** in Individuals Admitted for Heart Failure. J Am Geriatr Soc. 2018 Mar 6.
Bowles EJ, Wellman R, Feigelson HS, et al. Pharmacovigilance Study Team. Risk of heart failure in breast cancer patients after **anthracycline and trastuzumab** treatment: a retrospective cohort study. J Natl Cancer Inst. 2012 Sep 5;104(17):1293-305.
Boyle AJ, Jorde UP, Sun B, et al. Preoperative risk factors of bleeding and stroke during **LVAD support**: An analysis of over 900 HeartMate II outpatients. *J Am Coll Cardiol* 2013.
Bozkurt B, Aguilar D, Deswal A, et al. Contributory Risk and Management of **Comorbidities of Hypertension, Obesity, Diabetes Mellitus, Hyperlipidemia, and Metabolic Syndrome** in Chronic Heart Failure: A Scientific Statement From the American Heart Association. Circulation. 2016 Oct 31.
Braga JR, Austin PC, Ross HJ, et al. Importance of **Nonobstructive Coronary Artery Disease** in the Prognosis of Patients With Heart Failure. JACC Heart Fail. 2019 Jun;7(6):493-501.
Braga JR, Leong-Poi H, Rac VE, et al. Trends in the **Use of Cardiac Imaging** for Patients With Heart Failure in Canada. JAMA Netw Open. 2019 Aug 2;2(8):e198766.
Braunwald E. The **war against heart failure**: the Lancet lecture. Lancet. 2014 Nov 16.
Breathett K, Maffett S, Foraker RE, et al. Pilot Randomized Controlled Trial to Reduce Readmission for Heart Failure Using **Novel Tablet and Nurse Practitioner Education**. Am J Med. 2018 Mar 16.
Breathett K, Liu WG, et al. African Americans Are Less Likely to Receive Care by a Cardiologist During an Intensive Care Unit Admission for Heart Failure. JACC Heart Fail. 2018 May;6(5):413-420.
Briasoulis A, Palla M, Afonso L. Meta-Analysis of the Effects of **Carvedilol Versus Metoprolol** on All-Cause Mortality and Hospitalizations in Patients With Heart Failure. Am J Cardiol. 2015 Jan 31.
Brooks GC, Vittinghoff E, Iyer S, et al. Accuracy and Usability of a **Self-Administered 6-Minute Walk Test Smartphone Application**. Circ Heart Fail. 2015 Sep;8(5):905-13.
Bruce CR, Minard CG, Wilhelms LA, et al. **Caregivers of Patients With Left Ventricular Assist Devices**: Possible Impacts on Patients' Mortality and Interagency Registry for Mechanically Assisted Circulatory Support-Defined Morbidity Events. Circ Cardiovasc Qual Outcomes. 2017 Jan;10(1).
Bruckel J, Mehta A, Bradley SM, et al. **Variation in Do-Not-Resuscitate Orders** and Implications for Heart Failure Risk-Adjusted Hospital Mortality Metrics. JACC Heart Fail. 2017 Oct;5(10):743-752.
Buckley LF, Seoane-Vazquez E, Cheng JW, et al. Comparison of **Ambulatory, High-Dose, Intravenous Diuretic** Therapy to Standard Hospitalization and Diuretic Therapy for Treatment of Acute Decompensated Heart Failure. Am J Cardiol. 2016 Nov 1;118(9):1350-1355.
Burke MA, Givertz MM. Assessment and management of heart failure **after left ventricular assist device implantation**. Circulation. 2014 Mar 11;129(10):1161-6.
Burns KM, Byrne BJ, et al. New mechanistic and therapeutic targets for **pediatric heart failure**: report from a national heart, lung, and blood institute working group. Circulation. 2014 Jul 1;130(1):79-86.
Bursi F, McNallan SM, Redfield MM, et al. **Pulmonary pressures** and death in heart failure a community study. J Am Coll Cardiol2012; 59:222-231.
Butler J, Anker SD. The Ethics of Conducting Clinical Trials With **Sodium-Glucose Cotransporter-2 Inhibitors** in Heart Failure: Is Placebo Assignment Justified in Patients With Comorbid Diabetes Mellitus and Heart Failure? Circulation. 2017 Oct 17;136(16):1459-1461.
Butler J, et al; **EMPEROR** Trials Program. The potential role and rationale for treatment of **heart failure with sodium-glucose co-transporter 2 inhibitors**. Eur J Heart Fail. 2017 Nov;19(11):1390-1400.
Butt AA.; Chang C-C; Kuller L; et al. Risk of Heart Failure With **Human Immunodeficiency Virus** in the Absence of Prior Diagnosis of Coronary Heart Disease. Arch Intern Med. 2011;171(8):737-743.
Cadrin-Tourigny J, Shohoudi A, et al. **Decreased Mortality With Beta-Blockers in Patients With Heart Failure and Coexisting Atrial Fibrillation: An AF-CHF** Substudy. JACC Heart Fail. 2017 Jan 4.
Cammarano C, Silva M, Comee M, et al. Meta-Analysis of **Ivabradine** in Patients With Stable Coronary Artery Disease With and Without Left Ventricular Dysfunction. Clin Ther. 2016 Jan 30.
Canadian Cardiovascular Society (**CCS**) Heart Failure Management Primary Panel, Moe GW, Ezekowitz JA, O'Meara E, et al. The 2013 Canadian Cardiovascular Society Heart Failure Management Guidelines Update: focus on **rehabilitation and exercise and surgical coronary revascularization**. Can J Cardiol. 2014 Mar;30(3):249-63.
Canadian Hypertension Education Program. 2011 CHEP recommendations for the management of hypertension. http://hypertension.ca/chep/wp-content/uploads/2011/05/FullCHEPRecommendations_EN_2011.pdf
Carey SA, Bass K, Saracino G, et al. **Probability of Accurate Heart Failure Diagnosis** and the Implications for **Hospital Readmissions**. Am J Cardiol. 2017 Jan 5.
Carubelli V, Lombardi C, Lazzarini V, et al. **N-terminal pro-B-type natriuretic peptide-guided therapy** in patients hospitalized for acute heart failure. J Cardiovasc Med (Hagerstown). 2016;17:828-39.
Cardinale D, Colombo A, Bacchiani G, et al. Early detection of **anthracycline cardiotoxicity** and improvement with heart failure therapy. Circulation. 2015 Jun 2;131(22):1981-8.
Carr H, Cnattingius S, Granath F, et al. **Preterm Birth and Risk of Heart Failure** Up to Early Adulthood. J Am Coll Cardiol. 2017 May 30;69(21):2634-2642.
Caughey MC, Avery CL, Ni H, et al. Outcomes of Patients With **Anemia** and Acute Decompensated Heart Failure With Preserved Versus Reduced Ejection Fraction (from the ARIC Study Community Surveillance). Am J Cardiol. 2014 Dec 15;114(12):1850-4.
Caughey MC, Sueta CA, Stearns SC, et al. Recurrent Acute Decompensated Heart Failure Admissions for Patients With Reduced Versus Preserved Ejection Fraction (from the Atherosclerosis Risk in Communities Study). Am J Cardiol. 2018 Mar 28.
Cavigelli-Brunner A, Schweiger M, Knirsch W, et al. **VAD** as Bridge to Recovery in **Anthracycline-Induced Cardiomyopathy** and **HHV6 Myocarditis**. Pediatrics. 2014 Sep;134(3):e894-9.
Cedars AM. In Heart Failure, **Where You've Been** May be More Important than Where You Are: A Role for Patient Reported Outcomes. Am J Cardio.2017.
Chae CU, Albert CM, Moorthy MV, et al. **Vitamin E** supplementation and the risk of heart failure in women (Women's Health Study –**WHS**). Circulation 2012.
Chan AL, Wang MT, et al. Risk of digoxin intoxication caused by **clarithromycin**-digoxin interactions in heart failure patients: a population-based study. Eur J Clin Pharmacol. 2009 Aug 5.
Chan M, Tsuyuki R. **Heart failure in the elderly**. Curr Opin Cardiol. 2013 Jan;28(2):234-41.
Chandar M, et al. Perspectives of Health-Care Providers Toward **Advance Care Planning** in Patients With Advanced Cancer and Congestive Heart Failure. Am J Hosp Palliat Care. 2016 Mar 2.
Chandra A, et al. Effects of **Sacubitril/Valsartan on Physical & Social Activity Limitations** in Patients With Heart Failure: A Secondary Analysis of the PARADIGM-HF Trial. JAMA Cardiol. 2018 Apr 4.
Chandra A, Vaduganathan M, Lewis EF, et al; PARAGON-HF Investigators. **Health-Related Quality of Life** in Heart Failure With Preserved Ejection Fraction: The PARAGON-HF Trial. JACC Heart Fail. 2019 Jul 10.
Chang LL, DeVore AD, Granger BB, et al. Leveraging **Behavioral Economics** to **Improve Heart Failure Care** and **Outcomes**. Circulation. 2017 Aug 22;136(8):765-772
Chang PP, Wruck LM, Shahar E, et al. **Trends in Hospitalizations and Survival of Acute Decompensated Heart Failure** in Four US Communities (2005-2014): The Atherosclerosis Risk in Communities (**ARIC**) Study Community Surveillance. Circulation. 2018 Mar 8.
Chang PP, Wruck LM, Shahar E, et al. Trends in hospitalizations and survival of acute decompensated heart failure in four US communities (2005-2014): ARIC Study Community Surveillance. Circulation. 2018;138:12–24. doi: 10.1161/CIRCULATIONAHA.117.027551.
Chatterjee NA, Moorthy MV, Pester J, et al. **Sudden Death in Patients With Coronary Heart Disease** Without Severe Systolic Dysfunction. JAMA Cardiol. 2018 May 2.
Chatterjee P, Joynt Maddox KE. **US National Trends in Mortality** From Acute Myocardial Infarction and Heart Failure: Policy Success or Failure? JAMA Cardiol. 2018 Mar 14.

Chatterjee S, Moeller C, Shah N, et al. **Eplerenone** is not superior to older and less expensive aldosterone antagonists (**spironolactone**). Am J Med. 2012 Aug;125(8):817-25.

Chatterjee S, Biondi-Zoccai G, Abbate A, D'Ascenzo F, Castagno D, et al. Benefits **of β blockers in patients** with heart failure and reduced ejection fraction: network meta-analysis. BMJ 2013;346:f55.

Chaudhry SI et al. **Telemonitoring** in patients with heart failure (**Tele-HF**) . N Engl J Med 2010 Nov 16; [e-pub ahead of print]. (NS primary outcome)

Chaudhry SI, et al. **Risk factors for hospital admission** among older persons with newly diagnosed heart failure: from the Cardiovascular Health Study. J Am Coll Cardiol. 2013 Feb 12;61(6):635-42.

Chavez-MacGregor M, Niu J, Zhang N, et al. Cardiac Monitoring During Adjuvant **Trastuzumab**-Based Chemotherapy Among Older Patients With Breast Cancer. J Clin Oncol. 2015 Jul 1;33(19):2176-83.

Cheang MH, Rose G, et al. Current challenges in **palliative care provision for heart failure** in UK: a survey on the perspectives of palliative care professionals. Open Heart. 2015 Jan 15;2(1):e000188.

Chen CY, Stevenson LW, Stewart GC, et al. Real world effectiveness of **primary implantable cardioverter defibrillators** implanted during hospital admissions for exacerbation of heart failure or other acute co-morbidities: cohort study of older patients with heart failure. BMJ. 2015 Jul 14;351:h3529

Chen HH, Anstrom KJ, et al. Low-Dose **Dopamine** or Low-Dose **Nesiritide** in Acute Heart Failure With Renal Dysfunction: The **ROSE** Acute Heart Failure Randomized Trial. JAMA. 2013 Nov 18.

Chen J, Normand SLT, Wang Y, Krumholz HM. **National and regional trends in heart failure hospitalization and mortality rates** for Medicare beneficiaries, 1998-2008. JAMA 2011; 306:1669-1678.

Chen J, Long JB, Hurria A, et al. Incidence of Heart Failure or **Cardiomyopathy After Adjuvant Trastuzumab** Therapy for Breast Cancer. J Am Coll Cardiol. 2012 Nov 2.

Chen S, Purerfellner H, Meyer C, et al. **Rhythm control** for patients with atrial fibrillation complicated with heart failure in the contemporary era of catheter ablation: a stratified pooled analysis of randomized data. Eur Heart J. 2019 Jul 11.

Cherubini Antonio; Oristrell Joaquim; Pla Xavier; et al. The Persistent **Exclusion of Older Patients From Ongoing Clinical Trials** Regarding Heart Failure Arch Intern Med. 2011;171(6):550-556.

Cholley B, Caruba T, Grosjean S, et al. Effect of **Levosimendan** on **Low Cardiac Output Syndrome** in Patients With Low Ejection Fraction Undergoing Coronary Artery Bypass Grafting With Cardiopulmonary Bypass: The **LICORN** Randomized Clinical Trial. JAMA. 2017 Aug 8;318(6):548-556

Chow SL, Maisel AS, Anand I, et al; American Heart Association Clinical Pharmacology Committee of the Council on Clinical Cardiology; Council on Basic Cardiovascular Sciences; Council on Cardiovascular Disease in the Young; Council on Cardiovascular and Stroke Nursing; Council on Cardiopulmonary, Critical Care, Perioperative and Resuscitation; Council on Epidemiology and Prevention; Council on Functional Genomics and Translational Biology; and Council on Quality of Care and Outcomes Research. **Role of Biomarkers** for the Prevention, Assessment, and Management of Heart Failure: A Scientific Statement From the American Heart Association. Circulation. 2017 Apr 26.

Christiansen JR, Hamre H, Massey R, et al. Left Ventricular Function in Long-Term Survivors of **Childhood Lymphoma**. Am J Cardiol. 2014 May 17.

Christiansen MN, Køber L, Weeke P, et al. **Age-specific trends** in incidence, mortality and comorbidities of heart failure in Denmark, 1995 to 2012. Circulation. 2017;135:1214–1223.

Christopher PP, Stein MD. **Should a Prison Salt Trial Be Federally Funded**? Ann Intern Med. 2019 Mar 5.

Chuang CP, Jong YS, Wu CY, et al. Impact of **Triiodothyronine and N-Terminal Pro-B-Type Natriuretic Peptide** on the Long-Term Survival of Critically Ill Patients With Acute Heart Failure. Am J Cardiol. 2013 Dec 12

Chuzi S, Allen LA, Dunlay SM, Warraich HJ. **Palliative Inotrope Therapy**: A Narrative Review. JAMA Cardiol. 2019 Jul 3.

Cice G, Di Benedetto A, D'Isa S, et al. Effects of **telmisartan** added to angiotensin-converting enzyme inhibitors on mortality and morbidity in **hemodialysis patients with chronic heart failure**: a double-blind, placebo-controlled trial. J Am Coll Cardiol. 2010;56:1701-8.

Claggett B, Packer M, McMurray JJ, et al; **PARADIGM-HF** Investigators. Estimating the Long-Term Treatment Benefits of **Sacubitril-Valsartan**. N Engl J Med. 2015 Dec 3;373(23):2289-90.

Clark AL, Chyu J, Horwich TB. The **Obesity Paradox** in Men Versus Women With Systolic Heart Failure. Am J Cardiol. 2012 Apr 10.

Clark AL, Fonarow GC, Horwich TB. Impact of **cardiorespiratory fitness on the obesity paradox** in patients with systolic heart failure. Am J Cardiol. 2015 Jan 15;115(2):209-13.

Clark AL, Johnson MJ, Squire I. Does home **oxygen** benefit people with chronic heart failure? BMJ. 2011 Feb 4;342:d234. doi: 10.1136/bmj.d234.

Clark AL, Kalra PR, Petrie MC, et al. Change in **renal function associated with drug treatment** in heart failure: national guidance. Heart. 2019 Jun;105(12):904-910.

Cleland JGF, Daubert JC, Erdmann E, et al. The effect of cardiac resynchronization on morbidity and mortality in heart failure. (**CARE-HF**) N Engl J Med 2005; 352:1539-1549.

Cleland JG, Abraham WT, Linde C, et al. An individual patient meta-analysis of five randomized trials assessing the effects of **cardiac resynchronization therapy** on morbidity and mortality in patients with symptomatic heart failure. Eur Heart J 2013

Cleland JG, Zhang J, Pellicori P, Dicken et al. Prevalence and Outcomes of **Anemia** and Hematinic Deficiencies in Patients With Chronic Heart Failure. JAMA Cardiol. 2016 Aug1;1(5):539-547

Cleland JGF, Bunting KV, Flather MD, et al. **Beta-blockers for heart failure with reduced, mid-range, and preserved ejection fraction:** an individual patient-level analysis of double-blind randomized trials. Eur Heart J. 2017 Oct 10.

Cleland JGF, Bunting KV, Flather MD, et al; Beta-blockers in Heart Failure Collaborative Group. **Beta-blockers** for heart failure with **reduced, mid-range, and preserved ejection fraction**: an individual patient-level analysis of double-blind randomized trials. Eur Heart J. 2018 Jan 1;39(1):26-35.

Coles AH, Fisher K, Darling C, et al. Long-Term Survival for Patients With **Acute Decompensated** Heart Failure According to **Ejection Fraction Findings**. Am J Cardiol. 2014 Jul 2.

Collier TJ, Pocock SJ, McMurray JJ, et al. The impact of **eplerenone** at different levels of risk in patients with systolic heart failure and mild symptoms: insight from a novel risk score for prognosis derived from the **EMPHASIS-HF** trial. Eur Heart J. 2013 Jul 17.

Colucci VJ, Berry BD. Heart failure worsening and exacerbation after **venlafaxine** and **duloxetine** therapy. Ann Pharmacother. 2008 Jun;42(6):882-7. Epub 2008 Apr 29.

Conrad N, Judge A, Canoy D, et al. Temporal **Trends and Patterns in Mortality** After Incident Heart Failure: A Longitudinal Analysis of 86 000 Individuals. JAMA Cardiol. 2019 Sep 3.

Conrad N, Judge A, Tran J, et al. **Temporal trends** and patterns in **heart failure incidence**: a population-based study of 4 million individuals. Lancet. 2017 Nov 21. pii: S0140-6736(17)32520-5.

Cooper LB, Hammill BG, Peterson ED, et al. Consistency of **Laboratory Monitoring During Initiation of Mineralocorticoid Receptor Antagonist Therapy** in Patients With Heart Failure. JAMA. 2015 Nov 10;314(18):1973-5.

Cooper LB, Mentz RJ, Sun J, et al. **Psychosocial factors, exercise adherence, and outcomes** in heart failure patients.*Circ Heart Fail* 2015; DOI:10.1161/CIRCHEARTFAILURE.115.002327.

Cosmi F, Di Giulio P, Masson S, et al; GISSI-HF Investigators. **Regular wine consumption** in chronic heart failure: impact on outcomes, quality of life, and circulating biomarkers. Circ Heart Fail. 2015. May;8(3):428-37.

Costanzo MR, Stevenson LW, Adamson PB, et al. Interventions linked to decreased heart failure hospitalizations during **ambulatory pulmonary artery pressure monitoring**. *JACC: Heart Fail* 2016.

Cowie MR, Lobos AA. **Telemonitoring** for patients with heart failure. CMAJ. 2012 Mar 20;184(5):509-10.

Cowie MR et al. **Adaptive servo-ventilation** for central **sleep apnea** in systolic heart failure. (SERVE-HF) N Engl J Med 2015 Sep 1; [e-pub].

Cresci S, Kelly RJ, Cappola TP, et al. Clinical and **genetic** modifiers of long-term survival in heart failure. J Am Coll Cardiol 2009; 54:432-444). DOI:10.1016/j.jacc.2009.05.009.

Cubbon RM, Witte KK. **Cardiac resynchronisation therapy** for chronic heart failure and conduction delay. BMJ. 2009 Apr 28;338:b1265. doi: 10.1136/bmj.b1265.

Cubbon R, Ruff N, Groves D, et al. **Ambulatory heart rate** range predicts mode-specific mortality and hospitalisation in chronic heart failure. *Heart* 2015.

Curtis AB et al. **Biventricular pacing** for atrioventricular block and systolic dysfunction. (**Block HF**) N Engl J Med 2013 Apr 25; 368:1585.

Cvelich RG, Roberts SC, Brown JN. **Phosphodiesterase type 5 inhibitors** as adjunctive therapy in the management of systolic heart failure. Ann Pharmacother. 2011 Dec;45(12):1551-8.

Dai W, Kloner RA. Is inhibition of phosphodiesterase type 5 by **sildenafil** a promising therapy for volume-overload heart failure? Circulation. 2012 Mar 20;125(11):1341-3.

Dalén M, Lund LH, Ivert T, et al. **Survival after coronary artery bypass grafting** in patients with preoperative heart failure and preserved vs reduced ejection fraction. *JAMA Cardiol* 2016.

Dalzell JR, Abu-Arafeh A, Campbell RT. **Cardiotoxicity with 5-Fluorouracil based** (capecitabine)agents: rechallenge cannot currently be safely advised. Am J Cardiol. 2013 Feb 1;111(3):454.

Damasceno A, Mayosi BM, Sani M, et al. The Causes, Treatment, and Outcome of Acute Heart Failure in 1006 **Africans From 9 Countries**: Results of the Sub-Saharan Africa Survey of Heart Failure. Arch Intern Med. 2012 Sep 3:1-9.

Damman K, Solomon SD, Pfeffer MA, et al. **Worsening renal function** and outcome in heart failure patients with reduced and preserved ejection fraction and the impact of angiotensin receptor blocker treatment: data from the **CHARM**-study programme. Eur J Heart Fail. 2016 Jul 18.

Dang W, Yi A, Jhamnani S, Wang SY. Cost-Effectiveness of **Multidisciplinary Management Program and Exercise Training** Program in Heart Failure. Am J Cardiol. 2017 Oct 15;120(8):1338-1343.

Davidson PM, Newton PJ, Tankumpuan T, et al. **Multidisciplinary Management** of Chronic Heart Failure: Principles and Future Trends. Clin Ther. 2015 Sep 24.

Davis BR, Kostis JB, Simpson LM, et al. for the ALLHAT Collaborative Research Group. **Heart Failure** With Preserved and Reduced Left Ventricular Ejection Fraction in the Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial. Circulation. 2008 Nov 10. [Epub ahead of print] In **ALLHAT**, with adjudicated outcomes, **chlorthalidone** significantly reduced the occurrence of new-onset hospitalized HFPEF and HFREF compared with amlodipine and doxazosin. Chlorthalidone also reduced the incidence of new-onset HFPEF compared with lisinopril. Among high-risk hypertensive men and women, HFPEF has a better prognosis than HFREF.

Davis CC, Zelnak A, Eley JW, et al. Clinical Utility of Routine **Cardiac Monitoring** in Breast Cancer Patients Receiving **Trastuzumab**. Ann Pharmacother. 2016 Jun 15.

de Denus S, O'Meara E, Desai AS, et al. **Spironolactone Metabolites in TOPCAT** - New Insights into Regional Variation. N Engl J Med. 2017 Apr 27;376(17):1690-1692.

de Boer RA, Nayor M, deFilippi CR, et al. Association of **Cardiovascular Biomarkers** With Incident Heart Failure **With Preserved and Reduced Ejection Fraction**. JAMA Cardiol. 2018 Jan 10.

De la Espriella R, Santas E, Miñana G, et al. **Functional Mitral Regurgitation** Predicts Short-Term Adverse Events in Patients With Acute Heart Failure and Reduced Left Ventricular Ejection Fraction. Am J Cardiol. 2017 Oct 15;120(8):1344-1348.

De Marco M, et al. Influence of Left **Ventricular Stroke Volume** on Incident Heart Failure in a Population With Preserved Ejection Fraction (from the Strong Heart Study). Am J Cardiol. 2017 Jan 5.

deFilippi Christopher R.; de Lemos James A.; Christenson Robert H.; et al. Association of Serial Measures of **Cardiac Troponin T** Using a Sensitive Assay With Incident Heart Failure and Cardiovascular Mortality in Older Adults. JAMA. 2010;0(2010):jama.2010.1708.

Defilippi CR, de Lemos JA, Tkaczuk AT, et al. **Physical Activity**, Change in Biomarkers of Myocardial Stress and Injury, and Subsequent Heart Failure Risk in Older Adults. J Am Coll Cardiol. 2012 Nov2.

DeJong C, Kazi DS, Dudley RA, et al. Assessment of National Coverage and Out-of-Pocket **Costs for Sacubitril/Valsartan** Under Medicare Part D. JAMA Cardiol. 2019 Jul 10.

Del Campo M, Roberts G. Changes in **Warfarin Sensitivity** During Decompensated Heart Failure and Chronic Obstructive Pulmonary Disease. Ann Pharmacother. 2015Sep;49(9):962-8.

Denfeld QE, Winters-Stone K, Mudd JO, et al. Frequency of and Significance of **Physical Frailty** in Patients with Heart Failure. Am J Cardiol.2017

Desai AS, Stevenson LW. **Rehospitalization** for heart failure: predict or prevent? Circulation. 2012 Jul 24;126(4):501-6.

Desai AS. **Serial Natriuretic Peptide** (BNP) Measurements Are Not Useful in Heart Failure Management: The Art of Medicine Remains Long. Circulation. 2013 Jan 29;127(4):509-16.

Desai AS, McMurray JJ, et al. Effect of the angiotensin-receptor-neprilysin inhibitor **LCZ696 compared with enalapril on mode of death** in heart failure patients. Eur Heart J. 2015 Aug 7;36(30):1990-7.

Desai AS. **Intensive Management to Reduce Hospitalizations** in Patients With Heart Failure. Circulation. 2016 Apr 26;133(17):1704-7

Desai AS, Jhund PS. After **TOPCAT**: What to do now in Heart Failure with **Preserved Ejection Fraction**. Eur Heart J. 2016 Apr 13.

Desai AS, Solomon S, Claggett B, et al. **Factors Associated With Noncompletion During the Run-In** Period Before Randomization and Influence on the Estimated Benefit of LCZ696 in the **PARADIGM-HF** Trial. Circ Heart Fail. 2016 Jun;9(6).

Desai AS, Solomon SD, Shah AM, et al. Effect of **Sacubitril-Valsartan vs Enalapril** on Aortic Stiffness in Patients With Heart Failure and Reduced Ejection Fraction: A Randomized Clinical Trial. JAMA. 2019 Sep 2:1-10.

Desai AS, Claggett BL, Packer M, et al. Influence of **sacubitril/valsartan (LCZ696)** on 30-day readmission after heart failure hospitalization. (**Paradigm-HF**) J Am Coll Cardiol 2016;68:241–8.

Desai AS, Vardeny O, Claggett B, et al. Reduced Risk of **Hyperkalemia** During Treatment of Heart Failure With Mineralocorticoid Receptor Antagonists by Use of Sacubitril/Valsartan Compared With Enalapril: A Secondary Analysis of the **PARADIGM-HF** Trial. JAMA Cardiol. 2016 Nov 14.

Desai AS, Bhimaraj, et al. **Levosimendan** in patients with left ventricular Dysfunction undergoing cardiac surgery. *J Am Coll Cardiol* 2017.

Dewan P, Rørth R, Jhund PS, et al. Differential Impact of Heart Failure **With Reduced Ejection Fraction** on Men and Women. J Am Coll Cardiol. 2019 Jan 8;73(1):29-40.

Dharmarajan K, Masoudi FA, Spertus JA, et al. **Contraindicated Initiation of β-Blocker** Therapy in Patients Hospitalized for Heart Failure. JAMA Intern Med. 2013 Jun 24:1-3

Dharmarajan K, Hsieh AF, Kulkarni VT, et al. **Trajectories of risk after hospitalization for heart failure, acute myocardial infarction, or pneumonia**: retrospective cohort study. BMJ. 2015 Feb 5;350:h411.

Dickson G. **Gynescomastia**. Am Fam Physician. 2012 Apr 1;85(7):716-722.

Dicpinigaitis PV. **Angiotensin-converting enzyme inhibitor**-induced **cough**: ACCP evidence-based clinical practice guidelines. *Chest* 2006;129(suppl):169-73S.

Dinicolantonio JJ, Pasquale PD, Taylor RS, et al. **Low sodium** versus normal sodium diets in systolic heart failure: systematic review and meta-analysis. Heart. 2012 Aug 21. **Retracted** June 2013.

Djoussé L, Driver JA, Gaziano JM. Relation between modifiable **lifestyle factors** and lifetime risk of heart failure. JAMA. 2009 Jul 22;302(4):394-400.

Docherty KF, Campbell RT, Jhund PS, et al. **How robust are clinical trials in heart failure**? Eur Heart J. 2017 Feb 1;38(5):338-345.

Dodson JA, Fried TR, Van Ness PH, et al. Patient preferences for **deactivation of implantable cardioverter-defibrillators**. JAMA Intern Med 2013.

Dokainish H, Teo K, Zhu J, et al. **Global mortality** variations in patients with heart failure: results from the International Congestive Heart Failure (**INTER-CHF**) prospective cohort study. Lancet Glob Health. 2017 May 2.

Dorans KS, Mostofsky E, Levitan EB, et al. **Alcohol and incident heart failure** among middle-aged and elderly men: cohort of Swedish men. Circ Heart Fail. 2015 May;8(3):422-7.

Dorsheimer L, Assmus B, Rasper T, et al. Mutations contributing to clonal hematopoiesis are associated with **poor prognosis in chronic ischemic heart failure**. JAMA Cardiol. doi:10.1001/jamacardio.2018.3965

Doshi D, Ben-Yehuda O, Bonafede M, et al. Underutilization of coronary artery disease **testing** among patients hospitalized with new-onset heart failure. *J Am Coll Cardiol*; 2016; 68:450-458.

Dougherty CM, et al. A prospective randomized trial of **moderately strenuous aerobic exercise** after an implantable cardioverter defibrillator (ICD).*Circulation* 2015.

Doukky R, Avery E, Mangla A, et al. Impact of **Dietary Sodium Restriction** on Heart Failure Outcomes. JACC Heart Fail. 2016 Jan;4(1):24-35.

Dracup K, Moser DK, Pelter MM, et al. Randomized, controlled trial to improve **self-care** in patients with heart failure living in **rural areas**. Circulation. 2014 Jul 15;130(3):256-64.

Driscoll A, Currey J, Tonkin A, Krum H. **Nurse-led titration** of angiotensin converting enzyme inhibitors, beta-adrenergic blocking agents, and angiotensin receptor blockers for people with heart failure with reduced ejection fraction. Cochrane Database of Systematic Reviews 2015, Issue 12. Art. No.: CD009889. DOI: 10.1002/14651858.CD009889.pub2. Participants in the NLT group experienced fewer hospital admissions for any cause and an increase in survival and number of participants reaching target dose within a shorter time period. However, the quality of evidence regarding the proportion of participants reaching target dose was low and should be interpreted with caution. We found high-quality evidence supporting NLT as one strategy that may improve the optimisation of beta-adrenergic blocking agents resulting in a reduction in hospital admissions. Despite evidence of a dosedependent relationship of beta-adrenergic blocking agents, ACEIs, and ARBs with improving outcomes in patients with HFrEF, the translation of this evidence into clinical practice is poor. NLT is one strategy that facilitates the implementation of this evidence into practice.

Dunbar S, Dougherty C, Sears S, et al. Educational and psychological interventions to improve outcomes for recipients of **implantable cardioverter defibrillators** and their families. Circulation 2012.

Dunlay SM, Givertz MM, Aguilar D, et al. **Type 2 Diabetes Mellitus and Heart Failure**, A Scientific Statement From the American Heart Association and Heart Failure Society of America. J Card Fail. 2019 Jun 3.

Dunlay SM, Manemann SM, Chamberlain AM, et al. **Activities of Daily Living and Outcomes** in Heart Failure. Circ Heart Fail.2015 Feb 25. pii: CIRCHEARTFAILURE.114.001542. [Epub ahead of print]

Dunlay SM, Swetz KM, Mueller PS, Roger VL. **Advance Directives** in Community Patients With Heart Failure. Circ Cardiovasc Qual Outcomes. 2012 May 11.

Dworzynski K, Roberts E, Ludman A, et al; Guideline Development Group. **Diagnosing and managing acute heart failure in adults**: summary of **NICE** guidance. BMJ. 2014 Oct 8;349:g5695.

Earley A, Persson R, Garlitski AC, et al. Effectiveness of **implantable cardioverter defibrillators** for primary prevention of sudden cardiac death in subgroups a systematic review. Ann Intern Med. 2014 Jan 21;160(2):111-21.

Eaton CB, Abdulbaki AM, Margolis KL et al. **Racial and Ethnic Differences** in Incident Hospitalized Heart Failure in Postmenopausal Women: The Women's Health Initiative. Circulation. 2012 Aug 7;126(6):688-96.

Edelmann F, Gelbrich G, Düngen H-D, et al. **Exercise training** improves exercise capacity and diastolic function in patients with heart failure with preserved ejection fraction: results of the Ex-DHF (Exercise training in Diastolic Heart Failure) pilot study. J Am Coll Cardiol 2011;58:1780 –91.

Edelmann F, Wachter R, Schmidt AG, et al for the **Aldo-DHF** Investigators. Effect of **spironolactone on diastolic function** and exercise capacity in patients with heart failure with preserved ejection fraction: The Aldo-DHF randomized controlled trial. JAMA2013; 309:781-791.

Egiziano G et al. Improved outcomes in **heart failure** treated with **high-dose ACE inhibitors and ARBs**: a population-based study. Arch Intern Med [Epub ahead of print] 2 July 2012;

Egstrup M, Schou M, Tuxen CD, et al. Prediction of Outcome by **Highly Sensitive Troponin T** in Outpatients With Chronic Systolic Left Ventricular Heart Failure. Am J Cardiol. 2012 May 9.

Ejlersen H, et al. **Prognostic impact of physical activity prior to myocardial infarction**: Case fatality and subsequent risk of heart failure and death. Eur J Prev Cardiol. 2017 Jan 1:2047487317702046.

Eklind-Cervenka M, Benson L, Dahlstro¨m U, et al. Association of **candesartan vs losartan** with all-cause mortality in patients with **heart failure**. JAMA. 2011;305(2):175-182.

Ekman I, Chassany O, Komajda M et al. Heart rate reduction with **ivabradine** and health related quality of life in patients with chronic heart failure: results from the SHIFT study. Eur Heart J 2011

El-Jawahri A, et al. Randomized, Controlled Trial of an **Advance Care Planning Video** Decision Support Tool for Patients With Advanced Heart Failure. Circulation. 2016 Jul 5;134(1):52-60.

Ellenbogen Kenneth A., Gold Michael R., Meyer Timothy E., et al. Primary Results From the SmartDelay Determined AV Optimization: A Comparison to Other AV Delay Methods Used in Cardiac Resynchronization Therapy (**SMART-AV**) Trial: A Randomized Trial Comparing Empirical, Echocardiography-Guided, and Algorithmic Atrioventricular Delay Programming in Cardiac Resynchronization Therapy. Circulation published November 15, 2010, doi:10.1161/CIRCULATIONAHA.110.992552

Ellingsen Ø, Halle M, Conraads VM, et al; **SMARTEX** Heart Failure Study Group.. **High Intensity Interval Training** in Heart Failure Patients with Reduced Ejection Fraction. Circulation. 2017 Jan 12.

Ellison DH, Felker GM. **Diuretic Treatment in Heart Failure**. N Engl J Med. 2017 Nov 16;377(20):1964-1975.

Elming MB, Nielsen JC, Haarbo J, et al. **Age and Outcomes** of Primary Prevention Implantable Cardioverter Defibrillators in Patients with Non-Ischemic Systolic Heart Failure. Circulation. 2017 Sep 6.

Emdin CA, Callender T, Cao J, et al. Meta-Analysis of Large-Scale Randomized Trials to Determine the Effectiveness of Inhibition of the **Renin-Angiotensin Aldosterone System** in Heart Failure. Am J Cardiol. 2015 Apr 9

Engoren M, Schwann TA, Arslanian-Engoren C, et al. U-Shape Association Between **Hemoglobin A1c** and Late Mortality in Patients With Heart Failure After Cardiac Surgery. Am J Cardiol. 2013 Feb 4.

Epstein AM, Jha AK, Orav JE. The relationship between **hospital readmission rates and rehospitalizations**. N Engl J Med 2011; 365:2287-2295.

ESC Task Force for Diagnosis and Treatment of **Acute and Chronic Heart Failure 2008** of European Society of Cardiology, Dickstein K, Cohen-Solal A, Filippatos G, et al. ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure 2008: the Task Force for the Diagnosis and Treatment of Acute and Chronic Heart Failure 2008 of the European Society of Cardiology. Developed in collaboration with the Heart Failure Association of the ESC (HFA) and endorsed by the European Society of Intensive Care Medicine (ESICM). Eur Heart J. 2008 Oct;29(19):2388-442. Epub 2008 Sep 17. http://www.escardio.org/guidelines-surveys/esc-guidelines/GuidelinesDocuments/guidelines-HF-FT.pdf

ESC McMurray JJV, Adamopoulos S, Anker SD, et al. **ESC guidelines** for the diagnosis and treatment of acute and **chronic heart failure 2012**: The Task Force for the Diagnosis and Treatment of Acute and Chronic Heart Failure 2012 of the European Society of Cardiology. Developed in collaboration with the Heart Failure Association (HFA) of the ESC. Eur Heart J 2012.

Eurich DT, Marrie TJ, Minhas-Sandhu JK, et al. Risk of heart failure after **community acquired pneumonia**: prospective controlled study with 10 years of follow-up. BMJ. 2017 Feb 13;356:j413.

Evans JDW, Dobbin SJH, Pettit SJ, et al. **High-Sensitivity Cardiac Troponin** and New-Onset Heart Failure: A Systematic Review and Meta-Analysis of 67,063 Patients With 4,165 Incident Heart Failure Events. JACC Heart Fail. 2018 Mar;6(3):187-197.

Ewer MS, Ewer SM. **Troponin I** provides insight into cardiotoxicity and the anthracycline-**trastuzumab** interaction. J Clin Oncol 2010; 28: 3901-3904.

Eyal A, Roguin A. **Magnetic Resonance Imaging in Patients With Cardiac Implantable Electronic Devices**. Circulation. 2015 Oct 6;132(14):e176-8.

Ezekowitz JA, O'Meara E, et al. **2017 Comprehensive Update of the Canadian Cardiovascular Society (CCS)** Guidelines for the Management of Heart Failure. Canadian Journal of Cardiology. 2017.

Fadini GP, Avogaro A, Degli Esposti L, et al. Risk of **hospitalization for heart failure** in patients with type 2 diabetes newly treated with **DPP-4 inhibitors** or other oral glucose-lowering medications: a retrospective registry study on 127,555 patients from the Nationwide OsMed Health-DB Database. Eur Heart J. 2015 Jun 25.

Fang JC. Heart Failure With **Preserved Ejection Fraction**: A Kidney Disorder? Circulation. 2016 Aug 9;134(6):435-7

FDA Sep/12 notified healthcare profesionals about a possible increased risk of heart failure with Mirapex (**pramipexole**). Results of recent studies suggest a potential risk of heart failure that needs further review of available data.

FDA Aug/15 is alerting health care providers, patients, and caregivers about **serious adverse events associated with LVADs**. These adverse events include an increased rate of pump thrombosis

(blood clots inside the pump) with Thoratec's HeartMate II and a high rate of stroke with the HeartWare HVAD since approval of the devices. FDA is also aware of bleeding complications related to both the Thoratec HeartMate II and HeartWare HVAD. See the FDA Safety Communication for more detailed information.

Feijen EAM, Leisenring WM, Stratton KL, et al. Derivation of **Anthracycline and Anthraquinone Equivalence Ratios to Doxorubicin for Late-Onset Cardiotoxicity**. JAMA Oncol. 2019 Jan 31.

Feldman AM, Haller JA, DeKosky ST. **Valsartan/Sacubitril** for Heart Failure: **Reconciling Disparities** Between Preclinical and Clinical Investigations. JAMA. 2016 Jan 5;315(1):25-26.

Feldman T, Mauri L, Kahwash R, et al. A **Transcatheter InterAtrial Shunt Device** for the Treatment of Heart Failure with Preserved Ejection Fraction **(REDUCE LAP-HF I):** A Phase 2, Randomized, Sham-Controlled Trial. Circulation. 2017 Nov 15.

Feltner C, Jones CD, Cené CW, et al. **Transitional Care Interventions** to Prevent Readmissions for Persons With Heart Failure: A Systematic Review and Meta-analysis. Ann Intern Med. 2014 Jun 3;160(11):774-84.

Felker GM et al for the NHLBI Heart Failure Clinical Research Network. **Diuretic strategies** in patients with acute decompensated heart failure. (DOSE trial) N Engl J Med 2011 Mar 3; 364:797.

Felker GM, Anstrom KJ, Adams KF, et al. Effect of **natriuretic peptide-guided therapy** on hospitalization or cardiovascular mortality in high-risk patients with heart failure and reduced ejection fraction: a randomized clinical trial.JAMA. doi:10.1001/jama.2017.10565.

Fendler TJ, Spertus JA, Gosch KL, et al. Incidence and Predictors of **Cognitive Decline** in Patients with **Left Ventricular Assist Devices**. Circ Cardiovasc Qual Outcomes. 2015 Apr 29.

Fendler TJ, Nassif ME, Kennedy KF, et al. **Global Outcome** in Patients With **Left Ventricular Assist Devices**. Am J Cardiol. 2017 Jan 5.

Ferdinand KC, Elkayam U, Mancini D, et al. "Use of **Isosorbide Dinitrate and Hydralazine in African Americans** With Heart Failure 9 Years After **A-HeFT**". The American Journal of Cardiology. (2014).

Filion KB, Azoulay L, Platt RW, et al; **CNODES** Investigators. A Multicenter Observational Study of **Incretin-based Drugs and Heart Failure**. N Engl J Med. 2016 Mar 24;374(12):1145-54.

Fudim M, Cerbin LP, Devaraj S, et al. **Post-Traumatic Stress Disorder and Heart Failure** in Men Within the Veteran Affairs Health System. Am J Cardiol. 2018 Apr 11.

Miro´ O`, et al. **Predicting 30-day mortality for patients with acute heart failure** in the emergency department. A cohort study. Ann Intern Med. 2017. [Epub ahead of print]. doi:10.7326 /M16-2726

Fishbein DP, Hellkamp AS, Mark DB, et al. Use of the **six-minute walk distance to identify variations in treatment benefits from ICD and amiodarone**: Results from the Sudden Cardiac Death in Heart Failure Trial (SCD-HeFT). J Am Coll Cardiol 2014; DOI:10.1016/j.jacc.2014.02.602. Abstract

Fisher SA, Doree C, Mathur A, et al. **Stem cell therapy** for chronic ischaemic heart disease and congestive heart failure. Cochrane Database Syst Rev. 2016 Dec 24;12:CD007888.

Fisher SA, Brunskill SJ, Doree C, et al. **Stem cell therapy** for chronic ischaemic heart disease and congestive heart failure. Cochrane Database of Systematic Reviews 2014, Issue 4. Art. No.: CD007888. DOI: 10.1002/14651858.CD007888.pub2.

Fiuzat M, Wojdyla D, Kitzman D, et al. Relationship of **Beta-Blocker Dose** With Outcomes in Ambulatory Heart Failure Patients With Systolic Dysfunction: Results From the HF-ACTION (Heart Failure: A Controlled Trial Investigating Outcomes of Exercise Training) Trial. J Am Coll Cardiol. 2012 Apr 18.

Flather MD, Shibata MC, Coats AJ, et al. Randomized trial to determine the effect of **nebivolol** on mortality and cardiovascular hospital admission in elderly patients with heart failure (**SENIORS**). Eur Heart J 2005;26:215-25.

Flatt DM, Brown MC, Mizeracki AM, Ket al. **Mineralocorticoid Receptor Antagonists** in the Management of Heart Failure and Resistant Hypertension: A Review. JAMA Cardiol. 2016 Jul 13.

Fleetcroft R, Ford J, Gollop ND, et al. **Difficulty accessing data from randomised trials** of drugs for heart failure: a call for action. BMJ. 2015 Oct 21;351:h5002.

Fleming LM, Gavin M, Piatkowski G, et al. Derivation and Validation of a **30-Day Heart Failure Readmission Model**. Am J Cardiol. 2014 Aug 12.

Florido R, Kwak L, Lazo M, et al. Six-Year Changes in **Physical Activity and the Risk of Incident Heart Failure**: ARIC Study. Circulation. 2018 May 15;137(20):2142-2151.

Flynn KE, Piña IL, Whellan DJ, et al. Effects of exercise training on health status in patients with chronic heart failure: **HF-ACTION** randomized controlled trial. JAMA. 2009 Apr 8;301(14):1451-9.

Fonarow GC, Abraham WT, Albert NM, et al. OPTIMIZE-HF Investigators and Coordinators. Influence of beta-blocker continuation or withdrawal on outcomes in patients hospitalized with heart failure: findings from the OPTIMIZE-HF program. J Am Coll Cardiol. 2008 Jul 15;52(3):190-9. The continuation of beta-blocker therapy in patients hospitalized with decompensated HF is associated with lower post-discharge mortality risk and improved treatment rates. In contrast, withdrawal of beta-blocker therapy is associated with worse risk and propensity-adjusted mortality.

Fonarow GC, Albert NM, Curtis AB, et al. Associations Between Outpatient Heart Failure **Process-of-Care Measures** and Mortality. Circulation. 2011 Apr 19;123(15):1601-10.Current and emerging outpatient HF process measures are positively associated with patient survival. These HF measures may be useful for assessing and improving HF care.

Fonarow GC, Yancy CW, Hernandez AF, et al. Potential impact of **optimal implementation of evidence-based heart failure therapies** on **mortality**. Am Heart J. 2011 Jun;161(6):1024-1030.e3

Fonarow GC, Albert NM, Curtis AB, et al. Incremental **reduction in risk of death** associated with use of **guideline-recommended** therapies in patients with heart failure: a nested case-control analysis of **IMPROVE HF**. J Am Heart Assoc Cardiovasc Cerebrovasc Dis 2012.

Fong T, Lee AJ. **Pregabalin-Associated** Heart Failure Decompensation in a Patient With a History of Stage I Heart Failure. Ann Pharmacother. 2014 Apr25;48(8):1077-1081.

Fosbøl EL, Rørth R, Leicht BP, et al. **Association of Carpal Tunnel Syndrome** With Amyloidosis, Heart Failure, and Adverse Cardiovascular Outcomes. J Am Coll Cardiol. 2019 Jul 9;74(1):15-23.

Fowler NR, Johnson KG, Li J, et al. Use of **cardiac implantable electronic devices** in older adults with cognitive impairment. *JAMA Intern Med* 2014.

Franceschini N, Kopp JB, Barac A, et al. Association of **APOL1 With Heart Failure With Preserved Ejection Fraction** in Postmenopausal African American Women. JAMA Cardiol. 2018 Jul 3.

Francis GS, Greenberg BH, Hsu DT, et al. ACCF/AHA/ACP/HFSA/ISHLT 2010 clinical competence statement on management of patients with **advanced heart failure and cardiac transplant**: a report of the ACCF/AHA/ACP Task Force on Clinical Competence and Training. Circulation. 2010 Aug 10;122(6):644-72.

Freedland KE, Carney RM, Rich MW, et al. **Cognitive behavior therapy for depression** and self-care in heart failure patients: a randomized clinical trial [online September 28]. JAMA Intern Med. doi:10.1001 /jamainternmed.2015.5220.

Freeman JV, Yang J, Sung SH, et al. Effectiveness and Safety of **Digoxin Among Contemporary Adults** With Incident Systolic Heart Failure. Circ Cardiovasc Qual Outcomes. 2013 Sep 10.

Freiberg MS, et al. Association between **HIV infection** and the risk of heart failure with reduced ejection fraction and preserved ejection fraction in the antiretroviral therapy era: results from the **Veterans Aging Cohort** Study [online Apr 5, 2017].JAMA Cardiol. doi:10.1001/jamacardio.2017.0264

Freitas P, Aguiar C, Ferreira A, et al. Comparative Analysis of **Four Scores to Stratify Patients With Heart Failure** and Reduced Ejection Fraction. Am J Cardiol. 2017 Aug 1;120(3):443-449.

Friedman DJ, Singh JP, et al. Comparative effectiveness of **CRT-D versus defibrillator** alone in HF patients with moderate-to-severe chronic kidney disease. *J Am Coll Cardiol* 2015; 66:2618-2629.

Friedman DJ, et al. Association Between a **Prolonged PR Interval** and Outcomes of Cardiac Resynchronization Therapy: Report from the National Cardiovascular Data Registry. Circulation. 2016 Oct 19.

Frizzell JD, et al. **Prediction of 30-Day All-Cause Readmissions** in Patients Hospitalized for Heart Failure: Comparison of Machine Learning & Other Statistical Approaches. JAMA Cardiol. 2016 Oct 26.

Fu AZ, et al. Association Between Hospitalization for Heart Failure and **Dipeptidyl Peptidase-4 Inhibitors** in Patients With Type 2 Diabetes: An Observational Study. Diabetes Care. 2016 Jan 6.

Fumagalli S, Gasparini M, Landolina M, et al; Italian Clinical Service Project Centers. Determinants of All-Cause Mortality in Different Age Groups in Patients With Severe Systolic Left Ventricular Dysfunction Receiving an **Implantable Cardioverter Defibrillator** (from the Italian ClinicalService Multicenter Observational Project). Am J Cardiol. 2014 May 15;113(10):1691-6.

Gaasch WH. Deliberations on **Diastolic Heart Failure**. Am J Cardiol. 2016 Sep 29.

Gasparini M, Proclemer A, Klersy C, et al. Effect of **long-detection interval vs standard-detection interval** for implantable **cardioverter-defibrillators** on antitachycardia pacing and shock delivery: The ADVANCE III randomized clinical trial. JAMA 2013; 309:1903-1911.

Gazewood JD, Turner PL. **Heart Failure with Preserved Ejection Fraction**: Diagnosis and Management. Am Fam Physician. 2017;96(9):582-588.

Gaziano TA, Fonarow GC, et al. Cost-effectiveness Analysis of **Sacubitril/Valsartan** vs Enalapril in Patients With Heart Failure and Reduced Ejection Fraction. JAMA Cardiol. 2016 Jun 22.

Gelow JM, Mudd JO, Chien CV, Lee CS. **Usefulness of Cognitive Dysfunction** in Heart Failure to Predict Cardiovascular Risk at 180 Days. Am J Cardiol. 2015 Jan 7.

Georgiopoulou VV, Kalogeropoulos AP, Giamouzis G, et al. **Digoxin therapy does not** improve outcomes in patients with advanced heart failure on contemporary medical therapy. Circ Heart Fail. 2009;2:90 –97.

Georgiopoulou VV, Kalogeropoulos AP, Chowdhury R, et al. **Exercise Capacity**, Heart Failure Risk, and Mortality in Older Adults: The Health ABC Study. Am J Prev Med. 2017 Feb;52(2):144-153.

Gerber Y, Weston SA, Redfield MM, et al. A **Contemporary Appraisal of the Heart Failure Epidemic in Olmsted County**, Minnesota, 2000 to 2010. JAMA Intern Med. 2015 Apr 20.

Gerdes AM, Iervasi G. **Thyroid replacement** therapy and heart failure. Circulation. 2010 Jul 27;122(4):385-93.

Gerstein HC, Jung H, Rydén L, et al. Effect of Basal Insulin **Glargine** on First and Recurrent Episodes of **Heart Failure Hospitalization**: The **ORIGIN** Trial (Outcome Reduction With Initial Glargine Intervention). Circulation. 2018 Jan 2;137(1):88-90

Gerstein HC, Jung H, Rydén L, et al; **ORIGIN** Investigators. Effect of **Basal Insulin Glargine** on First and Recurrent Episodes of Heart Failure Hospitalization: The ORIGIN Trial (Outcome Reduction With Initial Glargine Intervention). Circulation. 2018 Jan 2;137(1):88-90.

Ghanbari Hamid; Dalloul Ghassan; Hasan Reema; et al. Effectiveness of **Implantable Cardioverter-Defibrillators** for the Primary Prevention of Sudden Cardiac Death in Women With Advanced Heart Failure: A Meta-analysis of Randomized Controlled Trials. Arch Intern Med. 2009;169(16):1500-1506.

Gheorghiade Mihai, Braunwald Eugene. A Proposed Model for **Initial Assessment and Management of Acute Heart Failure** Syndromes. JAMA. 2011;305(16):1702-1703.doi:10.1001/jama.2011.515

Gheorghiade M, Eugene Braunwald E. **Hospitalizations** for heart failure in the United States—a sign of hope. JAMA 2011; 306:1705-1706.

Gheorghiade M, et al. Effect of **aliskiren** on postdischarge mortality and heart failure readmissions among patients hospitalized for heart failure: The **ASTRONAUT** randomized trial. JAMA 2013.

Gheorghiade M, Greene SJ, Butler J, et al. Effect of **Vericiguat**, a Soluble Guanylate Cyclase Stimulator, on Natriuretic Peptide Levels in Patients With Worsening Chronic Heart Failure and Reduced Ejection Fraction: The **SOCRATES-REDUCED** Randomized Trial. JAMA. 2015 Dec 1;314(21):2251-2262.

Gilbert RE, Krum H. **Heart failure in diabetes**: effects of anti-hyperglycaemic drug therapy. Lancet. 2015 May 23;385(9982):2107-17.

Gillis AM, Kerr CR, Philippon F, et al. Impact of **cardiac resynchronization therapy** on hospitalizations in the resynchronization-defibrillation for ambulatory heart failure trial. Circulation. 2014 May 20;129(20):2021-30.

Gilstrap LG, DeFilippis EM, Stevenson LW. An Unintended **Consequence of the 21st-Century Cures Act** for Patients With Heart Failure. Circulation. 2017 Jul 11;136(2):123-125

Gislason GH, Rasmussen JN, Abildstrom SZ, et al. Increased mortality and cardiovascular morbidity associated with use of nonsteroidal anti-inflammatory drugs (**NSAIDs**) in chronic heart failure. Arch Intern Med. 2009 Jan 26;169(2):141-9.

Gissi-Hf Investigators. Effect of **n-3 polyunsaturated fatty acids** in patients with chronic heart failure (the **GISSI-HF** trial): a randomised, double-blind, placebo-controlled trial. Lancet. 2008 Aug 29. A simple and safe treatment with n-3 PUFA can provide a small beneficial advantage in terms of mortality and admission to hospital for cardiovascular reasons in patients with heart failure in a context of usual care.

Gissi-Hf Investigators. Effect of **rosuvastatin** in patients with chronic heart failure (the **GISSI-HF** trial): a randomised, double-blind, placebo-controlled trial. Lancet. 2008 Aug 29. [Epub ahead of print] Rosuvastatin 10 mg daily did not affect clinical outcomes in patients with chronic heart failure of any cause, in whom the drug was safe

Givertz MM. **Ventricular assist devices**: important information for patients and families. Circulation. 2011 Sep 20;124(12):e305-11.

Givertz MM, Anstrom KJ, Redfield MM, et al; NHLBI Heart Failure Clinical Research Network*. Effects of **Xanthine Oxidase Inhibition** in **Hyperuricemic** Heart Failure Patients: The Xanthine Oxidase Inhibition for Hyperuricemic Heart Failure Patients (EXACT-HF) Study. Circulation. 2015 May 19;131(20):1763-71.

Glynn P, Lloyd-Jones DM, Feinstein MJ, et al. **Disparities in Cardiovascular Mortality Related to Heart Failure in the United States**. J Am Coll Cardiol. 2019 May 14;73(18):2354-2355.

Goff ZD, Kichura AB, Chibnall JT, Hauptman PJ. A Survey of Unregulated Direct-to-Consumer Treatment Centers Providing **Stem Cells** for Patients With Heart Failure. JAMA Intern Med. 2017 Jul 24.

Gold M, Nath N, Green C, Atwater AR. Frequency of **Contact Allergy to Implanted Cardiac Devices**. JAMA Dermatol. 2019 Apr 3.

Gold MR, Thébault C, Linde C et al. Effect of QRS Duration and Morphology on **Cardiac Resynchronization Therapy** (CRT) Outcomes in Mild Heart Failure: Results From the Resynchronization Reverses Remodeling in Systolic Left Ventricular Dysfunction (REVERSE) Study. Circulation. 2012 Aug 14;126(7):822-9.

Goldberg RJ, Gurwitz JH, Saczynski JS, et al. Comparison of **Medication** Practices in Patients With Heart Failure and **Preserved Versus Those With Reduced Ejection** Fraction (Cardiovascular Research Network [CVRN]). Am J Cardiol. 2013 Feb 1.

Goldberger ZD, Goldberger AL. Therapeutic Ranges of Serum **Digoxin** Concentrations in Patients With Heart Failure. Am J Cardiol. 2012 Apr 11.

Goldberger ZD, Alexander GC. **Digitalis Use in Contemporary Clinical Practice**: Refitting the Foxglove. JAMA Intern Med. 2013 Nov 11.

Goldenberg I, Hall WJ, Beck CA, et al. Reduction of the risk of recurring heart failure events with cardiac resynchronization therapy: **MADIT-CRT** (Multicenter Automatic Defibrillator Implantation Trial with Cardiac Resynchronization Therapy). J Am Coll Cardiol 2011; 58:729-737.

Goldenberg I, Kutyifa V, Klein HU, et al. Survival with **cardiacresynchronization therapy** in mild heart failure. N Engl J Med. DOI: 10.1056/NEJMoa1401426.

Golwala H, Pandey A, Ju C, et al. Temporal trends and factors associated with **cardiac rehabilitation** referral among patients hospitalized with heart failure: Findings from Get With the Guidelines–Heart Failure Registry. *J Am Coll Cardiol* 2015; 66:917–926.

Gomes Neto M, Menezes MA, Carvalho VO. **Dance therapy** in patients with chronic heart failure: a systematic review and a meta-analysis. Clin Rehabil. 2014 May 21.

Gomes Neto M, Ferrari F, Helal L, et al. The impact of **high-intensity inspiratory muscle training on exercise capacity and inspiratory muscle strength in heart failure** with reduced ejection fraction: a systematic review and meta-analysis. Clin Rehabil. 2018 Jul 1:269215518784345.

Gonçalves A, Claggett B, Jhund PS, et al. **Alcohol consumption** and risk of heart failure: The Atherosclerosis Risk in Communities Study. *Eur Heart J* 215.

Gotsman I, Keren A, et al. Usefulness of Electrocardiographic Frontal **QRS-T Angle** to Predict Increased Morbidity and Mortality in Patients With Chronic Heart Failure. Am J Cardiol. 2013 Feb 27.

Grandin EW, Wand A, Zamani P, et al. Relation of **Body Mass Index** to Long-Term Survival After Cardiac Resynchronization Therapy. Am J Cardiol. 2016 Dec 15;118(12):1861-1867.

Grant JD, Jensen GL, et al. **Radiotherapy-Induced Malfunction in Contemporary Cardiovascular Implantable Electronic Devices**: Clinical Incidence and Predictors. JAMA Oncol. 2015 Jun 25.

Greenberg B, Neaton JD, Anker SD, et al. **Association of Rivaroxaban With Thromboembolic Events** in Patients With Heart Failure, Coronary Disease, and Sinus Rhythm: A Post Hoc Analysis of the COMMANDER HF Trial. JAMA Cardiol. 2019 Apr 24.

Greene SJ, Butler j, Albert NM, et al. **Medical Therapy for Heart Failure** With Reduced Ejection Fraction: The CHAMP-HF Registry. J Am Coll Cardiol. 2018 Jul; 72 (4) 351-366.

Groarke JD, Nohria A. **Anthracycline Cardiotoxicity**: A New Paradigm for an Old Classic. Circulation. 2015 May 6.

Grodin JL, Stevens SR, de las Funetes L, et al. Intensification of medication therapy for **cardiorenal syndrome** in acute decompensated heart failure. *J Card Fail* 2015.

Grodin JL, Sun JL, Anstrom KJ, et al. Implications of **Serum Chloride** Homeostasis in Acute Heart Failure (from **ROSE-AHF**). Am J Cardiol. 2016 Sep 30.

Grodin JL, et al. Implications of **Alternative Hepatorenal Prognostic Scoring Systems** in **Acute Heart Failure** (from **DOSE-AHF** and **ROSE-AHF**). Am J Cardiol. 2017 Jun 15;119(12):2003-2009

Groeneveld PW, Medvedeva EL, Walker L, et al. Outcomes of care for **ischemic coronary disease and chronic heart failure** in the Veterans Health Administration [online May 16, 2018]. JAMA Cardiol.

Grote Beverborg N, van der Wal HH, Klip IT, et al. Differences in Clinical Profile and Outcomes of **Low Iron Storage vs Defective Iron Utilization in Patients With Heart Failure**: Results From the DEFINE-HF and BIOSTAT-CHF Studies. JAMA Cardiol. 2019 Jun 12.

Gruson D, Pouleur AC, Makris K, et al. Systematic **vitamin D supplementation** and monitoring: improving outcomes in heart failure? Eur J Heart Fail. 2017 May;19(5):686-687.

Guazzi M, Vicenzi M, Arena R, Guazzi MD. **Pulmonary hypertension** in heart failure with preserved ejection fraction: a target of phosphodiesterase-5 inhibition (**sildenafil**) in a 1-year study. Circulation. 2011 Jul 12;124(2):164-74.

Guerrera M. et al. Therapeutic Uses of **Magnesium**. Am Fam Physician. 2009; 80(1):157-162.

Guirguis-Blake J. **Transitional Care Interventions** to Prevent Readmissions for Patients with Heart Failure. Am Fam Physician. 2016 Mar 1;93(5):401-3.

Gulati G, Grandin EW, Kennedy K, et al. **Preimplant Phosphodiesterase-5 Inhibitor Use** Is Associated With Higher Rates of Severe Early Right Heart Failure After Left Ventricular Assist Device Implantation. Circ Heart Fail. 2019 Jun;12(6):e005537.

Gulati R, Gersh BJ. **Percutaneous Coronary Intervention vs. Coronary Artery Bypass Grafting** in Patients With Left Ventricular Dysfunction: Do We Have the Evidence? Circulation. 2016 May 5.

Gupta A, Allen LA, et al. Association of the **Hospital Readmissions Reduction Program** Implementation With Readmission and Mortality Outcomes in Heart Failure. JAMA Cardiol. 2017 Nov 12.

Gupta D, Georgiopoulou VV, Kalogeropoulos AP, et al. **Dietary sodium** intake in heart failure. Circulation. 2012 Jul 24;126(4):479-85.

Gutzwiller FS, Schwenkglenks M, Blank PR, et al. Health economic assessment of ferric **carboxymaltose** in patients with iron deficiency and chronic heart failure based on the FAIR-HF trial: an analysis for the UK. Eur J Heart Fail 2012;14:782e790.

Hackam DG, Quinn RR, Ravani P, et al. Canadian Hypertension Education Program. The **2013 Canadian Hypertension Education Program (CHEP) Recommendations** for Blood Pressure Measurement, Diagnosis, Assessment of Risk, Prevention, and Treatment of Hypertension. Can J Cardiol. 2013 Mar 28.

Hall PS et al. **Reproductive factors** and incidence of heart failure hospitalization in the Women's Health Initiative. J Am Coll Cardiol 2017 May 15.

Halley CM, Houghtaling PL, Khalil MK, Thomas JD, Jaber WA. **Mortality rate in patients with diastolic dysfunction** and normal systolic function. Arch Intern Med. 2011;171(12): 1082-1087.

Halliday BP, Wassall R, Lota AS, et al. **Withdrawal of pharmacological treatment** for heart failure in patients with recovered dilated cardiomyopathy (TRED-HF): an open-label, pilot, randomised trial. Lancet. 2019;393:61-73.

Hallow KM, Helmlinger G, et al. Why do **SGLT2 inhibitors reduce heart failure hospitalization**? A differential volume regulation hypothesis. Diabetes Obes Metab. 2018 Mar;20(3):479-487.

Hamaguchi S, Kinugawa S, Tsuchihashi-Makaya M, et al. **Spironolactone** use at discharge was associated with improved survival in hospitalized patients with systolic heart failure. Am Heart J. 2010 Dec;160(6):1156-62.

Hamm CW, Bassand JP, Agewall S, et al. **ESC** Guidelines for the management of **acute coronary syndromes** in patients presenting without persistent ST-segment elevation: The Task Force for the management of acute coronary syndromes (ACS) in patients presenting without persistent ST-segment elevation of the European Society of Cardiology (ESC). Eur Heart J. 2011 Sep 21.

Hammond HK, Penny WF, Traverse JH, et al. **Intracoronary Gene Transfer** of Adenylyl Cyclase 6 in Patients With Heart Failure: A Randomized Clinical Trial. JAMA Cardiol. 2016 May 1;1(2):163-71.

Han JJ, Acker MA, Atluri P. **Left Ventricular Assist Devices**. Circulation. 2018 Dec 11;138(24):2841-2851.

Hasegawa K, Tsugawa Y, et al. **Frequent Utilization of the Emergency Department** for Acute Heart Failure Syndrome: A Population-Based Study. Circ Cardiovasc Qual Outcomes. 2014 Aug 19.

Hasenfuß G, Hayward C, Burkhoff D, et al; REDUCE LAP-HF study investigators. A **transcatheter intracardiac shunt device** for heart failure with preserved ejection fraction (**REDUCE LAP-HF**): a multicentre, open-label, single-arm, phase 1 trial. Lancet. 2016 Mar 26;387(10025):1298-304.

Hashim T, Elbaz S, Patel K, et al. A. **Digoxin** and 30-day All-cause Hospital Admission in Older Patients with Chronic Diastolic Heart Failure. Am J Med. 2013 Sep 17.

Hasin T, Gerber Y, McNallan SM, et al. Patients with heart failure have an **increased risk of incident cancer**. J Am Coll Cardiol 2013;62:881–6.

Hasin T, Gerber Y, Weston SA, et al. Heart Failure After Myocardial Infarction Is Associated With Increased **Risk of Cancer**. J Am Coll Cardiol. 2016 Jul 19;68(3):265-71.

Hasin T, Zalut T, Hasin Y. Managing the Patient with **Heart Failure in the Emergency Department**. Eur Heart J. 2018 Oct 7;39(38):3493-3495.

Hauptman PJ, Goff ZD, Vidic A, et al. Variability in Retail Pricing of **Generic Drugs** for Heart Failure. JAMA Intern Med. 2016 Nov 15.

Hawkins NM, Petrie MC, MacDonald MR, et al. Heart failure and **chronic obstructive pulmonary disease**. The quandary of **beta-blockers** and beta-agonists. J Am Coll Cardiol 2011; 57:2127-2138.

Hawkins NM, Scholes S, Bajekal M, et al. Community Care in England: Reducing **Socioeconomic Inequalities** in Heart Failure. Circulation. 2012 Jul 26.

Haykowsky MJ, et al. Meta-Analysis of **Aerobic Interval Training** on Exercise Capacity and Systolic Function in Patients With Heart Failure and Reduced Ejection Fractions. Am J Cardiol. 2013 Feb 21.

Haynes R, Judge PK, Staplin N, et al; UK HARP-III Collaborative Group. Effects of **Sacubitril/Valsartan Versus Irbesartan in Patients with Chronic Kidney Disease**: A Randomised Double-Blind Trial. Circulation. 2018 Jul 12.

Heart Failure Pathway Writing Committee, Yancy CW, Januzzi JL Jr, Allen LA, Et al. **2017 ACC Expert Consensus Decision Pathway for Optimization of Heart Failure Treatment**: Answers to 10 Pivotal Issues About Heart Failure With **Reduced Ejection Fraction**. J Am Coll Cardiol. 2017 Dec 13.

Hegde S, Claggett B, et al. **Physical Activity and Prognosis** in the Treatment of Preserved Cardiac Function Heart Failure with an Aldosterone Antagonist (**TOPCAT**) Trial. Circulation. 2017 Jun 21.

Hegde SM, et al. Physical activity and prognosis in the **TOPCAT** Trial (Treatment of Preserved Cardiac Function Heart Failure With an **Aldosterone Antagonist**). Circulation. 2017;136:982-992.

Hess PL, Hernandez AF, Bhatt DL, et al. **Sex and Race/Ethnicity** Differences in **Implantable Cardioverter-Defibrillator** Counseling and Use Among Patients Hospitalized With Heart Failure: Findings from the Get With The Guidelines-Heart Failure Program. Circulation. 2016 Aug 16;134(7):517-26

Heidenreich PA, Albert NM, Allen LA, et al. **Forecasting the impact of heart failure** in the United States. Circ Heart Fail 2013.

Heldman AW, Difede DL, et al. **Transendocardial Mesenchymal Stem Cells** and Mononuclear Bone Marrow Cells for Ischemic Cardiomyopathy: The TAC-HFT Randomized Trial. JAMA. 2013 Nov 18.

Heran BS, Musini VM, Bassett K, et al. **Angiotensin receptor blockers for heart failure**. Cochrane Database Syst Rev. 2012 Apr 18;4:CD003040. In patients with symptomatic HF and systolic

dysfunction or with preserved ejection fraction, ARBs compared to placebo or ACEIs do not reduce total mortality or morbidity. ARBs are better tolerated than ACEIs but do not appear to be as safe and well tolerated as placebo in terms of withdrawals due to adverse effects. Adding an ARB in combination with an ACEI does not reduce total mortality or total hospital admission but increases withdrawals due to adverse effects compared with ACEI alone.

Hernandez Adrian F.; Greiner Melissa A.; Fonarow Gregg C.; et al. Relationship Between **Early Physician Follow-up** and 30-Day Readmission Among Medicare Beneficiaries Hospitalized for Heart Failure. JAMA. 2010;303(17):1716-1722.

Hernandez AF, Mi X, Hammill BG, et al. Associations between **aldosterone antagonist therapy** and risks of mortality and readmission among patients with heart failure and reduced ejection fraction. JAMA 2012; 308:2097-2107.

Heusch G, Libby P, Gersh B, et al. **Cardiovascular remodelling** in coronary artery disease and heart failure. Lancet. 2014 May 12.

Heywood JT, Jermyn R, et al. Impact of practice-based management of pulmonary artery pressures in 2000 patients implanted with the CardioMEMS sensor. Circulation. 2017;135:1509–1517.

HFSA: Heart Failure Society of America, Lindenfeld J, Albert NM, Boehmer JP, et al. Evaluation of patients for ventricular dysfunction and heart failure: **HFSA 2010 comprehensive heart failure** practice guideline. J Card Fail **2010** Jun;16(6):e44-56. http://www.heartfailureguideline.org/home/3

Hilfiker-Kleiner D, Haghikia A, Berliner D, et al. **Bromocriptine** for the treatment of **peripartum cardiomyopathy**: a multicentre randomized study. Eur Heart J. 2017 Sep 14;38(35):2671-2679.

Hindricks G, Taborsky M, Glikson M, et al. **Implant-based multiparameter telemonitoring** of patients with heart failure **(IN-TIME)**: a randomized controlled trial. Lancet 2014; 384: 583–90.

Hioki H, et al. **Timing of Susceptibility** to Mortality & Heart Failure in Patients With Preexisting Atrial Fibrillation After Transcatheter Aortic Valve Implantation. Am J Cardiol. 2017 Nov1;120(9):1618-1625.

Hippisley-Cox J, Coupland C. **Diabetes treatments** and risk of heart failure, cardiovascular disease, and all cause mortality: cohort study in primary care. BMJ. 2016 Jul 12;354:i3477.

Ho EC, Parker JD, Austin PC, et al. Impact of **Nitrate Use** on Survival in Acute Heart Failure: A Propensity-Matched Analysis. J Am Heart Assoc. 2016 Feb 12;5(2).

Hohnloser SH, Israel CW. Current evidence base for use of the **implantable cardioverter-defibrillator**. Circulation. 2013 Jul 9;128(2):172-83.

Holland DJ, Kumbhani DJ, Ahmed SH, Marwick TH. Effects of Treatment on Exercise Tolerance, Cardiac Function, and Mortality in Heart Failure With **Preserved Ejection Fraction** A Meta-Analysis. J Am Coll Cardiol. 2011 Apr 19;57(16):1676-1686.

Holzmeister J, Leclercq C. **Implantable cardioverter defibrillators** and **cardiac resynchronisation therapy**. Lancet. 2011 Aug 20;378(9792):722-30.

Homma S, Thompson JLP, Pullicino PM, et al. **Warfarin and aspirin** in patients with **heart failure** and sinus rhythm. (**WARCEF**) N Engl J Med 2012. DOI: 10.1056/NEJMoa1202299.

Hoss S, Elizur Y, Luria D, et al. **Serum Potassium** Levels and Outcome in Patients With Chronic Heart Failure. Am J Cardiol. 2016 Dec 15;118(12):1868-1874.

House AA. Management of **Heart Failure in Advancing CKD**: Core Curriculum 2018. Am J Kidney Dis. 2018 Feb 23.

House AA, Wanner C, Sarnak MJ, et al; Conference Participants. **Heart failure in chronic kidney disease**: conclusions from a Kidney Disease: Improving Global Outcomes (KDIGO) Controversies Conference. Kidney Int. 2019 Apr 30.

Houstis NE, et al. **Exercise intolerance** in heart failure with preserved ejection fraction: diagnosing and ranking its causes using personalized o2 pathway analysis. Circulation. 2018;137:148–161.

Howden EJ, et al. **Reversing the Cardiac Effects of Sedentary Aging** in Middle Age-A Randomized Controlled Trial: Implications For Heart Failure Prevention. Circulation. 2018 Jan 8.

Howlett JG, McKelvie RS, Arnold JM, et al. **Canadian** Cardiovascular Society. Canadian Cardiovascular Society Consensus Conference guidelines on heart failure, update 2009: diagnosis and management of **right-sided heart failure, myocarditis, device therapy and recent important clinical trials**. Can J Cardiol. 2009 Feb;25(2):85-105.

Howlett JG, McKelvie RS, Costigan J, et al; **Canadian** Cardiovascular Society (**CCS**). The 2010 Canadian Cardiovascular Society guidelines for the diagnosis and management of heart failure update: Heart failure in **ethnic minority populations, heart failure and pregnancy, disease management, and quality improvement/assurance programs**. Can J Cardiol. 2010 Apr;26(4):185-202.

Howlett JG. **Specialist heart failure clinics** must evolve to stay relevant. Can J Cardiol. 2014 Mar;30(3):276-80.

Hsu JC, Solomon SD, Bourgoun M, et al. Predictors of super-response to **cardiac resynchronization therapy** and associated improvement in clinical outcome: The MADIT-CRT (Multicenter Automatic Defibrillator Implantation Trial With Cardiac Resynchronization Therapy) study. J Am Coll Cardiol 2012 59:2366-2373.

Hu LJ, Deng SB, et al. Additional Use of an **Aldosterone Antagonist** in Patients with Mild-to-Moderate Chronic Heart Failure: a systematic review and meta-analysis. Br J Clin Pharmacol. 2012 Oct 22.

Huang W, Chai SC, Lee SGS, et al. **Prognostic Factors** After Index Hospitalization for Heart Failure With **Preserved Ejection Fraction**. Am J Cardiol. 2017 Jun 15;119(12):2017-2020.

Hubers SA, Brown NJ. **Combined Angiotensin Receptor Antagonism and Neprilysin Inhibition**. Circulation. 2016 Mar 15;133(11):1115-24.

Hummel SL, DeFranco AC, Skorcz S, et al. Recommendation of **low-salt diet** and short-term outcomes in heart failure with preserved systolic function. Am J Med. 2009 Nov;122(11):1029-36.

Hunt SA, Abraham WT, Chin MH, et al. **2009 Focused Update Incorporated Into the ACC/AHA 2005 Guidelines for the Diagnosis and Management of Heart Failure** in Adults. A Report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. Circulation. 2009 Mar 26. [Epub ahead of print] http://circ.ahajournals.org/cgi/reprint/CIRCULATIONAHA.109.192065v1

Huynh QL, Negishi K, Blizzard L, et al. **Predictive Score for 30-Day Readmission** or Death in Heart Failure. JAMA Cardiol. 2016 Jun 1;1(3):362-4.

Huynh Q, Negishi K, De Pasquale CG, et al. **Validation of Predictive Score of 30-Day Hospital Readmission** or Death in Patients With Heart Failure. Am J Cardiol. 2018 Feb 1;121(3):322-329.

Ibrahim A, Baibars M, Alraies MC, Oliveira GH. Q: Should target **natriuretic peptide levels** be used for outpatient management of chronic heart failure? Cleve Clin J Med. 2012 Jan;79(1):22-5.

Ibrahim NE, Januzzi JL, Rabideau DJ, et al. Serial Heart Rates, Guideline-Directed **Beta Blocker** Use, and Outcomes in Patients With Chronic **Heart Failure** With **Reduced Ejection Fraction**. Am J Cardiol. 2017 Jun 15.

Imamura F, Lemaitre RN, King IB, et al. **Long-chain monounsaturated Fatty acids** and incidence of congestive heart failure in 2 prospective cohorts. Circulation. 2013 Apr 9;127(14):1512-21.

Imran TF, Shin HJ, et al. Meta-Analysis of the Usefulness of **Plasma Galectin-3** to Predict the Risk of Mortality in Patients With Heart Failure and in the General Population. Am J Cardio. 2017; 119:57-64.

In the Clinic: Heart Failure Lee R. Goldberg Ann Intern Med June 1, 2010 152:ITC6-1

Inampudi C, Parvataneni S, Morgan CJ, et al. **Spironolactone** Use and Higher Hospital Readmission for Medicare Beneficiaries With Heart Failure, Left Ventricular Ejection Fraction <45%, and Estimated Glomerular Filtration Rate <45 ml/min/1.73 m(2.). Am J Cardiol. 2014 Apr 18.

Inglis SC, Clark RA, McAlister FA, et al. **Structured telephone support or telemonitoring programmes** for patients with chronic heart failure. Cochrane Database Syst Rev. 2010 Aug 4;8:CD007228. Structured telephone support and telemonitoring are effective in reducing the risk of all-cause mortality and CHF-related hospitalisations in patients with CHF; they improve quality of life, reduce costs, and evidence-based prescribing.

Inglis SC, Clark RA, Dierckx R, et al. **Structured telephone support** or non-invasive **telemonitoring** for patients with heart failure. Cochrane Database Syst Rev. 2015 Oct 31;10:CD007228. For people with heart failure, structured telephone support and non-invasive home telemonitoring reduce the risk of all-cause mortality and heart failure-related hospitalisations; these interventions also demonstrated improvements in health-related quality of life and heart failure knowledge and self-care behaviours. Studies also demonstrated participant satisfaction with the majority of the interventions which assessed this outcome.

Inan OT, Baran et al. **Novel Wearable Seismocardiography and Machine Learning Algorithms** Can Assess Clinical Status of Heart Failure Patients. Circ Heart Fail. 2018 Jan;11(1):e004313.

Inohara T, Manandhar P, Kosinski AS, et al. **Association of Renin-Angiotensin Inhibitor Treatment With Mortality** and Heart Failure Readmission in Patients With Transcatheter Aortic Valve Replacement. JAMA. 2018 Dec 4;320(21):2231-2241.

Ip Dorothy, Syed Hafiz, Cohen Maurice. Digoxin specific antibody fragments (**Digibind**) in digoxin toxicity. BMJ 2009;339:b2884, doi: 10.1136/bmj.b2884 (Published 3 September 2009)

Isselbacher EM, Meyersohn NM, Sarma AA, et al. Case 38-2018: A **54-Year-Old Man with New Heart Failure**. N Engl J Med. 2018 Dec 13;379(24):2362-2372.

Jabbour A, Macdonald PS, Keogh AM, et al. Differences between **beta-blockers** in patients with chronic **heart failure and chronic obstructive pulmonary disease**: a randomized crossover trial. J Am Coll Cardiol. 2010 Apr 27;55(17):1780-7.

Jackevicius CA, de Leon NK, Lu L, et al. Impact of a **Multidisciplinary Heart Failure Post-hospitalization Program** on Heart Failure Readmission Rates. Ann Pharmacother. 2015 Nov;49(11):1189-96.

Jackson CE, Solomon SD, Gerstein HC, et al. **Albuminuria** in chronic heart failure: prevalence and prognostic importance (**Charm**). Lancet 2009; 374:543-550.

Jacobson AF, Senior R, Cerqueira MD, et al. **Myocardial iodine-123 meta-iodobenzylguanidine imaging** and cardiac events in heart failure results of the prospective ADMIRE-HF (AdreView Myocardial Imaging for Risk Evaluation in Heart Failure) study. J Am Coll Cardiol 2010; DOI:10.1016/j.jacc.2010.01.014.

Jaffe AS, Miller WL. Meta-Analyses and Interpretation of **Troponin** Values in Heart Failure. JACC Heart Fail. 2018 Mar;6(3):198-200.

Jain A, El-Khuffash AF, Kuipers BC, et al. Left Ventricular Function in Healthy Term **Neonates** During the Transitional Period. J Pediatr. 2016 Nov 28.

Jakovljevic, McDiarmid, Hallsworth, et al. Effect of **Left Ventricular Assist Device Implantation** and Heart Transplantation on Habitual Physical Activity and Quality of Life. The American Journal of Cardiology. 2014.

Jakovljevic DG, Yacoub MH, Schueler S, et al. **Left Ventricular Assist Device** as a Bridge to Recovery for Patients With Advanced Heart Failure. J Am Coll Cardiol. 2017 Apr 18;69(15):1924-1933.

Jankowska EA, Tkaczyszyn M, Suchocki T, et al. Effects of intravenous iron therapy in iron-deficient patients with **systolic heart failure**: a meta-analysis of randomized controlled trials. Eur J Heart Fail 2016;18:786e795.

Janssen RM, Berg M, Ovakim DH. Two cases of cardiac glycoside poisoning from accidental **foxglove** ingestion. CMAJ. 2016 Jul 12;188(10):747-50.

Januzzi JL Jr, Prescott MF, Butler J, et al. Association of **Change in N-Terminal Pro-B-Type Natriuretic Peptide** Following Initiation of Sacubitril-Valsartan Treatment With Cardiac Structure and Function in Patients With Heart Failure With Reduced Ejection Fraction. JAMA. 2019 Sep 2:1-11.

Januzzi JL Jr, Rehman SU, Mohammed AA, et al. Use of **amino-terminal pro-B-type natriuretic peptide** to guide outpatient therapy of patients with chronic left ventricular systolic dysfunction (**PROTECT**). J Am Coll Cardiol 2011; 58:1881-1889.

Januzzi JL, Troughton R. Are **Serial BNP Measurements Useful in Heart Failure Management**? Yes. Circulation. 2013 Jan 29;127(4):500-8.

Japp D, Shah A, Fisken S et al. **Mineralocorticoid receptor antagonists** in elderly patients with heart failure: a systematic review and meta-analysis. Age Ageing. 2017 Jan 9;46(1):18-25.

Jay SM, Murthy AC, Hawkins JF, et al. An **engineered bivalent neuregulin protects against doxorubicin-induced cardiotoxicity** with reduced proneoplastic potential. Circulation. 2013;128:152–161.

Jernberg T, Lindahl B, Alfredsson J, et al. Long-Term Effects of **Oxygen Therapy on Death or Hospitalization for Heart Failure in Patients With Suspected Acute Myocardial Infarction** Circulation. 2018 Dec 11;138(24):2754-2762.

Jessup M, Abraham WT, Casey DE, et al. **Focused Update: ACCF/AHA Guidelines for the Diagnosis and Management of Heart Failure in Adults**. A Report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. Circulation. **2009** Mar 26. [Epub ahead of print] http://circ.ahajournals.org/cgi/reprint/CIRCULATIONAHA.109.192064v1

Jessup M. The **heart failure paradox: an epidemic of scientific success**: presidential address at the american heart association 2013 scientific sessions. Circulation. 2014 Jun 24;129(25):2717-22.

Jhund PS, Fu M, et al; **PARADIGM-HF** Investigators and Committees. Efficacy and safety of LCZ696 (**sacubitril-valsartan**) **according to age**: insights from PARADIGM-HF. Eur Heart J. 2015 Jul 31.

Jhund PS, McMurray JJ. The **neprilysin pathway** in heart failure: a review and guide on the use of sacubitril/valsartan. Heart. 2016 May 20.

Jiang Y, Shorey S, Seah B, et al. The effectiveness of **psychological interventions** on **selfcare, psychological and health outcomes** in patients with chronic heart failure-A systematic review and meta-analysis. Int J Nurs Stud. 2017 Aug 19.

Jiawan A, Tandjung K. **New-Onset** Heart Failure. JAMA Cardiol. 2019 Mar 13.

Jilek C, Tzeis S, Vrazic H, et al. Safety of screening procedures with **handheld metal detectors** among patients with implanted **cardiac rhythm devices**. Ann Intern Med 2011; 155:587-592.

Johnson DB, Balko JM, Compton ML, et al. **Fulminant Myocarditis** with **Combination Immune Checkpoint Blockade**. N Engl J Med. 2016 Nov 3;375(18):1749-1755.

Jondeau Guillaume, Neuder Yannick, Eicher Jean-Christophe, et al. , and for the **B-CONVINCED** Investigators. B-CONVINCED: Beta-blocker CONtinuation Vs. INterruption in patients with Congestive heart failure hospitalizED for a decompensation episode. European Heart Journal Advance Access published on August 30, 2009, DOI 10.1093/eurheartj/ehp323.

Jones RH, Velazquez EJ, Michler RE, et al.; the **STICH** Hypothesis 2 Investigators. Coronary Bypass Surgery with or without Surgical Ventricular Reconstruction. N Engl J Med. 2009 Mar 29.

Jones CD, Loehr L, Franceschini N, et al. **Orthostatic hypotension** as a risk factor for incidence heart failure. The ARIC study. Hypertension 2012

Jonkman NH, Westland H, Groenwold RH, et al. Do **Self-Management Interventions** Work in Patients With Heart Failure? An Individual Patient Data Meta-Analysis. Circulation. 2016 Feb 12.

Jordan JH, Sukpraphrute B, Meléndez GC, et al. Early Myocardial Strain Changes During Potentially **Cardiotoxic Chemotherapy** May Occur as a Result of Reductions in Left Ventricular End-Diastolic Volume: The Need to Interpret Left Ventricular Strain With Volumes. Circulation. 2017 Jun 20;135(25):2575-2577.

Jorgenson, D. **Digoxin Dosing in Systolic Heart Failure**. RapidRx Q&A Jan 2007. Accessed online at: http://www.medicine.usask.ca/family/newsletters/rapid-rx/january-4-2007-pdf/Digoxin%20dosing%20in%20systolic%20heart%20failure.pdf

Jourdain P, Jondeau G, et al. Plasma brain **natriuretic peptideguided** therapy to improve outcome in heart failure: the STARS-BNP Multicenter Study. J Am Coll Cardiol. 2007;49(16):1733-1739.

Joy PS, Gopinathannair R, Olshansky B. Effect of **Ablation for Atrial Fibrillation on Heart Failure** Readmission Rates. Am J Cardiol. 2017 Nov 1;120(9):1572-1577.

Joynt Karen E, Orav E John, Jha AK. The Association Between **Hospital Volume and Processes**, Outcomes, and Costs of Care for Congestive Heart Failure. Ann Intern Med Jan 18, 11 154:94-102.

Kajimoto K, Minami Y, Sato N, et al. Etiology of Heart Failure and Outcomes in Patients Hospitalized for **Acute Decompensated Heart** Failure With Preserved or Reduced Ejection Fraction. Am J Cardiol. 2016 Dec 15;118(12):1881-1887.

Kajimoto K et al. **Gender Differences in Anemia & Survival** in Patients Hospitalized for Acute Decompensated Heart Failure With Preserved or Reduced Ejection Fraction. Am J Cardiol. 2017 Aug 1;120(3):435-442

Kajimoto K, Minami Y, Otsubo S, et al. Ischemic or Nonischemic Functional **Mitral Regurgitation** and Outcomes in Patients With **Acute Decompensated Heart Failure** With Preserved or Reduced Ejection Fraction. Am J Cardiol. 2017 Jun 15.

Kalahasty G, Ellenbogen KA. Management of the Patient With **Implantable Cardioverter-Defibrillator (ICD) Lead Failure**. Circulation 123: 1352-1354, doi:10.1161/CIRCULATIONAHA.110.986828

Kalogeropoulos AP, Fonarow GC, , et al. **Characteristics and Outcomes** of Adult Outpatients With Heart Failure and Improved or Recovered Ejection Fraction. JAMA Cardiol. 2016 Jul 6.

Kaluza J, Åkesson A, Wolk A. **Processed** and unprocessed **red meat consumption** and risk of heart failure: A prospective study of men. *Circ Heart Fail* 2014.

Kamimura D, Cain LR, Mentz RJ, et al. **Cigarette Smoking and Incident Heart Failure**: Insights From the Jackson Heart Study. Circulation. 2018 Apr 16.

Kaminsky BM, Pogue KT, et al. Effects of **Total Dose Infusion of Iron Intravenously** in Patients With Acute Heart Failure and Anemia (Hemoglobin < 13 g/dl). Am J Cardiol. 2016 Jun 15;117(12):1942-6.

Kamiya K, Masuda T, Matsue Y, et al. Complementary Role of **Arm Circumference to Body Mass Index** in Risk Stratification in Heart Failure. JACC Heart Fail. 2016 Feb 2.

Kane GC, Karon BL, Mahoney DW, et al. Progression of left ventricular **diastolic dysfunction** and risk of heart failure. JAMA. 2011 Aug 24;306(8):856-63.

Kannan L, Shaw PA, Morley MP, et al. **Thyroid Dysfunction in Heart Failure and** Cardiovascular Outcomes. Circ Heart Fail. 2018 Dec;11(12):e005266.

Kantharia B, Patel S, Kulkarni G, et al. **Reuse of explanted permanent pacemakers** donated by funeral homes. Am J Cardiol 2011

Kansagara Devan, Englander Honora, Salanitro Amanda, et al. **Risk Prediction Models for Hospital Readmission**: A Systematic Review. JAMA. 2011;306(15):1688-1698.doi:10.1001/jama.2011.1515

Kantor PF, Lougheed J, Dancea A, et al. Children's Heart Failure Study Group. Presentation, diagnosis, and medical management of **heart failure in children**: **Canadian Cardiovascular Society** guidelines. Can J Cardiol. 2013 Dec;29(12):1535-52.

Kao HH, Kao LT, et al. **Androgen Deprivation Therapy Use Increases the Risk of Heart Failure in Patients With Prostate Cancer**: A Population-Based Cohort Study. J Clin Pharmacol. 2018 Nov 7.

Kapoor JR, Heidenreich PA. **Obesity** and survival in patients with heart failure and preserved systolic function: A U-shaped relationship. Am Heart J 2010; 159:75-80.

Kapoor M, Schleinitz MD, Gemignani A, Wu WC. Outcomes of patients with chronic **heart failure and iron deficiency** treated with intravenous iron: a meta-analysis. Cardiovasc Hematol Disord Drug Targets 2013;13:35e44.

Kapur NK, Esposito ML, Bader Y, et al. **Mechanical Circulatory Support Devices** for Acute Right Ventricular Failure. Circulation. 2017 Jul 18;136(3):314-326.

Kato ET, Silverman MG, Mosenzon O, et al. Effect of **Dapagliflozin on Heart Failure and Mortality in Type 2 Diabetes Mellitus**. Circulation. 2019 Mar 18.

Kaul P, McAlister FA, Ezekowitz JA, et al. Resource use in the **last 6 months of life** among patients with heart failure in **Canada**. Arch Intern Med 2010: DOI: 10.1001/archinternmed.2010.365.

Kauta SR, et al. Diagnosis and treatment of **sleep disordered breathing** in hospitalized cardiac patients: A reduction in 30-day hospital readmission rates. *J Clin Sleep Med* 2014; 10:1051-1059.

Kavalieratos D, Gelfman LP, Tycon LE, et al. **Palliative Care in Heart Failure**: Rationale, Evidence, and Future Priorities**.** J Am Coll Cardiol. 2017 Oct 10;70(15):1919-1930.

Kawata H, Bao H, Curtis JP, et al. **Cardiac Resynchronization Defibrillator Therapy** for Nonspecific Intraventricular Conduction Delay **Versus Right Bundle Branch Block**. J Am Coll Cardiol. 2019 Jun 25;73(24):3082-3099.

Kelder JC, Cramer MJ, van Wijngaarden J, et al. The Diagnostic Value of Physical Examination and Additional Testing (eg. **NT-proBNP**) in Primary Care Patients With Suspected Heart Failure. Circulation. 2011 Nov 21.

Khalid U, Ather S, Bavishi C, et al. **Pre-Morbid Body Mass Index** and Mortality After Incident Heart Failure: The ARIC Study. J Am Coll Cardiol. 2014 Dec 30;64(25):2743-9.

Khan RF, Feder S, Goldstein NE, et al. **Symptom B**urden Among Patients Who Were **Hospitalized for Heart Failure**. JAMA Intern Med. 2015 Aug 17.

Khan SS, Butler J, Gheorghiade M. Management of **comorbid diabetes mellitus** and worsening heart failure. JAMA. 2014 Jun 18;311(23):2379-80.

Khan SS, Ning H, Shah SJ, et al. **10-Year Risk Equations** for Incident Heart Failure in the General Population. J Am Coll Cardiol. 2019 May 21;73(19):2388-2397.

Khanna A, White WB. The management of **hyperkalemia** in patients with cardiovascular disease. Am J Med. 2009 Mar;122(3):215-21.

Khawaja O, Kotler G, Gaziano JM, Djoussé L. Usefulness of **Desirable Lifestyle Factors** to Attenuate the Risk of Heart Failure Among Offspring Whose Parents Had Myocardial Infarction Before Age 55 Years. Am J Cardiol. 2012 Apr 18.

Khayat R, Jarjoura D, Porter K, et al. **Sleep disordered breathing** and post-discharge mortality in patients with acute heart failure. Eur Heart J. 2015 Jan 29.

Kiefer T, Park L, Tribouilloy C, et al. Association between **valvular surgery** and mortality among patients with **infective endocarditis** complicated by heart failure. JAMA 2011; 306:2239-2247.

Kini V, Soufi MK, Deo R, et al. **Appropriateness of primary prevention implantable cardioverter defibrillators** at time of generator replacement: Are indications still met? J Am Coll Cardiol 2014;

Kinch Westerdahl A, Sjöblom J, et al. **Implantable cardioverter-defibrillator** therapy before death: high risk for **painful shocks at end of life**. Circulation. 2014;129:422–429.

King M, Kingery, J, Caey, B. **Diagnosis and Evaluation** of Heart Failure. Am Fam Physician. 2012;85(12):1161-1168.

Kittleson Michelle M., Kobashigawa Jon A.. Management of **Advanced Heart Failure**: The Role of Heart **Transplantation**. Circulation 123: 1569-1574, doi:10.1161/CIRCULATIONAHA.110.972810

Kitzman DW, Brubaker P, Morgan T, et al. Effect of **caloric restriction or aerobic exercise training** on peak oxygen consumption and quality of life in obese older patients with heart failure with preserved ejection fraction: a randomized clinical trial.JAMA. doi:10.1001/jama.2015.17346.

Klingenberg R, Lüscher TF. **CANTOS:** a seductive song with several verses. Eur Heart J. 2018 Oct 7;39(38):3508-3510.

Køber L, Torp-Pedersen C, Carlsen JE, et al. A clinical trial of the angiotensin-converting-enzyme inhibitor trandolapril in patients with left ventricular dysfunction after myocardial infarction. Trandolapril Cardiac Evaluation (**TRACE**) Study Group. N Engl J Med. 1995 Dec 21;333(25):1670-6.

Kober L, Torp-Pedersen C, McMurray JJ,et al; **Dronedarone** Study Group. Increased mortality after dronedarone therapy for severe heart failure.N Engl J Med. 2008 Jun 19;358(25):2678-87.

Kober L, Thune JJ, Nielsen JC, et al. **Defibrillator Implantation** in Patients with Nonischemic Systolic Heart Failure. (**DANISH**) N Engl J Med. 2016 Aug 27.

Koehler F, Winkler S, Schieber M, et al. **Telemedical Interventional Monitoring in Heart Failure** (**TIM-HF**), a randomized, controlled intervention trial investigating the impact of telemedicine on mortality in ambulatory patients with chronic heart failure. Circulation 2010;12:1354-1362.

Koehler F, Koehler K, Deckwart O, etal. Efficacy of **telemedical interventional management in patients with heart failure** (TIM-HF2): a randomised, controlled, parallel-group, unmasked trial. Lancet. 2018 Aug 24.

Koifman E, et al. **Age-Dependent Effect** of Left Ventricular Ejection Fraction on Long-Term Mortality in Patients With Heart Failure (from the Heart Failure Survey in ISrael). Am J Cardiol. 2013 Sep 21.

Kolodziejczak M, Andreotti F, Kowalewski M, et al. **Implantable Cardioverter-Defibrillators for Primary Prevention** in Patients With Ischemic or Nonischemic Cardiomyopathy: A Systematic Review and Meta-analysis. Ann Intern Med. 2017 Jun 27

Konstam MA, Neaton JD, Dickstein K, et al. Effects of high-dose versus low-dose losartan on clinical outcomes in patients with heart failure (**HEAAL** study): a randomised, double-blind trial. Lancet 2009; DOI:10.1016/S0140-6736(09)61913-9.

Konstam MA, Abboud FM. **Ejection Fraction**: Misunderstood and Overrated (Changing the Paradigm in Categorizing Heart Failure). Circulation. 2017 Feb 21;135(8):717-719

Konstam MA, Abboud FM. **Ejection Fraction**: Misunderstood and Overrated (Changing the Paradigm in Categorizing Heart Failure). Circulation. 2017 Feb 21;135(8):717-719.

Konstam MA, Kiernan MS, Bernstein D, et al; American Heart Association Council on Clinical Cardiology; Council on Cardiovascular Disease in the Young; and Council on Cardiovascular Surgery and Anesthesia. Evaluation and Management of **Right-Sided Heart Failure**: A Scientific Statement From the American Heart Association. Circulation. 2018 Apr 12.

Koruth JS, Lala A, Pinney S, et al. The Clinical Use of **Ivabradine**. J Am Coll Cardiol. 2017 Oct 3;70(14):1777-1784.

Kosiborod M, et al. Lower Risk of Heart **Failure and Death in Patients Initiated on SGLT-2 Inhibitors** Versus Other Glucose-Lowering Drugs: The CVD-REAL Study. Circulation. 2017 May 18.

Kosmala W, Rojek A, et al. Effect of **aldosterone antagonism (spironolactone)** on exercise tolerance in heart failure with **preserved ejection fraction**. *J Am Coll Cardiol* 2016; 68:1823-34.

Kotecha T, Fox K. **Investigating suspected heart failure**. BMJ. 2013 Apr 24;346:f2442.

Kotecha D, Holmes J, Krum H, et al; on behalf of the Beta-Blockers in Heart Failure Collaborative Group. Efficacy of **β blockers** in patients with **heart failure plus atrial fibrillation**: an individual-patient data meta-analysis. Lancet. 2014 Sep 2.

Kotecha D, Manzano L, et al. Effect of **age and sex on** efficacy and tolerability of **Beta-blockers** in patients with heart failure with reduced ejection fraction: individual patient data meta-analysis. BMJ 2016;353:i1855.

Kotecha D, Flather MD, Altman DG, et al; **Beta-Blockers in Heart Failure** Collaborative Group. **Heart Rate and Rhythm** and the Benefit of Beta-Blockers in Patients With Heart Failure. J Am Coll Cardiol. 2017 Jun 20;69(24):2885-2896.

Kotecha D, Flather MD, Altman DG, et al. **Heart Rate and Rhythm and the Benefit of Beta-Blockers** in Patients With Heart Failure. J Am Coll Cardiol. 2017 Jun 20;69(24):2885-2896.

Kovesdy CP, Matsushita K, Sang Y, et al. **Serum potassium and adverse outcomes across the range of kidney function**: a CKD Prognosis Consortium meta-analysis. Eur Heart J. 2018 May 1;39(17):1535-1542.

Kpaeyeh JA Jr, Divoky L, Hyer JM, et al. Impact of **Renal Function on Survival After Cardiac Resynchronization Therapy**. Am J Cardiol. 2017 Jul 15;120(2):262-266

Kramer DB, Mitchell SL, Monteiro J, et al. Patient Activity and **Survival Following Implantable Cardioverter-Defibrillator Implantation**: **ALTITUDE** Activity Study. J Am Heart Assoc. 2015 May 15;4(5).

Kristensen SL, Kober L, Jhund PS, et al. **International geographic variation** in event rates in trials of heart failure with preserved and reduced ejection fraction. Circulation. 2015;131:43–53.

Kristensen SL, Mogensen UM, Jhund PS, et al. Clinical and **Echocardiographic Characteristics** and Cardiovascular Outcomes According to Diabetes Status in Patients with Heart Failure and Preserved Ejection Fraction. A Report from the Irbesartan in Heart Failure with Preserved Ejection Fraction Trial (**I-Preserve**). Circulation. 2017 Jan 4.

Kristensen SL, Mogensen UM, Jhund PS, et al. Clinical and Echocardiographic Characteristics and Cardiovascular Outcomes **According to Diabetes Status** in Patients With Heart Failure and Preserved Ejection Fraction: A Report From the **I-Preserve** Trial (**Irbesartan** in Heart Failure With **Preserved Ejection Fraction**). Circulation. 2017 Feb 21;135(8):724-735.

Krum H, Teerlink JR. **Medical therapy for chronic heart failure. Lancet. 2011** Aug 20;378(9792):713-21.

Ku E, Park J, Vidhun J, Campese V. The **hazards of dual renin-angiotensin blockade** in chronic kidney disease. Arch Intern Med. 2009 Jun 8;169(11):1015-8.

Kuenzli A, Bucher HC, et al. **Meta-analysis** of combined therapy with **angiotensin receptor antagonists versus ACE inhibitors** alone in patients with **heart failure**. PLoS One. 2010 Apr 1;5(4):e9946.

Kumar P, Patel A, Mounsey JP, et al. Effect of Left Ventricular Diastolic Dysfunction on Outcomes of **Atrial Fibrillation Ablation**. Am J Cardiol. 2014 May 17.

Kwon Y, et al. Effect of **sleep-disordered breathing** on appropriate implantable cardioverter-defibrillator therapy in patients with heart failure: systematic review and meta-analysis. *Circ Arrhythm* 2017.

Lainchbury JG, Troughton RW, Strangman KM, Frampton CM, Pilbrow A, Yandle TG, Hamid AK, Nicholls MG, Richards AM. N-terminal pro-B-type natriuretic peptide-guided treatment for chronic heart failure: results from the **BATTLESCARRED** (**NT-proBNP-Assisted** Treatment To Lessen Serial Cardiac Readmissions and Death) trial. J Am Coll Cardiol. 2009 Dec 29;55(1):53-60.

Laitinen TT, Puolakka E, Ruohonen S, et al. Association of **Socioeconomic Status** in Childhood With Left Ventricular Structure and Diastolic Function in Adulthood: The Cardiovascular Risk in Young Finns Study. JAMA Pediatr. 2017 Jun 26.

LaMonte MJ, Manson JE, Chomistek AK, et al. **Physical Activity and Incidence** of Heart Failure in Postmenopausal Women. JACC Heart Fail. 2018 Dec;6(12):983-995.

Landolina M, Gasparini M, Lunati M, et al. on behalf of the Cardiovascular Centers Participating in the ClinicalService Project. Long-Term Complications Related to **Biventricular Defibrillator Implantation**: Rate of Surgical Revisions and Impact on Survival: Insights From the Italian ClinicalService Database. Circulation. 2011 Jun 7;123(22):2526-2535.

Landolina M, Perego GB, Lunati M, et al. **Remote Monitoring** Reduces Healthcare Use and Improves Quality of Care in Heart Failure Patients With Implantable Defibrillators: The Evolution of Management Strategies of Heart Failure Patients With Implantable Defibrillators (EVOLVO) Study. Circulation. 2012 Jun 19;125(24):2985-92.

Landoni G, Lomivorotov VV, Alvaro G, et al. **Levosimendan** for Hemodynamic Support after Cardiac Surgery. (**CHEETAH**) N Engl J Med. 2017 Mar 21.

Lanfear DE, Hrobowski T, Peterson EL, et al. Association of **Beta Blocker Exposure** with Outcomes in Heart Failure Differs Between **African American** and White Patients. Circ Heart Fail. 2012 Jan 19.

Lara KM, Levitan EB, Gutierrez OM, et al. **Dietary Patterns** and Incident Heart Failure in U.S. Adults Without Known Coronary Disease. J Am Coll Cardiol. 2019 Apr 30;73(16):2036-2045.

Ledwidge M, Gallagher J, Conlon C, et al. **Natriuretic peptide–based screening** and collaborative care for heart failure: the **STOP-HF** randomized trial. JAMA. 2013;310(1):66-74.

Lee DS, Gona P, Vasan RS, et al. Relation of disease pathogenesis and **risk factors to heart failure with preserved or reduced ejection fraction**: insights from the Framingham Heart Study of the National Heart, Lung, and Blood Institute. Circulation 2009; 119:3070-3077.

Lee DS, Lee JS, Schull MJ, et al. Prospective **Validation of the Emergency Heart Failure Mortality Risk Grade** for Acute Heart Failure. Circulation. 2019 Feb 26;139(9):1146-1156.

Lee DS, Stukel TA, Austin PC, et al. Improved outcomes with early **collaborative care** of ambulatory heart failure patients discharged from the emergency department. Circulation. 2010 Nov 2;122(18):1806-14.

Lee DS, Stitt A, Austin PC, et al. **Prediction of heart failure mortality in emergent care**: a cohort study. Ann Intern Med. 2012 Jun 5;156(11):767-75.

Lehrke M, Marx N. Diabetes Mellitus and Heart Failure. Am J Cardiol. 2017 Jul 1;120(1S):S37-S47.

Lenneman AJ, Wang L, Wigger M, et al. Heart Transplant Survival Outcomes for **Adriamycin-Dilated Cardiomyopathy**. Am J Cardiol. 2012 Nov 27.

León H, Shibata MC, Dorgan M, et al. Effect of **fish oil** on arrhythmias and mortality: systematic review. BMJ 2008; DOI: 10.1136/bmj.a2931. Fish oil supplementation was associated with a significant reduction in deaths from cardiac causes but had no effect on arrhythmias or all cause mortality. Evidence to recommend an optimal formulation of EPA or DHA to reduce these outcomes is insufficient. Fish oils are a heterogeneous product, and the optimal formulations for DHA and EPA remain unclear.

Leong DP, McMurray JJV, Joseph PG, Yusuf S. From **ACE Inhibitors/ARBs to ARNIs** in Coronary Artery Disease and Heart Failure (Part 2/5). J Am Coll Cardiol. 2019 Aug 6;74(5):683-698.

Leong KTG, Wong LY, Aung KCY, et al. Risk Stratification Model for **30-Day Heart Failure Readmission** in a Multi-Ethnic South East Asian Community. Am J Cardiol. 2017.

Lerman BJ, Popat RA, Assimes TL, et al. Association Between Heart Failure and **Postoperative Mortality** Among Patients Undergoing Ambulatory Noncardiac Surgery. JAMA Surg. 2019 Jul 10.

Lerman BJ, Popat RA, Assimes TL, et al. Association of **Left Ventricular Ejection Fraction and Symptoms With Mortality After Elective Noncardiac Surgery** Among Patients With **Heart Failure**. JAMA. 2019 Feb 12;321(6):572-579.

Levitan Emily B.; Wolk Alicja; Mittleman Murray A. Consistency With the **DASH Diet** and Incidence of Heart Failure Arch Intern Med. 2009;169(9):851-857.

Levitan EB, Lewis CE, Tinker LF, et al. **Mediterranean and DASH** diet scores and mortality in women with heart failure: The Women's Health Initiative (WHI). Circ Heart Fail. 2013 Nov;6(6):1116-23.

Lewis GD, Malhotra R, Hernandez AF, et al. Effect of **Oral Iron Repletion on Exercise Capacity in Patients With Heart Failure** With **Reduced Ejection Fraction** and Iron Deficiency: The **IRONOUT HF** Randomized Clinical Trial. JAMA. 2017 May 16;317(19):1958-1966

Li N, Csepe TA, Hansen BJet al. **Adenosine-Induced Atrial Fibrillation**: Localized Reentrant Drivers in Lateral Right Atria due to Heterogeneous Expression of Adenosine A1 Receptors and GIRK4 Subunits in the Human Heart. Circulation. 2016 Jul 26

Li X, Zhang J, Huang J, et al. A multicenter, randomized, double-blind, parallel-group, placebo-controlled study of the effects of **qili qiangxin** capsules in patients with chronic heart failure. J Am Coll Cardiol. 2013 Sep 17;62(12):1065-72.

Liang Y, Pan W, et al. Meta-Analysis of Randomized Controlled Trials **Comparing Isolated Left Ventricular** and **Biventricular Pacing** in Patients With Chronic Heart Failure. AmJCardiol.2011Aug 1.

Lind M, Bounias I, Olsson M, et al. **Glycaemic control and incidence of heart failure** in 20 985 patients with type 1 diabetes: an observational study. Lancet 2011; published online June 25.

Lindblad AJ, Allan GM. **Aldosterone antagonists** in systolic heart failure. Can Fam Physician. 2014 Feb;60(2):e104.

Lindgren MP, PirouziFard M, Smith JG, et al. A Swedish Nationwide Adoption Study of the **Heritability of Heart Failure**. JAMA Cardiol. 2018 Jul 11.

Lindman BR. The **Diabetic Heart Failure With Preserved Ejection Fraction Phenotype**: Is it Real and Is It Worth Targeting Therapeutically? Circulation. 2017 Feb 21;135(8):736-740

Lindvall C, Chatterjee NA, et al. National Trends in the Use of **Cardiac Resynchronization** Therapy **With or Without Implantable Cardioverter-Defibrillator**. Circulation. 2016 Jan 19;133(3):273-81.

Lip GY, Shantsila E. **Anticoagulation versus placebo for heart failure** in sinus rhythm. Cochrane Database Syst Rev. 2014 Mar 28;3:CD003336. Based on the two major randomised trials (HELAS 2006; WASH 2004), there is no convincing evidence that oral anticoagulant therapy modifies mortality or vascular events in patients with heart failure and sinus rhythm

Lipinski MJ, Cauthen CA, Biondi-Zoccai GG, et al. Meta-analysis of randomized controlled trials of **statins** versus placebo in patients with heart failure. Am J Cardiol. 2009 Dec 15;104(12):1708-16.

Lipshultz SE, Scully RE, Lipsitz SR, et al. Assessment of **dexrazoxane as a cardioprotectant in doxorubicin-treated** children with high-risk acute lymphoblastic leukaemia: long-term follow-up of a prospective, randomised, multicentre trial. Lancet Oncol. 2010 Oct;11(10):950-61.

Löffler AI, Cappola TP, Fang J, et al. Effect of **renal function** on prognosis in chronic heart failure. Am J Cardiol. 2015 Jan 1;115(1):62-8.

Loh JC, Creaser J, Rourke DA, et al. **Temporal trends in treatment and outcomes for advanced heart failure** with reduced ejection fraction from 1993-2010: findings from a university referral center. Circ Heart Fail. 2013 May 1;6(3):411-9.

Long B, Koyfman A, Chin EJ. **Misconceptions in acute heart failure diagnosis** and Management in the Emergency Department. Am J Emerg Med. 2018 Jun 1.

Long B, Koyfman A, Gottlieb M. Management of **Heart Failure in the Emergency Department Setting**: An Evidence-Based Review of the Literature. J Emerg Med. 2018 Sep 26.

Long L, Mordi IR, Bridges C, et al. **Exercise-based cardiac rehabilitation for adults with heart failure**. Cochrane Database Syst Rev. 2019 Jan 29;1:CD003331.

Loop MS, Van Dyke MK, Chen L, Brown et al. Comparison of **Length of Stay, 30-Day Mortality, and 30-Day Readmission Rates** in Medicare Patients With Heart Failure and With Reduced Versus Preserved Ejection Fraction. Am J Cardiol. 2016 Jul 1;118(1):79-85.

Lorenz RA, Elwell RJ. **Pre-dosing metolazone** with loop diuretic combination regimens. Nephrol Nurs J. 2006 Jan-Feb;33(1):78-9.

Lotrionte M, Biondi-Zoccai G, Abbate A, et al. Review and Meta-Analysis of Incidence and Clinical Predictors of **Anthracycline Cardiotoxicity**. Am J Cardiol. 2013 Sep 25.

Lowrie R, Mair FS, Greenlaw N, et al. **Pharmacist** intervention in primary care to improve outcomes in patients with left ventricular systolic dysfunction. (**HOOPS**) Eur Heart J 2011.

Lozano Bahamonde A, Escolar Pérez V, Laskibar Asua A, et al. **Subcutaneous furosemide** in patients with **refractory heart failure**. BMJ Support Palliat Care. 2018 Jun 13.

Lu KJ, Kearney LG, Hare DL, et al. **Cardiorenal Anemia Syndrome** as a Prognosticator for Death in Heart Failure. Am J Cardiol. 2013 Jan 30.

Lund LH, Jurga J, Edner M, et al. Prevalence, correlates, and prognostic significance of **QRS prolongation in heart failure with reduced and preserved ejection fraction**. Eur Heart J 2012.

Lund LH, Benson L, Dahlström U, Edner M. Association between use of **renin angiotensin system antagonists** and mortality in patients with heart failure and **preserved ejection fraction**. JAMA 2012; 308:2108-2117.

Lund LH, Benson L, Dahlstrom U, et al. Association between use of **β-blockers and outcomes in patients with heart failure and preserved ejection fraction.** JAMA. doi:10.1001 /jama.2014.15241.

Luo N, Merrill P, Parikh KS, et al. **Exercise Training** in Patients With Chronic Heart Failure and Atrial Fibrillation. J Am Coll Cardiol. 2017 Apr 4;69(13):1683-1691.

Lytvyn Y, Bjornstad P, Udell JA, et al. **Sodium Glucose Cotransporter-2 Inhibition in Heart Failure**: Potential Mechanisms, Clinical Applications, and Summary of Clinical Trials. Circulation. 2017 Oct 24;136(17):1643-1658.

MacLeod-Glover N, Mink M, Yarema M, et al. **Digoxin toxicity**: Case for retiring its use in elderly patients? Can Fam Physician. 2016 Mar;62(3):223-8.

MacFadden DR, Crystal E, Krahn AD, et al. **Sex differences** in implantable cardioverter-defibrillator (**ICD**) outcomes: findings from a prospective defibrillator database. Ann Intern Med. 2012;156:195-203.

Macicek SM et al. Acute heart failure syndromes in the **pediatric** emergency department. Pediatrics 2009 Nov; 124:e898.

Mackenzie C, Syed J, Pollak PT, Koren G. Falling between the cracks: a case of **amiodarone toxicity**. CMAJ. 2011 Sep 6;183(12):1393-7.

Madelaire C, Gislason G, Kristensen SL, et al. **Low-Dose Aspirin in Heart Failure Not Complicated by Atrial Fibrillation**: A Nationwide Propensity-Matched Study. JACC Heart Fail. 2018 Feb;6(2):156-167.

Mahtani KR, Heneghan C, Onakpoya I, et al. **Reduced Salt Intake** for Heart Failure: A Systematic Review. JAMA Intern Med. 2018 Nov 5.

Maisel WH, Hauser RG, Hammill SC,et al. Recommendations from the Heart Rhythm Society Task Force on **Lead Performance** (ICD) Policies and Guidelines. Heart Rhythm. 2009;6:869–885.

Maisel A, Xue Y, van Veldhuisen DJ, et al. Effect of **Spironolactone** on 30-Day Death and Heart Failure Rehospitalization (from the **COACH** Study). Am J Cardiol. 2014 Sep 1;114(5):737-42.

Makani H, Messerli FH, Romero J, et al. Meta-Analysis of Randomized Trials of **Angioedema** as an Adverse Event of Renin-Angiotensin System Inhibitors. Am J Cardiol. 2012 Apr 20.

Makani H, Bangalore S, Desouza KA, et al. Efficacy and safety of **dual blockade** of the **renin-angiotensin system**: meta-analysis of randomised trials. BMJ. 2013 Jan 28;346:f360.

Malik A, Masson R, Singh S, et al. **Digoxin Discontinuation and Outcomes** in Patients With Heart Failure With Reduced Ejection Fraction. J Am Coll Cardiol. 2019 Aug 6;74(5):617-627

Mangoni AA, Jarmuzewska EA. The influence of **heart failure on the pharmacokinetics** of cardiovascular and non-cardiovascular drugs: a critical appraisal of the evidence. Br J Clin Pharmacol. 2018 Sep 7.

Manemann SM, Chamberlain AM, Boyd CM, et al. **Skilled nursing facility use** and hospitalizations in heart failure: A community linkage study. *Mayo Clin Proc* 2017; 92:490–499.

Manemann SM, Chamberlain AM, Roger VL, et al. **Multimorbidity and Functional Limitation** in Individuals with Heart Failure: A Prospective Community Study. J Am Geriatr Soc. 2018 Mar 30.

Mann DL. **Sphingosine 1-phosphate** as a therapeutic target in heart failure: more questions than answers. Circulation. 2012 Jun 5;125(22):2692-4.

Mann DL, Lee RJ, Coats AJ, et al. One-year follow-up results from **AUGMENT-HF**: A multicentre randomized controlled clinical trial of the efficacy of **left ventricular augmentation** with **Algisyl** in the treatment of heart failure. *Eur J Heart Fail* 2015.

Mant J, Abdallah AM, Swain S. Management of chronic heart failure in adults: Synopsis of the National Institute for Health and Clinical Excellence guideline (**NICE**). Ann Intern Med 2011; 155:252-259.

Mant J, Al-Mohammad A, Swain S, Laramée P; Guideline Development Group. Management of chronic **heart failure** in adults: synopsis of the National Institute For Health and clinical excellence guideline. (**NICE**). Ann Intern Med. 2011 Aug 16;155(4):252-9.

Mantel A, Holmqvist M, Andersson DC, et al. Association Between **Rheumatoid Arthritis** and Risk of Ischemic and Nonischemic Heart Failure. J Am Coll Cardiol. 2017 Mar 14;69(10):1275-1285.

Mantziari L, et al. Relation of **dosing of the Renin-Angiotensin system inhibitors** after **cardiac resynchronization therapy** (CRT) to long-term prognosis. Am J Cardiol. 2012 Jun 1;109(11):1619-25.

Mareev Y, Cleland JG. **Should β-Blockers** Be Used in Patients With **Heart Failure and Atrial Fibrillation**? Clin Ther. 2015 Sep 18.

Margulies KB, Hernandez AF, Redfield MM, et al. Effects of **Liraglutide** on Clinical Stability Among Patients With Advanced Heart Failure and Reduced Ejection Fraction: A Randomized Clinical Trial. JAMA. 2016 Aug 2;316(5):500-508

Marijon E, Leclercq C, Narayanan K, et al; **CeRtiTuDe** Investigators. **Causes-of-death** analysis of patients with **cardiac resynchronization therapy**: an analysis of the CeRtiTuDe cohort study. Eur Heart J. 2015 Sep 1.

Mark DB, Anstrom KJ, Sun JL, Clapp-Channing NE, Tsiatis AA, et al. Sudden Cardiac Death in Heart Failure Trial Investigators. (**SCD-HeFT**) Quality of life with **defibrillator** therapy or amiodarone in heart failure. N Engl J Med. 2008 Sep 4;359(10):999-1008. In a large primary-prevention population with moderately symptomatic heart failure, single-lead ICD therapy was not associated with any detectable adverse quality-of-life effects during 30 months of follow-up.

Mark DB, Cowper PA, Anstrom KJ, et al. **Economic and Quality-of-Life Outcomes of Natriuretic Peptide-Guided Therapy** for Heart Failure. J Am Coll Cardiol. 2018 Nov 27;72(21):2551-2562.

Martens P, et al. Changes in **Loop Diuretic Dose and Outcome After Cardiac Resynchronization Therapy** in Patients With Heart Failure and Reduced Left Ventricular Ejection Fractions. Am J Cardiol. 2017 Jul 15;120(2):267-273.

Martens P, Verbrugge FH, Nijst P, et al. Incremental benefit of **cardiac resynchronisation therapy** with versus without a defibrillator. Heart. 2017 Jul 17.

Martin N, Manoharan K, Thomas J, et al. **Beta-blockers** and **inhibitors of the renin-angiotensin aldosterone** system for chronic heart failure with preserved ejection fraction. Cochrane Database of Systematic Reviews 2018, Issue 6. Art. No.: CD012721. There is evidence that MRA treatment reduces heart failure hospitalisation in heart failure with preserverd ejection fraction, however the effects on mortality related outcomes and quality of life remain unclear. The available evidence for beta-blockers, ACEI, ARB and ARNI is limited and it remains uncertain whether these treatments have a role in the treatment of HFpEF in the absence of an alternative indication for their use.

Martindale JL, Wakai A, Collins SP, et al. **Diagnosing Acute Heart Failure in the Emergency Department**: A Systematic Review and Meta-analysis. Acad Emerg Med. 2016 Mar;23(3):223-42.

Martínez-Selles M, Doughty R N, Poppe K, et al. **Gender** and survival in patients with heart failure: interactions with diabetes and aetiology. Results from the MAGGIC individual patient meta-analysis. Eur J Heart Fail 2012. (survival better for **females** irrespective of ejection fraction)

Marwick TH, Shah SJ, Thomas JD. **Myocardial Strain in the Assessment** of Patients With Heart Failure: A Review. JAMA Cardiol. 2019 Feb 27.

Marzec LN, Peterson PN, Bao H, et al. Use of **Cardiac Resynchronization Therapy** Among Eligible Patients Receiving an Implantable Cardioverter Defibrillator: Insights From the National Cardiovascular Data Registry Implantable Cardioverter Defibrillator Registry. JAMA Cardiol. 2017 Jan 25.

Masip J, Peacock WF, Price S, et al; Acute Heart Failure Study Group of the Acute Cardiovascular Care Association and the Committee on Acute Heart Failure of the Heart Failure Association of the European Society of Cardiology. Indications and practical approach to **non-invasive ventilation in acute heart failure**. Eur Heart J. 2018 Jan 1;39(1):17-25.

Masoudi FA, Mi X, Curtis LH, et al. Comparative effectiveness of **cardiac resynchronization therapy** with an implantable cardioverter-defibrillator versus defibrillator therapy alone: a cohort study. Ann Intern Med. 2014 May 6;160(9):603-11.

Massie BM, Collins JF, Ammon SE, et al. **WATCH** Trial Investigators. Randomized trial of warfarin, aspirin, and clopidogrel in patients with chronic heart failure: the Warfarin and Antiplatelet Therapy in Chronic Heart Failure (WATCH) trial. Circulation. 2009 Mar 31;119(12):1616-24. Epub 2009 Mar 16. n=1587. The primary outcome measure and the mortality data do not support the primary hypotheses that warfarin is superior to aspirin and that clopidogrel is superior to aspirin.

Matlock D, Peterson P, Wang Y, et al. Variation in use of **dual-chamber implantable cardioverter-defibrillators**. Arch Intern Med 2012; 172:634-641.

Matlock DD, Allen LA. **Defibrillators, deactivation, decisions, and dying**. Comment on Patient preferences for deactivation of implantable cardioverter-defibrillators" JAMA Intern Med 2013.

Matsue Y, Damman K, Voors AA, et al. **Time-to-Furosemide Treatment** and Mortality in Patients Hospitalized With Acute Heart Failure. J Am Coll Cardiol. 2017 Jun 27;69(25):3042-3051

Matsushita K, Harada K, Miyazaki T, et al. **Younger- vs Older-Old Patients** with Heart Failure with **Preserved Ejection Fraction**. J Am Geriatr Soc. 2019 Jul 1.

Maw AM, Hassanin A, Ho PM, et al.**Diagnostic Accuracy of Point-of-Care Lung Ultrasonography and Chest Radiography** in Adults With Symptoms Suggestive of Acute Decompensated Heart Failure: A Systematic Review and Meta-analysis. JAMA Netw Open. 2019 Mar 1;2(3):e190703.

McAlister FA, Wiebe N, Ezekowitz JA, Leung AA, Armstrong PW. Meta-analysis: **beta-blocker dose, heart rate reduction**, and death in patients with heart failure. Ann Intern Med. 2009 Jun 2;150(11): 784-94. The magnitude of **heart rate reduction** is statistically significantly associated with the survival benefit of beta-blockers in heart failure, whereas the dose of beta-blocker is not.

McAlister, Finlay A., Zhang, Jianguo, Tonelli, M, et al. The safety of **combining angiotensin-converting-enzyme inhibitors with angiotensin-receptor blockers in elderly** patients: a population-based longitudinal analysis. CMAJ 2011 0: cmaj.101333.

McAlister FA, Ezekowitz JA, et al. **Renal Dysfunction** in Heart Failure Patients with Preserved versus Reduced Ejection Fraction: Impact of the New **CKD-EPI** Formula. Circ Heart Fail. 2012 Mar 22.

McAlister FA, Youngson E, Bakal JA, et al. Impact of **physician continuity** on death or urgent readmission after discharge among patients with heart failure. CMAJ. 2013 Aug 19.

McAlister FA, Youngson E, Kaul P, et al. Early **Follow-Up After a Heart Failure Exacerbation**: The Importance of Continuity. Circ Heart Fail. 2016 Sep;9(9).

McAlister FA, Youngson E, Kaul P. Patients With Heart Failure **Readmitted to the Original Hospital Have Better Outcomes Than Those Readmitted Elsewhere**. J Am Heart Assoc. 2017 May 10;6(5).

McAlister FA, Youngson E, Kaul P. Health Resource Implications of Heart Failure **Hospitalizations in Younger Patients Compared With Older Patients**. Circulation. 2017 Jul 25;136(4):424-427.

McAllister DA, Read SH, Kerssens J, et al. Incidence of **Hospitalization for Heart Failure and Case-Fatality** Among 3.25 Million People **With and Without Diabetes Mellitus**. Circulation. 2018 Dec 11;138(24):2774-2786.

McCallum W, Tighiouart H, Ku E, et al. Trends in **Kidney Function Outcomes Following RAAS Inhibition** in Patients With Heart Failure With Reduced Ejection Fraction. Am J Kidney Dis. 2019 Jul 11.

McCullough PA. How Trialists and Pharmaceutical **Sponsors Have Failed Us by Thinking That Acute Heart Failure Is a 48-Hour Illness**. Am J Cardiol. 2017 Aug 1;120(3):505-508.

McCormack J, McAlister FA, Kolber MR. **Higher medication doses in heart failure**? Can Fam Physician. 2017 Jan;63(1):e20.

McHugh K, DeVore AD, Wu J, et al. Heart Failure **With Preserved Ejection Fraction and Diabetes**: JACC State-of-the-Art Review. J Am Coll Cardiol. 2019 Feb 12;73(5):602-611.

McIlvennan CK, Allen LA. **Palliative care** in patients with heart failure. BMJ. 2016 Apr 14;353:i1010.

McKellar SH, Fang JC. An Age-Old Question: **What Is Too Old for Coronary Artery Bypass Grafting** in Heart Failure? Circulation. 2016 Nov 1;134(18):1325-1327

McKelvie RS, Moe GW, Cheung A, et al. The 2011 **Canadian Cardiovascular Society (CCS) heart failure management guidelines update: focus on sleep apnea, renal dysfunction, mechanical circulatory support, and palliative care**. Can J Cardiol. 2011 May-Jun;27(3):319-38.

McKelvie RS, Moe GW, Ezekowitz JA, et al. The **2012 canadian cardiovascular society (CCS) heart failure management guidelines** update: focus on **acute and chronic heart failure**.

Can J Cardiol. 2013 Feb;29(2):168-81. http://www.onlinecjc.ca/article/S0828-282X(12)01379-7/fulltext
McLellan J, Heneghan CJ, Perera R, et al. **B-type natriuretic peptide-guided treatment for heart failure**. Cochrane Database Syst Rev. 2016 Dec 22;12:CD008966. In patients with heart failure low-quality evidence showed a reduction in heart failure admission with NP-guided treatment while low-quality evidence showed uncertainty in the effect of NP-guided treatment for all-cause mortality, heart failure mortality, and all-cause admission. Uncertainty in the effect was further shown by very low-quality evidence for patient's quality of life. The evidence for adverse events and cost of treatment was low quality and we were unable to pool results.
McManus DD, et al. Recent Trends in the Incidence, Treatment, and Prognosis of Patients With **Heart Failure and Atrial Fibrillation** (the Worcester Heart Failure Study). Am J Cardiol. 2013 Feb 25.
McMurray JJ, Anand IS, et al.; on behalf of the **RED-HF** Committees and Investigators. Design of the Reduction of Events with **Darbepoetin** alfa in **Heart Failure** (RED-HF): a Phase III, anaemia correction, morbidity-mortality trial. Eur J Heart Fail. 2009 Aug;11(8):795-801.
McMurray, John J.V. **Systolic Heart Failure**. N Engl J Med **2010** 362: 228-238.
McMurray JJV, Adamopoulos S, Anker SD, et al. **ESC guidelines** for the diagnosis and treatment of acute and **chronic heart failure 2012**: The Task Force for the Diagnosis and Treatment of Acute and Chronic Heart Failure 2012 of the European Society of Cardiology. Developed in collaboration with the Heart Failure Association (HFA) of the ESC. Eur Heart J 2012; DOI:10.1093/eurheartj/ehs104.
McMurray JJV, Krum H, Abraham WT, et al. **Aliskiren, enalapril, or aliskiren and enalapril** in heart failure. (**Atmosphere**) N Engl J Med. DOI: 10.1056/NEJMoa1514859
McMurray JJV, Packer M, Desai AS, et al. **Angiotensin-neprilysin inhibition LCZ696 versus enalapril** in heart failure. (**Paradigm HF**) N Engl J Med. DOI: 10.1056/NEJMoa1409077.
McMurray JJV, Solomon SD, Inzucchi SE, et al. **Dapagliflozin** in patients with heart failure and reduced ejection fraction. (DAPA-HF) N Engl J Med. DOI: 10.1056/NEJMoa1911303.
McNaughton CD, Cawthon C, Kripalani S, et al. **Health literacy** and **mortality**: a cohort study of patients hospitalized for acute heart failure. J Am Heart Assoc. 2015 Apr 29;4(5).
McQuade CN, Mizus M, Wald JW, et al. **Brain-type natriuretic peptide** and amino-terminal pro– brain-type natriuretic peptide **discharge thresholds** for acute decompensated heart failure. A systematic review. Ann Intern Med. 2016. [Epub ahead of print].
Mebazaa A, Spiro TE, Büller HR, et al. Predicting the risk of **venous thromboembolism** in patients hospitalized with heart failure. Circulation. 2014 Jul 29;130(5):410-8.
Mebazaa A, Yilmaz MB, Levy P, et al. Recommendations on **pre-hospital and early hospital management of acute heart failure**: A consensus paper from the Heart Failure Association of the European Society of Cardiology, the European Society of Emergency Medicine, and the Society of Academic Emergency Medicine. *Eur Heart J* 2015.
Mediano MFF, Leifer ES, Cooper LS, et al. Influence of **Baseline Physical Activity Level on Exercise Training Response** and Clinical Outcomes in Heart Failure: The **HF-ACTION Trial**. JACC Heart Fail. 2018 Dec;6(12):1011-1019.
Medical Letter-Treatment Guidelines. **Heart Failure.** July 2009. (Updated Sept 2012) (Updated Jan 2015), (Updated **Apr 2019**)
Medina E, Sucharov CC, Nelson P, et al. **Molecular Changes in Children** with Heart Failure **Undergoing Left Ventricular Assist Device Therapy**. J Pediatr. 2016 Nov 29.
Mehra MR, Uriel N, Naka Y, et al; MOMENTUM 3 Investigators. A **Fully Magnetically Levitated Left Ventricular Assist Device** - Final Report. N Engl J Med. 2019 Mar 17.
Mehta LS, Watson KE, Barac A, et al; American Heart Association Cardiovascular Disease in Women and Special Populations Committee of the Council on Clinical Cardiology; Council on Cardiovascular and Stroke Nursing; and Council on Quality of Care and Outcomes Research. **Cardiovascular Disease and Breast Cancer**: Where These Entities Intersect: cientific Statement From the American Heart Association. Circulation. 2018 Feb 1.
Melgaard L, Gorst-Rasmussen A, Lane DA, et al. Assessment of the **CHA2DS2-VASc Score** in Predicting Ischemic Stroke, Thromboembolism, and Death in Patients With Heart Failure With and Without Atrial Fibrillation. JAMA. 2015 Aug 30:1-9.
Mehra MR, Domanski MJ. Should **left ventricular assist device** should be standard of care for patients with refractory heart failure who are not transplantation candidates?: left ventricular assist devices should be considered standard of care for patients with refractory heart failure who are not transplantation candidates. Circulation. 2012 Dec 18;126(25):3081-7.
Mehra MR, Naka Y, Uriel N, et al. A **Fully Magnetically Levitated Circulatory Pump** for Advanced Heart Failure. (**MOMENTUM 3**) N Engl J Med. 2016 Nov 16.
Mehra MR, Goldstein DJ, Uriel N, et al. Two-Year Outcomes with a **Magnetically Levitated Cardiac Pump** in Heart Failure. (**Momentum 3**) N Engl J Med. 2018 Mar 11.
Metra M, Teerlink JR. **Heart failure**. Lancet. 2017 Apr 28.
Mehta RA, Leimberger JD, van Diepen S, et al. **Levosimendan** in patients with left ventricular Dysfunction undergoing cardiac surgery. (**LEVO-CTS**) *N Engl J Med* 2017; DOI:10.1056/NEJMoa1616218.
Meléndez GC, et al. Frequency of Left Ventricular End-Diastolic Volume-Mediated Declines Ejection Fraction in Patients Receiving Potentially **Cardiotoxic Cancer Treatment**. Am J Cardiol. 2017 Mar 22.
Mentz RJ, Wojdyla D, Fiuzat M, et al. Association of **Beta-Blocker Use and Selectivity** With Outcomes in Patients With Heart Failure and Chronic Obstructive Pulmonary Disease (from **OPTIMIZE-HF**). Am J Cardiol. 2013 Feb 15;111(4):582-7.
Mentz RJ, Mi X, Sharma PP, et al. Relation of **dyspnea severity** on admission for acute heart failure with outcomes and costs. Am J Cardiol. 2015 Jan 1;115(1):75-81.
Merchant FM, Binney Z, Patel A, et al. Prevalence, predictors, and outcomes of **advance directives in implantable cardioverter defibrillator recipients**. *Heart Rhythm* 2017.
Merchant FM, Hoskins MH, Musat DL, et al. Incidence and Time Course for Developing Heart Failure With **High-Burden Right Ventricular Pacing**. Circ Cardiovasc Qual Outcomes. 2017 Jun;10(6).
Meta-analysis Global Group in Chronic Heart Failur. The **survival of patients with heart failure with preserved or reduced** left ventricular ejection fraction: an individual patient data meta-analysis. (**MAGGIC**) Eur Heart J. 2011 Aug 6.
Methawasin M, Strom JG, Slater RE, et al. Experimentally increasing the compliance of **titin through RNA binding** motif-20 (RBM20) inhibition improves diastolic function in a mouse model of heart failure with preserved ejection fraction. Circulation. 2016;134:1085–1099.
Metra M, Gheorghiade M, Bonow RO, Dei Cas L. **Postdischarge assessment** after a heart failure hospitalization: the next step forward. Circulation. 2010 Nov 2;122(18):1782-5.
Metra M, Ponikowski P, Cotter G, et al. Effects of **serelaxin** in subgroups of patients with acute heart failure: Results from RELAX-AHF. Eur Heart J 2013.
Metra M, Teerlink JR, Cotter G, et al. Effects of **Serelaxin** in Patients with Acute Heart Failure. N Engl J Med. 2019 Aug 22;381(8):716-726.
Miller AH, Nazeer S, Pepe P, Estes B, Gorman A, Yancy CW. Acutely decompensated heart failure in a county emergency department: a double-blind randomized controlled comparison of **nesiritide** versus placebo treatment. Ann Emerg Med. 2008 May;51(5):571-8. Epub 2008 Mar 4. Nesiritide (Natrecor), when added to standard therapy for heart failure in the emergency department, does not reduce return visits or hospitalizations over the subsequent 30 days as compared with standard therapy alone. (LOE = 1b)
Miller AL, Wang Y, Curtis J, Masoudi FA, Buxton AE, Wang TY. Optimal medical therapy use among patients receiving **implantable cardioverter/ defibrillators**: insights from the National Cardiovascular Data Registry [online Nov 14, 2011]. Arch Intern Med. doi10.1001/archinternmed.2011.466.
Miller LW, Rogers JG. Evolution of **Left Ventricular Assist Device Therapy** for Advanced Heart Failure: A Review. JAMA Cardiol. 2018 Apr 18.
Minami Y, et al. Effect of **Elevated C-Reactive Protein Level at Discharge** on Long-Term Outcome in Patients Hospitalized for Acute Heart Failure. Am J Cardiol. 2018 Apr 15;121(8):961-968.
Miró Ò, Gil V, Martín-Sánchez FJ, Herrero P, et al; **ICA-SEMES** Research Group.. **Morphine use** in the emergency department and outcomes of patients with acute heart failure: A propensity score-matching analysis based on the **EAHFE Registry**. Chest. 2017 Apr 11.
Miró Ò, Estruch R, et al. **Adherence to Mediterranean Diet and All-Cause Mortality** After an Episode of Acute Heart Failure: Results of the **MEDIT-AHF** Study. JACC Heart Fail. 2017 Nov 27.
Mitchell JE, Hellkamp AS, Mark DB, et al. **Thyroid function** in heart failure and impact on mortality. JACC Heart Fail 2013; 1:48-55.
Moayedi Y, Etchells E, Kobulnik J, Ross H. **Brain natriuretic peptide and shortness of breath** in the emergency department. CMAJ. 2018 Nov 19;190(46):E1361-E1363.
Moayedi Y, Kobulnik J. **Chronic heart failure** with **reduced ejection fraction**. CMAJ. 2015 Apr 21; 187(7):518.
Modin D, Jørgensen ME, Gislason G, et al**. Influenza Vaccine in Heart Failure**: Cumulative Number of Vaccinations, Frequency, Timing, and Survival: A Danish Nationwide Cohort Study. Circulation. 2018 Dec 10.
Moe GW, Ezekowitz JA, O'Meara E, et al. The **2014 canadian cardiovascular society heart failure management guidelines focus update**: anemia, biomarkers, and recent therapeutic trial implications. Can J Cardiol. 2015 Jan;31(1):3-16.
Mogensen UM, Køber L, et al; PARADIGM-HF Investigators and Committees. The effects of **sacubitril/valsartan** on coronary outcomes in **PARADIGM-HF**. Am Heart J. 2017 Jun;188:35-41.
Mogensen UM, et al; PARADIGM-HF Investigators and Committees. **Sacubitril/valsartan reduces serum uric acid** concentration, an independent predictor of adverse outcomes in PARADIGM-HF. Eur J Heart Fail. 2017 Nov 30.
Mohammed SF, Hussain I, Abou Ezzeddine OF, et al. Right ventricular function in heart failure with **preserved ejection fraction**: a community-based study. Circulation. 2014;130:2310–2320.
Morgan JM, Kitt S, Gill J, et al. Remote management of heart failure using **implantable electronic devices**. Eur Heart J. 2017 Aug 7;38(30):2352-2360.
Morrow DA, Velazquez EJ, DeVore AD, et al. Clinical Outcomes in Patients With **Acute Decompensated Heart Failure** Randomly Assigned to **Sacubitril/Valsartan or Enalapril in the PIONEER-HF** Trial. Circulation. 2019 Apr 8.
Moslehi JJ. Cardiovascular **Toxic Effects of Targeted Cancer Therapies**. N Engl J Med. 2016 Oct 13;375(15):1457-1467.
Moss AJ, Hall WJ, Cannom DS, et al. Cardiac-resynchronization therapy for the prevention of heart-failure events (**MADIT-CRT**). N Engl J Med 2009; DOI: 10.1056.NEJMa0906431.
Moss AJ et al for the MADIT-RIT Trial Investigators. Reduction in inappropriate therapy and mortality through ICD programming. (**MADIT-RIT**). N Engl J Med 2012 Nov 6.
Mostofsky E, Levitan EB, Wolk A, et al. **Chocolate Intake** and Incidence of Heart Failure: A Population-Based, Prospective Study of Middle-Aged and Elderly Women. Circ Heart Fail. 2010 Aug 16.
Mostofsky E, Rice MS, Levitan EB, Mittleman MA. Habitual **Coffee Consumption** and Risk of Heart Failure: A Dose-Response Meta-Analysis. Circ Heart Fail. 2012 Jun 26.
Motonaga KS, Dubin AM. **Cardiac resynchronization therapy** for pediatric patients with heart failure and congenital heart disease: a reappraisal of results. Circulation. 2014 May 6;129(18):1879-91.
Mozaffarian D, Lemaitre RN, King IB, et al. Circulating long-chain **ω-3 fatty acids** and incidence of congestive heart failure in older adults: the cardiovascular health study: a cohort study. Ann Intern Med. 2011 Aug 2;155(3):160-70.
Mujib M, Patel K, Fonarow GC, et al. **Angiotensin-converting Enzyme Inhibitors** and Outcomes in Heart Failure and **Preserved Ejection Fraction**. Am J Med. 2013 Mar 16.
Mulpuru SK, Madhavan M, McLeod CJ, et al. **Cardiac Pacemakers**: Function, Troubleshooting, and Management: Part 1 of a 2-Part Series. J Am Coll Cardiol. 2017 Jan 17;69(2):189-210.
Murad K, Goff DC Jr, Morgan TM, et al. Burden of **comorbidities and functional and cognitive impairments** in elderly patients at the initial diagnosis of heart failure and their impact on total mortality: The Cardiovascular Health Study.*JACC: Heart Failure* 2015:
Mutlak D, Lessick J, Carasso S et al. Utility of **Pulmonary Hypertension** for the Prediction of Heart Failure Following Acute Myocardial Infarction. Am J Cardiol. 2012 Feb 3.

Muzzarelli S et al. Frequency and Predictors of **Hyperkalemia** in Patients ≥60 Years of Age With Heart Failure Undergoing Intense Medical Therapy. Am J Cardiol. 2011 Dec 5.

Myhre PL, Claggett B, Ballantyne CM, et al. Association Between **Circulating Troponin Concentrations, Left Ventricular Systolic and Diastolic Functions**, and Incident Heart Failure in Older Adults. JAMA Cardiol. 2019 Sep 4.

Myhre PL, Vaduganathan M, Claggett BL, et al. Association of **Natriuretic Peptides With Cardiovascular Prognosis in Heart Failure** With Preserved Ejection Fraction: Secondary Analysis of the TOPCAT Randomized Clinical Trial. JAMA Cardiol. 2018 Aug 22.

Nagarajan V, Chamsi-Pasha M, Tang WH. The role of aldosterone receptor antagonists (**spironolactone, eplerenone**) in the management of heart failure: An update. Cleve Clin J Med. 2012 Sep;79(9):631-9.

Nagendran J, Bozso SJ, et al. **Coronary Artery Bypass** Surgery Improves Outcomes in Patients With Diabetes and Left Ventricular Dysfunction. J Am Coll Cardiol. 2018 Feb 27;71(8):819-827.

Nakamura M, Tanaka F, Nakajima S, et al. Comparison of the Incidence of Acute Decompensated Heart Failure Before and After the Major **Tsunami** in Northeast Japan. Am J Cardiol. 2012 Sep 19.

Narayan HK, Finkelman B, French B, et al. **Detailed echocardiographic phenotyping** in **breast cancer patients**: associations with ejection fraction decline, recovery, and heart failure symptoms over 3 years of follow-up. Circulation. 2017;135:1397–1412. (**Doxorubicin** and **trastuzumab**)

Nassif ME, Windsor S, Tang F, et al. **Dapagliflozin Effects** on Biomarkers, Symptoms, and Functional Status in Patients With Heart Failure With Reduced Ejection Fraction: The DEFINE-HF Trial. Circulation. 2019 Sep 16.

Nava S, Morales JL, Márquez MF, et al. **Reuse of Pacemakers**: Comparison of Short and Long-term Performance. Circulation. 2013 Mar 19;127(11):1177-1183.

Nawaf S. Al-Majed, Finlay A. McAlister, Jeffrey A. Bakal, et al. Meta-analysis: **Cardiac Resynchronization Therapy** for Patients With Less Symptomatic Heart Failure. Ann Intern Med E-313 Feb 14/11.

Nayor M, Enserro DM, Vasan RS, Xanthakis V. **Cardiovascular Health Status** and Incidence of Heart Failure in the **Framingham Offspring Study**. Circ Heart Fail. 2016 Jan;9(1):e002416.

Nazarian S, Hansford R, Roguin A, et al. A prospective evaluation of a protocol for **magnetic resonance imaging** of patients with **implanted cardiac devices**. Ann Intern Med 2011; 155:415-424.

Ndumele CE, Matsushita K, Sang Y, et al. **N-Terminal Pro-Brain Natriuretic Peptide** and Heart Failure Risk Among Individuals With and Without Obesity: The Atherosclerosis Risk in Communities (ARIC) Study. Circulation. 2016 Feb 16;133(7):631-8.

Neil CJ, Chong CR, et al. Occurrence of Tako-Tsubo Cardiomyopathy in Association with Ingestion of Serotonin/Noradrenaline Reuptake Inhibitors (**venlafaxine**). Heart Lung Circ. 2012 Jan 25.

Neubauer S, Redwood C. New mechanisms and concepts for **cardiac-resynchronization therapy**. N Engl J Med. 2014 Mar 20;370(12):1164-6.

Ng AY, Wong FK, Lee PH. Effects of a transitional **palliative care** model on patients with end-stage heart failure: study protocol for a randomized controlled trial. Trials. 2016 Mar 31

Nguyen PK, Rhee JW, Wu JC. Adult **Stem Cell** Therapy and Heart Failure, 2000 to 2016: A Systematic Review. JAMA Cardiol. 2016 Aug 24

Nguyen P et al. Comparison of Frequency of Cardiovascular Events and Mortality in Patients With Heart Failure Using Versus Not Using **Cocaine**. Am J Cardiol. 2017 Jun 15;119(12):2030-2034.

NICE: National Collaborating Centre for Acute and Chronic Conditions. **Chronic heart failure**. Management of chronic heart failure in adults in primary and secondary care. London (UK): National Institute for Health and Clinical Excellence (NICE); 2010 Aug. 45 p. (Clinical guideline; no. 108). http://www.nice.org.uk/nicemedia/live/13099/50526/50526.pdf

NICE: National Institute for Health and Clinical Excellence. **Ivabradine** for treating chronic heart failure. London (UK): National Institute for Health and Clinical Excellence (NICE); 2012 Nov.

NICE: National Institute for Health and Care Excellence. **Acute heart failure: diagnosing and managing acute heart failure in adults**. (Clinical Guideline CG187). **2014**. www.nice.org.k/guidance/cg187 .

NICE- National Institute for Health and Care Excellence. **Implantable cardioverter defibrillators and cardiac resynchronization therapy** for arrhythmias and heart failure (review of TA95 and TA120). London (UK): National Institute for Health and Care Excellence (NICE); 2014 Jun. 71 p. (Technology appraisal guidance; no. 314).

NICE: National Institute for Health and Care Excellence. **Chronic heart failure in adults: diagnosis and management** (NICE guideline NG106) 2018. https://www.nice.org.uk/guidance/ng106

Nichols GA, Reynolds K, et al. Comparison of **Risk of Re-hospitalization, All-Cause Mortality, and Medical Care Resource Utilization** in Patients With Heart Failure and Preserved Versus Reduced Ejection Fraction. Am J Cardiol. 2015 Jul 15.

Niehaus ED, Malhotra R, Cocca-Spofford D, et al. Repletion of Iron Stores With the Use of **Oral Iron Supplementatio**n in Patients With Systolic Heart Failure. J Card Fail. 2015 Aug;21(8):694-7.

Nieuwenhuis MM, Jaarsma T, van Veldhuisen DJ, et al. Long-Term Compliance With **Nonpharmacologic Treatment of Patients With Heart Failure**. Am J Cardiol. 2012 Apr 18.

Niizeki T, et al. Usefulness of **Albuminuria** as a Prognostic Indicator in Patients With Chronic Heart Failure Secondary to Ischemic or Idiopathic Dilated Cardiomyopathy. Am J Cardiol. 2013 Jan 22.

Nikolova AP, Hitzeman TC, Baum R, et al. Association of a novel diagnostic biomarker, the **plasma cardiac bridging integrator 1 score**, with heart failure with preserved ejection fraction and cardiovascular hospitalization [online Oct 31, 2018]. JAMA Cardiol. doi:10.1001/jamacardio.2018.3539.

Nochioka K, Querejeta Roca G, Claggett B, et al. **Right ventricular function, right ventricular–pulmonary artery coupling, and heart failure risk** in 4 US communities: the Atherosclerosis Risk In Communities (ARIC) Study [online August 15, 2018]. JAMA Cardiol.

Normand C, Kaye DM, Povsic TJ, Dickstein K. Beyond pharmacological treatment: an insight into **therapies that target specific aspects** of heart failure pathophysiology. Lancet. 2019 Mar 9;393(10175):1045-1055.

Nowbar AN, Mielewczik M, Karavassilis M, et al; **DAMASCENE** writing group. **Discrepancies in autologous bone marrow stem cell trials** and enhancement of ejection fraction (DAMASCENE): weighted regression and meta-analysis. BMJ. 2014 Apr 28;348:g2688.

Núñez J, Bayés-Genís A, Zannad F, et al. **Long-term potassium monitoring** and dynamics in heart failure and risk of mortality. Circulation. 2018;137:1320–1330.

Nyirenda MJ, Tang JI, Padfield PL, Seckl JR. **Hyperkalaemia**. BMJ. 2009 Oct 23;339:b4114. doi: 10.1136/bmj.b4114.

Oatmen KE, Zile MR, Burnett JC Jr, Spinale FG. **Bioactive Signaling in Next-Generation Pharmacotherapies** for Heart Failure: A Review. JAMA Cardiol. 2018 Nov 28.

O`Connor CM, Whellan DJ, Lee KL, et al. Efficacy and safety of exercise training in patients with chronic heart failure: **HF-ACTION** randomized controlled trial. JAMA. 2009 Apr 8;301(14):1439-50.

O'Connor CM, Starling RC, Hernandez AF, et al. Effect of **nesiritide** in patients with acute decompensated heart failure (**Ascend-HF**). N Engl J Med 2011;365:32-43.

O'Neal WT, Sandesara P, et al. **Gender Differences** in the Risk of Adverse Outcomes in Patients with Atrial Fibrillation and Heart Failure with Preserved Ejection Fraction. Am J Cardio. 2017.

Obokata M, Reddy YNV, Pislaru SV, et al. Evidence Supporting the Existence of a **Distinct Obese Phenotype** of Heart Failure With Preserved Ejection Fraction. Circulation. 2017 Jul 4;136(1):6-19.

Ohkuma T, Komorita Y, Peters SAE, Woodward M. **Diabetes as a risk factor** for heart failure in women and men: a systematic review and meta-analysis of 47 cohorts including 12 million individuals. Diabetologia. 2019 Jul 18.

Ohori T, Nozawa T, Ihori H, et al. Effect of Repeated **Sauna Treatment** on Exercise Tolerance and Endothelial Function in Patients With Chronic Heart Failure. Am J Cardiol. 2011 Sep 23.

Okada A, et al. Usefulness of the **Direct and/or Total Bilirubin** to Predict Adverse Outcomes in Patients With Acute Decompensated Heart Failure. Am J Cardiol. 2017 Jun 15;119(12):2035-2041.

Okin PM, Devereux RB, Kjeldsen SE, et al. Incidence of heart failure in relation to **QRS** duration during antihypertensive therapy: the LIFE study. J Hypertens. 2009 Oct 14.

Okonko DO, Grzeslo A, Witkowski T, et al. Effect of intravenous **iron sucrose** on exercise tolerance in anemic and nonanemic patients with symptomatic chronic heart failure and iron deficiency **FERRIC-HF**: a randomized, controlled, observer-blinded trial. J Am Coll Cardiol 2008;51:103e112.

Okumura N, Jhund PS, Gong J, et al. Importance of Clinical Worsening of **Heart Failure Treated in the Outpatient** Setting: Evidence from the Prospective Comparison of ARNI with ACEI to Determine Impact on Global Mortality and Morbidity in Heart Failure Trial (**PARADIGM-HF**). Circulation. 2016 Apr 20.

Oliveira GH, Mukerji S, et al. Incidence, predictors, and impact on survival of left ventricular systolic dysfunction and recovery in **advanced cancer patients**. Am J Cardiol. 2014 Jun 1;113(11):1893-8.

Ollendorf DA, Sandhu AT, Pearson SD. **Sacubitril-Valsartan** for the Treatment of Heart Failure: Effectiveness and Value. JAMA Intern Med. 2016 Feb 1;176(2):249-50.

Ollendorf DA, Sandhu AT, Pearson SD. **CardioMEMS HF** for the Management of Heart Failure-**Effectiveness and Value**. JAMA Intern Med. 2016 Oct 1;176(10):1551-1552.

Omar HR, Charnigo R, Guglin M. Prognostic Significance of Discharge **Hyponatremia** in Heart Failure Patients With Normal Admission Sodium (from the **ESCAPE** Trial). Am J Cardiol. 2017 Aug 15;120(4):607-615.

Omar HR, Charnigo R, Guglin M. **Ratio of Systolic Blood Pressure to Right Atrial Pressure**, a Novel Marker to Predict Morbidity and Mortality in Acute Systolic Heart Failure. Am J Cardiol. 2017 Jan 6.

Ong MK, Romano PS, Edgington S, et al; Better Effectiveness After Transition–Heart Failure (**BEAT-HF**) Research Group. Effectiveness of **remote patient monitoring** after discharge of hospitalized patients with heart failure: the Better Effectiveness After Transition–Heart Failure (BEAT-HF) randomized clinical trial [online Feb 8, 2016].JAMA Intern Med. doi:10.1001/jamainternmed.2015.7712.

Oreopoulos A, Padwal R, Kalantar-Zadeh K, Fonarow GC, Norris CM, McAlister FA. Body mass index and mortality in heart failure: a meta-analysis. Am Heart J. 2008 Jul;156(1):13-22. **Overweight** and obesity were associated with lower all-cause and cardiovascular mortality rates in patients with CHF and were not associated with increased mortality in any study.

Oskouie SK, Prenner SB, Shah SJ, et al. Differences in Repolarization Heterogeneity Among Heart Failure With Preserved Ejection Fraction Phenotypic Subgroups. Am J Cardiol. 2017 Aug 15;120(4):601-606.

Otto CM. Heartbeat: heart **failure induced by cancer therapy**. Heart. 2019 Jan;105(1):1-3.

Ouwerkerk W, et al. Determinants and clinical outcome of **uptitration of ACE-inhibitors and beta-blockers** in patients with heart failure: a prospective European study. Eur Heart J. 2017 Mar 11.

Owens AT, Jessup M. Should **left ventricular assist device** be standard of care for patients with refractory heart failure who are not transplantation candidates?: left ventricular assist devices should not be standard of care for transplantation-ineligible patients. Circulation. 2012 Dec 18;126(25):3088-94.

Packer M. **Obesity-Associated Heart Failure as a Theoretical Target for Treatment With Mineralocorticoid Receptor Antagonists**. JAMA Cardiol. 2018 Jul 25.

Packer M. **What causes sudden death** in patients with chronic heart failure and a reduced ejection fraction? Eur Heart J. 2019 Aug 7.

Packer M, Anker SD, Butler J, et al. Effects of **Sodium-Glucose Cotransporter 2 Inhibitors for the Treatment of Patients With Heart Failure**: Proposal of a Novel Mechanism of Action. JAMA Cardiol. 2017 Sep 1;2(9):1025-1029.

Packer M, Claggett B, Lefkowitz MP, et al. Effect of **neprilysin inhibition on renal function in patients with type 2 diabetes and chronic heart failure** who are receiving target doses of inhibitors of the renin-angiotensin system: a secondary analysis of the PARADIGM-HF trial. Lancet Diabetes Endocrinol. 2018 Apr 13.

Packer M, Colucci W, Fisher L, et al. Effect of **levosimendan** on the short-term clinical course of patients with acutely decompensated heart failure. JACC Heart Failure 2013; 1:103-11.

Packer M, McMurray JJV, Desai AS, et al: **PARADIGM-HF** Investigators and Coordinators. **Angiotensin-neprilysin inhibition and clinical progression** in surviving patients with heart failure. Circulation 2015;131:54–61.

Packer M, McMurray JJ. Importance of **endogenous compensatory vasoactive peptides** in broadening the effects of inhibitors of the renin-angiotensin system for the treatment of heart failure. Lancet. 2016 Dec 2.

Packer M, O'Connor C, McMurray JJV, et al. Effect of **ularitide** on cardiovascular mortality in acute heart failure. (**TRUE-AHF**) N Engl J Med. DOI: 10.1056/NEJMoa1601895.

Packer M, Poole-Wilson PA, Armstrong PW, et al. Comparative effects of low and high doses of the angiotensin-converting enzyme inhibitor, lisinopril, on morbidity and mortality in chronic heart failure. **ATLAS** Study Group. Circulation. 1999;100:2312-8.

Padwal R, McAlister FA, et al. The **obesity paradox** in heart failure patients with preserved versus reduced ejection fraction: a meta-analysis of individual patient data. Int J Obes (Lond). 2013 Oct 31.

Page RL 2nd, O'Bryant CL, Cheng D, et al. **Drugs That May Cause or Exacerbate Heart Failure**: A Scientific Statement From the **American Heart Association**. Circulation. 2016 Jul 11.

Palmer K, Bowles KA, Paton M, et al. Chronic Heart Failure and **Exercise Rehabilitation**: A Systematic Review and Meta-Analysis. Arch Phys Med Rehabil. 2018 Dec;99(12):2570-2582.

Pan A, Stiell IG, Dionne R, et al. **Prehospital use of furosemide** for the treatment of heart failure. Emerg Med J. 2014 Apr 4.

Pandey A, Garg S, Khunger M, et al. Dose-response relationship between **physical activity** and risk of heart failure: a meta-analysis. Circulation. 2015;132:1786–1794.

Pandey A, Golwala H, Sheng S, et al. Factors associated with and prognostic implications of **cardiac troponin elevation** in decompensated heart failure with preserved ejection fraction: findings from the American Heart Association Get With The Guidelines–Heart Failure program [online Dec 28, 2016].JAMA Cardiol. doi:10.1001 /jamacardio.2016.4726

Pandey A, LaMonte M, Klein L, et al. Relationship Between **Physical Activity, Body Mass Index**, and Risk of Heart Failure. J Am Coll Cardiol. 2017 Mar 7;69(9):1129-1142.

Pandey A, Keshvani N, Ayers C, et al. Association of **Cardiac Injury and Malignant Left Ventricular Hypertrophy** With Risk of Heart Failure in African Americans: The Jackson Heart Study. JAMA Cardiol. 2018 Dec 19.

Pandor A, Gomersall T, Stevens JW, et al. **Remote monitoring** after recent hospital discharge in patients with heart failure: a systematic review and network meta-analysis. Heart. 2013 May 16.

Pandor A, Thokala P, Gomersall T, et al. **Home telemonitoring** or structured telephone support programmes after recent discharge in patients with heart failure: systematic review and economic evaluation. Health Technol Assess. 2013 Aug;17(32):1-207, v-vi. doi: 10.3310/hta17320.

Pandey A, Cornwell WK 3rd, Willis B, et al. **Body Mass Index and Cardiorespiratory Fitness** in Mid-Life and Risk of Heart Failure Hospitalization in Older Age: Findings from the Cooper Center Longitudinal Study. JACC Heart Fail. 2017 Mar 30.

Panhwar MS, Kalra A, Gupta T, et al. Effect of **Influenza on Outcomes in Patients with Heart Failure**. JACC Heart Fail. 2019 Jan 2.

Pandey A, Omar W, et al. **Sex and Race Differences** in Lifetime Risk of Heart Failure with Preserved Ejection Fraction and Heart Failure with Reduced Ejection Fraction. Circulation. 2018 Jan 19.

Parikh K, Weitz H. Can a **bowel preparation exacerbate heart failure**? Cleveland Clinic Journal of Medicine 2011; 78(3):157-160; doi:10.3949/ccjm.77a.10025

Parikh KS, Lippmann SJ, Greiner M, et al. Scope of **Sacubitril/Valsartan** Eligibility After Heart Failure Hospitalization: Findings From the **GWTG-HF Registry** (Get With The Guidelines-Heart Failure). Circulation. 2017 May 23;135(21):2077-2080.

Park CS, Park JJ, Mebazaa A, et al. Characteristics, Outcomes, and **Treatment of Heart Failure With Improved Ejection Fraction**. J Am Heart Assoc. 2019 Mar 19;8(6):e011077.

Park JJ, Kim SH, Oh IY, et al. The Effect of **Door-to-Diuretic Time** on Clinical Outcomes in Patients With Acute Heart Failure. JACC Heart Fail. 2018 Apr;6(4):286-294.

Parker JD, Ross HJ. Chronic congestive heart failure - a **new therapeutic choice**. CMAJ. 2016 Nov 1;188(16):1137-1138

Pasini E, Aquilani R, Testa C, et al. **Pathogenic gut flora** in patients with chronic heart failure. *JACC: Heart Fail.*2015.

Pasternak B, Svanström H, Melbye M, et al. Association of Treatment With **Carvedilol vs Metoprolol** Succinate and Mortality in Patients With Heart Failure. JAMA Intern Med. 2014 Aug 31.

Patel AN, Henry TD, Quyyumi AA, et al; **ixCELL-DCM** Investigators. **Ixmyelocel-T** for patients with ischaemic heart failure: a prospective randomised double-blind trial. Lancet. 2016 Apr 5.

Patel N, et al. Temporal trends of **digoxin** use in patients hospitalized with heart failure: Analysis the American Heart Association Get With the Guidelines-Heart Failure Registry. *JACC Heart Fail* 2016.

Patel PA, Ali N, Roy A, et al. **Effects of Ivabradine on Hemodynamic and Functional Parameters in Left Ventricular Systolic Dysfunction**: a Systematic Review and Meta-analysis. J Gen Intern Med. 2018 Jul 18.

Patorno E, Pawar A, Franklin JM, et al. **Empagliflozin and the Risk of Heart Failure Hospitalization** in Routine Clinical Care: A First Analysis from the Empagliflozin Comparative Effectiveness and Safety (**EMPRISE**) Study. Circulation. 2019 Apr 8.

Pavri BB, Lokhandwala Y, Kulkarni GV, et al. **Reuse of explanted, resterilized implantable cardioverter-defibrillators**: a cohort study. Ann Intern Med. 2012 Oct 16;157(8):542-8.

Peacock WF, Chandra A, Char D, et al. **Clevidipine** in acute heart failure: Results of the PRONTO study. *Am Heart J* 2014.

Penn J, Goldenberg I, McNitt S, et al. Changes in drug utilization and outcome with **cardiac resynchronization therapy**: A **MADIT-CRT** substudy. *J Card Fail* 2015.

Perin EC, Willerson JT, Pepine CJ, et al. Effect of transendocardial delivery of **autologous bone marrow mononuclear cells** on functional capacity, left ventricular function and perfusion in chronic heart failure. The **FOCUS-CCTRN** trial. JAMA 2012

Peterson Pamela N., Shetterly Susan M., Clarke Christina L., et al. **Health Literacy** and Outcomes Among Patients With Heart Failure. JAMA. 2011;305(16):1695-1701.doi:10.1001/jama.2011.512.

Peterson PN, Varosy PD, Heidenreich PA, et al. Association of **single- vs dual-chamber ICDs** with mortality, readmissions, and complications among patients receiving an ICD for primary prevention. JAMA 2013; 309:2025-2034.

Pedersen SS, Chaitsing R, Szili-Torok T, et al. Patients' Perspective on **Deactivation of the Implantable Cardioverter-Defibrillator** Nearthe End of Life. Am J Cardiol. 2013 Mar 10.

Peterson N, Greiner MA, Qualls LG, et al. **QRS Duration, bundle-branch block** (esp LBBB) morphology, and outcomes among older patients with heart failure receiving cardiac resynchronization therapy. JAMA 2013; 310: 617-626.

Petrie MC, Jhund PS, She L, et al. **Ten-Year Outcomes After Coronary Artery Bypass Grafting** According to Age in Patients With Heart Failure and Left Ventricular Systolic Dysfunction: An Analysis of the Extended Follow-Up of the **STICH** Trial (Surgical Treatment for Ischemic Heart Failure). Circulation. 2016 Nov 1;134(18):1314-1324

Petrone AB, Gaziano JM, Djoussé L. **Alcohol Consumption** and Risk of Death in Male Physicians With Heart Failure. Am J Cardiol. 2014 Jul 18.

Pfeffer MA, Claggett B, Assmann SF, et al. **Regional variation** in patients and outcomes in the Treatment of Preserved Cardiac Function Heart Failure With an **Aldosterone Antagonist (TOPCAT)** trial. Circulation. 2015;131:34–42.

Pfeffer MA, Braunwald E. Treatment of Heart Failure With Preserved Ejection Fraction: Reflections on Its Treatment With an **Aldosterone Antagonist**. (TOPCAT: spironolactone). JAMA Cardiol. 2016 Apr 1;1(1):7-8.

Pfisterer M, Buser P, Rickli H, et al. **TIME-CHF** Investigators. **BNP**-guided vs symptom-guided heart failure therapy: Trial of Intensified vs Standard Medical Therapy in **Elderly Patients** With Congestive Heart Failure (TIME-CHF) randomized trial. JAMA. 2009 Jan 28;301(4):383-92. Heart failure therapy guided by N-terminal BNP did not improve overall clinical outcomes or quality of life compared with symptom-guided treatment. (BNP guided therapy increases dosages of evidence based medications but not significantly improve overall patient outcomes. Subgroup: The younger <75yr olds may respond better to BNP guided therapy than the >75yr olds.)

Pharmacist's Letter. **Nitrate comparison** chart. Mar, 2010.

Piccini JP, Berger JS, O`Connor CM. **Amiodarone** for the prevention of sudden cardiac death: a meta-analysis of randomized controlled trials. Eur Heart J. 2009 May;30(10):1245-53. Epub 2009 Mar 31.

Pierdomenico SD, Pierdomenico AM, Coccina F, et al. **Ambulatory Blood Pressure Parameters** and Heart Failure With Reduced or Preserved Ejection Fraction in Elderly Treated Hypertensive Patients. Am J Hypertens. 2016 Mar 18.

Pieske B, Tschöpe C, de Boer RA, et al. **How to diagnose heart failure with preserved ejection fraction**: the HFA-PEFF diagnostic algorithm: a consensus recommendation from the Heart Failure Association (HFA) of the European Society of Cardiology (ESC). Eur Heart J. 2019 Aug 31.

Piller LB, Baraniuk S, Simpson LM, et al. Long-term follow-up (**8.9yr**) of participants with **heart failure** in the Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial (**ALLHAT**). Circulation. 2011;124:1811–1818.

Pinho-Gomes AC, Rahimi K. Management of **blood pressure in heart failure**.Heart. 2019 Jan 23.

Piña IL, Zheng Q, She L, et al; on behalf of the **STICH** Trial Investigators. **Sex differences** in patients with ischemic heart failure undergoing **surgical revascularization**: results from the STICH trial (Surgical Treatment for Ischemic Heart Failure). Circulation. 2018;137:771–780.

Pitt B, Pfeffer MA, Assmann SF, et al. **Spironolactone** for heart failure with preserved ejection fraction. (**TOPCAT**) N Engl J Med 2014;370:1383-92.

Pocock SJ, Ariti CA, McMurray JJ, et al. **Predicting survival in heart failure**: a risk score based on 39 372 patients from 30 studies. Eur Heart J. 2012 Oct 24.

Pokorney SD, Mi X, et al. Use of **Antiarrhythmic** Medications in Medicare Part D Patients with An **Implantable Cardioverter-Defibrillator and Ventricular Tachycardia**. Am J Cardiol. 2017.

Ponikowski P, van Veldhuisen DJ, Comin-Colet J, et al; for the **CONFIRM-HF** Investigators. Beneficial effects of long-term **intravenous iron therapy** with **ferric carboxymaltose** in patients with symptomatic heart failure and iron deficiency†. Eur Heart J. 2014 Aug 31.

Ponikowski P, van Veldhuisen DJ, Comin-Colet J, et al. Beneficial effects of long-term intravenous iron therapy with **ferric carboxymaltose** in patients with symptomatic **heart failure** and iron deficiency. Eur Heart J 2015;36:657e668.

Ponikowski P, Voors AA, Anker SD, et al. **2016 ESC guidelines for the diagnosis and treatment of acute and chronic heart failure**: The Task Force for the diagnosis and treatment of acute and chronic heart failure of the European Society of Cardiology. Developed with the special contribution of the Heart Failure Association (HFA) of the ESC. Eur J Heart Fail. 2016 Aug;18(8):891-975.

Poole JE. Present guidelines for device implantation: clinical considerations and clinical challenges from **pacing, implantable cardiac defibrillator, and cardiac resynchronization therapy**. Circulation. 2014 Jan 21;129(3):383-94

Porapakkham Pramote; Porapakkham Pornwalee; Zimmet Hendrik; et al. **B-Type Natriuretic Peptide-Guided** Heart Failure Therapy: A Meta-analysis. Arch Intern Med. 2010;170(6):507-514.

Powell LH, Calvin JE Jr, Richardson D, et al. HART Investigators. **Self-management counseling** in patients with heart failure: the heart failure adherence and retention randomized behavioral trial. JAMA. 2010 Sep 22;304(12):1331-8

Pradhan A, Vohra S, Vishwakarma P, Sethi R. Review on sodium-glucose cotransporter 2 inhibitor (SGLT2i) in diabetes mellitus and heart failure. J Family Med Prim Care. 2019 Jun;8(6):1855-1862.

Preiss D, Campbell RT, Murray HM, et al. The effect of **statin** therapy on heart failure events: A collaborative meta-analysis of unpublished data from major randomized trials. *Eur Heart J* 2015.

Premchand RK, Sharma K, Mittal S, et al. Autonomic regulation therapy via left or right **cervical vagus nerve stimulation** in patients with chronic heart failure: results of the **ANTHEM-HF** trial.

J Card Fail. 2014 Aug 22. [Epub ahead of print]
Price JF, Kantor PF, et al. Incidence, Severity, and Association With Adverse Outcome of **Hyponatremia** in Children Hospitalized With Heart Failure. Am J Cardiol. 2016 Oct 1;118(7):1006-10.
Prinzen FW, Vernooy K, et al. **Cardiac Resynchronization Therapy**: State-of-the-Art-Current Applications, Guidelines, Ongoing Trials, & Areas of Controversy. Circulation.2013 Nov 26;128(22):2407-18.
Psotka MA, Teerlink JR. **Ivabradine**: Role in the Chronic Heart Failure Armamentarium. Circulation. 2016 May 24;133(21):2066-75.
Pufulete M;Maishman R;Dabner L;Mohiuddin S;Holling. Effectiveness and cost-effectiveness of serum B-type **natriuretic peptide testing** and monitoring in patients with heart failure in primary and secondary care: an evidence synthesis, cohort study and cost-effectiveness model. Health Technol Assess. 2017 Aug;21(40):1-150.
Pulignano G, Del Sindaco D, Di Lenarda A, et al. Incremental value of **gait speed** in predicting prognosis of heart failure older adults: Insights from the IMAGE-HF study. JACC Heart Fail 2016.
Pun PH, Sheng S, Sanders G. Prescription of Guideline-Recommended **Implantable Cardioverter Defibrillator and Cardiac Resynchronization Therapy** Among Patients Hospitalized with Heart Failure and Varying Degrees of Renal Function. Am J Cardio. 2017.
Qaseem A, Fihn SD, Williams S, Dallas P, Owens DK, Shekelle P; Clinical Guidelines Committee of the American College of Physicians. Diagnosis of **stable ischemic heart disease**(**SIHD**): summary of a clinical practice guideline from the American College of Physicians (ACP) /American College of Cardiology Foundation(ACCF)/American Heart Association (AHA)/American Association for Thoracic Surgery/Preventive Cardiovascular Nurses Association/Society of Thoracic Surgeons. Ann Intern Med. 2012 Nov 20;157(10):729-34.
Qi WX, Shen Z, Tang LN, et al. Congestive **heart failure** risk in **cancer patients** treated with **VEGFR-TKIs**: a systematic review and meta-analysis of 36 clinical trials. Br J Clin Pharmacol. 2014 Mar 25.
Qian F, Parzynski CS, Chaudhry SI, et al. **Racial differences** in heart failure outcomes: evidence from the Tele-HF Trial (Telemonitoring to Improve Heart Failure Outcomes). *JACC: Heart Failure* 2015; 3:531-538.
Qureshi WT, Zhang ZM, Chang PPet al. **Silent Myocardial Infarction** and Long-Term Risk of Heart Failure: The **ARIC** Study. J Am Coll Cardiol. 2018 Jan 2;71(1):1-8.
Radholm K, et al. **Canagliflozin** and **Heart Failure in** Type 2 Diabetes Mellitus: Results From the **CANVAS** Program (Canagliflozin Cardiovascular Assessment Study). Circulation. 2018 Mar 11.
Rahman I, Akesson A, Wolk A. Relationship between **age at natural menopause** and risk of heart failure. Menopause. 2014 May 12.
Rahman I, Bellavia A, Wolk A, et al. **Physical Activity** and Heart Failure Risk in a Prospective Study of Men. JACC Heart Fail. 2015 Aug 1.
Rahman I, Wolk A, Larsson SC. The relationship between **sweetened beverage consumption** and risk of heart failure in men. Heart. 2015 Nov 2.
Raman SV, Hor KN, Mazur W, et al. **Eplerenone** for early cardiomyopathy in **Duchenne muscular dystrophy**: a randomised, placebo-controlled trial. Lancet Neurol 2014; online Dec 30.
Rao MP, Al-Khatib SM, et al. **Sudden Cardiac Death** in Patients With Ischemic Heart Failure Undergoing Coronary Artery Bypass Grafting: Results From the **STICH** Randomized Clinical Trial (Surgical Treatment for Ischemic Heart Failure). Circulation. 2017 Mar 21;135(12):1136-1144.
Real J, Cowles E, Wierzbicki AS; Guideline Committee. **Chronic heart failure in adults**: summary of updated NICE guidance. BMJ. 2018 Sep 24;362:k3646.
Reddy SY, Warner H, Guttuso T, et al. **Gabapentin, estrogen, and placebo for treating hot fla**shes: a randomized controlled trial. Obstet Gynecol 2006;108:41-48.
Rajagopalan S, Arora A, Shafiq N, et al. Pharmacotherapy of heart failure with **normal ejection fraction (HFNEF)**-a systematic review. Br J Clin Pharmacol. 2011 Sep;72(3):369-80.
Ranasinghe I, Parzynski CS, Freeman JV, et al. **Long-Term Risk for Device-Related Complications** and Reoperations After Implantable Cardioverter-Defibrillator Implantation: An Observational Cohort Study. Ann Intern Med. 2016 May 3.
Reddy YNV, Carter RE, Obokata M, et al. A **Simple, Evidence-Based Approach to Help Guide Diagnosis of Heart Failure** with Preserved Ejection Fraction. Circulation. 2018 May 23.
Reddy VY, Exner DV, Cantillon DJ, et al. Percutaneous implantation of an entirely intracardiac **leadless pacemaker**. (**Leadless II**) N Engl J Med 2015;373:1125-35.
Redfield MM, et al. Effect of phosphodiesterase-5 inhibition (**sildenafil**) on exercise capacity & clinical status in heart failure with preserved ejection fraction: randomized clinical trial. (RELAX) JAMA 2013.
Redfield MM. Heart Failure with **Preserved Ejection Fraction**. N Engl J Med. 2016 Nov 10;375(19):1868-1877.
Reeves GR, Whellan DJ, Patel MJ, et al. Comparison of **Frequency of Frailty and Severely Impaired Physical Function** in Patients ≥60 Years Hospitalized With Acute Decompensated Heart Failure Versus Chronic Stable Heart Failure With Reduced and Preserved Left Ventricular Ejection Fraction. Am J Cardiol. 2016 Jun 15;117(12):1953-8.
Remme WJ, Swedberg K; The Task Force for the Diagnosis and Treatment of Heart Failure. Guidelines for the diagnosis and treatment of chronic heart failure. Eur Heart J. 2001;22(17):1527-1560.
Reynolds D, Duray GZ, Omar R, et al. A **leadless intracardiac transcatheter pacing system**. N Engl J Med. DOI: 10.1056/ NEJMoa1511643.
Reynolds K, Butler MG, Kimes TM, et al. Relation of **Acute Heart Failure Hospital Length of Stay** to Subsequent Readmission and All-Cause Mortality. Am J Cardiol. 2015 Aug 1;116(3):400-5
Rho RW, Patton KK, Poole JE, et al.. Important differences in mode of **death between men and women** with heart failure who would qualify for a primary prevention implantable cardioverter-defibrillator. Circulation. 2012 Nov 13;126(20):2402-7.
Richards AM, Lainchbury JG, Troughton RW, et al. **NT-proBNP** guided treatment for chronic heart failure: results from the Battlescarred trial. Circulation. 2008; 118:S1035-S1036.
Richardt D, Hanke T, Sievers HH. Two cases of heart failure after implantation of a **CoreValve prosthesis**. N Engl J Med. 2015 Mar 12;372(11):1079-80.
Richter S, Di Biase L, Hindricks G. **Atrial fibrillation ablation** in heart failure. Eur Heart J. 2019 Feb 21;40(8):663-671.
Rickard J, Bassiouny M, et al. Long-Term Outcomes in Patients With Ambulatory New York Heart Association Class III and IV Heart Failure Undergoing **Cardiac Resynchronization Therapy**. Am J Cardiol. 2015 Jan 1;115(1):82-5.
Rickard J, Michtalik H, Sharma R, et al. **Cardiac Resynchronization Therapy** in the Medicare Population. Technology Assessment Report. Rockville, MD: Agency for Healthcare Research and Quality. March 24, 2015. Contract HHSA 290-201-200007-1.
Rienstra M, Damman K, Mulder BA, et al. **Beta-blockers and outcome in heart failure and atrial fibrillation**. A meta-analysis. JACC:Heart Fail 2013; 1:21-28.
Rijal S, Shah RU, Saba S. **Extracting Versus Abandoning Sterile Pacemaker and Defibrillator Leads**. Am J Cardiol. 2015 Jan 31.
Rimm EB, Appel LJ, Chiuve SE, et al. Seafood Long-Chain **n-3 Polyunsaturated Fatty Acids and Cardiovascular Disease**: A Science Advisory From the American Heart Association. Circulation. 2018 May 17.
Ritter J M. Therapeutics: **Angiotensin converting enzyme inhibitors and angiotensin receptor blockers in hypertension**. BMJ 2011;342:doi:10.1136/bmj.d1673 (Published 7 April 2011)
Rivero-Ayerza M, Scholte Op Reimer W, et al. New-onset **atrial fibrillation** is an independent predictor of in-hospital mortality in hospitalized heart failure patients: results of the EuroHeart Failure Survey. Eur Heart J. 2008 Jul;29(13):1618-24. Epub 2008 May 31.
Roalfe AK, Mant J, Doust JA, et al. Development and initial validation of a simple clinical decision tool to predict the **presence of heart failure in primary care**: the **MICE (Male, Infarction, Crepitations, Edema) rule**. Eur J Heart Fail. 2012 Sep;14(9):1000-8.
Roberts DM, Galappatthy G, Dunuwille A, et al. Pharmacological treatment of **cardiac glycoside poisoning**. Br J Clin Pharmacol. 2015 Oct 27.
Roberts E, Ludman AJ, Dworzynski K, et al. The **diagnostic accuracy of the natriuretic peptides** in heart failure: systematic review and diagnostic meta-analysis in the acute setting. BMJ 2015;350;h910.
Rodondi N, Bauer DC, Cappola AR, et al. Subclinical thyroid dysfunction, cardiac function, and the risk of heart failure. The Cardiovascular Health study. J Am Coll Cardiol. 2008 Sep 30;52(14):1152-9. Compared with euthyroid older adults, those adults with **TSH>or=10.0 mU/l have a moderately increased risk of HF** and alterations in cardiac function but not older adults with TSH<10.0 mU/l. Clinical trials should assess whether the risk of HF might be ameliorated by thyroxine replacement in individuals with TSH>or=10.0 mU/l.
Rogers JG, Pagani FD, Tatooles AJ, et al. **Intrapericardial Left Ventricular Assist Device** for Advanced Heart Failure. N Engl J Med. 2017 Feb 2;376(5):451-460.
Rogers JG, Patel CB, Mentz RJ, et al. **Palliative Care** in Heart Failure: The **PAL-HF** Randomized, Controlled Clinical Trial. J Am Coll Cardiol. 2017 Jul 18;70(3):331-341
Rogers JK, McMurray JJ, Pocock SJ, et al. **Eplerenone** in patients with systolic heart failure & mild symptoms: analysis of repeat hospitalizations. (**Emphasis-HF**)Circulation. 2012 Nov 6;126(19):2317-23.
Rome BN, Kramer DB, Kesselheim AS. **FDA approval** of **cardiac implantable electronic devices** via original and supplement premarket approval pathways, 1979-2012. *JAMA*. doi:10.1001/jama.2013.284986.
Ross, Joseph S., Normand, Sharon-Lise T., Wang, Yun, et al. Hospital **Volume** and 30-Day **Mortality** for Three Common Medical Conditions. N Engl J Med 2010 362: 1110-1118.
Rossano JW, Shaddy RE. Update on Pharmacological **Heart Failure Therapies in Children**: Do Adult Medications Work in Children and if Not, Why Not? Circulation.2014 Feb 4;129(5):607-12.
Rossano JW, Shaddy RE. **Heart Failure in Children**: Etiology and Treatment. J Pediatr. 2014 Jun 11.
Rossignol P, Cleland JG, Bhandari S et al. Determinants and consequences of renal function variations with aldosterone blocker therapy in heart failure patients after myocardial infarction: insights from the eplerenone post-acute myocardial infarction heart failure efficacy and survival study. Circulation. 2012 Jan 17;125(2):271-9.
Rossignol P, Hernandez AF, Solomon SD, Zannad F. Heart failure **drug treatment**. Lancet. 2019 Mar 9;393(10175):1034-1044.
Rossignol P, Ménard J, Fay R, et al. **Eplerenone** survival benefits in heart failure patients post-myocardial infarction are independent from its diuretic and potassium-sparing effects: insights from an **EPHESUS** (Eplerenone Post-Acute Myocardial Infarction Heart Failure Efficacy and Survival Study) **EPHESUS** substudy. J Am Coll Cardiol 2011; 58:1958-1966.
Roth G, Poole J, Zaha R, et al. Use of **guideline-directed medications** for heart failure before **cardioverter-defibrillator implantation**. *J Am Coll Cardiol* 2016; 67:1062-1069.
Rothberger GD, Gadhvi S, Michelakis N, et al. Usefulness of **Serum Triiodothyronine (T3)** To Predict Outcomes in Patients Hospitalized With Acute Heart Failure. American Journal of Cardiology. 2016.
Rørth R, Wong C, Kragholm K, et al. **Return to the workforce** after first hospitalization for heart failure: a Danish nationwide cohort study. Circulation. 2016;134:999–1009.
Rorth R, Wong C, Kragholm K, et al. **Return to the Workfor**ce After First Hospitalization for Heart Failure: A Danish Nationwide Cohort Study. Circulation. 2016 Oct 4;134(14):999-1009.
Roy B, Pawar PP, Desai RV, et al. A Propensity-Matched Study of the Association of **Diabetes Mellitus With Incident Heart Failure** and Mortality Among Community-Dwelling Older Adults. Am J Cardiol. 2011 Sep 22.
Ruppar TM, Cooper PS, Mehr DR, et al. **Medication adherence interventions** improve heart failure mortality and readmission rates: systematic review and meta-analysis of controlled trials. J Am Heart Assoc. 2016;5:e002606 doi: 10.1161/JAHA.115.002606.
Ruschitzka F, Abraham WT, Singh JP, et al. **Cardiac-resynchronization therapy** in heart failure with a narrow QRS complex. (**EchoCRT**) N Engl J Med 2013; DOI: 10.1056/NEJMoa1306687.
Rush CJ, Campbell RT, Jhund PS, et al. Association is not causation: **treatment effects cannot be estimated** from observational data in heart failure. Eur Heart J. 2018 Oct 1;39(37):3417-3438.
Russo AM, Stainback RF, Bailey SR, et al. ACCF/HRS/AHA/ASE/HFSA/SCAI/SCCT/SCMR 2013 **Appropriate Use Criteria for Implantable Cardioverter-Defibrillators and Cardiac Resynchronization** Therapy: A Report of the American College of Cardiology Foundation Appropriate Use Criteria Task Force, Heart Rhythm Society, American Heart Association, American Society of Echocardiography, Heart Failure Society of America, Society for Cardiovascular Angiography and Interventions, Society of Cardiovascular Computed Tomography, and Society for Cardiovascular

Magnetic Resonance. Heart Rhythm. 2013 Mar 5
Russo RJ, Costa HS, Silva PD, et al. Assessing the **Risks Associated with MRI** in Patients **with a Pacemaker or Defibrillator**. N Engl J Med. 2017 Feb 23;376(8):755-764.
Ruwald MH, Ruwald AC, Jons C, et al. Effect of **metoprolol** (~64mg) **versus carvedilol** (~18mg) on outcomes in **MADIT-CRT** (Multicenter Automatic Defibrillator Implantation Trial with Cardiac Resynchronization Therapy). J Am Coll Cardiol 2013; 61:1518-1526.
Ruwald MH, Solomon SD, Foster E, et al. Left Ventricular Ejection Fraction Normalization in **Cardiac Resynchronization Therapy** and Risk of Ventricular Arrhythmias and Clinical Outcomes: Results from the **MADIT-CRT** Trial. Circulation. 2014 Oct 9.
Ruwald MH, Solomon SD, Foster E, et al. Left Ventricular Ejection Fraction Normalization in **Cardiac Resynchronization Therapy** and Risk of Ventricular Arrhythmias and Clinical Outcomes: Results From the Multicenter Automatic Defibrillator Implantation Trial With Cardiac Resynchronization Therapy (**MADIT-CRT**) Trial. Circulation. 2014 Dec 23;130(25):2278-86.
Sacks CA, Jarcho JA, Curfman GD. **Paradigm Shifts** in Heart-Failure Therapy - A Timeline. N Engl J Med. 2014 Sep 3.
Sadhu JS, Novak E, Mukamal KJ, et al. Association of **Alcohol Consumption After Development of Heart Failure** With Survival Among Older Adults in the Cardiovascular Health Study. JAMA Netw Open.2018;1(8):e186383.
Sagar S, Liu PP, Cooper LT Jr. **Myocarditis**. Lancet. 2011 Dec 16.
Saiki H, et al. **Risk of Heart Failure With Preserved Ejection Fraction** in **Older Women** After Contemporary **Radiotherapy for Breast Cancer**. Circulation. 2017 Apr 11;135(15):1388-1396.
Sakata Y, Shiba N, Takahashi J, et al. Clinical impacts of **additive use of olmesartan** in hypertensive patients with chronic heart failure: the supplemental benefit of an angiotensin receptor blocker in hypertensive patients with stable heart failure using olmesartan (**SUPPORT**) trial. Eur Heart J. 2015 Jan 30.
Salah K, Kok WE, Eurlings LW, et al. A novel discharge risk model for patients hospitalised for acute decompensated heart failure incorporating **N-terminal pro-B-type natriuretic peptide levels**: a European coLlaboration on Acute decompeNsated Heart Failure: ELAN-HF Score. Heart. 2013 Oct 31.
Salata BM, Sterling MR, et al. **Discharge Processes and 30-Day Readmission Rates** of Patients Hospitalized for Heart Failure on General Medicine and Cardiology Services. Am J Cardiol. 2018 Feb 7.
Salz T, Zabor EC, de Nully Brown P, et al. Preexisting Cardiovascular Risk and Subsequent **Heart Failure Among Non-Hodgkin Lymphoma Survivors**. J Clin Oncol. 2017 Dec 1;35(34):3837-3843.
Samala RV, Navas V, Saluke E, Ciocon JO. Heart failure in frail, older patients: We can do 'MORE'. Cleve Clin J Med. 2011 Dec;78(12):837-45.
Samsky MD, Ambrosy AP, Youngson E, et al. **Trends in Readmissions and Length of Stay** for Patients Hospitalized With Heart Failure in Canada and the United States. JAMA Cardiol. 2019 Apr 10.
Sandhu AT, Ollendorf DA, Chapman RH, et al. **Cost-effectiveness of sacubitril–valsartan** in patients with heart failure with reduced ejection fraction. Ann Intern Med. 2016.
Sano M. A new class of drugs for **heart failure: SGLT2** inhibitors reduce sympathetic overactivity. J Cardiol. 2018 May;71(5):471-476.
Santangeli P, Di Biase L, Russo AD, et al. Meta-analysis: Age and Effectiveness of Prophylactic **Implantable Cardioverter-Defibrillators** (**ICD**). Ann Intern Med November 2, 2010 153:592-599.
Santhanakrishnan R, Wang N, et al. **Atrial Fibrillation Begets Heart Failure and Vice Versa**: Temporal Associations and Differences in Preserved vs. Reduced Ejection Fraction. Circulation. 2016 Jan 8.
Sarrias A, Bayes-Genis A. Is **Sacubitril/Valsartan** (Also) an Antiarrhythmic Drug? Circulation. 2018 Aug 7;138(6):551-553
Sarwar CM, Papadimitriou L, Pitt B, et al. **Hyperkalemia** in Heart Failure. J Am Coll Cardiol. 2016 Oct 4;68(14):1575-89.
Sassone B, Gambetti S, Bertini M, et al. Relation of **QRS Duration** to Response to **Cardiac Resynchronization Therapy**. Am J Cardiol. 2015 Jan 15;115(2):214-9
Sato N, Gheorghiade M, Kajimoto K, et al; ATTEND Investigators. **Hyponatremia** and In-Hospital Mortality in Patients Admitted for Heart Failure(from the ATTEND Registry). Am J Cardiol. 2013 Jan 9.
Sato B, Yoshikawa D, Ishii H, et al. Relation of **Plasma Indoxyl Sulfate Levels** and Estimated Glomerular Filtration Rate to Left Ventricular Diastolic Dysfunction. Am J Cardiol. 2012 Dec 7.
Sauer AJ, Cole R, Jensen BC, et al. Practical guidance on the use of **sacubitril/valsartan for heart failure**. Heart Fail Rev. 2018 Dec 18.
Sawaya H, Sebaq IA, Plana JC, et al. Early detection and prediction of **cardiotoxicity in chemotherapy-treated patients**. Am J Cardiol2011; 107:1375-1380.
Sawyer DB. **Anthracyclines** and heart failure. N Engl J Med. 2013 Mar 21;368(12):1154-6.
Schaefer U, Zahn R, Abdel-Wahab M, et al; German TAVI Registry. Comparison of Outcomes of Patients With Left Ventricular Ejection Fractions ≤30% Versus ≥30% Having **Transcatheter Aortic Valve Implantation** (from the German Transcatheter Aortic Valve Interventions Registry). Am J Cardiol. 2014 Dec 18.
Schelbert EB, Fridman Y, Wong TC, et al. Temporal Relation Between **Myocardial Fibrosis** and Heart Failure With Preserved Ejection Fraction: Association With Baseline Disease Severity and Subsequent Outcome. JAMA Cardiol. 2017 Aug 2
Schichtel M, Wee B, Perera R, et al. **Clinician-targeted interventions to improve advance care planning** in heart failure: a systematic review and meta-analysis. Heart. 2019 May 22.
Schopfer DW, Whooley MA, Stamos TD. **Hospital compliance with performance** measures and 30-day outcomes in patients with heart failure. Am Heart J. 2012 Jul;164(1):80-6.
Schou M, Gustafsson F, Videbaek L, et al. **Extended heart failure clinic follow-up** in low-risk patients: a randomized clinical trial (NorthStar). Eur Heart J. 2012 Aug 8.
Schneider PM, Pellegrini CN, Wang Y, et al. Prevalence of **Guideline-Directed Medical Therapy** Among Patients Receiving **Cardiac Resynchronization Therapy Defibrillator Implantation** in the National Cardiovascular Data Registry During the Years 2006 to 2008. Am J Cardiol. 2014 Apr 1.
Schrage B, Uijl A, Benson L, et al. Association Between Use of Primary Prevention **Implantable Cardioverter-Defibrillators and Mortality** in Patients with Heart Failure: A Prospective Propensity-Score Matched Analysis from the Swedish Heart Failure Registry. Circulation. 2019 Sep 3.
Schwartz BG, Rezkalla S, Kloner RA. Cardiovascular effects of **cocaine**. Circulation. 2010 Dec 14;122(24):2558-69.
Sciarretta Sebastiano; Palano Francesca; Tocci G; et al. **Antihypertensive Treatment and Development of Heart Failure** in Hypertension: A Bayesian Network Meta-analysis of Studies in Patients With Hypertension and High Cardiovascular Risk. Arch Intern Med. 2010;0(2010):archinternmed.2010.427.
Scuffham PA, Ball J, Horowitz JD, et al. **Standard vs. intensified management of heart failure** to reduce healthcare costs: results of a multicentre, randomized controlled trial. Eur Heart J. 2017 May 20.
Sears SF, Woodrow L, Cutitta K, et al. A **Patient's Guide to Living Confidently With Chronic Heart Failure**. Circulation. 2013 Apr 2;127(13):e525-8.
Sedlak T, Bairey Merz CN, Shufelt C, et al. **Contraception** in patients with heart failure. Circulation. 2012 Sep 11;126(11):1396-400.
See I, Shehab N, Kegler SR, et al. Emergency department visits and hospitalizations for **digoxin toxicity**: United States, 2005 to 2010. Circ Heart Fail. 2014 Jan;7(1):28-34.
Seferovic JP, Claggett B, Seidelmann SB, et al. Influence of **sacubitril/valsartan on glycaemic control** in patients with heart failure and diabetes: a post-hoc analysis from the **PARADIGM-HF** trial. Lancet Diabetes Endocrinol 2017;
Sehn E, McDonald T, Lindblad AJ. **Sacubitril-valsartan**: novel therapy for heart failure. Can Fam Physician. 2017 Sep;63(9):697.
Seliger SL, Hong SN, Christenson RH, et al. **High-Sensitive Cardiac Troponin T** as an Early Biochemical Signature for Clinical and Subclinical Heart Failure: **MESA** (Multi-Ethnic Study of Atherosclerosis). Circulation. 2017 Apr 18;135(16):1494-1505
Selvaraj S, Klein I, Danzi S, et al. Association of **Serum Triiodothyronine** With B-Type Natriuretic Peptide and Severe Left Ventricular **Diastolic Dysfunction** in Heart Failure With Preserved Ejection Fraction. Am J Cardiol. 2012 Apr 11.
Selvaraj S, Claggett B, et al. **Systolic blood pressure** and cardiovascular outcomes in heart failure with preserved ejection fraction: an analysis of the **TOPCAT** trial. Eur J Heart Fail. 2017 Nov 16.
Selvaraj S, Bhatt DL, Claggett B, et al. **Lack of association between heart failure and incident cancer**. J Am Coll Cardiol 2018;71:1501–10.
Senthong V, Hudec T, Neale S, et al. Relation of **Red Cell Distribution Width** to **Left Ventricular End-Diastolic Pressure** and Mortality in Patients with and without Heart Failure. Am J Cardiol. 2017.
Serrano C, Cortés J, De Mattos-Arruda L, et al. **Trastuzumab-related cardiotoxicity** in the elderly: a role for cardiovascular risk factors. Ann Oncol. 2011 Aug 9.
Setoguchi S, Schneeweiss S, Avorn J, Katz JN, Weinblatt ME, Levin R, Solomon DH. **Tumor necrosis factor**-alpha antagonist use and heart failure in elderly patients with rheumatoid arthritis. Am Heart J. 2008 Aug;156(2):336-41. Epub 2008 Jun 17. TNFAs may increase the risk of both first hospitalization and exacerbation of HF in elderly patients with RA.
Setoguchi S, Warner Stevenson L, et al. Influence of **healthy candidate bias** in assessing clinical effectiveness for **implantable cardioverter-defibrillators**: cohort study of older patients with heart failure. BMJ. 2014 May 8;348:g2866.
Shah AM, Shah SJ, Anand IS, et al. Cardiac structure and function in heart failure with preserved ejection fraction: baseline findings from the echocardiographic study of the treatment of preserved cardiac function heart failure with an aldosterone antagonist tria-spironolactonel. (**TOPCAT**) Circ Heart Fail. 2013 Nov 18.
Shah AM, Claggett B, et al. Prognostic Importance of Impaired Systolic Function in Heart Failure With Preserved Ejection Fraction & the Impact of **Spironolactone**. Circulation. 2015 Aug 4;132(5):402-14.
Shah AM, Claggett B, Loehr LR, et al. **Heart Failure Stages** Among Older Adults in the Community: The Atherosclerosis Risk in Communities Study. Circulation. 2017 Jan17;135(3):224-240.
Shah ASV, Langrish JP, Nair H, et al. Global association of **air pollution** and heart failure: a systematic review and meta-analysis. Lancet 2013; online July 10.
Shah KS, Xu H, Matsouaka RA, et al. **Heart failure with preserved, borderline, and reduced ejection fraction**: 5-year outcomes. J Am Coll Cardiol 2017;XX:XXX–XXX.
Shah M, Avgil Tsadok M, Jackevicius CA, et al. Relation of **Digoxin Use in Atrial Fibrillation and the Risk of All-Cause Mortality** in Patients ≥65 Years of Age With Versus Without Heart Failure. Am J Cardiol. 2014 May 16.
Shah MR. STARBRITE: a randomized pilot trial of **BNP-guided** therapy in patients with advanced heart failure. Circulation. 2006;114(II):528.
Shah RV, Rong J, Larson MG, et al. **Associations of Circulating Extracellular RNAs With Myocardial Remodeling and Heart Failure**. JAMA Cardiol. 2018 Aug 8.
Shah SA, Kambur T, Chan C, et al. Relation of **Short-Term Heart Rate Variability** to Incident Heart Failure (from the Multi-Ethnic Study of Atherosclerosis). Am J Cardiol. 2013 Aug 15;112(4):533-40.
Shah SJ, Feldman T, Ricciardi MJ, et al. One-Year Safety and Clinical Outcomes of a Transcatheter **Interatrial Shunt Device for the Treatment of Heart Failure** With Preserved Ejection Fraction in the Reduce Elevated Left Atrial Pressure in Patients With Heart Failure (REDUCE LAP-HF I) Trial: A Randomized Clinical Trial. JAMA Cardiol. 2018 Aug 27
Shah SJ, Kitzman DW, Borlaug BA, et al. Phenotype-Specific Treatment of Heart Failure With **Preserved Ejection Fraction**: A Multiorgan Roadmap. Circulation. 2016 Jul 5;134(1):73-90.
Shah SJ, Lam CSP, Svedlund S, et al. Prevalence and correlates of **coronary microvascular dysfunction in heart failure** with preserved ejection fraction: PROMIS-HFpEF. Eur Heart J. 2018 Aug 27.
Shah SJ, Voors AA, McMurray JJV, et al. Effect of Neladenoson Bialanate on Exercise Capacity Among Patients With Heart Failure With Preserved Ejection Fraction: A Randomized Clinical Trial. JAMA. 2019 Jun 4;321(21):2101-2112.
Sharkey AT, Ghafar MZ, O'Keeffe ST, Mulkerrin EC. **Angiotensin receptor neprilysin inhibitors in older patients with heart failure**. BMJ Evid Based Med.2019 Feb;24(1):5-7.
Shantsila E, Lip GYH. **Antiplatelet versus anticoagulation treatment for patients with heart failure in sinus rhythm**. Cochrane Database of Systematic Reviews 2016, Issue 9. Art. No.: CD003333. There is evidence from RCTs to suggest that neither oral anticoagulation with warfarin or platelet inhibition with aspirin is better for mortality in systolic heart failure with sinus rhythm (high quality of the

evidence for all-cause mortality and moderate quality of the evidence for non-fatal cardiovascular events and major bleeding events). Treatment with warfarin was associated with a 20% reduction in non-fatal cardiovascular events but a twofold higher risk of major bleeding complications (high quality of the evidence). We saw a similar pattern of results for the warfarin versus clopidogrel comparison (low quality of the evidence). At present, there are no data on the role of oral anticoagulation versus antiplatelet agents in heart failure with preserved ejection fraction with sinus rhythm. Also, there were no data from RCTs on the utility of non-vitamin K antagonist oral anticoagulants compared to antiplatelet agents in heart failure with sinus rhythm.

Sharma A, Zhao X, Hammill BG, et al. Trends in **Noncardiovascular Comorbidities** Among Patients Hospitalized for Heart Failure: Insights From the **Get With The Guidelines-Heart Failure Registry**. Circ Heart Fail. 2018 Jun;11(6):e004646.

Sharma AK, Vegh E, Kandala J, et al. "Usefulness of **Hyponatremia** as a Predictor for Adverse Events in Patients With Heart Failure Receiving Cardiac Resynchronization Therapy". The American Journal of Cardiology. (2014).

Sharma A, Colvin-Adams M, Yancy CW. **Heart failure in African Americans**: Disparities can be overcome. Cleve Clin J Med. 2014 May;81(5):301-11.

Sharma K, Al Rifai M, Ahmed HM, et at. Usefulness of **Coronary Artery Calcium** to Predict Heart Failure with Preserved Ejection Fraction in Men Versus Women (From the Multi-Ethnic Study of Atherosclerosis). Am J Cardio. 2017

Sharp RP, Welch EB. Takotsubo cardiomyopathy as a complication of **electroconvulsive therapy**. Ann Pharmacother. 2011 Dec;45(12):1559-65.

Shelton RJ, Clark AL, Goode K, et al. A randomised, controlled study of rate versus rhythm control in patients with chronic **atrial fibrillation** and heart failure: (CAFE-II Study). Heart. 2009 Jun;95(11):924-30. Epub 2009 Mar 11.

Shen L, Jhund PS, Docherty KF, et al. Prior **Pacemaker Implantation and Clinical Outcomes** in Patients With Heart Failure and Preserved Ejection Fraction. JACC Heart Fail. 2019 Apr 3

Shen L, Jhund PS, Petrie MC, et al. **Declining Risk of Sudden Death in Heart Failure**. N Engl J Med. 2017 Jul 6;377(1):41-51.

Shibata MC, Leon H, Chatterley T, et al. Do **calcium channel blockers** increase the diagnosis of heart failure in patients with hypertension? Am J Cardiol. 2010 Jul 15;106(2):228-35.

Sieswerda E, van Dalen EC, Postma A, et al. Medical interventions for treating **anthracycline-induced symptomatic and asymptomatic cardiotoxicity** during and after treatment for childhood cancer. Cochrane Database of Systematic Reviews 2011, Issue 9. Art. No.: CD008011. DOI: 10.1002/14651858.CD008011.pub2.

Sinha SK, Crain B, Flickinger K, et al. Cardiovascular **implantable electronic device** function and longevity at autopsy: An underestimated resource.*Heart Rhythm* 2016 May 27.

Sipahi I,Carrigan TP, Rowland DY, Stambler BS, Fang JC. Impact of **QRS duration on clinical event reduction with cardiac resynchronization therapy**: metaanalysis of randomized controlled trials [published online June 13, 2011]. Arch Intern Med. 2011; 171 (16):1454-1462

Skrtic S, Cabrera C, Olsson M, et al. Contemporary **risk estimates** of **three HbA(1c) variables** in relation to heart failure following diagnosis of type 2 diabetes. Heart. 2017 Mar;103(5):353-358.

Slaughter MS, Rogers JG, Milano CA, et al. **HeartMate II** Investigators. Advanced heart failure treated with continuous-flow left ventricular assist device. N Engl J Med. 2009 Dec 3;361(23):2241-51.

Slim AM, Thomas H, Parish R, Mansi I. Comparison of outcomes of **illicit drug users** and nonusers hospitalized with heart failure. Am J Cardiol. 2012 Aug 15;110(4):558-61.

Smer A, et al. Meta-analysis of **Risk of Ventricular Arrhythmias** After Improvement in Left Ventricular Ejection Fraction During Follow-Up in Patients With **Primary Prevention Implantable Cardioverter Defibrillators**. Am J Cardiol. 2017 Jul 15;120(2):279-286.

Smith H, Battjes E, Yan S, et al. Chronic **Digoxin Toxicity Precipitated by Dronedarone**. Ann Pharmacother. 2014 Mar 31;48(7):923-927.

Sohail MR, Henrikson CA, Braid-Forbes MJ, Forbes KF, Lerner DJ. Mortality and Cost Associated With Cardiovascular **Implantable Electronic Device Infections**. Arch Intern Med. 2011 Sep 12.

Soliman OII, Akin S, Muslem R, et al; on behalf of the **EUROMACS** Investigators. **Derivation and validation of a novel right-sided heart failure model** after implantation of continuous flow left ventricular assist devices: the EUROMACS (European Registry for Patients with Mechanical Circulatory Support) Right-Sided Heart Failure Risk Score. Circulation 2018;137:891–906.

Solomon SD, Zile M, et al. The **angiotensin receptor neprilysin inhibitor LCZ696** in heart failure with preserved ejection fraction: phase 2 double-blind randomised controlled trial. Lancet 2012.

Solomon SD, Claggett B, Lewis EF, Desai et al; **TOPCAT** Investigators. Influence of ejection fraction on outcomes and efficacy of **spironolactone** in patients with heart failure with **preserved ejection** fraction. Eur Heart J. 2016 Feb 1;37(5):455-62.

Solomon SD, Claggett B, Desai AS, et al. Influence of Ejection Fraction on Outcomes and Efficacy of **Sacubitril/Valsartan** (LCZ696) in Heart Failure with Reduced Ejection Fraction: The Prospective Comparison of ARNI with ACEI to Determine Impact on Global Mortality and Morbidity in Heart Failure(**PARADIGM-HF**) Trial. Circ Heart Fail. 2016 Mar;9(3):e002744.

Solomon SD, Claggett B, Packer M, et al. Efficacy of **Sacubitril/Valsartan** Relative to a **Prior Decompensation**: The **PARADIGM-HF** Trial. JACC Heart Fail. 2016 Oct;4(10):816-22.

Solomon SD, McMurray JJV, Anand IS, et al. **Angiotensin-Neprilysin Inhibition** in Heart Failure with Preserved Ejection Fraction. N Engl J Med. 2019 Sep 1

Soubret A, Pang Y, Yu J, et al. Population **pharmacokinetics of serelaxin in patients with acute or chronic heart failure**, hepatic or renal impairment, or portal hypertension and in healthy subjects. Br J Clin Pharmacol. 2018 Jul 16.

Sperry BW, Ikram A, Hachamovitch R, et al. Efficacy of chemotherapy for light-chain **amyloidosis** in patients presenting with symptomatic heart failure. *J Am Coll Cardiol* 2016; 67:2941-2948.

Srivastava PK, Claggett BL, Solomon SD, et al. Estimated 5-Year Number Needed to Treat to Prevent Cardiovascular Death or Heart Failure Hospitalization With **Angiotensin Receptor-Neprilysin Inhibition vs Standard Therapy** for Patients With Heart Failure With Reduced Ejection Fraction: An Analysis of Data From the **PARADIGM-HF** Trial. JAMA Cardiol. 2018 Nov 28.

Starling RC. Advanced heart failure: **Transplantation, LVADs**, and beyond. Cleve Clin J Med. 2013 Jan;80(1):33-40.

Starling RC, Moazami N, Silvestry SC, et al. Unexpected Abrupt Increase in **Left Ventricular Assist Device Thrombosis**. N Engl J Med. 2013 Nov 27.

Stauffer Brett D.; Fullerton Cliff; Fleming Neil; et al. Effectiveness and Cost of a **Transitional Care Program** for Heart Failure: A Prospective Study With Concurrent Controls. Arch Intern Med. 2011;171(14):1238-1243.

Steckman DA, Varosy PD, Parzynski CS, et al. In-Hospital Complications Associated With **Reoperations of Implantable Cardioverter Defibrillators**. Am J Cardiol. 2014 May 16.

Steinberg L, White M, Arvanitis J, et al. Approach to **advanced heart failure at the end of life**. Can Fam Physician. 2017 Sep;63(9):674-680

Steinhaus DA, Mostofsky E, Levitan EB, et al. **Chocolate intake** and incidence of heart failure: Findings from the Cohort of Swedish men. *Am Heart J* 2016.

Steinke EE, Jaarsma T, Barnason SA, et al. on behalf of the Council on Cardiovascular and Stroke Nursing of the American Heart Association and the ESC Council on Cardiovascular Nursing and Allied Professions (CCNAP). **Sexual Counseling for Individuals With Cardiovascular Disease and Their Partners**: A Consensus Document From the American Heart Association and the ESC Council on Cardiovascular Nursing and Allied Professions (CCNAP). Circulation. 2013 Jul 29.

Steinberg BA, Zhao X, et al. **Trends in Patients Hospitalized** with Heart Failure and Preserved Left Ventricular Ejection Fraction - Prevalence, Therapies, and Outcomes. Circulation. 2012 May 21.

Stevenson LW. **Heart failure with better ejection fraction**: a modern diagnosis. Circulation. 2014 Jun 10;129(23):2364-7.

Stevenson LW. **Who Would Be Branded With Failure**? Circulation. 2017 Oct 10;136(15):1359-1361.

Stevenson WG, Hernandez AF, Carson PE, et al. Indications for **cardiac resynchronization therapy** (CRT): 2011 update from the Heart Failure Society of America (**HFSA**) guideline committee. J Card Fail 2012; 18:94-106.

Stewart S, Carrington MJ, Marwick TH, et al. Impact of **Home Versus Clinic-Based** Management of Chronic Heart Failure: The WHICH? (Which Heart Failure Intervention Is Most Cost-Effective & Consumer Friendly in Reducing Hospital Care) Multicenter, Randomized Trial. J Am Coll Cardiol. 2012 Oct 2;60(14):1239-48.

Stienen S, Salah K, Moons AH, et al. Rationale and design of **PRIMA II:** a multicenter, randomized clinical trial to study the impact of **in-hospital guidance** for **acute decompensated heart** failure treatment by a predefined **NT-PRoBNP target** on the reduction of readmIssion and Mortality rAtes. Am Heart J. 2014;168:30-6.

Stienen S, Salah K, Moons AH, et al. **NT-proBNP** (N-Terminal pro-B-Type Natriuretic Peptide)-Guided Therapy in Acute Decompensated Heart Failure: **PRIMA II** Randomized Controlled Trial (**Can NT-ProBNP-Guided Therapy** During Hospital Admission for Acute Decompensated Heart Failure Reduce Mortality and Readmissions?). Circulation. 2018 Apr 17;137(16):1671-1683.

Stienen S, Salah K, Moons AH, et al. **NT-proBNP-Guided Therapy in Acute Decompensated Heart Failure: The PRIMA II** Randomized Controlled Trial. Circulation. 2017 Dec 14.

STICH Trial Investigators, Petrie MC, Jhund PS, She L, et al. Ten-Year Outcomes After **Coronary Artery Bypass Grafting** According to Age in Patients With Heart Failure and Left Ventricular Systolic Dysfunction: An Analysis of the Extended Follow-Up of the **STICH** Trial (Surgical Treatment for Ischemic Heart Failure). Circulation. 2016 Aug 29.

Stone GW, Lindenfeld J, Abraham WT, et al; **COAPT** Investigators. **Transcatheter Mitral-Valve Repair** in Patients with Heart Failure. N Engl J Med. 2018 Sep 23.

Stout KK, Broberg CS, Book WM, et al. **American Heart Association** Council on Clinical Cardiology, Council on Functional Genomics and Translational Biology, and Council on Cardiovascular Radiology and Imaging. **Chronic Heart Failure in Congenital Heart Disease**: A Scientific Statement From the American Heart Association. Circulation. 2016 Feb 23;133(8):770-801.

Streng KW, Nauta JF, Hillege HL, et al. **Non-cardiac comorbidities in heart failure with reduced, mid-range and preserved ejection fraction**. Int J Cardiol. 2018 Nov 15;271:132-139.

Sud M, Wang X, Austin PC, et al. Presentation **blood glucose and death**, hospitalization, and future diabetes risk in patients with acute heart failure syndromes. Eur Heart J. 2015 Jan 8.

Sudharshan S, Novak E, Hock K, et al. **Use of Biomarkers** to Predict Readmission for Congestive Heart Failure. The American Journal of Cardiology (2016).

Sueta CA, Rodgers JE, Chang PP, et al. **Medication Adherence Based on Part D Claims** for Patients With Heart Failure After Hospitalization (from the Atherosclerosis Risk in Communities Study). Am J Cardiol. 2015 Aug 1;116(3):413-9.

Sulo G, Igland J, Vollset SE, et al. **Heart Failure Complicating Acute Myocardial Infarction**; Burden and Timing of Occurrence: A Nation-wide Analysis Including 86 771 Patients From the Cardiovascular Disease in Norway (CVDNOR) Project. J Am Heart Assoc. 2016 Jan 7;5(1).

Sulo G, Igland J, et al. **Prognostic Impact of In-Hospital and Postdischarge Heart Failure** in Patients With Acute Myocardial Infarction: A Nationwide Analysis Using Data From the Cardiovascular Disease in Norway (CVDNOR) Project. J Am Heart Assoc. 2017 Mar 15;6(3).

Summaries for patients: management of chronic **heart failure** in adults: guidelines from the National Institute For Health and clinical excellence. Ann Intern Med. 2011 Aug 16;155(4):I-42.

Sun D, Wang T, Heianza Y, et al. A **History of Asthma** From Childhood and Left Ventricular Mass in Asymptomatic Young Adults: The Bogalusa Heart Study. JACC Heart Fail. 2017 Jul;5(7):497-504.

Sun H, Olson KC, Gao C, et al. Catabolic Defect of **Branched-Chain Amino Acids** Promotes Heart Failure. Circulation. 2016 May 24;133(21):2038-49.

Sun LY, Tu JV, Coutinho T, et al. **Sex differences in outcomes of heart failure** in an ambulatory, population-based cohort from 2009 to 2013. CMAJ. 2018 Jul 16;190(28):E848-E854.

Sundaram V, Fang JC. **Gastrointestinal and Liver Issues** in Heart Failure. Circulation. 2016 Apr 26

Sundström J, Bruze G, Ottosson J, et al. **Weight Loss** and Heart Failure: A Nationwide Study of **Gastric Bypass Surgery Versus Intensive Lifestyle** Treatment. Circulation. 2017 Mar 3.

Suzuki S, Sagara K, Otsuka T, et al. A New Scoring System for Evaluating the Risk of **Heart Failure** Events in Japanese Patients With Atrial Fibrillation (**H_2ARDD**). Am J Cardiol. 2012 May 21.

Svanström H, Pasternak B, Hviid A. Association of treatment with **losartan vs candesartan** and mortality among patients with heart failure. JAMA 2012; 307: 1506-1512.

Swedberg K, Komajda M, Böhm M, et al. **Ivabradine** and outcomes in chronic heart failure (**SHIFT**): A randomised placebo-controlled study. Lancet 2010; DOI:10.1016/S01406736(10)61198-1.

Swerdlow CD, Ellenbogen KA. **Implantable cardioverter-defibrillator leads**:design, diagnostics, and management. Circulation. 2013 Oct 29;128(18):2062-71.

Swoboda PP, Plein S. Heart failure **in Diabetic patients**. Eur Heart J. 2018 May 21;39(20):1755-1757

Tachjian A, Maria V, Jahangir A. Use of herbal products and potential interactions in patients with cardiovascular diseases. J Am Coll Cardiol. 2010 Feb 9;55(6):515-25.

Tahhan AS, Vaduganathan M, Greene SJ, et al. Enrollment of Older Patients, Women, and Racial and Ethnic Minorities in Contemporary Heart Failure Clinical Trials: A Systematic Review. JAMA Cardiol. 2018 Aug 22.

Takeda A, Taylor SJC, Taylor RS, Khan F, Krum H, Underwood M. **Clinical service organisation** for heart failure. Cochrane Database of Systematic Reviews 2012, Issue 9. Art. No.: CD002752. DOI: 10.1002/14651858.CD002752.pub3. Amongst CHF patients who have previously been admitted to hospital for this condition there is now good evidence that case management type interventions led by a heart failure specialist nurse reduces CHF related readmissions after 12 months follow up, all cause readmissions and all cause mortality.

Takeda A, Martin N, Taylor RS, et al. **Disease management interventions for heart failure**. Cochrane Database Syst Rev. 2019 Jan 8;1:CD002752. We found limited evidence for the effect of disease management programmes on mortality due to heart failure, with few studies reporting this outcome. Case management may reduce all-cause mortality, and multidisciplinary interventions probably also reduce all-cause mortality, but clinic-based interventions had little or no effect on all-cause mortality. Readmissions due to heart failure or any cause were probably reduced by case-management interventions. Clinic-based interventions probably make little or no difference to heart failure readmissions and may result in little or no difference in readmissions for any cause. Multidisciplinary interventions may reduce the risk of readmission for heart failure or for any cause. There was a lack of evidence for adverse effects, and conclusions on quality of life remain uncertain due to poor-quality data.

Tang AS, Wells GA, Talajic M, et al. **Cardiac-resynchronization therapy** for mild-to-moderate heart failure. (**Raft**) N Engl J Med 2010; 363:2385-2395.

Tang L, Wu YY, Lip GY, et al. Heart failure and **risk of venous thromboembolism**: a systematic review and meta-analysis. Lancet Haematol. 2016 Jan;3(1):e30-44.

Tang WH, Wang Z, Fan Y, et al. Prognostic value of elevated levels of intestinal **microbe-generated metabolite trimethylamine-N-oxide** in patients with heart failure: refining the gut hypothesis. J Am Coll Cardiol. 2014 Nov 4;64(18):1908-14.

Taniguchi T, Shiomi H, Morimoto T, et al. **Incidence and Prognostic Impact** of Heart Failure Hospitalization During Follow-Up **After Primary Percutaneous Coronary Intervention** in ST-Segment Elevation Myocardial Infarction. Am J Cardiol. 2017 Mar 22.

Taniguchi T, Ohtani T, Kioka H, et al. **Liver Stiffness** Reflecting Right-Sided Filling Pressure Can Predict Adverse Outcomes in Patients With Heart Failure. JACC Cardiovasc Imaging. 2018 Jan 12.

Tavazzi L, Maggioni AP, Marchioli R, et al. Effect of **n-3 polyunsaturated fatty acids** in patients with chronic heart failure (the **GISSI-HF** trial): a randomised, double-blind, placebo-controlled trial. Lancet 2008;372:1223-1230

Tavazzi L, Swedberg K, Komajda M, et al. Efficacy and safety of **ivabradine** in chronic heart failure across the age spectrum: insights from the SHIFT study. Eur J Heart Fail. 2013 Nov;15(11):1296-303.

Tayal B, Gorcsan J 3rd, Bax JJ, et al. **Cardiac Resynchronization Therapy** in Patients With Heart Failure and Narrow QRS Complexes. J Am Coll Cardiol. 2018 Mar 27;71(12):1325-1333.

Taylor CJ, Hobbs FD, Marshall T, et al. From **breathless to failure**: symptom onset and diagnostic meaning in patients with heart failure-a qualitative study. BMJ Open. 2017 Mar 10;7(3):e013648.

Taylor CJ, Ordóñez-Mena JM, Roalfe AK, et al. **Trends in survival after a diagnosis of heart failure** in the United Kingdom 2000-2017: population based cohort study. BMJ. 2019 Feb 13;364:l223.

Taylor CJ, Ryan R, Nichols L, et al. **Survival following a diagnosis** of heart failure in primary care. Fam Pract. 2017 Apr 1;34(2):161-168.

Taylor KS, Verbakel JY, Feakins BG, et al. Diagnostic accuracy of **point-of-care natriuretic peptide testing** for chronic heart failure in ambulatory care: systematic review and meta-analysis. BMJ. 2018 May 21;361:k1450.

Taylor RS, Sagar VA, Davies EJ, et al. **Exercise-based rehabilitation** for heart failure. Cochrane Database Syst Rev. 2014 Apr 27;4:CD003331. This updated Cochrane review supports the conclusions of the previous version of this review that, compared with no exercise control, exercise-based rehabilitation does not increase or decrease the risk of all-cause mortality in the short term (up to 12-months' follow-up) but reduces the risk of hospital admissions and confers important improvements in health-related quality of life.

Taylor RS, Walker S, Ciani O, et al. **Exercise-based cardiac rehabilitation** for chronic heart failure: the **EXTRAMATCH II** individual participant data meta-analysis. Health Technol Assess. 2019 May;23(25):1-98.

Teerlink JR, Cotter G, Davidson BA, et al, for the RELAXin in Acute Heart Failure (**RELAX-AHF**) Investigators. **Serelaxin**, recombinant human relaxin-2, for treatment of acute heart failure (RELAX-AHF): a randomised, placebo-controlled trial. Lancet 2012; published online Nov 7.

Teerlink JR, Felker GM, McMurray JJV, et al, for the **COSMIC-HF** Investigators. Chronic Oral Study of Myosin Activation to Increase Contractility in Heart Failure (COSMIC-HF): a phase 2, pharmacokinetic, randomised, placebo-controlled trial. Lancet 2016; online Nov 30. (**omecamtiv mecarbil**)

Teerlink JR, Qian M, Bello NA, et al. **Aspirin** Does Not Increase Heart Failure Events in Heart Failure Patients: From the **WARCEF** Trial. JACC Heart Fail. 2017 Aug;5(8):603-610.

Terkelsen CJ, Jensen LO, Tilsted HH, et al. Health Care **System Delay** and Heart Failure in Patients With ST-Segment Elevation Myocardial Infarction Treated With Primary Percutaneous Coronary Intervention: Follow-up of Population-Based Medical Registry Data. Ann Intern Med. 2011 Sep 20;155(6):361-7.

Testani JM, Brisco MA, Turner JM, et al. **Loop Diuretic Efficiency**: A Metric of Diuretic Responsiveness with Prognostic Importance in Acute Decompensated Heart Failure. Circ Heart Fail. 2013 Dec 30.

Testani JM. Renal Subanalysis of the Acute Study of Clinical Effectiveness of **Nesiritide** in Decompensated Heart Failure (**ASCEND-HF**): The End of Nesiritide as a Cardiorenal Therapeutic? Circulation. 2014 Sep 16;130(12):936-8.

Teun van der Bom MD, Winter MM, Bouma BJ, et al. Effect of **valsartan on systemic right ventricular function**: a double-blind, randomized, placebo-controlled pilot trial. Circulation. 2013;127:322–330.

Thanassoulis George; Brophy James M.; Richard Hugues; et al. Gout, **Allopurinol** Use, and Heart Failure Outcomes. Arch Intern Med. 2010;170(15):1358-1364.

Thibault B, Ducharme A, Harel F, et al. **Left ventricular versus simultaneous biventricular pacing** in patients with heart failure and a QRS complex ≥ 120 milliseconds. (Greater-Earth) Circulation. 2011;124:2874 –2881.

Thibault B, Harel F, Ducharme A, et al; LESSER-EARTH Investigators. Cardiac Resynchronization Therapy in Patients With Heart Failure and a **QRS Complex <120** Milliseconds: The Evaluation of Resynchronization Therapy for Heart Failure (LESSER-EARTH) Trial. Circulation. 2013 Feb 26;127(8):873-81. (Potential harm seen)

Thibodeau JT, Turer AT, Gualano SK, et al. Characterization of a novel symptom of advanced heart failure: **Bendopnea**. *JACC Heart Fail* 2014; 2:24–31.

Thibodeau JT, Jenny BE, Maduka JO, et al. **Bendopnea** and risk of adverse clinical outcomes in ambulatory patients with systolic heart failure. Am Heart J. 2017 Jan;183:102-107.

Thomas GR, McDonald MA, Day J, et al. A Matched Cohort Study of Patients With End-Stage Heart Failure from **Anthracycline-Induced Cardiomyopathy** Requiring Advanced Cardiac Support. Am J Cardiol. 2016 Nov 15;118(10):1539-1544.

Thompson MP, Pagani FD, Liang Q, et al; Michigan Congestive Heart Failure Investigators. Center variation in Medicare spending for **durable left ventricular assist device implant hospitalizations** [online Jan 30, 2019]. JAMA Cardiol.

Thomson MR, Nappi JM, Dunn SP, et al. **Continuous versus intermittent** infusion of **furosemide** in acute decompensated heart failure. J Card Fail. 2010 Mar;16(3):188-93.

Tiburcy M, Hudson JE, Balfanz P, et al. Directed **engineered human myocardium** with advanced maturation for applications in heart failure modeling and repair. Circulation. 2017;135:1832–1847.

Toma A, Stahli BE, Gick M, et al. Comparison of Benefit of Successful **Percutaneous Coronary Intervention** for Chronic Total Occlusion in Patients with Versus Without Reduced (<40%) Left Ventricular Ejection Fraction. Am J Cardio. 2017

Toma M, McAlister FA, Coglianese EE, et al. **Testosterone Supplementation** in Heart Failure: A Meta-Analysis. Circ Heart Fail. 2012 Apr 17.

Tomdio A, Ritchie M, Miller AC. **Omega-3 Fatty Acids** and Cardiovascular Disease Prevention. Am Fam Physician. 2019 Aug 15;100(4):209-210.

Tomova GS, Nimbal V, Horwich TB. Relation between **hemoglobin A1c and outcomes in heart failure** patients with and without diabetes mellitus. Am J Cardiol 2012.

Torpy JM, Lynm C, Golub RM. JAMA **patient page**. **Heart failure**. JAMA. 2011 Nov 16;306(19):2175.

Tracy CM, Epstein AE, Darbar D, et al. **2012 ACCF/AHA/HRS** Focused Update of the 2008 guidelines for **device-based therapy of cardiac rhythm abnormalities**. A report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. Developed in collaboration with the American Association for Thoracic Surgery, Heart Failure Society of America, and Society of Thoracic Surgeons. J Am Coll Cardiol 2012.

Triposkiadis F, Butler J, Abboud FM, et al. The **continuous heart failure spectrum**: moving beyond an ejection fraction classification. Eur Heart J. 2019 Apr 8.

Tromp J,Maaten JT, Damman K, et al. Serum **Potassium Levels** and Outcome in Acute Heart Failure. (Data from the **PROTECT** and **COACH** trials). The American Journal of Cardiology (2016).

Tromp J, MacDonald MR, Tay WT, et al. **Heart Failure With Preserved Ejection Fraction** in the Young. Circulation. 2018 Dec 11;138(24):2763-2773.

Troughton RW, Frampton CM, Yandle TG, et al. Treatment of heart failure guided by plasma aminoterminal brain natriuretic peptide (**N-BNP**) concentrations. Lancet. 2000;355(9210):1126-1130.

Troughton RW, Frampton CM, Brunner-La Rocca HP, et al. Effect of **B-type natriuretic peptide-guided treatment** of chronic heart failure on total mortality and hospitalization: an individual patient meta-analysis. Eur Heart J. 2014 Mar 6.

Tsimploulis A, Lam PH, Arundel C, et al. **Systolic Blood Pressure** and Outcomes in Patients With **Heart Failure With Preserved Ejection Fraction**. JAMA Cardiol. 2018 Feb 14.

Tsujimoto T, Kajio H. **Abdominal Obesity** Is Associated With an Increased Risk of All-Cause Mortality in Patients With **HFpEF**. J Am Coll Cardiol. 2017 Dec 5;70(22):2739-2749.

Turagam MK, Garg J, Whang W, et al. **Catheter Ablation of Atrial Fibrillation** in Patients With Heart Failure: A Meta-analysis of Randomized Controlled Trials. Ann Intern Med. 2018 Dec 25.

Turakhia MP, Santangeli P, Winkelmayer WC, et al. Increased mortality associated with **digoxin** in contemporary patients with atrial fibrillation: findings from the **TREAT-AF** study. *J Am Coll Cardiol* 2014; 64:660–668.

Turakhia MP, et al. Healthcare Utilization and Expenditures Associated With **Appropriate and Inappropriate Implantable Defibrillator Shocks**. Circ Cardiovasc Qual Outcomes. 2017 Feb;10(2).

Tymińska A, Kapłon-Cieślicka A, Ozierański K, et al. **Anemia** at Hospital Admission and Its Relation to Outcomes in Patients With Heart Failure (from the Polish Cohort of 2 European Society of Cardiology Heart Failure Registries). Am J Cardiol. 2017 Jun 15;119(12):2021-2029.

Unroe KT, Greiner MA, Hernandez AF, et al. Resource use in the **last 6 months of life among Medicare** beneficiaries with heart failure, 2000-2007. Arch Intern Med 2010.

Udelson JE. Heart failure with **preserved ejection fraction**. Circulation. 2011 Nov 22;124(21):e540-3.

Udelson JE, Stevenson LW. The **Future of Heart Failure Diagnosis, Therapy, and Management**. Circulation. 2016 Jun 21;133(25):2671-86.
Unitt C, Montazeri K, Tolaney S, et al. **Breast cancer chemotherapy and your heart**. Circulation. 2014 Jun 24;129(25):e680-2.
Uriel N, Colombo PC, Cleveland JC, et al. Hemocompatibility-Related Outcomes in the **MOMENTUM 3** Trial at 6 Months: A Randomized Controlled Study of a **Fully Magnetically Levitated Pump** in Advanced Heart Failure. Circulation. 2017 May 23;135(21):2003-2012.
Vaduganathan M, Dei Cas A, Mentz RJ, et al; EVEREST Trial Investigators. **Mineralocorticoid Receptor Antagonist** Use in Hospitalized Patients With Heart Failure, Reduced Ejection Fraction, and Diabetes Mellitus (from the **EVEREST** Trial). Am J Cardiol. 2014 Jun 24.
Vaduganathan M, Greene SJ, Ambrosy AP, et al; **EVEREST** trial investigators. Relation of **Serum Uric Acid** Levels and Outcomes Among Patients Hospitalized for Worsening Heart Failure With Reduced Ejection Fraction (from the Efficacy of Vasopressin Antagonism in Heart Failure Outcome Study With Tolvaptan Trial). Am J Cardiol. 2014 Sep 16.
Vaduganathan M, Patel RB, Michel A, et al. **Mode of Death in Heart Failure** With Preserved Ejection Fraction. J Am Coll Cardiol. 2017 Feb 7;69(5):556-569.
Vaduganathan M, DeFilippis EM, Fonarow GC, et al. **Postmarketing Adverse Events** Related to the **CardioMEMS HF System**. JAMA Cardiol. 2017 Sep 18.
Vaduganathan M, Patel RB, Mentz RJ, et al. Sudden Death After Hospitalization for Heart Failure With Reduced Ejection Fraction (from the **EVEREST Trial**). Am J Cardiol. 2018 Apr 11.
Vaes B, et al. Value of Adding **Natriuretic Peptides** and Electrocardiographic Findings to Assess the Presence of Cardiac Dysfunction in Patients ≥ 80 Years of Age. Am J Cardiol. 2013 Jan 31.
Vamos M, Erath JW, Hohnloser SH. **Digoxin-associated mortality**: a systematic review and meta-analysis of the literature. Eur Heart J. 2015 May 4.
van Deursen VM, Hernandez AF, Stebbins A, et al. **Nesiritide**, Renal Function, and Associated Outcomes During Hospitalization for Acute Decompensated Heart Failure: Results From the Acute Study of Clinical Effectiveness of Nesiritide and Decompensated Heart Failure (**ASCEND-HF**). Circulation. 2014 Sep 16;130(12):958-65.
van Diepen S, Bakal JA, McAlister FA, Ezekowitz JA. Mortality and readmission of patients with heart failure, atrial fibrillation, or coronary artery disease **undergoing noncardiac surgery**: an analysis of 38 047 patients. Circulation. 2011 Jul 19;124(3):289-96.
van Doorn S, et al. Opportunistic **screening for heart failure with natriuretic peptides** in patients with atrial fibrillation: meta-analysis of individual participant data of four screening studies. Heart. 2018 Mar 16.
Van Spall HGC, Lee SF, Xie F, et al. Effect of **Patient-Centered Transitional Care Services on Clinical Outcomes** in Patients Hospitalized for Heart Failure: The PACT-HF Randomized Clinical Trial. JAMA. 2019 Feb 26;321(8):753-761.
van Veldhuisen DJ, Cohen-Solal A, et al.; **SENIORS** Investigators. Beta-blockade with nebivolol in elderly heart failure patients with impaired and preserved left ventricular ejection fraction: Data From SENIORS (Study of Effects of Nebivolol Intervention on Outcomes and Rehospitalization in Seniors With Heart Failure). J Am Coll Cardiol. 2009 Jun 9;53(23):2150-8. The effect of beta-blockade with nebivolol in elderly patients with HF in this study was similar in those with preserved and impaired EF.
van Veldhuisen DJ, Ponikowski P, van der Meer P, et al. Effect of **ferric carboxymaltose** on exercise capacity in patients with chronic heart failure and iron deficiency. Circulation. 2017;136:1374–1383.
Vanderpool RR, et al. Association between hemodynamic markers of **pulmonary hypertension and outcomes in heart failure with preserved ejection fraction** [online Mar 14, 2018]. JAMA Cardiol. doi:10.1001/jamacardio.2018.0128
Vassallo P, Trohman RG. Prescribing **amiodarone**: an evidence-based review of clinical indications. JAMA. 2007 Sep 19;298(11):1312-22
Vazir A, et al. Prognostic Importance of Temporal Changes in Resting **Heart Rate** in Heart Failure and **Preserved Ejection Fraction** From the **TOPCAT** Study-J Am Coll Cardiol HF. 2017;5:782-91
Vazir A, , et al. Association of **Resting Heart Rate and Temporal Changes in Heart Rate** With Outcomes in Participants of the Atherosclerosis Risk in Communities Study. JAMA Cardiol. 2018 Jan 24.
Vedel I, Khanassov V. **Transitional Care** for Patients With Congestive Heart Failure: A Systematic Review and Meta-Analysis. Ann Fam Med. 2015 Nov;13(6):562-71.
Velagaleti RS, Pencina MJ, Murabito JM, et al. Long-term trends in the incidence of heart failure after myocardial infarction. Circulation 2008; DOI: 10.1161/CIRCULATIONAHA.108.784215.
Velazquez EJ, Lee KL, Deja MA, et al. **Coronary-artery bypass surgery** (CABG) in patients with left ventricular dysfunction (**STITCH**). N Engl J Med 2011. DOI: 10.1056/NEJMoa1100356.
Velazquez EJ, Lee KL, Jones RH, et al. **Coronary-artery bypass surgery** in patients **with ischemic cardiomyopathy**. (**Stitches**) N Engl J Med. DOI: 10.1056/NEJMoa1602001.
Velazquez EJ, Morrow DA, DeVore AD, et al; PIONEER-HF Investigators. **Angiotensin-Neprilysin Inhibition in Acute Decompensated Heart Failure**. N Engl J Med. 2018 Nov 11.
Verbrugge FH, Duchenne J, Bertrand PB, et al. **Uptitration of Renin-Angiotensin system blocker and Beta-blocker therapy** in patients hospitalized for heart failure with reduced versus preserved left ventricular ejection fractions. Am J Cardiol. 2013 Dec 15;112(12):1913-20.
Verma A, Kalman JM, Callans DJ. Treatment of Patients With **Atrial Fibrillation and Heart Failure With Reduced Ejection Fraction**. Circulation. 2017 Apr 18;135(16):1547-1563.
Versteeg H, van den Broek KC, Theuns DA, et al. Effect of **cardiac resynchronization therapy**-defibrillator implantation on health status in patients with mild versus moderate symptoms of heart failure. Am J Cardiol. 2011 Oct 15;108(8):1155-9.
Vest AR, Wu Y, Hachamovitch R, et al. The **Heart Failure Overweight/Obesity Survival Paradox**: The Missing Sex Link. JACC Heart Fail. 2015 Sep 30.
Vieira J, Guimaraes G, de Andre P, et al. **Respiratory filter** reduces the cardiovascular effects associated with **diesel exhaust exposure**. *JACC Heart Fail* 2016; 4:55-64.
Vijayakumar S, et al. **Glucose-Lowering Therapies and Heart Failure** in Type 2 Diabetes Mellitus: Mechanistic Links, Clinical Data, and Future Directions. Circulation. 2018 Mar 6;137(10):1060-1073.
Vodovar N, Paquet C, Mebazaa A, et al. **Neprilysin, cardiovascular, and Alzheimer's diseases**: the therapeutic split? Eur Heart J. 2015 Jan 29.
von Lueder TG, Wang BH, Kompa AR, et al. **Angiotensin Receptor Neprilysin Inhibitor LCZ696** Attenuates Cardiac Remodeling and Dysfunction After Myocardial Infarction by Reducing Cardiac Fibrosis and Hypertrophy. Circ Heart Fail. 2015 Jan;8(1):71-8.
Wäßnig N, Günther M, Quick S, et al. Experience with the **Wearable Cardioverter-Defibrillator** in Patients at High Risk for Sudden Cardiac Death. Circulation. 2016 Jul 25
Wadhera RK, Joynt Maddox KE, Wasfy JH, et al. **Association of the Hospital Readmissions Reduction Program with mortality** among Medicare beneficiaries hospitalized for heart failure, acute myocardial infarction, and pneumonia [Dec 25, 2018]. JAMA
Waller DG, Waller JR. **{beta} blockers** for heart failure with reduced ejection fraction. BMJ. 2011 Sep 26;343:d5603. doi: 10.1136/bmj.d5603.
Wang AYM, Sanderson JE. Current perspectives on diagnosis of heart failure in long-term **dialysis patients**. Am J Kidney Dis. 2011;57:308–19.
Wang F, Harel-Sterling L, Cohen S, et al. Heart failure **risk predictions in adult patients** with congenital heart disease: a systematic review. Heart. 2019 Jul 26.
Wang L, Porter B, Maynard C, et al. **Predicting Risk of Hospitalization or Death** Among Patients With Heart Failure in the Veterans Health Administration. Am J Cardiol. 2012 Jul 21.
Wang L, Tan TC, et al. Major Cardiac Events and the Value of **Echocardiographic Evaluation** in Patients Receiving Anthracycline-Based Chemotherapy. Am J Cardiol. 2015 Aug 1;116(3):442-6.
Waqar S, Sarkar PK. **Exacerbation of psoriasis** with beta-blocker therapy. CMAJ. 2009 Jul 7;181(1-2):60.
Weeda ER, Nguyen E, White CM. The Role of **Ivabradine** in the Treatment of Patients With Cardiovascular Disease. Ann Pharmacother. 2016 Feb 25.
Weeks SG, Glantz SA, De Marco T, Rosen AB, Fleischmann KE. **Secondhand smoke** exposure and quality of life in patients with heart failure. Arch Intern Med. 2011;171(21):1887-1893.
Wei Li, Struthers Allan D, Fahey Tom et al. **Spironolactone** use and renal toxicity: population based longitudinal analysis. BMJ 2010;340:c1768
Weintraub Neal L., Collins Sean P., Pang Peter S., et al., and on behalf of the American Heart Association Council on Clinical Cardiology and Council on Cardiopulmonary, Critical Care, Perioperative and Resuscitation. **Acute Heart Failure Syndromes**: Emergency Department Presentation, Treatment, and Disposition: Current Approaches and Future Aims: A Scientific Statement From the American Heart Association (**AHA**). Circulation 122: 1975-1996; online before print as doi:10.1161/CIR.0b013e3181f9a223 http://circ.ahajournals.org/cgi/reprint/122/19/1975
Weintraub RG, Semsarian C, Macdonald P. **Dilated cardiomyopathy**. Lancet. 2017 Feb 9.
Wells, George, Parkash, Ratika, Healey, Jeffrey S., et al. **Cardiac resynchronization therapy** (**CRT**): a meta-analysis of randomized controlled trials. CMAJ 2011 0: cmaj.101685.
Whayne TF Jr. **Clinical Use of Digitalis**: A State of the Art Review. Am J Cardiovasc Drugs. 2018 Dec;18(6):427-440.
Whitbeck MG, Charnigo RJ, Khairy P, et al. **Increased mortality among patients taking digoxin**—analysis from the **AFFIRM** study. Eur Heart J 2012:
White MF, Kirschner J, Hamilton MA. **Self-care guide** for the heart failure patient. Circulation. 2014 Jan 21;129(3):e293-4
Whitley H, Lindsey W. **Sex-based** differences in drug activity. Am Fam Physician. 2009 Dec 1;80(11):1254-8.
Wienbergen H, Pfister O, Hochadel M, et al.Usefulness of **Iron Deficiency** Correction in Management of Patients With Heart Failure [from the Registry Analysis of Iron Deficiency-Heart Failure (**RAID-HF**) Registry]. Am J Cardiol. 2016 Dec 15;118(12):1875-1880.
Williams RP, Oakeshott P. **Diagnosis and management** of chronic heart failure. BMJ. 2014 Feb 12;348:g1429.
Wilson JR. **Rhetorical techniques** used in the reporting of **cardiac resynchronization trials** [published online June 13, 2011].Arch Intern Med. 2011;171(16): 1500-1502.
Wilson SS, Kwiatkowski GM, et al. Use of **nitroglycerin** by bolus prevents intensive care unit admission in patients with acute hypertensive heart failure. Am J Emerg Med. 2017 Jan;35(1):126-131.
Witte KK, Byrom R, Gierula J, et al. Effects of **vitamin D** on cardiac function in patients with chronic HF: The **VINDICATE** Study.*J Am Coll Cardiol* 2016.
Witteles RM, Bosch X. Myocardial Protection During **Cardiotoxic Chemotherapy**. Circulation. 2015 Nov 10;132(19):1835-45.
Wong FK, Ng AY, Lee PH, et al. Effects of a transitional **palliative care** model on patients with end-stage heart failure: a randomised controlled trial. Heart. 2016 Mar 11.
Wong FL, Bhatia S, Landier W, Francisco L, Leisenring W, Hudson MM, et al. Cost-effectiveness of the Children's Oncology Group long-term follow-up screening guidelines for **childhood cancer survivors** at risk for treatment-related heart failure. Ann Intern Med. 2014;160:672-83.
Woo CY, Strandberg EJ, Schmiegelow MD, et al. **Cost-Effectiveness** of Adding **Cardiac Resynchronization Therapy** to an **Implantable Cardioverter-Defibrillator** Among Patients With Mild Heart Failure. Ann Intern Med. 2015 Aug 25.
Woodruff AE, Kelley AM, Hempel CA, et al. **Discharge Diuretic Dose** and 30-Day Readmission Rate in Acute Decompensated Heart Failure. Ann Pharmacother. 2016 Mar 8.
Woods B, Hawkins N, Mealing S, et al. Individual patient data network meta-analysis of **mortality effects of implantable cardiac devices**. Heart. 2015 Aug 12.
Wu A. In the Clinic: **Heart Failure**. Ann Intern Med. 2018 Jun 5;168(11):ITC81-ITC96.
Wu AH, Levy WC, Welch KB, et al. Association Between **Bilirubin** and Mode of Death in Severe Systolic Heart Failure. Am J Cardiol. 2013 Jan 23.
Xin W, Wei W, Li X. Effects of **fish oil supplementation** on cardiac function in chronic heart failure: a meta-analysis of randomised controlled trials. Heart. 2012 Jul 3.
Yaku H, Kato T, Morimoto T, et al. Association of **Mineralocorticoid Receptor Antagonist Use With All-Cause Mortality** and Hospital Readmission in Older Adults With Acute Decompensated Heart Failure. JAMA Netw Open. 2019 Jun 5;2(6):e195892.

Yamauchi H, Yoshihisa A, Iwaya S, et al. Clinical Features of Patients With Decompensated Heart Failure After the Great East Japan **Earthquake**. Am J Cardiol. 2013 Apr 2.
Yamaguchi T, Kitai T, Miyamoto T, et al. Effect of **Optimizing Guideline-Directed Medical Therapy Before Discharge** on Mortality and Heart Failure Readmission in Patients Hospitalized With Heart Failure With Reduced Ejection Fraction. Am J Cardiol. 2018 Apr 15;121(8):969-974.
Yancy CW, Jessup M, Bozkurt B, et al. 2016 **ACC/AHA/HFSA focused update on new pharmacological therapy for heart failure: an update of the 2013 ACCF/AHA guideline** for the management of heart failure: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Clinical Practice Guidelines and the Heart Failure Society of America. Circulation. 2016.
Yancy CW, Jessup M, Bozkurt B, et al. **2017 ACC/AHA/HFSA Focused Update** of the 2013 ACCF/AHA Guideline for the **Management of Heart Failure**: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines and the Heart Failure Society of America. Circulation. 2017 Apr 28.
Yang JH, et al. **Angiotensin receptor blocker** in patients with ST segment elevation myocardial infarction with **preserved left ventricular** systolic function: prospective cohort study. BMJ. 2014 Nov 14.
Ye S, Cheng B, Lip GY, et al; **WARCEF** Investigators. **Bleeding Risk and Antithrombotic Strategy** in Patients With Sinus Rhythm and Heart Failure With Reduced Ejection Fraction Treated With Warfarin or Aspirin. Am J Cardiol. 2015 Jun 24.
Yeh ET, Chang HM. **Oncocardiology**-Past, Present, and Future: A Review. JAMA Cardiol. 2016 Aug 17.
Yeh Gloria Y.; McCarthy Ellen P.; Wayne Peter M.; et al. **Tai Chi Exercise** in Patients With Chronic Heart Failure: A Randomized Clinical Trial. Arch Intern Med. 2011;171(8):750-757.
Yeh JM, Nohria A, Diller L. Routine echocardiography screening for asymptomatic left ventricular dysfunction in **childhood cancer survivors**: a model-based estimation of the clinical and economic effects. Ann Intern Med. 2014;160: 661-71.
Yeung DF, Boom NK, Guo H, et al. Trends in the **incidence and outcomes** of heart failure in Ontario, Canada: 1997 to 2007. CMAJ. 2012 Aug 20.
Yeung DF, Van Dyke NK, et al. A comparison of **Chinese and non-Chinese Canadian patients hospitalized** with heart failure. BMC Cardiovasc Disord. 2013 Dec 10;13:114.
Yip GW, Wang M, Wang T et al. The Hong Kong diastolic heart failure study: a randomized controlled trial of **diuretics**, irbesartan and ramipril on quality of life, exercise capacity, left ventricular global and regional function in heart failure with a **normal ejection fraction**. Heart. 2008 94:573-580.
Ylänen K, Eerola A, Vettenranta K, et al. Three-dimensional echocardiography and cardiac magnetic resonance imaging in the **screening of long-term survivors of childhood cancer** after cardiotoxic therapy. Am J Cardiol. 2014 Jun 1;113(11):1886-92.
Yogasundaram H, Chappell MC, Braam B, Oudit GY. **Cardiorenal Syndrome and Heart Failure-Challenges** and Opportunities. Can J Cardiol. 2019 Apr 12.
York MK, Gupta DK, Reynolds CF, et al. **B-type natriutretic peptide** levels and mortality in patients with and without heart failure. J Am Coll Cardiol 2018;71:2079–88.
Young DR, Reynolds K, Sidell M, et al. Effects of **physical activity and sedentary time** on the risk of heart failure. Circ Heart Fail. 2014 Jan 1;7(1):21-7
Young LH, Viscoli CM, Schwartz GG, et al. **Heart Failure After Ischemic Stroke or TIA** in Insulin-Resistant Patients Without Diabetes Treated with **Pioglitazone**. (IRIS) Circulation. 2018 Jun 22.
Yousaf F, Collerton J, Kingston A, et al. Prevalence of **left ventricular dysfunction** in a UK community sample of **very old people**: The Newcastle 85+ Study. Heart 2012.
Yousaf F, Collerton J, Kingston A, et al. Prevalence of **left ventricular dysfunction** in a UK community sample of **very old people**: the Newcastle 85+ study. Heart. 2012 Aug 2.
Yu, Cheuk-Man, Chan, Joseph Yat-Sun, Zhang, Qing, et al. **Biventricular Pacing** in Patients with Bradycardia and Normal Ejection Fraction. N Engl J Med 2009 0: NEJMoa0907555.
Yu OH, Filion KB, Azoulay L, et al. **Incretin-Based Drugs and the Risk of Congestive Heart Failure.** Diabetes Care. 2014 Sep 9.
Yung D, Birnie D, Dorian P, et al. Survival after **implantable cardioverter-defibrillator implantation** in the elderly. Circulation 2013; 127:2383-2392.
Yuyun MF, Narayan HK, Ng LL. Prognostic Significance of **Adrenomedullin** in Patients With Heart Failure and With Myocardial Infarction. Am J Cardiol. 2015 Apr 1;115(7):986-991.
Zafrir B, Salman N, Amir O. Joint Impact of **Body Mass Index and Physical Capacity** on Mortality in Patients With Systolic Heart Failure. Am J Cardiol. 2014 Jan 15.
Zafrir B, Lund LH, Laroche C, et al; **ESC-HFA HF Long-Term Registry** Investigators. **Prognostic implications of atrial fibrillation in heart failure** with reduced, mid-range, and preserved ejection fraction: a report from 14 964 patients in the European Society of Cardiology Heart Failure Long-Term Registry. Eur Heart J. 2018 Oct 15.
Zamorano JL, Lancellotti P, Rodriguez Muñoz D, et al. **2016 ESC** position paper on cancer treatments and cardiovascular toxicity developed under the auspices of the ESC Committee for Practice Guidelines: The Task Force for **cancer treatments and cardiovascular toxicity** of the European Society of Cardiology (ESC). Eur Heart J. 2016 Aug 26. [Epub ahead of print]
Zannad F, McMurray JJV, Krum H, et al. **Eplerenone** in patients with systolic heart failure and mild symptoms. (**Emphasis-HF**) N Engl J Med 2011; 364:11-21.
Zannad F, Cannon CP, Cushman WC, et al; EXAMINE Investigators. Heart failure and mortality outcomes in patients with type 2 diabetes taking **alogliptin** versus placebo in **EXAMINE**: a multicentre, randomised, double-blind trial. Lancet. 2015 Mar 9.
Zannad F, Anker SD, Byra WM, et al. **Rivaroxaban in Patients with Heart Failure, Sinus Rhythm, and Coronary Disease**. (Commander HF) N Engl J Med. 2018 Aug 27.
Zannad F, Anker SD, Byra WM, et al; COMMANDER HF. **Rivaroxaban in Patients with Heart Failure, Sinus Rhythm, and Coronary Disease**. N Engl J Med. 2018 Aug 27.
Zhang Y, Fonarow GC, Sanders PW, et al. A Propensity-Matched Study of the Comparative Effectiveness of **Angiotensin Receptor Blockers Versus Angiotensin-Converting Enzyme Inhibitors** in Heart Failure Patients Age ≥65 Years. Am J Cardiol. 2011 Sep 3.
Zhang L, Lu Y, Jiang H, et al. Additional use of **trimetazidine** in patients with chronic heart failure: a meta-analysis. J Am Coll Cardiol. 2012 Mar 6;59(10):913-22.
Zhang Y, Guallar E, Blasco-Colmenares E, et al. Changes in Follow-Up Left Ventricular Ejection Fraction Associated With Outcomes in **Primary Prevention Implantable Cardioverter-Defibrillator and Cardiac Resynchronization Therapy Device Recipients.** J Am Coll Cardiol. 2015 Aug 4;66(5):524-31.
Zhao SX, et al. Clinical Characteristics and Outcome of **Methamphetamine-Associated Pulmonary Arterial Hypertension and Dilated Cardiomyopathy**. JACC Heart Fail. 2018 Mar;6(3):209-218.
Zhao W, Katzmarzyk PT, Horswell R, et al. **HbA1c and Heart Failure Risk** among Diabetic Patients. J Clin Endocrinol Metab. 2013 Dec 2.
Zheng SL;Chan FT;Nabeebaccus AA;Shah AM; eta l. Drug treatment effects on outcomes in heart failure with preserved ejection fraction: a systematic review and meta-analysis. Heart. 2017 Aug 5.
Zhou X, Xu W, Xu Y, et al**. Iron Supplementation Improves Cardiovascular Outcomes in Patients with Heart Failure**. Am J Med. 2019 Mar 7.
Ziaeian B, Kominski GF, Ong MK, et al. **National Differences in Trends for Heart Failure Hospitalizations by Sex and Race/Ethnicity**. Circ Cardiovasc Qual Outcomes. 2017 Jul;10(7).
Ziff OJ, Lane DA, Samra M, et al. **Safety and efficacy of digoxin**: systematic review and meta-analysis of observational and controlled trial data. BMJ. 2015 Aug 30;351:h4451.
Zile MR et al. for the **I-PRESERVE**. Prevalence and Significance of Alterations in **Cardiac Structure** and Function in Patients With Heart Failure and a Preserved Ejection Fraction. Circulation. 2011 Dec 6;124(23):2491-2501.
Zuchinali P, et al. Short-term effects of **high-dose caffeine** on cardiac arrhythmias in heart failure: a randomized clinical trial [online Oct 17, 16].JAMA Intern Med. doi:10.1001 /jamainternmed.2016.6374
Zusterzeel R, Selzman KA, Sanders WE, et al. **Cardiac Resynchronization Therapy in Women**: US Food and Drug Administration Meta-analysis of Patient-Level Data. JAMA Intern Med. 2014 Aug 1;174(8):1340-8
Zwi-Dantsis L, Huber I, Habib M, et al. Derivation and cardiomyocyte differentiation of induced pluripotent **stem cells** from heart failure patients. Eur Heart J. 2012 May 22.
Zwisler AD, Norton RJ, Dean SG, et al. **Home-based cardiac rehabilitation** for people with heart failure: A systematic review and meta-analysis. Int J Cardiol. 2016 Oct 15;221:963-9.

References: Major Lipid Trials

[1] Scandinavian Simvastatin Survival Study Group. Randomized trial of cholesterol lowering in 4444 patients with coronary heart disease: the Scandinavian Simvastatin Survival Study (**4S**). Lancet 1994;344:1383-9.

[2] Strandberg TE, Pyorala K, Cook TJ, et al; **4S** Group. Mortality and incidence of cancer during **10-year** follow-up of the Scandinavian Simvastatin Survival Study (4S). Lancet. 2004 Aug 28;364(9436):771-7. (Chonchol M, Cook T, Kjekshus J, Pedersen TR, Lindenfeld J. Simvastatin for secondary prevention of all-cause mortality and major coronary events in patients with mild chronic renal insufficiency. Am J Kidney Dis. 2007 Mar;49(3):373-82.)

[3] Long-Term Intervention with Pravastatin in Ischeamic Heart Disease (**LIPID**) Study Group. Prevention of cardiovascular events and death with pravastatin in patients with coronary heart disease and a broad range of initial cholesterol levels. N Engl J Med 1998; 339:1349-1357.

4 **LIPID** Study Group (Long-term Intervention with Pravastatin in Ischaemic Disease). Long-term effectiveness and safety of pravastatin in 9014 patients with coronary heart disease and average cholesterol concentrations: the LIPID trial follow-up. Lancet. 2002 Apr 20;359(9315):1379-87.

Hague WE, Simes J, Kirby A, et al; LIPID investigators. Long-Term Effectiveness and Safety of Pravastatin in Patients With Coronary Heart Disease: **16 Years of Follow-Up** of the **LIPID** Study. Circulation. 2016 Mar 25.

Simes J, Robledo KP, White HD, et al . **D-dimer** Predicts Long-Term Cause-Specific Mortality, Cardiovascular Events and Cancer in Stable Coronary Heart Disease Patients: The **LIPID** Study. Circulation. 2018 Jan 24.

[5]Sacks FM, Pfeffer MA, Moye LA, et al. The effect of pravastatin on coronary events after myocardial infarction in patients with average cholesterol levels (**CARE**). N Engl J Med 1996;335:1001-9. Tonelli M, et al. Proteinuria, impaired kidney function, and adverse outcomes in people with coronary disease: analysis of a previously conducted randomised trial (**CARE**). BMJ. 2006 May 19; [Epub ahead of print] The presence or absence of proteinuria on dipstick urinalysis may be used to refine estimates of risk based on kidney function alone.

[6] Heart Protection Study (**HPS**)- Preliminary data from: www.hpsinfo.org

[7] MRC/BHF Heart Protection Study Collaborative Group. MRC/BHF Heart Protection Study of cholesterol-lowering therapy and of antioxidant vitamin supplementation in a wide range of patients at increased risk of coronary heart disease death: early safety and efficacy experience (**HPS**). Eur Heart J 1999;20:725-41.

[8] Heart Protection Study Group.MRC/BHF **HPS** study of cholesterol lowering with simvastatin in 20,536 high-risk individuals: a randomised placebo-controlled trial. Lancet 2002 Jul 6;360(9326):7-22. (**11,609** of 32,145 pts in 4-6 wk run in treatment with simvastatin 40mg/d **were excluded**)

[9] Heart Protection Study Group.MRC/BHF **HPS** study of cholesterol lowering with simvastatin in 5,963 people with diabetes: a randomised placebo-controlled trial. Lancet 2003 Jun 14;361(9374):2005-16..

[10] Heart Protection Study Collaborative Group. Effects of cholesterol-lowering with simvastatin on stroke and other major vascular events in 20 536 people with cerebrovascular disease or other high-risk conditions. Lancet 2004 Mar 6;363(9411): 757-67.

(Heart Protection Study Group. **Lifetime cost effectiveness** of simvastatin in a range of risk groups and age groups derived from a randomised trial of 20 536 people. (**HPS**) BMJ. 2006 Nov 10; [Epub ahead of print])

Heart Protection Study (HPS) Collaborative Group. **C-reactive protein** concentration and the vascular benefits of statin therapy: an analysis of 20 536 patients in the Heart Protection Study. *Lancet* 2011; DOI:10.1016/S0140-6736(10)62174-5.

Hopewell JC, Parish S, Clarke R, et al. No impact of KIF6 genotype on vascular risk and statin response among 18 348 randomized patients in the Heart Protection Study. J Am Coll Cardiol 2011; DOI:10.1016/j.jacc.2011.02.015.

Heart Protection Study Collaborative Group. Effects on **11-year mortality and morbidity** of lowering LDL cholesterol with simvastatin for about 5 years in 20 536 high-risk individuals: a randomised controlled trial. Lancet 2011; online Nov 23.

[11]Cannon CP, Braunwald E, McCabe CH, et al. Pravastatin or Atorvastatin Evaluation and Infection Therapy-Thrombolysis in Myocardial Infarction 22 Investigators. Intensive versus moderate lipid lowering with statins after acute coronary syndromes. N Engl J Med. 2004 Apr 8;350(15):1495-504. Epub 2004 Mar 8. Erratum in: N Engl J Med. 2006 Feb 16;354(7):778. (Ahmed S, Cannon CP, Murphy SA, et al.Acute coronary syndromes and **diabetes**: Is intensive lipid lowering beneficial? Results of the **PROVE IT-TIMI 22** trial. Eur Heart J. 2006 Oct;27(19):2323-9. Epub 2006 Sep 5.)

Murphy SA, Cannon CP, Wiviott SD, McCabe CH, Braunwald E. Reduction in recurrent cardiovascular events with intensive lipid-lowering statin therapy compared with moderate lipid-lowering statin therapy after acute Coronary syndromes from the PROVE IT-TIMI 22 (Pravastatin or Atorvastatin Evaluation and Infection Therapy-Thrombolysis In Myocardial Infarction 22) trial. J Am Coll Cardiol. 2009 Dec 15;54(25):2358-62.

RxFiles PROVE IT Trial Summary: http://www.rxfiles.ca/rxfiles/uploads/documents/Lipid-QandA-Prove-It.pdf

[12] LaRosa JC. et al. Intensive Lipid Lowering with Atorvastatin in Patients with Stable Coronary Disease (**TNT**) . N Engl J Med. 2005 Mar 8;352 online. (InfoPOEMs: The benefit of intensive lipid therapy in patients with known heart disease is very modest: a number needed to treat (NNT) of 45 for 5 years to prevent any cardiovascular outcome. There was no difference in all-cause mortality between intensive and less intensive treatment groups (5.6% vs 5.7%), and the study was large enough and long enough to be able to detect such a benefit if one existed. Since the benefit of lipid lowering is greatest in patients with known disease, any benefit is certainly much less lower for patients without known disease who are at much lower risk. (LOE = 1b)) (**5461** of 15,464 pts in 8 wk open-label treatment with atorvastatin 10mg/d **were excluded**). McGowan MP; Treating to New Target (TNT) Study Group. There is no evidence for an increase in acute coronary syndromes after short-term abrupt discontinuation of statins in stable cardiac patients. Circulation. 2004 Oct 19;110(16):2333-5. Epub 2004 Oct 11. Shepherd J, et al. Effect of lowering LDL cholesterol substantially below currently recommended levels in patients with coronary heart disease and **diabetes**: the Treating to New Targets (TNT) study. Diabetes Care. 2006 Jun;29(6):1220-6. Deedwania P, et al. Treating to New Targets Investigators. Reduction of low-density lipoprotein cholesterol in patients with coronary heart disease and **metabolic syndrome**: analysis of the Treating to New Targets study. Lancet. 2006 Sep 9;368(9539):919-28. Wenger NK, Lewis SJ, Herrington DM, Bittner V, Welty FK; Treating to New Targets Study Steering Committee and Investigators. Outcomes of using high- or low-dose atorvastatin in patients **65 years of age or older** with stable coronary heart disease. Ann Intern Med. 2007 Jul 3;147(1):1-9. The analysis suggests that additional clinical benefit can be achieved by treating older patients with CHD more aggressively to reduce low-density lipoprotein cholesterol levels to less than 2.6 mmol/L (<100 mg/dL). The findings support the use of intensive low-density lipoprotein cholesterol-lowering therapy in high-risk older persons with established cardiovascular disease. Larosa JC, Grundy SM, Kastelein JJ, Kostis JB, Greten H; Treating to New Targets (TNT) Steering Committee and Investigators. Safety and Efficacy of Atorvastatin-Induced Very Low-Density Lipoprotein Cholesterol Levels in Patients With Coronary Heart Disease (a Post Hoc Analysis of the Treating to New Targets [TNT] Study). Am J Cardiol. 2007 Sep 1;100(5):747-52. Epub 2007 Jun 14. In conclusion, the present analysis adds support to the concept that for patients with established atherosclerotic cardiovascular disease, a further risk reduction without sacrifice of safety can be achieved by reducing LDL cholesterol to very low levels. (Barter P, Gotto AM, LaRosa JC, Maroni J, et al; Treating to New Targets Investigators (TNT). **HDL cholesterol, very low levels of LDL cholesterol**, and cardiovascular events. N Engl J Med. 2007 Sep 27;357(13):1301-10. In this post hoc analysis, HDL was predictive of major cardiovascular events in patients treated with statins. This relationship was also observed among patients with LDL cholesterol levels below 70 mg per deciliter.) Wenger NK, Lewis SJ, Welty FK, Herrington DM, Bittner V. Beneficial effects of aggressive LDL cholesterol lowering in **women** with stable coronary heart disease in the Treating to New Targets (TNT) study. Heart. 2007 Dec 10; [Epub ahead of print] Conclusion Intensive lipid-lowering treatment with atorvastatin 80 mg produced significant reductions in relative risk for major cardiovascular events compared with atorvastatin 10 mg in both women and men with stable CHD.

Shepherd J, Kastelein JJ, et al.; TNT (Treating to New Targets) Investigators. Intensive lipid lowering with atorvastatin in patients with coronary heart disease and **chronic kidney disease**: the TNT (Treating to New Targets) study. J Am Coll Cardiol. 2008 Apr 15;51(15):1448-54. [PubMed - in process] Aggressive lipid lowering with atorvastatin 80 mg was both safe and effective in reducing the excess of cardiovascular events in a high-risk population with CKD and CHD.

Shepherd J, Kastelein JP, Bittner VA, Carmena R, Deedwania PC, Breazna A, Dobson S, Wilson DJ, Zuckerman AL, Wenger NK; Treating to New Targets Steering Committee and Investigators. Intensive lipid lowering with atorvastatin in patients with coronary artery disease, diabetes, and chronic kidney disease. Mayo Clin Proc. 2008 Aug;83(8):870-9. The absolute risk reduction in patients with diabetes and CKD was substantial, yielding a number needed to treat of 14 to prevent 1 major cardiovascular event over 4.8 years. Patients with diabetes, stable coronary artery disease, and mild to moderate CKD experience marked reduction in cardiovascular events with intensive lipid lowering, in contrast to previous observations in patients with diabetes and end-stage renal disease.

Bangalore S, Messerli FH, Wun CC, et al. Treating to New Targets Steering Committee and Investigators. **J-curve** revisited: an analysis of blood pressure and cardiovascular events in the Treating to New Targets (TNT) trial. Eur Heart J. 2010 Sep 16.

Mora S, Wenger NK, DeMicco DA, et al. **Determinants of residual risk** in secondary prevention patients treated with high- versus low-dose statin therapy: the Treating to New Targets (**TNT**) study. Circulation. 2012;125:1979 –1987.

Ho JE, Waters DD, Kean A, et al; TNT Investigators. Relation of Improvement in Estimated Glomerular Filtration Rate With Atorvastatin to Reductions in Hospitalizations for Heart Failure (from the Treating to New Targets [TNT] Study). Am J Cardiol. 2012 Mar 27.

Shepherd J, Breazna A, Deedwania PC, et al; Treating to New Targets Steering Committee and Investigators. Relation Between **Change in Renal Function** and Cardiovascular Outcomes in **Atorvastatin**-Treated Patients (Treating to New Targets [**TNT**] Study). Am J Cardiol. 2016 Apr 15;117(8):1199-205.

[13] Pedersen TR, Faergeman O, et al. High-Dose Atorvastatin vs Usual-Dose Simvastatin for Secondary Prevention After Myocardial Infarction: The **IDEAL** Study: A Randomized Controlled Trial. JAMA.2005Nov16;294(19):2437-2445.

(InfoPOEMs: The intensive reduction of low-density lipoprotein (LDL) levels to well below 100 mg/dL (2.5 mmol/L) did not result in a significant reduction in the recurrence of major coronary events or all-cause mortality among patients with stable coronary artery disease. Intensive lowering is associated with an increased risk of discontinuing medication because of adverse events and significant drug costs. Aiming for an LDL of approximately 100 mg/dL (2.5 mmol/L) seems optimal for the majority of patients with stable disease. (LOE = 1b-))

Tikkanen MJ, Holme I, Cater NB, et al.; Incremental DEcrease through Aggressive Lipid Lowering Investigators. Comparison of efficacy and safety of atorvastatin (80 mg) to simvastatin (20 to 40 mg) in patients aged <65 versus >or=65 years with coronary heart disease (from the Incremental DEcrease through Aggressive Lipid Lowering [IDEAL] study). Am J Cardiol. 2009 Mar 1;103(5):577-82. Epub 2009 Jan 17. Rates of any reported serious adverse event were higher in older patients, but did not differ between the 2 statin groups. In conclusion, except for any CV events in the older group, significant reductions in primary and secondary end points were observed only in patients <65 years of age. The safety of atorvastatin (80 mg) and simvastatin (20 to 40 mg) was similar in patients aged <65 and >65 years with stable coronary disease.

Tikkanen MJ, Szarek M, Fayyad R, et al. IDEAL Investigators. Total cardiovascular disease burden: comparing intensive with moderate statin therapy insights from the IDEAL (Incremental Decrease in End Points Through Aggressive Lipid Lowering) trial. J Am Coll Cardiol. 2009 Dec 15;54(25):2353-7.

Pedersen TR, Cater NB, Faergeman O, et al. Comparison of atorvastatin 80 mg/day versus simvastatin 20 to 40 mg/day on frequency of cardiovascular events late (five years) after acute myocardial infarction (from the Incremental Decrease in End Points through Aggressive Lipid Lowering [IDEAL] trial). Am J Cardiol. 2010 Aug 1;106(3):354-9.

Stoekenbroek RM, Boekholdt SM, Fayyad R, et al. High-dose atorvastatin is superior to moderate-dose simvastatin in preventing peripheral arterial disease. (IDEAL) Heart. 2015 Jan 16.

RxFiles IDEAL Trial Summary: http://www.rxfiles.ca/rxfiles/uploads/documents/Lipid-QandA-IDEAL.pdf

[14] Colhoun HM, Betteridge DJ, Durrington PN, et al. Primary prevention of cardiovascular disease with atorvastatin in type 2 diabetes in the Collaborative Atovastatin Diabetes Study (CARDS). Lancet 2004;364:685-96. Colhoun HM, et al.; on behalf of the CARDS Investigators. Rapid emergence of effect of atorvastatin on cardiovascular outcomes in the Collaborative Atorvastatin Diabetes Study (CARDS). Diabetologia. 2005 Nov 12;:1-4 [Epub ahead of print] RESULTS: A reduction in the primary endpoint of major CVD events was apparent and statistically significant as soon as 18 months after treatment initiation. The effect of atorvastatin on CHD events was apparent by 6 months, and at 1 year was similar to the 37% relative risk reduction observed at trial closure.) (Neil HA, et al. **CARDS** Study Investigators. Analysis of efficacy and safety in patients **aged 65-75** years at randomization: Collaborative Atorvastatin Diabetes Study (CARDS). Diabetes Care. 2006 Nov;29(11):2378-84.)
Colhoun HM, Betteridge DJ, Durrington PN, et al.; CARDS Investigators. Effects of Atorvastatin on Kidney Outcomes and Cardiovascular Disease in Patients With Diabetes: An Analysis From the Collaborative Atorvastatin Diabetes Study (CARDS). Am J Kidney Dis. 2009 Jun 18. [Epub ahead of print] A modest beneficial effect of atorvastatin on **eGFR**, particularly in those with albuminuria, was observed. Atorvastatin did not influence albuminuria incidence. Atorvastatin was effective at decreasing CVD in those with and without a moderately decreased eGFR and achieved a high absolute benefit.

[15] Peter S Sever, Björn Dahlöf et al. Prevention of coronary and stroke events with atorvastatin in hypertensive patients who have average or lower-than-average cholesterol concentrations, in the **Anglo-Scandinavian Cardiac Outcomes Trial--Lipid Lowering Arm** (**ASCOT-LLA**): a multicentre randomised controlled trial Lancet 2003; **361:** 1149-58. Online April 2, 2003.
Sever PS, et al. The Anglo-Scandinavian Cardiac Outcomes Trial lipid lowering arm: extended observations 2 years after trial closure. Eur Heart J. 2008 Feb;29(4):499-508. Epub 2008 Jan 5. Carry-over benefits from those originally assigned atorvastatin but no longer taking the drug may account for unchanged relative risk reductions in most cardiovascular endpoints observed 2 years after ASCOT-LLA closed.
Sever PS, Poulter NR, Dahlof B, Wedel H; on behalf of the ASCOT investigators. Antihypertensive therapy and the benefits of atorvastatin in the Anglo-Scandinavian Cardiac Outcomes Trial: lipid-lowering arm extension. J Hypertens. 2009 Mar 21. [Epub ahead of print]
Sever PS, Chang CL, Gupta AK, et al. Anglo-Scandinavian Cardiac Outcomes Trial (Ascot): **11-year mortality follow-up** of the lipid-lowering arm in the UK. Eur Heart J 2011. (Less mortality mainly from less non-cardiovascular deaths)
Gupta A, Thompson D, Whitehouse A, et al. **Adverse events associated with unblinded**, but not with blinded, **statin therapy** in the Anglo-Scandinavian Cardiac Outcomes Trial-Lipid-Lowering Arm **(ASCOT-LLA):** a randomised double-blind placebo-controlled trial and its non-randomised non-blind extension phase. Lancet. 2017 May 2.
Gupta A, Mackay J, Whitehouse A, et al. Long-term mortality after blood pressure-lowering and lipid-lowering treatment in patients with hypertension in the Anglo-Scandinavian Cardiac Outcomes Trial (ASCOT) Legacy study: 16-year follow-up results of a randomised factorial trial. Lancet. 2018 Aug 24.

[16] Shepherd J, Cobbe SM, Ford I, et al. Prevention of coronary heart disease with pravastatin in men with hypercholesterolemia (**WOSCOPS**). N Engl J Med 1995;333:1383-9. Ford I, Murray H, Packard CJ, Shepherd J, Macfarlane PW, Cobbe SM; West of Scotland Coronary Prevention Study Group. Long-term follow-up of the West of Scotland Coronary Prevention Study. (Woscops) N Engl J Med. 2007 Oct 11;357(15):1477-86. In the period approximately 10 years after completion of the trial, the risk of death from coronary heart disease or nonfatal myocardial infarction was 10.3% in the placebo group and 8.6% in the pravastatin group (P=0.02); over the entire follow-up period, the rate was 15.5% in the placebo group and 11.8% in the pravastatin group (P<0.001). In this analysis, 5 years of treatment
with pravastatin was associated with a significant reduction in coronary events for a subsequent 10 years in men with hypercholesterolemia who did not have a history of myocardial infarction.
Logue J, Murray HM, Welsh P, et al. Obesity is associated with fatal coronary heart disease independently of traditional risk factors and deprivation (WOSCOPS). Heart 2011; DOI:10.1136/hrt.2010.211201.
McConnachie A, Walker A, Robertson M, et al. Long-term impact on healthcare resource utilization of statin treatment, and its cost effectiveness in the primary prevention of cardiovascular disease: a record linkage study. (WOSCOPS) Eur Heart J. 2013 Jul 9.
Ford I, Murray H, et al. Long-Term Safety and Efficacy of Lowering Low-Density Lipoprotein Cholesterol With Statin Therapy: **20-Year Follow-Up** of West of Scotland Coronary Prevention Study (**WOSCOPS**). Circulation. 2016 Mar 15;133(11):1073-80.
Natarajan P, Young R, Stitzielet NO, et al.. **Polygenic risk score identifies subgroup** with higher burden of atherosclerosis and greater relative **benefit from statin therapy** in the primary prevention setting. (**WOSCOPS**) *Circulation* 2017.
Vallejo-Vaz AJ, Robertson M, Catapano AL, et al. **LDL-Cholesterol Lowering for the Primary Prevention** of Cardiovascular Disease Among Men with Primary Elevations of LDL-Cholesterol Levels of 190 mg/dL or Above: Analyses from the **WOSCOPS** 5-year Randomised Trial and **20-year Observational Follow-Up.** Circulation. 2017 Sep 6.

[17] Downs JR, Clearfield M, Weis S, et al. Primary prevention of acute coronary events with lovastatin in men and women with average cholesterol levels. Results of (**AFCAPS/TexCAPS**). JAMA 1998;279:1615-22.
Clearfield M, Downs JR, Lee M, et al. Implications from the Air Force/Texas Coronary Atherosclerosis Prevention Study for the Adult Treatment Panel III Guidelines. Am J Cardiol. 2005 Dec 15;96(12):1674- 80. Epub 2005 Nov 2.
Cui Y, Watson DJ, Girman CJ, et al. Effects of increasing high-density lipoprotein cholesterol and decreasing low-density lipoprotein cholesterol on the incidence of first acute coronary events (from the Air Force/Texas Coronary Atherosclerosis Prevention Study). Am J Cardiol. 2009 Sep 15;104(6):829-34.

[18] Nakamura H, et al. **Primary prevention** of cardiovascular disease with pravastatin in Japan (**MEGA** Study): a prospective randomised controlled trial. Lancet. 2006 Sep 30;368(9542):1155-63. Treatment with a low dose of pravastatin reduces the risk of coronary heart disease in Japan by much the same amount as higher doses have shown in Europe and the USA.
Mizuno K, Nakaya N, Ohashi Y, et al; for the MEGA Study Group. Usefulness of Pravastatin in Primary Prevention of Cardiovascular Events in Women. Analysis of the Management of Elevated Cholesterol in the Primary Prevention Group of Adult Japanese (MEGA Study). Circulation. 2008 Jan 2; [Epub ahead of print] Treatment with pravastatin in women with elevated cholesterol but no history of cardiovascular disease provides a benefit similar to that seen in men, and this benefit is more marked in older women.

[19] Ridker PM, Danielson E, Fonseca FA, Genest J, et al. the **JUPITER** Study Group. Rosuvastatin to Prevent Vascular Events in Men and Women with Elevated C-Reactive Protein. N Engl J Med. 2008 Nov 9. [Epub ahead of print] In this trial of apparently healthy persons without hyperlipidemia but with elevated high-sensitivity C-reactive protein levels, rosuvastatin significantly reduced the incidence of major cardiovascular events. (Hlatky MA. Expanding the Orbit of Primary Prevention -- Moving beyond JUPITER. N Engl J Med. 2008 Nov 9. [Epub ahead of print])
Ridker PM, Danielson E, Fonseca FA, et al. JUPITER Trial Study Group. Reduction in C-reactive protein and LDL cholesterol and cardiovascular event rates after initiation of rosuvastatin: a prospective study of the JUPITER trial. Lancet. 2009 Apr 4;373(9670):1175-82. Epub 2009 Mar 28.
Everett BM, Glynn RJ, MacFadyen JG, Ridker PM. Rosuvastatin in the prevention of **stroke** among men and women with elevated levels of C-reactive protein: justification for the Use of Statins in Prevention: an Intervention Trial Evaluating Rosuvastatin (JUPITER). Circulation. 2010 Jan 5;121(1):143-50.
Mora S, Glynn RJ, Hsia J, Macfadyen JG, Genest J, Ridker PM. Statins for the Primary Prevention of Cardiovascular Events in Women With Elevated High-Sensitivity C-Reactive Protein or Dyslipidemia. Results From the Justification for the Use of Statins in Prevention: An Intervention Trial Evaluating Rosuvastatin (JUPITER) and Meta-Analysis of **Women** From Primary Prevention Trials. Circulation. 2010 Feb 22.
Glynn RJ, Koenig W, Nordestgaard BG, Shepherd J, Ridker PM. Rosuvastatin for primary prevention in **older persons** with elevated C-reactive protein and low to average low-density lipoprotein cholesterol levels: exploratory analysis of a randomized trial. Ann Intern Med. 2010 Apr 20;152(8):488-96, W174.
de Lorgeril Michel; Salen Patricia; Abramson John; et al. Cholesterol Lowering, Cardiovascular Diseases, and the Rosuvastatin-**JUPITER Controversy**: A Critical Reappraisal. Arch Intern Med. 2010;170(12):1032-1036.
Ridker PM, Genest J, Boekholdt SM, et al. JUPITER Trial Study Group. **HDL** cholesterol and residual risk of first cardiovascular events after treatment with potent statin therapy: an analysis from the JUPITER trial. Lancet. 2010 Jul 31;376(9738):333-9.
Ridker PM, MacFayden JG, Nordestgaard BG, et al. Rosuvastatin for primary prevention among individuals with elevated high-sensitivity C-reactive protein and 5% to 10% and 10% to 20% 10-year risk. Circ Cardiovasc Qual Outcomes 2010; DOI: 10.1161/circoutcomes.110938118.
Koenig W, Ridker PM. Rosuvastatin for primary prevention in patients with European systematic coronary risk evaluation **risk >5% or Framingham risk >20%:** Post hoc analyses of the JUPITER trial requested by the European health authorities. Eur Heart J 2010; DOI: 10.1093/eurheartj/ehq370.
Hsia J, MacFayden JG, Monyak J, Ridker PM. Cardiovascular event reduction and adverse events among subjects attaining low-density lipoprotein cholesterol <50 mg/dL with rosuvastatin. (JUPITER) J Am Coll Cardiol 2011; 57: 1666-1675.
Vidt Donald G., Ridker Paul M., Monyak JT, et al. Longitudinal Assessment of Estimated **Glomerular Filtration Rate** in Apparently Healthy Adults: A Post hoc Analysis from the JUPITER Study (Justification for the Use of Statins in Prevention: An Intervention Trial Evaluating Rosuvastatin). Clinical Therapeutics, Volume 33, Issue 6, June 2011, Pages 717-725, ISSN 0149-2918, DOI: 10.1016/j.clinthera.2011.05.004.
Novack V, Macfadyen J, Malhotra A, et al. The effect of rosuvastatin on **incident pneumonia**: results from the JUPITER trial. CMAJ. 2012 Mar 19.
Peña JM, Aspberg S, MacFadyen J, et al. Statin Therapy and Risk of Fracture: Results From the JUPITER Randomized Clinical Trial. JAMA Intern Med. 2014 Dec 1.
Ridker PM, Lonn E, Paynter NP, et al. **Primary Prevention** With Statin Therapy in the **Elderly**: New Meta-Analyses from the Contemporary **JUPITER** and **HOPE-3** Randomized Trials. Circulation. 2017 Apr 6.

[20] Implications of Recent Clinical Trials for the NCEP ATP Panel III Guidelines July **2004** {HPS: serum lipids at basline were determined on nonfasting samples and calculated by the direct LDL method. Most other trials determined on fasting samples and LDL-C calculated by the Friedewald equation. If HPS was calculated by the Friedewald eqation, the baseline LDL would be **~15% higher**. http://www.acc.org/clinical/adoptions/ncep_report.pdf
[21] Walsh, J.M., Pignone M. Drug Treatment of Hyperlipidemia in Women. JAMA. 2004 May 12;291(18):2243-2252.

[22] Bandolier: Cholesterol and Statins; Extra April 2004 http://www.jr2.ox.ac.uk/bandolier/Extraforbando/statin.pdf

[23] Cannon CP, Braunwald E, McCabe CH, Rader DJ, Rouleau JL, Belder R, Joyal SV, Hill KA, Pfeffer MA, Skene AM; Pravastatin or Atorvastatin Evaluation and Infection Therapy-Thrombolysis in Myocardial Infarction 22 Investigators. Intensive versus moderate lipid lowering with statins after acute coronary syndromes. N Engl J Med. 2004 Apr 8;350(15):1495-504. Epub 2004 Mar 08.

[24] Marco Studer, MD; Matthias Briel, MD; Bernd Leimenstoll, MD; et al. Effect of Different Antilipidemic Agents and Diets on Mortality A Systematic Review. Arch Intern Med. 2005;165:725-730. (InfoPOEMs: Only statin lipid-lowering drugs have been shown to decrease overall mortality in patients with high cholesterol but without evidence of heart disease. However, most patients treated with one of these drugs will not benefit: 228 have to be treated for 3.3 years to prevent 1 additional death during this period. In pts with known heart dx, statins & fish oil both have been shown to decrease mortality. Niacin, resins, & diet have not been shown to decrease mortality. Fibrates (gemfibrozil & others) actually increase overall mortality & at the same time decrease cardiac mortality. (LOE =1a))

[25] Committee of Principal Investigators (**WHO-Clof**). A co-operative trial in the primary prevention of ischeamic heart disease using clofibrate. British Heart Journal 1978;40:1069-1118.

26 BIP Study Group. Secondary prevention (n=3090) by raising HDL cholesterol and reducing triglycerides in patients with coronary artery disease. The bezafibrate infarction prevention (BIP) study. Circulation 2000;102:21-27. (Tenenbaum A, Motro M, Fisman EZ, et al. Bezafibrate for the secondary prevention of myocardial infarction in patients with metabolic syndrome. Arch Intern Med. 2005 May 23;165(10):1154-60 & McCormack J, Loewen P. The other side of the bezafibrate infarction prevention trial data. Arch Intern Med. 2005 Nov 14;165(20):2431-2; author reply 2432.) (Tenenbaum A, et al. Attenuation of progression of insulin resistance in patients with coronary artery disease by bezafibrate. Arch Intern Med. 2006 Apr 10;166(7):737-41.)
Goldenberg I, et al. Secondary prevention with bezafibrate therapy for the treatment of dyslipidemia: an extended follow-up of the BIP trial. J Am Coll Cardiol. 2008 Jan 29;51(4):459-65. The data demonstrate that bezafibrate therapy in the BIP trial was associated with significant long-term cardiovascular protection that was attenuated by an unbalanced usage of nonstudy LLDs during the course of the trial.
Goldenberg I, Boyko V, Tennebaum A, et al. Long-term benefit of high-density lipoprotein cholesterol-raising therapy with bezafibrate. (16yr follow up)Arch Intern Med 2009; 169: 508-514.
Klempfner R, Erez A, Sagit BZ, et al. **Elevated triglyceride level** is independently associated with increased all-cause mortality in patients with established coronary heart disease: Twenty-two-year follow-up of the bezafibrate infarction prevention study (**BIP**) and registry. Circ Cardiovasc Qual Outcomes 2016; 9:100-1088.

[27] Bloomfield Rubins A, Robins SJ, Collins D, et al. Gemfibrozil for the secondary prevention of coronary heart disease in men with low levels of high-density lipoprotein cholesterol (**VA-HIT**). N Engl J Med 1998; 339:1349-57.

28 **ACCORD** Study Group, Effects of Combination **Lipid** Therapy (**simvastatin** with fenofibrate) in Type 2 Diabetes Mellitus. N Engl J Med 2010 0: NEJMoa1001282.
Elam MB, Ginsberg HN, Lovato LC, Corson et al. Association of **Fenofibrate** Therapy With Long-term Cardiovascular Risk in Statin-Treated Patients With Type 2 Diabetes. (**ACCORDIAN**) JAMA Cardiol. 2016 Dec 28.

[29] Frick MH, Elo O, Haapa K, et al. Helsinki Heart Study (**HHS**): Primary-prevention trial with gemfibrozil in middle-aged men with dyslipidemia. Safety of treatment, changes in risk factors, and incidence of coronary heart disease. N Engl J Med 1987;317:1237-45. (Tenkanen L, et al. Gemfibrozil in the Treatment of Dyslipidemia: An **18-Year** Mortality Follow-up of the Helsinki Heart Study. (HHS) Arch Intern Med. 2006 Apr 10;166(7):743-8.)

[30] Taylor F, Huffman MD, Macedo AF, et al. Statins for the primary prevention of cardiovascular disease. Cochrane Database of Systematic Reviews 2013, Issue 1. Art. No.: CD004816. Reductions in all-cause mortality, major vascular events and revascularisations were found with no excess of adverse events among people without evidence of CVD treated with statins.

[31] . Brugts J, Yetgin T, Hoeks S, Gotto A, et al. The benefits of statins in people **without** established **cardiovascular disease** but with cardiovascular risk factors: meta-analysis of RCTs. BMJ 2009;338:2376. http://www.bmj.com/cgi/content/abstract/338/jun30_1/b2376
InfoPoems: Lowering cholesterol in 173 patients at risk for developing cardiovascular disease for slightly more than 4 years prevented 1 of them from dying prematurely. One major coronary event was prevented for every 81 patients, and one cerebrovascular event was prevented for every 245 patients treated. (LOE = 1a)

32 Jun M, Foote C, Lv J, et al. Effects of fibrates on cardiovascular outcomes: a systematic review and meta-analysis. Lancet. 2010 May 29;375(9729):1875-84.

33. Ridker PM, Rifai N, Cook NR, et al. Non-HDL cholesterol, apolipoproteins A-I and B100, standard lipid measures, lipid ratios, and CRP as risk factors for cardiovascular disease in women. JAMA. 2005 Jul 20;294(3):326-33.
(Nissen SE, Tuzcu EM, Schoenhagen P, et al.; Reversal of Atherosclerosis with Aggressive Lipid Lowering (REVERSAL) Investigators. Statin therapy, LDL cholesterol, C-reactive protein, and coronary artery disease. N Engl J Med. 2005 Jan 6;352(1):29-38.) (Nicholls SJ, et al. Effects of obesity on lipid-lowering, anti-inflammatory, and antiatherosclerotic benefits of atorvastatin or pravastatin in patients with coronary artery disease (from the **REVERSAL** Study). Am J Cardiol. 2006 Jun 1;97(11):1553-7. Epub 2006 Apr 6.)

34. Keech A, Simes RJ, Barter P, et al. **FIELD** study investigators. Effects of long-term fenofibrate therapy on cardiovascular events in 9795 people with type 2 diabetes mellitus (the FIELD study): randomised controlled trial. Lancet. 2005 Nov 26;366(9500):1849-61. INTERPRETATION: Fenofibrate did not significantly reduce the risk of the primary outcome of coronary events. It did reduce total cardiovascular events, mainly due to fewer non-fatal myocardial infarctions and revascularisations. The higher rate of starting statin therapy in patients allocated placebo might have masked a moderately larger treatment benefit. (But some **non-significant** concerns with fenofibrate vs placebo such as: an ↑ in cardiac mortality 2.2 vs 1.9%, an ↑ in total CVD events for those with previous CVD 25.5 vs 25.1%, an excess in non-cardiovascular disease deaths 4.4 vs 4% & an ↑ in total mortality 7.3 vs 6.6%). But may benefit albuminuria & retinopthy. (InfoPOEMs: In this study, patients with type 2 diabetes treated with fenofibrate (Antara, Lofibra, Tricor) had no significant reduction in coronary events compared with patients treated with placebo. There was a small reduction, however, in nonfatal myocardial infarctions, total cardiovascular disease, and revascularization. (LOE = 1b)) Keech AC, Mitchell P, Summanen PA, et al, for the FIELD study investigators. Effect of fenofibrate on the need for laser treatment for diabetic retinopathy (FIELD study): a randomised controlled trial. Lancet 2007;370(9600):1687-1697. In patients with type 2 diabetes mellitus fenofibrate (Antara, Lofibra, Tricor) modestly reduces the number of laser treatments for retinopathy. (LOE = 1b)
Rajamani K et al. Effect of fenofibrate on **amputation** events in people with type 2 diabetes mellitus (FIELD study): A prespecified analysis of a randomised controlled trial. Lancet 2009 May 23; 373:1780.
Davis TM, Ting R, Best JD, et al. Fenofibrate Intervention and Event Lowering in Diabetes Study investigators. Effects of fenofibrate on renal function in patients with type 2 diabetes mellitus: the Fenofibrate Intervention and Event Lowering in Diabetes (FIELD) Study. Diabetologia. 2011 Feb;54(2):280-90.
Ting RD, Keech AC, Drury PL, et al. FIELD Study Investigators. Benefits and safety of long-term fenofibrate therapy in people with type 2 diabetes and renal impairment: the FIELD Study. Diabetes Care. 2012 Feb;35(2):218-25.

35. Houslay E, et al. **Progressive coronary calcification despite** intensive lipid-lowering therapy: a randomised controlled trial. Heart. 2006 Jan 31; [Epub ahead of print]

36. Nissen SE, et al. Effect of Very High-Intensity Statin (rosuvastatin 40mg/d, 2yr, n=507) Therapy on Regression of Coronary Atherosclerosis: The **ASTEROID** Trial.JAMA. 2006 Mar 13; [Epub ahead of print]

37. Hooper L, et al. Risks and benefits of **omega 3 fats** for mortality, cardiovascular disease, and cancer: systematic review. BMJ. 2006 Mar 24; [Epub ahead of print]

38. Costa J, Borges M, David C, Carneiro AV. Efficacy of lipid lowering drug treatment for **diabetic and non-diabetic** patients: meta-analysis of randomised controlled trials. BMJ. 2006 Apr 3; [Epub ahead of print]

39. Manuel DG, et al. Effectiveness and efficiency of **different guidelines** on statin treatment for preventing deaths from coronary heart disease: **modelling study**. BMJ. 2006 Jun 17;332(7555):1419. Epub 2006 May 31.

40. Knopp RH, et al. Efficacy and Safety of Atorvastatin in the Prevention of Cardiovascular End Points in Subjects With Type 2 Diabetes: The Atorvastatin Study for Prevention of Coronary Heart Disease Endpoints in Non-Insulin-Dependent Diabetes Mellitus (**ASPEN**). Diabetes Care. 2006 Jul;29(7):1478-85.

41. Amarenco P, et al.; Stroke Prevention by Aggressive Reduction in Cholesterol Levels (**SPARCL**) Investigators. High-dose atorvastatin after stroke or transient ischemic attack. N Engl J Med. 2006 Aug 10;355(6):549-59. (Kent DM. Stroke--an equal opportunity for the initiation of statin therapy. N Engl J Med. 2006 Aug 10;355(6):613-5.) Amarenco P, Goldstein LB, Szarek M, Sillesen H, Rudolph AE, Callahan A 3rd, Hennerici M, Simunovic L, Zivin JA, Welch KM; SPARCL Investigators. Effects of Intense Low-Density Lipoprotein Cholesterol Reduction in Patients With Stroke or Transient Ischemic Attack. The Stroke Prevention by Aggressive Reduction in Cholesterol Levels (SPARCL) Trial. Stroke. 2007 Oct 25; [Epub ahead of print] As compared with having no change or an increase in LDL-C, achieving a >/=50% lowering was associated with a greater reduction in the risk of stroke and major coronary events with no increase in brain hemorrhages. Goldstein LB, Amarenco P, Szarek M, Callahan A 3rd, Hennerici M, Sillesen H, Zivin JA, Welch KM; On behalf of the SPARCL Investigators. Hemorrhagic stroke in the Stroke Prevention by Aggressive Reduction in Cholesterol Levels study. Neurology. 2007 Dec 12; [Epub ahead of print] Hemorrhagic stroke was more frequent in those treated with atorvastatin, in those with a hemorrhagic stroke as an entry event, in men, and increased with age. Those with Stage 2 hypertension at the last visit prior to the hemorrhagic stroke were also at increased risk. Treatment did not disproportionately affect the hemorrhagic stroke risk associated with these other factors. There were no relationships between hemorrhage risk and baseline low-density lipoprotein (LDL) cholesterol level or recent LDL cholesterol level in treated patients.
Sillesen H, Amarenco P, Hennerici MG, et al. on Behalf of the SPARCL Investigators. Atorvastatin Reduces the Risk of Cardiovascular Events in Patients With Carotid Atherosclerosis. A Secondary Analysis of the Stroke Prevention by Aggressive Reduction in Cholesterol Levels (SPARCL) Trial. Stroke. 2008 Oct 9. [Epub ahead of print] Consistent with the overall results of the SPARCL intention to treat population, intense lipid lowering with atorvastatin reduced the risk of cerebro- and cardiovascular events in patients with and without carotid stenosis. The carotid stenosis group may have greater benefit.
Amarenco P, Benavente O, Goldstein LB, et al.; on behalf of the SPARCL Investigators. Results of the Stroke Prevention by Aggressive Reduction in Cholesterol Levels (SPARCL) Trial by Stroke Subtypes. Stroke. 2009 Feb 19. [Epub ahead of print] Atorvastatin 80 mg/d is similarly efficacious in preventing strokes and other cardiovascular events, irrespective of baseline ischemic stroke subtype.
Goldstein LB, Amarenco P, Zivin J, Messig M, Altafullah I, Callahan A, Hennerici M, Macleod MJ, Sillesen H, Zweifler R, Welch KM; on behalf of the SPARCL Investigators. Statin Treatment and Stroke Outcome in the Stroke Prevention by Aggressive Reduction in Cholesterol Levels (SPARCL) Trial. Stroke. 2009 Sep 10.
Callahan Alfred; Amarenco Pierre; Goldstein Larry B.; et al. the SPARCL Investigators. Risk of Stroke and Cardiovascular Events After Ischemic Stroke or Transient Ischemic Attack in Patients With **Type 2 Diabetes or Metabolic Syndrome**: Secondary Analysis of the Stroke Prevention by Aggressive Reduction in Cholesterol Levels (SPARCL) Trial Arch Neurol. 2011;0(2011):archneurol.2011.146.

42. Hayward RA, Hofer TP, Vijan S. Narrative review: **lack of evidence** for recommended low-density lipoprotein treatment targets: a solvable problem. Ann Intern Med. 2006 Oct 3;145(7):520-30.

43. Cannon CP, Braunwald E, McCabe CH, et al. Pravastatin or Atorvastatin Evaluation and Infection Therapy-Thrombolysis in Myocardial Infarction 22 Investigators. Intensive versus moderate lipid lowering with statins after acute coronary syndromes. N Engl J Med. 2004 Apr 8;350(15):1495-504. Epub 2004 Mar 8. Erratum in: N Engl J Med. 2006 Feb 16;354(7):778. (Ahmed S, Cannon CP, Murphy SA, et al.Acute coronary syndromes and **diabetes**: Is intensive lipid lowering beneficial? Results of the **PROVE IT-TIMI 22** trial. Eur Heart J. 2006 Oct;27(19):2323-9. Epub 2006 Sep 5.)

Murphy SA, Cannon CP, Wiviott SD, McCabe CH, Braunwald E. Reduction in recurrent cardiovascular events with intensive lipid-lowering statin therapy compared with moderate lipid-lowering statin therapy after acute Coronary syndromes from the PROVE IT-TIMI 22 (Pravastatin or Atorvastatin Evaluation and Infection Therapy-Thrombolysis In Myocardial Infarction 22) trial. J Am Coll Cardiol. 2009 Dec 15;54(25):2358-62.

44. Nakamura H, et al. **Primary prevention** of cardiovascular disease with pravastatin in Japan (**MEGA** Study): a prospective randomised controlled trial. Lancet. 2006 Sep 30;368(9542):1155-63. Treatment with a low dose of pravastatin reduces the risk of coronary heart disease in Japan by much the same amount as higher doses have shown in Europe and the USA.
Mizuno K, Nakaya N, Ohashi Y, et al; for the MEGA Study Group. Usefulness of Pravastatin in Primary Prevention of Cardiovascular Events in Women. Analysis of the Management of Elevated Cholesterol in the Primary Prevention Group of Adult Japanese (MEGA Study). Circulation. 2008 Jan 2; [Epub ahead of print] Treatment with pravastatin in women with elevated cholesterol but no history of cardiovascular disease provides a benefit similar to that seen in men, and this benefit is more marked in older women.
45. Taylor AJ, et al. Arterial Biology for the Investigation of the Treatment Effects of Reducing Cholesterol **(ARBITER) 2**: a double-blind, placebo-controlled study of extended-release **niacin** on atherosclerosis progression in secondary prevention patients treated with statins. Circulation. 2004 Dec 7;110(23):3512-7. Epub 2004 Nov 10. Erratum in: Circulation. 2004 Dec 7;110(23):3615. Circulation. 2005 Jun 21;111(24):e446.
46. Thavendiranathan P, Bagai A, Brookhart MA, Choudhry NK. **Primary Prevention** of Cardiovascular Diseases With Statin Therapy: A **Meta-analysis** of Randomized Controlled Trials. Arch Intern Med. 2006 Nov 27;166(21):2307-13. Subjects taking statins for a mean of 4.3 years (n=42 848) had a lower incidence of heart attack, stroke, revascularization, and other events than controls. The authors estimate the following numbers needed to treat for 4.3 years: 60, to prevent one major coronary event; 268 for stroke; 61 for nonfatal myocardial infarction and 93 for revascularization. In patients without CV disease, statin therapy decreases the incidence of major coronary and cerebrovascular events and revascularizations but not coronary heart disease or overall mortality.
47. Wanner C, Krane V, Marz W, et al.; German Diabetes and Dialysis Study Investigators (**4D**). Atorvastatin in patients with type 2 diabetes mellitus undergoing hemodialysis. N Engl J Med. 2005 Jul 21;353(3):238-48.
Krane V, Schmidt KR, Gutjahr-Lengsfeld LJ, et al. Long-term effects following 4 years of randomized treatment with **atorvastatin** in patients with type 2 diabetes mellitus on **hemodialysis**. (**4D**) Kidney Int. 2016 Feb 17.

48. Crouse JR 3rd, Raichlen JS, Riley WA, Evans GW, Palmer MK, O'leary DH, Grobbee DE, Bots ML. Effect of Rosuvastatin 40mg od on Progression of Carotid Intima-Media Thickness in Low-Risk Individuals (n=984; Ros=702, placebo=282 over 2 years) With Subclinical Atherosclerosis: The **METEOR** Trial . JAMA. 2007Mar 25; [Epub ahead of print] Rosuvastatin treatment was associated with a 49% reduction in LDL-C level, a 34% reduction in total cholesterol level, an 8% increase in HDL-C level, and a 16% reduction in level of triglycerides. Serious adverse cardiovascular events were infrequent (6 participants [0.86%] had 8 events [1.1%] in the rosuvastatin group vs 0% in the placebo group) In middle-aged adults with an FRS of less than 10% and evidence of subclinical atherosclerosis, rosuvastatin resulted in statistically significant reductions in the rate of progression of maximum CIMT over 2 years vs placebo. Rosuvastatin did not induce disease regression.
49. Kjekshus J, Apetrei E, Barrios V, et al. the **CORONA** Group. **Rosuvastatin** in Older Patients (n=5011 over 32.8 months) with **Systolic Heart Failure**. N Engl J Med. 2007 Nov 5; [Epub ahead of print] Rosuvastatin did not reduce the primary outcome or the number of deaths from any cause in older patients with systolic heart failure, although the drug did reduce the number of cardiovascular hospitalizations. The drug did not cause safety problems. The drug did not cause safety problems. Rosuvastatin (Crestor) does not improve clinical outcomes in patients with heart failure and average cholesterol levels (low-density lipoprotein [LDL] = 137 mg/dl). (LOE = 1b)
Cleland JGF, McMurray JJV, Kjekshus J, et al. Plasma concentration of amino-terminal pro-brain natriuretic peptide in chronic heart failure: prediction of cardiovascular events and interaction with the effects of rosuvastatin: a report from CORONA (Controlled Rosuvastatin Multinational Trial in Heart Failure). J Am Coll Cardiol 2009; 54:1850-1859.
50. Murphy SA, Cannon CP, Wiviott SD, de et al Effect of intensive lipid-lowering therapy on mortality after acute coronary syndrome (a patient-level analysis of the Aggrastat to Zocor and Pravastatin or Atorvastatin Evaluation and Infection Therapy-thrombolysis in Myocardial Infarction 22 trials). Am J Cardiol. 2007 Oct 1;100(7):1047-51. Epub 2007 Jul 18. All-cause mortality was significantly reduced in the group with intensive statin therapy compared with the group with moderate statin therapy (3.6% vs 4.9%, hazard ratio 0.77, 95% confidence interval 0.63 to 0.95, p = 0.015), without significant interaction by trial (interaction p = 0.63). The reduction in all-cause mortality with intensive statin therapy was consistent across key subgroups.
51. Canner PL, Berge KG, Wenger NK, Stamler J, Friedman L, Prineas RJ, Friedewald W. Fifteen year mortality in Coronary Drug Project (**CDP**) patients: long-term benefit with niacin. J Am Coll Cardiol. 1986 Dec;8(6):1245-55.
52. de Lemos JA, Blazing MA, Wiviott SD, et al.; **A to Z Investigators**. Early intensive vs delayed conservative simvastatin strategy in patients with acute coronary syndromes: phase Z of A to Z trial. JAMA. 2004 Sep 15;292(11):1307-16. Epub 2004 Aug 30.
53. Afilalo J, Duque G, Steele R, et al. **Statins for secondary prevention in elderly patients**. J Am Coll Cardiol. 2008;51:37-45. The posterior median estimate of the number needed to treat to save 1 life was 28 (95% CI 15 to 56). CONCLUSIONS: Statins reduce all-cause mortality in elderly patients and the magnitude of this effect is substantially larger than had been previously estimated. {InfoPOEMs: Treating 28 elderly patients with coronary heart disease (CHD) for 5 years will prevent 1 of them from dying during that period. For every 38 people treated for 5 years, 1 nonfatal myocardial infarction will be prevented; for every 58 patients treated for 5 years, 1 stroke will be prevented. (LOE = 1a) }
54. Cholesterol Treatment Trialists' (**CTT**) Collaboration. Efficacy of cholesterol-lowering therapy in 18 686 people with **diabetes** in 14 randomised trials of statins: A meta-analysis. Lancet 2008; 371:117-125.
55. Strippoli GF, Navaneethan SD, Johnson DW, et al. Effects of statins in patients with **chronic kidney disease**: meta-analysis and meta-regression of randomised controlled trials. BMJ. 2008 Feb 25; [Epub ahead of print] Statins significantly reduce lipid concentrations and cardiovascular end points in patients with chronic kidney disease, irrespective of stage of disease, but no benefit on all cause mortality or the role of statins in primary prevention has been established. Reno-protective effects of statins are uncertain because of relatively sparse data and possible outcomes reporting bias.
56. Liakopoulos OJ, , et al. Impact of preoperative statin therapy on adverse **postoperative outcomes** in patients undergoing cardiac surgery: a meta-analysis of over 30 000 patients. Eur Heart Journal 2008; DOI:10.1093/eurheartj/ehn198.
57. ALLHAT Officers and Coordinators for the ALLHAT Collaborative Research Group. The Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial. Major outcomes in moderately hypercholesterolemic, hypertensive patients randomized to pravastatin vs usual care: The Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial (**ALLHAT-LLT**). JAMA. 2002 Dec 18;288(23):2998-3007.
Rahman M, Baimbridge C, Davis BR, et al. **ALLHAT** Collaborative Research Group. Progression of Kidney Disease in Moderately Hypercholesterolemic, Hypertensive Patients Randomized to Pravastatin Versus Usual Care: A Report From the Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial (ALLHAT). Am J Kidney Dis. 2008 Aug 1. [Epub ahead of print] In hypertensive patients with moderate dyslipidemia and decreased eGFR, pravastatin was not superior to usual care in preventing clinical renal outcomes.
Han BH, Sutin D, et al. Effect of **statin** treatment vs usual care on primary cardiovascular prevention among **older adults: the ALLHAT-LLT** randomized clinical trial [published online May 22, 2017]. JAMA Intern Med. doi:10.1001 /jamainternmed.2017.1442

58. Gissi-Hf Investigators. Effect of rosuvastatin in patients with chronic heart failure (the **GISSI-HF** trial): a randomised, double-blind, placebo-controlled trial. Lancet. 2008 Aug 29. [Epub ahead of print] Rosuvastatin 10 mg daily did not affect clinical outcomes in patients with chronic heart failure of any cause, in whom the drug was safe
59. Ridker PM, Danielson E, Fonseca FA, Genest J, et al. the **JUPITER** Study Group. Rosuvastatin to Prevent Vascular Events in Men and Women with Elevated C-Reactive Protein. N Engl J Med. 2008 Nov 9. [Epub ahead of print] In this trial of apparently healthy persons without hyperlipidemia but with elevated high-sensitivity C-reactive protein levels, rosuvastatin significantly reduced the incidence of major cardiovascular events. (Hlatky MA. Expanding the Orbit of Primary Prevention -- Moving beyond JUPITER. N Engl J Med. 2008 Nov 9. [Epub ahead of print])
Ridker PM, Danielson E, Fonseca FA, et al. JUPITER Trial Study Group. Reduction in C-reactive protein and LDL cholesterol and cardiovascular event rates after initiation of rosuvastatin: a prospective study of the JUPITER trial. Lancet. 2009 Apr 4;373(9670):1175-82. Epub 2009 Mar 28.
Everett BM, Glynn RJ, MacFadyen JG, Ridker PM. Rosuvastatin in the prevention of **stroke** among men and women with elevated levels of C-reactive protein: justification for the Use of Statins in Prevention: an Intervention Trial Evaluating Rosuvastatin (JUPITER). Circulation. 2010 Jan 5;121(1):143-50.
Mora S, Glynn RJ, Hsia J, Macfadyen JG, Genest J, Ridker PM. Statins for the Primary Prevention of Cardiovascular Events in Women With Elevated High-Sensitivity C-Reactive Protein or Dyslipidemia. Results From the Justification for the Use of Statins in Prevention: An Intervention Trial Evaluating Rosuvastatin (JUPITER) and Meta-Analysis of **Women** From Primary Prevention Trials. Circulation. 2010 Feb 22.
Glynn RJ, Koenig W, Nordestgaard BG, Shepherd J, Ridker PM. Rosuvastatin for primary prevention in **older persons** with elevated C-reactive protein and low to average low-density lipoprotein cholesterol levels: exploratory analysis of a randomized trial. Ann Intern Med. 2010 Apr 20;152(8):488-96, W174.
de Lorgeril Michel; Salen Patricia; Abramson John; et al. Cholesterol Lowering, Cardiovascular Diseases, and the Rosuvastatin-**JUPITER Controversy**: A Critical Reappraisal. Arch Intern Med. 2010;170(12):1032-1036.
Ridker PM, Genest J, Boekholdt SM, et al. JUPITER Trial Study Group. **HDL** cholesterol and residual risk of first cardiovascular events after treatment with potent statin therapy: an analysis from the JUPITER trial. Lancet. 2010 Jul 31;376(9738):333-9.
Ridker PM, MacFayden JG, Nordestgaard BG, et al. Rosuvastatin for primary prevention among individuals with elevated high-sensitivity C-reactive protein and 5% to 10% and 10% to 20% 10-year risk. Circ Cardiovasc Qual Outcomes 2010; DOI: 10.1161/circoutcomes.110938118.
Koenig W, Ridker PM. Rosuvastatin for primary prevention in patients with European systematic coronary risk evaluation **risk >5% or Framingham risk >20%:** Post hoc analyses of the JUPITER trial requested by the European health authorities. Eur Heart J 2010; DOI: 10.1093/eurheartj/ehq370.
Hsia J, MacFayden JG, Monyak J, Ridker PM. Cardiovascular event reduction and adverse events among subjects attaining low-density lipoprotein cholesterol <50 mg/dL with rosuvastatin. (JUPITER) J Am Coll Cardiol 2011; 57: 1666-1675.
Vidt Donald G., Ridker Paul M., Monyak JT, et al. Longitudinal Assessment of Estimated **Glomerular Filtration Rate** in Apparently Healthy Adults: A Post hoc Analysis from the JUPITER Study (Justification for the Use of Statins in Prevention: An Intervention Trial Evaluating Rosuvastatin). Clinical Therapeutics, Volume 33, Issue 6, June 2011, Pages 717-725, ISSN 0149-2918, DOI: 10.1016/j.clinthera.2011.05.004.
Novack V, Macfadyen J, Malhotra A, et al. The effect of rosuvastatin on **incident pneumonia**: results from the JUPITER trial. CMAJ. 2012 Mar 19.
RxFiles JUPITER Trial Overview: http://www.rxfiles.ca/rxfiles/uploads/documents/Lipid-Jupiter-trial-overview.pdf
60. Fellström BC, Jardine AG, Schmieder RE, et al. the **AURORA** Study Group. Rosuvastatin and Cardiovascular Events in Patients Undergoing Hemodialysis. N Engl J Med. 2009 Mar 30. [Epub ahead of print] In patients undergoing hemodialysis, the initiation of treatment with rosuvastatin lowered the LDL cholesterol level but had no significant effect on the composite primary end point of death from cardiovascular causes, nonfatal myocardial infarction, or nonfatal stroke.
61. Mills EJ, Rachlis B, et al. **Primary prevention** of cardiovascular mortality and events with statin treatments: a network meta-analysis involving more than 65,000 patients. J Am Coll Cardiol. 2008 Nov 25;52(22):1769-81.
62. Brugts J, Yetgin T, Hoeks S, Gotto A, et al. The benefits of statins in people **without** established **cardiovascular disease** but with cardiovascular risk factors: meta-analysis of RCTs. BMJ 2009;338:2376. http://www.bmj.com/cgi/content/abstract/338/jun30_1/b2376

InfoPoems: Lowering cholesterol in 173 patients at risk for developing cardiovascular disease for slightly more than 4 years prevented 1 of them from dying prematurely. One major coronary event was prevented for every 81 patients, and one cerebrovascular event was prevented for every 245 patients treated. (LOE = 1a)

63. Connor A, Tomson C. Should statins be prescribed for **primary prevention** of cardiovascular disease in patients with **chronic kidney disease**? BMJ. 2009 Aug 20;339:b2949. doi: 10.1136/bmj.b2949.
64. Schouten O, Boersma E, Hoeks SE, et al. Dutch Echocardiographic Cardiac Risk Evaluation Applying Stress Echocardiography Study Group. Fluvastatin and perioperative events in patients undergoing vascular surgery. (**Decrease III**) N Engl J Med. 2009 Sep 3;361(10):980-9. In patients undergoing vascular surgery, perioperative fluvastatin therapy was associated with an improvement in postoperative cardiac outcome.
65. Brown BG, Zhao XQ, Chait A, et al. Simvastatin and niacin, antioxidant vitamins, or the combination for the prevention of coronary disease. (**HATS**) N Engl J Med. 2001 Nov 29;345(22):1583-92.
66. Abourbih S, Filion KB, Joseph L, Schiffrin EL, Rinfret S, Poirier P, Pilote L, Genest J, et al. Effect of **fibrates** on lipid profiles and cardiovascular outcomes: a systematic review. Am J Med. 2009 Oct;122(10):962.e1-8. Epub 2009 Aug 19.
67. Sharma M, Ansari MT, Abou-Setta AM, et al. Systematic review: comparative effectiveness and harms of combination therapy and **monotherapy** for dyslipidemia. Ann Intern Med. 2009 Nov 3;151(9):622-30.
68. Navaneethan SD, Pansini F, Perkovic V, et al. HMG CoA reductase inhibitors (statins) for people with **chronic kidney disease not requiring dialysis**. Cochrane Database Syst Rev. 2009 Apr 15;(2):CD007784.
69. Taylor AJ, Villines TC, Stanek EJ, et al. Extended-Release Niacin or Ezetimibe and Carotid Intima-Media Thickness. (**ARBITER 6-HALTS**) N Engl J Med. 2009 Nov 15. [Epub ahead of print].
70. Chan KL, Teo K, Dumesnil JG, et al. Effect of lipid lowering with rosuvastatin on progression of aortic stenosis. (**Astronomer**) Circulation 2010; 121: 306-314.
71. Navaneethan SD, Nigwekar SU, Perkovic V, Johnson DW, Craig JC, Strippoli GF. HMG CoA reductase inhibitors **(statins) for dialysis** patients. Cochrane Database Syst Rev. 2009;(2):CD004289.
72. Navaneethan SD, Perkovic V, Johnson DW, Nigwekar SU, Craig JC, Strippoli GF. HMG CoA reductase inhibitors **(statins) for kidney transplant** recipients. Cochrane Database Syst Rev. 2009;(2):CD005019.
73. **ACCORD** Study Group, Effects of Combination **Lipid** Therapy (**simvastatin** with fenofibrate) in Type 2 Diabetes Mellitus. N Engl J Med 2010 0: NEJMoa1001282.
74. Triglyceride Coronary Disease Genetics Consortium and Emerging Risk Factors Collaboration, Sarwar N, Sandhu MS, Ricketts SL et al. **Triglyceride**-mediated pathways and coronary disease: collaborative analysis of 101 studies. Lancet. 2010 May 8;375(9726):1634-9.
75. Jun M, Foote C, Lv J et al. Effects of **fibrates** on cardiovascular outcomes: a systematic review and meta-analysis. Lancet. 2010 May 10.
76. Vuorio A, Kuoppala J, Kovanen PT, Humphries SE, et al. **Statins for children with familial hypercholesterolemia**. Cochrane Database of Systematic Reviews 2010, Issue 7. Art. No.: CD006401.
Statin treatment is an efficient lipid-lowering therapy in children with familial hypercholesterolemia. It seems to be safe in the short term but long-term safety is unknown. Children treated with statins should be carefully followed up by their pediatricians. Large long-term randomized controlled trials are needed to establish the long-term safety of statins.
77. Buchwald H, Rudser KD, Williams SE, et al. Overall mortality, incremental life expectancy, and cause of death at 25 years in the program on the **surgical control of the hyperlipidemias**. Ann Surg. 2010 Jun;251(6):1034-40.
78. McGuinness B, O`Hare J, Craig D, et al. Statins for the treatment of **dementia**. Cochrane Database Syst Rev. 2010 Aug 4;8:CD007514. There is insufficient evidence to recommend statins for the treatment of dementia. Analysis from the studies available, including one large RCT, indicate statins have no benefit on the outcome measures ADAS-Cog or MMSE. We need to await full results from CLASP 2008 before we can be certain.
79. Marrs JC, Saseen JJ. Effects of lipid-lowering therapy on reduction of cardiovascular events in patients with **end-stage renal disease requiring hemodialysis**. Pharmacotherapy. 2010 Aug;30(8):823-9.
80. Study of the Effectiveness of Additional Reductions in Cholesterol and Homocysteine (**SEARCH**) Collaborative Group. Intensive lowering of LDL cholesterol with 80 mg versus 20 mg simvastatin daily in 12 064 survivors of myocardial infarction: a double-blind randomised trial. The Lancet, Early Online Publication, 9 November 2010 doi:10.1016/S0140-6736(10)60310-8.
81. Cholesterol Treatment Trialists' (**CTT**) Collaboration. Efficacy and safety of more intensive lowering of LDL cholesterol: a meta-analysis of data from 170 000 participants in 26 randomised trials. The Lancet, Early Online Publication, 9 November 2010. doi:10.1016/S0140-6736(10)61350-5. In this analysis of patient data pooled from multiple studies, intensive statin therapy was more effective than less intensive statin therapy in reducing the rate of major cardiovascular events. Additionally, statins are more effective than controls in preventing major cardiovascular events. In spite of the authors' attempts to link these data to low-density lipoprotein (LDL) concentrations, none of the trials randomly assigned patients to specific LDL targets. (LOE = 1a) These authors pooled the patient-level data from 26 studies each involving at least 1000 patients and having at least 2 years of follow-up. Five of the trials compared intensive statin therapy with less intensive statin therapy and 21 compared statins with controls. Of the 5 trials comparing statin intensity, 2 evaluated 8659 patients with acute coronary syndromes (2.1 years of follow-up) and 3 evaluated 30,953 patients with stable coronary artery disease (5.8 years of follow-up). After 1 year of treatment, the LDL cholesterol levels decreased by an average 0.51 mmol/L (20 mg/dL). The annual rate of major vascular events cardiovascular death, nonfatal myocardial infarction, revascularization, or stroke) was 4.5% in the intensive therapy group and 5.3% in the less intense therapy group (number needed to treat [NNT] = 200 per year). Of the 14 trials comparing statin therapy with control (128,596 patients with 4.8 years of follow-up), 6 appear to be primary prevention studies and the remainder were for secondary prevention. In these 14 studies, after 1 year of treatment the LDL cholesterol levels decreased by 1.07 mmol/L (41 mg/dL). The annual rate of major vascular events was 2.8% in the patients taking statins compared with 3.6% in patients taking a control agent (NNT = 125 per year). Although they don't report the annual rate of death from any cause for each treatment group, the authors report the total death rate for the intensively treated patients plus the statin-treated patients (2.1%) compared with the rate of the less intensively treated patients plus control patients (2.3%). This works out to a number needed to treat of 500 per year. The authors also try to correlate the outcomes data with the LDL levels achieved by the various interventions. However, since none of the trials actually randomized patients to specific lipid targets, this information should be interpreted cautiously and is best used to generate hypotheses. If you subscribe to the lipid theory of atherogenesis, you will love this part of the study. If you subscribe to alternate theories (eg, inflammation, plaque stability, and so forth) or are a methodologic purist, you will be annoyed by the authors' extrapolations.
82. **SHARP** Collaborative Group. Study of Heart and Renal Protection (SHARP): Randomized trial to assess the effects of lowering low-density lipoprotein cholesterol among 9438 patients with chronic kidney disease. Am Heart J 2010; DOI:10.1016/j.ahj.2010.08.012. (Ezetimibe 10mg / simvastatin 20mg vs placebo)
Baigent C, Landray MJ, Reith C, et al. The effects of lowering LDL cholesterol with simvastatin plus ezetimibe in patients with chronic kidney disease (Study of Heart and Renal Protection-**SHARP**): a randomized placebo-controlled trial. Lancet 2011.
Haynes R, Lewis D, Emberson J, et al. Effects of lowering LDL cholesterol (ezetimibe + simvastatin) on progression of **kidney disease** (**Sharp trial**). J Am Soc Nephrol 2014.
Harbin M, Amadio A, Tejani A. Critical Appraisal of the SHARP Trial: The Results May Be Dull. Clin Ther. 2014 Dec 1;36(12):2112-7.
83. Athyros VG, Tziomalos K, Gossios TD, et al. Safety and efficacy of long-term statin treatment for cardiovascular events in patients with coronary heart disease and **abnormal liver tests** in the Greek Atorvastatin and Coronary Heart Disease Evaluation (**GREACE**) Study: A post hoc analysis. Lancet 2010; DOI:10.1016/S0140-6736(10)61272-X.
84. Petersen LK, Christensen K, Kragstrup J. Lipid-lowering treatment to the end? A review of observational studies and RCTs on cholesterol and mortality in **80+-year olds**. Age Ageing. 2010 Nov;39(6):674-80.
85. Taylor F, Ward K, Moore THM, Burke M, Davey Smith G, Casas JP, Ebrahim S. **Statins for the primary prevention** of cardiovascular disease. Cochrane Database of Systematic Reviews 2011, Issue 1. Art. No.: CD004816. DOI: 10.1002/14651858.CD004816.pub4. Although reductions in all-cause mortality, composite endpoints and revascularisations were found with no excess of adverse events, there was evidence of selective reporting of outcomes, failure to report adverse events and inclusion of people with cardiovascular disease. Only limited evidence showed that primary prevention with statins may be cost effective and improve patient quality of life. Caution should be taken in prescribing statins for primary prevention among people at low cardiovascular risk.
86. CDC: Centers for Disease Control & Prevention. **Prevalence, treatment, and control of high levels of low-density lipoprotein cholesterol—United States**, 1999-2002 & 2005-2008. MMWR Morb Mortal Wkly Rep 2011; 60:7-12.
87. Farzadfar F, Finucane MM, et al. **National, regional, and global trends in serum total cholesterol since 1980**: systematic analysis of health examination surveys and epidemiological studies with 321 country-years and 3.0 million participants. Lancet 2011.
88. Rahimi Kazem, Emberson Jonathan, McGale Paul, et al., PWM is acting on behalf of the PROSPER Executive. Effect of **statins on atrial fibrillation**: collaborative meta-analysis of published and unpublished evidence from randomised controlled trials. BMJ 342:doi:10.1136/bmj.d1250 (Published 16 Mar 2011)
89. Jackevicius Cynthia A, Tu Jack V, Ross Joseph S, et al. Use of **Fibrates in the United States and Canada**. JAMA. 2011;305(12):1217-1224.doi:10.1001/jama.2011.353
90. Mills EJ, Wu P, Chong G, et al. Efficacy and safety of statin treatment for cardiovascular disease: a **network meta-analysis** of 170,255 patients from 76 randomized trials. QJM. 2011 Feb;104(2):109-24.
91. Waters, David D., Ho, Jennifer E., DeMicco, David A., et al. Predictors of **New-Onset Diabetes in Patients Treated With Atorvastatin**: Results From 3 Large Randomized Clinical Trials (Ideal, TNT,Sparcl). J Am Coll Cardiol 2011 57: 1535-1545.
92. West AM, Anderson JD, Meyer CH, et al. The effect of **ezetimibe on peripheral arterial atherosclerosis** depends upon statin use at baseline. Atherosclerosis 2011; DOI:10.1016/j.atherosclerosis.2011.04.005.
93. National Institutes of Health. NIH stops clinical trial (**AIM-HIGH**) on combination cholesterol treatment [press release]. May 26, 2011. Available here. A trial of extended-release **niacin** (Niaspan, Abbott) given in addition to statin therapy in patients with a history of cardiovascular disease, high triglycerides, and low levels of HDL cholesterol has been halted prematurely, 18 months ahead of schedule, because niacin offered no additional benefits in this patient population. There was also a small, unexplained increase in ischemic stroke (1.6 vs 0.7%)in the high-dose, extended-release niacin group, in the Atherothrombosis Intervention in Metabolic Syndrome with Low HDL Cholesterol/High Triglyceride and Impact on Global Health Outcomes (AIM-HIGH) study, according to a statement from the **National Heart Lung and Blood Institute** (NHLBI), which sponsored it. N=3414, 32months. AIM-HIGH enrolled 3,414 participants in the US and Canada with a history of cardiovascular disease, low HDL cholesterol, and high triglycerides, who were all prescribed simvastatin and who were also randomized to either high-dose, extended-release niacin in gradually increasing doses up to 2000 mg per day (n=1718) or placebo (n=1696). Of the participants, 515 were given a second LDL-cholesterol-lowering drug, ezetimibe (Zetia, Merck/Schering-Plough), in order to maintain LDL-cholesterol levels at the target range between 40 and 80 mg/dL.
AIM-HIGH investigators. **Niacin** in patients with low HDL cholesterol levels receiving intensive statin therapy. N Engl J Med2011; DOI:10.1056/oa1107579.
Anderson TJ et al. Safety profile of extended-release niacin in the AIM-HIGH trial. N Engl J Med 2014 Jul 17; 371:288.
94. Holdaas H, et al. Assessment of LEscol in Renal Transplantation (**ALERT**) Study Investigators. Effect of fluvastatin on cardiac outcomes in renal transplant recipients: multicentre randomised placebo-controlled trial. Lancet. 2003 Jun 14;361(9374):2024-31.
95. Rossebø AB, Pedersen TR, Boman K, et al. **SEAS** Investigators. Intensive lipid lowering with simvastatin and ezetimibe in aortic stenosis. N Engl J Med. 2008 Sep 25;359(13):1343-56.
Green A, Ramey DR, Emneus M, et al. Incidence of **Cancer and Mortality** in Patients from the Simvastatin and Ezetimibe in Aortic Stenosis (**SEAS**) Trial. Am J Cardiol. 2014 Aug 27.
96. Preiss D, Seshasai SR, Welsh P, et al. Risk of **incident diabetes with intensive-dose compared with moderate-dose statin** therapy. JAMA 2011; 305:2556-2564.
97 n-3 fatty acid trials:
Saravanan P, Davidson NC, Schmidt EB, Calder PC. Cardiovascular effects of **marine omega-3 fatty acids**. Lancet. 2010 Aug 14;376(9740):540-50. Epub 2010 Jul 15.
Gruppo Italiano per lo Studio della Sopravvivenza nell'Infarto Miocardico. Dietary supplementation with n-3 polyunsaturated fatty acids and vitamin E after myocardial infarction: results of the **GISSIPrevenzione** trial. Lancet 1999;354:447- 55.
Pottala JV, Garg S, Cohen BE, Whooley MA, Harris WS. Blood eicosapentaenoic and docosahexaenoic acids predict all-cause mortality in patients with stable coronary heart disease: the Heart and Soul study. Circ Cardiovasc Qual Outcomes 2010;3: 406-12.
Burr ML, Fehily AM, Gilbert JF, et al. Effects of changes in fat, fish, and fibre intakes on death and myocardial reinfarction: Diet and Reinfarction Trial (**DART**). Lancet 1989;2:757-61.

Yokoyama M, Origasa H, Matsuzaki M,et al. Effects of eicosapentaenoic acid on major coronary events in hypercholesterolaemic patients (**JELIS**): a randomised open-label, blinded endpoint analysis. Lancet 2007;369:1090-8.
Tavazzi L, Maggioni AP, Marchioli R, et al. Effect of n-3 polyunsaturated fatty acids in patients with chronic heart failure (the **GISSI-HF** trial): a randomised, doubleblind, placebo-controlled trial. Lancet 2008; 372:1223-30.
Kromhout D, Giltay EJ, Geleijnse JM. n–3 Fatty acids and cardiovascular events after myocardial infarction (**Alpha Omega**). N Engl J Med 2010;363:2015-26.
De Caterina Raffaele. **n–3 Fatty Acids** in Cardiovascular Disease. N Engl J Med 2011; 364:2439-2450.
98. Kawut SM, Bagiella E, Lederer DJ, et al; on behalf of the **ASA-STAT Study** Group. Randomized Clinical Trial of **Aspirin and Simvastatin for Pulmonary Arterial Hypertension**: ASA-STAT. Circulation. 2011 Jun 28;123(25):2985-2993.
99. Liu ZL, Liu JP, Zhang AL, et al. **Chinese herbal medicines** for hypercholesterolemia. Cochrane Database Syst Rev. 2011 Jul 6;7:CD008305. Some herbal medicines may have cholesterol-lowering effects. Our findings have to be interpreted with caution due to high or unclear risk of bias of the included trials.
100. Sano M, Bell KL, Galasko D, et al. A randomized, double-blind, placebo-controlled trial of **simvastatin to treat Alzheimer disease**. Neurology. 2011 Aug 9;77(6):556-63. (no benefit)
101. Lee KH, Jeong MH, Kim HM, et al. Benefit of early statin therapy in patients with acute myocardial infarction who have **extremely low low-density lipoprotein cholesterol**. J Am Coll Cardiol 2011; 58:1664-1671.
102. Tonelli Marcello, Lloyd Anita, Clement F, et al. Efficacy of **statins for primary prevention** in people at low cardiovascular risk: a meta-analysis. CMAJ October 11, 2011 cmaj.101280; published ahead of print October 11, 2011, doi:10.1503/cmaj.101280
103. Schanberg L, Sandborg C, Barnhart HX, Ardoin SP, Yow E, Evans GW, et al. Use of atorvastatin in **systemic lupus erythematosus** in children and adolescents (**APPLE**). Arthritis Rheum 2011
104. Vale N, Nordmann AJ, Schwartz GG, et al. Statins for **acute coronary syndrome**. Cochrane Database of Systematic Reviews 2011, Issue 6. Art. No.: CD006870. DOI: 10.1002/14651858.CD006870.pub2. Based on available evidence, initiation of statin therapy within 14 days following ACS does not reduce death, myocardial infarction, or stroke up to four months, but reduces the occurrence of unstable angina at four months following ACS.
105. Nicholls SJ, Ballantyne CM, Barter PJ, et al. Effect of two intensive statin (**atrovastatin 80mg vs rosuvastatin 40mg**) regimens on progression of coronary disease. (**Saturn**) N Engl J Med 2011; DOI: 10.1056/NEJMoa1110874. SATURN trial, high doses of rosuvastatin and atorvastatin resulted in similar degrees of atherosclerosis regression, despite greater reductions in LDL levels with rosuvastatin.
106. Hayward RA, Krumholz HM. Three reasons to **abandon low-density lipoprotein targets**: an open letter to the Adult Treatment Panel IV of the National Institutes of Health. Circ Cardiovasc Qual Outcomes 2012.
107. Vandermeer ML et al. Association between use of statins and mortality among patients hospitalized with laboratory-confirmed **influenza virus infections**: a multistate study. J Infect Dis. 2012 Jan;205(1):13-9.
108. Kostis WJ, Cheng JQ, Dobrzynski JM, et al. Meta-analysis of **statin effects in women** versus men. J Am Coll Cardiol 2012; 59:572-582.
109. Newson RS, Felix JF, Heeringa J, et al. Association between **serum cholesterol and noncardiovascular mortality in older age**. J Am Geriatr Soc. 2011 Oct;59(10):1779-85.
110. Waubant E, Pelletier D, et al. behalf of the **ITN STAyCIS** Study Group; ITN020AI Study Management Team. Randomized controlled trial of **atorvastatin** in clinically isolated syndrome: The STAyCIS study. Neurology. 2012 Apr 10;78(15):1171-1178.
111. Gutierrez J, Ramirez G, Rundek T, Sacco RL. Statin therapy in the prevention of recurrent cardiovascular events: a **sex-based meta-analysis**. Arch Intern Med. 2012;172(12):909-918.
112. McKinney JS, Kostis WJ. Statin Therapy and the **Risk of Intracerebral Hemorrhage**: A Meta-Analysis of 31 Randomized Controlled Trials. Stroke. 2012 May 15.
113. Natsuaki M, Furukawa Y, Morimoto T, Sakata R, Kimura T; CREDO-Kyoto PCI/CABG Registry Cohort-2 Investigators. **Renal Function and Effect of Statin** Therapy on Cardiovascular Outcomes in Patients Undergoing Coronary **Revascularization** (from the CREDO-Kyoto PCI/CABG Registry Cohort-2). Am J Cardiol. 2012 Dec 1;110(11):1568-77.
114. Jun M, Zhu B, Tonelli M, et al. Effects of **fibrates in kidney disease**, a review and meta-analysis. J Am Coll Cardiol 2012 .
115. **HPS2-THRIVE** Collaborative. HPS2-THRIVE randomized placebo-controlled trial in 25 673 high-risk patients of **ER niacin/laropiprant**: trial design, pre-specified muscle and liver outcomes, and reasons for stopping study treatment. Eur Heart J. 2013 Feb 26.
HPS2-THRIVE Collaborative Group.Effects of **extended-release niacin with laropiprant** in high-risk patients. N Engl J Med 2014 Jul 17; 371:203.
116. Hou W, Lv J, Perkovic V, et al. Effect of **statin** therapy on cardiovascular and renal outcomes in patients with **chronic kidney disease**: a systematic review and meta-analysis. Eur Heart J. 2013 Mar 6.
117. Dormuth CR, Hemmelgarn BR, Paterson JM, et al. Use of **high potency statins** and rates of admission for **acute kidney injury**: multicenter, retrospective observational analysis of administrative databases. BMJ 2013.
118. Kruger P et al. A multicenter randomized trial of atorvastatin therapy in intensive care patients with **severe sepsis**. Am J Respir Crit Care Med 2013 Apr; 187:743.
119. Patel JM, Snaith C, Thickett DR, et al. Randomized double-blind placebo-controlled trial of 40 mg/day of **atorvastatin** in reducing the severity of **sepsis** in ward patients (**ASEPSIS** Trial). Crit Care. 2012 Dec 11;16(6):R231.
120. Wiger KJ, Manalac RJ, Blumenthal RS, et al. **Statins and cognition**: a systematic review and meta-analysis of short- and long-term cognitive effects. Mayo Clin Proc. 2013 Nov;88(11):1213-21
121. Wong WB, Lin VW, Boudreau D, Devine EB. **Statins in the prevention of dementia and Alzheimer's disease**: a meta-analysis of observational studies and an assessment of confounding. Pharmacoepidemiol Drug Saf. 2013 Apr;22(4):345-58.
122. Palmer SC, Navaneethan SD, Craig JC, et al. HMG CoA reductase inhibitors **(statins) for kidney transplant recipients**. Cochrane Database Syst Rev. 2014 Jan 28;1:CD005019. Statins may reduce cardiovascular events in kidney transplant recipients, although treatment effects are imprecise. Statin treatment has uncertain effects on overall mortality, stroke, kidney function, and toxicity outcomes in kidney transplant recipients. Additional studies would improve our confidence in the treatment benefits and harms of statins on cardiovascular events in this clinical setting.
123. Bangalore S, Fayyad R, Hovingh GK, et al; Treating to New Targets Steering Committee and Investigators. **Statin** and the Risk of **Renal-Related Serious Adverse Events**: Analysis from the IDEAL, TNT, CARDS, ASPEN, SPARCL, and Other Placebo-Controlled Trials. Am J Cardiol. 2014 Apr 3
124. Palmer SC, Navaneethan SD, Craig JC, et al. HMG CoA reductase inhibitors **(statins) for dialysis** patients. Cochrane Database Syst Rev. 2013 Sep 11;9:CD004289. Statins have little or no beneficial effects on mortality or cardiovascular events and uncertain adverse effects in adults treated with dialysis despite clinically relevant reductions in serum cholesterol levels.
125. McAuley DF, Laffey JG, O'Kane CM, et al; the **HARP-2** Investigators, for the Irish Critical Care Trials Group. **Simvastatin in the Acute Respiratory Distress Syndrome**. N Engl J Med. 2014 Sep 30.
126. Cholesterol Treatment Trialists' (**CTT**) Collaboration. Efficacy and safety of **LDL-lowering therapy among men and women**: meta-analysis of individual data from 174 000 participants in 27 randomised trials. Lancet 2015;online Jan 9.
127. Mega JL, Stitziel NO, Smith GJ, et al. Genetic risk, coronary heart disease events, and the clinical benefi t of statin therapy: an analysis of primary (Jupiter & Ascot) and secondary (Care & Prove It-Timi 22) prevention trials. Lancet 2015; online March 4.
128. Cannon CP, Blazing MA, Giugliano RP, et al. **Ezetimibe added to statin** therapy after acute coronary syndromes. (**Improve-It**) N Engl J Med. 10.1056/NEJMoa1410489.
Bohula EA, Giugliano RP, Cannon CP, et al. Achievement of dual **low-density lipoprotein** cholesterol and **high-sensitivity C-reactive protein** targets more frequent with the addition of **ezetimibe** to **simvastatin** and associated with better outcomes in **IMPROVE-IT**. Circulation. 2015;132:1224–1233. doi: 10.1161/CIRCULATIONAHA.115.018381
Murphy SA, Cannon CP, Blazing MA, et al. Reduction in Total Cardiovascular Events With **Ezetimibe/Simvastatin** Post-Acute Coronary Syndrome: The **IMPROVE-IT** Trial. J Am Coll Cardiol. 2016 Feb 2;67(4):353-61.
Giugliano RP, Wiviott SD, Blazing MA, et al. **Long-term Safety and Efficacy of Achieving Very Low Levels of Low-Density Lipoprotein Cholesterol** : A Prespecified Analysis of the **IMPROVE-IT** Trial. JAMA Cardiol. 2017 Mar 14.
Giugliano RP, Cannon CP, Blazing MA, et al. Benefit of **Adding Ezetimibe to Statin Therapy** on Cardiovascular Outcomes and Safety in Patients With vs. Without Diabetes: Results from **IMPROVE-IT**. Circulation. 2017 Dec 20.

129. Pandya A, Sy S, Cho S, Weinstein MC, Gaziano TA. **Cost-effectiveness of 10-year risk thresholds for initiation of statin therapy for primary prevention** of cardiovascular disease.JAMA. doi:10.1001/jama .2015.6822.
130. Pursnani A, Massaro JM, D'Agostino RB Sr, et al. **Guideline-based statin eligibility**, coronary artery calcification, and cardiovascular events. JAMA. doi:10.1001/jama .2015.7515.
131. O'Brien EC, Greiner MA, Xian Y, et al. Clinical Effectiveness of **Statin Therapy after Ischemic Stroke**: Primary Results from the Statin Therapeutic Area of the Patient-Centered Research into Outcomes Stroke Patients Prefer and Effectiveness Research (**PROSPER**) Study. Circulation. 2015 Aug 5.
132. Wang D, Liu B, Tao W, Hao Z, Liu M. **Fibrates for secondary prevention** of cardiovascular disease and stroke. Cochrane Database Syst Rev. 2015 Oct 25;10:CD009580. Moderate evidence showed that the fibrate class can be effective in the secondary prevention of composite outcome of non-fatal stroke, non-fatal MI, and vascular death. However, this beneficial effect relies on the inclusion of clofibrate data, a drug that was discontinued in 2002 due to its unacceptably large adverse effects. Further trials of the use of fibrates in populations with previous stroke and also against a background treatment with statins (standard of care) are required.
133. Nissen SE, Stroes E, Dent-Acosta RE, et al. Efficacy and tolerability of **evolocumab vs ezetimibe** in patients with **muscle-related statin intolerance**: the **GAUSS-3** randomized clinical trial. JAMA. doi:10.1001/jama.2016.3608.
134. O'Brien EC, Wu J, Schulte PJ, et al. **Statin use**, intensity, and 3-year clinical outcomes among **older patients** with coronary artery disease. Am Heart J. 2016 Mar;173:27-34.
135. Yusuf S, Bosch J, Dagenais G, et al. Cholesterol lowering in intermediate-risk persons without cardiovascular disease. (**Hope-3**) N Engl J Med. DOI: 10.1056/NEJMoa1600176.
Ridker PM, Lonn E, Paynter NP, et al. **Primary Prevention** With Statin Therapy in the **Elderly**: New Meta-Analyses from the Contemporary **JUPITER** and **HOPE-3** Randomized Trials. Circulation. 2017 Apr 6.
136. **USPSTF**: US Preventive Services Task Force. **Statin use for the primary prevention** of cardiovascular disease in adults: US Preventive Services Task Force **recommendation** statement.JAMA. doi:10.1001 /jama.2016.15450
137. Chou R, Dana T, Blazina I, et al. Screening for Dyslipidemia in Younger Adults: A **Systematic Review** for the U.S. Preventive Services Task Force (**USPSTF**). Ann Intern Med. 2016 Oct 18;165(8):560-564.
138. Ridker PM, Lonn E, Paynter NP, Glynn R, Yusuf S. **Primary Prevention With Statin Therapy in the Elderly**: New Meta-Analyses from the Contemporary **JUPITER** and **HOPE-3** Randomized Trials. Circulation. 2017 Apr 6.
139. Schandelmaier S, Briel M, Saccilotto R, Olu KK, Arpagaus A, Hemkens LG, Nordmann AJ. **Niacin for primary and secondary prevention** of cardiovascular events. Cochrane Database of Systematic Reviews 2017, Issue 6. Art. No.: CD009744.
140. **HPS3/TIMI55-REVEAL** Collaborative Group Effects of **Anacetrapib** in Patients with Atherosclerotic Vascular Disease. N Engl J Med. 2017 Aug 28.
141. Sabatine MS, Giugliano RP, Keech AC, et al. **Evolocumab** and clinical outcomes in patients with cardiovascular disease. (**Fourier**) N Engl J Med 2017
142. Hong SJ, Jeong HS, Ahn JC, et al. A Phase III, Multicenter, Randomized, Double-blind, Active Comparator Clinical Trial to Compare the Efficacy and Safety of Combination Therapy With **Ezetimibe and Rosuvastatin Versus Rosuvastatin Monotherapy** in Patients With Hypercholesterolemia: **I-ROSETTE** (Ildong Rosuvastatin & Ezetimibe for Hypercholesterolemia) Randomized Controlled Trial. Clin Ther. 2018 Feb;40(2):226-241.e4.
143. Cholesterol Treatment Trialists' (**CTT**) Collaboration. Efficacy and safety of **statin therapy in older people**: a meta-analysis of individual participant data from 28 randomised controlled trials. Lancet 2019; 393: 407–15.

See: Updated current FULL version on the **WEB** at **http://www.rxfiles.ca/rxfiles/uploads/documents/members/CHT-CVD-risk-table.pdf** or see page 2 in the RxFiles Drug Comparison Chart **BOOK**.

Historical notes: **Agents**: **↑↑LDL⇨HMG** +/- resin +/-ezetimibe; **↑↑LDL & ↑TG⇨HMG**; **↑↑LDL & ↓HDL⇨HMG** +/- fibrate/niacin; **Normal LDL & ↑↑TG**⇨fibrate/niacin/omega 3 fatty acid [23] or combo; **Normal LDL & ↓HDL**⇨fibrate/niacin or combo

LIPID LOWERING THERAPY: DYSLIPIDEMIA Comparison Chart

[1] Fodor JG, Frohlich JJ, Jacques JG et al. **Canadian** Recommendations for the management and treatment of dyslipidemia. CMAJ **2000**;162:1441-7.

[2] NCEP Expert Panel. Executive summary-3rd national cholesterol education program on detection, evaluation and treatment of high blood cholesterol in adults (**A**dult **T**reatment **P**anel **III**). JAMA **2001**;285:2486-97. Implications of Recent Clinical Trials for the NCEP ATP Panel III (ATP3) Guidelines July **2004** http://www.acc.org/clinical/adoptions/ncep_report.pdf

Ford ES, Li C, Zhao G, Pearson WS, Mokdad AH. **Hypertriglyceridemia** and its pharmacologic treatment among US adults. Arch Intern Med. 2009 Mar 23;169(6):572-8.

Stone NJ et al. **2013 ACC/AHA guideline** on the treatment of blood cholesterol to reduce atherosclerotic cardiovascular risk in adults: A report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. J Am Coll Cardiol 2013 Nov 12. (AHA-ACC ASCVD risk calculator 2013 http://my.americanheart.org/professional/StatementsGuidelines/PreventionGuidelines/Prevention-Guidelines_UCM_457698_SubHomePage.jsp)

Grundy SM, Stone NJ, Bailey AL, et al. **2018 AHA/ACC**/AACVPR/AAPA/ABC/ACPM/ADA/AGS/APhA/ASPC/NLA/PCNA Guideline on the **Management of Blood Cholesterol**: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. J Am Coll Cardiol. 2018 Nov 8.

Grundy SM, Stone NJ, Bailey AL, et al. **2018 AHA/ACC**/AACVPR/AAPA/ABC/ACPM/ADA/AGS/APhA/ASPC/NLA/PCNA Guideline on the **Management of Blood Cholesterol: Executive Summary**: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. J Am Coll Cardiol. 2018 Nov 3.

Wilson PWF, Polonsky TS, Miedema MD, et al. **Systematic Review for the 2018 AHA/ACC**/AACVPR/AAPA/ABC/ACPM/ADA/AGS/APhA/ASPC/NLA/PCNA Guideline on the **Management of Blood Cholesterol**: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. J Am Coll Cardiol. 2018 Nov 3.

[3] Knopp RH. Drug treatment of lipid disorders. N Eng J Med 1999;341:498-511.(Gibson K, Rindone JP. Experience with statin use in patients with chronic **hepatitis C infection**. Am J Cardiol. 2005 Nov 1;96(9):1278-9. Epub 2005 Sep 8)

[4] Davidson MH. Safety profiles for the HMG-CoA Reductase Inhibitors. Drugs 2001;61:197-206

[5] Link N, Tanner M. Hyperlipidemia: Part 1. Evaluation and dietary management. WJM 2001;175:246-250.

[6] Link N, Tanner M. Hyperlipidemia: Part 2. Pharmacologic management. WJM 2001;175:396-401.

[7] Anonymous. Choice of lipid-regulating drugs. Med Lett 2001;43:43-48.

Onofrei MD, et al. Safety of statin therapy in patients with preexisting liver disease. Pharmacotherapy. 2008 Apr;28(4):522-9.

Athyros VG, Tziomalos K, Gossios TD, et al. Safety and efficacy of long-term statin treatment for cardiovascular events in patients with coronary heart disease and **abnormal liver tests** in the Greek Atorvastatin and Coronary Heart Disease Evaluation (**GREACE**) Study: A post hoc analysis. Lancet 2010; DOI:10.1016/S0140-6736(10)61272-X.

Gillett RC Jr, Norrell A. Considerations for safe use of statins: **liver enzyme abnormalities and muscle toxicitiy**. Am Fam Physician. 2011 Mar 15;83(6):711-6.

[8] **Treatment Guidelines**: **Drugs for Lipids**. **The Medical Letter**: August, **2003**; (12) pp. 77-82 & March, **2005**; (3;31) pp. 15-22. Feb **2008** pages 9-16. Mar **2011**. Updated Jan **2014**. Updated Oct **2016**, Updated **Feb 2019**. Micromedex 2016; Drugs in Pregnancy and Lactation, 9th ed. Briggs GE, Freeman RK, Yaffe SJ, editors. Williams and Wilkins; Baltimore, MD: 2011.; Hansten & Horn-Drug Interactions 2005.

[9] Rizvi K, Hampson JP, Harvey JN. Do lipid-lowering drugs cause erectile dysfunction? A systematic review. Fam Pract 2002;19(1):95-8.

[10] Thompson PD, Clarkson P, Karas RH. Statin-associated **myopathy**. JAMA. 2003 Apr 2;289(13):1681-90. (Hansen KE, Hildebrand JP, Ferguson EE, Stein JH. Outcomes in 45 patients with statin-associated myopathy. Arch Intern Med. 2005 Dec 26;165(22):2671-6.) The SEARCH Collaborative Group. SLCO1B1 Variants and Statin-Induced Myopathy -- A Genomewide Study. N Engl J Med. 2008 Jul 23. [Epub ahead of print] We have identified common variants in **SLCO1B1** that are strongly associated with an increased risk of statin-induced **myopathy**. Genotyping these variants may help to achieve the benefits of statin therapy more safely and effectively.

Sathasivam S, Lecky B. Statin induced myopathy. BMJ. 2008 Nov 6;337:a2286. doi: 10.1136/bmj.a2286.

Joy T. R., Hegele R. A. Narrative Review: Statin-Related Myopathy. Ann Intern Med 2009; 858-868.

Mohaupt MG, Karas RH, Babiychuk EB, et al. Association between statin-associated myopathy and skeletal muscle damage. CMAJ. 2009 Jul 7;181(1-2):E11-8.

Voora D, Shah SH, Spasojevic I, Ali S, Reed CR, Salisbury BA, Ginsburg GS. The SLCO1B1*5 genetic variant is associated with statin-induced side effects. J Am Coll Cardiol. 2009 Oct 20;54(17):1609-16.

Bre wer HB Jr. Benefit -risk assessment of rosuvastatin 10 to 40 milli gram s. Am J Cardiol 2003; 92(suppl):23K–29K.

Fernandez G, Spatz ES, Jablecki C et al. **Statin myopathy**: A common dilemma not reflected in clinical trials Cleveland Clinic Journal of Medicine 2011; 78(6):393-403; doi:10.3949/ccjm.78a.10073

Mammen AL, Chung T, Christopher-Stine L, et al. **Autoantibodies** against 3-hydroxy-3-methylglutaryl-coenzyme a reductase (**HMGCR**) in patients with statin-associated autoimmune myopathy. Arthritis Rheum. 2010 Nov 19.

Lasker SS, Chowdhury TA. Myalgia while taking statins. BMJ. 2012 Aug 14;345:e5348.

Parker BA, Capizzi JA, Grimaldi AS, et al. The effect of statins on skeletal muscle function. (**STOMP**) Circulation 2012 .

Stroes ES, Thompson PD, Corsini A, et al. **European Atherosclerosis Society Consensus** Panel. Statin-associated muscle symptoms: impact on statin therapy-European Atherosclerosis Society Consensus Panel Statement on Assessment, Aetiology and Management. Eur Heart J. 2015 May 1;36(17):1012-22.

Mammen AL. **Statin-Associated Autoimmune Myopathy**. N Engl J Med. 2016 Feb 18;374(7):664-9.

[11] Herman, RJ. Drug interactions and the statins. CMAJ 1999;161:1281-6.

[12] Carswell CI, Plosker GL, Jarvis B. Rosuvastatin. Drugs. 2002;62(14):2075-85; discussion 2086-7.

[13] Rosuvastatin--a new lipid-lowering drug. Med Lett Drugs Ther. 2003 Oct 13;45(1167):81-3. Approved in Canada in 2003.

Ridker PM, Danielson E, Fonseca FA, Genest J, et al. the **JUPITER** Study Group. Rosuvastatin to Prevent Vascular Events in Men and Women with Elevated C-Reactive Protein. N Engl J Med. 2008 Nov 9. [Epub ahead of print] In this trial of apparently healthy persons without hyperlipidemia but with elevated high-sensitivity C-reactive protein levels, rosuvastatin significantly reduced the incidence of major cardiovascular events.

Glynn RJ, Danielson E, Fonseca FA, Genest J, et al. A Randomized Trial of Rosuvastatin in the Prevention of Venous **Thromboembolism**. (Jupiter) N Engl J Med. 2009 Mar 29. [Epub ahead of print]

Koenig W, Ridker PM. Rosuvastatin for primary prevention in patients with European systematic coronary risk evaluation **risk >5% or Framingham risk >20%:** Post hoc analyses of the JUPITER trial requested by the European health authorities. Eur Heart J 2010; DOI: 10.1093/eurheartj/ehq370.

[14] Alsheikh-Ali AA, Ambrose MS, Kuvin JT, Karas RH. The Safety of Rosuvastatin as Used in Common Clinical Practice. A Postmarketing Analysis. Circulation. 2005 May 23; [Epub ahead of print] (InfoPOEMs: The United States Federal Drug Administration (FDA), Health Canada, and European regulators have recently issued advisories to physicians regarding higher doses of rosuvastatin. These data -- though inherently limited by their voluntary nature and the possibility of reporting bias -- lend credence to concerns that rosuvastatin is less safe than other statins. It is also the only statin for which we do not have patient-oriented outcome data. (LOE = 2c))

[15] Jones P, et al. Comparative dose efficacy study of atorvastatin versus simvastatin, pravastatin, lovastatin and fluvastatin in patients with hypercholesterolemia (The **CURVES** study). Am J Cardiol 1998;81:582-7.

[16] Three new drugs for hyperlipidemia. Med Lett Drugs Ther. 2003 Mar 3;45(1151):17-9.

Bays HE, Moore PB, Drehobl MA, et al. Effectiveness and tolerability of ezetimibe in patients with primary hypercholesterolemia: pooled analysis of two phase II studies. *Clin Ther* 2001; 23:1209-30. (**low dose reduces LDL**)

[17] Grundy SM, Vega GL, McGovern ME, et al. Diabetes Multicenter Research Group. Efficacy, safety, and tolerability of once-daily niacin for the treatment of dyslipidemia associated with type 2 diabetes: results of the assessment of diabetes control and evaluation of the efficacy of niaspan trial. Arch Intern Med. 2002 Jul 22;162(14):1568-76.

[18] Elam MB, Hunninghake DB, Davis KB, et al. Effect of niacin on lipid and lipoprotein levels and glycemic control in patients with diabetes and peripheral arterial disease: the **ADMIT** study: A randomized trial. Arterial Disease Multiple Intervention Trial. JAMA. 2000 Sep 13;284(10):1263-70. (& What You Should Know About **Niacin**. Pharmacist's Letter. Dec, 2005).

Jackevicius CA, Tu JV, Ross JS, et al. Use of niacin in the United States and Canada. JAMA Intern Med 2013.

[19] Jacobson TA. Combination Lipid-Altering Therapy. Current Atherosclerosis Reports 2001;3:373-382.

[20] Mantel-Teeuwisse AK, Kloosterman ME, Maitland-van der Zee AH, et al. Drug-induced lipid changes. Drug Safety 2001;24:443-56.

[21] Unintended serum lipid level changes induced by some commonly used drugs. Drugs & Therapy Perspectives 2001; 17(23).

[22] Hayward RA, Hofer TP, Vijan S. Narrative review: lack of evidence for recommended low-density lipoprotein treatment targets: a solvable problem. Ann Intern Med. 2006 Oct 3;145(7):520-30.

[23] Berglund L, Brunzell JD, Goldberg AC, et al. Evaluation and treatment of **hypertriglyceridemia**: an Endocrine Society clinical practice guideline. J Clin Endocrinol Metab 2012; 97:2969.

Din JN, Newby DE, Flapan AD. Omega 3 fatty acids and cardiovascular disease--fishing for a natural treatment. BMJ. 2004 Jan 3;328(7430):30-5. & Omacor (Omega-3- acid Ethyl Esters), Pharmacist's Letter, Oct 2005 & Omega-3 Polyunsaturated Fatty Acids (**Omacor**) for Hypertriglyceridemia. The Medical Letter. Nov 7,2005. p 91-92. (O'Keefe JH Jr, et al. Effects of omega-3 fatty acids on resting heart rate, heart rate recovery after exercise, and heart rate variability in men with healed myocardial infarctions and depressed ejection fractions. Am J Cardiol. 2006 Apr 15;97(8):1127-30. Epub 2006 Mar 3.) (Fish Oil Supplements Medical Letter July 17,2006) (Pharmacists Letter. Omega-3 Fatty Acids: An Update. Aug 2007.)

Brunzell JD. Clinical practice. **Hypertriglyceridemia**. N Engl J Med. 2007 Sep 6;357(10):1009-17.

Saravanan P, Davidson NC, Schmidt EB, Calder PC. Cardiovascular effects of **marine omega-3 fatty acids**. Lancet. 2010 Aug 14;376(9740):540-50. Epub 2010 Jul 15.

Gruppo Italiano per lo Studio della Sopravvivenza nell'Infarto Miocardico. Dietary supplementation with n-3 polyunsaturated fatty acids and vitamin E after myocardial infarction: results of the **GISSIPrevenzione** trial. Lancet 1999;354:447- 55.

Pottala JV, Garg S, Cohen BE, Whooley MA, Harris WS. Blood eicosapentaenoic and docosahexaenoic acids predict all-cause mortality in patients with stable coronary heart disease: the Heart and Soul study. Circ Cardiovasc Qual Outcomes 2010;3: 406-12.

Burr ML, Fehily AM, Gilbert JF, et al. Effects of changes in fat, fish, and fibre intakes on death and myocardial reinfarction: Diet and Reinfarction Trial (**DART**). Lancet 1989;2:757-61.

Yokoyama M, Origasa H, Matsuzaki M,et al. Effects of eicosapentaenoic acid on major coronary events in hypercholesterolaemic patients (**JELIS**): a randomised open-label, blinded endpoint analysis. Lancet 2007;369:1090-8.

Tavazzi L, Maggioni AP, Marchioli R, et al. Effect of n-3 polyunsaturated fatty acids in patients with chronic heart failure (the **GISSI-HF** trial): a randomised, doubleblind, placebo-controlled trial. Lancet 2008; 372:1223-30.

Kromhout D, Giltay EJ, Geleijnse JM. n–3 Fatty acids and cardiovascular events after myocardial infarction (**Alpha Omega**). N Engl J Med 2010;363:2015-26.

De Caterina Raffaele. **n–3 Fatty Acids** in Cardiovascular Disease. N Engl J Med 2011; 364:2439-2450.

[25] Canadian Hypertension Society-**2014 Canadian** Hypertension **Recommendations** Working Group-downloadable Summary & Slides; www.hypertension.ca

[26] **Canadian 2008 Diabetes Guidelines (Sept 2008):** http://www.diabetes.ca/files/cpg2008/cpg-2008.pdf

Canadian 2003 Diabetes Guidelines http://www.diabetes.ca/cpg2003/download.aspx (Meltzer S, Leiter L, Daneman D, et al 1998. Clinical practice guidelines for the management of diabetes in Canada. CMAJ 1998;159 (8 Suppl).)

Canadian Diabetes 20013 Guidelines (April 2013): http://guidelines.diabetes.ca/

[27] Brown AF, Mangione CM, Saliba D, Sarkisian CA; California Healthcare Foundation/**American Geriatrics Society** Panel on Improving Care for Elders with Diabetes. Guidelines for improving the care of the older person with diabetes mellitus. J Am Geriatr Soc. **2003** May;51(5 Suppl Guidelines):S265-80.

28. Nissen S, Tuzcu E, et al. Effect of Intensive Compared With Moderate Lipid-Lowering Therapy on Progression of Coronary Atherosclerosis A Randomized Controlled Trial (**REVERSAL**). JAMA. 2004;291:1071-1080.

29. Heart Protection Study (**HPS**) Collaborative Group. Effects of cholesterol-lowering with simvastatin on stroke and other major vascular events in 20 536 people with cerebrovascular disease or other high-risk conditions. Lancet 2004 Mar 6;363(9411): 757-67. Heart Protection Study Group.MRC/BHF **HPS** study of cholesterol lowering with simvastatin in 20,536 high-risk individuals: a randomised placebo-controlled trial. Lancet 2002 Jul 6;360(9326):7-22. (**11,609** of 32,145 pts in 4-6 wk run in treatment with simvastatin 40mg/d **were excluded**)

Heart Protection Study Collaborative Group. Effects on **11-year mortality and morbidity** of lowering LDL cholesterol with simvastatin for about 5 years in 20 536 high-risk individuals: a randomised controlled trial. Lancet 2011; online Nov 23.

30. Cannon CP, Braunwald E, McCabe CH, ET AL. Comparison of Intensive and Moderate Lipid Lowering with Statins after Acute Coronary Syndromes. (**PROVE IT-TIMI 22**) N Engl J Med. 2004 Mar 8 (Ahmed S, Cannon CP, Murphy SA, Braunwald E. Acute coronary syndromes and **diabetes**: Is intensive lipid lowering beneficial? Results of the **PROVE IT-TIMI 22** trial. Eur Heart J. 2006 Oct;27(19):2323-9. Epub 2006 Sep 5.)

31. Colhoun HM, Betteridge DJ, et al. Primary prevention of cardiovascular disease with atorvastatin in type 2 diabetes in the Collaborative Atorvastatin Diabetes Study (**CARDS**): multicentre randomised placebo-controlled trial. Lancet. 2004 Aug 21;364(9435):685-96. Colhoun HM, Betteridge DJ, Durrington PN, et al.; CARDS Investigators. Effects of Atorvastatin on Kidney Outcomes and Cardiovascular Disease in Patients With Diabetes: An Analysis From the Collaborative Atorvastatin Diabetes Study (CARDS). Am J Kidney Dis. 2009 Jun 18. [Epub ahead of print] A modest beneficial effect of atorvastatin on eGFR, particularly in those with albuminuria, was observed. Atorvastatin did not influence albuminuria incidence. Atorvastatin was effective at decreasing CVD in those with and without a moderately decreased eGFR and achieved a high absolute benefit.

32. Sever PS, Dahlof B, Poulter NR, et al. Prevention of coronary and stroke events with atorvastatin in hypertensive patients who have average or lower-than-average cholesterol concentrations, in the Anglo-Scandinavian Cardiac Outcomes Trial--Lipid Lowering Arm (**ASCOT-LLA**): a multicentre randomised controlled trial. Lancet. 2003 Apr 5;361(9364):1149-58.

Sever PS, et al. The Anglo-Scandinavian Cardiac Outcomes Trial lipid lowering arm: extended **observations 2 years** after trial closure. Eur Heart J. 2008 Feb;29(4):499-508. Epub 2008 Jan 5. Carry-over benefits from those originally assigned atorvastatin but no longer taking the drug may account for unchanged relative risk reductions in most cardiovascular endpoints observed 2 years after ASCOT-LLA closed.

Sever PS, Poulter NR, Dahlof B, et al.; the ASCOT investigators. Antihypertensive therapy and the benefits of atorvastatin in the Anglo-Scandinavian Cardiac Outcomes Trial: lipid-lowering arm extension. J Hypertens. 2009 Mar 21. [Epub ahead of print]

33. De Lemos et al. Early Intensive vs a Delayed Conservative Simvastatin Strategy in Patients with Acute Coronary Syndromes Phase Z of the **A to Z Trial** JAMA. 2004 Sept 15;292 (11):1307-16.

34. LaRosa JC. et al. Intensive Lipid Lowering with Atorvastatin in Patients with Stable Coronary Disease (**TNT**) . N Engl J Med. 2005 Mar 8;352 online. (InfoPOEMs: The benefit of intensive lipid therapy in patients with known heart disease is very modest: a number needed to treat (NNT) of 45 for 5 years to prevent any cardiovascular outcome. There was no difference in all-cause mortality between intensive and less intensive treatment groups (5.6% vs 5.7%), and the study was large enough and long enough to be able to detect such a benefit if one existed. Since the benefit of lipid lowering is greatest in patients with known disease, any benefit is certainly much less lower for patients without known disease who are at much lower risk. (LOE = 1b)) (**5461** of 15,464 pts in 8 wk open-label treatment with atorvastatin 10mg/d **were excluded**)

McGowan MP; Treating to New Target (TNT) Study Group. There is no evidence for an increase in acute coronary syndromes after short-term abrupt discontinuation of statins in stable cardiac patients. Circulation. 2004 Oct 19;110(16):2333-5. Epub 2004 Oct 11. Shepherd J, et al. Effect of lowering LDL cholesterol substantially below currently recommended levels in patients with coronary heart disease and **diabetes**: the Treating to New Targets (TNT) study. Diabetes Care. 2006 Jun;29(6):1220-6. (Deedwania P, et al. Treating to New Targets Investigators. Reduction of low-density lipoprotein cholesterol in patients with coronary heart disease and **metabolic syndrome**: analysis of the Treating to New Targets study. Lancet. 2006 Sep 9;368(9539):919-28.) Wenger NK, Lewis SJ, Herrington DM, Bittner V, Welty FK; Treating to New Targets Study Steering Committee and Investigators. Outcomes of using high- or low-dose atorvastatin in patients **65 years of age or older** with stable coronary heart disease. Ann Intern Med. 2007 Jul 3;147(1):1-9. The analysis suggests that additional clinical benefit can be achieved by treating older patients with CHD more aggressively to reduce low-density lipoprotein cholesterol levels to less than 2.6 mmol/L (<100 mg/dL). The findings support the use of intensive low-density lipoprotein cholesterol-lowering therapy in high-risk older persons with established cardiovascular disease. Larosa JC, Grundy SM, Kastelein JJ, Kostis JB, Greten H; Treating to New Targets (TNT) Steering Committee and Investigators. Safety and Efficacy of Atorvastatin-Induced Very Low-Density Lipoprotein Cholesterol Levels in Patients With Coronary Heart Disease (a Post Hoc Analysis of the Treating to New Targets [TNT] Study). Am J Cardiol. 2007 Sep 1;100(5):747-52. Epub 2007 Jun 14. In conclusion, the present analysis adds support to the concept that for patients with established atherosclerotic cardiovascular disease, a further risk reduction without sacrifice of safety can be achieved by reducing LDL cholesterol to very low levels. (Barter P, Gotto AM, LaRosa JC, et al; Treating to New Targets Investigators (TNT). **HDL cholesterol, very low levels of LDL cholesterol**, and cardiovascular events. N Engl J Med. 2007 Sep 27;357(13):1301-10. In this post hoc analysis, HDL was predictive of major cardiovascular events in patients treated with statins. This relationship was also observed among patients with LDL cholesterol levels below 70 mg per deciliter.)

Wenger NK, Lewis SJ, Welty FK, Herrington DM, Bittner V. Beneficial effects of aggressive LDL cholesterol lowering in **women** with stable coronary heart disease in the Treating to New Targets (TNT) study. Heart. 2007 Dec 10; [Epub ahead of print] Conclusion Intensive lipid-lowering treatment with atorvastatin 80 mg produced significant reductions in relative risk for major cardiovascular events compared with atorvastatin 10 mg in both women and men

Targets) study. J Am Coll Cardiol. 2008 Apr 15;51(15):1448-54. [PubMed - in process] Aggressive lipid lowering with atorvastatin 80 mg was both safe and effective in reducing the excess of cardiovascular events in a high-risk population with CKD and CHD.
35. Ko DT, Mamdani M, Alter DA. Lipid-lowering therapy with statins in high-risk elderly patients: the treatment-risk paradox. JAMA. 2004 Apr 21;291(15):1864-70.
36. Wei L, Ebrahim S, Bartlett C, ET AL. Statin use in the secondary prevention of coronary heart disease in primary care: cohort study and comparison of inclusion and outcome with patients in randomised trials. BMJ. 2005 Apr 9;330(7495):821. Epub 2005 Mar 24.
37. Douglas G. Manuel, Peter Tanuseputro, Cameron Aet al. The 2003 Canadian recommendations for dyslipidemia management: Revisions are needed. CMAJ 2005 172: 1027-1031; doi:10.1503/cmaj.1040202
38. Graham DJ, Staffa JA, et al. Incidence of hospitalized rhabdomyolysis in patients treated with lipid-lowering drugs. JAMA. 2004 Dec 1;292(21):2585-90.(Per year of therapy, the number needed to treat to observe 1 case of rhabdomyolysis was 22,727 for statin monotherapy, 484 for older patients with diabetes mellitus who were treated with both a statin and fibrate, and ranged from 9.7 to 12.7 for patients who were treated with cerivastatin plus fibrate.)
39. Gardner CD, Coulston A, Chatterjee L, Rigby A, Spiller G, Farquhar JW. The effect of a **plant-based diet** on plasma lipids in hypercholesterolemic adults: a randomized trial. Ann Intern Med. 2005 May 3;142(9):725-33.
40. Sever PS, Poulter NR, Dahlof B, et al. Reduction in Cardiovascular Events With Atorvastatin in 2,532 Patients With Type 2 Diabetes: Anglo-Scandinavian Cardiac Outcomes Trial-Lipid-Lowering Arm (ASCOT-LLA). Diabetes Care. 2005 May;28(5):1151-1157.
41. Marco Studer, MD; Matthias Briel, MD; Bernd Leimenstoll, MD; et al. Effect of Different Antilipidemic Agents and Diets on Mortality -A Systematic Review. Arch Intern Med. 2005;165:725-730. (InfoPOEMs: Only statin lipid-lowering drugs have been shown to decrease overall mortality in patients with high cholesterol but without evidence of heart disease. However, most patients treated with one of these drugs will not benefit: 228 have to be treated for 3.3 years to prevent 1 additional death during this period. In patients with known heart disease, statins and fish oil both have been shown to decrease mortality. Niacin, resins, and diet have not been shown to decrease mortality. Fibrates (gemfibrozil and others) actually increase overall mortality and at the same time decrease cardiac mortality. (LOE = 1a))
42. Health Canada Warning July/05 for muscle related side effects possible with all statins http://www.hc-sc.gc.ca/english/protection/warnings/2005/2005_77.html
43. Rea TD, Breitner JC, Psaty BM, et al. Statin use and the risk of incident **dementia**: the cardiovascular health study. Arch Neurol. 2005 Jul;62(7):1047-51. CONCLUSIONS: In this cohort study, statin therapy was not associated with a decreased risk of dementia. (InfoPOEMs: In this prospective study, patients older than 65 years old taking statins developed dementia at the same rate as those not using statins. (LOE = 2b))
44. InfoPOEMs July, 2005. More adverse events with rosuvastatin than other statins. Bottom line: The United States Federal Drug Administration (FDA), Health Canada, and European regulators have recently issued advisories to physicians regarding higher doses of rosuvastatin. These data -- though inherently limited by their voluntary nature and the possibility of reporting bias- lend credence to concerns that rosuvastatin is less safe than other statins. It is also the only statin for which we do not have patient-oriented outcome data. (LOE = 2c). *Circulation 2005;111:3051-57.*
45. Wanner C, Krane V, Marz W, et al.; German Diabetes and Dialysis Study Investigators (4D). Atorvastatin in patients with type 2 diabetes mellitus undergoing hemodialysis. N Engl J Med. 2005 Jul 21;353(3):238-48.

Other articles:

Abaci O, Arat Ozkan A, Kocas C, et al. Impact of **rosuvastatin on contrast-induced acute kidney injury** in patients at high risk for nephropathy undergoing elective angiography. Am J Cardiol. 2015 Apr 1;115(7):867-71.
Abdallah MS, Kosiborod M, Tang F, et al. Patterns and predictors of **intensive statin therapy** among patients with **diabetes mellitus after acute myocardial infarction**. Am J Cardiol. 2014 Apr 15;113(8):1267-72.
Abdullah SM, Defina LF, Leonard D, et al. Longterm association of **LDL cholesterol with cardiovascular mortality** in individuals at low 10-year risk of atherosclerotic cardiovascular disease: results from the Cooper Center Longitudinal Study. Circulation. 2018;138:xx–xx.
Aberg JA, Sponseller CA, Ward DJ, et al. **Pitavastatin versus pravastatin** in adults with **HIV**-1 infection and dyslipidaemia (**INTREPID**): 12 week and 52 week results of a phase 4, multicentre, randomised, double-blind, superiority trial. Lancet HIV 2017; DOI:10.1016/S2352-3018(17)30075-9.
Abourbih S, Filion KB, Joseph L, Schiffrin EL, Rinfret S, Poirier P, Pilote L, et al. Effect of **fibrates** on lipid profiles and cardiovascular outcomes: a systematic review. Am J Med. 2009 Oct;122(10):962.e1-8. Epub 2009 Aug 19.
Abramson JD, Rosenberg HG, Jewell N, Wright JM. Should people at **low risk of cardiovascular disease take a statin**? BMJ. 2013 Oct 22;347:f6123.
Abramson J. **Statins in Persons at Low Risk of Cardiovascular Disease**. Am FamPhysician. 2017 Nov 1;96(9):Online.
ACC: Writing Committee, Lloyd-Jones DM, Morris PB, et al. 2017 Focused Update of the **2016 ACC Expert Consensus** Decision Pathway on the Role of **Non-Statin Therapies** for LDL-Cholesterol Lowering in the Management of Atherosclerotic Cardiovascular Disease Risk: A Report of the American College of Cardiology Task Force on Expert Consensus Decision Pathways. J Am Coll Cardiol. 2017 Aug 30.
ACCORD Study Group, Effects of Combination Lipid Therapy (simvastatin ≤ 40mg od +/- fenofibrate ≤ 160mg od) in Type 2 Diabetes Mellitus. N Engl J Med 2010 0: NEJMoa1001282. n=5518, 4.7yr.
Acharya T, Huang J, Tringali S, et al. **Statin use and the risk of kidney disease** with long term follow-up (8.4-years study). *Am J Cardiol* 2015.
Adams SP, Sekhon SS, Wright JM. **Lipid-lowering efficacy of rosuvastatin**. Cochrane Database Syst Rev. 2014 Nov 21;11:CD010254. The total blood total cholesterol, LDL-cholesterol and non-HDL-cholesterol-lowering effect of rosuvastatin was linearly dependent on dose. Rosuvastatin log dose-response data were linear over the commonly prescribed dose range. Based on an informal comparison with atorvastatin, this represents a three-fold greater potency. This review did not provide a good estimate of the incidence of harms associated with rosuvastatin because of the short duration of the trials and the lack of reporting of adverse effects in 44% of the placebo-controlled trials.
Adams SP, Tsang M,Wright JM. **Lipid-lowering efficacy of atorvastatin**. Cochrane Database of Systematic Reviews 2015, Issue 3. Art. No.: CD008226. DOI: 10.1002/14651858.CD008226.pub3. This update resulted in no change to the main conclusions of the review but significantly increases the strength of the evidence. Studies show that atorvastatin decreases blood total cholesterol and LDL-cholesterol in a linear dose-related manner over the commonly prescribed dose range.New findings include that atorvastatin is more than three-fold less potent than rosuvastatin, and that the cholesterollowering effects of atorvastatin are greater in females than in males and greater in non-familial than in familial hypercholesterolaemia. This review update does not provide a good estimate of the incidence of harms associated with atorvastatin because included trials were of short duration and adverse effects were not reported in 37% of placebo-controlled trials.
Adams SP, Sekhon SS, Tsang M, Wright JM. **Fluvastatin for lowering lipids**. Cochrane Database of Systematic Reviews 2018, Issue 3. Art. No.: CD012282. Fluvastatin lowers blood total cholesterol, LDL cholesterol and triglyceride in a dose-dependent linear fashion. Based on the effect on LDL cholesterol, fluvastatin is 12-fold less potent than atorvastatin and 46-fold less potent than rosuvastatin. This review did not provide a good estimate of the incidence of harms associated with fluvastatin because of the short duration of the trials and the lack of reporting of adverse effects in 56% of the placebo-controlled trials.
Afilalo J, Duque G, Steele R, et al. **Statins for secondary prevention in elderly patients**. J Am Coll Cardiol. 2008;51:37-45. The posterior median estimate of the number needed to treat to save 1 life was 28 (95% CI 15 to 56). CONCLUSIONS: Statins reduce all-cause mortality in elderly patients and the magnitude of this effect is substantially larger than had been previously estimated. (InfoPOEMs: Treating 28 elderly patients with coronary heart disease (CHD) for 5 years will prevent 1 of them from dying during that period. For every 38 people treated for 5 years, 1 nonfatal myocardial infarction will be prevented; for every 58 patients treated for 5 years, 1 stroke will be prevented. (LOE = 1a))
Afilalo J, Majdan AA, Eisenberg MJ. **Intensive statin** therapy in **acute coronary syndromes** and stable coronary heart disease: a comparative meta-analysis of randomised controlled trials. Heart 2007;93(8):914-921. <http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=1727734 9&dopt=Abstract> Intensive statin therapy will decrease overall mortality rates compared with lower doses in patients with a recent history of acute coronary syndrome (ACS) but not in patients with stable coronary heart disease. However, **80 patients must be treated to prevent 1 additional death over 2 years**. Intensive treatment decreases overall hospital admissions for heart failure in both groups and decreases major cardiac events in pts with stable coronary heart disease, but, again, the results are not striking. (LOE = 1a)
Ahmad Z. **Statin Intolerance**. Am J Cardiol. 2014 May 15;113(10):1765-1771.
Ahmadi A and Narula J.**Primary and secondary prevention**, or subclinical and clinical atherosclerosis. JACC Cardiovasc Imaging 2016 Oct 19.
Ahmadizar F, Souverein P, de Boer A, et al. **Under-treatment of hypertension and hypercholesterolemia in children and adolescents with type 1 diabetes**- Long term follow-up on time trends in the occurrence of cardiovascular disease, risk factors and medications use. Br J Clin Pharmacol. 2017 Dec 7.
Ahmadizar F, OchoaRosales C, Glisic M, et al. Associations of **statin use with glycaemic traits and incident type 2 diabetes**. Br J Clin Pharmacol. 2019 Mar 5.
Albayda J, Christopher-Stine L. Identifying statin-associated **autoimmune necrotizing myopathy**. Cleve Clin J Med. 2014 Dec;81(12):736-741.
Albright KC, Zhao H, Blackburn J, et al. **Racial differences in statin adherence** following hospital discharge for ischemic stroke. Neurology. 2017 May 9;88(19):1839-1848.
Akyea RK, Kai J, Qureshi N, et al. **Sub-optimal cholesterol response** to initiation of statins and future risk of cardiovascular disease. Heart. 2019 Apr 15.
Allan GM, Lindblad AJ, Comeau A, et al. **Simplified lipid guidelines**: Prevention and management of cardiovascular disease in primary care. **Can Fam Physician**. 2015 Oct;61(10):857-67.
AIM-HIGH: National Institutes of Health. NIH stops clinical trial on combination cholesterol treatment [press release]. May 26, 2011. Available here. A trial of extended-release **niacin** (Niaspan, Abbott) given in addition to statin therapy in patients with a history of cardiovascular disease, high triglycerides, and low levels of HDL cholesterol has been halted prematurely, 18 months ahead of schedule, because niacin offered no additional benefits in this patient population. There was also a small, unexplained increase in ischemic stroke (1.6 vs 0.7%)in the high-dose, extended-release niacin group, in the Atherothrombosis Intervention in Metabolic Syndrome with Low HDL Cholesterol/High Triglyceride and Impact on Global Health Outcomes (AIM-HIGH) study, according to a statement from the **National Heart Lung and Blood Institute** (NHLBI), which sponsored it. N=3414, 32months. AIM-HIGH enrolled 3,414 participants in the US and Canada with a history of cardiovascular disease, low HDL cholesterol, and high triglycerides, who were all prescribed simvastatin and who were also randomized to either high-dose, extended-release niacin in gradually increasing doses up to 2000 mg per day (n=1718) or placebo (n=1696). Of the participants, 515 were given a second LDL-cholesterol-lowering drug, ezetimibe (Zetia, Merck/Schering-Plough), in order to maintain LDL-cholesterol levels at the target range between 40 and 80 mg/dL.
AIM-HIGH investigators. **Niacin** in patients with low HDL cholesterol levels receiving intensive statin therapy. N Engl J Med2011; DOI:10.1056/oa1107579.
Akduman B, Tandberg DJ, O'Donnell CI, et al. Effect of Statins on Serum Prostate-specific Antigen (PSA) Levels. Urology. 2010 Jun 3.
Albright KC, Howard VJ, Howard G, et al. Age and Sex Disparities in Discharge **Statin Prescribing** in the **Stroke Belt**: Evidence From the Reasons for Geographic and Racial Differences in Stroke Study. J Am Heart Assoc. 2017 Aug 2;6(8).

Alenghat FJ, Davis AM. **Management of Blood Cholesterol**. JAMA. 2019 Feb 4.

Alexandre L, Clark AB, Bhutta HY, et al. **Statin** use is associated with reduced risk of histologic subtypes of **esophageal cancer**: a nested case-control analysis. Gastroenterology. 2014 Mar;146(3):661-8.

Al-Kindi SG, DeCicco A, Longenecker CT, et al. **Rate of Statin Prescription in Younger Patients** With Severe Dyslipidemia. JAMA Cardiol. 2017 Jan 4.

Ali-Alsheikh AA, Karas RH. **Ezetimibe**, and the combination of ezetimibe/simvastatin, and **risk of cancer**: a post-marketing analysis. *J Clin Lipidol* 2009; DOI:10.1016.2009.02.005.

Alpérovitch A, Kurth T, Bertrand M, et al. **Primary prevention** with lipid lowering drug and long term risk of vascular events in **older people**: population based cohort study. BMJ 2015;350:h2335.

Alsabbagh WM, Dagenais J, Yan L, et al. **Use and misuse of ezetimibe**: analysis of use and cost in Saskatchewan, a canadian jurisdiction with broad access. Can J Cardiol. 2014 Feb;30(2):237-43.

Alsheikh-Ali AA, Maddukuri PV, Han H, Karas RH. Effect of magnitude of lipid lowering on risk of **elevated liver enzymes, rhabdomyolysis, and cancer**. J Am Coll Cardiol 2007; 50:409-418. DOI: 10.1016/j.jacc.2007.02.073. Available at: http://content.onlinejacc.org. Risk of statin-associated elevated liver enzymes or rhabdomyolysis is not related to the magnitude of LDL-C lowering. However, the risk of cancer is significantly associated with lower achieved LDL-C levels.

Alsheikh-Ali AA, Trikalinos TA, Kent DM, Karas RH. Statins, low-density lipoprotein cholesterol, and risk of cancer. J Am Coll Cardiol. 2008 Sep 30;52(14):1141-7. There is an inverse association between on-treatment LDL-C and incident cancer. However, **statins**, despite producing marked reductions in LDL-C, are **not associated with an increased risk of cancer**.

Amarenco P, et al.; Stroke Prevention by Aggressive Reduction in Cholesterol Levels (**SPARCL**) Investigators. High-dose atorvastatin after stroke or transient ischemic attack. N Engl J Med. 2006 Aug 10;355(6):549-59. (Kent DM. Stroke--an equal opportunity for the initiation of statin therapy. N Engl J Med. 2006 Aug 10;355(6):613-5.) (InfoPOEMs: High-dose atorvastatin reduces the risk of recurrent stroke, but does not improve mortality rates. A reduction in the risk of transient ischemic attack (TIA) or unclassified stroke was partially offset by an increase in the risk of hemorrhagic stroke. (LOE = 1b)) Amarenco P, Goldstein LB, Szarek M, Sillesen H, Rudolph AE, Callahan A 3rd, Hennerici M, Simunovic L, Zivin JA, Welch KM; SPARCL Investigators. Effects of Intense Low-Density Lipoprotein Cholesterol Reduction in Patients With Stroke or Transient Ischemic Attack. The Stroke Prevention by Aggressive Reduction in Cholesterol Levels (SPARCL) Trial. Stroke. 2007 Oct 25; [Epub ahead of print] As compared with having no change or an increase in LDL-C, achieving a >/=50% lowering was associated with a greater reduction in the risk of stroke and major coronary events with no increase in brain hemorrhages. Goldstein LB, Amarenco P, Szarek M, Callahan A 3rd, Hennerici M, Sillesen H, Zivin JA, Welch KM; On behalf of the SPARCL Investigators. Hemorrhagic stroke in the Stroke Prevention by Aggressive Reduction in Cholesterol Levels study. Neurology. 2007 Dec 12; [Epub ahead of print] Hemorrhagic stroke was more frequent in those treated with atorvastatin, in those with a hemorrhagic stroke as an entry event, in men, and increased with age. Those with Stage 2 hypertension at the last visit prior to the hemorrhagic stroke were also at increased risk. Treatment did not disproportionately affect the hemorrhagic stroke risk associated with these other factors. There were no relationships between hemorrhage risk and baseline low-density lipoprotein (LDL) cholesterol level or recent LDL cholesterol level in treated patients.

Amarenco P, Labreuche J. Lipid management in the prevention of **stroke**: Review and updated meta-analysis of statins for stroke prevention. Lancet Neurol 2009; 8:453-463.

Amend KL, Landon J, Thyagarajan V, Niemcryk S, McAfee A. Incidence of **Hospitalized Rhabdomyolysis with Statin and Fibrate** Use in an Insured US Population (October). Ann Pharmacother. 2011 Sep 13. The number needed to harm was lower for combination statin-gemfibrozil therapy (**2753**) compared with that for statin therapy alone (**454,545**).

American Diabetes Association. (ADA 2016): Standards of Medical Care in Diabetes-2016: Summary of Revisions. Diabetes Care. (American Diabetes Association) 2016 Jan;39 Suppl 1:S4-5.

American Dietetic Association. Disorders of **lipid metabolism. Evidence-based nutrition practice guideline**. Chicago (IL): American Dietetic Association; 2011 Mar. https://www.adaevidencelibrary.com/tmp/prn9960934415842E340048AE5C7D4C4F2D.pdf

American College of Cardiology Foundation, , American Heart Association Task Force on Practice Guidelines, , Society for Cardiovascular Angiography and Interventions, , Levine, Glenn N., Bates, Eric R., Blankenship, Et al. **2011 ACCF/AHA/SCAI Guideline for Percutaneous Coronary Intervention**: Executive Summary. J Am Coll Cardiol 2011 0: j.jacc.2011.08.006. http://content.onlinejacc.org/cgi/reprint/j.jacc.2011.08.006v1.pdf

American College of Cardiology Foundation, , American Heart Association Task Force on Practice Guidelines, , American Association for Thoracic Surgery, , Society of Cardiovascular Anesthesiologists, , Society of Thoracic Surgeons, Hillis, L. David, Smith, Peter K., Anderson, Jeffrey L., et al. **2011 ACCF/AHA Guideline for Coronary Artery Bypass Graft Surgery**: Executive Summary. J Am Coll Cardiol 2011 0: j.jacc.2011.08.008. http://content.onlinejacc.org/cgi/reprint/j.jacc.2011.08.008v1.pdf

Anderson TJ, Grégoire J, Hegele RA, et al. Are the **ACC/AHA guidelines on the treatment of blood cholesterol a game changer**? A **perspective from the Canadian Cardiovascular Society** Dyslipidemia Panel. Can J Cardiol. 2014 Apr;30(4):377-80.

Anderson TJ et al. Safety profile of **extended-release niacin in the AIM-HIGH** trial. N Engl J Med 2014 Jul 17; 371:288.

Anderson TJ, Mancini GB, Genest J Jr, et al. The **New Dyslipidemia Guidelines: What Is the Debate**? Can J Cardiol. 2014 Nov 11.

Anderson TJ, Grégoire J, Pearson GJ, et al. **2016 Canadian Cardiovascular Society (CCS) guidelines** for the management of dyslipidemia for the prevention of cardiovascular disease in the adult. Can J Cardiol 2016 [accepted manuscript published online], doi: 10.1016/j.cjca.2016.07.510.

Anderson TJ, Grégoire J, Pearson GJ, et al. **2016 Canadian Cardiovascular Society (CCS) guidelines** for the management of **dyslipidemia for the prevention of cardiovascular disease in the** adult. Expanded rationale. Can J Cardiol 2016 [accepted manuscript published online], doi: 10.1016/j.cjca.2016.07.510.

Ando H, Tsuruoka S, Yanagihara H, et al. Effects of **grapefruit juice** on the pharmacokinetics of pitavastatin and **atorvastatin**. Br J Clin Pharmacol. 2005 Nov;60(5):494-7.

Antoniou T, Macdonald EM, Yao Z, et al. Association between **statin use and ischemic stroke or major hemorrhage in patients taking dabigatran** for atrial fibrillation. CMAJ. Online. Nov 21, 2016.

Arbel R, Hammerman A, Azuri J. Usefulness of **Ezetimibe Versus Evolocumab** as Add-On Therapy for Secondary Prevention of Cardiovascular Events in Patients With Type 2 Diabetes Mellitus. Am J Cardiol. 2019 Apr 15;123(8):1273-1276.

Arca M. **Atorvastatin** Efficacy in the Prevention of Cardiovascular Events in Patients with **Diabetes** Mellitus and/or Metabolic Syndrome. Drugs. 2007;67 Suppl 1:43-54. (Cards, Ascot-LLA, Greace, TNT, Prove-It, Aspen) In summary, several patient populations, from definitive, large-scale studies, are now available to corroborate the integral place of atorvastatin - in line with various regional and internationally accepted disease management guidelines - in the primary and secondary prevention of cardiovascular events in patients with diabetes and/or metabolic syndrome.

Arnold SV, Kosiborod M, Tang F, et al. Patterns of **Statin** Initiation, Intensification, and Maximization Among Patients Hospitalized **with an Acute Myocardial Infarction**. Circulation. 2014 Feb 4.

Arouche-Delaperche L, Allenbach Y, et al. Pathogenic role of **anti-SRP and anti-HMGCR antibodies** in necrotizing myopathies: Myofiber atrophy and impairment of muscle regeneration in necrotizing autoimmune myopathies. Ann Neurol. 2017 Feb 22.

Arrieta A, Hong JC, Khera R, et al. **Updated cost-effectiveness assessments of PCSK9 inhibitors** from the perspectives of health system and private payers: insights derived from the FOURIER study [online October 18, 2017]. JAMA Cardiol. 2017.

Arsenault BJ, Boekholdt SM, et al. Impact of **High-Dose Atorvastatin** Therapy and Clinical Risk Factors on Incident **Aortic Valve Stenosis** in Patients With Cardiovascular Disease (from TNT, IDEAL, and SPARCL). Am J Cardiol. 2014 Apr 15;113(8):1378-82.

Arya S, Khakharia A, Binney ZO, Det al. **Statins Have a Dose-Dependent Effect on Amputation and Survival in Peripheral Artery Disease** Patients. Circulation. 2018 Jan 12.

Arya S, Khakharia A, Binney ZO, et al. Association of **Statin Dose With Amputation and Survival in Patients With Peripheral Artery Disease**. Circulation. 2018 Apr 3;137(14):1435-1446.

Asch DA, Troxel AB, Stewart WF, et al. Effect of **Financial Incentives** to Physicians, Patients, or Both on Lipid Levels: A Randomized Clinical Trial. JAMA. 2015 Nov 10;314(18):1926-35.

Athyros VG, Tziomalos K, Gossios TD, et al.; GREACE Study Collaborative Group. Safety and efficacy of long-term statin treatment for cardiovascular events in patients with coronary heart disease and **abnormal liver tests** in the Greek Atorvastatin and Coronary Heart Disease Evaluation (**GREACE**) Study: a post-hoc analysis. Lancet. 2010;376(9756):1916-1922.

Babio N, Toledo E, Estruch R, et al; for the **PREDIMED** Study Investigators. **Mediterranean diets** and metabolic syndrome status in the PREDIMED randomized trial. CMAJ. 2014 Oct 14

Backes JM, Moriarty PM, Ruisinger JF, Gibson CA. Effects of once **weekly rosuvastatin** among patients with a prior statin intolerance. Am J Cardiol. 2007 Aug 1;100(3):554-5.

Bader T, Fazili J, Madhoun M, et al. Fluvastatin **Inhibits Hepatitis C** Replication in Humans. Am J Gastroenterol. 2008 Apr 9. [Epub ahead of print] FLV used as monotherapy in vivo showed suppressive effects of HCV clinically that are modest, variable, and often short-lived. These findings support "proof-of-concept" for pilot trials combining fluvastatin with standard therapy. Statins and fluvastatin, in particular, appear to be safe for use in hepatitis C.

Bach RG, Cannon CP, Giugliano RP, et al. Effect of **Simvastatin-Ezetimibe Compared With Simvastatin Monotherapy** After Acute Coronary Syndrome Among Patients 75 Years or Older: A Secondary Analysis of a Randomized Clinical Trial. JAMA Cardiol. 2019 Jul 17.

Backes JM, Moriarty PM, Ruisinger JF, Gibson CA. Effects of **once weekly rosuvastatin** among patients with a prior statin intolerance. Am J Cardiol 2007;100:554-5.

Bagdade J, Barter P, Quiroga C, et al. Effects of **Torcetrapib** and Statin Treatment on ApoC-III and Apoprotein-Defined Lipoprotein Subclasses (from the **ILLUMINATE** Trial). Am J Cardiol. 2017 Mar 18.

Baigent C, Keech A, Kearney PM, et al.; **Cholesterol Treatment Trialists'** (**CTT**) Collaborators. Efficacy & safety of cholesterol-lowering treatment: prospective meta-analysis of data from 90,056 participants in 14 randomised trials of statins. Lancet. 2005 Oct 8;366(9493):1267-78. Epub 2005 Sep 27. (InfoPOEMs: Statins reduce 5-year overall mortality, and specifically decrease cardiovascular mortality and morbidity. The patients at highest baseline risk derive the greatest benefit. (LOE = 1a))

Baigent C, Landray MJ, Reith C, et al. The effects of lowering LDL cholesterol with simvastatin plus ezetimibe in patients with chronic kidney disease (Study of Heart and Renal Protection-**SHARP**): a randomized placebo-controlled trial. Lancet 2011.

Balder JW, Rimbert A, Zhang X, et al. **Genetics, Lifestyle, and Low-Density Lipoprotein Cholesterol** in Young and Apparently Healthy Women. Circulation. 2018 Feb 20;137(8):820-831.

Ballantyne CM, Laufs U, Ray KK, et al. **Bempedoic acid plus ezetimibe** fixed-dose combination in patients with hypercholesterolemia and high CVD risk treated with maximally tolerated statin therapy. Eur J Prev Cardiol. 2019 Jul 29:2047487319864671.

Ballantyne CM, Shah S, Sapre A, et al. A Multiregional, Randomized Evaluation of the Lipid-Modifying Efficacy and Tolerability of **Anacetrapib** Added to Ongoing Statin Therapy in Patients With Hypercholesterolemia or Low High-Density Lipoprotein Cholesterol.

Banach M, Serban C, Sahebkar A, et al. Effects of **Coenzyme Q10** on Statin-Induced Myopathy: A Meta-analysis of Randomized Controlled Trials. Mayo Clin Proc. 2014 Nov 14.

Banaszewska B, et al. Effects of **simvastatin** and oral contraceptive agent on **polycystic ovary syndrome**: prospective randomized cross-over trial. J Clin Endocrinol Metab. 2006 Nov 14; [Epub ahead of print] n=48

Bang CN, Greve AM, La Cour M, et al. Effect of Randomized Lipid Lowering With **Simvastatin and Ezetimibe on Cataract** Development (from the Simvastatin and Ezetimibe in Aortic Stenosis Study-**SEAS**). Am J Cardiol. 2015 Dec 15;116(12):1840-4.

Bangalore S, Fayyad R, Hovingh GK, et al; Treating to New Targets Steering Committee and Investigators. **Statin** and the Risk of **Renal-Related Serious Adverse Events**: Analysis from the IDEAL, TNT, CARDS, ASPEN, SPARCL, and Other Placebo-Controlled Trials. Am J Cardiol. 2014 Apr 3

Bansal S et al. **Fasting compared with nonfasting triglycerides** and risk of cardiovascular events in women. JAMA 2007 Jul 18; 298:309-16.

Barakat AF, Saad M, Abuzaid A, et al. Perioperative Statin Therapy for Patients **Undergoing Coronary Artery Bypass Grafting**. Ann Thorac Surg. 2015 Dec 15.

Barbacki A, Fallavollita SA, Karamchandani J, Hudson M. **Immune-Mediated Necrotizing Myopathy and Dietary Sources of Statins**. Ann Intern Med. 2018 Feb 20. (ate Camargue red rice)

Barry AR. Point counterpoint: Should Patients Continue to Receive **Statins** Once They Reach **80 Years of Age**? The "Pro" side. CJHP. 2017;70(3):243-246

Barry AR, Beach JE, Pearson GJ. **Prevention and management of statin adverse effects**: A practical approach for pharmacists. Can Pharm J (Ott). 2018 Apr 4;151(3):179-188.

Barter PJ, Nicholls SJ, et al. Is **Cholesteryl Ester Transfer Protein Inhibition** an Effective Strategy to Reduce Cardiovascular Risk? CETP Inhibition as a Strategy to Reduce Cardiovascular Risk: The Pro Case. Circulation. 2015 Aug 4;132(5):423-32.

Barter PJ, Rye KA. **Targeting High-Density Lipoproteins** to Reduce Cardiovascular Risk: What Is the Evidence? Clin Ther. 2015 Aug 18.

Bartlett LE, Pratt N, Roughead EE. Does tablet **formulation** alone improve **adherence** and persistence: A comparison of **ezetimibe** fixed dose combination versus ezetimibe separate pill combination? Br J Clin Pharmacol. 2016 Aug 12.

Baruch L, Agarwal S, Gupta B, et al. Effect on serum lipid levels of switching dose of **ezetimibe from 10 to 5 mg**. Am J Cardiol. 2009 Jun 1;103(11):1568-71. Epub 2009 Apr 22.

Bateman BT, Hernandez-Diaz S, Fischer MA, Seely EW, Ecker JL, Franklin JM, et al. **Statins and congenital malformations**: cohort study. BMJ 2015;350:h1035.

Baudrand R, Pojoga LH, Vaidya A, et al. **Statin use and adrenal aldosterone production** in hypertensive and diabetic subjects. Circulation. 2015;132:1825–1833.

Bays HE, Averna M, Majul C, et al. Efficacy and Safety of **Ezetimibe Added to Atorvastatin** Versus Atorvastatin Uptitration or Switching to Rosuvastatin in Patients With Primary Hypercholesterolemia. Am J Cardiol. 2013 Sep 21.

Bazinet RP, Chu MW. **Omega-6 polyunsaturated fatty acids**: Is a broad cholesterol-lowering health claim appropriate? CMAJ. 2014 Apr 1;186(6):434-9.

Becker D. J., Gordon R. Y., et al. **Red Yeast Rice** for Dyslipidemia in Statin-Intolerant Patients: A Randomized Trial. Ann Intern Med 2009; 830-839.

Bedi P, Chalmers JD, Graham C, et al. A randomised control trial of **atorvastatin in bronchiectasis** patients infected with Pseudomonas aeruginosa- a proof of concept study. Chest. 2017 May 26.

Beeharry D, Coupe B, Benbow EW, Morgan J, Kwok S, Charlton-Menys V, et al. **Familial hypercholesterolaemia** commonly presents with **Achilles tenosynovitis**. Ann Rheum Dis 2006;65:312-5.

Bell KJL et al. **Monitoring adherence** to drug treatment by using **change in cholesterol concentration**: Secondary analysis of trial data. BMJ 2011 Jan 21; 342:d12.

Ben-Yehuda O, DeMaria AN. LDL-Cholesterol **Targets After the ACC/AHA 2013 Guidelines**: Evidence That Lower Is Better? J Am Coll Cardiol. 2014 Aug 5;64(5):495-7

Berg ML, Estes LL, Dierkhising RA, et al. Evaluation of Impact of Statin Use on Development of **CPK Elevation During Daptomycin** Therapy. Ann Pharmacother. 2014 Mar;48(3):320-7.

Berglind IA et al. **Hormone therapy and risk** of **cardiovascular outcomes** and mortality in women treated with statins. Menopause 2015 Apr; 22:369.

Berglund L, Brunzell JD, Goldberg AC, et al. Evaluation and treatment of **hypertriglyceridemia**: an **Endocrine Society** clinical practice guideline. J Clin Endocrinol Metab 2012; 97:2969.

Bero L, Oostvogel F, Bacchetti P, Lee K. Factors associated with findings of **published trials of drug-drug comparisons**: why some statins appear more efficacious than others. PLOS Med 2007;4:e184.

Bertagnolli MM, Hsu M, Hawk ET, et al. Statin use and **colorectal adenoma** risk: Results from the Adenoma Prevention with Celecoxib trial. Cancer Prev Res 2010. DOI:10.1158/1940-6207.CAPR-09-0271.

Berthold HK, et al. Effect of policosanol on lipid levels among patients with hypercholesterolemia or combined hyperlipidemia: a randomized controlled trial. JAMA. 2006 May 17;295(19):2262-9. In patients with hypercholesterolemia or combined hyperlipidemia, the sugar cane-derived policosanol in usual and high doses does not demons High-dose atorvastatin reduces the risk of recurrent stroke, but does not improve mortality rates. A reduction in the risk of transient ischemic attack (TIA) or unclassified stroke was partially offset by an increase in the risk of hemorrhagic stroke. (LOE = 1b) trate a reduction in lipid levels beyond placebo.

Berwanger O, Santucci EV, de Barros e Silva PGM, et al; for the **SECURE-PCI** Investigators. Effect of **loading dose of atorvastatin prior to planned percutaneous coronary intervention** on major adverse cardiovascular events in acute coronary syndrome: the SECURE-PCI randomized clinical trial [online Mar 11, 2018].JAMA. doi:10.1001 /jama.2018.2444

Besseling J, et al. Selection of individuals for **genetic testing for familial hypercholesterolaemia**: development and external validation of a prediction model for the presence of a mutation causing familial hypercholesterolaemia. Eur Heart J. 2016 Apr 3.

Bezin J, Mansiaux Y, Noize P, et al. Use of **lipid-lowering drugs and the risk of cataract**: a population-based nested case-control study. Clin Pharmacol Ther. 2018 Jul 10.

Bhatnagar D, Soran H, Durrington PN. **Hypercholesterolaemia** and its management. BMJ. 2008 Aug 21;337:a993. doi: 10.1136/bmj.a993.

Bhatt DL, Steg PG, Miller M, et al. Effects of **Icosapent Ethyl on Total Ischemic Events**: From REDUCE-IT. J Am Coll Cardiol. 2019 Jun 11;73(22):2791-2802.

Bhatt DL, Steg PG, Miller M, et al; REDUCE-IT Investigators. Cardiovascular Risk Reduction with **Icosapent Ethyl for Hypertriglyceridemia**. N Engl J Med. 2018 Nov 10.

Bhatt DL, et al; REACH Registry Investigators. International prevalence, recognition, and treatment of **cardiovascular risk factors in outpatients with atherothrombosis**. JAMA. 2006 Jan 11;295(2):180-9.

Bhattacharya S, McNeill G, Raja EA, et al. **Maternal gestational weight gain and offspring's risk of cardiovascular** disease and mortality. Heart. 2016 Sep 15;102(18):1456-63.

Bibbins-Domingo K, Grossman DC, Curry SJ, et al. **Statin Use for the Primary Prevention** of Cardiovascular Disease in Adults: US Preventive Services Task Force Recommendation (**USPSTF**) Statement. JAMA. 2016 Nov 15;316(19):1997-2007.

Biffi A, Devan WJ, Anderson CD, et al. Statin use and outcome **after intracerebral hemorrhage**: Case-control study and meta-analysis. Neurology. 2011 May 3;76(18):1581-8.

Billings FT, Hendricks PA, Schildcrout JS, et al. High-dose **perioperative atorvastatin** and **acute kidney injury following cardiac surgery**: a randomized clinical trial. *JAMA* 2016.

BIP Study Group. Secondary prevention ()n=3090) by raising HDL cholesterol and reducing triglycerides in patients with coronary artery disease. The bezafibrate infarction prevention (BIP) study. Circulation 2000;102:21-27. (Tenenbaum A, et al. Bezafibrate for the secondary prevention of myocardial infarction in patients with metabolic syndrome. Arch Intern Med. 2005 May 23;165(10):1154-60 & McCormack J, Loewen P. The other side of the bezafibrate infarction prevention trial data. Arch Intern Med. 2005 Nov 14;165(20):2431-2; author reply 2432. Tenenbaum A, et al. Attenuation of progression of insulin resistance in patients with coronary artery disease by bezafibrate. Arch Intern Med. 2006 Apr 10;166(7):737-41.) Goldenberg I, et al. Secondary prevention with bezafibrate therapy for the treatment of dyslipidemia: an extended follow-up of the BIP trial. J Am Coll Cardiol. 2008 Jan 29;51(4):459-65. The data demonstrate that bezafibrate therapy in the BIP trial was associated with significant long-term cardiovascular protection that was attenuated by an unbalanced usage of nonstudy LLDs during the course of the trial.

Birnbaum G, Cree B, Altafullah I, Zinser M, Reder AT. Combining beta interferon and **atorvastatin may increase disease** activity in **multiple sclerosis**. Neurology. 2008 Jun 4. [Epub ahead of print]

Biton Y, Goldenberg I, Kutyifa V, et al. Effects of **Statins on First and Recurrent Supraventricular Arrhythmias** in Patients With Mild Heart Failure (from the Multicenter Automatic Defibrillator Implantation Trial With Cardiac Resynchronization Therapy). Am J Cardiol. 2015 Oct 8.

Bittner V, Colantonio LD, Dai Y, et al. Association of Region and Hospital and Patient Characteristics With Use of **High-Intensity Statins After Myocardial Infarction** Among Medicare Beneficiaries. JAMA Cardiol. 2019 Jul 24.

Black S, Nicolay U, Del Giudice G, et al. Influence of **Statins on Influenza Vaccine** Response in Elderly Individuals. J Infect Dis. 2015 Oct 28.

Blaha MJ, Nasir K, Blumenthal RS. **Statin therapy for healthy men** identified as "increased risk." JAMA 2012; 307: 1489-1490.

Blanco M,Nombela F, CastellanosM, et al. **Statin treatment withdrawal** in ischemic stroke: a controlled randomized study. Neurology. 2007;69: 904-10

Blom DJ, Hala T, Bolognese M, et al; the **DESCARTES** Investigators. A 52-Week Placebo-Controlled Trial of **Evolocumab** in Hyperlipidemia. N Engl J Med. 2014 Mar 29.

Bodmer Michael; Brauchli Yolanda B.; Krahenbuhl Stephan; et al. Statin Use and Risk of **Gallstone** Disease Followed by Cholecystectomy. *JAMA*. 2009;302(18):2001-2007.

Bohula EA, Giugliano RP, Leiter LA, et al. Inflammatory and Cholesterol Risk in the **FOURIER** Trial (Further Cardiovascular Outcomes Research With PCSK9 Inhibition in Patients With Elevated Risk). Circulation. 2018 Mar 12.

Bohula EA, Giugliano RP, Leiter LA, et al. Inflammatory and Cholesterol Risk in the FOURIER Trial. Circulation. 2018 Jul 10;138(2):131-140.

Boehm JK, Williams DR, Rimm EB, Ryff C, Kubzansky LD. Relation Between **Optimism and Lipids in Midlife**. Am J Cardiol. 2013 Feb 21.

Boekholdt, SM, Arsenault BJ, Mora S, et al. Association of **LDL cholesterol, Non-HDL cholesterol, and apolipoprotein B levels** with risk of cardiovascular events among patients treated with statins. JAMA 2012; 307:1302-1309.

Boekholdt SM, Arsenault BJ, Hovingh GK, et al. Levels and Changes of **HDL Cholesterol and Apolipoprotein A-I** in Relation to Risk of Cardiovascular Events among Statin-Treated Patients: A Meta-Analysis. Circulation. 2013 Aug 21.

Boekholdt SM, Hovingh GK, Mora S, et al. **Very low levels of atherogenic lipoproteins** and the risk for cardiovascular events: a meta-analysis of statin trials. J Am Coll Cardiol. 2014 Aug 5;64(5):485-94.

IMPROVE-IT. Circulation. 2015;132:1224–1233. doi: 10.1161/CIRCULATIONAHA.115.018381
Bohula EA, Wiviott SD, Giugliano RP, et al. **Prevention of Stroke** with the Addition of **Ezetimibe** to Statin Therapy in Patients With Acute Coronary Syndrome in **IMPROVE-IT** (Improved Reduction of Outcomes: Vytorin Efficacy International Trial). Circulation. 2017 Dec 19;136(25):2440-2450.
Bonaca MP, Nault P, Giugliano RP, et al. Low-Density Lipoprotein Cholesterol Lowering With **Evolocumab** and Outcomes in Patients With Peripheral Artery Disease: Insights From the **FOURIER** Trial (Further Cardiovascular Outcomes Research With PCSK9 Inhibition in Subjects With Elevated Risk). Circulation. 2017 Nov 13.
Bonovas S, Filioussi K, Tsavaris N, Sitaras NM. **Statins and Cancer Risk**: A Literature-Based Meta-Analysis and Meta-Regression Analysis of 35 Randomized Controlled Trials. J Clin Oncol. 2006 Sep 25; [Epub ahead of print] Our findings do not support a protective effect of statins against cancer. However, this conclusion is limited by the relatively short follow-up periods (4.5 years on average) of the studies analyzed.
Bookstaver DA, Burkhalter NA, et al. Effect of **Coenzyme Q10 Supplementation (60mg po bid)** on Statin-Induced Myalgias. Am J Cardiol. 2012 May 17. n=76 no more effective than placebo
Bosch J, O'Donnell M, Swaminathan B, et al; HOPE-3 Investigators. Effects of **blood pressure and lipid lowering on cognition**: Results from the HOPE-3 study. Neurology. 2019 Feb 27.
Bosomworth NJ. Approach to identifying and **managing atherogenic dyslipidemia**: A metabolic consequence of obesity and diabetes. Can Fam Physician. 2013 Nov;59(11):1169-80.
Bosomworth, NJ. Evolution of **lipid management guidelines** Evidence might set you free. Canadian Family Physician, 60(7), 612-617. 2014.
Boulet J, Peña J, Hulten EA, et al. Statin Use and Risk of **Vascular Events Among Cancer Patients** After Radiotherapy to the Thorax, Head, and Neck. J Am Heart Assoc. 2019 Jul 2;8(13):e005996.
Bradley CK, Wang TY, Li S, et al. Patient-Reported **Reasons for Declining or Discontinuing Statin Therapy**: Insights From the PALM Registry. J Am Heart Assoc. 2019 Apr 2;8(7):e011765.
Brennan ET, Joy TR. Management strategies for **statin-associated muscle symptoms**: How useful is same-statin rechallenge? Can J Cardiol 2017; published online: March 1, 2017.
Briel M, Studer M, Glass TR, Bucher HC. Effects of statins on **stroke prevention** in patients with and without coronary heart disease: a meta-analysis of randomized controlled trials. Am J Med. 2004 Oct 15;117(8):596-606.
Briel M, et al. Effects of early treatment with **statins** on **short-term** clinical outcomes in **acute coronary syndromes**: a meta-analysis of randomized controlled trials. JAMA. 2006 May 3;295(17):2046-56. Based on available evidence, initiation of statin therapy within 14 days following onset of ACS does not reduce death, MI, or stroke up to 4 months. (see also InfoPOEMs July 2006)
Brindle P, et al. Accuracy and impact of **risk assessment** in the **primary prevention** of cardiovascular disease: a systematic review. Heart. 2006 Dec;92(12):1752-9. Epub 2006 Apr 18.
Brown C. **Canadian data provide window on statin use**. CMAJ. 2016 Mar 15;188(5):325.
Brown F, Singer A, Katz A, Konrad G. **Statin-prescribing trends for primary and secondary prevention** of cardiovascular disease. Can Fam Physician. 2017 Nov;63(11):e495-e503.
Bruderer S, Petersen-Sylla M, Boehler M, et al.Effect of **gemfibrozil or rifampicin** on the pharmacokinetics of **selexipag** and its active metabolite in healthy subjects. Br J Clin Pharmacol. 2017 Jul 17.
Brugts JJ, et al. **Benefits of statins in people without established cardiovascular disease** but with cardiovascular risk factors: meta-analysis of randomised controlled trials. BMJ. 2009 Jun 30;338:b2376. doi: 10.1136/bmj.b2376.
Brum J, Ramsey D, McRorie J, et al. Meta-Analysis of Usefulness of **Psyllium Fiber as Adjuvant Antilipid Therapy to Enhance Cholesterol Lowering Efficacy of Statins**. Am J Cardiol. 2018 Jul 4.
Brunham LR, Ruel I, Aljenedil S, et al. Canadian Cardiovascular Society Position Statement on **Familial Hypercholesterolemia**: Update 2018. Can J Cardiol. 2018 Dec;34(12):1553-1563.
Buchwald H, Rudser KD, Williams SE, et al. Overall mortality, incremental life expectancy, and cause of death at 25 years in the program on the **surgical control of the hyperlipidemias**. Ann Surg. 2010 Jun;251(6):1034-40.
Burgess S, Ference BA, Staley JR, et al; European Prospective **Investigation Into Cancer and Nutrition–Cardiovascular Disease** (**EPIC-CVD**) Consortium. Association of LPA variants with risk of coronary disease and implications for lipoprotein(a)-lowering therapies: a mendelian randomization analysis [online June 20, 2018]. JAMA Cardiol. doi:10.1001/jamacardio.2018.1470
Brunner NW, Ramanathan K, Wang H, Quan H, Khan NA. Effectiveness of **Statin** Prescribing on Reducing Mortality in **South Asian, Chinese, and White Patients With Diabetes**. Can J Cardiol. 2013 Feb 5.
Bucholz EM, et al. **Prevalence and Predictors of Cholesterol Screening, Awareness, and Statin Treatment Among US Adults With Familial Hypercholesterolemia** or Other Forms of Severe Dyslipidemia (1999-2014). Circulation. 2018 Mar 26.
Buettner C, Nir RR, Bertisch SM, et al. **Simvastatin and Vitamin D for Migraine Prevention**: A Randomized Controlled Trial. Ann Neurol. 2015 Sep 29.
Callahan Alfred; Amarenco Pierre; Goldstein Larry B.; et al. for the **SPARCL** Investigators. Risk of Stroke and Cardiovascular Events After Ischemic Stroke or Transient Ischemic Attack in Patients With **Type 2 Diabetes or Metabolic Syndrome**: Secondary Analysis of the Stroke Prevention by Aggressive Reduction in Cholesterol Levels (SPARCL) Trial Arch Neurol. 2011;0(2011):archneurol.2011.146.
Campitelli MA, Maxwell CJ, Maclagan LC, et al. One-year survival and admission to hospital for cardiovascular events among **older residents of long-term care facilities who were prescribed intensive- and moderate-dose statins**. CMAJ 2019;191:E32-9.
Canadian Adverse Reaction Newsletter Oct 2005: Statins and **memory loss**. http://www.hc-sc.gc.ca/dhp-mps/alt_formats/hpfb-dgpsa/pdf/medeff/carn-bcei_v15n4_e.pdf
Cancienne JM, Brockmeier SF, Rodeo SA, et al. Perioperative Serum Lipid Status and **Statin Use** Affect the Revision Surgery Rate After **Arthroscopic Rotator Cuff** Repair. Am J Sports Med. 2017 Aug 1:363546517717686.
Canner PL, Furberg CD, Terrin ML, McGovern ME. Benefits of niacin by glycemic status in patients with healed myocardial infarction (from the **Coronary Drug Project**). Am J Cardiol. 2005 Jan 15;95(2):254-7.
Cannon CP, Khan I, Klimchak AC, et al. Simulation of Lipid-Lowering Therapy Intensification in a Population With Atherosclerotic Cardiovascular Disease. JAMA Cardiol. 2017 Aug 2
Cannon CP, Steinberg BA, Murphy SA, et al. Meta-analysis of cardiovascular outcomes trials comparing **intensive versus moderate statin therapy**. J Am Coll Cardiol 2006; 48:438-445.
Cannon CP, Shah Sukrut, Dansky Hayes M, for the DEFINE Investigators. Safety of **Anacetrapib** in Patients with or at High Risk for Coronary Heart Disease. November 17, 2010 (10.1056/NEJMoa1009744)
Cannon CP, Cariou B, et al. Efficacy and safety of **alirocumab** in high cardiovascular risk patients with inadequately controlled hypercholesterolaemia on maximally tolerated doses of statins: the ODYSSEY COMBO II randomized controlled trial. Eur Heart J. 2015 Feb 16.
Cannon CP, Blazing MA, Giugliano RP, et al. **Ezetimibe added to statin** therapy after acute coronary syndromes. (**Improve-It**) N Engl J Med. 10.1056/NEJMoa1410489.
Canobbio MM, Warnes CA, Aboulhosn J, et al. Management of Pregnancy in Patients With **Complex Congenital Heart Disease**: A Scientific Statement for Healthcare Professionals From the American Heart Association. Circulation. 2017 Jan 12.
Cao X, Ejzykowicz F, Ramey DR, et al. Impact of **Switching From High-Efficacy Lipid-Lowering Therapies to Generic Simvastatin** on LDL-C Levels and LDL-C Goal Attainment Among High-Risk Primary and Secondary Prevention Populations in the United Kingdom. Clin Ther. 2015 Jan 24.
Cappellari M, Bovi P, Moretto G, et al. The **THRombolysis and STatins (THRaST)** study. Neurology. 2013 Feb 12;80(7):655-661.
Cardwell CR, Hicks BM, Hughes C, et al. **Statin Use After Colorectal Cancer** Diagnosis and Survival: A Population-Based Cohort Study. J Clin Oncol. 2014 Aug 4.
Cardwell CR, Mc Menamin U, Hughes CM, et al. **Statin use and survival from lung cancer**: a population-based cohort study. Cancer Epidemiol Biomarkers Prev. 2015 May;24(5):833-41.
Carroll MD, Lacher DA, Sorlie PD, Cleeman JI, Gordon DJ, Wolz M, Grundy SM, Johnson CL. **Trends in serum lipids** and lipoproteins of adults, **1960-2002**. JAMA. 2005 Oct 12;294(14):1773-81.
Carroll MD, Kit BK, Lacher DA, et al. Trends in **lipids and lipoproteins in US adults, 1988-2010**. JAMA 2012; 308:1545-1554.
Carroll MD, Mussolino ME, Wolz M, et al. Trends in **Apolipoprotein B, Non-High-Density Lipoprotein, and Low-Density Lipoprotein for Adults 60 Years and Older** by Use of Lipid-Lowering Medications: United States, 2005 to 2006 Through 2013 to 2014. Circulation. 2018 Jul 10;138(2):208-210.
Carter AA, Gomes T, Camacho X, et al. Risk of **incident diabetes** among patients treated with statins: a population-based study. BMJ 2013.
Catapano AL, Graham I, De Backer G, et al. Authors/Task Force Members; Additional Contributor. **2016 ESC/EAS Guidelines** for the Management of **Dyslipidaemias**: The Task Force for the Management of Dyslipidaemias of the European Society of Cardiology (ESC) and European Atherosclerosis Society (EAS)Developed with the special contribution of the European Assocciation for Cardiovascular Prevention & Rehabilitation (EACPR). Eur Heart J. 2016 Aug 27.
Caughey GE, Gabb GM, Ronson S, et al. Association of **statin exposure with histologically confirmed idiopathic inflammatory myositis** in an Australian population [online July 30, 2018]. JAMA Intern Med. doi:10.1001/jamainternmed.2018.2859
Cauley JA, et al. Women's Health Initiative Research Group. **Statin** use and **breast cancer**: prospective results from the Women's Health Initiative. J Natl Cancer Inst. 2006 May 17;98(10):700-7.
CDC: Centers for Disease Control & Prevention. **Prevalence, treatment, and control of high levels of low-density lipoprotein** cholesterol—United States, 1999-2002 & 2005-2008. MMWR Morb Mortal Wkly Rep 2011; 60:7-12.
Cederberg H, Stančáková A, Yaluri N, et al. **Increased risk of diabetes with statin** treatment is associated with impaired insulin sensitivity and insulin secretion: a 6 year follow-up study of the METSIM cohort. Diabetologia. 2015 Mar 10.
Chaffman MO, Webster WB, Winiecki JT. Efficacy and Safety Evaluation of a Large **Niacin Therapeutic Interchange Program** (May). Ann Pharmacother. 2013 Apr 23. (**Niaspan to Slo-Niacin**)
Chalasani N, Aljadhey H, Kesterson J, Murray MD, Hall SD. **Patients with elevated liver enzymes** are not at higher risk for statin hepatotoxicity. Gastroenterology. 2004 May;126(5):1287-92.
Chan D, Binks S, Nicholas JM, et al. Effect of **high-dose simvastatin** on **cognitive**, **neuropsychiatric**, and health-related quality-of-life measures in secondary progressive **multiple sclerosis**: secondary analyses from the **MS-STAT** randomised, placebo controlled trial. Lancet Neurol. 2017 Aug;16(8):591-600.
Chan KL, Teo K, Dumesnil JG, et al. Effect of lipid lowering with rosuvastatin on progression of **aortic stenosis**. (**Astronomer**)*Circulation* 2010; 121: 306-314.
Chang CH, Lin CH, Caffrey JL, et al. Risk of **Intracranial Hemorrhage** From **Statin** Use in Asians: A Nationwide Cohort Study. Circulation. 2015 Jun 9;131(23):2070-8.

Chapman MJ, Ginsberg HN, Amarenco P, et al. **Triglyceride-risk lipoproteins and high-density lipoprotein cholesterol** in patients at high risk of cardiovascular disease: evidence and guidance for management (**EAS**). Eur Heart J 2011; 32:1345-1361.
Chataway J, Schuerer N, Alsanousi A, et al. Effect of high-dose simvastatin on brain atrophy and disability in secondary progressive **multiple sclerosis** (**MS-STAT**): a randomised, placebo-controlled, phase 2 trial. Lancet 2014; online March 19.
Chen G, Farris MS, Cowling T, et al. Treatment and Low-Density Lipoprotein Cholesterol Management in **Patients Diagnosed With Clinical Atherosclerotic Cardiovascular Disease** in Alberta. Can J Cardiol. 2019 Jul;35(7):884-891.
Chen Y, Li D, Jing J, et al. Treatment Trends, Effectiveness, and Safety of **Statins on Lipid Goal Attainment in Chinese Percutaneous Coronary Intervention** Patients: a Multicenter, Retrospective Cohort Study. Clin Ther. 2017 Aug 11.
Cheung KS, Chen L, Chan EW, et al. **Statins reduce the progression of non-advanced adenomas to colorectal cancer**: a postcolonoscopy study in 187 897 patients. Gut. 2019 Feb 26.
Chiu H-F et al. **Statin use and the risk of liver cancer**: A population-based case–control study. Am J Gastroenterol 2011 May; 106:894.
Cholesterol Treatment Trialists' (**CTT**) Collaboration. Efficacy of cholesterol-lowering therapy in 18 686 people with **diabetes** in 14 randomised trials of statins: A meta-analysis. Lancet 2008; 371:117-125. Statin therapy should be considered for all diabetic individuals who are at sufficiently high risk of vascular events.
Cholesterol Treatment Trialists' (**CTT**) Collaboration. Efficacy and safety of more intensive lowering of LDL cholesterol: a meta-analysis of data from 170 000 participants in 26 randomised trials. The Lancet, Early Online Publication, 9 November 2010. doi:10.1016/S0140-6736(10)61350-5. Further reductions in LDL cholesterol safely produce definite further reductions in the incidence of heart attack, of revascularisation, and of ischaemic stroke, with each 1·0 mmol/L reduction reducing the annual rate of these major vascular events by just over a fifth. There was no evidence of any threshold within the cholesterol range studied, suggesting that reduction of LDL cholesterol by 2—3 mmol/L would reduce risk by about 40—50%.
Cholesterol Treatment Trialists' (**CTT**) Collaborators. The effects of lowering LDL cholesterol with statin therapy in people at low risk of vascular disease: meta-analysis of individual data from 27 randomised trials. Lancet 2012; online May 17.
Cholesterol Treatment Trialists' (**CTT**) Collaboration. **Efficacy and safety of LDL-lowering therapy among men and women**: meta-analysis of individual data from 174 000 participants in 27 randomised trials. Lancet 2015;online Jan 9.
Cholesterol Treatment Trialists' (**CTT**) Collaboration. Impact of **renal function** on the effects of **LDL cholesterol lowering with statin**-based regimens: meta-analysis of individual participant data from 28 randomised trials. Lancet Diabetes Endo. 2016 Jul 28.
Cholesterol Treatment Trialists' Collaboration (CTT) . Efficacy and safety of **statin therapy in older people**: a meta-analysis of individual participant data from 28 randomised controlled trials. Lancet 2019; 393: 407–15.
Chopra V, Wesorick DH, Sussman JB, et al. Effect of **Perioperative Statins** on Death, Myocardial Infarction, Atrial Fibrillation, and Length of Stay: A Systematic Review and Meta-analysis. Arch Surg. 2012 Feb;147(2):181-9.
Chou R, Dana T, Blazina I, et al. **Screening for Dyslipidemia in Younger Adults**: A Systematic Review for the U.S. Preventive Services Task Force (**USPSTF**). Ann Intern Med. 2016 Oct 18;165(8):560-564.
Chou R, Dana T, Blazina I, et al. **Statins for prevention of cardiovascular disease in adults**: evidence report and systematic review for the US Preventive Services Task Force (**USPSTF**). JAMA. doi:10.1001/jama.2015.15629
Chowdhury R, Stevens S, Gorman D, Pan A, Warnakula S, Chowdhury S, et al. Association between **fish consumption, long chain omega 3 fatty acids**, and risk of cerebrovascular disease: systematic review and meta-analysis. BMJ 2012;345:e6698.
Chuzi S, Pfenniger A, et al. Four Cases of **Cholesterol Management** Informed by the 2018 American Heart Association/American College of Cardiology Multisociety Guideline on the Management of Blood Cholesterol. JAMA Cardiol. 2019 Apr 10.

Cognition, Cognitive effects:

Galatti L, Polimeni G, Salvo F, Romani M, Sessa A, Spina E. Short-term **memory loss** associated with rosuvastatin. Pharmacotherapy. 2006 Aug;26(8):1190-2.
Gracias G, Garrison S, Allan GM. **Statins and cognitive impairment**. Can Fam Physician. 2014 Aug;60(8):e391.
King DS, Wilburn AJ, Wofford MR, Harrell TK, Lindley BJ, Jones DW. **Cognitive impairment** associated with atorvastatin and simvastatin. Pharmacotherapy. 2003 Dec;23(12):1663-7.
Padala KP, Padala PR, Potter JF. Simvastatin-induced **decline in cognition**. Ann Pharmacother. 2006 Oct;40(10):1880-3.
Morandi A, Hughes CG, Thompson JL, et al. **Statins and delirium** during critical illness: a multicenter, prospective cohort study*. Crit Care Med. 2014 Aug;42(8):1899-909.
Ong KL, Morris MJ, McClelland RL, et al. Relationship of **Lipids and Lipid-Lowering Medications With Cognitive Function**: The Multi-Ethnic Study of Atherosclerosis. Am J Epidemiol. 2018 Apr 1;187(4):767-776.
Peters JT, Garwood CL, Lepczyk M. **Behavioral changes with paranoia** in an elderly woman taking atorvastatin. Am J Geriatr Pharmacother. 2008 Mar;6(1):28-32.
Tatley M, Savage R. **Psychiatric adverse** reactions with statins, fibrates and ezetimibe: implications for the use of lipid-lowering agents. Drug Saf. 2007;30(3):195-201.
Wagstaff LR, Mitton MW, Arvik BM, Doraiswamy PM. Statin-associated **memory loss**: analysis of 60 case reports and review of the literature. Pharmacotherapy. 2003 Jul;23(7):871-80.

Clockaerts S, Van Osch GJ, Bastiaansen-Jenniskens YM, et al. Statin use is associated with **reduced incidence and progression of knee osteoarthritis** in the Rotterdam study. Ann Rheum Dis 2012;71:642–47.
Cohen JC, et al. Sequence variations in PCSK9, low LDL, and protection against coronary heart disease. N Engl J Med. 2006 Mar 23;354(12):1264-72.. These data indicate that moderate **lifelong reduction** in the plasma level of LDL cholesterol is associated with a substantial reduction in the incidence of coronary events, even in populations with a high prevalence of non-lipid-related cardiovascular risk factors.
Cohen DE, Anania FA, Chalasani N; National Lipid Association Statin Safety Task Force Liver Expert Panel. An assessment of **statin safety by hepatologists**. Am J Cardiol. 2006 Apr 17;97(8A):77C-81C. Epub 2006 Feb 3.
Colantonio LD, Baber U, Banach M, et al. **Contrasting** Cholesterol Management **Guidelines** for **Adults with CKD**. J Am Soc Nephrol. 2014 Nov 13.
Colantonio LD, Huang L, Monda KL, et al. **Adherence to High-Intensity Statins Following a Myocardial Infarction** Hospitalization Among Medicare Beneficiaries. JAMA Cardiol. 2017 Apr 19.
Colantonio LD, Rosenson RS, Deng L, et al. **Adherence to Statin Therapy Among US Adults** Between 2007 and 2014. J Am Heart Assoc. 2019 Jan 8;8(1):e010376.
Colhoun HM, Ginsberg HN, Robinson JG, et al. No effect of PCSK9 inhibitor **alirocumab** on the incidence of diabetes in a pooled analysis from 10 ODYSSEY Phase 3 studies. Eur Heart J. 2016 Jul 26.
Colivicchi F, Bassi A, Santini M, Caltagirone C. **Discontinuation of statin** therapy and clinical outcome after ischemic **stroke**. Stroke. 2007 Oct;38(10):2652-7. Epub 2007 Aug 30. A large number of patients discontinue their use of statins early after acute stroke. Moreover, patients discontinuing statins have a significantly increased mortality during the first year after the acute cerebrovascular event.
Collins GS, Altman DG. Predicting the adverse risk of statin treatment: an independent and external validation of **Qstatin risk scores** in the UK. Heart. 2012 Jul;98(14):1091-7.
Collins R, Reith C, Emberson J, et al. Interpretation of the **evidence for the efficacy and safety of statin therapy**. Lancet. 2016 Sep 6.
Conly J, Clement F, Tonelli M, et al. **Cost-effectiveness** of the use of low- and high-potency statins in people at **low cardiovascular risk**. CMAJ 2011;183:E1180-8.
Connor A, Tomson C. Should statins be prescribed for **primary prevention** of cardiovascular disease in patients with **chronic kidney disease**? BMJ. 2009 Aug 20;339:b2949. doi: 10.1136/bmj.b2949.
Cook NR, Ridker PM. **Further Insight Into the Cardiovascular Risk Calculator**: The Roles of Statins, Revascularizations, and Underascertainment in the Women's Health Study. JAMA Intern Med. 2014 Oct 6.
Cooper A, O'Flynn N; on behalf of the Guideline Development Group. **Risk assessment and lipi**d modification for primary and secondary prevention of cardiovascular disease: summary of **NICE** guidance. BMJ. 2008 May 31;336(7655):1246-1248. NICE May 2008 http://www.nice.org.uk/guidance/index.jsp?action=byID&o=11982
Corpechot C, Chazouillères O, Rousseau A, et al. A placebocontrolled trial of **bezafibrate i**n primary biliary cholangitis. **(BEZURSO**) N Engl J Med 2018;378: 2171-81.
Costa J, Borges M, David C, Carneiro AV. Efficacy of lipid lowering drug treatment for **diabetic and non-diabetic** patients: meta-analysis of randomised controlled trials. BMJ. 2006 Apr 3; [Epub ahead of print] In Primary prevention trials the major coronary event rates vs placebo were in diabetics 10 → 8% (not significant) & non-diabetics 8→ 6%. In Secondary prevention trials the major coronary event rates vs placebo: in diabetics 34 → 27% & non-diabetics 22 → 17%.
Cowell SJ, Newby DE, Prescott RJ, et al.; Scottish Aortic Stenosis and Lipid Lowering Trial, Impact on Regression (**SALTIRE**) Investigators. A randomized trial of intensive lipid-lowering therapy in calcific aortic stenosis. N Engl J Med. 2005 Jun 9;352(23):2389-97. CONCLUSIONS: Intensive lipid-lowering therapy does not halt the progression of calcific aortic stenosis or induce its regression. This study cannot exclude a small reduction in the rate of disease progression or a significant reduction in major clinical end points. Long-term, large-scale, randomized, controlled trials are needed to establish the role of statin therapy in patients with calcific aortic stenosis.
Crandall JP, Mather K, Rajpathak SN, et al. **Statin use and risk of developing diabetes**: results from the Diabetes Prevention Program. BMJ Open Diabetes Res Care. 2017 Oct 10;5(1):e000438.
Criner GJ, Connett JE, Aaron SD, et al. **Simvastatin** for the prevention of exacerbations in moderate-to-severe **COPD**. N Engl J Med. DOI: 10.1056/NEJMoa1403086.
Crossey E, Amar MJ, Sampson M, et al. A cholesterol-lowering **VLP vaccine that targets PCSK9**. Vaccine. 2015 Oct 26;33(43):5747-55.
Crouse JR 3rd, Raichlen JS, Riley WA, et al. Effect of Rosuvastatin 40mg od on Progression of Carotid Intima-Media Thickness in Low-Risk Individuals (n=984; Ros=702, placebo=282 over 2 years) With Subclinical Atherosclerosis: The **METEOR** Trial . JAMA. 2007 Mar 25; [Epub ahead of print] Rosuvastatin treatment was associated with a 49% reduction in LDL-C level, a 34% reduction in total cholesterol level, an 8% increase in HDL-C level, and a 16% reduction in level of triglycerides. Serious adverse cardiovascular events were infrequent (6 participants [0.86%] had 8 events [1.1%] in the rosuvastatin group vs 0% in the placebo group) In middle-aged adults with an FRS of less than 10% and evidence of subclinical atherosclerosis, rosuvastatin resulted in statistically significant reductions in the rate of progression of maximum CIMT over 2 years vs placebo. Rosuvastatin did not induce disease regression.
Cuchel M, Meagher EA, du Toit Theron H, et al; for the Phase 3 HoFH **Lomitapide** Study investigators. Efficacy and safety of a microsomal triglyceride transfer protein inhibitor in patients with homozygous familial hypercholesterolaemia: a single-arm, open-label, phase 3 study. Lancet. 2012 Nov 1.
Cuchel M, Bruckert E, Ginsberg HN, et al. **Homozygous familial hypercholesterolemia**: new insights and guidance for clinicians to improve detection and clinical management. A position paper from the consensus panel on familial hypercholesterolemia of the

Cuchel M, Meagher EA, et al. Efficacy and safety of a **microsomal triglyceride transfer protein inhibitor** in patients with homozygous familial hypercholesterolaemia: a single-arm, open-label, phase 3 study. Lancet. 2013 Jan 5;381(9860):40-6.
Culver AL, Ockene IS, Balasubramanian R, et al. Statin use and **risk of diabetes mellitus** in postmenopausal women in the Women's Health Initiative (**WHI**). Arch Intern Med 2012.
Curl K, LeBude B, Ruggiero N, et al. Frequency of Use of **Statins and Aspirin in Patients With Previous Coronary Artery Bypass Grafting**. Am J Cardiol. 2016 Apr 20.
Curtis M, Deng Y, Lee VV, et al. Effect of Dose and Timing of **Preoperative Statins on Mortality After Coronary Artery Bypass Surgery**. Ann Thorac Surg. 2017 Mar 15.
Cushman WC, Goff DC Jr. More **HOPE** for Prevention with Statins. N Engl J Med. 2016 Apr 2
Dale KM, Coleman CI, Henyan NN, Kluger J, White CM. Statins and **cancer risk**: a meta-analysis. JAMA. 2006 Jan 4;295(1):74-80.
Daniels SR, Greer FR; Committee on Nutrition. **Lipid screening and cardiovascular health in childhood. Pediatrics**. 2008 Jul;122(1):198-208.
Daniels SR. On the US Preventive Services Task Force (**USPSTF**). Statement on **Screening for lipid disorders in children and adolescents**. JAMA Pediatrics 2016.
Dansky HM, Bloomfield D, Gibbons P, et al. Efficacy and safety after cessation of treatment with the cholesteryl ester transfer protein inhibitor **anacetrapib (MK-0859)** in patients with primary hypercholesterolemia or mixed hyperlipidemia. Am Heart J. 2011 Oct;162(4):708-16.
Dagenais GR, Jung H, Lonn E, et al. Effects of **Lipid-Lowering and Antihypertensive Treatments in Addition to Healthy Lifestyles** in Primary Prevention: An Analysis of the HOPE-3 Trial. J Am Heart Assoc. 2018 Jul 22;7(15).
Dagenais GR, Lu J, Faxon DP, et al. Effects of Optimal Medical Treatment With or Without Coronary Revascularization on Angina and Subsequent Revascularizations in Patients With Type 2 Diabetes Mellitus and Stable Ischemic Heart Disease. Circulation. 2011 Mar 28. (**BARI 2D**)
D'Andrea E, Hey SP, Ramirez CL, Kesselheim AS. Assessment of the Role of Niacin in Managing Cardiovascular Disease Outcomes: A Systematic Review and Meta-analysis. JAMA Netw Open. 2019 Apr 5;2(4):e192224.
Darras P, Mattman A, Francis GA. **Nonfasting lipid testing**: the new standard for cardiovascular risk assessment. CMAJ. 2018 Nov 12;190(45):E1317-E1318.
Dasari TW, Cohen DJ, Kleiman NS, Keyes et al. Statin Therapy in Patients With **Chronic Kidney Disease Undergoing Percutaneous Coronary Intervention** (from the Evaluation of Drug Eluting Stents & Ischemic Events Registry). Am J Cardiol. 2013 Nov 23
Daskalopoulou SS, Mikhailidis DP. **Time for new low density lipoprotein cholesterol (LDL-C) targets**? Expert Opin Pharmacother. 2017 Aug 30:1-3.
David WS, Chad DA, Kambadakone A, et al. Case records of the Massachusetts General Hospital. Case 7-2012. A 79-year-old man with pain and **weakness in the legs**. N Engl J Med. 2012 Mar 8;366(10):944-54.
de Carvalho LSF, Campos AM, Sposito AC. Proprotein Convertase Subtilisin/Kexin Type 9 (**PCSK9**) Inhibitors **and Incident Type 2 Diabetes Mellitus**: A Systematic Review and Meta-analysis With Over 96,000 Patient-Years. Diabetes Care. 2017 Nov 27.
De Caterina Raffaele. **n–3 Fatty Acids** in Cardiovascular Disease. N Engl J Med 2011; 364:2439-2450.
de Ferranti SD, Rodday AM, Mendelson MM, Wong JB, et al. **Prevalence of familial hypercholesterolemia** in the 1999 to 2012 United States National Health and Nutrition Examination Surveys (NHANES). Circulation. 2016;133:1067–1072. d
de Ferranti SD, Rodday AM, Parsons SK, et al. **Cholesterol Screening and Treatment** Practices and Preferences: A Survey of **United States Pediatricians**. J Pediatr. 2017 Feb 13.
de Dios García-Díaz J, Corral-Bueno IM, Mesa-Latorre JM, et al. **Proprotein Convertase Subtilisin/Kexin Type 9 Antibody and Statin-Associated Autoimmune Myopathy**. Ann Intern Med. 2019 Feb 19.
de Jong HJ, Klungel OH, van Dijk L, et al. Use of **statins is associated with an increased risk of rheumatoid arthritis**. Ann Rheum Dis. 2011 Oct 6.
De Jong HJI, van Staa TP, Lalmohamed A, et al. Pattern of **risks of systemic lupus erythematosus** among statin users: a population-based cohort study. Ann Rheum Dis. 2017 Oct;76(10):1723-1730.
de Lorgeril Michel; Salen Patricia; Abramson John; et al. Cholesterol Lowering, Cardiovascular Diseases, and the Rosuvastatin-**JUPITER Controversy**: A Critical Reappraisal. Arch Intern Med. 2010;170(12):1032-1036.
De Vera MA, Choi H, Abrahamowicz M, Kopec J, Goycochea-Robles MV, Lacaille D. **Statin discontinuation** and **risk of acute myocardial infarction** in patients with rheumatoid arthritis: a population-based cohort study. Ann Rheum Dis. 2011 Mar 6.
de Waal BA, Buise MP, van Zundert AA. **Perioperative statin** therapy in patients at high risk for cardiovascular morbidity undergoing surgery: a review. Br J Anaesth. 2014 Sep 3.
DeBoer MD, Gurka MJ, Woo JG, et al. Severity of Metabolic Syndrome as a Predictor of Cardiovascular Disease Between Childhood and Adulthood: The Princeton Lipid Research Cohort Study. J Am Coll Cardiol. 2015 Aug 11;66(6):755-7.
Deedwania P, et al. Treating to New Targets Investigators. Reduction of low-density lipoprotein cholesterol in patients with coronary heart disease and **metabolic syndrome**: analysis of the Treating to New Targets (**TNT** study). Lancet. 2006 Sep 9;368(9539):919-28.
DeFilippis AP, Young R, McEvoy JW, et al. **Risk score overestimation**: the impact of individual cardiovascular risk factors and preventive therapies on the performance of the American Heart Association-American College of Cardiology-Atherosclerotic Cardiovascular Disease risk score in a modern multi-ethnic cohort. Eur Heart J. 2016 Jul 19
Dehghan M, Anand S, Mente A, et al. **Association of nutrients with blood lipids** in 19 countries and 5 continents: the **PURE** study. World Congress of Cardiology & Cardiovascular Health 2016; June 6, 2016; Mexico City, Mexico.Abstract OC06_01
Deloughery EP, Prasad V. If the **IMPROVE-IT Trial** Was Positive, as Reported, Why Did the FDA Denied Expanded Approval for **Ezetimibe and Simvastatin**? An Explanation of the Tipping Point Analysis. J Gen Intern Med. 2018 Jun 4.
Deljehier T, Pariente A, Miremont-Salamé G, et al. **Rhabdomyolysis** after co-administration of a **statin and fusidic acid**: an analysis of the literature and of the WHO database of adverse drug reactions. Br J Clin Pharmacol. 2018 Jan 16.
d'Emden MC, Jenkins AJ, Li L, et al; on behalf of the **FIELD** Study Investigators. Favourable effects of **fenofibrate** on lipids and cardiovascular disease in **women** with type 2 diabetes: results from the Fenofibrate Intervention and Event Lowering in Diabetes (FIELD) study. Diabetologia. 2014 Aug 23.
Derose SF, Green K, Marrett E, et al. **Automated outreach** to increase primary **adherence** to cholesterol-lowering medications. JAMA Intern Med. 2013 Jan 14;173(1):38-43.
Desai CS, Martin SS, Blumenthal RS. **Non-cardiovascular effects** associated with **statins**. BMJ. 2014 Jul 17;349:g3743.
Desai NR, Kohli P, Giugliano RP, et al. **AMG145**, a Monoclonal Antibody Against Proprotein Convertase Subtilisin Kexin Type 9, Significantly Reduces Lipoprotein(a) in Hypercholesterolemic Patients Receiving Statin Therapy: An Analysis From the LDL-C Assessment With Proprotein Convertase Subtilisin Kexin Type 9 Monoclonal Antibody Inhibition Combined With Statin Therapy (LAPLACE)-Thrombolysis in Myocardial Infarction (TIMI) 57 Trial. Circulation. 2013 Aug 27;128(9):962-9.
DeSantes K, Dodge A, Eickhoff J, et al. **Improving Universal Pediatric Lipid Screening**. J Pediatr. 2017 Jun 5.
Dewey FE, Gusarova V, O'Dushlaine C, et al. Inactivating variants in **ANGPTL4** and risk of coronary artery disease. N Engl J Med. DOI: 10.1056/NEJMoa1510926.
Dewey FE, Gusarova V, Dunbar RL, et al. Genetic and Pharmacologic Inactivation of **ANGPTL3** and Cardiovascular Disease. N Engl J Med. 2017 May 24.
Dhruva SS, Huang C, Spatz ES, et al. **Heterogeneity in Early Responses** in **ALLHAT** (Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial). Hypertension. 2017 Jul;70(1):94-102.
Di Angelantonio E et al. for the Emerging Risk Factors Collaboration. Major lipids, **apolipoproteins**, and risk of vascular disease. JAMA 2009 Nov 11; 302:1993. One approach supported by this study is to use nonfasting cholesterol profiles.
Diabetes Canada Clinical Practice Guidelines Expert Committee, Mancini GBJ, Hegele RA, Leiter LA. **Dyslipidemia**. Can J Diabetes. 2018 Apr;42 Suppl 1:S178-S185.
Dimmitt SB, Stampfer HG, Warren JB. The pharmacodynamic and clinical trial **evidence for statin dose**. Br J Clin Pharmacol. 2018 Feb 2.
Dolezelova E, Stein E, Derosa G, Maffioli P, Nachtigal P, Sahebkar A. Effect of **ezetimibe** on plasma adipokines: a systematic review and meta-analysis. Br J Clin Pharmacol. 2017 Feb 6.
Doran B, Guo Y, Xu J, et al. Prognostic Value of **Fasting Versus Nonfasting Low-Density Lipoprotein Cholesterol** Levels on Long-Term Mortality: Insight From the National Health and Nutrition Examination Survey III (NHANES-III). Circulation. 2014 Aug 12;130(7):546-53.
Dormuth CR, Hemmelgarn BR, Paterson JM, et al. Use of **high potency statins** and rates of admission for **acute kidney injury**: multicenter, retrospective observational analysis of administrative databases. BMJ 2013.
Dormuth CR, Filion KB, et al; Canadian Network for Observational Drug Effect Studies(CNODES) Investigators. **Higher potency statins and the risk of new diabetes**: multicentre, observational study of administrative databases. BMJ. 2014 May 29;348:g3244.
Dorresteijn JA, Boekholdt SM, van der Graaf Y, et al. **High-dose statin** therapy in patients with stable coronary artery disease: treating the right patients based on individualized prediction of treatment effect. (TNT) Circulation. 2013 Jun 25;127(25):2485-93.
Douglas K, O'Malley PG, Jackson JL. Meta-analysis: the effect of statins on **albuminuria**. Ann Intern Med. 2006 Jul 18;145(2):117-24.
Downs J, Good C. **New Cholesterol Guidelines**: Has Godot Finally Arrived? Ann Intern Med. 2014 Jan 28
Downs JR and O'Malley PG.**Management of dyslipidemia** for cardiovascular disease risk reduction: Synopsis of the 2014 U.S. **Department of Veterans Affairs and U.S. Department of Defense** clinical practice guideline. Ann Intern Med 2015 Jun 23.
Dowse GK, et al. **Changes in population cholesterol concentrations** and other cardiovascular risk factor levels after five years of the non-communicable disease intervention programme in Mauritius. BMJ 1995; 311: 1255–59. (switch from palm to soya oil)
Driver SL, Martin SS, Gluckman TJ, et al. **Fasting or Nonfasting Lipid Measurements**: It Depends on the Question. J Am Coll Cardiol. 2016 Mar 15;67(10):1227-34.
Drozda J. Jr., Messer JV, Spertus J, et al. **ACCF/AHA/AMA-PCPI 2011 performance measures for adults with coronary artery disease and hypertension**: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Performance Measures and the American Medical Association-Physician Consortium for Performance Improvement. J Am Coll Cardiol 2011;58:xxx–xxx. http://content.onlinejacc.org/cgi/reprint/j.jacc.2011.05.002v1.pdf
Du H, Li X, Su N, et al. Proprotein convertase subtilisin/kexin 9 inhibitors in reducing cardiovascular outcomes: a systematic review and meta-analysis. Heart. 2019 Mar 6.
Duell PB, Gidding SS, Andersen RL, et al. Longitudinal low density lipoprotein **cholesterol goal achievement and cardiovascular outcomes** among adult patients with familial hypercholesterolemia: The CASCADE FH registry. Atherosclerosis. 2019 Aug

Durrington PN, Soran H. **Cholesterol Levels** Should Play a More Important Role in Identifying Statin Recipients. Circulation. 2017 Feb 14;135(7):627-629.

Ebrahim S, Taylor FC, Brindle P. **Statins for the primary prevention** of cardiovascular disease. BMJ. 2014 Jan 27;348:g280.

Egan Amy, Colman Eric. Weighing the Benefits of **High-Dose Simvastatin against the Risk of Myopathy**. June 15, 2011 (10.1056/NEJMp1106689)

Egan BM, Li J, Qanungo S, Wolfman TE. Blood pressure and **cholesterol control in hypertensive hypercholesterolemic** patients **1988-2010**. Circulation 2013.

Egeland GM, Cao Z, Young TK. **Hypertriglyceridemic-waist phenotype and glucose intolerance among Canadian Inuit**: the International Polar Year Inuit Health Survey for Adults 2007-2008. CMAJ. 2011 Jun 14;183(9):E553-8.

Eijsvogels TMH, Januzzi J, Taylor B, et al. Impact of **Statin Use on Exercise-Induced Cardiac Troponin Elevations**. The American Journal of Cardiology (2014).

Ekhart C, de Jong LA, Gross-Martirosyan LD, van Hunsel FP. **Muscle rupture** associated with statin use. Br J Clin Pharmacol. 2016 Apr 13.

Elam MB, Ginsberg HN, Lovato LC, Corson et al. Association of **Fenofibrate** Therapy With Long-term Cardiovascular Risk in Statin-Treated Patients With Type 2 Diabetes. (**ACCORDIAN**) JAMA Cardiol. 2016 Dec 28.

Eliassen AH, Colditz GA, Rosner B, Willett WC, Hankinson SE. Serum lipids, lipid-lowering drugs, and the risk of **breast cancer**. Arch Intern Med. 2005 Oct 24;165(19):2264-71.

Elgendy IY, Mahmoud A, Huo T, et al. Meta-Analysis of 12 Trials Evaluating the Effects of **Statins on Decreasing Atrial Fibrillation** After Coronary Artery Bypass Grafting. Am J Cardiol. 2015 Mar 12.

Elgendy IY, Mahmoud A, Huo T, et al. Meta-analysis of 12 trials evaluating the effects of **statins on decreasing atrial fibrillation after coronary artery bypass grafting**. Am J Cardiol. 2015 Jun 1;115(11):1523-8.

Elgendy AY, Elgendy IY, Mahmoud AN, et al. **Statin Use** in Men **and New Onset of Erectile Dysfunction**: A Systematic Review and Meta-Analysis. Am J Med. 2017 Nov 13

Emerging Risk Factors Collaboration. Major Lipids, Apolipoproteins, and Risk of Vascular Disease. *JAMA*. 2009;302(18):1993-2000.Lipid assessment in vascular disease can be simplified by measurement of either total and HDL cholesterol levels or apolipoproteins without the need to fast and without regard to triglyceride.

Emerging Risk Factors Collaboration. Lipid-related markers and cardiovascular disease prediction. JAMA 2012; 307:2499-2506.

Emilsson L, García-Albéniz X, Logan RW, et al. Examining Bias in Studies of **Statin Treatment** and Survival in Patients With **Cancer**. JAMA Oncol. 2017 Aug 20

Engelter ST, Soinne L, Ringleb P, et al. **IV thrombolysis** and statins. Neurology. 2011 Aug 17.

Ericsson CG, Hamsten A, Nilsson J, et al. Angiographic assessment of effects of bezafibrate on progression of coronary artery disease in young male postinfarction patients. (**BECAIT**)Lancet. 1996 Mar 30;347(9005):849-53.

Eshaghi A, Kievit RA, Prados F, et al. Applying causal models to explore the **mechanism of action of simvastatin in progressive multiple sclerosis**. Proc Natl Acad Sci U S A. 2019 May 9.

Evangelista MT et al. **Simvastatin** as a novel therapeutic agent for **venous ulcers**: A randomized, double-blind, placebo-controlled trial. Br J Dermatol 2014 Feb 7.

Evangelista MT, Casintahan MF, Villafuerte LL. Simvastatin as a novel therapeutic agent **for venous ulcers**: a randomized, double-blind, placebo-controlled trial. Br J Dermatol. 2014 Feb 7.

Everett BM, Smith RJ, Hiatt WR. Reducing LDL with **PCSK9 Inhibitors** – The Clinical Benefit of Lipid Drugs. N Engl J Med. 2015 Oct 7.

Expert Panel on Integrated Guidelines for Cardiovascular Health and Risk Reduction in Children and Adolescents. Expert Panel on **Integrated Guidelines for Cardiovascular Health and Risk Reduction in Children and Adolescents**: Summary Report. (NHLBI: Daniels SR et al.) Pediatrics. 2011 Nov 14. http://www.nhlbi.nih.gov/guidelines/cvd_ped/

Ezetimibe: Using **half doses** of Zetia or Vytorin. Pharmacist's Letter Nov 2006.

Falk E, Mortensen MB. **Statin Therapy on the Basis of HOPE**: A European Perspective. J Am Coll Cardiol. 2016 Dec 27;68(25):2903-2906.

Farsaei S, Khalili H, Farboud ES, et al. Efficacy of **Topical Atorvastatin** for the Treatment of Pressure Ulcers: A Randomized Clinical Trial. Pharmacotherapy. 2013 Aug 12.

Farukhi Z, Mora S. The Future of Low-Density Lipoprotein Cholesterol in an Era of **Nonfasting Lipid Testing and Potent Low-Density Lipoprotein Lowering**. Circulation. 2018 Jan 2;137(1):20-23.

Farzadfar F, Finucane MM, Danaei G, et al. **National, regional, and global trends in serum total cholesterol since 1980**: systematic analysis of health examination surveys and epidemiological studies with 321 country-years and 3.0 million participants. Lancet 2011.

Fayad ZA, Mani V, Woodward M, et al, for the **dal-PLAQUE Investigators**. Safety and effi cacy of **dalcetrapib** on atherosclerotic disease using novel non-invasive multimodality imaging (dal-PLAQUE): a randomised clinical trial. Lancet 2011; online Sept 12.

FDA Mar/10 notified healthcare professionals and patients that, based on review of data from a large clinical trial and other sources, there is an increased risk of **muscle injury** in patients taking the highest approved dose of the cholesterol-lowering medication, Zocor (**simvastatin**) **80 mg**, compared to patients taking lower doses of simvastatin and possibly other drugs in the "statin" class. Reviewing preliminary data from one clinical trial, the agency found that muscle injury, including rhabdomyolysis, was more common among patients on the 80-mg dose of simvastatin versus a 20-mg dose (0.9% vs. 0.02%). In addition, 11 (0.02%) of the patients in the simvastatin-80-mg group developed rhabdomyolysis compared with no patients in the simvastatin-20-mg group.

FDA June/11: Food and Drug Administration drug safety communication: New restrictions, contraindications, and dose limitations for Zocor (simvastatin) to reduce the risk of muscle injury. June 8, 2011. Limit using the 80-mg dose unless the patient has already been taking the drug for 12 months and there is no evidence of myopathy.

FDA Nov/11 notified healthcare professionals the cholesterol-lowering medicine Trilipix (**fenofibric** acid) **may not lower a patient's risk of having a heart attack or stroke**.

FDA Feb/12 has approved important safety label changes for the class of cholesterol-lowering drugs known as statins. The changes include **removal of routine monitoring of liver enzymes** from drug labels. Information about the potential for generally **non-serious and reversible cognitive side effects** and reports of **increased blood sugar** and glycosylated hemoglobin (HbA1c) levels has been added to the statin labels. The **lovastatin** label has been extensively updated with new contraindications and dose limitations when it is taken with certain medicines that can increase the risk for **muscle injury**.

FDA Mar/12 notified healthcare professionals of updates to the prescribing information concerning interactions between **protease inhibitors (HIV & HCV)** and certain statin drugs. Protease inhibitors and statins taken together may raise the blood levels of statins and increase the risk for muscle injury (myopathy/ rhabdomyolysis).

Fei Y, Guyatt GH, Alexander PE, El et al. Addition of **Ezetimibe to statins** for patients at high cardiovascular risk: Systematic review of patient-important outcomes. J Eval Clin Pract. 2017 Jan 16.

Feinstein MJ, Achenbach CJ, Stone NJ, et al. A Systematic Review of the Usefulness of **Statin Therapy in HIV-Infected Patients**. Am J Cardiol. 2015 Jun15;115(12):1760-1766.

Feldman HH, Doody RS, Kivipelto M, et al. On behalf of the **LEADe** Investigators. Randomized controlled trial of atorvastatin in mild to moderate Alzheimer disease. LEADe. Neurology. 2010 Mar 3.

Fellström BC, Jardine AG, Schmieder RE, et al. the **AURORA** Study Group. Rosuvastatin and Cardiovascular Events in Patients Undergoing Hemodialysis. N Engl J Med. 2009 Mar 30. [Epub ahead of print] In patients undergoing hemodialysis, the initiation of treatment with rosuvastatin lowered the LDL cholesterol level but had no significant effect on the composite primary end point of death from cardiovascular causes, nonfatal myocardial infarction, or nonfatal stroke.

Feng CH, Miller CM, Tenney ME, et al. **Statin Use** Significantly Improves Overall Survival in High-Grade **Endometrial Cancer**. Int J Gynecol Cancer. 2016 Sep 19.

Feng Q, Wei WQ, Chaugai S, et al. Association Between **Low-Density Lipoprotein Cholesterol Levels and Risk for Sepsis** Among Patients Admitted to the Hospital With Infection. JAMA Netw Open. 2019 Jan 4;2(1):e187223.

Ference BA, Yoo W, Alesh I, et al. Effect of **long-term exposure** to lower **low-density lipoprotein cholesterol** beginning **early in life** on the risk of coronary heart disease: a Mendelian randomization analysis. J Am Coll Cardiol. 2012;60:2631-2639.

Ference BA et al. **Variation in *PCSK9* and *HMGCR* and risk of cardiovascular disease and diabetes**. N Engl J Med 2016 Dec 1; 375:2144.

Ference BA, Robinson JG, Brook RD, et al. **Variation in PCSK9 and HMGCR** and Risk of Cardiovascular Disease and Diabetes. N Engl J Med. 2016 Dec;375(22):2144-2153

Ference BA, et al. **Low-density lipoproteins cause atherosclerotic cardiovascular disease**. 1. Evidence from genetic, epidemiologic, & clinical studies. A consensus statement from the European Atherosclerosis Society Consensus Panel. *Euro Heart J* 2017.

Ference BA, Kastelein JJP, Ginsberg HN, et al. Association of **Genetic Variants Related to CETP Inhibitors and Statins** With Lipoprotein Levels and Cardiovascular Risk. JAMA. 2017 Sep 12;318(10):947-956

Ference BA, Cannon CP, Landmesser U, et al. **Reduction of low density lipoprotein**- cholesterol and cardiovascular events with proprotein convertase subtilisin-kexin type 9 (**PCSK9**) inhibitors and statins: an analysis of FOURIER, SPIRE, and the Cholesterol Treatment Trialists Collaboration. Eur Heart J. 2017 Aug 14.

Ference BA, Kastelein JJP, Ray KK, et al. Association of **triglyceride-lowering LPL variants and LDL-C–lowering LDLR variants** with risk of coronary heart disease [Jan 29, 2019]. JAMA. doi:10.1001/jama.2018.20045

Ference BA, Ray KK, Catapano AL, et al. Mendelian Randomization **Study of ACLY** and Cardiovascular Disease. N Engl J Med. 2019 Mar 14;380(11):1033-1042.

Fernández-Friera L, Fuster V, López-Melgar B, et al. **Normal LDL-Cholesterol Levels Are Associated With Subclinical Atherosclerosis** in the Absence of Risk Factors. J Am Coll Cardiol. 2017 Dec 19;70(24):2979-2991.

Ferrer-Garcia JC, et al. **Alternate-day** dosing of **atorvastatin**: effects in treating type 2 diabetic patients with dyslipidaemia. Acta Diabetol. 2006 Nov;43(3):75-8. LDL-C decreased 39% after the every-day period & 23% after the alternate-day atorvastatin dosing period ($p<0.05$). The target LDL-C concentration of <100 mg/dl was maintained in 19 patients (57.6%) in the alternate-day period. None of the 33 patients showed elevations in liver enzymes or creatine kinase during the alternate-day dosing period. Alternate-day dosing of atorvastatin could be an effective and safe alternative to daily-dosing in some type 2 diabetic patients.

Finegold JA, Manisty CH, Goldacre B, et al. What proportion of **symptomatic side effects** in patients taking **statins** are genuinely caused by the drug? Systematic review of randomized placebo-controlled trials to aid individual patient choice. Eur J Prevent Cardiol 2014.

Fitchett DH, Hegele RA, Verma S. **Statin intolerance**. Circulation. 2015 Mar 31;131(13):e389-91.

Fitzgerald K, Frank-Kamenetsky M, Shulga-Morskaya S, et al. Eff ect of an **RNA interference drug on the synthesis of proprotein convertase subtilisin/kexin type 9 (PCSK9)** and the concentration of serum LDL cholesterol in healthy volunteers: a randomised, single-blind, placebo-controlled, phase 1 trial. Lancet 2013; online Oct 3.

Fitzgerald K, White S, Borodovsky A, et al. A Highly Durable **RNAi Therapeutic Inhibitor** of PCSK9. N Engl J Med. 2016 Nov 13.

Fleg JL, Mete M, Howard BV, et al. Effect of statins alone versus statins plus ezetimibe on carotid atherosclerosis in type 2 diabetes: the **SANDS** (Stop Atherosclerosis in Native Diabetics Study) trial. J Am Coll Cardiol. 2008 Dec 16;52(25):2198-205. Reducing LDL-C to aggressive targets resulted in similar regression of CIMT in patients who attained equivalent LDL-C reductions from a statin alone or statin plus ezetimibe. Common carotid artery IMT increased in those achieving standard targets.

Fletcher B,et al.; AHA: Managing abnormal blood lipids: a **collaborative approach**. Circulation. 2005 Nov 15;112(20):3184-209.

Fleisher LA, Beckman JA, Brown KA, Calkins H, et al. ACC/AHA 2007 Guidelines on **Perioperative Cardiovascular** Evaluation and Care **for Noncardiac Surgery**. A Report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Writing Committee to Revise the 2002 Guidelines on Perioperative Cardiovascular Evaluation for Noncardiac Surgery). Circulation. 2007 Sep 27; [Epub ahead of print]

Flint AC, Kamel H, Navi BB, et al. **Inpatient statin use predicts improved ischemic stroke** discharge disposition. Neurology. 2012 May 22;78(21):1678-83.

Flint AC, Conell C, Rao VA, et al. Effect of **Statin Use During Hospitalization for Intracerebral Hemorrhage** on Mortality and Discharge Disposition. JAMA Neurol. 2014 Sep 22.

Floyd JS, Keckbert SR, Weiss SR, Carrel DS, Psaty BM. Use of **administrative data** to estimate the incidence of **statin-related rhabdomyolysis**. JAMA 2012; 307:1580-1583.

Folse H, Sternhufvud C, Andy Schuetz C, et al. Impact of **switching treatment from rosuvastatin to atorvastatin** on rates of cardiovascular events. Clin Ther. 2014 Jan 1

Fonarow GC, et al.; National Registry of MI 4 Investigators. Effect of statin use within the **first 24 hours** of admission for acute myocardial infarction on early morbidity and mortality. Am J Cardiol. 2005 Sep 1;96(5):611-6.

Fonarow GC, Keech AC, Pedersen TR, et al. **Cost-effectiveness** of **evolocumab therapy** for reducing cardiovascular events in patients with atherosclerotic cardiovascular disease [online August 23, 2017]. JAMA Cardiol. doi:10.1001/jamacardio.2017.2762.

Fonarow GC, van Hout B, Villa G, et al. Updated **Cost-effectiveness Analysis of Evolocumab** in Patients With Very High-risk Atherosclerotic Cardiovascular Disease. JAMA Cardiol. 2019 Jun 5.

Fong DS, Poon KY. **Recent statin use and cataract surgery**. Am J Ophthalmol 2012;153:222-8.

Fontana M, Asaria P, Moraldo M, et al. **Patient-accessible tool for shared decision making** in cardiovascular primary prevention. Circulation 2014.

Foody JM, et al. Hydroxymethylglutaryl-CoA reductase inhibitors in older persons with acute myocardial infarction: evidence for an **age-statin interaction**. J Am Geriatr Soc. 2006 Mar;54(3):421-30. Statin therapy is associated with lower mortality in older patients with AMI younger than 80 but not in those aged 80 and older, as a group.

Ford ES, Li C, Zhao G, Pearson WS, Mokdad AH. **Hypertriglyceridemia** and its pharmacologic treatment among US adults. Arch Intern Med. 2009 Mar 23;169(6):572-8.

Ford ES, Li C, Zhao G, Mokdad AH. Concentrations of low-density lipoprotein cholesterol and total cholesterol among **children and adolescents** in the United States. Circulation. 2009 Mar 3;119(8):1108-15. Epub 2009 Feb 16.

Ford I, Murray H, McCowan C, Packard CJ. Long Term Safety and Efficacy of Lowering LDL Cholesterol With Statin Therapy: **20-Year Follow-Up of West of Scotland Coronary Prevention Study**. Circulation. 2016 Feb 10.

Ford I, Murray H, Packard CJ, Shepherd J, Macfarlane PW, Cobbe SM; West of Scotland Coronary Prevention Study Group. Long-term follow-up of the West of Scotland Coronary Prevention Study. (Woscops) N Engl J Med. 2007 Oct 11;357(15):1477-86. In this analysis, 5 years of treatment with pravastatin was associated with a significant reduction in coronary events for a subsequent 10 years in men with hypercholesterolemia who did not have a history of myocardial infarction.

Ford I, Murray H, et al. Long-Term Safety and Efficacy of Lowering Low-Density Lipoprotein Cholesterol With Statin Therapy: **20-Year Follow-Up** of West of Scotland Coronary Prevention Study (**WOSCOPS**). Circulation. 2016 Mar 15;133(11):1073-80.

Ford I, Shah AS, Zhang R, et al. **High-Sensitivity Cardiac Troponin, Statin Therapy**, and Risk of Coronary Heart Disease. J Am Coll Cardiol. 2016 Dec 27;68(25):2719-2728.

Ford TJ, Rocchiccioli P. A keen **eye for risk**. (heterozygous familial hypercholesterolemia) BMJ. 2018 Feb 1;360:j5884.

Frank AP, Clegg DJ. JAMA Patient Page. **Dietary Guidelines for Americans**—Eat Less Fat. JAMA. 2016 May 3;315(17):1919

Freedman DS, Wang YC, Dietz WH, Xu JH, et al. **Changes and variability** in high levels of low-density lipoprotein cholesterol among **children**. Pediatrics. 2010 Aug;126(2):266-73. Epub 2010 Jul 19.

Freeman MW, Singh AK, Guidon AC, et al. Case 22-2019: A 65-Year-Old Woman with **Weakness, Dark Urine, and Dysphagia**. N Engl J Med. 2019 Jul 18;381(3):275-283

Frikke-Schmidt R, Nordestgaard BG, et al.. Association of loss-of-function mutations in the ABCA1 gene with high-density lipoprotein cholesterol levels and risk of ischemic heart disease. JAMA. 2008 Jun 4;299(21):2524-32. Lower plasma levels of HDL cholesterol due to heterozygosity for loss-of-function mutations in ABCA1 were not associated with an increased risk of IHD.

Fröhlich GM, Rufibach K, Enseleit F, et al. **Statins and the risk of cancer after heart transplantation**. Circulation. 2012 Jul 24;126(4):440-7.

Fuernau G, Eitel I, Kerber S et al. Impact of Chronic **Statin Pretreatment on Myocardial Damage** in ST-Elevation Myocardial Infarction (From the AIDA STEMI CMR Substudy). The American Journal of Cardiology (2014).

Gadarla M, Kearns AK, Thompson PD. Efficacy of **rosuvastatin (5 mg and 10 mg) twice a week** in patients intolerant to daily statins. Am J Cardiol. 2008 Jun 15;101(12):1747-8. Epub 2008 Apr 11.

Gagne JJ, Choudhry NK, Kesselheim AS, et al. Comparative effectiveness of **generic and brand-name statins** on patient outcomes: a cohort study. Ann Intern Med. 2014 Sep 16;161(6):400-7.

Gaist D, Goldstein LB, Cea Soriano L, et al. **Statins and the Risk of Intracerebral Hemorrhage** in Patients With Previous Ischemic Stroke or Transient Ischemic Attack. Stroke. 2017 Dec;48(12):3245-3251.

Ganda OP. **Deciphering cholesterol treatment guidelines**: a clinician's perspective. JAMA. 2015 Mar 10;313(10):1009-10.

Ganda OP, Plutzky J, Sanganalmath SK, et al. Efficacy and safety of **alirocumab among individuals with diabetes mellitus and atherosclerotic cardiovascular disease** in the **ODYSSEY** phase 3 trials. Diabetes Obes Metab. 2018 May 26.

Gandhi S, Mosleh W, Abdel-Qadir H, et al. **Statins and Contrast-induced Acute Kidney Injury with Coronary Angiography**. Am J Med. 2014 Oct;127(10):987-1000.

Gao X, Simon K, Schwarzschild M et al. Prospective Study of Statin Use and Risk of **Parkinson Disease** Arch Neurol. 2012;69(3):380-384.

Garg A, Sharma A, Krishnamoorthy P, et al. Role of **Niacin in Current Clinical Practice**: A Systematic Review. Am J Med. 2016 Oct 26.

Gaudet D, Watts GF, Robinson JG, et al. Effect of **Alirocumab** on Lipoprotein(a) Over >/=1.5 Years (from the Phase 3 **ODYSSEY** Program). Am J Cardiol. 2016 Sep 29.

Geng Q, Ren J, Song J, et al. Meta-analysis of the Effect of **Statins on Renal Function**.The American Journal of Cardiology (2014).

Gesquiere I, Hens B, der Van Schueren B, et al. Drug disposition before and after **gastric bypass**: **fenofibrate and posaconazole**. Br J Clin Pharmacol. 2016 Jul 1.

Giacoppo D, Capodanno D, Capranzano P, Meta-analysis of Randomized Controlled Trials of **Preprocedural Statin Administration** for **Reducing Contrast Induced Acute Kidney** In Patients Undergoing Coronary Catheterization. The American Journal of Cardiology (2014).

Gibson CM, Korjian S, et al. Safety and Tolerability of **CSL112,** a Reconstituted, Infusible, Plasma-Derived **Apolipoprotein A-I,** After Acute Myocardial Infarction: The **AEGIS-I** Trial (ApoA-I Event Reducing in Ischemic Syndromes I). Circulation. 2016 Nov 15.

Gidding SS, Prospero C, Hossain J, et al. A Double-Blind Randomized Trial of **Fish Oil to Lower Triglycerides** and Improve Cardiometabolic Risk in Adolescents. J Pediatr. 2014 Jul 7.

Gidding SS, Ann Champagne M, de Ferranti SD, et al. American Heart Association Atherosclerosis, Hypertension, and Obesity in the Young Committee of the Council on Cardiovascular Disease in the Young, Council on Cardiovascular and Stroke Nursing, Council on Functional Genomics and Translational Biology, and Council on Lifestyle and Cardiometabolic Health. The **Agenda for Familial Hypercholesterolemia**: A Scientific Statement From the American Heart Association (**AHA**). Circulation. 2015 Dec 1;132(22):2167-92.

Gill PJ, Harnden A, Karpe F. **Familial hypercholesterolaemia**. BMJ. 2012 May 11;344:e3228.

Gillett RC Jr, Norrell A. Considerations for safe use of statins: **liver enzyme abnormalities and muscle toxicitiy**. Am Fam Physician. 2011 Mar 15;83(6):711-6.

Giral P, Neumann A, Weill A, Coste J. **Cardiovascular effect of discontinuing statins** for primary prevention at the age of 75 years: a nationwide population-based cohort study in France. Eur Heart J. 2019 Jul 30.

Gissi-Hf Investigators. Effect of **rosuvastatin** in patients with chronic heart failure (the **GISSI-HF** trial): a randomised, double-blind, placebo-controlled trial. Lancet. 2008 Aug 29. [Epub ahead of print] Rosuvastatin 10 mg daily did not affect clinical outcomes in patients with chronic heart failure of any cause, in whom the drug was safe

Giugliano RP, Desai NR, Kohli P, et al, for the LAPLACE-TIMI 57 Investigators. Efficacy, safety, and tolerability of a monoclonal antibody to proprotein convertase subtilisin/kexin type 9 in combination with a statin in patients with hypercholesterolaemia (**LAPLACE-TIMI 57**): a randomised, placebocontrolled, dose-ranging, phase 2 study. Lancet 2012. (AMG145)

Giugliano RP, Mach F, Zavitz K, et al. Cognitive Function in a Randomized Trial of **Evolocumab**. N Engl J Med. 2017 Aug 17;377(7):633-643

Giugliano RP, Wiviott SD, Blazing MA, et al. **Long-term Safety and Efficacy of Achieving Very Low Levels of Low-Density Lipoprotein Cholesterol** : A Prespecified Analysis of the **IMPROVE-IT** Trial. JAMA Cardiol. 2017 Mar 14.

Giugliano RP, Pedersen TR, Jeong-Gun Park J-G, et al, on behalf of the **FOURIER** Investigators. Clinical efficacy and safety of achieving **very low LDL**-cholesterol concentrations with the **PCSK9** inhibitor **evolocumab**: a prespecified secondary analysis of the **FOURIER** trial. Lancet 2017; online Aug 28.

Giugliano RP, Keech A, Murphy SA, et al. Clinical efficacy and safety of **evolocumab** in high-risk patients receiving a statin: secondary analysis of patients with low LDL cholesterol levels and in those already receiving a maximal-potency statin in a

randomized clinical trial [online Nov 1, 2017]. JAMA Cardiol. doi:10.1001 /jamacardio.2017.3944.
Giugliano RP, Cannon CP, Blazing MA, et al. Benefit of **Adding Ezetimibe to Statin Therapy** on Cardiovascular Outcomes and Safety in Patients With vs. Without Diabetes: Results from **IMPROVE-IT**. Circulation. 2017 Dec 20.
Glasziou PP, Irwig L, Heritier S, Simes RJ, Tonkin A; LIPID Study Investigators. **Monitoring cholesterol levels**: measurement error or true change? Ann Intern Med. 2008 May 6;148(9):656-61.
Glynn RJ, Koenig W, Nordestgaard BG, et al. Rosuvastatin for primary prevention in **older persons** with elevated C-reactive protein and low to average low-density lipoprotein cholesterol levels: exploratory analysis of a randomized trial. Ann Intern Med. 2010 Apr 20;152(8):488-96, W174.
Go AS, et al. Atherosclerotic Disease, Vascular Function & Genetic Epidemiology (ADVANCE) Study. Statin & beta-blockers & the initial presentation of coronary heart disease. Ann Intern Med. 2006 Feb 21;144(4):229-38.
Go AS, Lee WY, Yang J, Lo JC, Gurwitz JH. Statin therapy and risks for death and hospitalization in chronic **heart failure**. JAMA. 2006 Nov 1;296(17):2105-11.
Godfrey LM, Erramouspe J, Cleveland KW. **Teratogenic Risk of Statins** in Pregnancy (October). Ann Pharmacother. 2012 Oct 2.
Godlee F. **Adverse effects of statins**. BMJ: British Medical Journal 348 (2014).
Goldberg AC, Hopkins PN, Toth PP, et al. **Familial hypercholesterolemia**: screening, diagnosis, and management of pediatric and adult patients. J Clin Lipidol 2011; 5:133-140.
Goldberg IJ, Reue K, Abumrad NA, et al. Deciphering the **Role of Lipid Droplets in Cardiovascular Disease**: A Report From the 2017 National Heart, Lung, and Blood Institute Workshop. Circulation. 2018 Jul 17;138(3):305-315.
Goldfine AB. Statins: Is It Really **Time to Reassess Benefits and Risks**? N Engl J Med. 2012 Apr 25.
Goldie C, Taylor AJ, Nguyen P, et al. **Niacin** therapy and the risk of **new-onset diabetes**: a meta-analysis of randomised controlled trials. Heart. 2015 Sep 14.
Goldstein LB, Nederkoorn PJ. **Statins and poststroke intracerebral hemorrhage**: Concern but increasing reassurance. Neurology. 2016 Apr 26;86(17):1570-1.
Golomb BA. Implications of statin adverse effects in the **elderly**. Expert Opin Drug Saf. 2005 May;4(3):389-97.
Golomb BA, Dimsdale JE, White HL, et al. Reduction in **blood pressure** with statins. Arch Intern Med 2008; 168: 721-727. Reductions in SBP and DBP occurred with hydrophilic and lipophilic statins and extended to normotensive subjects. These modest effects may contribute to the reduced risk of stroke and cardiovascular events reported on statins.
Golomb BA, Evans MA, Dimsdale JE, and White HL. Effects of **statins on energy and fatigue** with exertion: Results from a randomized controlled trial. Arch Intern Med 2012.
Golomb BA, Dimsdale JE, Koslik HJ, et al. **Statin effects on aggression**: Results from the UCSD Statin Study, a randomized controlled trial. *PLoS One* 2015.
Golomb BA, Dimsdale JE, Koslik HJ, et al. **Statin Effects on Aggression**: Results from the UCSD Statin Study, a Randomized Control Trial. PLoS One. 2015 Jul 1;10(7):e0124451.
Gooding HC, Rodday AM, Wong JB, et al. Application of **pediatric and adult guidelines** for treatment of **lipid levels** among us adolescents transitioning to young adulthood. *JAMA Pediatrics* 2015.
Gordon RY.; Cooperman T; Obermeyer W; et al. Marked Variability of Monacolin Levels in Commercial **Red Yeast Rice** Products: Buyer Beware! Arch Intern Med. 2010;170(19):1722-1727.
Gordin J, Haider A, Swaminathan RV et al. Impact of Long-term Statin Therapy on **Postprocedural Myocardial Infarction** in Patients Undergoing Nonemergency **Percutaneous Coronary Intervention**. Am J Cardiol. 2012 Aug 1.
Gotto AM Jr, Moon JE. **Recent clinical studies** of the effects of lipid-modifying therapies. Am J Cardiol. 2012 Jul;110(1 Suppl):15A-26A.
Gotto AM Jr, Moon JE. Management of cardiovascular risk: the importance of **meeting lipid targets**. Am J Cardiol. 2012 Jul;110(1 Suppl):3A-14A.
Gouni-Berthold I, Descamps OS, Fraass U, et al. Systematic review of published phase 3 data on **anti-PCSK9 monoclonal antibodies** in patients with hypercholesterolaemia. Br J Clin Pharmacol. 2016 Aug 1.
Grabowski DC, Lakdawalla DN, Goldman DP, et al. The large **social value resulting from use of statins** warrants steps to improve adherence and broaden treatment. Health Aff 31;2276-2285.
Gracias G, Garrison S, Allan GM. **Statins and cognitive impairment**. Can Fam Physician. 2014 Aug;60(8):e391.
Graham DJ, Staffa JA, Shatin D, et al. Incidence of **hospitalized rhabdomyolysis** in patients treated with lipid-lowering drugs. JAMA 2004; 292:2585-90.
Graham MJ, Lee RG, Brandt TA, et al. Cardiovascular and Metabolic Effects of **ANGPTL3** Antisense Oligonucleotides. N Engl J Med. 2017 May 24.
Greco A et al. Acute hepatitis caused by a **natural lipid-lowering product**: when "alternative" medicine is no "alternative" at all. J Hepatology 2009; 50:1273.
Green Lee A. Cholesterol-Lowering Therapy for **Primary Prevention**: Still Much We Don't Know. Arch Intern Med. 2010;170(12):1007-1008.
Green A, Ramey DR, Emneus M, et al. Incidence of **Cancer** and Mortality in Patients from the **Simvastatin and Ezetimibe** in **Aortic Stenosis** (**SEAS**) Trial. Am J Cardiol. 2014 Aug 27.
Gregoor PJ. Atorvastatin may cause **nightmares**. BMJ. 2006 Apr 22;332(7547):950.
Greve AM, Bang CN, Egstrup K, et al. Effect Modifications of Lipid Lowering Therapy on Progression of **Aortic Stenosis** (from the **SEAS** Study). Am J Cardio. 2017
Greving JP, Visseren FLJ, de Wit GA, et al. Statin treatment for **primary prevention** of vascular disease: whom to treat? **Cost-effectiveness analysis**. BMJ 2011;342:doi:10.1136/bmj.d1672 (30 March 2011). (seemed not cost-effective in low risk 1^0)
Grundy SM. Statins for All? Am J Cardiol. 2014 Sep 4.
Grundy SM, Stone NJ. 2018 American Heart Association/American College of Cardiology Multisociety Guideline on the **Management of Blood Cholesterol: Primary** Prevention. JAMA Cardiol. 2019 Apr 10.
Grundy SM, Stone NJ. 2018 American Heart Association/American College of Cardiology/Multisociety Guideline on the **Management of Blood Cholesterol-Secondary Prevention**. JAMA Cardiol. 2019 Apr 17.
Grundy SM, Stone NJ; Guideline Writing Committee for the 2018 Cholesterol Guidelines†. 2018 Cholesterol Clinical Practice Guidelines: Synopsis of the 2018 American Heart Association/American College of Cardiology/Multisociety Cholesterol Guideline. Ann Intern Med. 2019 May 28.
Guallar E, Laine C. **Controversy over clinical guidelines**: listen to the evidence, not the noise. *Ann Intern Med* 2014
Gudzune KA, Monroe AK, Sharma R, et al. Effectiveness of **combination therapy with statin and another lipid-modifying agent compared with intensified statin monotherapy**: a systematic review. Ann Intern Med. 2014 Apr 1;160(7):468-76.
Guedeney P, Claessen BE, Kalkman DN, et al. Residual **Inflammatory Risk in Patients With Low LDL Cholesterol Levels** Undergoing Percutaneous Coronary Intervention. J Am Coll Cardiol. 2019 May 21;73(19):2401-2409.
Guedeney P, Giustino G, Sorrentino S, et al. Efficacy and safety of **alirocumab and evolocumab**: a systematic review and meta-analysis of randomized controlled trials. Eur Heart J. 2019 Jul 3.
Guis S, et al. In vivo and in vitro characterization of **skeletal muscle metabolism** in patients with statin-induced adverse effects. Arthritis Rheum. 2006 Aug 15;55(4):551-7.
Gulliford M, Ravindrarajah R, Hamada S, et al. **Inception and deprescribing of statins** in people aged over 80 years: cohort study. Age Ageing. 2017 Nov 1;46(6):1001-1005.
Guo J, Meng F, Ma N, et al. Meta-Analysis of Safety of the **Coadministration of Statin With Fenofibrate** in Patients With Combined Hyperlipidemia. Am J Cardiol. 2012 Jul 26.
Guo J, Guo J, Li J, et al. **Statin treatment reduces the risk of poststroke seizures**. Neurology 2015;85:701–707.
Gupta A, Thompson D, Whitehouse A, et al. **Adverse events associated with unblinded**, but not with blinded, **statin therapy** in the Anglo-Scandinavian Cardiac Outcomes Trial-Lipid-Lowering Arm **(ASCOT-LLA):** a randomised double-blind placebo-controlled trial and its non-randomised non-blind extension phase. Lancet. 2017 May 2.
Gupta A, Mackay J, Whitehouse A, et al. Long-term **mortality after blood pressure-lowering and lipid-lowering treatment in patients with hypertension** in the Anglo-Scandinavian Cardiac Outcomes Trial (ASCOT) Legacy study: 16-year follow-up results of a randomised factorial trial. Lancet. 2018 Aug 24.
Gutierrez J, Ramirez G, Rundek T, Sacco RL. Statin therapy in the prevention of recurrent cardiovascular events: a **sex-based meta-analysis**. Arch Intern Med. 2012;172(12):909-918.
Ha V, Sievenpiper JL, de Souza RJ, et al. Effect of **dietary pulse intake (beans, lentils)** on established therapeutic lipid targets for cardiovascular risk reduction: a systematic review and meta-analysis of randomized controlled trials. CMAJ. 2014 Apr 7.
Haas ME, Levenson AE, Sun X, et al. The Role of **Proprotein Convertase Subtilisin/Kexin Type 9** in Nephrotic Syndrome-Associated Hypercholesterolemia. Circulation. 2016 Jul 5;134(1):61-72.
Hackam DG, Austin PC, Huang A, et al. Statins and **intracerebral hemorrhage**: a retrospective cohort study. Arch Neurol. doi:10.1001/archneurol.2011.228.
Hackam DG, Hegele RA. Cholesterol Lowering and **Prevention of Stroke**. Stroke. 2019 Jan 3:STROKEAHA118023167.
Hackam DG, Woodward M, Newby LK, et al. Statins and **intracerebral hemorrhage**: collaborative systematic review and meta-analysis. Circulation. 2011 Nov 15;124(20):2233-42.
Hagiwara N, Kawada-Watanabe E, Koyanagi R, et al. Lowdensity lipoprotein cholesterol targeting with **pitavastatin þ ezetimibe** for patients with **acute coronary syndrome** and **dyslipidaemia**: the **HIJ-PROPER** study, a prospective, open-label, randomized trial. Eur Heart J 2017;38:2264–2275.
Hague WE, Simes J, Kirby A, et al; LIPID investigators. Long-Term Effectiveness and Safety of Pravastatin in Patients With Coronary Heart Disease: **16 Years of Follow-Up** of the **LIPID** Study. Circulation. 2016 Mar 25.
Halava H, Korhonen MJ, Huupponen R, et al. **Lifestyle factors as predictors of nonadherence to statin** therapy among patients with and without cardiovascular comorbidities. CMAJ. 2014 Jun 23.
Halbert SC, French B, Gordon RY, et al. Tolerability of **red yeast rice** (2400 mg twice daily) versus pravastatin (20 mg twice daily) in patients with previous statin intolerance. Am J Cardiol 2010; 105:198-204.
Hammond G, Mashari Greenberger H, Liao M, Mosca L. Effect of gender, **caregiver**, on cholesterol control and statin use for secondary prevention among hospitalized patients with coronary heart disease. Am J Cardiol. 2012 Dec 1;110(11):1613-8.

Han BH, Sutin D, et al. Effect of **statin** treatment vs usual care on primary cardiovascular prevention among **older adults: the ALLHAT-LLT** randomized clinical trial [published online May 22, 2017]. JAMA Intern Med. doi:10.1001 /jamainternmed.2017.1442

Haney EM, et al. ***Screening and Treatment for Lipid Disorders in Children and Adolescents****: Systematic Evidence Review for the US Preventive Services Task Force.* Pediatrics. 2007 Jul;120(1):e189-214. Several key issues about screening and treatment of dyslipidemia in children and adolescents could not be addressed because of lack of studies, including effectiveness of screening on adult coronary heart disease or lipid outcomes, optimal ages and intervals for screening children, or effects of treatment of childhood lipid levels on adult coronary heart disease outcomes.

Hannah-Shmouni F, McLeod K, Sirrs S. **Recurrent exercise-induced rhabdomyolysis**. CMAJ. 2012 Mar 6;184(4):426-30.

Harada PH, Cook NR, Cohen DE, et al. Relation of **Alanine Aminotransferase Levels** to Cardiovascular Events and **Statin** Efficacy. Am J Cardiol. 2016 Jul 1;118(1):49-55.

Harbin M, Amadio A, Tejani A. Critical Appraisal of the **SHARP Trial**: The Results May Be Dull. Clin Ther. 2014 Dec 1;36(12):2112-7.

Harrison TN, Derose SF, Cheetham TC, et al. **Primary nonadherence to statin** therapy: patients' perception. Am J Manag Care 2013; 19: e133-e139.

Harrison SC, Holmes MV, Burgess S, et al. Genetic Association of Lipids and Lipid Drug Targets With **Abdominal Aortic Aneurysm**: A Meta-analysis.JAMA Cardiol. 2017 Nov 29.

Harshman LC, Wang X, Nakabayashi M, et al. **Statin** Use at the Time of **Initiation of Androgen Deprivation Therapy** and Time to Progression in Patients With Hormone-Sensitive **Prostate Cancer**. JAMA Oncol. 2015 Jul 1;1(4):495-504.

Harvey PD, Sabbagh MN, et al. **No evidence** of **neurocognitive adverse events** associated with **alirocumab** treatment in 3340 patients from 14 randomized Phase 2 and 3 controlled trials: a meta-analysis of individual patient data. Eur Heart J. 2017 Nov 27.

Hawkes N. An endorsement of **PCSK9 inhibitors** funded by … their manufacturers. BMJ. 2017 Feb 13;356:j712.

Hawkes N. Could **giving statins to over 75s** really save 8000 lives a year? BMJ. 2019 Apr 17;365:l1779.

Hayek S, Escaro FC, Sattar A, et al. Effect of **Ezetimibe** on Major Atherosclerotic Disease Events and All-Cause Mortality. Am J Cardiol. 2012 Dec 4.

Hayes JF, Lundin A, Wicks S, et al. Association of Hydroxylmethyl Glutaryl Coenzyme A Reductase Inhibitors, L-Type Calcium Channel Antagonists, and Biguanides With **Rates of Psychiatric Hospitalization and Self-Harm in Individuals** With Serious Mental Illness. JAMA Psychiatry. 2019 Jan 9.

Haynes R, Lewis D, Emberson J, et al. Effects of lowering LDL cholesterol (ezetimibe + simvastatin) on progression of **kidney disease** (**Sharp trial**). *J Am Soc Nephrol* 2014.

Hayward RA., Krumholz HM., Zulman DM., et al. **Optimizing Statin Treatment** for Primary Prevention of Coronary Artery Disease. Ann Intern Med January 19, 2010 152:69-77.

Hayward RA, Krumholz HM. Three reasons to **abandon low-density lipoprotein targets**: an open letter to the Adult Treatment Panel IV of the National Institutes of Health. Circ Cardiovasc Qual Outcomes 2012.

Hayward RA, Krumholz HM. **Three reasons to abandon low-density lipoprotein targets**: an open letter to the Adult Treatment Panel IV of the National Institutes of Health. Circ Cardiovasc Qual Outcomes. 2012 Jan;5(1):2-5.

Hayward RA. When to Start a **Statin Is a Preference-Sensitive Decision**. Circulation. 2017 Sep 19;136(12):1099-1101.

He Y, Li X, Gasevic D, Brunt E, et al. **Statins and Multiple Noncardiovascular Outcomes**: Umbrella Review of Meta-analyses of Observational Studies and Randomized Controlled Trials. Ann Intern Med. 2018 Oct 9.

Health Canada Jan/13: informing Canadians of a labelling update for all cholesterol-lowering drugs (also known as **statins**) regarding the risk of increased blood sugar levels and a small increased **risk of diabetes** among patients already at risk for the disease.

Heart Protection Study Group. **Lifetime cost effectiveness** of simvastatin in a range of risk groups and age groups derived from a randomised trial of 20 536 people. (**HPS**) BMJ. 2006 Nov 10; [Epub ahead of print]

Heart Protection Study (**HPS**) Collaborative Group. **C-reactive protein** concentration and the vascular benefits of statin therapy: an analysis of 20 536 patients in the Heart Protection Study. *Lancet* 2011.

Heart Protection Study Collaborative Group. (**HPS**) Effects on **11-year mortality and morbidity** of lowering LDL cholesterol with simvastatin for about 5 years in 20 536 high-risk individuals: a randomised controlled trial. Lancet 2011; online Nov 23.

Health Canada Oct/07 Foreign Product Alerts: **Red Yeast Rice, Red Yeast Rice/Policosonal Complex and Cholestrix** are promoted as dietary supplements for the treatment of high cholesterol. These products may contain **lovastatin**, a prescription medication for the treatment of high cholesterol that should only be taken under the guidance of a health professional.

Health Canada Nov/12: Merck Canada Inc., in consultation with Health Canada, would like to inform you of important safety recommendations on dosage related to the increased risk of **myopathy/rhabdomyolysis**, particularly with the 80 mg dose of ZOCOR® (**simvastatin**; also marketed as generics). An increased risk of myopathy/rhabdomyolysis within the recommended dose range for ZOCOR® (simvastatin) can also be seen with concomitant administration of certain medications.

Heath I, Evans S, Furberg C, et al. Report of the independent panel considering the **retraction of two articles** in The BMJ. (statins) BMJ. 2014 Aug 15;349:g5176.

Hegele RA. Improving the **Monitoring and Care of Patients With Familial Hypercholesterolemia**. J Am Coll Cardiol. 2016 Mar 22;67(11):1286-8.

Heller DJ, Coxson PG, Penko J, et al. Evaluating the Impact and **Cost-Effectiveness of Statin Use Guidelines for Primary Prevention** of Coronary Heart Disease and Stroke. Circulation. 2017 Jul 7.

Hernáez Á, Castañer O, Elosua R, et al. **Mediterranean diet** improves high-density lipoprotein function in high-cardiovascular-risk individuals: a randomized controlled trial. Circulation. 2017;135:633–643.

Hernandez I. Revisiting Outcomes-Based Pricing Propositions for the **PCSK9** Inhibitor **Evolocumab**. JAMA Intern Med. 2017 Aug 7.

Herttua K, Martikainen P, Batty GD, et al. **Poor Adherence to Statin and Antihypertensive** Therapies as Risk Factors for Fatal **Stroke**. J Am Coll Cardiol. 2016 Apr 5;67(13):1507-15.

Hess GP, Natarajan P, Faridi KF, et al. **Proprotein Convertase Subtilisin/Kexin Type 9 Inhibitor** Therapy: **Payer Approvals and Rejections**, **and Patient Characteristics** for Successful Prescribing. Circulation. 2017 Oct 30.

Hiatt WR, Smith RJ. Assessing the clinical **benefits of lipid-disorder drugs**. N Engl J Med. 2014 Jan 30;370(5):396-9

Hippisley-Cox J, Coupland C. Effect of statins on the mortality of patients with **ischaemic heart disease**: population based cohort study with nested case-control analysis. Heart. 2006 Jun;92(6):752-8. Epub 2005 Oct 10.

Hippisley-Cox Julia, Coupland Carol. **Unintended effects of statins** in men and women in England and Wales: population based cohort study using the QResearch database. BMJ 2010;340.

Hirayama K, Ota T, Harada K, et al. Impact of Paradoxical **Decrease in High-Density Lipoprotein** Cholesterol Levels After **Statin** Therapy on Major Adverse Cardiovascular Events in Patients with Stable Angina Pectoris. Clin Ther. 2016 Dec 26.

Hiukka A, Westerbacka J, Leinonen ES, et al. Long-term effects of fenofibrate on carotid intima-media thickness and augmentation index in subjects with type 2 diabetes mellitus. (Field) J Am Coll Cardiol. 2008 Dec 16;52(25):2190-7. Fenofibrate treatment was not associated with beneficial changes in IMT, augmentation index, or biomarkers of inflammation and endothelial function.

Hodis HN and Mack WJ.**Hormone therapy and risk of all-cause mortality** in women treated with statins. Menopause 2015 Apr; 22:363.

Hofer TP, Sussman JB, Hayward RA. New Studies **Do Not Challenge the American College of Cardiology/American Heart Association Lipid Guidelines**. Ann Intern Med. 2016 Feb 9.

Holdaas H, et al. Assessment of LEscol in Renal Transplantation (**ALERT**) Study Investigators. Effect of fluvastatin on cardiac outcomes in renal transplant recipients: multicentre randomised placebo-controlled trial. Lancet. 2003 Jun 14;361(9374):2024-31.

Holtzman CW, Wiggins BS, Spinler SA. Role of **P-glycoprotein** in statin drug interactions. Pharmacotherapy. 2006 Nov;26(11):1601-7.

Homer K, Robson J, Solaiman S, et al. **Reducing liver function tests for statin monitoring**: an observational comparison of two clinical commissioning groups. Br J Gen Pract. 2017 Mar;67(656):e194-e200.

Hong KN, Fuster V, Rosenson RS, et al. **How Low to Go With Glucose, Cholesterol, and Blood Pressure in Primary Prevention of CVD**. J Am Coll Cardiol. 2017 Oct 24;70(17):2171-2185.

Hong SJ, Jeong HS, Ahn JC, et al. A Phase III, Multicenter, Randomized, Double-blind, Active Comparator Clinical Trial to Compare the Efficacy and Safety of Combination Therapy With **Ezetimibe and Rosuvastatin Versus Rosuvastatin Monotherapy** in Patients With Hypercholesterolemia: **I-ROSETTE** (Ildong Rosuvastatin & Ezetimibe for Hypercholesterolemia) Randomized Controlled Trial. Clin Ther. 2018 Feb;40(2):226-241.e4.

Hooper L, et al. Risks and benefits of **omega 3 fats** for mortality, cardiovascular disease, and cancer: systematic review. BMJ. 2006 Mar 24; [Epub ahead of print] CONCLUSION: Long chain and shorter chain omega 3 fats do not have a clear effect on total mortality, combined cardiovascular events, or cancer. (InfoPOEMs: Overall, omega 3 fatty acid supplementation does not decrease mortality or cardiovascular disease as compared with placebo. This study combined both primary and secondary prevention; that is, it included people with and without coronary heart disease. (LOE = 1a)) (Brouwer IA, et al. SOFA Study Group. Effect of fish oil on ventricular tachyarrhythmia and death in patients with implantable cardioverter defibrillators: the Study on Omega-3 Fatty Acids and Ventricular Arrhythmia (SOFA) randomized trial. JAMA. 2006 Jun 14;295(22):2613-9. Our findings do not indicate evidence of a strong protective effect of intake of omega-3 PUFAs from fish oil against ventricular arrhythmia in patients with ICDs.)

Hopewell JC, Parish S, Clarke R, et al. No impact of **KIF6 genotype** on vascular risk and statin response among 18 348 randomized patients in the Heart Protection Study. J Am Coll Cardiol 2011; DOI:10.1016/j.jacc.2011.02.015.

Hou W, Lv J, Perkovic V, et al. Effect of **statin** therapy on cardiovascular and renal outcomes in patients with **chronic kidney disease**: a systematic review and meta-analysis. Eur Heart J. 2013 Mar 6.

Houslay E, et al. **Progressive coronary calcification despite** intensive lipid-lowering therapy: a randomised controlled trial. Heart. 2006 Jan 31; [Epub ahead of print]

Houslay ES, et al. **Scottish Aortic Stenosis** and Lipid Lowering Therapy, Impact on Regression trial Investigators. Progressive coronary calcification despite intensive lipid-lowering treatment: a randomised controlled trial. Heart. 2006 Sep;92(9):1207-12. Epub 2006 Jan 31.

Hovingh GK, Kastelein JJP, van Deventer SJH, et al. **Cholesterol ester transfer protein inhibition** by **TA-8995** in patients with mild dyslipidaemia (TULIP): a randomised, double-blind, placebo-controlled phase 2 trial. Lancet 2015; online June 3.

Hovingh GK, Ray KK, Boekholdt SM. Is **Cholesteryl Ester Transfer Protein Inhibition** an Effective Strategy to Reduce Cardiovascular Risk? CETP as a Target to Lower CVD Risk: Suspension of Disbelief? Circulation. 2015 Aug 4;132(5):433-40.

Hovingh GK, Gandra SR, McKendrick J, et al. Identification and **management of patients with statin-associated symptoms** in clinical practice: A clinician survey. Atherosclerosis. 2016 Feb;245:111-7.

Hoyland A, Mundal LJ, Igland J, et al. **Risk of Ischemic Stroke and Total Cerebrovascular Disease** in Familial Hypercholesterolemia. Stroke. 2018 Nov 21:STROKEAHA118023456.

HPS2-THRIVE Collaborative. HPS2-THRIVE randomized placebo-controlled trial in 25 673 high-risk patients of **ER niacin/laropiprant**: trial design, pre-specified muscle and liver outcomes, and reasons for stopping study treatment. Eur Heart J. 2013 Feb 26.
HPS2-THRIVE Collaborative Group.Effects of **extended-release niacin with laropiprant** in high-risk patients. N Engl J Med 2014 Jul 17; 371:203.
HPS3/TIMI55-REVEAL Collaborative Group **Effects of Anacetrapib in Patients with Atherosclerotic Vascular Disease.** N Engl J Med. 2017 Aug 28.
Hsue PY, Bittner VA, Betteridge J, et al. Impact of **female sex on lipid lowering**, clinical outcomes, and adverse effects in atorvastatin trials. Am J Cardiol. 2015 Feb 15;115(4):447-53.
Huang BZ, Chang JI, Li E, et al. Influence of **Statins** and Cholesterol on Mortality Among Patients With **Pancreatic Cancer**. J Natl Cancer Inst. 2016 Dec 31;109(5).
Huded CP, Becnk LR, Stone NJ et al. Relation of **Intensity of Statin Therapy** and Outcomes **After Transcatheter Aortic Valve Replacement**. Am J Cardio. 2017.
Huesch MD. Association of Baseline **Statin Use Among Older Adults Without Clinical Cardiovascular Disease** in the **SPRINT** Trial. JAMA Intern Med. 2018 Jan 22.
Hui LL, Kwok MK, Nelson EAS, et al. **Breastfeeding in Infancy and Lipid Profile in Adolescence**. Pediatrics. 2019 Apr 9.
Hulten E, et al. The effect of early, intensive statin therapy on **acute coronary syndrome**: a meta-analysis of randomized controlled trials. Arch Intern Med. 2006 Sep 25;166(17):1814-21. Early, intensive statin therapy reduces death and cardiovascular events after 4 months of treatment.
Huxley RR, Barzi F, Lam TH, et al; for the Asia Pacific Cohort Studies Collaboration and the Obesity in Asia Collaboration. Isolated Low Levels of **High-Density Lipoprotein** Cholesterol Are Associated With an Increased Risk of Coronary Heart Disease: An Individual Participant Data Meta-Analysis of 23 Studies in the Asia-Pacific Region. Circulation. 2011 Nov 8;124(19):2056-2064.
Ikeda M, et al. Different **anti-HCV** profiles of statins and their potential for combination therapy with interferon. Hepatology. 2006 Jul;44(1):117-25.
ICSI: Institute for Clinical Systems Improvement. Lipid management in adults. Bloomington (MN): Institute for Clinical Systems Improvement (ICSI); 2011 Oct.
Iggman D, Rosqvist F, Larsson A, et al. Role of **dietary fats** in modulating cardiometabolic risk during moderate weight gain: a randomized double-blind overfeeding trial (**LIPOGAIN** study). *J Am Heart Assoc* 2014
Ioannidis JPA. Inconsistent Guideline Recommendations for Cardiovascular Prevention and the Debate About Zeroing in on and Zeroing LDL-C Levels With **PCSK9** Inhibitors. JAMA. 2017 Aug 1;318(5):419-420.
Ioannidis JP. More than a billion people taking statins?: Potential implications of the **new cardiovascular guidelines**. JAMA. 2014 Feb 5;311(5):463-4
Iso H, et al.; JPHC Study Gp. Intake of **fish** & n3 fatty acids and risk of coronary heart disease among Japanese: the Japan Public Health Center-Based (JPHC) Study Cohort I. Circulation. 2006 Jan 17;113(2):195-202. Epub 2006 Jan 9.
Itoh H, Komuro I, Takeuchi M, et al; EMPATHY Investigators. Intensive Treat-to-Target **Statin Therapy** in High-Risk Japanese Patients With **Hypercholesterolemia and Diabetic Retinopathy**: Report of a Randomized Study. Diabetes Care. 2018 Apr 6.
Iwere RB, Hewitt J. **Myopathy** in older people receiving **statin** therapy: a systematic review and meta-analysis. Br J Clin Pharmacol. 2015 May 29.
Izquierdo-Palomares JM, Fernandez-Tabera JM, Plana MN, et al. **Chronotherapy versus conventional statins therapy** for the treatment of hyperlipidaemia. Cochrane Database Syst Rev. 2016 Nov 26;11:CD009462. Limited and low-quality evidence suggested that there were no differences between chronomodulated treatment with statins in people with hyperlipidaemia as compared to conventional treatment with statins, in terms of clinically relevant outcomes. Studies were short term and therefore did not report on our primary outcomes, cardiovascular clinical events or death. The review did not find differences in adverse events associated with statins between both regimens. Taking statins in the evening does not have an effect on the improvement of lipid levels with respect to morning administration. Further high-quality trials with longer-term follow-up are needed to confirm the results of this review.
Jackevicius Cynthia A, Tu Jack V, Ross Joseph S, et al. Use of **Fibrates in the United States and Canada**. JAMA. 2011;305(12):1217-1224.doi:10.1001/jama.2011.353
Jackevicius CA, Tu JV, Ross JS, et al. Use of **niacin** in the United States and Canada. JAMA Intern Med 2013. (Niaspan, Advicor…)
Jackson CL, Keeton JZ, Eason SJ, et al. **Identifying familial hypercholesterolemia** using a blood donor screening program with more than 1 million volunteer donors. JAMA Cardiol 2019 May 22.
Jacobson TA. **Toward "pain-free" statin prescribing**: clinical algorithm for diagnosis and management of **myalgia**. Mayo Clin Proc. 2008 Jun;83(6):687-700.
Jafri Haseeb, Alsheikh-Ali Alawi A., Karas Richard H. Meta-analysis: **Statin** Therapy Does Not Alter the Association Between Low Levels of High-Density Lipoprotein (**HDL**) Cholesterol and Increased Cardiovascular Risk. *Ann Intern Med December 21, 2010 153:800-808.*
Jaiswal S, Natarajan P, Silver AJ, et al. **Clonal hematopoiesis (CHIP)** and risk of atherosclerotic cardiovascular disease. N Engl J Med. DOI: 10.1056/NEJMoa1701719.
Jaspers NEM, Blaha MJ, Matsushita K, et al. **Prediction of individualized lifetime benefit** from cholesterol lowering, blood pressure lowering, antithrombotic therapy, and smoking cessation in apparently healthy people. Eur Heart J. 2019 May 18.
JBS3 Board. **Joint British Societies' consensus recommendations** for the prevention of cardiovascular disease (JBS3). Heart 2014.
Jefferson AA, Pearson SD. **Conflict of Interest** in Seminal **Hepatitis C** Virus and **Cholesterol** Management **Guidelines**. JAMA Intern Med. 2017 Jan 17.
Jellinger PS, Smith DA, Mehta AE, Ganda O, Handelsman Y, Rodbard HW, Shepherd MD, Seibel JA, **AACE** Task Force for Management of Dyslipidemia and Prevention of Atherosclerosis. American Association of Clinical Endocrinologists' guidelines for management of dyslipidemia and prevention of atherosclerosis. Endocr Pract 2012 Mar-Apr;18(Suppl 1):1-78.
Jellinger PS, Handelsman Y, Bell DS, et al. American Association of Clinical Endocrinologists (**AACE**) and American College of Endocrinology (**ACE**) Guidelines for **Management of Dyslip**idemia and Prevention of Atherosclerosis [online February 3, **2017**]. Endocr Pract. doi: 10.4158/EP171764.GL
Jenkins DJ, Wong JM, Kendall CW, et al. The effect of a plant-based low-carbohydrate ("**Eco-Atkins**") diet on body weight and blood lipid concentrations in hyperlipidemic subjects. Arch Intern Med. 2009 Jun 8;169(11):1046-54.
Jenkins DJA, Blanco Mejia S, Chiavaroli L, et al. Cumulative Meta-Analysis of the **Soy Effect Over Time**. J Am Heart Assoc. 2019 Jul 2;8(13):e012458.
Jenkins, David J.A., Chiavaroli, Laura, Wong, Julia M.et al. **Adding monounsaturated fatty acids to a dietary portfolio of cholesterol-lowering foods in hypercholesterolemia CMAJ 2010 182: 1961-1967.**
Jiang R, Zhao S, Wang R, et al. **Safety and Efficacy of Atorvastatin for Chronic Subdural Hematoma** in Chinese PatientsA Randomized ClinicalTrial. *JAMA Neurol.* 2018 Jul 30.
Jin J. **PCSK9 Inhibitors** for Treating High Cholesterol. JAMA. 2015 Dec 1;314(21):2320.
Jin J. **Lipid Disorders: Screening and Treatment**. JAMA. 2016 Nov 15;316(19):2056.
Johansen ME, Green LA. **Statin Use in Very Elderly Individuals**, 1999-2012. JAMA Intern Med. 2015 Aug 24.
Johnson PK, Mendelson MM, Baker A, et al. **Statin-Associated Myopathy in a Pediatric Preventive Cardiology** Practice. J Pediatr. 2017 Mar 29.
Jolliffe CJ, Janssen I. Distribution of **lipoproteins** by age and gender in **adolescents**. Circulation. 2006 Sep 5;114(10):1056-62. Epub 2006 Aug 28. For example, in 1-year increments for males starting at age 12 and extending to age 19 years, the high-risk thresholds for total cholesterol were 6.03, 5.83, 5.70, 5.70, 5.77, 5.88, 6.02, and 6.16 mmol/L.
Jones M, Tett S, Peeters GM, et al. **New-Onset Diabetes After Statin Exposure in Elderly Women**: The Australian Longitudinal Study on Women's Health. Drugs Aging. 2017 Mar;34(3):203-209.
Jones PH, Davidson MH. Reporting rate of **rhabdomyolysis with fenofibrate + statin** versus gemfibrozil + any statin. Am J Cardiol. 2005 Jan 1;95(1):120-2. The findings suggest that the use of fenofibrate in combination with statins results in fewer reports of rhabdomyolysis per million prescriptions dispensed than does the use of gemfibrozil.
Jones PH, Bays HE, Chaudhari U, et al. Safety of **Alirocumab** (A PCSK9 Monoclonal Antibody) from 14 Randomized Trials. Am J Cardiol. 2016 Dec 15;118(12):1805-1811.
Joseph P, Lonn E, Bosch J, et al; **HOPE-3** Investigators. **Long-term Effects of Statins, Blood Pressure-Lowering, and Both on Erectile Function** in Persons at Intermediate Risk for Cardiovascular Disease: A Substudy of the Heart Outcomes Prevention Evaluation-3 (HOPE-3) Randomized Controlled Trial. Can J Cardiol. 2018 Jan;34(1):38-44.
Joy TR, Monjed A, Zou GY, et al. N-of-1 (**single-patient**) trials for **statin-related myalgia**. Ann Intern Med 2014; 160:301-310.
Joyce N, Wellenius GA, Dore DD, et al. **Patterns of Lipid Lowering Therapy among Children Ages 8-20 Years**. J Pediatr. 2015 May 4.
Jukema JW, Szarek M, Zijlstra LE, et al. **Alirocumab** in Patients With Polyvascular Disease and Recent Acute Coronary Syndrome: ODYSSEY OUTCOMES Trial. J Am Coll Cardiol. 2019 Mar 18.
Jun M, Foote C, Lv J et al. Effects of **fibrates** on cardiovascular outcomes: a systematic review and meta-analysis. Lancet. 2010 May 10.
Jun M, Zhu B, Tonelli M, et al. Effects of **fibrates in kidney disease**, a review and meta-analysis. J Am Coll Cardiol 2012 .
Kaasenbrood L, Poulter NR, Sever PS, et al. Development and Validation of a Model to Predict **Absolute Vascular Risk Reduction by Moderate-Intensity Statin Therapy** in Individual Patients With Type 2 Diabetes Mellitus: The Anglo Scandinavian Cardiac Outcomes Trial, Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial, and Collaborative Atorvastatin Diabetes Study. (**Cards, Allhat, Ascot**) Circ Cardiovasc Qual Outcomes. 2016 May;9(3):213-21.
Kale MS, Bishop TF, Federman AD, Keyhani S. "**Top 5" lists top $5 billion**. Arch Intern Med 2011; DOI:10.1001/archinternmed.2011.501. (using **brand name vs generic statins**)
Kang EY, Chen TH, Garg SJ, et al. Association of **Statin Therapy With Prevention of Vision-Threatening Diabetic Retinopathy**. JAMA Ophthalmol. 2019 Jan 10.
Kang JH, Boumenna T, Stein JD, et al. Association of statin use and high serum cholesterol levels with **risk of primary open-angle glaucoma** [online May 2, 2019]. JAMA Ophthalmol. doi:10.1001/jamaophthalmol.2019.0900
Kang S, Liu Y, Liu XB. Effects of Aggressive **Statin Therapy on Patients With Coronary Saphenous Vein Bypass Grafts**: A Systematic Review and Meta-Analysis of Randomized, Controlled Trials. Clin Ther. 2013 Aug 7.

Kapoor AS, et al. Strength of evidence for **perioperative** use of statins to reduce cardiovascular risk: systematic review of controlled studies. BMJ. 2006 Nov 6; [Epub ahead of print] The evidence base for routine administration of statins to reduce perioperative cardiovascular risk is inadequate.
Karlson BW, Palmer MK, Nicholls SJ, et al. A **VOYAGER** Meta-Analysis of the Impact of Statin Therapy on **Low-Density Lipoprotein Cholesterol and Triglyceride Levels** in Patients With Hypertriglyceridemia. Am J Cardiol. 2016 May 1;117(9):1444-8.
Karmali KN, Goff DC Jr, Ning H, et al. A Systematic Examination of the **2013 ACC/AHA Pooled Cohort Risk Assessment Tool** for Atherosclerotic Cardiovascular Disease. J Am Coll Cardiol. 2014 Sep 9;64(10):959-68.
Kastelein JJ, Akdim F, Stroes ES, et al. Simvastatin **with or without ezetimibe** in familial hypercholesterolemia. (**ENHANCE** trial) N Engl J Med 2008; 358:1431-1443. In patients with familial hypercholesterolemia, combined therapy with ezetimibe and simvastatin did not result in a significant difference in changes in intima-media thickness, as compared with simvastatin alone, despite decreases in levels of LDL cholesterol and C-reactive protein.
Kastelein JJP, Besseling J, Shah S, et al. **Anacetrapib** as lipid-modifying therapy in patients with heterozygous familial hypercholesterolaemia (**REALIZE**): a randomised, double-blind, placebo-controlled, phase 3 study. Lancet 2015; online March 3.
Kastelein JJ, Ginsberg HN, Langslet G, et al. **ODYSSEY FH** I and FH II: 78 week results with **alirocumab** treatment in 735 patients with heterozygous familial hypercholesterolaemia. Eur Heart J. 2015 Sep 1.
Kataoka Y, John JS, Wolski K, et al. **Atheroma Progression in Hyporesponders to Statin Therapy**. Arterioscler Thromb Vasc Biol. 2015 Feb 26. pii: ATVBAHA.114.304477
Kato ET, Cannon CP, et al. Efficacy and Safety of **Adding Ezetimibe to Statin** Therapy Among Women and Men: Insight From IMPROVE-IT (Improved Reduction of Outcomes: Vytorin Efficacy International Trial). J Am Heart Assoc. 2017 Nov 18;6(11).
Kavousi M, Leening MJG, Nanchen D, et al. Comparison of application of the **ACC/AHA Guidelines, Adult Treatment Panel III guidelines, and European Society of Cardiology guidelines** for cardiovascular disease prevention in a European cohort. JAMA 2014.
Kawada-Watanabe E, Yamaguchi J, Kanbayashi K, et al. **Predictive Value of Baseline High-Sensitivity C-Reactive Protein Level and Renal Function** for Patients With Acute Coronary Syndrome Undergoing Aggressive Lipid-Lowering Therapy: A Subanalysis of HIJ-PROPER. Am J Cardiol. 2018 Sep 8.
Kawahara T, Nishikawa M, Kawahara C, et al. **Atorvastatin, etidronate**, or both in patients at high risk for atherosclerotic **aortic plaques**: a randomized, controlled trial. Circulation. 2013 Jun 11;127(23):2327-35.
Kawasaki R, Konta T, Nishida K. **Lipid-lowering medication is associated with decreased risk of diabetic retinopathy** and the need for treatment in patients with type 2 diabetes: A real-world observational analysis of a health claims database. Diabetes Obes Metab. 2018 Oct;20(10):2351-2360.
Kazi DS, Moran AE, Coxson PG, et al. **Cost-effectiveness of PCSK9** inhibitor therapy in patients with heterozygous familial hypercholesterolemia or atherosclerotic cardiovascular disease. JAMA 2016; 316:743-753.
Kazi DS, Penko J, Coxson PG, et al. Cost-effectiveness of **PCSK9** inhibitors in patients with atherosclerotic cardiovascular disease: an update based on the results of the **FOURIER** trial. JAMA. doi:10.1001/jama.2017.9924
Kazi DS, Penko J, Coxson PG, et al. **Cost-effectiveness of alirocumab**. A just-in-time analysis based on the **ODYSSEY Outcomes trial**. Ann Intern Med. 2018. [Epub ahead of print]. doi:10.7326/M18-1776.
Kazi DS, Lu CY, Lin GA, et al. **Nationwide Coverage and Cost-Sharing for PCSK9** Inhibitors Among **Medicare** Part D Plans. JAMA Cardiol. 2017 Sep 13.
Kearney S, Carr AS, McConville J, McCarron MO; on behalf of the Northern Ireland Neurology Network. **Rhabdomyolysis after co-prescription of statin and fusidic acid.** BMJ. 2012 Oct 9;345:e6562.
Keating AJ, Campbell KB, Guyton JR. **Intermittent nondaily dosing strategies** in patients with previous statin-induced myopathy. Ann Pharmacother. 2013
Keech A, Simes RJ, Barter P, et al. **FIELD** study investigators. Effects of long-term fenofibrate therapy on cardiovascular events in 9795 people with type 2 diabetes mellitus (the FIELD study): randomised controlled trial. Lancet. 2005 Nov 26;366(9500):1849-61. INTERPRETATION: Fenofibrate did not significantly reduce the risk of the primary outcome of coronary events. It did reduce total cardiovascular events, mainly due to fewer non-fatal myocardial infarctions and revascularisations. The higher rate of starting statin therapy in patients allocated placebo might have masked a moderately larger treatment benefit. (But some **non-significant** concerns with fenofibrate vs placebo such as: an ↑ in cardiac mortality 2.2 vs 1.9%, an ↑ in total CVD events for those with previous CVD 25.5 vs 25.1%, an excess in non-cardiovascular disease deaths 4.4 vs 4% & an ↑ in total mortality 7.3 vs 6.6%). But may benefit albuminuria & retinopthy. (InfoPOEMs: In this study, patients with type 2 diabetes treated with fenofibrate (Antara, Lofibra, Tricor) had no significant reduction in coronary events compared with patients treated with placebo. There was a small reduction, however, in nonfatal myocardial infarctions, total cardiovascular disease, and revascularization. (LOE = 1b)) Keech AC, Mitchell P, Summanen PA, et al, for the FIELD study investigators. Effect of fenofibrate on the need for laser treatment for diabetic retinopathy (FIELD study): a randomised controlled trial. Lancet 2007;370(9600):1687-1697. In patients with type 2 diabetes mellitus fenofibrate (Antara, Lofibra, Tricor) modestly reduces the number of laser treatments for retinopathy. (LOE = 1b) Scott R, O'Brien R, Fulcher G, Pardy C, d'Emden M, Tse D, Taskinen MR, Ehnholm C, Keech A; on behalf of the FIELD Study Investigators. The effects of fenofibrate treatment on cardiovascular disease risk in 9795 people with type 2 diabetes and various components of the metabolic syndrome: the FIELD study. Diabetes Care. 2008 Nov 4. [Epub ahead of print] MS components identify higher CVD risk in people with type 2 diabetes, so the absolute benefits of fenofibrate is likely to be greater when MS features are present. The highest risk and greatest benefits of fenofibrate are seen among those with marked hypertriglyceridemia.
Keene D, Price C, Shun-Shin MJ, et al. Effect on cardiovascular risk of high density lipoprotein targeted drug treatments **niacin, fibrates, and CETP inhibitors:** meta-analysis of randomised controlled trials including 117 411 patients. BMJ. 2014 Jul 18;349:g4379.
Kelly R. **Diet and Exercise** in the Management of Hyperlipidemia. American Family Physician. May1, 2010.
Khan AR, Bavishi C, Riaz H, et al. Increased Risk of Adverse **Neurocognitive Outcomes With Proprotein Convertase Subtilisin-Kexin Type 9 Inhibitors**. Circ Cardiovasc Qual Outcomes. 2017 Jan;10(1).
Khera AV, Plutzky J. Management of **low levels of high-density lipoprotein-cholesterol (HDL)**. Circulation. 2013 Jul 2;128(1):72-8.
Khera AV, Everett BM, Caulfield MP, et al. **Lipoprotein(a)** concentrations, Rosuvastatin therapy, and residual vascular risk: an analysis from the JUPITER Trial (Justification for the Use of Statins in Prevention: An Intervention Trial Evaluating Rosuvastatin). Circulation. 2014;129:635–642.
Khera AV, Qamar A, Reilly MP, et al. Effects of **niacin, statin, and fenofibrate** on circulating **proprotein convertase subtilisin/kexin type 9 levels** in patients with dyslipidemia. Am J Cardiol. 2015 Jan 15;115(2):178-82.
Khera AV et al. Diagnostic yield of **sequencing familial hypercholesterolemia genes** in patients with severe hypercholesterolemia. J Am Coll Cardiol 2016 Apr 3.
Khoury J, et al. Effect of a cholesterol-lowering diet on maternal, cord, and neonatal lipids, and **pregnancy** outcome: a randomized clinical trial. Am J Obstet Gynecol. 2005 Oct;193(4):1292-301. (InfoPOEMs: In this study of low-risk pregnant women, a diet rich in fish and low in other animal fats resulted in a marked decrease in the number of preterm births. These results seem too good to be true and further confirmatory evidence is needed. In the meantime, as long as the fish are free of toxins the potential benefit may be large and there is no apparent risk. (LOE = 1b))
Khunti K, Danese MD, Kutikova L, et al. Association of a **Combined Measure of Adherence and Treatment Intensity With Cardiovascular Outcomes in Patients With Atherosclerosis or Other Cardiovascular Risk Factors Treated With Statins and/or Ezetimibe**. JAMA Netw Open. 2018;1(8):e185554.
Khvorova A. **Oligonucleotide therapeutics** — a new class of cholesterol-lowering drugs. N Engl J Med 2017;376:3-7.
Kim CA, Kim DH. Statins Provide **Less Benefit in Populations with High Noncardiovascular Mortality Risk**: Meta-Regression of Randomized Controlled Trials. J Am Geriatr Soc. 2015 Jul;63(7):1413-9.
Kim CH, Han KA, Yu J, et al. Efficacy and Safety of Adding **Omega-3 Fatty Acids** in Statin-Treated Patients with Residual Hypertriglyceridemia: **ROMANTIC** (**Rosuvastatin**-OMAcor iN residual hyperTrIglyCeridemia), a Randomized, Double-blind, and Placebo-controlled Trial. Clin Ther. 2017 Dec 6.
Kim MC, Cho JY, Jeong HC, et al. Impact of **postdischarge statin withdrawal** on long-term outcomes in patients with acute myocardial infarction. Am J Cardiol. 2015 Jan 1;115(1):1-7.
Kim NH, Han KH, Choi J, et al. **Use of fenofibrate on cardiovascular outcomes** in statin users with metabolic syndrome: propensity matched cohort study. BMJ. 2019 Sep 27;366:l5125.
Kim S, Kim H, Kim E, et al. Utilization Patterns of **Lipid-lowering Therapies in Patients With Atherosclerotic Cardiovascular Disease or Diabetes**: A Population-Based Study in South Korea. Clin Ther. 2018 May 4.
Kim W, Yoon YE, Shin SH, et al. **Efficacy and Safety of Ezetimibe and Rosuvastatin Combination Therapy** Versus Those of Rosuvastatin Monotherapy in Patients With Primary Hypercholesterolemia. Clin Ther. 2018 May 29.
Kingwell BA, Chapman MJ. Future of **high-density lipoprotein infusion** therapies: potential for clinical management of vascular disease. Circulation. 2013 Sep 3;128(10):1112-21.
Kipfer S, Frigerio S, Hench J, et al. **Immune-mediated necrotizing myopathy linked to statin** use (atorvastatin). Lancet. 2015 Jun 11.
Kirkpatrick PJ, Turner CL, Smith C, Hutchinson PJ, Murray GD, for the **STASH** Collaborators. **Simvastatin** in **aneurysmal subarachnoid haemorrhage** (**STASH**): a multicentre randomised phase 3 trial. Lancet Neurol 2014; online May 16.
Kit BK, Carroll MD, Lacher DA, et al. **Trends in serum lipids among US youths** aged 6 to 19 years, 1988-2010. JAMA. 2012 Aug 8;308(6):591-600.
Kit BK, Kuklina E, Carroll MD, et al. Prevalence of and Trends in **Dyslipidemia and Blood Pressure Among US Children and Adolescents, 1999-2012**. JAMA Pediatr. 2015 Jan 19.
Kitas GD, Nightingale P, Armitage J, et al. Trial of **atorvastatin for the primary prevention of cardiovascular events** in patients with rheumatoid arthritis (TRACE RA): A multicenter, randomized, placebo controlled trial. Arthritis Rheumatol. 2019 Apr 15.
Kjærgaard KA, Christiansen MK, Schmidt M, et al. **Long-term cardiovascular risk in heterozygous familial hypercholesterolemia** relatives identified by cascade screening. J Am Heart Assoc. 2017;6:e005435.
Kjekshus J, Apetrei E, Barrios V, et al. the **CORONA** Group. Rosuvastatin in Older Patients with **Systolic Heart Failure**. N Engl J Med. 2007 Nov 5; [Epub ahead of print] Rosuvastatin did not reduce the primary outcome or the number of deaths from any cause in older patients with systolic heart failure, although the drug did reduce the number of cardiovascular hospitalizations. The drug did not cause safety problems. (Cleland JGF, McMurray JJV, Kjekshus J, et al. Plasma

Klein BE, et al. Statin use and incident nuclear **cataract**. JAMA. 2006 Jun 21;295(23):2752-8. (InfoPOEMs: Statin use is associated with a reduced incidence of nuclear cataracts, the most common type of age-related cataracts. However, this type of study design (prospective cohort study) does not prove a causal relationship between the use of statins and lower risk of developing cataracts. It is possible that other confounding variables (eg, genetics or patient compliance) are causally related. (LOE = 2b)) (Tan JS, Mitchell P, Rochtchina E, Wang JJ. Statin use and the long-term risk of incident cataract: the Blue Mountains Eye Study. Am J Ophthalmol. 2007 Apr;143(4):687-9. Epub 2006 Dec 20. Statin use was found to reduce by 50% the risk of cataract development, principally nuclear or cortical cataract subtypes.)

Klempfner R, Goldenberg I, Fisman EZ, et al. Comparison of **Statin Alone Versus Bezafibrate and Statin** Combination in Patients With Diabetes Mellitus and Acute Coronary Syndrome. Am J Cardiol. 2013 Oct 2.

Klempfner R, Erez A, Sagit BZ, et al. **Elevated triglyceride level** is independently associated with increased all-cause mortality in patients with established coronary heart disease: Twenty-two-year follow-up of the bezafibrate infarction prevention study (**BIP**) and registry. Circ Cardiovasc Qual Outcomes 2016; 9:100-1088.

Knowles JW, Howard WB, Karayan L, Baum et al. **Access to Non-Statin Lipid Lowering Therapies** in Patients at High-Risk of Atherosclerotic Cardiovascular Disease. Circulation. 2017 Apr 26.

Knowles JW, Howard WB, Karayan L, et al. **Access to Non-Statin Lipid Lowering Therapies in Patients at High-Risk** of Atherosclerotic Cardiovascular Disease. Circulation. 2017 Apr 26

Knowles JW, Rader DJ, Khoury MJ. **Cascade Screening for Familial Hypercholesterolemia** and the Use of Genetic Testing. JAMA. 2017 Jul 25;318(4):381-382.

Knopp RH, et al. Efficacy and Safety of Atorvastatin in the Prevention of Cardiovascular End Points in Subjects With Type 2 Diabetes: The Atorvastatin Study for Prevention of Coronary Heart Disease Endpoints in Non-Insulin-Dependent Diabetes Mellitus (**ASPEN**). Diabetes Care. 2006 Jul;29(7):1478-85.

Ko DT, Wijeysundera HC, Jackevicius CA, et al. **Diabetes** and cardiovascular events in older myocardial infarction patients prescribed intensive-dose and moderate-dose statins. Circ Cardiovasc Qual Outcomes 2013; 6: 315-22.

Koenig W. Low-Grade **Inflammation Modifies Cardiovascular Risk** Even at Very Low LDL-C Levels: Are We Aiming for a Dual Target Concept? Circulation. 2018 Jul 10;138(2):150-153.

Koehler P, Bröckelmann PJ, Hallek M, Kochanek M. **Bloodletting to Treat Severe Hypertriglyceridemia**. Ann Intern Med. 2019 Feb 26.

Köhler O et al. The effect of **concomitant treatment with SSRIs and statins**: A population-based study. Am J Psychiatry 2016 May 3.

Kohli-Lynch CN, Bellows BK, Thanassoulis G, et al. **Cost-effectiveness of Low-density Lipoprotein Cholesterol Level-Guided Statin Treatment** in Patients With Borderline Cardiovascular Risk. JAMA Cardiol. 2019 Aug 28.

Kokkinos PF, Faselis C, Myers J, et al. Interactive effects of **fitness and statin treatment** on mortality risk in veterans with dyslipidemia: a cohort study. Lancet 2012.

Kokkinos P, Faselis C, Myers J, et al. **Statin therapy, fitness, and mortality** risk in middle-aged **hypertensive male veterans**. Am J Hypertens. 2014 Mar;27(3):422-30.

Koopal C, Visseren FLJ, Westerink J, et al. Predicting the Effect of **Fenofibrate** on Cardiovascular Risk for Individual Patients With Type 2 **Diabetes Mellitus**. Diabetes Care. 2018 Feb 22.

Kopin Laurie, Lowenstein Charles, **In the Clinic: Dyslipidemia**. *Ann Intern Med* August 3, 2010 153:ITC2-1; doi:10.1059/0003-4819-153-3-201008030-01002.

Kopin L, Lowenstein C. **In the clinic. Dyslipidemia**. Ann Intern Med. 2017 Dec 15:ITC81-96.

Koren MJ, Scott R, Kim JB, et al. Efficacy, safety, and tolerability of a monoclonal antibody to proprotein convertase subtilisin/kexin type 9 as monotherapy in patients with hypercholesterolaemia (**MENDEL**): a randomised, double-blind, placebo-controlled, phase 2 study. Lancet 2012. (**AMG145**)

Koren MJ, Giugliano RP, Raal FJ, et al. Efficacy and Safety of Longer-Term Administration of **Evolocumab** (**AMG 145**) in Patients With Hypercholesterolemia: 52-Week Results From the Open-Label Study of Long-Term Evaluation Against LDL-C (OSLER) Randomized Trial. Circulation. 2014 Jan 14.

Koren MJ, Lundqvist P, Bolognese M, et al; **MENDEL-2** Investigators. Anti-PCSK9 Monotherapy for Hypercholesterolemia - The MENDEL-2 Randomized, Controlled Phase 3 Clinical Trial of **Evolocumab**. J Am Coll Cardiol. 2014 Mar 25.

Koren MJ, et al. Long-term Low-Density Lipoprotein Cholesterol-Lowering Efficacy, Persistence & Safety of **Evolocumab** in Treatment of Hypercholesterolemia: Results Up to 4 Years From Open-Label OSLER-1 Extension Study. JAMA Cardiol. 2017 Mar 14.

Koskinas KC;Siontis GCM;Piccolo R;Mavridis D;Raber. Effect of **statins and non-statin LDL-lowering medications on cardiovascular outcomes** in **secondary prevention**: a meta-analysis of randomized trials. Eur Heart J. 2017 Oct 23.

Koskinas KC, Windecker S, Pedrazzini G, et al**. Evolocumab** for Early Reduction of LDL-Cholesterol Levels in Patients with Acute Coronary Syndromes (EVOPACS). J Am Coll Cardiol. 2019 Aug 16..

Koskinen J, et al. Impact of **Lipid Measurements in Youth** in Addition to Conventional Clinic-Based Risk Factors on Predicting Preclinical Atherosclerosis in Adulthood: International Childhood Cardiovascular Cohort (i3C) Consortium. Circulation. 2017 Nov 23.

Koskinen J, et al. Impact of **lipid measurements in youth** in addition to conventional clinic-based risk factors on predicting preclinical atherosclerosis in adulthood: International Childhood Cardiovascular Cohort Consortium. Circulation. 2018;137:1246–1255.

Kostapanos MS, Elisaf MS. **Statins and mortality**: the untold story. Br J Clin Pharmacol. 2016 Dec 6.

Kostis WJ, Cheng JQ, Dobrzynski JM, et al. Meta-analysis of **statin effects in women** versus men. J Am Coll Cardiol 2012; 59:572-582.

Kostis JB, Dobrzynski JM. The Effect of **Statins on Erectile Dysfunction**: A Meta-Analysis of Randomized Trials. J Sex Med. 2014 Mar 29.

Krane V, Schmidt KR, Gutjahr-Lengsfeld LJ, et al. Long-term effects following 4 years of randomized treatment with **atorvastatin** in patients with type 2 diabetes mellitus on **hemodialysis**. (**4D**) Kidney Int. 2016 Feb 17.

Kreuter M, Bonella F, Maher TM, et al. Effect of **statins** on disease-related outcomes in patients with **idiopathic pulmonary fibrosis**. Thorax. 2016 Oct 5.

Kristensen ML, Christensen PM, Hallas J. The effect of **statins on average survival** in randomised trials, an analysis of end point postponement. BMJ Open. 2015 Sep 24;5(9):e007118.

Kristiansen O, Vethe NT, Fagerland MW, et al. A novel direct method to determine **adherence to atorvastatin therapy** in patients with coronary heart disease. Br J Clin Pharmacol. 2019 Sep 8.

Kromhout D, Gitay EJ, Geleijnse JM, et al. **N-3 fatty acids** and cardiovascular events after myocardial infarction. (**Alpha Omega Trial**)N Engl J Med 2010; DOI:10.1056.NEJM0a.1003603.

Kronish IM, Ross JS, Zhao H, et al. The Impact of **Hospitalization for Acute Myocardial Infarction on Adherence to Statins** Among Older Adults. Circ Cardiovasc Qual Outcomes. 2016 May 24.

Kruger PS, Harward ML, Jones MA, Joyce CJ, Kostner KM, Roberts MS, Venkatesh B. Continuation of **statin therapy in patients with presumed infection**: a randomized controlled trial. Am J Respir Crit Care Med 2011;183:774–781.

Kruger P et al. A multicenter randomized trial of atorvastatin therapy in intensive care patients with **severe sepsis**. Am J Respir Crit Care Med 2013 Apr; 187:743.

Krum H, et al. Impact of Statin Therapy on Clinical Outcomes in Chronic **Heart Failure** Patients According to Beta-Blocker Use: Results of **CIBIS II**. Cardiology. 2006 Sep 8;108(1):28-34 [Epub ahead of print]

Krumholz HM. The **new cholesterol and blood pressure guidelines**: Perspective on the path forward. JAMA 2014; DOI:10.1001/jama.2014.2634. Available at: Available at: https://jama.jamanetwork.com/journal.aspx

Krumholz HM. Treatment of Cholesterol in 2017. JAMA. 2017 Aug 1;318(5):417-418.

Kuehn BM. **Preventive Statin Use** Recommended by **US Task Force**. Circulation. 2017 Feb 21;135(8):806-807.

Kuklina Elena V.; Yoon Paula W.; Keenan Nora L.. **Trends** in High Levels of **Low-Density Lipoprotein** Cholesterol in the United States, 1999-2006. *JAMA*. 2009;302(19):2104-2110

Kumbhani DJ, Steg PG, Cannon CP, et al. REACH Registry Investigators. **Statin therapy and long-term adverse limb outcomes** in patients with peripheral artery disease: insights from the REACH registry. Eur Heart J. 2014 Nov 1;35(41):2864-72.

Kusters DM, Avis HJ, de Groot E, et al. **Ten-year follow-up** after initiation of **statin therapy in children with familial hypercholesterolemia**. JAMA. 2014 Sep 10;312(10):1055-7.

Kutner JS, Blatchford PJ, Taylor DH, et al. **Safety and benefit of discontinuing statin** therapy in the setting of advanced, life-limiting illness: a randomized clinical trial [online March 23, 2015]. JAMA InternMed. doi:10.1001/jamainternmed.2015.0289.

Lachaine J, et al. **Persistence and adherence** to cholesterol lowering agents: evidence from Regie de l'Assurance Maladie du Quebec data. Am Heart J. 2006 Jul;152(1):164-9.

Ladenson, Paul W., Kristensen, Jens D., Ridgway, E. Chester, et al. Use of the Thyroid Hormone Analogue **Eprotirome** in Statin-Treated Dyslipidemia. N Engl J Med 2010 362: 906-916.

Lai CC, Lee MG, Lee SH, Hsu et al. **Statin** treatment is associated with a decreased risk of active **tuberculosis**: an analysis of a nationally representative cohort. Thorax. 2016 Mar 3.

Lamina C, Kronenberg F; Lp(a)-GWAS-Consortium. Estimation of the **Required Lipoprotein(a)-Lowering Therapeutic Effect Size** for Reduction in Coronary Heart Disease Outcomes: A Mendelian Randomization Analysis. JAMA Cardiol. 2019 Apr 24.

Landmesser U, John Chapman M, Farnier M, et al, on behalf of the European Society of Cardiology (ESC) and the European Atherosclerosis Society (EAS). European Society of Cardiology/ European Atherosclerosis Society Task Force consensus statement on proprotein convertase subtilisin/kexin type 9 inhibitors: practical guidance for use in patients at very high cardiovascular risk. Eur Heart J 2017;38: 2245–2255.

Larosa JC, Pedersen TR, Somaratne R, Wasserman SM. Safety and Effect of **Very Low Levels of Low-Density Lipoprotein Cholesterol** on Cardiovascular Events. Am J Cardiol. 2013 Jan 30.

Lash TL, Riis AH, Ostenfeld EB, et al. Associations of **Statin Use With Colorectal Cancer Recurrence** and Mortality in a Danish Cohort. Am J Epidemiol. 2017 Sep 15;186(6):679-687.

Lasker SS, Chowdhury TA. **Myalgia** while taking statins. BMJ. 2012 Aug 14;345:e5348.

Last AR, Ference JD, Falleroni J. **Pharmacologic treatment of hyperlipidemia**. Am Fam Physician. 2011 Sep 1;84(5):551-8.

Last AR, Ference JD, Menzel ER. **Hyperlipidemia: Drugs for Cardiovascular Risk Reduction in Adults**. Am Fam Physician. 2017;95(2):78-87.

Laube R, Liu K. An unwanted complement: Rare case of **potential liver injury induced by an interaction between ginseng and atorvastatin**. Br J Clin Pharmacol. 2019 Apr 13.

Lauer MS. **PCSK9 Inhibitors**: Lots of Work Done, Lots More to Do. Ann Intern Med. 2016 May 3;164(9):624-5

Laufs U, Custodis F, Bohm M. HMG-CoA reductase inhibitors in chronic **heart failure**: potential mechanisms of benefit and risk. Drugs. 2006;66(2):145-54.

Lavie CJ, Milani RV, Mehra MR, et al. **Omega-3 polyunsaturated fatty acids** and cardiovascular disease. J Am Coll Cardiol 2009; 54: 585-594.

Law M, Rudnicka AR. **Statin safety**: a systematic review. Am J Cardiol. 2006 Apr 17;97(8A):52C-60C. Epub 2006 Feb 3. For statins other than cerivastatin, the incidence of rhabdomyolysis in 2 cohort studies was 3.4 (1.6 to 6.5) per 100,000 person-years, an estimate supported by data from 20 randomized controlled trials. Case fatality was 10%. Incidence was about 10 times greater when gemfibrozil was used in combination with statins. Incidence was higher (4.2 per 100,000 person-years) with lovastatin, simvastatin, or atorvastatin (which are oxidized by cytochrome P450 3A4 [CYP3A4], which is inhibited by many drugs) than pravastatin or fluvastatin (which are not oxidized by CYP3A4). In persons taking simvastatin, lovastatin, or atorvastatin, 60% of cases involved drugs known to inhibit CYP3A4 (especially erythromycin and azole antifungals), and 19% involved fibrates, principally gemfibrozil. The incidence of myopathy in patients treated with statins, estimated from cohort studies supported by randomized trials, was 11 per 100,000 person-years. For liver disease, randomized trials reported fewer hepatobiliary disorders in patients allocated statins than in those allocated placebo. The notification rate of liver failure to regulatory authorities was about 1 per million person-years of statin use. Randomized trials show no excess of renal disease or proteinuria in statin-allocated participants, and the decline in glomerular filtration rate was smaller with statins than with placebo. Evidence from 4 cohort studies and case reports suggests that statins cause peripheral neuropathy, but the attributable risk is small (12 per 100,000 person-years). No change in cognitive function was found in randomized trials of statins in elderly patients.

Layton JB, Kshirsagar AV, Simpson RJ Jr, et al. Effect of Statin Use on **Acute Kidney Injury Risk Following Coronary Artery Bypass Grafting**. Am J Cardiol. 2012 Dec 27.

Lazar LD, Pletcher MJ, Coxson PG, et al. **Cost-effectiveness of statin therapy for primary prevention** in a low-cost statin era. Circulation. 2011 Jul 12;124(2):146-53.

Leander K, Mälarstig A, Van't Hooft FM, et al. Circulating Proprotein Convertase Subtilisin/Kexin Type 9 (**PCSK9**) Predicts Future Risk of Cardiovascular Events Independently of Established Risk Factors. Circulation. 2016 Mar 29;133(13):1230-9.

Lebenthal Y, Horvath A, Dziechciarz P, et al. Are treatment targets for hypercholesterolemia evidence based in **children** ? Systematic review and meta-analysis of randomised controlled trials. Arch Dis Child. 2010 Sep;95(9):673-80.

Lecarpentier E, Morel O, Fournier T, Elefant E, Chavatte-Palmer P, Tsatsaris V. **Statins and Pregnancy**: Between Supposed Risks and Theoretical Benefits. Drugs. 2012 Apr 5.

Lee DSH, Markwardt S, Goeres L, et al. **Statins and physical activity** in older men: the Osteoporotic Fractures in Men Study [published online June 9, 2014]. JAMA Intern Med. doi:10.1001/jamainternmed.2014.2266.

Lee HY, et al. A Randomized, Multicenter, Double-blind, Placebo-controlled Study to Evaluate the Efficacy and the Tolerability of a Triple Combination of **Amlodipine/Losartan/Rosuvastatin** in Patients With Comorbid Essential Hypertension and Hyperlipidemia. Clin Ther. 2017 Nov 14.

Lee JW, Morris JK, Wald NJ. **Grapefruit Juice and Statins**. Am J Med. 2016 Jan;129(1):26-9.

Lee KH, Jeong MH, Kim HM, et al. Benefit of early statin therapy in patients with acute myocardial infarction who have **extremely low low-density lipoprotein cholesterol**. J Am Coll Cardiol 2011; 58:1664-1671.

Lee M, Saver JL, Wu YL, et al. Utilization of **Statins** Beyond the Initial Period **After Stroke** and 1-Year Risk of Recurrent Stroke. J Am Heart Assoc. 2017 Aug 2;6(8).

Lee SE, Chang HJ, Sung JM, et al. Effects of **Statins on Coronary Atherosclerotic Plaques**: The **PARADIGM** (Progression of AtheRosclerotic PlAque DetermIned by Computed TomoGraphic Angiography Imaging) Study. JACC Cardiovasc Imaging. 2018 Jun 8.

Leebmann J, Roeseler E, Julius U, et al; Pro(a)LiFe Study Group*. **Lipoprotein Apheresis** in Patients With Maximally Tolerated Lipid-Lowering Therapy, Lipoprotein(a)-Hyperlipoproteinemia, and Progressive Cardiovascular Disease: Prospective Observational Multicenter Study. Circulation. 2013 Dec 17;128(24):2567-76

Lehane PB, Lacey S, Hessey EW, et al. Effect of **concomitant statins on rituximab** efficacy in patients with rheumatoid arthritis. Ann Rheum Dis. 2014 Oct;73(10):1906-8.

Leibowitz M, Karpati T, Cohen-Stavi CJ, et al. Association Between Achieved **Low-Density Lipoprotein Levels and Major Adverse Cardiac Events** in Patients With Stable Ischemic Heart Disease Taking Statin Treatment. JAMA Intern Med. 2016 Jun 20.

Leiter LA, et al. Efficacy and safety of **alirocumab** in insulin-treated individuals with type 1 or type 2 diabetes and high cardiovascular risk: The **ODYSSEY DM-INSULIN** randomized trial. Diabetes Obes Metab. 2017 Dec;19(12):1781-1792.

Leiter LA, Teoh H, Kallend D, et al. **Inclisiran Lowers LDL-C and PCSK9 Irrespective of diabetes** Status: The ORION-1 Randomized Clinical Trial. Diabetes Care. 2018 Nov 28.

Lemstra M, Blackburn D. Nonadherence to statin therapy: discontinuation after a single fill. Can J Cardiol 2012;28:567-73.

Lenderink T, et al. Patients using statin treatment **within 24 h after admission** for ST-elevation acute coronary syndromes had lower mortality than non-users: a report from the first Euro Heart Survey on acute coronary syndromes. Eur Heart J. 2006 Aug;27(15):1799-804. Epub 2006 Jul 4.

Liakopoulos OJ, , et al. Impact of preoperative statin therapy on adverse **postoperative outcomes** in patients undergoing cardiac surgery: a meta-analysis of over 30 000 patients. Eur Heart Journal 2008; DOI:10.1093/eurheartj/ehn198.

Leoncini M, Toso A, Maioli M, et al. Early high-dose **rosuvastatin for Contrast-Induced Nephropathy Prevention** in Acute Coronary Syndrome. Results from Protective effect of Rosuvastatin and Antiplatelet Therapy On contrast-induced acute kidney injury and myocardial damage in patients with Acute Coronary Syndrome (PRATO-ACS Study). J Am Coll Cardiol. 2013 Sep 25.

Leong D, Wu PE. Proprotein convertase subtilisin-kexin type **9 (PCSK9) inhibitors**. CMAJ. 2019 Aug 12;191(32):E894

Leung AA, Nerenberg K, Daskalopoulou SS, et al; CHEP Guidelines Task Force. Hypertension Canada's **2016 CHEP guidelines** for blood pressure measurement, diagnosis, assessment of risk, prevention and treatment of hypertension. Can J Cardiol 2016 (accepted manuscript) doi: 10.1016/j.cjca.2016.02.066 www.onlinecjc.ca/article/S0828-282X(16)00192-6/pdf (accessed April 11, 2016). (**non fasting lipid testing option**)

Leuschen J, Mortensen EM, Frei CR, et al. Association of **Statin Use With Cataracts**: A Propensity Score-Matched Analysis. JAMA Ophthalmol. 2013 Sep 19.

Levin A, Hemmelgarn B, Culleton B, Tobe S, McFarlane P, Ruzicka M, Burns K, Manns B, White C, Madore F, Moist L, Klarenbach S, Barrett B, Foley R, Jindal K, Senior P, Pannu N, Shurraw S, Akbari A, Cohn A, Reslerova M, Deved V, Mendelssohn D, Nesrallah G, Kappel J, Tonelli M; Canadian Society of Nephrology. Guidelines for the **management of chronic kidney disease**. CMAJ. 2008 Nov 18;179(11):1154-62. http://www.cmaj.ca/cgi/data/179/11/1154/DC1/1

Lewis JH, Mortensen ME, Zweig S, Fusco MJ, Medoff JR, Belder R; Pravastatin in Chronic Liver Disease Study Investigators. Efficacy and safety of **high-dose pravastatin in hypercholesterolemic patients with well-compensated chronic liver disease**: results of a prospective, randomized, double-blind, placebo-controlled, multicenter trial. Hepatology. 2007;46(5):1453-1463.

Li DQ, Kim R, McArthur E, et al. Risk of adverse events among older adults following co-prescription of **clarithromycin and statins** not metabolized by cytochrome P450 3A4. CMAJ. 2014 Dec 22.

Li DQ, Kim RB, McArthur E, et al. **Statin Safety in Chinese**: A Population-Based Study of Older Adults. PLoS One. 2016 Mar 8;11(3):e0150990.

Li G, Mayer CL, Morelli D, et al. Effect of **simvastatin on CSF Alzheimer disease biomarkers** in cognitively normal adults. Neurology. 2017 Aug 18.

Li L, Sun T, Zhang P, et al. **Statins for primary prevention of venous thromboembolism**. Cochrane Database Syst Rev. 2011 Dec 7;12:CD008203. Available evidence showed that rosuvastatin was associated with a reduced incidence of VTE, but the evidence was limited to a single RCT.

Li M, Al-Sarraf A, Sinclair G, Frohlich J. **Fish odour syndrome**. CMAJ. 2011 Mar 21. (exacerbated by rosuvastatin)

Li P, McElligott S, Bergquist H, et al. Effect of the **medicare part d coverage gap** on medication use among patients with hypertension and hyperlipidemia. Ann Intern Med. 2012 Jun 5;156(11):776-84.

Li SS, Blanco Mejia S, et al. Effect of **Plant Protein on Blood Lipids**: A Systematic Review and Meta-Analysis of Randomized Controlled Trials. J Am Heart Assoc. 2017 Dec 20;6(12).

Li X, Zhou J. Impact of **postdiagnostic statin use on ovarian cancer** mortality: A systematic review and meta-analysis of observational studies. Br J Clin Pharmacol. 2018 Feb 17.

Li Z, Hou Z, Yin W, et al. Effects of **statin** therapy on progression of **mild non-calcified coronary plaque** assessed by serial coronary CT angiography: A multi-center prospective study. Am Heart J 2016.

Liakopoulos OJ, Kuhn EW, Slottosch I, et al. **Preoperative statin** therapy for patients undergoing cardiac surgery. Cochrane Database Syst Rev. 2012 Apr 18;4:CD008493. Preoperative statin therapy reduces the odds of post-operative AF and shortens the stay on the ICU and in the hospital. Statin pretreatment had no influence on perioperative mortality, stroke, myocardial infarction or renal failure. Since analysed studies included mainly patients undergoing myocardial revascularizations the results cannot be extrapolated to patients undergoing other cardiac procedures such as heart valve or aortic surgery.

Lilly SM, Mortensen EM, Frei CR, et al. Comparison of the risk of **psychological and cognitive disorders** between persistent and nonpersistent **statin users**. Am J Cardiol. 2014 Oct 1;114(7):1035-9.

Lim SY, Bae EH, Choi JS, et al. other Korea Acute Myocardial Infarction Registry Investigators. Effect on Short- and Long-Term Major Adverse Cardiac Events of Statin Treatment in Patients With Acute Myocardial Infarction and **Renal Dysfunction**. Am J Cardiol. 2012 Feb 20.

Lin HW, Ho YF, Lin FJ. **Statin use associated with lower risk of epilepsy** after intracranial haemorrhage: A population-based cohort study. Br J Clin Pharmacol. 2018 May 1.

Lin SM, Wang JH, Liang CC, et al. **Statin use is associated with decreased osteoporosis** and fracture risks in stroke patients. J Clin Endocrinol Metab. 2018 Jul 2.

Lin KD, Yang CY, Lee MY, et al. **Statin** Therapy Prevents the **Onset of Parkinson Disease** in Patients with Diabetes. Ann Neurol. 2016 Jul 29

Lincoff AM, Nicholls SJ, Riesmeyer JS, et al. **Evacetrapib** and Cardiovascular Outcomes in High-Risk Vascular Disease. N Engl J Med. 2017 May 18;376(20):1933-1942.

Lipinski MJ, Cauthen CA, Biondi-Zoccai GG, et al. Meta-analysis of randomized controlled trials of statins versus placebo in patients with **heart failure**. Am J Cardiol. 2009 Dec 15;104(12):1708-16.

Lipinski MJ, Benedetto U, et al. The impact of **proprotein convertase subtilisin-kexin type 9 serine protease inhibitors** on lipid levels and outcomes in patients with **primary hypercholesterolaemia**: a network meta-analysis. Eur Heart J. 2015 Nov 17.

Lippi G, Mattiuzzi C, Cervellin G. **Statins popularity**: A global picture. Br J Clin Pharmacol. 2019 May 11.

Liu G, Sterling NW, Kong L, et al. **Statins may facilitate Parkinson's disease**: Insight gained from a large, national claims database. Mov Disord. 2017 Jun;32(6):913-917.

Liu M, Alafris A, Longo AJ, Cohen H. Irreversible atorvastatin-associated **hearing loss**. Pharmacotherapy. 2012 Feb;32(2):e27-34. doi: 10.1002/PHAR.1040.

Liu ZL, Liu JP, Zhang AL, et al. **Chinese herbal medicines for hypercholesterolemia**. Cochrane Database Syst Rev. 2011 Jul 6;7:CD008305. Some herbal medicines may have cholesterol-lowering effects. Our findings have to be interpreted with caution due to high or unclear risk of bias of the included trials. {22 RCTs, n=2130, range of 1-6 months with mean duration 2.3 +/- 1.3 months, high or unclear risk of ibias, no outcome data (too short & too small), no SAEs; **Xuezhikang** most commonly used; possible TC lowering (-0.90mmol/L vs inositol nicotinate).

Liu Z, Joerg H, Hao H, et al. Efficacy of High-Intensity **Atorvastatin** for Asian Patients Undergoing **Percutaneous Coronary Intervention**. Ann Pharmacother. 2016 Jun 15.

Liu Z, Hao H, Yin C, Chu Y, Li J, Xu D. Therapeutic effects of **atorvastatin and ezetimibe compared with double-dose atorvastatin** in very elderly patients with acute coronary syndrome. Oncotarget. 2017 Feb 3.

Lloyd-Jones DM. Low-Density Lipoprotein Cholesterol and Drug Treatment to Lower Atherosclerotic Cardiovascular Disease Risk: Where Do We Stand? JAMA Cardiol. 2017 Aug 2

Lloyd-Jones DM, Morris PB, Ballantyne CM, et al. **2016 ACC Expert Consensus Decision Pathway on the Role of Non-Statin** Therapies for LDL Cholesterol Lowering in the Management of Atherosclerotic Cardiovascular Disease Risk: A Report of the American College of Cardiology Task Force on Clinical Expert Consensus Documents. J Am Coll Cardiol. 2016 Mar 28.

Lloyd-Jones DM. Role of **Nonstatin Therapies for Low-Density Lipoprotein Cholesterol Lowering** in Management of Atherosclerotic Cardiovascular Disease Risk. JAMA Cardiol. 2016 Nov 30.

Lloyd-Jones DM, Braun LT, Ndumele CE, et al. Use of Risk Assessment Tools to Guide **Decision-Making in the Primary Prevention of Atherosclerotic Cardiovascular Disease**: A Special Report From the American Heart Association and American College of Cardiology. J Am Coll Cardiol. 2018 Nov 3.

London MJ, Schwartz GG, Hur K, Henderson WG. Association of perioperative statin use with mortality and morbidity after major noncardiac surgery [online Dec 19, 2016]. JAMA Intern Med. doi:10.1001/jamainternmed.2016 .8005

Lopes RD, de Barros E Silva PGM, de Andrade Jesuíno I,et al. **Timing of Loading Dose of Atorvastatin** in Patients Undergoing **Percutaneous Coronary Intervention for Acute Coronary Syndromes**: Insights From the SECURE-PCI Randomized Clinical Trial. JAMA Cardiol. 2018 Sep 24.

Lotta LA, Stewart ID, Sharp SJ, et al. Association of **Genetically Enhanced Lipoprotein Lipase-Mediated Lipolysis and Low-Density Lipoprotein Cholesterol-Lowering Alleles With Risk of Coronary Disease and Type 2 Diabetes**. JAMA Cardiol. 2018 Oct 1;3(10):957-966.

Lozano P, Henrikson NB, Morrison CC, et al. **Lipid Screening in Childhood and Adolescence** for Detection of Multifactorial Dyslipidemia: Evidence Report and Systematic Review for the US Preventive Services Task Force. JAMA. 2016 Aug 9;316(6):634-44.

Lozano P, Henrikson NB, Dunn J, et al. Lipid **Screening in Childhood and Adolescence** for Detection of Familial Hypercholesterolemia: Evidence Report and Systematic Review for the US Preventive Services Task Force. JAMA. 2016 Aug 9;316(6):645-55.

Lu L, Krumholz HM, Tu JV, et al. Impact of **Drug Policy on Regional Trends in Ezetimibe Use**. Circ Cardiovasc Qual Outcomes. 2014 Jun 3.

Lu Z, Kou W, Du B, Wu Y, Zhao S, Brusco OA, Morgan JM, Capuzzi DM; Chinese Coronary Secondary Prevention Study Group. Effect of xuezhikang, an extract from **red yeast chinese rice**, on coronary events in a chinese population with previous myocardial infarction. Am J Cardiol. 2008 Jun 15;101(12):1689-93. Epub 2008 Apr 11. (n=~5000, 4.5years) In conclusion, long-term therapy with XZK significantly decreased the recurrence of coronary events and the occurrence of new CV events and deaths, improved lipoprotein regulation, and was safe and well tolerated.

Lüscher TF. **Lipids and lipid lowering**: current management with **statins and PCSK9 inhibitors**. European Heart Journal. 2018 Apr 7; 39(14): 1117-1120.

Ma C, Gurol ME, Huang Z, et al. Low-density lipoprotein cholesterol and **risk of intracerebral hemorrhage**: A prospective study. Neurology. 2019 Jul 30;93(5):e445-e457.

Ma T, Tien L, Fang CL, et al. **Statins and New-Onset Diabetes**: A Retrospective Longitudinal Cohort Study. Clin Ther. 2012 Aug 29.

Macchiaiolo M, Buonuomo PS, Valente P, et al. **Corneal Arcus** as First Sign of Familial Hypercholesterolemia. J Pediatr. 2013 Dec 3

Maccubbin DL, Chen F, Anderson JW, et al. Effectiveness and Safety of **Laropiprant** on Niacin-Induced Flushing. Am J Cardiol. 2012 Jun 7.

Macedo AF, Taylor FC, Casas JP, et al. **Unintended effects of statins** from **observational studies** in the general population: systematic review and meta-analysis. BMC Med. 2014 Mar 22;12:51.

Mach F, Baigent C, Catapano AL, et al. **2019 ESC/EAS Guidelines** for the management of dyslipidaemias: lipid modification to reduce cardiovascular risk. Eur Heart J. 2019 Aug 31.

Machan CM, Hrynchak PK, Irving EL. Age-related **cataract** is associated with type diabetes and statin use. Optom Vis Sci 2012; 89:1165-1171.

MacLean CH, et al. Effects of **omega-3 fatty acids on cancer risk**: a systematic review. JAMA. 2006 Jan 25;295(4):403-15.

Madsen CM, Varbo A, Nordestgaard BG. **Extreme high high-density lipoprotein cholesterol** is paradoxically associated with high **mortality** in men and women: two prospective cohort studies. Eur Heart J. 2017 Aug 21;38(32):2478-2486.

Madsen CM, Varbo A, Nordestgaard BG. Unmet need for **primary prevention in individuals with hypertriglyceridaemia not eligible for statin therapy** according to European Society of Cardiology/European Atherosclerosis Society guidelines: a contemporary population-based study. Eur Heart J. 2018 Feb 14;39(7):610-619.

Mahabadi AA, Mohlenkamp S. Lehmann N, et al. **CAC score** improves coronary and CV risk assessment above **statin indication** by ESC and AHA/ACC primary prevention guidelines. *JACC: Cardiovasc Imaging* 2016.

Majumdar SR, et al. Statins and outcomes in patients admitted to hospital with **community acquired pneumonia**: population based prospective cohort study. BMJ. 2006 Oct 23; [Epub ahead of print]

Makris UE, Alvarez CA, Wei W, et al. Association of **Statin Use With Risk of Back Disorder Diagnoses**. JAMA Intern Med. 2017 Jul 1;177(7):1044-1046.

Malhotra A, Redberg RF, Meier P. **Saturated fat does not clog the arteries**: coronary heart disease is a chronic inflammatory condition, the risk of which can be effectively reduced from healthy lifestyle interventions. Br J Sports Med. 2017 Apr 25.

Mamann N, Lemale J, Karsenty A, et al. **Intermediate-Term Efficacy and Tolerance** of Statins in Children. J Pediatr. 2019 Apr 30.

Mammen AL, Chung T, Christopher-Stine L, et al. **Autoantibodies** against 3-Hydroxy-3-methylglutaryl-coenzyme a reductase (HMGCR) in patients with **statin-associated autoimmune myopathy**. Arthritis Rheum 2010.

Mammen AL, Tiniakou E. Intravenous **Immune Globulin for Statin-Triggered Autoimmune Myopathy**. N Engl J Med. 2015 Oct 22;373(17):1680-2.

Mammen AL. **Statin-Associated Autoimmune Myopathy**. N Engl J Med. 2016 Feb 18;374(7):664-9.

Mampuya WM, Frid D, Rocco M, et al. Treatment strategies in patients with **statin intolerance**: the Cleveland Clinic experience. Am Heart J 2013; 166: 597-603.

Mamtani R, Lewis JD, Scott FI, et al. Disentangling the Association between **Statins, Cholesterol, and Colorectal Cancer**: A Nested Case-Control Study. PLoS Med. 2016 Apr 26

Mancini GB, Baker S, Bergeron J, et al. Diagnosis, prevention, and management of **statin adverse effects and intolerance**: proceedings of a Canadian Working Group Consensus Conference. Can J Cardiol. 2011 Sep-Oct;27(5):635-62.

Mancini GB, Tashakkor AY, Baker S, et al. Diagnosis, prevention, and management of **statin adverse effects and intolerance**: **canadian** working group consensus update. Can J Cardiol. 2013 Dec;29(12):1553-68.

Mani P, Uno K, St John J, et al. **Relation of High-Density Lipoprotein Cholesterol**:**Apolipoprotein A-I Ratio** to Progression of Coronary Atherosclerosis in Statin-Treated Patients. Am J Cardiol. 2014 Jun 18.

Mansi I, Frei CR, Pugh MJ, et al. **Statins and musculoskeletal conditions, arthropathies, and injuries**. JAMA Intern Med 3 Jun 2013, doi:10.1001/ jamainternmed.2013.6184.

Mansi I, Frei CR, Wang CP, et al. **Statins and New-Onset Diabetes** Mellitus and Diabetic Complications: A Retrospective Cohort Study of US Healthy Adults. J Gen Intern Med. 2015 Apr 28.

Mansi I et al. **Statins and new-onset diabetes** mellitus and diabetic complications: A retrospective cohort study of US healthy adults. J Gen Intern Med 2015 Nov; 30:1599.

Manuel DG, et al. Effectiveness and efficiency of **different guidelines** on statin treatment for preventing deaths from coronary heart disease: **modelling study**. BMJ. 2006 Jun 17;332(7555):1419. Epub 2006 May 31.

Marelli C, Gunnarsson C, Ross S, et al. **Statins and risk of cancer**. J Am Coll Cardiol 2011; 58:530-537. (no association found)

Majeed A. **Statins for primary prevention** of cardiovascular disease. BMJ. 2014 May 27;348:g3491.

Major RW, Cheung CK, Gray LJ, et al. **Statins and Cardiovascular Primary Prevention in CKD**: A Meta-Analysis. Clin J Am Soc Nephrol. 2015 Apr 1.

Marazzi G, Campolongo G, Pelliccia F, et al. Usefulness of **Low-Dose Statin Plus Ezetimibe and/or Nutraceuticals** in Patients With Coronary Artery Disease Intolerant to High-Dose Statin Treatment. Am J Cardiol. 2018 Oct 19.

Marazzi G, Pelliccia F, Campolongo G, et al. Usefulness of **Nutraceuticals (Armolipid Plus) Versus Ezetimibe** and Combination in Statin-Intolerant Patients With Dyslipidemia With Coronary Heart Disease. Am J Cardiol. 2015 Dec 15;116(12):1798-801.

Marcovecchio ML et al. **ACE inhibitors and statins in adolescents with type 1 diabetes**. (**AdDit**) N Engl J Med2017 Nov 2; 377:1733.

Marenzi G et al. **Myocardial infarct size** in patients on long-term **statin** therapy **undergoing primary percutaneous coronary intervention** for ST-elevation myocardial infarction. Am J Cardiol 2015 Dec 15; 116:1791.

Marrs JC, Saseen JJ. Effects of lipid-lowering therapy on reduction of cardiovascular events in patients with **end-stage renal disease requiring hemodialysis**. Pharmacotherapy. 2010 Aug;30(8):823-9.

Martin D, Schmidt R, Mortensen EM, et al. Association of **Statin** Therapy and **Risks of Cholelithiasis, Biliary Tract Diseases, and Gallbladder Procedures**: Retrospective Cohort Analysis of a US Population. Ann Pharmacother. 2015 Dec 24.

Martin JE, Cavanaugh TM, Trumbull L, et al. Incidence of adverse events with HMG-CoA reductase inhibitors in **liver transplant patients**. Clin Transplant. 2008 Jan-Feb;22(1):113-9. Overall, there was a general tolerability with a low incidence of adverse events, no incidence of severe complications, and no alterations in liver function tests in the study population with the use of LLA.

Martin SS, Metkus TS, Horne A, et al. Waiting for the National Cholesterol Education Program Adult Treatment **Panel IV Guidelines**, and in the Meantime, Some Challenges and Recommendations. Am J Cardiol. 2012 Apr 10.

Martin SS. Blaha MJ, Elshazly MB. **Friedewald estimated versus directly measured** low-density lipoprotein cholesterol and treatment implications. J Am Coll Cardiol 2013.

Martin SS, Blaha MJ, Elshazly MB, et al. Comparison of a **novel method vs the Friedewald equation** for estimating low-density lipoprotein cholesterol levels from the standard lipid profile. JAMA. doi:10.1001/jama.2013.280532.

Martin SS, Blaha MJ, Blankstein R, et al. **Dyslipidemia, coronary artery calcium, and incident atherosclerotic** cardiovascular disease: implications for statin therapy from the multi-ethnic study of atherosclerosis. Circulation. 2014 Jan 7;129(1):77-86.

Martin SS, Blumenthal RS. **Concepts and Controversies: The 2013 American** College of Cardiology/American Heart Association (**AHA**) Risk Assessment and Cholesterol Treatment Guidelines. Ann Intern Med. 2014 Jan 28

Martin SS, Khokhar AA, May HT, et al; Lipoprotein Investigators Collaborative (LIC). **HDL cholesterol subclasses**, myocardial infarction, and mortality in secondary prevention: the lipoprotein investigators collaborative. Eur Heart J. 2015 Jan 1;36(1):22-30.

Pdf Martin SS, Giugliano RP, Murphy SA, et al. Comparison of l**ow-density lipoprotein cholesterol** assessment by Martin/Hopkins estimation, Friedewald estimation, and preparative ultracentrifugation: insights from the FOURIER trial [online June 13, 2018]. JAMA Cardiol. doi:10.1001/jamacardio.2018.1533
Martínez-Sánchez P, Fuentes B, Martínez-Martínez M, et al. Treatment with **statins and ischemic stroke severity**: Does the dose matter? Neurology. 2013 May 7;80(19):1800-5.
Masuda J, Tanigawa T, Yamada T, et al. Effect of Combination Therapy of **Ezetimibe and Rosuvastatin** on Regression of Coronary **Atherosclerosis** in Patients With Coronary Artery Disease. Int Heart J. 2015 Apr 23.
Matthews A, Herrett E, Gasparrini A, et al. Impact of **statin related media coverage on use of statins**: interrupted time series analysis with UK primary care data. BMJ 2016;353:i3283.
Mayo Clinic Statin Choice Decision Aid https://statindecisionaid.mayoclinic.org/
Mazzanti G, Moro PA, Raschi E, et al. Adverse reactions to dietary supplements containing **red yeast rice**: assessment of cases from the Italian surveillance system. Br J Clin Pharmacol. 2017 Jan 17.
McAuley DF, Laffey JG, O'Kane CM, et al; the **HARP-2** Investigators, for the Irish Critical Care Trials Group. **Simvastatin in the Acute Respiratory Distress** Syndrome. N Engl J Med. 2014 Sep 30.
McConnachie A, Walker A, Robertson M, et al. Long-term impact on **healthcare resource utilization** of statin treatment, and its cost effectiveness in the **primary prevention** of cardiovascular disease: a record linkage study. Eur Heart J. 2013 Jul 9.
McCrindle BW, Kwiterovich PO, McBride PE, et al. Guidelines for lipid **screening in children and adolescents**: bringing evidence to the debate. Pediatrics. 2012 Aug;130(2):353-6.
McCrindle BW, Tyrrell PN, Kavey RE. Will **obesity** increase the proportion of children and **adolescents recommended for a statin**? Circulation. 2013 Nov 5;128(19):2162-5.
McCullough PA, et al. Efficacy and Safety of **Alirocumab** in High-Risk Patients With Clinical Atherosclerotic Cardiovascular Disease and/or Heterozygous Familial Hypercholesterolemia (from 5 Placebo-Controlled **ODYSSEY** Trials). Am J Cardiol. 2018 Apr 15;121(8):940-948.
McDonagh J. **Statin-Related Cognitive Impairment** in the Real World: You'll Live Longer, but You Might Not Like It. JAMA Intern Med. 2014 Dec 1;174(12):1889.
McGettigan P, Ferner RE. **PCSK9 inhibitors** for hypercholesterolaemia. BMJ. 2017 Jan 19;356:j188.
McGuinness B, O`Hare J, Craig D, et al. Statins for the treatment of **dementia**. Cochrane Database Syst Rev. 2010 Aug 4;8:CD007514. There is insufficient evidence to recommend statins for the treatment of dementia. Analysis from the studies available, including one large RCT, indicate statins have no benefit on the outcome measures ADAS-Cog or MMSE. We need to await full results from CLASP 2008 before we can be certain.
McGuinness B, Craig D, Bullock R, et al. **Statins for the prevention of dementia**. Cochrane Database Syst Rev. 2016 Jan 4;1:CD003160. There is good evidence that statins given in late life to people at risk of vascular disease do not prevent cognitive decline or dementia. Biologically, it seems feasible that statins could prevent dementia due to their role in cholesterol reduction and initial evidence from observational studies was very promising. However, indication bias may have been a factor in these studies and the evidence from subsequent RCTs has been negative. There were limitations in the included studies involving the cognitive assessments used and the inclusion of participants at moderate to high vascular risk only.
McKenney JM, et al. Safety and efficacy of long-term co-administration of **fenofibrate and ezetimibe** in patients with mixed hyperlipidemia. (N=587 48 wks) J Am Coll Cardiol. 2006 Apr 18;47(8):1584-7. Epub 2006 Mar 30.
McKenney JM, et al. Efficacy and safety of **torcetrapib**, a novel cholesteryl ester transfer protein inhibitor, in individuals with below-average high-density lipoprotein cholesterol levels on a background of atorvastatin. J Am Coll Cardiol. 2006 Nov 7;48(9):1782-90.
McKenney JM, Davidson MH, Jacobson TA, Guyton JR; National Lipid Association **Statin Safety Assessment Task Force**. Final conclusions and recommendations of the National Lipid Association Statin Safety Assessment Task Force. Am J Cardiol. 2006 Apr 17;97(8A):89C-94C. Epub 2006 Feb 28.
McKenney JM, Koren MJ, Kereiakes DJ, et al. Safety and efficacy of a monoclonal antibody to proprotein convertase subtilisin/kexin type 9 serine protease, **SAR236553/REGN727**, in patients with primary hypercholesterolemia receiving ongoing stable atorvastatin therapy. J Am Coll Cardiol 2012; 59: 2344-2353.
McKinney JS, Kostis WJ. **Statin therapy and the risk of intracerebral hemorrhage**: a meta-analysis of 31 randomized controlled trials. Stroke. 2012 Aug;43(8):2149-56.
McLean CC, Teft WA, Morse BL, et al. **Food Effect on Rosuvastatin** Disposition and Low-Density Lipoprotein Cholesterol. Clin Pharmacol Ther. 2017 Dec 8.
McMahon GM, Zeng X, Waikar SS. A **Risk Prediction Score** for Kidney Failure or Mortality in **Rhabdomyolysis**. JAMA Intern Med. 2013 Sep 2.
Medical Letter. **Pitavastatin (Livalo).** July 26, 2010.
Medical Letter. Drugs for **Hypertiglyceridemia**. Mar 4, 2013.
Mefford MT, Rosenson RS, Cushman M, et al. **PCSK9 Variants, LDL-Cholesterol, and Neurocognitive Impairment**: The REasons for Geographic and Racial Differences in Stroke (**REGARDS**) Study. Circulation. 2017 Nov 16.
Mefford MT, Rosenson RS, et al. **PCSK9** Variants, Low-Density Lipoprotein Cholesterol, and **Neurocognitive Impairment**: Reasons for Geographic and Racial Differences in Stroke Study (**REGARDS**). Circulation. 2018 Mar 20;137(12):1260-1269.
Mega JL, Stitziel NO, Smith GJ, et al. **Genetic risk, coronary heart disease events, and the clinical benefit of statin** therapy: an analysis of primary and secondary prevention trials. Lancet 2015; online March 4.
Mehta JL, et al. Comparison of mortality rates in statin users versus nonstatin users in a United States **veteran population**. Am J Cardiol. 2006 Oct 1;98(7):923-8. Epub 2006 Aug 7. The benefit observed in this study is unique because almost 1/2 the patients were >/=70 years of age when statin therapy was initiated.
Mendelson MM, Lyass A, O'Donnell C, et al. Association of **maternal prepregnancy dyslipidemia with adult offspring dyslipidemia** in excess of anthropometric, lifestyle, and genetic factors in the Framingham Heart Study. *JAMA Cardiol*2016.
Mercado C, DeSimone AK, Odom E, et al. Prevalence of **cholesterol treatment eligibility and medication use among adults—United States**, 2005-2012. *MMWR Morb Mortal Wkly Rep* 2015; 64:1305-1311.
Mergenhagen K, Ott M, Heckman K, et al. Low **Vitamin D** as a Risk Factor for the Development of **Myalgia in Patients Taking High-Dose Simvastatin**: A Retrospective Review. Clin Ther. 2014 Apr 14.
Meseguer E, Mazighi M, Lapergue B, et al. Outcomes after **thrombolysis in AIS according to prior statin use**: A registry and review. Neurology. 2012 Oct 23;79(17):1817-23.
Miedema MD, Lopez FL, Blaha MJ, et al. **Eligibility for Statin Therapy** According to **New Cholesterol Guidelines** and Prevalent Use of Medication to Lower Lipid Levels in an Older US Cohort: The Atherosclerosis Risk in Communities Study Cohort. JAMA Intern Med. 2014 Nov 17.
Mikolasevic I, Žutelija M, Mavrinac V, Orlic L. **Dyslipidemia in patients with chronic kidney disease**: etiology and management. Int J Nephrol Renovasc Dis. 2017 Feb 7;10:35-45.
Milionis HJ, Giannopoulos S, Kosmidou M, et al. **Statin therapy after first stroke** reduces 10-year stroke recurrence and improves survival. Neurology 2009; 72:1816-1822.
Miller M, et al. High attributable risk of elevated **C-reactive protein** level to conventional coronary heart disease risk factors: the Third National Health and Nutrition Examination Survey. Arch Intern Med. 2005 Oct 10;165(18):2063-8.
CONCLUSIONS: These data suggest that elevated CRP levels in the general population are in large measure attributable to traditional CHD risk factors. Moreover, CRP level elevation is rare in the absence of borderline or abnormal risk factors. As such, CRP measurements may have limited clinical utility as a screening tool beyond other known CHD risk factors.
Miller Michael, Stone Neil J., Ballantyne Christie, et al. and on behalf of the American Heart Association Clinical Lipidology, Thrombosis, and Prevention Committee of the Council on Nutrition, Physical Activity, and Metabolism, Council on Arteriosclerosis, Thrombosis and Vascular Biology, Council on Cardiovascular N. **Triglycerides and Cardiovascular Disease**: A Scientific Statement From American Heart Association (**AHA**). April 18, 2011. http://circ.ahajournals.org/cgi/reprint/CIR.0b013e3182160726v1
Mills EJ, Rachlis B, et al. **Primary prevention** of cardiovascular mortality and events with statin treatments: a network meta-analysis involving more than 65,000 patients. J Am Coll Cardiol. 2008 Nov 25;52(22):1769-81.
Mills EJ, Wu P, Chong G, et al. Efficacy and safety of statin treatment for cardiovascular disease: a **network meta-analysis** of 170,255 patients from 76 randomized trials. QJM. 2011 Feb;104(2):109-24.
Min KL, Park MS, Jung J et al. Comparison of Pharmacokinetics and Safety of a Fixed-Dose **Combination** of **Rosuvastatin** and **Ezetimibe** Versus Separate Tablets in Healthy Subjects. ClinTher. 2017.
Minicocci I, Pozzessere S, Prisco C, et al. Analysis of **Children and Adolescents with Familial Hypercholesterolemia**. J Pediatr. 2017 Apr;183:100-107.e3.
Mitchell JD, Fergestrom N, Gage BF, et al. Impact of **Statins on Cardiovascular Outcomes Following Coronary Artery Calcium Scoring**. J Am Coll Cardiol. 2018 Oct 31.
Mitka M. **Ezetimibe** Prescribing Fails to Keep Up With Evidence. JAMA. 2014 Mar 19.
Mittleman MA. A 39-year-old **woman with hypercholesterolemia**. JAMA. 2006 Jul 19;296(3):319-26.
Mittleman MA, Taylor WC, et al. Treatment of Blood **Cholesterol to Reduce Risk for Atherosclerotic Cardiovascular Disease: Grand Rounds** Discussion From the Beth Israel Deaconess Medical Center. Ann Intern Med. 2015 Aug 18;163(4):280-90.
Mochari-Greenberger H, Liao M, Mosca L. **Racial and Ethnic Differences** in Statin Prescription and Clinical Outcomes Among Hospitalized Patients With Coronary Heart Disease. Am J Cardiol. 2013 Nov 7.
Mohaupt MG, Karas RH, Babiychuk EB, et al. Association between **statin-associated myopathy** and skeletal muscle damage. CMAJ. 2009 Jul 7;181(1-2):E11-8.
Moleti M, Trimarchi F, Tortorella G, et al. Effects of **Maternal Iodine Nutrition and Thyroid Status** on Cognitive Development in Offspring: A Pilot Study. Thyroid. 2016 Feb;26(2):296-305.
Molina CA, Selim MH. **Continued statin treatment after acute intracranial hemorrhage**: fighting fire with fire. Stroke. 2013 Jul;44(7):2062-3.
Monami M, Sesti G, Mannucci E. **PCSK9 inhibitor therapy**: A systematic review and meta-analysis of metabolic and **cardiovascular outcomes in patients with diabetes**. Diabetes Obes Metab. 2018 Nov 28.
Monroe AK, Gudzune KA, Sharma R, et al. **Combination Therapy Versus Intensification of Statin Monotherapy**: An Update AHRQ Comparative Effectiveness Reviews. Rockville (MD): Agency for Healthcare Research and Quality (US); 2014 Feb.
Montori VM, Brito JP, Ting HH. **Patient-centered** and practical application of new high cholesterol **guidelines** to prevent cardiovascular disease. JAMA. 2014 Feb 5;311(5):465-6.
Mora S. **Nonfasting for Routine Lipid Testing**: From Evidence to Action. JAMA Intern Med. 2016 Apr 27.

Mora S, Chang CL, Moorthy MV, Sever PS. Association of **Nonfasting vs Fasting Lipid Levels** With Risk of Major Coronary Events in the Anglo-Scandinavian Cardiac Outcomes Trial-Lipid Lowering Arm. JAMA Intern Med. 2019 May 28.
Mora S, Glynn RJ, Ridker PM. High-density lipoprotein (**HDL**) cholesterol, size, particle number, and residual vascular risk after potent statin therapy. Circulation. 2013;128:1189–1197.
Mora S, Wenger NK, DeMicco DA, et al. **Determinants of residual risk** in secondary prevention patients treated with high- versus low-dose statin therapy: the Treating to New Targets (**TNT**) study. Circulation. 2012;125:1979 –1987.
Morandi A, Hughes CG, Thompson JL, et al. **Statins and delirium** during critical illness: a multicenter, prospective cohort study*. Crit Care Med. 2014 Aug;42(8):1899-909.
Moreyra AE, Wilson AC, Koraym A. Effect of combining psyllium **fiber with simvastatin** in lowering cholesterol. Arch Intern Med. 2005 May 23;165(10):1161-6.
Moriarity PM, Parhofer KG, Babirak SP, et al. **Alirocumab** in patients with heterozygous familial hypercholesterolemia undergoing lipoprotein apheresis: The ODYSSEY-ESCAPE trial. *Eur Heart J* 2016.
Mortensen MB, Afzal S, Nordestgaard BG, et al. **Primary Prevention With Statins: ACC/AHA Risk-Based Approach Versus Trial-Based Approaches** to Guide Statin Therapy. J Am Coll Cardiol. 2015 Dec 22;66(24):2699-709.
Mortensen MB, Fuster V, Muntendam P, et al. A **Simple Disease-Guided Approach to Personalize ACC/AHA-Recommended Statin Allocation in Elderly People**: The BioImage Study. J Am Coll Cardiol. 2016 Aug 30;68(9):881-91.
Mortensen MB, et al. **ACC/AHA** guidelines superior to **ESC/EAS guidelines** for **primary prevention with statins** in **non-diabetic Europeans**: the Copenhagen General Population Study. Eur Heart J. 2016 Nov 08;00:1-9.
Mortensen MB, Budoff MJ, Li D, et al. High **Quality Statin Trials Support the 2013 ACC/AHA Cholesterol Guidelines After HOPE-3**: The Multi-Ethnic Study of Atherosclerosis. Circulation. 2017 Jun 20.
Mortensen MB, Nordestgaard BG. Comparison of **five major guidelines for statin use in primary prevention** in a contemporary general population. Ann Intern Med. 2018;168:85-92.
Mortensen MB, Falk E. **Primary Prevention With Statins in the Elderly**. J Am Coll Cardiol. 2018 Jan 2;71(1):85-94.
Mumford SL, Schisterman EF, Siega-Riz AM, et al. A Longitudinal Study of Serum Lipoproteins in Relation to Endogenous Reproductive Hormones during the **Menstrual Cycle**: Findings from the BioCycle Study. J Clin Endocrinol Metab. 2010 Jun 9.
Mundal LJ, Igland J, Veierod MB, et al. Impact of **age on excess risk of coronary heart disease in patients with familial hypercholesterolaemia**. Heart. 2018 Apr 5.
Munkhaugen J, Sverre E, Otterstad JE, et al. **Medical and psychosocial factors** and **unfavourable low-density lipoprotein cholesterol control** in coronary patients. Eur J Prev Cardiol 2017.
Muñoz D, Uzoije P, Reynolds C, et al. **Polypill for Cardiovascular Disease Prevention** in an Underserved Population. N Engl J Med. 2019 Sep 19;381(12):1114-1123.
Muntner P, Levitan EB, Brown TM, et al. Trends in the **Prevalence, Awareness, Treatment** and Control of High Low Density Lipoprotein-Cholesterol Among **United States Adults** from 1999-2000 Through 2009-2010. Am J Cardiol. 2013 May 28.
Muntner P, Colantonio LD, Cushman M, et al. Validation of the **atherosclerotic cardiovascular disease pooled cohort risk equations**. JAMA 2014; DOI:10.1001/jama.2014.2630. Available at: https://jama.jamanetwork.com/journal.aspx.
Muntner P, Safford MM, Cushman M, and Howard G. Comment on the reports of **overestimation of ASCVD risk using the 2013 AHA/ACC risk equation**. Circulation 2014; 129:266-267.
Murphy SA, Cannon CP, Blazing MA, et al. Reduction in Total Cardiovascular Events With **Ezetimibe/Simvastatin** Post-Acute Coronary Syndrome: The **IMPROVE-IT** Trial. J Am Coll Cardiol. 2016 Feb 2;67(4):353-61.
Murphy SA, Pedersen TR, Gaciong ZA, et al. Effect of the **PCSK9 Inhibitor Evolocumab on Total Cardiovascular Events** in Patients With Cardiovascular Disease: A Prespecified Analysis From the FOURIER Trial. JAMA Cardiol. 2019 May 22.
Myers KD, Farboodi N, Mwamburi M, et al. Effect of **Access to Prescribed PCSK9 Inhibitors** on Cardiovascular Outcomes. Circ Cardiovasc Qual Outcomes. 2019 Aug;12(8):e005404.
Myocardial Infarction Genetics Consortium Investigators. Inactivating mutations in **NPC1L1** and protection from coronary heart disease. *N Engl J Med* 2014;
Myocardial Infarction Genetics and CARDIoGRAM Exome Consortia Investigators. Coding variation in **ANGPTL4, LPL, and SVEP1** and the risk of coronary disease. N Engl J Med. DOI: 10.1056/NEJMoa1507652.
Naci H, Brugts J, Ades T. **Comparative Tolerability and Harms of Individual Statins**: A Study-Level **Network Meta-Analysis** of 246 955 Participants From 135 Randomized Controlled Trials. Circ Cardiovasc Qual Outcomes. 2013 Jul 9.
Naci H, Dias S, Ades AE. Industry **sponsorship bias** in research findings: a network meta-analysis of **LDL cholesterol reduction** in randomised trials of statins. BMJ 2014;349:g5741.
Nakamura H, et al. **Primary prevention** of cardiovascular disease with pravastatin in Japan (**MEGA** Study): a prospective randomised controlled trial. Lancet. 2006 Sep 30;368(9542):1155-63.
Nanchen D, Gencer B, Muller O, et al. Prognosis of Patients with **Familial Hypercholesterolemia After Acute Coronary Syndromes**. Circulation. 2016 Jul 26.
Nanna MG, Navar AM, Zakroysky P, et al. Association of **Patient Perceptions of Cardiovascular Risk and Beliefs on Statin Drugs** With Racial Differences in Statin Use: Insights From the Patient and Provider Assessment of Lipid Management Registry. JAMA Cardiol. 2018 Jun 13.
Nardi K, Engelter S, Strbian D, et al, on behalf of the Lipid Profile in Thrombolysis Study Group. Lipid profiles and outcome in patients treated by **intravenous thrombolysis** for cerebral ischemia. Neurology 2012;79:1101–1108.
Nasir K, et al. Implications of **coronary artery calcium testing** among statin candidates according to American College of Cardiology/American Heart Association cholesterol management guidelines: **MESA**.J Am Coll Cardiol 2015; 66: 1657-1668.
Natarajan P, Young R, Stitzielet NO, et al.. **Polygenic risk score identifies subgroup** with higher burden of atherosclerosis and greater relative **benefit from statin therapy** in the primary prevention setting. (**WOSCOPS**) *Circulation* 2017.
Natarajan P, Young R, Stitziel NO, et al. **Polygenic risk score** identifies subgroup with higher burden of atherosclerosis and greater relative benefit from statin therapy in the primary prevention setting. (WOSCOPS) Circulation. 2017;135:2091–2101.
National Heart, Lung, and Blood Institute ARDS Clinical Trials Network. **Rosuvastatin** for **sepsis**-associated acute respiratory distress syndrome. (**ARDS**) N Engl J Med. DOI: 10.1056/NEJMoa1401520.
Natsuaki M, et al. **CREDO-Kyoto PCI/CABG** Registry Cohort-2 Investigators. Impact of Statin Therapy on Late Target Lesion Revascularization After **Sirolimus-Eluting Stent Implantation** (CREDO-Kyoto Registry Cohort-2). Am J Cardiol. 2012 Feb 28.
Natsuaki M, Furukawa Y, Morimoto T, Sakata R, Kimura T; CREDO-Kyoto PCI/CABG Registry Cohort-2 Investigators. **Renal Function and Effect of Statin** Therapy on Cardiovascular Outcomes in Patients Undergoing Coronary **Revascularization** (from the CREDO-Kyoto PCI/CABG Registry Cohort-2). Am J Cardiol. 2012 Dec 1;110(11):1568-77.
Naugler C, Sidhu D. Break the fast? Update on **patient preparation** for **cholesterol testing**. Can Fam Physician. 2014 Oct;60(10):895-897.
Navaneethan SD, Pansini F, Perkovic V, et al. HMG CoA reductase inhibitors (statins) for people with **chronic kidney disease not requiring dialysis**. Cochrane Database Syst Rev. 2009 Apr 15;(2):CD007784.
Navaneethan SD, Nigwekar SU, Perkovic V, Johnson DW, Craig JC, Strippoli GF. HMG CoA reductase inhibitors **(statins) for dialysis** patients. Cochrane Database Syst Rev. 2009;(2):CD004289.
Navaneethan SD, Perkovic V, Johnson DW, Nigwekar SU, Craig JC, Strippoli GF. HMG CoA reductase inhibitors **(statins) for kidney transplant** recipients. Cochrane Database Syst Rev. 2009;(2):CD005019.
Navar AM, Taylor B, Mulder H, et al. Association of **prior authorization and out-of-pocket costs with patient access to PCSK9 inhibitor therapy** [published online September 27, 2017].JAMA Cardiol. doi:10.1001/jamacardio.2017.3451.
Navar-Boggan AM, Peterson ED, D'Agostino RB, et al. **Hyperlipidemia in early adulthood increases** long-term risk of coronary heart disease. Circulation. 2015;131:451–458.
Navar-Boggan AM, Peterson ED, D'Agostino Sr RB, et al. One size may not fit all: Using **age- and sex-specific risk thresholds to guide statin** therapy. *J Am Coll Cardiol* 2015.
Navarese EP, Buffon A, Andreotti F, et al. Meta-Analysis of Impact of Different **Types and Doses of Statins on New-Onset Diabetes** Mellitus. Am J Cardiol. 2013 Jan 24.
Navarese EP, Kowalewski M, Andreotti F, et al. Meta-Analysis of **Time-Related Benefits of Statin** Therapy in Patients With Acute Coronary Syndrome Undergoing Percutaneous Coronary Intervention. Am J Cardiol. 2014 May 15;113(10):1753-1764.
Navarese EP, Kołodziejczak M, Schulze V, et al. Effects of **proprotein convertase subtilisin/kexin type 9 antibodies** (PCSK9) in adults with hypercholesterolemia. A systematic review and meta-analysis. Ann Intern Med. 2015.
Navarese EP, Kołodziejczak M, Kereiakes DJ, et al. **Proprotein convertase subtilisin/kexin type 9 monoclonal antibodies** for **acute coronary syndrome**. A narrative review. Ann Intern Med. 2016;164:600-7. doi:10.7326/M15-2994
Navarese EP, Robinson JG, Kowalewski M, et al. Association between **baseline LDL-C level and total and cardiovascular mortality** after LDL-C lowering: a systematic review and meta-analysis [online April 17, 2018].JAMA. doi:10.1001/jama.2018.2525
Nayor M, Vasan RS. Recent Update to the **US Cholesterol Treatment Guidelines: A Comparison With International Guidelines**. Circulation. 2016 May 3;133(18):1795-806
Needham DM, Colantuoni E, Dinglas VD, et al. **Rosuvastatin** versus placebo for **delirium** in intensive care and subsequent cognitive impairment in patients with sepsis-associated acute respiratory distress syndrome: an ancillary study to a randomised controlled trial. Lancet Respir Med. 2016 Jan 28.
Neil HA, et al. **CARDS** Study Investigators. Analysis of efficacy and safety in patients **aged 65-75** years at randomization: Collaborative Atorvastatin Diabetes Study (CARDS). Diabetes Care. 2006 Nov;29(11):2378-84.
New drug: **Advicor** (Niacin Extended-Release?Lovastatin). Pharmacist's Letter/Prescriber's Letter 2006;22(2):220220
Newman C, Tsai J, Szarek M, Luo D, Gibson E. Comparative safety of **atorvastatin 80 mg versus 10 mg** derived from analysis of 49 completed trials in 14,236 patients. Am J Cardiol. 2006 Jan 1;97(1):61-7. Epub 2005 Nov 15.
Newman CB, Preiss D, Tobert JA, et al. **Statin Safety and Associated Adverse Events**: A Scientific Statement From the **American Heart Association**. Arterioscler Thromb Vasc Biol. 2018 Dec 10:ATV0000000000000073.
Newman TB, Pletcher MJ, Hulley SB. Overly aggressive new guidelines for **lipid screening in children**: evidence of a broken process. Pediatrics. 2012 Aug;130(2):349-52.
Newman TB, Schroeder AR, Pletcher MJ. **Lipid screening in children**. JAMA Intern Med 2016.
Newson RS, Felix JF, Heeringa J, et al. Association between serum **cholesterol and noncardiovascular mortality in older age**. J Am Geriatr Soc. 2011 Oct;59(10):1779-85.
Ngo-Metzger Q, Gottfredson R. **Statin Use for the Primary Prevention of Cardiovascular Disease in Adults**. Am Fam Physician. 2017 Dec 15;96(12):805-806.
Nguyen CD, Andersson C, Jensen TB, et al. Statin treatment and **risk of recurrent venous thromboembolism**: a nationwide cohort study. BMJ Open. 2013 Nov 7;3(11):e003135.
Ni Chroinin D, Asplund K, Asberg S, et al. **Statin therapy and outcome after ischemic stroke**: systematic review and meta-analysis of observational studies and randomized trials. Stroke. 2013 Feb;44(2):448-56.
NICE clinical guideline CG181. **Lipid modification**: Cardiovascular risk assessment of blood lipids for the primary and secondary prevention of cardiovascular disease. July 2014.

NICE: National Institute for Health and Care Excellence (NICE). **Ezetimibe** for treating primary heterozygous-familial and non-familial hypercholesterolaemia. London (UK): National Institute for Health and Care Excellence (NICE); 2016 Feb 24.
NICE: National Institute for Health and Care Excellence. **Familial hypercholesterolaemia**: identification and management. Nov 2017. https://www.nice.org.uk/guidance/cg71/chapter/ Recommendations.
NICE: National Institute for Health and Care Excellence. **Familial hypercholesterolaemia**: identification and management. Nov 2017. https://www.nice.org.uk/guidance/cg71/chapter/ Recommendations
Nicholls SJ, et al. Effects of obesity on lipid-lowering, anti-inflammatory, and antiatherosclerotic benefits of atorvastatin or pravastatin in patients with coronary artery disease (from the **REVERSAL** Study). Am J Cardiol. 2006 Jun 1;97(11):1553-7. Epub 2006 Apr 6.
Nichols GA, Vupputuri S, Rosales AG. Change in **high-density lipoprotein** (HDL) cholesterol and risk of subsequent hospitalization for coronary artery disease or stroke among patients with type 2 diabetes mellitus. Am J Cardiol. 2011 Oct 15;108(8):1124-8.
Nicholls SJ, Puri R, Ballantyne CM, et al. Effect of infusion of **high-density lipoprotein mimetic containing recombinant apolipoprotein A-I Milano on coronary disease** in patients with an acute coronary syndrome in the MILANO-PILOT Trial: a randomized clinical trial [online July 25, 2018]. JAMA Cardiol. doi:10.1001/jamacardio.2018.2112
Nicholls SJ, Andrews J, Kastelein JJP, et al. Effect of serial **infusions of CER-001, a pre-β high-density lipoprotein mimetic, on coronary atherosclerosis** in patients following acute coronary syndromes in the CER-001 Atherosclerosis Regression Acute Coronary Syndrome Trial: a randomized clinical trial [online July 25, 2018]. JAMA Cardiol. doi:10.1001/jamacardio.2018.2121
Nicholls SJ, Brewer HB, Kastelein JJP, et al. Effects of the CETP inhibitor **evacetrapib** administered as monotherapy or in combination with statins on HDL and LDL cholesterol: a randomized controlled trial. JAMA. 2011;306(19):2099-2109.
Nicholls SJ, Ballantyne CM, Barter PJ, et al. Effect of two intensive statin (**atrovastatin 80mg vs rosuvastatin 40mg**) regimens on progression of coronary disease. (**Saturn**) N Engl J Med 2011; DOI: 10.1056/NEJMoa1110874.
Nicholls SJ. **Niacin's** effect on cardiovascular risk: have we finally learned our lesson? Cleve Clin J Med. 2014 May;81(5):275-7.
Nicholls SJ, Puri R, Anderson T, et al. Effect of **Evolocumab** on Progression of Coronary Disease in Statin-Treated Patients: The **GLAGOV** Randomized Clinical Trial. JAMA. 2016 Nov 15.
Nielsen SF, Nordestgaard BG, Bojesen SE. **Statin use and reduced cancer-related mortality**. N Engl J Med 2012;367:1792-802.
Nielsen SF, Nordestgaard BG. **Statin use before diabetes** diagnosis and risk of microvascular disease: a nationwide nested matched study. Lancet Diabetes Endocrinol. 2014 Nov;2(11):894-900.
Nielsen SF and Nordestgaard BG. **Negative statin-related news stories** decrease statin persistence and increase myocardial infarction and cardiovascular mortality: a nationwide prospective cohort study. *Eur Heart J* 2015.
Nielsen SF, Nordestgaard BG. **Negative statin-related news stories** decrease statin persistence and increase myocardial infarction and cardiovascular mortality: a nationwide prospective cohort study. Eur Heart J. 2015 Dec 1.
Nieuwkerk PT, Nierman MC, Vissers MN, et al. Intervention to **Improve Adherence** to Lipid-Lowering Medication and Lipid-Levels in Patients With an Increased Cardiovascular Risk. Am J Cardiol. 2012 May 21.
Nissen SE, et al. Effect of Very High-Intensity Statin (rosuvastatin 40mg/d, 2yr, n=507) Therapy on Regression of Coronary Atherosclerosis: The **ASTEROID** Trial.JAMA. 2006 Mar 13; [Epub ahead of print]
Nissen SE, Stroes E, Dent-Acosta RE, et al. Efficacy and tolerability of **evolocumab vs ezetimibe** in patients with **muscle-related statin intolerance**: the **GAUSS-3** randomized clinical trial. JAMA. doi:10.1001/jama.2016.3608.
Nissen SE. **Statin Denial**: An **Internet-Driven Cult With Deadly Consequences**. Ann Intern Med. 2017 Jul 25.
Nissen SE, Pillai SG, Nicholls SJ, et al. **ADCY9 genetic variants** and cardiovascular outcomes with **evacetrapib** in patients with high-risk vascular disease: a nested case-control study [online Mar 11, 2018].JAMA Cardiol. doi:10.1001 /jamacardio.2018.0569.
Nkemdirim Okere A, Renier CM. Effects of **Statins on Hospital Length of Stay** and All-Cause Readmissions Among Hospitalized Patients With a Primary Diagnosis of **Sepsis**. Ann Pharmacother. 2015 Dec;49(12):1273-83.
Nordestgaard BG et al. **Nonfasting triglycerides** and risk of myocardial infarction, ischemic heart disease, and death in men and women. JAMA 2007 Jul 18; 298:299-308.
Nordestgaard BG, Chapman MJ, Humphries SE, et al. **Familial hypercholesterolemia** is underdiagnosed and undertreated in the general population: guidance for clinicians to prevent coronary heart disease. Eur Heart J 2013.
Nordestgaard B, Varbo A. Lipids and cardiovascular disease 3: **Triglycerides and cardiovascular disease**. Lancet 2014; 384: 626–35.
Nordestgaard BG, Langsted A, Mora Set al. **Fasting is not routinely required** for determination of a **lipid profile**: clinical and laboratory implications including flagging at desirable concentration cut-points-a joint consensus statement from the **European** Atherosclerosis Society and European Federation of Clinical Chemistry and Laboratory Medicine. Eur Heart J. 2016 Apr 26
Nordestgaard BG. A Test in Context: **Lipid Profile, Fasting Versus Nonfasting**. J Am Coll Cardiol. 2017 Sep 26;70(13):1637-1646.
Noubiap JJ, Bigna JJ, Nansseu JR, et al. **Prevalence of dyslipidaemia among adults in Africa**: a systematic review and meta-analysis. Lancet Glob Health. 2018 Sep;6(9):e998-e1007.
Nozue T, Yamamoto S, Tohyama S, et al. Effects of **Serum n-3 to n-6 Polyunsaturated Fatty Acids Ratios** on Coronary Atherosclerosis in Statin-Treated Patients With Coronary Artery Disease. Am J Cardiol. 2013 Jan 1;111(1):6-11.
Nykänen AI, Holmström EJ, Tuuminen R, et al. **Donor Simvastatin Treatment** in Heart Transplantation: A Randomized and Blinded Clinical Trial. Circulation. 2019 Jul 29.
O'Brien EC, Greiner MA, Xian Y, et al. Clinical Effectiveness of **Statin Therapy after Ischemic Stroke**: Primary Results from the Statin Therapeutic Area of the Patient-Centered Research into Outcomes Stroke Patients Prefer and Effectiveness Research (**PROSPER**) Study. Circulation. 2015 Aug 5.
O'Brien EC, McCoy LA, Thomas L, et al. **Patient adherence to generic versus brand statin** therapy after acute myocardial infarction: Insights from the Can Rapid Stratification of Unstable Angina Patients Suppress Adverse Outcomes with Early Implementation of the American College of Cardiology/American Heart Association Guidelines Registry. Am Heart J. 2015 Jul;170(1):55-61.
O'Brien EC, Greiner MA, Xian Y, et al. Clinical Effectiveness of **Statin Therapy after Ischemic Stroke**: Primary Results from the Statin Therapeutic Area of the Patient-Centered Research into Outcomes Stroke Patients Prefer and Effectiveness Research (**PROSPER**) Study. Circulation. 2015 Aug 5.
O'Brien EC, Wu J, Schulte PJ, et al. **Statin use**, intensity, and 3-year clinical outcomes among **older patients** with coronary artery disease. Am Heart J. 2016 Mar;173:27-34.
O'Keefe JH, DiNicolantonio JJ, Lavie CJ. **Statins, Ezetimibe and Proprotein Convertase Subtilisin-kexin Type 9 (PCSK9)** inhibitors to Reduce Low-Density Lipoprotein-Cholesterol and Cardiovascular Events. Am J Cardio (2016)
O'Reilly M, Dillon E, Guo W, et al. **High density lipoprotein** proteomic composition, and not efflux capacity, reflects differential modulation of reverse cholesterol transport by saturated and monounsaturated fat diets. Circulation. 2016;133:1838–1850.
Odden MC, Pletcher MJ, Coxson PG, et al. **Cost-effectiveness** and population impact of **statins for primary prevention in adults aged 75 years or older** in the United States. Ann Intern Med. 2015;162:533-41.
Ofori-Asenso R, Ilomäki J, Tacey M, et al. **Predictors of first year nonadherence and discontinuation of statins** among older adults: a retrospective cohort study. Br J Clin Pharmacol Nov 2018.
Ogita M, et al. Impact of **Combined C-Reactive Protein and High-Density Lipoprotein Cholesterol Levels** on Long-Term Outcomes in Patients With Coronary Artery Disease After a First Percutaneous Coronary Intervention. Am J Cardiol. 2015 Jul 15.
Oh GC, Han JK, Han KH, et alS. Efficacy and Safety of Fixed-dose Combination Therapy With **Telmisartan and Rosuvastatin** in Korean Patients With Hypertension and Dyslipidemia: TELSTA-YU (TELmisartan-rosuvaSTAtin from YUhan), a Multicenter, Randomized, 4-Arm, Double-blind, Placebo-controlled, Phase III Study. Clin Ther. 2018 Apr 16.
Omer SB, Phadke VK, Bednarczyk RA, et al. Impact of **Statins on Influenza Vaccine** Effectiveness Against Medically Attended Acute Respiratory Illness. J Infect Dis. 2015 Oct 28.
Orngreen MC, Madsen KL, Preisler N, et al. **Bezafibrate** in **skeletal muscle fatty acid oxidation disorders**: A randomized clinical trial. Neurology. 2014 Feb 18;82(7):607-13.
Ong KL, Waters DD, Messig M, et al. Effect of **Change in Body Weight** on Incident Diabetes Mellitus in Patients With Stable Coronary Artery Disease Treated With Atorvastatin (from the Treating to New Targets Study). Am J Cardiol. 2014 May 15;113(10):1593-8.
Ong KL, Morris MJ, McClelland RL, et al. Relationship of **Lipids and Lipid-Lowering Medications With Cognitive Function**: The Multi-Ethnic Study of Atherosclerosis. Am J Epidemiol. 2018 Apr 1;187(4):767-776.
Onofrei MD, et al. Safety of statin therapy in patients with preexisting **liver disease**. Pharmacotherapy. 2008 Apr;28(4):522-9.
Onorato A, Sturm AC. **Heterozygous Familial Hypercholesterolemia**. Circulation. 2016 Apr 5;133(14):e587-9.
Oregon Health Sciences University. Drug class review on Statins (Aug 2006) http://www.ohsu.edu/drugeffectiveness/reports/documents/Statins%20Final%20Report%20Update%204%20Unshaded.pdf
ORIGIN trial investigators. **n-3 fatty acids** and cardiovascular outcomes in patients with dysglycemia. N Engl J Med 2012.
Ota T, Ishii H, Suzuki S, et al. Relation Between **Paradoxical Decrease in High-Density Lipoprotein Cholesterol** Levels After Statin Therapy and Adverse Cardiovascular Events in Patients With Acute Myocardial Infarction. Am J Cardiol. 2014 Dec 17.
Othman RA, Myrie SB, Mymin D, et al. **Thyroid Hormone Status** in **Sitosterolemia** Is Modified by **Ezetimibe**. J Pediatr. 2017 Jun 15.
Ott BR, Daiello LA, Dahabreh IJ, Springate BA, et al. **Do Statins Impair Cognition**? A Systematic Review and Meta- analysis of Randomized Controlled Trials. J Gen Intern Med. 2015 Jan 10.
Oza A, Lu N, Schoenfeld SR, et al. Survival benefit of **statin use in ankylosing spondylitis**: a general population-based cohort study. Ann Rheum Dis. 2017 Oct;76(10):1737-1742.
Packard CJ, Ford I, et al. Plasma Lipoproteins & Apolipoproteins as Predictors of Cardiovascular Risk and Treatment Benefit in the PROspective Study of Pravastatin in the Elderly at Risk (**PROSPER**). Circulation. 2005 Nov 7
(Ford I, Bezlyak V, Stott DJ, Sattar N, Packard CJ, Perry I, Buckley BM, Jukema JW, de Craen AJ, Westendorp RG, Shepherd J. Reduced glomerular filtration rate and its association with clinical outcome in older patients at risk of vascular events: secondary analysis. (Prosper) PLoS Med. 2009 Jan 20;6(1):e16.)
Page VJ, Davis D, Zhao XB, et al. Statin Use and **Risk of Delirium** in the Critically Ill. Am J Respir Crit Care Med. 2014 Jan 13
Pagidipati NJ, Navar AM, et al. Comparison of Recommended **Eligibility for Primary Prevention Statin** Therapy Based on the **US Preventive Services Task Force Recommendations vs the ACC/AHA Guidelines**. JAMA. 2017 Apr 18;317(15):1563-1567.

Paixao AR, Ayers CR, et al. Atherosclerotic Cardiovascular Disease Prevention: A Comparison Between the **Third Adult Treatment Panel and the New 2013 Treatment of Blood Cholesterol Guidelines**. Circ Cardiovasc Qual Outcomes. 2014 Aug 5.
Palmer SC, Craig JC, Navaneethan SD, et al. Benefits and Harms of Statin Therapy for Persons With **Chronic Kidney Disease**: A Systematic Review and Meta-analysis. Ann Intern Med. 2012 Aug 21;157(4):263-75.
Palmer SC, Navaneethan SD, Craig JC, et al. HMG CoA reductase inhibitors **(statins) for dialysis** patients. Cochrane Database Syst Rev. 2013 Sep 11;9:CD004289. Statins have little or no beneficial effects on mortality or cardiovascular events and uncertain adverse effects in adults treated with dialysis despite clinically relevant reductions in serum cholesterol levels.
Palmer SC, Navaneethan SD, Craig JC, et al. HMG CoA reductase inhibitors **(statins) for kidney transplant recipients**. Cochrane Database Syst Rev. 2014 Jan 28;1:CD005019. Statins may reduce cardiovascular events in kidney transplant recipients, although treatment effects are imprecise. Statin treatment has uncertain effects on overall mortality, stroke, kidney function, and toxicity outcomes in kidney transplant recipients. Additional studies would improve our confidence in the treatment benefits and harms of statins on cardiovascular events in this clinical setting.
Pandya A, Asch DA, Volpp KG, et al. **Cost-effectiveness of Financial Incentives for Patients and Physicians to Manage Low-Density Lipoprotein Cholesterol Levels**. JAMA Netw Open. 2018;1(5):e182008.
Pandya A, Sy S, Cho S, Weinstein MC, Gaziano TA. **Cost-effectiveness of 10-year risk thresholds for initiation of statin therapy for primary prevention** of cardiovascular disease.JAMA. doi:10.1001/jama .2015.6822.
Panza GA, Taylor BA, Roman W, et al. Changes in **muscle strength** in patients with **statin myalgia**. Am J Cardiol. 2014 Oct 15;114(8):1215-6.
Papazian L, Roch A, Charles PE, et al. Effect of Statin Therapy on Mortality in Patients With **Ventilator-Associated Pneumonia**: A Randomized Clinical Trial. JAMA. 2013 Oct 9.
Pape GA, Hunt JS, Butler KL, et al. **Team-based** care approach to **cholesterol management** in diabetes mellitus: 2-year cluster randomized controlled trial. Arch Intern Med. 2011 Sep 12;171(16):1480-6.
Parish E, Bloom T, Godlee F. **Statins for people at low risk**. BMJ. 2015 Jul 21;351:h3908.
Park Y, Jeong YH, Tantry US, et al. Accelerated platelet inhibition (with **clopidogrel**) by switching from **atorvastatin to a non-CYP3A4-metabolized statin** in patients with high platelet reactivity (ACCEL-STATIN) study. Eur Heart J 2012.
Parker BA, Augeri AL, Capizzi JA, et al. Effect of **Statins** on **Creatine Kinase Levels Before and After a Marathon Run**. Am J Cardiol. 2011 Oct 27. In conclusion, our results show that **statins increase exercise-related muscle injury**.
Parker BA, Capizzi JA, Grimaldi AS, et al. The effect of statins on skeletal muscle function. (Stomp:atorvastatin 80mg increased CKs) Circulation 2012 .
Parra D, Beckey NP, et al.; Veterans Integrated Service Network & Pharmacy Benefits Management Utilization Committee. Effect of **splitting simvastatin tablets** for control of low-density lipoprotein cholesterol. Am J Cardiol. 2005 Jun 15;95(12):1481-3.
Pasternak RC, et al. American College of Cardiology; American Heart Association; National Heart, Lung and Blood Institute. ACC/AHA/NHLBI Clinical Advisory on the Use and **Safety of Statins**. Circulation. 2002 Aug 20;106(8):1024-8.
Patel AM, Shariff S, Bailey DG, et al. Statin toxicity **(Cyp3A4) from macrolide** (clarithromycin, erythromycin, azithromycin) antibiotic coprescription: A population-based cohort study. Ann Intern Med 2013; 158:869-76.
Patel JM, Snaith C, Thickett DR, et al. Randomized double-blind placebo-controlled trial of 40 mg/day of **atorvastatin** in reducing the severity of **sepsis** in ward patients (**ASEPSIS** Trial). Crit Care. 2012 Dec 11;16(6):R231.
Patel KK, Taksler GB, Hu B, Rothberg MB. **Prevalence of elevated cardiovascular risks in young adults**: a cross-sectional analysis of National Health and Nutrition Examination Surveys. Ann Intern Med. 2017. [Epub ahead of print]. doi:10.7326/M16-2052
Patel MS, Kurtzman GW, Kannan S, et al. Effect of an **automated patient dashboard using active choice and peer comparison performance feedback** to physicians on **statin prescribing: the PRESCRIBE** cluster randomized clinical trial. JAMA Netw Open. 2018;1(3): e180818.
Pattanaik S, Malhotra S, et al. Comparison of **Alternate-day Atorvastatin** Treatment to Daily Treatment in Maintaining LDL-cholesterol Targets in Patients With Variable Coronary Risk Profile. J Cardiovasc Pharmacol. 2012 May;59(5):479-84. (inferior)
Patti G, et al. Randomized Trial of Atorvastatin for Reduction of Postoperative **Atrial Fibrillation** in Patients Undergoing Cardiac Surgery. Results of the **ARMYDA-3** (Atorvastatin for Reduction of MYocardial Dysrhythmia After cardiac surgery) Study. Circulation. 2006 Sep 25; [Epub ahead of print]
Patti G, Cannon CP, Murphy SA, et al. Clinical benefit of **statin pretreatment in patients undergoing percutaneous coronary intervention**: a collaborative patient-level meta-analysis of 13 randomized studies. Circulation. 2011 Apr 19;123(15):1622-32.
Pauff BR, Jiroutek MR, Holland MA, et al. **Statin Prescribing Patterns**: An Analysis of Data From Patients With Diabetes in the National Hospital Ambulatory Medical Care Survey Outpatient Department and National Ambulatory Medical Care Survey Databases, 2005-2010. Clin Ther. 2015 Apr 11.
Pauriah M, Elder DH, Ogston S, et al. **High-potency statin and ezetimibe** use and mortality in survivors of an acute myocardial infarction: a population-based study. *Heart* 2014.
Payne JM, Barton B, Ullrich NJ, et al. Randomized placebo-controlled study of **lovastatin** in children with **neurofibromatosis** type 1. Neurology. 2016 Dec 13;87(24):2575-2584.
Pedersen TR, Faergeman O, et al. High-Dose Atorvastatin vs Usual-Dose Simvastatin for Secondary Prevention After Myocardial Infarction: The **IDEAL** Study: A Randomized Controlled Trial. JAMA. 2005 Nov 16;294(19):2437-2445. (InfoPOEMs: The intensive reduction of low-density lipoprotein (LDL) levels to well below 100 mg/dL (2.5 mmol/L) did not result in a significant reduction in the recurrence of major coronary events or all-cause mortality among patients with stable coronary artery disease. Intensive lowering is associated with an increased risk of discontinuing medication because of adverse events and significant drug costs. Aiming for an LDL of approximately 100 mg/dL (2.5 mmol/L) seems optimal for the majority of patients with stable disease. (LOE = 1b-))
Pedersen SB, Langsted A, Nordestgaard BG. Nonfasting Mild-to-Moderate **Hypertriglyceridemia and Risk of Acute Pancreatitis**. JAMA Intern Med. 2016 Nov 7.
Pedersen TM, Stokholm J, Thorsen J, et al. **Antibiotics in Pregnancy Increase Children's Risk of Otitis Media and Ventilation Tubes**. J Pediatr. 2017 Jan 11.
Pelegrin S, Galtier F, Chalançon A, et al. **Effects of Nigella sativa seeds** (black cumin) on insulin secretion and lipid profile: a pilot study in healthy volunteers. Br J Clin Pharmacol. 2019 Mar 15.
Peña JM, Aspberg S, MacFadyen J, et al. **Statin Therapy and Risk of Fracture**: Results From the **JUPITER** Randomized Clinical Trial. JAMA Intern Med. 2014 Dec 1.
Pencina KM, Thanassoulis G, Wilkins JT, et al. **Trajectories of Non-HDL Cholesterol Across Midlife**: Implications for Cardiovascular Prevention. J Am Coll Cardiol. 2019 Jul 9;74(1):70-79
Pencina MJ, Navar-Boggan AM, D'Agostino RB Sr, et al. Application of **New Cholesterol Guidelines to a Population-Based Sample**. N Engl J Med. 2014 Mar 19.
Peng C, Ding Y, Yi X, et al. **Polymorphisms in CYP450 Genes** and the Therapeutic Effect of **Atorvastatin** on Ischemic Stroke: A Retrospective Cohort Study in Chinese Population. Clin Ther.2018 Feb 27.
Peng JA, Ancock BP, Conell C, et al. **Nonutilization of Statins** in a Community-Based Population with a History of Coronary Revascularization. Clin Ther. 2015 Dec 22.
Peng YC, Lin CL, Hsu WY, et al. **Statins are associated with a reduced risk of Cholangiocarcinoma**: a population-based case-control study. Br J Clin Pharmacol. 2015 Mar 25.
Penko J, Coxson PG, et al. **Updated cost-effectiveness analysis of PCSK9 inhibitors** in patients with atherosclerotic cardiovascular disease based on the results of the FOURIER trial [online Aug 22, 2017].JAMA. doi:10.1Pennisi G, Vacante M, Russo C, Malaguarnera M. Rhabdomyolysis Induced by **Rosuvastatin and Sildenafil**. South Med J. 2010 Sep 2.
Perak AM, Ning H, de Ferranti SD, et al. Long-term risk of atherosclerotic cardiovascular disease in US adults with the **familial hypercholesterolemia** phenotype. Circulation. 2016;134:9-19.
Perak AM, Ning H, Kit BK, et al. Trends in **Levels of Lipids and Apolipoprotein B** in US Youths Aged 6 to 19 Years, 1999-2016. JAMA. 2019 May 21;321(19):1895-1905.
Pérez de Isla L, Alonso R, Mata N, et al. **Predicting Cardiovascular Events in Familial Hypercholesterolemia**: The **SAFEHEART** Registry. Circulation. 2017 Mar 8.
Perk J, De Backer G, Gohlke H, et al**. European guidelines (ESC) on cardiovascular disease** in clinical practice (version 2012). Eur Heart J2012; DOI:10.1093/eurheartj/ehs092.
Peripheral Arterial Disease: ACC/AHA Guidelines for the Management of Patients With (Lower Extremity, Renal, Mesenteric, and Abdominal Aortic); A Collaborative Report From the AAVS/SVS, SCAI, SIR, SVMB, and the ACC/AHA Task Force on Practice Guidelines http://www.acc.org/clinical/guidelines/pad/summary.pdf
Persaud N, Maguire JL, Lebovic G, et al. TARGet Kids! collaboration. Association between serum **cholesterol and eating behaviours during early childhood**: a cross-sectional study. CMAJ. 2013 Aug 6;185(11):E531-6.
Peters SAE, Colantonio LD, Zhao H, et al. **Sex differences in high-intensity statin use following myocardial infarction** in the United States. J Am Coll Cardiol 2018;71:1729–37.
Petersen LK, Christensen K, Kragstrup J. Lipid-lowering treatment to the end? A review of observational studies and RCTs on cholesterol and mortality in **80+-year olds**. Age Ageing. 2010 Nov;39(6):674-80.
Petri M A, Kiani A N, Post W, et al. **Lupus** Atherosclerosis Prevention Study (LAPS). Ann Rheum Dis 2011;70:760-765 Published Online First: 21 December 2010 doi:10.1136/ard.2010.136762. (atorvastatin not help over 2yrs)
Pfizer April/08 In a study in patients with mild-to-moderate Alzheimer's disease (AD), the addition of Lipitor (atorvastatin calcium tablets) 80 mg to Aricept® (donepezil HCl) 10 mg showed no significant differences in cognition or global function (key measures of Alzheimer's progression) compared to placebo plus Aricept 10 mg. Furthermore, no statistically significant differences were seen on various cognitive, behavioral and functional secondary endpoints. However, the Lipitor arm was not associated with greater cognitive decline than the placebo arm in this trial. The results were presented today at the annual American Academy of Neurology meeting in Chicago. The 18-month study, called Lipitor's Effect on Alzheimer's Dementia (**LEADe**), included 640 patients and is the largest statin study in Alzheimer's disease.
Phan BA, Muñoz L, Shadzi P, et al. Effects of **Niacin** on Glucose Levels, Coronary Stenosis Progression, and Clinical Events in Subjects With Normal Baseline Glucose Levels (<100 mg/dl): A Combined Analysis of the Familial Atherosclerosis Treatment Study (FATS),HDL-Atherosclerosis Treatment Study (HATS), Armed Forces Regression Study (AFREGS), and Carotid Plaque Composition by MRI During Lipid-lowering (CPC) Study. Am J Cardiol. 2012 Nov 17.
Pharmacists Letter. Treatment of Hyperlipidemia in **Children and Adolescents**. January 2012**.**
Pharmacists Letter. **Niacin Abuse** in the Attempt to Alter Urine Drugs Tests. June 2007.

Pharmacists Letter. **Cardioviva** Probiotic to Reduce Cholesterol. Nov 2013.
Phillips PS, et al.; Scripps Mercy Clinical Research Center. Statin-associated **myopathy** with **normal creatine kinase** levels. Ann Intern Med. 2002 Oct 1;137(7):581-5.
Pignone M, **Aspirin, statins, or both drugs for the primary prevention** of coronary heart disease events in men: a cost-utility analysis. Ann Intern Med. 2006 Mar 7;144(5):326-36. Summary for patients in: Ann Intern Med. 2006 Mar 7;144(5):I29. (InfoPOEMs: From the viewpoint of cost to a third-party payer, the costs of aspirin alone are reasonable in men at low-risk for coronary heart disease (CHD); the addition of a statin to aspirin therapy in these men is above what is considered to be reasonable cost for prevention. However, the combination of aspirin and a statin is cost-effective when men are at high risk (10% or above). (LOE = 2a))
Pikula A, Beiser AS, Wang J, et al. **Lipid and lipoprotein measurements and the risk of ischemic vascular events**: **Framingham** Study. Neurology. 2015 Feb 3;84(5):472-9.
PILL Collaborative Group (2011) An International Randomised Placebo-Controlled Trial of a Four-Component Combination Pill ("**Polypill"**) in People with Raised Cardiovascular Risk. PLoS ONE 6(5): e19857. doi:10.1371/journal.pone.0019857.
Pilotto A, Gallina P, Panza F, et al.Relation of **Statin Use and Mortality in Community-Dwelling Frail Older Patients** With Coronary Artery Disease. Am J Cardiol. 2016 Dec 1;118(11):1624-1630.
Pittman DG, Fenton C, Chen W et al. Relation of Statin **Nonadherence** and Treatment Intensification. Am J Cardiol. 2012 Aug 6.
Pletcher MJ, Bibbins-Domingo K, Liu K, et al. **Nonoptimal Lipids Commonly Present in Young** Adults and Coronary Calcium Later in Life: The **CARDIA** (Coronary Artery Risk Development in Young Adults) Study. Ann Intern Med. 2010 Aug 3;153(3):137-46.
Pletcher MJ, Pignone M, Earnshaw S, et al. Using the **Coronary Artery Calcium Score to Guide Statin** Therapy: A Cost-Effectiveness Analysis. Circ Cardiovasc Qual Outcomes. 2014 Mar 1;7(2):276-284.
Pokharel Y, Gosch K, et al. Practice-Level Variation in **Statin Use** Among Patients With **Diabetes**: Insights From the **PINNACLE Registry**. J Am Coll Cardiol. 2016 Sep 20;68(12):1368-9
Polgreen LA, Cook EA, Brooks JM, et al. Increased **statin** prescribing does **not lower pneumonia risk**. Clin Infect Dis. 2015 Mar 10.
Polinski JM, Schneeweiss S, Maclure M, Marshall B, Ramsden S, Dormuth C. Time series evaluation of an intervention to increase **statin tablet splitting** by general practitioners. Clin Ther. 2011 Feb;33(2):235-43.
Poynter JN, Gruber SB, Higgins PDR, et al. Statins and the risk of colorectal cancer. N Engl J Med 2005;352:2184-92. (InfoPOEMs: This observational study found an association between statin use and a reduced risk of colorectal cancer. Large randomized controlled trials are needed to confirm this potential benefit before we begin recommending statins to our patients for this indication, given the relatively small absolute magnitude of benefit, the cost, and the findings of increased risk of cancer in some previous clinical trials. (LOE = 3b))
Pradhan AD, Aday AW, Rose LM, et al. **Residual Inflammatory Risk on Treatment With PCSK9 Inhibition and Statin Therapy**. Circulation. 2018 Jul 10;138(2):141-149.
Prasad V. **Statins, primary prevention, and overall mortality**. Ann Intern Med. 2014 Jun 17;160(12):867-9.
Preiss D, Seshasai SR, Welsh P, et al. Risk of **incident diabetes with intensive-dose compared with moderate-dose statin** therapy. JAMA 2011; 305:2556-2564. (New onset diabetes NNH=498, Cardiovascular events NNT=155 per year)
Preiss D, Tikkanen MJ, Welsh P, et al. Lipid-modifying therapies and risk of **pancreatitis**: A meta-analysis. JAMA 2012; 308:804-811.
Preiss D, Lloyd SM, Ford I, et al. **Metformin for non-diabetic** patients with coronary heart disease (the **CAMERA** study): A randomised controlled trial.*Lancet Diabetes Endocrinol*2013.
Preiss D, Campbell RT, Murray HM, et al. The effect of **statin therapy on heart failure** events: A collaborative meta-analysis of unpublished data from major randomized trials. *Eur Heart J* 2015.
Previsdomini M, Graziano E, Decosterd L, et al. **Severe rosuvastatin accumulation with rhabdomyolysis** due to drug interactions and low cardiac output syndrome. Br J Clin Pharmacol. 2019 May 3.
Puri R, Nissen SE, Libby P, et al. **C-Reactive Protein**, but not Low-Density Lipoprotein Cholesterol Levels, Associate With Coronary Atheroma Regression and Cardiovascular Events After Maximally Intensive Statin Therapy. Circulation. 2013 Nov 26;128(22):2395-403.
Puri R, Nissen SE, Shao M, et al. Impact of **Baseline Lipoprotein and C-Reactive Protein Levels** on Coronary Atheroma Regression Following High-Intensity Statin Therapy. Am J Cardiol. 2014 Aug 27.
Pursnani A;Massaro JM;D`Agostino RB Sr;O`Donnell C. **Guideline**-Based **Statin Eligibility**, **Cancer** Events, and **Noncardiovascular Mortality** in the Framingham Heart Study. J Clin Oncol. 2017 Jul 12:JCO2016713594.
Pursnani A, Massaro JM, D'Agostino RB Sr, et al. **Guideline-based statin eligibility**, coronary artery calcification, and cardiovascular events. JAMA. doi:10.1001/jama .2015.7515.
Qamar A, Giugliano RP, Bohula EA, et al. Biomarkers and Clinical Cardiovascular Outcomes With **Ezetimibe in the IMPROVE-IT Trial**. J Am Coll Cardiol. 2019 Aug 27;74(8):1057-1068.
Qamar A, Giugliano RP, Keech AC, et al. **Interindividual Variation in Low-Density Lipoprotein Cholesterol Level Reduction With Evolocumab**: An Analysis of FOURIER Trial Data. JAMA Cardiol. 2018 Dec 12.
Qaseem A, Hopkins RH, Sweet DE, et al. **Screening, Monitoring, and Treatment of Stage 1 to 3 Chronic Kidney Disease**: A Clinical Practice Guideline From the Clinical Guidelines Committee of the American College of Physicians (**ACP**). Ann Intern Med. 2013 Oct 22.
Raal FJ, Pilcher GJ, Panz VR, et al. Reduction in mortality in subjects with **homozygous familial hypercholesterolemia** associated with advances in lipid-lowering therapy. Circulation. 2011 Nov 15;124(20):2202-7.
Raal F, Scott R, Somaratne R, et al. Low-density lipoprotein cholesterol-lowering effects of **AMG 145**, a monoclonal antibody to proprotein convertase subtilisin/kexin type 9 serine protease in patients with heterozygous familial hypercholesterolemia: The Reduction of LDL-C with **PCSK9** Inhibition in Heterozygous Familial Hypercholesterolemia Disorder (**RUTHERFORD**) randomized trial.Circulation 2012.
Raal FJ, Honorpour N, Blom, et al. Inhibition of PCSK9 with **evolocumab** in **homozygous familial hypercholesterolemia** (**TESLA Part B**): A randomized, double-blind, placebo-controlled trial. Lancet 2014; DOI:10.1016/S0140-6736(14)61374-X.
Raal FJ, Stein EA, Dufour R, et al. PCSK9 inhibition with **evolocumab** (AMG145) in **heterozygous familial hypercholesterolemia** (**RUTHERFORD**-2): A randomized, double-blind, placebo-controlled trial. Lancet 2014.
Raal FJ, Blom DJ. **Anacetrapib** in familial hypercholesterolaemia: pros and cons. Lancet. 2015 Mar 2.
Rabar S, Harker M, O'Flynn N, et al; Guideline Development Group. **Lipid modification** and cardiovascular risk assessment for the primary and secondary prevention of cardiovascular disease: summary of updated **NICE** guidance. BMJ. 2014 Jul 17;349:g4356.
Rader DJ, Hovingh GK. Lipids and cardiovascular disease 2: **HDL and cardiovascular disease**. Lancet 2014; 384: 618–25.
Rahalkar AR, Ban MR, Hegele RA. Clinical equivalence of **proprietary and generic atorvastatin** in lipid clinic patients. Can J Cardiol. 2013 Apr;29(4):418-22.
Ramos R, Comas-Cufí M, Martí-Lluch R, et al. **Statins for primary prevention of cardiovascular events and mortality in old and very old adults with and without type 2 diabetes**: retrospective cohort study. BMJ. 2018 Sep 5;362:k3359.
Ray Kausik K.; Seshasai Sreenivasa Rao Kondapally; Erqou Sebhat; et al. Statins and All-Cause Mortality in High-Risk **Primary Prevention**: A Meta-analysis of 11 Randomized Controlled Trials Involving 65 229 Participants. Arch
Ray KK, Colhoun HM, Szarek M, et al. **Effects of alirocumab** on cardiovascular and metabolic outcomes after acute coronary syndrome in patients with or without diabetes: a prespecified analysis of the ODYSSEY OUTCOMES randomised controlled trial. Lancet Diabetes Endocrinol. 2019 Jul 1.
Ray KK, Corral P, Morales E, Nicholls SJ. Pharmacological lipid-modification **therapies for prevention of ischaemic heart disease**: current and future options. Lancet. 2019 Aug 24;394(10199):697-708
Ray KK, Ginsberg HN, Davidson MH, et al. Reductions in atherogenic lipids and major cardiovascular events: A pooled analysis of 10 ODYSSEY trials comparing **alirocumab** to control. *Circulation* 2016.
Ray KK, Leiter LA, et al. Alirocumab vs usual lipid-lowering care as add-on to statin therapy in individuals with **type 2 diabetes and mixed dyslipidaemia**: The ODYSSEY DM-DYSLIPIDEMIA randomized trial. Diabetes Obes Metab. 2018 Feb 13.
Ray KK, Stoekenbroek RM, Kallend D, et al. Effect of an **siRNA Therapeutic Targeting PCSK9 on Atherogenic Lipoproteins**: Pre-Specified Secondary End Points in **ORION 1**. Circulation. 2018 May 7.
Ray KK, Stoekenbroek RM, Kallend D, et al. Effect of an **siRNA Therapeutic Targeting PCSK9 on Atherogenic Lipoproteins**: Pre-Specified Secondary End Points in ORION 1. Circulation. 2018 May 7.
Ray KK, Stoekenbroek RM, Kallend D et al. Effect of 1 or 2 Doses of **Inclisiran on Low-Density Lipoprotein Cholesterol Levels**: One-Year Follow-up of the ORION-1 Randomized Clinical Trial. JAMA Cardiol. 2019 Sep 25.
Raymakers AJ, Sadatsafavi M, Sin DD, De Vera MA, Lynd LD. The impact of statin use on **all-cause mortality in patients with COPD**: a population based cohort study. Chest. 2017 Feb 12.
Raymakers AJN, Sadatsafavi M, Sin DD, De Vera MA, Lynd LD. The Impact of **Statin Drug Use on All-Cause Mortality in Patients With COPD**: A Population-Based Cohort Study. Chest. 2017 Sep;152(3):486-493.
Raymond C, Cho L, Rocco M, et al. **New cholesterol guidelines**: worth the wait? Cleve Clin J Med. 2014 Jan;81(1):11-9.
Reddy A, Huseman TL, Canamucio A, et al. **Patient and Partner Feedback** Reports to Improve **Statin Medication Adherence**: A Randomized Control Trial. J Gen Intern Med. 2016 Sep 9.
Reddy KJ, Singh M, Batsell RR, et al. Efficacy of combination **drug pulse therapy** in maintaining lipid levels in patients intolerant of daily statin use. J Clin Hypertens (Greenwich). 2009 Dec;11(12):766-8.
Reddy P, Ellington D, Zhu Y, et al. Serum concentrations and clinical effects of **atorvastatin in patients taking grapefruit juice** daily. Br J Clin Pharmacol. 2011 Apr 18. doi: 10.1111/j.1365-2125.2011.03996.x. (no major effect)
Redelmeier DA, Manzoor F, Thiruchelvam D. Association between **statin use and risk of dementia after a concussion** [online May 20, 2019]. JAMA Neurol. doi:10.1001/jamaneurol. 2019.1148
Redelmeier DA, Thiruchelvam D, Daneman N. **Delirium** after elective surgery among elderly patients taking statins. CMAJ. 2008 Sep 23;179(7):645-52.
Restrepo BJ, Rieger M. Denmark's Policy on **Artificial Trans Fat** and Cardiovascular Disease. Am J Prev Med. 2015 Aug 26.
Riaz H, Khan AR, Khan MS, et al. Meta-analysis of Placebo-Controlled Randomized Controlled Trials on the Prevalence of **Statin Intolerance**. Am J Cardiol. 2017 Jun 13.
Richardson K, Schoen M, French B, et al. **Statins and cognitive function**: a systematic review. Ann Intern Med. 2013 Nov 19;159(10):688-97.
Ridker PM, Pradhan A, MacFadyen JG et al. Cardiovascular benefits and **diabetes risks** of statin therapy in primary prevention: an analysis from the JUPITER trial. Lancet. 2012 Aug 11;380(9841):565-71.
Ridker PM, Cook NR. **Statins: new American guidelines** for prevention of cardiovascular disease. Lancet. 2013 Nov 30;382(9907):1762-5.

Ridker PM. Lipids and cardiovascular disease 1: **LDL cholesterol: controversies and future therapeutic directions** . Lancet 2014; 384: 607–17.

Ridker PM, Cook NR. The **Pooled Cohort Equations 3 Years On**: Building a Stronger Foundation. Circulation. 2016 Dec 6;134(23):1789-1791.

Ridker PM, Lonn E, Paynter NP, et al. **Primary Prevention** With Statin Therapy in the **Elderly**: New Meta-Analyses from the Contemporary **JUPITER** and **HOPE-3** Randomized Trials. Circulation. 2017 Apr 6.

Ridker PM. Mortality Differences Associated with Treatment Responses in **CANTOS and FOURIER**: Insights and Implications. Circulation. 2017 Dec 22.

Shah RV, Spahillari A, Mwasongwe S, et al. **Subclinical Atherosclerosis, Statin Eligibility**, and Outcomes in African American Individuals: The **Jackson Heart Study**. JAMA Cardiol. 2017 Mar 18.

Toth PP, Descamps O, Genest J, et al. Pooled Safety Analysis of **Evolocumab** in Over 6000 Patients From Double-Blind and Open-Label Extension Studies. Circulation. 2017 May 9;135(19):1819-1831

Riediger ND, Clara I. Prevalence of **metabolic syndrome in the Canadian** adult population. CMAJ 2011; DOI:10.1503/cmaj.110070.

Rist PM, Buring JE, Ridker PM, et al. **Lipid levels and the risk of hemorrhagic stroke among women**. Neurology. 2019 May 7;92(19):e2286-e2294.

Robinson JG. **Starting Primary Prevention Earlier With Statins.** Am J Cardiol. 2014 Aug 13.

Robinson JG, Farnier M, Krempf M, et al. Efficacy and safety of **alirocumab** in reducing lipids and cardiovascular events. (**ODYSSEY LONG TERM**) N Engl J Med. DOI: 10.1056/NEJMoa1501031.

Robinson JG, et al. Safety of Very Low Low-Density Lipoprotein Cholesterol Levels With **Alirocumab**: Pooled Data From Randomized Trials. J Am Coll Cardiol. 2017 Feb 7;69(5):471-482.

Robinson JG, Rosenson RS, Farnier M, et al. Safety of Very Low Low-Density Lipoprotein Cholesterol Levels With **Alirocumab**: Pooled Data From Randomized Trials. J Am Coll Cardiol. 2017 Feb 7;69(5):471-482.

Rocco MB. **Statins and diabetes risk**: Fact, fiction, and clinical implications. Cleve Clin J Med. 2012 Dec;79(12):883-93.

Rodriguez F, Olufade T, Heithoff K, et al. Frequency of **High-Risk Patients Not Receiving High-Potency Statin** (from a Large Managed Care Database). Am J Cardiol. 2015 Jan 15;115(2):190-5.

Rodriguez F, Maron DJ, Knowles JW, Virani et al. Association Between **Intensity of Statin Therapy and Mortality** in Patients With Atherosclerotic Cardiovascular Disease. JAMA Cardiol. 2016 Nov 9.

Rodriguez F, Maron DJ, Knowles JW, Virani SS, Lin S, Heidenreich PA. Association of **statin adherence with mortality** in patients with atherosclerotic cardiovascular disease [online Feb 13, 2019]). JAMA Cardiol. doi:10.1001/jamacardio.2018.4936

Roever L, Biondi-Zoccai G, Rao SV. **Lipid-Lowering** Therapy in Patients With **High Cardiovascular Risk**: **Dose or Combination**? Clin Ther. 2017 Feb 9.

Roselle H et al. Symptomatic hepatitis associated with the use of herbal **red yeast rice**. Ann Intern Med 2008; 149:516.

Rosenson R, Kent S, Brown T, et al. **Underutilization of high-intensity statin** therapy after hospitalization for coronary heart disease. *J Am Coll Cardiol* 2015; 65:270-7.

Rosenson RS, Colantonio LD, Burkholder GA, Chen L, Muntner P. Trends in Utilization of Statin Therapy and Contraindicated **Statin Use in HIV—Infected Adults Treated With Antiretroviral Therapy** From 2007 Through 2015. J Am Heart Assoc. 2018 Dec 18;7(24):e010345.

Rosenson RS, Farkouh ME, Mefford M, et al. **Trends in use of high-intensity statin therapy after myocardial infarction**, 2011 to 2014. J Am Coll Cardiol 2017;69:2696–706.

Roshandel G, Khoshnia M, Poustchi H, et al. Effectiveness of **polypill for primary and secondary prevention of cardiovascular diseases (PolyIran)**: a pragmatic, cluster-randomised trial. Lancet. 2019 Aug 24;394(10199):672-683.

Rosinger A, Carroll MD, Lacher D, et al. **Trends in Total Cholesterol, Triglycerides, and Low-Density Lipoprotein in US Adults**, 1999-2014. JAMA Cardiol. 2016 Nov 30.

Ross JS, Frazee SG, Garavaglia SB, et al. **Trends in Use of Ezetimibe After the ENHANCE** Trial, 2007 Through 2010. JAMA Intern Med. 2014 Jul 28.

Rossebø AB, Pedersen TR, Boman K, et al. the **SEAS** Investigators. Intensive Lipid Lowering with Simvastatin and Ezetimibe in Aortic Stenosis. N Engl J Med. 2008 Sep 2. [Epub ahead of print] (n=1873 52.2months) Simvastatin and ezetimibe did not reduce the composite outcome of combined aortic-valve events and ischemic events in patients with aortic stenosis. Such therapy reduced the incidence of ischemic cardiovascular events but not events related to aortic-valve stenosis. Cancer occurred more frequently in the simvastatin-ezetimibe group (105 vs. 70, P=0.01).

Rossignol M, Labrecque M, Cauchon M, et al. **Number of patients needed to prescribe statins in primary cardiovascular prevention**: mirage and reality. Fam Pract. 2018 Jul 23;35(4):376-382.

Roth EM, Bujas-Bobanovic M, Louie MJ, et al. Patient and Physician Perspectives on Mode of Administration of the PCSK9 Monoclonal Antibody **Alirocumab**, an Injectable Medication to Lower LDL-C Levels. Clin Ther. 2015 Aug 14.

Roth EM, Goldberg AC, Catapano AL, et al. Antidrug Antibodies in Patients Treated with **Alirocumab**. N Engl J Med. 2017 Mar 17.

Russo MW, Hoofnagle JH, Gu J, et al. Spectrum of **statin hepatotoxicity**: experience of the drug-induced liver injury network. Hepatology. 2014 Aug;60(2):679-86.

Ryan A, Heath S, Cook P. **Managing dyslipidaemia for the primary prevention** of cardiovascular disease. BMJ. 2018 Mar 23;360:k946.

Ryan A, Heath S, Cook P. **Dyslipidaemia and cardiovascular risk**. BMJ. 2018;360:k835

Sabatine MS, Giugliano RP. Low-Density Lipoprotein Cholesterol Treatment in the Proprotein Convertase Subtilisin/Kexin Type 9 Inhibitor Era: Getting Back on Target. JAMA Cardiol. 2017 Aug 2.

Sabatine MS, Giugliano RP, Wiviott SD, et al. Efficacy and safety of **evolocumab** in reducing lipids and cardiovascular events. (**OSLER**) N Engl J Med. DOI: 10.1056/NEJMoa1500858.

Sabatine MS, Leiter LA, Wiviott SD, et al. Cardiovascular safety and efficacy of the **PCSK9** inhibitor **evolocumab** in patients with and without diabetes and the effect of evolocumab on glycaemia and risk of new-onset diabetes: a prespecified analysis of the **FOURIER** randomised controlled trial. Lancet Diabetes Endocrinol 2017; online Sept 14.

Sabatine MS, Wiviott SD, Im K, et al. **Efficacy and safety of further lowering of low-density lipoprotein cholesterol in patients starting with very low levels**: a meta-analysis [August 1, 2018]. JAMA Cardiol. doi:10.1001/jamacardio.2018.2258

Sabatine MS, De Ferrari GM, Giugliano RP, et al. **Clinical Benefit of Evolocumab by Severity and Extent of Coronary Artery Disease**: An Analysis from FOURIER. Circulation. 2018 Apr 6.

Sahebkar A, Giua R, Pedone C. Impact of **Statin** Therapy on **Plasma Leptin Concentrations**: A Systematic Review and Meta-Analysis of Randomized Placebo-Controlled Trials. Br J Clin Pharmacol. 2016 Aug 11.

Saliba W, Rennert HS, Barnett-Griness O, et al. Association of **statin use with spontaneous intracerebral hemorrhage**: a cohort study. Neurology 2018;91:e400–e409.

Samuel S. Gidding. **Why cholesterol testing in children and adolescents matters**. JAMA Cardiol 2016.

Sandhu S, Wiebe N, Fried LF, Tonelli M. Statins for improving **renal outcomes**: a meta-analysis. J Am Soc Nephrol. 2006 Jul;17(7):2006-16. Epub 2006 Jun 8.

Sando KR, Michelle Knight P. **Nonstatin Therapies for Management of Dyslipidemia**: A Review. Clin Ther. 2015 Sep 24.

Sarma A, Cannon CP, de Lemos J, et al. The incidence of **kidney injury for patients treated with a high-potency versus moderate-potency statin** regimen after an acute coronary syndrome. J Am Heart Assoc. 2014 May 1 001/jama.2017.9924.

Sathiyakumar V, Park J, Golozar A, et al. **Fasting Versus Nonfasting** and Low-Density Lipoprotein Cholesterol Accuracy. Circulation. 2018 Jan 2;137(1):10-19.

Sathiyakumar V, Park J, Quispe R, et al. Impact of Novel **Low-Density Lipoprotein-Cholesterol Assessment on the Utility of Secondary Non-High-Density Lipoprotein-C and Apolipoprotein B Targets** in Selected Worldwide Dyslipidemia Guidelines. Circulation. 2018 Jul 17;138(3):244-254.

Sattar N, Toth PP, Blom DJ, et al. Effect of the Proprotein Convertase Subtilisin/Kexin Type 9 Inhibitor **Evolocumab** on Glycemia, Body Weight, and New-Onset Diabetes Mellitus.Am J Cardiol. 2017 Nov 1;120(9):1521-1527.

Schandelmaier S, Briel M, Saccilotto R, Olu KK, Arpagaus A, Hemkens LG, Nordmann AJ. **Niacin for primary and secondary prevention of cardiovascular events**. Cochrane Database of Systematic Reviews 2017, Issue 6. Art. No.: CD009744.
Moderate- to high-quality evidence suggests that niacin does not reduce mortality, cardiovascular mortality, non-cardiovascular mortality, the number of fatal or non-fatal myocardial infarctions, nor the number of fatal or non-fatal strokes but is associated with side effects. Benefits from niacin therapy in the prevention of cardiovascular disease events are unlikely.

Scheitz JF, MacIsaac RL, Abdul-Rahim AH, et al. **Statins and risk of poststroke hemorrhagic complications**. Neurology. 2016 Apr 26;86(17):1590-6.

Schiele F, Kristensen SD. The **anti-statin lobby strikes again**: time to set the record straight. Eur Heart J. 2018 Feb 1;39(5):335-336.

Schoenfeld SR, Lu L, Rai SK, et al. **Statin use and mortality in rheumatoid arthritis**: a general population-based cohort study. Ann Rheum Dis. 2016 Jul;75(7):1315-20.

Schwartz GG, Abt M, Bao W, et al. **Fasting triglycerides** predict recurrent ischemic events in patients with **acute coronary syndrome treated with statins**. J Am Coll Cardiol. 2015 Jun 2;65(21):2267-75.

Schwartz GG, Ballantyne CM, Barter PJ, et al. Association of **Lipoprotein(a)** With Risk of Recurrent Ischemic Events Following **Acute Coronary Syndrome**: Analysis of the dal-Outcomes Randomized Clinical Trial. JAMA Cardiol. 2017 Oct 25.

Schwartz GG, Steg PG, Szarek M, et al; ODYSSEY OUTCOMES Committees and Investigators. **Alirocumab and Cardiovascular Outcomes** after Acute Coronary Syndrome. N Engl J Med. 2018 Nov 7.

Schwing W, Hustak L, Taylor HC. Paradoxical Severe Decrease in HDL Cholesterol Due to **Rosiglitazone-Fenofibrate** Interaction. Endocr Pract. 2010 Jan 9:1-17. [Epub ahead of print]

Schulman KA, Balu S, Reed SD. **Specialty Pharmaceuticals for Hyperlipidemia** -Impact on Insurance Premiums. N Engl J Med. 2015 Oct 7.

Scranton RE, Young M, Lawler E, et al. Statin use and fracture risk: study of a US veterans population. Arch Intern Med. 2005 Sep 26;165(17):2007-12.

Seckl MJ, Ottensmeier CH, et al. Multicenter, Phase III, Randomized, Double-Blind, Placebo-Controlled Trial of **Pravastatin Added to First-Line Standard Chemotherapy in Small-Cell Lung Cancer (LUNGSTAR)**. J Clin Oncol. 2017 Feb 27:JCO2016697391

Serban M-C, Colantonio LD, Manthripragada AD, et al. **Statin intolerance** and risk of coronary heart events and all-cause mortality following myocardial infarction. J Am Coll Cardiol 2017;69:1386–95

Shah RV, Rubenfire M, Brook RD, et al. Heterogeneity in **statin indications within the 2013 american college of cardiology**/american heart association **guidelines**. Am J Cardiol. 2015 Jan 1;115(1):27-33.

Shah RV, Spahillari A, Mwasongwe S, et al. **Subclinical Atherosclerosis, Statin Eligibility**, and Outcomes in African American Individuals: The **Jackson Heart Study**. JAMA Cardiol. 2017 Mar 18.

Shantha GPS, Ramos J, Thomas-Hemak L, Pancholy SB. Association of **vitamin D** and incident statin induced myalgia - a retrospective cohort study. PLoS One. 2014;9:e88877.

Shapiro MD, Miles J, Tavori H, et al. **Diagnosing Resistance to a Proprotein Convertase Subtilisin/Kexin Type 9 Inhibitor**. Ann Intern Med. 2018 Mar 6;168(5):376-379.

Sharma M., Ansari M. T., Abou-Setta A. M., Systematic Review: Comparative Effectiveness and Harms of **Combinations of Lipid-Modifying Agents** and **High-Dose** Statin Monotherapy. *Ann Intern Med* 2009; 60520-144.

Sharma M, Ansari MT, Abou-Setta AM, et al. Systematic review: comparative **effectiveness and harms of combination therapy and monotherapy** for dyslipidemia. Ann Intern Med. 2009 Nov 3;151(9):622-30.

Shaya GE, Juraschek SP, Feldman DI, et al. Relation of Exercise Capacity to Risk of Development of **Diabetes** in Patients on **Statin** Therapy (the Henry Ford Exercise Testing Project). Am J Cardiol. 2017 Jun 15.

Shepherd J, Breazna A, Deedwania PC, et al; Treating to New Targets Steering Committee and Investigators. Relation Between **Change in Renal Function** and Cardiovascular Outcomes in **Atorvastatin**-Treated Patients (from the Treating to New Targets [**TNT**] Study). Am J Cardiol. 2016 Apr 15;117(8):1199-205.

Shewmon DA, Craig JM. **Creatine supplementation prevents statin-induced muscle toxicity**. Ann Intern Med. 2010 Nov 16;153(10):690-2. (n=12

Shin JY, Eberg M, Ernst P, Filion KB. **Statin Potency** and the Risk of Hospitalization for Community-Acquired **Pneumonia**. Br J Clin Pharmacol. 2016 Dec 9.

Shin S et al. Impact of intensive **LDL cholesterol lowering** on coronary artery **atherosclerosis progression**: A serial CT **angiography** study. JACC Cardiovasc Imaging 2016 Oct 19.

Shiu JR, Pearson GJ, Charrois TL, et al. Frequency of **Intensive Statin Therapy** in Patients With **Acute Coronary Syndrome** Admitted to a Tertiary Care Center. Am J Cardiol. 2011 Oct 6.

Shrank WH, Barlow JF, Brennan TA. New Therapies in the Treatment of High Cholesterol: An **Argument to Return to Goal-Based Lipid Guidelines**. JAMA. 2015 Aug 10

Shun-Shin MJ, Francis DP. Is this **muscle pain caused by my statin**? BMJ. 2017 Jun 23;357:j3030.

Siddiqui MK, Maroteau C, Veluchamy A, et al; **PREDICTION-ADR** Consortium. A **common missense variant of LILRB5 is associated with statin intolerance and myalgia**. Eur Heart J. 2017 Dec 21;38(48):3569-3575.

Siepmann T, Heinke D, Kepplinger J, et al. **Interaction of clopidogrel and statins** in secondary prevention after cerebral ischemia – a randomized, double-blind, double-dummy crossover-study. Br J Clin Pharmacol. 2014 May 6.

Silverman MG, Ference BA, Im K, et a. Association Between **Lowering LDL-C and Cardiovascular Risk Reduction** Among Different Therapeutic Interventions: A Systematic Review and Meta-analysis. JAMA. 2016 Sep 27;316(12):1289-1297.

Simard C, Poirier P. **Ezetimibe-associated myopathy** in monotherapy and in combination with a 3-hydroxy-3-methylglutaryl coenzyme A reductase inhibitor. Can J Cardiol. 2006 Feb;22(2):141-4.

Simes J, Robledo KP, White HD, et al . **D-dimer** Predicts Long-Term Cause-Specific Mortality, Cardiovascular Events and Cancer in Stable Coronary Heart Disease Patients: The **LIPID** Study. Circulation. 2018 Jan 24.

Simon TG, Duberg AS, Aleman S, et al. Lipophilic Statins and **Risk for Hepatocellular Carcinoma and Death** in Patients With Chronic Viral Hepatitis: Results From a Nationwide Swedish Population. Ann Intern Med. 2019 Aug 20.

Singh A et al. **Familial hypercholesterolemia among young adults with myocardial infarction**. J Am Coll Cardiol 2019 May 21; 73:2439.

Singh A, Gupta A, Collins BL, et al. **Familial Hypercholesterolemia** Among Young Adults With Myocardial Infarction. J Am Coll Cardiol. 2019 May 21;73(19):2439-2450.

Sinyavskaya L, Gauthier S, Renoux C, et al. Comparative effect of **statins on the risk of incident Alzheimer disease**. Neurology. 2017 Dec 15.

Sjolander M, Eriksson M, Glader E. **Inequalitites in medication adherence** to **statin treatment after stroke**: A nationwide observational study.2016(0);0:1-7

Skeldon SC, Carleton B, Brophy JM, et al. **Statin medications and the risk of gynecomastia**. Clin Endocrinol (Oxf). 2018 Oct;89(4):470-473.

Skulas-Ray AC, Wilson PWF, Harris WS, et al. **Omega-3 Fatty Acids for the Management of Hypertriglyceridemia**: A Science Advisory From the American Heart Association. Circulation. 2019 Aug 19:CIR0000000000000709.

Smit RAJ, et al. Higher visit-to-visit **low-density lipoprotein** cholesterol variability is associated with lower cognitive performance, lower cerebral blood flow, and greater white matter hyperintensity load in older subjects. Circulation 2016; 134:212-221.

Smith SC Jr. Defining Potential Use of Nonstatin Therapies to Lower Blood Cholesterol Levels. JAMA Cardiol. 2017 Aug 2

Smith SC Jr, et al. AHA/ACC guidelines for **secondary prevention** for patients with coronary and other atherosclerotic vascular disease: 2006 update: endorsed by the National Heart, Lung, and Blood Institute. Circulation. 2006 May 16;113(19):2363-72. http://circ.ahajournals.org/cgi/reprint/113/19/2363

Snipelisky D, Stancampiano F. An 85-year-old with **muscle pain**. (**simvastatin**) Cleve Clin J Med. 2014 Jan;81(1):27-30

Soran H, Schofield JD, Durrington PN. **Cholesterol, not just cardiovascular risk, is important** in deciding who should receive statin treatment. Eur Heart J. 2015 Nov 14;36(43):2975-83.

Sorensen PS, Lycke J, Erälinna JP, et al; for the **SIMCOMBIN** study investigators. **Simvastatin** as add-on therapy to interferon beta-1a for relapsing-remitting multiple sclerosis (SIMCOMBIN): a placebo-controlled randomised phase 4 trial. Lancet Neurol. 2011 Jul 8. (We found no beneficial effect of simvastatin)

Sousa-Uva M, Head SJ, Milojevic M, et al; Document Reviewers. **2017 EACTS Guidelines on perioperative medication in adult cardiac surgery**. Eur J Cardiothorac Surg. 2017 Oct 6.

Sparrow RT, Khan AM, Ferreira-Legere LE, et al. Effectiveness of Interventions Aimed at **Increasing Statin-Prescribing Rates** in Primary Cardiovascular Disease Prevention: A Systematic Review of Randomized Clinical Trials. JAMA Cardiol. 2019 Aug 28.

Spencer FA, et al.; National Registry of MI. Early **withdrawal of statin** therapy in patients with non-ST-segment elevation myocardial infarction: national registry of myocardial infarction. Arch Intern Med. 2004 Oct 25;164(19):2162-8.

Steen DL, Khan I, Ansell D, et al. **Retrospective examination of lipid-lowering treatment patterns in a real-world high-risk cohort in the UK** in 2014: comparison with the National Institute for Health and Care Excellence (NICE) 2014 lipid modification guidelines. BMJ Open. 2017 Feb 17;7(2):e013255.

Steg PG, Szarek M, Bhatt DL, et al. **Effect of Alirocumab** on Mortality After Acute Coronary Syndromes. Circulation. 2019 Jul 23;140(4):e171.

Stein EA, Dufour R, Gagne C, et al. Apolipoprotein B synthesis inhibition with **mipomersen** in heterozygous familial hypercholesterolemia: results of a randomized, double-blind, placebo-controlled trial to assess efficacy and safety as add-on therapy in patients with coronary artery disease. Circulation. 2012 Nov 6;126(19):2283-92.

Stein LH, Berger J, Tranquilli M, et al. Effect of Statin Drugs on **Thoracic Aortic Aneurysms**. Am J Cardiol. 2013 Oct 15;112(8):1240-1245.

Stein EA;Dann EJ;Wiegman A;Skovby F;Gaudet D;Sokal. Efficacy of **Rosuvastatin** in Children With **Homozygous Familial Hypercholesterolemia** and Association With Underlying Genetic Mutations. J Am Coll Cardiol. 2017 Aug 29;70(9):1162-1170.

Steiner MJ, Skinner AC, Perrin EM. **Fasting might not be necessary before lipid screening**: A nationally representative cross-sectional study. **Pediatrics** 2011; DOI:10.1542/peds.2011-0844.

Stenehjem K, Herren D, Pulver G, et al. Association of **Frequency of Lipid Testing With Changes in Lipid-Lowering Therapy**. JAMA Intern Med. 2017 Aug 28.

Stine NW, Chokshi DA. **Elimination of lipid levels from quality measures**: implications and alternatives. JAMA. 2014 Nov 19;312(19):1971-2.

Stoekenbroek RM, Boekholdt SM, Fayyad R, et al. **High-dose atorvastatin is superior to moderate-dose simvastatin** in preventing peripheral arterial disease. Heart. 2015 Jan 16.

Stone NJ, Robinson JG. **Potential for Net Benefit** Should Guide Preventive Therapy. Circulation. 2017 Feb 14;135(7):630-632.

Strandberg TE, et al. **Multifactorial intervention** to prevent recurrent cardiovascular events in patients **75 years or older**: the Drugs and Evidence-Based Medicine in the Elderly (**DEBATE**) study: a randomized, controlled trial. Am Heart J. 2006 Sep;152(3):585-92. (InfoPOEMs: First, the good news: Researchers were able, without unusual effort, to apply evidence-based guidelines to older elderly patients with cardiovascular disease (CVD) and achieve goal blood pressure and cholesterol levels in the majority. Now, the bad news: These interventions did not decrease the likelihood of the patients experiencing a cardiovascular problem over the next 3.4 years. The treated patients did not live any longer over this period, and the treatment did not delay deaths. (LOE = 1b)))

Strandberg TE, Kolehmainen L, Vuorio A. Evaluation and treatment of **older patients with hypercholesterolemia**: a clinical review. JAMA. 2014 Sep17;312(11):1136-44.

Streja E, Gosmanova EO, Molnar MZ, et al. Association of **continuation of statin therapy initiated before transition to chronic dialysis therapy** with mortality after dialysis initiation. JAMA Netw Open. 2018;1(6):e182311.

Stroes E, Colquhoun D, et al; **GAUSS-2** Investigators. Anti-PCSK9 Antibody Effectively Lowers Cholesterol in Patients with Statin Intolerance: GAUSS-2 Randomized, Placebo-controlled Phase 3 Clinical Trial of **Evolocumab**. J Am Coll Cardiol. 2014 Mar 25.

Stroes ES, Thompson PD, Corsini A, et al. European Atherosclerosis Society Consensus Panel. **Statin-associated muscle symptoms**: impact on statin therapy-**European** Atherosclerosis Society Consensus Panel Statement on Assessment, Aetiology and Management. Eur Heart J. 2015 May 1;36(17):1012-22.

Strom BL, Schinnar R, Karlawish J, et al. **Statin Therapy and Risk of Acute Memory Impairment**. JAMA Intern Med. 2015 Jun 8.

Sugerman DT, Livingston EH, Lynm C. JAMA **patient page. Statins**. JAMA. 2013 Apr 3;309(13):1419.

Sugiyama T, Tsugawa Y, Tseng C-H, et al. Different time trends of **caloric and fat intake between statin users** and nonusers among US adults: gluttony in the time of statins? online April 24, 2014]. JAMA Intern Med. doi:10.1001/jamainternmed.2014.1927.

Sun YE, Wang W, Qin J. **Anti-hyperlipidemia of garlic by reducing the level of total cholesterol and low-density lipoprotein**: A meta-analysis. Medicine (Baltimore). 2018 May;97(18):e0255.

Sullivan D, Olsson A G, Scott R, et al. Effect of a monoclonal antibody to **PCSK9** on low-density lipoprotein cholesterol levels in statin-intolerant patients. The **GAUSS** randomized trial. JAMA 2012. (**AMG145**)

Svendsen TK, Hansen PN, García Rodríguez LA, et al. **Statins and polyneuropathy** revisited: Case-control study in Denmark, 1999-2013. Br J Clin Pharmacol. 2017 Apr 1.

Swerdlow DI, Preiss D, Kuchenbaecker KB, et al. **HMG-coenzyme A reductase inhibition, type 2 diabetes, and bodyweight**: evidence from genetic analysis and randomised trials. Lancet. 2014 Sep 24.

Swiger KJ, Manalac RJ, Blumenthal RS et al. **Statins and Cognition:** A Systematic Review and Meta-analysis of Short- and Long-term Cognitive Effects. Mayo Clin Proc. 2013 Sep 27.

Swindle JP, Ye X, Mallick R, et al. **Colesevelam, Ezetimibe**, and Patients With Type 2 Diabetes Mellitus: Characteristics and Clinical Outcomes From a Health Care Database. Ann Pharmacother. 2014 Apr 16;48(7):847-855.

Rader DJ, Kastelein JJ. **Lomitapide and Mipomersen**: Two First-in-Class Drugs for Reducing Low-Density Lipoprotein Cholesterol in Patients With Homozygous Familial Hypercholesterolemia. Circulation. 2014 Mar 4;129(9):1022-32.

Rahimi Kazem, Emberson Jonathan, McGale Paul, et al., PWM is acting on behalf of the PROSPER Executive. Effect of **statins on atrial fibrillation**: collaborative meta-analysis of published and unpublished evidence from randomised controlled trials. BMJ 342:doi:10.1136/bmj.d1250 (Published 16 Mar 2011)

Rahimi K, Bhala N, Kamphuisen P, et al. Effect of statins on **venous thromboembolic events**: a meta-analysis of published and unpublished evidence from randomized controlled trials. PLoS Med 2012.

Rajamani K et al. Effect of fenofibrate on **amputation** events in people with type 2 diabetes mellitus (FIELD study): A prespecified analysis of a randomised controlled trial. Lancet 2009 May 23; 373:1780.

Rajpathak SN, Kumbhani DJ, Crandall J, et al. **Statin** therapy and risk of **developing type 2 diabetes**: a meta-analysis. Diabetes Care. 2009 Oct;32(10):1924-9.

Rahimi K, Majoni W, Merhi A et al. Effect of **statins on ventricular tachyarrhythmia**, **cardiac arrest, and sudden cardiac death**: a meta-analysis of published and unpublished evidence from randomized trials. Eur Heart J. 2012 Feb 3.

Rautio N, Jokelainen J, Oksa H, et al. Do **statins interfere with lifestyle intervention** in the prevention of diabetes in primary healthcare? One-year follow-up of the FIN-D2D project. BMJ 2012.

Ray KK, Bays HE, Catapano AL,et al; CLEAR Harmony Trial. Safety and Efficacy of **Bempedoic Acid to Reduce LDL Cholesterol**. N Engl J Med. 2019 Mar 14;380(11):1022-1032.

Ray KK, Cannon CP. Early time to benefit with intensive statin treatment: could it be the pleiotropic effects? Am J Cardiol. 2005 Sep 5;96(5A):54F-60F.

Ray KK, Landmesser U, Leiter LA, et al. **Inclisiran** in patients with high cardiovascular risk with elevated LDL cholesterol. (**Orion-1**) N Engl J Med 2017.

Rayman Margaret P., Stranges Saverio, Griffin Bruce A., et al. Effect of Supplementation With High-**Selenium** Yeast on Plasma Lipids: A Randomized Trial. Ann Intern Med May 17, 2011 154:656-665.

Redberg RF. Katz MH. **Healthy men should <u>not</u> take statins**. JAMA 2012; 307:1491-1492.

Reddy P, Ellington D, Zhu Y, et al. Serum concentrations and clinical effects of **atorvastatin in patients taking grapefruit juice** daily. Br J Clin Pharmacol. 2011 Apr 18. doi: 10.1111/j.1365-2125.2011.03996.x.

Reeves D, Springate DA, Ashcroft DM, et al. Can analyses of electronic patient records be independently and externally validated? The effect of **statins on the mortality of patients with ischaemic heart disease**: a cohort study with nested case-control analysis. BMJ Open. 2014 Apr 23;4(4):e004952.

Reindl Erin K, Wright Bradley M, Wargo Kurt A. **Alternate-Day Statin Therapy** for the Treatment of Hyperlipidemia. Ann Pharmacother 2010;44:1459-1470.

Reiss AB, Wirkowski E. Role of HMG-CoA Reductase Inhibitors in **Neurological Disorders** : Progress to Date. Drugs. 2007;67(15):2111-20.

Reynolds K, et al. A meta-analysis of the effect of **soy protein** supplementation on serum lipids. Am J Cardiol. 2006 Sep 1;98(5):633-40. Epub 2006 Jul 12.

Ridker PM, Rifai N, Cook NR, et al. Non-HDL cholesterol, apolipoproteins A-I and B100, standard lipid measures, lipid ratios, and CRP as risk factors for cardiovascular disease in women. JAMA. 2005 Jul 20;294(3):326-33.

Ridker PM, Danielson E, Fonseca FA, Genest J, et al. the **<u>JUPITER</u>** Study Group. Rosuvastatin to Prevent Vascular Events in Men and Women with Elevated C-Reactive Protein. N Engl J Med. 2008 Nov 9. [Epub ahead of print] In this trial of apparently healthy persons without hyperlipidemia but with elevated high-sensitivity C-reactive protein levels, rosuvastatin significantly reduced the incidence of major cardiovascular events.

Ridker PM, Tardif JC, Amarenco P, et ak, Lipid-reduction variability and antidrug-antibody formation with **bococizumab**. (**Spire**) N Engl J Med 2017.

Ridker PM, Revkin J, Amarenco P, et al. Cardiovascular efficacy and safety of **bococizumab** in high-risk patients. (**Spire**) N Engl J Med 2017

Ritchie, Susan K., Murphy, Emily C.-S., et al. **Universal Versus Targeted Blood Cholesterol Screening Among <u>Youth</u>:** The CARDIAC Project. Pediatrics 2010 0: peds.2009-2546.

Robinson JG, Smith B, Maheshwari N, Schrott H. **Pleiotropic effects** of statins: benefit beyond cholesterol reduction? A meta-regression analysis. J Am Coll Cardiol. 2005 Nov 15;46(10):1855-62. Epub 2005 Oct 24.

Robinson JG, Wang S, Jacobson TA. Meta-Analysis of Comparison of Effectiveness of Lowering **Apolipoprotein B Versus Low-Density Lipoprotein** Cholesterol and Nonhigh-Density Lipoprotein Cholesterol for Cardiovascular Risk Reduction in Randomized Trials. Am J Cardiol. 2012 Aug 17.

Robinson JG, Nedergaard BS, Rogers WJ, et al; **LAPLACE-2** Investigators. Effect of **evolocumab or ezetimibe** added to moderate- or high-intensity statin therapy on LDL-C lowering in patients with hypercholesterolemia: the LAPLACE-2 randomized clinical trial. JAMA. 2014 May 14;311(18):1870-82.

Roth EM, McKenney JM, Hanotin C, et al. Atorvastatin with or without an **antibody to PCSK9** in primary hypercholesterolemia. N EnglJ Med 2012. (REGN727/SAR236553)

Sabate Joan; Oda Keiji; Ros Emilio. **Nut Consumption** and Blood Lipid Levels: A Pooled Analysis of 25 Intervention Trials. Arch Intern Med. 2010;170(9):821-827.

Sabatine MS, Giugliano RP, Keech AC, et al. **Evolocumab** and clinical outcomes in patients with cardiovascular disease. (**Fourier**) N Engl J Med 2017.

Sailler L, Pereira C, Bagheri A, et al. Increased exposure to statins in patients developing **<u>chronic muscle diseases</u>**: a 2-year retrospective study.Ann Rheum Dis. 2008 May;67(5):614-9. Epub 2007 Sep 3. Patients who developed chronic muscle diseases after the age of 50, including DM/PM, had a higher than expected frequency of prior exposure to statins.

Sampathkumar K, et al. Extended release **nicotinic acid** - a novel oral agent for phosphate control. Int Urol Nephrol. 2006;38(1):171-4.

Sano M, Bell KL, Galasko D, et al. A randomized, double-blind, placebo-controlled trial of **simvastatin to treat Alzheimer disease**. Neurology. 2011 Aug 9;77(6):556-63. (no benefit)

Sattar N, Preiss D, Murray HM, et al. **Statins** and risk of incident **<u>diabetes</u>**: a collaborative meta-analysis of randomised statin trials. Lancet 2010; DOI:10.1016/S0140-6736(09)61965-6.

Savarese G, Gotto AM Jr, Paolillo S, et al. Benefits Of **Statins In Elderly** Subjects Without Established Cardiovascular Disease. A Meta-Analysis. J Am Coll Cardiol. 2013 Aug 14.

Schanberg L, Sandborg C, Barnhart HX, Ardoin SP, Yow E, Evans GW, et al. Use of atorvastatin in **systemic lupus erythematosus** in children and adolescents (**APPLE**). Arthritis Rheum 2011

Schedlbauer A, Davies P, Fahey T. Interventions to improve **adherence to lipid lowering** medication. Cochrane Database Syst Rev. 2010 Mar 17;3:CD004371.

Schelleman H, Bilker WB, Brensinger CM, et al. **Fibrate/statin initiation in warfarin** users and gastrointestinal bleeding risk. Am J Med. 2010 Feb;123(2):151-7.

Schmidt AF, Pearce LS, Wilkins JT, et al. **PCSK9 monoclonal antibodies** for the **primary and secondary prevention of cardiovascular disease**. Cochrane Database of Systematic Reviews 2017, Issue 4. Art. No.: CD011748.
Over short-term to medium-term follow-up, PCSK9 inhibitors reduced LDL-C. Studies with medium-term follow-up time (longest median follow-up recorded was 26 months) reported that PCSK9 inhibitors (compared with placebo) decreased CVD risk but may have increased the risk of any adverse events (driven by SPIRE-1 and -2 trials). Available evidence suggests that PCSK9 inhibitor use probably leads to little or no difference in mortality. Evidence on relative efficacy and safety when PCSK9 inhibitors were compared with active treatments was of low to very low quality (GRADE); follow-up times were short and events were few. Large trials with longer follow-up are needed to evaluate PCSK9 inhibitors versus active treatments as well as placebo. Owing to the predominant inclusion of high-risk patients in these studies, applicability of results to primary prevention is limited. Finally, estimated risk differences indicate that PCSK9 inhibitors only modestly change absolute risks (often to less than 1%).

Schmidt T, Battafarano DF, Mortensen EM, et al. Frequency of Development of **Connective Tissue Disease** in Statin-Users Versus Nonusers. Am J Cardiol. 2013 Jun 11.

Schouten O, Boersma E, Hoeks SE, et al. Dutch Echocardiographic Cardiac Risk Evaluation Applying Stress Echocardiography Study Group. Fluvastatin and perioperative events in patients undergoing vascular surgery. (**Decrease III**) N Engl J Med. 2009 Sep 3;361(10):980-9. In patients undergoing vascular surgery, perioperative fluvastatin therapy was associated with an improvement in postoperative cardiac outcome. (Dunkelgrun M et al. Bisoprolol and fluvastatin (fixed dose of 80 mg; **NS finding**) for the reduction of perioperative cardiac mortality and myocardial infarction in intermediate-risk patients undergoing noncardiovascular surgery: A randomized controlled trial (DECREASE-IV). Ann Surg 2009 Jun; 249:921.)

Schwartz JS. **Primary Prevention** of Coronary Heart Disease With Statins: It's Not About the Money. Circulation. 2011 Jul 12;124(2):130-2.

Schwartz GG, Olsson AG, Abt M, et al. effects of **dalcetrapib** in patients with a recent acute coronary syndrome. (**dal-OUTCOMES**) N Engl J Med2012 .

Semb AG, Kvien TK, Demicco D, et al. Effect of intensive lipid lowering on cardiovascular outcome in patients **with and without inflammatory joint disease**. Arthritis Rheum. 2012 May 10.

Sever P, Dahlof B, Poulter N, et al. Potential synergy between **lipid-lowering and blood-pressure-lowering** in the Anglo-Scandinavian Cardiac Outcomes Trial. (**ASCOT**) Eur Heart J 2006; 27:2982-2988.

Sever PS, Chang CL, Gupta AK, et al. The **Anglo-Scandinavian Cardiac Outcomes Trial (Ascot): 11-year mortality follow-up** of the lipid-lowering arm in the UK. Eur Heart J 2011

Shah RV, Goldfine AB. Statins and risk of **new-onset diabetes** mellitus. (**Patient page**) Circulation. 2012 Oct 30;126(18):e282-4.

Shalev V, Chodick G, Silber H, et al. **Continuation of statin treatment** and all-cause mortality. Arch Intern Med 2009; 169:260-268.

Shalev V, Goldshtein I, Porath A, et al. **Continuation of Statin Therapy and Primary Prevention** of Nonfatal Cardiovascular Events. Am J Cardiol. 2012 Sep 25.

Sharma M, Ansari MT, Abou-Setta AM, et al. Systematic review: comparative effectiveness and harms of <u>combination therapy and **monotherapy**</u> for dyslipidemia. Ann Intern Med. 2009 Nov 3;151(9):622-30.

<u>SHARP</u> Collaborative Group. Study of Heart and Renal Protection (SHARP): Randomized trial to assess the effects of lowering low-density lipoprotein cholesterol among 9438 patients with chronic kidney disease. Am Heart J 2010;

Shen L, Shah BR, Reyes EM, et al. Role of **diuretics, beta blockers, and statins** in increasing the risk of diabetes in patients with **impaired glucose tolerance**: reanalysis of data from the **NAVIGATOR** study. BMJ. 2013 Dec 9;347:f6745.

Siamopoulos KC, et al. Long-term treatment with **EPO** increases serum levels of high-density lipoprotein in patients with CKD. Am J Kidney Dis. 2006 Aug;48(2):242-9.

Sibley CT, Vavere AL, Gottlieb I, et al. **MRI-measured regression of carotid atherosclerosis** induced by statins with and without niacin in a randomised controlled trial: the NIA plaque study. Heart. 2013 Jul 19.

Sidhu D, Naugler C. **Fasting time and lipid levels** in a community-based population: a cross-sectional study [published online November 12, 2012]. Arch Intern Med. 10.1001/archinternmed.2012.3708.

Silbernagel G, Schöttker B, Appelbaum S, et al. **High-density lipoprotein (HDL) cholesterol**, coronary artery disease, and cardiovascular mortality. Eur Heart J. 2013 Sep 7.

Singh S, Singh PP, Singh AG, et al. **Statins** Are Associated With a **Reduced Risk of Hepatocellular Cancer**: A Systematic Review and Meta-analysis. Gastroenterology. 2012 Oct 12.

Smith S, Benjamin E, Bonow R, et al. **AHA/ACCF secondary prevention and risk reduction therapy** for patients with coronary and other atherosclerotic vascular disease: 2011 update: A guideline from the American Heart Association and American College of Cardiology Foundation. Circulation. 2011; DOI:10.1161/CIR.0b013e318235eb4d.

Sniderman AD, Thanassoulis G, Lawler PR, et al. Comparison of **Coronary Calcium Screening Versus Broad Statin** Therapy for Patients at Intermediate Cardiovascular Risk. Am J Cardiol. 2012 May 9.

Soler A, et al. Effectiveness and tolerance of atorvastatin for **antiretroviral therapy**-secondary dyslipemia. Med Clin (Barc). 2006 Jul 15;127(7):250-2.

Steenland K, Zhao L, Goldstein FC, Levey AI. **Statins and cognitive decline** in older adults with normal cognition or mild cognitive impairment. J Am Geriatr Soc. 2013 Sep;61(9):1449-55.

Stein EA, Mellis S, Yancopoulos GD, et al. Effect of a **monoclonal antibody to PCSK9** on LDL cholesterol. N Engl J Med 2012;366:1108-18.

Stein E A, Gipe D, Bergeron J et al. Effect of a monoclonal antibody to **PCSK9, REGN727/SAR236553**, to reduce low-density lipoprotein cholesterol in patients with heterozygous familial hypercholesterolaemia on stable statin dose with or without ezetimibe therapy: A phase 2 randomised controlled trial. Lancet 2012.

Stein JD, Newman-Casey PA, Talwar N, et al. The relationship between **statin use and open-angle glaucoma**. Ophthalmology. 2012 Oct;119(10):2074-81.

Study of the Effectiveness of Additional Reductions in Cholesterol and Homocysteine (**SEARCH**) Collaborative Group. Intensive lowering of LDL cholesterol with 80 mg versus 20 mg simvastatin daily in 12 064 survivors of myocardial infarction: a double-blind randomised trial. The Lancet, Early Online Publication, 9 November 2010 doi:10.1016/S0140-6736(10)60310-8.

Strippoli GF, Navaneethan SD, Johnson DW, et al. Effects of statins in patients with **chronic kidney disease**: meta-analysis and meta-regression of randomised controlled trials. BMJ. 2008 Feb 25; [Epub ahead of print] Statins significantly reduce lipid concentrations and cardiovascular end points in patients with chronic kidney disease, irrespective of stage of disease, but no benefit on all cause mortality or the role of statins in primary prevention has been established. Reno-protective effects of statins are uncertain because of relatively sparse data and possible outcomes reporting bias.

Subramanian S, Emami H, Vucic E, et al. High Dose **Atorvastatin Reduces Periodontal Inflammation**: A Novel Pleiotropic Effect of Statins. J Am Coll Cardiol. 2013; [In press]

Sugerman DT. JAMA **patient page. Blood lipids**. JAMA. 2013 Oct 23;310(16):1751.

Szarek M, White HD, Schwartz GG, et al. **Alirocumab** Reduces Total Nonfatal Cardiovascular and Fatal Events: The **ODYSSEY OUTCOMES Trial**. J Am Coll Cardiol. 2019 Feb 5;73(4):387-396.

Tada H, Kawashiri MA, Okada H, et al. Assessment of Coronary Atherosclerosis in Patients With **Familial Hypercholesterolemia** by Coronary Computed Tomography Angiography. Am J Cardiol. 2015 Jan 6.

Taguchi I, Iimuro S, Iwata H, et al. Highdose versus low-dose **pitavastatin** in Japanese patients with stable coronary artery disease (**REAL-CAD**): a randomized superiority trial. Circulation. 2018;137:1997–2009.

Tajeu GS, Booth JN 3rd, Colantonio LD, et al. **Incident Cardiovascular Disease Among Adults with Blood Pressure < 140/90 mm Hg**. Circulation. 2017 Jun 20.

Takano H, Ohba T, Yamamoto E, et al; PRIMITIVE Study Investigators. Usefulness of Rosuvastatin to **Prevent Periprocedural Myocardial Injury** in Patients Undergoing Elective Coronary Intervention. Am J Cardiol. 2013 Mar 16.

Takayama T, Komatsu S, Ueda Y, Fukushima et al; **ALTAIR** study group. Comparison of the Effect of **Rosuvastatin** 2.5 mg vs 20 mg on Coronary Plaque Determined by Angioscopy and Intravascular Ultrasound in Japanese With Stable Angina Pectoris (from the Aggressive Lipid-Lowering Treatment Approach Using Intensive Rosuvastatin for Vulnerable Coronary Artery Plaque [ALTAIR] Randomized Trial). Am J Cardiol. 2016 Apr 15;117(8):1206-12.

Talmud PJ, Shah S, Whittall R, et al. Use of **low-density lipoprotein cholesterol gene score** to distinguish patients with **polygenic and monogenic familial hypercholesterolemia**: a case-control study. Lancet 2013.

Talwar N, Musch DC, Stein JD. Association of Daily Dosage and Type of **Statin Agent With Risk of Open-Angle Glaucoma**. JAMA Ophthalmol. 2017 Jan 19.

Tanaka F, Makita S, et al; Iwate-Kenco Study Group. **Predictive Value of Lipoprotein Indices** for Residual Risk of Acute Myocardial Infarction and Sudden Death in Men With Low-Density Lipoprotein Cholesterol Levels <120 mg/dl. Am J Cardiol. 2013 Jul 4.

Tashakkor AY, Mancini GB. The Relationship Between **Skin Cholesterol Testing** and Parameters of Cardiovascular Risk: A Systematic Review. Can J Cardiol. 2013 Jul 10.

Taylor AJ, et al. Arterial Biology for the Investigation of the Treatment Effects of Reducing Cholesterol **(ARBITER) 2**: a double-blind, placebo-controlled study of extended-release **niacin** on atherosclerosis progression in secondary prevention patients treated with statins. Circulation. 2004 Dec 7;110(23):3512-7. Epub 2004 Nov 10. Erratum in: Circulation. 2004 Dec 7;110(23):3615. Circulation. 2005 Jun 21;111(24):e446.

Taylor AJ, Villines TC, Stanek EJ, et al. Extended-Release Niacin or Ezetimibe and Carotid Intima-Media Thickness. (**ARBITER 6-HALTS**) N Engl J Med. 2009 Nov 15. [Epub ahead of print].

Taylor BA. Does **Coenzyme Q10 Supplementation Mitigate Statin-Associated Muscle Symptoms**? Pharmacological and Methodological Considerations. Am J Cardiovasc Drugs. 2018 Apr;18(2):75-82.

Taylor F, Ward K, Moore THM, Burke M, Davey Smith G, Casas JP, Ebrahim S. **Statins for the primary prevention** of cardiovascular disease. Cochrane Database of Systematic Reviews 2011, Issue 1. Art. No.: CD004816. DOI: 10.1002/14651858.CD004816.pub4. Although reductions in all-cause mortality, composite endpoints and revascularisations were found with no excess of adverse events, there was evidence of selective reporting of outcomes, failure to report adverse events and inclusion of people with cardiovascular disease. Only limited evidence showed that primary prevention with statins may be cost effective and improve patient quality of life. Caution should be taken in prescribing statins for primary prevention among people at low cardiovascular risk.

Taylor F, Huffman MD, Macedo AF, et al. **Statins for the primary prevention** of cardiovascular disease. Cochrane Database Syst Rev. 2013 Jan 31;1:CD004816. DOI:10.1002/14651858.CD004816.pub5. Reductions in all-cause mortality, major vascular events and revascularisations were found with no excess of adverse events among people without evidence of CVD treated with statins.

Taylor FC, Huffman M, Ebrahim S. **Statin therapy for primary prevention** of cardiovascular disease [published online November 25, 2013]. JAMA. doi:10.1001/jama.2013.281348.

Taylor PC, Kremer JM, Emery P, et al. Lipid profile and effect of **statin** treatment in pooled phase II and phase III **baricitinib** studies. Ann Rheum Dis. 2018 Feb 20.

Taylor PC, Kremer JM, Emery P, et al. Lipid profile and effect of statin treatment in pooled phase II and phase III **baricitinib** studies. Ann Rheum Dis. 2018 Jul;77(7):988-995.

Te Morenga LA, Howatson AJ, Jones RM, et al. **Dietary sugars and cardiometabolic risk**: systematic review and meta-analyses of randomized controlled trials of the effects on blood pressure and lipids. Am J Clin Nutr. 2014 May 7.

Teichtahl AJ, Brady SR, Urquhart DM, et al. **Statins and tendinopathy**: a systematic review. Med J Aust. 2016 Feb 15;204(3):115-21. Tendon rupture is a rare occurrence among adults exposed to statin therapy. This review found no significantly consistent evidence for an association between statin exposure and an increased risk of tendon rupture. Evidence does, however, support a reduced risk of tendinopathy in adults treated with simvastatin. (LOE = 2a-)

Tejani AM. Point counterpoint: Should Patients Continue to Receive **Statins** Once They Reach **80 Years** of Age? The "Con" side. CJHP. 2017;70(3):243-24

Tenkanen L, et al. Gemfibrozil in the Treatment of Dyslipidemia: An **18-Year** Mortality Follow-up of the Helsinki Heart Study. (**HHS**) Arch Intern Med. 2006 Apr 10;166(7):743-8.

Tentzeris I, Rohla M, Jarai R, et al. Influence of **High-Dose Highly Efficient Statins** on Short-Term Mortality in Patients Undergoing Percutaneous Coronary Intervention (**PCI**) With Stenting for Acute Coronary Syndromes. Am J Cardiol. 2014 Jan 14.

Teo KK, Goldstein LB, Chaitman BR, et al. Extended-Release Niacin Therapy and Risk of **Ischemic Stroke** in Patients With Cardiovascular Disease: The Atherothrombosis Intervention in Metabolic Syndrome With Low HDL/High Triglycerides: Impact on Global Health Outcome (**AIM-HIGH**) Trial. Stroke. 2013 Jul 23.

Thanassoulis G, Sniderman AD, Pencina MJ. A Long-term Benefit Approach vs Standard Risk-Based Approaches for **Statin Eligibility in Primary Prevention**. JAMA Cardiol. 2018 Oct 24.

Thanassoulis G, Williams K, Altobelli KK, et al. **Individualized statin benefit** for determining **statin eligibility in the primary prevention of cardiovascular disease**. Circulation. 2016;133:1574–1581.

Thavendiranathan P, Bagai A, Brookhart MA, Choudhry NK. **Primary Prevention** of Cardiovascular Diseases With Statin Therapy: A **Meta-analysis** of Randomized Controlled Trials. Arch Intern Med. 2006 Nov 27;166(21):2307-13. Subjects taking statins for a mean of 4.3 years (n=42 848) had a lower incidence of heart attack, stroke, revascularization, and other events than controls. The authors estimate the following numbers needed to treat for 4.3 years: 60, to prevent one major coronary event; 268 for stroke; 61 for nonfatal myocardial infarction and 93 for revascularization. In patients without CV disease, statin therapy decreases the incidence of major coronary and cerebrovascular events and revascularizations but not coronary heart disease or overall mortality.

The STABILITY Investigators. **Darapladib** for Preventing Ischemic Events in Stable Coronary Heart Disease. N Engl J Med. 2014 Mar 30.

Thomas GS, Cromwell WC, Ali S, et al. **Mipomersen**, an apolipoprotein B synthesis inhibitor, reduces atherogenic lipoproteins in patients with severe hypercholesterolemia at high cardiovascular risk: a randomized, double-blind, placebo-controlled trial. J Am Coll Cardiol. 2013 Dec 10;62(23):2178-84.

Ting RD, Keech AC, Drury PL, et al; **FIELD** Study Investigators. Benefits and safety of long-term **fenofibrate** therapy in people with type 2 diabetes and renal impairment: the FIELD Study. Diabetes Care. 2012 Feb;35(2):218-25.

Tirosh A, Rudich A, Shochat T, et al. Changes in **triglyceride levels** and risk for coronary heart disease in young men. Ann Intern Med. 2007 Sep 18;147(6):377-85. Summary for patients in: Ann Intern Med. 2007 Sep 18;147(6):I45.

with persistently low triglyceride levels.
Tjia J, Kutner JS, Ritchie CS, et al. Perceptions of **Statin Discontinuation among Patients with Life-Limiting Illness**. J Palliat Med. 2017 May 18
Tleyjeh IM, Kashour T, Hakim FA, et al. Statins for the prevention and treatment of **infections**: a systematic review and meta-analysis. Arch Intern Med. 2009 Oct 12;169(18):1658-67.
Tobe SW, Stone JA, Brouwers M, et al. **Harmonization of guidelines** for the prevention and treatment of cardiovascular disease: the **C-CHANGE Initiative**. CMAJ. 2011 Sep 12.
Toleikyte I, Retterstøl K, Leren PT, Iversen PO. **Pregnancy outcomes in familial hypercholesterolemia**: a registry-based study. Circulation. 2011; 124:1606 –1614.
Thom S, Poulter N, Field J, et al; **UMPIRE** Collaborative Group. Effects of a **fixed-dose combination** on medication adherence and risk factors in patients with or at risk of CVD: the UMPIRE randomized clinical trial. JAMA. doi:10.1001/jama.2013.277064. (pollypill contained aspirin, simvastatin, lisinopril, and either atenolol or hydrochlorothiazide)
Thompson PD, Panza G, Zaleski A, et al. **Statin-Associated Side Effects**. J Am Coll Cardiol. 2016 May 24;67(20):2395-410.
Tice JA, Kazi DS, Pearson SD. **Proprotein convertase subtilisin/kexin type 9 (PCSK9) inhibitors** for treatment of high cholesterol levels: effectiveness and value [online December 14, 2015].JAMA Intern Med. doi:10.1001 /jamainternmed.2015.7248.
Tonelli M, Lloyd AM, Bello AK, et al. Statin use and the **risk of acute kidney injury** in older adults. BMC Nephrol. 2019 Mar 25;20(1):103.
Tonelli Marcello, Lloyd Anita, Clement F, et al. Efficacy of **statins for primary prevention** in people at low cardiovascular risk: a meta-analysis. CMAJ October 11, 2011 cmaj.101280; published ahead of print October 11, 2011, doi:10.1503/cmaj.101280
Tonelli M, Wanner C; for the Kidney Disease: Improving Global Outcomes (**KDIGO**) Lipid Guideline Development Work Group Members. **Lipid Management in Chronic Kidney Disease**: Synopsis of the Kidney Disease: Improving Global Outcomes 2013 Clinical Practice Guideline. Ann Intern Med. 2013 Dec 10.
Tonkin AM, et al J; LIPID Study Group. **Cost-effectiveness** of cholesterol-lowering therapy with pravastatin in patients with previous acute coronary syndromes **aged 65 to 74 years** compared with younger patients: results from the LIPID study. Am Heart J. 2006 Jun;151(6):1305-12. (InfoPOEMs: From the viewpoint of a health system, it is cost-effective to treat high-risk patients older than 65 years with pravastatin (Pravachol) no matter what their level of initial cholesterol level. The increased cost of treatment is partially offset by savings in other areas. This analysis did not take into account any effect on the quality of the life extension by pravastatin. (LOE = 2c))
Toth PP, Descamps O, Genest J, et al. Pooled Safety Analysis of **Evolocumab** in Over 6000 Patients From Double-Blind and Open-Label Extension Studies. Circulation. 2017 May 9;135(19):1819-1831
Toward Optimized Practice (**TOP**) Lipid Pathway Working Group. **Simplified lipid pathway**: **prevention and management** of cardiovascular disease risk in primary care clinical practice guideline. Edmonton, AB: Toward Optimized Practice; February 2015. http://www.topalbertadoctors.org/download/1655/Lipid%20Pathway%20CPG.pdf?_20150414080148 (accessed April 14, 2015).
Toward Optimized Practice (TOP) Lipid Pathway Working Group. **Simplified lipid pathway**: CVD risk in primary care. **Summary of the clinical practice guideline**. Lipid algorithm. Edmonton, AB: Toward Optimized Practice; February 2015. http://www.topalbertadoctors.org/download/1654/Lipid%20Pathway%20Summary.pdf?_20150414074824 (accessed April 14, 2015).
Trivedi D, Wellsted DM, Collard JB, et al. Simvastatin **improves the sexual health-related quality of life** in men aged 40 years and over with erectile dysfunction: additional data from the erectile dysfunction and statin trial. BMC Urol. 2014 Mar 5;14:24.
Tsimikas S, Gordts PLSM, Nora C, et al. **Statin therapy increases lipoprotein(a) levels**. Eur Heart J. 2019 May 20.
Tsimikas S, Viney NJ, Hughes SG, et al. **Antisense therapy targeting apolipoprotein(a):** a randomised, double-blind, placebo-controlled phase 1 study. Lancet 2015; online July 23.
Tsivgoulis G, et al. **Presymptomatic neuromuscular disorders** disclosed following statin treatment. Arch Intern Med. 2006 Jul 24;166(14):1519-24.
Tsivgoulis G, Katsanos AH, Sharma VK, et al. **Statin pretreatment** is associated with better outcomes in large artery atherosclerotic **stroke**. Neurology 2016;86:1103–1111.
Tsujita K, Sugiyama S, Sumida H, et al. Impact of Dual Lipid-Lowering Strategy With **Ezetimibe and Atorvastatin** on Coronary Plaque Regression in Patients With Percutaneous Coronary Intervention: The Multicenter Randomized Controlled **PRECISE-IVUS** Trial. J Am Coll Cardiol. 2015 Aug 4;66(5):495-507.
Tsuyuki RT, Rosenthal M, Pearson GJ. A Randomized Trial of a **Community-based approach to dyslipidemia management**: **Pharmacist prescribing** to achieve cholesterol Targets (RxACT Study). CPJ/RPC. Sept/Oct 2016:149(5).
Triglyceride Coronary Disease Genetics Consortium and Emerging Risk Factors Collaboration, Sarwar N, Sandhu MS, Ricketts SL et al. **Triglyceride**-mediated pathways and coronary disease: collaborative analysis of 101 studies. Lancet. 2010 May 8;375(9726):1634-9.
Turgeon R, Allan GM. **Statin-induced diabetes**: too sweet a deal? Can Fam Physician. 2013 Jul;59(7):e311.
Turgeon RD, Zarnke KB, Allan GM. Does **ezetimibe** modify clinical outcomes? Can Fam Physician. 2015 Mar;61(3):251.
Turgeon RD, Barry AR, Pearson GJ. **Familial hypercholesterolemia**: Review of diagnosis, screening, and treatment. Can Fam Physician. 2016 Jan;62(1):32-7. Review.
Turner JP, Shakib S, Singhal N, et al. **Statin use and pain in older people with cancer**: a cross-sectional study. J Am Geriatr Soc. 2014 Oct;62(10):1900-5.
Turner T, Stein EA. **Non-Statin Treatments** for Managing LDL Cholesterol and Their Outcomes. Clin Ther. 2015 Oct 14.
Ukaigwe A, Karmacharya P, Mahmood M, et al. Meta-Analysis on Efficacy of **Statins for Prevention of Contrast-Induced Acute Kidney Injury** in Patients Undergoing Coronary Angiography. Am J Cardiol. 2014 Aug 12.
Upadhyay A, Earley A, Lamont JL, et al. Lipid-Lowering Therapy in Persons With **Chronic Kidney Disease**: A Systematic Review and Meta-analysis. Ann Intern Med. 2012 Aug 21;157(4):251-62.
Urbina EM, de Ferranti SD. **Lipid Screening in Children and Adolescents**. JAMA. 2016 Aug 9;316(6):589-91
USPSTF: US Preventive Services Task Force. **Screening for lipid disorders in children and adolescents**. JAMA 2016; 316:625-633.
USPSTF: US Preventive Services Task Force. **Statin use for the primary prevention** of cardiovascular disease in adults: US Preventive Services Task Force (**USPSTF**) recommendation statement.JAMA. doi:10.1001 /jama.2016.15450
Uthman OA, Nduka C, Watson SI, et al. **Statin use and all-cause mortality** in people living with **HIV**: a systematic review and meta-analysis. BMC Infect Dis. 2018 Jun 5;18(1):258.
Valdes-Marquez E, Parish S, Clarke R, et al; METASTROKE Consortium of the ISGC. Relative effects of **LDL-C on ischemic stroke and coronary disease**: A Mendelian randomization study. Neurology. 2019 Mar 12;92(11):e1176-e1187.
Vale N, Nordmann AJ, Schwartz GG, et al. Statins for **acute coronary syndrome**. Cochrane Database of Systematic Reviews 2011, Issue 6. Art. No.: CD006870. DOI: 10.1002/14651858.CD006870.pub2. Based on available evidence, initiation of statin therapy within 14 days following ACS does not reduce death, myocardial infarction, or stroke up to four months, but reduces the occurrence of unstable angina at four months following ACS.
Vale N, Nordmann AJ, Schwartz GG, et al. **Statins for acute coronary syndrome**. Cochrane Database Syst Rev. **2014** Sep 1;9:CD006870. : Based on moderate quality evidence, due to concerns about risk of bias and imprecision, initiation of statin therapy within 14 days following ACS does not reduce death, myocardial infarction, or stroke up to four months, but reduces the occurrence of unstable angina at four months following ACS. Serious side effects were rare.
Vallejo-Vaz AJ, Robertson M, Catapano AL, et al. **LDL-Cholesterol Lowering for the Primary Prevention** of Cardiovascular Disease Among Men with Primary Elevations of LDL-Cholesterol Levels of 190 mg/dL or Above: Analyses from the **WOSCOPS** 5-year Randomised Trial and **20-year Observational Follow-Up.** Circulation. 2017 Sep 6.
van Breukelen-van der Stoep DF, van Zeben D, Klop B, et al. Marked underdiagnosis and **undertreatment** of **hypertension and hypercholesterolaemia in rheumatoid arthritis**. Rheumatology (Oxford). 2016 Mar 23
van de Woestijne AP, van der Graaf Y, Westerink J, et al. Effect of **statin therapy on incident type 2 diabetes mellitus** in patients with clinically manifest vascular disease. Am J Cardiol. 2015 Feb 15;115(4):441-6.
Van den Hoek HL, Bos WJW, De Boer A, van de Garde EMW. Statins and **prevention of infections**: systematic review and meta-analysis of data from large randomised placebo controlled trials. BMJ 2011;343:d7281.
van der Vaart T, Plasschaert E, Rietman AB et al. **Simvastatin for cognitive deficits** and behavioural problems in patients with neurofibromatosis type 1 (NF1-SIMCODA): a randomised, placebo-controlled trial. Lancet Neurol. 2013 Sep 30.
van Driel ML, Morledge MD, Ulep R, Shaffer JP, Davies P, Deichmann R. **Interventions to improve adherence to lipid-lowering medication**. Cochrane Database of Systematic Reviews 2016, Issue 12. Art. No.: CD004371. The evidence in our review demonstrates that intensification of patient care interventions improves short- and long-term medication adherence, as well as total cholesterol and LDL-cholesterol levels. Healthcare systems which can implement team-based intensification of patient care interventions may be successful in improving patient adherence rates to lipid-lowering medicines.
Van Horn L, et al. Recommended **Dietary Pattern to Achieve Adherence** to the American Heart Association/American College of Cardiology (**AHA/ACC**) Guidelines: A Scientific Statement From the American Heart Association. Circulation. 2016 Oct 27.
van Staa TP, Smeeth L, Ng ES, et al. The efficiency of cardiovascular risk assessment: do the **right patients get statin treatment**? Heart. 2013 Jun 4.
van Staa TP, Carr DF, O'Meara H, et al. Predictors and outcomes of increases in creatine phosphokinase levels or **rhabdomyolysis** risk during statin treatment. Br J Clin Pharmacol. 2014 Mar 6.
VanderBeek BL, Zacks DN, Talwar N, Nan B, Stein JD. Role of **statins** in the **development and progression of age-related macular degeneration**. Retina. 2013 Feb;33(2):414-22.
Vandermeer ML et al. Association between use of statins and mortality among patients hospitalized with laboratory-confirmed **influenza virus infections**: a multistate study. J Infect Dis. 2012 Jan;205(1):13-9.
Varbo A, Nordestgaard BG, Tybjaerg-Hansen A, et al. Nonfasting triglycerides, cholesterol, and **ischemic stroke** in the general population. Ann Neurol. 2011 Feb 18. doi: 10.1002/ana.22384.
Varbo A, Nordestgaard BG. Remnant cholesterol and **risk of ischemic stroke** in 112,512 individuals from the general population. Ann Neurol. 2019 Feb 5.
Varbo A, Benn M, et al. **Elevated remnant cholesterol** causes both low-grade inflammation and ischemic heart disease while low-density lipoprotein cholesterol causes ischemic heart disease without nflammation. Circulation2013.
Vaucher J, Marques-Vidal P, Preisig M, et al. Population and economic impact of the **2013 ACC/AHA guidelines compared with European guidelines** to prevent cardiovascular disease. *Eur Heart J* 2014.

Venkitachalam L, Wang K, Porath A, et al on behalf of the **REACH** Registry Investigators. **Global variation in the prevalence of elevated cholesterol** in outpatients with established vascular disease or 3 cardiovascular risk factors according to national indices of economic development and health system performance. Circulation 2012.

Verma AA, Jimenez MP, Subramanian SV, et al. **Race and Socioeconomic Differences** Associated With Changes in Statin Eligibility Under the **2013 American College of Cardiology/American Heart Association Cholesterol Guidelines**. Circ Cardiovasc Qual Outcomes. 2017 Sep;10(9)

Versmissen J, Oosterveer DM, Yazdanpanah M, et al. Efficacy of statins in **familial hypercholesterolaemia**: a long term cohort (8.5yr) study. BMJ. 2008 Nov 11;337:a2423. doi: 10.1136/bmj.a2423. In January 1990, 413 (21%) of the patients had started statin treatment, and during follow-up another 1294 patients (66%) started after a mean delay of 4.3 years. Most patients received simvastatin (n=1167, 33 mg daily) or atorvastatin (n=211, 49 mg daily). Lower statin doses than those currently advised reduced the risk of coronary heart disease to a greater extent than anticipated in patients with familial hypercholesterolaemia. With statin treatment, such patients no longer have a risk of myocardial infarction significantly different from that of the general population.

Vesper HW, Kuiper HC, Mirel LB, Johnson CL, Pirkle JL. Levels of plasma **trans-fatty acids** in non-Hispanic white adults in the United States in 2000 and 2009. JAMA. 2012 Feb 8;307(6):562-3.

Victor BM, Teal V, Ahedor L, et al. **Gender differences** in achieving optimal **lipid goals** in patients with coronary artery disease. Am J Cardiol. 2014 May 15;113(10):1611-5.

Viljoen A, Wierzbicki AS. **Investigating mixed hyperlipidaemia**. BMJ. 2011 Aug 25;343:d5146.

Villines TC, Stanek EJ, Devine PJ, et al. The **ARBITER-6 HALTS** Trial (Arterial Biology for the Investigation of the Treatment Effects of Reducing Cholesterol 6—HDL and LDL Treatment Strategies in Atherosclerosis). J Am Coll Cardiol 2010; DOI: 10.1016/j.jacc.2010.03.017.

Vinci SR, Rifas-Shiman SL, Cheng JK, et al. **Cholesterol testing among children and adolescents** during health visits. JAMA. 2014 May 7;311(17):1804-7.

Viney NJ, van Capelleveen JC, Geary RS, et al. **Antisense oligonucleotides** targeting **apolipoprotein(a)** in people with raised lipoprotein(a): two randomised, double-blind, placebo-controlled, dose-ranging trials. Lancet 2016; online Sept 21.

Vinogradova Y, Coupland C, Brindle P, et al. **Discontinuation and restarting** in patients on **statin treatment**: prospective open cohort study using a primary care database. BMJ. 2016 Jun 28;353:i3305.

Violi F, Calvieri C, Ferro D, Pignatelli P. **Statins as antithrombotic drugs**. Circulation. 2013 Jan 15;127(2):251-7.

Virani SS,Woodard LD,Wang D, et al. Correlates of **repeat lipid testing** in patients with coronary heart disease [published online July 1, 2013]. JAMA Intern Med. doi:10.1001/jamainternmed.2013.8198.

Virani SS, Woodard LD, Ramsey DJ, et al. **Gender disparities** in evidence-based statin therapy in patients with cardiovascular disease. Am J Cardiol. 2015 Jan 1;115(1):21-6.

Virani SS, Akeroyd JM, Nambi V, et al. Estimation of **Eligibility for Proprotein Convertase Subtilisin/Kexin Type 9 Inhibitors** and Associated Costs Based on the **FOURIER** Trial (Further Cardiovascular Outcomes Research With PCSK9 Inhibition in Subjects With Elevated Risk): Insights From the Department of Veterans Affairs. Circulation. 2017 Jun 20;135(25):2572-2574.

Vodnala D, Rubenfire M, Brook RD. **Secondary Causes** of Dyslipidemia. Am J Cardiol. 2012 Jun 1.

Voight BF, Peloso GM, Orho-Melander M, et al. Plasma **HDL cholesterol** and risk of myocardial infarction: a mendelian randomisation study. Lancet 2012; published online May 17. (not lower MI risk)

Vuorio A, Kuoppala J, Kovanen PT, Humphries SE, et al. **Statins for children with familial hypercholesterolemia**. Cochrane Database of Systematic Reviews 2010, Issue 7. Art. No.: CD006401. Statin treatment is an efficient lipid-lowering therapy in children with familial hypercholesterolemia. It seems to be safe in the short term but long-term safety is unknown. Children treated with statins should be carefully followed up by their pediatricians. Large long-term randomized controlled trials are needed to establish the long-term safety of statins.

Vuorio A, Kuoppala J, Kovanen PT, et al. **Statins for children with familial hypercholesterolemia**. Cochrane Database Syst Rev. 2017 Jul 7;7:CD006401. Statin treatment is an effective lipid-lowering therapy in children with familial hypercholesterolemia. No significant safety issues were identified. Statin treatment seems to be safe in the short term, but long-term safety remains unknown. Children treated with statins should be carefully monitored and followed up by their pediatricians and their care transferred to an adult lipidologist once they reach 18 years of age. Large long-term randomized controlled trials are needed to establish the long-term safety issues of statins.

Wagstaff LR, et al. Statin-associated **memory loss**: analysis of 60 case reports and review of the literature. Pharmacotherapy. 2003 Jul;23(7):871-80.

Wald DS, Bestwick JP, Wald NJ. **Child-parent screening for familial hypercholesterolaemia**: screening strategy based on a meta-analysis. BMJ. 2007 Sep 22;335(7620):599. Epub 2007 Sep 13. The proposed strategy of screening children and parents for familial hypercholesterolaemia could have considerable impact in preventing the medical consequences of this disorder in two generations simultaneously.

Wald DS, Bestwick JP, Morris JK, et al. **Child–parent familial hypercholesterolemia screening** in primary care. N Engl J Med 2016;375:1628-37.

Walldius G, Aastveit AH, Jungner I. Stroke mortality and the **apoB/apoA-I ratio**: results of the AMORIS prospective study. J Intern Med. 2006 Mar;259(3):259-66.

Wang C, Zheng Q, Zhang M, et al. **Lack of ethnic differences in the pharmacokinetics and pharmacodynamics of evolocumab between Caucasian and Asian populations**. Br J Clin Pharmacol. 2018 Sep 17.

Wang D, Liu B, Tao W, Hao Z, Liu M. **Fibrates for secondary prevention** of cardiovascular disease and stroke. Cochrane Database Syst Rev. 2015 Oct 25;10:CD009580. Moderate evidence showed that the fibrate class can be effective in the secondary prevention of composite outcome of non-fatal stroke, non-fatal MI, and vascular death. However, this beneficial effect relies on the inclusion of clofibrate data, a drug that was discontinued in 2002 due to its unacceptably large adverse effects. Further trials of the use of fibrates in populations with previous stroke and also against a background treatment with statins (standard of care) are required.

Wang KL, Liu CJ, Chao TF, Huang CM, Wu CH, Chen SJ, Chen TJ, Lin SJ, Chiang CE. **Statins, Risk of Diabetes**, and Implications on Outcomes in the General Population. J Am Coll Cardiol. 2012 Aug 2.

Wang KL, Liu CJ, Chao TF, et al. Risk of **New-Onset Diabetes Mellitus** Versus Reduction in Cardiovascular Events With Statin Therapy. Am J Cardiol. 2013 Nov 23

Wang X, Dong Y, Qi X, et al. Cholesterol levels and risk of **hemorrhagic stroke**: a systematic review and meta-analysis. Stroke. 2013 Jul;44(7):1833-9.

Wang Z, Zhang Y, Gao M, et al. Statin Therapy for the Prevention of **Atrial Fibrillation**: A Meta-analysis of Randomized Controlled Trials. Pharmacotherapy. 2011 Nov;31(11):1051-62.

Ward IM, Mortensen EM, Battafarano DF, et al. Association of **statins and risk of fractures** in a military health system: a propensity score-matched analysis. Ann Pharmacother. 2014 Nov;48(11):1406-14.

Warendorf JK, Vrancken AFJE, van Eijk RPA, et al. **Statins do not increase risk of polyneuropathy**: A case-control study and literature review. Neurology. 2019 Apr 30;92(18):e2136-e2144.

Warren JB, Dimmitt S, Stampfer H. **Cholesterol trials and mortality**. Br J Clin Pharmacol. 2016 Apr 4.

Warraich HJ, Salami JA, Khera R, et al. Trends in Use and Expenditures of **Brand-name Atorvastatin After Introduction of Generic Atorvastatin**. JAMA Intern Med. 2018 Mar 10.

Waters DD, et al. Effects of high-dose atorvastatin on **cerebrovascular events** in patients with stable coronary disease in the **TNT** (Treating to New Targets) study. J Am Coll Cardiol. 2006 Nov 7;48(9):1793-9. Epub 2006 Oct 17.

Waters, David D., Ho, Jennifer E., DeMicco, David A., et al. Predictors of **New-Onset Diabetes in Patients Treated With Atorvastatin**: Results From 3 Large Randomized Clinical Trials (Ideal, TNT,Sparcl). J Am Coll Cardiol 2011 57: 1535-1545.

Waters DD, Ho JE, Boekholdt SM, et al. Cardiovascular event reduction versus **new-onset diabetes during atorvastatin** therapy: effect of baseline risk factors for diabetes. J Am Coll Cardiol. 2013 Jan 15;61(2):148-52.

Waters DD. Are **Cholesterol Treatment Targets a Deterrent to Optimal Lipid-Lowering Therapy**? JAMA Cardiol. 2017 Nov 8.

Watkins Jack L, Atkinson Bradley J, Pagliaro Lance C. **Rhabdomyolysis** in a Prostate Cancer Patient Taking **Ketoconazole and Simvastatin**: Case Report and Review of the Literature. 1 February 2011, DOI 10.1345/aph.1P433. Ann Pharmacother ;45:e9.

Waubant E, Pelletier D, Mass M, et al. behalf of the **ITN STAyCIS** Study Group; ITN020AI Study Management Team. Randomized controlled trial of **atorvastatin** in clinically isolated syndrome: The STAyCIS study. Neurology. 2012 Apr 10;78(15):1171-1178.

Wei F, Crain AL, Whitebird RR, et al. Effects of **paroxetine and sertraline on low-density lipoprotein cholesterol**: an observational cohort study. CNS Drugs. 2009 Oct;23(10):857-65.

Wei WQ, Li X, Feng Q, et al. **LPA Variants are Associated with Residual Cardiovascular Risk** in Patients **Receiving Statins**. Circulation. 2018 Apr 27.

Wein T, Lindsay MP, Côté R, Foley N, Berlingieri J, Bhogal S, et al; Heart and Stroke Foundation **Canadian Stroke Best Practice Committees**. Canadian stroke best practice recommendations (**CSBPR**): Secondary prevention of stroke, sixth edition practice guidelines, update 2017. Int J Stroke. 2018 Jun;13(4):420-443.

Welsh JA, Sharma A, Abramson JL, et al. **Caloric sweetener consumption** and dyslipidemia among us adults. *JAMA* 2010; 303:1490-1497.

Werner JL, Christopher-Stine L, Ghazarian SR, et al. **Antibody levels** correlate with creatine kinase levels and strength in **anti-HMG-CoA** reductase-associated autoimmune myopathy. Arthritis Rheum. 2012 Aug 29.

West AM, Anderson JD, Meyer CH, et al. The effect of **ezetimibe on peripheral arterial atherosclerosis** depends upon statin use at baseline. Atherosclerosis 2011; DOI:10.1016/j.atherosclerosis.2011.04.005.

Westover M. Brandon; Bianchi Matt T.; Eckman Mark H.; et al. Statin Use Following **Intracerebral Hemorrhage**: A Decision Analysis. *Arch Neurol*. 2011;0(2011):archneurol.2010.356.

White CM. Therapeutic Potential and Critical Analysis of the PCSK9 Monoclonal Antibodies **Evolocumab** and **Alirocumab**. Ann Pharmacother. 2015 Dec;49(12):1327-35.

White HD, Steg PG, Szarek M, et al. **Effects of alirocumab on types of myocardial infarction**: insights from the ODYSSEY OUTCOMES trial. Eur Heart J. 2019 May 23.

White J et al. Association of **lipid fractions with risks for coronary artery disease and diabetes**. JAMA Cardiol 2016 Aug 3.

Wiegman A, et al. Efficacy and safety of statin therapy in **children** with familial hypercholesterolemia: a randomized controlled trial. JAMA. 2004 Jul 21;292(3):331-7.

Wiger KJ, Manalac RJ, Blumenthal RS, et al. **Statins and cognition**: a systematic review and meta-analysis of short- and long-term cognitive effects. Mayo Clin Proc. 2013 Nov;88(11):1213-21

Wiggins BS, Saseen JJ, Page RL 2nd, et al. Recommendations for Management of Clinically Significant **Drug-Drug Interactions With Statins** and Select Agents Used in Patients With Cardiovascular Disease: A Scientific Statement From the

Williams ED, Eastwood SV, Tillin T, et al. **Statin use** is associated with **reduced depressive symptoms** in Europeans, but **increased symptoms in ethnic minorities in UK**: An observational study. Br J Clin Pharmacol. 2015 Feb 2.

Winchester DE, Wen X, Xie L, et al. Evidence of **pre-procedural statin therapy** (PCI, CABG) a meta-analysis of randomized trials. J Am Coll Cardiol. 2010 Sep 28;56(14):1099-109. Epub 2010 Aug 31.

Wingo TS, Cutler DJ, Wingo AP, et al. Association of early-onset **Alzheimer disease with elevated low-density lipoprotein cholesterol levels** and rare genetic coding variants of APOB [online May 28, 2019]. JAMA Neurol. doi:10.1001/jamaneurol.2019.0648

Wise SJ, Nathoo NA, Etminan M, et al. **Statin use and risk for cataract**: a nested case-control study of 2 populations in Canada and the United States. Can J Cardiol. 2014 Dec;30(12):1613-9.

Witsch J, Al-Mufti F, Connolly ES, et al Statins and **perihemorrhagic edema in patients with spontaneous intracerebral hemorrhage**. Neurology. 2019 Apr 30;92(18):e2145-e2149.

Witztum JL, Gaudet D, Freedman SD, et al. **Volanesorsen and Triglyceride Levels** in Familial Chylomicronemia Syndrome. N Engl J Med. 2019 Aug 8;381(6):531-542.

Wolfe S. **Rosuvastatin**: winner in the statin wars, patients' health notwithstanding. BMJ. 2015 Mar 17;350:h1388.

Wojnicz R, et al. Usefulness of atorvastatin in patients (n=74) with heart failure due to inflammatory dilated cardiomyopathy and elevated cholesterol levels. Am J Cardiol. 2006 Mar 15;97(6):899-904. Epub 2006 Feb 3.

Wolk A, et al. Long-term **fatty fish consumption** and **renal cell carcinoma** incidence in women. JAMA. 2006 Sep 20;296(11):1371-6. Our study suggests that consumption of fatty fish may reduce the occurrence of renal cell carcinoma in women.

Won H, Ko Y, Shin D, et al. Efficacy of early intensive **rosuvastatin** therapy in patients with ST-segment elevation **myocardial infarction** undergoing primary percutaneous coronary intervention: randomized, placebo-controlled. European Heart Journal. 34.suppl 1. 2014.

Wong B, Kruse G, Kutikova L, et al. Cardiovascular Disease Risk Associated With **Familial Hypercholesterolemia**: A Systematic Review of the Literature. Clin Ther. 2016 May 31. pii: S0149-2918(16)30340-X.

Wong GK, Chan DY, Siu DY, et al; HDS-SAH Investigators. **High-dose simvastatin for aneurysmal subarachnoid hemorrhage**: multicenter randomized controlled double-blinded clinical trial. Stroke. 2015 Feb;46(2):382-8.

Wong H, Chahal N, Manlhiot C, et al. **Flaxseed** in Pediatric Hyperlipidemia: A Placebo-Controlled, Blinded, Randomized Clinical Trial of Dietary Flaxseed Supplementation for Children and Adolescents With Hypercholesterolemia. JAMA Pediatr. 2013 Jun 3:1-5.

Wong ND, Chuang J, Wong K, et al. **Residual dyslipidemia among United States adults treated with lipid modifying therapy** (data from National Health and Nutrition Examination Survey 2009-2010). Am J Cardiol. 2013 Aug 1;112(3):373-9.

Wong TY, Simó R, Mitchell P. **Fenofibrate** - a potential systemic treatment for **diabetic retinopathy**? Am J Ophthalmol. 2012 Jul;154(1):6-12.

Wong WB, Lin VW, Boudreau D, Devine EB. **Statins in the prevention of dementia and Alzheimer's disease**: a meta-analysis of observational studies and an assessment of confounding. Pharmacoepidemiol Drug Saf. 2013 Apr;22(4):345-58.

Wongwiwatthananukit S, et al. Efficacy and Safety of **Rosuvastatin** 10mg **Every Other Day** Compared with 10mg Once Daily in Patients with Hypercholesterolemia (November). Ann Pharmacother. 2006 Sep 26; [n=80 8week]

Wyman M, Lenoard M, Morledge T. **Coenzyme Q10**: A therapy for hypertension and statin-induced myalgia? Cleveland Clinic Journal of Medicine 2010; 77(7):435-442; doi:10.3949/ccjm.77a.09078

Yang YJ, Lee SH, Kim BS, et al. Combination Therapy of **Rosuvastatin and Ezetimibe** in Patients with High Cardiovascular Risk. Clin Ther. 2016 Dec 19.

Yasar S, Whitmer R. **Statin use and risk of Alzheimer disease**: A new view on an old relationship. Neurology. 2017 Dec 15.

Yeboah J, Polonsky TS, et al. **Utility of nontraditional risk markers in individuals ineligible for statin** therapy according to the 2013 American College of Cardiology/American Heart Association Cholesterol Guidelines. Circulation. 2015;132:916–922.

Yebyo HG, Aschmann HE, Puhan MA. Finding the balance between **benefits and harms when using statins** for primary prevention of cardiovascular disease. A modeling study. Ann Intern Med. 2018. [Epub ahead of print]. doi:10.7326/M18-1279

Yeh JS, Franklin JM, Avorn J, Landon J, Kesselheim AS. Association of **industry payments to physicians with the prescribing of brand-name statins** in Massachusetts [online May 9, 2016].JAMA Intern Med. doi:10.1001 /jamainternmed.2016.1709.

Young JM, Florkowski CM, Molyneux SL, et al. Effect of coenzyme Q(10) 200mg/d supplementation on simvastatin-induced myalgia. Am J Cardiol. 2007 Nov 1;100(9):1400-3. Epub 2007 Aug 16. n=44 12weeks In conclusion, **coenzyme Q(10) supplementation did not improve statin tolerance or myalgia**, although further studies are warranted.

Yoshimura S, Uchida K, et al. Randomized Controlled Trial of **Early Versus Delayed Statin Therapy in Patients With Acute Ischemic Stroke**: **ASSORT** Trial (Administration of Statin on Acute Ischemic Stroke Patient). Stroke. 2017 Nov;48(11):3057-3063.

Yu O, Eberg M, Benayoun S, et al. Use of **Statins** and the Risk of Death in Patients With **Prostate Cancer**. J Clin Oncol. 2013 Nov 4.

Yusuf S, Islam S, Chow CK, et al. Use of **secondary prevention drugs** for cardiovascular disease in the community in high-income, middle-income, and low-income countries (the PURE Study): a prospective epidemiological survey. Lancet 2011; DOI:10.1016/ S0140-6736(11)61215-4.

Yusuf S, Bosch J, Dagenais G, et al. **Cholesterol lowering** in intermediate-risk persons **without cardiovascular disease**. (**Hope-3**) N Engl J Med. DOI: 10.1056/NEJMoa1600176.

Yusuf S, Lonn E, Pais P, et al. **Blood-pressure and cholesterol** lowering in persons **without cardiovascular disease**. (**Hope-3**) N Engl J Med. DOI: 10.1056/NEJMoa1600177.

Zaharan NL, Williams D, Bennett K. Statins and Risk of Treated Incident **Diabetes** in a Primary Care Population. Br J Clin Pharmacol. 2012 Jul 30.

Zanni MV et al. 2013 American College of Cardiology-American Heart Association and **2004 Adult Treatment Panel III cholesterol guidelines applied to HIV**-infected patients with-without subclinical high-risk coronary plaque. AIDS 2014 Sep 10; 28:2061.

Zhan S, Tang M, Liu F, et al. **Ezetimibe for the prevention of cardiovascular disease and all-cause mortality events.** Cochrane Database Syst Rev. 2018 Nov 19;11:CD012502. Moderate- to high-quality evidence suggests that ezetimibe has modest beneficial effects on the risk of CVD endpoints, primarily driven by a reduction in non-fatal MI and non-fatal stroke, but it has little or no effect on clinical fatal endpoints. The cardiovascular benefit of ezetimibe might involve the reduction of LDL-C, total cholesterol and triglycerides. There is insufficient evidence to determine whether ezetimibe increases the risk of adverse events due to the low and very low quality of the evidence. The evidence for beneficial effects was mainly obtained from individuals with established atherosclerotic cardiovascular disease (ASCVD, predominantly with acute coronary syndrome) administered ezetimibe plus statins. However, there is limited evidence regarding the role of ezetimibe in primary prevention and the effects of ezetimibe monotherapy in the prevention of CVD, and these topics thus requires further investigation.

Zhang H, Plutzky J, Skentzos S, Morrison F, Mar P, Shubina M, et al. **Discontinuation of statins** in routine care settings. A cohort study. Ann Intern Med. 2013;158:526-34.

Zhang H, Plutzky J, Shubina M, et al. Continued **Statin** Prescriptions After **Adverse Reactions** and Patient Outcomes: A Cohort Study. Ann Intern Med. 2017 Jul 25.

Zhang H, Plutzky J, Shubina M, Turchin A. **Continued statin prescriptions after adverse reactions and patient outcomes**. A cohort study. Ann Intern Med. 2017. [Epub ahead of print]. doi:10.7326 /M16-0838

Zhang XL, Liu M, Qian J, et al. **Statin use and risk of kidney cancer**: a meta-analysis of observational studies and randomized trials. Br J Clin Pharmacol. 2013 Jul 23

Zhang W, Zhang Y, Li CW, et al. Effect of **Statins on COPD**: A Meta-Analysis of Randomized Controlled Trials. Chest. 2017 Dec;152(6):1159-1168.

Zhao YY, Weir MA, Manno M, et al. New **fibrate use and acute renal outcomes in elderly** adults: a population-based study. Ann Intern Med. 2012 Apr 17;156(8):560-9.

Zheng Z, Jayaram R, Jiang L, et al. **Perioperative Rosuvastatin** in Cardiac Surgery. (STICS) N Engl J Med. 2016 May 5;374(18):1744-53.

Zewinger S, et al. Relations between lipoprotein(a) concentrations, **LPA genetic variants**, and the risk of mortality in patients with established coronary heart disease: a molecular and genetic association study. Lancet Diabetes Endocrinol. 2017 May 26.

Zhang Y, Vittinghoff E, Pletcher MJ, et al. Associations of Blood Pressure and Cholesterol Levels During **Young Adulthood With Later Cardiovascular Events**. J Am Coll Cardiol. 2019 Jul 23;74(3):330-341

Zhou Z, Rahme E, Pilote L. Are **statins created equal**? Evidence from randomized trials of pravastatin, simvastatin, and atorvastatin for cardiovascular disease prevention. Am Heart J. 2006 Feb;151(2):273-81. (InfoPOEMs: The overall effectiveness of statin therapy on the most important outcomes -- decreasing mortality, heart attacks, and strokes -- is not different among the 3 major statins. These are the results from a meta-analysis; no study has directly compared equivalent doses of 2 statins. (LOE = 1a))

Ziff OJ, Werring DJ. **Statins after intracranial haemorrhage**: seizing a new opportunity? Br J Clin Pharmacol. 2018 Sep 7.

Zissimopoulos JM, Barthold D, Brinton RD, et al. **Sex and Race Differences** in the Association Between Statin Use and the Incidence of Alzheimer Disease. JAMA Neurol. 2016 Dec 12.

Zupec JF, Marrs JC, Saseen JJ. Evaluation of **Statin Prescribing for Secondary Prevention in Primary Care** Following New Guideline Recommendations. Ann Pharmacother. 2016 Jan;50(1):17-21.

References: RxFiles Post-MI

[1] Antman EM, Anbe DT, Armstrong PW, et al. **ACC/AHA guidelines** for the management of patients with ST-elevation myocardial infarction (**STEMI**); A report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Committee to Revise the 1999 Guidelines for the Management of patients with acute myocardial infarction). J Am Coll Cardiol. **2004** Aug 4;44(3):E1-E211. http://www.acc.org/clinical/guidelines/stemi/index.pdf
Antman EM, Hand M, Armstrong PW, et al. 2007 focused update of the ACC/AHA 2004 guidelines for the management of patients with ST-elevation myocardial infarction: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Writing Group to Review New Evidence and Update the ACC/AHA 2004 Guidelines for the Management of Patients With ST-Elevation Myocardial Infarction). ***Circulation* 2007**: DOI: 10.1161/CIRCULATIONAHA.107.188209. Available at: http://circ.ahajournals.org. *J Am Coll Cardiol* 2007: DOI:10.1016/j.jacc.2007.10.001. Available at: http://content.onlinejacc.org. http://content.onlinejacc.org/cgi/content/full/j.jacc.2007.10.001v1
Kushner, Frederick G., Hand, Mary, Smith, Sidney C., et al. **2009 Focused Updates**: ACC/AHA Guidelines for the Management of Patients With ST-Elevation Myocardial Infarction (Updating the 2004 Guideline and 2007 Focused Update) and ACC/AHA/SCAI Guidelines on Percutaneous Coronary Intervention (Updating the 2005 Guideline and 2007 Focused Update): A Report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. J Am Coll Cardiol 2009 0: j.jacc.2009.10.015 http://content.onlinejacc.org/cgi/reprint/j.jacc.2009.10.015v1.pdf
Mehta LS, Beckie TM, DeVon HA, et al. **Acute Myocardial Infarction in Women**: A Scientific Statement From the American Heart Association (**AHA 2016**). Circulation. 2016 Jan 25.
Ibanez B, James S, Agewall S, et al. **2017 ESC Guidelines** for the management of acute myocardial infarction in patients presenting with ST-segment elevation: The Task Force for the management of acute myocardial infarction in patients presenting with ST-segment elevation of the European Society of Cardiology (ESC). Eur Heart J. 2017 Aug 26.
O'Gara PT, Kushner FG, Ascheim DD et al. **2013 ACCF/AHA guideline for the management of st-elevation myocardial infarction**. (**STEMI**) A report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. Circulation 2012.

[2] Effect of ramipril on mortality and morbidity of survivors of acute myocardial infarction with clinical evidence of heart failure. The Acute Infarction Ramipril Efficacy (**AIRE**) Study Investigators. Lancet. 1993 Oct 2;342(8875):821-8.
[3] Yusuf S, Sleight P, Pogue J, et al., The Heart Outcomes Prevention Evaluation (**HOPE**) Study Investigators, Effects of an Angiotensin-Converting-Enzyme Inhibitor, Ramipril, on Cardiovascular Events in High-Risk Patients. N Engl J Med 2000 342: 145-153.
[4] Kober L, Torp-Pedersen C, Carlsen JE, et al. A clinical trial of the angiotensin-converting-enzyme inhibitor trandolapril in patients with left ventricular dysfunction after myocardial infarction. Trandolapril Cardiac Evaluation (**TRACE**) Study Group. N Engl J Med. 1995 Dec 21;333(25):1670-6.
[5] **GISSI-3**: effects of lisinopril and transdermal glyceryl trinitrate singly and together on 6-week mortality and ventricular function after acute myocardial infarction. Gruppo Italiano per lo Studio della Sopravvivenza nell'infarto Miocardico. Lancet. 1994 May 7;343(8906):1115-22.
[6] Packer M, Poole-Wilson PA, Armstrong PW, et al. Comparative effects of low and high doses of the angiotensin-converting enzyme inhibitor, lisinopril, on morbidity and mortality in chronic heart failure. **ATLAS** Study Group. Circulation. 1999 Dec 7;100(23):2312-8.
[7] The EURopean trial On reduction of cardiac events with Perindopril in stable coronary Artery disease Investigators. Efficacy of perindopril in reduction of cardiovascular events among patients with stable coronary artery disease: randomised, double-blind, placebo-controlled, multicentre trial (the **EUROPA** study). Lancet 2003; 362: 782-88.
[8] Swedberg K, Held P, Kjekshus J, et al. Effects of the early administration of enalapril on mortality in patients with acute myocardial infarction. Results of the Cooperative New Scandinavian Enalapril Survival Study II (**CONSENSUS II**) N Engl J Med. 1992 Sep 3;327(10):678-84.
[9] ISIS-4: a randomised factorial trial assessing early oral captopril, oral mononitrate, and intravenous magnesium sulphate in 58,050 patients with suspected acute myocardial infarction. **ISIS-4** (Fourth International Study of Infarct Survival) Collaborative Group. Lancet. 1995 Mar 18;345(8951):669-85.
[10] Pfeffer MA, Braunwald E, Moye LA, et al. Effect of captopril on mortality and morbidity in patients with left ventricular dysfunction after myocardial infarction. Results of the survival and ventricular enlargement trial. The **SAVE** Investigators. N Engl J Med. 1992 Sep 3;327(10):669-77.
[11] Major Outcomes in High-Risk Hypertensive Patients Randomized to Angiotensin-Converting Enzyme Inhibitor or Calcium Channel Blocker vs Diuretic. The Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial (**ALLHAT**). The ALLHAT Officers and Coordinators for the ALLHAT Collaborative Research Group. JAMA. 2002;288:2981-2997.
[12] Dickstein K, Kjekshus J. Effects of losartan and captopril on mortality and morbidity in high-risk patients after acute myocardial infarction: the **OPTIMAAL** randomised trial. Optimal Trial in Myocardial Infarction with Angiotensin II Antagonist Losartan.; OPTIMAAL Steering Committee of the OPTIMAAL Study Group. Lancet 2002 Sep 7;360(9335):752-60.
[13] Pfeffer MA, McMurray JJ, Velazquez EJ, et al. Valsartan in Acute Myocardial Infarction Trial Investigators (VALIANT). Valsartan, captopril, or both in myocardial infarction complicated by heart failure, left ventricular dysfunction, or both. N Engl J Med. 2003 Nov 13;349(20):1893-906. Epub 2003 Nov 10. (McMurray J, et al. The effect of valsartan, captopril, or both on atherosclerotic events after acute myocardial infarction: an analysis of the Valsartan in Acute Myocardial Infarction Trial (VALIANT). J Am Coll Cardiol. 2006 Feb 21;47(4):726-33. Epub 2006 Jan 26.) (McMurray J, et al. The effect of valsartan, captopril, or both on atherosclerotic events after acute myocardial infarction: an analysis of the Valsartan in Acute Myocardial Infarction Trial (VALIANT). J Am Coll Cardiol. 2006 Feb 21;47(4):726-33. Epub 2006 Jan 26.)
Califf RM, Lokhnygina Y, Velazquez EJ, McMurray JJ, et al. Usefulness of beta blockers in high-risk patients after myocardial infarction in conjunction with captopril and/or valsartan (from the VALsartan In Acute Myocardial Infarction [VALIANT] trial). Am J Cardiol. 2009 Jul 15;104(2):151-7. Epub 2009 Jun 3. PubMed PMID: 19576338. In conclusion, no evidence was found of adverse interactions between the angiotensin-receptor blocker valsartan and beta blockers or of a negative effect of the combination of valsartan, captopril, and beta blockers.
[14] Granger CB, McMurray JJ, Yusuf S, et al. CHARM Investigators and Committees. Effects of candesartan in patients with chronic heart failure and reduced left-ventricular systolic function intolerant to angiotensin-converting-enzyme inhibitors: the **CHARM-Alternative** trial. Lancet. 2003 Sep 6;362(9386):772-6. (Granger BB, et al.; for the CHARM investigators. Adherence to candesartan and placebo and outcomes in chronic heart failure in the CHARM programme: double-blind, randomised, controlled clinical trial. Lancet. 2005 Dec 10;366(9502):2005-2011.)
[15] McMurray JJ, Ostergren J, Swedberg K,et al.; CHARM Investigators and Committees. Effects of candesartan in patients with chronic heart failure and reduced left-ventricular systolic function taking angiotensin-converting-enzyme inhibitors: the **CHARM-Added** trial. Lancet. 2003 Sep 6;362(9386):767-71. (McMurray JJ, Young JB, Dunlap ME, et al. **Relationship of dose** of background angiotensin-converting enzyme inhibitor to the benefits of candesartan in Candesartan in Heart failure: Assessment of reduction in Mortality and morbidity (CHARM)-added trial. American Heart Journal 2006;151: 992-998)
[16] Parving HH, Lehnert H, Brochner-Mortensen J, et al. The effect of irbesartan on the development of diabetic nephropathy in patients with type 2 diabetes (**IRMA II**). Irbesartan in Patients with Type 2 Diabetes and Microalbuminuria Study Group. N Engl J Med 2001 Sep 20;345(12):870-8.
[17] Lewis EJ, Hunsicker LG, Clarke WR, et al. Renoprotective effect of the angiotensin-receptor antagonist irbesartan in patients with nephropathy due to type 2 diabetes (**IDNT**); Collaborative Study Group. N Engl J Med 2001 Sep 20;345(12):851-60.
[18] Brenner BM, Cooper ME, de Zeeuw D, et al. Effects of losartan on renal and cardiovascular outcomes in patients with type 2 diabetes and nephropathy; **RENAAL** Study Investigators. N Engl J Med 2001 Sep 20;345(12):861-9.
[19] Cicardi M, Zingale LC, Bergamaschini L, et al. Angioedema associated with angiotensin-converting enzyme inhibitor use: outcome after switching to a different treatment. Arch Intern Med. 2004 Apr 26;164(8):910-3.
[20] Pitt B, Remme W, Zannad F, et al.; **Eplerenone** Post-Acute Myocardial Infarction Heart Failure Efficacy and Survival Study Investigators. (**EPHESUS**) Eplerenone, a selective aldosterone blocker, in patients with left ventricular dysfunction after myocardial infarction. N Engl J Med. 2003 Apr 3;348(14):1309-21.
[21] Hjalmarson A, Elmfeldt D, Herlitz J, et al. Effect on mortality of metoprolol in acute myocardial infarction: a double blind randomised trial. *Lancet* 1981;ii:823-7.
[22] Janosi A, Ghali JK, Herlitz J, et al.; MERIT-HF Study Group. Metoprolol CR/XL in **postmyocardial** infarction patients with chronic heart failure: experiences from **MERIT-HF**. Am Heart J. 2003 Oct;146(4):721-8.
[23] Hjalmarson A, Goldstein S, Fagerberg B, et al. Effects of controlled-release metoprolol on total mortality, hospitalizations, and well-being in patients with heart failure: the Metoprolol CR/XL Randomized Intervention Trial in congestive heart failure (**MERIT-HF**). MERIT-HF Study Group. JAMA. 2000 Mar 8;283(10):1295-302.
[24] Gullestad L, Wikstrand J, et al.; for the MERIT-HF Study Group. What resting heart rate should one aim for when treating patients with heart failure with a beta-blocker? Experiences from the Metoprolol Controlled Release/Extended Release Randomized Intervention Trial in Chronic Heart Failure (MERIT-HF). J Am Coll Cardiol. 2005 Jan 18;45(2):252-9.
[25] Deedwania PC, et al. MERIT-HF Study Group. Efficacy, safety and tolerability of metoprolol CR/XL in patients with diabetes and chronic heart failure: experiences from MERIT-HF. Am Heart J. 2005 Jan;149(1):159-67.
[26] Randomised trial of intravenous atenolol among 16 027 cases of suspected acute myocardial infarction: **ISIS-1**. First International Study of Infarct Survival Collaborative Group. Lancet. 1986 Jul 12;2(8498):57-66.
[27] Dargie HJ. Effect of carvedilol on outcome after myocardial infarction in patients with left-ventricular dysfunction: the **CAPRICORN** randomised trial. Lancet. 2001 May 5;357(9266):1385-90.
[28] A randomized trial of propranolol in patients with acute myocardial infarction. I. Mortality results. JAMA. 1982 Mar 26;247(12):1707-14.
[29] Pedersen TR. The Norwegian Multicenter Study of Timolol after Myocardial Infarction. Circulation. 1983 Jun;67(6 Pt 2):I49-53.
[30] Boissel JP, Leizorovicz A, Picolet H, et al. Efficacy of acebutolol after acute myocardial infarction (**APSI** trial). The APSI Investigators. Am J Cardiol. 1990 Sep 25;66(9):24C-31C.
[31] Which Beta-blocker. Med Lett 2001;43:9-11. & Drugs for Hypertension, Treatment Guidelines from the Medical Letter 2003; Vol 1 (Issue 6) 33-40.
[32] Freemantle N, Cleland J, Young P, et al. Beta Blockade after myocardial infarction: systematic review and meta regression analysis. BMJ. 1999 Jun 26;318(7200):1730-7.
[33] Ko DT, Hebert PR, Coffey CS, et al. Adverse effects of beta-blocker therapy for patients with heart failure: a quantitative overview of randomized trials. Arch Intern Med. 2004 Jul 12;164(13):1389-94.
[34] Chen ZM, Pan HC, Chen YP, et al.; **COMMIT** (ClOpidogrel and Metoprolol in Myocardial Infarction Trial) collaborative group. Early intravenous then oral metoprolol in 45,852 patients with acute myocardial infarction: randomised placebo-controlled trial. Lancet. 2005 Nov 5;366(9497):1622-32. Second Chinese Cardiac Study COMMIT/CCS-2. Mean age 61, Fibrinolytic therapy 54%, Metoprolol 5mg IV over 2-3mins x 3 if HR & BP ok, then 15mins later 50mg po q6h Day 0-1, then 200mg controlled release od vs placebo x ~15days. ↓Reinfarction 2 vs 2.5%, ↓Ventricular fibrilation 2.5 vs 3 %, BUT ↑Cardiogenic shock 5 vs 3.9% (risk more with heart failure, systolic BP <120 & in the first 24hrs). INTERPRETATION: The use of early beta-blocker therapy in acute MI reduces the risks of reinfarction & ventricular fibrillation, but increases the risk of cardiogenic shock, esp. during the first day or so after admission. Consequently, it might generally be prudent to consider starting **beta-blocker therapy in hospital only when the haemodynamic condition after MI has stabilised**. (InfoPOEMs: The early use of metoprolol in patients with acute myocardial infarction who are also receiving thrombolytics and aspirin provides no short-term benefit compared with placebo. Since the early use, however, increases the risk of cardiogenic shock, it may be wise to delay starting metoprolol until the patient is hemodynamically stable. (LOE = 1b)).
[35] Poole-Wilson PA, Swedberg K, Cleland JG, et al.; Carvedilol Or Metoprolol European Trial Investigators. Comparison of carvedilol and metoprolol on clinical outcomes in patients with chronic heart failure in the Carvedilol Or Metoprolol European Trial (**COMET**): randomised controlled trial. Lancet. 2003 Jul 5;362(9377):7-13. (Metra M, Torp-Pedersen C, Swedberg K, et al. Influence of heart rate, blood pressure, and beta-blocker dose on outcome and the differences in outcome between carvedilol and metoprolol tartrate in patients with chronic heart failure: results from the COMET trial. Eur Heart J. 2005 Nov;26(21):2259-68. Epub 2005 Jul 21.)
[36] Borrello F, Beahan M, Klein L, et al. Reappraisal of beta-blocker therapy in the acute and chronic post-myocardial infarction period. Rev Cardiovasc Med. 2003;4 Suppl 3:S13-24.
[37] Scandinavian Simvastatin Survival Study Group. Randomized trial of cholesterol lowering in 4444 patients with coronary heart disease: the Scandinavian Simvastatin Survival Study (**4S**). Lancet 1994;344:1383-9.
[38] Heart Protection Study Group.MRC/BHF **HPS** study of cholesterol lowering with simvastatin in 20,536 high-risk individuals: a randomised placebo-controlled trial. Lancet 2002 Jul 6;360(9326):7-22.
[39] Peter S Sever, Björn Dahlöf et al. Prevention of coronary and stroke events with atorvastatin in hypertensive patients who have average or lower-than-average cholesterol concentrations, in the Anglo-Scandinavian Cardiac Outcomes Trial–Lipid Lowering Arm (**ASCOT-LLA**): a multicentre randomised controlled trial Lancet 2003; **361:** 1149-58. Online April 2, 2003. {RxFiles Q&A Summary: http://www.rxfiles.ca/acrobat/Lipid-Q&A-ASCOT.pdf }
[40] Cannon C, Braunwald E, McCabe C, et al. Comparison of Intensive and Moderate Lipid Lowering with Statins after Acute Coronary Syndromes (**PROVE IT-TIMI 22**). New Engl J Med 2004; 350. Online April 8, 2004. {RxFiles Q&A Summary: http://www.rxfiles.ca/acrobat/Lipid-Q&A-Prove-It.pdf }
[41] Schwartz G, Olsson A, Ezekowitz M, Ganz P, et al. Effects of atorvastatin on early recurrent ischemic events in acute coronary syndromes (**MIRACL**). JAMA 2001;285:1711-8.
[42] Long-Term Intervention with Pravastatin in Ischeamic Heart Disease (**LIPID**) Study Group. Prevention of cardiovascular events and death with pravastatin in patients with coronary heart disease and a broad range of initial cholesterol levels. N Engl J Med 1998; 339:1349-1357.
[43] Sacks FM, Pfeffer MA, Moye LA, et al. The effect of pravastatin on coronary events after myocardial infarction in patients with average cholesterol levels (**CARE**). N Engl J Med 1996;335:1001-9.
[44] Rosuvastatin--a new lipid-lowering drug. Med Lett Drugs Ther. 2003 Oct 13;45(1167):81-3.
[45] Carswell CI, Plosker GL, Jarvis B. Rosuvastatin. Drugs. 2002;62(14):2075-85; discussion 2086-7.
Ridker PM, Danielson E, Fonseca FA, Genest J, et al. the **JUPITER** Study Group. Rosuvastatin to Prevent Vascular Events in Men and Women with Elevated C-Reactive Protein. N Engl J Med. 2008 Nov 9. [Epub ahead of print] In this trial of apparently healthy persons without hyperlipidemia but with elevated high-sensitivity C-reactive protein levels, rosuvastatin significantly reduced the incidence of major cardiovascular events.
[46] Shepherd J, Blauw GJ, Murphy MB, et al.; PROSPER study group. PROspective Study of Pravastatin in the Elderly at Risk. Pravastatin in elderly individuals at risk of vascular disease (**PROSPER**): a randomised controlled trial. Lancet. 2002;360:1623-30.
[47] Yusuf S et al. Effects of clopidogrel in addition to aspirin in patients with acute coronary syndromes without ST segment elevation (Clopidogrel in unstable angina to prevent recurrent events (CURE). N Engl J Med 2001; 345: 494-502. Mean age 64, Major bleed 3.7 vs 2.7 %, (Budaj A, Yusuf S, Mehta SR, et al.; Clopidogrel in Unstable angina to prevent Recurrent Events (**CURE**) Trial Investigators. Benefit of clopidogrel in patients with acute coronary syndromes without ST-segment elevation in various risk groups. Circulation. 2002 Sep 24;106(13):1622-6.)
[48] Randomised trial of intravenous streptokinase, oral aspirin, both, or neither among 17,187 cases of suspected acute myocardial infarction: ISIS-2. ISIS-2 (Second International Study of Infarct Survival) Collaborative Group. Lancet. 1988 Aug 13;2(8607):349-60. Baigent C, Collins R, Appleby P, Parish S, Sleight P, Peto R. ISIS-2: 10 year survival among patients with suspected acute myocardial infarction in randomised comparison of intravenous streptokinase, oral aspirin, both, or neither. The ISIS-2 (Second International Study of Infarct Survival) Collaborative Group. BMJ. 1998 May 2;316(7141):1337-43.
Berger JS, Stebbins A, Granger CB, et al. Initial Aspirin Dose and Outcome Among ST-Elevation Myocardial Infarction Patients Treated With Fibrinolytic Therapy. Circulation. 2007 Dec 17; [Epub ahead of print] These data suggest that an **initial dose of 162 mg aspirin** may be as effective as and perhaps safer than 325 mg for the acute treatment of ST-elevation myocardial infarction.
[49] CAPRIE Steering Committee. A randomized, blinded trial of clopidogrel vs aspirin in patients at risk of ischemic events (**CAPRIE**). Lancet 1996; 348:1329-39.
[50] Sabatine MS, et al. Addition of Clopidogrel to Aspirin and Fibrinolytic Therapy for Myocardial Infarction with ST-Segment Elevation (**CLARITY-TIMI 28**). N Engl J Med. 2005 Mar 9; [Epub] (N=3491,Groups: Plavix 300mg x1 then 75mg od (median **4 doses** given) until angiography vs placebo had 30 day mortality of less than 5%, age <75yr Mean age 57, >2/3 of pts fibrin specific lytic, excluded high bleeding risk pts (1.9 vs 1.7% major bleeds), few CABG performed, thus select pts were studied, mechanism may be to prevent reocclusion) (InfoPOEMs: Adding clopidogrel to aspirin and fibrinolytic therapy during the first week in patients with ST- segment elevation myocardial infarction reduces the likelihood of recurrent myocardial infarction and ischemia leading to revascularization over a 30-day period (number needed to treat = 15). The short-term risk of major bleeding was low. This trial does not address how long patients should continue to take clopidogrel after the first week of treatment. (LOE = 1b)) (Sabatine MS, Cannon CP, Gibson CM, et al.; Clopidogrel as Adjunctive Reperfusion Therapy (CLARITY)-Thrombolysis in Myocardial Infarction (TIMI) 28 Investigators. Effect of clopidogrel pretreatment before percutaneous coronary intervention in patients with ST-elevation myocardial infarction treated with fibrinolytics: the **PCI-CLARITY** study. JAMA. 2005 Sep 14;294(10):1224-32. CONCLUSIONS: Clopidogrel pretreatment significantly reduces the incidence of cardiovascular death or ischemic complications both before and after PCI and without a significant increase in major or minor bleeding. These data add further support to the early use of clopidogrel in STEMI and the strategy of routine clopidogrel pretreatment in patients undergoing PCI).
[51] Chen ZM, Jiang LX, Chen YP, et al. **COMMIT** (ClOpidogrel and Metoprolol in Myocardial Infarction Trial) collaborative group. Addition of clopidogrel to aspirin in 45,852 patients with acute myocardial infarction: randomised placebo-controlled trial. Lancet. 2005 Nov 5;366(9497):1607-21. COMMIT/CCS-2 trial (Mean age 61, n=45,852, <24hr since MI symptom onset, primary PCI or high risk bleeding were excluded, 54% rec'd thrombolysis (primarily non fibrin specific: urokinase) , & <5% went on to have angiography, Plavix 75mg od (no loading dose) + ASA162mg od vs ASA 162mg od for a **mean of 15 days**, Death/MI/stroke 9.2 vs 10.1%, **Death** 7.5 vs 8.1%, Major Bleeding both equal ~0.6%, Minor bleeds 3.6 vs 3.1%). INTERPRETATION: In a wide range of patients with acute MI, adding clopidogrel 75 mg daily to aspirin and other standard treatments (such as fibrinolytic therapy) safely reduces mortality and major vascular events in hospital, and should be considered routinely.
[52] Bhatt DL, Fox KA, Hacke W, et al. Clopidogrel and Aspirin versus Aspirin Alone for the Prevention of Atherothrombotic Events. N Engl J Med. 2006 Mar 12; (**Charisma**) [Epub ahead of print] (InfoPOEMs: The use of the combination of clopidogrel (Plavix) and aspirin should be limited to carefully defined groups of patients with acute coronary syndromes. It is not recommended for the broader group of patients with coronary disease, cerebrovascular disease, or multiple risk factors such as diabetes, hyperlipidemia, & hypertension. (LOE = 1b))
[53] Wallentin L, Becker RC, Budaj A, et al. PLATO Investigators. Ticagrelor versus Clopidogrel in Patients with Acute Coronary Syndromes. N Engl J Med. 2009 Aug 30. (1o NNT=53/1yr, Major bleed non-CABG:including fatal intracranial NNH=143/1yr)
[54] Wiviott SD, Braunwald E, McCabe CH, et al.; the TRITON-TIMI 38 Investigators. Prasugrel versus Clopidogrel in atients with Acute Coronary Syndromes. N Engl J Med. 2007 Nov 4; [Epub ahead of print] In patients with acute coronary syndromes with scheduled percutaneous coronary intervention, prasugrel therapy was associated with significantly reduced rates of ischemic events, including stent thrombosis, but with an increased risk of major bleeding, including fatal bleeding. Overall mortality did not differ significantly between treatment groups.
[55] The **2017 Canadian Hypertension** Education Program **Recommendations** www.hypertension.ca
(Khan NA, McAlister FA, Campbell NR, Feldman RD, et al.; Canadian Hypertension Education Program. The 2004 Canadian recommendations for the management of hypertension: Part II--Therapy. Can J Cardiol. 2004 Jan;20(1):41-54.)
Canadian Hypertension Education Program. 2011 CHEP recommendations for the management of hypertension. http://hypertension.ca/chep/wp-content/uploads/2011/05/FullCHEPRecommendations_EN_2011.pdf
Hackam DG, Quinn RR, Ravani P, et al. Canadian Hypertension Education Program. The 2013 Canadian Hypertension Education Program (CHEP) Recommendations for Blood Pressure Measurement, Diagnosis, Assessment of Risk, Prevention, and Treatment of Hypertension. Can J Cardiol. 2013 Mar 28.
Canadian Hypertension Education Program. 2011 CHEP recommendations for the management of hypertension. http://hypertension.ca/chep/wp-content/uploads/2011/05/FullCHEPRecommendations_EN_2011.pdf
Dasgupta K, Quinn RR, Zarnke KB, et al. Canadian Hypertension Education Program. The **2014 Canadian Hypertension Education Program** Recommendations for Blood Pressure Measurement, Diagnosis, Assessment of Risk, Prevention, and Treatment of Hypertension.

Can J Cardiol. 2014 May;30(5):485-501.
Leung AA, Nerenberg K, Daskalopoulou SS, et al; CHEP Guidelines Task Force. Hypertension Canada's **2016 CHEP guidelines** for blood pressure measurement, diagnosis, assessment of risk, prevention and treatment of hypertension.
Can J Cardiol 2016 (accepted manuscript) doi: 10.1016/j.cjca.2016.02.066 www.onlinecjc.ca/article/S0828-282X(16)00192-6/pdf (accessed April 11, 2016).
Leung AA, Daskalopoulou SS, Dasgupta K, et al. **Hypertension Canada's 2017 Guidelines for Diagnosis, Risk Assessment, Prevention, and Treatment of Hypertension in Adults**. Can J Cardiol. 2017 May;33(5):557-576
Nerenberg KA, Zarnke KB, Leung AA, et al. **Hypertension Canada's 2018 guidelines** for diagnosis, risk assessment, prevention, and treatment of hypertension in adults and children. Can J Cardiol 2018; accepted for publication February 20, 2018.

[56] Genest J, McPherson R, Frohlich J, et al. **2009 Canadian** Cardiovascular Society/Canadian guidelines for the diagnosis and treatment of dyslipidemia and prevention of cardiovascular disease in the adult - 2009 recommendations. Can J Cardiol. 2009 Oct;25(10):567-79.
McPherson R, Frohlich J, Fodor G, Genest J. **Canadian 2006** Cardiovascular Society position statement -- Recommendations for the diagnosis and treatment of dyslipidemia and prevention of cardiovascular disease. Can J Cardiol. 2006 Sep;22(11):913-27. (Genest J, Frohlich J, Fodor G, et al.; Working Group on **Hypercholesterolemia** and Other Dyslipidemias. Recommendations for the management of dyslipidemia and the prevention of cardiovascular disease: summary of the **Canadian 2003 update**. CMAJ. 2003 Oct 28;169(9):921-4. http://www.cmaj.ca/cgi/data/169/9/921/DC1/1 Full Report.)
Anderson TJ, Grégoire J, Hegele RA, et al. **2012 Update of the Canadian Cardiovascular Society Guidelines** for the diagnosis and treatment of dyslipidemia for the prevention of cardiovascular disease in the adult.
Can J Cardiol 2013;29(2):151-67. www.onlinecjc.ca/article/S0828-282X(12)01510-3/fulltext (accessed February 5, 2013).
Anderson TJ, Grégoire J, Pearson GJ, et al. **2016** Canadian Cardiovascular Society guidelines for the management of **dyslipidemia** for the prevention of cardiovascular disease in the adult. Can J Cardiol 2016 [accepted manuscript online], doi: 10.1016/j.cjca.2016.07.510.

[57] Canadian 2008 Guidelines (Sept 2008): http://www.diabetes.ca/files/cpg2008/cpg-2008.pdf
Canadian 2003 Diabetes Guidelines http://www.diabetes.ca/cpg2003/download.aspx Harris SB, Lank CN. Recommendations from the Canadian Diabetes Association. 2003 guidelines for prevention and management of diabetes and related cardiovascular risk factors. Can Fam Physician. 2004 Mar;50:425-33. (Meltzer S, Leiter L, Daneman D, et al 1998. Clinical practice guidelines for the management of diabetes in Canada. CMAJ 1998;159 (8 Suppl)).

Canadian Diabetes 20013 Guidelines (April 2013): http://guidelines.diabetes.ca/

NOTE: Additional RxFiles Related Materials & Drug Comparison Charts: see www.RxFiles.ca {eg. Lipid Landmark Trials; Comparison Charts: ACEI, Beta-Blocker, Antithrombotic, Lipid Lowering}

Additional refs:

Abbasi J. **Do All Patients Need β-Blockers After a Heart Attack**? JAMA. 2018 Mar 6;319(9):853-855.
Abbate A, Van Tassell BW, Christopher S, et al. Effects of **Prolastin C (**Plasma-Derived Alpha-1 Antitrypsin) on the Acute Inflammatory Response in Patients With ST-Segment Elevation Myocardial Infarction (from the VCU-Alpha 1-RT Pilot Study). Am J Cardiol. 2015 Jan 1;115(1):8-12.
Abbate A, Kontos MC, Abouzaki NA, et al. Comparative Safety of Interleukin-1 Blockade With **Anakinra** in Patients With ST-Segment Elevation Acute Myocardial Infarction (from the VCU-ART and VCU-ART2 Pilot Studies). Am J Cardiol. 2015 Feb 1;115(3):288-92.
Abramsohn E, Decker C, Garavalia B, et al. 'I'm not just a heart. I'm a whole person here': A qualitative study of **women with MI to improve sexual outcomes**. JAHA 2013.
Abuzaid A, Fabrizio C, Felpel K, et al. **Oxygen Therapy** in Patients with Acute Myocardial Infarction: A Systemic Review and Meta-Analysis. Am J Med. 2018 Mar 5.
Acharya T, Aspelund T, Jonasson TF, et al. Association of **Unrecognized Myocardial Infarction With Long-term Outcomes** in Community-Dwelling Older Adults: The ICELAND MI Study. JAMA Cardiol. 2018 Oct 10.
ACCF/AHA 2011 Focused Update of the Guidelines for the Management of Patients With **Unstable Angina/Non-ST-Elevation Myocardial Infarction (Updating the 2007 Guideline):** A Report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. J Am Coll Cardiol 2011 0: j.jacc.2011.02.009. http://content.onlinejacc.org/cgi/reprint/j.jacc.2011.02.009v1.pdf
ACC/AHA/SCAI 2015 Focused Update on **Primary Percutaneous Coronary Intervention** for Patients With ST-Elevation Myocardial Infarction: An Update of 2011 ACCF/AHA/SCAI Guideline for Percutaneous Coronary Intervention and the 2013 ACCF/AHA Guideline for the Management of ST-Elevation Myocardial Infarction: Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines and the Society for Cardiovascular Angiography and Interventions. J Am Coll Cardiol. 2015 Oct 21. pii: S0735-1097(15)06797-2.
Adabag AS, Therneau TM, Gersh BJ, Weston SA, Roger VL. **Sudden death after** myocardial infarction. JAMA. 2008 Nov 5;300(17):2022-9. The risk of sudden cardiac death following MI in community practice has declined significantly over the past 30 years. Sudden cardiac death is independently associated with heart failure but not with recurrent ischemia.
Agarwal S, Sud K, Thakkar B, et al. **Changing Trends of Atherosclerotic Risk Factors** Among Patients With Acute Myocardial Infarction and Acute Ischemic Stroke. Am J Cardiol. 2017 Mar 31.
Agarwal M, Agrawal S, Garg L, et al. Effect of **Chronic Obstructive Pulmonary Disease** on In-Hospital Mortality and Clinical Outcomes After ST-Segment Elevation Myocardial Infarction. Am J Cardiol. 2017 May 15;119(10):1555-1559.
Andersson DP, Trolle Lagerros Y, Grotta A, et al. Association between treatment for **erectile dysfunction and death or cardiovascular outcomes after myocardial infarction**. Heart. 2017 Mar 9.
AHA Writing Group Members, Roger VL, Go AS, Lloyd-Jones DM, et al; on behalf of the American Heart Association Statistics Committee and Stroke Statistics Subcommittee, Roger VL, Turner MB; On behalf of the American Heart Association Heart Disease and Stroke Statistics Writing Group. Executive Summary: **Heart Disease and Stroke Statistics—2011 Update**: A Report From the American Heart Association. Circulation. 2011 Feb 1;123(4):459-463.
Akpek M, Kaya MG, Lam YY, et al. Relation of **Neutrophil/Lymphocyte Ratio to Coronary Flow** to In-Hospital Major Adverse Cardiac Events in Patients With ST-Elevated Myocardial Infarction Undergoing Primary Coronary Intervention. Am J Cardiol. 2012 May 17.
Albrektsen G, Heuch I, Løchen M-L, et al. **Lifelong gender gap** in risk of incident myocardial infarction: The **Tromsø Study**. *JAMA Intern Med* DOI:10.1001/JAMAINTERNMED.2016.5451.
Aldous SJ, Richards M, Cullen L et al. Diagnostic and prognostic utility of early measurement with **high-sensitivity troponin T assay** in patients presenting with chest pain. CMAJ. 2012 Mar 20;184(5):E260-8.
Aldrovandi A, Cademartiri F, Arduini D, et al. Computed tomography coronary **angiography** in patients with acute myocardial infarction with significant coronary stenosis. Circulation 2012.
Alpert JS, Thygesen K, Jaffe A, White HD. The **universal definition** of myocardial infarction: a consensus document: ischaemic heart disease. Heart. 2008 Oct;94(10):1335-41.
Akesson A, Weismayer C, Newby PK, et al. Combined effect of low-risk **dietary and lifestyle** behaviors in primary prevention of myocardial infarction in women. Arch Intern Med 2007; 167:2122-2127.
Akesson A, Larsson SC, Discacciati A, et al. **Low-Risk Diet and Lifestyle Habits** in the Primary Prevention of Myocardial Infarction in Men: A Population-Based Prospective Cohort Study. J Am Coll Cardiol. 2014 Sep 30;64(13):1299-306.
Alcántara C, Muntner P, Edmondson D, et al. Perfect storm: concurrent **stress and depressive symptoms** increase risk of myocardial infarction or death. Circ Cardiovasc Qual Outcomes. 2015 Mar;8(2):146-54.
Alnsasra H, Zahger D, Geva D, et al. Contemporary Determinants of Delayed Benchmark Timelines in Acute Myocardial Infarction in Men and Women. Am J Cardio. 2017
Amann U, Kirchberger I, Heier M, et al. Effect of **Renin-Angiotensin System Inhibitors on Long-Term Survival** in Patients Treated With Beta Blockers and Antiplatelet Agents After Acute Myocardial Infarction (from the MONICA/KORA Myocardial Infarction Registry). Am J Cardiol. 2014 Aug 1;114(3):329-35.
American College of Emergency Physicians Clinical Policies Subcommittee (Writing Committee) on Reperfusion Therapy for Acute ST-Segment Elevation Myocardial Infarction, Promes SB, Glauser JM, Smith MD, et al. Clinical Policy: **Emergency Department Management of Patients Needing Reperfusion Therapy for Acute ST-Segment Elevation Myocardial Infarction**. Ann Emerg Med. 2017 Nov;70(5):724-739.
Amier RP, Smulders MW, van der Flier WM, et al. Long-Term Prognostic Implications of **Previous Silent Myocardial Infarction** in Patients Presenting With Acute Myocardial Infarction. JACC Cardiovasc Imaging. 2018 Apr 13.
Amin AP, Salisbury AC, McCullough PA, et al. Trends in the incidence of **acute kidney injury** in patients hospitalized with acute myocardial infarction. Arch Intern Med. 2012;172(3):246-253.
Andell P, Koul S, Martinsson A, et al. Impact of **chronic obstructive pulmonary disease** on morbidity and mortality after myocardial infarction. *Open Heart* 2014.
Andell P, Erlinge D, Smith JG, et al. **β-blocker use and mortality in COPD** patients after myocardial infarction: a Swedish nationwide observational study. J Am Heart Assoc. 2015 Apr 8;4(4).
Anderson JL, Morrow DA. **Acute Myocardial Infarction**. N Engl J Med. 2017 May 25;376(21):2053-2064
Andersen MJ, Ersbøll M, Axelsson A, et al. **Sildenafil** and Diastolic Dysfunction After Acute Myocardial Infarction in Patients With Preserved Ejection Fraction:The Sildenafil and Diastolic Dysfunction After Acute Myocardial Infarction(SIDAMI) Trial. Circulation. 2013 Mar 19;127(11):1200-1208.
Andersohn F, Suissa S, Garbe E. Use of first- and second-generation **cyclooxygenase-2-selective** nonsteroidal antiinflammatory drugs & risk of **acute myocardial infarction**. Circulation. 2006 Apr 25;113(16):1950-7. Epub 2006 Apr 17. Current use of etoricoxib was associated with a 2.09-fold (95% confidence interval [CI], 1.10 to 3.97) risk of AMI compared with no use of NSAIDs during the prior year. Current use of rofecoxib (RR=1.29; 95% CI, 1.02 to 1.63), celecoxib (RR=1.56; 95% CI, 1.22 to 2.00), and diclofenac (RR=1.37; 95% CI, 1.17 to 1.59) also significantly increased the AMI risk. For current use of valdecoxib, the RR was 4.60 (95% CI, 0.61 to 34.51). RRs appeared to increase with higher daily doses of COX-2 inhibitors and were also increased in patients without major cardiovascular risk factors.
Andersson C, Lyngbæk S, Nguyen CD, et al. Association of **clopidogrel** treatment with risk of mortality and cardiovascular events following myocardial infarction in patients with and without **diabetes**. JAMA 2012; 308: 882-889.
Andersson C, Shilane D, Go AS, et al. **Beta-blocker therapy and cardiac events** among patients with newly diagnosed coronary heart disease.*J Am Coll Cardiol* 2014.
Anderson JL, Adams CD, Antman EM, et al. **2012 ACCF/AHA focused update** incorporated into the ACCF/AHA 2007 guidelines for the management of patients with **unstable angina/non-ST-elevation myocardial infarction**: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. Circulation. 2013;127:e663-828.
Anderson L, Taylor RS. **Cardiac rehabilitation** for people with heart disease: an overview of Cochrane systematic reviews. Cochrane Database of Systematic Reviews 2014, Issue 12. Art. No.: CD011273. DOI: 10.1002/14651858.CD011273.pub2. Exercise-based cardiac rehabilitation is an effective and safe therapy to be used in the management of clinically stable people following myocardial infarction or percutaneous coronary intervention or who have heart failure. Future RCTs of cardiac rehabilitation need to improve their reporting methods and reflect the real world practice better including the recruitment of higher risk people and consideration of contemporary models of cardiac rehabilitation delivery, and identify effective interventions for enhancing adherence to rehabilitation.
Antman EM, et al. Enoxaparin versus Unfractionated Heparin with Fibrinolysis for ST-Elevation Myocardial Infarction. (**EXTRACT-TIMI 25**)N Engl J Med. 2006 Mar 20; [Epub ahead of print] Conclusions In patients receiving fibrinolysis for ST-elevation myocardial infarction, treatment with enoxaparin throughout the index hospitalization is superior to treatment with unfractionated heparin for 48 hours but is associated with an increase in major bleeding episodes. (InfoPOEMs: For every 1000 patients treated with enoxaparin instead of unfractionated heparin there were 15 fewer nonfatal myocardial infarctions (MIs), 7 fewer urgent revascularizations, and 6 fewer deaths, but there were 4 additional episodes of nonfatal major bleeding. (LOE = 1b))
Andraws R, Berger JS, Brown DL. Effects of antibiotic therapy on outcomes of patients with coronary artery disease. A meta-analysis of randomized controlled trials. JAMA 2005;293:2641-47. (InfoPOEMs: Antibiotic therapy is no more effective than placebo in reducing the morbidity or mortality in patients with acute coronary syndromes. (LOE = 1a-))
Apple FS. Edging closer to early optimal patient management with **high-sensitivity cardiac troponin assay**. Circulation. 2011 Jul 12;124(2):127-9.
Armstrong PW. A comparison of pharmacologic therapy with/without timely coronary intervention vs. primary percutaneous intervention early after ST-elevation myocardial infarction: the **WEST** (Which Early ST-elevation myocardial infarction Therapy) study. Eur Heart J. 2006 Jun 6; [Epub ahead of print]
Armstrong PW, Boden WE. **Reperfusion Paradox** in ST-Segment Elevation Myocardial Infarction. Ann Intern Med. 2011 Sep 20;155(6):389-91.
Armstrong PW et al. **Fibrinolysis or primary PCI** in ST-segment elevation myocardial infarction. (**Stream**) N Engl J Med 2013 Mar 10.
Amsterdam EA, Wenger NK, Brindis RG, et al. **2014 AHA/ACC Guideline for the Management of Patients With Non-ST-Elevation Acute Coronary Syndromes-NSTE-ACS-:** Executive Summary: A Report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. Circulation. 2014 Sep 23.
Arora S, Stouffer GA, Kucharska-Newton AM, et al. Twenty Year Trends and **Sex Differences** in Young Adults Hospitalized With **Acute Myocardial Infarction**. Circulation. 2019 Feb 19;139(8):1047-1056.
Antoniou T, Gomes T, Mamdani MM, et al. **Trimethoprim-sulfamethoxazole induced hyperkalaemia in elderly patients receiving spironolactone**: nested case-control study. BMJ. 2011 Sep 12;343:d5228. doi: 10.1136/bmj.d5228.
Aradi D, Komócsi A, et al. Impact of clopidogrel and potent P2Y 12 -inhibitors on mortality and stroke in patients with acute coronary syndrome or undergoing percutaneous coronary intervention: a systematic review and meta-analysis. Thromb Haemost. 2013 Jan;109(1):93-101.
Arefalk G, Hambraeus K, Lind L, et al. **Discontinuation of Smokeless Tobacco** and Mortality Risk after Myocardial Infarction. Circulation. 2014 Jun 23.
Arnold SV, Spertus JA, Masoudi FA, et al. Beyond medication prescription as performance measures: **Optimal secondary prevention medication dosing** after AMI. J Am Coll Cardiol 2013.
Arnold SV, Masoudi FA, Rumsfeld JS, et al. Derivation and validation of a risk standardization **model for benchmarking hospital performance** for health-related quality of life outcomes after acute myocardial infarction. Circulation. 2014 Jan 21;129(3):313-20
Aronow WS. **Heart Failure Complicating Acute Mtyocardial Infarction**. Heart Fail Clin. 2017 Jul;13(3):513-525.
Aslibekyan S, Levitan EB, Mittleman MA. Prevalent **cocaine** use and myocardial infarction. Am J Cardiol. 2008 Oct 15;102(8):966-9. Epub 2008 Aug 5.
Assessment of the Safety and Efficacy of a New Treatment Strategy with Percutaneous Coronary Intervention (ASSENT-4 PCI) investigators. Primary versus tenecteplase-facilitated percutaneous coronary intervention in patients with ST-segment elevation acute myocardial infarction (**ASSENT-4 PCI**): randomised trial. Lancet. 2006 Feb 18;367(9510):569-78.
Assmus B, et al. Transcoronary transplantation of **progenitor cells** after myocardial infarction. N Engl J Med. 2006 Sep 21;355(12):*1222-32.*
Åstrand M, Amilon C, Röshammar D, et al. Pharmacokinetic-pharmacodynamic modelling of **platelet response to ticagrelor in stable coronary artery disease** and **prior myocardial infarction** patients. Br J Clin Pharmacol. 2018 Nov 10.
Atzema CL, Austin PC, Huynh T, Hassan A, Chiu M, Wang JT, Tu JV. Effect of **marriage on duration of chest pain** associated with acute myocardial infarction before seeking care. CMAJ. 2011 Jul 18.
Auffret, Oger, Leurent, et al. Efficacy of Pre-hospital Use of **Glycoprotein IIb/IIIa Inhibitors** in ST-Segment Elevation Myocardial Infarction before Mechanical Reperfusion in a Rapid-transfer Network (From the Acute Myocardial Infarction Registry of Brittany). The American Journal of Cardiology. 2014.
Auger N, Potter BJ, Smargiassi A, et al. Association between quantity and duration of **snowfall** and risk of myocardial infarction. CMAJ 2017 February 13:189:E235-42.
Aversano T et al. Outcomes of **PCI at hospitals with or without on-site cardiac surgery**. (**CPORT**) N Engl J Med 2012 Mar 25.
Aviña-Zubieta JA, Abrahamowicz M, De Vera MA, et al. Immediate and past cumulative effects of **oral glucocorticoids on the risk of acute myocardial infarction** in rheumatoid arthritis: a population-based study. Rheumatology. 2013;52:68-75.
Aviña-Zubieta JA, Mai A, Amiri N, et al. Risk of Myocardial Infarction and Stroke in Patients with **Granulomatosis with Polyangiitis**: A Population-Based Study. Arthritis Rheumatol. 2016 May 23.
Badertscher P, Boeddinghaus J, Twerenbold R, et al. Direct Comparison of the **0/1h and 0/3h Algorithms for Early Rule-Out of Acute Myocardial Infarction**. Circulation. 2018 Jun 5;137(23):2536-2538.
Bagai A, Jollis JG, et al. **Emergency department bypass** for ST-segment-elevation myocardial infarction patients identified with a prehospital electrocardiogram: a report from the American Heart Association Mission: Lifeline program. Circulation. 2013;128:352–359.
Baklanov DV, Kaltenbach LA, Marso SP, et al. The prevalence and outcomes of **transradial percutaneous coronary interventional** for ST-segment elevation myocardial infarction. J Am Coll Cardiol 2013.
Bally M, Dendukuri N, Rich B, et al. **Risk of acute myocardial infarction with NSAIDs** in real world use: Bayesian meta-analysis of individual patient data. BMJ. 2017 May 9;357:j1909
Bandosz P, O'Flaherty M, Drygas W, et al. **Decline in mortality from coronary heart disease** in Poland after socioeconomic transformation: modelling study. BMJ 2012;344:d8136.
Banerjee A, Silver LE, Heneghan C, et al. **Relative familial clustering** of cerebral versus coronary ischemic events. Circ CardiovascGenet 2011; DOI:10.1161/CIRCGENETICS.110.959114. (for MI but not stroke)
Bangalore Sripal, Kumar Sunil, Wetterslev Jørn, et al. **Angiotensin receptor blockers and risk of myocardial infarction**: meta-analyses and trial sequential analyses of 147,020 patients from randomised trials. BMJ 2011;342:doi:10.1136/bmj.d2234 (26 April 2011). –no ↑ MI.
Bangalore S, Fonarow GC, Peterson ED, et al. **Age and gender differences** in quality of care and outcomes for patients with ST-segment elevation myocardial infarction. Am J Cardiol 2012.
Bangalore S, Pursnani S, Kumar S, et al. **Percutaneous coronary intervention versus optimal medical therapy** for prevention of spontaneous myocardial infarction in subjects with stable ischemic heart disease. Circulation. 2013 Feb 19;127(7):769-81.
Bangalore S, Amoroso N, Fusaro M, Kumar S, Feit F. Outcomes with various **drug-eluting or bare-metal stents** in patients with ST-segment elevation myocardial infarction. Circ Cardiovasc Interv 2013.
Bangalore S, Makani H, Radford M, et al. **Clinical Outcomes with β-blockers for Myocardial Infarction** A Meta-Analysis of Randomized Trials. Am J Med. 2014 Jun 10.
Bangalore S, Bhatt DL, Steg PG, et al. **ß-blockers and cardiovascular events in patients with and without myocardial infarction**: Post hoc analysis from the **CHARISMA** trial. Circ Cardiovasc Qual Outcomes 2014.
Bangalore S, Toklu B, Kotwal A, et al. **Anticoagulant therapy** during primary percutaneous coronary intervention for acute myocardial infarction: a meta-analysis of randomized trials in the era of **stents and P2Y12 inhibitors**. BMJ. 2014 Nov 11;349:g6419.
Bangalore S, Gupta N, Guo Y, et al. Outcomes with **invasive versus conservative management of cardiogenic shock** complicating acute myocardial infarction. *Am J Med* 2015.
Barrabes JA, Gupta A, Porta-Sanchez A, et al. Comparison of **Electrocardiographic Characteristics** in **Men** Versus **Women** <55 Years with Acute Myocardial Infarction (a Virgo Sub-Study). Am J Cardio. 2017.
Barreto-Filho JA, Wang Y, Rathore SS, et al. **Transfer Rates From Nonprocedure Hospitals** After Initial Admission and Outcomes Among Elderly Patients With Acute Myocardial Infarction. JAMA Intern Med. 2013 Dec 2.
Bates ER. Evolution From Fibrinolytic Therapy to a **Fibrinolytic Strategy** for Patients With ST-Segment-Elevation Myocardial Infarction. Circulation. 2014 Sep 30;130(14):1133-5.

Batra G, Svennblad B, Held C, et al. **All types of atrial fibrillation in the setting of myocardial infarction** are associated with impaired outcome. Heart. 2016 Jun 15;102(12):926-33.

Beavers Craig James, Dunn Steven P, Macaulay Tracy E. The Role of Angiotensin Receptor Blockers in Patients with Angiotensin-Converting Enzyme Inhibitor**–Induced Angioedema**. Articles Ahead of Print published on 1 April 2011, DOI 10.1345/aph.1P630. Ann Pharmacother ;45:520-524.

Beckman AL, Bucholz EM, Zhang W, et al. **Sex Differences in Financial Barriers** and the Relationship to Recovery After Acute Myocardial Infarction. J Am Heart Assoc. 2016 Oct 14;5(10)

Beigel R, Fefer P, Rosenberg N, et al. Antiplatelet Effect of Thienopyridine (**Clopidogrel or Prasugrel**) Pretreatment in Patients Undergoing **Primary Percutaneous Intervention** for ST Elevation Myocardial Infarction. Am J Cardiol. 2013 Aug 22.

Bell Alan D., Roussin André, Cartier Raymond, et al. The Use of **Antiplatelet Therapy in the Outpatient Setting**: Canadian Cardiovascular Society (**CCS**) Guidelines. The Canadian journal of cardiology 1 May 2011 volume 27 issue 3 Pages S1-S59.

Bell KJL, Doust J, Glasziou P, et al. Recognizing the Potential for **Overdiagnosis**: Are **High-Sensitivity Cardiac Troponin Assays** an Example? Ann Intern Med. 2019 Feb 5.

Bengtson LG, Chen LY, Chamberlain AM, et al. **Temporal Trends** in the Occurrence and Outcomes of **Atrial Fibrillation** in Patients With Acute Myocardial Infarction (from the Atherosclerosis Risk in Communities Surveillance Study). Am J Cardiol. 2014 Jun 18.

Berger JS, Elliott L, Gallup D, et al. **Sex differences** in mortality following acute coronary syndromes. JAMA 2009; 302:874-882. Sex-based differences existed in 30-day mortality among patients with ACS and vary depending on clinical presentation. However, these differences appear to be largely explained by clinical differences at presentation and severity of angiographically documented disease.

Berry C, McClure JD, Oldroyd KG. Meta-Analysis of **Death and Myocardial Infarction** in the **DEFINE-FLAIR and iFR-SWEDEHEART** Trials. Circulation. 2017 Dec 12;136(24):2389-2391.

Berry JD et al. **Lifetime risks** of cardiovascular disease. N Engl J Med 2012 Jan 26; 366:321.

Bertaina M, Ferraro I, Omedè P, et al. Meta-analysis Comparing Complete or Culprit Only **Revascularization in Patients With Multivessel Disease Presenting With Cardiogenic Shock.** Am J Cardiol. 2018 Aug 22.

Berton G, Cordiano R, Cavuto F, et al. Predictors of **Ten-Year Event-Free Survival** in Patients With Acute Myocardial Infarction (from the Adria, Bassano, Conegliano, and Padova Hospitals [**ABC**] Study on Myocardial Infarction). Am J Cardiol. 2012 Jan 3.

Berwanger O, Lopes RD, Moia DDF, et al. **Ticagrelor Versus Clopidogrel** in Patients With STEMI Treated With Fibrinolysis: **TREAT Trial**. J Am Coll Cardiol. 2019 Jun 11;73(22):2819-2828.

Berwanger O, Nicolau JC, Carvalho AC, et al. **Ticagrelor vs Clopidogrel After Fibrinolytic Therapy in Patients With ST-Elevation Myocardial Infarction**: A Randomized Clinical Trial. (**TREAT**) JAMA Cardiol. 2018 Mar 11.

Bhaskaran K., Hajat S., Haines A., et al.. Short term **effects of temperature** on risk of myocardial infarction in England and Wales: time series regression analysis of the Myocardial Ischaemia National Audit Project (MINAP) registry. BMJ 2010;341:c3823, doi: 10.1136/bmj.c3823 (Published 10 August 2010).

Bhaskaran K, Hajat S, Armstrong B, Haines A, Herrett E, Wilkinson P, et al. The effects of hourly differences in **air pollution** on the risk of myocardial infarction: case crossover analysis of the MINAP database. BMJ 2011;343:d5531.

Bhaskaran K, Armstrong B, Hajat S, et al. **Heat** and risk of myocardial infarction: hourly level case-crossover analysis of MINAP database. BMJ. 2012 Dec 13;345:e8050.

Bhatt DL, Fox KA, Hacke W, et al. Clopidogrel and Aspirin versus Aspirin Alone for the Prevention of Atherothrombotic Events. N Engl J Med. 2006 Mar 12; (**Charisma**) [Epub ahead of print] (InfoPOEMs: The use of the combination of clopidogrel (Plavix) and aspirin should be limited to carefully defined groups of patients with acute coronary syndromes. It is not recommended for the broader group of patients with coronary disease, cerebrovascular disease, or multiple risk factors such as diabetes, hyperlipidemia, & hypertension. (LOE = 1b))

Bhatt DL, Bonaca MP, Bansilal S, et al. Reduction in Ischemic Events With **Ticagrelor in Diabetic Patients With Prior Myocardial Infarction in PEGASUS-TIMI 54**. J Am Coll Cardiol. 2016 Jun 14;67(23):2732-40.

Bhatt NS, Solhpour A, Balan P, et al. Comparison of In-Hospital Outcomes With **Low-Dose Fibrinolytic Therapy** Followed by Urgent Percutaneous Coronary Intervention Versus Percutaneous Coronary Intervention Alone for Treatment of ST-Elevation Myocardial Infarction. Am J Cardiol. 2013 Mar 10.

Bittl JA, Bates ER, Kaul S. **Extended dual antiplatelet therapy** in patients with prior myocardial infarction. JAMA Cardiol 2016; DOI:10.1001/jamacardio.2016.2252.

Bittner V, Colantonio LD, Dai Y, et al. Association of Region and Hospital and Patient Characteristics With Use of **High-Intensity Statins After Myocardial Infarction** Among Medicare Beneficiaries. JAMA Cardiol. 2019 Jul 24.

Bjorck Lena; Wallentin Lars; Stenestrand Ulf; et al. **Medication** in Relation to ST-Segment Elevation Myocardial Infarction in Patients With a First Myocardial Infarction: Swedish Register of Information and Knowledge About Swedish Heart Intensive Care Admissions (RIKS-HIA). Arch Intern Med. 2010;170(15):1375-1381.

Blackshear JL, Cutlip DE, Roubin GS, et al. for the **CREST** Investigators. Myocardial Infarction After **Carotid Stenting and Endarterectomy**: Results From the Carotid Revascularization Endarterectomy Versus Stenting Trial. Circulation. 2011 Jun 7;123(22):2571-2578.

Blin P, Dureau-Pournin C, Lassalle R, et al. **Outcomes in Post-Myocardial Infarction patients** similar to those of the **PEGASUS-TIMI 54** trial: a cohort study in the French national claims database. Br J Clin Pharmacol. 2017 Mar 26.

Boden H, Ahmed TA, Velders MA, et al. **Peak and Fixed-Time High-Sensitive Troponin** for Prediction of Infarct Size, Impaired Left Ventricular Function, & Adverse Outcomes in Patients With First ST-Segment Elevation Myocardial Infarction Receiving Percutaneous Coronary Intervention. Am J Cardiol. 2013 Feb 25.

Boden WE, O'rourke RA, Teo KK, Hartigan PM, et al. Optimal Medical Therapy with or without PCI for Stable Coronary Disease. **COURAGE** Trial Research Group. N Engl J Med. 2007 Mar 26; [Epub ahead of print] As an initial management strategy in patients with stable coronary artery disease, PCI did not reduce the risk of death, myocardial infarction, or other major cardiovascular events when added to optimal medical therapy. PCI does not lower the rates of myocardial infarction or death in patients with stable coronary artery disease who receive optimal medical treatment, a large trial concluded. The study, released early online by NEJM, randomized nearly 2300 patients either to PCI with optimal medical therapy (intensive pharmacologic treatment plus lifestyle intervention) or to optimal medical therapy alone. After a median follow-up of almost 5 years, 19% in the PCI group died or had MIs, compared with 18.5% who received medical therapy alone. PCI patients were more likely to be free of angina after 1 and 3 years, but there was no significant difference after 5 years. One-third of patients in the medical therapy group ultimately required revascularization, while 21% in the PCI group needed additional revascularization. An editorialist concludes: "Patients whose condition is clinically unstable, who have left main coronary artery disease, or in whom medical therapy has failed to control symptoms remain candidates for revascularization, but PCI should not play a major role as part of a secondary prevention strategy."

Boden H, Velders MA, van der Hoeven BL, et al. **In-Hospital Major Bleeding** and Its Clinical Relevance in Patients With ST Elevation Myocardial Infarction Treated With **Primary Percutaneous Coronary Intervention**. Am J Cardiol. 2013 Nov 15;112(10):1533-9.

Body R, Carley S, McDowell G, et al. Rapid exclusion of acute myocardial infarction in patients with undetectable **troponin using a high-sensitivity assay**. J Am Coll Cardiol. 2011 Sep 20;58(13):1332-9.

Body R, Cook G, Burrows G, et al. Can **emergency physicians 'rule in' and 'rule out'** acute myocardial infarction with clinical judgement? Emerg Med J. 2014 Nov;31(11):872-6.

Body R, Mueller C, Giannitsis E, et al. The Use of **Very Low Concentrations of High-sensitivity Troponin T to Rule Out** Acute Myocardial Infarction Using a Single Blood Test. Acad Emerg Med. 2016 Sep;23(9):1004-13.

Body R, Carlton E. **Understanding cardiac troponin** part 1: avoiding troponinitis. Emerg Med J. 2017 Aug 7.

Boeddinghaus J, Nestelberger T, Twerenbold R, et al. **Direct Comparison** of **Four Very Early Rule-Out Strategies for Acute Myocardial Infarction** Using High-Sensitivity Cardiac Troponin I. Circulation. 2017 Mar 10.

Boersma E; The **Primary Coronary Angioplasty vs. Thrombolysis** Group. Does time matter? A pooled analysis of randomized clinical trials comparing primary percutaneous coronary intervention and in-hospital fibrinolysis in acute myocardial infarction patients. Eur Heart J. 2006 Apr;27(7):779-88. Epub 2006 Mar 2.

Bogaty P, Brophy JM. **What to Do Following Fibrinolysis** for ST-Elevation Myocardial Infarction: **Reappraising Routine Percutaneous Intervention**. JAMA Intern Med. 2017 May 30.

Boghdady A, Elbadry MI. Comparison of Successful Myocardial Reperfusion and Adverse Events in Patients With ST-Elevation Myocardial Infarction Who Underwent Rescue Percutaneous Coronary Intervention After Failed Fibrinolytic Therapy **With Versus Without Manual Coronary Thrombus Aspiration**. Am J Cardiol. 2015 Oct 15;116(8):1185-92.

Bolli R, Chugh AR, D'Amario D, et al. **Cardiac stem cells** in patients with ischaemic cardiomyopathy (**SCIPIO**): initial results of a randomised phase 1 trial. Lancet 2011; published online Nov 14. DOI:10.1016/S0140- 6736(11)61590-0.

Bolland Mark J, Avenell Alison, Baron John A, et al, Effect of **calcium supplements** on risk of myocardial infarction and cardiovascular events: meta-analysis. BMJ 2010;341:c3691, doi: 10.1136/bmj.c3691 (Published 29 July 2010).

Bolland MJ, Grey A, Avenell A, et al. **Calcium supplements with or without vitamin D** and risk of cardiovascular events: reanalysis of the Women's Health Initiative limited access dataset and meta-analysis. BMJ 2011; DOI: doi:10.1136/bmj.d2040.

Bonaca MP, Wiviott SD, Braunwald E, et al. American College of Cardiology/American Heart Association/European Society of Cardiology/World Heart Federation **Universal Definition** of Myocardial Infarction Classification System and the **Risk of Cardiovascular Death**: Observations From the **TRITON-TIMI 38** Trial (Trial to Assess Improvement *in Therapeutic Outcomes by Optimizing Platelet Inhibition With Prasugrel-Thrombolysis in Myocardial Infarction 38). Circulation. 2012 Jan 31;125(4):577-83.*

Bonaca MP, Bhatt DL, Cohen M, et al; **PEGASUS-TIMI 54** Steering Committee and Investigators. Long-Term Use of **Ticagrelor** in Patients with Prior Myocardial Infarction. N Engl J Med. 2015 Mar 14.

Bonaca MP, Sabatine MS. **Antiplatelet therapy for long-term secondary prevention** after myocardial infarction. JAMA Cardiol 2016.

Bonaca MP, Goto S, Bhatt DL, et al. **Prevention of Stroke with Ticagrelor** in Patients with Prior Myocardial Infarction: Insights from **PEGASUS-TIMI 54**. Circulation. 2016 Sep 20;134(12):861-871.

Bonnefoy E, Steg PG, Boutitie F, et al. Comparison of primary angioplasty and pre-hospital fibrinolysis in acute myocardial infarction (**CAPTIM**) trial: a 5-year follow-up. Eur Heart J. 2009 Jul;30(13):1598-606. Epub 2009 May 8. The 5-year follow-up is consistent with the 30-day outcomes of the trial, showing similar mortality for primary percutaneous coronary intervention and a policy of pre-hospital lysis followed by transfer to an interventional center. In addition, for patients treated within 2 h of symptom onset, **5-year mortality was lower** with **pre-hospital lysis**.

Booth JN 3rd, Levitan EB, Brown TM, et al. Effect of Sustaining **Lifestyle Modifications (Nonsmoking, Weight Reduction, Physical Activity, and Mediterranean Diet**) After Healing of Myocardial Infarction, Percutaneous Intervention, or Coronary Bypass (from the REasons for Geographic and Racial Differences in Stroke Study). Am J Cardiol. 2014 Apr 1.

Boothroyd LJ, Lambert LJ, Segal E, et al. Comparison of Outcomes of **Ambulance Users and Nonusers** in ST Elevation Myocardial Infarction. Am J Cardiol. 2014 Aug 12.

Bøtker HE, Kharbanda R, Schmidt MR, et al. **Remote ischaemic conditioning before hospital admission, as a complement to angioplasty**, and effect on myocardial salvage in patients with acute myocardial infarction: a randomised trial. Lancet. 2010 Feb 27;375(9716):727-34.

Bradley EH, et al. Strategies for **Reducing the Door-to-Balloon Time** in Acute Myocardial Infarction. N Engl J Med. 2006 Nov 13; [Epub ahead of print]

Bradley EH, Curry LA, Spatz ES, et al. **Hospital strategies for reducing risk-standardized mortality** rates in acute myocardial infarction. Ann Intern Med. 2012;156:618-26.

Bradley SM, Borgerding JA, Wood GB, et al. **Incidence, Risk Factors, and Outcomes** Associated With In-Hospital Acute Myocardial Infarction. JAMA Netw Open. 2019 Jan 4;2(1):e187348.

Bradshaw PJ, et al. Validity of the GRACE (Global Registry of Acute Coronary Events) **acute coronary syndrome prediction model** for six month post-discharge death in an independent data set. Heart. 2006 Jul;92(7):905-9. Epub 2005 Dec 30.

Brandis Kepler S, Hasin T, Benyamini Y, et al. Frequency of **Sexual Activity and Long-term Survival after** Acute Myocardial Infarction. Am J Med. 2019 Jul 8.

Brandt R J, Myerson R, Coca M, et al. Hospital admissions for myocardial infarction and stroke before and after the **trans-fatty acid restrictions** in New York. JAMA Cardiol 2017.

Brauer R, Douglas I, Smeeth L. The association between **antipsychotic agents** and the risk of myocardial infarction: a systematic review. Br J Clin Pharmacol. 2011 Dec;72(6):871-8. doi: 10.1111/j.1365-2125.2011.04043.x.

Bravo CA, Hirji SA, Bhatt DL, et al. **Complete versus culprit-only revascularisation** in ST elevation myocardial infarction with multi-vessel disease. Cochrane Database of Systematic Reviews 2017, Issue 5. Art. No.: CD011986. Compared with culprit-only intervention, the complete revascularisation strategy may be superior due to lower proportions of longterm cardiovascular mortality, long-term revascularisation, and long-term non-fatal myocardial infarction, but these findings are based on evidence of very low quality. TSA also supports the need for more RCTs in order to draw stronger conclusions regarding the effects of complete revascularisation on long-term all-cause mortality, long-term cardiovascular mortality, and long-term non-fatal myocardial infarction.

Brener SJ, Mehran R, Dressler O et al. Diabetes Mellitus, Myocardial Reperfusion, and Outcome in Patients With Acute ST-Elevation Myocardial Infarction Treated With **Primary Angioplasty** (from **HORIZONS AMI**). Am J Cardiol. 2012 Jan 12.

Brener SJ, Oldroyd KG, Maehara A, et al. Outcomes in Patients With ST-Segment Elevation Acute Myocardial Infarction Treated With **Clopidogrel** Versus **Prasugrel** (from the **INFUSE-AMI** Trial). Am J Cardiol. 2014 May 1;113(9):1457-60.

Bresee LC, Knudtson ML, Zhang J, et al; the Alberta Kidney Disease Network (AKDN); the Alberta Provincial Project for Outcome Assessment in Coronary Heart Disease (APPROACH). **Likelihood of coronary angiography among First Nations** patients with acute myocardial infarction. CMAJ. 2014 May 20.

Bretler DM, Hansen PR, Sørensen R, et al. **Discontinuation of hormone replacement therapy** after myocardial infarction and short term risk of adverse cardiovascular events: nationwide cohort study. BMJ. 2012 Mar 27;344:e1802.

Briffa T, Hickling S, Knuiman M, et al. **Long term survival** after evidence based treatment of acute myocardial infarction and revascularisation: follow-up of population based Perth MONICA cohort, 1984-2005. BMJ. 2009 Jan 26;338:b36. doi: 10.1136/bmj.b36. The improving trends in 12 year survival after a definite acute myocardial infarction are associated with progressive use of evidence based treatments during the initial admission to hospital and in the 12 months after the event. These changes in the management of acute myocardial infarction are probably contributing to the continuing decline in mortality from coronary heart disease in Australia.

Brown DF, Jaffer FA, Baker JN, Gurol ME. Case records of the Massachusetts General Hospital. Case 28-2013. A 52-year-old man with **cardiac arrest after an acute myocardial infarction**. N Engl J Med. 2013 Sep 12;369(11):1047-54.

Brugts JJ, Knetsch AM, Mattace-Raso FU, Hofman A, Witteman JC. **Renal function and risk of myocardial infarction** in an elderly population: the Rotterdam Study. Arch Intern Med. 2005 Dec 12-26;165(22):2659-65.

Buchanan DM, Arnold SV, Gosch KL, et al. Association of **Smoking Status** With Angina and Health-Related Quality of Life After Acute Myocardial Infarction. Circ Cardiovasc Qual Outcomes. 2015 Aug 25.

Buchner S, Satzl A, Debl K, et al. Impact of **sleep-disordered breathing** on myocardial salvage and infarct size in patients with acute myocardial infarction. Eur Heart J. 2014 Jan;35(3):192-9

Bucholz EM, Rathore SS, Gosch K, et al. Effect of **living alone** on patient outcomes after hospitalization for acute myocardial infarction. Am J Cardiol. 2011 Oct 1;108(7):943-8.

Bucholz EM, Strait KM, Dreyer RP, et al. Effect of **Low Perceived Social Support** on Health Outcomes in Young Patients With Acute Myocardial Infarction: Results From the VIRGO (Variation in Recovery: Role of Gender on Outcomes of Young AMI Patients) Study. J Am Heart Assoc. 2014 Sep 30;3(5).

Bucholz EM, Ma S, Mormand SLT, et al. **Race, socioeconomic status, and life expectancy** after acute myocardial infarction.Circulation 2015.

Bucholz EM, Butala NM, Rathore SS, et al. **Sex Differences** in Long-Term Mortality after Myocardial Infarction: A Systematic Review. Circulation. 2014 Jul 22.

Bucholz EM, Normand SL, Wang Y, et al. Life **Expectancy and Years of Potential Life Lost** After Acute Myocardial Infarction **by Sex and Race**: A Cohort-Based Study of Medicare Beneficiaries. J Am Coll Cardiol. 2015 Aug 11;66(6):645-55.

Bucholz EM, Beckman AL, Krumholz HA, et al. **Excess weight and life expectancy** after acute myocardial infarction: The obesity paradox reexamined. Am Heart J. 2016 Feb;172:173-81.

Bucholz E, Krumholz H, Krumholz H. **Underweight, markers of cachexia, and mortality** in acute myocardial infarction: A prospective cohort study of elderly Medicare beneficiaries. PLOS Medicine 2016.

Bucholz EM, Butala NM, Normand SL, et al. Association of **Guideline-Based Admission Treatments and Life Expectancy After Myocardial Infarction in Elderly Medicare Beneficiaries**. J Am Coll Cardiol. 2016 May 24;67(20):2378-91.

Bucholz EM, Strait KM, Dreyer RP, et al. **Sex differences** in young patients with acute myocardial infarction: A VIRGO study analysis. Eur Heart J Acute Cardiovasc Care. 2016 Aug 2.

Bucholz EM, Butala NM, Ma S, et al. **Life Expectancy after Myocardial Infarction**, **According to Hospital Performance**. N Engl J Med. 2016 Oct 6;375(14):1332-1342.

Bucholz EM, Beckman BS, Kiefe CI, et al. **Life years gained from smoking-cessation** counselling after myocardial infarction. *Am J Prev Med* 2016;.

Buckley T, Hoo SY, Fethney J, et. al, Triggering of acute coronary occlusion by **episodes of anger**. Eur Heart J Acute Cardiovasc Care. 2015 Feb 23. pii: 2048872615568969. [Epub ahead of print] PubMed PMID: 25713468.

Budiman T, Snodgrass K, Komatsu Chang A. Evaluation of **Pharmacist Medication Education and Post-discharge Follow-up** in Reducing Readmissions in Patients With ST-Segment Elevation Myocardial Infarction (STEMI). Ann Pharmacother. 2015 Dec 17.

Bularga A, Lee KK, Stewart S, et al. **High-Sensitivity Troponin and The Application of Risk Stratification Thresholds** in Patients with Suspected Acute Coronary Syndrome. Circulation. 2019 Sep 1.

Bulluck H, Dharmakumar R, Arai AE, et al. Cardiovascular Magnetic Resonance in Acute ST-Segment-Elevation Myocardial Infarction: Recent Advances, Controversies, and Future Directions. Circulation. 2018 May 1;137(18):1949-1964.

Burns JD, Rabinstein AA, Roger VL. Incidence and predictors of **myocardial infarction after transient ischemic attack**: A population-based study. Stroke. 2001; DOI:10.1161/STROKEAHA.110.593723

Cabello JB, Burls A, Emparanza JI, et al. **Oxygen therapy** for acute myocardial infarction. Cochrane Database Syst Rev 2010; 6: CD007160.

Canto J G, Rogers W J, Goldberg R J et al. Association of age and **sex with myocardial infarction symptom** presentation and in-hospital mortality. JAMA 2012; 307:813-822. (Women under 55 having an MI are more likely to present without chest pain)

Cantor WJ et al. for the **TRANSFER-AMI** Trial Investigators. Routine early angioplasty after fibrinolysis for acute myocardial infarction. N Engl J Med 2009 Jun 25; 360:2705. These findings support making every effort to transfer STEMI patients who have received **fibrinolytic** therapy to a PCI-capable hospital and perform angiography promptly, rather than delaying such action. Critics will wonder (as do the authors) what might have been achieved with a strategy of routine early transfer followed by selective use of angiography, as opposed to the routine transfer-for-angiography strategy studied in this trial. (Verheugt, Freek W.A. Routine Angioplasty after Fibrinolysis -- How Early Should "Early" Be? N Engl J Med 2009 360: 2779-2781)

Canto JG, Kiefe CI, Roger WJ, et al; NRMI Investigators. **Number of coronary heart disease risk factors and mortality** in patients with first myocardial infarction. JAMA. 2011;306(19):2120-2127.

Canto JG, Kiefe CI, Rogers WJ, et al; NRMI Investigators. **Atherosclerotic Risk Factors** and Their Association With **Hospital Mortality** Among Patients With First Myocardial Infarction (from the National Registry of Myocardial Infarction). Am J Cardiol. 2012 Jul 26.

Carlton E, Greenslade J, Cullen L, et al. Evaluation of **high-sensitivity cardiac troponin I level**s in patients with suspected acute coronary syndrome [online June 1, 2016].JAMA Cardiol. doi:10.1001/jamacardio.2016.1309.

Carrero JJ, Evans M, Szummer K, et al. **Warfarin**, **kidney dysfunction**, and outcomes following acute myocardial infarction in patients with **atrial fibrillation**. (**SWEDEHEART**) JAMA. doi:10.1001/jama.2014.1334.

Cassidy A, Mukamal KJ, Liu L, et al. High **anthocyanin intake (blueberries, strawberries)** is associated with a reduced risk of myocardial infarction in young and middle-aged women (NHS II). Circulation 2013.

Cavender MA, Bhatt DL, Stone GW, et al. Consistent Reduction in Periprocedural Myocardial Infarction With **Cangrelor** as Assessed by Multiple Definitions: Findings From CHAMPION PHOENIX (Cangrelor Versus Standard Therapy to Achieve Optimal Management of Platelet Inhibition). Circulation. 2016 Sep 6;134(10):723-33.

Cenko E, Yoon J, Kedev S, et al. **Sex Differences in Outcomes After STEMI**: Effect Modification by Treatment Strategy and Age. JAMA Intern Med. 2018 Apr 9.

Cerisano G, Buonamici P, Valenti R, et al. Early short-term **doxycycline** therapy in patients with acute myocardial infarction and left ventricular dysfunction to prevent the ominous progression to adverse remodelling: the **TIPTOP** trial. Eur Heart J. 2014 Jan;35(3):184-91

Chan Paul S., Patel Manesh R., Klein Lloyd W., et al. **Appropriateness of Percutaneous Coronary Intervention (PCI)**. JAMA. 2011;306(1):53-61.doi:10.1001/jama.2011.916.

Chang M, Lee CW, Ahn JM, et al. **Coronary Artery Bypass Grafting Versus Drug-Eluting Stents** Implantation for Previous Myocardial Infarction. Am J Cardiol. 2016 Jul 1;118(1):17-22.
Chapman AR, Adamson PD, Mills NL. **Assessment and classification of patients with myocardial injury and infarction** in clinical practice. Heart. 2016 Nov 2. pii: heartjnl-2016-309530.
Chapman AR, Anand A, Boeddinghaus J, et al. Comparison of the Efficacy and Safety of **Early Rule Out Pathways** for Acute Myocardial Infarction. Circulation. 2016 Dec 29.
Chapman AR, Shah ASV, Lee KK, et al. **Long-Term Outcomes in Patients With Type 2 Myocardial Infarction** and Myocardial Injury. Circulation. 2018 Mar 20;137(12):1236-1245.
Chatterjee K, Gupta T, Goyal A, et al. Association of **Obesity** With In-Hospital Mortality of Cardiogenic Shock Complicating Acute Myocardial Infarction. Am J Cardiol. 2017 Mar 1.
Chatterjee P, Joynt Maddox KE. US National **Trends in Mortality From Acute Myocardial Infarction and Heart Failure**: Policy Success or Failure? JAMA Cardiol. 2018 Mar 14.
Chen HY, Gore JM, Lapane KL, et al. A **35-Year Perspective** (1975 to 2009) into the **Long-Term Prognosis and Hospital Management** of Patients Discharged from the Hospital After a First Acute Myocardial Infarction. Am J Cardiol. 2015 Apr 6.
Chen Jersey; Krumholz Harlan M.; Wang Yun; et al. Differences in Patient Survival After Acute Myocardial Infarction by Hospital **Capability of Performing Percutaneous Coronary Intervention**: Implications for Regionalization. Arch Intern Med. 2010;170(5):433-439.
Chen YL, Chang CL, et al. **Major Adverse Upper Gastrointestinal Events** in Patients with ST-Segment Elevation Myocardial Infarction Undergoing Primary Coronary Intervention and **Dual Antiplatelet Therapy**. Am J Cardiol. 2011 Sep 14. (Major GI 10.4% over 4yr)
Chen J, Hsieh AF, Dharmarajan K, et al. **National trends in heart failure hospitalization** after acute myocardial infarction for medicare beneficiaries: 1998-2010. Circulation. 2013 Dec 17;128(24):2577-84
Cheung NW, Wong VW, McLean M. The hyperglycemia: **intensive insulin infusion** in infarction (HI-5) study: a randomized controlled trial of insulin infusion therapy for myocardial infarction. Diabetes Care. 2006 Apr;29(4):765-70.
Chu DK, Kim LH, Young PJ, et al. Mortality and morbidity in acutely ill adults treated with **liberal versus conservative oxygen therapy (IOTA)**: a systematic review and meta-analysis. Lancet. 2018 Apr 28;391(10131):1693-1705.
Chung S-C, Gedeborg R, Nicholas O, et al. Acute myocardial infarction: a comparison of short-term **survival** in national outcome registries in **Sweden and the UK**. Lancet 2014; online Jan 23.
Cleland JG, et al.; Cardiac **Resynchronization**-Heart Failure (CARE-HF) Study. The effect of cardiac resynchronization on morbidity and mortality in heart failure. N Engl J Med. 2005 Apr 14;352(15):1539-49. Epub 2005 Mar 7.
Chen J et al. Recent **declines in hospitalizations for acute myocardial infarction** for Medicare fee-for-service beneficiaries: Progress and continuing challenges. Circulation 2010 Mar 23; 121:1322.
Cheung NW, et al. The Hyperglycemia: Intensive **Insulin Infusion** in Infarction (**HI-5**) study: a randomized controlled trial of insulin infusion therapy for myocardial infarction. Diabetes Care. 2006 Apr;29(4):765-70.
Choi JS, Kim YA, Kim MJ, et al. Relation Between Transient or Persistent **Acute Kidney Injury** and Long-Term Mortality in Patients With Myocardial Infarction. Am J Cardiol. 2013 Apr 1.
Choi JS, Kim YA, Kim HY, et al. Relation of serum **potassium level** to long-term outcomes in patients with acute myocardial infarction. Am J Cardiol. 2014 Apr 15;113(8):1285-90.
Choudhry NK, Singh JM, Barolet A, Tomlinson GA, Detsky AS. How should patients with unstable angina and non-ST-segment elevation myocardial infarction be managed? A meta-analysis of randomized trials. Am J Med. 2005 May;118(5):465-74 & ACP Journal Club .
Choudhry NK, Patrick AR, Antman EM, et al. Cost-effectiveness of providing **full drug coverage** to increase medication adherence in post-myocardial infarction Medicare beneficiaries. Circulation 2008; DOI: 10.1161/CIRCULATIONAHA.107.735605.
Choudhry NK, Avorn J, Glynn RJ, et al. **Full coverage** for preventive medications after myocardial infarction (**MI FREE**). N Engl J Med 2011. DOI: 10.1056/NEJMsa1107913.
Chu DK, Kim LH, Young PJ, et al. Mortality and morbidity in acutely ill adults treated **with liberal versus conservative oxygen therapy (IOTA)**: a systematic review and meta-analysis. Lancet. 2018 Apr 28;391(10131):1693-1705.
Chu TF, Rupnick MA, Kerkela R, et al. Cardiotoxicity associated with tyrosine kinase inhibitor **sunitinib**. Lancet. 2007 Dec 15;370(9604):2011-9.
Chung SC, Sundström J, Gale CP, et al. **Comparison of hospital variation in acute myocardial infarction care and outcome** between **Sweden and United Kingdom**: population based cohort study using nationwide clinical registries. BMJ. 2015 Aug 7;351:h3913
Cung TT, Morel O, Cayla G, et al. **Cyclosporine** before PCI in Patients with Acute Myocardial Infarction. (**CIRCUS**) N Engl J Med. 2015 Aug 30.
Claessen B, Dangas G, Weisz, et al. Prognostic impact of a chronic total occlusion in a non-infarct-related artery in patients with ST-segment elevation myocardial infarction: 3-year results from the **HORIZONS-AMI** trial. Eur Heart J 2012.
Claeys Marc J.; de Meester Antoine; Convens Carl; et al. Contemporary **Mortality Differences Between Primary Percutaneous Coronary Intervention and Thrombolysis** in ST-Segment Elevation Myocardial Infarction. Arch Intern Med. 2011;171(6):544-549.
Clark A, Lange T, Hallqvist J, et al. **Sleep** impairment and prognosis of acute myocardial infarction: a prospective cohort study. Sleep. 2014 May 1;37(5):851-8.
Clifford DM, Fisher SA, Brunskill SJ,et al. **Stem cell treatment** for acute myocardial infarction. Cochrane Database of Systematic Reviews 2012, Issue 2. Art. No.: CD006536. DOI: 10.1002/14651858.CD006536.pub3. Despite the high degree of heterogeneity observed, the results of this systematic review suggest that moderate improvement in global heart function is significant and sustained long-term.
Codner P, Vaduganathan M, Rechavia E, et al. **Clopidogrel Response Up to Six Months** After Acute Myocardial Infarction. Am J Cardiol. 2012 Apr 23.
Cohn JN. The message is clear: **prevent as well as treat acute myocardial infarction**. Circulation. 2013 Dec 17;128(24):2554-6
Colantonio LD, Huang L, Monda KL, et al. **Adherence to High-Intensity Statins** Following a Myocardial Infarction Hospitalization Among Medicare Beneficiaries. JAMA Cardiol. 2017 Apr 19.
Coles AH, Fisher KA, Darling C, et al. Recent Trends in **Post-Discharge Mortality** Among Patients With an Initial Acute Myocardial Infarction. Am J Cardiol. 2012 Jul 2.
Collet JP, Montalescot et al. **Percutaneous coronary intervention after fibrinolysis**: a multiple meta-analyses approach according to the type of strategy. J Am Coll Cardiol. 2006 Oct 3;48(7):1326-35. Epub 2006 Sep 14.
Comparison of Fondaparinux and Enoxaparin in Acute Coronary Syndromes. (**OASIS-5**) N Engl J Med. 2006 Mar 14; [Epub ahead of print] Conclusions Fondaparinux is similar to enoxaparin in reducing the risk of ischemic events at nine days, but it substantially reduces major bleeding and improves long term mortality and morbidity.
Connolly-Andersen AM, Hammargren E, Whitaker H, et al. Increased Risk of Acute Myocardial Infarction and Stroke **During Hemorrhagic Fever with Renal Syndrome**: A Self-Controlled Case Series Study. Circulation. 2014 Jan 7.
Cooper WO, et al Major **congenital malformations** after first-trimester exposure to **ACE inhibitors**. N Engl J Med. 2006 Jun 8;354(23):2443-51.
Cormier M, Lee TC. Chest pain and **supplemental oxygen**: too much of a good thing? [online Dec 12, 2016].JAMA Intern Med. doi: 10.1001/jamainternmed.2016.7612
Cornara S, Somaschini A, De Servi S et al. Prognostic Impact of in-**Hospital-Bleeding** in Patients with **ST-Elevation Myocardial Infarction** Treated by Primary Percutaneous Coronary Intervention. Am J Cardio. 2017
Corrada E, Ferrante G, Mazzali C, et al. **Eleven-Year Trends in Gender Differences of Treatments and Mortality** in ST-Elevation Acute Myocardial Infarction in Northern Italy, 2000 to 2010. Am J Cardiol. 2014 Aug 1;114(3):336-41.
Costa RA, Abizaid A, Lotan C, et al. Impact of **Thrombus Burden** on Outcomes After Standard Versus Mesh-Covered Stents in Acute Myocardial Infarction (from the MGuard for Acute ST Elevation Reperfusion Trial). Am J Cardiol. 2015 Jan 15;115(2):161-6.
Crane HM, Paramsothy P, Drozd DR, et al. **Types of Myocardial Infarction Among Human Immunodeficiency Virus**-Infected Individuals in the United States. JAMA Cardiol. 2017 Jan 4.
Cristell N, Cianflone D, Durante A, et al. High-sensitivity **C-reactive protein** (CRP) is within normal levels at the very onset of first ST-segment elevation acute myocardial infarction in 41% of case. J Am Coll Cardiol 2011; 58: 2654-2661.
Crowe E, Lovibond K, Gray H, et al. on behalf of the Guideline Development Group. Early management of **unstable angina and non-ST segment elevation myocardial infarction**: summary of **NICE** guidance. BMJ. 2010 Mar 24;340:c1134. doi: 10.1136/bmj.c1134.
Cubeddu RJ, Palacios IF, Blankenship JC, Horvath SA, et al. Outcome of Patients With ST-Segment Elevation Myocardial Infarction Undergoing Primary Percutaneous Coronary Intervention During **On- Versus Off-hours** (A Harmonizing Outcomes With RevasculariZatiON and Stents in Acute Myocardial Infarction [HORIZONS-AMI] Trial Substudy). Am J Cardiol. 2013 Jan 19.
Curry Leslie A., Spatz Erica, Cherlin Emily, et al. What Distinguishes **Top-Performing Hospitals** in Acute Myocardial Infarction Mortality Rates?: A Qualitative Study. *Ann Intern Med* March 15, 2011 154:384-390; doi:10.1059/0003-4819-154-6-201103150-00003
Curtis JR, Xie F, Chen L, et al. **Biomarker-related risk** for myocardial infarction and **serious infections in patients with rheumatoid arthritis**: a population-based study. Ann Rheum Dis. 2017 Dec 21.
Curzen N, Gurbel PA, Myat A, Bhatt DL, Redwood SR. What is the **optimum adjunctive reperfusion strategy** for primary percutaneous coronary intervention? Lancet 2013; 382: 633–43.
D'Ascenzo F, Taha S, Moretti C, et al. Meta-analysis of randomized controlled trials and adjusted observational results of use of **clopidogrel, aspirin, and oral anticoagulants** in patients undergoing **percutaneous coronary intervention**. Am J Cardiol. 2015 May 1;115(9):1185-93.
D'Onofrio G, Safdar B, Lichtman JH, et al. **Sex Differences** in Reperfusion in Young Patients With ST-Segment-Elevation Myocardial Infarction: Results From the **VIRGO** Study. Circulation. 2015 Apr 14;131(15):1324-32.
D'Souza M, Saaby L, Poulsen TS, et al. Comparison of Mortality in Patients With Acute Myocardial Infarction **Accidentally Admitted to Non-cardiology Departments Versus That in Patients Admitted to Coronary Care Units**. Am J Cardiol. 2014 Jul 30.
DAD study group. Class of **antiretroviral drugs** and the risk of myocardial infarction. N Engl J Med 2007; 356: 1723-1735. Increased exposure to protease inhibitors is associated with an increased risk of myocardial infarction, which is partly explained by dyslipidemia. We found no evidence of such an association for nonnucleoside reverse-transcriptase inhibitors; however, the number of person-years of observation for exposure to this class of drug was less than that for exposure to protease inhibitors. (23,437 pts followed for a median of 4.5yrs, there were 345 MIs).
Dahabreh Issa J., Paulus Jessica K.. Association of Episodic **Physical and Sexual Activity** With Triggering of Acute Cardiac Events: Systematic Review and Meta-analysis. JAMA. 2011;305(12):1225-1233.doi:10.1001/jama.2011.336
Dahal K, Hendrani A, Sharma PS, et al. **Aldosterone antagonist therapy and mortality in patients with ST-segment elevation myocardial infarction without heart failure**: a systematic review and meta-analysis [online May 21, 2018]. JAMA Intern Med.
Dahl Aarvik M, Sandven I, Dondo TB, et al. Effect of **Oral β-blocker Treatment on Mortality in Contemporary Post-myocardial Infarction Patients**. Eur Heart J Cardiovasc Pharmacother. 2018 Sep 6.
Dalager-Pedersen M, Sogaard M, Schonheyder HC, et al. Risk for myocardial infarction and stroke **after community-acquired bacteremia**: a 20-year population-based cohort study. Circulation. 2014;129:1387–1396.
Dalal F, Dalal HM, Voukalis C, et al. **Management of patients after primary percutaneous coronary intervention** for myocardial infarction. BMJ. 2017 Jul 20;358:j3237.
Damluji AA, Bandeen-Roche K, Berkower C, et al. **Percutaneous Coronary Intervention in Older Patients With ST-Segment Elevation Myocardial Infarction** and Cardiogenic Shock. J Am Coll Cardiol. 2019 Apr 23;73(15):1890-1900.
Danchin N, Puymirat E, Steg PG, et al. Five-Year Survival in Patients With ST-Segment-Elevation Myocardial Infarction According to **Modalities of Reperfusion Therapy**: The French Registry on Acute ST-Elevation and Non-ST-Elevation Myocardial Infarction (FAST-MI) 2005 Cohort. Circulation. 2014 Apr 22;129(16):1629-36.
Daneault B, Généreux P, Kirtane AJ, et al. Comparison of Three-Year Outcomes After **Primary Percutaneous Coronary Intervention** in Patients With Left Ventricular Ejection Fraction <40% Versus ≥40% (the HORIZONS-AMI Trial). Am J Cardiol. 2013 Jan 1;111(1):12-20.
Dangas George D., Caixeta Adriano, Mehran Roxana, et al., and for the Harmonizing Outcomes With Revascularization and **Stents** in Acute Myocardial Infarction (**HORIZONS-AMI**) Trial Investigators. Frequency and Predictors of Stent Thrombosis After Percutaneous Coronary Intervention in Acute Myocardial Infarction. Circulation 123: 1745-1756.
Dangas GD, Caixeta A, Mehran R, et al. Frequency and Predictors of **Stent Thrombosis After Percutaneous Coronary Intervention** (PCI) in Acute Myocardial Infarction. Circulation. 2011 Apr 26;123(16):1745-1756.
Dargie JH. Effect of carvedilol on outcome after myocardial infarction in patients with left-ventricular dysfunction: the **CAPRICORN** randomised trial. Lancet 2001; 357:1385–1390.
Dasari TW, Roe MT, et al. Impact of **Time of Presentation** on Process Performance and Outcomes in ST-Segment-Elevation Myocardial Infarction: A Report From the American Heart Association: Mission Lifeline Program. Circ Cardiovasc Qual Outcomes. 2014 Jul 29.
Das SR, Alexander K, Chen AY, et al. Impact of **body weight and extreme obesity** on the presentation, treatment, and in-hospital outcomes of 50 149 patients with ST-segment elevation myocardial infarction: Results from the NCDR. J Am Coll Cardiol 2011; 58:2642-50.
Davierwala PM, Leontyev S, Verevkin A, et al. **Temporal Trends in Predictors of Early and Late Mortality After Emergency Coronary Artery Bypass Grafting** for Cardiogenic Shock Complicating Acute Myocardial Infarction. Circulation. 2016 Oct 25;134(17):1224-1237.
Davis TME, Coleman RL, Holman RR; for the UKPDS Group. **Prognostic significance of silent myocardial infarction** in newly diagnosed type 2 diabetes mellitus: United Kingdom Prospective Diabetes Study **(UKPDS) 79**. Circulation. 2013;127:980–987.
Davis WT, Montrief T, Koyfman A, Long B. **Dysrhythmias and heart failure complicating acute myocardial infarction**: An emergency medicine review. Am J Emerg Med. 2019 Apr 27.
De Felice Francesco, Fiorilli Rosario, Parma Antonio, et al. Comparison of One-Year Outcome of Patients Aged **<75 Years Versus >=75 Years Undergoing 'Rescue' Percutaneous Coronary Intervention**, The American Journal of Cardiology, online 24 July 2011.
DeFilippis EM, Singh A, Divakaran S, et al. **Cocaine and Marijuana** Use Among Young Adults **With Myocardial Infarction**. J Am Coll Cardiol. 2018 Jun 5;71(22):2540-2551.
de Lemos JA. Increasingly sensitive assays for **cardiac troponins**: a review. JAMA. 2013 Jun 5;309(21):2262-9.
De Luca G, Suryapranata H, Ottervanger JP, Antman EM. **Time delay to treatment and mortality in primary angioplasty** for acute myocardial infarction: every minute of delay counts. Circulation. 2004;109(10):1223-1225.
De Luca G, Dirksen MT, Spaulding C, et al; DrugEluting Stent in Primary Angioplasty (**DESERT**) Cooperation. **Drug-eluting vs bare-metal stents** in primary angioplasty: a pooled patient-level meta-analysis of randomized trials. Arch Intern Med. 2012;172(8):611-621.
De Luca G, Dirksen MT, Spaulding C, et al; DESERT cooperation. Impact of **Age on Long-Term Outcome After Primary Angioplasty** With Bare-Metal or Drug-Eluting Stent (From the DESERT Cooperation). Am J Cardiol. 2013 May 7.
De Luca G, Biondi-Zoccai G, Marino P. Transferring patients with ST-segment elevation myocardial infarction for **mechanical reperfusion**: a meta-regression analysis of randomized trials. Ann Emerg Med. 2008 Dec;52(6):665-76.
De Oliveira PP, Gonzales V, Lopes RD, et al. **Serious infections** among unselected patients with ST-Elevation myocardial infarction treated with contemporary primary percutaneous coronary intervention. J Am Heart Assoc 2016.
de Winter RJ, Windhausen F, Cornel JH, et al. Invasive vs Conservative Treatment in Unstable Coronary Syndromes (ICTUS) Investigators. Early invasive vs selectively invasive management for acute coronary syndromes. N Engl J Med. 2005 Sep 15;353(11):1095-104.
Deckers JW, van Domburg RT, Akkerhuis M, Nauta ST. Relation of **Admission Glucose Levels**, Short- and Long-Term (20-Year) Mortality After Acute Myocardial Infarction. Am J Cardiol. 2013 Jul 15.
DeFilippis AP, Chapman AR, Mills NL, et al. **Assessment and Treatment of Patients** with Type 2 Myocardial Infarction and Acute Non-Ischemic Myocardial Injury. Circulation. 2019 Aug 16.
Deftereos S, Giannopoulos G, Angelidis C, et al. **Anti-Inflammatory Treatment With Colchicine** in Acute Myocardial Infarction: A Pilot Study. Circulation. 2015 Aug 11.
Dégano IR, Salomaa V, Veronesi G, et al. Acute myocardial Infarction Trends in Europe (**AMITIE**) Study Investigators. **twenty-five-year trends** in myocardial infarction attack and **mortality** rates, and case-fatality, in **six European populations**. Heart. 2015 Apr 8.
Deharo P, , et al. **Timing of Angiography** and Outcomes in High-Risk Patients With Non-ST-Segment-Elevation Myocardial Infarction **Managed Invasively**: Insights From the **TAO** Trial (Treatment of Acute Coronary Syndrome With **Otamixaban**). Circulation. 2017 Nov 14;136(20):1895-1907.
Dehghan A, Leening MJ, Solouki AM, et al. Comparison of Prognosis in **Unrecognized Versus Recognized Myocardial Infarction in Men Versus Women** >55 Years of Age (from the Rotterdam Study). Am J Cardiol. 2013 Oct 2.
Desch S, Stiermaier T, de Waha S, et al. **Thrombus aspiration** in patients with ST-elevation myocardial infarction presenting late after symptom onset. JACC Cardiovasc Interv 2015.
Devereaux PJ, Biccard BM, Sigamani A, et al. Association of **Postoperative High-Sensitivity Troponin Levels** With Myocardial Injury and 30-Day Mortality Among Patients Undergoing Noncardiac Surgery. JAMA. 2017 Apr 25;317(16):1642-1651.
Devereaux PJ, Duceppe E, Guyatt G, et al; MANAGE Investigators. **Dabigatran in patients with myocardial injury** after non-cardiac surgery (**MANAGE**): an international, randomised, placebo-controlled trial. Lancet. 2018 Jun 9;391(10137):2325-2334.
Deyell MW, Buller CE, Miller LH, et al. Impact of national clinical guideline recommendations for **revascularization** of persistently **occluded infarctrelated arteries** (**OAT trial**) on clinical practice in the United States. Arch Intern Med. doi:10.1001/archinternmed.2011.315.
Dharmarajan K, Hsieh AF, Kulkarni VT, et al. **Trajectories of risk after hospitalization for heart failure, acute myocardial infarction, or pneumonia**: retrospective cohort study. BMJ. 2015 Feb 5;350:h411.
Dhoot J, Tariq S, Erande A, et al. Effect of **Morbid Obesity** on In-Hospital Mortality and Coronary Revascularization Outcomes After Acute Myocardial Infarction in the United States. Am J Cardiol. 2013 Jan 26.
Digoxin (Ahmed A, et al. Digoxin and reduction in mortality and hospitalization in heart failure: a comprehensive post hoc analysis of the **DIG** trial. Eur Heart J. 2006 Jan;27(2):178-86. Epub 2005 Dec 8. & Adams KF Jr, et al. Relationship of serum digoxin concentration to mortality and morbidity in women in the digitalis investigation group trial: a retrospective analysis. J Am Coll Cardiol. 2005 Aug 2;46(3):497-504.
(InfoPOEMs: An intensive medical program with selective use of angiography and percutaneous coronary interventions is at least as good as a more aggressive strategy of catheterizing everyone. (LOE = 1b))
Devereaux P.J., Xavier Denis, Pogue Janice, et al, on behalf of the **POISE** (PeriOperative ISchemic Evaluation) Investigators. Characteristics and Short-Term Prognosis of Perioperative Myocardial Infarction in Patients Undergoing Noncardiac Surgery: A Cohort Study. Ann Intern Med April 19, 2011 154:523-528.
Dharmarajan K, McNamara RL, Wang Y, et al. **Age differences in hospital mortality** for acute myocardial infarction: implications for hospital profiling. Ann Intern Med. 2017. [Epub ahead of print]. doi:10.7326/M16-2871
Diagnosis and Management of Chronic Heart Failure in the Adult: **ACC/AHA 2005 Guideline Update** for the (J Am Coll Cardiol 2005) http://www.acc.org/clinical/guidelines/failure/index.pdf
Diener HC, Bogousslavsky J, Brass LM, et al.; MATCH investigators. Aspirin and clopidogrel compared with clopidogrel alone after recent ischaemic stroke or transient ischaemic attack in high-risk patients (**MATCH**): randomised, double-blind, placebo-controlled trial. Lancet. 2004 Jul 24;364(9431):331-7.
Dicpinigaitis PV. **Angiotensin-converting enzyme inhibitor**-induced **cough**: ACCP evidence-based clinical practice guidelines. *Chest* 2006;129(suppl):169-73S.
Dodson J,Wang Y, Sarwat C et al. **Bleeding Avoidance Strategies** and Outcomes in Patients ≥80 Years of Age With ST-Elevation Myocardial Infarction Undergoing Primary Percutaneous Coronary Intervention (NCDR CathPCI Registry). Am. J Cardiology 2012 2012 Apr 5.
Dodson JA, Hochman JS, Roe MT, et al. The Association of **Frailty With In-Hospital Bleeding Among Older Adults With Acute Myocardial Infarction**: Insights From the ACTION Registry. JACC Cardiovasc Interv. 2018 Nov 26;11(22):2287-2296.
Doll JA, Hellkamp A, Ho PM, et al. **Participation in Cardiac Rehabilitation Programs** Among Older Patients After Acute Myocardial Infarction. JAMA Intern Med. 2015 Aug 3.
Doll JA, Hellkamp A, Thomas L, et al. Effectiveness of **cardiac rehabilitation among older patients** after acute myocardial infarction. Am Heart J. 2015 Nov;170(5):855-64.
Doll JA, Li S, Chiswell K, et al. **Clopidogrel reloading** for patients with acute myocardial infarction already on clopidogrel therapy. Eur Heart J. 2018 Jan 14;39(3):193-200.
Dominguez-Rodriguez A, Abreu-Gonzalez P, de la Torre-Hernandez JM, Et al. Usefulness of Early Treatment With **Melatonin** to Reduce **Infarct** Size in Patients With ST-Segment Elevation Myocardial Infarction Receiving Percutaneous Coronary Intervention (From the Melatonin Adjunct in the Acute Myocardial Infarction Treated With Angioplasty Trial). Am J Cardiol. 2017 Aug 15;120(4):522-526.
Dondo TB, Hall M, West RM, et al. **Beta-blockers and mortality after acute myocardial infarction in patients without heart failure or ventricular dysfunction**. J Am Coll Cardiol 2017;69: 2710–20.
Douxfils J, Buckinx F, Mullier F, et al. **Dabigatran** Etexilate and Risk of Myocardial Infarction, Other Cardiovascular Events, Major Bleeding, and All-Cause Mortality: A Systematic Review and Meta-analysis of Randomized Controlled Trials. J Am Heart Assoc. 2014 Jun 6;3(3).
Dreyer RP, Wang Y, Strait KM, et al. **Gender Differences in the Trajectory of Recovery** in Health Status Among Young Patients With Acute Myocardial Infarction: Results From the Variation in Recovery: Role of Gender on Outcomes of Young AMI Patients (VIRGO) Study. Circulation. 2015 Jun 2;131(22):1971-80.
Dreyer RP, Ranasinghe I, Wang Y, et al. **Sex Differences** in the Rate, Timing, and Principal Diagnoses of 30-Day Readmissions in Younger Patients with Acute Myocardial Infarction. Circulation. 2015 Jul 21;132(3):158-66.
Dreyer RP, Dharmarajan K, Kennedy KF, et al. **Sex Differences** in 1-Year All-Cause Rehospitalization in Patients After Acute Myocardial Infarction: A Prospective Observational Study. Circulation. 2017 Feb 7;135(6):521-531.

Dreyer RP, Dharmarajan K, Hsieh AF, et al**. Sex Differences in Trajectories** of Risk After Rehospitalization for Heart Failure, Acute Myocardial Infarction, or Pneumonia. Circ Cardiovasc Qual Outcomes. 2017 May;10(5).

Dubreuil M, Louie-Gao Q, Peloquin CE, et al. Risk of myocardial infarction with use of selected **non-steroidal anti-inflammatory drugs in patients with spondyloarthritis and osteoarthritis**. Ann Rheum Dis. 2018 Apr 19.

Ducrocq G, Puymirat E, Steg PG, et al. **Blood transfusion, bleeding, anemia**, and survival in patients with acute myocardial infarction: **FAST-MI** registry. Am Heart J. 2015 Oct;170(4):726-734.e2.

Dunlay SM, Weston SA, Killian JM, et al. **Thirty-day rehospitalizations** after acute myocardial infarction. A cohort study. Ann Intern Med 2012; 157:11-18.

Dupre ME, George LK, Liu G, Peterson ED. The cumulative effect of **unemployment** on risks for acute myocardial infarction. Arch Intern Med 2012.

Dupre ME, George LK, Liu G, et al. Association Between **Divorce** and Risks for Acute Myocardial Infarction. Circ Cardiovasc Qual Outcomes. 2015 Apr 14.

Dzavik V, et al. Randomized Trial of **Percutaneous Coronary Intervention** for Subacute Infarct-Related **Coronary Artery Occlusion** to Achieve Long-Term Patency and Improve Ventricular Function. The Total Occlusion Study of Canada (**TOSCA**)-2 Trial. Circulation. 2006 Nov 14; [Epub ahead of print] PCI with stenting of a persistently occluded IRA in the subacute phase after MI effectively maintains long-term patency but has no effect on LV ejection fraction. On the basis of these findings and the lack of clinical benefit in the main Occluded Artery Trial, routine PCI is not recommended for stable patients with a persistently occluded IRA after MI.

Edwards M, Chang AM, Matsuura AC, Green M, Robey JM, Hollander JE. Relationship between **pain severity and outcomes** in patients presenting with potential acute coronary syndromes. Ann Emerg Med. 2011 Dec;58(6):501-7.

Effects of Fondaparinux on Mortality and Reinfarction in Patients With Acute ST-Segment Elevation Myocardial Infarction: The **OASIS-6** Randomized Trial. JAMA. 2006 Mar 14; [Epub ahead of print] CONCLUSION: In patients with STEMI, particularly those not undergoing primary percutaneous coronary intervention, fondaparinux significantly reduces mortality and reinfarction without increasing bleeding and strokes.

Eikelboom JW, et al. Unfractionated & **low-molecular-weight heparin** as adjuncts to thrombolysis in aspirin-treated patients with ST-elevation acute MI: a meta-analysis of the randomized trials. Circulation. 2005 Dec 20;112(25):3855-67. Epub 2005 Dec 12.

Eisenberg, Afilalo J, Lawler P, et al. **Cancer risk related to low-dose ionizing radiation** from cardiac imaging in patients after acute myocardial infarction. CMAJ 2011. DOI:10.1503/cmaj.100463.

Eitel I, Stiermaier T, Rommel KP, et al. Cardioprotection by combined **intrahospital remote ischaemic perconditioning and postconditioning** in ST-elevation myocardial infarction: the randomized **LIPSIA CONDITIONING** trial. Eur Heart J. 2015 Nov 21;36(44):3049-57.

Ejlersten M, Andersen ZJ, von Euler-Chelpin MC, Johansen et al. **Prognostic impact of physical activity prior** to myocardial infarction: Case fatality and subsequent risk of heart failure and death. Eur J Prev Cardiol. 2017 Jan 1:2047487317702046.

Ekerstad N et al. **Frailty** Is Independently Associated With Short-Term Outcomes for Elderly Patients With Non-ST-Segment Elevation Myocardial Infarction. Circulation. 2011 Nov 29;124(22):2397-404.

El-Hayek GE, Gershlick AH, Hong MK, et al. Meta-Analysis of Randomized Controlled Trials Comparing **Multivessel Versus Culprit-Only Revascularization** for Patients With ST-Segment Elevation Myocardial Infarction and Multivessel Disease Undergoing Primary Percutaneous Coronary Intervention. Am J Cardiol. 2015 Jun 1;115(11):1481-6.

Elbadawi A, Ha LD, Abuzaid AS, et al. Meta-Analysis of Randomized Trials on **Remote Ischemic Conditioning** during Primary Percutaneous Coronary Intervention in Patients with ST-Segment Elevation Myocardial Infarction. Am J Cardio.2017

Elkayam U, Jalnapurkar S, Barakkat MN, et al. **Pregnancy-associated acute myocardial infarction**: a review of contemporary experience in 150 cases between 2006 and 2011. Circulation. 2014 Apr 22;129(16):1695-702.

Ellis SG, Tendera M, de Belder MA, van Boven AJ, Widimsky P, Janssens L,et al. **FINESSE** Investigators. Facilitated PCI in patients with ST-elevation myocardial infarction. N Engl J Med. 2008 May 22;358(21):2205-17. Neither facilitation of PCI with reteplase plus abciximab nor facilitation with abciximab alone significantly improved the clinical outcomes, as compared with abciximab given at the time of PCI, in patients with ST-segment elevation myocardial infarction.

Erne P, Schoenenberger AW, Burckhardt D, et al. Effects of **percutaneous coronary interventions** in silent ischemia after myocardial infarction. The **SWISSI II** Randomized Controlled Trial. JAMA 2007; 297:1985-1991. Among patients with recent MI, silent myocardial ischemia verified by stress imaging, and 1- or 2-vessel coronary artery disease, PCI compared with anti-ischemic drug therapy reduced the long-term risk of major cardiac events.

Engstrøm T, Kelbæk H, Helqvist S, et al; DANAMI-3—PRIMULTI Investigators. **Complete revascularisation versus treatment of the culprit lesion** only in patients with ST-segment elevation myocardial infarction and multivessel disease (**DANAMI-3—PRIMULTI**): an open-label, randomized controlled trial. Lancet. 2015 Aug 15;386(9994):665-71.

Enezate TH, Omran J, Al-Dadah AS, et al. Comparison of Outcome of **Hospital Presentation** ST-Elevation Myocardial Infarction Treated by Percutaneous Coronary Intervention during **Off-Hours** Versus **on-Hours**. Am J Cardio. 2017

Epstein Andrew J., Polsky Daniel, Yang Feifei, et al. **Coronary Revascularization Trends** in the United States, 2001-2008. JAMA. 2011;305(17):1769-1776.doi:10.1001/jama.2011.551.

Erlinge D et al. **Bivalirudin versus heparin monotherapy** in myocardial infarction. N Engl J Med 2017 Aug27; [e-pub].

Ernstsen L, Rangul V, Nauman J, et al. Protective Effect of Regular **Physical Activity on Depression** After Myocardial Infarction: The **HUNT** Study. Am J Med. 2016 Jan;129(1):82-88.e1.

Ertelt K, et al. Comparison of **Outcomes and Prognosis With Versus Without Newly Diagnosed Diabetes** Mellitus After Primary Percutaneous Coronary Intervention for ST-Elevation Myocardial Infarction (the **HORIZONS-AMI** Study). Am J Cardiol. 2017 Jun 15;119(12):1917-1923.

Estévez-Loureiro R, Calviño-Santos R, López-Sainz A, et al. Long-Term Prognostic **Benefit of Field Triage and Direct Transfer** of Patients With ST-Segment Elevation Myocardial Infarction Treated by Primary Percutaneous Coronary Intervention. Am J Cardiol. 2013 Mar 14.

Everett BM, Brooks MM, Vlachos HEA, et al. **Troponin and cardiac events in stable ischemic heart disease** and diabetes. N Engl J Med 2015; 373:610 -20.

Faridi KF, Peterson ED, McCoy LA, et al. **Timing of First Postdischarge Follow-up and Medication Adherence** After Acute Myocardial Infarction. JAMA Cardiol. 2016 May 1;1(2):147-55.

Faulkenberg KD, Beavers JC, Finks SW. **Heparin Versus Bivalirudin** Monotherapy in the Setting of Primary Percutaneous Coronary Intervention for Patients With ST-Segment Elevation Myocardial Infarction. Ann Pharmacother. 2016 Feb;50(2):141-51.

Favaretto E, Roffi M, Frigo AC, et al. Meta-Analysis of Randomized Trials of **Postconditioning** in ST-Elevation Myocardial Infarction. Am J Cardiol. 2014 Jul 2.

FDA Nov/13: warning health care professionals of the rare but serious risk of heart attack and death with use of the cardiac nuclear stress test agents **Lexiscan (regadenoson) and Adenoscan (adenosine).**

FDA Nov/17 is alerting the public, health care providers, lab personnel, and lab test developers that **biotin (Vitamin B7)** can significantly interfere with certain lab tests and cause incorrect test results which may go undetected. Biotin in blood or other samples taken from patients who are ingesting high levels of biotin in dietary supplements can cause clinically significant incorrect lab test results. The FDA has seen an increase in the number of reported adverse events, including one death, related to biotin interference with lab tests. Biotin in patient samples can cause falsely high or falsely low results, depending on the test. Incorrect test results may lead to inappropriate patient management or misdiagnosis. For example, a falsely low result for troponin, a clinically important biomarker to aid in the diagnosis of heart attacks, may lead to a missed diagnosis and potentially serious clinical implications. The FDA has received a report that one patient taking high levels of biotin died following falsely low troponin test results when a troponin test known to have biotin interference was used. The FDA is aware of people taking high levels of biotin that would interfere with lab tests. Many dietary supplements promoted for hair, skin, and nail benefits contain biotin levels up to 650 times the recommended daily intake of biotin. Physicians may also be recommending high levels of biotin for patients with certain conditions such as multiple sclerosis (MS). Biotin levels higher than the recommended daily allowance may cause interference with lab tests.

Ferry AV, Anand A, Strachan FE, et al. **Presenting Symptoms in Men and Women** Diagnosed With Myocardial Infarction Using Sex-Specific Criteria. J Am Heart Assoc. 2019 Sep 3;8(17):e012307.

Fiocca L, Guagliumi G, et al. Characteristics and Outcomes of Patients With **ST-Segment Elevation Myocardial Infarction Excluded** from the Harmonizing Outcomes With Revascularization and Stents in Acute Myocardial Infarction (HORIZONS-AMI) Trial. Am J Cardiol. 2012 Oct 27.

Florido R, Ndumele CE, Kwak L, et la. **Physical Activity,** Obesity, and Subclinical Myocardial Damage. JACC Heart Fail. 2017 May;5(5):377-384.

Fortuni F, Crimi G, Angelini F, et al. **Early Complete Revascularization** in Hemodynamically Stable Patients With ST-Segment Elevation Myocardial Infarction and Multivessel Disease. Can J Cardiol. 2019 Aug;35(8):1047-1057.

Fosbol EL, Granger CB, Jollis JG, et al. The Impact of a Statewide **Pre-Hospital STEMI Strategy** to Bypass Hospitals Without Percutaneous Coronary Intervention Capability on Treatment Times. Circulation. 2013 Feb 5;127(5):604-12.

Fox KA, et al. Prediction of risk of death and myocardial infarction in the six months after presentation with acute coronary syndrome: prospective multinational observational study (**GRACE**). BMJ. 2006 Oct 10; [Epub ahead of print]

Fox KA, Poole-Wilson P, Clayton TC, et al. 5-year outcome of an interventional strategy in non-ST-elevation acute coronary syndrome: the British Heart Foundation RITA 3 randomised trial. Lancet. 2005 Sep 10-16;366(9489):914-20. (InfoPOEMs: In this study, patients with acute coronary syndromes when managed according to arteriography experience slightly better 5-year mortality rates (P=.054) than those managed conservatively. (LOE = 2b))

Fox KA, Steg PG, Eagle KA, et al. Decline in rates of death and heart failure in acute coronary syndromes, 1999-2006. JAMA. 2007 May 2;297(17):1892-900. In this multinational observational study, **GRACE**, improvements in the management of patients with ACS were associated with significant reductions in the rates of new heart failure and mortality and in rates of stroke and mycoardial infarction at 6 months. In patients with STEMI, hospital deaths decreased by 18 percentage points (95% CI, -5.3 to -1.9) and cardiogenic shock by -24 percentage points (95% CI, -4.3 to -0.5.)

Fox CS, Muntner P, Chen AY, et al. Short-term Outcomes of Acute Myocardial Infarction in Patients with **Acute Kidney Injury**: A Report from the National Cardiovascular Data Registry. Circulation. 2011 Dec 16.

Freiberg MS, Chang C-CH, Kuller LH, et al. **HIV infection and the risk of acute myocardial infarction** [online March 4, 2013]. JAMA Intern Med. doi:10.1001/jamainternmed.2013.3728.

Frencken JF, Donker DW, Spitoni C, et al. **Myocardial Injury in Patients With Sepsis** and Its Association With Long-Term Outcome. Circ Cardiovasc Qual Outcomes. 2018 Feb;11(2):e004040.

Fröbert O, Lagerqvist B, Olivecrona GK, et al. **Thrombus aspiration** during ST-segment elevation myocardial infarction. (**TASTE**) N Engl J Med 2013.

Frost L, Mostofsky E, Rosenbloom JI, Mukamal KJ, Mittleman MA. **Marijuana use** and long-term mortality among survivors of acute myocardial infarction. Am Heart J. 2013 Feb;165(2):170-5.

Fu S, Lv X, Fang Q, et al. **Oxygen therapy** for acute myocardial infarction: A systematic review and meta-analysis. Int J Nurs Stud. 2017 Sep;74:8-14.

Fuernau G, Eitel I, Kerber S et al. Impact of Chronic **Statin Pretreatment on Myocardial Damage** in ST-Elevation Myocardial Infarction (From the AIDA STEMI CMR Substudy). The American Journal of Cardiology (2014).

Fujino M, Ishihara M, Honda S, et al. Impact of **acute and chronic hyperglycemia** on in-hospital outcomes of patients with acute myocardial infarction. Am J Cardiol. 2014 Dec 15;114(12):1789-93.

Gaggin HK, Liu Y, Lyass A, et al. Incident **Type 2 Myocardial Infarction** in a Cohort of Patients Undergoing Coronary or Peripheral Arterial Angiography. Circulation. 2017 Jan 10;135(2):116-127.

Gao F, Lam C, Yeo KK, et al. Influence of **Ethnicity, Age, and Time on Sex Disparities** in Long-Term Cause-Specific Mortality After Acute Myocardial Infarction. J Am Heart Assoc.2016 ;e003760.

Garberich RF, Traverse JH, Claussen MT, et al. ST-segment–elevation myocardial infarction **diagnosed after hospital admission**. *Circulation*. 2014;129:1225–1232.

García Rodriguez LA, Cea-Soriano L, Martín-Merino E, Johansson S. **Discontinuation of low dose aspirin and risk of myocardial infarction**: case-control study in UK primary care. BMJ 2011;343:d4094.

Garzillo CL, Hueb W, Gersh B, et al. Association Between **Stress Testing-Induced Myocardial Ischemia and Clinical Events** in Patients With Multivessel Coronary Artery Disease. JAMA Intern Med. 2019 Jul 22.

Gast GCM, Pop VJM, Samsioe GN, et al. **Vasomotor menopausal symptoms** are associated with increased risk of coronary heart disease. Menopause 2011; 18:146-151.

Gelfand JM, et al. Risk of myocardial infarction in patients with **psoriasis**. JAMA. 2006 Oct 11;296(14):1735-41. Psoriasis may confer an independent risk of MI. The RR was greatest in young patients with severe psoriasis.

Gennaro G, Brener SJ, Redfors B, et al. Effect of **Smoking** on Infarct Size and Major Adverse Cardiac Events in Patients With Large Anterior ST-Elevation Myocardial Infarction (from the **INFUSE-AMI** Trial). Am J Cardiol. 2016 Oct 15;118(8):1097-1104.

Gerber Y, Rosen LJ, Goldbourt U, et al. **Smoking** status and long-term survival after first acute myocardial infarction. J Am Coll Cardiol 2009; 54:2382-2387.

Gerber Y, Melton LJ, Weston SA, et al. Association between **myocardial infarction and fractures**. An emerging phenomenon. Circulation 2011;

Gershlick AH, Stephens-Lloyd A, Hughes S, et al.; **REACT** Trial Investigators. **Rescue angioplasty after failed thrombolytic therapy** for acute myocardial infarction. N Engl J Med. 2005 Dec 29;353(26):2758-68.

Gershlick AH, Banning AP, Myat A, Verheugt FWA, Gersh BJ. Reperfusion therapy for STEMI: is there still a **role for thrombolysis in the era of primary percutaneous coronary intervention**? Lancet 2013; 382: 624–32.

Gharacholou S. Michael; Lopes Renato D.; Alexander Karen P.; et al. **Age and Outcomes** in ST-Segment Elevation Myocardial Infarction **Treated With Primary Percutaneous Coronary Intervention**: Findings From the **APEX-AMI** Trial. Arch Intern Med. 2011;171(6):559-567.

Gianstefani S, Douiri A, Delithanassis I, et al. Incidence and **Predictors of Early Left Ventricular Thrombus** After ST-Elevation Myocardial Infarction in the Contemporary Era of Primary Percutaneous Coronary Intervention. Am J Cardiol. 2014 Jan 14.

Gibson CM, Holmes D, Mikdadi G, et al**. Implantable Cardiac Alert System for Early Recognition** of ST-Segment Elevation Myocardial Infarction. J Am Coll Cardiol. 2019 Feb 25.

Giustino G, Harari R, Baber U, et al. Long-term Safety and Efficacy of **New-Generation Drug-Eluting Stents** in Women With Acute Myocardial Infarction: From the **Women** in Innovation and Drug-Eluting Stents (**WIN-DES**) Collaboration. JAMA Cardiol. 2017 Jun 28.

Gluckman TJ, Sachdev M, Schulman SP, Blumenthal RS. A simplified approach to the management of non-ST-segment elevation acute coronary syndromes. JAMA 2005; 293:349-57.

Goldberger JJ, Bonow RO, Cuffe M, Dyer A, Rosenberg Y, O'Rourke R, Shah PK, Smith SC Jr; PACE-MI Investigators. beta-Blocker use following myocardial infarction: **Low prevalence of evidence-based dosing**. Am Heart J. 2010 Sep;160(3):435-442.e1.

Go AS, et al. Atherosclerotic Disease, Vascular Function & Genetic Epidemiology (ADVANCE) Study. Statin & beta-blockers & the initial presentation of coronary heart disease. Ann Intern Med. 2006 Feb 21;144(4):229-38.

Go AS, Yang J, Gurwitz JH, Hsu J, Lane K, Platt R. Comparative effectiveness of **different beta-adrenergic antagonists** on mortality among adults with heart failure in clinical practice. Arch Intern Med. 2008 Dec 8;168(22):2415-21. Compared with atenolol, the adjusted risks of death were slightly higher with shorter-acting metoprolol tartrate but did not significantly differ for carvedilol in adults with heart failure. Our results should be interpreted cautiously and they suggest the need for randomized trials within real-world settings comparing a broader spectrum of beta-blockers for heart failure.

Goldberg A, Hammerman H, Petcherski S, Nassar M, Zdorovyak A, Yalonetsky S, Kapeliovich M, Agmon Y, Beyar R, Markiewicz W, Aronson D. **Hyponatremia** and Long-term Mortality in Survivors of Acute ST-Elevation Myocardial Infarction. Arch Intern Med. 2006 Apr 10;166(7):781-6.

Gimenez MR et al. **Sex-specific chest pain characteristics** in the early diagnosis of acute myocardial infarction. JAMA Intern Med 2013 Nov 25.

Goodacre S, Bradburn M, Cross E, Collinson P, Gray A, Hall A. The randomised assessment of treatment using **panel assay of cardiac markers** (**RATPAC**) trial: a randomised controlled trial of point-of-care cardiac markers in the emergency department. Heart 2010; 97: 190–96.

Goto K, Nikolsky E, Lansky AJ, et al. Impact of **Smoking** on Outcomes of Patients With ST-Segment Elevation Myocardial Infarction (from the HORIZONS-AMI Trial). Am J Cardiol. 2011 Aug 23.

Goyal A, Spertus JA, Gosch K, et al. Serum **potassium levels** and mortality in acute myocardial infarction. JAMA. 2012;307(2):157-164.

Goyal A, Gluckman TJ, Tcheng JE. What's in a Name? The New ICD-10 (10th Revision of the International Statistical Classification of Diseases and Related Health Problems) **Codes and Type 2 Myocardial Infarction**. Circulation. 2017 Sep 26;136(13):1180-1182.

Grace SL, Midence L, Oh P, et al. **Cardiac rehabilitation program** adherence and functional capacity among **women**: A randomized controlled trial. Mayo Clin Proc 2015.

Graham GN, Jones PG, Chan PS, et al. **Racial Disparities in Patient Characteristics and Survival After Acute Myocardial Infarction**. JAMA Netw Open. 2018;1(7):e184240.

Graham MM, Sessler DI, Parlow JL, Biccard BM, Guyatt G, Leslie K, et al. **Aspirin in patients with previous percutaneous coronary intervention undergoing noncardiac surgery**. Ann Intern Med. 2018;168: 237-44.

Granger CB, Bates ER, Jollis JG, et al. Improving Care of **STEMI** in the United States 2008 to 2012. J Am Heart Assoc. 2019 Jan 8;8(1):e008096.

Greco C, Pelliccia F, Tanzilli G, et al. Usefulness of **Local Delivery of Thrombolytics** Before Thrombectomy in Patients With ST-Segment Elevation Myocardial Infarction Undergoing Primary Percutaneous Coronary Intervention (the Delivery of Thrombolytics Before Thrombectomy in Patients With ST-Segment Elevation Myocardial Infarction Undergoing Primary Percutaneous Coronary Intervention [DISSOLUTION] Randomized Trial). Am J Cardiol. 2013 May 24.

Greenwood BN, Carnahan S, Huang L. Patient-physician gender concordance and **increased mortality among female heart attack patients**. Proc Natl Acad Sci U S A. 2018 Aug 6.

Grimaldi-Bensouda L, Alpérovitch A, Aubrun E, et al; the PGRx MI Group. Impact of **allopurinol** on risk of myocardial infarction. Ann Rheum Dis. 2014 Jan 6.

Grosso G, Sippl N, Kjellström B, et al. **Antiphospholipid Antibodies** in Patients With Myocardial Infarction. Ann Intern Med. 2018 Oct 23.

Gruberg L, Hellkamp AS, Thomas LE, et al. The Association of **Previous Revascularization** With In-Hospital Outcomes in Acute Myocardial Infarction Patients: Results From the National Cardiovascular Data Registry. JACC Cardiovasc Interv. 2015 Dec 28;8(15):1954-62.

Gu YL, Kampinga MA, Wieringa WG, et al. Intracoronary versus intravenous administration of **abciximab** in patients with ST-segment elevation myocardial infarction undergoing primary percutaneous coronary intervention with thrombus aspiration: the comparison of intracoronary versus intravenous abciximab administration during emergency reperfusion of ST-segment elevation myocardial infarction (CICERO) trial. Circulation. 2010 Dec 21;122(25):2709-17.

Gul M, Uyarel H, Ergelen M, et al. Prognostic Value of **Total Bilirubin** in Patients With ST-Segment Elevation Acute Myocardial Infarction Undergoing Primary Coronary Intervention. Am J Cardiol. 2012 Oct 24.

Gulliksson Mats; Burell Gunilla; Vessby Bengt; et al. Randomized Controlled Trial of **Cognitive Behavioral Therapy** vs Standard Treatment to Prevent Recurrent Cardiovascular Events in Patients With Coronary Heart Disease: Secondary Prevention in Uppsala Primary Health Care Project (SUPRIM). *Arch Intern Med*. 2011;171(2):134-140.

Gupta A, Wang Y, Spertus JA, et al. **Trends in acute myocardial** infarction in young patients and differences by **sex and race**, 2001 to 2010. J Am Coll Cardiol. 2014 Jul 29;64(4):337-45.

Gupta A, Das SR, Pandey A**. β-Blockers in myocardial infarction**: issues with standard admission orders sets [published online March 27, 2018].JAMA. doi:10.1001/jama.2018.0845

Gupta T, Harikrishnan P, Kolte D, et al. Trends in Management and Outcomes of ST-Elevation Myocardial Infarction in Patients With **End-Stage Renal Disease** in the United States. Am J Cardiol. 2015 Apr 15;115(8):1033-41.

Gupta T, Kolte D, Khera S, et al. Management and Outcomes of ST-Segment Elevation Myocardial Infarction in **US Renal Transplant Recipients**. JAMA Cardiol. 2017 Jan 11.

Haaf P, Drexler B, Reichlin T, et al. **High Sensitivity Cardiac Troponin** in the Distinction of Acute Myocardial Infarction from Acute Cardiac Non-Coronary Artery Disease. Circulation. 2012 May 23.

Hahn JY, Song YB, Kim EK, et al. **Ischemic Postconditioning** during Primary Percutaneous Coronary Intervention: The POST Randomized Trial. Circulation. 2013 Sep 25.

Hakulinen C, Pulkki-Råback L, Virtanen M, et al. **Social isolation and loneliness** as risk factors for myocardial infarction, stroke and mortality: UK Biobank cohort study of 479 054 men and women. Heart. 2018 Mar 27.

Hall HM, de Lemos JA, Enriquez JR, et al. Contemporary Patterns of **Discharge Aspirin Dosing After Acute Myocardial Infarction** in the United States: Results From the National Cardiovascular Data Registry (NCDR). Circ Cardiovasc Qual Outcomes. 2014 Aug 12.

Hall M, Dondo TB, Yan AT, et al. Association of **clinical factors and therapeutic strategies with improvements in survival** following non–ST-elevationmyocardial infarction, 2003-2013. JAMA. doi:10.1001/jama.2016.10766.

Hamm CW, Bassand JP, Agewall S, et al. **ESC** Guidelines for the management of **acute coronary syndromes** in patients presenting without persistent ST-segment elevation: The Task Force for the management of acute coronary syndromes (ACS) in patients presenting without persistent ST-segment elevation of the European Society of Cardiology (ESC). Eur Heart J. 2011 Sep 21.

Hammadah M, Kim JH, Samman Tahhan A, et al. Use of high-sensitivity **cardiac troponin** for the exclusion of inducible myocardial ischemia. A cohort study. Ann Intern Med.2018. [Epub ahead of print]. doi:10.7326/M18-0670

Han Y, Guo J, Zheng Y, et al; BRIGHT Investigators. **Bivalirudin vs heparin with or without tirofiban** during primary percutaneous coronary intervention in acute myocardial infarction: the **BRIGHT** randomized clinical trial. JAMA. 2015 Apr 7;313(13):1336-46.

Hanna EB, Glancy DL. **ST-segment depression and T-wave inversion**: Classification, differential diagnosis, and caveats Cleveland Clinic Journal of Medicine 2011; 78(6):404-414; doi:10.3949/ccjm.78a.10077

Hannan EL, Racz MJ, Walford G, et al. Long-term outcomes of coronary-artery bypass grafting versus stent implantation. N Engl J Med 2005; 352: 2174-83. (InfoPOEMs: Coronary artery bypass grafting (CABG) is associated with lower long-term mortality than percutaneous coronary interventions (PCI) with stenting for most anatomic groups in patients with multivessel disease, and a lower risk of requiring revascularization in the 3 years following intervention. Of course, this was an observational study and the groups were quite different at baseline, so we must be cautious about drawing firm treatment conclusions, even with appropriate statistical adjustments. Stenting is less invasive and is associated with lower unadjusted in-hospital mortality, so it remains a good option for many patients. (LOE = 2b))

Hannan EL, Racz M, Walford G. **Out-of-Hospital Deaths** Within 30 Days Following Hospitalization Where **Percutaneous Coronary Intervention** Was Performed. Am J Cardiol. 2011 Sep 29.

Hara M, Sakata Y, Nakatani D, et al; the OACIS Investigators. Comparison of 5-Year Survival After Acute Myocardial Infarction Using **Angiotensin-Converting Enzyme Inhibitor Versus Angiotensin II Receptor Blocker**. Am J Cardiol. 2014 Apr 18.

Hardin CC, Malhotra R, Petranović M, et al. Case 23-2019: A 52-Year-Old **Man with Fever, Cough, and Hypoxemia**. N Engl J Med. 2019 Jul 25;381(4):359-369.

Hardoon SL, Morris RW, Whincup PH, et al. Rising **adiposity** curbing decline in the incidence of myocardial infarction: 20-year follow-up of British men and women in the **Whitehall II cohort**. Eur Heart J 2011.

Hasin T, Gerber Y, Weston SA, et al. **Heart Failure** After Myocardial Infarction Is Associated With Increased Risk of Cancer. J Am Coll Cardiol. 2016 Jul 19;68(3):265-71.

Hausenloy DJ, Kharbanda RK, Møller UK, et al. Effect **of remote ischaemic conditioning on clinical outcomes** in patients with acute myocardial infarction (CONDI-2/ERIC-PPCI): a single-blind randomised controlled trial. Lancet. 2019 Sep 6.

Hayden M, Pignone M, Phillips C, et al. Aspirin for the primary prevention of cardiovascular events: a summary of the evidence for the U.S. Preventive Services Task Force. Ann Intern Med. 2002 Jan 15;136(2):161-72.

Heer T, et al. Acute Coronary Syndromes Registry Investigators. Beneficial effects of **abciximab** in patients with primary percutaneous intervention for acute ST segment elevation myocardial infarction in clinical practice. Heart. 2006 Oct;92(10):1484-9. Epub 2006 Apr 10.

Heitner JF, Senthilkumar A, Harrison JK, et al. Identifying the **Infarct-Related Artery in Patients With Non-ST-Segment-Elevation Myocardial Infarction**. Circ Cardiovasc Interv. 2019 May;12(5):e007305

Held C, Iqbal R, Lear SA, et al. **Physical activity levels**, ownership of goods promoting sedentary behavior and risk of myocardial infarction: results of the **INTERHEART** study. Eur Heart J 2012

Helin-Salmivaara A, et al. NSAID use and the risk of hospitalization for first **myocardial infarction** in the general population: a nationwide case-control study from Finland. Eur Heart J. 2006 Jul;27(14):1657-63. Epub 2006 May 26.

Held C, Iqbal R, Lear SA, et al. **Physical activity levels, ownership of goods** promoting sedentary behavior and risk of myocardial infarction: results of the INTERHEART study. Eur Heart J 2012

Herrett E, Shah AD, Boggon R, et al. Completeness and **diagnostic validity of recording acute myocardial infarction** events in primary care, hospital care, disease registry, and national mortality records: cohort study. BMJ. 2013 May 20;346:f2350.

Herrin J, Miller LE, Turkmani DF. National performance on **door-in to door-out time** among patients transferred for **primary percutaneous coronary intervention**. Arch Intern Med. 2011;171(21):1879-1886.

Herrmann J, Gersh B, Goldfinger J, et al. **Body Mass Index** and Acute and Long-term Outcomes After Acute Myocardial Infarction (from the Harmonizing Outcomes With Revascularization and Stents in Acute Myocardial Infarction [HORIZONS-AMI] Trial). The American Journal of Cardiology. 2014.

Herrett E, Bhaskaran K, Timmis A, et al. Association between **clinical presentations before myocardial infarction and coronary mortality**: a prospective population-based study using linked electronic records. Eur Heart J. 2014 Jul 19. pii: ehu286.

Hess C, Wang T, McCoy L, et al. **Unplanned Inpatient and Observation Rehospitalization** after Acute Myocardial Infarction: Insights from the **TRANSLATE-ACS** Study. Circulation. 2016;133:XX-XXX.

Hess CN, Peterson ED, Peng SA, et al. Use and outcomes of **triple therapy** among older patients with **acute myocardial infarction and atrial fibrillation**. J Am Coll Cardiol 2015;66:616–27.

Hess CN, Wang TY, McCoy LA, et al. **Unplanned Inpatient and Observation Rehospitalizations** After Acute Myocardial Infarction: Insights From the Treatment With Adenosine Diphosphate Receptor Inhibitors: Longitudinal Assessment of Treatment Patterns and Events After Acute Coronary Syndrome (**TRANSLATE-ACS**) Study. Circulation. 2016 Feb 2;133(5):493-501.

Hess CN, Kaltenbach LA, Doll JA, et al. **Race and Sex Differences** in Post-Myocardial Infarction Angina Frequency and Risk of 1-Year Unplanned Rehospitalization. Circulation. 2017 Feb 7;135(6):532-543.

Hess EP, Agarwal D, Chandra S, et al. Diagnostic accuracy of the **TIMI risk score** in patients with **chest pain** in the emergency department: a meta-analysis. CMAJ. 2010 Jun 7.

Heydari B, Abdullah S, Pottala JV, et al. Effect of **Omega-3 Acid Ethyl Esters** on Left Ventricular Remodeling After Acute Myocardial Infarction: The OMEGA-REMODEL Randomized Clinical Trial. Circulation. 2016 Aug 2;134(5):378-91

Hibbert B, Hayley B, Beanlands RS, et al. **Granulocyte colony-stimulating factor therapy** for stem cell mobilization following anterior wall myocardial infarction: the **CAPITAL STEM MI** randomized trial. CMAJ. 2014 Jun 16.

Hirakawa Y, et al. Effect of emergency **percutaneous coronary intervention** on in-hospital mortality of **very elderly** (80+ years of age) patients with acute myocardial infarction. Int Heart J. 2006 Sep;47(5):663-9.

Ho PM, Spertus JA, Masoudi FA, et al. Impact of **medication therapy discontinuation** on mortality after myocardial infarction. Arch Intern Med 2006; 166: 1842-1847.

Hoebers LP, Damman P, Claessen BE, et al. Predictive Value of Plasma **Glucose Level** on Admission for Short and Long Term Mortality in Patients With ST-Elevation Myocardial Infarction Treated With Primary Percutaneous Coronary Intervention. Am J Cardiol. 2011 Sep 23.

Hochman JS, et al. **Coronary Intervention** for **Persistent Occlusion** after Myocardial Infarction. (**OAT**) N Engl J Med. 2006 Nov 14; [Epub ahead of print] PCI did not reduce the occurrence of death, reinfarction, or heart failure, and there was a trend toward excess reinfarction during 4 years of follow-up in stable patients with occlusion of the infarct-related artery 3 to 28 days after myocardial infarction.

Hochman JS, et al.; **SHOCK** Investigators. Early revascularization and long-term survival in cardiogenic shock complicating acute myocardial infarction. JAMA. 2006 Jun 7;295(21):2511-5.

Hochman JS, Reynolds HR, Dzavík V, et al. for the Occluded Artery Trial Investigators. Long-Term Effects of **Percutaneous Coronary Intervention** of the Totally Occluded Infarct-Related Artery in the Subacute Phase After Myocardial Infarction. (**OAT**) Circulation. 2011 Oct 24.

Hoenig MR, Doust JA, Aroney CN, et al. Early invasive versus conservative strategies for **unstable angina and non-ST-elevation** myocardial infarction in the stent era. *Cochrane Database Syst Rev* 2006; 3:CD004815.

Hofmann R et al. **Oxygen therapy** in suspected acute myocardial infarction. (**DETO2X–SWEDEHEART**) N Engl J Med 2017 Aug 28; [e-pub].

Högström G, Nordström A, Nordström P. **High aerobic fitness** in late adolescence is associated with a reduced risk of myocardial infarction later in life: a nationwide cohort study in men. Eur Heart J. 2014 Jan 7

Hohnloser SH, Kuck KH, Dorian P, Roberts RS, et al; DINAMIT Investigators. Prophylactic use of an implantable cardioverter-defibrillator after acute myocardial infarction. N Engl J Med. 2004 Dec 9;351(24):2481-8.

Holme I, Retterstøl K, Norum KR, et al. **Lifelong benefits** on myocardial infarction mortality: **40-year follow-up** of the randomized Oslo diet and **antismoking study**. J Intern Med. 2016 Aug;280(2):221-7.

Honda S, Asaumi Y, Yamane T, et al. Trends in the clinical and pathological characteristics of **cardiac rupture** in patients with acute myocardial infarction over 35 years. J Am Heart Assoc. 2014 Oct 20;3(5):e000984.

Honkola J, Hookana E, Malinen S, et al. **Psychotropic medications** (antipsychotics & antidepressants) and the risk of sudden cardiac death during an acute coronary event. Eur Heart J. 2012 Mar;33(6):745-51.

Hooper L, Al-Khudairy L, Abdelhamid AS, et al. **Omega-6 fats for the primary and secondary prevention of cardiovascular disease**. Cochrane Database Syst Rev. 2018 Jul 18;7:CD011094. This is the most extensive systematic assessment of effects of omega-6 fats on cardiovascular health, mortality, lipids and adiposity to date, using previously unpublished data. We found no evidence that increasing omega-6 fats reduces cardiovascular outcomes other than MI, where 53 people may need to increase omega-6 fat intake to prevent 1 person from experiencing MI. Although benefits of omega-6 fats remain to be proven, increasing omega-6 fats may be of benefit in people at high risk of MI. Increased omega-6 fats reduce serum total cholesterol but not other blood fat fractions or adiposity.

Hsia J, Larson JC, Ockene JK, Sarto GE, Allison MA, et al.; Women's Health Initiative Research Group. Resting heart rate as a low tech predictor of coronary events in women: prospective cohort study. BMJ. 2009 Feb 3;338:b219. doi: 10.1136/bmj.b219.

Resting heart rate, a low tech and inexpensive measure of autonomic tone, independently predicts myocardial infarction or coronary death, but not stroke, in women.

Huang B, Yang Y, Zhu J, et al. Usefulness of the **Admission Shock Index** for Predicting Short-Term Outcomes in Patients With ST-Segment Elevation Myocardial Infarction. Am J Cardiol. 2014 Nov 1;114(9):1315-21.

Huang BT, Huang FY, Zuo ZL, et al. Meta-Analysis of Relation Between **Oral β-Blocker Therapy and Outcomes** in Patients With Acute Myocardial Infarction Who Underwent Percutaneous Coronary Intervention. Am J Cardiol. 2015 Jun 1;115(11):1529-38.

Huang SS, Chen YH, Chan WL, et al. Usefulness of the **CHADS2 Score** for Prognostic Stratification of Patients With Acute Myocardial Infarction. Am J Cardiol. 2014 Nov 1;114(9):1309-14.

Huber AH, Kampf JP, Kwan T, et al. Usefulness of Serum **Unbound Free Fatty Acid Levels** to Predict Death Early in Patients With ST-Segment Elevation Myocardial Infarction (from the Thrombolysis In Myocardial Infarction [TIMI] II Trial). Am J Cardiol. 2013 Oct 5

Huded CP, Johnson M, Kravitz K, et al. **4-Step Protocol for Disparities in STEMI** Care and outcomes in Women. J Am Coll Cardiol. 2018 May 15;71(19):2122-2132.

Huffman MD, Mohanan PP, Devarajan R, et al; Acute Coronary Syndrome Quality Improvement in Kerala (**ACS QUIK**) Investigators. Effect of a **quality improvement intervention** on clinical outcomes in patients in India with acute myocardial infarction: the ACS QUIK randomized clinical trial [Feb 13, 2018].JAMA. doi:10.1001/jama.2017 .21906

Hulten E, Villines TC, Cheezum MK, et al; CONFIRM Investigators. Usefulness of **Coronary Computed Tomography Angiography** to Predict Mortality and Myocardial Infarction Among Caucasian, African and East Asian Ethnicities (from the CONFIRM [Coronary CT Angiography Evaluation for Clinical Outcomes: An International Multicenter] Registry). Am J Cardiol. 2012 Dec 1.

Hurlen M, Abdelnoor M, Smith P, et al. Warfarin, aspirin, or both after myocardial infarction. (**WARIS-II**) N Engl J Med. 2002 Sep 26;347(13):969-74.

Hurt RD, Weston SA, Ebbert JO, et al. Myocardial infarction and sudden cardiac death in Olmsted County, Minnesota, **before and after smoke-free workplace laws** [online October 29, 2012]. Arch Intern Med.

Huynh T, Montigny M, Iftikhar U, et al. **Recurrent Cardiovascular Events in Survivors** of Myocardial Infarction With ST-Segment Elevation (from the **AMI-QUEBEC** Study). Am J Cardiol. 2018 Apr 15;121(8):897-902.

Ibanez B, Macaya C, Sanchez-Brunete V, et al. Effect of Early **Metoprolol** on Infarct Size in ST-Segment-Elevation Myocardial Infarction Patients Undergoing Primary Percutaneous Coronary Intervention: The Effect of Metoprolol in Cardioprotection During an Acute Myocardial Infarction (**METOCARD-CNIC**) Trial. Circulation. 2013 Oct 1;128(14):1495-503.

Ibanez B, James S, Agewall S, et al. **2017 ESC Guidelines** for the management of **acute myocardial infarction** in patients presenting with ST-segment elevation: The Task Force for the management of acute myocardial infarction in patients presenting with ST-segment elevation of the European Society of Cardiology (ESC). Eur Heart J. 2017 Aug 26.

Ibebuogu UN, Cercek B, Makkar R, et al. Comparison Between **Transradial and Transfemoral Percutaneous Coronary Intervention** in Acute ST-Elevation Myocardial Infarction. Am J Cardiol. 2012 Jul 25.

Iglesias JF, Muller O, Heg D, et al. Biodegradable **polymer sirolimus-eluting stents versus durable polymer everolimus-eluting stents** in patients with ST-segment elevation myocardial infarction (BIOSTEMI): a single-blind, prospective, randomised superiority trial. Lancet. 2019 Aug 30.

Iqbal MB, Ilsley C, Kabir T, et al. **Culprit vessel versus multivessel intervention** at the time of primary percutaneous coronary intervention in patients with ST-segment-elevation myocardial infarction and multivessel disease. *Circ Cardiovasc Qual Outcomes* 2014

Iqbal MB, Ilsley C, Kabir T, et al. London Heart Attack Centre (HAC) Group Investigators. **Culprit Vessel Versus Multivessel Intervention** at the Time of Primary Percutaneous Coronary Intervention in Patients With ST-Segment-Elevation Myocardial Infarction and Multivessel Disease: Real-World Analysis of 3984 Patients in London. Circ Cardiovasc Qual Outcomes. 2014 Nov;7(6):936-43.

Iqbal MB, Nadra IJ, Ding L, et al. **Culprit vessels versus multivessel versus in-hospital** staged intervention for patients with ST-segment elevation myocardial infarction and multivessel disease. JACC Cardiovasc Interv 2017.

Ishak M, Ali D, et al. Fast assessment and management of chest pain patients without ST-elevation in the pre-hospital gateway (**FamouS Triage**): ruling out a myocardial infarction at home with the **modified HEART score**. Eur Heart J Acute Card Care. 2017 Jan.

Jabre P, Jouven X, Adnet F, et al. **Atrial fibrillation and death after myocardial infarction**: a community study. Circulation. 2011;123:2094-100.

Jackevicius CA, Li P, Tu JV. Prevalence, predictors, and outcomes of primary **nonadherence after acute myocardial infarction**. Circulation 2008; DOI: 10.1161/CIRCULATIONAHA.107.706820.

Jacobs AK, Normand SLT, Massaro JM, et al. **Nonemergency PCI at hospitals with or without on-site cardiac surgery**. (**MASS COMM**) N Engl J Med2013: DOI: 10.1056/NEJMoa1300610.

Jacobs AK. The Challenge to Implement **Systems of Care** for ST-Segment-Elevation Myocardial Infarction. Circulation. 2016 Aug 2;134(5):375-7

Janszky I, Ljung R. **Shifts to and from daylight saving time** and incidence of myocardial infarction. N Engl J Med. 2008 Oct 30;359(18):1966-8.

Jernberg T, Johanson P, Held C, Svennblad B, Lindba¨ ck J, Wallentin L; **SWEDEHEART, RIKS-HIA**. Association between adoption of **evidence-based treatment and survival** for patients with ST-elevation myocardial infarction, 1996-2007. JAMA. 2011; 305(16):1677-1684.

Jena AB, Sun EC, Romley JA. Mortality Among High-Risk Patients With Acute Myocardial Infarction Admitted to US Teaching-Intensive **Hospitals in July**: A Retrospective Observational Study. Circulation. 2013 Dec 24;128(25):2754-63

Jensen LO et al. Influence of **Diabetes Mellitus** on Clinical Outcomes **Following Primary Percutaneous Coronary Intervention** in Patients With ST-Segment Elevation Myocardial Infarction. Am J Cardiol. 2011 Dec 5.

Jernberg T, Lindahl B, Alfredsson J, et al. Long-Term Effects of **Oxygen Therapy on Death or Hospitalization for Heart Failure** in Patients With Suspected Acute **Myocardial Infarction** Circulation. 2018 Dec 11;138(24):2754-2762.

Jiang W, Velazquez EJ, Kuchibhatla M, et al. Effect of **escitalopram** on mental stress-induced myocardial ischemia: results of the REMIT trial. JAMA. 2013 May 22;309(20):2139-49.

Jiang Z, Dreyer RP, Spertus JA, et al; China Patient-centered Evaluative Assessment of Cardiac Events (PEACE) Collaborative Group. **Factors associated with return to work after acute myocardial infarction** in China. JAMA Netw Open. 2018;1(7):e184831.

Jiang Z, Dreyer RP, Spertus JA, et al. Factors Associated With **Return to Work After Acute Myocardial Infarction** in China. JAMA Netw Open. 2018;1(7):e184831.

Jiddou MR, Pica M, Boura J, et al. Incidence of Myocardial Infarction With **Shifts to and From Daylight Savings Time**. Am J Cardiol. 2012 Dec 7.

Jinatongthai P, Kongwatcharapong J, Yoong FC. Comparative efficacy and safety of **reperfusion therapy** with **fibrinolytic agents** in patients with ST-segment elevation myocardial infarction: a systematic review and network meta-analysis. Lancet 2017; 390: 747–59.

Jinnouchi H, Sakakura K, Wada H, et al. Effect of Chronic **Statin** Treatment on Vascular Remodeling Determined by Intravascular Ultrasound in Patients With Acute Myocardial Infarction. Am J Cardiol. 2013 Dec 25

Johnston N, Bodegard J, Jerström S, et al. Effects of interactive patient **smartphone support app** on drug adherence and lifestyle changes in myocardial infarction patients: A randomized study. Am Heart J. 2016 Aug;178:85-94.

Jollis J, Al-Khalidi HR, Monk L, et al. Expansion of a regional ST-segment elevation myocardial infarction **system** to an **entire state**.Circulation 2012.

Jollis JG, Al-Khalidi HR, Roettig ML, et al. Impact of Regionalization of ST Elevation Myocardial Infarction Care on Treatment Times and Outcomes for **Emergency Medical Services Transported Patients** Presenting to Hospitals with Percutaneous Coronary Intervention: Mission: **Lifeline Accelerator-2**. Circulation. 2017 Nov 14

Jolly SS, Cairns JA, Yusuf S, et al; **TOTAL** Investigators. Outcomes after **thrombus aspiration** for ST elevation myocardial infarction: 1-year follow-up of the prospective randomised TOTAL trial. Lancet. 2015 Oct 12.

Jolly SS, James S, Džavík V, et al. **Thrombus Aspiration** in ST-Segment-Elevation Myocardial Infarction: An Individual Patient Meta-Analysis: Thrombectomy Trialists Collaboration. Circulation. 2017 Jan 10;135(2):143-152.

Jones DA, Gallagher S, Rathod KS, et al. Contemporary Analysis of Incidence and Outcomes of **Stent Thrombosis** Presenting as ST Elevation Myocardial Infarction in a Primary Percutaneous Coronary Intervention Cohort. Am J Cardiol. 2013 Sep 5.

Jones K, Saxon L, Cunningham W, Adams P; Guideline Development Group. **Secondary prevention for patients after a myocardial infarction**: summary of updated **NICE** guidance. BMJ. 2013 Nov 13;347:f6544.

Jones DS. The **puzzle of positive results--myocardial revascularization**. N Engl J Med. 2015 Feb 5;372(6):501-3.

Jouven X, Empana JP, Schwartz PJ, et al. Heart-rate profile during exercise as a predictor of sudden death. N Engl J Med 2005; 352: 1951-58. (InfoPOEMs: This study showed that a higher resting heart rate was associated with an increased risk of sudden death. We do not know whether any exercise or pharmacologic intervention in patients with an elevated heart rate would modify their risk. (LOE = 1b))

Joynt K, Blumenthal D, Orav EJ, et al. Association of **public reporting** for percutaneous coronary intervention with utilization and outcomes among Medicare beneficiaries with acute myocardial infarction. JAMA 2012; 308:1460-1468.

Jneid H, Anderson JL, Wright RS, et al. **2012 ACCF/AHA** focused update of the guideline for the management of patients with **unstable angina/non-ST-elevation myocardial infarction** (updating the 2007 guideline & replacing 2011 focused update). J Am Coll Cardiol. 2012;60(7):645-681.

Jneid H, et al. **2017 AHA/ACC Clinical Performance and Quality Measures** for Adults With ST-Elevation and Non-ST-Elevation Myocardial Infarction: Report of the American College of Cardiology/American Heart Association Task Force on Performance Measures. JACC 2017 Sep 14.

Jolly SS, Cairns JA, Yusuf S, et al. TOTAL Investigators. Randomized Trial of **Primary PCI with or without Routine Manual Thrombectomy**. N Engl J Med. 2015 Mar 16.

Juliard JM, Golmard JL, Himbert D, et al. Comparison of **Hospital Mortality** During ST-Segment Elevation Myocardial Infarction in the Era of Reperfusion Therapy in **Women Versus Men** and in Older Versus Younger Patients. Am J Cardiol. 2013 Mar 20.

Juo YY, Mantha A, Ebrahimi R, et al. **Incidence of Myocardial Infarction After High-Risk Vascular Operations** in Adults. JAMA Surg. 2017 Sep 6:e173360.

Kaehler J, Koester R, Billmann W, et al. 13-year follow-up of the German **angioplasty bypass surgery** investigation. Eur Heart J. 2005 Oct;26(20):2148-53. Epub 2005 Jun 23.

Kaikkonen KS, et al. **Family history** and the risk of sudden cardiac death as a manifestation of an acute coronary event. Circulation. 2006 Oct 3;114(14):1462-7. Epub 2006 Sep 25.

Kaier TE, Twerenbold R, Puelacher C, et al. Direct Comparison of **Cardiac Myosin-Binding Protein C with Cardiac Troponins** for the Early Diagnosis of Acute Myocardial Infarction. Circulation. 2017 Sep 26.

Kampourides N, Tziakas D, , et al. Usefulness of **matrix metalloproteinase-9 plasma levels** to identify patients with preserved left ventricular systolic function after acute myocardial infarction who could benefit from eplerenone. Am J Cardiol. 2012 Oct 15;110(8):1085-91.

Karam N, Bataille S, Marijon E, et al. Identifying Patients at Risk for **Pre-Hospital Sudden Cardiac Arrest** at the Early Phase of Myocardial Infarction: The **e-MUST** Study. Circulation. 2016 Oct 28.

Kastrati A, et al. Abciximab in Patients With Acute Coronary Syndromes Undergoing Percutaneous Coronary Intervention After Clopidogrel Pretreatment: The **ISAR-REACT 2** Randomized Trial. JAMA. 2006 Mar 13; [Epub ahead of print] CONCLUSIONS: Abciximab reduces the risk of adverse events in patients with non-ST-segment elevation ACS undergoing PCI after pretreatment with 600 mg of clopidogrel. The benefits provided by abciximab appear to be confined to patients presenting with an elevated troponin level.

Kastrati A et al. for the **ISAR-REACT 4** Trial Investigators. **Abciximab and heparin versus bivalirudin** for non–ST-elevation myocardial infarction. N Engl J Med 2011 Nov 13;

Kaul P, Fu Y, Westerhout CM, et al. Relative Prognostic Value of **Baseline Q Wave** and Time from Symptom Onset Among Men and Women With ST-Elevation Myocardial Infarction Undergoing Percutaneous Coronary Intervention. Am J Cardiol. 2012 Aug 21.

Kaul P, Federspiel JJ, Dai X, Stearns SC, et al. Association of **inpatient vs outpatient onset** of ST-elevation myocardial infarction with treatment and clinical outcomes. JAMA. 2014 Nov 19;312(19):1999-2007.

Kavsak PA, Neumann JT, Cullen L, et al. Clinical chemistry score versus high-sensitivity **cardiac troponin I and T tests alone to identify patients at low or high risk for myocardial infarction** or death at presentation to the emergency department. CMAJ. 2018 Aug 20;190(33):E974-E984.

Kaya MG, Uyarel H, Akpek M et al. Prognostic Value of **Uric Acid** in Patients With ST-Elevated Myocardial Infarction Undergoing Primary Coronary Intervention. Am J Cardiol. 2011 Nov 17.

Kedhi E, Fabris E, van der Ent M, et al. **Six months versus 12 months dual antiplatelet therapy after drug-eluting stent implantation in ST-elevation myocardial infarction (DAPT-STEMI)**: randomised, multicentre, non-inferiority trial. BMJ. 2018 Oct 2;363:k3793.

Keeley EC, Boura JA, Grines CL. Primary **angioplasty versus intravenous thrombolytic** therapy for acute myocardial infarction: a quantitative review of 23 randomised trials. Lancet. 2003 Jan 4;361(9351):13-20.

Keeley EC, Boura JA, et al. Comparison of primary and facilitated percutaneous coronary interventions for ST-elevation myocardial infarction: quantitative review of randomised trials. Lancet. 2006 Feb 18;367(9510):579-88. Erratum in: Lancet. 2006 May 20;367(9523):1656.

Keeley EC, Mehran R, Brener SJ, et al. Impact of **Multiple Complex Plaques** on Short- and Long-Term Clinical Outcomes in Patients Presenting With ST-Segment Elevation Myocardial Infarction (from the Harmonizing Outcomes With Revascularization and Stents in Acute Myocardial Infarction [**HORIZONS-AMI**]Trial). Am J Cardiol. 2014 May 15;113(10):1621-7.

Kelbæk H, Høfsten DE, Køber L, et al. **Deferred versus conventional stent implantation** in patients with ST-segment elevation myocardial infarction (**DANAMI 3-DEFER**): an open-label, randomised controlled trial. Lancet 2016; online April 3.

Keller, Till, Zeller, Tanja, Peetz, Dirk, et al. **Sensitive Troponin I Assay** in Early Diagnosis of Acute Myocardial Infarction. N Engl J Med 2009 361: 868-877. The use of a sensitive assay for troponin I improves early diagnosis of acute myocardial infarction and risk stratification, regardless of the time of chest-pain onset.

Keller T, Zeller T, Ojeda F, et al. **Serial changes in highly sensitive troponin I assay** (3hrs after)and early diagnosis of myocardial infarction.JAMA 2011; 306:2684-2693.

Keskin M, Kaya A, Tathsu A, et al. Effect of Adjunctive Thrombus Aspiration on in-Hospital and 3-Year Outcomes in Patients with ST-Segment Elevation Myocardial Infarction and **Large Native Coronary Artery Thrombus Burden**. Am J Cardio. 2017

Keskin M, Hayiroglu MI, Uzun AO, et al. Effect of **Nonalcoholic Fatty Liver Disease** on in-Hospital and Long-Term Outcomes in Patients with ST-Segment Elevation Myocardial Infarction. Am J Cardio. 2017.

Kesselheim AS, Bykov K, Avorn J, et al. Burden of changes in pill appearance for patients receiving **generic cardiovascular medications** after myocardial infarction: cohort and nested case-control studies. Ann Intern Med. 2014 Jul 15;161(2):96-103.

Khambaty T, Stewart JC, Gupta SK, et al. Association Between **Depressive Disorders** and Incident Acute Myocardial Infarction in Human Immunodeficiency Virus-Infected Adults: Veterans Aging Cohort Study. JAMA Cardiol. 2016 Aug 24.

Khan MS, Siddiqi TJ, Usman MS, et al. Meta-analysis Comparing Culprit Vessel Only **Versus Multivessel Percutaneous Coronary Intervention in Patients With Acute Myocardial Infarction** and Cardiogenic Shock. Am J Cardiol. 2018 Oct 26

Kharazmi Elham, Dossus Laure, Rohrmann Sabine, et al. **Pregnancy loss and risk of cardiovascular disease**: a prospective population-based cohort study (EPIC-Heidelberg). Heart hrt.2010.202226Published Online First: 1 December 2010 doi:10.1136/hrt.2010.202226.

Khawaja FJ, Shah ND, Lennon RJ, et al. Factors associated with 30-day **readmission rates after percutaneous coronary intervention** [published online November 28, 2011]. Arch Intern Med. doi:10.1001/archinternmed.2011.569.

Khera R, Jain S, Pandey A, et al. Comparison of **Readmission Rates** Following Acute Myocardial Infarction in 3 Patient Age Groups (18-44, 45-64, and >65 Years) in the USA. Am J Cardio. 2017

Khera S, Kolte D, Aronow WS, et al. Trends in **Acute Kidney Injury** and Outcomes After Early Percutaneous Coronary Intervention in Patients ≥75 Years of Age With Acute Myocardial Infarction. Am J Cardiol. 2013 Jul 15.

Khera S, Kolte D, Gupta T, et al. Temporal Trends and **Sex Differences** in Revascularization and Outcomes of ST-Segment Elevation Myocardial Infarction in Younger Adults in the United States. J Am Coll Cardiol. 2015 Nov 3;66(18):1961-72.

Kikkert WJ, Hoebers LP, Damman P, et al. Recurrent Myocardial Infarction **After Primary Percutaneous Coronary** Intervention for ST-Segment Elevation Myocardial Infarction. Am J Cardiol. 2013 Oct 3.

Kim HW, Klem I, Shah DJ, et al. Unrecognized **non-Q-wave** myocardial infarction: prevalence and prognostic significance in patients with suspected coronary disease. PLoS Med. 2009 Apr 21;6(4):e1000057. Epub 2009 Apr 21. In patients with suspected coronary disease, the prevalence of non-Q-wave UMI is more than 3-fold higher than Q-wave UMI. The presence of non-Q-wave UMI predicts subsequent mortality, and is incremental to LVEF.

Kim I, Kim MC, Sim DS, et al. Effect of the **Metabolic Syndrome** on Outcomes in Patients Aged <50 Years Versus >50 Years With Acute Myocardial Infarction. Am J Cardiol. 2018 Apr 11.

Kim JH, Malhotra R, Chiampas G et al, Cardiac arrest during **long-distance running** races. N Engl J Med 2012; 366:130-140.

Kim LK, Looser P, Swaminathan RV, et al. **Sex-Based Disparities** in Incidence, Treatment, and Outcomes of Cardiac Arrest in the United States, 2003-2012. J Am Heart Assoc. 2016 Jun 22;5(6).

Kim MC, Cho JY, Jeong HC, et al. Impact of **postdischarge statin withdrawal** on long-term outcomes in patients with acute myocardial infarction. Am J Cardiol. 2015 Jan 1;115(1):1-7.

Kim MC, Yun SC, Lee HB, et al. **Herpes Zoster** Increases the Risk of Stroke and Myocardial Infarction. J Am Coll Cardiol. 2017 Jul 11;70(2):295-296.

Kloner RA, et al. Impact of time to therapy and reperfusion modality on the efficacy of **adenosine** in acute myocardial infarction: the **AMISTAD-2** trial. Eur Heart J. 2006 Oct;27(20):2400-5. Epub 2006 Jun 16.

Kociol RD, Lopes RD, Clare R, et al. International variation in and factors associated with **hospital readmission after myocardial infarction (APEX-AMI)**. JAMA 2012; 307:66-74.

Koek HL, et al. Short- and long-term prognosis after acute myocardial infarction in **men versus women**. Am J Cardiol. 2006 Oct 15;98(8):993-9. Epub 2006 Aug 17. In conclusion, our findings in an unselected cohort (n=21,565) covering a complete nation indicate that the worse short- and long-term prognoses after an AMI in women compared with men may largely be explained by differences in age, whereas differences in co-morbidity, origin, infarct location, and reperfusion therapy seem to contribute little.

Koeth O, et al; PREMIR Investigators. Fate of Patients With **Prehospital Resuscitation** for ST-Elevation Myocardial Infarction and a High Rate of Early Reperfusion Therapy (Results from the **PREMIR** [Prehospital Myocardial Infarction Registry]). Am J Cardiol. 2012 Mar 31.

Koller L, Rothgerber DJ, Sulzgruber P, et al. History of **previous bleeding and C-reactive protein** improve assessment of bleeding risk in elderly patients (>/= 80 years) with myocardial infarction. (**Crusade risk score**) Thromb Haemost. 2015 Nov 2;114(5):1085-91.

Koltowski L, Koltowski-Haggstrom M, Filipiak KJ, et al. Quality of Life in Patients with ST-segment Elevation Myocardial Infarction Undergoing Percutaneous Coronary Intervention-**Radial versus Femoral Access** (From the OCEAN RACE Trial). The American Journal of Cardiology (2014).

Kontos MC, Lanfear DE, Gosch K, et al. Prognostic Value of **Serial N-Terminal Pro-Brain Natriuretic Peptide Testing** in Patients With Acute Myocardial Infarction. Am J Cardiol. 2017 Jul 15;120(2):181-185.

Kosiborod M, Inzucchi SE, Goyal A, et al. Relationship between spontaneous and iatrogenic **hypoglycemia** and mortality in patients hospitalized with acute myocardial infarction. JAMA. 2009 Apr 15;301(15):1556-64.

Kosmidou I, Embacher M, McAndrew T, et al. Early **Ventricular Tachycardia** or **Fibrillation** in Patients with ST-Elevation Myocardial Infarction Undergoing Primary Percutaneous Coronary Intervention and Impact on Mortality and Stent Thrombosis. Am J Cardio. 2017

Kosmidou I, et al. Incidence, Predictors, and Outcomes of **High-Grade Atrioventricular Block** in Patients with ST-Segment Elevation Myocardial Infarction Undergoing Primary Percutaneous Coronary Intervention (From the HORIZONS-AMI Trial. Am J Cardio. 2017.

Kovoor P, Lee AK, Carrozzi F, Wiseman V, Byth K, Zecchin R, Dickson C, King M, Hall J, Ross DL, et al. **Return to full normal activities** including work at two weeks after acute myocardial infarction. Am J Cardiol. 2006 Apr 1;97(7):952-8. Epub 2006 Feb 13.

Kramer JM, Curtis LH, Dupree CS, Pelter D, Hernandez A, Massing M, Anstrom KJ. Comparative effectiveness of **beta-blockers in elderly patients** with heart failure. Arch Intern Med. 2008 Dec 8;168(22):2422-8; discussion 2428-32. This elderly population, the comparative effectiveness of EBBBs vs non-EBBBs was similar for 1-year survival, whereas the rehospitalization rate was higher for patients receiving EBBBs.

Kristensen SL, Ahlehoff O, Lindhardsen J, et al. **Prognosis After First-Time Myocardial Infarction** in Patients With **Inflammatory Bowel Disease** According to Disease Activity: Nationwide Cohort Study. Circ Cardiovasc Qual Outcomes. 2014 Oct 14.

Kromhout D, Gitay EJ, Geleijnse JM, et al. **N-3 fatty acids** and cardiovascular events after myocardial infarction. (**Alpha Omega Trial**)N Engl J Med 2010; DOI:10.1056.NEJM0a.1003603.

Kronish IM, Ross JS, Zhao H, et al. The Impact of **Hospitalization for Acute Myocardial Infarction on Adherence to Statins** Among Older Adults. Circ Cardiovasc Qual Outcomes. 2016 May 24.

Krumholz HM,; American College of Cardiology; American Heart Association Task Force on **Performance Measures**; Writing Committee to Develop Performance Measures on ST-Elevation and Non-ST-Elevation Myocardial Infarction. **ACC/AHA** clinical performance measures for adults with ST-elevation and non-ST-elevation myocardial infarction: a report of the American College of Cardiology/American Heart Association Task Force on Performance Measures (Writing Committee to Develop Performance Measures on ST-Elevation and Non-ST-Elevation Myocardial Infarction). J Am Coll Cardiol. 2006 Jan 3;47(1):236-65.

Krumholz Harlan M.; Wang Yun; Chen Jersey; et al. Reduction in Acute Myocardial Infarction Mortality in the United States: Risk-Standardized **Mortality Rates** From 1995-2006. JAMA. 2009;302(7):767-773. Between 1995 and 2006, the risk-standardized hospital mortality rate for Medicare patients discharged with AMI showed a significant decrease, as did between-hospital variation.

Krumholz HM, Herrin J, Miller LE, et al. **Improvements in Door-to-Balloon Time** in the United States, 2005 to 2010. Circulation. 2011 Aug 30;124(9):1038-45.

Krumholz HM, Normand ST, Wang Y. **Twenty-Year Trends in Outcomes for Older Adults** With Acute Myocardial Infarction in the United States. JAMA Netw Open. 2019 Mar 1;2(3):e191938.

Kubesch NJ, Therming Jørgensen J, Hoffmann B, et al. Effects of **Leisure-Time and Transport-Related Physical Activities on the Risk of Incident and Recurrent Myocardial Infarction** and Interaction With Traffic-Related Air Pollution: A Cohort Study. J Am Heart Assoc. 2018 Jul 18;7(15).

Kubica J, Adamski P, Ostrowska M, et al. **Morphine delays and attenuates ticagrelor** exposure and action in patients with myocardial infarction: the randomized, double-blind, placebo-controlled IMPRESSION trial. Eur Heart J. 2016 Jan 14;37(3):245-52.

Kumbhani DJ, Shishehbor MH, Willis JM et al. Influence of **Gender** on Long-Term Mortality in Patients Presenting With Non-ST-Elevation Acute Coronary Syndromes Undergoing Percutaneous Coronary Intervention. Am J Cardiol. 2012 Apr 15;109(8):1087-91

Kunadian V, Qiu W, Bawamia B, et al. **Gender Comparisons** in Cardiogenic Shock During ST Elevation Myocardial Infarction Treated by Primary Percutaneous Coronary Intervention. Am J Cardiol. 2013 Sep 1;112(5):636-41.

Kuo H-K, Fujise K. **Human papillomavirus** and cardiovascular disease among US women in the National Health and Nutrition Examination Survey, 2003 to 2006. J Am Coll Cardiol 2011; 58: 2001-2006.

Kureshi F, Kennedy KF, Jones PG, et al. Association between **cardiac rehabilitation participation** and health status outcomes after acute myocardial infarction [online October 19, 2016].JAMA Cardiol. doi:10.1001 /jamacardio.2016.3458

Kurth T, et al. **Migraine** and risk of cardiovascular disease in **women**. JAMA. 2006 Jul 19;296(3):283-91. Erratum in: JAMA. 2006 Jul 19;296(3):1 p following 291. In this large, prospective cohort of women, active migraine with aura was associated with increased risk of major CVD, myocardial infarction, ischemic stroke, and death due to ischemic CVD, as well as with coronary revascularization and angina.

Kurtul A, Yarlioglues M, Murat SN, et al. Usefulness of the **Platelet-to-Lymphocyte Ratio** in Predicting Angiographic Reflow After Primary Percutaneous Coronary Intervention in Patients With Acute ST-Segment Elevation Myocardial Infarction. Am J Cardiol. 2014 Aug 1;114(3):342-7.

Kwok CS, Wong CW, Shufflebotham H, et al. Early Readmissions After Acute Myocardial Infarction. Am J Cardiol. 2017 Jun 15.

Kwong JC, Schwartz KL, Campitelli MA, et al. Acute Myocardial Infarction **after Laboratory-Confirmed Influenza Infection**. N Engl J Med. 2018 Jan 25;378(4):345-353.

Kytö V, Sipilä J, Rautava P. **Gender and In-hospital Mortality** of ST Segment Elevation Myocardial Infarction (from a Multihospital Nationwide Registry Study of 31,689 Patients). Am J Cardiol. 2015 Feb 1;115(3):303-6.

Laarman GJ, et al. **Paclitaxel-eluting versus uncoated** stents in primary percutaneous coronary intervention. (Passion trial)N Engl J Med. 2006 Sep 14;355(11):1105-13.

Ladwig KH, Fang X, Wolf K, et al. Comparison of **Delay Times Between Symptom Onset of an Acute ST-elevation Myocardial Infarction and Hospital Arrival in Men and Women** <65 Years Versus ≥65 Years of Age.: Findings From the Multicenter Munich Examination of Delay in Patients Experiencing Acute Myocardial Infarction (**MEDEA**) Study. Am J Cardiol. 2017 Dec 15;120(12):2128-2134.

Lagerqvist B, Fröbert O, Olivecrona GK, et al. Outcomes 1 Year after **Thrombus Aspiration** for Myocardial Infarction. N Engl J Med. 2014 Sep 1.

Lahoud R, Howe M, Krishnan SM, et al. Effect of Use of **Combination Evidence-Based Medical Therapy** After Acute Coronary Syndromes on Long-Term Outcomes. Am J Cardiol. 2011 Oct 17.

Lalmohamed A, Vestergaard P, Klop C, et al. Timing of Acute Myocardial Infarction in Patients Undergoing **Total Hip or Knee Replacement**: A Nationwide Cohort Study. Arch Intern Med. 2012 Jul 23:1-7.

Lamas GA, Goertz C, Boineau R, et al. Effect of **disodium EDTA chelation** regimen on cardiovascular events in patients with previous myocardial infarction. (**TACT**) JAMA 2013; 309: 1241-1250.

Lamas GA, Boineau R, Goertz C, Mark DB, Rosenberg Y, Stylianou M, et al; **TACT** (Trial to Assess Chelation Therapy) Investigators. Oral high-dose **multivitamins and minerals after myocardial infarction**. A randomized trial. Ann Intern Med. 2013;159:797-804.

Lambert Laurie; Brown Kevin; Segal Eli; et al. Association Between **Timeliness of Reperfusion** Therapy and Clinical Outcomes in ST-Elevation Myocardial Infarction. JAMA. 2010;303(21):2148-2155.

Lambert LJ, Brown KA, Boothroyd LJ, et al. **Transfer of Patients with ST-Elevation Myocardial Infarction for Primary Percutaneous Coronary Intervention: A Province-Wide** Evaluation of "Door-in to Door-Out" Delays at the First Hospital. Circulation. 2014 Apr 17.

Landi SN, Sandler RS, Pate V, et al. No Increase in Risk of Acute Myocardial Infarction in Privately Insured Adults **Prescribed Proton Pump Inhibitors vs Histamine-2 Receptor Antagonists** (2002-2014). Gastroenterology. 2018 Mar;154(4):861-873.e6.

Lane JR, Ben-Shachar G. Myocardial infarction in **healthy adolescents**. Pediatrics. 2007 Oct;120(4):e938-43.

Larsen KK, Agerbo E, Christensen B, Søndergaard J, Vestergaard M. Myocardial infarction and **risk of suicide**: a population-based case-control study. Circulation. 2010 Dec 7;122(23):2388-93.

Larsen AI, Tomey MI, Mehran R, et al. Comparison of Outcomes in Patients With ST-Segment Elevation Myocardial Infarction **Discharged on Versus Not on Statin** Therapy (from the Harmonizing Outcomes With Revascularization and Stents in Acute Myocardial Infarction Trial). Am J Cardiol. 2014 Apr 15;113(8):1273-9.

Larson DM, Menssen KM, Sharkey SW, Duval S, Schwartz RS, Harris J, Meland JT, Unger BT, Henry TD. **"False-positive" cardiac catheterization** laboratory activation among patients with suspected ST-segment elevation myocardial infarction. JAMA. 2007 Dec 19;298(23):2754-60.

Larsen AI, Nilsen DW, Yu J, et al. Long-term Prognosis of Patients Presenting With ST-Segment Elevation Myocardial Infarction With **No Significant Coronary Artery Disease** (from The **HORIZONS-AMI** Trial). Am J Cardiol. 2012 Dec 19.

Larsen GK, Seth M, Gurm HS. The ongoing importance of **smoking** as a powerful risk factor for ST-segment elevation myocardial infarction in young patients. JAMA Intern Med 2013.

Larsson SC, Burgess S, Michaëlsson K. Association of **Genetic Variants Related to Serum Calcium Levels** With Coronary Artery Disease and Myocardial Infarction. JAMA. 2017 Jul 25;318(4):371-380.

Laugsand LE, Vatten LJ, Platou C, Janszky I. **Insomnia** and the Risk of Acute Myocardial Infarction: A Population Study. Circulation. 2011 Oct 24.

Lavie C, Milani R, Ventura H, et al. **Impact of obesity** on outcomes in myocardial infarction. J Am Coll Cardiol 2011; 58:2651-53.

Lawler PR, Filion KB, Eisenberg MJ. Efficacy of **exercise-based cardiac rehabilitation** post-myocardial infarction: A systematic review and meta-analysis of randomized controlled trials. Am Heart J. 2011 Oct;162(4):571-584.e2.:

Lawler PR, Afilalo J, Eisenberg MJ, Pilote L. Exposure to **Low-Dose Ionizing Radiation** from Cardiac Imaging Among Patients With Myocardial Infarction. Am J Cardiol. 2011 Sep 29.

Lazzeri C, Valente S, Chiostri M et al. Usefulness of **Hyponatremia** in the Acute Phase of ST-Elevation Myocardial Infarction as a Marker of Severity. Am J Cardiol. 2012 Aug 2.

Lee CJ, Gerds TA, Carlson N, et al. Risk of **Myocardial Infarction in Anticoagulated Patients With Atrial Fibrillation**. J Am Coll Cardiol. 2018 Jul 3;72(1):17-26.

Le May MR, So DY, Dionne R, et al. A citywide (Ottawa) **protocol for primary PCI** in ST-segment elevation myocardial infarction. N Engl J Med. 2008 Jan 17;358(3):231-40.

Ledwoch J, Fuernau G, Desch S, et al. **Drug-eluting stents versus bare-metal stents** in acute myocardial infarction with cardiogenic shock. Heart. 2017 Aug;103(15):1177-1184.

Lee CW, Hwang I, Park CS, et al. Comparison of Intravascular Ultrasound and Histological Findings in Culprit Coronary Plaques Between ST-Segment Elevation and Non-ST-Segment Elevation Myocardial Infarction. Am J Cardiol. 2013 Apr 12. (more severe plaque rupture)

Lee G, Twerenbold R, Tanglay Y, et al. Clinical benefit of **high-sensitivity cardiac troponin I** in the detection of exercise-induced myocardial ischemia. Am Heart J 2015.

Lee JH, Bae MH, Yang DH, et al; Korea Acute Myocardial Infarction Registry Investigators. Prognostic value of the **age, creatinine, and ejection fraction** score (**ACEF**) for 1-year mortality in 30-day survivors who underwent **percutaneous coronary intervention** after acute myocardial infarction. Am J Cardiol. 2015 May 1;115(9):1167-73.

Leifheit-Limson EC, et al. **Sex Differences** in Cardiac Risk Factors, Perceived Risk, and Health Care Provider Discussion of Risk and Risk Modification Among Young Patients With Acute Myocardial Infarction: The VIRGO Study. J Am Coll Cardiol. 2015 Nov 3;66(18):1949-57.

Lemkes JS, Janssens GN, van der Hoeven NW, et al. **Coronary angiography** after cardiac arrest without ST-segment elevation. (COACT) N Engl J Med. DOI: 10.1056/NEJMoa1816897.

Lemkes JS, Janssens GN, van der Hoeven NW, et al. **Timing of revascularization in patients with transient ST-segment elevation myocardial infarction**: a randomized clinical trial. Eur Heart J. 2018 Oct 26.

León H, Shibata MC, Dorgan M, et al. Effect of **fish oil** on arrhythmias and mortality: systematic review. BMJ 2008; DOI: 10.1136/bmj.a2931. Fish oil supplementation was associated with a significant reduction in deaths from cardiac causes but had no effect on arrhythmias or all cause mortality. Evidence to recommend an optimal formulation of EPA or DHA to reduce these outcomes is insufficient. Fish oils are a heterogeneous product, and the optimal formulations for DHA and EPA remain unclear.

Leong DP, Smyth A, Teo KK, et al; INTERHEART Investigators*. Patterns of **Alcohol Consumption** and Myocardial Infarction Risk: Observations From 52 Countries in the INTERHEART Case-Control Study. Circulation. 2014 Jul 29;130(5):390-8.

Levesque LE, Brophy JM, Zhang B. Time variations in the risk of myocardial infarction among elderly users of **COX-2** inhibitors. CMAJ. 2006 May 23;174(11):1563-9. Epub 2006 May 2. A small proportion of patients using rofecoxib for the first time had their first MI shortly after starting the drug. This risk did not increase with the length of treatment and returned to baseline shortly after treatment was discontinued. More research is needed to identify those most susceptible to cardiotoxicity mediated by COX-2 inhibitor therapy.

Levine DA, Funkhouser EM, Houston TK, et al. Improving care after myocardial infarction using a 2-year **Internet-delivered intervention**: the Department of Veterans Affairs Myocardial Infarction–Plus cluster randomized trial. Arch Intern Med. 2011;171(21):1910-1917.

Levine GN, Bates ER, Blankenship JC, et al. 2011 **ACCF/AHA/SCAI** guideline for **percutaneous coronary intervention**: executive summary [published correction appears in Circulation. 2012;125(8):e411]. Circulation. 2011;124(23):2574-2609.

Levy B, Clere-Jehl R, Legras A, et al. **Epinephrine Versus Norepinephrine for Cardiogenic Shock** After Acute Myocardial Infarction. J Am Coll Cardiol. 2018 Jul 10;72(2):173-182.

Lexis CP, van der Horst IC, Lipsic E, et al; for the GIPS-III Investigators. Effect of **Metformin** on Left Ventricular Function After Acute Myocardial Infarction in Patients Without Diabetes: The GIPS-III Randomized Clinical Trial. JAMA. 2014 Mar 31.

Li J, Becker R, Rauch B, et al; OMEGA Study Group. Usefulness of **Heart Rate** to Predict One-Year Mortality in Patients With Atrial Fibrillation and Acute Myocardial Infarction (from the OMEGA Trial). Am J Cardiol. 2012 Dec 28.

Li J, Li X, Wang Q, et al. for the China PEACE Collaborative Group. ST-segment elevation myocardial infarction in **China from 2001 to 2011 (the China PEACE**-Retrospective Acute Myocardial Infarction Study): a retrospective analysis of hospital data. Lancet. 2014 Jun 23.

Li J, Chen Z, Gao X, et al. Meta-Analysis Comparing **Metoprolol and Carvedilol on Mortality Benefits in Patients With Acute Myocardial Infarction**. Am J Cardiol. 2017 Jul 29.

Li S, Chiuve SE, Flint A, et al. **Better Diet Quality and Decreased Mortality** Among Myocardial Infarction Survivors. JAMA Intern Med. 2013 Sep 2.

Li S, Flint A, Pai JK, et al. **Dietary fiber** intake and mortality among survivors of myocardial infarction: prospective cohort study. BMJ. 2014 Apr 29;348:g2659.

Lichtman JH, Leifheit-Limson EC, Watanabe E, et. al, **Symptom Recognition and Healthcare Experiences of Young Women** With Acute Myocardial Infarction. Circ Cardiovasc Qual Outcomes. 2015 Feb 24. pii: CIRCOUTCOMES.114.001612. [Epub ahead of print]

Lichtman JH, Leifheit-Limson EC, Watanabe E, et al. **Symptom recognition** and healthcare experiences of young **women** with acute myocardial infarction. Circ Cardiovasc Qual Outcomes. 2015 Mar;8(2 Suppl 1):S31-8.

Lichtman JH, et al. **Sex differences** in the presentation and perception of **symptoms** among young patients with myocardial infarction: evidence from the **VIRGO** study (Variation in Recovery: Role of Gender on Outcomes of Young AMI Patients). Circulation. 2018;137:781–790.

Liew R. **Implantable cardioverter defibrillators** (ICD) after acute myocardial infarction. BMJ. 2010 Nov 19;341:c5741. doi: 10.1136/bmj.c5741.

Lightwood JM, Glantz SA. Declines in Acute Myocardial Infarction After **Smoke-Free Laws** and Individual Risk Attributable to Secondhand Smoke. Circulation. 2009 Sep 21. [Epub ahead of print]

Likosky DS, Zhou W, Malenka DJ, et al. **Growth in Medicare Expenditures** for Patients With Acute Myocardial Infarction: A Comparison of 1998 Through 1999 and 2008. JAMA Intern Med. 2013 Sep 23.

Likosky DS, Van Parys J, Zhou W, et al. Association between **Medicare expenditure growth and mortality rates** in patients with acute myocardial infarction: a comparison from 1999 through 2014 [online Dec 20, 2017].JAMA Cardiol. doi:10 .1001/jamacardio.2017.4771

Lin ST, Chen CC, Tsang HY, et al. Association between **antipsychotic use and risk of acute myocardial infarction**: a nationwide case-crossover study. Circulation. 2014 Jul 15;130(3):235-43.

Lindahl B, Baron T, Erlinge D, et al. **Medical Therapy** for Secondary Prevention and Long-Term Outcome in Patients With Myocardial Infarction With Nonobstructive Coronary Artery Disease. (**MINOCA**) Circulation. 2017 Apr 18;135(16):1481-1489.
Lindau ST, Abramsohn E, Gosch K, et al. Patterns and **Loss of Sexual Activity** in the Year Following Hospitalization for Acute Myocardial Infarction (a United States National Multisite Observational Study). Am J Cardiol. 2012 May 15;109(10):1439-44.
Lindau ST, Abramsohn EM, Bueno H, et al. **Sexual activity and counseling** in the first month after acute myocardial infarction among younger adults in the United States and Spain: a prospective, observational study. Circulation. 2014 Dec 23;130(25):2302-9.
Lindau ST, Abramsohn E, Bueno H, et al. **Sexual activity and function** in the year after an acute myocardial infarction among younger women and men in the United States and Spain [online August 31, 2016].JAMA Cardiol. doi:10.1001/jamacardio.2016.2362.
Lindenauer PK, Lagu T, Rothberg MB, et al. **Income inequality** and 30 day outcomes after acute myocardial infarction, heart failure, and pneumonia: retrospective cohort study. BMJ. 2013 Feb 14;346:f521.
Lindhardsen J, Ahlehoff O, Gislason GH, et al. The risk of **myocardial infarction** in rheumatoid arthritis and diabetes mellitus: a Danish nationwide cohort study. Ann Rheum Dis. 2011 Jun;70(6):929-34.
Lindhardsen J, Ahlehoff O, Gislason GH et al. **Initiation and adherence to secondary prevention** pharmacotherapy after myocardial infarction in patients with **rheumatoid arthritis**: a nationwide cohort study. Ann Rheum Dis. 2012 Sep;71(9):1496-501.
Lipinski MJ, Escárcega RO, D'Ascenzo F, et al. A Systematic Review and Collaborative Meta-Analysis to Determine the Incremental Value of **Copeptin** for Rapid Rule-Out of Acute Myocardial Infarction. Am J Cardiol. 2014 May 1;113(9):1581-1591.
Lissåker CT, Norlund F, Wallert J, et al. **Persistent emotional distress after a first-time myocardial infarction** and its association to late cardiovascular and non-cardiovascular mortality. Eur J Prev Cardiol. 2019 Jun 3:2047487319841475.
Liu H, Tian Y, Xiang X, et al. **Air Pollution** and Hospitalization for **Acute Myocardial Infarction** in China. Am J Cardio. 2017.
Lloyd A, Steele L, Fotheringham J, et al. Pronounced increase in risk of acute ST-segment elevation myocardial infarction in **younger smokers**. Heart Published Online First: doi:10.1136/heartjnl- 2016- 309595
Loh JP, Pendyala LK, Kitabata H, et al. Comparison of **Outcomes After Percutaneous Coronary Intervention** Among Different Coronary Subsets (Stable and Unstable Angina Pectoris and ST-Segment and Non-ST-Segment Myocardial Infarction). Am J Cardiol. 2014 Jun 1;113(11):1794-801.
Loscalzo J.Is **oxygen therapy** beneficial in acute myocardial infarction? Simple question, complicated mechanism, simple answer. N Engl J Med 2017 Aug 28.
Lotz C, Ritter O, Muellenbach RM. **Assisted Beating** of the Ischemic Heart: How to Manage the Pulseless ST-Segment-Elevation Myocardial Infarction Patient. Circulation. 2014 Sep 23;130(13):1095-104.
Low AS, Symmons DP, Lunt M, et al. Relationship between exposure to **tumour necrosis factor inhibitor therapy and incidence and severity of myocardial infarction** in patients with rheumatoid arthritis. Ann Rheum Dis. 2017 Jan 10.
Low AS, Symmons DP, Lunt M, et al. Relationship between exposure to **tumour necrosis factor inhibitor** therapy and **incidence and severity of myocardial infarction** in patients with rheumatoid arthritis. Ann Rheum Dis. 2016 Apr;76(4):654-660.
Lu N, Misra D, Neogi T, et al. **Total Joint Arthroplasty** and the Risk of Myocardial Infarction - A General Population, Propensity Score-Matched Cohort Study. Arthritis Rheumatol. 2015 Aug 31.
Lunde K, et al. Intracoronary injection of mononuclear **bone marrow cells** in acute myocardial infarction. N Engl J Med. 2006 Sep 21;355(12):1199-209. With the methods used, we found no effects of intracoronary injection of autologous mononuclear BMC on global left ventricular function.
Lüscher TF. Myocardial **revascularization**: guideline-based therapy today. Eur Heart J. 2019 Jan 7;40(2):75-78.
Lüscher TF, Obeid S. From **Eisenhower's heart attack to modern management**: a true success story! Eur Heart J. 2017 Nov 1;38(41):3066-3069.
Mackay DF, Pell JP. Ten-Year Follow-Up of **the Impact of Scottish Smoke-Free Legislation** on Acute Myocardial Infarction. Circ Cardiovasc Qual Outcomes. 2019 Jul;12(7):e005392.
Madjid M, Miller CC, et al. **Influenza epidemics** and acute respiratory disease activity are associated with a surge in autopsy-confirmed coronary heart disease death: results from 8 years of autopsies in 34 892 subjects. Eur Heart J. 2007 Apr 17; [Epub ahead of print]
Maddox TM, Stanislawski MA, Grunwald GK, et al. **Nonobstructive coronary artery disease and risk** of myocardial infarction. JAMA. 2014 Nov 5;312(17):1754-63.
Mahajan VS, Jarolim P. How to **interpret elevated cardiac troponin levels**. Circulation. 2011 Nov 22;124(21):2350-4.
Mahajan N, Ference BA, Arora N, et al. Role of **Non-High-Density Lipoprotein** (non-HDL) Cholesterol in Predicting Cerebrovascular Events in Patients Following Myocardial Infarction. Am J Cardiol. 2012 Mar 31.
Makam RC, Erskine N, McManus DD, et al. **Decade-Long Trends (2001 to 2011) in the Use of Evidence-Based Medical Therapies** at the Time of **Hospital Discharge** for Patients Surviving Acute Myocardial Infarction. Am J Cardiol. 2016 Dec 15;118(12):1792-1797.
Malmberg K, Ryden L, Wedel H; DIGAMI 2 Investigators. Intense metabolic control by means of **insulin** in patients with diabetes mellitus and acute myocardial infarction (DIGAMI 2): effects on mortality and morbidity. Eur Heart J. 2005 Apr;26(7):650-61. Epub 2005 Feb 23.
(Malmberg K, et al. Randomized trial of insulin-glucose infusion followed by subcutaneous insulin treatment in diabetic patients with acute myocardial infarction (DIGAMI study): effects on mortality at 1 year. J Am Coll Cardiol. 1995 Jul;26(1):57-65. & Van den Berghe G, et al. Outcome benefit of intensive insulin therapy in the critically ill: Insulin dose versus glycemic control. Crit Care Med. 2003 Feb;31(2):359-66.) Diaz R, Goyal A, Mehta S, et al. Glucose-insulin-potassium therapy in patients with ST-segment elevation myocardial infarction. JAMA 2007; 298: 2399-2405.
Makrygiannis SS, Ampartzidou OS, Zairis MN, et al. Prognostic Usefulness of Serial **C-Reactive Protein** Measurements in ST-Elevation Acute Myocardial Infarction. Am J Cardiol. 2013 Jan 1;111(1):26-30.
Maniwa N, Fujino M, Nakai M, et al. **Anticoagulation combined with antiplatelet therapy** in patients with left ventricular thrombus after first acute myocardial infarction. Eur Heart J. 2017 Oct 3.
Mao TF, Bajwa A, Muskula P, et al. **Incidence of Left Ventricular Thrombus** in Patients With Acute ST-Segment Elevation Myocardial Infarction Treated with Percutaneous Coronary Intervention. Am J Cardiol. 2018 Jan 1;121(1):27-31.
Marso SP, Nauck MA, Monk Fries T, et al. **Myocardial Infarction Subtypes** in Patients With Type 2 Diabetes Mellitus and the Effect of **Liraglutide** Therapy (from the **LEADER** Trial). Am J Cardiol. 2018 Mar 15.
Masoudi FA, Bonow RO, Brindis RG, et al. ACC/AHA 2008 Statement on **Performance Measurement and Reperfusion Therapy**. A Report of the ACC/AHA Task Force on Performance Measures (Work Group to Address the Challenges of Performance Measurement and Reperfusion Therapy). Circulation. 2008 Nov 10. [Epub ahead of print]
Massoullié G, Wintzer-Wehekind J, Chenaf C, et al. **Prognosis and management of myocardial infarction**: Comparisons between the **French FAST-MI 2010 registry** and the French public health database. Arch Cardiovasc Dis. 2016 May;109(5):303-10.
Mathews R, Peterson ED, Li S, et al. Use of **Emergency Medical Service Transport** Among Patients With ST-Segment-Elevation Myocardial Infarction: Findings From the National Cardiovascular Data Registry Acute Coronary Treatment Intervention Outcomes Network Registry-Get With the Guidelines. Circulation. 2011 Jul 12;124(2):154-63.
Mathews R, Chen AY, Thomas L, et al. Differences in **Short-Term Versus Long-Term Outcomes** of Older **Black Versus White Patients With Myocardial Infarction**: Findings From the Can Rapid Risk Stratification of Unstable Angina Patients Suppress Adverse Outcomes With Early Implementation of American College of Cardiology/American Heart Association Guidelines (**CRUSADE**). Circulation. 2014 Aug 19;130(8):659-67.
Mathews R, Peterson ED, Honeycutt E, et al. **Early Medication Nonadherence** After Acute Myocardial Infarction: Insights into Actionable Opportunities From the Treatment with ADP receptor Inhibitors: Longitudinal Assessment of Treatment Patterns and Events After Acute Coronary Syndrome Study. Circ Cardiovasc Qual Outcomes. 2015 Jun 2.
Mathews R, Wang W, Kaltenbach LA, et al. **Hospital Variation in Adherence** Rates to Secondary Prevention Medications and the Implications on Quality. Circulation. 2018 Jan 31.
Mathews R, Wang W, Kaltenbach LA, Tet al. Hospital Variation in **Adherence** Rates to Secondary Prevention Medications and the Implications on Quality. Circulation. 2018 May 15;137(20):2128-2138.
Makkar RR, Smith RR, Cheng K, et al. Intracoronary **cardiosphere-derived cells** for heart regeneration after myocardial infarction (**CADUCEUS**): A prospective, randomised phase 1 trial. Lancet 2012. (stem cells)
Makrygiannis SS, Ampartzidou OS, Zairis MN, et al. Prognostic Usefulness of **Serial C-Reactive Protein Measurements** in ST-Elevation Acute Myocardial Infarction. Am J Cardiol. 2012 Oct 2.
Mariathas M, Allan R, Ramamoorthy S, et al. **True 99th centile of high sensitivity cardiac troponin** for hospital patients: prospective, observational cohort study. BMJ. 2019 Mar 13;364:l729
Mathias W Jr, Tsutsui JM, Tavares BG, et al. **Sonothrombolysis in ST-Segment Elevation Myocardial Infarction** Treated With Primary Percutaneous Coronary Intervention. J Am Coll Cardiol. 2019 Jun 11;73(22):2832-2842.
Mauri L, Kereiakes DJ, Yeh RW, et al. Twelve or 30 months of dual antiplatelet therapy after drug-eluting stents. (**DAPT**) N Engl J Med.
Mauri L, Silbaugh TS, Garg P,et al. **Drug-eluting** or bare-metal stents for acute myocardial infarction. N Engl J Med. 2008 Sep 25;359(13):1330-42. In patients presenting with acute myocardial infarction, treatment with drug-eluting stents is associated with decreased 2-year mortality rates and a reduction in the need for repeat revascularization procedures as compared with treatment with bare-metal stents.
McCabe JM, et al. Prevalence and Factors Associated With **False-Positive ST-Segment Elevation Myocardial Infarction Diagnoses** at Primary Percutaneous Coronary Intervention-Capable Centers: A Report From the Activate-SF Registry. Arch Intern Med. 2012 May 7.
McCabe JM, Armstrong EJ, Hoffmayer KS, et al. Impact of **door-to-activation time** on door-to-balloon time in primary percutaneous coronary intervention for ST-segment elevation myocardial infarctions. Circ Cardiovasc Qual Outcomes 2012.
McCabe JM, Kennedy KF, Eisenhauer AC, et al. Reporting Trends and Outcomes in ST-Segment-Elevation Myocardial Infarction National Hospital **Quality Assessment Programs**. Circulation. 2014 Jan 14
McCann GP, Khan JN, Greenwood JP, et al. **Complete Versus Lesion-Only Primary PCI**: The Randomized Cardiovascular **MR CvLPRIT** Substudy. J Am Coll Cardiol. 2015 Dec 22;66(24):2713-24.
McCarthy C, Murphy S, Cohen JA, et al. **Misclassification of Myocardial Injury** as Myocardial Infarction: Implications for Assessing Outcomes in Value-Based Programs. JAMA Cardiol. 2019 Mar 17.
McCarthy CP, Vaduganathan M, McCarthy KJ, et al. **Left Ventricular Thrombus** After Acute Myocardial Infarction: Screening, Prevention, and Treatment. JAMA Cardiol. 2018 May 9.
McCartney PJ, Eteiba H, Maznyczka AM, et al; T-TIME Group. Effect of **Low-Dose Intracoronary Alteplase** During Primary Percutaneous Coronary Intervention on Microvascular Obstruction in Patients With Acute Myocardial Infarction: A Randomized Clinical Trial. JAMA. 2019 Jan 1;321(1):56-68.
McCord J, Jneid H, et al. Management of **Cocaine-Associated Chest Pain and Myocardial Infarction**. A Scientific Statement From the American Heart Association Acute Cardiac Care Committee of the Council on Clinical Cardiology. Circulation online Mar 17,2008.
McEvoy JW, Chen Y, Ndumele CE, et al. Six-Year Change in **High-Sensitivity Cardiac Troponin T** and Risk of Subsequent Coronary Heart Disease, Heart Failure, and Death. JAMA Cardiol. 2016 Jun 8.
McNamara RL, et al. NRMI Investigators. Effect of **door-to-balloon time on mortality** in patients with ST-segment elevation myocardial infarction. J Am Coll Cardiol. 2006 Jun 6;47(11):2180-6. Epub 2006 May 15. InfoPOEMs: Mortality resulting from ST-segment elevation myocardial infarction (STEMI) is independently related to the time it takes to administer percutaneous coronary intervention (PCI) following presentation to the emergency department. The relationship is still seen in patients who present several hours after symptoms begin. If you have a choice of hospitals, find out their door-to-balloon times and send patients to the faster one. (LOE = 2b))
Mega JL et al. for the **ATLAS ACS 2–TIMI 51** Investigators. **Rivaroxaban** in patients with a recent **acute coronary syndrome**.N Engl J Med 2011 Nov 13. (but at baseline only 66% on BB, & 39% on ACEI)
Mega JL, Braunwald E, Murphy SA, et al. **Rivaroxaban** in patients stabilized after an **ST-elevation myocardial infarction**: Results from the **ATLAS ACS 2-TIMI 51** trial. J Am Coll Cardiol 2013.
Mehran R, Baber U, Steg PG, et al. **Cessation of dual antiplatelet treatment** and cardiac events after **percutaneous coronary intervention (PARIS):** 2 year results from a prospective observational study. Lancet 2013.
Mehta LS, Beckie TM, DeVon HA, et al. **Acute Myocardial Infarction in Women**: A Scientific Statement From the American Heart Association (**AHA 2016**). Circulation. 2016 Jan 25.
Mehta RH, et al. National Registry of Myocardial Infarction (NRMI) Investigators. Association of **Bleeding & In-Hospital Mortality** in Black & White Patients With ST-Segment-Elevation Myocardial Infarction Receiving Reperfusion. Circulation. 2012 Apr 10;125(14):1727-1734.
Mehta RH, et al. Recent Trends in the Care of Patients With Non-ST-Segment Elevation **Acute Coronary Syndromes**: Insights From the **CRUSADE** Initiative. Arch Intern Med. 2006 Oct 9;166(18):2027-34.
Mehta RH, Stebbins AS, Lopes RD, et al. Comparison of Incidence of **Bleeding and Mortality of Men Versus Women** With ST-Elevation Myocardial Infarction Treated With Fibrinolysis. Am J Cardiol. 2011 Nov 10.
Mehta SR, Cannon CP, Fox KA, et al. **Routine vs selective** invasive strategies in patients with acute coronary syndromes: a collaborative meta-analysis of randomized trials. JAMA. 2005 Jun 15;293(23):2908-17 & ACP Journal Club .
Mehta SR, Jolly SS, Cairns J, et al. Effects of **radial versus femoral artery access** in patients with acute coronary syndromes with or without ST-segment elevation. J Am Coll Cardiol 2012.
Mehta SR, Wood DA, Storey RF, et al. **Complete revascularization with multivessel PCI** for myocardial infarction. (COMPLETE) N Engl J Med. DOI: 10.1056/NEJMoa1907775.
Mehta SR, Yusuf S, Diaz R, et al.; **CREATE-ECLA** Trial Group Investigators. Effect of glucose-insulin-potassium infusion on mortality in patients with acute ST-segment elevation myocardial infarction: the CREATE-ECLA randomized controlled trial. JAMA. 2005 Jan 26;293(4):437-46. CONCLUSION: In this large, international randomized trial, high-dose GIK infusion had a neutral effect on mortality, cardiac arrest, and cardiogenic shock in patients with acute STEMI.
Menees DS, Peterson ED, Wang Y, et al. **Door-to-balloon time and mortality** among patients undergoing primary PCI. N Engl J Med 2013;369:901-9.
Mentias A, Raza MQ, Barakat AF, et al. Prognostic Significance of **Ischemic Mitral Regurgitation** on Outcomes in Acute ST-Elevation Myocardial Infarction Managed by Primary Percutaneous Coronary Intervention. Am J Cardiol. 2016 Sep 29.
Mercado MG, Smith DK, McConnon ML. Myocardial Infarction: Management of the **Subacute Period**. Am Fam Physician. 2013;88(9):581-588.
Messerli FH, Bangalore S. **Angiotensin Receptor Blockers Reduce** Cardiovascular Events, Including the Risk of Myocardial Infarction. Circulation. 2017 May 30;135(22):2085-2087.
Meyer-Saraei R, de Waha S, Eitel I, et al. **Thrombus aspiration** in non-ST-elevation myocardial infarction—12-month clinical outcome of the randomised **TATORT-NSTEMI** trial. Eur Heart J Acute Cardiovasc Care. 2015.
Michaëlsson K, Melhus H, Warensjö Lemming E, et al. Long term **calcium intake and rates of all cause and cardiovascular mortality**: community based prospective longitudinal cohort study. BMJ. 2013 Feb 12;346:f228.
Miedema MD, Newell MC, Duval S, et al. **Causes of delay and associated mortality in patients transferred** with ST-segment-elevation myocardial infarction. Circulation 2011; DOI: 10.1161/CIRCULATIONAHA.111.033118.
Miller AL, Simon D, Roe MT, et al. Comparison of **Delay Times** from Symptom Onset to Medical Contact in **Blacks Versus Whites** With Acute Myocardial Infarction. Am J Cardiol. 2017 Apr 15;119(8):1127-1134.
Millett ERC, Peters SAE, Woodward M. **Sex differences** in risk factors for myocardial infarction: cohort study of UK Biobank participants. BMJ. 2018 Nov 7;363:k4247.
Mills Nicholas L., Churchhouse Antonia M. D., Lee Kuan Ken, et al. Implementation of a **Sensitive Troponin I Assay** and Risk of Recurrent Myocardial Infarction and Death in Patients With Suspected Acute Coronary Syndrome. JAMA. 2011;305(12):1210-1216.
Mills NL, Lee KK, McAllister DA et al. Implications of lowering threshold of plasma **troponin** concentration in diagnosis of myocardial infarction: cohort study. BMJ. 2012 Mar 15;344:e1533.
Mir Arshid, Obafemi Adebisi, Young Amy, et al. Myocardial Infarction Associated With Use of the Synthetic Cannabinoid **K2**. Pediatrics 2011; peds.2010-3823; published ahead of print November 7, 2011
Mohammad MA, Koul S, Rylance R, et al. Association of **Weather With Day-to-Day Incidence of Myocardial Infarction**: A **SWEDEHEART N**ationwide Observational Study. JAMA Cardiol. 2018 Oct 24.
Mohammad MA, Karlsson S, Haddad J, et al. **Christmas, national holidays, sport events, and time factors as triggers of acute myocardial infarction**: SWEDEHEART observational study 1998-2013. BMJ. 2018 Dec 12;363:k4811.
Mohanan PP, Huffman MD, Baldridge AS, et al; ACS QUIK Investigators. **Microeconomic costs, insurance, and catastrophic health spending among patients with acute myocardial infarction** in India: substudy of a randomized clinical trial. JAMA Netw Open. 2019;2(5):e193831. doi:10.1001/jamanetworkopen.2019.3831
Mokhtari A et al. Diagnostic accuracy of high-sensitivity cardiac **troponin T** at presentation combined with history and ECG for ruling out major adverse cardiac events. Ann Emerg Med 2016 Jul 25.
Montaigne D, Marechal X, Modine T, et al. Daytime variation of perioperative myocardial injury in cardiac surgery and its prevention by **Rev-Erbα antagonism**: a single-centre propensity-matched cohort study and a randomised study. Lancet 2017; online Oct 26.
Montalescot G, Zeymer U, Silvain J, et al. **Intravenous enoxaparin or unfractionated heparin** in primary percutaneous coronary intervention for ST-elevation myocardial infarction: the international randomised open-label **ATOLL** trial. Lancet. 2011 Aug 20;378(9792):693-703.
Montalescot G, Hof AW, Lapostolle F, et al; the **ATLANTIC** Investigators. **Prehospital Ticagrelor** in ST-Segment Elevation Myocardial Infarction. N Engl J Med. 2014 Sep 1.
Moradkhan R, Sinoway LI. Revisiting the role of **oxygen therapy** in cardiac patients. J Am Coll Cardiol. 2010 Sep 21;56(13):1013-6.
Moran AE, Forouzanfar MH, Roth GA, et al. **Temporal trends** in ischaemic heart disease mortality in **21 world regions**, 1980–2010: the Global Burden of Disease 2010 Study. Circulation. 2014;129:1483–1492.
Moran AE, Forouzanfar MH, Roth G, et al. The **global burden of ischemic heart disease** in 1990 and 2010: the Global Burden of Disease 2010 Study. Circulation. 2014;129:1493–1501.
Morrow DA, de Lemos JA, Blazing MA, et al.; A to Z Investigators. Prognostic value of serial B-type natriuretic peptide testing during follow-up of patients with unstable coronary artery disease. JAMA. 2005 Dec 14;294(22):2866-71.
Mostofsky E, Maclure M, Sherwood JB, et al. Risk of acute myocardial infarction **after the death of a significant person on one's life be (bereavement).** The determinants of myocardial infarction onset study. Circulation 2012.
Mostofsky E, Maclure M, Tofler GH, et al. Relation of **Outbursts of Anger** and Risk of Acute Myocardial Infarction. Am J Cardiol. 2013 Apr 30.
Mostofsky E, Penner EA, Mittleman MA. **Outbursts of anger** as a trigger of acute cardiovascular events: a systematic review and meta-analysis. Eur Heart J. 2014 Mar 3.
Motivala, Apurva A., Cannon, Christopher P., Srinivas, Vankeepuram S., et al. Changes in **Myocardial Infarction Guideline Adherence** as a Function of Patient Risk: An End to Paradoxical Care? J Am Coll Cardiol 2011 58: 1760-1765.
Motovska Z, Hlinomaz O, Miklik R, et al. **Prasugrel versus ticagrelor** in patients with acute myocardial infarction treated with primary **percutaneous coronary intervention**: Multicenter randomized **PRAGUE-18** study. *Circulation*2016.
Mukamal KJ, Maclure M, Muller JE, Mittleman MA. An exploratory prospective study of **marijuana** use and mortality following acute myocardial infarction. Am Heart J. 2008 Mar;155(3):465-70. These preliminary results suggest possible hazards of marijuana for patients who survive acute myocardial infarction.
Musher DM, Abers MS, Corrales-Medina VF. **Acute Infection and Myocardial Infarction**. N Engl J Med. 2019 Jan 10;380(2):171-176.
Mustafic H, Jabre P, Caussin C, et al. Main **air pollutants** and myocardial infarction: A systematic review and meta-analysis. JAMA2012; 307:713-721.
Myerburg RJ. **Implantable cardioverter-defibrillators** after myocardial infarction. N Engl J Med. 2008 Nov 20;359(21):2245-53.
Myerson M, Coady S, Taylor H, et al. **Declining severity of myocardial infarction** from 1987 to 2002. The Atherosclerosis Risk in Communities (ARIC) Study. Circulation 2009; 119:503-514.
Najjar SS, Rao SV, Melloni C, et al. **REVEAL** Investigators. Intravenous **erythropoietin** in patients with **ST-segment elevation myocardial infarction** (STEMI): REVEAL: a randomized controlled trial. JAMA. 2011 May 11;305(18):1863-72.
Nakagawa S, et al. **Antipsychotics** and risk of first-time hospitalization for myocardial infarction: a population-based case-control study. J Intern Med. 2006 Nov;260(5):451-8.
Nakamura M, Tanaka K, Tanaka F, et al. Long-Term Effects of the **2011 Japan Earthquake and Tsunami** on Incidence of Fatal and Nonfatal Myocardial Infarction. Am J Cardiol. 2017 Aug 1;120(3):352-358.
Nakatani D, Sakata Y, Suna S, et al; Osaka Acute Coronary Insufficiency Study (OACIS) Investigators. Impact of **Beta Blockade** Therapy on Long-Term Mortality After ST-Segment Elevation Acute Myocardial Infarction (STEMI) in the Percutaneous Coronary Intervention Era. Am J Cardiol. 2012 Dec 7.
Nakatsuma K, Shiomi H, Watanabe H,, et al. Comparison of Long-term Mortality After Acute Myocardial Infarction Treated by Percutaneous Coronary Intervention in **Patients Living Alone versus Not Living Alone** at the Time of Hospitalization. The American Journal of Cardiology (2014).

Nallamothu BK, Normand SL, Wang Y, et al. Relation between **door-to-balloon times and** mortality after primary percutaneous coronary intervention over time: a retrospective study. Lancet. 2015 Mar 21;385(9973):1114-22.
Nauta ST, Deckers JW, van Domburg RT, Akkerhuis KM. **Sex-related trends in mortality** in hospitalized men and women after myocardial infarction between 1985 and 2008: equal benefit for women and men. Circulation. 2012 Oct 30;126(18):2184-9.
Navarese EP, De Luca G, Castriota F, et al. **Low-molecular-weight heparins vs unfractionated heparin** in the setting of percutaneous coronary intervention for ST-elevation myocardial infarction: A meta-analysis. J Thromb Haemost 2011.
Nawrot TS, Perez L, Künzli N, et al. Public health importance of triggers of myocardial infarction: A comparative risk assessment. Lancet 2011; DOI: 10.1016/S0140-6736(10)62296-9. A comparative risk assessment of various triggers for MI suggests that **cocaine** is most likely to trigger an event in an individual, but **traffic and exposure to air pollution** has the greatest effect on triggering an MI at the population level.
Nedkoff L, Knuiman M, Hung J, et al. **Improving 30-day case fatality** after incident myocardial infarction in people with diabetes between 1998 and 2010. Heart. 2015 Jun 15.
Nedkoff L, et al. **Comparative trends** in the **incidence of hospitalized myocardial infarction and coronary heart disease** in adults with and without diabetes mellitus in Western **australia** from 1998 to 2010. Circ Cardiovasc Qual Outcomes. 2014 Sep;7(5):708-17.
Nestelberger T, Boeddinghaus J, Wussler D, et al; APACE Investigators. **Predicting Major Adverse Events** in Patients With Acute Myocardial Infarction. J Am Coll Cardiol. 2019 Aug 20;74(7):842-854.
Nestelberger T, Cullen L, Lindahl B, et al. Diagnosis of acute myocardial infarction in the **presence of left bundle branch block**. Heart. 2019 May
Neumann JT, Sörenson NA, Schwemer T, et al. Diagnosis of myocardial infarction using a **high-sensitivity troponin I 1-hour algorithm** [online June 1, 2016].JAMA Cardiol. doi: 10.1001/jamacardio.2016.0695.
Neumann JT, Sörensen NA, Rübsamen N, et al. **Discrimination of patients with type 2 myocardial infarction**. Eur Heart J. 2017 Dec 14;38(47):3514-3520.
Neumann JT, Twerenbold R, Ojeda F, et al. **Application of High-Sensitivity Troponin** in Suspected Myocardial Infarction. N Engl J Med. 2019 Jun 27;380(26):2529-2540.
Newby DE, Adamson PD, Berry C, et al. **Coronary CT Angiography and 5-Year Risk of Myocardial Infarction**. (SCOT-HEART) N Engl J Med. 2018 Sep 6;379(10):924-933.
Newby KL, Jesse RL, Babb JD, et al. **ACCF 2012** Expert consensus document on practical clinical considerations in the **interpretation of troponin elevations**. J Am Coll Cardiol 2012.
Newman JD, Shimbo D, Baggett C, et al; **ARIC** Investigators. Trends in Myocardial Infarction Rates and Case Fatality by **Anatomical Location** in Four United States Communities, 1987 to 2008 (from the Atherosclerosis Risk in Communities Study). Am J Cardiol. 2013 Sep 21.
Ng FH, Tunggal P, Chu WM, et al. **Esomeprazole compared with famotidine** in the prevention of upper gastrointestinal bleeding in patients with acute coronary syndrome or myocardial infarction. Am J Gastroenterol. 2012 Mar;107(3):389-96.
NICE: Guidelines May 2007 Secondary prevention in primary and secondary care for patients following a myocardial infarction. http://guidance.nice.org.uk/CG48
NICE: National Institute for Health and Care Excellence. The **acute management of myocardial infarction** with ST-segment elevation. (Clinical guideline 167) 2013. http://guidance.nice.org.uk/CG167 .
NICE: National Institute for Health and Care Excellence. **Secondary prevention** in primary and secondary care for patients following a myocardial infarction. (Clinical guideline 172.) 2013. www.nice.org.uk/CG172 .
NCIE: National Institute for Health and Care Excellence. **Chest pain of recent onset**: assessment and diagnosis (clinical guideline CG95). Updated Nov 2016. https://www.nice.org.uk/ guidance/cg95.
Nikolsky E, Mehran R, Dangas GD, et al. Outcomes of Patients Treated With **Triple Antithrombotic Therapy** After Primary Percutaneous Coronary Intervention for ST-Elevation Myocardial Infarction (from the Harmonizing Outcomes with Revascularization and Stents in Acute Myocardial Infarction [**HORIZONS-AMI**] Trial). Am J Cardiol. 2011 Dec 21. In conclusion, in the setting of STEMI treated with primary PCI, the combination of aspirin, thienopyridine, and VKA results in an excess of bleeding complications.
Nikolsky E, Mehran R, Yu J, et al. Comparison of Outcomes of Patients With ST-Segment Elevation Myocardial Infarction With Versus Without Previous Coronary Artery Bypass Grafting (from the Harmonizing Outcomes With Revascularization and Stents in Acute Myocardial Infarction [**HORIZONS-AMI**] Trial). Am J Cardiol. 2013 Mar 8.
Norhammar A, Kjellström B, Habib N, et al. **Undetected Dysglycemia an Important Risk Factor** for Two Common Diseases Myocardial Infarction and Periodontitis: A Report From the PAROKRANK Study. Diabetes Care. 2019 Jun 10.
Novack V, Pencina M, Cohen DJ, et al. **Troponin criteria** for myocardial infarction after percutaneous coronary intervention. Arch Intern Med. 2012; 72(4):ioi110026.
Nudi F, Schillaci O, Di Belardino N, et al. **Temporal Trends in the Prevalence, Severity, and Localization** of Myocardial Ischemia and Necrosis at Myocardial Perfusion Imaging After Myocardial Infarction. Am J Cardiol. 2017 Oct 15;120(8):1238-1244
O'Brien C, Valsdottir L, Wasfy JH, et al. **Comparison of 30-Day Readmission Rates** After Hospitalization for Acute Myocardial Infarction in **Men Versus Women**. Am J Cardiol. 2017 Oct 1;120(7):1070-1076.
O'Brien EC, Rose KM, Suchindran CM, et al. **Temporal Trends in Medical Therapies** for ST- and Non-ST Elevation Myocardial Infarction: (from the Atherosclerosis Risk in Communities [ARIC] Surveillance Study). Am J Cardiol. 2012 Nov 17.
O'Connor SA, Garot P, Sanguineti F, et al. Meta-Analysis of the Impact on **Mortality of Noninfarct-Related Artery Coronary Chronic Total Occlusion** in Patients Presenting With ST-Segment Elevation Myocardial Infarction. Am J Cardiol. 2015 Jul 1;116(1):8-14.
O'Donnell CJ et al. Genome-wide association study for coronary artery calcification with follow-up in myocardial infarction. Circulation. 2011 Dec 20;124(25):2855-64.
O'Donoghue M, et al. **Lipoprotein-associated phospholipase A2** and its association with cardiovascular outcomes in patients with acute coronary syndromes in the PROVE IT-TIMI 22 (PRavastatin Or atorVastatin Evaluation and Infection Therapy-Thrombolysis In Myocardial Infarction) trial.Circulation. 2006 Apr 11;113(14):1745-52. Epub 2006 Mar 14.
O'Driscoll BR, Howard LS, Davison AG; British Thoracic Society. BTS guideline for **emergency oxygen** use in adult patients. Thorax. 2008 Oct;63 Suppl 6:vi1-68.
O'Donoghue ML, Glaser R, Cavender MA, et al; **LATITUDE-TIMI 60** Investigators. Effect of **Losmapimod** on Cardiovascular Outcomes in Patients Hospitalized With Acute Myocardial Infarction: A Randomized Clinical Trial. JAMA. 2016 Apr 4.
Odqvist M, Andersson PO, Tygesen H, et al. **High-Sensitivity Troponins and Outcomes After Myocardial Infarction**. J Am Coll Cardiol. 2018 Jun 12;71(23):2616-2624.
Ogunbayo GO, Misumida N, Olorunfemi O, et al. Comparison of Outcomes in Patients Having Acute Myocardial Infarction with Versus Without **Sickle-Cell Anemia**. Am J Cardio. 2017
O'Keefe JH Jr, et al. Effects of **omega-3 fatty acids** on resting heart rate, heart rate recovery after exercise, and heart rate variability in men with healed myocardial infarctions and depressed ejection fractions. Am J Cardiol. 2006 Apr 15;97(8):1127-30. Epub 2006 Mar 3.
Ørhn AM, Nielsen CS, Schirmer H, et al. **Pain Tolerance** in Persons With Recognized and Unrecognized Myocardial Infarction: A Population-Based, Cross-Sectional Study. J Am Heart Assoc. 2016 Dec 21;5(12).
Yamaji K, Kohsaka S, Morimoto T, et al. Relation of ST-segment Elevation Myocardial Infarction to **Daily Ambient Temperature and Air Pollutant Levels** in a Japanese Nationwide Percutaneous Coronary Intervention Registry (J-PCI). Am J Cardio. 2017.
Oldroyd KG. **Complete Immediate Revascularization** of the Patient With ST-Segment-Elevation Myocardial Infarction Is the New Standard of Care. Circulation. 2017 Apr 25;135(17):1571-1573.
Olgin JE, Pletcher MJ, Vittinghoff E, et al. **Wearable Cardioverter-Defibrillator** after Myocardial Infarction. (VEST) N Engl J Med. 2018 Sep 27;379(13):1205-1215.
Olsen Anne-Marie Schjerning, Fosbøl Emil L., Lindhardsen Jesper, et al. Duration of Treatment With **Nonsteroidal Anti-Inflammatory Drugs** (NSAIDS) and Impact on Risk of Death and Recurrent Myocardial Infarction in Patients With Prior Myocardial Infarction: A Nationwide Cohort Study. Circulation published May 9, 2011, doi:10.1161/CIRCULATIONAHA.110.004671
Ornato JP, Hand MM. **Warning signs** of a heart attack. Circulation. 2014 Mar 18;129(11):e393-5.
Osugi N, Suzuki S, Ishii H, et al. Impact of **Albuminuria** on the Incidence of Periprocedural Myocardial Injury in Patients Undergoing Elective Coronary Stent Implantation. Am J Cardiol. 2014 Apr 18.
Otaki Y, Gransar H, Berman DS, et al. Impact of **Family History of Coronary Artery Disease in Young** Individuals (from the CONFIRM Registry). Am J Cardiol. 2013 Feb 11.
Pack QR, Priya A, Lagu T, Pekow PS, et al. Association Between **Inpatient Echocardiography Use** and Outcomes in Adult Patients With Acute Myocardial Infarction. JAMA Intern Med. 2019 Jun 17.
Page, Maude, Doucet, Michel, Eisenberg, Mark J., et al. Temporal trends in **revascularization and outcomes** after acute myocardial infarction among the **very elderly**. CMAJ 2010 182: 1415-1420.
Pagidipati NJ, Hellkamp A, Thomas L, et al. Use of **Prescription Smoking Cessation Medications** After Myocardial Infarction Among Older Patients in Community Practice. JAMA Cardiol. 2017 Jul 19.
Pai JK, Mukamal KJ, Rimm EB. Long-term **alcohol consumption** in relation to all-cause and cardiovascular mortality among survivors of myocardial infarction: the Health Professionals Follow-up Study. Eur Heart J 2012.
Paine NJ, Bacon SL, Pelletier R, et al. Do **Women With Anxiety or Depression** Have Higher Rates of Myocardial Ischemia During Exercise Testing Than Men? Circ Cardiovasc Qual Outcomes. 2016 Jan;9(1):S53-61.
Paixao AR, de Lemos JA. **Acute troponin elevation** and the classification of myocardial infarction. JAMA. 2014 Nov 19;312(19):2032-3.
Palmer J, Lloyd A, Steele L, et al. **Differential Risk of ST-Segment Elevation Myocardial Infarction** in Male and Female Smokers. J Am Coll Cardiol. 2019 Jul 2;73(25):3259-3266.
Palmerini T, Mehran R, Dangas G, et al. Impact of **leukocyte count** (WBC) on mortality and bleeding in patients with myocardial infarction undergoing primary percutaneous coronary interventions: analysis from the harmonizing outcome with revascularization and stent in acute myocardial infarction trial. Circulation. 2011 Jun 21;123(24):2829-37.
Palmerini T, et al. Relation Between **White Blood Cell Count** and Final Infarct Size in Patients With ST-Segment Elevation Acute Myocardial Infarction Undergoing Primary Percutaneous Coronary Intervention (from the INFUSE AMI Trial). Am J Cardiol. 2013 Sep 21.
Panaich SS, Arora S, Patel N, et al. Comparison of **In-Hospital Mortality, Length of Stay, Postprocedural Complications, and Cost** of Single-Vessel Versus Multivessel Percutaneous Coronary Intervention in Hemodynamically Stable Patients With ST-Segment Elevation Myocardial Infarction (from Nationwide Inpatient Sample [2006 to 2012]). Am J Cardiol. 2016 Oct 1;118(7):950-8.
Pancholy SB, Shantha GP, Patel T, et al. **Sex Differences** in Short-term and Long-term All-Cause Mortality Among Patients With ST-Segment Elevation Myocardial Infarction Treated by **Primary Percutaneous Intervention**: A Meta-analysis. JAMA Intern Med. 2014 Nov 1;174(11):1822-30.
Pancholy S, Patel G, Pancholy M, et al. Association Between **Health Insurance Status** and In-Hospital Outcomes After ST-Segment Elevation Myocardial Infarction. Am J Cardiol. 2017 Oct 1;120(7):1049-1054.
Parashar S, et al. Time course of **depression** and outcome of myocardial infarction. Arch Intern Med. 2006 Oct 9;166(18):2035-43.
Pariente A, Fourrier-Réglat A, Ducruet T, Farrington P, et al. **Antipsychotic use and myocardial infarction** in older patients with treated dementia [published online Mar 26, 2012]. Arch Intern Med doi:10.1001/archinternmed.2012.28.
Park JJ, Jang HJ, Oh IY, et al. Prognostic Value of **Neutrophil to Lymphocyte Ratio** in Patients Presenting With ST-Elevation Myocardial Infarction Undergoing Primary Percutaneous Coronary Intervention. Am J Cardiol. 2012 Dec 27.
Park DW, Clare RM, Schulte PJ, et al. Extent, location, and clinical significance of **non-infarct-related coronary artery disease** among patients with ST-elevation myocardial infarction. JAMA. 2014 Nov 19;312(19):2019-27.
Park JS, Cha KS, Shin D, et al. Korea Working Group on Myocardial Infarction Investigators. Impact of **Non-Chest Pain Complaint** as a Presenting Symptom on Door-To-Balloon Time and Clinical Outcomes in Patients With Acute ST-Elevation Myocardial Infarction. Am J Cardiol. 2014 Dec 15;114(12):1801-9.
Park Y, Bateman BT, Kim DH, et al. Use of **haloperidol versus atypical antipsychotics and risk of in-hospital death in patients with acute myocardial infarction**: cohort study. BMJ. 2018 Mar 28;360:k1218.
Parodi G, Valenti R, Bellandi B, et al. Comparison of **prasugrel and ticagrelor** loading doses in ST-segment elevation myocardial infarction patients. J Am Coll Cardiol 2013; 61: 1601-1606.
Parsonage WA, Mueller C, Greenslade JH, et al. Validation of **NICE diagnostic guidance** for **rule out of myocardial infarction** using **high-sensitivity troponin tests**. Heart. 2016 Jun 10.
Pasupathy S, Air T, Dreyer RP, et al. Systematic review of patients presenting with suspected myocardial infarction and **nonobstructive coronary arteries**. Circulation. 2015 Mar 10;131(10):861-70.
Pasupathy S, et al. Early use of **N-Acetylcysteine (NAC) with Nitrate** Therapy in Patients Undergoing Primary Percutaneous Coronary Intervention for ST-Segment Elevation Myocardial Infarction Reduces Myocardial Infarct Size (The **NACIAM** Trial). Circulation. 2017 Jun 20.
Patel, MR, Smalling RW, Thiele H, et al. **Intra-aortic balloon counterpulsation** and infarct size in patients with acute anterior myocardial infarction **without shock**: The **CRISP AMI** randomized trial. JAMA 2011. (Not result in reduced infarct size)
Patel MR, Dehmer GJ, Hirshfeld JW, Smith PK, Spertus JA. **ACCF/SCAI/STS/AATS/AHA/ASNC/HFSA/SCCT 2012** appropriate use **criteria for coronary revascularization** focused update: A report of the American College of Cardiology Foundation Appropriate Use Criteria Task Force, Society for Cardiovascular Angiography and Interventions, Society of Thoracic Surgeons, American Association for Thoracic Surgery, American Heart Association, American Society of Nuclear Cardiology, and the Society of Cardiovascular Computed Tomography. J Am Coll Cardiol 2012
Patti G, Cannon CP, Murphy SA, et al. Clinical benefit of **statin pretreatment in patients undergoing percutaneous coronary intervention**: a collaborative patient-level meta-analysis of 13 randomized studies. Circulation. 2011 Apr 19;123(15):1622-32.
Patti G, Bárczi G, Orlic D, et al. Outcome comparison of **600- and 300-mg loading doses of clopidogrel** in patients undergoing primary PCI for STEMI. Results from the **ARMYDA-6 MI** (Antiplatelet Therapy for Reduction of Myocardial Damage During Angioplasty—Myocardial Infarction) randomized study. J Am Coll Cardiol 2011; 58:1592-1599.
Patti G, Cavallari I. **Extended duration dual antiplatelet therapy** in patients with myocardial infarction: A study-level meta-analysis of controlled randomized trials. Am Heart J. 2016 Jun;176:36-43.
Pauriah M, Elder DH, Ogston S, et al. High-potency **statin and ezetimibe** use and mortality in survivors of an acute myocardial infarction: a population-based study. *Heart* 2014.
Peberdy M, Ornato JP. Larkin GL, et al. Survival from in-hospital cardiac arrest **during nights and weekends**. JAMA 2008; 299:785-792.
Pedersen F, Butrymovich V, Kelbæk H, et al. **Short- and Long-Term Cause of Death** in Patients Treated With Primary PCI for STEMI. J Am Coll Cardiol. 2014 Nov 18;64(20):2101-8.
Pelletier R, Humphries KH, Shimony A, et al. **Sex-related** differences in **access to care** among patients with premature coronary syndrome. *CMAJ* 2014; DOI:10.1504/cmaj.131450.
Pelletier-Galarneau M, Hunter CRRN, Ascah KJ, et al. Randomized Trial Comparing the Effects of **Ticagrelor Versus Clopidogrel** on **Myocardial Perfusion** in Patients With Coronary Artery Disease. J Am Heart Assoc. 2017 May 2;6(5).
Perez MI, Musini VM, Wright JM. Effect of early treatment with **anti-hypertensive drugs** on short and long-term mortality in patients with an acute cardiovascular event. Cochrane Database Syst Rev. 2009 Oct 7;(4):CD006743.
Peters AE, Keeley EC. **Patient Engagement** Following Acute Myocardial Infarctionand Its Influence on Outcomes. Am J Cardiol. 2017 Nov 1;120(9):1467-1471.
Peters MN, Katz MJ, Moscona JC, et al. Effect of **Hurricane Katrina** on Chronobiology at Onset of Acute Myocardial Infarction During the Subsequent Three Years. Am J Cardiol. 2013 Jan 3.
Peters MN, Moscona JC, Katz MJ, et al. **Natural disasters** and myocardial infarction: the six years after hurricane katrina. Mayo Clin Proc. 2014 Apr;89(4):472-7.
Peters SAE, Bots SH, Woodward M. **Sex Differences** in the Association Between Measures of General and Central **Adiposity** and the Risk of Myocardial Infarction: Results From the UK Biobank. J Am Heart Assoc. 2018 Feb 28;7(5).
Peters SAE, Colantonio LD, Zhao H, et al. **Sex differences in high-intensity statin** use following myocardial infarction in the United States. J Am Coll Cardiol 2018;71:1729–37.
Pfortmueller CA, Funk GC, Marti G, et al. Diagnostic Performance of High-Sensitive **Troponin T in Patients With Renal Insufficiency**. Am J Cardiol. 2013 Sep 30.
Piccolo, Niglio, Spinelli, et al. **Reperfusion Correlates** and Clinical Outcomes of Right Ventricular Dysfunction in Patients with Inferior ST-segment Elevation Myocardial Infarction Undergoing Percutaneous Coronary Intervention. The American Journal of Cardiology. 2014.
Pickering J GJ, Cullen L, Flaws DF, et al. Assessment of the **European** Society of **Cardiology 0 hour/1hour algorithm to rule-out and rule-in** acute myocardial infarction. Circulation. 2016;134:XXX-XXX.
Pickering JW, Than MP, Cullen L, et al. **Rapid rule-out of myocardial infarction with a high-sensitivity cardiac troponin T measurement** below the limit of detection. A collaborative meta-analysis Ann Intern Med. 2017. [Epub ahead of print]. doi: 10.7326/M16-0562
Pickering JW, Young JM, George PM, et al. Validity of a Novel **Point-of-Care Troponin Assay** for Single-Test Rule-Out of Acute Myocardial Infarction. JAMA Cardiol. 2018 Oct 17.
Pimple P, Shah A, Rooks C, et al. Association between **anger and mental stress**-induced myocardial ischemia. Am Heart J. 2015 Jan;169(1):115-21.e2.
Pinto DS et al. for the National Registry of Myocardial Infarction Investigators. Benefit of **Transferring ST-Segment-Elevation Myocardial Infarction Patients for Percutaneous Coronary Intervention** Compared With Administration of **Onsite Fibrinolytic** Declines as Delays Increase. Circulation. 2011 Dec 6;124(23):2512-2521.
Pizarro G, Fernández-Friera L, Fuster V, et al. Long term benefit of **early pre-reperfusion metoprolol** administration in patients with acute myocardial infarction: results from the **METOCARD-CNIC** trial. J Am Coll Cardiol. 2014 Mar 24.
Podolecki T, Lenarczyk R, Kowalczyk J, et al. Effect of **Type of Atrial Fibrillation** on Prognosis in Acute Myocardial Infarction Treated Invasively. Am J Cardiol. 2012 Mar 20.
Podolecki T, Lenarczyk R, Kowalczyk J, et al. Significance of **Atrial Fibrillation** Complicating ST-Segment Elevation Myocardial Infarction. Am J Cardiol. 2017 Aug 15;120(4):517-521.
Pokorney SD, Miller AL, Chen AY, et al. **Implantable cardioverter-defibrillator use** among Medicare patients with low ejection fraction after acute myocardial infarction.JAMA. doi:10.1001 /jama.2015.6409.
Poole CD, Halcox JP, Jenkins-Jones S, et al. **Omega-3 Fatty Acids** and Mortality Outcome in Patients With and Without Type 2 Diabetes After Myocardial Infarction: A Retrospective, Matched-Cohort Study. ClinTher. 2012 Dec 12.
Postma S, Dambrink JH, Gosselink AT, et al. The influence of **system delay** on 30-day and on long-term mortality in patients with anterior versus non-anterior ST-segment elevation myocardial infarction: a cohort study. Open Heart. 2015 Apr 10;2(1):e000201.
Potter BJ, Matteau A, Mansour S, et al. Performance of a New **"Physician-Less" Automated System of Prehospital** ST-Segment Elevation Myocardial Infarction Diagnosis and **Catheterization Laboratory** Activation. Am J Cardiol. 2013 Apr 12.
Prasad Abhiram, Herrmann Joerg. Myocardial Infarction Due to **Percutaneous Coronary Intervention** (PCI). N Engl J Med 2011; 364:453-464.
Prasad A, Gersh BJ, Mehran R, et al. Effect of **Ischemia Duration and Door-to-Balloon Time** on Myocardial Perfusion in ST-Segment Elevation Myocardial Infarction: An Analysis From HORIZONS-AMI Trial (Harmonizing Outcomes with Revascularization and Stents in Acute Myocardial Infarction). JACC Cardiovasc Interv. 2015 Dec 28;8(15):1966-74.
Pristipino C, Roncella A, Pasceri V, Speciale G. Short-TErm Psychotherapy IN Acute Myocardial Infarction (**STEP-IN-AMI**) TRIAL: Final results. Am J Med. 2019 Jan 16.
Pu J, Ding S, Ge H, et al; **EARLY-MYO** Investigators. Efficacy and safety of a **pharmaco-invasive strategy with half-dose alteplase versus primary angioplasty in ST-segment-elevation myocardial infarctio**n: EARLY-MYO trial (Early Routine Catheterization After **Alteplase Fibrinolysis Versus Primary PCI** in Acute ST-SegmentElevation Myocardial Infarction). Circulation. 2017;136:1462–1473.
Puelacher C, Lurati Buse G, Seeberger D, et al. **Perioperative Myocardial Injury After Noncardiac Surgery**: Incidence, Mortality, and Characterization. Circulation. 2017 Dec 4.
Puymirat E, Aissaoui N, Coste P, et al. Comparison of efficacy and safety of a **standard versus a loading dose of clopidogrel** for acute myocardial infarction in patients >/= 75 years of age (from the **FAST-MI registry**). Am J Cardiol. 2011 Sep 15;108(6):755-9.
Puymirat E, Simon T, et al. Association of **changes in clinical characteristics** and management with improvement in survival among patients with ST-elevation myocardial infarction. (**FAST-MI**) JAMA 2012. (overall decreased but increase in proportion of women <60yrs)
Puymirat E, Riant E, Aissoui N, et al. **β blockers and mortality after myocardial infarction** in patients without heart failure: multicentre prospective cohort study. BMJ. 2016 Sep 20;354:i4801.
Puymirat E, Simon T, Cayla G, et al; USIK, USIC 2000, and **FAST-MI** investigators. **Acute Myocardial Infarction**: Changes in Patient Characteristics, Management, and 6-Month Outcomes **Over a Period of 20 Years in the FAST-MI Program** (French Registry of Acute ST-Elevation or Non-ST-Elevation Myocardial Infarction) 1995 to 2015. Circulation. 2017 Nov 14;136(20):1908-1919.
Pryu Bettger J et al. **Transitional care** after hospitalization for acute stroke or myocardial infarction. Ann Intern Med 2012 Sep 18; 157:407.

Qaseen A, Fihn SD, Dallas P, et al. Management of patients with **stable ischemic heart disease**: Executive summary of a clinical practice guideline from the American College of Physicians, American College of Cardiology Foundation/American Heart Association (AHA)/ American Association for Thoracic Surgery/Preventive Cardiovascular Nurses Association/Society of Thoracic Surgeons. Ann Intern Med 2012;

Qian F, Ling FS, Deedwania P, et al. Care and **outcomes of Asian acute myocardial infarction patients**: findings from the American Heart Association Get With The Guidelines—Coronary Artery Disease program (GWTG-CAD). Circ Cardiovasc Qual Outcomes 2012.

Quinn T, Johnsen S, Gale CP, et al; On behalf of the Myocardial Ischaemia National Audit Project (MINAP) Steering Group. Effects of **prehospital 12-lead ECG on** processes of care and mortality in acute coronary syndrome: a linked cohort study from the Myocardial Ischaemia National Audit Project. Heart. 2014 Apr 14.

Qureshi WT, Zhang ZM, Chang PPet al. **Silent Myocardial Infarction** and Long-Term Risk of Heart Failure: The **ARIC** Study. J Am Coll Cardiol. 2018 Jan 2;71(1):1-8.

Raber L, Yamaji K, Kelbaek H, et al. Five-year **clinical outcomes and intracoronary imaging findings of the COMFORTABLE AMI trial**: randomized comparison of biodegradable polymer-based biolimus-eluting stents with bare-metal stents in patients with acute ST-segment elevation myocardial infarction. Eur Heart J. 2019 Mar 9.

Rajagopalan S, Brook RD. Mortality from myocardial infarction **in chronic obstructive pulmonary disease**: minding and mending the 'Gap'. Heart. 2015 Apr 22.

Rallidis LS, Gialeraki A, Triantafyllis AS, et al. Characteristics and Long-Term **Prognosis** of Patients ≤35 Years of Age with ST Segment Elevation Myocardial Infarction and "Normal or Near Normal" Coronary Arteries. Am J Cardiol. 2017 Jun 13.

Ranasinghe I, Barzi F, Brieger D, et al. **Long-term mortality following interhospital transfer** for acute myocardial infarction. Heart. 2015 Jul1;101(13):1032-40.

Rao SV, Kaltenbach LA, Weintraub WS, et al. Prevalence and outcomes of **same-day discharge after elective percutaneous coronary intervention** among older adults. JAMA 2011; 306: 1461-1467.

Rasmussen MB, Stengaard C, Sørensen JT, et al. Comparison of **Acute Versus Subacute Coronary Angiography** in Patients With NON-ST-Elevation Myocardial Infarction (from the NONSTEMI Trial). Am J Cardiol. 2019 Jun 24.

Rathore SS, Curtis JP, Chen J, et al. National Cardiovascular Data Registry. Association of **door-to-balloon time** and mortality in patients admitted to hospital with ST elevation myocardial infarction: national cohort study. BMJ. 2009 May 19;338:b1807. doi: 10.1136/bmj.b1807.

Rauch Bernhard, Schiele Rudolf, Schneider Steffen, et al., and for the **OMEGA** Study Group OMEGA, a Randomized, Placebo-Controlled Trial to Test the Effect of Highly Purified **Omega-3 Fatty Acids** on Top of Modern Guideline-Adjusted Therapy After Myocardial Infarction Circulation published November 8, 2010, doi:10.1161/CIRCULATIONAHA.110.948562

Rautiainen S, Levitan EB, Orsini N, et al. Total **antioxidant capacity from diet** (fruits, vegetables , coffee & whole grains) and risk of myocardial infarction: a prospective cohort of women. Am J Med. 2012 Oct;125(10):974-80.

Reed GW, Rossi JE, Cannon CP. **Acute myocardial infarction**. Lancet. 2016 Aug 5.

Reichlin, Tobias, Hochholzer, Willibald, Bassetti, Stefano, et al. Early Diagnosis of Myocardial Infarction with **Sensitive Cardiac Troponin Assays**. N Engl J Med 2009 361: 858-867. The diagnostic performance of sensitive cardiac troponin assays is excellent, and these assays can substantially improve the early diagnosis of acute myocardial infarction, particularly in patients with a recent onset of chest pain.

Reichlin T, Irfan A, Twerenbold R, et al. Utility of absolute and relative changes in **cardiac troponin concentrations** in the early diagnosis of acute myocardial infarction. Circulation. 2011 Jul 12;124(2):136-45.

Reichlin T, Schindler C, Drexler B, et al. **One-hour rule-out and rule-in of acute myocardial infarction using high sensitivity cardiac troponin T**. Arch Intern Med 2012.

Reichlin T, Twerenbold R, Wildi K, et al. Prospective validation of a **1-hour algorithm** to rule-out and rule-in acute myocardial infarction using a **high-sensitivity cardiac troponin T assay**. *CMAJ* 2015.

Reichlin T, Cullen L, Parsonage WA, et al. **Two-hour Algorithm** for Triage Toward Rule-out and Rule-in of Acute Myocardial Infarction Using High-sensitivity Cardiac Troponin T. Am J Med. 2015 Apr;128(4):369-379.e4.

Reinstadler SJ, Eitel C, Thieme M, et al. Comparison of Characteristics of Patients aged **≤45 Years Versus >45 Years** With ST-Elevation Myocardial Infarction (from the **AIDA STEMI CMR** Substudy). Am J Cardiol. 2016 May 1;117(9):1411-6.

Reiter M, Twerenbold R, Reichlin T, et al. Early diagnosis of acute myocardial infarction in the elderly using more **sensitive cardiac troponin assays**. Eur Heart J. 2011 Jun;32(11):1379-89.

Rene AG, Généreux P, Ezekowitz M, et al. Impact of **Atrial Fibrillation** in Patients With ST-Elevation Myocardial Infarction Treated With Percutaneous Coronary Intervention (from the **HORIZONS-AMI** [Harmonizing Outcomes With Revascularization and Stents in Acute Myocardial Infarction] Trial). Am J Cardiol. 2013 Oct 3.

Reynolds HR, Srichai MB, Iqbal SN, et al. **Mechanisms of myocardial infarction in women** without angiographically obstructive coronary artery disease. Circulation. 2011;124:1414 –1425

Ridker PM, Danielson E, Fonseca FA, Genest J, et al. the **JUPITER** Study Group. Rosuvastatin to Prevent Vascular Events in Men and Women with Elevated C-Reactive Protein. N Engl J Med. 2008 Nov 9. [Epub ahead of print] In this trial of apparently healthy persons without hyperlipidemia but with elevated high-sensitivity C-reactive protein levels, rosuvastatin significantly reduced the incidence of major cardiovascular events.

Ridker PM et al. Antiinflammatory therapy with **canakinumab** for atherosclerotic disease. (**CANTOS**) N Engl J Med2017 Aug 27.

Ridker PM, MacFadyen JG, et al; **CANTOS** Trial Group. **Relationship of C-reactive protein** reduction to cardiovascular event reduction following treatment with **canakinumab**: a secondary analysis from the CANTOS randomised controlled trial. Lancet. 2017 Nov 13.

Ridker PM, Everett BM, Thuren T, et al. Antiinflammatory Therapy with **Canakinumab** for Atherosclerotic Disease. N Engl J Med. 2017 Sep 21;377(12):1119-1131.

Ritsinger V, Malmberg K, Mårtensson A, et al. **Intensified insulin-based glycaemic control after myocardial infarction**: mortality during 20 year follow-up of the randomised Diabetes Mellitus Insulin Glucose Infusion in Acute Myocardial Infarction (**DIGAMI 1**) trial. Lancet Diabetes Endocrinol. 2014 May 12

Roberts WC, Burks KH, Ko JM, Filardo G, Guileyardo JM. Commonalities of **Cardiac Rupture** (Left Ventricular Free Wall or Ventricular Septum or Papillary Muscle) During Acute Myocardial Infarction Secondary to Atherosclerotic Coronary Artery Disease. Am J Cardiol. 2015 Jan 1;115(1):125-140.

Rodríguez LA, Cea-Soriano L, Martín-Merino E, Johansson S. **Discontinuation of low dose aspirin and risk** of myocardial infarction: case-control study in UK primary care. BMJ. 2011 Jul 19;343:d4094.

Roger VL, Weston SA, Gerber Y, et al. Trends in **Incidence, Severity, and Outcome of Hospitalized Myocardial Infarction**. Circulation. 2010 Feb 8.

Romaguera R, Wakabayashi K, Laynez-Carnicero A, et al.. Association Between **Bleeding Severity** and Long-Term Mortality in Patients Experiencing Vascular Complications After **Percutaneous Coronary Intervention**. Am J Cardiol. 2011 Sep 29.

Rosamond WD, Chambless LE, Heiss G, et al. **Twenty-Two-Year Trends in Incidence of Myocardial Infarction**, Coronary Heart Disease **Mortality**, and Case Fatality in 4 US Communities, 1987-2008. Circulation. 2012 Apr 17;125(15):1848-57.

Rosenbloom JI, Mukamal KJ, Frost LE, Mittleman MA. **Alcohol Consumption** Patterns, Beverage Type, and Long-Term Mortality Among Women Survivors of Acute Myocardial Infarction. Am J Cardiol. 2011 Oct 17.

Rosenbloom JI, Wilker EH, Mukamal KJ, et al. **Residential proximity to major roadway** and 10-year all-cause mortality after myocardial infarction. Circulation. 2012 May 8;125(18):2197-203.

Rosenson RS, Farkouh ME, Mefford M, et al. Trends in use of **high-intensity statin therapy** after myocardial infarction, 2011 to 2014. J Am Coll Cardiol 2017;69:2696–706.

Ross, Joseph S., Normand, Sharon-Lise T., Wang, Yun, et al. Hospital **Volume** and 30-Day **Mortality** for Three Common Medical Conditions. N Engl J Med 2010 362: 1110-1118.

Rossignol P, Ménard J, Fay R, et al. **Eplerenone** survival benefits in heart failure patients post-myocardial infarction are independent from its diuretic and potassium-sparing effects: insights from an **EPHESUS** (Eplerenone Post-Acute Myocardial Infarction Heart Failure Efficacy and Survival Study) substudy. J Am Coll Cardiol 2011; 58:1958-1966.

Rothberg MB, Celestin C, Fiore LD, et al. Warfarin plus aspirin after myocardial infarction or the acute coronary syndrome: meta-analysis with estimates of risk and benefit. Ann Intern Med. 2005 Aug 16;143(4):241-50. (InfoPOEMs: Adding warfarin to aspirin prophylaxis does not affect overall death rates, though the combination decreases subsequent myocardial infarction risk ([NNT = 56) and, to a lesser degree, ischemic stroke risk (NNT = 221). As one might expect, major bleeding episodes occur more often with the added warfarin, though only in a small number of patients (1.5% vs 0.56%). (LOE = 1a))

Rothenbacher D, Dallmeier D, Mons U, et al. **Sexual Activity Patterns** Before Myocardial Infarction and Risk of Subsequent Cardiovascular Adverse Events. J Am Coll Cardiol. 2015 Sep 29;66(13):1516-7.

Rousan TA, Pappy RM, Chen AY, et al. **Impact of Diabetes Mellitus** on Clinical Characteristics, Management, and In-hospital Outcomes in Patients With Acute Myocardial Infarction (from the NCDR). Am J Cardiol. 2014 Jul 30.

Ruane L, Buckley T, Hoo SYS, et al. **Triggering of acute myocardial infarction by respiratory infection**. Intern Med J. 2017 May;47(5):522-529.

Rubini Gimenez M, Reiter M, Twerenbold R, et al. **Sex-specific chest pain characteristics** in the early diagnosis of acute myocardial infarction. JAMA Intern Med. 2014;174:241-9.

Rubini Gimenez M, Twerenbold R, Jaeger C, et al. **One-hour Rule-in and Rule-out** of Acute Myocardial Infarction Using **High-sensitivity Cardiac Troponin I**. Am J Med. 2015 Mar 31.

Rubini Giménez M, Twerenbold R, Boeddinghaus J, et al. Clinical Effect of **Sex-Specific Cutoff Values of High-Sensitivity Cardiac Troponin** T in Suspected Myocardial Infarction. JAMA Cardiol. 2016 Sep 21

Rubini Gimenez M, Badertscher P, Twerenbold R, et al. Impact of the US Food and Drug Administration-Approved Sex-Specific Cutoff Values for High-Sensitivity **Cardiac Troponin T** to Diagnose Myocardial Infarction. Circulation. 2018 Apr 24;137(17):1867-1869.

Ruzycki SM, Kachra R, Lyons K. A 71-year-old woman with an **asymptomatic postoperative troponin elevation**. CMAJ. 2019 Jan 7;191(1):E11-E14.

Rydén L, Buhlin K, Ekstrand E, et al. **Periodontitis** increases the risk of a first myocardial infarction: A report from the PAROKRANK study.*Circulation* 2016.

Sabaté M, Brugaletta S, Cequier A, et al. Clinical outcomes in patients with ST-segment elevation myocardial infarction treated with **everolimus-eluting stents versus bare-metal stents** (**EXAMINATION**): 5-year results of a randomised trial. Lancet 2015; online Oct 29.

Salisbury AC, Reid KJ, Alexander KP, et al. Diagnostic Blood Loss From **Phlebotomy and Hospital-Acquired Anemia During Acute Myocardial Infarction**. Arch Intern Med. 2011 Aug 8.

Salisbury AC, Amin AP, Reid KJ et al. **Red Blood Cell Indices** and Development ofHospital-Acquired Anemia During Acute Myocardial Infarction. Am J Cardiol. 2012 Jan 18.

Salisbury AC, Reid KJ, Marso SP, et al. **Blood transfusion** during acute myocardial infarction. *J Am Coll Cardiol*2014; 64:811-819.

Sandhu A, Seth M, Gurm H. **Daylight savings time** and myocardial infarction. Open Heart 1.1 (2014): e000019.

Sandoval Y, Jaffe AS. **Type 2 Myocardial Infarction**: JACC Review Topic of the Week. J Am Coll Cardiol. 2019 Apr 16;73(14):1846-1860.

Sandoval Y, Nowak R, deFilippi CR, et al. Myocardial Infarction **Risk Stratification With a Single Measurement of High-Sensitivity Troponin** I. J Am Coll Cardiol. 2019 Jul 23;74(3):271-282.

Schachinger V, et al. REPAIR-AMI Investigators. Intracoronary **bone marrow**-derived progenitor cells in acute myocardial infarction. N Engl J Med. 2006 Sep 21;355(12):1210-21.

Schelbert EB, Cao JJ, Sigurdsson S, et al. Prevalence and prognosis of unrecognized myocardial infarction determined by **cardiac magnetic resonance** in older adults. JAMA 2012; 308:890-897.

Schelde AB, Schmidt M, Madsen, M, et al. Impact of Comorbidity on the Risk of First-time Myocardial Infarction, Stroke, or Death **after Single-photon Emission Computed Tomography Myocardial Perfusion Imaging**. The American Journal of Cardiology (2014).

Scherrer JF, Chrusciel T, Garfield LD et al. Treatment-resistant and insufficiently treated **depression** and all-cause mortality following myocardial infarction. Br J Psychiatry. 2012 Feb;200:137-42.

Schieir O, Tosevski C, Glazier RH, et al. Incident myocardial infarction **associated with major types of arthritis** in the general population: a systematic review and meta-analysis. Ann Rheum Dis. 2017 Aug;76(8):1396-1404

Schjerning Olsen AM, Fosbøl EL, et al. Duration of treatment with nonsteroidal anti-inflammatory drugs and impact on risk of **death and recurrent myocardial infarction** in patients with prior myocardial infarction: a nationwide cohort study. Circulation. 2011;123: 2226-35.

Schjerning Olsen A, Fosbøl L, Lindhardsen J, et al. Long-term **cardiovascular risk of NSAID** use according to time passed after first-time myocardial infarction. A nationwide cohort study. Circulation 2012.

Schjerning Olsen A-M, Gislason GH, McGettigan P, et al. Association of **NSAID use with risk of bleeding and cardiovascular events in patients receiving antithrombotic therapy after myocardial infarction**. JAMA. doi:10.1001/jama.2015.0809.

Schmidt M, Jacobsen JB, et al. **25 year trends in first time hospitalisation** for acute myocardial infarction, subsequent short and long term mortality, and the prognostic impact of sex and comorbidity: a Danish nationwide cohort study. BMJ 2012;344:e356.

Schmidt M, Szépligeti S, Horváth-Puhó E, et al. Long-Term **Survival Among Patients With Myocardial Infarction Before Age 50** Compared With the General Population: A Danish Nationwide Cohort Study. Circ Cardiovasc Qual Outcomes. 2016 Aug 30.

Schomig A, Mehilli J, Mechanical Reperfusion in Patients with Acute Myocardial Infarction Presenting more than 12 Hours from Symptom Onset (**BRAVE-2**). JAMA. 2005 June 15;293:2865-2872.

Schulman-Marcus J, Goyal P, Swaminathan RV, et al. Comparison of Trends in Incidence, Revascularization, and In-Hospital Mortality in ST-Elevation Myocardial Infarction in Patients **With Versus Without Severe Mental Illness**. Am J Cardiol. 2016 May 1;117(9):1405-10.

Schulman SP, et al. **L-arginine** therapy in acute myocardial infarction: the Vascular Interaction With Age in Myocardial Infarction (VINTAGE MI) randomized clinical trial. JAMA. 2006 Jan 4;295(1):58-64.

Schwartz BG, Rezkalla S, Kloner RA. Cardiovascular effects of **cocaine**. Circulation. 2010 Dec 14;122(24):2558-69.

Scirica BM, Bonaca MP, Braunwald E, et al, TRA 2°P-TIMI 50 Steering Committee. **Vorapaxar** for secondary prevention of thrombotic events for patients with previous myocardial infarction: a prespecified subgroup analysis of the TRA 2°P-TIMI 50 trial. Lancet 2012.

Scott J, Howard B, Sinnett P, et al. **Variable methodological quality and use found in systematic reviews** referenced in STEMI clinical practice guidelines. Am J Emerg Med. 2017 Jun 14

SCOT-HEART Investigators, Newby DE, Adamson PD, Berry C, etal. **Coronary CT Angiography and 5-Year Risk of Myocardial Infarction**. N Engl J Med. 2018 Sep 6;379(10):924-933.

Secemsky EA, Ferro EG, Rao SV, et al. Association of physician variation in use of **manual aspiration thrombectomy** with outcomes following **primary percutaneous coronary intervention for ST-elevation myocardial infarction**: the National Cardiovascular Data Registry CathPCI Registry [online Jan 9, 2019]. JAMA Cardiol.doi:10.1001/jamacardio.2018.4472

Secemsky EA, Lange D, Ho JE, et al. Improvement in revascularization time after creation of a coronary catheterization laboratory at a public hospital. Arch Intern Med. doi:10.1001/archinternmed.2011.564.

Sehested TSG, Bjerre J, Ku S, et al. **Cost-effectiveness of Canakinumab for Prevention** of Recurrent Cardiovascular Events. JAMA Cardiol. 2019 Jan 16.

Selker HP, Beshansky JR, Sheehan PR, et al. Out-of-hospital administration of **intravenous-insulin-potassium** in patients with suspected acute coronary syndromes. (**Immediate**) JAMA 2012.

Selvaraj S, Bhatt DL, Stone GW. "**Off-hours" versus "on-hours**" presentation in ST-segment-elevation myocardial infarction: Findings from **CHAMPION PHOENIX**. *J Am Coll Cardiol* 2016.

Selvin E, Lazo M, Chen Y, et al. **Diabetes mellitus**, prediabetes, and incidence of subclinical myocardial damage. Circulation. 2014 Oct 14;130(16):1374 82.

Senecal EL, Rosenfield K, Caldera AE, et al. Case 36-2011 — A 93-Year-Old Woman with Shortness of Breath and Chest Pain. (**Takosubo cardiomyopathy**). N Engl J Med 2011; 365:2021-2028.

Sepehrvand N, James SK, Stub D, et al. Effects of **supplemental oxygen therapy** in patients with suspected acute myocardial infarction: a meta-analysis of randomised clinical trials. Heart. 2018 Mar 29.

Serebruany VL, Atar D. Viewpoint: **Central adjudication** of myocardial infarction in outcome-driven clinical trials—Common patterns in **TRITON, RECORD, and PLATO**? Thromb Haemost 2012.

Seronde MF, Geha R, Puymirat E, et al. **Discharge heart rate** and mortality after acute myocardial infarction. Am J Med. 2014 Jul 5.

Serrao GW, Lansky AJ, Mehran R et al. Predictors of **Left Ventricular Ejection Fraction Improvement** after Primary Stenting in ST-Segment Elevation Myocardial Infarction (From the **HORIZONS-AMI** Trial). Am J Cardio. 2017

Servey JT, Stephens M. **Cardiac Rehabilitation**: Improving Function and Reducing Risk. Am Fam Physician. 2016;94(1):37-43.

Shacham Y, Topilsky Y, Leshem-Rubinow E, et al. Comparison of **Left Ventricular Function** Following First ST-Segment Elevation Myocardial Infarction Treated With Primary Percutaneous Coronary Intervention in **Men Versus Women**. Am J Cardiol. 2014 Apr 1.

Shah AS, Newby DE, Mills NL. **High sensitivity cardiac troponin** in patients with chest pain. BMJ. 2013 Jul 22;347:f4222.

Shah ASV, Griffiths M, Lee KK, McAllister DA, Hunter AL, Cruickshank A, et al. **High sensitivity cardiac troponin and the under-diagnosis of myocardial infarction in women**: prospective cohort study. BMJ 2015;350:g7873.

Shah AS, Anand A, Sandoval Y et al; High-STEACS investigators. **High-sensitivity cardiac troponin** I at presentation in patients with suspected acute coronary syndrome: a cohort study. Lancet. 2015 Oct 7.

Shah ASV, Sandoval Y, Noaman A, et al. Patient selection for **high sensitivity cardiac troponin testing and diagnosis of myocardial infarction**: prospective cohort study. BMJ. 2017 Nov 7;359:j4788.

Shavadia JS, Chen AY, Fanaroff AC, et al. Intensive **Care Utilization in Stable Patients With ST-Segment Elevation Myocardial Infarction Treated With Rapid Reperfusion**. JACC Cardiovasc Interv. 2019 Apr 22;12(8):709-717.

Shavadia JS, Holmes DN, Thomas L, et al. Comparative **Effectiveness of β-Blocker Use Beyond 3 Years** After Myocardial Infarction and Long-Term Outcomes Among Elderly Patients. Circ Cardiovasc Qual Outcomes. 2019 Jul;12(7):e005103.

Shaya GE, Al-Mallah MH, Hung RK, et al. **High Exercise Capacity Attenuates** the Risk of Early Mortality After a First Myocardial Infarction: The Henry Ford Exercise Testing (**FIT**) Project. Mayo Clin Proc. 2016 Feb;91(2):129-39.

Shehata M. Impact of **Trimetazidine** on Incidence of Myocardial Injury and Contrast-Induced Nephropathy in Diabetic Patients With Renal Dysfunction Undergoing Elective Percutaneous Coronary Intervention. Am J Cardiol. 2014 May 16.

Shen YC, Hsia RY. Association between **ambulance diversion** and survival among patients with acute myocardial infarction. JAMA. 2011 Jun 15;305(23):2440-7.

Shen YC, Hsia RY. Association Between **Emergency Department Closure** and Treatment, Access, and Health Outcomes Among Patients With Acute Myocardial Infarction. Circulation. 2016 Nov 15;134(20):1595-1597.

Shahzad A, Kemp I, Mars C, et al, for the **HEAT-PPCI trial investigators. Unfractionated heparin versus bivalirudin** in primary percutaneous coronary intervention (HEAT-PPCI): an open-label, single centre, randomised controlled trial. Lancet 2014; online July 5.

Shibata T, Kawakami S, Noguchi T, et al. Prevalence, clinical features, and prognosis of acute myocardial infarction **due to coronary artery embolism**. Circulation. 2015;132:241–250

Shibata T, Kawakami S, Noguchi T, et al. Prevalence, Clinical Features, and Prognosis of Acute Myocardial Infarction Attributable to **Coronary Artery Embolism**. Circulation. 2015 Jul 28;132(4):241-50.

Shiomi H, et al; CREDO-Kyoto AMI investigators. Association of **onset to balloon and door to balloon time** with long term clinical outcome in patients with ST elevation acute myocardial infarction having primary percutaneous coronary intervention: observational study. BMJ. 2012 May 23;344:e3257.

Shrestha A, House DR, Welch JL. In Patients With ST-Segment Elevation Myocardial Infarction, **Which Fibrinolytic Agent Is the Safest and Most Effective**? Ann Emerg Med. 2018 Feb 24.

Siha H, Das D, Fu Y, et al. **Baseline Q waves** as a prognostic modulator in patients with ST-segment elevation: insights from the PLATO trial. CMAJ 2012;184:1135-42.

Simms A, Weston C, West R, et al. **Mortality and missed opportunities along the pathway of care** for ST elevation myocardial infarction: a national cohort study. Eur Heart J Acute Cardiovasc Care. 2014 Sep 16.

Singh A et al. **Familial hypercholesterolemia among young adults with myocardial infarction**. J Am Coll Cardiol 2019 May 21; 73:2439.

Shirani J, Pranesh S, Menhaji K, et al. **Dobutamine-Induced** Myocardial Ischemia and ST-Segment Elevation in Collateral-Dependent Myocardium. Am J Cardiol. 2013 Jul 15.

Silletta MG, Marfisi R, Levantesi G, et al. R; GISSI-Prevenzione Investigators. **Coffee consumption** and risk of cardiovascular events after acute myocardial infarction: results from the GISSI (Gruppo Italiano per lo Studio della Sopravvivenza nell'Infarto miocardico)-Prevenzione trial. Circulation. 2007 Dec 18;116(25):2944-51. Epub 2007 Dec 3. Coffee consumption does not increase the risk of cardiovascular events following acute myocardial infarction (AMI). (LOE = 1b)

Silva D, Cortez-Dias N, Jorge C et al. **Cystatin C** as Prognostic Biomarker in ST-Segment Elevation Acute Myocardial Infarction. Am J Cardiol. 2012 Feb 20.

Silvain J, Beygui F, Barthelemy O, et al. Efficacy and safety of **enoxaparin versus unfractionated heparin** during percutaneous coronary intervention: systematic review and meta-analysis. BMJ. 2012 Feb 3;344:e553.

Sim DS, Jeong MH, Ahn Y, et al; Other Korea Acute Myocardial Infarction Registry (KAMIR) Investigators. Benefit of **Percutaneous Coronary Intervention** in Early **Latecomers** With Acute ST-Segment Elevation Myocardial Infarction. Am J Cardiol. 2012 Jul 21.

Simpson TF, Rahman S, Goldschlager N. **Enhancing the Sgarbossa Criteria for the Diagnosis of ST Elevation Myocardial Infarction**. JAMA Intern Med. 2019 Feb 11.

Sims Michelle, Maxwell Roy, Bauld Linda, Gilmore Anna. Short term impact of **smoke-free legislation** in England: retrospective analysis of hospital admissions for **myocardial infarction**. BMJ 2010;340:c2161

Singh HS, Dangas GD, Guagliumi G, et al. Comparison of **Abciximab Versus Eptifibatide** During Percutaneous Coronary Intervention in ST-Segment Elevation Myocardial Infarction (from the HORIZONS-AMI Trial). Am J Cardiol. 2012 Oct 1;110(7):940-7.

Sinnaeve PR, Armstrong PW, Gershlick AH, et al; **STREAM** investigators*. ST-Segment-Elevation Myocardial Infarction Patients Randomized to a **Pharmaco-Invasive Strategy or Primary Percutaneous Coronary Intervention**: Strategic Reperfusion Early After Myocardial Infarction (STREAM) 1-Year Mortality Follow-Up. Circulation. 2014 Sep 30;130(14):1139-45.

Siontis KC, Barsness GW, Lennon RJ, et al. **Pharmacoinvasive and Primary Percutaneous Coronary Intervention Strategies** in ST-Elevation Myocardial Infarction (from the Mayo Clinic STEMI Network). Am J Cardiol. 2016 Jun 15;117(12):1904-10.

Sipilä JO, Gunn JM, Kauko T, et al. Association of **restaurant smoking ban** and the incidence of acute myocardial infarction in Finland. BMJ Open. 2016 Jan 29;6(1):e009320.

Siriwardena AN, Gwini SM, Coupland C. **Influenza vaccination, pneumococcal vaccination** and risk of AMI: Matched case-control study. CMAJ 2010; DOI:10.1503/cmaj.091891.

Skolnick AH et al. Comparison of Late Results of **Percutaneous Coronary Intervention** Among Stable Patients ≤65 Versus >65 Years of Age With an Occluded Infarct Related Artery (from the **Occluded Artery Trial**). Am J Cardiol. 2011 Dec 13 –no indication for routine PCI.

Smedegaard L, Numé AK, Charlot M, et al. **Return toWork** and Risk of Subsequent Detachment From Employment After Myocardial Infarction: Insights From Danish Nationwide Registries. J Am Heart Assoc. 2017Oct 4;6(10).

Smilowitz NR, Gupta N, Guo Y, et al. **Perioperative acute myocardial infarction** associated with non-cardiac surgery. European Heart Journal. 2017;38:2409-2417.

Smilowitz NR, Beckman JA, Sherman SE, Berger JS. **Hospital readmission after perioperative acute myocardial infarction** associated with noncardiac surgery. Circulation. 2018;137:2332–2339.

Smilowitz NR, Gupta N, Guo Y, et al. **Acute Myocardial Infarction During Pregnancy** and the Puerperium in the United States. Mayo Clin Proc. 2018 Jul 15.

Smith SC Jr, et al. **AHA/ACC guidelines for secondary prevention** for patients with coronary and other atherosclerotic vascular disease: **2006** update: endorsed by the National Heart, Lung, and Blood Institute. Circulation. 2006 May 16;113(19):2363-72. http://circ.ahajournals.org/cgi/reprint/113/19/2363

Smith SC Jr, Benjamin EJ, Bonow RO, et al.; World Heart Federation and the Preventive Cardiovascular Nurses Association. **AHA/ACCF secondary prevention** and risk reduction therapy for patients with coronary and other atherosclerotic vascular disease: 2011 update. Circulation. 2011;124(22):2458-2473.

Smits PC, Abdel-Wahab M, Neumann F-J, et al. **Fractional flow reserve–guided multivessel angioplasty in myocardial infarction**. (**Compare-Acute**) N Engl J Med. DOI: 10.1056/NEJMoa1701067.

Smolderen KG, et al. **Depression** treatment and health status outcomes in young patients with acute myocardial infarction: insights from the VIRGO study (Variation in Recovery: Role of Gender on Outcomes of Young AMI Patients). Circulation. 2017;135:1762–1764.

Smolderen KG, Buchanan DM, Gosch K, et al. **Depression** treatment and 1-year mortality following acute myocardial infarction: insights from the TRIUMPH registry (Translational ResearchInvestigating Underlying Disparities in Acute Myocardial Infarction Patients' Health Status). Circulation. 2017;135:1681-1689.

Smolina K, Wright FL, Rayner M, Goldacre MJ. Determinants of the **decline in mortality from acute myocardial infarction in England** between 2002 and 2010: linked national database study. BMJ 2012;344:d8059.

Smolina K, Wright FL, Rayner M, Goldacre MJ. **Long-Term Survival** and Recurrence After Acute Myocardial Infarction in **England**, 2004 to 2010. Circ Cardiovasc Qual Outcomes. 2012 Jun 26.

Smolina K, Ball L, Humphries KH, et al. **Sex Disparities** in Post-Acute Myocardial Infarction Pharmacologic Treatment **Initiation and Adherence**: Problem for Young **Women**. Circ Cardiovasc Qual Outcomes. 2015 Oct 13.

Smyth A, O'Donnell M, Lamelas P et al. **Physical Activity and Anger or Emotional Upset** as Triggers of Acute Myocardial Infarction. Circulation. 2016 ;134:1059-1067.

Sode BF, Dahl M, Nordestgaard BG. Myocardial infarction and other co-morbidities in patients with **chronic obstructive pulmonary disease**: a Danish Nationwide Study of 7.4 million individuals. Eur Heart J. 2011 Aug 29.

Solhpour A, Chang KW, Balan P, et al. Comparison of Outcomes for Patients **≥75 Years of Age** Treated With Pre-Hospital Reduced-Dose **Fibrinolysis** Followed by Percutaneous Coronary Intervention Versus Percutaneous Coronary Intervention Alone for Treatment of ST-Elevation Myocardial Infarction. Am J Cardiol. 2013 Oct 3.

Soliman EZ, Lopez F, O'Neal WT, et al. **Atrial Fibrillation** and Risk of ST-Segment Elevation versus Non-ST Segment Elevation Myocardial Infarction: The Atherosclerosis Risk in Communities (ARIC) Study. Circulation. 2015 Apr 27.

Solomon SD, Zelenkofske S, McMurray JJ, et al, for the Valsartan in Acute Myocardial Infarction Trial (**VALIANT**) Investigators. Sudden death in patients with myocardial infarction and left ventricular dysfunction, heart failure, or both. N Engl J Med 2005; 352: 2581-8. (InfoPOEMs: **Sudden death occurs in 1.4%** of patients during the first month after an acute myocardial infarction (AMI), & in approximately 0.14% per month after 2 years. Sudden death is more likely in patients with a lower ejection fraction. Although this suggests that early implantation of a cardiac defibrillator may be helpful, a previous trial did not find such a benefit, perhaps because this outcome is relatively rare and a larger, longer study would be needed to detect a statistically significant benefit. (LOE = 1b))

Solomon SD, Hee Shin S, Shah A, et al. Effect of the direct rennin inhibitor aliskiren on left ventricular remodelling following myocardial infarction *with systolic dysfunction.*(***ASPIRE***) *Eur Heart J 2011; 32: 1227–34.*

Sorita A, Ahmed A, Starr SR, Thompson KM, Reed DA, Prokop L, et al. **Off-hour presentation and outcomes** in patients with acute myocardial infarction: systematic review and meta-analysis. BMJ 2014;348:f7393.

Sousa-Uva M, Neumann FJ, Ahlsson A, et al; ESC Scientific Document Group . **2018 ESC/EACTS Guidelines on myocardial revascularization**. Eur J Cardiothorac Surg. 2018 Aug 27.

Spatz ES, Beckman AL, Desai NR, Krumholz HM. **Geographic variation** in trends and disparities in acute myocardial infarction hospitalization and **mortality by income levels**, 1999-2013 [online May 11, 2016]. JAMA Cardiol. doi:10.1001 /jamacardio.2016.0382.

Spaulding C, et al. **TYPHOON** Investigators. **Sirolimus-eluting versus uncoated** stents in acute myocardial infarction. N Engl J Med. 2006 Sep 14;355(11):1093-104.

Stacey RB, Leaverton PE, Schocken DD, et al. **Prediabetes** and the association with unrecognized myocardial infarction in the Multi-Ethnic Study of Atherosclerosis. *Am Heart J* 2015.

Spatz ES, Curry LA, Masoudi FA, et al. The Variation in Recovery: Role of **Gender** on Outcomes of Young AMI Patients (VIRGO) Classification System: A **Taxonomy for Young Women** With Acute Myocardial Infarction. Circulation. 2015 Nov 3;132(18):1710-8.

Stefanescu Schmidt AC, Kereiakes DJ, Cutlip DE, et al; **DAPT** Investigators.. **Myocardial Infarction Risk After Discontinuation of Thienopyridine Therapy** in the Randomized DAPT Study (Dual Antiplatelet Therapy). Circulation. 2017 May 2;135(18):1720-1732.

Steg G, James S, Atar D, et al. **ESC** guidelines for the management of **acute myocardial infarction** in patients presenting with ST-segment elevation: The Task Force on the management of ST-segment elevation acute myocardial infarction of the European Society of Cardiology (ESC). Eur Heart J **2012**.

Steg PG, Bhatt DL, Hamm CW, et al,CHAMPION Investigators. Effect of **cangrelor** on periprocedural outcomes in **percutaneous coronary interventions**: a pooled analysis of patient-level data. Lancet 2013; published online Sept 3.

Steg PG, van't Hof A, Hamm CW, et al. **Bivalirudin** started during emergency transport for primary PCI. (**EUROMAX**) N Engl J Med 2013. DOI: 10.1056/NEJMoa1311096.

Steinbeck G, Andresen D, Seidl K, et al. the **IRIS** Investigators. Defibrillator Implantation Early after Myocardial Infarction. N Engl J Med. 2009 Oct 8;361(15):1427-1436.

Steinke EE, Jaarsma T, Barnason SA, et al. on behalf of the Council on Cardiovascular and Stroke Nursing of the American Heart Association and the ESC Council on Cardiovascular Nursing and Allied Professions (CCNAP). **Sexual Counseling for Individuals With Cardiovascular Disease** and Their Partners: A Consensus Document From the American Heart Association and the ESC Council on Cardiovascular Nursing and Allied Professions (CCNAP). Circulation. 2013 Jul 29.

Steinman MA, Zullo AR, Lee Y, et al. Association of **β-blockers with functional outcomes, death, and rehospitalization in older nursing home residents after acute myocardial infarction** [online Dec 12, 2016].JAMA Intern Med. doi:10.1001/jamainternmed.2016.7701

Stenestrand U, Lindback J, Wallentin L; RIKS-HIA Registry. Long-term outcome of primary **percutaneous coronary intervention vs prehospital** and in-hospital thrombolysis for patients with ST-elevation myocardial infarction. JAMA. 2006 Oct 11;296(14):1749-56.

Stengaard C, Sørensen JT, Ladefoged SA, et al. Quantitative **Point-of-Care Troponin T Measurement** for Diagnosis and Prognosis in Patients With a Suspected Acute Myocardial Infarction. Am J Cardiol. 2013 Aug 14.

Stergiopoulos K, Brown DL. Initial coronary stent implantation with medical therapy vs **medical therapy alone for stable coronary artery disease**. Arch Intern Med 2012; 172:312-319.

Stergiopoulos K, Boden WE, Hartigan P, et al. **Percutaneous Coronary Intervention** Outcomes in Patients With Stable Obstructive Coronary Artery Disease and Myocardial Ischemia: A Collaborative Meta-analysis of Contemporary Randomized Clinical Trials. JAMA Intern Med. 2013 Dec 2.

Stolk LM, de Vries F, Ebbelaar C, et al. Risk of myocardial infarction in patients **with atrial fibrillation using vitamin K antagonists, aspirin or direct acting oral anticoagulants**. Br J Clin Pharmacol. 2017 Mar 22.

Stone GW, Witzenbichler B, Guagliumi G, et al.; **HORIZONS-AMI** Trial Investigators. **Bivalirudin** during primary PCI in acute myocardial infarction. N Engl J Med. 2008 May 22;358(21):2218-30. In patients with ST-segment elevation myocardial infarction who are undergoing primary PCI, anticoagulation with bivalirudin alone, as compared with heparin plus glycoprotein IIb/IIIa inhibitors, results in significantly reduced 30-day rates of major bleeding and net adverse clinical events.

Stone GW et al. for the **HORIZONS-AMI** Trial Investigators. **Paclitaxel-eluting stents** versus bare-metal stents in acute myocardial infarction. N Engl J Med 2009 May 7; 360:1946.

Stone GW, Witzenbichler B, Guagliumi G, et al, on behalf of the **HORIZONS AMI** Trial Investigators. Heparin plus a glycoprotein IIb/IIIa inhibitor versus **bivalirudin** monotherapy and **paclitaxel**-eluting stents versus bare-metal stents in acute myocardial infarction (HORIZONS AMI): final 3-year results from a multicentre, randomised controlled trial. Lancet 2011; DOI:10.1016/S0140-6736(11)60764-2.

Stone GW et al. **Intracoronary abciximab and aspiration thrombectomy** in patients with large anterior myocardial infarction: The **INFUSE-AMI** randomized trial. JAMA 2012 Mar 25.

Stone GW, Mehran R, Goldstein P, et al. **Bivalirudin Versus Heparin With or Without Glycoprotein IIb/IIIa Inhibitors in Patients With STEMI Undergoing Primary Percutaneous Coronary Intervention**: Pooled Patient-Level Analysis From the HORIZONS-AMI and EUROMAX Trials. J Am Coll Cardiol. 2015 Jan 6;65(1):27-38.

Stone GW. **Procedural anticoagulation** in myocardial infarction. N Engl J Med 2017 Aug 27.

Strauss MH, Hall AS. The **Divergent Cardiovascular Effects of Angiotensin Converting Enzyme Inhibitors and Angiotensin Receptor Blockers** on Myocardial Infarction and Death. Prog Cardiovasc Dis. 2015 Nov 14.

Strauss MH, Hall AS. **Angiotensin Receptor Blockers Do Not Reduce** Risk of Myocardial Infarction, Cardiovascular Death, or Total Mortality: Further Evidence for the ARB-MI Paradox. Circulation. 2017 May 30;135(22):2088-2090.

Stub D, Smith K, Bernard S, et al. **AVOID** Investigators. **Air Versus Oxygen** in ST-Segment Elevation Myocardial Infarction. Circulation. 2015 May 22.

Study of the Effectiveness of Additional Reductions in Cholesterol and Homocysteine (**SEARCH**) Collaborative Group. Effects of **Homocysteine-Lowering** With Folic Acid Plus Vitamin B12 vs Placebo on Mortality and Major Morbidity in Myocardial Infarction Survivors: A Randomized Trial. JAMA. 2010;303(24):2486-2494.

Sulo G, Vollset SE, Nygård O, et al. **Trends in Acute Myocardial Infarction Event Rates** and Risk of Recurrences After an Incident Event in **Norway 1994 to 2009** (from a Cardiovascular Disease in Norway Project). Am J Cardiol. 2014 Jun 1;113(11):1777-81.

Sulo G, Igland J, et al. **Heart Failure Complicating Acute Myocardial Infarction**; Burden & Timing of Occurrence: Nation-wide Analysis Including 86 771 Patients From the Cardiovascular Disease in Norway (CVDNOR) Project. J Am Heart Assoc. 2016 Jan 7;5(1).

Sulo G, Igland J, et al. **Prognostic Impact of In-Hospital and Postdischarge Heart Failure** in Patients With Acute Myocardial Infarction: A Nationwide Analysis Using Data From the Cardiovascular Disease in Norway (CVDNOR) Project. J Am Heart Assoc. 2017 Mar 15;6(3).

Sumner MD, Elliott-Eller M, Weidner G,et al. Effects of pomegranate juice consumption on myocardial perfusion in patients with coronary heart disease. Am J Cardiol. 2005 Sep 15;96(6):810-4.

Sundbøll J, Horváth-Puhó E, Adelborg K, et al. Higher risk of **vascular dementia** in myocardial infarction survivors. Circulation. 2018;137:567–577.

Sundström J, Hedberg J, Thuresson M, et al. **Low-Dose Aspirin Discontinuation** and Risk of Cardiovascular Events: A Swedish Nationwide, Population-Based Cohort Study. Circulation. 2017 Sep26;136(13):1183-1192

Svensson L, et al. Comparison of very early treatment with either fibrinolysis or percutaneous coronary intervention facilitated with **abciximab** with respect to ST recovery & infarct-related artery epicardial flow in patients with acute ST-segment elevation myocardial infarction: the Swedish Early Decision (SWEDES) reperfusion trial. Am Heart J. 2006 Apr;151(4):798.e1-7. CONCLUSIONS: Despite much shorter time delay to start of fibrinolysis than PCI, this did not result in signs of superior myocardial reperfusion. Epicardial flow in the infarct-related artery was better after invasive therapy, and there was a trend toward better clinical outcome after this treatment compared with after fibrinolysis.

Swerdel JN, Janevic TM, Cosgrove NM, Kostis JB; Myocardial Infarction Data Acquisition System (MIDAS 24) Study Group. The effect of **hurricane sandy** on cardiovascular events in new jersey. J Am Heart Assoc. 2014 Dec 8;3(6).

Szummer K, et al. **Improved outcomes in patients with ST-elevation myocardial infarction during the last 20 years** are related to implementation of evidence-based treatments: experiences from the **SWEDEHEART** registry 1995–2014. Eur Heart J 2017;38: 3056–3065.

Tachjian A, Maria V, Jahangir A. Use of **herbal products** and potential interactions in patients with cardiovascular diseases. J Am Coll Cardiol. 2010 Feb 9;55(6):515-25.

Tamis-Holland JE, Jneid H, Reynolds HR, et al. **Contemporary Diagnosis and Management** of Patients With Myocardial Infarction in the Absence of Obstructive Coronary Artery Disease: A Scientific Statement From the American Heart Association. Circulation. 2019 Mar 27:CIR0000000000000670

Tan NS, Goodman SG, Cantor WJ, et al; **TRANSFER-AMI** Investigators. Comparison of the Efficacy of **Pharmacoinvasive Management** for ST-Segment Elevation Myocardial Infarction in **Smokers Versus Non-Smokers** (from the Trial of Routine Angioplasty and Stenting After Fibrinolysis to Enhance Reperfusion in Acute Myocardial Infarction). Am J Cardiol. 2014 Oct 1;114(7):955-61.

Tandjung K, van Houwelingen KG, Jansen H, et al. Comparison of Frequency of **Periprocedural Myocardial Infarction** in Patients With and Without **Diabetes** Mellitus to Those With Previously Unknown but Elevated Glycated Hemoglobin Levels (from the TWENTE Trial). Am J Cardiol. 2012 Dec 1;110(11):1561-7.

Tang WH, Wu Y, Britt EB Jr, et al. Detectable subclinical myocardial necrosis is associated with cardiovascular risk in stable patients with **diabetes mellitus**. Diabetes Care 2013.

Tanglay Y, Twerenbold R, Lee G, et al. Incremental Value of a **Single High-sensitivity Cardiac Troponin** I Measurement to Rule Out Myocardial Ischemia. Am J Med. 2015 Jan 30.

Tanguay A, Brassard E, Lebon J, et al. Effectiveness of a **Prehospital Wireless 12-lead Electrocardiogram** and Cardiac Catheterization Laboratory Activation for ST-Elevation Myocardial Infarction. American Journal of Cardiology. 2016.

Taniguchi T, Shiomi H, Toyota T, et al. Effect of **Preinfarction Angina Pectoris** on Long-term Survival in Patients With ST-Segment Elevation Myocardial Infarction Who Underwent Primary Percutaneous Coronary Intervention. Am J Cardiol. 2014 Jul 29.

Tarantini G, D'amico G, Tellaroli P, et al. Meta-Analysis of the **Optimal Percutaneous Revascularization Strategy** in Patients with Acute Myocardial Infarction, Cardiogenic Shock and Multi-Vessel Coronary Artery Disease. Am J Cardio. 2017.

Tegn N, Abdelnoor M, Aaberge L, et al; **After Eighty study** investigators. **Invasive versus conservative strategy** in **patients aged 80 years or older** with non-ST-elevation myocardial infarction or unstable angina pectoris (After Eighty study): an open-label randomized controlled trial. Lancet. 2016;387:1057-65.

Tehrani DM, Seto AH. **Third universal definition** of myocardial infarction: update, caveats, differential diagnoses. Cleve Clin J Med. 2013 Dec;80(12):777-86.

Terkelsen CJ, Sørensen JT, Maeng M, et al. **System delay** and mortality among patients with STEMI treated with primary percutaneous coronary intervention. JAMA 2010; 304: 763-771.

Terkelsen CJ, Jensen LO, Tilsted HH, et al. Health Care **System Delay** and Heart Failure in Patients With ST-Segment Elevation Myocardial Infarction Treated With Primary Percutaneous Coronary Intervention: Follow-up of Population-Based Medical Registry Data. Ann Intern Med. 2011 Sep 20;155(6):361-7.

Than M, Cullen L, Reid CM, et al. **A 2-h diagnostic protocol** to assess patients with chest pain symptoms in the Asia-Pacifi c region (**ASPECT**): a prospective observational validation study. Lancet 2011; published online March 23. DOI:10.1016/S0140-6736(11)60310-3.

Than M, Cullen L, Aldous S, et al. **2-Hour accelerated diagnostic protocol** to assess patients with chest pain symptoms using contemporary troponins as the only biomarker. The ADAPT trial. J Am Coll Cardiol 2012.

The Writing Committee for the **TREAT** Study Group. **Ticagrelor vs clopidogrel after fibrinolytic** therapy in patients with ST-elevation myocardial infarction: a randomized clinical trial [online Mar 11, 2018].JAMA Cardiol. doi:10.1001 /jamacardio.2018.0612

Thiele H, et al. Leipzig **Prehospital Fibrinolysis** Group. ST-Segment Recovery and Prognosis in Patients With ST-Elevation Myocardial Infarction Reperfused by Prehospital Combination Fibrinolysis, Prehospital Initiated Facilitated Percutaneous Coronary Intervention, or Primary Percutaneous Coronary Intervention. Am J Cardiol. 2006 Nov 1;98(9):1132-9. Epub 2006 Sep 1.

Thiele H, Ohman EM, de Waha-Thiele S, et al. **Management of cardiogenic shock** complicating myocardial infarction: an update 2019. Eur Heart J. 2019 Aug 21;40(32):2671-2683.

Thiele H, Wöhrle J, Hambrecht R, et al. Intracoronary versus intravenous bolus **abciximab** during primary percutaneous coronary intervention in patients with acute ST elevation myocardial infarction: a randomised trial. Lancet 2012; online Feb 21.

Thiele H, Zeymer U, Neumann FJ, et al. **Intraaortic balloon support** for myocardial infarction with cardiogenic shock. (**IABP-Shock II**) N Engl J Med 2012.

Thiele H, Zeymer U, Neumann F-J, et al, on behalf of the Intraaortic Balloon Pump in cardiogenic shock II (**IABP-SHOCK II)** trial investigators. **Intra-aortic balloon counterpulsation** in acute myocardial infarction complicated by cardiogenic shock (IABP-SHOCK II): final 12 month results of a randomised, open-label trial. Lancet 2013; published online Sept 3.

Thiele H, Akin I, Sandri M, et al. **PCI strategies in patients with acute myocardial infarction and cardiogenic shock**. (**Culprit-Shock**) N Engl J Med. DOI: 10.1056/NEJMoa1710261.

Thiele H, Akin I, Sandri M, et al; CULPRIT-SHOCK Investigators. **One-Year Outcomes after PCI Strategies in Cardiogenic Shock**. N Engl J Med. 2018 Aug 25.

Thiele H, Zeymer U, Thelemann N, et al. **Intraaortic Balloon Pump in Cardiogenic Shock** Complicating Acute Myocardial Infarction: Long-Term 6-Year Outcome of the Randomized I**ABP-SHOCK II** Trial. Circulation. 2018 Nov 11.

Thomas JL, et al. Treatment and Outcomes of ST Segment Elevation Myocardial Infarction and Out-of-Hospital Cardiac Arrest in a Regionalized System of Care Based on **Presence or Absence of Initial Shockable Cardiac Arrest Rhythm**. Am J Cardiol. 2014 Oct 1;114(7):968-71.

Thomsen M, Nordestgaard BG. Myocardial Infarction and Ischemic Heart Disease in **Overweight and Obesity** With and Without Metabolic Syndrome. JAMA Intern Med. 2013 Nov 11.

Thrane PG, Kristensen SD, Olesen KKW, et al. 16-year follow-up of the Danish Acute Myocardial Infarction 2 (DANAMI-2) trial: **primary percutaneous coronary intervention vs. fibrinolysis** in ST-segment elevation myocardial infarction. Eur Heart J. 2019 Sep 2.

Thygesen K, Alpert JS, White HD, et al. **Universal definition of myocardial infarction**. *Circulation* 2007; DOI: 10.1161/CIRCULATIONAHA.107.187397. Available at: http://circ.ahajournals.org.

Thygesen K, Alpert JS, Jaffe AS, et al; the Writing Group on behalf of the Joint ESC/ACCF/AHA/WHF Task Force for the **Universal Definition of Myocardial Infarction**. Third Universal Definition of Myocardial Infarction. Circulation. 2012 Aug 24.

Thygesen K, Alpert JS, Jaffe AS, et al; Executive Group on behalf of the Joint European Society of Cardiology (ESC)/American College of Cardiology (ACC)/American Heart Association (AHA)/World Heart Federation (WHF) Task Force for the **Universal Definition of Myocardial Infarction**. Fourth Universal Definition of Myocardial Infarction (2018). J Am Coll Cardiol. 2018 Aug 23.

Thygesen K. What's new in the **Fourth Universal Definition of Myocardial infarction**? Eur Heart J. 2018 Nov 7;39(42):3757-3758.

Thune JJ, Hoefsten DE, Lindholm MG, et al.; Danish Multicenter Randomized Study on Fibrinolytic Therapy Versus Acute Coronary **Angioplasty** in Acute Myocardial Infarction (DANAMI)-2 Investigators. Simple risk stratification at admission to identify patients with reduced mortality from primary angioplasty. Circulation. 2005 Sep 27;112(13):2017-21.

Tisminetzky M, McManus DD, Gore JM, et al. **30-Year Trends in Patient Characteristics**, Treatment **Practices**, and Long-Term **Outcomes** of Adults Aged 35 to 54 Years Hospitalized With Acute Myocardial Infarction. Am J Cardiol. 2014 Jan 14.

Tisminetzky M, Coukos JA, McManus DD, et al. **Decade-Long Trends in the Magnitude, Treatment, and Outcomes of Patients Aged 30 to 54 Years** Hospitalized With ST-Segment Elevation and Non-ST-Segment Elevation Myocardial Infarction. Am J Cardiol. 2014 May 15;113(10):1606-10.

Toh S;Reichman ME;Graham DJ;Hampp C;Zhang R;Butler Prospective Postmarketing Surveillance of **Acute Myocardial Infarction in New Users of Saxagliptin**: A Population-Based Study**.** Diabetes Care. 2017 Nov 9.

Topaz G, Finkelstein A, Flint N, et al. Comparison of 30-day and Long-Term Outcomes and **Hospital Complications** Among **Patients <75 versus >75 Years** With ST-Elevation Myocardial Infarction Undergoing Percutaneous Coronary Intervention. Am J Cardio (2017).

Towfighi A, Markovic D, Ovbiagele B. National **Gender-Specific Trends** in Myocardial Infarction Hospitalization Rates Among Patients Aged 35 to 64 Years. Am J Cardiol. 2011 Aug 2.

Traverse JH, Henry TD, Ellis SG, et al. Effect of **intracoronary delivery of autologous bone marrow mononuclear cells** 2 to 3 weeks following acute myocardial infarction on left ventricular function: **LateTIM**E randomized trial [Nov 14, 2011]. JAMA. 2011;306(19):2110-2119.

Traverse JH, Henry TD, et al; Cardiovascular Cell Therapy Research Network-CCTRN. Effect of the Use and Timing of **Bone Marrow Mononuclear Cell Delivery** on Left Ventricular Function After Acute Myocardial Infarction: The **TIME** Randomized Trial. JAMA.2012Nov 6:1-10

Traverse JH, et al; Cardiovascular Cell Therapy Research Network (CCTRN). Effect of the use and timing of **bone marrow mononuclear cell delivery** on left ventricular function after acute myocardial infarction: the **TIME** randomized trial. JAMA. 2012 Dec 12;308(22):2380-9.

Traverse JH, Henry TD, Pepine CJ, et al. One-Year Follow-up of **Intracoronary Stem Cell Delivery** on Left Ventricular Function Following ST-Elevation Myocardial Infarction. JAMA. 2013 Nov 18.

Tricoci P et al for the **TRACER** Investigators. Thrombin-receptor antagonist **vorapaxar** in acute coronary syndromes. N Engl J Med2011 Nov 13

Tsai JP, Tian J, Wang WY, Ng AC. **Glycated hemoglobin versus fasting plasma glucose** as a predictor of left ventricular dysfunction after ST-elevation myocardial infarction. Can J Cardiol 2014.

Tu Jack V., Nardi Lorelei, Jiming Fang, et al., for the Canadian Cardiovascular Outcomes Research Team, National trends in rates of **death and hospital admissions related to acute myocardial infarction, heart failure and stroke, 1994-2004**. CMAJ 2009 180: E118-125.

Twerenbold R, Wildi K, Jaeger C, et al. Optimal Cutoff Levels of More **Sensitive Cardiac Troponin** Assays for the Early Diagnosis of Myocardial Infarction in Patients With **Renal Dysfunction**. Circulation. 2015 Jun 9;131(23):2041-50.

Twerenbold R, Jaeger C, Rubini Gimenez M,et al. Impact of **high-sensitivity cardiac troponin** on use of coronary angiography, cardiac stress testing, and time to discharge in suspected acute myocardial infarction. Eur Heart J. 2016 Jun 29

Twerenbold R, Boeddinghaus J, Nestelberger T, et al. Clinical Use of **High-Sensitivity Cardiac Troponin** in Patients With Suspected Myocardial Infarction. J Am Coll Cardiol. 2017 Aug 22;70(8):996-1012

Twerenbold R, Badertscher P, Boeddinghaus J, et al. **0/1-Hour Triage Algorithm for Myocardial Infarction in Patients with Renal Dysfunction**. Circulation. 2017 Nov 3.

Twerenbold R, Neumann JT, Sorensen NA, et al. Prospective Validation of the **0/1-h Algorithm** for Early Diagnosis of Myocardial Infarction. J Am Coll Cardiol. 2018 Aug 7;72(6):620-632.

Udell JA, Wang TY, Li S, et al. **Clinical trial participation** after myocardial infarction in a National Cardiovascular Data Registry. JAMA 2014; 312:841-843.

Udell JA, Bonaca MP, Collet JP, et al. **Long-term dual antiplatelet therapy** for secondary prevention of cardiovascular events in the subgroup of patients with previous myocardial infarction: a collaborative meta-analysis of randomized trials. Eur Heart J. 2015 Aug 31.

Unverzagt S, Wachsmuth L, Hirsch K, et al. **Inotropic agents and vasodilator** strategies for acute myocardial infarction complicated by cardiogenic shock or low cardiac output syndrome. Cochrane Database Syst Rev. 2014 Jan 2;1:CD009669. At present there are no robust and convincing data to support a distinct inotropic or vasodilator drug based therapy as a superior solution to reduce mortality in haemodynamically unstable patients with CS or low cardiac output complicating AMI.

Vaccarino Viola; Parsons Lori; Peterson Eric D.; et al. **Sex Differences** in Mortality After Acute Myocardial Infarction: Changes From **1994 to 2006**. Arch Intern Med. 2009;169(19):1767-1774.

Vaccarino V, Wilmot K, Al Mheid I, et al. **Sex Differences** in Mental Stress-Induced Myocardial Ischemia in Patients With Coronary Heart Disease. J Am Heart Assoc. 2016 Aug 24;5(9).

Vaccarino V, Sullivan S, Hammadah M, et al. **Mental Stress-Induced-Myocardial Ischemia** in Young Patients With Recent Myocardial Infarction: **Sex Differences** and Mechanisms. Circulation. 2018 Feb 20;137(8):794-805.

Vähätalo JH, Huikuri HV, Holmström LTA, et al. Association of **Silent Myocardial Infarction and Sudden Cardiac Death.** JAMA Cardiol. 2019 Jul 10.

Valenti R, Marrani M, Cantini G, et al. Impact of **chronic total occlusion revascularization** in patients with acute myocardial infarction treated by primary percutaneous coronary intervention. Am J Cardiol. 2014 Dec 15;114(12):1794-800.

Valentine CM, Tcheng JE, Waites T. Translating the Translation: What **Clinicians Should Know About the Fourth Universal Definition of Myocardial Infarction**. J Am Coll Cardiol. 2018 Nov 27;72(21):2668-2670.

Valgimigli M, et al. **STRATEGY** Investigators. **Tirofiban and sirolimus-eluting stent vs abciximab and bare-metal** stent for acute myocardial infarction: a randomized trial. JAMA. 2005 May 4;293(17):2109-17.

Valle JA, Zhang M, Dixon S, et al. Impact of **Pre-Procedural Beta Blockade** on Inpatient Mortality in Patients Undergoing Primary Percutaneous Coronary Intervention for ST Elevation Myocardial Infarction. Am J Cardiol. 2013 Mar 22.

Valley TS, Iwashyna TJ, Cooke CR, et al. **Intensive care use and mortality among patients with ST elevation myocardial infarction**: retrospective cohort study. BMJ. 2019 Jun 4;365:l1927

Van't Hof AW, Ten Berg J, Heestermans T, et al. Ongoing Tirofiban In Myocardial infarction Evaluation (**On-TIME**) 2 study group. Prehospital initiation of tirofiban in patients with ST-elevation myocardial infarction undergoing primary angioplasty (On-TIME 2): a multicentre, double-blind, randomised controlled trial. Lancet. 2008 Aug 16;372(9638):537-46. (n=491) or placebo (N=493) in addition to aspirin (500 mg), heparin (5000 IU), and clopidogrel (**600 mg**). Our finding that routine prehospital initiation of high-bolus dose tirofiban improved ST-segment resolution and clinical outcome after PCI, emphasises that further platelet aggregation inhibition besides high-dose clopidogrel is mandated in patients with STEMI undergoing PCI.

van Dalem J, Brouwers MCGJ, Stehouwer CDA, et al. Risk of a **first-ever acute myocardial infarction and all-cause mortality with sulphonylurea treatment**: A population-based cohort study. Diabetes Obes Metab. 2017 Nov 24.

Van de Werf F. **Drug-eluting stents** in acute myocardial infarction. N Engl J Med. 2006 Sep 14;355(11):1169-70.

Van de Werf F, Bax J, Betriu A, Blomstrom-Lundqvist C, Crea F, Falk V, et al. Management of **acute myocardial infarction** in patients presenting with persistent ST-segment elevation: The Task Force on the management of ST-segment elevation acute myocardial infarction of the **European Society of Cardiology** (**ESC**): Eur Heart J. 2008 Nov 12. [Epub ahead of print] http://www.escardio.org/guidelines-surveys/esc-guidelines/Pages/acs-st-segment-elevation.aspx

van der Linden N, Wildi K, Twerenbold R, et al. Combining High Sensitivity Cardiac **Troponin I** and Cardiac **Troponin T** in the Early Diagnosis of Acute Myocardial Infarction. Circulation. 2018 Apr 24.

van Nunen LX, Zimmermann FM, Tonino PAL, et al, for the **FAME** Study Investigators. Fractional fl ow reserve versus angiography for guidance of **PCI in patients with multivessel coronary artery disease** (**FAME**): **5-year follow**-up of a randomised controlled trial. Lancet 2015; online Aug 30.

van Waes JA, Nathoe HM, de Graaff JC, et al; Cardiac Health After Surgery (CHASE) Investigators. **Myocardial injury after noncardiac surgery** and its association with short-term mortality. Circulation. 2013 Jun 11;127(23):2264-71.

van Rooij E. **Cardiac Repair** after Myocardial Infarction. N Engl J Med. 2016 Jan 7;374(1):85-7.

Velagaleti RS, Pencina MJ, Murabito JM, et al. Long-term trends in the incidence of **heart failure** after myocardial infarction. Circulation 2008; DOI: 10.1161/CIRCULATIONAHA.108.784215.

Velásquez-Rodríguez J, Diez-Delhoyo F, Valero-Masa MJ, et al. **Prognostic Impact of Age and Hemoglobin** in Acute ST-Segment Elevation Myocardial Infarction Treated With Reperfusion Therapy. Am J Cardiol. 2017 Jun 15;119(12):1909-1916.

Velders MA, Boden H, van Boven AJ, et al. Influence of **Gender** on Ischemic Times and Outcomes After ST-Elevation Myocardial Infarction. Am J Cardiol. 2013 Feb 1;111(3):312-8.

Velders MA, Boden H, Hofma SH, et al. Outcome After ST Elevation Myocardial Infarction in Patients **With Cancer Treated With Primary Percutaneous Coronary Intervention**. Am J Cardiol. 2013 Sep 21.

Vilahur G, Gutiérrez M, Casani L, et al. Protective effects of **ticagrelor** on myocardial injury after infarction. Circulation. 2016;134:1708–1719.

VISION study investigators. Association between **postoperative troponin** levels and 30-day mortality among patients undergoing noncardiac surgery. JAMA 2012; 307:2295-2304.

Volpp KG, Troxel AB, Mehta SJ, et al. Effect of **Electronic Reminders, Financial Incentives, and Social Support** on Outcomes After Myocardial Infarction: The **HeartStrong** Randomized Clinical Trial. JAMA Intern Med. 2017 Jun 26.

Voors AA, Belonje AM, Zijlstra F, et al. A single dose of **erythropoietin** in ST-elevation myocardial infarction. Eur Heart J 2010; DOI:10.1093/eurheartj/ehq304.

Vora AN, et al. **Fibrinolysis** use among patients requiring interhospital transfer for ST-segment elevation myocardial infarction care: report from the US National Cardiovascular Data Registry [online Dec 8, 2014]. JAMA Intern Med. doi:10.1001/jamainternmed.2014.6573.

Vora AN, Peterson ED, Hellkamp AS, et al. **Care transitions** after acute myocardial infarction for transferred-in versus direct-arrival patients. *Circ Cardiovasc Qual Outcomes* 2016.

Vos NS, Fagel ND, Amoroso G, et al. **Paclitaxel-Coated Balloon Angioplasty Versus Drug-Eluting Stent** in Acute Myocardial Infarction: The REVELATION Randomized Trial. JACC Cardiovasc Interv. 2019 May 16.

Wadhera RK, Bhatt DL, Wang TY, et al. Association of **State Medicaid Expansion With Quality of Care and Outcomes for Low-Income Patients** Hospitalized With Acute Myocardial Infarction. JAMA Cardiol. 2019 Jan 16.

Wadhera RK, Joynt Maddox KE, Wasfy JH, et al. Association of the **Hospital Readmissions Reduction Program** with mortality among Medicare beneficiaries **hospitalized for heart failure, acute myocardial infarction, and pneumonia** [Dec 25, 2018]. JAMA. doi:10.1001/jama.2018.19232

Wald DS, Morris JK, ald NJ, et al. Randomized trial of **preventive angioplasty in myocardial infarction. (PRAMI)** N Engl J Med 2013.

Wallert J, Held C, Madison G, et al. Temporal Changes in myocardial infarction incidence rates are associated with periods of perceived **psychosocial stress**: A **SWEDEHEART** national registry study. Am Heart J. 2017:191:12-20

Wang OJ, Wang Y, Lichtman JH, et al.. "**America's Best Hospitals**" in the treatment of acute myocardial infarction. Arch Intern Med. 2007 Jul 9;167(13):1345-51. On average, admission to a ranked hospital for AMI was associated with a lower risk of 30-day mortality, although about one-third of the ranked hospitals fell outside the best performing quartile based on RSMR. Although ranked hospitals were much more likely to have an SMR significantly less than 1, many more nonranked hospitals had this distinction.

Wang OJ, Wang Y, Chen J, Krumholz HM. **Recent trends in hospitalization** for acute myocardial infarction. Am J Cardiol. 2012 Jun 1;109(11):1589-93.

Wang Tracy Y.; Fonarow Gregg C.;. Hernandez Adrian F; et al. The **Dissociation Between Door-to-Balloon Time** (DIDO) Improvement and Improvements in Other Acute Myocardial Infarction Care Processes and Patient Outcomes. Arch Intern Med. 2009;169(15):1411-1419.

Wang Tracy Y., Nallamothu Brahmajee K., Krumholz Harlan M., et al. Association of **Door-In to Door-Out Time** With Reperfusion Delays and Outcomes Among Patients Transferred for **Primary Percutaneous Coronary** Intervention. JAMA. 2011;305(24):2540-2547

Wang TY, Kaltenbach LA, Cannon CP, et al. Effect of **medication co-payment vouchers on P2Y12 inhibitor use** and major **adverse cardiovascular events among patients with myocardial infarction**: the **ARTEMIS** randomized clinical trial [Jan 8, 2018]. JAMA. doi:10.1001/jama.2018.19791

Wang Y, Li J, Zheng X, et al. **Risk Factors Associated With Major Cardiovascular Events 1 Year After Acute Myocardial Infarction**. JAMA Netw Open. 2018;1(4):e181079.

Wang Y, Peterson E, et al. **Door-to-balloon times** for patients with STsegment elevation myocardial infarction requiring **interhospital transfer** for **primary percutaneous coronary intervention**: a report from the national cardiovascular data registry. Am Heart J. 2011;161(1):76-83.

Wang Y, Wu B, Shu X. Meta-Analysis of Randomized Controlled Trials Comparing **Intracoronary and Intravenous Administration of Glycoprotein IIb/IIIa Inhibitors** in Patients With ST-Elevation Myocardial Infarction. Am J Cardiol. 2012 Jan 13.

Waqar S, Sarkar PK. **Exacerbation of psoriasis** with beta-blocker therapy. CMAJ. 2009 Jul 7;181(1-2):60.

Ward MJ, Kripalani S, Zhu Y, et al. Incidence of **Emergency Department Visits** for ST-Elevation Myocardial Infarction in a Recent Six-Year Period in the United States. Am J Cardiol. 2015 Jan 15;115(2):167-70.

Warren-Gash C et al. Laboratory-confirmed **respiratory infections as triggers for acute myocardial infarction and stroke**: A self-controlled case series analysis of national linked datasets from Scotland. Eur Respir J 2018 Mar; 51:1701794. (suggests influenza and pneumococcal vaccines useful)

Wei J, Rooks C, Ramadan R, et al. Meta-analysis of **mental stress-induced** myocardial ischemia and subsequent cardiac events in patients with coronary artery disease. Am J Cardiol. 2014 Jul 15;114(2):187-92.

Weintraub WS, Grau-Sepulveda MV, Weiss JM, et al. Comparative effectiveness of revascularization strategies (**PCI vs CABG**). N Engl J Med2012.

Wen YC, Hsiao FY, Chan KA, et al. **Acute Respiratory Infection** and **Use of Nonsteroidal Anti-Inflammatory Drugs** on Risk of Acute Myocardial Infarction: A Nationwide Case-Crossover Study. J Infect Dis. 2017 Feb 1.

Wennberg M, Strömberg U, Bergdahl IA, et al. Myocardial infarction in relation to **mercury and fatty acids from fish**: a risk-benefit analysis based on pooled Finnish and Swedish data in men. Am J Clin Nutr. 2012 Oct;96(4):706-13.

West RR, Jones DA, Henderson AH. **Rehabilitation** after myocardial infarction trial (**RAMIT**): multi-centre randomised controlled trial of comprehensive cardiac rehabilitation in patients following acute myocardial infarction. Heart. 2011 Dec 22

Wetmore JB, Tang F, Sharma A, et al. The association of **chronic kidney disease with the use of renin-angiotensin system inhibitors** after acute myocardial infarction. Am Heart J. 2015 Oct;170(4):735-43.

White DC, Grines CL, Grines LL, et al. Comparison of the usefulness of **enoxaparin versus warfarin** for prevention of left ventricular mural thrombus after anterior wall acute myocardial infarction. Am J Cardiol. 2015 May 1;115(9):1200-3.

Widimsky P, Wijns W, Fajadet J, et al. Reperfusion therapy for ST elevation acute **myocardial infarction in Europe**: description of the current situation in 30 countries. Eur Heart J 2010; 31:943-957.

Wildi K, Gimenez MR, Twerenbold R, et al. **Misdiagnosis** of Myocardial Infarction Related to Limitations of the Current Regulatory Approach to Define Clinical Decision Values for Cardiac Troponin. Circulation. 2015 Jun 9;131(23):2032-40.

Wijeysundera HC, Vijayaraghavan R, Nallamothu BK, et al. Rescue angioplasty or repeat fibrinolysis after **failed fibrinolytic therapy** for ST-segment myocardial infarction. A meta-analysis of randomized trials. J Am Coll Cardiol 2007; 49:422-30. Rescue PCI is associated with improved clinical outcomes for STEMI patients after failed fibrinolytic therapy, but these benefits must be interpreted in the context of potential risks. On the other hand, repeat fibrinolytic therapy is not associated with significant clinical improvement and may be associated with increased harm.

Windecker S, Bax JJ, Myat A, Stone GW, Marber MS. **Future treatment strategies** in ST-segment elevation myocardial infarction. Lancet 2013; 382: 644–53.

Windecker S, Kolh P, Alfonso F, et al. **2014 ESC/EACTS Guidelines on myocardial revascularization**. Eur Heart J 2014.

Witt BJ, Brown RD Jr, Jacobsen SJ, et al. A community-based study of **stroke incidence** after myocardial infarction. Ann Intern Med. 2005 Dec 6;143(11):785-92.

Wiviott SD, Morrow DA, Frederick PD, Antman EM, Braunwald E; National Registry of Myocardial Infarction. Application of the thrombolysis in myocardial infarction risk index in non-ST-segment elevation myocardial infarction: evaluation of patients in the National Registry of Myocardial Infarction. J Am Coll Cardiol. 2006 Apr 18;47(8):1553-8. Epub 2006 Mar 29.

Won H, Ko Y, Shin D, et al. Efficacy of early intensive **rosuvastatin** therapy in patients with ST-segment elevation **myocardial infarction** undergoing primary percutaneous coronary intervention: randomized, placebo-controlled. European Heart Journal. 34.suppl 1. 2014.

Wong CK, et al. **HERO-2** Investigators. Initial Q waves accompanying ST-segment elevation at presentation of acute myocardial infarction and 30-day mortality in patients given streptokinase therapy: an analysis from HERO-2. Lancet. 2006 Jun 24;367(9528):2061-7.

Wong CX, Sun MT, Lau DH, et al. Nationwide Trends in the Incidence of **Acute Myocardial Infarction in Australia**, 1993-2010. Am J Cardiol. 2013 Apr 12.

Wong GC, Welsford M, Ainsworth C, et al; members of the Secondary Panel. 2019 Canadian Cardiovascular Society/Canadian Association of Interventional Cardiology **Guidelines on the Acute Management of ST-Elevation Myocardial Infarction**: Focused Update on Regionalization and Reperfusion. Can J Cardiol. 2019 Feb;35(2):107-132.

Wood FO, Leonowicz NA, Vanhecke TE, et al. **Mortality** in Patients With ST-Segment Elevation Myocardial Infarction **Who Do Not Undergo Reperfusion**. Am J Cardiol. 2012 May 23.

Writing Committee Members., Al-Khatib SM, Yancy CW, Solis P, et al. **2016 AHA/ACC** Clinical Performance and Quality Measures for **Prevention of Sudden Cardiac Death**: A Report of the American College of Cardiology/American Heart Association Task Force on Performance Measures. J Am Coll Cardiol. 2016 Dec 14.

Xian Y, Wang TY, McCoy LA, et al. Association of **Discharge Aspirin Dose With Outcomes After Acute Myocardial Infarction**: Insights From the Treatment with ADP Receptor Inhibitors: Longitudinal Assessment of Treatment Patterns and Events after Acute Coronary Syndrome (**TRANSLATE-ACS**) Study. Circulation. 2015 Jul 21;132(3):174-81.

Xu X, Bao H, Strait K, et al. **Sex differences** in perceived **stress and early recovery** in young and middle-aged patients with acute myocardial infarction. Circulation 2015.

Yamaji K, Kohsaka S, Morimoto T, et al. Relation of ST-segment Elevation Myocardial Infarction to **Daily Ambient Temperature and Air Pollutant Levels** in a Japanese Nationwide Percutaneous Coronary Intervention Registry (J-PCI). Am J Cardio. 2017.

Yang JH, et al. **Angiotensin receptor blocker** in patients with ST segment elevation myocardial infarction with **preserved left ventricular systolic function**: prospective cohort study. BMJ. 2014 Nov 14.

Yasaitis LC, Berkman LF, Chandra A. Comparison of **Self-Reported and Medicare Claims**-Identified Acute Myocardial Infarction. Circulation. 2015 Mar 6.

Yasmina A, de Boer A, Deneer VH, et al. Patterns of **antiplatelet drug use after a first myocardial infarction during a 10-years** period. Br J Clin Pharmacol. 2016 Sep 23.

Yeh Robert W.; Go Alan S. Rethinking the **Epidemiology of Acute Myocardial Infarction**: Challenges and Opportunities. Arch Intern Med. 2010;170(9):759-764.

Yeh RW, Sidney S, Chandra M, et al. Population trends in the **incidence and outcomes** of acute myocardial infarction. N Engl J Med. 10 Jun 2010;362(23):2155-65.

Yerman T, Gan WQ, Sin DD. The influence of **gender on the effects of aspirin** in preventing myocardial infarction. BMC Med 2007; 5:29.

Yu J, Mehran R, Dangas GD, et al. Safety and efficacy of **high- versus low-dose aspirin** after primary percutaneous coronary intervention in ST-segment elevation myocardial infarction. JACC Cardiovasc Interv 2012; 5:1231-1238. (high-dose aspirin: ↑ major bleeding)

Yudi MB, Jones N, Fernando D, et al. **Management of Patients Aged ≥85 Years** With ST-Elevation Myocardial Infarction. Am J Cardiol. 2016 Jul 1;118(1):44-8.

Yusuf S, Mehta SR, Xie C, et al. **CREATE** Trial Group Investigators. Effects of reviparin, a low-molecular-weight heparin, on mortality, reinfarction, and strokes in patients with acute myocardial infarction presenting with ST-segment elevation. JAMA. 2005 Jan 26;293(4):427-35. CONCLUSIONS: In patients with acute ST-segment elevation or new left bundle-branch block MI, reviparin reduces mortality and reinfarction, without a substantive increase in overall stroke rates. There is a small absolute excess of life-threatening bleeding but the

Yuyun MF, Narayan HK, Ng LL. Prognostic Significance of **Adrenomedullin** in Patients With Heart Failure and With Myocardial Infarction. Am J Cardiol. 2015 Apr 1;115(7):986-991.

Zaman, S, Narayan A, Thiagalingam A, et al. **Long-term arrhythmia-free survival** in patients with severe left ventricular dysfunction and no inducible ventricular tachycardia post-myocardial infarction. Circulation 2013.
Zaman T, Agarwal S, Anabtawi AG, Patel NS, Ellis SG, Tuzcu EM, Kapadia SR. **Angiographic Lesion Severity** and Subsequent Myocardial Infarction. Am J Cardiol. 2012 Apr 10.
Zaman S, Narayan A, Thiagalingam A, et al. **Long-Term Arrhythmia-Free Survival** in Patients with Severe Left Ventricular Dysfunction and No Inducible Ventricular Tachycardia Post Myocardial Infarction. Circulation. 2013 Dec 31.
Zaman S, Kovoor P. **Sudden cardiac death early after myocardial infarction**: pathogenesis, risk stratification, and primary prevention. Circulation. 2014 Jun 10;129(23):2426-35.
Zhang D, Lv S, Song X, et al. **Fractional flow reserve versus angiography** for guiding percutaneous coronary intervention: a meta-analysis. Heart. 2015 Mar 15;101(6):455-62.
Zhang Z, Fang J, Gillespie C, et al. **Age-Specific Gender Differences** in In-Hospital Mortality by Type of Acute Myocardial Infarction. Am J Cardiol. 2012 Jan 13.
Zhang ZM, Rautaharju PM, Prineas RJ, et al. **Race and Sex Differences** in the Incidence and Prognostic Significance of Silent Myocardial Infarction in the Atherosclerosis Risk in Communities (ARIC) Study. Circulation. 2016 May 16.
Zhao YT, Weng CL, Chen ML, et al. Comparison of **glucose-insulin-potassium and insulin-glucose** as adjunctive therapy in acute myocardial infarction: a contemporary meta-analysis of randomised controlled trials. Heart. 2010 Oct;96(20):1622-6. Current evidence suggests that GIK with insulin does not reduce mortality in patients with AMI. However, studies of glycaemia are inconclusive and it remains possible that glycaemic control is beneficial.
Zhelev Z, Hyde C, Youngman E, Rogers M, Fleming S, Slade T, et al. **Diagnostic accuracy of single baseline measurement of Elecsys Troponin T high-sensitive assay** for diagnosis of acute myocardial infarction in emergency department: systematic review and meta-analysis. BMJ 2015;350:h15.
Zografos TA, Katritsis GD, Tsiafoutis I, et al. Effect of **One-Cycle Remote Ischemic Preconditioning** to Reduce Myocardial Injury During Percutaneous Coronary Intervention. Am J Cardiol. 2014 Apr 1.
Zuckerman IH, Yin X, Rattinger GB, et al. Effect of **exposure to evidence-based pharmacotherapy** on outcomes after acute myocardial infarction in **older adults**. J Am Geriatr Soc. 2012 Oct;60(10):1854-61.

[58] Yusuf S., Effect of potentially modifiable risk factors associated with myocardial infarction in 52 countries (the **INTERHEART** study): case-control study. Lancet 2004 (online version published Sept 3,2004)
[59] The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, & Treatment of High Blood Pressure (The **JNC 7**); JAMA. **2003** May;289(19):2560-72. (Complete report in Hypertension 2003;42:1206-1252)
[60] Anavekar NS, McMurray JJ, Velazquez EJ, et al. Relation between renal dysfunction and cardiovascular outcomes after myocardial infarction. N Engl J Med. 2004 Sep 23;351(13):1285-95. (Anand IS, Kuskowski MA, Rector TS, et al. Anemia & change in hemoglobin over time related to mortality & morbidity in patients with chronic heart failure: results from Val-HeFT. Circulation. 2005 Aug 23;112(8):1121-7. Epub 2005 Aug 15.)
Silletta MG, Marfisi R, Levantesi G, et al.; on behalf of the GISSI-Prevenzione Investigators. Coffee Consumption and Risk of Cardiovascular Events After Acute Myocardial Infarction. Results From the GISSI (Gruppo Italiano per lo Studio della Sopravvivenza nell'Infarto miocardico)-Prevenzione Trial. Circulation. 2007 Dec 3; [Epub ahead of print] No association between moderate coffee intake and cardiovascular events was observed in post-myocardial infarction patients.
[61] Antithrombotic Trialists' Collaboration (**ATC**). Collaborative meta-analysis of randomised trials of antiplatelet therapy for prevention of death, myocardial infarction, and stroke in high risk patients. BMJ. 2002 Jan 12;324(7329):71-86.

QT Prolongation: Online Extras

What can the pharmacist do to prevent Torsades de Pointes?

1. Watch for initiation of QT-prolonging drugs in patients at high risk of QT-prolongation (e.g. elderly, on other QT-prolongers, on loop diuretics, diagnosis of heart failure, female). Contact physician for ECG monitoring when risk appears high. Risk can be calculated using the Tisdale Risk Score, which does not require a baseline ECG (useful for community pharmacists).
2. Watch for drug interactions - which can cause drugs normally at low-risk of causing QT-prolongation to become high risk.
3. Be extra cautious in patients with chronic kidney disease - these patients are more likely to have electrolyte disturbances, and may be unable to properly excrete some drugs.

References for QT Prolongation and Torsades de Pointes:

1. Wolbrette D. Drugs that cause TdP & increase the risk of sudden cardiac death. Curr Card Reports 2004; 6: 379-84.
2. Wojciech Z & Lin D. Antipsychotic drugs and QT interval prolongation. Psychiatr Q 2003; 74(3): 291-306.
3. Taylor D. Antipsychotics and QT prolongation. Acta Psychiatr Scand 2003;107:85-95.
4. Vieweg W. New generation antipsychotic drugs and QTc interval prolongation. Prim Care Companion J Clin Psychiatry 2003;5 (5):205-15.
5. Roden D. Drug-induced prolongation of the QT interval. N Engl J Med 2004; 350: 1013-22.
6. Crouch M et al. Clinical relevance & management of drug-related QT interval prolongation. Pharmacotherapy 2003; 23(7):881-908.
7. Witchel H et al. Psychotropic drugs, cardiac arrhythmia, & sudden death. J Clin Psychopharmacol 2003; 23(1):58-77.
8. Brown et al. Cardiovascular effects of anti-psychotics. Clin Pharmacokinet 2004; 43(1): 38-56 (see Roden NEJM'08)
9. Gowda RM, et al. Torsade de pointes: the clinical considerations. Int J Cardiol. 2004;96:1
10. Sudden Arrhythmia Death Syndromes Foundation The long QT syndrome. SADS Foundation. Accessed from http://www.sads.org/LQTflyer.pdf (Cardiac Arrhythmia Reasearch & Education Foundation www.longqt.org)
11. Ray WA, et al. Oral erythromycin & the risk of sudden death from cardiac causes. N Engl J Med. 2004 Sep 9;351(11):1089-96.
12. Liu BA, Juurlink DN. Drugs and the QT interval - caveat doctor. N Engl J Med. 2004 Sep 9;351(11):1053-6.
13. Woeffel JA. Drug-Induced Long QT Interval & Sudden Cardiac Death. Pharmacist's Letter Nov 2004;20:201111
14. Al-Khatib SM, LaPointe NM, Kramer JM, Califf RM. What clinicians should know about the QT interval. JAMA. 2003 Apr 23-30;289(16):2120-7. Review. Erratum in: JAMA. 2003 Sep 10;290(10):1318.
15. Aström-Lilja et al. Drug-induced torsades de pointes: a review of the Swedish pharmacovigilance database. Pharmacoepidemiol Drug Saf.2008 Jun;17(6):587-92.
16. Tachjian A, Maria V, Jahangir A. Use of herbal products and potential interactions in patients with cardiovascular diseases. J Am Coll Cardiol. 2010 Feb 9;55(6):515-25.
17. Haugaa KH, Bos JM, Tarrell RF, Morlan BW, Caraballo PJ, Ackerman MJ. Institution-wide QT alert system identifies patients with a high risk of mortality. Mayo Clin Proc. 2013 Apr;88(4):315-25.
18. Tisdale JE, Jaynes HA, Kingery JR, et al. Development and Validation of a Risk Score to Predict QT Interval Prolongation in Hospitalized Patients. Circulation Cardiovascular quality and outcomes. 2013;6(4):479-487.

Additional references:

Abrams DJ, Perkin MA, Skinner JR. **Long QT syndrome**. BMJ. 2010 Jan 8;340:b4815. doi: 10.1136/bmj.b4815.

Abrams DJ, Macrae CA. **Long QT Syndrome**. Circulation. 2014 Apr 8;129(14):1524-9.

Abu-Zeitone A, Peterson DR, Polonsky B, et al. Efficacy of different **beta-blockers in the treatment of long QT syndrome**. J Am Coll Cardiol. 2014 Sep 30;64(13):1352-8. Although the 4 β-blockers are equally effective in reducing the risk of a first cardiac event in LQTS, their efficacy differed by genotype; nadolol was the only β-blocker associated with a significant risk reduction in patients with LQT2. Patients experiencing cardiac events during β-blocker therapy are at high risk for subsequent cardiac events, and propranolol is the least effective drug in this high-risk group.

AHA/ACCF-**Prevention of Torsade de Pointes in Hospital Settings**, Scientific Statement From American Heart Association and the American College of Cardiology Foundation. 2010. http://circ.ahajournals.org/cgi/reprint/CIRCULATIONAHA.109.192704

Arking DE, Pfeufer A, Post W, et al. A common genetic variant in the NOS1 regulator NOS1AP modulates cardiac repolarization. Nat Genet 2006; DOI: 10.1038/ng1790. Available at: http://www.nature.com/ng.

Auerbach DS, McNitt S, Gross RA, et al. **Genetic biomarkers for the risk of seizures** in long QT syndrome. Neurology. 2016 Oct 18;87(16):1660-1668.

Bagnall RD, Weintraub RG, Ingles J, et al. A Prospective Study of **Sudden Cardiac Death among Children and Young Adults**. N Engl J Med. 2016 Jun 23;374(25):2441-52.

Barsheshet A, Goldenberg I, O-Uchi J, et al. **Mutations in cytoplasmic loops of the KCNQ1** channel and the risk of life-threatening events: implications for mutation-specific response to Beta-blocker therapy in type 1 long-QT syndrome. Circulation. 2012;125:1988 –1996.

Basavarajaiah S, Wilson M, Whyte G, et al. Prevalence and significance of an isolated long QT interval in **elite athletes**. Eur Heart J. 2007 Dec;28(23):2944-9. Epub 2007 Oct 18. The prevalence of prolonged QTc in elite athletes is 0.4%. A QTc of >500 ms is highly suggestive of LQTS. A QTc of <500 ms in the absence of symptoms or familial disease is unlikely to represent LQTS in elite athletes.

Berger FA, Monadian N, de Groot NMS, et al. QTc-prolongation during **ciprofloxacin and fluconazole** combination therapy: prevalence and associated risk factors. Br J Clin Pharmacol. 2017 Oct 22.

Bibian C, Quilez RM, Gil J et al. Clinical Relevance Of The (S)-**Citalopram-Omeprazole** Interaction In Geriatric Patients. Br J Clin Pharmacol. 2013 Aug 7.

Blaufox AD, Tristani-Firouzi M, Seslar S, et al. Congenital Long **QT 3 in the Pediatric** Population. Am J Cardiol. 2012 Feb 21.

Boyce MJ, Baisley KJ,Warrington SJ. Pharmacokinetic Interaction between **domperidone and ketoconazole** leads to QT prolongation in healthy volunteers: randomized, placebo-controlled, double-blind, crossover study. Br J Clin Pharmacol 2012;73:411–21.

Buber J, Mathew J, Moss AJ, et al. Risk of Recurrent Cardiac Events **After Onset of Menopause** in Women With Congenital Long-QT Syndrome Types 1 and 2. Circulation. 2011 Jun 21;123(24):2784-91.

Calver L, Isbister GK. High dose **droperidol** and QT prolongation: analysis of continuous 12-lead recordings. Br J Clin Pharmacol. 2013 Oct 30.

Chambers KD, Beausejour Ladouceur V, Alexander ME, et al. **Cardiac Events During Competitive, Recreational, and Daily Activities in Children and Adolescents** With Long QT Syndrome. J Am Heart Assoc. 2017 Sep 21;6(9).

Chatterjee D. A case of **palpitation and pre-syncope**. BMJ. 2017 May 24;357:j2343.

Chew DS, Rezazadeh S, Miller RJ. **Recurrent Syncope** in the Emergency Department: A Lethal Cause Not for the Faint Hearted. JAMA Intern Med. 2017 Apr 10. (Torsades de pintes: TdP)

Chockalingam P, Crotti L, Girardengo G, et al. **Not all beta-blockers are equal** in the management of long QT syndrome types 1 and 2: higher recurrence of events under metoprolol. *J Am Coll Cardiol*. 2012;60:2092–2099.

Choi HK, et al. Population Pharmacokinetic-Pharmacodynamic Analysis to Compare the Effect of **Moxifloxacin** on QT Interval Prolongation Between Healthy Korean and Japanese Subjects. Clin Ther. 2016 Dec;38(12):2610-2621.

Chorin E, Hochstadt A, Granot Y, et al. **Grapefruit Juice prolongs the QT Interval** of Healthy Volunteers and Patients with Long QT syndrome. Heart Rhythm. 2019 Apr 22.

Chotsiri P, Wattanakul T, Hoglund R, et al. Population **pharmacokinetics** and electrocardiographic effects of **dihydroartemisinin-piperaquine** in healthy volunteers. Br J Clin Pharmacol. 2017 Jul 11

Chugh SS, Reinier K, Singh T, Uy-Evanado A, Socoteanu C, Peters D, Mariani R, Gunson K, Jui J. Determinants of Prolonged QT Interval and Their Contribution to Sudden Death Risk in Coronary Artery Disease. The Oregon Sudden Unexpected Death Study. Circulation. 2009 Jan 26. [Epub ahead of print] Diabetes mellitus and QTc-affecting drugs determined QTc prolongation and were predictors of SCD in coronary artery disease. However, idiopathic abnormal QTc prolongation was associated with 5-fold increased odds of SCD. A continued search for novel determinants of QTc prolongation such as genomic factors is likely to enhance risk stratification for SCD in coronary artery disease.

Crotti L, Tester DJ, et al. Long QT syndrome-associated mutations in **intrauterine fetal death**. JAMA. 2013 Apr 10;309(14):1473-82.

Cuneo BF, Strasburger JF, Yu S, Horigome H et al. **In Utero Diagnosis of Long QT Syndrome** by Magnetocardiography. Circulation. 2013 Nov 12;128(20):2183-91.

Danielsson B, Collin J, Jonasdottir Bergman G, et al. **Antidepressants and antipsychotics** classified with Torsades de Pointes arrhythmia risk and mortality in older adults – a Swedish nationwide study. Br J Clin Pharmacol. 2015 Nov 17.

Darpö B, Sager P, Macconell L et al. **Exenatide** at Therapeutic and Supratherapeutic Concentrations Does Not Prolong the QTc Interval in Healthy Subjects. Br J Clin Pharmacol. 2012 Aug 10.

Darpo B, Garnett C. **Early QT assessment** - how can our confidence in the data be improved? Br J Clin Pharmacol. 2012 Dec 24.

Darpo B, Karnad DR, Badilini F, et al. Are **women more susceptible than men** to drug-induced QT prolongation? Concentration-QTc modeling in a Phase 1 study with oral rac-sotalol. Br J Clin Pharmacol. 2013 Jul 2.

Darpo B, Ferber G, Siegl P, et al. Evaluation of the **QT** effect of a combination of **piperaquine and a novel anti-malarial drug candidate OZ439**, for the treatment of uncomplicated malaria. Br J Clin Pharmacol. 2015 May 13.

Darpo B, Zhou M, Bai SA, et al. Differentiating the Effect of an **Opioid Agonist** on Cardiac Repolarization From μ-Receptor-Mediated, Indirect Effects on the QT Interval: A Randomized, 3-Way Crossover Study in Healthy Subjects. Clin Ther. 2015 Dec 31.

Davis AM. **Torsades de Pointes: 50 Years Later**, Can We See It Coming? Circ Arrhythm Electrophysiol. 2016 Feb;9(2):e003850.

Davy M, Upward J, Arumugham T, et al. Cardiac Repolarization With **Gabapentin** Enacarbil in a Randomized, Double-Blind, Placebo- and Active-Controlled, Crossover Thorough QT/QTc Study in Healthy Adults. Clin Ther. 2013 Nov 27.

Dickstein LP, Franco KN, Rome ES, et al. Recognizing, managing medical consequences of **eating disorders** in primary care. Cleve Clin J Med. 2014 Apr;81(4):255-63.

Djeddi D, Kongolo G, Lefaix C, Mounard J, Léké A. Effect of **domperidone** on QT interval in neonates. J Pediatr. 2008 Nov;153(5):663-6. Epub 2008 Jun 27. This study shows a significant association between oral domperidone therapy and QTc prolongation. Two risk factors identified: advanced gestational age & serum potassium at the upper limit of normal.

Downes MA, Whyte IM, Isbister GK. QTc abnormalities in deliberate self-poisoning with **moclobemide**. Intern Med J. 2005 Jul;35(7):388-91.

Drake MJ, MacDiarmid S, Chapple CR, et al. Cardiovascular safety in refractory incontinent patients with overactive bladder receiving **add-on mirabegron therapy to solifenacin (BESIDE).** Int J Clin Pract. 2017 Apr 16.

Drew BJ, Ackerman MJ, Funk M, et al; American Heart Association Acute Cardiac Care Committee of the Council on Clinical Cardiology; Council on Cardiovascular Nursing; American College of Cardiology Foundation. **Prevention of torsade de pointes in hospital settings**: a scientific statement from the American Heart Association and the American College of Cardiology Foundation. J Am Coll Cardiol. 2010;55(9):934-947.

Ebrahim MA, Williams MR, Shepard S, et al. **Genotype Positive Long QT Syndrome** in Patients With Coexisting Congenital Heart Disease. Am J Cardiol. 2017 Jul 15;120(2):256-261.

Ehret GB, et al. Drug-Induced Long QT **Syndrome** in Injection Drug Users Receiving **Methadone**: High Frequency in Hospitalized Patients and Risk Factors. Arch Intern Med. 2006 Jun 26;166(12):1280-7.

EMA May/19: The European Medicines Agency's (EMA) Pharmacovigilance Risk Assessment Committee (PRAC) has recommended **revoking marketing authorizations for fenspiride medicines because of heart risks** (eg. QT), preventing them from being sold in the European Union (EU).

FDA Feb/10 notified healthcare professionals and patients that it is reviewing clinical trial data about a potentially serious effect on the heart from the use of Invirase (saquinavir) in combination with Norvir (ritonavir), antiviral medications given together to treat HIV infection. The data suggest that together the two drugs may affect the electrical activity of the heart, known as prolonged QT or PR intervals.

FDA Nov/10 is requesting that manufacturers of the painkiller **propoxyphene** pull the drug from the market because of concerns over cardiotoxicity. (Propoxyphene is marketed alone as Darvon & combined with acetaminophen as Darvocet.) The agency's request is based on data showing that, even when taken at therapeutic doses, the drug can lead to potentially dangerous changes in the heart's electrical activity, including prolonged PR & QT intervals & widened QRS complex. FDA advises clinicians to stop prescribing propoxyphene and to ask current users to discontinue the drug. FDA's MedWatch alert

FDA Dec/10 The injectable form of dolasetron mesylate (Anzemet) should not be used to prevent nausea or vomiting related to chemotherapy because the drug increases the risk for torsade de pointes, the FDA announced on Friday. The FDA recommends against using Anzemet injections in patients with congenital long-QT syndrome. The warning does not apply to Anzemet tablets because the risks for developing an abnormal heart rhythm are not as high as with the injections. FDA MedWatch alert (Free)

FDA July/11 FDA has added a warning to the label of the atypical antipsychotic quetiapine (Seroquel) cautioning about potential increases in the QT interval. Postmarketing cases of QT prolongation have been reported in some 17 patients, according to the *New York Times.* These patients had overdosed on quetiapine, had other illnesses, or were taking other medications that can cause electrolyte imbalance or QT prolongation.

FDA Aug/11 The antidepressant citalopram (marketed as Celexa) should not be prescribed at doses above 40 mg/day because higher dosages can cause arrhythmias, the FDA has warned.

FDA Sep/11 The U.S. Food and Drug Administration (FDA) is informing the public of an ongoing safety review of the anti-nausea drug Zofran (ondansetron, ondansetron hydrochloride and their generics). Ondansetron may increase the risk of developing abnormal changes(QT prolongation & torsades) in the electrical activity of the heart.

FDA July/12 Alerting clinicians that a single 32-mg intravenous dose of ondansetron (Zofran and generics) may lead to QT interval prolongation, which in turn may put patients at risk for torsades de pointes.

FDA Dec/12 is working with the manufacturers of all **32 mg dose Ondansetron** Injectable Products (brand and generic) to voluntarily recall them from the market due to QT serious cardiac toxicity.

FDA Mar/13 is warning the public that **azithromycin (Zithromax or Zmax)** can cause abnormal changes in the electrical activity of the heart that may lead to a potentially fatal irregular heart rhythm. Patients at particular risk for developing this condition include those with known risk factors such as existing **QT interval prolongation**, low blood levels of potassium or magnesium, a slower than normal heart rate, or use of certain drugs used to treat abnormal heart rhythms, or arrhythmias.

Freedman SB, Finkelstein Y. Route of **ondansetron** administration and ventricular arrhythmias. J Pediatr. 2017 May 22.

Funk KA, Bostwick JR. A Comparison of the Risk of QT Prolongation Among **SSRIs**. Ann Pharmacother. 2013 Oct;47(10):1330-41.

Gaba P, Bos JM, Cannon BC, et al. **Implantable cardioverter defibrillator** explantation for overdiagnosed or overtreated congenital long QT syndrome. DOI: 10.1016/j.hrthm.2015.12.008.

Giudicessi JR, Roden DM, Wilde AAM, et al. Classification and Reporting of Potentially **Proarrhythmic Common Genetic Variation in Long QT Syndrome Genetic Testing**. Circulation. 2018 Feb 6;137(6):619-630.

Gray B, Ingles J, Medi C, et al. Cardiovascular Effects of **Energy Drinks in Familial Long QT Syndrome**: A Randomized Cross-Over Study. Int J Cardiol. 2017 Mar 15;231:150-154

Grindrod KA, Nagge J. **Simplifying QT prolongation** for busy clinicians. Can Fam Physician. 2019 Apr;65(4):268-270.

Guo X, Li Z, Yu S, et al. Effects of **Metabolically Healthy and Unhealthy Obesity** on Prolongation of Corrected QT Interval. Am J Cardiol. 2017.

Gupta A, Mody P, Pandey A. Inappropriate Antibiotic Therapy in a Patient With Heart Failure and Prolonged QT Interval: A Teachable Moment. JAMA Intern Med. 2015 Nov 1;175(11):1748-9. (**quetiapine & moxifloxacin**)

Health Canada Aug/10 **Droperidol** Injection USP is associated with severe arrhythmia (eg. QT) and the Canadian Monograph of this product has been updated to reflect this risk.

Health Canada Nov/10 **Darvon-N (dextropropoxyphene) - Recall and Withdrawal in Canada** - Paladin Labs Inc. Paladin Labs Inc. in collaboration with Health Canada would like to inform healthcare professionals of the voluntary recall and withdrawal of the opioid analgesic Darvon-N (dextropropoxyphene) in Canada. (widen the QRS complex, prolong the QT interval and therefore increase the risk of serious abnormal heart rhythms.)

Health Canada Feb/12 has recently approved vandetanib (CAPRELSA) to treat medullary thyroid cancer in adult patients where either the tumour cannot be removed by surgery or it has spread from the thyroid gland to other parts of the body. CAPRELSA can cause serious QT heart rhythm changes which may result in sudden death, if left untreated.

Health Canada Mar/12: **Domperidone** should be used at the lowest possible dose. The risk of serious ventricular arrhythmias and sudden cardiac death may be higher in patients taking daily doses greater than 30 mg, and in patients over 60 years old.

Health Canada Oct/12: Ondansetron can cause a dose-dependent prolongation of the electrocardiographic-corrected QT interval (QTc), which can lead to Torsade de Pointes, a potentially life-threatening heart rhythm abnormality.

The new maximum recommended single intravenous (IV) dose of ZOFRAN ® is 16 mg infused over 15 minutes.

Health Canada Oct/13 has completed a safety review of the drug Sensipar (**cinacalcet**) that identified a possible link between the drug and abnormal heart rhythm (QT) associated with low blood calcium.

Health Canada Feb/14: **TELZIR** (fosamprenavir) should not be used with the antiarrhythmic drugs amiodarone, lidocaine (systemic), or quinidine, as this may cause serious and/or life-threatening reactions such as abnormal heart rhythm (arrhythmias). In addition, Telzir should not be used with delavirdine, another antiviral drug to treat HIV, because it may reduce the effectiveness of delavirdine.

Health Canada Mar/14: REMERON / REMERON RD (**mirtazapine**) – Abnormal Heart Rhythm - Merck Canada Inc. Cases of abnormal heart rhythm (eg. QT prolongation) have been reported with the antidepressant REMERON / REMERON RD (mirtazapine) mainly with drug overdose or when taking other drugs known to cause heart rhythm problems. The product information has been updated.

Health Canada Jun/14 Zofran (ondansetron) – Dosage and Administration of Intravenous Ondansetron in Geriatrics (>65 years of age) – GlaxoSmithKline Inc. Zofran (ondansetron) is associated with a risk of QT interval prolongation, which is expected to be greater with faster rate of infusion and larger doses for the intravenous administration. New dosing restrictions are recommended to mitigate this risk in elderly patients. The dosing restrictions for geriatrics are summarized below: In patients ≥75 years of age, the initial IV dose must not exceed 8 mg. In patients <75 years of age, the initial IV dose must not exceed 16 mg. Subsequent IV doses must not exceed 8 mg and may be given 4 and 8 hour after the initial dose. All IV doses must be diluted in 50–100 mL of saline or other compatible fluid. All IV doses must be infused over no less than 15 minutes.

Health Canada Jan/15 **Domperidone** Maleate - Association with Serious Abnormal Heart Rhythms and Sudden Death (Cardiac Arrest). Domperidone may be associated with a small increased risk of serious abnormal heart rhythms and sudden death. Prescribing information changes include a new recommended maximum daily dose, new restrictions of use and stronger warnings.

Health Canada June/16: **ATARAX (hydroxyzine)** is an antihistamine that can increase the risk of QT prolongation (QTP) and torsade de pointes (TdP) which may lead to dizziness, palpitations, syncope, seizures, and sudden cardiac death.

Health Canada Aug/17: Health Canada concluded that a link could not be established between **desloratadine** use and the development of **abnormal heart rhythm**. However, Health Canada will continue to monitor the safety of desloratadine.

Health Canada Mar/18: **Sertraline-** caution should be exercised, because of concentration dependent prolongation of the QTc interval.

Hibma JE, Kantarjian HM, DeAngelo DJ, et al. Effect of **inotuzumab ozogamicin on the QT interval in patients with hematologic malignancies** using QTc-Concentration Modelling. Br J Clin Pharmacol. 2018 Dec 8.

Higgins AY, Waks JW, Josephson ME. Influence of Gender on the Tolerability, Safety, and Efficacy of **Quinidine** Used for Treatment of Supraventricular and Ventricular Arrhythmias. Am J Cardiol. 2015 Oct 9. (QT prolongation)

Hough DW, Natarajan J, Vandebosch A, et al. Evaluation of the effect of **paliperidone** extended release and **quetiapine** on corrected QT intervals: a randomized, double-blind, placebo-controlled study. Int Clin Psychopharmacol. 2010 Sep 28.

Hunt K, Hughes CA, Hills-Nieminen C. **Protease Inhibitor**-Associated QT Interval Prolongation. Ann Pharmacother. 2011 Dec;45(12):1544-50.

Hyltén-Cavallius L, et al. Patients with **Long QT Syndrome** Due to Impaired hERG-encoded Kv11.1 Potassium Channel Have Exaggerated Endocrine Pancreatic and Incretin Function Associated with Reactive **Hypoglycemia**. Circulation. 2017 Feb 24.

Isbister GK, Page CB. Drug induced **QT prolongation: the measurement** and assessment of the QT interval in clinical practice. Br J Clin Pharmacol. 2012 Nov 20.

Isbister GK, Brown AL, Gill A, et al. **QT interval prolongation in opioid agonist treatment**: analysis of continuous 12-lead electrocardiogram recordings. Br J Clin Pharmacol. 2017 May 9.

Ishibashi K, Aiba T, Kamiya C, et al. Arrhythmia risk and **β-blocker therapy** in pregnant women with long QT syndrome. Heart. 2017 Mar 14.

Jackson H, Huisman LA, Sanatani S, Arbour LT. **Long QT syndrome**. CMAJ. 2011 Aug 9;183(11):1272-5.

Jardin CG, Putney D, Michaud S. Assessment of **drug-induced torsade de pointes** risk for hospitalized high-risk patients receiving QT-prolonging agents. Ann Pharmacother. 2014 Feb;48(2):196-202.

Jasiak NM, Bostwick JR. Risk of QT/QTc Prolongation Among **Newer Non-SSRI Antidepressants**. Ann Pharmacother. 2014 Dec;48(12):1620-1628.

Johnson JN, Ackerman MJ. **Competitive sports participation** in athletes with congenital long QT syndrome. JAMA. 2012 Aug 22;308(8):764-5.

Joyce DD, Bos JM, Haugaa KH, et al. Frequency and Cause of Transient **QT Prolongation After Surgery**. Am J Cardiol. 2015 Sep 3.

Kao WHL, Arking DE, Post W, et al. Genetic variations in nitric oxide synthase 1 adaptor protein are associated with sudden cardiac death in US white community-based populations. Circulation 2009; 119:940-951.

Katz DF, Sun J, Khatri V, et al. QTc Interval **Screening in an Opioid Treatment Program**. Am J Cardiol. 2013 Jun 29.

Kaufman ES, McNitt S, Moss AJ, Zareba W, et al. Risk of death in the long QT syndrome when a **sibling has died**. Heart Rhythm. 2008 Jun;5(6):831-6. Epub 2008 Mar 4.

Kempsford R, Allen A, Kelly K, et al. A Repeat-dose Thorough QT Study of Inhaled **Fluticasone Furoate (FF)/Vilanterol (VI)** Combination in Healthy Subjects. Br J Clin Pharmacol. 2013 Oct 4.

Kleiman RB, Shah RR, Morganroth J. Replacing the **Thorough QT Study**: Reflections of a baby in the bath water. Br J Clin Pharmacol. 2013 Nov 29

Kori S, Kellerman DJ, Voloshko P, Haugen G. Effects of a Supratherapeutic Dose of Investigational Orally **Inhaled Dihydroergotamine** (MAP0004) on QT Interval: A Randomized, Double-Blind, Active- and Placebo-Controlled Crossover Study in Healthy Volunteers. Clin Ther. 2012 Aug 20.

Krantz MJ, Martin J, et al. QTc Interval Screening in **Methadone** Treatment. Ann Intern Med. 2009 Jan 19. [Epub ahead print] Recommendation 1 (Disclosure): Clinicians should inform patients of arrhythmia risk when they prescribe methadone. Recommendation 2 (Clinical History): Clinicians should ask patients about any history of structural heart disease, arrhythmia, and syncope. Recommendation 3 (Screening): Obtain a pretreatment electrocardiogram for all patients to measure the QTc interval and a follow-up electrocardiogram within 30 days and annually. Additional electrocardiography is recommended if the methadone dosage exceeds 100 mg/d or if patients have unexplained syncope or seizures. Recommendation 4 (Risk Stratification): If the QTc interval is greater than 450 ms but less than 500 ms, discuss the potential risks and benefits with patients and monitor them more frequently. If the QTc interval exceeds 500 ms, consider discontinuing or reducing the methadone dose; eliminating contributing factors, such as drugs that promote hypokalemia; or using an alternative therapy. Recommendation 5 (Drug Interactions): Clinicians should be aware of interactions between methadone and other drugs that possess QT interval-prolonging properties or slow the elimination of methadone.

Laksman Z, Momciu B, Seong YW, et al. A Detailed Description and Assessment of **Outcomes** of Patients With Hospital Recorded QTc Prolongation. Am J Cardiol. 2015 Apr 1;115(7):907-11.

Lazzara R. **Antiarrhythmic drugs and torsade de pointes**. Eur Heart J. 1993 Nov;14 Suppl H:88-92. (**sotalol**)

Leitch A, McGinness P, Wallbridge D. Calculate the QT interval in patients taking drugs for dementia. BMJ. 2007 Sep 15;335(7619):557.

Loghin C, Haber H, Beasley CM, et al. Effects of **Atomoxetine** on the QT Interval in Healthy CYP2D6 Poor Metabolizers. Br J Clin Pharmacol. 2012 Jul 16.

Loke YK. The **thorough QT study** - do we need more of the same? Br J Clin Pharmacol. 2015 Dec 22.

Maljuric NM, Noordam R, Aarts N, et al. Use of selective **serotonin reuptake inhibitors and the heart-rate corrected QT** interval in a real-life setting: the population-based Rotterdam Study. Br J Clin Pharmacol. 2015 May 13.

Maluli HA, Meshkov AB. A short story of the **short QT syndrome**. Cleve Clin J Med. 2013 Jan;80(1):41-7.

Maron BJ, Haas TS, Ahluwalia A, et al. Demographics and Epidemiology of **Sudden Deaths in Young Competitive Athletes**: From the United States National Registry. Am J Med. 2016 Apr 1.

Mazzanti A, Maragna R, Vacanti G, et al. Interplay Between **Genetic Substrate, QTc Duration, and Arrhythmia Risk** in Patients With Long QT Syndrome. J Am Coll Cardiol. 2018 Apr 17;71(15):1663-1671.

Mazzanti A, Maragna R, Faragli A, et al. **Gene-specific therapy with mexiletine** reduces arrhythmic events in patients with long QT syndrome type 3. J Am Coll Cardiol. 2016;67:1053–1058.

Medical Letter –Treatment Guidelines: **Drugs for Cardiac Arrhythmias**. June 2007.

MHRA Dec/11 **Citalopram and escitalopram** are associated with dose-dependent QT interval prolongation and should not be used in those with: congenital long QT syndrome; known pre-existing QT interval prolongation; or in combination with other medicines that prolong the QT interval. ECG measurements should be considered for patients with cardiac disease, and electrolyte disturbances should be corrected before starting treatment. For citalopram, new restrictions on the maximum daily doses now apply: 40 mg for adults; 20 mg for patients older than 65 years; and 20 mg for those with hepatic impairment. For escitalopram, the maximum daily dose for patients older than 65 years is now reduced to 10 mg/day; other doses remain unchanged.

MHRA Apr/16 **Apomorphine with domperidone**: minimising risk of cardiac side effects. Patients receiving apomorphine and domperidone require an assessment of cardiac risk factors and ECG monitoring to reduce the risk of serious

arrhythmia related to QT-prolongation. https://www.gov.uk/drug-safety-update/apomorphine-with-domperidone-minimising-risk-of-cardiac-side-effects
MHRA'17: **Quinine** a reminder of dose-dependent QT-prolonging effects; updated medicine interactions.
Miceli JJ, Tensfeldt TG, Shiovitz T, et al. Effects of **Oral Ziprasidone and Oral Haloperidol** on QTc interval in patients with Schizophrenia or Schizoaffective disorder. Pharmacotherapy. 2010 Feb;30(2):127-35.
Mitchell JL, Cuneo BF, , et al. **Fetal Heart Rate** Predictors of **Long QT Syndrome**. Circulation. 2012 Dec 4;126(23):2688-95.
Moeller JR, Gummin DD, Nelson TJ, et al. Risk of Ventricular Arrhythmias and Association with **Ondansetron**. J Pediatr. 2016 Sep 21.
Moeller AD, Webber JC. Adverse effects of **therapeutic hypothermia** in a 55-year-old man with cardiac arrest. CMAJ. 2017 Oct 30;189(43):E1337-E1340
Moreno-Gutiérrez PA, Gaviria-Mendoza A, Cañón MM, et al. **High prevalence of risk factors in elderly** patients using drugs related to acquired Torsades de Pointes chronically in Colombia. Br J Clin Pharmacol. 2016 Apr 8
Moretti A, Bellin M, et al. Patient-specific induced **pluripotent stem-cell models** for long-QT syndrome. N Engl J Med 2010. Morganroth J, et al; CAPRIE Study Group. A randomized trial comparing the cardiac rhythm safety of moxifloxacin vs levofloxacin in elderly patients hospitalized with community-acquired pneumonia. Chest. 2005 Nov;128(5):3398-406.
Morris AD, Chen J, Lau E, Poh J. **Domperidone**-associated QT interval prolongation in non-oncologic pediatric patients: a review of the literature. Can J Hosp Pharm. 2016;69(3):224-30.
Morita H, Wu J, Zipes DP. The **QT syndromes**: long and short. Lancet. 2008 Aug 30;372(9640):750-63.
Moss AJ, Zareba W, Hall WJ, et al. Effectiveness and limitations of **beta-blocker** therapy in congenital long-QT syndrome.Circulation. 2000 Feb 15;101(6):616-23.
Muluneh B, Richardson DR, Hicks C, et al. Trials and Tribulations of **Corrected QT Interval Monitoring in Oncology**: Rationale for a Practice-Changing Standardized Approach. J Clin Oncol. 2019 Jul 16:JCO1900922.
Napolitano C, et al. **Genetic testing** in the long QT syndrome: development and validation of an efficient approach to genotyping in clinical practice. JAMA. 2005 Dec 21;294(23):2975-80.
Nebot N, Arkenau HT, Infante JR, et al. Evaluation of the effect of **dabrafenib** and metabolites on QTc interval in patients with BRAF V600-mutant tumours. Br J Clin Pharmacol. 2018 Apr;84(4):764-775.
Nelson S, Leung JG. Torsades de pointes after administration of low-dose **aripiprazole**. Ann Pharmacother. 2013 Feb;47(2):e11.
Newton-Cheh C, Eijgelsheim M, Rice KM, et al. **common variants** at ten loci influence QT interval duration in the QTGEN Study. Nature Genetics 2009; DOI:10.1038/ng.364.
Newton-Cheh Christopher, Lin Angela E., Baggish Aaron L., et al. Case 11-2011 — A 47-Year-Old Man with Systemic Lupus Erythematosus and Heart Failure. N Engl J Med 2011; 364:1450-1460. (Infiltrative cardiomyopathy & possible long-QT syndrome due to hydroxychloroquine)
Novick T, McMahon BA, Berliner A, Jaar BG. **Cinacalcet**-associated severe hypocalcemia resulting in torsades de pointes and cardiac arrest: a case for caution. Eur J Clin Pharmacol. 2016 Mar;72(3):373-5.
Nuttall GA, Eckerman KM, Jacob KA, et al. Does Low-dose **Droperidol** Administration Increase the Risk of Drug-induced QT Prolongation and Torsade de Pointes in the General Surgical Population? Anesthesiology. 2007 Oct;107(4):531-536. This indicates that the Food and Drug Administration black box warning for low dose droperidol is excessive and unnecessary.
O'Hare M, Maldonado Y, Munro J, et al. **Perioperative management** of patients with **congenital or acquired disorders of the QT interval**. Br J Anaesth. 2018 Apr;120(4):629-644.
Oteri A, Mazzaglia G, Pecchioli S, et al. Prescribing pattern of **antipsychotic drugs** during the years 1996-2010: a population-based database study in Europe with a focus on torsadogenic drugs. Br J Clin Pharmacol. 2016 Apr 6.
Petropoulou E, Jamshidi Y, Behr ER. The **genetics of pro-arrhythmic adverse drug reactions**. Br J Clin Pharmacol. 2013 Jul 9.
Phan DQ, Silka MJ, Lan YT, Chang RK. **Comparison of Formulas for Calculation of the Corrected QT Interval** in Infants and Young Children. J Pediatr. 2015 Apr;166(4):960-964.e2.
Phillips Mark; Sullivan B; Snyder B; et al. Effect of **Enzyte** on QT and QTc Intervals. Arch Intern Med. 010;170(15):1402-1404.
Rabkin SW, Cheng XJ. **Newer QT Correction Formulae** to Correct QT for Heart Rate Changes During Exercise. Am J Med Sci. 2016 Feb;351(2):133-9.
Rao GA, Mann JR, Shoaibi A, et al. **Azithromycin and levofloxacin** use and increased risk of cardiac arrhythmia and death. *Ann Fam Med* 2014; 12: 121-127.
Renoux C, Dell'Aniello S, Khairy P, et al. Ventricular tachyarrhythmia and sudden cardiac death with **domperidone** use in Parkinson's Disease. Br J Clin Pharmacol. 2016 Apr
Riad FS, Davis AM, Moranville MP, et al. **Drug induced QTc Prolongation**. The American Journal of Cardiology (2016).
Roden DM. Clinical practice. **Long-QT syndrome**. N Engl J Med. 2008 Jan 10;358(2):169-76.
Rodieux F, Nieto N, Sunthorn H, John G, Escher M. **Abiraterone acetate**-induced life-threatening torsade de pointes. Ann Pharmacother. 2015 Jan;49(1):152-3.
Roemer A, Stockwell T. Alcohol Mixed With **Energy Drinks** and Risk of Injury: A Systematic Review. J Stud Alcohol Drugs. 2017 Mar;78(2):175-183
Salem JE, Waintraub X, Courtillot C, et al. **Hypogonadism as a Reversible Cause of Torsades de Pointes** in Men. Circulation. 2018 Jul 3;138(1):110-113.
Salem J, Dureau P, Bachelot A, et al. Association of **Oral Contraceptives** With Drug-Induced QT Interval Prolongation in Healthy Nonmenopausal Women. JAMA Cardiol. 2018 Aug 1.
Sauer AJ, Newton-Cheh C. Clinical and genetic determinants of **torsade de pointes risk**. Circulation. 2012 Apr 3;125(13):1684-94.
Schächtele S, Tümena T, Gaßmann KG, et al. **Co-Prescription** of QT-Interval Prolonging Drugs: An Analysis in a Large Cohort of Geriatric Patients. PLoS One. 2016 May 18;11(5):e0155649.
Schwartz PJ, Priori SG, Cerrone M, et al. **Left cardiac sympathetic denervation** in the management of high-risk patients affected by the long-QT syndrome. Circulation. 2004 Apr 20;109(15):1826-33. Epub 2004 Mar 29.
Schwartz PJ, Spazzolini C, Priori SG, et al. Who are the long-QT syndrome patients who receive an **implantable cardioverter- defibrillator** and what happens to them?: data from the European Long-QT Syndrome Implantable Cardioverter-Defibrillator (LQTS ICD) Registry. Circulation. 2010 Sep 28;122(13):1272-82.
Schwartz PJ, Woosley RL. **Predicting the Unpredictable-Drug-Induced QT Prolongation and Torsades de Pointes**. J Am Coll Cardiol 2016;67:1639–50
Shah RR. Drug-Induced QT Interval Prolongation: Does **ethnicity** of the thorough QT study population matter? Br J Clin Pharmacol. 2012 Aug 7.
Shah SA, Szeto AH, Farewell R, et al. **Impact of High Volume Energy Drink Consumption** on Electrocardiographic and Blood Pressure Parameters: A Randomized Trial. J Am Heart Assoc. 2019 Jun 4;8(11):e011318.
Shen WK, Sheldon RS, Benditt DG, et al. **2017 ACC/AHA/HRS Guideline** for the Evaluation and Management of Patients With **Syncope**: Executive Summary: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines and the Heart Rhythm Society. J Am Coll Cardiol. 2017 Aug 1;70(5):620-663.
Shimizu W, Makimoto H, Yamagata K, et al. Association of **genetic and clinical aspects of congenital long QT syndrome** with life-threatening arrhythmias in Japanese patients [online Feb 13, 2019]. JAMA Cardiol.
Siddique SM, Shariff N, Vesuwala N, et al. **Metoclopramide** as a possible cause of prolonged QT syndrome and torsade de pointes in a patient with heart failure and renal insufficiency. Ann Intern Med. 2009 Apr 7;150(7):502-4.
Snipelisky D, Roberts M, Blackshear J. **Prolongation of a Prolonged QT: A Case** of an Undiagnosed Congenital Long QT Syndrome. JAMA Intern Med. 2014 Nov 1;174(11):1831-3.
Stahlmann R, Lode H. Safety considerations of **fluoroquinolones in the elderly**: an update. Drugs Aging 27 (3): 193-209, 2010.
Stefek B, Wolfe LT, Cohen M. Brugada Syndrome Associated With Adolescent **Loperamide Abuse**. Pediatrics. 2018 Sep 25. pii: e20181423.
Stollberger C, Huber JO, Finsterer J. **Antipsychotic drugs** and QT prolongation. Int Clin Psychopharmacol. 2005 Sep;20(5):243-51.
Strauss DG, Vicente J, Johannesen L, et al. A **Common Genetic Variant Risk Score** is Associated with Drug-Induced QT Prolongation and Torsade de Pointes Risk: A Pilot Study. Circulation. 2017 Feb 17.
Sugiyama A, Nakamura Y, Nishimura S, et al. Comparison of the effects of **levofloxacin** on QT/QTc interval assessed in both healthy Japanese and Caucasian subjects. Br J Clin Pharmacol 2012; 73: 455–9.
Sy RW, van der Werf C, Chatta IS, et al. Derivation and validation of a simple **exercise-based algorithm** for prediction of genetic testing in relatives of LQTS probands. Circulation. 2011;124:2187–2194.
Takasugi N, Goto H, Takasugi M, et al. Prevalence of **microvolt T-wave alternans** in patients with long QT syndrome and its association with torsade de pointes. Circ Arrhythm Electrophysiol. 2016;9:e003206.
Takaya T, Okamoto M, et al. Torsades de Pointes with QT prolongation related to **donepezil** use. J Cardiol. 2009 Dec;54(3):507-11.
Taubel J, Naseem A, Wang D, et al. Repeated supratherapeutic dosing of **strontium** ranelate 4g/d over 15 days does not prolong QTc interval in healthy volunteers. Br J Clin Pharmacol. 2012 Jan 29.
Taubel J, Lorch U, Ferber G, et al. **Insulin** at normal physiological levels does not prolong QTc interval in thorough QT studies performed in healthy volunteers. Br J Clin Pharmacol. 2012 Jul 10.
Terho HK, Tikkanen JT, Junttila JM, et al. Prevalence and Prognostic Significance of **Fragmented QRS Complex** in Middle-Aged Subjects With and Without Clinical or Electrocardiographic Evidence of Cardiac Disease. Am J Cardiol. 2014 Apr 18.

Thomas SH, Behr ER. **Pharmacological treatment** of acquired QT prolongation & torsades de pointes. Br J Clin Pharmacol. 2015 Jul 17.
Thottathil P, Acharya J, Moss AJ, et al. International Long QT Syndrome Investigative Group. Risk of cardiac events in patients with asthma and long-QT syndrome treated with **beta(2) agonists**. Am J Cardiol. 2008 Oct 1;102(7):871-4.
Tisdale JE, Jaynes HA, Kingery JR, et al. Development and Validation of a **Risk Score** to Predict QT Interval Prolongation in Hospitalized Patients. Circ Cardiovasc Qual Outcomes. 2013 May 28.
Tisdale JE. Drug-induced QT interval prolongation and torsades de pointes: **Role of the pharmacist** in risk assessment, prevention and management. Can Pharm J (Ott). 2016 May;149(3):139-52.
Tolbert D, Reid S, Harris S, et al. **Vigabatrin** Lacks Proarrhythmic Potential: Results from a Thorough QT/QTc Study in Healthy Volunteers. Clin Ther. 2017 Aug;39(8):1639-1648.
Tolbert D, Gordon J, Harris S, et al. A Thorough QT/QTc Study of **Clobazam** in Healthy Volunteers. Clin Ther. 2017 Sep 25. pii: S0149-2918(17)30941-4.
Tracz K, Owczuk R. Small doses of **droperidol do not present relevant torsadogenic actions**: a double-blinded, ondansetron-controlled study. Br J Clin Pharmacol. 2014 Oct 8.
Trifirò G, de Ridder M, Sultana J, et al. Use of **azithromycin** and risk of ventricular arrhythmia. CMAJ. 2017 Apr 18;189(15):E560-E568.
Tsujimoto T, Yamamoto-Honda R, Kajio H, et al. Vital signs, QT prolongation, and newly diagnosed cardiovascular disease during severe **hypoglycemia** in type 1 and type 2 diabetic patients. Diabetes Care 2013.
Vallecillo G et al. Risk of QTc prolongation in a cohort of opioid-dependent HIV-infected patients on **methadone** maintenance therapy. Clin Infect Dis 2013 Aug 14.
Van Dorn CS et al. **QTc Values Among Children and Adolescents** Presenting to the Emergency Department. Pediatrics. 2011 Dec;128(6):e1395-401.
Van Driest S, Wells Q, Stallings S, et al. Association of **arrhythmia-related genetic variants** with phenotypes documented in electronic medical records. *JAMA* 2016; 315:47-57.
van Gorp F, Whyte IM, et al. Clinical and ECG effects of **escitalopram** overdose. Ann Emerg Med. 2009 Sep;54(3):404-8.
van Gorp F, Duffull S, Hackett LP, Isbister GK. Population pharmacokinetics and pharmacodynamics of **escitolapram** in overdose and the effect of activated charcoal. Br J Clin Pharmacol 2012; 73: 402–10.
Vandael E, Vandenberk B, Vandenberghe J, et al. A **smart algorithm** for the prevention and risk management of QTc-prolongation based on the optimized **RISQ-PATH model**. Br J Clin Pharmacol. 2018 Aug 15.
Vandenberk B, Vandael E, Robyns T, et al. Which **QT Correction Formulae** to Use for QT Monitoring? J Am Heart Assoc. 2016 Jun 17;5(6).
Victor M, Castro VM, Clements CC, Murphy SN, et al. QT interval and antidepressant (**citalopram, escitalopram, amitriptyline**) use: A cross sectional study of electronic health records. BMJ 2013.
Viskin S, Postema PG, Bhuiyan ZA, et al. The response of the QT interval to the brief **tachycardia provoked by standing. A bedside test** for diagnosing long-QT syndrome. J Am Coll Cardiol 2010
Vrtovec B, Knezevic I, Poglajen G, et al. Relation of **B-Type Natriuretic Peptide** Level in Heart Failure to Sudden Cardiac Death in Patients With and Without QT Interval Prolongation. Am J Cardiol. 2012 Dec 27.
Wang M, Szepietowska B, Polonsky B, et al. Risk of Cardiac Events Associated With **Antidepressant Therapy in Patients With Long QT Syndrome**. Am J Cardiol. 2018 Jan 15;121(2):182-187.
Wang NC, Maggioni AP, Konstam MA, et al. Efficacy of Vasopressin Antagonism in Heart Failure Outcome Study With Tolvaptan (EVEREST) Investigators. Clinical implications of QRS duration in patients hospitalized with worsening **heart failure** & reduced left ventricular ejection fraction. JAMA. 2008 Jun 11;299(22):2656-66. A prolonged QRS duration appears common in patients with reduced LVEF who are hospitalized for heart failure and is an independent predictor of high postdischarge morbidity and mortality.
Wedam EF, Bigelow GE, Johnson RE, Nuzzo PA, Haigney MC. QT-Interval Effects of Methadone, Levomethadyl, and Buprenorphine in a Randomized Trial. Arch Intern Med. 2007 Dec 10;167(22):2469-75. **Buprenorphine is associated with less** QTc prolongation than levomethadyl or methadone and may be a safe alternative.
Weinberg G, Di Gregorio G, Hiller D, et al. Reversal of haloperidol-induced cardiac arrest by using lipid emulsion. Ann Intern Med. May 19;150(10):737-8.
Wilde AA, Moss AJ, Kaufman ES, et al. Clinical Aspects of **Type 3 Long-QT Syndrome**: An International Multicenter Study. Circulation. 2016 Sep 20;134(12):872-882.
Wiles JR, Leslie N, Knilans TK, et al. Prolonged QTc Interval in Association With Medium-Chain Acyl-Coenzyme A Dehydrogenase Deficiency. Pediatrics. 2014 May 5.
Yu T, Niu T. Giant inverted T waves and substantial QT interval prolongation induced by **azithromycin**: In an elderly woman with renal insufficiency. Can Fam Physician. 2014 Nov;60(11):1012-5.
Zamorano JL, Lancellotti P, Rodriguez Muñoz D, et al. **2016 ESC** position paper on **cancer treatments and cardiovascular toxicity** developed under the auspices of the ESC Committee for Practice Guidelines: The Task Force for cancer treatments and cardiovascular toxicity of the European Society of Cardiology (ESC). Eur Heart J. 2016 Aug 26. [Epub ahead of print]
Zeuli JD, Wilson JW, Estes LL. Effect of combined **fluoroquinolone and azole** use on QT prolongation in hematology patients. Antimicrob Agents Chemother. 2013 Mar;57(3):1121-7.
Zhang Y, Post WS, Dalal D, et al.. **QT-interval duration and mortality**: results from the Third National Health and Nutrition Examination Survey. Arch Intern Med. 2011;171(19):1727-1733.
Zhao C, Lv Y, Li X, et al. Effects of **Nemonoxacin on Thorough ECG QT/ QTc Interval**: A Randomized, Placebo- and Positive-Controlled Crossover Study in Healthy Chinese Adults. Clin Ther. 2018 May 23.
Zhou D, So K, Dymond AW, et al. Evaluation of the Effect of **Selumetinib** on Cardiac Repolarization: A Randomized, Placebo- and Positive-Controlled Crossover QT/QTc Study in Healthy Subjects. Clin Ther. 2016Nov 9.
Zipes DP, Camm AJ, Borggrefe M, et al; American College of Cardiology/American Heart Association Task Force; European Society of Cardiology Committee for Practice Guidelines; European Heart Rhythm Association; Heart Rhythm Society. **ACC/AHA/ESC 2006 Guidelines for Management of Patients With Ventricular Arrhythmias and the Prevention of Sudden Cardiac Death**: a report of the American College of Cardiology/American Heart Association Task Force and the European Society of Cardiology Committee for Practice Guidelines (writing committee to develop Guidelines for Management of Patients With Ventricular Arrhythmias and the Prevention of Sudden Cardiac Death): developed in collaboration with the European Heart Rhythm Association and the Heart Rhythm Society. Circulation. 2006 Sep 5;114(10):e385-484.

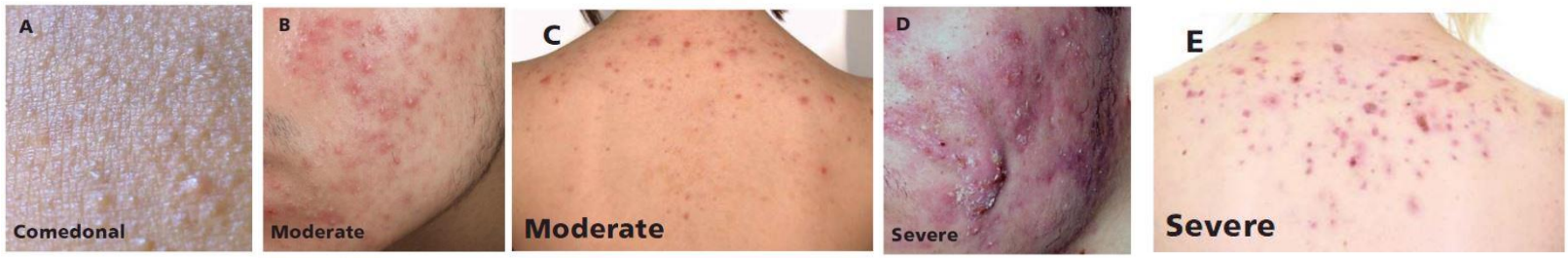
ACNE: Online Extras

Other acne drugs:

Salicylic Acid = SA▼x **Oxy, Clearasil, Neutrogena, others** Gels, lotions, toners, cleansers, sticks, pads, washes & astringents 0.5, 1, 2 & 3.5% PL	**Common:** less irritating than BPO, burning, stinging, pruritius & erythema **Serious**: rare systemic salicylate toxicity: nausea, vomiting, diarrhea, dizziness, loss of hearing, lethargy, psychic disturbances & hyperpnea ?protect from sun 8-12 weeks for noted improvement	✓ Used with topical retinoids to treat mild comedonal acne or 2nd line monotherapy agent[3] (also for seborrhea & psoriasis). **Not commonly recommended** (less potent than equal strength BPO). **D**: **↑ skin irritation or drying effect**: Abrasive or medicated soaps or cleansers; Acne preps (e.g., BPO, Resorcinol, Sulfur, Tretinoin); alcohol-containing topicals (After-shave lotions, perfumed toiletries, cosmetics/soaps with a strong drying effect); Isotretinoin DAILY or BID, 3-6% is keratolytic , OTC: $**10-15**

Tetracycline Lactation Ratings: a more conservative approach was used for acne (i.e. safe/likely safe changed to caution) as lactation data is only available for short-term courses versus the 8-12 weeks of therapy for acne.

Determining severity of acne (examples):



Reference: Canadian 2015 Acne Guidelines (Asai et al)

Benzoyl Peroxide Products:

Name	Active Ingredient	Base
Adasept	BPO 5%	Gel
Clean & Clear Continuous Control	BPO 5%	Lotion; water based
Clean & Clear Persa-Gel	BPO 5%	Gel; water based
Clinique Acne Solutions Clearing Moisturizer	BPO 2.5%	Lotion
Life Acne Medication	BPO 5%	gel
Medicated Acne Gel	BPO 5%	Gel
Nature's Cure Acne Treatment	BPO 5%	Cream
Obagi Clenziderm Acne Lotion	BPO 5%	Lotion; water based

List of Benzoyl Peroxide Products (discontinued)
Adasept B.P 5% acne gel; Clean & Clear Continuous Control = BPO 5% lotion = WATER based; CLEAN & CLEAR PERSA-GEL = BPO 5% gel = WATER BASED; OVERNIGHT ACNE CONTROL LOTION = BPO 3% lotion = WATER based; CLEAR ACNE TREATMENT CREAM = BPO 5% cream = WATER based; CLEAR PORE ON-THE SPOT ACNE TREATMENT, VANISHING = BPO 2.5% lotion; CLEAR SKIN TREATMENT REPAIRING LOTION = BPO 3.7% lotion; CLEAR ZONE ACNE SYSTEM SKIN PURIFYING MOISTURIZER = BPO 3.5% lotion; CLEARASIL STAYCLEAR ACNE TREATMENT CREAM BPO PLUS - VANISHING = BPO 5% cream; CLEARZ - IT = BPO 5% lotion; CLINIQUE ACNE SOLUTIONS CLEARING MOISTURIZER = BPO 2.5% lotion; CLINIQUE ACNE SOLUTIONS EMERGENCY LOTION = BPO 5% lotion; DERMACNE LOTION TRAITMENT 5% = BPO 5% lotion; DERMALOGICA SPECIAL CLEARING BOOSTER = BPO 5% lotion; LIFE ACNE MEDICATION = BPO 5% gel; MEDICATED ACNE GEL 5% = BPO 5% gel; NATURE'S CURE ACNE TREATMENT = BPO 5% cream; OBAGI CLENZIDERM ACNE LOTION = BPO 5% lotion; OXY 5 COVER UP FORMULA = BPO 5% cream; OXY 5 SENSITIVE SKIN VANISHING LOTION = BPO 2.5% lotion; OXY 5 VANISHING FORMULA = BPO 5% lotion; OXYDERM LOT 20% = BPO 20% lotion - Schedule F; OXYDERM LOTION 10% = BPO 10% lotion - Schedule F; OXYDERM LOTION 5% = BPO 5% lotion; PURE PEFECTION CLASSIC REPLENISHING CLEANSER = BPO 2.5% cream; PURE PERFECTION CLASSIC RENEWING CREME = BPO 2.5% cream; RODAN & FIELDS/PROACTIV SOLUTION:RENEWING CLEANSER = BPO 2.5% lotion; RODAN & FIELDS/PROACTIV SOLUTION:REPAIRING LOTION = BPO 2.5% lotion; SPECTRO ACNECARE DEEP PORE VANISHING LOTION = BPO 5% lotion; SPECTRO ACNECARE VANISHING LOTION FOR SENSITIVE SKIN = BPO 2.5% lotion; CLEAR ZONE ACNE SYSTEM SKIN PURIFYING WASH = BPO 3.5% liquid (WASH); PANOXYL CREAMY WASH 4% = BPO 4% (WASH)

References (ACNE – www.RxFiles.ca) :

[1] Abbas S, Goldberg JW, and Massaro M. Personal cleanser technology and clinical performance. Derm Ther 2004;17:35-42
[2] Magin P, Pond D, Smith W & Watson A. A systematic review of the evidence for 'myths and misconceptions' in acne management: diet, face-washing and sunlight. Family Practice 2005;22:62-70
[3] Katsambas AD, Stefanaki C, and Cunliffe WJ. Guidelines for Treating Acne. Clin Derm 2004;22:439-44
[4] Russell JJ. Topical therapy for Acne. American Family Physician. 2000;61(2):357-66
[5] Repchinsky, C. Patient Self-Care Helping Patients make therapeutic choices. 2002;Chapter 43:529-45.
[6] Layton AM. A review on the treatment of acne vulgaris. Int J clin Pract. 2006;60(1):64-72.
[7] Neely C et al. Health Care Guideline: Acne Management. 3rd ed. Institute for clinical systems improvement. 2006;May:1-33
[8] Poulin Y. Practical approach to the hormonal treatment of acne. J Cutan Med Surg 2005;8(4):16-21
[9] Work Group:; Strauss JS, Krowchuk DP, Leyden JJ, et al. **Guidelines** of care for acne vulgaris management. J Am Acad Dermatol. **2007 Feb 2**; [Epub ahead of print]
Asai Y, Baibergenova A, Dutil M, et al. **Management of acne: Canadian clinical practice guideline**. CMAJ **2015** [Early release published November 16, 2015].

Zaenglein AL, Pathy AL, Schlosser BJ, et al. **Guidelines** of care for the management of acne vulgaris. J Am Acad Dermatol (**AAD-American Academy of Dermatology**). 2016 Feb 15.
[10] Leyden JJ. A review of the use of combination therapies for the treatment of acne vulgaris. J Am Acad Dermatol. 2003 Sep;49(3 Suppl):S200-10.
[11] Agency for Healthcare Research and Quality, 2001
[12] Gray J, ed. Therapeutic Choices. 2003; 4th ed.
[13] AHFS, 2015 online, Micromedex 2015.
[14] Elliott R. Patient Self-Care Helping patients make therapeutic choices. 2002;1st ed.
[15] James WD. Clinical practice. Acne. N Engl J Med. 2005 Apr 7;352(14):1463-72.
[16] Dreno B. Topical Antibacterial Therapy for Acne Vulgaris. Drugs 2004;64(21):2389-97
[17] Ozolins M, Eady EA, Avery AJ, et al. comparison of **five antimicrobial regimens** for treatment of mild to moderate inflammation facial acne vulgaris in the community: randomized controlled trial. Lancet 2004;364:2188-95
[18] Lookingbill DP, Chalker DK, Lindholm JS, et al. Treatment of acne with a combination clindamycin/benzoyl peroxide gel compared with clindamycin gel, benzoyl peroxide gel and vehicle gel: combined results of two double-blind investigations. J Am Acad Dermatol 1997;37:590-5.
[19] Wolf JE Jr, Kaplan D, Kraus SJ, et al. A multicenter, randomized, investigator-blinded study. J Am Acad Dermatol 2003;49:Suppl:S211-S217
[20] Leyden JJ, Hickman JG, Jarratt MT, et al. The efficacy and safety of a combination benzoyl peroxide/clindamycin topical gel compared with benzoyl perosixde alone and a benzoyl peroxide/erythromycin combiantion product. J Cutan Med Surg 2001;5:37-42
[21] Cunliffe WJ, Holland KT, Bojar R, et al. A randomized, double-blind comparison of a clindamycin phosphate/benzoyl peroxide gel formulation and a matching clindamycin gel with respect to microbiologic activity and clinical efficacy in the topical treatment of acne vulgaris. Clin Ther 2002;24:1117-33
[22] Eady Ea, Cove JH, Holland KT, et al. Erythromycin resistant propionibacteria in antibiotic treated acne patients: association with therapeutic failure. Br J Dermatol 1989;121:51-7
[23] Simonart T & Dramaix M. Treatment of acne with topical antibiotics: lessons from clinical studies. Br J Derm 2005153:395-403.
[24] Bassett IB, Pannowitz DL, Barnetson RS. A comparative study of tea-tree oil versus benzoylperoxide in the treatment of acne. Med J Aust. 1990 Oct 15;153(8):455-8.
[25] Gammon WR, Meyer C, Lantis S, et al. Comparative efficacy of oral erythromycin versus oral tetracycline in the treatment of acne vulgaris. J Am Acad Dermatol. 1986;14:183-6
[26] Arowojolu AO, Gallo MF, Lopez LM, Grimes DA. **Combined oral contraceptive** pills for treatment of acne. Cochrane Database Syst Rev. 2012 Jul 11;7:CD004425.
[27] van Vloten WA. van Haselen CW. van Zuuren EJ. Gerlinger C. Heithecker R. The effect of 2 combined oral Contraceptives containing either drospirenone or cyproterone acetate on acne and seborrhea. [Clinical Trial. Journal Article. Multicenter Study. Randomized Controlled Trial] Cutis. 69(4 Suppl):2-15, 2002 Apr.
[28] Thorneycroft H. Gollnick H. Schellschmidt I. Superiority of a combined contraceptive containing drospirenone to a triphasic preparation containing norgestimate in acne treatment. [Clinical Trial. Journal Article. Multicenter Study. Randomized Controlled Trial] Cutis. 74(2):123-30, 2004 .
[29] Gollnick H. Current Concepts of the Pathogenesis of Acne Implications for Drug Treatment. Drugs 2003;63(15):1579-96.
[30] Katsambas A & Papakonstantinou A. Acne: Systemic Treatment. Clin Derm. 2004;22:412-8
[31] Cunliffe WJ, van de Kerkhof PCM, Caputo R, et al. Roaccutane treatment guidelines: results of an international survey. Dermatology 1997;194:351-7
[32] Layton AM, Knaggs H, Taylor J, et al. Isotretinoin for acne vulgaris 10 years later: a safe and successful treatment. Br J Dermatol 1993;129:292-6
[33] Wessels F, Anderson AN, Kropman K. The cost-effectiveness of isotretinoin in the treatment of acne. S Afr Med J 1999;89:780-4
[34] McLane, J. Analysis of common side effects of isotretinoin. J Am Acad Dermatol 2001;45:S188-94
[35] Marqueling AL & Zane LT. Depression and Suicidal Behavior in Acne Patients Treated with isotretinoin: A systematic review. Semin Cutan Med Surg 2005;24:92-102
Azoulay L, Blais L, Koren G, LeLorier J, Bérard A. Isotretinoin and the risk of depression in patients with acne vulgaris: a case-crossover study. J Clin Psychiatry. 2008 Apr;69(4):526-32. This is the first controlled study to find a statistically significant association between isotretinoin and depression. Because
depression could have serious consequences, close monitoring of isotretinoin users is indicated.
Sundström Anders, Alfredsson Lars, Sjölin-Forsberg Gunilla, et al. Association of **suicide attempts** with acne and treatment with isotretinoin: retrospective Swedish cohort study. BMJ 341:doi:10.1136/bmj.c5812 (Published 11 November 2010)
Singer S, Tkachenko E, Sharma P, et al. **Psychiatric Adverse Events in Patients Taking Isotretinoin** as Reported in a Food and Drug Administration Database From 1997 to 2017. JAMA Dermatol. 2019 Jul 3
[36] Cunliffe WJ, Layton AM. Oral isotretinoin: Patient selection and management. J Dermatol Treat 1993;4(suppl 2):S10-5
[37] Katsambas A, Papkonstantinou A. Acne: Systemic Treatment. Clin Derm 2004;22:412-8
[38] Goldsmith LA, bolognia JL, Callen JP, et al. American Academy of Dermatology Consensus Conference on the Safe and Optimal Use of Isotretinoin: Summary and recommendations. J Am Acad Dermatol 2004;50:900-6.
[39] Haroun M. Hormonal Therapy of Acne. J Cutan Med Surg 2005;6-10
[40] Simonart T, Dramaix M, De Maertelaer V. Efficacy of tetracyclines in the treatment of acne vulgaris: a review. Br J Dermatol. 2008 Feb;158(2):208-16. {InfoPOEMs 2008-Aug:There is no difference between tetracyclines regarding their efficacy in reducing lesion counts in acne. Although minocycline and doxycycline cost more, they require only once-daily dosing and may be better tolerated. There is no clear advantage to higher doses.}
41. Afra TP, Razmi T M, Narang T, et al. Topical **Tazarotene Gel, 0.1%, as a Novel Treatment Approach for Atrophic Postacne Scars**: A Randomized Active-Controlled Clinical Trial. JAMA Facial Plast Surg. 2018 Nov 15.

Other References:

http://www.mayoclinic.com/health/acne/DS00169, accessed September 18, 2006
Haider A & Shaw JC. Treatment of Acne Vulgaris. JAMA. 2004;292:726-735
Phototoxic effects of topical azelaic acid, benzoyl peroxide and adapalene were not detected when applied immediately before UVB to normal skin. Eur J Dermatol. 2004 Jul-Aug;14(4):235-7.

Additional info:

AADA Nov/10 American Academy of Dermatology Association (AADA) updated its position statement on the use of **isotretinoin**. http://www.aad.org/forms/policies/Uploads/PS/PS-Isotretinoin.pdf
Abdel Hay R, Shalaby K, Zaher H, et al. **Interventions for acne scars**. Cochrane Database of Systematic Reviews 2016, Issue 4. Art. No.: CD011946. DOI: 10.1002/14651858.CD011946.pub2. There is a lack of high-quality evidence about the effects of different interventions for treating acne scars because of poor methodology, underpowered studies, lack of standardised improvement assessments, and different baseline variables. There is moderate-quality evidence that injectable filler might be effective for treating atrophic acne scars; however, no studies have assessed long-term effects, the longest follow-up being 48 weeks in one study only. Other studies included active comparators, but in the absence of studies that establish efficacy compared to placebo or sham interventions, it is possible that finding no evidence of difference between two active treatments could mean that neither approach works. The results of this review do not provide support for the first-line use of any intervention in the treatment of acne scars. Although our aim was to identify important gaps for further primary research, it might be that placebo and or sham trials are needed to establish whether any of the active treatments produce meaningful patient benefits over the long term.
Adler BL, Kornmehl H, Armstrong AW. **Antibiotic Resistance** in Acne Treatment. JAMA Dermatol. 2017 Jun 21.
Agarwal US, Besarwal RK, Bhola K. Oral **isotretinoin** in different dose regimens or acne vulgaris: a randomized comparative trial. Indian J Dermatol Venereol Leprol. 2011 Nov-Dec;77(6):688-94.
Amichai B, Shemer A, Grunwald MH. Low-dose **isotretinoin** in the treatment of acne vulgaris. J Am Acad Dermatol. 2006 Apr;54(4):644-6.
Anderson KL, Dothard EH, Huang KE, et al. Frequency of **Primary Nonadherence** to Acne Treatment. JAMA Dermatol. 2015 Mar 20.
Arowojolu AO, Gallo MF, Lopez LM, Grimes DA, Garner SE. **Combined oral contraceptive** pills for treatment of acne. Cochrane Database Syst Rev. 2007 Jan 24;(1):CD004425. The three COCs evaluated in placebo-controlled trials are effective in reducing inflammatory and non-inflammatory facial acne lesions. Few differences were found between COC types in their effectiveness for treating acne.
Arowojolu AO, Gallo MF, Lopez LM, Grimes DA. **Combined oral contraceptive** pills for treatment of acne. Cochrane Database Syst Rev. 2012 Jul 11;7:CD004425. This update yielded six new trials but no change in conclusions. The six COCs evaluated in placebo-controlled trials are effective in reducing inflammatory and non-inflammatory facial acne lesions. Few important and consistent differences were found between COC types in their effectiveness for treating acne. How COCs compare to alternative acne treatments is unknown since only one trial addressed this issue. The use of standardized methods for assessing acne severity would help in synthesizing results across trials as well as aid in interpretation.
Asai Y, Baibergenova A, Dutil M, et al. **Management of acne: Canadian clinical practice guideline**. CMAJ **2015** [Early release published November 16, 2015].
Autret-Leca E, Kreft-Jais C, Elefant E, Cissoko H, Darrouzain F,Grimaldi-Bensouda L, Attia S, Jonville-Béra AP. **Isotretinoin exposure during pregnancy**: assessment of spontaneous reports in France. Drug Saf. 2010 Aug 1;33(8):659-65.
Barbaric J, Abbott R, Posadzki P, et al. **Light therapies for acne**. Cochrane Database of Systematic Reviews 2016, Issue 9. Art. No.: CD007917. High-quality evidence on the use of light therapies for people with acne is lacking. There is low certainty of the usefulness of MALPDT (red light) or ALA-PDT (blue light) as standard therapies for people with moderate to severe acne. Carefully planned studies, using standardised outcome measures, comparing the effectiveness of common acne treatments with light therapies would be welcomed, together with adherence to the Consolidated Standards of Reporting Trials (CONSORT) guidelines.
Barbieri JS et al. Duration of oral **tetracycline-class antibiotic therapy and use of topical retinoids** for the treatment of acne among general practitioners (GP): A retrospective cohort study. J Am Acad Dermatol2016 Dec; 75:1142.
Barbieri JS, Bhate K, Hartnett KP, Fleming-Dutra KE, Margolis DJ. Trends in **oral antibiotic prescription in dermatology**, 2008 to 2016 [online Jan 16, 2019]. JAMA Dermatol. doi:10.1001/jamadermatol.2018.4944
Bastawrous A, Silvester A, Batterbury M. **Laser refractive eye surgery**. BMJ2011;342:d2345. (20 April.) (CI: **isotretinoin**)
Berard A, Azoulay L, Koren G, Blais L, Perreault S, et al. **Isotretinoin, pregnancies, abortions and birth defects**: a population-based perspective. Br J Clin Pharmacol. 2007 Feb;63(2):196-205. Of the 90 women who became pregnant while on the drug, 76 terminated the pregnancy (84%), three had a spontaneous abortion (3%), two had trauma during delivery resulting in neonatal deaths (2%) and nine had a live birth (10%). Among the live births, only one had a congenital anomaly of the face and neck (11%).
Bernstein CN, et al. **Isotretinoin** Is Not Associated With **Inflammatory Bowel Disease**: A Population-Based Case-Control Study. Am J Gastroenterol. 2009 Jul 21. [Epub ahead of print]
Bozzo P, Chua-Gocheco A, Einarson A. Safety of **skin care products during pregnancy**. Can Fam Physician. 2011 Jun;57(6):665-7. (**tretinoin** & hydroquinone concern)
Brar G, Grewal P, Korownyk C. Is less more with **isotretinoin** and acne? Can Fam Physician. 2016 May;62(5):409. Epub 2016 May 12.
Brauer JA, Kazlouskaya V, Alabdulrazzaq H, et al. Use of a **Picosecond Pulse Duration Laser** With Specialized Optic for Treatment of Facial Acne Scarring. JAMA Dermatol. 2014 Nov 19.
Bremner JD, Shearer KD, McCaffery PK. Retinoic acid (**Isotretinoin**) and affective disorders (**depression**): the evidence for an association. J Clin Psychiatry. 2011 Aug 23.
Chien AL, Tsai J, Leung S, et al. Association of **systemic antibiotic treatment** of acne with skin microbiota characteristics [online Feb 13, 2019]. JAMA Dermatol. doi:10.1001/jamadermatol.2018.5221

Choi JS, Koren G, Nulman I. **Pregnancy and isotretinoin therapy**. CMAJ. 2013 Mar 19;185(5):411-3.

Costa CS, Bagatin E, Martimbianco ALC, et al. **Oral isotretinoin for acne.** Cochrane Database Syst Rev. 2018 Nov 24;11:CD009435. Evidence was low-quality for most assessed outcomes.We are unsure if isotretinoin improves acne severity compared with standard oral antibiotic and topical treatment when assessed by a decrease in total inflammatory lesion count, but it may slightly improve physician-assessed acne severity. Only one serious adverse event was reported in the isotretinoin group, which means we are uncertain of the risk of serious adverse effects; however, isotretinoin may result in more minor adverse effects.Heterogeneity in the studies comparing different regimens, doses, or formulations of oral isotretinoin meant we were unable to undertake meta-analysis. Daily treatment may be more effective than treatment for one week each month. None of the studies in this comparison reported serious adverse effects, or measured improvement in acne severity assessed by physician's global evaluation. We are uncertain if there is a difference in number of minor adverse effects, such as skin dryness, between doses/regimens.Evidence quality was lessened due to imprecision and attrition bias.

Crockett SD et al. **Isotretinoin** use and the risk of **inflammatory bowel disease**: A case–control study. Am J Gastroenterol 2010 Mar 30; [e-pub ahead of print].

Dawson AL, Dellavalle RP. **Acne vulgaris**. BMJ. 2013 May 8;346:f2634.

DeKlotz CMC, Roby KD, Friedlander SF. **Dietary Supplements, Isotretinoin, and Liver Toxicity in Adolescents**: A Retrospective Case Series. Pediatrics. 2017 Sep 1. (protein, creatine, herbal extracts)

Delost GR, Delost ME, Lloyd J. The impact of **chocolate consumption** on acne vulgaris in college students: A randomized crossover study. J Am Acad Dermatol. 2016 Jul;75(1):220-2.

Draelos ZD, et al. Two randomized studies demonstrate the efficacy and safety of **dapsone gel**, 5% for the treatment of acne vulgaris. J Am Acad Dermatol. 2007 Mar;56(3):439.e1-10. Epub 2007 Jan 17. Dapsone gel 5% (Aczone) is marginally more effective than placebo (NNT = 13, 9-23) in the treatment of acne vulgaris. At 12 weeks of treatment, less than half the patients in the treatment group received acne assessment scores of "none" or "minimal". No serious adverse events were reported, but data from follow-up longer than 3 months is forthcoming. (LOE = 1b)

Drugs in Pregnancy & Lactation, 9th Ed. Briggs GE,et al. Wilkins;Baltimore, MD.2011.

Eichenfield LF, Krakowski AC, Piggott C, et al. Evidence-based recommendations for the **diagnosis and treatment of pediatric acne**. Pediatrics. 2013 May;131 Suppl 3:S163-86.

Etminan M, Bird ST, Delaney JA, et al. **Isotretinoin and Risk for Inflammatory Bowel Disease**: A Nested Case-Control Study and Meta-analysis of Published and Unpublished Data. JAMA Dermatol. 2013 Feb 1;149(2):216-20.

Fanelli Matthew; Kupperman Eli; Lautenbach Ebbing; et al. **Antibiotics, Acne, and Staphylococcus aureus Colonization**. Arch Dermatol. 2011;0(2011):archdermatol.2011.67.

FDA Jun/14 is warning that certain over-the-counter (OTC) topical acne products can cause rare but serious and **potentially life-threatening allergic reactions or severe irritation**. Consumers should stop using their topical acne product and seek emergency medical attention immediately if they experience hypersensitivity reactions such as throat tightness; difficulty breathing; feeling faint; or swelling of the eyes, face, lips, or tongue. Consumers should also stop using the product if they develop hives or itching. The hypersensitivity reactions may occur within minutes to a day or longer after product use. **Sold under various brand names such as Proactiv, Neutrogena, MaxClarity, Oxy, Ambi, Aveeno, Clean & Clear, and as store brands.**

Freiman A, Barankin B. **Acne** (Five things you should know about acne). CMAJ. 2012 Sep 18;184(13):1497.

Garner SE, Eady EA, Popescu C, Newton J, Li WA. **Minocycline** for acne vulgaris: efficacy and safety.Cochrane Database Syst Rev. 2003;(1):CD002086.

Garner SE, Eady A, Bennett C, Newton JN, Thomas K, Popescu CM. **Minocycline** for acne vulgaris: efficacy and safety. Cochrane Database of Systematic Reviews 2012, Issue 8. Art. No.: CD002086. DOI: 10.1002/14651858.CD002086.pub2. Minocycline is an effective treatment for moderate to moderately-severe inflammatory acne vulgaris, but there is still no evidence that it is superior to other commonly-used therapies. This review found no reliable evidence to justify the reinstatement of its first-line use, even though the price-differential is less than it was 10 years ago. Concerns remain about its safety compared to other tetracyclines.

Goldgar C, Keahey DJ, Houchins J. Treatment options for acne **rosacea**. Am Fam Physician. 2009 Sep 1;80(5):461-8.

Goodfield MJ, Cox NH, Bowser A, et al. Advice on the **safe introduction and continued use of isotretinoin** in acne in the U.K. 2010. Br J Dermatol 2010;162:1172-9. http://www.bad.org.uk/Portals/_Bad/Guidelines/Clinical%20Guidelines/Isotretinoin%20Guidelines%202010.pdf

Graff DM, Bosse GM, Sullivan J. Case Report of **Methemoglobinemia** in a Toddler Secondary to Topical **Dapsone** Exposure. Pediatrics. 2016 Jul 8.

Halvorsen JA, Vleugels RA, Bjertness E, Lien L. A population-based study of acne and **body mass index** in adolescents. Arch Dermatol. 2012 Jan;148(1):131-2.

Hamilton Fiona, Car Josip, Layton Alison. **Acne vulgaris**. BMJ 2009;338:a2738, doi: 10.1136/bmj.a2738 (Published 5 June 2009)

Health Canada Sept/07 is advising consumers not to use **BuXie PaiDu XiaoDou Su** is used as an acne treatment and was found to contain the prescription drug rifampicin (**rifampin**).

Health Canada Feb/10 **Accutane** has been associated with cases of **severe skin reactions** (e.g. toxic epidermal necrolysis, Stevens-Johnson syndrome and erythema multiforme).

Health Canada Dec/15 is advising Canadians that the use of over-the-counter acne products applied to the skin containing **benzoyl peroxide** or **salicylic acid** may cause rare but **serious allergic reactions**.

Health Canada Sep/16 reinforces the importance of **preventing pregnancy** while taking the acne drug **isotretinoin** to avoid birth defects.

Henry D, Dormuth C, Winquist B, et al. Occurrence of pregnancy and **pregnancy** outcomes during **isotretinoin** therapy. CMAJ. 2016 Apr 25

Huang CF, Wang WM. **Radiotherapy-induced "solar" comedones**. CMAJ. 2012 Dec 11;184(18):2015.

Hurley MP, Stafford RS, Lane AT. Characterizing the Relationship Between **Free Drug Samples and Prescription Patterns for Acne** Vulgaris and Rosacea. JAMA Dermatol. 2014 Apr 16.

iPLEDGE (The iPLEDGE program is a computer-based risk management program designed to further the public health goal to eliminate fetal exposure to isotretinoin through a special restricted distribution program approved by the **FDA**. The program strives to ensure that: No female patient starts isotretinoin therapy if pregnant & No female patient on isotretinoin therapy becomes pregnant . This enhanced program is a SINGLE pregnancy risk management program for prescribing and dispensing all isotretinoin products (brand and generic products). The iPLEDGE program requires registration of all wholesalers distributing isotretinoin, all healthcare professionals prescribing isotretinoin, all pharmacies dispensing isotretinoin, and all male and female patients prescribed isotretinoin. This program is designed to create a verifiable link between the negative pregnancy test and the dispensing of the isotretinoin prescription to the female patient of childbearing potential. The iPLEDGE program requires that all patients meet qualification criteria and monthly program requirements. Before the patient receives his/her isotretinoin prescription each month, the prescriber must counsel the patient and document in the iPLEDGE system that the patient has been counseled about the risks of isotretinoin. There are also additional qualification criteria and monthly requirements for female patients of childbearing potential. As part of the ongoing risk management of isotretinoin products, it is crucial that a female of childbearing potential selects and commits to use two forms of effective contraception simultaneously for one month before, during, and for one month after isotretinoin therapy. She must have 2 negative urine or blood (serum) pregnancy tests with a sensitivity of at least 25 mIU/ml before receiving the initial isotretinoin prescription. The first pregnancy test is a screening test and can be conducted in the prescriber's office. The second pregnancy test must be done in a CLIA-certified laboratory according to the package insert. Each month of therapy, the patient must have a negative result from a urine or blood (serum) pregnancy test conducted by a CLIA-certified laboratory prior to receiving each prescription. https://www.ipledgeprogram.com/

Lee JW, Yoo KH, Park KY, Han TY, Li K, Seo SJ, Hong CK. Effectiveness of conventional, low-dose and intermittent oral isotretinoin in the treatment of acne: a randomized, controlled comparative study. Br J Dermatol. 2011 Jun;164(6):1369-75.

Lee YH, Scharnitz TP, Muscat J, et al. **Laboratory Monitoring During Isotretinoin Therapy** for Acne: A Systematic Review and Meta-analysis. JAMA Dermatol. 2015 Dec 2:1-10.

Lesens O, Haus-Cheymol R, Dubrous P, et al; Working Group on Cutaneous Infections in the Army. Methicillin-susceptible, **doxycycline-resistant** Staphylococcus aureus, Co^te d'Ivoire. Emerg Infect Dis. 2007;13(3):488-490.

Koo EB, Petersen TD, Kimball AB. Meta-analysis comparing efficacy of **antibiotics versus oral contraceptives in acne** vulgaris. J Am Acad Dermatol. 2014 May 28.

Kotori MG. Low-dose Vitamin "A" Tablets-treatment of Acne Vulgaris. Med Arch. 2015 Feb;69(1):28-30. doi: 10.5455/medarh.2015.69.28-30.

Kraft, John, Freiman, Anatoli. **Management of acne**. CMAJ 2011 0: cmaj.090374

Kundu RV, Patterson S, **Dermatologic Conditions in Skin of Color**: Part I. Special Considerations for Common Skin Disorders. Am Fam Physician. 2013;87(12):850-856.

Madden WS, Landells ID, Poulin Y, et al. **Treatment of acne vulgaris and prevention of acne scarring: Canadian consensus guidelines**. J Cutan Med Surg **2000**;4 Suppl 1:S2-13.

Maloney JM, Dietze P Jr, Watson D, et al. Treatment of Acne Using a **3-Milligram Drospirenone/20-Microgram Ethinyl Estradiol** Oral Contraceptive Administered in a 24/4 Regimen: A Randomized Controlled Trial. Obstet Gynecol. 2008 Oct;112(4):773-781.

Mandekou-Lefaki I, Delli F, Teknetzis A, Euthimiadou R, Karakatsanis G. Low-dose schema of isotretinoin in acne vulgaris. Int J Clin Pharmacol Res. 2003;23:41–6

Margolis David J.; Fanelli Matthew; Kupperman Eli; et al. Association of **Pharyngitis With Oral Antibiotic Use** for the Treatment of Acne: A Cross-sectional and Prospective Cohort Study. Arch Dermatol. 2011;0(2011):archdermatol.2011.355.

Marson JW, Baldwin HE. An Overview of Acne Therapy, Part 2: **Hormonal Therapy and Isotretinoin**. Dermatol Clin. 2019 Apr;37(2):195-203.

McIntee TJ, Bruckner AL. Challenges in optimizing **isotretinoin** use for acne vulgaris. JAMA Dermatol. 2013 Dec;149(12):1398.

McKeage K, Keating GM. Clindamycin/benzoyl peroxide gel (BenzaClin): a review of its use in the management of acne. Am J Clin Dermatol. 2008;9(3):193-204.

Medical Letter Nov 20/06. Extended release **minocycline** od (Solodyn) for acne

Medical Letter Feb 2016 (previously Nov 2008, Jan 2013 & **Feb 2016**). **Treatment Guidelines: Drugs for Acne & Rosacea**.

Menter A, Korman NJ, Elmets CA, Feldman SR, Gelfand JM, Gordon KB, Gottlieb A, Koo JY, Lebwohl M, Lim HW, Van Voorhees AS, Beutner KR, Bhushan R, American Academy of Dermatology. Guidelines of care for the management of psoriasis and psoriatic arthritis. Section 3. Guidelines of care for the management and treatment of **psoriasis with topical** therapies. J Am Acad Dermatol 2009 Apr;60(4):643-59.

MHRA Dec/17: **Isotretinoin** (Roaccutane): rare reports of **erectile dysfunction and decreased libido**.

Nagler AR, Milam EC, Orlow SJ. The use of oral **antibiotics before isotretinoin** therapy in patients with acne. J Am Acad Dermatol. 2015 Oct 29.

Nagpal M, De D, Handa S, et al. **Insulin Resistance** and **Metabolic Syndrome** in Young Men With Acne. JAMA Dermatol. 2015 Dec 23:1-5.

Nambudiri VE, Habib N, Arndt KA, et al. **Milia en plaque** of the Nose: Report of a Case and Successful Treatment With **Topical Tretinoin**. Pediatrics. 2014 Apr 7.

Neudorfer M, Goldshtein I, Shamai-Lubovitz O, et al. **Ocular Adverse Effects of Systemic Treatment With Isotretinoin**. Arch Dermatol. 2012 Apr 16.

Neuhaus CP, Nagler AR, Orlow SJ. **Teens, Acne, and Oral Contraceptive Pills**: The Need for Greater Clarity on When Teens Can Consent. JAMA Dermatol. 2017 Jan 11.

November 8, 2006 -- Medicis and Dow Pharmaceutical Sciences, Inc. announced that the U.S. Food and Drug Administration ("FDA") has approved **Ziana**(TM) (clindamycin phosphate 1.2% and tretinoin 0.025%) Gel. Ziana(TM) Gel is the first and only combination of clindamycin and tretinoin approved for once daily use for the topical treatment of acne vulgaris in patients 12 years or older.

Nov 8, 2006 -- QLT Inc. announced positive results of a Phase IV clinical trial of **Aczone**(TM) dapsone in more than 50 patients with G6PD deficiency that was performed to meet a post-approval commitment requested by the FDA. Mar/08 FDA removes G6PD screening & labeling requirements from the label. June 6/08 /CNW/ - QLT Inc. (NASDAQ: QLTI; TSX: QLT) announced today that Health Canada has completed its review of QLT USA, Inc.'s labeling supplement (SNDS) for Aczone(R) and has **removed the glucose-6-phosphate dehydrogenase (G6PD) screening** and blood monitoring requirements.

Owen CE. Treating acne with **high-dose isotretinoin**. JAMA. 2014 May 28;311(20):2121-2.

Perera E, Massie J, Phillips RJ. Treatment of Acne with Oral **Isotretinoin in Patients with Cystic Fibrosis**. Arch Dis Child. 2009 May 21. [Epub ahead of print] PubMed PMID: 19465582. Adolescents with cystic fibrosis and acne can be treated with oral isotretinoin. Oral isotretinoin should be considered for adolescents with cystic fibrosis who have acne associated with scarring, acne not clearing with topical and antibiotic treatment, acne associated with depression, or severe cystic acne.

Pickett H, Wiltz S. Adapelene/Benzoyl peroxide (**Epiduo/Tactuo**) for acne vulgaris. Am Fam Physician. 2011 Jun 15;83(12):1486-91.

Piette WW, Taylor S, Pariser D, Jarratt M, Sheth P, Wilson D. Hematologic safety of **dapsone gel, 5**%, for topical treatment of acne vulgaris. Arch Dermatol. 2008 Dec;144(12):1564-70. After treatment with dapsone gel, 5%, no clinical or laboratory evidence of drug-induced hemolytic anemia was noted in G6PD-deficient subjects with acne vulgaris.
Plensdore S, Livieratos M, Dada N. **Pigmentation Disorders**: Diagnosis and Management. Am Fam Physician. 2017;96(12):797-804.
Plovanich M,Weng QY, Mostaghimi A. Low usefulness of **potassium monitoring** among healthy young women taking **spironolactone** for acne [online March 23, 2015]. JAMA Dermatol. doi:10.1001/jamadermatol.2015.34.
Posadzki P, Car J. **Light Therapies** for Acne. JAMA Dermatol. 2018 Mar 14.
Racine A, Cuerq A, Bijon A, et al. **Isotretinoin** and Risk of **Inflammatory Bowel Disease**: A French Nationwide Study. Am J Gastroenterol. 2014 Feb 18.
Rasi A, Behrangi E, Rohaninasab M, Nahad ZM. Efficacy of fixed daily 20 mg of isotretinoin in moderate to severe scar prone acne. Adv Biomed Res. 2014 Mar 31;3:103. doi: 10.4103/2277-9175.129693.
Rehn L, Meririnne E, et al. Depressive symptoms & **suicidal ideation** during isotretinoin treatment: a 12-week follow-up study of male Finnish military conscripts. J Eur Acad Dermatol Venereol. 2009 Jun 11. [Epub ahead of print] On group level, isotretinoin seems not to be typically associated with treatment-emergent depression or suicidal ideation among young men. However, the possibility that individual patients may be susceptible for mood effects of isotretinoin as a rare idiosyncratic reaction can not be excluded.
Ryskina KL, Goldberg E, Lott B, et al. The Role of the Physician in Patient Perceptions of Barriers to Primary **Adherence** With Acne Medications. JAMA Dermatol. 2018 Feb 28.
Samycia M, Lam JM. **Infantile acne**. CMAJ. 2016 Dec 6;188(17-18):E540
Scope A, Agero AL, Dusza SW, Myskowski PL, Lieb JA, Saltz L, Kemeny NE, Halpern AC. Randomized double-blind trial of prophylactic oral **minocycline** and topical tazarotene for **cetuximab-associated** acne-like eruption. J Clin Oncol. 2007 Dec 1;25(34):5390-6. Prophylaxis with oral minocycline may be useful in decreasing the severity of the acneiform rash during the first month of cetuximab treatment. Topical tazarotene is not recommended for management of cetuximab-related rash.
Sinnott SJ, Bhate K, Margolis DJ, et al. **Antibiotics and acne**: an emerging iceberg of **antibiotic resistance**? Br J Dermatol. 2016 Dec;175(6):1127-1128.
Smith RN, Braue A, Varigos GA, Mann NJ. The effect of a **low glycemic load diet** on acne vulgaris and the fatty acid composition of skin surface triglycerides. J Dermatol Sci. 2008 Apr;50(1):41-52.
Spring LK, Krakowski AC, Alam M, et al. **Isotretinoin and Timing of Procedural Interventions**: A Systematic Review With Consensus Recommendations. JAMA Dermatol. 2017 Jun 28
Strauss JS, Krowchuk DP, Leyden JJ, Lucky AW, Shalita AR, Siegfried EC, et al.; **American Academy of Dermatology**/American Academy of Dermatology Association. **Guidelines of care for acne** vulgaris management. J Am Acad Dermatol. **2007** Apr;56(4):651-63. Epub 2007 Feb 5.
Strauss JS, Rapini RP, Shalita AR, Konecky E, Pochi PE, Comite H, Exner JH. Isotretinoin therapy for acne: results of a multicenter dose-response study. J Am Acad Dermatol. 1984 Mar;10(3):490-6.
Swartzentruber GS, Yanta JH, Pizon AF. **Methemoglobinemia as a complication of topical dapsone**. N Engl J Med. 2015 Jan 29;372(5):491-2.
Tangamornsuksan W, Lohitnavy M. Association Between **HLA-B*1301 and Dapsone-Induced Cutaneous Adverse Drug Reactions**: A Systematic Review and Meta-analysis. JAMA Dermatol. 2018 Mar 14.
Thiboutot D, Zaenglein A, Weiss J, et al. An aqueous gel fixed combination of clindamycin phosphate 1.2% and benzoyl peroxide 2.5% for the once-daily treatment of moderate to severe acne vulgaris: Assessment of efficacy and safety in 2813 patients. J Am Acad Dermatol. 2008 Sep 19. **Clindamycin-BPOO 2.5**% provides statistically significant greater efficacy than individual active ingredients and vehicle with a highly favorable safety and tolerability profile.
Thompson AE. JAMA **patient page**. Acne. JAMA. 2015 Feb 10; 313(6):640.
Titus S, Hodge J. **Diagnosis and Treatment of Acne**. Am Fam Physician. 2012;86(8):734-740.
Turowski CB, James WD. The efficacy and safety of amoxicillin, trimethoprim-sulfamethoxazole, and spironolactone for treatment-**resistant acne** vulgaris. Adv Dermatol. 2007;23:155-63.
Ugge H, Udumyan R, Carlsson J, et al. Acne in late adolescence and **risk of prostate cancer**. Int J Cancer. 2017 Dec 4.
van der Linden MMD, van Ratingen AR, van Rappard DC, et al. **DOMINO, doxycycline 40 mg vs. minocycline 100 mg** in the treatment of **rosacea**: a randomized, single-blinded, noninferiority trial, comparing efficacy and safety. Br J Dermatol. 2017 Jun;176(6):1465-1474.
van Zuuren EJ. **Rosacea**. N Engl J Med. 2017 Nov 2;377(18):1754-1764
Weinstock MA, Bingham SF, Lew RA, et al. Veterans Affairs Topical Tretinoin Chemoprevention (**VATTC**) Trial Group. Topical tretinoin therapy and all-cause mortality. A total of 1131 veterans were randomized. Their mean age was 71 years. Patients with a very high estimated short-term risk of death were excluded. Interventions Application of tretinoin, 0.1%, or vehicle control cream twice daily to the face and ears. Arch Dermatol. 2009 Jan;145(1):18-24. We observed an association of topical tretinoin therapy with death, but we do not infer a causal association that current evidence suggests is unlikely.
Werner CA, Papic MJ, Ferris LK, Schwarz EB. Promoting **Safe Use of Isotretinoin** by Increasing Contraceptive Knowledge. JAMA Dermatol. 2015 Feb 4.
Williams Hywel C, Dellavalle Robert P, Garner Sarah. **Acne vulgaris**. www.thelancet.com Published online August 30, 2011
Zaenglein AL, Pathy AL, Schlosser BJ, et al. **Guidelines** of care for the management of acne vulgaris. J Am Acad Dermatol. (**AAD-American Academy of Dermatology**) 2016 Feb 15.

For more information, topics and products see: **www.RxFiles.ca**

Web sites:
American Academy of Dermatology www.skincarephysicians.com/acnenet/FAQ.html www.aad.org/public/publications/pamphlets/common_acne.html?media=print
Medline Plus www.nlm.nih.gov/medlineplus/tutorials/acne/htm/index.htm
National Institute of Arthritis and Musculoskeletal and Skin Diseases www.niams.nih.gov/Health_Info/Acne/default.asp

Online Extras for TOPICAL CORTICOSTEROIDS Comparison Chart:

Eczema in Children – NICE guideline approach http://www.nice.org.uk/guidance/index.jsp?action=byID&o=11636

Tx Escalator ⇧			
			Systemic treatment
			Phototherapy
		Wet dressings	Wet dressings
		Topical calcineurin inhibitors	Topical calcineurin inhibitors
	Mild potency corticosteroids	Mild potency corticosteroids	Mild potency corticosteroids
	emolliants	emolliants	emolliants
	Mild	**Moderate**	**Severe**
	Atopic ezema severity		

Ridd M, Purdy S. Exacerbation of atopic eczema in children. BMJ. 2009 Aug 25;339:b2997.

Relative Absorption

Forearm	***1.0***
Sole	***0.14***
Back	***1.7***
Scalp	***3.5***
Forehead	***6.0***
Cheek	***13.0***
Scrotum	***42.0***

Cushing Syndrome (pituitary-adrenal axis suppression)**:**
- 50g of 0.05% clobetasol/wk or
- 500g of 1% hydrocortisone/wk
- in infants: a little as 1g/day x several days may ↓ HPA

References:

1. American Hospital Formulary System (AHFS) Drug Information 2009.
2. Merck Manual of Diagnosis and Therapy 1999 (http://www.merck.com/pubs/mmanual/tables/110tb1.htm access verified May 27, 2003)
3. WHO Model Prescibing Information: Drugs Used Dermatology, draft 1995.
4. Stoughton R. The vasoconstrictor assay in bioequivalence testing: practical concerns and recent developments. Int J Dermatol 1992; Suppl 1:26-28.
5. Brazzini B, Pimpinelli N. New & established topical corticosteroids in dermatology: clinical pharmacology and therapeutic use. Am J Clin Dermatol. 2002;3(1):47-58.
6. Korting HC, Unholzer A, Schafer-Korting M, Tausch I, Gassmueller J, Nietsch KH. Different skin thinning potential of equipotent medium-strength glucocorticoids. Skin Pharmacol Appl Skin Physiol. 2002 Mar-Apr;15(2):85-91.
7. FDA Issues Public Health Advisory Informing Health Care Providers of Safety Concerns Associated with the Use of Two Eczema Drugs, Elidel and Protopic Mar 10,2005 http://www.fda.gov/bbs/topics/ANSWERS/2005/ANS01343.html April/05 Health Canada http://www.hc-sc.gc.ca/english/protection/warnings/2005/2005_31.html CDA response: http://www.dermatology.ca/public-patients/atopic-dermatitis/calcineurin_e.php
8. Margolis DJ, Abuabara K, Hoffstad OJ, et al. Association Between Malignancy and Topical Use of Pimecrolimus. JAMA Dermatol. 2015 Feb 18.

Additional References:

Alabdulrazzaq F, Koren G. Topical corticosteroid use **during pregnancy**. Can Fam Physician. 2012 Jun;58(6):643-4.

Alikhan A, Mohammed ET, Lalor L. **White Spot on the Wrist**. Photo Quiz. Am Fam Physician. 2017:96(5):329-330 (**hypopigmentation**)

Andersen YMF, Egeberg A, Ban L, et al. **Association Between Topical Corticosteroid Use and Type 2 Diabetes** in Two European Population-Based Adult Cohorts. Diabetes Care. 2019 Apr 1.

Ashcroft DM, Dimmock P, Garside R, Stein K, Williams HC. Efficacy and tolerability of topical pimecrolimus and tacrolimus in the treatment of atopic dermatitis: meta-analysis of randomised controlled trials. BMJ 2005; 330:516-25**.** (InfoPOEMs: In comparison studies to date, tacrolimus is as effective as steroids in adults and is more effective in the higher concentration (0.1%) than weak corticosteroids in children. Pimecrolimus was less effective than potent steroids in adults, and has not been studied compared with weak corticosteroids. Neither has been studied in patients with corticosteroid-resistant lesions. These are expensive alternatives to corticosteroids. The Unites States Food and Drug Administration has issued a caution linking these drugs to cancer, and does not recommend them for children younger than 2 years. (LOE = 1a))

Arellano FM, Arana A, Wentworth CE, et al. **Lymphoma** among patients with atopic dermatitis and/or treated with topical immunosuppressants in the United Kingdom. J Allergy Clin Immunol. 2009 May;123(5):1111-6, 116.e1-13. Epub 2009 Apr 10. We did not find any cases of lymphoma in TCI users; however, the number of patients exposed to (topical calcineurin inhibitors) TCI was insufficient to study any possible association between lymphoma and these drugs. Our results show an association between lymphoma-especially skin lymphoma-and use of TCS. The risk increased with duration of exposure and potency of (topical corticosteroids) TCS.

Baumer JH. Guideline review: **atopic eczema** in children, NICE. Arch Dis Child. 2008 Apr 1; [Epub ahead of print]

Bieber T, Cork M, Ellis C, Girolomoni G, Groves R, Langley R, Luger T,Meurer M, Murrell D, Orlow S, Paller A, de Prost Y, Puig L, Ring J, Saurat JH,
Schwarz T, Shear N, Stingl G, Taieb A, Thestrup-Pedersen K; Pediatric Advisory Committee of the Food and Drug Administration. Consensus statement on the safety profile of topical calcineurin inhibitors. Dermatology. 2005;211(2):77-8.

Breneman D, Fleischer AB Jr, Abramovits W, et al.; for the Tacrolimus Ointment Study Group. Intermittent therapy for flare prevention and long-term disease control in stabilized atopic dermatitis: A randomized comparison of 3-times-weekly applications of tacrolimus ointment versus vehicle. J Am Acad Dermatol. 2008 Mar 20; [Epub ahead of print]

Breuer K, Werfel T, Kapp A. Safety and efficacy of topical calcineurin inhibitors in the treatment of childhood atopic dermatitis. Am J Clin Dermatol. 2005;6(2):65-77. (Topical calcineurin inhibitors have been proven to be effective and have a good safety profile during short-term and long-term use for up to 1 year with pimecrolimus and up to 4 years with tacrolimus. Given the lack of extensive experience with use of topical calcineurin inhibitors over longer periods, regular use of these agents, particularly in children, should be undertaken only after careful consideration of individual cases. Sun protection should also be advised.)

Butler DC, Heller MM, Murase JE. Safety of **dermatologic medications in pregnancy and lactation**: Part II. Lactation.
J Am Acad Dermatol. 2014 Mar;70(3):417.e1-10; quiz 427.

Chi CC, Kirtschig G, Baldo M, et al. Topical interventions for **genital lichen sclerosus**. Cochrane Database Syst Rev. 2011 Dec 7;12:CD008240. The current limited evidence demonstrates the efficacy of clobetasol propionate, mometasone furoate, and pimecrolimus in treating genital lichen sclerosus.

Chi CC, Wang SH, Mayon-White R, Wojnarowska F. **Pregnancy Outcomes After Maternal Exposure to Topical Corticosteroids**: A UK Population-Based Cohort Study. JAMA Dermatol. 2013 Sep 4.

Clark GW, Pope SM, Jaboori KA. Diagnosis and Treatment of **Seborrheic Dermatitis**. Am Fam Physician. 2015;91(3):185-190.

Coenraads PJ. **Hand eczema**. N Engl J Med. 2012 Nov 8;367(19):1829-37.

Cook BA, Warshaw EM. Role of topical **calcineurin inhibitors** in the treatment of **seborrheic dermatitis**: a review of pathophysiology, safety, and efficacy. Am J Clin Dermatol. 2009;10(2):103-18. doi: 10.2165/00128071-200910020-00003.

Cury Martins J, Martins C, Aoki V, et al. **Topical tacrolimus for atopic dermatitis**. Cochrane Database Syst Rev. 2015 Jul 1;7:CD009864. Tacrolimus 0.1% was better than low-potency corticosteroids pimecrolimus 1% and tacrolimus 0.03%. Results were equivocal when comparing both dose formulations to moderate-to-potent corticosteroids. Tacrolimus 0.03% was superior to mild corticosteroids and pimecrolimus. Both tacrolimus formulations seemed to be safe, and no evidence was found to support the possible increased risk of malignancies or skin atrophy with their use. The reliability and strength of the evidence was limited by the lack of data; thus, findings of this review should be interpreted with caution. We did not evaluate costs.

Dalziel K, Shaw S. **Lichen sclerosus**. BMJ. 2010 Feb 15;340:c731. doi: 10.1136/bmj.c731.

Dabade TS et al. **Wet dressing** therapy in conjunction with topical corticosteroids is effective for rapid control of severe pediatric atopic dermatitis: Experience with 218 patients over 30 years at Mayo Clinic. J Am Acad Dermatol 2012 Jul; 67:100.

Drugs for acne, rosacea and psoriasis. Treat Guidel Med Lett. 2005 Jul;3(35):49-56.

Eichenfield LF, Tom WL, Chamlin SL, et al. . Guidelines of care for the **management of atopic dermatitis**. Section 1. Diagnosis and assessment of atopic dermatitis.
J Am Acad Dermatol. 2014 Feb;70(2):338-51.

Eichenfield LF, Boguniewicz M, Simpson EL, et al. **Translating Atopic Dermatitis Management Guidelines Into Practice** for Primary Care Providers.
Pediatrics. 2015 Aug 3.

Eichenfield LF, Tom WL, Berger TG, et al. Guidelines of care for the **management of atopic dermatitis**. Section 2. Ma**nagement and treatment of atopic dermatitis with topical therapies**. J Am Acad Dermatol. 2014 Jul;71(1):116-32.

Felten R, Messer L, Moreau P, et al. **Osteonecrosis of the femoral head linked to topical steroids** for skin bleaching: a case report. Ann Intern Med. 2014 Nov 18;161(10):763-4.

Ference J, Last A. Choosing Topical Corticosteroids. Am Fam Phys **2009**;79(2): 135-140.

Forsyth EL, Millard TP. Diagnosis and pharmacological treatment of **chronic actinic dermatitis** in the elderly: an update. Drugs Aging. 2010 Jun 1;27(6):451-6.

Francis NA, Ridd MJ, Thomas-Jones E, et al. A randomised placebo-controlled trial of **oral and topical antibiotics for children with clinically infected eczema** in the community: the ChildRen with Eczema, Antibiotic Management (CREAM) study. Health Technol Assess. 2016 Mar;20(19):1-84. Our data suggest that oral and topical antibiotics have no effect, or a harmful effect, on subjective eczema severity in children with clinically infected eczema in the community.

Francis NA, Ridd MJ, Thomas-Jones E, et al. **Oral** and **Topical Antibiotics** for Clinically Infected **Eczema** in Children: A Pragmatic Randomized Controlled Trial in Ambulatory Care. Ann Fam Med. 2017 Mar;15(2):124-130.

Fraser, Lisa-Ann, Van Uum, Stan. Work-up for **Cushing** syndrome. CMAJ 2009 0: cmaj.090250.

Green C, Colquitt JL, Kirby J, Davidson P. Topical corticosteroids for atopic eczema: clinical and cost effectiveness of once-daily vs. more frequent use. Br J Dermatol 2005; 152:130-41. (InfoPOEMs: Patients should begin with once-daily dosing of topical corticosteroids for atopic eczema, increasing to twice or 3 times per day only if symptoms are not well controlled. (LOE = 1a-))

Haeck IM, Rouwen TJ, Timmer-de Mik L, et al. Topical corticosteroids in atopic dermatitis and the risk of **glaucoma and cataracts.** J Am Acad Dermatol. 2011 Feb;64(2):275-81.

Health Canada Mar/16 is informing Canadians that Jamp Pharma has initiated a voluntary recall of its product, **Jamp-Hydrocortisone Cream 1% (NPN 80057189), due to microbial contamination** with bacteria, yeast and mould.

Health Canada Mar/17 is advising Canadians that the unauthorized health product "**PureCare Herbal Cream**" may pose serious health risks. The product is promoted as a natural treatment for eczema and psoriasis in children and babies.

Health Canada testing confirmed the presence of a prescription steroid (clobetasol propionate) and another ingredient (phenoxylethanol) not declared on the product label.

Kohn LL, Kang Y, Antaya RJ. A randomized, controlled trial comparing **topical steroid application to wet versus dry skin in children with atopic dermatitis** AD). J Am Acad Dermatol. 2016 Aug;75(2):306-11.

Lebrum-Vignes B, Cleach L, Giraudeau B et al. Safety of topical corticosteroid use during **pregnancy**. Arch Dermatol 2012; 148(4):525-7.

Lenane P, Macarthur C, Parkin PC, et al. **Clobetasol propionate, 0.05%, vs hydrocortisone, 1%, for alopecia areata** in children: a randomized clinical trial. JAMA Dermatol. 2014 Jan;150(1):47-50.

Kalavala M, Mills C, Long C, & Finlay A. The **Fingertip Unit**: A Practical Guide for Topical Therapy in Children. Journal of Dermatological Treatment. 2007; 18: 319-320.

Kastarinen H, Oksanen T, Okokon EO, et al. **Topical anti-inflammatory agents for seborrhoeic dermatitis** of the face or scalp.Cochrane Database Syst Rev. 2014 May 19;5:CD009446. Topical steroids are an effective treatment for seborrhoeic dermatitis of the face and scalp in adolescents and adults, with no differences between mild and strong steroids in the short-term. There is some evidence of the benefit of topical calcineurin inhibitor or lithium salt treatment. Treatment with azoles seems as effective as steroids concerning short-term total clearance, but in other outcomes, strong steroids were more effective. Calcineurin inhibitor and azole treatment appeared comparable. Lithium salts were more effective than azoles in producing total clearance. Steroids are similarly effective to calcineurin inhibitors but with less adverse effects.

Kelso JM. Application of topical corticosteroids to sites of **positive immediate-type allergy skin tests** to relieve itching: results of a double-blind, placebo-controlled trial. Ann Allergy Asthma Immunol. 2007 Feb;98(2):182-4. The application of corticosteroid cream to sites of positive immediate-type allergy skin tests does not provide relief of itching; therefore, this practice should be abandoned. Instead, patients should be informed that any itching they may be experiencing will substantially resolve during the next 30 minutes and that application of such topical treatment will not hasten the relief of itching.

Kirtschig G, Middleton P, Bennett C, et al. Interventions for **bullous pemphigoid**. Cochrane Database Syst Rev. 2010 Oct 6;10:CD002292. Very potent topical steroids are effective and safe treatments for BP, but their use in extensive disease may be limited by side-effects and practical factors. Milder regimens (using lower doses of steroids) are safe and effective in moderate BP. Starting doses of prednisolone greater than 0.75 mg/kg/day do not give additional benefit, lower doses may be adequate to control disease and reduce the incidence and severity of adverse reactions. The effectiveness of adding plasma exchange, azathioprine or mycophenolate mofetil to corticosteroids, and combination treatment with tetracycline and nicotinamide needs further investigation.

Knight AK, Boxer M, Chandler MJ. **Alcohol**-induced rash caused by topical **tacrolimus**. Ann Allergy Asthma Immunol. 2005 Sep;95(3):291-2.

Kreuter A, et al. 1% pimecrolimus, 0.005% calcipotriol, and 0.1% betamethasone in the treatment of **intertriginous psoriasis**: a double-blind, randomized controlled study. Arch Dermatol. 2006 Sep;142(9):1138-43. The 1% **pimecrolimus was shown to be less potent than 0.1% betamethasone** in the treatment of IP. Considering the adverse-effect profile of long-term application of corticosteroids, occasional or intermittent rescue therapy with short-term topical corticosteroids and maintenance with a less potent agent, such as 1% pimecrolimus or 0.005% calcipotriol, might be appropriate for patients with IP in general practice. (InfoPOEMs: For intertriginous psoriasis (IP), betamethasone is more effective than calcipotriol; calcipotriol is more effective than placebo; & pimecrolimus is mimimally, if at all, effective. (LOE = 1b))

Lebrun-Vignes B, Le Cleach L, Giraudeau B, Chosidow O. Safety of **topical corticosteroid use during pregnancy**. Arch Dermatol. 2012 Apr;148(4):525-7.

Li AW, Yin ES, Antaya RJ. Topical Corticosteroid **Phobia** in **Atopic Dermatitis**: A Systematic Review. JAMA Dermatol. 2017 Jul 19.

Liu C, Zhou Z, Liu G, et al. Efficacy and safety of **dexamethasone ointment on recurrent aphthous ulceration**. Am J Med. 2012 Mar;125(3):292-301.

Lowther A, McCormick T, Nedorost S. Systemic contact dermatitis from propylene glycol. Dermatitis. 2008 Mar-Apr;19(2):105-8.

Manthripragada AD, Pinheiro SP, Macurdy TE, et al. **Off-Label Topical Calcineurin Inhibitor Use in Children**. Pediatrics. 2013 Oct 14.

Margolis DJ, Abuabara K, Hoffstad OJ, et al. Association Between **Malignancy** and Topical Use of **Pimecrolimus**. JAMA Dermatol. 2015 Feb 18.

Matterne U, Bohmer MM, Weisshaar E, et al. **Oral H1 antihistamines as `add-on` therapy to topical treatment for eczema**. Cochrane Database Syst Rev. 2019 Jan 22;1:CD012167. Based on the main comparisons, we did not find consistent evidence that H1 AH treatments are effective as 'add-on' therapy for eczema when compared to placebo; evidence for this comparison was of low and moderate quality. However, fexofenadine probably leads to a small improvement in patient-assessed pruritus, with probably no significant difference in the amount of treatment used to prevent eczema flares. Cetirizine was no better than placebo in terms of physician-assessed clinical signs nor patient-assessed symptoms, and we found no evidence that loratadine was more beneficial than placebo, although all interventions seem safe.The quality of evidence was limited because of poor study design and imprecise results.

Medical Letter. Treatment Guidelines. Drugs for **Allergic Disorders**. Aug 2007.

Medscape Mar 18, 2010 - Drugs for eczema made by Novartis AG and Astellas Pharma may need their warning labels expanded after dozens of new reported cases of cancer and infection in children, U.S. Food and Drug Administration staff said in documents released on Thursday. Agency scientists said **46 cancer cases and 71 infection** cases have been reported in patients aged 16 and younger from 2004 to 2008 with Novartis' Elidel and Astellas' Protopic. Both drugs -- also known as pimecrolimus and tacrolimus respectively -- already carry strong warnings about cancer and infection, but officials should consider expanding them to include the new post-marketing reports, they wrote.

Menter A, Korman NJ, Elmets CA, Feldman SR, Gelfand JM, Gordon KB, Gottlieb A, Koo JY, Lebwohl M, Lim HW, Van Voorhees AS, Beutner KR, Bhushan R, American Academy of Dermatology. Guidelines of care for the management of **psoriasis and psoriatic arthritis**. Section 3. Guidelines of care for the management and treatment of psoriasis with **topical** therapies. J Am Acad Dermatol 2009 Apr;60(4):643-59.

Millard AN, Stratman EJ. Assessment of **Topical Corticosteroid Prescribing, Counseling, and Communication Among Dermatologists and Pharmacists**. JAMA Dermatol. 2019 Mar 27.

Moreno G, Corbalan J, Penaloza B, et al. **Topical corticosteroids for treating phimosis** in boys. Cochrane Database Syst Rev. 2014 Sep 2;9:CD008973. Topical corticosteroids offer an effective alternative for treating phimosis in boys. Although sub optimal reporting among the included studies meant that the size of the effect remains uncertain, corticosteroids appear to be a safe, less invasive first-line treatment option before undertaking surgery to correct phimosis in boys.

Mose KF, Andersen F, Røpke MA, et al. Anti-inflammatory **potency testing of topical corticosteroids and calcineurin inhibitors** in human volunteers sensitized to **diphenylcyclopropenone.** Br J Clin Pharmacol. 2018 Apr 1.

Murase JE, Heller MM, Butler DC. Safety of **dermatologic medications in pregnancy and lactation**. J Am Acad Dermatol 2014;70:401-14 (part I) & 417-26 (part II).

Murase JE, Heller MM, Butler DC. Safety of **dermatologic medications in pregnancy and lactation**: Part I. Pregnancy. J Am Acad Dermatol. 2014 Mar;70(3):401.e1-14; quiz 415.

National Institute for Clinical Excellence (NICE). **Tacrolimus and pimecrolimus** for atopic eczema. London (UK): National Institute for Clinical Excellence (NICE); 2004 Aug. 45 p. (Technology appraisal; no. 82).
http://www.nice.org.uk/pdf/TA082guidance.pdf

National Institute for Clinical Excellence (NICE). Frequency of application of **topical corticosteroids for atopic eczema**. London (UK): National Institute for Clinical Excellence (NICE); 2004 Aug. 34 p. (Technology appraisal guidance; no. 81).

National Institute for Clinical Excellence (NICE). **Atopic eczema in children**: Management of atopic eczema in children from birth up to the age of 12 years.
http://www.nice.org.uk/guidance/index.jsp?action=byID&o=11901

Navarro-López V, et al. Effect of Oral Administration of a Mixture of **Probiotic Strains on SCORAD Index and Use of Topical Steroids** in Young Patients With Moderate Atopic Dermatitis: A Randomized Clinical Trial. JAMA Dermatol. 2017 Nov 8.

Paller AS, Lebwohl M, Fleischer AB, and the US/Canada Tacrolimus Ointment Study Group. **Tacrolimus** ointment is more effective than pimecrolimus cream with a similar safety profile in the treatment of atopic dermatitis: Results from 3 randomized, comparative studies. J Am Acad Dermatol 2005; 52:810-22.
(InfoPOEMs: Tacrolimus ointment is slightly more effective for the treatment of atopic dermatitis (AD) than pimecrolimus cream in pediatric and adult patients with moderate to severe disease. Adverse events are similar with both treatments. However, there is recent concern about the potential for an increased risk of skin cancer with prolonged use of either product. (LOE = 1b))

Paul C, et al. Safety and tolerability of 1% **pimecrolimus** cream among infants: experience with 1133 patients treated for up to 2 years. Pediatrics. 2006 Jan;117(1):e118-28. Epub 2005 Dec 15.

Plensdore S, Livieratos M, Dada N. **Pigmentation Disorders**: Diagnosis and Management. Am Fam Physician. 2017;96(12):797-804.

Prague JK, May S, Whitelaw BC. **Cushing's syndrome**. BMJ. 2013 Mar 27;346:f945.

Rashid RS, Shim TN. **Contact dermatitis**. BMJ. 2016 Jun 30;353:i3299.

Reitamo S, Ortonne JP, Sand C, et al.; European Tacrolimus Ointment Study Group. A multicentre, randomized, double-blind, controlled study of long-term treatment with 0.1% **tacrolimus** ointment in adults with moderate to severe atopic dermatitis. Br J Dermatol. 2005 Jun;152(6):1282-9.

Reitamo S, Rustin M, Harper J, et al. the 0·1% Tacrolimus Ointment Long-term Follow-up Study Group. A **4-year follow-up** study of atopic dermatitis therapy with 0.1% **tacrolimus** ointment in children and adult patients. Br J Dermatol. 2008 Jul 15. [Epub ahead of print] n=782. The safety profile of intermittent or continuous long-term application of 0.1% tacrolimus ointment for up to 4 years was consistent with that which has been established from shorter studies and gave no reason for concern. In addition, 0.1% tacrolimus ointment demonstrated sustained efficacy as reflected by the expression of high satisfaction with treatment by both patients and investigators.

Rigopoulos D, et al. Tacrolimus ointment 0.1% in pityriasis alba: an open-label, randomized, placebo-controlled study. Br J Dermatol. 2006 Jul;155(1):152-5. (InfoPOEMs: **Tacrolimus is an option for the treatment of pityriasis alba** (PA). Note that this drug has not been approved for use in children younger than 2 years and should be used in all patients for as short a time as possible since long-term use has been associated with an increased risk of lymphoma and skin cancer. Since PA is a self-limiting condition, with patients in the control group improving throughout the study, this expensive and potentially harmful agent should only be used after a careful discussion of the risks and benefits with patients and their parents. Moisturizers, sun block, and low-dose corticosteroids are first-line treatments. (LOE = 1b))

Rustin MH. The safety of **tacrolimus** ointment for the treatment of atopic dermatitis: a review. Br J Dermatol. 2007 Nov;157(5):861-73. Epub 2007 Sep 13.

Schwarz T, Kreiselmaier I, Bieber T, et al. A randomized, double-blind, vehicle-controlled study of 1% pimecrolimus cream in adult patients with **perioral dermatitis**.
J Am Acad Dermatol. 2008 Jul;59(1):34-40. Epub 2008 May 7. Adults with perioral dermatitis clinically improve faster with 1% pimecrolimus cream (Elidel) compared with inactive placebo, but after 1 month there is no longer any significant difference in response rates between active and control therapy. In this study, the subgroup of patients with a history of topical corticosteroid use received significantly more benefit from pimecrolimus cream. (LOE = 1b-)

Sidbury R, Davis DM, Cohen DE, et la. Guidelines of care for the management of **atopic dermatitis: Section 3. Management and treatment with phototherapy and systemic agents**. J Am Acad Dermatol. 2014 May 7. pii: S0190-9622(14)01264-X.

Sidbury R, Tom WL, Bergman JN, et al. Guidelines of care for the **management of atopic dermatitis: Section 4. Prevention of disease flares and use of adjunctive therapies and approaches**. J Am Acad Dermatol. 2014 Dec;71(6):1218-33.

SIGN: Scottish Intercollegiate Guidelines Network, 2011. Management of atopic eczema in primary care – a national clinical guideline [online]. Available: http://www.sign.ac.uk/pdf/sign125.pdf [Accessed 19 May 2011].

Sigurgeirsson B, Boznanski A, Todd G, et al. Safety and Efficacy of **Pimecrolimus** in **Atopic Dermatitis**: A 5-Year Randomized Trial. Pediatrics. 2015 Mar 23.

Song H, Adamson A, Mostaghimi A. **Medicare Part D Payments for Topical Steroids**: Rising Costs and Potential Savings. JAMA Dermatol. 2017 Aug 1;153(8):755-759.

Stein SL, Cifu AS. **Management of Atopic Dermatitis**. JAMA. 2016 Apr 12;315(14):1510-1

Tollefson MM, Bruckner AL; Section on Dermatology. **Atopic dermatitis**: skin-directed management. Pediatrics. 2014 Dec;134(6):e1735-44.

Usatine RP, Tinitigan M. Diagnosis and Treatment of **Lichen Planus**. Am Fam Physician. 2011;84(1):53-60.

van Velsen SGA et al. **Bone mineral density** in children with moderate to severe atopic dermatitis. J Am Acad Dermatol 2010 Nov; 63:824.

van Zuuren EJ, Fedorowicz Z, Christensen R, et al. **Emollients and moisturisers for eczema**. Cochrane Database of Systematic Reviews 2017, Issue 2. Art. No.: CD012119. Most moisturisers showed some beneficial effects, producing better results when used with active treatment, prolonging time to flare, and reducing the number of flares and amount of topical corticosteroids needed to achieve similar reductions in eczema severity. We did not find reliable evidence that one moisturiser is better than another.

Verma SB. **Topical corticosteroid misuse** in India is harmful and out of control. BMJ. 2015 Nov 25;351:h6079.

Weidinger S, Novak N. **Atopic dermatitis**. Lancet. 2015 Sep 11.

Woolner K, Sauder M. **Periorbital erythema** following **alcohol** ingestion during treatment with **topical tacrolimus**. CMAJ. 2016 Mar 15;188(5):368.

Xie H, Xiao X, Li J. Topical **Steroids** in **Chinese Cosmetics**. JAMA Dermatol. 2017 Jul 5.

Yao XJ, Zhang TD. **Psoriasis localized to the glans penis** in a 37-year-old man. (tacrolimus tx) CMAJ. 2018 Jun 18;190(24):E747.

Useful tables from Canadian Glaucoma Guidelines 2009:

Table 19—Staging each eye for glaucoma damage

Suspect	One or two of the following: IOP >21 mm Hg; suspicious disc or cup to disc (C/D) asymmetry of >0.2; suspicious 24-2 (or similar) VF defect
Early	Early glaucomatous disc features (e.g. C/D* <0.65) and (or) mild VF defect not within 10° of fixation (e.g. MD better than –6 dB on HVF 24-2)
Moderate	Moderate glaucomatous disc features (e.g. vertical C/D* 0.7–0.85) and (or) moderate VF defect not within 10° of fixation (e.g. MD from –6 to –12 dB on HVF 24-2)
Advanced	Advanced glaucomatous disc features (e.g. C/D* >0.9) and (or) VF defect within 10° of fixation† (e.g. MD worse than –12 dB on HVF 24-2)

Adapted from Damji et al.[160]

Please refer to text in order to decide whether a nerve exhibits characteristics of glaucomatous damage.

*Refers to vertical C/D ratio in an average size nerve. If the nerve is small, then a smaller C/D ratio may still be significant; conversely, a large nerve may have a large vertical C/D ratio and still be within normal limits.

†Also consider baseline 10-2 VF (or similar)

Note: MD, mean deviation; HVF, Humphrey Visual Field Analyzer.

Table 20—Suggested upper limit of initial target IOP for each eye

Stage	Suggested upper limit of target IOP. Modify based on longevity, QOL and risk factors for progression	Evidence
Suspect in whom a clinical decision is made to treat	24 mm Hg with at least 20% reduction from baseline	OHTS,[47] EGPS[325]
Early	20 mm Hg with at least 25% reduction from baseline	EMGTS,[48] CIGTS[326]
Moderate	17 mm Hg with at least 30% reduction from baseline	CNTGS,[12] AGIS[11]
Advanced	14 mm Hg with at least 30% reduction from baseline	AGIS,[11] Odberg[327]

Adapted from Damji et al.[160]

Note: Target IOP may need to be adjusted during the course of follow-up. Extremes of CCT may be helpful in the setting of target IOP. For example, if the cornea is very thin, this may encourage a more aggressive approach with more frequent follow-up.[161]

Table 21—Advantages and disadvantages of single and combined cataract and glaucoma procedures

Procedure	Advantages	Disadvantages
Phacoemulsification alone	Quick procedure with more rapid visual recovery	Postoperative IOP spike is a potential risk, particularly in patients with advanced VF loss
	Improved vision, which benefits QOL	Not regarded as a consistent or powerful means of lowering IOP
	May lower IOP a small amount in some patients	IOP should be watched closely in both the early postoperative period and later
Trabeculectomy alone	Quicker than combined procedure	Will not improve vision
	May achieve superior long-term IOP lowering than combined procedure or cataract alone	May cause or worsen cataract
Combined procedure	Minimizes anesthetic risk by combining 2 procedures in 1	May not be as effective at long-term IOP control as trabeculectomy alone
	Convenience to patient with 1 trip to operating room rather than 2	Increased risk of complications with 2 procedures rather than 1
	Cost savings	Slower visual recovery than doing cataract alone
	May blunt potentially damaging postoperative IOP spikes in patients with advanced VF loss	
	Opportunity to improve IOP control and improve vision at the same time with enhanced QOL	

References: *RxFiles* - Glaucoma

[1] Dipiro JT, Talbert RL, Yee GC, Matzke GR, Wells BG, Posey LM. *Pharmacotherapy: a pathophysiologic approach*. Fourth ed. Stamford, CT: Appleton and Lange; 1999:1470-75.

[2]Boucher M. Glaucoma: Keeping a close eye on your patients. *Pharmacy Practice* 2000; 16(2): 61-66

[3] Tsao S. The use of drugs in glaucoma patients. *CPJ* 2000; 133(7): 30-34.
[4] Micromedex 2017
[5] Khaw PT, Shah P, Elkington AR. Glaucoma--1: Diagnosis. BMJ. 2004 Jan 10;328(7431):97-9.
[6] Khaw PT, Shah P, Elkington AR. Glaucoma--2: Treatment. BMJ. 2004 Jan 17; 328(7431): 156-8.
[7] van der Valk R, Webers CA, Schouten JS, et al. Intraocular Pressure-Lowering Effects of All Commonly Used Glaucoma Drugs A **Meta-analysis** of Randomized Clinical Trials. Ophthalmology. **2005** May 24; [Epub ahead of print] Conclusion: This meta-analysis suggests that bimatoprost, travoprost, latanoprost, and timolol are the most effective intraocular pressure-reducing agents in POAG and OH patients.
[8] Reis R, dos Santos LC, Vila MP, Magacho L. Effects of travoprost 0.004% ophthalmic solution, six weeks after its laminated packaging had been removed, in primary open-angle glaucoma: a randomized, controlled, investigator-blinded study. Clin Ther. 2004 Dec;26(12):2121-7.
[9] Simmons ST, Dirks MS, Noecker RJ. Bimatoprost versus latanoprost in lowering intraocular pressure in glaucoma and ocular hypertension: results from parallel-group comparison trials. Adv Ther. 2004 Jul-Aug;21(4):247-62. Konstas AG, Hollo G, Irkec M, Tsironi S, Durukan I, Goldenfeld M, Melamed S. Diurnal IOP control with bimatoprost versus latanoprost in exfoliative glaucoma: a crossover, observer-masked, three-centre study. Br J Ophthalmol. 2007 Jun;91(6):757-60. Epub 2006 Nov 23. This crossover study suggests that better diurnal IOP control is obtained with bimatoprost than with latanoprost in patients with XFG. N=129.
Curran MP. Bimatoprost: a review of its use in open-angle glaucoma and ocular hypertension. Drugs Aging. 2009;26(12):1049-71. doi: 10.2165/11203210-000000000-00000.
Orme M, Collins S, Dakin H, Kelly S, Loftus J. Mixed treatment comparison and meta-regression of the efficacy and safety of prostaglandin analogues and comparators for primary open-angle glaucoma and ocular hypertension. Curr Med Res Opin. 2010 Mar;26(3):511-28.

[10] Doi LM, Melo LA Jr, Prata JA Jr. Effects of the combination of bimatoprost and latanoprost on intraocular pressure in primary open angle glaucoma: a randomised clinical trial. Br J Ophthalmol. 2005 May;89(5):547-9.

[11] Garcia-Sanchez J, Rouland JF, Spiegel D, et al. A comparison of the fixed combination of latanoprost and timolol with the unfixed combination of brimonidine and timolol in patients with elevated intraocular pressure. A six month, evaluator masked, multicentre study in Europe. Br J Ophthalmol. 2004 Jul;88(7):877-83.
[12] Johnson SM, Martinez M Freedman S. Management of glaucoma in pregnancy and lactation. Surv Opthalmol 2001;45:449-54.

AAO- American Academy of Ophthalmology Glaucoma Panel. **Primary open-angle glaucoma**. San Francisco (CA): American Academy of Ophthalmology; 2010. http://one.aao.org/ce/practiceguidelines/ppp_content.aspx?cid=93019a87-4649-4130-8f94-b6a9b19144d2
AAO-American Academy of Ophthalmology Glaucoma Panel. **Primary open-angle glaucoma suspect**. San Francisco (CA): American Academy of Ophthalmology; 2010. http://one.aao.org/CE/PracticeGuidelines/PPP_Content.aspx?cid=e2387c8a-e51c-4c21-be20-c30fbf4f3260
Alm A, Grunden JW, Kwok KK. **Five-year**, Multicenter Safety Study of Fixed-combination Latanoprost/Timolol (**Xalacom**) for Open-angle Glaucoma and Ocular Hypertension. J Glaucoma. 2010 May 29.
Alm A, Stjernschantz J. Effects on intraocular pressure and side effects of 0.005% latanoprost applied once daily, evening or morning. A comparison with timolol. Scandinavian Latanoprost Study Group. Ophthalmology. 1995 Dec;102(12):1743-52.
Alvan G, Calissendorff B, Seideman P, et al. **Absorption of ocular timolol**. Clin Pharmacokinet. 1980 Jan-Feb;5(1):95-100.
Alward WLM, van der Heide C, Khanna CL, et al; NEIGHBORHOOD Consortium. **Myocilin Mutations** in Patients With Normal-Tension Glaucoma. JAMA Ophthalmol. 2019 Feb 28.
Aldebert G, Faillie J, Buys D, et al. Association of anticholinergic drug use with risk for late age-related macular degeneration. JAMA Ophthalmology. 2018;136(7):770-78.
American Optometric Association. Care of the patient with open angle glaucoma. St. Louis (MO): American Optometric Association; **2010**. http://www.aoa.org/documents/CPG-9.pdf
American Optometric Association. Care of the patient with open angle glaucoma. 2nd ed. St. Louis (MO): American Optometric Association; 2002 Aug 17. http://www.aoa.org/documents/CPG-9.pdf
Aptel F, Cucherat M, Denis P. Efficacy and tolerability of prostaglandin analogs: a meta-analysis of randomized controlled clinical trials. J Glaucoma. 2008 Dec;17(8):667-73. The findings suggest a greater efficacy of bimatoprost compared with latanoprost and travoprost, although the incidence of hyperemia was lower with the latter 2 agents.
Arici MK, et al. The effect of **latanoprost**, bimatoprost, & **travoprost** on intraocular pressure after cataract surgery. J Ocul Pharmacol Ther. 2006 Feb;22(1):34-40. Our findings show that a single-dose topical of latanoprost and travoprost can prevent early postoperative IOP elevation after phacoemulsification surgery without any side effects.
Azuara-Blanco A, Burr J, Ramsay C, et al. Effectiveness of **early lens extraction** for the treatment of primary angle-closure glaucoma (**EAGLE**): a randomized controlled trial. Lancet. 2016 Oct 1;388(10052):1389-1397.
Barnett EM, Fantin A, Wilson BS, Kass MA, Gordon MO; **Ocular Hypertension Treatment Study** Group. The Incidence of Retinal Vein Occlusion in the Ocular Hypertension Treatment Study. Ophthalmology. 2010 Mar;117(3):484-488.
Basilious A, Buys YM. A woman with a family history of **glaucoma**. CMAJ. 2015 Jan 5.
Baskaran M, Foo RC, Cheng CY, et al. The **Prevalence and Types of Glaucoma** in an Urban Chinese Population: The Singapore Chinese Eye Study. JAMA Ophthalmol. 2015 May 14.
Becker ML, Huntington N, Woolf AD. **Brimonidine tartrate poisoning** in children: frequency, trends, and use of naloxone as an antidote. Pediatrics. 2009 Feb;123(2):e305-11. Epub 2009 Jan 5. All children < or =5 years of age with confirmed brimonidine ingestions should be medically evaluated and monitored for an extended period. Indications for the use of naloxone in brimonidine poisoning remain uncertain.
Belyea DA, Alhabshan R, Del Rio-Gonzalez AM, et al. **Marijuana Use** Among Patients With Glaucoma in a City With Legalized

Medical Marijuana Use. JAMA Ophthalmol. 2015 Dec 23:1-6.
Boland MV, Ervin AM, Friedman DS, et al. **Comparative effectiveness of treatments for open-angle glaucoma**: a systematic review for the u.s. Preventive services task force. (**USPSTF**) Ann Intern Med. 2013 Feb 19;158(4):271-9. Medical and surgical treatments for open- angle glaucoma lower intraocular pressure and reduce the risk for optic nerve damage over the short to medium term. Which treatments best prevent visual disability and improve patient-reported outcomes is unclear.
Bournias TE, Lai J. Brimonidine Tartrate 0.15%, Dorzolamide Hydrochloride 2%, and Brinzolamide 1% Compared as Adjunctive Therapy **to Prostaglandin Analogs**. Ophthalmology. 2009 Jul 8. [Epub ahead of print] The addition of brimonidine to a PGA provided greater IOP lowering than the addition of either dorzolamide or brinzolamide.
Brelén ME, Ng DS, Cheung CY. The Question of **Prescribing Calcium Supplements** to Patients at High Risk of Age-Related Macular Degeneration. JAMA Ophthalmol. 2019 Mar 21.
Canadian Ophthalmological Society Glaucoma Clinical Practice Guideline Expert Committee; Canadian Ophthalmological Society. **Canadian Ophthalmological Society** evidence-based clinical practice guidelines for the management of **glaucoma** in the adult eye. Can J Ophthalmol. 2009;44 Suppl 1:S7-93.
Cantor LB, Hoop JS, Morgan L. IOP-Lowering Efficacy of Bimatoprost 0.03% and Travoprost 0.004% in Patients with Glaucoma or Ocular Hypertension. Br J Ophthalmol. 2006 Jul 6; [Epub ahead of print]
Centofanti M, Oddone F, Gandolfi S, et al. Comparison of **Travoprost and Bimatoprost plus Timolol** Fixed Combinations in Open-Angle Glaucoma Patients Previously Treated with Latanoprost plus Timolol Fixed Combination.Am J Ophthalmol.2010 Aug 3.
Chan MPY, Broadway DC, Khawaja AP, et al. **Glaucoma and intraocular pressure in EPIC-Norfolk Eye Study**: cross sectional study. BMJ. 2017 Sep 13;358:j3889.
Charan NB, Lakshminarayan S. **Pulmonary** effects of topical **timolol**. Arch Intern Med. 1980 Jun;140(6):843-4.
Chauhan BC; Mikelberg FS; Balaszi AG; et al.; for the Canadian Glaucoma Study Group. Canadian Glaucoma Study: 2. **Risk Factors** for the Progression of Open-angle Glaucoma. *Arch Ophthalmol*. 2008;126(8):1030-1036.
Chauhan BC, Mikelberg FS, Artes PH, Balazsi AG, Leblanc RP, Lesk MR, Nicolela MT, Trope GE; for the Canadian Glaucoma Study Group. Canadian Glaucoma Study: 3. Impact of Risk Factors and Intraocular Pressure Reduction on the Rates of Visual Field Change. Arch Ophthalmol. 2010 Aug 9. Patients with abnormal **anticardiolipin antibody** levels and increasing age had faster visual field change. Modest IOP reduction in progressing patients significantly ameliorated the rate of visual field decline.
Chen EL, Kang KB. **Acute Onset of Blurry Vision** in a Young Man. JAMA Ophthalmol. 2019 Aug 22.
Chen HY, Lin CL, Lai SW, Kao CH. Association of **Selective Serotonin Reuptake Inhibitor Use** (SSRI) and Acute Angle-Closure Glaucoma. J Clin Psychiatry. 2016 Jun;77(6):e692-6.
Cheng JW, Cai JP, Li Y, Wei RL. A meta-analysis of topical **prostaglandin analogs** in the treatment of chronic angle-closure glaucoma. J Glaucoma. 2009 Dec;18(9):652-7.
Chiba T, et al. Effect of non-steroidal anti-inflammatory ophthalmic solution on intraocular pressure reduction by latanoprost in patients with primary open angle glaucoma or ocular hypertension. Br J Ophthalmol. 2006 Mar;90(3):314-7.
Collaborative Normal-Tension Glaucoma Study Group. (**CNGTS**) The effectiveness of **intraocular pressure reduction** in the treatment of normal-tension glaucoma. Am J Ophthalmol. 1998 Oct;126(4):498-505.
Cumberland PM, Russell-Eggitt I, Rahi JS. Visual Impairment Owing to Adverse Drug Reaction: Incidence and Routine Monitoring in the United Kingdom. Ophthalmology. 2014 Mar 5.
De Moraes CG, Juthani VJ, Liebmann JM, Teng CC, Tello C, Susanna R Jr, Ritch R. **Risk factors** for visual field progression in treated glaucoma. Arch Ophthalmol. 2011 May;129(5):562-8. (Especially peak IOP)
De Moraes CG, Mansouri K, Liebmann JM, et al. Association Between 24-Hour Intraocular Pressure Monitored With **Contact Lens Sensor and Visual Field Progression** in Older Adults With Glaucoma. JAMA Ophthalmol. 2018 May 24.
De Moraes CG, Sun A, Jarukasetphon R, et al. Association of **Macular Visual Field Measurements With Glaucoma Staging Systems**. JAMA Ophthalmol. 2018 Nov 8.
Dirks MS, et al. A 3-Month Clinical Trial Comparing the IOP-Lowering Efficacy of **Bimatoprost** and Latanoprost in Patients With Normal-Tension Glaucoma. Adv Ther. 2006 May-Jun;23(3):385-94. Bimatoprost was found to be more effective than latanoprost in lowering IOP in the patient with normal-tension glaucoma. Both drugs were efficacious and well tolerated.
Eadie BD, Etminan M, Carleton BC, et al. Association of Repeated Intravitreous **Bevacizumab Injections With Risk for Glaucoma Surgery**. JAMA Ophthalmol. 2017 Mar 16.
Etminan M, Mikelberg FS, Brophy JM. Selective **Serotonin Reuptake Inhibitors** and the Risk of Cataracts A Nested Case-Control Study. Ophthalmology. 2010 Mar 6.
Fahim A, Morice AH. Heightened **cough** sensitivity secondary to **latanoprost**. Chest. 2009 Nov;136(5):1406-7.
Fan BJ, Bailey JC, Igo RP Jr, et al. Association of a **Primary Open-Angle Glaucoma Genetic Risk Score** With Earlier Age at Diagnosis. JAMA Ophthalmol. 2019 Aug 22.
FDA: Nov/07 Cosmetic Eyelash-Lengthener Seized The FDA says U.S. marshals have seized more than 12,000 applicator tubes of Age Intervention Eyelash, a cosmetic promoted to increase eyelash growth, because of concerns it may cause eye damage. In a press release the agency said that the product is an "adulterated cosmetic" because it contains bimatoprost (Lumigan), used to treat elevated intraocular pressure. In patients taking the prescription drug, the agency said the extra dose of **bimatoprost** may decrease the treatment's effectiveness, leading to optic nerve damage. Other side effects could include macular edema and uveitis.The cosmetic's maker, Jan Marini Skin Research, responded that no cases of eye damage have been reported. It said it reformulated the product last year to remove bimatoprost and that "several other companies have copied [Marini's] discontinued product and continue to market their competing products with 'drug' claims for eyelash growth."
FDA Aug/18 Alcon Announces Voluntary Global Market Withdrawal of CyPass Micro-Stent for Surgical Glaucoma.
Feehan M, Munger MA, Cooper DK, et al. **Adherence to Glaucoma Medications** Over 12 Months in Two US Community Pharmacy Chains. J Clin Med. 2016 Sep 7;5(9).
Firth J, Hamel L, Kates J et al. **Visualizing Health Policy**. JAMA.2016;316(2):139

Garway-Heath DF, Crabb DP, Bunce C, et al. **Latanoprost** for open-angle glaucoma (**UKGTS**): a randomised, multicentre, placebo-controlled trial. Lancet 2014; online Dec 19.

Glaucoma Panel, Preferred Practice Patterns Committee. Primary open-angle glaucoma suspect. San Francisco (CA): American Academy of Ophthalmology (AAO); 2005. http://one.aao.org/asset.axd?id=2e86ca2e-9db0-43c9-b605-c004a82b6ea5

Goldberg I, Moloney G, McCluskey P. Topical ophthalmic medications: what potential for **systemic side effects** and interactions with Other medications. Med J Aust 2008;189:356-7.

Goldberg I, Gil Pina R, et al. **Bimatoprost 0.03%/timolol** 0.5% preservative-free ophthalmic solution versus **bimatoprost 0.03%/timolol 0.5% ophthalmic solution (Ganfort)** for glaucoma or ocular hypertension: a 12-week randomised controlled trial. Br J Ophthalmol. 2014 Mar 25.

Good TJ, Kimura AE, Mandava N, Kahook MY. Sustained elevation of intraocular pressure after intravitreal injections of **anti-VEGF** agents. Br J Ophthalmol. 2010 Aug 11.

Gracitelli CPB, et al. **Detection of glaucoma progression** in individuals of African descent compared with those of European descent [online Feb 15, 2018].JAMA Ophthalmol. doi:10.1001/jamaophthalmol.2017.6836

Ha A, Kim YK, Jeoung JW, et al. Association of **Angle Width** With Progression of Normal-Tension Glaucoma: A Minimum 7-Year Follow-up Study. JAMA Ophthalmol. 2018 Sep 20.

Han X, Souzeau E, Ong J-S, et al. **Myocilin gene** Gln368Ter variant penetrance and association with glaucoma in population-based and registry-based studies [online September 27, 2018]. JAMA Ophthalmol. doi:10.1001/jamaophthalmol.2018.4477

Hatanaka M, Grigera DE, Barbosa WL, Jordao M, Susanna R Jr. An eight-week, multicentric, randomized, interventional, open-label, phase 4, parallel comparison of the efficacy and tolerability of the fixed combination of timolol maleate 0.5%/brimonidine tartrate 0.2% versus fixed combination of timolol maleate 0.5%/dorzolamide 2% in patients with elevated intraocular pressure. J Glaucoma. 2008 Dec;17(8):674-9. Both fixed combinations were capable of significantly reducing the mean diurnal IOP, mean diurnal peak, and mean WDT peak after 8 weeks of treatment. Also, both fixed combinations are well tolerated with few side effects.

Health Canada July/19 is advising consumers that it has seized three unauthorized eye health products—**Digi Eye** contains neostigmine methylsulfate, **Kobayashi Aibon/Eyebon** Eyewash contains aminocaproic acid and **Sante FX Neo** contains neostigmine methylsulfate and aminocaproic acid—from a Glorious Cosmetics store in Edmonton, Alberta (10706, 82 Avenue NW) because they may pose serious health risks.

Heijl A, Leske MC, Bengtsson B, et al. Early Manifest Glaucoma Trial Group. (**EMGT**) Reduction of intraocular pressure and glaucoma progression: results from the Early Manifest Glaucoma Trial. Arch Ophthalmol. 2002 Oct;120(10):1268-79.

Helmer C, Malet F, et al. Is there a link between open-angle glaucoma and dementia? The 3C-alienor cohort. Ann Neurol. 2013 May 18.

Ho H, et al. Association of **systemic medication use with intraocular pressure** in a multiethnic Asian population: the Singapore Epidemiology of Eye Diseases study [online Jan 12, 2017].JAMA Ophthalmol. doi:10 .1001/jamaophthalmol.2016.5318

Hodge WG, Lachaine J, Steffensen I, Murray C, et al. The efficacy and harm of **prostaglandin analogues** for IOP reduction in Glaucoma patients compared to dorzolamide and brimonidine: a **systematic review**. Br J Ophthalmol. 2008 Jan;92(1):7-12. Latanoprost was found to be significantly superior to dorzolamide but not brimonidine. However, ocular adverse events were significantly fewer in latanoprost users than in brimonide users. Neither travoprost nor bimatoprost was compared to dorzolamide or brimonidine in the present literature.

Hoffmanová I, Sánchez D. **Metabolic acidosis and anaemia** associated with **dorzolamide** in a patient with impaired renal function. Br J Clin Pharmacol. 2018 Jan 14.

Hollands H, Johnson D, Hollands S, et al. Do findings on routine examination identify patients at risk for primary open-angle glaucoma? The rational clinical examination systematic review. JAMA. 2013 May 15;309(19):2035-42.

Honrubia F, Garcia-Sánchez J, Polo V, Martinez-de-la-Casa JM, Soto J. **Conjunctival hyperemia** with the use of **latanoprost** versus other prostaglandin analogues in patients with ocular hypertension or glaucoma: a meta-analysis of randomized clinical trials. Br J Ophthalmol. 2008 Nov 19. [Epub ahead of print] According to available data, the use of latanoprost is associated with a lower incidence of conjunctival hyperemia when compared to travoprost and bimatoprost in the treatment of patients with ocular hypertension or glaucoma.

Hong CJ, Trope GE. **Glaucoma**. CMAJ. 2014 Nov 24.

Horwitz A, Klemp M, Jeppesen J, et al. **Antihypertensive Medication Postpones the Onset of Glaucoma**: Evidence From a Nationwide Study. Hypertension. 2017 Feb;69(2):202-210.

Husain R, Do T, Lai J, et al. Efficacy of Phacoemulsification Alone vs Phacoemulsification With Goniosynechialysis in Patients With Primary Angle-Closure Disease: A Randomized Clinical Trial. JAMA Ophthalmol. 2019 Jul 11

Jampel HD, Chon BH, Stamper R, et al. Effectiveness of Intraocular Pressure-Lowering Medication **Determined by Washout.** JAMA Ophthalmol. 2014 Jan 30.

Jin J. JAMA **patient page. Glaucoma**. JAMA. 2014 May 14;311(18):1934.

Jonas JB, Aung T, Bourne RR, et al. **Glaucoma**. Lancet. 2017 May 31.

Kang JH, Boumenna T, Stein JD, et al. Association of statin use and high serum cholesterol levels with risk of primary open-angle glaucoma [online May 2, 2019]. JAMA Ophthalmol. doi:10.1001/jamaophthalmol.2019.0900

Kang JH, Willett WC, Rosner BA, et al. Association of **Dietary Nitrate Intake** With Primary Open-Angle Glaucoma: A Prospective Analysis From the Nurses' Health Study and Health Professionals Follow-up Study. JAMA Ophthalmol. 2016 Jan 14:1-11.

Kass MA, Gordon MO, Gao F, et al. for the Ocular Hypertension Treatment Study Group. Delaying Treatment of Ocular **Hypertension**: The Ocular Hypertension Treatment Study. Arch Ophthalmol. 2010 Mar;128(3):276-287.

Katz LJ, Cohen JS, Batoosingh AL, et al. Twelve-month, randomized, controlled trial of **bimatoprost 0.01%,** 0.0125%, and 0.03% in patients with glaucoma or ocular hypertension. Am J Ophthalmol. 2010 Apr;149(4):661-671.e1.

Kenigsberg PA. Changes in medical and surgical treatments of glaucoma between 1997 and 2003 in France. Eur J Ophthalmol. 2007 Jul-Aug;17(4):521-7. Between 1997 and 2003, new glaucoma drugs, primarily prostaglandins, improved intraocular pressure control and delayed surgery, reducing glaucoma surgery by 22%.

Khawaja AP, Chan MP, Broadway DC, et al. **Systemic medication** and intraocular pressure in a British population: the EPIC-Norfolk Eye Study. Ophthalmology. 2014 Aug;121(8):1501-7.

Kim MJ, Kim SH, Hwang YH, et al. Novel Screening Method for Glaucomatous Eyes With Myopic Tilted Discs: **The Crescent Moon Sign**. JAMA Ophthalmol. 2014 Aug 21.

King A, Azuara-Blanco A, Tuulonen A. **Glaucoma**. BMJ. 2013 Jun 11;346:f3518.

King AJ, Rotchford AP. Validity of the **Monocular Trial of Intraocular Pressure-Lowering at Different Time Points** in Patients Starting Topical Glaucoma Medication. JAMA Ophthalmol. 2016 May 5.

Konstas AG, Mikropoulos D, Dimopoulos AT, et al. Second line therapy with dorzolamide/timolol or latanoprost/timolol fixed combination versus adding dorzolamide/timolol fixed combination to latanoprost monotherapy. Br J Ophthalmol. 2008 Aug 14. [Epub ahead of print] This study showed DTFC, LTFC and the addition of DTFC to latanoprost significantly decrease the IOP compared to latanoprost alone, but the latter therapy regime obtains the greatest IOP reduction.

Konstas AG, Katsimbris JM, Lallos N, et al. Latanoprost 0.005% versus bimatoprost 0.03% in primary open-angle glaucoma patients. Ophthalmology. 2005 Feb;112(2):262-6.

Krakowski AC, Nguyen TA. **Inhibition of Angiofibromas** in a Tuberous Sclerosis Patient Using Topical **Timolol** 0.5% Gel. Pediatrics. 2015 Aug 24.

Kurtz S, Mann O. Incidence of hyperemia associated with bimatoprost treatment in naïve subjects and in subjects previously treated with latanoprost. Eur J Ophthalmol. 2009 May-Jun;19(3):400-3. The above findings suggest that patients already on prostaglandin therapy may be less likely to experience an increase in conjunctival hyperemia induced by bimatoprost.

Kwon YH, Fingert JH, et al. **Primary open-angle glaucoma**. (Mechanism of Disease) N Engl J Med. 2009 Mar 12;360(11):1113-24.

Landers J, Martin K, Sarkies N, Bourne R, Watson P. A Twenty-Year Follow-up Study of **Trabeculectomy**: Risk Factors and Outcomes. Ophthalmology. 2011 Dec 23.

Le JT, Viswanathan S, Tarver ME, et al. Assessment of the Incorporation of Patient-Centric Outcomes in Studies of Minimally Invasive Glaucoma **Surgical Devices**. JAMA Ophthalmol. 2016 Jul 7.

Leske MC, et al.; Early Manifest Glaucoma Trial Group. Factors for glaucoma progression and the effect of treatment: the early manifest glaucoma trial. Arch Ophthalmol. 2003 Jan;121(1):48-56.

Levy J, et al. **Topiramate**-induced bilateral angle-closure glaucoma. Can J Ophthalmol. 2006 Apr;41(2):221-5.

Liebmann JM, Cioffi GA. Nicking Glaucoma with **Nicotinamide**? N Engl J Med. 2017 May 25;376(21):2079-2081.

Lin CC, Hu CC, Ho JD, et al. **Obstructive sleep apnea and increased risk of glaucoma**: a population-based matched-cohort study. Ophthalmology. 2013 Aug;120(8):1559-64.

Lin HC, Kang JH, Jiang YD, et al. **Hypothyroidism** and the Risk of Developing Open-Angle **Glaucoma** A Five-Year Population-Based Follow-Up Study. Ophthalmology. 2010 Jun 15. Hypothyroid patients had a significantly increased risk of OAG development during the 5-year follow-up period. Levothyroxine seemed to be protective.

Lin HC, Stein JD, Nan B, et al. Association of **Geroprotective Effects of Metformin** and Risk of Open-Angle Glaucoma in Persons With Diabetes Mellitus. JAMA Ophthalmol. 2015 May 28.

Lin L, Zhao YJ, Chew PT, et al. Comparative Efficacy and Tolerability of **Topical Prostaglandin Analogues** for Primary Open-Angle Glaucoma and Ocular Hypertension. Ann Pharmacother. 2014 Dec;48(12):1585-1593.

Liu H, Li L, Wormstone IM, et al. Development and Validation of a **Deep Learning System to Detect Glaucomatous Optic Neuropathy** Using Fundus Photographs. JAMA Ophthalmol. 2019 Sep 12.

Liu JH, Medeiros FA, Slight JR, Weinreb RN. Diurnal and Nocturnal Effects of Brimonidine Monotherapy on Intraocular Pressure. Ophthalmology. 2010 Jul 20. [Epub ahead of print]

Maier PC, Funk J, Schwarzer G, Antes G, Falck-Ytter YT. Treatment of ocular hypertension and open angle glaucoma: meta-analysis of randomised controlled trials. BMJ. 2005 Jul 1; [Epub ahead of print] CONCLUSIONS: Lowering intraocular pressure in patients with ocular hypertension or manifest glaucoma is beneficial in reducing the risk of visual field loss in the long term.

Malihi M, Filho, Hodge D, et al. Long-Term Trends in **Glaucoma-Related Blindness** in Olmsted County, Minnesota. Ophthalmology 121.1:134-141. 2014.

Marquis RE, Whitson JT. Management of glaucoma: focus on pharmacological therapy. Drugs Aging. 2005;22(1):1-21.

Medical Letter. **Mitomycin solution (Mitosol)** for Glaucoma Surgery. March 18, 2013.

Morales DR, Dreischulte T, Lipworth BJ, et al. **Respiratory effect of beta-blocker eye drops** in asthma: population based study and meta-analysis of clinical trials. Br J Clin Pharmacol. 2016 May 10.

Moroi SE. **Eyelash Preservation** During Chemotherapy & Topical Prostaglandin Therapy.Arch Intern Med.2010;170(14):1269-1270.

Moyer VA; on behalf of the U.S. Preventive Services Task Force (**USPSTF**). **Screening for Glaucoma**: U.S. Preventive Services Task Force Recommendation Statement. Ann Intern Med. 2013 Jul 9.

Muller ME, van der Velde N, Krulder JW, van der Cammen TJ. Syncope and falls due to timolol eye drops. BMJ. 2006 Apr 22;332(7547):960-1.

Musch DC, Tarver ME, et al. Development of an **18-Item Measure of Symptom Burden** in Patients With Glaucoma From the Collaborative Initial Glaucoma Treatment Study's Symptom and Health Problem Checklist. JAMA Ophthalmol. 2017 Nov2.

Newman-Casey PA, Robin AL, Blachley T, et al. The Most Common Barriers to **Glaucoma Medication Adherence**: A Cross-Sectional Survey. Ophthalmology. 2015 Apr 23.

NICE April 2009 -- The National Institute for Health and Clinical Excellence (NICE) and the National Clinical Guideline Centre will issue a guideline to improve the diagnosis and management of chronic open angle glaucoma (COAG) and ocular hypertension (OHT). People who have COAG, who are suspected of having COAG or who have OHT should be offered a suite of tests including assessments of the eye pressure, the thickness of the cornea, the drainage area in the eye and field of vision, and an assessment and image of the appearance of the optic nerve heads. People at risk of developing glaucoma should be monitored regularly using tests similar to those used to diagnose glaucoma. The frequency of these tests will depend on how high the risk is of developing glaucoma. Clarity on monitoring intervals for testing people who have glaucoma or are at risk of developing it, and recommendations on follow-up of patients who turn out not to have glaucoma after a period of careful monitoring. Treatment with prostaglandins or beta-blockers to reduce high eye pressure in people with glaucoma or those at risk of the condition. After previous treatment switches, earlier consideration of alternative treatments for worsening glaucoma, such as surgery or laser treatment to avoid disease

progression. The guidance will be available at http://www.nice.org.uk/CG85
NICE: National Institute for Health and Care Excellence. **Glaucoma**: diagnosis and management. November 2017. www.nice.org.uk/guidance/ng81/resources/glaucoma-diagnosis-and-management-pdf-1837689655237.
Nouri-Mahdavi K, Zarei R, Caprioli J. Influence of Visual Field **Testing Frequency** on Detection of Glaucoma Progression With Trend Analyses. Arch Ophthalmol. 2011 Aug 8.
Nwanaji-Enwerem JC, Wang W, Nwanaji-Enwerem O, et al. Association of long-term **ambient black carbon exposure** and **oxidative stress allelic variants** with intraocular pressure in older men [online Nov 8, 2018]. JAMA Ophthalmol.
Ohringer G, Burke T, Shaikh A. Unilateral headache and loss of vision. (**Acute primary angle closure glaucoma**) BMJ. 2014 Feb 4;348:g1188.
Orme M, Collins S, Dakin H, Kelly S, Loftus J. Mixed treatment comparison and meta-regression of the efficacy and safety of prostaglandin analogues and comparators for primary open-angle glaucoma and ocular hypertension. Curr Med Res Opin. 2010 Mar;26(3):511-28.
Parikh R, et al. Choroidal drainage in the management of acute angle closure after **topiramate** toxicity. J Glaucoma. 2007 Dec;16(8):691-3.
Pasquale LR, et al. Prospective study of type 2 **diabetes mellitus** and risk of primary open-angle glaucoma in women. Ophthalmology. 2006 Jul;113(7):1081-6. Epub 2006 Jun 6.
Pasquale LR, Willett WC, Rosner BA, Kang JH. **Anthropometric measures** and their relation to incident primary open-angle glaucoma. Ophthalmology. 2010 Aug;117(8):1521-9. Epub 2010 Apr 10.
Passo MS, Palmer EA, Van Buskirk EM. **Plasma timolol** in glaucoma patients. Ophthalmology. 1984 Nov;91(11):1361-3.
Patil AJ, Vajaranant TS, Edward DP. **Bimatoprost** - a review. Expert Opin Pharmacother. 2009 Nov;10(16):2759-68.
Pelletier AL, Thomas J, Shaw FR. **Vision loss** in older persons. Am Fam Physician. 2009 Jun 1;79(11):963-70.
Pharmacist's Letter. Moving On Up: **Altitude** and Your Cardiac Patients. Feb 2010.
Pharmacist's Letter. **Systemic Effects of Ophthalmic Beta-Blockers**. Mar, 20101.
Pinnock C, Yip JL, Khawaja AP, et al. **Topical Beta-Blockers and Cardiovascular Mortality**: Systematic Review and Meta-Analysis with Data from the EPIC-Norfolk Cohort Study. Ophthalmic Epidemiol. 2016 Oct;23(5):277-84.
Pohl H, Tarnutzer AA. **Acute Angle-Closure Glaucoma**. N Engl J Med. 2018 Mar 8;378(10):e14.
Prager AJ, Liebmann JM, Cioffi GA, et al. **Self-reported Function, Health Resource Use, and Total Health Care Costs** Among Medicare Beneficiaries With Glaucoma. JAMA Ophthalmol. 2016 Jan 7.
Pronin S, Brown L, et al. **Measurement of Intraocular Pressure by Patients** With Glaucoma. JAMA Ophthalmol. 2017 Aug 31.
Quigley Harry A. **Glaucoma**. www.thelancet.com Published online March 30, 2011 DOI:10.1016/S0140-6736(10)61423-7.
Rahman MQ, Montgomery DM, Lazaridou MN. Surveillance of Glaucoma Medical Therapy in a Glasgow Teaching Hospital: 26 Years Experience. Br J Ophthalmol. 2009 Jul 23. [Epub ahead of print] Bimatoprost had a higher rate of discontinuation due to adverse effects (25%) than travoprost (16.3%), or latanoprost (12.4%), but this was only statistically significant between latanoprost and bimatoprost (p=0.0038).
Rao RC, Ballard TN, Chen TC. **Iris heterochromia and unilateral eyelash hypertrichosis** (**bimatoprost**). JAMA. 2015 May 19;313(19):1967-8.
Rouse B, Cipriani A, Shi Q, et al. Network Meta-analysis for Clinical Practice Guidelines: A Case Study on **First-Line Medical Therapies for Primary Open-Angle Glaucoma**. Ann Intern Med. 2016 May 17;164(10):674-82.
Refuse P, Buys Y. Medical use of cannabis for glaucoma. Can J Ophthalmol 2019;54:7-8.
Sabel BA, Gudlin J. **Vision restoration training for glaucoma**: a randomized clinical trial. JAMA Ophthalmol. 2014 Apr 1;132(4):381-9.
Saldanha IJ, Lindsley K, Do DV, et al. Comparison of Clinical Trial and Systematic Review **Outcomes for the 4 Most Prevalent Eye Diseases**. JAMA Ophthalmol. 2017 Aug 3
Saldanha IJ, Petris R, Han G, et al. **Research Questions** and Outcomes Prioritized by Patients With Dry Eye. JAMA Ophthalmol. 2018 Aug 16.
Sayner R, Carpenter DM, Blalock SJ, et al. Accuracy of Patient-Reported **Adherence** to Glaucoma Medications on a Visual Analog Scale Compared With Electronic Monitors. Clin Ther. 2015 Jul 8.
Schwartz LM, et al. A Clear-eyed View of **Restasis and Chronic Dry Eye Disease**. JAMA Intern Med. 2018 Feb 1;178(2):181-182.
Sherwood MB, et al. Twice-daily 0.2% brimonidine-0.5% timolol fixed-combo therapy vs monotherapy with timolol or brimonidine in patients with glaucoma or ocular hypertension: a 12-month randomized trial. Arch Ophthalmol. 2006 Sep;124(9):1230-8.
Shifera AS, Leoncavallo A, Sherwood M. Probable Association of an Attack of Bilateral Acute Angle-Closure Glaucoma With **Duloxetine**. Ann Pharmacother. 2014 Apr 14;48(7):936-939.
Skaat A, Rosman MS, Chien JL, et al. Effect of **Pilocarpine** Hydrochloride on the Schlemm Canal in Healthy Eyes and Eyes With Open-Angle Glaucoma. JAMA Ophthalmol. 2016 Jun 23.
Sleath BL, Blalock SJ, Muir KW, et al. Determinants of Self-Reported Barriers to Glaucoma Medicine **Administration and Adherence**: A Multisite Study. Ann Pharmacother. 2014 Apr 1;48(7):856-862.
Smith S, Fagien S, Whitcup SM, et al. **Eyelash growth** in subjects treated with **bimatoprost**: a multicenter, randomized, double-masked, vehicle-controlled, parallel-group study. J Am Acad Dermatol. 2012 May;66(5):801-6.
Sonty S, Donthamsetti V, Vangipuram G, Ahmad A. Long-term IOP lowering with bimatoprost in open-angle glaucoma patients poorly responsive to latanoprost. J Ocul Pharmacol Ther. 2008 Oct;24(5):517-20. Significant additional long-term IOP lowering may be achieved by switching to **bimatoprost** in patients with open-angle glaucoma who are not at target IOP with latanoprost.
Sorkhabi R, Alipanahi R, Eftakhari-Milani A, Ghojazadeh L. The Influence of Topical **Diclofenac** Sodium on the Ocular Hypotensive Effect of Latanoprost in Glaucoma Patients. J Glaucoma. 2010 Jun 23.
Stein JD, Newman-Casey PA, Niziol LM, et al. Association between the use of glaucoma medications and **mortality**.

Arch Ophthalmol. 2010 Feb;128(2):235-40.
Stein JD, Talwar N, Laverne AM, Nan B, Lichter PR. Trends in Use of **Ancillary Glaucoma Tests** for Patients with Open-Angle Glaucoma from 2001 to 2009. Ophthalmology. 2012 Jan 3.
Stein JD, Newman-Casey PA, Talwar N, et al. The relationship between **statin use and open-angle glaucoma**. Ophthalmology. 2012 Oct;119(10):2074-81.
Stein JD, Shekhawat N, Talwar N, et al. Impact of the Introduction of **Generic Latanoprost** on Glaucoma Medication Adherence. Ophthalmology. 2015 Feb 2.
Tanna AP, Rademaker AW, Stewart WC, Feldman RM. Meta-analysis of the Efficacy and Safety of {alpha}2-**Adrenergic Agonists**, **{beta}-Adrenergic** Antagonists, & **Topical Carbonic Anhydrase Inhibitors With Prostaglandin Analogs**. Arch Ophthalmol. 2010 Jul;128(7):825-33. All 3 classes are similarly effective in lowering mean diurnal IOP when used in combination with PGAs. The AA class is statistically significantly less effective in reducing IOP at trough compared with BBs and TCAIs. The types of adverse events that were identified varied among the different classes of adjunctive therapies.
Tisdale AK, Agrón E, Sunshine SB, et al. Association of **Dietary and Supplementary Calcium Intake** With Age-Related Macular Degeneration: Age-Related Eye Disease Study Report 39. JAMA Ophthalmol. 2019 Mar 21.
Trocme S, Hwang LJ, Bean GW, et al. The role of **benzalkonium chloride** in the occurrence of punctate keratitis: a meta-analysis of randomized, controlled clinical trials. Ann Pharmacother. 2010 Dec;44(12):1914-21.
Treatment Guidelines: The Medical Letter. Drugs for Some Common **Eye Disorders**. January 2007;5(53):1-3 ⇒ **Oct 2012**.
U.S. Preventive Services Task Force (**USPSTF**). Screening for glaucoma: recommendation statement. Rockville (MD): Agency for Healthcare Research and Quality (AHRQ); 2005 Mar. 9. http://www.ahrq.gov/clinic/3rduspstf/glaucoma/glaucrs.pdf
U.S. Preventive Services Task Force (**USPSTF**). Screening for glaucoma: recommendation statement. Rockville (MD): Agency for Healthcare Research and Quality (AHRQ); 2005 Mar. 9 http://www.ahrq.gov/clinic/uspstf/uspsglau.htm
Uusitalo H, Pillunat LE, Ropo A; Phase III Study Investigators. Efficacy and safety of **tafluprost** 0.0015% **versus latanoprost** 0.005% eye drops in open-angle glaucoma and ocular hypertension: 24-month results of a randomized, double-masked phase III study. Acta Ophthalmol. 2010 Feb;88(1):12-9.
van Issum C, Mavrakanas N, Schutz JS, Shaarawy T. **Topiramate-induced** acute bilateral angle closure and myopia: pathophysiology and treatment controversies. Eur J Ophthalmol. 2010 Nov 4. pii: 6E44A60D-B624-4EDA-9C14-7205923AE923.
Wang YE, Tseng VL, Yu F, et al. Association of **Dietary Fatty Acid Intake** With Glaucoma in the United States. JAMA Ophthalmol. 2017 Dec 21
Weinreb RN, Aung T, Medeiros FA. The **pathophysiology and treatment of glaucoma**: a review. JAMA. 2014 May 14;311(18):1901-11.
Wiggs JL, Yaspan BL, Hauser MA, et al. Common variants at **9p21 and 8q22** are associated with increased susceptibility to optic nerve degeneration in glaucoma. PLoS Genet. 2012 Apr;8(4):e1002654.
Wright TM, Freedman SF. Exposure to topical apraclonidine in children with glaucoma. J Glaucoma. 2009 Jun-Jul;18(5):395-8. In contrast to brimonidine, topical apraclonidine 0.5% can safely be administered for short-term treatment of most infants and children undergoing angle surgery for glaucoma, rarely producing systemic side effects.
Wu CM, Wu AM, Tseng VL, et al. Frequency of a diagnosis of glaucoma in individuals who **consume coffee, tea and/or soft drinks**. Br J Ophthalmol. 2017 Dec 14.
Yildirim N, Sahin A, Gultekin S. The effect of **latanoprost, bimatoprost, and travoprost** on circadian variation of intraocular pressure in patients with open-angle glaucoma. J Glaucoma. 2008 Jan-Feb;17(1):36-9. Latanoprost, bimatoprost, and travoprost were comparable in their ability to reduce IOP in open-angle glaucoma patients. On the basis of our data, the IOP reduction of these drugs is indistinguishable within statistical parameters.
Yonekawa Y, Vanderveen DK, Shah AS. **Congenital Glaucoma**. J Pediatr. 2013 Mar 13.
Zelefsky JR, Fine HF, Rubinstein VJ, Hsu IS, Finger PT. Escitalopram-induced uveal effusions and bilateral angle closure **glaucoma**. Am J Ophthalmol. 2006 Jun;141(6):1144-7.
Zhao PY, Rahmathullah R, Stagg BC, et al. A worldwide **price comparison** of glaucoma medications, laser trabeculoplasty, and trabeculectomy surgery [online Aug 30, 2018]. JAMA Ophthalmol.

Other drugs for Glaucoma:

- Osmotic Agents (used for acute rises in IOP)
    - Glycerol – onset 10 min; max effect in 1-2 hours
    - Mannitol – Onset 10-30min; max effect in 1 hour
- Cannabis, lower IOP by various modes of administration including inhalation, oral, intravenous, sublingual and topical
    - Topical
        - Poor ocular penetration due to high lipophilicity and low aqueous solubility of the cannabinoid extracts
        - Some studies have failed to find a hypotensive effect
        - Local irritation & corneal injury
    - Oral

        - Variable absorption, maximum hypotensive effect occurs between 60-90 min, duration of action between 3-4 hours
    - Smoked THC
        - Noted to lower intraocular pressure in 1971
        - AE: psychotropic effects (euphoria, dysphoria, decreased short-term memory, cognitive impairment, time distortion, decreased coordination, sleepiness), tachycardia, palpitations, systemic hypotension, conjunctival hyperemia, emphysema, possible lung cancer, addiction/tolerance, increased risk of motor vehicle accidents
    - Bottomline; Canadian Ophthalmological Society does not support medical use of cannabis for the treatment of glaucoma due to the short duration of action, the incidence of undesirable psychotropic and other systemic effects, and the absence of scientific evidenced showing a beneficial effect on the course of the disease. This is in contrast to other more effective and less harmful medical, laser, and surgical modalities for the treatment of glaucoma.

Intranasal Corticosteroids: Online Extras

Clinical use of selected allergy products

	rhinorrhea (runny nose)	sneezing	nasal congestion	sinusitis (acute or chronic)	nasal polyps	allergic conjunctivitis	urticaria (hives)
Intranasal steroids e.g. **NASONEX**, **OMNARIS**, **FLONASE**, etc.	✓	✓	✓	✓	✓	**sometimes** helps with ocular symptoms of allergic rhinitis	
Oral antihistamines e.g. **REACTINE**, **CLARITIN**, **ALLEGRA**, etc.	✓	✓	desloratadine or cetirizine may help			✓	✓ (and OK to use very high dose fexofenadine in unresponsive chronic urticaria, e.g. 240mg BID)
Ophthalmic antihistamines e.g. **PATANOL**, etc.						✓ (equally effective vs oral antihistamines)	
Intranasal antihistamines e.g. **LIVOSTIN** (Canada) **ASTELIN** (USA)	✓	✓	✓	**DYMISTA** (fluticasone/azelastine) combines an intranasal steroid with an intranasal antihistamine.			
Oral decongestants e.g. **SUDAFED**, etc. **Intranasal decongestants** e.g. **OTRIVIN**, etc.			✓ **short term use only!**	occasional benefit in acute sinusitis - **short term use only!**			
Intranasal antimuscarinics e.g. **ATROVENT nasal spray**	✓						
Leukotriene receptor antagonists e.g. **SINGULAIR**	✓ (relieves symptoms of allergic rhinitis, but inferior to intranasal steroids)						
Intranasal cromolyn e.g. **RHINARIS-CS**	✓ (relieves symptoms of allergic rhinitis, but inferior to intranasal steroids)						
Ophthalmic mast-cell stabilizers e.g. **OPTICROM**, **ALOMIDE**, **ALOCRIL**, etc.						✓ (requires ~10 days before onset)	
Sinus steroid implant e.g. **SINUVA**					✓		
Saline irrigation e.g. **NETI-POT**				✓ (small benefit)			

The Medical Letter on drugs and therapeutics. Medical Letter, Inc. May 8, 2017. Issue 1520. Drugs for Allergic Disorders.
Head K, Snidvongs K, Glew S, et al. **Saline irrigation for allergic rhinitis**. Cochrane Database of Systematic Reviews 2018, Issue 6. Art. No.: CD012597.

References – Intranasal Nasal Corticosteroids Comparative Chart (INCS) - **www.RxFiles.ca**

[1] Bousquet J. Van Cauwenberge P. Allergic Rhinitis and its Impact on Asthma (**ARIA**) In collaboration with the World Health Organization. Allergy 2002 Sept;57:841-855. http://www.whiar.com (access verified Dec 9/03)
[2] Salib RJ, Howarth PH. Safety and tolerability profiles of intranasal antihistamines and intranasal corticosteroids in the treatment of allergic rhinitis. **Drug Saf. 2003**;26(12):863-93.
[3] Micromedex 2018
[4] Yanez A, Rodrigo GJ. Intranasal corticosteroids versus topical H1 receptor antagonists for the treatment of allergic rhinitis: a systematic review with **meta-analysis**. Ann Allergy Asthma Immunol. 2002 Nov;89(5):479-84.
[5] Trangsrud AJ, Whitaker AL, Small RE. Intranasal corticosteroids for allergic rhinitis. Pharmacotherapy. 2002 Nov;22(11):1458-67.
[6] Nielsen LP, Mygind N, Dahl R. Intranasal corticosteroids for allergic rhinitis: superior relief? Drugs. 2001;61(11):1563-79.
[7] Weiner JM, Abramson MJ, Puy RM. Intranasal corticosteroids versus oral H1 receptor antagonists in allergic rhinitis: systematic review of randomised controlled trials. BMJ. 1998 Dec 12;317(7173):1624-9.
[8] Kaszuba SM, Baroody FM, deTineo M, et al.. Superiority of an intranasal corticosteroid compared with an oral antihistamine in the **as-needed** treatment of seasonal allergic rhinitis. Arch Intern Med. 2001 Nov 26;161(21):2581-7.
[9] Bachert C, El-Akkad T. Patient preferences and sensory comparisons of three intranasal corticosteroids for the treatment of allergic rhinitis. Ann Allergy Asthma Immunol. 2002 Sep;89(3):292-7.
[10] Shah SR, Miller C, et al. Two multicenter, randomized, single-blind, single-dose, crossover studies of specific sensory attributes of budesonide aqueous & fluticasone nasal spray. Clin Ther. 2003 Aug;25(8):2198-214.
[11] Lumry W, Hampel F, et al. A comparison of od triamcinolone acet. aqueous & bid beclomethasone diprop. aqueous nasal sprays in the treatment of seasonal allergic rhinitis. Allergy Asthma Proc. 2003 May-Jun;24(3):203-10.
[12] Sheth KK. Patient preferences and sensory comparisons of three intranasal corticosteroids for the treatment of allergic rhinitis. Ann Allergy Asthma Immunol. 2003 May;90(5):576; author reply 577.
[13] Waddell A.N.; Patel S.K.; Toma A.G.; Maw A.R. Intranasal steroid sprays in the treatment of rhinitis: is one better than another? Journal of Laryngology & Otology, 1 November 2003, vol. 117, no. 11, pp. 843-845(3)
[14] Therapeutic Choices 4rd edition, Canadian Pharmaceutical Association 2003
[15] **Treatment Guidelines**: **Drugs for Allergic Disorders**. The Medical Letter: Feb 2010. **May 2013.**
Wallace DV, Dykewicz MS, Bernstein DI, et al. Joint Task Force on Practice; American Academy of Allergy; Asthma & Immunology; American College of Allergy; Asthma and Immunology; Joint Council of Allergy, Asthma and Immunology. **The diagnosis and management of rhinitis: an updated practice parameter. J Allergy Clin Immunol. 2008** Aug;122(2 Suppl):S1-84.
Brozek JL, Bousquet J, Baena-Cagnani CE, et al. Global Allergy and Asthma European Network; Grading of Recommendations Assessment, Development and Evaluation Working Group. **Allergic Rhinitis and its Impact on Asthma** (**ARIA**) **guidelines**: **2010** revision. J Allergy Clin Immunol. 2010 Sep;126(3):466-76.
Seidman MD, Gurgel RK, Lin SY, et al**. Clinical practice guideline: allergic rhinitis executive summary. Otolaryngol Head Neck Surg. 2015** Feb;152(2):197-206.
Rosenfeld RM, Piccirillo JF, Chandrasekhar SS, et al. Clinical practice guideline (**AAO-HNSF**) update): **adult sinusitis executive summary**. Otolaryngol Head Neck Surg. 2015 Apr;152(4):598-609.
Wallace DV, Dykewicz MS, Oppenheimer J, et al. Pharmacologic Treatment of Seasonal Allergic Rhinitis: Synopsis of Guidance From the 2017 Joint Task Force on Practice Parameters. (**AAAAI**) Ann Intern Med. 2017 Nov 28.

[16] Compendium of Pharmaceuticals & Specialties –The Canadian Drug Reference for Health Professionals CPS 2016
[17] Benninger MS, Ahmad N, Marple BF. The safety of intranasal steroids. Otolaryngol Head Neck Surg. **2003 Dec**;129(6):739-750.
[18] Lieberman P. Best Practice Report: Rhinitis. May 2001 (Update March 2002). Available at: http://merck.praxis.md/index.asp?page=bpm_brief&article_id=BPM01AL07 (access verified Dec 9/02).
[19] Drugs in Pregnancy & Lactation, 9th Ed. Briggs GE,et al. Wilkins;Baltimore, MD.2011.
[20] Skoner DP, Rachelefsky GS, Meltzer EO, et al. Detection of **growth** suppression in children during treatment with intranasal beclomethasone dipropionate. Pediatrics. 2000 Feb;105(2):E23.
Skoner DP, Berger WE, Gawchik SM, et al. Intranasal Triamcinolone and Growth Velocity. Pediatrics. 2015 Jan 26.
[21] Wilson AM, Sims EJ, McFarlane LC, Lipworth BJ. Effects of intranasal corticosteroids on adrenal, bone, and blood markers of systemic activity in allergic rhinitis. J Allergy Clin Immunol. 1998 Oct;102(4 Pt 1):598-604.
[22] Pipkorn U, Pukander J, Suonpaa J, Makinen J, Lindqvist N. Long-term safety of budesonide nasal aerosol: a 5.5-year follow-up study. Clin Allergy. 1988 May;18(3):253-9.
[23] Lindqvist N, Balle VH, Karma P, Karja J, Lindstrom D, Makinen J, Pukander J, et al.Long-term safety and efficacy of budesonide nasal aerosol in perennial rhinitis. A 12-month multicentre study. Allergy. 1986 Apr;41(3):179-86.
[24] Bacharier LB, Raissy HH, Wilson L, et al. Long-term (3 yr) effect of **budesonide** on hypothalamic-pituitary-adrenal axis function in children with mild to moderate asthma. Pediatrics. 2004 Jun;113(6):1693-9.
[25] Wihl JA, Andersson KE, Johansson SA. Systemic effects of two nasally administered glucocorticosteroids. Allergy. 1997 Jun;52(6):620-6.
[26] Moller C, Ahlstrom H, Henricson KA, et al. Safety of nasal budesonide in the long-term (1-2 year -**growth**) treatment of children with perennial rhinitis. Clin Exp Allergy. 2003 Jun;33(6):816-22.(Murphy K, et al. Growth velocity in children with perennial allergic rhinitis treated with budesonide aqueous nasal spray. Ann Allergy Asthma Immunol. 2006 May;96(5):723-30. n=229 age 4-8yrs 1yr trial)
[27] Long-term effects of budesonide or nedocromil in children with asthma. The Childhood Asthma Management Program Research Group. N Engl J Med. 2000 Oct 12;343(15):1054-63.
[28] Agertoft L, Pedersen S. Effect of long-term treatment with inhaled budesonide on adult height in children with asthma. N Engl J Med. 2000 Oct 12;343(15):1064-9.
[29] Thorsson L, Borga O, et al. Systemic availability of budesonide after nasal administration of three different formulations: pressurized aerosol, aqueous pump spray, and powder. Br J Clin Pharmacol. 1999 Jun;47(6):619-24.
[30] Bolland MJ, Bagg W, Thomas MG, Lucas JA, Ticehurst R, Black PN. Cushing's syndrome due to interaction between inhaled corticosteroids and itraconazole. Ann Pharmacother. 2004 Jan;38(1):46-9.
[31] Wilson AM, et al.. Effects of repeated once daily dosing of three intranasal corticosteroids on basal & dynamic measures of hypothalamic-pituitary-adrenal-axis activity. J Allergy Clin Immunol. 1998 Apr;101(4 Pt 1):470-4.
[32] Allen DB, Meltzer EO, et al. No growth suppression in children treated with the maximum recommended dose of fluticasone propionate aqueous nasal spray for one year. Allergy Asthma Proc. 2002 Nov-Dec;23(6):407-13.
[33] Allen DB, Bronsky EA, LaForce CF, et al. Growth in asthmatic children treated with fluticasone propionate. Fluticasone Propionate Asthma Study Group. J Pediatr. 1998 Mar;132(3 Pt 1):472-7.
[34] Health Canada Endorsed Important Safety Information on FLUTICASONE PROPIONATE (FLONASE/ FLOVENT/ ADVAIR) and RITONAVIR (NORVIR/KALETRA) Jan 22, 2004
[35] Schenkel EJ, Skoner DP, Bronsky EA, et al. Absence of **growth** retardation in children with perennial allergic rhinitis after one year of treatment with mometasone furoate aqueous nasal spray. Pediatrics. 2000 Feb;105(2):E22.
[36] Nsouli Talal M. Nasal Steroids: Contralateral Hand-Nostril Technique Curbs Epistaxis American College of Allergy, Asthma, and Immunology meeting Nov 2003.
http://www.medscape.com/viewarticle/464241
[37] Howarth PH. A comparison of the anti-inflammatory properties of intranasal corticosteroids and antihistamines in allergic rhinitis. Allergy. 2000;55 Suppl 62:6-11.
[41] Vaidyanathan S, Barnes M, Williamson P, et al. Treatment of chronic rhinosinusitis with nasal polyposis with **oral steroids (prednisolone 25mg po od x 2wks) followed by topical steroids**: a randomized trial. Ann Intern Med. 2011 Mar 1;154(5):293-302.
[42] Head K, Snidvongs K, Glew S, et al. **Saline irrigation for allergic rhinitis**. Cochrane Database of Systematic Reviews 2018, Issue 6. Art. No.: CD012597. Saline irrigation may reduce patient-reported disease severity compared with no saline irrigation at up to three months in both adults and children with allergic rhinitis, with no reported adverse effects. No data were available for any outcomes beyond three months. The overall quality of evidence was low or very low. The included studies were generally small and used a range of different outcome measures to report disease severity scores, with unclear validation. This review did not include direct comparisons of saline types (e.g. different volume, tonicity).
43 Chong LY, Head K, Hopkins C, et al. Different types of intranasal steroids for chronic rhinosinusitis. Cochrane Database Syst Rev. 2016 Apr 26;4:CD011993. doi: 10.1002/14651858.CD011993.pub2. (Systematic review)

Additional information:

Ah-See KL, Mackenzie J, Practitioner G, Ah-See KW. Management of **chronic rhinosinusitis**. BMJ. 2012 Oct 30;345:e7054.
Al Sayyad JJ, Fedorowicz Z, Alhashimi D, Jamal A. Topical **nasal steroids** for intermittent and persistent allergic rhinitis in **children**. Cochrane Database Syst Rev. 2007 Jan 24;(1):CD003163. The three included trials provided some weak and unreliable evidence for the effectiveness of Beconase(R) and flunisolide used topically intranasally for the treatment of intermittent and persistent allergic rhinitis in children
Alt JA, DeConde AS, et al. **Quality of Life** in Patients With Chronic Rhinosinusitis and Sleep Dysfunction Undergoing **Endoscopic Sinus Surgery**: A Pilot Investigation of Comorbid Obstructive Sleep Apnea. JAMA Otolaryngol Head Neck Surg. 2015 Sep 10:1-9.
An update on the management of **hay fever in adults**. Drug Ther Bull. 2013 Mar;51(3):30-3.
Azelastine and fluticasone nasal spray: any advantage? Drug Ther Bull. 2014 Feb;52(2):21-4.
Bachert C, Mannent L, Naclerio RM, et al. Effect of Subcutaneous Dupilumab on Nasal Polyp Burden in Patients With Chronic Sinusitis and Nasal Polyposis: A Randomized Clinical Trial. JAMA. 2016 Feb 2;315(5):469-479. Adding subcutaneous dupilumab to the treatment regimen of adults with symptomatic chronic sinusitis and nasal polyposis despite at least 2 months of nasal steroid therapy alone significantly improves nasal symptom scores and reduces polyp size. (LOE = 1b)
Bachert C, Sousa AR, Lund VJ, et al. Reduced need for surgery in severe nasal polyposis with **mepolizumab**: Randomized trial. J Allergy Clin Immunol. 2017 Oct;140(4):1024-1031.e14.
Baroody FM, Brown D, Gavanescu L, et al. **Oxymetazoline adds to the effectiveness of fluticasone** furoate in the treatment of perennial allergic rhinitis. J Allergy Clin Immunol. 2011 Apr;127(4):927-34.
Barr JG, Al-Reefy H, Fox AT, et al. **Allergic rhinitis in children**. BMJ. 2014 Jul 1;349:g4153.
Bastianelli M, Kilty S. Chronic nasal congestion and hyposmia in a 22-year-old woman. (**chronic rhinosinusitis**) CMAJ. 2017 May 8;189(18):E667-E668.
Baysoy G, Arslan S, Karabay O, Uyan AP. **Nasal carriage of Staphylococcus aureus** in children with allergic rhinitis and the effect of intranasal fluticasone propionate treatment on carriage status. Int J Pediatr Otorhinolaryngol. 2006 Nov 8; [Epub ahead of print]
Beachler DC, Engels EA. **Chronic Sinusitis and Risk of Head and Neck Cancer** in the US Elderly Population. JAMA Otolaryngol Head Neck Surg. 2016 Sep 8.
Benninger M. **Diagnosis and management of nasal congestion**: the role of intranasal corticosteroids. Postgrad Med. 2009 Jan;121(1):122-31.
Bérard A, Sheehy O, Kurzinger ML, Juhaeri J. **Intranasal triamcinolone** use during **pregnancy** and the risk of adverse pregnancy outcomes. J Allergy Clin Immunol. 2016 Jul;138(1):97-104.e7.
Bergmark RW, Pynnonen M. **Diagnosis and First-Line Treatment of Chronic Sinusitis**. JAMA. 2017 Dec 19;318(23):2344-2345
Bird J, Biggs T, Thomas M, Salib R. **Adult acute rhinosinusitis**. BMJ. 2013 May 10;346:f2687.
Blaiss MS; Food and Drug Administration (U.S.); ACAAI-ACOG(American College of Allergy, Asthma, and Immunology and American College of Obstetricians and Gynecologists.). Management of rhinitis and asthma in **pregnancy**. Ann Allergy Asthma Immunol. 2003 Jun;90(6 Suppl 3):16-22.
Blaiss MS, Hammerby E, Robinson S, et al. The **burden of allergic rhinitis and allergic rhinoconjunctivitis on adolescents**: A literature review. Ann Allergy Asthma Immunol. 2018 Apr 4.
Brinkhaus B, Ortiz M, Witt CM, Roll et al. **Acupuncture** in patients with seasonal allergic rhinitis: a randomized trial. Ann Intern Med. 2013 Feb 19;158(4):225-34.
Brozek JL, Bousquet J, Baena-Cagnani CE, et al. Global Allergy and Asthma European Network; Grading of Recommendations Assessment, Development and Evaluation Working Group.
Allergic Rhinitis and its Impact on Asthma (**ARIA**) **guidelines**: **2010** revision. J Allergy Clin Immunol. 2010 Sep;126(3):466-76.
Campbell AP, Phillips KM, Hoehle LP, et al. **Depression symptoms** and lost productivity in chronic rhinosinusitis. Ann Allergy Asthma Immunol. 2017 Mar;118(3):286-289.
Carter A, Dattani N, Hannan SA. **Chronic rhinosinusitis**. BMJ. 2019 Feb 6;364:l131.
Castillo M, Scott NW, Mustafa MZ, et al. **Topical antihistamines and mast cell stabilisers for treating seasonal and perennial allergic conjunctivitis**. Cochrane Database Syst Rev. 2015 Jun 1;6:CD009566. It seems that all reported topical antihistamines and mast cell stabilisers reduce symptoms and signs of seasonal allergic conjunctivitis when compared with placebo in the short term. However, there is no long-term data on their efficacy. Direct comparisons of different antihistamines and mast cell stabilisers need to be interpreted with caution. Overall, topical antihistamines and mast cell stabilisers appear to be safe and well tolerated. We observed a large variability in outcomes reported. Poor quality of reporting challenged the synthesis of evidence.
Chadha NK, Chadha R. 10-minute consultation: sinusitis. BMJ. 2007 Jun 2;334(7604):1165.
Chong LY, Head K, Hopkins C, et al. **Different types of intranasal steroids for chronic rhinosinusitis**. Cochrane Database Syst Rev. 2016 Apr 26;4:CD011993. We found insufficient evidence to suggest that one type of intranasal steroid is more effective than another in patients with chronic rhinosinusitis, nor that the effectiveness of a spray differs from an aerosol. We identified no studies that compared drops with spray. It is unclear if higher doses result in better symptom improvements (low quality evidence), but there was moderate quality evidence of an increased risk of epistaxis as an adverse effect of treatment when higher doses were used. This included all levels of severity of epistaxis and it is likely that the proportion of events that required patients to discontinue usage is low due to the low numbers of withdrawals attributed to it. If epistaxis is limited to streaks of blood in the mucus it may be tolerated by the patient and it may be safe to continue treatment. However, it may be a factor that affects

compliance. There is insufficient evidence to suggest that the different types of corticosteroid molecule or spray versus aerosol have different effects. Lower doses have similar effectiveness but fewer side effects. Clearly more research in this area is needed, with specific attention given to trial design, disease-specific health-related quality of life outcomes and evaluation of longer-term outcomes and adverse effects.

Chong LY, Head K, Hopkins C, et al. **Intranasal steroids versus placebo or no intervention for chronic rhinosinusitis**. Cochrane Database Syst Rev. 2016 Apr 26;4:CD011996. Most of the evidence available was from studies in patients with chronic rhinosinusitis with nasal polyps. There is little information about quality of life (very low quality evidence). For disease severity, there seems to be improvement for all symptoms (low quality evidence), a moderate-sized benefit for nasal blockage and a small benefit for rhinorrhoea (moderate quality evidence). The risk of epistaxis is increased (high quality evidence), but these data included all levels of severity; small streaks of blood may not be a major concern for patients. It is unclear whether there is a difference in the risk of local irritation (low quality evidence).

Croft AM, Bager P, Kumar S. **Helminth therapy (worms) for allergic rhinitis**. Cochrane Database of Systematic Reviews 2012, Issue 4. Art. No.: CD009238. There is currently insufficient evidence on the efficacy, tolerability and likely costs of helminth therapy to support its use in the routine management of allergic rhinitis.

Creticos PS, et al. Immune Tolerance Network Group. Immunotherapy with a ragweed-toll-like receptor 9 agonist **vaccine** for allergic rhinitis. N Engl J Med. 2006 Oct 5;355(14):1445-55.

Demoly P, Piette V, Daures JP. Treatment of allergic rhinitis during **pregnancy**. Drugs. 2003;63(17):1813-20.

de Groot H, Brand PL, Fokkens WF, Berger MY. **Allergic rhinoconjunctivitis in children**. BMJ. 2007 Nov 10;335(7627):985-8.

de Vries et al. Reported **adverse drug reactions during the use of inhaled steroids** in children with asthma in the Netherlands. Eur J Clin Pharmacol. 2006 May;62(5):343-6. Epub 2006 Apr 1. Alteration of behaviour was the most frequently reported sADR. There are more indications that alterations of behaviour could be a real sADR of ICS. Non-fatal adrenal insufficiency was the only reported possible life threatening sADR. The association of hypertrichosis and teeth abnormalities after ICS in children has not been reported in the literature before.

Desrosiers M, Evans GE, Keith PK, et al. **Canadian clinical practice guidelines for acute and chronic rhinosinusitis**. Allergy Asthma Clin Immunol 2011;7:2. www.aacijournal.com/content/pdf/1710-1492-7-2.pdf

Dixon AE, Castro M, Cohen RI, et al. Efficacy of nasal **mometasone** for the treatment of **chronic sinonasal disease** in patients with inadequately controlled asthma. J Allergy Clin Immunol. 2014 Aug 28. pii: S0091-6749(14)00957-9.

Dixon AE et al. Efficacy of nasal **mometasone** for the treatment of **chronic sinonasal** disease in patients with inadequately controlled **asthma**. J Allergy Clin Immunol 2015 Mar; 135:701.

Durham SR, Creticos PS, Nelson HS, et al. Treatment effect of **sublingual immunotherapy tablets** and pharmacotherapies for seasonal and perennial allergic rhinitis: Pooled analyses. J Allergy Clin Immunol. 2016 Jul 15.

Eren E, Aktaş A, Arslanoğlu S, et al. Diagnosis of allergic rhinitis: inter-rater reliability and predictive value of **nasal endoscopic examination**: a prospective observational study. Clin Otolaryngol. 2013 Aug 28.

FDA May/18: Fluticasone Propionate Nasal Spray by Apotex Corp: **Recall - Due to Potential for Small Glass Particles**.

Frew AJ. **Sublingual immunotherapy**. N Engl J Med. 2008 May 22;358(21):2259-64. (Grass pollen sl tabs -Grazax is available in Europe)

Gevorgyan A, Segboer C, Gorissen R, et al. **Capsaicin for non-allergic rhinitis**. Cochrane Database Syst Rev. 2015 Jul 14;7:CD010591. Capsaicin may be an option in the treatment of idiopathic non-allergic rhinitis. It is given in the form of brief treatments, usually during the same day. It appears to have beneficial effects on overall nasal symptoms up to 36 weeks after treatment, based on a few, small studies (low-quality evidence). Well-conducted randomised controlled trials are required to further advance our understanding of the effectiveness of capsaicin in non-allergic rhinitis, especially in patients with non-allergic rhinitis of different types and severity, and using different methods of capsaicin application.

Gilbert C, Mazzotta P, Loebstein R, Koren G. Fetal safety of drugs used in the treatment of allergic rhinitis: a critical review. Drug Saf. 2005;28(8):707-19.

Gluth MB, McDonald DR, Weaver AL, et al. Management of **eustachian tube dysfunction** with nasal steroid spray: a prospective, randomized, placebo-controlled trial. Arch Otolaryngol Head Neck Surg. 2011 May;137(5):449-55. (not support steroid spray use)

Greiner AN, Hellings PW, Rotiroti G, Scadding GK. **Allergic rhinitis**. Lancet. 2011 Jul 21.

Hayward G, Heneghan C, Perera, R, Thompson M. Intranasal corticosteroids in management of **acute sinusitis**: a systematic review and meta-analysis. Ann Fam Med. 2012;10(3):241-249. (small therapeutic benefit in acute sinusitis, which may be greater with high doses and with courses of 21 days' duration

Head K, Chong LY, Piromchai P, et al. **Systemic and topical antibiotics for chronic rhinosinusitis**. Cochrane Database Syst Rev. 2016 Apr 26;4:CD011994. We found very little evidence that systemic antibiotics are effective in patients with chronic rhinosinusitis. We did find moderate quality evidence of a modest improvement in disease-specific quality of life in adults with chronic rhinosinusitis without polyps receiving three months of a macrolide antibiotic. The size of improvement was moderate (0.5 points on a five-point scale) and only seen at the end of the three-month treatment; by three months later no difference was found.Despite a general understanding that antibiotics can be associated with adverse effects, including gastrointestinal disturbances, the results in this review were very uncertain because the studies were small and few events were reported.No RCTs of topical antibiotics met the inclusion criteria.More research in this area, particularly evaluating longer-term outcomes and adverse effects, is required.

Head K, Chong LY, Hopkins C, et al. **Short-course oral steroids as an adjunct therapy for chronic rhinosinusitis**. Cochrane Database Syst Rev. 2016 Apr 26;4:CD011992. There might be an improvement in symptom severity, polyps size and condition of the sinuses when assessed using CT scans in patients taking oral corticosteroids when these are used as an adjunct therapy to antibiotics or intranasal corticosteroids, but the quality of the evidence supporting this is low orvery low (we are uncertain about the effect estimate; the true effect may be substantially different from the estimate of the effect). It is unclear whether the benefits of oral corticosteroids as an adjunct therapy are sustained beyond the short follow-up period reported (up to 30 days), as no longer-term data were available.There were no data in this review about the adverse effects associated with short courses of oral corticosteroids as an adjunct therapy.More research in this area, particularly research evaluating longer-term outcomes and adverse effects, is required.

Hissaria P, et al. Short course of systemic corticosteroids in **sinonasal polyposis**: a double-blind, randomized, placebo-controlled trial with evaluation of outcome measures. J Allergy Clin Immunol. 2006 Jul;118(1):128-33. Epub 2006 May 19. (InfoPOEMs: Fourteen days of oral prednisolone (50 mg daily) significantly improves nasal function scores and reduces polyp size. The duration of this benefit, however, is not clear. (LOE = 1b))

Hopkins C. Chronic **Rhinosinusitis with Nasal Polyps**. N Engl J Med. 2019 Jul 4;381(1):55-63.

Jacobsen L, Niggemann B, Dreborg S, et al. (The PAT investigator group). **Specific immunotherapy** has **long-term preventive effect of seasonal and perennial asthma: 10-year follow-up on the PAT** study. Allergy. 2007 Aug;62(8):943-8.

Jankowski R, Klossek JM, Attali V, Coste A, Serrano E. Long-term study of fluticasone propionate aqueous nasal spray in acute and maintenance therapy of **nasal polyposis**. Allergy. 2009 Jun;64(6):944-50. Epub 2009 Mar 3. The study demonstrated the efficacy of FPANS 200 microg bd in acute treatment and FPANS 200 microg od as a sufficient dose to maintain a long-term efficacy in the treatment for NP.

Jorissen M, Bachert C. Effect of **corticosteroids** on wound healing after endoscopic sinus surgery. Rhinology. 2009 Sep;47(3):280-6. These results suggest that treatment with MFNS following sinus surgery may improve wound healing, particularly in subjects with **nasal polyps**.

Kassel JC, King D, Spurling GK. **Saline nasal irrigation** for acute upper respiratory tract infections. Cochrane Database Syst Rev. 2010 Mar 17;(3):CD006821.

Kheirandish-Gozal L, Gozal D. Intranasal budesonide treatment for children with mild obstructive **sleep apnea syndrome**. Pediatrics. 2008 Jul;122(1):e149-55. A 6-week treatment with intranasal budesonide effectively reduced the severity of mild obstructive sleep apnea syndrome and the magnitude of the underlying adenoidal hypertrophy, and this effect persisted for at least 8 weeks after cessation of therapy. These findings justify the use of topical steroids as the initial therapeutic option in otherwise healthy children with mild obstructive sleep apnea.

Kim MK, Lee SY, Park HS, et al. A Randomized, Multicenter, Double-blind, Phase III Study to Evaluate the Efficacy on Allergic Rhinitis and Safety of a **Combination Therapy of Montelukast and Levocetirizine in Patients With Asthma and Allergic Rhinitis**. Clin Ther. 2018 Jun 24.

Kim JM, Lin SY, Suarez-Cuervo C, et al. **Allergen-Specific Immunotherapy** for Pediatric Asthma and Rhinoconjunctivitis: A Systematic Review. Pediatrics. 2013 May 6.

King D. What role for **saline nasal irrigation**? Drug Ther Bull. 2019 Apr;57(4):56-59.

Koltsidopoulos P, Papageorgiou E, Skoulakis C. Acute **sinusitis complicated with Pott puffy tumour**. CMAJ. 2019 Feb 11;191(6):E165.

Lange B, Lukat KF, Rettig K, et al. Efficacy, cost-effectiveness, and tolerability of **mometasone** furoate, levocabastine, and disodium cromoglycate nasal sprays in the treatment of seasonal allergic rhinitis. Ann Allergy Asthma Immunol. 2005 Sep;95(3):272-82.

Leger D, Annesi-Maesano I, Carat F, Rugina M, Chanal I, Pribil C, El Hasnaoui A, Bousquet J. Allergic rhinitis and its consequences on **quality of sleep**: An unexplored area. Arch Intern Med. 2006 Sep 18;166(16):1744-8.

Leopold DA, Elkayam D, Messina JC, et al. NAVIGATE II: randomized, double-blind trial of the **exhalation delivery system with fluticasone (EDS-FLU) for nasal polyposis**. J Allergy Clin Immunol. 2018 Jun 18.

Lin SY, Erekosima N, Kim JM, et al. **Sublingual immunotherapy** for the treatment of allergic rhinoconjunctivitis and asthma: a systematic review. JAMA. 2013; 309(12):1278-1288.

Marcus CL, Brooks LJ, Ward SD, et al. Diagnosis and management of **childhood obstructive sleep apnea syndrome**. Pediatrics. 2012 Sep;130(3):e714-55.

Marogna M, Bruno M, Massolo A, Falagiani P. Long-Lasting Effects of **Sublingual Immunotherapy** for House Dust Mites in Allergic Rhinitis with Bronchial Hyperreactivity: A Long-Term (13-Year) Retrospective Study in Real Life. Int Arch Allergy Immunol. 2006 Oct 2;142(1):70-78 [Epub ahead of print]

Martin BG, et al. Comparison of **fluticasone** propionate aqueous nasal spray and oral montelukast for the treatment of seasonal allergic rhinitis symptoms. Ann Allergy Asthma Immunol. 2006 Jun;96(6):851-7.

May JR, Dolen WK. Management of **Allergic Rhinitis**: A Review for the Community **Pharmacist**. Clin Ther. 2017 Oct 24

McCormack PL, Scott LJ. **Fluticasone furoate**: intranasal use in allergic rhinitis. Drugs. 2007;67(13):1905-15.

Medical Letter. Treatment Guidelines. Drugs for **Allergic Disorders**. Feb 2010.

Medical Letter. Fluticasone furoate (Veramyst) for Allergic Rhinitis. Nov 5, 2007.

Meltzer EO, Bachert C, Staudinger H. Treating acute rhinosinusitis: comparing efficacy and safety of **mometasone** furoate nasal spray, amoxicillin, and placebo. J Allergy Clin Immunol. 2005 Dec;116(6):1289-95. Epub 2005 Oct 24. (InfoPOEMs: The vast majority of patients with acute uncomplicated rhinosinusitis improve in 2 to 4 weeks without any specific treatment. Treatment with mometasone furoate nasal spray (Nasonex) 200 ug twice daily significantly reduces the time to resolution compared with amoxicillin alone or placebo. Patients who "must do something" may still find it easier and cheaper to try other modalities such as nasal saline. (LOE = 1b))

Meltzer EO, Andrews C, Journeay GE, Lim J, Prillaman BA, Garris C, et al. Comparison of patient preference for sensory attributes of **fluticasone furoate or fluticasone propionate** in adults with seasonal allergic rhinitis: a randomized, placebo-controlled, double-blind study. Ann Allergy Asthma Immunol. 2010 Apr;104(4):331-8.

Meltzer EO, Gates D, Bachert C. **Mometasone** furoate nasal spray increases the number of minimal-symptom days in patients with **acute rhinosinusitis**. Ann Allergy Asthma Immunol. 2012 Apr;108(4):275-9.

Moore P, Blakley B, Meen E. **Clinical predictors of chronic rhinosinusitis**: do the **Canadian** clinical practice guidelines for acute and chronic rhinosinusitis predict CT-confirmation of disease? J Otolaryngol Head Neck Surg. 2017 Dec 4;46(1):65.

Mounsey AL, Feller CM. **Capsaicin** for Nonallergic Rhinitis. Am Fam Physician. 2016 Aug 1;94(3):217-8.

Nasser M, Fedorowicz Z, Aljufairi H, McKerrow W. **Antihistamines used in addition to topical nasal steroids** for intermittent and persistent allergic rhinitis in children. Cochrane Database Syst Rev. 2010 Jul 7;7:CD006989. In view of the lack of evidence for the benefit or lack of benefit of antihistamine add-on therapy with topical nasal steroids for children with intermittent or persistent allergic rhinitis, it is important that clinicians are mindful of the adverse effects of antihistamines and the additional costs that may be incurred.

Okubo K, Nakashima M, Miyake N, Komatsubara M, Okuda M. Comparison of **fluticasone furoate and fluticasone propionate** for the treatment of Japanese cedar pollinosis. Allergy Asthma Proc. 2009 Jan;30(1):84-94.

Okubo K, Masuyama K, Imai T, et al. Efficacy and safety of the **SQ house dust mite sublingual immunotherapy** tablet in Japanese adults and adolescents with house dust mite-induced allergic rhinitis. J Allergy Clin Immunol. 2016 Nov 15.

Ozturk F, Bakirtas A, Ileri F, et al. Efficacy and tolerability of systemic **methylprednisolone** (oral) in children and adolescents with chronic rhinosinusitis: a double-blind, placebo-controlled randomized trial. J Allergy Clin Immunol. 2011 Aug;128(2):348-52.

Paton J, et al. **Adrenal responses** to low dose synthetic ACTH (Synacthen) in children receiving high dose **inhaled fluticasone**. Arch Dis Child. 2006 Oct;91(10):808-13. Epub 2006 Mar 23.

Patterson AM, Bonny AE, Shiels WE 2nd, Erwin EA. **Three-injection intralymphatic immunotherapy** in adolescents and young adults with **grass pollen** rhinoconjunctivitis. Ann Allergy Asthma Immunol. 2016;116:168e170.

Penagos M, et al. Efficacy of **sublingual immunotherapy** in the treatment of allergic rhinitis in pediatric patients 3 to 18 years of age: a meta-analysis of randomized, placebo-controlled, double-blind trials. Ann Allergy Asthma Immunol. 2006 Aug;97(2):141-8.

Pfaar O, Bachert C, Kuna P, et al. **Sublingual allergen immunotherapy with a liquid birch pollen** product in patients with seasonal allergic rhinoconjunctivitis with or without asthma. J Allergy Clin Immunol. 2019 Mar;143(3):970-977.

Pharmacist's Letter. Fluticasone furoate (Avamyst) for Allergic Rhinitis. Dec, 2007.

Plaut M, Alleric Rhinitis. N Engl J Med 2005;353:193-44.

Pokladnikova J, Meyboom RH, Vlcek J, Edwards RI. Can intranasal corticosteroids cause **migraine-like headache**? Cephalalgia. 2009 Mar;29(3):360-4. Epub 2008 Oct 22.

Radulovic S, Calderon MA, Wilson D, Durham S. **Sublingual immunotherapy** for allergic rhinitis. Cochrane Database of Systematic Reviews 2010, Issue 12. Art. No.: CD002893. DOI: 10.1002/14651858.CD002893.pub2. This updated review reinforces the conclusion of the original 2003 Cochrane Review that sublingual immunotherapy is effective for allergic rhinitis and has been proven to be a safe route of administration.

Ratner PH, Melchior A, Dunbar SA, et al. Pharmacokinetic Profile of **Beclomethasone** Dipropionate Hydrofluoroalkane After **Intranasal** Administration Versus **Oral Inhalation** in Healthy Subjects: Results of a Single-Dose, Randomized, Open-Label, 3-Period Crossover Study. Clin Ther. 2012 May 21.

Rimmer J, Fokkens W, Chong LY, et al. **Surgical versus medical interventions for chronic rhinosinusitis with nasal polyps**. Cochrane Database Syst Rev. 2014 Dec 1;12:CD006991. The evidence relating to the effectiveness of different types of surgery versus medical treatment for adults with chronic rhinosinusitis with nasal polyps is of very low quality. The evidence does not show that one treatment is better than another in terms of patient-reported symptom scores and quality of life measurements. The one positive finding from amongst the several studies examining a number of different comparisons must be treated with appropriate caution, in particular when the clinical significance of the measure is uncertain.As the overall evidence is of very low quality (serious methodological limitations, reporting bias, indirectness and imprecision) and insufficient to draw firm conclusions, further research to investigate this problem, which has significant implications for quality of life and healthcare service usage, is justified.

Rizvi AY, Panchal AS. **Timothy Grass Pollen Allergen Extract (Grastek)** for Allergic Rhinitis. Am Fam Physician. 2015 Dec 15;92(12):1096-7.

Rosenfeld RM, Piccirillo JF, Chandrasekhar SS, et al. **Clinical practice guideline** (update): **adult sinusitis** executive summary. **Otolaryngol Head Neck Surg**. 2015 Apr;152(4):598-609.

Rosenfeld RM. Clinical Practice. **Acute Sinusitis in Adults**. N Engl J Med. 2016 Sep 8;375(10):962-70

Rudmik L, Soler ZM. **Medical Therapies for Adult Chronic Sinusitis**: A Systematic Review. JAMA. 2015 Sep 1;314(9):926-39.

Rudmik L, Soler ZM, Smith TL, et al. Effect of **Continued Medical Therapy on Productivity Costs** for Refractory Chronic Rhinosinusitis. JAMA Otolaryngol Head Neck Surg. 2015 Oct 29:1-6.

Rudmik L, Xu Y, Liu M, et al. **Utilization Patterns of Topical Intranasal Steroid Therapy for Chronic Rhinosinusitis**: A Canadian Population-Based Analysis. JAMA Otolaryngol Head Neck Surg. 2016 Aug 25

Saleh HA, Durham SR. **Perennial rhinitis**. BMJ. 2007 Sep 8;335(7618):502-7.

Scadding G, Calderon M, Shamji MH, et al. Effect **of 2 years of treatment with sublingual grass pollen immunotherapy** on nasal response to allergen challenge at 3 years among patients with moderate to severe seasonal allergic rhinitis: the **GRASS** randomized clinical trial.JAMA. doi:10.1001 /jama.2016.21040.

Schroer B, Pien LC. **Nonallergic rhinitis**: Common problem, chronic symptoms. Cleve Clin J Med. 2012 Apr;79(4):285-93.

Simpson SA, Lewis R, van der Voort J, et al. Oral **or topical nasal steroids for hearing loss associated with otitis media** with effusion in children. Cochrane Database Syst Rev. 2011 May 11;5:CD001935. While oral steroids, especially when used in combination with an oral antibiotic, lead to a quicker resolution of OME in the short term, there is no evidence of longer-term benefit and no evidence that they relieve symptoms of hearing loss. We found no evidence of benefit from treatment of OME with topical intranasal steroids, alone or in combination with an antibiotic, either at short or longer-term follow up.

Skoner DP, Maspero J, Banerji D; and the Ciclesonide Pediatric Growth Study Group. Assessment of the Long-term Safety of Inhaled **Ciclesonide** on **Growth** in Children With Asthma. Pediatrics. 2007 Dec 10; [Epub ahead of print]n=661 1yr. Ciclesonide demonstrated no detectable effect on childhood growth velocity, even at the highest dosage, which may ease concerns about systemic adverse events.

Skoner DP, Berger WE, Gawchik SM, et al. **Intranasal Triamcinolone and Growth Velocity**. Pediatrics. 2015 Jan 26.

Slapak I, Skoupá J, Strnad P, Horník P. Efficacy of **isotonic nasal wash (seawater)** in the treatment and prevention of rhinitis in children. Arch Otolaryngol Head Neck Surg. 2008 Jan;134(1):67-74.

Small CB, Hernandez J, Reyes A, et al. Efficacy and safety of mometasone furoate nasal spray in **nasal polyposis**. J Allergy Clin Immunol. 2005 Dec;116(6):1275-1281. Epub 2005 Sep 26.

Snidvongs K, Kalish L, Sacks R, et al. **Topical steroid for chronic rhinosinusitis without polyps**. Cochrane Database Syst Rev. 2011 Aug 10;(8):CD009274. Topical steroid is a beneficial treatment for CRS without polyps and the adverse effects are minor. It may be included in a comprehensive treatment of CRS without polyps. Direct delivery of steroid to the sinuses may bring more beneficial effect.

Stelmach R, et al. Effect of treating allergic rhinitis with corticosteroids in patients with mild-to-moderate persistent **asthma**. Chest. 2005 Nov;128(5):3140-7.

Stjärne P, Olsson P, Alenius M. Use of mometasone furoate to prevent polyp relapse after endoscopic sinus surgery. Arch Otolaryngol Head Neck Surg. 2009 Mar;135(3):296-302. Postoperative use of mometasone furoate, 200 microg once daily, provided a statistically significant longer time to relapse of nasal polyps than did placebo in subjects with bilateral nasal polyposis who had undergone FESS. The ability of mometasone to prevent or prolong the time to relapse among subjects undergoing FESS is important because this may prolong the time to subsequent surgery.

Stjarne P, Mosges R, Jorissen M, Passali D, Bellussi L, Staudinger H, Danzig M. A randomized controlled trial of mometasone furoate nasal spray for the treatment of **nasal polyposis**. Arch Otolaryngol Head Neck Surg. 2006 Feb;132(2):179-85.

Stratakis N, Roumeliotaki T, Oken E, et al. **Fish and seafood consumption during pregnancy** and the risk of asthma and allergic rhinitis in childhood: a pooled analysis of 18 European and US birth cohorts. Int J Epidemiol. 2017 Oct 1;46(5):1465-1477.

Sur DKC, Plesa ML, **Chronic Nonallergic Rhinitis**. Am Fam Physician. 2018;98(3):171-176.

Sussman G, Sussman D, Sussman A. Intermittent **allergic rhinitis**. CMAJ. 2010 Jun 15;182(9):935-7.

Sur DK, Scandale S. Treatment of **allergic rhinitis**. Am Fam Physician. 2010 Jun 15;81(12):1440-6.

Sur DKC, Plesa ML. Treatment of **Allergic Rhinitis**. Am Fam Physician. 2015;92(11):985-992.

Tait S, Kallogjeri D, Suko J, et al. Effect of **budesonide added to large-volume, low-pressure saline sinus irrigation** for chronic rhinosinusitis: a randomized clinical trial [online June 7, 2018]. JAMA Otolaryngol Head Neck Surg. doi:10.1001/jamaoto.2018.0667

Van Hoecke H, Vandenbulcke L, Van Cauwenberge P. **Histamine and leukotriene receptor antagonism** in the treatment of allergic rhinitis : an update. Drugs. 2007;67(18):2717-26.

Venekamp RP, Thompson MJ, Hayward G, et al. **Systemic corticosteroids for acute sinusitis**. Cochrane Database Syst Rev. 2011 Dec 7;12:CD008115. Current evidence suggests that oral corticosteroids as an adjunctive therapy to oral antibiotics are effective for short-term relief of symptoms in acute sinusitis. However, data are limited and there is a significant risk of bias.

Venekamp RP, Bonten MJ, Rovers MM, et al. **Systemic corticosteroid monotherapy** for clinically diagnosed **acute rhinosinusitis**: a randomized controlled trial. CMAJ. 2012 Aug 7.

Venekamp RP, Thompson MJ, Rovers MM. **Systemic corticosteroid therapy** for acute sinusitis. JAMA. 2015 Mar 24-31;313(12):1258-9.

Wei CC, Adappa ND, Cohen NA. Use of **topical nasal therapies** in the management of Chronic rhinosinusitis. Laryngoscope. 2013 Apr 1.

Wheatley LM, Togias A. Clinical practice. **Allergic rhinitis**. N Engl J Med. 2015 Jan 29;372(5):456-63.

Williamson IG, Rumsby K, Benge S, Moore M, Smith PW, Cross M, Little P. **Antibiotics and topical nasal steroid for treatment of acute** maxillary sinusitis: a randomized controlled trial. JAMA. 2007 Dec 5;298(21):2487-96. Neither an antibiotic nor a topical steroid alone or in combination was effective as a treatment for acute sinusitis in the primary care setting.

Williamson I, Benge S, Barton S, et al. A double-blind randomised placebo-controlled trial of topical intranasal corticosteroids in 4- to 11-year-old children with **persistent bilateral otitis media** with effusion in primary care. Health Technol Assess. 2009 Aug;13(37): 1-144. Use of topical intranasal corticosteroids is very unlikely to be a clinically effective treatment for OME (glue ear) in the primary care setting.

Williamson Ian, Benge Sarah, Barton Sheila, et al. Topical intranasal corticosteroids in 4-11 year old children with **persistent bilateral otitis media** with effusion in primary care: double blind randomised placebo controlled trial. BMJ 2009;339:b4984, doi: 10.1136/bmj.b4984 (Published 16 December 2009) Topical steroids are unlikely to be an effective treatment for otitis media with effusion in general practice. High rates of natural resolution occurred by 1-3 months.

Wu EL, Riley CA, Hsieh MC, et al. **Chronic sinonasal** tract inflammation as a precursor to **nasopharyngeal carcinoma** and **sinonasal malignancy** in the United States. Int Forum Allergy Rhinol. 2017 May 23.

Zalmanovici A, Yaphe J. Steroids for acute sinusitis. Cochrane Database Syst Rev. 2007 Apr 18;(2):CD005149.For **acute sinusitis** confirmed by radiology or nasal endoscopy, current evidence is limited, but supports the use of INCS as a monotherapy or as an adjuvant therapy to antibiotics. Clinicians should weigh the modest but clinically important benefits against possible minor adverse events when prescribing therapy.

Zalmanovici Trestioreanu A, Yaphe J. **Intranasal steroids for acute sinusitis**. Cochrane Database Syst Rev. 2013 Dec 2;12:CD005149. Current evidence is limited for acute sinusitis confirmed by radiology or nasal endoscopy but supports the use of INCS as a monotherapy or as an adjuvant therapy to antibiotics.

Vaidyanathan S, Barnes M, Williamson P, et al. Treatment of chronic rhinosinusitis with nasal polyposis with **oral steroids followed by topical steroids**: a randomized trial. Ann Intern Med. 2011 Mar 1;154(5):293-302.

[1] Bagchus WM, Hust R, Maris F, Schnabel PG, Houwing NS. Important effect of food on the bioavailability of oral testosterone undecanoate. Pharmacotherapy. 2003 Mar;23(3):319-25.
[2] Bagchus WM, Hust R, Maris F, Schnabel P, Houwing N. Important Effect of Food on the Bioavailablility of Oral Testosterone Undecanoate. Pharmacotherapy 2003;23 (3):319-325.
[3] Gooren LJ. A ten-year safety study of the oral androgen testosterone undecanoate. J Androl. 1994 May-Jun;15(3):212-5.
[4] Gruenewald DA, Matsumoto AM. Testosterone Supplementation Therapy for Older Men: Potential Benefits and Risks. J Am Geriatr Soc. 2003 Jan;51(1):101-115.
Snyder PJ, Bhasin S, Cunningham GR, et al. **Effects of Testosterone Treatment in Older Men. (TTrials)** N Engl J Med. 2016 Feb 18;374(7):611-624.
Resnick SM, Matsumoto AM, Stephens-Shields AJ, et al. Testosterone treatment and cognitive function in older men with low testosterone and age-associated memory impairment. JAMA 2017;317(7):717-727.
Walther A, Breidenstein J, Miller R. Association of **testosterone treatment with alleviation of depressive symptoms in men**: a systematic review and meta-analysis [online Nov 14, 2018]. JAMA Psychiatry. doi:10.1001/jamapsychiatry.2018.2734.

[5] Tenover L. Male Hormone Replacement Therapy Including "Andropause". Endocrin and Metab Clinics of N America 1998;27(4):969-87.
[6] Vermeulen A. Decreased androgen levels and obesity in men. Ann Med. 1996 Feb;28(1):13-5.
[7] Wang C, Eyre DR, et al. Sublingual testosterone replacement improves muscle mass and strength, decreases bone resorption, and increases bone formation markers in hypogonadal men--a clinical research center study. J Clin Endocrinol Metab. 1996 Oct;81(10):3654-62.
[8] Morales A, Lunenfeld B. Investigation, treatment & monitoring of late-onset hypogonadism in males. Official ISSAM. International Society for the Study of the Aging Male.Aging Male.2002 Jun;5(2):74-86.
[9] Report of National Institute on Aging Advisory Panel on Testosterone Replacement in Men. J Clin Endocrinol Metab. 2001 Oct;86(10):4611-4.
[10] Heaton JP. POINT: Urologists should take an active role in the diagnosis and treatment of hypogonadism in the aging male. Can J Urol. 2002 Dec;9(6):1677-80.
[11] Wespes E, Schulman CC. Male andropause: myth, reality, and treatment. Int J Impot Res. 2002 Feb;14 Suppl 1:S93-8.
[12] Report of National Institute on Aging Advisory Panel on Testosterone Replacement in Men. J Clin Endocrinol Metab. 2001 Oct;86(10):4611-4.
[13] Morales A, Tenover JL. Androgen deficiency in the aging male: when, who, and how to investigate and treat. Urol Clin North Am. 2002 Nov;29(4):975-82.
[14] Tenover L. Male Hormone Replacement Therapy Including "Andropause". Endocrin and Metab Clinics of N America 1998;27(4):969-87.
Snyder PJ, Bhasin S, Cunningham GR, et al. Effects of **Testosterone Treatment in Older Men. (TTrials)** N Engl J Med. 2016 Feb 18;374(7):611-624.
Corona G, Rastrelli G, Morgentaler A, et al. Meta-analysis of Results of **Testosterone Therapy on Sexual Function** Based on International Index of Erectile Function Scores. Eur Urol. 2017 Apr 20. (useful if hypogonadal)

[15] Stas SN, Anastasiadis AG, Fisch H, Benson MC, Shabsigh R. Urologic aspects of andropause. Urology. 2003 Feb;61(2):261-6.
[16] Bhasin S, Bagatell CJ, Bremner WJ, Plymate SR, et al. Issues in testosterone replacement in older men. J Clin Endocrinol Metab. 1998 Oct;83(10):3435-48.
[17] Pope HG Jr, Cohane GH, Kanayama G, et al. Testosterone gel supplementation for men with refractory depression: a randomized, placebo-controlled trial. Am J Psychiatry 2003 Jan;160:105-11.
[18] Benkert O, Witt W, Adam W, Leitz A. Effects of testosterone undecanoate on sexual potency and the hypothalamic-pituitary-gonadal axis of impotent males. Arch Sex Behav. 1979 Nov;8(6):471-9.
[19] Fairfield WP, Treat M, Rosenthal DI, et al. Effects of testosterone and exercise on muscle leanness in eugonadal men with AIDS wasting. J Appl Physiol. 2001 Jun;90(6):2166-71.
[20]Bhasin S, Storer TW, et al. Effects of testosterone replacement with a nongenital, Androderm, in human immunodeficiency virus-infected men with low testosterone levels. J Clin Endocrinol Metab. 1998 Sep;83(9):3155-62.
[21] Rhoden E, Morgentaler A. Risks of **Testosterone-Replacement Therapy** and Recommendations for Monitoring. N Engl J Med 2004;350:482-492. (also Editorial pg 440-442)
Morales A, Bebb RA. Manjoo P, et al; **Canadian Men's Health Foundation Multidisciplinary Guidelines** Task Force on Testosterone Deficiency. Diagnosis and management of **testosterone deficiency syndrome in men**: clinical practice guideline. CMAJ 2015; early release online October 26, 2015. http://www.cmaj.ca/content/early/2015/10/26/cmaj.150033.full.pdf+html (accessed October 29, 2015)

[22] Pechersky AV, Mazurov VI, et al. Androgen administration in middle-aged and ageing men: effects of oral testosterone undecanoate on dihydrotestosterone, oestradiol and prostate volume. Int J Androl. 2002 Apr;25(2):119-25.
[23] Weiss EL, Bowers MB Jr, Mazure CM. Testosterone-patch-induced psychotic mania. Am J Psychiatry. 1999 Jun;156(6):969.

Additional references:
Abadilla KA, Dobs AS. **Topical testosterone supplementation** for the treatment of male hypogonadism. Drugs. 2012 Aug 20;72(12):1591-603.
Aditya I, Grober ED, Krakowsky Y**. Peyronie's disease** and testosterone deficiency: Is there a link? World J Urol. 2019 Mar 11.
Akturk HK, Nippoldt TB. **Low Testosterone in Men Should Be a Sign Rather Than a Number to Increase**: A Teachable Moment. JAMA Intern Med. 2016 Oct 10.
Alexander GC, Iyer G, Lucas E, et al. **Cardiovascular risks of exogenous testosterone** use among men: A systematic review and meta-analysis. Am J Med. 2016 Oct 14.
Algeffari M, Jayasena CN, et al. **Testosterone therapy for sexual dysfunction** in men with Type 2 diabetes: a systematic review and meta-analysis of randomized controlled trials. Diabet Med. 2018 Feb;35(2):195-202.
American College of Obstetricians and Gynecologists (**ACOG**). **Female sexual dysfunction**. Washington: American College of Obstetricians and Gynecologists (ACOG); 2011 Apr. 12 p. (ACOG practice bulletin; no. 119).
Anawalt BD, Hotaling JM, Walsh TJ, Matsumoto AM. **Performance of total testosterone measurement** to predict free testosterone for the biochemical evaluation of male hypogonadism. J Urol. 2012 Apr;187(4):1369-73.
Araujo AB, Esche GR, Kupelian V, O'donnell AB, Travison TG, Williams RE, Clark RV, McKinlay JB. Prevalence of Symptomatic Androgen Deficiency in Men. J Clin Endocrinol Metab. 2007 Aug 14; [Epub ahead of print]
Prevalence of symptomatic androgen deficiency in **men 30 and 79 y of age is 5.6%,** and increases substantially with age.
Arunakumari PS, Walker S. Reduced **sexual desire in women**. BMJ. 2009 Aug 10;339:b2371. doi: 10.1136/bmj.b2371.
Baggish AL, Weiner RB, Kanayama G, et al. Long term **anabolic-androgenic steroid use** is associated with **left ventricular dysfunction**. Circ Heart Fail 2010.
Baggish AL, Weiner RB, Kanayama G, et al. **Cardiovascular Toxicity of Illicit Anabolic-Androgenic Steroid Use**. Circulation. 2017 May 23;135(21):1991-2002.
Baillargeon J, Urban RJ, Ottenbacher KJ, et al. **Trends in androgen prescribing in the United States**, 2001 to 2011. JAMA Intern Med. 2013 Aug 12;173(15):1465-6.
Baillargeon J, Urban RJ, Kuo YF, et al. **Risk of Myocardial Infarction in Older Men** Receiving Testosterone Therapy. Ann Pharmacother. 2014 Jul 2.
Baillargeon J, Urban RJ, Morgentaler et al. **Risk of Venous Thromboembolism** in Men Receiving Testosterone Therapy. Mayo Clin Proc. 2015 Jul 15.
Baillargeon J, Kuo YF, Fang X, et al. **Long-Term Exposure to Testosterone Therapy** and the **Risk of High Grade Prostate Cancer**. J Urol. 2015 Jun 9.
Baillargeon J, Kuo YF, Westra JR, et al. Testosterone Prescribing in the United States, 2002-2016. JAMA. 2018 Jul 10;320(2):200-202.
Basaria, Shehzad, Coviello, Andrea D., Travison, Thomas G., et al. **Adverse Events** Associated with Testosterone Administration. (**TOM**) N Engl J Med 2010 0: NEJMoa1000485. In this population of older men with limitations in mobility and a high prevalence of chronic disease, the application of a testosterone gel was associated with an increased risk of cardiovascular adverse events. The small size of the trial and the unique population prevent broader inferences from being made about the safety of testosterone therapy.
Basaria S. **Male hypogonadism**. Lancet. 2013 Oct 9.
Basaria S. **Testosterone levels for evaluation of androgen deficiency**. JAMA. 2015 May 5;313(17):1749-50.
Basaria S, Harman SM, Travison TG et al. Effects of **Testosterone Administration for 3 Years on Subclinical Atherosclerosis** Progression in Older Men With Low or Low-Normal Testosterone Levels:
A Randomized Clinical Trial. JAMA. 2015 Aug 11;314(6):570-81.
Basson R, Brotto LA, Petkau AJ, Labrie F. Role of **androgens in women's sexual dysfunction**. Menopause. 2010 Sep-Oct;17(5):962-71.

Barton DL, Wender DB, Sloan JA, Dalton RJ, et al. RCT to evaluate transdermal testosterone in female cancer survivors with decreased libido; North Central Cancer Treatment. J Natl Cancer Inst. 2007 May 2;99(9):672-9.
{InfoPOEMs: In female cancer survivors, transdermal testosterone does not improve sexual desire even though it increases hormone levels. (LOE = 1b)}
Basson R. Clinical practice. Sexual desire and arousal disorders in **women**. N Engl J Med. 2006 Apr 6;354(14):1497-506.
Bawor M, Bami H, Dennis BB, et al. **Testosterone suppression in opioid users**: a systematic review and meta-analysis. Drug Alcohol Depend. 2015 Apr 1;149:1-9
Berkseth KE, Thirumalai A, Amory JK. Pharmacologic **Therapy in Men's Health: Hypogonadism**, Erectile Dysfunction, and Benign Prostatic Hyperplasia. Med Clin North Am. 2016 Jul;100(4):791-805.
Bhasin S, et al. Testosterone therapy in adult men with androgen deficiency syndromes: an **endocrine society clinical practice guideline**. J Clin Endocrinol Metab. **2006** Jun;91(6):1995-2010. Epub 2006 May 23. Erratum in: J Clin Endocrinol Metab. 2006 Jul;91(7):2688. We recommend making a diagnosis of androgen deficiency only in men with consistent symptoms and signs and unequivocally low serum testosterone levels. We suggest the measurement of morning total testosterone level by a reliable assay as the initial diagnostic test. We recommend confirmation of the diagnosis by repeating the measurement of morning total testosterone and in some patients by measurement of free or bioavailable testosterone level, using accurate assays. We recommend testosterone therapy for symptomatic men with androgen deficiency, who have low testosterone levels, to induce and maintain secondary sex characteristics and to improve their sexual function, sense of well-being, muscle mass and strength, and bone mineral density. We recommend against starting testosterone therapy in patients with breast or prostate cancer, a palpable prostate nodule or induration or prostate-specific antigen greater than 3 ng/ml without further urological evaluation, erythrocytosis (hematocrit > 50%), hyperviscosity, untreated obstructive sleep apnea, severe lower urinary tract symptoms with International Prostate Symptom Score (IPSS) greater than 19, or class III or IV heart failure. When testosterone therapy is instituted, we suggest aiming at achieving testosterone levels during treatment in the mid-normal range with any of the approved formulations, chosen on the basis of the patient's preference, consideration of pharmacokinetics, treatment burden, and cost. Men receiving testosterone therapy should be monitored using a standardized plan.
Bhasin S, Cunningham GR, Hayes FJ, et al. **Testosterone therapy in men with androgen deficiency syndromes**: an **Endocrine Society clinical practice** guideline. J Clin Endocrinol Metab **2010**;95:2536-59.
We recommend making a diagnosis of androgen deficiency only in men with consistent symptoms and signs and unequivocally low serum testosterone levels. We suggest the measurement of morning total testosterone level by a reliable assay as the initial diagnostic test. We recommend confirmation of the diagnosis by repeating the measurement of morning total testosterone and, in some men in whom total testosterone is near the lower limit of normal or in whom SHBG abnormality is suspected by measurement of free or bioavailable testosterone level, using validated assays. We recommend testosterone therapy for men with symptomatic androgen deficiency to induce and maintain secondary sex characteristics and to improve their sexual function, sense of well-being, muscle mass and strength, and bone mineral density. We recommend against starting testosterone therapy in patients with breast or prostate cancer, a palpable prostate nodule or induration or prostate-specific antigen greater than 4 ng/ml or greater than 3 ng/ml in men at high risk for prostate cancer such as African-Americans or men with first-degree relatives with prostate cancer without further urological evaluation, hematocrit greater than 50%, untreated severe obstructive sleep apnea, severe lower urinary tract symptoms with International Prostate Symptom Score above 19, or uncontrolled or poorly controlled heart failure. When testosterone therapy is instituted, we suggest aiming at achieving testosterone levels during treatment in the mid-normal range with any of the approved formulations, chosen on the basis of the patient's preference, consideration of pharmacokinetics, treatment burden, and cost. Men receiving testosterone therapy should be monitored using a standardized plan.
Bhasin S, Travison TG, Storer TW, et al. Effect of **testosterone supplementation** with and without a dual **5 alpha-reductase inhibitor** (dutasteride) on fat-free mass in men with suppressed testosterone production: a randomized controlled trial. *JAMA*. 2012; 307(9):931-939. n=139
Bhasin S, Brito JP, Cunningham GR, et al. **Testosterone Therapy in Men With Hypogonadism**: An **Endocrine Society Clinical Practice Guideline**. J Clin Endocrinol Metab. 2018 Mar 17.
Birnbaum W, Marshall L, Werner R, et al. **Oestrogen versus androgen in hormone-replacement therapy for complete androgen insensitivity syndrome**: a multicentre, randomised, double-dummy, double-blind crossover trial. Lancet Diabetes Endocrinol. 2018 Jul 31.
Blashill AJ, Safren SA. Sexual Orientation and **Anabolic-Androgenic Steroids** in US Adolescent Boys. Pediatrics. 2014 Feb 2.
Blevins CH, Wilson ME. **Klinefelter's** syndrome. BMJ. 2012 Dec 3;345:e7558.
Bodybuilding.com and FDA Nov/09 notified healthcare professionals and patients of a nationwide and international recall of all lots and expiration dates of 65 dietary supplement products that were sold through the Company's website, www.bodybuilding.com. FDA believes that the recalled products contain the following ingredients that are currently classified, or the FDA believes should be classified, as steroids: **"Superdrol," "Madol," "Tren," "Androstenedione," and/or "Turinabol."** Acute liver injury is known to be a possible harmful effect of using steroid-containing products. In addition, steroids may cause other serious long-term adverse health consequences in men, women, and children. These include shrinkage of the testes and male infertility, masculinization of women, breast enlargement in males, short stature in children, a higher predilection to misuse other drugs and alcohol, adverse effects on blood lipid levels, and increased risk of heart attack, stroke, and death.
Boskey ER, Taghinia AH, Ganor O. Association of **Surgical Risk With Exogenous Hormone Use in Transgender Patients**: A Systematic Review. JAMA Surg. 2018 Dec 5.
Braun SR. **Promoting "Low T"**: A Medical Writer's Perspective. JAMA Intern Med. 2013 Aug 12;173(15):1458-60.
Braunstein GD, et al. Safety & efficacy of a testosterone patch for the treatment of hypoactive sexual desire in surgically menopausal **women**: a randomized, placebo-controlled trial. Arch Intern Med. 2005 Jul 25;165(14):1582-9.
Brock G, et al. 9-Month Efficacy and Safety Study of Testosterone Solution 2% for **Sex Drive & Energy** in Hypogonadal Men: Results of 6-Month Open Label Extension of a 3-Month Double-Blind Study. J Urol. 2016 Apr 24.
Budoff MJ, Ellenberg SS, Lewis CE, et al. Testosterone treatment and **coronary artery plaque volume** in older men with low testosterone. JAMA 2017; 317:708-716.
Buster JE, Kingsberg SA, Aguirre O, et al. Testosterone patch for low sexual desire in surgically menopausal **women**: a randomized trial. Obstet Gynecol. 2005 May;105(5):944-52.
Bütikofer A, Figlio DN, Karbownik K, et al. Evidence that **prenatal testosterone transfer from male twins** reduces the fertility and socioeconomic success of their female co-twins. Proc Natl Acad Sci U S A. 2019 Mar 18.
Calof OM, Singh AB, Lee ML, et al. **Adverse events associated with testosterone replacement** in middle-aged and older men: a meta-analysis of randomized, placebo-controlled trials. J Gerontol 2005;60:1451-7.
Cappola AR. Testosterone therapy and **risk of cardiovascular disease** in men. JAMA 2013; 310:1805-1806.
Cervi A, Balitsky AK. **Testosterone use causing erythrocytosis**. CMAJ. 2017 Oct 16;189(41):E1286-E1288.
Cheetham TC, An J, et al. Association of testosterone replacement with **cardiovascular outcomes** among men with androgen deficiency [online Feb 21, 2017]. JAMA Intern Med. doi:10.1001/jamainternmed.2016.9546
Corona G, Rastrelli G, Morgentaler A, et al. Meta-analysis of Results of **Testosterone Therapy on Sexual Function** Based on International Index of Erectile Function Scores. Eur Urol. 2017 Apr 20.
Cunningham GR, Stephens-Shields AJ, Rosen RC, et al. **Testosterone Treatment and Sexual Function** in Older Men with Low Testosterone Levels. J Clin Endocrinol Metab. 2016 Jun 29:jc20161645.
Davis SR, Davison SL, Donath S, Bell RJ. Circulating androgen levels and self-reported sexual function in **women**. JAMA. 2005 Jul 6;294(1):91-6. CONCLUSIONS: No single androgen level is predictive of low female sexual function, and the majority of women with low dehydroepiandrosterone sulfate levels did not have low sexual function. (InfoPOEMs: Low total testosterone and free testosterone levels are not associated with low sexual desire and function in women. A serum dehydroepiandrosterone sulfate (DHEA) level below the aged-adjusted 10th percentile is a better marker for low sexual desire and function, but the majority of women with a low DHEA level do not have sexual dysfunction. There is no evidence to support measurement of serum testosterone in women with low sexual desire or function. The practice of prescribing exogenous testosterone for women with low sexual desire or function requires further study and should not be routine. (LOE = 2c))
Davis SR, et al. Efficacy and safety of a testosterone patch for the treatment of hypoactive sexual desire disorder in surgically menopausal women: a randomized, placebo-controlled trial. Menopause. 2006 May 25
Davis S, Papalia MA, Norman RJ, et al. Safety and efficacy of a testosterone metered-dose transdermal spray for treating decreased sexual satisfaction in **premenopausal women**: a randomized trial. Ann Intern Med. 2008 Apr 15;148(8):569-77. A daily 90-microL dose of transdermal testosterone improves self-reported sexual satisfaction for premenopausal women with reduced libido and low serum-free testosterone levels by a mean of **0.8 SSE per month**. The rate of SSEs with higher and lower testosterone doses did not differ from that with placebo.
Davis SR, Moreau M, Kroll R, et al. **APHRODITE** Study Team. Testosterone for **low libido in postmenopausal women** not taking estrogen. N Engl J Med. 2008 Nov 6;359(19):2005-17. In postmenopausal women not receiving estrogen therapy, treatment with a patch delivering 300 microg of testosterone per day resulted in a modest but meaningful improvement in sexual function. The long-term effects of testosterone, including effects on the breast, remain uncertain.
Davis SR, Evans AM, Humberstone A. **Application Site** Affects the Pharmacokinetics of Topical Testosterone Applied to the **Axilla Compared With the Inner Arm**. Clin Ther. 2014 Jul 26.
de Ronde W, Vogel S, Bui HN, Heijboer AC. Reduction in 24-hour plasma testosterone levels in subjects who **showered 15 or 30 minutes after application** of testosterone gel. Pharmacotherapy. 2011 Mar;31(3):248-52.
Dean JD, McMahon C, Guay A, et al. The **International Society for Sexual Medicine's (ISSM)** process of care for the **assessment and management of testosterone deficiency in adult men**. J Sex Med 2015;12:1660-86.
den Heijer M, Bakker A, Gooren L. **Long term hormonal treatment for transgender people**. BMJ. 2017 Nov 30;359:j5027.
Dhindsa S, Wilson MF, Dandona P. Changes in **Coronary Artery Plaque With Testosterone Therapy**. JAMA. 2017 Jun 20;317(23):2450
Dias JP, Melvin D, Shardell M, et al. Effects of **Transdermal Testosterone Gel or an Aromatase Inhibitor** on Prostate Volume in older men. J Clin Endocrinol Metab. 2016 Mar 7:jc20161111.

Dohle GR, Arver S, Bettocchi C, Kliesch S, Punab M, de Ronde W. Guidelines on male hypogonadism. Arnhem (The Netherlands): European Association of Urology; 2012 Feb.
Dohle GR, Arver S, Bettocchi C, et al. Guidelines on **male hypogonadism**. Arnhem-Netherlands: **European Association of Urology (EAU); 2014**. http://uroweb.org/wp-content/uploads/18-Male-Hypogonadism_LR.pdf
Eklund E, Berglund B, Labrie F, et al. **Serum androgen profile** and physical performance in **women Olympic athletes**. Br J Sports Med. 2017 Jun 23.
Elagizi A, Köhler TS, Lavie CJ. **Testosterone and Cardiovascular Health**. Mayo Clin Proc. 2018 Jan;93(1):83-100.
Elliott J, Kelly SE, Millar AC, et al. **Testosterone therapy in hypogonadal men**: a systematic review and network meta-analysis. BMJ Open. 2017 Nov 16;7(11):e015284.
Elraiyah T, Sonbol MB, Wang Z, et al. The **Benefits and Harms of Systemic Testosterone Therapy in Postmenopausal Women** With Normal Adrenal Function: A Systematic Review and Meta-analysis. J Clin Endocrinol Metab. 2014 Oct;99(10):3543-50.
Elsharkawy A, McPherson S, Masson S. Cholestasis secondary to anabolic steroid (**methandrostenolone**) use in young men. BMJ 2012; 344 doi: 10.1136/bmj.e468 (Published 2 February 2012)
Emmelot-Vonk MH, Verhaar HJ, Nakhai Pour HR, Aleman A, Lock TM, Bosch JL, Grobbee DE, van der Schouw YT. Effect of testosterone supplementation on functional mobility, cognition, and other parameters in older men: a randomized controlled trial. JAMA. 2008 Jan 2;299(1):39-52. Testosterone supplementation during 6 months to older men with a low normal testosterone concentration did not affect functional status or cognition but increased lean body mass and had mixed metabolic effects.
Endogenous Hormones, Prostate Cancer Collaborative Group, Roddam AW, Allen NE, Appleby P, Key TJ. **Endogenous sex hormones and prostate cancer**: a collaborative analysis of 18 prospective studies J Natl Cancer Inst. 2008 Feb 6;100(3):170-83. Epub 2008 Jan 29. In this collaborative analysis of the worldwide data on endogenous hormones and prostate cancer risk, serum concentrations of sex hormones were not associated with the risk of prostate cancer.
Evans-Brown M, Kimergård A, McVeigh J, et al. Is the breast cancer drug **tamoxifen being sold as a bodybuilding dietary supplement**? BMJ. 2014 Feb 13;348:g1476.
Farias JM, Tinetti M, Khoury M, et al. Low **Testosterone Concentration and Atherosclerotic Disease Markers in Male Patients With Type 2 Diabetes**. J Clin Endocrinol Metab. 2014 Oct 16
FDA May/09 notified healthcare professionals that it will require two prescription topical testosterone gel products, AndroGel 1% and Testim 1%, to include a boxed warning on the products' labels after receiving reports of adverse effects in **children** who were **inadvertently exposed** to testosterone through contact with another person being treated with these products. Of the fully reviewed cases, adverse events reported in these **children** included inappropriate enlargement of the genitalia (penis or clitoris), premature development of pubic hair, advanced bone age, increased libido and aggressive behavior.
FDA Aug/09 not to use body-building products marketed as containing **steroids or steroid-like substances** such as TREN-Xtreme, MASS Xtreme, ESTRO Xtreme, AH-89-Xtreme, HMG Xtreme, MMA-3 Xtreme, VNS-9 Xtreme, and TT-40-Xtreme..
FDA Nov/09 & IDS Sports notified consumers that five of the IDS's dietary supplement products (**Bromodrol, Dual Action Grow Tabs, Grow Tabs, Mass Tabs, and Ripped Tabs TR**) contain the following undeclared substances, which FDA considers to be steroids: "Madol," "Turinabol," "Superdrol," &/or "Androstenedione."
FDA Dec/09 for **S-DROL**: a voluntary recall by the manufacturer of one lot (lot# 810481, expiry date 01/2012) of S-DROL after FDA testing found it to contain undeclared desoxymethyltestosterone.
FDA Dec/09 warned consumers to stop using bodybuilding products manufactured by American Cellular Labs after they were found to contain unauthorized synthetic steroids in **TREN-Xtreme, MASS Xtreme, ESTRO Xtreme, AH-89-Xtreme, HMG Xtreme, MMA-3 Xtreme, VNS-9 Xtreme, TT-40-Xtreme.**
FDA Jan/10 & **MuscleMaster(dot)com**, Inc. notified consumers and healthcare professionals of the voluntary nationwide recall of all lots and expiration dates of the seventeen dietary supplements listed in the firm press release, sold between June 1, 2009 and November 17, 2009. FDA informed MuscleMaster(dot)com that it believes that the recalled products contain ingredients that are **steroids**.
FDA Oct/11 notified the manufacturer that lab analyses found that the product; **Uprizing 2.0** , sold as a testosterone booster, contains **superdrol**, a synthetic steroid, making it an unapproved new drug.
FDA Aug/13 Purity First Health Products is recalling two lots of **Healthy Life Chemistry B-50** (100 capsules), one lot of **Healthy Life Chemistry Multi-Mineral** (200 capsules) and all lot numbers for **Healthy Life Chemistry Vitamin C** (200 capsules). The B-50 capsules were found on testing by FDA to contain Methasterone (a schedule III controlled substance) and Dimethazine. Testing of the Multi-Mineral and Vitamin C capsules appear to indicate the presence of Dimethyltestosterone.
FDA Dec/13 is advising consumers to immediately stop using a product called **Mass Destruction**, marketed as a dietary supplement for muscle growth. The product is labeled to contain at least one synthetic anabolic steroid and has been linked to at least one reported serious illness.
FDA Feb/14 is investigating the **risk of stroke, heart attack, and death in men taking FDA-approved testosterone products**. We have been monitoring this risk and decided to reassess this safety issue based on the recent publication of two separate studies that each suggested an increased risk of cardiovascular events among groups of men prescribed testosterone therapy.
FDA Jun/14 is requiring manufacturers of testosterone products to include a general warning in the drug **labeling of all approved testosterone products about the risk of blood clots in the veins**.
FDA Mar/15 is requiring that the manufacturers of all approved prescription testosterone products change their labeling to clarify the approved uses of these medications. FDA is also requiring these manufacturers to add information to the labeling about a **possible increased risk of heart attacks and strokes** in patients taking testosterone. FDA cautions that prescription testosterone products are approved only for men who have low testosterone levels caused by certain medical conditions. The benefit and safety of these medications have not been established for the treatment of low testosterone levels due to aging, even if a man's symptoms seem related to low testosterone.
FDA Oct/16 approved class-wide labeling changes for all prescription testosterone products, adding a new Warning and updating the **Abuse and Dependence** section to include new safety information from published literature and case reports regarding the risks associated with abuse and dependence of **testosterone and other AAS (Anabolic Androgenic Steroids).** Abuse of testosterone, usually at doses higher than those typically prescribed and usually in conjunction with other AAS, is associated with serious safety risks affecting the heart, brain, liver, mental health, and endocrine system. Reported serious adverse outcomes include **heart attack, heart failure, stroke, depression, hostility, aggression, liver toxicity, and male infertility. Individuals abusing high doses of testosterone have also reported withdrawal symptoms, such as depression, fatigue, irritability, loss of appetite, decreased libido, and insomnia.** The new Warning will alert prescribers to the abuse potential of testosterone and the serious adverse outcomes, especially those related to heart and mental health that have been reported in association with testosterone/AAS abuse.
FDA May/17 Genetic Edge Compounds recalled all lot codes of **GEC Laxoplex dietary supplement capsules** distributed between February 2, 2015- May 2, 2017 to the retail level and consumer level. FDA analysis found GEC Laxoplex to be tainted with anabolic steroids and steroid like substances
FDA May/17: Dynamic Technical Formulations LLC. is voluntarily recalling all lots of **Tri-Ton**. This product was sold in 90 count bottles as a dietary supplement and includes all lot number and expiration dates of the product. FDA lab analysis of Tri-Ton was found to contain andarine and ostarine which are selective androgen receptor modulators (SARMs) that are considered unapproved drugs and anabolic steroid-like substances.
FDA Jul/17: Hardcore Formulations is voluntarily recalling all lots and expiration dates of **Ultra-Sten and D-Zine** capsules to the consumer level. These products are labeled to contain methylstenbolone (Ultra-Sten) and dymethazine (D-Zine), which are considered to be derivatives of anabolic steroids.
FDA Jul/17: Andropharm is voluntarily recalling all lots of **Sten Z and M1 Alpha capsules** to the consumer level because these products **contain derivatives of anabolic steroids** rendering them unapproved drugs for which safety and efficacy have not been established and therefore subject to recall.
Feldman HA, Longcope C, Derby CA, et al. **Age trends in the level of serum testosterone** and other hormones in middle-aged men: longitudinal results from the Massachusetts Male Aging Study. J Clin Endocrinol Metab 2002;87:589-98.
Finkelstein JS, Lee H, Burnett-Bowie S-AM, et al. **Gonadal steroids and body composition, strength, and sexual function in men**. N Engl J Med 2013;369:1011-22.
Finkle WD, Greenland S, Ridgeway GK, et al. Increased risk of nonfatal myocardial infarction following testosterone therapy prescription in men. *PLoS One* 2014.
Fitts RH, Peters JR, Dillon EL, et al. **Weekly versus monthly testosterone administration on fast and slow skeletal muscle fibers** in older adult males. J Clin Endocrinol Metab. 2015 Feb; 100(2):E223-31.
Fugh-Berman A. **Should family physicians screen for testosterone deficiency in men**? **No**: screening may be harmful, and benefits are unproven. Am Fam Physician. 2015 Feb 15
Fui MN, Grossmann M. **Hypogonadism** from **androgen deprivation therapy** in **identical twins**. Lancet. 2016 Jun 9.
Garnick MB. **Testosterone Replacement Therapy Faces FDA Scrutiny**. JAMA. 2014 Dec 11.
Gava G, Mancini I, Cerpolini S, et al. **Testosterone undecanoate and testosterone enanthate injections are both effective and safe in transmen over 5 years of administration**. Clin Endocrinol (Oxf). 2018 Jul 19.

Gaylis FD, Lin DW, Ignatoff JM, Amling CL, Tutrone RF, Cosgrove DJ. **Prostate cancer** in men using testosterone supplementation. J Urol. 2005 Aug;174(2):534-8; discussion 538.
Gault Emma Jane, Perry Rebecca J, Cole Tim J, et al. , on behalf of the British Society for Paediatric Endocrinology and Diabetes. Effect of **oxandrolone** and timing of pubertal induction on final height in Turner's syndrome: randomised, double blind, placebo controlled trial. *BMJ 2011;342:doi:10.1136/bmj.d1980 (Published 14 April 2011)*
Gettler LT, McDade TW, Feranil AB, Kuzawa CW. Longitudinal evidence that **fatherhood decreases testosterone** in human males. Proc Natl Acad Sci U S A. 2011 Sep 12.
Gettler LT, McKenna JJ, McDade TW, et al. Does **cosleeping** contribute to lower testosterone levels in **fathers**? Evidence from the Philippines. PLoS One. 2012;7(9):e41559. Epub 2012 Sep 5.
Gianatti EJ, Dupuis P, Hoermann R, et al. Effect of **Testosterone Treatment on Glucose Metabolism in men With Type 2 Diabetes**: A Randomized Controlled Trial. Diabetes Care. 2014 May 7.
Gianatti EJ et al. Effect of **testosterone treatment on constitutional and sexual symptoms in men with type 2 diabetes** in a randomized, placebo-controlled clinical trial. J Clin Endocrinol Metab 2014 Oct; 99:3821.
Glaser R, Dimitrakakis C. **Testosterone therapy in women**: myths and misconceptions. Maturitas. 2013 Mar;74(3):230-4.
Grant PM, Li X, Jacobson LP, et al. Effect of Testosterone Use on **Bone Mineral Density in HIV-Infected Men**. AIDS Res Hum Retroviruses. 2018 Nov 1.
Grashow R, Weisskopf MG, Miller KK, et al. **Association of Concussion Symptoms** With Testosterone Levels and Erectile Dysfunction in Former Professional US-Style Football Players. JAMA Neurol. 2019 Aug 26.
Green AL, Srivatsa A, Rodriguez-Galindo C. Delayed Diagnosis and **False Relapse** Due to **Paternal Testosterone** Use in Adrenocortical Carcinoma. Pediatrics. 2014 May 5.
Grossmann M, Matsumoto AM. A Perspective on **Middle-Aged and Older Men With Functional Hypogonadism**: Focus on **Holistic Management**. J Clin Endocrinol Metab. 2017 Mar 1;102(3):1067-1075.
Hackett G, Cole N, et al. **Testosterone Undecanoate** improves **Sexual Function** in Men with Type 2 diabetes and Severe Hypogonadism: Results from a 30 week randomized placebo controlled study. BJUInt. 2016 Apr 28.
Hackett G, Cole N, Mulay A, et al. **Long-term testosterone therapy in type 2 diabetes** is associated with reduced mortality without improvement in conventional cardiovascular risk factors. BJU Int. 2018 Sep 14.
Haider A, Zitzmann M, Doros G, et al. Incidence of **Prostate Cancer in Hypogonadal Men Receiving Testosterone Therapy**: Observations from 5-Year Median Followup of 3 Registries. J Urol. 2014 Jun 26.
Health Canada Feb /06 is warning consumers not to use the product M1T(methyl-1-testosterone) Andro Technologies, or any other supplements containing the synthetic steroid methyl-1-testosterone, due to such potentially serious health risks as liver disorders and hardening of the arteries. http://www.hc-sc.gc.ca/ahc-asc/media/advisories-avis/2006/2006_06_e.html
Health Canada July/07 is warning Canadians not to use the dietary supplement **MdMt**, or any other supplements containing the synthetic steroids methyl-1-testosterone or methyldienolone that are obtained without a prescription, due to potentially serious health risks including reduced fertility and liver disorders.
Health Canada Jul/14 is advising patients and healthcare professionals of new safety information regarding testosterone hormone replacement products and a risk of serious and **possibly life-threatening cardiovascular** (heart and blood vessel) problems.
Health Canada Jul/16 is informing Canadians that two unauthorized health products were seized from Next Level Fitness in Richmond and in Surrey,BC. The products **TRT** (**Testosterone Booster**) and **Freak'n Test** (**Testosterone Enhancer**) were labelled to contain a prescription drug substance (L-dopa) that may pose serious health risks to Canadians.
Heidelbaugh JJ. **Should family physicians screen for testosterone deficiency in men**? **Yes**: screening for testosterone deficiency is worthwhile for most older men. Am Fam Physician. 2015 Feb 15
Hembree WC, Cohen-Kettenis P, et al. Endocrine Society. Endocrine treatment of **transsexual persons**: an Endocrine Society clinical practice guideline. J Clin Endocrinol Metab 2009 Sep;94(9):3132-54. [
Herriman M, Fletcher L, Tchaconas A, et al. **Dietary Supplements and Young Teens**: Misinformation and Access Provided by Retailers. Pediatrics. 2017 Jan 2. (creatine, testosterone)
Horwitz H, Andersen JT, Dalhoff KP. Health consequences of androgenic anabolic steroid use. J Intern Med. 2018 Nov 20.
Houghton DE, Alsawas M, Barrioneuvo P, et al. Testosterone therapy and **venous thromboembolism**: A systematic review and meta-analysis. Thromb Res. 2018 Dec;172:94-103.
Huang G, Basaria S, Travison TG et al. Testosterone dose-response relationships in **hysterectomized women with or without oophorectomy**: effects on sexual function, body composition, muscle performance and physical function in a randomized trial. Menopause. 2013 Nov 25. (Testosterone enanthate 3, 6.25, 12.5, & 25mg IM qweekly x 24 weeks)
Idan Amanda, Griffiths Kaye A., Harwood D. Tim, et al. Long-Term Effects of **Dihydrotestosterone** Treatment on Prostate Growth in Healthy, Middle-Aged Men Without Prostate Disease: A Randomized, Placebo-Controlled Trial. Ann Intern Med November 16, 2010 153:621-632. (24 months has no beneficial or adverse effect on prostate growth, but decreases spinal BMD)
Islam RM, Bell RJ, Green S, et al. Safety and efficacy of **testosterone for women**: a systematic review and meta-analysis of randomised controlled trial data. Lancet Diabetes Endocrinol. 2019 Jul 25.
Jayasena CN, Alkaabi FM, Liebers CS, et al. A systematic review of randomised controlled trials investigating the **efficacy and safety of testosterone therapy for female sexual dysfunction in postmenopausal women**. Clin Endocrinol (Oxf). 2018 Nov 29.
Jones TH, Arver S, Behre HM, et al. **TIMES2** Investigators. Testosterone Replacement in Hypogonadal Men With Type 2 **Diabetes and/or Metabolic Syndrome** (the TIMES2 Study). Diabetes Care. 2011 Apr;34(4):828-37.
Jullian-Desayes I, Revol B, Chareyre E, Camus et al. Impact of **concomitant medications on obstructive sleep apnea**.Br J Clin Pharmacol. 2016 Oct 13.Kamerow D. **Getting your "T" up**. BMJ. 2014 Jan 10
Kaplan AL, Hu JC, Morgentaler A, et al. **Testosterone Therapy in Men With Prostate Cancer**. Eur Urol. 2015 Dec 21.
Kashanian JA, Brannigan RE. **Gonadotropin Interpretation** in a 25-Year-Old Man. JAMA. 2016 Mar 1;315(9):936-7.
Khaw KT, Dowsett M, Folkerd E, et al. Endogenous testosterone and mortality due to all causes, cardiovascular disease, and cancer in men. European Prospective Investigation into Cancer in Norfolk (EPIC-Norfolk) prospective population study. Circulation 2007; DOI: 10.1161/CIRCULATIONAHA.107.719005. In men, endogenous testosterone concentrations are inversely related to mortality due to cardiovascular disease and all causes. Low testosterone may be a predictive marker for those at high risk of cardiovascular disease.
Khazai B, Hill Golden S, Colangelo LA, et al. Association of **Endogenous Testosterone with Subclinical Atherosclerosis in Men**; the Multi-Ethnic Study of Atherosclerosis. Clin Endocrinol (Oxf). 2015 Dec 12.
Kimball A, Schorr M, Meenaghan E, et al. A randomized placebo-controlled **trial of low-dose testosterone therapy in women with anorexia nervosa**. J Clin Endocrinol Metab. 2019 Jun 20.
Kirk D, Misita C. Spuriously elevated testosterone measurements caused by **application of testosterone gel at or near the phlebotomy site**. Ann Pharmacother. 2013 Jan;47(1):e5.
Klein DA, Paradise SL, Goodwin ET, Caring for **Transgender and Gender-Diverse Persons**: What Clinicians Should Know. Am Fam Physician. 2018; 98(11): 645-653.
Köhler TS, Kim J, Feia K, et al. Prevalence of androgen deficiency in men with **erectile dysfunction**. Urology. 2008 Apr;71(4):693-7. Epub 2008 Mar 3. Androgen deficiency was quite common in men presenting with ED and correlated significantly with age, uncontrolled diabetes, hypercholesteremia, and anemia. Although additional prospective studies evaluating the effect of testosterone supplementation in this population are needed, clinicians, including urologists, should be keenly aware of the large overlap of patients with ED who might also have the entity, androgen deficiency in the aging male.
Kohn TP, Mata DA, Ramasamy R, et al. Effects of **Testosterone Replacement Therapy on Lower Urinary Tract Symptoms**: A Systematic Review and Meta-analysis. Eur Urol. 2016 Feb 10.
Layton JB, Li D, Meier CR, et al. **Testosterone Lab Testing** and Initiation in the United Kingdom and the United States, 2000-2011. J Clin Endocrinol Metab. 2014 Jan 1
Layton JB, Meier CR, Sharpless JL, et al. **Comparative safety of testosterone dosage forms** [online May 11, 2015]. JAMA. 2015. doi:10.1001/jamainternmed .2015.1573.
Layton JB, Kim Y, Alexander GC, Emery SL. Association between **direct-to-consumer advertising** and testosterone testing and initiation in the United States, 2009-2013.JAMA. doi:10.1001/jama.2016.21041
Layton JB, Li D, Meier CR, et al. **Injection Testosterone and Adverse Cardiovascular Events**: A Case-crossover Analysis. Clin Endocrinol (Oxf). 2018 Feb 15.
Leproult Rachel, Cauter Eve Van. Effect of 1 Week of **Sleep Restriction on Testosterone Levels** in Young Healthy Men. JAMA. 2011;305(21):2173-2174.doi:10.1001/jama.2011.710.
Liang JJ, Jolly D, Chan KJ, Safer JD. **Testosterone levels achieved by medically treated transgender women** in a United States Endocrinology clinic cohort.Endocr Pract. 2018 Feb;24(2):135-142.
Libby V, Lee M, Liu JH. Transgender health: **Hormonal management at 50 years and beyond**. Maturitas. 2019 Aug;126:34-37.
Loeb S, Folkvaljon Y, Damber JE, et al. Testosterone Replacement Therapy and Risk of **Favorable and Aggressive Prostate Cancer**. J Clin Oncol. 2017 May 1;35(13):1430-1436.
Loo SY, Azoulay L, Nie R, et al. **Cardiovascular and Cerebrovascular Safety** of Testosterone Replacement Therapy Among Aging Men with Low Testosterone Levels: A Cohort Study. Am J Med. 2019 Apr 3.
Lu PH, Masterman DA, Mulnard R, et al. Effects of Testosterone on Cognition and Mood in Male Patients With Mild **Alzheimer Disease** and Healthy Elderly Men. Arch Neurol. 2005 Dec 12; [Epub ahead of print] (InfoPOEMs: In this very small study, testosterone supplementation had negligible effects in men with Alzheimer's disease . (LOE = 2b))
Luo S, Au Yeung SL, Zhao JV, et al. Association of genetically predicted **testosterone with thromboembolism, heart failure, and myocardial infarction**: mendelian randomisation study in UK Biobank. BMJ. 2019 Mar 6;364:l476.
Malkin CJ, Pugh PJ, West JN, et al. Testosterone therapy in men with moderate severity **heart failure**: a double-blind randomized placebo controlled trial. Eur Heart J. 2005 Aug 10; [Epub ahead of print]
Marks LS, et al. Effect of Testosterone Replacement Therapy on Prostate Tissue in Men With Late-Onset Hypogonadism: A Randomized Controlled Trial. JAMA. 2006 Nov 15;296(19):2351-2361. (N=44 over 6 months) These preliminary

data suggest that in aging men with late-onset hypogonadism, 6 months of TRT normalizes serum androgen levels but appears to have little effect on prostate tissue androgen levels and cellular functions. Establishment of prostate safety for large populations of older men undergoing longer duration of TRT requires further study.
Martinez C, Suissa S, Rietbrock S, et al. Testosterone treatment and **risk of venous thromboembolism**: population based case-control study. BMJ. 2016 Nov 30;355:i5968.
Medical Letter: **Drugs for Female Sexual Dysfunction**. April 23, 2007.
Meeker JD, Ferguson KK. **Urinary Phthalate Metabolites** Are Associated With **Decreased Serum Testosterone** in Men, Women, and Children From NHANES 2011-2012. J Clin Endocrinol Metab. 2014 Aug 14
Meza J, Weaver K, Martin S. Testosterone therapy and risk recurrence after treatment of **prostate cancer**. Am Fam Physician. 2013 Oct 15;88(8).
Millar AC, Lau AN, Tomlinson G, et al. **Predicting low testosterone in aging men**: a systematic review. CMAJ. 2016 Jun 20.
Miller KK, Biller BM, Beauregard C, et al. Effects of testosterone replacement in androgen-deficient women with hypopituitarism: a randomized, double-blind, placebo-controlled study. J Clin Endocrinol Metab. 2006 May;91(5):1683-90. Epub 2006 Feb 14. This is the first randomized, double-blind, placebo-controlled study to show a positive effect of testosterone on bone density, body composition, and neurobehavioral function in women with severe androgen deficiency due to hypopituitarism.
Miner M, Heidelbaugh JJ, and Morgentaler A. **Testosterone Therapy and Cardiovascular Risk**: A Cautionary Tale. *Journal of Men's Health*11.1 (2014): 1-3.
Mogri M, Dhindsa S, Quattrin T, Ghanim H, Dandona P. **Testosterone Concentrations** In **Young Pubertal And Post-Pubertal Obese Males**. Clin Endocrinol (Oxf). 2012 Sep 13.
Mohler ER 3rd, Ellenberg SS, Lewis CE, et al. The Effect of **Testosterone on Cardiovascular Biomarkers** in the **Testosterone Trials**. J Clin Endocrinol Metab. 2018 Feb 1;103(2):681-688.
Morales A, Bebb RA. Manjoo P, et al; **Canadian Men's Health Foundation Multidisciplinary Guidelines** Task Force on Testosterone Deficiency. Diagnosis and management of **testosterone deficiency syndrome in men**: clinical practice guideline. CMAJ 2015; early release online October 26, 2015. http://www.cmaj.ca/content/early/2015/10/26/cmaj.150033.full.pdf+html (accessed October 29, 2015)

Morden NE, Woloshin S, Brooks CG, Schwartz LM. Trends in Testosterone **Prescribing for Age-related Hypogonadism** in Men With and Without Heart Disease. JAMA Intern Med. 2018 Dec 28.
Murphy EN, Miranda R. **Doubts** About Treating **Hypogonadism Due to Long-term Opioid Use With Testosterone Therapy**: A Teachable Moment. JAMA Intern Med. 2014 Dec 1;174(12):1892-3.

Mylonakis E, Koutkia P, Grinspoon S. Diagnosis and treatment of androgen deficiency in **human immunodeficiency virus**-infected men and women. Clin Infect Dis. 2001 Sep 15;33(6):857-64.
Nair KS, et al. **DHEA** (50mg) in elderly **women** and DHEA (75mg) or testosterone in **elderly men**. N Engl J Med. 2006 Oct 19;355(16):1647-59. (n= 2yr 87 males, 57 women) Men who received testosterone had a slight increase in fat-free mass, and men in both treatment groups had an increase in BMD at the femoral neck. Women who received DHEA had an increase in BMD at the ultradistal radius. Neither DHEA nor low-dose testosterone replacement in elderly people has physiologically relevant beneficial effects on body composition, physical performance, insulin sensitivity, or quality of life. {InfoPOEMS: There is no evidence that supplementation with dehydroepiandrosterone (DHEA) or testosterone has any meaningful clinical benefit for older patients with low serum levels of those hormones.}
Nguyen CP, Hirsch MS, Moeny D, et al. **Testosterone** and "**Age-Related Hypogonadism**"--**FDA Concerns**. N Engl J Med. 2015 Aug 20;373(8):689-91.
North American Menopause Society. NAMS Board of Trustees. The role of testosterone therapy in postmenopausal **women**: position statement of The North American Menopause Society. Menopause. 2005 Sep 1;12(5):497-511
[Epub ahead of print] CONCLUSIONS:
Postmenopausal women with decreased sexual desire associated with personal distress and with no other identifiable cause may be candidates for testosterone therapy. Testosterone treatment without concomitant estrogen therapy cannot be recommended because of a lack of evidence. When evaluating awoman for testosterone therapy, recommendations are to rule out causes not related to testosterone levels (eg, physical and psychosocial factors, medications) and to ensure that there is a physiologic cause for reduced testosterone levels (eg, bilateral oophorectomy). Laboratory testing of testosterone levels should be used only to monitor for supraphysiologic levels before and during therapy, not to diagnose testosterone insufficiency. Monitoring should also include subjective assessments of sexual response, desire, and satisfaction as well as evaluation for potential adverse effects. Transdermal patches and topical gels or creams are preferred over oral products because of first-pass hepatic effects documented with oral formulations. Custom-compounded products should be used with caution because the dosing may be more inconsistent than it is with government-approved products. Testosterone products formulated specifically for men have a risk of excessive dosing, although some clinicians use lower doses of these products in women. Testosterone therapy is contraindicated in women with breast or uterine cancer or in those with cardiovascular or liver disease. It should be administered at the lowest dose for the shortest time that meets treatment goals. Counseling regarding the potential risks and benefits should be provided before initiating therapy.
Ohlsson C, Barrett-Connor E, Bhasin S, et al. **High serum testosterone is associated with reduced risk of cardiovascular events** in elderly men. **The MrOS** (osteoporotic fractures in men) Study in Sweden. J Am Coll Cardiol 2011; 58:1674-1681.
Ohlsson C, Wallaschofski H, Lunetta KL, et al. **Genetic** determinants of serum **testosterone** concentrations in men. PLoS Genet. 2011 Oct;7(10):e1002313.
Okun MS, et al. Testosterone therapy in men with **Parkinson** disease: results of the TEST-PD Study. Arch Neurol. 2006 May;63(5):729-35.
Orme C, Imaeda S. Images in clinical medicine. **Eschar formation from testosterone patch.** N Engl J Med. 2012 May 3;366(18):e28.
Orwoll E, et al. **Osteoporotic Fractures** in Men Study Group. Endogenous testosterone levels, physical performance, and fall risk in older men. Arch Intern Med. 2006 Oct 23;166(19):2124-31. Falls were common among older men. Fall risk was higher in men with lower bioavailable testosterone levels. The effect of testosterone level was independent of poorer physical performance, suggesting that the effect of testosterone on fall risk may be mediated by other androgen actions.
Ottenbacher KJ, et al. Androgen treatment and **muscle strength** in elderly men: a meta-analysis. J Am Geriatr Soc. 2006 Nov;54(11):1666-73.
Paduch DA, Brannigan RE, Fuchs EF, et al. The **Laboratory Diagnosis of Testosterone Deficiency**. Urology. 2014 Feb 16
Paduch DA, Polzer PK, Ni X, et al. Testosterone Replacement in Androgen-Deficient Men With **Ejaculatory Dysfunction**: A Randomized Controlled Trial. J Clin Endocrinol Metab. 2015 Jul 9
Page ST, Amory JK, Bowman ED, et al. Exogenous **testosterone** (T) alone or with finasteride increases **physical performance**, grip, strength, and lean body mass in older men with low serum T. J Clin Endocrinol Metab 2005;90:1502-10.
Page ST. **Testosterone, cardiovascular disease, and mortality** in men: living in the dark. Lancet Diabetes Endocrinol. 2014 Apr 25.
Palmert Mark R, Dunkel Leo. **Delayed Puberty**. N Engl J Med 2012; 366:443-453.
Pantalone KM, Faiman C. **Male hypogonadism**: More than just a low testosterone. Cleve Clin J Med. 2012 Oct;79(10):717-725.
Pearson J, Blackman MR. Longitudinal effects of **aging on serum total and free testosterone levels** in healthy men. J Clin Endocrinol Metab 2001;86:724-31.
Perry-Keene D. Low **Testosterone in Men**. Australian Prescriber.2014;37:196-200
Petering RC, Brooks NA. **Testosterone Therapy**: Review of Clinical Applications. Am Fam Physician. 2017;96(7):441-449.
Pharmacists Letter. **Testim** (Testosterone 1% gel). June 2007.
Pikwer M, Giwercman A, Bergström U, et al. Association between testosterone levels and risk of future **rheumatoid arthritis** in men: a population-based case-control study. Ann Rheum Dis. 2013 Apr 3.
Ponce OJ, et al. The **efficacy & adverse events of testosterone replacement** therapy in hypogonadal men: A systematic review and meta-analysis of randomized, placebo-controlled trials. J Clin Endocrinol Metab. 2018 Mar 17.
Popat VB, Calis KA, Kalantaridou SN, et al. Bone Mineral Density in Young Women With Primary Ovarian Insufficiency: Results of a Three-Year Randomized Controlled Trial of Physiological **Transdermal Estradiol and Testosterone** Replacement. J Clin Endocrinol Metab. 2014 Jun 6:jc20134145.
Qaseem A, Snow V, Denberg TD, Casey DE Jr, Forciea MA, Owens DK, Shekelle P, Clinical Efficacy Assessment Subcommittee of the American College of Physicians. **Hormonal testing** and pharmacologic treatment of erectile dysfunction: a clinical practice guideline from the American College of Physicians. Ann Intern Med 2009 Nov 3;151(9):639-49.
Raynor MC, Carson CC, Pearson MD, Nix JW. **Androgen deficiency in the aging male**: a guide to diagnosis and testosterone replacement therapy. **Can J Urol. 2007** Dec;14 Suppl 1:63-8.
Resnick SM, Matsumoto AM, Stephens-Shields AJ, et al. Testosterone treatment and **cognitive function** in older men with low testosterone and age-associated memory impairment. JAMA 2017; 317:717-727.
Roy CN, Snyder PJ, Stephens-Shields AJ, et al. Association of testosterone levels with **anemia** in older men: a controlled clinical trial. JAMA Intern Med. doi:10.1001/jamainternmed.2016.9540
Ruige JB, Ouwens DM, Kaufman JM. **Beneficial and Adverse Effects of Testosterone on the Cardiovascular System** in Men. J Clin Endocrinol Metab. 2013 Sep 24.
Rosenthal BD, et al. Adjunctive use of AndroGel(testosterone gel) with sildenafil to treat erectile dysfunction in men with acquired androgen deficiency syndrome after failure using sildenafil alone.Urology.2006Mar;67(3):571-4.
Ross JL, Kushner H, Kowal K, et al. Androgen Treatment Effects on **Motor Function, Cognition, and Behavior in Boys with Klinefelter Syndrome**. J Pediatr. 2017 Mar 10.
Salem JE, Waintraub X, Courtillot C, et al. **Hypogonadism as a Reversible Cause of Torsades de Pointes** in Men. Circulation. 2018 Jul 3;138(1):110-113.
Sargis RM, Davis AM. **Evaluation and Treatment of Male Hypogonadism**. JAMA. 2018 Mar 17.
Saxbe DE, Schetter CD, et al. **High paternal testosterone** may **protect against postpartum depressive symptoms in fathers**, but confer risk to mothers and children. Hormones and Behavior, 2017; 95.
Schwartz LM, Woloshin S. **Low "t" as in "template"**: how to sell disease. JAMA Intern Med. 2013 Aug 12;173(15):1460-2.

Shahabi S, He S, Kopf M, Mariani M, Petrini J, et al. (2013) **Free Testosterone Drives Cancer Aggressiveness:** Evidence from US Population Studies. PLoS ONE 8(4): e61955.
Sharma R, Oni OA, Gupta K, et al. **Normalization of testosterone** level is associated with r**educed incidence of myocardial infarction and mortality** in men. Eur Heart J. 2015 Aug 6.
Shifren JL, et al. Testosterone patch for the treatment of hypoactive sexual desire disorder in naturally menopausal **women**: results from the INTIMATE NM1 Study. Menopause. 2006 Aug 22; [Epub ahead of print]
Shimon I, Eshed V, Doolman R, Sela BA, Karasik A, Vered I. **Alendronate for osteoporosis** in men with androgen-repleted hypogonadism. Osteoporos Int. 2005 Dec;16(12):1591-6. Epub 2005 Mar 15.
Snyder PJ, Bhasin S, Cunningham GR, et al. Effects of **Testosterone Treatment in Older Men. (TTrials)** N Engl J Med. 2016 Feb 18;374(7):611-624.
Somboonporn W, Davis S, Seif M, Bell R, Davis S. Testosterone for peri- and postmenopausal **women**. Cochrane Database Syst Rev. 2005 Oct 19;(4):CD004509.
Spack NP. Management of **transgenderism**. JAMA. 2013 Feb 6;309(5):478-84.
Spitzer M, Basaria S, Travison TG, et al. Effect of **testosterone replacement on response to sildenafil** citrate in men with erectile dysfunction: a parallel, randomized trial. Ann Intern Med. 2012 Nov 20;157(10):681-91.
Spratt DI, et al. **Subcutaneous Injection of Testosterone** is an Effective and Preferred **Alternative to Intramuscular Injection**: Demonstration in Female-to-Male Transgender Patients. J Clin Endocrinol Metab. 2017 Apr 3.
Srinivas-Shankar U et al. Effects of **testosterone** on muscle strength, physical function, body composition, and quality of life in intermediate-frail and frail elderly men: A randomized, double-blind, placebo-controlled study. J Clin Endocrinol Metab 2010 Feb; 95:639.
Stanworth RD, Kapoor D, Channer KS, Jones TH. Statin therapy is associated with lower total but not bioavailable or free testosterone in men with type 2 diabetes. Diabetes Care. 2008 Dec 29. [Epub ahead of print] Assessing androgen status using TT in men with type 2 diabetes treated with statins, particularly **atorvastatin**, may potentially lead to diagnostic error. BT or FT are recommended for the assessment of hypogonadism in this group if TT levels are borderline.
Sugerman DT. JAMA **patient page. Low testosterone**. JAMA. 2013 Nov 6;310(17):1872.
Swerdloff R, Anawalt BD. Clinical decisions. **Testosterone-replacement therapy**. N Engl J Med. 2014 Nov 20;371(21):2032-4.
Snyder PJ, Kopperdahl DL, et al. Effect of testosterone treatment on volumetric **bone density and strength** in older men with low testosterone: a controlled clinical trial. JAMA Intern Med. doi:10.1001/jamainternmed.2016.9539
Tanrikut C, Goldstein M, Rosoff JS, Lee RK, Nelson CJ, Mulhall JP. **Varicocele** as a risk factor for androgen deficiency and effect of repair. BJU Int. 2011 Mar 24. doi: 10.1111/j.1464-410X.2010.10030.x.
Toma M, McAlister FA, Coglianese EE, et al. **Testosterone Supplementation in Heart Failure**: A Meta-Analysis. Circ Heart Fail. 2012 Apr 17.
Traish AM, Haider A, Doros G, Saad F. **Long-term testosterone therapy in hypogonadal men** ameliorates elements of the metabolic syndrome: an observational, long-term registry study. Int J Clin Pract. 2013 Oct 15.
Traish AM, et al. Long-Term Testosterone Therapy **Improves Cardiometabolic Function** & Reduces Risk of Cardiovascular Disease in Men with Hypogonadism. J Cardiovasc Pharmacol Ther. 2017 Jan 1:1074248417691136.
Travison TG, Vesper HW, Orwoll E et al. **Harmonized Reference Ranges** for Circulating **Testosterone Levels** in Men of Four Cohort Studies in the USA and Europe. J Clin Endocrinol. Metab. 2017. Online.
Vigen R, O'Donnell CI, Barón AE, Grunwald GK, Maddox TM, Bradley SM, et al. Assoiation of **testosterone therapy with mortality, myocardial infarction, and stroke** in men with low testosterone levels. JAMA. 2013 Nov 6;310(17):1829-36. doi:10.1001/jama.2013.280386.
Wallis CJ, Lo K, Lee Y, et al. **Survival and cardiovascular events** in men treated with **testosterone replacement therapy**: intention-to-treat observational cohort study. Lancet Diabetes Endocrinol. 2016 Jun;4(6):498-506.
Walter LC, Bertenthal D, Lindquist K, Konety BR. **PSA screening** among elderly men with limited life expectancies. JAMA. 2006 Nov 15;296(19):2336-42.
Wang C, Nieschlag E, Swerdloff R, et al. **Investigation, treatment, and monitoring** of late-onset hypogonadism in males: ISA, ISSAM, EAU, EAA, and ASA recommendations. J Androl 2009;30:1-9.
Weickhardt AJ, Doebele RC, Purcell WT, et al. Symptomatic **reduction in free testosterone levels secondary to crizotinib** use in male cancer patients. Cancer. 2013 Apr 12.
Welliver RC Jr, Wiser HJ, et al. Validity of **Midday Total Testosterone Levels** in Older Men with Erectile Dysfunction. J Urol. 2014 Feb 8. pii: S0022-5347(14)00115-3.
Westley CJ, Amdur RL, Irwig MS. High Rates of **Depression and Depressive Symptoms** among Men Referred for Borderline Testosterone Levels. J Sex Med. 2015 Jun 30.
Wibral M, Dohmen T, Klingmüller D, et al. Testosterone administration **reduces lying** in men. PLoS One. 2012;7(10):e46774.
Wierman ME, Basson R, Davis SR, Khosla S, et al. **Androgen therapy in women**: an Endocrine Society Clinical Practice guideline. J Clin Endocrinol Metab. 2006 Oct;91(10):3697-710. Epub 2006 Oct 3.
Wierman ME, Arlt W, Basson R, et al. **Androgen therapy in women**: a reappraisal: an endocrine society clinical practice guideline. J Clin Endocrinol Metab. **2014** Oct;99(10):3489-510.
Wu, Frederick C.W., Tajar, Abdelouahid, Beynon, Jennifer M. et al; the EMAS Group, **Identification of Late-Onset Hypogonadism** in Middle-Aged and Elderly Men. N Engl J Med 2010 0: NEJMoa0911101. Late-onset hypogonadism can be defined by the presence of at least three sexual symptoms associated with a total testosterone level of less than 11 nmol per liter (3.2 ng per milliliter) and a free testosterone level of less than 220 pmol per liter (64 pg per milliliter).
Wunder DM, et al.; Swiss HIV Cohort Study. Androgen and gonadotropin patterns differ in **HIV-1-**infected men who develop lipoatrophy during antiretroviral therapy: a case-control study. HIV Med. 2008 Jul;9(6):427-32.
Wylie K, Rees M, Hackett G, et al. **Androgens, health and sexuality in women and men**. Hum Fertil (Camb). 2010 Dec;13(4):277-97.
Xu L, Freeman G, Cowling BJ, Schooling CM. **Testosterone therapy and cardiovascular events** among men: a systematic review and meta-analysis of placebo-controlled randomized trials. BMC Med. 2013 Apr 18;11:108.
Yassin A, Haider A, Haider KS, et al. **Testosterone Therapy in Men With Hypogonadism** Prevents Progression From Prediabetes to Type 2 Diabetes: Eight-Year Data From a Registry Study. Diabetes Care. 2019 Mar 12.
Yeap BB, Alfonso H, Chubb SA, et al. In **Older Men an Optimal Plasma Testosterone Is Associated With Reduced All-Cause Mortality** and Higher Dihydrotestosterone With Reduced Ischemic Heart Disease Mortality, While Estradiol Levels Do Not Predict Mortality. J Clin Endocrinol Metab. 2013 Nov 20.
Zarrouf FA, Artz S, Griffith J, Sirbu C, Kommor M. **Testosterone and depression**: systematic review and meta-analysis. J Psychiatr Pract. 2009 Jul;15(4):289-305.

[24] Padero MC, Bhasin S, Friedman TC. Androgen supplementation in older women: too much hype, not enough data. J Am Geriatr Soc. 2002 Jun;50(6):1131-40. (Barton DL, Wender DB, Sloan JA, et al. Randomized controlled trial to evaluate transdermal testosterone in female cancer survivors with decreased libido; North Central Cancer Treatment Group protocol N02C3.J Natl Cancer Inst. 2007 May 2;99(9):672-9. Increased testosterone level did not translate into improved libido, possibly because women on this study were estrogen depleted.) (El-Hage G, Eden JA, Manga RZ. A double-blind, randomized, placebo-controlled trial of the effect of testosterone cream on the sexual motivation of menopausal hysterectomized women with hypoactive sexual desire disorder. Climacteric. 2007 Aug;10(4):335-43.Testosterone cream significantly improved sexual scores in menopausal women with low sexual desire. It was effective, easy to use and had no side-effects over the 3-month period of active treatment. It offers a novel and acceptable method of administering testosterone to menopausal women.) Davis SR, Nijland EA. Pharmacological Therapy for Female Sexual Dysfunction : Has Progress Been Made? Drugs. 2008;68(3):259-264.

References:

Gerstein HC, Colhoun HM, Dagenais GR, et al; REWIND Investigators. Dulaglutide and renal outcomes in type 2 diabetes: an exploratory analysis of the **REWIND** randomised, placebo-controlled trial. Lancet. 2019;394:131-138. https://doi.org/10.1016/S0140-6736(19)31150-X.

Husain M, Birkenfeld AL, Donsmark M, et al. For the **PIONEER 6** investigators. Oral semaglutide and cardiovascular outcomes in patients with type 2 diabetes. N Engl J Med. June 11, 2019. https://doi.org/10.1056/NEJMoa1901118.

Marso SP, Daniels GH, Brown-Frandsen K, et al. Liraglutide and Cardiovascular Outcomes in Type 2 Diabetes. (**LEADER**) N Engl J Med. 2016 Jun 13

Marso SP, Bain SC, Consoli A, et al. Semaglutide and Cardiovascular Outcomes in Patients with Type 2 Diabetes. (**SUSTAIN-6**) N Engl J Med. 2016 Nov 10;375(19):1834-1844.

McMurray JJV, Solomon SD, Inzucchi SE, Køber Let al; **DAPA-HF** Trial Committees and Investigators. Dapagliflozin in Patients with Heart Failure and Reduced Ejection Fraction. N Engl J Med. 2019 Sep 19.

Neal B, Perkovic V, Mahaffey KW, de Zeeuw D, Fulcher G, Erondu N, Shaw W, Law G, Desai M, Matthews DR; **CANVAS** Program Collaborative Group. Canagliflozin and Cardiovascular and Renal Events in Type 2 Diabetes. N Engl J Med. 2017 Aug 17;377(7):644-657. doi: 10.1056/NEJMoa1611925. Epub 2017 Jun 12. PubMed PMID:28605608.

Perkovic V, Jardine MJ, Neal B, Bompoint S; **CREDENCE** Trial Investigators. Canagliflozin and Renal Outcomes in Type 2 Diabetes and Nephropathy. N Engl J Med. 2019 Apr 14.

Wiviott SD, Raz I, Bonaca MP, Mosenzon O, Kato ET, Cahn A, Silverman MG, Zelniker TA, Kuder JF, Murphy SA, Bhatt DL, Leiter LA, McGuire DK, Wilding JPH,Ruff CT, Gause-Nilsson IAM, Fredriksson M, Johansson PA, Langkilde AM, Sabatine MS; **DECLARE–TIMI 58** Investigators. Dapagliflozin and Cardiovascular Outcomes in Type 2 Diabetes. N Engl J Med. 2019 Jan 24;380(4):347-357. doi:10.1056/NEJMoa1812389. Epub 2018 Nov 10.

Zinman B, Wanner C, Lachin JM, Fitchett D, Bluhmki E, Hantel S, Mattheus M, Devins T, Johansen OE, Woerle HJ, Broedl UC, Inzucchi SE; **EMPA-REG OUTCOME** Investigators. Empagliflozin, Cardiovascular Outcomes, and Mortality in Type 2 Diabetes. N Engl J Med. 2015 Nov 26;373(22):2117-28.doi:10.1056/NEJMoa1504720. Epub 2015 Sep 17. PubMed PMID: 26378978.

Death/MACE (MACE: Major adverse cardiovascular event)

1. Drug manufacturers must establish CV safety (one-sided upper boundary of 95% CI ≤ 1.3) vs comparator (typically placebo) in a RCT for all new agents in ↑ CV risk patients.[1] FDA
2. Metformin vs conventional diet; obese >120% IBW & small sample n=753; ↓ **all-cause mortality NNT 14/10.7 yr**, and ↓ **MI NNT=14/10.7 yr**.[2] UKPDS-34 10 yr observational follow-up ↓ **all-cause mortality NNT=14/~20 yr**, and ↓ **MI NNT=16/~20 yr**.[3] UKPDS-80
3. Intensive HbA1c target (included gliclazide) vs standard HbA1c target; MACE 10% vs 10.6% p=NS, all-cause mortality 8.9% vs 9.6% p=NS.[4] ADVANCE
4. Intensive therapy (chlorpropamide, glipizide[USA], glibenclamide or insulin) vs conventional diet; all-cause mortality 17.9% vs 18.9% p=NS, MI 14.7% vs 17.4% p=NS, and stroke 5.6% vs 5% p=NS.[5] UKPDS-33 10 yr observational follow-up ↓ **all-cause mortality NNT=29/~20 yr**, and ↓ **MI NNT=36/~20 yr**.[3] UKPDS-80
5. SU (2nd or 3rd generation) vs control (diet, placebo, other antihyperglycemic); all-cause mortality OR 1.12 (0.96-1.3, I^2=0%), CV mortality OR 1.12 (0.87-1.42, I^2=12%), MI OR 0.92 (0.76-1.12, I^2=NR), stroke OR 1.16 (0.81-1.66, I^2=NR).[6]
6. Metformin vs glipizide; Chinese, small sample n=304, & medically undertreated 100% CAD, but ≤10% taking ACEi; Metformin ↓ **MACE NNT=10/5 yr**.[7] SPREAD-DIMCAD
7. Pioglitazone vs placebo; T2DM & high CV risk; ↓ **MACE NNT=50/2.9 yr**,[8] PROACTIVE insulin resistance & recent TIA/stroke; ↓**MACE NNT=36/4.8 yr**.[9] IRIS
8. Rosiglitazone vs placebo; ↑ **MACE** 2.9% vs 2.1% p=0.08 (NS), trial stopped 5 mons early,[10] DREAM ↑ MI NNH=167 & CV death 0.87% vs 0.39% p=0.06.[10] Rosiglitazone vs glyburide ↑ **MACE NNH 63/4 yr**.[12] ADOPT
9. Acarbose vs placebo; impaired glucose tolerance; ↓ **MACE NNT 40/3.3 yr**.[13] STOP-NIDDM Acarbose vs placebo; coronary heart disease (Chinese) HR 0.98 95% CI, 0.86-1.11, p=0.73.[13] ACE
10. Saxagliptin vs placebo; MACE 7.3% vs 7.2%, **non-inferior** (p<0.001), but not superior (p=0.99).[14] SAVOR-TIMI 53 Alogliptin vs placebo; MACE 11.3% vs 11.8%, **non-inferior** (p<0.001), but not superior (p=0.32).[15] EXAMINE Sitaglipin MACE vs placebo; MACE 9.6% vs 9.6%, **non-inferior** (p<0.001), but not superior (p=0.65).[16] TECOS Meta-analysis(SAVOR-TIMI 53, EXAMINE, TECOS) MACE RR 0.99 (95% CI, 0.93-1.06, I^2=0%).[17]
11. Linagliptin vs placebo; MACE 12.4% vs 12.1% **non-inferior** (p<0.001), but not superior (p=0.74).[18] CARMELINA Linagliptin vs glimepiride: MACE 11.8% vs 12% non-inferior (p<0.001) but not superior.CAROLINA2019
12. Liraglutide vs placebo; **MACE** 13% vs 14.9%, **superior** (p=0.01, **NNT=53/3.8 yr**), but results neutral in North America subgroup; ↓ **CV death NNT=77/3.8 yr** and ↓ **all-cause mortality NNT 72/3.8 yr**.[19] LEADER Semaglutide SC weekly vs placebo; MACE **superior**; (nephropathy was better; however, retinopathy complications were worse).[20] SUSTAIN6
13. Lixisenatide vs placebo (post-ACS); MACE 13.4% vs 13.2%, **non-inferior** (p<0.001), not superior (p=0.81).[21] ELIXA
14. Exenatide extended release vs placebo (~70% CVD, ~30% primary prevention); MACE 11.4% vs 12.2% over median 3.2 yr, **non-inferior** (p<0.001), but not superior (p=0.06).[22] EXSCEL Dulaglutide[USA] CV trial
19. Intensive insulin vs standard insulin; T1DM population; ~11 yr observational follow up ↓ **MACE NNT=23/ ~17 yr**.[32] DCCT, [33] EDIC
20. Insulin basal/bolus vs conventional diet; all-cause mortality 18.6% vs 19.9% p=NS, MI 15.8% vs 17.9%

Death/MACE (MACE: Major adverse cardiovascular event)- cont'd

p=NS, and stroke 5.4% vs 5.0% p=NS.[5] UKPDS-33 10 yr observational follow-up ↓ **all-cause mortality NNT=29/~20 yr**, and ↓ **MI NNT=36/~20 yr**.[3] UKPDS-80

21. Greater insulin use (any & bolus) with intensive therapy vs standard therapy; ↑ **MACE NNT=33/3.5 yr** and ↑**CV death NNT=125/3.5 yr**.[34] ACCORD
    Insulin degludec vs insulin glargine (T2DM; ~50/50 split bolus vs bolus/basal baseline & no difference between basal/bolus insulin use between groups at the end of study): MACE 8.5% vs 9.3% (95% CI 0.78- 1.06; p<0.001 non-inferiority).[34a] DEVOTE

Weight (weight gain/loss variable, diabetic agents used in conjunction with diet and lifestyle interventions as well as other concomitant medications)

A1. Metformin: ↓ 2.9 kg/4 yr [1] ADOPT
A2. Sulfonylureas: ↑ 1.6 kg/4 yr [1] ADOPT
A3. Pioglitazone: ↑ 3.6 kg/3 yr [2] PROACTIVE
A4. Rosiglitazone: ↑ 4.8 kg/4 yr; rosiglitazone statistically significant ↑ weight vs. both metformin & glyburide [1] ADOPT
A5. Acarbose: ↓1.15 kg/3 yr [3] STOP-NIDDM
A6. Repaglinide: ↑ ~1.7 kg/12-24 wks;[4,5] nateglinide: ↑ 0.7-1 kg/16-24 wks[4.6]
A7. DPP4-inhibitors (generally considered neutral)[7]
- saxagliptin ↓ 0.4 kg/2.1 year (similar to placebo) [8] SAVOR-TIMI 53
- alogliptin ↑ 1 kg/18 months (similar to placebo) [9] EXAMINE
- sitagliptin ↑ ≤ 0.5 kg/12 weeks[10]

A8. GLP-1 agonists
- exenatide ↓ 2.8 kg/24-52 weeks[11]
- liraglutide ↓ 2.3 kg/3.8 yr [12] LEADER
- dulaglutide ↓1.3-3 kg/5-52 weeks[13]

A9. SGLT2 inhibitors[14]
- canagliflozin ↓ 2.8-4 kg/4-52 weeks[15,16] CANTATA-M
- dapagliflozin ↓ 2 kg/12-52 weeks[17]
- empagliflozin ↓ ~1.5-2 kg/3.1 y[18] EMPA-REG

A10. Insulin

ongoing, estimated completed 2018.[23] REWIND Albiglutide CV trial ongoing, estimated completed 2018.[24] HARMONY Semaglutide PO CV trial semaglutide po vs placebo: MACE, non-inferior; ↓ all-cause death 1.4% vs 2.8% 2ndy endpoint 2019. PIONEER-6

15. Empagliflozin vs placebo; **MACE** 10.5% vs 12.1%, **superior** (p=0.04, **NNT=63/3.1 yr**); **↓ CV death NNT=46/3.1 yr** and **↓ all-cause mortality NNT 39/3.1 yr**.[25] EMPA-REG Canagliflozin vs placebo; **MACE** 26.9/1000ptyrs (2.7%/yr) vs 31.5/1000ptyrs (3.15%/yr), **superior** (p=0.02, **NNT~220/yr**), f/u duration 3.6yr, no signfigant difference in components of primary composite or death; ↑ MACE in 1st 30 days (n=13 vs n=1, p=NS, non-dose related); ↓ MACE (NS) after 30 days (HR 0.89, 95% CI 0.64, 1.25); numeric imbalance not present in non-CANVAS trials. [26,27,27a] CANVAS Dapagliflozin vs placebo; MACE 8.8% vs 9.4% p<0.001 **non-inferior**, but not superior p=0.17; ↓ CV death & HF hospitalization combo outcome.[28] DECLARE
16. Ertugliflozin CV trial ongoing, estimated completed 2019.[29] VERTIS CV Sotagliflozin CV trial ongoing, estimated completed 2022. SCORE
17. Basal insulin (glargine) vs standard care; all-cause mortality 15.2% vs 15.4% p=NS, MI 5.4% vs 5.2% p=NS, and stroke 5.3 vs 5.1% p=NS.[30] ORIGIN
18. Basal insulin vs basal/bolus insulin; small sample n=152; CV mortality 3.8% vs 6.7% p=NS, MACE 20% vs 32% p=NS.[31]

HF/Edema- cont'd

29. Repaglinide vs rosiglitazone: peripheral edema 0% vs 3.2%, p=N/A.[9]
30. Saxagliptin vs placebo; **↑ hospitalization for HF NNH=143/2.1 yr**; however, subgroup without a history of HF at baseline **↑ hospitalization for HF NNH=147/2.1 yr**, subgroup eGFR <60 mL/min **↑ hospitalization for HF NNH=68/2.1 yr** & no difference from 12 months on (HR 1.05, 95% CI 0.81-1.35).[10, 11] SAVOR-TIMI 53 Alogliptin vs placebo; hospitalization for HF 3.9% vs 3.3% p=0.22; subgroup without a history of HF at baseline **↑ hospitalization for HF NNH=111/1.5 yr**.[12,13] EXAMINE Sitaglipin vs placebo; hospitalization for HF 3.1% vs 3.1% p=0.98; and neutral results when adjusted for baseline HF (aHR 1.00, 95% CI 0.83-1.20 [unpublished data]).[14,15] TECOS Meta-analysis(SAVOR-TIMI 53, EXAMINE, TECOS) HF admission RR 1.12 (95% CI, 1.00-1.25, I^2=42%).[16] FDA warnings for both saxagliptin & alogliptin.[17] Linagliptin vs placebo; hospitalization for heart failure 6.0% vs 6.5% for an absolute incidence rate difference of −0.27 (95% CI, −0.82 to 0.28), with no significant difference between the 2 treatment groups (HR, 0.90; 95% CI, 0.74-1.08; P = .26).CARMELINA
31. Liraglutide vs placebo; hospitalization for HF: 4.7% vs 5.3% p=0.14.[18] LEADER Lixisenatide vs placebo; hospitalization for HF: 4.0% vs 4.2% p=0.75.[19] ELIXA
32. Empagliflozin vs placebo; hospitalization for HF: 2.7% vs 4.1% p=0.002.[20] EMPA-REG Empagliflozin in HF patients (regardless of diabetes status) ongoing trial estimated to be complete 2020 EMPEROR-Reduced & Preserved. Canagliflozin vs placebo; hospitalization for HF: 5.5/1000ptyrs (0.55%/yr) vs 8.7/1000ptyrs (0.87%/yr) (HR 0.67, 95% CI 0.52-0.87) follow up 3.6yr but exploratory.[27a] CANVAS Dapagliflozin vs placebo; hospitalization for HF: 2.5%/1000 patient year vs 3.3%/1000 patient year HR0.73 (95% CI 0.61-0.88) but exploratory.[28] DECLARE Dapagliflozin 10mg po once daily vs placebo; composite primary outcome: worsening HF (hospitalization or urgent visit resulting in IV therapy for heart failure) or CV death:
16.3% vs 21.2% p=<0.001. DAPA-HF
33. Basal insulin (glargine) vs standard care; hospitalization for HF 4.9% vs 5.5% p=NS.[21] ORIGIN
34. Basal insulin vs basal/bolus insulin; small sample n=152; HF 1.3% vs 5.3% p=NS.[22] ArchInternMed1997

Other/Additional Trials Recently Published

35. Pioglitazone & Rosiglitazone FDA +/- Health Canada warnings/label changes:
    - ?↑ HF (see above) [1] PROACTIVE, [2] RECORD, [3] DREAM, [4, 5]
    - ?↑ fractures ♀; pioglitazone vs placebo 5.1 vs 2.5%, calculated p=0.005 ?↑ fractures ♀ **NNH=38/2.9 yr** (unpublished PROACTIVE data).[6] Rosiglitazone vs MF ↑ fractures ♀ **NNH=24/4 yr**, rosiglitazone vs glyburide ↑ fractures ♀ **NNH=17/4 yr**.[8] ADOPT Post marketing data: pioglitazone exposure in women associated **0.8 excess fractures (distal upper and lower limbs)/100 patient-years** vs comparator treated group.[8] No ↑ risk in males.[8,9]
    - intensive therapy vs standard therapy; avg weight ↑ 3.5 kg vs 0.4 kg/3.5 y; weight ↑ >10 kg 28% vs 14% p<0.00[19] ACCORD
    - Note: detemir -1.27 to -0.8 kg vs NPH (glargine no difference vs NPH)[20]

HF/Edema

22. MF should be considered 1st line in HF patients with eGFR > 30 mL/min [Grade D, Consensus].[1] CDA'13
23. Retrospective cohort (n=10,920 patients hospitalized with HF); MF vs SU **↓ all-cause mortality aHR 0.85 (95% CI 0.75-0.98)**, MF + SU vs MF **↓ all-cause mortality aHR 0.89 (95% 0.82-0.96),** MF + insulin vs SU neutral aHR0.96 (95% CI 0.82-1.13), MF+SU+insulin neutral aHR 0.94 (0.77-1.15).[2]
24. Intensive A1C target (included gliclazide) vs standard A1C target; HF (HF death, HF hospitalization, worsening NYHA class) 3.9% vs 4.1% p=NS.[3] ADVANCE
25. Glyburide vs rosiglitazone; **↓HF** (serious events) **NNT 167/3.5 yr, ↓HF** (total events) **NNT=67/3.5 yr.**[4] ADOPT
26. Pioglitazone vs placebo; **↑ hospitalization for HF NNH=50/2.9 yr** (not adjudicated), **↑ edema (without HF) NNH=8/2.9 yr**.[5] PROACTIVE
27. Rosiglitazone +meformin or SU vs control; **↑ hospitalization for HF or HF death NNH=69/5.5 yr**.[6] RECORD Rosiglitazone vs placebo; **↑ HF NNT=250/3 yr**.[7] DREAM
28. Acarbose vs placebo; impaired glucose tolerance; HF 0% vs 0.3% p=N/A.[8] STOP-NIDDM

Other- continued

or sitagliptin/metformin of which n=58 cases were hospitalized (n=4 cases admitted to the ICU), n=2 cases of hemorrhagic or necrotizing pancreatitis.[27] Listed adverse event for other agents (e.g., liraglutide) in product monograph.

40. Incretin agents (DPP-4 inhibitors and GLP-1 agonists) ?↑ pancreatic cancer: n=13 pancreatic cancer cases suspected of being associated with all incretin-based therapies (July 31, 2014).[24,28]
41. Liraglutide: ?↑ thyroid C-cell tumor (including medullary thyroid carcinoma) in animal studies (both genders, dose-dependent, and treatment-duration-dependent).[29]
42. ?↑/↓ GI (nausea, diarrhea, vomiting) AE with long acting agents[30,31]: **↑ GI AE**: taspoglutide once weekly 59% vs exenatide BID 35% (clinical development of taspoglutide has been stopped).[32] **↓ GI AE:** Exenatide once weekly 28% vs exenatide BID 48%, albiglutide once weekly 29.8% vs liraglutide daily 52%, exenatide once weekly 19.1% vs liraglutide daily 44.5%.[33] DURATION-5,[34] HARMONY-7,[35] DURATION-6 Neutral GI: dulaglutide once weekly 39.4% vs liraglutide daily 38.3%.[36] AWARD-6
43. SGLT-2 inhibitors FDA +/- Health Canada warnings/label changes:
    - ?↑ diabetic ketoacidosis; n=5 Canadian cases, some requiring hospitalization (May 2016); n= 73 US cases (n=44 T2DM cases, n=15T1DM cases, n=13 NR) (Mar 2013-2015) all requiring hospitalization or emergency department care.[37,38]
    - ?↑ urosepsis & pyelonephritis; n=19 cases requiring hospitalizations (canagliflozin [n=10 cases] and dapagliflozin [n=9 cases]), of which n=4 cases required ICU admission and n=2 cases required hemodialysis (Mar 2013-Oct 2014).[38]
    - ?↑ AKI; n=2 Canadian cases (Canagliflozin) (Oct 2015); n=101 US cases (Mar 2013-Oct 2015), of which n=96 cases required hospitalization (n=22 cases required ICU admission), n=15 cases required hemodialysis, and n=4 cases resulted in death. ~50% of cases occurred within 1 month of drug initiation; empagliflozin not included in review due to recent approval.[39,40]
    - ?↑ fracture; canagliflozin 100 mg-300 mg vs placebo follow up 3.6yr; 15.4/1000ptyrs (1.54%/yr) vs 11.9/1000ptyrs (1.19%/yr) NNT= 285/yr (HR 1.26, 95% CI 1.04-1.52),. CANVAS ?↓BMD (total hips, lumbar spine, femoral neck, & distal forearm).[41]
    - ?↑ lower limb amputation; canagliflozin 100-300 mg vs placebo follow up 3.6yr; ↑ all amputation 6.3/1000ptyrs (.63%/yr) vs 3.4/1000ptyrs (0.34%/yr) NNH=345/yr (HR 1.97, 95% CI 1.41-2.75) & ↑ major amputation (ankle, below/above knee) 1.8/1000ptyrs (0.18%/yr) vs 0.9/1000ptyrs (0.09%/yr) NNH>1000/yr (HR 2, 95% CI 1.08-3.82) .CANVAS Other trials neutral.e.g.,CANVAS-R [42,43] May2017 FDA: canaglifozin -increased risk of leg and foot amputations. https://www.fda.gov/Drugs/DrugSafety/ucm557507.htm?source=govdelivery&utm_medium=email&utm_source=govdelivery
44. ?↑UTI; SGLT2 inhibitor vs placebo: **OR 1.34 (1.03-1.74, I^2=0%)**, vs active agent: OR 1.42 (1.06-1.9, I^2=25%). ↑ genital tract infection; SGLT2 inhibitor vs placebo **OR 3.50 (2.46-4.99, I^2=0%)**, vs active agent: OR 5.06 (3.44-7.45, I^2=0%).[44]

- ?↑ diabetic macular edema: retrospective cohort, TZD users vs nonusers ↑ macular edema 1 yr follow up aOR 2.3 (1.5-3.6) & 10 yr follow up HR 2.3 (1.7-3.0).[10] Cross-section of **ACCORD** ↑macular edema aOR, 0.97 (0.67-1.40).[11] Note- only rosiglitazone has a warning.[12]

36. Piog: ?↑ bladder cancer; France, retrospective observational cohort pioglitazone exposure vs other diabetic agent HR 1.22 (1.03-1.43), pioglitazone exposure **cumulative dose > 28 000** mg vs other diabetic agent HR 1.75 (1.22-2.5), pioglitazone **exposure >12 months** vs other diabetic agent HR 1.28 (1.09-1.51).[13] US, prospective observational cohort (5 yr interim analysis) pioglitazone exposure vs never exposed HR 1.2 (0.9-1.5), pioglitazone exposure >12 months vs never exposed HR 1.4 (0.9-2.1), & piogltazone exposure >24 months vs never exposed HR 1.4 (1.03-2.0).[14] FDA calculated pioglitazone >12 months associated **27.5 excess cases of bladder cancer /100,000 person-yrs** vs never exposed.[15,16]
37. Rosigltazone FDA +/- Health Canada warnings/label changes: restricted access- in Canada (SK-EDS) due to ?↑ CV events- see MACE/mortality.[17-21]
38. DPP-4 inhibitors FDA +/- Health Canada warnings/label changes:
    - ?↑ HF risk with saxagliptin and alogliptin (see above).[10, 11] **SAVOR-TIMI 53**,[12,13] **EXAMINE**,[16, 22]
    - ?↑ arthralgia risk; n=33 cases of severe arthralgia, of which n=10 cases were hospitalized due to disabling joint pain; n=8 cases reported a positive rechallenge (2006-2013).[23]
39. Incretin agents (DPP-4 inhibitors and GLP-1 agonists) ?↑ pancreatitis:[24] Meta-analysis of SAVOR-TIMI 53, EXAMINE, & TECOS (n=36,395) demonstrated ↑ acute pancreatitis **OR 1.79 (1.13-2.82) and ARI of 0.13%** vs placebo.[24a] US case control study; incretin agent (exenatide or sitagliptin) within 30 days **OR 2.24 (95% CI, 1.36-3.68)**.[25] FDA: n=30 cases of pancreatitis with exenatide of which n=21 cases hospitalized, n=3 cases reported positive rechallenge.[26] FDA: n=88 cases of pancreatitis with sitagliptin
45. Dapagliflozin: ? ↑ bladder/breast cancer; approved by FDA 2014 (rejected in 2012 due to breast & bladder cancer concerns). Dapagliflozin vs control; bladder cancer: n=10 cases vs n=1 case & breast cancer: n=12 cases vs n= 3 cases (up to 2013).
46. Canagliflozin 100mg once daily vs placebo: ↓primary composite outcome of ESKD, doubling of SCr & renal or CV death: 11.1% vs 15.5% p= 0.00001. **CREDENCE**
47. FDA Warning (May 2019): SGLT-2 inhibitors associated with Fournier Gangrene.

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References: Death/MACE

1. U.S. Department of Health and Human Services Food and Drug Administration Center for Drug Evaluation and Research. Guidance for industry: diabetes mellitus—evaluating cardiovascular risk in new antidiabetic therapies to treat type 2 diabetes. www.fda.gov/downloads/drugs/guidancecomplianceregulatoryinformation/guidances/ucm071627.pdf (accessed July 12 2016).
2. Effect of intensive blood-glucose control with metformin on complications in overweight patients with type 2 diabetes (UKPDS 34). UK Prospective Diabetes Study (UKPDS) Group. Lancet. 1998 Sep 12;352(9131):854-65.
3. Holman RR, Paul SK, Bethel MA, Matthews DR, Neil HA. 10-year follow-up of intensive glucose control in type 2 diabetes. N Engl J Med. 2008 Oct 9;359(15):1577-89.
4. ADVANCE Collaborative Group, Patel A, MacMahon S, Chalmers J, Neal B, Billot L, Woodward M, Marre M, Cooper M, Glasziou P, Grobbee D, Hamet P, Harrap S, Heller S, Liu L, Mancia G, Mogensen CE, Pan C, Poulter N, Rodgers A, Williams B, Bompoint S, de Galan BE, Joshi R, Travert F. Intensive blood glucose control and vascular outcomes in patients with type 2 diabetes. N Engl J Med. 2008 Jun 12;358(24):2560-72.
5. Intensive blood-glucose control with sulphonylureas or insulin compared with conventional treatment and risk of complications in patients with type 2 diabetes (UKPDS 33). UK Prospective Diabetes Study (UKPDS) Group. Lancet. 1998 Sep 12;352(9131):837-53.
6. Varvaki Rados D, Catani Pinto L, Reck Remonti L, Bauermann Leitão C, Gross JL. The Association between Sulfonylurea Use and All-Cause and Cardiovascular Mortality: A Meta-Analysis with Trial Sequential Analysis of Randomized Clinical Trials. PLoS Med. 2016 Apr 12;13(4):e1001992.
7. Hong J, Zhang Y, Lai S, Lv A, Su Q, Dong Y, Zhou Z, Tang W, Zhao J, Cui L, Zou D, Wang D, Li H, Liu C, Wu G, Shen J, Zhu D, Wang W, Shen W, Ning G; SPREAD-DIMCAD Investigators. Effects of metformin versus glipizide on cardiovascular outcomes in patients with type 2 diabetes and coronary artery disease. Diabetes Care. 2013 May;36(5):1304-11.
8. Dormandy JA, Charbonnel B, Eckland DJ, Erdmann E, Massi-Benedetti M, Moules IK, Skene AM, Tan MH, Lefèbvre PJ, Murray GD, Standl E, Wilcox RG, Wilhelmsen L, Betteridge J, Birkeland K, Golay A, Heine RJ, Korányi L, Laakso M, Mokán M, Norkus A, Pirags V, Podar T, Scheen A, Scherbaum W, Schernthaner G, Schmitz O,Skrha J, Smith U, Taton J; PROactive Investigators. Secondary prevention of macrovascular events in patients with type 2 diabetes in the PROactive Study (PROspective pioglitAzone Clinical Trial In macroVascular Events): a randomized controlled trial. Lancet. 2005 Oct 8;366(9493):1279-89.
9. Kernan WN, Viscoli CM, Furie KL, Young LH, Inzucchi SE, Gorman M, Guarino PD, Lovejoy AM, Peduzzi PN, Conwit R, Brass LM, Schwartz GG, Adams HP Jr, Berger L Carolei A, Clark W, Coull B, Ford GA, Kleindorfer D, O'Leary JR, Parsons MW, Ringleb P, Sen S, Spence JD, Tanne D, Wang D, Winder TR; IRIS Trial Investigators. Pioglitazone after Ischemic Stroke or Transient Ischemic Attack. N Engl J Med. 2016 Apr 7;374(14):1321-31.
10. DREAM (Diabetes REduction Assessment with ramipril and rosiglitazone Medication) Trial Investigators, Gerstein HC, Yusuf S, Bosch J, Pogue J, Sheridan P, Dinccag N, Hanefeld M, Hoogwerf B, Laakso M, Mohan V, Shaw J, Zinman B, Holman RR. Effect of rosiglitazone on the frequency of diabetes in patients with impaired glucose tolerance or impaired fasting glucose: a randomised controlled trial. Lancet. 2006 Sep 23;368(9541):1096-105.
11. Nissen SE, Wolski K. Effect of rosiglitazone on the risk of myocardial infarction and death from cardiovascular causes. N Engl J Med. 2007 Jun 14;356(24):2457-71. Epub 2007 May 21.
12. Viberti G, Kahn SE, Greene DA, Herman WH, Zinman B, Holman RR, Haffner SM, Levy D, Lachin JM, Berry RA, Heise MA, Jones NP, Freed MI. A diabetes outcome progression trial (ADOPT): an international multicenter study of the comparative efficacy of rosiglitazone, glyburide, and metformin in recently diagnosed type 2 diabetes. Diabetes Care. 2002 Oct;25(10):1737-43.
13. Chiasson JL, Gomis R, Hanefeld M, Josse RG, Karasik A, Laakso M. The STOP-NIDDM Trial: an international study on the efficacy of an alpha-glucosidase inhibitor to prevent type 2 diabetes in a population with impaired glucose tolerance: rationale, design, and preliminary screening data. Study to Prevent Non-Insulin-Dependent Diabetes Mellitus. Diabetes Care. 1998 Oct;21(10):1720-5.
14. Scirica BM, Bhatt DL, Braunwald E, Steg PG, Davidson J, Hirshberg B, Ohman P, Frederich R, Wiviott SD, Hoffman EB, Cavender MA, Udell JA, Desai NR, Mosenzon O, McGuire DK, Ray KK, Leiter LA, Raz I; SAVOR-TIMI 53 Steering Committee and Investigators. Saxagliptin and cardiovascular outcomes in patients with type 2 diabetes mellitus. N Engl J Med. 2013 Oct 3;369(14):1317-26.
15. White WB, Cannon CP, Heller SR, Nissen SE, Bergenstal RM, Bakris GL, Perez AT, Fleck PR, Mehta CR, Kupfer S, Wilson C, Cushman WC, Zannad F; EXAMINE Investigators. Alogliptin after acute coronary syndrome in patients with type 2diabetes. N Engl J Med. 2013 Oct 3;369(14):1327-35.
16. Green JB, Bethel MA, Armstrong PW, Buse JB, Engel SS, Garg J, Josse R, Kaufman KD, Koglin J, Korn S, Lachin JM, McGuire DK, Pencina MJ, Standl E, Stein PP, Suryawanshi S, Van de Werf F, Peterson ED, Holman RR; TECOS Study Group. Effect of Sitagliptin on Cardiovascular Outcomes in Type 2 Diabetes. N Engl J Med. 2015 Jul 16;373(3):232-42.
17. Barry AR, Turgeon RD. DPP-4 Inhibitors: The Seinfeld of Oral Antihyperglycemics. Can J Hosp Pharm. 2016 May-Jun;69(3):253-4.
18. Cardiovascular and Renal Microvascular Outcome study with Linagliptin in patients with Type 2 Diabetes Mellitus (CARMELINA). NCT01897532. Available: https://clinicaltrials.gov/ct2/show/NCT01897532. (Accessed July 16 2016).

19. Marso SP, Daniels GH, Brown-Frandsen K, Kristensen P, Mann JF, Nauck MA, Nissen SE, Pocock S, Poulter NR, Ravn LS, Steinberg WM, Stockner M, Zinman B, Bergenstal RM, Buse JB; LEADER Steering Committee on behalf of the LEADER Trial Investigators. Liraglutide and Cardiovascular Outcomes in Type 2 Diabetes. N Engl J Med. 2016 Jun 13.
20. Nainggolan L. Now Novo Says Semaglutide Cuts CV Risk: SUSTAIN-6 Top-line Data. http://www.medscape.com/viewarticle/862644 (accessed June 24, 2016).
21. Pfeffer MA, Claggett B, Diaz R, Dickstein K, Gerstein HC, Køber LV, Lawson FC, Ping L, Wei X, Lewis EF, Maggioni AP, McMurray JJ, Probstfield JL, Riddle MC, Solomon SD, Tardif JC; ELIXA Investigators. Lixisenatide in Patients with Type 2 Diabetes and Acute Coronary Syndrome. N Engl J Med. 2015 Dec 3;373(23):2247-57.
22. Holman RR, Bethel MA, Mentz RJ, et al. Effects of Once-Weekly Exenatide on Cardiovascular Outcomes in Type 2 Diabetes. N Engl J Med. 2017 Sep 14. doi: 10.1056/NEJMoa1612917. {Exenatide Study of Cardiovascular Event Lowering Trial (EXSCEL): A Trial To Evaluate Cardiovascular Outcomes After Treatment With Exenatide Once Weekly In Patients With Type 2 Diabetes Mellitus. NCT01144338. Available: https://clinicaltrials.gov/ct2/show/NCT01144338?term=EXSCEL&rank=1 (accessed July 21, 2016).}
23. Researching Cardiovascular Events With a Weekly Incretin in Diabetes (REWIND). NCT01394952. Available: https://clinicaltrials.gov/ct2/show/NCT01394952?term=REWIND&rank=1 (accessed July 21, 2016).
24. Effect of Albiglutide, When added to Standard Blood Glucose Lowering Therapies, on Major Cardiovascular Events in Subjects With Type 2 Diabetes Mellitus. NCT02465515. Available: https://clinicaltrials.gov/ct2/show/NCT02465515?term=HARMONY+and+albiglutide&rank=1 (accessed July 21, 2016).
25. Zinman B, Wanner C, Lachin JM, Fitchett D, Bluhmki E, Hantel S, Mattheus M, Devins T, Johansen OE, Woerle HJ, Broedl UC, Inzucchi SE; EMPA-REG OUTCOME Investigators. Empagliflozin, Cardiovascular Outcomes, and Mortality in Type 2 Diabetes. N Engl J Med. 2015 Nov 26;373(22):2117-28.
26. CANVAS- CANagliflozin cardiovascular Assessment Study. NCT01032629. Available: https://clinicaltrials.gov/ct2/show/NCT01032629?term=Canvas&rank=1 (accessed July 21 2016).
27. Center for Drug Evaluation and Research. Canagliflozin: Summary Review Available: http://www.accessdata.fda.gov/drugsatfda_docs/nda/2013/204042Orig1s000SumR.pdf (accessed July 21 2016).
27a. Neal B, Perkovic V, Mahaffey KW, de Zeeuw D, et al. CANVAS Program Collaborative Group. Canagliflozin and Cardiovascular and Renal Events in Type 2 Diabetes. N Engl J Med. 2017 Jun 12.
28. Multicenter Trial to Evaluate the Effect of Dapagliflozin on the Incidence of Cardiovascular Events (DECLARE-TIMI58). NCT01730534. Available: https://clinicaltrials.gov/ct2/show/NCT01730534?term=DECLARE+and+dapagliflozin&rank=1 (accessed July 21, 2016).
Wiviott SD, Raz I, Bonaca MP, et al; DECLARE–TIMI 58 Investigators. Dapagliflozin and Cardiovascular Outcomes in Type 2 Diabetes. N Engl J Med. 2018 Nov 10.
29. Cardiovascular Outcomes Following Ertugliflozin Treatment in Type 2 Diabetes Mellitus Participants with Vascular Disease, The VERTIS CV Study (MK-8835-004). NCT01986881. Available: https://clinicaltrials.gov/ct2/show/NCT01986881?term=Ertugliflozin+and+cardiovascular&rank=1 (accessed July 21 2016).
30. ORIGIN Trial Investigators, Gerstein HC, Bosch J, Dagenais GR, Díaz R, Jung H, Maggioni AP, Pogue J, Probstfield J, Ramachandran A, Riddle MC, Rydén LE, Yusuf S. Basal insulin and cardiovascular and other outcomes in dysglycemia. N Engl J Med. 2012 Jul 26;367(4):319-28.
31. Abraira C, Colwell J, Nuttall F, Sawin CT, Henderson W, Comstock JP, Emanuele NV, Levin SR, Pacold I, Lee HS. Cardiovascular events and correlates in the Veterans Affairs Diabetes Feasibility Trial. Veterans Affairs Cooperative Study on Glycemic Control and Complications in Type II Diabetes. Arch Intern Med. 1997 Jan 27;157(2):181-8.
32. DCCT Research Group. The effect of intensive treatment of diabetes on the development and progression of long-term complications in insulin-dependent diabetes mellitus. The Diabetes Control and Complications Trial Research Group. N Engl J Med 1993; 329: 977- 86.
33. Epidemiology of Diabetes Interventions and Complications (EDIC). Design, implementation, and preliminary results of a long-term follow-up of the Diabetes Control and Complications Trial cohort. Diabetes Care. 1999 Jan;22(1):99-111.
34. Action to Control Cardiovascular Risk in Diabetes Study Group, Gerstein HC, Miller ME, Byington RP, Goff DC Jr, Bigger JT, Buse JB, Cushman WC, Genuth S, Ismail-Beigi F, Grimm RH Jr, Probstfield JL, Simons-Morton DG, Friedewald WT. Effects of intensive glucose lowering in type 2 diabetes. N Engl J Med. 2008 Jun 12;358(24):2545-59.
34a. Marso SP, McGuire DK, Zinman Bet al. DEVOTE Study Group. Efficacy and Safety of Degludec versus Glargine in Type 2 Diabetes. N Engl J Med. 2017 Jun 12.
35. Rodríguez-Gutiérrez R, Montori VM. Glycemic Control for Patients With Type 2 Diabetes Mellitus: Our Evolving Faith in the Face of Evidence. Circ Cardiovasc Qual Outcomes. 2016 Sep;9(5):504-12.

References: Weight

1. Viberti G, Kahn SE, Greene DA, Herman WH, Zinman B, Holman RR, Haffner SM, Levy D, Lachin JM, Berry RA, Heise MA, Jones NP, Freed MI. A diabetes outcome progression trial (ADOPT): an international multicenter study of the comparative efficacy of rosiglitazone, glyburide, and metformin in recently diagnosed type 2 diabetes. Diabetes Care. 2002 Oct;25(10):1737-43.
2. Dormandy JA, Charbonnel B, Eckland DJ, Erdmann E, Massi-Benedetti M, Moules IK, Skene AM, Tan MH, Lefèbvre PJ, Murray GD, Standl E, Wilcox RG, Wilhelmsen L, Betteridge J, Birkeland K, Golay A, Heine RJ, Korányi L, Laakso M, Mokán M, Norkus A, Pirags V, Podar T, Scheen A, Scherbaum W, Schernthaner G, Schmitz O,Skrha J, Smith U, Taton J; PROactive Investigators. Secondary prevention of macrovascular events in patients with type 2 diabetes in the PROactive Study (PROspective pioglitAzone Clinical Trial In macroVascular Events): a randomized controlled trial. Lancet. 2005 Oct 8;366(9493):1279-89.
3.Chiasson JL, Gomis R, Hanefeld M, Josse RG, Karasik A, Laakso M. The STOP-NIDDM Trial: an international study on the efficacy of an alpha-glucosidase inhibitor to prevent type 2 diabetes in a population with impaired glucose tolerance: rationale, design, and preliminary screening data. Study to Prevent Non-Insulin-Dependent Diabetes Mellitus. Diabetes Care. 1998 Oct;21(10):1720-5.
4. Rosenstock J, Hassman DR, Madder RD, Brazinsky SA, Farrell J, Khutoryansky N, Hale PM; Repaglinide Versus Nateglinide Comparison Study Group. Repaglinide versus nateglinide monotherapy: a randomized, multicenter study. Diabetes Care. 2004 Jun;27(6):1265-70.
5. GlucoNorm ® (repaglinide tablets) Product Monograph. Novo Nordisk Canada Inc. ON, Canada. June 3, 2015
6. Starlix® (nateglinide tablets) Product Monograph. Novartis Pharmaceuticals Canada Inc. QB, Canada. June 10, 2011

6. Richard KR, Shelburne JS, Kirk JK. Tolerability of dipeptidyl peptidase-4 inhibitors: a review. Clin Ther. 2011 Nov;33(11):1609-29. doi:10.1016/j.clinthera.2011.09.028. Epub 2011 Nov 8.
7. Canadian Diabetes Association 2013 Clinical. Practice *Guidelines* for the Prevention and Management of Diabetes in Canada. Can J *Diabetes* 2013;37(suppl 1), pg S126-8.
8. Scirica BM, Bhatt DL, Braunwald E, Steg PG, Davidson J, Hirshberg B, Ohman P, Frederich R, Wiviott SD, Hoffman EB, Cavender MA, Udell JA, Desai NR, Mosenzon O, McGuire DK, Ray KK, Leiter LA, Raz I; SAVOR-TIMI 53 Steering Committee and Investigators. Saxagliptin and cardiovascular outcomes in patients with type 2 diabetes mellitus. N Engl J Med. 2013 Oct 3;369(14):1317-26.
9. White WB, Cannon CP, Heller SR, Nissen SE, Bergenstal RM, Bakris GL, Perez AT, Fleck PR, Mehta CR, Kupfer S, Wilson C, Cushman WC, Zannad F; EXAMINE Investigators. Alogliptin after acute coronary syndrome in patients with type 2diabetes. N Engl J Med. 2013 Oct 3;369(14):1327-35.
10. Scott R, Wu M, Sanchez M, Stein P. Efficacy and tolerability of the dipeptidyl peptidase-4 inhibitor sitagliptin as monotherapy over 12 weeks in patients with type 2 diabetes. Int J Clin Pract. 2007 Jan;61(1):171-80.
11. Vilsbøll T, Christensen M, Junker AE, Knop FK, Gluud LL. Effects of glucagon-like peptide-1 receptor agonists on weight loss: systematic review and meta-analyses of randomised controlled trials. BMJ. 2012 Jan 10;344:d7771. doi:10.1136/bmj.d7771.
12. Marso SP, Daniels GH, Brown-Frandsen K, Kristensen P, Mann JF, Nauck MA, Nissen SE, Pocock S, Poulter NR, Ravn LS, Steinberg WM, Stockner M, Zinman B, Bergenstal RM, Buse JB; LEADER Steering Committee on behalf of the LEADER Trial Investigators. Liraglutide and Cardiovascular Outcomes in Type 2 Diabetes. N Engl J Med. 2016 Jun 13.
13. Edwards KL, Minze MG. Dulaglutide: an evidence-based review of its potential in the treatment of type 2 diabetes. Core Evid. 2015 Jan 9;10:11-21.
14. Scheen AJ. SGLT2 Inhibitors: Benefit/Risk Balance. Curr Diab Rep. 2016 Oct;16(10):92.
15. Yang XP, Lai D, Zhong XY, Shen HP, Huang YL. Efficacy and safety of canagliflozin in subjects with type 2 diabetes: systematic review and meta-analysis. Eur J Clin Pharmacol. 2014 Oct;70(10):1149-58.
16. Stenlöf K, Cefalu WT, Kim KA, Jodar E, Alba M, Edwards R, Tong C, Canovatchel W, Meininger G. Long-term efficacy and safety of canagliflozin monotherapy in patients with type 2 diabetes inadequately controlled with diet and exercise: findings from the 52-week CANTATA-M study. Curr Med Res Opin. 2014 Feb;30(2):163-75.
17. Vasilakou D, Karagiannis T, Athanasiadou E, et al. Sodium-glucose cotransporter 2 inhibitors for type 2 diabetes: a systematic review and meta-analysis. Ann Intern Med. 2013;159:262–74.
18. Zinman B, Wanner C, Lachin JM, Fitchett D, Bluhmki E, Hantel S, Mattheus M, Devins T, Johansen OE, Woerle HJ, Broedl UC, Inzucchi SE; EMPA-REG OUTCOME Investigators. Empagliflozin, Cardiovascular Outcomes, and Mortality in Type 2 Diabetes. N Engl J Med. 2015 Nov 26;373(22):2117-28.
19. Action to Control Cardiovascular Risk in Diabetes Study Group, Gerstein HC, Miller ME, Byington RP, Goff DC Jr, Bigger JT, Buse JB, Cushman WC, Genuth S, Ismail-Beigi F, Grimm RH Jr, Probstfield JL, Simons-Morton DG, Friedewald WT. Effects of intensive glucose lowering in type 2 diabetes. N Engl J Med. 2008 Jun 12;358(24):2545-59.
20. Canadian Optimal Medication Prescribing & Utilization Service (**COMPUS**), 2008; Current Topics, Diabetes: http://cadth.ca/index.php/en/compus/current-topics/-dm1 (www.cadth.ca)
{Long-acting IAs: Metaanalysis of Clinical Outcomes: http://cadth.ca/media/compus/reports/compus_Long-Acting-Insulin-Analogs-Report_Clinical-Outcomes.pdf }
{Rapid Acting IAs: Metaanalysis of Clinical Outcomes: http://cadth.ca/media/compus/reports/compus_Rapid-Acting-Insulin-Analogues-Report_Clinical=Outcomes.pdf }

{Optimal Therapy Recommendations for Prescribing and Use of Insulin Analogues: http://cadth.ca/media/pdf/compus_IA_OT_rec_report.pdf Final Report: January 2009}
{Grade Evidence Profiles of Long and Rapid Acting Insulin Analogues: http://cadth.ca/media/compus/reports/compus_GRADE-REPORT.pdf }

References: HF/Edema

1. Canadian Diabetes Association 2013 Clinical. Practice *Guidelines* for the Prevention and Management of Diabetes in Canada. Can J *Diabetes* 2013;37(suppl 1), pg S126-8.
2. Andersson C, Olesen JB, Hansen PR, Weeke P, Norgaard ML, Jørgensen CH, Lange T, Abildstrøm SZ, Schramm TK, Vaag A, Køber L, Torp-Pedersen C, Gislason GH. Metformin treatment is associated with a low risk of mortality in diabetic patients with heart failure: a retrospective nationwide cohort study. Diabetologia. 2010 Dec;53(12):2546-53.
3. ADVANCE Collaborative Group, Patel A, MacMahon S, Chalmers J, Neal B, Billot L, Woodward M, Marre M, Cooper M, Glasziou P, Grobbee D, Hamet P, Harrap S, Heller S, Liu L, Mancia G, Mogensen CE, Pan C, Poulter N, Rodgers A, Williams B, Bompoint S, de Galan BE, Joshi R, Travert F. Intensive blood glucose control and vascular outcomes in patients with type 2 diabetes. N Engl J Med. 2008 Jun 12;358(24):2560-72.
4. Viberti G, Kahn SE, Greene DA, Herman WH, Zinman B, Holman RR, Haffner SM, Levy D, Lachin JM, Berry RA, Heise MA, Jones NP, Freed MI. A diabetes outcome progression trial (ADOPT): an international multicenter study of the comparative efficacy of rosiglitazone, glyburide, and metformin in recently diagnosed type 2 diabetes. Diabetes Care. 2002 Oct;25(10):1737-43.
5. Dormandy JA, Charbonnel B, Eckland DJ, Erdmann E, Massi-Benedetti M, Moules IK, Skene AM, Tan MH, Lefèbvre PJ, Murray GD, Standl E, Wilcox RG, Wilhelmsen L, Betteridge J, Birkeland K, Golay A, Heine RJ, Korányi L, Laakso M, Mokán M, Norkus A, Pirags V, Podar T, Scheen A, Scherbaum W, Schernthaner G, Schmitz O, Skrha J, Smith U, Taton J; PROactive Investigators. Secondary prevention of macrovascular events in patients with type 2 diabetes in the PROactive Study (PROspective pioglitAzone Clinical Trial In macroVascular Events): a randomized controlled trial. Lancet. 2005 Oct 8;366(9493):1279-89.
6. Home PD, Pocock SJ, Beck-Nielsen H, Curtis PS, Gomis R, Hanefeld M, Jones NP, Komajda M, McMurray JJ; RECORD Study Team. Rosiglitazone evaluated for cardiovascular outcomes in oral agent combination therapy for type 2 diabetes(RECORD): a multicentre, randomised, open-label trial. Lancet. 2009 Jun 20;373(9681):2125-35.
7. DREAM (Diabetes REduction Assessment with ramipril and rosiglitazone Medication) Trial Investigators, Gerstein HC, Yusuf S, Bosch J, Pogue J, Sheridan P, Dinccag N, Hanefeld M, Hoogwerf B, Laakso M, Mohan V, Shaw J, Zinman B, Holman RR. Effect of rosiglitazone on the frequency of diabetes in patients with impaired glucose tolerance or impaired fasting glucose: a randomised controlled trial. Lancet. 2006 Sep 23;368(9541):1096-105.
8. Chiasson JL, Gomis R, Hanefeld M, Josse RG, Karasik A, Laakso M. The STOP-NIDDM Trial: an international study on the efficacy of an alpha-glucosidase inhibitor to prevent type 2 diabetes in a population with impaired glucose tolerance: rationale, design, and preliminary screening data. Study to Prevent Non-Insulin-Dependent Diabetes Mellitus. Diabetes Care. 1998 Oct;21(10):1720-5.
9. GlucoNorm ® (repaglinide tablets) Product Monograph. Novo Nordisk Canada Inc. ON, Canada. June 3, 2015
10. Scirica BM, Bhatt DL, Braunwald E, Steg PG, Davidson J, Hirshberg B, Ohman P, Frederich R, Wiviott SD, Hoffman EB, Cavender MA, Udell JA, Desai NR, Mosenzon O, McGuire DK, Ray KK, Leiter LA, Raz I; SAVOR-TIMI 53 Steering Committee and Investigators. Saxagliptin and cardiovascular outcomes in patients with type 2 diabetes mellitus. N Engl J Med. 2013 Oct 3;369(14):1317-26.
11. Scirica BM, Braunwald E, Raz I, Cavender MA, Morrow DA, Jarolim P, Udell JA, Mosenzon O, Im K, Umez-Eronini AA, Pollack PS, Hirshberg B, Frederich R, Lewis BS, McGuire DK, Davidson J, Steg PG, Bhatt DL; SAVOR-TIMI 53 Steering Committee and Investigators. Heart Failure, Saxagliptin, and Diabetes Mellitus: Observations from the SAVOR-TIMI 53 Randomized Trial. Circulation. 2015 Oct 13;132(15):e198.
12. White WB, Cannon CP, Heller SR, Nissen SE, Bergenstal RM, Bakris GL, Perez AT, Fleck PR, Mehta CR, Kupfer S, Wilson C, Cushman WC, Zannad F; EXAMINE Investigators. Alogliptin after acute coronary syndrome in patients with type 2diabetes. N Engl J Med. 2013 Oct 3;369(14):1327-35.
13. Zannad F, Cannon CP, Cushman WC, Bakris GL, Menon V, Perez AT, Fleck PR, Mehta CR, Kupfer S, Wilson C, Lam H, White WB; EXAMINE Investigators. Heart failure and mortality outcomes in patients with type 2 diabetes taking alogliptin versus placebo in EXAMINE: a multicentre, randomised, double-blind trial. Lancet. 2015 May 23;385(9982):2067-76.
14. Green JB, Bethel MA, Armstrong PW, Buse JB, Engel SS, Garg J, Josse R, Kaufman KD, Koglin J, Korn S, Lachin JM, McGuire DK, Pencina MJ, Standl E, Stein PP, Suryawanshi S, Van de Werf F, Peterson ED, Holman RR; TECOS Study Group. Effect of Sitagliptin on Cardiovascular Outcomes in Type 2 Diabetes. N Engl J Med. 2015 Jul 16;373(3):232-42.
15. European Society of Cardiology Press Office. New TECOS analysis adds heart failure data for sitagliptin. http://www.escardio.org/The-ESC/Press-Office/Press-releases/Last-5-years/new-tecos-analysis-adds-heart-failure-data-for-sitagliptin (accessed July 16 2016).
16. Barry AR, Turgeon RD. DPP-4 Inhibitors: The Seinfeld of Oral Antihyperglycemics. Can J Hosp Pharm. 2016 May-Jun;69(3):253-4.
17. FDA Drug Safety Communication: FDA adds warnings about heart failure risk to labels of type 2 diabetes medicines containing saxagliptin and alogliptin. Available: http://www.fda.gov/Drugs/DrugSafety/ucm486096.htm (accessed July 16 2016).
18. Marso SP, Daniels GH, Brown-Frandsen K, Kristensen P, Mann JF, Nauck MA, Nissen SE, Pocock S, Poulter NR, Ravn LS, Steinberg WM, Stockner M, Zinman B, Bergenstal RM, Buse JB; LEADER Steering Committee on behalf of the LEADER Trial Investigators. Liraglutide and Cardiovascular Outcomes in Type 2 Diabetes. N Engl J Med. 2016 Jun 13.
19. Pfeffer MA, Claggett B, Diaz R, Dickstein K, Gerstein HC, Køber LV, Lawson FC, Ping L, Wei X, Lewis EF, Maggioni AP, McMurray JJ, Probstfield JL, Riddle MC, Solomon SD, Tardif JC; ELIXA Investigators. Lixisenatide in Patients with Type 2 Diabetes and Acute Coronary Syndrome. N Engl J Med. 2015 Dec 3;373(23):2247-57.
20. Zinman B, Wanner C, Lachin JM, Fitchett D, Bluhmki E, Hantel S, Mattheus M, Devins T, Johansen OE, Woerle HJ, Broedl UC, Inzucchi SE; EMPA-REG OUTCOME Investigators. Empagliflozin, Cardiovascular Outcomes, and Mortality in Type 2 Diabetes. N Engl J Med. 2015 Nov 26;373(22):2117-28.
21. ORIGIN Trial Investigators, Gerstein HC, Bosch J, Dagenais GR, Díaz R, Jung H, Maggioni AP, Pogue J, Probstfield J, Ramachandran A, Riddle MC, Rydén LE, Yusuf S. Basal insulin and cardiovascular and other outcomes in dysglycemia. N Engl J Med. 2012 Jul 26;367(4):319-28.
22. Abraira C, Colwell J, Nuttall F, Sawin CT, Henderson W, Comstock JP, Emanuele NV, Levin SR, Pacold I, Lee HS. Cardiovascular events and correlates in the Veterans Affairs Diabetes Feasibility Trial. Veterans Affairs Cooperative Study on Glycemic Control and Complications in Type II Diabetes. Arch Intern Med. 1997 Jan 27;157(2):181-8.
23. McMurray JJV, Solomon SD, Inzucchi SE; DAPA-HF Trial Committees and Investigators. Dapagliflozin in Patients with Heart Failure and Reduced Ejection Fraction. N Engl J Med. 2019 Sep 19. doi: 10.1056/NEJMoa1911303.

References: Other

1. Dormandy JA, Charbonnel B, Eckland DJ, Erdmann E, Massi-Benedetti M, Moules IK, Skene AM, Tan MH, Lefèbvre PJ, Murray GD, Standl E, Wilcox RG, Wilhelmsen L, Betteridge J, Birkeland K, Golay A, Heine RJ, Korányi L, Laakso M, Mokán M, Norkus A, Pirags V, Podar T, Scheen A, Scherbaum W, Schernthaner G, Schmitz O,Skrha J, Smith U, Taton J; PROactive Investigators. Secondary prevention of macrovascular events in patients with type 2 diabetes in the PROactive Study (PROspective pioglitAzone Clinical Trial In macroVascular Events): a randomized controlled trial. Lancet. 2005 Oct 8;366(9493):1279-89.
2. Home PD, Pocock SJ, Beck-Nielsen H, Curtis PS, Gomis R, Hanefeld M, Jones NP, Komajda M, McMurray JJ; RECORD Study Team. Rosiglitazone evaluated for cardiovascular outcomes in oral agent combination therapy for type 2 diabetes(RECORD): a multicentre, randomised, open-label trial. Lancet. 2009 Jun 20;373(9681):2125-35.
3. DREAM (Diabetes REduction Assessment with ramipril and rosiglitazone Medication) Trial Investigators, Gerstein HC, Yusuf S, Bosch J, Pogue J, Sheridan P, Dinccag N, Hanefeld M, Hoogwerf B, Laakso M, Mohan V, Shaw J, Zinman B, Holman RR. Effect of rosiglitazone on the frequency of diabetes in patients with impaired glucose tolerance or impaired fasting glucose: a randomised controlled trial. Lancet. 2006 Sep 23;368(9541):1096-105.
4. Manufacturers of Some Diabetes Drugs to Strengthen Warning on Heart Failure Risk-Companies Will Include Boxed Warning on Drug Label. Available: http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/2007/ucm108966.htm (accessed July 21 2016).
5. Updated labelling for diabetes drug ACTOS and risk of heart failure. Available: http://www.healthycanadians.gc.ca/recall-alert-rappel-avis/hc-sc/2008/13269a-eng.php (accessed July 21 2016).
   Information for Healthcare Professionals Rosiglitazone maleate (marketed as Avandia, Avandamet, and Avandaryl). Available: http://www.fda.gov/Drugs/DrugSafety/PostmarketDrugSafetyInformationforPatientsandProviders/ucm143406.htm#2007_7 (accessed July 21 2016).
6. Dormandy J, Bhattacharya M, van Troostenburg de Bruyn AR; PROactive investigators. Safety and tolerability of pioglitazone in high-risk patients with type 2 diabetes: an overview of data from PROactive. Drug Saf. 2009;32(3):187-202.
7. Viberti G, Kahn SE, Greene DA, Herman WH, Zinman B, Holman RR, Haffner SM, Levy D, Lachin JM, Berry RA, Heise MA, Jones NP, Freed MI. A diabetes outcome progression trial (ADOPT): an international multicenter study of the comparative efficacy of rosiglitazone, glyburide, and metformin in recently diagnosed type 2 diabetes. Diabetes Care. 2002 Oct;25(10):1737-43.
8. Observation of an Increased Incidence of Fractures in Female Patients Who Received Long-Term Treatment with ACTOSO (pioglitazone HOI) Tablets for Type 2 Diabetes Mellitus.
   Available:http://www.fda.gov/downloads/Safety/MedWatch/SafetyInformation/SafetyAlertsforHumanMedicalProducts/UCM153896.pdf (accessed July 21 2016).
9. Clinical Trial Observation of an Increased Incidence of Fractures in Female Patients Who Received Long-Term Treatment with Avandia® (rosiglitazone maleate) Tablets for Type 2 Diabetes Mellitus. Available:
   http://www.fda.gov/downloads/Safety/MedWatch/SafetyInformation/SafetyAlertsforHumanMedicalProducts/UCM153903.pdf (accessed July 21 2016).
10. Idris I, Warren G, Donnelly R. Association between thiazolidinedione treatment and risk of macular edema among patients with type 2 diabetes. Arch Intern Med. 2012 Jul 9;172(13):1005-11.
11. Ambrosius WT, Danis RP, Goff DC Jr, Greven CM, Gerstein HC, Cohen RM, Riddle MC, Miller ME, Buse JB, Bonds DE, Peterson KA, Rosenberg YD, Perdue LH, Esser BA, Seaquist LA, Felicetta JV, Chew EY; ACCORD Study Group. Lack of association between thiazolidinediones and macular edema in type 2 diabetes: the ACCORD eye substudy. Arch Ophthalmol. 2010 Mar;128(3):312-8.

12. Association of Avandia (rosiglitazone) and Avandamet (rosiglitazone/metformin) with new onset and/or worsening of macular edema-for health professionals. Available: http://www.healthycanadians.gc.ca/recall-alert-rappel-avis/hc-sc/2005/14308a-eng.php (accessed July 21 2016).
13. Neumann A, Weill A, Ricordeau P, Fagot JP, Alla F, Allemand H. Pioglitazone and risk of bladder cancer among diabetic patients in France: a population-based cohort study. Diabetologia. 2012 Jul;55(7):1953-62.
14. Lewis JD, Ferrara A, Peng T, Hedderson M, Bilker WB, Quesenberry CP Jr, Vaughn DJ, Nessel L, Selby J, Strom BL. Risk of bladder cancer among diabetic patients treated with pioglitazone: interim report of a longitudinal cohort study. Diabetes Care. 2011 Apr;34(4):916-22.
15. ACTOS (pioglitazone hydrochloride) – Potential association with bladder cancer. Available: http://www.healthycanadians.gc.ca/recall-alert-rappel-avis/hc-sc/2012/15854a-eng.php (accessed July 21 2016).
16. FDA Drug Safety Communication: Update to ongoing safety review of Actos (pioglitazone) and increased risk of bladder cancer. Available: http://www.fda.gov/Drugs/DrugSafety/ucm259150.htm (accessed July 21 2016).
17. DREAM (Diabetes REduction Assessment with ramipril and rosiglitazone Medication) Trial Investigators, Gerstein HC, Yusuf S, Bosch J, Pogue J, Sheridan P, Dinccag N, Hanefeld M, Hoogwerf B, Laakso M, Mohan V, Shaw J, Zinman B, Holman RR. Effect of rosiglitazone on the frequency of diabetes in patients with impaired glucose tolerance or impaired fasting glucose: a randomised controlled trial. Lancet. 2006 Sep 23;368(9541):1096-105.
18. Nissen SE, Wolski K. Effect of rosiglitazone on the risk of myocardial infarction and death from cardiovascular causes. N Engl J Med. 2007 Jun 14;356(24):2457-71. Epub 2007 May 21.
19. Viberti G, Kahn SE, Greene DA, Herman WH, Zinman B, Holman RR, Haffner SM, Levy D, Lachin JM, Berry RA, Heise MA, Jones NP, Freed MI. A diabetes outcome progression trial (ADOPT): an international multicenter study of the comparative efficacy of rosiglitazone, glyburide, and metformin in recently diagnosed type 2 diabetes. Diabetes Care. 2002 Oct;25(10):1737-43.
20. AVANDIA, AVANDAMET, AVANDARYL-Important New Restrictions on the Use of Rosiglitazone Products Due to Information on Cardiovascular Related Events: For Health Professionals. Available: http://www.healthycanadians.gc.ca/recall-alert-rappel-avis/hc-sc/2010/14591a-eng.php (accessed July 21 2016).
21. FDA Drug Safety Communication: FDA requires removal of some prescribing and dispensing restrictions for rosiglitazone-containing diabetes medicines. Available http://www.fda.gov/Drugs/DrugSafety/ucm376389.htm (accessed July 21 2016).
22. FDA Drug Safety Communication: FDA adds warnings about heart failure risk to labels of type 2 diabetes medicines containing saxagliptin and alogliptin. Available: http://www.fda.gov/Drugs/DrugSafety/ucm486096.htm (accessed July 21 2016).
23. FDA Drug Safety Communication: FDA warns that DPP-4 inhibitors for type 2 diabetes may cause severe joint pain. Available: http://www.fda.gov/Drugs/DrugSafety/ucm459579.htm (accessed July 21 2016).
24. FDA Drug Safety Communication: FDA investigating reports of possible increased risk of pancreatitis and pre-cancerous findings of the pancreas from incretin mimetic drugs for type 2 diabetes http://www.fda.gov/Drugs/DrugSafety/ucm343187.htm (accessed July 21 2016).
24a. Tkáč I, Raz I. Combined Analysis of Three Large Interventional Trials With Gliptins Indicates Increased Incidence of Acute Pancreatitis in Patients With Type 2 Diabetes. Diabetes Care. 2017 Feb;40(2):284-286. doi: 10.2337/dc15-1707. Epub 2016 Sep 22.
25. Singh S, Chang HY, Richards TM, Weiner JP, Clark JM, Segal JB. Glucagonlike peptide 1-based therapies and risk of hospitalization for acute pancreatitis in type 2 diabetes mellitus: a population-based matched case-control study. JAMA Intern Med. 2013 Apr 8;173(7):534-9.
26. Postmarket Drug Safety Information for Healthcare Professionals: Exenatide (marketed as Byetta)- 8/2008 update. Available: http://www.fda.gov/Drugs/DrugSafety/PostmarketDrugSafetyInformationforPatientsandProviders/ucm124713. htm (accessed July 21 2016).
27. Postmarket Drug Safety Information for Healthcare Professionals: Acute pancreatitis and sitagliptin (marketed as Januvia and Jaumet) Available: http://www.fda.gov/Drugs/DrugSafety/PostmarketDrugSafetyInformationforPatientsandProviders/ucm124713.htmhttp://www.fda.gov/Drugs/DrugSafety/PostmarketDrugSafetyInformationforPatientsandProviders/DrugSafetyInformationforHeathcareProfessionals/ucm183764.htm (accessed July 21 2016).
28. Canadian Adverse Reaction Newsletter: Incretin-based therapies and the risk of pancreatic cancer. http://www.fda.gov/Drugs/DrugSafety/PostmarketDrugSafetyInformationforPatientsandProviders/ucm124713.htmIncretin-based therapies and the risk of pancreatic cancer. Canadian Adverse Reaction Newsletter 2014;24;4. Available: http://www.hc-sc.gc.ca/dhp-mps/medeff/bulletin/carn-bcei_v24n4-eng.php (accessed July 21 2016).
29. Victoza (liraglutide [rDNA origin]) Injection: REMS - Risk of Thyroid C-cell Tumors, Acute Pancreatitis. Available: http://www.fda.gov/Safety/MedWatch/SafetyInformation/SafetyAlertsforHumanMedicalProducts/ucm258826.htm (accessed July 12, 2016).
30. Madsbad S. Review of head-to-head comparisons of glucagon-like peptide-1 receptor agonists. Diabetes Obes Metab. 2016 Apr;18(4):317-32.
31. Trujillo JM, Nuffer W, Ellis SL. GLP-1 receptor agonists: a review of head-to-head clinical studies. Ther Adv Endocrinol Metab. 2015 Feb;6(1):19-28.
32. Rosenstock J, Balas B, Charbonnel B et al. The fate of taspoglutide, a weekly GLP-1 receptor agonist, versus twice-daily exenatide for type 2 diabetes. Diabetes Care 2013; 36: 498–504.
33. Blevins T, Pullman J, Malloy J etal. DURATION-5: exenatide once weekly resulted in greater improvements in glycemic control compared with exenatide twice daily in patients with type 2 diabetes. J Clin Endocrinol Metab 2011; 96: 1301–1310.
34. Pratley RE, Nauck MA, Barnett AH etal. Once-weekly albiglutide versus once-daily liraglutide in patients with type 2 diabetes inadequately con- trolled on oral drugs (HARMONY 7): a randomised, open-label, multicentre, non-inferiority phase 3 study. Lancet Diabetes Endocrinol 2014; 2: 289–297.
35. 31. Buse JB, Nauck M, Forst T et al. Exenatide once weekly versus liraglutide once daily in patients with type 2 diabetes (DURATION-6): a randomised, open-label study. Lancet 2013; 381: 117–124.
36. Dungan KM, Povedano ST, Forst T etal. Once-weekly dulaglutide versus once-daily liraglutide in metformin-treated patients with type 2 diabetes (AWARD-6): a randomised, open-label, phase 3, non-inferiority trial. Lancet 2014; 384: 1349–1357.
37. Summary Safety Review- SGLT2 Inhibitors (canagliflozin, dapagliflozin, empagliflozin)- Assessing the risk of the body producing high levels of acid in the blood (diabetic ketoacidosis). Available: http://www.hc-sc.gc.ca/dhp-mps/medeff/reviews-examens/sglt2-2-eng.php (accessed July 12, 2016).
38. FDA Drug Safety Communication: FDA revises labels of SGLT2 inhibitors for diabetes to include warnings about too much acid in the blood and serious urinary tract infections. Available: http://www.fda.gov/Drugs/DrugSafety/ucm475463.htm (accessed July 21 2016).
39. Summary Safety Review- SGLT2 Inhibitors INVOKANA (canagliflozin) and FORXIGA (dapagliflozin)- Evaluation of a Potential Risk of Acute Kidney Injury. Available: http://www.hc-sc.gc.ca/dhp-mps/medeff/reviews-examens/sglt2-eng.php (accessed July 21 2016).
40. FDA Drug Safety Communication: FDA strengthens kidney warnings for diabetes medicines canagliflozin (Invokana, Invokamet) and dapagliflozin (Farxiga, Xigduo XR). Available: http://www.fda.gov/Drugs/DrugSafety/ucm505860.htm (accessed July 12, 2016).
41. FDA Drug Safety Communication: FDA revises label of diabetes drug canagliflozin (Invokana, Invokamet) to include updates on bone fracture risk and new information on decreased bone mineral density. Available: http://www.fda.gov/Drugs/DrugSafety/ucm461449.htm (accessed July 21 2016).
42. FDA Drug Safety Communication: Interim clinical trial results find increased risk of leg and foot amputations, mostly affecting the toes, with the diabetes medicine canagliflozin (Invokana, Invokamet); FDA to investigate. Available: http://www.fda.gov/Drugs/DrugSafety/ucm500965.htm (accessed July 21 2016).
43. Drug safety update Canagliflozin (Invokana, Vokanamet): signal of increased risk of lower extremity amputations observed in trial in high cardiovascular risk patients. Avaliable: https://www.gov.uk/drug-safety-update/canagliflozin-invokana-vokanamet-signal-of-increased-risk-of-lower-extremity-amputations-observed-in-trial-in-high-cardiovascular-risk-patients (accessed July 21 2016).
44. Vasilakou D, Karagiannis T, Athanasiadou E, Mainou M, Liakos A, Bekiari E,Sarigianni M, Matthews DR, Tsapas A. Sodium-glucose cotransporter 2 inhibitors for type 2 diabetes: a systematic review and meta-analysis. Ann Intern Med. 2013 Aug 20;159(4):262-74.
45. Lin HW, Tseng CH. A Review on the Relationship between SGLT2 Inhibitors and Cancer. Int J Endocrinol. 2014;2014:719578.
46. Faillie JL, Yu OH, Yin H, Hillaire-Buys D, Barkun A, Azoulay L. Association of Bile Duct and Gallbladder Diseases With the Use of Incretin-Based Drugs in Patients With Type 2 Diabetes Mellitus. JAMA Intern Med. 2016 Oct 1;176(10):1474-1481.

Online Extras

Table 3: Combination Therapy +/- Insulin in Type 2 Diabetes [i,ii,73]

Drug combination	↓ in A1C	Hypo -glyc	Wt	Comments (long-term clinical outcomes not studied!)
MF + SU dose-dependent	↓↓↓	↑↑	↑/↓	◆**MF combos: result in less wt gain than SU combos**
SU + TZD [iv]	↓↓	↑↑	↑↑	◆if MF initially, may add SU e.g. **gliclazide** or repaglinide
MF + repaglinide [v]	↓↓	↑	↑	◆if SU initially, may add MF or TZD; SU+MF may further ↓A1C by 1.7%; 1 study ↑ mortality[iii]; but ADVANCE neutral*
MF + DPP-4 sita/saxa/lina-	↓↓	-	-/↓	◆MF+ pioglitazone: positive lipid effects, but ↑ edema/HF
MF + TZD [vi,vii,viii]	↓↓↓	-/↑	↑	◆MF+ rosiglitazone: lower A1C but ↑ edema/HF
MF + acarbose [ix]	↓	-	↓↓	◆MF+ acarbose: ↓ wt & PPG, but ↑ GI AE
MF+canagliflozin+SU	↓↓↓	↑↑	-/↓	◆MF+ DPP-4 inhibitor: ↓ wt, PPG. {↑ hypoglycemia if with SU}
exenatide+TZD [pio]	↓↓↓	↑↑	↑↑	◆MF+ canagliflozin: ↓ wt, PPG & hypoglycemia unless with insulin/SU
exenatide+MF+SU [70] liraglutide+MF+SU	↓↓↓	↑↑	↓	◆exenatide+pioglitatzone vs insulin tx: =A1c ; less wt↑ QATAR
MF+DPP4+DAPA	↓↓↓	-/↑	↓↓	◆empagliflozin+MF±other : ↓wt, some hypoglycemia, ↓BP ↓death NNT=38/3yrs & ↓CV death A1C=7.8%, EMPA-REG
Insulin monotherapy	↓↓↓	↑↑↑	↑↑↑	◆tight BG control but **hypoglycemia/weight gain**
Insulin + MF (FINFAT STUDY [x])	↓↓↓	↑	↑/↓	◆**↓ insulin resistance**; preferred in obese less wt gain; patient; superior to insulin+SU; insulin sparing ~20-25%
Insulin + SU (UKPDS 57 ultralente @ evening)	↓↓↓	↑↑	↑↑	◆evening basal insulin; lower A1C & less hypoglycemia than insulin alone; caution in elderly (hypoglycemia)
Insulin + acarbose	↓↓	↑↑↑	↑↑↑	◆↓ PPG diet high in Carbs; also ↓ wt & triglycerides
Insulin+ pioglitazone	↓↓[xi]	↑↑↑	↑↑↑	◆↓insulin resistance; but harms (**↑ wt, edema & risk of HF** [xii])
Insulin+ repaglinide	↓↓	↑↑	↑↑	◆option to ↓ PPG;↑wt more than metformin non-obese Lund'09
Insulin basal + GLP-1 (e.g. exenatide, liraglutide)	↓↓	↑/↓	↑/↓↓	◆if A1C <8, ↓ initial insulin dose ~20%. ↑N/V & diarrhea, ↓wt (reasonable combo alternative; can be high cost)
Insulin + 3 orals*	↓↓↓	↑↑↑↑	↑↑↑	◆**ACCORD**: >50% on 3 orals+insulin; A1C=6.4 vs 7.5% **↑ death** *
***ACCORD**: baseline A1C=8.3%, wt=93kg & very aggressive intervention (>50% on 3 orals + insulin); ↓A1C to 6.4% but ↑ death NNH=95 /3.5yr (& ↑wt. & hypoglycemia). In **ADVANCE**: baseline A1C=7.5%, wt=78kg; most on SU **gliclazide + MF**; ↓A1C to 6.5% & ↓ microvascular NNT=67 /5yr (esp. nephropathy) but also ↑ severe hypoglycemia NNT=83 /5yr & ↑ hospitalizations NNH=42 /5yr.				
Note: benefits for trials often given in relative numbers for multiple years (~10yrs in UKPDS); however AEs often only reported in absolute numbers over one year. This has the effect of minimizing the quantification of harms & exaggerating the benefits.				

Individualize targets: More aggressive: young adult with recent diagnosis STENO-2; **Less aggressive in frail elderly** [32]. **ACCORD A1C** arm halted due to ↑death NNH= 95 / 3.5yr in aggressive target group (A1C <6 Achieved=6.4) vs standard target group (A1C: 7-7.9 Achieved=7.5); patients with established T2DM at high CV risk ~ 10 yr hx.
Deprescribing: http://deprescribing.org/wp-content/uploads/2015/11/deprescribing_algorithms2016_AHG_vf-cc-Sept-2016-InDesign.pdf

REFERENCES

Aakre KM, Watine J, Bunting PS, et al. **Self-monitoring of blood glucose** in patients with diabetes who do not use insulin—are guidelines evidence-based? Diabet Med 2012;29:1226–36.
Abbasi A, Peelen LM, Corpeleijn E, et al. **Prediction models** for risk of developing type 2 diabetes: systematic literature search and independent external validation study. BMJ. 2012 Sep 18;345:e5900.
Abbassi A, Juszczyk D, van Jaarsveld CHM, et al. **Body Mass Index** and Incident Type 1 and Type 2 Diabetes in Children and Young Adults: A Retrospective Cohort Study. J Endocrine Society. May 2017;1(5):524-537.
Abdel Shaheed C, Carland JE, Graham GG, et al. Is the use of **metformin in patients undergoing dialysis** hazardous for life? A systematic review of the safety of metformin in patients undergoing dialysis. Br J Clin Pharmacol. 2019 Aug 31.
Abrahami D, Douros A, Yin H, etal **. Incretin based drugs and risk of cholangiocarcinoma** among patients with type 2 diabetes: population based cohort study. BMJ 2018;363:k4880.
Abrahami D, Douros A, Yin H, et al. **Dipeptidyl peptidase-4 inhibitors and incidence of inflammatory bowel disease** among patients with type 2 diabetes: population based cohort study. BMJ. 2018 Mar 21;360:k872.
Abrahami D, Douros A, Yin H, et al. **Sodium-Glucose Cotransporter 2 Inhibitors** and the Risk of Fractures Among Patients With Type 2 Diabetes. Diabetes Care. 2019 Jul 11.
Abuissa H, Jones PG, Marso SP, et al. **ACE or ARB** for prevention of type 2 diabetes a meta-analysis of randomized clinical trials. J Am Coll Cardiol. 2005 Sep 6;46(5):821-6.
AACE Diabetes Mellitus Practice Guidelines Task Force. **American** Assoc. of Clinical **Endocrinologists** medical **guidelines** for clinical practice for the management of diabetes mellitus. Endocr Pract. **2007** May-Jun;13 Suppl 1:1-68.
AACE Garber AJ, et al. **AACE-ACE-Consensus** statement-American Assoc Clinical Endocrinologists and College of Endocrinology-**Comprehensive Type 2 Diabetes Management Algorithm 2018** Executive Summary. Endocr Pract. 2018 Jan;24(1):91-120.
Abdelghaffar S, Attia AM. **Metformin added to insulin therapy for type 1 diabetes** mellitus in adolescents. Cochrane Database Syst Rev. 2009 Jan 21;(1):CD006691. There is some evidence suggesting improvement of metabolic control in poorly controlled adolescents with type 1 diabetes, on addition of metformin to insulin therapy. Stronger evidence is required from larger studies, carried out over longer time periods to document the long-term effects on metabolic control, health-related quality of life as well as morbidity and mortality in those patients.
ACC/AHA 2017 Whelton PK, Carey RM, et al. **2017 ACC/AHA**/AAPA/ABC/ACPM/AGS/APhA/ASH/ASPC/NMA/PCNA **Guideline for the Prevention, Detection, Evaluation, and Management of High Blood Pressure** in Adults: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. Hypertension. 2017 Nov 13.
ACCORD Study Group, **Effects of Intensive Blood-Pressure Control in Type 2 Diabetes Mellitus.** N Engl J Med 2010 0: NEJMoa1001286
ACCORD Study Group, **Effects of Combination Lipid Therapy (simvastatin with fenofibrate) in Type 2 Diabetes Mellitus.** N Engl J Med 2010 0: NEJMoa1001282.
ACCORD Action to Control Cardiovascular Risk in Diabetes Study Group. Effects of Intensive **Glucose** Lowering in Type 2 Diabetes. N Engl J Med. 2008 Jun 6. [Epub ahead of print]
ACCORD Riddle MC, Ambrosius WT, Brillon DJ, et al. Epidemiologic relationships between **A1C and all-cause mortality** during a median 3.4 year follow up of glycemic treatment in the ACCORD. Diabetes Care 2010; 33:983-990.
ACCORD Study Group and ACCORD Eye Study Group, Effects of Medical Therapies on **Retinopathy** Progression in Type 2 Diabetes. N Engl J Med 2010 0: NEJMoa1001288.
ACCORD Ismail-Beigi F, Craven T, Banerji MA. Effect of intensive treatment of hyperglycaemia on **microvascular** outcomes in type 2 diabetes: an analysis of the ACCORD randomised trial.The Lancet, Early Online Publication, 29 June 2010 doi:10.1016/S0140-6736(10)60576-4.

ACCORD Study Group. Long-term effects of intensive glucose lowering on cardiovascular outcomes. N Engl J Med 2011 Mar 3; 364:818.
ACCORD Anderson RT, Narayan KM, Feeney P, et al. Action to Control Cardiovascular Risk in Diabetes (ACCORD) Investigators. Effect of intensive glycemic lowering on health-related quality of life in type 2 diabetes: ACCORD trial. Diabetes Care. 2011 Apr;34(4):807-12.
ACCORD Schwartz AV, Margolis KL, Sellmeyer DE, et al. Intensive Glycemic Control Is Not Associated With **Fractures or Falls** in the ACCORD Randomized Trial. Diabetes Care. 2012 Jul;35(7):1525-31.
ACCORD Fonseca V, McDuffie R, Calles J, et al. Determinants of **weight gain** in the Action to Control Cardiovascular Risk in Diabetes (Acord) trial.Diabetes Care 2013 .
ACCORD Margolis KL, O'Connor PJ, Morgan TM, et al. Outcomes of **Combined Cardiovascular Risk Factor Management** Strategies in Type 2 Diabetes: The ACCORD Randomized Trial. Diabetes Care. 2014 Mar 4.
ACCORD Gerstein HC, Miller ME, Ismail-Beigi F, et al, for the ACCORD Study Group. Effects of **intensive glycaemic control** on ischaemic heart disease: analysis of data from the randomised, controlled ACCORD trial. Lancet 2014; online Aug 1.
ACCORD 9-Year Effects of 3.7 Years of **Intensive Glycemic Control** on **Cardiovascular Outcomes**. Diabetes Care. 2016 Jan 28. pii: dc152283
ACCORD Action to Control Cardiovascular Risk in Diabetes Follow-On (**ACCORDION**) Eye Study Group and the Action to Control Cardiovascular Risk in Diabetes Follow-On (ACCORDION) Study Group. Persistent Effects of **Intensive Glycemic Control on Retinopathy** in Type 2 Diabetes in the Action to Control Cardiovascular Risk in Diabetes (**ACCORD**) Follow-On Study. Diabetes Care. 2016 Jul;39(7):1089-100
ACCORD Study Group.. **Nine-Year Effects of 3.7 Years** of Intensive Glycemic Control on Cardiovascular Outcomes. Diabetes Care. 2016 May;39(5):701-8.
ADA: American Diabetes Association. Standards of **Medical Care in Diabetes-2018 Abridged for Primary Care Providers**. Clin Diabetes. 2018 Jan;36(1):14-37.
Adamsson Eryd S, Gudbjörnsdottir S, Manhem K, et al. **Blood pressure and complications** in individuals with type 2 diabetes and no previous cardiovascular disease: national population based cohort study. BMJ. 2016 Aug 4;354:i4070.
Adane AA, Mishra GD, Tooth LR. **Diabetes in Pregnancy and Childhood Cognitive Development**: A Systematic Review. Pediatrics. 2016 May;137(5).
Adimadhyam S, Schumock GT, Calip GS, et al. Increased **risk of mycotic infections associated with sodium-glucose co-transprter 2 inhibitors**- a prescription sequence symmetry analysis. Br J Clin Pharmacol. 2018 Oct 7.
Adler AI, Shaw EJ, Stokes T, Ruiz F; Guideline Development Group. **Newer agents** for blood glucose control in type 2 diabetes: summary of **NICE guidance**. BMJ. 2009 May 22;338:b1668. doi: 10.1136/bmj.b1668. http://www.nice.org.uk/nicemedia/pdf/CG87ShortGuideline.pdf
Adler AI, Ting S, Dent R, Latimer N. **NICE guidance on dapagliflozin** with insulin for type 1 diabetes. Lancet Diabetes Endocrinol. 2019 Sep 2.
Abdul-Ghani M, Migahid O, et al. Combination Therapy With **Exenatide Plus Pioglitazone Versus Basal/Bolus Insulin** in Poorly Controlled Patients With Type 2 Diabetes on Sulfonylurea Plus Metformin: The Qatar Study. Diabetes Care. 2017 Jan 17.
ADVANCE Collaborative Group. Intensive Blood Glucose Control and Vascular Outcomes in Patients with Type 2 Diabetes. N Engl J Med. 2008 Jun 6. [Epub ahead of print] (Poulter NR. Blood pressure and glucose control in subjects with diabetes: new analyses from ADVANCE. J Hypertens. 2009 May;27 Suppl 1:S3-8. Additional blood pressure lowering and intensive glucose control, as achieved in ADVANCE, produce independent benefits and, when combined, substantially reduced cardiovascular mortality and all-cause mortality and improved renal outcomes.) Zoungas S, de Galan BE, Ninomiya T, et al. on behalf of the ADVANCE Collaborative Group. The combined effects of routine blood pressure lowering and intensive glucose control on macrovascular and microvascular outcomes in patients with type 2 diabetes; new results from ADVANCE. Diabetes Care. 2009 Aug 3. [Epub ahead of print] The effects of routine blood pressure lowering and intensive glucose control were independent of one another and when combined produced additional reductions in clinically relevant outcomes.
Afkarian M, Sachs MC, Kestenbaum B, et al. **Kidney disease** and increased mortality risk in type 2 diabetes. J Am Soc Nephrol Jan 24, 2013.
Afkarian M, Zelnick LR, Hall YN, Heagerty et al. Clinical Manifestations of **Kidney Disease** Among US Adults With Diabetes,1988-2014. JAMA. 2016 Aug 9;316(6):602-10.
AFSSAPS June/11 The antidiabetes drug **pioglitazone** (marketed in the U.S. as **Actos) is to be taken off the market in France because of concerns over a "slightly increased risk" for bladder cancer**, Bloomberg reports.
Agarwal MM, Dhatt GS, et al. **Gestational** diabetes mellitus: simplifying the **international association** of diabetes and pregnancy diagnostic algorithm using fasting plasma glucose. (IADPSG) Diabetes Care. 2010 Sep;33(9):2018-20.
Aggarwal N;Singla A;Mathieu C;et al. **Metformin extended-release** versus immediate-release: an international, randomized, double-blind, head-to-head trial in pharmacotherapy-naive patients with type 2 diabetes. Diabetes Obes Metab. 2017 Aug 31.
Aguiar EJ, Morgan PJ, Collins CE, et al. Efficacy of the Type 2 Diabetes Prevention Using **LifeStyle Education Program RCT (Pulse).** Am J Prev Med. 2015 Oct 30.
Agus MSD, Steil GM, Wypij D, et al. **Tight glycemic control versus standard care** after pediatric cardiac surgery. (**SPECS**) N Engl J Med 2012.
Agus MS, Wypij D, Hirshberg EL, et al. **Tight Glycemic Control in Critically Ill Children**. N Engl J Med. 2017 Jan 24.
Ahlqvist E, Storm P, Käräjämäki A, et al. **Novel subgroups of adult-onset diabetes** and their association with outcomes: a data-driven cluster analysis of six variables.Lancet Diabetes Endocrinol. 2018 Mar 1. (**5 groups**)
Ahmadizar F, et al. **Undertreatment of hypertension and hypercholesterolaemia in children and adolescents with type 1 diabetes**: long-term follow-up on time trends in the occurrence of cardiovascular disease, risk factors and medications use. Br J Clin Pharmacol. 2018 Apr;84(4):776-785.
Ahmadizar F, OchoaRosales C, Glisic M, et al. **Associations of statin use with glycaemic traits** and incident type 2 diabetes. Br J Clin Pharmacol. 2019 Mar 5.
Ahmann A, Rodbard HW, Rosenstock J, et al. Efficacy and safety of **liraglutide** versus placebo added to basal insulin analogues (with or without metformin) in patients with type 2 diabetes: a randomized, placebo-controlled trial. Diabetes Obes Metab. 2015 Jul 14.
Ahmann AJ, Capehorn M, Charpentier G, et al. Efficacy and Safety of Once-Weekly **Semaglutide** Versus Exenatide ER in Subjects With Type 2 Diabetes (SUSTAIN 3): A 56-Week, Open-Label, Randomized Clinical Trial. Diabetes Care. 2017 Dec 15.
Ahmed HM, Khraishah H, Cho L. **Cardioprotective anti-hyperglycaemic medications**: a review of clinical trials. Eur Heart J. 2017 Dec 9.
Ahn CH, Han KA, Yu JM, et al. Efficacy and safety of **gemigliptin**, a dipeptidyl peptidase-4 inhibitor, in patients with type 2 diabetes mellitus inadequately controlled with combination treatment of metformin and sulphonylurea: a 24-week, multicentre, randomized, double-blind, placebo-controlled study (TROICA study). Diabetes Obes Metab. 2016 Dec 27.
Ahren B, Leguizamo Dimas A, Miossec P, et al. Efficacy and Safety of **Lixisenatide** Once-Daily Morning or Evening Injections in Type 2 Diabetes Inadequately Controlled on Metformin (GetGoal-M). Diabetes Care. 2013 Mar 27.
Ahren B, Hirsch IB, Pieber TR, et al. Efficacy and Safety of **Liraglutide Added to Capped Insulin** Treatment in Subjects With Type 1 Diabetes: the **ADJUNCT TWO** Randomized Trial. Diabetes Care. 2016 Aug 4.
Aiello LP, Ayala AR, Antoszyk AN, et al; Diabetic Retinopathy Clinical Research Network. Assessing the Effect of **Personalized Diabetes Risk Assessments During Ophthalmologic Visits** on Glycemic Control: A Randomized Clinical Trial. JAMA Ophthalmol. 2015 Aug;133(8):888-96.
Ajay Varanasi, Natalie Bellini, Deepti Rawal, et al. **Liraglutide** as Additional Treatment in Type 1 Diabetes *Eur J Endocrinol* 2011 EJE-11-0330
Akilen R, Tsiami A, Devendra D, et al. Glycated Haemoglobin and Blood Pressure-Lowering Effect of **Cinnamon** in Multi-Ethnic Type 2 Diabetic Patients in the UK: A Randomized, Placebo-Controlled, Double-Blind Clinical Trial. Diab Med. 2010;27:1159-1167.
Akinpelua OV, Mujica-Motaa M, Daniela SJ. Is type 2 diabetes mellitus associated with alterations in **hearing**?: a systematic review and meta-analysis. Laryngoscope 2013; August 14. doi: 10.1002/lary.24354.
Akirov A, Grossman A, Shochat T, et al. **Mortality among hospitalized patients with hypoglycemia: insulin-related and non-insulin related**. J Clin Endocrinol Metab. 2016 Nov 17:jc20162653.
Al Hamarneh YN, Charrois T, Lewanczuk R, et al. **Pharmacist intervention for glycaemic control** in the community (the RxING study). BMJ Open 2013;3(9):e003154
Al Hamarneh YN, Siemens RL, Townsend KJ. **Top 10 things pharmacists should consider when they interact with patients with type 2 diabetes**. Can J Diabetes 2017; DOI: http://dx.doi.org/10.1016/j.jcjd.2017.08.247.
Al Hamarneh YN, Hemmelgarn BR, Hassan I, et al. The Effectiveness of **Pharmacist Interventions on Cardiovascular Risk** in Adult Patients with Type 2 Diabetes: The Multicentre Randomized Controlled R(x)EACH Trial. Can J Diabetes. 2017 Sep 28.
Al Khalifah RA et al. **Metformin or oral contraceptives for adolescents with polycystic ovarian syndrome**: A meta-analysis. Pediatrics 2016 May; 137:e20154089.
Al Khalifah RA, Florez ID, Dennis B, et al. **Metformin or Oral Contraceptives** for Adolescents With **Polycystic Ovarian Syndrome**: A Meta-analysis. Pediatrics. 2016 May;137(5).
Al Khalifah RA, Alnhdi A, Alghar H, et al. The effect of **adding metformin to insulin therapy** for type 1 diabetes mellitus children: A systematic review and meta-analysis. Pediatr Diabetes. 2017 Feb 1.
Al Nofal A, Lteif A. **Thiazide Diuretics** in the Management of Young Children with Central **Diabetes Insipidus**. J Pediatr. 2015 Jun 27.
Al-Arouj M, Bouguerra R, Buse J, et al. Recommendations for management of diabetes during **Ramadan**. Diabetes Care. 2005 Sep;28(9):2305-11.
Al-Sofiani ME, Yanek LR, Faraday N, et al. Diabetes and Platelet **Response to Low-Dose Aspirin**. J Clin Endocrinol Metab. 2018 Dec 1;103(12):4599-4608.
Albers JW, Herman WH, Pop-Busui R, et al. for the **DCCT/EDIC** Research Group. Effect Of Prior Intensive Insulin Treatment During The Diabetes Control And Complications Trial (DCCT) On **Peripheral Neuropathy** In Type 1 Diabetes During The Epidemiology Of Diabetes Interventions, And Complications (EDIC) Study. Diabetes Care. 2010 Feb 11.
Alberti KG, Zimmet P, Shaw J; IDF Epidemiology Task Force Consensus Group. The **metabolic syndrome**--a new worldwide definition. Lancet. 2005 Sep 24-30;366(9491):1059-62.
Aldasouqi S, Mora S, Bhalla G, et al. **Fasting-Evoked En Route Hypoglycemia in Diabetes** (FEEHD): An Overlooked Form of Hypoglycemia in Clinical Practice. Int J Endocrinol. 2018 Oct 24;2018:1528437.
Alegre-Díaz J, Herrington W, López-Cervantes M, et al. Diabetes and **Cause-Specific Mortality in Mexico City**. N Engl J Med. 2016 Nov 17;375(20):1961-1971.
Aleppo G, Ruedy KJ, Riddlesworth TD, et al. **REPLACE-BG**: Randomized Trial Comparing **Continuous Glucose Monitoring With and Without Routine Blood Glucose Monitoring** in Well-Controlled Adults With Type 1 Diabetes. Diabetes Care. 2017 Feb 16.
Alexopoulos AS, Blair R, Peters AL. Management of **Preexisting Diabetes in Pregnancy**: A Review. JAMA. 2019 May 14;321(18):1811-1819.

Algeffari M, Jayasena CN, MacKeith P, et al. **Testosterone therapy for sexual dysfunction** in men with Type 2 diabetes: a systematic review and meta-analysis of randomized controlled trials. Diabet Med. 2018 Feb;35(2):195-202.
Ali A, Cheng AY, Yu CH. Breaking down **barriers to initiating insulin**: Insulin prescription pad. Can Fam Physician. 2015 May;61(5):445-7.
Ali K, Harnden A, Edge JA. **Type 1 diabetes in children**. BMJ. 2011 Feb 16;342:d294. doi: 10.1136/bmj.d294.
Ali MK, Bullard KM, Saaddine JB, et al. **Achievement of goals in U.S. diabetes care**, 1999–2010. N Engl J Med 2013;368: 1613-24.
Ali MK, Bullard KM, Gregg EW, Del Rio C. A **cascade of care** for diabetes in the United States: visualizing the gaps. Ann Intern Med. 2014 Nov 18;161(10):681-9.
Ali MK, Singh K, Kondal D, et al. Effectiveness of a **Multicomponent Quality Improvement Strategy** to Improve Achievement of Diabetes Care Goals: A Randomized, Controlled Trial. Ann Intern Med. 2016 Jul 12.
Ali MK, McKeever Bullard K, Imperatore G, et al. Reach and Use of **Diabetes Prevention Services in the United States**, 2016-2017. JAMA Netw Open. 2019;2(5):e193160.
Allegretti AS, Zhang W, Zhou W, et al. Safety and Effectiveness of **Bexagliflozin in Patients** With Type 2 Diabetes Mellitus and Stage 3a/3b CKD. Am J Kidney Dis. 2019 May 13.
Allen RW, Schwartzman E, Baker WL, et al. **Cinnamon** use in type 2 diabetes: an updated systematic review and meta-analysis. Ann Fam Med. 2013 Sep-Oct;11(5):452-9.
Alpañés M, Álvarez-Blasco F, et al. **Combined oral contraceptives plus spironolactone compared with metformin in women with polycystic ovary syndrome**: a one-year randomized clinical trial. Eur J Endocrinol. 2017 Nov;177(5):399-408.
Alqudah A, McKinley MC, McNally R, et al. **Risk of pre-eclampsia in women taking metformin**: a systematic review and meta-analysis. Diabet Med. 2018 Feb;35(2):160-172.
Alvarez-Blasco F, et al. Prevalence and characteristics of the **polycystic ovary syndrome** in overweight and obese women. Arch Intern Med. 2006 Oct 23;166(19):2081-6.
*Amate J, Lopez-Cuadrado T, Almendro N, et al. Effectiveness and safety of **glimepiride and iDPP4, associated with metformin** in second line pharmacotherapy of type 2 diabetes mellitus: systematic review and meta-analysis. Int J Clin Pract. 2015 Feb 16.*
Amblee A, Lious D, Fogelfeld L. Combination of **Saxagliptin and Metformin** is Effective as Initial Therapy in New Onset Type 2 Diabetes Mellitus With Severe Hyperglycemia. J Clin Endocrinol Metab. 2016 May 4.
*Amed S, Nuernberger K, McCrea P, et al. Adherence to Clinical Practice Guidelines in the Management of **Children, Youth, and Young Adults with Type 1** Diabetes-A Prospective Population Cohort Study. J Pediatr. 2013 Mar 21.*
Amed S, Dean H, Sellers EA, et al. **Risk factors for medication-induced** diabetes and type 2 diabetes. J Pediatr. 2011 Aug;159(2):291-6.
*American Heart Association Nutrition Committee, Lichtenstein AH, Appel LJ, Brands M, et al. **Diet and lifestyle recommendations revision 2006**: a scientific statement from the American Heart Association Nutrition Committee. Circulation 2006 Jul 4;114(1):82-96.*
American College of Obstetricians and Gynecologists (**ACOG**). **Polycystic ovary syndrome**. Washington (DC): American College of Obstetricians and Gynecologists (ACOG); 2009 Oct. 14 p. (ACOG practice bulletin; no. 108).
American College of Sports Medicine, American Diabetes Association. **Exercise and type 2 diabetes**: American College of Sports Medicine and the American Diabetes Association: joint position statement. Med Sci Sports Exerc 2010 Dec;42(12):2282-303.
American Diabetes Association (ADA 2016): Standards of Medical Care in **Diabetes-2016: Summary of Revisions**. Diabetes Care. (American Diabetes Association) 2016 Jan;39 Suppl 1:S4-5.
Amin S, Lux A, O'Callaghan F. The journey **of metformin from glycaemic control to mTOR inhibition and the suppression of tumor growth**. Br J Clin Pharmacol. 2018 Oct 5.
Amin R, Turner C, van Aken S, Bahu TK, et al. The relationship between **microalbuminuria and glomerular filtration** rate in young type 1 diabetic subjects: The Oxford Regional Prospective Study. Kidney Int. 2005 Oct;68(4):1740-9.
Aminian A, Zajichek A, Arterburn DE, et al. Association of **Metabolic Surgery With Major Adverse Cardiovascular Outcomes** in Patients With Type 2 Diabetes and Obesity. JAMA. 2019 Sep 2.
Amori RE, et al. Efficacy and safety of **incretin therapy** in type 2 diabetes: systematic review and meta-analysis. JAMA. 2007 Jul 11;298(2):194-206. Incretin therapy offers an alternative option to currently available hypoglycemic agents for nonpregnant adults with type 2 diabetes, with modest efficacy & a favorable weight-change profile. Careful postmarketing surveillance for adverse effects, especially among the DPP4 inhibitors, & continued evaluation in longer-term studies and in clinical practice are required to determine the role of this new class among current pharmacotherapies for type 2 diabetes.
Andersen SE, Christensen M. **Hypoglycaemia when Adding Sulphonylurea to Metformin**: A Systematic Review and Network Meta-analysis. (gliclazide) Br J Clin Pharmacol. 2016 Jul 18.
Andersen YMF, Egeberg A, Ban L, et al. Association Between Topical Corticosteroid Use and Type 2 Diabetes in Two European Population-Based Adult Cohorts. Diabetes Care. 2019 Jun;42(6):1095-1103
Anderson RJ, Bahn GD, Moritz TE, et al.; for the **VADT** Study Group. Blood Pressure and Cardiovascular Disease risk in the Veterans Affairs Diabetes Trial (VADT) Diabetes Care. 2010 Nov 8. DBP <70 mmHg elevated CVD risk.
Anderson TJ, Grégoire J, Hegele RA, et al. **2012 Update of the Canadian Cardiovascular Society (CCS) Guidelines for the diagnosis and treatment of dyslipidemia** for the prevention of cardiovascular disease in the adult. Can J Cardiol 2013;29(2):151-67. www.onlinecjc.ca/article/S0828-282X(12)01510-3/fulltext (accessed February 5, 2013).
Andrews RC, Cooper AR, Montgomery AA, et al. **Diet or diet plus physical activity versus usual care** in patients with newly diagnosed type 2 diabetes: the Early ACTID randomised controlled trial. Lancet 2011; June 25.
Andrews MA, O'Malley PG. Diabetes **overtreatment in elderly** individuals: risky business in need of better management. JAMA. doi:10.1001 /jama.2014.4563.
Andrade Susan E, Lo Joan C, Roblin Douglas, et al. **Antipsychotic Medication Use Among Children** and Risk of Diabetes Mellitus. Pediatrics 2011; peds.2011-0855; ahead of print November 21, 2011.
Anjana RM, Deepa M, Pradeepa R, et al. **Prevalence of diabetes and prediabetes in 15 states of India**: results from the ICMR-INDIAB population-based cross-sectional study. Lancet Diabetes Endocrinol. 2017 Jun 7
Anthonisen NR, Skeans MA, Wise RA, et al.; Lung Health Study Research Group. The effects of a **smoking cessation** intervention on 14.5-year mortality: a randomized clinical trial. Ann Intern Med. 2005 Feb 15;142(4):233-9.
Antonetti DA, Klein R, Gardner TW. **Diabetic retinopathy**. N Engl J Med. 2012 Mar 29;366(13):1227-39.
AntvorskovJC, HalldorssonTI, JosefsenK, etal . Association between **maternal gluten intake and type 1 diabetes in offspring**: national prospective cohort study in Denmark. BMJ 2018;362:k3547.
Anyanwagu U, Mamza J, Mehta R, et al. Cardiovascular events and **all-cause mortality with insulin versus glucagon-like peptide-1 analogue** in type 2 diabetes. Heart. 2016 May 23.
Anyanwagu U, Mamza J, Gordon J, et al. **Premixed vs basal-bolus insulin regimen** in Type 2 diabetes: comparison of clinical outcomes from randomized controlled trials and real-world data. Diabet Med. 2017 Dec;34(12):1728-1736.
Apolzan JW, Venditti EM, Edelstein SL, et al. **Long-term weight loss with metformin or lifestyle intervention** in the Diabetes Prevention Program Outcomes Study. (DPPOS) Ann Intern Med. 2019 Apr 23.
Arad Y, Fonseca V, Peters A, et al. Beyond the **Monofilament for the Insensate Diabetic Foot**: A systematic review of randomized trials to prevent the occurrence of plantar foot ulcers in patients with diabetes. Diabetes Care. 2011 Apr;34(4):1041-6.
Araki E, Tanizawa Y, Tanaka Y, et al. Long-term treatment with **empagliflozin** as add-on to oral antidiabetes therapy in Japanese patients with type 2 diabetes mellitus. Diabetes Obes Metab. 2015 Jul;17(7):665-74.
Araki E, Inagaki N, Tanizawa Y, et al. Efficacy and safety of once-weekly **dulaglutide** in combination with sulphonylurea and/or biguanide compared with once-daily insulin glargine in Japanese patients with type 2 diabetes: a randomized, open-label, phase III, non-inferiority study. Diabetes Obes Metab. 2015 Jul 14.
Araneta MR, Grandinetti A, Chang HK. **A1C and diabetes diagnosis among Filipino Americans, Japanese Americans, and Native Hawaiians**. Diabetes Care. 2010 Dec;33(12):2626-8.
Araneta MR, Kanaya AM, Hsu WC, et al. **Optimum BMI** Cut Points to Screen **Asian** Americans for Type 2 Diabetes. Diabetes Care. 2015 May;38(5):814-20.
Arcani R, Martinez S, Gayet S. **Sitagliptin and Angioedema**: A Case Report. Ann Intern Med. 2017 May 30.
Areosa Sastre A, Vernooij RW, Gonzalez-Colaco Harmand M, et al. Effect of the **treatment of Type 2 diabetes mellitus on the development of cognitive impairment and dementia**. Cochrane Database Syst Rev. 2017 Jun 15;6:CD003804. We found no good evidence that any specific treatment or treatment strategy for Type 2 diabetes can prevent or delay cognitive impairment. The best available evidence related to the comparison of intensive with standard glycaemic control strategies. Here there was moderate-quality evidence that the strategies do not differ in their effect on global cognitive functioning over 40 to 60 months.
Aroda VR, Edelstein SL, Goldberg RB, eta l. Diabetes Prevention Program Research Group. Long-term **Metformin Use and Vitamin B12 Deficiency** in the Diabetes Prevention Program Outcomes Study. J Clin Endocrinol Metab. 2016 Apr;101(4):1754-61.
Aronson R, Brown RE, Li A, et al. **Optimal Insulin Correction Factor in Post-High-Intensity Exercise Hyperglycemia in Adults With Type 1 Diabetes**: The **FIT** Study. Diabetes Care. 2018 Nov 19.
Aronson R, Umpierrez G, Stager W, et al. **Insulin glargine/lixisenatide fixed-ratio combination improves glycaemic variability** and control without increasing hypoglycaemia. Diabetes Obes Metab. 2018 Nov 13.
Aronson R, Brown RE, Li A, et al. Optimal **Insulin Correction Factor in Post-High-Intensity Exercise Hyperglycemia in Adults** With Type 1 Diabetes: **The FIT Study**. Diabetes Care. 2018 Nov 19.
Armato JP, DeFronzo RA, Abdul-Ghani M, et al. Successful treatment of **prediabetes in clinical practice using physiological assessment** (STOP DIABETES). Lancet Diabetes Endocrinol. 2018 Sep 13.
Armstrong DG, Lavery LA; Diabetic Foot Study Consortium. **Negative pressure wound** therapy after partial diabetic foot amputation: a multicentre, randomised controlled trial. Lancet. 2005 Nov 12;366(9498):1704-10.
Armstrong DG, Boulton AJM, Bus SA. **Diabetic Foot Ulcers and Their Recurrence**. N Engl J Med. 2017 Jun 15;376(24):2367-2375.
Armstrong MJ, Houlihan DD, Rowe IA, et al. Safety and efficacy of **liraglutide** in patients with type 2 diabetes and elevated liver enzymes: individual patient data meta-analysis of the LEAD program. Aliment Pharmacol Ther. 2013 Jan;37(2):234-42.
Armstrong MJ, Gaunt P, Aithal GP, et al; **LEAN** trial team, **Liraglutide** safety and efficacy in patients with non-alcoholic steatohepatitis (LEAN): a multicentre, double-blind, randomised, placebo-controlled phase 2 study. Lancet. 2015 Nov 19.
Aroda VR, Henry RR, Han J, et al. Efficacy of **GLP-1 Receptor Agonists and DPP-4 Inhibitors**: Meta-Analysis and Systematic Review. Clin Ther. 2012 May 17.
Aroda VR, et al. The effect of adding **insulin degludec** in patients with type 2 diabetes inadequately controlled with **metformin and liraglutide**: double-blind randomized controlled trial (BEGIN: ADD TO GLP-1 Study). Diabetes Obes Metab. 2016 Mar 18.
Aroda VR, et al. Efficacy & Safety of **LixiLan**, a Titratable Fixed-Ratio Combination of **Insulin Glargine Plus Lixisenatide** in Type 2 Diabetes Inadequately Controlled on Basal Insulin and Metformin: The LixiLan-L Randomized Trial. Diabetes Care. 2016 Sep 20.

Aroda VR, Rosenstock J, Terauchi Y, et al. PIONEER 1: Randomized Clinical Trial Comparing the **Efficacy and Safety of Oral Semaglutide** Monotherapy with Placebo in Patients with Type 2 Diabetes. Diabetes Care. 2019 Jun 11.

Aronson R, Reznik Y, Conget I, et al. Sustained efficacy of **insulin pump therapy**, compared with multiple daily injections, in type 2 diabetes: 12-month data from the OpT2mise randomized trial. Diabetes Obes Metab. 2016 Feb 8.

Arslanian S, Bacha F, Grey M, et al. Evaluation and Management of **Youth-Onset Type 2 Diabetes**: A Position Statement by the American Diabetes Association. Diabetes Care. 2018 Dec;41(12):2648-2668.

Arterburn D, McCulloch D. **Bariatric Surgery for Type 2 Diabetes**: Getting Closer to the Long-term Goal. JAMA. 2016 Mar 22-29;315(12):1276-7.

Aschner PJ, Chan J, Owens DR, et al, **EASIE** investigators. **Insulin glargine versus sitagliptin** in insulin-naive patients with type 2 diabetes mellitus uncontrolled **on metformin** (EASIE): a multicentre, randomised, open-label trial. Lancet 2012; online June 9.

ASCEND Study Collaborative Group. Effects of **Aspirin for Primary Prevention** in Persons with Diabetes Mellitus. N Engl J Med. 2018 Aug 26.

ASCEND Study Collaborative Group. Effects of **n-3 Fatty Acid Supplements** in Diabetes Mellitus. N Engl J Med. 2018 Aug 26.

Ashwell SG, Gebbie J, Home PD. Twice-daily compared with once-daily insulin **glargine** in people with Type 1 diabetes using meal-time **insulin aspart**. Diabet Med. 2006 Aug;23(8):879-86.

Atkin S. Commentary: controversies in NICE guidance on management of type 2 diabetes. BMJ 2008;336:1308-1309.

Athauda D, Maclagan K, Skene SS, et al. **Exenatide** once weekly versus placebo in **Parkinson's** disease: a randomised, double-blind, placebo-controlled trial. Lancet. 2017 Aug 3.

Atkinson MA, Eisenbarth GS, Michels AW. **Type 1 diabetes**. Lancet. 2014 Jan 4;383(9911):69-82

Augustine P, Gent R, Louise J, et al. **Pancreas size and exocrine function is decreased in young children** with recent-onset Type 1 diabetes. Diabet Med. 2019 May 15.

Auzanneau M, Lanzinger S, Bohn B, et al; DPV Initiative. **Area Deprivation and Regional Disparities** in Treatment and Outcome Quality of 29,284 Pediatric Patients With Type 1 Diabetes in Germany: A Cross-sectional Multicenter DPV Analysis. Diabetes Care. 2018 Dec;41(12):2517-2525.

Avandaryl (Rosiglitazone/Glimepiride) Medical Letter Mar 13,2006.

Avery L, Flynn D, van Wersch A, et al. Changing **Physical Activity Behavior** in Type 2 Diabetes: A systematic review and meta-analysis of behavioral interventions. Diabetes Care. 2012 Dec;35(12):2681-9.

Avgerinos I, Karagiannis T, Malandris K, et al. **Glucagon-like peptide-1 receptor agonists and microvascular outcomes in type 2 diabetes**: A systematic review and meta-analysis. Diabetes Obes Metab. 2018 Jul 29.

Avogaro A, Fadini GP. The **pleiotropic cardiovascular effects of dipeptidyl peptidase-4 inhibitors**. Br J Clin Pharmacol. 2018 Apr 17.

Aylsworth A, Dean Z, VanNorman C, et al. **Dapagliflozin** for the Treatment of Type 2 Diabetes Mellitus. Ann Pharmacother. 2014 Jun 20;48(9):1202-1208.

Azhary H, Farooq MU, Bhanushali M, Majid A, Kassab MY. **Peripheral neuropathy**: differential diagnosis and management. Am Fam Physician. 2010 Apr 1;81(7):887-92.

Azoulay L, Yin H, Filion KB, et al. The use of **pioglitazone and the risk of bladder cancer** in people with type 2 diabetes: nested case-control study. BMJ 2012; DOI:10.1136/bmj.e3645

Azoulay L, Filion KB, Platt RW, et al. **Incretin based drugs and the risk of pancreatic cancer**: international multicentre cohort study. BMJ 2016;352:i581. 3

Azoulay L, Filion KB, Platt RW, et al. Association Between **Incretin-Based Drugs and the Risk of Acute Pancreatitis**. JAMA Intern Med. 2016 Aug 1.

Azoulay L, Suissa S. **Sulfonylureas and the Risks of Cardiovascular Events and Death**: A Methodological Meta-Regression Analysis of the Observational Studies.Diabetes Care. 2017 May;40(5):706-714.

Babenko AP, et al. Activating mutations in the ABCC8 gene in neonatal diabetes mellitus. N Engl J Med. 2006 Aug 3;355(5):456-66.

Bach RG, Brooks MM, Lombardero M, et al., **BARI 2D** Investigators. **Rosiglitazone** and oucomes for patients with diabetes mellitus and coronary artery disease in the Bypass Angioplasty Revascularization Investigation 2 Diabetes (BARI 2D) trial. Circulation. 2013;128:785–794.

Bae JP, Duan R, Fu H, et al. Risk Factors for **Nocturnal Hypoglycemia** in **Insulin**-Treated Patients With Type 2 Diabetes: A Secondary Analysis of Observational Data Derived From an Integrated Clinical Trial Database. Clin Ther. 2017 Aug 3.

Baerlocher MO, Asch M, Myers A. **Metformin and intravenous contrast**. CMAJ. 2013 Jan 8;185(1):E78.

Baidal DA, Ricordi C, Berman DM, Alvarez et al. **Bioengineering of an Intraabdominal Endocrine Pancreas**. N Engl J Med. 2017 May 11;376(19):1887-1889.

Bajaj HS, Abouhassan T, Ahsan MR, et al. **Diabetes Canada Position Statement** for People with Types 1 and 2 Diabetes Who **Fast During Ramadan**. Can J Diabetes. 2018 Apr 27.

Bajaj HS, Barnes T, Nagpal S, et al. **Diabetes Canada position statement on recreational cannabis use** in adults and adolescents with type 1 and type 2 diabetes. Can J Diabetes 2019 (accepted manuscript). doi: https://doi.org/10.1016/j.jcjd.2019.05.010.

Baker WL, Gutierrez-Williams G, White CM, Kluger J, Coleman CI. Effect of **cinnamon on glucose control** and lipid parameters. Diabetes Care. 2008 Jan;31(1):41-3. Epub 2007 Oct 1. Cinnamon does not appear to improve A1C, FBG, or lipid parameters in patients with type 1 or type 2 diabetes.

Bakrania K, et al. Associations of **moderate-to-vigorous-intensity physical activity** and body mass index with glycated haemoglobin within the general population: a cross-sectional analysis of the 2008 Health Survey for England. BMJ Open. 2017 Apr 3;7(4):e014456.

Bakris G, et al. Differences in glucose tolerance between fixed-dose **antihypertensive drug combinations** in people with **metabolic syndrome**. Diabetes Care. 2006 Dec;29(12):2592-7.

Bakris GL, Agarwal R, Chan JC, et al; Mineralocorticoid Receptor Antagonist Tolerability Study–Diabetic Nephropathy (**ARTS-DN**) Study Group. Effect of **Finerenone on Albuminuria** in Patients With Diabetic Nephropathy: A Randomized Clinical Trial. JAMA. 2015 Sep 1;314(9):884-94.

Bailey Clifford J, Gross Jorge L, Pieters Anne, et al., Effect of **dapagliflozin** in patients with type 2 diabetes who have inadequate glycaemic control with metformin: a randomised, double-blind, placebo-controlled trial, The Lancet, Volume 375, Issue 9733, 26 June 2010-2 July 2010, Pages 2223-2233

Bailey Clifford J. The challenge of **managing coexistent type 2 diabetes and obesity**. BMJ 2011;342:doi:10.1136/bmj.d1996 (Published 13 April 2011)

Bailey TS, Grunberger G, Bode BW, et al. **American** Association of Clinical Endocrinologists and American College of Endocrinology 2016 **Outpatient Glucose Monitoring Consensus Statement**. Endocr Pract. 2016 Feb;22(2):231-61.

Bain S, Druyts E, Balijepalli C, et al. **Cardiovascular events** and allcause mortality associated with **sulphonylureas** compared with other antihyperglycaemic drugs: a Bayesian meta-analysis of survival data. Diabetes Obes Metab. 2017;19:329-35.

Balducci S, D'Errico V, Haxhi J, et al; Italian Diabetes and Exercise Study 2 (IDES_2) Investigators. Effect of a Behavioral Intervention Strategy on **Sustained Change in Physical Activity and Sedentary Behavior** in Patients With Type 2 Diabetes: The IDES_2 Randomized Clinical Trial. JAMA. 2019 Mar 5;321(9):880-890.

Baldwin D, Zander J, Munoz C, et al. A Randomized Trial of Two Weight-Based Doses of **Insulin Glargine and Glulisine** in Hospitalized Subjects With Type 2 Diabetes and **Renal Insufficiency**. Diabetes Care. 2012 Jun 14.

Balena R, Hensley IE, Miller S, et al. Combination therapy with GLP-1 receptor agonists and basal insulin: a systematic review of the literature. Diabetes Obes Metab. 2012 Oct 15.

Balk EM, Earley A, Raman G, et al. **Combined Diet and Physical Activity Promotion Programs** to Prevent Type 2 Diabetes Among Persons at Increased Risk: A Systematic Review for the Community Preventive Services Task Force. Ann Intern Med. 2015 Jul 14

Bally L, Thabit H, Hartnell S, et al. **Closed-Loop Insulin Delivery for Glycemic Control** in Noncritical Care. N Engl J Med. 2018 Jun 25.

Balsells M, García-Patterson A, Solà I, Roqué M, Gich I, Corcoy R. **Glibenclamide (glyburide), metformin, and insulin for the treatment of gestational diabetes**: a systematic review and meta-analysis. BMJ 2015;350:h102.

Bancks MP, Pletcher MJ, Kertesz SG, et al. **Marijuana use** and risk of prediabetes and diabetes by middle adulthood: the Coronary Artery Risk Development in Young Adults (CARDIA) study. Diabetologia. 2015 Sep 13.

Bancks MP, Ning H, Allen NB, et al. Long-Term **Absolute Risk for Cardiovascular Disease Stratified by Fasting Glucose Level**. Diabetes Care. 2019 Jan 7.

Bang Heejung, Edwards Alison M., Bomback Andrew S., Development and Validation of a **Patient Self-assessment Score for Diabetes Risk**. Ann Intern Med December 1, 2009 151:775-783.

Bangalore S, Kumar S, Lobach I, et al. **Blood pressure targets in subjects with type 2 diabetes mellitus/impaired fasting glucose**: Observations from traditional and Bayesian random-effects meta-analyses of randomized trials. Circulation 2011. DOI: 10.1161/CIRCULATIONAHA.110.016337.

Bangalore S, Fakheri R, Toklu B, Messerli FH. Diabetes mellitus as a **compelling indication for using renin angiotensin system blockers**: systematic review and meta-analysis of randomized trials. BMJ 2016;352:i438.

Bannister CA, Poole CD, Jenkins-Jones S, et al. **External Validation of the UKPDS Risk Engine** in Incident Type 2 Diabetes: A Need for New Type 2 Diabetes-Specific Risk Equations. Diabetes Care. 2014 Feb;37(2):537-45.

Bannister CA, Holden SE, Jenkins-Jones S, et al. Can people with type 2 diabetes **live longer** than those without? A comparison of mortality in people **initiated with metformin or sulphonylurea** monotherapy and matched, non-diabetic controls. Diabetes Obes Metab. 2014 Jul 7.

Bao Y, Ma X, Li H, et al. Glycated haemoglobin **A1c for diagnosing** diabetes in **Chinese** population: cross sectional epidemiological survey. BMJ. 2010 May 17

Bao W, Tobias DK, Bowers K, et al. **Physical activity and sedentary behaviors** associated with risk of progression from gestational diabetes mellitus to type 2 diabetes mellitus: a prospective cohort study. JAMA Intern Med. 2014 Jul 1;174(7):1047-55.

Bao W, Yeung E, Tobias DK, et al. **Long-term risk of type 2 diabetes mellitus in relation to BMI** and weight change among women with a history of gestational diabetes mellitus: a prospective cohort study. Diabetologia. 2015 Mar 22.

Bao W, Tobias DK, Hu FB, et al. Pre-pregnancy **potato consumption** and risk of gestational diabetes mellitus: prospective cohort study. BMJ. 2016 Jan 12;352:h6898.

Barer Y, Cohen O, Cukierman-Yaffe T The effect of **glycemic control on cardiovascular disease** in individuals with **type 2 diabetes** with pre-existing cardiovascular disease - a systematic review and meta-analysis. Diabetes Obes Metab. 2018 Nov 13.

Barnard ND, et al. A **low-fat vegan diet** improves glycemic control and cardiovascular risk factors in a randomized clinical trial in individuals with type 2 diabetes. Diabetes Care. 2006 Aug;29(8):1777-83.

Barnett AH, Huisman H, Jones R, et al. **Linagliptin for patients aged 70 years or older** with type 2 diabetes inadequately controlled with common antidiabetes treatments: a randomised, double-blind, placebo-controlled trial. *Lancet* 2013; online Aug 13.

Barnett AH, et al. An open, randomized, parallel-group study to compare the efficacy and safety profile of **inhaled human insulin (Exubera) with metformin** as adjunctive therapy in patients with type 2 diabetes poorly controlled on a sulfonylurea. Diabetes Care. 2006 Jun;29(6):1282-7.

Barnett AH, Arnoldini S, Hunt B, et al. **Switching from sitagliptin to liraglutide to manage patients with type 2 diabetes** in the UK: A long-term cost-effectiveness analysis**.** Diabetes Obes Metab. 2018 Apr 13.

Barone BB, Yeh HC, Snyder CF, et al. Long-term All-Cause **Mortality in Cancer Patients** With Preexisting Diabetes Mellitus: A Systematic Review and Meta-analysis. JAMA. 2008 Dec 17;300(23):2754-64. Patients diagnosed with cancer who have preexisting diabetes are at increased risk for long-term, all-cause mortality compared with those without diabetes.

BARI 2D study group. A randomized trial of therapies for type 2 diabetes and coronary artery disease. *N Engl J Med.* 2009; 360:2503-2515.

Barrett HL, Gatford KL, Houda CM, et al. Maternal and neonatal circulating markers of metabolic and cardiovascular risk in the **Metformin in Gestational** Diabetes (**MIG**) trial: Responses to maternal metformin versus insulin treatment. Diabetes Care 2013;36:529–36.

Barrett EJ, Liu Z, Khamaisi M, et al. **Diabetic Microvascular Disease**: An **Endocrine Society** Scientific Statement. J Clin Endocrinol Metab. 2017 Dec 1;102(12):4343-4410

Barry E, Finnikin S. A **borderline HBA(1c) result**. BMJ. 2019 Apr 11;365:l1361.

Barry E, Roberts S, Oke J, et al. **Efficacy and effectiveness of screen and treat policies** in prevention of type 2 diabetes: systematic review and meta-analysis of screening tests and interventions. BMJ 2017;356:i6538.

Baskerville R, et al Impact of **accelerometer and pedometer** use on physical activity and glycaemic control in people with Type 2 diabetes: a systematic review and meta-analysis. Diabet Med. 2017 May;34(5):612-620.

Basu S, Yoffe P, Hills N, Lustig RH. The relationship of **sugar to population-level diabetes prevalence**: an econometric analysis of repeated cross-sectional data. PLoS One. 2013;8(2):e57873.

Basu S, Sussman JB, Berkowitz SA, et al. **Validation of Risk Equations for Complications** of Type 2 Diabetes (**RECODe**) Using Individual Participant Data From Diverse Longitudinal Cohorts in the U.S. Diabetes Care. 2017 Dec 21.

Basu S, Yudkin JS, Kehlenbrink S, et al. Estimation of **global insulin use for type 2 diabetes**, 2018-30: a microsimulation analysis. Lancet Diabetes Endocrinol. 2018 Nov 20.

Batabyal P, Vander Hoorn S, Christophi C, Nikfarjam M. Association of **Diabetes Mellitus and Pancreatic Adenocarcinoma**: A Meta-Analysis of 88 Studies. Ann Surg Oncol. 2014 Mar 9.

Battelino T, Phillip M, Bratina N, et al. Effect of **continuous glucose monitoring** on hypoglycemia in type 1 diabetes. Diabetes Care 2011;34:795–800.

Battelino T, Nimri R, Dovc K, Phillip M, Bratina N. **Prevention of Hypoglycemia With Predictive Low Glucose Insulin Suspension** in Children With Type 1 Diabetes: A Randomized Controlled Trial. Diabetes Care. 2017 Jun;40(6):764-770.

Baum A, Scarpa J, Bruzelius E, et al. Targeting weight loss interventions to reduce cardiovascular complications of type 2 diabetes: a machine learning-based post-hoc analysis of heterogeneous treatment effects in the **Look AHEAD** trial. Lancet Diabetes Endocrinol. 2017 Jul 12.

Bazerbachi F, Nazarian S, Alraiyes AH, et al. Q: Is **hemoglobin A1c an accurate measure of glycemic control** in all diabetic patients? Cleve Clin J Med. 2014 Mar;81(3):146-9.

Beddhu S, Greene T, Boucher R, et al. Intensive **systolic blood pressure control and incident chronic kidney disease** in people with and without diabetes mellitus: secondary analyses of two randomised controlled trials. Lancet Diabetes Endocrinol 2018; online April 20

Becerra-Tomás N, Estruch R, Bulló M, et al. Increased Serum **Calcium Levels and Risk of Type 2 Diabetes** in Individuals at High Cardiovascular Risk. Diabetes Care. 2014 Aug 19.

Beck RW, Riddlesworth TD, Ruedy K, et al: **DIAMOND** Study Group. **Continuous glucose monitoring** versus usual care in patients with type 2 diabetes receiving multiple daily insulin injections. A randomized trial. Ann Intern Med. 2017. [Epub ahead of print]. doi:10.7326/M16-2855

Beck RW, Riddlesworth T, Ruedy K, et al; **DIAMOND** Study Group. Effect of **continuous glucose monitoring** on glycemic control in adults with type 1 diabetes using insulin injections: the DIAMOND randomized clinical trial.JAMA. doi:10.1001/jama.2016.19975

Becker M, Galler A, Raile K. **Meglitinide Analogues** in Adolescent Patients With **HNF1A-MODY (MODY 3**). Pediatrics. 2014 Mar;133(3):e775-9.

Beckles ZL, Edge JA, Mugglestone MA, et al; Guideline Development Group. Diagnosis and management of **diabetes in children and young people**: summary of updated **NICE** guidance. BMJ. 2016 Jan 27;352:i139.

Behary P, Tharakan G, Alexiadou K, et al. **Combined GLP-1, Oxyntomodulin, and Peptide YY Improves Body Weight and Glycemia** in Obesity and Prediabetes/Type 2 Diabetes: A Randomized, Single-Blinded, Placebo-Controlled Study. Diabetes Care. 2019 Aug;42(8):1446-1453.

Belalcazar LM, Ballantyne CM. Looking Back at **Look AHEAD** Through the Lens of Recent Diabetes Outcome Trials. Circulation. 2017 Feb 21;135(8):720-723.

Belfort R, et al. A placebo-controlled trial of **pioglitazone** in subjects with **nonalcoholic steatohepatitis**. N Engl J Med. 2006 Nov 30;355(22):2297-307. (n=55 6months) In this proof-of-concept study, the administration of pioglitazone 45mg/d led to metabolic and histologic improvement in subjects with nonalcoholic steatohepatitis. Larger controlled trials of longer duration are warranted to assess the long-term clinical benefit of pioglitazone.

Bellamy L, Casas JP, Hingorani AD, et al. Type 2 diabetes mellitus after **gestational diabetes**: a systematic review and meta-analysis. Lancet. 2009 May 23;373(9677):1773-1779.

Bello O, Mohandas C, Shojee-Moradie F, et al. Black African men with early type 2 diabetes have **similar muscle, liver and adipose tissue insulin sensitivity** to white European men despite lower visceral fat. Diabetologia. 2019 May;62(5):835-844.

Ben Q, Xu M, Ning X, et al. Diabetes mellitus and risk of **pancreatic cancer**: A meta-analysis of cohort studies. Eur J Cancer. 2011 Sep;47(13):1928-37.

Benjamin D, Colombi M, Hindupur SK, et al. **Syrosingopine sensitizes cancer cells to killing by metformin**. Sci Adv. 2016 Dec 23;2(12):e1601756.

Bennett Wendy L., Maruthur Nisa M., Singh Sonal, et al. **Comparative Effectiveness and Safety of Medications for Type 2 Diabetes**: An Update Including New Drugs and 2-Drug Combinations. *Ann Intern Med* E-336published ahead of print March 14, 2011. Evidence supports metformin as a first-line agent to treat type 2 diabetes. Most 2-drug combinations similarly reduce hemoglobin A1c levels, but some increased risk for hypoglycemia and other adverse events.

Bennett WL, Odelola OA, Wilson LM,et al. **Evaluation of guideline recommendations** on oral medications for type 2 diabetes mellitus: a systematic review. Ann Intern Med. 2012 Jan 3;156(1 Pt 1):27-36

Benoit SR, Hora I, Albright AL, Gregg EW. **New directions in incidence and prevalence** of diagnosed diabetes in the USA. BMJ Open Diabetes Res Care. 2019 May 28;7(1):e000657.

Bergenstal RM, Johnson M, Passi R, et al. **Automated insulin dosing guidance** to optimize insulin management in patients with type 2 diabetes: a multicentre, randomised controlled trial. Lancet 2019; published online Feb 23.

Bergenstal RM, Wysham C, Macconell L, et al. for the **DURATION-2** Study Group. Efficacy and safety of **exenatide once weekly versus sitagliptin or pioglitazone** as an adjunct to metformin for treatment of type 2 diabetes (DURATION-2): a randomised trial. Lancet. 2010 Jun 25.

Bergenstal RM, Gal RL, Connor CG, Gubitosi-Klug R, Kruger D, et al. **Racial differences** in the relationship of glucose concentrations and **hemoglobin A1c levels**. Ann Intern Med. 2017. [Epub ahead of print]. doi:10.7326/M16-2596

Berghella V, Caissutti C, Saccone G, Khalifeh A. **The One Step approach** for diagnosing gestational diabetes is associated **with better perinatal outcomes than using the Two Step approach**: Evidence of Randomized Clinical Trials. Am J Obstet Gynecol. 2019 Jan 31.

Bergmark BA, Bhatt DL, McGuire DK, et al. **Metformin Use and Clinical Outcomes** among Patients with Diabetes with or without Heart Failure or Kidney Dysfunction: Observations from the SAVOR-TIMI 53 Trial. Circulation. 2019 Jul 31.

Berkelmans GFN, Gudbjornsdottir S, Visseren FLJ, et al. Prediction of **individual life-years gained** without cardiovascular events from lipid, blood pressure, glucose, and aspirin treatment based on data of more than 500 000 patients with **Type 2 diabetes mellitus**. Eur Heart J. 2019 Jan 9.

Berkowitz SA, Krumme AA, Avorn J, et al. **Initial choice of oral glucose-lowering medication for diabetes mellitus**: a patient-centered comparative effectiveness study [online October 27, 2014]. JAMA Intern Med. doi:10.1001/jamainternmed.2014.5294.

Berria R, et al. **Reduction in hematocrit** level after **pioglitazone** treatment is correlated with decreased plasma free testosterone level, not hemodilution, in women with polycystic ovary syndrome.Clin Pharmacol Ther. 2006 Aug;80(2):105-14. Epub 2006 Jun 30.

Bersoff-Matcha SJ, Chamberlain C, Cao C, et al. **Fournier Gangrene Associated With Sodium-Glucose Cotransporter-2 Inhibitors**: A Review of Spontaneous Postmarketing Cases. Ann Intern Med. 2019 May 7.

Besser RE, Flanagan SE, Mackay DG, et al. **Prematurity and Genetic Testing for Neonatal Diabetes**. Pediatrics. 2016 Sep;138(3).

Bethel MA, Patel RA, Merrill P, et al. **Cardiovascular outcomes with glucagon-like peptide-1 receptor agonists** in patients with type 2 diabetes: a meta-analysis. Lancet Diabetes Endocrinol. 2017 Dec 5.

Bethel MA, McMurray JJV. Class Effect for **Sodium Glucose-Cotransporter-2 Inhibitors in Cardiovascular Outcomes**: Implications for the Cardiovascular Disease Specialist. Circulation. 2018 Mar 20;137(12):1218-1220.

Beyerlein A, Wehweck F, Ziegler AG, Pflueger M. **Respiratory Infections** in Early Life and the Development of Islet **Autoimmunity in Children** at Increased Type 1 Diabetes Risk: Evidence From the **BABYDIET** Study. JAMA Pediatr. 2013 Jul 1.

Beyerlein A, Donnachie E, Jergens S, et al. **Infections in Early Life** and Development of **Type 1 Diabetes**. JAMA. 2016 May 3;315(17):1899-901.

Bharucha AE, Kudva YC, Prichard DO. **DIABETIC GASTROPARESIS**. Endocr Rev. 2019 May 13.

Bhupathiraju SN, Pan A, Manson JE, et al. Changes in **coffee** intake and subsequent risk of type 2 diabetes: three large cohorts of US men and women. Diabetologia. 2014 Apr 26.

Biggio JR Jr et al. **Fetal anomalies in obese women**: The contribution of diabetes. Obstet Gynecol 2010 Feb; 115:290.

Bihan H, Fysekidis M, Harbuz V, Reach G, Cohen R. **False-positive blood glucose and ketone** values with **lightening cream**. Ann Intern Med. 2011 Nov 1;155(9):649.

Billeter AT, Scheurlen KM, Probst P, et al. **Meta-analysis of metabolic surgery versus medical treatment for microvascular complications in patients with type 2 diabetes mellitus.** Br J Surg. 2018 Feb;105(3):168-181.

Bilik D, McEwen LN, Brown MB, et al. **Thiazolidinediones and Fractures**: Evidence from Translating Research into Action for Diabetes. J Clin Endocrinol Metab. 2010 Jul 14.

Billings LK, Doshi A, Gouet D, et al. Efficacy and Safety of **IDegLira Versus Basal-Bolus Insulin** Therapy in Patients With Type 2 Diabetes **Uncontrolled on Metformin and Basal Insulin**; **DUAL VII** Randomized Clinical Trial. Diabetes Care. 2018 Feb 26.

Billionnet C, Mitanchez D, Weill A, et al. **Gestational diabetes** and adverse **perinatal outcomes** from 716,152 births in France in 2012. Diabetologia. 2017 Feb 15.

Birkeland KI, Jørgensen ME, Carstensen B, et al. Cardiovascular mortality and morbidity in patients with type 2 diabetes following initiation of **sodium-glucose co-transporter-2** inhibitors versus other glucose-lowering drugs (**CVD-REAL** Nordic): a multinational observational analysis. Lancet Diabetes Endocrinol. 2017 Aug 3.

Birkenhäger-Gillesse EG, den Elzen WP, Achterberg WP, et al. Association Between **Glycosylated Hemoglobin and Cardiovascular Events and Mortality in Older Adults** without Diabetes Mellitus in the General Population: The **Leiden 85-Plus Study**. J Am Geriatr Soc. 2015 Jun;63(6):1059-66.

BIRTH-GENE (BIG) Study Working Group, Huang T, Wang T, Zheng Y, et al. **Association of Birth Weight With Type 2 Diabetes and Glycemic Traits**: A Mendelian Randomization Study. JAMA Netw Open. 2019 Sep 4;2(9):e1910915.

Bjerregaard LG, Jensen BW, Ängquist L, et al. Change in **Overweight from Childhood to Early Adulthood and Risk of Type 2 Diabetes**. N Engl J Med. 2018 Apr 5;378(14):1302-1312.

Bjornstad P, Schafer M, Truong U, et al. **Metformin Improves Insulin Sensitivity and Vascular Health** in Youth With **Type 1 Diabetes Mellitus**. Circulation. 2018 Dec 18;138(25):2895-2907.

Black C, et al. **Meglitinide** analogues for type 2 diabetes mellitus. Cochrane Database Syst Rev. 2007 Apr 18;(2):CD004654. Meglitinides may offer an alternative oral hypoglycaemic agent of similar potency to metformin, and may be indicated where side effects of metformin are intolerable or where metformin is contraindicated. However, there is no evidence available to indicate what effect meglitinides will have on important long-term outcomes, particularly mortality.

Blackberry ID, Furler JS, Best JD, et al. Effectiveness of general practice based, practice **nurse led telephone coaching** on glycaemic control of type 2 diabetes: the Patient Engagement And Coaching for Health (PEACH) pragmatic cluster randomised controlled trial. BMJ. 2013 Sep 18;347:f5272.

Blair JC, McKay A, Ridyard C, et al. **Continuous subcutaneous insulin infusion versus multiple daily injection** regimens in children and young people at diagnosis of type 1 diabetes: pragmatic randomised controlled trial and economic evaluation. BMJ. 2019 Apr 3;365:l1226.

Blenner SR, Köllmer M, Rouse AJ, et al. Privacy Policies of **Android Diabetes Apps** and Sharing of Health Information. JAMA. 2016 Mar 8;315(10):1051-2.

Blevins T, Pieber TR, G, et al. Randomized double-blind clinical trial comparing basal **insulin peglispro and insulin glargine, in combination with prandial insulin lispro**, in patients with type 2 diabetes: **IMAGINE 4**. Diabetes Obes Metab. 2016 May 28.

Blickle J. **Thiazolidinediones: donnees cliniques et perspectives** (French language). Diabetes Metab 2001;27:279-285.

Blind E, Dunder K, de Graeff PA, and Abadie E. **Rosiglitazone: a European regulatory perspective**. Diabetologia 2010; DOI:10.1007/s00125-010-1992-5.

Blomgren KB, Sundström A, Steineck G, Wiholm BE. Obesity and treatment of diabetes with **glyburide** may both be risk factors for **acute pancreatitis**. Diabetes Care. 2002 Feb;25(2):298-302.

Blomster JI, Zoungas S, Chalmers J, et al. The relationship between **alcohol consumption** and vascular complications and mortality in individuals with type 2 diabetes. Diabetes Care. 2014;37:1353-1359.

Blonde L, Jendle J, Gross J, et al. Once-weekly **dulaglutide versus bedtime insulin glargine**, both in combination with prandial insulin lispro, in patients with type 2 diabetes (AWARD-4): a randomised, open-label, phase 3, non-inferiority study.

Blonde L, Rosenstock J, Del Prato S, et al. Switching to **iGlarLixi Versus Continuing Daily or Weekly GLP-1 RA** in Type 2 Diabetes Inadequately Controlled by GLP-1 RA and Oral Antihyperglycemic Therapy: The LixiLan-G Randomized Clinical Trial. Diabetes Care. 2019 Sep 17.

Blotsky AL, Rahme E, Dahhou M, et al. **Gestational diabetes associated with incident diabetes** in childhood and youth: a retrospective cohort study. CMAJ. 2019 Apr 15;191(15):E410-E417.

Blumer I, Hadar E, Hadden DR, et al. **Diabetes and pregnancy**: an endocrine society clinical practice guideline. J Clin Endocrinol Metab. 2013 Nov;98(11):4227-49.

Blumer I, Clement M. Type 2 Diabetes, Hypoglycemia, and **Basal Insulins**: Ongoing Challenges. Clin Ther. 2016 Nov 18. pii: S0149-2918(16)30779-2.

Blundell J, Finlayson G, Axelsen M, et al. Effects of once-weekly **semaglutide** on appetite, energy intake, control of eating, food preference and body weight in subjects with obesity. Diabetes Obes Metab. 2017 Mar 7.

Bobo WV, Cooper WO, Stein CM et al. **Antipsychotics and the Risk of Type 2 Diabetes** Mellitus in Children and Youth. JAMA Psychiatry. 2013 Aug 21.

Bodmer M, Meier C, Krähenbühl S, Jick SS, Meier CR. Metformin, sulfonylureas, or other antidiabetes drugs and the risk of lactic acidosis or hypoglycemia: a nested case-control analysis. Diabetes Care. 2008 Nov;31(11):2086-91. Epub 2008 Sep 9. **Lactic acidosis** during current use of oral antidiabetes drugs was very rare and was associated with concurrent comorbidity. Hypoglycemic episodes were substantially more common among sulfonylurea users than among users of metformin.

Bodmer M, Becker C, Meier C et al. Use of Antidiabetic Agents and the Risk of **Pancreatic Cancer**: A Case-Control Analysis. Am J Gastroenterol. 2012 Jan 31. (Metformin reduced risk in women)

Boeri L, Capogrosso P, Ventimiglia E, et al. Undiagnosed **prediabetes is highly prevalent in primary infertile men** -results from a cross-sectional study. BJU Int. 2018 Oct 16.

Boghossian NS, Hansen NI, Bell EF, et al; Eunice Kennedy Shriver National Institute of Child Health and Human Development Neonatal Research Network. Outcomes of **Extremely Preterm Infants Born to Insulin-Dependent Diabetic Mothers**. Pediatrics. 2016 May 13.

Bogun M, Inzucchi SE. **Inpatient** management of diabetes and hyperglycemia. Clin Ther. 2013 May;35(5):724-33.

Bohula EA, Scirica BM, Inzucchi SE, et al; CAMELLIA-TIMI 61 Steering Committee Investigators. Effect of **lorcaserin on prevention and remission of type 2 diabetes in overweight and obese patients** (CAMELLIA-TIMI 61): a randomised, placebo-controlled trial. Lancet. 2018 Oct 3. pii: S0140-6736(18)32328-6.

Bolen S, Feldman L, Vassy J, et al. Systematic Review: Comparative Effectiveness and Safety of Oral Medications for Type 2 Diabetes Mellitus. Ann Intern Med. 2007 Jul 16; [Epub ahead of print] Compared with newer, more expensive agents (thiazolidinediones, alpha-glucosidase inhibitors, and meglitinides), older agents (second-generation sulfonylureas and metformin) have similar or superior effects on glycemic control, lipids, and other intermediate end points.

Bolen S, Tseng E, Hutfless S, et al. **Diabetes medications for adults with type 2 diabetes**: An update. Comparative Effectiveness Review No. 173. Rockville (MD): Agency for Healthcare Research and Quality (US); 2016 Apr. No. 16-EHC013-EF.

Bolli GB, Munteanu M, Dotsenko S, et al. Efficacy and safety of **lixisenatide** once daily vs. placebo in people with Type 2 diabetes insufficiently controlled on **metformin (GetGoal-F1).** Diabet Med. 2014 Feb;31(2):176-84.

Bolli GB, Wysham C, Fisher M, et al. A **post-hoc pooled analysis to evaluate the risk of hypoglycaemia with insulin glargine 300 U/mL (Gla-300) versus 100 U/mL (Gla-100**) over wider nocturnal windows in individuals with type 2 diabetes on a basal-only insulin regimen. Diabetes Obes Metab. 2018 Aug 29.

Bolinder J, Ljunggren O, Johansson L, et al. **Dapagliflozin** maintains glycaemic control while reducing weight and body fat mass over 2 years in patients with type 2 diabetes mellitus inadequately controlled on metformin. Diabetes Obes Metab. 2013 Aug 1.

Bolinder J, Antuna R, Geelhoed-Duijvestijn P, et al. **Novel glucose-sensing technology** and hypoglycaemia in type 1 diabetes: a multicentre, non-masked, randomised controlled trial. Lancet. 2016 Sep 9.

Bolinder J, Antuna R, Geelhoed-Duijvestijn P, et al. **Novel glucose-sensing technology** and hypoglycaemia in type 1 diabetes: a multicentre, non-masked, randomised controlled trial. Lancet 2016; online Sept 12.

Bommer C, Heesemann ECN, Sagalova V, et al. The **global economic burden of diabetes in adults** aged 20–79: a cost-of-illness study. Lancet Diabetes Endocrinol 2017; online April 26.

Bonds Denise E, Miller Michael E, Bergenstal Richard M, et al. The association between symptomatic, severe **hypoglycaemia** and mortality in type 2 diabetes: retrospective epidemiological analysis of the **ACCORD** study. BMJ 2010;340:b4909, doi: 10.1136/bmj.b4909 (Published 8 January 2010)

Bonfig W, Kapellen T, Dost A, Fritsch M, Rohrer T, Wolf J, et al. **Growth in children and adolescents** with type 1 diabetes. J Pediatr 2012;160:900-3.

Bonifacio E, Ziegler A-G, Klingensmith G, et al; **Pre-POINT** Study Group. Effects of **high-dose oral insulin** on immune responses in children at high risk for type 1 diabetes: the Pre-POINT randomized clinical trial. JAMA. doi:10.1001/jama.2015.2928.

Boniol M, Franchi M, Bota M, et al. **Incretin-Based Therapies and the Short-Term Risk of Pancreatic Cancer**: Results From Two Retrospective Cohort Studies. Diabetes Care. 2017 Nov 16.

Booth GL, Kapral MK, Fung K, & Tu JV. Relation between age and cardiovascular disease in men and women with **diabetes compared with nondiabetic** people: a population-based retrospective cohort study. Lancet 2006; 368: 29-36.

Booth GL, Luo J, Park AL, et al. Influence of **environmental temperature on risk of gestational diabetes**. CMAJ. 2017 May 15;189(19):E682-E689.

Booth H, Khan O, Prevost T, et al. Incidence of type 2 **diabetes after bariatric surgery**: population-based matched cohort study. Lancet Diabetes Endocrinol. 2014 Nov 3;2(12):963-968.

Bordeleau L, Yakubovich N, Dagenais GR, et al. for the **ORIGIN** Trial Investigators. The Association of **Basal Insulin Glargine and/or n-3 Fatty Acids With Incident Cancers** in Patients With Dysglycemia. Diabetes Care. 2014 Feb 26.

Bosetti C, Rosato V, Li D, et al. Diabetes, **antidiabetic medications** and **pancreatic cancer risk**: an analysis from the international pancreatic cancer case-control consortium. Ann Oncol. 2014 Jul 23.

Bosi E, Choudhary P, de Valk HW, et al. Efficacy and safety of **suspend-before-low insulin pump technology** in hypoglycaemia-prone adults with type 1 diabetes(SMILE): an open-label randomised controlled trial. Lancet Diabetes Endocrinol. 2019 Jun;7(6):462-472.

Botha S, Forde L, et al. Effect of **non-surgical weight management on weight and glycaemic control** in people with type 2 diabetes: A comparison of interventional and non-interventional outcomes at 3 years. Diabetes Obes Metab. 2017 Nov 27.

Boughton CK, Bally L, Martignoni F, et al. **Fully closed-loop insulin delivery** in inpatients receiving nutritional support: a two-centre, open-label, randomised controlled trial. Lancet Diabetes Endocrinol. 2019 May;7(5):368-377.

Boussageon R, Bejan-Angoulvant T, Saadatian-Elahi M, et al. Effect of **intensive glucose lowering treatment on all cause mortality, cardiovascular death, and microvascular events in type 2 diabetes**: meta-analysis of randomised controlled trials.

BMJ 2011;343:d4169.
Boussageon R, Supper I, Bejan-Angoulvant T, et al. **Reappraisal of metformin** efficacy in the treatment of type 2 diabetes: a meta-analysis of randomised controlled trials. PLoS Med. 2012 Apr;9(4):e1001204.
Boussageon R, Gueyffier F, Cornu C. **Metformin** as **firstline** treatment for type 2 diabetes: **are we sure**? BMJ. 2016 Jan 8;352:h6748.
Bowen ME, Xuan L, Lingvay I, Halm EA. **Random Blood Glucose**: A Robust Risk Factor For Type 2 Diabetes. J Clin Endocrinol Metab. 2015 Feb 4:jc20144116.
Bowker SL, et al. Increased **cancer-related mortality** for patients with type 2 diabetes who use sulfonylureas or insulin. Diabetes Care. 2006 Feb;29(2):254-8. (InfoPOEMs: Death due to cancer seems to be more prevalent in patients with type 2 diabetes treated with either insulin or a sulfonylurea than in patients treated with metformin (Glucophage). It may be that hyperinsulinemia increases cancer risk, or that metformin is protective. Another explanation could be that, although cancer is related to certain medication use, it is not caused by their use. We need a controlled study to answer these questions. (LOE = 2b))
Bowman P, Sulen A, Barbetti F, et al. **Effectiveness and safety of long-term treatment with sulfonylureas** in patients with neonatal diabetes due to KCNJ11 mutations: an international cohort study. Lancet Diabetes Endocrinol 2018; published online June 1.
Bragg F, Li L, Bennett D, et al. Association of **random plasma glucose levels** with the risk for cardiovascular disease among Chinese adults without known diabetes. *JAMA Cardiol* 2016.
Bragg F, Holmes MV, Iona A, et al; China Kadoorie Biobank Collaborative Group. Association between diabetes and cause-specific **mortality in rural and urban areas of China**. JAMA. doi:10.1001 /jama.2016.19720
Brauer R, Bhaskaran K, Chaturvedi N, et al. **Glitazone** Treatment and Incidence of **Parkinson's** Disease among People with Diabetes: A Retrospective Cohort Study. PLoS Med. 2015 Jul 21;12(7):e1001854.
Bressler NM, Beck RW, Ferris FL 3rd. **Panretinal photocoagulation** for proliferative diabetic retinopathy. N Engl J Med. 2011 Oct 20;365(16):1520-6.
Bressler NM, Varma R, Doan QV, et al. **Underuse** of the health care system by persons with diabetes mellitus and **diabetic macular edema** in the United States. JAMA Ophthalmol. 2014;132(2):168-173.
Bril F, Biernacki DM, Kalavalapalli S, et al. Role of **Vitamin E for Nonalcoholic Steatohepatitis in Patients With Type 2 Diabetes**: A Randomized Controlled Trial. Diabetes Care. 2019 Aug;42(8):1481-1488
Bril V., England J., Franklin G.M., et al. Evidence-based guideline: Treatment of **painful diabetic neuropathy**: Report of the American Academy of Neurology (**AAN**), the American Association of Neuromuscular and Electrodiagnostic Medicine, and the American Academy of Physical Medicine and Rehabilitation. Neurology May 17, 2011 76:1758-1765; published ahead of print April 11, 2011. http://www.neurology.org/content/early/2011/04/08/WNL.0b013e3182166ebe.full.pdf+html
Brinkhues S, Dukers-Muijrers NHTM, Hoebe CJPA, et al. **Socially isolated individuals** are more prone to have newly diagnosed and prevalent type 2 diabetes mellitus - the Maastricht study. BMC Public Health. 2017 Dec 19;17(1):955.
Brito JP, Montori VM, Davis AM. **Metabolic surgery in the treatment algorithm for type 2 diabetes**: a joint statement by international diabetes organizations. doi:10.1001/jama.2016 .20563
Brock C, Hansen CS, Karmisholt J, et al. **Liraglutide treatment reduced interleukin 6** in adults with type 1 diabetes but did not improve established autonomic or polyneuropathy. Br J Clin Pharmacol. 2019 Jul 24.
Broglio F, Mannucci E, Napoli R, et al. Beneficial effect of **lixisenatide after 76 weeks** of treatment in patients with type 2 diabetes mellitus: A meta-analysis from the GetGoal programme. Diabetes Obes Metab. 2016 Oct 20.
Brown JB, Conner C, Nichols GA. **Secondary failure of metformin** monotherapy in clinical practice. Diabetes Care. 2010 Mar;33(3):501-6. Epub 2009 Dec 29.
Brown J;Grzeskowiak L;Williamson K;et al. **Insulin for the treatment of women with gestational diabetes**. Cochrane Database Syst Rev. 2017 Nov 5;11:CD012037. The main comparison in this review is insulin versus oral anti-diabetic pharmacological therapies. Insulin and oral anti-diabetic pharmacological therapies have similar effects on key health outcomes. The quality of the evidence ranged from very low to moderate, with downgrading decisions due to imprecision, risk of bias and inconsistency. For the other comparisons of this review (insulin compared with non-pharmacological interventions, different insulin analogues or different insulin regimens), there is insufficient volume of high-quality evidence to determine differences for key health outcomes. Long-term maternal and neonatal outcomes were poorly reported for all comparisons. The evidence suggests that there are minimal harms associated with the effects of treatment with either insulin or oral anti-diabetic pharmacological therapies. The choice to use one or the other may be down to physician or maternal preference, availability or severity of GDM. Further research is needed to explore optimal insulin regimens. Further research could aim to report data for standardised GDM outcomes.
Brown TJ, Brainard J, Song F, et al. **Omega-3, omega-6, and total dietary polyunsaturated fat for prevention** and treatment of type 2 diabetes mellitus: systematic review and meta-analysis of randomised controlled trials. BMJ. 2019 Aug 21;366:l4697.
Brownstein JS, Murphy SN, Goldfine AB, et al. Rapid identification of **myocardial infarction risk** associated with diabetes medications using electronic medical records. Diabetes Care. 2010 Mar;33(3):526-31. Epub 2009 Dec 15.
Bruderer SG, Bodmer M, Jick SS, et al. Poorly controlled type 2 diabetes mellitus is associated with a decreased risk of incident **gout**: a population-based case-control study. Ann Rheum Dis. 2015 Sep;74(9):1651-8.
Brunner S, Stecher L, Ziebarth S, et al. **Excessive gestational weight gain** prior to glucose screening and the risk of **gestational** diabetes: a meta-analysis. Diabetologia. 2015 Jul 4.
Bruno G, Spadea T, Picariello R, et al; Piedmont Study Group for Diabetes Epidemiology. **Early Life Socioeconomic Indicators** and Risk of Type 1 Diabetes in Children and Young Adults. J Pediatr. 2012 Oct 17.
Bruno G, Spadea T, Picariello R, et al. Early life **socioeconomic indicators** and risk of type 1 diabetes in children and young adults. J Pediatr. 2013 Mar;162(3):600-605.e1.
Bryan RN, Bilello M, Davatzikos C, et al. Effect of **diabetes on brain structure**: The Action to Control Cardiovascular Risk in Diabetes MRI imaging baseline data. Radiology. 2014 Apr 14.
Bu W, Song L, Zhao D, et al. **Insulin therapy and the risk of colorectal cancer** in patients with type 2 diabetes: a meta-analysis of observational studies. British Journal of Clinical Pharmacology. 2014.
Buchleitner AM, Martínez-Alonso M, Hernández M, Solà I, Mauricio D. **Perioperative glycaemic control** for diabetic patients undergoing surgery. Cochrane Database Syst Rev. 2012 Sep 12;9:CD007315. The included trials did not demonstrate significant differences for most of the outcomes when targeting intensive perioperative glycaemic control compared with conventional glycaemic control in patients with diabetes mellitus. However, posthoc analysis indicated that intensive glycaemic control was associated with an increased number of patients experiencing hypoglycaemic episodes.
Buckley LF, Dixon DL, Wohlford GF 4th, et al. **Intensive Versus Standard Blood Pressure** Control in **SPRINT**-Eligible Participants of the **ACCORD-BP** Trial. Diabetes Care. 2017 Sep 25.
Bulugahapitiya U, Siyambalapitiya S, Sithole J, Idris I. Is diabetes a **coronary risk equivalent**? Systematic review and meta-analysis. Diabet Med. 2009 Feb;26(2):142-8. This meta-analysis found no evidence to support the contention that diabetes alone is a coronary heart disease (CHD) risk equivalent to a history of prior myocardial infarction (MI). The blanket use of aspirin and statins for patients with type 2 diabetes, regardless of their lipid levels, is not supported by the evidence. (LOE = 2a)
Burant CF, Viswanathan P, Marcinak J, et al. **TAK-875** (FFAR1) versus placebo or glimepiride in type 2 diabetes mellitus: a phase 2, randomised, double-blind, placebo-controlled trial. Lancet 2012; online Feb 27.
Burcu M, Zito JM, Safer DJ, et al. **Association of Antidepressant Medications With Incident Type 2 Diabetes** Among Medicaid-Insured Youths. JAMA Pediatr. 2017 Oct 16.
Burr JF, Shephard RJ, Riddell MC. **Physical activity** in type 1 diabetes mellitus: Assessing risks for physical activity clearance and prescription. Can Fam Physician. 2012 May;58(5):533-5.
Burr J, Shephard R, Riddell M. Prediabetes and type 2 diabetes mellitus: Assessing risks for **physical activity clearance and prescription**. Can Fam Physician March 2012 58: 280-284.
Buse JB, Ginsberg HN, Bakris GL, et al. American Heart Association; American Diabetes Association. **Primary prevention of cardiovascular diseases in people with diabetes mellitus**: a scientific statement from the American Heart Association and the American Diabetes Association. Circulation. 2007 Jan 2;115(1):114-26. Epub 2006 Dec 27.
Buse JB et al. **Liraglutide** once a day versus exenatide twice a day for type 2 diabetes: A 26-week randomised, parallel-group, multinational, open-label trial (**LEAD-6**). Lancet 2009 Jul 4; 374:39.
Buse JB, Drucker DJ, Taylor KL, et al. for the DURATION-1 Study Group. **DURATION-1**: **Exenatide Once Weekly** Produces Sustained Glycemic Control and Weight Loss Over 52 Weeks. Diabetes Care. 2010 Mar 9.
Buse JB, Sesti G, Schmidt WE, et al. for the Liraglutide Effect and Action in Diabetes (**LEAD**)-6 Study Group. Switching to once-daily liraglutide from twice-daily exenatide further improves glycemic control in patients with type 2 diabetes using oral agents. Diabetes Care. 2010 Mar 23.
Buse JB, Bergenstal RM, Glass LC, et al. Use of **Twice-Daily Exenatide** in Basal Insulin-Treated Patients With Type 2 Diabetes: A Randomized, Controlled Trial. Ann Intern Med. 2010 Dec 6.
Buse JB, Nauck M, Forst T, et al. **Exenatide once weekly versus liraglutide** once daily in patients with type 2 diabetes (**DURATION-6**): a randomised, open-label study. Lancet 2012; online Nov 7.
Buse JB, Vilsbøll T, Thurman J, et al; on behalf of the NN9068-3912 (**DUAL-II**) Trial Investigators. Contribution of **Liraglutide** in the **Fixed-Ratio** Combination of **Insulin Degludec and Liraglutide** (IDegLira). Diabetes Care. 2014 Aug 11.
Buse JB, Peters A, Russell-Jones D, et al. Is **insulin the most effective injectable antihyperglycaemic therapy**?. Diabetes Obes Metab. 2014 Oct 17.
Buse JB, Rodbard HW, et al.**IMAGINE 5** Investigators. Randomized Clinical Trial Comparing **Basal Insulin Peglispro and Insulin Glargine** in Patients With Type 2 Diabetes Previously Treated With Basal Insulin: IMAGINE 5. Diabetes Care. 2015 Nov 17.
Buse JB, Bethel MA, Green JB, et al. **Pancreatic Safety of Sitagliptin** in the **TECOS** Study. Diabetes Care. 2016 Sep 14.
Buse JB et al. **Pancreatic safety** of **sitagliptin** in the **TECOS** study. Diabetes Care 2017 Feb; 40:164.
Buse JB, Garg SK, Rosenstock J, et al. **Sotagliflozin in Combination With Optimized Insulin Therapy in** Adults With Type 1 Diabetes: The North American inTandem1 Study. Diabetes Care. 2018 Jun 24.
Buse JB, Carlson AL, Komatsu M, et al. **Fast-acting insulin aspart versus insulin aspart** in the setting of insulin degludec-treated type 1 diabetes: Efficacy and safety from a randomized double-blind trial. Diabetes Obes Metab. 2018 Sep 26.
Busse D, Tang W, Scheerer MF, et al. Comparison of **pharmacokinetics and the exposure- response relationship of dapagliflozin** between adolescent/young adult and adult patients with type 1 diabetes mellitus. Br J Clin Pharmacol. 2019 May 11.
Butala NM, Johnson BK, Dziura JD, et al. **Decade-long trends in mortality** among patients with and without diabetes mellitus at a major academic medical center. JAMA Intern Med. 2014 Jul 1;174(7):1187-8.
Butalia S, Gutierrez L, Lodha A, et al. Short- and long-term outcomes of **metformin compared with insulin alone in pregnancy**: a systematic review and meta-analysis. Diabet Med. 2017 Jan;34(1):27-36.
Butler AE, Campbell-Thompson M, Gurlo T, et al. Marked **expansion of exocrine and endocrine pancreas with incretin therapy** in humans with increased exocrine **pancreas dysplasia** and the potential for glucagon-producing neuroendocrine tumors. Diabetes. 2013 Jul;62(7):2595-604.
Butler J, Anker SD. The Ethics of Conducting Clinical Trials With **Sodium-Glucose Cotransporter-2 Inhibitors in Heart Failure**: Is Placebo Assignment Justified in Patients With Comorbid Diabetes Mellitus and Heart Failure? Circulation. 2017 Oct 17;136(16):1459-1461.
Butler J, Hamo CE, Filippatos G, et al; **EMPEROR** Trials Program. The potential role and rationale for treatment of **heart failure with sodium-glucose co-transporter 2 inhibitors**. Eur J Heart Fail. 2017 Nov;19(11):1390-1400.
Cahn A, Melzer-Cohen C, Pollack R, et al. Acute **renal outcomes with sodium-glucose co-transporter-2 inhibitors**: **Real-world data** analysis. Diabetes Obes Metab. 2018 Sep 12.

Cai X, Yang W, Gao X, et al. The Association Between the Dosage of **SGLT2 Inhibitor and Weight Reduction** in Type 2 Diabetes Patients: A Meta-Analysis. Obesity (Silver Spring). 2018 Jan;26(1):70-80.

Callahan Alfred; Amarenco Pierre; Goldstein Larry B.; et al. for the **SPARCL** Investigators. Risk of Stroke and Cardiovascular Events After Ischemic Stroke or Transient Ischemic Attack in Patients With Type 2 Diabetes or Metabolic Syndrome: Secondary Analysis of the Stroke Prevention by Aggressive Reduction in Cholesterol Levels (SPARCL-**atorvastatin**) Trial Arch Neurol. 2011;0(2011):archneurol.2011.146.

Callaghan BCC, Cheng HT, Stables CL et al. **Diabetic neuropathy**: clinical manifestations and current treatments. Lancet Neurol 2012; 11: 521–34.

Callaghan BC, Little AA, Feldman EL, Hughes RAC. Enhanced **glucose control for preventing and treating diabetic neuropathy**. Cochrane Database of Systematic Reviews 2012, Issue 6. Art. No.: CD007543. According to high-quality evidence, enhanced glucose control significantly prevents the development of clinical neuropathy and reduces nerve conduction and vibration threshold abnormalities in type 1 diabetes mellitus. In type 2 diabetes mellitus, enhanced glucose control reduces the incidence of clinical neuropathy, although this was not formally statistically significant (P = 0.06). However, enhanced glucose control does significantly reduce nerve conduction and vibration threshold abnormalities. Importantly, enhanced glucose control significantly increases the risk of severe hypoglycemic episodes, which needs to be taken into account when evaluating its risk/benefit ratio.

Camelo CastilloW, Boggess K, Stürmer T, et al. Association of adverse **pregnancy outcomes with glyburide vs insulin** in women with gestational diabetes [online March 30, 2015]. JAMA Pediatr. doi:10.1001/jamapediatrics.2015.74.

Cameron AR, Morrison VL, Levin D, Mohan et al. **Anti-Inflammatory Effects of Metformin** Irrespective of Diabetes Status. Circ Res. 2016 Aug 19;119(5):652-65.

Cameron FJ, Wherrett DK. Care of **diabetes in children and adolescents**: controversies, changes, and consensus. Lancet. 2015 May 23;385(9982):2096-106.

Campbell Matthew D, Walker Mark, Ajjan Ramzi A, et al. An **additional bolus of rapid-acting insulin** to **normalise postprandial cardiovascular risk factors** following a high-carbohydrate high-fat meal in patients with type 1 diabetes: A randomised controlled trial. Diab Vasc Dis Res. 2017 Mar 1:1479164117698918.

Campbell PT, Newton CC, Patel AV, Jacobs EJ, Gapstur SM. Diabetes and cause-specific mortality in a prospective cohort of one million u.s. Adults. Diabetes Care. 2012 Sep;35(9):1835-44.

Carnethon MR, De Chavez PJ, Biggs ML, et al. Association of **weight status with mortality** in adults with incident diabetes. JAMA. 2012 Aug 8;308(6):581-90. (normal weight had higher mortality)

Canadian Hypertension Education Program 2016 Recommendations www.hypertension.ca **Canadian Hypertension Education Program (CHEP).**

Canadian Diabetes Association Clinical Practice Guidelines Expert Committee. **Pharmacologic management of type 2 diabetes: 2016 interim update**. Can J Diabetes 2016 guidelines.diabetes.ca/cdacpg_resources/JCJD_6921.pdf (accessed May 2, 2016).

Canadian Diabetes Association Clinical Practice Guidelines Expert Committee. **Table 1. Antihyperglycemic agents for use in type 2 diabetes**. April 2016. guidelines.diabetes.ca/cdacpg_resources/Ch13_Table1_Antihyperglycemic_agents_type_2_2016.pdf(accessed May 2, 2016).

Canadian Diabetes Association Clinical Practice Guidelines Expert Committee. Addendum to policies, guidelines and consensus statements: **pharmacologic management of type 2 diabetes: 2015 interim update**. Figure 2. Antihyperglycemic medications and renal function. Can J Diabetes 2015;39:440.guidelines.diabetes.ca/cdacpg_resources/Ch13_Fig2_Antihyperglycemic_medications_and_renal_function_2016.pdf(May 2, 2016).

Capodanno D, Angiolillo DJ. **Aspirin for Primary Cardiovascular Risk Prevention** and Beyond in Diabetes Mellitus. Circulation. 2016 Oct 11.

Carbone S, Dixon DL, Buckley LF, Abbate A. **Glucose-Lowering Therapies** for Cardiovascular Risk Reduction in type 2 Diabetes Mellitus: State-of-the-Art Review. Mayo Clin Proc. 2018 Nov;93(11):1629-1647.

Cardoso CRL, Leite NC, Carlos FO, et al. Efficacy and Safety of **Diacerein** in Patients With Inadequately Controlled Type 2 Diabetes: A Randomized Controlled Trial. Diabetes Care. 2017 Oct;40(10):1356-1363.

Carey IM, Critchley JA, DeWilde S, et al. **Risk of Infection in Type 1 and Type 2 Diabetes** Compared With the General Population: A Matched Cohort Study. Diabetes Care. 2018 Jan 12.

Carlsen SM, Martinussen MP, Vanky E. Metformin's Effect on **First-Year Weight Gain (on offspring)**: A Follow-up Study. Pediatrics. 2012 Oct 15.

Carlsson LMS, Peltonen M, Ahlin S, et al. **Bariatric surgery** and prevention of type 2 diabetes in Swedish Obese Subjects. (**SOS**) N Engl J Med 2012; 367:695-704.

Carlsson S, Andersson T, Araghi M, et al. **Smokeless tobacco** (**snus**) is associated with an increased risk of type 2 diabetes: results from five pooled cohorts. J Intern Med. 2017 Feb 6.

Carlsson S, Andersson T, Talbäck M, Feychting M. Incidence and prevalence of **type 2 diabetes by occupation**: results from all Swedish employees. Diabetologia. 2019 Sep 17. doi: 10.1007/s00125-019-04997-5.

Carmody D, Naylor RN, Philipson LH. **Insulin dosing in pediatric diabetic ketoacidosis**: where to start? JAMA. 2015 Jun 9;313(22):2274-5.

Carrasquillo O, Lebron C, Alonzo Y, et al. Effect of a **Community Health Worker Intervention Among Latinos** With Poorly Controlled Type 2 Diabetes: The **Miami Healthy Heart Initiative** Randomized Clinical Trial. JAMA Intern Med. 2017 Jul 1;177(7):948-954

Carretero Gómez J, Arévalo Lorido JC, Gómez Huelgas R, et al. **Combination Therapy With Glucagon-Like Peptide-1 Receptor Agonists and Sodium-Glucose Cotransporter 2 Inhibitors in Older Patients With Type 2 Diabetes**: A Real-World Evidence Study. Can J Diabetes. 2018 Sep 8.

Carnevale R, Silvestri R, Loffredo L, et al. **Oleuropein**, a component of extra virgin olive oil, lowers postprandial glycaemia in healthy subjects. Br J Clin Pharmacol. 2018 Mar 26.

Carson AP, Reynolds K, Fonseca VA, et al. Comparison of **A1C** and fasting glucose criteria to **diagnose diabetes** among U.S. adults. Diabetes Care. 2010 Jan;33(1):95-7. Epub 2009 Oct 6.

Carstensen B, Read S, Friis S, et al. **Cancer incidence** in persons with **type 1 diabetes**: a five country study of 9000 cancers in type 1 diabetic individuals. Diabetologia 2016; doi:10.1007/s00125-016-3884-9.

Carter P., Gray L. J., Troughton J., Khunti K., Davies M. J. **Fruit and vegetable intake** and incidence of type 2 diabetes mellitus: systematic review and meta-analysis. BMJ 2010;341:c4229, doi: 10.1136/bmj.c4229

Carter S, Clifton PM, Keogh JB. Effect of Intermittent Compared With Continuous **Energy Restricted Diet on Glycemic Control in Patients With Type 2 Diabetes**A Randomized Noninferiority Trial. *JAMA Network Open*.2018;1(3):e180756.

Casas JP, et al. Effect of inhibitors of the **renin-angiotensin system** and other antihypertensive drugs on **renal outcomes**: systematic review and meta-analysis. Lancet. 2005 Dec 10;366(9502):2026-2033. INTERPRETATION: The benefits of ACE inhibitors or ARBs on renal outcomes in placebo-controlled trials probably result from a blood-pressure-lowering effect. In patients with diabetes, additional renoprotective actions of these substances beyond lowering blood pressure remain unproven, and there is uncertainty about the greater renoprotection seen in non-diabetic renal disease.

*Casey BM, Duryea EL, Abbassi-Ghanavati M, et al. **Glyburide in Women With Mild Gestational** Diabetes: A Randomized Controlled Trial. Obstet Gynecol. 2015 Aug;126(2):303-9.*

*Catalano PM, McIntyre HD, Cruickshank JK, et al. **HAPO** Study Cooperative Research Group. The **hyperglycemia and adverse pregnancy outcome study**: associations of GDM and obesity with pregnancy outcomes. Diabetes Care. 2012 Apr;35(4):780-6.*

*Caughey GE, Preiss AK, Vitry AI, et al. Comorbid **Diabetes and COPD: Impact of corticosteroid** use on diabetes complications. Diabetes Care. 2013 Jun 4.*

Cavender MA, Scirica BM, Raz I, et al. **Cardiovascular Outcomes** of Patients in **SAVOR-TIMI 53** by Baseline Hemoglobin A1c. Am J Med. 2016 Mar;129(3):340.e1-8.

Cavender MA, White WB, Jarolim P, et al. **Serial Measurement of High-Sensitivity Troponin I** and Cardiovascular Outcomes in Patients With Type 2 Diabetes Mellitus in the **EXAMINE** Trial (Examination of Cardiovascular Outcomes With **Alogliptin** Versus Standard of Care). Circulation. 2017 May 16;135(20):1911-1921.

*Caverly TJ, Fagerlin A, Zikmund-Fisher BJ, et al. **Appropriate Prescribing for Patients With Diabetes at High Risk for Hypoglycemia**: National Survey of Veterans Affairs Health Care Professionals. JAMA Intern Med. 2015 Oct 26:1-3.*

*Cebul RD, Love TE, Jain AK, Hebert CJ. **Electronic health records** and quality of diabetes care. N Engl J Med. 2011 Sep 1;365(9):825-33.*

*Cederberg H, Stančáková A, Yaluri N, et al. Increased risk of **diabetes with statin** treatment is associated with impaired insulin sensitivity and insulin secretion: a 6 year follow-up study of the METSIM cohort. Diabetologia. 2015 Mar 10.*

*Cefalu WT, Leiter LA, Yoon K-H, et al. Efficacy and safety of **canagliflozin versus glimepiride** in patients with type 2 diabetes inadequately controlled with metformin (CANTATA-SU): 52 week results from a randomised, double-blind, phase 3 non-inferiority trial. Lancet 2013; online July 12.*

Cefalu WT, Leiter LA, de Bruin TW, et al. **Dapagliflozin**`s Effects on Glycemia and Cardiovascular Risk Factors in High-Risk Patients With Type 2 Diabetes: A 24-Week, Multicenter, Randomized, Double-Blind, Placebo-Controlled Study With a 28-Week Extension. Diabetes Care. 2015 Apr 7

Cefalu WT, Kaul S, Gerstein HC, et al. **Cardiovascular Outcomes Trials in Type 2 Diabetes**: Where Do We Go From Here? Reflections From a Diabetes Care Editors' Expert Forum. Diabetes Care. 2018 Jan;41(1):14-31.

Cespedes EM, Bhupathiraju SN, Li Y, et al. Long-term changes in **sleep duration**, energy balance and risk of type 2 diabetes. Diabetologia. 2015 Nov 2.

Chacra A, Gantz I, Mendizabal G, et al. A randomised, double-blind, trial of the safety and efficacy of **omarigliptin** (a once-weekly DPP-4 inhibitor) in subjects with type 2 diabetes and renal impairment. Int J Clin Pract. 2017 Apr 27. d

Chalew SA. The continuing challenge of **outcome disparities in children** with diabetes. Pediatrics. 2015 Mar;135(3):552-3.

*Chalasani N et al. The diagnosis and management of **non-alcoholic fatty liver disease** (**NAFLD**): Practice guideline by the American Association for the Study of Liver Diseases, American College of Gastroenterology, and the American Gastroenterological Association. Hepatology 2012 Jun; 55:2005.*

Chalia M, Subramanian T. Type 2 Diabetes Presenting With **Persistent Chorea**. JAMA Neurol. 2018 Dec 21.

Chamberlain JJ, Doyle-Delgado K, Peterson L, Skolnik N. Diabetes Technology: Review of the **2019 American Diabetes Association Standards of Medical Care** in Diabetes. Ann Intern Med. 2019 Aug 13.

Chamberlain JJ, Herman WH, Leal S, et al. **Pharmacologic Therapy for Type 2 Diabetes**: Synopsis of the 2017 **American Diabetes Association (ADA)** Standards of Medical Care in Diabetes. Ann Intern Med. 2017 Mar 14.

Chamberlain JJ, Kalyani RR, Leal S, et al. **Treatment of Type 1 Diabetes: Synopsis of the 2017 American Diabetes Association (ADA)** Standards of Medical Care in Diabetes. Ann Intern Med. 2017 Sep 12.

Chamberlain JJ, Johnson EL, Leal S, et al. **Cardiovascular Disease and Risk Management: Review of the American Diabetes Association Standards** of Medical Care in Diabetes 2018. Ann Intern Med. 2018 Apr 3.

*Chan JC, Sui Y, Oldenburg B, et al; for the JADE and PEARL Project Team. Effects of **Telephone-Based Peer Support** in Patients With Type 2 Diabetes Mellitus Receiving Integrated Care: A Randomized Clinical Trial. JAMA Intern Med. 2014 Apr 28.*
*Chang CH, Lin JW, Wu LC, Lai MS, Chuang LM. Oral Insulin Secretagogues, Insulin, and **Cancer Risk** in Type 2 Diabetes Mellitus. J Clin Endocrinol Metab. 2012 May 4.*
Chang H-Y, Singh S, Mansour O, et al. Association between **sodium-glucose cotransporter 2 inhibitors** and lower extremity amputation among patients with type 2 diabetes [online August 13, 2018]. JAMA Intern Med. doi:10.1001/jamainternmed.2018.3034
*Chang YC, Chuang LM, Lin JW, et al. **Cardiovascular risks associated with second-line oral antidiabetic agents added to metformin** in patients with Type 2 diabetes: a nationwide cohort study. Diabet Med. 2015 Nov;32(11):1460-9.*
*Chanoine JP, Hampl S, Jensen C, et al. Effect of **orlistat** on weight and body composition in obese adolescents. A randomized controlled trial. JAMA 2005;293:2873-83.* (InfoPOEMs: Orlistat (Xenical), in combination with diet, exercise, & behavioral modification, improves weight management in obese adolescents. No major safety issues were identified after 1 year, but further follow-up for sustained weight management and safety is important. (LOE = 1b))
Charbonnel B, et al. Efficacy & safety of the dipeptidyl peptidase-4 inhibitor **sitagliptin** added to metformin therapy in patients with type 2 diabetes inadequately controlled with metformin alone. Diabetes Care. 2006 Dec;29(12):2638-43.
Charpentier G, et al. Should **postprandial hyperglycaemia** in prediabetic and type 2 diabetic patients be treated? Drugs. 2006;66(3):273-86.
Chatterjee Ranee; Yeh Hsin-Chieh; Shafi Tariq; et al. **Serum and Dietary Potassium** and Risk of Incident Type 2 Diabetes Mellitus: The Atherosclerosis Risk in Communities (ARIC) Study. Arch Intern Med. 2010;170(19):1745-1751.
Chatterjee S. **Neck Pain, Stiffness, and Periorbital Edema** in a Man With Diabetes. (Diabetic scleredema) JAMA. 2016 Mar 15;315(11):1159-1160.
Chatterjee S, Khunti K, Davies MJ. **Type 2 diabetes**. Lancet. 2017 Feb 9.
Chatterton H, Younger T, Fischer A, Khunti K; on behalf of the Programme Development Group. **Risk identification and interventions** to prevent type 2 diabetes in adults at high risk: summary of **NICE** guidance. BMJ. 2012 Jul 12;345:e4624.
Chen CB, Lin M, Eurich DT, Johnson JA. Safety of **Concomitant Metformin and Proton Pump Inhibitor Use**: A Population Retrospective Cohort Study. Clin Ther. 2016 Apr 6.
Chen HM, Yang YH, Chen KJ, et al. **Antidepressants reduced risk of mortality** in patients with diabetes mellitus: a population-based cohort study in Taiwan. J Clin Endocrinol Metab. 2019 Jul 2.
Chen HP, Shieh JJ, Chang CC, et al. **Metformin decreases hepatocellular carcinoma** risk in a dose-dependent manner: population-based and in vitro studies. Gut. 2013 Apr;62(4):606-15.
Chen HS, Wu TE, Jap TS, Hsiao LC, Lee SH, Lin HD. Beneficial effects of insulin on glycemic control and beta-cell function in newly diagnosed type 2 diabetes with severe hyperglycemia after short-term intensive insulin therapy. Diabetes Care. 2008 Oct;31(10):1927-32. Epub 2008 Jun 12. n=50. A 6-month course of insulin therapy, compared with OAD treatment, could more effectively achieve adequate glycemic control and significant improvement of beta-cell function in new-onset type 2 diabetic patients with severe hyperglycemia.
Chen M, Sun Q, Giovannucci E, Mozaffarian D, et al. **Dairy consumption** and risk of type 2 diabetes: 3 cohorts of US adults and an updated meta-analysis. BMC Med. 2014 Nov 25;12:215.
Cheng AY, Fantus IG. Oral antihyperglycemic therapy for type 2 diabetes mellitus. **CMAJ**. **2005** Jan 18;172(2):213-26.
Cheng J, Zhang W, Zhang X, et al. Effect of **Angiotensin-Converting Enzyme Inhibitors and Angiotensin II Receptor Blockers** on All-Cause Mortality, Cardiovascular Deaths, and Cardiovascular Events in Patients **With Diabetes** Mellitus: A Meta-analysis. JAMA Intern Med. 2014 Mar 31.
Cheng JWM, Colucci VJ, Kalus JS, Spinler SA. Managing Diabetes and **Preventing Heart Disease**: Have We Found a Safe and Effective Agent? Ann Pharmacother. 2018 Dec 5:1060028018816466.
Cherney DZ, Udell JA. Use of **Sodium Glucose Cotransporter 2 Inhibitors** in the Hands of **Cardiologists**: With Great Power Comes Great Responsibility. Circulation. 2016 Dec 13;134(24):1915-1917.
Cherney DZI, Zinman B, Inzucchi SE, et al. Effects of **empagliflozin** on the **urinary albumin-to-creatinine ratio** in patients with type 2 diabetes and established cardiovascular disease: an exploratory analysis from the **EMPA-REG OUTCOME** randomised, placebo-controlled trial. Lancet Diabetes Endocrinol 2017; online June 27.
Chetan MR, Charlton MH, Thompson C, etal. The **Type 1 diabetes 'honeymoon' period is five times longer in men who exercise**: a case-control study. Diabet Med. 2018 Aug 17.
Chiang JL, Kirkman MS, Laffel LM, et al; on behalf of the Type 1 Diabetes Sourcebook Authors. **Type 1 Diabetes Through the Life Span**: A Position Statement of the American Diabetes Association. Diabetes Care. 2014 Jun 16.
Chiang JL, Maahs DM, Garvey KC, et al. Type 1 Diabetes **in Children and Adolescents**: A Position Statement by the American Diabetes Association. Diabetes Care. 2018 Aug 9.
Chiasson JL, Josse RG, Gomis R, Hanefeld M, Karasik A, Laakso M; **STOP-NIDDM** Trial Research Group. Acarbose treatment and the risk of cardiovascular disease and hypertension in patients with impaired glucose tolerance: the STOP-NIDDM trial. JAMA. 2003 Jul 23;290(4):486-94.
Chiew AL, Wright DFB, Dobos NM, et al. "**Massive" metformin overdose**. Br J Clin Pharmacol. 2018 Mar 13.
Chilton R, Tikkanen I, Cannon CP, et al. Effects of **empagliflozin** on blood pressure and markers of arterial stiffness and vascular resistance in patients with type 2 diabetes. Diabetes Obes Metab. 2015 Dec;17(12):1180-93.
Ching Sun GE, Kashyap SR, Nasr C. **Diabetes therapy and cancer risk**: Where do we stand when treating patients? Cleve Clin J Med. 2014 Oct;81(10):620 628.
Chiquette E, Ramirez G, Defronzo R. A meta-analysis comparing the effect of **thiazolidinediones on cardiovascular risk factors**. Arch Intern Med. 2004 Oct 25;164(19):2097-104.
Chiu WC, Ho WC, Liao DL, et al. Progress of **Diabetic Severity and Risk of Dementia**. J Clin Endocrinol Metab. 2015 Jul 9
Chlebowski RT, McTiernan A, Wactawski-Wende J, et al. Diabetes, **Metformin, and Breast Cancer** in Postmenopausal Women. J Clin Oncol. 2012 Jun 11.
Choi B, Lee S, Kim SM, et al. **Dipeptidyl Peptidase-4 Induces Aortic Valve Calcification by Inhibiting** Insulin-Like Growth Factor-1 Signaling in Valvular Interstitial Cells. Circulation. 2017 May 16;135(20):1935-1950.
Cho SK, Kim CO, Park ES, et al. **Verapamil decreases** the glucose-lowering effect of **metformin** in healthy volunteers. Br J Clin Pharmacol. 2014 Jul 24.
Choo VL, Viguiliouk E, Blanco Mejia S, etal . Food sources of **fructose-containing sugars and glycaemic control**: systematic review and meta-analysis of controlled intervention studies. BMJ 2018;363:k4644.
Chon S, Rhee SY, Ahn KJ, et al. Long-term effects on glycaemic control and **beta-cell preservation of early intensive treatment** in patients with newly diagnosed type 2 diabetes: A multicentre randomized trial. Diabetes Obes Metab. 2017 Dec 22
*Chow E, Bernjak A, Williams S, et al. Risk of **cardiac arrhythmias** during **hypoglycemia** in patients with type 2 diabetes and cardiovascular risk. Diabetes. 2014 May;63(5):1738-47.*
Chow LS, Odegaard AO, Bosch TA, et al. **Twenty year fitness trends** in young adults and incidence of prediabetes and diabetes: the **CARDIA** study. Diabetologia. 2016 May 16.
Chowdhury TA, Wright R, Yaqoob MM. Using **metformin** in the presence of **renal disease**. BMJ. 2015 Apr 14;350:h1758.
Chowdhury TA, Shah R. Reducing the risk of diabetes. BMJ. 2015 Sep 22;351:h4595.
Chowdhury TA, Cheston H, Claydon A. Managing adults with **diabetes in hospital during an acute illness**. BMJ. 2017 Jun 22;357:j2551.
Christine PJ, Auchincloss AH, Bertoni AG, et al. Longitudinal Associations Between **Neighborhood Physical and Social Environments** and Incident Type 2 Diabetes Mellitus: The Multi-Ethnic Study of Atherosclerosis (MESA). JAMA Intern Med. 2015 Jun 29.
Chudyk Anna, Petrella Robert J.. Effects of **Exercise** on Cardiovascular Risk Factors in Type 2 Diabetes: A meta-analysis Diabetes Care May 2011 34:1228-1237; doi:10.2337/dc10-1881
Claggett B, Lachin JM, Hantel S, et al. Long-term **benefit of empagliflozin on life expectancy** in patients with type 2 diabetes mellitus and established cardiovascular disease. Survival estimates from the EMPA-REG OUTCOME trial. Circulation 2018;138:1599-601.
Clifton P. Do **Dipeptidyl Peptidase IV (DPP-IV) Inhibitors** Cause **Heart Failure**? Clin Ther. 2014 Dec 1;36(12):2072-9.
Claesen M, Gillard P, De Smet F, et al. **Mortality** in individuals treated with **glucose-lowering agents**: a large, controlled cohort study. J Clin Endocrinol Metab. 2016;101:461-469.
Clery P, Stahl D, Ismail K, et al. Systematic review and meta-analysis of the efficacy of **interventions for people with Type 1 diabetes mellitus and disordered eating.** Diabet Med. 2017 Dec;34(12):1667-1675.
Cloutier L, Lamarre-Cliche M. **Hypertension in Adults With Type 2 Diabetes**: A Review of Blood Pressure Measurement Methods, Targets and Therapy. Can J Diabetes. 2018 Apr;42(2):188-195.
Coca SG, Ismail-Beigi F, Haq N, Krumholz HM, Parikh CR. Role of intensive glucose control in development of **renal end points** in type 2 diabetes mellitus: systematic review and meta-analysis. Arch Intern Med. 2012;172 (10):761-769.
Cogen AL, Desai K, Elder D, Rosenbach M. Acute **Photodistributed Exanthematous Pustulosis Associated With Liraglutide** Treatment. JAMA Dermatol. 2019 Aug 7.
Cohen D. Has **pancreatic damage from glucagon suppressing** drugs been underplayed? BMJ 2013;346:f3680.
COIITSS Study Investigators, Annane D, Cariou A, Maxime V, et al. Corticosteroid treatment and intensive insulin therapy for **septic shock** in adults: a randomized controlled trial. JAMA. 2010 Jan 27;303(4):341-8.
Colberg SR, Sigal RJ, Yardley JE et al. **Physical Activity/Exercise and Diabetes**: A Position Statement of the American Diabetes Association (**ADA**). Diabetes Care.2016;39(11):2065-2079.
Colberg SR, Sigal RJ, Yardley JE, et al. **Physical Activity/Exercise and Diabetes**: A Position Statement of the **American Diabetes Association (ADA)**. Diabetes Care. 2016 Nov;39(11):2065-2079.
Collins GS, Altman DG. External validation of **QDSCORE**((R)) for predicting the 10-year risk of developing Type 2 diabetes. Diabet Med. 2011 May;28(5):599-607. doi: 10.1111/j.1464-5491.2011.03237.x
Colmers IN, Bowker SL, Majumdar SR, Johnson JA. Use of **thiazolidinediones (esp. pioglitazone) and the risk of bladder cancer** among people with type 2 diabetes: a meta-analysis. CMAJ. 2012 Jul 3.
Comi RJ. Incorporating **New Medications in Diabetes Care**. Ann Intern Med. 2015 Nov 3;163(9):719-20.
Cone CJ, Bachyrycz AM, Murata GH. **Hepatotoxicity Associated with Metformin** Therapy in Treatment of Type 2 Diabetes Mellitus with Nonalcoholic Fatty Liver Disease**.** Ahead of Print 1Oct2010. Ann Pharmacother ;44:1655-1659.
Conlin PR, Colburn J, Aron D, et al. Synopsis of the **2017 U.S. Department of Veterans Affairs/U.S. Department of Defense** clinical practice guideline: management of type 2 diabetes mellitus. Ann Intern Med. 2017;167:655-63. doi:10.7326 /M17-1362
Connelly KA, Yan AT, Leiter LA, et al. **Cardiovascular Implications of Hypoglycemia** in Diabetes Mellitus. Circulation. 2015 Dec 15;132(24):2345-50.
Constantino MI, Molyneaux L, Limacher-Gisler F, et al. **Long-Term Complications and Mortality in Young-Onset Diabetes**: Type 2 diabetes is more hazardous and lethal than type 1 diabetes. Diabetes Care. 2013 Jul 11.

Cooke D, Hurel SJ, Casbard A, et al. Randomized controlled trial to assess the impact of **continuous glucose monitoring** on HbA1c in insulin-treated diabetes (MITRE Study). . Diabet. Med. 2009 May;26:540–7.

Cooper MN, de Klerk NH, Jones TW, et al. **Clinical and demographic risk factors associated with mortality** during early adulthood in a population-based cohort of **childhood-onset type 1 diabetes**. Diabet Med. 2014 Dec;31(12):1550-8.

Copeland KC, Silverstein J, Moore KR, et al. **Management of Newly Diagnosed Type 2 Diabetes Mellitus (T2DM) in Children and Adolescents. (AAP, ADA, AAFP, AND, Ped Endo Soc)** Pediatrics. 2013 Jan 28.

Coppell Kirsten J, Kataoka Minako, Williams Sheila M, et al. **Nutritional intervention** in patients with type 2 diabetes who are hyperglycaemic despite optimised drug treatment—Lifestyle Over and Above Drugs in Diabetes (LOADD) study: randomised controlled trial. BMJ 2010;341:c3337.

Corella D, Carrasco P, et al. **Mediterranean diet** reduces the adverse effect of the TCF7L2-rs7903146 polymorphism on cardiovascular risk factors and stroke incidence: A randomized controlled trial in a high-cardiovascular-risk population. Diabetes Care 2013.

Cornel JH, Bakris GL, Stevens SR, et al. Effect of **Sitagliptin** on **Kidney Function** and Respective Cardiovascular Outcomes in Type 2 Diabetes: Outcomes From **TECOS**. Diabetes Care. 2016 Dec;39(12):2304-2310.

Cosentino F, Grant PJ, Aboyans V, et al. **2019 ESC Guidelines** on diabetes, pre-diabetes, and cardiovascular diseases developed in collaboration with the EASD. Eur Heart J. 2019 Aug 31.

Costanzo P, Cleland JG, Pellicori P, et al. The **obesity paradox in type 2 diabetes** mellitus: relationship of body mass index to prognosis: a cohort study. Ann Intern Med. 2015 May 5;162(9):610-8.

Courcoulas AP, Goodpaster BH, Eagleton JK, et al. **Surgical vs Medical** Treatments for Type 2 Diabetes Mellitus: A Randomized Clinical Trial. JAMA Surg. 2014 Jun 4.

Cousminer DL, Ahlqvist E, Mishra R, et al. First Genome-Wide Association Study of Latent Autoimmune Diabetes in Adults Reveals Novel **Insights Linking Immune and Metabolic Diabetes**. Diabetes Care. 2018 Nov;41(11):2396-2403.

Coustan DR. Pharmacological management of **gestational diabetes**: an overview. Diabetes Care. 2007 Jul;30 Suppl 2:S206-8. Review. Erratum in: Diabetes Care. 2007 Dec;30(12):3154.

Cowie CC, et al. **Prevalence** of **diabetes and impaired fasting glucose** in adults in the **U.S.** population: National Health And Nutrition Examination Survey 1999-2002. Diabetes Care. 2006 Jun;29(6):1263-8.

Cox DJ, Gonder-Frederick LA, Singh H, et al. **Predicting and Reducing Driving Mishaps** Among Drivers With Type 1 Diabetes. Diabetes Care. 2017 Apr 12.

Cradock KA, OLaighin G, Finucane FM, et al. **Diet Behavior Change** Techniques in Type 2 Diabetes: A Systematic Review and Meta-analysis. Diabetes Care. 2017 Dec;40(12):1800-1810.

Craig J. Currie, Chris D. Poole, Sara Jenkins-Jones, et al. Mortality After Incident **Cancer** in People With and Without Type 2 Diabetes: Impact of **metformin on survival**. Diabetes Care February 2012 35:299-304; published ahead of print Jan 20, 2012.

Crandall JP, Mather K, Rajpathak SN, et al. **Statin use and risk of developing diabetes**: results from the **Diabetes Prevention Program (DPP)**. BMJ Open Diabetes Res Care. 2017 Oct 10;5(1):e000438.

Crawford F, Cezard G, Chappell FM, et al. A systematic review and individual patient data meta-analysis of prognostic factors for **foot ulceration** in people with diabetes: the international research collaboration for the prediction of diabetic foot ulcerations (PODUS). Health Technol Assess. 2015 Jul;19(57):1-210.

Creamer J, Attridge M, Ramsden M, et al. **Culturally appropriate health education** for Type 2 diabetes in ethnic minority groups: an updated Cochrane Review of randomized controlled trials. Diabet Med. 2016 Feb;33(2):169-83

Creanga AA, Bradley HM, McCormick C, Witkop CT. Use of metformin in **polycystic ovary syndrome.** Obstet Gynecol 2008;111:959-968. {Info POEMs: Metformin induces ovulation in women with polycystic ovarian syndrome (PCOS). Metformin plus clomiphene induces ovulation and results in early pregnancy for clomiphene-resistant women. Data are insufficient to determine whether metformin increases live births in women with PCOS. Future studies should compare metformin head-to-head with clomiphene as the primary treatment. (LOE = 1a-)}

Creatore, Maria Isabella, Moineddin, Rahim, Booth, Gillian, et al. Age- and sex-related prevalence of diabetes mellitus among **immigrants to Ontario**, Canada. CMAJ 2010 0: cmaj.091551.

Creatore MI, Glazier RH, Moineddin R, et al. Association of **neighborhood walkability** with change in overweight, obesity, and diabetes.JAMA. doi:10.1001/jama.2016.5898.

Crowley MJ, Diamantidis CJ, McDuffie JR, et al. Clinical Outcomes of **Metformin Use in Populations With Chronic Kidney Disease, Congestive Heart Failure, or Chronic Liver Disease**: A Systematic Review. Ann Intern Med. 2017 Jan 3.

Crowley MJ, Maciejewski ML. Revisiting **NPH Insulin for Type 2 Diabetes: Is** a Step Back the Path Forward? JAMA. 2018 Jul 3;320(1):38-39.

Crume TL, Ogden L, Maligie M, et al. Long-Term Impact of Neonatal **Breastfeeding** on Childhood Adiposity and Fat Distribution Among Children Exposed to Diabetes In Utero. Diabetes Care Mar 2011 34:641-645.

Crump C, Sundquist J, Winkleby MA, Sieh W, Sundquist K. **Physical fitness** among Swedish military conscripts and long-term risk for type 2 diabetes mellitus: a cohort study. Ann Intern Med. 2016. [Epub ahead of print]. doi:10.7326/M15-2002

Cummings DE, Arterburn DE, Westbrook EO, et al. **Gastric bypass surgery vs intensive lifestyle** and medical intervention for type 2 **diabetes**: the **CROSSROADS** randomised controlled trial. Diabetologia. 2016 May;59(5):945-53.

Cryer PE, Axelrod L, Grossman AB, et al.; Endocrine Society. Evaluation and management of adult **hypoglycemic disorders**: an Endocrine Society Clinical Practice Guideline. J Clin Endocrinol Metab. 2009 Mar;94(3):709-28.

Cryer PE. Mechanisms of **hypoglycemia-associated autonomic failure** in diabetes. N Engl J Med. 2013 Jul 25;369(4):362-72.

CTFPHC: Canadian Task Force on Preventive Health Care. Recommendations on **screening for type 2 diabetes in adults**. CMAJ. 2012 Oct 16;184(15):1687-96.

Cui J, Philo L, Nguyen P et al. **Sitagliptin** versus **placebo** in the treatment of **nonalcoholic fatty liver disease**: A randomized controlled trial. *Journal of Hepatology*, 2016.

Cukierman-Yaffe T, Bosch J, Diaz R, et al. for the **ORIGIN** Investigators. Effects of **basal insulin glargine and omega-3 fatty acid on cognitive** decline and probable cognitive impairment in people with dysglycaemia: a substudy of the ORIGIN trial. Lancet Diabetes Endocrinol. 2014 May 30. pii: S2213-8587(14)70062-2.

Cummings DM, Kirian K, Howard G, et al. Consequences of Comorbidity of Elevated **Stress and/or Depressive Symptoms** and Incident Cardiovascular Outcomes in Diabetes: Results From the REasons for the Geographic And Racial Differences in Stroke (**REGARDS**) Study. Diabetes Care. 2015 Nov 17.

Cummings DM, Lutes LD, Littlewood K, et al. **Randomized Trial of a Tailored Cognitive Behavioral Intervention** in Type 2 Diabetes With Comorbid Depressive and/or Regimen-Related Distress Symptoms: 12-Month Outcomes From COMRADE. Diabetes Care. 2019 May;42(5):841-848.

Cundy T, Ackermann E, Ryan EA. **Gestational diabetes**: new criteria may triple the prevalence but effect on outcomes is unclear. BMJ. 2014 Mar 11

Currie CJ, Peters JR, Tynan A, Evans M, Heine RJ, Bracco OL, Zagar T, Poole CD. **Survival as a function of HbA(1c)** in people with type 2 diabetes: a retrospective cohort study. Lancet. 2010 Jan 26. [Epub ahead of print]

Currie CJ et al. **Mortality and other important diabetes-related outcomes with insulin** vs other antihyperglycemic therapies in type 2 diabetes. J Clin Endocrinol Metab 2013; 98: 668-77.

Currie O, Williman J, Mangin D, et al. Comparative risk of **new-onset diabetes following commencement of antipsychotics** in New Zealand: a population-based clustered multiple baseline time series design. BMJ Open. 2019 Feb 21;9(2):e022984.

Cusi K, Orsak B, Bril F, et al. Long-term **pioglitazone** treatment for patients with **nonalcoholic steatohepatitis** and prediabetes or type 2 diabetes mellitus. A randomized, controlled trial. Ann Intern Med. 2016.

D'Aiuto F, Gkranias N, Bhowruth D, et al; TASTE Group. Systemic effects of **periodontitis treatment** in patients with type 2 diabetes: a 12 month, single-centre, investigator-masked, randomised trial. Lancet Diabetes Endocrinol.2018 Dec;6(12):954-965.

D'Alessio D, Haring HU, Charbonnel B, et al. Comparison of **insulin glargine and liraglutide** added to oral agents in patients with poorly controlled type 2 diabetes. Diabetes Obes Metab. 2015 Feb;17(2):170-8.

D'Anna R et al. **Myo-inositol supplementation** for prevention of gestational diabetes in obese pregnant women: A randomized controlled trial. Obstet Gynecol 2015 Aug; 126:310.

Dabelea D, Rewers A, Stafford JM, et al; **SEARCH** for Diabetes in youth Study Group. Trends in the Prevalence of **Ketoacidosis** at Diabetes Diagnosis: The SEARCH for Diabetes in Youth Study. Pediatrics. 2014 Apr;133(4):e938-45.

*Dabelea D, Mayer-Davis EJ, Saydah S, et al; **SEARCH** for Diabetes in **Youth** Study. **Prevalence** of **type 1 and type 2** diabetes among **children and adolescents** from 2001 to 2009. JAMA. 2014 May 7;311(17):1778-86.*

Dabelea D, Stafford JM, Mayer-Davis EJ, et al. Association of **Type 1 Diabetes vs Type 2 Diabetes** Diagnosed During Childhood and Adolescence With **Complications During Teenage Years** and Young Adulthood. JAMA. 2017 Feb 28;317(8):825-835.

Dagenais GR, Lu J, Faxon DP, et al. Effects of Optimal Medical Treatment With or Without Coronary Revascularization on Angina and Subsequent Revascularizations in Patients With Type 2 Diabetes Mellitus and Stable Ischemic Heart Disease. Circulation. 2011 Mar 28. (BARI 2D)

Dagogo-Jack S;Liu J;Eldor R;Amorin G;Johnson J;Hil. Efficacy and safety of the addition of **ertugliflozin** in patients with type 2 diabetes mellitus inadequately controlled with metformin and sitagliptin: The **VERTIS SITA2** placebo-controlled randomized study. Diabetes Obes Metab. 2017 Sep 17.

Dahlqvist S, Rosengren S, Gudbjörnsdottir S, et al. Risk of **atrial fibrillation** in people with **type 1** diabetes compared with matched controls from the general population: a prospective case-control study. Lancet Diabetes Endocrinol 2017; online August 21.

Dailey George. **Early and Intensive Therapy** for Management of Hyperglycemia and Cardiovascular Risk Factors in Patients With Type 2 Diabetes. Clinical Therapeutics, Volume 33, Issue 6, June 2011

Dailey, George. "**Empagliflozin for the treatment of type 2 diabetes mellitus**: An overview of safety and efficacy based on Phase 3 trials." Journal of diabetes 7.4 (2015): 448-461.

Daly B, Toulis KA, Thomas N, et al. Increased risk of **ischemic heart disease, hypertension, and type 2 diabetes** in women with previous **gestational diabetes** mellitus, a target group in general practice for preventive interventions: A population-based cohort study. PLoS Med. 2018 Jan 16;15(1):e1002488.

Daly N, Carroll C, Flynn I, et al. Evaluation of **point-of-care maternal glucose measurements** for the diagnosis of gestational diabetes mellitus. BJOG. 2016 Aug 17.

Dambha-Miller H, Cooper AJ, Simmons RK, et al. **Patient-centred care**, health behaviours and cardiovascular risk factor levels in people with recently diagnosed type 2 diabetes: 5-year follow-up of the **ADDITION-Plus** trial cohort. BMJ Open. 2016 Jan 6;6(1):e008931.

Danaei G, Lawes CMM, et al. Global and regional mortality from ischaemic heart disease and stroke attributable to **higher-than-optimum blood glucose** concentration: comparative risk assessment. Lancet 2006; 368: 1651-1659.

Danaei G, Finucane MM, Lu Y, et al, on behalf of the Global Burden of Metabolic Risk Factors of Chronic Diseases Collaborating Group (Blood Glucose). **National, regional, and global trends in fasting plasma glucose and diabetes** prevalence since 1980: systematic analysis of health examination surveys and epidemiological studies with 370 country-years and 2.7 million participants. Lancet 2011.

Dandjinou M, Sheehy O, Bérard A. **Antidepressant use during pregnancy and the risk of gestational diabetes mellitus**: a nested case-control study. BMJ Open. 2019 Oct 1;9(9):e025908.

Dandona P, Mathieu C, Phillip M, et al. Efficacy and safety of **dapagliflozin** in patients with inadequately controlled type 1 diabetes **(DEPICT-1):** 24 week results from a multicentre, double-blind, phase 3, randomised controlled trial. Lancet Diabetes Endocrinol 2017; online Sept 14.

Dandona P, Mathieu C, Phillip M, et al. Efficacy and Safety of **Dapagliflozin in Patients With Inadequately Controlled Type 1 Diabetes**: The **DEPICT-1 52-Week Study**. Diabetes Care. 2018 Oct 23.

Dangas GD, Farkouh ME, Sleeper LA, et al. **FREEDOM** Investigators. Long-Term Outcome **of PCI Versus CABG in Insulin and Non-Insulin-Treated Diabetic Patients**: Results From the FREEDOM Trial. J Am Coll Cardiol. 2014 Sep 23;64(12):1189-97.

Dankner R, Agay N, Olmer L, et al. **Metformin Treatment and Cancer Risk**: Cox Regression Analysis with Time-Dependent Covariates of 320,000 Individuals with Incident Diabetes Mellitus. Am J Epidemiol. 2019 Jul 3.

Danne T, et al. Liraglutide in an **Adolescent Population with Obesity**: A Randomized,Double-Blind, Placebo-Controlled 5-Week Trial to Assess Safety, Tolerability, and Pharmacokinetics of Liraglutide in Adolescents Aged 12-17 Years. J Pediatr. 2016 Dec 13.

Danne T, Nimri R, Battelino T, et al. **International Consensus on Use of Continuous Glucose Monitoring**. Diabetes Care. 2017 Dec;40(12):1631-1640.

Das SR, Everett BM, Birtcher KK, et al. 2018 ACC Expert Consensus Decision Pathway on Novel Therapies for **Cardiovascular Risk Reduction in Patients With Type 2 Diabetes and Atherosclerotic Cardiovascular Disease**: A Report of the American College of Cardiology Task Force on Expert Consensus Decision Pathways. J Am Coll Cardiol. 2018 Nov 24.

Dasgupta K, Quinn RR, Zarnke KB, et al. Canadian Hypertension Education Program. The **2014 CHEP-Canadian Hypertension** Education Program Recommendations for Blood Pressure Measurement, Diagnosis, Assessment of Risk, Prevention, and Treatment of Hypertension. Can J Cardiol. 2014 May;30(5):485-501.

Dave CV, Schneeweiss S, Kim D, et al. Sodium–glucose cotransporter-2 inhibitors and the **risk for severe urinary tract infections**. A population-based cohort study. Ann Intern Med. 2019. [Epub ahead of print]. doi:10.7326/M18-3136

Dave CV, Schneeweiss S, Patorno E. Association of Sodium-Glucose Cotransporter 2 Inhibitor Treatment With **Risk of Hospitalization for Fournier Gangrene** Among Men. JAMA Intern Med. 2019 Sep 3.

Dave CV, Schneeweiss S, Patorno E Comparative **risk of genital infections associated with sodium-glucose co-transporter-2 inhibitors**. Diabetes Obes Metab. 2018 Sep 12.

Davis CL, Pollock NK, Waller JL, et al. **Exercise dose** and diabetes risk in overweight and obese children: a randomized controlled trial. JAMA. 2012 Sep 19;308(11):1103-12.

Davis WA, Hamilton EJ, Bruce DG, Davis TME. **Development and Validation of a Simple Hip Fracture Risk Prediction Tool for Type 2 Diabetes**: The Fremantle Diabetes Study Phase I. Diabetes Care. 2018 Nov 19.

Davies G, Lobanova L, Dawicki W, et al. **Metformin** inhibits the development, and promotes the resensitization, of **treatment-resistant breast cancer**. PLoS One. 2017 Dec 6;12(12):e0187191.

Davies ML, Pham DQ, Drab SR. **GLP1-RA Add-on Therapy** in Patients with Type 2 Diabetes Currently on a Bolus Containing **Insulin** Regimen. Pharmacotherapy. 2016 Aug;36(8):893-905.

Davies MJ, Heller S, Skinner TC, et al; Diabetes Education and Self Management for Ongoing and Newly Diagnosed Collaborative. Effectiveness of the diabetes education and self management for ongoing and newly diagnosed (DESMOND) programme for people with newly diagnosed type 2 diabetes: cluster randomised controlled trial. BMJ. 2008 Mar 1;336(7642):491-5. Epub 2008 Feb 14. Erratum in: BMJ. 2008 Apr 9;336(7649):doi:10.1136/bmj.39553.528299.AD. A 6-hour well-constructed educational intervention given to patients with newly diagnosed diabetes was no better than usual care in improving their overall glucose control over 1 year of evaluation. However, the intervention resulted in a greater average weight loss and prompted more patients to quit smoking, though these results were not the primary goal of the intervention. (LOE = 1b-)

Davies MJ, Chubb BD, Smith IC, et al. Cost-utility analysis of **liraglutide compared with sulphonylurea or sitagliptin**, all as add-on to metformin monotherapy in Type 2 diabetes mellitus. Diabet Med. 2012 Mar;29(3):313-20.

Davies MJ, Bergenstal R, Bode B, et al. Efficacy of **Liraglutide for Weight Loss** Among Patients With Type 2 Diabetes: The **SCALE** Diabetes Randomized Clinical Trial. JAMA. 2015 Aug 18;314(7):687-99.

Davies MJ, Bain SC, et al. Efficacy and Safety of **Liraglutide** Versus Placebo as Add-on to Glucose-Lowering Therapy in Patients With Type 2 Diabetes and Moderate **Renal Impairment (LIRA-RENAL**): A Randomized Clinical Trial. Diabetes Care. 2015 Dec 17.

Davies MJ, D'Alessio DA, Fradkin J, et al. Management of Hyperglycemia in Type 2 Diabetes, 2018. A Consensus Report by **the American Diabetes Association (ADA) and the European Association for the Study of Diabetes (EASD**). Diabetes Care. 2018 Oct 4. pii: dci180033.

Davies MJ, Gray LJ, et al. A **community based primary prevention programme** for type 2 diabetes integrating identification and lifestyle intervention for prevention: the **Let`s Prevent Diabetes** cluster randomised controlled trial. Prev Med. 2016 Mar;84:48-56.

Davies MJ, Russell-Jones D, Selam JL, et al. **Basal insulin peglispro versus insulin glargine** in insulin-naive type 2 diabetes: IMAGINE 2 randomized trial. Diabetes Obes Metab. 2016 Jun 28.

Davies M, Pieber TR, Hartoft-Nielsen ML, et al. Effect of Oral **Semaglutide** Compared With Placebo and Subcutaneous Semaglutide on Glycemic Control in Patients With Type 2 Diabetes: A Randomized Clinical Trial.JAMA. 2017 Oct 17;318(15):1460-1470.

Davis TME, Coleman RL, Holman RR; for the UKPDS Group. **Prognostic significance of silent myocardial infarction** in newly diagnosed type 2 diabetes mellitus: United Kingdom Prospective Diabetes Study **(UKPDS) 79**. Circulation. 2013;127:980–987.

Davoren P. **Safe prescribing of metformin** in diabetes. Australian Prescriber. AN INDEPENDENT REVIEW (2014): 2.

DCCT/EDIC Research Group. Intensive Diabetes Therapy and **Glomerular Filtration** Rate in Type 1 Diabetes. N Engl J Med. 2011 Nov 12.

DCCT/EDIC Research Group. Association between **7 years** of intensive treatment of type 1 diabetes and long-term **mortality**. JAMA. doi:10.1001/jama.2014.16107.

DCCT/EDIC Research Group. Intensive Diabetes Therapy and **Ocular Surgery** in Type 1 Diabetes. N Engl J Med. 2015 Apr 30;372(18):1722-1733.

DCCT/EDIC Research Group. Frequency of evidencebased screening for **retinopathy** in type 1 diabetes. N Engl J Med 2017;376:1507-16.

DCCT/EDIC Diabetes Control and Complications Trial (**DCCT**)/Epidemiology of Diabetes Interventions and Complications (**EDIC**) Study Research Group. **Intensive Diabetes Treatment and Cardiovascular Outcomes in Type 1 Diabetes**: The **DCCT/EDIC Study 30-Year Follow-up**. Diabetes Care. 2016 May;39(5):686-93.

De Berardis G, Sacco M, Strippoli GF, et al. **Aspirin for primary prevention** of cardiovascular events in people with diabetes: meta-analysis of randomised controlled trials. BMJ. 2009 Nov 6;339:b4531. doi: 10.1136/bmj.b4531.

de Boer H, et al. Glycaemic control without weight gain in insulin requiring type 2 diabetes: 1-year results of the **GAME** regimen. Diabetes Obes Metab. 2006 Sep;8(5):517-23. All patients were treated with the GAME regimen, a combination of **glimepiride** administered at 20:00 hours for nocturnal glycaemic control, **insulin aspart** three times daily for meal-related glucose control and metformin.

de Boer IH, Kestenbaum B, Rue TC, et al. Diabetes Control and Complications Trial (**DCCT**)/Epidemiology of Diabetes Interventions and Complications (**EDIC**) Study Research Group. Insulin therapy, hyperglycemia, and hypertension in type 1 diabetes mellitus. Arch Intern Med. 2008 Sep 22;168(17):1867-73. Hyperglycemia is a risk factor for incident hypertension in type 1 diabetes, and intensive insulin therapy reduces the long-term risk of developing hypertension.

de Boer IH.; Rue Tessa C.; Cleary Patricia A.; et al.; for the Diabetes Control and Complications Trial/Epidemiology of Diabetes Interventions and Complications Study Research Group. **Long-term Renal Outcomes** of Patients With Type 1 Diabetes Mellitus and Microalbuminuria: An Analysis of the Diabetes Control and Complications Trial/Epidemiology of Diabetes Interventions and Complications Cohort **DCCT/EDIC**. Arch Intern Med. 2011;171(5):412-420.

de Boer IH., Rue Tessa C., Hall Yoshio N., et al. Temporal **Trends in the Prevalence of Diabetic Kidney Disease** in the United States. JAMA. 2011;305(24):2532-2539.doi:10.1001/jama.2011.861.

de Boer IH, Bangalore S, Benetos A, et al. **Diabetes and Hypertension**: A Position Statement by the American Diabetes Association. Diabetes Care. 2017 Sep;40(9):1273-1284

de Boer IH, Bakris G, Cannon CP. Individualizing Blood Pressure Targets for People With **Diabetes and Hypertension**: **Comparing the ADA and the ACC/AHA Recommendations**. JAMA. 2018 Mar 15.

De Buck E, Borra V, Carlson JN, et al. First aid **glucose administration routes for symptomatic hypoglycaemia**. Cochrane Database Syst Rev. 2019 Apr 11;4:CD013283. When providing first aid to individuals with hypoglycaemia, oral glucose administration results in a higher blood glucose concentrations after 20 minutes when compared with buccal administration of glucose. A difference in plasma glucose concentration could not be demonstrated, when administering a dextrose gel, defined as "a combined oral and buccal mucosal route" compared to oral administration of a glucose tablet or solution. In the specific population of children with concomitant malaria and respiratory illness, sublingual sugar results in a higher blood glucose concentration after 20 minutes when compared with oral administration.

De Cosmo S, Copetti M, Lamacchia O, et al. Development and Validation of a Predicting Model of All-Cause Mortality in Patients With Type 2 Diabetes Mellitus. Diabetes Care. 2013 May 1.

de Ferranti SD, de Boer IH, Fonseca V, et al. **Type 1 Diabetes** Mellitus and **Cardiovascular Disease**: A Scientific Statement From the **American Heart Association** and **American Diabetes Association**. Diabetes Care. 2014 Oct;37(10):2843-2863.

De Franco E, Flanagan SE, Houghton JA, et al. The effect of early, comprehensive **genomic testing on clinical care in neonatal diabetes**: an international cohort study. Lancet 2015; online July 29.

DeFronzo RA, Tripathy D, Schwenke DC, et al. for **ACT NOW**. **Pioglitazone for Diabetes Prevention** in Impaired Glucose Tolerance. N Engl J Med 2011; 364:1104-1115. {↓progression to T2DM (incidence of 2.1 vs 7.6%/yr; NNT=19/yr) but ↑weight (3.9 vs 0.77kg) & edema (12.9 vs 6.4%)}.

de Goffau MC, Fuentes S, van den Bogert B, et al. **Aberrant gut microbiota** composition at the onset of type 1 diabetes in young children. Diabetologia. 2014 Jun 15.

de Havenon A, Majersik JJ, Tirschwell DL, et al. **Blood pressure, glycemic control, and white matter hyperintensity progression** in type 2 diabetics(ACCORD MIND). Neurology. 2019 Mar 12;92(11):e1168-e1175.

de la Hera JM, García-Ruiz JM, Martínez-Camblor P, et al. Real **Incidence of Diabetes Mellitus in a Coronary Disease Population**. Am J Cardiol. 2012 Nov 17.

de Jager Jolien, Kooy Adriaan, Lehert Philippe et al. Long term treatment with **metformin** in patients with type 2 diabetes and risk of **vitamin B-12 deficiency**: randomised placebo controlled trial. BMJ 2010;340

De Leo V, Musacchio MC, Morgante G, Piomboni P, Petraglia F. Metformin treatment is effective in obese teenage girls with PCOS. Hum Reprod. 2006 Jun 19; [Epub ahead of print]

De Pablo-Fernandez E, Goldacre R, Pakpoor J, et al. Association between **diabetes and subsequent Parkinson disease**: A record-linkage cohort study. Neurology. 2018 Jun 13.

de Vathaire F, El-Fayech C, Ben Ayed FF, et al. **Radiation dose to the pancreas** and risk of diabetes mellitus in childhood cancer survivors: a retrospective cohort study. Lancet Oncol. 2012 Aug 22.

de Vos CC, Meier K, Zaalberg PB, et al. **Spinal cord stimulation** in patients with painful **diabetic neuropathy**: A multicentre randomized clinical trial. Pain. 2014 Aug 29.

de Zeeuw D, Akizawa T, Audhya P, et al. **Bardoxolone** methyl in type 2 diabetes and stage 4 chronic kidney disease. (Beacon) N Engl J Med 2013. DOI: 10.1056/NEJMoa1306033.

Deeks ED. **Linagliptin**: a review of its use in the management of type 2 diabetes mellitus. Drugs. 2012 Sep 10;72(13):1793-824.

Dejgaard TF, Johansen NB, Frandsen CS, et al. Effects of **liraglutide** on cardiovascular risk factors in patients with **type 1 diabetes**. Diabetes Obes Metab. 2016 Dec 9.

Delahanty LM, Dalton KM, Porneala B, et al. Improving diabetes outcomes through **lifestyle change** - A randomized controlled trial. Obesity (Silver Spring). 2015 Sep;23(9):1792-1799.

Delea TE, Edelsberg JS, Hagiwara M, Oster G, Phillips LS. Use of **thiazolidinediones and risk of heart failure in people with type 2 diabetes**: a retrospective cohort study. Diabetes Care. 2003 Nov;26(11):2983-9.

Dempsey PC et al. Benefits for type 2 diabetes of interrupting **prolonged sitting** with brief bouts of **light walking** or **simple resistance** activities. Diabetes Care 2016 Jun; 39:964.

Denig P, Schuling J, Haaijer-Ruskamp F, et al. Effects of a **patient oriented decision aid** for prioritising treatment goals in diabetes: pragmatic randomised controlled trial. BMJ. 2014 Sep 25;349:g5651.

Dennis JM, Henley WE, Weedon MN, et al; MASTERMIND Consortium. **Sex and BMI Alter the Benefits and Risks of Sulfonylureas and Thiazolidinediones** in Type 2 Diabetes: A Framework for Evaluating Stratification Using Routine Clinical and Individual Trial Data. Diabetes Care. 2018 Aug 2.

Dennis JM, Shields BM, Henley WE, et al. Disease progression and treatment response in data-driven subgroups of type 2 diabetes compared with models based on simple clinical features: an analysis using clinical trial data. Lancet Diabetes Endocrinol. 2019 Apr 29.

Deprescribing Guideline and Algorithms (Benzodiazepine receptor agonits, Proton pump inhibitors, Antipsychotics, Antihyperglycemic) http://deprescribing.org/resources/deprescribing-guidelines-algorithms/

Desai Shrey; Brinker Allen; Swann Joslyn; et al. **Sitagliptin-Associated Drug Allergy**: Review of Spontaneous Adverse Event Reports Arch Intern Med. 2010;170(13):1169-1171.

Despres, JP, Golay A, Sjostrom L. Effects of **rimonabant** on metabolic risk factors in overweight patients with dyslipidemia (**Rio-Lipids**). N Engl J Med 2005;353:2121-34. (Weight loss: **6.7kg** at 1yr by repeated-measures method)

Devries JH, Bain SC, Rodbard HW, et al. Sequential Intensification of **Metformin Treatment in Type 2 Diabetes With Liraglutide Followed by Randomized Addition of Basal Insulin** (**detemir**) Prompted by A1C Targets. Diabetes Care. 2012 May 18.

Dhatariya K. Should **inpatient hyperglycaemia** be treated? BMJ. 2013 Jan 17;346:f134.

Dhatariya K, Bain SC, Buse JB, et al. The Impact of **Liraglutide** on Diabetes-Related Foot Ulceration and Associated Complications in Patients With Type 2 Diabetes at High Risk for Cardiovascular Events: Results From the LEADER Trial. Diabetes Care. 2018 Aug 2.

Dhulkotia JS, Ola B, Fraser R, et al. **Oral hypoglycemic agents vs insulin in management of gestational diabetes**: a systematic review and metaanalysis. Am J Obstet Gynecol. 2010 Nov;203(5):457.e1-9.

Diabetes Canada Clinical Practice Guidelines Expert Committee, Lipscombe L, Booth G, Butalia S, et al. **Pharmacologic Glycemic Management of Type 2 Diabetes in Adults. Can J Diabetes. 2018** Apr;42 Suppl 1:S88-S103.

Diabetes Canada Clinical Practice Guidelines Expert Committee, Ekoe JM, Goldenberg R, Katz P. **Screening for Diabetes in Adults**. Can J Diabetes. 2018 Apr;42 Suppl 1:S16-S19.

Diabetes Canada Clinical Practice Guidelines Expert Committee, Wherrett DK, Ho J, Huot C, Legault L, et al. **Type 1 Diabetes in Children and Adolescents**. Can J Diabetes. 2018 Apr;42 Suppl 1:S234-S246.

Diabetes Canada Clinical Practice Guidelines Expert Committee, Bebb R, Millar A, Brock G. **Sexual Dysfunction** and Hypogonadism in Men With Diabetes. Can J Diabetes. 2018 Apr;42 Suppl 1:S228-S233.

Diabetes Canada Clinical Practice Guidelines Expert Committee, Poirier P, Bertrand OF, Leipsic J, Mancini GBJ, Raggi P, Roussin A. **Screening for the Presence of Cardiovascular Disease**. Can J Diabetes. 2018 Apr;42 Suppl 1:S170-S177.

Diabetes Canada Clinical Practice Guidelines Expert Committee, Malcolm J, Halperin I, Miller DB, et al. **In-Hospital Management** of Diabetes. Can J Diabetes. 2018 Apr;42 Suppl 1:S115-S123.

Diabetes Canada Clinical Practice Guidelines Expert Committee, Imran SA, Agarwal G, et al. **Targets for Glycemic Control**. Can J Diabetes. 2018 Apr;42 Suppl 1:S42-S46.

Diabetes Canada Clinical Practice Guidelines Expert Committee, Lipscombe L, Booth G, Butalia S, et al. **Pharmacologic Glycemic Management** of Type 2 Diabetes in Adults. Can J Diabetes. 2018 Apr;42 Suppl 1:S88-S103.

Diabetes Canada Clinical Practice Guidelines Expert Committee, Yale JF, Paty B, Senior PA. **Hypoglycemia**. Can J Diabetes. 2018 Apr;42 Suppl 1:S104-S108.

Diabetes Canada Clinical Practice Guidelines Expert Committee, Sievenpiper JL, Chan CB, Dworatzek PD, Freeze C, Williams SL. **Nutrition Therapy**. Can J Diabetes. 2018 Apr;42 Suppl 1:S64-S79.

Diabetes Canada Clinical Practice Guidelines Expert Committee, Crowshoe L, Dannenbaum D, Green M, et al. Type 2 **Diabetes and Indigenous Peoples**. Can J Diabetes. 2018 Apr;42 Suppl 1:S296-S306.

Diabetes Canada Clinical Practice Guidelines Expert Committee, Meneilly GS, Knip A, Miller DB, Sherifali D, et al. **Diabetes in Older People**. Can J Diabetes. 2018 Apr;42 Suppl 1:S283-S295.

Diabetes Canada Clinical Practice Guidelines Expert Committee, Wharton S, Pedersen SD, Lau DCW, Sharma AM. **Weight Management** in Diabetes. Can J Diabetes. 2018 Apr;42 Suppl 1:S124-S129.

Diabetes Canada Clinical Practice Guidelines Expert Committee, Stone JA, Houlden RL, Lin P, et al. **Cardiovascular Protection** in People With Diabetes. Can J Diabetes. 2018 Apr;42 Suppl 1:S162-S169.

Diabetes Canada Clinical Practice Guidelines Expert Committee, Grossman LD, Roscoe R, Shack AR. **Complementary and Alternative Medicine** for Diabetes. Can J Diabetes. 2018 Apr;42 Suppl 1:S154-S161.

Diabetes Canada Clinical Practice Guidelines Expert Committee, Goguen J, Gilbert J. **Hyperglycemic Emergencies in Adults**. Can J Diabetes. 2018 Apr;42 Suppl 1:S109-S114.

Diabetes Canada Clinical Practice Guidelines Expert Committee, Senior PA, AlMehthel M, Miller A, Paty BW. **Diabetes and Transplantation**. Can J Diabetes. 2018 Apr;42 Suppl 1:S145-S149.

Diabetes Canada Clinical Practice Guidelines Expert Committee, Imran SA, Agarwal G, Bajaj HS, Ross S. **Targets for Glycemic Control.** Can J Diabetes. 2018 Apr;42 Suppl 1:S42-S46.

Diabetes Canada Clinical Practice Guidelines Expert Committee, Altomare F, Kherani A, Lovshin J. **Retinopathy.** Can J Diabetes. 2018 Apr;42 Suppl 1:S210-S216.

Diabetes Canada Clinical Practice Guidelines Expert Committee, Tardif JC, L'Allier PL, Fitchett DH. Management of **Acute Coronary Syndromes**. Can J Diabetes. 2018 Apr;42 Suppl 1:S190-S195.

Diabetes Canada Clinical Practice Guidelines Expert Committee, Sigal RJ, Armstrong MJ, Bacon SL, Boulé NG, Dasgupta K, Kenny GP, Riddell MC. **Physical Activity and Diabetes**. Can J Diabetes. 2018 Apr;42 Suppl 1:S54-S63.

Diabetes Canada Clinical Practice Guidelines Expert Committee, Berard LD, Siemens R, Woo V. Monitoring **Glycemic Control**. Can J Diabetes. 2018 Apr;42 Suppl 1:S47-S53.

Diabetes Canada Clinical Practice Guidelines Expert Committee, McFarlane P, Cherney D, Gilbert RE, Senior P. **Chronic Kidney Disease** in Diabetes. Can J Diabetes. 2018 Apr;42 Suppl 1:S201-S209.

Diabetes Canada Clinical Practice Guidelines Expert Committee, Altomare F, Kherani A, Lovshin J. **Retinopathy.** Can J Diabetes. 2018 Apr;42 Suppl 1:S210-S216.

Diabetes Canada Clinical Practice Guidelines Expert Committee, Bril V, Breiner A, Perkins BA, Zochodne D. **Neuropathy**. Can J Diabetes. 2018 Apr;42 Suppl1:S217-S221.

Diabetes Canada Clinical Practice Guidelines Expert Committee, McGibbon A, Adams L, Ingersoll K, Kader T, Tugwell B. **Glycemic Management in Adults With Type1 Diabetes**. Can J Diabetes. 2018 Apr;42 Suppl 1:S80-S87.

Diabetes Canada Clinical Practice Guidelines Expert Committee, Embil JM, Albalawi Z, Bowering K, Trepman E. **Foot Care.** Can J Diabetes. 2018 Apr;42 Suppl1:S222-S227.

Diabetes Canada Clinical Practice Guidelines Expert Committee, Houlden RL, Berard L, Lakoff JM, Woo V, Yale JF. **Diabetes and Driving**. Can J Diabetes. 2018 Apr;42 Suppl 1:S150-S153.

Diabetes Canada Clinical Practice Guidelines Expert Committee, Punthakee Z, Goldenberg R, Katz P. Definition, Classification and Diagnosis of Diabetes, **Prediabetes and Metabolic Syndrome**. Can J Diabetes. 2018 Apr;42 Suppl 1:S10-S15.

Diabetes Canada Clinical Practice Guidelines Expert Committee, Mancini GBJ, Hegele RA, Leiter LA. **Dyslipidemia**. Can J Diabetes. 2018 Apr;42 Suppl 1:S178-S185.

Diabetes Canada Clinical Practice Guidelines Expert Committee, Prebtani APH, Bajaj HS, Goldenberg R, Mullan Y. Reducing the Risk of Developing Diabetes. Can J Diabetes. 2018 Apr;42 Suppl 1:S20-S26.

Diabetes Canada Clinical Practice Guidelines Expert Committee, Feig DS, Berger H, Donovan L, Godbout A, Kader T, Keely E, Sanghera R. **Diabetes and Pregnancy.** Can J Diabetes. 2018 Apr;42 Suppl 1:S255-S282.

Diabetes Control and Complications Trial (**DCCT**)/Epidemiology of Diabetes Interventions and Complications (**EDIC**) Study Research Group. Intensive Diabetes Treatment and Cardiovascular Outcomes in Type 1 Diabetes: The DCCT/EDIC Study **30-Year Follow-up**. Diabetes Care. 2016 Feb 9.

Diabetes Prevention Program (**DPP**) Research Group. Long-term effects of **lifestyle intervention** or metformin on diabetes development and microvascular complications over 15-year follow-up: the **Diabetes Prevention Program** Outcomes Study. Lancet Diabetes Endocrinol. 2015 Sep 11.

Diabetes Prevention Program Research Group. Long-term effects of **lifestyle intervention or metformin** on diabetes development and microvascular omplications over 15-year follow-up: the Diabetes Prevention Program Outcomes Study. Lancet Diabetes Endocrinol. 2015 Sep 11.

Diabetes Prevention Program Research Group. Effects of withdrawal from metformin on the development of diabetes in the diabetes prevention program. Diabetes Care. 2003 Apr;26(4):977-80. The primary analysis of the DPP demonstrated that metformin decreased the risk of diabetes by 31%. The washout study shows that 26% of this effect can be accounted for by a pharmacological effect of metformin that did not persist when the drug was stopped. After the washout the incidence of diabetes was still reduced by 25%.) (Eddy DM, Schlessinger L, Kahn R. Clinical outcomes and cost-effectiveness of strategies for managing people at high risk for diabetes. Ann Intern Med. 2005 Aug 16;143(4):251-64. Summary for patients in: Ann Intern Med. 2005 Aug 16;143(4):I22.) (Lindstrom J, et al. Finnish Diabetes Prevention Study Group. (FDPS) Sustained reduction in the incidence of type 2 diabetes by lifestyle intervention: follow-up of the Finnish Diabetes Prevention Study. Lancet. 2006 Nov 11;368(9548):1673-9. (InfoPOEMs: Diet and exercise are effective in delaying the diagnosis of diabetes in patients at increased risk. (LOE = 2b))

Diabetes Prevention Program Research Group, Knowler WC, Fowler SE, Hamman RF, et al. 10-year follow-up of diabetes incidence and weight loss in the Diabetes Prevention Program Outcomes Study. Lancet. 2009 Nov 14;374(9702):1677-86.

Diabetes Prevention Program Research Group. Long-term **Effects of Metformin on Diabetes Prevention**: Identification of Subgroups That Benefited Most in the Diabetes Prevention Program and Diabetes Prevention Program Outcomes Study. Diabetes Care. 2019 Apr;42(4):601-608.

Diamant M et al. Safety and efficacy of **once-weekly exenatide compared with insulin glargine** titrated to target in patients with type 2 diabetes over 84 weeks. Diabetes Care [Epub ahead of print] 22 February 2012; doi:10.2337/dc11-1233.

Dicembrini I, Nreu B, Mannucci E, et al. Sodium-glucose co-transporter-2 **(SGLT-2) inhibitors and cancer**: A meta-analysis of randomized controlled trials. Diabetes Obes Metab. 2019 Apr 11.

Digman C, Klein AK, Pittas AG. Leukopenia and thrombocytopenia caused by **thiazolidinediones**. Ann Intern Med. 2005 Sep 20;143(6):465-6.

Dills DG, Schneider J. Clinical evaluation of **glimepiride versus glyburide in NIDDM in** a double-blind comparative study. Glimepiride/Glyburide Research Group. Horm Metab Res. 1996 Sep;28(9):426-9.

DiMeglio LA, Evans-Molina C, Oram RA. **Type 1 diabetes**. Lancet. 2018 Jun 16;391(10138):2449-2462.

Ding Y, Yao P, Li H, et al. Evaluation of **combined radiofrequency and chemical blockade of multi-segmental lumbar sympathetic ganglia** in painful diabetic peripheral neuropathy. J Pain Res. 2018 Jul 26;11:1375-1382.

Dipietro L, Gribok A, Stevens MS, et al. **Three 15-min Bouts of Moderate Postmeal Walking** Significantly Improves 24-h Glycemic Control in Older People at Risk for Impaired Glucose Tolerance. Diabetes Care. 2013 Jun 11.

Dixon JB, le Roux CW, Rubino F, Zimmet P. **Bariatric surgery** for type 2 diabetes. Lancet. 2012 Jun 8.

Diamant Michaela, Van Gaal Luc, Stranks Stephen, et al., Once **weekly exenatide** compared with insulin glargine titrated to target in patients with type 2 diabetes (**DURATION-3**): an open-label randomised trial, The Lancet, Volume 375, Issue 9733, 26 June 2010-2 July 2010

DiNicolantonio JJ, O'Keefe JH, Lucan SC. **Added Fructose**: A Principal Driver of Type 2 Diabetes Mellitus and Its Consequences. Mayo Clin Proc. 2015 Jan 26.

Dionne JM, Harris KC, Benoit G, et al. **Hypertension Canada's 2017 Guidelines for the Diagnosis, Assessment, Prevention, and Treatment of Pediatric Hypertension**. Can J Cardiol. 2017 May;33(5):577-585

DiPersio JF. **Diabetic stem-cell "mobilopathy"**. N Engl J Med. 2011 Dec 29;365(26):2536-8.

Dixon JB, O'Brien PE, Playfair J, et al. Adjustable **gastric banding** and conventional therapy for type 2 diabetes: a randomized controlled trial. JAMA. 2008 Jan 23;299(3):316-23. Participants randomized to surgical therapy were more likely to achieve remission of type 2 diabetes through greater weight loss.

Dobson R, Whittaker R, Jiang Y, et al. Effectiveness of **text message based, diabetes self management support programme** (**SMS4BG**): two arm, parallel randomised controlled trial. BMJ. 2018 May 17;361:k1959.

Dodd JM, Louise J, Deussen AR, et al. **Effect of metformin in addition to dietary and lifestyle advice for pregnant women who are overweight or obese**: the GRoW randomised, double-blind, placebo-controlled trial. Lancet Diabetes Endocrinol. 2018 Dec 4.

Doki K, Darwich AS, Achour B, et al.Implications of inter-correlation between hepatic **CYP3A4-CYP2C8** enzymes for the evaluation of drug-drug interactions: a case study with **repaglinide**. Br J Clin Pharmacol. 2018 Jan 30.

Donin AS, Nightingale CM, Owen CG, et al. **Regular Breakfast Consumption** and Type 2 Diabetes Risk Markers in 9- to 10-Year-Old Children in the Child Heart and Health Study in England (CHASE): A Cross-Sectional Analysis. PLoS Med. 2014 Sep 2;11(9):e1001703

Donnelly LA, Doney AS, Hattersley AT, Morris AD, Pearson ER. The effect of **obesity on glycaemic response** to metformin or sulphonylureas in Type 2 diabetes. Diabet Med. 2006 Feb;23(2):128-33.

Donner T, Muñoz M. **Update on insulin** therapy for type 2 diabetes. J Clin Endocrinol Metab. 2012 May;97(5):1405-13.

Donovan L, Hartling L, Muise M, et al. **Screening tests for gestational diabetes**: a systematic review for the u.s. Preventive services task force (USPSTF). Ann Intern Med. 2013 Jul 16;159(2):115-22. The OGCT and fasting plasma glucose level (at a threshold of 4.7 mmol/L [85 mg/dL]) by 24 weeks' gestation are good at identifying women who do not have GDM. The OGCT is better at identifying women who have GDM. The OGCT has not been validated for the IADPSG diagnostic criteria.

Dormandy JA, Charbonnel B, Eckland DJ, et al. PROactive investigators. Secondary prevention of macrovascular events in patients with type 2 diabetes in the PROactive Study (PROspective pioglitAzone Clinical Trial In macroVascular Events): a randomised controlled trial. (**PROACIVE**) Lancet. 2005 Oct 8;366(9493):1279-89. (Jarvinen H. The PROactive study: some answers, many questions. -**more heart failures, weight gain & more edema**. Lancet. 2005 Oct 8;366(9493):1241-2.) INTERPRETATION: Pioglitazone reduces the composite of all-cause mortality, non-fatal myocardial infarction, and stroke in patients with type 2 diabetes who have a high risk of macrovascular events. (**n=5328 34.5months** follow-up, Pioglitazone vs placebo, primary endpoint not significant, secondary endpoint of composite of all-cause mortality, non-fatal MI & stroke was 11.6 vs 13.6%, more to hospital with heart failure 6 vs 4%, 22% vs 13% edema, weight gain ↑ 3.6kg vs 0.4kg decrease) (InfoPOEMs: In patients with type 2 diabetes and comorbid macrovascular disease, 3 years of intensive diabetes care using pioglitazone did not significantly prevent further complications or mortality compared with placebo. (LOE = 1b))
Wilcox R, Kupfer S, and Erdmann E. Effects of pioglitazone on major adverse cardiovascular events in high-risk patients with type 2 diabetes: Results from Prospective Pioglitazone Clinical Trial in Macrovascular Events (**PROactive 10**). Am Heart J 2008; DOI:10.1016/j.ahj.2007.11.029 In patients with advanced type 2 diabetes at high risk for cardiovascular events, pioglitazone treatment resulted in significant risk reductions in MACE composite end points to 3 years.

Dormuth CR, Carney G, Carleton B, et al. Thiazolidinediones and **fractures in men and women**. *Arch Intern Med*. 2009; 169:1395-1402.

Dou J;Ma J;Liu J;et al. Efficacy and safety of **saxagliptin in combination with metformin** as initial therapy in Chinese patients with type 2 diabetes: Results from the START study, a multicentre, randomized, double-blind, active-controlled, phase 3 trial. Diabetes Obes Metab. 2017 Sep 19.

Douglas IJ, Evans SJ, Pocock S, Smeeth L. The risk of **fractures associated with thiazolidinediones**: a self-controlled case-series study. PLoS Med. 2009 Sep;6(9):e1000154. Epub 2009 Sep 29.

Douros A, Dell'Aniello S, Yu OHY, Filion KB, Azoulay L, Suissa S. **Sulfonylureas as second line drugs in type 2 diabetes** and the risk of cardiovascular and hypoglycaemic events: population based cohort study. BMJ 2018;362:k2693.

Douros A, Yin H, Yu OHY, et al. Pharmacologic **Differences of Sulfonylureas and the Risk of Adverse Cardiovascular and Hypoglycemic Events**. Diabetes Care. 2017 Sep 1.

DREAM (Diabetes REduction Assessment with ramipril and rosiglitazone Medication) Trial Investigators; Gerstein HC, et al. Effect of **rosiglitazone** on the frequency of diabetes in patients with impaired glucose tolerance or impaired fasting glucose: a randomised controlled trial. Lancet. 2006 Sep 23;368(9541):1096-105. Cardiovascular event rates were much the same in both groups, although 14 (0.5%) participants in the rosiglitazone group and two (0.1%) in the placebo group developed heart failure (p=0.01). (InfoPOEMs: Patients at increased risk of developing diabetes were less likely to develop diabetes if taking rosiglitazone (Avandia) than if given a placebo. We don't know how well rosiglitazone compares with other interventions also known to delay diabetes: diet and exercise, metformin, or acarbose. We also don't know if clinically relevant outcomes are improved. (LOE = 1b));
(Montori VM, Isley WL, Guyatt GH. Waking up from the DREAM of preventing diabetes with drugs. BMJ. 2007 Apr 28;334(7599):882-4.)
(Nathan DM, Berkwits M. Trials that matter: rosiglitazone, ramipril, and the prevention of type 2 diabetes. Ann Intern Med. 2007 Mar 20;146(6):461-3.)

Driessen JH, de Vries F, van Onzenoort H, et al. The use of **incretins and fractures** - a meta-analysis on population-based real life data. Br J Clin Pharmacol. 2016 Oct 25.

Drouin-Chartier JP, Zheng Y, Li Y, et al. Changes in **Consumption of Sugary Beverages and Artificially Sweetened Beverages** and Subsequent Risk of Type 2 Diabetes: Results From Three Large Prospective U.S. Cohorts of Women and Men. Diabetes Care. 2019 Oct 3. doi: 10.2337/dc19-0734

Drucker DJ, et al. The incretin system: **glucagon-like peptide-1 receptor agonists** and **dipeptidyl peptidase-4 inhibitors** in type 2 diabetes. Lancet. 2006 Nov 11;368(9548):1696-705. (eg. exenatide, liraglutide, sitagliptin, vildagliptin)

Du H, Li L, Bennett D, et al. **Fresh fruit consumption** in relation to incident diabetes and diabetic vascular complications: A 7-y prospective study of 0.5 million Chinese adults. PLoS Med. 2017 Apr 11;14(4):e1002279.

Du J, Liang L, Fang H, et al. Efficacy and safety of **saxagliptin compared with acarbose** in Chinese patients with type 2 diabetes mellitus uncontrolled on metformin monotherapy: Results of a Phase IV open-label randomized controlled study (the **SMART** study). Diabetes Obes Metab. 2017 Mar 14.

Du YT, Rayner CK, Jones KL, et al. **Gastrointestinal Symptoms in Diabetes**: Prevalence, Assessment, Pathogenesis, and Management. Diabetes Care. 2018 Mar;41(3):627-637.

Duan-Porter W, Goldstein KM, McDuffie JR, et al. Reporting of **Sex Effects** by Systematic Reviews on Interventions for Depression, Diabetes, and Chronic Pain. Ann Intern Med. 2016 Aug 2;165(3):184-93

Duckworth W, Abraira C, Moritz T, et al. Glucose Control and Vascular Complications in Veterans with Type 2 Diabetes. N Engl J Med. 2008 Dec 17. (**VADT** study) Intensive glucose control in patients with poorly controlled type 2 diabetes had no significant effect on the rates of major cardiovascular events, death, or microvascular complications.

Dumville JC, Deshpande S, O`Meara S, et al. **Foam dressings for healing diabetic foot ulcers**. Cochrane Database Syst Rev. 2011 Sep 7;9:CD009111. Currently there is no research evidence to suggest that foam wound dressings are more effective in healing foot ulcers in people with diabetes than other types of dressing however all trials in this field are very small.

Dumville JC, Deshpande S, O`Meara S, et al. **Hydrocolloid dressings** for healing **diabetic foot ulcers**. Cochrane Database Syst Rev. 2012 Feb 15;2:CD009099. Currently there is no research evidence to suggest that any type of hydrocolloid wound dressing is more effective in healing diabetic foot ulcers than other types of dressing.

Dumville JC, Hinchliffe RJ, Cullum N, et al. **Negative pressure wound therapy** for treating foot wounds in people with diabetes mellitus. Cochrane Database Syst Rev. 2013 Oct 17;10:CD010318. There is some evidence to suggest that negative pressure wound therapy is more effective in healing post-operative foot wounds and ulcers of the foot in people with DM compared with moist wound dressings. However, these findings are uncertain due to the possible risk of bias in the original studies.

Dumville JC, Lipsky BA, Hoey C, et al. **Topical antimicrobial agents for treating foot ulcers in people with diabetes**. Cochrane Database Syst Rev. 2017 Jun 14;6:CD011038. The randomised controlled trial data on the effectiveness and safety of topical antimicrobial treatments for diabetic foot ulcers is limited by the availability of relatively few, mostly small, and often poorly designed trials. Based on our systematic review and analysis of the literature, we suggest that: 1) use of an antimicrobial dressing instead of a non-antimicrobial dressing may increase the number of diabetic foot ulcers healed over a medium-term follow-up period (low-certainty evidence); and 2) there is probably little difference in the risk of adverse events related to treatment between systemic antibiotics and topical antimicrobial treatments based on the available studies (moderate-certainty evidence). For each of the other outcomes we examined there were either no reported data or the available data left us uncertain as to whether or not there were any differences between the compared treatments. Given the high, and increasing, frequency of diabetic foot wounds, we encourage investigators to undertake properly designed randomised controlled trials in this area to evaluate the effects of topical antimicrobial treatments for both the prevention and the treatment of infection in these wounds and ultimately the effects on wound healing.

Duncan GE. Prevalence of diabetes and impaired fasting glucose levels among **US adolescents**: National Health and Nutrition Examination Survey, 1999-2002. Arch Pediatr Adolesc Med. 2006 May;160(5):523-8.

Dungan KM, Povedano ST, Forst T, et al. Once-weekly dulaglutide versus once-daily liraglutide in metformin-treated patients with type 2 diabetes (AWARD-6): a randomised, open-label, phase 3, non-inferiority trial. Lancet 2014; online July 11.

Dungan KM, Povedano ST, Forst T, et al. Once-weekly **dulaglutide versus once-daily liraglutide** in metformin-treated patients with type 2 diabetes (AWARD-6): a randomised, open-label, phase 3, non-inferiority trial. Lancet 2014; 384: 1349–57.

Dungan KM, Raz I, Skrivanek Z, et al. Achieving the composite endpoint of glycated haemoglobin <7.0%, no weight gain and no hypoglycaemia in the once-weekly **dulaglutide AWARD** programme. Diabetes Obes Metab. 2015 Sep 12.

Dungan KM, Weitgasser R, Perez Manghi F, et al. A 24-week Study to Evaluate the Efficacy and Safety of Once Weekly **Dulaglutide** Added on to **Glimepiride** in Type 2 Diabetes (AWARD-8). Diabetes Obes Metab. 2016 Jan 22.

Dunkler D, Dehghan M, Teo KKet al. **Diet and Kidney Disease** in High-Risk Individuals With Type 2 Diabetes Mellitus. JAMA Intern Med. 2013 Aug 12.

Dunlay SM, Givertz MM, Aguilar D, et al. Type 2 Diabetes Mellitus **and Heart Failure**, A Scientific Statement From the American Heart Association and Heart Failure Society of America. J Card Fail. 2019 Jun 3.

Dunseath GJ, Bright D, Jones C, et al. Performance evaluation of a **self-administered home oral glucose tolerance test kit** in a controlled clinical research setting. Diabet Med. 2019 Apr 10.

Dunstan DW, Kingwell BA, Larsen R, et al. Breaking up **prolonged sitting** reduces postprandial glucose and insulin responses. Diabetes Care. 2012 May;35(5):976-83.

Durso SC. Using clinical guidelines designed for **older adults** with diabetes mellitus and complex health status. JAMA. 2006 Apr 26;295(16):1935-40.

Duvivier BM, Schaper NC, Hesselink MK, et al. Breaking sitting with **light activities vs structured exercise**: a randomised crossover study demonstrating benefits for glycaemic control and insulin sensitivity in type 2 diabetes. Diabetologia. 2016 Dec 1.

Eakin EG, Winkler EA, Dunstan DW, et al. Living Well With Diabetes: 24-Month Outcomes From a Randomized Trial of **Telephone-Delivered Weight Loss and Physical Activity Intervention** to Improve Glycemic Control. Diabetes Care. 2014 Mar 21.

Echouffo-Tcheugui JB, Simmons RK, Prevost AT, et al. Long-term effect of **population screening** for diabetes on cardiovascular morbidity, self-rated health, and health behavior. Ann Fam Med. 2015 Mar;13(2):149-57.

Eckel RH, et al. Preventing **cardiovascular risk and diabetes**. A call to action from the American Diabetes Association and the American Heart Association. Circulation 2006; DOI: 10.1161/CIRCULATIONAHA.106.176583. http://www.circulationaha.org

Eckel RH, Henry RR, Yue P, et al. Effect of **Ranolazine** Monotherapy on Glycemic Control in Subjects With Type 2 Diabetes. Diabetes Care. 2015 Jun 6.

Edelman S, et al. A double-blind, placebo-controlled trial assessing **pramlintide** treatment in the setting of intensive insulin therapy in type 1 diabetes. Diabetes Care. 2006 Oct;29(10):2189-95.

Edelman SV, Liu R, Johnson J, et al. **AUTONOMY**: The First Randomized Trial Comparing Two Patient-Driven Approaches to Initiate and Titrate **Prandial Insulin Lispro** in Type 2 Diabetes. Diabetes Care. 2014 Aug;37(8):2132-40.

Edmonds M, et al. **Sucrose octasulfate dressing** versus control dressing in patients with neuroischaemic diabetic foot ulcers (**Explorer**): an international, multicentre, double-blind, randomised, controlled trial. Lancet Diabetes Endocrinol 2017; online Dec 20.

Edwards J, Stapley S. **Debridement of diabetic foot ulcers**. Cochrane Database Syst Rev. 2010 Jan 20;(1):CD003556. There is evidence to suggest that hydrogel increases the healing rate of diabetic foot ulcers compared with gauze dressings or standard care and larval therapy resulted in significantly greater reduction in wound area than hydrogel.

Egan AG, Blind E, Dunder K, et al. **Pancreatic safety of incretin-based drugs**--FDA and EMA assessment. N Engl J Med. 2014 Feb 27;370(9):794-7.

Egi M, Finfer S, Bellomo R. **Glycemic control in the ICU**. Chest. 2011 Jul;140(1):212-20.

Ehrlich SF, Hedderson MM, Xu F, Ferrara A. **Diagnostic thresholds for pregnancy hyperglycemia**, maternal weight status and the risk of childhood obesity in a diverse Northern California cohort using health care delivery system data. PLoS One. 2019 May 10;14(5):e0216897.

Ehrmann DA. **Polycystic ovary** syndrome. N Engl J Med. 2005 Mar 24;352(12):1223-36.

Ekström N, Schiöler L, Svensson AM, et al. Effectiveness and safety of **metformin** in 51 675 patients with type 2 diabetes and different levels of **renal function**: a cohort study from the Swedish National Diabetes Register. BMJ Open. 2012 Jul 13;2(4).

Ekström N, Svensson AM, Miftaraj M, Franzén et al. Cardiovascular safety of glucose-lowering agents as **add-on medication to metformin** treatment in type 2 diabetes: report from the Swedish National Diabetes Register. Diabetes Obes Metab. 2016 Jun 10.

El-Khatib FH, Balliro C, Hillard MA, et al. Home use of a **bihormonal bionic pancreas versus insulin pump therapy** in adults with type 1 diabetes: a multicentre randomised crossover trial. Lancet. 2016 Dec 20

El Messaoudi S, Nederlof R, Zuurbier CJ, et al. Effect of **metformin pretreatment on myocardial injury during coronary artery bypass surgery** in patients without diabetes (**MetCAB**): a double-blind, randomised controlled trial. Lancet Diabetes Endocrinol. 2015 Aug;3(8):615-623.

Elashoff M, Matveyenko AV, Gier B, Elashoff R, Butler PC. **Pancreatitis, pancreatic, and thyroid cancer** with glucagon-like peptide-1-based therapies (**sitagliptin, exenatide**). Gastroenterology. 2011 Jul;141(1):150-6.

Elder DA, Herbers PM, Weis T et al. **β-cell Dysfunction in Adolescents** and **Adults** with Newly Diagnosed Type 2 Diabetes Mellitus. J Pediatr. 2012 Jan 10.

Ellis K, Mulnier H, Forbes A. Perceptions of insulin use in type 2 diabetes in primary care: a thematic synthesis. BMC Fam Pract. 2018 May 22;19(1):70.

EMA July/11 The European Medicines Agency (EMA) has reached a decision:pioglitazone (Actos, Takeda), opting to recommend new contraindications & warnings be added to the drug label, noting that there is a small increased risk of bladder cancer.

Emerging Risk Factors Collaboration, Diabetes mellitus, **fasting blood glucose** concentration, & risk of vascular disease: a collaborative meta-analysis of 102 prospective studies, Lancet, Volume 375, Issue 9733, 26 June 2010-2 July 2010, Pages 2215-2222.

Emerging Risk Factors Collaboration. Diabetes Mellitus, Fasting Glucose, and Risk of Cause-Specific Death. N Engl J Med 2011; 364:829-841.

Eng C, Kramer CK, Zinman B, Retnakaran R. **Glucagon-like peptide-1 receptor agonist and basal insulin combination** treatment for the management of type 2 diabetes: a systematic review and meta-analysis. Lancet 2014; online Sept 12. http://dx.doi.org/10.1016/S0140-6736(14)61335-0.

Engebretson SP, Hyman LG, Michalowicz BS, et al. The effect of nonsurgical **periodontal therapy** on hemoglobin A1c levels in persons with type 2 diabetes and chronic periodontitis: a randomized clinical trial. JAMA. 2013 Dec 18;310(23):2523-32

Engen Hanem LG, Stridsklev S, Júlíusson PB, et al. **Metformin use in PCOS** pregnancies increases the risk of offspring overweight at 4 years of age; follow-up of two RCTs. J Clin Endocrinol Metab. 2018 Feb 27.

ERBP: Guideline development group. Clinical Practice Guideline on management of patients with **diabetes and chronic kidney disease stage 3b or higher** (eGFR <45 mL/min). Nephrol Dial Transplant. 2015 May;30 Suppl 2:ii1-142.

Eskicioglu P, Halas J, Sénéchal M, et al. **Peer Mentoring** for Type 2 Diabetes Prevention in First Nations Children. Pediatrics. 2014 May 12.

Esposito K., Maiorino M. I., Ciotola M., et al. Effects of a **Mediterranean-Style Diet** on the Need for Antihyperglycemic Drug Therapy in Patients With Newly Diagnosed Type 2 Diabetes: A Randomized Trial. Ann Intern Med 2009; 306-314.

Esposito K, Maiorino MI, Petrizzo M, et al. The Effects of a **Mediterranean Diet** on Need for Diabetes Drugs and Remission of Newly Diagnosed Type 2 Diabetes: Follow-up of a Randomized Trial. Diabetes Care. 2014 Apr 10.

*Esposito K, Maiorino MI, Petrizzo M, et al. The Effects of a **Mediterranean Diet on Need** for **Diabetes Drugs** and Remission of Newly Diagnosed Type 2 Diabetes: Follow-up of a Randomized Trial. Diabetes Care. 2014 Apr 10.*

Eurich DT, Majumdar SR, McAlister FA, Tsuyuki RT, Johnson JA. Improved clinical outcomes associated with **metformin** in patients with diabetes and **heart failure**. Diabetes Care. 2005 Oct;28(10):2345-51.

Eurich DT, McAlister FA, Blackburn DF, Majumdar SR, Tsuyuki RT, Varney J, Johnson JA. Benefits and harms of antidiabetic agents in patients with diabetes and heart failure: systematic review. BMJ. 2007 Aug 30; [Epub ahead of print] **Metformin was the only** antidiabetic agent not associated with harm in patients with heart failure and diabetes. It was associated with reduced all cause mortality in two of the three studies.

Eurich DT, Simpson S, Senthilselvan A, et al. **Comparative safety and effectiveness of sitagliptin** in patients with type 2 diabetes: retrospective population based cohort study. BMJ. 2013 Apr 25;346:f2267.

Evans JR, Michelessi M, Virgili G. Laser photocoagulation for proliferative **diabetic retinopathy**. Cochrane Database of Systematic Reviews 2014, Issue 11. Art. No.: CD011234. DOI: 10.1002/14651858.CD011234.pub2. This review provides evidence that laser photocoagulation is beneficial in treating proliferative diabetic retinopathy. We judged the evidence to be moderate or low, depending on the outcome. This is partly related to reporting of trials conducted many years ago, after which panretinal photocoagulation has become the mainstay of treatment of proliferative diabetic retinopathy. Future Cochrane Reviews on variations in the laser treatment protocol are planned. Future research on laser photocoagulation should investigate the combination of laser photocoagulation with newer treatments such as anti-vascular endothelial growth factors (anti- VEGFs).

Evans V, Roderick P, Pollock AM. Adequacy of clinical trial evidence of **metformin fixed-dose combinations** for the treatment of type 2 diabetes mellitus in India. BMJ Glob Health. 2018 Mar 6;3(2):e000263.

Even JL, Crosby CG, Song Y, McGirt MJ, Devin CJ. Effects of **epidural steroid injections** on blood glucose levels in patients with diabetes mellitus. Spine (Phila Pa 1976). 2012 Jan 1;37(1):E46-50.

Everett BM, Donath MY, Pradhan AD, et al. Anti-Inflammatory Therapy With **Canakinumab for the Prevention and Management of Diabetes**. J Am Coll Cardiol. 2018 May 29;71(21):2392-2401.

Evert AB, Boucher JL, Cypress M, et al. **Nutrition Therapy** Recommendations for the Management of Adults With Diabetes. Diabetes Care. 2013 Oct 9.

Evert AB, Dennison M, Gardner CD, et al. **Nutrition Therapy** for Adults With Diabetes or Prediabetes: A Consensus Report. Diabetes Care. 2019 May;42(5):731-754.

Exalto LG, Biessels GJ, Karter AJ, et al. Risk score for prediction of 10 year dementia risk in individuals with type 2 diabetes: a cohort study. Lancet Diabetes Endocrinol. 2013 Nov;1(3):183-90.

Fadini GP, et al. Intraclass differences in the risk of hospitalization for **heart failure among patients with type 2 diabetes initiating a dipeptidyl peptidase-4 inhibitor or sulphonylurea**: Results from **OsMed Health-DB registry**. Diabetes Obes Metab. 2017Apr 21.

Fadini GP;Bonora BM;Mayur S;et al. **Dipeptidyl peptidase-4 inhibitors moderate the risk of genitourinary tract infections associated with sodium-glucose co-transporter-2 inhibitors**. Diabetes Obes Metab. 2017 Oct 20.

Fadini GP, Frison V, Simioni N, et al. **Changes in the Prescription of Glucose-Lowering Medications** in Patients With Type 2 Diabetes Mellitus After a Cardiovascular Event: A Call to Action From the DATAFILE Study. J Am Heart Assoc. 2019 Jul 16;8(14):e012244.

Fagherazzi G, Gusto G, Clavel-Chapelon F, et al. **ABO and Rhesus blood groups** and risk of type 2 diabetes: evidence from the large E3N cohort study. Diabetologia. 2014 Dec 23.

Faillie JL, Yu OH, Yin H, et al. Association of **Bile Duct and Gallbladder Diseases With the Use of Incretin-Based Drugs** in Patients With Type 2 Diabetes Mellitus. JAMA Intern Med. 2016 Aug 1

Falk J, Friesen KJ, Okunnu A, et al. Patterns, Policy and Appropriateness: A 12-Year Utilization Review of **Blood Glucose Test Strip Use** in Insulin Users. Can J Diabetes. 2017 Apr 11.

Fang R, Deng X **Electronic messaging intervention** for management of cardiovascular risk factors in type 2 diabetes mellitus: A randomised controlled trial**.** J Clin Nurs. 2017 Jul 12.

Farias JM, Tinetti M, Khoury M, et al. Low **Testosterone Concentration and Atherosclerotic Disease** Markers in Male Patients With Type 2 Diabetes. J Clin Endocrinol Metab. 2014 Oct 16

Farmer A, Wade A, Goyder E, et al. Impact of **self-monitoring of blood glucose** in the management of patients with non-insulin treated diabetes: open parallel group randomised trial. BMJ 2007; DOI: 10.1136/bmj.39247.447431. Evidence is not convincing of an effect of self monitoring blood glucose, with or without instruction in incorporating findings into self care, in improving glycaemic control compared with usual care in reasonably well controlled non-insulin treated patients with type 2 diabetes. (see also Pharmacist's Letter Sept 2007) (Peel E, Douglas M, Lawton J. Self monitoring of blood glucose in type 2 diabetes: longitudinal qualitative study of patients' perspectives. BMJ. 2007 Sep 8;335(7618):493. Epub 2007 Aug 30.)

O'Kane MJ, Bunting B, Copeland M, Coates VE; on behalf of the **ESMON** study group. Efficacy of self monitoring of blood glucose in patients with newly diagnosed type 2 diabetes (ESMON study): randomised controlled trial. BMJ. 2008 Apr 17; [Epub ahead of print] In patients with newly diagnosed type 2 diabetes self monitoring of blood glucose concentration has no effect on glycaemic control but is associated with higher scores on a depression subscale. Simon J, Gray A, Clarke P, Wade A, Neil A, Farmer A; on behalf of the Diabetes Glycaemic Education and Monitoring Trial Group. Cost effectiveness of self monitoring of blood glucose in patients with non-insulin treated type 2 diabetes: economic evaluation of data from the **DiGEM** trial. BMJ. 2008 Apr 17; [Epub ahead of print] Self monitoring of blood glucose with or without additional training in incorporating the results into self care was associated with higher costs and lower quality of life in patients with non-insulin treated type 2 diabetes. In light of this, and no clinically significant differences in other outcomes, self monitoring of blood glucose is unlikely to be cost effective in addition to standardised usual care.

Gomes, Tara, Juurlink, David N, Shah, Baiju R, et al. Blood glucose test strips: options to reduce usage. CMAJ 2009 0: cmaj.091017.

Cameron, Chris, Coyle, Doug, Ur, Ehud, Klarenbach, Scott. Cost-effectiveness of self-monitoring of blood glucose in patients with type 2 diabetes mellitus managed without insulin. CMAJ 2009 0: cmaj.090765.

Gomes T, Martins D, Tadrous M, et al. Association of a **Blood Glucose Test Strip Quantity-Limit Policy** With Patient Outcomes: A Population-Based Study. JAMA Intern Med. 2016 Nov 7

Farmer AJ, Perera R, Ward A, et al. Meta-analysis of individual patient data in randomised trials of self monitoring of blood glucose (**SMBG**) in people with non-insulin treated type 2 diabetes. BMJ. 2012 Feb 27;344:e486.

Farmer A. Use of **HbA1c in the diagnosis of diabetes**. BMJ. 2012 Nov 1;345:e7293.

Farid D, Rosenberg E, and Bartlett G. Importance of education in managing type 2 diabetes during **Ramadan**. Canadian Family Physician 60.6 (2014): 508-510.

Farkouh ME et al. for the **FREEDOM** Trial Investigators. Strategies for multivessel revascularization in patients with diabetes. N Engl J Med 2012 Nov 4; [e-pub ahead of print]. (**CABG** vs PCI)

Farrar D, Simmonds M, Bryant M, et al. **Hyperglycaemia and risk of adverse perinatal outcomes**: systematic review and meta-analysis. BMJ. 2016 Sep 13;354:i4694

Farrell B, Black C, Thompson W, et al. **Deprescribing antihyperglycemic agents** in older persons: Evidence-based clinical practice guideline. Can Fam Physician. 2017 Nov;63(11):832-843.

Farren M, Daly N, McKeating A, et al. The Prevention of Gestational Diabetes Mellitus With **Antenatal Oral Inositol Supplementation**: A Randomized Controlled Trial. Diabetes Care. 2017 Mar 21.

Faruque LI, Wiebe N, Ehteshami-Afshar A, et al. Effect of **telemedicine on glycated hemoglobin** in diabetes: a systematic review and meta-analysis of randomized trials. CMAJ. 2016 Oct 31.

Faurschou M, Ahlstrom MG, Lindhardsen J, et al. Risk of Diabetes Mellitus among Patients Diagnosed with **Giant Cell Arteritis or Granulomatosis with Polyangiitis**: Comparison with the General Population. J Rheumatol. 2016 Oct 15.

Fayehun AF, Olowookere OO, Ogunbode AM, et al. **Walking prescription** of 10 000 steps per day in patients with type 2 diabetes mellitus: a randomised trial in Nigerian general practice. Br J Gen Pract. 2018 Feb;68(667):e139-e145.

Fazeli Farsani S, Souverein PC, et al. **Long term trends in oral antidiabetic drug use** among **children and adolescents** in the Netherlands. Br J Clin Pharmacol. 2015 Feb 12.

FDA Aug/09 Patients with diabetes who take therapeutic products containing nonglucose sugars (e.g., **peritoneal dialysis solution and some immunoglobulins**) can have falsely elevated readings from blood glucose test strips that use glucose dehydrogenase pyrroloquinoline quinone (**GDH-PQQ**) technology, according to an FDA public health notification. The strips are in wide use, and we have provided a link to a listing of the affected products. The FDA cites 13 deaths associated with hypoglycemia not detected by the test strips, which cannot distinguish between lucose and other sugars such as maltose and xylose. Ten patients were receiving icodextrin peritoneal dialysis solution. The FDA advises physicians to avoid using GDH-PQQ test strips in health care facilities and to rely, instead, on laboratory assays of glucose — especially in patients taking the therapeutic products listed in the alert. Interfering products containing nonglucose sugars include icodextrin peritoneal dialysis solution, certain immunoglobulins, abatacept (Orencia, Bristol-Myers Squibb), tositumomab (Bexxar, GlaxoSmithKline), and any product containing or metabolized into maltose, galactose, or xylose. Several test strips and associated monitors use GDH-PQQ methodology:

ACCU-CHEK (Roche), FreeStyle (Abbott Diabetes Care), TRUEtest (Home Diagnostics), CoZmonitor blood glucose module (for use with the Deltec Cozmo insulin pump, Smiths Medical MD), and OmniPod insulin management system (Insulet).

FDA Sep/10 & Takeda, conducted a planned analysis of the study data at the five-year mark, and submitted their results to FDA. Overall, there was no statistically significant association between **Actos exposure and bladder cancer risk**. However, further analyses were also performed looking at how long patients were on Actos and the total amount of the drug they received during that time. An increased risk of bladder cancer was observed among patients with the longest exposure to Actos, as well as in those exposed to the highest cumulative dose of Actos. FDA notified healthcare professionals and patients that the Agency is reviewing data from an ongoing, ten-year epidemiological study designed to evaluate whether Actos (pioglitazone) is associated with an increased risk of bladder cancer.

FDA May/11 Updated risk evaluation and mitigation strategy **(REMS) to restrict access to rosiglitazone**-containing medicines including Avandia, Avandamet, and Avandaryl. May 18, 2011. http://www.fda.gov/Drugs/DrugSafety/ucm255005.htm

FDA June/11 **Victoza** (liraglutide [rDNA origin]) Injection: REMS - Risk of **Thyroid C-cell Tumors, Acute Pancreatitis**. http://www.fda.gov/Safety/MedWatch/SafetyInformation/SafetyAlertsforHumanMedicalProducts/ucm258826.htm

FDA June/11 drug safety communication: Update to ongoing safety review of **Actos (pioglitazone) and increased risk of bladder cancer**- use for more than 12 months linked to an increased risk of bladder cancer. http://www.fda.gov/Drugs/DrugSafety/ucm259150.htm

FDA Mar/13 is evaluating unpublished new findings by a group of academic researchers that suggest an increased risk of **pancreatitis and pre-cancerous cellular** changes called pancreatic duct metaplasia in patients with type 2 diabetes treated with a class of drugs called incretin mimetics **(glucagonlike peptide-1 (GLP-1) agonists and the DPP-4 inhibitors, or "gliptins**). These findings were based on examination of a small number of pancreatic tissue specimens taken from patients after they died from unspecified causes.

FDA Aug/13 Nova Diabetes Care initiated a **voluntary recall of 21 lots of the Nova Max Glucose Test Strips** distributed both in the USA and outside the continental USA.

FDA May/15 is warning that the type 2 diabetes medicines **canagliflozin**, **dapagliflozin**, and **empagliflozin** may lead to **ketoacidosis**, a serious condition where the body produces high levels of blood acids called ketones that may require hospitalization. FDA is continuing to investigate this safety issue and will determine whether changes are needed in the prescribing information for this class of drugs, called sodium-glucose cotransporter-2 (SGLT2) inhibitors.

FDA Aug/15 The U.S. Food and Drug Administration (FDA) is warning that the type 2 diabetes medicines **sitagliptin, saxagliptin, linagliptin, and alogliptin** may cause joint pain that can be severe and disabling **joint pain**.

FDA Sep/15 The U.S. Food and Drug Administration (FDA) has strengthened the warning for the type 2 diabetes medicine **canagliflozin (Invokana, Invokamet)** related to the increased risk of bone fractures and added new information about **decreased bone mineral density**.

FDA Dec/15 safety review has resulted in adding warnings to the labels of a specific class of type 2 diabetes medicines called **sodium-glucose cotransporter-2 (SGLT2) inhibitors** about the risks of too much **acid in the blood and of serious urinary tract infections**.

FDA Dec/15 is **eliminating the Risk Evaluation and Mitigation Strategy (REMS) for rosiglitazone**-containing type 2 diabetes medicines, which are approved as Avandia, Avandamet, Avandaryl, and generics.
The REMS is no longer necessary to ensure that the benefits of rosiglitazone medicines outweigh their risks.

FDA Apr/16 safety review has found that type 2 diabetes medicines containing **saxagliptin and alogliptin** may increase the risk of **heart failure**, particularly in patients who already have heart or kidney disease.

FDA Apr/16 is also requiring manufacturers to revise the labeling to recommend that the measure of **kidney function** used to determine whether a patient can receive **metformin** be changed from one based on a single laboratory parameter (blood creatinine concentration) to one that provides a better estimate of renal function (i.e., glomerular filtration rate estimating equation (eGFR)). Metformin is contraindicated in patients with an eGFR below 30 mL/minute/1.73 m2.

FDA Apr/16 **Dexcom** Inc. is recalling the **Continuous Glucose Monitoring Systems** because the audible alarm may not activate in the receiver piece when low or high glucose levels (hypoglycemia or hyperglycemia) are detected. Relying on this product for notification of low or high blood sugar could result in serious adverse consequences, including death as the auditory alarm may not sound and users might not be notified of low or high blood sugar.

FDA June/16 has strengthened the existing warning about the risk of **acute kidney injury** for the type 2 diabetes medicines **canagliflozin** (Invokana, Invokamet) and **dapagliflozin** (Farxiga, Xigduo XR). Based on recent reports, we have revised the warnings in the drug labels to include information about acute kidney injury and added recommendations to minimize this risk.

FDA Dec/16: As a result of an updated review, the FDA has concluded that use of the type 2 diabetes medicine **pioglitazone** (Actos, Actoplus Met, Actoplus Met XR, Duetact, Oseni) may be linked to an **increased risk of bladder cancer**.

FDA May/17: Based on new data from two large clinical trials, the FDA has concluded that the type 2 diabetes medicine **canagliflozin** (Invokana, Invokamet, Invokamet XR) causes an **increased risk of leg and foot amputations**. FDA is requiring new warnings, including the most prominent Boxed Warning, to be added to the canagliflozin drug labels to describe this risk.

FDA Aug/18: is warning that cases of a rare but serious infection of the genitals and area around the genitals have been reported with the class of type 2 diabetes medicines called sodium-glucose cotransporter-2 (SGLT2) inhibitors. This serious rare infection, called necrotizing fasciitis of the perineum, is also referred to as Fournier's gangrene.

Fedewa MV, Gist NH, Evans EM, Dishman RK. **Exercise and Insulin Resistance in Youth**: A Meta-Analysis. Pediatrics. 2013 Dec 2.

Fedorko L et al. **Hyperbaric oxygen** therapy does not reduce indications for amputation in patients with diabetes with nonhealing ulcers of the lower limb: A prospective, double-blind, randomized controlled clinical trial. Diabetes Care 2016 Mar; 39:392.

Feghali MN, Scifres CM. **Novel therapies for diabetes** mellitus **in pregnancy**. BMJ. 2018 Jul 16;362:k2034.

Feig DS, Donovan LE, Corcoy R, et al, on behalf of the **CONCEPTT** Collaborative Group. **Continuous glucose monitoring in pregnant women** with type 1 diabetes (CONCEPTT): a multicentre international randomised controlled trial. Lancet 2017; online Sept 15

Feig DS, Donovan LE, Corcoy R, et al. **Continuous glucose monitoring** in women with **type 1 diabetes in pregnancy** (**CONCEPTT**): a multicentre international randomised controlled trial. Lancet 2017. doi:S0140-6736(17)32400-5.

Feldman AL, Griffin SJ, Ahern AL, et al. Impact of **weight maintenance** and loss on diabetes risk and burden: a population-based study in 33,184 participants. BMC Public Health. 2017 Feb 6;17(1):170.

Fenger M, Hansen DL, Worm D, et al. **Gastric bypass surgery** reveals independency of obesity and diabetes mellitus type 2. BMC Endocr Disord. 2016 Nov 9;16(1):59.

Ferdinand KC, Izzo JL, Lee J, et al. **Antihyperglycemic and Blood Pressure Effects of Empagliflozin** in Black Patients With Type 2 Diabetes Mellitus and Hypertension. Circulation. 2019 Apr 30;139(18):2098-2109.

Fernández A, Quan J, Moffet H, et al. **Adherence** to newly prescribed diabetes medications among **insured Latino and white patients** with diabetes [online Jan 23, 2017].JAMA Intern Med. doi:10 .1001/jamainternmed.2016.8653

Ferrannini E, Ramos SJ, Salsali A, et al. **Dapagliflozin** monotherapy in type 2 diabetic patients with inadequate glycemic control by diet and exercise: a randomized, double-blind, placebo-controlled, phase 3 trial. Diabetes Care. 2010 Oct;33(10):2217-24.

Ferrannini E. The **target of metformin** in type 2 diabetes. N Engl J Med. 2014 Oct 16;371(16):1547-8.

Ferrannini E, DeFronzo RA. Impact of **glucose-lowering drugs on cardiovascular disease** in type 2 diabetes. Eur Heart J. 2015 Sep 7;36(34):2288-96.

Ferrannini E, Mark M, Mayoux E. CV Protection in the **EMPA-REG OUTCOME Trial**: A "Thrifty Substrate" Hypothesis. Diabetes Care. 2016 Jul;39(7):1108-14.

Filion KB, Azoulay L, Platt RW, et al; **CNODES** Investigators. A Multicenter Observational Study of **Incretin-based Drugs and Heart Failure**. N Engl J Med. 2016 Mar 24;374(12):1145-54.

Filion KB, Douros A, Azoulay L, et al. **Sulfonylureas** as Initial Treatment for Type 2 Diabetes and the **Risk of Adverse Cardiovascular Events**: A Population-based Cohort Study. Br J Clin Pharmacol. 2019 Jul 5.

Finne P, Groop PH, Arffman M, et al. Cumulative **Risk of End-Stage Renal Disease** Among Patients With Type 2 Diabetes: A Nationwide Inception Cohort Study. Diabetes Care. 2019 Jan 28.

Finne P, Reunanen A, Stenman S, Groop PH, Gronhagen-Riska C. Incidence of end-stage **renal disease** in patients with type 1 diabetes. JAMA. 2005 Oct 12;294(14):1782-7. CONCLUSIONS: With regard to ESRD, the prognosis of type 1 diabetes has improved during the past 4 decades. Children diagnosed as having diabetes before age 5 years have the most favorable prognosis. Overall, incidence of ESRD appears to be lower than previously estimated.

Finucane MM, Stevens GA, Cowan MJ. **National, regional, and global trends in body-mass index since 1980**: systematic analysis of health examination surveys and epidemiological studies with 960 country-years and 9.1 million participants. Lancet 2011; DOI: 10.1016/S0140-6736(10)62035-5.

Fioretto P, Del Prato S, Buse JB, et al; DERIVE Study Investigators. Efficacy and Safety of **Dapagliflozin in Patients with Type 2 Diabetes** and Moderate **Renal Impairment** (Chronic Kidney Disease Stage 3A): The **DERIVE Study**. Diabetes Obes Metab. 2018 Jun 11.

Fioretto P, Zambon A, Rossato M, et al. **SGLT2 Inhibitors and the Diabetic Kidney**. Diabetes Care. 2016 Aug;39 Suppl 2:S165-71.

Fischer HH, Fischer IP, Pereira RI, et al. **Text Message Support for Weight Loss** in Patients With Prediabetes: A Randomized Clinical Trial. Diabetes Care. 2016 Feb 9.

Fitchett D, Zinman B, Wanner C, et al. Heart failure outcomes with **empagliflozin** in patients with type 2 diabetes at high cardiovascular risk: results of the **EMPA-REG OUTCOME**(R) trial. Eur Heart J. 2016 Jan 26.

Fitchett D, Cheng A, Connelly K, et al. A Practical Guide to the Use of **Glucose-Lowering Agents With Cardiovascular Benefit or Proven Safety**. Can J Cardiol. 2017 Jul;33(7):940-942.

Fitchett D, Butler J, van de Borne P, et al. Effects of **empagliflozin** on risk for cardiovascular death and **heart failure** hospitalization across the spectrum of heart failure risk in the **EMPA-REG OUTCOME**® trial. Eur Heart J. 2017 Aug 28.

Fitchett D, Inzucchi SE, Lachin JM, et al; **EMPA-REG** OUTCOME Investigators. **Cardiovascular Mortality Reduction** With **Empagliflozin** in Patients With Type 2 Diabetes and Cardiovascular Disease. J Am Coll Cardiol. 2018 Jan 23;71(3):364-367.

Fitzgerald E, Mathieu S, Ball A. Metformin associated **lactic acidosis**. BMJ. 2009 Sep 16;339:b3660. doi: 10.1136/bmj.b3660.

Fitzpatrick SL, Golden SH, Stewart K, et al. Effect of **DECIDE** (**Decision-making Education** for Choices In Diabetes Everyday) Program Delivery Modalities on Clinical and Behavioral Outcomes in Urban African Americans With Type 2 Diabetes: A Randomized Trial. Diabetes Care. 2016 Dec;39(12):2149-2157.

FLAT-SUGAR Trial Investigators. Glucose Variability in a 26-Week Randomized Comparison of Mealtime Treatment With **Rapid-Acting Insulin Versus GLP-1 Agonist** in Participants With Type 2 Diabetes at High Cardiovascular Risk. Diabetes Care. 2016 Jun;39(6):973-81.

Flory J, Lipska K. **Metformin in 2019**. JAMA. 2019 Apr 22.

Flory JH, Hennessy S. **Metformin Use Reduction in Mild to Moderate Renal Impairment**: Possible Inappropriate Curbing of Use Based on Food and Drug Administration Contraindications. JAMA Intern Med. 2015 Jan 5.

Flory J. Will **Cardiovascular Outcomes** Data on **Newer Diabetes Drugs** Bury the Older Agents? JAMA Intern Med. 2017 Jan 17.

Fonseca VA, Lavery LA, Thethi TK, et al. **Metanx** (L-methylfolate, methylcobalamin, and pyridoxal-5`-phosphate) in Type 2 Diabetes with Peripheral Neuropathy: A Randomized Trial. Am J Med. 2012 Dec 5. pii: S0002-9343(12)00586-4.

Fonseca V, McDuffie R, Calles J, et al. Determinants of **weight gain** in the Action to Control Cardiovascular Risk in Diabetes (Acord) trial.Diabetes Care 2013 .

Fortmann AL, Gallo LC, Garcia MI, et al. Dulce Digital: An mHealth SMS-Based Intervention Improves Glycemic Control in Hispanics With Type 2 Diabetes. Diabetes Care. 2017 Jun 9.

Forouhi NG, Misra A, Mohan V, et al. **Dietary and nutritional approaches for prevention and management of type 2 diabetes**. BMJ. 2018 Jun 13;361:k2234.

Fottrell E, Ahmed N, Morrison J, et al. **Community groups or mobile phone messaging to prevent and control type 2 diabetes** and intermediate hyperglycaemia in Bangladesh (DMagic): a cluster-randomised controlled trial. Lancet Diabetes Endocrinol. 2019 Mar;7(3):200-212.

Fouqueray P, Pirags V, Diamant M, et al. The Efficacy and Safety of Imeglimin as Add-on Therapy in Patients With Type 2 Diabetes Inadequately Controlled With Sitagliptin Monotherapy. Diabetes Care. 2014 Apr 10.

Foushee JA, Goodbar NH, Kelly JL, et al. Cerebrovascular Accident in a High-Risk Patient During the Early Initiation Phase With **Canagliflozin**. Ann Pharmacother. 2014 Apr 16;48(8):1066-1069.

Fox CS, Golden SH, Anderson C, et al. Update on **Prevention of Cardiovascular Disease in Adults With Type 2 Diabetes Mellitus** in Light of Recent Evidence: A Scientific Statement From the American Heart Association (AHA) and the American Diabetes Association (ADA). Diabetes Care. 2015 Aug 5.

Fralick M, Kim SC, Schneeweiss S, et al. **Fracture risk after initiation of use of canagliflozin**. A multidatabase cohort study. Ann Intern Med. 2018. [Epub ahead of print]. doi:10.7326/M18-0567

Franco OH, de Laet C, Peeters A, Jonker J, Mackenbach J, Nusselder W. Effects of **physical activity** on life expectancy with cardiovascular disease. Arch Intern Med. 2005 Nov 14;165(20):2355-60.

Franciosi M, Lucisano G, Pellegrini F, et al. ROSES Study Group. Role of **self-monitoring of blood glucose** and intensive education in patients with Type 2 diabetes not receiving insulin. A pilot randomized clinical trial. Diabet Med. 2011 Jul;28(7):789-96.

Franks, Paul W., Hanson, Robert L., Knowler, William C., et al. **Childhood Obesity**, Other Cardiovascular Risk Factors, and **Premature Death**. N Engl J Med 2010 362: 485-493.

Frid A, Hirsch L, Gaspar R, et al. Scientific Advisory Board for the Third Injection Technique Workshop. **New injection recommendations for patients with diabetes**. Diabetes Metab. 2010 Sep;36 Suppl 1:S3-18.

Frei A, Senn O, Chmiel C, et al. Implementation of the **Chronic Care Model** in Small Medical Practices Improves Cardiovascular Risk But Not Glycemic Control. Diabetes Care. 2014 Feb 10.

Forster DA, Moorhead AM, et al. Advising women with **diabetes in pregnancy to express breastmilk in late pregnancy** (Diabetes and Antenatal Milk Expressing [**DAME**]): a multicentre, unblinded, randomized controlled trial. Lancet 2017; 389: 2204–13.

Forst T, Guthrie R, Goldenberg R, et al. Efficacy and safety of **canagliflozin** over 52 weeks in patients with type 2 diabetes on background metformin and pioglitazone. Diabetes Obes Metab. 2014 Feb 15.

Fournier JP, Yin H, Yu OH, et al. **Metformin and low levels of thyroid-stimulating hormone** in patients with type 2 diabetes mellitus. CMAJ. 2014 Sep 22.

Fox CS, et al. Trends in the Incidence of **Type 2 Diabetes Mellitus From the 1970s to the 1990s.** The Framingham Heart Study. Circulation. 2006 Jun 19; [Epub ahead of print]

Fox CS. **Weighty** Matters: Balancing Weight Gain with Cardiovascular Risk among Patients with Type 1 Diabetes Mellitus on Intensive **Insulin** Therapy. Circulation. 2013 Jan 15;127(2):157-9.

Fralick M, Schneeweiss S, Patorno E. **Risk of Diabetic Ketoacidosis** after Initiation of an **SGLT2 Inhibitor**. N Engl J Med. 2017 Jun 8;376(23):2300-2302.

Franciosi M, Lucisano G, Lapice E, et al. **Metformin therapy and risk of cancer** in patients with type 2 diabetes: systematic review. PLoS One. 2013 Aug 2;8(8):e71583.

Franco M, Bilal U, Urduñez P, et al. **Population-wide weight loss and regain in relation to diabetes** burden and cardiovascular mortality in Cuba 1980-2010: repeated cross sectional surveys and ecological comparison of secular trends. BMJ 2013;346:f1515.

Franks AS, Lee PH, George CM. **Pancreatitis**: a potential complication of **liraglutide**? Ann Pharmacother. 2012 Nov;46(11):1547-53.

Frederiksen B, Kroehl M, Lamb MM, et al. **Infant Exposures and Development of Type 1 Diabetes** Mellitus: The Diabetes Autoimmunity Study in the Young (DAISY). JAMA Pediatr. 2013 Jul 8. These results suggest the safest age to introduce solid foods in children at increased genetic risk for T1DM is between 4 and 5 months of age. Breastfeeding while introducing new foods may reduce T1DM risk.

Frias JP, Nauck MA, Van J, et al. Efficacy and safety of **LY3298176, a novel dual GIP and GLP-1 receptor agonist, in patients with type 2 diabetes**: a randomised, placebo-controlled and active comparator-controlled phase 2 trial. Lancet. 2018 Oct 3. pii: S0140-6736(18)32260-8.

Frias JP, Zimmer Z, Lam RLH, et al. Double-blind, randomized clinical trial assessing the **efficacy and safety of early initiation of sitagliptin during metformin uptitration** in the treatment of patients with type 2 diabetes: The CompoSIT-M study. Diabetes Obes Metab. 2019 Jan 4.

Frid AH, Kreugel G, Grassi G, et al. **New Insulin Delivery Recommendations**. Mayo Clin Proc. 2016 Sep;91(9):1231-55.

Friis AM, Johnson MH, Cutfield RG, et al. **Kindness Matters**: A Randomized Controlled Trial of a Mindful Self-Compassion Intervention Improves Depression, Distress, and HbA1c Among Patients With Diabetes. Diabetes Care. 2016 Jun 22.

Frosch DL, Uy V, Ochoa S, Mangione CM. Evaluation of a **behavior support intervention** for patients with poorly controlled diabetes [published online October 10, 2011]. Arch Intern Med. doi:10.1001/archinternmed.2011.497.

Frøssing S, Nylander M, Chabanova E, et al. Effect of **liraglutide** on ectopic fat in **polycystic ovary syndrome**: A randomized clinical trial. Diabetes Obes Metab. 2017 Jul 6.

Fu AZ, Johnston SS, Ghannam A, et al. Association Between Hospitalization for **Heart Failure and Dipeptidyl Peptidase-4 Inhibitors** in Patients With Type 2 Diabetes: An Observational Study. Diabetes Care. 2016 Jan 6.

Fukuoka Y, Gay CL, Joiner KL, Vittinghoff E. A Novel **Diabetes Prevention Intervention Using a Mobile App**: A Randomized Controlled Trial With Overweight Adults at Risk. Am J Prev Med. 2015 May 29.

Fuller NR, Sainsbury A, Caterson ID, et al. Effect of a **high-egg diet on cardiometabolic risk factors in people with type 2 diabetes**: the Diabetes and Egg (DIABEGG) Study-randomized weight-loss and follow-up phase. Am J Clin Nutr. 2018 May 7.

Fullerton B, Jeitler K, Seitz M, et al. **Intensive glucose control versus conventional glucose control for type 1 diabetes** mellitus. Cochrane Database Syst Rev. 2014 Feb 14;2:CD009122. Tight blood sugar control reduces the risk of developing microvascular diabetes complications. The evidence of benefit is mainly from studies in younger patients at early stages of the disease. Benefits need to be weighed against risks including severe hypoglycaemia, and patient training is an important aspect in practice. The effects of tight blood sugar control seem to become weaker once complications have been manifested. However, further research is needed on this issue. Furthermore, there is a lack of evidence from RCTs on the effects of tight blood sugar control in older patient populations or patients with macrovascular disease. There is no firm evidence for specific blood glucose targets and treatment goals need to be individualised taking into account age, disease progression, macrovascular risk, as well as the patient's lifestyle and disease management capabilities.

Fullerton B, Siebenhofer A, Jeitler K, et al. **Short-acting insulin analogues versus regular human insulin** for adult, non-pregnant persons with type 2 diabetes mellitus. Cochrane Database Syst Rev. 2018 Dec 17;12:CD013228.
Our analysis found no clear benefits of short-acting insulin analogues over regular human insulin in people with type 2 diabetes. Overall, the certainty of the evidence was poor and results on patient-relevant outcomes, like all-cause mortality, microvascular or macrovascular complications and severe hypoglycaemic episodes were sparse.

Funch D, Mortimer K, Ziyadeh NJ, et al. **Liraglutide use** and evaluation of pancreatic outcomes in a US commercially insured population. Diabetes Obes Metab. 2019 Apr 4.

Furie KL, Viscoli CM, Gorman M, et al; **IRIS** Trial Investigators. Effects of **pioglitazone on cognitive function** in patients with a recent ischaemic stroke or TIA: a report from the IRIS trial. J Neurol Neurosurg Psychiatry. 2017 Sep 22.

Furler J, O'Neal D, Speight J, et al. **Supporting insulin initiation** in type 2 diabetes in primary care:results of the Stepping Up pragmatic cluster randomized controlled clinical trial. BMJ. 2017 Mar 8;356:j783.

Furmli S, Elmasry R, Ramos M, Fung J. **Therapeutic use of intermittent fasting for people with type 2 diabetes as an alternative to insulin**. BMJ Case Rep. 2018 Oct 9;2018. pii: bcr-2017-221854.

Furtado RHM, Bonaca MP, Raz I, et al. **Dapagliflozin and Cardiovascular Outcomes** in Patients With Type 2 Diabetes Mellitus and Previous Myocardial Infarction. Circulation. 2019 May 28;139(22):2516-2527.

Gabel K, Kroeger CM, Trepanowski JF, et al. Differential Effects of **Alternate-Day Fasting Versus Daily Calorie Restriction on Insulin Resistance**. Obesity (Silver Spring). 2019 Jul 22.

Gæde P, Oellgaard J, Carstensen B, et al. **Years of life gained** by multifactorial intervention in patients with type 2 diabetes mellitus and **microalbuminuria**: 21 years follow-up on the **Steno-2** randomised trial. Diabetologia. 2016 Aug 16.

Gagnum V, Stene LC, Jenssen TG, et al. Causes of **death in childhood-onset Type 1 diabetes**: long-term follow-up. Diabet Med. 2016 Mar 21.

Gagnum V, Stene LC, Leivestad T, et al. Long-term **Mortality** and End-Stage **Renal Disease** in **a Type 1 Diabetes** Population Diagnosed at Age 15-29 Years in **Norway**. Diabetes Care. 2017 Jan;40(1):38-45.

Gagnum V, Saeed M, Stene LC, et al. **Low Incidence of End-Stage Renal Disease in Childhood-Onset Type 1 Diabetes Followed for Up to 42 Years**. Diabetes Care. 2017 Oct 12.

Ganie MA, Khurana ML, Nisar S, et al. Improved Efficacy of Low-Dose **Spironolactone and Metformin** Combination Than Either Drug Alone in the Management of Women With Polycystic Ovary Syndrome (PCOS): A Six-Month, Open-Label Randomized Study. J Clin Endocrinol Metab. 2013 Sep;98(9):3599-607.

Galaviz KI, Weber MB, Straus A, et al. Global Diabetes Prevention Interventions: A Systematic Review and Network Meta-analysis of the **Real-World Impact on Incidence, Weight, and Glucose**. Diabetes Care. 2018 Jul;41(7):1526-1534.

Gallo S, Charbonnel B, Goldman A, et al. **Long-term efficacy and safety of ertugliflozin in patients with type 2 diabetes** mellitus inadequately controlled with metformin monotherapy: 104-week VERTIS MET trial. Diabetes Obes Metab. 2019 Jan 7.

Gallwitz B, Guzman J, Dotta F, et al. **Exenatide twice daily versus glimepiride** for prevention of glycaemic deterioration in patients with type 2 diabetes with metformin failure (**EUREXA**): an open-label, randomised controlled trial. Lancet 2012; online June 9.

Gallwitz B, Rosenstock J, Rauch J, et al. **Two-year efficacy and safety of linagliptin compared with glimepiride** in patients with type 2 diabetes inadequately controlled **on metformin**: a randomized, double-blind, noninferiority trial. Lancet 2012.

Gamble JM, Clarke A, Myers KJ, et al. **Incretin-based medications** for type 2 diabetes: an overview of reviews. Diabetes Obes Metab. 2015 Jul;17(7):649-58.

Gamble J-M, Chibrikov E, Twells LK, et al. Association of **insulin dosage with mortality** or major adverse cardiovascular events: a retrospective cohort study. Lancet Diabetes Endocrinol 2016; online Nov 16.

Gamble JM, et al. Examining the risk of **depression or self-harm** associated with **incretin-based therapies** used to manage hyperglycaemia in patients with type 2 diabetes: a cohort study using the UK Clinical Practice Research Datalink. BMJ Open. 2018 Oct 8;8(10):e023830.

Ganie MA, Khurana ML, Nisar S, et al. Improved Efficacy of Low-Dose **Spironolactone and Metformin** Combination Than Either Drug Alone in the Management of Women With Polycystic Ovary Syndrome (PCOS): A Six-Month, Open-Label Randomized Study.

J Clin Endocrinol Metab. 2013 Sep;98(9):3599-607.
Gantz I, Okamoto T, Ito Y, et al. A randomized, placebo- and **sitagliptin**-controlled trial of the safety and efficacy of **omarigliptin**, a once-weekly dipeptidyl peptidase-4 inhibitor, in Japanese patients with type 2 diabetes. Diabetes Obes Metab. 2017 Apr 27.
Garber A et al. **Liraglutide** versus glimepiride monotherapy for type 2 diabetes (**LEAD-3 Mono**): A randomised, 52-week, phase III, double-blind, parallel-treatment trial. Lancet 2009 Feb 7; 373:473.
Garber AJ, Abrahamson MJ, Barzilay JI, et al. **AACE** Comprehensive **Diabetes Management Algorithm** 2013. Endocr Pract. 2013 Mar-Apr;19(2):327-36.
Garber AJ, Abrahamson MJ, Barzilay JI, et al. Consensus statement by the **American Associations of Clinical Endocrinologists and American College of Endocrinology** on the **Comprehensive type 2 Diabetes Management Algorithm-2016** Executive Summary Endocr Pract. 2016 Jan;22(1):84-113.
Garber AJ, Abrahamson MJ, Barzilay JI, et al. CONSENSUS STATEMENT BY THE AMERICAN ASSOCIATION OF CLINICAL ENDOCRINOLOGISTS (AACE) AND AMERICAN COLLEGE OF ENDOCRINOLOGY (ACE) ON THE **COMPREHENSIVE TYPE 2 DIABETES MANAGEMENT ALGORITHM - 2019 EXECUTIVE SUMMARY**. Endocr Pract. 2019 Jan;25(1):69-100.
Garber AJ, et al. Consensus Statement: **American Association of Clinical Endocrinologits and American Collge of Endocrinology** on the **Comprehensive Type 2 Diabetes Mangaement Algorithm- 2017** Executive Summary. Endocr Pract. 2017 Jan 17.
Garber AJ, et al. **AACE-ACE-Consensus** statement-American Assoc Clinical Endocrinologists and College of Endocrinology-**Comprehensive Type 2 Diabetes Management Algorithm 2018** Executive Summary. Endocr Pract. 2018 Jan;24(1):91-120.
Gardner C, Wylie-Rosett J, Gidding SS, et al. **Nonnutritive sweeteners**: Current use and health perspectives. A scientific statement from the American Heart Association and the American Diabetes Association. Circulation 2012; 126:509-519. (Aspartame, acesulfame-K, neotame, saccharin, and sucralose)
Garg R, Chen W, Pendergrass M. Acute **pancreatitis** in type 2 diabetes treated with **exenatide or sitagliptin**: a retrospective observational pharmacy claims analysis. Diabetes Care. 2010 Nov;33(11):2349-54. Epub 2010 Aug 3.
Garg SK, Henry RR, Banks P, et al. Effects of **sotagliflozin** added to insulin in patients with type 1 diabetes. (**inTandem3**) N Engl J Med. DOI: 10.1056/NEJMoa1708337.
Garrison A. Screening, Diagnosis, and Management of **Gestational Diabetes** Mellitus. Am Fam Physician. 2015 Apr 1;91(7):460-467.
Garvey WT, Ryan DH, Henry R, et al. **Prevention of type 2 diabetes** in subjects with prediabetes and metabolic syndrome treated with phentermine and **topiramate** extended release. Diabetes Care. 2014 Apr;37(4):912-21.
Gazzina S, Alberici A, Padovani A, et al. **Myoclonic dystonia (DYT11) responsive to insulin therapy**: A case report. Neurology. 2017 Aug 1;89(5):517-518.
Gee BT, Nansel TR, Liu A. **Reduction of hypoglycaemic events with a behavioural intervention**: a randomized clinical trial for paediatric patients with Type 1 diabetes mellitus. Diabet Med. 2017 Mar;34(3):340-347.
Gegick C, Altheimer M. Comparison of effect of **thiazolidinediones on cardiovascular risk factors**: observations from a clinical practice. Endocr Pract 2001;7:162-169.
Geijselaers SL, Sep SJ, Stehouwer CD, et al. Glucose regulation, **cognition, and brain MRI** in type 2 diabetes: a systematic review. Lancet Diabetes Endocrinol. 2014 Aug 22.
Geiss LS, Wang J, Cheng YJ, et al. **Prevalence and incidence trends for diagnosed diabetes among adults aged 20 to 79 years, United States, 1980-2012**. JAMA. 2014 Sep 24;312(12):1218 26.
Gellad WF, Zhao X, Thorpe CT, et al. Dual Use of Department of Veterans Affairs and Medicare Benefits and Use of **Test Strips** in Veterans With Type 2 Diabetes Mellitus. JAMA Intern Med. 2014 Nov 10.
Geller AI, Shehab N, Lovegrove MC, et al. National estimates of **insulin-related hypoglycaemia** and errors leading to emergency department visits and hospitalizations [online March 10, 2014]. JAMA Intern Med. 2013.
Geldsetzer P, Manne-Goehler J, Theilmann M, et al. **Diabetes and hypertension in India**: a nationally representative study of 1.3 million adults [online Jan 29, 2018].JAMA Intern Med. doi:10.1001/jamainternmed.2017.8094
Genest J, McPherson R, Frohlich J, et al. **2009 Canadian** Cardiovascular Society/Canadian guidelines for the diagnosis and treatment of dyslipidemia and prevention of cardiovascular disease in the adult - 2009 recommendations. Can J Cardiol. 2009 Oct;25(10):567-79.
Geng DF, Jin DM, Wu W, Liang YD, Wang JF. Angiotensin converting enzyme inhibitors for **prevention of new-onset type 2 diabetes mellitus**: A meta-analysis of 72,128 patients. Int J Cardiol. 2012 Jul 16.
George CM, Will K, Howard-Thompson A. Management of **blood glucose with noninsulin therapies** in type 2 diabets. Am Fam Physician. 2015 Jul 1;92(1):2734.
Georgianos PI, Agarwal R. **Ambulatory Blood Pressure Reduction With SGLT-2 Inhibitors**: Dose-Response Meta-analysis and Comparative Evaluation With Low-Dose Hydrochlorothiazide. Diabetes Care. 2019 Apr;42(4):693-700.
Gepner Y, Golan R, Harman-Boehm I, et al. Effects of Initiating **Moderate Alcohol Intake** on Cardiometabolic Risk in Adults With Type 2 Diabetes: A 2-Year Randomized, Controlled Trial. Ann Intern Med. 2015 Oct 13.
Gerich J, Raskin P, Jean-Louis L, Purkayastha D, Baron MA. PRESERVE-beta: two-year efficacy and safety of initial combination therapy with **nateglinide** or glyburide **plus metformin**. Diabetes Care. 2005 Sep;28(9):2093-9.
Gerstein HC, Colhoun HM, Dagenais GR, et al. **Dulaglutide and cardiovascular outcomes** in type 2 diabetes (**REWIND):** a double-blind, randomised placebo-controlled trial. Lancet 2019; online June 10. http://dx.doi.org/10.1016/S0140-6736(19)31149-3.
Gerstein HC, Colhoun HM, Dagenais GR, et al. **Dulaglutide and renal outcomes** in type 2 diabetes: an exploratory analysis of the **REWIND** randomised, placebo-controlled trial. Lancet 2019; online June 10. http://dx.doi.org/10.1016/S0140-6736(19)31150-X.
Gerstein HC, Ratner RE, Cannon CP, et al. the **APPROACH** Study Group. Effect of Rosiglitazone on Progression of Coronary Atherosclerosis in Patients With Type 2 Diabetes Mellitus and Coronary Artery Disease. The Assessment on the Prevention of Progression by **Rosiglitazone** on Atherosclerosis in Diabetes Patients With Cardiovascular History Trial. Circulation. 2010 Mar 1
Gerstein HC, Miller ME, Ismail-Beigi F, et al, for the **ACCORD** Study Group. Effects of **intensive glycaemic control** on **ischaemic heart disease**: analysis of data from the randomised, controlled ACCORD trial. Lancet 2014; online Aug 1.
Gerstein HC, et al; **ORIGIN** Investigators. Effect of **Basal Insulin Glargine on First and Recurrent Episodes of Heart Failure Hospitalization**: The ORIGIN Trial (Outcome Reduction With Initial Glargine Intervention). Circulation. 2018 Jan 2;137(1):88-90.
Gibb FW, Teoh WL, Graham J, et al. Risk of death following admission to a UK hospital with **diabetic ketoacidosis**. Diabetologia. 2016 Jul 11.
Gibson DM. Estimates of the Percentage of US Adults With Diabetes Who Could Be **Screened for Diabetic Retinopathy** in Primary Care Settings. JAMA Ophthalmol. 2019 Jan 31.
Gilbert MP, Bain SC, Franek E, ET AL; and the LEADER Publication Committee on behalf of the **LEADER** Trial Investigators**. Effect of Liraglutide** on Cardiovascular Outcomes in Elderly Patients: A Post Hoc Analysis of a Randomized Controlled Trial. Ann Intern Med. 2018 Dec 4.
Gillett M, Royle P, Snaith A, et al. **Non-pharmacological interventions** to **reduce the risk of diabetes** in people with impaired glucose regulation: a systematic review and economic evaluation. Health Technol Assess. 2012 Aug;16(33):1-236, iii-iv.
Gillies CL, Abrams KR, et al. **Pharmacological and lifestyle interventions to prevent or delay type 2 diabetes** in people with impaired glucose tolerance: systematic review and meta-analysis. BMJ. 2007 Jan 19; [Epub ahead of print] Lifestyle and pharmacological interventions reduce the rate of progression to type 2 diabetes in people with impaired glucose tolerance. Lifestyle interventions seem to be at least as effective as drug treatment. (InfoPOEMs: Diet, exercise, or diet and exercise changes, at least those in study situations, will slow the progression of diabetes by approximately 50% in patients with impaired glucose tolerance. Drug therapy with either oral diabetes drugs or the weight loss drug orlistat (Xenical) will also slow progression. The preventive effect of the drugs is not maintained when they are stopped, and research has not been conducted for long enough to determine whether diabetes onset is prevented or just delayed. (LOE = 1a))
Gilbert C, Valois M, Koren G. **Pregnancy** outcome after first-trimester exposure to **metformin**: a meta-analysis. Fertil Steril. 2006 Sep;86(3):658-63. Epub 2006 Jul 31. On the basis of the limited data available today, there is no evidence of an increased risk for major malformations when metformin is taken during the first trimester of pregnancy. Large studies are needed to corroborate these preliminary results.
Gilbert RE, Krum H. **Heart failure in diabetes**: effects of anti-hyperglycaemic drug therapy. Lancet. 2015 May 23;385(9982):2107-17.
Gilbert-Ouimet M, Ma H, Glazier R, et al. Adverse effect of **long work hours on incident diabetes in 7065 Ontario workers** followed for 12 years. BMJ Open Diabetes Res Care. 2018 Jul 2;6(1):e000496.
Gilsanz P, Albers K, Beeri MS, et al. **Traumatic brain injury associated with dementia risk** among people with type 1 diabetes. Neurology. 2018 Oct 3; 91(17):e1611-e1618.
Gilstrap LG, Chernew ME, Nguyen CA, et al. Association Between Clinical Practice Group **Adherence to Quality Measures and Adverse Outcomes** Among Adult Patients With Diabetes. JAMA Netw Open. 2019 Aug 2;2(8):e199139.
Gin H;Rorive M;Gautier S;Condomines M;Saint Aroman. Treatment by a moisturizer of **xerosis** and cracks of the feet in men and women with diabetes: a randomized, double-blind, placebo-controlled study. Diabet Med. 2017 Sep;34(9):1309-1317.
Giorgino F, Benroubi M, Sun JH, et al. Efficacy and Safety of Once-Weekly **Dulaglutide Versus Insulin Glargine** in Patients With Type 2 Diabetes on **Metformin and Glimepiride** (**AWARD-2**). Diabetes Care. 2015 Jun 18.
Giovannucci, Edward, Harlan, David M., Archer, Michael C., et al. **Diabetes and Cancer**: A Consensus Report. CA Cancer J Clin 2010 0: caac.20078.
Giugliano D, Maiorino MI, Bellastella G, et al. GLP-1 receptor agonists for **prevention of cardiorenal outcomes** in type 2 diabetes: An updated meta-analysis including the REWIND and PIONEER 6 trials. Diabetes Obes Metab. 2019 Aug 2.
Given JE, Loane M, Garne E, et al. **Metformin exposure in first trimester of pregnancy** and risk of all or specific **congenital anomalies**: exploratory case-control study. BMJ. 2018 Jun 25;361:k2477.
Glatstein MM, Djokanovic N, Garcia-Bournissen F, Finkelstein Y, Koren G. Use of **hypoglycemic drugs during lactation**. Can Fam Physician. 2009 Apr;55(4):371-3.
Glueck CJ, Salehi M, Sieve L, Wang P. Growth, motor, and social development in **breast- and formula-fed infants of metformin**-treated women with polycystic ovary syndrome. J Pediatr. 2006 May;148(5):628-632.
Godino JG, van Sluijs EMF, Marteau TM, et al. **Lifestyle advice combined with personalized estimates of genetic or phenotypic risk** of type 2 diabetes, and objectively measured physical activity: a randomized controlled trial. PLoS Med 2016. doi:10.1371/journal.pmed.1002185.
Goff LM. **Ethnicity and Type 2 diabetes** in the UK. Diabet Med. 2019 Jan 6.
Gokhale M, Buse JB, Gray CL, et al. **Dipeptidyl-peptidase-4 inhibitors and pancreatic cancer**: a cohort study. Diabetes Obes Metab. 2014 Dec;16(12):1247-56.
Goldberg N, Fralick M. **Sodium-glucose cotransporter 2 inhibitors** for treating diabetes mellitus. CMAJ. 2017 May 23;189(20):E724.
Goldberg RB, Holman R, Drucker DJ. Clinical decisions. **Management of type 2 diabetes**. N Engl J Med. 2008 Jan 17;358(3):293-7.
Goldberg R, Temprosa M, Otvos J, et al. **Lifestyle and metformin** treatment favorably influence lipoprotein subfraction distribution in the Diabetes Prevention Program. J Clin Endocrinol Metab 2013.

Goldberg RB, Aroda VR, et al; Diabetes Prevention Program (**DPP**) Research Group. Effect of **Long-Term Metformin** and **Lifestyle** in the Diabetes Prevention Program and Its **Outcome Study on Coronary Artery Calcium**. Circulation. 2017 Jul 4;136(1):52-64.
Goldberg RB, Kendall DM, Deeg MA, et al. A comparison of **lipid** and glycemic effects of **pioglitazone and rosiglitazone** in patients with type 2 diabetes and dyslipidemia. Diabetes Care. 2005 Jul;28(7):1547-54.
Goldenberg RM, Cheng AYY, Punthakee Z, Clement M. **CDA** Position statement: use of glycated hemoglobin (**A1C**) in the diagnosis of type 2 diabetes mellitus in adults. Can J Diabetes 2011;35:247-9.
Goldenberg RM, Berard LD, Cheng AY, et al. **SGLT2 Inhibitor-associated Diabetic Ketoacidosis**: Clinical Review and Recommendations for Prevention and Diagnosis. Clin Ther. 2016 Dec;38(12):2654-2664.e1.
Goldenberg RM. Choosing **Dipeptidyl Peptidase-4 Inhibitors, Sodium-glucose Cotransporter-2 Inhibitors, or Both, as Add-ons to Metformin**: Patient Baseline Characteristics Are Crucial. Clin Ther. 2017 Nov 22.
Goldfine AB, et al. **Family history** of diabetes is a major determinant of endothelial function. J Am Coll Cardiol. 2006 Jun 20;47(12):2456-61. Epub 2006 May 30.
Goldfine Allison B., Fonseca Vivian, Jablonski Kathleen A., Et al. and for the TINSAL-T2D (Targeting Inflammation Using Salsalate in Type 2 Diabetes) Study Team. The Effects of **Salsalate** on Glycemic Control in Patients With Type 2 Diabetes: A Randomized Trial. *Ann Intern Med* March 16, 2010
Goldfine AB, Phua EJ, Abrahamson MJ. Glycemic management in patients with **coronary artery disease and prediabetes** or type 2 diabetes mellitus. Circulation. 2014 Jun 17;129(24):2567-73.
Goldman J, White JR Jr. New **Insulin Glargine 300 U/mL** for the Treatment of Type 1 and Type 2 Diabetes Mellitus. Ann Pharmacother. 2015 Oct;49(10):1153-61.
Goldman-Levine JD. **Combination Therapy When Metformin Is Not an Option** for Type 2 Diabetes. Ann Pharmacother. 2015 Jun;49(6):688-699. Epub 2015 Mar 13.
Goldner MG, Knatterud GL, Prout TE. Effects of hypoglycemic agents on vascular complications in patients with adult-onset diabetes. 3. Clinical implications of **UGDP** results. JAMA. 1971 Nov;218(9):1400-10.
Goldstein JN, McCrary M, Lipska KJ. Is the **Over-the-Counter Availability of Human Insulin** in the United States Good or Bad? JAMA Intern Med. 2018 Jul 16.
Goldstein JN, Patel RM, Bland K, Hicks LS. Frequency of Sale and Reasons for **Purchase of Over-the-Counter Insulin** In the United States. JAMA Intern Med. 2019 Feb 18.
Golledge J, Moxon J, Pinchbeck J, et al. Association between **metformin prescription and growth rates of abdominal aortic aneurysms**. Br J Surg. 2017 Oct;104(11):1486-1493.
Golledge J, Singh TP Systematic review and meta-analysis of clinical trials examining the effect of **hyperbaric oxygen therapy** in people with diabetes-related lower limb ulcers. Diabet Med. 2019 Jul;36(7):813-826
Gomes T, Martins D, Tadrous M, et al. Association of a **Blood Glucose Test Strip Quantity-Limit Policy** With Patient Outcomes: A Population-Based Study. JAMA Intern Med. 2016 Nov 7
Gommans YMM, Runhaar J, Jacobs ML, Bierma-Zeinstra SMA. The Effect of Prolonged **Glucosamine** Usage on HbA1c Levels and New-Onset Diabetes Mellitus in Overweight and Obese Middle-Aged Women. Am J Med. 2017 Jun;130(6):731-737.e6.
Goncalves E, Bell DSH. **Combination Treatment of SGLT2 Inhibitors and GLP-1 Receptor Agonists**: Symbiotic Effects on Metabolism and Cardiorenal Risk. Diabetes Ther. 2018 Apr 5.
Gong Q, Zhang P, Wang J, et al. **Morbidity and mortality after lifestyle intervention** for people with impaired glucose tolerance: 30-year results of the Da Qing Diabetes Prevention Outcome Study. Lancet Diabetes Endocrinol. 2019 Jun;7(6):452-461.
Gong Z, Aragaki AK, Chlebowski RT, et al. Diabetes, metformin and incidence of and death from **invasive cancer in postmenopausal women**: Results from the women's health initiative (**WHI**). Int J Cancer. 2016 Apr 15;138(8):1915-27.
Gonzalez-Perez A, Schlienger RG, Rodríguez LA. **Acute pancreatitis** in association with type 2 diabetes and **antidiabetic drugs**: a population-based cohort study. Diabetes Care. 2010 Dec;33(12):2580-5.
Goring S, Hawkins N, Wygant G, et al. **Dapagliflozin** compared with other oral anti-diabetes treatments when added to metformin monotherapy: a systematic review and network meta-analysis. Diabetes Obes Metab. 2013 Nov 14.
Goossens ME, Buntinx F, Zeegers MP, et al. Influence of **metformin intake on the risk of bladder cancer** in type 2 diabetes patients. Br J Clin Pharmacol. 2015 Aug 10.
Gorricho J, Garjón J, Alonso A, et al. Use of oral antidiabetic agents and **risk of community-acquired pneumonia**: a nested case-control study. Br J Clin Pharmacol. 2017 Mar 11.
Goto A, Arah OA, Goto M, et al. **Severe hypoglycaemia and cardiovascular disease**: systematic review and meta-analysis with bias analysis. BMJ. 2013 Jul 29;347:f4533.
Goyder E, Irwig L, Payne N. Should we **screen for type 2 diabetes**? No. BMJ. 2012 Jul 9;345:e4516.
Gough SC, Bode B, Woo V, Rodbard HW, et al. NN9068-3697 (DUAL-I) trial investigators. Efficacy and safety of a fixed-ratio combination of insulin **degludec and liraglutide** (IDegLira) compared with its **components given alone**: results of a phase 3, open-label, randomised, 26-week, treat-to-target trial in insulin-naïve patients with type 2 diabetes. Lancet Diabetes Endocrinol. 2014 Nov;2(11):885-93.
Groop PH, Cooper ME, Perkovic V, et al. **Linagliptin Lowers Albuminuria** on Top of Recommended Standard Treatment in Patients With Type 2 Diabetes and Renal Dysfunction. Diabetes Care. 2013 Sep 11.
Graal MB, Wolffenbuttel HR. The use of **sulphonylureas in the elderly**. Drugs and Aging 1999;15(6):471-81.
Graff SK, Mario FM, Ziegelmann P, et al. Effects of **orlistat vs. metformin** on weight loss-related clinical variables in women with **PCOS**: systematic review and meta-analysis. Int J Clin Pract. 2016 May 26.
Gray KE, Katon JG, LeBlanc ES, et al. **Vasomotor symptom characteristics**: are they risk factors for incident diabetes? Menopause. 2017 Dec 4.
Gray LJ, Dales J, Brady EM, et al. Safety and effectiveness of **non-insulin glucose-lowering agents** in the treatment of people with type 2 diabetes who observe **Ramadan**: a systematic review and meta-analysis. Diabetes Obes Metab. 2015 Jul;17(7):639-48.
Green JB, Bethel MA, Armstrong PW, et al; **TECOS** Study Group. Effect of **Sitagliptin** on Cardiovascular Outcomes in Type 2 Diabetes. N Engl J Med. 2015 Jun 8.
Greene JA, Riggs KR. Why is there **no generic insulin**? Historical origins of a modern problem. N Engl J Med. 2015 Mar 19;372(12):1171-5.
Gregg B, Connor CG, Ruedy KJ, et al; Pediatric Diabetes Consortium. **Body mass index changes** in youth in the first year after type 1 diabetes diagnosis. J Pediatr. 2015 May;166(5):1265-1269.e1.
Gregg EW, Cheng YJ, Saydah S, et al. Trends in **death rates among US adults with and without diabetes between 1997 and 2006**.Diabetes Care 2012; 35:1252-1257.
Gregg EW, Chen H, Wagenknecht LE, et al. Association of an **intensive lifestyle** intervention with remission of type 2 diabetes. (**Look Ahead**) JAMA. 2012;308(23): 2489-2496.
Gregg EW, Li Y, Wang J, et al. Changes in **diabetes-related complications in the United States**, 1990-2010. N Engl J Med. 2014 Apr 17;370(16):1514-23.
Gregg EW, Lin J, Bardenheier B, et al. Impact of **Intensive Lifestyle Intervention on Disability-Free Life Expectancy**: The **Look AHEAD Study**. Diabetes Care. 2018 Mar 15.
Grennan D. Diabetic Foot **Ulcers**. JAMA. 2019 Jan 1;321(1):114.
Griebeler ML, Morey-Vargas OL, Brito JP, et al. **Pharmacologic interventions for painful diabetic neuropathy**. An umbrella systematic review and comparative effectiveness network meta-analysis. Ann Intern Med. 2014;161:639-49. doi:10.7326/M14-0511
Griffin SJ, Borch-Johnsen K, Davies MJ, et al. Eff ect of early **intensive multifactorial therapy on 5-year cardiovascular outcomes** in individuals with type 2 diabetes detected by screening (**ADDITION-Europe**):a cluster-randomised trial. Lancet 2011; published online June 25
Grimaldi-Bensouda L, Cameron D, Marty M, et al. Risk of **breast cancer by individual insulin use** - an international multicenter study. Diabetes Care. 2013 Aug 15.
Grohmann B, Espin S, Gucciardi E. **Patients' experiences of diabetes education** teams integrated into primary care. Can Fam Physician. 2017 Feb;63(2):e128-e136
Gross Jorge L., Kramer Caroline K., Leitão Cristiane B., et al. , for the Diabetes and Endocrinology Meta-analysis Group (DEMA). Effect of Antihyperglycemic **Agents Added to Metformin** and a Sulfonylurea on Glycemic Control and Weight Gain in Type 2 Diabetes: A Network Meta-analysis. Ann Intern Med May 17, 2011 154:672-679.
Grøntved A, Rimm EB, Willett WC, et al. A Prospective Study of **Weight Training** and Risk of Type 2 Diabetes Mellitus in Men. Arch Intern Med. 2012 Aug 6:1-7.
Grøntved A, Pan A, Mekary RA, et al. **Muscle-Strengthening and Conditioning** Activities and Risk of Type 2 Diabetes: A Prospective Study in Two Cohorts of US Women. PLoS Med. 2014 Jan;11(1):e1001587
Grover SA, Kaouache M, Rempel P, et al. Years of **life lost** and healthy life-years lost from diabetes and cardiovascular disease in **overweight and obese people**: a modelling study. Lancet Diabetes Endocrinol. 2014 Dec 4.
Grün B, Kiessling MK, Burhenne J, et al. **Trimethoprim-metformin interaction** and its genetic modulation by **OCT2** and **MATE1** transporters. Br J Clin Pharmacol. 2013 Nov;76(5):787-96.
Grunberger G, Chang A, Garcia Soria G, et al. Monotherapy with the once-weekly GLP-1 analogue **dulaglutide** for 12 weeks in patients with Type 2 diabetes: dose-dependent effects on glycaemic control in a randomized, double-blind, placebo-controlled study. Diabet Med. 2012 Oct;29(10):1260-7.
Grundy SM. **Metabolic syndrome**: connecting and reconciling cardiovascular and diabetes worlds. J Am Coll Cardiol. 2006 Mar 21;47(6):1093-100. Epub 2006 Feb 23.
Grundy SM, et al. American Heart Association; National Heart, Lung, and Blood Institute. Diagnosis and management of the **metabolic syndrome**: an American Heart Association/National Heart, Lung, and Blood Institute Scientific Statement. Circulation. 2005 Oct 25;112(17):2735-52. Epub 2005 Sep 12. Erratum in: Circulation. 2005 Oct 25;112(17):e297. Circulation. 2005 Oct 25;112(17):e298.
Grøntved A, Hu FB. **Television viewing** and risk of type 2 diabetes, cardiovascular disease, and all-cause mortality: a meta-analysis. JAMA. 2011 Jun 15;305(23):2448-55.
Gu T, Ma J, Zhang Q, et al. **Comparative effect of saxagliptin and glimepiride** with a composite endpoint of adequate glycaemic control without hypoglycaemia and without weight gain in patients uncontrolled with metformin therapy: Results from the SPECIFY study, a 48-week, multi-centre, randomized, controlled trial. Diabetes Obes Metab. 2018 Dec 5.
Guja C, Frias JP, Somogyi A, et al. Effect of **exenatide QW or** placebo, both added to titrated **insulin glargine**, in uncontrolled type 2 diabetes: The **DURATION-7** randomized study. Diabetes Obes Metab. 2018 Feb 23.
Gujral UP, Narayan KM, Pradeepa RG, et al. **Comparing Type 2 Diabetes**, Prediabetes, and Their Associated Risk Factors in **Asian Indians in India and in the U.S.:** The **CARRS** and **MASALA** Studies. Diabetes Care. 2015 Apr 15.
Gulliford MC, Charlton J, Latinovic R. Risk of Diabetes Associated With Prescribed **Glucocorticoids** in a Large Population. Diabetes Care. 2006 Dec;29(12):2728-2729. The researchers found that the adjusted odds ratio for diabetes associated with 3 or more prescriptions for oral glucorticoids was 1.36. Such patients appeared to account for about 2% of incident cases of diabetes.

Gunderson EP, Hurston SR, Ning X, et al. Study of Women, Infant Feeding and Type 2 Diabetes After GDM Pregnancy Investigators. **Lactation and Progression to Type 2 Diabetes** Mellitus After Gestational Diabetes Mellitus: A Prospective Cohort Study. Ann Intern Med. 2015 Nov 24:889-898.
Gunderson EP, Lewis CE, Lin Y, et al. **Lactation Duration and Progression to Diabetes** in Women Across the Childbearing Years: The 30-Year CARDIA Study. JAMA Intern Med. 2018 Mar 1;178(3):328-337.
Guo M, Ding J, Li J, et al. **SGLT2 inhibitors and risk of stroke** in patients with type 2 diabetes: A systematic review and meta-analysis. Diabetes Obes Metab. 2018 Mar 23.
Guo J, Erqou SA, Miller RG, et al. The role of **coronary artery calcification testing in incident coronary artery disease risk** prediction in type 1 diabetes. Diabetologia. 2018 Nov 14.
Gupta AK, Dahlof B, et al. Anglo-Scandinavian Cardiac Outcomes Trial Investigators. Determinants of new-onset diabetes among 19,257 hypertensive patients randomized in the Anglo-Scandinavian Cardiac Outcomes Trial--Blood Pressure Lowering Arm and the relative influence of antihypertensive medication. (**ASCOT**) Diabetes Care. 2008 May;31(5):982-8. Epub 2008 Jan 30. Baseline FPG >5 mmol/l, BMI, and use of an atenolol +/- diuretic regimen were among the major determinants of NOD in hypertensive patients. The model developed from these data allows accurate prediction of NOD among hypertensive subjects.
Gupta T, Hudson M. Update on **Glucose Management Among Noncritically Ill Patients Hospitalized on Medical and Surgical Wards**. J Endocrine Society. 2017 Apr;1(4)247-259.
Habib G, Khazin F, Chernin M. Continuous blood glucose monitoring in a patient with type-2 diabetes treated with **intra-articular betamethasone** injection at the knee joint. Arthritis Rheum. 2013 Oct 7.
Hackam DG, Quinn RR, Ravani P, et al. Canadian Hypertension Education Program. The **2013 Canadian Hypertension Education Program (CHEP) Recommendations** for Blood Pressure Measurement, Diagnosis, Assessment of Risk, Prevention, and Treatment of Hypertension. Can J Cardiol. 2013 Mar 28.
Hagopian W, Lee H-S, Liu E, et al. Co-occurrence of **type 1 diabetes and celiac disease** autoimmunity in the **TEDDY** prospective cohort. Pediatrics. 2017;140(5): e20171305
Haidar A, Legault L, Dallaire M, et al. Glucose-responsive insulin and glucagon delivery (dual-hormone **artificial pancreas**) in adults with type 1 diabetes: a randomized crossover controlled trial. CMAJ. 2013 Mar 5;185(4):297-305.
Haidar A, Legault L, Messier V, et al. Comparison of dual-hormone **artificial pancreas**, single-hormone artificial pancreas, and conventional insulin pump therapy for glycaemic control in patients with type 1 diabetes: an open-label randomised controlled crossover trial. Lancet Diabetes Endocrinol. 2014 Nov 26.
Haidar A, Legault L, Messier V, et al. Comparison of dual-hormone **artificial pancreas**, single-hormone artificial pancreas, and conventional insulin pump therapy for glycaemic control in patients with type 1 diabetes: an open-label randomised controlled crossover trial. Lancet Diabetes Endocrinol. 2015 Jan;3(1):17-26.
Hakola L, Miettinen ME, Syrjälä E, et al. Association of **Cereal, Gluten, and Dietary Fiber Intake With Islet Autoimmunity** and Type 1 Diabetes. JAMA Pediatr. 2019 Aug 12.
Halberg IB, Lyby K, Wassermann K, et al. Efficacy and safety of **oral basal insulin** versus **subcutaneous insulin glargine** in type 2 diabetes: a randomised, double-blind, phase 2 trial. Lancet Diabetes Endocrinol. 2019 Jan 21.
Hall H, Perelman D, Breschi A, et al. **Glucotypes reveal new patterns of glucose dysregulation**. PLoS Biol. 2018 Jul 24;16(7):e2005143.
Hallahan B, Ryan T, Hibbeln JR, et al. Efficacy of **omega-3** highly unsaturated fatty acids in the treatment of **depression**. Br J Psychiatry. 2016 Apr 21.
Hallow KM, Helmlinger G, Greasley PJ, et al. Why do **SGLT2 inhibitors reduce heart failure hospitalization**? A differential volume regulation hypothesis. Diabetes Obes Metab. 2018 Mar;20(3):479-487.
Halperin F, Ding SA, Simonson DC, et al. **Roux-en-Y Gastric Bypass Surgery or Lifestyle** With Intensive Medical Management in Patients With Type 2 Diabetes: Feasibility and 1-Year Results of a Randomized Clinical Trial. JAMA Surg. 2014 Jun 4.
Hals IK, Fiskvik Fleiner H, Reimers N, et al. Investigating **optimal beta-cell-preserving treatment** in latent autoimmune diabetes in adults: Results from a 21-month randomized trial. Diabetes Obes Metab. 2019 May 30.
Halvorsen YD, Lock JP, Zhou W, et al. A 24-week, randomized, double-blind, active-controlled clinical **trial comparing bexagliflozin with sitagliptin** as an adjunct to metformin for the treatment of type 2 diabetes in adults. Diabetes Obes Metab. 2019 Jun 4
Hamada S, Gulliford MC. **Antidiabetic and cardiovascular drug utilisation** in patients diagnosed with type 2 diabetes mellitus **over the age of 80 years**: a population-based cohort study. Age Ageing. 2015 Jul;44(4):566-73.
Hamada S, Gulliford MC. Mortality in Individuals **Aged 80 and Older** with Type 2 Diabetes Mellitus in Relation to **Glycosylated Hemoglobin**, Blood Pressure, and Total Cholesterol. J Am Geriatr Soc. 2016 Jul;64(7):1425-31.
Hambling CE, et al. **Older people with Type 2 diabetes, including those with chronic kidney disease or dementia**, are commonly **overtreated with sulfonylurea or insulin therapies**. Diabet Med. 2017 Sep;34(9):1219-1227.
Hamood R, Hamood H, Merhasin I, et al. Diabetes **After Hormone Therapy in Breast Cancer Survivors**: A Case-Cohort Study. J Clin Oncol. 2018 Apr 24:JCO2017763524.
Handelsman Y, Mechanick JI, Blonde L, et al. **AACE** Task Force for Developing Diabetes **Comprehensive Care Plan**. American Association of Clinical Endocrinologists medical guidelines for clinical practice for developing a diabetes mellitus comprehensive care plan. Endocr Pract 2011 Mar-Apr;17(Suppl 2):1-53.
Hajna S, Ross NA, Joseph L, et al. **Neighbourhood Walkability** and Daily Steps in Adults with Type 2 Diabetes. PLoS One. 2016 Mar 18;11(3):e0151544.
Handelsman Y, Henry RR, Bloomgarden ZT, et al. American Association of Clinical Endocrinologists and **American** College of Endocrinology-Association of **SGLT-2 Inhibiotors and diabeteic ketoacidosis**. Endocr Pract. 2016 Jun 1.
Hanefeld M, Monnier L, Schnell O, et al. Early Treatment with **Basal Insulin Glargine** in People with Type 2 Diabetes: Lessons from **ORIGIN** and Other Cardiovascular Trials. Diabetes Ther. 2016 Jun;7(2):187-201.
Hansen LJ, Siersma V, Beck-Nielsen H, de Fine Olivarius N. **Structured personal care** of type 2 diabetes: a **19-year follow-up** of the study Diabetes Care in General Practice (**DCGP**). Diabetologia 2013, online 8 April.
Harder T, Roepke K, Diller N, et al. **Birth weight, early weight gain**, and subsequent risk of type 1 **diabetes**: systematic review and meta-analysis. Am J Epidemiol. 2009 Jun 15;169(12):1428-36. Epub 2009 Apr 10. This meta-analysis indicates that high birth weight and increased early weight gain are risk factors for type 1 diabetes.
Harjutsalo V, Forsblom C, Groop PH. **Time trends in mortality** in patients with type 1 diabetes: nationwide population based cohort study. BMJ. 2011 Sep 8;343:d5364. doi: 10.1136/bmj.d5364.
Haring HU, Merker L, Seewaldt-Becker E, et al. **Empagliflozin** As Add-on to Metformin Plus Sulfonylurea in Patients With Type 2 Diabetes: A 24-week, randomized, double-blind, placebo-controlled trial. Diabetes Care. 2013 Aug 20.
Harper W, Clement M, Goldenberg R, et al. **Pharmacologic management of type 2 diabetes – 2015 interim update. Can J Diabetes** 2015;39:250-2. http://guidelines.diabetes.ca/Browse/Chapter13_2015 (accessed August 10, 2015)
Harris DL, Weston PJ, Signal M, Chase JG, Harding JE. **Dextrose gel for neonatal hypoglycaemia** (the Sugar Babies Study): a randomised, double-blind, placebo-controlled trial. Lancet 2013; published online Sept 25.
Hart HE, Rutten GE, Bontje KN, Vos RC. **Overtreatment of older patients with type 2 diabetes mellitus in primary care**. Diabetes Obes Metab. 2018 Apr;20(4):1066-1069.
Hart T, Milner R, Cifu A. **Management of a Diabetic Foot**. JAMA. 2017 Oct 10;318(14):1387-1388.
Hartling L, Dryden DM, Guthrie A, et al. Screening and diagnosing **gestational diabetes** mellitus. Evid Rep Technol Assess. 2012 Oct; 210:1-327.
Hartling L, Dryden DM, Guthrie A, et al. Benefits and Harms of Treating **Gestational Diabetes Mellitus**: A Systematic Review and Meta-analysis for the U.S. Preventive Services Task Force and the National Institutes of Health Office of Medical Applications of Research. Ann Intern Med. 2013 May 28.
Hattersley AT, Thorens B. Type 2 **Diabetes, SGLT2 Inhibitors, and Glucose Secretion**. N Engl J Med. 2015 Sep 3;373(10):974-6.
Haw JS, Galaviz KI, Straus AN, et al. **Long-term Sustainability of Diabetes Prevention Approaches**: A Systematic Review and Meta-analysis of Randomized Clinical Trials. JAMA Intern Med. 2017 Nov 6.
Hay J, Wittmeier K, MacIntosh A, et al. **Physical activity** intensity and type 2 diabetes risk in overweight youth: a randomized trial. Int J Obes (Lond). 2016 Apr;40(4):607-14
Hayashi A, Oguchi H, Kozawa Y, et al. **Daily walking is effective for the management of pregnant women with gestational diabetes** mellitus. J Obstet Gynaecol Res. 2018 Jul 5.
Hayes JF, Lundin A, Wicks S, et al. Association of Hydroxylmethyl Glutaryl Coenzyme A Reductase Inhibitors, L-Type Calcium Channel Antagonists, and Biguanides With Rates of **Psychiatric Hospitalization and Self-Harm in Individuals** With Serious Mental Illness. JAMA Psychiatry. 2019 Jan 9.
Hayward RA, Reaven PD, Wiitala WL, et al; **VADT** Investigators. **Follow-up of glycemic control and cardiovascular outcomes** in type 2 diabetes. N Engl J Med. 2015 Jun 4;372(23):2197-206.
HbA1c targets in type 2 diabetes: guidelines and evidence. Drug Ther Bull. 2013 Apr;51(4):42-5.
Heaf J. **Metformin in chronic kidney disease**: time for a rethink. Perit Dial Int. 2014 Jun;34(4):353-7.
Hedderson MM, Brown SD, Ehrlich SF, et al. A Tailored Letter Based on Electronic Health Record Data Improves Gestational Weight Gain Among Women With Gestational Diabetes: The Gestational Diabetes` Effects on Moms (GEM) Cluster-Randomized Controlled Trial. Diabetes Care. 2018 Apr 18.
Heianza Y, Kato K, Kodama S, et al. Risk of the development of Type 2 diabetes in relation to overall **obesity, abdominal obesity and the clustering of metabolic abnormalities** in Japanese individuals: does metabolically healthy overweight really exist? The Niigata Wellness Study. Diabet Med. 2015 May;32(5):665-72.
Health Canada Dec/05 Association of **AVANDIA** & **AVANDAMET** with new onset and/or worsening of **macular edema** http://www.hc-sc.gc.ca/dhp-mps/medeff/advisories-avis/prof/2005/avandia_avandamet_hpc-cps_e.html
Health Canada Jan/06 & July/07 Association of **AVANDIA** & 6 reports of parotid gland enlargement http://www.hc-sc.gc.ca/dhp-mps/medeff/bulletin/carn-bcei_v16n1_e.html#2
Health Canada Apr/07 is warning consumers from The Hong Kong Department of Health found **Lanmei Keili Ji to be adulterated with gliclazide**, a hypoglycaemic agent (lowers blood sugar).
Health Canada May/07 is advising consumers not to use **Xiaokeshuping Jiangtangning Jiaonang** capsules in Hong Kong to contain the undeclared pharmaceutical drugs phenformin, rosiglitazone, and glibenclamide, which may be used in diabetes to lower blood sugar.
Health Canada May& June/07 is advising consumers & health professionals about heart risks with **Avandia** http://www.hc-sc.gc.ca/dhp-mps/medeff/advisories-avis/public/2007/avandia_pc-cp_3_e.html
Health Canada Sept/07 is advising consumers not to use foreign health products due to concerns about possible side-effects: **Jacaranda**, **Queenmer Fat Loss**, **Li Da Dai Dai Hua Jiao Nang, J-minus** and **Jelimel Slimming Capsules**. These products are promoted for

weight loss and have been found to be adulterated with the prescription drug sibutramine. Sibutramine is used for treating obesity and should only be taken under the supervision of a health professional. **Junyu Jiaonanyihao** has been found to contain the undeclared prescription drugs sibutramine and dexamethasone, as well as phenolphthalein, which is currently prohibited in Canada.. **Heng Tong Jiangtangning Jiaonang** was found to contain the prohibited drug phenformin, and the prescription drug glibenclamide (glyburide) which should only be taken under the supervision of a health professional.

Health Canada Nov/07 Rosiglitazone (**AVANDIA**®) is no longer approved as monotherapy for type 2 diabetes, except when metformin use is contraindicated or not tolerated. Rosiglitazone is no longer approved for use in combination with a sulfonylurea, except when metformin is contraindicated or not tolerated. Treatment with all rosiglitazone products is now contraindicated in patients with any stage of heart failure (i.e., NYHA Class I, II, III or IV).

Health Canada April/08 warns that Singapore's Health Sciences Authority (HSA) advised the public not to use the product **Power 1 Walnut**, because it was found to contain the prescription drugs sildenafil and glibenclamide.

Health Canada April/08 is advising consumers not to use The Hong Kong Department of Health advised the public not to use the product **Tian Sheng Yi Bao** because it was found to contain two pharmaceutical products, glibenclamide and phenformin.

Health Canada June/08 **Nangen Zengzhangsu** (may also be known as Nangen or Nangeng), Sanbianwan, Jiu Bian Wang, Tian Huang Gu Shen Dan, Zui Xian Dan Gong Shi Zi, and Power Up. The Hong Kong Department of Health has warned consumers not to use these herbal/proprietary Chinese medicine products promoted for erectile dysfunction because they have been found to contain sildenafil and/or glibenclamide.

Health Canada June/08 **Zhong Hua Niu Bian**. Zhong Hua Niu Bian is an herbal/proprietary Chinese medicine product promoted for erectile dysfunction. Singapore's Health Sciences Authority has warned against the use of this product because it has been found to contain sildenafil, glibenclamide, tadalafil and sibutramine

Health Canada Nov/08 is advising consumers not to use foreign health products due to concerns about possible side-effects: The Hong Kong Department of Health warned consumers not to buy or use **Lu Quan** because it contains undeclared glibenclamide and sildenafil.

Health Canada Nov/10 AVANDIA®/AVANDAMET®/AVANDARYL® is now indicated only in patients with type 2 diabetes mellitus for whom all other oral antidiabetic agents, in monotherapy or in combination, do not result in adequate glycemic control or are inappropriate due to contraindications or intolerance. Prior to starting or renewing a prescription for **AVANDIA®/AVANDAMET®/ AVANDARYL®,** physicians should consider whether a rosiglitazone-containing product is an appropriate therapeutic choice, and if so: Document the eligibility of patients to meet the above criteria; Counsel each patient on the risks and benefits of AVANDIA®/AVANDAMET®/ AVANDARYL®, including the cardiovascular risks; and Obtain the patient's written informed consent to take the drug.

Health Canada Nov/11 **Pancre-Plus** The Hong Kong Department of Health warned that this counterfeit Chinese medicine contains an unauthorized drug (phenformin) and a prescription drug (glyburide)**. Tian Ma Tu Chung Seven Leave Ginseng, Vall-Boon Tongkat Al, and Pao Ni Kang** The Singapore Health Sciences Authority warned that these traditional herbal products contain prescription and over-the-counter drugs (dexamethasone, ketoconazole, repaglinide, pheniramine, and chlorpheniramine).

Health Canada Apr/12 has recently completed a safety assessment of the available data for **rosiglitazone-ACTOS**, an oral anti-diabetic drug, and the label was updated to reflect the potential risk of **bladder cancer** in treated patients.

Health Canada May/12 1. **Jin Yu Tang Tai Han Kang Pai Pu Ling Jiao Nang; TangBaoKouFuYiDaoSuJiaoNang; Tangren 365 Kangxunpai sangge huoyisu jiaonang; Tong Ren Xiu Fu Kou Fu Yi Dao Su.** The Hong Kong Department of Health warned that these products contain a combination of prescription drugs (metformin, glibenclamide [also known as glyburide], rosiglitazone, glimepiride, hydrochlorothiazide) and unauthorized drugs (phenolphthalein, phenformin).

Health Canada Jan/13: informing Canadians of a labelling update for all cholesterol-lowering drugs (also known as **statins**) regarding the risk of increased blood sugar levels and a small increased **risk of diabetes** among patients already at risk for the disease.

Health Canada Apr/14: **San Xiao Ping Tang Jin Qi Jiao Nang**: The Hong Kong Department of Health warned consumers not to use this product after it was found to contain phenformin, pioglitazoneand glibenclamide**.**

Health Canada June/15 **Forxiga, Invokana**: Health Canada begins safety review of diabetes drugs known as SGLT2 inhibitors and risk of **ketoacidosis**.

Health Canada Jul/17 is advising Canadians that Novo Nordisk A/S has updated a voluntary recall of insulin cartridge holders used in certain lots of its **NovoPen Echo and NovoPen 5 insulin pens**. The company detected that the **cartridge holders may crack** or break if exposed to certain chemicals, such as some cleaning agents.

HEALTHY Study Group, A **School-Based Intervention** for Diabetes Risk Reduction. N Engl J Med 2010 0: NEJMoa1001933.

Health Canada Aug/15: Co-administration of **repaglinide and clopidogrel** (a CYP2C8 inhibitor) may lead to a significant decrease in blood glucose levels due to a drug-drug interaction. The concomitant use of repaglinide and clopidogrel is now contraindicated.

Health Canada May/16 **SGLT2 Inhibitors** [INVOKANA (canagliflozin), FORXIGA (dapagliflozin), XIGDUO (dapagliflozin/metformin), JARDIANCE (empagliflozin)] - Risk of **Diabetic Ketoacidosis** - Janssen Inc., Boehringer Ingelheim (Canada) Ltd. Serious, sometimes life-threatening and fatal cases of diabetic ketoacidosis (DKA) have been reported in patients on sodium glucose co-transporter 2 (SGLT2) inhibitors for type 1 and type 2 diabetes. In a number of these cases, the presentation of the condition was atypical with only moderately increased blood glucose levels observed. SGLT2 inhibitors are NOT indicated for treatment of type 1 diabetes mellitus and should not be used in type 1 diabetes.

Health Canada Aug/16: Hong Kong Department of Health-**TANGKE TEGONGYIHAOJIAONANG** undeclared phenformin and glibenclamide.

Health Canada Sep/17: **INVOKANA** (**canagliflozin**) and **INVOKAMET** (**canagliflozin** and metformin) - Risk of Lower Limb **Amputation** - Janssen Inc.

Health Canada Jan/18 - Summary safety review – **dipeptidylpeptidase-4 inhibitors – assessing the potential risk of a skin reaction (bullous pemphigoid).** January 25, 2018.

Health Canada Jun/18: Jamp-Glucose 50 and Jamp-Glucose 75 – Risk of False Negative Oral Glucose Challenge or Tolerance Test Results. Jamp Pharma Corporation has voluntarily recalled three (3) lots of Jamp-Glucose 50 and three (3) lots of Jamp-Glucose 75 because they contain significantly less D-glucose than what is declard on the label.

Heerspink HJ, Perkins BA, Fitchett DH, et al. **Sodium Glucose Cotransporter 2 Inhibitors** in the Treatment of Diabetes: Cardiovascular and Kidney Effects, Potential Mechanisms and Clinical Applications. Circulation. 2016 Jul 28

Heerspink HJ, Desai M, Jardine M, et al.**Canagliflozin** Slows Progression of **Renal** Function Decline Independently of Glycemic Effects. J Am Soc Nephrol. 2016 Aug 18

Heerspink HJ, Perkins BA, Fitchett DH, et al. **Sodium Glucose Cotransporter 2 Inhibitors** in the Treatment of Diabetes Mellitus: **Cardiovascular and Kidney Effects**, Potential Mechanisms, and Clinical Applications. Circulation. 2016 Sep 6;134(10):752-72.

Heerspink HJL, Parving HH, Andress DL, et al**. Atrasentan and renal events in patients with type 2 diabetes** and chronic kidney disease (SONAR): a double-blind, randomised, placebo-controlled trial. Lancet. 2019 Apr 12.

Heianza Y, Hara S, Arase Y, et al. **HbA(1c)** 5.7-6.4% and impaired fasting plasma glucose for diagnosis of prediabetes and risk of progression to diabetes in Japan (**TOPICS 3**): a longitudinal cohort study. Lancet. 2011 Jun 24.

Heikes KE, et al. **Diabetes Risk Calculator**: a simple tool for detecting undiagnosed diabetes and pre-diabetes. Diabetes Care. 2008 May;31(5):1040-5. Epub 2007 Dec 10. The Diabetes Risk Calculator is the only currently available noninvasive screening tool designed and validated to detect both pre-diabetes and undiagnosed diabetes in the U.S. population.

Heine RJ, Van Gaal LF, Johns D, et al.; GWAA Study Group. **Exenatide** versus insulin glargine in patients with suboptimally controlled type 2 diabetes: a randomized trial. Ann Intern Med. 2005 Oct 18;143(8):559-69.

Heinemann L, et al. **Real-time continuous glucose monitoring** in adults with type 1 diabetes and impaired hypoglycaemia awareness or severe hypoglycaemia treated with multiple daily insulin injections (**HypoDE**): a multicentre, randomised controlled trial. Lancet. 2018 Feb 15.

Heisler Michele, Vijan Sandeep, Makki Fatima, et al. Diabetes Control With Reciprocal Peer Support Versus Nurse Care Management: A Randomized Trial. *Ann Intern Med* October 19, 2010 153:507-515.

Helle EIT, Biegley P, Knowles JW, et al. **First Trimester Plasma Glucose Values** in Women without Diabetes are Associated with Risk for Congenital Heart Disease in Offspring. J Pediatr. 2017 Dec 13.

Helminen O, Aspholm S, Pokka T, et al. **HbA1c Predicts Time to Diagnosis of Type 1 Diabetes in Children** at Risk. Diabetes. 2015 May;64(5):1719-27.

Hemmingsen B, Lund SS, Gluud C, et al. Targeting **intensive glycaemic control versus targeting conventional glycaemic control** for type 2 diabetes mellitus. Cochrane Database of Systematic Reviews 2011, Issue 6. Art. No.: CD008143. DOI: 10.1002/14651858.CD008143.pub2. The included trials did not show significant differences for all-cause mortality and cardiovascular mortality when targeting intensive glycaemic control compared with conventional glycaemic control. Targeting intensive glycaemic control reduced the risk of microvascular complications while increasing the risk of hypoglycaemia. Furthermore, intensive glycaemic control might reduce the risk of non-fatal myocardial infarction in trials exclusively dealing with glycaemic control in usual care settings.

Hemmingsen B, Lund SS, Gluud C, et al. **Intensive glycaemic control for patients with type 2 diabetes**: systematic review with meta-analysis and trial sequential analysis of randomised clinical trials. BMJ. 2011 Nov 24;343:d6898.

Hemmingsen B, Christensen LL, Wetterslev J, et al. Comparison of **metformin and insulin versus insulin alone** for type 2 diabetes: systematic review of randomised clinical trials with meta-analyses and trial sequential analyses. BMJ. 2012 Apr 19;344:e1771.

Hemmingsen B, Schroll JB, Lund SS, et al. **Sulphonylurea monotherapy** for patients with type 2 diabetes mellitus. Cochrane Database Syst Rev. 2013 Apr 30;4:CD009008. There is insufficient evidence fromRCTs to support the decision as to whether to initiate sulphonylureamonotherapy. Data on patientimportant outcomes are lacking.

Hemmingsen B, Lund SS, Gluud C, et al. **Targeting intensive glycaemic control versus targeting conventional glycaemic control** for type 2 diabetes mellitus. Cochrane Database Syst Rev. 2013 Nov 11;11:CD008143. Although we have been able to expand the number of participants by 16% in this update, we still find paucity of data on outcomes and the bias risk of the trials was mostly considered high. Targeting intensive glycaemic control compared with conventional glycaemic control did not show significant differences for all-cause mortality and cardiovascular mortality. Targeting intensive glycaemic control seemed to reduce the risk of microvascular complications, if we disregard the risks of bias, but increases the risk of hypoglycaemia and serious adverse events.

Hemmingsen B, Schroll JB, Wetterslev J, et al. **Sulfonylurea versus metformin monotherapy** in patients with type 2 diabetes: a Cochrane systematic review and meta-analysis of randomized clinical trials and trial sequential analysis. CMAJ Open. 2014 Jul 22;2(3):E162 75.

Hemmingsen B, Sonne DP, Metzendorf MI, et al. **Insulin secretagogues** for **prevention or delay of type 2 diabetes mellitus** and its associated complications in persons at increased risk for the development of type 2 diabetes mellitus. Cochrane Database Syst Rev. 2016 Oct 17;10:CD012151. There is insufficient evidence to demonstrate whether insulin secretagogues compared mainly with placebo reduce the risk of developing T2DM and its associated complications in people at increased risk for the development of T2DM. Most trials did not investigate patient-important outcomes.

Hemmingsen B, Sonne DP, Metzendorf MI, et al. **Dipeptidyl-peptidase (DPP)-4 inhibitors and glucagon-like peptide (GLP)-1 analogues** for **prevention or delay of type 2 diabetes mellitus** and its associated complications in people at increased risk for the development of type 2 diabetes mellitus. Cochrane Database Syst Rev. 2017 May 10;5:CD012204. There is no firm evidence that DPP-4 inhibitors or GLP-1 analogues compared mainly with placebo substantially influence the risk of T2DM and especially its associated complications in people at increased risk for the development of T2DM. Most trials did not investigate patient-important outcomes.

Hemmingsen B, Gimenez-Perez G, Mauricio D, et al. **Diet, physical activity or both for prevention or delay of type 2 diabetes mellitus** and its associated complications in people at increased risk of developing type 2 diabetes mellitus. Cochrane Database Syst Rev. 2017 Dec 4;12:CD003054. There is no firm evidence that diet alone or physical activity alone compared to standard treatment influences the risk of T2DM and especially its associated complications in people at increased risk of developing

T2DM. However, diet plus physical activity reduces or delays the incidence of T2DM in people with IGT. Data are lacking for the effect of diet plus physical activity for people with intermediate hyperglycaemia defined by other glycaemic variables. Most RCTs did not investigate patient-important outcomes.

Heinemann L, Fleming GA, Petrie JR, et al. **Insulin pump risks and benefits**: a clinical appraisal of pump safety standards, adverse event reporting and research needs. A Joint Statement of the European Association for the Study of Diabetes and the American Diabetes Association Diabetes Technology Working Group. Diabetologia. 2015 Mar 18.

Hendley J. **Are you well controlled**? BMJ. 2018 Nov 22;363:k3119

Heneka MT, Fink A, Doblhammer G. Effect of **pioglitazone** medication on the incidence of **dementia**. Ann Neurol. 2015 May 14.

Henry RR, Mudaliar S, Kanitra L, Woloschak M, Balena R; for the T-Emerge 3 Study Group. Efficacy and Safety of **Taspoglutide** in Patients with Type 2 Diabetes Inadequately Controlled with Metformin Plus Pioglitazone over 24 Weeks: T-Emerge 3 Trial. J Clin Endocrinol Metab. 2012 Apr 26.

Henry RR, Murray AV, Marmolejo MH, et al. **Dapagliflozin**, **metformin XR, or both**: initial pharmacotherapy for type 2 diabetes, a randomised controlled trial. Int J Clin Pract. 2012 May;66(5):446-56.

Henry RR, Thakkar P, Tong C, et al. Efficacy and Safety of **Canagliflozin**, a Sodium Glucose Cotransporter 2 Inhibitor, as Add-On to Insulin in Patients With Type 1 Diabetes. Diabetes Care. 2015 Oct 20.

Herber-Gast GC, Mishra GD. Early severe **vasomotor** menopausal symptoms are **associated with diabetes**. Menopause. 2014 Jan 6.

Herkert DM, Vijayakumar P, Luo J, et al. **Cost-related insulin underuse** among patients with diabetes [published online December 3, 2018]. JAMA Int Med.

Hermida RC, Ayala DE, Mojón A, et al. **Bedtime ingestion of hypertension medications** reduces the risk of new-onset type 2 diabetes: a randomized controlled trial. Diabetologia. 2015 Sep 23.

Hernandez AF, Green JB, Janmohamed S, et al. **Albiglutide and cardiovascular outcomes in patients with type 2 diabetes** and cardiovascular disease (**Harmony Outcomes**): a double-blind, randomised placebo-controlled trial. Lancet. 2018 Oct 1.

Herold KC, Bundy BN, Long SA, et al. An anti-CD3 antibody, **teplizumab,** in relatives at risk for type 1 diabetes. N Engl J Med. DOI: 10.1056/NEJMoa1902226.

Hiatt WR, Kaul S, Smith RJ. The **cardiovascular safety of diabetes drugs—insights from the rosiglitazone experience**. N Engl J Med 2013; DOI:10.1056/NEJMp1309610. Available here.

Hicks BM, Yin H, Yu OHY, Pollak MN, Platt RW, Azoulay L. **Glucagon-like peptide-1 analogues and risk of breast cancer** in women with type 2 diabetes: population based cohort study using the UK Clinical Practice Research Datalink. BMJ 2016;355:i5340.

Hidayat K, Du X, Shi BM. **Risk of fracture** with dipeptidyl peptidase-4 inhibitors, glucagon-like peptide-1 receptor agonists, or sodium-glucose cotransporter-2 inhibitors in real-world use: systematic review and meta-analysis of observational studies. Osteoporos Int. 2019 May 27.

Higurashi T, Hosono K, Takahashi H, et al. **Metformin** for chemoprevention of metachronous colorectal **adenoma or polyps** in post-polypectomy patients without diabetes: a multicentre double-blind, placebo-controlled, randomised phase 3 trial. Lancet Oncol. 2016 Mar 2.

Hill NE, Campbell C, Buchanan P, et al.Biochemical, Physiological and Psychological Changes **During Endurance Exercise** in People With **Type 1 Diabetes**. J Diabetes Sci Technol. 2016 Sep 30.

Hillier TA, et al. **Screening for gestational diabetes** mellitus: a systematic review for the U.S. Preventive Services Task Force. Ann Intern Med. 2008 May 20;148(10):766-75. Limited evidence suggests that gestational diabetes treatment after 24 weeks improves some maternal and neonatal outcomes. Evidence is even more sparse for screening before 24 weeks` gestation.

Hillmer M, Sandoval GA, Elliott JA, et al. Diabetes risk reduction in primary care: Evaluation of the Ontario Primary Care Diabetes Prevention Program. Can J Public Health. 2017 Jun 16;108(2):e176-e184.

Hingorani A, LaMuraglia GM, Henke P, et al. The management of **diabetic foot**: A clinical practice guideline by the Society for Vascular Surgery in collaboration with the **American** Podiatric Medical Association and the Society for Vascular Medicine. J Vasc Surg. 2016 Feb;63(2 Suppl):3S-21S.

Hinkle S, Laughon S, Catov J, Olsen J, Bech B. **First trimester coffee and tea intake and risk of gestational diabetes mellitus**: a study within a national birth cohort. BJOG. 2015 Feb;122(3):420-8.

Hinkle SN, Buck Louis GM, Rawal S,et al. A longitudinal study of **depression and gestational diabetes** in pregnancy and the postpartum period. Diabetologia. 2016 Sep 19.

Hippisley-Cox J, Coupland C, Robson J, Sheikh A, Brindle P. **Predicting risk of type 2 diabetes** in England and Wales: prospective derivation and validation of **QDScore**. BMJ. 2009 Mar 17;338:b880. doi: 10.1136/bmj.b880.

Hippisley-Cox J, Coupland C. Development and validation of risk prediction equations to **estimate future risk of blindness and lower limb amputation** in patients with diabetes: cohort study. BMJ 2015;351:h5441.

Hippisley-Cox J, Coupland C. Diabetes treatments and **risk of amputation, blindness, severe kidney failure, hyperglycaemia, and hypoglycaemia**: open cohort study in primary care. BMJ 2016;352:i1450.

Hippisley-Cox J, Coupland C. **Diabetes treatments and risk of heart failure**, cardiovascular disease, and all cause mortality: cohort study in primary care.BMJ. 2016 Jul 12;354:i3477.

Hippisley-Cox J, Coupland C. Development and validation of **QDiabetes-2018** risk prediction algorithm to estimate future risk of type 2 diabetes: cohort study. BMJ. 2017 Nov 20;359:j5019.

Hirsch IB. The Future of the **GLP-1 Receptor Agonists**. JAMA. 2019 Mar 23.

Hirschfeld G, von Glischinski M, Blankenburg M, et al. **Screening for Peripheral Neuropathies in Children** With Diabetes: A Systematic Review. Pediatrics. 2014 Apr 7.

Hirst JA, Farmer AJ, Feakins BG, et al. Quantifying the effects of **diuretics and beta-blockers** on glycaemic control in diabetes mellitus - a systematic review and meta-analysis. Br J Clin Pharmacol. 2014 Nov 6.

Hitchings AW, Lai D, Jones PW, et al. **Metformin** in severe exacerbations of **chronic obstructive pulmonary disease**: a randomised controlled trial. Thorax. 2016 Feb 25.

Ho PM, Rumsfeld JS, Masoudi FA, et al. Effect of **medication nonadherence** on hospitalization and mortality among patients with diabetes mellitus. Arch Intern Med 2006; 166: 1836-1841.

Ho JM, Juurlink DN. Considerations when prescribing **trimethoprim-sulfamethoxazole**. CMAJ. 2011 Oct 11.

Hober D, Sane F. **Enteroviruses** and type 1 diabetes. BMJ. 2011 Feb 3;342:c7072. doi: 10.1136/bmj.c7072.

Hochsmann C, Muller O, Ambuhl M, et al. Novel **Smartphone Game Improves Physical Activity Behavior** in Type 2 Diabetes. Am J Prev Med. 2019 Jul;57(1):41-50.

Holden SE, Jenkins-Jones S, Currie CJ. Association between **Insulin Monotherapy versus Insulin plus Metformin** and the Risk of All-Cause **Mortality** and Other Serious Outcomes: A Retrospective Cohort Study. PLoS One. 2016 May 6;11(5):e0153594.

Holman RR, Thorne KI, Farmer AJ, Davies MJ, Keenan JF, Paul S, Levy JC; the **4-T Study** Group. Addition of Biphasic, Prandial, or Basal Insulin to Oral Therapy in Type 2 Diabetes. N Engl J Med. 2007 Sep 21; [Epub ahead of print] A single analogue-insulin formulation added to **metformin & sulfonylurea** resulted in a glycated hemoglobin level of 6.5% or less in a minority of patients at 1 year. The addition of biphasic or prandial insulin aspart reduced levels more than the addition of basal insulin detemir but were associated with greater risks of hypoglycemia and weight gain.

Holman, Rury R., Farmer, Andrew J., Davies, Melanie J., et al. the **4-T** Study Group, **Three-Year Efficacy of Complex Insulin Regimens in Type 2 Diabetes.**N Engl J Med 2009 0: NEJMoa0905479.

Holman RR, Paul SK, Bethel MA, Neil HA, Matthews DR. Long-Term Follow-up after Tight Control of Blood Pressure in Type 2 Diabetes. N Engl J Med. 2008 Sep 10. [Epub ahead of print] (**UKPDS 81**) The benefits of previously improved blood-pressure control were not sustained when between-group differences in blood pressure were lost. Early improvement in blood-pressure control in patients with both type 2 diabetes and hypertension was associated with a reduced risk of complications, but it appears that good blood-pressure control must be continued if the benefits are to be maintained.

Holman RR, Paul SK, Bethel MA, Matthews DR, Neil HA. **10-Year Follow-up** of Intensive Glucose Control in Type 2 Diabetes. (**UKPDS-80**) N Engl J Med. 2008 Sep 10. [Epub ahead of print] Despite an early loss of glycemic differences, a continued reduction in microvascular risk and emergent risk reductions for myocardial infarction and death from any cause were observed during 10 years of post-trial follow-up. A continued benefit after metformin therapy was evident among overweight patients.

Holman RR, Sourij H, Califf RM. **Cardiovascular outcome trials of glucose-lowering drugs** or strategies in type 2 diabetes. Lancet. 2014 Jun 7;383(9933):2008-2017.

Holman RR, Coleman RL, Chan JCN, et al, for the **ACE** Study Group. Effects of **acarbose** on cardiovascular and diabetes outcomes in patients with coronary heart disease and impaired glucose tolerance (ACE): a randomised, double-blind, placebo-controlled trial. Lancet Diabetes Endocrinol 2017; online Sept 13.

Holman RR, Bethel MA, Mentz RJ, et al. Effects of **Once-Weekly Exenatide** on Cardiovascular Outcomes in Type 2 Diabetes. (**EXSCEL**) N Engl J Med. 2017 Sep 14.

Holmes RS, Crabtree E, McDonagh MS Comparative **effectiveness and harms of long-acting insulins for type 1 and type 2 diabetes**: A systematic review and meta-analysis. Diabetes Obes Metab. 2018 Dec 15.

Holst C, Becker U, Jørgensen ME, et al. **Alcohol** drinking patterns and risk of **diabetes**: a cohort study of 70,551 men and women from the general Danish population. Diabetologia. 2017 Jul 27.

Holstein A, Plaschke A, Egberts EH. Lower incidence of **severe hypoglycaemia in patients with type 2 diabetes treated with glimepiride versus glibenclamide**. Diabetes Metab Res Rev. 2001 Nov-Dec;17(6):467-73.

Holzinger Ulrike, Warszawska Joanna, Kitzberger Reinhard. **Real-Time Continuous Glucose Monitoring** in Critically Ill Patients: A prospective randomized trial. Diabetes Care March 2010 33:467-472.;

Holzmann MJ, Rathsman B, Eliasson N, et al. Long-term prognosis in patients with **type 1 and 2 diabetes mellitus after coronary artery bypass grafting**. *J Am Coll Cardiol* 2015; 65:1644-1652.

Home P. **Cardiovascular outcome trials of glucose-lowering medications**: an update. Diabetologia. 2019 Jan 3.

Home PD;Bergenstal RM;Bolli GB;Ziemen M;Rojeski M;. Glycaemic control and hypoglycaemia during 12 months of randomized treatment with insulin glargine 300 U/mL versus glargine 100 U/mL in people with **type 1 diabetes** (**EDITION** 4). Diabetes Obes Metab. 2017 Jun 29.

Home P, Mant J, Diaz J, Turner C; Guideline Development Group. Management of type 2 diabetes: summary of updated **NICE guidance**. BMJ. **2008** Jun 7;336(7656):1306-8. http://www.nice.org.uk/guidance/index.jsp?action=byID&o=11983

Home PD, Pocock SJ, Beck-Nielsen H, et al. Rosiglitazone evaluated for cardiovascular outcomes in oral agent combination therapy for type 2 diabetes (**RECORD**): A multicentre, randomised, open-label trial. *Lancet* 2009; DOI:10.1016/S0140-6736(09)60953-3 Addition of rosiglitazone to glucose-lowering therapy in people with type 2 diabetes is confirmed to increase the risk of heart failure and of some fractures, mainly in women. Although the data are inconclusive about any possible effect on myocardial infarction, rosiglitazone does not increase the risk of overall cardiovascular morbidity or mortality compared with standard glucose-lowering drugs

Home PD, Bolli GB, Mathieu C, et al. Modulation of **insulin dose titration using a hypoglycaemia-sensitive algorithm**: insulin **glargine versus neutral protamine Hagedorn** insulin in insulin-naive people with type 2 diabetes. Diabetes Obes Metab. 2015 Jan;17(1):15-22.

Home PD; et al; Glycaemic control and hypoglycaemia during 12 months of randomized treatment with **insulin glargine 300 U/mL versus glargine 100 U/mL** in people with type 1 diabetes (**EDITION 4**). Diabetes Obes Metab. 2017 Jun 29.

Hong ES, Khang AR, Yoon JW, et al. Comparison between **sitagliptin as add-on therapy to insulin** and insulin dose-increase therapy in uncontrolled Korean type 2 diabetes: CSI study. Diabetes Obes Metab. 2012 Sep;14(9):795-802.

Hong J, Zhang Y, Lai S, et al. Effects of **metformin versus glipizide** on cardiovascular outcomes in patients with type 2 diabetes and coronary artery disease. Diabetes Care 2012.

Hong KN, Fuster V, Rosenson RS, et al. **How Low to Go With Glucose, Cholesterol, and Blood Pressure in Primary Prevention of CVD**. J Am Coll Cardiol. 2017 Oct 24;70(17):2171-2185.

Hong JL, Buse JB, Jonsson Funk M, et al. The Risk of **Acute Pancreatitis After Initiation of Dipeptidyl Peptidase 4 Inhibitors**: Testing a Hypothesis of Subgroup Differences in Older U.S. Adults. Diabetes Care. 2018 Apr 4.

Honsek C, Kabisch S, Kemper M, et al. **Fibre supplementation for the prevention of type 2 diabetes** and improvement of glucose metabolism: the randomized controlled Optimal Fibre Trial (OptiFiT). Diabetologia. 2018 Jun;61(6):1295-1305.

Hood KK, Iturralde E, Rausch J, et al. **Preventing Diabetes Distress in Adolescents With Type 1 Diabetes**: Results One Year After Participation in the STePS Program. Diabetes Care. 2018 Jun 19.

Hooper P, Boucher MC, Cruess A, et al. **Canadian Ophthalmological Society** evidence-based clinical practice guidelines for the management of **diabetic retinopathy**. Can J Ophthalmol 2012;47:1–30. http://www.eyesite.ca/resources/CPGs/COS-Diabetic-Retinopathy_e.pdf (accessed June 19, 2012

Hooper P, Boucher MC, Cruess A, et al. Excerpt from the **Canadian Ophthalmological Society** evidence-based clinical practice guidelines for the **management of diabetic retinopathy**. Can J Ophthalmol. 2017 Nov;52 Suppl 1:S45-S74.

Horikawa C, Yoshimura Y, Kamada C, et al. **Dietary intake** in Japanese patients with type 2 diabetes: Analysis from Japan Diabetes Complications Study. J Diabetes Investig. 2014 Mar 23;5(2):176-87.

Horvath K, Koch K, Jeitler K, et al. Effects of treatment in women with **gestational diabetes** mellitus: systematic review and meta-analysis. BMJ. 2010 Apr 1.

Hou C, Xu Q, Diao S, et al. **Mobile phone applications and self-management of diabetes**: A systematic review with meta-analysis, meta-regression of 21 randomized trials and GRADE. Diabetes Obes Metab. 2018 Mar 27.

Hou WH, Chang KC, Li CY, et al. **Dipeptidyl peptidase-4 inhibitor use is associated with decreased risk of fracture** in patients with type 2 diabetes: a population-based cohort study. Br J Clin Pharmacol. 2018 May 16.

House Andrew A.; Eliasziw Misha; Cattran Daniel C.; et al. Effect of **B-Vitamin Therapy** on Progression of Diabetic Nephropathy: A Randomized Controlled Trial. *JAMA*. 2010;303(16):1603-1609.

Housden L, Wong ST, Dawes M. Effectiveness of **group medical visits for improving diabetes care**: a systematic review and meta-analysis. CMAJ. 2013 Sep 17;185(13):E635-44.

Hovorka R, Kumareswaran K, Harris J, Allen JM, Elleri D, Xing D, et al. **Overnight closed loop insulin delivery (artificial pancreas)** in adults with type 1 diabetes: crossover randomised controlled studies. BMJ 2011;342:1855.

Howard BV, et al. Coronary heart disease risk equivalence in diabetes depends on **concomitant risk factors**. Diabetes Care. 2006 Feb;29(2):391-7.

Howard BV, Manson JE, Stefanick ML, Beresford SA, et al. **Low-fat dietary pattern** and weight change over 7 years: the Women's Health Initiative Dietary Modification Trial. JAMA. 2006 Jan 4;295(1):39-49. (InfoPOEMs: Following the long-term recommendations to reduce dietary fat and increase consumption of fruits, vegetables, and whole grains does not cause weight gain among postmenopausal women. (LOE = 2b))

Howard BV, et al. **Low-fat dietary** pattern and risk of cardiovascular disease: the Women's Health Initiative Randomized Controlled Dietary Modification Trial. JAMA. 2006 Feb 8;295(6):655-66.

Howard BV, Roman MJ, Devereux RB, et al. Effect of **lower targets for blood pressure and LDL** cholesterol on atherosclerosis in diabetes: The **SANDS** randomized trial. JAMA. 2008;299:1678-1689. Reducing LDL-C and SBP to lower targets resulted in regression of carotid IMT and greater decrease in left ventricular mass in individuals with type 2 diabetes. Clinical events were lower than expected and did not differ significantly between groups. Further follow-up is needed to determine whether these improvements will result in lower long-term CVD event rates and costs and favorable risk-benefit outcomes.

Howard-Thompson A, Khan M, Jones M eta al. Type 2 Diabetes Mellitus: **Outpatient Insulin Management**. Am Fam Physician. 2018;97(1):29-37.

Howse PM, Chibrikova LN, Twells LK, et al. Safety and Efficacy of **Incretin-Based Therapies** in Patients With Type 2 Diabetes Mellitus and **CKD**: A Systematic Review and Meta-analysis. Am J Kidney Dis. 2016 Aug 12.

Hruby A, Meigs JB, O'Donnell CJ, Jacques PF, McKeown NM. Higher **magnesium** intake reduces risk of impaired glucose and insulin metabolism and progression from prediabetes to diabetes in middle-aged americans. Diabetes Care. 2014 Feb;37(2):419-27.

Hsiao FY, et al. **Thiazolidinediones** and Cardiovascular Events in Patients with Type 2 Diabetes Mellitus: A Retrospective Cohort Study of over 473 000 Patients Using the National Health Insurance Database in Taiwan. Drug Saf. 2009;32(8):675-90.

Hsu A, Gan S, Cenzer-Stijacic I, et al. **Glycemic Control and Functional Decline in Nursing Home** Residents With Diabetes. JAMA Intern Med. 2016 Nov 21.

Hsu CC, Almulaifi A, Chen JC, et al. Effect of **Bariatric Surgery vs Medical Treatment** on Type 2 **Diabetes** in Patients With Body Mass Index Lower Than 35: Five-Year Outcomes. JAMA Surg. 2015 Sep 16:1-8.

Hsu JC, Ross-Degnan D, Wagner AK, et al. How Did Multiple **FDA Actions** Affect the Utilization and Reimbursed Costs of **Thiazolidinediones** in US Medicaid? Clin Ther. 2015 May 11.

Htike ZZ, Zaccardi F, Papamargaritis D, et al. Efficacy and safety of **glucagon-like peptide-1 receptor agonists** in type 2 diabetes: A systematic review and mixed-treatment comparison analysis. Diabetes Obes Metab. 2016 Dec 15.

Hu E, Pan A, Malik V, Sun Q. **White rice consumption** and risk of type 2 diabetes: meta-analysis and systematic review. BMJ 2012;344:e1454.

Hua X, Carvalho N, Tew M, et al. **Expenditures** and Prices of **Antihyperglycemic Medications in the United States**: 2002-2013. JAMA. 2016 Apr 5;315(13):1400-2.

Huang CJ, Wang WT, Sung SH, et al. Blood glucose reduction by **diabetic drugs with minimal hypoglycaemia risk for cardiovascular outcomes**: Evidence from meta-regression analysis of randomized controlled trials. Diabetes Obes Metab. 2018 May 2.

Huang ES, Laiteerapong N, Liu JY, et al. **Rates of Complications and Mortality in Older Patients** With Diabetes Mellitus: The Diabetes and Aging Study. JAMA Intern Med. 2013 Dec 9

Huang ES. Potential **Overtreatment of Older, Complex Adults** With Diabetes. JAMA. 2015 Sep 22-29;314(12):1280-1.

Huang ES. Management of **diabetes mellitus in older people with comorbidities**. BMJ. 2016 Jun 15;353:i2200.

Huang Y, Cai X, Qiu M, et al. **Prediabetes** and the **risk of cancer**: a meta-analysis. Diabetologia. 2014 Sep 11.

Huang ES, Davis AM. **Glycemic Control in Older Adults** With Diabetes Mellitus. JAMA. 2015 Oct 13;314(14):1509-10.

Huang W, Mirza RG, Molitch ME. What Does This **Retina Examination** Show? (**Diabetic retinopathy**) JAMA. 2015 Dec 15;314(23):2555-2556.

Huang Y, Cai X, Mai W, et al. Association between **prediabetes** and risk of cardiovascular disease and all cause mortality: systematic review and meta-analysis. BMJ. 2016 Nov 23;355:i5953.

Hughes RC, Rowan JA. **Pregnancy** in women with Type 2 diabetes: who takes **metformin** and what is the outcome? Diabet Med. 2006 Mar;23(3):318-22.

Hughes R. Investigation of **peripheral neuropathy**. BMJ. 2010 Nov 5;341:c6100. doi: 10.1136/bmj.c6100.

Hughes RC, Moore MP, Gullam JE, et al. An **Early Pregnancy HbA1c ≥5.9%** (41 mmol/mol) Is Optimal for Detecting Diabetes and Identifies Women at Increased Risk of **Adverse Pregnancy Outcomes**. Diabetes Care. 2014 Nov;37(11):2953-9.

Hui E, Bravis V, Hassanein M, et al. Management of people with diabetes wanting to fast during **Ramadan**. BMJ 2010;340:c3053.

Humphrey LL, Kansagara D, Qaseem A; High Value Care Committee of the American College of Physicians. **World Health Organization Guidelines on Medicines for Diabetes Treatment Intensification**: Commentary From the American College of Physicians High Value Care Committee. Ann Intern Med. 2018 Sep 18;169(6):398-400.

Huang Y, Hessami-Booshehri M. **Acanthosis nigricans** at sites of insulin injection in a man with diabetes. CMAJ. 2018 Nov 26;190(47):E1390.

Hung SC, Chang YK, Liu JS, et al. **Metformin** use and **mortality in patients with advanced chronic kidney disease**: national, retrospective, observational, cohort study. Lancet Diabetes Endocrinol. 2015 Aug;3(8):605-614.

Hung YC, Lin CC, Chen HJ, et al. **Severe hypoglycemia and hip fracture** in patients with type 2 diabetes: a nationwide population-based cohort study. Osteoporos Int. 2017 Apr 3.

Hunt B, Kragh N, McConnachie CC, et al. **Long-Term Cost-Effectiveness of Two GLP-1 Receptor Agonists** for the Treatment of Type 2 Diabetes Mellitus in the Italian Setting: Liraglutide Versus Lixisenatide. Clin Ther. 2017 Jun 15.

Huo L, Magliano DJ, Rancière F, et al. Impact of **age at diagnosis and duration of type 2 diabetes on mortality** in Australia 1997-2011. Diabetologia. 2018 Feb 22.

Huo X, Gao L, Guo L, et al. **Risk of non-fatal cardiovascular diseases in early-onset versus late-onset** type 2 diabetes in China: a cross-sectional study. Lancet Diabetes Endocrinol. 2015 Dec 15.

Huo X, Krumholz HM, Bai X, et al. Effects of **Mobile Text Messaging on Glycemic Control** in Patients With Coronary Heart Disease and Diabetes Mellitus. Circ Cardiovasc Qual Outcomes. 2019 Sep;12(9):e005805.

Husain M, Birkenfeld AL, Donsmark M, et al; PIONEER 6 Investigators. **Oral Semaglutide and Cardiovascular Outcomes** in Patients with Type 2 Diabetes. N Engl J Med. 2019 Jun 11.

Hussain MA, Al-Omran M, Salata K, et al. Population-based secular **trends in lower-extremity amputation** for diabetes and peripheral artery disease. CMAJ 2019;191:E955-61.

Hussein H, Zaccardi F, Khunti K, et al. **Cardiovascular efficacy and safety** of sodium-glucose co-transporter-2 inhibitors and glucagon-like peptide-1 receptor agonists: a systematic review and network meta-analysis. Diabet Med. 2019 Apr;36(4):444-452.

Hutchison AT, Regmi P, Manoogian ENC, et al. **Time-Restricted Feeding** Improves Glucose Tolerance in Men at Risk for Type 2 Diabetes: A Randomized Crossover Trial. Obesity (Silver Spring). 2019 May;27(5):724-732.

Huxley R, Barzi F, Woodward M. Excess risk of **fatal coronary heart disease** associated with **diabetes** in men and **women**: meta-analysis of 37 prospective cohort studies. BMJ. 2005 Dec 21; [Epub ahead of print]

Huxley RR, Peters SA, Mishra GD, Woodward M. Risk of all-cause **mortality and vascular events in women versus men** with type 1 diabetes: a systematic review and meta-analysis. Lancet Diabetes Endocrinol. 2015 Mar;3(3):198-206.

Hwang TS, Hagag AM, Wang J, et al. Automated **quantification of nonperfusion areas in 3 vascular plexuses with optical coherence tomography angiography in eyes of patients with diabetes** [online June 14, 2018]. JAMA Ophthalmol.doi:10.1001/jamaophthalmol.2018.2257

Hyman I, Shakya Y, Jembere N, et al. Provider- and patient-related determinants of **diabetes self-management** among recent immigrants: Implications for systemic change. Can Fam Physician. 2017 Feb;63(2):e137-e144.
Ibanez L, et al. Metformin therapy during puberty delays menarche, prolongs pubertal growth, and augments adult height: a randomized study in **low-birth-weight girls** with early-normal onset of puberty. J Clin Endocrinol Metab. 2006 Jun;91(6):2068-73. Epub 2006 Feb 21. (InfoPOEMs: Three years of metformin treatment resulted in a mean increase of at least an additional 3.5 cm of adult height in girls with history of low birth weight (LBW) and onset of puberty at 8 to 9 years of age. Larger studies are needed to assess safety, and to address girls with early-normal onset of puberty associated with insulin resistance but without history of LBW. (LOE = 1b-))
Ibañez J, Izquierdo M, Argüelles I, et al. Twice-weekly **progressive resistance training** decreases abdominal fat and improves insulin sensitivity in older men with type 2 diabetes. Diabetes Care. 2005 Mar;28(3):662-7.
IDF: International Diabetes Federation. **Bariatric surgical** and procedural interventions in the treatment of obese patients with type 2 diabetes 2011 http://www.idf.org/webdata/docs/IDF-Position-Statement-Bariatric-Surgery.pdf
Idris I, Warren G, Donnelly R. Association between **thiazolidinedione treatment and risk of macular edema** among patients with type 2 diabetes [published online June 11, 2012]. Arch Intern Med. doi:10.1001/archinternmed
Ilany J, et al. Effect of **prandial treatment timing adjustment, based on continuous glucose monitoring**, in patients with type 2 diabetes uncontrolled with once-daily basal insulin: randomized, phase IV. Diabetes Obes Metab. 2018 May;20(5):1186-1192.
Ijas H, Vaarasmaki M, Morin-Papunen L, et al. **Metformin should be considered in the treatment of gestational diabetes**: a prospective randomised study. BJOG. 2011 Jun;118(7):880-5.
Ijas H, Vaarasmaki M, Saarela T, et al. A follow-up of a randomised study of **metformin and insulin in gestational diabetes** mellitus: growth and development of the children at the age of 18 months. BJOG. 2014 Jul 16.
Ikramuddin S, Korner J, Lee W-J, et al. **Roux-en-Y gastric bypass** vs intensive medical management for the control of type 2 diabetes, hypertension, and hyperlipidemia: The Diabetes Surgery Study randomized clinical trial. JAMA 2013; 309:2240-2249.
Ikramuddin S, Billington CJ, Lee WJ, et al. **Roux-en-Y gastric bypass for diabetes** (the Diabetes Surgery Study): 2-year outcomes of a 5-year, randomised, controlled trial. Lancet Diabetes Endocrinol. 2015 Jun;3(6):413-22.
Ikramuddin S, Korner J, Lee WJ, et al. Durability of Addition of **Roux-en-Y Gastric Bypass to Lifestyle Intervention and Medical Management** in Achieving Primary Treatment Goals for Uncontrolled Type 2 Diabetes in Mild-to-Moderate Obesity: A Randomized Control Trial. Diabetes Care. 2016 Jun 16.
Imamura F, O'Connor L, Ye Z, et al. **Consumption of sugar sweetened beverages, artificially sweetened beverages, and fruit juice** and incidence of type 2 **diabetes**: systematic review, meta-analysis, and estimation of population attributable fraction. BMJ. 2015 Jul 21;351:h3576.
Imamura F, Fretts A, Marklund M, et al; Fatty Acids and Outcomes Research Consortium (FORCE). **Fatty acid biomarkers of dairy fat consumption and incidence of type 2 diabetes**: A pooled analysis of prospective cohort studies. PLoS Med. 2018 Oct 10;15(10):e1002670.
Imfeld P, Bodmer M, Jick SS, Meier CR. **Metformin**, Other Antidiabetic Drugs, and **Risk of Alzheimer's** Disease: A Population-Based Case-Control Study. J Am Geriatr Soc. 2012 Mar 28. **International** Expert Comittee. International Expert Committee Report on the Role of the **A1C Assay in the Diagnosis of Diabetes**. Diabetes Care. 2009 Jun 5. [Epub ahead of print]
Inagaki N, Atsumi Y, Oura T et al. Efficacy and Safety Profile of **Exenatide Once Weekly** Compared With Insulin Once Daily in Japanese Patients With Type 2 Diabetes Treated With Oral Antidiabetes Drug(s): Results From a 26-Week, Randomized, Open-Label, Parallel-Group, Multicenter, Noninferiority Study. Clin Ther. 2012 Aug 9.
Inagaki N, Kondo K, Yoshinari T, et al. Efficacy and safety of **canagliflozin** in Japanese patients with type 2 diabetes: a randomized, double-blind, placebo-controlled, 12-week study. Diabetes Obes Metab. 2013 Jun 19.
Inge TH, Laffel LM, Jenkins TM, et al. Comparison of **Surgical and Medical Therapy for Type 2 Diabetes in Severely Obese Adolescents**. JAMA Pediatr. 2018 Mar 12.
Inoue H, Tamaki Y, Kashihara Y, et al. Efficacy of **DPP-4 inhibitors, GLP-1 analogues, and SGLT2 inhibitors as add-ons to metformin monotherapy** in T2DM patients: A model-based meta-analysis (149/150). Br J Clin Pharmacol. 2018 Nov 5.
Insel RA, Dunne JL, Atkinson MA, et al. **Staging presymptomatic type 1 diabetes**: a scientific statement of **JDRF**, the **Endocrine** Society, and the **American** Diabetes Association. Diabetes Care. 2015 Oct;38(10):1964-74.
Institute for Safe Medication Practices. Perspectives **(pancreatitis, cancer…) on GLP-1 agents** for diabetes. 18 Apr 2013. www.ismp.org/QuarterWatch/pdfs/2012Q3.pdf .
InterAct Consortium. Consumption of **sweet beverages** and type 2 diabetes incidence in European adults: results from **EPIC-InterAct**. Diabetologia 2013; DOI:10.1007/s00125-013-2899-8.
InterAct Consortium. **Dietary fibre** and incidence of type 2 diabetes in eight European countries: the **EPIC-InterAct Study** and a meta-analysis of prospective studies. Diabetologia. 2015 May 29.
International Association of Diabetes and **Pregnancy** Study Groups Consensus Panel. International Association of Diabetes and Pregnancy Study Groups Recommendations on the Diagnosis and Classification of Hyperglycemia in Pregnancy. Diabetes Care March 2010 33:676-682
International **Hypoglycaemia** Study Group. Glucose concentrations of **less than 3.0 mmol**/L (54 mg/dL) should be reported in clinical trials: a joint position statement of the American Diabetes Association and the European Association for the Study of Diabetes. Diabetes Care. 2017;40(1):155-157.
International Diabetes Federation and Diabetes and Ramadan International Alliance. **Diabetes and Ramadan**: Practical Guidelines. April 2016. http://www.daralliance.org/daralliance/wp-content/uploads/IDF-DAR-Practical-Guidelines_15-April-2016_low.pdf Accessed December 11, 2016.
International Hypoglycaemia Study Group. **Hypoglycaemia, cardiovascular disease, and mortality in diabetes**: epidemiology, pathogenesis, and management. Lancet Diabetes Endocrinol. 2019 Mar 26.
Inzucchi SE, Bergenstal RM, Buse JB, et al. **Management of Hyperglycemia in Type 2 Diabetes**: A Patient-Centered Approach: Position Statement of the American Diabetes Association (**ADA**) and the European Association for the Study of Diabetes(**EASD**). Diabetes Care. 2012 Apr 19.
Inzucchi SE, Lipska KJ, Mayo H, et al. **Metformin** in patients with type 2 diabetes and **kidney disease**: a systematic review. JAMA. 2014 Dec 24-31;312(24):2668-75.
Inzucchi SE, Bergenstal RM, Buse JB, et al. **Management of hyperglycaemia in type 2 diabetes, 2015:** a patient-centred approach. Update to a Position Statement of the American Diabetes Association (**ADA**) and the European Association for the Study of Diabetes(**EASD**).. Diabetologia. 2015 Mar;58(3):429-42.
Inzucchi SE, Viscoli CM, Young LH, et al. **Pioglitazone Prevents Diabetes** in Insulin-Resistant Patients With Cerebrovascular Disease. Diabetes Care. 2016 Jul 27
Inzucchi SE, Iliev H, Pfarr E, et al. **Empagliflozin** and Assessment of **Lower-Limb Amputations** in the **EMPA-REG OUTCOME** Trial. Diabetes Care. 2017 Nov 13.
Inzucchi SE, Zinman B, Fitchett D, et al. How Does **Empagliflozin Reduce Cardiovascular Mortality**? Insights From a Mediation Analysis of the EMPA-REG OUTCOME Trial. Diabetes Care. 2018 Feb;41(2):356-363.
Ioannides-Demos LL, Proietto J, McNeil JJ. Pharmacotherapy for **obesity**. Drugs. 2005;65(10):1391-418.
Iqbal Z, Azmi S, Yadav R, et al. **Diabetic Peripheral Neuropathy**: Epidemiology, Diagnosis, and Pharmacotherapy. Clin Ther. 2018 Apr 27.
Ishihara H, Yamaguchi S, et al. Efficacy and safety of **ipragliflozin** as add-on therapy to insulin in Japanese patients with type 2 diabetes mellitus (IOLITE): a multi-centre, randomized, placebo-controlled, double-blind study. Diabetes Obes Metab. 2016 Jul 20.
Ishikawa S, Shimano M, Watarai M, et al. Impact of **Sitagliptin on Carotid Intima-Media Thickness** in Patients With Coronary Artery Disease and Impaired Glucose Tolerance or Mild Diabetes Mellitus. Am J Cardiol. 2014 May 16.
Ishoy PL, Knop FK, Broberg BV, et al. Effect of **GLP-1 receptor agonist treatment on body weight in obese antipsychotic-treated** patients with schizophrenia: a randomized, placebo-controlled trial. Diabetes Obes Metab. 2016 Sep 26.
Ismail-Beigi Faramarz, Moghissi Etie, Tiktin Margaret, et al. **Individualizing Glycemic Targets** in Type 2 Diabetes Mellitus: Implications of Recent Clinical Trials. *Ann Intern Med* April 19, 2011 154:554-559.
Ismail-Beigi F. Clinical practice. **Glycemic management of type 2 diabetes mellitus**. N Engl J Med. 2012 Apr 5;366(14):1319-27.
Ismail-Beigi F, Craven TE, O`Connor PJ, et al. Combined intensive **blood pressure and glycemic** control does not produce an additive benefit on microvascular outcomes in type 2 diabetic patients. (**ACCORD**) Kidney Int. 2012 Mar;81(6):586-94.
Ismail-Beigi F, Moghissi E, Kosiborod M, et al. **Shifting Paradigms in the Medical Management of Type 2 Diabetes**: Reflections on Recent Cardiovascular Outcome Trials. J Gen Intern Med. 2017 May 26.
Iványi T, Fövényi J, Faludi P, et al. Long-Term Effects (up to 132 weeks) of Adding **Exenatide** to a Regimen of Metformin and/or Sulfonylurea in Type 2 Diabetes: An Uncontrolled, Open-Label Trial in Hungary. Clin Ther. 2012 May 16.
Iversen, L., Bygum, A. **Diabetic dermopathy**. BMJ 2018;363:k4882.
Jabbour SA, Hardy E, Sugg J, et al; Study 10 Group. **Dapagliflozin** Is Effective as Add-on Therapy to Sitagliptin With or Without Metformin: A 24-Week, Multicenter, Randomized, Double-Blind, Placebo-Controlled Study. Diabetes Care. 2014 Mar;37(3):740-50.
Jabbour S;Seufert J;Scheen A;et al. **Dapagliflozin** in patients with type 2 diabetes mellitus: A pooled analysis of safety data from phase IIb/III clinical trials. Diabetes Obes Metab. 2017 Sep 26.
Jackson GL, Smith VA, Edelman D, et al. **Intermediate diabetes outcomes in patients managed by physicians, nurse practitioners, or physician assistants**. A cohort study. Ann Intern Med. 2018. [Epub ahead of print]. doi:10.7326/M17-1987
Jacobson AM, Braffett BH, Cleary PA, et al. The **Long-Term Effects of Type 1 Diabetes** Treatment and Complications on Health-Related Quality of Life: A 23-year follow-up of the Diabetes Control and Complications/Epidemiology of Diabetes Interventions and Complications cohort. Diabetes Care. 2013 Jul 8.
Jaiswal M, Divers J, Dabelea D, et al. Prevalence of and Risk Factors for Diabetic **Peripheral Neuropathy** in **Youth** With Type 1 and Type 2 Diabetes: SEARCH for Diabetes in Youth Study. Diabetes Care. 2017 Jul 3
Jakubowicz D, Wainstein J, Ahrén B, et al. **High-energy breakfast with low-energy dinner** decreases overall daily hyperglycaemia in type 2 diabetic patients: a randomised clinical trial. Diabetologia. 2015 Mar 1.
Jamerson KA. Should Certain **Antihyperglycemic Medications Be Preferred Over Antihypertensive Medications for Blood Pressure Control** in Special Populations With Diabetes Mellitus? Circulation. 2019 Apr 30;139(18):2110-2112.
James PA, Oparil S, Carter BL, et al. **2014** evidence-based guideline for the management of **high blood pressure in adults**: report from the panel members appointed to the Eighth Joint National Committee (**JNC 8**). JAMA. doi:10.1001/jama.2013.284427.
Jampol LM, Bressler NM, Glassman AR. Revolution to a new standard treatment of **diabetic macular edema**. JAMA. doi:10.1001 /jama.2014.2536.
Jansson SP, Andersson DK, Svärdsudd K. Effects of fasting blood **glucose, diabetes treatment, blood pressure** and anti-hypertension treatment on cardiovascular disease incidence: a 30-year follow-up study of 740 incident patients with Type 2 diabetes.

Diabet Med. 2013 Mar;30(3):349-57.
Januzzi JL Jr., Butler J, Jarolim P, et al. Effects of **canagliflozin** on cardiovascular biomarkers in older adults with type 2 diabetes. J Am Coll Cardiol 2017;70:704–12.
Jarskog LF, Hamer RM, Catellier DJ, et al; for the METS Investigators. **Metformin for Weight Loss** and Metabolic Control in Overweight Outpatients With **Schizophrenia** and Schizoaffective Disorder. Am J Psychiatry. 2013 Jul 12.
Jeffcoate WJ, Vileikyte L, Boyko EJ, et al. Current Challenges and Opportunities in the Prevention and **Management of Diabetic Foot Ulcers**. Diabetes Care. 2018 Apr;41(4):645-652.
Jenkins DJ, Kendall CW, McKeown-Eyssen G, et al. Effect of a **low-glycemic index or a high-cereal fiber** diet on type 2 diabetes: a randomized trial. JAMA. 2008 Dec 17;300(23):2742-53. In the low-glycaemic diet, beans, peas, lentils, nuts, pasta, and briefly boiled rice were emphasised. Breads (including pumpernickel, rye pita, and quinoa and flaxseed) and breakfast cereals (including large-flake oatmeal and oat bran) were emphasised in the low-glycaemic diet. In patients with type 2 diabetes, 6-month treatment with a low-glycemic index diet resulted in moderately lower HbA(1c) levels compared with a high-cereal fiber diet.
Jenkins DJA, Kendall CWC, Augustin LSA, et al. Effect of **legumes** as part of a **low glycemic index diet** on glycemic control and cardiovascular risk factors in type 2 diabetes [online October 22, 2012. Arch Intern Med. doi:10.1001/2013.jamainternmed.70.
Jenkins DJ, Kendall CW, Vuksan V, et al. Effect of Lowering the **Glycemic Load With Canola Oil** on Glycemic Control and Cardiovascular Risk Factors: A Randomized Controlled Trial. Diabetes Care. 2014 Jun 14.
Jess T, Jensen BW, Andersson M, et al. **Inflammatory Bowel Disease Increases Risk of Type 2 Diabetes** in a Nationwide Cohort Study. Clin Gastroenterol Hepatol. 2019 Aug 5.
Ji L, Ma J, Li H, et al. **Dapagliflozin** as Monotherapy in Drug-Naive Asian Patients With Type 2 Diabetes Mellitus: A Randomized, Blinded, Prospective Phase III Study. Clin Ther. 2013 Dec 27
Ji L, Liu J, Yang J, et al. Comparative effectiveness of **metformin monotherapy in extended release and immediate release formulations** for the treatment of type 2 diabetes in treatment-naive Chinese patients: Analysis of results from the CONSENT trial. Diabetes Obes Metab. 2017 Dec 11.
Ji Q. Treatment Strategy for Type 2 **Diabetes with Obesity**: Focus on **Glucagon-Like Peptide-1 Receptor Agonists**. Clin Ther. 2017 May 16.
Jiang L, Johnson A, Pratte K, et al. Long-term Outcomes of Lifestyle Intervention to **Prevent Diabetes in American Indian and Alaska Native Communities**: The Special Diabetes Program for Indians Diabetes Prevention Program. Diabetes Care. 2018 Jul;41(7):1462-1470.
Jiang L, Wang K, Lo K, et al. Sex-specific Association of **Circulating Ferritin Levels and Risk of Type 2 Diabetes**: A Dose-response Meta-analysis of Prospective Studies. J Clin Endocrinol Metab. 2019 May 10
Jiao J, Liu G, Shin HJ, et al. **Dietary fats and mortality** among patients with type 2 diabetes: analysis in two population based cohort studies. BMJ. 2019 Jul 2;366:l4009.
Jin J. **Starting Insulin Treatment** for Diabetes. JAMA. 2014 Jun 11;311(22):2347.
Johansen MY, MacDonald CS, Hansen KB, et al. Effect of an Intensive Lifestyle Intervention on Glycemic Control in Patients With Type 2 Diabetes: A Randomized Clinical Trial. JAMA. 2017 Aug 15;318(7):637-646
Johnsen SP, et al. Risk and short-term prognosis of myocardial infarction among users of antidiabetic drugs. Am J Ther. 2006 Mar-Apr;13(2):134-40.
Johnson JF, Parsa R, Bailey RA. Real-world Clinical Outcomes Among Patients With Type 2 Diabetes Receiving **Canagliflozin** at a Specialty Diabetes Clinic: Subgroup Analysis by Baseline HbA(1c) and Age. Clin Ther. 2017 May 8.
Johnston R, Uthman O, Cummins E, et al. **Canagliflozin, dapagliflozin and empagliflozin monotherapy** for treating type 2 diabetes: systematic review and economic evaluation. Health Technol Assess. 2017 Jan;21(2):1-218.
Johnston Stephen S., Conner Christopher, Aagren Mark, et al. Evidence Linking **Hypoglycemic Events to an Increased Risk of Acute Cardiovascular Events** in Patients With Type 2 Diabetes. Diabetes Care May 2011 34:1164-1170; published ahead of print March 18, 2011, doi:10.2337/dc10-1915
Jokela M, et al. Trajectories of glycaemia, insulin sensitivity, and insulin secretion before diagnosis of type 2 diabetes: an analysis from the Whitehall II study. Lancet. 2009 Jun 8. [Epub ahead of print] In this study, we show changes in glucose concentrations, insulin sensitivity, and insulin secretion as much as 3-6 years before diagnosis of diabetes. The description of biomarker trajectories leading to diabetes diagnosis could contribute to more-accurate risk prediction models that use repeated measures available for patients through regular check-ups.
Johnston KC, Bruno A, Pauls Q, et al. Intensive vs Standard Treatment of Hyperglycemia and **Functional Outcome in Patients With Acute Ischemic Stroke**: The SHINE Randomized Clinical Trial. JAMA. 2019 Jul 23;322(4):326-335.
Jones LV, Ray A, Moy FM, et al. Techniques of **monitoring blood glucose during pregnancy** for women with pre-existing diabetes. Cochrane Database Syst Rev. 2019 May 23;5:CD009613. Two new studies (406 women) have been incorporated to one of the comparisons for this update. Although the evidence suggests that CGM in comparison to intermittent glucose monitoring may reduce hypertensive disorders of pregnancy, this did not translate into a clear reduction for pre-eclampsia, and so this result should be viewed with caution. No differences were observed for other primary outcomes for this comparison.
Jones M, Tett S, Peeters GM, et al. **New-Onset Diabetes** After **Statin Exposure in Elderly Women**: The Australian Longitudinal Study on Women's Health. Drugs Aging. 2017 Mar;34(3):203-209.
Joseph JJ, Echouffo-Tcheugui JB, Carnethon MRet al. The association of **ideal cardiovascular health with incident type 2 diabetes mellitus**: the Multi-Ethnic Study of Atherosclerosis. Diabetologia. 2016 Jun 8.
Joseph JJ, Bennett A, Echouffo Tcheugui JB, et al. **Ideal cardiovascular health, glycaemic status and incident type 2 diabetes mellitus**: the REasons for Geographic and Racial Differences in Stroke (**REGARDS**) study. Diabetologia. 2019 Jan 15.
Joseph S, Kim R, Ravindran RD, et al. Effectiveness of **Teleretinal Imaging-Based Hospital Referral Compared With Universal Referral in Identifying Diabetic Retinopathy**: A Cluster Randomized Clinical Trial. JAMA Ophthalmol. 2019 May 9.
Joshi PH, Kalyani RR, Blumenthal RS, Donner TW. **Cardiovascular effects of noninsulin**, glucose-lowering agents: need for more outcomes data. Am J Cardiol. 2012 Nov 6;110(9 Suppl):32B-42B.
Josse RG, Majumdar SR, Zheng Y, et al. **Sitagliptin and risk of fractures** in type 2 diabetes: Results from the **TECOS** trial. Diabetes Obes Metab. 2016 Oct 6.
Jovanovski E, Khayyat R, Zurbau A, et al. Should **Viscous Fiber Supplements Be Considered in Diabetes Control**? Results From a Systematic Review and Meta-analysis of Randomized Controlled Trials. Diabetes Care. 2019 Jan 7.
Juonala M, Jääskeläinen P, Sabin MA, et al. **Higher Maternal Body Mass Index** Is Associated with an Increased Risk for Later Type 2 Diabetes in Offspring. J Pediatr. 2012 Dec 19. Kaisari P, Yannakoulia M, Panagiotakos DB. Eating
Juurlink David N, Gomes Tara, Lipscombe Lorraine L, et al. Adverse cardiovascular events during treatment with pioglitazone and **rosiglitazone**: population based cohort study. BMJ 2009;339:b2942, doi: 10.1136/bmj.b2942 (Published 18 August 2009)
Juurlink DN, Gomes T, Shah BR, et al. Adverse **cardiovascular events** during treatment with **glyburide (glibenclamide) or gliclazide** in a high-risk population. Diabet Med. 2012 Dec;29(12):1524-8.
Juvenile Diabetes Research Foundation **Continuous Glucose Monitoring** Study JDRF Group, Tamborlane WV, Beck RW, Bode BW, et al. Continuous glucose monitoring and intensive treatment of type 1 diabetes. N Engl J Med. 2008 Oct 2;359(14):1464-76. Epub 2008 Sep 8.
Justesen TI, et al. **Albumin-to-creatinine ratio** in random urine samples might replace 24-h urine collections in screening for micro- and macroalbuminuria in pregnant woman with type 1 diabetes. Diabetes Care. 2006 Apr;29(4):924-5.
Kaakeh Y, Kanjee S, Boone K, Sutton J. **Liraglutide-induced acute kidney injury**. Pharmacotherapy 2012;32:e7-11.
Kadowaki T, Inagaki N, et al. Efficacy and safety of **canagliflozin** as add-on therapy to **teneligliptin** in Japanese patients with type 2 diabetes mellitus: results of a 24-week, randomised, double-blind, placebo-controlled trial. Diabetes Obes Metab. 2017 Feb 8.
Kadowaki T, Inagaki N, Kondo K, et al. Efficacy and safety of **teneligliptin added to canagliflozin** monotherapy in Japanese patients with type 2 diabetes mellitus: A multicentre, randomized, double-blind, placebo-controlled, parallel-group comparative study. Diabetes Obes Metab. 2017 Aug 8.
Kahal H, Abouda G, Rigby AS, et al. Glucagon-like peptide-1 analogue, **liraglutide, improves liver fibrosis** markers in obese women with **polycystic ovary syndrome** and nonalcoholic fatty liver disease. Clin Endocrinol (Oxf). 2013 Nov 21.
Kahkoska AR, Shay CM, Crandell J, et al. **Association of Race and Ethnicity With Glycemic Control and Hemoglobin A1c Levels in Youth With Type 1 Diabetes**. JAMA Netw Open. 2018;1(5):e181851.
Kahleova H, Belinova L, Malinska H, et al. Eating two larger meals a day (**breakfast and lunch**) is more effective than **six smaller meals** in a reduced-energy regimen for patients with type 2 diabetes: a randomised crossover study. Diabetologia. 2014 May 18.
Kahn PA, Wagner NE, Gabbay RA. **Underutilization of Glucagon** in the Prehospital Setting. Ann Intern Med. 2017 Dec 26.
Kahn R, Buse J, Ferrannini E, Stern M; American Diabetes Association; European Association for the Study of Diabetes. The **metabolic syndrome**: time for a critical appraisal: joint statement from the American Diabetes Association and the European Association for the Study of Diabetes. Diabetes Care. 2005 Sep;28(9):2289-304.
Kahn SE, Haffner SM, Heise MA, et al. Glycemic Durability of Rosiglitazone, Metformin, or Glyburide Monotherapy. (**ADOPT** trial) N Engl J Med. 2006 Dec 4; [Epub ahead of print] Calculated monotherapy failure at 5 years was 15% with rosiglitazone, 21% with metformin, and 34% with glyburide. Kaplan-Meier analysis showed a cumulative incidence of monotherapy failure at 5 years of 15% with rosiglitazone, 21% with metformin, and 34% with glyburide. This represents a risk reduction of 32% for rosiglitazone, as compared with metformin, and 63%, as compared with glyburide (P<0.001 for both comparisons). The difference in the durability of the treatment effect was greater between rosiglitazone and glyburide than between rosiglitazone and metformin. Glyburide was associated with a lower risk of cardiovascular events (including congestive heart failure) than was rosiglitazone (P<0.05), and the risk associated with metformin was similar to that with rosiglitazone. Rosiglitazone was associated with more weight gain, edema and fractures than either metformin or glyburide but with fewer gastrointestinal events than metformin and with less hypoglycemia than glyburide (P<0.001 for all comparisons). An editorialist criticizes the study's use of fasting glucose rather than glycated hemoglobin to ascertain failure. When looked at from the latter standpoint, he writes, rosiglitazone shows "a clinically less impressive effect. "Given the modest glycemic benefit of rosiglitazone (with the risk of fluid retention & weight gain) & higher cost (including the need for more statins and diuretics), metformin remains the logical choice when initiating pharmacotherapy for type 2 diabetes. (**n=4360 median 4yrs**) .Feb/07 Health Canada Avandia fracture warning: http://www.hc-sc.gc.ca/dhp-mps/medeff/advisories-avis/prof/2007/avandia_hpc-cps_3_e.html & May/07 for Actos http://www.hc-sc.gc.ca/dhp-mps/medeff/advisories-avis/prof/2007/actos_hpc-cps_2_e.html
Kaku K, Isaka H, Sakatani T, Toyoshima J. Efficacy and safety of **ipragliflozin add-on therapy to insulin** in Japanese patients with type 1 diabetes mellitus: A randomized, double-blind, phase 3 trial. Diabetes Obes Metab. 2019 Jun 7.
Kaku K, Kuroda S, Ishida K, et al. Efficacy and safety of **trelagliptin in combination with insulin therapy in Japanese patients with type 2 diabetes**: Results from a randomized, Phase IV study. Diabetes Obes Metab. 2018 Jun 4.
Kaku K, Yamada Y, Watada H, et al. Safety and efficacy of **once-weekly semaglutide** vs additional oral antidiabetic drugs in Japanese people with inadequately controlled type 2 diabetes: A randomized trial. Diabetes Obes Metab. 2018 Jan 11.

Kao SL, Chan CL, Tan B, Lim CC, Dalan R, Gardner D, Pratt E, Lee M, Lee KO. An unusual outbreak of hypoglycemia. N Engl J Med. 2009 Feb 12;360(7):734-6. No abstract available. Hypoglycaemia outbreak linked to contamination of illegal **sexual-enhancement drugs with glyburide**.

Kahn SE, et al. **Rosiglitazone-associated fractures** in type 2 diabetes: an Analysis from A Diabetes Outcome Progression Trial (ADOPT). Diabetes Care. 2008 May;31(5):845-51. Epub 2008 Jan 25. Further investigation into the risk factors and underlying pathophysiology for the increased fracture rate in women taking rosiglitazone is required to relate them to preclinical data and better understand the clinical implications of and possible interventions for these findings.

Kahn R, Alperin P, Eddy D, et al. Age at initiation and frequency of **screening** to detect type 2 diabetes: a cost-effectiveness analysis. Lancet 2010; DOI:10.1016/s0140-6736(09)62162-0.

Kahn SE, Cooper ME, Del Prato S. Pathophysiology and treatment of type 2 diabetes: **perspectives on the past, present, and future**. Lancet. 2013 Dec 3

Kaiwar C, Fernandes GC, Rieder CR, et al. Teaching NeuroImages: The **lentiform fork sign: An MRI pattern of metformin**-associated encephalopathy. Neurology. 2015 Aug 18;85(7):655.

Kajbaf F, Lalau JD. The criteria for **metformin-associated lactic acidosis**: the quality of reporting in a large pharmacovigilance database. Diabet Med. 2012 Sep 21.

Kaku K, Yamada Y, Watada H, et al. Safety and efficacy of once-weekly **semaglutide** vs additional oral antidiabetic drugs in Japanese people with inadequately controlled type 2 diabetes: A randomized trial. Diabetes Obes Metab. 2018 Jan 11.

Kamel KS, Halperin ML. **Acid-base problems in diabetic ketoacidosis**. N Engl J Med. 2015 Feb 5;372(6):546-54.

Kamiko K, Aoki K, Kamiyama H, et al. Comparison of the administration of **teneligliptin** every day versus every other day in Japanese patients with type 2 diabetes: A randomized non-inferior test. J Clin Pharmacol. 2014 Aug 27.

Kanamori T, Takeshita Y, Isobe Y, et al. **Mealtime dosing of a rapid-acting insulin analog reduces glucose variability and suppresses daytime cardiac sympathetic activity**: a randomized controlled study in hospitalized patients with type 2 diabetes. BMJ Open Diabetes Res Care. 2018 Oct 31;6(1):e000588.

Kanaya AM, Herrington D, Vittinghoff E, et al. Impaired fasting glucose and cardiovascular outcomes in **postmenopausal women** with coronary artery disease. Ann Intern Med. 2005 May 17;142(10):813-20. (Among postmenopausal women with coronary artery disease, the 2003 definition for impaired fasting glucose was **not** associated with increased risk for new CHD, stroke or TIA, or CHF).

Kanji Jamil N.; Anglin Rebecca E. S.; Hunt Dereck L.; et al. Does This Patient With Diabetes Have Large-Fiber **Peripheral Neuropathy**? *JAMA*. 2010;303(15):1526-1532.

Kanters S, Wilkinson L, Vrazic H, et al. Comparative efficacy of **once-weekly semaglutide versus SGLT-2 inhibitors** in patients inadequately controlled with one to two oral antidiabetic drugs: a systematic literature review and network meta-analysis. BMJ Open. 2019 Jul 23;9(7):e023458.

Kao SL, Chan CL, et al. An unusual outbreak of hypoglycemia. N Engl J Med. 2009 Feb 12;360(7):734-6. No abstract available. Hypoglycaemia outbreak linked to contamination of **illegal sexual-enhancement drugs** with glyburide.

Kaplan A, Abidi E, El-Yazbi A, Eid A, Booz GW, Zouein FA. **Direct cardiovascular impact of SGLT2 inhibitors**: mechanisms and effects. Heart Fail Rev. 2018 May;23(3):419-437.

Kapoor K, George P, Miller M. **Cardiovascular Outcomes Trials in Type 2 Diabetes Mellitus**. Cardiology. 2016 Jun 15;135(2):108-126.

Kappel BA, Lehrke M, Schütt K, et al. Effect of **Empagliflozin** on the Metabolic Signature of Patients With Type 2 Diabetes Mellitus and Cardiovascular Disease. Circulation. 2017 Sep 5;136(10):969-972.

Kar P, Plummer MP, Bellomo R, et al. **Liberal Glycemic Control in Critically Ill Patients** With Type 2 Diabetes: An Exploratory Study. Crit Care Med. 2016 Jun 16.

Karagiannis T, Paschos P, Paletas K, Matthews DR, Tsapas A. **Dipeptidyl peptidase-4 inhibitors** (DPP-4) for treatment of type 2 diabetes mellitus in the clinical setting: systematic review and meta-analysis. BMJ 2012;344:e1369.

Karagiannis T, Liakos A, et al. Efficacy and safety of **once-weekly glucagon-like peptide 1 receptor agonists** for the management of type 2 diabetes: a systematic review and meta-analysis of randomized controlled trials. Diabetes Obes Metab. 2015 Jul 15.

Karges B, et al. Association of **Insulin Pump Therapy vs Insulin Injection** Therapy With Severe Hypoglycemia, Ketoacidosis, & Glycemic Control Among Children, Adolescents, and Young Adults With Type 1 Diabetes. JAMA. 2017 Oct 10;318(14):1358-1366.

Karslioglu French E, Donihi AC, Korytkowski MT. Diabetic **ketoacidosis and hyperosmolar hyperglycemic syndrome**: review of acute decompensated diabetes in adult patients. BMJ. 2019 May 29;365:l1114.

Karstoft K, Winding K, Knudsen SH, et al. Mechanisms behind the superior effects of **interval vs continuous training on glycaemic control** in individuals with type 2 diabetes: a randomised controlled trial. Diabetologia. 2014 Aug 7.

Karter AJ, Warton EM, Lipska KJ, et al. Development and Validation of a **Tool** to Identify Patients With Type 2 Diabetes at **High Risk** of **Hypoglycemia**-Related Emergency Department or Hospital Use. JAMA Intern Med. 2017 Aug 21.

Karter AJ, Moffet HH, Liu JY, et al. **Surveillance of Hypoglycemia**-Limitations of Emergency Department and Hospital Utilization Data. JAMA Intern Med. 2018 Apr 16.

Kashyap SR, Bhatt DL, Wolski K, et al. **Metabolic effects of bariatric surgery** in patients with moderate obesity and type 2 **diabetes**: Analysis of a randomized control trial comparing surgery with intensive medical treatment. (**STAMPEDE**) Diabetes Care 2013 .

Kato ET, Silverman MG, Mosenzon O, et al. Effect of **Dapagliflozin** on Heart Failure and Mortality in Type 2 Diabetes Mellitus. (Declare-TIMI-58) Circulation. 2019 May 28;139(22):2528-2536

Katz PM, Leiter LA. The Role of the **Kidney and SGLT2 Inhibitors** in Type 2 Diabetes. Can J Diabetes. 2015 Dec;39 Suppl 5:S167-75.

Kaul Sanjay, Bolger Ann F., Herrington David, et al. **Thiazolidinedione Drugs and Cardiovascular Risks**. A Science Advisory From the American Heart Association and American College of Cardiology Foundation. Circulation published February 23, 2010, doi:10.1161/CIR.0b013e3181d34114.

Kaul S. Is the Mortality Benefit With **Empagliflozin** in Type 2 Diabetes Mellitus Too Good To Be True? (**Empa-Reg**) Circulation. 2016 Jul 12;134(2):94-6.

Kaul P, Bowker SL, Savu A, et al. Association between **maternal diabetes, being large for gestational age and breast-feeding on being overweight or obese in childhood**. Diabetologia. 2018 Nov 13.

Kawamori R et al. **Voglibose** for prevention of type 2 diabetes mellitus: A randomised, double-blind trial in Japanese individuals with impaired glucose tolerance. Lancet 2009 May 9; 373:1607.

Kazda CM, Frias J, Foga I, et al. Treatment with the **Glucagon Receptor Antagonist LY2409021** Increases Ambulatory Blood Pressure in Patients with Type 2 Diabetes. Diabetes Obes Metab. 2017 Feb 13.

KDOQI. KDOQI Clinical Practice Guidelines and Clinical Practice Recommendations for **Diabetes and Chronic Kidney Disease**. Am J Kidney Dis. 2007 Feb;49(2 Suppl 2):S12-154.

Ke C, Sohal P, Qian H, et al. **Diabetes in the young**: a population-based study of **South Asian, Chinese and White people**. Diabet Med. 2014 Dec 4.

Ke C, Lau E, Shah BR, et al. **Excess Burden of Mental Illness and Hospitalization in Young-Onset Type 2 Diabetes**: A Population-Based Cohort Study. Ann Intern Med. 2019 Jan 15.

Kelly TN, Bazzano LA, Fonseca VA, Thethi TK, Reynolds K, He J. **Glucose Control and Cardiovascular Disease** in Type 2 Diabetes. Ann Intern Med. 2009 Jul 20.

Kelsey MM, Braffett BH, Geffner ME, et al. **Menstrual Dysfunction** in Girls from the Treatment Options for Type 2 Diabetes in Adolescents and **Youth** (**TODAY**) Study. J Clin Endocrinol Metab. 2018 Apr 24.

Kempf K, Altpeter B, Berger J, et al. Efficacy of the **Telemedical Lifestyle intervention** Program **TeLiPro** in Advanced Stages of Type 2 Diabetes: A Randomized Controlled Trial. Diabetes Care. 2017 Jul;40(7):863-871.

Kemps H, Kränkel N, Dörr M, et al; European Association of Preventive Cardiology (EAPC). **Exercise training for patients with type 2 diabetes and cardiovascular disease**: What to pursue and how to do it. A Position Paper of the European Association of Preventive Cardiology (EAPC). Eur J Prev Cardiol. 2019 Jan 14:2047487318820420.

Keoki Williams L, Padhukasahasram B, Ahmedani BK, et al. Differing Effects of **Metformin on Glycemic Control by Race-Ethnicity**. J Clin Endocrinol Metab. 2014 Jun 12

Kendall DM, et al. Improvement of glycemic control, triglycerides, and HDL cholesterol levels with **muraglitazar**, a dual (alpha/gamma) peroxisome proliferator-activated receptor activator, in patients with type 2 diabetes inadequately controlled with metformin monotherapy: A double-blind, randomized, pioglitazone-comparative study. Diabetes Care. 2006 May;29(5):1016-23.

Kendall D, Vail A, Amin R, et al. **Metformin in Obese Children and Adolescents**: The **MOCA** Trial. J Clin Endocrinol Metab. 2012 Nov 21.

Kent BD, Grote L, Ryan S, et al. Diabetes Mellitus prevalence and control in **Sleep Disordered Breathing**: the European Sleep Apnea Cohort (ESADA) study. Chest. 2014 May 15.

Kerfoot BP, Gagnon DR, McMahon GT, et al. A Team-Based Online Game Improves Blood Glucose Control in Veterans With Type 2 Diabetes: A Randomized, Controlled Trial. Diabetes Care. 2017 Aug 8.

Kern E, VanWagner LB, Yang GY, Rinella ME. **Liraglutide-induced autoimmune hepatitis**. JAMA Intern Med. 2014 Jun 1;174(6):984-7.

Kernan WN, Viscoli CM, Furie KL, et al. **Pioglitazone** after ischemic stroke or transient ischemic attack. (**IRIS**) N Engl J Med. DOI: 10.1056/NEJMoa1506930.

Kernan WN, Viscoli CM, Dearborn JL, et al; Insulin Resistance Intervention After Stroke (**IRIS**) Trial Investigators. Targeting **pioglitazone** hydrochloride therapy after stroke or transient ischemic attack according to pretreatment risk for stroke or myocardial infarction [online September 18, 2017].JAMA Neurol. doi:10.1001/jamaneurol.2017.2136

Kernan WN, Viscoli CM, Dearborn JL, et al. Targeting **Pioglitazone** Hydrochloride Therapy After **Stroke** or Transient Ischemic Attack According to Pretreatment Risk for Stroke or Myocardial Infarction. JAMA Neurol. 2017 Sep 18.

Kerr JL, Timpe EM, Petkewicz KA. **Bromocriptine** mesylate for glycemic management in type 2 diabetes mellitus. Ann Pharmacother. 2010 Nov;44(11):1777-85.

Khashan AS, Kenny LC, Lundholm C, et al. Mode of **obstetrical delivery and type 1 diabetes**: a sibling design study. Pediatrics. 2014 Sep;134(3):e806-13.

Khetan AK, Rajagopalan S. **Prediabetes**. Can J Cardiol. 2018 May;34(5):615-623.

Khoza S, Barner JC, Bohman TM, Rascati K, Lawson K, Wilson JP. Use of **antidepressant agents** and the risk of type 2 diabetes. Eur J Clin Pharmacol. 2011 Nov 26.

Khunti K, Chatterjee S, Gerstein HC, et al. **Do sulphonylureas still have a place in clinical practice**? Lancet Diabetes Endocrinol. 2018 Feb 28.

Khunti K, et al. Randomised controlled trial of **near-patient testing for glycated haemoglobin** in people with type 2 diabetes mellitus. Br J Gen Pract. 2006 Jul;56(528):511-7. (InfoPOEMs: Rapid testing of glycated hemoglobin in office settings does not save money or improve glycemic control compared with usual care. (LOE = 2b))

Khunti K, Gray LJ, Skinner T, et al. Effectiveness of a **diabetes education** and self management programme (**DESMOND**) for people with newly diagnosed type 2 diabetes mellitus: three year follow-up of a cluster randomised controlled trial in primary care.

BMJ 2012;344:e2333.
Khunti K, Davies M. Should we **screen for type 2 diabetes**: Yes. BMJ. 2012 Jul 9;345:e4514.
*Kilpatrick ES, Atkin SL. Using **haemoglobin A1c to diagnose** type 2 diabetes or to identify people at high risk of diabetes. BMJ. 2014 Apr 25;348:g2867.*
Kim C, Aroda VR, et al; **Diabetes Prevention Program** (**DPP**) Outcomes Study Group. **Androgens, irregular menses, and risk of diabetes** and coronary artery calcification in the Diabetes Prevention Program. J Clin Endocrinol Metab. 2017 Dec 6.
Kim JD, Park CY, Cha BY, et al. Comparison of Adherence to Glimepiride/Metformin Sustained Release Once-daily Versus Glimepiride/Metformin Immediate Release BID Fixed-combination Therapy Using the Medication Event Monitoring System in Patients With Type 2 Diabetes. Clin Ther. 2018 May 2.
Kim SC, Schneeweiss S, Glynn RJ, et al. **Dipeptidyl peptidase-4 inhibitors** in type 2 diabetes may reduce the risk of **autoimmune diseases**: a population-based cohort study. Ann Rheum Dis. 2015 Nov;74(11):1968-75.
Kim EK, Kwak SH, Jung HS, et al. The Effect of **a Smartphone-Based, Patient-Centered Diabetes Care System in Patients With Type 2 Diabetes**: A Randomized, Controlled Trial for 24 Weeks. Diabetes Care. 2018 Oct 30.
Kiran T, Kopp A, Moineddin R, et al. Unintended consequences of **delisting routine eye exams** on retinopathy screening for people with diabetes in Ontario, Canada. CMAJ. 2013 Feb 19;185(3):E167-73.
Kirkman MS, et al. Treating **postprandial hyperglycemia** (**acarbose** 100mg tid vs placebo) does not appear to delay progression of early type 2 diabetes: the early diabetes intervention program. Diabetes Care. 2006 Sep;29(9):2095-101.
Ameliorating postprandial hyperglycemia did not appear to delay progression of early type 2 diabetes. Factors other than postprandial hyperglycemia may be greater determinants of progression of diabetes. Alternatively, once FPG exceeds 126 mg/dl, beta-cell failure may no longer be remediable.
Kirkman MS, Briscoe VJ, Clark N, et al. **Diabetes in older adults**. Diabetes Care. 2012 Dec;35(12):2650-64.
Kirpichnikov D, McFarlane SI, Sowers JR. Metformin: an update. Ann Intern Med. 2002 Jul 2;137(1):25-33.
Kirsh SR, Aron DC. Choosing targets for **glycaemia, blood pressure and low-density lipoprotein cholesterol in elderly** individuals with diabetes mellitus. Drugs Aging. 2011 Dec 1;28(12):945-60.
Kitzmiller JL, Block JM, Brown FM, et al. **Managing preexisting diabetes for pregnancy**: summary of evidence and consensus recommendations for care. Diabetes Care. 2008 May;31(5):1060-79.
Kivimäki M, Virtanen M, Kawachi I, et al. **Long working hours, socioeconomic status**, and the risk of incident type 2 diabetes: a meta-analysis of published and unpublished data from 222 120 individuals. Lancet Diabetes Endocrinol. 2014 Sep 24.
Kiviniemi AM, Lepojärvi ES, Tulppo MP, et al. **Prediabetes and Risk for Cardiac Death** Among Patients With Coronary Artery Disease: The ARTEMIS Study. Diabetes Care. 2019 May 10.
Klarenbach S, Cameron C, Singh S, Ur E. Cost-effectiveness of **second-line antihyperglycemic therapy in patients with type 2 diabetes mellitus inadequately controlled on metformin**. CMAJ. 2011 Oct 3. For most patients with type 2 diabetes that is inadequately controlled with metformin monotherapy, the addition of a sulphonylurea represents the most cost-effective second-line therapy.
Klatman EL, Jenkins AJ, Ahmedani MY, et al. Blood glucose meters and test strips: global market and challenges to access in low-resource settings. Lancet Diabetes Endocrinol. 2018 Jul 30.
Kleefstra N, et al. Chromium tx has no effect in patients with poorly controlled, insulin-treated type 2 diabetes in an obese Western population: a randomized, double-blind, placebo-controlled trial. Diabetes Care. 2006 Mar;29(3):521-5.
Klein R, Klein BE. Body Fat Distribution and Diabetic Retinopathy in People With Type 2 Diabetes. JAMA. 2016 Apr 26
Klein S, Sheard NF, Pi-Sunyer X, et al.Weight management through lifestyle modification for the prevention and management of type 2 diabetes: rationale and strategies. Diabetes Care 2004 Aug;27(8):2067-73.
Klein-Schwartz W, Stassinos GL, Isbister GK. Treatment of **sulfonylurea and insulin overdose**. Br J Clin Pharmacol. 2015 Nov 9.
Klimentidis YC, Chen Z, Arora A, et al. Association of **physical activity** with lower type 2 diabetes incidence is weaker among individuals at high genetic risk. Diabetologia. 2014 Oct 2.
Kloecker DE, Zaccardi F, Baldry E, et al. Efficacy **of low- and very-low-energy diets in people with type 2 diabetes mellitus**: A systematic review and meta-analysis of interventional studies. Diabetes Obes Metab. 2019 Mar 29.
Knip Mikael, Virtanen Suvi M, Seppä Karri, et al.. for the Finnish TRIGR Study Group. **Dietary Intervention** in Infancy and Later Signs of Beta-Cell Autoimmunity. N Engl J Med 2010; 363:1900-1908.
Knowler WC, Barrett-Connor E, Fowler SE, et al.; **Diabetes Prevention Program** Research Group. Reduction in the incidence of type 2 diabetes with lifestyle intervention or metformin. N Engl J Med. 2002 Feb 7;346(6):393-403
Kodner C, Anderson L, Pohlgeers K. **Glucose Management in Hospitalized Patients**. Am Fam Physician. 2017;96(10):648-654.
Koenigsberg MR, Corliss J. **Diabetes Self-Management**: Facilitating Lifestyle Change. Am Fam Physician. 2017;96(6):362-370.
Koekkoek PS, Kappelle LJ, van den Berg E, et al. **Cognitive function** in patients with diabetes mellitus: guidance for daily care. Lancet Neurol. 2015 Mar;14(3):329-40.
Koivusalo SB, Rönö K, Klemetti MM, et al. **Gestational Diabetes Mellitus Can Be Prevented** by **Lifestyle Intervention**: The Finnish Gestational Diabetes Prevention Study (**RADIEL**): A Randomized Controlled Trial. Diabetes Care. 2015 Jul 29.
Kohan DE, Fioretto P, Tang W, et al. Long-term study of patients with type 2 diabetes and moderate renal impairment shows that **dapagliflozin** reduces weight and blood pressure but does not improve glycemic control. Kidney Int. 2013 Sep 25.
Kohler S, Kaspers S, Salsali A, et al. Analysis of **Fractures in Patients With Type 2 Diabetes Treated With Empagliflozin** in Pooled Data From Placebo-Controlled Trials and a Head-to-Head Study Versus Glimepiride. Diabetes Care. 2018 Jun 15.
Koivusalo SB, Rono K, Klemetti MM, et al. **Gestational diabetes** mellitus can be prevented by **lifestyle intervention**: the Finnish Gestational Diabetes Prevention study (**RADIEL**): a randomized controlled trial. Diabetes Care. 2015;Jul 29.
Kong L, Nilsson IAK, Gissler M, Lavebratt C. Associations of Maternal Diabetes and Body Mass Index With **Offspring Birth Weight and Prematurity**. JAMA Pediatr. 2019 Feb 25.
Kooy A, et al. Long-term effects of **metformin** on metabolism and microvascular and macrovascular disease in patients with type 2 diabetes mellitus. Arch Intern Med. 2009 Mar 23;169(6):616-25.
Kordes S, Pollack MN, Zwinderman AH, et al. **Metformin** in patients with **advanced pancreatic cancer**: a double-blind, randomised, placebocontrolled phase 2 trial. Lancet Oncol 2015; online June 9.
Korhonen P, Heintjes EM, Williams R, et al. **Pioglitazone** use and **risk of bladder cancer** in patients with type 2 diabetes: retrospective cohort study using datasets from four European countries. BMJ. 2016 Aug 16;354:i3903.
Korownyk C, Ivers N, Allan GM. Strategies for **initiating insulin** in type 2 diabetes. Can Fam Physician. 2011 May;57(5):562.
Kosiborod M, Cavender MA, et al; **CVD-REAL** Investigators and Study Group.. Lower Risk of **Heart Failure and Death in Patients Initiated on SGLT-2 Inhibitors Versus Other Glucose-Lowering Drugs**: The CVD-REAL Study. Circulation. 2017 May 18.
Kosiborod M, Lam CSP, Kohsaka S, et al. Lower Cardiovascular Risk Associated with **SGLT-2i** in >400,000 Patients: The **CVD-REAL 2 Study**. J Am Coll Cardiol. 2018 Mar 7.
Kotsani K, Antonopoulou V, Kountouri A, et al. The role of **telenursing** in the management of Diabetes Type 1: A randomized controlled trial. Int J Nurs Stud. 2018 Jan 6;80:29-35.
Kouyoumdjian FG, Lai W, Orkin A, et al. A 25-year-old woman with **diabetes in custody**. CMAJ. 2016 Dec 6;188(17-18):1249-1250
Kovacs CS, Seshiah V, Swallow R, et al. on behalf of the EMPA-REG PIO™ trial investigators. **Empagliflozin** improves glycaemic and weight control as add-on therapy to pioglitazone or pioglitazone plus metformin in patients with type 2 diabetes: a 24-week, randomized, placebo-controlled trial. Diabetes Obes Metab. 2013 Aug 1.
Koves IH, Leu MG, Spencer S, et al; **Diabetic Ketoacidosis** Guideline Development Workgroup. Improving care for pediatric diabetic ketoacidosis. Pediatrics. 2014 Sep;134(3):e848-56.
KnipM, Akerblom HK, Becker D, et al; **TRIGR** Study Group. **Hydrolyzed infant formula** and early β-cell autoimmunity: a randomized clinical trial. JAMA. doi:10.1001/jama.2014.5610.
Kramer CK, Campbell S, Retnakaran R. **Gestational diabetes and the risk of cardiovascular disease in women**: a systematic review and meta-analysis. Diabetologia. 2019 Mar 7.
Kraus WE, Bhapkar M, Huffman KM, et al; CALERIE Investigators. 2 years of **calorie restriction and cardiometabolic risk** (CALERIE): exploratory outcomes of a multicentre, phase 2, randomised controlled trial. Lancet Diabetes Endocrinol. 2019 Sep;7(9):673-683.
Kraut JA, Madias NE. **Lactic Acidosis**. N Engl J Med. 2014 Dec 11;371(24):2309-2319.
Krentz AJ, Bailey CJ. Oral antidiabetic agents : current role in type 2 diabetes mellitus. **Drugs**. **2005**;65(3):385-411.
Kridin K, Bergman R. Assessment of the prevalence of **mucosal involvement in bullous pemphigoid** [online Jan 9, 2019]. JAMA Dermatol. doi:10.1001/jamadermatol.2018.5049
Kridin K, Bergman R. Association of **Bullous Pemphigoid With Dipeptidyl-Peptidase 4 Inhibitors** in Patients With Diabetes: Estimating the Risk of the New Agents and Characterizing the Patients. JAMA Dermatol. 2018 Aug 8.
Kristensen KL, Pottegard A, Hallas J, et al. **Metformin** treatment does not affect the risk of ruptured **abdominal aortic aneurysms**. J Vasc Surg. 2017 May 12.
Kristensen SL, Rørth R, Jhund PS, et al. **Cardiovascular, mortality, and kidney outcomes with GLP-1 receptor agonists** in patients with type 2 diabetes: a systematic review and meta-analysis of cardiovascular outcome trials. Lancet Diabetes Endocrinol 2019; published online Aug 14.
Kropff J, Choudhary P, Neupane S, et al. Accuracy and Longevity of an **Implantable Continuous Glucose Sensor** in the **PRECISE** Study: A 180-Day, Prospective, Multicenter, Pivotal Trial. Diabetes Care. 2017 Jan;40(1):63-68.
Kuan IHS, Savage RL, Duffull SB, Walker RJ, Wright DFB. The Association **between Metformin Therapy and Lactic Acidosis**. Drug Saf. 2019 Aug 1.
Kuenen JC, Borg R, Kuik DJ, et al. ADAG Study Group. Does **glucose variability influence** the relationship between mean plasma glucose and **HbA1c levels in type 1** and type 2 diabetic patients? Diabetes Care. 2011 Aug;34(8):1843-7.
Kuhadiya ND, Dhindsa S, Ghanim H, et al. **Addition of Liraglutide** to Insulin in Patients With Type 1 Diabetes: A Randomized Placebo-Controlled Clinical Trial of 12 Weeks. Diabetes Care. 2016 Apr 5.
Kuhadiya ND, Ghanim H, Mehta A, et al. **Dapagliflozin as Additional Treatment to Liraglutide and Insulin** in Patients With Type 1 Diabetes. J Clin Endocrinol Metab. 2016 Aug 4
Kumar S, Jang HC, et al. Efficacy and safety of once-daily **insulin degludec/insulin aspart compared with once- daily insulin glargine** in participants with Type 2 diabetes: a randomized, treat-to-target study. Diabet Med. 2017 Feb;34(2):180-188.
Kumar M, Chapman A, Javed S,et al. The Investigation and Treatment of **Diabetic Gastroparesis**. Clin Ther. 2018 May 7.
Kumaraguru J, Flanagan SE, Greeley SA, et al. **Tooth discoloration** in patients with neonatal diabetes after transfer onto glibenclamide: a previously unreported side effect. Diabetes Care. 2009 Aug;32(8):1428-30. Epub 2009 May 12.

Kunte H, Busch MA, Trostdorf K, et al. **Hemorrhagic transformation** of ischemic stroke in diabetics on **sulfonylureas**. Ann Neurol. 2012 Nov;72(5):799-806.
Kunutsor SK, Seidu S, Khunti K. **Aspirin** for **primary prevention** of cardiovascular and all-cause mortality events in **diabetes**: updated meta-analysis of randomized controlled trials. Diabet Med. 2016 Apr 17.
Kuppermann N, Ghetti S, Schunk JE, et al. Clinical Trial of **Fluid Infusion Rates for Pediatric Diabetic Ketoacidosis**. N Engl J Med. 2018 Jun 14;378(24):2275-2287.
Kühtreiber WM, Tran L, Kim T, et al. Long-term **reduction in hyperglycemia in advanced type 1 diabetes**: the value of induced aerobic glycolysis with **BCG vaccinations**. NPJ Vaccines. 2018 Jun 21;3:23.
Kuzik N, Myette-Côté É, Carson V, et al. Evaluating the Effects of **Metformin Use on Height** in Children and Adolescents: A Meta-analysis of Randomized Clinical Trials. JAMA Pediatr. 2015 Sep 28:1-8.
Kwak SH, Hwang YC, Won JC, et al. Comparison of **Gemigliptin and Dapagliflozin Effects on Glycemic Variability** in Type 2 Diabetes: A Randomized, Open-Label, Active-Controlled, 12-Week Study (STABLE II Study). Diabetes Obes Metab. 2019 Sep 10.
Kyrø C, Tjønneland A, Overvad K, et al. Higher **Whole-Grain Intake Is Associated with Lower Risk of Type 2 Diabetes** among Middle-Aged Men and Women: The Danish Diet, Cancer, and Health Cohort. J Nutr. 2018 Sep 1;148(9):1434-1444.
Lablanche S, Vantyghem M-C, Kessler L, et al, on behalf of the TRIMECO trial investigators. **Islet transplantation versus insulin therapy in patients with type 1 diabetes** with severe hypoglycaemia or poorly controlled glycaemia after kidney transplantation (TRIMECO): a multicentre, randomised controlled trial. Lancet Diabetes Endocrinol; published online May 15.
Lacy ME, Wellenius GA, Sumner AE, et al. Association of **sickle trait with hemoglobin A1c** in African Americans.JAMA. doi:10.1001/jama.2016 .21035
Lago RM, Singh PP, Nesto RW. Congestive heart failure and cardiovascular death in patients with prediabetes and type 2 diabetes given thiazolidinediones: a meta-analysis of randomized clinical trials. Lancet. 2007 Sep 29;370(9593):1129-36. Congestive heart failure in patients given TZDs might not carry the risk that is usually associated with congestive heart failure which is caused by progressive systolic or diastolic dysfunction of the left ventricle. Longer follow-up and better characterisation of such patients is needed to determine the effect of TZDs on overall cardiovascular outcome.
Lai SW, Muo CH, Liao KF, et al. Risk of **acute pancreatitis in type 2 diabetes** and risk reduction on anti-diabetic drugs: a population-based cohort study in Taiwan. Am J Gastroenterol. 2011 Sep;106(9):1697-704.
Laine MK, Eriksson JG, Kujala UM, et al. A former career as a male **elite athlete**-does it protect against type 2 diabetes in later life? Diabetologia. 2013 Nov 21.
Laiteerapong N, Cifu AS. **Screening for Prediabetes and Type 2 Diabetes Mellitus**. JAMA. 2016 Feb 16;315(7):697-8.
Laiteerapong N, Cooper JM, Skandari MR, et al. **Individualized Glycemic Control** for U.S. Adults With Type 2 Diabetes: A Cost-Effectiveness Analysis. Ann Intern Med. 2017 Dec 12.
Lajara R, Aguilar R, et al. Efficacy and Safety of **Linagliptin** in Subjects With Long-Standing Type 2 Diabetes Mellitus (>10 Years): Evidence From Pooled Data of Randomized, Double-Blind, Placebo-Controlled, Phase III Trials. Clin Ther. 2014 Sep 15.
Lake A, Arthur A, Byrne C, et al. The effect of **hypoglycaemia during hospital admission on health-related outcomes** for people with diabetes: a systematic review and meta-analysis. Diabet Med. 2019 Aug 23. doi: 10.1111/dme.14115.
Lalau JD. **Lactic acidosis** induced by **metformin**: incidence, management and prevention. Drug Saf. 2010 Sep 1;33(9):727-40. doi: 10.2165/11536790-000000000-00000.
Lalau JD, Kajbaf F, Bennis Y, et al. **Metformin** Treatment in Patients With Type 2 Diabetes and **Chronic Kidney Disease Stages 3A, 3B, or 4.** Diabetes Care. 2018 Jan 5.
Lalau JD and Race JM. Metformin and lactic acidosis in diabetic humans. Diabetes, Obesity and Metabolism 2000;2:131-137.
Lamain-de Ruiter M, Kwee A, Naaktgeboren CA, et al. External validation of prognostic models to predict **risk of gestational diabetes** mellitus in one Dutch cohort: prospective multicentre cohort study. BMJ. 2016 Aug 30;354:i4338.
Lamanna C, Monami M, Marchionni N, et al. Effect of **metformin on cardiovascular events and mortality**: a meta-analysis of randomized clinical trials. Diabetes Obes Metab. 2011 Mar;13(3):221-8.
Lambert BL, et al. Diabetes risk associated with use of **olanzapine, quetiapine, and risperidone** in veterans health administration patients with schizophrenia. Am J Epidemiol. 2006 Oct 1;164(7):672-81. Epub 2006 Aug 30.
Landi SN, Radke S, Engel SM, et al. Association of Long-term **Child Growth and Developmental Outcomes With Metformin vs Insulin Treatment for Gestational Diabetes**. JAMA Pediatr. 2018 Dec 3.
Landon MB, Thom E, Spong CY, et al. A planned randomized clinical trial of treatment for mild gestational diabetes mellitus. J Matern Fetal Neonatal Med. 2002 Apr;11(4):226-31.
Landon MB et al. A multicenter, randomized trial of treatment for mild **gestational diabetes**. N Engl J Med 2009 Oct 1; 361:1339.
Lane W, Bailey TS, Gerety G, et al. Effect of insulin **degludec vs insulin glargine** U100 on hypoglycemia in patients with type 1 diabetes: the **SWITCH 1** randomized clinical trial.JAMA. doi:10.1001/jama.2017.7115
Lane W, Weinrib S, Rappaport J, et al. The effect of addition of **liraglutide** to high-dose intensive insulin therapy: a randomized prospective trial. Diabetes Obes Metab. 2014 Mar 3.
Langan RC, Zawistoski KJ. Update on **Vitamin B12 Deficiency**. Am Fam Physician. 2011 Jun 15;83(12):1425-1430.
Langan, RC, Goodgred AJ, **Vitamin B12 Deficiency**: Recognition and Management. Am Fam Physician. 2017;96(6):384-389.
Langer O, Conway DL, Berkus MD, Xenakis EM, Gonzales O. A comparison of glyburide and insulin in women with **gestational diabetes mellitus**. N Engl J Med. 2000 Oct 19;343(16):1134-8. In women with gestational diabetes, glyburide is a clinically effective alternative to insulin therapy.
Langran T, Nanda N, Bataveljic A, et al. Supporting the management of type 2 diabetes with **pharmacist-led reviews**: an observational analysis. BMJ Open 2017;7(3).
Lansang MC, Hustak LK. **Glucocorticoid-induced diabetes and adrenal suppression**: How to detect and manage them. Cleve Clin J Med. 2011 Nov;78(11):748-56.
Lanspa MJ, Krinsley JS, Hersh AM, et al. **Percent of time in range 70-139mg/dL is associated with reduced mortality** among critically ill patients receiving intravenous insulin infusion. Chest. 2019 Jun 12
*Lapolla A, Frison V, Bettio M, et al. Correlation Between Baseline Characteristics and Clinical Outcomes in a Large Population of Diabetes Patients Treated with **Liraglutide** in a Real-World Setting in Italy. Clin Ther. 2015 Jan 24.*
*Larkin ME, Barnie A, Braffett BH, et al. **Musculoskeletal Complications** in Type 1 Diabetes. Diabetes Care. 2014 Apr 10.*
Larsson SC, Scott RA, Traylor M, Langenberg et al. Type 2 diabetes, glucose, insulin, BMI, and **ischemic stroke** subtypes: Mendelian randomization study. Neurology. 2017 Aug 1;89(5):454-460.
Lash RW, Lucas DO, Illes J. **Preventing Hypoglycemia** in Type 2 Diabetes. J Clin Endocrinol Metab. 2018 Mar 5.
Lasserson D, Fox R, Farmer A. **Late onset type 1 diabetes**. BMJ. 2012 Apr 30;344:e2827.
Lauffenburger JC, Lewey J, Jan S, et al. Effectiveness of **Targeted Insulin-Adherence Interventions** for Glycemic Control Using Predictive Analytics Among Patients With Type 2 Diabetes: A Randomized Clinical Trial. JAMA Netw Open. 2019 Mar 1;2(3):e190657.
Launer LJ, Miller ME, Williamson JD, et al; **ACCORD MIND** investigators. Effects of **intensive glucose lowering** on **brain** structure and function in people with type 2 diabetes: a randomised open-label substudy. Lancet Neurol. 2011 Nov;10(11):969-77.
Lavalle-Gonzalez F, Januszewicz A, Davidson J, et al. Efficacy and safety of **canagliflozin** compared with placebo and sitagliptin in patients with type 2 diabetes on background metformin monotherapy: a randomised trial; Diabetologia. 2013;56:2582-2592.
Lavine Joel E., Schwimmer Jeffrey B., Van Natta Mark L., et al., for the **Nonalcoholic Steatohepatitis** Clinical Research Network. Effect of **Vitamin E or Metformin** for Treatment of Nonalcoholic Fatty Liver Disease in Children and Adolescents: The TONIC Randomized Controlled Trial. *JAMA*. 2011;305(16):1659-1668.
Lawrenson JG, Graham-Rowe E, Lorencatto F, et al. Interventions to **increase attendance for diabetic retinopathy screening**. Cochrane Database of Systematic Reviews 2018, Issue 1. Art. No.: CD012054. The results of this review provide evidence that QI interventions targeting patients, healthcare professionals or the healthcare system are associated with meaningful improvements in DRS attendance compared to usual care. There was no statistically significant difference between interventions specifically aimed at DRS and those which were part of a general QI strategy for improving diabetes care. This is a significant finding, due to the additional benefits of general QI interventions in terms of improving glycaemic control, vascular risk management and screening for other microvascular complications. It is likely that further (but smaller) improvements in DRS attendance can also be achieved by increasing the intensity of a particular QI component or adding further components.
Lazar HL, McDonnell MM, Chipkin S, et al. Effects of **aggressive versus moderate glycemic** control on clinical outcomes in diabetic **coronary artery bypass graft patients**. Ann Surg. 2011 Sep;254(3):458-63; discussion 463-4.
Lazarus B, Wu A, Shin J-I, et al. Association of **metformin use with risk of lactic acidosis across the range of kidney function**: a community-based cohort study [online June 4, 2018]. JAMA Intern Med. doi:10.1001/jamainternmed.2018.0292
Le Roux CW, Astrup A, Fujioka K, et al, for the **SCALE** Obesity and Prediabetes NN8022-1839 Study Group. 3 years of **liraglutide** versus placebo for type 2 **diabetes** risk reduction and **weight management** in individuals with prediabetes: a randomised, double-blind trial. Lancet 2017; online Feb 22.
Leal I, Romio SA, Schuemie M, et al. **Prescribing pattern** of glucose lowering drugs in The United Kingdom in the last decade: a focus on the effects of safety warnings about rosiglitazone. Br J Clin Pharmacol. 2012 Jul 30.
Lean ME, Leslie WS, Barnes AC, et al. **Primary care-led weight management** for **remission of type 2 diabetes** (**DiRECT**): an open-label, cluster-randomised trial. Lancet. 2017 Dec 4.
Lean MEJ, Leslie WS, Barnes AC, et al. **Durability of a primary care-led weight-management intervention for remission of type 2 diabetes:** 2-year results of the DiRECT open-label, cluster-randomised trial. Lancet Diabetes Endocrinol.2019 Mar 5.
Lebovitz HE, Dole JF, Patwardhan R, et al**. Rosiglitazone monothreapy is effective in patients with type 2 diabetes**. J Clin Endocrinol Metab 2001;86:280-8.
Ledesma G, Umpierrez GE, Morley JE, et al. Efficacy and safety of **linagliptin to improve glucose control** in older people with type 2 diabetes on stable insulin therapy: A randomized trial. Diabetes Obes Metab. 2019 Jul 12.
Lee Phillip H, Stockton M David, Franks Andrea S. **Acute Pancreatitis Associated with Liraglutide.** Articles Ahead of Print published on 1 April 2011, DOI 10.1345/aph.1P714. Ann Pharmacother ;45:e22.
Lee SG, Lee HJ, Yoon MS, Kim DH. **Association of Dipeptidyl Peptidase 4 Inhibitor Use With Risk of Bullous Pemphigoid in Patients With Diabetes**. JAMA Dermatol. 2019 Jan 9.
Lee SJ, Boscardin WJ, Stijacic Cenzer I, Huang ES, Rice-Trumble K, Eng C. The **risks and benefits of implementing glycemic control guidelines in frail older adults** with diabetes mellitus. J Am Geriatr Soc. 2011 Apr;59(4):666-72.
Lee JM, Wu EL, Tarini B, et al. Diagnosis of diabetes using **hemoglobin A1c: should recommendations in adults be extrapolated to adolescents**?. J Pediatr. 2011 Jun;158(6):947-952.e1-3.
Lee JM, Wu EL, Tarini B, et al. **Diagnosis of diabetes using hemoglobin A1c**: should recommendations in adults be extrapolated to **adolescents**?. J Pediatr. 2011 Jun;158(6):947-952.e1-3.
Lee YY, Lin YM, Leu WJ, et al. **Sliding-scale insulin** used for blood glucose control: a meta-analysis of randomized controlled trials. Metabolism. 2015 Sep;64(9):1183-92.

Leese GP, Stratton IM, et al. Four Nations Diabetic Retinopathy Screening Study Group. Progression of diabetes **retinal status** within community screening programs and potential implications for screening intervals. Diabetes Care. 2015 Mar;38(3):488-94.
Lega IC, Austin PC, Gruneir A, et al. Association between **metformin therapy and mortality after breast cancer**: a population-based study. Diabetes Care. 2013 Oct;36(10):3018-26.
Lega IC, Bronskill SE, Campitelli MA, et al. Sodium glucose cotransporter 2 inhibitors and **risk of genital mycotic and urinary tract infection**: A population-based study of older women and men with diabetes. Diabetes Obes Metab. 2019 Jul 2
Lega IC, Wilton AS, Austin PC, et al. The temporal relationship between **diabetes and cancer**: A population-based study. Cancer. 2016 Jul 11.
Legro RS, Arslanian SA, Ehrmann DA, et al. Diagnosis and Treatment of **Polycystic Ovary Syndrome**: An **Endocrine Society** Clinical Practice Guideline. J Clin Endocrinol Metab. 2013 Oct 22.
Legro RS, Barnhart HX, Schlaff WD, et al. Cooperative Multicenter Reproductive Medicine Network. Clomiphene, metformin, or both for infertility in the polycystic ovary syndrome. N Engl J Med. 2007 Feb 8;356(6):551-66. Clomiphene is superior to metformin in achieving live birth in infertile women with the polycystic ovary syndrome, although multiple birth is a complication. InfoPOEMs: Clomiphene is more effective than metformin for enhancing fertility in women with polycystic ovary syndrome (PCOS). This study did not find that the combination of clomiphene and metformin was more effective than clomiphene alone. (LOE = 1b)
Legro RS, Zaino RJ, Demers LM, Kunselman AR, Gnatuk CL, Williams NI, Dodson WC. The effects of metformin and rosiglitazone, alone and in combination, on the ovary and endometrium in polycystic ovary syndrome. Am J Obstet Gynecol. 2007 Apr;196(4):402.e1-10; discussion 402.e10-1.
Lehrke M, Marx N, Patel S, et al. Safety and Tolerability of **Linagliptin** in Patients With Type 2 Diabetes: A Comprehensive Pooled Analysis of 22 Placebo-Controlled Studies. Clin Ther. 2014 Jul 8.
Lehrke M, Marx N. **Diabetes Mellitus and Heart Failure**. Am J Cardiol. 2017 Jul 1;120(1S):S37-S47.
Leibowitz G, Cahn A, Bhatt DL, et al. Impact of treatment with **saxagliptin** on glycaemic stability and beta-cell function in the **SAVOR-TIMI 53** study. Diabetes Obes Metab. 2015 May;17(5):487-94.
Leiter LA, et al.; International Prandial Glucose Regulation Study Group. **Postprandial glucose** regulation: new data and new implications. Clin Ther. 2005;27 Suppl B:S42-56.
Leiter LA, Cefalu WT, de Bruin TW, et al. **Dapagliflozin** Added to Usual Care in Individuals with Type 2 Diabetes Mellitus with Preexisting Cardiovascular Disease: A 24-Week, Multicenter, Randomized, Double-Blind, Placebo-Controlled Study with a 28-Week Extension. J Am Geriatr Soc. 2014 Jun 2.
Leiter LA, Teoh H, Braunwald E, et al. Efficacy and Safety of **Saxagliptin** in Older Participants in the **SAVOR-TIMI 53** Trial. Diabetes Care. 2015 Mar 10.
Lennerz B, Barton A, Bernstein RK, et al. Management of **type 1 diabetes with a very low–carbohydrate diet**. Pediatrics. 2018;141(6):e20173349
Leonard CE, Brensinger CM, Aquilante CL, et al. Comparative Safety of **Sulfonylureas and the Risk of Sudden Cardiac Arrest and Ventricular Arrhythmia**. Diabetes Care. 2018 Feb 2.
Leonetti F, Capoccia D, Coccia F, et al. Obesity, type 2 diabetes mellitus, and other comorbidities: a prospective cohort study of **laparoscopic sleeve gastrectomy vs medical treatment** [online ahead of print April 16, 2012]. Arch Surg. 2012.
Leong A, Rahme E, Dasgupta K. **Spousal diabetes** as a diabetes risk factor: A systematic review and meta-analysis. BMC Med. 2014 Jan 24;12(1):12.
LeRoith D, Biessels GJ, Braithwaite SS, et al. **Treatment of Diabetes in Older Adults**: An Endocrine Society* Clinical Practice Guideline. J Clin Endocrinol Metab. 2019 May 1;104(5):1520-1574.
Leslie BR, Gerwin LE, Taylor SI. Sodium–glucose cotransporter-2 inhibitors**: lack of a complete history delays diagnosis**. Ann Intern Med. 2019;171:421-6. doi:10.7326/M19-1463.
Leung AA, Nerenberg K, Daskalopoulou SS, et al; CHEP Guidelines Task Force. Hypertension Canada's **2016 CHEP guidelines** for blood pressure measurement, diagnosis, assessment of risk, prevention and treatment of hypertension. Can J Cardiol 2016 (accepted manuscript) doi: 10.1016/j.cjca.2016.02.066 www.onlinecjc.ca/article/S0828-282X(16)00192-6/pdf (accessed April 11, 2016).
Leung AA, Daskalopoulou SS, Dasgupta K, et al. **Hypertension Canada's 2017 Guidelines for Diagnosis, Risk Assessment, Prevention, and Treatment of Hypertension in Adults**. Can J Cardiol. 2017 May;33(5):557-576
Levengood TW, Peng Y, Xiong KZ, et al. **Team-Based Care** to Improve Diabetes Management: A Community Guide Meta-analysis. Am J Prev Med. 2019 Jul;57(1):e17-e26.
Levin P, Zhou S, Durden E, et al. Clinical and Economic Outcomes Associated With the **Timing of Initiation of Basal Insulin** in Patients With Type 2 Diabetes Mellitus Previously Treated With Oral Antidiabetes Drugs. Clin Ther. 2015 Dec 8.
Lewin A, DeFronzo RA, Patel S, et al. Initial Combination of **Empagliflozin and Linagliptin** in Subjects With Type 2 Diabetes.Diabetes Care. 2015 Jan 29.
Lexis CP, van der Horst IC, Lipsic E, et al; for the GIPS-III Investigators. Effect of **Metformin** on Left Ventricular Function **After Acute Myocardial Infarction** in Patients Without Diabetes: The **GIPS-III** Randomized Clinical Trial. JAMA. 2014 Mar 31.
Lewis EJH, Perkins BA, Lovblom LE, et al. Effect of **omega-3 supplementation** on **neuropathy in type 1 diabetes**: A 12-month pilot trial. Neurology. 2017 Jun 13;88(24):2294-2301.
Lewis JD, Ferrara A, Peng T, et al. Risk of **Bladder Cancer Among Diabetic Patients Treated With Pioglitazone**: Interim report of a longitudinal cohort study. Diabetes Care. 2011 Apr;34(4):916-22. In this cohort of patients with diabetes, short-term use of pioglitazone was not associated with an increased incidence of bladder cancer, but use for more than 2 years was weakly associated with increased risk.
Lewis J, Lipp A. **Pressure-relieving** interventions for treating **diabetic foot ulcers**. Cochrane Database Syst Rev. 2012 Nov 2;1:CD002302. DOI: 10.1002/14651858.CD002302.pub2. Non-removable, pressure-relieving casts are more effective in healing diabetes related plantar foot ulcers than removable casts, or dressings alone. Non-removable devices, when combined with Achilles tendon lengthening were more successful in one forefoot ulcer study than the use of a non-removable cast alone.
Lewis JD, Habel LA, Quesenberry CP, et al. **Pioglitazone** Use and Risk of **Bladder Cancer** and Other Common Cancers in Persons With Diabetes. JAMA. 2015 Jul 21;314(3):265-77.
Ley SH, Hamdy O, Mohan V, et al. Prevention and management of type 2 diabetes: **dietary components and nutritional strategies**. Lancet. 2014 Jun 7;383(9933):1999-2007.
Li G, Zhang P, Wang J, et al. Cardiovascular mortality, all-cause mortality, and diabetes incidence after **lifestyle intervention for people with impaired glucose tolerance in the Da Qing Diabetes Prevention Study**: a 23-year follow-up study. *Lancet Diabetes Endocrinol* 2014.
Li J, Rice MS, Huang T, et al. **Circulating prolactin concentrations and risk of type 2 diabetes** in US women. Diabetologia. 2018 Oct 11.
Li J, Tong Y, et al. Effects on **All-Cause Mortality and Cardiovascular Outcomes** in Patients With Type 2 Diabetes by Comparing **Insulin With Oral Hypoglycemic** Agent Therapy: A Meta-Analysis of Randomized Controlled Trials. Clin Ther. 2016 Jan 7.
Li L, Shen J, Bala MM, et al. **Incretin treatment and risk of pancreatitis** in patients with type 2 diabetes mellitus: systematic review and meta-analysis of randomised and non-randomised studies. BMJ. 2014 Apr 15.
Li L, Li S, Deng K, et al. **Dipeptidyl peptidase-4 inhibitors and risk of heart failure** in type 2 diabetes: systematic review and meta-analysis of randomised and observational studies. BMJ 2016;352:i610.
Li M, Fallin MD, Riley A, et al. The Association of **Maternal Obesity** and Diabetes With **Autism** and Other Developmental Disabilities. Pediatrics. 2016 Jan 29.
Li M, Li S, Chavarro JE, et al. Prepregnancy Habitual Intakes of Total, Supplemental, and Food **Folate and Risk of Gestational Diabetes Mellitus**: A Prospective Cohort Study. Diabetes Care. 2019 Apr 22.
Li R, Zhang P, Barker LE, et al. **Cost-effectiveness of interventions to prevent** and control diabetes mellitus: a systematic review. Diabetes Care. 2010 Aug;33(8):1872-94.
Li S, Wang YY, Cui J, et al. Are low **levels of serum bicarbonate associated with risk of progressing to impaired fasting glucose/diabetes**? A single-centre prospective cohort study in Beijing, China. BMJ Open. 2018 Jul 23;8(7):e019145.
Li W, Risacher SL, Huang E, et al. Type 2 diabetes mellitus is associated with **brain atrophy and hypometabolism** in the ADNI cohort. Neurology. 2016 Aug 9;87(6):595-600
Li Yanfeng, Burrows Nilka Ríos, Gregg Edward W., et al. **Declining** Rates of Hospitalization for Nontraumatic **Lower-Extremity Amputation** in the Diabetic Population Aged 40 Years or Older: U.S., 1988–2008. Diabetes Care February 2012 35:273-277.
Li YF, Geiss LS, Burrows NR, et al. **Awareness of prediabetes—United States**, 2005-2010. MMWR Morb Mortal Wkly Rep 2013; 62;209-212.
Li Y, Hu Y, Ley SH, et al. **Sulfonylurea Use and Incident Cardiovascular Disease** Among Patients With Type 2 Diabetes: Prospective Cohort Study Among Women. Diabetes Care. 2014 Aug 22.
Li Y, Hu Y, Ley SH, Rajpathak S, Hu FB. **Sulfonylurea** use and incident **cardiovascular disease** among patients with type 2 diabetes: prospective cohort study among women. Diabetes Care. 2014 Nov;37(11):3106-13.
Li Y, Ley SH, Tobias DK, Chiuve SE, et al. **Birth weight** and later life adherence to unhealthy lifestyles in predicting type 2 diabetes: prospective cohort study. BMJ. 2015 Jul 21;351:h3672.
Li Y, Gao X, Winkelman JW, et al. Association between **sleeping difficulty** and type 2 diabetes in women. Diabetologia. 2016 Jan 28.
Li X, Du T, Li W, et al. Efficacy and Safety of **Weight-Based Insulin Glargine Dose** Titration Regimen Compared With Glucose Level- and Current Dose-Based Regimens in Hospitalized Patients With Type 2 Diabetes: A Randomized, Controlled Study. Clin Ther. 2014 Jul 22.
Li X, Wang J, Shen X, et al. **Higher blood pressure predicts diabetes** and enhances long-term risk of cardiovascular disease events in individuals with impaired glucose tolerance: Twenty-three-year follow-up of the Daqing diabetes prevention study. J Diabetes. 2018 Dec 16.
Lian F, Li G, Chen X, et al. **Chinese Herbal Medicine Tianqi** Reduces Progression From Impaired Glucose Tolerance to Diabetes: A Double-Blind, Randomized, Placebo-Controlled, Multicenter Trial. J Clin Endocrinol Metab. 2014 Jan 16
Liang C, Bertoia ML, Ding Y, et al. **Exenatide use and incidence of pancreatic and thyroid cancer:** A retrospective cohort study. Diabetes Obes Metab. 2018 Nov 25.
Liao WC, Tu YK, Wu MS, et al. Blood glucose concentration and **risk of pancreatic cancer**: systematic review and dose-response meta-analysis. BMJ. 2015 Jan 2;349:g7371.
Liao HW, Saver JL, Wu YL, et al. **Pioglitazone** and cardiovascular outcomes in patients with **insulin resistance, pre-diabetes and type 2 diabetes**: a systematic review and meta-analysis. BMJ Open. 2017 Jan 5;7(1):e013927.
Libman H, Jiang ZG, Tapper EB, et al. How Would You Manage This **Patient With Nonalcoholic Fatty Liver Disease**?: Grand Rounds Discussion From Beth Israel Deaconess Medical Center. Ann Intern Med. 2019 Aug 6;171(3):199-207.
Libman IM, Miller KM, et al.; T1D Exchange Clinic Network Metformin RCT Study Group. Effect of **Metformin Added to Insulin on Glycemic Control Among Overweight/Obese Adolescents With Type 1 Diabetes**: A Randomized Clinical Trial. JAMA. 2015 Dec 1;314(21):2241-2250.

Ligthart S, van Herpt TT, Leening MJ, et al. **Lifetime risk of developing impaired glucose metabolism** and eventual progression from **prediabetes to type 2 diabetes**: a prospective cohort study. Lancet Diabetes Endocrinol. 2016 Jan;4(1):44-51.
Lim S, et al. Efficacy and safety of initial combination therapy with **gemigliptin** and **metformin** compared with monotherapy with either drug in patients with type 2 diabetes: double-blind randomized controlled trial (**INICOM**). Diabetes Obes Metab. 2016 Sep 13.
Lin HC, Stein JD, Nan B, et al. Association of **Geroprotective Effects of Metformin** and Risk of Open-Angle Glaucoma in Persons With Diabetes Mellitus. JAMA Ophthalmol. 2015 May 28.
Lincoff AM, Tardif JC, Schwartz GG, et al; the AleCardio Investigators. Effect of **Aleglitazar** on Cardiovascular Outcomes After Acute Coronary Syndrome in Patients With Type 2 Diabetes Mellitus: The AleCardio Randomized Clinical Trial. JAMA. 2014 Mar 30.
Lind M, Bounias I, Olsson M, Gudbjörnsdottir S, et al. **Glycaemic control and incidence of heart failure** in 20 985 patients with type 1 diabetes: an observational study. Lancet 2011; published online June 25.
Lind M, Garcia-Rodriguez LA, Booth GL, et al. **Mortality trends** in patients with and without diabetes in Ontario, **Canada and the UK** from 1996 to 2009: a population-based study. Diabetologia. 2013 Jun 22.
Lind M, Hirsch IB, Tuomilehto J, et al. **Liraglutide** in people treated for type 2 diabetes with **multiple daily insulin injections**: randomised clinical trial (MDI Liraglutide trial). BMJ. 2015 Oct 28;351:h5364.
Lind M, Pivodic A, Svensson AM, et al. **HbA(1c) level as a risk factor for retinopathy and nephropathy** in children and adults with type 1 diabetes: Swedish population based cohort study. BMJ. 2019 Aug 28;366:l4894.
Lind M, Polonsky W, et al. **Continuous glucose monitoring vs conventional therapy** for glycemic control in adults with type 1 diabetes treated with multiple daily insulin injections: the **GOLD** randomized clinical trial.JAMA. doi:10.1001 /jama.2016.19976
Lind M, Svensson AM, Kosiborod M, et al. **Glycemic control and excess mortality** in type 1 diabetes. N Engl J Med. 2014 Nov 20;371(21):1972-82.
Lindblad AJ, Garrison S, Michael Allan G. **Glucagonlike peptide 1 analogs** in diabetes care. Can Fam Physician. 2017 May;63(5):371
*Linder K, Schleger F, Kiefer-Schmidt I, et al. **Gestational Diabetes** Impairs Human **Fetal Postprandial Brain Activity**. J Clin Endocrinol Metab. 2015 Oct 14:jc20152692.*
Lindstrom J, et al. **Finnish Diabetes** Prevention Study Group. (FDPS) Sustained reduction in the incidence of type 2 diabetes by **lifestyle** intervention: follow-up of the Finnish Diabetes Prevention Study. Lancet. 2006 Nov 11;368(9548):1673-9.
Lingaiah S, Morin-Papunen L, Risteli J, Tapanainen JS. **Metformin** decreases bone turnover markers in polycystic ovary syndrome: a post hoc study. Fertil Steril. 2019 Jun 18.
Lingvay I, Catarig A-M, Frias JP, et al. Efficacy and safety of **once-weekly semaglutide versus daily canagliflozin** as add-on to metformin in patients with type 2 diabetes (SUSTAIN 8): a double-blind, randomised controlled phase 3b trial. Lancet Diabetes Endocrinol 2019; published online Sep 17.
Lingvay I, Desouza CV, Lalic KS, et al. A 26-Week Randomized Controlled Trial of **Semaglutide Once Daily Versus Liraglutide and Placebo** in Patients With Type 2 Diabetes Suboptimally Controlled on Diet and Exercise With or Without Metformin. Diabetes Care. 2018 Jul 19.
Lingvay I, Leiter LA. Use of GLP-1 RAs in Cardiovascular Disease Prevention: A Practical Guide. Circulation. 2018 May 22;137(21):2200-2202.
Lingvay I, Manghi FP, García-Hernández P, et al; **DUAL V Investigators**. Effect of Insulin **Glargine Up-titration vs Insulin Degludec/Liraglutide** on Glycated Hemoglobin Levels in Patients With Uncontrolled Type 2 Diabetes: The DUAL V Randomized Clinical Trial. JAMA. 2016 Mar 1;315(9):898-907.
Linz PE, Lovato LC, Byington RP, et al. Paradoxical **Reduction in HDL**-C with **Fenofibrate and Thiazolidinedione** Therapy In Type 2 Diabetes: the ACCORD Lipid Trial. Diabetes Care. 2013 Dec 2.
Linz PE, Lovato LC, Byington RP, et al. **Paradoxical Reduction in HDL-C with Fenofibrate and Thiazolidinedione** Therapy In Type 2 Diabetes: the ACCORD Lipid Trial. Diabetes Care. 2013 Dec 2
Lipman TH, Levitt Katz LE, et al. **Increasing Incidence of Type 1 Diabetes in Youth: Twenty years** of the Philadelphia Pediatric Diabetes Registry. Diabetes Care. 2013 Jan 22.
Lipscombe LL, Levesque L, Gruneir A, et al. **Antipsychotic drugs and hyperglycemia** in older patients with diabetes. Arch Intern Med. 2009 Jul 27;169(14):1282-9.
Lipska KJ, Flory JH, Hennessy S, Inzucchi S, et al. Citizen Petition to the US Food and Drug Administration to **Change Prescribing Guidelines: The Metformin** Experience. Circulation. 2016 Nov 1;134(18):1405-1408.
Lipska KJ, Laiteerapong N. **Lack of Glycemic Legacy Effects** in the Veterans Affairs Diabetes Trial. N Engl J Med. 2019 Jun 6;380(23):2266-2267.
Lipska KJ, Parker MM, Moffet HH, et al. Association of **Initiation of Basal Insulin Analogs vs Neutral Protamine Hagedorn Insulin With Hypoglycemia-Related Emergency Department** Visits or Hospital Admissions and With Glycemic Control in Patients With Type 2 Diabetes. JAMA. 2018 Jul 3;320(1):53-62.
Lipska KJ, Ross JS, Van Houten HK, et al. Use and **out-of-pocket costs** of insulin for type 2 diabetes mellitus from 2000 through 2010. JAMA. doi:10.1001/jama.2014.6316.
Lipska KJ, Ross JS, Wang Y, et al. **National Trends** in US Hospital Admissions for **Hyperglycemia and Hypoglycemia** Among Medicare Beneficiaries, 1999 to 2011. JAMA Intern Med. 2014 Jul 1;174(7):1116-24.
Lipska KJ, Ross JS, Miao Y, et al. Potential **Overtreatment of Diabetes Mellitus in Older Adults** With Tight Glycemic Control. JAMA Intern Med. 2015 Jan 12.
Lipsky BA, Aragón-Sánchez J, et al; International Working Group on the Diabetic Foot., Peters EJ. **IWGDF guidance** on the **diagnosis and management of foot infections** in persons with diabetes. Diabetes Metab Res Rev. 2016 Jan;32 Suppl 1:45-74.
Liu SC, Tu YK, Chien MN, et al. Effect of **antidiabetic agents added to metformin on glycaemic control, hypoglycaemia and weight** change in patients with type 2 diabetes: a network meta-analysis. Diabetes Obes Metab. 2012 Sep;14(9):810-20.
Liu R, Li L, Yang M, et al. Systematic review of the effectiveness of **hyperbaric oxygenation therapy** in the management of chronic **diabetic foot ulcers**. Mayo Clin Proc. 2013 Feb;88(2):166-75.
Liu J, Wang LN. Peroxisome proliferator-activated receptor gamma agonists (rosiglitazone, **pioglitazone**) for preventing recurrent stroke and other vascular events in patients with stroke or transient ischaemic attack. Cochrane Database Syst Rev. 2014 Jan 8;1:CD010693. PPAR-gamma agonists were demonstrated to **reduce recurrent stroke and total events** of cardiovascular death, non-fatal myocardial infarction or non-fatal stroke, and improve insulin sensitivity and the stabilisation of carotid plaques.
Liu J, Li L, Deng K, et al. **Incretin based treatments and mortality** in patients with type 2 diabetes: systematic review and meta-analysis. BMJ. 2017 Jun 8;357:j2499.
Liu J, Wang LN Peroxisome proliferator-activated receptor gamma agonists (**Pioglitazone & rosiglitazone**) for **preventing recurrent stroke and other vascular events in people with stroke or transient ischaemic attack**. Cochrane Database Syst Rev. 2017 Dec 2;12:CD010693. Peroxisome proliferator-activated receptor gamma agonists probably reduce recurrent stroke and total events of cardiovascular death, non-fatal myocardial infarction or non-fatal stroke, and may improve insulin sensitivity and the stabilisation of carotid plaques. Their effects on adverse events are uncertain. Our conclusions should be interpreted with caution considering the small number and the quality of the included studies. Further well-designed, double-blind RCTs with large samples are required to assess the efficacy and safety of PPAR-γ agonists in the secondary prevention of stroke and related vascular events in people with stroke or TIA.
Livingstone SJ, Looker HC, Hothersall EJ, et al. Risk of **cardiovascular disease and total mortality** in adults with type 1 diabetes: Scottish registry linkage study. PLoS Med. 2012 Oct;9(10):e1001321.
Livingstone SJ, Levin D, Looker HC, et al. Estimated **life expectancy** in a Scottish cohort with type 1 diabetes, 2008-2010. JAMA. doi:10.1001 /jama.2014.16425.
Lo A, Lorenz K, Cor K, Simpson SH. **Factors Affecting Number of Diabetes Management Activities** Provided by Pharmacists. Can J Diabetes. 2016 Dec;40(6):535-542.
Lo C, Toyama T, Wang Y, et al. **Insulin and glucose-lowering agents for treating people with diabetes and chronic kidney disease**. Cochrane Database Syst Rev. 2018 Sep 24;9:CD011798. Evidence concerning the efficacy and safety of glucose-lowering agents in diabetes and CKD is limited. SGLT2 inhibitors and GLP- 1 agonists are probably efficacious for glucose-lowering and DPP-4 inhibitors may be efficacious for glucose-lowering. Additionally, SGLT2 inhibitors probably reduce BP, heart failure, and hyperkalaemia but increase genital infections, and slightly increase creatinine. The safety profile for GLP-1 agonists is uncer tain. No further conclusions could be made for the other classes of glucose-lowering agents including insulin. More high quality studies are required to help guide th erapeutic choice for glucose-lowering in diabetes and CKD.
Lo SC, Yang YS, Kornelius E, et al. Early **cardiovascular risk and all-cause mortality** following an incident of **severe hypoglycaemia**: A population-based cohort study. Diabetes Obes Metab. 2019 Apr 11.
Lofvenborg JE, Andersson T, Dorkhan M, et al. **Sweetened beverage intake** and risk of latent autoimmune diabetes in adults (LADA) and type 2 diabetes. European Journal of Endocrinology (2016):175:605-614.
Loke YK, Singh S, Furberg CD. Long-term use of thiazolidinediones and **fractures** in type 2 diabetes: a meta-analysis. CMAJ. 2009 Jan 6;180(1):32-9. Epub 2008 Dec 10. Long-term thiazolidinedione use doubles the risk of fractures among women with type 2 diabetes, without a significant increase in risk of fractures among men with type 2 diabetes.
Loke Yoon Kong, Kwok Chun Shing, Singh Sonal. Comparative **cardiovascular effects of thiazolidinediones**: systematic review and meta-analysis of observational studies. BMJ 342:doi:10.1136/bmj.d1309 (17 Mar 2011)
Lombardo F, Passanisi S, Caminiti L, et al. High prevalence of **skin reactions among pediatric patients with type 1 diabetes** using new technologies: the alarming role of colophonium. Diabetes Technol Ther. 2019 Aug 29. doi: 10.1089/dia.2019.0236.
Long JA, Jahnle EC, Richardson DM, Loewenstein G, Volpp KG. **Peer mentoring** and financial incentives to improve glucose control in african american veterans: a randomized trial. Ann Intern Med. 2012 Mar 20;156(6):416-24.
Long AN, Atwell CL, Yoo W, Solomon SS. **Vitamin B(12) deficiency** associated with concomitant **metformin and proton pump inhibitor** use. Diabetes Care. 2012 Dec;35(12):e84.
*Long GH, Cooper AJ, Wareham NJ, et al. **Healthy Behavior Change and Cardiovascular Outcomes** in Newly Diagnosed Type 2 Diabetes Patients: A Cohort Analysis of The **ADDITION-Cambridge** Study. Diabetes Care. 2014 Mar 21.*
Lonn EM, Gerstein HC, Sheridan P, Smith S, Diaz R, Mohan V, Bosch J, Yusuf S, Dagenais GR; DREAM (Diabetes REduction Assessment with ramipril and rosiglitazone Medication) and **STARR** Investigators. Effect of ramipril and of rosiglitazone on carotid intima-media thickness in people with impaired glucose tolerance or impaired fasting glucose: STARR (STudy of Atherosclerosis with Ramipril and Rosiglitazone). J Am Coll Cardiol. 2009 Jun 2;53(22):2028-35. One thousand four hundred twenty-five people with IGT and/or IFG but without cardiovascular disease or diabetes were randomized to ramipril 15 mg/day or its placebo and to rosiglitazone 8 mg/day or its placebo with a 2 x 2 factorial design for 3years. In people with IGT and/or IFG without cardiovascular disease and diabetes, treatment with ramipril had a neutral effect on CIMT, whereas rosiglitazone modestly reduced CIMT progression.
Look AHEAD Research Group. Cardiovascular effects of intensive lifestyle intervention in type 2 diabetes. N Engl J Med 2013. DOI: 10.1056/NEJMoa1212914.
Lopez D, Luque-Fernandez MA, Steele A, et al. **"Nonfunctional" Adrenal Tumors** and the Risk for Incident Diabetes and Cardiovascular Outcomes: A Cohort Study. Ann Intern Med. 2016 Aug 2
Lopez PE, Evans M, King BR, et al. A randomized comparison of **three prandial insulin dosing algorithms for children and adolescents with Type 1 diabetes**. Diabet Med. 2018 Jun 5.

Loprinzi PD. Association of **Accelerometer-Assessed Sedentary Behavior** With Diabetic Retinopathy in the United States. JAMA Ophthalmol. 2016 Aug 4.

Lord JM, Flight IH, Norman RJ. Insulin-sensitising drugs (metformin, troglitazone, rosiglitazone, pioglitazone, D-chiro-inositol) for **polycystic ovary syndrome**. Cochrane Database Syst Rev. 2003;(3):CD003053.

Lorenzo C, Haffner SM. **Performance characteristics of the new definition of diabetes**: the insulin resistance atherosclerosis study. Diabetes Care. 2010 Feb;33(2):335-7. Epub 2009 Oct 30.

Lotstein DS, Seid M, Klingensmith G, et al; for the SEARCH for Diabetes in Youth Study Group. **Transition From Pediatric to Adult Care** for Youth Diagnosed With Type 1 Diabetes in Adolescence. Pediatrics. 2013 Mar 25.

Lotta LA, Wittemans LBL, Zuber V, et al. Association of **Genetic Variants Related to Gluteofemoral vs Abdominal Fat Distribution With Type 2 Diabetes**, Coronary Disease, and Cardiovascular Risk Factors. JAMA. 2018 Dec 25;320(24):2553-2563.

Louie JC, Markovic TP, Perera N, et al. A randomized controlled trial investigating the effects of a **low-glycemic index** diet on pregnancy outcomes in **gestational** diabetes mellitus. Diabetes Care. 2011 Nov;34(11):2341-6.

Lovvik TS, Carlsen SM, Salvesen O, et al. Use of **metformin to treat pregnant women with polycystic ovary syndrome (PregMet2)**: a randomised, double-blind, placebo-controlled trial. Lancet Diabetes Endocrinol. 2019 Apr;7(4):256-266.

Lowe WL Jr, Scholtens DM, Lowe LP, et al; HAPO Follow-up Study Cooperative Research Group. Association of **Gestational Diabetes With Maternal Disorders of Glucose Metabolism and Childhood Adiposity**. JAMA. 2018 Sep 11;320(10):1005-1016.

Lowe WL Jr, Lowe LP, Kuang A, et al; HAPO Follow-up Study Cooperative Research Group. **Maternal glucose levels during pregnancy and childhood adiposity** in the Hyperglycemia and Adverse Pregnancy Outcome Follow-up Study. Diabetologia. 2019 Jan 15.

Lu J, Ma X, Zhou J, et al. Association of **Time in Range**, as Assessed by Continuous Glucose Monitoring, **With Diabetic Retinopathy in Type 2 Diabetes**. Diabetes Care. 2018 Nov;41(11):2370-2376.

Lu WR, Defilippi J, Braun A. **Unleash metformin**: reconsideration of the contraindication in patients with **renal impairment**. Ann Pharmacother. 2013 Nov;47(11):1488-97.

Lu ZX, Walker KZ, O'Dea K, Sikaris KA, Shaw JE. **A1C for screening and diagnosis** of type 2 diabetes in routine clinical practice. Diabetes Care. 2010 Apr;33(4):817-9. Epub 2010 Jan 12.

Lubowsky ND, Siegel R, Pittas AG. Management of glycemia in patients with **diabetes mellitus and CKD**. Am J Kidney Dis. 2007 Nov;50(5):865-79.

Ludvigsson JF, Neovius M, Söderling J, et al. Maternal Glycemic Control in Type 1 Diabetes and the **Risk for Preterm Birth**: A Population-Based Cohort Study. Ann Intern Med. 2019 Apr 23.

Ludvigsson Johnny, Krisky David, Casas Rosaura, **GAD65 Antigen Therapy** in Recently Diagnosed Type 1 Diabetes Mellitus. N Engl J Med 2012; 366:433-442. (not effective)

Lum E, Jimenez G, Huang Z, et al. Decision Support and Alerts of **Apps for Self-management of Blood Glucose** for Type 2 Diabetes. JAMA. 2019 Apr 16;321(15):1530-1532.

Lund SS, Tarnow L, Astrup AS, et al. Effect of adjunct **metformin** treatment in patients with type-1 diabetes and persistent inadequate glycaemic control. A randomized study. PLoS ONE. 2008;3(10):e3363. Epub 2008 Oct 9.

Lund Søren S, Tarnow Lise, Frandsen Merete, et al. Combining insulin with **metformin** or an insulin secretagogue (repaglinide) in non-obese patients with type 2 diabetes: 12 month, randomised, double blind trial. BMJ 2009;339:b4324, doi:10.1136/bmj.b4324 (Published 9 November 2009

Lundkvist P, et al. **Dapagliflozin** once-daily & **exenatide** once-weekly dual therapy: A 24-week randomized, placebo-controlled, phase II study examining effects on body weight & prediabetes in obese adults without diabetes. Diabetes Obes Metab. 2016 Aug 23.

Lung Derrick D., Olson Kent R.. Hypoglycemia in Pediatric **Sulfonylurea Poisoning**: An 8-Year Poison Center Retrospective Study. Pediatrics 2011; 127:6 e1558-e1564; ahead of print May 23, 2011, doi:10.1542/peds.2010-3235.

Lung TW, Petrie D, Herman WH, et al. **Severe hypoglycemia and mortality** after cardiovascular events for type 1 diabetic patients in sweden. Diabetes Care. 2014 Nov;37(11):2974-81.

Luo J, Avorn J, Kesselheim AS. Trends in **Medicaid Reimbursements for Insulin** From 1991 Through 2014. JAMA Intern Med. 2015 Aug 24.

Luo G, Liu H, Lu H. **Glucagon-like peptide-1(GLP-1)** receptor agonists: potential to **reduce fracture risk** in diabetic patients? Br J Clin Pharmacol. 2016 Jan;81(1):78-88

Luo X, Dai W, Chee M, et al. Association of Diabetes With Central **Corneal Thickness** Among a Multiethnic Asian Population. JAMA Netw Open. 2019;2(1):e186647.

Luo J, Khan NF, Manetti T, et al. Implementation of a **health plan program for switching from analogue to human insulin and glycemic control among Medicare beneficiaries** with type 2 diabetes [Jan 29, 2019]. JAMA. doi:10.1001/jama.2018.21364

Luo J, Manson JE, Weitlauf JC, et al. **Personality traits and diabetes incidence among postmenopausal women**. Menopause. 2019 Jan 21.

Luoto R, Kinnunen TI, Aittasalo M, Kolu P, Raitanen J, et al. (2011) Primary **Prevention of Gestational Diabetes Mellitus** and Large-for-Gestational-Age Newborns by **Lifestyle Counseling**: A Cluster-Randomized Controlled Trial. PLoS Med 8(5): e1001036. doi:10.1371/journal.pmed.1001036

Lv J, Perkovic V, Foote CV, et al. **Antihypertensive agents for preventing diabetic kidney disease**. Cochrane Database Syst Rev. 2012 Dec 12;12:CD004136. doi: 10.1002/14651858.CD004136.pub3.
ACEi were found to prevent new onset DKD and death in normoalbuminuric people with diabetes, and could therefore be used in this population. More data are needed to clarify the role of ARB and other drug classes in preventing DKD.

Lv C, Chen C, Chen Q, et al. **Multiple pregnancies and the risk of diabetes mellitus in postmenopausal women**. Menopause. 2019 May 6.

Ly TT, Nicholas JA, et al. Effect of **sensor-augmented insulin pump** therapy and automated insulin suspension vs standard insulin pump therapy on hypoglycemia in patients with type 1 diabetes: a randomized clinical trial. JAMA. 2013;310(12):1240-1247.

Lycett D, Nichols L, Ryan R, et al. The association between **smoking cessation and glycaemic control** in patients with type 2 diabetes: a THIN database cohort study. Lancet Diabetes Endocrinol. 2015 Jun;3(6):423-30.

Lynch EB, Mack L, Avery E, et al. Randomized Trial of a **Lifestyle Intervention for Urban Low-Income African Americans** with Type 2 Diabetes. J Gen Intern Med. 2019 Apr 8.

Lyon C, Fields H, Langner S, DeSanto K. **Diabetes Education and Glycemic Control**. Am Fam Physician. 2018 Feb 15;97(4):269-270.

Lytvyn Y, Bjornstad P, Udell JA, et al. **Sodium Glucose Cotransporter-2 Inhibition in Heart Failure**: Potential Mechanisms, Clinical Applications, and Summary of Clinical Trials. Circulation. 2017 Oct 24;136(17):1643-1658.

Ma Y, Hébert JR, et al. **All-cause, cardiovascular, and cancer mortality** rates in postmenopausal white, black, Hispanic, and Asian women with and without diabetes in the United States: The Women's Health Initiative (WHI), 1993-2009. Am J Epidemiol 2013.

Maahs DM, Daniels SR, de Ferranti SD, et al; American Heart Association Atherosclerosis, Hypertension and Obesity in Youth Committee of the Council on Cardiovascular Disease in the Young, Council on Clinical Cardiology, Council on Cardiovascular and Stroke Nursing, Council for High Blood Pressure Research, and Council on Lifestyle and Cardiometabolic Health. **Cardiovascular disease risk factors in youth with diabetes mellitus**: a scientific statement from the american heart association. Circulation. 2014 Oct 21;130(17):1532-58

Maahs DM, DeSalvo D, Pyle L, et al. Effect of **acetaminophen on CGM glucose** in an outpatient setting. Diabetes Care. 2015 Oct;38(10):e158-9.

MacCallum L, Consiglio G, MacKeigan L, et al. Uptake of **community pharmacist-delivered MedsCheck Diabetes medication review** service in Ontario between 2010 and 2014. Can J Diabetes 2017; published online March 18, 2017.

MacFarlane LA, Jin Y, Franklin PD, et al. **Assessment for Perioperative Hyperglycemia** Prior to Total Joint Replacement in Patients With and Without Diabetes. JAMA Netw Open. 2019 Sep 4;2(9):e1910589.

Macintosh MC, et al. **Perinatal mortality & congenital** anomalies in babies of women with type 1 or type 2 diabetes in England, Wales, and Northern Ireland: population based study. BMJ. 2006 Jul 22;333(7560):177. Epub 2006 Jun 16.

Mackin ST, Nelson SM, Kerssens JJ, et al. **Diabetes and pregnancy**: national trends over a 15 year period. Diabetologia. 2018 Jan 11.

Mackin ST, Nelson SM, Wild SH, et al. **Factors associated with stillbirth** in women with diabetes. Diabetologia. 2019 Jul 29.

Macrae D, Grieve R, Allen E, et al. A randomized trial of **hyperglycemic control in pediatric intensive care**. N Engl J Med 2014;370:107-18.

Madenidou AV, Paschos P, Karagiannis T, et al. **Comparative Benefits and Harms of Basal Insulin Analogues for Type 2 Diabetes**: A Systematic Review and Network Meta-analysis. Ann Intern Med. 2018 Jul 10.

Madjd A, Taylor MA, Delavari A, et al. Beneficial effects of **replacing diet beverages with water** on type 2 diabetic obese women following a hypo-energetic diet: A randomized, 24-week clinical trial. Diabetes Obes Metab. 2016 Oct 16.

Madsen KS, Kahler P, Kahler LKA, et al. Metformin and second- or third-generation sulphonylurea combination therapy for adults with type 2 diabetes mellitus. Cochrane Database Syst Rev. 2019 Apr 18;4:CD012368. There is inconclusive evidence whether M+S combination therapy compared with metformin plus another glucose-lowering intervention results in benefit or harm for most patient-important outcomes (mortality, SAEs, macrovascular and microvascular complications) with the exception of hypoglycaemia (more harm for M+S combination).

Madsen LR, Baggesen LM, Richelsen B, Thomsen RW**. Effect of Roux-en-Y gastric bypass surgery on diabetes remission** and complications in individuals with type 2 diabetes: a Danish population-based matched cohort study. Diabetologia. 2019 Feb 6.

Maggard-Gibbons M, Maglione M, Livhits M, et al. **Bariatric surgery** for weight loss and glycemic control in nonmorbidly obese adults with diabetes: A systematic review. JAMA 2013; 309:2250-2261.

Magliano DJ, Islam RM, Barr ELM, et al. **Trends in incidence of total or type 2 diabetes**: systematic review. BMJ. 2019 Sep 11;366:l5003.

Mahabaleshwarkar R, Gohs F, Mulder H, et al. Patient and Provider Factors Affecting Clinical Inertia in Patients With **Type 2 Diabetes on Metformin Monotherapy**. Clin Ther. 2017 Aug;39(8):1658-1670.e6.

Mahaffey KW, Jardine MJ, Bompoint S, et al. **Canagliflozin and Cardiovascular and Renal Outcomes** in Type 2 Diabetes Mellitus and Chronic Kidney Disease in Primary and Secondary Cardiovascular Prevention Groups. Circulation. 2019 Aug 27;140(9):739-750.

Mainous AG 3rd, Tanner RJ, Jo A, et al. Prevalence of Prediabetes and **Abdominal Obesity** Among Healthy-Weight Adults: 18-Year Trend. Ann Fam Med. 2016 Jul;14(4):304-10.

Mahaffey KW, Hafley G, Dickerson S, et al. Results of a reevaluation of cardiovascular outcomes in the **RECORD** trial (rosiglitazone). Am Heart J2013; 166:240-249.e1.

Mainous AG 3rd, Schatz DA. Is It **Time to Prioritize Diabetes Prevention** in Practice? J Am Board Fam Med. 2019 Jul-Aug;32(4):457-459.

Mainous AG 3rd, Tanner RJ, Anton SD, et al. **Physical Activity** and Abnormal Blood Glucose Among Healthy Weight Adults. Am J Prev Med. 2017 Jan 13.

Majumdar SR, Hemmelgarn BR, Lin M, McBrien K, Manns BJ, Tonelli M. **Hypoglycemia Associated With Hospitalization** and Adverse Events in Older People: Population-based cohort study. Diabetes Care. 2013 Oct 2.

Makam AN, Nguyen OK. An **Evidence-Based Medicine** Approach to **Antihyperglycemic Therapy** in Diabetes Mellitus **to Overcome Overtreatment**. Circulation. 2017 Jan 10;135(2):180-195.

Malanda UL, Welschen LM, Riphagen II, et al. **Self-monitoring of blood glucose** in patients with type 2 diabetes mellitus who are not using insulin. Cochrane Database Syst Rev. 2012 Jan 18;1:CD005060. From this review, we conclude that when diabetes duration is

over one year, the overall effect of self-monitoring of blood glucose on glycaemic control in patients with type 2 diabetes who are not using insulin is small up to six months after initiation and subsides after 12 months. Furthermore, based on a best-evidence synthesis, there is no evidence that SMBG affects patient satisfaction, general well-being or general health-related quality of life. More research is needed to explore the psychological impact of SMBG and its impact on diabetes specific quality of life and well-being, as well as the impact of SMBG on hypoglycaemia and diabetic complications.

Malanda UL, Bot SD, Kostense PJ, et al. Effects of **self-monitoring of glucose** on distress and self-efficacy in people with non-insulin-treated type 2 diabetes: a randomized controlled trial. Diabet Med. 2015 Jul 14.

Malik VS, Popkin BM, Bray GA, et al. **Sugar-sweetened beverages** and risk of metabolic syndrome and type 2 diabetes: A meta-analysis. Diabetes Care 2010: 33:2477-2483.

Malmenäs M, Bouchard JR, Langer J. Retrospective Real-World Adherence in Patients With Type 2 Diabetes Initiating Once-Daily **Liraglutide** 1.8 mg or Twice-Daily **Exenatide** 10 µg. Clin Ther. 2013 May 1.

Mamtani R, Haynes K, Bilker WB, et al. Association between longer therapy with **thiazolidinediones and risk of bladder cancer**: a cohort study. J Natl Cancer Inst. 2012 Sep 19;104(18):1411-21.

Mancia G, Cannon CP, Tikkanen I, et al. Impact of **Empagliflozin** on **Blood Pressure in** Patients With Type 2 Diabetes Mellitus and Hypertension by Background Antihypertensive Medication. Hypertension.2016 ;68 :000-000.

Mancini GB, Cheng AY, Connelly K, et al. **Diabetes for Cardiologists**: Practical Issues in Diagnosis and Management. Can J Cardiol. 2017 Mar;33(3):366-377.

Mandel EI, Curhan GC, Hu FB, Taylor EN. **Plasma bicarbonate** and risk of type 2 diabetes mellitus. CMAJ. 2012 Sep 18;184(13):E719-25.

Mangione CM, et al. TRIAD Study Group. The association between quality of care and the intensity of diabetes **disease management programs**. Ann Intern Med. 2006 Jul 18;145(2):107-16. Summary for patients in: Ann Intern Med. 2006 Jul 18;145(2):I41.

Mann DM, Carson AP, Shimbo D, Fonseca V, Fox CS, Muntner P. Impact of **A1C screening criterion on the diagnosis of pre-diabetes** among U.S. adults. Diabetes Care. 2010 Oct;33(10):2190-5.

Mann JFE, Ørsted DD, Brown-Frandsen K, et al. **Liraglutide** and **renal outcomes** in type 2 diabetes. (**Leader**) N Engl J Med 2017;377: 839-48.

Manns BJ, Tonelli M, Zhang J, et al Enrolment in **primary care networks**: impact on outcomes and processes of care for patients with diabetes. CMAJ. 2012 Feb 7;184(2):E144-52.

Mansi I, Frei CR, Wang CP, et al. **Statins and New-Onset Diabetes** Mellitus and Diabetic Complications: A Retrospective Cohort Study of US Healthy Adults. J Gen Intern Med. 2015 Apr 28.

Margel D, Urbach DR, Lipscombe LL, et al. **Metformin** Use and All-Cause and **Prostate Cancer**-Specific Mortality Among Men With Diabetes. J Clin Oncol. 2013 Sep 1;31(25):3069-3075.

Magnus MC, Olsen SF, Granström C, et al. **Infant Growth and Risk of Childhood-Onset Type 1 Diabetes** in Children From 2 Scandinavian Birth Cohorts. JAMA Pediatr. 2015 Dec 7;169(12):e153759.

Mahaffey KW;Neal B;Perkovic V;et al. **Canagliflozin** for Primary and Secondary Prevention of Cardiovascular Events: Results From the **CANVAS** Program (Canagliflozin Cardiovascular Assessment Study). Circulation. 2017 Nov 13.

Mahaffey KW, et al; CANVAS Program Collaborative Group. Canagliflozin for primary and secondary prevention of cardiovascular events: results from the **CANVAS** Program (**Canagliflozin** Cardiovascular Assessment Study). Circulation. 2018;137:323–334.

Marcovecchio ML et al. **ACE inhibitors and statins** in adolescents with **type 1 diabetes**. (**AdDit**) N Engl J Med2017 Nov 2; 377:1733.

Marcum ZA et al. Mortality associated with **metformin versus sulfonylurea** initiation: A cohort study of veterans with **diabetes and chronic kidney disease**. J Gen Intern Med 2018 Feb; 33:155.

Margulies KB, Hernandez AF, Redfield MM, et al. Effects of **Liraglutide** on Clinical Stability Among Patients **With Advanced Heart Failure** and Reduced Ejection Fraction: A Randomized Clinical Trial. JAMA. 2016 Aug 2;316(5):500-508

Margolis KL, O`Connor PJ, Morgan TM, et al. Outcomes of **Combined Cardiovascular Risk Factor Management** Strategies in Type 2 Diabetes: The **ACCORD** Randomized Trial. Diabetes Care. 2014 Mar 4.

Marshall SM, Flyvbjerg A. Prevention and early detection of **vascular complications** of diabetes. BMJ. 2006 Sep 2;333(7566):475-80.

Marso SP, Daniels GH, Brown-Frandsen K, et al. **Liraglutide and cardiovascular outcomes** in type 2 diabetes. (**Leader**) N Engl J Med. DOI: 10.1056/NEJMoa1603827.

Marso SP, Bain SC, Consoli A, et al. **Semaglutide** and Cardiovascular Outcomes in Patients with Type 2 Diabetes. **(Sustain-6)** N Engl J Med. 2016 Sep 15

Marso SP, Bain SC, Consoli A, et al; **SUSTAIN-6 Investigators**.. **Semaglutide** and Cardiovascular Outcomes in Patients with Type 2 Diabetes. N Engl J Med. 2016 Nov 10;375(19):1834-1844.

Marso SP, McGuire DK, Zinman B, et al. Efficacy and Safety of **Degludec versus Glargine** in Type 2 Diabetes. (**DEVOTE**) N Engl J Med. 2017 Jun 12

Marso SP, Nauck MA, Monk Fries T, et al. **Myocardial Infarction Subtypes** in Patients With Type 2 Diabetes Mellitus and the Effect of **Liraglutide** Therapy (from the **LEADER** Trial). Am J Cardiol. 2018 Mar 15.

Martin J, et al. **Cromium Picolinate** Supplementation Attenuates Body Weight Gain and Increases Insulin Sensitivity in Subjects With Type 2 Diabetes. Diabetes Care. Volume 29;8: 2006

Martinez J, Laswell E, Cailor S, et al. Frequency and Impact of **Pharmacist Interventions** in Clinical Trial Patients With Diabetes. Clin Ther. 2017 Mar 9.

Martinez-Ceron E, Barquiel B, et al. Effect of **Continuous Positive Airway Pressure on Glycemic Control** in Patients with Obstructive Sleep Apnea and Type 2 Diabetes. A Randomized Clinical Trial. Am J Respir Crit Care Med. 2016 Aug 15;194(4):476-85.

Martinez-Valbuena I, Valenti-Azcarate R, Amat-Villegas I, et al. **Amylin as a potential link between type 2 diabetes and Alzheimer's** disease. Ann Neurol. 2019 Aug 3.

Martis R, Crowther CA, Shepherd E, et al. **Treatments for women with gestational diabetes mellitus**: an overview of Cochrane systematic reviews. Cochrane Database Syst Rev. 2018 Aug 14;8:CD012327.

Maruthur NM, Ma Y, Delahanty LM, et al; for the Diabetes Prevention Program Research Group. **Early Response to Preventive Strategies** in the Diabetes Prevention Program. J Gen Intern Med. 2013 Jul 17.

Maruthur NM, Tseng E, Hutfless S, et al. Diabetes Medications as **Monotherapy or Metformin-Based Combination** Therapy for Type 2 Diabetes: A Systematic Review and Meta-analysis. Ann Intern Med. 2016 Apr 19.

Mason SA, Rasmussen B, van Loon LJC, et al. **Ascorbic acid supplementation improves postprandial glycaemic control and blood pressure in people with type 2 diabetes**: Findings of a randomized cross-over trial. Diabetes Obes Metab. 2018 Nov 4.

Mathieu C, Rodbard HW, Cariou B, et al. A comparison of adding **liraglutide versus a single daily dose of insulin aspart to insulin degludec** in subjects with type 2 diabetes (BEGIN: VICTOZA ADD-ON). Diabetes Obes Metab. 2014 Jan 20.

Mathieu C, Ranetti AE, Li D, et al. A Randomized, Double-Blind, Phase 3 Trial of Triple Therapy With **Dapagliflozin** Add-on to **Saxagliptin** Plus **Metformin** in Type 2 Diabetes. Diabetes Care. 2015 Aug 5.

Mathieu C, Zinman B, Hemmingsson JU, et al. Efficacy and Safety of **Liraglutide Added to Insulin** Treatment in Type 1 Diabetes: The **ADJUNCT ONE** Treat-To-Target Randomized Trial. Diabetes Care. 2016 Oct;39(10):1702-10.

Matsuhisa M, Koyama M, Cheng X, et al. New insulin **glargine 300 U/ml versus glargine 100** U/ml in Japanese adults with type 1 diabetes using basal and mealtime insulin: glucose control and hypoglycaemia in a randomized controlled trial (EDITION JP 1). Diabetes Obes Metab. 2016 Apr;18(4):375-83.

Matthews DE, Beatty SJ, Grever GM, et al. Comparison of 2 Population Health Management Approaches to Increase **Vitamin B12 Monitoring** in Patients Taking **Metformin**. Ann Pharmacother. 2016 Oct;50(10):840-6.

Matthews DR, Paldánius PM, Proot P, et al. Glycaemic durability of an early combination therapy with **vildagliptin and metformin versus sequential metformin monotherapy** in newly diagnosed type 2 diabetes (VERIFY): a 5-year, multicentre, randomised, double-blind trial. Lancet. 2019 Sep 17.

Matuleviciene-Anängen V, Rosengren A, Svensson AM, et al. **Glycaemic control and excess risk of major coronary events** in persons with type 1 diabetes. Heart. 2017 Jul 14.

Mauer M, Zinman B, Gardiner R, et al. Renal and retinal effects of **enalapril and losartan in type 1** diabetes. N Engl J Med. 2009 Jul 2;361(1):40-51. Early blockade of the renin-angiotensin system in patients with type 1 diabetes did not slow nephropathy progression but slowed the progression of retinopathy.

Mauras N, Beck R, Xing D, et al. A randomized clinical trial to assess the efficacy and safety of **real-time continuous glucose monitoring** in the management of type 1 diabetes in **young children** aged 4 to <10 years. Diabetes Care. 2012 Feb;35(2):204-10.

May AL, Kuklina EV, Yoon PW. Prevalence of Cardiovascular Disease Risk Factors Among US **Adolescents**, 1999-2008. Pediatrics. 2012 May 21. (14% increase in prediabetes/diabetes)

Mayer-Davis EJ, Lawrence JM, Dabelea D, et al. **Incidence trends of type 1 and type 2 diabetes among youths**, 2002–2012. N Engl J Med 2017;376:1419-29.

Mayor S. Sixty seconds on…drinking and diabetes. BMJ. 2017 Aug 2;358:j3672

Mazzone T, Meyer PM, Feinstein SB, et al. Effect of pioglitazone compared with glimepiride on carotid intima-media thickness in type 2 diabetes. (**CHICAGO**) A randomized trial. *JAMA* 2006; 298:doi:10.1001/jama.296.21.joc60158. Over an 18-month treatment period in patients with type 2 DM, pioglitazone slowed progression of CIMT compared with glimepiride.

McAdam-Marx C, Nguyen H, Schauerhamer MB, et al. Glycemic Control and Weight Outcomes for **Exenatide Once Weekly Versus Liraglutide** in Patients with Type 2 Diabetes: A 1-Year Retrospective Cohort Analysis. Clin Ther. 2016 Nov 23.

McAllister DA, Hughes KA, Lone N, et al. **Stress hyperglycaemia** in hospitalised patients and their 3-year risk of diabetes: a Scottish retrospective cohort study. PLoS Med. 2014 Aug 19;11(8):e1001708.

McAuley PA, Artero EG, Sui X, et al. **Fitness, fatness, and survival** in adults with prediabetes. Diabetes Care. 2014 Feb;37(2):529-36. CRF markedly modifies the relationship between adiposity and mortality in persons with prediabetes. Unfit individuals have a higher and fit individuals have a lower mortality risk irrespective of adiposity level in this high-risk group.

McBain H, Mulligan K, Haddad M, et al. **Self management interventions** for type 2 diabetes in adult people with severe mental illness. Cochrane Database Syst Rev. 2016 Apr 27;4:CD011361. Evidence is insufficient to show whether type 2 diabetes self management interventions for people with severe mental illness are effective in improving outcomes. Researchers must conduct additional trials to establish efficacy, and to identify the active ingredients in these interventions and the people most likely to benefit from them.

McBrien K, Rabi DM, Campbell N, et al. **Intensive and Standard Blood Pressure** Targets in Patients With Type 2 Diabetes Mellitus: Systematic Review and Meta-analysis. Arch Intern Med. 2012 Aug 6:1-8.

McCall KL, Craddock D, Edwards K. Effect of **Angiotensin**-Converting Enzyme Inhibitors and **Angiotensin II** Type 1 Receptor Blockers on the Rate of New-Onset Diabetes Mellitus: A Review and Pooled Analysis. Pharmacotherapy. 2006 Sep;26(9):1297-306.

McCartney CR, Marshall JC. CLINICAL PRACTICE. **Polycystic Ovary Syndrome**. N Engl J Med. 2016 Jul 7;375(1):54-64.

McCombie L, Leslie W, Taylor R, et al. **Beating type 2 diabetes into remission**. BMJ. 2017 Sep 13;358:j4030.
McCoy RG, Van Houten HK, Ross JS, et al. **HbA1c overtesting and overtreatment among US adults** with controlled type 2 diabetes, 2001-13: observational population based study. BMJ 2015;351:h6138.
McCoy RG, Lipska KJ, Yao X, Ross JS, Montori VM, Shah ND. **Intensive treatment and severe hypoglycemia** among adults with type 2 diabetes [online June 6, 2016].JAMA Intern Med. doi:10.1001/jamainternmed.2016.2275.
McCrimmon RJ, Ryan CM, Frier BM. Diabetes and **cognitive dysfunction**. Lancet. 2012 Jun 8.
McDonagh MS, Selph S, Ozpinar A, et al. Systematic Review of the Benefits and Risks of **Metformin in Treating Obesity in Children** Aged 18 Years and Younger. JAMA Pediatr. 2013 Dec 16
McGovern A, Tippu Z, Hinton W, et al. Comparison of medication **adherence and persistence** in type 2 diabetes: A systematic review and meta-analysis. Diabetes Obes Metab. 2017 Nov 14.
McGrath K. Edi, R, **Diabetic Kidney Disease**: Diagnosis, Treatment, and Prevention. Am Fam Physician. 2019;99(12):751-759.
McGuire H, Longson D, Adler A, et al. Management of **type 2 diabetes in adults**: summary of updated **NICE** guidance. BMJ. 2016 Apr 6
McGuire DK, Alexander JH, Johansen O.E., et al. **Linagliptin Effects on Heart Failure and Related Outcomes in Individuals with Type 2 Diabetes** at High Cardiovascular and Renal Risk in **CARMELINA**. Circulation 2018. in press doi: 10.1161/CIRCULATIONAHA.118.038352.
McInnes G, Evans M, Del Prato S, et al. Cardiovascular and **heart failure safety profile of vildagliptin**: a meta-analysis of 17 000 patients. Diabetes Obes Metab. 2015 Nov;17(11):1085-92.
McInnes N, Smith A, Otto R, et al. Piloting a **Remission Strategy in Type 2 Diabetes**: Results of a Randomized Controlled Trial. J Clin Endocrinol Metab. 2017 Mar 15.
McIntosh EC, Nation DA; Alzheimer's Disease Neuroimaging Initiative. Importance of **Treatment Status in Links Between Type 2 Diabetes and Alzheimer Disease**. Diabetes Care. 2019 Mar 4.
McMullan CJ, Schernhammer ES, Rimm EB, et al. **Melatonin** secretion and the incidence of type 2 diabetes. JAMA. 2013 Apr 3;309(13):1388-96.
McMurray JJV, Solomon SD, Inzucchi SE, et al. **Dapagliflozin in patients with heart failure and reduced ejection fraction**. (DAPA-HF) N Engl J Med. DOI: 10.1056/NEJMoa1911303.
McPherson R, Frohlich J, Fodor G, Genest J. **Canadian 2006** Cardiovascular Society position statement -- Recommendations for the diagnosis and treatment of **dyslipidemia** and prevention of cardiovascular disease. Can J Cardiol. 2006 Sep;22(11):913-27.
McTavish L, Krebs JD, Weatherall M, et al. **Weight-based hypoglycaemia** treatment protocol for adults with Type 1 diabetes: a randomized crossover clinical trial. Diabet Med. 2015 Sep;32(9):1143-8.
McTavish L, Corley B, Weatherall M, et al. Weight-based **carbohydrate treatment of hypoglycaemia** in people with Type 1 diabetes using insulin pump therapy: a randomized crossover clinical trial. Diabet Med. 2018 Mar;35(3):339-346.
Mearns ES, Saulsberry WJ, White CM, et al. Efficacy and safety of **antihyperglycaemic drug regimens added to metformin and sulphonylurea** therapy in Type 2 diabetes: a network meta-analysis. Diabet Med. 2015 Dec;32(12):1530-40.
Medical Letter May 23,2005: **Pramlintide** for Diabetes.
Medical Letter Jan 30,2006: **Pioglitazone/Metformin** (Actoplus met)
Medical Letter Jan 1,2007: **Sitagliptin** (Januvia); Medical Letter. Sitagliptin/Metformin (Janumet) for Type 2 Diabetes. June 4,2007.
Medical Letter Jan 29,2007: **Pioglitazone/glimepiride** (Duetact)
Medical Letter. **Liraglutide** (Victoza) for Type 2 Diabetes. April 5,2010.
Medical Letter. **Continuous Glucose Monitoring**. May 2, 2011.
Medical Letter. **Canagliflozin** (Invokana) for Type 2 Diabetes. May 13, 2013.
Medical Letter. **Dapagliflozin** (Farxiga) for Type 2 Diabetes. February 17, 2014.
Megia A, Naf S, Herranz L, et al. The usefulness of **HbA1c in postpartum reclassification of gestational** diabetes. BJOG. 2012 Apr 24.
Melander O, Maisel AS, Almgren P, et al. **Plasma proneurotensin** and incidence of diabetes, cardiovascular disease, breast cancer, and mortality. JAMA 2012; 308:1469-1475.
Melsom T, Schei J, Stefansson VT, et al. **Prediabetes** and Risk of **Glomerular Hyperfiltration and Albuminuria** in the General Nondiabetic Population: A Prospective Cohort Study. Am J Kidney Dis. 2015 Dec 16.
Menard J, Payette H, Baillargeon JP, Maheux P, et al. Efficacy of **intensive multitherapy** for patients with type 2 diabetes mellitus: a randomized controlled trial. CMAJ. 2005 Nov 17; [Epub ahead of print]
Mendes R, Sousa N, Almeida A, et al. **Exercise prescription** for patients with type 2 diabetes-a synthesis of international recommendations: narrative review. Br J Sports Med.2015 Dec 30.
Mendez-Figueroa H, Schuster M, Maggio L, et al. **Gestational Diabetes Mellitus and Frequency of Blood Glucose Monitoring**: A Randomized Controlled Trial. Obstet Gynecol. 2017 Jul;130(1):163-170.
Meneilly GS. **Diabetes in the elderly**. Med Clin North Am. 2006 Sep;90(5):909-23.
Menke A, Casagrande S, Geiss L, Cowie CC. **Prevalence of and trends** in diabetes among adults in the United States, 1988-2012.JAMA. doi:10.1001 /jama.2015.10029.
Meng X, Xu S, Chen G, Derwahl M, Liu C. **Metformin and thyroid disease**. J Endocrinol. 2017 Feb 14.
Menke A, Casagrande S, Cowie CC. Prevalence of **Diabetes in Adolescents Aged 12to 19 Years** in the United States, 2005-2014. JAMA. 2016 Jul 19;316(3):344-5.
Menon V, Lincoff AM. **Cardiovascular safety evaluation** in the development of new drugs for diabetes mellitus. Circulation. 2014 Jun 24;129(25):2705-13.
Menon V, Aggarwal B. Why are we doing **cardiovascular outcome trials** in type 2 diabetes? Cleve Clin J Med. 2014 Nov;81(11):665-71.
Merino J; CHARGE Consortium Nutrition Working Group. Quality of **dietary fat and genetic risk of type 2 diabetes**: individual participant data meta-analysis. BMJ. 2019 Jul 25;366:l4292.
Merlotti C, Morabito A, Pontiroli AE. **Prevention of type 2 diabetes**; a systematic review and meta-analysis of different intervention strategies. Diabetes Obes Metab. 2014 Jan 29.
Mesotten D, Gielen M, Sterken C, et al. **Neurocognitive development** of children 4 years after critical illness and treatment with tight glucose control: a randomized controlled trial [published online October 17, 2012]. JAMA. doi: 10.1001/jama.201212424.
Meyer EJ, Gabb G, Jesudason D. **SGLT2 Inhibitor-Associated Euglycemic Diabetic Ketoacidosis**: A South Australian Clinical Case Series and Australian Spontaneous Adverse Event Notifications. Diabetes Care. 2018 Apr;41(4):e47-e49.
Meyerovitch J, Zlotnik M, Yackobovitch-Gavan M, et al. **Real-Life Glycemic Control** in Children with Type 2 Diabetes: A Population-Based Study. J Pediatr. 2017 Jul 7.
MHRA Sep/12 There have been reports of **acute pancreatitis** associated with drugs in the **dipeptidylpeptidase-4 (DPP-4) inhibitor** class of antidiabetic agents ('gliptins').
MHRA Dec/15: Storing home use **GlucoMen LX Sensor test strips incorrectly**, especially in high humidity, can lead to falsely high readings.
MHRA Apr/16 **SGLT2 inhibitors**: updated advice on the risk of **diabetic ketoacidosis**. Test for raised ketones in patients with ketoacidosis symptoms, even if plasma glucose levels are near-normal. https://www.gov.uk/drug-safety-update/sglt2-inhibitors-updated-advice-on-the-risk-of-diabetic-ketoacidosis
MHRA June/16 **Canagliflozin** (Invokana▼ , Vokanamet▼): signal of increased risk of **lower extremity amputations** observed in trial in high cardiovascular risk patients.
MHRA June/16 **TRUEyou blood glucose test strips** - certain lots of test strips may give incorrect low blood glucose results that could lead to undetected hyperglycaemia.
MHRA Aug/16: The manufacturer, Nipro Diagnostics, found an issue with the packaging meaning that test strips in specific lots are not sealed properly. This can affect how the strips measure blood glucose levels and could lead to undetected high blood glucose (hyperglycaemia) which can have serious health implications. People using these test strips, which are used in **TRUEresult, TRUEresult twist, and TRUEtrack blood glucose meters**, are asked to check if they use affected blood glucose test strips with the lot numbers below.
Miao Jonasson J, Hendryx M, Manson JE, et al. **Personality traits and the risk** of coronary heart disease or stroke in women with diabetes - an epidemiological study based on the Women's Health Initiative. Menopause. 2019 Oct;26(10):1117-1124.
Middleton P, Crowther CA, Simmonds L. Different intensities of **glycaemic control for pregnant women with pre-existing diabetes**. Cochrane Database Syst Rev. 2012 Aug 15;8:CD008540. In a very limited body of evidence, few differences in outcomes were seen between very tight and tight-moderate glycaemic control targets in pregnant women with pre-existing type 1 diabetes, including actual glycaemic control achieved. There is evidence of harm (increased pre-eclampsia, caesareans and birthweights greater than 90th centile) for `loose` control (FBG above 7 mmol/L). Future trials comparing interventions, rather than glycaemic control targets, may be more feasible particularly for pregnant women with type 2 diabetes.
Mishra SC, Chhatbar KC, Kashikar A, Mehndiratta A. **Diabetic foot**. BMJ. 2017Nov 16;359:j5064.
Mikkelsen KH, Knop FK, Frost M, Hallas J, et al. Use of **Antibiotics and Risk of Type 2 Diabetes**: A Population-Based Case-Control Study. J Clin Endocrinol Metab. 2015 Aug 27:jc20152696.
Miller ME, Bonds DE, Gerstein HC, et al. **ACCORD** Investigators. The effects of baseline characteristics, glycaemia treatment approach, and glycated haemoglobin concentration on the risk of severe hypoglycaemia: post hoc epidemiological analysis of the ACCORD study. BMJ. 2010 Jan 8;340:b5444. doi: 10.1136/bmj.b5444.
Miller ME, Williamson JD, Gerstein HC, et al.; **ACCORD** Investigators. Effects of randomization to intensive glucose control on **adverse events, cardiovascular disease, and mortality** in older versus younger adults in the ACCORD Trial. Diabetes Care 2014;37:634–43.
Mingrone G, Panunzi S, De Gaetano A, et al. **Bariatric surgery versus conventional** medical therapy for type 2 **diabetes**. N Engl J Med 2012. DOI: 10.1056/NEJMoa1200111.
Mingrone G, Panunzi S, De Gaetano A, et al. **Bariatric–metabolic surgery** versus conventional medical treatment in obese patients with type 2 diabetes: 5 year follow-up of an open-label, single-centre, randomised controlled trial. Lancet 2015; 386: 964–73.
Miras AD, Pérez-Pevida B, Aldhwayan M, et al. **Adjunctive liraglutide treatment** in patients with persistent or recurrent type 2 diabetes after metabolic surgery (GRAVITAS): a randomised, double-blind, placebocontrolled trial. Lancet Diabetes Endocrinol 2019; online June 4.
Miremberg H, Ben-Ari T, Betzer T, et al. The impact of a daily **smartphone-based feedback** system among women with **gestational diabetes** on compliance, glycemic control, satisfaction, and pregnancy outcome: a randomized controlled trial. Am J Obstet Gynecol. 2018 Apr;218(4):453.e1-453.e7.
Mishriky BM, Powell JR, Wittwer JA, et al. **Do GLP-1RAs and SGLT-2is reduce cardiovascular events** in black patients with type 2 diabetes? A systematic review and meta-analysis. Diabetes Obes Metab. 2019 Jun 5.
Misra S, Oliver NS. **Diabetic ketoacidosis in adults**. BMJ. 2015 Oct 28;351:h5660.
Mitanchez D, Burguet A, Simeoni U. Infants Born to Mothers with **Gestational Diabetes** Mellitus: Mild Neonatal Effects, a Long-term Threat to Global Health. J Pediatr. 2013 Dec 10

Moelands SV, Lucassen PL, Akkermans RP, et al. **Alpha-glucosidase inhibitors for prevention or delay of type 2 diabetes mellitus** and its associated complications in people at increased risk of developing type 2 diabetes mellitus. Cochrane Database Syst Rev. 2018 Dec 28;12:CD005061. AGI may prevent or delay the development of T2DM in people with IGT. There is no firm evidence that AGI have a beneficial effect on cardiovascular mortality or cardiovascular events.

Monami M, Dicembrini I, Antenore A, Mannucci E. **Dipeptidyl peptidase-4 inhibitors and bone fractures**: a meta-analysis of randomized clinical trials. Diabetes Care. 2011 Nov;34(11):2474-6. (May reduce fractures)

Monami M, Dicembrini I, Mannucci E. **Dipeptidyl peptidase-4 inhibitors and pancreatitis risk**: a meta-analysis of randomized clinical trials. Diabetes Obes Metab. 2013 Jul 9.

Monami M, Nreu B, Scatena A, et al. **Safety issues with glucagon-like peptide-1 receptor agonists (pancreatitis, pancreatic cancer and cholelithiasis):** Data from randomized controlled trials. Diabetes Obes Metab. 2017 Feb 28.

Monami M, Liistro F, Scatena A, et al. Short and medium-term efficacy of sodium glucose co-transporter-2 **(SGLT-2) inhibitors**: A meta-analysis of randomized clinical trials. Diabetes Obes Metab. 2018 Jan 12.

Moghissi ES, Korytkowski MT, DiNardo M, et al. American Association of Clinical Endocrinologists and American Diabetes Association consensus statement on **inpatient glycemic control**. *Endocr Pract* 2009;15:1-17.

Moghissi ES, Korytkowski MT, DiNardo M, et al.; American Association of Clinical Endocrinologists; American Diabetes Association. American Association of Clinical Endocrinologists and American Diabetes Association consensus statement on **inpatient glycemic** control. Diabetes Care. 2009 Jun;32(6):1119-31. Epub 2009 May 8.

Mohamed Q, Gillies MC, Wong TY. Management of **diabetic retinopathy**: a systematic review. JAMA. 2007 Aug 22;298(8):902-16.

Mohan M, Al-Talabany S, McKinnie A, et al. A randomized controlled trial of **metformin on left ventricular hypertrophy in patients with coronary artery disease without diabetes**: the MET-REMODEL trial. Eur Heart J. 2019 Apr 17.

Moin T, Li J, Duru OK, et al. **Metformin prescription for insured** adults with prediabetes from 2010 to 2012: a retrospective cohort study. Ann Intern Med. 2015 Apr 21;162(8):542-8.

Mokashi A, Young M. When you **suspect diabetes in a child**. Can Fam Physician. 2018 Jan;64(1):32-35.

Mokhlesi B, Temple KA, Tjaden AH, et al; RISE Consortium. **Association of Self-Reported Sleep and Circadian Measures** With Glycemia in Adults With Prediabetes or Recently Diagnosed Untreated Type 2 Diabetes. Diabetes Care. 2019 Jul;42(7):1326-1332.

Moll E, et al. Effect of clomifene citrate plus metformin & **clomifene plus placebo** on induction of ovulation in women with newly diagnosed polycystic ovary syndrome: randomised double blind clinical trial. BMJ. 2006 Jun 24;332(7556):1485. Epub 2006 Jun 12.

Moore LE, Clokey D, Rappaport VJ, Curet LB. Metformin compared with **glyburide** in **gestational** diabetes: a randomized controlled trial. Obstet Gynecol. 2010 Jan;115(1):55-9.

Monami M, et al. **Three-year mortality** in diabetic patients treated with different **combinations of insulin secretagogues and metformin**. Diabetes Metab Res Rev. 2006 Apr 24; [Epub ahead of print]

Monami M, Colombi C, Balzi D, et al. **Metformin and Cancer** Occurrence in Insulin-treated type 2 diabetic patients. Diabetes Care. 2010 Oct 27. [Epub ahead of print]

Monami M, Lamanna C, Desideri CM, Mannucci E. DPP-4 inhibitors and lipids: systematic review and meta-analysis. Adv Ther. 2012 Jan;29(1):14-25.

Monami M, Genovese S, Mannucci E. **Cardiovascular safety of sulfonylureas**: a meta-analysis of randomized clinical trials. Diabetes Obes Metab. 2013 Apr 17.

Monami M, Nardini C, Mannucci E. Efficacy and safety of **sodium glucose co-transport-2 inhibitors** in type 2 diabetes: a meta-analysis of randomized clinical trials. Diabetes Obes Metab. 2014;16:457-466

Monami M, Nardini C, Mannucci E. Efficacy and safety of **sodium glucose co-transport-2 inhibitors** in type 2 diabetes: a meta-analysis of randomized clinical trials. Diabetes Obes Metab. 2013 Dec 5.

Mongraw-Chaffin M, Bertoni AG, Golden SH, et al. Association of **Low Fasting Glucose and HbA1c** With Cardiovascular Disease and Mortality: The MESA Study. J Endocr Soc. 2019 Mar 1;3(5):892-901.

Montori VM, Fernández-Balsells M. **Glycemic Control** in Type 2 Diabetes: **Time for an Evidence-Based About-Face**?. Ann Intern Med. 2009 Apr 20.

Montvida O, Green JB, Atherton J, Paul SK. Treatment with **incretins does not increase the risk of pancreatic diseases** compared to older anti-hyperglycaemic drugs, **when added to metformin**: real world evidence in people with Type 2 diabetes. Diabet Med. 2018 Oct 10.

Moore EM, Mander AG, Ames D, et al. Increased risk of **cognitive impairment** in patients with diabetes is associated with **metformin**. Diabetes Care. 2013 Oct;36(10):2981-7.

Moran A, Brundy B, Becker DJ, et al. **Interleukin-1 antagonism** (canakinumab & anakinra) in type 1 diabetes of recent onset: two multicentre, randomised, double-blind, placebo-controlled trials. Lancet 2013; online April 5.

Moreland EC, et al. Use of a blood **glucose monitoring manual** to enhance monitoring adherence in adults with diabetes: a randomized controlled trial. Arch Intern Med. 2006 Mar 27;166(6):689-95.

Morello CM, Christopher ML, Ortega L, et al. Clinical Outcomes Associated With a **Collaborative Pharmacist-Endocrinologist Diabetes Intense Medical Management** "Tune Up" Clinic in Complex Patients. Ann Pharmacother. 2016 Jan;50(1):8-16.

Moreno-Castilla C, Hernandez M, Bergua M, et al. **Low-Carbohydrate Diet** for the Treatment of Gestational Diabetes: A randomized controlled trial. Diabetes Care. 2013 Apr 5.

Morey MC, Pieper CF, Edelman DE, et al. **Enhanced fitness**: a randomized controlled trial of the effects of home-based physical activity counseling on glycemic control in older adults with prediabetes mellitus. J Am Geriatr Soc. 2012 Sep;60(9):1655-62.

Morgan CL, Poole CD, Evans M, et al. What Next **after Metformin**? A Retrospective Evaluation of the Outcome of Second-Line, Glucose-Lowering Therapies in People with Type 2 Diabetes. J Clin Endocrinol Metab. 2012 Oct 17.

Moreira-Lucas TS, Duncan AM, Rabasa-Lhoret R, et al. Effect of **vitamin D supplementation** on oral **glucose tolerance** in individuals with low vitamin D status and increased risk for developing type 2 diabetes (EVIDENCE): a double-blind, randomized, placebo-controlled clinical trial. Diabetes Obes Metab. 2016 Sep 26.

Morley LC, Tang T, Yasmin E, Norman RJ, Balen AH. **Insulin-sensitising drugs (metformin, rosiglitazone, pioglitazone, Dchiro-inositol) for women with polycystic ovary syndrome, oligo amenorrhoea and subfertility**. Cochrane Database of Systematic Reviews 2017, Issue 11. Art. No.: CD003053. Our updated review suggests that metformin alone may be beneficial over placebo for live birth, although the evidence quality was low. When metformin was compared with clomiphene citrate, data for live birth were inconclusive, and our findings were limited by lack of evidence. Results differed by body mass index (BMI), emphasising the importance of stratifying results by BMI. An improvement in clinical pregnancy and ovulation suggests that clomiphene citrate remains preferable to metformin for ovulation induction in obese women with PCOS.

Morrison JA, Glueck CJ, Horn PS, et al. **Childhood predictors** of adult type 2 diabetes at 9- and 26-year follow-ups. Arch Pediatr Adolesc Med. 2010 Jan;164(1):53-60.

Morrison F, Shubina M, Turchin A. **Encounter frequency** and serum glucose level, blood pressure, and cholesterol level control in patients with diabetes mellitus. Arch Intern Med. 2011;171(17):1542-1550.

Mosenzon O, Blicher TM, Rosenlund S, et al; PIONEER 5 Investigators. Efficacy and safety of **oral semaglutide** in patients with type 2 diabetes and moderate renal impairment (**PIONEER 5**): a placebo-controlled, randomised, phase 3a trial. Lancet Diabetes Endocrinol. 2019 Jul;7(7):515-527.

Mosenzon O, Wei C, Davidson J, et al. Incidence of **Fractures in Patients With Type 2 Diabetes in the SAVOR-TIMI 53** (**saxagliptin**)Trial. Diabetes Care. 2015 Sep 10.

Mosenzon O, Leibowitz G, Bhatt DL, et al. Effect of **Saxagliptin** on Renal Outcomes in the **SAVOR-TIMI 53** Trial. Diabetes Care. 2017 Jan;40(1):69-76.

Mosenzon O, Wiviott SD, Cahn A, et al. Effects of d**apagliflozin** on development and progression of kidney disease in patients with type 2 diabetes: an analysis from the **DECLARE-TIMI 58** randomised trial. Lancet Diabetes Endocrinol. 2019 Jun 10.

Movahedi M, Beauchamp ME, Abrahamowicz M, et al. Risk of Incident **Diabetes Associated with Dose and Duration of Oral Glucocorticoid Therapy** in Patients with Peumatoid Arthritis. Arthritis Rheumatol. 2015 Dec 14.

Moyer VA. Screening for **Gestational Diabetes** Mellitus: U.S. Preventive Services Task Force Recommendation Statement. Ann Intern Med. 2014 Jan 14

Mozaffarian D, Kamineni A, Prineas RJ, Siscovick DS. **Metabolic syndrome** and mortality in older adults: the Cardiovascular Health Study. Arch Intern Med. 2008 May 12;168(9):969-78. These findings suggest limited utility of MetS for predicting total or CVD mortality in older adults compared with assessment of fasting glucose and blood pressure alone.

Muka T, Nano J, Jaspers L, et al. Associations of **steroid sex hormones and sex hormone-binding globulin with the risk of type 2 diabetes** in women: a population-based cohort study and meta-analysis. Diabetes. 2016 Oct 10.

Muka T, Asllanaj E, Avazverdi N, et al. **Age at natural menopause** and risk of type 2 diabetes: a prospective cohort study. Diabetologia. 2017 Jul 18

Mullan Rebecca J.; Montori Victor M.; Shah Nilay D.; et al. The Diabetes Mellitus Medication Choice **Decision Aid**: A Randomized Trial. Arch Intern Med. 2009;169(17):1560-1568.

Muller-Wieland D, Kellerer M, Cypryk K, et al. Efficacy and safety of **dapagliflozin or dapagliflozin plus saxagliptin versus glimepiride as add-on to metformin** in patients with type 2 diabetes. Diabetes Obes Metab. 2018 Jun 27.

Munch L, Bennich BB, Overgaard D, et al. Management of people with Type 2 diabetes shared between a **specialized outpatient clinic and primary health care is noninferior to management in a specialized outpatient clinic**: a randomized, noninferiority trial. Diabet Med. 2019 Jul;36(7):854-861.

Munshi MN, Florez H, Huang ES, et al. Management of **Diabetes in Long-term Care and Skilled Nursing Facilities**: A Position Statement of the **American** Diabetes Association (ADA). Diabetes Care. 2016 Feb;39(2):308-18.

Munshi MN, Slyne C, Segal AR, et al. **Simplification of Insulin Regimen** in Older Adults and Risk of Hypoglycemia. JAMA Intern Med. 2016 Jun 6.

Muraki I, Imamura F, Manson JE, et al. **Fruit consumption** and risk of type 2 diabetes: results from three prospective longitudinal cohort studies. BMJ. 2013 Aug 28;347:f5001.

Murdoch C, Unwin D, Cavan D, et al. **Adapting diabetes medication for low carbohydrate management** of type 2 diabetes: a practical guide. Br J Gen Pract. 2019 Jul;69(684):360-361.

Muraki I, Rimm ER, Willett WC, et al. **Potato consumption** and risk of type 2 diabetes: results from three prospective cohort studies. Diabeties Care 2016;39:376–84.

Murphy CE. Review of the safety and efficacy of **exenatide once weekly** for the treatment of type 2 diabetes mellitus. Ann Pharmacother. 2012 Jun;46(6):812-21.

Murphy HR, Rayman G, Lewis K, et al. Effectiveness of continuous glucose monitoring in pregnant women with diabetes: randomised clinical trial. BMJ. 2008 Sep 25;337:a1680. doi: 10.1136/bmj.a1680. **Continuous glucose monitoring** during pregnancy is associated with improved glycaemic control in the third trimester, lower birth weight, and reduced risk of macrosomia.

Murphy HR, Stewart ZA. **Automated insulin delivery**: what's new, needed, and next? Lancet. 2016 Dec 19

Musen G, Tinsley LJ, Marcinkowski KA, et al. **Cognitive Function Deficits Associated With Long-Duration Type 1 Diabetes** and Vascular Complications. Diabetes Care. 2018 Jun 5.

Muskiet MHA, Tonneijck L, Huang Y, et al. **Lixisenatide and renal outcomes in patients with type 2 diabetes and acute coronary syndrome**: an exploratory analysis of the **ELIXA r**andomised, placebo-controlled trial. Lancet Diabetes Endocrinol. 2018 Oct 1. pii: S2213-8587(18)30268-7.

Muskiet MHA, Wheeler DC, Heerspink HJL. New **pharmacological strategies for protecting kidney function** in type 2 diabetes. Lancet Diabetes Endocrinol. 2018 Dec 19.

Musso G, Cassader M, Paschetta E, et al. **Thiazolidinediones and Advanced Liver Fibrosis** in Nonalcoholic Steatohepatitis: A Meta-analysis. JAMA Intern Med. 2017 Feb 27.

Musso G, Gambino R, Cassader M, Paschetta E. Efficacy and safety of **dual SGLT 1/2 inhibitor sotagliflozin in type 1 diabetes**: meta-analysis of randomised controlled trials. BMJ. 2019 Apr 9;365:l1328.

Mutluoglu M, Lipsky BA. **Diabetic foot osteomyelitis**. CMAJ. 2016 Dec 6;188(17-18):E535.

Nachum Z, Zafran N, Salim R, et al. **Glyburide Versus Metformin and Their Combination for the Treatment of Gestational Diabetes** Mellitus: A Randomized Controlled Study. Diabetes Care. 2017 Mar;40(3):332-337.

Naci H, Lehman R, Wouters OJ, et al. Rethinking the **appraisal and approval of drugs for type 2 diabetes**. BMJ. 2015 Oct 9;351:h5260.

Nagel AK, Ahmed-Sarwar N, Werner PM, et al. **Dipeptidyl Peptidase-4 Inhibitor-Associated Pancreatic Carcinoma**: A Review of the **FAERS** Database. Ann Pharmacother. 2016 Jan;50(1):27-31.

Nahas R, Moher M. **Complementary and alternative medicine** for the treatment of type 2 diabetes. Can Fam Physician. 2009 Jun;55(6):591-6. Chromium, and possibly gymnema, appears to improve glycemic control. Fibre, green tea, and fenugreek have other benefits but there is little evidence that they substantially improve glycemic control. Further research on bitter melon and cinnamon is warranted. There is no complementary and alternative medicine research addressing microvascular or macrovascular clinical outcomes.

Naik Aanand D.; Palmer Nynikka; Petersen Nancy J.; et al. Comparative Effectiveness of **Goal Setting in Diabetes Mellitus Group Clinics**: Randomized Clinical Trial. *Arch Intern Med*. 2011;171(5):453-459.

Nakhla M, Rahme E, Simard M, et al. **Risk of ketoacidosis in children** at the time of diabetes mellitus diagnosis by primary caregiver status: a population-based retrospective cohort study. CMAJ. 2018 Apr 9;190(14):E416-E421.

Nansel TR, Iannotti RJ, Liu A. **Clinic-integrated behavioral intervention** for families of youth with type 1 diabetes: randomized clinical trial. Pediatrics. 2012 Apr;129(4):e866-73.

Nassif ME, Windsor S, Tang F, et al. **Dapagliflozin Effects** on Biomarkers, Symptoms, and Functional Status in Patients With Heart Failure With Reduced Ejection Fraction: The DEFINE-HF Trial. Circulation. 2019 Sep 16.

Nathan DM, et al. Management of hyperglycemia in type 2 diabetes: a **consensus algorithm** for the initiation and adjustment of therapy: a consensus statement from the **American Diabetes Association** and the **European Association** for the Study of Diabetes. Diabetes Care. 2006 Aug;29(8):1963-72.

Nathan DM, et al.; Diabetes Control and Complications Trial/Epidemiology of Diabetes Interventions and Complications (**DCCT/EDIC**) Study Research Group. **Intensive diabetes treatment and cardiovascular disease in patients with type 1** diabetes. N Engl J Med. 2005 Dec 22;353(25):2643-53. (InfoPOEMs: This extension of the Diabetes Control and Complications Trial (DCCT) trial provides the first high-quality evidence that intensive treatment of Type 1 diabetes reduces the risk of adverse cardiovascular outcomes. Although the relative risk reduction was greater than 50%, the absolute risk reduction (0.42 per 100 patient years; NNT=25 over 10years) was modest. Note that this effect has not been shown in patients with Type 2 diabetes, although many patients and physicians believe otherwise, and data regarding all-cause mortality or adverse effects of intensive treatment (such as hypoglycemic episodes or traffic accidents) are not reported.. (LOE = 1b)) Diabetes Control and Complications Trial/Epidemiology of Diabetes Interventions and Complications (DCCT/EDIC) Research Group. Modern-Day Clinical Course of Type 1 Diabetes Mellitus After 30 Years' Duration: The Diabetes Control and Complications Trial/Epidemiology of Diabetes Interventions and Complications and Pittsburgh Epidemiology of Diabetes Complications Experience (1983-2005). Arch Intern Med. 2009;169(14):1307-1316.

Nathan DM, Buse JB, Davidson MB, Ferrannini E, Holman RR, Sherwin R, Zinman B. Medical management of hyperglycaemia in type 2 diabetes mellitus: a **consensus algorithm** for the initiation and adjustment of therapy : A consensus statement from the American Diabetes Association (**ADA**) and the European Association for the Study of Diabetes. Diabetologia. 2008 Oct 22. http://care.diabetesjournals.org/misc/MedicalManagementofHyperglycemia.pdf

Nathan DM. Diabetes: **Advances in Diagnosis and Treatment**. JAMA. 2015 Sep 8;314(10):1052-1062.

Nau KC. Lorenzetti RC, Cucuzzela M et al. **Glycemic control in Hospitalized Patents not in Intensive Care**: Beyond Sliding Scale. American Family Pysician. May 1, 2010.

Nauck M, Araki A, Hehnke U, et al. **Risk of hypoglycaemia in people aged >/=65 years receiving linagliptin**: pooled data from 1489 individuals with type 2 diabetes mellitus. Int J Clin Pract. 2018 Oct;72(10):e13240.

Nauck M, Weinstock RS, Umpierrez GE, et al. Efficacy and Safety of **Dulaglutide** Versus Sitagliptin After 52 Weeks in Type 2 Diabetes in a Randomized Controlled Trial (AWARD-5). Diabetes Care. 2014 Apr 17.

Nauck M, Rizzo M, Johnson A, et al. Once-Daily **Liraglutide Versus Lixisenatide as Add-on to Metformin** in Type 2 Diabetes: A 26-Week Randomized Controlled Clinical Trial. Diabetes Care. 2016 Jun 16.

Nauck MA. A Critical Analysis of the Clinical Use of **Incretin-Based Therapies**: The benefits by far outweigh the potential risks. Diabetes Care. 2013 May 6.

Nauck MA, Buse JB, Mann JFE, et al. Health-related quality of life in people with type 2 diabetes participating in the LEADER trial. Diabetes Obes Metab. 2018 Sep 27

Nauck MA, Jensen TJ, Rosenkilde C, et al. **Neoplasms Reported With Liraglutide or Placebo in People With Type 2 Diabetes**: Results From **the LEADER** Randomized Trial. Diabetes Care. 2018 Jun 13.

Nauck MA, Meier JJ, Cavender MA, et al. Cardiovascular Actions and Clinical Outcomes With **Glucagon-Like Peptide-1 Receptor Agonists and Dipeptidyl Peptidase-4 Inhibitors**. Circulation. 2017 Aug 29;136(9):849-870

Nauck MA, Muus Ghorbani ML, Kreiner E, et al. Effects of **Liraglutide Compared With Placebo on Events of Acute Gallbladder or Biliary Disease** in Patients With Type 2 Diabetes at High Risk for Cardiovascular Events in the LEADER Randomized Trial. Diabetes Care. 2019 Aug 9.

Navarro-González JF, Mora-Fernández C, Muros de Fuentes M, et al. Effect of **pentoxifylline** on renal function and urinary albumin excretion in patients with **diabetic kidney disease**: the **PREDIAN** trial. J Am Soc Nephrol. 2015 Jan;26(1):220-9.

NAVIGATOR Study Group, Effect of **Nateglinide** on the Incidence of Diabetes and Cardiovascular Events. N Engl J Med 2010 0: NEJMoa1001122.

NAVIGATOR Study Group, Effect of **Valsartan** on the Incidence of Diabetes and Cardiovascular Events. N Engl J Med 2010 0: NEJMoa1001121.

NCD Risk Factor Collaboration (NCD-RisC). Effects of **diabetes definition on global surveillance** of diabetes prevalence & diagnosis: pooled analysis of 96 population-based studies with 331 288 participants. Lancet Diabetes Endocrinol. 2015 Aug;3(8):624-37.

NCD Risk Factor Collaboration (NCD-RisC). **Worldwide trends in diabetes since 1980**: a pooled analysis of 751 population-based studies with 4·4 million participants. Lancet 2016; online April 6.

Neal B, Perkovic V, Mahaffey KW, et al. **Canagliflozin** and Cardiovascular and Renal Events in Type 2 Diabetes. (**CANVAS**) N Engl J Med. 2017 Jun 12.

Negrotto L, Farez MF, Correale J. Immunologic Effects of **Metformin and Pioglitazone** Treatment on **Metabolic Syndrome and Multiple Sclerosis**. JAMA Neurol. 2016 Mar 7.

Nerenberg KA, Zarnke KB, Leung AA, et al. **Hypertension Canada's 2018 guidelines for diagnosis, risk assessment, prevention, and treatment of hypertension in adults and children**. Can J Cardiol 2018; February 20, 2018.

Nestler JE. Metformin for the treatment of the polycystic ovary syndrome. N Engl J Med. 2008 Jan 3;358(1):47-54.

Nesto RW, et al. **Thiazolidinedione use**, fluid retention, and congestive heart failure: a consensus statement from the American Heart Association and American Diabetes Association. Diabetes Care. 2004 Jan;27(1):256-63.

Neuen BL, Ohkuma T, Neal B, et al. **Cardiovascular and Renal Outcomes With Canagliflozin According to Baseline Kidney Function**: Data from the CANVAS Program. Circulation. 2018 Jun 25.

Neuen BL, Young T, Heerspink HJL, et al. **SGLT2 inhibitors for the prevention of kidney failure** in patients with type 2 diabetes: a systematic review and meta-analysis. Lancet Diabetes Endocrinol. 2019 Sep 5.

Neuenschwander M, Ballon A, Weber KS, et al. **Role of diet in type 2 diabetes incidence**: umbrella review of meta-analyses of prospective observational studies. BMJ. 2019 Jul 3;366:l2368.

Neugebauer R, Fireman B, Roy JA, O'Connor PJ. Impact of Specific **Glucose-Control Strategies on Microvascular and Macrovascular Outcomes** in 58,000 Adults With Type 2 Diabetes. Diabetes Care. 2013 Jul 22.

Neumann A, Weill A, Ricordeau P, Fagot JP, Alla F, Allemand H. **Pioglitazone and risk of bladder cancer** among diabetic patients in France: a population-based cohort study. Diabetologia. 2012 Mar 31.

New JP, Ajjan R, Pfeiffer AF, et al. **Continuous glucose monitoring** in people with diabetes: the randomized controlled Glucose Level Awareness in Diabetes Study (GLADIS). Diabet Med. 2015 May;32(5):609-17.

Newman JD, Schwartzbard AZ, Weintraub HS, et al. Primary Prevention of Cardiovascular Disease in Diabetes Mellitus. J Am Coll Cardiol. 2017 Aug 15;70(7):883-893.

Ngueta G, Ndjaboue R. Lifetime **marijuana use in relation to insulin resistance** in lean, overweight, and obese US adults. J Diabetes. 2019 Jun 1.

NICE recommends **liraglutide** for diabetes triple therapy Feb/10 http://www.nice.org.uk/newsroom/news/newsdiabetes.jsp http://www.nice.org.uk/nicemedia/live/13248/51313/51313.pdf

NICE: National Collaborating Centre for Chronic Conditions. **Type 2 diabetes**. The management of type 2 diabetes. London (UK): National Institute for Health and Clinical Excellence ; 2009 May.

NICE Mar 2011 Clinical Guideline 119. **Diabetic foot** - inpatient management of people with diabetic foot ulcers and infection. http://www.nice.org.uk/nicemedia/live/13416/53556/53556.pdf

NICE: National Institute for Health and Clinical Excellence. **Exenatide prolonged-release** suspension for injection in combination with oral antidiabetic therapy for the treatment of type 2 diabetes. London (UK): National Institute for Health and Clinical Excellence (NICE); 2012 Feb. http://www.nice.org.uk/nicemedia/live/13670/58205/58205.pdf

NICE: National Institute for Health and Clinical Excellence. **Preventing type 2 diabetes: risk identification and interventions** for individuals at high risk. PHG38. 2012. http://guidance.nice.org.uk/PH38 .

NICE: National Institute for Health and Care Excellence (**NICE**). **Dapagliflozin** in combination therapy for treating type 2 diabetes. London (UK): National Institute for Health and Care Excellence (NICE); 2013 Jun.

NICE: National Institute for Health and Care Excellence (NICE). **Empagliflozin** in combination therapy for treating type 2 diabetes. London (UK): National Institute for Health and Care Excellence (NICE); 2015 Mar.

NICE: National Institute for Health and Care Excellence. **Type 1 diabetes in adults**: diagnosis and management. (NICE guideline 17.) 2015. http://www.nice.org.uk/guidance/ng17.

***NICE**: National Collaborating Centre for Women & Children's Health. **Diabetes in pregnancy**: management of diabetes and its complications from preconception to the postnatal period. London (UK): National Institute for Health and Care Excellence (NICE); 2015*

NICE: National Clinical Guideline Centre. **Type 1 diabetes in adults**: diagnosis and management. London (UK): National Institute for Health and Care Excellence (NICE); 2015.

NICE: National Collaborating Centre for Women's and Children's Health. **Diabetes (type 1 and type 2) in children and young people**: diagnosis and management. London (UK): National Institute for Health and Care Excellence (NICE); 2015.

NICE: National Institute for Health and Care Excellence (NICE). **Diabetic foot problems**: prevention and management. London (UK): National Institute for Health and Care Excellence (NICE); 2015.

NICE: National Institute for Health and Care Excellence (**NICE**). **Type 2 diabetes in adults**: management. London (UK): National Institute for Health and Care Excellence (NICE); 2015 Dec.

Nice-Sugar. Hypoglycemia and risk of death in critically ill patients. N Engl J Med 2012;367:1108-18.

Nichols GA, et al. **Normal fasting plasma glucose** and risk of type 2 diabetes diagnosis. Am J Med. 2008 Jun;121(6):519-24. The strong independent association between the level of normal fasting plasma glucose and the incidence of diabetes after controlling for other risk factors suggests that diabetes risk increases as fasting plasma glucose levels increase, even within the currently accepted normal range.

Nichols GA, Joshua-Gotlib S, Parasuraman S. Independent contribution of **A1c, systolic blood pressure, and LDL cholesterol** control to risk of cardiovascular disease hospitalizations in type 2 diabetes: An observational cohort study. J Gen Intern Med 2013.

Nicholson W, Bolen S, Witkop CT, Neale D, Wilson L, Bass E. Benefits and Risks of Oral Diabetes Agents Compared With Insulin in Women With Gestational Diabetes: A Systematic Review. Obstet Gynecol. 2009 Jan;113(1):193-205. No substantial maternal or neonatal outcome differences were found with the use of glyburide or metformin compared with use of insulin in women with GDM.

Nicklas JM, Zera CA, England LJ, et al. A **web-based lifestyle intervention** for women with recent **gestational diabetes** mellitus: a randomized controlled trial. Obstet Gynecol. 2014 Sep;124(3):563-70.

Nielsen SF, Nordestgaard BG. **Statin use before diabetes** diagnosis and risk of microvascular disease: a nationwide nested matched study. Lancet Diabetes Endocrinol. 2014 Nov;2(11):894-900.

Nielsen RE, Laursen MF, Vernal DL, et al. Risk of **diabetes in children and adolescents exposed to antipsychotics**: a nationwide 12-year case-control study. J Am Acad Child Adolesc Psychiatry. 2014 Sep;53(9):971-979.e6.

NINDS Exploratory Trials in Parkinson Disease (NET-PD) FS-ZONE Investigators. **Pioglitazone in early Parkinson's disease**: a phase 2, multicentre, double-blind, randomised trial. Lancet Neurol. 2015 Jun 23.

Ning G, Bi Y, Wang T, Xu M, Xu Y, Huang Y, et al. Relationship of **urinary bisphenol A** concentration to risk for prevalent type 2 diabetes in Chinese adults. A cross-sectional analysis. Ann Intern Med. 2011;155:368-74.

Nissen SE, Wolski K, Topol EJ. Effect of **Muraglitazar** on Death and Major Adverse Cardiovascular Events in Patients With Type 2 Diabetes Mellitus JAMA. 2005;294:(doi:10.1001/jama.294.20.joc50147). Oct/05

Nissen SE, Nicholls SJ, Wolski K, et al.;for the **PERISCOPE** Investigators. Comparison of **Pioglitazone vs Glimepiride** on Progression of Coronary Atherosclerosis in Patients With Type 2 Diabetes: The PERISCOPE Randomized Controlled Trial. JAMA. 2008 Mar

31; [Epub ahead of print] In patients with type 2 diabetes and coronary artery disease, treatment with pioglitazone resulted in a significantly lower rate of progression of coronary atherosclerosis compared with glimepiride.
Niven DJ, Rubenfeld GD, Kramer AA, et al. Effect of published scientific evidence on **glycemic control in adult intensive care units**. JAMA Intern Med. 2015 May 1;175(5):801-9.
Njeru JW, Wieland ML, Kwete G, et al. Diabetes Mellitus Management Among Patients with **Limited English Proficiency**: A Systematic Review and Meta-Analysis. J Gen Intern Med. 2017 Dec 18.
Njike VY, Ayettey R, Petraro P, et al. **Walnut ingestion** in adults at risk for diabetes: effects on body composition, diet quality, and cardiac risk measures. BMJ Open Diabetes Res Care. 2015 Oct 19;3(1):e000115.
Nobis S, Lehr D, Ebert DD, et al. Efficacy of a Web-Based Intervention With **Mobile Phone Support** in Treating **Depressive Symptoms in Adults With Type 1 and Type 2 Diabetes**: A Randomized Controlled Trial. Diabetes Care. 2015 Feb 20.
Noble D et al. **Risk models and scores for type 2 diabetes**: systematic review. BMJ. 2011 Nov 28;343:d7163.
Noe A, Howard C, Thuren T, et al. Pharmacokinetic and Pharmacodynamic Characteristics of Single-Dose **Canakinumab** in Patients With Type 2 Diabetes Mellitus. Clin Ther. 2014 Sep 17.
Noon MJ, Khawaja A, Ishtiaq O, et al. **Fasting** with diabetes: a prospective observational study. BMJ Global Health. 2016;1:e000009.
Nordmann AJ, et al. Effects of **low-carbohydrate vs low-fat diets** on weight loss & cardiovascular risk factors: a meta-analysis of randomized controlled trials. Arch Intern Med. 2006 Feb 13;166(3):285-93. (InfoPOEMs: People interested in weight loss can choose either a low-fat, reduced calorie diet or a low-carbohydrate, non-calorie-restricted diet to lose a small but sustained amount of weight. The effect on cardiovascular outcomes of either diet are not known, though each has different effects on lipid levels, which may or may not translate into an actual effect on patient-oriented outcomes that matter. (LOE = 1a))
Norhammar A, Kjellström B, Habib N, et al. **Undetected Dysglycemia** an Important Risk Factor for Two Common Diseases **Myocardial Infarction and Periodontitis**: A Report From the PAROKRANK Study. Diabetes Care. 2019 Jun 10.
Noronha JC, Nishi SK, Braunstein CR, et al. The Effect of **Liquid Meal Replacements on Cardiometabolic Risk Factors in Overweight/Obese Individuals With Type 2 Diabetes**: A Systematic Review and Meta-analysis of Randomized Controlled Trials. Diabetes Care. 2019 Mar 28.
Norris SL, Kansagara D, Bougatsos C, Fu R; U.S. Preventive Services Task Force. **Screening adults** for type 2 diabetes: a review of the evidence for the U.S. Preventive Services Task Force. Ann Intern Med. 2008 Jun 3;148(11):855-68. Review. Summary for patients in: Ann Intern Med. 2008 Jun 3;148(11):I30. Direct evidence is lacking on the health benefits of detecting type 2 diabetes by either targeted or mass screening, and indirect evidence also fails to demonstrate health benefits for screening general populations. Persons with hypertension probably benefit from screening, because blood pressure targets for persons with diabetes are lower than those for persons without diabetes. Intensive lifestyle and pharmacotherapeutic interventions reduce the progression of prediabetes to diabetes, but few data examine the effect of these interventions on long-term health outcomes.
Norwood P, Liutkus JF, Haber H, et al. Safety of **Exenatide Once Weekly** in Patients With Type 2 Diabetes Mellitus Treated With a Thiazolidinedione Alone or in Combination With Metformin for 2 Years. Clin Ther. 2012 Sep 29.
Norwood P, Chen R, Jaeckel E, et al. Rates of **hypoglycaemia** are lower in patients treated with **insulin degludec/liraglutide (IDegLira) than with IDeg or insulin glargine** regardless of the hypoglycaemia definition used. Diabetes Obes Metab. 2017 Apr 17.
Notley SR, Poirier MP, Sigal RJ, et al. **Exercise Heat Stress** in Patients With and Without Type 2 Diabetes. JAMA. 2019 Oct 8;322(14):1409-1411
Nowicka P, Santoro N, Liu H, et al. Utility of **hemoglobin a1c for diagnosing prediabetes and diabetes** in obese children and adolescents. Diabetes Care. 2011 Jun;34(6):1306-11.
NPS – Australia – Sitagliptin / Januvia Review: http://www.nps.org.au/health_professionals/publications/nps_radar/issues/current/august_2008/sitagliptin
Nygren M, Carstensen J, Koch F, et al. Experience of a **serious life event** increases the risk for childhood type 1 diabetes: the ABIS population-based prospective cohort study. Diabetologia. 2015 Apr 14.
Nyström T, Holzmann MJ, Eliasson B, et al. Glycemic control in type 1 diabetes and long-term risk of cardiovascular events or death after **coronary artery bypass grafting**. *J Am Coll Cardiol* 2015; 66:535-543.
Nyström T, James SK, Lindahl B, et al; DETO2X-SWEDEHEART Investigators. **Oxygen Therapy in Myocardial Infarction** Patients With or Without Diabetes: A Predefined Subgroup Analysis From the DETO2X-AMI Trial. Diabetes Care. 2019 Aug 31.
O'Brien MJ, Bullard KM, Zhang Y, et al. Performance of the **2015 US Preventive Services Task Force Screening Criteria for Prediabetes** and Undiagnosed Diabetes. J Gen Intern Med. 2018 Apr 12.
O'Brien MJ, Karam SL, Wallia A, et al. Association of **Second-line Antidiabetic Medications With Cardiovascular Events Among Insured Adults With Type Diabetes**. JAMA Netw Open. 2018;1(8):e186125.
O'Brien MJ, Lee JY, Carnethon MR, et al. Detecting Dysglycemia Using the 2015 United States Preventive Services Task Force Screening Criteria: A Cohort Analysis of Community Health Center Patients. PLoS Med. 2016 Jul 12;13(7):e1002074.
O'Brien MJ, Sacks DB. **Point-of-Care Hemoglobin A1c**. JAMA. 2019 Sep 12.
O'Connor L, Imamura F, Lentjes MA, Khaw et al. Prospective associations and population impact of **sweet beverage intake** and type 2 diabetes, and effects of substitutions with alternative beverages. Diabetologia. 2015 May 6.
O'Keeffe DT, Maraka S, Rizza RA. **HbA1c in the Evaluation** of Diabetes Mellitus. JAMA. 2016 Feb 9;315(6):605-6.
Ockrim Z, Yorston D. Managing diabetic **retinopathy**. BMJ. 2010 Oct 25;341:c5400. doi: 10.1136/bmj.c5400.
Odawara M, Miyagawa J, Iwamoto N, et al. Once-weekly glucagon-like peptide-1 receptor agonist **dulaglutide** significantly decreases glycated haemoglobin compared with once-daily **liraglutide** in Japanese patients with type 2 diabetes: 52 weeks of treatment in a randomized phase III study. Diabetes Obes Metab. 2016 Mar;18(3):249-57.
Oh TJ, Moon JH, Choi SH, et al. **Body-weight fluctuation and incident diabetes mellitus**, cardiovascular disease, and mortality: a 16-year prospective cohort study. J Clin Endocrinol Metab. 2018 Nov 29.
Ohara T, Doi Y, Ninomiya T, et al. **Glucose tolerance status** and **risk of dementia** in the community: The Hisayama Study. Neurology. 2011 Sep 20;77(12):1126-34.
Ohkuma T, Komorita Y, Peters SAE, Woodward M. Diabetes as a **risk factor for heart failure** in women and men: a systematic review and meta-analysis of 47 cohorts including 12 million individuals. Diabetologia. 2019 Jul 18.
Ohkuma T, Peters SAE, Woodward M. **Sex differences in the association between diabetes and cancer**: a systematic review and meta-analysis of 121 cohorts including 20 million individuals and one million events. Diabetologia. 2018 Jul 20.
Olansky L. Q: Do **incretin drugs** for type 2 diabetes increase the risk of **acute pancreatitis**? Cleve Clin J Med. 2010 Aug;77(8):503-5.
Olausson EA, Störsrud S, Grundin H, et al. A Small Particle Size Diet Reduces Upper Gastrointestinal Symptoms in Patients With **Diabetic Gastroparesis**: A Randomized Controlled Trial. Am J Gastroenterol. 2014 Jan 14.
Olson DE, Rhee MK, Herrick K, et al. **Screening** for diabetes and pre-diabetes with proposed **A1C-based diagnostic criteria**. Diabetes Care. 2010 Oct;33(10):2184-9.
Onady G, Stolfi A. Insulin and oral agents for managing **cystic fibrosis**-related diabetes. Cochrane Database Syst Rev. 2005 Jul 20;(3):CD004730.
O'Neil PM, Birkenfeld AL, McGowan B, et al. Efficacy and safety of **semaglutide compared with liraglutide** and placebo for weight loss in patients with obesity: a randomised, double-blind, placebo and active controlled, dose-ranging, phase 2 trial. Lancet. 2018 Aug 25;392(10148):637-649.
Oram RA, McDonald TJ, Shields BM, et al. on behalf of the UNITED Team. Most People With **Long-Duration Type 1 Diabetes** in a Large Population-Based Study Are **Insulin Microsecretors**. Diabetes Care. 2014 Dec 17.
Orban T, Bundy B, Becker DJ, et al. the Type 1 Diabetes TrialNet **Abatacept** Study Group. Co-stimulation modulation with abatacept in patients with recent-onset type 1 diabetes: a randomised, double-blind, placebo-controlled trial. Lancet. 2011 Jun 28.
Orchard TJ, et al.; **Diabetes Prevention Program** Research Group. The effect of metformin and intensive lifestyle intervention on the metabolic syndrome: the Diabetes Prevention Program randomized trial. Ann Intern Med. 2005 Apr 19;142(8):611-9 & ACP Journal Club . Summary for patients in: Ann Intern Med. 2005 Apr 19;142(8):I46.
Orchard TJ, Nathan DM, Zinman B, et al. Association between **7 years of intensive treatment of type 1 diabetes** and long-term **mortality**. JAMA. 2015 Jan 6;313(1):45-53.
ORIGIN trial investigators**. n-3 fatty acids** and cardiovascular outcomes in patients with dysglycemia. N Engl J Med 2012.
ORIGIN Trial Investigators. **Basal insulin** (glargine) and cardiovascular and other outcomes in dysglycemia. N Engl J Med 2012 Jun 11
ORIGIN Trial Investigators. **Cardiovascular and Other Outcomes** Postintervention With **Insulin Glargine and Omega-3 Fatty Acids** (**ORIGINALE**). Diabetes Care. 2015 Dec 17.
ORIGIN Trial Investigators. Cardiovascular and Other Outcomes Postintervention With Insulin **Glargine and Omega-3 Fatty Acids** (**ORIGINALE**). Diabetes Care. 2016 May;39(5):709-16.
Orkaby AR, Cho K, Cormack J, et al. **Metformin vs sulfonylurea use and risk of dementia** in US veterans aged $65 years with diabetes. Neurology 2017;89:1877–1885.
Orozco LJ, Buchleitner AM, Gimenez-Perez G, Roqué i Figuls M, Richter B, Mauricio D. **Exercise or exercise and diet for preventing type 2 diabetes mellitus**. Cochrane Database of Systematic Reviews 2008, Issue 3. Art. No.: CD003054. DOI:10.1002/14651858.CD003054.pub3. Interventions aimed at increasing exercise combined with diet are able to decrease the incidence of type 2 diabetes mellitus in high risk groups (people with impaired glucose tolerance or the metabolic syndrome). There is a need for studies exploring exercise only interventions and studies exploring the effect of exercise and diet on quality of life, morbidity and mortality, with special focus on cardiovascular outcomes.
Oster RT, Johnson JA, Hemmelgarn BR, et al. Recent epidemiologic trends of diabetes mellitus **among status Aboriginal adults**. CMAJ. 2011 Sep 6;183(12):E803-8.
Ou HT, Chang KC, Li CY, et al. Comparative **cardiovascular risks of dipeptidyl peptidase-4 inhibitors** with other 2(nd) and 3(rd) line antidiabetic drugs in patients with type 2 diabetes. Br J Clin Pharmacol. 2017 Jan 21
Ou HT, Lee TY, Du YF, Li CY. **Comparative risks of diabetes-related complications of basal insulins**: a longitudinal population-based cohort of type 1 diabetes 1999-2013 in Taiwan. Br J Clin Pharmacol. 2017 Oct 26.
Ou SM, Shih CJ, Chao PW, et al. Effects on Clinical Outcomes of **Adding Dipeptidyl Peptidase-4 Inhibitors Versus Sulfonylureas to Metformin** Therapy in Patients With Type 2 Diabetes Mellitus. Ann Intern Med. 2015 Oct 13.
Ou SM, Chen HT, Kuo SC, et al. **Dipeptidyl peptidase-4 inhibitors** and cardiovascular risks in patients with pre-existing **heart failure**. Heart. 2016 Sep 19.
Ovalle F, Grimes T, Xu G, et al. **Verapamil and beta cell function in adults with recent-onset type 1 diabetes**. Nat Med. 2018 Jul 9.
Overbeek JA, Heintjes EM, Prieto-Alhambra D, et al. Type 2 Diabetes Mellitus Treatment **Patterns Across Europe**: A Population-Based Multi-Database Study. Clin Ther. 2017 Mar 22.
Overbeek JA, van Herk-Sukel MPP, Vissers PAJ, et al. Type 2 Diabetes, but Not Insulin (Analog)Treatment, Is Associated With More **Advanced Stages of Breast Cancer**: A National Linkage of Cancer and Pharmacy Registries.

Owei I, Umekwe N, Stentz F, et al. Running title: **amino acids and prediabetes risk** in blacks and whites. Metabolism. 2019 Jun 19.

Oyama J, Murohara T, Kitakaze M, et al. The Effect of **Sitagliptin** on **Carotid Artery Atherosclerosis** in Type 2 Diabetes: The **PROLOGUE** Randomized Controlled Trial. PLoS Med. 2016 Jun 28;13(6):e1002051.

Owens DR, Swallow R, Dugi KA, Woerle HJ. Efficacy and safety of **linagliptin** in persons with type 2 diabetes inadequately controlled by a combination of metformin and sulphonylurea: a 24-week randomized study. Diabet Med. 2011 Nov;28(11):1352-61.

Owolabi MO, Yaria JO, Daivadanam M, et al; COUNCIL Initiative. Gaps in Guidelines for the **Management of Diabetes in Low- and Middle-Income Versus High-Income Countries-A Systematic Review**. Diabetes Care. 2018 May;41(5):1097-1105.

Øyen N, Diaz LJ, Leirgul E, et al. **Prepregnancy diabetes and offspring risk of congenital heart disease**: a nationwide cohort study. Circulation. 2016;133:2243–2253.

Ozen G, Pedro S, Holmqvist ME, et al. **Risk of diabetes mellitus associated with disease-modifying antirheumatic drugs** and statins in rheumatoid arthritis. Ann Rheum Dis. 2017 May;76(5):848-854.

Packer M, Anker SD, Butler J et al. Effects of **Sodium-Glucose Cotransporter 2 Inhibitors** for the Treatment of Patients With **Heart Failure**: Proposal of a Novel Mechanism of Action. JAMA Cardiol. 2017 Aug 2

Padwal RS, Gabr RQ, Sharma AM, et al. Effect of **gastric bypass surgery** on the absorption and bioavailability of **metformin**. Diabetes Care. 2011 Jun;34(6):1295-300.

Pagidipati NJ, Navam AM, Pieper KS, et al; on behalf of the TECOS Study Group. **Secondary prevention of cardiovascular disease** in patients with type 2 diabetes: international insights from the **TECOS** trial (Trial Evaluating Cardiovascular Outcomes With **Sitagliptin**). Circulation. 2017;136:1193–1203.

Paisley A, Yadav R, Younis N, Rao-Balakrishna P, Soran H. **Dapagliflozin**: a review on efficacy, clinical effectiveness and safety. Expert Opin Investig Drugs. 2013;22(1):131-140.

Pal K, Eastwood SV, Michie S, Farmer AJ, Barnard ML, Peacock R, et al. **Computer-based diabetes self-management interventions** for adults with type 2 diabetes mellitus. Cochrane Database Syst Rev2013;3:CD008776. Computer-based diabetes self- management interventions to manage type 2 diabetes appear to have a small beneficial effect on blood glucose control and the effect was larger in the mobile phone subgroup. There is no evidence to show benefits in other biological outcomes or any cognitive, behavioural or emotional outcomes.

Paldus B, Lee MH, O'Neal DN**. Insulin pumps** in general practice. Aust Prescr. 2018 Dec;41(6):186-190.

Palmer SC, Mavridis D, Nicolucci A, et al. Comparison of **Clinical Outcomes** and Adverse Events Associated With **Glucose-Lowering Drugs** in Patients With Type 2 Diabetes: A Meta-analysis. JAMA. 2016 Jul 19;316(3):313-24.

Palomba S, et al. A randomized controlled trial evaluating metformin pre-treatment and co-administration in non-obese insulin-resistant women with **polycystic ovary** syndrome treated with controlled ovarian stimulation plus timed intercourse or intrauterine insemination. Hum Reprod. 2005 Jun 15.

Palomba S, Orio F Jr, et al. Prospective parallel randomized, double-blind, double-dummy controlled clinical trial comparing clomiphene citrate & metformin as the first-line treatment for ovulation induction in nonobese anovulatory women with polycystic ovary syndrome. J Clin Endocrinol Metab. 2005 Jul;90(7):4068-74. (InfoPOEMs: In nonobese women with polycystic ovary syndrome, metformin is more effective than clomiphene for improving the rate of conception. (LOE = 1b))

Pan A, Schernhammer ES, Sun Q, et al. **Rotating night shift work** and risk of type 2 diabetes: two prospective cohort studies in women. PLoS Med 2011;8:e1001141.

Pan A, Sun Q, Bernstein AM, Manson JE,Willett WC, Hu FB. Changes in **red meat consumption** and subsequent risk of type 2 diabetes mellitus: three cohorts of US men and women [online June 17, 2013]. JAMA Intern Med.

Pan A, Wang Y, Talaei M, et al. ***Relation of active, passive, and quitting smoking*** *with incident type 2 diabetes: a systematic review and meta-analysis. Lancet Diabetes Endocrinol. 2015 Sep 17.*

Pan SW, Yen YF, Kou YR, et al. The risk of **tuberculosis** disease in type 2 diabetes patients initiating **metformin** versus sulfonylureas. Chest. 2017 Dec 15.

Pace R, Brazeau AS, Meltzer S, et al. Conjoint Associations of **Gestational Diabetes and Hypertension With Diabetes**, Hypertension, and Cardiovascular Disease in Parents: A Retrospective Cohort Study. Am J Epidemiol. 2017 Nov 15;186(10):1115-1124.

Panchaud A, Rousson V, Vial T, et al. **Pregnancy outcomes in women on metformin** for diabetes **or other indications** among those seeking teratology information services. Br J Clin Pharmacol. 2017 Dec 7.

Pandey A, Swift DL, McGuire DK, et al. **Metabolic Effects of Exercise Training** Among Fitness Nonresponsive Patients With Type 2 Diabetes Mellitus: The **HART-D** Study. Diabetes Care. 2015 Jun 17.

Pandeya N, Huxley RR, Chung HF, et al. **Female reproductive history and risk of type 2 diabetes**: a prospective analysis of 126,721 women. Diabetes Obes Metab. 2018 Apr 25.

Paneni F, Lüscher TF. **Cardiovascular Protection in the Treatment of Type 2 Diabetes**: A Review of Clinical Trial Results Across Drug Classes. Am J Cardiol. 2017 Jul 1;120(1S):S17-S27

Pantalone KM, Kattan MW, Yu C, et al. The Risk of Overall Mortality in Patients with Type 2 Diabetes Receiving **Glipizide, Glyburide, or Glimepiride** Monotherapy: A Retrospective Analysis. Diabetes Care. 2010 Mar 9.

Pantell MS, Prather AA, Downing JM, et al. Association of **Social and Behavioral Risk Factors With Earlier Onset of Adult Hypertension and Diabetes**. JAMA Netw Open. 2019 May 3;2(5):e193933.

Panunzi S, Carlsson L, De Gaetano A, et al. Determinants of **Diabetes Remission** and Glycemic Control **After Bariatric Surgery**. Diabetes Care. 2016 Jan;39(1):166-74.

Papa G, et al. Safety of Type 2 Diabetes Treatment With **Repaglinide Compared With Glibenclamide in Elderly** People: A randomized, open-label, two-period, cross-over trial. Diabetes Care. 2006 Aug;29(8):1918-20.

Papademetriou V et al. **Chronic kidney disease** and intensive glycemic control increase cardiovascular risk in patients with type 2 diabetes. (Accord) Kidney Int 2015 Mar; 87:649.

Papak J, Kansagara D. Management of **hyperglycemia in a hospitalized patient** with diabetes mellitus and cardiovascular disease. Am J Cardiol. 2012 Nov 6;110(9 Suppl):24B-31B.

Paramasivam SS, Chinna K, Singh AKK, et al. **Continuous glucose monitoring results in lower HbA1c in Malaysian women with insulin-treated gestational diabetes**: a randomized controlled trial. Diabet Med. 2018 Apr 16.

Park J, Park SW, Yoon KH, et al. Efficacy and safety of **evogliptin** monotherapy in patients with type 2 diabetes and moderately elevated glycated haemoglobin levels after diet and exercise. Diabetes Obes Metab. 2017 Apr 27.

Park SK, Garland CF, Gorham ED, et al. **Plasma 25-hydroxyvitamin D concentration** and risk of type 2 diabetes and pre-diabetes: 12-year cohort study. PLoS One. 2018 Apr 19;13(4):e0193070.

Parekh TM, Raji M, Lin Y-L, et al.. **Hypoglycemia after antimicrobial drug prescription** for older patients using sulfonylureas [online September 1, 2014]. JAMA Intern Med.

Park K. How low to go with glucose control http://www.australianprescriber.com/magazine/32/2/30/1

Paschou SA, Dede AD, Anagnostis PG, et al. Type 2 diabetes and **osteoporosis**: a guide to optimal management. J Clin Endocrinol Metab. 2017 June 21.

Pasternak B, Ueda P, Eliasson B, et al. Use of sodium glucose cotransporter 2 inhibitors and **risk of major cardiovascular events and heart failure**: Scandinavian register based cohort study. BMJ. 2019 Aug 29;366:l4772.

Patel A; ADVANCE Collaborative Group, MacMahon S, Chalmers J, Neal B, et al. Effects of a fixed combination of perindopril and indapamide on macrovascular and microvascular outcomes in patients with type 2 diabetes mellitus (the **ADVANCE** trial): a randomised controlled trial. Lancet. 2007 Sep 8;370(9590):829-40. Routine administration of a fixed combination of perindopril and indapamide to patients with type 2 diabetes was well tolerated and reduced the risks of major vascular events, including death. Although the confidence limits were wide, the results suggest that over 5 years, one death due to any cause would be averted among every 79 patients assigned active therapy. (InfoPOEMs: Perindopril (Aceon) plus indapamide (Lozol) is better than placebo in decreasing clinically relevant events in patients with type 2 diabetes who are at high risk of cardiovascular complications. Whether the combination is better than other medications -- like aspirin -- isn't addressed by this study. (LOE = 1b))

Patel YR, Kirkman MS, Considine RV, et al. Effect of **acarbose** to delay progression of carotid intima-media thickness in early diabetes. [Early Diabetes Intervention Program (EDIP)] Diabetes Metab Res Rev. 2013 Oct;29(7):582-91.

Patil HR, Al Badarin FJ, Shami HA, et al. Meta-Analysis of Effect of **Dipeptidyl Peptidase-4 Inhibitors on Cardiovascular Risk** in Type 2 Diabetes Mellitus. Am J Cardiol. 2012 Jun 14.

Patorno E, Goldfine AB, Schneeweiss S, et al. Cardiovascular outcomes associated with **canagliflozin** versus other non-gliflozin antidiabetic drugs: population based cohort study. BMJ. 2018 Feb 6;360:k119.

Patorno E, Pawar A, Franklin JM, et al**. Empagliflozin and the Risk of Heart Failure** Hospitalization in Routine Clinical Care: A First Analysis from the Empagliflozin Comparative Effectiveness and Safety (EMPRISE) Study. Circulation. 2019 Apr 8.

Patorno E, Gopalakrishnan C, Brodovicz KG, et al. **Cardiovascular safety of linagliptin compared with other oral glucose-lowering** agents in patients with type 2 diabetes: A sequential monitoring programme in routine care. Diabetes Obes Metab. 2019 Apr 2.

Patterson CC, Harjutsalo V, Rosenbauer J, et al. Trends and cyclical variation in the **incidence of childhood type 1 diabetes** in 26 European centres in the 25 year period 1989-2013: a multicentre prospective registration study. Diabetologia. 2018 Nov 28.

Pavela J, Suresh R, Blue RS, et al. MANAGEMENT OF **DIABETES DURING AIR TRAVEL**: A SYSTEMATIC LITERATURE REVIEW OF CURRENT RECOMMENDATIONS AND THEIR SUPPORTING EVIDENCE. Endocr Pract. 2018 Feb;24(2):205-219.

Pawaskar M, Tuttle KR, Li Q, et al. Observational Study of Kidney Function and Albuminuria in Patients With Type 2 Diabetes Treated With **Exenatide BID Versus Insulin Glargine**. Ann Pharmacother. 2014 May;48(5):571-6.

Payk SL, Drew RH, Smith JD, et al. **Sulfonylurea Prescribing Patterns After** the Introduction of **DPP-4 Inhibitors and GLP-1 Receptor Agonists**. Clin Ther. 2015 May 26.

Paynter NP, Mazer NA, Pradhan AD, et al.. **Cardiovascular Risk Prediction** in Diabetic Men and Women Using **Hemoglobin A1c** vs Diabetes as a High-Risk Equivalent. Arch Intern Med. 2011 Jul 25.

Paz Levy D, Sheiner E, Wainstock T, et al. Evidence that children born at early term (37-38 6/7 weeks) are at increased risk for diabetes and obesity-related disorders. Am J Obstet Gynecol. 2017 Jul 18.

Pearson ER, et al.; Neonatal Diabetes International Collaborative Group. Switching **from insulin to oral sulfonylureas** in patients with diabetes due to Kir6.2 mutations. N Engl J Med. 2006 Aug 3;355(5):467-77.

Pearson-Stuttard J, Zhou B, Kontis V, et al. Worldwide burden of **cancer attributable to diabetes** and high body-mass index: a comparative risk assessment. Lancet Diabetes Endocrinol. 2017 Nov 28.

Pearson-Stuttard J, Zhou B, Kontis V, et al. Worldwide burden of **cancer attributable to diabete**s and high body-mass index: a comparative risk assessment. Lancet Diabetes Endocrinol. 2018 Jun;6(6):e6-e15.

Pedersen SD, Kang J, Kline GA. **Portion control plate** for weight loss in obese patients with type 2 diabetes mellitus: a controlled clinical trial. Arch Intern Med. 2007 Jun 25;167(12):1277-83.

Peltier A, Goutman SA, Callaghan BC. **Painful diabetic neuropathy**. BMJ. 2014 May 6;348:g1799.

Peña PA, Pérez-Díaz I, Pulido-Ayala AK, et al. Association of **Grit Scores With Treatment Adherence and Biomarkers** in Patients With Type 2 Diabetes. JAMA Netw Open. 2019 Sep 4;2(9):e1911476.

Pergola Pablo E., Raskin Philip, Toto Robert D., et al. for the **BEAM** Study Investigators. **Bardoxolone** Methyl and Kidney Function in CKD with Type 2 Diabetes. June 24, 2011 (10.1056/NEJMoa1105351)

Perkovic V, Heerspink HL, Chalmers J, et al. **Intensive glucose control improves kidney outcomes** in patients with type 2 diabetes. (**Advance**) Kidney Int. 2013 Jan 9.

Perkovic V, Agarwal R, Fioretto P, et al. Conference Participants.. Management of patients with **diabetes and CKD**: conclusions from a "Kidney Disease: Improving Global Outcomes" (KDIGO) Controversies Conference. Kidney Int. 2016 Dec;90(6):1175-1183.
Perkovic V, Jardine MJ, Neal B, et al. **Canagliflozin and Renal Outcomes** in Type 2 Diabetes and Nephropathy. N Engl J Med. 2019 Apr 14.
Perkovic V, Zeeuw D, Mahaffey KW, et al. **Canagliflozin and renal outcomes** in type 2 diabetes: results from the CANVAS Program randomised clinical trials. Lancet Diabetes Endocrinol. 2018 Jun 21.
Perreault L, Pan Q, Mather KJ, et al., for the Diabetes Prevention Program Research Group. Effect of **regression from prediabetes to normal glucose** regulation on long-term reduction in diabetes risk: results from the Diabetes Prevention Program Outcomes Study (**DPPOS**) . Lancet 2012; online June 9.
Perreault L, Temprosa M, Mather KJ, et al; for the Diabetes Prevention Program (**DPP**) Research Group. **Regression From Prediabetes to Normal Glucose Regulation** Is Associated With Reduction in Cardiovascular Risk: Results From the Diabetes Prevention Program Outcomes Study. Diabetes Care. 2014 Jun 26.
Perreault L. **EMPA-REG OUTCOME**: The **Endocrinologist's Point of View**. Am J Med. 2017 May 12.
Perrett KP, Jachno K, Nolan TM, Harrison LC. Association of **Rotavirus Vaccination With the Incidence of Type 1 Diabetes in Children.** JAMA Pediatr. 2019 Jan 22.
Persaud N, Bedard M, Boozary AS, et al;(CLEAN Meds) Study Team. Effect on Treatment **Adherence of Distributing Essential Medicines at No Charge**: The CLEAN Meds Randomized Clinical Trial. JAMA Intern Med. 2019 Oct 7. doi: 10.1001/jamainternmed.2019.4472.
Persson M, Shah PS, Rusconi F, et al. Association of **Maternal Diabetes With Neonatal Outcomes of Very Preterm and Very Low-Birth-Weight Infants**: An International Cohort Study. JAMA Pediatr. 2018 Jul 2.
Pescovitz MD, Greenbaum CJ, Krause-Steinrauf H, et al. Type 1 Diabetes TrialNet Anti-CD20 Study Group. **Rituximab**, B-lymphocyte depletion, and preservation of beta-cell function. N Engl J Med. 2009 Nov 26;361(22):2143-52.
Peters AL, Henry RR, Thakkar P, Tong C, Alba M. **Diabetic Ketoacidosis** With **Canagliflozin**, a Sodium-Glucose Cotransporter 2 Inhibitor, in Patients With Type 1 Diabetes. Diabetes Care. 2016 Apr;39(4):532-8.
Peters AL, Ahmann AJ, et al. Diabetes Technology-**Continuous Subcutaneous Insulin Infusion Therapy and Continuous Glucose Monitoring in Adults**: An Endocrine Society Clinical Practice Guideline. J Clin Endocrinol Metab. 2016 Sep 2:jc20162534
Peters AL, Ahmann AJ, Battelino T, Evert A, et al. **Diabetes technology-continuous subcutaneous insulin infusion** therapy and continuous glucose monitoring in adults: an **Endocrine Society** clinical practice guideline. J Clin Endocrinol Metab. 2016 Nov;101(11):3922-37.
Peters SAE, Huxley RR, Woodward M. **Diabetes as a risk factor for stroke** in women compared with men: a systematic review and meta-analysis of 64 cohorts, including 775 385 individuals and 12 539 strokes. Lancet 2014; online March 7.
Peters SA, Huxley RR, Diabetes as **risk factor for incident coronary heart disease in women** compared with men: a systematic review and meta-analysis of 64 cohorts including 858,507 individuals and 28,203 coronary events. Diabetologia. 2014 May 25.
Peterson K, et al. Management of **Type 2 diabetes inYouth**: An Update. Am Fam Physician 2007;76:658-64.
Petrie JR, Chaturvedi N, Ford I, et al. **Cardiovascular and metabolic effects** of **metformin** in patients with type 1 diabetes (**REMOVAL**): a double-blind, randomised, placebo-controlled trial. Lancet Diabetes Endocrinol. 2017 Jun 9.
Petrillo LA, Gan S, Jing B, et al. **Hypoglycemia in Hospice Patients** With Type 2 Diabetes in a National Sample of Nursing Homes. JAMA Intern Med. 2017 Dec 26
Pettus J, McNabb B, Eckel RH, et al. The effect of **ranolazine on glycemic control** in patients with type 2 diabetes treated with either glimepiride or metformin. Diabetes Obes Metab. 2016 Jan 8.
Petrykiv S, Sjöström CD, Greasley PJ, et al. Differential Effects of **Dapagliflozin** on **Cardiovascular Risk Factors at Varying Degrees of Renal Function**. Clin J Am Soc Nephrol. 2017 May 8;12(5):751-759.
Pezzella AT, Holmes SD, Pritchard G, et al. Impact of **perioperative glycemic control strategy on patient survival after coronary bypass surgery**. Ann Thorac Surg. 2014 Oct;98(4):1281-5.
Pfeffer MA, Claggett B, Diaz R, et al; **ELIXA** Investigators. **Lixisenatide** in Patients with Type 2 Diabetes and Acute Coronary Syndrome. N Engl J Med. 2015 Dec 3;373(23):2247-57.
Pham SV, Chilton RJ. **EMPA-REG OUTCOME: The Cardiologist's Point of View**. Am J Cardiol. 2017 Jul 1;120(1S):S53-S58.
Pharmacist's Letter May 2006: Byetta (**Exenatide**) for **Weight Loss**.
Pharmacist's Letter July 2006: **Sitagliptin** (Januvia) and Vildagliptin (Galvus) for Diabetes. (see also Medical Letter Jan 1,2007 Sitagliptin) (see also Vildagliptin. Emerging Drug List CADTH Nov/06; (FDA:concern of skin toxicity in primates http://cws.huginonline.com/N/134323/PR/200611/1087811_5_2.html)
Pharmacist's Letter Sept 2006. The use of Glitazones in persons with congestive heart failure (see also DREAM & PROACTIVE trial results)
Pharmacist's Letter: **Treatment of type 2 diabetes mellitus**. Nov 2006
Pharmacist's Letter. Treatment of Diabetes in women who are **pregnant**. Sept 2007.
Pharmacist's Letter. Metformin-Induced **Vitamin B12 Deficiency**: Can it Lead to Peripheral Neuropathy? Aug,2009.
Pharmacist's Letter. **Fasting in the Patient with Diabetes**. July 2011.
Pharmacist's Letter. Comparison of **GLP-1 Agonists (Bydureon, Byetta, and Victoza).** March 2012.
Philis-Tsimikas A, Billings LK, Busch R, et al. Superior efficacy of insulin **degludec/liraglutide versus insulin glargine U100** as add-on to sodium-glucose co-transporter-2 inhibitor therapy: A randomized clinical trial in people with uncontrolled type 2 diabetes. Diabetes Obes Metab. 2019 Feb 13.
Phillip M, Battelino T, Atlas E, et al. Nocturnal glucose control with an **artificial pancreas** at a diabetes camp. N Engl J Med. 2013 Feb 28;368(9):824-33.
Phillips LS, Grunberger G, Miller E, Patwardhan R, et al.. **Once- and twice-daily dosing with rosiglitazone improves glycemic control** in patients with type 2 diabetes. Diabetes Care. 2001 Feb;24(2):308-15.
Phrommintikul A, Wongcharoen W, Kumfu S, et al. Effects of **Dapagliflozin vs. Vildagliptin** on Cardiometabolic Parameters in Diabetic Patients with Coronary Artery Disease: A Randomised Study. Br J Clin Pharmacol. 2019 Feb 14.
Phung OJ; Scholle JM.; Talwar M; et al. Effect of **Noninsulin Antidiabetic Drugs Added to Metformin** Therapy on Glycemic Control, Weight Gain, and Hypoglycemia in Type 2 Diabetes. JAMA. 2010;303(14):1410-1418.
Phung OJ, Schwartzman E, Allen RW, et al. **Sulphonylureas and risk of cardiovascular** disease: systematic review and meta-analysis. Diabet Med. 2013 Oct;30(10):1160-71.
Piccinni C, Motola D, Marchesini G, Poluzzi E. Assessing the Association of **Pioglitazone Use and Bladder Cancer** Through Drug Adverse Event Reporting. Diabetes Care. 2011 Apr 22
Pickup JC. **Insulin-pump** therapy for type 1 diabetes mellitus. N Engl J Med. 2012 Apr 26;366(17):1616-24.
Pickup JC, Reznik Y, Sutton AJ. Glycemic Control During **Continuous Subcutaneous Insulin Infusion Versus Multiple Daily Insulin Injections** in Type 2 Diabetes: Individual Patient Data Meta-analysis and Meta-regression of Randomized Controlled Trials. Diabetes Care. 2017 May;40(5):715-722.
Pickwell K, Siersma V, Kars M, et al. **Predictors of Lower-Extremity Amputation** in Patients With an **Infected Diabetic Foot Ulcer**. Diabetes Care. 2015 Feb 9.
Pieber TR, Bode B, Mertens A, et al. Efficacy and safety of oral **semaglutide** with flexible dose adjustment **versus sitagliptin** in type 2 diabetes (PIONEER 7):
a multicentre, open-label, randomised, phase 3a trial. Lancet Diabetes Endocrinol. 2019 Jun 6.
Pierce DA, Russell G, Pirkle JL Jr. Incidence of **Hypoglycemia in Patients With Low eGFR** Treated With Insulin and Dextrose for Hyperkalemia. Ann Pharmacother. 2015 Dec;49(12):1322-6.
Pignone Michael, Alberts Mark J., Colwell John A., et al. **Aspirin for Primary Prevention of Cardiovascular Events in People With Diabetes**. A Position Statement of the American Diabetes Association (**ADA**), a Scientific Statement of the American Heart Association (**AHA**), and an Expert Consensus Document of the American College of Cardiology Foundation (ACCF). Circulation published May 27, **2010**, doi:10.1161/CIR.0b013e3181e3b133 http://circ.ahajournals.org/cgi/reprint/CIR.0b013e3181e3b133v1
Pillay J, Armstrong MJ, Butalia S, et al. **Behavioral Programs for Type 1 Diabetes** Mellitus: A Systematic Review and Meta-analysis. Ann Intern Med. 2015 Sep 29.
Pillay J, Armstrong MJ, Butalia S, et al. **Behavioral Programs for Type 2 Diabetes** Mellitus: A Systematic Review and NetworkMeta-analysis for Effect Moderation. Ann Intern Med. 2015 Sep 29.
Pillay J, Chordiya P, Dhakal S, et al. **Behavioral programs** for diabetes mellitus. Evidence Report/Technology Assessment No. 221. AHRQ Publication No. 15-E003-EF. Rockville, MD: Agency for Healthcare Research and Quality; September 2015.
Pimouguet, Clement, Le Goff, Melanie, Thiebaut, Rodolphe, et al. **Effectiveness of disease-management programs for improving diabetes care: a meta-analysis.** CMAJ 2011 183: E115-127.
Pinelli NR, Hurren KM. Efficacy and safety of long-acting **glucagon-like peptide-1 receptor agonists** compared with exenatide twice daily and sitagliptin in type 2 diabetes mellitus: a systematic review and meta-analysis. Ann Pharmacother. 2011 Jul;45(7-8):850-60.
Pi-Sunyer FX, et al. RIO-North America Study Group. Effect of rimonabant, a cannabinoid-1 receptor blocker, on weight and cardiometabolic risk factors in overweight or obese patients: RIO-North America: a randomized controlled trial. JAMA. 2006 Feb 15;295(7):761-75. (InfoPOEMs: Rimonabant (Acomplia) is minimally effective for obese or overweight patients for achieving sustained weight loss. Less than half the subjects initially enrolled in this study completed the protocol at 1 year. Of those remaining in the study, only one fourth lost a clinically significant amount of weight (10% or more) and, as with other weight-loss drugs, the patients who stopped taking the medicine after 1 year regained the weight. (LOE = 1b-))
Pierce SA, Chung AH, Black KK. Evaluation of **vitamin B12 monitoring** in a veteran population on long-term, high-dose **metformin** therapy. Ann Pharmacother. 2012 Nov;46(11):1470-6.
Pippitt K, Li M, Gurgle HE. **Diabetes Mellitus: Screening and Diagnosis**. Am Fam Physician. 2016;93(2):103-109.
Pitchika A, Jolink M, Winkler C, et al. Associations of **maternal type 1 diabetes with childhood adiposity and metabolic health in the offspring**: a prospective cohort study. Diabetologia. 2018 Jul 14.
Pittas AG, Dawson-Hughes B, Sheehan P, et al. **Vitamin D supplementation** and prevention of type 2 diabetes. (D2d trial) N Engl J Med. DOI: 10.1056/NEJMoa1900906.

Platt KD, Thompson AN, Lin P, et al. Assessment of **Self-monitoring of Blood Glucose in Individuals With Type 2 Diabetes Not Using Insulin**. JAMA Intern Med. 2018 Dec 10.

Plosker G. **Dapagliflozin**: A Review of its Use in Type 2 Diabetes Mellitus. Drugs. 2012;72(17):2289-2312.

Plourde G, Klein AV, Dent R. **Impaired awareness of hypoglycemia** in a man with type 1 diabetes. CMAJ. 2014 Jul 8;186(10):770-1. doi: 10.1503/cmaj.131391. Epub 2014 Feb 10.

Pollock C, Stefansson B, Reyner D, et al. **Albuminuria-lowering effect of dapagliflozin alone and in combination with saxagliptin** and effect of **dapagliflozin and saxagliptin on glycaemic control in patients with type 2 diabetes and chronic kidney disease** (DELIGHT): a randomised, double-blind, placebo-controlled trial. Lancet Diabetes Endocrinol. 2019 Apr 12.

Polonsky KS. The past **200 years in diabetes**. N Engl J Med. 2012 Oct 4;367(14):1332-40.

Polonsky WH, Hessler D, Ruedy KJ, Beck RW; **DIAMOND** Study Group. The Impact of **Continuous Glucose Monitoring** on Markers of Quality of Life in Adults With **Type 1 Diabetes**: Further Findings From the DIAMOND Randomized Clinical Trial. Diabetes Care. 2017 Jun;40(6):736-741.

Polycystic Ovary Syndrome (PCOS)Writing Committee. American Association of Clinical Endocrinologists position statement on metabolic and cardiovascular consequences of polycystic ovary syndrome. Endocr Pract 2005 Mar- Apr;11(2):125-34. http://www.aace.com/clin/guidelines/PCOSpositionstatement.pdf (Moll E, et al. Effect of clomifene citrate plus metformin and **clomifene citrate plus placebo** on induction of ovulation in women with newly diagnosed polycystic ovary syndrome: randomised double blind clinical trial. BMJ. 2006 Jun 13; Epub ahead of print. **Metformin is not an effective** addition to clomifene citrate as the primary method of inducing ovulation in women with polycystic ovary syndrome.)

Poolsup N, Suksomboon N, Plordplong N. Effect of **vitamin D supplementation** on insulin resistance and glycaemic control in **prediabetes**: a systematic review and meta-analysis. Diabet Med. 2016 Mar;33(3):290-9.

Pop-Busui R, Boulton AJ, Feldman EL, et al. **Diabetic Neuropathy**: A Position Statement by the **American Diabetes Association (ADA)**. Diabetes Care. 2017 Jan;40(1):136-154.

Poppy A, Retamal-Munoz C, Cree-Green M, et al. Reduction of **Insulin Related Preventable Severe Hypoglycemic** Events in Hospitalized Children. Pediatrics. 2016 Jul;138(1).

Porepa, Liane, Ray, Joel G, Sanchez-Romeu, Paula, Booth, Gillian L. Newly diagnosed diabetes mellitus as a risk factor for **serious liver disease**. CMAJ 2010 0: cmaj.092144.

Powe CE, Allard C, Battista MC, et al. Heterogeneous Contribution of **Insulin Sensitivity and Secretion Defects** to **Gestational** Diabetes Mellitus. Diabetes Care. 2016 Jun;39(6):1052-5.

Powers MA, Bardsley J, Cypress M, et al. **Diabetes Self-Management Education** and Support in Type 2 Diabetes: A Joint Position Statement of the American Diabetes Association (**ADA**), the American Association of Diabetes Educators, and the Academy of Nutrition and Dietetics. J Acad Nutr Diet. 2015 Jun 2.

Pozzilli P, Norwood P, Jodar E, et al. A placebo-controlled, randomised trial of the addition of once weekly GLP-1 receptor agonist **dulaglutide to titrated daily insulin glargine** in patients with type 2 diabetes (**AWARD-9**). Diabetes Obes Metab. 2017 Mar 14.

Pozzobon D, Ferreira PH, Dario AB, et al. Is there an association between **diabetes and neck and back pain**? A systematic review with meta-analyses. PLoS One. 2019 Feb 21;14(2):e0212030.

Practice Committee of the American Society for Reproductive Medicine. **Role of metformin for ovulation induction in infertile patients with polycystic ovary syndrome (PCOS):** a guideline. Fertil Steril. 2017 Sep;108(3):426-41.

Pradhan A, Vohra S, Vishwakarma P, Sethi R. Review on sodium-glucose cotransporter 2 inhibitor (**SGLT2i) in diabetes mellitus and heart failure**. J Family Med Prim Care. 2019 Jun;8(6):1855-1862.

Pratley R, Amod A, Hoff ST, et al. Oral **semaglutide versus subcutaneous liraglutide** and placebo in type 2 diabetes (**PIONEER 4**): a randomised, double-blind, phase 3a trial. Lancet 2019 Jun 7.; online June 8. http://dx.doi.org/10.1016/S0140-6736(19)31271-1.

Pratley RE, Aroda VR, Lingvay I, et al. **Semaglutide versus dulaglutide** once weekly in patients with type 2 diabetes (**SUSTAIN 7):** a randomised, open-label, phase 3b trial. Lancet Diabetes Endocrinol 2018; online Jan 31.

Pratley RE, Emerson SS, Franek E, et al. Cardiovascular safety and lower severe hypoglycaemia of **insulin degludec versus insulin glargine U100** in patients with type 2 diabetes aged 65 years or older: Results from DEVOTE (DEVOTE 7). Diabetes Obes Metab. 2019 Mar 8.

Pratley RE, Nauck M, Bailey T, et al. for 1860-LIRA-DPP-4 Study Group. **Liraglutide versus sitagliptin** for patients with type 2 diabetes who did not have adequate glycaemic control with metformin: a 26-week, randomised, parallel-group, open-label trial. Lancet. 2010 Apr 24;375(9724):1447-1456.

Preiss D, Lloyd SM, Ford I, et al. **Metformin for non-diabetic** patients with coronary heart disease (the **CAMERA** study): A randomised controlled trial.*Lancet Diabetes Endocrinol*2013.

Preiss D, Seshasai SR, Welsh P, et al. Risk of **incident diabetes with intensive-dose compared with moderate-dose statin** therapy. JAMA 2011; 305:2556-2564. (New onset diabetes NNH=498, Cardiovascular events NNT=155 per year)

Priest JR, Yang W, Reaven G, et al. **Maternal Midpregnancy Glucose** Levels and Risk of Congenital Heart Disease in Offspring. JAMA Pediatr. 2015 Oct 12:1-5.

Prospective Studies Collaboration and Asia Pacific Cohort Studies Collabroation. **Sex-specific relevance of diabetes** to occlusive vascular and other mortality: a collaborative meta-analysis of individual data from 980 793 adults from 68 prospective studies. Lancet Diabetes Endocrinol 2018; online May 8.

Puar TH, Khoo JJ, Cho LW, Xu Y, Chen YT, Chuo AM, Poh CB, Ng JM. Association between **glycemic control and hip fracture**. J Am Geriatr Soc. 2012 Aug;60(8):1493-7.

Punthakee Z, Miller ME, Simmons DL, et al. **ACCORD** Group of Investigators. **Durable change in glycaemic control** following intensive management of type 2 diabetes in the ACCORD clinical trial. Diabetologia. 2014 Oct;57(10):2030-7.

Purnell JQ, Hokanson JE, Cleary PA, et al. The effect of excess **weight gain with intensive diabetes mellitus treatment** on cardiovascular disease risk factors and atherosclerosis in type 1 diabetes mellitus: results from the Diabetes Control and Complications Trial/Epidemiology of Diabetes Interventions and Complications Study (**DCCT/EDIC**) Study. Circulation. 2013;127:180–187.

Pyatak EA, et al. **Occupational Therapy Intervention Improves Glycemic Control** and Quality of Life Among Young Adults With Diabetes: Resilient, Empowered, Active Living With Diabetes (REAL Diabetes) Randomized Trial. Diabetes Care. 2018 Jan 19.

Qaseem A, Humphrey LL, Sweet DE, et al. for the Clinical Guidelines Committee of the American College of Physicians (**ACP**). **Oral Pharmacologic Treatment of Type 2 Diabetes Mellitus**: A Clinical Practice Guideline From the American College of Physicians. Ann Intern Med. 2012 Feb 7;156(3):218-231.

Qaseem A, Chou R, Humphrey LL, Shekelle P; for the Clinical Guidelines Committee of the American College of Physicians. **Inpatient Glycemic Control**: Best Practice Advice From the Clinical Guidelines Committee of the American College of Physicians. Am J Med Qual. 2013 May 24.

Qaseem A, Barry MJ, Humphrey LL, et al. **Oral pharmacologic treatment of type 2 diabetes mellitus**: a clinical practice guideline update from the **American College of Physicians (ACP).** Ann Intern Med. 2017. [Epub ahead of print]. doi:10.7326/M16-1860

Qaseem A, Wilt TJ, et al. **Hemoglobin A1c Targets for Glycemic Control With Pharmacologic Therapy for Nonpregnant Adults With Type 2 Diabetes Mellitus**: A Guidance Statement Update From the **American College of Physicians (ACP).** Ann Intern Med. 2018 Mar 6.

Qi J, He P, Yao H, et al. **Cancer risk among patients with type 2 diabetes**: A real-world study in Shanghai, China. J Diabetes. 2019 May 8.

Qian F, Liu G, Hu FB, et al. Association Between **Plant-Based Dietary Patterns and Risk of Type 2 Diabetes**: A Systematic Review and Meta-analysis. JAMA Intern Med. 2019 Jul 22.

Qiu M, Shen W, Song X, et al. Effects of **prediabetes mellitus alone or plus hypertension** on subsequent occurrence of cardiovascular disease and diabetes mellitus: longitudinal study. Hypertension. 2015 Mar;65(3):525-30.

Rabizadeh S, Nakhjavani M, Esteghamati A. **Cardiovascular and Renal Benefits of SGLT2 Inhibitors**: A Narrative Review. Int J Endocrinol Metab. 2019 Apr 22;17(2):e84353.

Radhakutty A, Burt MG. **Management of Endocrine Disease**: Critical review of the evidence underlying **management of glucocorticoid-induced hyperglycaemia**. Eur J Endocrinol. 2018 Jul 10.

Radholm K, Figtree G, Perkovic V, et al. **Canagliflozin** and **Heart Failure** in Type 2 Diabetes Mellitus: Results From the **CANVAS** Program (Canagliflozin Cardiovascular Assessment Study). Circulation. 2018 Mar 11.

Raebel MA, Xu S, Goodrich GK, et al. **Initial Antihyperglycemic Drug Therapy** Among 241 327 Adults With Newly Identified Diabetes From 2005 Through 2010: A Surveillance, Prevention, and Management of Diabetes Mellitus (SUPREME-DM) Study. Ann Pharmacother. 2013 Oct;47(10):1280-91.

Raghavan S, Vassy JL, Ho YL, et al. Diabetes Mellitus-Related **All-Cause and Cardiovascular Mortality** in a National Cohort of Adults. J Am Heart Assoc. 2019 Feb 19;8(4):e011295.

Rahman F, McEvoy JW, Ohkuma T, et al. Effects of Blood Pressure Lowering on Clinical Outcomes According to **Baseline Blood Pressure and Cardiovascular Risk in Patients With Type 2 Diabetes Mellitus**. Hypertension. 2019 Apr 29:HYPERTENSIONAHA11812414.

Rajan KB, Arvanitakis Z, Lynch EB, et al. **Cognitive decline** following incident and preexisting diabetes mellitus in a population sample. Neurology 2016;87:1681–1687.

Rajendran R, Hodgkinson D, Rayman G. Patients with diabetes **requiring emergency department care for hypoglycaemia**: characteristics and long-term outcomes determined from multiple data sources. Postgrad Med J. 2015 Feb;91(1072):65-71.

Rajkumar AP, Horsdal HT, Wimberley T, et al. Endogenous and **Antipsychotic-Related Risks for Diabetes Mellitus** in Young People With Schizophrenia: A Danish Population-Based Cohort Study. Am J Psychiatry. 2017 Jan 20:appiajp201616040442.

Rajkumar AP, Horsdal HT, Wimberley T, et al. Endogenous and **Antipsychotic-Related Risks for Diabetes Mellitus in Young People With Schizophrenia**: A Danish Population-Based Cohort Study. Am J Psychiatry. 2017 Jan 20:appiajp201616040442.

Rajpathak SN, Kumbhani DJ, Crandall J, et al. **Statin** therapy and risk of developing type 2 diabetes: a meta-analysis. Diabetes Care. 2009 Oct;32(10):1924-9.

Ramachandran A, Riddle MC, et al. Relationship between **A1C and fasting plasma glucose in dysglycemia or type 2 diabetes**: an analysis of baseline data from the ORIGIN trial. Diabetes Care. 2012 Apr;35(4):749-53.

Raman P, Shepherd E, Dowswell T, et al. Different methods and settings for **glucose monitoring for gestational diabetes during pregnancy**. Cochrane Database of Systematic Reviews 2017, Issue 10. Art. No.: CD011069. Evidence from 11 RCTs assessing different methods or settings for glucose monitoring for GDM suggests no clear differences for the primary outcomes or other secondary outcomes assessed in this review. However, current evidence is limited by the small number of RCTs for the comparisons assessed, small sample sizes, and the variable methodological quality of the RCTs.

Ramos R, Comas-Cufí M, Martí-Lluch R, et al. **Statins for primary prevention of cardiovascular events** and mortality in old and very old adults with and without type 2 diabetes: retrospective cohort study. BMJ. 2018 Sep 5;362:k3359.

Rawshani A, Sattar N, Franzén S, et al. **Excess mortality and cardiovascular disease in young adults with type 1 diabetes** in relation to age at onset: a nationwide, register-based cohort study. Lancet. 2018 Aug 11;392(10146):477-486.

Ran M, Wang Y. Images in Clinical Medicine. Generalized **Granuloma Annulare** Associated with Diabetes Mellitus. N Engl J Med. 2016 Sep 8;375(10):e21

Ranc K, Jørgensen ME, Friis S, et al. **Mortality after cancer** among patients with diabetes mellitus: effect of diabetes duration and treatment. Diabetologia. 2014 Mar 15.

Randolph AC, Lin YL, Volpi E, Kuo YF. **Tricyclic Antidepressant and/or γ-Aminobutyric Acid-Analog Use Is Associated With Fall Risk** in Diabetic Peripheral Neuropathy. J Am Geriatr Soc. 2019 Jan 29

Rangarajan S, Bone NB, Zmijewska AA, et al. **Metformin reverses established lung fibrosis in a bleomycin model**. Nat Med. 2018 Jul 2.

Rascati KL et al. **Progression to insulin** for patients with diabetes mellitus using the Texas medicaid database. Clin Ther. 2011 Dec;33(12):2016-20. (slower progression with metformin/TZD than sulfonylurea/TZD)

Rasmussen BS, Yderstraede KB, Carstensen B, et al. Substantial reduction in the number of **amputations** among patients with diabetes: a cohort study over 16 years. Diabetologia. 2015 Nov 22.

Rawla P, Vellipuram AR, Bandaru SS, Pradeep Raj J. **Euglycemic diabetic ketoacidosis**: a diagnostic and therapeutic dilemma. Endocrinol Diabetes Metab Case Rep. 2017 Sep 4;2017.

Rawlings AM, Sharrett AR, Schneider AL, et al. **Diabetes in midlife and cognitive change** over **20 years**: a cohort study. Ann Intern Med. 2014 Dec 2;161(11):785-93.

Rawshani A, Rawshani A, Franzén S, et al. **Mortality and cardiovascular disease in type 1 and type 2 diabetes**. N Engl J Med 2017;376:1407-18.

Rawshani A, Rawshani A, Franzén S, et al. **Range of Risk Factor Levels**: Control, Mortality, and Cardiovascular Outcomes in Type 1 Diabetes Mellitus. Circulation. 2017 Apr 18;135(16):1522-1531.

Rawshani A, Rawshani A, Franzén S, et al. Risk Factors, Mortality, and Cardiovascular Outcomes in Patients with Type 2 Diabetes. N Engl J Med. 2018 Aug 16;379(7):633-644.

Ray JG, et al. **Breast size** and risk of type 2 diabetes mellitus. CMAJ. 2008 Jan 29;178(3):289-95. A large bra cup size at age 20 may be a predictor of type 2 diabetes mellitus in middle-aged women.

Ray KK, Seshasai SR, Wijesuriya S, et al. Effect of **intensive control of glucose on cardiovascular outcomes** and death in patients with diabetes mellitus: a meta-analysis of randomized controlled trials. Lancet 2009; 373: 1765-72.

Raz I, Wilson PW, Strojek K, et al. Effects of prandial versus fasting glycemia on cardiovascular outcomes in type 2 diabetes: the **HEART2D** trial. Diabetes Care. 2009 Mar;32(3):381-6. Treating diabetic survivors of AMI with prandial versus basal strategies achieved differences in fasting blood glucose, less-than-expected differences in postprandial blood glucose, similar levels of A1C, and no difference in risk for future cardiovascular event rates.

Razmaria AA. **Diabetic Neuropathy**. JAMA. 2015 Nov 24;314(20):2202.

Reaven PD, Emanuele NV, Wiitala WL, et al; VADT Investigators. **Intensive Glucose Control** in Patients with Type 2 Diabetes - 15-Year Follow-up. N Engl J Med. 2019 Jun 6;380(23):2215-2224.

Rebarber A, Dolin C, Fields JC, et al. **Screening** approach for **gestational** diabetes in **twin pregnancies**. Am J Obstet Gynecol. 2014 Dec;211(6):639.e1-5.

Reboldi G, Gentile G, Angeli F, et al. Effects of **intensive blood pressure reduction on myocardial infarction and stroke in diabetes**: a meta-analysis in 73 913 patients. J Hypertens 2011; 29:1253-1269.

Reddy M, Rilstone S, Cooper P, et al. **Type 1 diabetes in adults**: supporting self management. BMJ. 2016 Mar 10;352:i998.

Reddy M, Jugnee N, El Laboudi A, et al. A randomized controlled pilot study of **continuous glucose monitoring** and **flash glucose monitoring** in people with **Type 1 diabetes** and impaired awareness of hypoglycaemia. Diabet Med. 2018 Apr;35(4):483-490.

Reed M, Huang J, Graetz I, et al. Outpatient **electronic health records** and the clinical care and outcomes of patients with diabetes mellitus. Ann Intern Med 2012.

Reeds Dominic N., Patterson Bruce W., Okunade Adewole, et al. **Ginseng and Ginsenoside** Re Do Not Improve β-Cell Function or Insulin Sensitivity in Overweight and Obese Subjects With Impaired Glucose Tolerance or Diabetes. Diabetes Care May 2011 34:1071-1076; published ahead of print March 16, 2011, doi:10.2337/dc10-2299

Regensteiner JG, Golden S, Huebschmann AG, et al. **Sex Differences** in the Cardiovascular Consequences of Diabetes Mellitus: A Scientific Statement From the American Heart Association. Circulation. 2015 Dec 7.

Rehackova L, Arnott B, Araujo-Soares V, et al. Efficacy and acceptability of **very low energy diets** in overweight and obese people with Type 2 diabetes mellitus: a systematic review with meta-analyses. Diabet Med. 2016 May;33(5):580-91.

Reis JP, Loria CM, Sorlie PD, et al. **Lifestyle factors** and risk for new-onset diabetes: a population-based cohort study. Ann Intern Med. 2011 Sep 6;155(5):292-9.

Repaske DR. **Medication-induced diabetes mellitus**. Pediatr Diabetes. 2016 Sep;17(6):392-7.

REPOSE Study Group. Relative effectiveness of **insulin pump treatment over multiple daily injections** and structured education during flexible intensive insulin treatment for type 1 diabetes: cluster randomised trial (REPOSE). BMJ. 2017 Mar 30;356:j1285

Restivo DA, Casabona A, Frittitta L, et al**. Efficacy of Botulinum Toxin-A for treating cramps in diabetic neuropathy**. Ann Neurol. 2018 Sep 17.

Retnakaran R, Zinman B. **Thiazolidinediones** and clinical outcomes in type 2 diabetes. *Lancet* 2009; DOI:10.1016/S0140-6736(09)61029-1.

Retnakaran, Ravi, Shah, Baiju R. **Mild glucose intolerance in pregnancy** and risk of cardiovascular disease: a population-based cohort study. CMAJ 2009 0: cmaj.090569

Retnakaran R, Kramer CK, Ye C, et al. **Fetal Sex and Maternal Risk** of **Gestational Diabetes** Mellitus: The Impact of Having a Boy. Diabetes Care. 2015 Feb 18.

Retnakaran R, Shah BR. **Fetal Sex and the Natural History of Maternal Risk of Diabetes** During and After **Pregnancy**. J Clin Endocrinol Metab. 2015 May 20

Retnakaran R, Shah BR. **Glucose screening in pregnancy and future risk of cardiovascular disease** in women: a retrospective, population-based cohort study. Lancet Diabetes Endocrinol. 2019 May;7(5):378-384.

Reusch J, Stewart MW, Perkins CM, et al. Efficacy and safety of **once-weekly** glucagon-like peptide 1 receptor agonist **albiglutide** (**HARMONY 1** trial): 52- week primary endpoint results from a randomized, double-blind, placebo-controlled trial in patients with type 2 diabetes mellitus not controlled on **pioglitazone, with or without metformin**. Diabetes Obes Metab. 2014 Dec;16(12):1257-64.

Reusch JE, Manson JE. **Management of Type 2 Diabetes in 2017**: **Getting to Goal**. JAMA. 2017 Mar 1.

Rewers A, Dong F, Slover RH, et al. Incidence of **diabetic ketoacidosis at diagnosis of type 1 diabetes** in Colorado **youth**, 1998-2012. JAMA. 2015 Apr 21;313(15):1570-2.

Reynolds AN, Mann JI, Williams S, et al. **Advice to walk after meals** is more effective for lowering postprandial glycaemia in type 2 diabetes mellitus than advice that does not specify timing: a randomised crossover study. Diabetologia. 2016 Oct 17

Reznik Y, Cohen O, Aronson R, et al; for the OpT2mise Study Group. **Insulin pump treatment compared with multiple daily injections** for treatment of type 2 diabetes (**OpT2mise**): a randomised open-label controlled trial. Lancet. 2014 Jul 2.

Rhee MK, Ho YL, Raghavan S, et al. Random **plasma glucose predicts the diagnosis of diabetes**. PLoS One. 2019 Jul 19;14(7):e0219964.

Rho YH, Lu N, Peloquin CE, et al. Independent **impact of gout** on the **risk of diabetes mellitus** among women and men: a population-based, BMI-matched cohort study. Ann Rheum Dis. 2016 Jan;75(1):91-5.

Richter B, Bandeira-Echtler E, Bergerhoff K, Clar C, Ebrahim Sh. **Rosiglitazone** for type 2 diabetes mellitus. Cochrane Database Syst Rev. 2007 Jul 18;(3):CD006063. Eighteen trials which randomised 3888 people to rosiglitazone treatment were identified. Longest duration of therapy was four years with a median of 26 weeks. Published studies of at least 24 weeks rosiglitazone treatment in people with type 2 diabetes mellitus did not provide evidence that patient-oriented outcomes like mortality, morbidity, adverse effects, costs and health-related quality of life are positively influenced by this compound. Metabolic control measured by glycosylated haemoglobin A1c (HbA1c) as a surrogate endpoint did not demonstrate clinically relevant differences to other oral antidiabetic drugs. Occurrence of oedema was significantly raised (OR 2.27, 95% confidence interval (CI) 1.83 to 2.81). The single large RCT (ADOPT - A Diabetes Outcomes Progression Trial) indicated increased cardiovascular risk.

Richter B, Bandeira-Echtler E, et al.. **Pioglitazone** for type 2 diabetes mellitus. Cochrane Database Syst Rev. 2006 Oct 18;(4):CD006060. Until new evidence becomes available, the benefit-risk ratio of pioglitazone remains unclear. Different therapeutic indications for pioglitazone of the two big U.S. and European drug agencies should be clarified to reduce uncertainties amongst patients and physicians.

Richter B, Bandeira-Echtler E, Bergerhoff K, Lerch CL. Dipeptidyl peptidase-4 (DPP-4) inhibitors (**sitagliptin and vildagliptin**) for type 2 diabetes mellitus. Cochrane Database Syst Rev. 2008 Apr 16;(2):CD006739.

Riddell MC, Gallen IW, Smart CE, et al.**Exercise management in** type 1 diabetes: a consensus statement. Lancet Diabetes Endocrinol. 2017 Jan 23.

Riddle MC, Yki-Jarvinen H, Bolli GB, et al. One-year sustained glycaemic control and less hypoglycaemia with new **insulin glargine 300 U/ml compared with 100 U/ml** in people with type 2 diabetes using basal plus meal-time insulin: the EDITION 1 12-month randomized trial, including 6-month extension. Diabetes Obes Metab. 2015 Sep;17(9):835-42.

Ried-Larsen M, Johansen MY, MacDonald CS, et al. Type 2 **diabetes remission 1 year after an intensive lifestyle intervention**: A secondary analysis of a randomized clinical trial**.** Diabetes Obes Metab. 2019 Jun 5.

Rigby MR, Dimeglio LA, et al. Targeting of memory T cells with **alefacept** in new-onset **type 1 diabetes** (T1DAL study): 12 month results of a randomised, double-blind, placebo-controlled phase 2 trial. Lancet Diabetes Endocrinol. 2013 Dec;1(4):284-94.

Ripsin CM, Kang H, Urban RJ. **Management of blood glucose in type 2 diabetes mellitus**. Am Fam Physician. 2009 Jan 1;79(1):29-36.

RISE Consortium. Impact of **insulin and metformin versus metformin alone on b-cell function in youth with impaired glucose tolerance** or recently diagnosed type 2 diabetes. Diabetes Care 2018;41:June 2018.

RISE Consortium Investigators. **Lack of Durable Improvements in β-Cell Function Following** Withdrawal of Pharmacological Interventions in Adults With Impaired Glucose Tolerance or Recently Diagnosed Type 2 Diabetes. Diabetes Care. 2019 Jun 9.

RISE Consortium; RISE Consortium Investigators. Effects of Treatment of Impaired Glucose Tolerance or Recently Diagnosed Type 2 Diabetes With Metformin Alone or in Combination With Insulin Glargine on β-Cell Function: Comparison of Responses In Youth And Adults. Diabetes. 2019 Jun 9.

Ritsinger V, Malmberg K, Mårtensson A, et al. **Intensified insulin**-based glycaemic control **after myocardial infarction**: mortality during 20 year follow-up of the randomised Diabetes Mellitus Insulin Glucose Infusion in Acute Myocardial Infarction (**DIGAMI 1**) trial. Lancet Diabetes Endocrinol. 2014 May 12.

Ritzel R, Harris SB, Baron H, et al. A Randomized Controlled Trial Comparing **Efficacy and Safety of Insulin Glargine 300 Units/mL Versus 100 Units/mL in Older People With Type 2 Diabetes**: Results From the SENIOR Study. Diabetes Care. 2018 Jun 12.

Ritzel R, Roussel R, et al. Patient-level meta-analysis of the **EDITION** 1, 2 and 3 studies: glycaemic control and hypoglycaemia with new **insulin glargine 300 U/ml versus glargine 100** U/ml in type 2 diabetes. Diabetes Obes Metab. 2015 Sep;17(9):859-67.

Ritzel R; et al. Better glycaemic control and less hypoglycaemia with **insulin glargine 300 U/mL vs glargine 100 U/mL**: 1-year patient-level meta-analysis of the **EDITION** clinical studies in people with type 2 diabetes. Diabetes Obes Metab. 2017 Sep 1.

*Roberts RO, Knopman DS, Przybelski SA, et al. Association of type 2 diabetes with brain atrophy and **cognitive impairment**. Neurology. 2014 Apr 1;82(13):1132-41.*

Roberts AL, Agnew-Blais JC, Spiegelman D, et al. **Posttraumatic Stress Disorder** and Incidence of Type 2 Diabetes Mellitus in a Sample of Women: A 22-Year Longitudinal Study. JAMA Psychiatry. 2015 Jan 7.
Robling M, McNamara R, Bennert K, et al. The effect of the **Talking Diabetes consulting skills intervention** on glycaemic control and quality of life in children with type 1 diabetes: cluster randomised controlled trial (**DEPICTED** study). BMJ 2012;344:e2359
Robson J, Smithers H, Chowdhury T, et al. **Reduction in self-monitoring of blood glucose** in type 2 diabetes: an observational controlled study in east London. Br J Gen Pract. 2015 Apr; 65(633):e256-63.
Rocco MB. **Statins and diabetes risk**: Fact, fiction, and clinical implications. Cleve Clin J Med. 2012 Dec;79(12):883-93.
Rock CL, Flatt SW, et al. Weight Loss, Glycemic Control, and Cardiovascular Disease Risk Factors in Response to **Differential Diet Composition in a Weight Loss** Program in Type 2 Diabetes: A Randomized Controlled Trial. Diabetes Care. 2014 Apr 23.
Rockette-Wagner B, Edelstein S, Venditti EM, et al; Diabetes Prevention Program (**DPP**) Research Group. The impact of **lifestyle intervention on sedentary time in** individuals at high risk of diabetes. Diabetologia. 2015 Apr 8.
Rockette-Wagner B, Storti KL, Dabelea D, et al. **Activity and Sedentary Time 10 Years** After a Successful **Lifestyle Intervention**: The Diabetes Prevention Program (**DPPOS**). Am J Prev Med. 2017 Mar;52(3):292-299.
Rodbard HW, Jellinger PS, Davidson JA, et al. Statement by an American Association of Clinical Endocrinologists/American College of Endocrinology Consensus Panel on Type 2 Diabetes Mellitus: **Algorithm for Glycemic Control**. Endocr Pract. 2009 September-October 1;15(6):540-559.
Rodriguez BL, et al. Prevalence of cardiovascular disease risk factors in U.S. **children and adolescents** with diabetes: the **SEARCH** for diabetes in youth study. Diabetes Care. 2006 Aug;29(8):1891-6.
Rodriguez-Gutierrez R, Lipska KJ, McCoy RG. **Intensive Glycemic Control** in Type 2 Diabetes Mellitus-A **Balancing Act** of Latent Benefit and Avoidable Harm: A Teachable Moment. JAMA Intern Med. 2016 Mar 1;176(3):300-1.
Rodriguez-Gutierrez R, Lipska KJ, McCoy RG, et al; **Hypoglycemia** as a Quality Measure in Diabetes Study Group. Hypoglycemia as an indicator of good diabetes care. BMJ. 2016 Mar 7;352:i1084.
Rodríguez-Gutiérrez R, Montori VM. **Glycemic Control** for Patients With Type 2 Diabetes Mellitus: Our **Evolving Faith in the Face of Evidence**. Circ Cardiovasc Qual Outcomes. 2016 Sep;9(5):504-12.
Rodbard HW, Tripathy D, et al. **Adding fast-acting insulin aspart** to basal insulin significantly improved glycaemic control in patients with type 2 diabetes: A randomized, 18-week, open-label, phase 3 trial (onset 3). Diabetes Obes Metab. 2017 Mar 27.
Roglic G, Norris SL. **Medicines for Treatment Intensification in Type 2 Diabetes and Type of Insulin in Type 1 and Type 2 Diabetes in Low-Resource Settings**: Synopsis of the World Health Organization Guidelines on Second- and Third-Line Medicines and Type of Insulin for the Control of Blood Glucose Levels in Nonpregnant Adults With Diabetes Mellitus. Ann Intern Med. 2018 Sep 18;169(6):394-397.
Romeo GR, Abrahamson MJ. The **2015 Standards for Diabetes Care**: Maintaining a Patient-Centered Approach. Ann Intern Med. 2015 Mar 24.
Romeo GR, Abrahamson MJ. The **2015 standards for diabetes care**: maintaining a patient-centered approach. Ann Intern Med. 2015 Jun 2;162(11):785-6.
Rondags SM, de Wit M, Twisk JW, et al. Effectiveness of **HypoAware**, a Brief Partly Web-Based **Psychoeducational Intervention** for Adults With Type 1 and Insulin-Treated Type 2 Diabetes and Problematic Hypoglycemia: A Cluster Randomized Controlled Trial. Diabetes Care. 2016 Oct 20.
Rondinelli M, Rossi A, Gandolfi A, et al. Use of **Liraglutide** in the **Real World** and Impact at **36 Months** on Metabolic Control, Weight, Lipid Profile, Blood Pressure, Heart Rate, and Renal Function. Clin Ther. 2016 Dec 8.
Rooney NJ, Morant S, Guest C. **Investigation into the value of trained glycaemia alert dogs to clients with type I diabetes**. PLoS One. 2013 Aug 7;8(8):e69921.
Roos N, Kieler H, Sahlin L, Ekman-Ordeberg G, Falconer H, Stephansson O. Risk of **adverse pregnancy outcomes in women with polycystic ovary syndrome**: population based cohort study. BMJ 2011;343:d6309.
Rosenstock J, Allison D, Birkenfeld AL, et al; PIONEER 3 Investigators. Effect of Additional Oral **Semaglutide vs Sitagliptin** on Glycated Hemoglobin in Adults With Type 2 Diabetes Uncontrolled With Metformin Alone or With Sulfonylurea: The PIONEER 3 Randomized Clinical Trial. JAMA. 2019 Mar 23.
Rosenstock J, Aronson R, Grunberger G, et al. Benefits of **LixiLan**, a Titratable Fixed-Ratio Combination of Insulin **Glargine Plus Lixisenatide**, Versus Insulin **Glargine and Lixisenatide Monocomponents** in Type 2 Diabetes Inadequately Controlled With Oral Agents: The LixiLan-O Randomized Trial. Diabetes Care. 2016 Aug 15.
Rosenstock J, Balas B, Charbonnel B, et al; T-emerge 2 Study Group. The Fate of **Taspoglutide**, a Weekly GLP-1 Receptor Agonist, Versus Twice-Daily Exenatide for Type 2 Diabetes: The T-emerge 2 trial. Diabetes Care. 2013 Mar;36(3):498-504.
Rosenstock J, Cheng A, Ritzel R, et al. More Similarities Than Differences Testing **Insulin Glargine 300 Units/mL Versus Insulin Degludec 100 Units/mL** in Insulin-Naive Type 2 Diabetes: The Randomized Head-to-Head BRIGHT Trial. Diabetes Care. 2018 Aug 13.
Rosenstock J, Cheng A, Ritzel R, et al. More Similarities Than Differences Testing **Insulin Glargine 300 Units/mL Versus Insulin Degludec 100 Units/mL** in Insulin-Naive Type 2 Diabetes: The Randomized Head-to-Head BRIGHT Trial. Diabetes Care. 2018 Oct; 41(10):2147-2154.
Rosenstock J, Chuck L, Gonzalez-Ortiz M, et al. Initial Combination Therapy With **Canagliflozin Plus Metformin** Versus Each Component as Monotherapy for Drug-Naive Type 2 Diabetes. Diabetes Care. 2016 Jan 19.
Rosenstock J, Diamant M, Aroda VR, et al; LixiLan PoC Study Group. Efficacy and Safety of **LixiLan**, a Titratable Fixed-Ratio Combination of **Lixisenatide and Insulin Glargine, Versus Insulin Glargine** in Type 2 Diabetes Inadequately Controlled on **Metformin** Monotherapy: The LixiLan Proof-of-Concept Randomized Trial. Diabetes Care. 2016 Jun 9.
Rosenstock J, Fonseca VA, Gross JL, et al;for the **Harmony-6** Study Group. Advancing Basal Insulin Replacement in Type 2 Diabetes Inadequately Controlled With Insulin **Glargine Plus Oral Agents**: A Comparison of Adding **Albiglutide**, a Weekly GLP-1 Receptor Agonist, Versus Thrice-Daily Prandial Insulin **Lispro**. Diabetes Care. 2014 Jun 4.
Rosenstock J, Franco D, Korpachev V, et al. **Inhaled Technosphere Insulin** Versus Inhaled Technosphere Placebo in Insulin-Naive Subjects With Type 2 Diabetes Inadequately Controlled on Oral Antidiabetes Agents. Diabetes Care. 2015 Aug 7.
Rosenstock J; Frias J; Pall D;et al. Effect of **ertugliflozin** on glucose control, body weight, blood pressure and bone density in type 2 diabetes mellitus inadequately controlled on metformin monotherapy (**VERTIS MET**). Diabetes Obes Metab. 2017 Aug 31.
Rosenstock J, Guerci B, Hanefeld M, et al; **GetGoal Duo-2** Trial Investigators. Prandial Options to Advance Basal Insulin Glargine Therapy: Testing **Lixisenatide Plus Basal Insulin Versus Insulin Glulisine Either as Basal-Plus or Basal-Bolus** in Type 2 Diabetes: The GetGoal Duo-2 Trial. Diabetes Care. 2016 May 23.
Rosenstock J, Guerci B, Hanefeld M, et al. Prandial Options to Advance Basal Insulin Glargine Therapy: Testing **Lixisenatide Plus Basal Insulin Versus Insulin Glulisine** Either as Basal-Plus or Basal-Bolus in Type 2 Diabetes: The GetGoal Duo-2 Trial. Diabetes Care. 2016 May 23. pii: dc160014.
Rosenstock J, Hansen L, Zee P, et al. Dual Add-on Therapy in Type 2 Diabetes Poorly Controlled With Metformin Monotherapy: A Randomized Double-Blind Trial of **Saxagliptin Plus Dapagliflozin** Addition Versus Single Addition of **saxagliptin or Dapagliflozin to Metformin**. Diabetes Care. 2014 Oct 28.
Rosenstock J, Hansen L, Zee P, Li Y, Cook W, Hirshberg B, Iqbal N. Dual Add-on Therapy in Type 2 Diabetes Poorly Controlled With **Metformin** Monotherapy: A Randomized Double-Blind Trial of **Saxagliptin** Plus Dapagliflozin Addition Versus Single Addition of Saxagliptin or **Dapagliflozin** to Metformin. Diabetes Care. 2014 Oct 28.
Rosenstock J, Jelaska A, Frappin G, et al. Improved Glucose Control With Weight Loss, Lower Insulin Doses, and No Increased Hypoglycemia With **Empagliflozin** Added to Titrated Multiple Daily Injections of Insulin in Obese Inadequately Controlled Type 2 Diabetes. Diabetes Care. 2014 Jun 14.
Rosenstock J, Kahn SE, Johansen OE, et al; CAROLINA Investigators. Effect of **linagliptin vs glimepiride** on major adverse cardiovascular outcomes in patients with type 2 diabetes: the CAROLINA randomized clinical trial [published September 19, 2019]. JAMA. doi:10.1001/jama.2019.13772
Rosenstock J, Perkovic V, Johansen OE, et al; CARMELINA Investigators. Effect of **Linagliptin vs Placebo** on Major Cardiovascular Events in Adults With Type 2 Diabetes and High Cardiovascular and Renal Risk: The CARMELINA Randomized Clinical Trial. JAMA. 2018 Nov 9.
Rosenstock J, Raccah D, Koranyi L, et al. Efficacy and Safety of **Lixisenatide** Once Daily Versus Exenatide Twice Daily in Type 2 Diabetes Inadequately Controlled on Metformin: A 24-Week, Randomized, Open-Label, Active-Controlled Study (GetGoal-X). Diabetes Care. 2013 May 22.
Rosenstock J, Rood J, Cobitz A, Biswas N, Chou H, Garber A. Initial treatment with rosiglitazone/metformin fixed-dose combination therapy compared with monotherapy with either rosiglitazone or metformin in patients with uncontrolled type 2 diabetes. Diabetes Obes Metab. 2006 Nov;8(6):650-60.
Rosenstock J, Seman LJ, Jelaska A, et al. Efficacy and safety of **empagliflozin**, a sodium glucose cotransporter 2 (SGLT2) inhibitor, as add-on to metformin in type 2 diabetes with mild hyperglycaemia. Diabetes Obes Metab. 2013 Aug 1.
Rosenstock J, Wilson C, Fleck P. **Alogliptin versus glipizide** monotherapy in elderly type 2 diabetes mellitus patients with mild hyperglycaemia: a prospective, double-blind, randomized, 1-year study. Diabetes Obes Metab. 2013 Mar 26.
Rosenzweig JL, Bakris GL, Berglund LF, et al. Primary **Prevention of ASCVD and T2DM** in Patients at Metabolic Risk: An Endocrine Society* Clinical Practice Guideline. J Clin Endocrinol Metab. 2019 Jul 31.
Ross R, Hudson R, Stotz PJ, Lam M. Effects of **exercise amount and intensity** on abdominal obesity and **glucose tolerance** in obese adults. A randomized trial. Ann Intern Med. 2015;162:325-34.
Roumie CL, Chipman J, Min JY, et al. Association of Treatment With **Metformin vs Sulfonylurea** With Major Adverse Cardiovascular Events Among Patients With Diabetes and Reduced Kidney Function. JAMA. 2019 Sep 19:1-11.
Roumie CL, Greevy RA, Grijalva CG, et al. Association between **intensification of metformin treatment with insulin vs sulfonylureas** and cardiovascular events and all-cause mortality among patients with diabetes. JAMA. doi:10.1001/jama.2014.4312.
Roumie CL, Hung AM, Greevy RA, Grijalva CG, Liu X, Murff HJ, et al. Comparative effectiveness of **sulfonylurea and metformin monotherapy on cardiovascular events** in type 2 diabetes mellitus. A cohort study. Ann Intern Med. 2012;157:601-10.
Roumie CL, Min JY, Greevy RA, et al. Risk of **hypoglycemia** following intensification of **metformin treatment with insulin versus sulfonylurea**. CMAJ. 2016 Jan 25.
Rousan TA, Pappy RM, Chen AY, et al. Impact of Diabetes Mellitus on Clinical Characteristics, Management, and In-hospital Outcomes in Patients With Acute **Myocardial Infarction (from the NCDR**). Am J Cardiol. 2014 Jul 30.

Roussel R, d'Emden MC, Fisher M, et al. Glycaemic control and hypoglycaemia in people with type 2 diabetes **switching** from twice-daily basal insulin to once-daily **insulin glargine 300 U/mL or insulin glargine 100 U/mL** (**EDITION 1** and **EDITION 2** subgroup analysis). Diabetes Obes Metab. 2017 Jul 24.

Roussel R, Duran Garcia S, Zhang Y, et al. Double-blind, **randomized clinical trial comparing the efficacy and safety of continuing or discontinuing the dipeptidyl peptidase-4 inhibitor sitagliptin when initiating insulin glargine therapy in patients with type 2 diabetes**: The **CompoSIT-I** Study. Diabetes Obes Metab. 2018 Nov 4.

Roussel Ronan; Travert Florence; Pasquet Blandine; et al.; for the Reduction of Atherothrombosis for Continued Health (REACH) Registry Investigators. **Metformin Use and Mortality** Among Patients With Diabetes and Atherothrombosis. Arch Intern Med. 2010;170(21):1892-1899.

Roustit M, Blondel E, Villier C, Fonrose X, Mallaret MP. Symptomatic hypoglycemia associated with **trimethoprim/sulfamethoxazole and repaglinide** in a diabetic patient. Ann Pharmacother 44 (4): 764-7, 2010.

Rowan JA, Rush EC, Obolonkin V, Battin M, Wouldes T, Hague WM. **Metformin in Gestational Diabetes**: The Offspring Follow-Up (**MiG TOFU**): Body composition at 2 years of age. Diabetes Care. 2011 Oct;34(10):2279-84.

Rowan JA, Rush EC, Plank LD, et al. **Metformin in gestational diabetes**: the offspring follow-up (MiG TOFU): body composition and metabolic outcomes at 7-9 years of age. BMJ Open Diabetes Res Care. 2018 Apr 13;6(1):e000456.

Roy MS, Affouf M. Six-year progression of **retinopathy** and associated risk factors in African american patients with type 1 diabetes mellitus: the new jersey 725. Arch Ophthalmol. 2006 Sep;124(9):1297-306.

Roze S, Smith-Palmer J, Valentine W, et al. **Cost-effectiveness of continuous subcutaneous insulin infusion** versus **multiple daily injections** of insulin in Type 1 diabetes: a systematic review. Diabet Med. 2015 Nov;32(11):1415-24.

Ruan Y, Bally L, Thabit H, et al. **Hypoglycaemia incidence** and recovery during home use of **hybrid closed-loop insulin delivery** in adults with type 1 diabetes. Diabetes Obes Metab. 2018 Mar 25.

Rubin DM, Kreider AR, Matone M, et al. **Risk for Incident Diabetes** Mellitus Following Initiation of **Second-Generation Antipsychotics** Among Medicaid-Enrolled Youths. JAMA Pediatr. 2015 Apr 6

Rubin KH, Glintborg D, Nybo M, et al. Development and Risk Factors of **Type 2 Diabetes in a Nationwide Population of Women With PolycysticOvary Syndrome**. J ClinEndocrinolMetab. 2017 Oct 1;102(10):3848-3857

Rubino F, Nathan DM, Eckel RH, et al; Delegates of the Second Diabetes Surgery Summit. **Metabolic surgery in the treatment algorithm for type 2 diabetes**: a joint statement by international diabetes organizations. Diabetes Care. 2016;39(6): 861-877.

Rudnicka AR, Nightingale CM, Donin AS, et al. Sleep Duration and Risk of Type 2 Diabetes. Pediatrics. 2017;140(3):e20170338

Ruiter R et al. **Lower risk of cancer in patients on metformin** in comparison with those on sulfonylurea derivatives: Results from a large population-based follow-up study. Diabetes Care 2012 Jan; 35:119.

Ruospo M, Saglimbene VM, Palmer SC, et al. **Glucose targets for preventing diabetic kidney disease and its progression**. Cochrane Database Syst Rev. 2017 Jun 8;6:CD010137. This review suggests that people who receive intensive glycaemic control for treatment of diabetes had comparable risks of kidney failure, death and major cardiovascular events as people who received less stringent blood glucose control, while experiencing small clinical benefits on the onset and progression of microalbuminuria and myocardial infarction. The adverse effects of glycaemic management are uncertain. Based on absolute treatment effects, the clinical impact of targeting an HbA1c < 7% or blood glucose < 6.6 mmol/L is unclear and the potential harms of this treatment approach are largely unmeasured.

Rushakoff RJ, Sullivan MM, MacMaster HW, et al. Association between a **virtual glucose management service and glycemic control** in hospitalized adult patients. An observational study. Ann Intern Med. 2017;166:621-7. doi:10.7326 /M16-1413

Russell-Jones D, Cuddihy RM, Hanefeld M, et al. **DURATION-4** Study Group. Efficacy and safety of **exenatide once weekly** versus metformin, pioglitazone, and sitagliptin used as monotherapy in drug-naive patients with type 2 diabetes (DURATION-4): a 26-week double-blind study. Diabetes Care. 2012 Feb;35(2):252-8.

Russell-Jones D, et al. **Fast-Acting Insulin Aspart** Improves Glycemic Control in Basal-Bolus Treatment for Type 1 Diabetes: a 26-Week Multicenter, Active-Controlled, Treat-to-Target, Randomized, Parallel-Group Trial (Onset 1). Diabetes Care. 2017 Mar 29.

Russell SJ, El-Khatib FH, Sinha M, et al. Outpatient Glycemic Control with a **Bionic Pancreas** in Type 1 Diabetes. N Engl J Med. 2014 Jun 15.

Ryden L, Grant PJ, Anker SD, et al. **ESC Guidelines on diabetes, pre-diabetes, and cardiovascular diseases** developed in collaboration with the EASD: Summary. Eur Heart J 2013

Rydén L, Shahim B, Mellbin L. Clinical Implications of **Cardiovascular Outcome Trials** in Type 2 Diabetes: From **DCCT** to **EMPA-REG**. Clin Ther. 2016 Apr 20

Ryu SY, Coutu JP, Rosas HD, et al. Effects of insulin resistance on **white matter microstructure** in middle-aged and older adults. Neurology. 2014 May 27;82(21):1862-70.

Sabanayagam C, Banu R, Chee ML, et al. Incidence and progression of **diabetic retinopathy**: a systematic review. Lancet Diabetes Endocrinol. 2018 Jul 10.

Sabin MA, Magnussen CG, Juonala M, et al. **Insulin and BMI** as Predictors of Adult Type 2 Diabetes Mellitus. Pediatrics. 2015 Jan;135(1):e144-51.

Sacks DB, JohnWG. **Interpretation of hemoglobin A1C** values. JAMA. doi:10.1001 /jama.2014.6342.

Saenz A, Fernandez-Esteban I, Mataix A, et al. Metformin monotherapy for type 2 diabetes mellitus. **Cochrane** Database Syst Rev. 2005 Jul 20;(3):CD002966. CONCLUSIONS: Metformin may be the first therapeutic option in the diabetes mellitus type 2 with overweight or obesity, as it may prevent some vascular complications, and mortality. Metformin produces beneficial changes in glycaemia control, and moderated in weight, lipids, insulinaemia and diastolic blood pressure. Sulphonylureas, alpha-glucosidase inhibitors, thiazolidinediones, meglitinides, insulin, and diet fail to show more benefit for glycaemia control, body weight, or lipids, than metformin.

Safford MM. **Comparative effectiveness** research and outcomes of diabetes treatment. JAMA. doi:10.1001/jama.2014.4313.

Saito M, Kaibara A, Kadokura T, et al. Pharmacokinetic and Pharmacodynamic Modeling for **Renal Function Dependent Urinary Glucose Excretion Effect of Ipragliflozin**, a Selective Sodium Glucose Cotransporter 2 (SGLT2) Inhibitor, Both in Healthy Subjects and Patients with Type 2 Diabetes Mellitus. Br J Clin Pharmacol. 2019 Apr 26.

Saito T, Watanabe M, Nishida J, et al; **Zensharen Study** for Prevention of Lifestyle Diseases Group. **Lifestyle modification and prevention** of type 2 diabetes in overweight Japanese with impaired fasting glucose levels: a randomized controlled trial. Arch Intern Med. 2011;171(15):1352-1360.

Saito Y, et al. **Low-Dose Aspirin for Primary Prevention** of Cardiovascular Events in Patients with Type 2 **Diabetes:10-year Follow-up (JPAD)** of a Randomized Controlled Trial. Circulation. 2016 Nov 15.

Salas-Salvadó. J, Bullo M, Babio N et al. Reduction in the incidence of type 2 diabetes with the **Mediterranean Diet**: Results of the PREDIMED-Reus Nutrition Intervention Randomized trial. Diabetes Care 2011;34:14–19.

Salas-Salvadó J, Bulló M, Estruch R, et al. Prevention of diabetes with **Mediterranean diets**: a subgroup analysis of a randomized trial. Ann Intern Med. 2014 Jan 7;160(1):1-10.

Sala-Vila A, Díaz-López A, et al. **Dietary Marine ω-3 Fatty Acids** and Incident Sight-Threatening **Retinopathy** in Middle-Aged and Older Individuals With Type 2 Diabetes: Prospective Investigation From the PREDIMED Trial. JAMA Ophthalmol. 2016 Aug 18.

Salehi M, Gastaldelli A, D'Alessio DA. Blockade of **glucagon-like peptide 1 receptor** corrects postprandial hypoglycemia after gastric bypass. Gastroenterology 2014;146:669–680.

Salpeter SR, Buckley NS, Kahn JA, Salpeter EE. Meta-analysis: **metformin** treatment in persons at **risk for diabetes mellitus**. Am J Med. 2008 Feb;121(2):149-157.e2. Using metformin to treat patients at risk for diabetes decreases their likelihood of developing diabetes over a 3-year period. Longer studies are needed to determine whether the likelihood of diabetes is truly decreased or simply delayed. We have no research to tell us whether, in the long run, patients live longer or live better if they are treated at this stage of (pre)diabetes. (LOE = 1a)

Salpeter SR, Greyber E, Pasternak GA, et al. Risk of fatal and nonfatal **lactic acidosis with metformin** use in type 2 diabetes mellitus. Cochrane Database Syst Rev. 2010 Jan 20;(1):CD002967. No evidence assoc. metformin with ↑lactic acidosis.

Salsali A, Kim G, Woerle HJ, et al. Cardiovascular safety of **empagliflozin** in patients with type 2 diabetes: a meta-analysis of data from randomized placebo-controlled trials. Diabetes Obes Metab. 2016 Jul 4.

Salvo F, Moore N, Arnaud M, et al. **Addition of dipeptidyl peptidase-4 inhibitors to sulphonylureas** and risk of **hypoglycaemia**: systematic review and meta-analysis. BMJ. 2016 May 3;353:i2231

Sanabria-Martínez G, García-Hermoso A, Poyatos-León R, et al. Effectiveness of **physical activity interventions** on preventing gestational diabetes mellitus and excessive maternal weight gain: a meta-analysis. BJOG. 2015 Jun 3.

Sandbæk A, Griffin SJ, Sharp SJ, et al. Effect of Early **Multifactorial Therapy Compared With Routine Care** on Microvascular Outcomes at 5 Years in People With Screen-Detected Diabetes: A Randomized Controlled Trial: The **ADDITION-Europe** Study. Diabetes Care. 2014 Jul;37(7):2015-23.

Sandbæk A, Griffin SJ, Sharp SJ, et al. Effect of Early Multifactorial Therapy Compared With Routine Care on Microvascular Outcomes at 5 Years in People With Screen-Detected Diabetes: A Randomized Controlled Trial: The ADDITION-Europe Study. Diabetes Care. 2014 Jul;37(7):2015-23.

Sano M. A new class of drugs for **heart failure: SGLT2 inhibitors** reduce sympathetic overactivity. J Cardiol. 2018 May;71(5):471-476.

Santamaria A, Alibrandi A, Di Benedetto A, et al. Clinical and metabolic outcomes in pregnant women at risk for gestational diabetes mellitus supplemented with myo-inositol: a secondary analysis from 3 RCTs. Am J Obstet Gynecol. 2018 Sep;219(3):300.e1-300.e6.

Santema KTB;Stoekenbroek RM; et al. **Hyperbaric Oxygen Therapy** in the **Treatment of Ischemic Lower Extremity Ulcers** in Patients With Diabetes: Results of the DAMO2CLES Multicenter Randomized Clinical Trial. Diabetes Care. 2017 Oct 26.

Santoro AB, Botton MR, Struchiner CJ, et al. Influence of **pharmacogenetic polymorphisms and demographic variables on metformin** pharmacokinetics in an admixed Brazilian cohort. Br J Clin Pharmacol. 2018 Jan 20.

Santos-Lozano JM, Rada M, Lapetra J, et al. Prevention of type 2 diabetes in prediabetic patients by using **functional olive oil enriched in oleanolic acid**: The PREDIABOLE study, a randomized controlled trial. Diabetes Obes Metab. 2019 Jul 31.

Sanyal, Arun J., Chalasani, Naga, Kowdley, Kris V., et al. the **NASH CRN, Pioglitazone**, Vitamin E, or Placebo for Nonalcoholic Steatohepatitis. N Engl J Med 2010 0: NEJMoa0907929.

Saremi A, Bahn GD, Reaven PD; Veterans Affairs Diabetes Trial (**VADT**). A Link Between **Hypoglycemia and Progression of Atherosclerosis in the Veterans Affairs Diabetes Trial (VADT).** Diabetes Care. 2016 Mar;39(3):448-54.

Satija A, Bhupathiraju SN, Rimm EB, et al. **Plant-Based Dietary Patterns** and Incidence of Type 2 Diabetes in US Men and Women: Results from Three Prospective Cohort Studies. PLoS Med. 2016 Jun 14;13(6):e1002039.

Sattar N, McConnachie A, Shaper AG, et al. Can **metabolic syndrome** usefully predict cardiovascular disease and diabetes? Outcome data from two prospective studies. Lancet. 2008 May 21. [Epub ahead of print] Metabolic syndrome and its components are associated with type 2 diabetes but have weak or no association with vascular risk in elderly populations, suggesting that attempts to define criteria that simultaneously predict risk for both cardiovascular disease and diabetes are unhelpful.

Sattar N, Preiss D, Murray HM, et al. **Statins** and risk of incident **diabetes**: a collaborative meta-analysis of randomised statin trials. *Lancet* 2010; DOI:10.1016/S0140-6736(09)61965-6.

Sattar N, McLaren J, Kristensen SL, et al. **SGLT2 Inhibition** and cardiovascular events: why did **EMPA-REG** Outcomes **surprise** and what were the likely **mechanisms**? Diabetologia. 2016 Apr 25.

Sattar N, McGuire DK. **Pathways to Cardiorenal Complications in Type 2 Diabetes Mellitus**: A Need to Rethink. Circulation. 2018 Jul 3;138(1):7-9.

Sattar N, Rawshani A, Franzén S, et al. **Age at Diagnosis of Type 2 Diabetes Mellitus and Associations With Cardiovascular and Mortality Risks** Findings From the Swedish National Diabetes Registry. Circulation. 2019 Apr 8.

Saudek CD, Derr RL, Kalyani RR. Assessing glycemia in diabetes using **self-monitoring** blood glucose and hemoglobin A1c. JAMA. 2006 Apr 12;295(14):1688-97.

Sauer WH, Cappola AR, Berlin JA, Kimmel SE. Insulin sensitizing pharmacotherapy for prevention of myocardial infarction in patients with diabetes mellitus. Am J Cardiol. 2006 Mar 1;97(5):651-4. Epub 2006 Jan 6.

Saulsberry WJ, Coleman CI, Mearns ES, et al. Comparative efficacy and safety of **antidiabetic drug regimens added to stable and inadequate metformin and thiazolidinedione** therapy in type 2 diabetes. Int J Clin Pract. 2015 Jul 28.

Sawatsky L, Halipchuk J, Wicklow B. **Type 2 diabetes in a four-year-old child**. CMAJ. 2017 Jul 4;189(26):E888-E890

Sawin G, Shaughnessy AF. **Glucose control in Hospitalized Patients**. American Family Pysician. May 1, 2010.

Sayers A, Thayer D, Harvey JN, et al. Evidence for a **persistent, major excess** in all cause **admissions to hospital in children with type-1 diabetes**: results from a large Welsh national matched community cohort study. BMJ Open. 2015 Apr13;5(4):e005644.

Schauer PR, Kashyap SR, Wolski K, et al. **Bariatric surgery versus intensive medical therapy** in obese patients with **diabetes**. N Engl J Med 2012. DOI: 10.1056/NEJMoa1200225.

Schauer PR, Bhatt DL, Kirwan JP, et al. **Bariatric Surgery versus Intensive Medical Therapy for Diabetes** -5-Year Outcomes. (**Stampede**) N Engl J Med. 2017 Feb 16;376(7):641-651.

Scheen AJ, Finet al. **RIO-Diabetes** Study Group. Efficacy and tolerability of **rimonabant** (20mg/d)in overweight or obese patients with type 2 diabetes: a randomised controlled study. Lancet. 2006 Nov 11;368(9548):1660-72. (n=1047 1yr) These data indicate that 20 mg/day rimonabant, in combination with diet and exercise, can produce a clinically meaningful reduction in bodyweight and improve HbA1c and a number of cardiovascular and metabolic risk factors in overweight or obese patients with type 2 diabetes inadequately controlled by metformin or sulphonylureas.

Scheen AJ. Series: Implications of the recent CVOTs in type 2 diabetes: Impact on guidelines: The endocrinologist point of view. Diabetes Res Clin Pract. 2019 May 18.

Schellenberg ES, Dryden DM, Vandermeer B, et al. Lifestyle Interventions for Patients With and at Risk for Type 2 Diabetes: A Systematic Review and Meta-analysis. Ann Intern Med. 2013 Oct 15;159(8):543-51.

Schenck S Jr, Niewerth M, Klotsche J, et al. **Comorbidity of type 1 diabetes mellitus in patients with juvenile idiopathic arthritis**. J Pediatr 2017;192:196-203.

Schernthaner G, Gross J, Rosenstock J, Guarisco M, et al. **Canagliflozin** Compared With **Sitagliptin** for Patients With Type 2 Diabetes Who Do Not Have Adequate Glycemic Control With Metformin Plus Sulfonylurea: A 52-week randomized trial. Diabetes Care. 2013 September;36(9):2508-15.

Schernthaner G, Schernthaner-Reiter MH, Schernthaner GH. **EMPA-REG** and Other Cardiovascular Outcome Trials of Glucose-lowering Agents: Implications for Future Treatment Strategies in Type 2 Diabetes Mellitus. Clin Ther. 2016 May 19.

Scherrer JF, Salas J, Norman SB, et al. Association Between Clinically Meaningful **Posttraumatic Stress Disorder Improvement and Risk of Type 2 Diabetes**. JAMA Psychiatry. 2019 Aug 21.

Schmid R, Vollenweider P, Bastardot F, et al. Validation of **7 Type 2 Diabetes Mellitus Risk Scores** in a Population-Based Cohort: CoLaus Study. Arch Intern Med. 2012 Jan 23;172(2):188-9.

Schmidt EM, Barnes J, Chen C, et al. **Patient and Health Care Factors** Associated With Long-term Diabetes Complications Among Adults With and Without Mental Health and Substance Use Disorders. JAMA Netw Open. 2019 Sep 4;2(9):e1912060.

Schmidt MI, Bracco PA, Yudkin JS, et al**. Intermediate hyperglycaemia to predict progression** to type 2 diabetes (ELSA-Brasil): an occupational cohort study in Brazil. Lancet Diabetes Endocrinol 2019; publishe Feb 2.

Schmidt S, Schelde B, Nørgaard K. Effects of **advanced carbohydrate counting** in patients with Type 1 diabetes: a systematic review. Diabet Med. 2014 Aug;31(8):886-96.

Schmidt CB, van Loon BJP, Vergouwen ACM, et al. Systematic review and meta-analysis of **psychological interventions in people with diabetes and elevated diabetes-distress**. Diabet Med. 2018 Jun 13.

Schoenborn NL, Crossnohere NL, Bridges JFP, et al**. Patient Perceptions of Diabetes Guideline Frameworks** for Individualizing Glycemic Targets. JAMA Intern Med. 2019 Sep 16.

Schoeps A, van Ewijk R, Kynast-Wolf G, et al.**Ramadan Exposure In Utero and Child Mortality** in Burkina Faso: Analysis of a Population-Based Cohort Including 41,025 Children. Am J Epidemiol. 2018 Oct 1;187(10):2085-2092.

Scholl JH, van Eekeren R, van Puijenbroek EP. Six cases of (severe) **hypoglycaemia associated with gabapentin** use in both diabetic and non diabetic patients. Br J Clin Pharmacol. 2014 Nov 11.

Schorr M, Hemmelgarn BR, Tonelli M, et al; for the Alberta Kidney Disease Network. Assessment of **serum creatinine and kidney function among incident metformin users**. CJD 2013;37:226-30.

Schramm TK, Gislason GH, Vaag A, et al. **Mortality and cardiovascular risk associated with different insulin secretagogues compared with metformin** in type 2 diabetes, with or without a previous myocardial infarction: a nationwide study. Eur Heart J. 2011 Aug;32(15):1900-8. Monotherapy with the most used ISs, including glimepiride, glibenclamide, glipizide, and tolbutamide, seems to be associated with increased mortality and cardiovascular risk compared with metformin. Gliclazide and repaglinide appear to be associated with a lower risk than other ISs.

Schwartz AV, et al. **Thiazolidinedione** use and **bone loss** in older diabetic adults. J Clin Endocrinol Metab. 2006 Sep;91(9):3349-54. Epub 2006 Apr 11.

*Schwartz AV, Vittinghoff E, Bauer DC, et al. Study of Osteoporotic Fractures (SOF) Research Group; Osteoporotic Fractures in Men (MrOS) Research Group; Health, Aging, and Body Composition (Health ABC) Research Group. Association of **BMD and FRAX score with risk of fracture** in older adults with type 2 diabetes. JAMA. 2011 Jun 1;305(21):2184-92.*

Schwarz PEH, Timpel P, Harst L, et al. **Blood Sugar Regulation for Cardiovascular Health Promotion and Disease Prevention**: JACC Health Promotion Series. J Am Coll Cardiol. 2018 Oct 9;72(15):1829-1844.

*Schwing W, Hustak L, Taylor HC. Paradoxical Severe Decrease in HDL Cholesterol Due to **Rosiglitazone-Fenofibrate** Interaction. Endocr Pract. 2010 Jan 9:1-17. [Epub ahead of print]*

Schwingshackl L, Missbach B, Dias S, et al. Impact of different training modalities on glycaemic control and blood lipids in patients with type 2 diabetes: a systematic review and network meta-analysis. Diabetologia. 2014 Jul 5.

Scirica BM, Braunwald E, Raz I, et al; for the **SAVOR-TIMI 53** Steering Committee and Investigators. **Heart Failure, Saxagliptin** and Diabetes Mellitus: Observations from the SAVOR - TIMI 53 Randomized Trial. Circulation. 2014 Sep 4.

Schwingshackl L, Missbach B, Dias S, et al. Impact of different training modalities on **glycaemic control and blood lipids** in patients with type 2 diabetes: a systematic review and network meta-analysis. Diabetologia. 2014 Jul 5.

Scirica BM, Bhatt DL, Braunwald E, et al. Saxagliptin and cardiovascular outcomes in patients with type 2 diabetes mellitus. (**Savor-Timi 53**) N Engl J Med 2013; DOI:10.1056/NEJMoa1307684. Available here.

Scirica BM, Bhatt DL, Braunwald E, et al. Prognostic Implications of **Biomarker Assessments** in Patients With Type 2 **Diabetes at High Cardiovascular Risk**: A Secondary Analysis of a Randomized Clinical Trial. JAMA Cardiol. 2016 Sep 28.

Scirica BM, Mosenzon O, Bhatt DL, et al. Cardiovascular Outcomes According to **Urinary Albumin and Kidney Disease** in Patients With Type 2 Diabetes at High Cardiovascular Risk: Observations From the **SAVOR-TIMI 53** Trial. JAMA Cardiol. 2017 Dec 6.

Scott LJ. Exenatide extended-release (Bydureon) : a review of its use in type 2 diabetes mellitus. Drugs. 2012 Aug 20;72(12):1679-707.

Scott DA, Boye KS, Timlin L, et al. A network meta-analysis to compare glycaemic control in patients with type 2 diabetes treated with exenatide once weekly or liraglutide once daily in comparison with insulin glargine, exenatide twice daily or placebo. Diabetes Obes Metab. 2013 Mar;15(3):213-23.

Scott R, Morgan J, Zimmer Z, et al. A **randomized clinical trial of the efficacy and safety of sitagliptin compared with dapagliflozin** in patients with type 2 diabetes mellitus and mild renal insufficiency: The CompoSIT-R study. Diabetes Obes Metab. 2018 Dec;20(12):2876-2884.

Seaquist ER, Anderson J, Childs B, et al. **Hypoglycemia and diabetes**: a report of a workgroup of the American Diabetes Association (**ADA**) and the Endocrine Society. Diabetes Care. 2013 May;36(5):1384-95.

Seaquist ER. Addressing the **burden of diabetes**. JAMA. doi:10.1001/jama.2014.6451.

Segar MW, Vaduganathan M, Patel KV, et al. Machine Learning to Predict the **Risk of Incident Heart Failure Hospitalization Among Patients With Diabetes**: The WATCH-DM Risk Score. Diabetes Care. 2019 Sep 13.

Seidu S, Achana FA, Gray LJ, et al. Effects of **glucose-lowering** and multifactorial interventions on **cardiovascular and mortality outcomes**: a meta-analysis of randomized control trials. Diabet Med. 2016 Mar;33(3):280-9.

Seino Y, et al. Efficacy and safety of **alogliptin** added to metformin in Japanese patients with type 2 diabetes: a randomized, double-blind, placebo-controlled trial with an open-label, long-term extension study. Diabetes Obes Metab. 2012 Oct;14(10):927-36.

Selph S, Dana T, Blazina I, et al. **Screening** for Type 2 **Diabetes** Mellitus: A Systematic Review for the U.S. Preventive Services Task Force (**USPSTF**). Ann Intern Med. 2015 Apr 14.

*Selva Olid A, Sola I, Barajas-Nava LA, et al. **Systemic antibiotics for treating diabetic foot infections**. Cochrane Database Syst Rev. 2015 Sep 4;9:CD009061.* The evidence for the relative effects of different systemic antibiotics for the treatment of foot infections in diabetes is very heterogeneous and generally at unclear or high risk of bias. Consequently it is not clear if any one systemic antibiotic treatment is better than others in resolving infection or in terms of safety. One non-inferiority trial suggested that ertapenem with or without vancomycin is more effective in achieving clinical resolution of infection than tigecycline. Otherwise the relative effects of different antibiotics are unclear. The quality of the evidence is low due to limitations in the design of the included trials and important differences between them in terms of the diversity of antibiotics assessed, duration of treatments, and time points at which outcomes were assessed. Any further studies in this area should have a blinded assessment of outcomes, use standardised criteria to classify severity of infection, define clear outcome measures, and establish the duration of treatment.

Selvin E, Coresh J, Golden SH, et al. Glycemic control and coronary heart disease risk in persons with and without diabetes: the atherosclerosis risk in communities study. Arch Intern Med. 2005 Sep 12;165(16):1910-6.

Selvin E, Bolen S, Yeh HC, et al.. Cardiovascular outcomes in trials of oral diabetes medications: a systematic review. Arch Intern Med. 2008 Oct 27;168(19):2070-80. Meta-analysis suggested that, compared with other oral diabetes agents and placebo, **metformin was moderately protective and rosiglitazone possibly harmful**, but lack of power prohibited firmer conclusions.

Selvin, Elizabeth, Steffes, Michael W., Zhu, Hong, et al. **Glycated Hemoglobin** (A1c), Diabetes, and Cardiovascular Risk in Nondiabetic Adults. (ARIC study) N Engl J Med 2010 362: 800-811.

Selvin E, Steffes MW, Gregg E, et al. Performance of **A1C for the classification and prediction of diabetes**. Diabetes Care. 2011 Jan;34(1):84-9.

Selvin E, Parrinello CM, Sacks DB, Coresh J. Trends in **prevalence and control of diabetes** in the United States, 1988–1994 and 1999–2010. Ann Intern Med. 2014;160:517-25.

Selvin E, Wang D, Lee AK, et al. **Identifying trends in undiagnosed diabetes** in U.S. adults by using a confirmatory definition. Ann Intern Med. 2017. [Epub ahead of print]. doi:10 .7326/M17-1272

Selvin E, Wang D, Matsushita K, et al. **Prognostic implications of single-sample confirmatory testing for undiagnosed diabetes**. A prospective cohort study. Ann Intern Med. 2018. [Epub ahead of print]. doi:10.7326/M18-0091

Sen Gupta P, Green AN, Chowdhury TA. **Hypoglycaemia**. BMJ. 2011 Feb 16;342:d567. doi: 10.1136/bmj.d567.

Sénat M-V, Affres H, et al; Groupe de Recherche en Obstétrique et Gynécologie (**GROG**). Effect of **glyburide vs subcutaneous insulin** on perinatal complications for women with **gestational diabetes**: a randomized clinical trial [online May 1, 2018]. JAMA. doi:10.1001/jama.2018.4072

Senniappan S, Alexandrescu S, Tatevian N, Shah et al. **Sirolimus** therapy in infants with severe hyperinsulinemic hypoglycemia. N Engl J Med. 2014 Mar 20;370(12):1131-7.

Senthinathan A, Kelly V, Dzingina M et al. **Hyperglycaemia** in acute coronary syndromes: summary of NICE guidance. BMJ. 2011 Oct 26;343:d6646.

Seong JM, Yee J, Gwak HS. **DPP-4 inhibitors lower the risk of autoimmune disease** in patients with type 2 diabetes mellitus: A nationwide population-based cohort study. Br J Clin Pharmacol. 2019 Apr 9.

Serwylo O, Friesen K, Falk J, et al. Opportunity Cost and Policy: A Utilization Review of **Self-Monitoring of Blood Glucose** in Manitoba, Canada. Clin Ther. 2016 Mar 2.

Setiawan VW, Stram DO, Porcel J, et al. **Pancreatic Cancer Following** Incident **Diabetes in African Americans and Latinos**: The Multiethnic Cohort. J Natl Cancer Inst. 2018 Jun 18.

Shah B, Berger JS, Amoroso NS, et al. **Periprocedural glycemic control** in patients with diabetes mellitus undergoing **coronary angiography** with possible percutaneous coronary intervention. Am J Cardiol. 2014 May 1;113(9):1474-80.

Shah HS, Gao H, Morieri ML, et al. **Genetic Predictors** of Cardiovascular **Mortality** During Intensive Glycemic Control in Type 2 Diabetes: Findings From the **ACCORD** Clinical Trial. Diabetes Care. 2016 Aug 15.

Shah HS, Morieri ML, Marcovina SM, et al. Modulation of **GLP-1 Levels by a Genetic Variant** That Regulates the Cardiovascular Effects of Intensive Glycemic Control in ACCORD. Diabetes Care. 2017 Nov 28.

Shah R. **Assessing the risk of diabetes**. BMJ. 2015 Sep 3;351:h4525.

Shah S, Baez EA, Felipe DL et al. **Advanced Glycation Endproducts** in Children with Diabetes. J Pediatr. 2013 Aug 3.

Shahi N, Tobe SW. Thresholds and Targets for Hypertension Management of Type 2 Diabetes Mellitus Remain at 130/80 mmHg: What's the Evidence? Can J Diabetes. 2017 Dec 20.

Shahraz S, Pittas AG, Saadati M, et al. Change in **Testing, Awareness of Hemoglobin A1c Result, and Glycemic Control in US Adults**, 2007-2014. JAMA. 2017 Nov 14;318(18):1825-1827.

Shai I, Schwarzfuchs D, Henkin Y, et al. Dietary Intervention Randomized Controlled Trial (DIRECT) Group. Weight loss with a low-carbohydrate, Mediterranean, or low-fat diet. N Engl J Med. 2008 Jul 17;359(3):229-41. Mediterranean and low-carbohydrate diets may be effective alternatives to low-fat diets. The more favorable effects on lipids (with the low-carbohydrate diet) and on glycemic control (with the Mediterranean diet) suggest that personal preferences and metabolic considerations might inform individualized tailoring of dietary interventions. (Elhayany A, Lustman A, Abel R, et al. A low carbohydrate Mediterranean diet improves cardiovascular risk factors and diabetes control among overweight patients with type 2 diabetes mellitus: a 1-year prospective randomized intervention study. Diabetes Obes Metab. 2010 Mar;12(3):204-9.)

Shan Z, Li Y, Zong G, et al. Rotating **night shift work and adherence to unhealthy lifestyle** in predicting risk of type 2 diabetes: results from two large US cohorts of female nurses. BMJ. 2018 Nov 21;363:k4641.

Shan Z, Ma H, Xie M, et al. **Sleep duration and risk of type 2 diabetes**: a meta-analysis of prospective studies. Diabetes Care. 2015 Mar;38(3):529-37.

Shang Y, Marseglia A, Fratiglioni L, et al. **Natural history of prediabetes** in older adults from a population-based longitudinal study. J Intern Med. 2019 Jun 4.

Shapiro AR. **FDA Approval of Nonadjunctive Use of Continuous Glucose Monitors** for Insulin Dosing: A Potentially Risky Decision. JAMA. 2017 Sep 14.

Sharma S, Kerry C, Atkins H, et al. The **Ipswich Touch Test**: a simple and novel method to screen patients with diabetes at home for increased risk of foot ulceration. Diabet Med. 2014 Sep;31(9):1100-3.

Sharma A, Kandlakunta H, Nagpal SJS, et al. Model to Determine Risk of **Pancreatic Cancer in Patients With New-Onset Diabetes**. Gastroenterology. 2018 Sep;155(3):730-739.e3.

Sharp SA, Rich SS, Wood AR, et al. Development and **Standardization of an Improved Type 1 Diabetes Genetic Risk Score for Use in Newborn Screening** and Incident Diagnosis. Diabetes Care. 2019 Feb;42(2):200-207.

Shaw JE, Punjabi NM, Naughton MT, et al. The Effect of Treatment of **Obstructive Sleep Apnea on Glycemic Control in Type 2 Diabetes**. Am J Respir Crit Care Med. 2016 Feb 29.

Shen HN, Yang CC, Chang YH, et al. Risk of **Diabetes Mellitus after First-Attack Acute Pancreatitis**: A National Population-Based Study. Am J Gastroenterol. 2015 Nov 3.

Shen L, Shah BR, Reyes EM, et al. Role of **diuretics, beta blockers, and statins** in increasing the risk of diabetes in patients with impaired glucose tolerance: reanalysis of data from the NAVIGATOR study. BMJ. 2013 Dec 9;347:f6745.

Sherifali D, Nerenberg K, Pullenayegum E, Cheng JE, Gerstein HC. The Effect of **Oral Antidiabetic Agents on Glycated Hemoglobin Levels**: A Systematic Review and Meta-Analysis. Diabetes Care. 2010 May 18.

Sherifali D, Greb JL, Amirthavasar G, et al. Effect of **computer-generated tailored feedback** on glycemic control in people with diabetes in the community: a randomized controlled trial. Diabetes Care. 2011 Aug;34(8):1794-8.

*Sherifali D, Bai JW, Kenny M, et al. **Diabetes self-management programmes** in older adults: a systematic review and meta-analysis. Diabet Med. 2015 Nov;32(11):1404-14.*

Sherr JL, Hermann JM, Campbell F, et al; T1D Exchange Clinic Network, the DPV Initiative, and the National Paediatric Diabetes Audit and the Royal College of Paediatrics and Child Health registries. Use of **insulin pump therapy** in children and adolescents with **type 1 diabetes** and its impact on metabolic control: comparison of results from three large, transatlantic paediatric registries. Diabetologia. 2015 Nov 7.

Sherry N, Hagopian W, Ludvigsson J, et al. for the Protégé Trial Investigators. **Teplizumab** for treatment of type 1 diabetes (Protégé study): 1-year results from a randomised, placebo-controlled trial. Lancet. 2011 Jun 28.

Sheth KN, Elm JJ, Molyneaux BJ, et al. Safety and efficacy of **intravenous glyburide** (RP-1127) on brain swelling after large hemispheric infarction: a phase 2 randomised, double-blind, placebo-controlled clinical trial. Lancet Neurol 2016; online 23.

Shih CJ, Chen HT, Kuo SC, et al. Comparative effectiveness of **angiotensin-converting-enzyme inhibitors and angiotensin II receptor blockers** in patients with type 2 diabetes and retinopathy. CMAJ. 2016 Mar 21.

Shin JI. Second-line **Glucose-Lowering Therapy in Type 2 Diabetes Mellitus**. Curr Diab Rep. 2019 Jul 8;19(8):54.

Shivaswamy V, Boerner B, Larsen J. **Post-transplant diabetes mellitus**: Causes, treatment, and impact on outcomes. Endocr Rev. 2015 Dec 9:er20151084.

Shojania KG, et al. Effects of **quality improvement strategies** for type 2 diabetes on glycemic control: a meta-regression analysis. JAMA. 2006 Jul 26;296(4):427-40.

Shurraw S, Hemmelgarn B, Lin M, et al; for the Alberta Kidney Disease Network. Association between **glycemic control and adverse outcomes** in people with diabetes mellitus and **chronic kidney disease**: a population-based cohort study. Arch Intern Med. 2011;171(21):1920-1927. {Lower A1C benefits renal function, but avoid A1Cs of <6.5%. e.g. U shaped curve for mortality (↑ mortality <6.5% & >9%)}

Shyangdan DS, Royle P, Clar C, et al. **Glucagon-like peptide analogues** (exenatide, liraglutide) for type 2 diabetes mellitus. Cochrane Database Syst Rev. 2011 Oct 5;10:CD006423. GLP-1 agonists are effective in improving glycaemic control.

Siafis S, Papazisis G. Detecting a potential **safety signal of antidepressants and type 2 diabetes: a pharmacovigilance-pharmacodynamic study**. Br J Clin Pharmacol. 2018 Jun 28.

Sieri S, Krogh V, Berrino F, et al. **Dietary glycemic load** and index and risk of coronary heart disease in a large italian cohort: the EPICOR study. Arch Intern Med. 2010 Apr 12;170(7):640-7.

SIGMA Type 2 Diabetes Consortium. Association of **a low-frequency variant in HNF1A** with type 2 diabetes in a Latino population. (SIGMA) JAMA. doi:10.1001/jama.2014.6511.

Sillars B, Davis WA, Hirsch IB, et al. **Sulphonylurea-metformin combination therapy**, cardiovascular disease and all-cause mortality: the Fremantle Diabetes Study. Diabetes Obes Metab. 2010 Sep;12(9):757-65.

Silverman RA, Thakker U, Ellman T, et al. **Hemoglobin A1c as a screen** for previously undiagnosed prediabetes and diabetes in an acute-care setting. Diabetes Care. 2011 Sep;34(9):1908-12.

Silverstein J, Klingensmith G, Copeland K, et al. Care of children and adolescents with type 1 diabetes: a statement of the American Diabetes Association. Diabetes Care 2005 Jan;28(1):186-212.

Simha V, Shah P. **Perioperative Glucose Control** in Patients With Diabetes Undergoing Elective Surgery. JAMA. 2019 Jan 7.

Simmons D, McElduff A, McIntyre HD, et al. **Gestational Diabetes Mellitus**: **NICE for the U.S**.? A Comparison of the American Diabetes Association and the American College of Obstetricians and Gynecologists Guidelines With the U.K. National Institute for Health and Clinical Excellence Guidelines: Response to Holt et al. Diabetes Care. 2010 Mar;33(3):e48.

Simmons RK, Echouff o-Tcheugui JB, Sharp SJ, et al. **Screening** for type 2 diabetes and population mortality over 10 years (**ADDITION-Cambridge**): a cluster-randomised controlled trial. Lancet 2012.

Simmons RK, Griffin SJ, Witte DR, et al. Effect of population **screening** for type 2 diabetes and **cardiovascular risk** factors on mortality rate and cardiovascular events: a controlled trial among 1,912,392 Danish adults. Diabetologia. 2017 Aug 23.

Simmons RK, Griffin SJ, Lauritzen T, et al. Effect of **screening** for type 2 diabetes on risk of **cardiovascular disease** and mortality: a controlled trial among 139,075 individuals diagnosed with diabetes in Denmark between 2001 and 2009. Diabetologia doi:10.1007/s00125-017-4299-y

Simmons RK, Sharp SJ, Sandbaek A, et al. Does early **intensive multifactorial treatment** reduce total cardiovascular burden in individuals with screen-detected diabetes? Findings from the ADDITION-Europe cluster-randomized trial. Diabet Med. 2012 Nov;29(11):e409-e416.

Simmons RK, Borch-Johnsen K, Lauritzen T, et al. A randomised trial of the effect and cost-effectiveness of early **intensive multifactorial therapy** on 5-year cardiovascular outcomes in individuals with screen-detected type 2 diabetes: the Anglo-Danish-Dutch Study of Intensive Treatment in People with Screen-Detected Diabetes in Primary Care (**ADDITION-Europe**) study. Health Technol Assess. 2016 Aug;20(64):1-86.

Simpson SH, Majumdar SR, Tsuyuki RT, Eurich DT, Johnson JA. Dose-response relation between **sulfonylurea drugs and mortality** in type 2 diabetes mellitus: a population-based cohort study. CMAJ. 2006 Jan 17;174(2):169-74. (Bell DS. Do sulfonylurea drugs increase the risk of cardiac events? CMAJ. 2006 Jan 17;174(2):185-6.) (Evans JM, et al. Risk of mortality and adverse cardiovascular outcomes in type 2 diabetes: a comparison of patients treated with sulfonylureas and metformin. Diabetologia. 2006 Mar 9; [Epub ahead of print])

Simpson SH, Gamble JM, Mereu L, et al. Effect of **aspirin** dose on mortality and cardiovascular events in people with **diabetes**: a meta-analysis. J Gen Intern Med. 2011 Nov;26(11):1336-44.

Simpson SH, Lee J, Choi S, et al. **Mortality risk among sulfonylureas**: a systematic review and network meta-analysis. Lancet Diabetes Endocrinol. 2015 Jan;3(1):43-51.

Simpson SH, Lin M, Eurich DT. **Medication Adherence** Affects Risk of New Diabetes Complications: A Cohort Study. Ann Pharmacother. 2016 Jun 15.

Simpson TC, Needleman I, Wild SH, Moles DR, Mills EJ. Treatment of **periodontal disease** for glycaemic control in people with diabetes. Cochrane Database Syst Rev. 2010 May 12;5:CD004714. There is some evidence of improvement in metabolic control in people with diabetes, after treating periodontal disease.

Sinclair AJ, Paolisso G, et al. European Diabetes Working Party for Older People. **European** Diabetes Working Party for **Older People 2011 clinical guidelines** for type 2 diabetes mellitus. Executive summary. Diabetes Metab. 2011 Nov;37 Suppl 3:S27-38.

Sinclair AJ, Bode B, Harris S, et al. Efficacy and Safety of **Canagliflozin** in Individuals **Aged 75 and Older** with Type 2 Diabetes Mellitus: A Pooled Analysis. J Am Geriatr Soc. 2016 Mar;64(3):543-52.

Singh S, Chang HY, et al. Glucagonlike Peptide 1-Based (sitagliptin, exenatide) Therapies & Risk of Hospitalization for Acute Pancreatitis in Type 2 Diabetes Mellitus: A Population-Based Matched Case-Control Study. JAMA Intern Med. 2013 Feb 25:1-6.

Singh S, Loke YK, Furberg CD. **Thiazolidinediones and Heart Failure**: A Teleo-Analysis.Diabetes Care. 2007 May 29; [Epub ahead of print] Our teleo-analysis confirms the increased magnitude of the risk of heart failure with thiazolidinediones. We estimate the Number-Needed-to-Harm with thiazolidinediones to be around 50 over 2.2 years.

Singh S, Singh PP, Singh AG, et al. Anti-Diabetic Medications and the Risk of Hepatocellular Cancer: A Systematic Review and Meta-Analysis. Am J Gastroenterol. 2013 Feb 5.

Singh S, Wright EE Jr, Kwan AY, et al. **Glucagon-like peptide-1 receptor agonists compared with basal insulins** for the treatment of type 2 diabetes mellitus: a systematic review and meta-analysis. Diabetes Obes Metab. 2016 Oct 7.

*Siraj ES, Rubin DJ, Riddle MC, et al; ACCORD Investigators. **Insulin Dose** and Cardiovascular Mortality in the **ACCORD** Trial. Diabetes Care. 2015 Nov;38(11):2000-8.*

Siskind D, Hahn M, Correll CU, et al. **Glucagon-like peptide-1 receptor agonists for antipsychotic-associated cardio-metabolic risk factors**: A systematic review and individual participant data meta-analysis. Diabetes Obes Metab. 2018 Sep 5.

*Siu AL. **Screening for Abnormal Blood Glucose and Type 2 Diabetes Mellitus**: U.S. Preventive Services Task Force Recommendation (**USPSTF**) Statement. Ann Intern Med. 2015 Oct 27.*

Sjostrom L, Peltonen M, Jacobson P, et al. Association of **bariatric surgery** with long-term remission of type 2 diabetes and with microvascular and macrovascular complications. JAMA. doi:10.1001/jama.2014.5988.

Skipper N, Gaulke A, Sildorf SM, et al. Association of Type 1 **Diabetes With Standardized Test Scores of Danish Schoolchildren**. JAMA. 2019 Feb 5;321(5):484-492.

Skovgaard R, Jon Ploug U, Hunt B, Valentine WJ. Evaluating the **Cost** of Bringing People with Type 2 Diabetes Mellitus to **Multiple Targets of Treatment in Canada**. Clin Ther. 2015 Aug 1;37(8):1677-88.

Skrtic S, Cabrera C, Olsson M, et al. Contemporary **risk estimates of three HbA(1c) variables** in relation to heart failure following diagnosis of type 2 diabetes. Heart. 2017 Mar;103(5):353-358.

Skyler JS, Bergenstal R, Bonow RO, Buse J, Deedwania P, Gale EA, Howard BV, Kirkman MS, Kosiborod M, Reaven P, Sherwin RS; American Diabetes Association; American College of Cardiology Foundation; American Heart Association. Intensive glycemic control and the prevention of cardiovascular events: implications of the **ACCORD, ADVANCE, and VADT diabetes trials**: a position statement of the American Diabetes Association and a scientific statement of the American College of Cardiology Foundation and the American Heart Association. Diabetes Care. 2009 Jan;32(1):187-92. Epub 2008 Dec 17.

Sluik D, Buijsse B, Muckelbauer R, et al. **Physical Activity** and Mortality in Individuals With Diabetes Mellitus: A Prospective Study and Meta-analysis. Arch Intern Med. 2012 Aug 6:1-11.

SMBG: Type 2 Diabetes and **Monitoring** your Blood Sugar –**Patient Pamphlet** . http://www.cadth.ca/media/pdf/smbg-nb_eng.pdf

Smetana GW, Nathan DM, Dugdale DC, Burns RB. To **What Target Hemoglobin A1c Level Would You Treat This Patient** With Type 2 Diabetes?: Grand Rounds Discussion From Beth Israel Deaconess Medical Center. Ann Intern Med. 2019 Oct 1;171(7):505-513.

Smith A, Harris C, **Type 1 Diabetes: Management** Strategies. Am Fam Physician. 2018;98(3):154-162.

Smith AD, Crippa A, Woodcock J, et al. **Physical activity and incident type 2 diabetes mellitus**: a systematic review and dose-response meta-analysis of prospective cohort studies. Diabetologia. 2016 Oct 17. Review.

Smith JD, Mills E, Carlisle SE. Treatment of **Pediatric Type 2 Diabetes**. Ann Pharmacother. 2016 Jun 15.

Smith NL, et al. **New-onset diabetes** and risk of all-cause and **cardiovascular mortality**: the Cardiovascular Health Study. Diabetes Care. 2006 Sep;29(9):2012-7. Our findings indicate that there may be a mortality differential soon after diabetes onset in older adults and suggest that long-term macrovascular damage from atherosclerosis may not be primarily responsible for increased risk.

Smith S M, Paul G, Kelly A, et al. **Peer support** for patients with type 2 diabetes: cluster randomised controlled trial. *BMJ 342:doi:10.1136/bmj.d715 (Published 15 February 2011)*

Smith-Strom H, Igland J, Ostbye T, et al. The Effect of **Telemedicine** Follow-up Care on Diabetes-Related **Foot Ulcers**: A Cluster Randomized Controlled Noninferiority Trial. Diabetes Care. 2017 Nov 29.

Smolders EJ, Colbers A, de Kanter CTMM, et al. **Metformin and daclatasvir**: absence of a pharmacokinetic-pharmacodynamic drug interaction in healthy volunteers. Br J Clin Pharmacol. 2017 May 5.

Snyder MJ, Gibbs LM, Lindsay TJ. Treating Painful **Diabetic Peripheral Neuropathy**: An Update. Am Fam Physician. 2016 Aug 1;94(3):227-34

Sodi R, McKay K, Dampetla S, Pappachan JM. Monitoring glycaemic control in patients with **diabetes mellitus**. BMJ. 2018 Nov 20;363:k4723.

Soedamah-Muthu SS, Vergouwe Y, Costacou T, et al. **Predicting major outcomes in type 1 diabetes**: a model development and validation study. Diabetologia. 2014 Sep 4.

Sofi F, Cesari F, Abbate R, Gensini GF, Casini A. Adherence to **Mediterranean diet** and health status: meta-analysis. BMJ 2008;337:a1344.

Solomon Daniel H., Massarotti Elena, Garg Rajesh, et al. Association Between **Disease-Modifying Antirheumatic Drugs and Diabetes Risk** in Patients With Rheumatoid Arthritis and Psoriasis. JAMA. 2011;305(24):2525-2531.

Solomon SD, Chew E, Duh EJ, et al. **Diabetic Retinopathy**: A Position Statement by the **American Diabetes Association**. Diabetes Care. 2017 Mar;40(3):412-418.

Son JW, Jang EH, Kim MK et al. Usefulness of **Albuminuria** as Predictor for Coronary Artery Stenosis, Regardless of Estimated Glomerular Filtration Rate, in Patients With Type 2 Diabetes Mellitus. Am J Cardiol. 2012 Aug 1.

Sosenko JM, Skyler JS, Mahon J, et al. **Validation of the Diabetes Prevention Trial-Type 1 Risk Score** in the TrialNet Natural History Study. Diabetes Care. 2011 Aug;34(8):1785-7.

Sorkin JD, et al.The relation of **fasting** & **2h postchallenge** plasma glucose concentrations to mortality:data from the Baltimore Longitudinal Study of Aging with a critical review of the literature. Diabetes Care.2005Nov;28(11):2626-32.
(InfoPOEMs: Higher fasting blood glucose levels or 2-hour postprandial blood glucose levels in middle-aged men are predictive of subsequent mortality. However, that doesn't necessarily mean that lowering their blood glucose with therapy reduces that mortality; this was not demonstrated in the United Kingdom Prospective Diabetes Study (UK Prospective Diabetes Study [UKPDS] Group. Lancet 1998;352:837-53). (LOE = 1b))

Sorli CH, Harashima S-i, Tsoukas GM, et al. Efficacy and safety of once-weekly **semaglutide** monotherapy versus placebo in patients with type 2 diabetes (**SUSTAIN 1**): a double-blind, randomised, placebocontrolled, parallel-group, multinational, multicentre, phase 3a trial. Lancet Diabetes Endocrinol 2017; online Jan 16.

Soylemez Wiener R, Wiener DC, Larson RJ. Benefits and risks of tight glucose control in **critically ill** adults: a meta-analysis. JAMA. 2008 Aug 27;300(8):933-44. In critically ill adult patients, tight glucose control is not associated with significantly reduced hospital mortality but is associated with an increased risk of **hypoglycemia**.

Spanakis EK, Umpierrez GE, Siddiqui T, et al. "Association of **glucose concentrations at hospital discharge with readmissions and mortality**: A nationwide cohort study." J Clin Endocrinol Metab. 2019 May 1.

Spanopoulos D, Barrett B, Busse M, et al. Prescription of **DPP-4 Inhibitors** to Type 2 Diabetes Mellitus Patients **With Renal Impairment**: A UK Primary Care Experience. Clin Ther. 2017 Dec 12.

Spaulonci CP, Bernardes LS, Trindade TC, et al. Randomized trial of **metformin vs insulin in the management of gestational** diabetes. Am J Obstet Gynecol. 2013 Jul;209(1):34.e1-34.e7.

Spence JD, Viscoli CM, Inzucchi SE, et al; IRIS Investigators. **Pioglitazone therapy in patients with stroke and prediabetes**: a post hoc analysis of the IRIS randomized clinical trial [online Feb 7, 2019]. JAMA Neurol. doi:10.1001/jamaneurol.2019.0079

Sperl-Hillen J, Beaton S, Fernandes O, et al. Comparative effectiveness of **patient education methods** for type 2 diabetes: a randomized controlled trial [published online October 10, 2011]. Arch Intern Med. doi:10.1001/archinternmed .2011.507.

Springer SC, Silverstein J, Copeland K, et al. Management of **Type 2 Diabetes Mellitus in Children and Adolescents**. Pediatrics. 2013 Jan 28.

Srinivasan S, et al. Randomized, controlled trial of metformin for obesity & insulin resistance in children & adolescents: improvement in body composition and fasting insulin. J Clin Endocrinol Metab. 2006 Jun;91(6):2074-80. Epub 2006 Apr 4. (InfoPOEMs: For obese 9- to 18-year-olds, metformin (1g twice daily) resulted in a mean weight loss of approximately 10 pounds at the end of 6 months of treatment. Larger and longer studies are needed to support the effectiveness and safety of this regimen. (LOE = 1b-))

Staels B. **Cardiovascular Protection by Sodium Glucose Cotransporter 2 Inhibitors**: Potential Mechanisms. Am J Cardiol. 2017 Jul 1;120(1S):S28-S36.

Stage TB, Pedersen RS, Damkier P, et al. Intake of **St. John's wort improves the glucose tolerance** in healthy subjects that ingest metformin compared to metformin alone. Br J Clin Pharmacol. 2014 Sep 16.

Stanek KR, Youngkin EM, Pyle LL, et al. Prevalence, Characteristics and Diabetes **Management in Children with Comorbid Autism Spectrum Disorder and Type 1 Diabetes**. Pediatr Diabetes. 2019 Mar 26.

Stankiewicz M, Norman R. Diagnosis and management of **polycystic ovary syndrome**: a practical guide. Drugs. 2006;66(7):903-12.

Steenkamp DW, Alexanian SM, Sternthal E. Approach to the patient with **atypical diabetes**. CMAJ. 2014 Jun 10;186(9):678-684.

Stefani M, Roberts DM. Complex decisions in the use of extracorporeal treatments in **acute metformin overdose**: which modality, when and how to measure the effect. Br J Clin Pharmacol. 2018 Sep 8.

Steinberg WM, Rosenstock J, Wadden TA, et al. Impact of **Liraglutide** on Amylase, Lipase, and Acute Pancreatitis in Participants With Overweight/Obesity and Normoglycemia, Prediabetes, or Type 2 Diabetes: Secondary Analyses of Pooled Data From the **SCALE** Clinical Development Program. Diabetes Care. 2017 May 4.

Steineck I, Cederholm J, Eliasson B, et al; Swedish National Diabetes Register. **Insulin pump therapy, multiple daily injections, and cardiovascular mortality** in 18 168 people with type 1 diabetes: observational study. BMJ. 2015 Jun 22;350:h3234.

Stenlof K, Cefalu WT, Kim KA, et al. Efficacy and safety of **canagliflozin** monotherapy in subjects with type 2 diabetes mellitus inadequately controlled with diet and exercise. Diabetes Obes Metab. 2013 Apr;15(4):372-82.

Stephens NA, Sparks LM. Resistance to the Beneficial Effects of **Exercise** in Type 2 Diabetes: Are Some Individuals Programmed to Fail? J Clin Endocrinol Metab. 2014 Nov 20:jc20142545.

Stern RJ, Murphy EJ. **Metformin** as Initial Oral Therapy in Type 2 Diabetes. JAMA. 2015 Jun 23-30;313(24):2484-5.

Steven S, Hollingsworth KG, Al-Mrabeh A, et al. **Very-Low-Calorie Diet and 6 Months of Weight Stability** in Type 2 Diabetes: Pathophysiologic Changes in Responders and Nonresponders. Diabetes Care. 2016 Mar 21.

Stevens RJ, Ali R, Bankhead CR, et al. **Cancer outcomes** and all-cause mortality in adults allocated to **metformin**: systematic review and collaborative meta-analysis of randomised clinical trials. Diabetologia. 2012 Oct;55(10):2593-603.

Stewart ZA, Wilinska ME, Hartnell S, et al. **Closed-Loop Insulin Delivery during Pregnancy** in Women with Type 1 Diabetes. N Engl J Med. 2016 Aug 18;375(7):644-54

Stokes A, Preston SH. **Deaths Attributable to Diabetes in the United States**:Comparison of Data Sources and Estimation Approaches. PLoS One. 2017 Jan 25;12(1):e0170219.

Stokes A, Collins JM, Grant BF, et al. Obesity Progression Between **Young Adulthood and Midlife and Incident Diabetes**: A Retrospective Cohort Study of U.S. Adults. Diabetes Care. 2018 May;41(5):1025-1031.

Stone MA, Camosso-Stefinovic J, Wilkinson J, de Lusignan S, Hattersley A, Khunti K. **Incorrect and incomplete coding and classification of diabetes**: a systematic review. Diabet Med 2010;27:491-7.

Strain WD, Hope SV, Green A, et al. **Type 2 diabetes mellitus in older people**: a brief statement of key principles of modern day management including the assessment of frailty. A national collaborative stakeholder initiative. Diabet Med. 2018 Apr 7.

Strain WD, Lukashevich V, et al. Individualised treatment targets for **elderly** patients with type 2 diabetes using **vildagliptin** add-on or lone therapy (INTERVAL): a 24 week, randomised, double-blind, placebo-controlled study. Lancet 2013; online May 23.

Strauss SM, Rosedale MT, Pesce MA, et al. The Potential for **Glycemic Control Monitoring and Screening** for Diabetes at **Dental Visits** Using Oral Blood. Am J Public Health. 2015 Feb 25:e1-e6.

Stringhini S, Tabak AG, Akbaraly TN, et al. Contribution of **modifiable risk factors** to social inequalities in type 2 diabetes: prospective Whitehall II cohort study. BMJ. 2012 Aug 21;345:e5452.

Strippoli GF, Craig MC, Schena FP, Craig JC. Role of blood pressure targets and specific antihypertensive agents used to prevent **diabetic nephropathy** and delay its progression. J Am Soc Nephrol. 2006 Apr;17 Suppl 2:S153-5. On the basis of available RCT evidence, ACEi are the only agents with proven renal benefit in patients who have diabetes with no nephropathy and the only agents with proven survival benefit in patients who have diabetes with nephropathy.

Strong WB, Malina RM, Blimkie CJ, et al. Evidence based **physical activity** for school-age **youth**. J Pediatr. 2005 Jun;146(6):732-7. (InfoPOEMs: Children should participate in at least 60 minutes of moderate to vigorous physical activity every day to avoid obesity and improve lipid levels and blood pressure. Encourage parents to turn off their child's television and find activities for them that are developmentally appropriate and fun. (LOE = 1a))

Strongman H, D`Oca K, Langerman H, et al. Comparison of diabetes-associated secondary healthcare utilization between alternative oral **antihyperglycaemic dual therapy combinations** with metformin in patients with type 2 diabetes: an observational cohort study. Diabetes Obes Metab. 2015 Jun;17(6):573-80.

Stranges S, Marshall JR, Natarajan R, et al. Effects of Long-Term Selenium 200ug daily Supplementation on the Incidence of Type 2 Diabetes: A Randomized Trial. Ann Intern Med. 2007 Jul 9; [Epub ahead of print]
Selenium supplementation does not seem to prevent type 2 diabetes, and it may increase risk for the disease. (but this was a secondary analysis of the Nutritional Prevention of Cancer- NPC trial)

Strich D, Balagour L, Shenker J, et al. **Lower Basal Insulin Dose is Associated with Better Control** in Type 1 Diabetes. J Pediatr. 2016 Dec 12.

Strychar I. **Diet** in the management of weight loss. CMAJ. 2006 Jan 3;174(1):56-63.

Sturmer T, Marquis MA, Zhou H, et al. **Cancer** Incidence Among Those Initiating Insulin Therapy With **Glargine Versus Human NPH** Insulin. Diabetes Care. 2013 Jul 22.

Suissa S. **Mortality Reduction in EMPA-REG** OUTCOME Trial: Beyond the Antidiabetes Effect. Diabetes Care. 2018 Feb;41(2):219-223.

Sumarsono A, Everett BM, McGuire DK, et al. Trends in **Aggregate Use and Associated Expenditures of Antihyperglycemic Therapies** Among US Medicare Beneficiaries Between 2012 and 2017. JAMA Intern Med. 2019 Sep 30. doi: 10.1001/jamainternmed.2019.3884.

Sumner AE, Duong MT, Aldana PC, et al. **A1C Combined** With **Glycated Albumin** Improves Detection of **Prediabetes in Africans**: The Africans in America Study. Diabetes Care. 2015 Dec 17.

Sun F, Wu S, Wang J, et al. Effect of **Glucagon-Like Peptide-1 Receptor Agonists on Lipid Profiles** Among Type 2 Diabetes: A Systematic Review and Network Meta-Analysis. Clin Ther. 2014 Dec 29.

Sun JK, Keenan HA, Cavallerano JD, et al. Protection from **retinopathy** and other complications in patients with type 1 diabetes of extreme duration: the **joslin 50-year medalist study**. Diabetes Care. 2011 Apr;34(4):968-74.

Sun L, Xie C, Wang G, et al. **Gut microbiota and intestinal FXR mediate the clinical benefits of metformin**. Nat Med. 2018 Nov 5.

Sun Qi; Spiegelman Donna; van Dam Rob M.; Miet al. White Rice, **Brown Rice**, and Risk of Type 2 Diabetes in US Men and Women. Arch Intern Med. 2010;170(11):961-969.

Sundelin EIO, Gormsen LC, Heebøll S, et al. **Hepatic exposure of metformin** in patients with non-alcoholic fatty liver disease. Br J Clin Pharmacol. 2019 Apr 11

Sundstrom J, et al. Clinical value of the **metabolic syndrome** for long term prediction of total and cardiovascular mortality: prospective, population based cohort study. BMJ. 2006 Apr 15;332(7546):878-82. Epub 2006 Mar 1.

Sussman JB, Kent DM, Nelson JP, Hayward RA. Improving diabetes prevention with benefit based **tailored treatment**: risk based reanalysis of Diabetes Prevention Program. BMJ. 2015 Feb 19;350:h454.

*Sussman JB, Kerr EA, Saini SD, et al. **Rates of deintensification of blood pressure and glycemic medication** treatment based on levels of control and life expectancy in older patients with diabetes mellitus [online October 26, 2015]. JAMA Intern Med. doi:10.1001/jamainternmed.2015.5110*

Svedbo Engström M, Leksell J, Johansson UB, et al. What is important for you? A qualitative interview study of living with diabetes and experiences of diabetes care to establish a basis for a **tailored Patient-Reported Outcome** Measure for the Swedish National Diabetes Register. BMJ Open. 2016 Mar 24;6(3):e010249.

Svensson E, Baggesen LM, Johnsen SP, et al. Early Glycemic Control and Magnitude of **HbA(1c) Reduction Predict Cardiovascular Events and Mortality**: Population-Based Cohort Study of 24,752 Metformin Initiators. Diabetes Care. 2017 Apr 12.

Swoboda PP, Plein S. **Heart failure in Diabetic patients.** Eur Heart J. 2018 May 21;39(20):1755-1757

Syngelaki A, Nicolaides KH, Balani J, et al. **Metformin** versus Placebo in **Obese Pregnant Women** without Diabetes Mellitus. N Engl J Med. 2016 Feb 4;374(5):434-43.

Tabák AG, Herder C, Rathmann W, Brunner EJ, Kivimäki M. **Prediabetes**: a high-risk state for diabetes development. Lancet. 2012 Jun 8.

Tabesh M, Magliano DJ, Koye DN, Shaw JE. The effect of **nurse prescribers on glycaemic control in type 2 diabetes**: A systematic review and meta-analysis. Int J Nurs Stud. 2017 Aug 31.

Tam WH, Ma RC, Ozaki R, et al. In Utero Exposure to **Maternal Hyperglycemia Increases Childhood Cardiometabolic Risk** in Offspring. Diabetes Care. 2017 Mar 9.

Tamborlane WV, Barrientos-Pérez M, Fainberg U, et al; Ellipse Trial Investigators. **Liraglutide** in Children and Adolescents with Type 2 Diabetes. N Engl J Med. 2019 Apr 28.

Tancredi M, Rosengren A, Svensson AM, et al. **Excess Mortality among Persons with Type 2 Diabetes**. N Engl J Med. 2015 Oct 29;373(18):1720-32.

Tang H, Fang Z, Wang T, et al. Meta-Analysis of Effects of **Sodium-Glucose Cotransporter 2 Inhibitors** on **Cardiovascular Outcomes** and All-Cause Mortality Among Patients With Type 2 Diabetes Mellitus. Am J Cardiol. 2016 Aug 31.

Tang H, Cui W, Li D, et al. **Sodium-glucose co-transporter 2 inhibitors in addition to insulin** therapy for management of type 2 diabetes mellitus: A meta-analysis of randomized controlled trials. Diabetes Obes Metab. 2016 Sep 6.

Tang H, Li D, Zhang J, et al. **Sodium-glucose cotransporter 2 inhibitors** and risk of adverse renal outcomes among type 2 diabetes patients: a network and cumulative meta-analysis of randomized controlled trials. Diabetes Obes Metab. 2017 Feb 27

Tang H, Dai Q, Shi W, et al. **SGLT2 inhibitors and risk of cancer** in type 2 diabetes: a systematic review and meta-analysis of randomized controlled trials. Diabetologia. 2017 Jul 19.

Tang H, Yang K, Song Y, et al. Meta-analysis of the association between **sodium-glucose co-transporter-2 inhibitors and risk of skin cancer** among patients with type 2 diabetes. Diabetes Obes Metab. 2018 Jul 23.

Tang T, Lord JM, Norman RJ, et al. Insulin-sensitising drugs (**metformin**, rosiglitazone, pioglitazone, D-chiro-inositol) for women with **polycystic ovary syndrome**, oligo amenorrhoea and subfertility. Cochrane Database Syst Rev. 2009 Oct 7;(4):CD003053. In agreement with the previous review, metformin is still of benefit in improving clinical pregnancy and ovulation rates.

Tang T, Lord JM, Norman RJ, et al. Insulin-sensitising drugs (**metformin**, rosiglitazone, pioglitazone, D-chiro-inositol) for women with polycystic ovary syndrome, oligo amenorrhoea and subfertility. Cochrane Database Syst Rev. 2010 Jan 20;(1):CD003053.

Targher G, Zoppini G, Mantovani W, et al. Comparison of Two **Creatinine-Based Estimating Equations** in Predicting All-Cause and Cardiovascular Mortality in Patients With Type 2 Diabetes. Diabetes Care. 2012 Jul 26.

Tarry-Adkins JL, Aiken CE, Ozanne SE. Neonatal, infant, and childhood **growth following metformin versus insulin treatment for gestational diabetes**: A systematic review and meta-analysis. PLoS Med. 2019 Aug 6;16(8):e1002848.

Tauschmann M, Thabit H, Bally L, et al, APCam11 Consortium. **Closed-loop insulin delivery in suboptimally controlled type 1 diabetes**: a multicentre, 12-week randomised trial. Lancet. 2018 Oct 1.

Tay J, de Bock MI, Mayer-Davis EJ. **Low-carbohydrate diets** in type 2 diabetes. Lancet Diabetes Endocrinol. 2019 Jan 15.

Taylor SI, Leslie BR. **Cardiovascular outcome trials of diabetes drugs**: lessons learned. J Clin Invest. 2018 Mar 1;128(3):893-896.

Teede HJ, Misso ML, Costello MF, et al. **Recommendations** from the international evidence-based guideline for the **assessment and management of polycystic ovary syndrome**. Fertil Steril. 2018 Jul 12.

Teeuw WJ, Gerdes VE, Loos BG. Effect of **periodontal treatment** on glycemic control of diabetic patients: a systematic review and meta-analysis. Diabetes Care. 2010 Feb;33(2):421-7.

Terra SG, Focht K, Davies M, et al. Phase III, efficacy and safety study of **ertugliflozin** monotherapy in people with type 2 diabetes mellitus inadequately controlled with diet and exercise alone. Diabetes Obes Metab. 2017 Jan 24.

Testa MA et al. Comparative effectiveness of **basal-bolus versus premix** analog insulin on glycemic variability and patient-centered outcomes during insulin intensification in type 1 and type 2 diabetes: A randomized, controlled, crossover trial. J Clin Endocrinol Metab 2012 Oct; 97:3504.

Tertti K, Ekblad U, Koskinen P, et al. **Metformin Vs Insulin in Gestational Diabetes**. A Randomized Study Characterizing Metformin Patients Needing Additional Insulin. Diabetes Obes Metab. 2012 Sep 28.

Tessier DM, Meneilly GS. Diabetes in an **older woman** living in a **long-term care residence**. CMAJ. 2015 Mar 3; 187(4):269-71.

*Thabit H, Tauschmann M, Allen JM, et al; APCam Consortium and AP@home Consortium. **Home Use of an Artificial Beta Cell in Type 1 Diabetes**. N Engl J Med. 2015 Sep 17.*

Thanabalasingham Gaya, Owen Katharine R. Diagnosis and management of **maturity onset diabetes of the young** (**MODY**). BMJ 2011;343:doi:10.1136/bmj.d6044 (Published 19 October 2011)
Thankappan KR, Sathish T, Tapp RJ, et al. A **peer-support lifestyle intervention for preventing type 2 diabetes** in India: A cluster-randomized controlled trial of the Kerala Diabetes Prevention Program. PLoS Med. 2018 Jun 6;15(6):e1002575.
Thayer S, Aguilar R, Korrer S, Chow W. HbA(1c) Outcomes in Patients Treated With **Canagliflozin Versus Sitagliptin** in US Health Plans. Clin Ther. 2017 Sep 21.
Thereaux J, Lesuffleur T, Czernichow S, et al. Association between **bariatric surgery and rates of continuation, discontinuation, or initiation of antidiabetes treatment 6 years later** [online Feb 14, 2018].JAMA Surg. doi:10.1001 /jamasurg.2017.6163
Thethi T, Fonseca V. **Comparing diabetes drugs-helping clinical decisions**? Lancet. 2012 Nov 6.
Thiering E, Cyrys J, Kratzsch J, et al. Long-term exposure to traffic-related **air pollution** and insulin resistance in children: results from the GINIplus and LISAplus birth cohorts. Diabetologia. 2013 May 11.
Thind H;Lantini R;Balletto BL, et al. The effects of **yoga** among adults with type 2 diabetes: A systematic review and meta-analysis. Prev Med. 2017 Sep 4;105:116-126.
Tirosh A, Shai I, Tekes-Manova D, et al.; Israeli Diabetes Research Group. **Normal fasting plasma glucose** levels and type 2 diabetes in young men. N Engl J Med. 2005 Oct 6;353(14):1454-62.
Thabit H, Hartnell S, Allen JM, et al. **Closed-loop insulin delivery** in inpatients with type 2 diabetes: a randomised, parallel-group trial. Lancet Diabetes Endocrinol. 2016 Nov 8.
TheHeart.org: Steno-2 news release: http://www.theheart.org/article/842047.do#
TheHeart.org: ACCORD – intensive glucose control arm halted early - news release: http://www.theheart.org/article/842113.do
Thomas D, Elliott EJ. Low **glycaemic index**, or low glycaemic load, diets for diabetes mellitus. Cochrane Database Syst Rev. 2009 Jan 21;(1):CD006296. A low-GI diet can improve glycaemic control in diabetes without compromising hypoglycaemic events.
Thomas NJ, Jones SE, Weedon MN, et al. **Frequency and phenotype of type 1 diabetes in the first six decades of life**: a cross-sectional, genetically stratified survival analysis from UK Biobank. Lancet Diabetes Endocrinol. 2017 Nov 30.
Thomas RL, Dunstan F, Luzio SD et al. Incidence of **diabetic retinopathy** in people with type 2 diabetes mellitus attending the Diabetic Retinopathy Screening Service for Wales: retrospective analysis. BMJ. 2012 Feb 22;344:e874.
Thompson AE. JAMA patient page. **Hypoglycemia**. JAMA. 2015 Mar 24-31;313(12):1284.
Thomsen RW, Pedersen L, Moller N, et al. ***Incretin-Based Therapy and Risk of Acute Pancreatitis****: A Nationwide Population-Based Case-Control Study. Diabetes Care. 2015 Jan 29.*
Thomsen RW, Pedersen L, Moller N, et al. **Incretin-based therapy and risk of acute pancreatitis**: a nationwide population-based case-control study. Diabetes Care. 2015 Jan.
Thompson PL, Davis TM. Cardiovascular Effects of Glucose-Lowering Therapies for Type 2 Diabetes: **New Drugs** in Perspective. Clin Ther. 2016 Nov 15. pii: S0149-2918(16)30793-7.
Thornton PS, Stanley CA, De Leon DD, et al. Recommendations from the **Pediatric Endocrine Society** for Evaluation and Management of **Persistent Hypoglycemia in Neonates**, Infants, and Children. J Pediatr. 2015 May 6.
Thrasher J. **Pharmacologic Management of Type 2 Diabetes Mellitus**: Available Therapies. Am J Cardiol. 2017 Jul 1;120(1S):S4-S16.
Tieu J, Middleton P, McPhee AJ, Crowther CA. **Screening** & subsequent management for **gestational diabetes** for improving maternal and infant health.Cochrane Database Syst Rev. 2010 Jul 7;7:CD007222. There was insufficient evidence to determine if screening for gestational diabetes, or what types ofscreening, can improve maternal and infant health outcomes.
Tikkanen-Dolenc H, Wadén J, Forsblom C, et al; **FinnDiane** Study Group. **Physical Activity** Reduces Risk of Premature Mortality in Patients With Type 1 Diabetes With and Without Kidney Disease. Diabetes Care. 2017 Oct 16.
Tin W, Brunskill G, Kelly T, Fritz S. 15-year follow-up of recurrent "**hypoglycemia**" in **preterm infants**. Pediatrics. 2012 Dec;130(6):e1497-503.
Tinahones FJ, Gallwitz B, Nordaby M, et al. **Linagliptin as add-on to empagliflozin and metformin** in patients with type 2 diabetes: Two 24-week randomized, double-blind, double-dummy, parallel-group trials. Diabetes Obes Metab. 2016 Oct 20.
Ting RZ, et al. Risk factors of **vitamin B12 deficiency** in patients receiving metformin. Arch Intern Med. 2006 Oct 9;166(18):1975-9. Our results indicate an increased risk of vitamin B(12) deficiency associated with current dose and duration of metformin use despite adjustment for many potential confounders
Ting RD, Keech AC, Drury PL, et al. FIELD Study Investigators. Benefits and safety of long-term **fenofibrate** therapy in people with type 2 diabetes and renal impairment: the FIELD Study. Diabetes Care. 2012 Feb;35(2):218-25.
Tirosh A et al. Adolescent **BMI trajectory and risk of diabetes versus coronary disease**. N Engl J Med 2011 Apr 7; 364:1315.
Tobalem M, Uçkay I. Images in clinical medicine. Evolution of a **diabetic foot infection**. N Engl J Med. 2013 Dec 5;369(23):2252.
Tobe SW, Stone JA, Brouwers M, et al. **Harmonization of guidelines** for the prevention and treatment of cardiovascular disease: the **C-CHANGE Initiative**. CMAJ. 2011 Sep 12.
Tobias DK, Zhang C, van Dam RM, Bowers K, Hu FB. **Physical activity before and during pregnancy** and risk of gestational diabetes mellitus: a meta-analysis. Diabetes Care. 2011 Jan;34(1):223-9.
Tobias DK, Hu FB, Chavarro J, et al. **Healthful Dietary Patterns** and Type 2 Diabetes Mellitus Risk Among Women With a History of Gestational Diabetes Mellitus. Arch Intern Med. 2012 Sep 17:1-7.
Tobias DK, Pan A, Jackson CL, et al. **Body-mass index and mortality** among adults with incident type 2 diabetes. N Engl J Med. 2014 Jan 16
Tobias DK, Stuart JJ, Li S, et al. Association of history of **gestational diabetes** with long-term cardiovascular disease risk in a large prospective cohort of US women [online October 16, 2017].JAMA Intern Med. doi:10.1001/jamainternmed.2017.2790
Tocci G, Paneni F, Palano F, et al. **Angiotensin-Converting Enzyme Inhibitors, Angiotensin II Receptor Blockers** and **Diabetes**: A Meta-Analysis of Placebo-Controlled Clinical Trials. Am J Hypertens. 2011 May;24(5):582-90.
TODAY Study Group. A clinical trial to maintain *glycemic control in youth* with type 2 diabetes. N Engl J Med 2012.
TODAY Study Group. **Retinopathy** in Youth With Type 2 Diabetes Participating in the TODAY Clinical Trial. Diabetes Care. 2013 Jun;36(6):1772-4.
TODAY Study Group. Rapid Rise in **Hypertension and Nephropathy** in Youth With Type 2 Diabetes: The TODAY clinical trial. Diabetes Care. 2013 Jun;36(6):1735-41.
TODAY Study Group. Effects of Metformin, Metformin Plus Rosiglitazone, and Metformin Plus Lifestyle on Insulin Sensitivity and **β-Cell Function** in TODAY. Diabetes Care. 2013 Jun;36(6):1749-57.
TODAY Study Group. Safety and Tolerability of the Treatment of **Youth-Onset** Type 2 Diabetes: The TODAY experience. Diabetes Care. 2013 Jun;36(6):1765-71.
Toh S, Hampp C, et al. Risk for hospitalized **heart failure** among new users of **saxagliptin, sitagliptin**, and other antihyperglycemic drugs. A retrospective cohort study. Ann Intern Med. 2016. [Epub ahead of print]. doi:10.7326/M15-2568
Toh S;Reichman ME;Graham DJ;Hampp C;Zhang R;Butler Prospective Postmarketing Surveillance of **Acute Myocardial Infarction in New Users of Saxagliptin**: A Population-Based Study**.** Diabetes Care. 2017 Nov 9.
Tolman KG, Freston JW, Kupfer S, Perez A. **Liver Safety** in Patients with Type 2 Diabetes Treated with **Pioglitazone**: Results from a 3-Year, Randomized, Comparator-Controlled Study in the US. Drug Saf. 2009;32(9):787-800.
Tom WL, et al. The effect of short-contact topical **tretinoin** therapy for **foot ulcers** in patients with diabetes. Arch Dermatol. 2005 Nov;141(11):1373-7. (InfoPOEMs: This small study provides some support for a daily 10-minute application of 0.05% topical tretinoin to diabetic ulcers. (LOE = 1b-))
Tomova GS, Nimbal V, Horwich TB. Relation between **hemoglobin A1c and outcomes in heart failure** patients with and without diabetes mellitus. Am J Cardiol 2012.
Torimoto K, Okada Y, Goshima Y, et al. Addition of **canagliflozin** to insulin **improves glycaemic control** and reduces insulin dose in patients with type 2 diabetes mellitus: A randomized controlled trial. Diabetes Obes Metab. 2019 May 10.
Torpy Janet M., Golub Robert M.. **Diabetes patient page**. JAMA. 2011;305(24):2592.doi:10.1001/jama.2011.741.
Toulis KA, Bilezikian JP, Thomas GN, et al. Initiation of **dapagliflozin** and treatment-emergent **fractures**. Diabetes Obes Metab. 2017 Nov 30.
Touma C, Pannain S. Does **lack of sleep cause diabetes**? Cleve Clin J Med. 2011 Aug;78(8):549-58.
Toumpanakis A, Turnbull T, Alba-Barba I. Effectiveness of **plant-based diets in promoting well-being in the management of type 2 diabetes**: a systematic review. BMJ Open Diabetes Res Care. 2018 Oct 30;6(1):e000534
Toyama T, Neuen BL, Jun M, et al. Effect of **SGLT2 inhibitors on cardiovascular, renal and safety outcom**es in patients with type 2 diabetes mellitus and chronic kidney disease: a systematic review and meta-analysis. Diabetes Obes Metab. 2019 Jan 29.
Tran L, Zielinski A, Roach AH, et al. Pharmacologic Treatment of Type 2 **Diabetes**: **Injectable Medications**. Ann Pharmacother. 2015 Jun;49(6):700-714.
Trasande L, Lampa E, Lind L, et al. Population attributable risks and costs of **diabetogenic chemical exposures** in the elderly. J Epidemiol Community Health. 2016 Oct 27.
Tricco AC, Ivers NM, Grimshaw JM, et al. Eff ectiveness of **quality improvement strategies** on the management of diabetes: a systematic review and meta-analysis. Lancet 2012; online June 9.
Tricco AC, Ashoor HM, Antony J, et al. Safety, effectiveness, and cost effectiveness of **long acting versus intermediate acting insulin for patients with type 1 diabetes**: systematic review and network meta-analysis. BMJ. 2014 Oct 1;349:g5459.
Trief PM, Fisher L, Sandberg J, et al. Two for one? Effects of a couples **intervention on partners** of persons with Type 2 diabetes: a randomized controlled trial. Diabet Med. 2018 Nov 28.
Tripathy D, Schwenke DC, Banerji M, et al. Diabetes Incidence and Glucose Tolerance after **Termination of Pioglitazone** Therapy: Results from **ACT NOW**. J Clin Endocrinol Metab. 2016 May;101(5):2056-62.
Trujillo JM, Nuffer W. **Albiglutide**: A New GLP-1 Receptor Agonist for the Treatment of Type 2 Diabetes. Ann Pharmacother. 2014 Nov;48(11):1494 1501.
Tseng CL, Soroka O, Maney M, et al. Assessing **Potential Glycemic Overtreatment in Persons at Hypoglycemic Risk**. JAMA Intern Med. 2013 Dec 9
Tseng KS, Lin C, Lin YS, et al. Risk of **Head and Neck Cancer** in Patients With Diabetes Mellitus: A Retrospective Cohort Study in Taiwan. JAMA Otolaryngol Head Neck Surg. 2014 Jul 24:1-8.
Tseng E, Greer RC, O'Rourke P, et al. Survey of primary care providers' knowledge of **screening for, diagnosing and managing prediabetes**. J Gen Intern Med. 2017 Jul 20.
Tsilas CS, de Souza RJ, Mejia SB, et al. Relation of **total sugars, fructose and sucrose** with **incident type 2 diabetes**: a systematic review and meta-analysis of prospective cohort studies. CMAJ. 2017 May 23;189(20):E711-E720
Tsilidis K, Kasimis J, Lopez D, Ntzani EE, Ioannadis JP. **Type 2 diabetes and cancer**: umbrella review of meta-analyses of observational studies. BMJ 2015;350:g7707.
Tso LO, Costello MF, Albuquerque LE, et al. **Metformin treatment before and during IVF or ICSI in women with polycystic ovary syndrome**. Cochrane Database Syst Rev. 2014 Nov 18;11:CD006105. This review found no conclusive evidence that metformin treatment

before or during ART cycles improved live birth rates in women with PCOS. However, the use of this insulin-sensitising agent increased clinical pregnancy rates and decreased the risk of OHSS.
Tsugawa Y, Mukamal KJ, Davis RB, et al. Should the **Hemoglobin A1c** Diagnostic Cutoff Differ Between Blacks and Whites?: A Cross-sectional Study. Ann Intern Med. 2012 Aug 7;157(3):153-9.
Tsujimoto T, Kajio H, Shapiro MF, et al. **Risk of All-Cause Mortality in Diabetic Patients Taking β-Blockers**. Mayo Clin Proc. 2018 Apr;93(4):409-418.
Tuccori M, Filion KB, Yin H, Yu OH, Platt RW, Azoulay L. **Pioglitazone** use and risk of **bladder cancer**: population based cohort study. BMJ2016;352:i1541.
Tufail A, Kapetanakis VV, Salas-Vega S, et al. An observational study to assess if **automated diabetic retinopathy** image assessment software can replace one or more steps of manual imaging grading and to determine their cost-effectiveness. Health Technol Assess. 2016 Dec;20(92):1-72.
Tung EL, Davis AM, Laiteerapong N. **Glycemic Control in Nonpregnant Adults With Type 2 Diabetes**. JAMA. 2018 Jun 19;319(23):2430-2431.
Turner RM, Kwok CS, Chen-Turner C, et al. **Thiazolidinediones** and associated risk of **Bladder Cancer**: a Systematic Review and Meta-analysis. Br J Clin Pharmacol. 2013 Dec 10
Turgeon RD, Banh HL, Korownyk C. **Is diabetes a coronary artery disease equivalent**? Can Fam Physician. 2013 Dec;59(12):1306
Tuomi T, Santoro N, Caprio S, et al. The **many faces of diabetes**: a disease with increasing heterogeneity. Lancet. 2013 Dec 3
Turksoy K, Frantz N, Quinn L, et al. **Automated Insulin Delivery**-The Light at the End of the Tunnel. J Pediatr. 2017 Apr 7.
Turin TC, Saad N, Jun M, Tonelli et al. **Lifetime risk** of diabetes among **First Nations and non-First Nations people**. CMAJ. 2016 Sep 19
Tuttle KR, Lakshmanan MC, Rayner B, et al. **Dulaglutide versus insulin glargine in patients with type 2 diabetes** and moderate-to-severe chronic kidney disease (AWARD-7): a multicentre, open-label, randomised trial. Lancet Diabetes Endocrinol 2018; online June 14.
Tylee T, Hirsch IB. **Costs Associated With Using Different Insulin** Preparations. JAMA. 2015 Aug 18;314(7):665-6.
Tuttle KR, McKinney TD, Davidson JA, et al. Effects of once-weekly **dulaglutide on kidney function** in patients with type 2 diabetes in phase II and III clinical trials. Diabetes Obes Metab. 2016 Oct 21.
Tzoulaki Ioanna, Molokhia Mariam, Curcin Vasa, et al. **Risk of cardiovascular disease** and all cause mortality among patients with type 2 diabetes prescribed **oral antidiabetes drugs**: retrospective cohort study using UK general practice research database. BMJ 2009;339:b4731, doi: 10.1136/bmj.b4731 (Published 3 December 2009)
Udell JA, Bhatt DL, Braunwald E, et al. **Saxagliptin** and Cardiovascular Outcomes in Patients With Type 2 Diabetes Mellitus and **Moderate or Severe Renal Impairment**: Observations From the SAVOR-TIMI 53 Trial. Diabetes Care. 2014 Dec 31.
Udell JA, Yuan Z, Rush T, et al. **Cardiovascular Outcomes** and Risks After Initiation of a **Sodium Glucose Co-Transporter 2 Inhibitor**: Results From the **EASEL** Population-Based Cohort Study. Circulation. 2017 Nov 13.
Ueda P, Svanström H, Melbye M, et al. **Sodium glucose cotransporter 2 inhibitors and risk of serious adverse events**: nationwide register based cohort study. BMJ. 2018 Nov 14;363:k4365.
Umpierre D, Ribeiro PB, Kramer CK, et al. Physical **Activity** Advice Only or Structured **Exercise** Training and Association With HbA1c Levels in Type 2 Diabetes: Systematic Review & Meta-analysis. JAMA.2011;305(17):1790-1799.
Umpierrez GE, Hellman R, Korytkowski MT, et al. Management of **hyperglycemia in hospitalized patients** in non-critical care setting: an endocrine society clinical practice guideline. J Clin Endocrinol Metabol 2012; 97:16-38.
Umpierrez G, Povedano ST, Manghi FP, et al. Efficacy and Safety of **Dulaglutide** Monotherapy **Versus Metformin** in Type 2 Diabetes in a Randomized Controlled Trial (AWARD-3). Diabetes Care. 2014 May 19.
Umpierrez GE, Pasquel FJ. **Management of Inpatient Hyperglycemia** and Diabetes in Older Adults. Diabetes Care. 2017 Apr;40(4):509-517.
Umpierrez GE, O`Neal D, DiGenio A, et al. **Lixisenatide** reduces glycaemic variability in insulin-treated patients with type 2 diabetes. Diabetes Obes Metab. 2017 Mar 3.
UKPDS-34. Effect of intensive blood-glucose control with metformin on complications in overweight patients with type 2 diabetes. Lancet. 1998 Sep 12;352(9131):854-65. Erratum in: Lancet 1998 Nov 7;352(9139):1558.
Usher-Smith JA, Thompson MJ, Sharp SJ, Walter FM. Factors associated with the presence of **diabetic ketoacidosis** at diagnosis of diabetes in children and young people: a systematic review. BMJ 2011;343:d4092.
U.S. Preventive Services Task Force. **Screening** for type 2 **diabetes mellitus** in adults: (USPSTF) U.S. Preventive Services Task Force recommendation statement. Ann Intern Med. 2008 Jun 3;148(11):846-54.
U.S. Preventive Services Task Force. **Screening** for **gestational diabetes** mellitus: (USPSTF) U.S. Preventive Services Task Force recommendation statement. Ann Intern Med. 2008 May 20;148(10):759-65.
Uusitalo U, Liu X, Yang J, et al; **TEDDY** Study Group. Association of Early Exposure of **Probiotics** and **Islet Autoimmunity** in the TEDDY Study. JAMA Pediatr. 2015 Nov 9:1-9.
Xu T, Magnusson Hanson LL, et al. **Workplace bullying** and violence as risk factors for type 2 diabetes: a multicohort study and meta-analysis. Diabetologia. 2017 Nov 13.
VA/DoD clinical practice guideline: Management of Type 2 Diabetes Mellitus in Primary Care Work Group. **VA/DoD clinical practice** guideline for the management of **type 2 diabetes mellitus in primary care**. Version 5.0. Washington (DC): Department of Veterans Affairs, Department of Defense; 2017 Apr.
Vaccaro O, Masulli M, Nicolucci A, et al, for the **Thiazolidinediones Or Sulphonylureas** Cardiovascular Accidents Intervention Trial (**TOSCA.IT**) study group. Effects on the incidence of cardiovascular events of the addition of **pioglitazone versus sulfonylureas** in patients with type 2 diabetes **inadequately controlled with metformin** (TOSCA.IT): a randomised, multicentre trial. Lancet Diabetes Endocrinol 2017; online Sept 13.
Valdes AM, Andrew T, Gardner JP, Kimura M, Oelsner E, Cherkas LF, Aviv A, Spector TD. Obesity, cigarette smoking, and telomere length in women. Lancet. 2005 Aug 20-26;366(9486):662-4.
Valencia WM, Florez H. How to **prevent the microvascular complications** of type 2 diabetes beyond glucose control. BMJ. 2017 Jan 17;356:i6505.
Valentine N, Van de Laar FA, van Driel ML. Adenosine-diphosphate (ADP) receptor antagonists (**clopidogrel, dipyridamole**) for the prevention of cardiovascular disease in type 2 **diabetes** mellitus. Cochrane Database Syst Rev. 2012 Nov 14;11:CD005449. doi: 10.1002/14651858.CD005449.pub2. The available evidence for ADP receptor antagonists in patients with diabetes mellitus is limited and most trials do not report outcomes for patients with diabetes separately.
Valladares T, Cardoso MR, Aldrighi JM. Higher **serum levels of vitamin D are associated with lower blood glucose levels**. Menopause. 2019 Jan 18.
van Baar MJB, van Ruiten CC, Muskiet MHA, et al. **SGLT2 Inhibitors in Combination Therapy**: From Mechanisms to Clinical Considerations in Type 2 Diabetes Management. Diabetes Care. 2018 Aug;41(8):1543-1556.
van Dalem J, Brouwers MC, Stehouwer CD, et al. Risk of **hypoglycaemia in users of sulphonylureas compared with metformin** in relation to renal function and sulphonylurea metabolite group: population based cohort study. BMJ. 2016 Jul 13;354:i3625.
van Dalem J, Brouwers MCGJ, Stehouwer CDA, et al. Risk of a **first-ever acute myocardial infarction and all-cause mortality with sulphonylurea treatment**: A population-based cohort study. Diabetes Obes Metab. 2017 Nov 24.
van Dam RM, Hu FB. Coffee consumption and risk of type 2 diabetes. A systematic review. JAMA 2005; 294:97-104. (InfoPOEMs Habitual coffee drinking is associated with a reduced risk for type 2 diabetes. The lowest risk reduction occurred among individuals consuming 6 or more cups of filtered coffee daily. Decaffeinated and caffeinated brews are equally effective. (LOE = 2a-):)
Van de Laar FA, Lucassen PL, Akkermans RP, et al. Alpha-glucosidase inhibitors for type 2 diabetes mellitus. Cochrane Database Syst Rev. 2005 Apr 18;(2):CD003639 & ACP Journal Club . AUTHORS' CONCLUSIONS: It remains unclear whether alpha-glucosidase inhibitors influence mortality or morbidity in patients with type 2 diabetes. Conversely, they have a significant effect on glycemic control and insulin levels, but no statistically significant effect on lipids and body weight. These effects are less sure when alpha-glucosidase inhibitors are used for a longer duration. Acarbose dosages higher than 50 mg TID offer no additional effect on glycated hemoglobin but more adverse effects instead. Compared to sulphonylurea, alpha-glucosidase inhibitors lower fasting and post-load insulin levels and have an inferior profile regarding glycemic control and adverse effects.
Van de Werf F. **Prevention of Cardiovascular Events in Patients With Diabetes**: How Beneficial Is Dual Antiplatelet Therapy? Circulation. 2017 May 2;135(18):1675-1676.
van de Woestijne AP, van der Graaf Y, Westerink J, et al. Effect of **statin therapy on incident type 2 diabetes** mellitus in patients with clinically manifest vascular disease. Am J Cardiol. 2015 Feb 15;115(4):441-6.
Van der Berg J, Stehouwer C, Bosma H, et al. Associations of total amount and patterns of **sedentary behaviour** with type 2 diabetes and the metabolic syndrome: the Maastricht study. Diabetologia 2016; doi:10.1007/s00125-015-3861-8.
van der Heijden AA, Ortegon MM, Niessen LW, et al. Prediction of coronary heart disease risk in a general, pre-diabetic, and diabetic population during 10 years of follow-up: accuracy of the Framingham, SCORE, and UKPDS risk functions: The Hoorn Study. Diabetes Care. 2009 Nov;32(11):2094-8. The use of the Framingham function for prediction of the first CHD event is likely to overestimate an individual`s absolute CHD risk. In CHD prevention, application of the **SCORE and UKPDS** functions might be useful in the absence of a more valid tool.
van der Leeuw J, van Dieren S, Beulens JW, et al. The **validation of cardiovascular risk scores** for patients with type 2 diabetes mellitus. Heart. 2014 Sep 25.
van Dieren S, Beulens JW, Kengne AP, et al. **Prediction models for the risk of cardiovascular disease** in patients with type 2 diabetes: a systematic review. Heart. 2011 Dec 18.
van Dijk JW, Venema M, van Mechelen W, Stehouwer CD, Hartgens F, van Loon LJ. Effect of **moderate-intensity exercise versus activities of daily living** on 24-hour blood glucose homeostasis in male patients with type 2 diabetes. Diabetes Care. 2013 Nov;36(11):3448-53.
Van Gaal LF, Rissanen AM, Scheen AJ, et al. **RIO-Europe** Study Group. Effects of the cannabinoid-1 receptor blocker rimonabant on weight reduction and cardiovascular risk factors in overweight patients: 1-year experience from the RIO-Europe study. Lancet. 2005 Apr 16-22;365(9468):1389-97. Erratum in: Lancet. 2005 Jul 30-Aug 5;366(9483):370.
van Meijel LA, van den Heuvel-Bens SP, Zimmerman LJ, et al. Effect of **Automated Bolus Calculation** on Glucose Variability and Quality of Life in Patients With Type 1 Diabetes on CSII Treatment. Clin Ther.2018 Mar 1.
van Raalte DH, Bjornstad P, Persson F, et al. The **Impact of Sotagliflozin** on Renal Function, Albuminuria, Blood Pressure, and Hematocrit in Adults With Type 1 Diabetes. Diabetes Care. 2019 Aug 1.
van Son J, Nyklicek I, Pop VJ, et al. The Effects of a **Mindfulness-Based Intervention** on Emotional Distress, Quality-of-Life, and HbA1c in Outpatients With Diabetes (DiaMind): A randomized controlled trial. Diabetes Care. 2012 Nov 27.
Vanderheiden A, Harrison L, Warshauer J, et al. Effect of **Adding Liraglutide vs Placebo to a High-Dose Insulin Regimen** in Patients With Type 2 Diabetes: A Randomized Clinical Trial. JAMA Intern Med. 2016 Jun 6.
Varghese D, Kirkwood CK, Carroll NV. Prevalence of **Antidiabetic and Antilipidemic Medications** in **Children and Adolescents** Treated With **Atypical Antipsychotics** in a Virginia Medicaid Population. Ann Pharmacother. 2016 Mar 23.
Vanky E, Stridsklev S, Heimstad R, et al. Metformin Versus Placebo from First Trimester to Delivery in Polycystic Ovary Syndrome: A Randomized, Controlled Multicenter Study. J Clin Endocrinol Metab. 2010 Oct 6.
Vashisht R, Jung K, Schuler A, et al. Association of **Hemoglobin A1c Levels With Use of Sulfonylureas, Dipeptidyl Peptidase 4 Inhibitors, and Thiazolidinediones in Patients With Type 2 Diabetes** Treated With MetforminAnalysis From the Observational Health Data Sciences and Informatics Initiative. JAMA Netw Open. 2018;1(4):e181755.

Vasilakou D, Karagiannis T, Athanasiadou E, et al. **Sodium–glucose cotransporter 2 inhibitors** for type 2 diabetes. A systematic review and meta-analysis. Ann Intern Med. 2013;159:262-74.

Vasileiou V, Kyratzoglou E, Paschou SA, et al. The impact of **environmental temperature on the diagnosis of gestational diabetes** mellitus. Eur J Endocrinol. 2018 Jan 23.

Vassy JL, Dasmahapatra P, Meigs JB, et al. **Genotype prediction of adult type 2 diabetes** from **adolescence** in a multiracial population. Pediatrics. 2012 Nov;130(5):e1235-42.

Vause TD, Cheung AP, Sierra S, Claman P, Graham J, Guillemin JA, Lapensée L, Steward S, Wong BC. Ovulation induction in polycystic ovary syndrome. J Obstet Gynaecol Can. 2010 May;32(5):495-502. Ovulation Induction in **Polycystic Ovary Syndrome SOGC-2010** http://sogc.org/guidelines/documents/gui242CPG1005E.pdf

Vavanikunnel J, Charlier S, Becker C, et al. Association Between Glycemic Control and **Risk of Fracture** in Diabetic Patients: A Nested Case-Control Study. J Clin Endocrinol Metab. 2019 May 1;104(5):1645-1654.

Vellanki P, Rasouli N, Baldwin D, et al; Linagliptin Inpatient Research Group. **Glycaemic Efficacy and Safety of Linagliptin** compared to Basal-Bolus Insulin Regimen in Patients with Type 2 Diabetes Undergoing Non-Cardiac Surgery: A Multicenter Randomized Clinical Trial. Diabetes Obes Metab. 2018 Nov 20.

Verbraak FD, Abramoff MD, Bausch GCF, et al. **Diagnostic Accuracy of a Device for the Automated Detection of Diabetic Retinopathy** in a Primary Care Setting. Diabetes Care. 2019 Feb 14.

Verma S, Mazer CD, Al-Omran M, et al. Cardiovascular Outcomes and Safety of Empagliflozin in Patients With Type 2 Diabetes Mellitus and **Peripheral Artery Disease**: A Subanalysis of **EMPA-REG OUTCOME**. Circulation. 2017 Nov 13.

Verma S, Bhatt DL, Bain SC, et al. Effect of **Liraglutide** on Cardiovascular Events in Patients With Type 2 Diabetes Mellitus and Polyvascular Disease: Results of the LEADER Trial. Circulation. 2018 May 15;137(20):2179-2183.

Verma S, Leiter LA, Mazer CD, et al. **Liraglutide Reduces Cardiovascular Events and Mortality in Type 2 Diabetes Mellitus Independently of Baseline Low-Density Lipoprotein Cholesterol Levels and Statin Use**. (Leader) Circulation. 2018 Oct 9;138(15):1605-1607.

Verma S, Mazer CD, Yan AT, et al; EMPA-HEART CardioLink-6 Investigators. **Effect of Empagliflozin on Left Ventricular Mass** in Patients with Type 2 Diabetes and Coronary Artery Disease: The EMPA-HEART CardioLink-6 Randomized Clinical Trial. Circulation. 2019 Aug 22.

Vetter ML, Cardillo S, Rickels MR, Iqbal N. Narrative review: effect of **bariatric surgery** on type 2 diabetes mellitus. Ann Intern Med. 2009 Jan 20;150(2):94-103.

Vetter C, Dashti HS, Lane JM, et al. **Night Shift Work, Genetic Risk, and Type 2 Diabetes** in the UK Biobank. Diabetes Care. 2018 Apr;41(4):762-769.

Vigersky RA, Fonda SJ, Chellappa M, et al. Short- and long-term effects of **real-time continuous glucose monitoring** in patients with type 2 diabetes. Diabetes Care. 2012 Jan;35(1):32-8.

Viguiliouk E, Kendall CW, Kahleová H, et al. Effect of **vegetarian dietary patterns on cardiometabolic risk factors in diabetes**: A systematic review and meta-analysis of randomized controlled trials. Clin Nutr. 2018 Jun 13.

Vijan Sandeep. **In the Clinic: Type 2 Diabetes**. *Ann Intern Med* March 2, 2010 152:ITC3-1; doi:10.1059/0003-4819-152-5-201003020-01003. **Updated ITC2 Mar 3, 2015.**

Vijan S, Sussman JB, Yudkin JS, et al. Effect of **Patients' Risks and Preferences on Health Gains** With Plasma Glucose Level Lowering in Type 2 Diabetes Mellitus. JAMA Intern Med. 2014 Jun 30.

Vijayakumar S, Vaduganathan M, Butler J. **Glucose-Lowering Therapies and Heart Failure** in Type 2 Diabetes Mellitus: Mechanistic Links, Clinical Data, and Future Directions. Circulation. 2018 Mar 6;137(10):1060-1073.

Viljoen A, Hoxer CS, Johansen P, et al. Evaluation of the long-term **cost-effectiveness of once-weekly semaglutide versus dulaglutide** for treatment of type 2 diabetes mellitus in the UK. Diabetes Obes Metab. 2018 Oct 25.

Villegas K, Meier JL, Long M, et al. The Effect of **Proton Pump Inhibitors on Glycemic Control** in Patients with Type 2 Diabetes. Metab Syndr Relat Disord. 2019 Feb 7.

Vilsboll T, Ekholm E, Johnsson E, et al. **Dapagliflozin Plus Saxagliptin Add-on Therapy Compared With Insulin** in Patients With Type 2 Diabetes Poorly Controlled by Metformin With or Without Sulfonylurea Therapy: A Randomized Clinical Trial. Diabetes Care. 2019 Jun 4.

Vimalananda VG, Palmer JR, Gerlovin H, et al. **Night-shift work** and incident diabetes among African American women. Diabetologia. 2015 Jan 14.

Viner R, White B, Christie D. **Type 2 diabetes in adolescents**: a severe phenotype posing major clinical challenges and public health burden. Lancet. 2017 Jun 3;389(10085):2252-2260

Vinik AI, Shapiro DY, et al. A Randomized-Withdrawal, Placebo-Controlled Study Evaluating the Efficacy and Tolerability of **Tapentadol** Extended Release in Patients With Chronic, Painful Diabetic Peripheral **Neuropathy**. Diabetes Care. 2014 May 21.

Vinik AI. **Diabetic Sensory and Motor Neuropathy**. N Engl J Med. 2016 Apr 14

Virtanen M, Ervasti J, Mittendorfer-Rutz E, et al. Trends of Diagnosis-Specific **Work Disability** After Newly Diagnosed Diabetes: A Four-Year Nationwide Prospective Cohort Study. Diabetes Care. 2015 Aug 6.

Viscoli CM et al. **Pioglitazone** and risk for bone fracture: Safety data from a randomized clinical trial. J Clin Endocrinol Metab 2017 Mar; 102:914.

Vistisen D, Andersen GS, Hansen CS, et al. Prediction of First Cardiovascular Disease Event in Type 1 Diabetes: The **Steno T1 Risk Engine**. Circulation. 2016 Feb 17.

Vitamin E in Neuroprotection Study (**VENUS**) Investigators, Hor CP, Fung WY, Ang HA, et al. Efficacy of Oral Mixed **Tocotrienols** in **Diabetic Peripheral Neuropathy**: A Randomized Clinical Trial. JAMA Neurol. 2018 Jan 29.

Vo MT, Uratsu CS, Estacio KR, et al. **Prompting Patients with Poorly Controlled Diabetes to Identify Visit Priorities Before Primary Care Visits**: a Pragmatic Cluster Randomized Trial. J Gen Intern Med. 2019 Feb 11.

Vos RC, van Avendonk MJ, Jansen H, et al. **Insulin monotherapy compared with the addition of oral glucose-lowering agents to insulin** for people with type 2 diabetes already on insulin therapy and inadequate glycaemic control. Cochrane Database Syst Rev. 2016 Sep 18;9:CD006992. The addition of all oral glucose-lowering agents in people with type 2 diabetes and inadequate glycaemic control who are on insulin therapy has positive effects on glycaemic control and insulin requirements. The addition of sulphonylureas results in more hypoglycaemic events. Additional weight gain can only be avoided by adding metformin to insulin. Other well-known adverse effects of oral glucose-lowering agents have to be taken into account when prescribing oral glucose-lowering agents in addition to insulin therapy.

Vos RC, Rutten GEHM. **Oral Hypoglycemic Agents Added to Insulin Monotherapy** for Type 2 Diabetes. JAMA. 2017 Oct 17;318(15):1489-1490.

Wadden TA, Berkowitz RI, Womble LG, et al. Randomized trial: **lifestyle modification & pharmacotherapy** for obesity. N Engl J Med 2005;353:2111-20. Combo of sibutramine & group lifestyle modifications resulted in more weight loss (**12.1 kg** at 1yr) then either alone.

Wahrenberg H, Hertel K, Leijonhufvud BM, Persson LG, Toft E, Arner P. Use of **waist circumference** to predict insulin resistance: retrospective study. BMJ. 2005 Jun 11;330(7504):1363-4. Epub 2005 Apr 15.

Waldrop G, Zhong J, Peters M, Rajagopalan S. **Incretin-Based Therapy for Diabetes**: What a Cardiologist Needs to Know. J Am Coll Cardiol 2016;67:1488–96.

Waldfogel JM, Nesbit SA, Dy SM, et al. Pharmacotherapy for **diabetic peripheral neuropathy pain** and quality of life: A systematic review. Neurology. 2017 Mar 24

Wallia A, MolitchME. **Insulin therapy** for type 2 diabetes mellitus. JAMA. doi:10.1001 /jama.2014.5951.

Walker EA, et al. **Adherence** to preventive medications: predictors and outcomes in the Diabetes Prevention Program. Diabetes Care. 2006 Sep;29(9):1997-2002.

Wan W, Skandari MR, Minc A, et al. Cost-effectiveness of **Continuous Glucose Monitoring for Adults** With Type 1 Diabetes Compared With Self-Monitoring of Blood Glucose: the **DIAMOND** Randomized Trial. Diabetes Care. 2018 Apr 12.

Wang Amy T, McCoy Christopher P, Murad Mohammad Hassan, Montori Victor M. Association between **industry affiliation** and position on cardiovascular risk with **rosiglitazone**: cross sectional systematic review. BMJ 2010;340:c1344, doi: 10.1136/bmj.c1344 (Published 18 March 2010).

Wang B, Wang F, Zhang Y, et al. Effects of **RAS inhibitors** on **diabetic retinopathy**: a systematic review and meta-analysis. Lancet Diabetes Endocrinol. 2015 Apr;3(4):263-74.

Wang C, Mamza J, Idris I. **Biphasic vs basal bolus insulin** regimen in Type 2 diabetes: a systematic review and meta-analysis of randomized controlled trials. Diabet Med. 2015 May;32(5):585-94.

Wang C, Wei Y, Zhang X, et al. A randomized clinical trial of **exercise during pregnancy** to **prevent gestational diabetes mellitus** and improve pregnancy outcome in overweight and obese pregnant women. Am J Obstet Gynecol. 2017 Apr;216(4):340-351.

Wang C, Zhou Y, Kong Z, et al. The **renoprotective effects of sodium-glucose cotransporter 2 inhibitors** versus placebo in patients with type 2 diabetes with or without prevalent kidney disease: A systematic review and meta-analysis. Diabetes Obes Metab. 2018 Dec 18.

Wang H, Romano G, Frustaci ME, et al. **Fulranumab** for treatment of diabetic peripheral neuropathic pain: A randomized controlled trial. Neurology. 2014 Aug 12;83(7):628-37.

Wang H, Liu Y, Tian Q, et al. **Incretin-based therapies and risk of pancreatic cancer** in patients with type 2 diabetes: a meta-analysis of randomised controlled trials. Diabetes Obes Metab. 2017 Nov 30.

Wang H, Wender-Ozegowska E, Garne E, et al. **Insulin analogues use in pregnancy** among women with pregestational diabetes mellitus and risk of congenital anomaly: a retrospective population-based cohort study. BMJ Open. 2018 Feb 24;8(2):e014972.

Wang J, Huang J, Li W, et al. Polyethylene glycol loxenatide (**PEX168**) in subjects with renal impairment: A pharmacokinetic study. Br J Clin Pharmacol. 2019 Aug 8.

Wang L, Gao P, Zhang M, et al. Prevalence and Ethnic Pattern of **Diabetes and Prediabetes in China** in 2013. JAMA. 2017 Jun 27;317(24):2515-2523.

Wang R, Kim BV, van Wely M, et al. Treatment strategies for **women with WHO group II anovulation**: systematic review and network meta-analysis. BMJ. 2017 Jan 31;356:j138.

Wang SY, Andrews CA, Herman WH, et al. Incidence and risk factors for developing **diabetic retinopathy** among youths with type 1 or type 2 diabetes throughout the United States. Ophthalmology 2016 Nov 30. pii: S0161e6420(16)30997-6.

Wang SY, Andrews CA, Gardner TW, et al. **Ophthalmic screening** patterns among youths with diabetes enrolled in a large US managed care network [online Mar 23, 2017].JAMA Ophthalmol. doi:10.1001 /jamaophthalmol.2017.0089

Wang T, Wang F, Gou Z, et al. Using real-world data to evaluate the association of **incretin-based therapies with risk of acute pancreatitis**: a meta-analysis of 1 324 515 patients from observational studies. Diabetes Obes Metab. 2015 Jan;17(1):32-41.

Wang T, Hong JL, Gower EW, et al. **Incretin-Based Therapies and Diabetic Retinopathy**: Real-World Evidence in Older U.S. Adults. Diabetes Care. 2018 Jul 16.

Wang T, Huang T, Li Y, et al. **Low birthweight and risk of type 2 diabetes**: a Mendelian randomisation study. Diabetologia. 2016 Jun 23.

Wang T, Lu J, Su Q, et al Ideal **Cardiovascular Health Metrics and Major Cardiovascular Events** in Patients With Prediabetes and Diabetes. JAMA Cardiol. 2019 Jul 31.

Wang W, Nevarez L, Filippova E, et al. **Efficacy and safety of once-weekly dulaglutide versus insulin glargine in mainly Asian patients with type 2 diabetes mellitus** on metformin and/or a sulphonylurea: A 52-week open-label, randomized phase III trial. Diabetes Obes Metab. 2018 Aug 21.

Wang Y, Lee DC, Brellenthin AG, et al. Association of **Muscular Strength and Incidence of Type 2 Diabetes**. Mayo Clin Proc. 2019 Apr;94(4):643-651.

Wang Z;Sun J;Han R;Fan D;Dong X;Luan Z;Xiang R;Zha. Efficacy and safety of **sodium-glucose cotransporter-2 inhibitors** versus **dipeptidyl peptidase-4 inhibitors** as monotherapy or add-on to metformin in patients with type 2 diabetes mellitus: A systematic review and meta-analysis. Diabetes Obes Metab. 2017 Jun 28.

Wannamethee SG, Shaper AG, Lennon L, Morris RW. Metabolic Syndrome vs **Framingham Risk Score** for Prediction of Coronary Heart Disease, Stroke, and Type 2 Diabetes Mellitus. Arch Intern Med. 2005 Dec 26;165(22):2644-50.

Wannamethee S. Goya; Shaper A. Gerald; Whincup Peter H.; et al. Impact of Diabetes on **Cardiovascular Disease Risk and All-Cause Mortality in Older Men**: Influence of Age at Onset, Diabetes Duration, and Established and Novel Risk Factors. *Arch Intern Med*. 2011;171(5):404-410.

Wanner C, Inzucchi SE, Lachin JM, et al. **Empagliflozin and progression of kidney disease** in type 2 diabetes. (**Empa-Reg Outcome**) N Engl J Med. DOI: 10.1056/NEJMoa1515920.

Wanner C. **EMPA-REG OUTCOME**: The **Nephrologist's Point of View**. Am J Cardiol. 2017 Jul 1;120(1S):S59-S67.

Wanner C, Lachin JM, Inzucchi SE, et al.; on behalf of the **EMPA-REG OUTCOME** Investigators. **Empagliflozin** and clinical outcomes in patients with type 2 diabetes mellitus, established cardiovascular disease, and **chronicic kidney disease**. Circulation. 2018;137:119–129. doi: 10.1161/CIRCULATIONAHA.117.028268.

Wanner C, Marx N. **SGLT2 inhibitors**: the future for treatment of type 2 diabetes mellitus and other chronic diseases. Diabetologia. 2018 Oct;61(10):2134-2139.

Warren B, Pankow JS, Matsushita K, et al. **Comparative prognostic performance of definitions of prediabetes**: a prospective cohort analysis of the Atherosclerosis Risk in Communities (ARIC) study. Lancet Diabetes Endocrinol 2016; online Nov 15.

Wasag DR, Gregory JW, Dayan C, Harvey JN; Brecon Group. **Excess all-cause mortality before age 30** in **childhood onset type 1 diabetes**: data from the **Brecon Group Cohort** in Wales. Arch Dis Child. 2017 Aug 31.

Wasko MC, Hubert HB, Lingala VB, et al. ***Hydroxychloroquine and risk of diabetes*** *in patients with rheumatoid arthritis. JAMA. 2007 Jul 11;298(2):187-93.*

Watada H, Kaneko S, Komatsu M, et al. Superior **HbA1c control with the fixed-ratio combination of insulin degludec and liraglutide** (IDegLira) compared with </=50 units insulin degludec in Japanese subjects with type 2 diabetes in a phase 3, double-blind, randomised trial. Diabetes Obes Metab. 2019 Aug 18.

Watts NB, Bilezikian JP, Usiskin K, et al. Effects of **canagliflozin** on **fracture risk** in patients with type 2 diabetes mellitus. J Clin Endocrinol Metab 2016;101:157-66.

Waugh N, Cummins E, Royle P, et al. Newer agents for blood glucose control (glucagon-like peptide-1 (GLP-1) analogue ***exenatide****; dipeptidyl peptidase-4 (DPP-4) inhibitors* ***sitagliptin*** *and* ***vildagliptin****; the long-acting insulin analogues,* ***glargine*** *and* ***detemir****) in type 2 diabetes: systematic review and economic evaluation. Health Technol Assess. 2010 Jul;14(36):1-248.*

Waugh N, Royle P, Clar C, et al. ***Screening for hyperglycaemia in pregnancy****: a rapid update for the National Screening Committee. Health Technol Assess. 2010 Sep;14(45):1-183.* The evidence base has improved since the last HTA review in 2002. There is now good evidence for treatment of oral drugs instead of insulin and it looks increasingly as if FPG could be the test of choice.

Waugh NR, Shyangdan D, Taylor-Phillips S, et al. **Screening for type 2 diabetes**: a short report for the National Screening Committee. Health Technol Assess. 2013 Aug;17(35):1-90.

Wei L, Lai EC, Kao-Yang YH, et al. Incidence of type 2 diabetes mellitus in **men receiving steroid 5α-reductase inhibitors**: population based cohort study. BMJ. 2019 Apr 10;365:l1204.

Weiner JZ, Gopalan A, Mishra P, et al. **Use and Discontinuation of Insulin Treatment Among Adults Aged 75 to 79** Years With Type 2 Diabetes. JAMA Intern Med. 2019 Sep 23.

Weinger K, Beverly EA, Lee Y, Sitnokov L, Ganda OP, Caballero AE. The effect of a **structured behavioral intervention** on poorly controlled diabetes: a randomized controlled trial [published online October 10, 2011]. Arch Intern Med.

Weinstein G, Maillard P, Himali JJ, et al. **Glucose indices are associated with cognitive and structural brain measures** in young adults. Neurology 2015;84:2329–2337.

Weir DL, McAlister FA, Senthilselvan A, Minhas- Sandu JK, Eurich DT. **Sitagliptin** use in patients with diabetes and **heart failure**: a population based retrospective cohort study. J Am Coll Cardiol HF 2014;2:XXX–XXX.

Welch G, Zagarins SE, Santiago-Kelly P, et al. An **Internet-Based Diabetes Management Platform** Improves Team Care and Outcomes in an Urban Latino Population. Diabetes Care. 2015 Jan 29.

Wells G., Kelly S., Johnston A., et al. New drugs for **type 2 diabetes**: **Second-line therapy** - science report. Ottawa (ON): Canadian Agency for Drugs and Technologies in Health; 2017 Sep.

Welschen LM, Bloemendal E, Nijpels G, Dekker JM, Heine RJ, Stalman WA, Bouter LM. Self-monitoring of blood glucose in patients with type 2 diabetes who are not using insulin. Diabetes Care 2005; 28:1510-17. (InfoPOEMs: Intensive monitoring of blood glucose in patients with type 2 diabetes not using insulin results in a small decrease in hemoglobin A1c (HbA1c) levels but does not change fasting blood glucose levels. Urine glucose monitoring works just as well. More casual monitoring of blood glucose, such as once a day, has not been studied. There is a strong possibility that the weak study design was largely responsible for the difference seen in the study. Blood glucose monitoring is expensive: At the intense level of monitoring used in some of these studies (6 times a day), the cost of the monitoring strips alone can be $2000 US per year. (LOE = 1a))

Wen CP, et al. Increased mortality risks of pre-diabetes (**impaired fasting glucose**) in Taiwan. Diabetes Care. 2005 Nov;28(11):2756-61. CONCLUSIONS: There was an overall J-shaped relationship between all-cause mortality and FBG. IFG, when defined as 110-125 mg/dl, is an independent risk factor and should be aggressively treated as a disease because its subsequent mortality risks for CVD and diabetes were significantly increased. The newly defined IFG at 100-125 mg/dl did not have the predictive power for later increases in CVD or diabetes mortality.

Weng J, Li Y, Xu W, et al. Effect of intensive insulin therapy on beta-cell function and glycaemic control in patients with newly diagnosed type 2 diabetes: a multicentre randomized parallel-group trial. Lancet. 2008 May 4;371(9626):1753-1760. Early intensive insulin therapy in patients with newly diagnosed type 2 diabetes has favourable outcomes on recovery and maintenance of beta-cell function and protracted glycaemic remission compared with treatment with oral hypoglycaemic agents.

Weng J, Zhou Z, Guo L, et al; **T1D** China Study Group. Incidence of **type 1 diabetes in China, 2010-13**: population based study. BMJ. 2018 Jan 3;360:j5295.

Wermeling PR, Gorter KJ, Stellato RK, et al. Effectiveness and cost-effectiveness of **3-monthly versus 6-monthly monitoring** of well-controlled type 2 diabetes patients: a pragmatic randomised controlled patient-preference equivalence trial in primary care (EFFIMODI study). Diabetes Obes Metab. 2014 Mar 17.

Wernicke JF, et al. A randomized controlled trial of **duloxetine** in diabetic peripheral **neuropathic** pain. Neurology. 2006 Oct 24;67(8):1411-20. (InfoPOEMs: In this study, duloxetine (Cymbalta) 60 mg daily was more effective than placebo in reducing pain from neuropathy in pts with diabetes. Higher doses of duloxetine didn't provide much additional benefit. The biases in this study favor treatment, so it is likely that the real benefit is less than what these investigators observed. Finally, we don't know if duloxetine is any more effective than other treatments used for painful diabetic neuropathy. (LOE = 2b-))

Wentworth JM, Burton P, Laurie C, et al. Five-Year Outcomes of a Randomized Trial of **Gastric Band Surgery** in Overweight but Not Obese People With Type 2 Diabetes. Diabetes Care. 2017 Feb 19.

Wernroth ML, Svennblad B, Fall K, et al. **Dog Exposure** During the First Year of Life and Type 1 Diabetes in Childhood. JAMA Pediatr. 2017 May 1

Wexler DJ, Macias-Konstantopoulos W, Forcione DG, et al. Case 23-2018: A 36-Year-Old Man with Episodes of Confusion and Hypoglycemia. N Engl J Med. 2018 Jul 26;379(4):376-385. (insulinoma)

Wharam JF, Zhang F, Eggleston EM, Lu et al. **Diabetes Outpatient Care and Acute Complications** Before and After **High-Deductible Insurance Enrollment**: A Natural Experiment for Translation in Diabetes (NEXT-D) Study. JAMA Intern Med. 2017 Jan 9.

Wharam JF, Lu CY, Zhang F, et al. **High-deductible insurance and delay in care for the macrovascular complications of diabetes**. Ann Intern Med. 2018. [Epub ahead of print]. doi:10.7326/M17-3365

Wherrett DK, Bundy B, Becker DJ, et al, and the Type 1 Diabetes TrialNet GAD Study Group. Antigen-based therapy with **glutamic acid decarboxylase (GAD) vaccine** in patients with recent-onset type 1 diabetes: a randomised double-blind trial. Lancet 2011; published online June 27. DOI:10.1016/S0140-6736(11)60895-7.

White JS, Hamad R, Li X, et al. **Long-term effects of neighbourhood deprivation** on diabetes risk: quasi-experimental evidence from a refugee dispersal policy in Sweden. Lancet Diabetes Endocrinol. 2016 Apr 27.

White J, Swerdlow DI, Preiss D, et al. Association of **lipid fractions** with risks for coronary artery disease and diabetes [online August 3, 2016].JAMA Cardiol. doi:10.1001 /jamacardio.2016.1884.

White JS, Hamad R, Li X, et al. **Long-term effects of neighbourhood deprivation** on diabetes risk: quasi-experimental evidence from a refugee dispersal policy in Sweden. Lancet Diabetes Endocrinol. 2016 Jun;4(6):517-24.

White NH, Sun W, Cleary PA, et al. Effect of Prior Intensive Therapy in Type 1 Diabetes Mellitus on 10-year Progression of **Retinopathy** in the **DCCT/EDIC**: Comparison of Adults and Adolescents. Diabetes. 2010 Feb 11.

White SL, Pasupathy D, Sattar N, et al; UPBEAT Consortium. Metabolic profiling of **gestational diabetes** in obese women during pregnancy. Diabetologia. 2017 Aug 1.

White WB, Cannon CP, Heller SR, et al. **Alogliptin** after acute coronary syndrome in patients with type 2 diabetes. (**EXAMINE**) N Engl J Med 2013; DOI:10.1056/NEJMoa1305889. Available here.

White WB, Jalil F, Cushman WC, et al. Average Clinician-Measured **Blood Pressures and Cardiovascular Outcomes** in Patients With Type 2 Diabetes Mellitus and Ischemic Heart Disease in the **EXAMINE** Trial. J Am Heart Assoc. 2018 Oct 16;7(20):e009114.

White WB, Kupfer S, Zannad F, et al; **EXAMINE** Investigators. Cardiovascular Mortality in Patients With Type 2 Diabetes and **Recent Acute Coronary Syndromes** From the EXAMINE Trial. Diabetes Care. 2016 Jun 11. (alogliptin)

Whitten JS. **Liraglutide** (Saxenda) for **Weight Loss**. Am Fam Physician. 2016 Jul 15;94(2):161-6.

Wicklow BA, Sellers EAC, Sharma AK, et al. Association of Gestational Diabetes and Type 2 Diabetes Exposure In Utero With the Development of Type 2 Diabetes in First Nations and Non-First Nations Offspring. JAMA Pediatr. 2018 Jun 11.

Wiberg S, Hassager C, Schmidt H, et al. **Neuroprotective** Effects of the Glucagon-Like Peptide-1 Analog **Exenatide** After Out-of-Hospital Cardiac Arrest: A Randomized Controlled Trial. Circulation. 2016 Nov 12.

Wild SH, Hanley J, Lewis SC, et al. **Supported Telemonitoring** and Glycemic Control in People with Type 2 Diabetes: The Telescot Diabetes Pragmatic Multicenter Randomized Controlled Trial. PLoS Med. 2016 Jul 26;13(7):e1002098.

Wilding JP, Hardy K. **Glucagon-like peptide-1 analogues** for type 2 diabetes. BMJ. 2011 Feb 16;342:d410. doi: 10.1136/bmj.d410.

Wilding JP, Woo V, Soler NG, Pahor A, Sugg J, Rohwedder K, et al. Long-term efficacy of **dapagliflozin** in patients with type 2 diabetes mellitus receiving high doses of insulin. A randomized trial. Ann Intern Med. 2012;156: 405-15.

Wilding JP, Ferrannini E, Fonseca VA, et al. Efficacy and safety of **ipragliflozin** in patients with type 2 diabetes inadequately controlled on metformin: a dose-finding study. Diabetes Obes Metab. 2012 Nov 19.

Wilding JP, Charpentier G, Hollander P, et al. Efficacy and safey of **canagliflozin** in patients with type 2 diabetes mellitus inadequately controlled with metformin and sulphonylurea: a randomised trial. Int J Clin Pract. 2013 Dec;67(12):1267-1282.

Wile DJ and Toth C. Association of metformin, elevated homocysteine, and methylmalonic acid levels and clinically worsened diabetic peripheral neuropathy. Diabetes Care 2010 Jan; 33:156. (depressed **vitamin B12,** cobalamin levels)

Willi SM, Miller KM, DiMeglio LA, et al; T1D Exchange Clinic Network. **Racial-ethnic disparities** in management and outcomes among children with type 1 diabetes. Pediatrics. 2015 Mar;135(3):424-34.

Williams T, Mortada R, Porter S. Diagnosis and Treatment of **Polycystic Ovary Syndrome**. Am Fam Physician. 2016 Jul 15;94(2):106-13.

Williams R;de Vries F;Kothny W;Serban C;Lopez-Leon. **Cardiovascular safety** of **vildagliptin** in patients with type 2 diabetes: A European multi-database, non-interventional post-authorization safety study. Diabetes Obes Metab. 2017 Mar 24.

Williamson JD, Launer LJ, Bryan RN, et al. **Cognitive Function and Brain Structure** in Persons With Type 2 Diabetes Mellitus After Intensive Lowering of Blood Pressure and Lipid Levels: A Randomized Clinical Trial. JAMA Intern Med. 2014 Feb 3.

Wilson Jennifer F. **In the Clinic: Diabetic Ketoacidosis**. Ann Intern Med January 5, 2010 152:ITC1-1; doi:10.1059/0003-4819-152-1-201001050-01001.

Wilson Jennifer F.. In the Clinic: The **Polycystic Ovary Syndrome**. Ann Intern Med February 1, 2011 154:ITC2-1.

Wimot EG, Edwardson CL, Achana FA, et al. **Sedentary time in adults** and the association with diabetes, cardiovascular disease and death: Systematic review and meta-analysis. Diabetologia 2012; 55:2895-2905.

Winkelmayer WC, Setoguchi S, Levin R, Solomon DH. Comparison of **Cardiovascular Outcomes in Elderly Patients With Diabetes Who Initiated Rosiglitazone vs Pioglitazone Therapy**. Arch Intern Med. 2008 Nov 24;168(21):2368-75. Our findings from a large population-based cohort of US seniors are compatible with an increased risk of all-cause mortality and congestive heart failure in patients initiating therapy with rosiglitazone compared with similar patients initiating therapy with pioglitazone.

Wise J. **The wrong diabetes: how C peptide testing might help**. BMJ. 2019 Jun 25;365:l4352.

Wittenbecher C, Kuxhaus O, Boeing H, et al. Associations of **short stature and components of height** with incidence of type 2 diabetes: mediating effects of cardiometabolic risk factors. Diabetologia. 2019 Sep 9. doi:10.1007/s00125-019-04978-8.

Wiviott SD, Raz I, Bonaca MP, et al; **DECLARE–TIMI 58** Investigators. **Dapagliflozin and Cardiovascular Outcomes in Type 2 Diabetes**. N Engl J Med. 2018 Nov 10.

Wong CA, et al. Effect of **financial incentives** on **glucose monitoring adherence** and glycemic control among adolescents & young adults with type 1 diabetes: randomized clinical trial [online Oct 23, 2017].JAMA Pediatr. doi:10.1001 /jamapediatrics.2017.3233

Wong MG, Perkovic V, Chalmers J, et al. ADVANCE-ON Collaborative Group. **Long-term Benefits of Intensive Glucose** Control for **Preventing End-Stage Kidney Disease**: **ADVANCE-ON**. Diabetes Care. 2016 Mar 22.

Wong TY, Simó R, Mitchell P. **Fenofibrate** - a potential systemic treatment for **diabetic retinopathy**? Am J Ophthalmol. 2012 Jul;154(1):6-12.

Woo VC. A Review of the Clinical Efficacy and Safety of **Insulin Degludec and Glargine 300 U/mL** in the Treatment of Diabetes Mellitus. Clin Ther. 2017 Feb 7.

Wood GC, Mirshahi T, Still CD, Hirsch AG. Association of **DiaRem Score** With Cure of Type 2 Diabetes Following **Bariatric Surgery**. JAMA Surg. 2016 Apr 20.

Woodmansey C, McGovern AP, McCullough KA, et al. Incidence, demographics, and clinical characteristics of **diabetes of the exocrine pancreas (type 3c)**: a retrospective cohort study. Diabetes Care 2017;dc170542.

Wright AD, Cull CA, Macleod KM, Holman RR; for the UKPDS Group. Hypoglycemia in Type 2 diabetic patients randomized to and maintained on monotherapy with diet, sulfonylurea, metformin, or insulin for 6 years from diagnosis: UKPDS73. J Diabetes Complications. 2006 Nov-Dec;20(6):395-401. More on basal insulin reported hypoglycemia (3.8% per year) than diet (0.1%), sulfonylurea (1.2%), or metformin (0.3%) therapy, but less than on basal and prandial insulin (5.3%) (all P<.0001). **Low hypoglycemia rates** seen during the first 6 years of intensive glucose lowering therapy in Type 2 diabetes are unlikely to have a major impact on attempts to achieve guideline glycemic targets when sulfonylurea, metformin, or insulin are used as monotherapy.

Wright A, Burden AC, Paisey RB, Cull CA, Holman RR; U.K. Prospective Diabetes Study Group. Sulfonylurea inadequacy: efficacy of addition of insulin over 6 years in patients with type 2 diabetes in the U.K. Prospective Diabetes Study (**UKPDS 57**). Diabetes Care. 2002 Feb;25(2):330-6.

Wright AK, Kontopantelis E, Emsley R, et al. **Cardiovascular Risk and Risk Factor Management** in Type 2 Diabetes: A Population-Based Cohort Study Assessing Sex Disparities. Circulation. 2019 Apr 15.

Wright AK, Kontopantelis E, Emsley R, et al. Life Expectancy and Cause-Specific **Mortality in Type 2 Diabetes**: A Population-Based Cohort Study Quantifying Relationships in **Ethnic Subgroups**. Diabetes Care. 2016 Dec 20.

Writing Group for the TRIGR Study Group, Knip M, Åkerblom HK, et al. Effect of **Hydrolyzed Infant Formula** vs Conventional Formula on Risk of Type 1 Diabetes: The TRIGR Randomized Clinical Trial. JAMA. 2018 Jan 2;319(1):38-48.

Writing Committee for the Type 1 Diabetes **TrialNet Oral Insulin** Study Group, Krischer JP, Schatz DA, Bundy B, et al. Effect of **Oral Insulin** on **Prevention of Diabetes in Relatives of Patients** With Type 1 Diabetes: A Randomized Clinical Trial. JAMA. 2017 Nov 21;318(19):1891-1902.

Wu HY, Peng YS, Chiang CK, et al. Diagnostic Performance of Random Urine Samples Using **Albumin Concentration vs Ratio of Albumin to Creatinine** for Microalbuminuria Screening in Patients With Diabetes Mellitus: A Systematic Review and Meta-analysis. JAMA Intern Med. 2014 May 5.

Wu JW, Azoulay L, Majdan A, et al. Long-Term Use of **Long-Acting Insulin Analogs and Breast Cancer** Incidence in Women With Type 2 Diabetes. J Clin Oncol. 2017 Sep 27:JCO2017734491.

Wu L, Norman G, Dumville JC, O'Meara S, Bell-Syer SE. **Dressings for treating foot ulcers** in people with diabetes: an overview of systematic reviews. Cochrane Database Syst Rev. 2015 Jul 14;7:CD010471. There is currently no robust evidence for differences between wound dressings for any outcome in foot ulcers in people with diabetes (treated in any setting). Practitioners may want to consider the unit cost of dressings, their management properties & patient preference when choosing dressings.

Wu RR, Jin H, Gao K, et al. Metformin for treatment of **antipsychotic-induced amenorrhea and weight gain** in women with first-episode schizophrenia: a double-blind, randomized, placebo-controlled study. Am J Psychiatry. 2012 Aug 1;169(8):813-21.

Wu SS, Yen HH. Images in clinical medicine. Pneumatosis cystoides intestinalis (due to **acarbose**). N Engl J Med. 2011 Aug 25;365(8):e16.

Wu S, Chai S, Yang J, et al. Gastrointestinal Adverse Events of **Dipeptidyl Peptidase 4 Inhibitors** in Type 2 Diabetes: A Systematic Review and Network Meta-analysis. Clin Ther. 2017 Aug 18.

Wysham C, Bhargava A, Chaykin L, et al. Effect of insulin **degludec vs insulin glargine** U100 on hypoglycemia in patients with type 2 diabetes: the **SWITCH 2** randomized clinical trial.JAMA. doi:10.1001/jama.2017.7117

Wysham CH, Rosenstock J, Vetter ML, et al. Efficacy and tolerability of the **new autoinjected suspension of exenatide once weekly** versus exenatide twice daily in patients with type 2 diabetes. Diabetes Obes Metab. 2017 Jul 7.

Xiang AH, Chow T, Martinez MP, et al. **Hemoglobin A1c Levels During Pregnancy and Risk of Autism** Spectrum Disorders in Offspring. JAMA. 2019 Jun 9.

Xiang AH, Wang X, Martinez MP, et al. Association of **maternal diabetes with autism** in offspring. JAMA. 2015 Apr 14;313(14):1425-34.

Xiang AH, Wang X, Martinez MP, et al. **Maternal Type 1 Diabetes and Risk of Autism** in Offspring. JAMA. 2018 Jun 23.

Xie J, Ikram MK, Cotch MF, et al. Association of **Diabetic Macular Edema** and Proliferative Diabetic Retinopathy With Cardiovascular Disease: A Systematic Review and Meta-analysis. JAMA Ophthalmol. 2017 May 4

Xie Y, Agiro A, Bowman K, DeVries A. **Lowering Cost Share May Improve Rates of Home Glucose Monitoring** Among Patients with Diabetes Using Insulin. J Manag Care Spec Pharm. 2017 Aug;23(8):884-891.

Xie Y, Bowe B, Li T, et al. **Higher blood urea nitrogen** is associated with increased risk of incident diabetes mellitus. Kidney Int. 2017 Dec 7.

Xing Z, Tang L, Chen J, et al. Association of **predicted lean body mass and fat mass with cardiovascular events** in patients with type 2 diabetes mellitus. CMAJ. 2019 Sep 23;191(38):E1042-E1048.

Xu G, Liu B, Sun Y, et al. **Prevalence of diagnosed type 1 and type 2 diabetes among US adults in 2016 and 2017**: population based study. BMJ. 2018 Sep 4;362:k1497.

Xu H, Verre MC. **Type 2 Diabetes Mellitus in Children.** Am Fam Physician. 2018; 98(9): 590-594.

Xu Y, Tan DHY, Lee JY Evaluating the impact of **self-monitoring of blood glucose frequencies on glucose control** in patients with type 2 diabetes who do not use insulin: A systematic review and meta-analysis. Int J Clin Pract. 2019 Apr 29:e13357.

Xu Y, Wang L, He J, et al; 2010 China Noncommunicable Disease Surveillance Group. Prevalence and control of **diabetes in Chinese** adults. JAMA. 2013 Sep 4;310(9):948-59.

Yabiku K, Mutoh A, et al. Effects of **Oral Antidiabetic Drugs on Changes in the Liver-to-Spleen Ratio** on Computed Tomography and Inflammatory Biomarkers in Patients With Type 2 Diabetes and Nonalcoholic Fatty Liver Disease. Clin Ther. 2017 Feb 6.

Yaffe K, Falvey C, Hamilton N, et al. Diabetes, Glucose Control, and 9-Year **Cognitive Decline** Among Older Adults Without Dementia Diabetes and Risk of Cognitive Decline. Arch Neurol. 2012 Jun 18:1-6.

Yaffe K, Falvey CM, Hamilton N, Harris TB, et al. Association between **hypoglycemia and dementia** in a biracial cohort of older adults with diabetes mellitus. JAMA Intern Med. 2013 Jul 22;173(14):1300-6.

Yaghi S, Furie KL, Viscoli CMet al. **Pioglitazone Prevents Stroke in Patients with a Recent TIA or Ischemic Stroke**: A Planned Secondary Analysis of the **IRIS** Trial. Circulation. 2017 Oct 30.

Yamada T, Shojima N, Noma H, et al. **Sodium-glucose co-transporter-2 inhibitors as add-on therapy to insulin for type 1** diabetes mellitus: Systematic review and meta-analysis of randomized controlled trials. Diabetes Obes Metab. 2018 Feb 16.

Yamada T, Kamata R, Ishinohachi K, et al. **Biosimilar vs originator insulins**: Systematic review and meta-analysis. Diabetes Obes Metab. 2018 Mar 14.

Yamaoka K, Tango T. Efficacy of **lifestyle education** to prevent type 2 diabetes: a meta-analysis of randomized controlled trials. Diabetes Care. 2005 Nov;28(11):2780-6.

Yang CP, Li CI, Liu CS, et al. Variability of **fasting plasma glucose** increased risks of diabetic **polyneuropathy** in T2DM. Neurology. 2017 Mar 7;88(10):944-951.

Yang JJ, Yu D, Wen W, et al. Association of Diabetes With **All-Cause and Cause-Specific Mortality in Asia**: A Pooled Analysis of More Than 1 Million Participants. JAMA Netw Open. 2019 Apr 5;2(4):e192696.

Yang W, Ma J, Yuan G, et al. Determining the **optimal fasting glucose target** for patients with type 2 diabetes: results of the multicentre, open-label, randomized-controlled FPG GOAL trial. Diabetes Obes Metab. 2019 Apr 1

Yang X, So WY, Ma RC, et al. Low HDL Cholesterol, **Metformin Use and Cancer** Risk in Type 2 Diabetes – the Hong Kong Diabetes Registry. Diabetes Care. 2010 Oct 27.

Yang XJ, Zou SF, Xu Y, et al. The influence of **intensive lifestyle intervention** on patients with isolated impaired fasting glucose: a meta-analysis. J Adv Nurs. 2016 May 29.

Yang Y, Hu X, Zhang Q, Zou R. Diabetes mellitus and **risk of falls** in older adults: a systematic review and meta-analysis. Age Ageing. 2016 Nov;45(6):761-767.

Yassin A, Haider A, Haider KS, et al. **Testosterone Therapy in Men With Hypogonadism Prevents Progression** From Prediabetes to Type 2 Diabetes: Eight-Year Data From a Registry Study. Diabetes Care. 2019 Mar 12.

Yau CK, Eng C, Cenzer IS, Boscardin WJ, Rice-Trumble K, Lee SJ. **Glycosylated hemoglobin** and functional decline in community-dwelling nursing home-eligible **elderly** adults with diabetes mellitus. J Am Geriatr Soc. 2012 Jul;60(7):1215-21.

Yeboah P, Hsu FC, Bertoni AG, Yeboah J. **Body Mass Index, Change in Weight, Body Weight Variability and Outcomes** in Type 2 Diabetes Mellitus (from the ACCORD Trial). Am J Cardiol. 2019 Feb 15;123(4):576-581.

Yeh HC, Brown TT, Maruthur N, et al. Comparative Effectiveness and Safety of Methods of **Insulin Delivery and Glucose Monitoring** for Diabetes Mellitus: A Systematic Review and Meta-analysis. Ann Intern Med. 2012 Jul 10:E-508.

Yeoh E, Choudhary P, Nwokolo M, et al. Interventions That **Restore Awareness of Hypoglycemia** in Adults With Type 1 Diabetes: A Systematic Review and Meta-analysis. Diabetes Care. 2015 Aug;38(8):1592-609.

Yeung Wing-Chi G, Rawlinson William D, Craig Maria E. **Enterovirus infection** and type 1 diabetes mellitus: systematic review and meta-analysis of observational molecular studies. BMJ 2011;342:doi:10.1136/bmj.d35 (3 Feb 2011)

Yi Y, Norris AW, Wang K, et al. **Abnormal Glucose Tolerance** in Infants and Young Children with Cystic Fibrosis. Am J Respir Crit Care Med. 2016 Jul 22

Yin M, Zhou J, Gorak EJ, Quddus F. **Metformin Is Associated With Survival Benefit in Cancer** Patients With Concurrent Type 2 Diabetes: A Systematic Review and Meta-Analysis. Oncologist. 2013 Nov 20.

Yki-Jarvinen Hannele, Drug Therapy: T**hiazolidinedione**s. N Engl J Med 2004;351:1106-18.

Yoon S, Cho H, Kim J, et al. **Brain changes in overweight/obese** and normal-weight adults with type 2 diabetes mellitus. Diabetologia. 2017 Apr 27.

You WP, Henneberg M. Type 1 **diabetes prevalence increasing globally and regionally**: the role of natural selection and life expectancy at birth. BMJ Open Diabetes Res Care. 2016 Mar 2;4(1):e000161.

Young LA, Buse JB, Weaver MA, et al; Monitor Trial Group. **Glucose self-monitoring in** non–insulin-treated type 2 diabetes in primary care settings: a randomized trial [published online June 10, 2017].JAMA Intern Med. doi:10.1001 /jamainternmed.2017.1233

Young LH, Wackers FJ, Chyun DA, et al. Cardiac outcomes after **screening** for asymptomatic coronary artery disease in patients with type 2 diabetes: the DIAD study: a randomized controlled trial. JAMA. 2009 Apr 15;301(15):1547-55.

Young LH, Viscoli CM, Curtis JP, et al, for the **IRIS** investigators. **Cardiac outcomes after ischemic stroke or transient ischemic attack**: effects of **pioglitazone** in patients with insulin resistance without diabetes mellitus. Circulation. 2017;135:1882–1893.

Young LH, Viscoli CM, Curtis JP, et al. **Cardiac Outcomes** After Ischemic Stroke or Transient Ischemic Attack: Effects of **Pioglitazone** in Patients With Insulin Resistance Without Diabetes Mellitus. (IRIS) Circulation. 2017 May 16;135(20):1882-1893.

Young LH, Viscoli CM, Schwartz GG, et al. **Heart Failure After Ischemic Stroke or TIA in Insulin-Resistant Patients Without Diabetes Treated with Pioglitazone**. Circulation. 2018 Jun 22.

Yska JP, van Roon EN, de Boer A, et al. **Remission of Type 2 Diabetes** Mellitus in Patients After Different Types of **Bariatric Surgery**: A Population-Based Cohort Study in the United Kingdom. JAMA Surg. 2015 Sep 30:1-8.

Yu CH. "Safety" technology: a hidden cause of **diabetic ketoacidosis**. CMAJ. 2012 Mar 20;184(5):557-8.

Yu M, Van Brunt K, Varnado OJ, Boye KS. Patient-reported outcome results in patients with type 2 diabetes treated with once-weekly dulaglutide: data from the AWARD phase III clinical trial programme. Diabetes Obes Metab. 2016 Apr;18(4):419-24.

Yu MG, Keenan HA, Shah HS, et al. **Residual β cell function and monogenic variants** in long-duration type 1 diabetes patients. J Clin Invest. 2019 Jul 2;130.

Yu OH, Filion KB, Azoulay L, et al. **Incretin-Based Drugs** and the **Risk of Congestive Heart Failure**. Diabetes Care. 2014 Sep 9. pii: DC_141459.

Yu X, et al. The effectiveness of **traditional Chinese medicine-based lifestyle interventions** on biomedical, psychosocial, and behavioral outcomes in individuals with type 2 diabetes: systematic review with meta-analysis. Int J Nurs Stud. 2018 Apr;80:165-180.

Yu X, Jiang D, Wang J, et al. **Metformin prescription and aortic aneurysm**: systematic review and meta-analysis. Heart. 2019 Apr 1.

Yuan T, Zhao W, Wang L, et al. Continuous Subcutaneous Insulin Infusion as an Effective Method of **Desensitization** Therapy for Diabetic Patients with **Insulin Allergy**: A 4-year Single-Center Experience. Clin Ther. 2016 Oct 25.
Yuan Z;DeFalco FJ;Ryan PB;et al. **Risk of lower extremity amputations** in people with type 2 diabetes mellitus treated with **sodium-glucose co-transporter-2 inhibitors** in the USA: A retrospective cohort study. Diabetes Obes Metab. 2017 Sep 12.
Yuqian Bao, Xiaojing Ma, Huating Li et al. **Glycated haemoglobin A1c** for **diagnosing diabetes** in Chinese population: cross sectional epidemiological survey; BMJ 2010;340.
Zaccardi F, Htike ZZ, Webb DR, Khunti K, Davies MJ. Benefits and harms of **once-weekly glucagon-like peptide-1 receptor agonist** (dulaglutide, exenatide, taspoglutide) treatments. A systematic review and network meta-analysis. Ann Intern Med. 2016;164:•••-••. doi:10.7326/M15-2722
Zaccardi F, Davies MJ, Dhalwani NN, et al. Trends in hospital **admissions** for **hypoglycaemia** in England: a retrospective, observational study. Lancet Diabetes Endocrinol. 2016 Aug;4(8):677-85.
Zaccardi F, Dhalwani NN, Dales J, et al. Comparison of **glucose-lowering agents after dual therapy failure in type 2 diabetes**: A systematic review and network meta-analysis of randomized controlled trials. Diabetes Obes Metab. 2017 Dec 5.
Zaharia OP, Strassburger K, Strom A, et al. Risk of diabetes-associated **diseases in subgroups of patients with recent-onset diabetes**: a 5-year follow-up study. Lancet Diabetes Endocrinol. 2019 Sep;7(9):684-694.
Zanders MM, Haak HR, van Herk-Sukel MP, et al. Impact of **cancer on adherence to glucose-lowering drug treatment** in individuals with diabetes. Diabetologia. 2015 Feb 1.
Zang L, Liu Y, et al. Efficacy and safety of **liraglutide versus sitagliptin, both in combination with metformin**, in Chinese patients with type 2 diabetes: a 26-week, open-label, randomised, active comparator clinical trial. Diabetes Obes Metab. 2016 Apr 7.
Zeller M, Danchin N, Simon D, et al. French Registry of Acute ST-Elevation and Non-ST-Elevation Myocardial Infarction investigators. Impact of Type of Preadmission **Sulfonylureas** on Mortality and Cardiovascular Outcomes in Diabetic Patients with Acute Myocardial Infarction. J Clin Endocrinol Metab. 2010 Aug 11.
Zelniker TA, Braunwald E. Cardiac and Renal Effects of Sodium-Glucose Co-Transporter 2 Inhibitors in Diabetes: JACC State-of-the-Art Review. J Am Coll Cardiol. 2018 Jul 24.
Zelniker TA, Wiviott SD, Raz I, et al. Comparison of the Effects of **Glucagon-Like Peptide Receptor Agonists and Sodium-Glucose Co-Transporter 2 Inhibitors** for Prevention of Major Adverse Cardiovascular and Renal Outcomes in Type 2 Diabetes Mellitus: A Systematic Review and Meta-Analysis of Cardiovascular Outcomes Trials. Circulation. 2019 Feb 21.
Zelniker TA, Wiviott SD, Raz I, et al. **SGLT2 inhibitors for primary and secondary prevention of cardiovascular and renal outcomes in type 2 diabetes**: a systematic review and meta-analysis of cardiovascular outcome trials. Lancet. 2018 Nov 9.
Zhang C, et al. A prospective study of pregravid physical activity and **sedentary behaviors** in relation to the risk for **gestational** diabetes mellitus. Arch Intern Med. 2006 Mar 13;166(5):543-8.
Zhang H, Goldberg SI, Hosomura N, et al. **Lifestyle Counseling and Long-term Clinical Outcomes** in Patients With Diabetes. Diabetes Care. 2019 Aug 1.
Zhang J, Chi H, Wang T, et al. Effects of **Orthostatic Hypotension on Cognition** in Type 2 Diabetes Mellitus. Ann Neurol. 2019 Aug 9.
Zhang L, Li Y, Wang C, et al. **Early menarche is associated with an increased risk** of type 2 diabetes in rural Chinese women and is partially mediated by BMI: the Henan Rural Cohort Study. Menopause. 2019 Jul 29.
Zhang L, Tamilia M. **Euglycemic diabetic ketoacidosis associated with the use of a sodium-glucose cotransporter-2 inhibitor**. CMAJ. 2018 Jun 25;190(25):E766-E768.
Zhang X, Harmsen WS, Mettler TA, et al. Continuation of **metformin use after a diagnosis of cirrhosis** significantly improved survival of patients with diabetes. Hepatology. 2014 May 3.
Zhang Xinzhi; Saaddine Jinan B.; Chou Chiu-Fang; et al. Prevalence of **Diabetic Retinopathy** in the United States, 2005-2008. JAMA. 2010;304(6):649-656.
Zhang Y, Gong Y, Xue H, et al. Vitamin D and gestational diabetes mellitus: a systematic review based on data free of Hawthorne effect. BJOG. 2017 Dec 15.
Zhang Y, Pan XF, Chen J, et al. Combined **lifestyle factors and risk of incident type 2 diabetes** and prognosis among individuals with type 2 diabetes: a systematic review and meta-analysis of prospective cohort studies. Diabetologia. 2019 Sep 4.
Zhang ZJ, Zheng ZJ, Kan H, et al. **Reduced risk of colorectal cancer with metformin** therapy in patients with type 2 diabetes: a meta-analysis. Diabetes Care. 2011 Oct;34(10):2323-8.
Zhang ZJ, Zheng ZJ, Shi R, Su Q, Jiang Q, Kip KE. **Metformin for Liver Cancer Prevention** in Patients with Type 2 Diabetes: A Systematic Review and Meta-Analysis. J Clin Endocrinol Metab. 2012 Apr 20.
Zhao D, Luo S, Xu W, et al. Efficacy and Safety of **Hyperbaric Oxygen** Therapy Used in Patients **With Diabetic Foot**: A Meta-Analysis of Randomized Clinical Trials. Clin Ther. 2017 Sep 18.
Zhao L, Sheng X, Zhou S, et al. **Metformin versus insulin for gestational diabetes** mellitus: a meta-analysis. Br J Clin Pharmacol. 2015 Apr 29.
Zhao W, Katzmarzyk PT, Horswell R, et al. **Aggressive blood pressure control increases coronary heart disease** risk among diabetic patients. Diabetes Care 2013.
Zhao W, Katzmarzyk PT, Horswell R, et al.. **Body mass index** and the risk of all-cause **mortality** in patients with type 2 diabetes mellitus. *Circulation*. 2014;130:2143–2151.
Zhang X, et al. Legacy Effect of **Intensive Blood Glucose Control on Cardiovascular Outcomes** in Patients With Type 2 Diabetes and Very High Risk or Secondary Prevention of Cardiovascular Disease: A Meta-analysis of Randomized Controlled Trials. Clin Ther. 2018 Apr 12.
Zheng F, Yan L, Yang Z, et al. **HbA(1c), diabetes and cognitive decline**: the English Longitudinal Study of Ageing. Diabetologia. 2018 Jan 25.
Zheng SL, Roddick AJ, Aghar-Jaffar R, et al. Association Between Use of **Sodium-Glucose Cotransporter 2 Inhibitors, Glucagon-like Peptide 1 Agonists, and Dipeptidyl Peptidase 4 Inhibitors With All-Cause Mortality** in Patients With Type 2 Diabetes: A Systematic Review and Meta-analysis. JAMA. 2018 Apr 17;319(15):1580-1591.
Zhou JB, Bai L, Wang Y, et al. The benefits and risks of **DPP4-inhibitors vs. sulfonylureas** for patients with type 2 diabetes: accumulated evidence from randomised controlled trials. Int J Clin Pract. 2015 Dec 28.
Zhou W, Sailani MR, Contrepois K, et al. **Longitudinal multi-omics of host-microbe dynamics** in prediabetes. Nature. 2019 May;569(7758):663-671.
Zhou X, Pang Z, Gao W, et al. Performance of an A1C and **Fasting Capillary Blood Glucose** Test for Screening Newly Diagnosed Diabetes and Pre-Diabetes Defined by an Oral Glucose Tolerance Test in Qingdao, China. Diabetes Care. 2010 Mar;33(3):545-50. Epub 2009 Dec 10.
Zhou Z, Lindley RI, Rådholm K, et al. **Canagliflozin and Stroke** in Type 2 Diabetes Mellitus. Stroke. 2018 Dec 28:STROKEAHA118023009.
Zhu B, Ge X, Huang K, et al. **Folic Acid Supplement Intake in Early Pregnancy Increases Risk of Gestational Diabetes Mellitus**: Evidence From a Prospective Cohort Study. Diabetes Care. 2016 Mar;39(3):e36-7.
Zhu Q, Tong Y, Wu T, et al. Comparison of the Hypoglycemic Effect of **Acarbose** Monotherapy in Patients With Type 2 Diabetes Mellitus Consuming an **Eastern or Western Diet**: A Systematic Meta-analysis. Clin Ther. 2013 Apr 18.
Zhu Y, Sidell MA, Arterburn D, et al. **Racial/Ethnic Disparities** in the Prevalence of Diabetes and Prediabetes by BMI: Patient Outcomes Research To Advance Learning (PORTAL) Multisite Cohort of Adults in the U.S. Diabetes Care. 2019 Sep 19. doi: 10.2337/dc19-0532.
Zhu Z, Shen Z, Lu Y, Zhong S, Xu C. Increased risk of **bladder cancer with pioglitazone** therapy in patients with diabetes: A meta-analysis. Diabetes Res Clin Pract. 2012 Jun 15.
Ziegler D, Low PA, Litchy WJ, et al. Efficacy and safety of antioxidant treatment with **α-lipoic acid** over 4 years in **diabetic polyneuropathy**: the **NATHAN 1** trial. Diabetes Care. 2011 Sep;34(9):2054-60.
Ziegler AG, Rewers M, Simell O, et al. **Seroconversion to multiple islet autoantibodies** and risk of progression to diabetes in children. JAMA. 2013;309 (23):2473-2479.
Zinman B, Bhosekar V, Busch R, et al. **Semaglutide once-weekly as add-on to SGLT-2 inhibitor therapy** in type 2 diabetes (SUSTAIN 9): a randomised, placebo-controlled trial. Lancet Diabetes Endocrinol 2019; published online March 1.
Zinman B, Harris SB, Neuman J, et al. Low-dose combination therapy with **rosiglitazone and metformin** to prevent type 2 diabetes mellitus (**CANOE** trial): A double-blind randomised controlled study. Lancet 2010; DOI: 10.1016/S0140-6736(10)60746-5.
Zinman B, Wanner C, Lachin JM, et al; **EMPA-REG OUTCOME**. **Empagliflozin**, Cardiovascular Outcomes, and Mortality in Type 2 Diabetes. N Engl J Med. 2015 Sep 17.
Zinman B, Inzucchi SE, Lachin JM, et al. **Empagliflozin** and **Cerebrovascular Events** in Patients With Type 2 Diabetes Mellitus at High Cardiovascular Risk. (**Empa-Reg**) Stroke. 2017 May;48(5):1218-1225.
Zinman B, Marso SP, Poulter NR, et al. Day-to-day fasting glycaemic variability in **DEVOTE**:associations with **severe hypoglycaemia and cardiovascular outcomes (DEVOTE 2).** Diabetologia. 2017 Sep 15
Zoungas S et al. **Severe hypoglycemia** and risks of vascular events and death (**Advance**). N Engl J Med 2010 Oct 7; 363:1410. During a median follow-up period of 5 years, 231 patients (2.1%) had at least one severe hypoglycemic episode; 150 had been assigned to intensive glucose control (**2.7%** of the 5571 patients in that group), and 81 had been assigned to standard glucose control (1.5% of the 5569 patients in that group).
Zoungas S, Chalmers J, Neal B, et al; the **ADVANCE-ON** Collaborative Group. **Follow-up of Blood-Pressure Lowering and Glucose Control** in Type 2 Diabetes. N Engl J Med. 2014 Sep 19.
Zoungas S et al. Effects of **intensive glucose control on microvascular outcomes** in patients with type 2 diabetes: a meta-analysis of individual participant data from randomised controlled trials. Lancet [Epub ahead of print] 29 March 2017.
Zou H, Zhou B, Xu G. **SGLT2 inhibitors**: a novel choice for the combination therapy in diabetic kidney disease. Cardiovasc Diabetol. 2017 May 16;16(1):65.

Tuomilehto J, Lindstrom J, Eriksson JG, et al.; Finnish Diabetes Prevention Study Group. Prevention of type 2 diabetes mellitus by changes in lifestyle among subjects with impaired glucose tolerance. N Engl J Med. 2001 May 3;344(18):1343-50.
Sigal RJ, Kenny GP, Boule NG, et al. Effects of aerobic training, resistance training, or both on glycemic control in type 2 diabetes: a randomized trial. Ann Intern Med. 2007 Sep 18;147(6):357-69.
Summary for patients in: Ann Intern Med. 2007 Sep 18;147(6):I16. Either aerobic or resistance training alone improves glycemic control in type 2 diabetes, but the improvements are greatest with **combined aerobic and resistance training**.)
Li G, Zhang P, Wang J, et al. The long-term effect of lifestyle interventions to prevent diabetes in the China Da Qing Diabetes Prevention Study: a **20-year follow-up** study. Lancet. 2008 May 24;371(9626):1783-9.
Group-based lifestyle interventions over 6 years can prevent or delay diabetes for up to 14 years after the active intervention. However, whether lifestyle intervention also leads to reduced CVD and mortality remains unclear.
Martínez-González MA, Fuente-Arrillaga CD, et al. Adherence to Mediterranean diet and risk of developing diabetes: prospective cohort study. BMJ. 2008 May 29. [Epub ahead of print]
Coppell Kirsten J, Kataoka Minako, Williams Sheila M, et al. **Nutritional intervention in patients with type 2 diabetes who are hyperglycaemic despite optimised drug treatment—Lifestyle Over and Above Drugs in Diabetes (LOADD) study: randomised controlled trial.**BMJ 2010
Look AHEAD Group. Long-term Effects of a **Lifestyle** Intervention on Weight and Cardiovascular Risk Factors in Individuals With Type 2 Diabetes Mellitus: Four-Year Results of the Look AHEAD Trial. Arch Intern Med. 2010;170(17):1566-1575.

Church TS.; Blair SN.; Cocreham S; et al. Effects of **Aerobic and Resistance Training** on Hemoglobin A1c Levels in Patients With Type 2 Diabetes: A Randomized Controlled Trial(**HART-D**). JAMA. 2010;304(20):2253-2262.
Balducci Stefano; Zanuso Silvano; Nicolucci Antonio; et al. for the Italian Diabetes Exercise Study (**IDES**) Investigators. Effect of an Intensive Exercise Intervention Strategy on Modifiable Cardiovascular Risk Factors in Subjects With Type 2 Diabetes Mellitus: A Randomized Controlled Trial: The Italian Diabetes and Exercise Study (IDES). Arch Intern Med. 2010;170(20):1794-1803.
Tobias DK, Zhang C, van Dam RM, Bowers K, Hu FB. **Physical activity before and during pregnancy** and risk of gestational diabetes mellitus: a meta-analysis. Diabetes Care. 2011 Jan;34(1):223-9.
Chudyk Anna, Petrella Robert J.. Effects of **Exercise** on Cardiovascular Risk Factors in Type 2 Diabetes: A meta-analysis Diabetes Care May 2011 34:1228-1237; doi:10.2337/dc10-1881
Salas-Salvadó J, Bulló M, Babio N, et al.; **PREDIMED** Study Investigators. Reduction in the incidence of type 2 diabetes with the Mediterranean diet: results of the PREDIMED-Reus nutrition intervention randomized trial. Diabetes Care 2011;34:14–19.
Mayo Clinic [website]. ***Mediterranean diet****: choose this heart-healthy diet option.* Rochester, MN: Mayo Clinic; 2010. Available from: www.mayoclinic.com/health/mediterranean-diet/CL00011 . Accessed 2011 May 24.
Estruch R, Ros E, Salas-Salvadó J, et al; the **PREDIMED** Study Investigators. Primary Prevention of Cardiovascular Disease with a **Mediterranean Diet**. N Engl J Med. 2013 Feb 25.
Look AHEAD Research Group. Cardiovascular effects of intensive lifestyle intervention in type 2 diabetes. N Engl J Med 2013. DOI: 10.1056/NEJMoa1212914.
Canada's food guide to healthy eating. Website: **http://www.hc-sc.gc.ca/fn-an/food-guide-aliment/index_e.html**
Health Canada's Fitness and Healthy Living. Website: **http://www.hc-sc.gc.ca/hppb/fitness** ; CADTH Diabetes Self Management Action Plan: http://www.cadth.ca/media/compus/pdf/C1109-Self-Management-Action-Plan-e.pdf
Impact of Intensive Lifestyle and Metformin Therapy on Cardiovascular Disease Risk Factors in the Diabetes Prevention Program. Diabetes Care. 2005 Apr;28(4):888-894.
Charpentier G, Riveline JP, Varroud-Vial M. Management of drugs affecting blood glucose in diabetic patients with renal failure. Diabetes Metab 2000;26 Suppl 4:73-85
Lalau JD and Race JM. Metformin and lactic acidosis in diabetic humans. Diabetes, Obesity and Metabolism 2000;2:131-137.
Lalau JD, Kajbaf F, Bennis Y, et al. Metformin Treatment in Patients With Type 2 Diabetes and Chronic Kidney Disease Stages 3A, 3B, or 4. Diabetes Care. 2018 Jan 5.
Micromedex 2017; Drugs in Pregnancy & Lactation, 10th Ed. Briggs GE,et al. Wilkins;Baltimore, MD.2017.
Hansten & Horn-Drug Interactions 2008.
Rosenstock J. Management of type 2 diabetes mellitus in the elderly. Drugs & Aging 2001;18(1)31-44.
Fisman EZ, Tenenbaum A, et al. Oral antidiabetic treatment in patients with coronary disease: time-related increased mortality on combined glyburide/metformin therapy over a 7.7-year follow-up. Clin Cardiol. 2001 Feb;24(2):151-8.
Gale, EAM. Lessons from the glitazones: a story of drug development. Lancet 2001;357:1870-75.
Moses R, Slobodniuk R, Boyages S, Colagiuri S et al. Effect of repaglinide addition to metformin monotherapy on glycemic control in patients with type 2 diabetes. Diabetes Care 1999 Jan;22(1):119-124
Fonseca V, Rosenstock J, Patwardhan R, Salzman A. Effect of metformin and rosiglitazone combination therapy in patients with type 2 diabetes mellitus. JAMA 2000;283(13):1695-1702.
Einhorn D, et al. Pioglitazone hydrochloride in combination with metformin in the treatment of type 2 diabetes mellitus: a randomized, placebo-controlled study. The pioglitazone 027 study group. Clin Ther 2000 2000;1395-1409.
[1]Rosenstock J; Rood J; Cobitz A; Biswas N; Chou H; Garber A. Initial treatment with rosiglitazone/metformin fixed-dose combination therapy compared with monotherapy with either rosiglitazone or metformin in patients with uncontrolled type 2 diabetes. Diabetes Obes Metab. 2006; 8(6):650-60.
Rosenstock J, Brown A, Fisher J, Jain A et al. Efficacy and safety of acarbose in metformin-treated patients with type 2 diabetes. Diabetes Care 1998;21(12):2050-2055.
Yki-Jarvinen H, Ryysy L, Nikkila K, et al. Comparison of bedtime insulin regimens in patients with type 2 diabetes mellitus: a randomized controlled trial. Ann Intern Med 1999;130:389-96.
Kooy A, de Jager J, Lehert P, Bets D, Wulffelé MG, Donker AJ, Stehouwer CD. Long-term effects of metformin on metabolism and microvascular and macrovascular disease in patients with type 2 diabetes mellitus. Arch Intern Med. 2009 Mar 23;169(6):616-25.
Raskin P, Rendell M, Riddle MC et al. A randomized trial of rosiglitazone therapy in patients with inadequately controlled insulin-treated type 2 diabetes. Diabetes Care 2001 Jul;24(7):1226-32
Krentz AJ, Bailey CJ, Melander A. Thiazolidinediones for type 2 diabetes: new agents reduce insulin resistance but need long term clinical trials. BMJ 2000;321:252-3.
Chehade AM, Mooradian AD. A rational approach to drug therapy of type 2 diabetes mellitus. Drugs 2000;60(1):95-113.
Drug Information Handbook 17th Edition. Lacy CF et al (editors). American Pharmaceutical Association. Lexi-Comp Inc, Hudson Ohio, 2008-2009 edition.
Boctor, MA. Diabetes Mellitus in Therapeutic Choices (3rd edition). Gray, Jean (editor). Canadian Pharmacists Association. Web-com Ltd, Ottawa, ON, 2000.
Management of Type II Diabetes. Clinical Trends in Pharmacy Practice, 3rd issue, 1997 (p46-52).
Campbell IW. Antidiabetic drugs present and future. Drugs 2000; 60 (5): 1017-28.
Rendell MS and Kirchain WR. Pharmacotherapy of Type 2 Diabetes Mellitus. Ann Pharmacother 2000; 34:878-95.
Yki-Jarvinen, H. Management of Type 2 Diabetes Mellitus and cardiovascular risk- lessons from intervention trials. Drugs 2000; 60(5): 975-83.
Meltzer S, Leiter L, Daneman D. et al 1998 Clinical practice guidelines for the management of diabetes in **Canada**. CMAJ **1998**;159 (8 Suppl).
American Diabetes Association: Clinical Practice Recommendations 2003, Diabetes Care 2003 26:Supplement 1.
(**Standards of Medical Care in Diabetes-2006**-American-Diabetes-Association http://care.diabetesjournals.org/cgi/content/full/29/suppl_1/s4)(Nathan DM, et al. Management of hyperglycemia in type 2 diabetes: a **consensus algorithm** for the initiation and adjustment of therapy: a consensus statement from the **American Diabetes Association** and the **European Association** for the Study of Diabetes. Diabetes Care. 2006 Aug;29(8):1963-72.)
American Diabetes Association (ADA). Standards of medical care in diabetes. IV. **Prevention/delay of type 2 diabetes**. Diabetes Care 2007 Jan;30(Suppl 1):S7-8.
American Diabetes Association (ADA). Standards of medical care in diabetes. VI. **Prevention and management of diabetes complications. Diabetes Care 2007** Jan;30(Suppl 1):S15-24. http://care.diabetesjournals.org/cgi/content/full/30/suppl_1/S4#SEC14
American Diabetes Association (ADA). Standards of medical care in diabetes--2008. Diabetes Care. 2008 Jan;31 Suppl 1:S12-54. http://care.diabetesjournals.org/cgi/content/full/31/Supplement_1/S12
American Diabetes Association. Standards of medical care in diabetes--2009. Diabetes Care. **2009** Jan;32 Suppl 1:S1-97. http://care.diabetesjournals.org/content/vol32/Supplement_1/
Nathan DM, Buse JB, Davidson MB, Ferrannini E, Holman RR, Sherwin R, Zinman B; American Diabetes Association; European Association for Study of Diabetes. Medical management of **hyperglycemia** in type 2 diabetes: a consensus algorithm for the initiation and adjustment of therapy: a consensus statement of the ADA and the European Association for the Study of Diabetes. Diabetes Care. **2009** Jan;32(1):193-203.
Epub 2008 Oct 22. http://care.diabetesjournals.org/cgi/reprint/32/1/193?maxtoshow=&HITS=10&hits=10&RESULTFORMAT=&author1=nathan&fulltext=hyperglycemia&searchid=1&FIRSTINDEX=0&sortspec=relevance&resourcetype=HWCIT .
Hobbs C, Pogach L, Aron D, et al. **VA/DoD (Veterans Affaris/ Dept of Defense) clinical practice guideline for the management of diabetes mellitus**. Version 4.0. http://www.healthquality.va.gov/diabetes/DM2010_FUL-v4e.pdf . Aug **2010**.
ADA Diabetes Guidelines- Standards of Medical Care in Diabetes—**2010** http://care.diabetesjournals.org/content/33/Supplement_1/S11.full.pdf+html
ADA American Diabetes Association. **Diagnosis and Classification** of Diabetes Mellitus Diabetes Care January 2010 33:S62-S69; doi:10.2337/dc10-S062.
ADA- American Diabetes Association. Standards of Medical Care in Diabetes—**2011** Diabetes Care January 2011 34:S11-S61; doi:10.2337/dc11-S011. http://care.diabetesjournals.org/content/34/Supplement_1/S11.full.pdf+html
ADA 2012: American Diabetes Association Position Statement: **Executive Summary**: Standards of Medical Care in Diabetes—2012Diabetes Care January 2012 35:S4-S10; doi:10.2337/dc12-s004 http://care.diabetesjournals.org/content/35/Supplement_1/S4.full.pdf
ADA 2012: American Diabetes Association Position Statement: **Diagnosis and Classification** of Diabetes MellitusDiabetes Care January 2012 35:S64-S71; doi:10.2337/dc12-s064 http://care.diabetesjournals.org/content/35/Supplement_1/S64.full.pdf
ADA 2012: American Diabetes Association Position Statement: **Standards of Medical Care** in Diabetes—2012Diabetes Care January 2012 35:S11-S63; doi:10.2337/dc12-s011. http://care.diabetesjournals.org/content/35/Supplement_1/S11.full.pdf
Inzucchi SE, Bergenstal RM, Buse JB, et al. **Management of Hyperglycemia in Type 2 Diabetes**: A Patient-Centered Approach: Position Statement of the American Diabetes Association (**ADA**) and the European Association for the Study of Diabetes(**EASD**). Diabetes Care. 2012 Apr 19.
ADA 2013: American Diabetes Association. Clinical practice recommendations. Diabetes Care 2013; 36:S1-S110. http://care.diabetesjournals.org/content/36/Supplement_1.toc
ADA 2014: American Diabetes Association. Standards of Medical Care in Diabetes. Diabetes Care January 2014 37:S14-S80; doi:10.2337/dc14-S014. http://care.diabetesjournals.org/content/37/Supplement_1.toc
ADA 2015: Standards of medical care in diabetes--2015: summary of revisions. Diabetes Care. 2015 Jan;38 Suppl:S4.
ADA 2016: Standards of Medical Care in Diabetes-2016: Summary of Revisions. Diabetes Care. (American Diabetes Association) 2016 Jan;39 Suppl 1:S4-5.
ADA 2017: American Diabetes Association.. 8. Pharmacologic Approaches to Glycemic Treatment. Diabetes Care. 2017 Jan;40(Suppl 1):S64-S74.
ADA 2017: American Diabetes Association.. 13. Management of Diabetes in Pregnancy. Diabetes Care. 2017 Jan;40(Suppl 1):S114-S119.

ADA 2018: American Diabetes Association. 14. Diabetes Care **in the Hospital**: Standards of Medical Care in Diabetes-2018. Diabetes Care. 2018 Jan;41(Suppl 1):S144-S151.
ADA 2018: American Diabetes Association. 13. Management of Diabetes in **Pregnancy**: Standards of Medical Care in Diabetes-2018. Diabetes Care. 2018 Jan;41(Suppl 1):S137-S143.
ADA 2018: American Diabetes Association. 12. **Children and Adolescents**: Standards of Medical Care in Diabetes-2018. Diabetes Care. 2018 Jan;41(Suppl 1):S126-S136.
ADA 2018: American Diabetes Association. 11. **Older Adults**: Standards of Medical Care in Diabetes-2018. Diabetes Care. 2018 Jan;41(Suppl 1):S119-S125.
ADA 2018: American Diabetes Association. 9. **Cardiovascular Disease and Risk Management**: Standards of Medical Care in Diabetes-2018. Diabetes Care. 2018 Jan;41(Suppl 1):S86-S104.
ADA 2018: American Diabetes Association. 8. **Pharmacologic Approaches** to Glycemic Treatment: Standards of Medical Care in Diabetes-2018. Diabetes Care. 2018 Jan;41(Suppl 1):S73-S85.
ADA 2018: American Diabetes Association. 7. **Obesity Management** for the Treatment of Type 2 Diabetes: Standards of Medical Care in Diabetes-2018. Diabetes Care. 2018 Jan;41(Suppl 1):S65-S72.
ADA 2018: American Diabetes Association. 6. **Glycemic Targets**: Standards of Medical Care in Diabetes-2018. Diabetes Care. 2018 Jan;41(Suppl 1):S55-S64.
ADA 2018: American Diabetes Association. 5. **Prevention or Delay of Type 2 Diabetes**: Standards of Medical Care in Diabetes-2018. Diabetes Care. 2018 Jan;41(Suppl 1):S51-S54.
ADA 2018: American Diabetes Association. 4. **Lifestyle Management**: Standards of Medical Care in Diabetes-2018. Diabetes Care. 2018 Jan;41(Suppl 1):S38-S50.
ADA 2018: American Diabetes Association. 2. **Classification and Diagnosis of Diabetes**: Standards of Medical Care in Diabetes-2018. Diabetes Care. 2018 Jan;41(Suppl 1):S13-S27.

ADA 2019: Summary of Revisions: **Standards of Medical Care** in Diabetes-2019. Diabetes Care. 2019 Jan;42(Suppl 1):S4-S6.
ADA 2019: American Diabetes Association. 6. **Glycemic Targets**: Standards of Medical Care in Diabetes-2019. Diabetes Care. 2019 Jan;42(Suppl 1):S61-S70.
ADA 2019: American Diabetes Association. 9. **Pharmacologic Approaches to Glycemic Treatment**: Standards of Medical Care in Diabetes-2019. Diabetes Care. 2019 Jan;42(Suppl 1):S90-S102.
ADA 2019: American Diabetes Association. 10. **Cardiovascular Disease** and Risk Management: Standards of Medical Care in Diabetes-2019. Diabetes Care. 2019 Jan;42(Suppl 1):S103-S123.
ADA 2019: American Diabetes Association. 12. **Older Adults**: Standards of Medical Care in Diabetes-2019. Diabetes Care. 2019 Jan;42(Suppl 1):S139-S147.
ADA 2019: American Diabetes Association. 14. Management of **Diabetes in Pregnancy**: Standards of Medical Care in Diabetes-2019. Diabetes Care. 2019 Jan;42(Suppl 1):S165-S172.

[1] **Treatment Guidelines**: Drugs for Type 2 Diabetes. **The Medical Letter**: September, **2002**; (1) pp. 1-6. Updated Aug 2005, Aug 2011, Mar 2014 & **Updated Jan 2017.**
[1] Brown AF, Mangione CM, Saliba D, Sarkisian CA; California Healthcare Foundation/**American Geriatrics Society** Panel on Improving Care for Elders with Diabetes. Guidelines for improving the care of the older person with diabetes mellitus. J Am Geriatr Soc. **2003** May;51(5 Suppl Guidelines):S265-80.
Greenfield Sheldon, Billimek John, Pellegrini Fabio, Comorbidity Affects the Relationship Between Glycemic Control and Cardiovascular Outcomes in Diabetes: A Cohort Study . Ann Intern Med December 15, 2009 151:854-860; doi:10.1059/0003-4819-151-12-200912150-00005.
Lee SJ, Boscardin WJ, Stijacic Cenzer I, Huang ES, Rice-Trumble K, Eng C. The risks and benefits of implementing glycemic control guidelines in **frail older adults** with diabetes mellitus. J Am Geriatr Soc. 2011 Apr;59(4):666-72.
[1] **Canadian 2003 Diabetes Guidelines** http://www.diabetes.ca/cpg2003/download.aspx
Canadian 2008 Guidelines (Sept 2008): http://www.diabetes.ca/files/cpg2008/cpg-2008.pdf
(Bhattacharyya OK, Estey EA, Cheng AY; Canadian Diabetes Association 2008. Update on the Canadian Diabetes Association 2008 clinical practice guidelines. Can Fam Physician. 2009 Jan;55(1):39-43.)
Canadian Diabetes 20013 Guidelines (April 2013): http://guidelines.diabetes.ca/
Harper W, Clement M, Goldenberg R, et al. **Pharmacologic management of type 2 diabetes – 2015 interim update. Can J Diabetes** 2015;39:250-2. http://guidelines.diabetes.ca/Browse/Chapter13_2015 (accessed August 10, 2015)
Canadian Hypertension Education Program 2017 Recommendations www.hypertension.ca **Canadian Hypertension Education Program (CHEP).**
Canadian Diabetes Association Clinical Practice Guidelines Expert Committee. **Pharmacologic management of type 2 diabetes: 2016 interim update**. Can J Diabetes 2016 guidelines.diabetes.ca/cdacpg_resources/JCJD_6921.pdf (accessed May 2, 2016).
Canadian Diabetes Association Clinical Practice Guidelines Expert Committee. **Table 1. Antihyperglycemic agents for use in type 2 diabetes**. April 2016. guidelines.diabetes.ca/cdacpg_resources/Ch13_Table1_Antihyperglycemic_agents_type_2_2016.pdf(accessed May 2, 2016).
Canadian Diabetes Association Clinical Practice Guidelines Expert Committee. Addendum to policies, guidelines and consensus statements: **pharmacologic management of type 2 diabetes: 2015 interim update**. Figure 2. Antihyperglycemic medications and renal function. Can J Diabetes 2015;39:440.guidelines.diabetes.ca/cdacpg_resources/Ch13_Fig2_Antihyperglycemic_medications_and_renal_function_2016.pdf(May 2, 2016).
Canadian Diabetes Association Clinical Practice Guidelines Expert Committee. Pharmacologic management of type 2 diabetes: 2016 interim update. (**Leader: liraglutide**) Can J Diabetes 2016;40:484-6. www.canadianjournalofdiabetes.com/article/S1499-2671(16)30592-5/pdf (accessed December 6, 2016).
Canadian Diabetes Association Clinical Practice Guidelines Expert Committee. Pharmacologic management of type 2 diabetes: 2016 interim update. (**Empa-Reg: empagliflozin**) Can J Diabetes 2016;40:193-5. www.canadianjournalofdiabetes.com/article/S1499-2671(16)00072-1/pdf (accessed December 6, 2016).
Diabetes Canada Clinical Practice Guidelines Expert Committee, Lipscombe L, Booth G, Butalia S, et al. **Pharmacologic Glycemic Management of Type 2 Diabetes in Adults. Can J Diabetes. 2018** Apr;42 Suppl 1:S88-S103.
Diabetes Canada Clinical Practice Guidelines Expert Committee, Tobe SW, Gilbert RE, Jones C, et al. **Treatment of Hypertension**. Can J Diabetes. 2018 Apr;42 Suppl 1:S186-S189.
Diabetes Canada Clinical Practice Guidelines Expert Committee, Robinson DJ,Coons M, Haensel H, et al. **Diabetes and Mental Health**. Can J Diabetes. 2018 Apr;42 Suppl 1:S130-S141.
Diabetes Canada Clinical Practice Guidelines Expert Committee, Ekoe JM, Goldenberg R, Katz P. **Screening for Diabetes in Adults**. Can J Diabetes. 2018 Apr;42 Suppl 1:S16-S19.
Diabetes Canada Clinical Practice Guidelines Expert Committee, Wherrett DK, Ho J, Huot C, Legault L, et al. **Type 1 Diabetes in Children and Adolescents**. Can J Diabetes. 2018 Apr;42 Suppl 1:S234-S246.

Clinical Knowledge Summary - Diabetes – NHS – **UK**: Link http://www.cks.library.nhs.uk/diabetes_type_2
AHRQ-**USA**: Clinicians Summary: http://www.effectivehealthcare.ahrq.gov/ehc/products/155/720/ECBCM_Oral%20Meds%20T2%20Diab_Clinician06282011.pdf; Full Report: http://www.effectivehealthcare.ahrq.gov/ehc/products/155/644/CER27_OralDiabetesMeds_20110623.pdf
AHRQ-USA: Patients Summary: http://www.effectivehealthcare.ahrq.gov/ehc/products/155/721/OralMedT2Diab_consumer.pdf
Mayo Clinic – **Shared Decision Making** – diabetes tools: http://dev.shareddecisions.mayoclinic.org/decision-aids-for-diabetes/diabetes-medication-management/

Health Canada – Advisory on rosiglitazone (Avandia) (June 01, 2007) http://www.hc-sc.gc.ca/dhp-mps/medeff/advisories-avis/prof/2007/avandia_hpc-cps_4_e.html
Important Advice for Managing Your Patients

In Canada, Avandia® is NOT approved for use:
- with insulin therapy
- with the combination of metformin AND a sulfonylurea
- in patients with pre-diabetes.

Avandia® is contraindicated in patients with NYHA Class III and IV cardiac status.
Avandia® should be used with caution in any patient with NYHA Class I and II cardiac status.

All patients should be monitored for signs and symptoms of fluid retention, edema, and rapid weight gain.
The dose of Avandia® used in combination with a sulfonylurea should not exceed 4mg daily.

More links, information and a RxFiles Q&A Summary available at: http://www.rxfiles.ca/Rosiglitazone-CV-Controversy.htm

---

[i] Micromedex 2017; Drugs in Pregnancy & Lactation, 10th Ed. Briggs GE,et al. Wilkins;Baltimore, MD.2017.
.; Hansten & Horn-Drug Interactions 2016.
[ii] Rosenstock J. Management of type 2 diabetes mellitus in the elderly. Drugs & Aging 2001;18(1)31-44.
[iii] Fisman EZ, Tenenbaum A, et al. Oral antidiabetic treatment in patients with coronary disease: time-related increased mortality on combined glyburide/metformin therapy over a 7.7-year follow-up. Clin Cardiol. 2001 Feb;24(2):151-8.
[iv] Gale, EAM. Lessons from the glitazones: a story of drug development. Lancet 2001;357:1870-75.
[v] Moses R, Slobodniuk R, Boyages S, Colagiuri S et al. Effect of repaglinide addition to metformin monotherapy on glycemic control in patients with type 2 diabetes. Diabetes Care 1999 Jan;22(1):119-124
[vi] Fonseca V, Rosenstock J, Patwardhan R, Salzman A. Effect of metformin and rosiglitazone combination therapy in patients with type 2 diabetes mellitus. JAMA 2000;283(13):1695-1702.
[vii] Einhorn D, et al. Pioglitazone hydrochloride in combination with metformin in the treatment of type 2 diabetes mellitus: a randomized, placebo-controlled study. The pioglitazone 027 study group. Clin Ther 2000 2000;1395-1409.
[viii] Rosenstock J; Rood J; Cobitz A; Biswas N; Chou H; Garber A. Initial treatment with rosiglitazone/metformin fixed-dose combination therapy compared with monotherapy with either rosiglitazone or metformin in patients with uncontrolled type 2 diabetes. Diabetes Obes Metab. 2006; 8(6):650-60.
[ix] Rosenstock J, Brown A, Fisher J, Jain A et al. Efficacy and safety of acarbose in metformin-treated patients with type 2 diabetes. Diabetes Care 1998;21(12):2050-2055.
[x] Yki-Jarvinen H, Ryysy L, Nikkila K, et al. Comparison of bedtime insulin regimens in patients with type 2 diabetes mellitus: a randomized controlled trial. Ann Intern Med 1999;130:389-96.
Kooy A, de Jager J, Lehert P, Bets D, Wulffelé MG, Donker AJ, Stehouwer CD. Long-term effects of metformin on metabolism and microvascular and macrovascular disease in patients with type 2 diabetes mellitus. Arch Intern Med. 2009 Mar 23;169(6):616-25.
[xi] Raskin P, Rendell M, Riddle MC et al. A randomized trial of rosiglitazone therapy in patients with inadequately controlled insulin-treated type 2 diabetes. Diabetes Care 2001 Jul;24(7):1226-32
[xii] Krentz AJ, Bailey CJ, Melander A. Thiazolidinediones for type 2 diabetes: new agents reduce insulin resistance but need long term clinical trials. BMJ 2000;321:252-3.

Additional articles SMBG meters:

Aakre KM, Watine J, Bunting PS, et al. **Self-monitoring of blood glucose** in patients with diabetes who do not use insulin—are guidelines evidence-based? Diabet Med 2012;29:1226–36.

Battelino T et al. Effect of continuous glucose monitoring on hypoglycemia in type 1 diabetes. Diabetes Care 2011; 34:795.

Bergenstal RM et al. Effectiveness of sensor-augmented insulinpump therapy in type 1 diabetes. N Engl J Med 2010; 363:311.

Blevins TC et al. Statement by the American Association of Clinical Endocrinologists Consensus Panel on Continuous Glucose Monitoring. Endocr Pract 2010; 16:730.

Butalia S. Rabi D. To test or not to test? Self-monitoring blood glucose in patients with type 2 diabetes managed without insulin. Open Medicine, North America, 4, may. 2010.

Cameron, C., Viranti, A., Dean, H., et al. Utilization and Expenditure on Blood Glucose Test Strips in Canada. Canadian Journal of Diabetes. 2010;34(1):34-40.

CADTH Rapid Response: Blood Glucose Monitors and Test Strips: A Review of the Comparative Clinical Evidence and Cost-Effectiveness. Apr 2011. Accessed at: http://www.cadth.ca/media/pdf/htis/april-2011/L0256%20SMBG%20Test%20Strips%20and%20Monitors%20Final.pdf

Canadian Diabetes Association (CDA) plans to launch a **compassionate use program** to assist people with diabetes who have difficulty covering the costs of blood glucose monitoring supplies http://www.diabetes.ca/

Cornish A, Chase HP. Navigating **Airport Security** with an Insulin Pump and/or Sensor. Diabetes Technol Ther. 2012 Nov;14(11):984-5.

Falk J, et al. Patterns, Policy and Appropriateness: A 12-Year Utilization Review of **Blood Glucose Test Strip Use** in Insulin Users. Can J Diabetes. 2017 Apr 11.

Farmer AJ, Perera R, Ward A, et al. **Meta-analysis** of individual patient data in randomised trials of self monitoring of blood glucose (**SMBG**) in people with non-insulin treated type 2 diabetes. BMJ. 2012 Feb 27;344:e486. {SMBG does not appreciably improve control in T2DM patients not on insulin. ↓A1C only marginally 8.3%⇨8.05%.}

FDA Aug/10 and CDC have noted a progressive increase in the reports of bloodborne infection transmission over the past 10 to 15 years (**primarily hepatitis B virus**), resulting from shared use of fingerstick and point-of-care [POC] blood testing devices.

FDA Aug/13 Nova Diabetes Care initiated a voluntary **recall of 21 lots of the Nova Max Glucose Test Strips** distributed both in the USA and outside the continental USA.

FDA Jan/14 Nipro Diagnostics initiated a voluntary recall and replacement of a limited number of **TRUEbalance and TRUEtrack Blood Glucose Meters** distributed both in the United States and outside the United States. The company determined that certain isolated TRUEbalance and TRUEtrack Blood Glucose Meters have an incorrect factory-set unit of measure that displays the glucose result in mmoi/L rather than mg/dl. If a consumer were not to notice the incorrect unit of measure, it is possible that the meter result could be read as a lower than expected blood glucose result. BACKGROUND: There are 501 affected TRUEbalance meters and 105 affected TRUEtrack meters that were distributed in the United States from September 2008 to May 2013. The company is sending notifications to pharmacies, durable medical equipment providers, mail order companies and distributors where the TRUEbalance and TRUEtrack meters are recommended or sold in the United States.

FDA Mar/14 Abbott is conducting a recall for the **FreeStyle Blood Glucose Meter and the FreeStyle Flash Blood Glucose Meter**. When used with the Abbott FreeStyle test strips, the FreeStyle Blood Glucose Meter and the FreeStyle Flash Blood Glucose Meter may produce mistakenly low blood glucose results.

FDA Apr/14 is advising people with diabetes and health care professionals to stop using **GenStrip Blood Glucose Test Strips** because the strips may report incorrect blood glucose levels.

FDA Jun/14 Diabetic Supply of Suncoast, Inc. initiated a nationwide voluntary recall of all **BMB-BA006A Advocate Redi-Code+ blood glucose test strip** lots manufactured by BroadMaster Bio-Tech Corp due to a labeling error which could result in confusion about which meter models the Redi-Code+ BMB-BA006A blood glucose test strips are designed to be used with. In the incorrect labeling, the test strips model (BMB-BA006A) was omitted.

FDA Jan/16 Arkray is recalling the **SPOTCHEM II Basic PANEL-1 Reagent Test Strip** and SPOTCHEM II Glucose Reagent Test Strip because they may report falsely low blood glucose levels.

Franciosi M, Lucisano G, Pellegrini F, et al. ROSES Study Group. Role of **self-monitoring of blood glucose** and intensive education in patients with Type 2 diabetes not receiving insulin. A pilot randomized clinical trial. Diabet Med.2011Jul;28(7):789-96.

Gellad WF, Zhao X, Thorpe CT, et al. Dual Use of Department of Veterans Affairs and Medicare Benefits and Use of **Test Strips** in Veterans With Type 2 Diabetes Mellitus. JAMA Intern Med. 2014 Nov 10.

Gillett M., Dallosso H. M., Dixon S., et al. Delivering the diabetes education and self management for ongoing and newly diagnosed (DESMOND) programme for people with newly diagnosed type 2 diabetes:cost effectiveness analysis.BMJ 2010;341:c4093

Gomes T, Martins D, Tadrous M, et al. Association of a **Blood Glucose Test Strip Quantity-Limit Policy** With Patient Outcomes: A Population-Based Study. JAMA Intern Med. 2016 Nov 7

Health Canada Mar/14: Informing Canadians that when Abbott FreeStyle glucose test strips are used with certain devices, there is a potential for users to receive a lower-than-actual blood sugar reading.

JDRF CGM Study Group. Continuous glucose monitoring and intensive treatment of type 1 diabetes. N Engl J Med 2008; 359:1464.

Lau, D. The Cost of Diabetes: A Game Changer. Canadian Journal of Diabetes, Mar '10.

Malanda UL, Bot SD, Kostense PJ, et al. Effects of **self-monitoring of glucose** on distress and self-efficacy in people with non-insulin-treated type 2 diabetes: a randomized controlled trial. Diabet Med. 2015 Jul 14.

Mcintosh B., Yu C., Lal A. et al. Efficacy of self-monitoring of blood glucose in patients with type 2 diabetes mellitus managed without insulin: a systematic review and meta-analysis. Open Medicine, North America, 4, may. 2010. Also article in CPJ, Sep 2010 @ http://www.cpjournal.ca/doi/pdf/10.3821/1913-701X-143.5.218; Commentary by Johnson in **CPJ, Sep 2010** @ http://www.cpjournal.ca/doi/pdf/10.3821/1913-701X-143.5.216.

Medical Letter. **Continuous Glucose Monitoring**. May 2, 2011.

MHRA June/16 TRUEyou blood glucose test strips - certain lots of test strips may give incorrect low blood glucose results that could lead to undetected hyperglycaemia.

Ontario Aug 2013: introducing limitations in funding for diabetes test strips. And these new restrictions are okay with the Canadian Diabetes Association, which worked with the government to ensure that new self-management of diabetes reflects the best evidence and clinical experience available. According to a notice posted on the Ontario Public Drug Programs (OPDP) website, research indicates that Blood Glucose Test Strips (BGTS) have a limited clinical benefit for many patients who don't take insulin. Based on this evidence, Ontario will restrict the number of BGTS allowed in a 365-day period, while ensuring continued access to those who need test strips to manage their blood sugar. The province's Health Network System (HNS) will track and determine the reimbursement level based on each patient's diabetes treatment. Under the new rules, patients managing diabetes with insulin will be allowed 3,000 BGTS a year, while patients managing diabetes with anti-diabetes medication with high risk of causing hypoglycemia will get 400 BGTS. Patients managing diabetes using anti-diabetes medication with low risk of causing hypoglycemia and those who are managing diabetes through diet/lifestyle therapy only will be allowed 200 BGTS.

Pickup John C, Freeman Suzanne C, Sutton Alex J. Glycaemic control in type 1 diabetes during real time **continuous glucose monitoring** compared with self monitoring of blood glucose: meta-analysis of randomised controlled trials using individual patient data. BMJ 2011;343:doi:10.1136/bmj.d3805 (7 July 2011)

Polonsky WH, Hessler D, Ruedy KJ, Beck RW; DIAMOND Study Group. The Impact of Continuous Glucose Monitoring on Markers of Quality of Life in Adults With Type 1 Diabetes: Further Findings From the DIAMOND Randomized Clinical Trial. Diabetes Care. 2017 Jun;40(6):736-741.

Rabi, D., Johnson, J., Edwards, J. Self-monitoring of blood glucose for individuals with type 2 diabetes not using insulin: Leaving no cornerstone unturned. Canadian Journal of Diabetes, March 2010. Accessed June 24 2010 at: SMBG: Type 2 Diabetes and **Monitoring** your Blood Sugar –**Patient Pamphlet**. http://www.cadth.ca/media/pdf/smbg-nb_eng.pdf

Riveline JP, Schaepelynck P, et al. Assessment of patient-led or physician-driven continuous glucose monitoring in patients with poorly controlled type 1 diabetes using basal-bolus insulin regimens: a 1-year multicenter study. Diabetes Care. 2012 May;35(5):965-71.

Robson J, Smithers H, Chowdhury T, et al. **Reduction in self-monitoring of blood glucose** in type 2 diabetes: an observational controlled study in east London. Br J Gen Pract. 2015 Apr; 65(633):e256-63.

Serwylo O, Friesen K, Falk J, et al. Opportunity Cost and Policy: A Utilization Review of **Self-Monitoring of Blood Glucose** in Manitoba, Canada. Clin Ther. 2016 Mar 2.

Vigersky RA, Fonda SJ, et al. Short- and long-term effects of real-time continuous glucose monitoring in patients with type 2 diabetes. Diabetes Care. 2012 Jan;35(1):32-8.

Woo, V., Cheng, A., Hanna, A., et al. Self-monitoring of Blood Glucose in Individuals with Type 2 Diabetes Not Using Insulin: Commentary. Canadian Journal of Diabetes, March 2010. Accessed June 24 2010.

Young LA, Buse JB, Weaver MA, et al; Monitor Trial Group. **Glucose self-monitoring** in non–insulin-treated type 2 diabetes in primary care settings: a randomized trial [online June 10, 2017].JAMA Intern Med. doi:10.1001 /jamainternmed.2017.1233

References (SMBG)

[i] Cameron C, Coyle D, Ur E, Klarenbach S. Cost-effectiveness of self-monitoring of blood glucose in patients with type 2 diabetes mellitus managed without insulin. **CMAJ**. 2010 Jan 12;182(1):28-34. {Summary also in DailyPOEMs: 01Apr2010; https://www.essentialevidenceplus.com/content/poem/120401 }

[ii] Kolb H, Kempf K, Martin S, Stumvoll M, Landgraf R. On what evidence-base do we recommend self-monitoring of blood glucose? Diabetes Res Clin Pract. 2010 Feb;87(2):150-156.

[iii] O'Kane MJ, Pickup J. Self-monitoring of blood glucose in diabetes: is it worth it? Ann Clin Biochem. 2009 Jul;46(Pt 4):273-82.

[iv] Farmer AJ, Wade AN, French DP, Simon J, Yudkin P, Gray A, Craven A, Goyder L, Holman RR, Mant D, Kinmonth AL, Neil HA; **DiGEM** Trial Group. Blood glucose self-monitoring in type 2 diabetes: a randomised controlled trial. Health Techno Assess. 2009 Feb;13(15):iii-iv, ix-xi, 1-50.

[v] Varanauskiene E. Can blood glucose self-monitoring improve treatment outcomes in type 2 diabetes? Diabetes Res Clin Pract. 2008 Dec 15;82 Suppl 2:S112-7.

[vi] Towfigh A, Romanova M, Weinreb JE, Munjas B, Suttorp MJ, Zhou A, Shekelle PG. Self-monitoring of blood glucose levels in patients with type 2 diabetes mellitus not taking insulin: a meta-analysis. Am J Manag Care. 2008 Jul;14(7):468-75.

[vii] Majumdar SR. Self-monitoring of blood glucose was not cost-effective in non-insulin-treated type 2 diabetes. ACP J Club. 2008 Nov-Dec;149(4):4-5.

[viii] French DP, Wade AN, Yudkin P, Neil HA, Kinmonth AL, Farmer AJ. Self-monitoring of blood glucose changed non-insulin-treated Type 2 diabetes patients' beliefs about diabetes and self-monitoring in a randomized trial. Diabet Med. 2008 Oct;25(10):1218-28. {No change in diabetes-related health behaviours.}

[ix] O'Kane MJ, Pickup J. Self-monitoring of blood glucose in diabetes: is it worth it? Ann Clin Biochem. 2009 Jul;46(Pt 4):273-82.

[x] Mansell K, Blackburn D, Eurich D. Do postprandial glucose levels add important clinical information when fasting glucose levels are near normal in non-insulin-dependent patients with type 2 diabetes? CPJ 2010;142(6):298-302. Accessed on line Feb 11, 2010 at http://www.cpjournal.ca/perlserv/?request=get-document&doi=10.3821%2F1913-701X-142.6.298&ct=1

[xi] Malanda UL, Welschen LM, Riphagen II, et al. Self-monitoring of blood glucose in patients with type 2 diabetes mellitus who are not using insulin. **Cochrane** Database Syst Rev. 2012 Jan 18;1:CD005060. {From this review, we conclude that when diabetes duration is over one year, the overall effect of self-monitoring of blood glucose on glycaemic control in patients with type 2 diabetes who are not using insulin is small up to six months after initiation and subsides after 12 months. Furthermore, based on a best-evidence synthesis, there is no evidence that SMBG affects patient satisfaction, general well-being or general health-related quality of life. More research is needed to explore the psychological impact of SMBG and its impact on diabetes specific quality of life and well-being, as well as the impact of SMBG on hypoglycaemia and diabetic complications.}

[xii] O'Kane MJ, Bunting B, Copeland M, Coates VE; ESMON study group. Efficacy of self monitoring of blood glucose in patients with newly diagnosed type 2 diabetes (**ESMON** study): randomised controlled trial. BMJ. 2008;336(7654):1174-7.

[xiii] Simon J, Gray A, Clarke P, Wade A, Neil A, Farmer A; Diabetes Glycaemic Education and Monitoring Trial Group. Cost effectiveness of self monitoring of blood glucose in patients with non-insulin treated type 2 diabetes: economic evaluation of data from the **DiGEM** trial. BMJ. 2008 May 24;336(7654):1177-80.

[xiv] **COMPUS Optimal Therapy Report**: **Cost Effectiveness** of Blood Glucose Test Strips in the Management of Adult Patients with Diabetes Mellitus. May 2009. Accessed Feb 04, 2010 at http://www.cadth.ca/media/pdf/BGTS_Consolidated_Economic_Report.pdf

[xv] Simon J, Gray A, Clarke P, Wade A, Neil A, Farmer A; Diabetes Glycaemic Education and Monitoring Trial Group. Cost effectiveness of self monitoring of blood glucose in patients with non-insulin treated type 2 diabetes: economic evaluation of data from the DiGEM trial. BMJ. 2008 May 24;336(7654):1177-80.

[xvi] Parkin CG, Hinnen D, Campbell RK, Geil P, Tetrick DL, Polonsky WH. Effective use of paired testing in type 2 diabetes: practical applications in clinical practice. Diabetes Educ. 2009 Nov-Dec;35(6):915-27.

[xvii] **Canadian Diabetes Association 2008** clinical practice guidelines for the prevention and management of diabetes in Canada. *Can J Diabetes*. [Internet]. 2008 Sep [cited 2008 Jan 17];32(Suppl 1): S168-S180. Available from: http://www.diabetes.ca/files/cpg2008/cpg-2008.pdf

Note: see Diabetes and Pregnancy Recommendations, *page s170 and s174*

[xviii] **COMPUS Optimal Therapy Report**: **Systematic Review** of Use of Blood Glucose Test Strips for the Management of Diabetes Mellitus. May 2009. Accessed Feb 04, 2010 at http://www.cadth.ca/media/pdf/BGTS_SR_Report_of_Clinical_Outcomes.pdf

[xix] RxFiles **Diabetes – Glucose Control- Landmark Trials and Links**. Accessed online at: http://www.rxfiles.ca/rxfiles/uploads/documents/CHT-Diabetes-Landmark-Trials-Links.pdf

[xx] Regier L, Jensen B. RxFiles Diabetes Glucose Control – Landmark Trials & Links. Access online at: http://www.rxfiles.ca/rxfiles/uploads/documents/CHT-Diabetes-Landmark-Trials-Links.pdf

[xxi] Holman R, Sanjoy P, Bethel MA, Matthews D, Neil A. 10-Year Follow-up of Intensive Glucose Control in Type 2 Diabetes. (**UKPDS-80**). N Engl J Med 2008;359:1-13.

[xxii] **Canadian 2008 Guidelines (Sept 2008). Accessed at** http://www.diabetes.ca/files/cpg2008/cpg-2008.pdf
{Also, Bhattacharyya OK, Estey EA, Cheng AY; Canadian Diabetes Association 2008. Update on the Canadian Diabetes Association 2008 clinical practice guidelines. Can Fam Physician. 2009 Jan;55(1):39-43.}

[xxiii] Nauck MA, El-Ouaghlidi A, Vardarli I. Self-monitoring of blood glucose in diabetes mellitus: arguments for an individualized approach. Dtsch Arztebl Int. 2009 Sep;106(37):587-94.

[xxiv] RxFiles **ACCORD** Trial Summary: Accessed online at: http://www.rxfiles.ca/rxfiles/uploads/documents/Diabetes-Targets-ACCORD-A1C.pdf

[xxv] Brown AF, Mangione CM, Saliba D, Sarkisian CA; California Healthcare Foundation/**American Geriatrics Society** Panel on Improving Care for Elders with Diabetes. Guidelines for improving the care of the older person with diabetes mellitus. J Am Geriatr Soc. **2003** May;51(5 Suppl Guidelines):S265-80.

[xxvi] Currie CJ, Peters JR, Tynan A, Evans M, Heine RJ, Bracco OL, Zagar T, Poole CD. Survival as a function of HbA(1c) in people with type 2 diabetes: a retrospective cohort study. Lancet. 2010 Jan 26. [Epub ahead of print]

Clinical Resource, Comparison of Blood Glucose Meters. Pharmacist's Letter/Prescriber's Letter. February 2018.

Extras for Insulin Pen Delivery Devices:

Discontinued Insulin Devices

AutoPen 24 (3ml penfill) A) green – up to 21 units 1-21 units in 1 unit increments B) blue – up to 42 units 2-42 units in 2 unit increments		**LANTUS** (glargine) ◆ free with Lantus insulin	◆ has side-mounted injection button ◆ small white numbers on a dark background; does not have number window (e.g. number not magnified.) ◆ does **NOT** have dial back capabilities, dose must be wasted if overdialed ◆ if insufficient insulin in cartridge, number remaining on dial will show remaining dose to be given
Novolin-Pen Junior (3ml penfill) {Green, Yellow} 1-35 units in ½ unit increments	 [Novo-Pen Junior was replaced by **NovoPen Echo**'2013]	**NOVOLIN GE** (Toronto, NPH, 30/70, 40/60, 50/50) **LEVEMIR** (detemir) **NOVORAPID, FIASP** (aspart) **NOVOMIX 30** (aspart + aspart protamine) **TRESIBA** (degludec)	◆ small increments useful: children & insulin sensitive pts ◆ does **NOT** have dial back capability; barrel and cartridge holder should be pulled apart & button reset to correct dose ◆ small white numbers on a black background ◆ if insufficient insulin in cartridge, number remaining on dial will show remaining dose to be given
HumaPen Luxura (3ml cartridge) {Champagne, Burgundy} 1-60 units in 1 unit increments	 [HumanPen Luxura was replaced by **HumaPen Savvio**]	**HumuLIN** (R, N, 30/70) **HumaLOG** (lispro) **HumaLOG** Mix25 (lispro+lispro protamine) **HumaLOG** Mix50 (lispro+lispro protamine)	◆ has dial back capability, decreases wastage ◆ audible click on dialing doses ◆ dark numbers on a white background ◆ if insufficient insulin in cartridge, number remaining on dial will show remaining dose to be given ◆ Luxura last up to 6 years
Humalog Pen **Humalog Mix Pen** 1-60 units in 1 unit increments	 [Humulog Pens were replaced by **Humalog KwikPen**'2011]	**HumaLOG** (lispro) **HumaLOG MIX 25 & MIX 50** (lispro + lispro protamine)	◆ window magnification **NOT** as clear as other pens ◆ may use a symbol instead of 0 to indicate dose complete ◆ has dial back capability, decreases wastage ◆ audible click on dialing doses ◆ dark numbers on a white background
Humulin N Pen 1-60 units in 1 unit increments	 [Humulin N Pen was replaced by **Humulin N KwikPen**'2011]	**HumuLIN N** [Humulog and Humulin N Pens were replaced by Humalog and Humulin N KwikPen'2011]	

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References: CPS product monographs 2008 (e-CPS accessed 12 Sep, 2008); *Product information leaflets. See also RxFiles Drug Comparison Charts / BOOK – diabetes pages 24-26 (www.RxFiles.ca).*

Additional References:
Errors Associated with Pen Injectors. Pharmacist's Letter Nov 2008.
Gibney MA, Arce CH, Byron KJ, Hirsch LJ. Skin and subcutaneous adipose layer thickness in adults with diabetes at sites used for insulin injections: implications for needle length recommendations. Curr Med Res Opin. 2010 Jun;26(6):1519-30.
Hofman PL, Behrensdorf Derraik JG, et al. Defining the ideal injection techniques when using 5-mm needles in children and adults. Diabetes Care. 2010 Jun 28.
Israel-Bultman Harma, Hyllested-Winge Jacob, Kolaczynski Marcin, et al. Comparison of Preference for NovoPen(R) 4 With Previous Insulin Pen Treatments After 12 Weeks in Adult Patients With Type 1 and Type 2 Diabetes: A Multicenter Observational Study, Clinical Therapeutics, Volume 33, Issue 3, March 2011, Pages 346-357
Jet injectors (eg. AdvantaJet, Medi-Jector) avoid the use of needles, are expensive, & require frequent cleaning.

INSULIN Comparison Chart

1. DeWitt DE, Hirsch IB. Outpatient insulin therapy in type 1 and type 2 diabetes mellitus: scientific review. JAMA. 2003 May 7;289(17):2254-64.
2. Drug Information Handbook 10TH edition. Lacy CF et al (editors). American Pharmaceutical Association. Lexi-Comp Inc, Hudson Ohio, 2002-2003 edition.
3. Boctor, MA. Diabetes Mellitus in Therapeutic Choices (3rd edition). Gray, Jean (editor). Canadian Pharmacists Association. Web-com Ltd, Ottawa, ON, 2000.
4. Micromedex 2018.
5. Yki-Jarvinen H, Ryysy L, Nikkila K, et al. Comparison of bedtime insulin regimens in patients with type 2 diabetes mellitus: a randomized controlled trial. (FINFAT STUDY) Ann Intern Med 1999;130:389-96.
6. Meltzer S, Leiter L, Daneman D. et al 1998 Clinical practice guidelines for the management of diabetes in **Canada**. CMAJ **1998**;159 (8 Suppl).
7. Hermann LS. Optimizing therapy for insulin-treated Type 2 Diabetes Mellitus. Drugs & Aging 2000;17(4):283-94.
8. Insulin glargine (Lantus), a new long-acting insulin. Med Lett Drugs Ther. 2001 Aug 6;43(1110):65-6.
9. Insulin aspart, a new rapid-acting insulin. Med Lett Drugs Ther. 2001 Oct 15;43(1115):89-90.
10. American Diabetes Association: Clinical Practice Recommendations 2003, Diabetes Care 2003 26:Supplement 1
11. Writing Team For The Diabetes Control And Complications Trial/Epidemiology Of Diabetes Interventions And Complications Research Group. Sustained effect of intensive treatment of type 1 diabetes mellitus on development and progression of diabetic nephropathy: the Epidemiology of Diabetes Interventions and Complications (EDIC) study. JAMA. 2003 Oct 22;290(16):2159-67.
12. Diabetes Control and Complications Trial Research Group. The effect of intensive treatment of diabetes on the development and progression of long-term complications in insulin-dependent diabetes mellitus. N Engl J Med. 1993;329:977-986.
13. Intensive blood-glucose control with sulphonylureas or insulin compared with conventional treatment and risk of complications in patients with type 2 diabetes (UKPDS 33). UK Prospective Diabetes Study (UKPDS) Group. Lancet. 1998 Sep 12;352(9131):837-53.
14. Yki-Jarvinen H, Ryysy L, Nikkila K, et al. Comparison of bedtime insulin regimens in patients with type 2 diabetes mellitus. A randomized, controlled trial. Ann Intern Med. 1999 Mar 2;130(5):389-96.
15. Wright A, Burden AC, Paisey RB, Cull CA, Holman RR; U.K. Prospective Diabetes Study Group. Sulfonylurea inadequacy: efficacy of addition of insulin over 6 years in patients with type 2 diabetes in the U.K. Prospective Diabetes Study (UKPDS 57). Diabetes Care. 2002 Feb;25(2):330-6.
16. Ohkubo Y, Kishikawa H, Araki E, Miyata T, Isami S, Motoyoshi S, Kojima Y, Furuyoshi N, Shichiri M. Intensive insulin therapy prevents the progression of diabetic microvascular complications in Japanese patients with non-insulin-dependent diabetes mellitus: a randomized prospective 6-year study. Diabetes Res Clin Pract. 1995 May;28(2):103-17.
17. Rosenstock J, Schwartz SL, Clark CM Jr, et al. Basal insulin therapy in type 2 diabetes: 28-week comparison of insulin glargine (HOE 901) and NPH insulin. Diabetes Care. 2001 Apr;24(4):631-6.
18. New Drugs: Lantus (insulin glargine injection). in Pharmacists Letter Mar 2005;21(3):210319.
19. Mayfield JA, White RD. Insulin therapy for type 2 diabetes: rescue, augmentation, and replacement of beta-cell function. Am Fam Physician. 2004 Aug 1;70(3):489-500. Erratum in: Am Fam Physician. 2004 Dec 1;70(11):2079-80.
20. Harjutsalo V, Podar T, Tuomilehto J. Cumulative incidence of type 1 diabetes in 10,168 siblings of Finnish young-onset type 1 diabetic patients. Diabetes 2005; 54:563-69. (InfoPOEMs- The cumulative risk of type 1 diabetes up to ages 10, 20, 30, 40, and 50 years in brothers and sisters of patients with childhood-onset diabetes is 1.5%, 4.1%, 5.5%, 6.4%, and 6.9%, respectively. A young age at diagnosis of diabetes in the index case is the strongest predictor of the risk of type 1 diabetes in siblings. The risk in siblings is also increased with increasing maternal and paternal age at birth and male sex. (LOE = 1b))
21. Hirsch IB. Insulin analogues. N Engl J Med. 2005 Jan 13;352(2):174-83.
22. **Treatment Guidelines**: Drugs for Diabetes. **The Medical Letter**: August, **2005**; (3) pp. 57-62.
23. Rosenstock J, Zinman B, Murphy LJ, et al. **Inhaled insulin** improves glycemic control when substituted for or added to oral combination therapy in type 2 diabetes: a randomized, controlled trial. Ann Intern Med. 2005 Oct 18;143(8):549-58. CONCLUSIONS: Inhaled insulin improved overall glycemic control and hemoglobin A1c level when added to or substituted for dual oral agent therapy with an insulin secretagogue and sensitizer. Consistent with other insulin therapies, hypoglycemia and mild weight gain occurred. Pulmonary function showed no between-group differences.
24. Comparison of insulins Pharmacist's Letter/Prescriber's Letter 2006;22(2):220217
25. van den Berghe G, Wouters P, Weekers F, Verwaest C, Bruyninckx F,et al. Intensive insulin therapy in the **critically ill patients**. N Engl J Med. 2001 Nov 8;345(19):1359-67.
26. Van den Berghe G, Wilmer A, Hermans G, et al. Intensive insulin therapy in the **medical ICU**. N Engl J Med. 2006 Feb 2;354(5):449-61. CONCLUSIONS: Intensive insulin therapy significantly reduced morbidity but not mortality among all patients in the medical ICU. Although the risk of subsequent death and disease was reduced in patients treated for three or more days, these patients could not be identified before therapy. Further studies are needed to confirm these preliminary data. (InfoPOEMs: Intensive insulin treatment of patients in the medical intensive care unit (ICU) is helpful if patients spend at least 3 days in the unit. Unfortunately, those with a shorter stay may be harmed, and physicians were unable to accurately predict who would actually stay 3 or more days (36% of those predicted to stay at least 3 days were discharged sooner in this study). (LOE = 1b))
27. Nathan DM, et al.; Diabetes Control and Complications Trial/Epidemiology of Diabetes Interventions and Complications (**DCCT/EDIC**) Study Research Group. Intensive diabetes treatment and cardiovascular disease in patients with type 1 diabetes. N Engl J Med. 2005 Dec 22;353(25):2643-53. (InfoPOEMs: This extension of the Diabetes Control and Complications Trial (DCCT) trial provides the first high-quality evidence that intensive treatment of Type 1 diabetes reduces the risk of adverse cardiovascular outcomes. Although the relative risk reduction was greater than 50%, the absolute risk reduction (0.42 per 100 patient years; NNT=25 over 10years) was modest. Note that this effect has not been shown in patients with Type 2 diabetes, although many patients and physicians believe otherwise, and data regarding all-cause mortality or adverse effects of intensive treatment (such as hypoglycemic episodes or traffic accidents) are not reported.. (LOE = 1b))
28. Van den Berghe G, Schoonheydt K, Becx P, Bruyninckx F, Wouters PJ. Insulin therapy protects the central and peripheral nervous system of intensive care patients. Neurology. 2005;64:1348-53.
29. Fiallo-Scharer R, Horner B, McFann K, Walravens P, Chase HP. **Mixing rapid-acting** insulin analogues with insulin **glargine** in children with type 1 diabetes mellitus. J Pediatr. 2006 Apr;148(4):481-4. There were no significant differences in glycemic control between children who mixed IG in the same syringe with a RAI analogue compared with children who took separate injections.
30. Garg S, Rosenstock J, et al. Efficacy & safety of preprandial human **insulin inhalation** powder versus injectable insulin in pts with type 1 diabetes. Diabetologia. 2006 May;49(5):891-9. Epub 2006 Feb 28.
31. Barnett AH, et al. An open, randomized, parallel-group study to compare the efficacy and safety profile of **inhaled human insulin (Exubera) with metformin** as adjunctive therapy in patients with type 2 diabetes poorly controlled on a sulfonylurea. Diabetes Care. 2006 Jun;29(6):1282-7.
32. Hermansen K, et al. A 26-week, randomized, parallel, treat-to-target trial **comparing insulin detemir with NPH** insulin as add-on therapy to oral glucose-lowering drugs in insulin-naive people with type 2 diabetes. Diabetes Care. 2006 Jun;29(6):1269-74. In both groups, 70% of participants achieved an A1C < or =7.0%, but the proportion achieving this without hypoglycemia was higher with insulin detemir than with NPH insulin (26 vs. 16%, P = 0.008). Compared with NPH insulin, the risk for all hypoglycemia with insulin detemir was reduced by 47% (P < 0.001) and nocturnal hypoglycemia by 55% (P < 0.001). Mean weight gain was 1.2 kg with insulin detemir and 2.8 kg with NPH insulin (P < 0.001), and the difference in baseline-adjusted final weight was -1.58 (P < 0.001).
33. Siebenhofer A, et al. **Short acting insulin analogues versus regular** human insulin in patients with diabetes mellitus. Cochrane Database Syst Rev. 2006 Apr 19;(2):CD003287.
34. Cheung NW, Wong VW, McLean M. The hyperglycemia: intensive insulin infusion in infarction (HI-5) study: a randomized controlled trial of insulin infusion therapy for myocardial infarction. Diabetes Care. 2006 Apr;29(4):765-70. (InfoPOEMs: Intensive control of blood glucose in patients with known diabetes or in patients with hyperglycemia at the time of admission for acute myocardial infarction (AMI) does not decrease either short-term or long-term mortality. (LOE = 1b-))
35. Inhaled insulin (**Exubera**). Med Lett Drugs Ther. 2006 Jul 17;48(1239):57-8. {dry powder, rapid acting, not yet in Canada; no difference in HbA1c from regular/NPH based regimens; pts may prefer over sc; CI in COPD, smoking; long term lung safety unknown; $$$$}
36. Pearson ER, et al. Neonatal Diabetes International Collaborative Group. Switching **from insulin to oral sulfonylureas** in pts with diabetes due to Kir6.2 mutations. N Engl J Med. 2006 Aug 3;355(5):467-77.
37. Babenko AP, et al. Activating mutations in the ABCC8 gene in neonatal diabetes mellitus. N Engl J Med. 2006 Aug 3;355(5):456-66.
38. Mooradian AD, Bernbaum M, Albert SG. Narrative review: a rational approach to starting insulin therapy. Ann Intern Med. 2006 Jul 18;145(2):125-34.
39. Health Canada Insulin Products update Sept/06 http://www.hc-sc.gc.ca/iyh-vsv/alt_formats/cmcd-dcmc/pdf/insulin_e.pdf .
40. Ballani P, Tran MT, Navar MD, Davidson MB. Clinical experience with **U-500 regular insulin** in obese, markedly insulin-resistant type 2 diabetic patients. Diabetes Care. 2006 Nov;29(11):2504-5.

41. Ceglia L, Lau J, Pittas AG. Meta-analysis: efficacy and safety of **inhaled insulin** therapy in adults with diabetes mellitus. Ann Intern Med. 2006 Nov 7;145(9):665-75.
42. Budnitz DS, et al. National surveillance of emergency department visits for outpatient **adverse drug events**. JAMA. 2006 Oct 18;296(15):1858-66. In an analysis of routine surveillance data from 63 US hospitals, adverse drug events accounted for an estimated 2.5% of emergency department visits for unintentional injury and 0.6% of visits for all causes. About a third were allergic reactions and another third were unintentional overdoses, particularly of drugs that need regular monitoring such as digoxin and warfarin. Insulin and warfarin were implicated in over a quarter of all serious events. Insulin, warfarin, and digoxin accounted for more than 40% of serious events among people aged over 65.
43. Dunn C, Curran MP. **Inhaled human insulin** (Exubera): a review of its use in adult patients with diabetes mellitus. Drugs. 2006;66(7):1013-32.
44. Shapiro AM, et al. International trial of the **Edmonton protocol** for **islet transplantation**. N Engl J Med. 2006 Sep 28;355(13):1318-30. Out of the 36 patients given transplants in an uncontrolled trial, 16 had stopped using insulin by the end of the first year, but only five were still independent of insulin a year later. Only one was cured for the full three years of the trial.
45. Barnett AH, et al. An open, randomized, parallel-group study to compare the efficacy and safety profile of **inhaled human insulin** (Exubera) with glibenclamide as adjunctive therapy in patients with type 2 diabetes poorly controlled on metformin. Diabetes Care. 2006 Aug;29(8):1818-25.
46. Cheung NW, et al. The Hyperglycemia: **Intensive Insulin Infusion in Infarction** (**HI-5**) study: a randomized controlled trial of insulin infusion therapy for myocardial infarction. Diabetes Care. 2006 Apr;29(4):765-70.
47. Martin CL, et al. **DCCT/EDIC** Research Group. **Neuropathy** among the diabetes control and complications trial cohort 8 years after trial completion. Diabetes Care. 2006 Feb;29(2):340-4.
48. Skyler JS, Jovanovic L, Klioze S, Reis J, Duggan W; Inhaled Human Insulin Type 1 Diabetes Study Group. Two-year safety and efficacy of inhaled human insulin (**Exubera**) in adult patients with type 1 diabetes. Diabetes Care. 2007 Mar;30(3):579-85. Treatment group differences in lung function between EXU and s.c. insulin in adult patients with type 1 diabetes are small, develop early, and are nonprogressive for up to 2 years of therapy.
49. McMahon GT, Arky RA. **Inhaled insulin** for diabetes mellitus. N Engl J Med. 2007 Feb 1;356(5):497-502.
50. Taylor R, Davison JM. **Type 1 diabetes and pregnancy**. BMJ. 2007 Apr 7;334(7596):742-5.
51. Diabetes Control and Complications Trial/Epidemiology of Diabetes Interventions and Complications Study Research Group; (**DCCT/EDIC**) Jacobson AM, Musen G, Ryan CM, et al. Long-term effect of diabetes and its treatment on cognitive function. N Engl J Med. 2007 May 3;356(18):1842-52. **No evidence of substantial long-term declines in cognitive function** was found in a large group of patients with type 1 diabetes who were carefully followed for an average of 18 years, despite relatively high rates of recurrent severe hypoglycemia. Forty percent of the cohort reported having had at least one hypoglycemic coma or seizure.
52. Horvath K, Jeitler K, Berghold A, et al. Long-acting insulin analogues versus NPH insulin (human isophane insulin) for type 2 diabetes mellitus. Cochrane Database Syst Rev. 2007 Apr 18;(2):CD005613. Our analysis suggests, if at all only a minor clinical benefit of treatment with long-acting insulin analogues for patients with diabetes mellitus type 2 treated with "basal" insulin regarding symptomatic nocturnal hypoglycaemic events. Until long-term efficacy and safety data are available, we suggest a cautious approach to therapy with **insulin glargine or detemir**.
53. Gandhi GY, Nuttall GA, Abel MD, et al. Intensive intraoperative insulin therapy versus conventional glucose management during cardiac surgery: a randomized trial. Ann Intern Med. 2007 Feb 20;146(4):233-43. Intensive insulin therapy during cardiac surgery does not reduce perioperative death or morbidity. The increased incidence of death and stroke in the intensive treatment group raises concern about routine implementation of this intervention.
54. Pharmacist's Letter. Treatment of Diabetes in women who are **pregnant**. Sept 2007.
55. Bryden KS, et al. Eating habits, body weight, and insulin misuse. A longitudinal study of teenagers and young adults with type 1 diabetes. Diabetes Care. 1999 Dec;22(12):1956-60.
56. Holman RR, Thorne KI, Farmer AJ, Davies MJ, Keenan JF, Paul S, et al.; the **4-T Study** Group. Addition of Biphasic, Prandial, or Basal Insulin to Oral Therapy in Type 2 Diabetes. (4T) N Engl J Med. 2007 Sep 21; [Epub ahead of print] A single analogue-insulin formulation added to metformin and sulfonylurea resulted in a glycated hemoglobin level of 6.5% or less in a minority of patients at 1 year. The addition of biphasic or prandial insulin aspart reduced levels more than the addition of basal insulin detemir but were associated with greater risks of hypoglycemia and weight gain. (InfoPOEMs: Patients choosing biphasic or prandial insulin regiments should be prepared to gain approximately **10 pounds to 12 pounds** and expect **4 to 8 moderate or severe episodes of hypoglycemia per year**. Basal insulin was a bit less effective as measured by the change in glycated hemoglobin (Hb A1C), but resulted in less weight gain & much less hypoglycemia. Of course, we don't know whether any of these regiments improve long-term clinical outcomes in these patients. If you are going to add insulin for a patient with poorly controlled Type 2 diabetes, it makes sense to start with a single dose of basal insulin for most patients, and to focus primarily on those patients with an initial Hb A1C of more than 8.5%. (LOE = 1b))

    Holman, Rury R., Farmer, Andrew J., Davies, Melanie J., et al. the 4-T Study Group, **Three-Year** Efficacy of Complex Insulin Regimens in Type 2 Diabetes.N Engl J Med 2009 0: NEJMoa0905479. Patients who added a basal or prandial insulin-based regimen to oral therapy had better glycated hemoglobin control than patients who added a biphasic insulin-based regimen. Fewer hypoglycemic episodes and less weight gain occurred in patients adding basal insulin.
57. Pharmacists Letter. Exubera. Oct 2007.
58. Norris JM, Yin X, Lamb MM, Barriga K, et al. **Omega-3** polyunsaturated fatty acid intake and islet autoimmunity in children at increased risk for type 1 diabetes. JAMA. 2007 Sep 26;298(12):1420-8. Dietary intake of omega-3 fatty acids is associated with reduced risk of IA in children at increased genetic risk for type 1 diabetes.
59. Weston C, Walker L, Birkhead J; National Audit of Myocardial Infarction Project, National Institute for Clinical Outcomes Research. Early impact of insulin treatment on mortality for hyperglycaemic patients without known diabetes who present with an **acute coronary syndrome**. Heart. 2007 Dec;93(12):1542-6. Epub 2007 May 13. In non-diabetic patients with acute coronary syndrome and hyperglycaemia, treatment with insulin was associated with a reduction in the relative risk of death, evident within 7 days of admission, which persists at 30 days.
60. Datta S, Qaadir A, Villanueva G, Baldwin D. Once-daily insulin glargine versus 6-hour sliding scale regular insulin for control of hyperglycemia after a bariatric surgical procedure: a randomized clinical trial. Endocr Pract 2007;13(3):225-31.
61. Yeldandi RR, Lurie A, Baldwin D. Comparison of once-daily glargine insulin with twice-daily NPH/regular insulin for control of hyperglycemia in inpatients after cardiovascular surgery. Diabetes Technology & Therapeutics 2006;8(6):609-16.
62. Hofman PL, Lawton SA, Peart JM, et al. An angled insertion technique using 6-mm needles markedly reduces the risk of intramuscular injections in children and adolescents. Diabetic Medicine 2007;74(12):1400-1405. (InfoPOEMs: A pinched technique with angled insertion using 6-mm needles most reliably results in the appropriately placed subcutaneous injection of insulin in children with diabetes. This same needle-size used in the abdominal site also resulted in the least amount of injection pain. (LOE = 2b))
63. Goebel-Fabbri AE, Fikkan J, et al. **Insulin restriction and associated morbidity and mortality** in women with type 1 diabetes. Diabetes Care. 2008 Mar;31(3):415-9. Epub 2007 Dec 10. Our data demonstrate that insulin restriction is associated with increased rates of diabetes complications and increased mortality risk. Mortality associated with insulin restriction appeared to occur in the context of eating disorder symptoms, rather than other psychological distress.
64. Hassan K, Rodriguez LM, Johnson SE, et al. A randomized, controlled trial comparing twice-a-day insulin glargine mixed with rapid-acting insulin analogs versus standard neutral protamine Hagedorn (NPH) therapy in newly diagnosed type 1 diabetes. Pediatrics. 2008 Mar;121(3):e466-72. Epub 2008 Feb 25. Glycemic control with insulin glargine mixed with a rapid-acting insulin analog given twice daily seems significantly more effective than the standard therapy in newly diagnosed type 1 diabetes. Furthermore, it decreases pain and burden of injections for children with diabetes by allowing patients to **mix glargine with rapid**-acting insulin analog.
65. Coustan DR. Pharmacological management of **gestational diabetes**: an overview. Diabetes Care. 2007 Jul;30 Suppl 2:S206-8. Review. Erratum in: Diabetes Care. 2007 Dec;30(12):3154.
66. Bretzel RG, Nuber U, Landgraf W, et al. **Once-daily basal insulin glargine** versus thrice-daily prandial insulin lispro in people with type 2 diabetes on oral hypoglycaemic agents (APOLLO): an open randomised controlled trial. Lancet. 2008 Mar 29;371(9618):1073-84. A therapeutic regimen involving the addition of either basal or prandial insulin analogue is equally effective in lowering haemoglobin A(1c). We conclude that insulin glargine provides a simple and effective option that is more satisfactory to patients than is lispro for early initiation of insulin therapy, since it was associated with a lower risk of hypoglycaemia, fewer injections, less blood glucose self monitoring, and greater patient satisfaction than was insulin lispro.

postitive mast cells, known to be sensitive to sodium cromolyn, may contribute to the destructive immune process mediated in response to exogenous insulin. Mast cell stabilizing therapy with topical **cromolyn** may reverse early and prevent new **lipoatrophic** lesions.

68. Cope JU, Morrison AE, Samuels-Reid J. Adolescent use of **insulin** and patient-controlled analgesia **pump** technology: a 10-year Food and Drug Administration retrospective study of adverse events. Pediatrics. 2008 May;121(5):e1133-8. A total of 1674 reports were identified: 1594 for insulin pumps and 53 for patient-controlled analgesic pumps. In reports of insulin pump events, there were 13 reported deaths, 2 reports that indicated possible suicide attempts, and several additional reports indicating severe hypoglycemic or hyperglycemic events that seemed to be device-related.
69. Guideline Development Group. Management of diabetes from **preconception to the postnatal** period: summary of NICE guidance. BMJ. 2008 Mar 29;336(7646):714-7.
70. Crowther CA, Hiller JE, Moss JR, et al. Australian Carbohydrate Intolerance Study in Pregnant Women (**ACHOIS**) Trial Group. Effect of treatment of gestational diabetes mellitus on pregnancy outcomes. N Engl J Med. 2005 Jun 16;352(24):2477-86. Epub 2005 Jun 12.
71. Rowan JA, Hague WM, Gao W, Battin MR, et al; **MiG** Trial Investigators. **Metformin** versus insulin for the treatment of gestational diabetes. N Engl J Med. 2008 May 8;358(19):2003-15. In women with gestational diabetes mellitus, metformin (alone or with supplemental insulin) is not associated with increased perinatal complications as compared with insulin. The women preferred metformin to insulin.
72. Langer O, Conway DL, Berkus MD, Xenakis EM, Gonzales O. A comparison of **glyburide and insulin** in women with gestational diabetes mellitus. N Engl J Med. 2000 Oct 19;343(16):1134-8. In women with gestational diabetes, glyburide is a clinically effective alternative to insulin therapy.
73. Gangemi A, Salehi P, Hatipoglu B, Martellotto J, Barbaro B, Kuechle JB, Qi M, Wang Y, Pallan P, Owens C, Bui J, West D, Kaplan B, Benedetti E, Oberholzer J. **Islet transplantation** for brittle type 1 diabetes: the UIC protocol.Am J Transplant. 2008 Jun;8(6):1250-61. Epub 2008 Apr 29. Four subjects (Group 1) received the Edmonton immunosuppression regimen (daclizumab, sirolimus, tacrolimus). Six subjects (Group 2) received the University of Illinois protocol (etanercept, exenatide and the Edmonton regimen).Combined treatment of etanercept and exenatide improves islet graft function and facilitates achievement of insulin-independence with less islets.
74. Vardi M, Jacobson E, Nini A, Bitterman H. Intermediate acting versus long acting insulin for type 1 diabetes mellitus. Cochrane Database Syst Rev. 2008 Jul 16;(3):CD006297. Long acting insulin preparations seem to exert a beneficial effect on nocturnal glucose levels. Their effect on the overall diabetes control is clinically unremarkable. Their use as a basal insulin regimen for type 1 diabetes mellitus warrants further substantiation.
75. Rosenstock J, Davies M, Home PD, Larsen J, Koenen C, et al. A randomised, 52-week, treat-to-target trial comparing **insulin detemir with insulin glargine** when administered as add-on to glucose-lowering drugs in insulin-naive people with type 2 diabetes. Diabetologia. 2008 Jan 16; [Epub ahead of print] Supplementation of oral agents with detemir or glargine achieves clinically important improvements in glycaemic control with low risk of hypoglycaemia. Non-inferiority was demonstrated for detemir using higher insulin doses (mainly patients on twice daily dosing); weight gain was somewhat reduced with once daily insulin detemir.
76. Soylemez Wiener R, Wiener DC, Larson RJ. Benefits and risks of **tight glucose control in critically ill** adults: a meta-analysis. JAMA. 2008 Aug 27;300(8):933-44. In critically ill adult patients, tight glucose control is not associated with significantly reduced hospital mortality but is associated with an increased risk of hypoglycemia.
77. de Boer IH, Kestenbaum B, Rue TC, et al. Diabetes Control and Complications Trial (**DCCT**)/Epidemiology of Diabetes Interventions and Complications (**EDIC**) Study Research Group. Insulin therapy, hyperglycemia, and hypertension in type 1 diabetes mellitus. Arch Intern Med. 2008 Sep 22;168(17):1867-73. Hyperglycemia is a risk factor for incident hypertension in type 1 diabetes, and intensive insulin therapy reduces the long-term risk of developing hypertension.
78. Qayyum R, Bolen S, Maruthur N, et al. Systematic Review: Comparative Effectiveness and Safety of Premixed Insulin Analogues in Type 2 Diabetes. Ann Intern Med. 2008 Sep 15. [Epub ahead of print]
79. Murphy HR, Rayman G, Lewis K, et al; Effectiveness of **continuous glucose monitoring** in pregnant women with diabetes: randomised clinical trial. BMJ. 2008 Sep 25;337:a1680. doi: 10.1136/bmj.a1680. Continuous glucose monitoring during pregnancy is associated with improved glycaemic control in the third trimester, lower birth weight, and reduced risk of macrosomia.
80. Juvenile Diabetes Research Foundation Continuous Glucose Monitoring Study Group, Tamborlane WV, Beck RW, Bode BW, et al. **Continuous glucose monitoring** and intensive treatment of type 1 diabetes. N Engl J Med. 2008 Oct 2;359(14):1464-76. Epub 2008 Sep 8.
81. Weng J et al. Effect of **intensive insulin** therapy on β-cell function and glycaemic control in patients with **newly diagnosed** type 2 diabetes: A multicentre randomised parallel-group trial. Lancet 2008 May 24; 371:1753.
82. Chen HS, Wu TE, Jap TS, Hsiao LC, Lee SH, Lin HD. Beneficial effects of insulin on glycemic control and beta-cell function in **newly diagnosed** type 2 diabetes with severe hyperglycemia after short-term **intensive insulin** therapy. Diabetes Care. 2008 Oct;31(10):1927-32. Epub 2008 Jun 12. n=50. A 6-month course of insulin therapy, compared with OAD treatment, could more effectively achieve adequate glycemic control and significant improvement of beta-cell function in new-onset type 2 diabetic patients with severe hyperglycemia.
83. Nathan DM, Buse JB, Davidson MB, Ferrannini E, Holman RR, Sherwin R, Zinman B. Medical management of hyperglycaemia in type 2 diabetes mellitus: a **consensus algorithm** for the initiation and adjustment of therapy : A consensus statement from the American Diabetes Association (**ADA**) and the European Association for the Study of Diabetes. Diabetologia. 2008 Oct 22. http://care.diabetesjournals.org/misc/MedicalManagementofHyperglycemia.pdf
84. Ludvigsson J, Faresjo M, Hjorth M, et al. **GAD treatment** and insulin secretion in recent-onset type 1 diabetes. N Engl J Med. 2008 Oct 30;359(18):1909-20. Epub 2008 Oct 8.
85. Arabi YM, Dabbagh OC, Tamim HM, et al. Intensive versus conventional insulin therapy: a randomized controlled trial in medical and surgical **critically ill patients**. Crit Care Med. 2008 Dec;36(12):3190-7. Intensive insulin therapy was not associated with improved survival among medical surgical intensive care unit patients and was associated with increased occurrence of hypoglycemia. Based on these results, we do not advocate universal application of intensive insulin therapy in intensive care unit patients.
86. Esposito K, Ciotola M, Maiorino MI, et al. Addition of neutral protamine lispro insulin or insulin glargine to oral type 2 diabetes regimens for patients with suboptimal glycemic control: a randomized trial. Ann Intern Med. 2008 Oct 21;149(8):531-9. Similar glycemic control occurred with the addition of NPL or glargine insulin to oral regimens in patients with poorly controlled type 2 diabetes. Hypoglycemia was similar in the 2 groups, but sample size limited the ability to make a definite safety assessment.
87. Hollander P, Cooper J, Bregnhøj J, Pedersen CB. A 52-week, multinational, open-label, parallel-group, noninferiority, treat-to-target trial comparing **insulin detemir with insulin glargine** in a basal-bolus regimen with mealtime insulin aspart in patients with type 2 diabetes. Clin Ther. 2008 Nov;30(11):1976-87. When used as indicated as part of a basal-bolus regimen in patients with T2DM who had previously received other insulin and/or OAD regimens, detemir was noninferior to glargine in its effects on overall glycemic control. Both basal insulins were associated with clinically relevant reductions in hyperglycemia. Both were well tolerated, with no significant difference in the frequency of hypoglycemia or AEs.
88. Pharmacist's Letter. **How Much Insulin is Too Much**? Jan 2009.
89. Ashwell SG, Gebbie J, Home PD. Twice-daily compared with once-daily insulin glargine in people with Type 1 diabetes using meal-time insulin aspart. Diabet Med. 2006 Aug;23(8):879-86.
90. Ashwell SG, Gebbie J, Home PD. Optimal timing of injection of once-daily insulin glargine in people with Type 1 diabetes using insulin lispro at meal-times. Diabet Med. 2006 Jan;23(1):46-52.
91. Lund SS, Tarnow L, Astrup AS, et al. Effect of adjunct **metformin** treatment in patients with type-1 diabetes and persistent inadequate glycaemic control. A randomized study. PLoS ONE. 2008;3(10):e3363. Epub 2008 Oct 9.
92. NeedleAid Ensures: injection at the proper angle & depth & shields the needle. Useful for visually impaired. http://www.needleaid.com/
93. Hirsch IB. **Sliding scale** insulin--time to stop sliding. JAMA. 2009 Jan 14;301(2):213-4.
94. Singh SR, Ahmad F, Lal A, et al. Efficacy and safety of insulin analogues for the management of diabetes mellitus: a meta-analysis. CMAJ 2009;180(4):385-97. Online at: http://www.cmaj.ca/cgi/reprint/180/4/385 Rapid-and long-acting insulin analogues offer little benefit relative to conventional insulins in terms of glycemic control or reduced hypoglycemia. Long-term, high-quality studies are needed to determine whether insulin analogues reduce the risk of long-term complications of diabetes.
95. Cameron CG, Bennett HA. Cost-effectiveness of insulin analogues for diabetes mellitis. CMAJ 2009;180(4):400-7. http://www.cmaj.ca/cgi/reprint/180/4/400 . The cost-effectiveness of insulin analogues depends on the type of insulin analogue and whether the patient receiving the treatment has type 1 or type 2 diabetes. With the exception of rapid-acting insulin analogues in type 1 diabetes, routine use of insulin analogues, especially long-acting analogues in type 2 diabetes, is unlikely to represent an efficient use of finite health care resources.
96. Siebenhofer-Kroitzsch A, Horvath K, Plank J. Insulin analogues: too much noise about small benefits. CMAJ. 2009 Feb 17;180(4):369-70. http://www.cmaj.ca/cgi/reprint/180/4/369
97. Beardsall K, Vanhaesebrouck S, Ogilvy-Stuart AL, et al. **Early insulin therapy in very-low-birth-weight infants.** N Engl J Med. 2008 Oct 30;359(18):1873-84.
98. **NICE-SUGAR** Study Investigators, Finfer S, Chittock DR, Su SY, Blair D, et al. **Intensive** versus conventional glucose control in **critically ill** patients. N Engl J Med. 2009 Mar 26;360(13):1283-97. Epub 2009 Mar 24. In this

to 108 mg per deciliter.
Griesdale DE, de Souza RJ, van Dam RM, et al. Intensive insulin therapy and mortality among critically ill patients: a meta-analysis including NICE-SUGAR study data. CMAJ. 2009 Apr 14;180(8):821-7. Epub 2009 Mar 24.
99. Montori VM, Fernández-Balsells M. **Glycemic Control** in Type 2 Diabetes: **Time for an Evidence-Based About-Face**?. Ann Intern Med. 2009 Apr 20.
100. Ray KK, Seshasai SR, et al. Effect of **intensive control of glucose on cardiovascular outcomes** and death in patients with diabetes mellitus: a meta-analysis of randomized controlled trials. Lancet 2009; 373: 1765-72.
101. Perez, Norma, Moisan, Jocelyne, Sirois, Caroline, Poirier, Paul, Gregoire, Jean-Pierre. **Initiation of insulin** therapy in elderly patients taking oral antidiabetes drugs. CMAJ 2009 180: 1310-1316.
102. Glargine & cancer: FDA Jul/09 : Early Communication About Safety of Lantus (insulin glargine): http://www.fda.gov/Drugs/DrugSafety/PostmarketDrugSafetyInformationforPatientsandProviders/DrugSafetyInformationforHeathcareProfessionals/ucm169722.htm ; http://www.diabetologia-journal.org/cancer.html ; Related links: http://www.medscape.com/viewarticle/705198?src=mp&spon=34&uac=93517FV ; http://www.nationalpost.com/life/health/story.html?id=4578946f-1f50-426e-b92a-bc0f7dd86eed ; http://www.hc-sc.gc.ca/ahc-asc/media/advisories-avis/_2009/2009_115-eng.php ; http://www.endo-society.org/advocacy/policy/upload/Statement-for-Patients-on-Insulin-Glargine.pdf
Currie CJ, Poole CD, Gale EA. The influence of glucose-lowering therapies on cancer risk in type 2 diabetes. Diabetologia. 2009 Jul 2. [Epub ahead of print]
Hemkens LG, Grouven U, Bender R, Günster C, Gutschmidt S, Selke GW, Sawicki PT. Risk of malignancies in patients with diabetes treated with human insulin or insulin analogues: a cohort study. Diabetologia. 2009 Jun 30. [Epub ahead of print]
Jonasson JM, Ljung R, Talbäck M, Haglund B, Gudbjörnsdóttir S, Steineck G. Insulin glargine use and short-term incidence of malignancies-a population-based follow-up study in Sweden. Diabetologia. 2009 Jul 9. [Epub ahead of print]
Ruiter R, Visser LE, van Herk-Sukel MP, et al. Risk of cancer in patients on insulin glargine and other insulin analogues in comparison with those on human insulin: results from a large population-based follow-up study. Diabetologia. 2011 Sep 29.
Wu JW, Azoulay L, Majdan A, et al. Long-Term Use of **Long-Acting Insulin Analogs and Breast Cancer** Incidence in Women With Type 2 Diabetes. J Clin Oncol. 2017 Sep 27:JCO2017734491.
103. Pérez N, Moisan J, Sirois C, Poirier P, Grégoire JP. **Initiation of insulin** therapy in elderly patients taking oral antidiabetes drugs. CMAJ. 2009 Jun 23;180(13):1310-6
104. Bolli GB, Kerr D, Thomas R, et al. Comparison of a multiple daily insulin injection regimen (basal once-daily glargine plus mealtime lispro) and continuous subcutaneous insulin infusion (lispro) in type 1 diabetes: a randomized open parallel multicenter study. Diabetes Care. 2009 Jul;32(7):1170-6. Epub 2009 Apr 23. In unselected people with type 1 diabetes naive to CSII or insulin glargine, glycemic control is no better with the more expensive CSII therapy compared with glargine-based MDI therapy.
105. Lingvay I, Legendre JL, Kaloyanova PF, et al. **Insulin-Based** versus Triple Oral Therapy for Newly-Diagnosed Type 2 Diabetes: Which is Better? Diabetes Care. 2009 Jul 10. [Epub ahead of print] When compared with a clinically equivalent treatment regimen, insulin-based therapy is effective, did not cause greater weight gain or hypoglycemia, nor decrease compliance, treatment satisfaction, or QoL. Insulin is safe, well-accepted, and effective for ongoing treatment of patients with newly-diagnosed type 2 diabetes.
106. Pollex EK, Feig DS, Lubetsky A, Yip PM, Koren G. Insulin **Glargine** Safety in **Pregnancy**: a Transplacental Transfer Study. Diabetes Care. 2009 Oct 6. [Epub ahead of print]
107. Dejgaard A, Lynggaard H, Råstam J, Krogsgaard Thomsen M. No evidence of increased risk of **malignancies** in patients with diabetes treated with insulin **detemir**: a meta-analysis. Diabetologia. 2009 Oct 17.
108. Van den Berghe G, Mesotten D, Vanhorebeek I. Intensive insulin therapy in the intensive care unit. CMAJ. 2009 Apr 14;180(8):799-800. Epub 2009 Mar 24.
109. Pescovitz MD, Greenbaum CJ, et al. Type 1 Diabetes TrialNet Anti-CD20 Study Group. **Rituximab**, B-lymphocyte depletion, and preservation of beta-cell function. N Engl J Med. 2009 Nov 26;361(22):2143-52.
110. Wilson Jennifer F. **In the Clinic: Diabetic Ketoacidosis**. Ann Intern Med January 5, 2010 152:ITC1-1; doi:10.1059/0003-4819-152-1-201001050-01001.
111. Misso ML, Egberts KJ, Page M, O'Connor D, Shaw J. Continuous subcutaneous insulin infusion (**CSII**) **versus multiple insulin** injections for type 1 diabetes mellitus. Cochrane Database Syst Rev. 2010 Jan 20;(1):CD005103.
112. Hernández-Díaz S, Adami HO. Diabetes therapy and **cancer risk**: causal effects and other plausible explanations. Diabetologia. 2010 Feb 23.
113. Hovorka R, Allen JM, Elleri D, et al. Manual **closed-loop insulin delivery** in children and adolescents with type 1 diabetes: a phase 2 randomised crossover trial. Lancet. 2010 Feb 27;375(9716):743-51.
114. Egi M et al. **Hypoglycemia** and outcome in critically ill patients. Mayo Clin Proc 2010 Mar; 85:217.
115. Barton AL, Gilbertson HR, Donath SM and Cameron FJ. Is bedtime **supper** necessary for older children with diabetes using **glargine insulin** in multiple daily injection regimens?. Diabet Med. 2010 Feb;27:238-41.
116. Gibney MA, Arce CH, et al. Skin & subcutaneous adipose layer thickness in adults with diabetes at sites used for insulin injections:implications for **needle length** recommendations. Curr Med Res Opin.2010Jun;26(6):1519-30.
117. Nguyen TM, Renukuntla VS, Heptulla RA. **Mixing Insulin Aspart With Detemir** Does Not Affect Glucose Excursion In Children With Type 1 Diabetes Mellitus. Diabetes Care. 2010 May 26.
118. Giovannucci, Edward, Harlan, David M., Archer, Michael C., et al. **Diabetes and Cancer**: A Consensus Report. CA Cancer J Clin 2010 0: caac.20078.
119. Hovorka R, Allen JM, Elleri D, et al. Manual closed-loop insulin delivery in children and adolescents with type 1 diabetes: a phase 2 randomised crossover trial. Lancet. 2010 Feb 27;375(9716):743-51.
120. Rosenstock Julio, Lorber Daniel L, Gnudi Luigi, et al., Prandial inhaled insulin plus basal insulin glargine versus twice daily biaspart insulin for type 2 diabetes: a multicentre randomised trial, The Lancet, Volume 375, Issue 9733, 26 June 2010-2 July 2010, Pages 2244-2253
121. Bergenstal, Richard M., Tamborlane, William V., Ahmann, Andrew, et al. the **STAR 3** Study Group, Effectiveness of **Sensor-Augmented Insulin-Pump** Therapy in Type 1 Diabetes. N Engl J Med 2010 0: NEJMoa1002853.
122. Miser William F., Arakaki R, Jiang H et al., Randomized, open-label, parallel-group evaluations of **basal-bolus therapy versus** insulin lispro **premixed** therapy in patients with type 2 diabetes mellitus failing to achieve control with starter insulin treatment and continuing oral antihyperglycemic drugs: A noninferiority intensification substudy of the DURABLE trial, Clinical Therapeutics, Volume 32, Issue 5, May 2010, Pages 896-908.
123. Hofman PL, Behrensdorf Derraik JG, et al. Defining the ideal injection techniques when using **5-mm needles** in children and adults. Diabetes Care. 2010 Jun 28.
124. Campbell PT, Deka A, Jacobs EJ, et al. Prospective study reveals associations between **colorectal cancer** and type 2 diabetes mellitus or insulin use in men. Gastroenterology. 2010 Oct;139(4):1138-46.
125. Grimaldi-Bensouda L, Marty M, Pollak M.; et al. The international study of insulin and cancer (**ISICA**). Lancet. 2010 Sep 4;376(9743):769-70.
126. Zhao YT, Weng CL, Chen ML, et al. Comparison of **glucose-insulin-potassium and insulin-glucose** as adjunctive therapy in acute myocardial infarction: a contemporary meta-analysis of randomised controlled trials. Heart. 2010 Oct;96(20):1622-6. Current evidence suggests that GIK with insulin does not reduce mortality in patients with AMI. However, studies of glycaemia are inconclusive & it remains possible that glycaemic control is beneficial.
127. Knip Mikael, Virtanen Suvi M, Seppä Karri, et al.. for the Finnish TRIGR Study Group. **Dietary Intervention** in Infancy and Later Signs of Beta-Cell Autoimmunity. N Engl J Med 2010; 363:1900-1908.
128. Frid A, Hirsch L, Gaspar R, et al. Scientific Advisory Board for the Third Injection Technique Workshop. **New injection recommendations** for patients with diabetes. Diabetes Metab. 2010 Sep;36 Suppl 1:S3-18.
129. Pharmacist's Letter. Insulin **Pump Therapy**. Dec 2010.
130. Dhulkotia JS, Ola B, Fraser R, et al. **Oral hypoglycemic agents vs insulin in management of gestational diabetes**: a systematic review and metaanalysis. Am J Obstet Gynecol. 2010 Nov;203(5):457.e1-9.
131. Pollex E, Moretti ME, Koren G,et al. Safety of Insulin **Glargine Use in Pregnancy**: A Systematic Review and Meta-Analysis (January). Ann Pharmacother.2011 Jan 4.
132. Kansagara Devan, Fu Rongwei, Freeman Michele, et al. **Intensive Insulin Therapy in Hospitalized Patients**: A Systematic Review. Ann Intern Med February 15, 2011 154:268-282.
133. Qaseem Amir, Humphrey Linda L., Chou Roger, et al. and for the Clinical Guidelines Committee of the American College of Physicians. Use of **Intensive Insulin Therapy for the Management of Glycemic Control in Hospitalized Patients**: A Clinical Practice Guideline From the American College of Physicians. Ann Intern Med February 15, 2011 154:260-267.
134. Zinman Bernard, Fulch e Greg r, Rao Paturi V. **Insulin degludec**, an ultra-long-acting basal insulin, once a day or three times a week versus insulin glargine once a day in patients with type 2 diabetes: a 16-week, randomised, open-label, phase 2 trial. The Lancet, Early Online Publication, 10 March 2011. doi:10.1016/S0140-6736(10)62305-7
135. Morgan CL, Evans M, Toft AD, et al. Clinical Effectiveness of Biphasic Insulin **Aspart 30:70** Vs Biphasic Human Insulin 30 in UK General Clinical Practice: A Retrospective Database Study. Clin Ther.2011Jan;33(1):27-35.
136. Hovorka R, Kumareswaran K, Harris J, Allen JM, Elleri D, Xing D, et al. **Overnight closed loop insulin delivery (artificial pancreas)** in adults with type 1 diabetes: crossover randomised controlled studies. BMJ 2011;342:1855.
137. Buse JB, Wolffenbuttel BH, Herman WH, et al. **DURAbility** of Basal versus Lispro mix 75/25 insulin Efficacy (DURABLE) Trial: Comparing the durability of lispro mix 75/25 and glargine. Diabetes Care. 2011 Feb;34(2):249-55.
138. Hamaty M. **Insulin treatment for type 2 diabetes**: When to start, which to use *Cleveland Clinic Journal of Medicine* 2011; 78(5):332-342; doi:10.3949/ccjm.78a.10051.
139. Korownyk C, Ivers N, Allan GM. Strategies for **initiating insulin** in type 2 diabetes. Can Fam Physician. 2011 May;57(5):562.
140. Umpierrez GE, Hor T, Smiley D, et al. Comparison of inpatient insulin regimens with **detemir plus aspart versus neutral protamine Hagedorn plus regular** in medical patients with type 2 diabetes. (DEAN) J Clin Endocrinol Metab 2009; 94:564–569.
141. Umpierrez GE, Smiley D, Jacobs S, et al. Randomized study of basal-bolus insulin therapy in the inpatient management of patients with type 2 diabetes undergoing general surgery (RABBIT 2 surgery). Diabetes Care 2011; 34:256–261.
142. Umpierrrez GE, Smiley D, Zisman A, et al. Randomized study of basal-bolus insulin therapy in the inpatient management of patients with type 2 diabetes (RABBIT 2 trial). Diabetes Care 2007; 30:2181–2186.
143. Umpierez GE. How to manage type 2 diabetes in **medical and surgical patients in the hospital**. Cleveland Clinic Journal of Medicine 2011; 78(6):379-384; doi:10.3949/ccjm.78gr.11001.

144. Rogal SS, Ukomadu C, Levy BD, Loscalzo J. Clinical problem-solving. A sweet source of abdominal pain. (Glycogenic hepatopathy) N Engl J Med. 2011 May 5;364(18):1762-7.
145. Ajay Varanasi, Natalie Bellini, Deepti Rawal, et al. **Liraglutide** as Additional Treatment in Type 1 Diabetes *Eur J Endocrinol* 2011 EJE-11-0330.
146. Levin Philip A., Zhang Quanwu, Mersey James H., et al. Glycemic Control With Insulin **Glargine Plus Insulin Glulisine** Versus Premixed Insulin Analogues in Real-World Practices: A Cost-Effectiveness Study With a Randomized Pragmatic Trial Design, Clinical Therapeutics, In Press, Corrected Proof, Available online 30 June 2011.
147. Pickup John C, Freeman Suzanne C, Sutton Alex J. Glycaemic control in type 1 diabetes during real time **continuous glucose monitoring** compared with self monitoring of blood glucose: meta-analysis of randomised controlled trials using individual patient data. BMJ 2011;343:doi:10.1136/bmj.d3805 (7 July 2011)
148. Zachariah S, Sheldon B, Shojaee-Moradie F, et al. **Insulin detemir reduces weight gain** as a result of reduced food intake in patients with type 1 diabetes. Diabetes Care. 2011 Jul;34(7):1487-91.
149. Petznick A. **Insulin management** of type 2 diabetes mellitus. Am Fam Physician. 2011 Jul 15;84(2):183-90.
150. Cohen D. The prickly problem of **access to insulin**. BMJ. 2011 Sep 14;343:d5782. doi: 10.1136/bmj.d5782.
151. Blair JC, Peak M, Gregory JW. What is the best way to deliver subcutaneous **insulin to infants, children, and young people** with type 1 diabetes mellitus? BMJ. 2011 Sep 2;343:d5221.
152. Ruiter R, Visser LE, van Herk-Sukel MP, et al. Risk of **cancer in patients on insulin glargine and other insulin analogues** in comparison with those on human insulin: results from a large population-based follow-up study. Diabetologia. 2011 Sep 29.
153. Rascati KL, Richards KM, Lopez D, et al. **Progression to Insulin** for Patients with Diabetes Mellitus Using the Texas Medicaid Database. Clin Ther. 2011 Nov 17.
154. Bellolio MF, Gilmore RM, Stead LG. **Insulin for** glycaemic control in acute **ischaemic stroke**. Cochrane Database Syst Rev. 2011;(9): CD005346. Starting intravenous insulin within the first 24 hours of acute ischemic stroke to maintain normoglycemia does not reduce death or dependency but increases the risk for hypoglycemia.
155. Gray CS,Hildreth AJ, Sandercock PA, et al;GISTTrialists Collaboration. **Glucose-potassium-insulin infusions** in the management of post-stroke hyperglycaemia: the UK Glucose Insulin in Stroke Trial (GIST-UK). Lancet Neurol. 2007;6:397-406.
156. Tibaldi JM. Intensifying insulin therapy in type 2 diabetes mellitus: dosing options for **insulin analogue premixes**. Clin Ther. 2011 Nov;33(11):1630-42.
157. Rascati KL et al. **Progression to insulin** for patients with diabetes mellitus using the Texas medicaid database. Clin Ther. 2011 Dec;33(12):2016-20. (slower progression with metformin/TZD than sulfonylurea/TZD)
158. Lee P, Chang A, Blaum C, Vlajnic A, Gao L, Halter J. Comparison of safety and efficacy of **insulin glargine and neutral protamine hagedorn** insulin in older adults with type 2 diabetes mellitus: results from a pooled analysis. J Am Geriatr Soc. 2012 Jan;60(1):51-9.
159. Ng KW, Allen ML, Desai A et al. **Cardioprotective effects of insulin**: how intensive insulin therapy may benefit cardiac surgery patients. Circulation. 2012 Feb 7;125(5):721-8.
160. Heller S, Buse J, Fisher M, et al, on behalf of the **BEGIN Basal-Bolus Type 1** Trial Investigators. **Insulin degludec**, an ultra-longacting basal insulin, **versus insulin glargine** in basal-bolus treatment with mealtime insulin aspart in type 1 diabetes (BEGIN Basal-Bolus Type 1): a phase 3, randomised, open-label, treat-to-target non-inferiority trial. Lancet 2012; 379: 1489–97.
161. Garber AJ, King AB, Del Prato S, et al, on behalf of the NN1250–3582 (BEGIN BB T2D) Trial Investigators. **Insulin degludec**, an ultra-longacting basal insulin, **versus insulin glargine** in basal-bolus treatment with mealtime insulin aspart in type 2 diabetes (**BEGIN Basal-Bolus Type 2**): a phase 3, randomised, open-label, treat-to-target non-inferiority trial. Lancet 2012; 379: 1498–507.
162. Lau AN, Tang T, Halapy H, Thorpe K, Yu CH. **Initiating insulin** in patients with type 2 diabetes. CMAJ. 2012 Apr 2.
163. Pickup JC. **Insulin-pump** therapy for type 1 diabetes mellitus. N Engl J Med. 2012 Apr 26;366(17):1616-24.
164. Donner T, Muñoz M. **Update on insulin** therapy for type 2 diabetes. J Clin Endocrinol Metab. 2012 May;97(5):1405-13.
165. Lasserson D, Fox R, Farmer A. **Late onset type 1 diabetes**. BMJ. 2012 Apr 30;344:e2827.
166. Mauras N, Beck R, Xing D, et al. A randomized clinical trial to assess the efficacy and safety of **real-time continuous glucose monitoring** in the management of type 1 diabetes in young children aged 4 to <10 years. Diabetes Care. 2012 Feb;35(2):204-10.
167. Aschner PJ, Chan J, Owens DR, et al, **EASIE** investigators. **Insulin glargine versus sitagliptin** in insulin-naive patients with type 2 diabetes mellitus uncontrolled on metformin (EASIE): a multicentre, randomised, open-label trial. Lancet 2012; online June 9.
168. **ORIGIN** Trial Investigators. Basal insulin (glargine) and cardiovascular and other outcomes in dysglycemia. N Engl J Med 2012 Jun 11; [e-pub ahead of print].
169. Chang CH, Lin JW, Wu LC, Lai MS, Chuang LM. Oral Insulin Secretagogues, Insulin, and **Cancer Risk** in Type 2 Diabetes Mellitus. J Clin Endocrinol Metab. 2012 May 4.
170. Baldwin D, Zander J, Munoz C, et al. A Randomized Trial of Two Weight-Based Doses of **Insulin Glargine and Glulisine** in Hospitalized Subjects With Type 2 Diabetes and **Renal Insufficiency**. Diabetes Care. 2012 Jun 14.
171. Rosso C, Corvol JC, Pires C, et al. Intensive Versus Subcutaneous Insulin in Patients With **Hyperacute Stroke**: Results From the Randomized **INSULINFARCT** Trial. Stroke. 2012 Jun 14.
172. Mathiesen ER, Hod M, Ivanisevic M, et al. Maternal Efficacy and Safety Outcomes in a Randomized, Controlled Trial Comparing **Insulin Detemir With NPH** Insulin in 310 **Pregnant** Women With Type 1 Diabetes. Diabetes Care. 2012 Jul 30.
173. Yeh HC, Brown TT, et al. Comparative Effectiveness and Safety of Methods of **Insulin Delivery and Glucose Monitoring** for Diabetes Mellitus: A Systematic Review and Meta-analysis. Ann Intern Med. 2012 Jul 10:E-508.
174. Rosso C, Corvol JC, Pires C, et al. **Intensive Versus Subcutaneous Insulin** in Patients With **Hyperacute Stroke**: Results From the Randomized INSULINFARCT Trial. Stroke. 2012 Sep;43(9):2343-9.
175. Gale EA. **Newer insulins** in type 2 diabetes. BMJ. 2012 Sep 11;345:e4611.
176. Testa MA et al. Comparative effectiveness of **basal-bolus versus premix** analog insulin on glycemic variability and patient-centered outcomes during insulin intensification in type 1 and type 2 diabetes: A randomized, controlled, crossover trial. J Clin Endocrinol Metab 2012 Oct; 97:3504.
177. Cornish A, Chase HP. Navigating **Airport Security** with an Insulin Pump and/or Sensor. Diabetes Technol Ther. 2012 Nov;14(11):984-5.
178. Freemantle N, Meneghini L, Christensen T, et al. **Insulin degludec** improves health-related quality of life (SF-36((R))) compared with insulin glargine in people with Type 2 diabetes starting on basal insulin: a meta-analysis of phase 3a trials. Diabet Med. 2013 Feb;30(2):226-32.
179. Thalange N, Bereket A, Larsen J, et al. Insulin analogues (**detemir vs NPH**) in children with Type 1 diabetes: a 52-week randomized clinical trial. Diabet Med. 2013 Feb;30(2):216-25.
180. Fox CS. **Weighty** Matters: Balancing Weight Gain with Cardiovascular Risk among Patients with Type 1 Diabetes Mellitus on Intensive **Insulin** Therapy. Circulation. 2013 Jan 15;127(2):157-9.
181. Zinman B, Philis-Tsimikas A, Cariou B, et al; NN1250-3579 (BEGIN Once Long) Trial Investigators. **Insulin degludec versus insulin glargine** in insulin-naive patients with type 2 diabetes: a 1-year, randomized, treat-to-target trial (BEGIN Once Long). Diabetes Care. 2012 Dec;35(12):2464-71.
182. Muller N, Frank T, Kloos C, et al. Randomized Crossover Study to Examine the Necessity of an **Injection-to-Meal Interval** in Patients With Type 2 Diabetes Mellitus and Human Insulin. Diabetes Care. 2013 Jan 22.
183. Haidar A, Legault L, et al. Glucose-responsive insulin and glucagon delivery (dual-hormone **artificial pancreas**) in adults with type 1 diabetes: a randomized crossover controlled trial. CMAJ. 2013 Mar 5;185(4):297-305.
184. Phillip M, Battelino T, Atlas E, et al. Nocturnal glucose control with an **artificial pancreas** at a diabetes camp. N Engl J Med. 2013 Feb 28;368(9):824-33.
185. Balena R, Hensley IE, Miller S, et al. Combination therapy with **GLP-1 receptor agonists and basal insulin**: a systematic review of the literature. Diabetes Obes Metab. 2012 Oct 15.
186. Currie CJ et al. **Mortality and other important diabetes-related outcomes** with insulin vs other antihyperglycemic therapies in type 2 diabetes. J Clin Endocrinol Metab 2013; 98: 668-77.
187. Wang L, Wei W, Miao R, et al with **insulin glargine** or neutral protamine Hagedorn insulin: a comparative retrospective database study. BMJ Open. 2013 Apr 30;3(4).
188. Meneghini L, Kesavadev J, Demissie M, et al. Once-daily initiation of **basal insulin as add-on to metformin**: a 26-week, randomized, treat-to-target trial comparing **insulin detemir with insulin glargine** in patients with type 2 diabetes. Diabetes Obes Metab. 2013 Feb 19.
189. Bergenstal RM, Klonoff DC, Garg SK, et al; the ASPIRE In-Home Study Group. **Threshold-Based Insulin-Pump** Interruption for Reduction of Hypoglycemia. N Engl J Med. 2013 Jun 22.
190. Jacobi J, Bircher N, Krinsley J, Agus M, et al. Guidelines for the use of an **insulin infusion** for the management of hyperglycemia in **critically ill patients**. Crit Care Med. 2012 Dec;40(12):3251-76.
191. Dailey GE, Gao L, Aurand L, et al. Impact of diabetes duration on **hypoglycaemia** in patients with type 2 diabetes treated with insulin **glargine or NPH** insulin. Diabetes Obes Metab. 2013 May 17.
192. Ly TT, Nicholas JA, et al. Effect of **sensor-augmented insulin pump** therapy and automated insulin suspension vs standard insulin pump therapy on hypoglycemia in patients with type 1 diabetes: a randomized clinical trial.

193. Grimaldi-Bensouda L, Cameron D, Marty M, et al. Risk of **breast cancer by individual insulin use** - an international multicenter study. Diabetes Care. 2013 Aug 15.
194. Ziegler R, Cavan DA, Cranston I, et al. Use of an **Insulin Bolus Advisor** Improves Glycemic Control in Multiple Daily Insulin Injection (MDI) Therapy Patients With Suboptimal Glycemic Control: First results from the ABACUS trial. Diabetes Care. 2013 Jul 30.
195. Sturmer T, Marquis MA, Zhou H, et al. **Cancer** Incidence Among Those Initiating Insulin Therapy With **Glargine Versus Human NPH** Insulin. Diabetes Care. 2013 Jul 22.
196. Spaulonci CP, Bernardes LS, Trindade TC, et al. Randomized trial of **metformin vs insulin in the management of gestational** diabetes. Am J Obstet Gynecol. 2013 Jul;209(1):34.e1-34.e7.
197. Geller AI, Shehab N, Lovegrove MC, et al. National estimates of **insulin-related hypoglycaemia** and errors leading to emergency department visits and hospitalizations [online March 10, 2014]. JAMA Intern Med. 2013.
198. Wallace JP, Wallace JL, McFarland MS. Comparing dosing **of Basal insulin analogues detemir and glargine**: is it really unit-per-unit and dose-per-dose? Ann Pharmacother. 2014 Mar;48(3):361-8.
199. Habel LA, Danforth KN, Quesenberry CP, et al. Cohort study of insulin **glargine and risk of breast, prostate, and colorectal cancer** among patients with diabetes. Diabetes Care. 2013 Dec;36(12):3953-60.
200. Mathieu C, Rodbard HW, Cariou B, et al. A comparison of adding **liraglutide** versus a single daily dose of **insulin aspart to insulin degludec** in subjects with type 2 diabetes (BEGIN: VICTOZA ADD-ON). Diabetes Obes Metab. 2014 Jan 20.
201. Bordeleau L, Yakubovich N, Dagenais GR, et al. for the ORIGIN Trial Investigators. The Association of **Basal Insulin Glargine and/or n-3 Fatty Acids With Incident Cancers** in Patients With Dysglycemia. Diabetes Care. 2014 Feb 26.
202. Pawaskar M, Tuttle KR, et al. Observational Study of Kidney Function and Albuminuria in Patients With Type 2 Diabetes Treated With **Exenatide BID Versus Insulin Glargine**. Ann Pharmacother. 2014 May;48(5):571-6.
203. Lane W, Weinrib S, Rappaport J, et al. The effect of addition of **liraglutide to high-dose intensive insulin** therapy: a randomized prospective trial. Diabetes Obes Metab. 2014 Mar 3.
204. Bu W, Song L, Zhao D, et al. **Insulin therapy and the risk of colorectal cancer** in patients with type 2 diabetes: a meta-analysis of observational studies. British Journal of Clinical Pharmacology. 2014.
205. The **ORIGIN** trial investigators, Gilbert RE, Mann JF, Hanefeld M, Spinas G, et al. Basal **insulin glargine** and microvascular outcomes in dysglycaemic individuals: results of the Outcome Reduction with an Initial Glargine Intervention (ORIGIN) trial. Diabetologia. 2014 Apr 26.
206. Fulcher GR, Christiansen JS, Bantwal G, et al. Comparison of Insulin **Degludec/Insulin Aspart and Biphasic Insulin Aspart 30** in Uncontrolled, Insulin-Treated Type 2 Diabetes: A Phase 3a, Randomized, Treat-to-Target Trial. Diabetes Care. 2014 May 9.
207. Wallia A, MolitchME. **Insulin therapy** for type 2 diabetes mellitus. JAMA. doi:10.1001 /jama.2014.5951.
208. Cukierman-Yaffe T, Bosch J, Diaz R, et al. for the **ORIGIN** Investigators. Effects of **basal insulin glargine and omega-3 fatty acid on cognitive** decline and probable cognitive impairment in people with dysglycaemia: a substudy of the ORIGIN trial. Lancet Diabetes Endocrinol. 2014 May 30. pii: S2213-8587(14)70062-2.
209. Jin J. **Starting Insulin Treatment** for Diabetes. JAMA. 2014 Jun 11;311(22):2347.
210. Reznik Y, Cohen O, Aronson R, et al, for the **OpT2mise** Study Group. **Insulin pump treatment compared with multiple daily injections** for treatment of type 2 diabetes (OpT2mise): a randomised open-label controlled trial. Lancet 2014; online July 3.
211. Rosenstock J, Fonseca VA, Gross JL, et al;for the Harmony-6 Study Group. Advancing Basal Insulin Replacement in Type 2 Diabetes Inadequately Controlled With Insulin **Glargine Plus Oral Agents**: A Comparison of Adding **Albiglutide**, a Weekly GLP-1 Receptor Agonist, Versus Thrice-Daily Prandial Insulin **Lispro**. Diabetes Care. 2014 Jun 4.
212. Russell SJ, El-Khatib FH, Sinha M, et al. Outpatient Glycemic Control with a **Bionic Pancreas** in Type 1 Diabetes. N Engl J Med. 2014 Jun 15.
213. Tinahones FJ, Gross JL, Onaca A, et al. **Insulin lispro low mixture twice daily versus basal insulin glargine once daily and prandial insulin lispro** once daily in patients with type 2 diabetes requiring insulin intensification: a randomized phase IV trial. Diabetes Obes Metab. 2014 Apr 11.
214. Reznik Y, Cohen O, Aronson R, et al; for the **OpT2mise** Study Group. **Insulin pump treatment compared with multiple daily injections** for treatment of type 2 diabetes (OpT2mise): a randomised open-label controlled trial. Lancet. 2014 Jul 2.
215. Davies MJ, Gross JL, Ono Y, et al.; on behalf of the BEGIN BB T1 study group. Efficacy and safety of **insulin degludec given as part of basal-bolus treatment with mealtime insulin aspart** in type 1 diabetes: a 26-week randomized, open-label, treat-to-target non-inferiority trial. Diabetes Obes Metab. 2014 Apr 7.
216. Riddle MC, Bolli GB, Ziemen M, et al. New Insulin **Glargine 300 Units/mL Versus Glargine 100** Units/mL in People With Type 2 Diabetes Using Basal and Mealtime Insulin: Glucose Control and Hypoglycemia in a 6-Month Randomized Controlled Trial (EDITION 1). Diabetes Care. 2014 Jul 30. pii: DC_140991.
217. Santos Cavaiola T, Edelman S. **Inhaled Insulin**: A Breath of Fresh Air? A Review of Inhaled Insulin. Clin Ther. 2014 Jul 17.
218. Li X, Du T, Li W, et al. Efficacy and Safety of **Weight-Based Insulin Glargine Dose** Titration Regimen Compared With Glucose Level- and Current Dose-Based Regimens in Hospitalized Patients With Type 2 Diabetes: A Randomized, Controlled Study. Clin Ther. 2014 Jul 22.
219. Edelman SV, Liu R, Johnson J, et al. **AUTONOMY**: The First Randomized Trial Comparing Two Patient-Driven Approaches to Initiate and **Titrate Prandial Insulin Lispro** in Type 2 Diabetes. Diabetes Care. 2014 Aug;37(8):2132-40.
220. Tricco AC, Ashoor HM, Antony J, et al. Safety, effectiveness, and cost effectiveness of **long acting versus intermediate acting insulin for patients with type 1 diabetes**: systematic review and network meta-analysis. BMJ. 2014 Oct 1;349:g5459.
221. Buse JB, Vilsbøll T, Thurman J, et al; on behalf of the NN9068-3912 (DUAL-II) Trial Investigators. Contribution of Liraglutide in the Fixed-Ratio Combination of Insulin Degludec and Liraglutide (IDegLira). Diabetes Care. 2014 Aug 11.
222. Gough SC, Bode B, Woo V, et al; the NN9068-3697 (DUAL-I) trial investigators. Efficacy and safety of a fixed-ratio combination of **insulin degludec and liraglutide** (**IDegLira**) compared with its components **given alone**: results of a phase 3, open-label, randomised, 26-week, treat-to-target trial in insulin-naïve patients with type 2 diabetes. Lancet Diabetes Endocrinol. 2014 Sep 1.
223. Nallasamy K, Jayashree M, Singhi S, et al. **Low-Dose vs Standard Dose Insulin in Pediatric Diabetic Ketoacidosis**: A Randomized Clinical Trial. JAMA Pediatr. 2014 Sep 29.
224. Haidar A, Legault L, Messier V, et al. Comparison of dual-hormone artificial pancreas, single-hormone artificial pancreas, and conventional insulin pump therapy for glycaemic control in patients with type 1 diabetes: an open-label randomised controlled crossover trial. Lancet Diabetes Endocrinol. 2014 Nov 26.
225. Sabin MA, Magnussen CG, Juonala M, et al. **Insulin and BMI** as Predictors of Adult Type 2 Diabetes Mellitus. Pediatrics. 2015 Jan;135(1):e144-51.
226. Nuffer W, Trujillo JM, Ellis SL. **Technosphere Insulin (Afrezza):** A New, Inhaled Prandial Insulin. Ann Pharmacother. 2015 Jan;49(1):99-106.
227. Yki-Jarvinen H, Bergenstal R, Ziemen M, et al. New **Insulin Glargine 300 Units/mL Versus Glargine 100 Units/mL** in People With Type 2 Diabetes Using Oral Agents and Basal Insulin: Glucose Control and Hypoglycemia in a 6-Month Randomized Controlled Trial (EDITION 2). Diabetes Care. 2014 Dec;37(12):3235-43. Gla-300 was as effective as Gla-100 and associated with a lower risk of hypoglycemia during the night and at any time of the day.
228. Buse JB, Peters A, Russell-Jones D, et al. Is **insulin the most effective injectable antihyperglycaemic therapy**?. Diabetes Obes Metab. 2014 Oct 17.
229. Haidar A, Legault L, Messier V, et al. Comparison of dual-hormone **artificial pancreas**, single-hormone artificial pancreas, and conventional insulin pump therapy for glycaemic control in patients with type 1 diabetes: an open-label randomised controlled crossover trial. Lancet Diabetes Endocrinol. 2015 Jan;3(1):17-26.
230. Home PD, Bolli GB, Mathieu C, et al. Modulation of insulin dose titration using a **hypoglycaemia-sensitive algorithm**: insulin glargine versus neutral protamine Hagedorn insulin in insulin-naive people with type 2 diabetes. Diabetes Obes Metab. 2015 Jan;17(1):15-22.
231. Greene JA, Riggs KR. Why is there **no generic insulin**? Historical origins of a modern problem. N Engl J Med. 2015 Mar 19;372(12):1171-5.
232. Heinemann L, Fleming GA, Petrie JR, et al. **Insulin pump risks and benefits**: a clinical appraisal of pump safety standards, adverse event reporting and research needs. A Joint Statement of the

European Association for the Study of Diabetes and the American Diabetes Association Diabetes Technology Working Group. Diabetologia. 2015 Mar 18.
233. Bonifacio E, Ziegler A-G, Klingensmith G, et al; **Pre-POINT** Study Group. Effects of **high-dose oral insulin** on immune responses in children at **high risk for type 1 diabetes**: the Pre-POINT randomized clinical trial. JAMA. doi:10.1001/jama.2015.2928.
234. Zhao L, Sheng X, Zhou S, et al. **Metformin versus insulin for gestational diabetes** mellitus: a meta-analysis. Br J Clin Pharmacol. 2015 Apr 29.
235. Ali A, Cheng AY, Yu CH. Breaking down **barriers to initiating insulin**: Insulin prescription pad. Can Fam Physician. 2015 May;61(5):445-7.
236. Tran L, Zielinski A, Roach AH, et al. Pharmacologic Treatment of Type 2 **Diabetes: Injectable Medications**. Ann Pharmacother. 2015 Jun;49(6):700-714.
237. Wang C, Mamza J, Idris I. **Biphasic vs basal bolus insulin** regimen in Type 2 diabetes: a systematic review and meta-analysis of randomized controlled trials. Diabet Med. 2015 May;32(5):585-94.
238. Luo J, Avorn J, Kesselheim AS. **Trends in Medicaid Reimbursements for Insulin** From 1991 Through 2014. JAMA Intern Med. 2015 Aug 24.
239. Tylee T, Hirsch IB. **Costs Associated With Using Different Insulin** Preparations. JAMA. 2015 Aug 18;314(7):665-6.
240. Steineck I, Cederholm J, Eliasson B, et al; Swedish National Diabetes Register. **Insulin pump therapy, multiple daily injections, and cardiovascular mortality** in 18 168 people with type 1 diabetes: observational study. BMJ. 2015 Jun 22;350:h3234.
241. Goldman J, White JR Jr. New **Insulin Glargine 300 U/mL** for the Treatment of Type 1 and Type 2 Diabetes Mellitus. Ann Pharmacother. 2015 Oct;49(10):1153-61.
242. Lee YY, Lin YM, Leu WJ, et al. **Sliding-scale insulin** used for blood glucose control: a meta-analysis of randomized controlled trials. Metabolism. 2015 Sep;64(9):1183-92.
243. Buse JB, Rodbard HW, Trescoli Serrano C, et al.**IMAGINE 5** Investigators. Randomized Clinical Trial Comparing Basal **Insulin Peglispro and Insulin Glargine** in Patients With Type 2 Diabetes Previously Treated With Basal Insulin: IMAGINE 5. Diabetes Care. 2015 Nov 17.
244. Buse JB, Rodbard HW, Trescoli Serrano C, et al.**IMAGINE 5** Investigators. Randomized Clinical Trial Comparing Basal **Insulin Peglispro and Insulin Glargine** in Patients With Type 2 Diabetes Previously Treated With Basal Insulin: IMAGINE 5. Diabetes Care. 2015 Nov 17.
245. Roze S, Smith-Palmer J, Valentine W, et al. **Cost-effectiveness of continuous subcutaneous insulin infusion versus multiple daily injections** of insulin in Type 1 diabetes: a systematic review. Diabet Med. 2015 Nov;32(11):1415-24.
246. **ORIGIN** Trial Investigators. **Cardiovascular and Other Outcomes** Postintervention With **Insulin Glargine and Omega-3 Fatty Acids** (**ORIGINALE**). Diabetes Care. 2015 Dec 17.
247. Lingvay I, Manghi FP, García-Hernández P, et al; **DUAL V Investigators**. Effect of Insulin **Glargine Up-titration vs Insulin Degludec/Liraglutide** on Glycated Hemoglobin Levels in Patients With Uncontrolled Type 2 Diabetes: The **DUAL V** Randomized Clinical Trial. JAMA. 2016 Mar 1;315(9):898-907.
248. Boghossian NS, Hansen NI, Bell EF, et al; Eunice Kennedy Shriver National Institute of Child Health and Human Development Neonatal Research Network. Outcomes of **Extremely Preterm Infants** Born to Insulin-Dependent Diabetic Mothers. Pediatrics. 2016 May 13.
249. Herrera KM, Rosenn BM, Foroutan J, et al. Randomized controlled trial of **insulin detemir versus NPH** for the treatment of pregnant women with diabetes. Am J Obstet Gynecol. 2015 Sep;213(3):426.e1-7.
250. Holden SE, Jenkins-Jones S, Currie CJ. Association between **Insulin Monotherapy versus Insulin plus Metformin** and the Risk of All-Cause Mortality and Other Serious Outcomes: A Retrospective Cohort Study. PLoS One. 2016 May 6;11(5):e0153594.
251. Munshi MN, Slyne C, Segal AR, et al. Simplification of Insulin Regimen in Older Adults and **Risk of Hypoglycemia**. JAMA Intern Med. 2016 Jun 6.
252. Zargham H, O'Brien E. **Cutaneous sarcoidosis** at insulin injection sites. CMAJ. 2016 Jun 14;188(9):674.
253. Frid AH, Kreugel G, Grassi G, et al. **New Insulin Delivery Recommendations**. Mayo Clin Proc. 2016 Sep;91(9):1231-55.
254. Peters AL, Ahmann AJ, et al. Diabetes Technology-**Continuous Subcutaneous Insulin Infusion Therapy and Continuous Glucose Monitoring in Adults**: An **Endocrine Society Clinical Practice Guideline**. J Clin Endocrinol Metab. 2016 Sep 2:jc20162534
255. Fath M, Danne T, Biester T, et al. **Faster-acting insulin aspart** provides faster onset and greater early exposure vs insulin aspart in children and adolescents with type 1 diabetes mellitus. Pediatr Diabetes. 2017 Feb 6.
256. Strich D, Balagour L, Shenker J, et al. **Lower Basal Insulin Dos**e is Associated with Better Control in Type 1 Diabetes. J Pediatr. 2016 Dec 12.
257. Yuan T, Zhao W, Wang L, et al. Continuous Subcutaneous **Insulin Infusion** as an Effective Method of **Desensitization Therapy** for Diabetic Patients with **Insulin Allergy**: A 4-year Single-Center Experience. Clin Ther. 2016 Oct 25.
258. Russell-Jones D, et al. **Fast-Acting Insulin Aspart** Improves Glycemic Control in Basal-Bolus Treatment for Type 1 Diabetes: a 26-Week Multicenter, Active-Controlled, Treat-to-Target, Randomized, Parallel-Group Trial (Onset 1). Diabetes Care. 2017 Mar 29.
259. Turksoy K, Frantz N, Quinn L, et al. **Automated Insulin Delivery**-The Light at the End of the Tunnel. J Pediatr. 2017 Apr 7.
260. **REPOSE** Study Group. Relative effectiveness of **insulin pump treatment over multiple daily injections** and structured education during flexible intensive insulin treatment for type 1 diabetes: cluster randomised trial (REPOSE). BMJ. 2017 Mar 30;356:j1285
261. Baidal DA, Ricordi C, Berman DM, Alvarez et al. **Bioengineering of an Intraabdominal Endocrine Pancreas**. N Engl J Med. 2017 May 11;376(19):1887-1889.
262. Pickup JC, Reznik Y, Sutton AJ. Glycemic Control During **Continuous Subcutaneous Insulin Infusion Versus Multiple Daily Insulin Injections** in Type 2 Diabetes: Individual Patient Data Meta-analysis and Meta-regression of Randomized Controlled Trials. Diabetes Care. 2017 May;40(5):715-722.
263. Campbell Matthew D, Walker Mark, Ajjan Ramzi A, et al. An **additional bolus of rapid-acting insulin** to **normalise postprandial cardiovascular risk factors** following a high-carbohydrate high-fat meal in patients with type 1 diabetes: A randomised controlled trial. Diab Vasc Dis Res. 2017 Mar 1:1479164117698918.
264. Baidal DA, Ricordi C, Berman DM, Alvarez et al. **Bioengineering of an Intraabdominal Endocrine Pancreas**. N Engl J Med. 2017 May 11;376(19):1887-1889.
265. Pickup JC, Reznik Y, Sutton AJ. **Glycemic Control During Continuous Subcutaneous Insulin Infusion Versus Multiple Daily Insulin Injections** in Type 2 Diabetes: Individual Patient Data Meta-analysis and Meta-regression of Randomized Controlled Trials. Diabetes Care. 2017 May;40(5):715-722.
266. Marso SP, McGuire DK, Zinman B, et al. Efficacy and Safety of **Degludec versus Glargine** in Type 2 Diabetes. (**DEVOTE**) N Engl J Med. 2017 Jun 12
267. Lane W, Bailey TS, Gerety G, et al. Effect of **insulin degludec vs insulin glargine** U100 on hypoglycemia in patients with type 1 diabetes: the **SWITCH 1** randomized clinical trial. JAMA. doi:10.1001/jama.2017.7115
268. Wysham C, Bhargava A, Chaykin L, et al. Effect of **insulin degludec vs insulin glargine** U100 on hypoglycemia in patients with type 2 diabetes: the **SWITCH 2** randomized clinical trial. JAMA. doi:10.1001/jama.2017.7117
269. Wu JW, Azoulay L, Majdan A, et al. Long-Term Use of **Long-Acting Insulin Analogs and Breast Cancer** Incidence in Women With Type 2 Diabetes. J Clin Oncol. 2017 Sep 27:JCO2017734491.

ADA 2018: American Diabetes Association. 13. Management of Diabetes in **Pregnancy**: Standards of Medical Care in Diabetes-2018. Diabetes Care. 2018 Jan;41(Suppl 1):S137-S143.
ADA 2018: American Diabetes Association. 12. **Children and Adolescents**: Standards of Medical Care in Diabetes-2018. Diabetes Care. 2018 Jan;41(Suppl 1):S126-S136.
ADA 2018: American Diabetes Association. 11. **Older Adults**: Standards of Medical Care in Diabetes-2018. Diabetes Care. 2018 Jan;41(Suppl 1):S119-S125. Jan;41(Suppl 1):S86-S104.
ADA 2018: American Diabetes Association. 8. **Pharmacologic Approaches** to Glycemic Treatment: Standards of Medical Care in Diabetes-2018. Diabetes Care. 2018 Jan;41(Suppl 1):S73-S85.
271. Anyanwagu U, Mamza J, Gordon J, et al. **Premixed vs basal-bolus insulin** regimen in Type 2 diabetes: comparison of clinical outcomes from randomized controlled trials and real-world data. Diabet Med. 2017 Dec;34(12):1728-1736.
272. Gerstein HC, Jung H, Rydén L, et al. Effect of Basal Insulin **Glargine** on First and Recurrent Episodes of **Heart Failure** Hospitalization: The **ORIGIN** Trial (Outcome Reduction With Initial Glargine Intervention). Circulation. 2018 Jan 2;137(1):88-90
273. Howard-Thompson A, Khan M, Jones M eta al. Type 2 Diabetes Mellitus: **Outpatient Insulin Management**. Am Fam Physician. 2018;97(1):29-37.
274. Gazzina S, Alberici A, Padovani A, et al. **Myoclonic dystonia (DYT11) responsive to insulin therapy**: A case report. Neurology. 2017 Aug 1;89(5):517-518.
275. Gerstein HC, Jung H, Rydén L, et al; **ORIGIN** Investigators. Effect of Basal Insulin **Glargine** on First and Recurrent Episodes of **Heart Failure Hospitalization**: The ORIGIN Trial (Outcome Reduction With Initial Glargine Intervention). Circulation. 2018 Jan 2;137(1):88-90.
276. Home PD;Bergenstal RM;Bolli GB;Ziemen M;Rojeski M;. Glycaemic control and hypoglycaemia during 12 months of randomized treatment with **insulin glargine 300 U/mL versus glargine 100 U/mL** in people with type 1 diabetes (**EDITION 4**). Diabetes Obes Metab. 2017 Jun 29.
277. Yamada T, Kamata R, Ishinohachi K, et al. **Biosimilar vs originator insulins**: Systematic review and meta-analysis. Diabetes Obes Metab. 2018 Mar 14.
278. Crowley MJ, Maciejewski ML. Revisiting **NPH Insulin for Type 2 Diabetes**: Is a Step Back the Path Forward? JAMA. 2018 Jul 3;320(1):38-39.
279. Lipska KJ, Parker MM, Moffet HH, et al. Association of **Initiation of Basal Insulin Analogs vs Neutral Protamine Hagedorn Insulin With Hypoglycemia**-Related Emergency Department Visits or Hospital Admissions and With Glycemic Control in Patients With Type 2 Diabetes. JAMA. 2018 Jul 3;320(1):53-62.
280. Madenidou AV, Paschos P, Karagiannis T, et al. Comparative **Benefits and Harms of Basal Insulin Analogues for Type 2 Diabetes**: A Systematic Review and Network Meta-analysis. Ann Intern Med. 2018 Jul 10.
281. Blair J, McKay A, Ridyard C, et al. **Continuous subcutaneous insulin infusion versus multiple daily injections in children and young people** at diagnosis of type 1 diabetes: the **SCIPI** RCT. Health Technol Assess. 2018 Aug;22(42):1-112.
282. Lopez PE, Evans M, King BR, et al. A randomized comparison of **three prandial insulin dosing algorithms for children and adolescents** with Type 1 diabetes. Diabet Med. 2018 Jun 5.
283. Rosenstock J, Cheng A, Ritzel R, et al. More Similarities Than Differences Testing **Insulin Glargine 300 Units/mL Versus Insulin Degludec 100 Units/mL** in Insulin-Naive Type 2 Diabetes: The Randomized Head-to-Head BRIGHT Trial. Diabetes Care. 2018 Oct; 41(10):2147-2154.
284. Holmes RS, Crabtree E, McDonagh MS. Comparative effectiveness and **harms of long-acting insulins for type 1 and type 2 diabetes**: A systematic review and meta-analysis. Diabetes Obes Metab. 2018 Dec 15.
285. Luo J, Khan NF, Manetti T, et al. Implementation of a health plan program for **switching from analogue to human insulin** and glycemic control among Medicare beneficiaries with type 2 diabetes [Jan 29, 2019]. JAMA. doi:10.1001/jama.2018.21364
286. Bergenstal RM, Johnson M, Passi R, et al. **Automated insulin dosing guidance** to optimize insulin management in patients with type 2 diabetes: a multicentre, randomised controlled trial. Lancet 2019; published online Feb 23.
287. Goldstein JN, Patel RM, Bland K, Hicks LS. **Frequency of Sale and Reasons for Purchase** of Over-the-Counter Insulin In the United States. JAMA Intern Med. 2019 Feb 18.
288. Paldus B, Lee MH, O'Neal DN. Insulin **pumps in general practice**. Aust Prescr. 2018 Dec;41(6):186-190
289. Blonde L, Rosenstock J, Del Prato S, et al. Switching to **iGlarLixi Versus Continuing Daily or Weekly GLP-1 RA** in Type 2 Diabetes Inadequately Controlled by GLP-1 RA and Oral Antihyperglycemic Therapy: The LixiLan-G Randomized Clinical Trial. Diabetes Care. 2019 Sep 17.
290. Philis-Tsimikas A, Billings LK, Busch R, et al. Superior efficacy of insulin **degludec/liraglutide versus insulin glargine U100** as add-on to sodium-glucose co-transporter-2 inhibitor therapy: A randomized clinical trial in people with uncontrolled type 2 diabetes. Diabetes Obes Metab. 2019 Feb 13.
291. Health Canada Jun/19: is advising patients and health care providers that certain older **Medtronic MiniMed 508 and MiniMed Paradigm insulin pumps** distributed between 2010 and 2015, may be vulnerable to cybersecurity risks.

CADTH: Starting Insulin in T2DM: http://www.cadth.ca/media/pdf/c1109-guide-to-starting-insulin-final-e.pdf

References - Diabetes Trials: Landmark Outcome and Prevention (www.RxFiles.ca)

[1] **DCCT** Reasearch Group. The effect of intensive treatment of diabetes on the development and progression of long-term complications in insulin-dependent diabetes mellitus. N Engl J Med. 1993 Sep 30;329(14):977-86.

[2] Nathan DM, Cleary PA, Backlund JY, Genuth SM, Lachin JM, Orchard TJ, Raskin P, Zinman B; Diabetes Control and Complications Trial/Epidemiology of Diabetes Interventions and Complications (**DCCT/EDIC**) Study Research Group. Intensive diabetes treatment and cardiovascular disease in patients with type 1 diabetes. N Engl J Med. 2005 Dec 22;353(25):2643-53.

de Boer IH, Kestenbaum B, Rue TC, et al. Diabetes Control and Complications Trial (**DCCT**)/Epidemiology of Diabetes Interventions and Complications (**EDIC**) Study Research Group. Insulin therapy, hyperglycemia, and hypertension in type 1 diabetes mellitus. Arch Intern Med. 2008 Sep 22;168(17):1867-73. Hyperglycemia is a risk factor for incident hypertension in type 1 diabetes, and intensive insulin therapy reduces the long-term risk of developing hypertension.

{Diabetes Control and Complications Trial/Epidemiology of Diabetes Interventions and Complications (DCCT/EDIC) Research Group. Modern-Day Clinical Course of Type 1 Diabetes Mellitus After **30 Years'** Duration: The Diabetes Control and Complications Trial/Epidemiology of Diabetes Interventions and Complications and Pittsburgh Epidemiology of Diabetes Complications Experience (1983-2005). Arch Intern Med. 2009;169(14):1307-1316.}

White NH, Sun W, Cleary PA, et al. Effect of Prior Intensive Therapy in Type 1 Diabetes Mellitus on 10-year Progression of **Retinopathy** in the DCCT/EDIC: Comparison of Adults and Adolescents. Diabetes. 2010 Feb 11.

Albers JW, Herman WH, Pop-Busui R, et al. for the DCCT/EDIC Research Group. Effect Of Prior Intensive Insulin Treatment During The Diabetes Control And Complications Trial (DCCT) On **Peripheral Neuropathy** In Type 1 Diabetes During The Epidemiology Of Diabetes Interventions, And Complications (EDIC) Study. Diabetes Care. 2010 Feb 11.

de Boer Ian H.; Rue Tessa C.; Cleary Patricia A.; et al.; for the Diabetes Control and Complications Trial/Epidemiology of Diabetes Interventions and Complications Study Research Group. **Long-term Renal Outcomes** of Patients With Type 1 Diabetes Mellitus and Microalbuminuria: An Analysis of the Diabetes Control and Complications Trial/Epidemiology of Diabetes Interventions and Complications Cohort **DCCT/EDIC**. Arch Intern Med. 2011;171(5):412-420.

DCCT/EDIC Research Group. Intensive Diabetes Therapy and **Glomerular Filtration** Rate in Type 1 Diabetes. N Engl J Med. 2011; 365:2366.

Purnell JQ, Hokanson JE, Cleary PA, et al. The effect of excess **weight gain** with intensive diabetes mellitus treatment on cardiovascular disease risk factors and atherosclerosis in type 1 diabetes mellitus: results from the Diabetes Control and Complications Trial/Epidemiology of Diabetes Interventions and Complications Study (**DCCT/EDIC**) Study. Circulation. 2013;127:180–187.

DCCT/EDIC Research Group. Association between **7 years** of intensive treatment of type 1 diabetes and long-term **mortality**. JAMA. doi:10.1001/jama.2014.16107.

DCCT/EDIC Research Group. Intensive Diabetes Therapy and **Ocular Surgery** in Type 1 Diabetes. N Engl J Med. 2015 Apr 30;372(18):1722-1733.

Diabetes Control and Complications Trial (**DCCT**)/Epidemiology of Diabetes Interventions and Complications (**EDIC**) Study Research Group. Intensive Diabetes Treatment and Cardiovascular Outcomes in Type 1 Diabetes: The **DCCT/EDIC** Study **30-Year Follow-up**. Diabetes Care. 2016 May;39(5):686-93.

DCCT/EDIC Research Group. Frequency of evidencebased screening for **retinopathy** in type 1 diabetes. N Engl J Med 2017;376:1507-16.

[3] Intensive blood-glucose control with sulphonylureas or insulin compared with conventional treatment and risk of complications in patients with type 2 diabetes (**UKPDS 33**). (UKPDS) Group. Lancet. 1998 Sep 12;352(9131):837-53.

[4] Salpeter SR, Buckley NS, Kahn JA, Salpeter EE. **Meta-analysis: metformin** treatment in persons at risk for diabetes mellitus. Am J Med 2008;121:149-157.e2. {InfoPOEMS: Using metformin to treat patients at risk for diabetes decreases their likelihood of developing diabetes over a 3-year period. Longer studies are needed to determine whether the likelihood of diabetes is truly decreased or simply delayed. We have no research to tell us whether, in the long run, patients live longer or live better if they are treated at this stage of (pre)diabetes. (LOE = 1a)}

[5] Nissen SE, Wolski K. Effect of Rosiglitazone on the Risk of Myocardial Infarction and Death from Cardiovascular Causes. N Engl J Med. 2007 May 21; [Epub ahead of print] http://content.nejm.org/cgi/content/full/NEJMoa072761

[6] DeFronzo Ralph A., Tripathy Devjit, Schwenke Dawn C., et al. for the **ACT NOW** Study. **Pioglitazone for Diabetes Prevention** in Impaired Glucose Tolerance. N Engl J Med 2011; 364:1104-1115.

ACT-NOW: ↓progression to T2DM (annual incidence of diabetes was 2.1 vs 7.6%/yr; NNT=19/yr) but ↑weight (3.9kg vs 0.77kg) & edema (12.9 vs 6.4%).

Loke Yoon Kong, Kwok Chun Shing, Singh Sonal. Comparative cardiovascular effects of thiazolidinediones: systematic review and meta-analysis of observational studies. BMJ 342:doi:10.1136/bmj.d1309

Tripathy D, Schwenke DC, Banerji M, et al. Diabetes Incidence and Glucose Tolerance after Termination of Pioglitazone Therapy: Results from ACT NOW. J Clin Endocrinol Metab. 2016 May;101(5):2056-62.

[7] Montori VM, Isley WL, Guyatt GH. Waking up from the DREAM of preventing diabetes with drugs. BMJ 2007;28;334(7599):882-4. Accessed online: http://www.bmj.com/cgi/content/extract/334/7599/882

[8] Weng J et al. Effect of intensive insulin therapy on β-cell function and glycaemic control in patients with newly diagnosed type 2 diabetes: A multicentre randomised parallel-group trial. *Lancet* 2008 May 24; 371:1753.

[9] Effect of intensive blood-glucose control with metformin on complications in overweight patients with type 2 diabetes (**UKPDS 34**). UK Prospective Diabetes Study (UKPDS) Group. Lancet. 1998 Sep 12;352(9131):854-65. Erratum.

[10] Ohkubo Y, Kishikawa H, Araki E, Miyata T,et al. Intensive insulin therapy prevents the progression of diabetic microvascular complications in Japanese patients with non-insulin-dependent diabetes mellitus: a randomized prospective 6-year study. Diabetes Res Clin Pract. 1995 May;28(2):103-17. (**Kumamoto** study)

[11] Dormandy JA, et al. Secondary prevention of macrovascular events in patients with type 2 diabetes in the **PROactive** Study. (PROspective pioglitAzone Clinical Trial in macroVascular Events): a RCT. Lancet. 2005; 366: 1279-1289. {InfoPOEMs Aug 2008: Pioglitazone (Actos), unlike its chemical cousin rosiglitazone (Avandia), does not seem to increase the likelihood of cardiovascular events (N Engl J Med. 2007;356:2457-2471). The researchers conducting this study stretched -- and broke -- the scientific method when claiming benefit, but any claims of benefit are specious. (LOE = 1a-)}

[12] Action to Control Cardiovascular Risk in Diabetes Study Group, Gerstein HC, Miller ME, Byington RP, et al. Effects of intensive glucose lowering in type 2 diabetes. N Engl J Med. 2008 Jun 12;358(24):2545-59. {RxFiles Trial Summary: **ACCORD** }

Miller ME, Bonds DE, Gerstein HC, et al. **ACCORD** Investigators. The effects of baseline characteristics, glycaemia treatment approach, and glycated haemoglobin concentration on the risk of severe hypoglycaemia: post hoc epidemiological analysis of the ACCORD study. BMJ. 2010 Jan 8;340:b5444. doi: 10.1136/bmj.b5444.

ACCORD Study Group and ACCORD Eye Study Group, Effects of Medical Therapies on **Retinopathy** Progression in Type 2 Diabetes. N Engl J Med 2010 0: NEJMoa1001288.

Ismail-Beigi F, Craven T, Banerji MA. Effect of intensive treatment of hyperglycaemia on **microvascular** outcomes in type 2 diabetes: analysis of ACCORD randomised trial.The Lancet, Early Online, 29June10 doi:10.1016/S0140-6736(10)60576-4.

[7b]**: ACCORD** Study Group. Long-term effects of intensive glucose lowering on cardiovascular outcomes. N Engl J Med 2011 Mar 3; 364:818.

ACCORD Anderson RT, Narayan KM, Feeney P, et al. Action to Control Cardiovascular Risk in Diabetes (ACCORD) Investigators. Effect of intensive glycemic lowering on health-related quality of life in type 2 diabetes: ACCORD trial. Diabetes Care. 2011 Apr;34(4):807-12.

Launer LJ, Miller ME, Williamson JD, et al; **ACCORD MIND**. Effects of **intensive glucose lowering** on **brain** structure and function in people with type 2 diabetes: a randomised open-label substudy. Lancet Neurol. 2011 Nov;10(11):969-77.

ACCORD Fonseca V, McDuffie R, Calles J, et al. Determinants of **weight gain** in the Action to Control Cardiovascular Risk in Diabetes (Acord) trial.Diabetes Care 2013 .

Gerstein HC, Miller ME, Ismail-Beigi F, et al, for the ACCORD Study Group. Effects of intensive glycaemic control on ischaemic heart disease: analysis of data from the randomised, controlled **ACCORD** trial. Lancet 2014; online Aug 1.

Miller ME, Williamson JD, Gerstein HC, et al.; **ACCORD** Investigators. Effects of randomization to intensive glucose control on **adverse events, cardiovascular disease, and mortality** in older versus younger adults in the ACCORD Trial. Diabetes Care 2014;37:634–43.

ACCORD Action to Control Cardiovascular Risk in Diabetes Follow-On (**ACCORDION**) Eye Study Group and the Action to Control Cardiovascular Risk in Diabetes Follow-On (ACCORDION) Study Group. Persistent Effects of **Intensive Glycemic Control on Retinopathy** in Type 2 Diabetes in the Action to Control Cardiovascular Risk in Diabetes (**ACCORD**) Follow-On Study. Diabetes Care. 2016 Jul;39(7):1089-100

ACCORD Study Group.. **Nine-Year Effects of 3.7 Years** of Intensive Glycemic Control on Cardiovascular Outcomes. Diabetes Care. 2016 May;39(5):701-8.

[13] ADVANCE Collaborative Group, Patel A, MacMahon S, Chalmers J, Neal B, Billot L, Woodward M, Marre M, Cooper M, Glasziou P, Grobbee D, Hamet P, Harrap S, Heller S, Liu L, Mancia G, Mogensen CE, Pan C, Poulter N, Rodgers A, Williams B, Bompoint S, de Galan BE, Joshi R, Travert F. Intensive blood glucose control and vascular outcomes in patients with type 2 diabetes. N Engl J Med. 2008 Jun 12;358(24):2560-72.
Patel A; **ADVANCE** Collaborative Group, MacMahon S, Chalmers J, Neal B, Woodward M, et al. Effects of a fixed combination of perindopril and indapamide on macrovascular and microvascular outcomes in patients with type 2 diabetes mellitus (the ADVANCE trial): a randomised controlled trial. Lancet. 2007 Sep 8;370(9590):829-40. {RxFiles Trial Summary: **ADVANCE** http://www.rxfiles.ca/rxfiles/uploads/documents/Diabetes-ADVANCE-trial.pdf }
Zoungas S, de Galan BE, Ninomiya T, et al. the ADVANCE Collaborative Group. The combined effects of routine blood pressure lowering and intensive glucose control on **macrovascular and microvascular** outcomes in patients with type 2 diabetes; new results from ADVANCE. Diabetes Care. 2009 Aug 3. [Epub ahead of print] The effects of routine blood pressure lowering and intensive glucose control were independent of one another and when combined produced additional reductions in clinically relevant outcomes.
Zoungas S et al. **Severe hypoglycemia** and risks of vascular events and death (Advance). N Engl J Med 2010 Oct 7; 363:1410. During a median follow-up period of 5 years, 231 patients (2.1%) had at least one severe hypoglycemic episode; 150 had been assigned to intensive glucose control (2.7% of the 5571 patients in that group), and 81 had been assigned to standard glucose control (1.5% of the 5569 patients in that group).
Perkovic V, Heerspink HL, Chalmers J, et al. Intensive glucose control improves kidney outcomes in patients with type 2 diabetes. (Advance) Kidney Int. 2013 Jan 9.
Zoungas S, Chalmers J, Neal B, et al; the **ADVANCE-ON** Collaborative Group. **Follow-up of Blood-Pressure Lowering and Glucose Control** in Type 2 Diabetes. N Engl J Med. 2014 Sep 19.
Wong MG, Perkovic V, Chalmers J, et al. **ADVANCE-ON** Collaborative Group. Long-term Benefits of Intensive Glucose Control for Preventing End-Stage Kidney Disease: ADVANCE-ON. Diabetes Care. 2016 Mar 22.

[14] Gaede P, Lund-Andersen H, Parving HH, Pedersen O. Effect of a multifactorial intervention on mortality in type 2 diabetes. (**STENO-2**) N Engl J Med. 2008 Feb 7;358(6):580-91.
Gæde P, Oellgaard J, Carstensen B, et al. Years of life gained by multifactorial intervention in patients with type 2 diabetes mellitus and microalbuminuria: 21 years follow-up on the Steno-2 randomised trial. Diabetologia. 2016 Aug 16.

[15] UGDP.
[16] Duckworth W, Abraira C, Moritz T, et al. Glucose Control and Vascular Complications in Veterans with Type 2 Diabetes. N Engl J Med. 2008 Dec 17. (**VADT** study) Intensive glucose control in patients with poorly controlled type 2 diabetes had no significant effect on the rates of major cardiovascular events, death, or microvascular complications. {InfoPOEMs Mar09: Like the ACCORD and ADVANCE studies, this trial provides additional evidence that intensive glucose control does not improve outcomes in patients with type 2 diabetes mellitus. It is important to note that these patients had well-controlled hypertension (mean blood pressure = 126/68) and well-controlled hyperlipidemia (mean low-density lipoprotein = 80 mg/dL).}
Anderson RJ, Bahn GD, Moritz TE, et al.; for the **VADT** Study Group. Blood Pressure and Cardiovascular Disease risk in the Veterans Affairs Diabetes Trial (VADT) Diabetes Care. 2010 Nov 8. DBP <70 mmHg elevated CVD risk.
Hayward RA, Reaven PD, Wiitala WL, et al; **VADT** Investigators. **Follow-up of glycemic control and cardiovascular outcomes** in type 2 diabetes. N Engl J Med. 2015 Jun 4;372(23):2197-206.
Reaven PD, Emanuele NV, Wiitala WL, et al; VADT Investigators. Intensive Glucose Control in Patients with Type 2 Diabetes - 15-Year Follow-up. N Engl J Med. 2019 Jun 6;380(23):2215-2224.
[17] Lindstrom J, Ilanne-Parikka P, et al. Sustained reduction in the incidence of type 2 diabetes by lifestyle intervention: follow-up of the **Finnish** Diabetes Prevention Study. The Lancet. 2006; 368:1673-1679.
Uusitupa M, Peltonen M, Lindström J, et al. 2009 **Ten-Year** Mortality and Cardiovascular Morbidity in the Finnish Diabetes Prevention Study—Secondary Analysis of the Randomized Trial. PLoS ONE 4(5): e5656. doi:10.1371/journal.pone.0005656.
[18] Knowler WC, Barret-Connor E, et al. Reduction in the incidence of type 2 diabetes with lifestyle intervention or metformin. (**DPP** trial) N Engl J Med. 2002; 346: 393-403.
Diabetes Prevention Program Research Group, Knowler WC, Fowler SE, Hamman RF, et al. 10-year follow-up of diabetes incidence and weight loss in the Diabetes Prevention Program Outcomes Study. Lancet. 2009 Nov 14;374(9702):1677-86.
Goldberg R, Temprosa M, Otvos J, et al. **Lifestyle and metformin** treatment favorably influence lipoprotein subfraction distribution in the Diabetes Prevention Program. J Clin Endocrinol Metab 2013.
Perreault L, Temprosa M, Mather KJ, et al; for the Diabetes Prevention Program (DPP) Research Group. Regression From Prediabetes to Normal Glucose Regulation Is Associated With Reduction in Cardiovascular Risk: Results From the Diabetes Prevention Program Outcomes Study. Diabetes Care. 2014 Jun 26.
Rockette-Wagner B, Edelstein S, Venditti EM, et al; Diabetes Prevention Program (**DPP**) Research Group. The impact of **lifestyle intervention on sedentary time in** individuals at high risk of diabetes. Diabetologia. 2015 Apr 8.
Diabetes Prevention Program Research Group. Long-term effects of lifestyle intervention or metformin on diabetes development and microvascular complications over **15-year** follow-up: the Diabetes Prevention Program Outcomes Study. Lancet Diabetes Endocrinol. 2015 Sep 11.
Rockette-Wagner B, Storti KL, et al. **Activity and Sedentary Time 10 Years** After a Successful **Lifestyle Intervention**: The **Diabetes Prevention Program** (**DPPOS**). Am J Prev Med. 2017 Mar;52(3):292-299.
Goldberg RB, Aroda VR, et al; Diabetes Prevention Program (**DPP**) Research Group. Effect of **Long-Term Metformin** and **Lifestyle** in the Diabetes Prevention Program and Its **Outcome Study on Coronary Artery Calcium**. Circulation. 2017 Jul 4;136(1):52-64.
Crandall JP, Mather K, Rajpathak SN, et al. **Statin use and risk of developing diabetes**: results from the **Diabetes Prevention Program (DPP)**. BMJ Open Diabetes Res Care. 2017 Oct 10;5(1):e000438.
Kim C, Aroda VR, Goldberg RB, et al; Diabetes Prevention Program (DPP) Outcomes Study Group. **Androgens, irregular menses, and risk of diabetes and coronary artery calcification** in the Diabetes Prevention Program. J Clin Endocrinol Metab. 2017 Dec 6.
Diabetes Prevention Program Research Group. Long-term Effects of Metformin on Diabetes Prevention: Identification of Subgroups That Benefited Most in the Diabetes Prevention Program and Diabetes Prevention Program Outcomes Study. Diabetes Care. 2019 Apr;42(4):601-608.

[19] Ramachandran A, Snehalatha C, Mary S, Mukesh B, Bhaskar AD, Vijay V; Indian Diabetes Prevention Programme (**IDPP**). Diabetologia. 2006 Feb;49(2):289-97. Epub 2006 Jan 4. n=531 over 2.5yrs
Ramachandran A, Snehalatha C, Mary S, Selvam S, Kumar CK, Seeli AC, Shetty AS. Pioglitazone does not enhance the effectiveness of lifestyle modification in preventing conversion of impaired glucose tolerance to diabetes in Asian Indians: results of the Indian Diabetes Prevention Programme-2 (**IDPP-2**). Diabetologia. 2009 Mar 10. [Epub ahead of print]
[20] Chiasson JL, Josse RG, et al. Acarbose for prevention of type 2 diabetes mellitus: the **STOP-NIDDM** randomized trial. The Lancet. 2002; 359: 2072-2077.
[21] Chiasson JL, Josse RG, Gomis R, et al. Acarbose Treatment and the Risk of Cardiovascular Disease and Hypertension in Patients with Impaired Glucose Tolerance: The STOP-NIDDM Trial. JAMA 2003; 290(4): 486-494.
[22] Torgerson JS, Boldrin MN, et al. XENical in the Prevention of Diabetes in Obese Subjects (**XENDOS**) Study. Diabetes Care. 2004; 27: 155-161.
[23] **DREAM** (Diabetes REduction Assessment with ramipril and rosiglitazone Medication) Trial Investigators; Gerstein HC, Yusuf S, Bosch J, et al. Effect of **rosiglitazone** on the frequency of diabetes in patients with impaired glucose tolerance or impaired fasting glucose: a randomised controlled trial. Lancet. 2006 Sep 23;368(9541):1096-105. Erratum in: Lancet 2006;18;368:1770.
DREAM On (Diabetes Reduction Assessment with Ramipril and Rosiglitazone Medication Ongoing Follow-up) Investigators. Long-term effect of rosiglitazone and/or ramipril on the incidence of diabetes. Diabetologia. 2010 Nov.
Holman RR, Zinman B, Yusuf S, Sheridan PM, Anand SS, Bosch JJ, Conget I, et al. **Incidence of Diabetes Following Ramipril or Rosiglitazone Withdrawal**. (DREAM) trial. Diabetes Care. 2011 Apr 22.
[24] **DREAM** Trial Investigators; Bosch J, Yusuf S, Gerstein HC, et al.Effect of **ramipril** on the incidence of diabetes. N Engl J Med. 2006 Oct 12;355(15):1551-62. Epub 2006 Sep 15.
Holman RR, Zinman B, Yusuf S, Sheridan PM, Anand SS, Bosch JJ, Conget I, et al. **Incidence of Diabetes Following Ramipril or Rosiglitazone Withdrawal**. (DREAM) trial. Diabetes Care. 2011 Apr 22.
[25] **NAVIGATOR** Study Group, Effect of **Nateglinide** on the Incidence of Diabetes and Cardiovascular Events. N Engl J Med 2010 0: NEJMoa1001122. **NAVIGATOR** Study Group, Effect of **Valsartan** on the Incidence of Diabetes and Cardiovascular Events. N Engl J Med 2010 0: NEJMoa1001121.

[26] Holman R, Sanjoy P, Bethel MA, Matthews D, Neil A. 10-Year Follow-up of Intensive Glucose Control in Type 2 Diabetes. (**UKPDS-80**). N Engl J Med 2008;359:1-13. {(SU/Insulin vs control: ↓ MI 19.6⇨16.8 per 1000 patient-yrs RR=0.85 (CI: 0.74-0.97); ↓ Death 30.3⇨26.8 per 1000 patient-yrs RR=0.87 (CI: 0.79-0.96)); (MF vs control: ↓ MI, 21.1⇨14.8 per 1000 patient-yrs RR=0.67 (CI: 0.51-0.89); ↓ Death 33.1⇨25.9 per 1000 patient-yrs RR=0.73 (CI: 0.59-0.89)). {Daily POEM: "The advantages of tight blood sugar control seen in the United Kingdom Prospective Diabetes Study (UKPDS) trial were maintained and to some extent extended during a 10-year nonrandomized follow-up period, even though all patients quickly had similar glycohemoglobin levels. The benefit was most pronounced with metformin. Note that patients in the "intensive therapy" group had a mean glycohemoglobin of approximately 8% at the end of the randomized portion of the study, and the recent ACCORD study found that more aggressive control offered no benefit and may be harmful (N Engl J Med 2008;358:2545-59, POEM #100825). (LOE = 2b)"}

[27] AACE: THE DIAGNOSIS AND MANAGEMENT OF PRE-DIABETES IN THE CONTINUUM OF HYPERGLYCEMIA. July 2008. Accessed online at: http://www.aace.com/meetings/consensus/hyperglycemia/hyperglycemia.pdf

[28] Canadian Optimal Medication Prescribing & Utilization Service (**COMPUS**), Current Topics, Diabetes: http://cadth.ca/index.php/en/compus/current-topics/-dm1 (www.cadth.ca)

[29] Montori V, Fernandez-Balsells M. Glycemic Control in Type 2 Diabetes: Time for an Evidence-Based About Face? Ann Int Med 2009; 150(11). Available at: http://www.annals.org/cgi/content/full/0000605-200906020-00118v1 on 2009 Apr 21.

[30] Salpeter SR, Buckley NS, Kahn JA, Salpeter EE. **Meta-analysis: metformin** treatment in persons at risk for diabetes mellitus. Am J Med 2008;121:149-157.e2. {InfoPOEMS: Using metformin to treat patients at risk for diabetes decreases their likelihood of developing diabetes over a 3-year period. Longer studies are needed to determine whether the likelihood of diabetes is truly decreased or simply delayed. We have no research to tell us whether, in the long run, patients live longer or live better if they are treated at this stage of (pre)diabetes. (LOE = 1a)}

[31] Nissen SE, Wolski K. Effect of Rosiglitazone on the Risk of Myocardial Infarction and Death from Cardiovascular Causes. N Engl J Med. 2007 May 21; [Epub ahead of print] http://content.nejm.org/cgi/content/full/NEJMoa072761

[32] DeFronzo Ralph A., Tripathy Devjit, Schwenke Dawn C., et al. for the **ACT NOW** Study. **Pioglitazone for Diabetes Prevention** in Impaired Glucose Tolerance. N Engl J Med 2011; 364:1104-1115.
ACT-NOW: ↓progression to T2DM (annual incidence of diabetes was 2.1 vs 7.6%/yr; NNT=19/yr) but ↑weight (3.9kg vs 0.77kg) & edema (12.9 vs 6.4%).
Loke Yoon Kong, Kwok Chun Shing, Singh Sonal. Comparative cardiovascular effects of thiazolidinediones: systematic review and meta-analysis of observational studies. BMJ 342:doi:10.1136/bmj.d1309
Tripathy D, Schwenke DC, Banerji M, et al. Diabetes Incidence and Glucose Tolerance after Termination of Pioglitazone Therapy: Results from ACT NOW. J Clin Endocrinol Metab. 2016 May;101(5):2056-62.

[33] Montori VM, Isley WL, Guyatt GH. Waking up from the DREAM of preventing diabetes with drugs. BMJ 2007;28;334(7599):882-4. Accessed online: http://www.bmj.com/cgi/content/extract/334/7599/882

[34] Weng J et al. Effect of intensive insulin therapy on β-cell function and glycaemic control in patients with newly diagnosed type 2 diabetes: A multicentre randomised parallel-group trial. *Lancet* 2008 May 24; 371:1753.

[35] Knowler WC, Hamman RF, Edelstein SL, et al. Prevention of type 2 diabetes with troglitazone in the diabetes prevention program. Diabetes. 2005; 54: 1150-1156.

[36] Chiasson JL, Josse RG, Gomis R, et al. Acarbose Treatment and the Risk of Cardiovascular Disease and Hypertension in Patients with Impaired Glucose Tolerance: The STOP-NIDDM Trial. JAMA 2003; 290(4): 486-494.

[37] AACE: THE DIAGNOSIS AND MANAGEMENT OF PRE-DIABETES IN THE CONTINUUM OF HYPERGLYCEMIA. July 2008. Accessed online at: http://www.aace.com/meetings/consensus/hyperglycemia/hyperglycemia.pdf

[38] Canadian Optimal Medication Prescribing & Utilization Service (**COMPUS**), Current Topics, Diabetes: http://cadth.ca/index.php/en/compus/current-topics/-dm1 (www.cadth.ca)

[39] Montori V, Fernandez-Balsells M. Glycemic Control in Type 2 Diabetes: Time for an Evidence-Based About Face? Ann Int Med 2009; 150(11). Available at: http://www.annals.org/cgi/content/full/0000605-200906020-00118v1 on 2009 Apr 21.

[40] Wiener RS, Wiener DC, Larson RJ. Benefits and risks of tight glucose control in critically ill adults: a meta-analysis. JAMA. 2008 Aug 27;300(8):933-44. In critically ill adult patients, tight glucose control is not associated with significantly reduced hospital mortality but is associated with an increased risk of hypoglycemia.
Arabi YM, Dabbagh OC, Tamim HM, et al. Intensive versus conventional insulin therapy: a randomized controlled trial in medical and surgical critically ill patients. Crit Care Med. 2008 Dec;36(12):3190-7.
NICE-SUGAR Study Investigators, Finfer S, Chittock DR, Su SY, Blair D, et al. Intensive versus conventional glucose control in critically ill patients. N Engl J Med. 2009 Mar 26;360(13):1283-97. Epub 2009 Mar 24. In this large, international, randomized trial, we found that intensive glucose control increased mortality among adults in the ICU: a blood glucose target of 180 mg or less per deciliter resulted in lower mortality than did a target of 81 to 108 mg per deciliter.

[31] Home PD, Pocock SJ, Beck-Nielsen H, Curtis PS, Gomis R, Hanefeld M, Jones NP, Komajda M, McMurray JJ; RECORD Study Team. Rosiglitazone evaluated for cardiovascular outcomes in oral agent combination therapy for type 2 diabetes (RECORD): a multicentre, randomised, open-label trial. Lancet. 2009 Jun 20;373(9681):2125-35. {Commentary & limitations: http://www.medscape.com/viewarticle/704038 }
Komajda M, McMurray JJ, Beck-Nielsen H, et al. Heart failure events with rosiglitazone in type 2 diabetes: data from the RECORD clinical trial. Eur Heart J 2010; DOI: 10.1093/eurheartj/ehp604.
Home PD, Pocock SJ, Beck-Nielsen H, et al. Rosiglitazone evaluated for cardiovascular outcomes in oral agent combination therapy for type 2 diabetes (RECORD): a multicentre, randomised, open-label trial. Lancet 2009;373:2125-2135.
Avenell A, Cook JA, MacLennan GS, McPherson GC; **RECORD** trial group. Vitamin D supplementation and type 2 **diabetes**. Age Ageing. 2009;38(5):606-609.

[32] Griffin SJ, Borch-Johnsen K, Davies MJ, et al. Eff ect of early **intensive multifactorial therapy on 5-year cardiovascular outcomes** in individuals with type 2 diabetes detected by screening (**ADDITION-Europe**):a cluster-randomised trial. Lancet 2011; published online June 25. {In 2014, another publication showed that the 5 year microvascular event rates were also not significantly reduced. (Sandbaek, et al. Diabetes Care. 2014 Jul;37(7):2015-23.)}

Recent Trials, Post-2015

[33]. Scirica BM, Bhatt DL, Braunwald E, et al. **SAVOR-TIMI 53** Steering Committee and Investigators. Saxagliptin and cardiovascular outcomes in patients with type 2 diabetes mellitus. N Engl J Med. 2013 Oct 3;369(14):1317-26. doi: 10.1056/NEJMoa1307684. Link to trial summary: http://www.rxfiles.ca.ezproxy.shirp.ca/rxfiles/uploads/documents/SAVOR-TIMI-53-Saxagliptin-CV-Outcomes-Trial-Summary.pdf

[34]. White WB, Cannon CP, Heller SR et al. **EXAMINE** Investigators. Alogliptin after acute coronary syndrome in patients with type 2 diabetes. N Engl J Med. 2013 Oct 3;369(14):1327-35. doi: 10.1056/NEJMoa1305889.

[35]. Pfeffer MA, Claggett B, Diaz R, et al. Lixisenatide in Patients with Type 2 Diabetes and Acute Coronary Syndrome. **(ELIXA)** N Engl J Med. 2015 Dec 3;373(23):2247 - 57
Link to trial summary: http://www.rxfiles.ca/rxfiles/uploads/documents/Lixisenatide-ELIXA%20Trial%20Summary.pdf

[36]. Green JB, Bethel MA, Armstrong PW, et al. Effect of Sitagliptin on Cardiovascular Outcomes in Type 2 Diabetes. (**TECOS**) N Engl J Med. 2015 Jul 16;373(3):232-42. doi: 10.1056/NEJMoa1501352. Epub 2015 Jun 8. Erratum in: N Engl J Med. 2015 Aug 6;373(6):586. Link to trial summary: http://www.rxfiles.ca/rxfiles/uploads/documents/TECOS-Trial-Summary.pdf

[37]. Marso SP, Bain SC, Consoli A, Eliaschewitz FG, Jódar E, Leiter LA, et al ; **SUSTAIN-6** Investigators.. Semaglutide and Cardiovascular Outcomes in Patients with Type 2 Diabetes. N Engl J Med. 2016 Nov 10;375(19):1834-1844.

[38]. Marso SP, Daniels GH, Brown-Frandsen K, et al. Liraglutide and Cardiovascular Outcomes in Type 2 Diabetes. (**LEADER**) N Engl J Med. 2016 Jun 13.
Link to trial summary: http://www.rxfiles.ca/rxfiles/uploads/documents/Leader-Liraglutide%20VICTOZA%20and%20Cardiovascular%20Outcomes%20in%20Type%202%20Diabetes.pdf

[39]. Zinman B, Wanner C, Lachin JM, et al.; **EMPA-REG** OUTCOME Investigators. Empagliflozin, Cardiovascular Outcomes, and Mortality in Type 2 Diabetes. N Engl J Med. 2015 Sep 17.
Link to trial summary: http://www.rxfiles.ca/rxfiles/uploads/documents/EMPA-REG%20Trial%20Summary.pdf
Zinman B, Inzucchi SE, Lachin JM, et al. **Empagliflozin** and **Cerebrovascular Events** in Patients With Type 2 Diabetes Mellitus at High Cardiovascular Risk. (**Empa-Reg**) Stroke. 2017 May;48(5):1218-1225.

[40]. Jiang L, Johnson A, Pratte K, et al. Long-term Outcomes of Lifestyle Intervention to Prevent Diabetes in American Indian and Alaska Native Communities:
The Special Diabetes Program for Indians Diabetes Prevention Program. (**SDPI-DP**) Diabetes Care. 2018 Jul;41(7):1462-1470.

Additional References

ADA-American Diabetes Association Guidelines- Standards of Medical Care in Diabetes—**2014** http://care.diabetesjournals.org/content/37/Supplement_1.toc
ADA, ACC & AHA Position Statement - Intensive Glycemic Control & the prevention of CV Events - Jan/2009 Implications of ACCORD, ADVANCE & VA Diabetes Trials (ePublished - accessed Dec 30, 2008) http://care.diabetesjournals.org/misc/finaldc9026.pdf
ADA 2018: American Diabetes Association. 8. **Pharmacologic Approaches** to Glycemic Treatment: Standards of Medical Care in Diabetes-2018. Diabetes Care. 2018 Jan;41(Suppl 1):S73-S85.
ADA 2018: American Diabetes Association. 7. **Obesity Management** for the Treatment of Type 2 Diabetes: Standards of Medical Care in Diabetes-2018. Diabetes Care. 2018 Jan;41(Suppl 1):S65-S72.
ADA 2018: American Diabetes Association. 5. **Prevention or Delay of Type 2 Diabetes**: Standards of Medical Care in Diabetes-2018. Diabetes Care. 2018 Jan;41(Suppl 1):S51-S54.
ADA 2018: American Diabetes Association. 4. **Lifestyle Management**: Standards of Medical Care in Diabetes-2018. Diabetes Care. 2018 Jan;41(Suppl 1):S38-S50.
American College of Sports Medicine, American Diabetes Association. **Exercise and type 2 diabetes**: American College of Sports Medicine and the American Diabetes Association: joint position statement. Med Sci Sports Exerc 2010 Dec;42(12):2282-303.
Andrews RC, Cooper AR, Montgomery AA, et al. **Diet or diet plus physical activity versus usual care** in patients with newly diagnosed type 2 diabetes: the Early ACTID randomised controlled trial. Lancet 2011; June 25.
Avery L, Flynn D, van Wersch A, et al. Changing **Physical Activity Behavior** in Type 2 Diabetes: A systematic review and meta-analysis of behavioral interventions. Diabetes Care. 2012 Dec;35(12):2681-9.
Baum A, Scarpa J, Bruzelius E, et al. Targeting weight loss interventions to reduce cardiovascular complications of type 2 diabetes: a machine learning-based post-hoc analysis of heterogeneous treatment effects in the **Look AHEAD** trial. Lancet Diabetes Endocrinol. 2017 Jul 12.
Belalcazar LM, Ballantyne CM. Looking Back at **Look AHEAD** Through the Lens of Recent Diabetes Outcome Trials. Circulation. 2017 Feb 21;135(8):720-723.
BMJ 2009;338:b800. Mar 2009. Editorials: **Tight contro**l of blood glucose in long standing type 2 diabetes. Accessed at http://www.bmj.com/cgi/content/full/338/mar05_2/b800?ct
Boussageon R, Bejan-Angoulvant T, Saadatian-Elahi M, et al. Effect of **intensive glucose lowering treatment on all cause mortality, cardiovascular death**, and microvascular events in type 2 diabetes: meta-analysis of randomised controlled trials. BMJ 2011;343:d4169.
Bulugahapitiya U, Siyambalapitiya S, Sithole J, Idris I. Is diabetes a coronary risk equivalent? Systematic review and meta-analysis. Diabet Med. 2009;26:142-8. {InfoPOEMs Apr09: This meta-analysis found no evidence to support the contention that diabetes alone is a coronary heart disease (CHD) risk equivalent to a history of prior myocardial infarction (MI). The blanket use of aspirin and statins for patients with type 2 diabetes, regardless of their lipid levels, is not supported by the evidence. (LOE = 2a)}
Burr J, Shephard R, Riddell M. Prediabetes and type 2 diabetes mellitus: Assessing risks for physical activity clearance and prescription. Can Fam Physician March 2012 58: 280-284.
Chatterton H, Younger T, Fischer A, Khunti K; on behalf of the Programme Development Group. **Risk identification and interventions** to prevent type 2 diabetes in adults at high risk: summary of **NICE** guidance. BMJ. 2012 Jul 12;345:e4624.
Coca SG, Ismail-Beigi F, Haq N, Krumholz HM, Parikh CR. Role of intensive glucose control in development of renal end points in type 2 diabetes mellitus: systematic review & meta-analysis. Arch Intern Med. 2012;172 (10):761-769
Collins GS, Altman DG. External validation of **QDSCORE**((R)) for predicting the 10-year risk of developing Type 2 diabetes. Diabet Med. 2011 May;28(5):599-607. doi: 10.1111/j.1464-5491.2011.03237.x
Coppell KJ, Kataoka M, Williams SM, et al. **Nutritional intervention** in patients with type 2 diabetes who are hyperglycaemic despite optimised drug treatment—Lifestyle Over and Above Drugs in Diabetes (LOADD) study: randomised controlled trial. BMJ 2010;341:c3337.
Defronzo RA, Banerji M, Bray GA, et al. Actos Now for the prevention of diabetes (**ACT NOW**) study. BMC Endocr Disord. 2009 Jul 29;9:17. (pioglitazone)
DeFronzo Ralph A., Tripathy Devjit, Schwenke Dawn C., et al. for the **ACT NOW** Study. **Pioglitazone for Diabetes Prevention** in Impaired Glucose Tolerance. N Engl J Med 2011; 364:1104-1115.
Dipietro L, Gribok A, Stevens MS, et al. **Three 15-min Bouts of Moderate Postmeal Walking** Significantly Improves 24-h Glycemic Control in Older People at Risk for Impaired Glucose Tolerance. Diabetes Care. 2013 Jun 11.
Elhayany A, Lustman A, Abel R, et al. A low carbohydrate **Mediterranean diet** improves cardiovascular risk factors and diabetes control among overweight patients with type 2 diabetes mellitus: a 1-year prospective randomized intervention study. Diabetes Obes Metab. 2010 Mar;12(3):204-9.
Esposito K, Maiorino MI, Petrizzo M, et al. The Effects of a **Mediterranean Diet** on Need for Diabetes Drugs and Remission of Newly Diagnosed Type 2 Diabetes: Follow-up of a Randomized Trial. Diabetes Care. 2014 Apr 10.
Franks, Paul W., Hanson, Robert L., Knowler, William C., et al. **Childhood Obesity**, Other Cardiovascular Risk Factors, and **Premature Death**. N Engl J Med 2010 362: 485-493.
Garvey WT, Ryan DH, Henry R, et al. **Prevention of type 2 diabetes** in subjects with prediabetes and metabolic syndrome treated with phentermine and **topiramate** extended release. Diabetes Care. 2014 Apr;37(4):912-21.
Gillett M, Royle P, Snaith A, et al. **Non-pharmacological interventions** to **reduce the risk of diabetes** in people with impaired glucose regulation: a systematic review and economic evaluation. Health Technol Assess. 2012 Aug;16(33):1-236, iii-iv.
Gregg EW, Chen H, Wagenknecht LE, et al. Association of an **intensive lifestyle** intervention with remission of type 2 diabetes. (**Look Ahead**) JAMA. 2012;308(23): 2489-2496.
Haw JS, Galaviz KI, Straus AN, et al. **Long-term Sustainability of Diabetes Prevention Approaches**: A Systematic Review and Meta-analysis of Randomized Clinical Trials. JAMA Intern Med. 2017 Nov 6.
Haynes RB, Haynes GA. What does it take to put an ugly fact through the heart of a beautiful hypothesis? Evid Based Med. 2009 Jun;14(3):68-9. http://ebm.bmj.com/cgi/content/full/14/3/68?linkType=FULL&journalCode=ebmed&resid=14/3/68
Hayward RA, Reaven PD, Wiitala WL, et al; **VADT** Investigators. **Follow-up of glycemic control and cardiovascular outcomes** in type 2 diabetes. N Engl J Med. 2015 Jun 4;372(23):2197-206.
Heianza Y, Hara S, Arase Y, et al. **HbA(1c)** 5.7-6.4% and impaired fasting plasma glucose for diagnosis of prediabetes and risk of progression to diabetes in Japan (**TOPICS 3**): a longitudinal cohort study. Lancet. 2011 Jun 24.
Hemmingsen B, Lund SS, Gluud C, et al. Targeting **intensive glycaemic control versus targeting conventional glycaemic control** for type 2 diabetes mellitus. Cochrane Database of Systematic Reviews 2011, Issue 6. Art. No.: CD008143. DOI: 10.1002/14651858.CD008143.pub2. The included trials did not show significant differences for all-cause mortality and cardiovascular mortality when targeting intensive glycaemic control compared with conventional glycaemic control. Targeting intensive glycaemic control reduced the risk of microvascular complications while increasing the risk of hypoglycaemia. Furthermore, intensive glycaemic control might reduce the risk of non-fatal myocardial infarction in trials exclusively dealing with glycaemic control in usual care settings.
Hemmingsen B, Lund SS, Gluud C, et al. **Intensive glycaemic control for patients with type 2 diabetes**: systematic review with meta-analysis and trial sequential analysis of randomised clinical trials. BMJ. 2011 Nov 24;343:d6898.
Hemmingsen B, Sonne DP, Metzendorf MI, et al. **Dipeptidyl-peptidase (DPP)-4 inhibitors and glucagon-like peptide (GLP)-1 analogues for prevention or delay of type 2 diabetes mellitus** and its associated complications in people at increased risk for the development of type 2 diabetes mellitus. Cochrane Database Syst Rev. 2017 May 10;5:CD012204. There is no firm evidence that DPP-4 inhibitors or GLP-1 analogues compared mainly with placebo substantially influence the risk of T2DM and especially its associated complications in people at increased risk for the development of T2DM. Most trials did not investigate patient-important outcomes.
Hippisley-Cox J, Coupland C, Robson J, Sheikh A, Brindle P. **Predicting risk of type 2 diabetes** in England and Wales: prospective derivation and validation of **QDScore**. BMJ. 2009 Mar 17;338:b880. doi: 10.1136/bmj.b880.
Holman, Rury R., Farmer, Andrew J., Davies, Melanie J., et al. the **4-T** Study Group, Three-Year Efficacy of Complex Insulin Regimens in Type 2 Diabetes.N Engl J Med 2009 0: NEJMoa0905479.
Holman RR, Sourij H, Califf RM. **Cardiovascular outcome trials** of glucose-lowering drugs or strategies in type 2 diabetes. Lancet. 2014 Jun 7;383(9933):2008-2017.
Ismail-Beigi Faramarz, Moghissi Etie, Tiktin Margaret, et al. **Individualizing Glycemic Targets** in Type 2 Diabetes Mellitus: **Implications of Recent Clinical Trials**. Ann Intern Med April 19, 2011 154:554-559.
Johnston Stephen S., Conner Christopher, Aagren Mark, et al. Evidence Linking **Hypoglycemic Events to an Increased Risk of Acute Cardiovascular Events** in Patients With Type 2 Diabetes. Diabetes Care May 2011 34:1164-1170.
Kahn HS, Cheng YJ, Thompson TJ, Imperatore G, Gregg EW. Two risk-scoring systems for **predicting incident diabetes mellitus** in U.S. adults age 45 to 64 years. Ann Intern Med. 2009 Jun 2;150(11):741-51. Basic information identified adults at high risk for diabetes. Additional data from fasting blood tests better identified those at extreme risk.
Karagiannis T, Paschos P, Paletas K, Matthews DR, Tsapas A. **Dipeptidyl peptidase-4 inhibitors** (DPP-4) for treatment of type 2 diabetes mellitus in the clinical setting: systematic review and meta-analysis. BMJ 2012;344:e1369.
Kawamori R, Tajima N, et al. Voglibose Ph-3 Study Group. **Voglibose** for prevention of type 2 diabetes mellitus: a randomised, double-blind trial in Japanese individuals with impaired glucose tolerance. Lancet. 2009 May 9;373(9675):1607-14.
Le Roux CW, Astrup A, Fujioka K, et al, for the **SCALE** Obesity and Prediabetes NN8022-1839 Study Group. 3 years of **liraglutide** versus placebo for **type 2 diabetes risk reduction** and weight management in individuals with prediabetes:

a randomised, double-blind trial. Lancet 2017; online Feb 22.
Lean MEJ, Leslie WS, Barnes AC, et al. **Primary care-led weight management for remission of type 2 diabetes (DiRECT)**: an open-label, cluster-randomised trial. Lancet 2017; published online Dec 5.
Li G, Zhang P, Wang J, et al. Cardiovascular mortality, all-cause mortality, and diabetes incidence after **lifestyle intervention for people with impaired glucose tolerance in the Da Qing Diabetes Prevention Study**: a 23-year follow-up study. *Lancet Diabetes Endocrinol* 2014.
Li R, Zhang P, Barker LE, et al. **Cost-effectiveness of interventions to prevent** and control diabetes mellitus: a systematic review. Diabetes Care. 2010 Aug;33(8):1872-94.
Lilly M, Godwin M. Treating **prediabetes with metformin**: systematic review and meta-analysis. Can Fam Physician. 2009 Apr;55(4):363-9. Metformin decreases the rate of conversion from prediabetes to diabetes. This was true at higher dosage (850 mg twice daily) & lower dosage (250 mg twice or 3 times daily); in people of varied ethnicity; & even when a sensitivity analysis was applied to the data. The number needed to treat was between 7 & 14 for treatment over a 3-year period.
Lind M, Bounias I, Olsson M, Gudbjörnsdottir S, et al. **Glycaemic control and incidence of heart failure** in 20 985 patients with type 1 diabetes: an observational study. Lancet 2011; published online June 25.
Loke Yoon Kong, Kwok Chun Shing, Singh Sonal. Comparative **cardiovascular effects of thiazolidinediones**: systematic review and meta-analysis of observational studies. BMJ 342:doi:10.1136/bmj.d1309
Long GH, Cooper AJ, Wareham NJ, et al. **Healthy Behavior Change** and Cardiovascular Outcomes in Newly Diagnosed Type 2 Diabetes Patients: A Cohort Analysis of The **ADDITION-Cambridge** Study. Diabetes Care. 2014 Mar 21.
Look AHEAD Group. Long-term Effects of a **Lifestyle** Intervention on Weight and Cardiovascular Risk Factors in Individuals With Type 2 Diabetes Mellitus: Four-Year Results of the Look AHEAD Trial. Arch Intern Med. 2010;170(17):1566-1575.
Look AHEAD Research Group. Cardiovascular effects of intensive lifestyle intervention in type 2 diabetes. N Engl J Med 2013. DOI: 10.1056/NEJMoa1212914.
Look AHEAD Research Group. **Eight-year weight losses with an intensive lifestyle** intervention: the look AHEAD study. Obesity (Silver Spring). 2014 Jan;22(1):5-13.
Luoto R, Kinnunen TI, Aittasalo M, Kolu P, Raitanen J, et al. (2011) Primary **Prevention of Gestational Diabetes Mellitus** and Large-for-Gestational-Age Newborns by **Lifestyle Counseling**: A Cluster-Randomized Controlled Trial. PLoS Med 8(5): e1001036. doi:10.1371/journal.pmed.1001036
Maruthur NM, Ma Y, Delahanty LM, et al; for the Diabetes Prevention Program Research Group. **Early Response to Preventive Strategies** in the Diabetes Prevention Program (**DPP**). J Gen Intern Med. 2013 Jul 17.
Merlotti C, Morabito A, Pontiroli AE. **Prevention of type 2 diabetes**; a systematic review and meta-analysis of different intervention strategies. Diabetes Obes Metab. 2014 Jan 29.
Montori V, Fernandez-Balsells M. **Glycemic Control** in Type 2 Diabetes: Time for an Evidence-Based About Face? Ann Int Med 2009; 150(11). Available at: http://www.annals.org/cgi/content/full/0000605-200906020-00118v1 on 2009 Apr 21.
Mozaffarian D, Kamineni A, Carnethon M, et al. **Lifestyle** risk factors and new-onset diabetes mellitus in older adults. Arch Intern Med 2009; 169:798-807.
NICE: National Institute for Health and Clinical Excellence. Preventing type 2 diabetes: risk identification and interventions for individuals at high risk. PHG38. 2012. http://guidance.nice.org.uk/PH38 .
Orozco LJ, Buchleitner AM, Gimenez-Perez G, Roqué i Figuls M, Richter B, Mauricio D. **Exercise or exercise and diet for preventing type 2 diabetes mellitus**. Cochrane Database of Systematic Reviews 2008, Issue 3. Art. No.: CD003054. DOI:10.1002/14651858.CD003054.pub3. Interventions aimed at increasing exercise combined with diet are able to decrease the incidence of type 2 diabetes mellitus in high risk groups (people with impaired glucose tolerance or the metabolic syndrome). There is a need for studies exploring exercise only interventions and studies exploring the effect of exercise and diet on quality of life, morbidity and mortality, with special focus on cardiovascular outcomes.
Perreault L, Pan Q, Mather KJ, et al., for the Diabetes Prevention Program Research Group. Effect of **regression from prediabetes to normal glucose regulation** on long-term reduction in diabetes risk: results from the Diabetes Prevention Program Outcomes Study. Lancet 2012; online June 9.
Pillay J, Armstrong MJ, Butalia S, et al. **Behavioral Programs for Type 1 Diabetes** Mellitus: A Systematic Review and Meta-analysis. Ann Intern Med. 2015 Sep 29.
Pillay J, Armstrong MJ, Butalia S, et al. **Behavioral Programs for Type 2 Diabetes** Mellitus: A Systematic Review and NetworkMeta-analysis for Effect Moderation. Ann Intern Med. 2015 Sep 29.
Ray KK, Seshasai SR, Wijesuriya S, et al. Effect of **intensive control of glucose on cardiovascular outcomes** and death in patients with diabetes mellitus: a meta-analysis of randomized controlled trials. Lancet 2009; 373: 1765-72.
Reis JP, Loria CM, Sorlie PD, et al. Lifestyle factors and risk for new-onset diabetes: a population-based cohort study. Ann Intern Med. 2011 Sep 6;155(5):292-9.
Rock CL, Flatt SW, et al. Weight Loss, Glycemic Control, and Cardiovascular Disease Risk Factors in Response to **Differential Diet Composition in a Weight Loss** Program in Type 2 Diabetes: A Randomized Controlled Trial. Diabetes Care. 2014 Apr 23.
Rosenstock J, Klaff LJ, Schwartz S, et al. Effects of **Exenatide** and Lifestyle Modification on Body Weight and Glucose Tolerance in Obese Subjects With and Without Prediabetes. Diabetes Care. 2010 Mar 23. n=152 over 24weeks.
Saito T, Watanabe M, Nishida J, et al; **Zensharen Study** for Prevention of Lifestyle Diseases Group. **Lifestyle modification and prevention** of type 2 diabetes in overweight Japanese with impaired fasting glucose levels: a randomized controlled trial. Arch Intern Med. 2011;171(15):1352-1360.
Saitz R. How Much Evidence Do We Need to Change Practices in Which We Firmly Believe? Enough already! Randomized trials show that tight glucose control in patients with long-standing type 2 diabetes isn't beneficial. *http://general-medicine.jwatch.org/cgi/content/full/2009/730/1#R9*
Salas-Salvadó J, Bulló M, Estruch R, et al. Prevention of diabetes with **Mediterranean diets**: a subgroup analysis of a randomized trial. Ann Intern Med. 2014 Jan 7;160(1):1-10.
Sandbæk A, Griffin SJ, Sharp SJ, et al. Effect of Early **Multifactorial Therapy Compared With Routine Care** on Microvascular Outcomes at 5 Years in People With Screen-Detected Diabetes: A Randomized Controlled Trial: The **ADDITION-Europe** Study. Diabetes Care. 2014 Jul;37(7):2015-23.
Schellenberg ES, Dryden DM, Vandermeer B, et al. **Lifestyle Interventions** for Patients With and at Risk for Type 2 Diabetes: A Systematic Review and Meta-analysis. Ann Intern Med. 2013 Oct 15;159(8):543-51.
Scirica BM, Bhatt DL, Braunwald E, et al. **Saxagliptin** and cardiovascular outcomes in patients with type 2 diabetes mellitus. (**Savor-Timi 53**) N Engl J Med 2013; DOI:10.1056/NEJMoa1307684. Available here.
Shurraw S, Hemmelgarn B, Lin M, et al; for the Alberta Kidney Disease Network. Association between **glycemic control and adverse outcomes** in people with diabetes mellitus and **chronic kidney disease**: a population-based cohort study. Arch Intern Med. 2011;171(21):1920-1927.
Tikkanen-Dolenc H, Wadén J, Forsblom C, et al; **FinnDiane Study Group**. **Physical Activity Reduces Risk of Premature Mortality in Patients With Type 1 Diabetes** With and Without Kidney Disease. Diabetes Care. 2017 Oct 16.
Tocci G, Paneni F, Palano F, et al. **Angiotensin-Converting Enzyme Inhibitors, Angiotensin II Receptor Blockers** and Diabetes: A Meta-Analysis of Placebo-Controlled Clinical Trials. Am J Hypertens. 2011 May;24(5):582-90.
TODAY Study Group. A clinical trial to maintain glycemic control in **youth with type 2 diabetes**. N Engl J Med 2012.
Writing Committee for the Type 1 Diabetes **TrialNet Oral Insulin** Study Group, Krischer JP, Schatz DA, Bundy B, et al. Effect of **Oral Insulin** on **Prevention of Diabetes in Relatives of Patients** With Type 1 Diabetes: A Randomized Clinical Trial. JAMA. 2017 Nov 21;318(19):1891-1902.
Yates T, Haff ner SM, Schulte PJ, et al. Association between change in **daily ambulatory activity** and cardiovascular events in people with impaired glucose tolerance (NAVIGATOR trial): a cohort analysis. Lancet 2014; online Dec 20.
Zhang H, Gao C, Fang L, Zhao HC, Yao SK. **Metformin and reduced risk of hepatocellular carcinoma** in diabetic patients: a meta-analysis. Scand J Gastroenterol. 2012 Nov 9.
Zinman B, Harris SB, Gerstein HC, Young TK, Raboud JM, Neuman J, Hanley AJ. Preventing type 2 diabetes using combination therapy: design and methods of the CAnadian Normoglycaemia Outcomes Evaluation (**CANOE**) trial. Diabetes Obes Metab. 2006 Sep;8(5):531-7.
Zinman B, Harris SB, Neuman J, et al. Low-dose combination therapy with **rosiglitazone & metformin** to prevent type 2 diabetes mellitus (**CANOE**): A double-blind randomised controlled study. Lancet 2010; DOI: 10.1016/S0140-6736(10)60746-5.

References (DIABETES Landmark Trials: Summary of RCT Evidence for Lipid, ASA & BP Trials)
1) Colhoun HM, Betteridge DJ, Durrington PN, et al. Primary prevention of cardiovascular disease with atorvastatin in type 2 diabetes in the Collaborative Atorvastatin Diabetes Study (CARDS): multicentre randomised placebo-controlled trial. *Lancet* 2004; 364 (9435): 685-96.
2) Collins R, Armitage J, Parish S, Sleigh P, Peto R. Heart Protection Study Collaborative Group: MRC/BHF Heart Protection Study of cholesterol-lowering with simvastatin in 5,963 people with diabetes: a randomised placebo-controlled trial. *Lancet* 2003; 361: 2005–2016.
3) Sever PS, Poulter NR, Dahlöf B, et al. Reduction in cardiovascular events with atorvastatin in 2,532 patients with Type 2 Diabetes. Anglo-Scandinavian Cardiac Outcomes Trial – Lipid Lowering Arm. (ASCOT-LLA) *Diabetes Care* 2005; 28: 1151-1157.
4) Knopp RH, d'Emden M, Smilde JG, Pocock SJ. Efficacy and safety of atorvastatin in the prevention of cardiovascular end points in subjects with type 2 diabetes: the Atorvastatin Study for Prevention of Coronary Heart Disease Endpoints in non-insulin-dependent diabetes mellitus (ASPEN). *Diabetes Care* 2006;29:1478-85.
5) The ALLHAT Officers & Coordinators for the ALLHAT Collaborative Research Group. Major Outcomes in Moderately Hypercholesterolemic, Hypertensive Patients Randomized to Pravastatin vs Usual Care. The Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial (ALLHAT-LLT). *JAMA* 2002; 288: 2998-3007.
6) Shepherd J, Cobbe SM, Ford I, et al. Prevention of Coronary Heart Disease with Pravastatin in Men with Hypercholesterolemia. *NEJM* 1995; 333 (20): 1301-7.
7) Downs JR, Clearfield M, Weis S, et al. Primary prevention of acute coronary events with lovastatin in men and women with average cholesterol levels: results of AFCAPS/TexCAPS. Air Force/Texas Coronary Atherosclerosis Prevention Study. *JAMA* 1998; 279: 1615-22.
8) Shepherd J, Blauw GJ, Murphy MB, et al. Pravastatin in elderly individuals at risk of vascular disease (PROSPER): a randomised controlled trial. *Lancet* 2002; 360: 1623-30.
9) Nakamura H, Arakawa K, Itakura H, et al. Primary prevention of cardiovascular disease with pravastatin in Japan (MEGA study): a prospective randomised controlled trial. *Lancet* 2006; 368: 1155-63.
10) Cholesterol Treatment Trialists' (CTT) Collaborators. Efficacy of cholesterol-lowering therapy in 18,686 people with diabetes in 14 randomised trials of statins: a meta-analysis. *Lancet* 2008; 371: 117-125.
11) Vijan S, Hayward RA. Pharmacologic lipid-lowering therapy in type 2 diabetes mellitus: background paper for the American College of Physicians. *Ann Intern Med* 2004; 140: 650-658.
12) Dalhousie University - Academic Detailing Service. Statins and Cardiovascular Disease. April 2005. Available from: http://cme.medicine.dal.ca/files/statins.pdf. Accessed on: June 11, 2011.
13) Atorvastatin reduced major cardiovascular disease events in type 2 diabetes mellitus. *ACP Journal Club* 2005; 142(2): 29.
14) Hackam DG. Should a statin be routinely prescribed for primary prevention of cardiovascular disease in diabetes mellitus? *CMAJ* 2004; 171(8): 857.
15) Garg A. Statins for all patients with type 2 diabetes: not so soon. *Lancet* 2004; 364 (9435): 641-642.
16) Costa J, Borges M, David C, Carneiro AV. Efficacy of lipid lowering drug treatment for diabetic and non-diabetic patients: meta-analysis of randomised controlled trials. *BMJ* 2006; doi: 10.1136/bmj.38793.468449.AE.
17) Koskinen P, Manttari M, Manninen V, et al. Coronary Heart Disease Incidence in NIDDM Patients in the Helsinki Heart Study. *Diabetes Care* 1992; 15(7): 820-825.
18) DeBerardis G, Sacco M, Strippoli GFM, et al. Aspirin for primary prevention of cardiovascular events in people with diabetes: meta-analysis of randomized controlled trials. *BMJ* 2009; doi:10.1136/bmjb4531.
19) NHS. Regional Drug and Therapeutics Centre – Drug Update. Aspirin for primary prevention of cardiovascular disease. July 2010, No. 65. Available from: http://www.nyrdtc.nhs.uk/docs/dud/DU_65_Aspirin.pdf Accessed on: June 12, 2011.
20) Zhang C, Sun A, Zhang P, et al. Aspirin for primary prevention of cardiovascular events in patients with diabetes: A meta-analysis. *Diabetes Research and Clinical Practice* 2010; 87: 211-218.
21) Sattar N, Preiss D, Murray HM, et al. Statins and risk of incident diabetes: a collaborative meta-analysis of randomised statin trials. *Lancet* 2010; 375: 735-42.
22) Statin use increases risk for diabetes. ACP Journal Club 2010; 152(6): JC6-7.
23) Coleman CI, Reinhart K, Kluger J, White CM. The effect of statins on the development of new-onset type 2 diabetes: a meta-analysis of randomised controlled trials. *Curr Med Res Opin* 2008; 24: 1359-62.
24) Ogawa H, Nakayama M, Morimoto T, et al. Low dose aspirin for primary prevention of atherosclerotic events in patients with type 2 diabetes. *JAMA* 2008;300:2134-41.
Saito Y, et al. **Low-Dose Aspirin for Primary Prevention** of Cardiovascular Events in Patients with Type 2 **Diabetes:10-year Follow-up (JPAD)** of a Randomized Controlled Trial. Circulation. 2016 Nov 15.
25) Belch J, MacCuish A, Campbell I, et al. The prevention of progression of arterial disease and diabetes (POPADAD) trial: factorial randomised placebo controlled trial of aspirin and antioxidants in patients with diabetes and asymptomatic peripheral arterial disease. *BMJ*. 2008; 337:a1840.
26) Fitchett D and Kraw M. Vascular Protection in People with Diabetes. Canadian Diabetes Association Clinical Practice Guidelines Expert Committee. *Can J Diabetes* 2008; 32(Suppl 1):S102–S106.
27) Bell AD, Roussin A, Cartier R, et al. The Use of Antiplatelet Therapy in the Outpatient Setting: Canadian Cardiovascular Society Guidelines. *Canadian Journal of Cardiology* 2011; 27: S1-S59.
28) ADA- American Diabetes Association. Standards of Medical Care in Diabetes—2011 Diabetes Care. January 2011 34:S11-S61; doi:10.2337/dc11-S011. http://care.diabetesjournals.org/content/34/Supplement_1/S11.full.pdf+html
29) Pignone M, Alberts MJ, Colwell JA, et al. Aspirin for primary prevention of cardiovascular events in people with diabetes. A position statement of the American Diabetes Association, American Heart Association, and an expert consensus document of the American College of Cardiology Foundation. *Circulation* 2010; 121: 2694-2701.
30) Preiss D, Seshasai SR, Welsh P, et al. Risk of incident diabetes with intensive-dose compared with moderate-dose statin therapy: a meta-analysis. *JAMA*. 2011 Jun 22;305(24):2556-64.
31) Mogensen CE, Neldam S, Tikkanen I, Oren S, et al. Randomised controlled trial of dual blockade of renin-angiotensin system in patients with hypertension, microalbuminuria, and non-insulin dependent diabetes: the candesartan and lisinopril microalbuminuria (CALM) study. *BMJ* 2000;321:1440-4.
32) Patel A; ADVANCE Collaborative Group, MacMahon S, Chalmers J, Neal B, et al. Effects of a fixed combination of perindopril and indapamide on macrovascular and microvascular outcomes in patients with type 2 diabetes mellitus (the ADVANCE trial): a randomised controlled trial. *Lancet* 2007 Sep 8;370(9590):829-40.
33) Weber MA, Bakris GL, Jamerson K, et al. Cardiovascular events during differing hypertension therapies in patients with diabetes. *J Am Coll Cardiol* 2010; 56: 77-85.
34) Whelton PK, Barzilay J, Cushman WC, et al. ALLHAT Collaborative Research Group. Clinical outcomes in antihypertensive treatment of type 2 diabetes, impaired fasting glucose concentration, and normoglycemia:Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial (ALLHAT). *Arch Intern Med* 2005;165:1401-1409.
35) Antithrombotic Trialists' Collaboration. Collaborative meta-analysis of randomized trials of antiplatelet therapy for prevention of death, myocardial infarction, and stroke in high-risk patients. *BMJ* 2002; 324: 71-86.
36)Antithrombotic Trialists' Collaboration. Aspirin in the primary and secondary prevention of vascular disease: collaborative meta-analysis of individual participant data from randomised trials. *Lancet* 2009; 373: 1849-60.
37) Benazepril plus amlodipine reduced cardiovascular events more than benazepril plus hydrochlorothiazide with or without diabetes. *ACP Journal Club* 2010; 153(4).
38) ACCORD Study Group. Effects of Intensive Blood-Pressure Control in Type 2 Diabetes Mellitus. N Engl J Med. 2010 Mar 14.
39) ACCORD Study Group. Effects of Combination Lipid Therapy in Type 2 Diabetes Mellitus. *N Engl J Med*. 2010 Mar 18. Supplement App: http://www.nejm.org/doi/suppl/10.1056/NEJMoa1001282/suppl_file/nejm_accord_1563sa1.pdf
40) Allan GM, Ivers N, and McCormack J. Type 2 diabetes and ASA. Tools for Practice. *Canadian Family Physician.* 2010; 56: 664.
41) Vijan S and Hayward R. Treatment of Hypertension in Type 2 Diabetes Mellitus: Blood pressure goals, choice of agents and setting priorities in diabetes care. *Ann Intern Med.* 2003;138:593-602.
42) Hansson L, Zanchetti A, Carruthers SG, et al. Effects of intensive blood-pressure lowering and low-dose aspirin in patients with hypertension: principal results of the Hypertension Optimal Treatment (HOT) randomised trial. HOT Study Group. *Lancet*. 1998;351:1755-62.
43) UK Prospective Diabetes Study Group. Tight blood pressure control and risk of macrovascular and microvascular complications in type 2 diabetes: UKPDS 38. BMJ 1998;317:703-13.
44) UK Prospective Diabetes Study Group. Efficacy of atenolol and captopril in reducing risk of macrovascular and microvascular complications in type 2 diabetes: UKPDS 39. BMJ 1998;317:713-20.
45) Cooper-DeHoff RM, Gong Y, Handberg EM et al. Tight blood pressure control and cardiovascular outcomes among hypertensive patients with diabetes and coronary heart disease. JAMA. 2010; Jul 7; 304(1): 61-8.
46) Issues in Hypertension 2011, Dalhousie CME Academic Detailing Service, June 2011, http://cme.medicine.dal.ca/ad_resources.htm
47) Grossman E, Messerli FH, Goldbourt U. High blood pressure and DM: are all antihypertensives created equal? *Arch Intern Med*. 2000; 160(16): 2447-52.
48) Turnbull F, Neal B, Algert C, et al. Effects of different blood pressure-lowering regimens on major cardiovascular events in individuals with and without diabetes mellitus: results of prospectively designed overviews of randomized trials. *Arch Intern Med*. 2005; 165(12): 1410-9.
49) Balamuthusamy S, Molnar J, Adigopula S, Arora R. Comparative analysis of beta-blockers with other antihypertensive agents on cardiovascular outcomes in hypertensive patients with diabetes mellitus: a systematic review and meta-analysis. *Am J Ther*. 2009; 16(2): 133-142.
50) Yusuf S, Teo KK, Pogue J, et al for the ONTARGET investigators. Telmisartan, ramipril, or both in patients at high risk for vascular events. N Engl J Med 2008: 358:1547-155.
Mancia G, Schumacher H, Redon J, et al. **Blood pressure targets** recommended by guidelines and incidence of cardiovascular and renal events in the Ongoing Telmisartan Alone and in Combination With Ramipril Global Endpoint Trial (**ONTARGET**). Circulation. 2011;124:1727–1736.
51) Mancia G, Laurent S, Agabiti-Rosei E, Ambrosioni E, Burnier M, Caulfield MJ, et al. Reappraisal of European guidelines on hypertension management: a European Society of Hypertension Task Force document. J Hypertens 2009 Nov;27(11):2121-58.
52) Messerli FH, Mancia G, Conti CR, Hewkin AC, Kupfer S, Champion A, et al. Dogma disputed: can aggressively lowering blood pressure in hypertensive patients with coronary artery disease be dangerous? Ann Intern Med 2006 Jun 20;144(12):884-93.
53) Reboldi G, Gentile G, Angeli F, Ambrosio G, Mancia G, Verdecchia P. Effects of intensive blood pressure reduction on myocardial infarction and stroke in diabetes: a meta-analysis in 73,913 patients. J Hypertens. 2011 Jul;29(7):1253-69.
54) Coca SG, Ismail-Beigi F, Haq N, Krumholz HM, Parikh CR. Role of intensive glucose control in development of **renal end points** in type 2 diabetes mellitus: systematic review and meta-analysis. Arch Intern Med. 2012;172 (10):761-769.
55) Emdin CA, Rahimi K, Neal B, et al. Blood pressure lowering in type 2 diabetes: a systematic review and meta-analysis. JAMA. doi:10.1001/jama.2014.18574.
56) Bhatt DL, Steg PG, Mehta SR, et al. Ticagrelor in patients with diabetes and stable coronary artery disease with a history of previous percutaneous coronary intervention (**THEMIS-PCI**): a phase 3, placebo-controlled, randomised trial. Lancet. 2019 Aug 30.
Steg PG, Bhatt DL, Simon T, et al. Ticagrelor in patients with stable coronary disease and diabetes. (**THEMIS**) N Engl J Med. DOI: 10.1056/NEJMoa1908077.

Other Resources
ACC/AHA 2017 Whelton PK, Carey RM, et al. **2017 ACC/AHA**/AAPA/ABC/ACPM/AGS/APhA/ASH/ASPC/NMA/PCNA **Guideline for the Prevention, Detection, Evaluation, and Management of High Blood Pressure** in Adults:
A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. Hypertension. 2017 Nov 13.
Aspirin and/or antioxidants did not prevent CV events in diabetes and peripheral arterial disease. *ACP Journal Club* 2009; 150(1).
Canadian Hypertension Education Program. 2011 CHEP recommendations for the management of hypertension. http://hypertension.ca/chep/wp-content/uploads/2011/05/FullCHEPRecommendations_EN_2011.pdf. Accessed August 28, 2011.
Cheng J, Zhang W, Zhang X, et al. Effect of **Angiotensin-Converting Enzyme Inhibitors and Angiotensin II Receptor Blockers** on All-Cause Mortality, Cardiovascular Deaths, and Cardiovascular Events in Patients **With Diabetes** Mellitus: A Meta-analysis. JAMA Intern Med. 2014 Mar 31.
Current evidence shows no overall benefit of aspirin for primary prevention of cardiovascular disease in diabetes. *ACP Journal Club* 2010; 152(4).
Do statins cause diabetes? *Pharmacist's Letter/Prescriber's Letter* 2009; 25(1):250110.
Hypertension treatment in patients with diabetes. In DynaMed [database online]. EBSCO Publishing.http://search.ebscohost.com/login.aspx?direct=true&site=dynamed&id=113862. Updated June 10, 2011. Accessed August 21, 2011.
Ismail-Beigi F, Craven TE, O`Connor PJ, et al. Combined intensive **blood pressure and glycemic** control does not produce an additive benefit on microvascular outcomes in type 2 diabetic patients. (**ACCORD**) Kidney Int. 2012 Mar;81(6):586-94.
Kerr E, Lucatorto MA, Holleman R, et al. **Monitoring performance for blood pressure** management among patients with **diabetes** mellitus. Arch Intern Med 2012.
Leiter L, Genest J, Harris SB, et al. Dyslipidemia. Canadian Diabetes Association Clinical Practice Guidelines Expert Committee. *Can J Diabetes* 2008; 32(Suppl 1):S107–S114.
Lv J, Perkovic V, Foote CV, et al. **Antihypertensive agents for preventing diabetic kidney disease**. Cochrane Database Syst Rev. 2012 Dec 12;12:CD004136. doi: 10.1002/14651858.CD004136.pub3.
ACEi were found to prevent new onset DKD and death in normoalbuminuric people with diabetes, and could therefore be used in this population. More data are needed to clarify the role of ARB and other drug classes in preventing DKD.
Marcovecchio ML et al. **ACE inhibitors and statins in adolescents with type 1 diabetes. (AdDit)** N Engl J Med2017 Nov 2; 377:1733.
Nicolucci A. Aspirin for primary prevention of cardiovascular events in diabetes. Still an open question. *JAMA* 2008; 300: 2180-1.
Richie DM and McClendon KS. Role of statins for the primary prevention of cardiovascular disease in patients with Type 2 Diabetes Mellitus. *Am J Health-Syst Pharm*. 2007; 64: 1603-10.
Sampson UK, Linton MF, and Fazio S. Are statins diabetogenic? *Current Opinion in Cardiology*. 2011; 26: 342-347.

Snow V, Aronson MD, Hornbake R, et al. Lipid control in the management of Type 2 Diabetes Mellitus: A clinical practice guideline from the American College of Physicians. *Ann Intern Med* 2004; 140: 644-649.
Vamos EP, Harris M, Millett C, et al. Association of **systolic and diastolic blood pressure** and all cause mortality in people with newly diagnosed type 2 diabetes: retrospective cohort study. BMJ. 2012 Aug 30;345:e5567.
Zhao W, Katzmarzyk PT, Horswell R, et al. **Aggressive blood pressure control increases coronary heart disease risk among diabetic** patients. Diabetes Care 2013.

Extras

- ASCEND (A Study of Cardiovascular Events iN Diabetes) and ACCEPT-D (Aspirin and Simvastatin Combination for Cardiovascular Events Prevention Trial in Diabetes). These are large, ongoing studies that will enrol up to 15,000 participants with anticipated completion dates of 2011 and 2013, respectively.

ETDRS 5 yrs, n=3,711	T1DM & T2DM plus diabetic retinopathy; ~50% of pts with hx of CV disease <10% hx of MI or stroke	aspirin 2 x 325mg/day vs placebo	◆ 1°: all-cause mortality, 12.1 vs 14.9, RR 0.91 [99% CI, 0.75 to 1.11, p=0.24] ◆ 2°: cardiovascular mortality, 9.3 vs 11.2, RR 0.87 [99% CI, 0.7 to 1.1, p=0.12] ◆ 2°: fatal or non-fatal MI, 9.1 vs 12.3, RR 0.83 [99% CI, 0.66 to 1.04] ◆ 2°: fatal or non-fatal stroke, 4.5 vs 3.8, RR 1.17 [99% CI, 0.79 to 1.28] -no evidence of harmful effects of aspirin

ETDRS Investigators. Aspirin effects on mortality and morbidity in patients with diabetes mellitus. Early Treatment Diabetic Retinopathy Study Report 14. *JAMA* 1992; 268(10); 1292-1300.

- From Circulation 2010: Intervention patients experienced a decreased risk of nonfatal or fatal MI (RR 0.85, 95% CI 0.73–1.00). In contrast, stroke occurred more frequently with aspirin, although the difference was not statistically significant (RR 1.18, 99% CI 0.88 –1.58). Men appeared to derive more benefit from aspirin than women for prevention of MI (RR for men 0.74, 99% CI 0.54 –1.00; RR for women 0.91, 99% CI 0.65–1.28), but this difference was not statistically significant and could represent a chance finding.
- From CCS 2011: For the predetermined secondary endpoint of fatal or nonfatal MI, the difference was significant at 5 years (RR 0.72, 99% CI 0.55-0.95) but not at 7 years (RR 0.83, 99% CI 0.66-1.04).

💻 Online Extras:

Metabolic Syndrome: condition characterized by a distinctive cluster of abnormalities including: abdominal obesity, HTN, dyslipidemia, insulin resistance & dysglycemia.

In-Hospital Considerations (insulin considered a "high-risk" medication due to administration errors & risk of harm)

- Scheduled basal, bolus & correction (supplemental) insulin is preferred over "sliding-scale" insulin as ↓hyperglycemia DC(A,1A)
- Targets: noncritically ill (e.g. medicine ward) FBG: 5-8, random BG <10; critically ill (e.g. ICU) FBG 6-10 mmol/L DC(D) (targeting ↓ levels controversial eg 4.4-6.1 CV surgery) NICE-SUGAR

CAD Risk in Diabetes

- Diabetes confers ↑ CAD risk such that those with diabetes, ♂ age ≥45 or ♀ age ≥50yr, are considered to be at high CAD risk. For specific estimates, see a risk calculator (e.g. UKPDS).[i]

NNTs in T2DM - (Standardized for 5 yrs)

- ↓ Mortality: Metformin 2550mg/d in obese NNT=7/5yrs UKPDS-34
- ↑ Mortality: intensive blood glucose control (A1C target=6); NNH=66/5yrs ACCORD
- Blood pressure control: ?HOT trial??
- Major CHD Event: Atorvastatin 10mg daily; NNT=26/5yrs CARDS

Considerations for patient during Ramadan.

- Ensure adequate fluid intake for safety, especially critical for some medications (metformin, insulin, ACEI, ARB)
- Metformin: 1000mg at sunset meal; 500mg at pre-dawn meal
- Sulfonylureas: if daily, dose given at sunset meal; if twice a day, give larger amount prior to sunset meal

Additional references:

ADA 2013: American Diabetes Association. Clinical practice recommendations. Diabetes Care 2013; 36:S1-S110. http://care.diabetesjournals.org/content/36/Supplement_1.toc
ADA 2014: American Diabetes Association. Standards of Medical Care in Diabetes. Diabetes Care January 2014 37:S14-S80; doi:10.2337/dc14-S014. http://care.diabetesjournals.org/content/37/Supplement_1.toc
ADA 2015: Standards of medical care in diabetes--2015: summary of revisions. Diabetes Care. 2015 Jan;38 Suppl:S4.
ADA 2016: Standards of Medical Care in Diabetes-2016: Summary of Revisions. Diabetes Care. (American Diabetes Association) 2016 Jan;39 Suppl 1:S4-5.
ADA 2017: American Diabetes Association.. 8. Pharmacologic Approaches to Glycemic Treatment. Diabetes Care. 2017 Jan;40(Suppl 1):S64-S74.
ADA 2017: American Diabetes Association.. 13. Management of Diabetes in Pregnancy. Diabetes Care. 2017 Jan;40(Suppl 1):S114-S119.
ADA 2018: American Diabetes Association. 14. Diabetes Care **in the Hospital**: Standards of Medical Care in Diabetes-2018. Diabetes Care. 2018 Jan;41(Suppl 1):S144-S151.
ADA 2018: American Diabetes Association. 13. Management of Diabetes in **Pregnancy**: Standards of Medical Care in Diabetes-2018. Diabetes Care. 2018 Jan;41(Suppl 1):S137-S143.
ADA 2018: American Diabetes Association. 12. **Children and Adolescents**: Standards of Medical Care in Diabetes-2018. Diabetes Care. 2018 Jan;41(Suppl 1):S126-S136.
ADA 2018: American Diabetes Association. 11. **Older Adults**: Standards of Medical Care in Diabetes-2018. Diabetes Care. 2018 Jan;41(Suppl 1):S119-S125.
ADA 2018: American Diabetes Association. 9. **Cardiovascular Disease and Risk Management**: Standards of Medical Care in Diabetes-2018. Diabetes Care. 2018 Jan;41(Suppl 1):S86-S104.
ADA 2018: American Diabetes Association. 8. **Pharmacologic Approaches** to Glycemic Treatment: Standards of Medical Care in Diabetes-2018. Diabetes Care. 2018 Jan;41(Suppl 1):S73-S85.
ADA 2018: American Diabetes Association. 7. **Obesity Management** for the Treatment of Type 2 Diabetes: Standards of Medical Care in Diabetes-2018. Diabetes Care. 2018 Jan;41(Suppl 1):S65-S72.
ADA 2018: American Diabetes Association. 5. **Prevention or Delay of Type 2 Diabetes**: Standards of Medical Care in Diabetes-2018. Diabetes Care. 2018 Jan;41(Suppl 1):S51-S54.
ADA 2018: American Diabetes Association. 4. **Lifestyle Management**: Standards of Medical Care in Diabetes-2018. Diabetes Care. 2018 Jan;41(Suppl 1):S38-S50.
Bodmer M, Becker C, Meier C et al. Use of Antidiabetic Agents and the Risk of Pancreatic Cancer: A Case-Control Analysis. Am J Gastroenterol. 2012 Jan 31. (metformin reduced risk in women)
Brunström M, Carlberg B. Effect of **antihypertensive treatment** at different blood pressure levels in patients with diabetes mellitus: systematic review and meta-analyses. BMJ. 2016 Feb 24;352:i717.
Canadian Diabetes Association Clinical Practice Guidelines Expert Committee. Pharmacologic management of type 2 diabetes: 2016 interim update. Can J Diabetes 2016 guidelines.diabetes.ca/cdacpg_resources/JCJD_6921.pdf (accessed May 2, 2016).
Canadian Diabetes Association Clinical Practice Guidelines Expert Committee. Table 1. Antihyperglycemic agents for use in type 2 diabetes. April 2016. guidelines.diabetes.ca/cdacpg_resources/Ch13_Table1_Antihyperglycemic_agents_type_2_2016.pdf(accessed May 2, 2016).
Canadian Diabetes Association Clinical Practice Guidelines Expert Committee. Addendum to policies, guidelines and consensus statements: pharmacologic management of type 2 diabetes: 2015 interim update. Figure 2. Antihyperglycemic medications and renal function. Can J Diabetes 2015;39:440.guidelines.diabetes.ca/cdacpg_resources/Ch13_Fig2_Antihyperglycemic_medications_and_renal_function_2016.pdf(May 2, 2016).
Chamberlain JJ, Rhinehart AS, Shaefer CF Jr, et al. **Diagnosis and Management of Diabetes**: Synopsis of the **2016 American Diabetes Association (ADA)** Standards of Medical Care in Diabetes. Ann Intern Med. 2016 Mar 1.
Cheng J, Zhang W, Zhang X, et al. Effect of **Angiotensin-Converting Enzyme Inhibitors and Angiotensin II Receptor Blockers** on All-Cause Mortality, Cardiovascular Deaths, and Cardiovascular Events in Patients **With Diabetes** Mellitus: A Meta-analysis. JAMA Intern Med. 2014 Mar 31.
Chow E, Bernjak A, Williams S, et al. Risk of **cardiac arrhythmias during hypoglycemia** in patients with type 2 diabetes and cardiovascular risk. Diabetes. 2014 May;63(5):1738-47.
Cohen D. Has **pancreatic damage from glucagon suppressing drugs** been underplayed? BMJ 2013;346:f3680.
Copeland KC, Silverstein J, Moore KR, et al. **Management of Newly Diagnosed Type 2 Diabetes Mellitus (T2DM) in Children and Adolescents. (AAP, ADA, AAFP, AND, Ped Endo Soc)** Pediatrics. 2013 Jan 28.
Diabetes Canada Clinical Practice Guidelines Expert Committee, Lipscombe L, Booth G, Butalia S, et al. **Pharmacologic Glycemic Management of Type 2 Diabetes in Adults. Can J Diabetes. 2018** Apr;42 Suppl 1:S88-S103.
Diabetes Control and Complications Trial (**DCCT**)/Epidemiology of Diabetes Interventions and Complications (**EDIC**) Study Research Group. Intensive Diabetes Treatment and Cardiovascular Outcomes in Type 1 Diabetes: The DCCT/EDIC Study **30-Year Follow-up**. Diabetes Care. 2016 Feb 9.
Egan AG, Blind E, Dunder K, et al. **Pancreatic safety of incretin-based drugs**--FDA and EMA assessment. N Engl J Med. 2014 Feb 27;370(9):794-7.
Estruch R, Ros E, Salas-Salvadó J, et al; the **PREDIMED** Study Investigators. Primary Prevention of Cardiovascular Disease with a **Mediterranean Diet**. N Engl J Med. 2013 Feb 25.

Fried LF, Emanuele N, Zhang JH, et al. **Combined angiotensin inhibition** for the treatment of diabetic nephropathy. (**VA Nephron-D**) N Engl J Med 2013. DOI: 10.1056/NEJMoa1303154.
Garber AJ, Abrahamson MJ, Barzilay JI, et al. **AACE Comprehensive Diabetes Management Algorithm 2013**. Endocr Pract. 2013 Mar-Apr;19(2):327-36.
Geiss LS, Wang J, Cheng YJ, et al. **Prevalence and incidence trends for diagnosed diabetes among adults aged 20 to 79 years, United States, 1980-2012.** JAMA. 2014 Sep 24;312(12):1218 26.
Gillett M, Royle P, Snaith A, et al. **Non-pharmacological interventions** to **reduce the risk of diabetes** in people with impaired glucose regulation: a systematic review and economic evaluation. Health Technol Assess. 2012 Aug;16(33):1-236, iii-iv.
Gregg EW, Li Y, Wang J, et al. Changes in **diabetes-related complications in the United States**, 1990-2010. N Engl J Med. 2014 Apr 17;370(16):1514-23.
Green JB, Bethel MA, Armstrong PW, et al; **TECOS** Study Group. Effect of **Sitagliptin** on Cardiovascular Outcomes in Type 2 Diabetes. N Engl J Med. 2015 Jun 8.
Grundy SM, Stone NJ, Bailey AL, et al. **2018 AHA/ACC**/AACVPR/AAPA/ABC/ACPM/ADA/AGS/APhA/ASPC/NLA/PCNA Guideline on the **Management of Blood Cholesterol**: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. J Am Coll Cardiol. 2018 Nov 8.
Grundy SM, Stone NJ, Bailey AL, et al. **2018 AHA/ACC**/AACVPR/AAPA/ABC/ACPM/ADA/AGS/APhA/ASPC/NLA/PCNA Guideline on the **Management of Blood Cholesterol: Executive Summary**: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. J Am Coll Cardiol. 2018 Nov 3.
Hayward RA, Reaven PD, Wiitala WL, et al; **VADT** Investigators. **Follow-up of glycemic control and cardiovascular outcomes** in type 2 diabetes. N Engl J Med. 2015 Jun 4;372(23):2197-206.
Hemmingsen B, Lund SS, Gluud C, et al. **Targeting intensive glycaemic control versus targeting conventional glycaemic control** for type 2 diabetes mellitus. Cochrane Database Syst Rev. 2013 Nov 11;11:CD008143. Although we have been able to expand the number of participants by 16% in this update, we still find paucity of data on outcomes and the bias risk of the trials was mostly considered high. Targeting intensive glycaemic control compared with conventional glycaemic control did not show significant differences for all-cause mortality and cardiovascular mortality. Targeting intensive glycaemic control seemed to reduce the risk of microvascular complications, if we disregard the risks of bias, but increases the risk of hypoglycaemia and serious adverse events.
Inzucchi SE, Bergenstal RM, Buse JB, et al. **Management of Hyperglycemia in Type 2 Diabetes**: A Patient-Centered Approach: Position Statement of the American Diabetes Association (**ADA**) and the European Association for the Study of Diabetes(**EASD**). Diabetes Care. 2012 Apr 19.
Inzucchi SE, Bergenstal RM, Buse JB, et al. **Management of hyperglycaemia in type 2 diabetes, 2015**: a patient-centred approach. Update to a Position Statement of the American Diabetes Association (**ADA**) and the European Association for the Study of Diabetes(**EASD**).. Diabetologia. 2015 Mar;58(3):429-42.
Ismail-Beigi F, Craven TE, O`Connor PJ, et al. Combined intensive **blood pressure and glycemic** control does not produce an additive benefit on microvascular outcomes in type 2 diabetic patients. (**ACCORD**) Kidney Int. 2012 Mar;81(6):586-94.
James PA, Oparil S, Carter BL, et al. **2014** evidence-based guideline for the management of high blood pressure in adults: report from the panel members appointed to the Eighth Joint National Committee (**JNC 8**). JAMA. doi:10.1001/jama.2013.284427.
Kirkman MS, Briscoe VJ, Clark N, et al. **Diabetes in older adults**. Diabetes Care. 2012 Dec;35(12):2650-64.
Leung AA, Nerenberg K, Daskalopoulou SS, et al; CHEP Guidelines Task Force. Hypertension Canada's **2016 CHEP guidelines** for blood pressure measurement, diagnosis, assessment of risk, prevention and treatment of hypertension. Can J Cardiol 2016 (accepted manuscript) doi: 10.1016/j.cjca.2016.02.066 www.onlinecjc.ca/article/S0828-282X(16)00192-6/pdf (accessed April 11, 2016).
Leung AA, Daskalopoulou SS, Dasgupta K, et al. **Hypertension Canada's 2017 Guidelines for Diagnosis, Risk Assessment, Prevention, and Treatment of Hypertension in Adults**. (CHEP) Can J Cardiol. 2017 May;33(5):557-576
Lv J, Perkovic V, Foote CV, et al. **Antihypertensive agents for preventing diabetic kidney disease**. Cochrane Database Syst Rev. 2012 Dec 12;12:CD004136. doi: 10.1002/14651858.CD004136.pub3.
ACEi were found to prevent new onset DKD and death in normoalbuminuric people with diabetes, and could therefore be used in this population. More data are needed to clarify the role of ARB and other drug classes in preventing DKD.
Nichols GA, Joshua-Gotlib S, Parasuraman S. Independent contribution of **A1c, systolic blood pressure, and LDL cholesterol** control to risk of cardiovascular disease hospitalizations in type 2 diabetes: An observational cohort study. J Gen Intern Med 2013.
Pillay J, Armstrong MJ, Butalia S, et al. **Behavioral Programs for Type 1 Diabetes** Mellitus: A Systematic Review and Meta-analysis. Ann Intern Med. 2015 Sep 29.
Pillay J, Armstrong MJ, Butalia S, et al. **Behavioral Programs for Type 2 Diabetes** Mellitus: A Systematic Review and NetworkMeta-analysis for Effect Moderation. Ann Intern Med. 2015 Sep 29.
Qaseem A, Humphrey LL, Sweet DE, et al. for the Clinical Guidelines Committee of the American College of Physicians (**ACP**). Oral Pharmacologic Treatment of Type 2 Diabetes Mellitus: A Clinical Practice Guideline From the American College of Physicians. Ann Intern Med. 2012 Feb 7;156(3):218-231.
Romeo GR, Abrahamson MJ. The **2015 Standards for Diabetes Care**: Maintaining a Patient-Centered Approach. Ann Intern Med. 2015 Mar 24.
Roumie CL, Greevy RA, Grijalva CG, et al. Association between **intensification of metformin treatment with insulin vs sulfonylureas** and cardiovascular events and all-cause mortality among patients with diabetes. JAMA. doi:10.1001/jama.2014.4312.
Scirica BM, Bhatt DL, Braunwald E, et al. **Saxagliptin** and cardiovascular outcomes in patients with type 2 diabetes mellitus. (**Savor-Timi 53**) N Engl J Med 2013; DOI:10.1056/NEJMoa1307684. Available here.
Selvin E, Parrinello CM, Sacks DB, Coresh J. Trends in **prevalence and control of diabetes** in the United States, 1988–1994 and 1999–2010. Ann Intern Med. 2014;160:517-25.
Springer SC, Silverstein J, Copeland K, et al. Management of **Type 2 Diabetes Mellitus in Children and Adolescents**. Pediatrics. 2013 Jan 28.
Stevens PE, Levin A; Kidney Disease: Improving Global Outcomes Chronic Kidney Disease Guideline Development Work Group Members*. (KDIGO) Evaluation and management of chronic kidney disease: synopsis of the kidney disease: improving global outcomes 2012 clinical practice guideline. Ann Intern Med. 2013 Jun 4;158(11):825-30.
White WB, Jalil F, Cushman WC, et al. Average Clinician-Measured **Blood Pressures** and Cardiovascular Outcomes in Patients With Type 2 Diabetes Mellitus and Ischemic Heart Disease in the **EXAMINE** Trial. J Am Heart Assoc. 2018 Oct 16;7(20):e009114.
Wilson PWF, Polonsky TS, Miedema MD, et al. **Systematic Review for the 2018 AHA/ACC**/AACVPR/AAPA/ABC/ACPM/ADA/AGS/APhA/ASPC/NLA/PCNA Guideline on the **Management of Blood Cholesterol**: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. J Am Coll Cardiol. 2018 Nov 3.
Wu HY, Huang JW, Lin HJ, et al. Comparative effectiveness of **renin-angiotensin system blockers and other antihypertensive drugs in patients with diabetes**: systematic review and bayesian network meta-analysis. BMJ. 2013 Oct 24;347:f6008. (superiority of using ACE inhibitors)
Zhao W, Katzmarzyk PT, Horswell R, et al. **Aggressive blood pressure control increases coronary heart disease** risk among diabetic patients. Diabetes Care 2013.

[i] UKPDS Risk Engine (University of Oxford). Accessed online Aug 10, 2011at http://www.dtu.ox.ac.uk/riskengine/ .

References: Weight Loss Agents – COMPARISON CHART – www.RxFiles.ca

[1] Therapeutic Choices 4rd Edition, 2003 , (For Herbal warnings see Health Canada. http://www.hc-sc.gc.ca/dhp-mps/advisories-avis/index_e.html)

[2] Micromedex 2016

[3] Li Z, Maglione M, Tu W, Mojica W,et al. Meta-analysis: pharmacologic treatment of **obesity**. Ann Intern Med. 2005 Apr 5;142(7):532-46. CONCLUSIONS: Sibutramine, orlistat, phentermine, probably diethylpropion, bupropion, probably fluoxetine, and topiramate promote modest weight loss when given along with recommendations for diet. Sibutramine and orlistat are the 2 most-studied drugs. (InfoPOEMs: On the basis of flimsy evidence of benefit, The American College of Physicians recommends drug therapy for the treatment of obesity. They also recommend gastric bypass surgery, performed by an experienced surgeon, for patients with marked obesity and other risk factors for premature death. (LOE = 5))

[4] Jain A. Treating **obesity** in individuals and populations. BMJ. 2005 Dec 10;331(7529):1387-1390.

[5] Padwal R, Li SK, Lau DC. Long-term pharmacotherapy for obesity and overweight. **Cochrane** Database Syst Rev. 2004;(3):CD004094. REVIEWERS' CONCLUSIONS: Studies evaluating the long-term efficacy of anti-obesity agents are limited to orlistat and sibutramine. Both drugs appear modestly effective in promoting weight loss; however, interpretation is limited by high attrition rates. Longer and more methodologically rigorous studies of anti- obesity drugs that are powered to examine endpoints such as mortality and cardiovascular morbidity are required to fully evaluate any potential benefit of such agents.

[6] Stats Canada Obesity, 2014. Retrieved from http://www.statcan.gc.ca/pub/82-625-x/2015001/article/14185-eng.htm on November 11, 2016.

[7] de Gonzalez Amy Berrington, Hartge Patricia, Cerhan James R., et al. Body-Mass Index and Mortality among 1.46 Million White Adults. N Engl J Med 2010; 363:2211-2219.

[8] Jakicic JM, Marcus BH, Gallagher KI, Napolitano M, Lang W. Effect of exercise duration and intensity on weight loss in overweight, sedentary women: a randomized trial. JAMA. 2003 Sep 10;290(10):1323-30.

[9] Knowler WC, Barrett-Connor E, Fowler SE et al. Diabetes Prevention Program Research Group. Reduction in the incidence of type 2 diabetes with lifestyle intervention or metformin. N Engl J Med. 2002 Feb 7;346(6):393-403.

[10] Schnohr P, O'Keefe JH, Marott JL, Lange P, Jensen GB. Dose of jogging and long-term mortality: the Copenhagen City Heart Study. J Am Coll Cardiol. 2015 Feb 10;65(5):411-9.

[11] Howard BV, Manson JE, Stefanick ML, Beresford SA, et al. **Low-fat dietary pattern** and weight change over 7 years: the Women's Health Initiative Dietary Modification Trial. JAMA. 2006 Jan 4;295(1):39-49. (InfoPOEMs: Following the long-term recommendations to reduce dietary fat and increase consumption of fruits, vegetables, and whole grains does not cause weight gain among postmenopausal women. (LOE = 2b))

[12] Nordmann AJ, et al. Effects of **low-carbohydrate vs low-fat diets** on weight loss & cardiovascular risk factors: a meta-analysis of randomized controlled trials. Arch Intern Med. 2006 Feb 13;166(3):285-93. (InfoPOEMs: People interested in weight loss can choose either a low-fat, reduced calorie diet or a low-carbohydrate, non-calorie-restricted diet to lose a small but sustained amount of weight. The effect on cardiovascular outcomes of either diet are not known, though each has different effects on lipid levels, which may or may not translate into an actual effect on patient-oriented outcomes that matter. (LOE = 1a))

[13] Strychar I. **Diet** in the management of weight loss. CMAJ. 2006 Jan 3;174(1):56-63.

Foster GD, Wyatt HR, Hill JO, et al. A randomized trial of a low-carbohydrate diet for obesity. N Engl J Med. 2003 May 22;348(21):2082-90.

Stern L, Iqbal N, Seshadri P, et al. The effects of low-carbohydrate versus conventional weight loss diets in severely obese adults: one-year follow-up of a randomized trial. Ann Intern Med. 2004 May 18;140(10):778-85.

Dansinger ML, Gleason JA, et al. Comparison of the Atkins, Ornish, Weight Watchers, and Zone diets for weight loss and heart disease risk reduction: a randomized trial. JAMA. 2005 Jan 5;293(1):43-53.

Gardner CD, Kiazand A, Alhassan S, et al. Comparison of the Atkins, Zone, Ornish, and LEARN diets for change in weight and related risk factors among overweight premenopausal women: the A TO Z Weight Loss Study: a randomized trial. JAMA. 2007 Mar 7;297(9):969-77. Erratum in: JAMA. 2007 Jul 11;298(2):178.

Look AHEAD Research Group, Pi-Sunyer X, Blackburn G, Brancati FL, Bray GA, Et al. Reduction in weight and cardiovascular disease risk factors in individuals with type 2 diabetes: one-year results of the look AHEAD trial. Diabetes Care. 2007 Jun;30(6):1374-83. Epub 2007 Mar 15.

Dietary Guidelines for Americans (DGA) 2010. Full Guideline: http://www.health.gov/dietaryguidelines/dga2010/DietaryGuidelines2010.pdf, Summary: http://www.cnpp.usda.gov/Publications/DietaryGuidelines/2010/PolicyDoc/ExecSumm.pdf

[14] **SOS** Sjostrom L, Narbro K, Sjostrom CD, et al.; Swedish Obese Subjects Study (**SOS**). Effects of **bariatric surgery** on mortality in Swedish obese subjects. N Engl J Med. 2007 Aug 23;357(8):741-52. Bariatric surgery for severe obesity is associated with long-term weight loss and decreased overall mortality.

Sjostrom L, et al.; Swedish Obese Subjects (**SOS**) Study Scientific Group. Lifestyle, diabetes, and cardiovascular risk factors 10 years after bariatric surgery. N Engl J Med. 2004 Dec 23;351(26):2683-93. After two years, the weight had increased by 0.1 percent in the control group and had decreased by 23.4 percent in the surgery group (P<0.001). After 10 years, the weight had increased by 1.6 percent and decreased by 16.1 percent, respectively (P<0.001). Energy intake was lower and the proportion of physically active subjects higher in the surgery group than in the control group throughout the observation period. Two- and 10-year rates of recovery from diabetes, hypertriglyceridemia, low levels of high-density lipoprotein cholesterol, hypertension, and hyperuricemia were more favorable in the surgery group than in the control group, whereas recovery from hypercholesterolemia did not differ between the groups. The surgery group had lower 2- and 10-year incidence rates of diabetes, hypertriglyceridemia, and hyperuricemia than the control group; differences between the groups in the incidence of hypercholesterolemia and hypertension were undetectable.

Sjöström L et al. Effects of bariatric surgery on **cancer incidence** in obese patients in Sweden (Swedish Obese Subjects Study-**SOS**): A prospective, controlled intervention trial. Lancet Oncol 2009 Jun 24; [e-pub ahead of print].

Sjostrom L, Narbro K, Sjostrom CD, et al. Eff ects of bariatric surgery on mortality in Swedish obese subjects (Swedish Obese Subjects Study-**SOS**). N Engl J Med 2007; 357: 741–52.

Sjostrom L, Peltonen M, Jacobson P, et al. Bariatric surgery and long-term cardiovascular events. (**SOS**) JAMA. 2012;307(1):56-65.

Adams TD, Gress RE, Smith SC, et al. Long-term mortality after **gastric bypass** surgery. N Engl J Med. 2007 Aug 23;357(8):753-61. Long-term total mortality after gastric bypass surgery was significantly reduced, particularly deaths from diabetes, heart disease, and cancer. However, the rate of death from causes other than disease was higher in the surgery group than in the control group.)

Dixon JB, O'Brien PE, Playfair J, et al. Adjustable **gastric banding** and conventional therapy for type 2 diabetes: a randomized controlled trial. JAMA. 2008 Jan 23;299(3):316-23.

Karmali, Shahzeer, Stoklossa, Carlene Johnson, Sharma, Arya, et al. **Bariatric surgery**: A primer. Can Fam Physician 2010 56: 873-879.

Mechanick JI, Kushner RF, Sugerman HJ, Gonzalez-Campoy JM, Collazo-Clavell ML, Guven S, Spitz AF, Apovian CM, Livingston EH, Brolin R, Sarwer DB, Anderson WA, Dixon J. American Association of Clinical Endocrinologists, The Obesity Society, and American Society for Metabolic & Bariatric Surgery Medical guidelines for clinical practice for the **perioperative nutritional, metabolic, and nonsurgical support** [trunc]. Endocr Pract 2008 Jul-Aug;14 Suppl 1:1-83.

Heber David, Greenway Frank L ., Kaplan L ee M., et al. **Endocrine and Nutritional Management of the Post-Bariatric Surgery Patient**: An Endocrine Society Clinical Practice Guideline. Journal of Clinical Endocrinology & Metabolism, November 2010, 95 (11):4823–4843. http://www.endo-society.org/guidelines/final/upload/FINAL-Standalone-Post-Bariatric-Surgery-Guideline-Color.pdf

IDF: International Diabetes Federation. **Bariatric surgical** and procedural interventions in the treatment of obese patients with type 2 diabetes 2011 http://www.idf.org/webdata/docs/IDF-Position-Statement-Bariatric-Surgery.pdf

Søvik TT, Aasheim ET, Taha O, et al. Weight loss, cardiovascular risk factors, and quality of life after **gastric bypass and duodenal switch**: a randomized trial. Ann Intern Med. 2011 Sep 6;155(5):281-91.

Michalsky M, Kramer RE, Fullmer MA, et al. Developing criteria for **pediatric/adolescent bariatric surgery** programs. Pediatrics 2011;128:Suppl 2:S65-S70

Heneghan HM, Meron-Eldar S, Brethauer SA, et al.Effect of Bariatric Surgery on Cardiovascular Risk Profile. Am J Cardiol. 2011 Aug 29.

Romy S, Donadini A, Giusti V, et al. Gastric Bypass vs Gastric Banding for Morbid Obesity: A Case-Matched Study of 442 Patients. Arch Surg. 2012 Jan 16.

Schroeder R, Garrison JM Jr, Johnson MS. Treatment of adult obesity with bariatric surgery. Am Fam Physician. 2011 Oct 1;84(7):805-14.

Himpens J, Cadière GB, Bazi M, et al. Long-term outcomes of laparoscopic adjustable gastric banding. Arch Surg. 2011 Jul;146(7):802-7.

Mingrone G, Panunzi S, De Gaetano A, et al. **Bariatric surgery versus conventional medical therapy** for type 2 diabetes. N Engl J Med 2012. DOI: 10.1056/NEJMoa1200111.

Schauer PR, Kashyap SR, Wolski K, et al. **Bariatric surgery versus intensive medical therapy** in obese patients with diabetes. N Engl J Med 2012. DOI: 10.1056/NEJMoa1200225.

Leonetti F, et al. Obesity, type 2 diabetes mellitus, and other comorbidities: a prospective cohort study of **laparoscopic sleeve gastrectomy vs medical treatment** [online ahead of print April 16, 2012]. Arch Surg. 2012.

Carlsson LMS, Peltonen M, Ahlin S, et al. **Bariatric surgery and prevention of type 2 diabetes** in Swedish Obese Subjects. (**SOS**) N Engl J Med 2012; 367:695-704.

Olbers T, Gronowitz E, Werling M, et al. Two-year outcome of **laparoscopic Roux-en-Y gastric bypass in adolescents** with severe obesity: results from a Swedish Nationwide Study (AMOS). Int J Obes (Lond). 2012 Sep 25.

Arterburn D, Powers JD, Toh S, et al. Comparative effectiveness of **laparoscopic adjustable gastric banding (AGB) vs laparoscopic gastric bypass (RYGB)** [online October 29, 2014]. JAMA Surg. doi:10.1001/jamasurg.2014.1674.

Dupree CE, Blair K, Steele SR, et al. **Laparoscopic Sleeve Gastrectomy** in Patients With Preexisting Gastroesophageal Reflux Disease : A National Analysis. JAMA Surg. 2014 Feb 5.

Risstad H, Søvik TT, EngströmM, et al. **Five-year** outcomes after **laparoscopic gastric bypass and laparoscopic duodenal switch** in patients with body mass index of 50 to 60: a randomized clinical trial [online February 4, 2015]. JAMA Surg. doi:10.1001/jamasurg.2014.3579.

Parent B, Martopullo I, Weiss NS, et al. **Bariatric surgery in women of childbearing age, timing between an operation and birth**, and associated perinatal complications [online October 19, 2016].

Inge TH, Jenkins TM, Xanthakos SA, et al. Long-term outcomes of **bariatric surgery** in **adolescents** with severe obesity(**FABS-5+):** a prospective follow-up analysis. Lancet Diabetes Endocrinol. 2017 Jan 5.

Olbers T, Beamish AJ, Gronowitz E, et al. Laparoscopic **Roux-en-Y gastric bypass** in **adolescents** with severe obesity (**AMOS**): a prospective, 5-year, Swedish nationwide study. Lancet Diabetes Endocrinol. 2017 Jan 5.

[15] Coniff RF, Shapiro JA, Seaton TB. Long-term efficacy and safety of acarbose in the treatment of obese subjects with non-insulin-dependent diabetes mellitus. Arch Intern Med. 1994 Nov 14;154(21):2442-8.

[16] Chiasson JL, Josse RG, Gomis R, et al.; **STOP-NIDDM** Trial Research Group. Acarbose treatment and the risk of cardiovascular disease and hypertension in patients with impaired glucose tolerance: the STOP-NIDDM trial. JAMA. 2003 Jul 23;290(4):486-94.

[17] Yki-Jarvinen H, Ryysy L, Nikkila K, et al. Comparison of bedtime insulin regimens in patients with type 2 diabetes mellitus: a randomized controlled trial. (**FINFAT** study) Ann Intern Med 1999;130:389-96.

[18] Jorenby DE, et al.; Varenicline Phase 3 Study Group. Efficacy of varenicline, an alpha4beta2 nicotinic acetylcholine receptor partial agonist, vs placebo or sustained-release bupropion for smoking cessation: a randomized controlled trial. JAMA. 2006 Jul 5;296(1):56-63.

[19] Torgerson JS, Hauptman J, Boldrin MN, Sjostrom L. XENical in the prevention of diabetes in obese subjects (**XENDOS**) study: a randomized study of orlistat as an adjunct to lifestyle changes for the prevention of type 2 diabetes in obese patients. Diabetes Care. 2004 Jan;27(1):155-61. Erratum in: Diabetes Care. 2004 Mar;27(3):856.

[20] Maahs D, de Serna DG, Kolotkin RL, Ralston S, Sandate J, Qualls C, Schade DS. Randomized, double-blind, placebo-controlled trial of orlistat for weight loss in adolescents.Endocr Pract. 2006 Jan-Feb;12(1):18-28.

[21] Khera R, Murad MH, Chandar AK, Dulai PS, Wang Z, Prokop LJ, Loomba R, Camilleri M, Singh S. Association of Pharmacological Treatments for Obesity With Weight Loss and Adverse Events: A Systematic Review and Meta-analysis. JAMA. 2016 Jun 14;315(22):2424-34. doi: 10.1001/jama.2016.7602. Review.

[22]Norris SL, Zhang X, Avenell A, et al. Efficacy of pharmacotherapy for weight loss in adults with type 2 diabetes mellitus: a meta-analysis. Arch Intern Med. 2004 Jul 12;164(13):1395-404.

[23] Chanoine JP, Hampl S, Jensen C, et al. Effect of **orlistat** on weight and body composition in obese adolescents. A randomized controlled trial. JAMA 2005;293:2873-83. n=539 54week (InfoPOEMs: Orlistat (Xenical), in combination with diet, exercise, & behavioral modification, improves weight management in obese adolescents. No major safety issues were identified after 1 year, but further follow-up for sustained weight management and safety is important. (LOE = 1b))

(Dunican KC, Desilets AR, Montalbano JK. Pharmacotherapeutic options for overweight adolescents. Ann Pharmacother. 2007 Sep;41(9):1445-55. Epub 2007 Jul 24.)

Rogovik, Alexander L., Goldman, Ran D. Pharmacologic **treatment of pediatric obesity**. Can Fam Physician 2011 57: 195-197.

[24] Pharmacist's Letter May 2006: Byetta (**Exenatide**) for **Weight Loss**.

[25] Saenz A, Fernandez-Esteban I, Mataix A, et al. Metformin monotherapy for type 2 diabetes mellitus. **Cochrane** Database Syst Rev. 2005 Jul 20;(3):CD002966. CONCLUSIONS: Metformin may be the first therapeutic option in the diabetes mellitus type 2 with overweight or obesity, as it may prevent some vascular complications, and mortality. Metformin produces beneficial changes in glycaemia control, and moderated in weight, lipids, insulinaemia and diastolic blood pressure. Sulphonylureas, alpha-glucosidase inhibitors, thiazolidinediones, meglitinides, insulin, and diet fail to show more benefit for glycaemia control, body weight, or lipids, than metformin.

Park MH, Kinra S, Ward KJ, et al. Metformin for obesity in children and adolescents: a systematic review. Diabetes Care. 2009 Sep;32(9):1743-5. Epub 2009 Jun 5.

Kendall D, Vail A, Amin R, et al. **Metformin** in Obese Children and Adolescents: The **MOCA** Trial. J Clin Endocrinol Metab. 2012 Nov 21.

[26]Norris SL, Zhang X, Avenell A, Gregg E, Schmid CH, Lau J. Pharmacotherapy for weight loss in adults with type 2 diabetes mellitus. Cochrane Database Syst Rev. 2005 Jan 25;(1):CD004096.

[27] Toplak H, Hamann A, Moore R, Masson E, et al. Efficacy and safety of topiramate in combination with metformin in the treatment of obese subjects with type 2 diabetes: a randomized, double-blind,placebo-controlled study. Int J Obes (Lond). 2006 May 16;epub ahead of print.

[28] Pittler MH, Ernst E. **Complementary therapies** for reducing body weight: a systematic review. Int J Obes (Lond). 2005 Sep;29(9):1030-8.

[29] Rocha, Tiago, Joana S. Amaral, and Maria Beatriz PP Oliveira. "Adulteration of Dietary Supplements by the Illegal Addition of Synthetic Drugs: A Review." *Comprehensive Reviews in Food Science and Food Safety* 15.1 (2016): 43-62.

[30] **PREDIMED** Estruch R, Ros E, Salas-Salvadó J, Covas MI, Corella D, Arós F, Gómez-Gracia E, Ruiz-Gutiérrez V, Fiol M, Lapetra J, Lamuela-Raventos RM, Serra-Majem L, Pintó X, Basora J, Muñoz MA, Sorlí JV, Martínez JA, Martínez-González MA; PREDIMED Study Investigators. Primary prevention of cardiovascular disease with a Mediterranean diet. N Engl J Med. 2013 Apr 4;368(14):1279-90. Retracted & then republished in June 2018.

[31] Wadden TA, Berkowitz RI, Womble LG, et al. Randomized trial: **lifestyle modification & pharmacotherapy** for obesity. N Engl J Med 2005;353:2111-20. Combo of sibutramine & group lifestyle modifications resulted in more weight loss (**12.1 kg** at 1yr) then either alone.

[32] Berkowitz R., Fujioka K., Daniels SR., et al. Effects of Sibutramine treatment in obese adolescents: a randomized trial. Ann Intern Med 2006; 145(2): 81-90. n=498 1yr

[33] Berkowitz RI, Wadden TA, Tershakovec AM, et al. Behavior therapy and sibutramine for the treatment of adolescent obesity: a randomized controlled trial. JAMA. 2003 Apr 9;289(14):1805-12. n=82 RCT 6month, Open label 6month

[34] Wadden, T., Berkowitz, L., Womble, D. et al. Effects of Sibutramine Plus Orlistat in Obese Women Following 1 Year of Treatment by Sibutramine Alone: A Placebo-Controlled Trial. Obesity Research 2000; 8(6): 431-7.

[35] Sari, R., Balci, MK., Cakir, M., et al. Comparison of Efficacy of Sibutramine or Orlistat Versus Their Combination in Obese Women. Endocrine Research 2004; 30(2): 159-167.

[36] Kaya, A., Aydin, N., Topsever, P., et al. Efficacy of Sibutramine, orlistat and combination therapy on short-term weight management in obese patients. Biomedicine & Pharmacotherapy 2004; (58): 582-587.

[38] Trichopoulou A, Costacou T, Bamia C, Trichopoulos D. Adherence to a Mediterranean diet and survival in a Greek population. New England Journal of Medicine. 2003 Jun 26;348(26):2599-608.

[39] Shai I, Schwarzfuchs D, Henkin Y, Shahar DR, Witkow S, Greenberg I, Golan R, Fraser D, Bolotin A, Vardi H, Tangi-Rozental O. Weight loss with a low-carbohydrate, Mediterranean, or low-fat diet. New England Journal of Medicine. 2008 Jul 17;359(3):229-41.

[40] Review: What Does the PREDIMED Trial Retraction & Reboot Mean for the Mediterranean Diet? Available from http://blogs.plos.org/absolutely-maybe/2018/06/14/what-does-the-predimed-trial-retraction-re-boot-mean-for-the-mediterranean-diet/

[41] Mancini JG, Filion KB, Atallah R, Eisenberg MJ. Systematic Review of the Mediterranean Diet for Long-Term Weight Loss. Am J Med. 2016 Apr;129(4):407-415.e4.

Additional refs:

AAP: American Academy of Pediatrics: Policy Statement: Children, Adolescents, Obesity, and the **Media**. Council on Communications and Media. Pediatrics 2011; 128:1 201-208; doi:10.1542/peds.2011-1066

Aaron DG, Siegel MB. **Sponsorship** of National Health Organizations by **Two Major Soda Companies**. Am J Prev Med.2016 Oct 10.

Abbassi A, Juszczyk D, van Jaarsveld CHM, et al. Body Mass Index and **Incident Type 1 and Type 2 Diabetes** in Children and Young Adults: A Retrospective Cohort Study. J Endocrine Society. May 2017;1(5):524-537.

Abed HS, Wittert GA, et al. Effect of weight reduction and cardiometabolic risk factor management on symptom burden and severity in patients with **atrial fibrillation**: a randomized clinical trial. JAMA. 2013 Nov 20;310(19):2050-60.

ACOG: Bariatric surgery and **pregnancy**. June,2009 http://mail.ny.acog.org/website/SMIPodcast/BariatricSurgery.pdf

ACOG: Practice Bulletin No 156: **Obesity in Pregnancy**. Obstet Gynecol. 2015 Dec;126(6):e112-26.

ACOG: Committee on Adolescent Health Care. Committee Opinion No. 714: **Obesity in Adolescents**. Obstet Gynecol. 2017 Sep;130(3):e127-e140.

Acosta AA et al. Prevalence of **Persistent Prehypertension** in Adolescents. J Pediatr. 2011 Dec 6.

Acosta A, Streett S, Kroh MD, et al. White Paper **AGA: POWER - Practice Guide on Obesity and Weight Management, Education and Resources**. Clin Gastroenterol Hepatol. 2017 Feb 24.

Adab P, Pallan MJ, Lancashire ER. Effectiveness of a **childhood obesity prevention programme delivered through schools**, targeting 6 and 7 year olds: cluster randomised controlled trial (**WAVES** study). BMJ 2018;360:k211.

Adab P, Pallan M, Whincup PH. **Is BMI the best measure of obesity**? BMJ. 2018 Mar 29;360:k1274.

Adabag S, Huxley RR, Lopez FL, et al. Obesity-related risk of **sudden cardiac death**: the Atherosclerosis Risk in Communities study. Heart 2014;10.1136/heartjnl-2014-306238.

Adamo KB, Colley RC, Hadjiyannakis S, et al. **Physical Activity and Sedentary Behavior** in Obese Youth. J Pediatr. 2015 Feb 12.

Adam S, Ammori B, Soran H, et al. **Pregnancy after bariatric surgery**: screening for gestational diabetes. BMJ. 2017 Feb 3;356:j533.

Adams TD, Gress RE, Smith SC, Halverson RC, et al. Long-term mortality after **gastric bypass surgery**. N Engl J Med. 2007 Aug 23;357(8):753-61.

Adams TD, Davidson LE, Litwin SE, et al. Health benefits of gastric **bypass surgery after 6 years**. JAMA 2012; 308:1122-1131.

Adams TD, Davidson LE, Litwin SE, et al. **Weight and metabolic outcomes 12 years after gastric bypass**. N Engl J Med2017;358:1143-55

Afshin A, Babalola D, et al. **Information Technology and Lifestyle**: A Systematic Evaluation of Internet and Mobile Interventions for Improving Diet, Physical Activity, Obesity, Tobacco, and Alcohol Use. J Am Heart Assoc. 2016 Aug 31;5(9).

Afzal S, Tybjærg-Hansen A, Jensen GB, et al. Change in **Body Mass Index Associated With Lowest Mortality** in Denmark, 1976-2013. JAMA. 2016 May 10;315(18):1989-96.

Agatston A. Why **america is fatter** and sicker than ever. Circulation. 2012 Jul 3;126(1):e3-5.

Aguirre Castaneda RL, Kumar S, Voigt RG, et al. Childhood **Attention-Deficit/Hyperactivity Disorder**, Sex, and Obesity: A Longitudinal Population-Based Study. Mayo Clin Proc. 2016 Feb 3.

Aguirre EK, Mytton OT, Monsivais P. **Liberalising agricultural policy for sugar in Europe** risks damaging public health. BMJ. 2015 Oct 27;351:h5085.

Ahern AL, Wheeler GM, Aveyard P, et al. **Extended and standard duration weight-loss programme referrals for adults in primary care (WRAP):** a randomised controlled trial. Lancet. 2017 May 3.

Al Khatib HK, et al. **Sleep extension** is a feasible lifestyle intervention in free-living adults who are habitually short sleepers: a potential strategy for decreasing intake of free sugars? A randomized controlled pilot study. Am J Clin Nutr. 2018 Jan 1;107(1):43-53.

Alba D, Wu L, Cawthon PMet al. **Changes in lean mass, absolute and relative muscle strength, and physical performance after gastric bypass surgery**. J Clin Endocrinol Metab. 2019 Jan 16.

Alfonso-Cristancho R, King WC, Mitchell JE, et al. Longitudinal Evaluation of **Work Status and Productivity After Bariatric Surgery**. JAMA. 2016 Oct 18;316(15):1595-1597.

Alhurani RE, Vassilaki M, Aakre JA, et al. Decline in Weight and Incident **Mild Cognitive Impairment**: Mayo Clinic Study of Aging. JAMA Neurol. 2016 Feb 1.

Allison DB, Gadde KM, Timothy W, et al. Controlled-release **phentermine/topiramate** in severely obese adults: A randomized controlled trial (**EQUIP**). Obesity 2011; DOI:10.1038/oby.2011.330.

Allison DB, Gadde KM, Garvey WT, et al. Controlled-release **phentermine/topiramate** in severely obese adults: a randomized controlled trial (EQUIP). Obesity (Silver Spring). 2012 Feb;20(2):330-42.

Alley DE, Chang VW. The changing relationship of **obesity and disability**, 1988-2004. JAMA. 2007 Nov 7;298(17):2020-7. Recent cardiovascular improvements have not been accompanied by reduced disability within the obese older population. Rather, obese participants surveyed during 1999-2004 were more likely to report functional impairments than obese participants surveyed during 1988-1994, and reductions in ADL impairment observed for nonobese older individuals did not occur in those who were obese. Over time, declines in obesity-related mortality, along with a younger age at onset of obesity, could lead to an increased burden of disability within the obese older population.

Althoff T, Sosič R, Hicks JL, et al. Large-scale physical activity data reveal **worldwide activity inequality**. Nature. 2017 Jul 10.

Alvarez-Blasco F, et al. Prevalence and characteristics of the **polycystic ovary syndrome** in overweight and obese women. Arch Intern Med. 2006 Oct 23;166(19):2081-6.

Amies-Cull B, Briggs ADM, Scarborough P. Estimating the potential impact of the UK government's **sugar reduction programme on child and adult health**: modelling study. BMJ. 2019 Apr 17;365:l1417.

Aminian A, Andalib A, Khorgami Z, et al. Who Should Get **Extended Thromboprophylaxis After Bariatric Surgery**?: A Risk Assessment Tool to Guide Indications for Post-discharge Pharmacoprophylaxis. Ann Surg. 2016 Mar 8.

Aminian A, Zajichek A, Arterburn DE, et al. Association of **Metabolic Surgery With Major Adverse Cardiovascular Outcomes** in Patients With Type 2 Diabetes and Obesity. JAMA. 2019 Sep 2.

Amstrong-Javors A, Pratt J, Kharasch S. **Wernicke Encephalopathy** in Adolescents **after Bariatric Surgery**: Case Report and Review. Pediatrics. 2016;138(6):e20161039.

Anderson JJ, Celis-Morales CA, Mackay DF, et al. Adiposity among 132 479 UK Biobank participants; contribution of sugar intake vs other macronutrients. Int J Epidemiol. 2017 Apr 1;46(2):492-501.

Anderson JW, et al. **Low-dose orlistat** effects on body weight of mildly to moderately overweight individuals: a 16 week, double-blind, placebo-controlled trial. Ann Pharmacother. 2006 Oct;40(10):1717-23. Epub 2006 Aug 29.

Azad MB, Abou-Setta AM, Chauhan BF, et al. **Nonnutritive sweeteners and cardiometabolic health**: a systematic review and meta-analysis of randomized controlled trials and prospective cohort studies. CMAJ. 2017 Jul 17;189(28):E929-E939

Anderson SE, Gooze RA, Lemeshow S, et al. Quality of early **maternal-child relationship** and risk of adolescent obesity. Pediatrics. 2012 Jan;129(1):132-40.
Anderson SE, Andridge R, Whitaker RC. **Bedtime in Preschool-Aged Children** and Risk for Adolescent Obesity. J Pediatr. 2016 Jul 8.
Anderson SE, Whitaker RC. Association of **Self-regulation With Obesity in Boys vs Girls** in a US National Sample. JAMA Pediatr. 2018 Jul 16.
Angelakis E, Merhej V, Raoult D. Related actions of **probiotics and antibiotics** on gut microbiota and weight modification. Lancet Infect Dis. 2013 Oct;13(10):889-99.
Angell SY, Cobb LK, Curtis CJ, et al. Change in **Trans Fatty Acid Content of Fast-Food** Purchases Associated With New York City's Restaurant Regulation: A Pre-Post Study. Ann Intern Med. 2012 Jul 17;157(2):81-6.
Angerås O, Albertsson P, Karason K, et al. Evidence for **obesity paradox in patients with ACS**: a report from the Swedish Coronary Angiography and Angioplasty Registry. Eur Heart J 2012.
Antoniotti GS, Coughlan M, Salamonsen LA, et al. Obesity associated **advanced glycation end products within the human uterine cavity adversely impact endometrial function** and embryo implantation competence. Hum Reprod. 2018 Apr 1;33(4):654-665.
Antony B, Jones G, Venn A, et al. Association between childhood overweight measures and adulthood **knee pain, stiffness and dysfunction**: a 25-year cohort study. Ann Rheum Dis. 2015 Apr; 74(4):711-7.
Anzman-Frasca S, Carmichael Djang H, Halmo MM, et al. Estimating impacts of a **Breakfast in the Classroom program** on school outcomes [online November 10, 2014]. JAMA Pediatr. doi:10.1001/jamapediatrics.2014.2042.
Anzman-Frasca S, Mueller MP, Sliwa S, et al. Changes in children's **meal orders following healthy menu modifications** at a regional US restaurant chain. Obesity (Silver Spring). 2015 May;23(5):1055-62.
Aparicio HJ, Himali JJ, Beiser AS, et al. Overweight, Obesity, and Survival After **Stroke** in the Framingham Heart Study. J Am Heart Assoc. 2017 Jun 24;6(6)
Apovian CM, et al. Best practice guidelines in **pediatric**/adolescent **weight loss surgery**. Obes Res. 2005 Feb;13(2):274-82.
Apovian CM, Gokce N. **Obesity and cardiovascular** disease. Circulation. 2012 Mar 6;125(9):1178-82.
Apovian CM, Aronne LJ, Bessesen DH, et al. **Pharmacological Management of Obesity: An Endocrine Society Clinical Practice Guideline**. J Clin Endocrinol Metab. 2015 Jan 15:jc20143415.
Apovian CM, Aronne LJ. The 2013 American Heart Association/American College of Cardiology/The Obesity Society Guideline for the Management of Overweight and Obesity in Adults: What Is New **About Diet, Drugs, and Surgery** for Obesity? Circulation. 2015 Oct 20;132(16):1586-91.
Appel LJ, Clark JM, Yeh H-C, et al. **Comparative effectiveness** of **weight-loss interventions** in clinical practice. (**POWER**) N Engl J Med 2011. DOI: 10.1056/NEJMoa1108660.
Araneta MR, Kanaya AM, Hsu WC, et al. Optimum BMI Cut Points to **Screen Asian Americans for Type 2 Diabetes**. Diabetes Care. 2015 May;38(5):814-20.
Araújo J, Severo M, Ramos E. **Sleep Duration** and Adiposity During Adolescence. Pediatrics. 2012 Oct 1.
Archer E, Shook RP, Thomas DM, et al. 45-year trends in **women's use of time and household management** energy expenditure.PLoS One 2013.
Ard J. **Obesity in the US**: what is the best role for **primary care**? BMJ. 2015 Feb 5; 350:g7846.
Argenta PA, Kassing M, Truskinovsky AM, Svendsen CA. **Bariatric surgery and endometrial pathology** in asymptomatic morbidly obese women: a prospective, pilot study. BJOG. 2013 Jun;120(7):795-800.
Armstrong S, Lazorick S, Hampl S, et al. **Physical Examination Findings** Among Children and Adolescents With Obesity: An Evidence-Based Review. Pediatrics. 2016 Jan 27.
Armstrong SC, Skinner AC. Defining "Success" in **Childhood Obesity Interventions in Primary Care**. Pediatrics. 2016 Sep 12.
Arnold AJ, Tkach A, Wile DJ. **Copper deficiency myeloneuropathy** in a patient with previous bariatric surgery. CMAJ. 2019 Aug 6;191(31):E866
Arnold M, Pandeya N, Byrnes G, et al. **Global burden of cancer attributable to high body-mass index** in 2012: a population-based study. Lancet Oncol 2014; online Nov 24. http://dx.doi.org/10.1016/S1470-2045(14)71123-4.
Arnold M, Jiang L, Stefanick ML, et al. Duration of Adulthood Overweight, Obesity, and **Cancer Risk** in the Women's Health Initiative: A Longitudinal Study from the United States. PLoS Med. 2016 Aug 16;13(8):e1002081.
Arnoldussen IAC, Gustafson DR, Leijsen EMC, et al. Adiposity is related to **cerebrovascular and brain volumetry outcomes** in the RUN DMC study. Neurology. 2019 Aug 27;93(9):e864-e878.
Aron-Wisnewsky J, Prifti E, Belda E, et al. Major **microbiota dysbiosis in severe obesity**: fate after bariatric surgery. Gut. 2018 Jun 13.
Arslan Alan A.; Helzlsouer Kathy J.; Kooperberg Charles; et al. Anthropometric Measures, Body Mass Index, and **Pancreatic Cancer**: A Pooled Analysis From the Pancreatic Cancer Cohort Consortium (PanScan). Arch Intern Med. 2010;170(9):791-802.
Artaud F, Dugravot A, Sabia S, et al. **Unhealthy behaviours and disability** in older adults: **Three-City Dijon** cohort study. BMJ. 2013 Jul 23;347:f4240.
Arterburn DE, Courcoulas AP. Bariatric surgery for obesity and metabolic conditions in adults. BMJ. 2014 Aug 27;349:g3961.
Arterburn D, Powers JD, Toh S, et al. Comparative effectiveness of **laparoscopic adjustable gastric banding (AGB) vs laparoscopic gastric bypass (RYGB)** [online October 29, 2014]. JAMA Surg. doi:10.1001/jamasurg.2014.1674.
Arterburn DE, Olsen MK, Smith VA, et al. Association between **bariatric surgery and long-term survival**. JAMA. 2015 Jan 6;313(1):62-70.
Arterburn D, McCulloch D. **Bariatric Surgery for Type 2 Diabetes**: Getting Closer to the Long-term Goal. JAMA. 2016 Mar 22-29;315(12):1276-7.
Arterburn D, Gupta A. **Comparing the outcomes** of **sleeve gastrectomy and Roux-en-Y gastric bypass** for severe obesity. JAMA. doi:10.1001/jama.2017.20449
Arterburn D, Wellman R, Emiliano A, et al. Comparative **effectiveness and safety of bariatric procedures** for weight loss. A PCORnet cohort study. Ann Intern Med. 2018. [Epub ahead of print]. doi:10.7326/M17-2786
Arya R, Gillespie CW, Cnaan Aet al. Obesity and overweight as **CAE comorbidities** and differential drug response modifiers. Neurology. 2016 Mar 30
Asarnow LD, McGlinchey E, Harvey AG. Evidence for a Possible Link between **Bedtime and Change in Body Mass Index**. Sleep. 2015 Jul 13.
Astbury NM, Aveyard P, Nickless A, et al. **Doctor Referral of Overweight People to Low Energy total diet replacement** T**reatment (DROPLET**): pragmatic randomized controlled trial. BMJ. 2018 Sep 26;362:k3760.
Atallah R, Filion KB, Wakil S, et al. **Long-term effects of 4 popular diets** (**Atkins, South Beach, Zone, or Weight Watchers**) on weight loss and cardiovascular risk factors: A systematic review of randomized controlled trials. Circ Cardiovasc Qual Outcomes 2014; 7:815-827.
Auerback BJ, Wolf FM, Hikida A, et al**. Fruit Juice** and Change in BMI: A Meta-Analysis. Pediatrics.2017;139(a):e20162454
Aune D, Saugstad OD, Henriksen T, et al. **Maternal body mass index and the risk of fetal death**, stillbirth, and infant death: a systematic review and meta-analysis. JAMA. 2014 Apr 16;311(15):1536-46.
Aune D, Sen A, Norat T, et al. Body Mass Index, Abdominal Fatness and **Heart Failure** Incidence and Mortality: A Systematic Review and Dose-Response Meta-Analysis of Prospective Studies. Circulation. 2016 Jan 8.
Aune D, Sen A, Prasad M, et al. **Body mass index and all cause mortality**: systematic review and non-linear dose-response meta-analysis of 230 prospective studies with 3.74 million deaths among 30.3 million participants. BMJ 2016;353:i1256.
Aung L, Lee W-J, Chen SC, et al. **Bariatric surgery** for patients with **early-onset vs late-onset type 2 diabetes** [online June 1, 2016].JAMA Surg. doi:10.1001/jamasurg.2016.1130.
Australain Therapeutic Good Administration:**OMG Slim** capsules contains Undeclaredsibutramine and orlistat.
Australian Therapeutic Goos Administration Oct/15 : **ActiveSlim slimming capsules** contains undeclared sibutramine.

Aveyard P, Lewis A, Tearne S, et al. **Screening and brief intervention for obesity in primary care**: a parallel, two- arm, randomised trial. Lancet 2016; online Oct 24.
Axelsson KF, Werling M, Eliasson B, et al. **Fracture Risk After Gastric Bypass Surgery**: A Retrospective Cohort Study. J Bone Miner Res. 2018 Jul 16.
Azad MB, Sharma AK, de Souza RJ, et al; Canadian Healthy Infant Longitudinal Development Study Investigators. Association between **artificially sweetened beverage consumption** during pregnancy and infant body mass index [online May 9, 2016]. JAMA Pediatr. doi:10.1001 /jamapediatrics.2016.0301.
Backx EM, Tieland M, Borgonjen-van den Berg KJ, et al. **Protein intake and lean body mass preservation** during energy intake restriction in overweight older adults. Int J Obes (Lond). 2016 Feb;40(2):299-304.
Bucholz EM, Beckman AL, Krumholz HA, et al. Excess weight and **life expectancy after acute myocardial infarction**: The obesity paradox reexamined. Am Heart J. 2016 Feb;172:173-81.
Bailey Clifford J. The challenge of managing **coexistent type 2 diabetes and obesity**. BMJ 2011;342:doi:10.1136/bmj.d1996 (Published 13 April 2011)
Bailey DP, Savory LA, Denton SJ, et al. The **Hypertriglyceridemic Waist**, Waist-to-Height Ratio, and Cardiometabolic Risk. J Pediatr. 2012 Nov 6.
Bailey LC, Forrest CB, Zhang P, et al. **Association of Antibiotics in Infancy** With Early Childhood Obesity. JAMA Pediatr. 2014 Sep 29.
Bailey-Davis L, Horst M, Hillemeier MM, Lauter A. Obesity Disparities Among **Elementary-Aged Children**: Data From School-Based BMI Surveillance. Pediatrics. 2012 Dec;130(6):1102-9.
Bajos N et al. **Sexuality and obesity**, a gender perspective: Results from French national random probability survey of sexual behaviours. BMJ 2010 Jun 15; 340:c2573.
Bajos N, Wellings K, Laborde C, Moreau C; for the CSF Group. **Sexuality and obesity**, a gender perspective: results from French national random probability survey of sexual behaviours. BMJ 2010;340:c2573.
Baker JL, Olsen LW, Sørensen TI. **Childhood** body-mass index and the risk of **coronary heart disease** in adulthood. N Engl J Med. 2007 Dec 6;357(23):2329-37.
Baker SS, Baker RD. **Early Exposure to Dietary Sugar and Salt**. Pediatrics. 2015 Feb 2.
Baker SS, Baker RD. A **Varied and Diverse Diet** Can Lead to Increasing BMI for Poor Children. Pediatrics. 2016 Feb 11.
Bakker LE, Boon MR, van der Linden RA, et al. **Brown adipose tissue** volume in healthy lean south Asian adults compared with white Caucasians: a prospective, case-controlled observational study. Lancet Diabetes Endocrinol. 2014 Mar;2(3):210-7.
Bakker EA, Lee DC, Sui X, et al. Association of **Resistance Exercise**, Independent of and Combined With **Aerobic Exercise**, With the Incidence of **Metabolic Syndrome**. Mayo Clin Proc. 2017 Aug;92(8):1214-1222
Bakrania K, et al. Associations of moderate-to-vigorous-intensity physical activity and body mass index with **glycated haemoglobin** within the general population: a cross-sectional analysis of the 2008 Health Survey for England. BMJ Open. 2017 Apr 3;7(4):e014456.
Bal S, Ying GS, Tomlinson L, et al. Association of Weight **Gain Acceleration With Risk of Retinopathy** of Prematurity. JAMA Ophthalmol. 2019 Sep 5
Bangalore S, Fayyad R, Laskey R, et al. **Body-Weight Fluctuations** and Outcomes in Coronary Disease. N Engl J Med. 2017 Apr 6;376(14):1332-1340.
Bao W, Yeung E, Tobias DK, et al. Long-term **risk of type 2 diabetes** mellitus in relation to BMI and weight change among women with a history of gestational diabetes mellitus: a prospective cohort study. Diabetologia. 2015 Mar 22.
Baranowski T, Abdelsamad D, Baranowski J et al. Impact of an **Active Video Game** on Healthy Children's Physical Activity. Pediatrics. 2012 Mar;129(3):e636-42.
Barkin SL, Heerman WJ, Sommer EC, et al. Effect of a **behavioral intervention for underserved preschool-age children on change in body mass index:** a randomized clinical trial [August 7, 2018]. JAMA. doi:10.1001/jama.2018.9128
Barnes RD, White MA, Martino S, et al. A randomized controlled trial comparing **scalable weight loss treatments in primary care**. Obesity (Silver Spring). 2014 Dec;22(12):2508-16.
Barnes RD, White MA, Martino S, Grilo CM. A randomized controlled trial comparing **scalable weight loss treatments in primary care**. Obesity (Silver Spring). 2014 Dec;22(12):2508-16.
Barnes RD, Ivezaj V, Martino S, et al. Back to Basics? No Weight Loss from **Motivational Interviewing Compared to Nutrition Psychoeducation** at One-Year Follow-Up. Obesity (Silver Spring). 2017 Dec;25(12):2074-2078.
Barnett TA, et al. **Sedentary Behaviors** in Today's Youth: Approaches to the **Prevention and Management of Childhood Obesity**: A Scientific Statement From the **American Heart Association (AHA)**. Circulation. 2018 Sep 11;138(11):e142-e159.
Barrington WE, Schenk JM, Etzioni R, Arnold et al. Difference in Association of Obesity With **Prostate Cancer Risk** Between US African American and Non-Hispanic White Men in the Selenium and Vitamin E Cancer Prevention Trial (**SELECT**). JAMA Oncol. 2015 Jun
Barton Garry R, et al. **Lifestyle interventions** for knee pain in overweight and obese adults aged ≥45: economic evaluation of randomised controlled trial. BMJ 2009;339:b2273, doi: 10.1136/bmj.b2273 (Published 18 August 2009)
Basatemur E, Gardiner J, Williams C, et al.**Maternal Prepregnancy BMI and Child Cognition**: A Longitudinal Cohort Study. Pediatrics. 2013 Jan;131(1):56-63.
Basu S, Yoffe P, Hills N, Lustig RH. The relationship of **sugar to population-level diabetes prevalence**: an econometric analysis of repeated cross-sectional data. PLoS One. 2013;8(2):e57873.
Batac J, Hamade M, Hamade H, Glickman L. **Abdominoplasty in the Obese Patient**: Risk versus Reward. Plast Reconstr Surg. 2019 Apr;143(4):721e-726e.
Batsis JA, Sahakyan KR, et al. **Normal Weight Obesity and Mortality** in United States Subjects ≥60 Years of Age (from the Third National Health and Nutrition Examination Survey). Am J Cardiol. 2013 Nov 15;112(10):1592-8.
Batsis JA, Gill LE, Masutani RK, et al. **Weight Loss Interventions in Older Adults with Obesity**: A Systematic Review of Randomized Controlled Trials Since 2005. J Am Geriatr Soc. 2017 Feb;65(2):257-268.
Bauditz J, Norman K, Biering H, Lochs H, Pirlich M. Severe weight loss caused by chewing gum (**sorbitol**). BMJ. 2008 Jan 12;336(7635):96-7.
Bauer KW, Lumeng JC, Sonneville KR. **Parenting in an Obesogenic Environment**:Ghosts at the Dinner Table. Pediatrics. 2018 Mar 6.
Bazan IS, Fares WH. Review of the Ongoing Story of **Appetite Suppressants, Serotonin Pathway, and Pulmonary Vascular Disease**. Am J Cardiol. 2016 May 15;117(10):1691-6.
Bazzano LA, Hu T, Reynolds K, et al. Effects of **low-carbohydrate and low-fat diets**: a randomized trial. Ann Intern Med. 2014 Sep 2;161(5):309-18.
Bazzocchi A, Diano D. **Dual-energy x-ray absorptiometry** in obesity. CMAJ. 2014 Jan 7;186(1):48
Beavers KM, Beavers DP, Nesbit BA, et al. Effect of an **18-month physical activity and weight loss intervention** on body composition in overweight and obese older adults. Obesity (Silver Spring). 2014 Feb;22(2):325-31.
Bech BH, Obel C, Henriksen TB, Olsen J. Effect of reducing **caffeine** intake on birth weight and length of gestation: randomised controlled trial. BMJ. 2007 Jan 26; [Epub ahead of print] A moderate reduction in caffeine intake in the second half of pregnancy has no effect on birth weight or length of gestation.
Beets, Michael W., Bornstein, Daniel, Dowda, Marsha, et al. Compliance With National Guidelines for **Physical Activity** in U.S. Preschoolers: Measurement and Interpretation. Pediatrics 2011 127: 658-664.
Behary P, Tharakan G, Alexiadou K, et al. **Combined GLP-1, Oxyntomodulin, and Peptide YY Improves Body Weight** and Glycemia in Obesity and Prediabetes/Type 2 Diabetes: A Randomized, Single-Blinded, Placebo-Controlled Study. Diabetes Care. 2019 Aug;42(8):1446-1453.
Behrens G, Matthews CE, Moore SC, et al. Body size and physical activity in relation to incidence of **chronic obstructive pulmonary disease**. CMAJ. 2014 Jul 7.
Belcher BR, Berrigan D, Papachrisotopoulou A, et al. Effects of **Interrupting Children's Sedentary Behaviors With Activity** on Metabolic Function: A Randomized Trial. J Clin Endocrinol Metab. 2015 Aug 27:jc20152803.
Bell JA, Carslake D, O'Keeffe LM, et al. Associations of **Body Mass and Fat Indexes With Cardiometabolic Traits**. J Am Coll Cardiol. 2018 Dec 18;72(24):3142-3154.
Bell JA, Hamer M, Batty GD, et al. Combined effect of **physical activity and leisure time sitting** on long-term risk of incident obesity and metabolic risk factor clustering. *Diabetologia* 2014

Beltrand J et al.**Post-Term Birth** is Associated with Greater Risk of Obesity in Adolescent Males. J Pediatr. 2011 Dec 6.
Ben-Menachem E. Weight issues for people with **epilepsy**-A review. Epilepsia. 2007;48 Suppl 9:42-5.
Ben Q, An W, Jiang Y et al. Body Mass Index Increases Risk for **Colorectal Adenomas** Based on Meta-Analysis. Gastroenterology. 2012 Jan 11.
Benedict C et al. **Acute sleep deprivation** enhances the brain's response to hedonic food stimuli: An fMRI study. J Clin Endocrinol Metab 2012 Jan 18.
Bennett GG, Foley P, Levine E, et al. Behavioral Treatment for **Weight Gain Prevention Among Black Women** in Primary Care Practice: A Randomized Clinical Trial. JAMA Intern Med. 2013 Aug 26.
Bennett WL, Gilson MM, Jamshidi R, et al. Impact of bariatric surgery on **hypertensive** disorders in pregnancy: retrospective analysis of insurance claims data. BMJ 2010;340:c1662, doi: 10.1136/bmj.c1662 (Published 13 April 2010)
Bennett WL, Wilson RF, Zhang A, et al. Methods for Evaluating Natural Experiments in Obesity: A Systematic Review. Ann Intern Med. 2018 May 1:1-10.
Bentham J, di Cesare M, Bilano V, et al. NCD Risk Factor Collaboration (**NCD-RisC**). **Worldwide trends in body-mass index, underweight, overweight, and obesity from 1975 to 2016**: a pooled analysis of 2416 population-based measurement studies in 128·9 million children, adolescents, and adults. Lancet 2017 (published online 10 Oct)
Berge JM, Maclehose R, Loth KA, et al. **Parent Conversations About Healthful Eating and Weight**: Associations With Adolescent Disordered Eating Behaviors. JAMA Pediatr. 2013 Jun 24:1-7.
Berge JM, Rowley S, Trofholz A, et al. Childhood Obesity and Interpersonal Dynamics During **Family Meals**. Pediatrics. 2014 Oct 13.
Berge JM, Wall M, Hsueh TF, et al. The Protective Role of **Family Meals** for Youth Obesity: 10-Year Longitudinal Associations. J Pediatr. 2014 Sep 27.
Berge JM, Wall M, Hsueh T-F, Fulkerson JA, Larson N, Neumark-Sztainer D. The protective role of **family meals** for youth obesity: 10-year longitudinal associations. J Pediatr 2015;166:296-301.
Berge JM, Meyer CS, Loth K, et al. **Parent/Adolescent Weight Status Concordance** and Parent Feeding Practices. Pediatrics. 2015 Aug 24.
Berger NA. **Young Adult Cancer: Influence of the Obesity** Pandemic. Obesity (Silver Spring). 2018 Apr;26(4):641-650.
Bernhardt AM, Wilking C, Adachi-Mejia AM, et al. How **television fast food marketing aimed at children** compares with adult advertisements. PLoS One. 2013 Aug 28;8(8):e72479.
Bernhardt AM, Wilking C, Gottlieb M, et al. Children's Reaction to **Depictions of Healthy Foods in Fast-Food Television Advertisements**. JAMA Pediatr. 2014 Mar 31.
Bernstein JT, L'Abbé MR. **Added sugars on nutrition labels**: a way to support population health in Canada. CMAJ. 2016 Oct 18;188(15):E373-E374.
Bertoia ML, et al. Changes in Intake of **Fruits and Vegetables** and Weight Change in United States Men and Women Followed for Up to 24 Years: Analysis from Three Prospective Cohort Studies. PLoS Med. 2015 Sep 22;12(9):e1001878.
Bertoia ML, Rimm EB, Mukamal KJ, et al. **Dietary flavonoid intake** and weight maintenance: three prospective cohorts of 124 086 US men and women followed for up to 24 years. BMJ. 2016 Jan 28;352:i17.
Berz JP, Singer MR, Guo X et al. use of a **DASH food group** score to predict excess weight gain in adolescent girls in the National Growth and Health Study. Arch Pediatr Adolesc Med 2011; 165:540-546.
Beyerlein A, Schiessl B, Lack N, et al. Associations of **gestational weight loss** with birth-related outcome: a retrospective cohort study. *BJOG* 2011*;* **118***:* 55– 61.
Bhaskaran K, dos-Santos-Silva I, Leon DA, et al. Association of **BMI with overall and cause-specific mortality**: a population-based cohort study of 3·6 million adults in the UK. Lancet Diabetes Endocrinol 2018; online Oct 30.
Bhaskaran K, Douglas I, Forbes H, et al. **Body-mass index** and risk of **22 specific cancers**: a population-based cohort study of 5·24 million UK adults. Lancet. 2014 Aug 30;384(9945):755-65.
Bhatt DL, Aminian A, Kashyap SR, et al. Cardiovascular Biomarkers After **Metabolic Surgery Versus Medical Therapy for Diabetes**. J Am Coll Cardiol. 2019 Jul 16;74(2):261-263.
Bhattacharya S, McNeill G, Raja EA, et al. **Maternal gestational weight gain** and **offspring's risk of cardiovascular disease** and mortality. Heart. 2016 Sep 15;102(18):1456-63.
Bhatti JA, Nathens AB, Thiruchelvam D, et al. **Self-harm emergencies after bariatric surgery**: a population-based cohort study.JAMA Surg. doi:10.1001/jamasurg.2015.3414.
Bhaumik S. The public health **threat** from **sugary drinks** in India. BMJ. 2014 Oct 21;349:g6216.
Bianchi-Hayes J, Calixte R, Huang J, et al. **Healthcare Utilization by Obese** and Overweight **Children**. J Pediatr. 2015 Jan 6.
Bibbins-Domingo K, Coxson P, Pletcher MJ, Lightwood J, Goldman L. **Adolescent** overweight and future adult **coronary heart disease**. N Engl J Med. 2007 Dec 6;357(23):2371-9.
Bickham DS, Blood EA, Walls CE et al. Characteristics of **Screen Media** Use Associated With Higher BMI in Young Adolescents. Pediatrics. 2013 Apr 8.
Biddiss E, Irwin J. Active **video games** to promote physical activity in children and youth: a systematic review. Arch Pediatr Adolesc Med. 2010;164(7):664-672.
Biehl A, Hovengen R, Grøholt EK, et al. **Parental marital status** and childhood overweight and obesity in Norway: a nationally representative cross-sectional study. BMJ Open. 2014 Jun 4;4(6):e004502.
Billeter AT, Scheurlen KM, Probst P, et al. Meta-analysis of **metabolic surgery versus medical treatment for microvascular complications in patients with type 2 diabetes** mellitus. Br J Surg. 2018 Feb;105(3):168-181.
Birken C, Hamilton J. **Obesity in a young child**. CMAJ. 2014 Apr 1;186(6):443-4.
Birken CS, Tu K, Oud W, et al. Determining rates of overweight and **obese status in children using electronic medical records**: Cross-sectional study. Can Fam Physician. 2017 Feb;63(2):e114-e122.
Birkmeyer NJ, Dimick JB, Share D, et al. Michigan Bariatric Surgery Collaborative. Hospital **complication rates with bariatric surgery** in Michigan. JAMA. 2010 Jul 28;304(4):435-42.
Birkmeyer JD, Finks JF, O'Reilly A, et al. **Surgical skill and complication rates after bariatric surgery**. N Engl J Med 2013; 369:1434-42.
Bjerregaard LG, Jensen BW, Ängquist L, et al. Change in **Overweight from Childhood to Early Adulthood and Risk of Type 2 Diabetes**. N Engl J Med. 2018 Apr 5;378(14):1302-1312.
Bjørge T, Sørensen HT, Grotmol T, et al. **Fetal growth and childhood cancer**: a population-based study. Pediatrics. 2013 Nov;132(5):e1265-75.
Blake-Lamb TL, Locks LM, Perkins ME, et al. **Interventions** for **Childhood Obesity** in the **First 1,000 Days** A Systematic Review. Am J Prev Med. 2016 Feb 8.
Blazeby JM, Byrne J, Welbourn R. What is the **most effective operation** for adults with severe and complex obesity? BMJ. 2014 Mar 14;348:g1763.
Bleich SN. A Road Map for **Sustaining Healthy Eating Behavior**. N Engl J Med. 2018 Aug 9;379(6):507-509.
Bleich SN, Vercammen KA, Koma JW, Li Z. Trends in **Beverage Consumption** Among Children and Adults, 2003-2014. Obesity (Silver Spring). 2017 Nov 14.
Bleich SN, Segal J, Wu Y, et al. Systematic Review of **Community-Based Childhood Obesity Prevention** Studies. Pediatrics. 2013 Jun 10.
Bliddal H, Leeds AR, Stigsgaard L, Astrup A, Christensen R. Weight loss as **treatment for knee osteoarthritis symptoms** in obese patients: 1-year results from a randomised controlled trial. Ann Rheum Dis. 2011 Oct;70(10):1798-803.
Block JP. The **Calorie-Labeling** Saga - Federal Preemption and Delayed **Implementation of Public Health Law**. N Engl J Med. 2018 May 23.
Block JP, Condon SK, Kleinman K, et al. **Consumers' estimation of calorie** content at **fast food restaurants**: cross sectional observational study. BMJ. 2013 May 23;346:f2907.
Block JP, Bailey LC, Gillman MW, et al; PCORnet Antibiotics and Childhood Growth Study Group. Early **antibiotic exposure and weight outcomes** in young children. Pediatrics. 2018;142(6):e20180290
Blumenthal SR, Castro VM, Clements CC, et al. An Electronic Health Records Study of Long-Term **Weight Gain Following Antidepressant Use.** JAMA Psychiatry. 2014 Jun 4.
Bocca G, Corpeleijn E, Stolk RP, et al. Results of a **multidisciplinary** treatment program in **3-year-old to 5-year-old** overweight or obese children: a randomized, controlled clinical trial [online Oct 29, 2012]. Arch Pediatr Adolesc Med.
Boerlage TC, van de Laar AW, Westerlaken S, et al. **Gastrointestinal symptoms and food intolerance 2 years after laparoscopic Roux-en-Y gastric bypass** for morbid obesity. Br J Surg. 2016 Dec 19.

Bogart LM, Elliott MN, Cowgill BO, et al. Two-Year BMI Outcomes From a **School-Based Intervention** for Nutrition and Exercise: A Randomized Trial. Pediatrics. 2016 May;137(5).
Boggs DA, Rosenberg L, Cozier YC, et al. General and abdominal **obesity and risk of death among black women**. N Engl J Med. 2011 Sep 8;365(10):901-8.
Bohula EA, Wiviott SD, McGuire DK, et al; CAMELLIA–TIMI 61 Steering Committee and Investigators. **Cardiovascular Safety of Lorcaserin** in Overweight or Obese Patients. N Engl J Med. 2018 Sep 20;379(12):1107-1117.
Bolhuis DP, Lakemond CM, de Wijk RA, et al. **Consumption with large sip sizes** increases food intake and leads to underestimation of the amount consumed. PLoS One. 2013;8(1):e53288.
Bonham MP, Dordevic AL, Ware RS, et al. Evaluation of a **Commercially Delivered Weight Management Program** for **Adolescents**. J Pediatr. 2017 Mar 7.
Boone-Heinonen J, Gordon-Larsen P, Kiefe CI, et al. **Fast food restaurants and food stores**: longitudinal associations with diet in young to middle-aged adults: the CARDIA study. *Arch Intern Med*. 2011;171(13):1162-1170.
Booth HP, Prevost TA, Wright AJ, et al. Effectiveness of **behavioural weight loss interventions** delivered in a primary care setting: a systematic review and meta-analysis. Fam Pract. 2014 Oct 8.
Booth H, Khan O, Prevost T, et al. Incidence of type 2 **diabetes after bariatric surgery**: population-based matched cohort study. Lancet Diabetes Endocrinol. 2014 Nov 3;2(12):963-968.
Borges MC, Louzada ML, de Sá TH, et al. **Artificially Sweetened Beverages** and the Response to the Global Obesity Crisis. PLoS Med. 2017 Jan 3;14(1):e1002195.
Bosomworth NJ. **Normal-weight central obesity**: Unique hazard of the toxic waist. Can Fam Physician. 2019 Jun;65(6):399-408.
Bosomworth NJ. The **downside of weight loss**. Realistic intervention in bodyweight trajectory. Can Fam Physician 2012;58: 517-23.
Botha S, Forde L, et al. Effect of **non-surgical weight management on weight and glycaemic control in people with type 2 diabetes**: A comparison of interventional and non-interventional outcomes at 3 years. Diabetes Obes Metab. 2017 Nov 27.
Bout-Tabaku S, Michalsky MP, Jenkins TM, et al. Musculoskeletal Pain, Self-reported Physical Function, and Quality of Life in the Teen-Longitudinal Assessment of **Bariatric Surgery** (Teen-LABS) Cohort. JAMA Pediatr. 2015 Apr 27.
Bouchard C, et al. The response to long-term **overfeeding** in **identical twins**. N Engl J Med. 1990 May 24;322(21):1477-82.
Boulton J, Hashem KM, Jenner KH, et al. How much **sugar is hidden in drinks** marketed to children? A survey of fruit juices, juice drinks and smoothies. BMJ Open. 2016 Mar 23;6(3):e010330.
Boutelle KN, Norman GJ, Rock CL, Rhee KE, Crow SJ. Guided **Self-Help for the Treatment of Pediatric Obesity**. Pediatrics. 2013 Apr 1.
Boutelle KN, Rhee KE, Liang J, et al. Effect of **attendance of the child** on body weight, energy intake, and physical activity in childhood obesity treatment: a randomized clinical trial [online May 30, 2017].JAMA Pediatr. doi:10.1001
Boyland Emma J., Harrold Joanne A., Kirkham Tim C., et al. **Food Commercials** Increase Preference for Energy-Dense Foods, Particularly in Children Who Watch More Television. Pediatrics 2011; 128:1 e93-e100; ahead of print June 27, 2011.
Boyland EJ, Harrold JA, Dovey TM, et al. Food choice and overconsumption: effect of a premium **sports celebrity endorser**. J Pediatr. 2013 Aug;163(2):339-43.
Boynton-Jarrett R, Rosenberg L, Palmer JR, et al. **Child and Adolescent Abuse** in Relation to Obesity in Adulthood: The Black Women's Health Study. Pediatrics. 2012 Jul 2.
Bradley D, Magkos F, Klein S. Effects of **bariatric surgery** on glucose homeostasis and type 2 diabetes. Gastroenterology. 2012 Oct;143(4):897-912.
Bragg MA, Yanamadala S, Roberto CA, et al. **Athlete Endorsements in Food Marketing**. Pediatrics. 2013 Oct 7.
Brandkvist M, Bjørngaard JH, Ødegård RA, et al. **Quantifying the impact of genes** on body mass index during the obesity epidemic: longitudinal findings from the HUNT Study. BMJ. 2019 Jul 3;366:l4067.
Brauer P, Connor Gorber S, Shaw E, et al.; **Canadian Task Force on Preventive Health Care**. (**CTFPHC**) Recommendations for **prevention of weight gain and use of behavioural and pharmacologic interventions to manage overweight and obesity** in adults in primary care. CMAJ. 2015 Jan 26.
Brault MC, Turcotte O, Aimé A, et al. **Body Mass Index Accuracy in Preadolescents**: Can We Trust Self-Report or Should We Seek **Parent Report**? JPediatr. 2015 May 15.
Braun JM, Chen A, Romano ME, et al. Prenatal **perfluoroalkyl substance exposure** and child adiposity at 8 years of age: The HOME study. Obesity (Silver Spring). 2015 Nov 11.
Bravata DM, Smith-Spangler C, Sundaram V, et al. Using **pedometers** to increase physical activity and health. A systematic review. JAMA 2007; 298:2296-2304.
Bray GA, Smith SR, de Jonge L, et al. Effect of **dietary protein** content on weight gain, energy expenditure, and body composition during overeating: a randomized controlled trial. JAMA. 2012;307(1):47-55.
Bray GA, Ryan DH. **Medical therapy** for the patient with obesity. Circulation. 2012 Apr 3;125(13):1695-703.
Bray GA, Frühbeck G, Ryan DH, Wilding JP. **Management of obesity.** Lancet. 2016 Feb 8.
Bray GA, Heisel WE, Afshin A, et al. The **Science of Obesity Management**: An **Endocrine Society Scientific Statement**. Endocr Rev. 2018 Mar 6.
Brennan LK, Brownson RC, Orleans CT. **Childhood obesity policy research and practice**: evidence for policy and environmental strategies. Am J Prev Med. 2014 Jan;46(1):e1-16.
Briggs AD, Mytton OT, Kehlbacher A, et al. Overall and **income specific effect** on prevalence of overweight and obesity of 20% sugar sweetened drink tax in UK: econometric and comparative risk assessment modelling study. BMJ. 2013 Oct 31;347:f6189.
Broccoli S, Davoli AM, Bonvicini L, et al. Motivational Interviewing to Treat Overweight Children: 24-Month Follow-Up of a Randomized Controlled Trial. Pediatrics. 2016 Jan;137(1):1-10.
Brotman LM, Dawson-McClure S, Huang KY et al. Early Childhood **Family Intervention** and Long-term Obesity Prevention Among High-risk Minority Youth. Pediatrics. 2012 Feb 6.
Brown JC, Caan BJ, Prado CM, et al. **Body Composition and Cardiovascular Events in Patients With Colorectal Cancer**: A Population-Based Retrospective Cohort Study. JAMA Oncol. 2019 May 16.
Brown TJ, Mead E, Ells LJ. **Behavior-Changing Interventions for Treating Overweight or Obesity** in Children Aged 6 to 11 Years. JAMA Pediatr. 2019 Feb 18.
Bruyndonckx L, Hoymans VY, De Guchtenaere A, et. al. **Diet, Exercise, and Endothelial Function** in Obese Adolescents. Pediatrics. 2015 Feb 9. pii: peds.2014-1577.
Bruze G, Holmin TE, Peltonen M, et al. Associations of **bariatric surgery with changes in interpersonal relationship status**: results from 2 Swedish cohort studies [online Mar 28, 2018].JAMA Surg. doi:10.1001/jamasurg.2018.0215
Budu-Aggrey A, Brumpton B, Tyrrell J, et al. Evidence of a **causal relationship between body mass index and psoriasis**: A mendelian randomization study. PLoS Med. 2019 Jan 31;16(1):e1002739.
Burgoine T, Forouhi NG, Griffin SJ, et al. Associations between **exposure to takeaway food outlets**, takeaway food consumption, and body weight in Cambridgeshire, UK: population based, cross sectional study. BMJ. 2014 Mar 13;348:g1464.
Burke GL, Bertoni AG, Shea S, et al. The impact of obesity on cardiovascular disease risk factors and subclinical vascular disease: the Multi-Ethnic Study of Atherosclerosis. Arch Intern Med. 2008 May 12;168(9):928-35. These data confirm the epidemic of obesity in most but not all racial and ethnic groups. The observed **low prevalence of obesity in Chinese American** participants indicates that high rates of obesity should not be considered inevitable.
BurkeMA, Heiland FW. **Evolving societal norms of obesity**: what is the appropriate response? JAMA. doi:10.1001/jama.2017.18947
Buscot M-J, Thompson RJ, Juonala M, et al. **BMI Trajectories** Associated With Resolution of Elevated **Youth BMI** and Incident Adult Obesity. Peds. 2018; 141(1):e20172003
Butryn ML, Forman EM, Lowe MR, et al. Efficacy of **environmental and acceptance-based enhancements** to **behavioral weight loss treatment**: The **ENACT** trial. Obesity (Silver Spring). 2017 May;25(5):866-872.
Cahill AG, Haire-Joshu D, Cade WT, et al. **Weight Control Program and Gestational Weight Gain in Disadvantaged Women** with Overweight or Obesity: A Randomized Clinical Trial. Obesity (Silver Spring). 2018 Mar;26(3):485-491.
Cai L, Wu Y, Wilson RF, et al. Effect of Childhood Obesity Prevention Programs on **Blood Pressure**: A Systematic Review and Meta-Analysis. Circulation. 2014 Feb 19.
Cai X, Qiu SH, Yin H, et al. **Pedometer intervention** and weight loss in overweight and obese adults with Type 2 diabetes: a meta-analysis. Diabet Med. 2016 Aug;33(8):1035-44.
Caleyachetty R, Thomas GN, Toulis KA, et al. **Metabolically Healthy Obese** and Incident Cardiovascular Disease Events Among 3.5 Million Men and Women. JACC. 2017;70(12):1429-37

Campbell KJ, Lioret S, McNaughton SA, et al. A **Parent-Focused Intervention** to Reduce Infant Obesity Risk Behaviors: A Randomized Trial. Pediatrics. 2013 Mar 4.
Campos GM, Rabl C, et al. Factors associated with weight loss after **gastric bypass**. Arch Surg. 2008 Sep;143(9):877-883; discussion 884. Gastric bypass results in substantial weight loss in most patients. Diabetes and larger pouch size are independently associated with poor weight loss after GBP.
Camps G, Mars M, et al. **Empty calories and phantom fullness**: a randomized trial studying the relative effects of energy density and viscosity on gastric emptying determined by MRI and satiety. Am J Clin Nutr. 2016 Jul;104(1):73-80.
Canadian Physical Activity Guidelines-Jan 2011. Clinical Practice Guideline Development Report. Canadian Society for Exercise Physiology. http://www.csep.ca/CMFiles/Guidelines/CPAGuideline_Report_JAN2011.pdf
Cantor J, Breck A, Elbel B. Correlates of **Sugar-Sweetened Beverages** Purchased for Children at **Fast-Food Restaurants**. Am J Public Health. 2016 Nov;106(11):2038-2041.
Carlson JA, Schipperijn J, Kerr J, et al. **Locations of Physical Activity** as Assessed by GPS in Young Adolescents. Pediatrics. 2015 Dec 8.
Carlsson LMS, Peltonen M, Ahlin S, et al. **Bariatric surgery and prevention of type 2 diabetes** in Swedish Obese Subjects. (**SOS**) N Engl J Med 2012; 367:695-704.
Caro JC, Corvalán C, Reyes M, et al. Chile's 2014 **sugar-sweetened beverage tax and changes in prices and purchases of sugar-sweetened beverages**: An observational study in an urban environment. PLoS Med. 2018 Jul 3;15(7):e1002597.
Carter AR, Borges MC, Benn M, et al. Combined Association of Body Mass Index and Alcohol Consumption With **Biomarkers for Liver Injury and Incidence of Liver Disease**: A Mendelian Randomization Study. JAMA Netw Open. 2019 Mar 1;2(3):e190305
Carter PJ, Taylor BJ, Williams SM, Taylor RW. Longitudinal analysis of **sleep in relation to BMI and body fat in children**: the **FLAME** study. BMJ 2011;342:d2712.
Carreras-Torres R, Johansson M, Haycock PC, et al. Role of **obesity in smoking behaviour**: Mendelian randomisation study in UK Biobank. BMJ. 2018 May 16;361:k1767.
Carslake D, Davey Smith G, Gunnell D, et al. Confounding by ill health in the observed association between **BMI and mortality**: evidence from the **HUNT** Study using offspring BMI as an instrument. Int J Epidemiol. 2017 Dec 1.
Caruso ML, Cullen KW. Quality and Cost of **Student Lunches Brought From Home**. JAMA Pediatr. 2014 Nov 24.
Casazza K, Fontaine KR, Astrup A, et al. **Myths, presumptions, and facts** about obesity. N Engl J Med. 2013 Jan 31;368(5):446-54.
Casperson SL, Hall C, Roemmich JN. **Postprandial energy metabolism** and substrate oxidation in response to the inclusion of a **sugar**- or **non-nutritive sweetened beverage** with meals differing in protein content. BMC Nutrition. 2017;3:49
Catalano PM, Shankar K. **Obesity and pregnancy**: mechanisms of short term and long term adverse consequences for mother and child. BMJ. 2017 Feb 8;356:j1
Caunca MR, Gardener H, Simonetto M, et al. Measures of obesity are **associated with MRI markers of brain aging**: The Northern Manhattan Study. Neurology. 2019 Jul 24.
Cavaignac E, Lafontan V, Reina N, et al. Obesity has no adverse effect on the outcome of **unicompartmental knee replacement** at a minimum follow-up of seven years. Bone Joint J. 2013 Aug;95-B(8):1064-8.
Cawley J, Willage B, Frisvold D. Pass-through of a **tax on sugar**-sweetened beverages at the Philadelphia International Airport. JAMA. 2017.doi:10.1001/jama.2017.16903
Celis-Morales C, Lyall DM, Guo Y, et al. **Sleep characteristics** modify the association of genetic predisposition with obesity and anthropometric measurements in 119,679 UK Biobank participants. Am J Clin Nutr. 2017 Mar 1.
Celis-Morales C, Lyall DM, Guo Y, et al. Sleep characteristics modify the association of genetic predisposition with obesity and anthropometric measurements in 119,679 UK Biobank participants. Am J Clin Nutr. 2017 Mar 1.
Cerhan JR, Moore SC, Jacobs EJ, et al. A pooled analysis of **waist circumference** and mortality in 650 000 adults.*Mayo Clin Proc* 2014; 89: 335-345.
Cespedes Feliciano EM, Rifas-Shiman SL, Quante M, et al. **Chronotype, Social Jet Lag, and Cardiometabolic Risk** Factors in Early Adolescence. JAMA Pediatr. 2019 Sep 16.
Chakravarty EF, Hubert HB, Lingala VB, Fries JF. **Reduced disability and mortality among aging runners**: a 21-year longitudinal study.Arch Intern Med. 2008 Aug 11;168(15):1638-46. Vigorous exercise (running) at middle and older ages is associated with reduced disability in later life and a notable survival advantage.
Chalasani N et al. The diagnosis and management of **non-alcoholic fatty liver disease (NAFLD):** Practice guideline by the American Association for the Study of Liver Diseases, American College of Gastroenterology, and the American Gastroenterological Association. Hepatology 2012 Jun; 55:2005.
Chang AR, Grams ME, Ballew SH, et al; CKD Prognosis Consortium (CKD-PC). **Adiposity and risk of decline in glomerular filtration rate**:meta-analysis of individual participant data in a global consortium. BMJ. 2019 Jan 10;364:k5301.
Chang J, Kashyap SR. The **protein-sparing modified fast** for obese patients with type 2 **diabetes**: What to expect. Cleve Clin J Med. 2014 Sep;81(9):557-565.
Chang SH, Stoll CR, Song J, et al. The Effectiveness and Risks of **Bariatric Surgery**: An Updated Systematic Review and Meta-analysis, 2003-2012. JAMA Surg. 2013 Dec 18
Chang T, Choi H, Richardson CR, et al. Implications of **teen birth for overweight and obesity in adulthood**. Am J Obstet Gynecol. 2013 Apr 12.
Chang T, Ravi N, Plegue MA, et al. **Inadequate Hydration, BMI, and Obesity** Among US Adults: NHANES 2009-2012. Ann Fam Med. 2016 Jul;14(4):320-4.
Chang Y, Kim BK, Yun KE, et al. **Metabolically healthy obesity** and **coronary artery calcification**. *J Am Coll Cardiol*2014.
Chang Y, Kim BK, Yun KE, et al. **Metabolically healthy obesity** and **coronary artery calcification**. J Am Coll Cardiol. 2014 Apr 17.
Chang Y, Ryu S, Choi Y, et al. **Metabolically Healthy Obesity** and Development of Chronic **Kidney Disease**: A Cohort Study. Ann Intern Med. 2016 Feb 9.
Chaput JP, Ferraro ZM, Prud'homme D, Sharma AM. Widespread **misconceptions** about obesity. Can Fam Physician. 2014 Nov;60(11):973-5.
Charakida M, Khan T, Johnson W, et al. **Lifelong patterns of BMI** and cardiovascular phenotype in individuals aged 60-64 years in the 1946 British birth cohort study: an epidemiological study. Lancet Diabetes Endocrinol. 2014 May 20.
Chatterjee K, Gupta T, Goyal A, et al. Association of Obesity With In-Hospital Mortality of Cardiogenic Shock **Complicating Acute Myocardial Infarction**. Am J Cardiol. 2017 Mar 1.
Chavez-Tapia NC, Tellez-Avila FI, Barrientos-Gutierrez T, Mendez-Sanchez N, Lizardi-Cervera J, Uribe M. **Bariatric surgery for non-alcoholic steatohepatitis** in obese patients. Cochrane Database Syst Rev. 2010 Jan 20;(1):CD007340.
Chazelas E, Srour B, Desmetz E, et al. **Sugary drink consumption and risk of cancer**: results from NutriNet-Santé prospective cohort. BMJ. 2019 Jul 10;366:l2408.
Chen Y, Copeland WK, Vedanthan R, et al. Association between body mass index and cardiovascular disease mortality in east Asians and south Asians: pooled analysis of prospective data from the Asia Cohort Consortium. BMJ. 2013 Oct 1;347:f5446.
Chen G, Ratcliffe J, Olds T, et al. **BMI, Health Behaviors, and Quality of Life** in Children and Adolescents: A School-Based Study. Pediatrics. 2014 Mar 3.
Chen GL, Kubat E, Eisenberg D. Prevalence of **anemia 10 years after Roux-en-Y gastric bypass** in a single veterans affairs medical center. JAMA Surg2017. doi:10.1001/jamasurg.2017.3158.
Chen Z, Salam MT, Alderete TL, et al. Effects of **Childhood Asthma** on the Development of Obesity among School-aged Children. Am J Respir Crit Care Med. 2017 Jan 19.
Cheung EL, Bell CS, Samuel JP, et al. **Race and Obesity in Adolescent Hypertension**. Pediatrics. 2017;139(5):e20161433
Chevrot A, Kayem G, Coupaye M, et al. Impact of **bariatric surgery on fetal growth restriction**: experience of a perinatal and bariatric surgery center. Am J Obstet Gynecol 2016;214:655.e1–7.
Childerhose JE, Tarini BA. Understanding Outcomes in **Adolescent Bariatric Surgery**. Pediatrics. 2015 Aug;136(2):e312-4.
Ching CK, Chen SPL, Lee HHC, et al. **Adulteration of proprietary Chinese medicines** and health products with undeclared drugs: experience of a tertiary toxicology laboratory in Hong Kong. Br J Clin Pharmacol. 2017 Oct 1. (esp. sibutramine)
Chirinos JA, Gurubhagavatula I, Teff K, et al. **CPAP, weight loss, or both for obstructive sleep apnea**. N Engl J Med 2014;370: 2265-75.
Chlebowski RT, Luo J, Anderson GL, et al. Weight loss and **breast cancer incidence in postmenopausal women**. Cancer. 2018 Oct 8.

Choi S, Kim K, Kim SM, et al. Association of **Obesity or Weight Change With Coronary Heart Disease** Among Young Adults in South Korea. JAMA Intern Med. 2018 Jun 18.
Choi HK, Zhang Y. **Bariatric surgery as urate-lowering therapy** in severe obesity. Ann Rheum Dis. 2014 May;73(5):791-3.
Chriqui JF, Pickel M, Story M. Influence of school competitive food and beverage policies on obesity, consumption, and availability: a systematic review. JAMA Pediatr. 2014 Mar;168(3):279-86.
Chriqui JF, Turner L, Taber DR, Chaloupka FJ. Association Between **District and State Policies** and US Public Elementary School Competitive Food and Beverage Environments. JAMA Pediatr. 2013 Jun 10:1-9.
Christian NJ, KingWC, Yanovski SZ, Courcoulas AP, Belle SH. **Validity of self-reported weights following bariatric surgery (Labs-2)** [online November 4, 2013]. JAMA. doi:10.1001 /jama.2013.281043.
Christopher RJ, Morgan ME, Tang Y, et al. Pharmacokinetics and Tolerability of **Lorcaserin** in Special Populations: Elderly Patients and Patients with Renal or Hepatic Impairment. Clin Ther. 2017 Mar 29.
Chun S, Choi Y, Chang Y, et al. **Sugar-sweetened carbonated beverage consumption** and coronary artery calcification in asymptomatic men and women. *Am Heart J* 2016.
Chuang J, Zeller MH, Inge T, Crimmins N. **Bariatric Surgery** for Severe Obesity in **Two Adolescents With Type 1 Diabetes**. Pediatrics. 2013 Sep 23.
Claussnitzer M, Dankel SN, Kim K-H, et al. **FTO obesity variant** circuitry and adipocyte browning in humans. N Engl J Med. DOI: 10.1056/NEJMoa1502214.
Cleo G, Glasziou P, Beller E, et al. **Habit-based interventions for weight loss** maintenance in adults with overweight and obesity: a randomized controlled trial. Int J Obes (Lond). 2018 Apr 23.
Cloutier MM, Wiley J, Huedo-Medina T, et al. Outcomes from a **Pediatric Primary Care Weight Management Program**: Steps to Growing Up Healthy. J Pediatr. 2015 Jun 11.
Coates AE, Hardman CA, Halford JCG, et al. **Social Media Influencer Marketing and Children's Food Intake**: A Randomized Trial. Pediatrics. 2019 Mar 4.
Cogswell ME, Gunn JP, Yuan K, Park S, Merritt R. **Sodium and Sugar in Complementary Infant and Toddler Foods** Sold in the United States. Pediatrics. 2015 Feb 2.
Cohen DA, Han B, Nagel CJ, et al. The First National Study of **Neighborhood Parks**: Implications for Physical Activity. Am J Prev Med. 2016 Oct;51(4):419-26.
Cohen JFW, Richardson SA, Cluggish SA, et al. Effects of choice architecture and **chef-enhanced meals** on the selection and consumption of healthier school foods: a randomized clinical trial [online March 23, 2015]. JAMA Pediatr. doi:10.1001/jamapediatrics.2014.3805.
Cohen PA, Maller G, DeSouza R, et al. Presence of **banned drugs in dietary supplements following FDA recalls**. JAMA. 2014 Oct 22 29;312(16):1691-3.
Colchero MA, Popkin BM, Rivera JA, et al. **Beverage purchases from stores in Mexico** under the **excise tax on sugar** sweetened beverages: observational study. BMJ. 2016 Jan 6;352:h6704.
Coles N, Birken C, Hamilton J. **Emerging treatments for severe obesity in children and adolescents**. BMJ. 2016 Sep 29;354:i4116.
Colin P, Eleveld DJ, Struys MM, et al. **Moxifloxacin** dosing in post-bariatric surgery patients. Br J Clin Pharmacol. 2013 Dec 9
Collins, Clare E., Okely, Anthony D., Morgan, Philip J., et al. **Parent Diet Modification, Child Activity**, or Both in Obese Children: An RCT. (at **24 months**) Pediatrics 2011 127: 619-627.
Collin LJ, Judd S, Safford M, et al. Association of **Sugary Beverage Consumption With Mortality Risk in US Adults**: A Secondary Analysis of Data From the REGARDS Study. JAMA Netw Open. 2019 May 3;2(5):e193121.
Colman E. **Food and Drug Administration's (FDA) Obesity Drug Guidance** Document: A Short History. Circulation. 2012 May 1;125(17):2156-64.
Cologne J, Takahashi I, French B, et al. Association of Weight **Fluctuation With Mortality in Japanese Adults**. JAMA Netw Open. 2019 Mar 1;2(3):e190731.
Colquitt JL, Picot J, Loveman E, Clegg AJ. **Surgery for obesity**. Cochrane Database Syst Rev. 2009 Apr 15;(2):CD003641.
Colquitt JL, Pickett K, Loveman E, et al. **Surgery for weight loss in adults**. Cochrane Database Syst Rev. 2014 Aug 8;8:CD003641. Surgery results in greater improvement in weight loss outcomes and weight associated comorbidities compared with non-surgical interventions, regardless of the type of procedures used. When compared with each other, certain procedures resulted in greater weight loss and improvements in comorbidities than others. Outcomes were similar between RYGB and sleeve gastrectomy, and both of these procedures had better outcomes than adjustable gastric banding. For people with very high BMI, biliopancreatic diversion with duodenal switch resulted in greater weight loss than RYGB. Duodenojejunal bypass with sleeve gastrectomy and laparoscopic RYGB had similar outcomes, however this is based on one small trial. Isolated sleeve gastrectomy led to better weight-loss outcomes than adjustable gastric banding after three years follow-up. This was based on one trial only. Weight-related outcomes were similar between laparoscopic gastric imbrication and laparoscopic sleeve gastrectomy in one trial. Across all studies adverse event rates and reoperation rates were generally poorly reported. Most trials followed participants for only one or two years, therefore the long-term effects of surgery remain unclear.
Conason A, Teixeira J, Hsu CH, et al. **Substance Use Following Bariatric Weight Loss Surgery**. Arch Surg. 2012 Oct 15:1-6. (alcohol)
Cornier MA, Deprés JP, Davis N, et al. **Assessing adiposity**: a scientific statement from the American Heart Association (AHA). Circulation2011; DOI: 10.1161/CIR0b013e318233bc6a.
Cortese S, Ramos Olazagasti MA, Klein RG, et al. Obesity in Men With **Childhood ADHD**: A 33-Year Controlled, Prospective, Follow-up Study. Pediatrics. 2013 May 20.
Cortese S, Moreira-Maia CR, St Fleur D, et al. Association Between **ADHD** and Obesity: A Systematic Review and Meta-Analysis. Am J Psychiatry. 2016 Jan;173(1):34-43.
Council on School Health; Committee on Nutrition. **Snacks, sweetened beverages, added sugars, and schools**. Pediatrics. 2015 Mar;135(3):575-83.
Coughlin JW, Brantley PJ, Champagne CM, et al. The impact of continued intervention on weight: **Five-year results from the weight loss maintenance trial**. Obesity (Silver Spring). 2016 May;24(5):1046-53.
Coulman KD, Hopkins J, Brookes ST, et al; BARIACT working group.. A **Core Outcome Set** for the Benefits and Adverse Events of Bariatric and Metabolic Surgery: The **BARIACT** Project. PLoS Med. 2016 Nov 29;13(11):e1002187.
Courcoulas AP, Christian NJ, Belle SH, et al. **Weight change and health outcomes at 3 years after bariatric surgery** among individuals with severe obesity (**LABS**) [online Nov 4, 2013]. JAMA. doi:10.1001/jama.2013.280928.
Courcoulas AP, Goodpaster BH, Eagleton JK, et al. **Surgical vs Medical** Treatments for Type 2 Diabetes Mellitus: A Randomized Clinical Trial. JAMA Surg. 2014 Jun 4.
Courcoulas AP, Yanovski SZ, Bonds D, et al. **Long-term Outcomes of Bariatric Surgery**: A National Institutes of Health Symposium. JAMA Surg. 2014 Oct 1.
Courcoulas AP, Belle SH, Neiberg RH, et al. **Three-Year Outcomes of Bariatric Surgery vs Lifestyle** Intervention for Type 2 Diabetes Mellitus Treatment: A Randomized Clinical Trial. JAMA Surg. 2015 Jul 1.
Courcoulas AP, King WC, Belle SH, et al. **Seven-year weight trajectories and health outcomes in the Longitudinal Assessment of Bariatric Surgery** (**LABS**) Study [online Dec 6, 2017].JAMA Surg. doi:10.1001 /jamasurg.2017.5025
Coutinho T, Goel K, Correa de Sá D, et al. **Combining body mass index with measures of central obesity** in the assessment of mortality in subjects with coronary heart disease. Role of "normal weight central obesity." J Am Coll Cardiol 2012; 61:553-560.
Cnattingius S, Villamor E, Johansson S, et al. **Maternal obesity** and **risk of preterm delivery**. JAMA. 2013 Jun 12;309(22):2362-70.
Cradock AL, Barrett JL, Giles CM, et al. **Promoting Physical Activity** With the **Out of School Nutrition and Physical Activity** (**OSNAP**) Initiative: A Cluster-Randomized Controlled Trial. JAMA Pediatr. 2015 Dec 7:1-9.
Crane MM, Lutes LD, Ward DS, et al. A randomized trial testing the efficacy of a **novel approach to weight loss among men** with overweight and obesity. Obesity (Silver Spring). 2015 Dec;23(12):2398-405.
Creatore MI, Glazier RH, Moineddin R, et al. Association of neighborhood walkability with change in overweight, obesity, and diabetes.JAMA. doi:10.1001/jama.2016.5898.
Cresswell JA, Campbell OM, De Silva MJ, Filippi V. Effect of maternal obesity on **neonatal death** in sub-Saharan Africa: multivariable analysis of 27 national datasets. Lancet. 2012 Aug 8.
Crosbie E, Schillinger D, Schmidt LA. State Preemption to Prevent Local **Taxation of Sugar-Sweetened Beverages**. JAMA Intern Med. 2019 Jan 22.

Crockett RA, King SE, Marteau TM, et al. **Nutritional labelling for healthier food or non-alcoholic drink purchasing and consumption**. Cochrane Database of Systematic Reviews 2018, Issue 2. Art. No.: CD009315. Findings from a small body of low-quality evidence suggest that nutritional labelling comprising energy information on menus may reduce energy purchased in restaurants. The evidence assessing the impact on consumption of energy information on menus or on a range of food options in laboratory settings suggests a similar effect to that observed for purchasing, although the evidence is less definite and also of low quality.

Crume TL, Ogden L, Maligie M, et al. Long-Term Impact of Neonatal **Breastfeeding** on Childhood Adiposity and Fat Distribution Among Children Exposed to Diabetes In Utero. Diabetes Care Mar 2011 34:641-645.

Crume TL, Ogden L, Daniels S, Hamman RF, Norris JM, Dabelea D. The Impact of **In Utero Exposure to Diabetes** on Childhood Body Mass Index Growth Trajectories: The EPOCH Study. J Pediatr. 2011 Jun;158(6):941-6.

Cummings DE, Arterburn DE, Westbrook EO, et al. **Gastric bypass surgery vs intensive lifestyle** and medical intervention for type 2 **diabetes**: the **CROSSROADS** randomised controlled trial. Diabetologia. 2016 May;59(5):945-53.

Cunningham SA, Kramer MR, Narayan KMV. **Incidence of childhood obesity in the United States**. N Engl J Med 2014;370: 403-11.

Curioni C, Andre C. **Rimonabant** for overweight or obesity. Cochrane Database Syst Rev. 2006 Oct 18;(4):CD006162. Compared with placebo, rimonabant 20 mg produced a 4.9 kg greater reduction in body weight in trials with one-year results. The use of rimonabant after one year produces modest weight loss of approximately 5%. Even modest amounts of weight loss may be potentially beneficial. The observed results should be interpreted with some caution, though, since the evaluated studies presented some deficiencies in methodological quality. Studies with longer follow-ups after the end of treatment and of more rigorous quality should be done before definitive recommendations can be made regarding the role of this new medication in the management of overweight or obese patients.

Daepp MIG, Gortmaker SL, Wang YC, et al. **WIC Food Package Changes**: Trends in Childhood Obesity Prevalence. Pediatrics. 2019 Apr 1.

Dalbeth N, Chen P, White M, et al. Impact of **bariatric surgery on serum urate targets** in people with morbid obesity and diabetes: a prospective longitudinal study. Ann Rheum Dis 2014;73:797–802.

Daly N, Farren M, McKeating A, et al. A Medically Supervised **Pregnancy Exercise Intervention** in Obese Women: A Randomized Controlled Trial. Obstet Gynecol. 2017 Nov;130(5):1001-1010.

Dangardt F, Charakida M, Georgiopoulos G, et al. Association between fat mass through adolescence and arterial stiffness: a population-based study from The Avon Longitudinal Study of Parents and Children. Lancet Child Adolesc Health. 2019 May 21.

Daniels LA, Mallan KM, Nicholson JM, et al. Outcomes of an **Early Feeding Practices** Intervention to Prevent Childhood Obesity. Pediatrics. 2013 Jun 10.

Daniels LA, Mallan KM, Nicholson JM, et al. An **Early Feeding Practices** Intervention for Obesity Prevention. Pediatrics. 2015 Jun 8.

Daniels SR, Hassink SG; Committee on Nutrition. The Role of the **Pediatrician in Primary Prevention of Obesity**. Pediatrics. 2015 Jun 29.

Danielsson P, Kowalski J, Ekblom O, Marcus C. Response of **severely obese children and adolescents to behavioral treatment** [online October 29, 2012]. Arch Pediatr Adolesc Med. doi:10.1001/2013.jamapediatrics.319.

Danne T, et al. **Liraglutide** in an **Adolescent** Population with Obesity: Randomized,Double-Blind, Placebo-Controlled 5-Week Trial to Assess Safety, Tolerability, and Pharmacokinetics of Liraglutide in Adolescents Aged 12-17 Years. J Pediatr. 2016 Dec 13.

Dansinger ML, Gleason JA, Griffith JL, Selker JP, Schaefer EJ. **Comparison of the Atkins, Ornish, Weight Watchers, and Zone** diets for weight loss and heart disease risk reduction: a randomized trial. JAMA 2005;293:43-53.

Daraki V, Roumeliotaki T, Chalkiadaki G, et al. Low maternal **vitamin D status in pregnancy** increases the risk of childhood obesity. Pediatr Obes. 2018 Jan 28.

Darmasseelane K, Hyde MJ, Santhakumaran S, et al. **Mode of delivery** and offspring body mass index, overweight and obesity in adult life: a systematic review and meta-analysis. PLoS One. 2014 Feb 26;9(2)

Datar A, Nicosia N. Association of **exposure to communities with higher ratios of obesity** with increased body mass index and risk of overweight and obesity among parents and children [online Jan 22, 2018]. JAMA Pediatr. doi:10.1001 /jamapediatrics.2017.4882

Daubenmier J, Moran PJ, Kristeller J, et al. Effects of a **mindfulness-based weight loss intervention** in adults with obesity: A randomized clinical trial. Obesity (Silver Spring). 2016 Mar 9.

Daumit GL, Dickerson FB, Wang NY, et al. A **Behavioral Weight-Loss Intervention in Persons with Serious Mental Illness**. N Engl J Med. 2013 Mar 21.

Davidson LE, Adams TD, Kim J, et al. Association of **patient age** at **gastric bypass surgery** with long-term all-cause and cause-specific **mortality** [online February 10, 2016].JAMA Surg. doi:10.1001/jamasurg.2015.5501.

Davidson MH, Tonstad S, Oparil S, et al. Changes in cardiovascular risk associated with **phentermine and topiramate extended-release** in participants with comorbidities and a body mass index >27. (**CONQUER**) Am J Cardiol 2013 .

Davies GA, Maxwell C, McLeod L, et al., Society of Obstetricians and Gynaecologists of Canada. **Obesity in pregnancy**. (**SOGC**) J Obstet Gynaecol Can 2010 Feb;32(2):165-73.

Davies MJ, Bergenstal R, Bode B, et al. Efficacy of **Liraglutide** for **Weight Loss** Among Patients With Type 2 Diabetes: The **SCALE** Diabetes Randomized Clinical Trial. JAMA. 2015 Aug 18;314(7):687-99.

Davies MJ, Aronne LJ, Caterson ID, et al; Satiety and Clinical Adiposity – **Liraglutide** Evidence in individuals with and without diabetes (**SCALE**) study groups. Liraglutide and cardiovascular outcomes in adults with overweight or obesity: A post hoc analysis from SCALE randomized controlled trials. Diabetes Obes Metab. 2017 Sep 26.

Davis CL, Pollock NK, Waller JL, et al. **Exercise dose** and diabetes risk in overweight and obese children: a randomized controlled trial. JAMA. 2012 Sep 19;308(11):1103-12.

Dawes AJ, Maggard-Gibbons M, Maher AR, et al. **Mental Health Conditions** Among Patients Seeking and Undergoing **Bariatric Surgery**: A Meta-analysis. JAMA. 2016 Jan 12;315(2):150-163.

Davoli AM, Broccoli S, Bonvicini L, et al. **Pediatrician-led Motivational Interviewing** to Treat Overweight Children: An RCT. Pediatrics. 2013 Oct 21.

de Boer IH, Katz R, Fried LF, et al. Obesity and change in **estimated GFR** among older adults. Am J Kidney Dis. 2009 Dec;54(6):1043-51. Epub 2009 Sep 25.

de la Haye K, Dijkstra JK, Lubbers MJ, et al. The dual role of **friendship and antipathy** relations in the marginalization of overweight children in their peer networks: The TRAILS Study. PLoS One. 2017 Jun 7;12(6):e0178130.

de Ferranti SD, Milliren CE, Denhoff ER, et al. **Providing food to treat adolescents** at risk for cardiovascular disease. Obesity (Silver Spring). 2015 Oct;23(10):2109-17.

De Jong A, Jung B, Chanques G, et al. **Obesity and mortality in critically ill patients**: another case of the simpson paradox? Chest. 2012 Jun;141(6):1637-8.

de Oliveira Otto MC, Anderson CAM, Dearborn JL, et al. **Dietary Diversity**: Implications for **Obesity Prevention in Adult Populations: A Science Advisory From the American Heart Association (AHA)**. Circulation. 2018 Sep 11;138(11):e160-e168.

de Ruyter JC, Olthof MR, Seidell JC, Katan MB. A trial of **sugar-free or sugar-sweetened beverages** and body weight in children. N Engl J Med 2012; DOI:10.1056/NEJMoa1203034. Available at: http://www.nejm.org.

de Vries HJ, Kooiman TJ, van Ittersum MW, et al. Do **activity monitors** increase physical activity in adults with overweight or obesity? A systematic review and meta-analysis. Obesity (Silver Spring). 2016 Oct;24(10):2078-91.

de Zwaan M, Herpertz S, Zipfel S, et al. Effect of **Internet**-Based Guided **Self**-**help** vs **Individual Face**-**to**-**Face** Treatment on Full or Subsyndromal **Binge Eating** Disorder in Overweight or Obese Patients: The INTERBED Randomized Clinical Trial. JAMA Psychiatry. 2017 Aug 2.

Deboer MD, Scharf RJ, Demmer RT. **Sugar-Sweetened Beverages** and Weight Gain in 2- to 5-Year-Old Children. Pediatrics. 2013 Aug 5.

Dehghani P, Habib B, Windle SB, et al. **Smokers and Postcessation Weight Gain** After Acute Coronary Syndrome. J Am Heart Assoc. 2017 Apr 18;6(4)

Dehlendorff C, Andersen KK, Olsen TS. Body Mass Index and **Death by Stroke**: No Obesity Paradox. JAMA Neurol. 2014 Jun 2.

DeMaria EJ. **Bariatric surgery** for morbid obesity. N Engl J Med. 2007 May 24;356(21):2176-83.

Dennis EA, Dengo AL, Comber DL, et al. **Water consumption** increases weight loss during a hypocaloric diet intervention in middle-aged and older adults. Obesity (Silver Spring). 2010 Feb;18(2):300-7. Epub 2009 Aug 6.

Depommier C, Everard A, Druart C, et al. **Supplementation with Akkermansia muciniphila** in overweight and obese human volunteers: a proof-of-concept exploratory study. Nat Med. 2019 Jul 1.

Deshpande G, Mapanga RF, Essop MF. Frequent **Sugar-Sweetened Beverage Consumption** and the Onset of Cardiometabolic Diseases: Cause for Concern? J Endocr Soc. 2017 Nov 2;1(11):1372-1385.

Desilets A, Dhakal-Karki S, Dunican K. Role of metformin for weight management in patients without type 2 diabetes. Ann Pharmacother 2008;42:817-26.

Dhana K, Haines J, Liu G, et al. Association between **maternal adherence to healthy lifestyle practices and risk of obesity in offspring**: results from two prospective cohort studies of mother-child pairs in the United States. BMJ. 2018 Jul 4;362:k2486.

Dhingra R, Sullivan L, Jacques PF, et al. **Soft drink consumption** & risk of developing cardiometabolic risk factors and the metabolic syndrome in middle-aged adults in the community. Circulation 2007; DOI: 0.1161/circulationaha.107.689935.

Dhurandhar EJ, Dawson J, Alcorn A, et al. The effectiveness of **breakfast** recommendations on weight loss: a randomized controlled trial. Am J Clin Nutr. 2014 Jun 4.

Dias KA, Green DJ, Ingul CB, et al. **Exercise and Vascular Function** in Child Obesity: A Meta-Analysis. Pediatrics. 2015 Aug 10.

Dietary Guidelines for Americans (DGA) 2010. Full Guideline: http://www.health.gov/dietaryguidelines/dga2010/DietaryGuidelines2010.pdf, Summary: http://www.cnpp.usda.gov/Publications/DietaryGuidelines/2010/PolicyDoc/ExecSumm.pdf

Dietz WH, Baur LA, Hall K, et al. **Management of obesity**: improvement of health-care training and systems for prevention and care. Lancet. 2015 Feb 18.

Dimick JB, Nicholas LH, Ryan AM, et al. **Bariatric surgery complications** before vs after implementation of a national policy **restricting coverage to centers of excellence**. JAMA. 2013 Feb 27;309(8):792-9.

Dimick JB, Birkmeyer NJ, Finks JF, et al. Composite **Measures for Profiling Hospitals** on **Bariatric Surgery Performance**. JAMA Surg. 2013 Oct 16.

Ding SA, Simonson DC, Wewalka M, et al. **Adjustable Gastric Band Surgery or Medical Management** in Patients with Type 2 Diabetes: a Randomized Clinical Trial. J Clin Endocrinol Metab. 2015 Apr 24

Disantis KI, Birch LL, Davey A, et al. **Plate Size** and Children's Appetite: Effects of Larger Dishware on Self-Served Portions and Intake. Pediatrics. 2013 Apr 8.

Dixon JB, O'Brien PE, Playfair J, et al. Adjustable **gastric banding** and conventional therapy for type 2 diabetes: a randomized controlled trial. JAMA. 2008 Jan 23;299(3):316-23. Participants randomized to surgical therapy were more likely to achieve remission of type 2 diabetes through greater weight loss.

Dixon JB, le Roux CW, Rubino F, Zimmet P. **Bariatric surgery** for **type 2 diabetes**. Lancet. 2012 Jun 8.

Dixon JB, Straznicky NE, Lambert EA et al. **Laparoscopic adjustable gastric banding** and other devices for the management of obesity. Circulation. 2012 Aug 7;126(6):774-85.

Dixon JB, Schachter LM, O'Brien PE, et al. **Surgical vs conventional** therapy for weight loss treatment of obstructive **sleep apnea**: a randomized controlled trial. JAMA. 2012;308(11):1142-1149.

Dobbins M, Husson H, DeCorby K, et al. **School-based physical activity programs** for promoting physical activity and fitness in **children and adolescents** aged 6 to 18. Cochrane Database Syst Rev. 2013 Feb 28;2:CD007651. doi: 10.1002/14651858.CD007651.pub2. The evidence suggests the ongoing implementation of school-based physical activity interventions at this time, given the positive effects on behavior and one physical health status measure. However, given these studies are at a minimum of moderate risk of bias, and the magnitude of effect is generally small, these results should be interpreted cautiously. Additional research on the long-term impact is needed.

Dodd JM, Grivell RM, Crowther CA, Robinson JS. Antenatal interventions for **overweight or obese pregnant women**: a systematic review of randomised trials. BJOG. 2010 Oct;117(11):1316-26. This meta-analysis of randomized trials of antenatal dietary or exercise interventions for overweight or obese pregnant women identified no credible improvement in outcomes for the mothers or their newborns. (LOE = 1a-)

Dodd JM, Turnbull D, McPhee AJ, Duessen AR, Grivell RM, Yelland LN, et al. **Antenatal lifestyle advice** for women who are overweight or obese: LIMIT randomised trial. BMJ 2014;348:g1285.

Dolan P, Afaneh C, Symer M, et al. Assessment of **Public Attitudes Toward Weight Loss Surgery** in the United States. JAMA Surg. 2018 Dec 12.

Dombrowski SU, Knittle K, Avenell A, et al. **Long term maintenance of weight loss with non-surgical interventions** in obese adults: systematic review and meta analyses of randomised controlled trials. British Medical Journal 348 (2014).

Donin AS, Nightingale CM, Owen CG, et al. **Takeaway meal consumption** and risk markers for coronary heart disease, type 2 diabetes and obesity in children aged 9-10 years: a cross-sectional study. Arch Dis Child. 2017 Dec 3.

Donnellan E, Wazni OM, Kanj M, et al. Association between **pre-ablation bariatric surgery and atrial fibrillation** recurrence in morbidly obese patients undergoing atrial fibrillation ablation. Europace. 2019 Jul 15.

Döring N, Ghaderi A, Bohman B, et al. **Motivational Interviewing** to Prevent Childhood Obesity: A Cluster RCT. Pediatrics. 2016 May;137(5).

Dorman RB, Miller CJ, Leslie DB, et al. Risk for **hospital readmission following bariatric surgery**. PLoS One. 2012;7(3):e32506.

Douglas IJ, Langham J, Bhaskaran K, et al. **Orlistat and the risk of acute liver injury**: self controlled case series study in UK Clinical Practice Research Datalink. BMJ. 2013 Apr 12;346:f1936.

Douglas IJ, Bhaskaran K, Batterham RL, et al. The Effectiveness of **Pharmaceutical Interventions for Obesity**: Weight Loss With **Orlistat and Sibutramine** in a United Kingdom Population-Based Cohort. Br J Clin Pharmacol. 2014 Dec 31.

Douglas IJ, Bhaskaran K, Batterham RL, et al. **Bariatric Surgery in the United Kingdom**: A Cohort Study of Weight Loss and Clinical Outcomes in Routine Clinical Care. PLoS Med. 2015 Dec 22;12(12):e1001925.

Drager LF, Brunoni AR, Jenner R, et al. Effects of **CPAP on body weight** in patients with obstructive sleep apnoea: a meta-analysis of randomised trials. Thorax. 2014 Nov 28.

Drake KM, Beach ML, Longacre MR, et al. Influence of **Sports, Physical Education, and Active Commuting** to School on Adolescent Weight Status. Pediatrics. 2012 Jul 16.

Dreyfus J, Jacobs DR Jr, Mueller N, et al. **Age at Menarche** and Cardiometabolic Risk in Adulthood: The Coronary Artery Risk Development in Young Adults Study. J Pediatr. 2015 May 8.

Drugs Associated with weight gain. Pharmacist's Letter Mar 2007.

Duffey Kiyah J.; Gordon-Larsen Penny; Shikany James M.; et al. **Food Price and Diet** and Health Outcomes: 20 Years of the CARDIA Study. Arch Intern Med. 2010;170(5):420-426.

Dumanovsky T, Huang CY, Nonas CA, et al. **Changes in energy content of lunchtime purchases from fast food** restaurants after introduction of **calorie labelling**: cross sectional customer surveys. BMJ 2011;343:d4464.

Durrer Schutz D, Busetto L, Dicker D, et al. **European Practical and Patient-Centred Guidelines for Adult Obesity** Management in Primary Care. Obes Facts. 2019;12(1):40-66. (EASO)

Dushay J, Gao C, Gopalakrishnan GS, et al. Short-term **exenatide** treatment leads to significant weight loss in a subset of obese women without diabetes. Diabetes Care. 2012 Jan;35(1):4-11.

Eather N, Morgan PJ, Lubans DR. Improving the fitness and physical activity levels of primary school children: Results of the **Fit-4-Fun** group randomized controlled trial. Prev Med. 2013 Jan;56(1):12-9.

Eaton CB, Hartman SJ, Perzanowski E, et al. A Randomized Clinical Trial of a **Tailored Lifestyle Intervention** for Obese, Sedentary, Primary Care Patients. Ann Fam Med. 2016 Jul;14(4):311-9.

Ebbeling CB, Swain JF, Feldman HA, et al. Effects of **dietary composition on energy expenditure** during weight-loss maintenance.JAMA 2012; 307:2627-2634.

Ebbeling CB, Feldman HA, Chomitz VR, et al. A randomized trial of **sugar-sweetened beverages** and adolescent body weight. N Engl J Med 2012; DOI:10.1056/NEJMoa1203388. Available at: http://www.nejm.org.

Ebbeling CB, Feldman HA, Klein GL, et al. Effects of a **low carbohydrate diet on energy expenditure** during weight loss maintenance: randomized trial. BMJ. 2018 Nov 14;363:k4583.

Eckel N, Li Y, Kuxhaus O, et al. Transition from metabolic healthy to unhealthy phenotypes and association with **cardiovascular disease risk across BMI categories in 90257 women** (the Nurses' Health Study): 30 year follow-up from a prospective cohort study. Lancet Diabetes Endocrinol 2018; published online May 30. FDA Jun/18: Liquid-filled Intragastric Balloons by Apollo Endosurgery and ReShape Lifesciences: Letter to Health Care Providers - New Labeling About Potential Risks.

Eckel RH. Clinical practice. **Nonsurgical management of obesity in adults**. N Engl J Med. 2008 May 1;358(18):1941-50.

Edelman S, et al. A double-blind, placebo-controlled trial assessing **pramlintide** treatment in the setting of intensive insulin therapy in type 1 diabetes. Diabetes Care. 2006 Oct;29(10):2189-95.

Ehrlich SF, Hedderson MM, Xu F, Ferrara A. **Diagnostic thresholds for pregnancy hyperglycemia**, maternal weight status and the risk of childhood obesity in a diverse Northern California cohort using health care delivery system data. PLoS One. 2019 May 10;14(5):e0216897.

Eid GM, McCloskey CA, Eagleton JK, et al. **StomaphyX vs a Sham** Procedure for Revisional Surgery to Reduce Regained Weight in Roux-en-Y Gastric Bypass Patients : A Randomized Clinical Trial. JAMA Surg. 2014 Feb 19.

Eisenberg MJ, Atallah R, Grandi SM, Windle SB, Berry EM. **Legislative approaches** to tackling the obesity epidemic. CMAJ. 2011 May 2.

Ejlerskov KT, Sharp SJ, Stead M, et al. **Supermarket policies on less-healthy food at checkouts**: Natural experimental evaluation using interrupted time series analyses of purchases. PLoS Med. 2018 Dec 18;15(12):e1002712.

Ek A, Lewis Chamberlain K, Sorjonen K, et al. A **Parent Treatment Program for Preschoolers With Obesity**: A Randomized Controlled Trial. Pediatrics. 2019 Jul 12.

Elbel B, Cantor J, Mijanovich T. Potential effect of the New York City policy regarding **sugared beverages**. N Engl J Med. 2012 Aug 16;367(7):680-1.

Elbel B, Mijanovich T, Dixon LB, et al. **Calorie labeling, Fast food purchasing and restaurant visits**. Obesity (Silver Spring). 2013 Oct 17.

Eder L, Thavaneswaran A, Chandran V, et al. Obesity is associated with a lower probability of achieving sustained minimal disease activity state among patients with **psoriatic arthritis**. Ann Rheum Dis. 2014 Jan 15.

Eliassen AH, et al. Adult weight change and risk of postmenopausal **breast cancer**. JAMA. 2006 Jul 12;296(2):193-201.

Elks CE, Heude B, de Zegher F, et al. Associations Between **Genetic Obesity Susceptibility and Early Postnatal Fat and Lean Mass**: An Individual Participant Meta-analysis. JAMA Pediatr. 2014 Oct 20.

Elnahas A, Jackson TD, Okrainec A, et al. The effect of the **Ontario** Bariatric Network on **health services utilization after bariatric surgery**: a retrospective cohort study. CMAJ Open. 2016 Sep 14;4(3):E489-E495

Emerging Risk Factors Collaboration. Separate and combined associations of **body-mass index and abdominal adiposity** with cardiovascular disease: collaborative analysis of 58 prospective studies.Lancet 2011;online Mar11/11.

Emery CF, Olson KL, Bodine A, et al. **Dietary intake** mediates the relationship of body fat to pain. Pain. 2017 Feb;158(2):273-277.

Emmons KM, Doubeni CA, Fernandez ME, et al. National Institutes of Health Pathways to Prevention Workshop: Methods for Evaluating Natural Experiments in Obesity. Ann Intern Med. 2018 May 1.

Emond JA, Bernhardt AM, Gilbert-Diamond D, et al. Commercial **Television Exposure, Fast Food Toy Collecting, and Family Visits to Fast Food Restaurants** among Families Living in Rural Communities. J Pediatr. 2015 Oct 22.

Emond JA, Smith ME, Mathur SJ, et al. **Children's Food and Beverage Promotion on Television** to Parents. Pediatrics. 2015 Nov 9.

Emond JA, Lasigan RK, Ramanujam A et al. Randomized Exposure to **Food Advertisements** and Eating in the Absence of Hunger Among Prescholers. Pediatrics.2016;138(6):e20162361

Edmonson MB, Eickhoff JC. **Weight gain and obesity** in infants and young children exposed to **prolonged antibiotic prophylaxis** [online Dec 27, 2016].JAMA Pediatr. doi:10.1001 /jamapediatrics.2016.3349

Endres LK, Straub H, McKinney C, et al. Community Child Health Network of the Eunice Kennedy Shriver National Institute of Child Health and Human Development. **Postpartum weight retention** risk factors and relationship to obesity at 1 year. Obstet Gynecol. 2015 Jan;125(1):144-52.

Eng DS, Gebremariam A, Meeker JD, Peterson K, Padmanabhan V, Lee JM. **Bisphenol A** and chronic disease risk factors in US children. Pediatrics. 2013;132(3).

Epstein LH, et al. A randomized trial of the effects of reducing **television viewing and computer use** on body mass index in young children. Arch Pediatr Adolesc Med. 2008 Mar;162(3):239-45. Reducing television viewing and computer use may have an important role in preventing obesity and in lowering BMI in young children, and these changes may be related more to changes in energy intake than to changes in physical activity.

Eriksson MK, Hagberg L, Lindholm L, et al. **Quality of Life and Cost-effectiveness** of a 3-Year Trial of **Lifestyle** Intervention in Primary Health Care. Arch Intern Med. 2010 Sep 13;170(16):1470-9.

Erlandson M, Ivey LC, Seikel K. Update on **Office-Based Strategies** for the Management of Obesity. Am Fam Physician. 2016;94(5):361-368.

Ersoy A, Baran B, Ersoy C, Kahvecioglu S, Akdag I. Calcineurin inhibitors and post-transplant weight gain. Nephrology (Carlton). 2008 Mar 5; [Epub ahead of print] Only pretransplant BMI, creatinine clearance, **cyclosporine A** usage, being hypertensive and dysplipidemic were independent predictors of weight gain at the 12th month. Our results suggested that the type of immunosuppression may affect post-transplant weight gain.

Ervin RS, Kit BK, Carroll MD, Ogden CL. **Consumption of added sugar** among US children and adolescents, 2005-2008. NCHS data brief, 87, March 2012.

Erythropel HC, Kong G, deWinter TM, et al. Presence of **High-Intensity Sweeteners in Popular Cigarillos of Varying Flavor Profiles**. JAMA. 2018 Oct 2 ;320(13):1380-1383.

Espeland MA, Lewis CE, Bahnson J, et al. Impact of weight loss on **ankle-brachial index and interartery blood pressures**.Obesity (Silver Spring). 2014 Apr;22(4):1032-41.

Estruch R, et al. Effect of a **high-fat Mediterranean diet** on bodyweight and waist circumference: a prespecified secondary outcomes analysis of the **PREDIMED** randomised controlled trial. Lancet Diabetes Endocrinol. 2016 Aug;4(8):666-76.

Estruch R, Ros E, Salas-Salvadó J, et al. Primary **Prevention of Cardiovascular Disease with a Mediterranean Diet** Supplemented with Extra-Virgin Olive Oil or Nuts. (**PREDIMED**) N Engl J Med. 2018 Jun 13.

Fakhouri TH, Hughes JP, Brody DJ, et al. **Physical Activity and Screen-Time** Viewing Among Elementary School-Aged Children in the United States From 2009 to 2010. JAMA Pediatr. 2013 Jan 7:1-7.

Faith MS, Hittner JB, Hurston SR, et al; SWIFT Offspring Study Investigators. **Association of Infant Temperament With Subsequent Obesity** in Young Children of Mothers With Gestational Diabetes Mellitus. JAMA Pediatr. 2019 Mar 11.

Faith MS, Van Horn L, Appel LJ,et al. Evaluating **Parents and Adult Caregivers as "Agents of Change**" for Treating Obese Children: Evidence for Parent Behavior Change Strategies and Research Gaps: A Scientific Statement From the American Heart Association (AHA). Circulation. 2012 Mar 6;125(9):1186-1207.

Falbe J, Rosner B, Willett WC, Sonneville et al. Adiposity and different types of **screen time**. Pediatrics. 2013 Dec;132(6):e1497-505.

Fariello RM, Pariz JR, Spaine DM, et al. Association between **obesity and alteration of sperm** DNA integrity and mitochondrial activity. BJU Int. 2012 Feb 2.

Farrant B, Utter J, Ameratunga S, et al. Prevalence of **severe obesity among New Zealand adolescents** and associations with health risk behaviors and emotional well being. J Pediatr 2013.

Faulkner G, Cohn TA. Pharmacologic and nonpharmacologic strategies for weight gain and metabolic disturbance in patients treated with **antipsychotic** medications. Can J Psychiatry. 2006 Jul;51(8):502-11. Review. Erratum in: Can J Psychiatry. 2006 Aug;51(9):620. Although difficult, the prevention of weight gain and the promotion of weight loss are possible for individuals treated with antipsychotic medications. Further research, including diabetes prevention studies, is required. We suggest a pathway for the management of weight gain and emerging metabolic disturbance.

Faulkner JL, Kennard S, Huby AC, et al. **Progesterone Predisposes Females to Obesity**-Associated Leptin-Mediated Endothelial Dysfunction via Upregulating Endothelial MR (Mineralocorticoid Receptor) Expression. Hypertension. 2019 Sep;74(3):678-686.

Fedorka PN, Murali SB, Rajaratnam DR. **Abdominal Pain and Vomiting in a Pregnant Woman Who Has Had a Gastric Bypass Procedure**. JAMA. 2019 Feb 20.

FDA approves **Orlistat for OTC**, Pharmacist's Letter Mar 2007.

FDA Nov/08 Fashion Sanctuary announced a recall of **Zhen De Shou Fat Loss** Capsules because FDA analysis found the product to contain undeclared sibutramine, an FDA approved drug used as an appetite suppressant for weight loss.

FDA Jan/09 notified consumers not to take Venom **HYPERDRIVE 3.0**, a product sold as a dietary supplement but containing sibutramine.

FDA Mar/09 Herbal **Xenicol** (found to contain cetilistat, an obesity drug not approved in the U.S.) along with **Slimbionic** and **Xsvelten** (both containing sibutramine, a prescription-only weight loss drug) have been added to the list of tainted dietary supplements. There are now **72 products** on the list. http://www.fda.gov/bbs/topics/NEWS/2009/NEW01977.html

FDA Apr/09: **ABC Beauty Supply** & FDA notified consumers and healthcare professionals of a recall of 34 dietary supplement products. FDA lab analyses identified undeclared **sibutramine**, an FDA- approved drug, used as an appetite suppressant for weight loss. http://www.fda.gov/oc/po/firmrecalls/universalabc04_09.html **(34 products listed)**

FDA July/09 notified healthcare professionals that four weight loss dietary supplements sold and marketed by the firm (**Slimbionic, One Weight Loss Pill, SlimDemand Capsules, Botanical Weight Loss**) contain sibutramine.

FDA Aug/09 notified healthcare professionals and patients that it is reviewing new safety information regarding reports of liver-related adverse events in patients taking orlistat. **Orlistat** is marketed in the United States as a prescription product, Xenical, and as an over-the-counter (OTC) product, Alli. Between 1999 and October 2008, 32 reports of serious liver injury, including **6 cases of liver failure**, in patients using orlistat were submitted to FDA's Adverse Event Reporting System. The most commonly reported adverse events described in the 32 reports of serious liver injury were jaundice, weakness, and abdominal pain.

FDA Nov/09 & GMP Herbal Products notified consumers and healthcare professionals of a recall of **Pai You Guo**, a weight loss dietary supplement, due to the presence sibutramine & phenolphthalein.

FDA 2010: Orlistat n=13 severe liver injury https://www.fda.gov/drugs/drugsafety/postmarketdrugsafetyinformationforpatientsandproviders/ucm213038.htm

FDA Jan/10 notified consumers and healthcare professionals about a counterfeit and potentially harmful version of **Alli 60 mg capsules** (120 count refill kit). The **counterfeit** version contained the controlled substance sibutramine and did not contain orlistat, the active ingredient.

FDA July/10 analysis of **Que She** found that it contains: fenfluramine – a stimulant drug withdrawn from the U.S. market in 1997 after studies demonstrated that it caused serious heart valve damage, propranolol – a prescription beta blocker drug that can pose a risk to people with bronchial asthma and certain heart conditions, sibutramine – a controlled substance and prescription weight loss drug, sibutramine was the subject of a recent study whose preliminary findings showed an association between sibutramine use and increased risk of heart attack and stroke in patients who have a history of heart disease, & ephedrine – a stimulant drug that is legally marketed over-the-counter for temporary relief of asthma but can pose a risk to people with certain cardiovascular conditions.

FDA Aug/10 lab analysis of **Solo Slim** was found to contain the undeclared drug ingredient Didesmethyl Sibutramine.

FDA July/10 lab analysis of **Slim-30** Herb Supplement distributed by the company was found to contain undeclared N-Desmethyl Sibutramine and traces of Sibutramine.

FDA July/10 lab analysis of this herb supplement, **Joyful Slim** Herb Supplement, was found to contain the undeclared drug, desmethyl sibutramine.

FDA Oct/10 notified consumers that **Slimming Beauty Bitter Orange Slimming Capsules** contain the active pharmaceutical ingredient sibutramine, a prescription-only drug which is a stimulant.

FDA Oct/10 Abbott Laboratories notified healthcare professionals and patients about the **voluntary withdrawal of Meridia (sibutramine)**, from the U.S. market because of clinical trial data indicating an increased risk of heart attack and stroke.

FDA Dec/10 has received multiple reports of adverse events associated with the use of **Fruta Planta**, including several cardiac events and one death. FDA laboratory analysis confirmed that Fruta Planta contains sibutramine.

FDA Jan/11 laboratory analysis confirmed that **Celerite Slimming Capsules** contain sibutramine

FDA Mar/11 lab analysis of **Svelte 30** orange & gray capsules determined that the product contains Sibutramine.

FDA Mar/11 notified Biotab Nutraceuticals, Inc. that two lots of counterfeit product purporting to be **Extenze** contain undeclared drug ingredients. Specifically, lot 0709241 contains tadalafil and sildenafil, and lot 0509075 contains tadalafil and sibutramine.

FDA Mar/11 laboratory analyses of **Celerite Slimming Tea**: Recall - were found to contain undeclared Sibutramine.

FDA May/11 laboratory analysis confirmed that "**Slim Xtreme Herbal Slimming Capsule**" contains sibutramine.

FDA July/11 is advising consumers not to purchase or use "**Slim Forte Slimming Capsules**," "**Slim Forte Slimming Coffee**," and "**Botanical Slimming Soft Gel & Slim Forte Double Power Slimming Capsules**. FDA laboratory analysis confirmed that these products contain sibutramine.

FDA Dec/11 took joint action against several companies selling over-the-counter **hCG products** that falsely and illegally claim to promote weight loss. Labeled "homeopathic" by the seven companies who received the letters, the products contain human chorionic gonadotropin (hCG), a hormone produced during pregnancy by cells that form the placenta. 1. HCG Diet Direct LLC- HCG Diet Homeopathic Drops, 2. The hCG Drops LLC- Homeopathic HCG, 3. HCG Platinum LLC; RightWay Nutrition- HCG Platinum, HCG Platinum X-30, HCG Platinum X-14, 4. Nutri Fusion Systems LLC- HCG Fusion 30, HCG Fusion 43, 5. www.resetthebody.com; www.theoriginalhcgdrops.com-Homeopathic Original HCG, Homeopathic HCG, 6. Hcg-miracleweightloss.com- HCG Extra Weight Loss Homeopathic Drops, 7. Natural Medical Supply- Alcohol Free hCG Weight Loss Formula.

FDA Feb/12 **Healthy People Co.** notified the public of a recall of the company's dietary supplements sold under the brand names Healthy People Co. FDA lab analysis confirmed the presence of Sibutramine and Tadalafil, making these products unapproved new drugs. (**Mince Belle Dietary Supplement, PERFECT Men Dietary Supplement , EVERLAX Dietary Supplement, EVER Slim Dietary Supplement, Herbal Drink Acai-man Mangosteen Dietary Supplement, EVER SLIM Shake Mix Dietary Supplement**)

FDA Feb/12 is advising consumers not to purchase or use "**Japan Weight Loss Blue**," a product for weight loss sold on various websites, laboratory analysis confirmed that "Japan Weight Loss Blue" contains sibutramine, analogs of sibutramine, and ephedrine alkaloids.

FDA Apr/12 laboratory analysis confirmed that "**Japan Rapid Weight Loss Diet Pills Yellow**" contains sibutramine and phenolphthalein.

FDA Oct/12 is advising consumers not to purchase or use "**Ultimate Formula Bee Pollen Capsules (Ultimate Formula)**," or "**Zi Xiu Tang Bee Pollen Capsules**," also referred to as "**Zi Xiu Tang Beauty, Face & Figure Capsule**," products promoted and sold for weight loss because they contain sibutramine.

FDA Dec/12 is advising consumers not to purchase or use "**SLIMDIA Revolution**," a product promoted and sold for weight loss on various websites, including www.pinkfatty.com, and in some retail stores since it contains Sibutramine.

FDA Jan/13 is advising consumers not to purchase or use "**MAXILOSS** Weight Advanced," a product promoted and sold for weight loss on various websites, includingwww.dreamlifeweightloss.com, and in some retail stores since it contains sibutramine.

FDA Feb/13 Olaax Corp announced a nationwide recall of the company's dietary supplement sold under the brand name **Maxiloss Weight Advanced Softgels** to the user level, because FDA testing found the Maxiloss Weight Advanced product to contain Sibutramine.

FDA Jun/13 FDA laboratory analysis confirmed that **"Bethel 30", & "XIYOUJI QINGZHI CAPSULE**" & **JaDera** contains sibutramine. .

FDA Jun/13 A sample of **Extreme Body Slim, Fat Zero, Fruit & Plant Slimming, & Paiyouji Plus** all contains silbutramine.

FDA Jun/13 Beta Labs has recalled certain lots of **Oxyphen, Phentalene, Phen FX, and Red Vipers** because they contain 1,3 dimethylamylamine (DMAA), the FDA announced over the weekend. The products are used as pre-workout stimulants and for weight loss, but the agency has previously warned that DMAA can be dangerous: it can elevate blood pressure and lead to cardiovascular complications. One distributor, GNC, faces FDA seizure of over 3000 cases of two other DMAA-containing products, **Jack3d and OxyElitePro**. Although the manufacturer of those supplements has ceased production, GNC continues to sell its remaining stocks, according to the *New York Times*.

FDA July/13 **Meizi Revolution, Strawberry Balance** contains silbutramine.

FDA Aug/13 Herbal Give Care LLC issued a voluntarily recall of all lots of **Esbelin silouttete** and **Esbelin siloutte Herbal Blend with L-Carnitine** (30 Capsules), to the consumer level. The products have been found to contain undeclared Sibutramine, N-Desmethylsibutramine, and N-di-Desmethylsibutramine.

FDA Aug/13 Bethel Nutritional Consulting, Inc., New York, NY, is voluntarily recalling **Quick Thin and Bethel Advance** to the consumer level. These products have been found to contain Sibutramine and Phenolphthalein, and may pose a threat to consumers.

FDA Aug/13 CTV Best Group announced that it is conducting a voluntary nationwide recall of all lots of a dietary supplement products distributed by the company under the names **BEST SLIM 40 Pills** to the consumer level. Testing by FDA revealed the presence of Sibutramine in Best Slim.

FDA Aig/13 Herbal Give Care LLC is voluntarily recalling all lots of **Esbelder man (30 capsules), Esbelder fem (30 capsules) and Esbelder siloutte** (30 capsules) to the consumer level. The products have been found to contain undeclared

Sibutramine, N-Desmethylsibutramine, and N-di-Desmethylsibutramine.

FDA Sep/13 laboratory analysis confirmed that **Shou Fu Ti Tun Guo Xiang Xing Jian Fei Jiao Nang** contains sibutramine.

FDA Oct/13: B@B Trade, Inc., Florida is voluntarily recalling all lots of **Slim Fortune, Lidiy, and Slim Expert** to the consumer level. The FDA laboratory analysis of these dietary supplements found to contain undeclared Sibutramine.

FDA Oct/13 is advising consumers not to purchase or use **Perfect Body Solutions or Burn 7**. FDA laboratory analyses confirmed that Perfect Body Solutions and Burn 7 contain sibutramine.

FDA Oct/13 is advising consumers not to purchase or use **Dr. Mao Slimming Capsules**. FDA laboratory analysis confirmed that Dr. Mao Slimming Capsules contain sibutramine.

FDA Oct/13 is advising consumers not to purchase or use **Bella Vi Insane Amp'd or Bella Vi Amp'd Up.** FDA laboratory analyses confirmed that Bella Vi Insane Amp'd and Bella Vi Amp'd Up contain sibutramine.

FDA Nov/13 **SlimExtra Herbal** capsules contain silbutramine.

FDA Dec/13 laboratory analysis found the **Burn 7 Capsules** to contain undeclared Sibutramine.

FDA Jan/14 is advising consumers not to purchase or use **Magic Slim or Dream Body Slimming Capsule**, products promoted and sold for weight loss and sold on various websites and in some stores, since FDA lab analysis confirmed they contains sibutramine.

FDA Jan/14 **Citrus Fit Gold, Hot Detox & Thinogenics** contains sibutramine. **Tonic Life BP** contains phenolphthalein.

FDA Feb/14: MyNicKnaxs, LLC notified the public it is recalling all lots of "**Reduce Weight Fruta Planta**". FDA lab analysis of the product found Reduce Weight Fruta Planta to contain 10.2 mg of Phenolphthalein.

FDA Mar/14 is advising consumers not to purchase or use **Vitaccino Coffee**, a product promoted and sold for weight loss. FDA laboratory analysis confirmed that Vitaccino Coffee contains sibutramine.

FDA Mar/14: New Life Nutritional Center is recalling all lots of "**Super Fat Burner capsules, Maxi Gold capsules and Esmeralda softgels**" to the user level after FDA analysis revealed the products contain undeclared active pharmaceutical ingredients: sibutramine, phenolphthalein or a combination of both sibutramine and phenolphthalein.

FDA Mar/14: **Bella Vi Insane Bee Pollen Capsules, Bella Vi BTrim Ultimate Boost, Bella Vi BTrim Max, Bella Vi Extreme Accelerator, Bella Vi Insane Amp'd, and Bella Vi Amp'd U**, contain silbutramine with or without phenolphthalein.

FDA Mar/14: GlaxoSmithKline (GSK) Consumer Healthcare is **voluntarily recalling** all alli weight loss products from U.S. and Puerto Rico retailers as the company believes that some packages of the product were tampered with and may contain product that is not authentic **Alli**.

FDA Apr/14: FDA analysis on **New You** contains silbutramine.

FDA Apr/14 has tested multiple **Zi Xiu Tang Bee Pollen** products from various distributors in the United States (US). All products that have been tested, including those that claim to be "genuine" and "anti-counterfeit," have been found to contain one or both of the undeclared drug ingredients sibutramine and Phenolphthalein.

FDA Apr/14 laboratory analysis confirmed that **Infinity & Lite Fit** USA contains sibutramine.

FDA Apr/14: Nature's Universe notified the public it is recalling all lots of **Thinogenics** product sold prior to February 6, 2014 to the user level after FDA analysis revealed that the affected product contained undeclared sibutramine.

FDA May/14 laboratory analysis confirmed that **Slim Trim U & Natural Body Solution** contains sibutramine.

FDA May/14 is advising consumers not to purchase or use **Asset Bee Pollen**, a product promoted and sold for weight loss because it contains sibutramine.

FDA May/14 is advising consumers not to purchase or use **Asset Bold**, a product promoted and sold for weight loss. FDA laboratory analysis confirmed that Asset Bold contains sibutramine.

FDA Jun/14 laboratory analysis confirmed that **La Jiao Shou Shen** contains sibutramine

FDA Jun/14 laboratory analysis confirmed that **Sliming Diet** contains sibutramine.

FDA July/14 laboratory analysis confirmed that **Mix Fruit Slimming, Lingzhi Cleansed Slim Tea, 24 Ince, Lipo 8 Burn Slim, Sliming (sic) Diet By Pretty, & Trim-Fast Slimming Softgel** contains sibutramine.

FDA July/14: **Vitaccino Coffee, Collagen Slim, & Sulami** contains sibutramine.

FDA July/14: **Fruta Bio, Jianfeijindan Activity Girl, & LTD Japanese Chinese Formula pill** for weight reduction contains sibutramine and/or phenolphthalein.

FDA Aug/14 Regeneca Worldwide a division of VivaCeuticals, Inc., is conducting a voluntary nationwide recall of its **RegenESlim appetite control dietary supplement**, lot # EX0616R15814 and lot #11414RE5516, because FDA analysis confirmed the presence of DMAA.

FDA Sep/14 laboratory analysis confirmed that **Best Line Suplemento Alimenticio Capsules** contains sibutramine.

FDA Sep/14 laboratory analysis confirmed that **Japan Hokkaido Slimming Weight Loss Pills** contain sibutramine, benzocaine, phenolphthalein and diclofenac.

FDA Sep/14 laboratory analysis confirmed that **Mezo** contains benzylsibutramine, a substance structurally similar to sibutramine.

FDA Sep/14 laboratory analysis confirmed that **Mezo** contains benzylsibutramine, a substance structurally similar to sibutramine.

FDA Oct/14 laboratory analysis confirmed that **Sit and Slim II** contains sibutramine.

FDA Nov/14 is advising consumers not to purchase or use **V26 Slimming Coffee**. FDA laboratory analysis confirmed that V26 Slimming Coffee contains sibutramine.

FDA Nov/14: REFA Enterprises is voluntarily recalling one lot each of: **Forever Beautiful Bee Pollen** (UPC # 6333090804632), **Forever Beautiful Infinity** (UPC # 633090804649). The products have been found to contain undeclared Sibutramine or a combination of both Sibutramine and Phenolphthalein through FDA laboratory analyses.

FDA Nov/14 is advising consumers not to purchase or use **Bee Slim, Bee Thin & Super Extreme Accelerator**. FDA laboratory analysis confirmed that they contain sibutramine.

FDA Nov/14 laboratory analysis confirmed that **Slim-Vie** containssibutramine.

FDA Dec/14 Bethel Nutritional Consulting, Inc. is recalling one lot of **SLIM-K Capsules** to the consumer level. The firm was informed by the US Food and Drug Administration (FDA) that a sample of SLIM-K collected and tested by the FDA was found to contain sibutramine, desmethylsibutramine, and phenolphthalein.

FDA Dec/14 Bethel Nutritional Consulting, Inc. is recalling one lot of **B-Lipo Capsules** to the consumer level. The firm was informed by the US Food and Drug Administration (FDA) that a sample of B-Lipo Capsules collected and tested by the FDA was found to contain lorcaserin.

FDA Feb/15 laboratory analysis confirmed that **Lean Body Extreme** contains sibutramine, desmethyl sibutramine, phenolphthalein, and sildenafil.

FDA Feb/15 laboratory analysis confirmed that **Nine Slim, & Seven Slim** contains phenolphthalein.

FDA Mar/15 laboratory analysis confirmed that **Elimulating Weight & Toxin Keeping Beauty** contains sibutramine

FDA Mar/15 laboratory analysis confirmed that **Black Mamba Hyperrush & L-Carnitine Sob Strengthening Version Slimming Miracle Capsule** contains sibutramine.

FDA Mar/15 laboratory analysis confirmed that **Green Algae** Combination by Crane Beauty contains lorcaserin.

FDA May/15 laboratory analysis confirmed that **Li Da Dai Dai Hua Slimming Capsule** contains sibutramine.

FDA May/15 laboratory analysis confirmed that **Slim Forte Slimming Capsule** contains sibutramine.

FDA Apr/15 laboratory analysis confirmed that **Superior** contains sibutramine.

FDA May/15 **Yanhee Slim & iNSANE Bee Pollen** contains undeclared lorcaserin; **EDGE Amplified Weight Release** contains undeclared phenolphthalein and fluoxetine; **iNDiGO & BtRim Max** contains undeclared phenolphthalein.

FDA May/15: **Nine Slim & Seven Slim** contains undeclared phenolphthalein.

FDA May/15: **Oxy ELITE Pro Super Thermogenic** contains undeclared fluoxetine.

FDA May/15: **Elimulating Weight & Toxin Keeping Beauty & L-Carnitine Sob Strengthening Version Slimming Miracle Capsule** contains undeclared sibutramine.

FDA May/15: **Lean Body Extreme** contains undeclared sibutramine, desmethyl sibutramine, phenolphthalein & sildenafil.

FDA May/15: **Diablos Eca Fire Caps** contains undeclared sildenafil, phenolphthalein, sibutramine & deisobutylbenzylsibutramine.

FDA July 15: **Black Mamba Hyperrush & Ultra ZX** contains Undeclared sibutramine and phenolphthalein.

FDA July 15:**Botanical Slimming (Red) & Xcel** contains Undeclared fluoxetine.

FDA July 15:**Green Algae Combination** by Crane Beauty contains Undeclared lorcaserin.

FDA July 15:**Natural Max Slimming** contains Undeclared sildenafil, fluoxetine, and sibutramine.

FDA July 15: **Ultimate Boost & Xcel Advanced** contains Undeclared phenolphthalein.

FDA Sep/15: **Miracle Diet 30** has been found to contain undeclared **phenolphthalein.**

FDA Oct/15 **Lida DaiDaiHua** contains undeclared sibutramine & phenolphthalein.

FDA Sep/15: **Miracle Diet 30** has been found to contain undeclared phenolphthalein.

FDA Oct/15 laboratory analysis confirmed that **Xtreme Fat Burner Capsules** contains phenolphthalein.

FDA Oct/15 laboratory analysis confirmed that **Tip-Top Shape, Lishou Slimming Coffee, & Basha Nut 100% Fruit Soft Gel Capsules** contains sibutramine.

FDA Nov/15 laboratory analysis confirmed that **Super Herbs** contains sibutramine and desmethylsiburamine.

FDA Nov/15 laboratory analysis confirmed that **Zero Fat & SPCARET Princess Diet** contains sibutramine.

FDA Dec/15 laboratory analysis confirmed that **Thirty Plus** contains sibutramine.

FDA Dec/15 Lipo Escultura Corp. of Brooklyn, NY (dba JAT Productos Naturales Corp., and JAT Natural Products Corp.): recalling all **Lipo Escultura** within expiry to the consumer level since contains sibutramine and diclofenac..

FDA Dec/15 laboratory analysis confirmed that **Evolve Bee Pollen, Jenesis, Prime Bee Pollen & Oasis Bee Pollen** contains sibutramine.

FDA Dec/15: laboratory analysis confirmed that **La'Trim Plus** contains sibutramine.

FDA's Dec/15 analysis found the **Smart Lipo** products to contain undeclared sibutramine, desmethylsibutramine, and phenolphthalein.

FDA Dec/15 BeeXtreme LLC is recalling all lots of **La' Trim Plus, Jenesis and Oasis products** from the market. Recent Analysis by the Food and Drug Administration has found undeclared Sibutramine and Phenolphthalein.

FDA Jan/16 analysis of **Pink Bikini** (white capsules, blue capsules and gold capsules) and **Shorts on the Beach** (blue capsules and gold capsules) found these products to be tainted with Sibutramine, Phenolphthalein, and/or Diclofenac.

FDA Mar/16 laboratory analysis confirmed that **Propell Platinum** contains sibutramine.

FDA Mar/16 laboratory analysis confirmed that **ENVY BP** contains sibutramine.

FDA Apr/16 Super Herbs is voluntarily recalling all bottles of **SUPER HERBS**, light green and dark green capsules to the consumer level after FDA laboratory testing found SUPER HERBS to contain sibutramine, desmethylsibutramine, and/or phenolphthalein.

FDA May/16 laboratory analysis confirmed that **3rd Degree & Black Gold X** contains sibutramine.

FDA May/16 laboratory analysis confirmed that **Black Label X** contains sildenafil.

FDA May/16 laboratory analysis confirmed that **Step 2 contains** sibutramine.

FDA June/16: The Body Shot Bar is voluntarily recalling all lots distributed March 1- May 6 2016 of **Step 2 60 gold capsule** (350MG per) capsules to the consumer level. Step 2 has been found positive for Sibutramine.

FDA July/16: FDA laboratory analysis confirmed that **Dream Body Extreme Gold** contains sibutramine, fluoxetine and sildenafil.

FDA July/16: FDA laboratory analysis confirmed that **Dream Body Original Formula, SBF Bee Pollen & Extra Slim Plus Acai Berry Weight Loss Formula** contains sibutramine.

FDA July/16: Dream Body Weight Loss is voluntarily recalling all lots of **Dream Body Extreme Gold 800mg 30 gold capsules, Dream Body 450mg 30 white capsules, and Dream Body Advanced 400mg 30 purple capsules** to the consumer level. The **Dream Body Extreme 800mg Gold, Dream Body 450mg and Dream Body Advanced 400mg** have been found to contain sibutramine.

FDA July 16 laboratory analysis confirmed that **Slim Fit X, & Mang Luk Power Slim Detox** contains sibutramine and desmethylsibutramine.

FDA July 16 laboratory analysis confirmed that **Mang Luk Power Slim, Maxx Easy** contains sibutramine.

FDA July/16 laboratory analysis confirmed that **Xcelerated Weight Loss Charged Up, Xcelerated Weight Loss Turbo Charge** contains sibutramine.

FDA July/16 laboratory analysis confirmed that **Xcelerated Weight Loss Ultra Max** contains phenolphthalein and sildenafil.

FDA Jul/16 laboratory analysis confirmed that **Zi Xiu Tang Beauty Face & Figure Capsule** contains phenolphthalein and fluoxetine.

FDA Jul/16 laboratory analysis confirmed that **Ultimate Lean** contains sibutramine and desmethylsibutramine.

FDA Aug/16 laboratory analysis confirmed that **Natural Eruption** contains sibutramine.

FDA Aug/16 laboratory analysis confirmed that **Citrus' Fit** contains sibutramine and desmethylsibutramine.

FDA Aug/16 laboratory analysis confirmed that **Adelgazantes R-II** contains sibutramine.

FDA Oct/16 laboratory analysis confirmed that **Zi Su Body Fat Health II** contains sibutramine and phenolphthalein.

FDA Nov/16 laboratory analysis confirmed that **ABX Weight Loss** contains sibutramine.

FDA Nov/16 Love My Tru Body is voluntarily recalling all of **Skinny Bee Diet 500 mg** to the consumer level after FDA laboratory testing found Skinny Bee Diet to contain sibutramine, desmethylsibutramine, and/phenolphthalein.

FDA Dec/16 Ultimate Body–Tox is voluntarily recalling all lots of **Ultimate Body Tox PRO** capsules to the consumer level. FDA analyses of this product found it to contain undeclared sibutramine.
FDA Dec/16 laboratory analysis confirmed that **Queen Slimming Soft Gel** contains sibutramine.
FDA Jan/17: **ABX Weight Loss, Ultimate Body Tox** has undeclared sibutramine.
FDA Jan/17: **Accelerator Boost** has undeclared phenolphthalein.
FDA Jan/17: **Results & Zi Su Body Fat Health II** has undeclared sibutramine and phenolphthalein.
FDA Jan/17: **Skinny Bee Diet** has undeclared desmethylsibutramine, sibutramine, and phenolphthalein.
FDA Jan/17: **Supreme Slim 5.7** has undeclared phenolphthalein and sildenafil.
FDA Feb/17 laboratory analysis confirmed that **Lean Extreme Max, Slimming Plus Advanced, Platinum Weight Solution – Fat Loss Metabolizer & X-treme Beauty Slim** contains sibutramine.
FDA Mar/17 analyzed samples of **La Bri's Body Health Atomic** and found it to contain the undeclared ingredient sibutramine.
FDA Jul/17: **EZ Weight Loss TX** is voluntarily recalling all lots of **La Bri's Body Health Atomic and Xplode capsules** to the consumer level since it was tainted with sibutramine.
FDA Aug/17 laboratory analysis confirmed that **Physic Candy – Curve & Physic Candy**-Define contains sibutramine.
FDA Oct/17 laboratory analysis confirmed that **A1 Slim** contains sibutramine and phenolphthalein.
FDA Mar/18: Bella All Natural is voluntarily recalling its **Diet Capsules labeled as Bella**, Lot Number MFD:10.15.2017 EXP: 10.14.2019, to the consumer level. This recall has been initiated due to presence of sibutramine.
FDA 2010: **Orlistat** https://www.fda.gov/drugs/drugsafety/postmarketdrugsafetyinformationforpatientsandproviders/ucm213038.htm
FDA Jul/18: laboratory analysis confirmed that **Asunsa contains sibutramine, N-desmethylsibutramine, benzylsibutramine, phenolphthalein and diclofenac**.
FDA July/18: laboratory analysis confirmed that **Lyn DTOX FS3 contains sibutramine and N-desmethylsibutramine**.
FDA Aug/18: is advising consumers **not to purchase or use Nuvitra**, a product promoted for weight loss. This product was identified during an examination of international mail shipments. FDA laboratory analysis confirmed that Nuvitra **contains sibutramine and fluoxetine**.
FDA Sep/18: laboratory analysis confirmed that Slimming Capsule contains sibutramine and phenolphthalein.
FDA Sep/18: laboratory analysis confirmed that BodySlim Herbal & Easy 2 Slim contains sibutramine.
FDA Oct/18: laboratory analysis confirmed that Green Lean Body Capsule * Baschi Quick Slimming Capsule contains sibutramine and N-desmethylsibutramine.
FDA Oct/18: laboratory analysis confirmed that Shengan Natural Model, Like Slim Coffee & In Shape contains sibutramine.
FDA Oct/18: Fat Burners Zone is voluntarily **recalling 1 lot of Zero Xtreme, capsules to the consumer level**. FDA analysis has found Zero Xtreme to be **tainted with sibutramine.**
FDA Jan/19: laboratory analysis confirmed that **Slimina contains sibutramine**.
FDA Jan/19: laboratory analysis confirmed that **GoLean Detox & Slimmer Extreme Thermogenic Formula** contains sibutramine and phenolphthalein.
FDA Jan/19: laboratory analysis confirmed that **Slim Bio Capsules** contain sibutramine, N-desmethylsibutramine, sildenafil, tadalafil, benproperine and diphenhydramine.
FDA Jan/19: laboratory analysis confirmed that **Ultra Fit, 1 Day Diet** contains sibutramine and N-desmethylsibutramine.
FDA Feb/19: **GoLean Detox Capsules by GoLean Detox USA: Recall** - Due to Presence of Undeclared Sibutramine and Phenolphthalein.Pdf Guo W, Key TJ, Reeves GK. Accelerometer compared with questionnaire measures of physical activity in relation to body size and composition: a large cross-sectional analysis of UK Biobank. BMJ Open. 2019 Jan 29;9(1):e024206.
FDA Jun/19: laboratory analysis confirmed that **Adelgasin Plus, Lishou Fuling Jiaonang & Absolute Nine Slim** contains sibutramine and N-desmethyl sibutramine.
FDA Jun/19: laboratory analysis confirmed that **Super Slimming Herb & Detoxi Slim** contains sibutramine.
FDA July/19: laboratory analysis confirmed that **Reduktis Max** contains sibutramine.
FDA Sep/19: laboratory analysis confirmed that **Love in S contains sibutramine and N-desmethylsibutramine**.
FDA Sep/19: laboratory analysis confirmed that **Sheaya Lender contains sibutramine and fluoxetine**.
Fedele DA, Cushing CC, Fritz A, et al. **Mobile Health Interventions** for Improving Health Outcomes in Youth: A Meta-analysis. JAMA Pediatr. 2017 May 1;171(5):461-469.
Feinmann J. **Low calorie and low carb diets for weight loss** in primary care. BMJ. 2018 Mar 13;360:k1122.
Fenger M, Hansen DL, Worm D, et al. **Gastric bypass surgery** reveals independency of obesity and **diabetes** mellitus type 2. BMC Endocr Disord. 2016 Nov 9;16(1):59.
Fernandez C, Kasper NM, Miller AL, et al. Association of **Dietary Variety and Diversity** With Body Mass Index in US Preschool Children. Pediatrics. 2016 Feb 11.
Field AE, Inge TH, Belle SH, et al. Association of Obesity Subtypes in the **Longitudinal Assessment of Bariatric Surgery Study and 3-Year Postoperative Weight Change**. Obesity (Silver Spring). 2018 Nov 13.
Fildes A, Charlton J, Rudisill C, Littlejohns P, et al. **Probability of an Obese Person Attaining Normal Body Weight**: Cohort Study Using Electronic Health Records. Am J Public Health. 2015 Jul 16:e1-e6.
Finkelstein Eric A.; Zhen Chen; Nonnemaker James; et al. Impact of Targeted **Beverage Taxes** on Higher- and Lower-Income Households. Arch Intern Med. 2010;170(22):2028-2034.
Finkelstein EA, Tan YT, Malhotra R, et al. A Cluster Randomized Controlled Trial of an **Incentive-Based Outdoor Physical Activity Program**. J Pediatr. 2013 Feb 14.
Finkelstein EA, Graham WC, Malhotra R. **Lifetime Direct Medical Costs of Childhood Obesity**. Pediatrics. 2014 Apr 7.
Finkelstein EA, Kruger E. Meta- and **cost-effectiveness analysis of commercial weight loss strategies**. Obesity (Silver Spring). 2014 Sep;22(9):1942-51. (Weight Watchers & Qsymia good options)
Finks JF, Dimick JB. An Updated **National Institutes of Health Consensus Panel on Bariatric Surgery**. JAMA Surg. 2014 Oct 1.
Finucane MM, Stevens GA, Cowan MJ. **National, regional, and global trends in body-mass index since 1980**: systematic analysis of health examination surveys and epidemiological studies with 960 country-years and 9.1 million participants. Lancet 2011; DOI: 10.1016/S0140-6736(10)62035-5.
Fisher DP, Johnson E, Haneuse S, et al. Association between **bariatric surgery and macrovascular disease outcomes in patients with type 2 diabetes and severe obesity** [Oct 16, 2018]. JAMA. doi:10.1001/jama.2018.14619
Flaherty MR. "**Fat Letters**" in Public Schools: Public Health Versus Pride.Pediatrics. 2013 Aug 19.
Flegal KM, Carroll MD, Ogden CL, Curtin LR. Prevalence and Trends in **Obesity Among US Adults, 1999-2008**. JAMA. 2010 Jan 13.
Flegal KM, Carroll MD, Kit BK, Ogden CL. **Prevalence of obesity and trends in the distribution of body mass index** among us adults, 1999-2010. JAMA 2012.
Flegal KM, Kit BK, Oprana H, Graubard BI. Association of **all-cause mortality with overweight and obesity** using standard body mass index categories: a systematic review and meta-analysis. *JAMA*. 2012;309(1):71-82.

Flegal KM, Kruszon-Moran D, Carroll MD, et al. **Trends in obesity** among **adults in the United States, 2005 to 2014**.JAMA. doi:10.1001 /jama.2016.6458.
Fleming JW, McClendon KS, Riche DM. New obesity agents: **lorcaserin and phentermine/topiramate**. Ann Pharmacother. 2013 Jul;47(7-8):1007-16.
Fleming-Milici F, Harris JL, Sarda V, Schwartz MB. Amount of Hispanic Youth Exposure to Food and Beverage **Advertising** on Spanish- and English-Language Television. JAMA Pediatr. 2013 Jun 17:1-6.
Flint E, Cummins S, Sacker A. Associations between **active commuting, body fat, and body mass index**: population based, cross sectional study in the United Kingdom. BMJ. 2014 Aug 19;349:g4887.
Floegel A, Pischon T. **Low carbohydrate-high protein diets**. BMJ. 2012 Jun 19;344:e3801.
Flum DR, Belle SH, KingWC, et al; Longitudinal Assessment of Bariatric Surgery (**LABS**) Consortium. Perioperative safety in the longitudinal assessment of bariatric surgery. N Engl J Med. 2009;361(5):445-454.
Folkvord F, Anschütz DJ, Nederkoorn C, et al. **Impulsivity, "Advergames,"** and Food Intake. Pediatrics. 2014 May 5.
Forbes JD, Azad MB, Vehling L, et al. Association of **Exposure to Formula in the Hospital and Subsequent Infant Feeding Practices** With Gut Microbiota and Risk of Overweight in the First Year of Life. JAMA Pediatr. 2018 Jun 4:e181161.
Ford AL, Bergh C, Södersten P, Sabin MA, Hollinghurst S, Hunt LP, Shield JP. Treatment of childhood obesity by **retraining eating behaviour (device)**: randomised controlled trial. BMJ. 2009 Jan 5;340:b5388. doi: 10.1136/bmj.b5388.
Ford ES, Maynard LM, Li C. **Trends in mean waist circumference and abdominal obesity among US adults, 1999-2012**. JAMA. 2014 Sep 17;312(11):1151-3.
Forslund A, Staaf J, Kullberg J, et al. Uppsala Longitudinal Study of **Childhood Obesity**: Protocol Description. Pediatrics. 2014 Jan 13
Foster GD, Wyatt HR, Hill JO, et al. A randomized trial of a low-carbohydrate diet for obesity. N Engl J Med 2003;348:2082-90.
Foster Gary D.; Borradaile Kelley E.; Sanders Mark H.; et al. for the Sleep AHEAD Research Group of the Look AHEAD Research Group. A Randomized Study on the Effect of Weight Loss on Obstructive **Sleep Apnea** Among Obese Patients With Type 2 Diabetes: The Sleep AHEAD Study. Arch Intern Med. 2009;169(17):1619-1626.
Foster GD, Wyatt HR, Hill JO, et al. Weight and metabolic outcomes after 2 years on a **low-carbohydrate versus low-fat diet**: a randomized trial. Ann Intern Med. 2010 Aug 3;153(3):147-57.
Foster C, Richards J, ThorogoodM, HillsdonM. **Remote and web 2.0 interventions for promoting physical activity**. Cochrane Database of Systematic Reviews 2013, Issue 9. Art. No.: CD010395. DOI: 10.1002/14651858.CD010395.pub2.
We found consistent evidence to support the effectiveness of remote and web 2.0 interventions for promoting PA. These interventions have positive, moderate sized effects on increasing self-reported PA and measured cardio-respiratory fitness, at least at 12 months.
Fothergill E, Guo J, Howard L, et al. Persistent metabolic adaptation 6 years after "**The Biggest Loser**" **competition**. Obesity (Silver Spring). 2016 May 2.
Fourkala EO, Burnell M, et al. Association of **skirt size and postmenopausal breast cancer** risk in older women: cohort study within the UK Collaborative Trial of Ovarian Cancer Screening (UKCTOCS). BMJ Open. 2014 Sep 24;4(9):e005400.
Fournier A and Zureik M. Estimate of deaths due to valvular insufficiency attributable to the use of **benfluorex** in France.Pharmacoepidemiol Drug Saf 2012.
Fowler SP, Williams K, Hazuda HP. **Diet Soda Intake** Is Associated with Long-Term Increases in Waist Circumference in a Biethnic Cohort of Older Adults: The San Antonio Longitudinal Study of Aging. J Am Geriatr Soc. 2015 Mar 17.
Foy AJ, Mandrola J, Liu G, et al. Relation of Obesity to New-Onset **Atrial Fibrillation and Atrial Flutter** in Adults. Am J Cardiol. 2018 Feb 6.
Franco M, Bilal U, Urduñez P, et al. Population-wide **weight loss and regain in relation to diabetes burden and cardiovascular mortality in Cuba** 1980-2010: repeated cross sectional surveys and ecological comparison of secular trends. BMJ 2013;346:f1515.
Franks, Paul W., Hanson, Robert L., Knowler, William C., et al. **Childhood Obesity**, Other Cardiovascular Risk Factors, and Premature Death. N Engl J Med 2010 362: 485-493.
Freedman DS, Berenson G. Tracking of **BMI** z scores for **severe obesity**. Pediatrics. 2017;140(3):e20171072
Freedman DS, Goodman A, Contreras OA, et al. Secular Trends in **BMI and Blood Pressure Among Children and Adolescents**: The Bogalusa Heart Study. Pediatrics. 2012 Jun 4.
Freedman DS, Butte NF, Taveras EM, et al. The **limitations** of transforming very **high body mass indexes into z-scores** among 8.7 million 2- to 4-year-old children. J Pediatr 2017 Apr 19.
Freitas Júnior IF, Christofaro DG, Codogno JS, et al. The Association between Skipping Breakfast and Biochemical Variables in Sedentary Obese Children and Adolescents. J Pediatr. 2012 Jun 7.
Friedemann C, Heneghan C, Mahtani K, Thompson M, Perera R, Ward AM. **Cardiovascular disease risk** in healthy children and its association with body mass index: systematic review and meta-analysis. BMJ 2012;345:e4759
Friel S, Chopra M, Satcher D. Unequal weight: equity oriented **policy responses to the global obesity epidemic**. BMJ. 2007 Dec 15;335(7632):1241-3.
Field AE, Sonneville KR, Crosby RD, et al. Prospective Associations of Concerns About Physique and the Development of Obesity, **Binge Drinking, and Drug Use** Among Adolescent Boys and Young Adult Men. JAMA Pediatr. 2013 Nov 4.
Franckle R, Adler R, Davison K. Accelerated **weight gain among children during summer versus school year** and related racial/ethnic disparities: a systematic review. Prev Chronic Dis. 2014 Jun 12;11:E101.
Freisling H, Arnold M, Soerjomataram I, et al. Comparison of general obesity and **measures of body fat distribution in older adults in relation to cancer risk**: meta-analysis of individual participant data of seven prospective cohorts in Europe. Br J Cancer. 2017 May 23;116(11):1486-1497.
Freitas PD, Ferreira PG, Silva AG, et al. The Role of **Exercise** in a Weight-Loss Program on Clinical Control in Obese Adults with **Asthma**. A Randomized Controlled Trial. Am J Respir Crit Care Med. 2017 Jan 1;195(1):32-42.
French SA, Sherwood NE, Veblen-Mortenson S, et al. Multicomponent **Obesity Prevention Intervention in Low-Income Preschoolers**: Primary and Subgroup Analyses of the NET-Works Randomized Clinical Trial, 2012-2017. Am J Public Health. 2018 Dec;108(12):1695-1706.
Fröhlich G, Pott W, Albayrak O, et al. Conditions of **Long-term Success in a Lifestyle** Intervention for Overweight and Obese Youths. Pediatrics. 2011 Oct;128(4):e779-85.
Fryar CD and Ervin RB. **Caloric intake from fast food among adults**: United States, 2007-2010. NCHS data brief 2013; 113.
FSRH Guideline (April 2019) **Overweight, Obesity and Contraception**. BMJ Sex Reprod Health. 2019 Apr;45(Suppl 2):1-69.
Fuller NR, Pearson S, Lau NS, et al. An **intragastric balloon** in the treatment of obese individuals with metabolic syndrome: a randomized controlled study. Obesity (Silver Spring). 2013 Aug;21(8):1561-70.
Gabbert, Charles, Donohue, Michael, Arnold, John, et al. **Adenovirus 36** and Obesity in Children and Adolescents. Pediatrics 2010 0: peds.2009-3362.
Gadde KM, Allison DB, Ryan DH. Et al. Effects of low-dose, controlled-release, **phentermine plus topiramate** combination on weight and associated comorbidities in overweight and obese adults (**CONQUER**): a randomised, placebo-controlled, phase 3 trial. www.thelancet.com Published online April 11, 2011 DOI:10.1016/S0140-6736(11)60205-5.
Gadde KM, Kopping MF, Wagner HR, et al. **Zonisamide** (400mg day) for Weight Reduction in Obese Adults: A 1-Year Randomized Controlled Trial. Arch Intern Med. 2012 Oct 15:1-8.
Gallagher D, Rosenn B, Toro-Ramos T, et al. **Greater Neonatal Fat-Free Mass and Similar Fat Mass** Following a Randomized Trial to Control Excess Gestational Weight Gain. Obesity (Silver Spring). 2018 Mar;26(3):578-587.
Garaulet M, Gómez-Abellán P, Alburquerque-Béjar JJ, et al. **Timing of food intake** predicts weight loss effectiveness. Int J Obes (Lond). 2013 Jan 29.
Garber AJ, Abrahamson MJ, Barzilay JI, et al. **AACE Comprehensive Diabetes Management Algorithm** 2013. Endocr Pract. 2013 Mar-Apr;19(2):327-36.
García AL, Raza S, Parrett A, Wright et al. **Nutritional content of infant commercial weaning foods** in the UK. Arch Dis Child. 2013 Oct;98(10):793-7.
Garcia CM, Meltzer JA, Chan KN, et al. A Validation Study of the **PAWPER** (**Pediatric Advanced Weight Prediction in the Emergency Room**) **Tape**-A New Weight Estimation Tool. J Pediatr. 2015 Jul;167(1):173-177.e1.

Gardner CD, Kiazand A, et al. Comparison of the **Atkins, Zone, Ornish, and LEARN** diets for change in weight and related risk factors among overweight premenopausal women. JAMA 2007;297:969-77. [Erratum, JAMA 2007;298:178.]

Gardner C, Wylie-Rosett J, Gidding SS, et al. **Nonnutritive sweeteners**: Current use and health perspectives. A scientific statement from the American Heart Association and the American Diabetes Association. Circulation 2012; 126:509-519. (Aspartame, acesulfame-K, neotame, saccharin, and sucralose)

Gardner CD, Trepanowski JF, Del Gobbo LC, et al. Effect of **Low-Fat vs Low-Carbohydrate Diet** on 12-Month Weight Loss in Overweight Adults and the Association With Genotype Pattern or Insulin Secretion: The DIETFITS Randomized Clinical Trial. JAMA. 2018 Feb 20;319(7):667-679.

Garrel D. Is the treatment of **obesity futile?: NO**. Can Fam Physician. 2012 May;58(5):509-10.

Garrido-Miguel M, Cavero-Redondo I, Álvarez-Bueno C, et al. **Prevalence and Trends of Overweight and Obesity in European Children** From 1999 to 2016: A Systematic Review and Meta-analysis. JAMA Pediatr. 2019 Aug 5:e192430.

Garvey WT, Ryan DH, Look M, et al. Two-year sustained weight loss and metabolic benefits with controlled-release **phentermine/topiramate** in obese and overweight adults (SEQUEL): a randomized, placebo-controlled, phase 3 extension study. Am J Clin Nutr. 2012 Feb;95(2):297-308.

Garvey WT, Ryan DH, Henry R, et al. Prevention of type 2 diabetes in subjects with prediabetes and metabolic syndrome treated with **phentermine and topiramate** extended release. Diabetes Care. 2014 Apr;37(4):912-21.

Garvey WT, Mechanick JI, Brett EM, et al. Reviewers of the **AACE/ACE Obesity Clinical Practice Guidelines**. American Association of Clinical Endocrinologists and American College of Endocrinology Clinical Practice Guidelines for **Comprehensive medical Care of Patients with Obesity** –Executive Summary. Endocr Pract. 2016 May 24.

GBD 2015 Obesity Collaborators. **Health effects of overweight and obesity in 195 countries over 25 years**. N Engl J Med. DOI: 10.1056/NEJMoa1614362.

Gelfer M, Mang E, Duhaney T, Campbell N. Calls for **restricting the marketing of unhealthy foods** to children ignored by policy makers: What can we do? Can Fam Physician. 2014 Nov;60(11):969-71.

Geoffroy MC, Power C, Touchette E, et al. Childcare and Overweight or Obesity over **10 Years of Follow-Up**. J Pediatr. 2012 Nov 6.

Gesquiere I, Hens B, der Van Schueren B, et al. **Drug disposition before and after gastric bypass**: fenofibrate and posaconazole. Br J Clin Pharmacol. 2016 Jul 1.

Gerber JS, Bryan M, Ross RK, et al. **Antibiotic Exposure** During the First 6 Months of Life and Weight Gain During Childhood. JAMA. 2016 Mar 22-29;315(12):1258-65.

Gesquiere I, Darwich AS, Van der Schueren B, et al. **Drug disposition** and modelling before and after gastric bypass: immediate and controlled release metoprolol formulations. Br J Clin Pharmacol. 2015 Apr 27.

Gesell SB, Tesdahl E, Ruchman E. The Distribution of **Physical Activity in an After-school Friendship Network**. Pediatrics. 2012 May 28.

Geserick M, Vogel M, Gausche R, et al. **Acceleration of BMI in Early Childhood and Risk of Sustained Obesity**. N Engl J Med. 2018 Oct 4;379(14):1303-1312.

Giel KE, Zipfel S, Alizadeh M, et al. **Stigmatization of obese individuals** by human resource professionals: an experimental study. BMC Public Health. 2012 Jul 16;12:525.

Gilbert-Diamond D, Li Z, Adachi-Mejia AM, et al. Association of a television in the bedroom with increased adiposity gain in a nationally representative sample of children and adolescents. JAMA Pediatr. 2014 May;168(5):427-34.

Gibson TM, Park Y, Robien K, et al. Body Mass Index and **Risk of Second Obesity-Associated Cancers** After Colorectal Cancer: A Pooled Analysis of Prospective Cohort Studies. J Clin Oncol. 2014 Sep 29.

Gillman MW, Rifas-Shiman S, Berkey CS, Field AE, Colditz GA. Maternal **gestational diabetes**, birth weight, and adolescent obesity. Pediatrics. 2003 Mar;111(3):e221-6.

Gillman MW, Rifas-Shiman SL, Fernandez-Barres S, et al. **Beverage Intake** During Pregnancy and Childhood Adiposity. Pediatrics. 2017;140(2):e20170031

Glance LG, Li Y, Osler TM, Mukamel DB, Dick AW. Impact of Obesity on Mortality and Complications in **Trauma Patients**. Ann Surg. 2013 Nov 20.

Glaser Pediatric Research Network Obesity Study Group. **Metformin** Extended Release Treatment of Adolescent Obesity: A 48-Week Randomized, Double-Blind, Placebo-Controlled Trial With 48-Week Follow-up. Arch Pediatr Adolesc Med. 2010;164(2):116-123.

Global Burden of Metabolic Risk Factors for Chronic Diseases Collaboration (BMI Mediated Effects). Metabolic mediators of the effects of **body-mass index, overweight, and obesity** on coronary heart disease and stroke: a pooled analysis of 97 prospective cohorts with 1·8 million participants. Lancet. 2013 Nov 21.

Gloy VL, Briel M, Bhatt DL, et al. **Bariatric surgery versus non-surgical treatment** for obesity: a systematic review and meta-analysis of randomised controlled trials. BMJ. 2013 Oct 22;347:f5934.

Gluck ME, Alonso-Alonso M, Piaggi P, et al. **Neuromodulation targeted to the prefrontal cortex** induces changes in energy intake and weight loss in obesity. Obesity (Silver Spring). 2015 Nov;23(11):2149-56.

Gnatiuc L, Alegre-Díaz J, Wade R, et al. **General and Abdominal Adiposity and Mortality** in Mexico City: Prospective Study of 150 000 Adults. Ann Intern Med. 2019 Aug 13.

Godfrey KM, Reynolds RM, Prescott SL, et al. Influence of **maternal obesity on the long-term health of off spring**. Lancet Diabetes Endocrinol 2016; online Oct 12.

Godino JG, Merchant G, Norman GJ, et al. Using **social and mobile tools** for weight loss in overweight and obese young adults (Project SMART): a 2 year, parallel-group, randomised, controlled trial. Lancet Diabetes Endocrinol. 2016 Jul 14

Goffredo M, Mass K, Parks EJ,et al. Role of **Gut Microbiota and Short Chain Fatty Acids** in Modulating Energy Harvest and Fat Partitioning in Youth. J Clin Endocrinol Metab. 2016 Sep 20:jc20161797.

Gogebakan O, Kohl A, Osterhoff MA, et al. Effects of weight loss and long-term weight maintenance with **diets varying in protein and glycemic index** on cardiovascular risk factors: the Diet, Obesity, and Genes (**DiOGenes**) study, a randomized controlled trial. Circulation. 2011;124:2829 –2838.

Golden NH, Yang W, Jacobson MS, et al. Expected Body Weight in Adolescents: Comparison Between **Weight-for-Stature and BMI Methods**. Pediatrics. 2012 Dec;130(6):e1607-13.

Golden NH, Schneider M, Wood C, **AAP** Committee on Nutrition. Preventing **Obesity and Eating Disorders in Adolescents**. Pediatrics. 2016;138(3):e20161649

Goldschmidt Andrea B., Stein Richard I., Saelens Brian E., et al. Importance of **Early Weight Change** in a Pediatric Weight Management Trial. Pediatrics 2011

Goldschmidt AB, Khoury J, Jenkins TM, et al. Adolescent Loss**-of-Control Eating** and Weight Loss Maintenance **After Bariatric Surgery**. Pediatrics. 2017 Dec 13.

Goldstein RF, Abell SK, Ranasinha S, et al. Association of **gestational weight gain** with **maternal and infant outcomes**: a systematic review and meta-analysis.JAMA. doi:10.1001/jama.2017.3635

Golomb BA, Koperski S, White HL. Association between more frequent **chocolate consumption** and lower body mass index. Arch Intern Med. 2012 Mar 26;172(6):519-21.

Golomb I, Ben David M, et al. **Diminution in long-term metabolic effect** of **laparoscopic sleeve gastrectomy**: a retrospective analysis [online August 5, 2015].JAMA Surg. doi:10.1001/jamasurg.2015.2202.

Gong L, Yuan F, Teng J, et al. Weight Loss, Inflammatory Markers, and Improvements of Iron Status in Overweight and Obese Children. J Pediatr. 2014 Feb 8

Goodbar NH, Foushee JA, Eagerton DH, et al. Effect of the **Human Chorionic Gonadotropin Diet** on Patient Outcomes (May). Ann Pharmacother. 2013 Apr 19.

Goodpaster Bret H.; DeLany James P.; Otto Amy D.; et al. Effects of **Diet and Physical Activity Interventions** on Weight Loss and Cardiometabolic Risk Factors in Severely Obese Adults: A Randomized Trial. *JAMA*. 2010;0(2010):jama.2010.1505.

Gopinath B, Hardy LL, Baur LA, et al. **Physical Activity and Sedentary Behaviors** and Health-Related Quality of Life in Adolescents. Pediatrics. 2012 Jun 11.

Gorin AA, Lenz EM, Cornelius T, et al. Randomized Controlled Trial Examining the **Ripple Effect of a Nationally Available Weight Management Program on Untreated Spouses**. Obesity (Silver Spring). 2018 Feb 1.

Gortmaker SL, Swinburn BA, Levy D, et al. Changing the future of obesity: **science, policy, and action**. Lancet. 2011 Aug 27;378(9793):838-47.

Gould JC. **Bariatric surgery** as a highly effective intervention for diabetes Arch Surg 2012; DOI:10.1001/archsurg.2012.227.
Govindan M, GurmR, Mohan S, et al. **Gender differences** in physiologic markers and health behaviors associated with childhood obesity. Pediatrics 2013.
Graff M, Scott RA, Justice AE, et al. **Genome-wide physical activity interactions** in adiposity – A meta-analysis of 200,452 adults. PLoS Genet. 2017 Apr 27;13(4):e1006528.
Graff SK, Mario FM, Ziegelmann P, et al. Effects of **orlistat vs. metformin** on weight loss-related clinical variables in women with **PCOS**: systematic review and meta-analysis. Int J Clin Pract. 2016 May 26.
Graham L, Murty G, Bowrey DJ. **Taste, Smell and Appetite Change After Roux-en-Y** Gastric Bypass Surgery. Obes Surg. 2014 Mar 8.
Granell R, Henderson AJ, Evans DM, et al. Effects of **BMI, Fat Mass, and Lean Mass on Asthma** in Childhood: A Mendelian Randomization Study. PLoS Med. 2014 Jul 1;11(7):e1001669.
Gray Linsay; Lee I-Min; et al. **Body Weight** in Early and Mid-Adulthood in Relation to Subsequent Coronary Heart Disease Mortality**: 80-Year Follow-up** in the Harvard Alumni Study. Arch Intern Med. 2011;171(19):1768-1770.
Green CA, Yarborough BJ, Leo MC, et al. The **STRIDE** Weight Loss and Lifestyle Intervention for Individuals **Taking Antipsychotic Medications**: A Randomized Trial. Am J Psychiatry. 2014 Sep 15.
Greenhalgh S. Making China safe for Coke: how **Coca-Cola shaped obesity science and policy in China**. BMJ 2019;354:k5050. 10.1136/bmj.k5050.
Greenlee H, Shi Z, Sardo Molmenti CL, Rundle A, Tsai WY. Trends in Obesity Prevalence in Adults With a History of **Cancer**: Results From the US National
Greenway FL, Fujioka K, Plodkowski RA, et al. Effect of **naltrexone plus bupropion** on weight loss in overweight and obese adults (**COR-I**): a multicentre, randomised, double-blind, placebo-controlled, phase 3 trial. Lancet 2010;
Gregg B, Connor CG, Ruedy KJ, et al; Pediatric Diabetes Consortium. Body mass index changes in youth in the **first year after type 1 diabetes diagnosis**. J Pediatr. 2015 May;166(5):1265-1269.e1.
Gregson J, Kaptoge S, Bolton T, et al; Emerging Risk Factors Collaboration. **Cardiovascular Risk Factors Associated With Venous Thromboembolism**. JAMA Cardiol. 2019 Jan 16.
Grenda TR, Pradarelli JC, Thumma JR, et al. Variation in Hospital Episode **Costs** With **Bariatric Surgery**. JAMA Surg. 2015 Sep 16:1-7.
Gribsholt SB, Pedersen AM, Svensson E, et al. Prevalence of **Self-reported Symptoms After Gastric Bypass Surgery** for Obesity. JAMA Surg. 2016 Jan 6:1-9.
Gribsholt SB, Svensson E, Richelsen B, et al. Rate of Acute Hospital Admissions Before and After **Roux-en-Y Gastric Bypass Surgery**: A Population-based Cohort Study. Ann Surg. 2016 Dec 16.
Grief SN, Miranda RLF. **Weight Loss Maintenance**. Am Fam Physician. 2010 Sep 15;82(6):630-634.
Grimes CA, Riddell LJ, Campbell KJ, Nowson CA. **Dietary salt intake, sugar-sweetened beverage consumption**, and obesity risk. Pediatrics. 2013 Jan;131(1):14-21.
Grivell RM, Yelland LN, Deussen A, et al. **Antenatal dietary and lifestyle advice** for women who are overweight or obese and the effect on fetal growth and adiposity: the LIMIT randomised trial. BJOG. 2016 Jan;123(2):233-43.
Grøntved A, Hu FB. **Television viewing** and risk of type 2 diabetes, cardiovascular disease, and all-cause mortality: a meta-analysis. JAMA. 2011 Jun 15;305(23):2448-55.
Grover SA, Kaouache M, Rempel P, et al. **Years of life lost** and healthy life-years lost from diabetes and cardiovascular disease in overweight and obese people: a modelling study. Lancet Diabetes Endocrinol. 2014 Dec 4.
Gross RS, Mendelsohn AL, Fierman AH, et al. **Food insecurity** and obesogenic **maternal infant feeding styles** and practices in low-income families. Pediatrics. 2012 Aug;130(2):254-61.
Grube B, Chong PW, Lau KZ, et al. A **Natural Fiber Complex (Litramine IQP G-002AS)** Reduces Body Weight in the Overweight and Obese: A Double-Blind, Randomized, Placebo-Controlled Study. Obesity (Silver Spring). 2012 Jun 25.
Gudzune KA, Doshi RS, Mehta AK, et al. Efficacy of **Commercial Weight-Loss Programs**: An Updated Systematic Review. Ann Intern Med. 2015 Apr 7;162(7):501-512.
Guerra PH, Nobre MR, da Silveira JA, et al. **School-based physical activity and nutritional education** interventions on body mass index: A meta-analysis of randomised community trials - Project PANE. Prev Med. 2014 Jan 16;61C:81-89.
Gujral UP, Vittinghoff E, et al. **Cardiometabolic Abnormalities Among Normal-Weight Persons** From Five Racial/Ethnic Groups in the United States: A Cross-sectional Analysis of Two Cohort Studies. Ann Intern Med. 2017 May 2;166(9):628-636.
Guillemette L, Durksen A, Rabbani R, et al. **Intensive gestational glycemic management and childhood obesity**: a systematic review and meta-analysis. Int J Obes (Lond). 2017 Apr 4.
Guo F, Garvey WT. Trends in **Cardiovascular Health Metrics** in Obese Adults: National Health and Nutrition Examination Survey (NHANES), 1988-2014. J Am Heart Assoc. 2016 Jul 13;5(7).
Guo F, Garvey WT. Cardiometabolic Disease Staging Predicts Effectiveness of Weight Loss Therapy to Prevent Type 2 Diabetes: Pooled Results- Phase III Clinical Trials Assessing **Phentermine/Topiramate** Extended Release. Diabetes Care. 2017 Apr 28.
Haas WC, Moore JB, Kaplan M, Lazorick S. Outcomes from a medical weight loss program: primary **care clinics versus weight loss clinics**. Am J Med. 2012 Jun;125(6):603.e7-603.e11.
Hagström H, Tynelius P, Rasmussen F. **High BMI in late adolescence predicts future severe liver disease and hepatocellular carcinoma**: a national, population-based cohort study in 1.2 million men. Gut. 2017 Mar 20.
Haines J, McDonald J, O'Brien A, Sherry et al. **Healthy Habits, Happy Homes**: Randomized Trial to Improve Household Routines for Obesity Prevention Among Preschool-Aged Children. JAMA Pediatr. 2013 Sep 9.
Håkanson BS, Lundell L, Bylund A, Thorell A. **Comparison of Laparoscopic 270° Posterior Partial Fundoplication vs Total Fundoplication** for the Treatment of Gastroesophageal Reflux Disease: A Randomized Clinical Trial. JAMA Surg. 2019 Mar 6.
Halawi H, Khemani D, Eckert D, et al. Effects of **liraglutide on weight, satiation, and gastric functions** in obesity: a randomised, placebo-controlled pilot trial. Lancet Gastroenterol Hepatol. 2017 Dec;2(12):890-899.
Hales CM, Fryar CD, Carroll MD, et al. **Trends in Obesity and Severe Obesity Prevalence in US Youth and Adults** by Sex and Age, 2007-2008 to 2015-2016. JAMA. 2018 Mar 23.
Hales CM, Fryar CD, Carroll MD, et al. Differences in **Obesity Prevalence by Demographic Characteristics and Urbanization Level** Among Adults in the United States, 2013-2016. JAMA. 2018 Jun 19;319(23):2419-2429.
Halford JC, Harrold JA, Boyland EJ, Lawton CL, Blundell JE. Serotonergic drugs : effects on appetite expression and use for the treatment of obesity. Drugs. 2007;67(1):27-55.
Hall KD, Bemis T, Brychta R, et al. **Calorie for Calorie, Dietary Fat Restriction Results in More Body Fat Loss than Carbohydrate** Restriction in People with Obesity. Cell Metab. 2015 Aug 12.
Hall KD, Ayuketah A, Brychta R, et al. **Ultra-Processed Diets Cause Excess Calorie Intake and Weight Gain**: An Inpatient Randomized Controlled Trial of Ad Libitum Food Intake. Cell Metab. 2019 May 10.
Halperin F, Ding SA, et al. **Roux-en-Y Gastric Bypass** Surgery or Lifestyle With Intensive Medical Management in Patients With Type 2 Diabetes: Feasibility and 1-Year Results of a Randomized Clinical Trial. JAMA Surg. 2014 Jun 4.
Hamad GG, Helsel JC, Perel JM, et al. The effect of **gastric bypass on the pharmacokinetics of serotonin reuptake inhibitors**. Am J Psychiatry. 2012 Mar;169(3):256-63.
Hamer M, Batty GD. Association of **body mass index and waist-to-hip ratio with brain structure**: UK Biobank study. Neurology. 2019 Feb 5;92(6):e594-e600.
Hamer M, O'Donovan G, Stensel D, et al. **Normal-Weight Central Obesity** and Risk for Mortality. Ann Intern Med. 2017 Apr 25:1-2.
Hampl SE, Borner KB, Dean KM, et al.Patient Attendance and Outcomes in a **Structured Weight Management Program**. J Pediatr. 2016 Jun 8. pii: S0022-3476(16)30240-2.
Han JC, Lawlor DA, Kimm SY. **Childhood obesity**. Lancet. 2010 May 15;375(9727):1737-48. Epub 2010 May 5.
Hankinson AL, Daviglus ML, Bouchard C, et al. Maintaining a high **physical activity level over 20 years** and weight gain. JAMA 2010; 304: 2603-2610.
Hanks AS, Just DR, Wansink B. **Preordering School Lunch** Encourages Better Food Choices by Children. JAMA Pediatr. 2013 May 3:1-2.
Hansel B, Roussel R, Elbez Y, et al; **REACH** Registry Investigators. **Cardiovascular risk** in relation to body mass index and use of evidence-based preventive medications in patients with or at risk of atherothrombosis. Eur Heart J. 2015 Aug 4.
Hansen AR, Duncan DT, Tarasenko YN, et al. Generational shift in **parental perceptions of overweight among school-aged children**. Pediatrics. 2014 Sep;134(3):481-8.
Hansen L, Netterstrøm MK, Johansen NB, et al. **Metabolically Healthy Obesity and Ischemic Heart Disease**: A 10-Year Follow-Up of the Inter99 Study. J Clin Endocrinol Metab. 2017 Jun 1;102(6):1934-1942.
Hanson M, Barker M, Dodd JM, et al. Interventions to **prevent maternal obesity** before conception, during pregnancy, and post partum. Lancet Diabetes Endocrinol 2016; online Oct 12
Harari A, Endo B, Nishimoto S, et al. Risk of Advanced Papillary **Thyroid Cancer** in Obese Patients. Arch Surg. 2012 May 21:1-7.

Harder T, Roepke K, Diller N, et al. **Birth weight, early weight gain**, and subsequent risk of type 1 **diabetes**: systematic review and meta-analysis. Am J Epidemiol. 2009 Jun 15;169(12):1428-36. Epub 2009 Apr 10. This meta-analysis indicates that high birth weight and increased early weight gain are risk factors for type 1 diabetes.

Hardman CA, Ferriday D, Kyle L, et al. So **Many Brands and Varieties to Choose from**: Does This Compromise the Control of Food Intake in Humans? PLoS One. 2015 Apr 29;10(4)

Harnack L, Oakes JM, Elbel B, et al. Effects of **Subsidies and Prohibitions on Nutrition in a Food Benefit Program**: A Randomized Clinical Trial. JAMA Intern Med. 2016 Sep 19.

Harris JA, Byhoff E, Perumalswami CR, et al. The Relationship of Obesity to **Hospice Use** and Expenditures: A Cohort Study. Ann Intern Med. 2017 Feb 7.

Harris KC, Kuramoto LK, Schulzer M, et al. Effect of **school-based physical activity interventions** on body mass index in children: a meta-analysis. CMAJ. 2009 Mar 31;180(7):719-26.

Harris R, Card TR, Delahooke T, et al. Obesity Is the Most **Common Risk Factor for Chronic Liver Disease**: Results From a Risk Stratification Pathway Using Transient Elastography. Am J Gastroenterol. 2019 Aug 27.

Harrison ME, Norris ML, Obeid N, et al. Systematic review of the effects of **family meal frequency** on psychosocial outcomes in youth. Can Fam Physician. 2015 Feb;61(2):e96-e106.

Hart Carole L, Morrison David S, Batty G David, et al. Effect of **body mass index and alcohol** consumption on **liver disease**: analysis of data from two prospective cohort studies. BMJ 2010

Harvey J, Krukowski R, Priest J, West D. Log Often, Lose More: **Electronic Dietary Self-Monitoring for Weight Loss**. Obesity (Silver Spring). 2019 Mar;27(3):380-384.

Hasegawa K, Tsugawa Y, Chang Y, et al. Risk of an **asthma exacerbation after bariatric surgery** in adults. J Allergy Clin Immunol. 2015 Feb 7.

Havrankova J. Is the treatment of **obesity futile?: YES**. Can Fam Physician. 2012 May;58(5):508-10.

Hawkes C, Smith TG, Jewell J, et al. **Smart food policies** for obesity prevention. Lancet. 2015 Jun 13;385(9985):2410-21.

Hawkins DR, Kazmierski K, Hansen A, et al. Trends in **Weight Loss Efforts Among US Adolescents** With Overweight and Obesity. JAMA Pediatr. 2018 Jun 25.

Hay J, Wittmeier K, MacIntosh A, et al. **Physical activity intensity** and type 2 diabetes risk in overweight youth: a randomized trial. Int J Obes (Lond). 2016 Apr;40(4):607-14

Hayes A, Chevalier A, D'Souza M, et al . Early childhood obesity: Association with **healthcare expenditure** in Australia. Obesity (Silver Spring). 2016 Jul 6.

Healton CG, et al. **Smoking, obesity, and their co-occurrence** in the United States: cross sectional analysis. BMJ. 2006 May 12; [Epub ahead of print] 23.5% of adults were obese, 22.7% smoked, and 4.7% smoked and were obese.

Health Canada April 2007: The **Safe Use of Health Products** for Weight Loss. http://www.hc-sc.gc.ca/iyh-vsv/med/weight-amaigr_e.html

Health Canada Apr/07 is warning consumers about **Bitter orange** & cardiovascular reactions in the Canadian Adverse Reactions April 2007 Newsletter.

Health Canada Apr/07 is warning consumers from the Hong Kong Department of Health found **Lexscl Fat Rapid Loss capsules to be adulterated with sibutramine** and thyroid hormones.

Health Canada via July/07 Medsafe also advised the public not to use the product **Dai Dai Hua Jiao Nang** because it was found to contain sibutramine.

Health Canada Aug/07 is advising Canadians of a recall in the United States of one lot of **Metaboslim Apple Cider Vinegar**, which is marketed as a dietary supplement, because it has been found to contain sibutramine, a prescription medication that should only be taken under medical supervision.

Health Canada Sept/07 is advising consumers not to use foreign health products due to concerns about possible side-effects: **Jacaranda**, **Queenmer Fat Loss**, **Li Da Dai Dai Hua Jiao Nang**, **J-minus** and **Jelimel Slimming Capsules**. These products are promoted for weight loss and have been found to be adulterated with the prescription drug sibutramine. Sibutramine is used for treating obesity and should only be taken under the supervision of a health professional. **Junyu Jiaonanyihao** has been found to contain the undeclared prescription drugs sibutramine and dexamethasone, as well as phenolphthalein, which is currently prohibited in Canada.. **Heng Tong Jiangtangning Jiaonang** was found to contain the prohibited drug phenformin, and the prescription drug glibenclamide (glyburide) which should only be taken under the supervision of a health professional.

Health Canada Jan/08 is warning Canadians not to use the unauthorized product **Physio Care Lida Dai Dai Hua Jiao Nang Slimming Capsules** (batch number 28012007 / expiration date: Jan 2009). This product is promoted for weight loss and has been found to contain a derivative of the prescription drug sibutramine.

Health Canada April/08 is advising consumers not to use **Xian Zhi Wei II** was found to contain sibutramine and phenolphthalein, which are not meant for self-care and may cause serious side effects.

Health Canada Aug/08 is advising consumers not to use 9 foreign health products due to concerns about possible side-effects: **Dan Bai Shou Shen Su** was found to contain undeclared thyroid hormones and sibutramine. **Karntien and Karntien Easy to Slim** were adulterated with sibutramine and a compound that is similar in structure to sibutramine (N-desmethylsibutramine). **More Slim** was found to contain the undeclared pharmaceutical ingredient sibutramine. **Soloslim** was found to contain an undeclared substance similar in structure to the prescription drug sibutramine. It also contains the prescription drug L-carnitine, as well as synephrine, which is not authorized for sale in weight loss products in Canada.

Health Canada Aug/08 is advising consumers not to use 8 foreign health products due to concerns about possible side-effects: The Hong Kong Department of Health warned against the use of Natural (Xin Yi Dai) and Lasmi because Natural (Xin Yi Dai) was found to contain sibutramine and phenolphthalein, and Lasmi was found to contain sibutramine and spironolactone. The Hong Kong Department of Health warned against the use of AA Qu Feng Shu Jin Wan because it was found to contain the undeclared pharmaceutical ingredient dexamethasone. Apisate contained fenfluramine and Energy ll contained sibutramine. Obat Asam Urat and Asam Urat both contained dexamethasone, phenylbutazone and piroxicam. The Hong Kong Department of Health warned against the use of Slim 3in1 (Xiao Nan zhi Bao) because it was found to contain the undeclared pharmaceutical ingredients sibutramine and phenolphthalein.

Health Canada Sep/08 is advising consumers not to use 2 foreign health products due to concerns about possible side-effects: The Hong Kong Department of Health warned against the use of **Hanguo shoushen yihao** (meiti xing) because it was found to contain the undeclared pharmaceutical ingredient sibutramine. The Hong Kong Department of Health warned against the use of **ARMA - Sin Gang San** and New ARMA - Sin Gang San because they were found to contain the undeclared pharmaceutical ingredients sibutramine and fenfluramine.

Health Canada Nov/08 is advising that the Hong Kong Department of Health warned consumers not to buy or use **Fat Killer, Carbohydrate Cut and Sugar-Carbohydrate Cut** because they contain sibutramine and an unauthorised substance similar in structure to sibutramine.

Health Canada Jan 2009 is advising consumers not to use 4 foreign products: **Zhuang Tjar Gere** because it contains the undeclared prescription drugs sildenafil & tadalafil, **Zhixhue** Capsules manufactured by Vital Pharmaceutical Holdings Ltd. due to concerns of serious side- effects including liver dysfunction, **Tonik Warisan Banjar** because it contains undeclared dexamethasone & **Healthily Slim** because it contains sibutramine.

Health Canada Mar/09 Foreign Product: **68 Weight Loss Products**; Best-life Fat Burning Capsules; Bevidan;Huiji Yin Chiao Chieh Tu Pien & Relacore. Plus Lami, Linglongquxian, Menergy M-Essence, Nyal Day & Night Cold & Flu Fighter (AUST L 146264), Nyal Cold & Flu Fighter (AUST L 146263), 999 Radix Notoginseng, Batch no. 0807021, Slim Pure, Carbohydrate, Kalomee, K Carbohydrate, K Tighten Slim, & K Slimming Pills. http://www.hc-sc.gc.ca/ahc-asc/media/advisories-avis/_fpa-ape_2009/index-eng.php

Health Canada June/09 Foreign Product Alerts: **Jia Yi Jian** (undeclared sibutramine & tadalafil); **Shan Dian Qiang Xiao Shou** (undeclared sibutramine & phenolphthalein).

Health Canada June/09 is warning consumers not to use the unauthorized product **Slim Magic Herbal**, which is promoted as a weight-loss product, as it was found to contain an undeclared pharmaceutical ingredient similar to the prescription drug sibutramine.

Health Canada is warning consumers not to use the unauthorized product **Nutural Slim**, which is promoted as a weight-loss product, as it was found to contain the undeclared pharmaceutical ingredient sibutramine and also an undeclared pharmaceutical ingredient similar to sibutramine.

Health Canada June/09 warns of foreign Product Alerts: ***Herbal Xenicol*** because it contains undeclared cetilistat. ***BioEmagrecim***, which the FDA had previously warned contained sibutramine, was also found to contain fluoxetine, furosemide and fenproporex. Products: ***Slimbionic***, ***Xsvelten***, ***999 Fitness Essence***, ***24" ince***, ***Light Some***, ***Paiyouji***, ***Pearl White Slimming***, & ***Reducing Weight Easily*** contain undeclared pharmaceutical ingredients (sibutramine and/or phenolphthalein) and/or excessive levels of lead, and may cause serious health effects..

Health Canada Aug/09 is advising via Singapore Health Sciences Authority (HSA) that **Delima Raja Urat** contains undeclared dexamethasone, chlorpheniramine, pheniramine and sibutramine.

Health Canada Dec/09 is advising Canadians not to use certain Acai Berry products after a large number of shipments of adulterated products were stopped at the border. The product names include: **Anti-Aging Acai Berry, Guarana Blast, Brazillian Pure, Anti-aging Vital Rez V, Weight Loss VitalAcai, Dietary Supplement Acai Power Blast and Muscle Mass**. These products for anti-aging and weight loss were found to contain undeclared sildenafil.

Health Canada Dec/09 is warning consumers not to use "**RevolutionDS Weight Loss**", an unauthorized health product promoted for weight loss, because it contains benzylpiperazine (BZP), and may pose serious health risks.

Health Canada Jan/10 informs that U.S. FDA: **Pai You Guo** contains sibutramine and phenolphthalein. Hong Kong Department of Health: **Ku Xiu Ba Xiang Jian Fei Wan** contains sibutramine and an unauthorized substance similar to sibutramine; **Super Slim (Yani)** contains sibutramine and phenolphthalein; **SHoufsy** contains sibutramine & **MIGAC (sic) FAT BURMING (sic) FACTOR** contains sibutramine.

Health Canada Jan/10 is warning consumers not to use the unauthorized product "**The Slimming Coffee**," which was previously sold as "**Lose Weight Coffee**," because it was found to contain sibutramine.

Health Canada Mar/10 is warning Canadians that an unauthorized health product, "**Herbal Diet Natural**" has been found on the Canadian market and contains an undeclared pharmaceutical ingredient similar to the prescription drug sibutramine.

Health Canada is warning Canadians that an unauthorized health product, "**West Pharm Therma Lean Fat Burner Energizer**" was found on the Canadian market. West Pharm Therma Lean Fat Burner Energizer contains Ephedrine and caffeine, which combined together, may cause serious and possibly fatal adverse effects.

Health Canada Apr/10 is warning Canadians that an unauthorized health product, "Slim-30" distributed in Ontario and Quebec by Duxx Enterprises Inc., contains an undeclared pharmaceutical ingredient similar to the prescription drug, sibutramine.

Health Canada May/10 is advising consumers not to use the following foreign health products due to concerns about possible adverse reactions: 1. **Ba Bao Xiao Ke Dan** The Hong Kong Department of Health warned consumers not to buy or use Ba Bao Xiao Ke Dan after it was found to contain undeclared glibenclamide. 2. **Seven Slim 7 Seshou** (Qingchun Shaonüxing, Jieshixing, Guifurenxing, Songchixing), Shoushen Jiaoguan-Tinei Yundong Wan (Jian Xiabanshen, Jian Quanshen Feipang) The Hong Kong Department of Health warned consumers not to buy or use the six products listed above after they were found to contain undeclared sibutramine and phenolphthalein.

Health Canada May/10 is advising consumers not to use 1. **Botanical Slimming 100% Natural Soft Gel, also sold as Meizitang** The Australian Therapeutic Goods Administration warned consumers not to buy or use this product after it was found to contain undeclared sibutramine. 2. **Marsha Slim Plus** The Hong Kong Department of Health warned consumers not to buy or use Marsha Slim Plus after it was found to contain undeclared sibutramine, an unauthorized substance similar to sibutramine and phenolphthalein. 3**. S&S Super Slender** The Hong Kong Department of Health warned consumers not to buy or use S&S Super Slender after two samples were found to contain agent similar to sibutramine. One of the tested samples also contained undeclared sibutramine and phenolphthalein.

Health Canada June/10 is advising consumers not to use the following foreign health products due to concerns about possible adverse reactions: 1. **COMECOO, ZHONGCAOYAO-JIANKANGJIANFEI** The Hong Kong Department of Health warned consumers not to buy or consume these two products after they were found to contain undeclared phenolphthalein, sibutramine and two unauthorized substances similar to sibutramine. 2. **Qingzhi Santian Shou** The Hong Kong Department of Health warned consumers not to buy or consume Qingzhi Santian Shou after it was found to contain undeclared sibutramine and an unauthorized substance similar to sibutramine.

Health Canada July/10 is advising consumers not to use the following foreign health product(s) 1.. **Po Chai Pills** (capsule form) The Hong Kong Department of Health warned consumers not to buy or use this product after it was found to contain undeclared sibutramine and phenolphthalein. Sibutramine is a prescription drug and should only be used under the supervision of a health care practitioner while phenolphthalein is no longer authorized for sale in Canada because it may cause cancer. Po Chai Pills (capsule form) has been recalled by the manufacturer. 2. **LiPO-8 Cap and Glucomi 600 Cap** Hong Kong Department of Health warned consumers not to buy or use these products because they contain undeclared sibutramine.

Health Canada July/10 is advising consumers not to use the following foreign health products due to concerns about possible adverse reactions: **1 Body Beautiful** The Hong Kong Department of Health warned consumers not to buy or consume *1 Body Beautiful* after it was found to contain undeclared phenolphthalein and sibutramine. 2. **USA Yaku Cell Slimming Capsules, Dong Gua Pai You Su, Qing Gua Pai You Su, and Mu Gua Pai You Su** The Hong Kong Department of Health warned consumers not to buy or consume these four products after they were found to contain undeclared phenolphthalein, sibutramine and an unauthorized substance similar to sibutramine.

Health Canada Aug/10 is advising consumers not to use the following foreign health product(s): **Que She** The U.S. FDA warned consumers not to buy or use Que She after it was found to contain undeclared fenfluramine, propranolol, sibutramine and ephedrine. **Sheng Yuan Fang** The Hong Kong Department of Health (HKDH) warned consumers not to buy or use Sheng Yuan Fang after it was found to contain undeclared phenolphthalein and sibutramine.

Health Canada Sep/10 is advising consumers not to use : **Joyful Slim Herb** Supplement The U.S. FDA informed consumers of a recall of one lot (#101408) of Joyful Slim Herb Supplement after FDA tests found it to contain undeclared desmethyl sibutramine. The lot is being voluntarily recalled nationwide in the U.S. by the company J & H Besta Corp.

Health Canada Oct/10 is informing healthcare practitioners and Canadians that Abbott Laboratories is **voluntarily withdrawing the prescription weight-loss drug sibutramine**, which is marketed as Meridia®, from the Canadian market.

Health Canada Nov/10 **Amana Care Seven Slim Herbal Capsules**: The Israel Ministry of Health informed consumers that it found the product Amana Care Seven Slim Herbal Capsules to contain undeclared sibutramine and residue of sildenafil.

Health Canada Nov/10 is advising consumers not to use the following foreign health products due to concerns about possible adverse reactions: **1. Goya–Bitter Melon - Miyura Fit'x Capsules** contained undeclared phenolphthalein and sibutramine **2. Solo Slim Extra Strength - Revivexxx Extra Strength** contained undeclared didesmethyl sibutramine.

Health Canada Nov/10 "**Fat Burner No. 1**" (labelled in Chinese characters translated as "**Qian Mei Yin Zi**", an unauthorized Chinese herbal weight loss medicine, is being voluntarily recalled by Ying Tai TCM Supplying Ltd. after Health Canada lab tests revealed the product contains two pharmaceutical ingredients: a chemical similar to sibutramine (N,N- didesmethylsibutramine), and sildenafil.

Health Canada Dec/10 is advising consumers not to use the following foreign health products due to concerns about possible adverse reactions: 1. **Slimming Beauty Bitter Orange Slimming Capsule (Slimming Beauty)** The U.S. Food and Drug Administration warned consumers not to buy or use Slimming Beauty after FDA lab tests revealed that this product contains undeclared sibutramine.

Health Canada Jan/11 The product **Synerate**, manufactured for Strive and distributed by Upper 49th, is being voluntarily recalled from the Canadian market because of the risk of serious, potentially fatal adverse effects from the combination of the ingredients in the product. Synerate, a product used for weight loss or body building, contains caffeine and synephrine, which is similar to ephedrine.

Health Canada Feb/11 is advising consumers not to use the following foreign health products due to concerns about possible adverse reactions: **1. Fruta Planta, Reduce Weight Fruta Planta** The U.S. FDA warned consumers not to buy or use Fruta Planta and Reduce Weight Fruta Planta after FDA lab tests revealed that this product contains undeclared sibutramine. **2. Slimming Factor** The Australian TGA warned consumers not to buy or use Slimming Factor after TGA lab tests confirmed the presence of the undeclared substances sibutramine, fenfluramine and phenolphthalein. According to the TGA release, the product is sold over the Internet.

Health Canada Mar/11 is advising consumers not to use the following foreign health products due to concerns about possible adverse reactions: 1. **Celerite Slimming Capsules**: The U.S. FDA informed consumers of a company recall of CeleriteTM Slimming Capsules after it was found to contain undeclared sibutramine. 2. **Herbal Flos Lonicerae** (Herbal Xenicol) Natural Weight Loss Formula: The product was found to contain undeclared sibutramine at more than twice the dose that was normally prescribed before sibutramine was removed from the UK market in 2010.

Health Canada May/11 is advising consumers not to use the following foreign health products due to concerns about possible adverse reactions: **1. Dr. Health Series CM Factor** The Hong Kong Department of Health warned consumers not to buy or use this product after it was found to contain an unauthorized substance similar to sibutramine that may pose similar health risks.

Health Canada July/11 is advising consumers not to use the following foreign health products due to concerns about possible adverse reactions: **1. Slim Xtreme Herbal Slimming Capsules** The U.S. Food and Drug Administration informed consumers of a voluntary recall after *Slim Xtreme Herbal Slimming Capsules* was found to contain undeclared sibutramine.

Health Canada Aug/11 is advising consumers not to use the following foreign health products due to concerns about possible adverse reactions: **1. Celerite Slimming Tea** The U.S. FDA informed consumers of a company recall of Celerite Slimming Tea after it was found to contain undeclared sibutramine. **2. Pink Lady for Women Capsules, St Nirvana Herbal Slimming Capsules** The Australian TGA warned consumers not to use these products after Pink Lady for Women Capsules was found to contain undeclared tadalafil while St Nirvana Herbal Slimming Capsules was found to contain undeclared sibutramine and phenolphthalein. According to the TGA advisories, these products are sold over the Internet. **3. Fifteen products promoted for weight loss** The Hong Kong Department of Health (HKDH) warned consumers not to buy or use these 15 products after they were found to contain at least one of the following undeclared substances: phenolphthalein, sibutramine, and/or an unauthorized substance similar to sibutramine.

Health Canada Oct/11 is advising Canadians not to use these foreign health products as they may pose a health risk. **Slim Forte Slimming Capsules**, **Slim Forte Double Power Slimming Capsules**, **Slim Forte Slimming Coffee** and **Meizitang Botanical Slimming Soft Gel**-The U.S. Food and Drug Administration warned that these weight loss products contain an unauthorized drug (sibutramine). **OxyELITE Pro capsules and Pure Fat Three Days Reduce Weight capsules**-The Australian Therapeutic Goods Administration warned that these weight loss products contain an unauthorized drug (sibutramine), or a prescription drug (yohimbine).

Health Canada Nov/11 is advising Canadians not to use these foreign health products as they may pose a health risk. 1. **Metabolic Advantage** The Singapore Health Sciences Authority warned that this weight-loss product contains prescription drugs (thyroid hormones). 2. **Tian Ma Tu Chung Seven Leave Ginseng, Vall-Boon Tongkat Al,** and **Pao Ni Kang** The Singapore Health Sciences Authority warned that these traditional herbal products contain prescription and over-the-counter drugs (dexamethasone, ketoconazole, repaglinide, pheniramine, and chlorpheniramine). 3. **Slimming Kapsul** The Hong Kong Department of Health warned that this weight-loss product contains an unauthorized drug (sibutramine) and a prescription drug (spironolactone). 4. **Pancre-Plus** The Hong Kong Department of Health warned that this counterfeit Chinese medicine contains an unauthorized drug (phenformin) and a prescription drug (glyburide).

Health Canada Jan/12 advises: 1)**17 weight loss products (see Alert for a complete list)** A-Slim 100% Natural Slimming Capsule, Acai Berry Soft Gel ABC, Advanced Slim 5 >DaiDaiHuaJiaoNang, Dream Body Slimming Capsule, Fruit Plant Lossing Fat Capsule, Health Slimming Coffee, Ja Dera 100% Natural Weight Loss Supplement, Leisure 18 Slimming Coffee, Lishou, Magic Slim Tea, Magic Slim Weight Reduction Capsule, P57 Hoodia, Pai You Guo Slim Tea, PhentraBurn Slimming Capsules, Slender Slim 11 Tengda. The U.S. Food and Drug Administration warned that these weight loss products contain unauthorized drugs (sibutramine, phenolphthalein). **2. Slimina weightloss capsules, S-shape slim capsules** The Australian Therapeutic Goods Administration warned that these weight loss products contain prescription drugs (propranolol, nifedipine) and/or unauthorized drugs (sibutramine, fenfluramine, phenolphthalein). **3. Cardiotium, Paidusu, SlimEasy Herbs Capsule, Tianran Zuanshi Xianweisu** The Hong Kong Department of Health warned that these health products contain prescription drugs (losartan, atorvastatin, thyroxine) and/or unauthorized drugs (sibutramine, phenolphthalein).

Health Canada May/12 1. **CanSui; Lexscl Fat Rapid Loss Capsule; The Extreme-thin Fat Burning Bomb; Xiu Zhi Su L-Carnitine Slimming Capsule** The Hong Kong Department of Health warned that these weight loss products contain unauthorized drugs (sibutramine, phenolphthalein). 2. **Lipro Diet Pills; Xiyouji Qingzhi** weight loss capsules The Australian Therapeutic Goods Administration warned that these weight loss products contain an unauthorized drug (sibutramine).

Health Canada June/12 **1. Japan Weight Loss Blue, Japan Rapid Weight Loss Diet Pills Green; Japan Rapid Weight Loss Diet Pills Yellow:** The U.S. Food and Drug Administration warned that these weight loss products contain prescription drugs (sibutramine, ephedrine alkaloids) and unauthorized drugs (phenolphthalein, and substances similar to sibutramine). **2. Mince Belle; Everlax; Ever Slim; Ever Slim Shake Mix (Strawberry); Ever Slim Shake Mix (Chocolate); Acai-Man Mangosteen Herbal Drink; Perfect Men:** The U.S. Food and Drug Administration informed of a recall because these weight loss and sexual enhancement products contain prescription drugs (sibutramine or tadalafil).

Health Canada Jun/12 testing has identified that the weight loss product "**ZXT Gold**" bee pollen capsules contain hidden pharmaceutical ingredients (sibutramine and phenolphthlalein).

Health Canada Aug/12: Burnaby, B.C. Store (**U-Box**) Selling Potentially Dangerous Weight Loss Products. Further to our previous communications, Health Canada is advising Canadians that four products promoted for weight loss have been seized from "U-Box," a store in Burnaby, B.C. Health Canada testing has identified they contain hidden drug ingredients (sibutramine and phenolphthalein) that may pose serious health risks. Caffeine was also found in some of the products and was not listed on the product label.

Health Canada is advising Canadians that three unauthorized products "**Goya Bittermelon", "S-organic Cocoa+L-carnitine", or "KaBaNa L-Carnitine 360 Slimming Coffee**", promoted for weight loss have been seized from "Cube Inc.", a box-store in Richmond, B.C. These products contain hidden drug ingredients (sibutramine and phenolphthalein) that may pose serious health risks. Caffeine was also found in two products and was not listed on the product label.

Health Canada Apr/13 **1. Diet Garcinia Forte; Shan Dian Shou; Aulura Energy Dietary Supplement** The Hong Kong Department of Health has advised consumers not to use these products after they were found to contain sibutramine and phenolphthalein, drug ingredients that were not declared on their product label.

Health Canada Aug/13 is advising Canadians not to use these foreign health products as they may pose a health risk. **1. Brazilian Slimming Coffee, Leisure 18 Slimming Coffee, 7 Days Slimming Coffee, Brazilian 7 Days Slimming Coffee, Beauty Secret Slimming Coffee, Body Beauty 5 Days Slimming Coffee, Leisure 18 Slimming Mango Juice, Leisure 18 Slimming Orange Juice, Authentic Leisure 18 Slimming Orange Juice, Super Slim Orange Juice, Coffee Fashion Slimming** The Hong Kong Department of Health has advised consumers not to use these products after they were found to contain the undeclared drug ingredients sibutramine and/or phenolphthalein. http://healthycanadians.gc.ca/recall-alert-rappel-avis/hc-sc/2013/34859a-eng.php **5. Best Slim capsules, Meizi Evolution Botanical Slimming soft gel capsules** The Australian Therapeutic Goods Administration warned consumers not to use these products after they were found to contain the undeclared drug sibutramine.

Health Canada Nov/13 is advising Canadians not to use these foreign health products as they may pose a health risk. These products have been found by regulators in other countries to contain drug ingredients or soy milk allergens that are not declared on the product labels, or a high level of microbial contamination. Prescription drugs should only be taken under the supervision of a healthcare professional. These products are not authorized for sale in Canada and have not been found on the Canadian market, but they may have been brought into the country by travellers or purchased over the Internet:

1. **Aisiyuan V26 Slimming Granules, AcaiBerry Living-XS, and 4C Cosmoslim** , http://healthycanadians.gc.ca/recall-alert-rappel-avis/hc-sc/2013/36269a-eng.php ;
2. **MAXILOSS Weight Advanced** http://healthycanadians.gc.ca/recall-alert- rappel-avis/hc-sc/2013/36197a-eng.php;
3. **ESV Extra Strong Version, MSV Strong Version, RL Rapid Loss, My Slimmer Me (MSM) soft gel capsules, Natural Miaotiaoyishen capsules, and Paiyouji Natural Slimming Capsules** http://healthycanadians.gc.ca/recall-alert-rappel-avis/hc-sc/2013/36521a-eng.php.

Health Canada Feb/14: 1. **Lightning 10.0+, LV Shou Reduces Fat, and STB Summit of the Thin Body S Woman Degreasing Burning Pill** The Hong Kong Department of Health warned consumers not to use this product after it was found to

contain sibutramine, phenolphthalein, and indomethacin.

Health Canada Apr/14 has seized the unauthorized drug, "**L-Showm Weight Loss Pills**", being sold at the U-Box store, located at 2809-4500 Kingsway, Burnaby, BC. Health Canada testing: contained an undisclosed ingredient, phenolphthalein.

Health Canada Apr/14: Four unauthorized drugs being sold at two SVN FUEL stores - one in Burnaby and one in Coquitlam, B.C. - were seized by Health Canada as they contain ingredients that are potentially dangerous to the health of consumers. The products, and the unapproved ingredients they contain, include **Jack3d** (DMAA (1, 3-dimethylamylamine), **Red Rockets** (ephedrine and caffeine), **West Pharm Therma Lean** (ephedrine and caffeine), and **OxyElite Pro** (1, 3-dimethylamylamine HCl and Yohimbe Bark extract). They were being promoted for weight management.

Health Canada May/14 **Esbelin siloutte te, Esbelin Siloutte Herbal blend with L-Carnitine, Esbelder man, Esbelder fem, Esbelder siloutte** contains Sibutramine, N-Desmethylsibutramine, and N-di-Desmethylsibutramine; **Instant Slim** contains sibutramine and phenolphthalein.

Health Canada May/14 One lot of **Lite Fit USA** (Lot Number 13165, Exp. 05/17) is being voluntarily recalled in the U.S. after analysis by the U.S. Food and Drug Administration revealed the lot contains the undeclared prescription drug sibutramine.

Health Canada May/14: 1. **Slim Fortune, Lidiy & Slim Expert:** FDA found sibutramine; 2. **Dr. Mao Slimming capsules, Perfect Body Solutions, Burn 7**: FDA found sibutramine; **Bella Vi Insane Amp'd Up, Be Inspired, Goodliness Fat Reducing capsules, Jimpness Beauty Fat Loss capsules**: FDA found sibutramine and phenolphthalein.

Health Canada June/14: **Asset Extreme, Asset Extreme Plus, Meizitang Citrus, Slimming Diet Berry Plus, Citrus Fit Gold, Hot Detox, Thinogenics** contains sibutramine. **Tonic Life BP & Slimfast** capsules contains phenolphthalein . **Dr. Ming's Chinese Capsule, Magic Slim and Apple's Quick Impact Weight Loss** contains sibutramine and phenolphthalein.

Health Canada July/14: **Bella Vi Insane Bee Pollen Capsules, Bella Vi BTrim Ultimate Boost, Bella Vi BTrim Max, Bella Vi Extreme Accelerator**: The United States Food and Drug Administration (FDA) warned consumers not to use these products after they were found to contain undeclared sibutramine and/or phenolphthalein. **Super Fat Burner capsules, Maxi Gold capsules, and Esmeralda softgels**: The United States Food and Drug Administration (FDA) warned consumers not to use these products after they were found to contain undeclared sibutramine and phenolphthalein. **Powerful leg-slimming capsules, Pink grain herbal slimming capsules, and Night fat-burning capsules**: The Australian Therapeutic Goods Administration (TGA) warned consumers not to use these products after they were found to contain undeclared phenolphthalein and diclofenac. The product, Night fat-burning slimming capsules, was also found to contain undeclaredtheophylline. **Zi Xiu Tang Pollen capsule and Zi Xiu Tang Beauty Face and Figure capsule**: The Australian Therapeutic Goods Administration (TGA) warned consumers not to use these products after they were found to contain undeclared sibutramine, phenolphthalein, diclofenac, and ibuprofen. The product, Zi Xiu Tang Beauty Face and Figure capsule, was also found to contain undeclared glibenclamide, and indomethacin.

Heath Canada Aug/14: The Australian Therapeutic Goods Administration (TGA) warned consumers not to use the product **Sanovera Starter capsules**, the Hong Kong Department of Health warned consumers not to use the product **Yanhee Slim** and the United States Food and Drug Administration (FDA) warned consumers not to use the products **Infinity, Asset Bee Pollen, Asset Bold, Slim Trim U, and Natural Body Solution** after they were found to contain undeclared sibutramine. The Australian Therapeutic Goods Administration (FDA) warned consumers not to use **3x Slimming Powder Capsules** after it was found to contain undeclared sibutramine and phenolphthalein.

Health Canada Sep/14: **La Jiao Shou Shen, B-Perfect, Diet Master, Super Slim, Slim Max**: The United States Food and Drug Administration (FDA) warned consumers not to use these products after they were found to contain undeclared sibutramine and phenolphthalein.

Health Canada Dec/14 is following up with Rapha Biotech Inc. **RAPHA Vitamin B1** (NPN: 80036493) -- undeclared ingredients: sibutramine, desmethyl sibutramine.

Health Canada Dec/14: The United States Food and Drug Administration (FDA) warned consumers not to use the products **Lingzhi Cleansed Slim Tea, Trim-Fast Slimming Softgel, Sliming Diet By Pretty White, Lipo 8 Burn Slim, and Best Line Suplemento Alimenticio Capsules**. Tthe Hong Kong Department of Health warned consumers not to use the products **Slim Perfect Arm and Slim Perfect Legs** and the Australian Therapeutics Goods Administration (TGA) warned consumers not to use the product **Slyn Both Green capsules** after they were found to contain undeclaredsibutramine. The United States Food and Drug Administration (FDA) also warned consumers not to use the product **Mezo** after it was found to contain benzylsibutramine. **Mix Fruit Slimming**: The United States Food and Drug Administration (FDA) warned consumers not to use this product after it was found to contain undeclared sibutramine and phenolphthalein.

Health Canada Jan/15: **Star Majestic Slimming**- Undeclared sibutramine & phenolphthalein via Australian Therapeutic Goods Administration. **Sit and Slim II**-Undeclared sibutramine & phenolphthalein via FDA.

Health Canada Mar/15 advises- FDA Mar/15 **Bee Slim** & **Bee Thin** has undeclaried silbutramine. Singapore Health Sciences Authority Mar/15 **Nutri Drops Grapefruit Diet**: Undeclared sibutramine, benzyl sibutramine & phenolphthalein.

Health Canada Mar/15 advisory regarding "**Altimate Fat Burner Maximum Burn" being sold by Nature's** Source in Vaughan, Ont., the Department received a complaint about the product also being sold at Nature's Source, 2391 Trafalgar Rd., Unit #6 in Oakville, Ont. Altimate Fat Burner Maximum Burn is an unauthorized health product labelled to contain DHEA, yohimbe, caffeine and ephedrine.

Health Canada Jun/15 requests quarantine of drugs linked to **Zhejiang Hisun Pharma** due to data integrity concerns.

Health Canada Aug/15-FDA has **Akttive Capsules & Zero Xtreme Capsules** with undeclared silbutramine.

Health Canada Mar/16 says A**sia Black, Black Widow 25, Burn Fat Now, Extreme Stack, Fataway Ultimate Stack, MaxOut Body, Metabolic Accelerator, Methyldrene Original 25 Dietary Supplements, ThermoFX, Thermogenic Fat Burner & Thin and Slim Naturally** by FDA contains undeclared salicylic acid.

Health Canada Mar/16 says **BASCHI Quick Slimming capsules** by Australian Therapeutic Goods Administration contains undeclared sibutramine.

Health Canada Mar/16 says **Basha Nut 100% Fruit Soft Gel Capsules, Ultimate Herbal Slimcap, Lishou Slimming Coffee, Meizi Super Power Fruits Herbal Slimming Formula, NATUREAL & Tip-Top Shape by FDA** contains undeclared sibutramine.

Health Canada Mar/16 says **Miracle Diet 30 & Xtreme Fat Burner Capsules** by FDA contains undeclared phenolphthalein.

Health Canada Mar/16 says **New Queen Slimming soft gel capsules** by Australian Therapeutic Goods Administration contains undeclared sibutramine.

Health Canada Mar/16 says **Perfect Slim Fast Track Slim & Slyn Both** by FDA contains undeclared fluoxetine

Health Canada Mar/16 says **Pink Bikini and Shorts on the Beach Blue Edition & Pink Bikini and Shorts on the Beach Blue Gold Edition** by FDA contains undeclared sibutramine and phenolphthalein.

Health Canada Mar/16 says **Super Herbs** by FDA contains undeclared sibutramine and desmethylsibutramine

Health Canada June/16: Australian Therapeutic Goods Administration-**Excellence Losing Weight** capsules contains undeclared silbutramine.

Health Canada June/16: Australian Therapeutic Goods Administration- **Natural Model capsules** contains undeclared sibutramine and phenolphthalein

Health Canada July/16: FDA says **Dynamizm Capsules, ENVY BP, Propell Platinum, Xerophagy Capsules, & Sextra** contains undeclared sibutramine.

Health Canada July/16: FDA says **Eradicate Capsules** undeclared sibutramine and desmethylsibutramine.

Health Canada July/16: Australian Therapeutic Goods Administration says **Leisure Slimming capsules** contains undeclared sibutramine and phenolphthalein.

Health Canada July/16: Australian Therapeutic Goods Administration says **U Slimming and U Plus Slimming capsules** undeclared sibutramine, phenolphthalein, diclofenac, and lignocaine.

Health Canada Aug/16 is advising consumers not to use the weight loss product **AlgoSlim**, distributed via mail order by E Sélection. The package does not contain unauthorized AlgoSlim and instead contains an authorized product, Slite-T, from a lot that expired in June 2012.

Health Canada July/16 **Exhilarate** undeclared sibutramine, desmethylsibutramine, phenolphthalein.

Health Canada Aug/16: FDA- **Dream Body 450mg, Dream Body Original Formula, Dream Body Advanced 400mg, Extra Slim Plus Acai Berry Weight Loss Formula, Lose Weight Coffee & SBF Bee Pollen** undeclared silbutramine.

Health Canada Aug/16: Hong Kong Department of Health- **Lose Weight Coffee** undeclared silbutramine.

Health Canada Aug/16: FDA- **Dream Body Advanced + Acai Weight Loss & Cleanse, & Dream Body Extreme Gold** undeclared sibutramine, fluoxetine, and sildenafil.

Health Canada Oct/16: **Adelganzantes R-II, Mang Luk Power Slim, Xcelerated Weight Loss Charged Up, & Xcelerated Weight Loss Turbo Charge**-Undeclared sibutramine by United States Food and Drug Administration.

Health Canada Oct/16: **B-finn**- Undeclared orlistat and 2-(diphenylmethyl)pyrrolidine (desoxy-D2PM)by Hong Kong Department of Health.

Health Canada Oct/16: **Citrus' Fit, Mang Luk Power Slim Detox, Slim Fit X, & Ultimate Lean** -Undeclared sibutramine and desmethylsibutramine by United States Food and Drug Administration.

Health Canada Oct/16: **Double S-** Undeclared sibutramine by Hong Kong Department of Health.

Health Canada Oct/16: **Maxx Easy**-Undeclared sibutramine and lorcaserin, and orlistat by United States Food and Drug Administration.

Health Canada Oct/16: **Mi Show Slimming capsules**- Undeclared sibutramine by Australian Therapeutic Goods Administration.

Health Canada Oct/16: **Xcelerated Weight Loss Ultra Max**- Undeclared phenolphthalein and sildenafil by United States Food and Drug Administration.

Health Canada Oct/16: **Zi Xiu Tang Beauty Face and Figure Capsule**- Undeclared phenolphthalein and fluoxetine by United States Food and Drug Administration.

Health Canada Nov/16: **Natural Eruption** has undeclared sibutramine by the United States Food and Drug Administration.

Health Canada Dec/16 reports: Australian Therapeutic Goods Administration: **Bee Sexy Slimming capsules** undeclared sibutramine; Australian Therapeutic Goods Administration: **Biolo World Slimming capsules**-undeclared sibutramine and phenolphthalein; Hong Kong Department of Health: **ele Slim Shot**-undeclared orlistat.

Health Canada Jan/17 wishes to advise Canadians that **hCG (human chorionic gonadotropin)** is not authorized or proven as a weight loss aid, and could pose serious health risks.

Health Canada Mar/17: **Queen Slimming Soft Gel** contains undeclared sibutramine

Health Canada Mar/17: VIP **Bio Mangosteen Complex** contains undeclared sibutramine & phenolphthalein.

Health Canada Mar/17: **CA NI Slim BELLANCE** has undeclared orlistat by the Hong Kong Department of Health.

Health Canada Mar/17: **Lean Extreme Max & X-treme Beauty Slim** has undeclared sibutramine by the FDA.

Health Canada Mar/17: **Platinum Max Strength Blue Pill Version, Slimming Plus Advanced & Platinum Weight Loss Solution** has undeclared sibutramine & phenolphthalein by the FDA.

Health Canada May/17: **Anyang Herbal Blue** by Singapore Health Sciences Authority has undeclared sibutramine.

Health Canada May/17: **Anyang Herbal Red** by Singapore Health Sciences Authority has undeclared diclofenac, phenolphthalein, and sibutramine.

Health Canada May/17: **Change Me Herbal Slimming Capsules & Ultimate & Herbal Slim Weight** Loss capsules by Australia Therapeutic Goods Administration has undeclared sibutramine.

Health Canada June/17: **Lose Weight capsules** has undeclared sibutramine and diclofenac by Australia Therapeutic Goods Administration.

Health Canada June/17: **Slim-Vie Slimming Capsules** has undeclared sibutramine, sildenafil, and phenolphthalein by Australia Therapeutic Goods Administration.

Health Canada Apr/19: is aware of Canadian and international reports of various complications, including some with a fatal outcome, associated with the use of intragastric balloons for weight loss therapy.

HEALTHY Study Group, A **School-Based Intervention** for Diabetes Risk Reduction. N Engl J Med 2010 0: NEJMoa1001933.

Heath GW, Parra DC, Sarmiento OL, et al; for the Lancet Physical Activity Series Working Group. **Evidence-based intervention** in physical activity: lessons from around the **world**. Lancet. 2012 Jul 17.

Heber David, Greenway Frank L ., Kaplan L ee M., et al. **Endocrine and Nutritional Management of the Post-Bariatric Surgery Patient**: An Endocrine Society Clinical Practice Guideline. Journal of Clinical Endocrinology & Metabolism, November 2010, 95 (11):4823–4843. http://www.endo-society.org/guidelines/final/upload/FINAL-Standalone-Post-Bariatric-Surgery-Guideline-Color.pdf

Helander EE, Wansink B, Chieh A. **Weight Gain over the Holidays** in Three Countries. N Engl J Med. 2016 Sep 22;375(12):1200-2.

Hellec B, Campbell-Scherer D, Michael Allan G. The skinny on **BMI and mortality**. Can Fam Physician. 2015 Nov;61(11):970.

Henderson DC, et al. A double-blind, placebo-controlled trial of **sibutramine (n=21) for clozapine**-associated weight gain. Acta Psychiatr Scand. 2007 Feb;115(2):101-5. Sibutramine treatment did not show significant weight loss compared with placebo in clozapine-treated patients with schizophrenia or schizoaffective disorder.

Henderson M, Benedetti A, Barnett TA, et al. Influence of **Adiposity, Physical Activity, Fitness, and Screen Time** on Insulin Dynamics Over 2 Years in Children. JAMA Pediatr. 2016 Feb 8.

Heneghan HM, Meron-Eldar S, Brethauer SA, et al.Effect of **Bariatric Surgery** on Cardiovascular Risk Profile. Am J Cardiol. 2011 Aug 29.

Henriksson P, Henriksson H, Tynelius P, et al. **Fitness and Body Mass Index During Adolescence and Disability Later in Life**: A Cohort Study. Ann Intern Med. 2019 Feb 12.

Herrmann J, Gersh B, Goldfinger J, et al. Body Mass Index and Acute and Long-term Outcomes **After Acute Myocardial Infarction** (from the Harmonizing Outcomes With Revascularization and Stents in Acute Myocardial Infarction [HORIZONS-AMI] Trial). The American Journal of Cardiology. 2014.

Heymsfield SB, Wadden TA. **Mechanisms, Pathophysiology, and Management** of **Obesity**. N Engl J Med. 2017 Jan 19;376(3):254-266.

Hill AP, Zuckerman KE, Fombonne E. **Obesity and Autism**. Pediatrics. 2015 Nov 2.

Hill JO, Wyatt HR, Peters JC. **Energy balance** and obesity. Circulation. 2012 Jul 3;126(1):126-32.

Hillier TA, Pedula KL, Schmidt MM, Mullen JA, Charles MA, Pettitt DJ. Childhood Obesity and Metabolic Imprinting: The Ongoing Effects of Maternal Hyperglycemia. Diabetes Care. 2007 May 22; [Epub ahead of print] Our results in a multi-ethnic US population suggest that increasing **hyperglycemia in pregnancy is associated with an increased risk of childhood obesity**.

Hillier TA, Pedula KL, Vesco KK, et al. Impact of **Maternal Glucose and Gestational Weight Gain on Child Obesity** over the First Decade of Life in Normal Birth Weight Infants. Matern Child Health J. 2016 May 6.

Himpens J, Cadière GB, Bazi M, et al. Long-term outcomes of **laparoscopic adjustable gastric banding**. Arch Surg 2011; DOI:10.1001/archsurg.2011.45.

Hingle M, Nichter M, Medeiros M, Grace S. **Texting for health**: The use of participatory methods to develop healthy lifestyle messages for teens. J Nutr Educ Behav 2013; 45:12-19.

Hjorth S, Näslund I, Andersson-Assarsson JC, et al. **Reoperations after bariatric surgery** in 26 years of follow-up of the Swedish Obese Subjects Study [online Ja 2, 2019]. JAMA Surg. doi:10.1001/jamasurg.2018.5084

Huf SW, Volpp KG, Asch DA, Bair E, Venkataramani A. Association of **Medicaid Healthy Behavior Incentive Programs** with smoking cessation, weight loss, and annual preventive health visits. JAMA Netw Open. 2018;1(8): e186185. doi:10.1001/jamanetworkopen.2018.6185

Ho M, Garnett SP, Baur L, et al. Effectiveness of **Lifestyle Interventions** in Child Obesity: Systematic Review With Meta-analysis. Pediatrics. 2012 Nov 19.

Ho M, et al. Impact of **Dietary and Exercise Interventions** on Weight Change and Metabolic Outcomes in Obese **Children and Adolescents**: A Systematic Review and Meta-analysis of Randomized Trials. JAMA Pediatr. 2013 Jun 17:1-11.

Hohwü L, Li J, et al. **Severe maternal stress** exposure due to bereavement before, during and after pregnancy and risk of overweight and obesity in young adult men: a Danish National Cohort Study. PLoS One. 2014 May 14;9(5):e97490.

Hoffman J, Frerichs L, Story M, et al. An **Integrated Clinic-Community Partnership** for Child Obesity Treatment: A Randomized Pilot Trial. Pediatrics. 2017 Dec 13.

Hollands GJ, Shemilt I, Marteau TM, et al. **Portion, package or tableware size for changing selection and consumption of food, alcohol and tobacco**. Cochrane Database of Systematic Reviews 2015, Issue 9. Art. No.: CD011045. DOI: 10.1002/14651858.CD011045.pub2. This review found that people consistently consume more food and drink when offered larger-sized portions, packages or tableware than when offered smaller-sized versions. This suggests that policies and practices that successfully reduce the size, availability and appeal of larger-sized portions, packages, individual units and tableware can contribute to meaningful reductions in the quantities of food (including non-alcoholic beverages) people select and consume in the immediate and short term. However, it is uncertain whether reducing portions at the smaller end of the size range can be as effective in reducing food consumption as reductions at the larger end of the range. We are unable to highlight clear implications for tobacco or alcohol policy due to identified gaps in the current evidence base.

Holme I, Tonstad S. **Survival in elderly men** in relation to midlife and current BMI. Age Ageing. 2015 Jan 21. pii: afu202.

Hong JL, Meier CR, Sandler RS, et al. Risk of **colorectal cancer after initiation of orlistat**: matched cohort study. BMJ. 2013 Aug 27;347:f5039.

Hooper L, Abdelhamid A, Moore HJ, et al. Effect of **reducing total fat intake** on body weight: systematic review and meta-analysis of randomised controlled trials and cohort studies. BMJ. 2012 Dec 6;345:e7666.

Hornack SE, Nadler EP, Wang J, et al. **Sleeve Gastrectomy for Youth With Cognitive Impairment** or Developmental Disability. Pediatrics. 2019 Apr 15.

Horvath K, Jeitler K, Siering U, et al. **Long-term effects of weight-reducing interventions in hypertensive patients**. Arch Intern Med 2008; 168:571-580.

Howard JB, Skinner AC, Ravanbakht SN, et al. Obesogenic Behavior and Weight-Based Stigma **in Popular Children's Movies**, 2012 to 2015. Pediatrics. 2017 Nov 20.

Hoyt LT, Kushi LH, Leung CW, et al. **Neighborhood influences** on girls' obesity risk across the transition to adolescence. Pediatrics. 2014 Nov;134(5):942-9.

Hsu C-Y et al. Body mass index and risk for **end-stage renal disease**. Ann Intern Med 2006 Jan 3; 144:21-8.

Hu Y, He JR, Liu FH, et al. Effectiveness of a **Kindergarten-Based Intervention** for Preventing Childhood Obesity. Pediatrics. 2017 Nov 10.

Huang JS, Chun S, Sandhu A, Terrones L. Quality Improvement in Childhood Obesity Management through the **Maintenance of Certification Process**. J Pediatr. 2013 Jun 26.

Huang TT, Cawley JH, Ashe M, et al. **Mobilisation of public support** for policy actions to prevent obesity. Lancet. 2015 Jun 13;385(9985):2422-31.

Huang G, Parikh PB, Malhotra A, et al. Relation of Body Mass Index and **Gender to Left Atrial Size and Atrial Fibrillation**. Am J Cardiol. 2017 Jul 15;120(2):218-222.

Hudda MT, Fewtrell MS, Haroun D, et al. Development and validation of a **prediction model for fat mass in children and adolescents**: meta-analysis using individual participant data. BMJ. 2019 Jul 24;366:l4293.

Huh, Susanna Y., Rifas-Shiman, Sheryl L., Taveras, Elsie M., et al. Timing of **Solid Food Introduction** and Risk of Obesity in **Preschool-Aged Children**. Pediatrics 2011 0: peds.2010-0740.

Hunger JM, Tomiyama AJ. **Weight Labeling** and Obesity: A Longitudinal Study of Girls Aged 10 to 19 Years. JAMA Pediatr. 2014 Apr 28.

Hunt K, Wyke S, et al. A **gender-sensitised weight loss and healthy living programme** for overweight and obese men delivered by **Scottish Premier League football** clubs (FFIT): a pragmatic randomised controlled trial. Lancet. 2014 Jan 20.

Huppke B, Ellenberger D, Hummel H, et al. Association of Obesity With **Multiple Sclerosis Risk and Response to First-line Disease Modifying Drugs** in Children. JAMA Neurol. 2019 Jul 15.

Hurst Y, Fukuda H. Effects of changes in **eating speed** on obesity in patients with diabetes: a secondary analysis of longitudinal health check-up data. BMJ Open. 2018 Feb 12;8(1):e019589.

Hutchison AT, Liu B, Wood RE, et al. Effects of **Intermittent Versus Continuous Energy Intakes on Insulin Sensitivity and Metabolic Risk in Women with Overweight**. Obesity (Silver Spring). 2019 Jan;27(1):50-58.

Hsu CC, Almulaifi A, Chen JC, et al. Effect of **Bariatric Surgery vs Medical Treatment** on Type 2 Diabetes in Patients With Body Mass Index Lower Than 35: Five-Year Outcomes. JAMA Surg. 2015 Sep 16:1-8.

Iannotti RJ, Wang J. Trends in **Physical Activity, Sedentary Behavior, Diet, and BMI** Among US Adolescents, 2001-2009. Pediatrics. 2013 Sep 16.

Ibrahim AM, Ghaferi AA, Thumma JR, et al. Variation in Outcomes at **Bariatric Surgery** Centers of Excellence. JAMA Surg. 2017 Jul 1;152(7):629-636.

Ibrahim AM, Thumma JR, Dimick JB. **Reoperation** and Medicare expenditures **after laparoscopic gastric band surgery** [online May 17, 2017].JAMA Surg. doi:10.1001/jamasurg .2017.1093

IDF: International Diabetes Federation. **Bariatric surgical** and procedural interventions in the treatment of obese patients with type 2 diabetes 2011 http://www.idf.org/webdata/docs/IDF-Position-Statement-Bariatric-Surgery.pdf

Ignat M, Vix M, Imad I, et al. Randomized trial of **Roux-en-Y gastric bypass versus sleeve gastrectomy** in achieving excess weight loss. Br J Surg. 2016 Nov 30.

Ikramuddin S, Korner J, Lee W-J, et al. **Roux-en-Y gastric bypass** vs intensive medical management for the control of type 2 diabetes, hypertension, and hyperlipidemia: The Diabetes Surgery Study randomized clinical trial. JAMA 2013; 309:2240-2249.

Ikramuddin S, Blackstone RP, Brancatisano A, et al. Effect of **reversible intermittent intra-abdominal vagal nerve blockade** on morbid obesity: the ReCharge randomized clinical trial. JAMA. doi:10.1001/jama.2014.10540.

Ikramuddin S, Billington CJ, Lee WJ, et al. **Roux-en-Y gastric bypass for diabetes** (the Diabetes Surgery Study): 2-year outcomes of a 5-year, randomised, controlled trial. Lancet Diabetes Endocrinol. 2015 Jun;3(6):413-22.

Ikramuddin S, Korner J, Lee WJ, et al. Durability of Addition of **Roux-en-Y Gastric Bypass to Lifestyle Intervention and Medical Management** in Achieving Primary Treatment Goals for Uncontrolled Type 2 Diabetes in Mild-to-Moderate Obesity: A Randomized Control Trial. Diabetes Care. 2016 Jun 16.

Ikramuddin S, et al. **Lifestyle intervention & medical management with vs without Roux-en-Y gastric bypass** & control of hemoglobin A1c, LDL cholesterol, & systolic blood pressure at 5 years-Diabetes Surgery Study. JAMA. doi:10.1001/jama.2017.20813

Imamura F, O'Connor L, Ye Z, et al. **Consumption of sugar sweetened beverages, artificially sweetened beverages, and fruit juice** and incidence of type 2 **diabetes**: systematic review, meta-analysis, and estimation of population attributable fraction. BMJ. 2015 Jul 21;351:h3576.

Inge TH, Zeller MH, Lawson ML, Daniels SR. A critical appraisal of evidence supporting a **bariatric surgical** approach to weight management for **adolescents**. J Pediatr. 2005 Jul;147(1):10-9.

Inge TH. **Bariatric surgery** to treat obesity and diabetes in adolescents. Obesity 2012; September 21, 2012; San Antonio, TX.

Inge TH, Zeller MH, Jenkins TM, et al. Perioperative outcomes of **adolescents undergoing bariatric surgery**: the Teen–Longitudinal Assessment of Bariatric Surgery (**Teen-LABS**) Study [published online November 4, 2013]. JAMA Pediatr. doi:10.1001/jamapediatrics.2013.4296.

Inge TH, Zeller MH, Jenkins TM, et al. **Perioperative Outcomes** of Adolescents Undergoing **Bariatric Surgery**: The Teen-Longitudinal Assessment of Bariatric Surgery (Teen-LABS) Study. JAMA Pediatr. 2013 Nov 4.

Inge TH, King WC, Jenkins TM, et al. The effect of **obesity in adolescence** on adult health status. Pediatrics. 2013 Dec;132(6):1098-104.

Inge TH et al. Weight loss and health status 3 years after **bariatric surgery in adolescents. (Teen-LABS)** N Engl J Med 2015 Nov 6.
Inge TH, Jenkins TM, Xanthakos SA, et al. Long-term outcomes of **bariatric surgery** in **adolescents** with severe obesity(**FABS-5+):** a prospective follow-up analysis. Lancet Diabetes Endocrinol. 2017 Jan 5.
Inge TH, Laffel LM, Jenkins TM, et al. Comparison of **Surgical and Medical Therapy for Type 2 Diabetes in Severely Obese Adolescents**. JAMA Pediatr. 2018 Mar 12.
Inge TH, Courcoulas AP, Jenkins TM, et al. **Five-year outcomes of gastric bypass in adolescents as compared with** adults. (Teen-LABS) N Engl J Med. DOI: 10.1056/NEJMoa1813909.
Institute of Medicine. Accelerating Progress in **Obesity Prevention:** Solving the Weight of the Nation. Washington, DC: National Academies Press, 2012.
InterAct Consortium. Long-Term Risk of Incident Type 2 Diabetes and **Measures of Overall and Regional Obesity**: The EPIC-InterAct Case-Cohort Study. PLoS Med. 2012 Jun;9(6):e1001230. (**waist circumference**)
InterAct Consortium. Consumption of **sweet beverages** and type 2 diabetes incidence in European adults: results from **EPIC-InterAct**. Diabetologia 2013; DOI:10.1007/s00125-013-2899-8.
Ioannides-Demos LL, Proietto J, McNeil JJ. **Pharmacotherapy** for obesity. Drugs. 2005;65(10):1391-418.
Ioannides-Demos LL, et al. Safety of **drug therapies** used for weight loss and treatment of obesity. Drug Saf. 2006;29(4):277-302.
Ip P, Ho FK, Louie LH, et al. **Childhood Obesity and Physical Activity-Friendly School Environments**. J Pediatr. 2017 Oct 4.
Isganaitis E, Venditti S, Matthews TJ, et al. **Maternal obesity and the human milk metabolome**: associations with infant body composition and postnatal weight gain. Am J Clin Nutr. 2019 Apr 4
Islami F, Goding Sauer A, Gapstur SM, et al. Proportion of **Cancer Cases Attributable to Excess Body Weight** by US State, 2011-2015. JAMA Oncol. 2018 Dec 27.
Isong IA, Richmond T, Kawachi I, et al. **Childcare Attendance and Obesity Risk**. Pediatrics.2016 ;138(5) :e20161539
Isong IA, Rao SR, Bind MA, et al. **Racial and Ethnic Disparities** in Early Childhood Obesity. Pediatrics. 2017 Dec 21.
Jacobs Eric J.; Newton Christina C.; Wang Yiting; et al. **Waist Circumference and All-Cause Mortality** in a Large US Cohort. Arch Intern Med. 2010;170(15):1293-1301.
Jacobson BC, et al. Body-mass index and symptoms of **gastroesophageal** reflux in women. N Engl J Med. 2006 Jun 1;354(22):2340-8.
Jago R, Davison KK, Thompson JL, Page AS, Brockman R, Fox KR. **Parental Sedentary Restriction**, Maternal Parenting Style, and Television Viewing Among 10- to 11-Year-Olds. Pediatrics. 2011 Aug 22.
Jakicic JM, Marcus BH, Lang W, Janney C. Effect of exercise on 24-month weight loss maintenance in overweight women. Arch Intern Med. 2008 Jul 28;168(14):1550-9; discussion 1559-60. The addition of **275 mins/wk of physical activity**, in combination with a reduction in energy intake, is important in allowing overweight women to sustain a weight loss of more than 10%. Interventions to facilitate this level of physical activity are needed.
Jakicic JM, Tate DF, Lang W, et al. Effect of a **stepped-care intervention approach** on weight loss in adults: a randomized clinical trial. JAMA. 2012 Jun 27;307(24):2617-26.
Jakicic JM, Davis KK, Rogers RJ, et al. Effect of **Wearable Technology** Combined With a **Lifestyle Intervention** on Long-term Weight Loss: The **IDEA** Randomized Clinical Trial. JAMA. 2016 Sep 20;316(11):1161-1171.
Jakobsen GS, Småstuen MC, Sandbu R, et al. Association of **bariatric surgery vs medical obesity** treatment with long-term medical complications and obesity-related comorbidities. JAMA. doi:10.1001/jama.2017.21055
Jakubowicz D, Barnea M, Wainstein J, et al. **High Caloric intake at breakfast vs. dinner** differentially influences weight loss of overweight and obese women. Obesity (Silver Spring). 2013 Dec;21(12):2504-12.
Jarman M, Yuan Y, Pakseresht M, et al. Patterns and trajectories of **gestational weight gain**: a prospective cohort study. CMAJ Open. 2016 Jun 23;4(2):E338-45
James WPT, Caterson ID, Coutinho W, et al. Effect of **sibutramine on cardiovascular outcomes** in overweight and obese subjects (**Scout**) . N Engl J Med 2010;363:905-17.
Jansen PW, Verlinden M, Dommisse-van Berkel A, et al. **Teacher and peer reports of overweight and bullying** among young primary school children. Pediatrics. 2014 Sep;134(3):473-80.
Jarskog LF, Hamer RM, Catellier DJ, et al; for the METS Investigators. **Metformin for Weight Loss** and Metabolic Control in Overweight Outpatients With **Schizophrenia** and Schizoaffective Disorder. Am J Psychiatry. 2013 Jul 12.
Jebb SA, Ahern AL, Olson AD et al. Primary care referral to a **commercial provider (Weight Watchers) for weight loss treatment versus standard care**: a randomized controlled trial. Lancet 2011
Jebeile H, Gow ML, Baur LA, et al. Association of **Pediatric Obesity Treatment**, Including a Dietary Component, **With Change in Depression and Anxiety**: A Systematic Review and Meta-analysis. JAMA Pediatr. 2019 Sep 16:e192841.
Jebeile H, Mijatovic J, Louie JC, et al. A systematic review and meta-analysis of **energy intake and weight gain in pregnancy**. Am J Obstet Gynecol 2016;214(4):465–83.
Jenkins DJ, Wong JM, Kendall CW, et al. The effect of a plant-based low-carbohydrate ("**Eco-Atkins**") diet on body weight and blood lipid concentrations in hyperlipidemic subjects. Arch Intern Med. 2009 Jun 8;169(11):1046-54.
Jensen ET, van der Burg JW, O'Shea TM, et al. The Relationship of **Maternal Prepregnancy Body Mass Index and Pregnancy Weight Gain to Neurocognitive Function** at Age 10 Years among Children Born Extremely Preterm. J Pediatr. 2017 Mar 21.
Jensen MD, Ryan DH, Apovian CM, et al. **2013 AHA/ACC/TOS** Guideline for the Management of Overweight and Obesity in Adults: A Report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines and The Obesity Society. Circulation. 2013 Nov 12.
Jess T. **Microbiota, antibiotics, and obesity**. N Engl J Med. 2014 Dec 25;371(26):2526-8.
Ji Q. Treatment Strategy for **Type 2 Diabetes with Obesity**: Focus on **Glucagon-Like Peptide-1 Receptor Agonists**. Clin Ther. 2017 May 16.
Jia H, Lubetkin EI. Trends in **quality-adjusted life-years** lost contributed by smoking and obesity. Am J Prev Med 2010; DOI: 10.1016/j.amepre.2009.09.043.
Jick H, Vasilakis C, Weinrauch LA, et al. A population-based study of **appetite-suppressant drugs and the risk of cardiac-valve regurgitation**. N Engl J Med 1998; 339: 719–24.
Jin J. JAMA **PATIENT PAGE**. **Specific Medications for Weight Loss**. JAMA. 2015 Aug 18;314(7):742.
Jin J. **Screening for Obesity in Children and Adolescents**. (Patient information) JAMA. 2017 Jun 20;317(23):2460
Jo H, Schieve LA, Sharma AJ, et al. **Maternal prepregnancy body mass index** and child psychosocial development at 6 years of age. Pediatrics. 2015 May;135(5)
Joffe G, Takala P, Tchoukhine E, et al.. Orlistat in **Clozapine- or Olanzapine**-Treated Patients With Overweight or Obesity: A 16-Week Randomized, Double-Blind, Placebo-Controlled Trial. J Clin Psychiatry. 2008 Mar 11;:e1-e6 [Epub ahead of print] Without a hypocaloric diet, the effect of orlistat in overweight/obese clozapine-or olanzapine-treated patients is modest and may only be seen in men.
Johansson Kari, Neovius Martin, Lagerros Ylva Trolle, et al. Effect of a very low energy diet on moderate and severe obstructive **sleep apnoea** in obese men: a randomised controlled trial. BMJ 2009;339:b4609, doi: 10.1136/bmj.b4609 (3 Dec 2009)
Johansson Kari, Hemmingsson Erik, Harlid Richard, et al. Longer term effects of **very low energy diet on obstructive sleep apnoea** in cohort derived from randomised controlled trial: prospective observational follow-up study. BMJ 2011;342:doi:10.1136/bmj.d3017 (Published 1 June 2011)
Johansson K, Sundström J, Marcus C, et al. **Risk of symptomatic gallstones and cholecystectomy** after **very low calorie diet or low calorie diet in a commercial weight loss program**: 1-year matched cohort study.Int J Obes (Lond). 2013 May 22.
Johansson K et al. **Outcomes of pregnancy after bariatric surgery**. N Engl J Med 2015 Feb 26; 372:814.
Johansson S, Villamor E, Altman M, et al. **Maternal overweight and obesity in early pregnancy and risk of infant mortality**: a population based cohort study in Sweden. BMJ 2014;349:g6572.
Johnston BC, Kanters S, Bandayrel K, et al. Comparison of **weight loss among named diet programs** in overweight and obese adults: ameta-analysis. JAMA. doi:10.1001/jama.2014.10397.
Johnston CA, Rost S, Miller-Kovach K, et al. A randomized controlled trial of a **community-based behavioral counseling** program. Am J Med. 2013 Dec;126(12):1143.e19-24.
Johnson G, Oliver MN. **Lorcaserin** (belviq) for weight loss. Am Fam Physician. 2014 Dec 15;90(12):863-6.

Johnson RK. Reducing Intakes of **Sugar Sweetened Beverages** is Vital to Improving Our Nation's Health. Circulation. 2016 Jan 11.
Johnson RK, Lichtenstein AH, Anderson CAM, et al; **American Heart Association Nutrition Committee** of the Council on Lifestyle and Cardiometabolic Health; Council on Cardiovascular and Stroke Nursing; Council on Clinical Cardiology; Council on Quality of Care and Outcomes Research; and Stroke Council. Low-Calorie Sweetened Beverages and Cardiometabolic Health: A Science Advisory From the American Heart Association. Circulation. 2018 Aug 28;138(9):e126-e140.
Jolly K, Aveyard P. Provision of **commercial weight management programmes**. Lancet. 2011 Sep 7.
Jolly K, Lewis A, Beach J, et al. Comparison of range of **commercial or primary care led weight reduction programmes** with minimal intervention control for weight loss in obesity: Lighten Up randomised controlled trial. BMJ 2011;343:d6500.
Joo J, Williamson SA, Vazquez AI, et al. The influence of **15-week exercise training on dietary patterns** among young adults. Int J Obes (Lond). 2019 Jan 18.
Joosten SA, Hamilton GS, Naughton MT. Impact of **Weight Loss Management in OSA**. Chest. 2017 Feb 6.
Josaphat KJ, Kugathasan TA, E R Reid R, et al. **Use of Active Workstations** in Individuals with Overweight or Obesity: A Systematic Review. Obesity (Silver Spring). 2019 Mar;27(3):362-379.
Juonala M, Magnussen CG, Berenson GS, et al. **Childhood adiposity, adult adiposity, and cardiovascular risk factors**. N Engl J Med 2011;365:1876-85.
Juonala M, Jääskeläinen P, Sabin MA, et al. Higher Maternal Body Mass Index Is Associated with an Increased **Risk for Later Type 2 Diabetes** in Offspring. J Pediatr. 2012 Dec 19.
K Stephens S, J Cobiac L, Veerman JL. Improving **diet and physical activity** to reduce population prevalence of overweight and obesity: An overview of current evidence. Prev Med. 2014 Feb 15;62C:167-178.
Kaisari P, Yannakoulia M, Panagiotakos DB. **Eating Frequency** and Overweight and Obesity in Children and Adolescents: A Meta-analysis. Pediatrics. 2013 Apr 8.
Kahan S, Manson JE. **Obesity Treatment**, Beyond the Guidelines: Practical Suggestions for Clinical Practice. JAMA. 2019 Mar 21.
Kahn R. A Cautionary Tale of Warning Messages on Food Products: The Case of **Sugar-Sweetened Beverages**. Ann Intern Med. 2018 Feb 13.
Kakinami L, Henderson M, Delvin EE, et al. Association between different **growth curve definitions** of overweight and obesity and cardiometabolic risk in children. CMAJ. 2012 Apr 30.
Kalarchian MA, Levine MD, Arslanian SA, et al. **Family-based treatment** of severe pediatric obesity: randomized, controlled trial. Pediatrics. 2009 Oct;124(4):1060-8. Epub 2009 Sep 28.
Kaltenbach T, Crockett S, Gerson LB. Are **lifestyle** measures effective in patients with **gastroesophageal reflux disease**? An evidence-based approach. Arch Intern Med. 2006 May 8;166(9):965-71. Weight loss and head of bed elevation are effective lifestyle interventions for GERD. There is no evidence supporting an improvement in GERD measures after cessation of tobacco, alcohol, or other dietary interventions.
Kammire DE, Walkup MP, Ambrosius WT, et al. Effect of Weight Change Following Intentional Weight Loss on **Bone Health in Older Adults with Obesity**. Obesity (Silver Spring). 2019 Sep 4.
Kant AK, Whitley MI, Graubard BI. **Away from home meals**: associations with biomarkers of chronic disease and dietary intake in American adults, **NHANES** 2005-2010. Int J Obes (Lond). 2014 Oct 16.
Kantor ED, Udumyan R, Signorello LB, et al. Adolescent body mass index and erythrocyte sedimentation rate in relation to **colorectal cancer risk**. Gut. 2015 May 18.
Kaplan RC, Avilés-Santa ML, Parrinello CM, et al. Body mass index, sex, and cardiovascular disease risk factors among **hispanic/latino** adults: Hispanic community health study/study of latinos. J Am Heart Assoc. 2014 Jul 9;3(4).
Karmali, Shahzeer, Stoklossa, Carlene Johnson, Sharma, Arya, et al. **Bariatric surgery**: A primer. Can Fam Physician 2010 56: 873-879.
Kashyap SR, Bhatt DL, Wolski K, et al. **Metabolic effects of bariatric surgery** in patients with moderate obesity and type 2 diabetes: Analysis of a randomized control trial comparing surgery with intensive medical treatment. (**STAMPEDE**) Diabetes Care 2013 .
Kato PM, Cole SW, Bradlyn AS, Pollock BH. A **video game** improves behavioural outcomes in adolescents and young adults with cancer: a randomized trial. Pediatrics. 2008;122(2):e305-e317.
Kaulfers, Anne-Marie D., Bean, Judy A., Inge, Thomas H., Dolan, et al. **Bone Loss in Adolescents After Bariatric Surgery**. Pediatrics 2011 0: peds.2010-0785.
Kaviani S, vanDellen M, Cooper JA. Daily **Self-Weighing to Prevent Holiday-Associated Weight Gain** in Adults. Obesity (Silver Spring). 2019 Jun;27(6):908-916.
Keag OE, Norman JE, Stock SJ. Long-term risks and benefits associated with **cesarean delivery for mother, baby, and subsequent pregnancies**: Systematic review and meta-analysis. PLoS Med. 2018 Jan 23;15(1):e1002494.
Kearns CE, Apollonio D, Glantz SA. **Sugar industry sponsorship** of germ-free rodent studies **linking sucrose to hyperlipidemia and cancer**: an historical analysis of internal documents. PLoS Biol 2017;359:e2003460.
Kelly AS, Barlow SE, Rao G, et al. **Severe obesity in children and adolescents**: identification, associated health risks, and treatment approaches: A scientific statement from the American Heart Association (AHA). Circulation 2013.
Kelly Y, Patalay P, Montgomery S, et al. **BMI Development and Early Adolescent Psychological Well-Being** : UK Millennium Cohort Study: Pediatrics.2016;138(6):e20160967
Kendall D, Vail A, Amin R, et al. **Metformin in Obese Children and Adolescents**: The **MOCA** Trial. J Clin Endocrinol Metab. 2012 Nov 21.
Kenney EL, Gortmaker SL. **United States Adolescents' Television, Computer, Videogame, Smartphone, and Tablet Use**: Associations with Sugary Drinks, Sleep, Physical Activity, and Obesity. J Pediatr. 2016 Dec 9.
Kerling EH, Hilton JM, Thodosoff JM, et al. Effect of **Prenatal Docosahexaenoic Acid Supplementation on Blood Pressure in Children** With Overweight Condition or Obesity: A Secondary Analysis of a Randomized Clinical Trial. JAMA Netw Open. 2019 Feb 1; 2(2): e190088.
Keyserling TC, Sheridan SL, Draeger LB, et al. A comparison of **live counseling with a web-based** lifestyle and medication intervention to reduce coronary heart disease risk: a randomized clinical trial [onlineMay 26, 2014]. JAMA Intern Med. 10.1001/jamainternmed.2014.1984.
Khalife N, Kantomaa M, Glover V, et al. Childhood **attention-deficit/hyperactivity disorder** symptoms are risk factors for obesity and physical inactivity in adolescence. J Am Acad Child Adolesc Psychiatry. 2014 Apr;53(4):425-36.
Khan NA, Raine LB, Drollette ES, et al. Impact of the **FITKids Physical Activity Intervention** on Adiposity in Prepubertal Children. Pediatrics. 2014 Apr;133(4):e875-83.
Khera AV, Chaffin M, Wade KH, et al. **Polygenic Prediction of Weight and Obesity** Trajectories from Birth to Adulthood. Cell. 2019 Apr 18;177(3):587-596.e9
Khera R, Murad MH, Chandar AK, et al. Association of **Pharmacological Treatments for Obesity With Weight Loss and Adverse Events**: A Systematic Review and Meta-analysis. JAMA. 2016 Jun 14;315(22):2424-34.
Khera R, Pandey A, Chandar AK, et al. Effects of **Weight-Loss Medications on Cardiometabolic Risk Profiles**: A Systematic Review and Network Meta-analysis. Gastroenterology. 2018 Apr;154(5):1309-1319.e7.
Klebanoff MJ, Corey KE, Samur S, et al. Cost-effectiveness **Analysis of Bariatric Surgery for Patients With Nonalcoholic Steatohepatitis Cirrhosis**. JAMA Netw Open. 2019 Feb 1;2(2):e190047.
Kohl HW 3rd, Craig CL, Lambert EV, et al; for the Lancet Physical Activity Series Working Group. The pandemic of physical inactivity: **global action** for public health. Lancet. 2012 Jul 17.
Kong L, Nilsson IAK, Gissler M, Lavebratt C. **Associations of Maternal Diabetes and Body Mass Index** With Offspring Birth Weight and Prematurity. JAMA Pediatr. 2019 Feb 25.
Kiel DW, Dodson EA, Artal R, Boehmer TK, Leet TL. **Gestational weight gain and pregnancy outcomes** in obese women: how much is enough? Obstet Gynecol. 2007 Oct;110(4):752-8. Limited or no weight gain in obese pregnant women has favorable pregnancy outcomes.
Kilpeläinen TO, Qi L, Brage S, et al. Physical Activity Attenuates the Influence of **FTO Variants on Obesity Risk**: A Meta-Analysis of 218,166 Adults and 19,268 Children. PLoS Med. 2011 Nov;8(11):e1001116.
Kim BJ, Lee SH, Jung KH, et al; For Korean Stroke Registry investigators. Dynamics of **obesity paradox** after stroke, related to time from onset, age, and causes of death. Neurology. 2012 Aug 15.
Kim K, Choi S, Park SM. Association of **High Body Mass Index and Hepatocellular Carcinoma** in Patients With **Chronic Hepatitis B Virus Infection**: A Korean Population-Based Cohort Study. JAMA Oncol. 2018 Mar 22.
Kim SY, Sharma AJ, et al. Association of **Maternal Body Mass Index**, Excessive Weight Gain, and Gestational Diabetes Mellitus With Large-for-Gestational-Age Births. Obstet Gynecol. 2014 Apr;123(4):737-44.

King WC, Belle SH, Hinerman AS, et al. **Patient Behaviors and Characteristics Related to Weight Regain After Roux-en-Y Gastric Bypass**: A Multicenter Prospective Cohort Study. Ann Surg. 2019 Apr 4.
King MA, Nkoy FL, Maloney CG, et al. Physicians and **Physician Trainees Rarely Identify or Address Overweight/Obesity** in Hospitalized Children. J Pediatr. 2015 Jul 29.
King WC, Chen JY, Mitchell JE, et al. Prevalence of **Alcohol Use Disorders Before and After Bariatric Surgery**. JAMA. 2012 Jun18:1-10.
King WC, Chen JY, Belle SH, et al. Change in **Pain and Physical Function** Following Bariatric Surgery for Severe Obesity. JAMA. 2016 Apr 5;315(13):1362-71.
King WC, Hinerman AS, Belle SH, et al. Comparison of the **performance of common measures of weight regain after bariatric surgery for association with clinical outcomes**. JAMA. doi:10.1001/jama.2018.1443
Kipping RR, Jago R, Lawlor DA. **Obesity in children. Part 1**: Epidemiology, measurement, risk factors, and screening. BMJ. 2008 Oct 15;337:a1824. doi: 10.1136/bmj.a1824.
Kipping RR, Jago R, Lawlor DA. **Obesity in children. Part 2**: Prevention and management. BMJ. 2008 Oct 22;337:a1848. doi: 10.1136/bmj.a1848.
Kirk S, Brehm B, Saelens BE et al. Role of **Carbohydrate Modification** in Weight Management among Obese Children: A Randomized Clinical Trial. J Pediatr. 2012 Feb 28.
Kitahara CM, Flint AJ, Berrington de Gonzalez A, et al. Association between **Class III Obesity** (BMI of 40-59 kg/m2) and **Mortality**: A Pooled Analysis of 20 Prospective Studies. PLoS Med. 2014 Jul 8;11(7):e1001673.
Kivimäki M, Luukkonen R, Batty GD, et al. **Body mass index and risk of dementia**: Analysis of individual-level data from 1.3 million individuals. Alzheimers Dement. 2017 Nov 21.
Kjær MM, Lauenborg J, Breum BM, Nilas L. The risk of **adverse pregnancy outcome after bariatric surgery**: a nationwide register-based matched cohort study. Am J Obstet Gynecol. 2013 Jun;208(6):464.e1-5.
Klebanoff MJ, Chhatwal J, Nudel JD, et al. **Cost-effectiveness of Bariatric Surgery in Adolescents** With Obesity. JAMA Surg. 2016 Oct 26.
Klein DJ, et al. A Randomized, Double-Blind, Placebo-Controlled Trial of **Metformin** Treatment of Weight Gain Associated With Initiation of **Atypical Antipsychotic** Therapy in Children and Adolescents. Am J Psychiatry. 2006 Dec;163(12):2072-2079. (n=39 16weeks age 10-17) Metformin 850mg bid therapy is safe and effective in abrogating weight gain, decreased insulin sensitivity, and abnormal glucose metabolism resulting from treatment of children and adolescents with atypicals.
Knäuper B, Carrière K, Frayn M, et al. The Effects of **If-Then Plans on Weight Loss:** Results of the McGill CHIP Healthy Weight Program Randomized Controlled Trial. Obesity (Silver Spring). 2018 Jun 28.
Knell G, Li Q, Pettee Gabriel K, et al. **Long-Term Weight Loss and Metabolic Health in Adults Concerned With Maintaining or Losing Weight**: Findings From NHANES. Mayo Clin Proc. 2018 Aug 10.
Köchli S, Endes K, Infanger D, et al. **Obesity, Blood Pressure, and Retinal Vessels**: A Meta-analysis. Pediatrics. 2018 May 9.
Koehestanie P, de Jonge C, Berends FJ, et al. The effect of the **endoscopic duodenal-jejunal bypass liner** on obesity and type 2 diabetes mellitus, a multicenter randomized controlled trial. Ann Surg. 2014 Dec;260(6):984-92.
Kodner C, Hartman DR. **Complications of Adjustable Gastric Banding** Surgery for Obesity. Am Fam Physician. 2014;89(10):813-818.
Kolt GS, Schofield GM, Kerse N, et al. Healthy steps trial: **pedometer-based** advice and physical activity for low-active older adults. Ann Fam Med. 2012 May;10(3):206-12.
Kokkinos P, Myers J, Kokkinos JP, et al. **Exercise Capacity and Mortality** in Black and White Men. Circulation. 2008 Jan 22; [Epub ahead of print] Exercise capacity is a strong predictor of all-cause mortality in blacks and whites. The relationship was inverse and graded, with a similar impact on mortality outcomes for both blacks and whites.
Kokkvoll A, Grimsgaard S, Steinsbekk S, et al. Health in **overweight children: 2-year follow-up of Finnmark Activity School**-a randomised trial. Arch Dis Child. 2014 Nov 20.
Kong L, Norstedt G, Schalling M, et al. The Risk of **Offspring Psychiatric Disorders in the Setting of Maternal Obesity and Diabetes**. Pediatrics. 2018 Aug 9.
Koolhaas CM, Dhana K, Schoufour JD, et al. Impact of **physical activity** on the association of overweight and obesity with cardiovascular disease: The **Rotterdam Study**. Eur J Prev Cardiol. 2017 Jan 1:2047487317693952
Koroukian SM, Dong W, Berger NA. Changes in Age Distribution of **Obesity-Associated Cancers**. JAMA Netw Open. 2019 Aug 2;2(8):e199261.
Korre M, Porto LG, Farioli A, et al. Effect of Body Mass Index on **Left Ventricular Mass in Career Male Firefighters**. Am J Cardiol. 2016 Aug 31.
Koutoukidis DA, Astbury NM, Tudor KE, et al. Association of **Weight Loss Interventions With Changes in Biomarkers of Nonalcoholic Fatty Liver Disease**: A Systematic Review and Meta-analysis. JAMA Intern Med. 2019 Jul 1.
Kouvari M, Panagiotakos DB, Yannakoulia M, et al. Transition from **metabolically benign to metabolically unhealthy obesity** and 10-year cardiovascular disease incidence: the ATTICA cohort study. Metabolism. 2019 Jan 10.
Koyama S, Sairenchi T, Shimura N, et al. Association between **Timing of Adiposity Rebound** and Body Weight Gain during **Infancy**. J Pediatr. 2015 Feb;166(2):309-12.
Kramer CK, Zinman B, Retnakaran R. Are **metabolically healthy overweight and obesity benign conditions**? A systematic review and meta-analysis. Ann Intern Med. 2013;159:758-69.
Kramer MR, Raskind IG, Van Dyke ME, et al. **Geography of Adolescent Obesity in the U.S.,** 2007-2011. Am J Prev Med. 2016 Dec;51(6):898-909.
Kraus WE, Bhapkar M, Huffman KM, et al. **2 years of calorie restriction and cardiometabolic risk** (CALERIE): exploratory outcomes of a multicentre, phase 2, randomised controlled trial. Lancet Diabetes Endocrinol. 2019 Jul 11.
Kriemler Susi, Zahner Lukas, Schindler Christian, et al. Effect of **school based physical activity programme** (**KISS**) on fitness and adiposity in primary schoolchildren: cluster randomised controlled trial. BMJ 2010;340:c785, (23 Feb 2010).
Kriska A, Delahanty L, Edelstein S, et al. **Sedentary Behavior and Physical Activity** in Youth With **Recent Onset of Type 2 Diabetes**. Pediatrics. 2013 Feb 11.
Krishnaswami J, Martinson M, Wakimoto P, et al. **Community-engaged interventions** on diet, activity, and weight outcomes in U.S. schools: a systematic review. Am J Prev Med. 2012 Jul;43(1):81-91.
Kritchevsky SB, Lovato L, Handing EP, et al. **Exercise's effect on mobility disability** in older adults with and without obesity: The LIFE study randomized clinical trial. Obesity (Silver Spring). 2017 Jul;25(7):1199-1205.
Kubo A, Ferrara A, Windham GC, et al. **Maternal hyperglycemia during pregnancy** predicts adiposity of the offspring. Diabetes Care. 2014 Nov;37(11):2996-3002.
Kubzansky LD, Bordelois P, Jun HJ, et al. The Weight of **Traumatic Stress**: A Prospective Study of Posttraumatic Stress Disorder Symptoms and Weight Status in Women. JAMA Psychiatry. 2013 Nov 20.
Kuk JL, Rotondi M, Sui X, et al. Individuals with **obesity but no other metabolic risk factors are not at significantly elevated all-cause mortality risk** in men and women. Clin Obes. 2018 Jul 12.
Kullgren JT, Troxel AB, Loewenstein G, et al. **Individual- versus group-based financial incentives** for weight loss: A randomized controlled trial. Ann Intern Med 2013; 158:505-514.
Kumanyika SK, Obarzanek E, Stettler N, et al. **Population-Based Prevention of Obesity**. The Need for Comprehensive Promotion of Healthful Eating, Physical Activity, and Energy Balance. A Scientific Statement From American Heart Association Council on Epidemiology and Prevention, Interdisciplinary Committee for Prevention (Formerly the Expert Panel on Population and Prevention Science). Circulation. 2008 Jun 30. [Epub ahead of print]
Kurnool S, Nguyen NH, Proudfoot J, et al. **High body mass index** is associated with increased risk of treatment failure and surgery in biologic-treated patients with **ulcerative colitis**. Aliment Pharmacol Ther. 2018 Jun;47(11):1472-1479.
Kushner RF. Clinical **assessment and management** of adult obesity. Circulation. 2012 Dec 11;126(24):2870-7.
Kushner RF, Ryan DH. **Assessment and lifestyle management** of patients with obesity: clinical recommendations from systematic reviews. JAMA. 2014 Sep 3;312(9):943-52.
Kwok CS, Pradhan A, Khan MA, et al. **Bariatric surgery** and its impact on **cardiovascular disease** and mortality: A systematic review and meta-analysis. Int J Cardiol. 2014 Apr 15;173(1):20-28.
Kwon S, Janz KF, Letuchy EM, et al. Developmental Trajectories of **Physical Activity, Sports, and Television Viewing** During Childhood to Young Adulthood: Iowa Bone Development Study. JAMA Pediatr. 2015 May 18.
Kyrgiou M, Kalliala I, Markozannes G, et al. **Adiposity and cancer** at major anatomical sites: umbrella review of the literature. BMJ 2017;356:j477. [ie. colon and rectum, liver, gallbladder, pancreas, kidney, thyroid, breast (postmenopausal), endometrium, ovary, oesophagus (adenocarcinoma), and gastric cardia, as well as meningioma and multiple myeloma.]

Ladabaum U, Mannalithara A, Myer PA, et al. **Obesity**, Abdominal Obesity, **Physical Activity**, and **Caloric Intake** in U.S. Adults: 1988-2010. Am J Med. 2014 Mar 10.
Lagiou P, Sandin S, Lof M, et al. **Low carbohydrate-high protein diet** (Atkins-type diet) and incidence of cardiovascular diseases in Swedish women: prospective cohort study. BMJ. 2012 Jun 26;344:e4026.
Lahti-Pulkkinen M, Bhattacharya S, Wild SH, et al. **Consequences of being overweight** or obese during pregnancy **on diabetes in the offspring:** a record linkage study in Aberdeen, Scotland. Diabetologia. 2019 Jun 19.
Lakshman R, Elks CE, Ong KK. **Childhood Obesity**. Circulation. 2012 Oct 2;126(14):1770-1779.
Lamerton TJ, Torquati L, Brown WJ. **Overweight and obesity as major, modifiable risk factors for urinary incontinence in young to mid-aged women**: a systematic review and meta-analysis. Obes Rev. 2018 Sep 19.
Land SR, et al. Patient-Reported Symptoms and Quality of Life During Treatment With **Tamoxifen** or **Raloxifene** for Breast Cancer Prevention: The NSABP Study of Tamoxifen and Raloxifene (STAR) P-2 Trial. JAMA. 2006 Jun 5; [Epub ahead of print] No significant differences existed between the tamoxifen and raloxifene groups in patient-reported outcomes for physical health, mental health, and depression, although the tamoxifen group reported better sexual function. Although mean symptom severity was low among these postmenopausal women, those in the tamoxifen group reported more gynecological problems, vasomotor symptoms, leg cramps, and bladder control problems, whereas women in the raloxifene group reported more musculoskeletal problems, dyspareunia, and weight gain.)
Lang JE, Bunnell H, Hossain J, et al. Being overweight or obese and the **development of asthma**. Pediatrics. 2018;142(6):e20182119.
Lang JE, Fitzpatrick AM, Mauger DT, et al. Overweight/obesity status in preschool children associates with worse **asthma** but robust improvement on inhaled corticosteroids. J Allergy Clin Immunol. 2017 Dec 8.
Larsen JR, et al. Effect of **Liraglutide** Treatment on Prediabetes and Overweight or **Obesity in Clozapine- or Olanzapine-Treated Patients** With Schizophrenia Spectrum Disorder: A Randomized Clinical Trial. JAMA Psychiatry. 2017 Jul 1;74(7):719-728
Larsen Thomas Meinert, Dalskov Stine-Mathilde, van Baak Marleen, et al. for the Diet, Obesity, and Genes (**Diogenes**) Project. **Diets with High or Low Protein Content and Glycemic Index** for Weight-Loss Maintenance. N Engl J Med 2010; 363:2102-2113. In this large European study, a modest increase in protein content and a modest reduction in the glycemic index led to an improvement in study completion and maintenance of weight loss.
Lassale C, Tzoulaki I, Moons KGM, et al. Separate and combined associations of **obesity** and **metabolic health** with **coronary heart disease**: a pan-European case-cohort analysis. European Heart J. 2017;00: 1-12
Lasserre AM, Glaus J, Vandeleur CL, et al. **Depression With Atypical Features and Increase in Obesity**, Body Mass Index, Waist Circumference, and Fat Mass: A Prospective, Population-Based Study. JAMA Psychiatry. 2014 Jun 4.
Lau DC, Douketis JD, Morrison KM, Hramiak IM, Sharma AM, Ur E; Obesity Canada Clinical Practice Guidelines Expert Panel. **2006 Canadian clinical practice guidelines on the management & prevention of obesity in adults & children** Summary http://www.cmaj.ca/cgi/reprint/176/8/S1 Complete guidelines http://www.cmaj.ca/cgi/data/176/8/S1/DC1/1 CMAJ. 2007 Apr 10;176(8):S1-13.
Lauby-Secretan B, Scoccianti C, Loomis D, et al. **Body Fatness and Cancer**--Viewpoint of the **IARC** Working Group. N Engl J Med. 2016 Aug 25;375(8):794-8.
Lauche R, Langhorst J, Lee MS, et al. A systematic review and meta-analysis on the effects of **yoga** on weight-related outcomes. Prev Med. 2016 Apr 4.
Lawlor DA, Benfield L, Logue J, et al. Association between general and central adiposity in **childhood**, and change in these, with cardiovascular risk factors in **adolescence**: prospective cohort study. BMJ **341**:doi:10.1136/bmj.c6224 (25Nov10).
Lazzati A, De Antonio M, Paolino L, et al. **Natural history of adjustable gastric banding**: lifespan and revisional rate. A nationwide study on administrative data on 53,000 patients. Ann Surg 2017;265:439–445.
Leahey TM, Thomas G, Fava JL, et al. Adding Evidence-Based Behavioral Weight Loss Strategies to a **Statewide Wellness Campaign**: A Randomized Clinical Trial. Am J Public Health. 2014 May 15.
Leahey TM, Subak LL, Fava J, et al. Benefits of adding small **financial incentives or optional group meetings to a web-based** statewide obesity initiative. Obesity (Silver Spring). 2015 Jan;23(1):70-6.
Lean MEJ, Astrup A, Roberts SB. Making progress on the **global crisis of obesity and weight management**. BMJ. 2018 Jun 13;361:k2538.
Lean M, Finer N. **ABC of obesity**. Management: part II--**drugs**. BMJ. 2006 Oct 14;333(7572):794-7. Available online at: http://bmj.bmjjournals.com/cgi/content/full/333/7572/794 (Oct 17, 2006). (McMillan DC, et al. ABC of obesity. Obesity and **cancer**. BMJ. 2006 Nov 25;333(7578):1109-11. Lawlor DA, et al. ABC of obesity: obesity and **vascular disease**. BMJ. 2006 Nov 18;333(7577):1060-3. Wild SH, et al. ABC of obesity. Risk factors for **diabetes and coronary heart disease**. BMJ. 2006 Nov 11;333(7576):1009-11. Lean M, Lara J, Hill JO. ABC of obesity. Strategies for **preventing** obesity.BMJ. 2006 Nov 4;333(7575):959-62. Kral JG. ABC of obesity. Management: Part III--surgery. BMJ. 2006 Oct 28;333(7574):900-3.: Lean M, Finer N. ABC of obesity. **Management**: part II--drugs. BMJ. 2006 Oct 14;333(7572):794-7. Avenell A, Sattar N, Lean M. ABC of obesity. Management: Part I—**behaviour** change, diet, and activity. BMJ. 2006 Oct 7;333(7571):740-3. Han TS, Sattar N, Lean M. ABC of obesity. **Assessment** of obesity and its clinical implications. BMJ. 2006 Sep 30;333(7570):695-8. Haslam D, Sattar N, Lean M. ABC of obesity. Obesity--**time to wake up**. BMJ. 2006 Sep 23;333(7569):640-2. Ramsay JE. ABC of obesity. **Obesity and reproduction**. BMJ. 2006 Dec 2;333(7577):1159-62. Lean M, Gruer L, Alberti G, Sattar N. ABC of obesity. Obesity--**can we turn the tide**? BMJ. 2006 Dec 16;333(7581):1261-4. Reilly JJ, Wilson D. ABC of obesity. **Childhood obesity**. BMJ. 2006 Dec 9;333(7580):1207-10.
Lean ME, Leslie WS, Barnes AC, et al. **Primary care-led weight management for remission of type 2 diabetes (DiRECT):** an open-label, cluster-randomised trial. Lancet. 2017 Dec 4.
Lear SA, Teo K, Gasevic D, et al. The association between ownership of common **household devices** and obesity and diabetes in high, middle and low income countries. CMAJ. 2014 Feb 10.
Leblanc ES, O'Connor E, Whitlock EP, et al. Effectiveness of **primary care-relevant treatments** for obesity in adults: a systematic evidence review for the US Preventive services task force. (USPSFT) Ann Intern Med. 2011Oct 4;155(7):434-47.
Lee AM, Gurka MJ, DeBoer MD. Trends in **Metabolic Syndrome Severity** and Lifestyle Factors Among Adolescents. Pediatrics. 2016 Feb 9.
Lee I-Min; Djousse Luc; Sesso Howard D.; et al. **Physical Activity** and Weight Gain Prevention. JAMA. 2010;303(12):1173-1179. (Maintain weight if average **60mins** a day moderate-intensity activity)
Lee JM, Gebremariam A, Vijan S, Gurney JG. **Excess Body Mass Index-Years**, a Measure of Degree and Duration of Excess Weight, and Risk for Incident Diabetes. Arch Pediatr Adolesc Med. 2011 Sep 12
Lee JM, Wasserman R, Kaciroti N, et al. **Timing of Puberty** in Overweight Versus Obese Boys. Pediatrics. 2016 Jan 27.
Leff DR, Heath D. **Surgery for obesity** in adulthood. BMJ. 2009 Sep 22;339:b3402. doi: 10.1136/bmj.b3402.
Legro RS, Dodson WC, Gnatuk CL, et al. Effects of Gastric Bypass Surgery on **Female Reproductive Function**. J Clin Endocrinol Metab. 2012 Oct 12.
Lent MR, Benotti PN, Mirshahi T, et al. **All-Cause and Specific-Cause Mortality Risk After Roux-en-Y Gastric Bypass** in Patients With and Without Diabetes. Diabetes Care. 2017 Oct;40(10):1379-1385.
Leonetti F, et al. Obesity, type 2 diabetes mellitus, and other comorbidities: a prospective cohort study of **laparoscopic sleeve gastrectomy vs medical treatment** [online ahead of print April 16, 2012]. Arch Surg. 2012.
Lewis KH, Fischer H, Ard J, et al. Safety and Effectiveness of **Longer-Term Phentermine Use**: Clinical Outcomes from an Electronic Health Record Cohort. Obesity (Silver Spring). 2019 Apr;27(4):591-602.
Lewis KH, Zhang F, Arterburn DE, et al. Comparing Medical **Costs** and Use After **Laparoscopic Adjustable Gastric Banding and Roux-en-Y Gastric Bypass**. JAMA Surg. 2015 Jun 3.
Leyland KM, Judge A, Javaid MK, et al. Obesity and the relative risk of **replacement surgery in knee osteoarthritis** patients: A prospective cohort study. Arthritis Rheumatol. 2015 Nov 10.
Liang L, Meyerhoefer C, Wang J. **Obesity Counseling** by Pediatric Health Professionals: An Assessment Using Nationally Representative Data. Pediatrics. 2012 Jun 4.
Li DK, Miao M, Zhou Z, et al. Urine **bisphenol-a level** in relation to obesity and overweight in school-age children. PLoS One. 2013 Jun 12;8(6):e65399.
Li Donghui; Morris Jeffrey S.; et al. Body Mass Index and Risk, Age of Onset, and Survival in Patients With **Pancreatic Cancer**. JAMA. 2009;301(24):2553-2562.
Li DK, Chen H, Ferber J, et al. **Infection and antibiotic use** in infancy and risk of childhood obesity: a longitudinal birth cohort study. Lancet Diabetes Endocrinol. 2016 Nov 1.
Li JS, Barnett TA, Goodman E, et al; on behalf of the American Heart Association Atherosclerosis, Hypertension and Obesity in the Young Committee of the Council on Cardiovascular Disease in the Young, Council on Epidemiology and Prevention, and Council on Nutrition, Physical Activity and Met. Approaches to the Prevention and Management of Childhood Obesity: The Role of **Social Networks** and the Use of **Social Media** and Related Electronic

Technologies: A Scientific Statement From the American Heart Association. Circulation. 2013 Jan 15;127(2):260-267.
Li K, Haynie D, Lipsky L, et al. Changes in **Moderate-to-Vigorous Physical Activity Among Older Adolescents**. Pediatrics. 2016 Sep 26.
Li M, Fallin MD, Riley A, et al. The Association of Maternal Obesity and Diabetes With **Autism** and Other **Developmental Disabilities**. Pediatrics. 2016 Jan 29.
Li W, Han J, Qureshi AA. Obesity and risk of incident **psoriatic arthritis** in US women. Ann Rheum Dis. 2012 May 9.
Li Z, Heber D. Managing **weight loss expectations**: the challenge and the opportunity. JAMA. 2014 Apr 2;311(13):1348-9.
Licht H, Murray M, Vassaur J, et al. The Relationship of Obesity to Increasing Health-Care Burden in the Setting of **Orthopaedic Polytrauma**. J Bone Joint Surg Am. 2015 Nov 18;97(22):e73.
Liem ET, van Buuren S, Sauer PJ, et al. **Growth during Infancy and Childhood**, and Adiposity at Age 16 Years: Ages 2 to 7 Years Are Pivotal. J Pediatr. 2012 Sep 14.
LifeCycle Project-Maternal Obesity and Childhood Outcomes Study Group. Association of **gestational weight gain with adverse maternal and infant outcomes** [online May 7, 2019]. JAMA. doi:10.1001/jama.2019.3820
Ligibel JA, Alfano CM, Courneya KS, et al. **American Society of Clinical Oncology (ASCO)** Position Statement on **Obesity and Cancer**. J Clin Oncol. 2014 Oct 1.
Lin, Wen-Yuan, Tsai, Shin-Li, Albu, Jeanine B., et al. **Body mass index and all-cause mortality in a large Chinese** cohort. CMAJ 2011 183: E329-336.
Lin JS, O'Connor E, Whitlock EP, Beil TL. **Behavioral counseling to promote physical activity** and a healthful diet to prevent cardiovascular disease in adults: a systematic review for the US Preventive services task force. (**USPSTF**) Ann Intern Med. 2010 Dec 7;153(11):736-50.
Lin SL, Leung GM, Lam TH, et al. Timing of **Solid Food Introduction** and Obesity: Hong Kong's "Children of 1997" Birth Cohort. Pediatrics. 2013 Apr 8.
Lin WY, Chan CC, Liu YL, et al. Performing different kinds of **physical exercise differentially attenuates the genetic effects on obesity** measures: Evidence from 18,424 Taiwan Biobank participants. PLoS Genet. 2019 Aug 1;15(8):e1008277.
Linderman GC, Lu J, Lu Y, et al. Association of **Body Mass Index With Blood Pressure** Among 1.7 Million Chinese Adults. JAMA Netw Open. 2018;1(4):e181271.
Ling J, Robbins LB, Wen F, Zhang N. **Lifestyle Interventions in Preschool Children**: A Meta- analysis of Effectiveness. Am J Prev Med. 2017 Feb 22.
Lisan Q, Van Sloten T, et al. Association of **Positive Airway Pressure Prescription With Mortality in Patients With Obesity and Severe Obstructive Sleep Apnea**: The Sleep Heart Health Study. JAMA Otolaryngol Head Neck Surg. 2019 Apr 11.
Lisonkova S, Muraca GM, Potts J, et al. Association between **prepregnancy body mass index and severe maternal morbidity**.JAMA. doi:10.1001/jama.2017.16191
Little P, Stuart B, Hobbs FR, et al. Randomised controlled trial and economic analysis of an **internet-based weight management programme: POWeR+** (Positive Online Weight Reduction). Health Technol Assess. 2017 Jan;21(4):1-62.
Liu Bette, Balkwill Angela, Reeves Gillian et al. on behalf of the Million Women Study Collaborators. Body mass index and risk of **liver cirrhosis** in middle aged UK women: prospective study. BMJ 2010
Liu G, Dhana K, Furtado JD, et al. **Perfluoroalkyl substances** and changes in body weight and resting metabolic rate in response to weight-loss diets: A prospective study. PLoS Med. 2018 Feb 13;15(2):e1002502.
Liu JB, Ban KA, Berian JR, et al. **Concurrent bariatric operations** and association with perioperative outcomes: registry based cohort study. BMJ. 2017 Sep 26;358:j4244
Liu PH, Wu K, Ng K, et al. Association of Obesity With Risk of **Early-Onset Colorectal Cancer** Among Women. JAMA Oncol. 2018 Oct 11.
Livingston EH, Langert J. The impact of **age** and medicare status on **bariatric** surgical outcomes. Arch Surg. 2006 Nov;141(11):1115-20; discussion 1121. Limiting bariatric surgical procedures to those younger than 65 years is warranted because of the high morbidity and mortality associated with these operations in older patients.
Livingstone KM, Celis-Morales C, Papandonatos GD, et al. **FTO genotype** and weight loss: a systematic review and meta-analysis of 9563 individual participant data from eight randomised controlled trials. BMJ 2016;354:i4707.
Lloyd-Richardson EE, Jelalian E, Sato AF, et al. Two-Year Follow-up of an **Adolescent Behavioral Weight** Control Intervention. Pediatrics. 2012 Aug;130(2):e281-8.
Lobstein T, Jackson-Leach R, Moodie ML, et al. **Child and adolescent obesity**: part of a bigger picture. Lancet. 2015 Feb 18.
Lombard C, Deeks A, Jolley D, et al. A **low intensity, community based lifestyle programme** to prevent weight gain in women with young children: cluster randomised controlled trial. BMJ. 2010 Jul 13;341:c3215. doi: 10.1136/bmj.c3215.
Lomenick JP, El-Sayyid M, Smith WJ. Effect of **levo-thyroxine treatment** on weight and body mass index in children with acquired hypothyroidism. J Pediatr. 2008 Jan;152(1):96-100. Epub 2007 Oct 24. Most children treated for acquired hypothyroidism exhibited little short-term or long-term change in weight or BMI despite near-normalization of TSH. Those children who lost weight tended to have severe hypothyroidism and to have only a small weight loss.
Longitudinal Assessment of Bariatric Surgery (**LABS**) Consortium, **Perioperative Safety in the Longitudinal Assessment of Bariatric Surgery.** N Engl J Med 2009 361: 445-454
Lønnberg AS, Skov L, Skytthe A, et al. Association of **psoriasis with the risk for type 2 diabetes mellitus and obesity** [online April 27, 2016].JAMA Derm. doi:10.1001/jamadermatol.2015.6262.
Look AHEAD Research Group. **Eight-year weight losses with an intensive lifestyle** intervention: the look AHEAD study. Obesity (Silver Spring). 2014 Jan;22(1):5-13.
Lopez RB, Heatherton TF, Wagner DD. **Media multitasking** is associated with higher risk for obesity and increased responsiveness to rewarding food stimuli. Brain Imaging Behav. 2019 Mar 1.
Lopez-Nava G et al. **Endoscopic sleeve gastroplasty** with 1-year follow-up: Factors predictive of success. Endosc Int Open 2016 Jan 15.
Losina Elena, Walensky Rochelle P., Reichmann William M., et al. Impact of Obesity and **Knee Osteoarthritis** on Morbidity and Mortality in Older Americans. *Ann Intern Med* February 15, 2011 154:217-226.
Loth KA, Maclehose RF, Fulkerson JA, et al. **Food-Related Parenting Practices** (clean up plate) and Adolescent Weight Status: A Population-Based Study. Pediatrics. 2013 Apr 22.
Lotta LA, Wittemans LBL, Zuber V, et al. Association of **Genetic Variants Related to Gluteofemoral vs Abdominal Fat Distribution** With Type 2 Diabetes, Coronary Disease, and Cardiovascular Risk Factors. JAMA. 2018 Dec 25;320(24):2553-2563.
Louzada ML, Campagnolo PD, Rauber F, Vitolo MR. Long-term Effectiveness of **Maternal Dietary Counseling** in a Low-Income Population: A Randomized Field Trial. Pediatrics. 2012 May 7.
Love TJ, Zhu Y, Zhang Y, et al. Obesity and the risk of **psoriatic arthritis**: a population-based study. Ann Rheum Dis 2012;71:1273–7.
Lovely R, Hossain J, Ramsey JP, et al. Obesity-related increase of **gamma prime fibrinogen** concentration in children and its reduction by physical activity-based lifestyle intervention: a randomized controlled study. J Pediatr 2013.
Lu B, Hiraki LT, Sparks JA, et al. Being overweight or obese and risk of **developing rheumatoid arthritis** among women: a prospective cohort study. Ann Rheum Dis. 2014 Nov;73(11):1914-22.
Ludwig DS and Currie J. The association between **pregnancy weight gain and birthweight**: A within-family comparison. Lancet 2010 Aug 5;
Ludwig J, Sanbonmatsu L, Gennetian L, et al. **Neighborhoods**, obesity, and diabetes-a randomized social experiment. N Engl J Med2011; 365:1509-1519.
Ludwig DS. **Weight loss strategies for adolescents**: a 14-year-old struggling to lose weight. JAMA. 2012 Feb 1;307(5):498-508.
Ludwig DS, Ebbeling CB. The **Carbohydrate-Insulin Model** of Obesity: Beyond "Calories In, Calories Out". JAMA Intern Med. 2018 Jul 2.
Lumeng JC. **Infant Eating Behaviors** and Risk for Overweight. JAMA. 2016 Nov 15;316(19):2036-2037
Lumeng JC, Kaciroti N, Sturza J, et al. Changes in Body Mass Index Associated With **Head Start Participation**. Pediatrics. 2015 Jan 12.
Lumeng JC, Taveras EM, Birch L, et al. **Prevention of obesity in infancy and early childhood**: a national institutes of health workshop. JAMA Pediatr. 2015 May 1;169(5):484-90.
Lumeng JC, Wendorf K, Pesch MH, et al. Overweight Adolescents and **Life Events in Childhood**. Pediatrics. 2013 Nov 11.
Lumeng JC, Miller AL, Horodynski MA, et al. **Improving self-regulation for obesity** prevention in **Head Start**: a randomized controlled trial. Pediatrics. 2017;139(5):e20162047

Lundahl A, Kidwell KM, Nelson TD. **Parental Underestimates of Child Weight**: A Meta-analysis. Pediatrics. 2014 Feb 2.
Luo J, Chlebowski RT, Hendryx M, et al. Intentional Weight Loss and **Endometrial Cancer** Risk. J Clin Oncol. 2017 Feb 6:JCO2016705822.
Lupi JL, Haddad MB, Gazmararian JA, et al. **Parental Perceptions** of Family and Pediatrician Roles in Childhood Weight Management. J Pediatr. 2014 Apr 7.
Lusk Anne C.; Mekary Rania A.; Feskanich Diane; et al. **Bicycle Riding, Walking, and Weight Gain** in Premenopausal Women. Arch Intern Med. 2010;170(12):1050-1056.
Lustig RH, Mulligan K, Noworolski SM, et al. **Isocaloric fructose restriction** and metabolic improvement in children with obesity and metabolic syndrome. Obesity (Silver Spring). 2015 Oct 26.
Lv N, Azar KMJ, Rosas LG, et al. **Behavioral lifestyle interventions** for moderate and severe obesity: A systematic review. Prev Med. 2017 Jul;100:180-193.
Lv Y, Yuan J, Mao C, et al. Association of **Body Mass Index With Disability in Activities of Daily Living Among Chinese Adults 80 Years** of Age or Older. JAMA Netw Open. 2018;1(5):e181915.
Lyall DM, Celis-Morales C, Ward J, et al. Association of **body mass index with cardiometabolic disease in the UK Biobank**: a mendelian randomization study [online July 5, 2017].JAMA Cardiol. doi:10.1001 /jamacardio.2016.5804
Lyngbakken M, Omland T, Nordstrand N, et al. Effect of weight loss on **subclinical myocardial injury**: A clinical trial comparing gastric bypass surgery and intensive lifestyle intervention. *Eur J Prev Cardiol* 2015.
Ma C, Avenell A, Bolland M, et al. Effects of **weight loss interventions** for adults who are obese on mortality, cardiovascular disease, and cancer: systematic review and meta-analysis. BMJ. 2017 Nov 14;359:j4849.
Ma J, Yank V, Xiao L, et al. Translating the Diabetes Prevention Program **lifestyle intervention into primary care**: a randomized trial [online December 10, 2012]. Arch Intern Med. doi:10.1001/2013.jamainternmed.987.
Ma J, McKeown NM, Hwang SJ, et al. **Sugar-Sweetened Beverage** Consumption Is Associated With Change of Visceral Adipose Tissue Over 6 Years of Follow-Up. Circulation. 2016 Jan 26;133(4):370-7.
Ma RCW, Schmidt MI, Tam WH, McIntyre HD, Catalano PM. **Clinical management of pregnancy in the obese mother**: before conception, during pregnancy, and post partum. Lancet Diabetes Endocrinol 2016; online Oct 12.
Macbrayne CE, Blum JD, Kiser JJ. **Tenofovir, Emtricitabine, and Darunavir/Ritonavir Pharmacokinetics** in an HIV-Infected Patient **After Roux-en-Y Gastric Bypass** Surgery. Ann Pharmacother. 2014 Jun;48(6):816-9.
Macfarlane DJ, Taylor LH, Cuddihy TF. Very short **intermittent vs continuous bouts of activity** in sedentary adults. Prev Med. 2006 Oct;43(4):332-6. Epub 2006 Jul 27.
Mackenzie H, Markar SR, Askari A, et al. **Obesity surgery and risk of cancer**. Br J Surg. 2018 Jul 13.
Mackey RH, Belle SH, Courcoulas AP, et al; Longitudinal Assessment of Bariatric Surgery Consortium Writing Group. Distribution of 10-year and lifetime predicted risk for cardiovascular disease prior to surgery in the longitudinal assessment of **bariatric surgery**-2 study. Am J Cardiol. 2012 Oct 15;110(8):1130-7.
Maciejewski ML, Livingston EH, Smith VA, et al. **Survival** among high-risk patients **after bariatric surgery**. JAMA. 2011 Jun 15;305(23):2419-26.
Maciejewski M, Livingston EH, Smith VA, et al. **Health expenditures** among high-risk patients after gastric bypass and matched controls. Arch Surg 2012; 147:633-640.
Maciejewski ML, Arterburn DE, Van Scoyoc L, et al. **Bariatric surgery** and **long-term durability of weight loss** [online August 31, 2016]. JAMA Surg. doi:10.1001/jamasurg.2016.2317.
Madjd A, Taylor MA, Delavari A, et al. Effect of a **Long Bout Versus Short Bouts of Walking on Weight Loss During a Weight-Loss Diet**: A Randomized Trial. Obesity (Silver Spring). 2019 Apr;27(4):551-558.
Madsen K, Thompson H, Adkins A, Crawford Y. School-Community Partnerships: A Cluster-Randomized Trial of an **After-School Soccer Program**. JAMA Pediatr. 2013 Feb 25:1-6.
Madsen LR, Baggesen LM, Richelsen B, Thomsen RW. Effect of **Roux-en-Y gastric bypass surgery on diabetes remission and complications** in individuals with **type 2 diabetes**: a Danish population-based matched cohort study. Diabetologia. 2019 Feb 6.
Magarey, Anthea M., Perry, Rebecca A., Baur, Louise A., et al. **A Parent-Led Family-Focused Treatment Program** for Overweight Children Aged 5 to 9 Years: The PEACH RCT**.** Pediatrics 2011 127: 214-222.
Maggard MA, et al. Meta-analysis: **surgical treatment** of obesity. Ann Intern Med. 2005 Apr 5;142(7):547-59. Summary for patients in: Ann Intern Med. 2005 Apr 5;142(7):I55.
Maggard-Gibbons M, Maglione M, Livhits M, et al. **Bariatric surgery** for weight loss and glycemic control in nonmorbidly obese adults with diabetes: A systematic review. JAMA 2013; 309:2250-2261.
Magge SN, Prasad D, Koren D, et al. **Prediabetic Obese** Adolescents have a More Atherogenic Lipoprotein Profile Compared with Normoglycemic Obese Peers. J Pediatr. 2012 May 22.
Maglio C, Peltonen M, Neovius M, et al. Effects of **bariatric surgery on gout** incidence in the **Swedish Obese Subjects** study: a non-randomised, prospective, controlled intervention trial. Ann Rheum Dis. 2016 Apr;76(4):688-693.
Maglione MA, Maggard Gibbons M, Livhits M, et al. **Bariatric Surgery** and Nonsurgical Therapy in Adults With Metabolic Conditions and a Body Mass Index of 30.0 to 34.9 kg/m². Comparative Effectiveness Review No. 82.
Mainous AG 3rd, Tanner RJ, Jo A, et al. Prevalence of **Prediabetes and Abdominal Obesity** Among Healthy-Weight Adults: 18-Year Trend. Ann Fam Med. 2016 Jul;14(4):304-10.
Makary MA, Clarke JM, Shore AD, et al. **Medication utilization** and annual health care costs in patients with type 2 diabetes mellitus **before and after bariatric surgery**. Arch Surg. 2010 Aug;145(8):726-31.
Mancini JG, Filion KB, Atallah R, et al. Systematic Review of the **Mediterranean Diet** for Long-term Weight Loss. Am J Med. 2015 Dec 22.
Manco M, Dallapiccola B. **Genetics of Pediatric Obesity**. Pediatrics. 2012 Jun 4.
Manco M, Mosca A, De Peppo F, et al. The Benefit of **Sleeve Gastrectomy** in Obese Adolescents on **Nonalcoholic Steatohepatitis** and Hepatic Fibrosis. JPediatr. 2016 Sep 30.
Maniccia Dayna M., Davison Kirsten K., Marshall Simon J., et al. A Meta-analysis of Interventions That Target Children's **Screen Time for Reduction**. Pediatrics 2011; 128:1 e193-e210; doi:10.1542/peds.2010-2353
Manini TM, et al. Daily activity **energy expenditure** and mortality among older adults. JAMA. 2006 Jul 12;296(2):171-9.
Marcus MD, Foster GD, El Ghormli L, et al. Shifts in **BMI Category and Associated Cardiometabolic Risk**: Prospective Results From HEALTHY Study. Pediatrics. 2012 Apr;129(4):e983-91.
Marteau TM, Hollands GJ, Shemilt I, et al. **Downsizing**: policy options to reduce portion sizes to help tackle obesity. BMJ Dec 2, 2015.
Martin CK, Bhapkar M, Pittas A, et al; Comprehensive Assessment of Long-term Effects of **Reducing Intake of Energy (CALERIE)** Phase 2 Study Group. Effect of calorie restriction on mood, quality of life, sleep, and sexual function in healthy nonobese adults: the CALERIE 2 randomized clinical trial [published online May 2, 2016].JAMA Intern Med. doi:10.1001/jamainternmed.2016.1189.
Martin RM, Patel R, Kramer MS, et al. Effects of promoting longer-term and exclusive **breastfeeding** on adiposity and insulin-like growth factor-I at age 11.5 years: a randomized trial. JAMA. 2013 Mar 13;309(10):1005-13.
Martínez Steele E, Baraldi LG, Louzada ML, et al. **Ultra-processed foods** and **added sugars** in the US diet: evidence from a nationally representative cross-sectional study. BMJ Open. 2016 Mar 9;6(3):e009892.
Martino JL, Stapleton RD, Wang M, et al. **Extreme obesity and outcomes** in **critically ill patients**. Chest. 2011 Nov;140(5):1198-206.
Maruyama K, Sato S, Ohira T, et al. The joint impact on being overweight of self reported behaviours of **eating quickly and eating until full**: cross sectional survey. BMJ. 2008 Oct 21;337:a2002. doi: 10.1136/bmj.a2002.
Masa JF, Corral J, Alonso ML, et al. Efficacy of Different Treatment Alternatives for **Obesity Hypoventilation Syndrome. Pickwick Study**. Am J Respir Crit Care Med. 2015 Jul 1;192(1):86-95.
Mason F, Farley A, Pallan M et al. Effectiveness of a **brief behavioural intervention to prevent weight gain over the Christmas holiday period**: randomised controlled trial. BMJ 2018;363:k4867.
Mason KE, Pearce N CS. Associations between **fast food and physical activity environments** and adiposity in mid-life: cross-sectional, observational evidence from UK Biobank. Lancet Public Health 2017; online Dec 12.
Matlaga BR, Shore AD, Magnuson T, Clark JM, Johns R, Makary MA. Effect of **gastric bypass surgery** on **kidney stone disease**. J Urol. 2009 Jun;181(6):2573-7. Epub 2009 Apr 16.
Mayer-Davis EJ, et al. **Breast-Feeding** and Risk for Childhood Obesity: Does maternal diabetes or obesity status matter? Diabetes Care. 2006 Oct;29(10):2231-7. These data provide support for all mothers to breast-feed their infants to reduce the risk for childhood overweight.
McCallum Z, et al. Outcome data from the **LEAP** (Live, Eat and Play) trial: a randomized controlled trial of a primary care intervention for childhood overweight/mild obesity. Int J Obes (Lond). 2006 Dec 12; [Epub ahead of print]

McDonnell WM, Bhattacharya R, Halldorson JB. Fulminant Hepatic Failure After Use of the Herbal Weight-Loss Supplement **Exilis**. Ann Intern Med. 2009 Nov 3;151(9):673-674.

McCusker RR, Goldberger BA, Cone EJ. **Caffeine** content of energy drinks, carbonated sodas, and other beverages. J Anal Toxicol. 2006 Mar;30(2):112-4.

McDonagh MS, Selph S, Ozpinar A, et al. Systematic Review of the Benefits and Risks of **Metformin** in Treating Obesity in Children Aged 18 Years and Younger. JAMA Pediatr. 2013 Dec 16

McDonald SD, Han Z, Mulla S, et al., on behalf of the Knowledge Synthesis Group. Overweight and **obesity in mothers** and **risk of preterm birth** and low birth weight infants: systematic review and meta-analyses. BMJ 2010;341:c3428

McDow KB, Nguyen DT, Herrick KA, Akinbami LJ. **Attempts to Lose Weight** Among Adolescents Aged 16-19 in the United States, 2013-2016. NCHS Data Brief. 2019 Jul;(340):1-8.

McHill AW, Phillips AJ, Czeisler CA, et al. **Later circadian timing of food intake** is associated with increased body fat. Am J Clin Nutr. 2017 Sep 6.

McMillan-Price J, et al. Comparison of **4 diets** of varying glycemic load on weight loss and cardiovascular risk reduction in overweight and obese young adults: a randomized controlled trial. Arch Intern Med. 2006 Jul 24;166(14):1466-75.

McNicholas C, Zhao Q, Secura G, et al. **Contraceptive failures** in overweight and obese combined hormonal contraceptive users. Obstet Gynecol. 2013 Mar;121(3):585-92.

McTigue K, et al. **Mortality and cardiac and vascular outcomes** in extremely obese women. JAMA. 2006 Jul 5;296(1):79-86.

Mead E, Atkinson G, Richter B, et al. **Drug interventions for the treatment of obesity in children and adolescents**. Cochrane Database of Systematic Reviews 2016, Issue 11. Art. No.: CD012436. This systematic review is part of a series of associated Cochrane reviews on interventions for obese children and adolescents and has shown that pharmacological interventions (metformin, sibutramine, orlistat and fluoxetine) may have small effects in reduction in BMI and bodyweight in obese children and adolescents. However, many of these drugs are not licensed for the treatment of obesity in children and adolescents, or have been withdrawn. Trials were generally of low quality with many having a short or no post-intervention followup period and high dropout rates (overall dropout of 25%). Future research should focus on conducting trials with sufficient power and long-term follow-up, to ensure the long-term effects of any pharmacological intervention are comprehensively assessed. Adverse events should be reported in a more standardised manner specifying amongst other things the number of participants experiencing at least one adverse event. The requirement of regulatory authorities (US Food and Drug Administration and European Medicines Agency) for trials of all new medications to be used in children and adolescents should drive an increase in the number of high quality trials.

Mechanick JI, Youdim A, Jones DB, et al. Clinical practice guidelines for the **perioperative nutritional, metabolic, and nonsurgical support of the bariatric surgery** patient-**2013 update**: Cosponsored by American Association of Clinical Endocrinologists (AACE) , The Obesity Society (TOS), and American Society for Metabolic & Bariatric Surgery (ASMBS). Obesity (Silver Spring). 2013 Mar;21 Suppl 1:S1-S27.

Medical Letter: Treatment Guidelines –**Diet, Drugs and Surgery for Weight Loss**. April 2008. Updated 2011. **Updated Feb 2015.**

Medical Letter: **ReShape and Orbera –Two Gastric Balloon Devices for Weight Loss**. Aug 13, 2015.

Mediterranean diet: [Mayo Clinic website] choose this heart-healthy diet option. Rochester, MN: Mayo Clinic; 2010. Available from: www.mayoclinic.com/health/mediterranean-diet/CL00011 . Accessed 2011 May 24.

Mehta S, Lopez ME, Chumpitazi BP et al. Clinical characteristics and risk factors for symptomatic pediatric **gallbladder disease**. Pediatrics. 2012 Jan;129(1):e82-8.

Meijer RI, van Wagensveld BA, Siegert CE, Eringa EC, Serné EH, Smulders YM. **Bariatric surgery** as a novel treatment for type 2 diabetes mellitus: a systematic review. Arch Surg 2011; 146: 744–50.

Meinhardt U, Witassek F, Petrò R, et al. **Strength training and physical activity** in boys: a randomized trial. Pediatrics. 2013 Dec;132(6):1105-11.

Melnick EM, Li M. Association of Plate Design With **Consumption of Fruits and Vegetables Among Preschool Children**. JAMA Pediatr. 2018 Aug 6.

Mendoza JA, Watson K, Baranowski T, et al. The **Walking School Bus** and Children's Physical Activity: A Pilot Cluster Randomized Controlled Trial. Pediatrics. 2011 Aug 22.

Menke A, Rust KF, et al. Associations Between **Trends in Race/Ethnicity, Aging, and Body Mass Index With Diabetes Prevalence in the United States**: A Series of Cross-sectional Studies. Ann Intern Med. 2014 Sep 2;161(5):328-35.

Menke MN, King WC, White GE, et al. **Conception rates and contraceptive use after bariatric surgery among women with infertility**: Evidence from a prospective multicenter cohort study. Surg Obes Relat Dis. 2019 Jan 11.

Merritt MA, Riboli E, Murphy N, et al. **Reproductive factors** and risk of **mortality** in the European Prospective Investigation into **Cancer and Nutrition**; a cohort study. BMC Med. 2015 Oct 30;13:252.

Merola JF, Ghoroghchian PP, Samuels MA, et al. Clinical problem-solving. **At a loss**. N Engl J Med. 2012 Jul 5;367(1):67-72. (Wernicke's encephalopathy-**thiamine** deficiency post bariatric surgery)

Messier SP, et al. **Exercise and dietary** weight loss in overweight and obese older adults with knee osteoarthritis: the Arthritis, Diet, and Activity Promotion Trial. Arthritis Rheum. 2004 May;50(5):1501-10.

Messier SP, Mihalko SL, Legault C, et al. Effects of **intensive diet and exercise** on knee joint loads, inflammation, and clinical outcomes among overweight and obese adults with knee osteoarthritis: the IDEA randomized clinical trial. JAMA. 2013 Sep 25;310(12):1263-73.

Messier SP, Resnik AE, Beavers DP, et al. **Intentional Weight Loss** for Overweight and Obese **Knee Osteoarthritis Patients**: Is More Better? Arthritis Care Res (Hoboken). 2018 Jun 18.

Metcalf B, Henley W, Wilkin T. **Effectiveness of intervention** on physical activity of children: systematic review and meta-analysis of controlled trials with objectively measured outcomes (EarlyBird 54). BMJ. 2012 Sep 27;345:e5888.

Meyer KA, Guilkey DK, Ng SW, et al. Sociodemographic Differences in **Fast Food Price Sensitivity**. JAMA Intern Med. 2014 Jan 13

MHRA Feb/12 Herbal sliming products found to contain potentially dangerous undeclared pharmaceuticals: **Expelling Grease Slimming Abdomen, V12 Fruit Slimming, 100% Natural Weight Loss Coffee, Leisure 18 Slimming Orange Juice, Fashion Slimming Milk Shake, Langli, Ya Buk & Fruit and vegetables lose weight**. MHRA has received advice from the Danish Medicines Agency that these unlicensed products have been tested and found to contain the Prescription Only Medicine Sibutramine.

MHRA Feb/12 Following a safety alert issued in October 2010 about slimming products containing Paiyouji the Agency has received a further complaint about a product called **'Paiyouji Plus - Fast Acting Slimming Tea'**. This product has been tested by the Agency and, as in the case of other Paiyouji products, found to contain sibutramine.

MHRA Nov/12 has received advice from the Danish Medicines Agency that this unlicensed product, **Ultra Slim** has been tested and found to contain the Prescription Only Medicine Sibutramine.

MHRA Feb/13 is advising consumers not to use the products specified below due to sibutramine content. Product: **Fashion Slimming Coffee, L-Carnitine + P57, L-CarnitinL 360 Slimming Coffee, Brazil Potent Slimming Coffee sachets, Coffee 26 Original sachets, Coffee Nature Fashion Slimming sachets, Slender Capsule, Slim-1.**

Michalsky M, Kramer RE, Fullmer MA, et al. Developing **criteria for pediatric/adolescent bariatric surgery** programs. Pediatrics 2011;128:Suppl 2:S65-S70

Michalsky MP, Inge TH, Simmons M, et al; the Teen-LABS Consortium. Cardiovascular Risk Factors in Severely Obese Adolescents: The **Teen Longitudinal Assessment of Bariatric Surgery (Teen-LABS)** Study. JAMA Pediatr. 2015 Mar 2.

Michalsky MP, Inge TH, Jenkins TMet al; **Teen-LABS Consortium. Cardiovascular Risk Factors After Adolescent Bariatric Surgery**. Pediatrics. 2018 Jan 8.

Miller AC, Polgreen LA, Segre EM, Polgreen PM. Variations in **Marginal Taste Perception** by Body Mass Index Classification: A Randomized Controlled Trial. J Acad Nutr Diet. 2019 Jul 25.

Miller AD, Smith KM. Medication and nutrient administration considerations after **bariatric surgery**. Am J Health-Syst Pharm. 2006;63:1852-1857.

Miller PE, Perez V. **Low-calorie sweeteners** and body weight and composition: a meta-analysis of randomized controlled trials and prospective cohort studies. Am J Clin Nutr. 2014 Sep;100(3):765-77.

Mingrone G, Panunzi S, De Gaetano A, et al. **Bariatric surgery versus conventional medical therapy** for type 2 diabetes. N Engl J Med 2012. DOI: 10.1056/NEJMoa1200111.

Miras AD, Pérez-Pevida B, Aldhwayan M, et al. Adjunctive **liraglutide** treatment in patients **with persistent or recurrent type 2 diabetes after metabolic surgery** (GRAVITAS): a randomised, double-blind, placebocontrolled trial. Lancet Diabetes Endocrinol 2019; online June 4.

Mital S, Nguyen HV. Incremental Cost-Effectiveness of **Aspiration Therapy vs Bariatric Surgery** and No Treatment for Morbid Obesity. Am J Gastroenterol. 2019 Sep;114(9):1470-1477.

Mitchell JA, Rodriguez D, Schmitz KH et al. **Sleep Duration** and Adolescent Obesity. Pediatrics. 2013 Apr 8.

Mitchell JE, Christian NJ, Flum DR, et al. **Postoperative behavioral variables** and weight change 3 years after bariatric surgery [online April 20, 2016].JAMA Surg. doi:10.1001 /jamasurg.2016.0395.

Mnatzaganian G, Ryan P, Norman PE, et al. Smoking, body **weight, physical exercise** and risk of **lower limb total joint replacement** in a population-based cohort of men. Arthritis Rheum. 2011 Jul 11.

Moin T. **Obesity Management and Prevention**: More Questions Than Answers. JAMA Intern Med. 2016 May 2

Mokhlesi B, Masa JF, Brozek JL, et al. Evaluation and Management of **Obesity Hypoventilation Syndrome**. An Official American Thoracic Society Clinical Practice Guideline. Am J Respir Crit Care Med. 2019 Aug 1;200(3):e6-e24.

Mokry LE, Ross S, Timpson NJ, et al. **Obesity and Multiple Sclerosis**: A Mendelian Randomization Study. PLoS Med. 2016 Jun 28;13(6):e1002053.

Moleres A, Rendo-Urteaga T, Zulet MA, et al. EVASYON Study Group. **Obesity Susceptibility Loci** on Body Mass Index and Weight Loss in Spanish Adolescents after a Lifestyle Intervention. J Pediatr. 2012 May 18.

Molyneaux E, Poston L, Ashurst-Williams S, et al. Obesity and **Mental Disorders During Pregnancy and Postpartum**: A Systematic Review and Meta-analysis. Obstet Gynecol. 2014 Apr;123(4):857-67.

Mongraw-Chaffin M, Foster MC, Anderson CAM, et al. Metabolically Healthy Obesity, Transition to Metabolic Syndrome, and Cardiovascular Risk. J Am Coll Cardiol. 2018 May 1;71(17):1857-1865.

Montanha MC, Magon TFDS, Alcantara CDS, et al. **Reduced bioavailability of oral amoxicillin tablets compared to suspensions** in RYGB bariatric subjects. Br J Clin Pharmacol. 2019 Jun 19.

Montgomery JR, Waits SA, Dimick JB, Telem DA. **Risks of Bariatric Surgery Among Patients With End-stage Renal Disease**. JAMA Surg. 2019 Sep 25.

Moore M, Hopkins J, Wainwright P. **Primary care management of patients after weight loss surgery**. BMJ. 2016 Mar 10;352:i945.

Moore SM, Borawski EA, Love TE, et al. **Two family interventions to reduce BMI in low-income urban youth**: a randomized trial. Pediatrics. 2019; 143(6):e20182185

Mor A, Antonsen S, Kahlert J, et al. **Prenatal exposure to systemic antibacterials** and overweight and obesity in Danish schoolchildren: a prevalence study. Int J Obes (Lond). 2015 Oct;39(10):1450-5.

Moran AJ, Block JP, Goshev SG, et al. Trends in **Nutrient Content of Children's Menu** Items in U.S. Chain Restaurants. Am J Prev Med. 2016 Dec 27.

Morandi A, Meyre D, Lobbens S, et al. Estimation of **newborn risk** for child or adolescent obesity: lessons from longitudinal birth cohorts. PLoS One. 2012;7(11):e49919.

Morandi A, Tommasi M, Soffiati F, et al. **Prevention of obesity in toddlers** (PROBIT): a randomised clinical trial of responsive feeding promotion from birth to 24 months. Int J Obes (Lond). 2019 Jul 3.

Morgan DJR, Ho KM, Platell C. Incidence and Determinants of **Mental Health Service Use After Bariatric Surgery**. JAMA Psychiatry. 2019 Sep 25.

Morgan PJ, Collins CE, Plotnikoff RC, et al. The `**Healthy Dads, Healthy Kids**` community randomized controlled trial: A community-based healthy **lifestyle program for fathers and their children**. Prev Med. 2014 Apr;61:90-9.

Morgan PJ, Young MD, Lloyd AB, et al. **Involvement of Fathers** in Pediatric Obesity Treatment and Prevention Trials: A Systematic Review. Pediatrics. 2017 Feb;139(2).

Morrison KM, Xu L, Tarnopolsky M, et al. **Screening for dysglycemia** in overweight youth presenting for weight management. Diabetes Care. 2012 Apr;35(4):711-6.

Morton JM, Garg T, Leva N. Association of **Laparoscopic Gastric Bypass Surgery With Telomere Length** in Patients With Obesity. JAMA Surg. 2018 Dec 19.

Mourtakos SP, Tambalis KD, Panagiotakos DB et al. **Maternal lifestyle** characteristics during pregnancy, and the risk of obesity in the offspring: a study of 5,125 children. BMC Pregnancy Childbirth. 2015 Mar 21;15:66.

Moyer VA; on behalf of the U.S. Preventive Services Task Force **(USPSTF). Screening** for and Management of Obesity in Adults: U.S. Preventive Services Task Force Recommendation Statement. Ann Intern Med. 2012 Jun 26.

Moylan A, Appelbaum N, Clarke J, et al. Assessing the Agreement of **5 Ideal Body Weight Calculations** for Selecting Medication Dosages for Children With Obesity. JAMA Pediatr. 2019 Apr 1.

Mozaffarian Dariush, Hao Tao, Rimm Eric B., eft al. Changes in **Diet and Lifestyle and Long-Term Weight Gain** in Women and Men. N Engl J Med 2011; 364:2392-2404.

Mueller JA, Patel T, Halawa A, et al. **Warfarin dosing and body mass index.** Ann Pharmacother. 2014 May;48(5):584-8.

Murali SB, Mshs MD. Interpretation of **Vitamin B12 Status After a Roux-en-Y Gastric Bypass**. JAMA. 2019 Jul 26.

Murtagh L, Ludwig DS. **State intervention** in life-threatening childhood obesity. JAMA 2011;306:206-7

Must A, M Phillips S, Naumova EN. Occurance and **Timing of Childhood Overweight and Mortality**: Findings from the Third Harvard Growth Study. J Pediatr. 2011 Dec 17.

Muth ND, Dietz WH, Magge SN, et al. **Public Policies to Reduce Sugary Drink Consumption** in Children and Adolescents. Pediatrics. 2019 Apr;143(4).

Mutsaerts MAQ et al. Randomized trial of a **lifestyle program in obese infertile women**. N Engl J Med 2016 May 19; 374:1942.

Nackers LM, Appelhans BM, Segawa E, et al. Associations between body mass index and **sexual functioning** in midlife women: the Study of Women's Health Across the Nation. Menopause. 2015 Mar 23.

Nagy M, Gill A, Adams T, et al. **Stress-induced suppression of food intake** in overweight and obese adolescents. Psychosom Med. 2019 Jul 10.

Naparstek J, Wing RR, Xu X, Leahey TM. **Internet-delivered obesity treatment** improves symptoms of and risk for depression. Obesity (Silver Spring). 2017 Apr;25(4):671-675.

Nascimento SL, Pudwell J, Surita FG, et al. The effect of **physical exercise strategies on weight loss in postpartum** women: a systematic review and meta-analysis. Int J Obes (Lond). 2013 Sep 19.

Naude CE, Visser ME, Nguyen KA, et al. Effects of **total fat intake on bodyweight in children**. Cochrane Database of Systematic Reviews 2018, Issue 2. Art. No.: CD012960. We were unable to reach firm conclusions. Limited evidence from three trials that randomised children to a lower total fat intake (30% or less TE) versus usual or modified fat intake, but with no intention to reduce weight, showed small reductions in body mass index, total- and LDL-cholesterol at some time points with lower fat intake compared to controls, and no consistent differences in effects on weight, high-density lipoprotein (HDL) cholesterol or height. Associations in cohort studies that related total fat intake to later measures of body fatness in children were inconsistent and the quality of this evidence was mostly very low.

NCD Risk Factor Collaboration. **Trends in adult body-mass index in 200 countries** from 1975 to 2014: a pooled analysis of 1698 population-based measurement studies with 19·2 million participants. Lancet 2016; 387: 1377–96.

NCD Risk Factor Collaboration (NCD-RisC). **Worldwide trends in body-mass index, underweight, overweight, and obesity** from 1975 to 2016: a pooled analysis of 2416 population-based measurement studies in 128·9 million children, adolescents, and adults. Lancet. 2017 Oct 10.

NCD Risk Factor Collaboration (NCD-RisC). **Trends in adult body-mass index in 200 countries** from 1975 to 2014: a pooled analysis of 1698 population-based measurement studies with 19·2 million participants. Lancet. 2016 Apr 2;387(10026):1377-1396.

Ndumele CE, Coresh J, Lazo M, et al. Obesity, **subclinical myocardial injury, and incident heart failure**. JACC Heart Fail. 2014 Dec;2(6):600-7.

Ndumele CE, Matsushita K, Lazo M, et al. Obesity and **Subtypes of Incident Cardiovascular Disease**. J Am Heart Assoc. 2016 Jul 28;5(8).

Nedeltcheva Arlet V., Kilkus Jennifer M., Imperial Jacqueline, et al. **Insufficient Sleep** Undermines Dietary Efforts to Reduce Adiposity. Ann Intern Med October 5, 2010 153:435-441; doi:10.1059/0003-4819-153-7-201010050-00006.

Nelson DW, Blair KS, Martin MJ. Analysis of Obesity-Related Outcomes and Bariatric Failure Rates With the **Duodenal Switch vs Gastric Bypass** for Morbid Obesity. Arch Surg. 2012 Sep 1;147(9):847-54.

Neovius M, Narbro K, Keating C, et al. Health care use during **20 years following bariatric surgery**. JAMA. 2012;308(11):1132-1141.

Neovius M, Bruze G, Jacobson P, et al. **Risk of suicide and non-fatal self-harm after bariatric surgery**: results from two matched cohort studies. Lancet Diabetes Endocrinol 2018; online Jan 9.
Neuhouser ML, Aragaki AK, Prentice RL, et al. Overweight, Obesity, and **Postmenopausal Invasive Breast Cancer Risk**: A Secondary Analysis of the Women's Health Initiative Randomized Clinical Trials.JAMA Oncol. 2015 Jun 11.
Ng M, Fleming T, Robinson M, et al. **Global, regional, and national prevalence of overweight and obesity in children and adults** during 1980-2013: a systematic analysis for the Global Burden of Disease Study 2013. Lancet. 2014 May 28.
Ngueta G, Ndjaboue R. Lifetime **marijuana use in relation to insulin resistance** in lean, overweight, and obese US adults. J Diabetes. 2019 Jun 1.
Nguyen CT, Zhou S, Shanahan W, et al. **Lorcaserin** in Obese and Overweight Patients Taking Prohibited Serotonergic Agents: A Retrospective Analysis. Clin Ther. 2016 May 17.
Nguyen NT et al. A prospective randomized trial of laparoscopic gastric **bypass versus laparoscopic adjustable gastric banding** for the treatment of morbid obesity: Outcomes, quality of life, and costs. Ann Surg 2009 Oct; 250:631.
Niranjan U, Wright NP. Should we treat **subclinical hypothyroidism** in obese children? BMJ. 2016 Mar 16
Nishtar S, Gluckman P, Armstrong T. **Ending childhood obesity**: a time for action. Lancet. 2016 Jan 22.
Nissen SE, Nicholls SJ, Wolski K, et al. Effect of rimonabant on progression of atherosclerosis in patients with abdominal obesity and coronary artery disease. The **STRADIVARIUS** randomized controlled trial. JAMA 2008; 299: 1547-1560.
NICE Obesity Guidelines Dec 2006 http://www.nice.org.uk/guidance/CG43/?c=91500
NICE: National Institute for Health and Care Excellence. Managing overweight and obesity among **children and young people**: **lifestyle weight management services**. (Public Health Guideline PH47). 2013. www.nice.org.uk/guidance/PH47.
NICE: National Institute for Health and Care Excellence. **Behaviour change**: individual approaches. (Public Health Guideline PH49). 2014. www.nice.org.uk/guidance/PH49.
NICE: National Institute for Health and Care Excellence. **Managing overweight and obesity in adults**—lifestyle weight management services. (Public Health Guideline PH53). 2014. www.nice.org.uk/guidance/PH53.
NCIE: National Institute for Health and Care Excellence, 2014. **Obesity: identification, assessment and management of overweight and obesity in children, young people and adults** (CG189) [online]. Available: https://www.nice.org.uk/guidance/cg189/ [Accessed 21 January 2015].
NICE: National Institute for Health and Care Excellence. **Maintaining a healthy weight and preventing excess weight gain** among children and adults. Public Health Guideline. Publication expected 2015. www.nice.org.uk/guidance/indevelopment/GID-PHG78.
NICE: National Institute for Health and Care Excellence. **Maintaining a healthy weight and preventing excess weight gain among adults and children**. London (UK): National Institute for Health and Care Excellence (NICE); 2015 Mar 13.
Nicholls SJ, et al. Effects of obesity on lipid-lowering, anti-inflammatory, and antiatherosclerotic benefits of **atorvastatin** or **pravastatin** in patients with coronary artery disease (from the REVERSAL Study). Am J Cardiol. 2006 Jun 1;97(11): 1553-7. Epub 2006 Apr 6.
Nissen SE, Wolski KE, et al. Effect of **naltrexone-bupropion** on major adverse cardiovascular events in overweight and obese patients with cardiovascular risk factors: a randomized clinical trial (**Light**) .JAMA. doi:10.1001/jama .2016.1558.
Nokoff N, Thurston J, Hilkin A, et al. Sex Differences in **Effects of Obesity on Reproductive Hormones and Glucose Metabolism** in Early Puberty. J Clin Endocrinol Metab. 2019 Apr 15.
Nordestgaard BG, Palmer TM, Benn M, et al. The effect of elevated body mass index on **ischemic heart disease risk**: causal estimates from a mendelian randomisation approach. PLoS Med. 2012 May;9(5):e1001212.
Nordestgaard LT, Tybjærg-Hansen A, Nordestgaard BG, et al. Body Mass Index and **Risk of Alzheimer Disease**: a Mendelian Randomization Study of 399,536 Individuals. J Clin Endocrinol Metab. 2017 May 9.
Nordström P, Pedersen NL, Gustafson Y, et al. Risks of **Myocardial Infarction, Death, and Diabetes** in Identical Twin Pairs With Different Body Mass Indexes. JAMA Intern Med. 2016 Aug 1.
Nourse SE, Olson I, Popat RA, et al. **Live Video Diet and Exercise Intervention** in Overweight and Obese Youth: Adherence and Cardiovascular Health. J Pediatr. 2015 Jul 4.
Novak NL, Brownell KD. Role of **policy and government** in the obesity epidemic. Circulation. 2012 Nov 6;126(19):2345-52.
O'Brien Paul E.; Sawyer Susan M.; Laurie Cheryl; et al. Laparoscopic Adjustable **Gastric Banding** in Severely Obese **Adolescents**: A Randomized Trial. *JAMA*. 2010;303 (6):519-526.
O'Brien PD, Hinder LM, Callaghan BC, et al. **Neurological consequences of obesity**. Lancet Neurol. 2017 Jun;16(6):465-477.
O'Brien PE, MacDonald L, Anderson M, et al. Long-term outcomes after **bariatric surgery: 15-year follow-up** of adjustable gastric banding and a systematic review of the bariatric surgical literature. (Core) Ann Surg 2013; 257:87-94.
O'Brien R, Johnson E, Haneuse S, et al. **Microvascular outcomes in patients with diabetes after bariatric surgery** versus usual care. A matched cohort study. Ann Intern Med. 2018. [Epub ahead of print].
O'Byrne ML, et al. Effect of Obesity and Underweight Status on **Perioperative Outcomes of Congenital Heart Operations in Children, Adolescents, and Young Adults**: Data from the Society of Thoracic Surgeons Database. Circulation. 2017 Jun 16.
O'Byrne ML, Kim S, Hornik CP, et al. Effect of Obesity and Underweight Status on **Perioperative Outcomes of Congenital Heart Operations in Children, Adolescents, and Young Adults**: An Analysis of Data from the Society of Thoracic Surgeons Database. Circulation. 2017 Jun 16.
Ochs-Balcom HM, Preus L, Nie J, et al. **Physical activity modifies genetic susceptibility to obesity** in postmenopausal women. Menopause. 2018 May 14.
O'Connor GT et al. Prospective study of sleep-disordered breathing and **hypertension**: The Sleep Heart Health Study. Am J Respir Crit Care Med 2009 Jun 15; 179:1159.
O'Connor L, Imamura F, Lentjes MA, Khaw et al. Prospective associations and population impact of **sweet beverage intake** and type 2 diabetes, and effects of substitutions with alternative beverages. Diabetologia. 2015 May 6.
O'Neil PM, Miller-Kovach K, Tuerk PW, et al. Randomized controlled trial of a **nationally available weight control program tailored for adults** with type 2 diabetes. Obesity (Silver Spring). 2016 Nov;24(11):2269-2277.
Ode KL, Gray HL, Ramel SE, et al. Decelerated Early Growth in Infants of **Overweight and Obese Mothers**. J Pediatr. 2012 Jul 19.
Ogden CL, Carroll MD, Flegal KM. High body mass index for age among **US children and adolescents, 2003-2006**. JAMA. 2008 May 28;299(20):2401-5. The prevalence of high BMI for age among children and adolescents showed no significant changes between 2003-2004 and 2005-2006 and no significant trends between 1999 and 2006.
Ogden CL, Carroll MD, Curtin LR, McDowell MA, Tabak CJ, Flegal KM. **Prevalence** of overweight and obesity in the **United States, 1999-2004**. JAMA. 2006 Apr 5;295(13):1549-55. The prevalence of overweight among children and adolescents and obesity among men increased significantly during the 6-year period from 1999 to 2004; among women, no overall increases in the prevalence of obesity were observed. These estimates were based on a 6-year period and suggest that the increases in body weight are continuing in men and in children and adolescents while they may be leveling off in women.
Ogden Cynthia L.; Carroll Margaret D.; Curtin Lester R.; et al. Prevalence of High **Body Mass Index** in **US Children and Adolescents**, 2007-2008. JAMA. 2010;0(2010):2009.2012.
Ogden CL, Carroll MD, Kit BK, Flegal KM. **Prevalence of obesity and trends in body mass index** among us children and adolescents, 1999-2010. JAMA 2012.
Ogden CL, Carroll MD, Kit BK, Flegal KM. **Prevalence of childhood and adult obesity in the United States, 2011-2012**. JAMA. 2014 Feb 26;311(8):806-14.
Ogden CL, Carroll MD, Lawman HG, et al. **Trends in obesity** prevalence among **children and adolescents in the United States, 1988-1994 through 2013-2014**.JAMA. doi:10.1001/jama.2016 .6361.
Ogden CL, Fakhouri TH, Carroll MD, et al. Prevalence of Obesity Among Adults, by **Household Income and Education** – United States, 2011-2014. MMWR Morb Mortal Wkly Rep. 2017 Dec 22;66(50):1369-1373
Ogden CL, Fryar CD, Hales CM, et al. Differences in **Obesity Prevalence by Demographics and Urbanization in US Children** and Adolescents, 2013-2016. JAMA. 2018 Jun 19;319(23):2410-2418.
Oh TJ, Moon JH, Choi SH, et al. **Body-weight fluctuation and incident diabetes mellitus, cardiovascular disease, and mortality**: a 16-year prospective cohort study. J Clin Endocrinol Metab. 2018 Nov 29.
Ohlsson C, Bygdell M, Nethander M, et al. **BMI change during puberty is an important determinant of adult type 2 diabetes risk** in men. J Clin Endocrinol Metab. 2018 Dec 4.

Okabayashi K, Ashrafian H, Hasegawa H, et al. Body mass index category as a risk factor for **colorectal adenomas**: a systematic review and meta-analysis. Am J Gastroenterol. 2012 Aug;107(8):1175-85.

Olbers T, Gronowitz E, Werling M, et al. Two-year outcome of **laparoscopic Roux-en-Y gastric bypass in adolescents** with severe obesity: results from a Swedish Nationwide Study (AMOS). Int J Obes (Lond). 2012 Sep 25.

Olbers T, Beamish AJ, Gronowitz E, et al. Laparoscopic **Roux-en-Y gastric bypass** in **adolescents** with severe obesity (**AMOS**): a prospective, 5-year, Swedish nationwide study. Lancet Diabetes Endocrinol. 2017 Jan 5.

Ollendorf DA, Cameron CG, Pearson SD. Effectiveness and Value of **Treatment Options for Obesity**-A Report for the California Technology Assessment Forum. JAMA Intern Med. 2016 Jan 4:1-3.

Ong KL, Waters DD, Messig M, et al. Effect of **Change in Body Weight on Incident Diabetes** Mellitus in Patients With Stable Coronary Artery Disease Treated With Atorvastatin (from the Treating to New Targets Study). Am J Cardiol. 2014 May 15;113(10):1593-8.

Omalu BI, Ives DG, Buhari AM, Lindner JL, Schauer PR, Wecht CH, Kuller LH. Death rates & causes of death after **bariatric surgery** for Pennsylvania residents, 1995 to 2004. Arch Surg. 2007 Oct;142(10):923-8; discussion 929. There was a substantial excess of deaths owing to suicide and coronary heart disease. Careful monitoring of bariatric surgical procedures and more intense follow-up could likely reduce the long-term case fatality rate in this patient population.

O'Neil PM, Birkenfeld AL, McGowan B, et al. Efficacy and safety of **semaglutide compared with liraglutide and placebo for weight loss** in patients with obesity: a randomised, double-blind, placebo and active controlled, dose-ranging, phase 2 trial. Lancet. 2018 Aug 25;392(10148):637-649.

Ordway MR, Sadler LS, Holland ML, et al. A **Home Visiting Parenting Program and Child Obesity**: A Randomized Trial. Pediatrics. 2018 Jan 16.

Ortega FB, Ruiz JR, Labayen I, et al; HELENA project group. **Health inequalities** in urban adolescents: role of physical activity, diet, and genetics. Pediatrics. 2014 Apr;133(4):e884-95.

Oskrochi Y, Majeed A, Easton G. **Bariatric surgery**. BMJ. 2015 Jul 30;351:h3802.

Ostendorf DM, Caldwell AE, Creasy SA, et al. **Physical Activity Energy Expenditure and Total Daily Energy Expenditure in Successful Weight Loss Maintainers**. Obesity (Silver Spring). 2019 Mar;27(3):496-504.

Østergaard Pedersen J, Heitmann B L, Schnohr P, and Grønbæk M. The combined influence of leisure-time **physical activity and weekly alcohol** intake on fatal ischaemic heart disease and all-cause mortality. Eur Heart J 2008; DOI:10.1093/eurheartj/ehm574.

Osto E, Doytcheva P, Corteville C, et al. Rapid and body weight-independent improvement of endothelial and high-density lipoprotein function after **Roux-en-Y gastric bypass**: role of glucagon-like peptide-1. Circulation. 2015;131:871–881.

Otten Jennifer J.; Jones Katherine E.; et al. Effects of **Television Viewing** Reduction on Energy Intake and Expenditure in Overweight and Obese Adults: A Randomized Controlled Trial. Arch Intern Med. 2009;169(22):2109-2115.

Oude Luttikhuis H, Baur L, Jansen H, Shrewsbury VA, O'Malley C, Stolk RP, Summerbell CD. Interventions for treating **obesity in children. Cochrane** Database Syst Rev. 2009 Jan 21;(1):CD001872. While there is limited quality data to recommend one treatment program to be favoured over another, this review shows that combined behavioural lifestyle interventions compared to standard care or self-help can produce a significant and clinically meaningful reduction in overweight in children and adolescents. In obese adolescents, consideration should be given to the use of either orlistat or sibutramine, as an adjunct to lifestyle interventions, although this approach needs to be carefully weighed up against the potential for adverse effects.

Overberg J, Hummel T, Krude H, Wiegand S. Differences in **taste sensitivity** between obese and non-obese children and adolescents. Arch Dis Child. 2012 Sep 20.

Owen-Smith A, Kipping R, Donovan J, et al. A **NICE** example? Variation in provision of **bariatric surgery** in England. BMJ. 2013 May 1;346:f2453.

Pacanowski CR, Levitsky DA. **Frequent Self-Weighing** and Visual Feedback for Weight Loss in Overweight Adults. J Obes. 2015;2015

Packer M. **Obesity-Associated Heart Failure as a Theoretical Target for Treatment With Mineralocorticoid Receptor Antagonists**. JAMA Cardiol. 2018 Jul 25

Padwal RS, Majumdar SR. **Drug treatments for obesity**: orlistat, sibutramine, and rimonabant. Lancet. 2007 Jan 6;369(9555):71-7.

Padwal RS, Pajewski NM, Allison DB, Sharma AM. Using the **Edmonton obesity staging system to predict mortality** in a population-representative cohort of people with overweight and obesity. CMAJ. 2011 Aug 15.

Padwal RS, Klarenbach SW, Wang X, et al. A **Simple Prediction Rule** for All-Cause Mortality in a Cohort Eligible for **Bariatric Surgery**. JAMA Surg. 2013 Oct 16.

Padwal R, McAlister FA, et al. The **obesity paradox in heart failure** patients with preserved versus reduced ejection fraction: a meta-analysis of individual patient data. Int J Obes (Lond). 2013 Oct 31.

Padwal R, Leslie WD, Lix LM, et al. Relationship Among **Body Fat Percentage, Body Mass Index, and All-Cause Mortality**: A Cohort Study. Ann Intern Med. 2016 Mar 8.

Pagani LS, Nguyen AK, Fitzpatrick C. Prospective associations between early long-term **household tobacco smoke** exposure and subsequent indicators of metabolic risk at age 10. Nicotine Tob Res. 2015 Jun 11.

Page KA, Chan O, Arora J, et al. Effects of **fructose vs glucose** on regional cerebral blood flow in brain regions involved with appetite and reward pathways. JAMA 2013; 309:63-67.

Pakhale S, Baron J, Dent R, et al. Effects of weight loss on **airway responsiveness** in obese adults with **asthma**: does weight loss lead to reversibility of asthma? Chest. 2015 Jun;147(6):1582-90.

Pakpour AH, Gellert P, Dombrowski SU, et. al. **Motivational Interviewing** With Parents for Obesity: An RCT. Pediatrics. 2015 Feb 9. pii: peds.2014-1987.

Palamara KL, Mogul HR, Peterson SJ, Frishman WH. Obesity: new perspectives and pharmacotherapies. Cardiol Rev. 2006 Sep-Oct;14(5):238-58.

Pan L, Freedman DS, Park S, et al. **Changes in Obesity** Among US Children Aged 2 Through 4 Years Enrolled in WIC During 2010-2016. JAMA. 2019 Jun 18;321(23):2364-2366.

Pan L, May AL, Wethington H, et al. Incidence of Obesity Among **Young US Children Living in Low-Income** Families, 2008-2011. Pediatrics. 2013 Dec;132(6):1006-13.

Panagiotopoulos C, Ronsley R, Davidson J. Increased Prevalence of **Obesity** and **Glucose Intolerance** in Youths Treated With Second-Generation **Antipsychotic** Medications. Can J Psychiatry. 2009;54(11):743-749

Panagiotou OA, Markozannes G, Adam GP, et al. Comparative **Effectiveness and Safety of Bariatric Procedures** in Medicare-Eligible Patients: A Systematic Review. JAMA Surg. 2018 Sep 5:e183326.

Pandey A, Cornwell WK 3rd, Willis B, et al. Body Mass Index and **Cardiorespiratory Fitness in Mid-Life and Risk of Heart Failure Hospitalization** in Older Age: Findings from the Cooper Center Longitudinal Study. JACC Heart Fail. 2017 Mar 30.

Pan L, Park S, Slayton R, et al. Trends in **Severe Obesity Among Children Aged 2 to 4 Years** Enrolled in Special Supplemental Nutrition Program for Women, Infants, and Children From 2000 to 2014. JAMA Pediatr. 2018 Jan 8.

Pantel H, Hwang J, Brams D, et al. Effect of **incentive spirometry** on postoperative hypoxemia and pulmonary complications **after bariatric surgery**: a randomized clinical trial [online Jan 11, 2017]. JAMA Surg. doi:10.1001/jamasurg.2016.4981

Panunzi S, Carlsson L, De Gaetano A, et al. Determinants of **Diabetes Remission** and Glycemic Control **After Bariatric Surgery**. Diabetes Care. 2016 Jan;39(1):166-74.

Papadakis GE, Hans D, Rodriguez EG, et al. **Menopausal hormone therapy** is associated with reduced total and visceral **adiposity**, the OsteoLaus cohort. J Clin Endocrinol Metab. 2018 Mar 27.

Parent B, Martopullo I, Weiss NS, et al. **Bariatric surgery in women of childbearing age, timing** between an operation and birth, and associated perinatal complications [online October 19, 20].

Park SH, Huh TL, Kim SY, et al. Antiobesity effect of **Gynostemma pentaphyllum extract (actiponin):** a randomized, double-blind, placebo-controlled trial. Obesity (Silver Spring). 2014 Jan;22(1):63-71.

Park YM, White AJ, Jackson CL, et al. Association of Exposure to **Artificial Light at Night While Sleeping With Risk of Obesity** in Women. JAMA Intern Med. 2019 Jun 10.

Parker M, Rifas-Shiman SL, Oken E, et al. Second Trimester Estimated **Fetal Weight** and Fetal Weight Gain Predict Childhood Obesity. J Pediatr. 2012 Jun 7.

Parkin L, Sweetland S, Balkwill A, et al. the **Million Women Study Collaborators**. **Body Mass Index, Surgery, and Risk of Venous Thromboembolism** in Middle-Aged Women: A Cohort Study. Circulation. 2012 Apr 17;125(15):1897-1904.

Parkin P, Connor Gorber S, Shaw E, et al; **Canadian Task Force on Preventive Health Care**. Recommendations for **growth monitoring, and prevention and management of overweight and obesity in children and youth in primary care**. CMAJ. 2015 Mar 30.

Parks EP, Kumanyika S, Moore RH, et al. Influence of **Stress in Parents** on Child Obesity and Related Behaviors. Pediatrics. 2012 Oct 22.
Parr EB, Coffey VG, Cato LE, et al. A randomized trial of **high-dairy-protein, variable-carbohydrate diets and exercise** on body composition in adults with obesity. Obesity (Silver Spring). 2016 May;24(5):1035-45.
Parretti HM, Aveyard P, Blannin A, et al. Efficacy of **water preloading** before main meals as a strategy for weight loss in primary care patients with obesity: RCT. Obesity (Silver Spring). 2015 Aug 3.
Pastor-Villaescusa B, Cañete MD, Caballero-Villarraso J, et al. Metformin for obesity in prepubertal and pubertal children: a randomized controlled trial. Pediatrics. 2017;140(1):e20164285
Patalay P, Hardman CA. **Comorbidity, Codevelopment, and Temporal Associations** Between Body Mass Index and Internalizing Symptoms From Early Childhood to Adolescence. JAMA Psychiatry. 2019 Mar 20.
Patel AI, Ritchie L. Striving for meaningful policies to **reduce sugar-sweetened beverage intake** among young children. Pediatrics. 2013 Sep;132(3):566-8.
Patel MS, Asch DA, Rosin R, et al. Framing **Financial Incentives** to Increase **Physical Activity** Among Overweight and Obese Adults: A Randomized, Controlled Trial. Ann Intern Med. 2016 Feb 16.
Patel MS, Benjamin EJ, Volpp KG, et al. Effect of a **game-based intervention** designed to enhance social incentives to **increase physical activity** among families: the **BE FIT** randomized clinical trial [online October 2, 2017].JAMA Intern Med. doi:10.1001/jamainternmed.2017.3458
Patel MS, Small DS, Harrison JD, et al. Effectiveness of Behaviorally Designed **Gamification Interventions With Social Incentives** for Increasing Physical Activity Among Overweight and Obese Adults Across the United States: The STEP UP Randomized Clinical Trial. JAMA Intern Med. 2019 Sep 9:1-9.
Paul IM, Savage JS, Anzman-Frasca S, et al. Effect of a responsive **parenting educational intervention on childhood weight outcomes at 3 years of age**: the INSIGHT randomized clinical trial [August 7, 2018]. JAMA. doi:10.1001/jama.2018.9432
Pearl RL, Himmelstein MS, Puhl RM, et al. Weight **bias internalization in a commercial weight management sample**: prevalence and correlates. Obes Sci Pract. 2019 Jul 11;5(4):342-353.
Pearson-Stuttard J, Zhou B, Kontis V, et al. Worldwide burden of **cancer attributable** to diabetes and high body-mass index: a comparative risk assessment. Lancet Diabetes Endocrinol. 2017 Nov 28.
Pearson-Stuttard J, Zhou B, Kontis V, et al. Worldwide burden of **cancer attributable** to diabetes and high body-mass index: a comparative risk assessment. Lancet Diabetes Endocrinol. 2018 Jun;6(6):e6-e15.
Pedersen SD, Kang J, Kline GA. **Portion control plate** for weight loss in obese patients with type 2 diabetes mellitus: a controlled clinical trial. Arch Intern Med. 2007 Jun 25;167(12):1277-83.
Pei Z, Heinrich J, Fuertes E, et al. **Cesarean Delivery** and Risk of Childhood Obesity. J Pediatr. 2014 Feb 5.
Peng L, Wang J, Li F. Weight reduction for **non-alcoholic fatty liver disease** (NAFLD). Cochrane Database Syst Rev. 2011 Jun 15;6:CD003619. The sparse data and high risk of bias preclude us from drawing any definite conclusion on lifestyle programme or **orlistat** for treatment of NAFLD.
Pepino MY, Okunade AL, Eagon JC, et al. Effect of **Roux-en-Y Gastric Bypass Surgery**: Converting 2 **Alcoholic Drinks** to 4. JAMA Surg. 2015 Aug 5.
Perez AJ, Kebbe M, Holt NL, et al. **Parent Recommendations** to Enhance Enrollment in Multidisciplinary Clinical Care for Pediatric Weight Management. J Pediatr. 2018 Jan;192:122-129.
Perez LG, Arredondo EM, Elder JP, et al. **Evidence-based obesity treatment interventions for Latino adults** in the U.S.: a systematic review. Am J Prev Med. 2013 May;44(5):550-60.
Perez-Cornago A, Appleby PN, Pischon T, et al. Tall height and obesity are associated with an increased risk of **aggressive prostate cancer**: results from the EPIC cohort study. BMC Med. 2017 Jul 13;15(1):115
Perri MG, Limacher MC, von Castel-Roberts K, et al. Comparative effectiveness of **three doses of weight-loss counseling**: two-year findings from the rural **LITE** trial. Obesity (Silver Spring). 2014 Nov;22(11):2293-300.
Perry CL, Creamer MR. The Childhood Obesity Epidemic: **Lessons Learned from Tobacco**. J Pediatr. 2013 Sep 5.
Persson M, Cnattingius S, Villamor E, et al. **Risk of major congenital malformations** in relation to maternal overweight and obesity severity: cohort study of 1.2 million singletons. BMJ. 2017 Jun 14;357:j2563
Persson M, Razaz N, Edstedt Bonamy AK, et al. **Maternal Overweight and Obesity and Risk of Congenital Heart Defects**. J Am Coll Cardiol. 2019 Jan 8;73(1):44-53.
Peterli R, et al. Laparoscopic **Sleeve Gastrectomy Versus Roux-Y-Gastric Bypass** for Morbid Obesity-3-Year Outcomes of the Prospective Randomized Swiss Multicenter Bypass Or Sleeve Study (SM-BOSS). Ann Surg. 2017 Mar;265(3):466-473.
Peterli R, Wölnerhanssen BK, Peters T, et al. Effect of **laparoscopic sleeve gastrectomy vs laparoscopic Roux-en-Y gastric bypass** on weight loss in patients with morbid obesity: the SM-BOSS randomized clinical trial.JAMA. doi:10.1001/jama.2017.20897
Peterlin BL, Rosso AL, Williams MA, et al. **Episodic migraine** and obesity and the influence of age, race, and sex. Neurology. 2013 Oct 8;81(15):1314-21.
Peters JC, Wyatt HR, Foster GD, et al. The effects of **water and non-nutritive sweetened beverages** on weight loss during a 12-week weight loss treatment program. Obesity (Silver Spring). 2014 Jun;22(6):1415-21.
Petrick JL, Kelly SP, Liao LM, et al. Body weight trajectories and risk of **oesophageal and gastric cardia adenocarcinomas**: a pooled analysis of NIH-AARP and PLCO Studies. Br J Cancer. 2017 Feb 14.
Pharmacist's Letter. **PolyGlycopleX (PGX)** for Weight Loss. April 2010.
Pharmacist's Letter. **Raspberry ketone** for Weight Loss. May 2012.
Pharmacist's Letter. **Bariatric Surgery and Medication Use**. Canadian Pharmacist's Letter. Dec 2013.
Phelan S, Hagobian T, Brannen A, et al. Effect of an **internet-based program on weight loss for low-income postpartum women**: a randomized clinical trial.JAMA. doi:10.1001/jama.2017.7119
Phillips L, Singer MA. Peripheral neuropathy due to **dinitrophenol** used for weight loss: something old, something new. Neurology. 2013 Feb 19;80(8):773-4.
Phillips CM, Perry IJ. Does **Inflammation Determine Metabolic Health Status** in Obese and Nonobese Adults? J Clin Endocrinol Metab. 2013 Aug 26.
Pi-Sunyer X, Astrup A, Fujioka K, et al. A randomized, controlled trial of **3.0 mg of liraglutide** in weight management (**SCALE**). N Engl J Med 2015;373:11-22.
Piaggi P. **Metabolic Determinants** of Weight Gain in Humans. Obesity (Silver Spring). 2019 May;27(5):691-699.
Piercy KL, Troiano RP, Ballard RM, et al. The **Physical Activity Guidelines** for Americans. JAMA. 2018 Nov 12.
Pinsonneault L, Déry V. Family physicians and treatment of **pediatric obesity**: findings drawn from the creation of clinical practice **guidelines**. Can Fam Physician. 2012 May;58(5):e238, 502.
Pinto AM, Fava JL, Hoffmann DA, Wing RR. **Combining behavioral weight loss treatment and a commercial program (Weight Watchers)**: a randomized clinical trial. Obesity (Silver Spring). 2013 Apr;21(4):673-80.
Pitts SI, Maruthur NM, Langley GE, et al. **Obesity, Diabetes, and the Risk of Invasive Group B Streptococcal Disease** in Nonpregnant Adults in the United States. Open Forum Infect Dis. 2018 Jun 8;5(6):ofy030.
Plachta-Danielzik S, Kehden B, Landsberg B, et al. Attributable Risks for Childhood Overweight: Evidence for **Limited Effectiveness of Prevention**. Pediatrics. 2012 Sep 3.
Plourde G. Preventing and **managing pediatric obesity. Recommendations for family physicians**. Can Fam Physician. 2006 Mar;52:322-8.
Podolsky SH. Historical Perspective on the Rise and Fall and Rise of **Antibiotics and Human Weight Gain**. Ann Intern Med. 2017 Jan 17;166(2):133-138
Poirier P, Cornier MA, Mazzone T. **Bariatric surgery and cardiovascular risk factors**: A scientific statement from the American Heart Association (**AHA**). Circulation. 2011; DOI: 10.1161/CIR.0b013e3182149099. http://circ.ahajournals.org/cgi/reprint/123/15/1683
Polonsky HM, Bauer KW, Fisher JO, et al. Effects of a **breakfast in the classroom initiative** on obesity in urban school-aged children: a cluster randomized controlled trial [online Feb 25, 2019]. JAMA Pediatr.
Pomeranz JL,Mozaffarian D, Micha R. Can the government require **health warnings on sugar-sweetened beverage advertisements**? JAMA.doi:10.1001/jama.2017.19209

Pope L, Hansen D, Harvey J. Examining the **Weight Trajectory of College Students**. J Nutr Educ Behav. 2016 Dec 3.

Popov VB, Ou A, Schulman AR, et al. The Impact of **Intragastric Balloons** on Obesity-Related Co-Morbidities: A Systematic Review and Meta-Analysis. Am J Gastroenterol. 2017 Jan 24.

Post RE, Mainous AG 3rd, Gregorie SH, et al. The influence of **physician acknowledgment** of patients' weight status on patient perceptions of overweight and obesity in the United States. Arch Intern Med 2011;171:316–21.

Poston L, Caleyachetty R, Cnattingius S, et al. **Preconceptional and maternal obesity**: epidemiology and health consequences. Lancet Diabetes Endocrinol 2016; online Oct 12.

Powell LM, Nguyen BT. **Fast-Food and Full-Service Restaurant** Consumption Among Children and Adolescents: Effect on Energy, Beverage, and Nutrient Intake. Arch Pediatr Adolesc Med. 2012 Nov 5:1-7.

Powell LM, Nguyen BT, Dietz WH. Energy and Nutrient Intake From **Pizza** in the United States. Pediatrics. 2015 Jan 19.

Pozuelo-Carrascosa DP, Sánchez-López M, Cavero-Redondo I, et al. Obesity as a Mediator between **Cardiorespiratory Fitness and Blood Pressure in Preschoolers**. J Pediatr. 2016 Nov 29.

Prachand VN, Davee RT, Alverdy JC. Duodenal Switch Provides Superior Weight Loss in the Super-Obese (BMI >/=50kg/m2) Compared With Gastric Bypass. Ann Surg. 2006 Oct;244(4):611-9.

Preganancy: May/09 Obese women (BMI, 30 or higher) should gain only 11 to 20 pounds during a singleton pregnancy, according to new guidelines from the Institute of Medicine. The guidelines update the IOM's previous recommendations, issued in 1990. The group continues to recommend that: underweight women (BMI lower than 18.5) gain 28-40 pounds; normal-weight women (BMI, 18.5-24.9) gain 25-35 pounds; overweight women (BMI, 25.0-29.9) gain 15-25 pounds. Weight gain should be higher for multiple pregnancies. Excessive weight gain, the IOM notes, is associated with increased risk for gestational diabetes, pregnancy-associated hypertension, and delivery of large-for-gestational-age infants, among other outcomes. The group says that clinicians should supplement these guidelines with individualized counseling about diet and exercise. In addition, preconception counseling should stress the importance of conceiving at a normal BMI. http://www.iom.edu/Object.File/Master/68/110/Report%20Brief%20-%20Weight%20Gain%20During%20Pregnancy.pdf

Proietti M, Lane DA, Lip GY. Relation of **Nonvalvular Atrial Fibrillation** to Body Mass Index (from the SPORTIF Trials). Am J Cardiol. 2016 Jul 1;118(1):72-8.

Proudfoot NA, King-Dowling S, Cairney J, et al. **Physical Activity and Trajectories of Cardiovascular Health Indicators** During Early Childhood. Pediatrics. 2019 Jun 11.

Puder JJ, Marques-Vidal P, Schindler C, et al. Effect of **multidimensional lifestyle intervention** on fitness and adiposity in predominantly migrant preschool children-Ballabeina: cluster randomised controlled trial. BMJ. 2011 Oct 13;343:d6195.

Puhl RM, Peterson JL, Luedicke J. **Parental Perceptions of Weight Terminology** That Providers Use With Youth. Pediatrics. 2011 Sep 26.

Puhl RM, Peterson JL, Luedicke J. **Weight-based victimization**: bullying experiences of weight loss treatment-seeking youth. Pediatrics. 2013 Jan;131(1):e1-9.

Puhl RM, Wall MM, Chen C, et al. **Experiences of weight teasing** in adolescence and weight-related outcomes in adulthood: A 15-year longitudinal study. Prev Med. 2017 Apr 24;100:173-179.

Purcell K, Sumithran P, Prendergast LA, et al. The effect of **rate of weight loss on long-term weight management**: a randomized controlled trial. Lancet Diabetes Endocrinol. 2014 Oct 15;2(12):954-962.

Puzziferri N, Roshek TB, Mayo HG, Gallagher R, Belle SH, Livingston EH. **Long-term follow-up after bariatric surgery**: a systematic review. JAMA. doi:10.1001/jama.2014.10706.

Puzziferri N, Almandoz JP. **Sleeve Gastrectomy** for Weight Loss. JAMA. 2018 Jan 16;319(3):316.

Qi Q, Chu AY, Kang JH, et al. **Sugar-sweetened beverages** and genetic risk of obesity. N Engl J Med published 2012; DOI:10.1056/NEJMoa1203039. Available at: http://www.nejm.org.

Qi Q, Li Y, Chomistek AK, et al. **Television watching**, leisure time physical activity, and the genetic predisposition in relation to body mass index in women and men. Circulation. 2012 Oct 9;126(15):1821-7.

Qi Q, Chu AY, Kang JH, Huang, J, Rose LM, Jensen MK, et al. **Fried food consumption, genetic risk**, and body mass index: gene-diet interaction analysis in three US cohort studies. BMJ 2014;348:g1610.

Qizilbash N, Gregson J, Johnson ME, et al. **BMI and risk of dementia** in two million people over two decades: a retrospective cohort study. Lancet Diabetes Endocrinol. 2015 Jun;3(6):431-6.

Quattrin T, Roemmich JN, Paluch R, et al. Efficacy of **Family-Based Weight Control Program** for Preschool Children in Primary Care. Pediatrics. 2012 Sep 17.

Raebel MA, Newcomer SR, Reifler LM, et al. Chronic use of **opioid medications before and after bariatric surgery**. JAMA. doi:10.1001/jama.2013.278344.

Rahman I, Wolk A, Larsson SC. The relationship between **sweetened beverage** consumption and risk of **heart failure** in men. Heart. 2015 Nov 2.

Raja-Khan N, Agito K, Shah J, et al. **Mindfulness-based stress reduction** in women with overweight or obesity: A randomized clinical trial. Obesity (Silver Spring). 2017 Jul 7.

Ramaraju GA, Teppala S, Prathigudupu K, et al. Association between **obesity and sperm quality**. Andrologia. 2017 Sep 19.

Ramsey Buchanan L, Rooks-Peck CR, Finnie RK, et al. **Reducing Recreational Sedentary Screen Time**: A Community Guide Systematic Review. Am J Prev Med. 2016 Mar;50(3):402-15.

Rank M, Siegrist M, Wilks D, et al. The **cardio-metabolic risk** of **moderate and severe obesity in children and adolescents**. J Pediatr 2013.

Rank M, Wilks DC, Foley L, et al. Health-Related **Quality of Life and Physical Activity in Children and Adolescents 2 Years after an Inpatient Weight-Loss Program**. J Pediatr. 2014 Jul 16.

Rao G. **Office-based strategies** for the management of obesity. Am Fam Physician. 2010 Jun 15;81(12):1449-56 ; quiz 1429.

Rao G, Burke LE, Spring BJ, et al. on behalf of the American Heart Association Obesity Committee of the Council on Nutrition, Physical Activity and Metabolism, Council on Clinical Cardiology, Council on Cardiovascular Nursing, Council on the Kidney in Cardiovascular Disease, and Stroke Cou. **New and Emerging Weight Management Strategies** for Busy Ambulatory Settings: A Scientific Statement From the American Heart Association * Endorsed by the Society of Behavioral Medicine. Circulation. 2011 Sep 6;124(10):1182-1203.

Rao G, Powell-Wiley TM, Ancheta I, et al. Identification of **Obesity and Cardiovascular Risk in Ethnically and Racially Diverse Populations**: A Scientific Statement From the **American Heart Association**. Circulation. 2015 Jul 6.

Raut A, Lee TC, McDonald EG. "**Explainable" weight loss** [published online January 17, 2017]. JAMA Intern Med. doi:10.1001/jamainternmed.2016 .8693

Razaz N, Tedroff K, Villamor E, et al. **Maternal Body Mass Index** in Early Pregnancy and **Risk of Epilepsy** in Offspring. JAMA Neurol. 2017 Apr 3.

Read J. Leighton, Shortell Stephen M.. **Interactive Games** to Promote Behavior Change in Prevention and Treatment. JAMA. 2011;305(16):1704-1705.

Reames BN, Finks JF, Bacal D, et al. Changes in **bariatric surgery procedure** use in Michigan, 2006-2013. JAMA. 2014 Sep 3;312(9):959-61.

Reeves GK, Pirie K, Beral V, Green J, Spencer E, Bull D; Million Women Study Collaboration. **Cancer incidence and mortality in relation to body mass index** in the Million Women Study: cohort study. BMJ. 2007 Dec 1;335(7630):1134. Epub 2007 Nov 6. Increasing body mass index is associated with a significant increase in the risk of cancer for 10 out of 17 specific types examined. Among postmenopausal women in the UK, 5% of all cancers (about 6000 annually) are attributable to being overweight or obese. For endometrial cancer and adenocarcinoma of the oesophagus, body mass index represents a major modifiable risk factor; about half of all cases in postmenopausal women are attributable to overweight or obesity.

Reges O, et al. Association of **bariatric surgery using laparoscopic banding, Roux-en-Y gastric bypass, or laparoscopic sleeve gastrectomy** vs usual care obesity management with all-cause mortality.JAMA. doi:10.1001/jama .2017.20513

Rehm CD, Drewnowski A. Trends in Energy Intakes by Type of **Fast Food** Restaurant Among US Children From 2003 to 2010. JAMA Pediatr. 2015 Mar 30.

Reichkendler MH, Rosenkilde M, Auerbach PL, et al. Only **minor additional metabolic health benefits of high as opposed to moderate dose physical exercise** in young, moderately overweight men. Obesity (Silver Spring). 2014 May;22(5):1220-32. doi: 10.1002/oby.20226

Reicks M, Redden JP, Mann T, et al. **Photographs in lunch tray compartments** and vegetable consumption among children in elementary school cafeterias. JAMA 2012.

Reilly JJ, et al. **Physical activity** to prevent obesity in **young children**: cluster randomized controlled trial. BMJ. 2006 Oct 6; [Epub ahead of print] Physical activity can significantly improve motor skills but did not reduce body mass index in young children in this trial.

Reis JP, Loria CM, Lewis CE, et al. Association between **duration of overall and abdominal obesity beginning in young adulthood** and coronary artery calcification in middle age. JAMA. 2013 Jul 17;310(3):280-8.

Renehan AG, et al. **Body-mass index and incidence of cancer**: a systematic review and meta-analysis of prospective observational studies. Lancet. 2008 Feb 16;371(9612):569-78. Increased BMI is associated with increased risk of common and less common malignancies. For some cancer types, associations differ between sexes and populations of different ethnic origins.

Rejeski W. Jack; Brubaker Peter H.; Goff David C., et al. Translating **Weight Loss and Physical Activity Programs** Into the Community to Preserve Mobility in Older, Obese Adults in Poor Cardiovascular Health. Arch Intern Med. 2011;171(10):880-886.

Rejeski WJ, Ip EH, Bertoni AG, et al. **Lifestyle change and mobility** in obese adults with type 2 diabetes. (**Look Ahead**) N Engl J Med. 2012 Mar 29;366(13):1209-17.

Resnicow K, McMaster F, Bocian A, et al. **Motivational Interviewing** and **Dietary Counseling** for Obesity in Primary Care: An RCT. Pediatrics. 2015 Mar 30.

Reznik M, Wylie-Rosett J, Kim M, Ozuah PO. **Physical activity during school** in urban minority kindergarten and first-grade students. Pediatrics. 2013 Jan;131(1):e81-7.

Riaz H, Khan MS, Siddiqi TJ, et al. Association Between **Obesity and Cardiovascular Outcomes** A Systematic Review and Meta-analysis of Mendelian Randomization Studies. JAMA Netw Open. 2018;1(7):e183788.

Rich S, Rubin L, Walker AM, et al. **Anorexigens and pulmonary hypertension** in the United States: results from the surveillance of North American Pulmonary Hypertension. Chest 2000; 117: 870–74.

Richards J, Thorogood M, Hillsdon M, Foster C. **Face-to-face versus remote and web 2.0 interventions for promoting physical activity**. Cochrane Database Syst Rev. 2013 Sep 30;9:CD010393. There is insufficient evidence to assess whether face-to-face interventions or remote and web 2.0 approaches are more effective at promoting PA.

Richardson CR, Newton TL, Abraham JJ, Sen A, Jimbo M, Swartz AM. A meta-analysis of **pedometer**-based walking interventions and weight loss. Ann Fam Med. 2008 Jan-Feb;6(1):69-77. Using pedometers to guide physical activity, even when not accompanied by dietary interventions, promotes modest weight loss among sedentary and obese or overweight individuals. (LOE = 2a)

Richelsen B, et al. Effect of Orlistat on Weight Regain and Cardiovascular Risk Factors Following a Very-Low-Energy Diet in Abdominally Obese Patients: A 3-year randomized, placebo-controlled study. Diabetes Care. 2007 Jan;30(1):27-32. The addition of orlistat to lifestyle intervention was associated with maintenance of an extra 2.4 kg weight loss after VLED for up to 3 years in obese subjects. The combination of orlistat and lifestyle intervention was associated with a reduced occurrence of type 2 diabetes.

Riddoch CJ, Leary SD, Ness AR, et al. Prospective associations between objective measures of **physical activity** and fat mass in 12-14 year old children: the Avon Longitudinal Study of Parents and Children (ALSPAC). BMJ. 2009 Nov 26;339:b4544. doi: 10.1136/bmj.b4544.

Rijks JM, Plat J, Dorenbos E, et al. Association of **TSH With Cardiovascular Disease Risk in Overweight and Obese Children During Lifestyle Intervention**. J Clin Endocrinol Metab. 2017 Jun 1;102(6):2051-2058.

Rillamas-Sun E, Lacroix AZ, Waring ME,et al. Obesity and Late-Age **Survival Without Major Disease or Disability in Older Women**. JAMA Intern Med.2013 Nov 11.

Ring Madsen L, Espersen R, Rejnmark L, et al. Effect of **calcium citrate vs calcium carbonate on elevated parathyroid hormone after Roux-en-Y gastric bypass**. A double-blinded, randomized trial. Clin Endocrinol (Oxf). 2018 Aug 14.

Risstad H, Søvik TT, EngströmM, et al. **Five-year** outcomes after **laparoscopic gastric bypass and laparoscopic duodenal switch** in patients with body mass index of 50 to 60: a randomized clinical trial [online February 4, 2015]. JAMA Surg. doi:10.1001/jamasurg.2014.3579.

Ritzwoller DP, Glasgow RE, Sukhanova AY, et al. **Economic Analyses of the Be Fit Be Well Program**: A Weight Loss Program for Community Health Centers. J Gen Intern Med. 2013 Jun 4.

Roager HM, Vogt JK, Kristensen M, et al. **Whole grain-rich diet** reduces body weight and systemic low-grade inflammation without inducing major changes of the gut microbiome: a randomised cross-over trial. Gut. 2017 Nov 1.

Roberto CA, Lawman HG, LeVasseur MT, et al. Association of a **beverage tax on sugar-sweetened and artificially sweetened beverages with changes in beverage prices** and sales at chain retailers in a large urban setting [May 14, 2019]. JAMA. doi:10.1001/jama.2019.4249

Roberto CA, Swinburn B, Hawkes C, et al. Patchy progress on **obesity prevention**: emerging examples, entrenched barriers, and new thinking. Lancet. 2015 Jun 13;385(9985):2400-9.

Roberto CA, Wong D, Musicus A, et al. The Influence of **Sugar-Sweetened Beverage** Health Warning Labels on Parents' Choices. Pediatrics. 2016 Jan 14.

Roberto CA, Lawman HG, LeVasseur MT, et al. Association of a **Beverage Tax on Sugar-Sweetened and Artificially Sweetened Beverages** With Changes in Beverage Prices and Sales at Chain Retailers in a Large Urban Setting. JAMA. 2019 May 14;321(18):1799-1810.

Roberts SB, Das SK, Suen VMM, et al. **Measured energy content of frequently purchased restaurant meals**: multi-country cross sectional study. BMJ 2018;363:kk4864.

Robertson C, Archibald D, Avenell A, et al. Systematic reviews of and **integrated report** on the quantitative, qualitative and economic evidence base for the management of obesity in **men**. Health Technol Assess. 2014 May;18(35):1-424.

Robinson E, Sutin AR. **Parental Perception of Weight Status and Weight Gain Across Childhood**. Pediatrics. 2016 May;137(5).

Robertson J, Schaufelberger M, Lindgren M, et al. **Higher Body Mass Index** in Adolescence **Predicts Cardiomyopathy Risk in Midlife**: Long-Term Follow-Up Among Swedish Men. Circulation. 2019 May 28.

Robinson L, Ojha S, Symonds ME, Budge H. Body Mass Index as a Determinant of **Brown Adipose Tissue** Function in Healthy Children. J Pediatr. 2013 Nov 14.

Robinson TN, Matheson DM, Kraemer HC, et al. A randomized controlled trial of **culturally tailored dance and reducing screen time** to prevent weight gain in low-income African American girls: Stanford GEMS. Arch Pediatr Adolesc Med. 2010 Nov;164(11):995-1004.

Rock Cheryl L.; Flatt Shirley W.; Sherwood Nancy E.; et al. Effect of a **Free Prepared Meal and Incentivized Weight Loss Program** on Weight Loss and Weight Loss Maintenance in Obese and Overweight Women: A Randomized Controlled Trial. *JAMA*. 2010;0(2010):jama.2010.1503.

Rock CL, Flatt SW, Pakiz B, et al. **Weight loss, glycemic control, and cardiovascular disease** risk factors in response to differential diet composition in a weight loss program in type 2 diabetes: a randomized controlled trial. Diabetes Care. 2014 Jun;37(6):1573-80.

Rock CL, et al. Results of Exercise & Nutrition to Enhance Recovery & Good Health for You (**ENERGY**) Trial: Behavioral **Weight Loss Intervention in Overweight or Obese Breast Cancer Survivors**. J Clin Oncol. 2015 Oct 1;33(28):3169-76.

Rock CL, Flatt SW, Pakiz B, et al. Randomized clinical trial of **portion-controlled prepackaged foods** to promote weight loss.Obesity (Silver Spring). 2016 Jun;24(6):1230-7.

Rodd C, Sharma AK. Recent **trends in the prevalence of overweight and obesity among Canadian children**. CMAJ. 2016 May 9.

Rogers PJ, Hogenkamp PS, de Graaf C, et al. Does **low-energy sweetener consumption** affect energy intake and body weight? A systematic review, including meta-analyses, of the evidence from human and animal studies. Int J Obes (Lond). 2016 Mar;40(3):381-94.

Roggero P, Gianni ML, Amato O, et al. Growth and Fat-Free Mass Gain in **Preterm Infants** After Discharge: A Randomized Controlled Trial. Pediatrics. 2012 Oct 29.

Rogovik AL, Chanoine JP, Goldman RD. Pharmacotherapy and weight-loss supplements for treatment of **paediatric obesity**. Drugs. 2010 Feb 12;70(3):335-46.

Rogovik, Alexander L., Goldman, Ran D. Pharmacologic **treatment of pediatric obesity**. Can Fam Physician 2011 57: 195-197.

Rohailla S, Jackson TD, Fralick M. **Bariatric surgery**. CMAJ. 2017 Aug 8;189(31):E1017.

Roman YM, Dominguez MC, Easow TM, et al. **Effects of intermittent versus continuous dieting on weight and body composition in obese and overweight people: a systematic review and meta-analysis of randomized controlled trials.** Int J Obes (Lond). 2018 Sep 11.

Rommel J, Simpson R, Mounsey JP, et al. Effect of Body Mass Index, Physical Activity, Depression, and Educational Attainment on High-Sensitivity C-Reactive Protein in Patients With **Atrial Fibrillation.** Am J Cardiol. 2012 Nov 2.

Rondinelli M, Rossi A, Gandolfi A, et al. Use of **Liraglutide** in the Real World and Impact at **36 Months** on Metabolic Control, Weight, Lipid Profile, Blood Pressure, Heart Rate, and Renal Function. Clin Ther. 2016 Dec 8.

Rooney D, Herkenrath S, Priegnitz C, et al. Choosing an adequate **test to determine fitness for air travel** in obese individuals. Chest. 2019 Aug 13.

Roos N, Neovius M, Cnattingius S, et al. **Perinatal outcomes after bariatric surgery**: nationwide population based matched cohort study. BMJ. 2013 Nov 12;347:f6460.

Rosen ED. Burning Fat by **Bugging the System**. N Engl J Med. 2016 Mar 3;374(9):885-7.

Rosenbaum DL, Espel HM, Butryn ML, et al. **Daily self-weighing** and weight gain prevention: a longitudinal study of college-aged women. J Behav Med. 2017 Jul 8

Rosenstock J, Hollander P, Gadde KM, et al.; OBD-202 Study Group. A randomized, double-blind, placebo-controlled, multicenter study to assess the efficacy and safety of topiramate controlled release in the treatment of obese type 2 diabetic patients. Diabetes Care. 2007 Jun;30(6):1480-6. Epub 2007 Mar 15.

Rosinger AY, Bethancourt H, Francis LA. Association of Caloric Intake From Sugar-Sweetened Beverages With Water Intake Among US Children and Young Adults in the 2011-2016 National Health and Nutrition Examination Survey. JAMA Pediatr. 2019 Apr 22.

Ross PA, Newth CJ, Leung D, et al. **Obesity** and **Mortality** Risk in **Critically Ill Children**. Pediatrics. 2016 Feb 16.

Ross R, Lam M, Blair SN, et al. Trial of Prevention and Reduction of Obesity Through **Active Living** in Clinical Settings: A Randomized Controlled Trial. Arch Intern Med. 2012 Feb 27. (over 2yrs)

Rousseau C, Jean S, Gammache P, et al. Change in **fracture risk and fracture** pattern after **bariatric surgery**: nested case-control study. BMJ 2016;354:i3794

Roy SM, Spivack JG, Faith MS, et al. **Infant BMI** or Weight-for-Length and Obesity Risk in Early Childhood. Pediatrics. 2016 May;137(5).

Rozier MD, Ghaferi AA, Rose A, et al. Patient **Preferences for Bariatric Surgery**: Findings From a Survey Using Discrete Choice Experiment Methodology. JAMA Surg. 2018 Nov 28:e184375.

Rubin LH, Gustafson D, Hawkins KL, et al. **Midlife adiposity predicts cognitive decline** in the prospective Multicenter AIDS Cohort Study. Neurology. 2019 Jul 16;93(3):e261-e271.

Rucker D, Padwal R, Li SK, Curioni C, Lau DC. Long term **pharmacotherapy** for obesity and overweight: **updated meta-analysis**. BMJ. 2007 Nov 15; [Epub ahead of print] Attrition rates averaged 30-40%. Compared with placebo, orlistat reduced weight by 2.9 kg (95% confidence interval 2.5 kg to 3.2 kg), sibutramine by 4.2 kg (3.6 kg to 4.7 kg), and rimonabant by 4.7 kg (4.1 kg to 5.3 kg). Patients receiving active drug treatment were significantly more likely to achieve 5% and 10% weight loss thresholds. Orlistat reduced the incidence of diabetes and improved concentrations of total cholesterol and low density lipoprotein cholesterol, blood pressure, and glycaemic control in patients with diabetes but increased rates of gastrointestinal side effects and slightly lowered concentrations of high density lipoprotein. Sibutramine lowered concentrations of high density lipoprotein cholesterol and triglycerides but raised blood pressure and pulse rate. Rimonabant improved concentrations of high density lipoprotein cholesterol and triglycerides, blood pressure, and glycaemic control in patients with diabetes but increased the risk of mood disorders. Orlistat, sibutramine, and rimonabant modestly reduce weight, have differing effects on cardiovascular risk profiles, and have specific adverse effects.

Rueda-Clausen CF, Padwal RS. **Pharmacotherapy for weight loss**. BMJ. 2014 Jun 6;348:g3526.

Ryan Donna H.; Johnson William D.; Myers Valerie H.; et al. **Nonsurgical** Weight Loss for Extreme Obesity in Primary Care Settings: Results of the Louisiana Obese Subjects Study (**LOSS**). Arch Intern Med. 2010;170(2):146-154.

Ryckman KK, Feenstra B, Shaffer JR, Bream EN, Geller F, Feingold E, et al. Replication of a **genome-wide association** study of birth weight in preterm neonates. J Pediatr 2011.

Ryder JR, Edwards NM, et al. Changes in **Functional Mobility and Musculoskeletal Pain** After Bariatric Surgery in Teens With Severe Obesity: Teen-Longitudinal Assessment of Bariatric Surgery (LABS) Study. JAMA Pediatr. 2016 Jul 18.

Sabhaney V, Boutis K, Yang G, et al. **Bone Fractures** in Children: Is There an Association with Obesity? J Pediatr. 2014 May 13.

Saccomani S, Lui-Filho JF, Juliato CR, et al. Does **obesity increase the risk of hot flashes** among midlife women? A population-based study. Menopause. 2017 May 29.

Sacks FM, Bray GA, Carey VJ, Smith SR, et al. Comparison of **weight-loss diets** with different compositions of fat, protein, and carbohydrates. N Engl J Med. 2009 Feb 26;360(9):859-73. Reduced-calorie diets result in clinically meaningful weight loss regardless of which macronutrients they emphasize.

Sahakyan KR, Somers VK, Rodriguez-Escudero JP, et al. **Normal-weight central obesity**: implications for total and cardiovascular mortality. Ann Intern Med. 2015: 163:827-35.

Salehi M, Gastaldelli A, D'Alessio DA. **Beta-cell sensitivity to glucose is impaired after gastric bypass surgery**. Diabetes Obes Metab. 2017 Nov 20.

Salminen P, et al. Effect of **laparoscopic sleeve gastrectomy vs laparoscopic Roux-en-Y gastric bypass** on weight loss at 5 years among patients with morbid obesity: the **SLEEVEPASS** randomized clinical trial.JAMA. doi:10.1001/jama.2017.20313

Samaha FF, Iqbal N, Seshadri P, et al. A low-carbohydrate as compared with a low-fat diet in severe obesity. N Engl J Med 2003; 348:2074-81.

Samartzis D, Karppinen J, Chan D, et al. The association of **lumbar intervertebral disc degeneration** on magnetic resonance imaging with body mass index in overweight and obese adults: a population-based study. Arthritis Rheum. 2012 May;64(5):1488-96.

Samuel-Hodge CD, Holder-Cooper JC, Gizlice Z, et al. **Family PArtners in Lifestyle Support** (**PALS**): **Family-based** weight loss for African American adults with type 2 diabetes. Obesity (Silver Spring). 2017 Jan;25(1):45-55.

Sanchez-Vaznaugh EV, Sánchez BN, Crawford PB, et al. Association between **competitive food and beverage policies** in elementary schools and childhood overweight/obesity trends: differences by neighborhood socioeconomic resources. JAMA Pediatr. 2015 May 4;169(5)

Sandberg ME, Bengtsson C, Källberg H, et al. Overweight decreases the chance of achieving good response and low disease activity in early **rheumatoid arthritis**. Ann Rheum Dis. 2014 Nov;73(11):2029-33.

Sanders LM, Perrin EM, Yin HS, et al; on behalf of the Greenlight Study Team. "**Greenlight Study**": A Controlled Trial of **Low-Literacy, Early Childhood Obesity Prevention**. Pediatrics. 2014 May 12.

Santos RG, Durksen A, Rabbanni R, et al. Effectiveness of **Peer-Based Healthy Living Lesson Plans** on Anthropometric Measures and Physical Activity in Elementary School Students: A Cluster Randomized Trial. JAMA Pediatr. 2014 Feb 10.

Sarwer DB, Spitzer JC,Wadden TA, et al. Changes in **sexual functioning and sex hormone levels** in women following **bariatric surgery** [published online November 4, 2013]. JAMA Surg. doi:10.1001/jamasurg.2013.5022.

Savir S, Kalchiem-Dekel O, Naggan L, Maimon N. **Respiratory deterioration** following laparoscopic adjustable **gastric banding**: A three-year follow-up of over 3,000 subjects. Respir Med. 2016 Jun;115:66-71.

Savoye, Mary, Nowicka, Paulina, Shaw, Melissa, et al. **Long-term Results of an Obesity Program** in an Ethnically Diverse **Pediatric** Population. Pediatrics 2011 0: peds.2010-0697.

Sawyer MG, Harchak T, Wake M, Lynch J. **Four-Year** Prospective Study of BMI and Mental Health Problems in Young **Children**. Pediatrics. 2011 Oct;128(4):677-84.

Scally CP, Varban OA, Carlin AM, et al. Michigan Bariatric Surgery Collaborative. **Video Ratings** of Surgical Skill and Late Outcomes of Bariatric Surgery. JAMA Surg. 2016 Apr 13:e160428.

Schaefer L, Plotnikoff RC, Majumdar SR, et al. **Outdoor Time** Is Associated with Physical Activity, Sedentary Time, and Cardiorespiratory Fitness in Youth. J Pediatr. 2014 Jul 17.

Scharf RJ, Demmer RT, Deboer MD. Longitudinal evaluation of **milk type** consumed and weight status in preschoolers. Arch Dis Child. 2013 Mar 18.

Schauer PR, Kashyap SR, Wolski K, et al. **Bariatric surgery versus intensive medical therapy** in obese patients with diabetes. N Engl J Med 2012. DOI: 10.1056/NEJMoa1200225.

Schauer PR, Bhatt DL, Kirwan JP, et al. **Bariatric Surgery versus Intensive Medical Therapy for Diabetes - 3-Year** Outcomes. (**Stampede**) N Engl J Med. 2014 Mar 31.

Schauer DP, Arterburn DE, Livingston EH, et al. Impact of **Bariatric Surgery** on **Life Expectancy** in Severely Obese Patients With Diabetes: A Decision Analysis. Ann Surg. 2015 May;261(5):914-919.

Schauer PR, Bhatt DL, Kirwan JP, et al. **Bariatric Surgery versus Intensive Medical Therapy for Diabetes -5-Year Outcomes**. . (**Stampede**) N Engl J Med. 2017 Feb 16;376(7):641-651.

Scheelbeek PFD, Cornelsen L, Marteau TM, et al. Potential impact on prevalence of obesity in the UK of a **20% price increase in high sugar snacks**: modelling study. BMJ. 2019 Sep 4;366:l4786

Scheen AJ, Finet al. **RIO-Diabetes Study Group**. Efficacy and tolerability of rimonabant in overweight or obese patients with type 2 diabetes: a randomised controlled study. Lancet. 2006 Nov 11;368(9548):1660-72.

Scheinker D, Valencia A, Rodriguez F. Identification of Factors Associated With Variation in **US County-Level Obesity Prevalence Rates** Using Epidemiologic vs Machine Learning Models. JAMA Netw Open. 2019 Apr 5;2(4):e192884.

Scherrer JF, Salas J, Lustman PJ, et al. The Role of Obesity in the Association Between Posttraumatic Stress Disorder and Incident Diabetes. JAMA Psychiatry. 2018 Aug 8.

Schiavon CA, et al. Effects of **Bariatric Surgery in Obese Patients With Hypertension**: The **GATEWAY** Randomized Trial (Gastric Bypass to Treat Obese Patients With Steady Hypertension). Circulation. 2018 Mar 13;137(11):1132-1142.

Schievink WI, Goseland A, Cunneen S. Bariatric surgery as a possible risk factor for spontaneous intracranial hypotension. Neurology. 2014 Nov 11;83(20):1819-22.

Schijns W, Homan J, van der Meer L, et al. **Efficacy of oral compared with intramuscular vitamin B-12 supplementation after Roux-en-Y gastric bypass**: a randomized controlled trial. Am J Clin Nutr. 2018 Jul 1;108(1):6-12.

Schillinger D, Jacobson MF. Science and Public Health on Trial: **Warning Notices** on **Advertisements for Sugary Drinks**. JAMA. 2016 Oct 18;316(15):1545-1546.

Schlam TR, Wilson NL, Shoda Y, et al. **Preschoolers' Delay of Gratification** Predicts their Body Mass 30 Years Later. J Pediatr. 2012 Aug 18.

Schmidt M, Johannesdottir SA, et al. **Obesity in young men**, and individual and combined risks of type 2 diabetes, cardiovascular morbidity and death before 55 years of age: a Danish 33-year follow-up study. BMJ Open. 2013 Apr 29;3(4).

Schnohr P, O'Keefe JH, Marott JL, et al. **Dose of Jogging** and Long-Term Mortality: The Copenhagen City Heart Study. J Am Coll Cardiol. 2015;65(5):411-419.

Schrempft S, van Jaarsveld CHM, Fisher A, et al. **Variation in the Heritability of Child Body Mass Index by Obesogenic Home Environment.** JAMA Pediatr. 2018 Oct 1.

Schroeder R, Garrison JM Jr, Johnson MS. Treatment of adult obesity with **bariatric surgery**. Am Fam Physician. 2011 Oct 1;84(7):805-14.

Schroeder R, Harrison TD. McGraw SL. **Treatment of Adult Obesity with Bariatric Surgery**. Am Fam Physician. 2016;93(1):31-37.

Schulman AR, Tavakkoli A, Thompson CC, et al. **Making the Connection**. (bariatric surgery) N Engl J Med. 2017 Feb 2;376(5):476-482

Schulman E, Bartlett SJ, et al. Overweight and Obesity **Reduce the Likelihood of Achieving Sustained Remission in Early Rheumatoid Arthritis**: Results from the Canadian Early Arthritis Cohort Study. Arthritis Care Res (Hoboken). 2017 Nov 30.

Schuster MA, Elliott MN, Bogart LM, et al. Changes in **Obesity Between Fifth and Tenth Grades**: A Longitudinal Study in Three Metropolitan Areas. Pediatrics. 2014 Nov 10.

Schulte EM, Avena NM, Gearhardt AN. **Which foods may be addictive**? The roles of processing, fat content, and glycemic load. PLoS One. 2015 Feb 18;10(2):e0117959.

Schwartz AE, Leardo M, Aneja S, et al. Effect of a **School-Based Water Intervention** on Child Body Mass Index and Obesity. JAMA Pediatr. 2016 Jan 19:1-8.

Schwartz BS, Bailey-Davis L, Bandeen-Roche K, et al. **Attention Deficit Disorder, Stimulant Use**, and Childhood Body Mass Index Trajectory. Pediatrics. 2014 Mar 17.

Schwartz MB, Schneider GE, Choi Y-Y, et al. Association of a **community campaign for better beverage choices with beverage purchases from supermarkets** [online Mar 6, 2017]. JAMA Intern Med. doi:10.1001/jamainternmed.2016 .9650

Schwartz MB, Schneider GE, Choi YY, et al. Association of a **community campaign for better beverage choices with beverage purchases from supermarkets** [online Mar 6, 2017]. *JAMA Intern Med* 2017

Schwarzfischer P, Gruszfeld D, Stolarczyk A, et al. **Physical Activity and Sedentary Behavior** From 6 to 11 Years. Pediatrics. 2018 Dec 3.

Schwarzfuchs D, Golan R, Shai I. **Four-year follow-up** after two-year **dietary interventions**. N Engl J Med. 2012 Oct 4;367(14):1373-4.

Scirica BM, Bohula EA, Dwyer JP, et al. **Lorcaserin and Renal Outcomes in Obese and Overweight Patients** in the CAMELLIA-TIMI 61 Trial. Circulation. 2019 Jan 15;139(3):366-375.

Scott FI, Horton DB, Mamtani R, et al. **Administration of Antibiotics** to Children Before Age 2 Years Increases Risk for Childhood Obesity. Gastroenterology. 2016 Mar 18.

Seema Kumar, Jobayer Hossain, Nicole Nader, et al. Decreased Circulating Levels of **Spexin** in Obese Children. *The Journal of Clinical Endocrinology & Metabolism*, 2016.

Selvin E, Paynter NP, Erlinger TP. The effect of weight loss on **C-reactive protein**: a systematic review.Arch Intern Med. 2007 Jan 8;167(1):31-9.

Semla TP, Ruser C, Good CB, et al. Pharmacotherapy for **Weight Management in the VHA**. J Gen Intern Med. 2017 Apr;32(Suppl 1):70-73.

Shah N, Braverman E. Measuring Adiposity in Patients: The Utility of **Body Mass Index (BMI), Percent Body Fat, and Leptin.** PLoS ONE 7(4): e33308.

Shai I, Schwarzfuchs D, Henkin Y, et al. Dietary Intervention Randomized Controlled Trial (DIRECT) Group. Weight loss with a low-carbohydrate, Mediterranean, or low-fat diet. N Engl J Med. 2008 Jul 17;359(3):229-41. **Mediterranean** and **low-carbohydrate diets** may be effective alternatives to low-fat diets. The more favorable effects on lipids (with the low-carbohydrate diet) and on glycemic control (with the Mediterranean diet) suggest that personal preferences and metabolic considerations might inform individualized tailoring of dietary interventions.

Shai I, Schwarzfuchs D, Henkin Y, et al. Weight loss with a **low-carbohydrate, Mediterranean, or low-fat diet**. N Engl J Med 2008;359:229-41.

Shankar P, Boylan M, Sriram K. **Micronutrient deficiencies** (vitamins) after bariatric surgery. Nutrition. 2010 Nov-Dec;26(11-12):1031-7.

Shapiro JR, Koro T, Doran N, et al. **Text4Die**t: A randomized controlled study using **text messaging** for weight loss behaviors. Prev Med. 2012 Aug 27. pii: S0091-7435(12)00384-2.

Sharifi M, Franz C, Horan CM, et al. Cost-Effectiveness of a **Clinical Childhood Obesity Intervention**. Pediatrics. 2017;140(5):e20162998

Sharma AM. **Inequalities in access to bariatric surgery** in Canada. CMAJ. 2016 Mar 15;188(5):317-8.

Sharma S, Batsis JA, Coutinho T, et al. Normal-weight central obesity and **mortality** risk in older adults with coronary artery disease. *Mayo Clin Proc* 2016.

Shaw RJ, Bosworth HB, Silva SS, et al. **Mobile health messages** help sustain recent weight loss. Am J Med. 2013 Nov;126(11):1002-9.

Shaw Tronieri J, Wadden TA, Berkowitz RI, et al. A Randomized Trial of **Lorcaserin and Lifestyle Counseling** for Maintaining Weight Loss Achieved with a Low-Calorie Diet**.** Obesity (Silver Spring). 2018 Feb;26(2):299-309.

Sherwood NE, Crain AL, Martinson BC, et al. **Enhancing long-term weight loss maintenance: 2 year results from the Keep It Off** randomized controlled trial. Prev Med. 2012 Dec 28. pii: S0091-7435(12)00631-7.

Shihab HM, Meoni LA, Chu AY, et al. Body mass index and risk of incident **hypertension** over the life course: The Johns Hopkins Precursors Study. Circulation 2012.

Shin DW, Yun JM, Shin JH, et al. Enhancing physical activity and **reducing obesity through smartcare and financial incentives**: A pilot randomized trial. Obesity (Silver Spring). 2017 Feb;25(2):302-310.

Showell NN, Fawole O, Segal J, et al. A Systematic Review of **Home-Based Childhood Obesity Prevention** Studies. Pediatrics. 2013 Jun 10.

Shubeck S, Dimick JB, Telem DA. **Long-term Outcomes Following Bariatric Surgery**. JAMA. 2018 Jan 16;319(3):302-303.

Shuval K, Nguyen BT, Yaroch AL, et al. **Accelerometer** determined **sedentary behavior** and dietary quality among US adults. Prev Med. 2015 Jul 2;78:38-43.

Siavash Dastjerdi M, et al. An open-label pilot study of the combination therapy of **metformin and fluoxetine** for weight reduction. Int J Obes (Lond). 2006 Sep 12; [Epub ahead of print]

Siddiqui SA, et al. Obesity and survival after radical **prostatectomy**: A 10-year prospective cohort study. Cancer. 2006 Aug 1;107(3):521-9. (InfoPOEMs: In spite of worse baseline disease status, obesity does not affect survival or other outcomes in men undergoing radical prostatectomy for prostate cancer. (LOE = 1b))

Sievenpiper JL, de Souza RJ, Mirrahimi A, et al. Effect of **Fructose** on Body Weight in Controlled Feeding Trials: A Systematic Review and Meta-analysis. Ann Intern Med. 2012 Feb 21;156(4):291-304.

Sievert K, Hussain SM, Page MJ, et al. **Effect of breakfast** on weight and energy intake: systematic review and meta-analysis of randomised controlled trials. BMJ. 2019 Jan 30; 364:l42.

Sigal RJ, Alberga AS, Goldfield GS, et al. Effects of **Aerobic Training, Resistance Training, or Both** on Percentage Body Fat and Cardiometabolic Risk Markers in Obese Adolescents: The Healthy Eating Aerobic and Resistance Training in Youth Randomized Clinical Trial. JAMA Pediatr. 2014 Sep 22.

SIGN: Scottish Intercollegiate Guidelines Network (**SIGN**). **Management of obesity**. A national clinical guideline. Edinburgh (Scotland): Scottish Intercollegiate Guidelines Network (SIGN); 2010 Feb.

Silver LD, Ng SW, et al. Changes in prices, sales, consumer spending, and beverage consumption one year after a **tax on sugar-sweetened beverages** in Berkeley, California, US: A before-and-after study. PLoS Med. 2017 Apr 18;14(4):e1002283.

Silveira JA, Taddei JA, Guerra PH, et al. The effect of **participation in school-based nutrition education** interventions on body mass index: A meta-analysis of randomized controlled community trials. Prev Med. 2013 Mar;56(3-4):237-43.

Silveira PP, Gaudreau H, Atkinson L, et al. **Genetic Differential Susceptibility to Socioeconomic** Status and Childhood Obesogenic Behavior: Why Targeted Prevention May Be the Best Societal Investment. JAMA Pediatr. 2016 Feb 1.

Silverwood RJ, Pierce M, Thomas C, et al. Association between Younger Age When First Overweight and Increased **Risk for CKD**. J Am Soc Nephrol. 2013 Apr 4.

Sim LA, Lebow J, Billings M. **Eating Disorders** in Adolescents With a History of Obesity. Pediatrics. 2013 Sep 9.

Sim LA, Lebow J, Wang Z, Koball A, Murad MH. **Brief Primary Care Obesity Interventions**: A Meta-analysis. Pediatrics. 2016 Sep 12

Simonson DC, Halperin F, Foster K, et al. Clinical and Patient-Centered Outcomes in Obese Type 2 Diabetes Patients 3 Years After Randomization to **Roux-en-Y Gastric Bypass Surgery Versus Intensive Lifestyle Management**: The **SLIMM-T2D** Study. Diabetes Care. 2018 Feb 6.

Simpson SA, Shaw C, McNamara R. What is the most effective way to **maintain weight loss** in adults? BMJ. 2011 Dec 28;343:d8042.

Singapore Health Sciences Authority July/15: **Skinny 22**" contains Undeclared phenolphthalein.

Singh GM, Micha R, Khatibzadeh S, et al; Global Burden of Diseases Nutrition and Chronic Diseases Expert Group (NutriCoDE). Estimated **Global**, Regional, and National Disease Burdens Related to **Sugar-Sweetened Beverage Consumption** in 2010. Circulation. 2015 Jun 29.

Singh GM, Micha R, Khatibzadeh et al; Global Burden of Diseases Nutrition and Chronic Diseases Expert Group (NutriCoDE). Global, Regional, and National Consumption of **Sugar-Sweetened Beverages, Fruit Juices, and Milk**: A Systematic Assessment of Beverage Intake in 187 Countries. PLoS One. 2015 Aug 5;10(8):e0124845.

Singh-Manoux A, Czernichow S, Elbaz A, et al. Obesity phenotypes in midlife and **cognition** in early old age: The Whitehall II cohort study. Neurology. 2012 Aug 21;79(8):755-62.

Sinha R, et al. Prevalence of **impaired glucose tolerance** among children and adolescents with marked obesity. N Engl J Med. 2002 Mar 14;346(11):802-10. Erratum in: N Engl J Med 2002 May 30;346(22):1756.

Sjostrom L, et al.; Swedish Obese Subjects (**SOS**) Study Scientific Group. Lifestyle, diabetes, and cardiovascular risk factors 10 years after bariatric surgery. N Engl J Med. 2004 Dec 23;351(26):2683-93. After two years, the weight had increased by 0.1 percent in the control group and had decreased by 23.4 percent in the surgery group (P<0.001). After 10 years, the weight had increased by 1.6 percent and decreased by 16.1 percent, respectively (P<0.001). Energy intake was lower and the proportion of physically active subjects higher in the surgery group than in the control group throughout the observation period. Two- and 10-year rates of recovery from diabetes, hypertriglyceridemia, low levels of high-density lipoprotein cholesterol, hypertension, and hyperuricemia were more favorable in the surgery group than in the control group, whereas recovery from hypercholesterolemia did not differ between the groups. The surgery group had lower 2- and 10-year incidence rates of diabetes, hypertriglyceridemia, and hyperuricemia than the control group; differences between the groups in the incidence of hypercholesterolemia and hypertension were undetectable.

Sjöström L et al. Effects of bariatric surgery on **cancer incidence** in obese patients in Sweden (Swedish Obese Subjects Study-**SOS**): A prospective, controlled intervention trial. Lancet Oncol 2009 Jun 24; [e-pub ahead of print].

Sjostrom L, Narbro K, Sjostrom CD, et al. Eff ects of bariatric surgery on mortality in Swedish obese subjects (Swedish Obese Subjects Study-**SOS**). N Engl J Med 2007; 357: 741–52.

Sjostrom L, Peltonen M, Jacobson P, et al. Bariatric surgery and long-term cardiovascular events. (**SOS**) JAMA. 2012;307(1):56-65. During a median 15 years' follow-up, significantly fewer surgery patients than controls experienced a first cardiovascular event (199 vs. 234 patients; adjusted hazard ratio, 0.67). Cardiovascular mortality was similarly reduced with bariatric surgery (HR, 0.47).

Sjöholm K, Anveden A, Peltonen M, et al. Evaluation of Current Eligibility Criteria for Bariatric Surgery: **Diabetes prevention** and risk factor changes in the **Swedish Obese Subjects (SOS)**study. Diabetes Care. 2013 Jan 28.

Sjostrom L, Peltonen M, Jacobson P, et al. Association of **bariatric surgery with long-term remission of type 2 diabetes** and with microvascular and macrovascular complications. JAMA. doi:10.1001/jama.2014.5988.

Skilton MR, Marks GB, Ayer JG, et al. **Weight Gain in Infancy and Vascular Risk** Factors in Later Childhood. Pediatrics. 2013 May 27.

Skinner AC, Steiner MJ, Perrin EM. **Self-Reported Energy Intake** by Age in Overweight and Healthy-Weight Children in NHANES, 2001-2008. Pediatrics. 2012 Sep 10.

Skinner AC, Perrin EM, Skelton JA. **Prevalence of obesity and severe obesity in US children**, 1999-2014. Obesity (Silver Spring). 2016 May;24(5):1116-23

Skinner AC, Skelton JA. Prevalence and **Trends in Obesity and Severe Obesity Among Children in the United States, 1999-2012**. JAMA Pediatr. 2014 Apr 7.

Skinner AC, Perrin EM, Moss LA, et al. **Cardiometabolic Risks and Severity of Obesity** in Children and Young Adults. N Engl J Med. 2015 Oct;373(14):1307-17.

Skinner AC, Ravanbakht SN, Skelton JA, et al. **Prevalence of Obesity and Severe Obesity in US Children**, 1999-2016. Pediatrics. 2018 Feb 26.

Smallwood SR, Morris MM, Fallows SJ, Buckley JP. Physiologic Responses and **Energy Expenditure of Kinect** Active Video Game Play in Schoolchildren. Arch Pediatr Adolesc Med. 2012 Sep 24:1-5.

Smetana GW, Jones DB, Wee CC. **Should This Patient Have Weight Loss Surgery**?: Grand Rounds Discussion From Beth Israel Deaconess Medical Center. Ann Intern Med. 2017 Jun 6;166(11):808-817.

Smith GD, Sterne JA, Abigail F, et al. The association between **BMI and mortality** using offspring BMI as an indicator of own BMI: large intergenerational mortality study. BMJ 2009;339:b5043, doi: 10.1136/bmj.b5043 (22 Dec 2009)

Smith JJ, Morgan PJ, Plotnikoff RC, et al. **Smart-Phone Obesity Prevention Trial** for Adolescent Boys in Low-Income Communities: The ATLAS RCT. Pediatrics. 2014 Sep;134(3):e723-31.

Smith SR, Weissman NJ, Anderson CM, et al. Multicenter, placebo-controlled trial of **lorcaserin** for weight management (**Bloom**). N Engl J Med 2010;363:245-56.

Sofi F, Cesari F, Abbate R, Gensini GF, Casini A. Ad herence to **Mediterranean diet** and health status: meta-analysis. BMJ 2008;337:a1344.

Solbrig L, Whalley B, Kavanagh DJ, et al. **Functional imagery training versus motivational interviewing for weight loss**: a randomised controlled trial of brief individual interventions for overweight and obesity. Int J Obes (Lond). 2018 Sep 5.

Soltani-Arabshahi Razieh, Wong Bob, Feng Bing-Jian, et al. Obesity in Early Adulthood as a Risk Factor for **Psoriatic Arthritis**. *Arch Dermatol.* 2010;146(7):721-726.

Song M, Hu FB, Wu K, et al. **Trajectory of body shape** in early and middle life and all cause and cause specific mortality: results from two prospective US cohort studies. BMJ 2016;353:i2195.

Song Y, Ma J, Wang HJ, et al. **Trends of Age at Menarche** and Association with Body Mass Index in Chinese School-Aged Girls, 1985-2010. J Pediatr. 2014 Sep 17.

Sonneville KR, Horton NJ, et al. Longitudinal Associations Between **Binge Eating** and Overeating and Adverse Outcomes Among Adolescents and Young Adults: Does Loss of Control Matter? Arch Pediatr Adolesc Med. 2012 Dec 10:1-7.

Søvik TT, Aasheim ET, Taha O, Engstro¨m M, et al. Weight loss, cardiovascular risk factors, and quality of life **after gastric bypass and duodenal switch**. A randomized trial. Ann Intern Med. 2011;155: 281-91.
Snook KR, Hansen AR, Duke CH, et al. Change in **Percentages of Adults With Overweight or Obesity Trying to Lose Weight**, 1988-2014. JAMA. 2017 Mar 7;317(9):971-973
Spadola CE, Wagner EF, Varga LM, et al. A Qualitative Examination of **Increased Alcohol Use after Bariatric Surgery** among Racially/Ethnically Diverse Young Adults. Obes Surg. 2017 Nov 19.
Spaniolas K, Yang J, Crowley S, et al. Association of **Long-term Anastomotic Ulceration After Roux-en-Y Gastric Bypass** With Tobacco Smoking. JAMA Surg. 2018 Jun 20.
Sparks JA, Chang SC, Nguyen US, et al. **Weight change in the early rheumatoid arthritis** period and risk for subsequent mortality among women with RA and matched comparators. Arthritis Rheumatol. 2017 Nov 30.
Spring B, Schneider K, McFadden HG, et al. Multiple behavior changes in diet and activity: A randomized controlled trial using **mobile technology**. Arch Intern Med 2012; 172:789-796.
Spring B, Duncan JM, Janke EA, et al. Integrating **technology into standard weight loss treatment**: a randomized controlled trial [online December 10, 2012]. Arch Intern Med. doi:10.1001/jamainternmed.2013.1221.
Spyropoulos C, Kehagias I, Panagiotopoulos S, Mead N, Kalfarentzos F. **Revisional bariatric surgery**: 13-year experience from a tertiary institution. Arch Surg. 2010 Feb;145(2):173-7.
Sridhar SB, Darbinian J, Ehrlich SF, et al. **Maternal gestational weight gain** and offspring risk for childhood overweight or obesity. Am J Obstet Gynecol. 2014 Apr 12.
Stacy SL, Buchanich JM, Ma ZQ, et al. **Maternal Obesity, Birth Size, and Risk of Childhood Cancer** Development. Am J Epidemiol. 2019 May 20
Stampanoni Bassi M, Iezzi E, et al. **Obesity worsens central inflammation and disability in multiple sclerosis**. Mult Scler. 2019 Jun 4:1352458519853473.
Stark LJ, Spear Filigno S, Bolling C, et al. **Clinic and Home-Based Behavioral Intervention for Obesity in Preschoolers**: A Randomized Trial. J Pediatr. 2017 Nov 14.
Steffen KJ, King WC, White GE, et al. Changes in **sexual functioning in women and men in the 5 years after bariatric surgery** [online Feb 20, 2019]. JAMA Surg.
Stegenga H, Haines A, Jones K, Wilding J; Guideline Development Group. Identification, **assessment, and management of overweight and obesity**: summary of updated **NICE** guidance. BMJ. 2014 Nov 27;349:g6608.
Steinberg DM, Tate DF, Bennett GG, et al. **Daily self-weighing** and adverse psychological outcomes: a randomized controlled trial. Am J Prev Med. 2014 Jan;46(1):24-9.
Stephansson O, Johansson K, Söderling J, et al. **Delivery outcomes in term births after bariatric surgery**: Population-based matched cohort study. PLoS Med. 2018 Sep 26;15(9):e1002656.
Stern JS, Peerson J, Mishra AT, et al. Efficacy and tolerability of a novel herbal formulation (**Sphaeranthus indicus & Garcinia mangostana**) for weight management. Obesity (Silver Spring). 2013 May;21(5):921-7.
Stessman J, Jacobs JM, Ein-Mor E, Bursztyn M. Normal body mass index **rather than obesity** predicts greater mortality in **elderly people**: the Jerusalem longitudinal study. J Am Geriatr Soc. 2009 Dec;57(12):2232-8. Epub 2009 Nov 17.
Stewart ST, Cutler DM, Rosen AB. Forecasting the effects of obesity and smoking on U.S. **life expectancy**. N Engl J Med. 2009 Dec 3;361(23):2252-60. PubMed
Stevens VJ, Brantley PJ, et al. Weight Loss Maintenance (WLM) Collaborative Research Group. Comparison of strategies for sustaining weight loss: the weight loss maintenance randomized controlled trial. JAMA. 2008 Mar 12;299(10):1139-48. The majority of individuals who successfully completed an initial behavioral weight loss program maintained a weight below their initial level. Monthly brief **personal contact** provided modest benefit in sustaining weight loss, whereas an interactive technology-based intervention provided early but transient benefit. N=1032, 30months
Steinsbekk S, Belsky D, Guzey IC, et al. **Polygenic Risk**, **Appetite Traits**, and Weight Gain in Middle Childhood: A Longitudinal Study. JAMA Pediatr. 2016 Feb 1;170(2):e154472.
Stenberg E, Szabo E, Ågren G, et al. Closure of **mesenteric defects in laparoscopic gastric bypass**: a multicentre, randomised, parallel, open-label trial. Lancet 2016; online Feb 16.
Still CD, Wood GC, Benotti P, et al. **Preoperative prediction** of type 2 diabetes remission **after Roux-en-Y** gastric bypass surgery: a retrospective cohort study. Lancet Diabetes Endocrinol. 2014 Jan;2(1):38-45.
Stokes A, Collins JM, Grant BF, et al. **Obesity Progression Between Young Adulthood and Midlife and Incident Diabetes**: A Retrospective Cohort Study of U.S. Adults. Diabetes Care. 2018 May;41(5):1025-1031.
Stotland NE. **Obesity and pregnancy**. BMJ. 2008 Dec 15;337:a2450. doi: 10.1136/bmj.a2450.
Stothard KJ, Tennant PW, Bell R, Rankin J. Maternal overweight and obesity and the risk of **congenital anomalies**: a systematic review and meta-analysis. JAMA. 2009 Feb 11;301(6):636-50. Maternal obesity is associated with an increased risk of a range of structural anomalies, although the absolute increase is likely to be small.
Straker LM, Abbott RA, Smith AJ. To **remove or to replace traditional electronic games**? A crossover randomised controlled trial on the impact of removing or replacing home access to electronic games on physical activity and sedentary behaviour in children aged 10-12 years. BMJ Open. 2013 Jul 1;3(6).
Strømmen M, Helland A, Kulseng B, et al. Bioavailability of **Methadone After Sleeve Gastrectomy**: A Planned Case Observation. Clin Ther. 2016 May 12.
Stuart A and Källen K. **Risk of abdominal surgery in pregnancy among women who have undergone bariatric surgery**. Obstet Gynecol 2017 Apr 4.
Sturgiss E, van Weel C. **The 5 As framework for obesity management**: Do we need a more intricate model? Can Fam Physician. 2017 Jul;63(7):506-508.
Sturgiss E, Jay M, Campbell-Scherer D, et al. **Challenging assumptions in obesity research**. BMJ. 2017 Nov 22;359:j5303.
Sturm R, An R, Segal D, Patel D. A **cash-back rebate program** for healthy food purchases in South Africa. Results from scanner data. Am J Prev Med 2013.
Styne DM, Arslanian SA, Connor EL, et al. **Pediatric Obesity-Assessment, Treatment, and Prevention**: An **Endocrine Society** Clinical Practice Guideline. J Clin Endocrinol Metab. 2017 Mar 1;102(3):709-757.
Subak LL, King WC, Belle SH, et al. **Urinary Incontinence** Before and After Bariatric Surgery. JAMA Intern Med. 2015 Jun 22.
Suglia SF, Chambers EC, Rosario A, Duarte CS. **Asthma and obesity in three-year-old urban children**: role of sex and home environment. J Pediatr. 2011 Jul;159(1):14-20.e1.
Suglia SF, Solnick S, Hemenway D. **Soft Drinks Consumption** Is Associated with Behavior Problems in 5-Year-Olds. J Pediatr. 2013 Aug 19.
Sui X, LaMonte MJ, Laditka JN, et al. Cardiorespiratory **fitness** and adiposity as mortality predictors in older adults. JAMA. 2007 Dec 5;298(21):2507-16. In this study population, fitness was a significant mortality predictor in older adults, independent of overall or abdominal adiposity.
Clinicians should consider the importance of preserving functional capacity by recommending regular physical activity for older individuals, normal-weight and overweight alike.
Sullivan S, Stein R, Jonnalagadda S, et al. **Aspiration therapy** leads to weight loss in obese subjects: a pilot study. Gastroenterology. 2013 Dec;145(6):1245-1252.e5
Sumithran P, Prendergast LA, Delbridge E, et al. Long-term persistence of **hormonal adaptations** to weight loss. N Engl J Med. 2011 Oct 27;365(17):1597-604.
Sun Qi, Townsend Mary K, Okereke Olivia I, et al. Adiposity and weight change in mid-life in relation to healthy **survival after age 70** in women: prospective cohort study**.** BMJ 2009;339:b3796, doi: 10.1136/bmj.b3796 Tabák AG, Svetkey LP,
Sun Y, Liu B, Snetselaar LG, et al. Association of Normal-Weight Central Obesity With All-Cause and Cause-Specific **Mortality Among Postmenopausal Women**. JAMA Netw Open. 2019 Jul 3;2(7):e197337.
Sun YQ, Burgess S, Staley JR, et al. **Body mass index and all cause mortality** in HUNT and UK Biobank studies: linear and non-linear mendelian randomisation analyses. BMJ. 2019 Mar 26;364:l1042.
Sundström J, Bruze G, Ottosson J, et al. Weight Loss and **Heart Failure**: A Nationwide Study of **Gastric Bypass Surgery** Versus Intensive Lifestyle Treatment. Circulation. 2017 Mar 3.
Sung H, Siegel RL, Torre LA, et al. Global **patterns in excess body weight and the associated cancer burden**. CA Cancer J Clin. 2018 Dec 12.
Sung H, Siegel RL, Rosenberg PS, et al. **Emerging cancer trends among young adults in the USA**: analysis of a population-based cancer registry. Lancet Public Health. 2019 Feb 1.
Surén P, Gunnes N, Roth C, et al. **Parental Obesity and Risk of Autism** Spectrum Disorder. Pediatrics. 2014 Apr 7.

Sutin AR, Terracciano A. **Perceived weight discrimination** and obesity. PloS One. 2013 Jul 24;8(7):e70048.
Svensson PA, Anveden Å, Romeo S, et al. **Alcohol consumption and alcohol problems** after bariatric surgery in the Swedish obese subjects study. Obesity (Silver Spring). 2013 Dec;21(12):2444-51.
Swinburn BA, Sacks G, Hall KD, et al. The **global obesity pandemic**: shaped by global drivers and local environments. Lancet. 2011 Aug 27;378(9793):804-14.
Swinburn B, Kraak V, Rutter H, et al. Strengthening of accountability systems to create **healthy food environments** and reduce global obesity. Lancet. 2015 Feb 18.
Tate DF, et al. A randomized trial comparing human e-mail counseling, computer-automated tailored counseling, and no counseling in an Internet weight loss program. Arch Intern Med. 2006 Aug 14-28;166(15):1620-5.
Taber DR, Chriqui JF, Perna FM, et al. Weight status among adolescents in States that **govern competitive food nutrition content**. Pediatrics. 2012 Sep;130(3):437-44.
Taber DR, Chriqui JF, Powell L, et al. Association Between State **Laws Governing School Meal Nutrition Content** and Student Weight Status: Implications for New USDA School Meal Standards. JAMA Pediatr. 2013 Apr 8:1-8.
Tabet M, Flick LH, Tuuli MG, et al. **Prepregnancy body mass index** in a first uncomplicated pregnancy and outcomes of a second pregnancy. Am J Obstet Gynecol. 2015 Jun 20.
Tal A, Zuckerman S, Wansink B. Watch What You Eat: **Action-Related Television Content** Increases Food Intake. JAMA Intern Med. 2014 Sep 1.
Taubes G. The **science of obesity**: what do we really know about what makes us fat? An essay by Gary Taubes. BMJ. 2013 Apr 15;346:f1050.
Taubes G. What if **sugar** is worse than just empty calories? An essay by Gary Taubes. BMJ. 2018 Jan 3;360:j5808.
Taveras EM, Rifas-Shiman SL, Oken E, Gunderson EP, Gillman MW. **Short sleep duration** in infancy and risk of childhood overweight. Arch Pediatr Adolesc Med. 2008 Apr;162(4):305-11. Daily sleep duration of less than 12 hours during infancy appears to be a risk factor for overweight and adiposity in preschool-aged children.
Taveras EM, Gillman MW, Peña MM, et al. Chronic **Sleep Curtailment and Adiposity**. Pediatrics. 2014 May 19.
Taveras EM, Marshall R, Kleinman KP, et al. Comparative Effectiveness of **Childhood Obesity Interventions** in **Pediatric Primary Care**: A Cluster-Randomized Clinical Trial. JAMA Pediatr. 2015 Apr 20.
Taveras EM, Marshall R, Sharifi M, et al. Comparative Effectiveness of Clinical-**Community Childhood Obesity Interventions**: A Randomized Clinical Trial. JAMA Pediatr. 2017 Aug 7;171(8):e171325.
Taylor BJ, Gray AR, Galland BC, et al. **Targeting Sleep, Food, and Activity in Infants** for Obesity Prevention: An RCT. Pediatrics. 2017 Feb 27.
Taylor JA, Simpson EA. Categorizing **weight loss in breastfed infants**: a good first step. Pediatrics. 2015 Jan;135(1):e174-5.
Taylor PN, Richmond R, Davies N, et al. Paradoxical relationship between **body mass index and thyroid hormone levels**; a study using Mendelian Randomization. J Clin Endocrinol Metab. 2015 Nov 23:jc20153505.
Taylor RW, Williams SM, Dawson AM, et al. What factors influence uptake into **family-based obesity treatment** after weight screening? J Pediatr. 2013 Dec;163(6):1657-1662.e1.
Taylor RW, Cox A, Knight L, et al. A **Tailored Family-Based Obesity Intervention**: A Randomized Trial. Pediatrics. 2015 Jul 20.
Taylor RW, Williams SM, Fangupo LJ, et al. Effect of a **baby-led approach** to **complementary feeding on infant growth and overweight**: a randomized clinical trial [published online July 10, 2017].JAMA Pediatr. doi:10.1001/jamapediatrics.2017.1284
Tchoukhine E, Takala P, et al. Orlistat in **clozapine- or olanzapine**-treated patients with overweight or obesity: a 16-week open-label extension phase and both phases of a randomized controlled trial. J Clin Psychiatry. 2010 Aug 24.
Te Morenga L, Mallard S and Mann J. **Dietary sugars** and body weight: systematic review and meta-analyses of randomized controlled trials and cohort studies. BMJ 2012.
ter Bogt Nancy C. W.; Bemelmans Wanda J. E.; Beltman FW.; et al. Preventing Weight Gain by **Lifestyle Intervention in a General Practice Setting**: Three-Year Results of a Randomized Controlled Trial. Arch Intern Med. 2011;171(4):306-313.
Terada T, Johnson JA, Norris C, et al. Severe obesity is associated with increased risk of early complications and extended length of stay following **coronary artery bypass grafting surgery**. *J Am Heart Assoc*. 2016. 2016 Jun 1;5(6).
Terry-McElrath YM, Turner L, Sandoval A, Johnston LD, Chaloupka FJ. **Commercialism** in US elementary and secondary **school nutrition environments**: trends from 2007 to 2012 online January 13, 2014. *JAMA Pediatr*.
Terry-McElrath YM, O'Malley PM, Johnston LD. Potential Impact of **National School Nutritional Environment Policies**: Cross-sectional Associations With US Secondary Student Overweight/Obesity, 2008-2012. JAMA Pediatr. 2014 Nov 17.
Tester JM, Phan TT, Tucker JM, et al. Characteristics of **Children 2 to 5 Years of Age With Severe Obesity**. Pediatrics. 2018 Feb 27.
Thacker P. **Coca-Cola's secret influence** on medical and science journalists. BMJ. 2017 Apr 5;357:j1638.
The Global BMI Mortality Collaboration. Body-mass index and **all-cause mortality**: individual-participant-data meta-analysis of 239 prospective studies in four continents. Lancet 2016 online July 13.
The Natalie S.; Suchindran Chirayath; North Kari E.; et al. Association of **Adolescent Obesity With Risk of Severe Obesity in Adulthood**. JAMA. 2010;304(18):2042-2047
Thereaux J, Lesuffleur T, Czernichow S, et al. Association between **bariatric surgery and rates of continuation, discontinuation, or initiation of antidiabetes treatment** 6 years later [online Feb 14, 2018].JAMA Surg. doi:10.1001 /jamasurg.2017.6163
Thomas JG, Bond DS, Raynor HA, et al. **Comparison of Smartphone-Based Behavioral Obesity Treatment** With Gold Standard Group Treatment and Control: A Randomized Trial. Obesity (Silver Spring). 2019 Apr;27(4):572-580.
Thomas JG, Leahey TM, Wing RR. An **Automated Internet Behavioral Weight Loss Program** by Physician Referral: A Randomized, Controlled Trial. Diabetes Care. 2014 Nov 17.
Thomas JG, Raynor HA, Bond DS, et al. Weight loss in **Weight Watchers Online with and without an activity tracking device** compared to control: A randomized trial. Obesity (Silver Spring). 2017 Jun;25(6):1014-1021.
Thompson DR, Obarzanek E, Franko DL, et al. **Childhood** overweight and cardiovascular disease risk factors: The National Heart, Lung, and Blood Institute Growth and Health Study. J Pediatr 2007; 150: 18-25.
Thompson AE. **Childhood Obesity**. JAMA. 2015 Aug 25;314(8):850.
Thomsen M, Nordestgaard BG. **Myocardial Infarction and Ischemic Heart Disease** in Overweight and Obesity With and Without Metabolic Syndrome. JAMA Intern Med. 2013 Nov 11.
Thomson CA, Garcia DO, Wertheim BC, et al. **Body shape, adiposity index, and mortality** in postmenopausal women: Findings from the **Women`s Health Initiative**. Obesity (Silver Spring). 2016 May;24(5):1061-9.
Thorn JE, Delellis N, Chandler JP, Boyd K. Parent and Child Self-Reports of **Dietary Behaviors, Physical Activity, and Screen Time**. J Pediatr. 2012 Oct 9.
Thorndike AN, Gelsomin ED, McCurley JL, Levy DE. **Calories Purchased by Hospital Employees** After Implementation of a Cafeteria Traffic Light-Labeling and Choice Architecture Program. JAMA Netw Open. 2019 Jul 3;2(7):e196789
Thurston RC, Ewing LJ, Low CA, et al. Behavioral weight loss for the **management of menopausal hot flashes**: a pilot study. Menopause. 2014 Jun 23.
Tiberio SS, Kerr DC, Capaldi DM, et al. Parental Monitoring of **Children's Media Consumption**: The Long-term Influences on Body Mass Index in Children. JAMA Pediatr. 2014 Mar 17.
Tindle HA et al. Risk of **suicide after long-term follow-up from bariatric surgery**. Am J Med 2010 Nov; 123:1036.
Ting R, Dugré N, Allan GM, et al**. Ketogenic diet for weight loss**. Can Fam Physician. 2018 Dec;64(12):906.
Tirosh A et al. Adolescent **BMI trajectory and risk of diabetes versus coronary disease**. N Engl J Med 2011 Apr 7; 364:1315.
Tobias DK, Pan A, Jackson CL, et al. Body-mass index and **mortality** among adults with incident **type 2 diabetes**. N Engl J Med. 2014 Jan 16
Tobias DK, Chen M, Manson JE, et al. Effect of **low-fat diet interventions versus other diet interventions** on long-term weight change in adults: a systematic review and meta-analysis. Lancet Diabetes Endocrinol. 2015 Oct 29.
Toews I, Lohner S, Küllenberg de Gaudry D, et al. Association between **intake of non-sugar sweeteners and health outcomes**: systematic review and meta-analyses of randomised and non-randomised controlled trials and observational studies. BMJ. 2019 Jan 2;364:k4718.
Tolete P, Knupp K, Karlovich M, et al. **Lorcaserin therapy** for severe epilepsy of childhood onset: A case series. Neurology. 2018 Oct 30;91(18):837-839

Topol E, Bousser MG, Fox KA, et al. **Rimonabant** for prevention of cardiovascular events (**CRESCENDO**): a randomised, multicenter, placebo-controlled trial. Lancet 2010: 376:517-23.

Torlinska B, Nichols L, Mohammed MA, et al. Patients treated for **hyperthyroidism** are at increased risk of becoming obese: findings from a large prospective secondary care cohort. Thyroid. 2019 Aug 2.

Torp-Pedersen C, Caterson I, et al,on the behalf of the **SCOUT** Investigators. Cardiovascular responses to weight management and sibutramine in high-risk subjects: an analysis from the SCOUT trial. Eur Heart J. 2007 Jun 26; [Epub ahead of print]

Six-week treatment with sibutramine appears to be efficacious, tolerable and safe in this high-risk population for whom sibutramine is usually contraindicated.

Torpy JM, Lynm C, Glass RM. JAMA **patient page. Bariatric surgery**. JAMA. 2010 Feb 10;303(6):576.

Torrijos-Niño C, Martínez-Vizcaíno V, Pardo-Guijarro MJ, et al. Physical Fitness, Obesity, and **Academic Achievement** in Schoolchildren. J Pediatr. 2014 Mar 29.

Towbin A, et al. **Beriberi** after gastric bypass surgery in adolescence. J Pediatr. 2004 Aug;145(2):263-7.

Trasande L, Attina TM, Blustein J. Association between **urinary bisphenol A concentration** and obesity prevalence in children and adolescents. JAMA. 2012 Sep 19;308(11):1113-21.

Trasande L, Spanier AJ, Sathyanarayana S, Attina TM, Blustein J. **Urinary phthalates** and increased insulin resistance in adolescents. Pediatrics. 2013;132(3).

Trepanowski JF, Kroeger CM, Barnosky A, et al. Effect of **Alternate-Day Fasting on Weight Loss, Weight Maintenance, and Cardioprotection** Among Metabolically Healthy Obese Adults: A Randomized Clinical Trial. JAMA Intern Med. 2017 May 1.

Trichopoulou A, Bamia C, Trichopoulos D. Anatomy of health effects of **Mediterranean diet**: Greek EPIC prospective cohort study. BMJ. 2009 Jun 23;338:b2337. doi: 10.1136/bmj.b2337. Some food groups in the Mediterranean diet are more important than others in promoting health and longer life, according to this prospective cohort study from the Greek segment of the European Prospective Investigation into Cancer and nutrition (EPIC). The researchers investigated the importance of individual components of the diet and found that eating more vegetables, fruits, nuts, pulses, and olive oil, and drinking moderate amounts of alcohol is linked to people living longer, whereas following a Mediterranean diet high in seafood and cereals and low in dairy products was not an indicator of longevity.

Trikudanathan S, Pedley A, Massaro JM, et al. Association of **Female Reproductive Factors** with Body Composition: The Framingham Heart Study. J Clin Endocrinol Metab. 2012 Oct 23.

Trinh A, Campbell M, Ukoumunne OC, et al. **Physical Activity** and 3-Year BMI Change in Overweight and Obese Children. Pediatrics. 2013 Jan 14.

Tronieri JS, Wadden TA, Walsh OA, et al. Effects of **liraglutide plus phentermine** in adults with obesity following 1year of treatment by liraglutide alone: A randomized placebo-controlled pilot trial. Metabolism. 2019 Mar 20.

Trost SG, Sundal D, Foster GD, et al. Effects of a Pediatric Weight Management Program **With and Without Active Video Games**: A Randomized Trial. JAMA Pediatr. 2014 Mar 3.

Truby H, et al. Randomised controlled trial of **four commercial weight loss programmes** in the UK: initial findings from the BBC "diet trials". BMJ. 2006 Jun 3;332(7553):1309-14. Epub 2006 May 23. Erratum in: BMJ. 2006 Jun 17;332(7555):1418.

Tsai WS, Inge TH, Burd RS. **Bariatric surgery** in adolescents: recent national trends in use and in-hospital outcome. Arch Pediatr Adolesc Med. 2007 Mar;161(3):217-21.

Tsai AG, Wadden TA. **In the Clinic: Obesity**. Ann Intern Med Sep 3, 2013:ITC3-2.

Tsai AG, Bessesen DH. **Obesity- In the Clinic**. Ann Intern Med. **2019** Mar 5;170(5):ITC33-ITC48.

Tsujimoto T, Kajio H. **Abdominal Obesity** Is Associated With an Increased Risk of All-Cause Mortality in Patients With **HFpEF**. J Am Coll Cardiol. 2017 Dec 5;70(22):2739-2749.

Tuah NAA, Amiel C, Qureshi S, Car J, Kaur B, Majeed A. **Transtheoretical model** for dietary and physical exercise modification in weight loss management for overweight and obese adults. Cochrane Database of Systematic Reviews 2011, Issue 10. Art. No.: CD008066. DOI: 10.1002/14651858.CD008066.pub2. TTM SOC and a combination of physical activity, diet and other interventions resulted in minimal weight loss, and there was no conclusive evidence for sustainable weight loss.

Tucker JM, Tucker LA, Lecheminant J, et al. Obesity increases risk of **declining physical activity over time in women**: A prospective cohort study. Obesity (Silver Spring). 2013 Mar 20.

Tun HM, et al; Canadian Healthy Infant Longitudinal Development (**CHILD**) Study Investigators. Roles of **birth mode and infant gut microbiota in intergenerational transmission of overweight and obesity from mother to offspring** [online Feb 19, 2018].JAMA Pediatr. doi:10.1001/jamapediatrics.2017.5535

Tuomilehto HP, Seppa JM, Partinen MM, Peltonen M, Gylling H, Tuomilehto JO, et al. Lifestyle Intervention with Weight Reduction-First Line Treatment in Mild Obstructive **Sleep Apnea**. Am J Respir Crit Care Med. 2008 Nov 14. [Epub ahead of print]

Turchiano M, Sweat V, Fierman A, Convit A. Obesity, Metabolic Syndrome, and Insulin Resistance in **Urban High School Students** of Minority Race/Ethnicity. Arch Pediatr Adolesc Med. 2012 Sep 24:1-7.

Turer CB, Montaño S, Lin H, et al. **Pediatricians' communication** about weight with overweight latino children and their parents. Pediatrics. 2014 Nov;134(5):892-9.

Turner L, Chaloupka FJ. Encouraging Trends in Student Access to **Competitive Beverages** in US Public Elementary Schools, 2006-2007 to 2010-2011.

Twarog JP, Politis MD, Woods EL, et al. **Is obesity becoming the new normal**? Age, gender and racial/ethnic differences in parental misperception of obesity as being 'About the Right Weight'. Int J Obes (Lond). 2016 Mar 22

Twells L, Gregory D, Reddigan J, et al. **Current and predicted prevalence of obesity in Canada**: a trend analysis. Canadian Medical Association Open Access Journal 2.1 E18-E26. 2014.

Twig G, Afek A, Shamiss A, et al. Adolescence **BMI and Trends in adulthood Mortality**: A Study of 2.16 Million Adolescents. J Clin Endocrinol Metab. 2014 Mar 6

Twig G, Ben-Ami Shor D, Furer A, et al. **Adolescent Body Mass Index** and Cardiovascular Disease-specific **Mortality** by Midlife. J Clin Endocrinol Metab. 2017 Jun 9.

Twig G, Yaniv G, Levine H, et al. **Body-Mass Index in 2.3 Million Adolescents** and Cardiovascular Death in Adulthood. N Engl J Med. 2016 Apr 13

Tyrrell J, Richmond RC, Palmer TM, et al; Early Growth Genetics (EGG) Consortium. Genetic Evidence for Causal Relationships Between **Maternal Obesity-Related Traits and Birth Weight**. JAMA. 2016 Mar 15;315(11):1129-1140.

Ul-Haq Z, Mackay DF, Fenwick E, Pell JP. Meta-Analysis of the Association between Body Mass Index and **Health-Related Quality of Life** among Children and Adolescents, Assessed Using the Pediatric Quality of Life Inventory Index. J Pediatr. 2012 Sep 5.

Urban LE, McCrory MA, Dallal GE, et al. Accuracy of **stated energy contents of restaurant foods**. JAMA. 2011 Jul 20;306(3):287-93.

Urban LE, Lichtenstein AH, Gary CE, et al. The **energy content of restaurant foods** without stated calorie information. JAMA Intern Med. 2013 Jul 22;173(14):1292-9.

Urban LE, McCrory MA, Dallal GE, et al. Accuracy of **stated energy contents of restaurant foods**. JAMA. 2011;306(3):287-293.

Urban LE, et al. Energy Contents of Frequently **Ordered Restaurant Meals** & Comparison with Human Energy Requirements & US Department of Agriculture Database Information: Multisite Randomized Study. J Acad Nutr Diet. 2016 Jan 19.

USPSTF- US Preventive Services Task Force, **Screening** for Obesity in **Children and Adolescents**: US Preventive Services Task Force Recommendation Statement Pediatrics 2010 0: peds.2009-2037

The USPSTF recommends that clinicians screen children aged 6 years and older for obesity and offer them or refer them to intensive counseling and behavioral interventions to promote improvements in weight status (grade B recommendation).

USPSTF- U.S. Preventive Services Task Force. **Screening** for obesity in **adults**: recommendations and rationale. Ann Intern Med. 2003 Dec 2;139(11):930-2.

USPSTF: US Preventive Services Task Force. **Screening for and management of obesity in adults**: US Preventive Services Task Force recommendation statement. Ann Intern Med 2012.

USPSTF: US Preventive Services Task Force. **Behavioral counseling interventions** to promote a healthful diet and physical activity for cardiovascular disease prevention in adults: US Preventive Services Task Force recommendation statement. Ann Intern Med 2012.

USPSTF-US Preventive Services Task Force. **Screening for obesity in children and adolescents**: US Preventive Services Task Force recommendation statement. JAMA. doi:10.1001/jama.2017.6803

USPSTF: US Preventive Services Task Force. **Behavioral weight loss interventions** to prevent obesity-related morbidity and mortality in adults: US Preventive Services Task Force recommendation statement [Sept 18, 2018]. JAMA.

USPSTF: LeBlanc ES, Patnode CD, Webber EM, et al. **Behavioral and pharmacotherapy weight loss interventions** to prevent obesity-related morbidity and mortality in adults: updated evidence report and systematic review for the US Preventive Services Task Force [Sept 18, 2018]. JAMA. Boland CL, Harris JB, Harris KB. **Pharmacological Management of Obesity** in **Pediatric Patients**. Ann Pharmacother. 2015 Feb;49(2):220-232.

USPSTF: Curry SJ, Krist AH, Owens DK, et al. **Behavioral Weight Loss Interventions** to Prevent Obesity-Related **Morbidity and Mortality in Adults**: US Preventive Services Task Force Recommendation Statement. JAMA. 2018 Sep 18;320(11):1163-1171.

VA/DoD: Management of Overweight and Obesity Working Group. **VA/DoD clinical practice guideline** for screening and management of overweight and **obesity**. Washington: Department of Veterans Affairs, Department of Defense; 2014.

Vale S, Trost SG, Rêgo C, et al. **Physical Activity, Obesity Status**, and Blood Pressure in Preschool Children. J Pediatr. 2015 May 8.

Valgeirsdottir H, Vanky E, Sundström-Poromaa I, et al. Prenatal exposures and birth indices, and subsequent **risk of polycystic ovary syndrome**: a national registry-based cohort study. BJOG. 2018 Jun 12.

Vallabhan MK, Jimenez EY, Nash JL, et al. **Motivational Interviewing** to Treat Adolescents With Obesity: A Meta-analysis. Pediatrics. 2018 Oct 22.

Vallis M, Piccinini-Vallis H, Sharma AM, Freedhoff Y. Clinical Review: **Modified 5 As: Minimal intervention for obesity counseling** in primary care. Can Fam Physician. 2013 Jan;59(1):27-31.

Valle JA, O'Donnell CI, Armstrong EJ, Bradley et al. **Guideline Recommended Medical Therapy** for Cardiovascular Diseases in the Obese: Insights From the Veterans Affairs Clinical Assessment, Reporting, and Tracking (CART) Program. J Am Heart Assoc. 2016 May 16;5(5).

Van Cleave J, Gortmaker SL, Perrin JM. **Dynamics of obesity and chronic health conditions among children** and youth. JAMA. 2010 Feb 17;303(7):623-30.

van de Langenberg D, Hoekstra T, Twisk JW, et al. **Weight Fluctuation during Childhood** and Cardiometabolic Risk at Young Adulthood. J Pediatr. 2015 Feb;166(2):313-318.e1.

van der Baan-Slootweg O, Benninga MA, Beelen A, et al. **Inpatient treatment** of children and adolescents with severe obesity in the Netherlands: a randomized clinical trial. JAMA Pediatr. 2014 Sep 1;168(9):807-14.

van der Boon RM, Chieffo A, Dumonteil N, et al; PRAGMATIC-Plus Researchers. Effect of Body Mass Index on Short- and Long-term Outcomes After **Transcatheter Aortic Valve Implantation**. Am J Cardiol. 2012 Oct 24.

van Emmerik NM, Renders CM, van de Veer M, et al. High **cardiovascular risk** in severely obese young children and adolescents. Arch Dis Child. 2012 Jul 23.

van Gameren-Oosterom HB, van Dommelen P, Schönbeck Y, et al. Prevalence of overweight in dutch children with **down syndrome**. Pediatrics. 2012 Dec;130(6):e1520-6.

van Rossem L, Wijga AH, Gehring U, et al. **Maternal Gestational and Postdelivery Weight Gain** and Child Weight. Pediatrics. 2015 Oct 19.

Vander Ploeg KA, McGavock J, Maximova K, et al. **School-Based Health Promotion and Physical Activity** During and After School Hours. Pediatrics. 2014 Jan 13

Vandevijvere S, Chow CC, Hall KD, et al. **Increased food energy supply** as a major driver of the obesity epidemic: a global analysis. Bull World Health Organ. 2015 Jul 1;93(7):446-56.

Vanherweghem JL, et al. Rapidly progressive **interstitial renal fibrosis** in young women: association with **slimming regimen** including **Chinese herbs**. Lancet. 1993 Feb 13;341(8842):387-91.

Varban OA, Cassidy RB, Bonham A, et al; Michigan Bariatric Surgery Collaborative. Factors associated with **achieving a body mass index of less than 30 after bariatric surgery** [online July 26, 2017].JAMA Surg. doi:10.1001/jamasurg.2017.2348

Velickovic K, Wayne D, Leija HAL, et al. **Caffeine exposure induces browning features** in adipose tissue in vitro and in vivo. Sci Rep. 2019 Jun 24;9(1):9104.

Vemmos K, Ntaios G, Spengos K, et al. Association between obesity and **mortality after acute first-ever stroke**: the obesity-stroke paradox. Stroke. 2011 Jan;42(1):30-6.

Vesco KK, Leo MC, Karanja N, et al. One-year **postpartum outcomes** following a weight management intervention in pregnant women with obesity. Obesity (Silver Spring). 2016 Oct;24(10):2042-9.

Vest AR, Heneghan HM, Agarwal S, et al. Bariatric surgery and **cardiovascular outcomes**: A systematic review. Heart 2012.

Vest AR, Heneghan HM, Schauer PR, Young JB. **Surgical management of obesity** and the relationship to cardiovascular disease. Circulation. 2013 Feb 26;127(8):945-59.

Vest AR, Wu Y, Hachamovitch R, et al. The **Heart Failure Overweight/Obesity Survival Paradox**: The Missing Sex Link. JACC Heart Fail. 2015 Sep 30.

Vetter ML, Cardillo S, Rickels MR, Iqbal N. Narrative review: effect of bariatric surgery on **type 2 diabetes** mellitus. Ann Intern Med. 2009 Jan 20;150(2):94-103.

Viana RB, Naves JPA, Coswig VS, et al. Is **interval training the magic bullet for fat loss**? A systematic review and meta-analysis comparing moderate-intensity continuous training with high-intensity interval training (HIIT). Br J Sports Med. 2019 Feb 14.

Viera AJ, Antonelli R. Potential Effect of **Physical Activity Calorie Equivalent Labeling** on Parent Fast Food Decisions. Pediatrics. 2015 Jan 26.

Vilar-Gomez E, Martinez-Perez Y, Calzadilla-Bertot L, et al. **Weight loss through lifestyle modification** significantly reduces features of **nonalcoholic steatohepatitis**. Gastroenterology 2015;149:367–378.

Villamor E, Cnattingius S. **Interpregnancy** weight change and risk of adverse pregnancy outcomes: a population-based study. Lancet. 2006 Sep 30;368(9542):1164-70.

Villamor E, Tedroff K, Peterson M, et al. Association Between **Maternal Body Mass Index in Early Pregnancy and Incidence of Cerebral Palsy**. JAMA. 2017 Mar 7;317(9):925-936.

Villareal DT, et al. **Bone mineral density** response to caloric restriction-induced weight loss or exercise-induced weight loss: A randomized controlled trial. Arch Intern Med. 2006 Dec 11-25;166(22):2502-10. CR-induced weight loss, but not EX-induced weight loss, is associated with reductions in BMD at clinically important sites of fracture. These data suggest that EX should be an important component of a weight loss program to offset adverse effects of CR on bone.

Villareal DT, Chode S, Parimi N, et al. **Weight loss, exercise, or both** and physical function in obese older adults. N Engl J Med 2011; 364: 1218-29.

Villareal DT, Aguirre L, Gurney AB, et al. **Aerobic or Resistance Exercise, or Both**, in Dieting Obese Older Adults. N Engl J Med. 2017 May 18;376(20):1943-1955.

Vilsbøll T, Christensen M, Junker AE, et al. Effects of **glucagon-like peptide-1 receptor agonists** (exenatide, liraglutide) on weight loss: systematic review and meta-analyses of randomised controlled trials. BMJ 2011;343:d7771.

Vinter CA, Jensen DM, Ovesen P, Beck-Nielsen H, Jørgensen JS. The **LiP (Lifestyle in Pregnancy)** study: a randomized controlled trial of lifestyle intervention in 360 obese pregnant women. Diabetes Care 2011;34:2502–7.

Vinter CA, Jorgensen JS, Ovesen P, et al. Metabolic effects of **lifestyle intervention in obese pregnant women**. Results from the randomized controlled trial `Lifestyle in Pregnancy` (LiP). Diabet Med. 2014 Nov;31(11):1323-30.

Virji A, Murr MM. Caring for patients after **bariatric surgery**. Am Fam Physician. 2006;73:1403-1408.

Vistisen D, Witte DR, Tabák AG, et al. **Patterns of Obesity Development** before the Diagnosis of Type 2 Diabetes: The Whitehall II Cohort Study. PLoS Med. 2014 Feb 11;11(2)

Vivante A, Golan E, Tzur D, et al. Body mass index in 1.2 million adolescents and risk for **end-stage renal disease** [onlineOctober 29, 2012]. Arch Intern Med.

Voils CI, Olsen MK, Gierisch JM, et al. **Maintenance of Weight Loss After Initiation of Nutrition Training**: A Randomized Trial. Ann Intern Med. 2017 Feb 21.

Volpp KG, John LK, Troxel AB, Norton L, Fassbender J, Loewenstein G. **Financial incentive-based** approaches for weight loss: a randomized trial. JAMA. 2008 Dec 10;300(22):2631-7.

Wabitsch M, Funcke JB, Lennerz B, et al. **Biologically inactive leptin** and early-onset extreme obesity. N Engl J Med. 2015 Jan;372(1):48-54.

Wade KH, Chiesa ST, Hughes AD, Chaturvedi N, Chaet al. Assessing the causal role of **body mass index on cardiovascular health** in young adults: Mendelian randomization and recall-by-genotype analyses. Circulation. 2018 Nov 13;138(20):2187-2201.

Wadden TA, Volger S, Sarwer DB, et al. A two-year randomized trial of obesity **treatment in primary care** practice. (**POWER-UP**) N Engl J Med 2011. DOI: 10.1056/NEJMoa1109220.

Wadden TA, Butryn ML, Hong PS, et al. **Behavioral treatment** of obesity in patients encountered in **primary care** settings: a systematic review. JAMA. 2014 Nov 5;312(17):1779-91.

Wahi G, Parkin PC, Beyene J, et al. Effectiveness of interventions aimed at **reducing screen time** in children: a systematic review and meta-analysis of randomized controlled trials. Arch Pediatr Adolesc Med. 2011 Nov;165(11):979-86.

Wake Melissa, Baur Louise A, Gerner Bibi, et al. Outcomes and costs of **primary care surveillance** and intervention for overweight or obese children: the LEAP 2 randomised controlled trial. BMJ 2009;339:b3308, doi: 10.1136/bmj.b3308

Wake M, Lycett K, Clifford SA, et al. **Shared care obesity management in 3-10 year old children**: 12 month outcomes of **HopSCOTCH** randomised trial. BMJ. 2013 Jun 10;346:f3092.
Wake M, Lycett K. **Let's Call It As It Is**: On Results, Reach, and Resolution in Population-Based Obesity Trials. Pediatrics. 2014 Sep;134(3):e846-7.
Wake M, Clifford S, Lycett K, et al. **Natural BMI Reductions and Overestimation of Obesity Trial Effectiveness**. Pediatrics. 2015 Jan 12.
Walter S, Mejía-Guevara I, Estrada K, et al. Association of a **Genetic Risk Score** With Body Mass Index Across Different Birth Cohorts. JAMA. 2016 Jul 5;316(1):63-69.
Wang DD, Leung CW, Li Y, et al. **Trends in dietary quality** among adults in the United States, 1999 through 2010 [published online September 1,2014]. JAMA Intern Med. doi:10.1001/jamainternmed.2014.3422.
Wang G, Hu FB, Mistry KB, et al. Association Between **Maternal Prepregnancy Body Mass Index and Plasma Folate** Concentrations With Child Metabolic Health. JAMA Pediatr. 2016 Jun 13:e160845.
Wang Lu; Lee I-Min; Manson JoAnn E.; et al. **Alcohol** Consumption, Weight Gain, and Risk of Becoming Overweight in Middle-aged and Older Women. Arch Intern Med. 2010;170(5):453-461.
Wang T, Heianza Y, Sun D. Improving adherence to **healthy dietary patterns, genetic risk, and long term weight gain**: **gene-diet interaction** analysis in two prospective cohort studies. BMJ2018;360:j5644
Wang YC, McPherson K, Marsh T, et al. Health and economic burden of the projected obesity **trends in the USA and the UK**. Lancet. 2011 Aug 27;378(9793):815-25.
Wang YC, Pamplin J, Long MW, et al. Severe Obesity In Adults **Cost State Medicaid Programs Nearly $8 Billion** In 2013. Health Aff (Millwood). 2015 Nov 1;34(11):1923-31.
Wansink B, Tal A, Shimizu M. First foods most: after 18-hour **fast**, people drawn to **starches first and vegetables last**. Arch Intern Med. 2012 Jun 25;172(12):961-3.
Wansink B, Shimizu M, Brumberg A. Association of **nutrient-dense snack combinations** with calories and vegetable intake. Pediatrics. 2013 Jan;131(1):22-9.
Wansink B, van Ittersum K, Payne CR. **Larger Bowl Size** Increases the Amount of Cereal Children Request, Consume, and Waste. J Pediatr. 2013 Nov 16.
Ward ZJ et al. Simulation of **growth trajectories of childhood obesity into adulthood**. N Engl J Med 2017 Nov 30; 377:2145.
Warkentin LM, Majumdar SR, Johnson JA, et al. Weight loss required by the severely obese to achieve clinically important differences in **health-related quality of life**: two-year prospective cohort study. BMC Med. 2014 Oct 15;12:175.
Waters E, de Silva-Sanigorski A, Hall BJ, et al. **Interventions for preventing obesity in children**. Cochrane Database Syst Rev 2011; 12:CD001871. Obesity-prevention programs targeted to children that emphasize improving nutrition and physical-activity levels are generally effective and worth the investment, according to a review of evidence on obesity-intervention strategies around the world.
Wee Christina C. A 52-Year-Old Woman With Obesity: Review of **Bariatric Surgery**. *JAMA*. 2009;302(10):1097-1104.
Wee CC, Hamel MB, Apovian CM, et al. Expectations for weight loss and **willingness to accept risk** among patients seeking **weight loss surgery**. JAMA Surg. 2013 Mar 1;148(3):264-71.
Weinberg CR, Supariwala A, Mian Z, et al. Effect of Body Mass Index on Outcome in Patients With Suspected **Coronary Artery Disease Referred for Stress Echocardiography**. Am J Cardiol. 2013 Aug 29.
Weiner JP, Goodwin SM, Chang HY, et al. Impact of **bariatric surgery on health care costs** of obese persons. JAMA Surg 2012.
Weir Matthew A.; Beyea Michael M.; Gomes Tara; et al. **Orlistat and Acute Kidney Injury**: An Analysis of 953 Patients. *Arch Intern Med*. 2011;171(7):703-704.
Weiss R, et al. Obesity and the **metabolic syndrome** in children and adolescents. N Engl J Med. 2004 Jun 3;350(23):2362-74.
Weiss EP, Albert SG, Reeds DN, et al. Effects of **matched weight loss from calorie restriction, exercise, or both** on cardiovascular disease risk factors: a randomized intervention trial. Am J Clin Nutr. 2016 Sep;104(3):576-86.
Welbourn R, le Roux CW, Owen-Smith A, et al. Why the **NHS should do more bariatric surgery**; how much should we do? BMJ. 2016 May 11;353:i1472.
Welsh JA, Sharma A, Abramson JL, et al. **Caloric sweetener consumption** and dyslipidemia among us adults. JAMA 2010; 303:1490-1497.
Wen LM, Baur LA, Simpson JM, et al. Effectiveness of **home based early intervention on children's BMI** at age 2: randomised controlled trial. BMJ. 2012 Jun 26;344:e3732.
Wen JP, Wen LY, Zhao YJ et al. Effect of **bariatric surgery on sexual function and sex hormone levels** in obese patients: a meta-analysis. J Endocr Soc. 2018 Feb 1; 2(2):117-132.
Wen X, Kong KL, Eiden RD, et al. **Sociodemographic differences** and infant dietary patterns. Pediatrics. 2014 Nov;134(5):e1387-98.
Weng SF, Redsell SA, Swift JA, et al. Systematic review and meta-analyses of **risk factors for childhood overweight** identifiable during infancy. Arch Dis Child. 2012 Oct 29.
Weng SF, Redsell SA, Nathan D, et al. **Estimating Overweight Risk in Childhood** From Predictors **During Infancy**. Pediatrics. 2013 Jul 15.
Wennberg P, Gustafsson PE, Dunstan DW, et al. **Television viewing and low leisure-time physical activity** in adolescence independently predict the metabolic syndrome in mid-adulthood. Diabetes Care. 2013 Jul;36(7):2090-7.
Wentworth JM, Burton P, Laurie C, et al. **Five-Year Outcomes** of a Randomized Trial of **Gastric Band Surgery** in Overweight but Not Obese People With Type 2 Diabetes. Diabetes Care. 2017 Feb 19.
Werling M, Olbers T, Fändriks L, et al. **Increased postprandial energy expenditure** may explain superior long term weight loss after **Roux-en-Y gastric bypass** compared to vertical banded gastroplasty. PLoS One. 2013;8(4):e60280.
WGO Practice Guidelines Obesity - August 2009 http://www.worldgastroenterology.org/assets/downloads/en/pdf/guidelines/22_obesity.pdf
Whalen DJ, Belden AC, Barch D, et al. **Emotion Awareness** Predicts Body Mass Index Percentile Trajectories in Youth. J Pediatr. 2015 Oct;167(4):821-828.e4.
Wharton S, Kuk JL, Petrova L, et al. Effectiveness of a **Community-Based Weight Management Program** for Patients Taking Antidepressants and/or Antipsychotics. Obesity (Silver Spring). 2019 Sep;27(9):1539-1544.
White GE, Courcoulas AP, King WC. **Drug- and alcohol-related mortality risk after bariatric surgery**: evidence from a 7-year prospective multicenter cohort study. Surg Obes Relat Dis. 2019 Apr 17.
White J, Jago R. Prospective Associations Between **Physical Activity** and Obesity Among Adolescent Girls: Racial Differences and Implications for Prevention Physical Activity and Obesity Among Girls. Arch Pediatr Adolesc Med. 2012 Jun 1;166(6):522-7.
Whitten JS. **Liraglutide (Saxenda) for Weight Loss**. Am Fam Physician. 2016 Jul 15;94(2):161-6.
Whooten RC, Perkins ME, Gerber MW, et al. Effects of **Before-School Physical Activity** on Obesity Prevention and Wellness. Am J Prev Med. 2018 Apr;54(4):510-518.
Wieland LS, Falzon L, Sciamanna CN et al. **Interactive computer-based interventions** for weight loss or weight maintenance in overweight or obese people. Cochrane Database of Systematic Reviews 2012, Issue 8. Art. No.: CD007675.
Wilding JPH, Mooney V, Pile R. Should obesity be **recognised as a disease?** BMJ. 2019 Jul 17;366:l4258.
Wilfley DE, Saelens BE, Stein RI, et al. Dose, Content, and Mediators of **Family-Based Treatment** for Childhood Obesity: A Multisite Randomized Clinical Trial. JAMA Pediatr. 2017 Oct 30.
Wilhelm SM, Young J, Kale-Pradhan PB. Effect of **Bariatric Surgery on Hypertension**: A Meta-analysis. Ann Pharmacother. 2014 Jun;48(6):674-82.
Whitlock EP, O'Connor EA, Williams SB, Beil TL, Lutz KW. **Effectiveness of Weight Management Interventions** in **Children**: A Targeted Systematic Review for the USPSTF. Pediatrics. 2010 Jan 18.
Williams DE, et al. Prevalence of impaired **fasting glucose** and its relationship with cardiovascular disease risk factors in US adolescents, 1999-2000. Pediatrics. 2005 Nov;116(5):1122-6.
Willett KC, Alsharhan M, Durand C, et al. Dosing of **enoxaparin** for venous thromboembolism prophylaxis in obese patients. Ann Pharmacother. 2013 Dec;47(12):1717-20
Wilson CL, Liu W, Yang JJ, et al. Genetic and clinical factors associated with obesity among **adult survivors of childhood cancer**: A report from the St. Jude Lifetime Cohort. Cancer. 2015 May 11.
Wilson DM, Abrams SH, Aye T, Lee PD, Lenders C, Lustig RH, Osganian SV, Feldman HA; Glaser Pediatric Research Network Obesity Study Group. **Metformin** extended release treatment of adolescent obesity: a 48-week randomized, double-blind, placebo-controlled trial with 48-week follow-up. Arch Pediatr Adolesc Med. 2010 Feb;164(2):116-23.

Wing RR, et al. A **self-regulation program** for maintenance of weight loss. (STOP Regain)N Engl J Med. 2006 Oct 12;355(15):1563-71. As compared with receiving quarterly newsletters, a self-regulation program based on daily weighing improved maintenance of weight loss, particularly when delivered face to face.

Wing RR, Tate DF, Espeland MA; Study of Novel Approaches to Weight Gain Prevention (**SNAP**) Research Group. **Innovative self-regulation strategies** to reduce weight gain in young adults: the Study of Novel Approaches to Weight Gain Prevention (SNAP) randomized clinical trial [published online May 2, 2016].JAMA Intern Med. doi:10.1001/jamainternmed.2016.1236.

Winkle RA, Mead RH, Engel G, et al. The impact of **obesity on atrial fibrillation**: Patient characteristics, long-term outcomes and complications. *Heart Rhythm* 2017.

Winther A, Ahmed LA, Furberg AS, et al. **Leisure time computer** use and adolescent bone health-findings from the Tromsø Study, Fit Futures: a cross-sectional study. BMJ Open. 2015 Apr 22;5(6):e006665.

Woloshin S, Schwartz LM. The New Weight-Loss Drugs, **Lorcaserin and Phentermine-Topiramate**: Slim Pickings? JAMA Intern Med. 2014 Feb 10.

Woo Baidal JA, Taveras EM. Protecting Progress against Childhood Obesity – The **National School Lunch Program**. N Engl J Med. 2014 Oct 29.

Woo Baidal JA, Locks LM, Cheng ER, et al. **Risk Factors** for **Childhood Obesity** in the **First 1,000 Days**: A Systematic Review. Am J Prev Med. 2016 Feb 8.

Wood CT, Linthavong O, Perrin EM, et al; ELGAN Study Investigators. **Antecedents of Obesity Among Children Born Extremely Preterm**. Pediatrics. 2018 Oct 5.

Wood CT, Skinner AC, Yin HS, et al. **Bottle Size and Weight Gain** in Formula-Fed Infants. Pediatrics. 2016 Jun 7.

Wood GC, Mirshahi T, Still CD, Hirsch AG. Association of **DiaRem Score** With Cure of Type 2 **Diabetes Following Bariatric Surgery**. JAMA Surg. 2016 Apr 20.

Wood MH, Carlin AM, Ghaferi AA, et al. **Association of Race With Bariatric Surgery Outcomes**. JAMA Surg. 2019 Mar 6:e190029.

Woodard GA, Encarnacion B, PerazaJ, et al. **Halo effect for bariatric surgery**. Arch Surg 2011; 10:1185-1190.

Wotton CJ, Goldacre MJ. Age at **obesity and association with subsequent dementia**: record linkage study. Postgrad Med J. 2014 Oct;90(1068):547 51.

Wu RR, Zhao JP, Jin H, et al. Lifestyle intervention and **metformin for treatment of antipsychotic-induced** weight gain: a randomized controlled trial. JAMA. 2008 Jan 9;299(2):185-93.Lifestyle intervention and metformin alone and in combination demonstrated efficacy for antipsychotic-induced weight gain. Lifestyle intervention plus metformin showed the best effect on weight loss. Metformin alone was more effective in weight loss and improving insulin sensitivity than lifestyle intervention alone.

Xi B, Mi J, Zhao M, et al; on behalf of Public Health Youth Collaborative and Innovative Study Group of Shandong University (PHYCISG-SDU). **Trends in Abdominal Obesity** Among US Children and Adolescents. Pediatrics. 2014 Jul 21.

Xiao Q, Keadle SK, Hollenbeck AR, et al. **Sleep Duration and Total and Cause-Specific Mortality** in a Large US Cohort: Interrelationships With Physical Activity, Sedentary Behavior, and Body Mass Index. Am J Epidemiol. 2014 Oct 3.

Xu H, Cupples LA, Stokes A, et al. Association of **Obesity With Mortality** Over 24 Years of Weight History Findings From the Framingham Heart Study. JAMA Netw Open. 2018;1(7):e184587.

Yancy William S Jr; Westman Eric C.; McDuffie Jennifer R.; et al. A Randomized Trial of a **Low-Carbohydrate** Diet vs **Orlistat Plus a Low-Fat** Diet for Weight Loss. Arch Intern Med. 2010;170(2):136-145.

Yancy WS Jr, Mayer SB, Coffman CJ, et al. Effect of **Allowing Choice of Diet on Weight Loss**: A Randomized Trial. Ann Intern Med. 2015 Jun 16;162(12):805-14.

Yamakawa M, Yorifuji T, Inoue S, et al. **Breastfeeding** and Obesity Among Schoolchildren: A Nationwide Longitudinal Survey in Japan. JAMA Pediatr. 2013 Aug 12.

Yang K, Turk MT, Allison VL, et al. Body mass index **self-perception and weight management behaviors** during late adolescence. J Sch Health. 2014 Oct;84(10):654-60.

Yang L, Colditz GA. Prevalence of **Overweight and Obesity in the United States**, 2007-2012. JAMA Intern Med. 2015 Jun 22.

Yang Q, Zhang Z, Gregg EW, et al. Added **sugar intake** and cardiovascular diseases mortality among US adults.*JAMA Intern Med* 2014

Yanovski JA, Parikh SJ. Effects of **Calcium Supplementation** on Body Weight and Adiposity in Overweight and Obese Adults: A Randomized Trial. Ann Intern Med 2009; 821-829. (No effect)

Yanovski SZ, Yanovski JA. **Long-term Drug Treatment for Obesity**: A Systematic and Clinical Review. JAMA. 2013 Nov 14.

Yau PL, Castro Bs MG, Tagani A, et al. Obesity and Metabolic Syndrome and Functional and Structural **Brain Impairments** in Adolescence. Pediatrics. 2012 Sep 3.

Yeung EH, Sundaram R, Ghassabian A, et al. **Parental Obesity** and Early Childhood Development. Pediatrics. 2017 Jan 2.

Yin HS, Sanders LM, Rothman RL, et al. **Parent health literacy** and "obesogenic" feeding and physical activity-related infant care behaviors. J Pediatr. 2014 Mar;164(3):577-583.

Yoon S, Cho H, Kim J, et al. **Brain changes** in overweight/obese and normal-weight adults with type 2 diabetes mellitus. Diabetologia. 2017 Apr 27.

Yoong SL, Chai LK, Williams CM, et al. Systematic review and meta-analysis of **interventions targeting sleep** and their impact on child body mass index, diet, and physical activity. Obesity (Silver Spring). 2016 May;24(5):1140-7.

Young MD, Callister R, Collins CE, et al. Efficacy of a **gender-tailored intervention** to prevent weight regain in **men** over 3 years: A weight loss maintenance RCT. Obesity (Silver Spring). 2017 Jan;25(1):56-65.

Yska JP, van Roon EN, de Boer A, et al. **Remission of Type 2 Diabetes** Mellitus in Patients After Different Types of **Bariatric Surgery**: A Population-Based Cohort Study in the United Kingdom. JAMA Surg. 2015 Sep 30:1-8.

Yu EW, Kim SC, Sturgeon DJ, et al. **Fracture risk after Roux-en-Y gastric bypass vs adjustable gastric banding among Medicare beneficiares** [online May 15, 2019]. JAMA Surg. doi:10.1001/jamasurg.2019.1157

Yu EW, Wewalka M, Ding SA, et al. Effects of **Gastric Bypass and Gastric Banding on Bone Remodeling** in Obese Patients with Type 2 Diabetes. J Clin Endocrinol Metab. 2015 Nov 24:jc20153437.

Yu E, Ley SH, Manson JE, et al. **Weight history and all-cause and cause-specific mortality** in three prospective cohort studies. Ann Intern Med. 2017;166:613-20. doi:10.7326 /M16-1390

Yuan C, Gaskins AJ, Blaine AI, et al. Association Between **Cesarean Birth and Risk of Obesity in Offspring** in Childhood, Adolescence, and Early Adulthood. JAMA Pediatr. 2016 Nov 7;170(11):e162385.

Zabarsky G, Beek C, Hagman E, et al. Impact of Severe Obesity on **Cardiovascular Risk Factors** in Youth. J Pediatr. 2018 Jan;192:105-114.

Zhang C, Hediger ML, Albert PS, et al. Association of **Maternal Obesity With Longitudinal Ultrasonographic Measures of Fetal Growth**: Findings From the NICHD Fetal Growth Studies-Singletons. JAMA Pediatr. 2017 Nov 13.

Zhang R, Borisenko O, Telegina I, et al. Systematic review of **risk prediction models for diabetes after bariatric surgery**. Br J Surg. 2016 Oct;103(11):1420-7.

Zhao W, Katzmarzyk PT, Horswell R, et al. **Body mass index** and the risk of all-cause **mortality** in patients with type 2 diabetes mellitus. *Circulation*. 2014;130:2143–2151.

Zheng JS, Liu H, Zhao YM, et al. **Complementary Feeding** and Childhood Adiposity in Preschool-Aged Children in a Large Chinese Cohort. J Pediatr. 2014 Dec 6.

Zheng W, McLerran DF, and Rolland B. Association between BMI and **risk of death** in more than one million Asians. New Engl J Med 2011; 364:719-729.

Zheng W, Xiang YT, Xiang YQ, et al. Efficacy and safety of **adjunctive topiramate for schizophrenia**: a meta-analysis of randomized controlled trials. Acta Psychiatr Scand 2016;134:385–98.

Zheng Y, Manson JE, Yuan C, et al. Associations of **weight gain from early to middle adulthood with major health outcomes later in life** .JAMA. doi:10.1001/jama.2017.7092

Zhong Y, Auchincloss AH, Lee BK, et al. The Short-Term Impacts of the **Philadelphia Beverage Tax** on Beverage Consumption. Am J Prev Med. 2018 Apr 11.

Zhu, Yeyi, et al. **Maternal dietary intakes of refined grains** during pregnancy and growth through the first 7 years of life among children born to women with gestational diabetes. American Journal of Clinical Nutrition. doi:10.3945/ajcn.116.136291

Zong G, Eisenberg DM, Hu FB, et al. **Consumption of meals prepared at home** and risk of type 2 diabetes: an analysis of two prospective cohort studies. PLoS Med 2016;13:e1002052.

[37] Despres, JP, Golay A, Sjostrom L. Effects of **rimonabant** on metabolic risk factors in overweight patients with dyslipidemia (**Rio-Lipids**). N Engl J Med 2005;353:2121-34. (Weight loss: **6.7kg** at 1yr by repeated-measures method)

Pi-Sunyer FX, et al. RIO-North America Study Group. Effect of **rimonabant**, a cannabinoid-1 receptor blocker, on weight and cardiometabolic risk factors in overweight or obese patients: **RIO-North America**: a randomized controlled trial. JAMA. 2006 Feb 15;295(7):761-75. In this multicenter trial, treatment with 20 mg/d of rimonabant plus diet for **2 years** promoted modest but sustained reductions in weight and waist circumference and favorable changes in cardiometabolic risk factors. {InfoPOEMs: Rimonabant (Acomplia) is minimally effective for obese or overweight patients for achieving sustained weight loss. Less than half the subjects initially enrolled in this study completed the protocol at 1 year. Of those remaining in the study, only one fourth lost a clinically significant amount of weight (10% or more) and, as with other weight-loss drugs, the patients who stopped taking the medicine after 1 year regained the weight. (LOE = 1b-)

Van Gaal LF, Rissanen AM, Scheen AJ, et al. **RIO-Europe** Study Group. Effects of the cannabinoid-1 receptor blocker **rimonabant** on weight reduction and cardiovascular risk factors in overweight patients: 1-year experience from the RIO-Europe study. Lancet. 2005 Apr 16-22;365(9468):1389-97. Erratum in: Lancet. 2005 Jul 30-Aug 5;366(9483):370. (n=1507, weight loss at 1 year: placebo -1.8kg (±6.4), rimonabant 5mg/d -3.4kg (±5.7), rimonabant 20mg/d -6.6kg (±7.2) (p<0.001). {Medscape article on rimonabant in RIO-Diabetes: http://www.medscape.com/viewarticle/546739_print}

Christensen R, Kristensen PK, Bartels EM, Bliddal H, Astrup A. Efficacy and safety of the weight-loss drug rimonabant: a meta-analysis of randomised trials. Lancet. 2007 Nov 17;370(9600):1706-13. Our findings suggest that 20 mg per day rimonabant increases the risk of **psychiatric adverse events**--ie, depressed mood disorders and anxiety-despite depressed mood being an exclusion criterion in these trials. Taken together with the recent US Food and Drug Administration finding of increased risk of suicide during treatment with rimonabant, we recommend increased alertness by physicians to these potentially severe psychiatric adverse reactions. { InfoPOEMs Jan08: These authors searched several databases for double-blind randomized trials of rimonabant for weight loss in patients with a body mass index higher than 30 (27 if the patient also had an obesity-related comorbid condition such as diabetes). Two reviewers independently assessed the quality of the included studies using the Jadad score. The authors don't describe looking for unpublished studies. Four trials (4105 patients) were included in this analysis. After 1 year, patients taking rimonabant lost an average of 4.7 kg more than did those given placebo. Additionally, 25% of patients taking rimonabant lost at least 10% of their baseline weight compared with 7% of control patients (number needed to treat = 5.3; 95% CI, 4.8 - 6). However, patients taking rimonabant were more likely to have unspecified serious adverse events (4% vs 6%; number needed to treat to harm [NNTH] = 58; 95% CI, 33 - 295). Additionally, 3% of patients taking rimonabant developed depression compared with 1.4% of control patients (NNTH = 63; 95% CI, 41-150). Although it's not formally addressed in this study, the authors mention recent Food and Drug Administration reports of increased suicide risk in patients taking rimonabant.}

Topol E, Bousser MG, Fox KA, et al. Rimonabant for prevention of cardiovascular events (**CRESCENDO**): a randomised, multicenter, placebo-controlled trial. Lancet 2010: 376:517-23.

Extras (RxFiles Herbal Weight Loss

Energy Drinks

Health Canada: Safe Use of Energy Drinks. Accessed online at http://www.hc-sc.gc.ca/hl-vs/iyh-vsv/food-aliment/boissons-energ-drinks-eng.php. {Excessive drinking of energy drinks or mixing them with alcohol can have serious health effects. Energy drinks are meant to supply mental and physical stimulation for a short period of time. They usually contain caffeine, taurine (an amino acid, one of the building blocks of protein), vitamins and glucuronolactone, a carbohydrate. Energy drinks should not be confused with sports drinks such as Gatorade® or Powerade®. Sports drinks re-hydrate the body and provide sugars, which the body burns to create energy and replenish electrolytes.}

Glucomannan (in PGX PolyGlycopleX) Plant fibre water-soluble: unabsorbable polysaccharide (glucose + mannose). May ↓LDL, ↓gastric emptying & improve BG control. Conflicting evidence. SE: gas, bloating, etc.

◆General References 7,8,9,10,11,12

WEIGHT LOSS – "HERBAL / NATURAL" PRODUCTS

1 Stevens T, Qadri A, Zein NN. Two patients with acute liver injury associated with use of the herbal weight-loss supplement hydroxycut. Ann Intern Med. 2005 Mar 15;142(6):477-8 .

2 Walsh DE, Yaghoubian V, Behforooz A. Effect of glucomannan on obese patients: a clinical study. Int J Obes. 1984;8(4):289-93.

3 Copeland P. How Successful are commercial weight-loss programs? Nat Clin Pract Endocrinol Metab. 2006;2:658-659.

4 Bui L, Nguyen D, Ambrose P. Blood pressure and heart rate effects following a single dose of bitter orange. Ann Pharmacother 2006;40:53-7.

5 Nykamp D, Fackih M, Compton A. Possible association of acute lateral-wall myocardial infarction and bitter orange supplement. Ann Pharmacother 2004;38:812-6.

6 Heymsfield S, Allison D, Vasselli J, et al. Garcinia cambogia (hydroxycitric acid) as a potential antiobesity agent: a randomized controlled trial. JAMA 1988;280:1596-1600.

7 Natural Medicines Comprehensive Database 2006.

8 Pharmacists Letter. Problems with Weight Loss Products. Jan 2006

9 Robinson R., Griffith J., Nahata M., et al. Herbal Weight-loss supplement misadventures per a regiona poison centre. Ann Pharmacother 2004;38:787-90.

10 Pittler M, Ernst E. Dietary supplements for body weight reduction: a systematic review. Am J Clin Nutr 2004;79:529-36. {InfoPOEMS July 14, 2004. Evidence weak that any commonly used alternative products are effective for reducing weight in moderately overweight individuals. None of the products have been studied for longer than 3 months.}

11 Dwyer J, Allison D, Coates P. Dietary Supplements in Weight Reduction. J Am Diet Assoc 2005;105:S80-S86.

12 Micromedex 2012

13 National Institutes of Health. Dietary Supplements for Weight Loss. Accessed online 24 September 2019 at https://ods.od.nih.gov/factsheets/WeightLoss-Consumer/

Additional references:

Australain Therapeutic Good Administration:**OMG Slim** capsules contains Undeclaredsibutramine and orlistat.

Australian Therapeutic Goos Administration Oct/15 : **ActiveSlim slimming capsules** contains undeclared sibutramine.

Berz JP, Singer MR, Guo X et al. use of a **DASH food group** score to predict excess weight gain in adolescent girls in the National Growth and Health Study. Arch Pediatr Adolesc Med 2011; 165:540-546.

Bliddal H, Leeds AR, Stigsgaard L, Astrup A, Christensen R. Weight loss as **treatment for knee osteoarthritis** symptoms in obese patients: 1-year results from a randomised controlled trial. Ann Rheum Dis. 2011 Oct;70(10):1798-803.

Canadian Physical Activity Guidelines-Jan 2011. Clinical Practice Guideline Development Report. Canadian Society for Exercise Physiology. http://www.csep.ca/CMFiles/Guidelines/CPAGuideline_Report_JAN2011.pdf

CARE Study Group. Maternal **caffeine intake during pregnancy** and risk of fetal growth restriction: a large prospective observational study. BMJ. 2008 Nov 3;337:a2332. doi: 10.1136/bmj.a2332. Caffeine consumption during pregnancy was associated with an increased risk of fetal growth restriction and this association continued throughout pregnancy. Sensible advice would be to reduce caffeine intake before conception and throughout pregnancy.

Carter PJ, Taylor BJ, Williams SM, et al. Longitudinal analysis of **sleep in relation to BMI and body fat in children**: the **FLAME** study. BMJ 2011;342:d2712.

Cheng M, Hu Z, et al. **Caffeine intake and atrial fibrillation** incidence: Dose response meta-analysis of prospective cohort studies. *Canadian J Cardiol* 2014.

Davies GA, Maxwell C, McLeod L, et al., Society of Obstetricians and Gynaecologists of Canada. **Obesity in pregnancy**. (**SOGC**) J Obstet Gynaecol Can 2010 Feb;32(2):165-73.

Dietary Guidelines for Americans (DGA) 2010. Full Guideline: http://www.health.gov/dietaryguidelines/dga2010/DietaryGuidelines2010.pdf , Executive summary: http://www.cnpp.usda.gov/Publications/DietaryGuidelines/2010/PolicyDoc/ExecSumm.pdf

Eisenberg MJ, Atallah R, Grandi SM, Windle SB, Berry EM. **Legislative approaches** to tackling the obesity epidemic. CMAJ. 2011 May 2.

FDA Dec/08 alerted consumers nationwide not to purchase or consume more than **25 different products** marketed for weight loss because they contain undeclared,

active pharmaceutical ingredients that may put consumers' health at risk. The undeclared active pharmaceutical ingredients in some of these products include sibutramine (a controlled substance), rimonabant (a drug not approved for marketing in the United States), phenytoin (an anti-seizure medication), and phenolphthalein (a solution used in chemical experiments and a suspected cancer causing agent). The weight loss products, some of which are marked as "dietary supplements," are promoted and sold on various web sites and in some retail stores. FDA advises consumers who use the products to stop taking them and consult their healthcare professional immediately as the health risks posed by these products can be serious (for example, high blood pressure, seizures, tachycardia, palpitations, heart attack or stroke). FDA also encourages consumers to seek guidance from healthcare professional before purchasing weight loss products. See the FDA News Release for a listing of the names of the 25 referenced products. Read the MedWatch 2008 safety summary, including links to http://www.fda.gov/medwatch/safety/2008/safety08.htm#Weight

FDA May/09 warned consumers to immediately stop using **Hydroxycut products by Iovate Health Sciences**, Inc. Hydroxycut products are associated with a number of **serious liver injuries**. Hydroxycut products are dietary supplements that are marketed for weight-loss, as fat burners, as energy-enhancers, as low carb diet aids, and for water loss under the Iovate and MuscleTech brand names. FDA has received 23 reports of serious health problems ranging from jaundice and elevated liver enzymes, an indicator of potential liver injury, to liver damage requiring liver transplant. One death due to liver failure has been reported to FDA. Other health problems reported include seizures; cardiovascular disorders; and rhabdomyolysis, a type of muscle damage that can lead to other serious health problems such as kidney failure.

FDA Jan/10 notified consumers and healthcare professionals about a counterfeit and potentially harmful version of **Alli 60 mg capsules** (120 count refill kit). The **counterfeit version** contained the controlled substance sibutramine and did not contain orlistat, the active ingredient.

FDA July/10 analysis of **Que She** found that it contains: fenfluramine – a stimulant drug withdrawn from the U.S. market in 1997 after studies demonstrated that it caused serious heart valve damage, propranolol – a prescription beta blocker drug that can pose a risk to people with bronchial asthma and certain heart conditions, sibutramine – a controlled substance and prescription weight loss drug, sibutramine was the subject of a recent study whose preliminary findings showed an association between sibutramine use and increased risk of heart attack and stroke in patients who have a history of heart disease, & ephedrine –a stimulant drug that is legally marketed over-the-counter for temporary asthma relief but can pose a risk to people with cardiovascular disease.

FDA Aug/10 lab analysis of **Solo Slim** was found to contain the undeclared drug ingredient Didesmethyl Sibutramine.

FDA July/10 lab analysis of **Slim-30** Herb Supplement distributed by the company was found to contain undeclared N-Desmethyl Sibutramine & Sibutramine.

FDA July/10 lab analysis of this herb supplement, **Joyful Slim** Herb Supplement, was found to contain the undeclared drug, desmethyl sibutramine.

FDA Oct/10 notified consumers that **Slimming Beauty Bitter Orange Slimming Capsules** contain sibutramine, a prescription-only drug which is a stimulant.

FDA Dec/10 has received multiple reports of adverse events associated with the use of **Fruta Planta**, including several cardiac events and one death. FDA lab analysis confirmed that Fruta Planta contains sibutramine.

FDA Jan/11 laboratory analysis confirmed that **Celerite Slimming Capsules** contain sibutramine

FDA Mar/11 lab analysis of **Svelte 30** orange & gray capsules determined that the product contains Sibutramine.

FDA Mar/11 notified Biotab Nutraceuticals, Inc. that two lots of counterfeit product purporting to be **Extenze** contain undeclared drug ingredients. Specifically, lot 0709241 contains tadalafil and sildenafil, and lot 0509075 contains tadalafil and sibutramine.

FDA Mar/11 laboratory analyses of **Celerite Slimming Tea**: Recall - were found to contain undeclared Sibutramine.

FDA May/11 laboratory analysis confirmed that "**Slim Xtreme Herbal Slimming Capsule**" contains sibutramine.

FDA July/11 is advising consumers not to purchase or use "**Slim Forte Slimming Capsules**," "**Slim Forte Slimming Coffee**," and "**Botanical Slimming Soft Gel & Slim Forte Double Power Slimming Capsules**. FDA laboratory analysis confirmed that these products contain sibutramine.

FDA Dec/11 took joint action against several companies selling over-the-counter **hCG products** that falsely and illegally claim to promote weight loss. Labeled "homeopathic" by the seven companies who received the letters, the products contain human chorionic gonadotropin (hCG), a hormone produced during pregnancy by cells that form the placenta. 1. HCG Diet Direct LLC- HCG Diet Homeopathic Drops, 2. The hCG Drops LLC- Homeopathic HCG, 3. HCG Platinum LLC; RightWay Nutrition- HCG Platinum, HCG Platinum X-30, HCG Platinum X-14, 4. Nutri Fusion Systems LLC- HCG Fusion 30, HCG Fusion 43, 5. www.resetthebody.com; www.theoriginalhcgdrops.com-Homeopathic Original HCG, Homeopathic HCG, 6. Hcg-miracleweightloss.com- HCG Extra Weight Loss Homeopathic Drops, 7. Natural Medical Supply- Alcohol Free hCG Weight Loss Formula.

FDA Feb/12 is advising consumers not to purchase or use "**Japan Weight Loss Blue**," a product for weight loss sold on various websites, laboratory analysis confirmed that "Japan Weight Loss Blue" contains sibutramine, analogs of sibutramine, and ephedrine alkaloids.

FDA Apr/12 laboratory analysis confirmed that "**Japan Rapid Weight Loss Diet Pills Yellow**" contains sibutramine and phenolphthalein.

FDA Dec/12 is advising consumers not to purchase or use "SLIMDIA Revolution," a product promoted and sold for weight loss on various websites, including www.pinkfatty.com, and in some retail stores since it contains Sibutramine.

FDA Jan/13 is advising consumers not to purchase or use "**MAXILOSS** Weight Advanced," a product promoted and sold for weight loss on various websites, includingwww.dreamlifeweightloss.com, and in some retail stores since it contains sibutramine.

FDA Feb/13 Olaax Corp announced a nationwide recall of the company's dietary supplement sold under the brand name **Maxiloss Weight Advanced Softgels** to the

user level, because FDA testing found the Maxiloss Weight Advanced product to contain Sibutramine.

FDA Jun/13 FDA laboratory analysis confirmed that "**Bethel 30", & "XIYOUJI QINGZHI CAPSULE**" & **JaDera** contains sibutramine. .

FDA Jun/13 A sample of **Extreme Body Slim, Fat Zero, Fruit & Plant Slimming, & Paiyouji Plus** all contains silbutramine.

FDA Jun/3 Beta Labs has recalled certain lots of **Oxyphen, Phentalene, Phen FX, and Red Vipers** because they contain 1,3 dimethylamylamine (DMAA), the FDA announced over the weekend. The products are used as pre-workout stimulants and for weight loss, but the agency has previously warned that DMAA can be dangerous: it can elevate blood pressure and lead to cardiovascular complications. One distributor, GNC, faces FDA seizure of over 3000 cases of two other DMAA-containing products, **Jack3d and OxyElitePro**. Although the manufacturer of those supplements has ceased production, GNC continues to sell its remaining stocks, according to the New York Times.

FDA July/13 **Meizi Revolution, Strawberry Balance** contains silbutramine.

FDA Aug/13 Herbal Give Care LLC issued a voluntarily recall of all lots of **Esbelin silouttete** and **Esbelin siloutte Herbal Blend with L-Carnitine** (30 Capsules), to the consumer level. The products have been found to contain undeclared Sibutramine, N-Desmethylsibutramine, and N-di-Desmethylsibutramine.

FDA Aug/13 Bethel Nutritional Consulting, Inc., New York, NY, is voluntarily recalling **Quick Thin and Bethel Advance** to the consumer level. These products have been found to contain Sibutramine and Phenolphthalein, and may pose a threat to consumers.

FDA Aug/13 CTV Best Group announced that it is conducting a voluntary nationwide recall of all lots of a dietary supplement products distributed by the company under the names **BEST SLIM 40 Pills** to the consumer level. Testing by FDA revealed the presence of Sibutramine in Best Slim.

FDA Aig/13 Herbal Give Care LLC is voluntarily recalling all lots of **Esbelder man (30 capsules), Esbelder fem (30 capsules) and Esbelder siloutte** (30 capsules) to the consumer level. The products have been found to contain undeclared Sibutramine, N-Desmethylsibutramine, and N-di-Desmethylsibutramine.

FDA Sep/13 laboratory analysis confirmed that **Shou Fu Ti Tun Guo Xiang Xing Jian Fei Jiao Nang** contains sibutramine.

FDA Oct/13: B@B Trade, Inc., Florida is voluntarily recalling all lots of **Slim Fortune, Lidiy, and Slim Expert** to the consumer level. The FDA laboratory analysis of these dietary supplements found to contain undeclared Sibutramine.

FDA Oct/13 is advising consumers not to purchase or use **Perfect Body Solutions or Burn 7.** FDA laboratory analyses confirmed that Perfect Body Solutions and Burn 7 contain sibutramine.

FDA Oct/13 is advising consumers not to purchase or use **Dr. Mao Slimming Capsules**. FDA laboratory analysis confirmed that Dr. Mao Slimming Capsules contain sibutramine.

FDA Oct/13 is advising consumers not to purchase or use **Bella Vi Insane Amp'd or Bella Vi Amp'd Up.** FDA laboratory analyses confirmed that Bella Vi Insane Amp'd and Bella Vi Amp'd Up contain sibutramine.

FDA Nov/13 **SlimExtra Herbal** capsules contain silbutramine.

FDA Dec/13 laboratory analysis found the **Burn 7 Capsules** to contain undeclared Sibutramine.

FDA Jan/14 is advising consumers not to purchase or use **Magic Slim or Dream Body Slimming Capsule**, products promoted and sold for weight loss and sold on various websites and in some stores, since FDA lab analysis confirmed they contains sibutramine.

FDA Jan/14 **Citrus Fit Gold, Hot Detox & Thinogenics** contains sibutramine. **Tonic Life BP contains** phenolphthalein.

FDA Mar/14 is advising consumers not to purchase or use **Vitaccino Coffee**, a product promoted and sold for weight loss. FDA laboratory analysis confirmed that Vitaccino Coffee contains sibutramine.

FDA Mar/14: New Life Nutritional Center is recalling all lots of "**Super Fat Burner capsules, Maxi Gold capsules and Esmeralda softgels**" to the user level after FDA analysis revealed the products contain undeclared active pharmaceutical ingredients: sibutramine, phenolphthalein or a combination of both sibutramine and phenolphthalein.

FDA Mar/14: **Bella Vi Insane Bee Pollen Capsules, Bella Vi BTrim Ultimate Boost, Bella Vi BTrim Max, Bella Vi Extreme Accelerator, Bella Vi Insane Amp'd, and Bella Vi Amp'd U**, contain silbutramine with or without phenolphthalein.

FDA Apr/14: FDA analysis on **New You** contains silbutramine.

FDA Apr/14 has tested multiple **Zi Xiu Tang Bee Pollen** products from various distributors in the United States (US). All products that have been tested, including those that claim to be "genuine" and "anti-counterfeit," have been found to contain one or both of the undeclared drug ingredients sibutramine and Phenolphthalein.

FDA Apr/14 laboratory analysis confirmed that **Infinity & Lite Fit** USA contains sibutramine.

FDA Apr/14: Nature's Universe notified the public it is recalling all lots of **Thinogenics** product sold prior to February 6, 2014 to the user level after FDA analysis revealed that the affected product contained undeclared sibutramine.

FDA May/14 laboratory analysis confirmed that **Slim Trim U & Natural Body Solution** contains sibutramine.

FDA May/14 is advising consumers not to purchase or use **Asset Bee Pollen**, a product promoted and sold for weight loss because it contains sibutramine.

FDA May/14 is advising consumers not to purchase or use **Asset Bold**, a product promoted and sold for weight loss. FDA laboratory analysis confirmed that

Asset Bold contains sibutramine.

FDA Jun/14 laboratory analysis confirmed that **La Jiao Shou Shen** contains sibutramine.

FDA Jun/14 laboratory analysis confirmed that **Sliming Diet** contains sibutramine.

FDA July/14 laboratory analysis confirmed that **Mix Fruit Slimming, Lingzhi Cleansed Slim Tea, 24 Ince, Lipo 8 Burn Slim, Sliming (sic) Diet By Pretty, & Trim-Fast Slimming Softgel** contains sibutramine.

FDA July/14: **Vitaccino Coffee, Collagen Slim, & Sulami** contains sibutramine.

FDA July/14: **Fruta Bio, Jianfeijindan Activity Girl, & LTD Japanese Chinese Formula** pill for weight reduction contains sibutramine and/or phenolphthalein.

FDA Aug/14 Regeneca Worldwide a division of VivaCeuticals, Inc., is conducting a voluntary nationwide recall of its **RegenESlim appetite control dietary** supplement, lot # EX0616R15814 and lot #11414RE5516, because FDA analysis confirmed the presence of DMAA.

FDA Sep/14 laboratory analysis confirmed that **Best Line Suplemento Alimenticio Capsules** contains sibutramine.

FDA Sep/14 laboratory analysis confirmed that **Japan Hokkaido Slimming Weight Loss Pills** contain sibutramine, benzocaine, phenolphthalein and diclofenac.

FDA Sep/14 laboratory analysis confirmed that **Mezo** contains benzylsibutramine, a substance structurally similar to sibutramine.

FDA Oct/14 laboratory analysis confirmed that **Sit and Slim II** contains sibutramine.

FDA Nov/14 is advising consumers not to purchase or use **V26 Slimming Coffee**. FDA laboratory analysis confirmed sibutramine.

FDA Nov/14: REFA Enterprises is voluntarily recalling one lot each of: **Forever Beautiful Bee Pollen** (UPC # 6333090804632), **Forever Beautiful Infinity** (UPC # 633090804649). The products have been found to contain undeclared Sibutramine or a combination of both Sibutramine and Phenolphthalein through FDA laboratory analyses.

FDA Nov/14 is advising consumers not to purchase or use **Bee Slim, Bee Thin & Super Extreme Accelerator**. FDA laboratory analysis confirmed that they contain sibutramine.

FDA Nov/14 laboratory analysis confirmed that **Slim-Vie** containssibutramine.

FDA Dec/14 Bethel Nutritional Consulting, Inc. is recalling one lot of **SLIM-K Capsules** to the consumer level. The firm was informed by the US Food and Drug Administration (FDA) that a sample of SLIM-K collected and tested by the FDA was found to contain sibutramine, desmethylsibutramine, and phenolphthalein.

FDA Dec/14 Bethel Nutritional Consulting, Inc. is recalling one lot of **B-Lipo Capsules** to the consumer level. The firm was informed by the US Food and Drug Administration (FDA) that a sample of B-Lipo Capsules collected and tested by the FDA was found to contain lorcaserin.

FDA Feb/15 laboratory analysis confirmed that **Lean Body Extreme** contains sibutramine, desmethyl sibutramine, phenolphthalein, and sildenafil.

FDA Feb/15 laboratory analysis confirmed that **Nine Slim, & Seven Slim** contains phenolphthalein.

FDA Mar/15 laboratory analysis confirmed that **Elimulating Weight & Toxin Keeping Beauty** contains sibutramine

FDA Mar/15 laboratory analysis confirmed that **Black Mamba Hyperrush & L-Carnitine Sob Strengthening Version Slimming Miracle Capsule** contains sibutramine.

FDA May/15 laboratory analysis confirmed that **Li Da Dai Dai Hua Slimming Capsule** contains sibutramine.

FDA May/15 laboratory analysis confirmed that **Slim Forte Slimming Capsule** contains sibutramine.

FDA Apr/15 laboratory analysis confirmed that **Superior** contains sibutramine.

FDA May/15: **Nine Slim & Seven Slim** contains undeclared phenolphthalein.

FDA May/15: **Oxy ELITE Pro Super Thermogenic** contains undeclared fluoxetine.

FDA May/15: **Elimulating Weight & Toxin Keeping Beauty & L-Carnitine Sob Strengthening Version Slimming Miracle Capsule** contains undeclared sibutramine.

FDA May/15: **Lean Body Extreme** contains undeclared sibutramine, desmethyl sibutramine, phenolphthalein & sildenafil.

FDA May/15: **Diablos Eca Fire Caps** contains undeclared sildenafil, phenolphthalein, sibutramine & deisobutylbenzylsibutramine.

FDA July 15: **Black Mamba Hyperrush & Ultra ZX** contains Undeclared sibutramineand phenolphthalein.

FDA July 15:**Botanical Slimming (Red) & Xcel** contains Undeclared fluoxetine.

FDA July 15:**Green Algae Combination** by Crane Beauty contains Undeclared lorcaserin.

FDA July 15:**Natural Max Slimming** contains Undeclared sildenafil, fluoxetine, andsibutramine.

FDA July 15: **Ultimate Boost & Xcel Advanced** contains Undeclared phenolphthalein.

FDA Oct/15 **Kaboom Action Strips** 12 Pack contains undeclared sulfoaildenafil.

FDA Oct/15 **Lida DaiDaiHua** contains undeclared sibutramine & phenolphthalein.

FDA Sep/15: **Miracle Diet 30** has been found to contain undeclared phenolphthalein.

FDA Oct/15 laboratory analysis confirmed that **Xtreme Fat Burner Capsules** contains phenolphthalein.

FDA Oct/15 laboratory analysis confirmed that **Tip-Top Shape, Lishou Slimming Coffee, & Basha Nut 100% Fruit Soft Gel Capsules** contains sibutramine.
FDA Dec/15 laboratory analysis confirmed that **Evolve Bee Pollen, Jenesis, Prime Bee Pollen & Oasis Bee Pollen** contains sibutramine.
FDA Dec/15: laboratory analysis confirmed that **La'Trim Plus** contains sibutramine.
FDA's Dec/15 analysis found the **Smart Lipo** products to contain undeclared sibutramine, desmethylsibutramine, and phenolphthalein.
FDA Dec/15 BeeXtreme LLC is recalling all lots of **La' Trim Plus, Jenesis and Oasis products** from the market. Recent Analysis by the Food and Drug Administration has found undeclared Sibutramine and Phenolphthalein.

Finucane MM, Stevens GA, Cowan MJ. **National, regional, and global trends in body-mass index since 1980**: systematic analysis of health examination surveys and epidemiological studies with 960 country-years and 9.1 million participants. Lancet 2011; DOI: 10.1016/S0140-6736(10)62035-5.
Folkvord F, Anschütz DJ, Nederkoorn C, et al. **Impulsivity, "Advergames**," and Food Intake. Pediatrics. 2014 May 5.
Grasser EK, Dulloo AG, Montani JP. Cardiovascular and cerebrovascular effects in response to red bull consumption combined with mental stress. Am J Cardiol. 2015 Jan 15;115(2):183-9.
Health Canada April 2007: The **Safe Use of Health Products** for Weight Loss. http://www.hc-sc.gc.ca/iyh-vsv/med/weight-amaigr_e.html
Health Canada Apr/07 is warning consumers about **Bitter orange** & cardiovascular reactions in the Canadian Adverse Reactions April 2007 Newsletter.
Health Canada Apr/07 is warning consumers from the Hong Kong Department of Health found **Lexscl Fat Rapid Loss capsules to be adulterated with sibutramine** and thyroid hormones.
Health Canada via July/07 Medsafe also advised the public not to use the product **Dai Dai Hua Jiao Nang** because it was found to contain sibutramine.
Health Canada Aug/07 is advising Canadians of a recall in the United States of one lot of **Metaboslim Apple Cider Vinegar**, which is marketed as a dietary supplement, because it has been found to contain sibutramine, a prescription medication that should only be taken under medical supervision.
Health Canada Sept/07 is advising consumers not to use foreign health products due to concerns about possible side-effects: **Jacaranda**, **Queenmer Fat Loss**, **Li Da Dai Dai Hua Jiao Nang**, **J-minus** and **Jelimel Slimming Capsules**. These products are promoted for weight loss and have been found to be adulterated with the prescription drug sibutramine. Sibutramine is used for treating obesity and should only be taken under the supervision of a health professional. **Junyu Jiaonanyihao** has been found to contain the undeclared prescription drugs sibutramine and dexamethasone, as well as phenolphthalein, which is currently prohibited in Canada.. **Heng Tong Jiangtangning Jiaonang** was found to contain the prohibited drug phenformin, and the prescription drug glibenclamide (glyburide) which should only be taken under the supervision of a health professional.
Health Canada Jan/08 is warning Canadians not to use the unauthorized product **Physio Care Lida Dai Dai Hua Jiao Nang Slimming Capsules** (batch number 28012007 / expiration date: Jan 2009). This product is promoted for weight loss and has been found to contain a derivative of the prescription drug sibutramine.
Health Canada April/08 is advising consumers not to use **Xian Zhi Wei II** was found to contain sibutramine and phenolphthalein, which are not meant for self-care and may cause serious side effects.
Health Canada Aug/08 is advising consumers not to use 9 foreign health products due to concerns about possible side-effects: **Dan Bai Shou Shen Su** was found to contain undeclared thyroid hormones and sibutramine. **Karntien and Karntien Easy to Slim** were adulterated with sibutramine and a compound that is similar in structure to sibutramine (N-desmethylsibutramine). **More Slim** was found to contain the undeclared pharmaceutical ingredient sibutramine. **Soloslim** was found to contain an undeclared substance similar in structure to the prescription drug sibutramine. It also contains the prescription drug L-carnitine, as well as synephrine, which is not authorized for sale in weight loss products in Canada.
Health Canada Aug/08 is advising consumers not to use 8 foreign health products due to concerns about possible side-effects: The Hong Kong Department of Health warned against the use of Natural (Xin Yi Dai) and Lasmi because Natural (Xin Yi Dai) was found to contain sibutramine and phenolphthalein, and Lasmi was found to contain sibutramine and spironolactone. The Hong Kong Department of Health warned against the use of AA Qu Feng Shu Jin Wan because it was found to contain the undeclared pharmaceutical ingredient dexamethasone. Apisate contained fenfluramine and Energy ll contained sibutramine. Obat Asam Urat and Asam Urat both contained dexamethasone, phenylbutazone and piroxicam. The Hong Kong Department of Health warned against the use of Slim 3in1 (Xiao Nan zhi Bao) because it was found to contain the undeclared pharmaceutical ingredients sibutramine and phenolphthalein.
Health Canada Sep/08 is advising consumers not to use 2 foreign health products due to concerns about possible side-effects: The Hong Kong Department of Health warned against the use of **Hanguo shoushen yihao** (meiti xing) because it was found to contain the undeclared pharmaceutical ingredient

sibutramine. The Hong Kong Department of Health warned against the use of **ARMA - Sin Gang San** and New ARMA - Sin Gang San because they were found to contain the undeclared pharmaceutical ingredients sibutramine and fenfluramine.

Health Canada Nov/08 is advising that the Hong Kong Department of Health warned consumers not to buy or use **Fat Killer, Carbohydrate Cut and Sugar-Carbohydrate Cut** because they contain sibutramine and an unauthorised substance similar in structure to sibutramine.

Health Canada Jan 2009 is advising consumers not to use 4 foreign products: **Zhuang Tjar Gere** because it contains the undeclared prescription drugs sildenafil & tadalafil, **Zhixhue** Capsules manufactured by Vital Pharmaceutical Holdings Ltd. due to concerns of serious side- effects including liver dysfunction, **Tonik Warisan Banjar** because it contains undeclared dexamethasone & **Healthily Slim** because it contains sibutramine.

Health Canada Mar/09 Foreign Product: **68 Weight Loss Products**; Best-life Fat Burning Capsules; Bevidan;Huiji Yin Chiao Chieh Tu Pien & Relacore. Plus Lami, Linglongquxian, Menergy M-Essence, Nyal Day & Night Cold & Flu Fighter (AUST L 146264), Nyal Cold & Flu Fighter (AUST L 146263), 999 Radix Notoginseng, Batch no. 0807021, Slim Pure, Carbohydrate, Kalomee, K Carbohydrate, K Tighten Slim, & K Slimming Pills. http://www.hc-sc.gc.ca/ahc-asc/media/advisories-avis/_fpa-ape_2009/index-eng.php

Health Canada June/09 Foreign Product Alerts: **Jia Yi Jian** (undeclared sibutramine & tadalafil); **Shan Dian Qiang Xiao Shou** (undeclared sibutramine & phenolphthalein).

Health Canada June/09 is warning consumers not to use the unauthorized product **Slim Magic Herbal**, which is promoted as a weight-loss product, as it was found to contain an undeclared pharmaceutical ingredient similar to the prescription drug sibutramine.

Health Canada is warning consumers not to use the unauthorized product **Nutural Slim**, which is promoted as a weight-loss product, as it was found to contain the undeclared pharmaceutical ingredient sibutramine and also an undeclared pharmaceutical ingredient similar to sibutramine.

Health Canada June/09 warns of foreign Product Alerts: ***Herbal Xenicol*** because it contains undeclared cetilistat. ***BioEmagrecim***, which the FDA had previously warned contained sibutramine, was also found to contain fluoxetine, furosemide and fenproporex. Products: ***Slimbionic***, ***Xsvelten***, ***999 Fitness Essence***, ***24" ince***, ***Light Some***, ***Paiyouji***, ***Pearl White Slimming***, & ***Reducing Weight Easily*** contain undeclared pharmaceutical ingredients (sibutramine and/or phenolphthalein) and/or excessive levels of lead, and may cause serious health effects..

Health Canada Aug/09 is advising via Singapore Health Sciences Authority (HSA) that **Delima Raja Urat** contains undeclared dexamethasone, chlorpheniramine, pheniramine and sibutramine.

Health Canada Dec/09 is advising Canadians not to use certain Acai Berry products after a large number of shipments of adulterated products were stopped at the border. The product names include: **Anti-Aging Acai Berry, Guarana Blast, Brazillian Pure, Anti-aging Vital Rez V, Weight Loss VitalAcai, Dietary Supplement Acai Power Blast and Muscle Mass**. These products for anti-aging and weight loss were found to contain undeclared sildenafil.

Health Canada Dec/09 is warning consumers not to use "**RevolutionDS Weight Loss**", an unauthorized health product promoted for weight loss, because it contains benzylpiperazine (BZP), and may pose serious health risks.

Health Canada Dec/09 is advising consumers not to use **Show Party**: Hong Kong Department of Health warned consumers not to buy or consume [shou-shen pai] after it was found to contain undeclared sibutramine and phenolphthalein.

Health Canada Jan/10 informs that U.S. FDA: **Pai You Guo** contains sibutramine and phenolphthalein. Hong Kong Department of Health: **Ku Xiu Ba Xiang Jian Fei Wan** contains sibutramine and an unauthorized substance similar to sibutramine; **Super Slim (Yani)** contains sibutramine and phenolphthalein; **SHoufsy** contains sibutramine & **MIGAC (sic) FAT BURMING (sic) FACTOR** contains sibutramine.

Health Canada Jan/10 is warning consumers not to use the unauthorized product "**The Slimming Coffee**," which was previously sold as "**Lose Weight Coffee**," because it was found to contain sibutramine.

Health Canada Mar/10 is warning Canadians that an unauthorized health product, "**Herbal Diet Natural**" has been found on the Canadian market and contains an undeclared pharmaceutical ingredient similar to the prescription drug sibutramine.

Health Canada is warning Canadians that an unauthorized health product, "**West Pharm Therma Lean Fat Burner Energizer**" was found on the Canadian market. West Pharm Therma Lean Fat Burner Energizer contains Ephedrine and caffeine, which combined together, may cause serious and possibly fatal adverse effects.

Health Canada Apr/10 is warning Canadians that an unauthorized health product, "**Slim-30**" distributed in Ontario and Quebec by Duxx Enterprises Inc., contains an undeclared pharmaceutical ingredient similar to the prescription drug, sibutramine.

Health Canada May/10 is advising consumers not to use the following foreign health products due to concerns about possible adverse reactions: 1. **Ba Bao Xiao Ke Da**n The Hong Kong Department of Health warned consumers not to buy or use Ba Bao Xiao Ke Dan after it was found to contain undeclared glibenclamide. 2. **Seven Slim 7 Seshou** (Qingchun Shaonüxing, Jieshixing, Guifurenxing, Songchixing), Shoushen Jiaoguan-Tinei Yundong Wan (Jian Xiabanshen, Jian Quanshen Feipang) The Hong Kong Department of Health warned consumers not to buy or use the six products listed above after they were found to contain undeclared sibutramine and phenolphthalein.

Health Canada May/10 is advising consumers not to use 1. **Botanical Slimming 100% Natural Soft Gel, also sold as Meizitang** Australian Therapeutic Goods

Administration warned consumers not to buy or use this product after it was found to contain undeclared sibutramine. 2. **Marsha Slim Plus** Hong Kong Department of Health warned consumers not to buy or use Marsha Slim Plus after it was found to contain undeclared sibutramine, an unauthorized substance similar to sibutramine and phenolphthalein. 3. **S&S Super Slender** The Hong Kong Department of Health warned consumers not to buy or use S&S Super Slender after two samples were found to contain agent similar to sibutramine. One of the tested samples also contained undeclared sibutramine and phenolphthalein.

Health Canada June/10 is advising consumers not to use the following foreign health products due to concerns about possible adverse reactions: 1. **COMECOO**, **ZHONGCAOYAO-JIANKANGJIANFEI** The Hong Kong Department of Health warned consumers not to buy or consume these two products after they were found to contain undeclared phenolphthalein, sibutramine and two unauthorized substances similar to sibutramine. 2. **Qingzhi Santian Shou** The Hong Kong Department of Health warned consumers not to buy or consume Qingzhi Santian Shou after it was found to contain undeclared sibutramine and an unauthorized substance similar to sibutramine.

Health Canada July/10 is advising consumers not to use the following foreign health product(s) 1. **Po Chai Pills** (capsule form) The Hong Kong Department of Health warned consumers not to buy or use this product after it was found to contain undeclared sibutramine and phenolphthalein. Sibutramine is a prescription drug and should only be used under the supervision of a health care practitioner while phenolphthalein is no longer authorized for sale in Canada because it may cause cancer. Po Chai Pills (capsule form) has been recalled by the manufacturer. 2. **LiPO-8 Cap and Glucomi 600 Cap** The Hong Kong Department of Health warned consumers not to buy or use these products because they contain undeclared sibutramine.

Health Canada July/10 is advising consumers not to use the following foreign health products due to concerns about possible adverse reactions: **1 Body Beautiful** The Hong Kong Department of Health warned consumers not to buy or consume *1 Body Beautiful* after it was found to contain undeclared phenolphthalein and sibutramine. 2. **USA Yaku Cell Slimming Capsules, Dong Gua Pai You Su, Qing Gua Pai You Su, and Mu Gua Pai You Su** The Hong Kong Department of Health warned consumers not to buy or consume these four products after they were found to contain undeclared phenolphthalein, sibutramine and an unauthorized substance similar to sibutramine.

Health Canada Aug/10 is advising consumers not to use the following foreign health product(s): **Que She** The U.S. FDA warned consumers not to buy or use Que She after it was found to contain undeclared fenfluramine, propranolol, sibutramine and ephedrine. **Sheng Yuan Fang** The Hong Kong Department of Health (HKDH) warned consumers not to buy or use Sheng Yuan Fang after it was found to contain undeclared phenolphthalein and sibutramine.

Health Canada Sep/10 is advising consumers not to use : **Joyful Slim** Herb Supplement The U.S. FDA informed consumers of a recall of one lot (#101408) of Joyful Slim Herb Supplement after FDA tests found it to contain undeclared desmethyl sibutramine. The lot is being voluntarily recalled nationwide in the U.S. by the company J & H Besta Corp.

Health Canada Nov/10 **Amana Care Seven Slim Herbal Capsules**: The Israel Ministry of Health informed consumers that it found the product Amana Care Seven Slim Herbal Capsules to contain undeclared sibutramine and residue of sildenafil.

Health Canada Nov/10 is advising consumers not to use the following foreign health products due to concerns about possible adverse reactions: **1. Goya–Bitter Melon - Miyura Fit'x Capsules** contained undeclared phenolphthalein and sibutramine **2. Solo Slim Extra Strength - Revivexxx Extra Strength** contained undeclared didesmethyl sibutramine

Health Canada Nov/10 "**Fat Burner No. 1**" (labelled in Chinese characters translated as "**Qian Mei Yin Zi**", an unauthorized Chinese herbal weight loss medicine, is being voluntarily recalled by Ying Tai TCM Supplying Ltd. after Health Canada lab tests revealed the product contains two pharmaceutical ingredients: a chemical similar to sibutramine (N,N- didesmethylsibutramine), and sildenafil.

Health Canada Dec/10 is advising consumers not to use the following foreign health products due to concerns about possible adverse reactions: 1. **Slimming Beauty Bitter Orange Slimming Capsule (Slimming Beauty)** The U.S. Food and Drug Administration warned consumers not to buy or use Slimming Beauty after FDA lab tests revealed that this product contains undeclared sibutramine.

Health Canada Jan/11 The product **Synerate**, manufactured for Strive and distributed by Upper 49th, is being voluntarily recalled from the Canadian market because of the risk of serious, potentially fatal adverse effects from the combination of the ingredients in the product. Synerate, a product used for weight loss or body building, contains caffeine and synephrine, which is similar to ephedrine.

Health Canada Feb/11 is advising consumers not to use the following foreign health products due to concerns about possible adverse reactions: **1. Fruta Planta, Reduce Weight Fruta Planta** The U.S. FDA warned consumers not to buy or use Fruta Planta and Reduce Weight Fruta Planta after FDA lab tests revealed that this product contains undeclared sibutramine. **2. Slimming Factor** The Australian TGA warned consumers not to buy or use Slimming Factor after TGA lab tests confirmed the presence of the undeclared substances sibutramine, fenfluramine and phenolphthalein. According to the TGA release, the product is sold over the Internet.

Health Canada Mar/11 is advising consumers not to use the following foreign health products due to concerns about possible adverse reactions: 1. **Celerite Slimming Capsules**: The U.S. FDA informed consumers of a company recall of CeleriteTM Slimming Capsules after it was found to contain undeclared sibutramine. 2. **Herbal Flos Lonicerae** (Herbal Xenicol) Natural Weight Loss Formula: The product was found to contain undeclared

sibutramine at more than twice the dose that was normally prescribed before sibutramine was removed from the UK market in 2010.

Health Canada May/11 is advising consumers not to use: 1. **Dr. Health Series CM Factor** The Hong Kong Department of Health warned consumers not to buy or use this product after found to contain substance similar to sibutramine.

Health Canada July/11 is advising consumers not to use the following foreign health products due to concerns about possible adverse reactions:
1. **Slim Xtreme Herbal Slimming Capsules** The U.S. Food and Drug Administration informed consumers of a voluntary recall after Slim Xtreme Herbal Slimming Capsules was found to contain undeclared sibutramine.

Health Canada Aug/11 is advising consumers not to use the following foreign health products due to concerns about possible adverse reactions:
1. Celerite Slimming Tea The U.S. FDA informed consumers of a company recall of Celerite Slimming Tea after it was found to contain undeclared sibutramine. **2. Pink Lady for Women Capsules, St Nirvana Herbal Slimming Capsules** The Australian TGA warned consumers not to use these products after Pink Lady for Women Capsules was found to contain undeclared tadalafil while St Nirvana Herbal Slimming Capsules was found to contain undeclared sibutramine and phenolphthalein. According to the TGA advisories, these products are sold over the Internet. **3. Fifteen products promoted for weight loss** The Hong Kong Department of Health (HKDH) warned consumers not to buy or use these 15 products after they were found to contain at least one of the following undeclared substances: phenolphthalein, sibutramine, and/or an unauthorized substance similar to sibutramine.

Health Canada Oct/11 is advising Canadians not to use these foreign health products as they may pose a health risk. **Slim Forte Slimming Capsules**, **Slim Forte Double Power Slimming Capsules**, **Slim Forte Slimming Coffee** and **Meizitang Botanical Slimming Soft Gel**-The U.S. Food and Drug Administration warned that these weight loss products contain an unauthorized drug (sibutramine). **OxyELITE Pro capsules and Pure Fat Three Days Reduce Weight capsules**- The Australian Therapeutic Goods Administration warned that these weight loss products contain an unauthorized drug (sibutramine), or a prescription drug (yohimbine).

Health Canada Nov/11 is advising Canadians not to use these foreign health products as they may pose a health risk. 1. **Metabolic Advantage** The Singapore Health Sciences Authority warned that this weight-loss product contains prescription drugs (thyroid hormones). 2. **Tian Ma Tu Chung Seven Leave Ginseng, Vall-Boon Tongkat Al,** and **Pao Ni Kang** The Singapore Health Sciences Authority warned that these traditional herbal products contain prescription and over-the-counter drugs (dexamethasone, ketoconazole, repaglinide, pheniramine, and chlorpheniramine). 3. **Slimming Kapsul** The Hong Kong Department of Health warned that this weight-loss product contains an unauthorized drug (sibutramine) and a prescription drug (spironolactone). 4. **Pancre-Plus** The Hong Kong Department of Health warned that this counterfeit Chinese medicine contains an unauthorized drug (phenformin) and a prescription drug (glyburide).

Health Canada Jan/12 advises: 1)**17 weight loss products (see Alert for a complete list)** A-Slim 100% Natural Slimming Capsule, Acai Berry Soft Gel ABC, Advanced Slim 5 >DaiDaiHuaJiaoNang, Dream Body Slimming Capsule, Fruit Plant Lossing Fat Capsule, Health Slimming Coffee, Ja Dera 100% Natural Weight Loss Supplement, Leisure 18 Slimming Coffee, Lishou, Magic Slim Tea, Magic Slim Weight Reduction Capsule, P57 Hoodia, Pai You Guo Slim Tea, PhentraBurn Slimming Capsules, Slender Slim 11 Tengda. The U.S. Food and Drug Administration warned that these weight loss products contain unauthorized drugs (sibutramine, phenolphthalein). **2. Slimina weightloss capsules, S-shape slim capsules** The Australian Therapeutic Goods Administration warned that these weight loss products contain prescription drugs (propranolol, nifedipine) and/or unauthorized drugs (sibutramine, fenfluramine, phenolphthalein). **3. Cardiotium, Paidusu, SlimEasy Herbs Capsule, Tianran Zuanshi Xianweisu** The Hong Kong Department of Health warned that these health products contain prescription drugs (losartan, atorvastatin, thyroxine) and/or unauthorized drugs (sibutramine, phenolphthalein).

Health Canada May/12 1. **CanSui; Lexscl Fat Rapid Loss Capsule; The Extreme-thin Fat Burning Bomb; Xiu Zhi Su L-Carnitine Slimming Capsule** The Hong Kong Department of Health warned that these weight loss products contain unauthorized drugs (sibutramine, phenolphthalein). 2. **Lipro Diet Pills; Xiyouji Qingzhi** weight loss capsules The Australian Therapeutic Goods Administration warned that these weight loss products contain an unauthorized drug (sibutramine).

Health Canada June/12 **1. Mince Belle; Everlax; Ever Slim; Ever Slim Shake Mix (Strawberry); Ever Slim Shake Mix (Chocolate); Acai-Man Mangosteen Herbal Drink; Perfect Men:** The U.S. Food and Drug Administration informed of a recall because these weight loss and sexual enhancement products contain prescription drugs (sibutramine or tadalafil). **2. Japan Weight Loss Blue, Japan Rapid Weight Loss Diet Pills Green; Japan Rapid Weight Loss Diet Pills Yellow:** The U.S. Food and Drug Administration warned that these weight loss products contain prescription drugs (sibutramine, ephedrine alkaloids) and unauthorized drugs (phenolphthalein, and substances similar to sibutramine).

Health Canada Jun/12 testing has identified that the weight loss product "**ZXT Gold**" bee pollen capsules contain sibutramine and phenolphthlalein.

Health Canada is advising Canadians that three unauthorized products "**Goya Bittermelon", "S-organic Cocoa+L-carnitine", or "KaBaNa L-Carnitine 360 Slimming Coffee**", promoted for weight loss have been seized from "Cube Inc.", a box-store in Richmond, B.C. These products contain hidden drug ingredients (sibutramine and phenolphthalein) that may pose serious health risks. Caffeine was also found in two products and was not listed on the product label.

Health Canada Aug/13 is advising Canadians not to use these foreign health products as they may pose a health risk. **1. Brazilian Slimming Coffee, Leisure 18 Slimming Coffee, 7 Days Slimming Coffee, Brazilian 7 Days Slimming Coffee, Beauty Secret Slimming Coffee, Body Beauty 5 Days Slimming Coffee, Leisure 18 Slimming Mango Juice, Leisure 18 Slimming Orange Juice, Authentic Leisure 18 Slimming Orange Juice, Super Slim Orange Juice, Coffee Fashion Slimming** The Hong Kong Department of Health has advised consumers not to use these products after they were found to contain the undeclared drug ingredients sibutramine and/or phenolphthalein. http://healthycanadians.gc.ca/recall-alert-rappel-avis/hc-sc/2013/34859a-eng.php **5. Best Slim capsules, Meizi Evolution Botanical Slimming soft gel capsules** The Australian Therapeutic Goods Administration warned consumers not to use these products after they were found to contain the undeclared drug sibutramine.

Health Canada Nov/13 is advising Canadians not to use these foreign health products as they may pose a health risk. These products have been found by regulators in other countries to contain drug ingredients or soy milk allergens that are not declared on the product labels, or a high level of microbial contamination. Prescription drugs should only be taken under the supervision of a healthcare professional. These products are not authorized for sale in Canada and have not been found on the Canadian market, but they may have been brought into the country by travellers or purchased over the Internet:

1. **Aisiyuan V26 Slimming Granules, AcaiBerry Living-XS, and 4C Cosmoslim** , http://healthycanadians.gc.ca/recall-alert-rappel-avis/hc-sc/2013/36269a-eng.php ;
2. **MAXILOSS Weight Advanced** http://healthycanadians.gc.ca/recall-alert- rappel-avis/hc-sc/2013/36197a-eng.php;
3. **ESV Extra Strong Version, MSV Strong Version, RL Rapid Loss, My Slimmer Me (MSM) soft gel capsules, Natural Miaotiaoyishen capsules, and Paiyouji Natural Slimming Capsules** http://healthycanadians.gc.ca/recall-alert-rappel-avis/hc-sc/2013/36521a-eng.php.

Health Canada Feb/14: 1. **Lightning 10.0+, LV Shou Reduces Fat, and STB Summit of the Thin Body S Woman Degreasing Burning Pill** The Hong Kong Department of Health warned consumers not to use this product after it was found to contain sibutramine, phenolphthalein, and indomethacin.

Health Canada Apr/14 has seized the unauthorized drug, "**L-Showm Weight Loss Pills**", being sold at the U-Box store, located at 2809-4500 Kingsway, Burnaby, BC. Health Canada testing found that it contained an undisclosed ingredient, phenolphthalein.

Health Canada Apr/14: Four unauthorized drugs being sold at two SVN FUEL stores - one in Burnaby and one in Coquitlam, B.C. - were seized by Health Canada as they contain ingredients that are potentially dangerous to the health of consumers. The products, and the unapproved ingredients they contain, include **Jack3d** (DMAA (1, 3-dimethylamylamine), **Red Rockets** (ephedrine and caffeine), **West Pharm Therma Lean** (ephedrine and caffeine), and **OxyElite Pro** (1, 3-dimethylamylamine HCl and Yohimbe Bark extract). They were being promoted for weight management.

Health Canada May/14 **Esbelin siloutte te, Esbelin Siloutte Herbal blend with L-Carnitine, Esbelder man, Esbelder fem, Esbelder siloutte** contains Sibutramine, N-Desmethylsibutramine, and N-di-Desmethylsibutramine; **Instant Slim** contains sibutramine and phenolphthalein.

Health Canada May/14 One lot of **Lite Fit USA** (Lot Number 13165, Exp. 05/17) is being voluntarily recalled in the U.S. after analysis by the U.S. Food and Drug Administration revealed the lot contains the undeclared prescription drug sibutramine.

Health Canada May/14: 1. **Slim Fortune, Lidiy & Slim Expert**: FDA found sibutramine; 2. **Dr. Mao Slimming capsules, Perfect Body Solutions, Burn 7**: FDA found sibutramine; **Bella Vi Insane Amp'd Up, Be Inspired, Goodliness Fat Reducing capsules, Jimpness Beauty Fat Loss capsules**: FDA found sibutramine and phenolphthalein.

Health Canada June/14: **Asset Extreme, Asset Extreme Plus, Meizitang Citrus, Slimming Diet Berry Plus, Citrus Fit Gold, Hot Detox, Thinogenics c**ontains sibutramine. **Tonic Life BP & Slimfast capsules** contains phenolphthalein . **Dr**. **Ming's Chinese Capsule**, **Magic Slim and Apple's Quic**k **Impact Weight Loss** contains sibutramine and phenolphthalein.

Health Canada July/14: **Bella Vi Insane Bee Pollen Capsules, Bella Vi BTrim Ultimate Boost, Bella Vi BTrim Max, Bella Vi Extreme Accelerator**: The United States Food and Drug Administration (FDA) warned consumers not to use these products after they were found to contain undeclared sibutramine and/or phenolphthalein. **Super Fat Burner capsules, Maxi Gold capsules, and Esmeralda softgels**: The United States Food and Drug Administration (FDA) warned consumers not to use these products after they were found to contain undeclared sibutramine and phenolphthalein. **Powerful leg-slimming capsules, Pink grain herbal slimming capsules, and Night fat-burning capsules**: The Australian Therapeutic Goods Administration (TGA) warned consumers not to use these products after they were found to contain undeclared phenolphthalein and diclofenac. The product, Night fat-burning slimming capsules, was also found to contain undeclaredtheophylline. **Zi Xiu Tang Pollen capsule and Zi Xiu Tang Beauty Face and Figure capsule**: The Australian Therapeutic Goods Administration (TGA) warned consumers not to use these products after they were found to contain undeclared sibutramine, phenolphthalein, diclofenac, and ibuprofen. The product, Zi Xiu Tang Beauty Face and Figure capsule, was also found to contain undeclared glibenclamide, and indomethacin.

Heath Canada Aug/14: The Australian Therapeutic Goods Administration (TGA) warned consumers not to use the product **Sanovera Starter** capsules, the Hong Kong Department of Health warned consumers not to use the product **Yanhee Slim** and the United States Food and Drug Administration (FDA) warned consumers not to use the products **Infinity, Asset Bee Pollen, Asset Bold, Slim Trim U, and Natural Body Solution** after they were found to contain undeclared sibutramine. The Australian Therapeutic Goods Administration (FDA) warned consumers not to use **3x Slimming Powder Capsules** after it was found to contain undeclared sibutramine and phenolphthalein.

Health Canada Dec/14 is following up with Rapha Biotech Inc. **RAPHA Vitamin B1** (NPN: 80036493) -- undeclared ingredients: sibutramine, desmethyl sibutramine. **Rapha Diet** (700 mg, 270 Capsules) -- undeclared ingredient: caffeine.

Health Canada Dec/14: The United States Food and Drug Administration (FDA) warned consumers not to use the products **Lingzhi Cleansed Slim Tea, Trim-Fast Slimming Softgel, Sliming Diet By Pretty White, Lipo 8 Burn Slim, and Best Line Suplemento Alimenticio Capsules**. Tthe Hong Kong Department of Health warned consumers not to use the products **Slim Perfect Arm and Slim Perfect Legs** and the Australian Therapeutics Goods Administration (TGA) warned consumers not to use the product **Slyn Both Green capsules** after they were found to contain undeclaredsibutramine. The United States Food and Drug Administration (FDA) also warned consumers not to use the product **Mezo** after it was found to contain benzylsibutramine. **Mix Fruit Slimming**: The United States Food and Drug Administration (FDA) warned consumers not to use this product after it was found to contain undeclaredsibutramine and phenolphthalein.

Health Canada Dec/14: **Hydro-Lean** was seized from two Calgary stores because the label indicates it contains a combination of ingredients that can cause serious health risks (ephedrine and caffeine).

Health Canada Jan/15: **Star Majestic Slimming**- Undeclared sibutramine & phenolphthalein via Australian Therapeutic Goods Administration. **Sit and Slim II**-Undeclared sibutramine & phenolphthalein via FDA.

Health Canada Mar/15 advises- FDA Mar/15 **Bee Slim & Bee Thin** has undeclaried silbutramine. Singapore Health Sciences Authority Mar/15 **Nutri Drops Grapefruit Diet**: Undeclared sibutramine, benzyl sibutramine & phenolphthalein.

Health Canada Mar/15 advisory regarding "**Altimate Fat Burner Maximum Burn**" being sold by Nature's Source in Vaughan, Ont., the Department received a complaint about the product also being sold at Nature's Source, 2391 Trafalgar Rd., Unit #6 in Oakville, Ont. Altimate Fat Burner Maximum Burn is an unauthorized health product labelled to contain DHEA, yohimbe, caffeine and ephedrine.

Health Canada Jun/15 requests quarantine of drugs linked to **Zhejiang Hisun Pharma** due to data integrity concerns.

Health Canada Aug/15-FDA has **Akttive Capsules & Zero Xtreme Capsules** with undeclared silbutramine.

Health Canada Oct/16: **Adelganzantes R-II, Mang Luk Power Slim, Xcelerated Weight Loss Charged Up, & Xcelerated Weight Loss Turbo Charge**- Undeclared sibutramine by United States Food and Drug Administration.

Health Canada Oct/16: **B-finn**- Undeclared orlistat and 2-(diphenylmethyl)pyrrolidine (desoxy-D2PM)by Hong Kong Department of Health.

Health Canada Oct/16: **Citrus' Fit, Mang Luk Power Slim Detox, Slim Fit X, & Ultimate Lean** -Undeclared sibutramine and desmethylsibutramine by United States Food and Drug Administration.

Health Canada Oct/16: **Double S**- Undeclared sibutramine by Hong Kong Department of Health.

Health Canada Oct/16: **Maxx Easy**-Undeclared sibutramine and lorcaserin, and orlistat by United States Food and Drug Administration.

Health Canada Oct/16: **Mi Show Slimming capsules**- Undeclared sibutramine by Australian Therapeutic Goods Administration.

Health Canada Oct/16: **Xcelerated Weight Loss Ultra Max**- Undeclared phenolphthalein and sildenafil by United States Food and Drug Administration.

Health Canada Oct/16: **Zi Xiu Tang Beauty Face and Figure Capsule**- Undeclared phenolphthalein and fluoxetine by United States FDA.

Jebb SA, Ahern AL, Olson AD et al. Primary care **referral to a commercial provider** for weight loss treatment versus standard care: a randomized controlled trial. Lancet 2011

Jensen MD, Ryan DH, Apovian CM, et al. **2013 AHA/ACC/TOS Guideline** for the Management of **Overweight and Obesity in Adults**: A Report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines and The Obesity Society. Circulation. 2013 Nov 12.

Kodner C, Hartman DR. **Complications of Adjustable Gastric Banding Surgery** for Obesity. Am Fam Physician. 2014;89(10):813-818.

Lee JM, Gebremariam A, Vijan S, Gurney JG. **Excess Body Mass Index-Years**, a Measure of Degree and Duration of Excess Weight, and Risk for Incident Diabetes. Arch Pediatr Adolesc Med. 2011 Sep 12

McDonnell WM, et al. Fulminant Hepatic Failure After Use of the Herbal Weight-Loss Supplement **Exilis**. Ann Intern Med. 2009 Nov 3;151(9):673-674.

Mediterranean diet: [Mayo Clinic website] choose this heart-healthy diet option. Rochester, MN: Mayo Clinic; 2010. Available from: www.mayoclinic.com/health/mediterranean-diet/CL00011 . Accessed 2011 May 24.

Medical Letter. Treatment Guidelines. **Diet, Drugs & Surgery for weight loss**. April 2011.

MHRA Feb/12 Herbal sliming products found to contain potentially dangerous undeclared pharmaceuticals: **Expelling Grease Slimming Abdomen, V12 Fruit Slimming, 100% Natural Weight Loss Coffee, Leisure 18 Slimming Orange Juice, Fashion Slimming Milk Shake, Langli, Ya Buk & Fruit and vegetables lose weight**. MHRA has received advice from the Danish Medicines Agency that these unlicensed products have been tested and

found to contain the Prescription Only Medicine Sibutramine.

MHRA Feb/12 Following a safety alert issued in October 2010 about slimming products containing Paiyouji the Agency has received a further complaint about a product called '**Paiyouji Plus - Fast Acting Slimming Tea**'. This product has been tested by the Agency and, as in the case of other Paiyouji products, found to contain sibutramine.

MHRA Nov/12 has received advice from the Danish Medicines Agency that this unlicensed product, **Ultra Slim** has been tested and found to contain the Prescription Only Medicine Sibutramine.

MHRA Feb/13 is advising consumers not to use the products specified below due to sibutramine content. Product names: **Fashion Slimming Coffee, L-Carnitine + P57, L-CarnitinL 360 Slimming Coffee, Brazil Potent Slimming Coffee sachets, Coffee 26 Original sachets, Coffee Nature Fashion Slimming sachets, Slender Capsule, Slim-1.**

Mozaffarian Dariush, Hao Tao, Rimm Eric B., eft al. Changes in **Diet and Lifestyle and Long-Term Weight Gain** in Women and Men. N Engl J Med 2011; 364:2392-2404.

Padwal RS, Pajewski NM, Allison DB, Sharma AM. Using the **Edmonton obesity staging system to predict mortality** in a population-representative cohort of people with overweight and obesity. CMAJ. 2011 Aug 15.

Pharmacist's Letter: Health Benefits of Drinking Green Tea. Nov 2006.

Pharmacist's Letter. **PolyGlycopleX (PGX)** for Weight Loss. April 2010.

Pharmacist's Letter. **Raspberry ketone** for Weight Loss. May 2012.

Pharmacist's Letter. **Green Coffee Extract** for Weight Loss. Sept 2012.

Poirier P, Cornier MA, Mazzone T. **Bariatric surgery and cardiovascular risk factors**: A scientific statement from the American Heart Association (**AHA**). Circulation. 2011; DOI: 10.1161/CIR.0b013e3182149099. http://circ.ahajournals.org/cgi/reprint/123/15/1683

Read J. Leighton, Shortell Stephen M.. **Interactive Games** to Promote Behavior Change in Prevention and Treatment. JAMA. 2011;305(16):1704-1705.

Safe Use of Health Products for Weight Loss. Health Canada April 2007 http://www.hc-sc.gc.ca/iyh-vsv/med/weight-amaigr_e.html

Savitz DA, Chan RL, Herring AH, et al. **Caffeine** and miscarriage risk. Epidemiology. 2008 Jan;19(1):55-62. There is little indication of possible harmful effects of caffeine on miscarriage risk within the range of coffee and caffeine consumption reported, with a suggested reporting bias among women with losses before the interview.

Singapore Health Sciences Authority July/15: **Skinny 22**" contains Undeclared phenolphthalein.

Søvik TT, Aasheim ET, Taha O, Engstro¨m M, et al. Weight loss, cardiovascular risk factors, and quality of life **after gastric bypass and duodenal switch**. A randomized trial. Ann Intern Med. 2011;155: 281-91.

Spring B, Schneider K, McFadden HG, et al. Multiple behavior changes in diet and activity: A randomized controlled trial using **mobile technology**. Arch Intern Med 2012; 172:789-796.

Stern JS, Peerson J, Mishra AT, et al. Efficacy and tolerability of a novel herbal formulation (**Sphaeranthus indicus & Garcinia mangostana**) for weight management. Obesity (Silver Spring). 2013 May;21(5):921-7.

Striano P, Zara F, Minetti C, Striano S. Chitosan may decrease serum valproate and increase the risk of seizure reappearance. BMJ. 2009 Sep 24;339:b3751. doi: 10.1136/bmj.b3751.

Tirosh A et al. Adolescent **BMI trajectory and risk of diabetes versus coronary disease**. N Engl J Med 2011 Apr 7; 364:1315.

Twells L, Gregory D, Reddigan J, et al. **Current and predicted prevalence of obesity in Canada**: a trend analysis. Canadian Medical Association Open Access Journal 2.1 E18-E26. 2014.

van der Hoeven N, Visser I, Schene A, et al. Severe **hypertension related to caffeinated coffee and tranylcypromine**: a case report. Ann Intern Med. 2014 May 6;160(9):657-8.

Vanherweghem JL, et al. Rapidly progressive **interstitial renal fibrosis** in young women: association with **slimming regimen** including **Chinese herbs**. Lancet. 1993 Feb 13;341(8842):387-91.

Villareal DT, Chode S, Parimi N, et al. **Weight loss, exercise, or both** and physical function in obese older adults. N Engl J Med 2011; 364: 1218-29.

Weng X, Odouli R, Li DK. Maternal **caffeine** consumption during **pregnancy** and the risk of miscarriage: a prospective cohort study. Am J Obstet Gynecol. 2008 Jan 24; [Epub ahead of print] Our results demonstrated that high doses of caffeine intake during pregnancy increase the risk of miscarriage, independent of pregnancy-related symptoms.

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Thyroid: Online Extras

1. Other hypothyroid tests: Thyroid peroxidase (TPO) is a key enzyme in thyroid hormonogenesis. Nearly all patients with Hashimoto's thyroiditis will have antibodies to TPO. An **Anti-TPO test** can help identify an autoimmune cause of hypothyroidism. A **bone mineral density test** (BMD) may also be indicated in some patients with long-standing hypothyroidism (esp. in the elderly) to rule out osteoporosis associated with levothyroxine treatment.

2. Other hyperthyroid tests: A **differential I-131** can be valuable for diagnosis once TSH test shows hyperthyroidism (e.g. thyroiditis has ↓ I-131U, Graves' has diffuse I-131U). **TSH receptor antibodies** (TRAbs) can be used when I-131 testing is contraindicated (e.g. in pregnancy). Graves' disease typically has the presence of both blocking and stimulating TRAbs. An **ECG** may also be clinically indicated in hyperthyroidism in patients with cardiac disease (hyperthyroidism is one risk factor for the development of atrial fibrillation and other arrhythmias). A **bone mineral density test** (BMD) may also be indicated (esp. in the elderly) to rule out osteoporosis.

3. Management of thyroid nodules: Do TSH & ultrasound as part of initial workup. Then:

Categorization of nodules based on degree of suspicious features and the likelihood of malignancy [21,22]	Threshold size for Fine Needle Aspiration	Likelihood of malignancy
High suspicion Solid hypoechoic nodule or solid hypoechoic component of partially cystic nodule with ≥1 of the following features: Irregular margins Microcalcification Taller-than-wide shape Rim calcification with small extrusive soft tissue component Evidence of extrathyroidal extension	≥ 1 cm	> 70-90%
Intermediate suspicion Hypoechoic solid nodule with smooth margin without the following: Microcalcifications Extrathyroidal extension Taller-than-wide shape	≥ 1 cm	10-20 %
Low suspicion Isoechoic or hyperechoic solid nodule, or partially cystic nodule with eccentric solid area without any ultrasonographic features	≥ 1.5 cm	5-10%
Very low suspicion Spongiform or partially cystic without any ultrasonographic features	≥ 2 cm	< 3%
Purely cystic nodules	No biopsy required	< 1%

References: THYROID DISORDERS

[1] Toward Optimized Practice Clinical Practice Guideline Working Group. Clinical practice guidelines: investigation and management of primary thyroid dysfunction. Edmonton AB: Toward Optimized Practice Program: 2014 Update Available from: http://www.topalbertadoctors.org/cpgs/1620428 (accessed January 2017).

[2] American Association of Clinical Endocrinologists and American Thyroid Association. Clinical Practice Guidelines for Hypothyroidism in Adults: Co-Sponsored by the American Association of Clinical Endocrinologists and the American Thyroid Association. Endocr Pract 2012;18(6):989-1028. Available from: https://www.aace.com/publications/guidelines (accessed January 2017).

[3] Sherman SI, Talbert RL,Thyroid disorders. In JT DiPiro, RL Talbert, GC Yee, et al (eds), Pharmacotherapy: A Pathophysiological Approach, 9th ed. On-line. www.accesspharmacy.com. New York, McGraw-Hill, 2014 (accessed January 2017).

[4] American Thyroid Association Professional Guidelines. Available from: http://www.thyroid.org/professionals/ata-professional-guidelines/ (accessed January 2017).

[5] British Thyroid Association. UK Guidelines for the Use of Thyroid Function Tests. Available from: http://www.british-thyroid-association.org/sandbox/bta2016/uk_guidelines_for_the_use_of_thyroid_function_tests.pdf (accessed January 2017).

[6] Surks MI, Ortiz E, Daniels GH, Sawin CT, Col NF, Cobin RH, Franklyn JA, Hershman JM, Burman KD, Denke MA, Gorman C, Cooper RS, Weissman NJ. Subclinical thyroid disease: scientific review and guidelines for diagnosis and management. JAMA. 2004 Jan 14;291(2):228-38.

[7] Gharib H, Tuttle RM, Baskin HJ, Fish LH, Singer PA, McDermott MT. Subclinical thyroid dysfunction: a joint statement on management from the American Association of Clinical Endocrinologists, the American Thyroid Association, and the Endocrine Society. J Clin Endocrinol Metab. 2005 Jan;90(1):581-5; discussion 586-7.

[8] Jensen KA. Update on Nonmalignant Thyroid Disorders. Pharmacy Practice. Continuing Education Lesson. June 2009

[9] Vaidya B, Pearce SH. Management of hypothyroidism in adults. BMJ. 2008 Jul 28;337:a801. doi: 10.1136/bmj.a801

[10] U.S. Preventive Services Task Force. Screening for thyroid disease:recommendation statement. Ann Intern Med. 2004 Jan 20;140(2):125-7.
U.S. Preventive Services Task Force. Screening for Thyroid Dysfunction: U.S. Preventive Services Task Force Recommendation Statement. Ann Intern Med. 2015;162:641-650. doi:10.7326/M15-0483.

[11] Ross DS. Ross DS. Subclinical hyperthyroidism in nonpregnant adults. In: UpToDate Online. UpToDate Waltham, MA. Available from: www.uptodate.com (accessed January 2017).
Donangelo I, Braunstein GD. Update on Subclinical Hyperthyroidism. Am Fam Physician. 2011;83(8):933-938.

Hyland KA, Arnold AM, Lee JS, Cappola AR. Persistent Subclinical Hypothyroidism and Cardiovascular Risk in the Elderly: The Cardiovascular Health Study. J Clin Endocrinol Metab. 2012 Nov 16.
Biondi B, Cooper DS. Subclinical Hyperthyroidism. N Engl J Med. 2018 Jun 21;378(25):2411-2419.
Feller M, Snel M, Moutzouri E, et al. Association of Thyroid Hormone Therapy With Quality of Life and Thyroid-Related Symptoms in Patients With Subclinical Hypothyroidism: A Systematic Review and Meta-analysis. JAMA. 2018 Oct 2;320(13):1349-1359.

[12] Compendium of Therapeutic Choices 7th Edition
[13] Micromedex 2017 Truven Health Analytics Inc.
[14] Repchinsky, C. Compendium of Pharmaceuticals and Specialties (CPS), Ottawa: Canadian Pharmacists Association, 2017.
[15] Lexi-Comp 2017.
[16] Lau E. The 2008-2009 Drug Handbook and Formulary; The Hospital for Sick Children. Toronto: The Hospital for Sick Children, 2008.
[17] Dipchand A, Friedman J. The Hospital for Sick Children Handbook of Pediatrics. Toronto: The Hospital for Sick Children, 2008
[18] Pharmacist's Letter. Drugs & Substances that **Reduce Absorption** of Levothyroxine. Dec 2008.
[19] Briggs GG, Freeman RK, Sumner JY. Drugs in Pregnancy and Lactation 11th Edition. Williams & Wilkins, Baltimore, 2017.
[20] Villar HCCE, Saconato H, Valente O, Atallah ÁN. Thyroid hormone replacement for subclinical hypothyroidism. *Cochrane Database of SystematicReviews* 2007, Issue 3.Art. No.:CD003419.DOI: 10.1002/14651858.CD003419.pub2.
[21] Haugen BR Md, Alexander EK, Bible KC, et al. **2015 American Thyroid Association Management Guidelines for Adult Patients with Thyroid Nodules and Differentiated Thyroid Cancer**. Thyroid. 2015 Oct 14.
[22] Song JSA, Hart RD. **Fine-needle aspiration biopsy** of **thyroid nodules**: Determining when it is necessary. Can Fam Physician. 2018 Feb;64(2):127-128.
[23] Bartalena L, Bogazzi F, Chiovato L, et al. **2018 European Thyroid Association (ETA) Guidelines for the Management of Amiodarone-Associated Thyroid Dysfunction**. Eur Thyroid J. 2018 Mar;7(2):55-66.
[24] Kahaly GJ, Bartalena L, Hegedüs L, et al. **2018 European Thyroid Association Guideline** for the Management of **Graves' Hyperthyroidism**. Eur Thyroid J. 2018 Aug;7(4):167-186.
25. Chen AX, Leung AM, Korevaar TI. Thyroid Function and Conception. New England Journal of Medicine. 2019 Jul 11;381(2):178-81.

Additional References:

Abalovich M, Amino N, Barbour LA, Cobin RH, De Groot LJ, Glinoer D, Mandel SJ, Stagnaro-Green A. Management of thyroid dysfunction during pregnancy and postpartum: an Endocrine Society Clinical Practice Guideline. J Clin Endocrinol Metab. 2007 Aug;92(8 Suppl):S1-47.
Abraham P, Avenell A, Watson WA, Park CM, Bevan JS. Antithyroid drug regimen for treating Graves' hyperthyroidism. *Cochrane Database of Systematic Reviews* 2005, Issue 2. Art. No.: CD003420. DOI: 10.1002/14651858.CD003420.pub3.
Abu-Shama Y, Cuny T. **Pemberton's Sign in a Patient with a Goiter**. N Engl J Med. 2018 May 31;378(22):e31.
Adam MA, et al. Rethinking the current American Joint Committee on **Cancer TNM staging system for medullary thyroid cancer** [online June 21, 2017].JAMA Surg. doi:10.1001/jamasurg.2017.1665
Ahn HS, Kim HJ, Welch HG. Korea's **thyroid-cancer "epidemic"**- screening and overdiagnosis. N Engl J Med. 2014 Nov 6;371(19):1765-7.
Akhtar MA, Agrawal R, Brown J, et al. **Thyroxine replacement for subfertile women** with euthyroid autoimmune thyroid disease or subclinical hypothyroidism. Cochrane Database Syst Rev. 2019 Jun 25;6:CD011009. We could draw no clear conclusions in this systematic review due to the very low to low quality of the evidence reported.
Akturk HK, Chindris AM, Hines JM, Set al. **Over-the-Counter "Adrenal Support"** Supplements Contain Thyroid and Steroid-Based Adrenal Hormones. Mayo Clin Proc. 2018 Mar;93(3):284-290.
Al-Qurayshi Z, Hauch A, Srivastav S, et al. A National Perspective of the Risk, Presentation, and Outcomes of **Pediatric Thyroid Cancer**. JAMA Otolaryngol Head Neck Surg. 2016 Mar 31
Alexander EK, Kennedy GC, Baloch ZW, et al. **Preoperative diagnosis of benign thyroid nodules** with indeterminate cytology. N Engl J Med 2012. DOI: 10.1056/NEJMoa1203208.
American Thyroid Association; Endocrine Society; American Association of Clinical Endocrinologists. Joint statement on the U.S. Food and Drug Administration's decision regarding bioequivalence of levothyroxine sodium. Thyroid. 2004 Jul;14(7):486.
Andersen SL, Knøsgaard L, Olsen J, et al. **Maternal thyroid function,** use of antithyroid drugs in early pregnancy and birth defects. J Clin Endocrinol Metab. 2019 Aug 13.
Andersen SL, Olsen J, Laurberg P. **Antithyroid Drug Side Effects** in the Population and in **Pregnancy**. J Clin Endocrinol Metab. 2016 Jan 27
Appelhof BC, Fliers E, Wekking EM, Schene AH, Huyser J, Tijssen JG, Endert E, van Weert HC, Wiersinga WM. Combined therapy with levothyroxine and liothyronine in two ratios, compared with levothyroxine monotherapy in primary hypothyroidism: a double-blind, randomized, controlled clinical trial. J Clin Endocrinol Metab. 2005 May;90(5):2666-74
Aronson R, Offman HJ, Joffe RT, Naylor CD. Triiodothyronine augmentation in the treatment of refractory depression. A meta-analysis. Arch Gen Psychiatry. 1996 Sep;53(9):842-8.
Arnason T, Clarke DB, Imran SA. Hyperthyroidism caused by a **pituitary adenoma**. CMAJ. 2011 Aug 9;183(11):E757.
Aschebrook-Kilfoy B, James B, et al. Risk Factors for Decreased **Quality of Life in Thyroid Cancer** Survivors: Initial Findings from the North American Thyroid Cancer Survivorship Study. Thyroid. 2015 Dec;25(12):1313-21.
Åsvold BO, Vatten LJ, Midthjell K, Bjøro T. **Serum TSH within the reference range** as a predictor of future hypothyroidism and hyperthyroidism: 11-year follow-up of the HUNT Study in Norway. J Clin Endocrinol Metab. 2012 Jan;97(1):93-9.
Åsvold BO, Vatten LJ, Bjøro T, et al; Thyroid Studies Collaboration. **Thyroid Function Within the Normal Range and Risk of Coronary Heart Disease**: An Individual Participant Data Analysis of 14 Cohorts. JAMA Intern Med. 2015 Apr 20.
Aubert CE, Bauer DC, da Costa BR, et al. The association between subclinical **thyroid dysfunction and dementia**: the Health, Aging and Body Composition (Health ABC) Study. Clin Endocrinol (Oxf). 2017 Aug 29.
Azim S, Nasr C**. Subclinical hypothyroidism**: When to treat. Cleve Clin J Med. 2019 Feb;86(2):101-110.
Azizi F, Takyar M, Madreseh E, Amouzegar A. Long-term **Methimazole Therapy in Juvenile Graves' Disease**: A Randomized Trial. Pediatrics. 2019 May;143(5).
Bahn, Rebecca S. **Graves' Ophthalmopathy**. N Engl J Med 2010 362: 726-738.
Banerjee M, Wiebel JL, et al. Use of imaging tests after primary treatment of thyroid cancer in the United States: population based retrospective cohort study evaluating death and recurrence. BMJ. 2016 Jul 20;354:i3839.
Bano A, Chaker L, al. Thyroid function and the **risk of non-alcoholic fatty liver disease**: The Rotterdam Study. J Clin Endocrinol Metab. 2016 Jun 7:jc20161300.
Bano A, Dhana K, Chaker L, et al. Association of **Thyroid Function With Life Expectancy** With and Without Cardiovascular Disease: The Rotterdam Study. JAMA Intern Med. 2017 Sep 18.
Bano A, Chaker L, Mattace-Raso FU, et al. **Thyroid Function and the Risk of Atherosclerotic Cardiovascular Morbidity and Mortality**: The Rotterdam Study. Circ Res. 2017 Oct 31.
Bano A, Chaker L, Schoufour J, et al. **High circulating free thyroxine levels may increase the risk of frailty**: The **Rotterdam Study**. J Clin Endocrinol Metab. 2017 Nov 6.
Barczyński M, Konturek A, Gołkowski F, Hubalewska-Dydejczyk A, Cichoń S, Nowak W. Five-Year Follow-up of a Randomized Clinical Trial of **Unilateral Thyroid Lobectomy** with or Without Postoperative Levothyroxine Treatment. World J Surg. 2010 Feb 4. Prophylactic LT4 treatment significantly decreased the recurrence rate of nodular goiter in the contralateral thyroid lobe and the need for completion thyroidectomy, mostly among patients with iodine deficiency.

Barroso-Sousa R, Barry WT, et al. Incidence of Endocrine Dysfunction Following the Use of Different **Immune Checkpoint Inhibitor Regimens**: A Systematic Review and Meta-analysis. JAMA Oncol. 2017 Sep 28.
Bathgate G, Karra E, Khoo B. **New diagnosis of hyperthyroidism in primary care**. BMJ. 2018 Aug 24;362:k2880.
Bauer DC, McPhee SJ: Thyroid Disease. In: SJ McPhee, WF Ganong (eds), Pathophysiology of Disease: An Introduction to Clinical Medicine, 5th ed. On-line. www.statref.com. New York, McGraw-Hill, 2006. (accessed September 2009).
Baumgartner C, da Costa BR, Collet TH, et al. **Thyroid Function Within the Normal Range, Subclinical Hypothyroidism and the Risk of Atrial Fibrillation**. Circulation. 2017 Oct 23.
Becker DV, Braverman LE, Delange F, et al. **Iodine supplementation** for pregnancy and lactation—United States and Canada: recommendations of the American Thyroid Association. Thyroid 2006; 16: 949–51.
Bekkering GE, Agoritsas T, Lytvyn L, et al. **Thyroid hormones treatment for subclinical hypothyroidism**: a clinical practice guideline. BMJ. 2019 May 14;365:l2006.
Belliveau MJ, Jordan DR. **Thyroid eye disease**. CMAJ. 2013 Jun 11;185(9):797.
Bengtsson C, Padyukov L, Källberg H, et al. Thyroxin substitution and the risk of developing **rheumatoid arthritis**; results from the Swedish population-based EIRA study. Ann Rheum Dis. 2014 Jun 1;73(6):1096-100.
Benhadi N, Wiersinga WM, Reitsma JB, Vrijkotte TG, Bonsel GJ. **Higher maternal TSH levels in pregnancy** are associated with increased risk for miscarriage, fetal or neonatal death. *Eur J Endocrinol* 2009;160:985-91.
Biondi B, Cappola AR, Cooper DS. **Subclinical Hypothyroidism**: A Review. JAMA. 2019 Jul 9;322(2):153-160.
Biondi B, Cooper DS. The clinical significance of subclinical thyroid dysfunction. Endocr Rev. 2008 Feb;29(1):76-131. Epub 2007 Nov 8.
Birk-Urovitz E, Elisabeth Del Giudice M, Meaney C, et al. **Use of thyroid-stimulating hormone tests for identifying primary hypothyroidism** in family medicine patients. Can Fam Physician. 2017 Sep;63(9):e389-e394.
Bisschop PH, van Trotsenburg AS. Images in clinical medicine. **Neonatal thyrotoxicosis**. N Engl J Med. 2014 Mar 27;370(13):1237.
Blum MR, Bauer DC, Collet TH, et al; Thyroid Studies Collaboration. **Subclinical thyroid dysfunction and fracture risk**: a meta-analysis. JAMA. 2015 May 26;313(20):2055-65.
Bochukova E et al. A **Mutation in the Thyroid Hormone Receptor Alpha Gene**. N Engl J Med. 2011 Dec 14.
Bogazzi F, Bartalena L, Martino E. Approach to the patient with **amiodarone-induced thyrotoxicosis**. J Clin Endocrinol Metab. 2010 Jun;95(6):2529-35.
Bongers PJ, Kluijfhout WP, Devon K, et al. Long-term Risk of **Thyroid Cancer After Initially Negative Thyroid Biopsy Results**. JAMA Otolaryngol Head Neck Surg. 2019 Apr 18.
Booms S, Hill E, Kulhanek L, et al. **Iodine Deficiency** and Hypothyroidism From Voluntary Diet Restrictions in the US: Case Reports. Pediatrics. 2016 May 10.
Borkar DS, Homayounfar G, Tham VM, et al. Association Between **Thyroid Disease and Uveitis**: Results From the Pacific Ocular Inflammation Study. JAMA Ophthalmol. 2017 May 4.
Brose MS, Nutting CM, Jarzab B, et al, on behalf of the DECISION investigators. **Sorafenib** in radioactive iodine-refractory, locally advanced or metastatic diff erentiated thyroid **cancer**: a randomised, double-blind, phase 3 trial. Lancet 2014; published online April 24.
Bremner AP, Feddema P, Leedman PJ, et al. **Age-related changes in thyroid function**: a longitudinal study of a community-based cohort. J Clin Endocrinol Metab. 2012 May;97(5):1554-62. Aging is associated with increased serum TSH concentrations, with no change in free T4 concentrations. The largest TSH increase is in people with the lowest TSH at baseline. This suggests that the TSH increase arises from age-related alteration in the TSH set point or reduced TSH bioactivity rather than occult thyroid disease.
Brent GA. Clinical practice. Graves' disease. N Engl J Med. 2008 Jun12;358(24):2594-605
Brito JP, Morris JC, Montori VM. **Thyroid cancer: zealous imaging** has increased detection and treatment of low risk tumours. BMJ. 2013 Aug 27;347:f4706.
Brito JP, Hay ID, Morris JC. **Low risk papillary thyroid cancer**. BMJ. 2014 Jun 16;348:g3045.
Burch HB. **Drug Effects** on the Thyroid. N Engl J Med. 2019 Aug 22;381(8):749-761.
Burch HB, Cooper DS. A young woman with palpitations, **goitre** and low thyroid-stimulating hormone. CMAJ. 2014 Mar 4;186(4):289-91.
Burch HB, Burman KD, Cooper DS, et al. A 2015 Survey of Clinical Practice Patterns in the Management of **Thyroid Nodules**. J Clin Endocrinol Metab. 2016 Mar 25:jc20161155.
Burman KD, Wartofsky L. Clinical Practice. **Thyroid Nodules**. N Engl J Med. 2015 Dec 10;373(24):2347-56.
Burns RB, Bates CK, Hartzband P, Smetana GW. Should We Treat for Subclinical Hypothyroidism?: Grand Rounds Discussion From Beth Israel Deaconess Medical Center. Ann Intern Med. 2016 Jun 7;164(11):764-70.
Burton BN, Okwuegbuna O, Jafari A, et al. Association of Preoperative Anemia With 30-Day Morbidity and Mortality Among Patients With Thyroid Cancer Who Undergo Thyroidectomy. JAMA Otolaryngol Head Neck Surg. 2018 Nov 29.
Cabanillas ME, McFadden DG, Durante C. **Thyroid cancer**. Lancet. 2016 May 27.
Calsolaro V, Niccolai F, Pasqualetti G, et al. **Hypothyroidism in the Elderly:** Who Should Be Treated and How? J Endocr Soc. 2018 Nov 19;3(1):146-158.
Cappola AR, Cooper DS. **Screening and treating subclinical thyroid disease**: getting past the impasse. Ann Intern Med. 2015 May 5;162(9):664-5.
Cappola AR, Desai AS, Medici M, et al. Thyroid and Cardiovascular Disease: Research Agenda for **Enhancing Knowledge, Prevention, and Treatment**. Thyroid. 2019 May 13.
Carle A, Andersen SL, Boelaert K, Laurberg P. Management of Endocrine Disease: **Subclinical Thyrotoxicosis**: Prevalence, Causes and Choice of Therapy. Eur J Endocrinol. 2017 Mar 8.
Carvalho GA, Paz-Filho G, Mesa Junior CO, Graf H. Management of Endocrine Disease: Pitfalls on the **replacement therapy for primary and central hypothyroidism** in adults. Eur J Endocrinol. 2018 Feb 28.
Casassus B. Risks of reformulation: French patients complain after **Merck modifies levothyroxine pills**. BMJ. 2018 Feb 16;360:k714.
Cassio A, Monti S, Rizzello A, et al. Comparison between **Liquid and Tablet Formulations of Levothyroxine** in the Initial Treatment of Congenital Hypothyroidism. J Pediatr. 2013 Jan 10.
Chaker L, Cappola AR, Mooijaart SP, et al. Clinical aspects of **thyroid function during ageing**. Lancet Diabetes Endocrinol. 2018 Jul 12.
Chaker L, van den Berg ME, Niemeijer MN, et al. **Thyroid Function** and **Sudden Cardiac Death**: A Prospective Population-Based Cohort Study. Circulation. 2016 Sep 6;134(10):713-22.
Chaker L, Wolters FJ, Bos D, et al. Thyroid function and the **risk of dementia**: The Rotterdam Study. Neurology. 2016 Oct 18;87(16):1688-1695.
Chiappa V, Anderson MA, Barrett CD, et al. Case 24-2019: A 39-Year-Old Woman with **Palpitations, Abdominal Pain, and Vomiting**. N Engl J Med. 2019 Aug 8;381(6):567-577.
Chen AX, Leung AM, Korevaar TIM. **Thyroid Function and Conception**. N Engl J Med. 2019 Jul 11;381(2):178-181.
Cheng W, Ma C, Fu H, et al. **Low- or high-dose radioiodine remnant ablation for differentiated thyroid carcinoma**: a meta-analysis. J Clin Endocrinol Metab. 2013 Apr;98(4):1353-60.
Cibas ES, Baloch ZW, Fellegara G, et al. A prospective assessment defining the limitations of **thyroid nodule pathologic evaluation**. Ann Intern Med. 2013 Sep 3;159(5):325-32.
Clyde PW, Harari AE, Getka EJ, Shakir KM. Combined levothyroxine plus liothyronine compared with levothyroxine alone in primary hypothyroidism: a randomized controlled trial. JAMA. 2003 Dec 10;290(22):2952-8.
Cohen RN, Davis AM. Management of Adult Patients With **Thyroid Nodules and Differentiated Thyroid Cancer**. JAMA. 2017 Jan 24;317(4):434-435.
Cook R, Fortescue-Webb D, Taft R; NIHR Dissemination Centre. **Repeat thyroid function tests** for healthy older people are not needed. BMJ. 2019 Mar 1;364:l805.
Cooper DS. Antithyroid drugs. N Engl J Med. 2005 Mar 3;352(9):905-17.
Cooper DS. Approach to the patient with subclinical hyperthyroidism. J Clin Endocrinol Metab. 2007 Jan;92(1):3-9.
Cooper DS. Hyperthyroidism. Lancet. 2003 Aug 9;362(9382):459-68.
Cooper DS, Biondi B. Subclinical thyroid disease. Lancet. 2012 Jan 20.
Costeira MJ, Oliveira P, Santos NC, et al. Psychomotor development of children from an **iodine-deficient region**. J Pediatr. 2011 Sep;159(3):447-53.
Counts D, Varma SK. Hypothyroidism in children. Pediatr Rev. 2009 Jul;30(7):251-8.
Dhillon-Smith RK, Middleton LJ, Sunner KK, et al. **Levothyroxine in Women with Thyroid Peroxidase Antibodies** before Conception. N Engl J Med. 2019 Mar 23.
Dhital R, Basnet S, Poudel DR. Impact of **Hypothyroidism on Occurrence and Outcome of Acute Coronary Syndrome** from the National Inpatient Sample. Am J Cardiol. 2017 Dec 15;120(12):2160-2163.
Durante C, Costante G, Lucisano G, et al. The **natural history of benign thyroid nodules**. JAMA. doi:10.1001/jama.2015.0956.
Davies Louise; Welch H. Gilbert. **Thyroid Cancer** Survival in the United States: Observational Data From 1973 to 2005. Arch Otolaryngol Head Neck Surg. 2010;136(5):440-444.
Davies L, Welch HG. Current **Thyroid Cancer** Trends in the United States. JAMA Otolaryngol Head Neck Surg. 2014 Feb 20.
Davis FB, LaMantia RS, Spaulding SW, Wehmann RE, Davis PJ. **Estimation of a physiologic replacement** dose of levothyroxine in elderly patients with hypothyroidism. Arch Intern Med. 1984; 144(9):1752-4.

Davies L, Hendrickson CD, Hanson GS. Experience of US Patients Who Self-identify as Having an **Overdiagnosed Thyroid Cancer**: A Qualitative Analysis. JAMA Otolaryngol Head Neck Surg. 2017 Mar 9.
De Groot L, Abalovich M, Alexander EK, et al. 2012 Management of thyroid dysfunction during **pregnancy and postpartum: an Endocrine Society clinical practice guideline**. J Clin Endocrinol Metab 97:2543–2565.
De Leo S, Pearce EN. **Autoimmune thyroid disease during pregnancy**. Lancet Diabetes Endocrinol. 2017 Dec 12.
De Pergola G, Ciampolillo A, Alò D, et al. Free Triiodothyronine is associated with **smoking** habit, independently of obesity, body fat distribution, insulin, and metabolic parameters. J Endocrinol Invest. 2010 Jul 13.
Dickens LT, Cifu AS, Cohen RN. Diagnosis and Management of **Thyroid Disease During Pregnancy and the Postpartum Period**. JAMA. 2019 May 3.
Dickerman AL, Barnhill JW. **Abnormal thyroid function tests in psychiatric patients**: a red herring? Am J Psychiatry. 2012 Feb 1;169(2):127-33.
Drake MT. **Hypothyroidism in Clinical Practice**. Mayo Clin Proc. 2018 Sep;93(9):1169-1172.
Drugs for thyroid disorders. Treat Guidel Med Lett. 2009 Aug;7(84):57-64; quiz 2p following 64.
Du Puy R, Poortvliet RKE, Snel M, et al. Associations of **elevated anti-TPO antibodies** with thyroid function, survival, functioning and depressive symptoms in the oldest old: the Leiden 85-plus Study. Thyroid. 2019 Aug 6.
Duclos A, Peix JL, Colin C et al. Influence of **experience on performance of individual surgeons in thyroid surgery**: prospective cross sectional multicentre study. BMJ. 2012 Jan 10;344:d8041.
Durante C, Grani G, Lamartina L, et al. The Diagnosis and Management of **Thyroid Nodules**: A Review. JAMA. 2018 Mar 6;319(9):914-924.
Escobar-Morreale HF, Botella-Carretero JI, Gómez-Bueno M, Galán JM, Barrios V, Sancho J. Thyroid hormone replacement therapy in primary hypothyroidism: a randomized trial comparing L-thyroxine plus liothyronine with L-thyroxine alone. Ann Intern Med. 2005 Mar 15;142(6):412-24.
Faber J, Galløe AM. Changes in bone mass during prolonged subclinical hyperthyroidism due to L-thyroxine treatment: a meta-analysis. Eur J Endocrinol. 1994 Apr;130(4):350-6.
Fagin JA, Wells SA Jr. Biologic and Clinical Perspectives on **Thyroid Cancer**. N Engl J Med. 2016 Sep 15;375(11):1054-67
FDA Propylthiouracil-Induced Liver Failure June/09 FDA has identified 32 AERS cases (22 adult and 10 pediatric) of serious liver injury associated with propylthiouracil use. Of the adult cases, 12 deaths and 5 liver transplants occurred. Among the pediatric patients, 1 case resulted in death and 6 in liver transplants. In contrast, for methimazole 5 AERS cases of serious liver injury were identified. All five cases were in adult patients and 3 resulted in death. (**April 21, 2010**: Propylthiouracil: FDA has added a Boxed Warning to the label for propylthiouracil, to include information about reports of severe liver injury and acute liver failure, some of which have been fatal, in adult and pediatric patients using this medication. A boxed warning has been added to the hyperthyroidism drug propylthiouracil (PTU) to alert clinicians about the drug's risk for severe liver injury, the FDA announced on Wednesday. The new labeling is based in part on postmarketing safety reports of severe liver injury — including 15 deaths — in 23 adult and 11 pediatric patients taking PTU. A warning about the potential dangers of the drug was issued by the agency last June. The FDA recommends that PTU only be used in patients who cannot tolerate methimazole or other treatments for hyperthyroidism and in women just before and during their first trimester of pregnancy. Patients will now receive a medication guide upon filling a prescription for PTU. FDA drug safety communication)
FDA Nov/15: advising that rare cases of **underactive thyroid have been reported in infants following the use of contrast media containing iodine**, also called "contrast dye," for X-rays and other medical imaging procedures. In all of the reported cases, the infants were either premature or had other serious underlying medical conditions. Available evidence leads FDA to believe that this rare occurrence is usually temporary and resolves without treatment or any lasting effects. See the Drug Safety Communication for a data summary and a list of approved Approved Iodinated Contrast Media Products.
FDA Aug/18: alerts drug makers of a recall of porcine thyroid API from Sichuan Friendly Pharmaceutical Co., Limited, China was just added to the FDA Recalls webpage.
Fiore E, Rago T, Provenzale MA, Scutari M, et al. L-thyroxine-treated patients with **nodular goiter** have lower serum TSH and lower frequency of **papillary thyroid cancer**: results of a cross-sectional study on 27 914 patients. Endocr Relat Cancer. 2010 Feb 18;17(1):231-9.
Fleiner HF, Bjøro T, Midthjell K, et al. Prevalence of **thyroid dysfunction in autoimmune and type 2 diabetes**. The population-based **HUNT** Study in Norway. J Clin Endocrinol Metab. 2015 Nov 19:jc20153235.
Fournier JP, Yin H, Yu OH, et al. **Metformin and low levels of thyroid-stimulating hormone** in patients with type 2 diabetes mellitus. CMAJ. 2014 Sep 22.
Franklyn JA, Maisonneuve P, Sheppard M, Betteridge J, Boyle P. Cancer incidence and mortality after radioiodine treatment for hyperthyroidism: a population-based cohort study. Lancet. 1999 Jun 19;353(9170):2111-5.
Friedman, Diana, Richard L. Reed, and Arshag D. Mooradian. The **prevalence of overmedication** with levothyroxine in **ambulatory elderly** patients. Age 1992 15(1):9-13.
Gaitonde DY, Rowley KD, and Sweeny LB. **Hypothyroidism**: An Update. Am Fam Physician. 2012;86(3):244-251.
Garin MC, Arnold AM, Lee JS, et al. **Subclinical thyroid dysfunction** and **hip fracture** and bone mineral density in older adults: the cardiovascular health study. J Clin Endocrinol Metab. 2014 Aug;99(8):2657-64.
Gastaldi R, Poggi E, Mussa A, Weber et al. **Graves Disease in Children**: Thyroid-Stimulating Hormone Receptor Antibodies as Remission Markers. J Pediatr. 2014 Feb 8
Gerdes AM, Iervasi G. Thyroid replacement therapy and **heart failure**. Circulation. 2010 Jul 27;122(4):385-93.
Gencer B, Collet TH, Virgini V, et al. **Subclinical Thyroid Dysfunction and the Risk of Heart Failure** Events: An Individual Participant Data Analysis from Six Prospective Cohorts. Circulation. 2012 Jul 19.
Gharib H, Papini E, Garber JR,et al; **AACE/ACE/AME** Task Force on Thyroid Nodules. American Association of Clinical Endocrinologists and American College of Endocrinology-Association Medici Endo-Guidelines: Diagnosis and Management of **Thyroid Nodules**-2016 Update . Endocr Pract. 2016 May;22(5):622-39.
Glinoer D, Riahi M, Grün JP, Kinthaert J. Risk of **subclinical hypothyroidism in pregnant** women with asymptomatic autoimmune thyroid disorders. *J Clin Endocrinol Metab* 1994;79:197-204.
Giovanella L. Increased cancer incidence after radioiodine treatment for hyperthyroidism. Cancer. 2008 Jan 1;112(1):220; author reply 220-1.
Giri A, Edwards TL, LeGrys VA, et al. **Subclinical hypothyroidism** and risk for incident ischemic stroke among postmenopausal women. Thyroid. 2014 Aug;24(8):1210-7.
Glatstein MM, Garcia-Bournissen F, Giglio N, Finkelstein Y, Koren G. Pharmacologic treatment of hyperthyroidism during lactation. Can Fam Physician. 2009 Aug;55(8):797-8.
Glinoer D, de Nayer P, Bex M; Belgian Collaborative Study Group on Graves' Disease. Effects of l-thyroxine administration, TSH-receptor antibodies and smoking on the risk of recurrence in Graves' hyperthyroidism treated with antithyroid drugs: a double-blind prospective randomized study. Eur J Endocrinol. 2001 May;144(5):475-83.
Goffredo P, Thomas SM, Dinan MA, et al. Patterns of use and cost for inappropriate **radioactive iodine** treatment for thyroid cancer in the United States: use and misuse. JAMA Intern Med. 2015 Apr 1;175(4):638-40.
Granfors M, Akerud H, Skogö J, et al. **Targeted thyroid testing during pregnancy** in clinical practice. Obstet Gynecol. 2014 Jul;124(1):10-5.
Grant CS. **Papillary Thyroid Cancer**: Strategies for Optimal Individualized Surgical Management. Clin Ther. 2014 Apr 30.
Grogan RH, Mitmaker EJ, Hwang J, et al. A Population-Based Prospective Cohort Study of Complications after **Thyroidectomy in the Elderly**. J Clin Endocrinol Metab. 2012 Mar 14.
Guldvog I, Reitsma LC, Johnsen L, et al. Thyroidectomy Versus Medical Management for **Euthyroid Patients With Hashimoto Disease and Persisting Symptoms**: A Randomized Trial. Ann Intern Med. 2019 Mar 12.
Gupta A, Ly S, Castroneves LA, et al. How Are **Childhood Thyroid Nodules Discovered**: Opportunities for Improving Early Detection. J Pediatr. 2013 Dec 14
Gupta A, Arora N, Gruntmanis U. **Unnecessary Thyroid Ultrasonography in the Evaluation of Laboratory Thyroid Abnormalities**. JAMA Intern Med. 2017 Oct 30.
Haentjens P, Van Meerhaeghe A, Poppe K, Velkeniers B. Subclinical thyroid dysfunction and mortality: an estimate of relative and absolute excess all-cause mortality based on time-to-event data from cohort studies. Eur J Endocrinol. 2008 Sep;159(3):329-41.
Hanley P, Lord K, Bauer AJ. **Thyroid Disorders in Children and Adolescents**: A Review. JAMA Pediatr. 2016 Oct 1;170(10):1008-1019
Harjai KJ, Licata AA. Effects of **amiodarone** on thyroid function. Ann Intern Med. 1997 Jan 1;126(1):63-73.
Hayley B, Birnie D, Chow BJ. Cardiac effects of **panhypopituitarism** in a 71-year-old woman. CMAJ. 2014 Mar 18;186(5):366-9.
Haymart MR, Banerjee M, Stewart AK, et al.Use of **radioactive iodine for thyroid cancer**. JAMA. 2011 Aug 17;306(7):721-8.
Health Canada Nov/11 is advising Canadians not to use these foreign health products as they may pose a health risk. **1. Metabolic Advantage** The Singapore Health Sciences Authority warned that this weight-loss product contains prescription drugs (thyroid hormones).
Health Canada May/14 has requested a stop sale and recall of the product "**Thyroid Gland**" (NPN 80044198). The action has been taken because the product contains the prescription drug ingredient thyroid.
Hirshoren N, Kaganov K, Weinberger JM, et al. **Thyroidectomy Practice After Implementation of the 2015 American Thyroid Association Guidelines** on Surgical Options for Patients With Well-Differentiated Thyroid Carcinoma. JAMA Otolaryngol Head Neck Surg. 2018 Mar 29.

Ho AL, Grewal RK, Leboeuf R, Sherman EJ, et al. **Selumetinib**-enhanced radioiodine uptake in advanced thyroid **cancer**. N Engl J Med. 2013 Feb 14;368(7):623-32.
Hoang TD, Olsen CH, Mai VQ, et al. **Desiccated thyroid extract compared with levothyroxine** in the treatment of hypothyroidism: a randomized, double-blind, crossover study. J Clin Endocrinol Metab. 2013;98:1982-90.
Holsinger FC, Ramaswamy U, Cabanillas ME, et al. Measuring the Extent of **Total Thyroidectomy for Differentiated Thyroid Carcinoma** Using Radioactive Iodine Imaging: Relationship With Serum Thyroglobulin and Clinical Outcomes. JAMA Otolaryngol Head Neck Surg. 2014 Apr 3.

Howe CG, Eckel SP, Habre R, et al. Association of **Prenatal Exposure to Ambient and Traffic-Related Air Pollution With Newborn Thyroid Function**- Findings From the Children's Health Study. JAMA Netw Open. 2018;1(5):e182172.
Hung CL, Yeh CC, Sung PS, et al. Is Partial or **Total Thyroidectomy Associated with Risk of Long-Term Osteoporosis**: A Nationwide Population-Based Study. World J Surg. 2018 Mar 14.
Hung SH, Chung SD, Lin HC. **Thyroxin Use is Associated with Increased Risk of Thyroid Cancer** in Patients with Hypothyroidism. Journal Clinical Pharmacology. 2017;00:1-5.
Hung ML, Wu JX, Li N, et al. Association of Radioactive **Iodine** Administration After Reoperation With Outcomes Among Patients With **Recurrent or Persistent Papillary Thyroid Cancer**. JAMA Surg. 2018 Aug 15.
Iglesias P, Ridruejo E, Muñoz A, et al. **Thyroid Function Tests and Mortality in Aged Hospitalized Patients**: A 7-Year Prospective Observational Study. J Clin Endocrinol Metab. 2013 Oct 30.
Ikomi C, Cole CR, Vale E, et al. **Hypothyroidism and Iodine Deficiency** in Children on Chronic Parenteral Nutrition. Pediatrics. 2018 Mar 1.
Imaizumi M, Ohishi W, Nakashima E, et al. Association of **Radiation Dose With Prevalence of Thyroid Nodules** Among Atomic Bomb Survivors Exposed in Childhood (2007-2011). JAMA Intern Med. 2014 Dec 29.
Inoue M, Arata N, Koren G, Ito S. Hyperthyroidism during pregnancy. Can Fam Physician. 2009 Jul;55(7):701-3.
Iyer NG, Morris LG, Tuttle RM, et al. Rising incidence of **second cancers in patients with low-risk (T1N0) thyroid cancer who receive radioactive iodine** therapy. Cancer. 2011 Oct 1;117(19):4439-46.
Jansen TA, Korevaar TIM, Mulder TA, et al. **Maternal thyroid function** during pregnancy and child brain morphology: a time window-specific analysis of a prospective cohort. Lancet Diabetes Endocrinol. 2019 Jun 28.
Jefferys A, Vanderpump M, Yasmin E. **Thyroid Dysfunction and Reproductive Health**. The Obstetrician and Gynaecologist.2015;17:39-45
Jin J. **Screening for Thyroid Cancer**. JAMA. 2017 May 9;317(18):1920
Johns LE, Ferguson KK, Cantonwine DE, et al. **Subclinical Changes in Maternal Thyroid Function** Parameters in Pregnancy and Fetal Growth. J Clin Endocrinol Metab. 2017 Dec 26.
Jonklaas J, Bianco AC, Bauer AJ, et al. GUIDELINES FOR THE **TREATMENT OF HYPOTHYROIDISM**. Thyroid. 2014 Sep 29. (American Thyroid Association)
Kaluarachchi DC, Allen DB, Eickhoff JC, et al. Thyroid-Stimulating Hormone **Reference Ranges for Preterm Infants**. Pediatrics. 2019 Jul 16.
Kannan L, Shaw PA, Morley MP, et al. Thyroid Dysfunction in **Heart Failure and Cardiovascular Outcomes**. Circ Heart Fail. 2018 Dec;11(12):e005266.
Karch A, Thomas SL. **Autoimmune thyroiditis** as a risk factor for **stroke**: A historical cohort study. Neurology. 2014 Apr 9.
Kelly DM, Lynch T, Casserly LF. **Abdominal tremor in thyrotoxicosis**. Neurology. 2017 Sep 26;89(13):1424-1425.
Kharlip J, Cooper DS. Recent developments in hyperthyroidism. Lancet. 2009 Jun 6;373(9679):1930-2.
Kilberg MJ, Rasooly IR, LaFranchi SH, et al. **Newborn Screening** in the US May Miss Mild Persistent **Hypothyroidism**. J Pediatr. 2018 Jan;192:204-208.
Kim BB, Ku YH, Han JY, et al. Relation of **Triiodothyronine to Subclinical Myocardial Injury** in Patients With Chest Pain. Am J Cardiol. 2013 Jan 30.
Klein Hesselink EN, Klein Hesselink MS, de Bock GH, et al. Long-Term **Cardiovascular Mortality** in Patients With Differentiated **Thyroid Carcinoma**: An Observational Study. J Clin Oncol. 2013 Oct 7.
Klubo-Gwiezdzinska J, Auh S, Gershengorn M, et al. Association of **Thyrotropin Suppression With Survival Outcomes** in Patients With Intermediate- and High-Risk Differentiated **Thyroid Cancer**. JAMA Netw Open. 2019 Feb 1;2(2):e187754.
Kluijfhout WP, Rotstein LE, Pasternak JD. **Well-differentiated thyroid cancer**: Thyroidectomy or lobectomy? CMAJ. 2016 Dec 6;188(17-18):E517-E520
Know MA. **Thyroid Nodules**. Am Fam Physician. 2013;88(3):193-196.
Korevaar TI, Chaker L, Jaddoe VW, et al. **Maternal and Birth Characteristics are Determinants of Offspring Thyroid Function**. J Clin Endocrinol Metab. 2015 Nov 19
Korevaar TIM, Derakhshan A, Taylor PN, et al. Association of Thyroid Function **Test Abnormalities and Thyroid Autoimmunity** With Preterm Birth: A Systematic Review and Meta-analysis. JAMA. 2019 Aug 20;322(7):632-641.
Korzeniewski SJ, Grigorescu V, Kleyn M et al. Transient Hypothyroidism at 3-Year Follow-Up among Cases of Congenital Hypothyroidism Detected by **Newborn Screening**. J Pediatr. 2012 Aug 7.
Korzeniewski SJ, Grigorescu V, Kleyn M, et al. Performance metrics after changes in screening protocol for **congenital hypothyroidism**. Pediatrics. 2012 Nov;130(5):e1252-60.
Kumar P, De P. **Elephantiasic pretibial myxoedema**. BMJ. 2018;360:k945
Kuroda M, Kuroda K, Segawa T, et al. **Levothyroxine supplementation** improves serum anti-Müllerian hormone levels in **infertile** patients with Hashimoto's thyroiditis. J Obstet Gynaecol Res. 2018 Jan 3.
Labourier E, Shifrin A, Busseniers AE, et al. **Molecular testing** for miRNA, mRNA and DNA on fine needle aspiration improves the preoperative **diagnosis of thyroid nodules** with indeterminate cytology. J Clin Endocrinol Metab. 2015 May 12:
Ladenson, Paul W., Kristensen, Jens D., Ridgway, E. Chester, et al. Use of the Thyroid Hormone Analogue **Eprotirome** in Statin-Treated Dyslipidemia. N Engl J Med 2010 362: 906-916.
LaFranchi S. Treatment and prognosis of congenital hypothyroidism . In: UpToDate Online. UpToDate Waltham, MA. Available from: www.uptodate.com (accessed September 2009).
Liamis G, Filippatos TD, Liontos A, Elisaf MS. Management of Endocrine Disease: **Hypothyroidism-associated hyponatremia**: Mechanisms, implications and treatment. Eur J Endocrinol. 2016 Aug 2.
Lain SJ, et al. Association between **borderline neonatal thyroid-stimulating hormone concentrations** and educational and developmental outcomes: a population-based record-linkage study. Lancet Diabetes Endo. 2016 Jul 21.
Laurberg P, Wallin G, Tallstedt L, Abraham-Nordling M, Lundell G, Tørring O. TSH-receptor autoimmunity in Graves' disease after therapy with anti-thyroid drugs, surgery, or radioiodine: a 5-year prospective randomized study. Eur J Endocrinol. 2008 Jan;158(1):69-75.
Lawrence N, Cheetham T, Elder C. **How do paediatricians use and monitor antithyroid drugs** in the UK? A clinician survey. Clin Endocrinol (Oxf). 2019 Jun 10.
Lazarus JH, Bestwick JP, Channon S, et al. **Antenatal thyroid screening** and childhood cognitive function. N Engl J Med 2012; 366:493-50. Prenatal screening and treatment for hypothyroidism do not lead to improved cognitive function in offspring at age 3 years.
Lee JY, Chung JH, Lee YJ, et al. **Propylthiouracil-induced nonspecific interstitial pneumonia**. Chest. 2011 Mar;139(3):687-90.
LeFevre ML. **Screening for Thyroid Dysfunction**: U.S. Preventive Services Task Force (**USPSTF**) Recommendation Statement. Ann Intern Med. 2015 Mar 24.
Levie D, Korevaar TIM, Bath SC, et al. **Thyroid Function in Early Pregnancy**, Child IQ, and Autistic Traits: a Meta-analysis of Individual-participant Data. J Clin Endocrinol Metab. 2018 May 10.
L'Heureux A, Wieland DR, Weng CH, et al. Association Between **Thyroid Disorders and Colorectal Cancer Risk** in Adult Patients in Taiwan. JAMA Netw Open. 2019 May 3;2(5):e193755.
Lim H, Devesa SS, Sosa JA, et al. **Trends in Thyroid Cancer** Incidence and Mortality in the United States, 1974-2013. JAMA. 2017 Mar 31.
Liu JB, Sosa JA, Grogan RH, et al. Variation of **Thyroidectomy**-Specific Outcomes Among Hospitals and Their Association With Risk Adjustment and Hospital Performance. JAMA Surg. 2017 Nov 29:e174593.
Lucas-Herald A, Jones J, Attaie M, et al. Diagnostic and Predictive Value of **Ultrasound and Isotope Thyroid Scanning**, Alone and in Combination, in Infants Referred with Thyroid-Stimulating Hormone Elevation on **Newborn Screening**. J Pediatr. 2014 Jan 9
Luft MJ, Aldrich SL, Poweleit E, et al. Thyroid Function Screening in **Children and Adolescents With Mood and Anxiety Disorders**. J Clin Psychiatry. 2019 Aug 6;80(5).
Ma C, Xie J, Wang H, Li J, Chen S. **Radioiodine therapy versus antithyroid medications for Graves' disease.** Cochrane Database Syst Rev. 2016;(2):CD010094. The only antithyroid drug investigated in the two included trials was methimazole, which might limit the applicability of our findings with regard to other compounds such as propylthiouracil. Results from two RCTs suggest that radioiodine treatment is associated with an increased risk of Graves' ophthalmopathy. Our findings suggest some benefit from radioiodine treatment for recurrence of hyperthyroidism (relapse) but there is uncertainty about the magnitude of the effect size.
Mallick U, Harmer C, Yap B, et al. Ablation with **low-dose radioiodine and thyrotropin alfa in thyroid cancer**. N Engl J Med 2012;366:1674-85.

Manning SC. Rethinking the **Growth Pattern of Thyroid Cancer** in Young Patients Based on the Fukushima Database. JAMA Otolaryngol Head Neck Surg. 2017 Nov 16.
Marcocci Claudio, Kahaly George J, Krassas Gerasimos E., et al. for the European Group on Graves' Orbitopathy. **Selenium and the Course of Mild Graves' Orbitopathy**. N Engl J Med 2011; 364:1920-1931.
Martin AT, Pinney SM, Xie C, et al. **Headache Disorders** May Be a Risk Factor for the Development of New Onset **Hypothyroidism**. Headache. 2016 Sep 27.
Marwali EM, Boom CE, Budiwardhana N, et al. Oral **Triiodothyronine** for Infants and Children **Undergoing Cardiopulmonary Bypass**. Ann Thorac Surg. 2017 Feb 6.
Marx H, Amin P, Lazarus JH. Hyperthyroidism and pregnancy. BMJ. 2008 Mar 22;336(7645):663-7.
Mascarella MA, Milad D, Richardson K, et al**. Preoperative Risk Index** Among Patients Undergoing Thyroid or Parathyroid Surgery. JAMA Otolaryngol Head Neck Surg. 2019 Sep 5.
Maynard MA, Marino-Enriquez A, Fletcher JA, et al. Thyroid hormone inactivation in **gastrointestinal stromal tumors**. N Engl J Med. 2014 Apr 3;370(14):1327-34.
McAninch EA, Rajan KB, Miller CH, et al. Systemic **Thyroid Hormone Status During Levothyroxine Therapy In Hypothyroidism**: A Systematic Review and Meta-Analysis. J Clin Endocrinol Metab. 2018 Aug 15.
McGrath N, Hawkes CP, McDonnell CM, et al. Incidence of **Congenital Hypothyroidism Over 37 Years in Ireland**. Pediatrics. 2018 Sep 21.
McLeod DS, Caturegli P, Cooper DS, et al. Variation in rates of autoimmune thyroid disease by **race/ethnicity** in US military personnel. JAMA. 2014 Apr 16;311(15):1563-5
McNally LJ, Ofiaeli CI, Oyibo SO. **Treatment-refractory hypothyroidism**. BMJ. 2019 Feb 25;364:l579.
McQueen MJ. Laboratory Reference Intervals: SI and Traditional Units. E-Therapeutics Online. Canadian Pharmacists Association. Ottawa, Ontario. www.e-therapeutics.ca (accessed September 2009).
Medical Letter, Inc. **Drugs for Hypothyroidism**. Treat Guidel Med Lett.. 2015;57(1480):147-50.
Medici M, Timmermans S, Visser W, et al. **Maternal thyroid hormone parameters during early pregnancy** and birth weight: the Generation R Study. J Clin Endocrinol Metab. 2013 Jan;98(1):59-66.
Medici M, Direk N, Visser WE, et al. Thyroid Function Within the Normal Range and the Risk of **Depression**: A Population-Based Cohort Study. J Clin Endocrinol Metab. 2014 Feb 24
Meltzer C, Hull M, Sundang A, Adams JL. Association Between Annual Surgeon **Total Thyroidectomy Volume and Transient and Permanent Complications**. JAMA Otolaryngol Head Neck Surg. 2019 Jul 25.
Meng X, Xu S, Chen G, Derwahl M, Liu C. **Metformin and thyroid disease**. J Endocrinol. 2017 Feb 14.
Metso S, Auvinen A, Huhtala H, Salmi J, Oksala H, Jaatinen P. Increased cancer incidence after radioiodine treatment for hyperthyroidism. Cancer. 2007 May 15;109(10):1972-9.
Metso S, Jaatinen P, Huhtala H, Auvinen A, Oksala H, Salmi J. Increased cardiovascular and cancer mortality after radioiodine treatment for hyperthyroidism. J Clin Endocrinol Metab. 2007 Jun;92(6):2190-6.
Meuwese CL, Gussekloo J, de Craen AJ, et al. **Thyroid status** and **renal function** in **older** persons in the general population. J Clin Endocrinol Metab. 2014 Aug;99(8):2689-96.
Mitchell JE, Hellkamp AS, Mark DB, et al. Thyroid function in **heart failure** and impact on mortality. JACC Heart Fail 2013; 1:48-55.
Modesto T, Tiemeier H, et al. **Maternal Mild Thyroid Hormone Insufficiency in Early Pregnancy and Attention deficit/ Hyperactivity Disorder** Symptoms in Children. JAMA Pediatr. 2015 Sep 1;169(9):838-845.
Mohamed M, Fernando R, Arora A. **Airway obstruction** after the development of **Hashimoto's thyroiditis**. BMJ. 2014 Feb 24;348:g1643.
Moleti M, Trimarchi F, Tortorella G, et al. Effects of **Maternal Iodine Nutrition and Thyroid Status** on Cognitive Development in Offspring: A Pilot Study. Thyroid. 2016 Feb;26(2):296-305.
Morris LG, Tuttle RM, Davies L. Changing Trends in the Incidence of **Thyroid Cancer** in the United States. JAMA Otolaryngol Head Neck Surg. 2016 Apr 14
Moubayed SP, Urken ML. **Thyroid nodules**. CMAJ. 2016 Dec 6;188(17-18):1259.
Muller I, Premawardhana LD. **Hypercalcaemia with undetectable parathormone levels**. BMJ. 2018 Nov 8;363:k4074. (Graves disease)
Nakamura H et al. Comparison of methimazole and propylthiouracil in patients with hyperthyroidism caused by Graves' disease. J Clin Endocrinol Metab. 2007 Jun;92(6):2157 -62.
Negro R, Formoso G, Mangieri T, et al. **Levothyroxine** treatment in **euthyroid pregnant women** with autoimmune thyroid disease: effects on obstetrical complications. *J Clin Endocrinol Metab* 2006;91:2587-91.
Negro R, Schwartz A, Gismondi R, et al. **Increased Pregnancy Loss Rate** in Thyroid Antibody Negative Women with TSH Levels between 2.5 and 5 in the First Trimester of Pregnancy. J Clin Endocrinol Metab.2010Jun 9.
Nelson S, Haig C, McConnachie A, etal . **Maternal thyroid function and child educational attainment**: prospective cohort study. BMJ 2018;360:k452. 10.1136/bmj.k452.
Newman CM, Price A, Davies DW, Gray TA, Weetman AP. **Amiodarone** and the thyroid: a practical guide to the management of thyroid dysfunction induced by amiodarone therapy. Heart. 1998 Feb;79(2):121-7.
Nexo MA, Watt T, Pedersen J, et al. Increased Risk of **Long-Term Sickness Absence**, Lower Rate of **Return to Work**, and Higher Risk of **Unemployment** and Disability Pensioning for Thyroid Patients: A Danish Register-Based Cohort Study. J Clin Endocrinol Metab. 2014 Jun 17:jc20134468.
Ng SM, Anand D, Weindling AM. High versus low dose of initial thyroid hormone replacement for congenital hypothyroidism. *Cochrane Database of Systematic Reviews* 2009, Issue 1. Art. No.: CD006972. DOI: 10.1002/14651858.CD006972.pub2.
Nolte MR, Muller R, Siggelkow H, et al. **Prophylactic application of thyrostatic drugs during excessive iodine exposure** in euthyroid patients with thyroid autonomy: a randomized study. Eur J Endocrinol. 1996;134(3):337-341.
Oakley GM, Curtin K, Pimentel R, et al. Establishing a Familial Basis for Papillary **Thyroid Carcinoma** Using the Utah Population Database. JAMA Otolaryngol Head Neck Surg. 2013 Oct 3.
Ohtsuru A, Midorikawa S, Ohira T, et al. Incidence of **thyroid cancer among children and young adults in Fukushima**, Japan, screened with 2 rounds of ultrasonography within 5 years of the 2011 Fukushima Daiichi nuclear power station accident [online Nov 29, 2018]. JAMAOtolaryngol Head Neck Surg. doi:**10.1001/jamaoto.2018.3121**
Orouji Jokar T, Fourman LT, Lee H, et al. **Higher TSH levels** within the normal range are associated with unexplained **infertility**. J Clin Endocrinol Metab. 2017 Dec 19.
Othman RA, Myrie SB, Mymin D, et al. **Thyroid Hormone Status in Sitosterolemia Is Modified by Ezetimibe**. J Pediatr. 2017 Jun 15.
Overcash RT, Marc-Aurele KL, Hull AD, Ramos GA. **Maternal Iodine Exposure**: A Case of Fetal Goiter and Neonatal Hearing Loss. Pediatrics. 2016 Mar 22.
Pajamäki N, Metso S, Hakala T, et al. Long-term **cardiovascular morbidity** and mortality in patients treated for **differentiated thyroid cancer**. Clin Endocrinol (Oxf). 2017 Nov 20.
Park S, Oh C, Cho H, et al. Association between **screening and the thyroid cancer "epidemic**" in South Korea: evidence from a nationwide study. BMJ 2016;355:i5745.
Pasqualetti G, Pagano G, Rengo G, Ferrara N, Monzani F. **Subclinical Hypothyroidism and Cognitive Impairment**: Systematic Review and Meta-Analysis. J Clin Endocrinol Metab. 2015;100(11):4240-8.
Patel D, Li P, Bauer AJ, Castelo-Soccio L. **Screening Guidelines for Thyroid Function in Children** With **Alopecia Areata**. JAMA Dermatol. 2017 Sep 27.
Patel KN, Angell TE, Babiarz J, et al. Performance of a **genomic sequencing classifier** for the preoperative diagnosis of cytologically **indeterminate thyroid nodules** [online May 23, 2018].JAMA Surg. doi:10.1001/jamasurg .2018.1153.
Pearce EN. Management of **Thyrotoxicosis: Preconception, Pregnancy, and the Postpartum Period**.Endocr Pract. 2018 Oct 5.
Perros P, Kendall-Taylor P, Neoh C, Frewin S, Dickinson J. A prospective study of the effects of radioiodine therapy for hyperthyroidism in patients with minimally active graves' ophthalmopathy. J Clin Endocrinol Metab. 2005 Sep;90(9):5321-3.
Persani L, Brabant G, Dattani M, et al. 2018 European Thyroid Association (ETA) Guidelines on the **Diagnosis and Management of Central Hypothyroidism**. Eur Thyroid J. 2018 Oct;7(5):225-237.
Peterson SJ, McAninch EA, Bianco AC. Is a **Normal TSH Synonymous** with "**Euthyroidism**" in **Levothyroxine Monotherapy**? J Clin Endocrinol Metab. 2016 Oct 4:jc20162660.
Plowden TC, Schisterman EF, Sjaarda LA, et al. **Thyroid stimulating hormone, anti-thyroid antibodies and pregnancy outcomes**. Am J Obstet Gynecol. 2017 Sep 13.
Pollock AJ, Seibert T, Allen DB. Severe and Persistent **Thyroid Dysfunction Associated with Tetracycline**-Antibiotic Treatment in Youth. J Pediatr. 2016 Apr 5
Pramyothin P, Leung AM, Pearce EN, Malabanan AO, Braverman LE. Clinical problem-solving. A hidden solution. N Engl J Med. 2011 Dec 1;365(22):2123-7.
Qian ZJ, Jin MC, Meister KD, Megwalu UC. **Pediatric thyroid cancer incidence** and mortality trends in the United States, 1973-2013 [online May 23, 2019]. JAMA Otolaryngol Head Neck Surg. doi:10.1001/jamaoto.2019.0898
Rawal S, Tsai MY, Hinkle SN, et al. A Longitudinal Study of **Thyroid Markers across Pregnancy** and the Risk of **Gestational Diabetes**. J Clin Endocrinol Metab. 2018 Jun 7.
Reiners C, Biko J, Haenscheid H, et al. Twenty-Five Years after **Chernobyl**: Outcome of **Radioiodine Treatment** in Children and Adolescents with Very-High-Risk Radiation-Induced Differentiated **Thyroid Carcinoma**. J Clin Endocrinol Metab. 2013 Apr 24.

Rhee CM, Bhan I, Alexander EK, Brunelli SM. Association between **iodinated contrast media exposure** and incident hyperthyroidism and hypothyroidism. Arch Intern Med. 2012;172(2):153-159.
Rijks JM, Plat J, Dorenbos E, et al. Association of **TSH With Cardiovascular Disease Risk in Overweight and Obese Children During** Lifestyle Intervention. J Clin Endocrinol Metab. 2017 Jun 1;102(6):2051-2058.
Rivkees SA, Mattison DR. **Ending propylthiouracil-induced liver failure** in children. N Engl J Med. 2009 Apr 9;360(15):1574-5.
Roberts L, McCahon D, Johnson O, et al. **Stability of thyroid function in older adults**: the Birmingham Elderly Thyroid Study. Br J Gen Pract. 2018 Oct;68(675):e718-e726.
Roberts L, McCahon D, Johnson O, et al. Stability of **thyroid function in older adults: the Birmingham Elderly Thyroid Study**. Br J Gen Pract. 2018 Oct;68(675):e718-e726.
Roos A, Linn-Rasker SP, van Domburg RT, Tijssen JP, Berghout A. The starting dose of levothyroxine in primary hypothyroidism treatment: a prospective, randomized, double-blind trial. Arch Intern Med. 2005 Aug 8 22;165(15):1714-20.
Rosenbaum RL, Barzel US. **Levothyroxine replacement dose for primary hypothyroidism decreases with age**. Ann Intern Med. 1982; 96(1):53-5
Rosenthal LJ, Goldner WS, O'Reardon JP. **T3 Augmentation** in Major Depressive Disorder: Safety Considerations. Am J Psychiatry 168:10, October 2011.
Ross DS. Thionamides in the treatment of Graves'disease. In: UpToDate Online. UpToDate Waltham, MA. Available from: www.uptodate.com (accessed September 2009).
Ross DS. Thyroid function in nonthyroidal illness. In: UpToDate Online. UpToDate Waltham, MA. Available from: www.uptodate.com (accessed September 2009).
Ross DS. Treatment of Hypothyroidism. In: UpToDate Online. UpToDate Waltham, MA. Available from: www.uptodate.com (accessed September 2009).
Ross DS. Treatment of Graves' Hyperthyroidism. In: UpToDate Online. UpToDate Waltham, MA. Available from: www.uptodate.com (accessed September 2009)
Ross DS. **Radioiodine therapy for hyperthyroidism**. N Engl J Med. 2011 Feb 10;364(6):542-50.
Rothberger GD, Gadhvi S, Michelakis N, et al. Usefulness of **Serum Triiodothyronine (T3) To Predict Outcomes in Patients Hospitalized With Acute Heart Failure**. American Journal of Cardiology. 2016.
Rugge JB, Bougatsos C, Chou R. **Screening and Treatment of Thyroid Dysfunction**: An Evidence Review for the U.S. Preventive Services Task Force (**USPSTF**). Ann Intern Med. 2014 Oct 28.
Sahli Z, Najafian A, Kahan S, et al. One-Hour Postoperative Parathyroid Hormone Levels Do Not Reliably Predict **Hypocalcemia After Thyroidectomy**. World J Surg. 2017 Dec 31.
Santoro AB, Struchiner CJ, Suarez-Kurtz G. **L-thyroxine doses** required for TSH suppression in patients with differentiated **thyroid cancer**: Effect of a novel UGT1 marker, rs11563250A > G. Br J Clin Pharmacol. 2016 Aug 16
Samuels MH, Kolobova I, Niederhausen M, et al. Effects of **Altering Levothyroxine (L-T4) Doses on Quality of Life, Mood, and Cognition** in L-T4 Treated Subjects. J Clin Endocrinol Metab. 2018 May 1;103(5):1997-2008.
Sattar N, Lazare F, Kacer M, et al. **Celiac disease** in children, adolescents, and young adults with autoimmune thyroid disease. J Pediatr. 2011 Feb;158(2):272-5.e1.
Sawicka-Gutaj N, Ruchala M, Feldt-Rasmussen U, et al. Patients with **benign thyroid diseases experience an impaired sex life**. Thyroid. 2018 Jul 24.
Sawka AM, Brierley JD, Ezzat S, et al. Managing newly diagnosed **thyroid cancer**. CMAJ. 2014 Mar 4;186(4):269-75.
Schlumberger M, Catargi B, Borget I, et al. Strategies of **radioiodine ablation in patients with low-risk thyroid cancer**. N Engl J Med 2012;366:1663-73.
Schlumberger M, Leboullex S, Catargi B, et al. Outcome after **ablation in patients with low-risk thyroid cancer** (**ESTIMABL1**): 5-year follow-up results of a randomised, phase 3, equivalence trial. Lancet Diabetes Endocrinol 2018; published online May 25.
Schlumberger M, Tahara M, Wirth LJ, et al. **Lenvatinib** versus placebo in radioiodine-refractory **thyroid cancer**. N Engl J Med. 2015 Feb 12;372(7):621-30.
Schvartz C, Bonnetain F, Dabakuyo S, et al. Impact on overall **survival of radioactive iodine in low-risk differentiated thyroid cancer** patients. J Clin Endocrinol Metab 2012 February 16
Scratch SE, Hunt RW, Thompson DK, et al. Free thyroxine levels after **very preterm birth and neurodevelopmental** outcomes at age 7 years. Pediatrics. 2014 Apr;133(4):e955-63.
Selvaraj S, Klein I, Danzi S, et al. Association of Serum **Triiodothyronine** With B-Type Natriuretic Peptide and Severe Left Ventricular **Diastolic Dysfunction in Heart Failure** With Preserved Ejection Fraction. Am J Cardiol. 2012 Apr 11.
Seo GH, Kim TH, Chung JH. **Antithyroid Drugs and Congenital Malformations**: A Nationwide Korean Cohort Study. Ann Intern Med. 2018 Jan 23.
Seymour M, Morton A. Unilateral facial swelling in a thyrotoxic patient. BMJ. 2017 Feb 9;356:j534.
Sharkia M, Michaud S, Berthier MT, et al. Thyroid function from birth to adolescence in **prader-willi syndrome**. J Pediatr. 2013 Sep;163(3):800-5.
Sharma A, Stan MN. **Thyrotoxicosis**: Diagnosis and Management. Mayo Clin Proc. 2019 Mar 25.
Shields B, Hill A, Bilous M, Knight B, Hattersley AT, Bilous RW, Vaidya B. Cigarette smoking during pregnancy is associated with alterations in maternal and fetal thyroid function. J Clin Endocrinol Metab. 2009 Feb;94(2):570-4.
Shin DW, Suh B, Lim H, et al. J-shaped Association between Post-operative **Levothyroxine Dosage and Fracture Risk** in Thyroid Cancer Patients: a Retrospective Cohort Study. J Bone Miner Res. 2018 Feb 15.
Siegmann EM, Müller HHO, Luecke C, et al. Association of **Depression and Anxiety Disorders With Autoimmune Thyroiditis**: A Systematic Review and Meta-analysis. JAMA Psychiatry. 2018 May 2.
Skelin M, Lucijanić T, Amidžić Klarić D, et al. Factors Affecting Gastrointestinal Absorption of Levothyroxine: A Review. Clin Ther. 2017 Jan 30.
Smith-Bindman R, Lebda P, Feldstein VA, et al. Risk of **Thyroid Cancer Based on Thyroid Ultrasound Imaging** Characteristics: Results of a Population-Based Study. JAMA Intern Med. 2013 Aug 26.
Smith TJ, Kahaly GJ, Ezra DG, et al. **Teprotumumab** for Thyroid-Associated **Ophthalmopathy**. N Engl J Med. 2017 May 4;376(18):1748-1761
Spaans E, Schroor E, Groenier K, et al. **Thyroid Disease and Type 1 Diabetes** in Dutch Children: A Nationwide Study (**Young Dudes-3**). J Pediatr. 2017 Jun 2
Spencer L, Bubner T, Bain E, et al. **Screening and subsequent management for thyroid dysfunction pre-pregnancy and during pregnancy for improving maternal and infant health**. Cochrane Database Syst Rev. 2015 Sep 21;9:CD011263. Based on the existing evidence, though universal screening for thyroid dysfunction in pregnancy increases the number of women diagnosed with hypothyroidism who can be subsequently treated, it does not clearly impact (benefit or harm) maternal and infant outcomes.While universal screening versus case finding for thyroid dysfunction increased diagnosis and subsequent treatment, we found no clear differences for the primary outcomes: pre-eclampsia or preterm birth. No clear differences were seen for secondary outcomes, including miscarriage and fetal or neonatal death; data were lacking for the primary outcome: neurosensory disability for the infant as a child, and for many secondary outcomes. Though universal screening versus no screening for hypothyroidism similarly increased diagnosis and subsequent treatment, no clear difference was seen for the primary outcome: neurosensory disability for the infant as a child (IQ < 85 at three years); data were lacking for the other primary outcomes: pre-eclampsia and preterm birth, and for the majority of secondary outcomes.For outcomes assessed using the GRADE approach the evidence was considered to be moderate or high quality, with any downgrading of the evidence based on the presence of wide confidence intervals crossing the line of no effect.More evidence is needed to assess the benefits or harms of different screening methods for thyroid dysfunction in pregnancy, on maternal, infant and child health outcomes. Future trials should assess impacts on use of health services and costs, and be adequately powered to evaluate the effects on short- and long-term outcomes.
Stagnaro-Green A, Roman SH, Cobin RH, el-Harazy E, Alvarez-Marfany M, Davies TF. Detection of **at-risk pregnancy** by means of highly sensitive assays for thyroid autoantibodies. *JAMA* 1990;264:1422-5.
Stagnaro-Green A, Abalovich M, Alexander E, et al. Guidelines of the American Thyroid Association (**ATA**) for the diagnosis and management of **thyroid disease during pregnancy** and postpartum. Thyroid 2011;21.
Stagnaro-Green A. **Screening pregnant women for overt thyroid disease**. JAMA. 2015 Feb 10; 313(6):565-6.
Stuckey B, Kent G, Ward L, Brown S, Walsh J. **Postpartum thyroid dysfunction** and the long-term risk of **hypothyroidism**: results from a 12 year follow-up study of women with and without postpartum thyroid dysfunction. Clin Endocrinol (Oxf). 2010 Feb 23. Women who present with postpartum hypothyroidism or have positive TPOAb are at particularly high risk.
Sweeney LB, Stewart C, Gaitonde DY. **Thyroiditis**: An Integrated Approach. Am Fam Physician. 2014;90(6):389-396.
Tallstedt L, Lundell G, Tørring O, Wallin G, Ljunggren JG, Blomgren H, Taube A. Occurrence of ophthalmopathy after treatment for Graves' hyperthyroidism. The Thyroid Study Group. N Engl J Med. 1992 Jun 25;326(26):1733-8.
Taylor PN, Albrecht D, Scholz A, et al. **Global epidemiology of hyperthyroidism and hypothyroidism**. Nat Rev Endocrinol. 2018;14:301-316.
Taylor PN, Minassian C, Rehman A, et al. **TSH Levels and Risk of Miscarriage** in Women on Long-Term Levothyroxine: A Community-Based Study. J Clin Endocrinol Metab. 2014 Jul 24
Thangaratinam S, Tan A, Knox E, Kilby MD, Franklyn J, Coomarasamy A. Association between **thyroid autoantibodies and miscarriage and preterm** birth: meta-analysis of evidence. BMJ 2011;342:d2616.

Thayakaran R, Adderley NJ, Sainsbury C, et al. **Thyroid replacement therapy**, thyroid stimulating hormone concentrations, and long term health outcomes in patients with hypothyroidism: longitudinal study. BMJ. 2019 Sep 3;366:l4892.
Thyroid®. Product monograph. ERFA Canada. Available from: http://thyroid.erfa.net/index.php/en/thyroid-monograph.html (accessed September 2009).
Topliss DJ. Clinical Update in Aspects of the Management of **Autoimmune Thyroid Diseases**. Endocrinol Metab (Seoul). 2016 Dec;31(4):493-499.
Torlinska B, Nichols L, Mohammed MA, et al. Patients treated for hyperthyroidism are at increased **risk of becoming obese**: findings from a large prospective secondary care cohort. Thyroid. 2019 Aug 2.
Tuttle RM, Fagin JA, Minkowitz G, et al. **Natural history and tumor volume kinetics of papillary thyroid cancers** during active surveillance [online August 31, 2017]. JAMA Otolaryngol Head Neck Surg. doi:10.1001/jamaoto .2017.1442
Tzakas P, Sit SW. Progressive impairment of cognition and motor function: **Hashimoto encephalopathy**. CMAJ. 2011 Feb 14.
Ukrainski MB, Pribitkin EA, et al. Increasing Incidence of **Thyroid Nodules and Thyroid Cancer**: Does Increased Detection of a Subclinical Reservoir Justify the Associated Anxiety and Treatment? Clin Ther. 2015 Aug 17.
Vaidya B, Pearce SH. Management of hypothyroidism in adults. BMJ. 2008 Jul 28;337:a801. doi: 10.1136/bmj.a801.
Vaidya B, Pearce SH. Diagnosis and management of **thyrotoxicosis**. BMJ. 2014 Aug 21;349:g5128.
Valderrabano P, Khazai L, Thompson ZJ, et al. Association of **tumor size with histologic and clinical outcomes among patients with cytologically indeterminate thyroid nodules** [online July 19, 2018].JAMA Otolaryngol Head Neck Surg. doi:10.1001/jamaoto.2018.1070
Vanderpump MPJ, Lazarus JH, Smyth PP, et al, on behalf of the British Thyroid Association UK Iodine Survey Group. **Iodine status of UK schoolgirls**: a cross-sectional survey. *Lancet* 2011; published online June 2.
Vaccarella S, Franceschi S, Bray F, et al. **Worldwide Thyroid-Cancer Epidemic**? The Increasing Impact of **Overdiagnosis**. N Engl J Med. 2016 Aug 18;375(7):614-7
Vergamini LB, Frazier AL, Abrantes FL, et al. Increase in the Incidence of **Differentiated Thyroid Carcinoma** in **Children**, Adolescents, and Young Adults: A Population-Based Study. J Pediatr. 2014 Mar 12.
Virili C, Antonelli A, Santaguida MG, et al. **Gastrointestinal Malabsorption of Thyroxine**. Endocr Rev. 2018 Nov 23.
Vigone MC, Caiulo S, Di Frenna M, et al. Evolution of Thyroid Function in **Preterm Infants** Detected by Screening for **Congenital Hypothyroidism**. J Pediatr. 2014 Feb 8
Virgini VS, Rodondi N, Cawthon PM, Harrison SL, Hoffman AR, Orwoll ES, Ensrud KE, Bauer DC; **Osteoporotic Fractures** in Men (MrOS) Research Group. **Subclinical Thyroid Dysfunction** and Frailty Among Older Men. J Clin Endocrinol Metab. 2015;100(12):4524-32.
Viswanathan L, Vigersky RA. The effect of **herbal medications on thyroid hormone economy** and estrogen-sensitive hepatic proteins in a patient with prostate cancer. Arch Intern Med. 2012 Jan 9;172(1):58-60. (PC-SPES)
Vrijkotte TGM, Hrudey EJ, Tickler TB. Early maternal thyroid function during gestation is associated with fetal growth, particularly in male newborns. J Clin Endocrinol. Metab. 2017. Online
Walter MA, Briel M, Christ-Crain M, Bonnema SJ, Connell J, Cooper DS, Bucher HC, Müller-Brand J, Müller B. Effects of antithyroid drugs on radioiodine treatment: systematic review and meta-analysis of randomized controlled trials. BMJ. 2007 Mar 10;334(7592):514.
Walter MA, Christ-Crain M, Muller B. Graves' disease. N Engl J Med. 2008 Sep 25;359(13):1407; author reply 1409.
Wang H, Gao H, Chi H, et al. Effect of **Levothyroxine on Miscarriage** Among Women With Normal Thyroid Function and Thyroid Autoimmunity Undergoing In Vitro Fertilization and Embryo Transfer: A Randomized Clinical Trial. JAMA. 2017 Dec 12;318(22):2190-2198.
Waldenlind K, Saevarsdottir S, Bengtsson Cet al. Risk of **Thyroxine-Treated Autoimmune Thyroid Disease Associated With Disease Onset in Patients With Rheumatoid Arthritis**. JAMA Netw Open.2018;1(6):e183567.
Wallner LP, Reyes-Gastelum D, Hamilton AS, et al. **Patient-Perceived Lack of Choice in Receipt of Radioactive Iodine** for Treatment of Differentiated Thyroid Cancer. J Clin Oncol. 2019 Jul 8:JCO1802228.
Walshaw PD, Gyulai L, Bauer M, et al. **Adjunctive thyroid hormone treatment in rapid cycling bipolar disorder**: A double-blind placebo-controlled trial of levothyroxine (L-T(4)) and triiodothyronine (T(3)). Bipolar Disord. 2018 Jun 4.
Watanabe K, Kajiwara K. Spontaneous remission of a large **thyroid tumour**. (possible **methotrexate** reaction) CMAJ. 2016 Apr 5
Welch HG, Doherty GM. **Saving Thyroids - Overtreatment of Small Papillary Cancers**. N Engl J Med. 2018 Jul 26;379(4):310-312.
Welsh KJ, Soldin SJ. DIAGNOSIS OF ENDOCRINE DISEASE: **How reliable are free thyroid and total T3 hormone assays**? Eur J Endocrinol. 2016 Dec;175(6):R255-R263.
Wen LL, Lin LY, et al. Association Between Serum **Perfluorinated Chemicals** and Thyroid Function in U.S. Adults: The National Health and Nutrition Examination Survey 2007-2010. J Clin Endocrinol Metab. 2013 Jul 17.
Wirth LJ, Ross DS, Randolph GW, et al. Case records of the Massachusetts General Hospital. Case 5-2013. A 52-year-old woman with a **mass in the thyroid**. N Engl J Med. 2013 Feb 14;368(7):664-73.
Wirth CD, Blum MR, da Costa BR, et al. Subclinical Thyroid Dysfunction and the **Risk for Fractures**: A Systematic Review and Meta-analysis. Ann Intern Med. 2014 Aug 5;161(3):189-99.
Xing M, Alzahrani AS, Carson KA, et al. Association between BRAF V600E mutation and mortality in patients with papillary **thyroid cancer**. JAMA. 2013 Apr 10;309(14):1493-501.
Yamamoto J, Donovan LE. **Managing thyroid disease in women planning pregnancy**. CMAJ. 2017 Jul 17;189(28):E940.
Yamamoto JM, Benham JL, Nerenberg KA, Donovan LE. Impact of **levothyroxine therapy on obstetric, neonatal and childhood outcomes** in women with subclinical hypothyroidism diagnosed in pregnancy: a systematic review and meta-analysis of randomised controlled trials. BMJ Open. 2018 Sep 8;8(9):e022837.
Yim CH. Update on the Management of **Thyroid Disease during Pregnancy**. Endocrinol Metab (Seoul). 2016 Aug 16.
Yip L, Carty SE. Expanding the Options for Patient-Guided Decision Making in **Papillary Thyroid Cancer**. JAMA. 2018 Jan 2;319(1):76-77.
Yoo F, Chaikhoutdinov I, Mitzner R, et al. Characteristics of Incidentally Discovered **Thyroid Cancer**. JAMA Otolaryngol Head Neck Surg. 2013 Oct 10.
Zanocco KA, Hershman JM, Leung AM. Active **Surveillance of Low-Risk Thyroid Cancer**. JAMA. 2019 Apr 30.
Zhang B, Tian J, Pei S, et al. Machine Learning-Assisted System for **Thyroid Nodule Diagnosis**. Thyroid. 2019 Mar 30
Zung A, Yehieli A, Blau A, Almashanu S. Characteristics of **Delayed Thyroid Stimulating Hormone Elevation in Neonatal Intensive Care Unit Newborns**. J Pediatr. 2016 Nov;178:135-140.e1.

Hypothyroid

Akhoundi FH, Ghorbani A, Soltani A, Meysamie A. **Favorable functional outcomes in acute ischemic stroke patients with subclinical hypothyroidism**. Neurology. 2011 Jun 29.
Akhtar MA, Agrawal R, Brown J, et al. Thyroxine replacement for subfertile women with euthyroid autoimmune thyroid disease or subclinical hypothyroidism. Cochrane Database Syst Rev. 2019 Jun 25;6:CD011009. We could draw no clear conclusions in this systematic review due to the very low to low quality of the evidence reported
Alexander EK, Marqusee E, Lawrence J, et al. Timing and magnitude of increases in levothyroxine requirements during **pregnancy** in women with hypothyroidism. N Engl J Med. 2004 Jul 15;351(3):241-9.
Bach-Huynh TG, Nayak B, Loh J, et al. Timing of Levothyroxine Administration Affects Serum Thyrotropin Concentration. J Clin Endocrinol Metab. 2009 Jul 7. [Epub ahead of print]. Non-fasting regimens of levothyroxine administration are associated with higher and more variable serum thyrotropin concentrations. If a specific serum thyrotropin goal is desired, thereby avoiding iatrogenic subclinical thyroid disease, then fasting ingestion of levothyroxine ensures that thyrotropin concentrations remain within the narrowest target range.
Bahn RS, Burch HB, Cooper DS, et al; American Thyroid Association; American Association of Clinical Endocrinologists. Hyperthyroidism and other causes of thyrotoxicosis: management guidelines of the American Thyroid Association and American Association of Clinical Endocrinologists. Endocr Pract. 2011 May-Jun;17(3):456-520.
Balhara B, Misra M, Levitsky LL. Clinical monitoring guidelines for **congenital hypothyroidism**: Laboratory outcome data in the first year of life. J Pediatr 2011;158:532-7.
Bekkering GE, Agoritsas T, Lytvyn L, et al. **Thyroid hormones treatment for subclinical hypothyroidism**: a clinical practice guideline. BMJ. 2019 May 14;365:l2006.
Biondi B, Cappola AR, Cooper DS. **Subclinical Hypothyroidism**: A Review. JAMA. 2019 Jul 9;322(2):153-160.
Bolk Nienke; Visser Theo J.; Nijman Judy; et al. Effects of **Evening** vs Morning **Levothyroxine Intake**: A Randomized Double-blind Crossover Trial. Arch Intern Med. 2010;170(22):1996-2003.

Booms S, Hill E, Kulhanek L, et al. **Iodine Deficiency** and Hypothyroidism From Voluntary Diet Restrictions in the US: Case Reports. Pediatrics. 2016 May 10.
Bunevicius R, Kazanavicius G, Zalinkevicius R, Prange AJ Jr. Effects of **thyroxine as compared with thyroxine plus triiodothyronine** in patients with hypothyroidism. N Engl J Med 1999;340:424-429.
Canaris GJ, Manowitz NR, Mayor G, Ridgway EC. The Colorado thyroid disease prevalence study. Arch Intern Med 2000;160:526-34.
Capalbo D, Lucariello A, Saccà L, et al. Long-term cardiovascular effects of levothyroxine therapy in young adults with congenital hypothyroidism. J Clin Endocrinol Metab. 2008 Jul;93(7):2486-91. Epub 2008 Apr 29.
Cappola AR, Fried LP, Arnold AM, et al. Thyroid status, cardiovascular risk, and mortality in older adults. JAMA. 2006;295(9):1033-1041.
Cappola AR. **Levothyroxine prescription**: not as simple as it seems. JAMA. 2014 Jun 25;311(24):2532-3.
Casey BM, Thom EA, Peaceman AM, et al. Treatment of **subclinical hypothyroidism or hypothyroxinemia in pregnancy**. N Engl J Med 2017;376:815-25.
Chaker L, Bianco AC, Jonklaas J, et al. **Hypothyroidism (Seminar)**. Lancet. 2017 Mar 20.
Cleary-Goldman J, et al. **Maternal thyroid hypofunction and pregnancy outcome.** Obstet Gynecol. 2008 Jul;112(1):85-92.
Clemens Kristin, Payne William, Van Uum Stan H.M.. **Central hypothyroidism** Can Fam Physician June 2011 57: 677-680.
Clemens K, Van Uum S. A **pituitary mass** as consequence of a **decimal error in levothyroxine dose**. CMAJ. 2012 Jan 16.
Committee on Patient Safety and Quality Improvement; Committee on Professional Liability. ACOG Committee Opinion No. 381: Subclinical hypothyroidism in pregnancy. Obstet Gynecol. 2007 Oct;110(4):959-60.
Connelly KJ, Boston BA, Pearce EN, et al. Congenital hypothyroidism caused by excess prenatal **maternal iodine ingestion**. J Pediatr. 2012 Oct;161(4):760-2.
Cooper DS, Halpern R, Wood LC, Levin AA, Ridgway EC. L-thyroxine therapy in subclincial hypothyroidism. A double-blind, placebo-controlled trial. Ann Intern Med 1984;101:18-24.
Cooper DS and Pearce EN.**Subclinical hypothyroidism and hypothyroxinemia in pregnancy** — still no answers. N Engl J Med 2017 Mar 2; 376:876.
Dahl AR, Iqbal AM, Lteif AN, et al. **Mild subclinical hypothyroidism** is associated with paediatric **dyslipidaemia**. Clin Endocrinol (Oxf). 2018 May 30.
Danese MD, Ladenson PW, Meinert CL, Powe NR. Clinical review 115: effect of thyroxine therapy on serum lipoproteins in patients with mild thyroid failure: a quantitative review of the literature. J Clin Endocrinol Metab. 2000;85(9):2993-3001.
Davis FB, LaMantia RS, Spaulding SW, Wehmann RE, Davis PJ. Estimation of a **physiologic replacement dose of levothyroxine in elderly patients** with hypothyroidism. Arch Intern Med. 1984; 144(9):1752-4.
Deshauer S, Wyne A. **Subclinical hypothyroidism in pregnancy**. CMAJ. 2017 Jul 17;189(28):E941
Ertaş B, Veyseller B, Karataş A, et al. **Hypoparathyroidism in Total Thyroidectomy** due to Benign Thyroid Diseases. Clin Ther. 2018 Apr 20.FDA Nov/15 is advising that rare cases of underactive thyroid have been reported in infants following the use of **contrast media containing iodine**, also called "contrast dye," for X-rays and other medical imaging procedures. In all of the reported cases, the infants were either premature or had other serious underlying medical conditions. Available evidence leads FDA to believe that this rare occurrence is usually temporary and resolves without treatment or any lasting effects. See the Drug Safety Communication for a data summary and a list of approved Approved Iodinated Contrast Media Products.
Feller M, Snel M, Moutzouri E, et al. Association of **Thyroid Hormone Therapy With Quality of Life and Thyroid-Related Symptoms in Patients With Subclinical Hypothyroidism**: A Systematic Review and Meta-analysis. JAMA. 2018 Oct 2;320(13):1349-1359.
FDA Aug/18: **Westminster Pharmaceuticals, LLC. Issues Voluntary Nationwide Recall of Levothyroxine and Liothyronine (Thyroid Tablets, USP) Due to Risk of Adulteration.**
Flynn RW, et al. Serum **Thyroid-Stimulating Hormone Concentration** and Morbidity from **Cardiovascular Disease and Fractures** in Patients on Long-Term Thyroxine Therapy. J Clin Endocrinol Metab. 2009 Nov 11.
Fox CS, Pencina MJ, D'Agostino RB, et al. Relations of thyroid function to **body weight**: cross-sectional and longitudinal observations in a community-based sample. Arch Intern Med. 2008 Mar 24;168(6):587-92.
Friedman, Diana, Richard L. Reed, and Arshag D. Mooradian. The prevalence of **overmedication with levothyroxine** in ambulatory elderly patients. Age 1992 15(1):9-13.
Fruzza AG, Demeterco-Berggren C, Jones KL. Unawareness of the Effects of **Soy Intake** on the Management of Congenital Hypothyroidism. Pediatrics. 2012 Aug 20.
Furukawa S, Yamamoto S, Todo Y, et al. Association between **subclinical hypothyroidism** and **diabetic nephropathy** in patients with type 2 diabetes mellitus. Endocr J. 2014Aug 7.
Gaitonde DY, Rowley KD, and Sweeny LB. **Hypothyroidism**: An Update. Am Fam Physician. 2012;86(3):244-251.
Gammage MD, Parle JV, Holder RL, Roberts LM, Hobbs FD, Wilson S, et al. Association between serum free thyroxine concentration and atrial fibrillation. Arch Intern Med 2007;167:928-34.
Garber JR, Cobin RH, Gharib H, et al. Clinical Practice Guidelines for **Hypothyroidism** in Adults: Co-sponsored by American Association of Clinical Endocrinologists (**AACE**) and the American Thyroid Association (**ATA**). Endocr Pract. 2012 Sep 11:1-207.
Gencer B, Collet TH, Virgini V, et al. **Subclinical Thyroid Dysfunction and the Risk of Heart Failure** Events: An Individual Participant Data Analysis from Six Prospective Cohorts. Circulation. 2012 Jul 19.
Ghassabian A, El Marroun H, Peeters RP, et al. Downstream effects of **maternal hypothyroxinemia in early pregnancy**: nonverbal IQ and brain morphology in school-age children. J Clin Endocrinol Metab 2014; 99: 2383-90.
Giri A, Edwards TL, LeGrys VA, et al. **Subclinical hypothyroidism** and risk for incident ischemic stroke among postmenopausal women. Thyroid. 2014 Aug;24(8):1210-7.
Girling J, Nelson-Piercy C. Hypothyroidism in pregnancy: Three unresolved issues. BMJ. 2007 Aug 25;335(7616):362.
Granfors M, Akerud H, Berglund A, et al. **Thyroid Testing and Management of Hypothyroidism During Pregnancy**: A Population-based Study. J Clin Endocrinol Metab. 2013 Jul;98(7):2687-92.
Grebe SK, Cooke RR, Ford HC, et al. Treatment of hypothyroidism with once **weekly thyroxine**. J Clin Endocrinol Metab. 1997 Mar;82(3):870-5.
Grob F, Van Vliet G. Avoiding the **Overdiagnosis of Congenital Hypothyroidism in Premature Newborns**. Pediatrics. 2019 Jul 16.
Grozinsky-Glasberg S, Fraser A, Nahshoni E, Weizman A, Leibovici L. **Thyroxine-triiodothyronine combination therapy versus thyroxine** monotherapy for clinical hypothyroidism: meta-analysis of randomized controlled trials. J Clin Endocrinol Metab 2006;91:2592-2599.
Hak AE, Pols HA, Visser TJ, et al. Subclinical hypothyroidism is an independent risk factor for **atherosclerosis** and myocardial infarction in elderly women: the Rotterdam Study. Ann Intern Med. 2000 Feb 15;132(4):270-8.
Health Canada Apr/17: Rare cases of **hypothyroidism following Iodinated Contrast Media (ICM) exposure** have been reported, particularly in term and preterm infants.
Heather N, Hall K, Neas K et al. Growth and development in a child with **resistance to thyroid hormone** and ectopic thyroid gland. Pediatrics. 2012 Mar;129(3):e817-20.
Hennessey JV, Espaillat R. Diagnosis and Management of **Subclinical Hypothyroidism in Elderly** Adults: A Review of the Literature. J Am Geriatr Soc. 2015 Jul 22.
Hennessey JV, Klein I, et al. Aggressive Case Finding: A **Clinical Strategy for the Documentation of Thyroid Dysfunction**. Ann Intern Med. 2015 Aug 18;163(4):311-2.
Herrick B. Subclinical hypothyroidism. Am Fam Physician. 2008 Apr 1;77(7):953-5.
Hoang TD, Olsen CH, Mai VQ, et al. **Desiccated thyroid extract compared with levothyroxine** in the treatment of hypothyroidism: a randomized, double-blind, crossover study. J Clin Endocrinol Metab. 2013;98:1982-90.
Hyland KA, Arnold AM, Lee JS, Cappola AR. Persistent **Subclinical Hypothyroidism and Cardiovascular Risk** in the Elderly: The Cardiovascular Health Study. J Clin Endocrinol Metab. 2012 Nov 16.
Iyasere CA, Simmons LH, Fintelmann FJ, Dighe AS. **Case 38-2014**: An 87 year old man with sore throat, hoarseness, fatigue and dyspnea. N Engl J Med. 2014 Dec 11;371(24):2321-2327.
Iwasaki Y, Fukaya K. **Woltman's Sign of Hypothyroidism**. N Engl J Med. 2018 Oct 4;379(14):e23.
Ineck BA, Ng TM. Effects of subclinical hypothyroidism and its treatment on serum lipids. Ann Pharmacother 2003;37:725-30.
Jang SY, Dooley MA, Joy MS. Impact of severe **hypothyroidism on cyclophosphamide** disposition and routes of metabolism and transport in a patient with treatment-resistant lupus nephritis. Ann Pharmacother. 2013 Jul;47(7-8):e35.
Jones DE, Hart K, Shapira SK, et al. Identification of **Primary Congenital Hypothyroidism Based on Two Newborn Screens** - Utah, 2010-2016. MMWR Morb Mortal Wkly Rep. 2018 Jul 20;67(28):782-785.
Jonklaas J, Bianco AC, Bauer AJ, et al. GUIDELINES FOR THE **TREATMENT OF HYPOTHYROIDISM**. Thyroid. 2014 Sep 29. (American Thyroid Association)
Jorde R, Waterloo K, Storhaug H, Nyrnes A, et al. Neuropsychological function and symptoms in subjects with subclinical hypothyroidism and the effect of thyroxine treatment. J Clin Endocrinol Metab 2006;91:145-53.
Julià H, Benaiges D, Mollà P, et al. **Changes in Thyroid Replacement Therapy after Bariatric Surgery**: Differences between Laparoscopic Roux-en-Y Gastric Bypass and Laparoscopic Sleeve Gastrectomy. Obes Surg. 2019 Apr 25.

Kim J. Images in clinical medicine. **Myxedema**. N Engl J Med. 2015 Feb 19;372(8):764.

Kim JS, Zhang Y, Chang Y, et al. **Subclinical hypothyroidism** and incident **depression** in young and middle age adults. J Clin Endocrinol Metab. 2018 Feb 2.

Kong WM, Sheikh MH, Lumb PJ, Naoumova RP, Freedman DB, Crook M, et al. A 6-month randomized trial of thyroxine treatment in women with mild subclinical hypothyroidism. Am J Med 2002;112:348-54.

Lechner MG, Vyas CM, Hamnvik OR, et al. **Risk Factors** for New Hypothyroidism During **Tyrosine Kinase Inhibitor** Therapy in Advanced Nonthyroidal Cancer Patients. Thyroid. 2018 Apr;28(4):437-444.

Lee Jennifer S.; Buzkova Petra; Fink Howard A.; et al. Subclinical Thyroid Dysfunction and Incident **Hip Fracture** in Older Adults Arch Intern Med. 2010;170(21):1876-1883.

Levine Richard J, Vatten Lars J, Horowitz Gary L, **Pre-eclampsia**, soluble fms-like tyrosine kinase 1, and the risk of reduced thyroid function: nested case-control and population based study**.** BMJ 2009;339:b4336, doi: 10.1136/bmj.b4336 (Published 17 November 2009)

Li Y, Shan Z, Teng W, et al. Abnormalities of maternal thyroid function during pregnancy affect neuropsychological development of their children at 25-30 months. Clin Endocrinol (Oxf). 2009 Oct 31.

Lin HC, Kang JH, Jiang YD, et al. Hypothyroidism and the Risk of Developing Open-Angle **Glaucoma** A Five-Year Population-Based Follow-Up Study. Ophthalmology. 2010 Jun 15. Hypothyroid patients had a significantly increased risk of OAG development during the 5-year follow-up period. Levothyroxine seemed to be protective.

Liu H, Shan Z, Li C, et al. **Maternal subclinical hypothyroidism**, thyroid autoimmunity, and the risk of miscarriage: a prospective cohort study. Thyroid 2014; 24: 1642-9.

Loh JA, Wartofsky L, Jonklaas J, Burman KD.The magnitude of increased levothyroxine requirements in hypothyroid pregnant women depends upon the etiology of the hypothyroidism. Thyroid. 2009;19:269-275.

Maraka S, O'Keeffe DT, Montori VM. **Subclinical Hypothyroidism During Pregnancy**-Should You Expect This When You Are Expecting?: A Teachable Moment. JAMA Intern Med. 2015 May 4.

Maraka S, Ospina NM, O'Keeffe DT, et al. **Subclinical hypothyroidism in pregnancy**: a systematic review and meta-analysis. Thyroid 2016; 26: 580-90.

Maraka S, Mwangi R, McCoy RG, et al. **Thyroid hormone treatment among pregnant women with subclinical hypothyroidism**: US national assessment. BMJ. 2017 Jan 25;356:i6865.

Marwali EM, Boom CE, Budiwardhana N, et al. **Oral Triiodothyronine** for Infants and Children **Undergoing Cardiopulmonary Bypass**. Ann Thorac Surg. 2017 Feb 6.

McAninch EA, Bianco AC. The **History and Future** of **Treatment** of **Hypothyroidism**. Ann Intern Med. 2016 Jan 5;164(1):50-6.

McDermott Michael T. **In the Clinic**: **Hypothyroidism**. Ann Intern Med December 1, 2009 151:ITC6-1.

McMahon B, Kamath S. Pancytopenia in a Patient With Hypothyroidism. (**Vitamin B12: pernicious anemia**) JAMA. 2016 Apr 19;315(15):1648-9.

Medical Letter, Inc. **Drugs for Hypothyroidism**. Treat Guidel Med Lett.. 2015;57(1480):147-50.

Mohamed M, Fernando R, Arora A. **Airway obstruction** after the development of Hashimoto's thyroiditis. BMJ. 2014 Feb 24;348:g1643.

Moleti M, Trimarchi F, Tortorella G, et al. F. Effects of **Maternal Iodine Nutrition** and Thyroid Status on Cognitive Development in Offspring: A Pilot Study. Thyroid. 2015 Nov 20.

Moon S, Kong SH, Choi HS, et al. Relation of **Subclinical Hypothyroidism is Associated With Cardiovascular Events and All-Cause Mortality** in Adults With High Cardiovascular Risk. Am J Cardiol. 2018 May 16.

Nazarpour S, Ramezani Tehrani F, Simbar M, Tohidi M, et al. Effects of **levothyroxine treatment on pregnancy outcomes** in pregnant women with autoimmune thyroid disease. Eur J Endocrinol 2017; 176: 253-65.

Negro R, Schwartz A, Gismondi R, Tinelli A, Mangieri T, Stagnaro-Green A. **Universal Screening Versus Case Finding** for Detection and Treatment of Thyroid Hormonal Dysfunction During **Pregnancy**. J Clin Endocrinol Metab. 2010 Feb 3.

Negro R, Stagnaro-Green A. Diagnosis and management of **subclinical hypothyroidism in pregnancy**. BMJ. 2014 Oct 6;349:g4929.

Niranjan U, Wright NP. Should we treat **subclinical hypothyroidism** in **obese children**? BMJ. 2016 Mar 16

Noten AM, Loomans EM, Vrijkotte TG, et al. **Maternal hypothyroxinaemia** in early **pregnancy** and school performance in 5-year-old offspring. Eur J Endocrinol. 2015 Aug 25.

Nygaard B, Jensen EW, Kvetny J, Jarlov A, Faber J. Effect of **combination therapy with thyroxine (T4) and 3,5,3′-triiodothyroxine versus T4 monotherapy** in patients with hypothyroidism, a double-blind, randomised cross-over study. Eur J Endocrinol 2009;161:895-902.

Panicker V, Saravanan P, Vaidya B, et al. Common variation in the **DIO2 gene predicts baseline** psychological well-being and response to **combination thyroxine plus triiodothyronine** therapy in hypothyroid patients. J Clin Endocrinol Metab 2009;94:1623-1629.

Park S, Jeon MJ, Song E et al. Clinical Features of Early and Late Postoperative Hypothyroidism after Lobectomy. J Clin Endocrinol. Metab. 2017. Online.

Parle J, Roberts L, Wilson S, et al. A Randomized Controlled Trial of the Effect of Thyroxine Replacement on **Cognitive Function** in Community-Living Elderly Subjects with Subclinical Hypothyroidism: The Birmingham Elderly Thyroid Study. J Clin Endocrinol Metab. 2010 May 25. This RCT provides no evidence for treating elderly subjects with SCH with T4 replacement therapy to improve cognitive function.

Parsaik AK, Singh B, Roberts RO, et al. Hypothyroidism and **Risk of Mild Cognitive Impairment** in **Elderly** Persons: A Population-Based Study. JAMA Neurol. 2013 Dec 30.

Pasqualetti G, Pagano G, Rengo G, Ferrara N, Monzani F. **Subclinical Hypothyroidism** and Cognitive Impairment: Systematic Review and Meta-Analysis. J Clin Endocrinol Metab. 2015;100(11):4240-8.

Papaleontiou M, Cappola AR. **Thyroid-Stimulating Hormone in the Evaluation of Subclinical Hypothyroidism**. JAMA. 2016 Oct 18;316(15):1592-1593.

Peckham S, Lowery D, Spencer S. Are **fluoride levels in drinking water associated with hypothyroidism** prevalence in England? A large observational studyof GP practice data and fluoride levels in drinking water. J Epidemiol Community Health. 2015 Feb 24. pii: jech-2014-204971.

Pecina J, Garrison GM, Bernard ME. **Levothyroxine dosage** is associated with stability of thyroid-stimulating hormone values. Am J Med. 2014 Mar;127(3):240-5.

Peeters RP. **Subclinical Hypothyroidism**. N Engl J Med. 2017 Jun 29;376(26):2556-2565.

Peterson SJ, McAninch EA, Bianco AC. Is a **Normal TSH Synonymous** with "**Euthyroidism**" in **Levothyroxine Monotherapy**? J Clin Endocrinol Metab. 2016 Oct 4:jc20162660.

Plowden TC, Schisterman EF, Sjaarda LA, et al. **Subclinical hypothyroidism** and thyroid autoimmunity are not associated with fecundity, pregnancy loss, or live birth. J Clin Endocrinol Metab 2016; 101: 2358-65.

Practice Committee of the American Society for Reproductive Medicine. **Subclinical hypothyroidism** in the **infertile female population**: a guideline. Fertil Steril. 2015 Sep;104(3):545-53.

Ramadhan A, Tamilia M. **Treatment-refractory** hypothyroidism. CMAJ. 2012 Feb 7;184(2):205-9. (May have a **supervised test for levothyroxine absorption**)

Razvi S, Ingoe L, Keeka G, et al. The beneficial effect of L-thyroxine on cardiovascular risk factors, endothelial function, and quality of life in subclinical hypothyroidism: randomized, crossover trial. J Clin Endocrinol Metab 2007;92:1715-23.

Razvi S, Weaver JU, Butler TJ, Pearce SHS. **Levothyroxine treatment of subclinical hypothyroidism**, fatal and nonfatal cardiovascular events, and mortality. Arch Intern Med 2012.

Reid SM, Middleton P, Cossich MC, Crowther CA. Interventions for **clinical and subclinical hypothyroidism in pregnancy**. Cochrane Database Syst Rev. 2010 Jul 7;7:CD007752.
Levothyroxine treatment of clinical hypothyroidism in pregnancy is already standard practice given the documented benefits from earlier non-randomised studies. Whether levothyroxine should be utilised in autoimmune and subclinical hypothyroidism remains to be seen, but it may prove worthwhile, given a possible reduction in preterm birth and miscarriage.Selenomethionine as an intervention in women with thyroid autoantibodies is promising, particularly in reducing postpartum thyroiditis. There is a probable low incidence of adverse outcomes from levothyroxine and selenomethionine. High-quality evidence is lacking and large-scale randomised trials are urgently needed in this area. Until evidence for or against universal screening becomes available, targeted thyroid function testing in pregnancy should be implemented in women at risk of thyroid disease and levothyroxine utilised in hypothyroid women.

Reid SM, Middleton P, Cossich MC, et al. Interventions for **clinical and subclinical hypothyroidism pre-pregnancy and during pregnancy**. Cochrane Database Syst Rev. **2013** May 31;5:CD007752. doi: 10.1002/14651858.CD007752.pub3. This review found no difference between levothyroxine therapy and a control for treating pregnant euthyroid women with thyroid peroxidase antibodies for the outcome of pre-eclampsia, however a reduction in preterm birth and a trend towards reduced miscarriage with levothyroxine was shown. This review also showed no difference for pre-eclampsia or preterm birth when selenium was compared with placebo, however a promising reduction in postpartum thyroiditis was shown. Childhood neurodevelopmental delay was not assessed by any trial included in the review.Given that this review is based on four trials of moderate risk of bias, with only two trials contributing data (n = 284), there is insufficient evidence to recommend the use of one intervention for clinical or subclinical hypothyroidism pre-pregnancy or during pregnancy over another, for improving maternal, fetal, neonatal & childhood outcomes.

Rhee CM, Curhan GC, Alexander EK, et al. **Subclinical Hypothyroidism and Survival**: The Effects of Heart Failure and Race. J Clin Endocrinol Metab. 2013 May 29.

Rodondi N, Newman AB, Vittinghoff E, et al. Subclinical hypothyroidism and the risk of heart failure, other cardiovascular events, and death. Arch Intern Med. 2005;165(21):2460-2466.

Rodondi N, Aujesky D, Vittinghoff E, Cornuz J, Bauer DC. Subclinical hypothyroidism and the risk of coronary heart disease: a meta-analysis. Am J Med. 2006;119(7):541-551.

Rosenbaum RL, Barzel US. Levothyroxine replacement dose for **primary hypothyroidism** decreases with age. Ann Intern Med. 1982; 96(1):53-5

Saba C, Guilmin-Crepon S, Zénaty D, et al. Early determinants of thyroid function outcome in children with **congenital hypothyroidism and a normally located thyroid gland**: a regional cohort study. Thyroid. 2018 Jul 3.

Salerno M, Oliviero U, Lettiero T, et al. Long-term cardiovascular effects of levothyroxine therapy in young adults with congenital hypothyroidism. J Clin Endocrinol Metab. 2008 Jul;93(7):2486-91. Epub 2008 Apr 29.

Samuels MH, Kolobova I, Smeraglio A, et al. The effects of levothyroxine replacement or suppressive therapy on **health status, mood and cognition**. J Clin Endocrinol Metab. 2014 Jan 13
Sawka AM, Jonklaas J. **Hypothyroidism**. CMAJ. 2015 Feb 17;187(3):205. doi: 10.1503/cmaj.141596.
Sharma AK, Vegh E, Orencole M, et al. Association of **hypothyroidism with adverse events in patients with heart failure receiving cardiac resynchronization therapy**. Am J Cardiol. 2015 May 1;115(9):1249-53.
Shields BM, Knight BA, Hill AV, et al. Five-year follow-up for women with **subclinical hypothyroidism in pregnancy**. J Clin Endocrinol Metab. 2013 Dec;98(12):E1941-5.
Shin DY, Kim EK, Lee EJ. Role of Ultrasonography in Outcome Prediction in Subclinical Hypothyroid Patients Treated with Levothyroxine. Endocr J. 2009 Oct 10.
Shrestha RT, Malabanan A, Haugen BR, et al. **Adverse Event Reporting** in Patients Treated with **Thyroid Hormone Extract**. Endocr Pract. 2017 Feb 22.
Simonsick Eleanor M.; Newman Anne B.; Ferrucci Luigi; et al. for the Health ABC Study **Subclinical Hypothyroidism** and Functional Mobility in **Older** Adults. Arch Intern Med. 2009;169(21):2011-2017.
Singh S, Duggal J, Molnar J, Maldonado F, Barsano CP, Arora R. Impact of subclinical thyroid disorders on coronary heart disease, cardiovascular and all-cause mortality: a meta-analysis. Int J Cardiol. In press.
Smallridge RC, Sangaralingham LR, Mwangi R, et al. Comparison of **Incident Cardiovascular Event Rates Between Generic and Brand l-Thyroxine** for the Treatment of Hypothyroidism. Mayo Clin Proc. 2019 Jul;94(7):1190-1198.
Søgaard M, Farkas DK, Ehrenstein V, et al. **Hypothyroidism** and hyperthyroidism and breast cancer risk: a nationwide cohort study. Eur J Endocrinol. 2016 Apr;174(4):409-14.
Stagnaro-Green A, Abalovich M, Alexander E, et al. Guidelines of the American Thyroid Association (**ATA**) for the diagnosis and management of **thyroid disease during pregnancy** and postpartum. Thyroid 2011;21.
Stott DJ, Gussekloo J, et al. Study protocol; Thyroid hormone Replacement for Untreated older adults with **Subclinical hypothyroidism** - randomised placebo controlled Trial (**TRUST**). BMC Endocr Disord. 2017 Feb 3;17(1):6.
Stott DJ, Rodondi N, Kearney PM, et al. **Thyroid Hormone Therapy for Older Adults with Subclinical Hypothyroidism**. (**Trust**) N Engl J Med. 2017 Apr 3.
Sullivan SA. **Hypothyroidism in Pregnancy**. Clin Obstet Gynecol. 2019 Jun;62(2):308-319.
Taguchi T. **Brittle Nails and Hair Loss in Hypothyroidism**. N Engl J Med. 2018 Oct 4;379(14):1363.
Tan ZS, Beiser A, Vasan RS, Au R, et al. Thyroid function and the risk of Alzheimer disease: the Framingham Study. Arch Intern Med. 2008 Jul 28;168(14):1514-20. Low and high thyrotropin levels were associated with an increased risk of incident AD in women but not in men.
Taylor PN, Iqbal A, et al. **Falling Threshold for Treatment** of Borderline Elevated Thyrotropin Levels-Balancing Benefits and Risks: Evidence From a Large Community-Based Study. JAMA Intern Med. 2013 Oct 7.
Taylor PN, Richmond R, Davies N, et al. Paradoxical relationship between **body mass index and thyroid hormone levels**; a study using Mendelian Randomization. J Clin Endocrinol Metab. 2015 Nov 23:jc20153505.
Teng X, Shan Z, Li C, et al. **Iron Deficiency May Predict Greater Risk for Hypothyroxinemia**: A Retrospective Cohort Study of Pregnant Women in China. Thyroid. 2018 Jul 3.
Torpy Janet M., Lynm Cassio, Golub Robert M. JAMA Patient Page: **Hyperthyroidism**. JAMA. 2011;306(3):330.doi:10.1001/jama.306.3.330
Turner MR, Camacho X, Fischer HD, Austin PC, Anderson GM, Rochon PA, et al. **Levothyroxine dose and risk of fractures** in older adults: nested case-control study. BMJ 2011;342:d2238.
Unnikrishnan AG, Kalra S, Sahay RK, Bantwal G, John M, Tewari N. Prevalence of **hypothyroidism in adults**: an epidemiological study in eight cities of **India**. *Indian J Endocr Metab* 2013;17:647-52.
Vanderpump MP, Tunbridge WM, French JM, Appleton D, Bates D, Clark F, et al. The incidence of thyroid disorders in the community: a twenty-year follow-up of the Whickham survey. Clin Endocrinol 1995;43:55-68.
Villar HC, Saconato H, Valente O, Atallah AN. Thyroid hormone replacement for subclinical hypothyroidism. Cochrane Database Syst Rev. 2007;(3):CD003419.
Virgini VS, Rodondi N, Cawthon PM, Harrison SL, Hoffman AR, Orwoll ES, Ensrud KE, Bauer DC; Osteoporotic Fractures in Men (MrOS) Research Group. **Subclinical Thyroid Dysfunction** and Frailty Among Older Men. J Clin Endocrinol Metab. 2015;100(12):4524-32.
Wiles KS, Jarvis S, Nelson-Piercy C. Are we **overtreating subclinical hypothyroidism** in pregnancy? BMJ. 2015 Oct 12;351:h4726.
Wolter P, Stefan C, Decallonne B, et al. The clinical implications of sunitinib-induced hypothyroidism: a prospective evaluation. Br J Cancer. 2008 Aug 5;99(3):448-54.
Woo CH, Lizarda A, Tucker R, Mitchell ML, Vohr G, OhW, Phornphutkul C. **Congenital hypothyroidism** with a delayed thyroid-stimulating hormone (TSH) elevation in very premature infants: Incidence and growth and developmental outcomes. J Pediatr 2011;158:538-42.
Yassa L, Marqusee E, Fawcett R, Alexander EK. Thyroid Hormone Early Adjustment in **Pregnancy** (The THERAPY) Trial. J Clin Endocrinol Metab. 2010 May 12.
Ybarra M, Dos Santos TJ, Pinheiro CTC, et al. **Rectal Levothyroxine** for the **Treatment of Hypothyroidism**: A Case Study. Pediatrics. 2018 Jul 12.

Hyperthyroid

Bahn R, Levy E, Wartofsky L. Graves' disease. J Clin Endocrinol Metab. 2007 Nov;92(11):2 p following 14A.
Bahn, Rebecca S. **Graves' Ophthalmopathy**. N Engl J Med 2010 362: 726-738.
Bahn RS, Burch HS, Cooper DS, et al. The role of propylthiouracil in the management of Graves' disease in adults: report of a meeting jointly sponsored by the American Thyroid Association and the Food and Drug Administration. Thyroid. 2009;19:673-674.
Bahn RS, Burch HB, Cooper DS, et al; American Thyroid Association; American Association of Clinical Endocrinologists. **Hyperthyroidism and other causes of thyrotoxicosis**: management guidelines of the American Thyroid Association and American Association of Clinical Endocrinologists. Endocr Pract. 2011 May-Jun;17(3):456-520.
Banigé M, Polak M, Luton D; Research Group for Perinatal Dysthyroidism (RGPD) Study Group. Prediction of **Neonatal Hyperthyroidism**. J Pediatr. 2018 Jun;197:249-254.e1.
Bauer DC, Rodondi N, Stone KL, Hillier TA; Study of Osteoporotic Fractures Research Group: Universities of California (San Francisco), Pittsburgh, Minnesota (Minneapolis); Kaiser Permanente Center for Health Research, Portland. Thyroid hormone use, hyperthyroidism and mortality in older women. Am J Med. 2007 Apr;120(4):343-9.
Biondi B, Cooper DS. Subclinical **Hyperthyroidism**. N Engl J Med. 2018 Jun 21;378(25):2411-2419.
Bogazzi F, Tomisti L, Rossi G, et al.. Glucocorticoids are preferable to thionamides as first-line treatment for **amiodarone-induced** thyrotoxicosis due to destructive thyroiditis: a matched retrospective cohort study. . J Clin Endocrinol Metab. 2009 Jul 21. [Epub ahead of print]
Bogazzi F, Bartalena L, Martino E. Approach to the patient with **amiodarone-induced thyrotoxicosis**. J Clin Endocrinol Metab. 2010 Jun;95(6):2529-35.
Brito JP, Castaneda-Guarderas A, Gionfriddo MR, et al. Development and Pilot Testing of an Encounter Tool for **Shared Decision Making About the Treatment of Graves' Disease**. Thyroid. 2015 Nov;25(11):1191-8.
Burch HB, Cooper DS. Management of **Graves Disease**: A Review. JAMA. 2015 Dec 15;314(23):2544-2554.
Chen CH, Xirasagar S, Lin CC, et al. Risk of adverse perinatal outcomes with **antithyroid treatment during pregnancy**: a nationwide population-based study. BJOG. 2011 Oct;118(11):1365-73.
Chen WT, Chi CC. Associations of **HLA genotypes with antithyroid drug-induced agranulocytosis**: a systematic review and meta-analysis of pharmacogenomics studies. Br J Clin Pharmacol. 2019 May 20.
Chattaway JM. Klepser TB. Propylthiouracil versus methimazole in treatment of Graves' disease during pregnancy. Ann Pharmacother. 2007;41:1018-1022.
Chen H. Pre-operative management of patients with Graves' disease. Surgery. 2008 Feb;143(2):292-3. Epub 2007 Dec 21.
Chung SD, Chen YK, Chen YH et al. **Hyperthyroidism** and female urinary incontinence: a population-based cohort study. Clin Endocrinol (Oxf). 2011 Nov;75(5):704-8.
Collet T-H, Gussekloo J, Bauer DC, et al; Thyroid Studies Collaboration.**Subclinical hyperthyroidism** and the risk of coronary heart disease and mortality [online April 23, 2012]. Arch Intern Med.
Cooper DS, Rivkees SA. Putting **propylthiouracil** in perspective. J Clin Endocrinol Metab. 2009;94:1881-1882.
De Leo S, Lee SY, Braverman LE. **Hyperthyroidism**. Lancet. 2016 Mar 30
Donangelo I, Braunstein GD. Update on **Subclinical Hyperthyroidism**. Am Fam Physician. 2011;83(8):933-938.
Donangelo I, Suh SY. **Subclinical Hyperthyroidism**: When to Consider Treatment. Am Fam Physician. 2017;95(11):710-716.
Douchement D, Rakza T, Holder M, Bonne NX, Fayoux P. **Choanal Atresia** Associated With Tracheoesophageal Fistula: The Spectrum of **Carbimazole** Embryopathy. Pediatrics. 2011 Aug 1.
Dunne P, Kaimal N, Macdonald J, et al. **Iodinated contrast-induced thyrotoxicosis**. CMAJ. 2013 Feb 5;185(2):144-7.

England RJ, Atkin S. Total thyroidectomy is best operation for thyrotoxicosis. BMJ. 2007 Apr 7;334(7596):710.
Franklyn JA, Boelaert K. **Thyrotoxicosis**. Lancet. 2012 Mar 2.
Gastaldi R, Poggi E, Mussa A, Weber et al. **Graves Disease in Children**: Thyroid-Stimulating Hormone Receptor Antibodies as Remission Markers. J Pediatr. 2014 Feb 8
Kampmann JP, Johansen K, Hansen JM, Helweg J. **Propylthiouracil** in human milk. Revision of a dogma. Lancet. 1980;1:736-737.
Kitahara CM, Berrington de Gonzalez A, Bouville A, et al. Association of **Radioactive Iodine Treatment With Cancer Mortality in Patients** With Hyperthyroidism. JAMA Intern Med. 2019 Jul 1.
Kravets I. **Hyperthyroidism**: **Diagnosis and Treatment**. Am Fam Physician. 2016;93(5):363-370.
Kummer S, Hermsen D, Distelmaier F. **Biotin Treatment** Mimicking Graves' Disease. N Engl J Med. 2016 Aug 18;375(7):704-6
Laurberg P, Andersen SL. Endocrinology in Pregnancy: **Pregnancy and the incidence, diagnosing and therapy of Graves' disease**. Eur J Endocrinol. 2016 Jun 8.
Laurberg P, Wallin G, Tallstedt L, Abraham-Nordling M, Lundell G, Torring O. **TSH-receptor autoimmunity in Graves' disease** after therapy with anti-thyroid drugs, surgery, or radioiodine: a 5-year prospective randomized study. Eur J Endocrinol 2008;158:69-75.
Leblicq C, Duval M, Carmant L, et al. Rising serum thyroxine levels and **chorea** in graves' disease. Pediatrics. 2013 Feb;131(2):e616-9.
Liu J, Fu J, Xu Y, Wang G. **Antithyroid Drug Therapy for Graves' Disease** and Implications for Recurrence. Int J Endocrinol. 2017;2017:3813540.
Majlesi N, Greller HA, McGuigan MA, Caraccio T, Su MK, Chan GM. Thyroid storm after **pediatric levothyroxine ingestion**. Pediatrics. 2010 Aug;126(2):e470-3. Epub 2010 Jul 19.
Marriott C, George C. New onset **atrial fibrillation, prominent chest wall veins, and dyspnoea**. BMJ. 2018 Oct 11;363:k3779. (hyperthyroidism)
Medical Letter, Inc. Drugs for hypothyroidism and hyperthyroidism. Treat Guidel Med Lett. 2006 Apr;4(44):17-24.
Nygaard B. Hyperthyroidism. Am Fam Physician. 2007 Oct 1;76(7):1014-6.
Ochs N, Auer R, Bauer DC, Nanchen D, et al. Meta-analysis: subclinical thyroid dysfunction and the risk for coronary heart disease and mortality. Ann Intern Med. 2008 Jun 3;148(11):832-45. Epub 2008 May 19.
Ortiz GA et al. **Propylthiouracil-induced lupus, antiphospholipid syndrome**, and stroke in a patient with graves hyperthyroidism. Arch Neurol. 2011 Dec;68(12):1587-90.
Pantalone K Nasr C. **Approach to a low TSH level**: Patience is a virtue *Cleveland Clinic Journal of Medicine* 2010; 77(11):803-811; doi:10.3949/ccjm.77a.10056.
Pearce EN. Diagnosis and management of thyrotoxicosis. BMJ. 2006 Jun 10;332(7554):1369-73.
Pusl T, Jaehnig H, Dorn R. Thyrotoxicosis: a lesson from the **slaughterhouse**. Ann Intern Med. 2011 Nov 1;155(9):646.
Regelmann MO, Sullivan CK, Rapaport R. Thyroid "Vise" in an Infant With **Neonatal Graves' Disease**. Pediatrics. 2013 Sep 16.
Rhee EP, et al. Case records of the Massachusetts General Hospital. Case 4-2012. A 37-year-old man with muscle pain, weakness, and weight loss. (**thyrotoxic periodic paralysis**) N Engl J Med. 2012 Feb 9;366(6):553-60.
Rivkees SA, Mattison DR. Ending **propylthiouracil-induced liver failure** in children. N Engl J Med. 2009;360:1574-1575.
Ross DS. **Radioiodine therapy for hyperthyroidism**. N Engl J Med. 2011 Feb 10;364(6):542-50.
Ross DS, Burch HB, Cooper DS, et al. **2016 American Thyroid Association** (**ATA**) Guidelines for Diagnosis and Management of **Hyperthyroidism and other causes of Thyrotoxicosis**. Thyroid. 2016 Aug 12.
Sarezky MD, Corwin DJ, Harrison VS, et al. **Hyperthyroidism** Presenting With Pathologic Fractures. Pediatrics. 2016 Jan 8.
Shi M, Li X, Peng J. **Localised myxoedema complicating Graves' disease**. BMJ 2016 Jan 19; 352:i156.
Simon M, Rigou A, Le Moal J, et al. Epidemiology of **childhood hyperthyroidism** in France: a nationwide population-based study. J Clin Endocrinol Metab. 2018 May 28.
Smith TJ, Hegedüs L. **Graves' Disease.** N Engl J Med. 2016 Oct20;375(16):1552-1565.
Tallstedt L, Lundell G, Torring O, et al. Occurrence of **ophthalmopathy** after treatment for Graves' hyperthyroidism. The Thyroid Study Group. N Engl J Med. 1992;326:1733-1738.
Takata K, Amino N, Kubota S, et al. Benefit of short-term iodide supplementation to antithyroid drug treatment of thyrotoxicosis due to Graves' disease. Clin Endocrinol (Oxf). 2009 Nov 11.
Toderian AB, Lawson ML. Use of **Antihistamines After Serious Allergic Reaction to Methimazole** in Pediatric Graves' Disease. Pediatrics. 2014 Apr 28.
Tsang W, Houlden RL. **Amiodarone-induced** thyrotoxicosis: a review. Can J Cardiol. 2009 Jul;25(7):421-4
Toft A, Sandeep TC. Radioiodine treatment of hyperthyroidism. BMJ. 2007 Mar 10;334(7592):483-4.
Torpy JM, Lynm C, Golub RM. JAMA patient page. **Hyperthyroidism**. JAMA. 2011 Jul 20;306(3):330.
van der Kaay DC, Wasserman JD, Palmert MR. Management of **Neonates Born to Mothers With Graves' Disease**. Pediatrics. 2016 Mar 15.
Weetman AP. Investigating **low thyroid stimulating hormone** (TSH) level. BMJ. 2013 Nov 20;347:f6842.
Wang MT, Lee WJ, Huang TY, et al. **Antithyroid Drug related Hepatotoxicity** in **Hyperthyroidism** Patients: A Population‐based Cohort Study. British Journal of Clinical Pharmacology **.** 2014.
Wilhelm SM, McHenry CR. **Total Thyroidectomy** Is Superior to Subtotal Thyroidectomy for Management of Graves' Disease in the United States. World J Surg. 2009 Dec 23.
US Food and Drug Administration. Information for healthcare professionals - propylthiouracil-induced liver failure. June 4, 2009. Available at: http://www.fda.gov/Drugs/DrugSafety/PostmarketDrugSafetyInformationforPatientsandProviders/DrugSafetyInformationforHeathcareProfessionals/ucm162701.htm . Accessed February 9, 2010.

Given these potential adverse effects, the FDA issued an alert on June 4, 2009 that noted the risk of serious liver injury, including liver failure and death, with the use of PTU in adult (1:10,000) and pediatric (1:2,000) patients. These conferences focused on the relative safety of methimazole compared with PTU.[11-14,16] Approximately 30% of patients treated with PTU will have 1- to 2-fold elevations of serum aminotransferase levels. The liver disease associated with PTU can be severe. In the Adverse Event Reporting System (AERS), approximately 22 adult (12 deaths, 5 hepatic transplants) and 10 pediatric (1 death, 6 hepatic transplants) cases of serious hepatic injury associated with PTU treatment were reported. Methimazole, by contrast, was associated with 5 adult cases of serious hepatic injury with 3 deaths. In a system that may overlap with AERS, the United Network for Organ Sharing reported 23 hepatic transplants from 1990 to 2007 (16 adult, 7 children) related to PTU-associated hepatic failure.[11-13,16] Concurrently, no liver transplants related to the use of methimazole were reported. The average PTU dose in children and adults requiring liver transplant was 300 mg daily. Liver failure occurred between 6 and 450 days after starting treatment (median 120 days). Furthermore, there were 2 reports of serious maternal liver disease during pregnancy and 2 reports of liver injury in fetuses of mothers who ingested PTU during pregnancy.[11-14,16]

Zhao SX, Liu W, Liang J, et al; China Consortium for the Genetics of Autoimmune Thyroid Disease. Assessment of **Molecular Subtypes in Thyrotoxic Periodic Paralysis and Graves Disease** Among Chinese Han Adults: A Population-Based Genome-Wide Association Study. JAMA Netw Open. 2019 May 3;2(5):e193348.

Guidelines

AACE/AME Task Force on Thyroid Nodules. American Association of Clinical Endocrinologists and Associazione Medici Endocrinologi medical guidelines for clinical practice for the diagnosis and management of thyroid nodules. Endocr Pract. 2006 Jan-Feb;12(1):63-102.
American Association of Clinical Endocrinologists-**AACE**. American Association of Clinical Endocrinologists medical guidelines for clinical practice for the evaluation and treatment of hyperthyroidism and hypothyroidism. Endocr Pract. 2002 Nov-Dec;8(6):457-69.
American Thyroid Association (ATA) Guidelines Taskforce on Thyroid Nodules and Differentiated Thyroid Cancer, Cooper DS, Doherty GM, Haugen BR, Kloos RT, Lee SL, Mandel SJ, Mazzaferri EL, McIver B, Pacini F, Schlumberger M, Sherman SI, Steward DL, Tuttle RM. Revised American Thyroid Association management guidelines for patients with **thyroid nodules and differentiated thyroid cancer**. Thyroid. **2009** Nov;19(11):1167-214.
American Thyroid Association (ATA) Guidelines Task Force, Kloos RT, Eng C, Evans DB, Francis GL, Gagel RF, Gharib H, Moley JF, Pacini F, Ringel MD, Schlumberger M, Wells SA Jr. **Medullary thyroid cancer**:

management guidelines of the American Thyroid Association. Thyroid 2009 Jun;19(6):565-612.
American Thyroid Association (**ATA**): Stagnaro-Green A, Abalovich M, Alexander E, et al. Guidelines of the American Thyroid Association (**ATA**) for the diagnosis and management of **thyroid disease during pregnancy** and postpartum. Thyroid 2011;21.
American Thyroid Association (**ATA**); American Association of Clinical Endocrinologists-AACE. Bahn Chair RS, Burch HB, Cooper DS, et al. **Hyperthyroidism** and other causes of thyrotoxicosis: management guidelines of the American Thyroid Association and American Association of Clinical Endocrinologists. Thyroid. 2011 Jun;21(6):593-646.
American Thyroid Association (**ATA**); Smallridge RC, Ain KB, Asa SL, et al. American Thyroid Association **Anaplastic Thyroid Cancer** Guidelines Taskforce. American Thyroid Association guidelines for management of patients with anaplastic thyroid cancer. Thyroid. 2012 Nov;22(11): 1104-39.
American Thyroid Association (**ATA**); Ross DS, Burch HB, Cooper DS, et al. **2016 American Thyroid Association** (**ATA**) Guidelines for Diagnosis and Management of **Hyperthyroidism and other causes of Thyrotoxicosis**. Thyroid. 2016 Aug 12.
Abalovich M, Amino N, Barbour LA, Cobin RH, De Groot LJ, Glinoer D, Mandel SJ, Stagnaro-Green A. Management of thyroid dysfunction during **pregnancy and postpartum**: an Endocrine Society Clinical Practice Guideline. J Clin Endocrinol Metab. 2007 Aug;92(8 Suppl):S1-47.
Alexander EK, Pearce EN, Brent GA, et al. 2016 Guidelines of the **American Thyroid Association** for the Diagnosis and **Management of Thyroid Disease during Pregnancy and the Postpartum**. Thyroid. 2017 Jan 6.
Bahn RS, Burch HB, Cooper DS, et al; American Thyroid Association; American Association of Clinical Endocrinologists. **Hyperthyroidism and other causes of thyrotoxicosis**: management guidelines of the American Thyroid Association and American Association of Clinical Endocrinologists. Endocr Pract. 2011 May-Jun;17(3):456-520.
Bartalena L, Bogazzi F, Chiovato L, et al. **2018 European Thyroid Association (ETA) Guidelines for the Management of Amiodarone-Associated Thyroid Dysfunction**. Eur Thyroid J. 2018 Mar;7(2):55-66.
Cohen JI, Salter KD; American Thyroid Association-**ATA**; American Association of Clinical Endocrinologists; Associazione Medici Endocrinologi. Thyroid disorders: evaluation and management of thyroid nodules. Oral Maxillofac Surg Clin North Am. 2008 Aug;20(3):431-43.
Cooper DS, Doherty GM, Haugen BR, Kloos RT, Lee SL, Mandel SJ, Mazzaferri EL, McIver B, Sherman SI, Tuttle RM, The American Thyroid Association Guidelines Taskforce. Management guidelines for patients with **thyroid nodules and differentiated thyroid cancer**. Thyroid 2006 Feb;16(2):109-42.
Cooper DS, Doherty GM, Haugen BR, et al. Revised American Thyroid Association management guidelines for patients with **thyroid nodules and differentiated thyroid cancer**. Thyroid 2009;19:1167-214.
De Groot L, Abalovich M, Alexander EK, et al. **2012** Management of thyroid dysfunction during **pregnancy and postpartum: an Endocrine Society clinical practice guideline**. J Clin Endocrinol Metab 97:2543–2565.
Garber JR, Cobin RH, Gharib H, et al. Clinical Practice Guidelines for **Hypothyroidism** in Adults: Co-sponsored by American Association of Clinical Endocrinologists (**AACE**) and the American Thyroid Association (**ATA**). Endocr Pract. 2012 Sep 11:1-207.
Gharib H, Tuttle MH, Baskin J, Fish LH, Singer PA, McDermott MT. **Subclinical** thyroid dysfunction: a joint statement on management from the American Association of Clinical Endocrinologists, the American Thyroid Association, and the Endocrine Society. J Clin Endocrin Metab 2005;90:581-5.
Gharib H, Tuttle RM, Baskin HJ, Fish LH, Singer PA, McDermott MT; American Association of Clinical Endocrinologists/American Thyroid Association/Endocrine Society. **Subclinical** thyroid dysfunction: a joint statement on management from the American Association of Clinical Endocrinologists, the American Thyroid Association, and the Endocrine Society. Endocr Pract. 2004 Nov-Dec;10(6):497-501.
Gharib H, Papini E, Paschke R, et al. AACE/AME/ETA Task Force on Thyroid Nodules. American Association of Clinical Endocrinologists, Associazione Medici Endocrinologi, and European Thyroid Association medical guidelines for clinical practice for the diagnosis and management of **thyroid nodules**: executive summary of recommendations. J Endocrinol Invest. 2010;33(5 Suppl):51-6.
Gharib H, Papini E, Garber JR,et al; **AACE/ACE/AME** Task Force on Thyroid Nodules. American Association of Clinical Endocrinologists and American College of Endocrinology-Association Medici Endo-Guidelines: Diagnosis and Management of **Thyroid Nodules**-2016 Update . Endocr Pract. 2016 May;22(5):622-39.
Helfand M, Redfern CC. Clinical guideline, part 2. **Screening** for thyroid disease: an update. American College of Physicians [published correction appears in Ann Intern Med. 1999;130(3):246]. Ann Intern Med. 1998;129(2):144-158.
Haugen BR Md, Alexander EK, Bible KC, et al. **2015 American Thyroid Association Management Guidelines for Adult Patients with Thyroid Nodules and Differentiated Thyroid Cancer**. Thyroid. 2015 Oct 14.
Inoue M, Arata N, Koren G, Ito S. Hyperthyroidism during **pregnancy**. Can Fam Physician. 2009 Jul;55(7):701-3.
Jonklaas J, Bianco AC, Bauer AJ, et al. GUIDELINES FOR THE **TREATMENT OF HYPOTHYROIDISM**. Thyroid. 2014 Sep 29. (American Thyroid Association)
Kahaly GJ, Bartalena L, Hegedüs L, et al. **2018 European Thyroid Association Guideline** for the Management of **Graves' Hyperthyroidism**. Eur Thyroid J. 2018 Aug;7(4):167-186.
Screening for thyroid disease: recommendation statement. Ann Intern Med 2004 Jan 20;140(2):125-7.
The Endocrine Society. Management of thyroid dysfunction during **pregnancy and postpartum**: an Endocrine Society clinical practice guideline. Chevy Chase (MD): The Endocrine Society; 2007. 79 p.
UK guidelines for the use of thyroid function **tests**. 2006. http://www.acb.org.uk/docs/TFTguidelinefinal.pdf
USPSTF- U.S. Preventive Services Task Force. Screening for thyroid disease: recommendation statement. Ann Intern Med. 2004 Jan 20;140(2):125-7.
USPSTF- US Preventive Services Task Force. Screening for congenital hypothyroidism: US Preventive Services Task Force reaffirmation recommendation. Ann Fam Med 2008 Mar-Apr;6(2):166.
USPSTF- US Preventive Services Task Force. Recommendation statement. Screening for thyroid disease. 2004. www.ahrq.gov/clinic/3ruspstf/thyroid/thyrrs.htm#recommendations
USPSTF: US Preventive Services Task Force. Screening for thyroid cancer: US Preventive Services Task Force recommendation statement [published May 9,2017]

Web Sites:

Access information for patients with hypothyroidism prepared by the American College of Physicians.
www.acponline.org/patients_families/diseases_conditions/hypothyroidism/

Access information for patients with hypothyroidism prepared by the National Library of Medicine of the National Institutes of Health.
www.nlm.nih.gov/medlineplus/ency/article/000353.htm

Access information for patients with hypothyroidism prepared by the American Thyroid Association.
www.thyroid.org/patients/patient_brochures/hypothyroidism.html

American Thyroid Association. Questions and answers about potassium iodide (KI). http://www.thyroid.org/professionals/publications/statements/ki/02_04_09_ki_qa.html Accessed March 17, 2011.

US Nuclear Regulatory Commission. Use of potassium iodide. Available at: http://www.nrc.gov/about-nrc/emerg-preparedness/about-emerg-preparedness/potassium-iodide-use.html Accessed March 17, 2011.

ONLINE EXTRAS: IDIOPATHIC HIRSUTISM

Other Agents	**Prednisone** (Glucocorticoid) 1, 5ⓒ, 50ⓒmg tab; {1mg/ml prednisolone soln}	- Suppresses adrenal function	- Classic & Nonclassic congenital adrenal hyperplasia (NCCAH)	-Less effective compared to OCs or anti-androgens[1]	Uncontrolled diabetes, Obesity	- Changes typical of Cushing syndrome (weight gain, bone loss), adrenal atrophy	5-7.5mg po daily $12 (5mg tab)
	Ketoconazole NIZORAL 200ⓒmg tab ☎▼	- Adrenal enzyme inhibitor	- For patients with Cushing's syndrome while waiting definite therapy	-Similar efficacy to CPA 2-50mg[20]	Hepatic dysfunction Pregnancy, BF	- Gynecomastia, dry skin, **hepatotoxicity**, adrenocortical suppression	200mg po daily $41 (200mg tab)
	Leuprolide Acetate (GnRH analog) LUPRON(SC): Vial 5mg/ml✗ ® LUORON DEPOT (IM)☎▼: 3.75, 7.5, 11.25, 22.5✗, 30✗ mg ELIGARD (SC)✗▼: 7.5, 22.5, 30, 45mg	- Potent inhibitor of ovarian steroidogenesis by suppressing LH & FSH	- Severe hyperandrogenism of ovarian origin that does not respond to other drugs	-Similar efficacy to CPA 2-50mg, but more adverse effects[20]	Pregnancy, BF Osteoporosis	- Osteoporosis - Reversable induced menopause	3.75-7.5mg monthly IM, with 25-50ug transdermal estradiol 445_{$415 + $24-30}$
	MetFORMIN GLUCOPHAGE 500ⓒ, 850mg tab	- improves insulin sensitivity	- Used in polycystic ovary syndrome (PCOS). - Not effective for idiopathic hirsutism	-Small benefit compared to placebo[23] -Inferior to OC or anti-androgen therapy for idiopathic hirsutism[23]	Renal failure	- Gastrointestinal upset (minimize by starting low dose 250mg daily, then titrate)	500-2000mg/day (given 250-1000mg BID) $13-21 (500mg tab)

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References for Hirsutism, Idiopathic - Tables & Figures (RxFiles.ca)
http://www.rxfiles.ca/rxfiles/uploads/documents/members/Hirsutism-Treatment-Figure-Drug-Chart.pdf

RxFiles provides objective, comparative, evidence informed drug information for drug therapy decision making. One hallmark of the program is the academic detailing service or "office visit discussions" provided for physicians/others in Saskatchewan, Canada. A second hallmark that has evolved is the RxFiles Drug Therapy Charts book. For more information on our academic detailing, book, app or online info & services, see our website at www.RxFiles.ca.

hirsutism: a consensus statement by the Androgen Excess and Polycystic Ovary Syndrome Society. Human Reproduction Update Advanced Access published November 6, 2011
[2] Rosenfield, RL. Hirsutism. N Engl J Med 2005;353:2578-88
[3] e-CPS, Toronto, ON: Canadian Pharmacists Association. www-e-therapeutics-ca (accessed 2011 November)
[4] DRUGDEX System. Greenwood Village, CO: Thomson Micromedex. www.thomsonhc.com (accessed 2011 November)
[5] Kumar R, St John J, Devendra D. 10-MinuteConsultation: Hirsutism. BMJ 2009;339:b3090 doi: 10.1136/bmj.b3090
[6] Sathyapalan T, Atkin SL.. Rational Testing: Investigating hirsutism. BMJ 2009;338:912 doi:10.1136/bmj.b912
[7] Koulouri O, Conway GS. Clinical Review: Management of hirsutism. BMJ 2009;338:b847 doi:10.1136/bmj.b847
[8] Harrison S, Somani N, Bergfeld W. Update on the management of hirsutism. Cleveland Clinic J Med 2010;77(6): 338-98.
[9] Hamzavi I, Tan E, Shapiro J, Lui H. A randomized bilateral vehicle-controlled study of eflornithine cream combined with laser treatment versus laser treatment alone for facial hirsutism in women. J Am Acad Dermatol 2007;57:54-9.
[10] Smith SR, Piacquadio DJ, Beger B, Littler C. Eflornithine Cream Combined with Laser Therapy in the Management of Unwanted Facial Hair Growth in Women: A Randomized Trial. Dermatol Surg 2006;32:1237–1243.
[11] Wolf JE, Shander D, Huber F, Jackson J, Lin CS, Mathes BM et al. Randomized, double-blind clinical evaluation of the efficacy and safety of topical eflornithine HCl 13.9% cream in the treatment of women with facial hair. Int J Dermat 2007;46:94 –98.
[12] Regier L, Downey S. Contraceptive, Combination Hormonal Products – Prescription. *RxFiles drug comparison charts*. 8th ed. Saskatoon, SK: RxFiles; 2011. Available from: http://www.rxfiles.ca/rxfiles/uploads/documents/members/CHT-OCs-Color.pdf (accessed 2011 December)
[13] Batukan C, Muderris II. Efficacy of a new oral contraceptive containing drospirenone and ethinyl estradiol in the long-term treatment of hirsutism. Fertil Steril 2006;85:436–40.
[14] Batukan C, Muderris II, Ozcelik B, Ozturk A. Comparison of two oral contraceptives containing either drospirenone or cyproterone acetate in the treatment of hirsutism. Gyne Endocrin 2007;23(1):38–44.
[15] Breitkopf DM, Rosen MP, Young SL, Nagamani M. Efficacy of second versus third generation oral contraceptives in the treatment of hirsutism. Contraception 2003;67:349–353.
[16] Bunka D, Hall J. YAZ / YASMIN: Safety Considerations related to Venous Thromboembolism (VTE). *RxFiles Q&A*. Saskatoon, SK: RxFiles; 2011. Available from: http://www.rxfiles.ca/rxfiles/uploads/documents/Yaz-Yasmin-Q-A.pdf (accessed 2011 December)
[17] Brown J, Farquhar C, Lee O, Toomath R, Jepson RG. Spironolactone versus placebo or in combination with steroids for hirsutism and/or acne. Cochrane Database of Systematic Reviews 2009, Issue 2. Art. No.: CD000194. DOI: 10.1002/14651858.CD000194.pub2.
[18] Swiglo BA, Cosma M, Flynn DN, Kurtz DM, Labella ML, Mullan RJ, Erwin PJ, Montori VM. Clinical review: antiandrogens for the treatment of hirsutism: a systematic review and metaanalyses of randomized controlled trials. J Clin Endocrinol Metab 2008b;93:1153–1160.
[19] Karakurt F. Comparison of the Clinical Efficacy of Flutamide and Spironolactone plus Ethinyloestradiol/Cyproterone Acetate in the Treatment of Hirsutism: a Randomised Controlled Study. *Adv Ther.* 2008;25(4):321–328.
[20] van der Spuy ZM, Le Roux PA, Matjila MJ. Cyproterone acetate for hirsutism. Cochrane Database of Systematic Reviews 2003, Issue 4. Art. No.: CD001125. DOI: 10.1002/14651858.CD001125.
[21] Brahm J, Brahm M, Segovia R, Latorre R, Zapata R, Poniachik J et al. Acute and fulminant hepatitis induced by flutamide: Case series report and review of the literature. Ann Hepatology 2011;10(1):93-98.

[22] Calaf J, Lopez E, Millet A, Alcaniz J, Fortuny A, Vidal O, Callejo J, Escobar-Jimenez F, Torres E, Espinos JJ. Long-term efficacy and tolerability of flutamide combined with oral contraception in moderate to severe hirsutism: a 12-month, double-blind, parallel clinical trial. J Clin Endocrinol Metab 2007;92:3446–3452.

[23] Cosma M, Swiglo BA, Flynn DN, Kurtz DM, LaBella ML, Mullan RJ, et al. Insulin Sensitizers for the Treatment of Hirsutism: A Systematic Review and Metaanalyses of Randomized Controlled Trials. J Clin Endocrinol Metab 2008;93:1135–1142.

Additional references:

Alpañés M, Álvarez-Blasco F, Fernández-Durán E, et al. **Combined oral contraceptives plus spironolactone** compared with metformin in women with polycystic ovary syndrome: a one-year randomized clinical trial. Eur J Endocrinol. 2017 Nov;177(5):399-408.

Barrionuevo P, Nabhan M, Altayar O, et al. **Treatment Options for Hirsutism**: A Systematic Review and Network Meta-Analysis. J Clin Endocrinol Metab. 2018 Apr 1;103(4):1258-1264.

Legro RS, Arslanian SA, Ehrmann DA, et al. Diagnosis and Treatment of **Polycystic Ovary Syndrome**: An Endocrine Society Clinical Practice Guideline. J Clin Endocrinol Metab. 2013 Oct 22.

Liu K, Motan T, Claman P. **SOGC No. 350-Hirsutism**: Evaluation and Treatment. J Obstet Gynaecol Can. 2017 Nov;39(11):1054-1068.

Martin KA, Anderson RR, Chang RJ, et al. **Evaluation and Treatment of Hirsutism in Premenopausal Women: An Endocrine Society Clinical Practice Guideline**. J Clin Endocrinol Metab. 2018 Mar 7.

McCartney CR, Marshall JC. CLINICAL PRACTICE. **Polycystic Ovary Syndrome**. N Engl J Med. 2016 Jul 7;375(1):54-64.

Mimoto MS, Oyler JL, Davis AM. **Evaluation and Treatment of Hirsutism** in Premenopausal Women. JAMA. 2018 Mar 9.

van Zuuren EJ, Fedorowicz Z, Carter B, Pandis N. **Interventions for hirsutism** (excluding laser and photoepilation therapy alone). Cochrane Database Syst Rev. 2015 Apr 28;4:CD010334. doi: 10.1002/14651858.CD010334.pub2. Treatments may need to incorporate pharmacological therapies, cosmetic procedures, and psychological support. For mild hirsutism there is evidence of limited quality that OCPs are effective. Flutamide 250 mg twice daily and spironolactone 100 mg daily appeared to be effective and safe, albeit the evidence was low to very low quality. Finasteride 5 mg daily showed inconsistent results in different comparisons, therefore no firm conclusions can be made. As the side effects of antiandrogens and finasteride are well known, these should be accounted for in any clinical decision-making. There was low quality evidence that metformin was ineffective for hirsutism and although GnRH analogues showed inconsistent results in reducing hirsutism they do have significant side effects.Further research should consist of well-designed, rigorously reported, head-to-head trials examining OCPs combined with antiandrogens or 5α-reductase inhibitor against OCP monotherapy, as well as the different antiandrogens and 5α-reductase inhibitors against each other. Outcomes should be based on standardised scales of participants' assessment of treatment efficacy, with a greater emphasis on change in quality of life as a result of treatment.

van Zuuren EJ, Fedorowicz Z. Interventions for Hirsutism. JAMA. 2015 Nov 3;314(17):1863-1864.

Williams T, Mortada R, Porter S. Diagnosis and Treatment of **Polycystic Ovary Syndrome**. Am Fam Physician. 2016 Jul 15;94(2):106-13.

Barkun A, N Chiba, R Enns, et al. Commonly used preparations for colonoscopy: Efficacy, tolerability and safety – A Canadian Association of Gastroenterology position paper. Can J Gastroenterol 2006;20(11):699-710.

Wexner SD, Beck DE, Baron TH, et al. A consensus document on bowel preparation before colonoscopy: Prepared by a task force from the American Society of Colon and Rectal Surgeons (ASCRS), the American Society for Gastrointestinal Endoscopy (ASGE), and the Society of American Gastrointestinal and Endoscopic Surgeons(SAGES). Dis Colon Rectum 2006;49:792-809.

Rex DK, Johnson DA, Anderson JC, Schoenfeld PS, MD, Burke CA, Inadomi J. American College of Gastroenterology Guidelines for Colorectal Cancer Screening 2008. Am J Gastroenterol 2009; 104:739–750; doi:10.1038/ajg.2009.104; published online 24 February 2009.

Parra-Blanco A, Nicolas-Perez D, Gimeno-Garcia A et al. The timing of bowel preparation before colonoscopy determines the quality of cleansing, and is a significant factor contributing to the detection of flat lesions: a randomized study. World J Gastroenterol 2006;12:6161–6.

Hassan C, Bretthauer M, Kaminski MF, et al. Bowel preparation for colonoscopy: European Society of Gastrointestinal Endoscopy (ESGE) Guideline. Endoscopy 2013; 45: 142.150.

Rostom A, Jolicoeur E, Dube C et al. A randomized prospective trial comparing different regimens of oral sodium phosphate and polyethylene glycol-based lavage solution in the preparation of patients for colonoscopy. Gastrointest Endosc 2006;64:544–52.

Aoun E, Abdul-Baki H, Azar C et al. A randomized single-blind trial of split-dose PEG-electrolyte solution without dietary restriction compared with whole dose PEG-electrolyte solution with dietary restriction for colonoscopy preparation. Gastrointest Endosc 2005;62:213–8.

Canadian Pharmacist's Letter June 2012. PL Detail – Document #280628

Caldera F, Selby L. How to avoid common pitfalls with bowel preparation agents. Gastrointestinal endoscopy 2001; 73: 346-348.

Belsey J, Crosta C, Epstein O, et al. Meta-analysis: the relative efficacy of oral bowel preparations for colonoscopy 1985 – 2010. Aliment Pharmacol Ther 2011; 35:222–237.

KilgoreTW, AbdinoorAA, SzaryNM et al. Bowel preparation with split-dose polyethylene glycol before colonoscopy: a meta-analysis of randomized controlled trials. Gastroint Endosc 2011; 73:1240 – 1245.

Elitsur R, Butcher L, Vicki L, Elitsur Y. Polyethylene glycol 3350 based colon cleansing protocol: 2d vs 4d head to head comparison. World J Gastrointest Endosc 2013 April 16; 5(4): 165-168 ISSN 1948-5190 (online).

Samarasena JB, Muthusamy VR, Jamal MM. Split-dosed MiraLAX/Gatorade is an effective, safe, and tolerable option for bowel preparation in low-risk patients: a randomized controlled study. Am J Gastroenterol. 2012 Jul;107(7):1036-42. doi: 10.1038/ajg.2012.115. Epub 2012 May 8.

McKenna T, Macgill A, Porat G, Friedenberg FK. Colonoscopy preparation: polyethylene glycol with Gatorade is as safe and efficacious as four liters of polyethylene glycol with balanced electrolytes. Dig Dis Sci. 2012 Dec;57(12):3098-105. doi: 10.1007/s10620-012-2266-5. Epub 2012 Jun 19.

Moraveji S, Casner N, Bashashati M, et al. The role of oral simethicone on the adenoma detection rate and other quality indicators of screening colonoscopy: a randomized, controlled, observer-blinded clinical trial. Gastrointest Endosc. 2019;90(1):141-149. doi: 10.1016/j.gie.2019.03.018. Epub 2019 Mar 26.

Phatak, Uma P. Johnson, Susanne. Husain, Sohail Z. Pashankar, Dinesh S. Two-day bowel preparation with polyethylene glycol 3350 and bisacodyl: a new, safe, and effective regimen for colonoscopy in children. Journal of Pediatric Gastroenterology & Nutrition. 53(1):71-4, 2011 Jul.

Turner D, Levine A, Weiss B et al. on behalf of the Israeli Society of Pediatric Gastroenterology and Nutrition. Evidence-based recommendations for bowel cleansing before colonoscopy in children: a report from a national working group. Endoscopy 2010; 42:1063-1070.

Turner D, Benchimol EI , Dunn H et al. Pico-Salax versus poly-ethylene glycol for bowel cleanout before colonoscopy in children-a randomized controlled trial. Endoscopy 2009; 41:1038-1045.

Sharara A, Abou Mrad RR. The modern bowel preparation in colonoscopy. Gastroenterol Clin N Am 2013; 42:577-598.

Envestvedt BK, Tofani C, Laine L et al. 4L split-dose polyethylene glycol is superior to other bowel preparations, based on systematic review and meta-analysis. Clin Gastro and Hepatol 2012;10:1225-1231.

Walia R, Steffen R, Feinberg L et al. Tolerability, safety and efficacy of PEG 3350 as a 1 day bowel preparation in children. J Pediatr Gastroenterol Nutr 2013; 56(2): 225-8.

Terry N, Chen-Lim, Ely E et al. Polyethylene glycol powder solution versus senna for bowel preparation for colonoscopy in children. JPGN 2013; 56(2):215-219.

Hunter A, Mamula P. Bowel preparation for pediatric colonoscopy procedures. J Pediatr Gastroenterol Nutr 2010; 51:254–261.

Abbas MI, Nylund CM, Bruch CJ, et al. Prospective evaluation of 1-day polyethylene glycol-3350 bowel preparation regimen in children. J Pediatr Gastroenterol Nutr 2013;56:220–4.

Bucci C, Zingone F, Schettino P et al. Same-day regimen as an alternative to split preparation for colonoscopy: a systematic review with meta-analysis. Gastroenterol Res Pract. 2019;7476023. doi: 10.1155/2019/7476023. eCollection 2019.

Mo Y, Gandhi S, Orsini J. **Possible GoLytely-Associated Cardiac Arrest: A case report** and literature review. J Pharm Pract. 2019; epub ahead of print. PMID: 3072797.

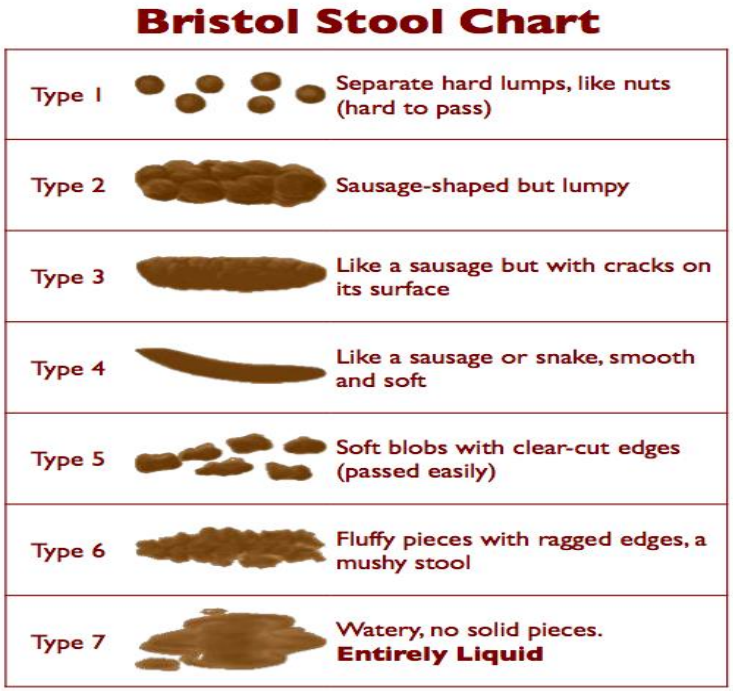
Parekh P. Oldfield E, Johnson D. Bowel preparation for colonoscopy: what is best and necessary for quality? Curr Opin Gastroenterol 2019;35(1):51-7.

Additional articles:

Di Nardo G, Aloi M, Cucchiara S, et al. **Bowel Preparations for Colonoscopy**: An RCT. Pediatrics. 2014 Jul 7.

Radaelli F, Paggi S, Hassan C, et al. **Split-dose preparation for colonoscopy** increases adenoma detection rate: a randomised controlled trial in an organised screening programme. Gut. 2015 Dec 9.

The Bristol Stool Chart: a validated tool to correlate stool consistency with colonic transit time. Use with patients for assessment & monitoring.



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REFERENCES: MANAGEMENT OF CONSTIPATION

GENERAL REFERENCES:

e-CPS (2018), Dynamed (2018)

Bowles-Jordan J. Constipation (Chapter 31), Therapeutic Choices for Minor Ailments, 1st edition. Canadian Pharmacists Association. Toronto, ON. 2013.

Bowles-Jordan J. Constipation (Chapter 31), Patient Self-Care, 2nd edition. Canadian Pharmacists Association. Toronto, ON. 2010.

Chaun H. Gastrointestinal Disorders: Constipation in Adults. Therapeutic Choices. Available at: https://www.e-therapeutics.ca/tc.showChapter.action. Accessed August 20, 2012.

GUIDELINES, POSITION STATEMENTS, ETC:

American College of Gastroenterology:

Ford AC, Moayyedi P, Lacy BE et al. American College of Gastroenterology monograph on the management of irritable bowel syndrome and chronic idiopathic constipation. Am J Gastroenterol. 2014 Aug;109 Suppl 1:S2-S26.

Mahadevan U, Kane S. American Gastroenterological Association Institute medical position statement on the use of gastrointestinal medications in pregnancy. Gastroenerology 2006;131:278-82.

American Gastroenterology Association:

American Gastroenterological Association (AGA) , Bharucha AE, Dorn SD, Lembo A, Pressman A. American gastroenterological association medical position statement on constipation. Gastroenterology. 2013 Jan;144(1):211-7.

Bharucha AE, Pemberton JH, Locke GR 3rd. American gastroenterological association technical review on constipation. Gastroenterology. 2013 Jan;144(1):218-38.

Crockett SD, Greer KB, Heidelbaugh JJ, Falck-Ytter Y, Hanson BJ, Sultan S; American Gastroenterological Association Institute Clinical Guidelines Committee. American Gastroenterological Association Institute Guideline on the Medical Management of **Opioid-Induced Constipation**. Gastroenterology. **2019** Jan;156(1):218-226.

Canadian Association of Gastroenterology:

Andrews CN, Storr M. The pathophysiology of chronic constipation. Can J Gastroenterol. 2011 Oct;25 Suppl B:16B-21B. Review.

Camilleri M. New treatment options for chronic constipation: mechanisms, efficacy and safety. Can J Gastroenterol. 2011 Oct;25 Suppl B:29B-35B. Review.

Gray JR. What is chronic constipation? Definition and diagnosis. Can J Gastroenterol. 2011 Oct;25 Suppl B:7B-10B.

Liu LW. Chronic constipation: current treatment options. Can J Gastroenterol. 2011 Oct;25 Suppl B:22B-28B. Review.

Pare P. The approach to diagnosis and treatment of chronic constipation: suggestions for a general practitioner. Can J Gastroenterol. 2011 Oct;25 Suppl B:36B-40B.

Sanchez MI, Bercik P. Epidemiology and burden of chronic constipation. Can J Gastroenterol. 2011 Oct;25 Suppl B:11B-15B. Review.

Storr M, Storr M. Chronic constipation: current management and challenges. Can J Gastroenterol. 2011 Oct;25 Suppl B:5B-6B.

Canadian Paediatric Society. 2011 Position Statement: Managing functional constipation in children. Paediatric Child Health 2011; 16(10):661-5.

National Institute for Health and Clinical Excellence. Constipation in children and young people: Evidence Update June 2012.

CHRONIC CONSTIPATION:

Andrews CN, Storr M. The pathophysiology of chronic constipation. Can J Gastroenterol. 2011 Oct;25 Suppl B:16B-21B. Review.

Battistella M. Current and future therapies for the management of chronic constipation. Canadian Council on Continuing Education in Pharmacy. February/March 2012.

Bowles-Jordan J. Constipation (Chapter 31), Patient Self-Care, 2nd edition. Canadian Pharmacists Association. Toronto, ON. 2010.

Bungard T, Yakiwchuk E, Foisy M, Brocklebank C. Drug interactions involving warfarin: practice tool & practical management tips. CPJ 2011, 144(1):21-25.

Camilleri M. New treatment options for chronic constipation: mechanisms, efficacy and safety. Can J Gastroenterol. 2011 Oct;25 Suppl B:29B-35B. Review.

Canadian Agency for Drugs & Technologies in Health. Rapid Response Report: Dioctyl Sulfosuccinate or Docusate (Calcium or Sodium) for the Prevention or Management of Constipation: A Review of the Clinical Effectiveness. Available at:http://www.cadth.ca/media/pdf/htis/jul-2014/RC0561%20Stool%20Softeners%20Final.pdf . Accessed September 2014.

Coggrave M,Wiesel P, Norton CC.Management of faecal incontinence and constipation in adults with central neurological diseases. Cochrane Database of Systematic Reviews 2006, Issue 2. Art. No.: CD002115. DOI: 10.1002/14651858.CD002115.pub3.

Ford AC, Talley NJ. Laxatives for chronic constipation in adults. BMJ. 2012 Oct 1;345:e6168.

Ford AC, Suares NC. Effect of laxatives and pharmacological therapies in chronic idiopathic constipation: systematic review and meta-analysis. Gut. 2011 Feb;60(2):209-18.

Gal-Ezer S, Shaoul R. The safety of mineral oil in the treatment of constipation--a lesson from prolonged overdose. Clin Pediatr (Phila). 2006 Nov;45(9):856-8.

Gray JR. What is chronic constipation? Definition and diagnosis. Can J Gastroenterol. 2011 Oct;25 Suppl B:7B-10B.

Johanson JF, Kralstein J. Chronic constipation: a survey of the patient perspective. Aliment Pharmacol Ther. 2007 Mar 1;25(5):599-608.

Lee-Robichaud H, Thomas K, Morgan J, Nelson RL. Lactulose versus Polyethylene Glycol for Chronic Constipation. Cochrane Database of Systematic Reviews 2010, Issue 7. Art. No.: CD007570. DOI: 10.1002/14651858.CD007570.pub2.

Leung L, Riutta T, Kotecha J, Rosser W. Chronic constipation: an evidence-based review. J Am Board Fam Med. 2011 Jul-Aug;24(4):436-51.

Liu LW. Chronic constipation: current treatment options. Can J Gastroenterol. 2011 Oct;25 Suppl B:22B-28B. Review.

Kirkman MS, Zimmerman DR, Filippini SA. Marked deterioration in glycemic control with change in brand of lactulose syrup. South Med J. 1995 Apr;88(4):492-3.

Kumagai Y, Amano H, Sasaki Y, et al. Effect of single and multiple doses of **elobixibat**, an ileal bile acid transporter inhibitor, on **chronic constipation**: a randomised controlled trial. Br J Clin Pharmacol. 2018 Jun 29.

Müller-Lissner SA, Kamm MA, Scarpignato C, Wald A. Myths and misconceptions about chronic constipation. Am J Gastroenterol. 2005 Jan;100(1):232-42.

Panda H, Andrews CN. Constipation in a 40-year-old woman. CMAJ. 2016 Mar 1;188(4):277-8.

Pare P. The approach to diagnosis and treatment of chronic constipation: suggestions for a general practitioner. Can J Gastroenterol. 2011 Oct;25 Suppl B:36B-40B.

Pharmacist 's Letter Detail Document, Treatment of Constipation in Adults. Pharmacist's Letter. April 2013.

Sanchez MI, Bercik P. Epidemiology and burden of chronic constipation. Can J Gastroenterol. 2011 Oct;25 Suppl B:11B-15B. Review.
Sharif F, Crushell E, O'Driscoll K, Bourke B. Liquid paraffin: a reappraisal of its role in the treatment of constipation. Arch Dis Child. 2001 Aug;85(2):121-4. Review.
Stern T, Davis AM. **Evaluation and Treatment** of Patients With Constipation. JAMA. 2016 Jan 12;315(2):192-193.
Storr M, Storr M. Chronic constipation: current management and challenges. Can J Gastroenterol. 2011 Oct;25 Suppl B:5B-6B.
Sugerman DT. Constipation (**patient page**). JAMA. 2013 Oct 2;310(13):1416.
Wald A. **Constipation: Advances in Diagnosis and Treatment**. JAMA. 2016 Jan 12;315(2):185-191.
Wald A. Constipation (**patient page**). JAMA. 2016 Jan 12;315(2):214.

GERIATRICS:

Battistella M. Current and future therapies for the management of chronic constipation. Canadian Council on Continuing Education in Pharmacy. February/March 2012.
Bowles-Jordan J. Constipation (Chapter 31), Patient Self-Care, 2nd edition. Canadian Pharmacists Association. Toronto, ON. 2010.
Gallegos-Orozco JF, Foxx-Orenstein AE, Sterler SM, Stoa JM. Chronic constipation in the elderly. Am J Gastroenterol. 2012 Jan;107(1):18-25; quiz 26.
Gandell D, Straus SE, Bundookwala M et al. Treatment of constipation in older people. CMAJ. 2013 May 14;185(8):663-70. doi:10.1503/cmaj.120819. Epub 2013 Jan 28.
Lee JK. Gastrointestinal Disorders and Nutrition (Chapter 11), Fundamentals of Geriatric Pharmacotherapy: An evidence-based approach. American Society of Health-Systems Pharmacists. Bethesda, MD. 2010.
Weir MA, Fleet JL, Vinden C, et al. Hyponatremia and **Sodium Picosulfate** Bowel Preparations in Older Adults. Am J Gastroenterol. 2014 Mar 4.
Vazquez Roque M, Bouras EP. Epidemiology and management of **chronic constipation** in elderly patients. Clin Interv Aging. 2015 Jun 2;10:919-30.

PALLIATIVE CARE:

Battistella M. Current and future therapies for the management of chronic constipation. Canadian Council on Continuing Education in Pharmacy. February/March 2012.
Bowles-Jordan J. Constipation (Chapter 31), Patient Self-Care, 2nd edition. Canadian Pharmacists Association. Toronto, ON. 2010.
Candy B, Jones L, Goodman ML, Drake R, Tookman A. Laxatives or methylnaltrexone for the management of constipation in palliative care patients. Cochrane Database of Systematic Reviews 2011, Issue 1. Art. No.: CD003448. DOI:10.1002/14651858.CD003448.pub3.
Downing M, ed. Medical Care of the Dying, 4th ed. Victoria Hospice Society. Victoria, BC; 2006.
Fraser Health Hospice Palliative Care Symptom Guidelines. Available at: http://www.fraserhealth.ca/professionals/hospice_palliative_care/
Health Canada. Association of RELISTOR (methylnaltrexone) subcutaneous injection with gastrointestional perforation. 2010. Available at: http://www.hc-sc.gc.ca/dhp-mps/alt_formats/pdf/medeff/advisories-avis/prof/2010/relistor_hpc-cps-eng.pdf (accessed August 14, 2012).
Hospital Pharmacists' Special Interest Group in Palliative Care. Care Beyond Cure: Management of Pain and Other Symptoms, 4th ed. APES Quebec, Canada; 2009.
McNicol ED, Boyce D, Schumann R, Carr DB. Mu-opioid antagonists for opioid-induced bowel dysfunction. Cochrane Database of Systematic Reviews 2008, Issue 2. Art. No.: CD006332. DOI: 10.1002/14651858.CD006332.pub2.
Pereia JL, Associates. The Pallium Palliative Pocketbook: a peer-reviewed, referenced resource. 1st Canadian ed. Edmonton, Canada: The Pallium Project; 2008.

PEDIATRICS:

Auth MK, Vora R, Farrelly P, Baillie C. Childhood constipation. BMJ. 2012 Nov 13;345:e7309.
Battistella M. Current and future therapies for the management of chronic constipation. Canadian Council on Continuing Education in Pharmacy. February/March 2012.
Biggs WS, Dery WH. Evaluation and treatment of constipation in infants and children. Am Fam Physician. 2006 Feb 1;73(3):469-77. Review.
Bowles-Jordan J. Constipation (Chapter 31), Patient Self-Care, 2nd edition. Canadian Pharmacists Association. Toronto, ON. 2010.
Canadian Paediatric Society. 2011 Position Statement: Managing functional constipation in children. Paediatric Child Health 2011; 16(10):661-5.
Constipation Guideline Committee of the North American Society for Pediatric Gastroenterology, Hepatology and Nutrition. Evaluation and treatment of constipation in infants and children: recommendations of the North American Society for Pediatric Gastroenterology, Hepatology and Nutrition. J Pediatr Gastroenterol Nutr. 2006 Sep;43(3):e1-13.
Gordon M, Naidoo K, Akobeng AK, Thomas AG. Osmotic and stimulant laxatives for the management of childhood constipation. CochraneDatabase of Systematic Reviews 2012, Issue 7. Art.No.:CD009118. DOI: 10.1002/14651858.CD009118.pub2.
López J, Botrán M, García A, et al. Constipation in the Critically Ill Child: Frequency and Related Factors. J Pediatr. 2015 Aug 5. pii: S0022-3476(15)00684-8.

National Institute for Health and Clinical Excellence. Constipation in children and young people: Evidence Update June 2012.
Nurko S, Zimmerman LA. Evaluation and Treatment of Constipation in Children and Adolescents. Am Fam Physician. 2014;90(2):82-90.
Pharmacist's Letter Detailed Document, Treatment of Constipation in Children. Pharmacist's Letter. February 2012.
Rajindrajith S, Devanarayana NM, Weerasooriya L, et al. Quality of life and somatic symptoms in children with constipation: a school-based study. J Pediatr. 2013 Oct;163(4):1069-1072.e1.
Tabbers MM, DiLorenzo C, Berger MY, et al. Evaluation and treatment of functional constipation in infants and children: evidence-based recommendations from ESPGHAN and NASPGHAN. J Pediatr Gastroenterol Nutr. 2014 Feb;58(2):258-74.

PREGNANCY:

Battistella M. Current and future therapies for the management of chronic constipation. Canadian Council on Continuing Education in Pharmacy. February/March 2012.
Bowles-Jordan J. Constipation (Chapter 31), Patient Self-Care, 2nd edition. Canadian Pharmacists Association. Toronto, ON. 2010.
Jewell D, Young G. Interventions for treating constipation in pregnancy. Cochrane Database of Systematic Reviews 2001, Issue 2. Art. No.: CD001142. DOI: 10.1002/14651858.CD001142.
Mahadevan U, Kane S. American Gastroenterological Association Institute medical position statement on the use of gastrointestinal medications in pregnancy. Gastroenerology 2006;131:278-82.
Pharmacist's Letter Detailed Document, Gastrointestinal drug use in pregnancy. Pharmacist's Letter. 2006, updated June 2009.
Rungsiprakarn P, Laopaiboon M, Sangkomkamhang US, et al. Interventions for treating **constipation in pregnancy**. Cochrane Database Syst Rev. 2015 Sep 4;9:CD011448.
Trottier M, Erebara A, Bozzo P. Treating constipation during pregnancy. Can Fam Physician. 2012 Aug;58(8):836-8.

OPIOID-INDUCED CONSTIPATION:

Al-Huniti N, Chapel S, Xu H, et al. Population pharmacokinetics of **naloxegol** in a population of 1,247 healthy subjects and patients. Br J Clin Pharmacol. 2015 Aug 28.
Candy B, Jones L, Goodman ML, Drake R et al. Laxatives or methylnaltrexone for the management of constipation in palliative care patients. *Cochrane Database of Systematic Reviews* 2011, Issue 1. Art. No.: CD003448. DOI: 10.1002/14651858.CD003448.pub3.
Camilleri M. Opioid-induced constipation: challenges and therapeutic opportunities. Am J Gastroenterol. 2011 May;106(5):835-42.
Canadian Guideline for Safe and Effective Use of Opioids for Chronic NonCancer Pain© 2010 National Opioid Use Guideline Group (NOUGG).
McNicol ED, Boyce D, Schumann R, Carr DB. Mu-opioid antagonists for opioid-induced bowel dysfunction. *Cochrane Database of Systematic Reviews* 2008, Issue 2. Art. No.: CD006332. DOI: 10.1002/14651858.CD006332.pub2.
Bennett M, Cresswell H. Factors influencing constipation in advanced cancer patients: a prospective study of opioid dose, dantron dose and physical functioning. Palliat Med. 2003 Jul;17(5):418-22.
Carson S, Thakurta S, Low A, et al. Drug Class Review: Long-Acting Opioid Analgesics: Final Update 6 Report [Internet]. Portland (OR): Oregon Health & Science University; 2011 Jul. Available from: http://www.ncbi.nlm.nih.gov/books/NBK62335/.Accessed September 2012.
Chou R, Clark E, Helfand M. Comparative efficacy and safety of long-acting oral opioids for chronic non-cancer pain: a systematic review. J Pain Symptom Manage. 2003 Nov;26(5):1026-48.
Clark AJ, Ahmedzai SH, Allan LG et al. Efficacy and safety of transdermal fentanyl and sustained-release oral morphine in patients with cancer and chronic non-cancer pain. Curr Med Res Opin. 2004 Sep;20(9):1419-28.
Crighton IM, Martin PH, Hobbs GJ et al. A comparison of the effects of intravenous tramadol, codeine, and morphine on gastric emptying in human volunteers. Anesth Analg. 1998 Aug;87(2):445-9.
Daeninck PJ, Bruera E. Reduction in constipation and laxative requirements following opioid rotation to methadone: a report of four cases. J Pain Symptom Manage. 1999 Oct;18(4):303-9.
Leonard J, Baker DE. **Naloxegol**: Treatment for Opioid-Induced Constipation in Chronic Non-Cancer Pain. Ann Pharmacother. 2015 Mar;49(3):360-365.
Luthra P, Burr NE, Brenner DM, et al. Efficacy of **pharmacological therapies for the treatment of opioid-induced constipation**: systematic review and network meta-analysis. Gut. 2018 May 5.
Mercadante S, Casuccio A, Fulfaro F et al. Switching from morphine to methadone to improve analgesia and tolerability in cancer patients: a prospective study. J Clin Oncol. 2001 Jun 1;19(11):2898-904.
Mikus G, Trausch B, Rodewald C et al. Effect of codeine on gastrointestinal motility in relation to CYP2D6 phenotype. Clin Pharmacol Ther. 1997 Apr;61(4):459-66.
NICE: National Institute for Health and Care Excellence (NICE). **Naloxegol** for treating opioid-induced constipation. London (UK): National Institute for Health and Care Excellence (NICE); 2015 Jul.
Pappagallo M. Incidence, prevalence, and management of opioid bowel dysfunction. Am J Surg. 2001 Nov;182(5A Suppl):11S-18S.
Quigley C. Opioids in people with cancer-related pain. Clin Evid (Online).2008 Jul 31;2008.
Radbruch L, Sabatowski R, Loick G et al. Constipation and the use of laxatives: a comparison between transdermal fentanyl and oral morphine. Palliat Med. 2000 Mar;14(2):111-9.
Rowland M. Opioid induced constipation. 2009. Canadian Council on Continuing Education.
Sykes NP. The relationship between opioid use and laxative use in terminally ill cancer patients. Pall Med 1998; 12:375-382.
Tassinari D, Sartori S, Tamburini E et al. Adverse effects of transdermal opiates treating moderate-severe cancer pain in comparison to long-acting morphine: a meta-analysis and systematic review of the literature. J Palliat Med. 2008 Apr;11(3):492-501.
Walsh D. Palliative Medicine. Saunders/Elsevier. Philadelphia, PA.

Wirz S, Wittmann M, Schenk M et al. Gastrointestinal symptoms under opioid therapy: a prospective comparison of oral sustained-release hydromorphone, transdermal fentanyl, and transdermal buprenorphine. Eur J Pain. 2009 Aug;13(7):737-43.
Wirz S, Wartenberg HC, Nadstawek J. Less nausea, emesis, and constipation comparing hydromorphone and morphine? A prospective open-labeled investigation on cancer pain. Support Care Cancer. 2008 Sep;16(9):999-1009.
Wolff RF, Aune D, Truyers C et al. Systematic review of efficacy and safety of buprenorphine versus fentanyl or morphine in patients with chronic moderate to severe pain. Curr Med Res Opin.2012 May;28(5):833-45.
Canadian Agency for Drugs & Technologies in Health. Common Drug Review: Final Recommendation for Oxycodone Hydrochloride/Naloxone Hydrochloride Resubmission, 2012. Available at: http://www.cadth.ca/media/cdr/complete/cdr_complete_Targin_2_Jan-27-12_e.pdf. Accessed September 2012.
Clemens KE, Mikus G. Combined oral prolonged-release oxycodone and naloxone in opioid-induced bowel dysfunction: review of efficacy and safety data in the treatment of patients experiencing chronic pain. Expert Opin Pharmacother. 2010 Feb;11(2):297-310.
Löwenstein O, Leyendecker P, Lux EA et al. Efficacy and safety of combined prolonged-release oxycodone and naloxone in the management of moderate/severe chronic non-malignant pain: results of a prospectively designed pooled analysis of two randomised, double-blind clinical trials. BMC Clin Pharmacol. 2010 Sep 29;10:12.
Löwenstein O, Leyendecker P, Hopp M et al. Combined prolonged-release oxycodone and naloxone improves bowel function in patients receiving opioids for moderate-to-severe non-malignant chronic pain: a randomised controlled trial. Expert Opin Pharmacother. 2009 Mar;10(4):531-43.
Meissner W, Leyendecker P, Mueller-Lissner S et al. A randomised controlled trial with prolonged-release oral oxycodone and naloxone to prevent and reverse opioid-induced constipation. Eur J Pain. 2009 Jan;13(1):56-64.
Pharmacist's Letter. New drug: Targin (oxycodone/naloxone). Pharmacist's Letter/Prescriber's Letter 2010;26(12):261219.
Rentz AM, Yu R, Müller-Lissner S, Leyendecker P. Validation of the Bowel Function Index to detect clinically meaningful changes in opioid-induced constipation. J Med Econ. 2009;12(4):371-83.
Sandner-Kiesling A, Leyendecker P, Hopp M et al. Long-term efficacy and safety of combined prolonged-release oxycodone and naloxone in the management of non-cancer chronic pain. Int J Clin Pract. 2010 May;64(6):763-74.
Schutter U, Grunert S, Meyer C et al. Innovative pain therapy with a fixed combination of prolonged-release oxycodone/naloxone: a large observational study under conditions of daily practice. Curr Med Res Opin. 2010 Jun;26(6):1377-87.
Simpson K, Leyendecker P, Hopp M et al. Fixed-ratio combination oxycodone/naloxone compared with oxycodone alone for the relief of opioid-induced constipation in moderate-to-severe noncancer pain. Curr Med Res Opin. 2008 Dec;24(12):3503-12.
Ueberall MA, Müller-Lissner S, Buschmann-Kramm C, Bosse B. The Bowel Function Index for evaluating constipation in pain patients: definition of a reference range for a non-constipated population of pain patients. J Int Med Res. 2011;39(1):41-50.
Chamberlain BH, Cross K, Winston JL et al. Methylnaltrexone treatment of opioid-induced constipation in patients with advanced illness. J Pain Symptom Manage. 2009 Nov;38(5):683-90.
Gatti A, Sabato AF. Management of opioid-induced constipation in cancer patients: focus on methylnaltrexone. Clin Drug Investig. 2012 May 1;32(5):293-301.
Health Canada. Health Canada endorsed important safety information on Relistor (methylnaltrexone bromide): association of Relistor subcutaneous injection with gastrointestinal perforation. July 28th, 2010.
Lipman AG, Karver S, Cooney GA et al. Methylnaltrexone for opioid-induced constipation in patients with advanced illness: a 3-month open-label treatment extension study. J Pain Palliat Care Pharmacother. 2011;25(2):136-45.
Michna E, Weil AJ, Duerden M et al. Efficacy of subcutaneous methylnaltrexone in the treatment of opioid-induced constipation: a responder post hoc analysis. Pain Med. 2011 Aug;12(8):1223-30.
Michna E, Blonsky ER, Schulman S et al. Subcutaneous methylnaltrexone for treatment of opioid-induced constipation in patients with chronic, nonmalignant pain: a randomized controlled study. J Pain. 2011 May;12(5):554-62. doi: 10.1016/j.jpain.2010.11.008. Epub 2011 Mar 22.
Slatkin NE, Lynn R, Su C et al. Characterization of abdominal pain during methylnaltrexone treatment of opioid-induced constipation in advanced illness: a post hoc analysis of two clinical trials. J Pain Symptom Manage. 2011 Nov;42(5):754-60.
Slatkin N, Thomas J, Lipman AG et al. Methylnaltrexone for treatment of opioid-induced constipation in advanced illness patients. J Support Oncol. 2009 Jan-Feb;7(1):39-46.
Thomas J, Karver S, Cooney GA et al. Methylnaltrexone for opioid-induced constipation in advanced illness. N Engl J Med. 2008 May 29;358(22):2332-43.
Caraceni A, Hanks G, Kaasa S et al. European Palliative Care Research Collaborative (EPCRC); European Association for Palliative Care (EAPC). Use of opioid analgesics in the treatment of cancer pain: evidence-based recommendations from the EAPC. Lancet Oncol. 2012 Feb;13(2):e58-68.
Goodheart CR, Leavitt SB. Managing Opioid-induced Constipation in Ambulatory Care Patients, 2006. Pain Treatment Topics. Available at: http://pain-topics.org/pdf/Managing_Opioid-Induced_Constipation.pdf. Accessed September 2012.
Larkin PJ, Sykes NP, Centeno C et al; European Consensus Group on Constipation in Palliative Care. The management of constipation in palliative care: clinical practice recommendations. Palliat Med. 2008 Oct;22(7):796-807. Review. Erratum in: Palliat Med. 2009 Jun;23(4):376.
National Comprehensive Cancer Network, Inc. Practice Guidelines in Oncology – v.1.2010. Palliative Care.
NHS Lothian Palliative Care Guidelines: Constipation. Available at: http://www.palliativecareguidelines.scot.nhs.uk/documents/Constipationfinal.pdf. Accessed September 2012.
Quigley C. Opioid switching to improve pain relief and drug tolerability. Cochrane Database of Systematic Reviews 2004, Issue 3. Art. No.: CD004847. DOI: 10.1002/14651858.CD004847.
Mercadante S, Ferrera P, Adile C. High doses of oxycodone-naloxone combination may provide poor analgesia. Support Care Cancer. 2011 Sep;19(9):1471-2. Epub 2011 Jun 9.
Ford AC, Brenner DM, Schoenfeld PS. Efficacy of Pharmacological Therapies for the Treatment of Opioid-Induced Constipation: Systematic Review and Meta-Analysis. Am J Gastroenterol. 2013 Jun 11.
Medical Letter. Lubiprostone (Amitiza) for opioid-induced constipation. 2013; 55(1418): 47-48.

Crockett SD, Greer KB, Heidelbaugh JJ, et al; AGAICG Committee. American Gastroenterological Association Institute Guideline on the Medical Management of **Opioid-Induced Constipation**. Gastroenterology. 2018 Oct 16.

Webster LR, Israel RJ Oral **methylnaltrexone does not negatively impact analgesia in patients with opioid-induced constipation and chronic noncancer pain**. J Pain Res. 2018 Aug 13;11:1503-1510.

Brenner DM, Hu Y, Datto C, et al. A Randomized, Multicenter, Prospective, Crossover, Open-Label Study of Factors Associated With **Patient Preferences for Naloxegol or PEG 3350 for Opioid-Induced Constipation.** Am J Gastroenterol. 2019 May 3.

Additional Laxative References:

Abbott R, Ayres I, Hui E, Hui KK. Effect of **perineal self-acupressure** on constipation: a randomized controlled trial. J Gen Intern Med. 2015 Apr;30(4):434-9. Perineal self-massage, in addition to standard treatment approaches, significantly improves quality of life and measures of bowel function in patients with functional constipation. You can take a few minutes to explain the process or you can show a short (2-minute) video in which one of the authors explains the technique: http://tinyurl.com/perinealmassage. (LOE = 1b-)

Antoniou T, Juurlink DN. **Loperamide abuse**. CMAJ. 2017 Jun 12;189(23):E803.

Barichella M, Pacchetti C, Bolliri C, et al. **Probiotics and prebiotic fiber** for constipation associated with Parkinson disease: An RCT. Neurology. 2016 Aug 19.

Bell MM. **Lipoid pneumonia (mineral oil):** An unusual and preventable illness in elderly patients. Can Fam Physician. 2015 Sep;61(9):775-7.

Beinvogl B, Sabharwal S, et al. Are We Using **Abdominal Radiographs** Appropriately in the Management of Pediatric Constipation? J Pediatr. 2017 Dec;191:179-183.

Boland JW, Boland EG. Pharmacological therapies for **opioid induced constipation** in adults with **cancer**. BMJ. 2017 Aug 2;358:j3313

Brooks AJ, Smith PJ, Cohen R, Collins. UK guideline on **transition of adolescent and young persons with chronic digestive diseases from paediatric to adult care**. Gut. 2017 Feb 21.

Bucci C et al. **Optimal bowel cleansing for colonoscopy**: Split the dose! A series of meta-analyses of controlled studies. Gastrointest Endosc 2014 Oct; 80:566.

Calzo JP, Sonneville KR, Scherer EA, et al. **Gender Conformity** and Use of Laxatives and Muscle-Building Products in Adolescents and Young Adults. Pediatrics. 2016 Aug;138(2).

Carlisle BJ, Craft G, Harmon JP, et al. **PEG and Thickeners: A Critical Interaction Between Polyethylene Glycol Laxative and Starch-Based Thickeners**. J Am Med Dir Assoc. 2016 Sep 1;17(9):860-1.

CDC Jul/16: CDC has recommended that clinicians avoid using **liquid docusate** as it investigates a multistate outbreak of healthcare-associated *Burkholderia cepacia* infections.

Choi N-K et al. **Acute renal failure following oral sodium phosphate** bowel preparation: A nationwide case-crossover study. Endoscopy 2014 Jun; 46:465.

Christie J, Shroff S, Shahnavaz N, et al. A Randomized, Double-Blind, Placebo-Controlled Trial to Examine the Effectiveness of **Lubiprostone on Constipation** Symptoms and Colon Transit Time in Diabetic Patients. Am J Gastroenterol. 2016 Dec 6.

Dimidi E, Cox C, Grant R, et al. **Perceptions of Constipation** Among the General Public and People With Constipation Differ Strikingly From Those of General and Specialist Doctors and the Rome IV Criteria. Am J Gastroenterol. 2019 Jun 4.

Fakheri RJ, Volpicelli FM. Things We Do for No Reason: **Prescribing Docusate for Constipation** in Hospitalized Adults. J Hosp Med. 2019 Feb;14(2):110-113.

FDA Jan/14 is warning that the over-the-counter constipation drug **sodium phosphate** (marketed as **Fleet**, and generics) has been tied to heart and kidney damage and even death when patients exceed the recommended dose. The agency has identified over 50 serious adverse events related to dehydration and electrolyte disturbances (sodium, calcium, and phosphate) with both the oral and rectal formulations. Most cases occurred in older adults and children younger than 5 years.

FDA Jan/18 Magno-Humphries Laboratories, Inc., is voluntarily **recalling** one lot of **Basic Drugs Brand of Senna Laxative tablets**, 8.6mg Sennosides to the consumer level due to a customer complaint that their bottle labeled as Senna Laxative actually contained Basic Drugs Brand of Naproxen Sodium 220mg.

DuPont HL. Persistent Diarrhea: A Clinical Review. JAMA. 2016 Jun 28;315(24):2712-23.

Eggleston W, Clark KH, Marraffa JM. **Loperamide Abuse** Associated With Cardiac Dysrhythmia and Death. Ann Emerg Med. 2016 Apr 26.

Ferguson CC, Gary MP, Diaz M, et al. Reducing **Unnecessary Imaging** for Patients with **Constipation** in thePediatric Emergency Department. Peds.2017;140(1):e20162290

Freedman SB, Rodean J, Hall M, et al. **Delayed Diagnoses** in **Children** with **Constipation**: Multicenter Retrospective Cohort Study. J Pediatr. 2017 Jul;186:87-94.e16

Gordon M, MacDonald JK, Parker CE, et al. **Osmotic and stimulant laxatives for the management of childhood constipation**.Cochrane Database Syst Rev. 2016 Aug 17;8:CD009118. The pooled analyses suggest that PEG preparations may be superior to placebo, lactulose and milk of magnesia for childhood constipation. GRADE analyses indicated that the overall quality of the evidence for the primary outcome (number of stools per week) was low or very low due to sparse data, inconsistency (heterogeneity), and high risk of bias in the studies in the pooled analyses. Thus, the results of the pooled analyses should be interpreted with caution because of quality and methodological concerns, as well as clinical heterogeneity, and short follow-up. There is also evidence suggesting the efficacy of liquid paraffin (mineral oil). There is no evidence to demonstrate the superiority of lactulose when compared to the other agents studied, although there is a lack of placebo controlled studies. Further research is needed to investigate the long term use of PEG for childhood constipation, as well as the role of liquid paraffin. The optimal dose of PEG also warrants further investigation.

Gregorio GV, Gonzales MLM, Dans LF, Martinez EG. **Polymer-based oral rehydration solution for treating acute watery diarrhoea**. Cochrane Database of Systematic Reviews 2016, Issue 12. Art. No.: CD006519. Polymer-based ORS shows advantages compared to glucose-based ORS (at ≥ 310 mOsm/L). Comparisons favoured polymer-based ORS over ORS ≤ 270 but analysis was underpowered.

Gu P, Lew D, Oh SJ, Vipani A, et al. Comparing the Real-World Effectiveness of **Competing Colonoscopy Preparations**: Results of a Prospective Trial. Am J Gastroenterol. 2019 Feb;114(2):305-314. (Miralax, Moviprep, Suprep)

Health Canada Jul/17 is advising Canadians that Bayer Inc. is voluntarily recalling **RestoraLAX 45 + 10** Value Pack sold at Costco Canada due to a potential **choking hazard**. The recalled product may contain deposits such as clumps or lumps. The presence of these deposits may pose a choking hazard.

Health Canada Jul/17 is advising Canadians that Bayer Inc. is expanding its voluntary recall to include specific lots of **RestoraLAX 30+7 B**onus Packs sold at various retailers across

Canada due to a potential **choking hazard**.
Horton N, Garber A, Hasson H, et al. Impact of **Single- vs. Split-Dose Low-Volume Bowel Preparations** on Bowel Movement Kinetics, Patient Inconvenience, and Polyp Detection: A Prospective Trial. Am J Gastroenterol. 2016 Jul 5.
Jin J. JAMA **patient page. Over-the-counter laxatives**. JAMA. 2014 Sep 17;312(11):1167.
Koppen IJN, Vriesman MH, Saps M, et al. **Prevalence of Functional Defecation Disorders in Children**: A Systematic Review and Meta-Analysis. J Pediatr. 2018 Apr 12.
Kovacic K, Sood MR, Mugie S, et al. A multicenter study on **childhood constipation and fecal incontinence**: effects on quality of life. J Pediatr. 2015 Jun;166(6):1482-1487
Kurowski J, Kaur S, Katsogridakis Y, et al. **Educational Module** Improves Emergency Department Evaluation for Suspected Constipation. J Pediatr. 2015 Jul 7.
Larkin PJ, Cherny NI, La Carpia D, et al. **Diagnosis, assessment and management of constipation in advanced cancer**: ESMO Clinical Practice Guidelines. Ann Oncol. 2018 Jul 17.
Lee TC, McDonald EG, Bonnici A, Tamblyn R. Pattern of Inpatient Laxative Use: Waste Not, Want Not. JAMA Intern Med. 2016 Jun 20.
Livingston MH, Shawyer AC, Rosenbaum PL, et al. **Glycerin Enemas and Suppositories in Premature Infants**: A Meta-analysis. Pediatrics. 2015 Jun;135(6):1093-1106. Epub 2015 May 18. Review.
Liu Z, Yan S, Wu J, et al. **Acupuncture** for Chronic Severe Functional Constipation: A Randomized, Controlled Trial. Ann Intern Med. 2016 Sep 13.
Mallon D, Vernacchio L, Trudell E, et al. **Shared care**: a quality improvement initiative to optimize primary care management of constipation. Pediatrics. 2015 May;135(5):e1300-7.
MacMillan TE, Kamali R, Cavalcanti RB. Missed Opportunity to **Deprescribe: Docusate** for Constipation in Medical Inpatients. Am J Med. 2016 Sep;129(9):1001.e1-7.
Modi RM, Hinton A, Pinkhas D, et al. Implementation of a **Defecation Posture Modification Device**: Impact on Bowel Movement Patterns in Healthy Subjects. J Clin Gastroenterol. 2018 Oct 22.
Nee J, Zakari M, Sugarman MA, et al. **Efficacy of Treatments for Opioid-induced Constipation**: A Systematic Review and Meta-Analysis. Clin Gastroenterol Hepatol. 2018 Jan 25.
Nelson AD, Camilleri M, Chirapongsathorn S, et al. Comparison of efficacy of pharmacological treatments for **chronic idiopathic constipation**: a systematic review and network meta-analysis. Gut. 2016 Jun 10.
Nguyen GC, Smalley WE, Vege SS, Carrasco-Labra A, Clinical Guidelines Committee. American Gastroenterological Association Institute guideline on the medical management of **microscopic colitis**. Gastroenterology. 2016 Jan;150(1):242-6.
Panda H, Andrews CN. Constipation in a **40-year-old woman**. CMAJ. 2016 Mar 1;188(4):277-8.
Pasay D, Guirguis M, Shkrobot R, et al. Association of Dissemination of an Educational Communication Tool With **Docusate** Administration. JAMA Intern Med. 2017 Aug 7.
Peery AF, Sandler RS, Ahnen DJ, et al. Constipation and a low-fiber diet are not associated with **diverticulosis**. Clin Gastroenterol Hepatol. 2013 Dec;11(12):1622-7.
Rahimi RS, Singal AG, Cuthbert JA, Rockey DC. **Lactulose vs polyethylene glycol 3350-electrolyte solution for treatment of overt hepatic encephalopathy**: the HELP randomized clinical trial [online September 22, 2014]. JAMA Intern Med. doi:10.1001/jamainternmed.2014.4746.
Riddle MS, DuPont HL, Connor BA. ACG Clinical Guideline: Diagnosis, Treatment, and Prevention of **Acute Diarrheal Infections in Adults**. Am J Gastroenterol. 2016 Apr 12.
Riddle MS et al. ACG clinical guideline: Diagnosis, treatment, and prevention of **acute diarrheal infections** in adults. Am J Gastroenterol 2016 May; 111:602.
Schoenfeld P;Lacy BE;Chey WD;Lembo AJ;Kurtz CB;Rea Low-Dose **Linaclotide (72 mug) for Chronic Idiopathic Constipation**: A 12-Week, Randomized, Double-Blind, Placebo-Controlled Trial. Am J Gastroenterol. 2017 Aug 22.
Schuster BG, Kosar L, Kamrul R. **Constipation in older adults**: Stepwise approach to keep things moving. Can Fam Physician. 2015 Feb;61(2):152-8.
Shah BJ, Rughwani N, Rose S. **Constipation-In the Clinic**. Ann Intern Med. 2015 Apr 7;162(7):ITC1.
Sharifi-Rad L, et al. Effects of **Interferential Electrical Stimulation Plus Pelvic Floor Muscles** Exercises on Functional Constipation in Children: A Randomized Clinical Trial. Am J Gastroenterol. 2017 Dec 19.
Sharma BC, et al. Randomized controlled trial comparing **lactulose plus albumin versus lactulose alone for treatment of hepatic encephalopathy**. J Gastroenterol Hepatol. 2017 Jun;32(6):1234-1239.
Song M, Wu K, Meyerhardt JA, et al. **Fiber Intake** and **Survival After Colorectal Cancer Diagnosis**. JAMA Oncol. 2017Nov 2.
Stern T, Davis AM. **Evaluation and Treatment** of Patients With Constipation. JAMA. 2016 Jan 12;315(2):192-193.
Stollman N, Smalley W, Hirano I, AGA Institute Clinical Guidelines Committee. American Gastroenterological Association Institute guideline on the management of acute diverticulitis. Gastroenterology. 2015 Dec;149(7):1944-9.
Tharner A, Jansen PW, et al. Bidirectional Associations between **Fussy Eating and Functional Constipation** in Preschool Children. J Pediatr. 2015 Jan;166(1):91-96.e1.
van Engelenburg-van Lonkhuyzen ML, Bols EM, et al. Effectiveness of **Pelvic Physiotherapy in Children With Functional Constipation** Compared With Standard Medical Care. Gastroenterology. 2017 Jan;152(1):82-91.
Vriesman MH, Velasco-Benitez CA, et al. Assessing Children's Report of **Stool Consistency: Agreement Between the Pediatric Rome III Questionnaire and the Bristol Stool Scale**. J Pediatr. 2017 Sep 11.
Wald A. **Constipation: Advances in Diagnosis and Treatment**. JAMA. 2016 Jan 12;315(2):185-191.
Wald A. Constipation (**patient page**). JAMA. 2016 Jan 12;315(2):214.
Wald A. JAMA **Patient Page**. **Treating Constipation With Medications**. JAMA. 2016 Mar 22-29;315(12):1299.
Wijdicks EF. **Hepatic Encephalopathy**. N Engl J Med. 2016 Oct 27;375(17):1660-1670.
Wojtyniak K, Horvath A, et al. **Lactobacillus casei rhamnosus Lcr35 in the Management of Functional Constipation in Children**: A Randomized Trial. J Pediatr. 2017 Mar 8
Woodward S, Norton C, Chiarelli P. **Biofeedback for treatment of chronic idiopathic constipation in adults**. Cochrane Database Syst Rev. 2014 Mar 26;3:CD008486. Currently there is insufficient evidence to allow any firm conclusions regarding the efficacy and safety of biofeedback for the management of people with chronic constipation. We found low or very low quality evidence from single studies to support the effectiveness ofbiofeedback for the management of people with chronic constipation and dyssynergic defecation. However, the majority of trials are of poor methodological quality and subject to bias. Further well-designed randomised controlled trials with adequate sample sizes, validated outcome measures (especially patient reported outcome measures) and long-term follow-up are required to allow definitive conclusions to be drawn.

Gu P, Lew D, Oh SJ, Vipani A, et al. Comparing the Real-World Effectiveness of **Competing Colonoscopy Preparations**: Results of a Prospective Trial. Am J Gastroenterol. 2019 Feb;114(2):305-314. (**Miralax, Moviprep, Suprep**)

Migaly J, Bafford AC, Francone TD, et al; Clinical Practice Guidelines Committee of the American Society of Colon and Rectal Surgeons. The American Society of Colon and Rectal Surgeons **Clinical Practice Guidelines for the Use of Bowel Preparation** in Elective Colon and Rectal Surgery. Dis Colon Rectum. 2019 Jan;62(1):3-8.

Zawaly K, Rumbolt C, Abou-Setta AM, et al. The Efficacy of **Split-Dose Bowel Preparations for Polyp Detection**: A Systematic Review and Meta-Analysis. Am J Gastroenterol. 2019 Jun;114(6):884-892.

Cochrane reviews CD:

- TNF-a for induction: data not combined. One RCT indicates single infusion may induce remission. CDP571 may induce remission; no evidence for etanercept. Need longer f/u to assess SE such as TB & lymphoma.
- MTX for induction: data not combined. Evidence from a single large trial suggests benefit of MTX 25 mg IM weekly for induction of remission & complete withdrawal from steroids in refractory disease. No evidence supports lower dose PO MTX.
- CsA for induction: low dose PO CsA does not induce remission. Higher PO or IV doses not adequately evaluated, but ↑risk SE such as nephrotoxicity. One study found clinical improvement on unvalidated scale, but remission not assessed.
- AZA and 6-MP effective for inducing remission (NNT=5); OR increases after 17 weeks of tx; NNT=3 for steroid sparing effect; NNT for SE=14.
- Budesonide: superior to placebo for induction & superior to mesalamine; budesonide was inferior to prednisone/prednisolone, but fewer SE. Note: in disease limited to ileum or ascending colon.
- Natalizumab: superior to placebo for induction, but trials halted after 2 cases fatal progressive multifocal leukoencephalopathy in MS.
- Corticosteroids superior to enteral nutrition therapy for induction.
- 5-ASA not superior to placebo in maintaining remission in CD.
- PO budesonide 6 mg/day not effective in maintaining remission.
- Anti-tubercular tx for maintaining remission: may be effective when remission induced by corticosteroids combined with anti-TB tx; however, this is based on subgroup analyses of 2 trials with small numbers
- Corticosteroids (maintenance): not effective and increased AE.
- Probiotics (maintenance): Lactobacilli GC, E. coli strain Nissle 1917, VSL#3, Saccharomyces boulardii-all not effective, but may be due to small sample size
- AZA (maintenance): effective NNT=7 for maintenance; NNT=3 for steroid sparing; NNH=19.

Cochrane reviews UC:

- 5-ASA superior to placebo to induce remission in UC & trended towards benefit over sulfasalazine (SSZ). However, cost an issue, therefore SSZ generally preferred. 5-ASA has fewer SE than SSZ. 5-ASA not associated with male infertility, but SSZ is.
- 5-ASA superior to placebo in maintaining remission for UC (NNT=6). 5-ASA NOT superior to SSZ (NNT= -19), indicating SSZ superior. HOWEVER, many trials required tolerance of SSZ as part of inclusion criteria (Bergman 2006)
- Transdermal nicotine superior to placebo for inducing remission in UC, however no benefit was seen when compared to standard therapy (oral prednisone or mesalamine). More patients on transdermal nicotine withdrew due to AE then placebo or standard therapy.
- Only 2 small trials identified for CsA; could not be pooled as major differences in design & patients involved. Quick response rates in severe disease appear beneficial, but long-term effects unknown.
- In moderate-severe, refractory disease, infliximab induces remission. NNT=5 at 8 weeks (based on ACT studies alone)
- Systematic review: Combination topical & oral 5ASA superior to oral 5ASA for induction of remission of mild-mod UC. Intermittent topical 5ASA superior to oral for prevention of relapse of quiescent UC.[Ford et al.]

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Pregnancy:

- **Guidelines:** Nguyen GC, Seow CH, Maxwell C, et al; IBD in Pregnancy Consensus Group. Canadian Association of Gastroenterology. The Toronto Consensus Statements for the Management of Inflammatory Bowel Disease in Pregnancy. Gastroenterology. 2016 Mar;150(3):734-757.e1.
    - TNF-α inhibitors: Consider D/C 22-24wks gestation if ↓ relapse risk (e.g. sustained remession durring the 12 months before conception, no active disease on endoscopy or imaging during the preconception period, no prior secondary loss of response to anti-TNF therapy or dose escaltion, demonstrated therapeutic levels of anti-TNF therapy, no prior intestinal resections, and no hospitalizations in the past 36 months).
- IBD Patient Information- Pregnancy (University of Saskatchewan Multidisciplinary Inflammatory Bowel Disease Clinic): http://mdibdc.com/images/userImages/files/IBD%20and%20Pregnancy%20Module.pdf

RxFiles – Inflammatory Bowel Disease - References:

[1] Kornbluth A, Sachar DB; **Ulcerative colitis practice guidelines in adults (update)**: **American** College of Gastroenterology (**ACG**), Practice Parameters Committee. Am J Gastroenterol. 2004 Jul;99(7):1371-85.
Ko CW, Singh S, Feuerstein JD, et al; **AGA** Institute Clinical Guidelines Committee. American Gastroenterological Association Institute **Guideline on the Management of Mild-to-Moderate Ulcerative Colitis**. Gastroenterology. 2018 Dec 18.
Lichtenstein GR, Loftus EV, Isaacs KL, et al. **ACG Clinical Guideline: Management of Crohn's Disease** in Adults. Am J Gastroenterol. 2018 Apr;113(4):481-517.
Nguyen GC et al. **AGA**: **American** Gastroenterological Institute guideline on the **management of Crohn's disease after surgical resection**. Gastroenterology 2016 Nov 10.

[2] Dipiro JT, Schade RR. Inflammatory Bowel Disease. In: DipiroJT, Talbert RL, Yee GC, Matzke GR, Wells BG, Posey LM, eds. Pharmacotherapy: a pathophysiologic approach. Toronto, McGraw-Hill, 2005:649-64.
[3] Sandborn WJ, Feagan BG. Review article: mild to moderate Crohn's disease--defining the basis for a new treatment algorithm. Aliment Pharmacol Ther. 2003 Aug 1;18(3):263-77.
[4] Bergman R, Parkes M. Systematic review: the use of mesalazine in inflammatory bowel disease. Aliment Pharmacol Ther. 2006 Apr 1;23(7):841-55.
[5] Hanauer SB, Sandborn W; Practice Parameters Committee of the American College of Gastroenterology. Management of Crohn's disease in adults. Am J Gastroenterol. 2001; Mar;96(3):635-43
[6] Hanauer SB, Stromberg U. Oral Pentasa in the treatment of active Crohn's disease: A meta-analysis of double-blind, placebo-controlled trials. Clin Gastroenterol Hepatol. 2004; May;2(5):379-88.
[7] Simms L, Steinhart AH. **Budesonide** for maintenance of remission in Crohn's disease. **Cochrane** Database Syst Rev. 2001;(1):CD002913.
[8] Ardizzone S, Maconi G, Russo A, et al. Randomised controlled trial of azathioprine and 5-aminosalicylic acid for treatment of steroid dependent ulcerative colitis. Gut. 2006; Jan;55(1):47-53.
[9] Sandborn W, Sutherland L, Pearson D, May G, Modigliani R, Prantera C. Azathioprine or 6-mercaptopurine for inducing remission of Crohn's disease. Cochrane Database Syst Rev. 2000;(2):CD000545.
[10] Panaccione R, Fedorak RN, Aumais G, Bernstein CN, Bitton A, Croitoru K, Enns R, Feagan B, Fishman M, Greenberg G, Griffiths A, Marshall JK, Rasul I, Sadowski D, Seidman E, Steinhart H, Sutherland L, Walli E, Wild G, Williams CN, Zachos M; Canadian Association of Gastroenterology. **Canadian Association of Gastroenterology Clinical Practice Guidelines**: the use of infliximab in Crohn's disease. Can J Gastroenterol. 2004 Aug;18(8):503-8.
[11] Pearson DC, May GR, Fick G, Sutherland LR. Azathioprine for maintaining remission of Crohn's disease. **Cochrane** Database Syst Rev. 2000;(2):CD000067.
[12] Rutgeerts P, Sandborn WJ, Feagan BG, et al. Infliximab for induction and maintenance therapy for ulcerative colitis. N Engl J Med. 2005 Dec 8;353(23):2462-76. Erratum in: N Engl J Med. 2006 May 18;354(20):2200.
[13] SickKids Drug Handbook and Formulary 2006-2007 (25th Ed). Hospital for Sick Children, Toronto, ON, Canada.
[14] IBD guideline team, Cincinnati Children's Hospital Medical Centre: evidence-based care guideline for management of inflammatory bowel disease (IBD), http://www.cincinnatichildrens.org/svc/alpha/h/health-policy/ev-based/ibd.htm Guideline 29 pages 1-16, May 9, 2006.
[15] Pediatric Dosing Handbook, Health Sciences Centre, Winnipeg, MB.
[16] Micromedex 2010
[17] Kane SV. Systematic review: adherence issues in the treatment of ulcerative colitis. Aliment Pharmacol Ther. 2006 Mar 1;23(5):577-85.
[18] Cohen RD, Woseth DM, Thisted RA, et al. A meta-analysis and overview of the literature on treatment options for left-sided ulcerative colitis and ulcerative proctitis. Am J Gastroenterol. 2000 May;95(5):1263-76.
[19] Marteau P, Crand J, Foucault M, Rambaud JC. Use of mesalazine slow release suppositories 1 g three times per week to maintain remission of ulcerative proctitis: a randomised double blind placebo controlled multicentre study. Gut. 1998 Feb;42(2):195-9.
[20] Beattie RM, Croft NM, Fell JM, Afzal NA, Heuschkel RB. Inflammatory bowel disease. Arch Dis Child. 2006 May;91(5):426-32. Review. PMID: 16632672

[21] Simms L, Steinhart AH. **Budesonide** for maintenance of remission in Crohn's disease. **Cochrane** Database Syst Rev. 2001;(1):CD002913.
[22] Sandborn 2003 - duplicate
[23] SickKids Drug Handbook and Formulary 2006-2007 (25th Ed). Hospital for Sick Children, Toronto, ON, Canada.
[24] IBD guideline team, Cincinnati Children's Hospital Medical Centre: evidence-based care guideline for management of inflammatory bowel disease (IBD), http://www.cincinnatichildrens.org/svc/alpha/h/health-policy/ev-based/ibd.htm Guideline 29 pages 1-16, May 9, 2006.
[25] Pediatric Dosing Handbook, Health Sciences Centre, Winnipeg, MB.
[26] Micromedex 2018
[27] Lichtenstein GR, Abreu MT, Cohen R, Tremaine W; American Gastroenterological Association. **American Gastroenterological Association Institute technical review** on **corticosteroids**, **immunomodulators**, and **infliximab** in inflammatory bowel disease. Gastroenterology. 2006 Mar;130(3):940-87.
[28] Lichtenstein GR - Duplicate
[29] Siegel CA, Hur C, Korzenik JR, Gazelle GS, et al. Risks and benefits of infliximab for the treatment of Crohn's disease. Clin Gastroenterol Hepatol. 2006 Aug;4(8):1017-24; quiz 976. Epub 2006 Jul 14.
[30] Alfadhli AA, McDonald JW, Feagan BG. Methotrexate for induction of remission in refractory Crohn's disease. **Cochrane** Database Syst Rev. 2005 Jan 25;(1):CD003459.
[31] Carter MJ, Lobo AJ, Travis SP; IBD Section, British Society of Gastroenterology. Guidelines for the management of inflammatory bowel disease in adults. Gut. 2004 Sep;53 Suppl 5:V1-16.
[32] Escher JC, Taminiau JA, Nieuwenhuis EE, Buller HA, Grand RJ. Treatment of inflammatory bowel disease in childhood: best available evidence. Inflamm Bowel Dis. 2003 Jan;9(1):34-58.
[33] Mack DR, Young R, Kaufman SS, Ramey L, Vanderhoof JA. Methotrexate in patients with Crohn's disease after 6-mercaptopurine. J Pediatr. 1998 May;132(5):830-5.
[34] Pham CQ, Efros CB, Berardi RR. Cyclosporine for severe ulcerative colitis. Ann Pharmacother. 2006 Jan;40(1):96-101. Epub 2005 Dec 20.
[35] Lichtenstein GR, Duplicate.
[36] Belluzzi A, Brignola C, Campieri M, et al. Effect of an enteric-coated fish-oil preparation on relapses in Crohn's disease. N Engl J Med. 1996 Jun 13;334(24):1557-60.
[37] Romano C, Cucchiara S, Barabino A, et al. Usefulness of omega-3 fatty acid supplementation in addition to mesalazine in maintaining remission in pediatric Crohn's disease: a double-blind, randomized, placebo-controlled study. World J Gastroenterol. 2005 Dec 7;11(45):7118-21.
[38] MacLean CH, Mojica WA, Newberry SJ, et al. Systematic review of the effects of n**-3 fatty acids** in inflammatory bowel disease. Am J Clin Nutr. 2005 Sep;82(3):611-9.

Additional IBD References

1: MacLean CH, Mojica WA, Newberry SJ, et al. Systematic review of the effects of n**-3 fatty acids** in inflammatory bowel disease. Am J Clin Nutr. 2005 Sep;82(3):611-9.
2: Romano C, Cucchiara S, Barabino A, et al. Usefulness of omega-3 fatty acid supplementation in addition to mesalazine in maintaining remission in pediatric Crohn's disease: a double-blind, randomized, placebo-controlled study. World J Gastroenterol. 2005 Dec 7;11(45):7118-21.
3: Belluzzi A, Brignola C, Campieri M, et al. Effect of an enteric-coated fish-oil preparation on relapses in Crohn's disease. N Engl J Med. 1996 Jun 13;334(24):1557-60.
1: Thukral C, Cheifetz A, Peppercorn MA. Anti-tumour necrosis factor therapy for ulcerative colitis : evidence to date.Drugs. 2006;66(16):2059-65.
2: Gisbert JP, Gomollon F, Mate J, Pajares JM. Role of 5-aminosalicylic acid (5-ASA) in treatment of inflammatory bowel disease: a systematic review.Dig Dis Sci. 2002 Mar;47(3):471-88.
3: Akobeng AK, Gardener E. Oral 5-aminosalicylic acid for maintenance of medically-induced remission in Crohn's Disease. Cochrane Database Syst Rev. 2005 Jan 25;(1):CD003715.
4: Summers RW, Switz DM, Sessions JT Jr, et al. National Cooperative Crohn's Disease Study: results of drug treatment. Gastroenterology. 1979 Oct;77(4 Pt 2):847-69.
5: Malchow H, Ewe K, Brandes JW, Goebell H, Ehms H, Sommer H, Jesdinsky H. European Cooperative Crohn's Disease Study (ECCDS): results of drug treatment. Gastroenterology. 1984 Feb;86(2):249-66.
6: Bergman R, Parkes M. **Systematic review**: the use of **mesalazine** in inflammatory bowel disease. Aliment Pharmacol Ther. 2006 Apr 1;23(7):841-55.
7: Feagan BG. 5-ASA therapy for active Crohn's disease: old friends, old data, and a new conclusion. Clin Gastroenterol Hepatol. 2004 May;2(5):376-8.
8: Sandborn WJ, Feagan BG. Review article: mild to moderate Crohn's disease--defining the basis for a new treatment algorithm. Aliment Pharmacol Ther. 2003 Aug 1;18(3):263-77.
9: Kane SV, Schoenfeld P, Sandborn WJ, Tremaine W, Hofer T, Feagan BG. The effectiveness of budesonide therapy for Crohn's disease. Aliment Pharmacol Ther. 2002 Aug;16(8):1509-17.
10: Hanauer SB, Stromberg U. Oral Pentasa in the treatment of active Crohn's disease: A meta-analysis of double-blind, placebo-controlled trials. Clin Gastroenterol Hepatol. 2004 May;2(5):379-88.
11: Rutgeerts P, Sandborn WJ, Feagan BG, et al. Infliximab for induction and maintenance therapy for ulcerative colitis. N Engl J Med. 2005 Dec 8;353(23):2462-76. Erratum in: N Engl J Med. 2006 May 18;354(20):2200.
12: Hanauer SB, Feagan BG, Lichtenstein GR, et al.; ACCENT I Study Group. Maintenance infliximab for Crohn's disease: the ACCENT I randomised trial.Lancet. 2002 May 4;359(9317):1541-9.
13: Sands BE, Anderson FH, Bernstein CN, et al. Infliximab maintenance therapy for fistulizing Crohn's disease. N Engl J Med. 2004 Feb 26;350(9):876-85.
14: Rutgeerts P, D'Haens G, Targan S, et al. Efficacy & safety of retreatment with anti-tumor necrosis factor antibody (infliximab) to maintain remission in Crohn's disease. Gastroenterology. 1999 Oct;117(4):761-9.
15: Present DH, Rutgeerts P, Targan S, et al. Infliximab for the treatment of fistulas in patients with Crohn's disease. N Engl J Med. 1999 May 6;340(18):1398-405. (Targan SR, et al. A short-term study of chimeric monoclonal antibody cA2 to tumor necrosis factor alpha for Crohn's disease. Crohn's Disease cA2 Study Group. N Engl J Med. 1997 Oct 9;337(15):1029-35.)
16: Panaccione R, Fedorak RN, Aumais G, et al. **Canadian Association of Gastroenterology**. Canadian Association of Gastroenterology Clinical Practice Guidelines: the use of infliximab in Crohn's disease. Can J Gastroenterol. 2004 Aug;18(8):503-8.
17: Siegel CA, Hur C, Korzenik JR, Gazelle GS, et al. Risks and benefits of infliximab for the treatment of Crohn's disease. Clin Gastroenterol Hepatol. 2006 Aug;4(8):1017-24; quiz 976. Epub 2006 Jul 14.
18: Sandborn WJ. Evidence-based treatment algorithm for mild to moderate Crohn's disease. Am J Gastroenterol. 2003 Dec;98(12 Suppl):S1-5.
19: Hanauer SB, Sandborn W; **Practice Parameters Committee of the American College of Gastroenterology**. Management of Crohn's disease in adults. Am J Gastroenterol. 2001 Mar;96(3):635-43.
20: Papi C, Luchetti R, Gili L, Montanti S, Koch M, Capurso L. **Budesonide** in the treatment of Crohn's disease: a **meta-analysis**. Aliment Pharmacol Ther. 2000 Nov;14(11):1419-28.
21: Sandborn WJ, Hanauer SB. Infliximab in the treatment of Crohn's disease: a user's guide for clinicians. Am J Gastroenterol. 2002 Dec;97(12):2962-72.
22: Cunliffe RN, Scott BB. Review article: monitoring for drug side-effects in inflammatory bowel disease. Aliment Pharmacol Ther. 2002 Apr;16(4):647-62.
23: Carter MJ, Lobo AJ, Travis SP; IBD Section, British Society of Gastroenterology. **Guidelines** for the management of inflammatory bowel disease in adults. Gut. 2004 Sep;53 Suppl 5:V1-16.
24: Lichtenstein GR, Abreu MT, Cohen R, Tremaine W; American Gastroenterological Association. **American Gastroenterological Association** Institute technical review on corticosteroids, immunomodulators, and **infliximab** in inflammatory bowel disease. Gastroenterology. 2006 Mar;130(3):940-87.
25: Escher JC, Taminiau JA, Nieuwenhuis EE, Buller HA, Grand RJ. Treatment of inflammatory bowel disease in childhood: best available evidence. Inflamm Bowel Dis. 2003 Jan;9(1):34-58.
26: Chapman TM, Plosker GL, Figgitt DP. VSL#3 probiotic mixture: a review of its use in chronic inflammatory bowel diseases. Drugs. 2006;66(10):1371-87.
27: Beattie RM, Croft NM, Fell JM, Afzal NA, Heuschkel RB. Inflammatory bowel disease. Arch Dis Child. 2006 May;91(5):426-32. Review. PMID: 16632672
Deepak P, Sifuentes H, Sherid M, et al. **T-Cell Non-Hodgkin's Lymphomas** Reported to the FDA AERS With **Tumor Necrosis Factor-Alpha**(TNF-α) Inhibitors: REFURBISH Study. Am J Gastroenterol. 2013 Jan;108(1):99-105. (increased
28: Podolsky DK. Inflammatory bowel disease. N Engl J Med. 2002 Aug 8;347(6):417-29.
29: Simms L, Steinhart AH. **Budesonide** for maintenance of remission in Crohn's disease. **Cochrane** Database Syst Rev. 2001;(1):CD002913.
30: Alfadhli AA, McDonald JW, Feagan BG. Methotrexate for induction of remission in refractory Crohn's disease. **Cochrane** Database Syst Rev. 2005 Jan 25;(1):CD003459.
31: Sandborn W, Sutherland L, Pearson D, May G, Modigliani R, Prantera C. Azathioprine or 6-mercaptopurine for inducing remission of Crohn's disease. Cochrane Database Syst Rev. 2000;(2):CD000545.
32: Akobeng AK, Zachos M. Tumor necrosis factor-alpha antibody for induction of remission in Crohn's disease. **Cochrane** Database Syst Rev. 2004;(1):CD003574.
33: Zachos M, Tondeur M, Griffiths AM. Enteral nutritional therapy for inducing remission of Crohn's disease. **Cochrane** Database Syst Rev. 2001;(3):CD000542.
34: McDonald JW, Feagan BG, Jewell D, Brynskov J, Stange EF, Macdonald JK. Cyclosporine for induction of remission in Crohn's disease. **Cochrane** Database Syst Rev. 2005 Apr 18;(2):CD000297.
35: Macdonald JK, McDonald JW. Natalizumab for induction of remission in Crohn's disease. **Cochrane** Database Syst Rev. 2006 Jul 19;3:CD006097.
36: Steinhart AH, Ewe K, Griffiths AM, Modigliani R, Thomsen OO. Corticosteroids for maintenance of remission in Crohn's disease. **Cochrane** Database Syst Rev. 2003;(4):CD000301.
37: Rolfe VE, Fortun PJ, Hawkey CJ, Bath-Hextall F. **Probiotics** for maintenance of remission in Crohn's disease. **Cochrane** Database Syst Rev. 2006 Oct 18;(4):CD004826.
38: Pearson DC, May GR, Fick G, Sutherland LR. Azathioprine for maintaining remission of Crohn's disease. **Cochrane** Database Syst Rev. 2000;(2):CD000067.
39: Otley A, Steinhart AH. Budesonide for induction of remission in Crohn's disease. **Cochrane** Database Syst Rev. 2005 Oct 19;(4):CD000296.
40: Sutherland L, Macdonald JK. **Oral 5-aminosalicylic acid for maintenance** of remission in ulcerative colitis. **Cochrane** Database Syst Rev. 2006 Apr 19;(2):CD000544.
41: Sutherland L, Macdonald JK. **Oral 5-aminosalicylic acid for induction** of remission in ulcerative colitis. **Cochrane** Database Syst Rev. 2006 Apr 19;(2):CD000543.
42: Lawson MM, Thomas AG, Akobeng AK. Tumour necrosis factor alpha blocking agents for induction of remission in ulcerative colitis. **Cochrane** Database Syst Rev. 2006 Jul 19;3:CD005112.
43: McGrath J, McDonald JW, Macdonald JK. Transdermal nicotine for induction of remission in ulcerative colitis. **Cochrane** Database Syst Rev. 2004 Oct 18;(4):CD004722.

44: Shibolet O, Regushevskaya E, Brezis M, Soares-Weiser K. Cyclosporine A for induction of remission in severe ulcerative colitis. **Cochrane** Database Syst Rev. 2005 Jan 25;(1):CD004277.
45: Ardizzone S, Maconi G, Russo A, et al. Randomised controlled trial of azathioprine and 5-aminosalicylic acid for treatment of steroid dependent ulcerative colitis. Gut. 2006 Jan;55(1):47-53. Epub 2005 Jun 21.
46: Kornbluth A, Sachar DB; **Practice Parameters Committee of the American College of Gastroenterology. Ulcerative colitis practice guidelines in adults (update)**: American College of Gastroenterology, Practice Parameters Committee. Am J Gastroenterol. 2004 Jul;99(7):1371-85.
47: Collins P, Rhodes J. Ulcerative colitis: diagnosis and management. BMJ. 2006 Aug 12;333(7563):340-3.
48: Marteau P, Crand J, Foucault M, Rambaud JC. Use of mesalazine slow release suppositories 1 g three times per week to maintain remission of ulcerative proctitis: a randomised double blind placebo controlled multicentre study. Gut. 1998 Feb;42(2):195-9.
49: Hanauer SB, Sandborn WJ, Kornbluth A, et al. Delayed-release oral mesalamine at 4.8 g/day (800 mg tablet) for the treatment of moderately active ulcerative colitis: the ASCEND II trial. Am J Gastroenterol. 2005 Nov;100(11):2478-85.
50: Pham CQ, Efros CB, Berardi RR. Cyclosporine for severe ulcerative colitis. Ann Pharmacother. 2006 Jan;40(1):96-101. Epub 2005 Dec 20.
51: Mack DR, Young R, Kaufman SS, Ramey L, Vanderhoof JA. Methotrexate in patients with Crohn's disease after 6-mercaptopurine. J Pediatr. 1998 May;132(5):830-5.
52: Sandborn WJ. Rational selection of oral 5-aminosalicylate formulations and prodrugs for the treatment of ulcerative colitis. Am J Gastroenterol. 2002 Dec;97(12):2939-41.
53: Cohen RD, Woseth DM, Thisted RA, et al. A meta-analysis and overview of the literature on treatment options for left-sided ulcerative colitis and ulcerative proctitis. Am J Gastroenterol. 2000 May;95(5):1263-76.
54: Marshall JK, Irvine EJ. Rectal corticosteroids versus alternative treatments in ulcerative colitis: a meta-analysis. Gut. 1997 Jun;40(6):775-81.
55: Ogata H, Matsui T, Nakamura M, et al. A randomised dose finding study of oral tacrolimus (FK506) therapy in refractory ulcerative colitis. Gut. 2006 Sep;55(9):1255-62. Epub 2006 Feb 16.
56: D'Haens G, Daperno M. Advances in biologic therapy for ulcerative colitis and Crohn's disease. Curr Gastroenterol Rep. 2006 Dec;8(6):506-12.
57: Medical Letter Mar 26,2007. Once daily mesalamine (Lialda) for ulcerative colitis.
58: Sands BE, Anderson FH, Bernstein CN, Chey WY, et al. Infliximab maintenance therapy for fistulizing Crohn's disease. N Engl J Med. 2004 Feb 26;350(9):876-85.
59. Jarnerot G, Hertervig E, Friis-Liby I, Blomquist L, et al. Infliximab as rescue therapy in severe to moderately severe ulcerative colitis: a randomized, placebo-controlled study. Gastroenterology. 2005 Jun;128(7):1805-11.
60. Sandborn WJ, Rutgeerts P, Enns R, Hanauer SB, et al. **Adalimumab** Induction Therapy for Crohn Disease Previously Treated with Infliximab. A Randomized Trial. Ann Intern Med. 2007 Apr 30; [Epub ahead of print] n=325. Adalimumab induces remissions more frequently than placebo in adults with Crohn disease who cannot tolerate infliximab or have symptoms despite receiving infliximab therapy.
61. Gisbert JP, Gonzalez-Lama Y, Mate J. **Systematic review:Infliximab** therapy in ulcerative colitis. Aliment Pharmacol Ther. 2007Jan 1;25(1):19-37. Infliximab is more effective than placebo, with an NNT from 3 to 5, for the treatment of moderate-to-severe UC, achieving clinical remission in 40% of the patients at approximately 9 months of follow-up. Further studies are necessary to confirm the long-term efficacy of infliximab in ulcerative colitis.
62. Bartelds GM, Wijbrandts CA, Nurmohamed MT, et al. Clinical response to adalimumab: relationship to **anti-adalimumab antibodies** and serum adalimumab concentrations in rheumatoid arthritis. Ann Rheum Dis. 2007 Jul;66(7):921-6. Epub 2007 Feb 14. Serum antibodies against adalimumab are associated with lower serum adalimumab concentrations and non-response to adalimumab treatment.
63. Sandborn WJ, Feagan BG, Stoinov S, et al; PRECISE 1 Study Investigators. **Certolizumab** pegol for the treatment of Crohn's disease. N Engl J Med. 2007 Jul 19;357(3):228-38.
64. Schreiber S, Khaliq-Kareemi M, Lawrance IC, et al; PRECISE 2 Study Investigators. Maintenance therapy with **certolizumab** pegol for Crohn's disease. N Engl J Med. 2007 Jul 19;357(3):239-50.
65. Colombel JF, Sandborn WJ, Rutgeerts P, et al. **Adalimumab** for maintenance of clinical response and remission in patients with Crohn's disease: the CHARM trial. Gastroenterology. 2007 Jan;132(1):52-65. Epub 2006 Nov 29.
66. Sandborn WJ, Hanauer SB, Rutgeerts P, et al **Adalimumab** for maintenance treatment of Crohn's disease: results of the CLASSIC II trial. Gut. 2007 Sep;56(9):1232-9. Epub 2007 Feb 13. Adalimumab induced and maintained clinical remission for up to 56 weeks in patients with moderate to severe Crohn's disease naive to anti-TNF treatment.
67. Headstrom PD, Rulyak SJ, Lee SD. Prevalence of and risk factors for **vitamin B(12) deficiency** in patients with Crohn's disease. Inflamm Bowel Dis. 2007 Sep 20; [Epub ahead of print] Vitamin B(12) abnormalities are common in patients with CD and patients with a prior ileal or ileocolonic resection are at particular risk.
68. Langan RC, Gotsch PB, Krafczyk MA, et al. **Ulcerative Colitis**: Diagnosis and Treatment. American Family Physician. Nov 1, 2007.
69. Kruis W, Fric P, Pokrotnieks J, et al. Maintaining remission of ulcerative colitis with the probiotic **Escherichia coli Nissle 1917** is as effective as with standard mesalazine. Gut. 2004 Nov;53(11):1617-23.
70. Rembacken BJ, Snelling AM, et al. **Non-pathogenic Escherichia** coli versus mesalazine for the treatment of ulcerative colitis: a randomised trial. Lancet. 1999 Aug 21;354(9179):635-9.
71. Velayos FS, Terdiman JP, Walsh JM. Effect of **5-aminosalicylate** use on **colorectal cancer** and dysplasia risk: a systematic review and metaanalysis of observational studies. Am J Gastroenterol. 2005 Jun;100(6):1345-53.
72. Nikolaus S, Schreiber S. **Diagnostics** of inflammatory bowel disease. Gastroenterology. 2007 Nov;133(5):1670-89.
73. Roberts SE, Williams JG, Yeates D, Goldacre MJ. Mortality in patients with and without **colectomy** admitted to hospital for ulcerative colitis and Crohn's disease: record linkage studies. BMJ. 2007 Nov 17;335(7628):1033. Epub 2007 Oct 30. In England, the clinical threshold for elective colectomy in people with inflammatory bowel disease may be too high. Further research is now required to establish the threshold criteria and optimal timing of elective surgery for people with poorly controlled inflammatory bowel disease.
74. Langan RC, Gotsch PB, Krafczyk MA, Skillinge DD. **Ulcerative colitis**: diagnosis and treatment. Am Fam Physician. 2007 Nov 1;76(9):1323-30.
75. Panés J, Gomollón F, Taxonera C, Hinojosa J, Clofent J, Nos P. **Crohn's disease** : a review of current treatment with a focus on **biologics**. Drugs. 2007;67(17):2511-37.
76. Turner D, Grossman AB, Rosh J, et al. **Methotrexate** following unsuccessful thiopurine therapy in pediatric Crohn's disease. Am J Gastroenterol. 2007 Dec;102(12):2804-12.
77. Orholm M, Fonager K, Sørensen HT. Risk of ulcerative colitis and Crohn's disease among **offspring of patients** with chronic inflammatory bowel disease. Am J Gastroenterol. 1999 Nov;94(11):3236-8.
78. Behm B, et al. Tumor necrosis factor-alpha antibody for maintenace of remission in Crohn`s disease. **Cochrane** Database Syst Rev. 2008 Jan 23;(1):CD006893. Infliximab 5 mg/kg or 10 mg/kg, given every 8 weeks, is effective for the maintenance of remission and maintenance of fistula healing in patients who have responded to infliximab induction therapy. Adalimumab 40 mg weekly or every other week is effective for the maintenance of remission in patients who have responded to adalimumab induction therapy. Certolizumab pegol 400 mg every 4 weeks is effective for the maintenance of remission in patients who have responded to certolizumab induction therapy.
79. D'Haens G, Baert F, van Assche G, et al; Belgian Inflammatory Bowel Disease Research Group; North-Holland Gut Club. **Early combined immunosuppression** or conventional management in patients with newly diagnosed Crohn's disease: an open randomised trial. Lancet. 2008 Feb 23;371(9613):660-7.
80. Feagan BG, et al. Omega-3 free fatty acids for maintenance of remission in Crohn disease: **EPIC** RCT. JAMA. 2008 Apr 9;299(14):1690-7. In these trials, **omega-3 free fatty acids was not effective** for the prevention of relapse in Crohn disease.
81. Cummings JR, Keshav S, Travis SP. **Medical management of Crohn's disease**. BMJ. 2008 May 10;336(7652):1062-6.
82. Akobeng AK. **Crohn's disease**: current treatment options. Arch Dis Child. 2008 May 2. [Epub ahead of print]
83. Gisbert JP, Gomollón F. Common misconceptions in the diagnosis and management of **anemia** in inflammatory bowel disease. Am J Gastroenterol. 2008 May;103(5):1299-307.
84. Health Canada June/08 Reports of serious **liver injury** in patients receiving **Tysabri**, occurring as early as 6 days after first dose. Tysabri product label has been updated for liver injury, hypersensitivity reactions and herpes infections.
85. Kulnigg S, et al.. A novel intravenous iron formulation for anemia in inflammatory bowel disease: the **ferric carboxymaltose** (FERINJECT) randomized controlled trial. Am J Gastroenterol. 2008 May;103(5):1182-92. Epub 2008 Mar 26.
86. Ferguson CB, Mahsud-Dornan S, Patterson RN. Inflammatory bowel disease in **pregnancy**. BMJ. 2008 Jul 3;337:a427. doi: 10.1136/bmj.39566.681458.BE.
87. Brar H, Einarson A. Effects and treatment of inflammatory bowel disease during **pregnancy**. Can Fam Physician. 2008 Jul;54(7):981-3.
88. Strate LL, Liu YL, Syngal S, et al. **Nut, corn, and popcorn consumption** and the incidence of diverticular disease. JAMA. 2008 Aug 27;300(8):907-14. In this large, prospective study of men without known diverticular disease, nut, corn, and popcorn consumption did not increase the risk of diverticulosis or diverticular complications. The recommendation to avoid these foods to prevent diverticular complications should be reconsidered.
89. Kitazaki S, Mitsuyama K, Masuda J, et al. Clinical trial: comparison of **alendronate** & alfacalcidol in glucocorticoid-associated osteoporosis in patients with ulcerative colitis. Aliment Pharmacol Ther. 2008 Nov 25. [Epub ahead of print] Our study indicates that alendronate is a safe, well tolerated, and more effective therapy than alfacalcidol for preventing glucocorticoid-associated bone loss in patients with ulcerative colitis.
90. **Infliximab** for the treatment of acute exacerbations of ulcerative colitis **NICE** Guidance Dec 2008 http://www.nice.org.uk/TA163
91. Kane S, Ford J, Cohen R, Wagner C. **Absence of Infliximab** in Infant Sera and **Breast Milk** From Nursing Mothers Receiving Therapy for Crohn's Disease Before and After Delivery. J Clin Gastroenterol. 2009 Jan 12. [Epub ahead of print]n=3. Infliximab was detected in the mothers' sera, but not in the breast milk of nursing mothers or in the sera of the breast-fed newborns. Data from this small series of patients suggest that infliximab was not transferred from mother to child, either in utero or through breast milk. These data suggest that mothers receiving infliximab should not be discouraged from nursing their children.
92. Turner D, Zlotkin SH, Shah PS, Griffiths AM. **Omega 3 fatty acids** (fish oil) for maintenance of remission in Crohn's disease. Cochrane Database Syst Rev. 2009 Jan 21;(1):CD006320. Omega 3 fatty acids are safe but probably ineffective for maintenance of remission in CD. The existing data do not support routine maintenance treatment of Crohn's disease with omega 3 fatty acids.
93. Prefontaine E, Sutherland LR, Macdonald JK, Cepoiu M. **Azathioprine** or 6-mercaptopurine for maintenance of remission in Crohn's disease. Cochrane Database Syst Rev. 2009 Jan 21;(1):CD000067. Azathioprine and 6-mercaptopurine are more effective than placebo for maintenance of remission in Crohn's disease. Higher response rates were obtained with azathioprine than 6-mercaptopurine. However, the one study evaluating 6-mercaptopurine used a relatively low dose of the drug. Future studies should look at the effect of higher doses of 6-mercaptopurine. There is weak evidence for a steroid sparing effect with azathioprine treatment.
94. Benchimol EI, Seow CH, Otley AR, Steinhart AH. **Budesonide** for maintenance of remission in Crohn's disease. Cochrane Database Syst Rev. 2009 Jan 21;(1):CD002913. Budesonide is not more effective than placebo or weaning prednisolone for maintenance of remission in Crohn's disease. Some modest benefits are noted in patients receiving budesonide compared with placebo in terms of lower CDAI scores and longer time to relapse of disease. However, these benefits are offset by higher treatment-related adverse event rates and more frequent adrenocorticoid suppression in patients receiving budesonide. Therefore, budesonide is **not recommended** for maintenance of remission in Crohn's disease.
95. Regueiro M, Schraut W, Baidoo L, Kip KE, Sepulveda AR, Pesci M, Harrison J, Plevy SE. **Infliximab** prevents Crohn's disease recurrence **after ileal resection**. Gastroenterology. 2009 Feb;136(2):441-50.e1; quiz 716. Epub 2008 Oct 31.

96. Miele E, Pascarella F, Giannetti E, Quaglietta L, Baldassano RN, Staiano A. Effect of a Probiotic Preparation (VSL#3) on Induction and Maintenance of Remission in Children With Ulcerative Colitis. Am J Gastroenterol. 2009 Jan 20. [Epub ahead of print] This is the first pediatric, n=29, randomized, placebo-controlled trial that suggests the efficacy and safety of a highly concentrated mixture of **probiotic bacterial strains (VSL#3**) in active UC and demonstrates its role in maintenance of remission.
97. Levine A, Kori M, Dinari G, Broide E, Shaoul R, Yerushalmi B, On A, Bujanover Y, Pröls M, Greinwald R; Israeli Pediatric Budesonide Study Group. Comparison of two dosing methods for induction of response and remission with **oral budesonide** in active pediatric Crohn's disease: A randomized placebo-controlled trial. Inflamm Bowel Dis. 2009 Feb 19. [Epub ahead of print] Group 1: Standard dose budesonide (9 mg/day) for 7 weeks followed by 6 mg budesonide daily for an additional 3 weeks. Group 2: Induction with 12 mg/day for the first month followed by the same regimen as Group 1. Use of an induction dose of budesonide followed by a budesonide taper resulted in a trend to higher rates of clinical remission and a decrease in inflammation, without an increase in steroid-associated side effects. Budesonide was also useful for patients with ileocolonic disease.
98. Patel H, Barr A, Jeejeebhoy KN. **Renal effects** of long-term treatment with **5-aminosalicylic acid**. Can J Gastroenterol. 2009 Mar;23(3):170-6. The present study is the first to demonstrate a significant dose- and treatment duration-dependant decline in CrCl. The risks need to be further evaluated because 5-ASA is widely used for long-term maintenance therapy in patients with IBD.
99. Meggitt SJ, Gray JC, Reynolds NJ. Azathioprine dosed by thiopurine methyltransferase activity for moderate-to-severe atopic eczema: a double-blind, randomised controlled trial. Lancet. 2006 Mar 11;367(9513):839-46.
100. Barnes PJ, Adcock IM. **Glucocorticoid resistance** in inflammatory diseases. Lancet. 2009 May 30;373(9678):1905-17.
101. Hindorf U, Johansson M, Eriksson A, Kvifors E, Almer SH. **Mercaptopurine** treatment should be considered in azathioprine intolerant patients with inflammatory bowel disease. Aliment Pharmacol Ther. 2009 Mar 15;29(6):654-61. Epub 2008 Dec 22.
102. Peyrin-Biroulet L, Deltenre P, Ardizzone S, D'Haens G, et al. **Azathioprine and 6-Mercaptopurine** for the Prevention of Postoperative Recurrence in Crohn's Disease: A Meta-Analysis. Am J Gastroenterol. 2009 Jun 30. [Epub ahead of print]
103. Sandborn WJ, Rutgeerts P, Feagan BG, et a;l **Colectomy** Rate Comparison After Treatment of Ulcerative Colitis With Placebo or **Infliximab**. Gastroenterology. 2009 Jul 10. [Epub ahead of print] Patients with moderately-to-severely active ulcerative colitis treated with infliximab were less likely to undergo colectomy through 54 weeks than those receiving placebo.
104. Bernstein CN, et al. **Isotretinoin** Is Not Associated With **Inflammatory Bowel Disease**: A Population-Based Case-Control Study. Am J Gastroenterol. 2009 Jul 21. [Epub ahead of print]
105. Cassinotti A, Actis GC, Duca P, et al. Maintenance Treatment With **Azathioprine** in Ulcerative Colitis: Outcome and Predictive Factors After Drug Withdrawal. Am J Gastroenterol. 2009 Jul 21. [Epub ahead of print
106. Sadowski DC, Bernstein CN, et al.; the CAG Crohn's Consensus Group. **Canadian** Association of Gastroenterology Clinical Practice Guidelines: The use of **tumour necrosis factor-alpha antagonist** therapy in Crohn's disease. Can J Gastroenterol. 2009 Mar;23(3):185-202.
107, **Drugs for Inflammatory Bowel Disease**. Treatment Guidelines- Medical Letter Sept 2009, Mar 2012, Aug 2014 & **Updated July 2018.**
108. Lichtenstein GR, Hanauer SB, Sandborn WJ; Practice Parameters Committee of **American College of Gastroenterology** (ACG). Management of **Crohn's disease** in adults. Am J Gastroenterol. 2009 Feb;104(2):465-83; quiz 464, 484. Epub 2009 Jan 6.
109. Hart AR. **Linoleic Acid**, a Dietary N-6 Polyunsaturated Fatty Acid, and the Aetiology of Ulcerative Colitis - A European Prospective Cohort Study. Gut. 2009 Jul 23. [Epub ahead of print]
110. Assasi N, Blackhouse G, Xie F, Gaebel K, Marshall J, Irvine EJ, Giacomini M, Robertson D, Campbell K, Hopkins R, Goeree R. Anti-TNF-α drugs for refractory inflammatory bowel disease: Clinical- and cost-effectiveness analyses [Technology report number 120] and Overview of anti-TNF-α drugs for refractory inflammatory bowel disease [Technology overview number 52].
111. Beaugerie L, Brousse N, Bouvier AM, et al. for the CESAME Study Group. **Lymphoproliferative** disorders in patients receiving **thiopurines** for inflammatory bowel disease: a prospective observational cohort study. Lancet. 2009 Oct 16. [Epub ahead of print]
FDA Apr/11 Warning of Tumor Necrosis Factor (TNF) blockers, Azathioprine and/or Mercaptopurine: Update on Reports of Hepatosplenic T-Cell Lymphoma in Adolescents and Young Adults.
Chiorean MV, Pokhrel B, Adabala J, et al. Incidence and risk factors for lymphoma in a single-center inflammatory bowel disease population. Dig Dis Sci. 2011 May;56(5):1489-95.
Deepak P, Sifuentes H, Sherid M, et al. **T-Cell Non-Hodgkin's Lymphomas** Reported to the FDA AERS With **Tumor Necrosis Factor-Alpha**(TNF-α) Inhibitors: REFURBISH Study. Am J Gastroenterol. 2013 Jan;108(1):99-105. (increased with TNF use + thiopurines)
Khan N, Abbas AM, Lichtenstein GR, et al. Risk of **lymphoma in patients with ulcerative colitis treated with thiopurines**: a nationwide retrospective cohort study. Gastroenterology 2013;145:1007–1015.
Health Canada Mar/14: IMURAN (azathioprine) or PURINETHOL (mercaptopurine) - Association with a Type of Blood Cancer - Hepatosplenic T-Cell Lymphoma - Triton Pharma Inc. and Teva Canada Ltd.
Ertz-Archambault N, Kosiorek H, Taylor GE, et al. Association of Therapy for Autoimmune Disease With Myelodysplastic Syndromes (MDS etc…) and Acute Myeloid Leukemia. JAMA Oncol. 2017 Feb 2. (azathioprine exposure)

112. Gisbert JP. Safety of immunomodulators and biologics for the treatment of inflammatory bowel disease during **pregnancy and breast-feeding**. Inflamm Bowel Dis. 2009 Nov 2.
113. **WGO Practice Guidelines** Inflammatory bowel disease: a global perspective - June 2009 http://www.worldgastroenterology.org/assets/downloads/en/pdf/guidelines/21_inflammatory_bowel_disease.pdf
114. Hoes JN, Jacobs JW, Verstappen SM, Bijlsma JW, Van der Heijden GJ. Adverse events of low- to medium-dose oral **glucocorticoids** in inflammatory diseases: a meta-analysis. Ann Rheum Dis. 2009 Dec;68(12):1833-8. Epub 2008 Dec 9.
115. Papay P, Reinisch W, Ho E, Gratzer C, et al.. The Impact of **Thiopurines** on the Risk of **Surgical Recurrence** in Patients With Crohn's Disease After First Intestinal Surgery. Am J Gastroenterol. . [Epub ahead of print]
116. Rosh JR, Lerer T, Markowitz J, et al. Retrospective Evaluation of theSafety and Effect of **Adalimumab** Therapy (RESEAT) in **pediatric** Crohn's disease. Am J Gastroenterol. 2009 Dec;104(12):3042-9.
117. Seow CH, Newman A, Irwin SP, Steinhart AH, Silverberg MS, Greenberg GR. **Trough serum infliximab**: a predictive factor of clinical outcome for infliximab treatment in acute ulcerative colitis. Gut. 2010 Jan;59(1):49-54.
(Maser EA, Villela R, Silverberg MS, Greenberg GR. Association of trough serum infliximab to clinical outcome after scheduled maintenance treatment for Crohn's disease. Clin Gastroenterol Hepatol. 2006 Oct;4(10):1248-54. Epub 2006 Aug 22.)
118. Sandborn WJ, Korzenik J, Lashner B, et al. Once Daily Dosing of Delayed-Release Oral Mesalamine (400 mg Tablet) for Maintenance of Remission of Ulcerative Colitis: The **QDIEM** Trial. Gastroenterology. 2010 Jan 8.[Epub ahead of print]
119. Sandborn WJ, Regula J, Feagan BG, et al. Delayed-release oral mesalamine 4.8 g/day (800-mg tablet) is effective for patients with moderately active ulcerative colitis. Gastroenterology. 2009 Dec;137(6):1934-43.e1-3. Epub 2009 Sep 18. (**ASCEND III**)
120. Marshall JK, Thabane M, Steinhart AH, Newman JR, Anand A, Irvine EJ. **Rectal 5-aminosalicylic acid** for induction of remission in ulcerative colitis. Cochrane Database Syst Rev. 2010 Jan 20;(1):CD004115.
121. El-Matary W, Vandermeer B, Griffiths AM. **Methotrexate** for maintenance of remission in ulcerative colitis. Cochrane Database Syst Rev. 2009 Jul 8;(3):CD007560.
122. Hyams JS, Lerer T, Griffiths A, et al. Outcome Following **Infliximab** Therapy in **Children With Ulcerative Colitis**. Am J Gastroenterol. 2010 Jan 26.
123. Wasan SK, Baker SE, Skolnik PR, Farraye FA. A Practical Guide to **Vaccinating t**he Inflammatory Bowel Disease Patient. Am J Gastroenterol. 2010 Jan 26. [Epub ahead of print]
Rahier JF, Ben-Horin S, Chowers Y, et al. on behalf of the European Crohn's and Colitis Organisation (ECCO). **European evidence-based Consensus** on the prevention, diagnosis and management of opportunistic infections in inflammatory bowel disease. J Crohns Colitis. 2009 Jun;3(2):47-91.
124. Farraye FA, Odze RD, Eaden J, Itzkowitz SH. **AGA** technical review on the diagnosis and management of colorectal **neoplasia in inflammatory bowel disease**. Gastroenterology. 2010 Feb;138(2):746-74.
125. Farraye FA, Odze RD, Eaden J, Itzkowitz SH; **AGA** Institute Medical Position Panel on Diagnosis and Management of Colorectal **Neoplasia in Inflammatory Bowel Disease**, McCabe RP, Dassopoulos T, Lewis JD, et al. AGA medical position statement on the diagnosis and management of colorectal neoplasia in inflammatory bowel disease. Gastroenterology. 2010 Feb;138(2):738-45.
NICE: Guideline 118 Mar 2011. **Colonoscopic surveillance** for prevention of colorectal cancer in people with ulcerative colitis, Crohn's disease or adenomas. http://www.nice.org.uk/nicemedia/live/13415/53641/53641.pdf Guick Guide http://www.nice.org.uk/nicemedia/live/13415/53592/53592.pdf
Lieberman DA, Rex DK, Winawer SJ, et al. Guidelines for Colonoscopy Surveillance After Screening and Polypectomy: A Consensus Update by the US Multi-Society Task Force on Colorectal Cancer. Gastroenterology. 2012 Sep;143(3):844-57.
126. Sorrentino D, Paviotti A, Terrosu G, Avellini C, Geraci M, Zarifi D. Low dose maintenance therapy with **infliximab prevents postsurgical recurrence of Crohn's** disease. Clin Gastroenterol Hepatol. 2010 Feb 4.
127. Afif W, Loftus EV Jr, Faubion WA, Kane SV, Bruining DH, Hanson KA, Sandborn WJ. Clinical Utility of Measuring Infliximab and **Human Anti-Chimeric Antibody Concentrations** in Patients With Inflammatory Bowel Disease. Am J Gastroenterol. 2010 Feb 9.
128. Bezabeh S, Flowers CM, Kortepeter C, Avigan M. Review article: clinically significant **liver injury** in patients treated with **natalizumab** (TYSABRI). Aliment Pharmacol Ther. 2010 Feb 16.
129. Fournier MR, Klein J, Minuk GY, Bernstein CN. Changes in **Liver Biochemistry** During **Methotrexate** Use for Inflammatory Bowel Disease. Am J Gastroenterol. 2010 Feb 16. Methotrexate is commonly associated with LET abnormalities, but these frequently normalize while still on therapy, and in only 5% will drug discontinuation be necessary. Liver biopsies rarely have substantive abnormalities
130. Tan CS, Koralnik IJ. **Progressive multifocal leukoencephalopathy** (PML) and other disorders caused by JC virus: clinical features and pathogenesis. Lancet Neurol. 2010 Apr;9(4):425-37.
131. Schreiber S, Colombel JF, Bloomfield R, et al. Increased Response and Remission Rates in Short-Duration Crohn's Disease With Subcutaneous **Certolizumab** Pegol: An Analysis of **PRECiSE 2** Randomized Maintenance Trial Data. Am J Gastroenterol. 2010 Mar 16.f
132. Colombel, Jean Frederic, Sandborn, William J., Reinisch, Walter, et al., the **SONIC** Study Group, **Infliximab, Azathioprine, or Combination** Therapy for Crohn's Disease. N Engl J Med 2010 362: 1383-1395.
Cosnes J, Bourrier A, Laharie D, et al. Early administration of **azathioprine vs conventional management** of Crohn's disease: a randomized controlled trial. Gastroenterology 2013;145:758–765.
Panés J, López-SanRomán A, Bermejo F, et al. Early **azathioprine** therapy is no more effective than placebo for newly diagnosed Crohn's disease. Gastroenterology 2013;145:766–774.
133. Gisbert JP, Linares PM, McNicholl AG, Maté J, Gomollón F. Meta-analysis: the efficacy of **azathioprine and mercaptopurine** in ulcerative colitis. Aliment Pharmacol Ther. 2009 Jul 1;30(2):126-37. Epub 2009 Apr 15.
134. Gisbert JP, Niño P, Cara C, Rodrigo L. Comparative effectiveness of **azathioprine** in Crohn's disease and ulcerative colitis: prospective, long-term, follow-up study of 394 patients. Aliment Pharmacol Ther. 2008 Jul;28(2):228-38. Epub 2008 May 12.
135. Crockett SD et al. **Isotretinoin** use and the risk of **inflammatory bowel disease**: A case–control study. Am J Gastroenterol 2010 Mar 30; [e-pub ahead of print].

136. NICE 2010: Use of tumour necrosis factor alpha (TNF a) inhibitors (**adalimumab, and infliximab** [review]) for **Crohn's** disease (review of TA40) http://guidance.nice.org.uk/TA187
137. Ducharme J, Pelletier C, Zacharias R. The safety of **infliximab infusions** in the community setting. Can J Gastroenterol. 2010 May;24(5):307-11.
138. Jones DW, Finlayson SR. Trends in **Surgery for Crohn's** Disease in the Era of Infliximab. Ann Surg. 2010 Jun 25.
139. Gisbert JP. Safety of immunomodulators and biologics for the treatment of inflammatory bowel disease during **pregnancy and breast-feeding**. Inflamm Bowel Dis. 2010 May;16(5):881-95.
140. Bermejo F, López-Sanromán A, Algaba A, et al. **Mercaptopurine rescue after azathioprine-induced liver injury** in inflammatory bowel disease. Aliment Pharmacol Ther. 2010 Jan;31(1):120-4.
141. van Rheenen PF, Van de Vijver E, Fidler V. **Faecal calprotectin for screening** of patients with suspected inflammatory bowel disease: diagnostic meta-analysis. BMJ. 2010 Jul 15;341
142. Turner D, Griffiths AM. Acute severe **ulcerative colitis in children**: Asystematic review. Inflamm Bowel Dis. 2010 Jul 19.
143. Hussain SW, Pardi DS. **Inflammatory bowel disease in the elderly**. Drugs Aging. 2010 Aug 1;27(8):617-24. doi: 10.2165/11537340-000000000-00000.
144. Teruel C, Román AL, Bermejo F, et al. Outcomes of **Pregnancies Fathered** by Inflammatory Bowel Disease Patients Exposed to **Thiopurines**. Am J Gastroenterol. 2010 Aug 10.
145. Van Assche G, Vermeire S, Rutgeerts P. Management of **acute severe ulcerative colitis**. Gut. 2010 Oct 28.
146. Chi AC, Neville BW, Krayer JW, Gonsalves WC. **Oral manifestations** of systemic disease. Am Fam Physician. 2010 Dec 1;82(11):1381-8. (Oral cavity changes may be first sign of Crohn's disease)
147. Kane SV, Acquah LA. **Placental transport of immunoglobulins**: a clinical review for gastroenterologists who prescribe therapeutic monoclonal antibodies to women during conception and pregnancy. Am J Gastroenterol. 2009;104:228-233.
148. Mahadevan U, Cucchiara S, Hyams JS, et al. The London position statement of the World Congress of Gastroenterology on **Biological Therapy for IBD with the European Crohn's and Colitis Organisation: Pregnancy and Pediatrics**. Am J Gastroenterol. 2010 Dec 14.
149. Hyams JS, Lerer T, Griffiths A, et al. Pediatric Inflammatory Bowel Disease Collaborative Research Group. Outcome following **infliximab therapy in children with ulcerative colitis**. Am J Gastroenterol. 2010 Jun;105(6):1430-6.
150. Hyams JS, Lerer T, Mack D, Bousvaros A, et al. Outcome Following **Thiopurine Use in Children With Ulcerative Colitis**: A Prospective Multicenter Registry Study. Am J Gastroenterol. 2011 Jan 11.
151. Kornbluth A, Sachar DB; Practice Parameters Committee of the American College of Gastroenterology (**ACG**). **Ulcerative colitis practice guidelines in adults: American College Of Gastroenterology**, Practice Parameters Committee. Am J Gastroenterol. **2010** Mar;105(3):501-23.
152. Tursi A, Brandimarte G, Papa A, et al. Treatment of relapsing mild-to-moderate ulcerative colitis with the **probiotic VSL#3** as adjunctive to a standard pharmaceutical treatment: a double-blind, randomized, placebo-controlled study. Am J Gastroenterol. 2010 Oct;105(10):2218-27.
153. Marteau P, Probert CS, Lindgren S, et al. Combined **oral and enema treatment with Pentasa (mesalazine)** is superior to oral therapy alone in patients with extensive mild/moderate active ulcerative colitis: a randomised, double blind, placebo controlled study. Gut. 2005 Jul;54(7):960-5.
154. Safdi M, DeMicco M, Sninsky C, et al. A double-blind comparison of **oral versus rectal mesalamine** versus combination therapy in the treatment of distal ulcerative colitis. Am J Gastroenterol. 1997 Oct;92(10):1867-71.
155. Timmer A, McDonald JW, Macdonald JK. **Azathioprine and 6-mercaptopurine** for maintenance of remission in ulcerative colitis. Cochrane Database Syst Rev. 2007 Jan 24;(1):CD000478.
156. Goodhand JR, Kamperidis N, Nguyen H, et al. Application of the WHO **fracture risk assessment tool (FRAX) to predict need for DEXA scanning** and treatment in patients with inflammatory bowel disease at risk of osteopo rosis.Aliment Pharmacol Ther. 2011 Mar;33(5):551-8.
157. Riquelme AJ, Calvo MA, Guzmán AM, Depix MS, García P, Pérez C, Arrese M, Labarca JA. Saccharomyces cerevisiae fungemia after Saccharomyces boulardii treatment in immunocompromised patients. J Clin Gastroenterol. 2003 Jan;36(1):41-3.
158. Singh JA, Wells GA, Christensen R, et al. **Adverse effects of biologics**: a network meta-analysis and Cochrane overview. Cochrane Database of Systematic Reviews 2011, Issue 2. Art. No.: CD008794. DOI: 10.1002/14651858.CD008794.pub2. Overall, in the short term biologics were associated with significantly higher rates of total adverse events, withdrawals due to adverse events and TB reactivation. Some biologics had a statistically higher association with certain adverse outcomes compared to control, but there was no consistency across the outcomes so caution is needed in interpreting these results.
159. Bernstein CN, Fried M, Krabshuis JH, Cohen H, Eliakim R, Fedail S, et al. **World Gastroenterology Organization Practice Guidelines** for the diagnosis and management of IBD in 2010. Inflamm Bowel Dis. 2010 Jan;16(1):112-24.
160. Nikfar S, Ehteshami-Ashar S, Rahimi R, et al. Systematic review and meta-analysis of the efficacy and tolerability of **nicotine preparations in active ulcerative colitis**. Clin Ther. 2010 Dec;32(14):2304-15. The findings from this meta-analysis do not support the efficacy or tolerability of nicotine preparations in inducing remission in UC.
161. Yarur AJ, Deshpande AR, Pechman DM, et al. Inflammatory Bowel Disease Is Associated With an **Increased Incidence of Cardiovascular Events**. Am J Gastroenterol. 2011 Mar 8.
162. **NICE**: Guideline 118 Mar 2011. **Colonoscopic surveillance** for prevention of colorectal cancer in people with ulcerative colitis, Crohn's disease or adenomas. http://www.nice.org.uk/nicemedia/live/13415/53641/53641.pdf Guick Guide http://www.nice.org.uk/nicemedia/live/13415/53592/53592.pdf
163. Ford AC, Sandborn WJ, Khan KJ, Hanauer SB, Talley NJ, Moayyedi P. Efficacy of **Biological Therapies in Inflammatory Bowel Disease**: Systematic Review and Meta-Analysis. Am J Gastroenterol. 2011 Mar 15.
164. Wee JS, Marinaki A, Smith CH. Life threatening **myelotoxicity secondary to azathioprine** in a patient with atopic eczema and normal thiopurine methyltransferase activity. BMJ. 2011 Mar 25;342:d1417. doi: 10.1136/bmj.d1417.
165. Khan KJ, Dubinsky MC, Ford AC, Ullman TA, Talley NJ, Moayyedi P. Efficacy of **immunosuppressive therapy for inflammatory bowel disease**: a systematic review and meta-analysis. Am J Gastroenterol. 2011 Apr;106(4):630-42.
166. Khan KJ, Ullman TA, Ford AC, Abreu MT, Abadir A, Marshall JK, Talley NJ, Moayyedi P. **Antibiotic therapy in inflammatory bowel disease**: a systematic review and meta-analysis. Am J Gastroenterol. 2011 Apr;106(4):661-73.
167. Talley NJ, Abreu MT, Achkar J for the American College of Gastroenterology (**ACG**) IBD Task Force. An evidence-Based Systematic Review on **Medical Therapies for Inflammatory Bowel Disease**. Am J Gastroenterol. 2011 Apr;106(Supp 1).
168. Ford AC, Achkar JP, Khan KJ, et al. Efficacy of **5-aminosalicylates in ulcerative colitis**: systematic review and meta-analysis. Am J Gastroenterol. 2011 Apr;106(4):601-16. Epub 2011 Mar 15.
169. Bartelds Geertje M., Krieckaert Charlotte L. M., Nurmohamed Michael T., et al. Development of Antidrug **Antibodies Against Adalimumab** and Association With Disease Activity and Treatment Failure During Long-term Follow-up. JAMA. 2011;305(14):1460-1468.doi:10.1001/jama.2011.406
170. Korswagen LA, Bartelds GM, Krieckaert CL, et al. Venous and arterial **thromboembolic events in adalimumab-treated patients with antiadalimumab antibodies**: a case series and cohort study. Arthritis Rheum. 2011 Apr;63(4):877-83. doi: 10.1002/art.30209.
171. Chande N, McDonald JW, Macdonald JK, Wang JJ. Unfractionated or low-molecular weight **heparin** for induction of remission in ulcerative colitis. Cochrane Database Syst Rev. 2010 Oct 6;(10):CD006774.
172. Chiorean MV, Pokhrel B, Adabala J, et al. Incidence and risk factors for **lymphoma** in a single-center inflammatory bowel disease population. Dig Dis Sci. 2011 May;56(5):1489-95. (not higher than general population)
173. Frankel Jonathan K, Packer Clifford D. Cushing's Syndrome Due to Antiretroviral **Ritonaivr-Budesonide Interaction**. Articles Ahead of Print published on 1 June 2011, DOI 10.1345/aph.1P731. Ann Pharmacother ;45:823-824.
174. Booth Ronald A., Ansari Mohammed T., Loit Evelin, et al. Assessment of **Thiopurine S-Methyltransferase Activity in Patients Prescribed Thiopurines**: A Systematic Review. Ann Intern Med June 21, 2011 154:814-823.
175. Mahadevan U, Cucchiara S, Hyams JS, et al. The London Position Statement of the World Congress of Gastroenterology on **Biological Therapy for IBD** with the European Crohn's and Colitis Organisation: **pregnancy and pediatrics**. Am J Gastroenterol. 2011 Feb;106(2):214-23; quiz 224.
176. Baumgart DC, Macdonald JK, Feagan B. **Tacrolimus** (FK506) for induction of remission in refractory ulcerative colitis. Cochrane Database Syst Rev. 2008;(3):CD007216.
177. Ford AC, Bernstein CN, Khan KJ, Abreu MT, Marshall JK, Talley NJ, et al. **Glucocorticosteroid therapy** in inflammatory bowel disease: systematic review and meta-analysis. Am J Gastroenterol. 2011 Apr;106(4):590-9.
178. Sang LX, Chang B, Zhang WL, Wu XM, Li XH, Jiang M. Remission induction and maintenance effect of **probiotics** on ulcerative colitis: a meta-analysis. World J Gastroenterol [Internet]. 2010 Apr 21 [cited 2011 Jun 2];16(15):1908-15.
179. Sherlock ME, Seow CH, Steinhart AH, Griffiths AM. **Oral budesonide** for induction of remission in ulcerative colitis. Cochrane Database Syst Rev. 2010;(10):CD007698.
180. Wall GC, Schirmer LL, Anliker LE, Tigges AE. Pharmacotherapy for **acute pouchitis**. Ann Pharmacother. 2011 Sep;45(9):1127-37.
181. FDA Nov/11 FDA continues to receive reports of a rare cancer of white blood cells (known as **Hepatosplenic T-Cell Lymphoma** or **HSTCL**, primarily in adolescents and young adults being treated for Crohn's disease and ulcerative colitis with medicines known as tumor necrosis factors (TNF) blockers, as well as with azathioprine, and/or mercaptopurine. TNF blockers include Remicade (infliximab), Enbrel (etanercept), Humira (adalimumab), Cimzia (certolizumab pegol) and Simponi (golimumab).
182. Briggs GG, Freeman RK, Sumner JY. Drugs in Pregnancy and Lactation 9th Edition. Williams & Wilkins, Baltimore, 2011.
183. Danese S, Fiocchi C. **Ulcerative colitis**. N Engl J Med. 2011 Nov 3;365(18):1713-25.
184. Peyrin-Biroulet L, Khosrotehrani K, Carrat F, et al. Cesame Study Group. Increased risk for **nonmelanoma skin cancers** in patients who receive **thiopurines** for inflammatory bowel disease. Gastroenterology. 2011 Nov;141(5):1621-1628.e5.
Long MD, Martin CF, Pipkin CA, et al. Risk of melanoma and nonmelanoma skin cancer among patients with inflammatory bowel disease. Gastroenterology. 2012 Aug;143(2):390-399.e1.
Abbas AM, Almukhtar RM, Loftus EV, et al. Risk of **Melanoma and Non-Melanoma Skin Cancer in Ulcerative Colitis Patients Treated With Thiopurines**: A Nationwide Retrospective Cohort. Am J Gastroenterol. 2014 Sep 23.
185. Sanaee F, Clements JD, Waugh AW, et al. Drug-disease interaction: **Crohn's disease elevates verapamil** plasma concentrations but reduces response to the drug proportional to disease activity. Br J Clin Pharmacol. 2011 Nov;72(5):787-97. doi: 10.1111/j.1365-2125.2011.04019.x.
186. Hoentjen F, et al "Long-term effectiveness and tolerability of allopurinol and thiopurine combination therapy in inflammatory bowel disease patients" *ACG* 2011; Abstract 27. http://www.medpagetoday.com/MeetingCoverage/ACG/29402
187. Natekar A, Pupco A, Bozzo P and Koren G. Safety of **azathioprine use during pregnancy**. Can Fam Physician December 2011 57: 1401-1402.
188. Leiper K, Martin K, Ellis A, et al. Randomised placebocontrolled trial of **rituximab** (anti-CD20) in active ulcerative colitis. Gut 2011;60:1520 –1526.
189. Wilkins T, Jarvis K, Patel J. Diagnosis and management of Crohn's disease. American Family Physician December 2011; 84(12):1365-75.
190. Jess T, Frisch M, Jørgensen KT, Pedersen BV, Nielsen NM. Increased risk of inflammatory bowel disease in women with endometriosis: a nationwide Danish cohort study. Gut. 2011 Dec 19.
191. Kappelman MD, Horvath-Puho E, Sandler RS, et al. **Thromboembolic risk** among Danish children and adults with inflammatory bowel diseases: a populationbased nationwide study. Gut 2011;60:937–943.
192. Sandborn WJ, van Assche G, Reinisch W et al. **Adalimumab** Induces and Maintains Clinical Remission in Patients With Moderate-to-Severe Ulcerative Colitis. Gastroenterology. 2011 Nov 4.
193. Merrill A, Millham F. Increased Risk of **Postoperative Deep Vein Thrombosis and Pulmonary Embolism** in Patients With Inflammatory Bowel Disease: A Study of National Surgical Quality Improvement Program Patients. Arch Surg. 2011 Oct 17.
194. Molodecky NA et al. Increasing **incidence and prevalence** of the inflammatory bowel diseases with time, based on systematic review. Gastroenterology. 2012 Jan;142(1):46-54.e42.
195. Louis E et al. Groupe D'etudes Thérapeutiques Des Affections Inflammatoires Digestives. Maintenance of remission among patients with Crohn's disease on **antimetabolite therapy after infliximab therapy is stopped**. (**STORI**) Gastroenterology. 2012 Jan;142(1):63-70.e5.
196. Ananthakrishnan AN, Khalili H, Higuchi LM, et al. Higher predicted **vitamin d** status is associated with reduced risk of Crohn's disease. Gastroenterology. 2012 Mar;142(3):482-9.
197. Prantera C, Lochs H, Grimaldi M et al. **Rifaximin**-extended intestinal release induces remission in patients with moderately active Crohn's disease. Gastroenterology. 2012 Mar;142(3):473-481.e4.
198. Ananthakrishnan AN, Higuchi LM, Huang ES, et al. Aspirin, **Nonsteroidal Anti-inflammatory Drug Use**, and Risk for Crohn Disease and Ulcerative Colitis: A Cohort Study (NHS). Ann Intern Med. 2012 Mar 6;156(5):350-9.
199. National Institute for Health and Clinical Excellence (**NICE**). **Colonoscopic surveillance** for prevention of colorectal cancer in people with ulcerative colitis, Crohn's disease or adenomas. London (UK): National Institute for Health and Clinical Excellence (NICE); 2011 Mar. (Guideline no. 118).
200. Ford AC, Khan KJ, Achkar JP, et al. Efficacy of **oral vs. topical, or combined oral and topical 5-aminosalicylates**, in **Ulcerative Colitis**: systematic review and meta-analysis. Am J Gastroenterol. 2012 Feb;107(2):167-76. Combined 5-ASA therapy appeared superior to oral 5-ASAs for induction of remission of mildly to moderately active UC. Intermittent topical 5-ASAs appeared superior to oral 5-ASAs for preventing relapse of quiescent UC.
201. Fiehn C, Vay S. **Golimumab can induce flares** of inflammatory bowel disease: Report of three cases with enteropathic spondyloarthritis or ankylosing spondylitis and comorbid colitis. Arthritis Rheum. 2011 Jul 18.
202. Levesque BG, Loftus EV Jr. Initiating **azathioprine for Crohn's disease**. Clin Gastroenterol Hepatol. 2012 May;10(5):460-5.
203. Rutgeerts P, Van Assche G, Sandborn WJ, et al. **Adalimumab** Induces and Maintains Mucosal Healing in Patients With **Crohn's** Disease: Data From the **EXTEND** Trial. Gastroenterology. 2012 May;142(5):1102-1111.e2.
204. Román M, Cabaleiro T, Ochoa D, et al. Validation of a Genotyping Method for Analysis of **TPMT Polymorphisms**. Clin Ther. 2012 Mar 13.
205. Lakhi N, Govind A. **Unplanned pregnancy** in a woman with **Crohn** disease. Can Fam Physician. 2012 May;58(5):531-2.
206. Chabok A, Påhlman L, Hjern F, Haapaniemi S, Smedh K; AVOD Study Group. Randomized clinical trial of **antibiotics** in acute uncomplicated **diverticulitis**. Br J Surg. 2012 Apr;99(4):532-9.
207. Crandall WV, Margolis PA, Kappelman MD, et al. Improved Outcomes in a **Quality Improvement Collaborative for Pediatric Inflammatory Bowel Disease**. Pediatrics. 2012 Apr;129(4):e1030-e1041
208. Clarke K, Regueiro M. **Stopping immunomodulators and biologics** in inflammatory bowel disease patients in remission. Inflamm Bowel Dis. 2012 Jan;18(1):174-9.

209. Dignass A, Van Assche G, Lindsay JO, et al; European Crohn's and Colitis Organisation (**ECCO**). The **second European evidence-based Consensus** on the diagnosis and management of **Crohn's disease**: Current management. J Crohns Colitis. 2010 Feb;4(1):28-62.
210. Ford AC, Khan KJ, Sandborn WJ, Kane SV, Moayyedi P. **Once-daily dosing vs. conventional dosing schedule of mesalamine** and relapse of quiescent ulcerative colitis: systematic review and meta-analysis. Am J Gastroenterol. 2011 Dec;106(12):2070-7.
211. Baumgart DC, Sandborn WJ. **Crohn's disease**. Lancet. 2012 Aug 17.
212. Ordás I, Eckmann L, Talamini M, et al. **Ulcerative colitis**. Lancet. 2012 Aug 17.
213. Hollands GJ, Whitwell SC, Parker RA, et al. Effect of communicating DNA based risk assessments for Crohn's disease on **smoking cessation**: randomised controlled trial. BMJ. 2012 Jul 20;345:e4708.
214. Sandborn WJ, Ghosh S, Panes J, et al; Study A3921063 Investigators. **Tofacitinib**, an oral Janus kinase inhibitor, in active ulcerative colitis. N Engl J Med. 2012 Aug 16;367(7):616-24.
215. Sands BE, Sandborn WJ, Creed TJ, et al. **Basiliximab** does not increase efficacy of corticosteroids in patients with steroid-refractory ulcerative colitis. Gastroenterology. 2012 Aug;143(2):356-364.e1.
216. Hyams JS, Griffiths A, Markowitz J, et al. Safety and efficacy of **adalimumab** for moderate to severe **Crohn's** disease in **children**. Gastroenterology. 2012 Aug;143(2):365-374.e2.
217. Jess T, Simonsen J, Jørgensen KT, et al. Decreasing risk of **colorectal cancer** in patients with inflammatory bowel disease over 30 years. Gastroenterology. 2012 Aug;143(2):375-381.e1.
218. Herrinton LJ, Liu L, Levin TR, et al. Incidence and mortality of **colorectal adenocarcinoma** in persons with inflammatory bowel disease from 1998 to 2010. Gastroenterology. 2012 Aug;143(2):382-9.
219. Long MD, Martin CF, Pipkin CA, et al. Risk of **melanoma and nonmelanoma** skin cancer among patients with inflammatory bowel disease. Gastroenterology. 2012 Aug;143(2):390-399.e1.
220. Tursi A. Advances in the management of **colonic diverticulitis**. CMAJ. 2012 Sep 18;184(13):1470-6.
221. Laharie D, Bourreille A, Branche J, et al, Groupe d'Etudes Thérapeutiques des Aff ections Infl ammatoires Digestives. **Ciclosporin versus infl iximab** in patients with severe ulcerative colitis refractory to intravenous steroids: a parallel, open-label randomised controlled trial. Lancet 2012 Oct.
222. Hiraoka S, Kato J, Suzuki H, Yamamoto K. **Readministration of Calcineurin Inhibitors** for Ulcerative Colitis (October). Ann Pharmacother. 2012 Oct 2.
223. Kronman MP, Zaoutis TE, Haynes K, et al. **Antibiotic Exposure** and IBD Development Among Children: A Population-Based Cohort Study. Pediatrics. 2012 Sep 24.
224. Reinisch W, Feagan BG, Rutgeerts PJ, et al. **Infliximab concentration** and clinical outcome in patients with ulcerative colitis. Gastroenterology 2012; 142 (suppl 1): S114.
225. Khalili H, Higuchi LM, Ananthakrishnan AN, et al. **Hormone Therapy** Increases Risk of Ulcerative Colitis but not Crohn's Disease. Gastroenterology. 2012 Jul 27.
226. Sandborn WJ, Gasink C, Gao LL, et al; CERTIFI Study Group. **Ustekinumab** induction and maintenance therapy in refractory Crohn's disease. N Engl J Med. 2012 Oct 18;367(16):1519-28.
227. Sandborn WJ, Travis S, Moro L, et al. Once-Daily **Budesonide MMX® Extended-Release Tablets** Induce Remission in Patients With Mild to Moderate Ulcerative Colitis: Results From the CORE I Study. Gastroenterology. 2012 Aug 11.
228. Shaw SY, Blanchard JF, Bernstein CN. Association between Early Childhood **Otitis Media** and Pediatric Inflammatory Bowel Disease: An Exploratory Population-Based Analysis. J Pediatr. 2012 Oct 17.
229. Van Assche G, D'Haens G, Noman M, et al. Randomized, double-blind comparison of 4 mg/kg versus 2 mg/kg intravenous **cyclosporine** in severe ulcerative colitis. Gastroenterology. 2003 Oct;125(4):1025-31.
230. Deepak P, Sifuentes H, Sherid M, et al. **T-Cell Non-Hodgkin's Lymphomas** Reported to the FDA AERS With **Tumor Necrosis Factor-Alpha**(TNF-α) Inhibitors: REFURBISH Study. Am J Gastroenterol. 2013 Jan;108(1):99-105. (increased with TNF use + thiopurines)
231. Nanda KS, Cheifetz AS, Moss AC. Impact of **Antibodies to Infliximab** on Clinical Outcomes and Serum Infliximab Levels in Patients With Inflammatory Bowel Disease (IBD): A Meta-Analysis. Am J Gastroenterol. 2013 Jan;108(1):40-7.
232. NICE: National Institute for Health and Clinical Excellence **(NICE). Crohn's disease**: management in adults, children and young people. London (UK): National Institute for Health and Clinical Excellence (NICE); 2012 Oct. http://www.nice.org.uk/nicemedia/live/13936/61001/61001.pdf
233. Ford AC, Moayyedi P, Hanauer SB. **Ulcerative colitis**. BMJ. 2013 Feb 5;346:f432.
234. Neovius M, Arkema EV, Blomqvist P, Ekbom et al Patients with **ulcerative colitis miss more days of work** than the general population, even following colectomy. Gastroenterology. 2013 Mar;144(3):536-43.
235. Etminan M, Bird ST, Delaney JA, et al. **Isotretinoin and Risk for Inflammatory Bowel Disease**: A Nested Case-Control Study and Meta-analysis of Published and Unpublished Data. JAMA Dermatol. 2013 Feb 1;149(2):216-20.
236. Sadr-Azodi O, Mattsson F, Bexlius TS, et al. Association of Oral **Glucocorticoid** Use With an Increased Risk of **Acute Pancreatitis**: A Population-Based Nested Case-Control Study. JAMA Intern Med. 2013 Feb 25:1-6.
237. Figueroa JJ, Loftus EV Jr, Harmsen WS, et al. **Peripheral neuropathy** incidence in inflammatory bowel disease: A population-based study.Neurology. 2013 Apr 10.
238. Deboer MD, Denson LA. Delays in Puberty, Growth, and Accrual of **Bone Mineral Density in Pediatric Crohn's** Disease: Despite Temporal Changes in Disease Severity, the Need for Monitoring Remains. J Pediatr. 2013 Mar 22.
239. Adams SM, Bornemann PH. **Ulcerative Colitis**. Am Fam Physician. 2013;87(10):699-705.
240. Cheifetz AS. **Management of active Crohn disease**. JAMA. 2013 May 22;309(20):2150-8.
241. Li WQ, Han JL, Chan AT, Qureshi AA. **Psoriasis, psoriatic arthritis** and increased risk of incident Crohn's disease in US women. Ann Rheum Dis. 2013 Mar 16.
242. Ford AC, Peyrin-Biroulet L. **Opportunistic Infections** With Anti-**Tumor Necrosis Factor**-alpha Therapy in Inflammatory Bowel Disease: Meta-Analysis of Randomized Controlled Trials. Am J Gastroenterol. 2013 May 7.
243. Björnsson ES, Bergmann OM, Björnsson HK, et al. Incidence, presentation, and outcomes in patients with **drug-induced liver injury** in the general population of iceland. Gastroenterology. 2013 Jun;144(7):1419-1425.e3. In a population-based study in Iceland, the incidence of DILI was the highest reported to date. Amoxicillin-clavulanate was the most commonly implicated agent. The highest risk of hepatotoxicity was associated with **azathioprine and infliximab**, but the actual number of cases attributed to these agents was small.
244. Erdener SE, Kansu T, Arsava EM, Dericioglu N. Brain MRI evolution of **metronidazole intoxication** (ataxia, dysarthria). Neurology. 2013 May 7;80(19):1816-7.
245. Hovde O, Kempski-Monstad I, Smastuen MC, et al. **Mortality** and causes of death in **Crohn`s disease**: results from 20 years of follow-up in the IBSEN study. Gut. 2013 Jun 6.
246. Feagan BG et al. **Vedolizumab** as induction and maintenance therapy for **ulcerative colitis**. (Gemini 1) N Engl J Med 2013 Aug 22; 369:699.
247. Sandborn WJ et al. **Vedolizumab** as induction and maintenance therapy for **Crohn's** disease. (Gemini 2) N Engl J Med 2013 Aug 22; 369:711. -
248. Nielsen OH, Ainsworth MA. **Tumor necrosis factor inhibitors** for inflammatory bowel disease. N Engl J Med. 2013 Aug 22;369(8):754-62.
249. Jess T, Horvath-Puho E, Fallingborg J, et al. **Cancer Risk in Inflammatory Bowel Disease** According to Patient Phenotype and Treatment: A Danish Population-Based Cohort Study. Am J Gastroenterol. 2013 Aug 27
250. Lennard L. Implementation of **TPMT testing**. Br J Clin Pharmacol. 2013 Aug 21.TPMT testing is cost-effective and the major role is in the identification of the TPMT deficient individual prior to the start of thiopurine drugs.
251. Tursi A, Brandimarte G, Elisei W, et al. Randomised clinical trial: **mesalazine and/or probiotics** in maintaining remission of symptomatic uncomplicated diverticular disease – a double-blind, randomised, placebo-controlled study. Aliment Pharmacol Ther. 2013 Oct;38(7):741-51.
252. Frolkis AD, Dykeman J, Negrón ME, et al. **Risk of Surgery** for Inflammatory Bowel Diseases Has Decreased Over Time: A Systematic Review and Meta-analysis of Population-Based Studies. Gastroenterology. 2013 Nov;145(5):996-1006.
253. Cosnes J, Bourrier A, Laharie D, et al. Early administration of **azathioprine vs conventional management** of Crohn's disease: a randomized controlled trial. Gastroenterology 2013;145:758–765.
254. Panés J, López-SanRomán A, Bermejo F, et al. Early **azathioprine** therapy is no more effective than placebo for newly diagnosed Crohn's disease. Gastroenterology 2013;145:766–774.
255. Khalili H, Ananthakrishnan AN, Konijeti GG, et al. **Physical activity** and risk of inflammatory bowel disease: prospective study from the Nurses' Health Study cohorts. BMJ. 2013 Nov 14;347:f6633. (Inversely associated with **Crohn's** but not ulcerative colitis)
256. Khan N, Abbas AM, Lichtenstein GR, et al. Risk of **lymphoma in patients with ulcerative colitis treated with thiopurines**: a nationwide retrospective cohort study. Gastroenterology 2013;145:1007–1015.
257. Ananthakrishnan AN, Khalili H, Konijeti GG, et al. A prospective study of **long-term intake of dietary fiber and risk of Crohn's disease and ulcerative colitis**. Gastroenterology 2013;145:970–977.
258. Rungoe C, Basit S, Ranthe MF, et al. Risk of **ischemic heart disease** in patients with inflammatory bowel disease: a nationwide Danish cohort study. Gut 2013;62:689–694.
259. Kristensen SL, Ahlehoff O, Lindhardsen J, et al. Disease activity in inflammatory bowel disease is associated with increased **risk of myocardial infarction, stroke and cardiovascular death** a Danish nationwide cohort study. Plos One 2013;8:e56944.
260. Terdiman JP, Gruss CB, Heidelbaugh JJ, et al. American Gastroenterological Association Institute **Guideline on the Use of Thiopurines, Methotrexate, and Anti-TNF-α Biologic Drugs for the Induction and Maintenance of Remission** in Inflammatory Crohn's Disease. Gastroenterology. 2013 Dec;145(6):1459-63.
261. Dassopoulos T, Sultan S, Falck-Ytter YT, et al. American Gastroenterological Association Institute **Technical Review on the Use of Thiopurines, Methotrexate, and Anti-TNF-α Biologic Drugs for the Induction and Maintenance of Remission** in Inflammatory Crohn's Disease. Gastroenterology. 2013 Dec;145(6):1464-1478.e5.
262. Vuitton L, Koch S, Peyrin-Biroulet L. **Preventing postoperative recurrence in Crohn's** disease: what does the future hold? Drugs. 2013 Nov;73(16):1749-59.
263. Lazzerini M, Martelossi S, Magazzù G, et al. Effect of **thalidomide** on clinical remission in children and adolescents with refractory Crohn disease: a randomized clinical trial. JAMA. 2013 Nov 27;310(20):2164-73.
264. Wingate KE, Jacobson K, Issenman R, et al. **25-Hydroxyvitamin D** Concentrations in Children with Crohn's Disease Supplemented with Either **2000 or 400 IU Daily** for 6 Months: A Randomized Controlled Study. J Pediatr. 2014 Jan 11
265. Waugh N, Cummins E, Royle P, et al. **Faecal calprotectin testing** for differentiating amongst inflammatory and non-inflammatory bowel diseases: systematic review and economic evaluation. Health Technol Assess. 2013 Nov;17(55):1-212. Faecal calprotectin can be a highly sensitive way of detecting IBD, although there are inevitably trade-offs between sensitivity and specificity, with some false positives (IBS with positive calprotectin) if a low calprotectin cut-off is used. In most cases, a negative calprotectin rules out IBD, thereby sparing most people with IBS from having to have invasive investigations, such as colonoscopy.
266. van der Valk ME, Mangen MJ, Leenders M, et al. **COIN** study group and the Dutch Initiative on Crohn and Colitis. Healthcare costs of inflammatory bowel disease have shifted from **hospitalisation and surgery** towards **anti-TNFα therapy**: results from the COIN study. Gut. 2014 Jan;63(1):72-9.
267. Feagan BG, Sandborn WJ, Lazar A, et al. **Adalimumab** therapy is associated with reduced risk of hospitalization in patients with ulcerative colitis. Gastroenterology. 2014 Jan;146(1):110-118
268. Sandborn WJ, Feagan BG, Marano C, et al. Subcutaneous **Golimumab Maintains** Clinical Response in Patients With Moderate-to-Severe **Ulcerative Colitis**. Gastroenterology. 2014 Jan;146(1):96-109
269. Sandborn WJ, Feagan BG, Marano C, et al. Subcutaneous **Golimumab Induces** Clinical Response and Remission in Patients With Moderate-to-Severe **Ulcerative Colitis**. Gastroenterology. 2014 Jan;146(1):85-95
270. Ban L, Tata LJ, Fiaschi L, et al. Limited Risks of Major **Congenital Anomalies** in Children of Mothers With IBD and Effects of Medications. Gastroenterology. 2014 Jan;146(1):76-84
271. Lin KK, Mahadevan U. **Etrolizumab**: Anti-β7-A Novel Therapy for UlcerativeColitis. Gastroenterology. 2014 Jan;146(1):307-9
292. Long MD, Martin C, Sandler RS, et al. Increased risk of **herpes zoster** among 108 604 patients with **inflammatory bowel disease**. Aliment Pharmacol Ther. 2013 Feb;37(4):420-9.
293. Chatu S, Subramanian V, Saxena S, et al. The role of **thiopurines in reducing the need for surgical resection in Crohn's** disease: a systematic review and meta-analysis. Am J Gastroenterol. 2014 Jan;109(1):23-34.
294. Walters TD, Kim MO, Denson LA, et al. Increased Effectiveness of Early Therapy With **Anti-Tumor Necrosis Factor-α vs an Immunomodulator in Children With Crohn's** Disease. Gastroenterology. 2014 Feb;146(2):383-91.
295. Konidari A, Anagnostopoulos A, Bonnett LJ, et al. **Thiopurine monitoring** in children with inflammatory bowel disease: a systematic review. Br J Clin Pharmacol. 2014 Mar 5.
296. Feagan BG, McDonald JW, Panaccione R, et al. **Methotrexate in combination with infliximab** is **no more effective** than infliximab alone in patients with **Crohn's** disease. Gastroenterology. 2014 Mar;146(3):681-688.
297. Nguyen GC, Bernstein CN, Bitton A, et al. Consensus statements on the risk, prevention, and treatment of **venous thromboembolism** in inflammatory bowel disease: canadian association of gastroenterology. Gastroenterology. 2014 Mar;146(3):835-848
298. Panaccione R, Ghosh S, Middleton S, et al. Combination Therapy With **Infliximab and Azathioprine Is Superior** to Monotherapy With Either Agent in Ulcerative Colitis. Gastroenterology. 2013 Oct 25.
299. National Clinical Guideline Centre. **Ulcerative colitis. Management in adults, children** and young people. London (UK): National Institute for Health and Care Excellence (NICE); 2013 Jun.
300. Nielsen OH, Loftus EV, Jess T. Safety of **TNF-α inhibitors during IBD pregnancy**: a systematic review. BMC Med 2013;11:174.
301. Laakso S, Valta H, Verkasalo M, et al. Compromised **Peak Bone Mass** in Patients with Inflammatory Bowel Disease-A Prospective Study. J Pediatr. 2014 Mar 17.
302. Osterman MT, Sandborn WJ, Colombel JF, et al. Increased risk of **malignancy with adalimumab combination therapy, compared with monotherapy**, for Crohn's disease. Gastroenterology. 2014 Apr
303. Solomon DH, Kremer JM, Fisher M, et al. Comparative **cancer risk associated with methotrexate**, other non-biologic and biologic disease-modifying anti-rheumatic drugs. Semin Arthritis Rheum. 2014 Feb;43(4):489-97.

304. Racine A, Cuerq A, Bijon A, et al. **Isotretinoin** and Risk of **Inflammatory Bowel Disease**: A French Nationwide Study. Am J Gastroenterol. 2014 Feb 18.
305. Health Canada Mar/14: IMURAN (**azathioprine**) or PURINETHOL (**mercaptopurine**) - Association with a Type of Blood Cancer - **Hepatosplenic T-Cell Lymphoma** - Triton Pharma Inc. and Teva Canada Ltd.
306. Vester-Andersen MK, Prosberg MV, Jess T, et al. Disease Course and **Surgery Rates in Inflammatory Bowel Disease**: A Population-Based, 7-Year Follow-Up Study in the Era of Immunomodulating Therapy. Am J Gastroenterol. 2014 Mar 18.
307. Williams CJ, Peyrin-Biroulet L, Ford AC. Systematic review with meta-analysis: **malignancies with anti-tumour necrosis factor-α therapy in inflammatory bowel disease**. Aliment Pharmacol Ther. 2014 Mar;39(5):447-58.
308. Lamore RF 3rd, Hechenbleikner EM, Ha C, et al. **Perioperative Glucocorticoid Prescribing** Habits in Patients With Inflammatory Bowel Disease : A Call for Standardization. JAMA Surg. 2014 Mar 19.
309. Miehlke S, Madisch A, Kupcinskas L, et al; BUC-60/COC Study Group. **Budesonide Is More Effective Than Mesalamine** or Placebo in Short-term Treatment of **Collagenous Colitis**. Gastroenterology. 2014 May;146(5):1222-1230.
310. Osterman MT et al. **Comparative** effectiveness of **infliximab** and **adalimumab** for Crohn's disease. Clin Gastroenterol Hepatol 2014 May; 12:811.
311. Vermeire S, O'Byrne S, Keir M, et al. **Etrolizumab** as induction therapy for **ulcerative colitis**: a randomised, controlled, phase 2 trial. Lancet 2014; online May 9. http://dx.doi.org/10.1016/S0140-6736(14)60661-9.
312. Williams CJ, Peyrin-Biroulet L, Ford AC. Systematic review with meta-analysis: **malignancies** with **anti-tumour necrosis factor-α therapy in inflammatory bowel disease**. Aliment Pharmacol Ther. 2014 Mar;39(5):447-58.
313. Ross H, Steele SR, Varma M, Dykes S, Cima R, Buie WD, Rafferty J, Standards Practice Task Force of the **American Society of Colon and Rectal Surgeons**. Practice parameters for the **surgical treatment of ulcerative colitis**. Dis Colon Rectum. 2014 Jan;57(1):5-22.
314. Danese S, Fiorino G, Peyrin-Biroulet L, et al. **Biological agents for moderately to severely active ulcerative colitis**. A systematic review and network meta-analysis. Ann Intern Med. 2014;160:704-11.
315. Jin J. JAMA **patient page. Inflammatory bowel disease**. JAMA. 2014 May 21;311(19):2034.
316. Terdiman JP, Gruss CB, Heidelbaugh JJ, Sultan S, Falck-Ytter YT, AGA Institute Clinical Practice and Quality Management Committee. American Gastroenterological Association Institute guideline on the use of **thiopurines, methotrexate, and anti-TNF-**a biologic drugs for the induction and maintenance of remission in inflammatory **Crohn's** disease. Gastroenterology. 2013 Dec;145(6):1459-63.
317. Forrest CB, Crandall WV, Bailey LC, et al. Effectiveness of **Anti-TNFα for Crohn Disease: Research in a Pediatric** Learning Health System. Pediatrics. 2014 Jun 16.
318. Nyboe Andersen N, Pasternak B, et al. Association between **tumor necrosis factor-α antagonists and risk of cancer** in patients with inflammatory bowel disease. JAMA. 2014 Jun 18;311(23):2406-13.
319. Bickston SJ, Behm BW, Tsoulis DJ, et al. **Vedolizumab** for induction and maintenance of remission in ulcerative colitis. Cochrane Database Syst Rev. 2014 Aug 8;8:CD007571. Moderate to high quality data from four studies shows that vedolizumab is superior to placebo for induction of clinical remission and response and endoscopic remission in patients with moderate to severely active ulcerative colitis and prevention of relapse in patients with quiescent ulcerative colitis. Moderate quality data from one study suggests that vedolizumab is superior to placebo for prevention of relapse in patients with quiescent ulcerative colitis. Adverse events appear to be similar to placebo. Future trials are needed to define the optimal dose, frequency of administration and long-term efficacy and safety of vedolizumab used for induction and maintenance therapy of ulcerative colitis.
320. Cooper WO, Cheetham TC, Li DK et al. Brief report: Risk of **adverse fetal outcomes** associated with **immunosuppressive medications** for chronic immune-mediated diseases in **pregnancy**. Arthritis Rheumatol. 2014 Feb;66(2):444-50.
321. Stobaugh DJ, Deepak P. Effect of **Tumor Necrosis Factor-α Inhibitors** on Drug-Induced **Pancreatitis** in Inflammatory Bowel Disease. Ann Pharmacother. 2014 Oct;48(10):1282-7.
322. Ananthakrishnan AN et al. **Colonoscopy** is associated with a reduced risk for colon cancer and mortality in patients with inflammatory bowel diseases. Clin Gastroenterol Hepatol 2014 Jul 17.
323. Bernstein CN, Nugent Z, Targownik LE, et al. Predictors and **risks for death in a population-based study of persons with IBD** in Manitoba. Gut. 2014 Sep 16. pii: gutjnl-2014-307983.
324. Abbas AM, Almukhtar RM, Loftus EV, et al. Risk of **Melanoma and Non-Melanoma Skin Cancer in Ulcerative Colitis Patients Treated With Thiopurines**: A Nationwide Retrospective Cohort. Am J Gastroenterol. 2014 Sep 23.
325. Kristensen SL, Ahlehoff O, Lindhardsen J, et al. Prognosis after first-time **myocardial infarction** in patients with inflammatory bowel disease according to disease activity: Nationwide cohort study. Circ Cardiovasc Qual Outcomes2014
326. Raithatha N, Mehrtens S, Mouyis M, et al. **Rash and fever after sulfasalazine** use. BMJ. 2014 Oct 8;349:g5655.
327. Cheifetz A. JAMA **patient page. Crohn disease**. JAMA. 2014 Oct 22-29;312(16):1708.
328. Guiddir T, Frémond ML, Triki TB, et al. Anti-TNF-α Therapy May Cause **Neonatal Neutropenia**. Pediatrics. 2014 Oct;134(4):e1189-93. (**ulcerative colitis with infliximab**)
329. Ananthakrishnan AN, Long MD, Martin CF, et al. **Sleep disturbance and risk of active disease in patients with Crohn's disease and ulcerative colitis**. Clin Gastroenterol Hepatol. 2013 Aug;11(8):965-71.
330. Jess T, Lopez A, Andersson M, et al. **Thiopurines and Risk of Colorectal Neoplasia** in Patients With Inflammatory Bowel Disease: A Meta-analysis. Clin Gastroenterol Hepatol. 2014 Jun 4.
331. Casteele NV et al. The relationship between **infliximab concentrations, antibodies** to infliximab and disease activity in Crohn's disease. Gut 2014 Oct 21.
332. Adedokun OJ, Sandborn WJ, Feagan BG, et al. Association between **serum concentration of infliximab** and efficacy in adult patients with ulcerative colitis. Gastroenterology. 2014 Dec;147(6):1296-1307.e5.
333. De Cruz P, Kamm MA, Hamilton AL, et al. **Crohn's disease management after intestinal resection**: a randomised trial. Lancet 2014; online Dec 24. http://dx.doi.org/10.1016/S0140-6736(14)61908-5.
334. Kalla R, Ventham NT, Satsangi J, Arnott ID. **Crohn's disease**. BMJ. 2014 Nov 19;349:g6670.
335. Singh S, Garg SK, Pardi DS, et al. Comparative Efficacy of **Biologic Therapy in Biologic-Naive Patients With Crohn** Disease: A Systematic Review and Network Meta-analysis. Mayo Clin Proc. 2014 Dec;89(12):1621-35.
336. Smith MA, Mohammad RA. **Vedolizumab**: An **α4β7 Integrin Inhibitor** for Inflammatory Bowel Diseases. Ann Pharmacother. 2014 Dec;48(12):1629-1635.
337. Hazlewood GS et al. **Comparative effectiveness of immunosuppressants and biologics for inducing and maintaining remission in Crohn's** disease: A network meta-analysis. Gastroenterology 2015 Feb; 148:344.
338. Avni T, Bieber A, Steinmetz T, et al. Treatment of **anemia in inflammatory bowel disease**--systematic review and meta-analysis. PLoSOne. 2013 Dec 2;8(12)
339. Lankisch PG, Apte M, Banks PA. **Acute pancreatitis**. Lancet. 2015 Jan 20.
340. Singh H, Nugent Z, Brownell M, Targownik LE, Roos LL, Bernstein CN. **Academic Performance** among Children with Inflammatory Bowel Disease: A Population-Based Study. J Pediatr. 2015 Jan 15.
341. Vande Casteele N, Ferrante M, Van Assche G, et al**. Trough Concentrations (3-7 ug/ml) of Infliximab** Guide Dosing for Patients with Inflammatory Bowel Disease. (TAXIT) Gastroenterology. 2015 Feb 24
342. Beaugerie L, Itzkowitz SH. **Cancers** complicating inflammatory bowel disease. N Engl J Med. 2015 Apr 9;372(15):1441-52.
343. Monteleone G, Neurath MF, Ardizzone S, et al. **Mongersen**, an oral SMAD7 antisense oligonucleotide, and Crohn's disease. N Engl J Med. 2015 Mar 19;372(12):1104-13.
344. Goel RM, Hullah E. Images in clinical medicine. **Orofacial fistulae** associated with Crohn's disease. N Engl J Med. 2015 May 28;372(22):e29.
345. Hedin C, van der Gast CJ, Rogers GB, et al. Siblings of patients with Crohn's disease exhibit a biologically relevant dysbiosis in **mucosal microbial metacommunities**. Gut. 2015 Apr 8.
346. Mosli MH, Zou G, Garg SK, et al. **C-Reactive Protein, Fecal Calprotectin, and Stool Lactoferrin** for Detection of Endoscopic Activity in Symptomatic Inflammatory Bowel Disease Patients: A Systematic Review and Meta-Analysis. Am J Gastroenterol. 2015 May 12.
347. Oliva-Hemker M, Hutfless S, Al Kazzi ES, et al. Clinical Presentation and Five-Year Therapeutic Management of **Very Early-Onset Inflammatory Bowel Disease** in a Large North American Cohort. J Pediatr. 2015 May 15.
348. Moayyedi P et al. **Fecal microbiota transplantation** induces remission in patients with active **ulcerative coli**tis in a randomized controlled trial. Gastroenterology 2015 Jul; 149:102.
349. Rossen NG, Fuentes S, van der Spek MJ, et al. Findings From a Randomized Controlled Trial of **Fecal Transplantation** for Patients With **Ulcerative Colitis**. Gastroenterology. 2015 Jul;149(1):110-118.e4.
350. Bewtra M, Newcomb CW, Wu Q, Chen L, Xie F, Roy JA, et al. **Mortality associated with medical therapy versus elective colectomy in ulcerative colitis.** A cohort study. Ann Intern Med. 2015;163:•••-•••. doi:10.7326/M14-0960
351. Wang Y, MacDonald JK, Vandermeer B, et al. Methot**rexate for maintenance of remission in ulcerative colitis**. Cochrane Database Syst Rev. 2015 Aug 11;8:CD007560.
352. Fuller-Thomson E, West KJ, Sulman J, et al. **Childhood Maltreatment Is Associated with Ulcerative Colitis** but Not Crohn's Disease: Findings from a Population-based Study. Inflamm Bowel Dis. 2015 Jul 30.
353. Khanna R, Bressler B, Levesque BG, et al, for the **REACT** Study Investigators. Early combined **immunosuppression for the management of Crohn's disease** (REACT): a cluster randomised controlled trial. Lancet 2015; online Sept 3.
354. Aguirre A, Nugent CA. Images in Clinical Medicine: **Oral Manifestation of Crohn's Disease**. N Engl J Med. 2015 Sep 24;373(13):1250.
355. Mozdiak E, O'Malley J, Arasaradnam R. **Inflammatory bowel disease**. BMJ. 2015 Sep 24;351:h4416.
356. Rosen MJ, Dhawan A, Saeed SA. **Inflammatory Bowel Disease in Children and Adolescents**. JAMA Pediatr. 2015 Sep 28:1-8.
357. Wang Y, MacDonald JK, Benchimol EI, et al. **Type I interferons** for induction of remission in **ulcerative colitis**. Cochrane Database Syst Rev. 2015 Sep 14;9:CD006790.
Moderate quality evidence suggests that type I IFNs are not effective for the induction of remission in UC. In addition, there are concerns regarding the tolerability of this class of treatment.
358. Katsanos KH et al. Increased risk of **oral cancer in patients with inflammatory bowel diseases**. Clin Gastroenterol Hepatol 2015 Oct 20.
359. Teich N, Mohl W, Bokemeyer B, et al; German IBD Study Group*. **Azathioprine-induced acute pancreatitis** in patients with inflammatory bowel diseases - a prospective study on incidence and severity. J Crohns Colitis. 2015 Oct 13.
360. Bressler B, Marshall JK, Bernstein CN, et al; Toronto Ulcerative Colitis Consensus Group. Clinical practice guidelines for the medical management of **nonhospitalized ulcerative colitis**: the **Toronto consensus**. Gastroenterology. 2015 May;148(5):1035-1058.e3.
361. Centor RM. **Acute Uncomplicated Diverticulitis**: What to Do Until We Have Better Data. Ann Intern Med. 2015 Nov 19.
362. Cleynen I, Moerkercke WV, Billiet T, et al. Characteristics of **Skin Lesions Associated With Anti-Tumor Necrosis Factor Therapy** in Patients With Inflammatory Bowel Disease: A Cohort Study. Ann Intern Med. 2015 Dec 8:10-22.
363. Hawkey CJ, Allez M, Clark MM, et al. **Autologous Hematopoetic Stem Cell Transplantation for Refractory Crohn Disease**: A Randomized Clinical Trial. JAMA. 2015 Dec 15;314(23):2524-2534.
364. Scherkenbach LA, Stumpf JL. **Methotrexate** for the Management of **Crohn's Disease** in Children. Ann Pharmacother. 2016 Jan;50(1):60-9.
365. Cleynen I, Boucher G, Jostins L, et al. **Inherited determinants of Crohn's disease** and ulcerative colitis phenotypes: a genetic association study. Lancet 2015; online Oct 19.
366. Daunton A, Langman G, Goulding JM. A **cutaneous presentation** of a common condition. (**Crohn's** Disease) BMJ. 2015 Dec 17;351:h6711.
367. Holtman GA, Lisman-van Leeuwen Y, Reitsma JB, et al. **Noninvasive Tests** for **Inflammatory Bowel Disease**: A Meta-analysis. Pediatrics. 2016 Jan;137(1):1-11.
368. Pdf Brotherton CS et al. Avoidance of **fiber** is associated with greater risk of Crohn's disease flare in a 6-month period. Clin Gastroenterol Hepatol 2015 Dec 31.
369. Huang V, Fedorak R. A 29-year-old woman with **Crohn** disease considering **pregnancy**. CMAJ. 2016 Feb 2;188(2):131-2.
370. Seah D, De Cruz P. Review article: the practical **management of acute severe ulcerative colitis**. Aliment Pharmacol Ther. 2016 Feb;43(4):482-513.
371. Torres J, Boyapati RK, Kennedy NA, et al. Systematic Review of Effects of Withdrawal of **Immunomodulators** or **Biologic Agents** From Patients With **Inflammatory Bowel Disease**. Gastroenterology. 2015 Dec;149(7):1716-30.
372. Harbord M, Annese V, Vavricka SR, et al; **European** Crohn's and Colitis Organisation [**ECCO**]. The First **European Evidence-based Consensus on Extra-intestinal Manifestations in Inflammatory Bowel Disease**. J Crohns Colitis. 2015 Nov 27.
373. Carbonnel F, Colombel JF, Filippi J, et al. **Methotrexate** Is Not Superior to Placebo for Inducing Steroid-Free Remission, but Induces Steroid-Free Clinical Remission in a Larger Proportion of Patients With **Ulcerative Colitis**. Gastroenterology. 2016 Feb;150(2):380-388.e4.
374. Miligkos M, Papamichael K, Casteele NV, et al. Efficacy and Safety Profile of **Anti-Tumor Necrosis Factor-α Versus Anti-integrin Agents** for the Treatment of **Crohn Disease**: A Network Meta-analysis of Indirect Comparisons. Clin Ther. 2016 Apr 15.
375. Nyboe Andersen N, Gørtz S, Frisch M, et al. **Reduced risk of UC (ulcerative colitis) in families affected by appendicitis**: a Danish national cohort study. Gut. 2016 Apr 26.
376. Sandborn WJ, Feagan BG, Wolf DC, et al; **TOUCHSTONE** Study Group. **Ozanimod** Induction and Maintenance Treatment for **Ulcerative Colitis**. N Engl J Med. 2016 May 5;374(18):1754-62.
377. DeFilippis EM, Sockolow R, Barfield E. **Health Care Maintenance for the Pediatric** Patient With Inflammatory Bowel Disease. Pediatrics. 2016 Aug 3.
378. Gubatan J et al. Low serum **vitamin D** during remission increases risk of clinical relapse in patients with **ulcerative colitis**. Clin Gastroenterol Hepatol 2016 Jun 3.

379. Kabbani TA et al. Association of **vitamin D** level with clinical status in **inflammatory bowel disease**: A 5-year longitudinal study. Am J Gastroenterol 2016 May; 111:712.
380. Li Y, Stocchi L, Cherla D, et al. Association of **Preoperative Narcotic Use** With Postoperative Complications and Prolonged Length of Hospital Stay in Patients With Crohn Disease. JAMA Surg. 2016 Aug 1;151(8):726-34
381. Nørgård BM, Magnussen B, Larsen MD, et al. Reassuring results on birth outcomes in children fathered by men treated with **azathioprine/6-mercaptopurine within 3 months before conception**: a nationwide cohort study. Gut. 2016 Jul 25.
382. Nunes T, Etchevers MJ, García-Sánchez Vet al. Impact of **Smoking Cessation** on the Clinical Course of **Crohn's Disease** Under Current Therapeutic Algorithms: A Multicenter Prospective Study. Am J Gastroenterol. 2016 Mar;111(3):411-9.
383. Vutcovici M, Bitton A, Ernst P, et al. Inflammatory bowel disease and risk of **mortality in COPD**. Eur Respir J. 2016 May;47(5):1357-64.
384. Fiorino G, Cortes PN, Ellul P, et al. **Discontinuation of Infliximab** in Patients With **Ulcerative Colitis** Is Associated With **Increased Risk of Relapse**: A Multinational Retrospective Cohort Study. Clin Gastroenterol Hepatol. 2016 Jun 16. pii: S1542-3565(16)30313-5.
385. Laine L, Kaltenbach T, Barkun A, et al. **SCENIC** international consensus statement on surveillance and **management of dysplasia in inflammatory bowel disease**. Gastrointest Endosc. 2015 Mar;81(3):489-501.
386. Mocko P, Kawalec P, Pilc A. **Safety Profile of Biologic Drugs** in the Therapy of **Ulcerative Colitis:** A Systematic Review and Network Meta-Analysis. Pharmacotherapy. 2016 Aug;36(8):870-9.
387. Mowat C, Arnott I, Cahill A, et al. **Mercaptopurine versus placebo** to **prevent recurrence of Crohn's Disease** after surgical resection (**TOPPIC**): a Multicenttre, double-blind, randomized controlled trial. Lancet Gastroenterol Hepatol. 2016 Aug 30.
388. Gomollón F, Dignass A, Annese V, et al; **ECCO** (* FG and *AD contributed equally to this work, AD, FG and PG acted as convenors of the consensus). 3. **EUROPEAN** Evidence-based consensus on the **diagnosis and management** of **Crohn's disease 2016:** Part 1: Diagnosis and medical management. J Crohns Colitis. 2016 Sep 22.
Gionchetti P, Dignass A, Danese S, et al; **ECCO**.. 3rd European Evidence-based Consensus on the Diagnosis and Management of **Crohn's Disease 2016**: Part 2: **Surgical Management and Special Situations**. J Crohns Colitis. 2017 Feb;11(2):135-149.
389. Colombel JF et al. **Management strategies** to improve outcomes of patients with inflammatory bowel diseases. Gastroenterology 2016 Oct 5;.
390. Mahadevan U et al. Drug **safety and risk of adverse outcomes for pregnant patients with inflammatory bowel diseases**. Gastroenterology 2016 Oct 18.
391. Romano C, Syed S, Valenti S, et al. **Management of Acute Severe Colitis in Children With Ulcerative Colitis in the Biologics Era**. Pediatrics. 2016 May;137(5).
392. Nguyen GC et al. **AGA**: **American** Gastroenterological Institute guideline on the **management of Crohn's disease after surgical resection**. Gastroenterology 2016 Nov 10.
393. Regueiro M et al. **AGA**: **American** Gastroenterological Association **technical review on the management of Crohn's disease after surgical resection**. Gastroenterology 2016 Nov 10.
394. Torres J, Mehandru S, Colombel JF, Peyrin-Biroulet L. **Crohn's disease**. Lancet. 2016 Nov 30.
395. Ungaro R, Mehandru S, Allen PB, et al. **Ulcerative colitis**. Lancet. 2016 Nov 30. pii: S0140-6736(16)32126-2.
396. Ananthakrishnan AN. **Filgotinib** for Crohn's disease-expanding treatment options. Lancet. 2016 Dec 14.
397. Feagan BG, Sandborn WJ, Gasink C, et al. **Ustekinumab** as Induction and Maintenance Therapy for Crohn's Disease. (UNITI-IM-UNITI) N Engl J Med. 2016 Nov 17;375(20):1946-1960.
398. Forsmark CE, Swaroop Vege S, Wilcox CM. **Acute Pancreatitis**. N Engl J Med. 2016 Nov 17;375(20):1972-1981 (azathioprine, 6-mercaptopurine, didanosine, valproic acid,angiotensin-converting–enzyme inhibitors, and mesalamine)
399. Jeuring SF, van den Heuvel TR, Liu LY, et al. Improvements in the **Long-Term Outcome of Crohn`s Disease Over the Past Two Decades** and the Relation to Changes in Medical Management: Results from the Population-Based IBDSL Cohort. Am J Gastroenterol. 2016 Dec 6.
400. MacDonald JK, Nguyen TM, Khanna R, et al. **Anti-IL-12/23p40 antibodies** for induction of remission in Crohn's disease. Cochrane Database Syst Rev. 2016 Nov 25;11:CD007572. High quality evidence suggests that **ustekinumab** is effective for induction of clinical remission and clinical improvement in patients with moderate to severe Crohn's disease. Moderate to high quality evidence suggests that the optimal dosage of ustekinumab is 6 mg/kg. **Briakinumab** and ustekinumab appear to be safe. Moderate quality evidence suggests no increased risk of serious adverse events. Future studies are required to determine the long-term efficacy and safety of ustekinumab in patients with moderate to severe Crohn's disease.
401. Marion JF et al. **Chromoendoscopy** is more effective than standard colonoscopy in detecting dysplasia during long-term surveillance of patients with colitis. Clin Gastroenterol Hepatol 2015 Dec 1.
402. Vermeire S, Schreiber S, Petryka R, et al. Clinical remission in patients with moderate-to-severe Crohn's disease treated with **filgotinib** (the **FITZROY** study): results from a phase 2, double-blind, randomised, placebo-controlled trial. Lancet. 2016 Dec 14.
403. Ertz-Archambault N, Kosiorek H, Taylor GE, et al. Association of Therapy for Autoimmune Disease With **Myelodysplastic Syndromes and Acute Myeloid Leukemia**. JAMA Oncol. 2017 Feb 2. (**azathioprine exposure**)
404. Narula N, Steinhart AH. **Preventive care** for a 35-year-old woman with **inflammatory bowel disease**. CMAJ. 2017 Feb 13;189(6):E243-E244.
405. Paramsothy S, Kamm MA, Kaakoush NO, et al. **Multidonor intensive faecal microbiota transplantation** for active **ulcerative colitis**: a randomised placebo-controlled trial. Lancet 2017; online Feb 14.
406. Bouhnik Y, Carbonnel F, Laharie D, et al; **GETAID CREOLE** Study Group.. Efficacy of **adalimumab** in patients with **Crohn's** disease and symptomatic **small bowel stricture**: a multicentre, prospective, observational cohort (CREOLE) study. Gut. 2017 Jan 24.
407. Desai RJ, Bateman BT, Huybrechts KF, et al. **Risk of serious infections associated with use of immunosuppressive agents in pregnant women** with autoimmune inflammatory conditions: cohort study. BMJ. 2017 Mar 6;356:j895.
408. Feagan BG, Sandborn WJ, D'Haens G, et al. Induction therapy with the selective interleukin-23 inhibitor **risankizumab** in patients with moderate-to-severe **Crohn's** disease: a randomised, double-blind, placebo-controlled phase 2 study. Lancet 2017; online April 12.
409. Kugathasan S, Denson LA, Walters TD, et al. **Prediction of complicated disease course** for children newly diagnosed with **Crohn's** disease: a multicentre inception cohort study. Lancet 2017; online March 1.
410. Sandborn WJ, Wolf DC, Kosutic G, et al. Effects of Transient and Persistent **Anti-drug Antibodies** to **Certolizumab** Pegol: Longitudinal Data from a 7-Year Study in **Crohn's** Disease. Inflamm Bowel Dis. 2017 Apr 13.
411. Sandborn WJ, Su C, Sands BE, et al. **Tofacitinib** as induction and maintenance therapy for **ulcerative colitis**. (**Octave Sustain**) N Engl J Med 2017; 376: 1723-36.
412. Varkas G, Thevissen K, De Brabanter G, et al. An induction or flare of arthritis and/or sacroiliitis by **vedolizumab** in inflammatory bowel disease: a case series. Ann Rheum Dis. 2017 May;76(5):878-881.
413. Danese S, Fiorino G, Raine T, et al. **ECCO Position Statement on the Use of Biosimilars for Inflammatory Bowel Disease**-An Update. J Crohns Colitis. 2017 Jan;11(1):26-34.
414. Miloslavsky EM, Stone JH, Moy AP. Case 14-2017 - A 20-Year-Old Man with Pain and **Swelling of the Left Calf and a Purpuric Rash**. N Engl J Med. 2017 May 11;376(19):1868-1877
415. Stritzke AI, Seow CH. **Inflammatory bowel disease in pregnancy**. CMAJ. 2017 May 8;189(18):E669.
416. Nguyen GC, Seow CH, Maxwell C, et al; IBD in Pregnancy Consensus Group.; **Canadian Association of Gastroenterology.. The Toronto Consensus Statements for the Management of Inflammatory Bowel Disease in Pregnancy**. Gastroenterology. 2016 Mar;150(3):734-757.
417. Bafeta A, Yavchitz A, Riveros C, Batista R, Ravaud P. Methods and reporting studies assessing **fecal microbiota transplantation**. A systematic review. Ann Intern Med. 2017. [Epub ahead of print]. doi:10 .7326/M16-2810
418. Malarcher CA, Wheaton AG, Liu Y, et al. **Hospitalizations for Crohn's Disease** - **United States**, 2003-2013. MMWR Morb Mortal Wkly Rep. 2017 Apr 14;66(14):377-381.
419. Vermeire S, Sandborn WJ, Danese S, et al. **Anti-MAdCAM antibody (PF-00547659) for ulcerative colitis**: the **TURANDOT** study. Lancet 2017; online May 17.
420. Benchimol EI, Bernstein CN, Bitton A, et al. **Trends in Epidemiology of Pediatric Inflammatory Bowel Disease** in Canada: Distributed Network Analysis of Multiple Population-Based Provincial Health Administrative Databases. Am J Gastroenterol. 2017 Apr 18.
421. Enns RA, Hookey L, Armstrong D, et al. Clinical practice **guidelines** for the use of **video capsule endoscopy**. Gastroenterology 2017;152:497-514. https://www.cag-acg.org/images/publications/VCE_guidelines_in_Gastro_Jan2017.pdf (accessed June 14, 2017).
422. Kulaylat AS, Kulaylat AN, Schaefer EW, et al. Association of **Preoperative Anti-Tumor Necrosis Factor Therapy With Adverse Postoperative Outcomes in Patients Undergoing Abdominal Surgery for Ulcerative Colitis**. JAMA Surg. 2017 Jun 14:e171538.
423. Oliveira SB, Monteiro IM. **Diagnosis and management of inflammatory bowel disease in children**. BMJ. 2017 May 31;357:j2083.
424. Cohen BL, Sachar DB. **Update on anti-tumor necrosis factor agents and other new drugs for inflammatory bowel disease**. BMJ. 2017 Jun 19;357:j2505.
425. Gisbert JP, Marín AC, Chaparro M. The **Risk of Relapse after Anti-TNF Discontinuation** in Inflammatory Bowel Disease: Systematic Review and Meta-Analysis. Am J Gastroenterol. 2016 May;111(5):632-47.
426. Torres J, Boyapati RK, Kennedy NA, et al. Systematic Review of **Effects of Withdrawal of Immunomodulators or Biologic Agents** From Patients With Inflammatory Bowel Disease. Gastroenterology. 2015 Dec;149(7):1716-30.
427. Farraye FA, Melmed GY, Lichtenstein GR, Kane SV. **ACG Clinical Guideline: Preventive Care** in Inflammatory Bowel Disease. Am J Gastroenterol. 2017 Feb;112(2):241-258.
428. Benchimol EI, Kaplan GG, Otley AR, et al. Rural and Urban Residence During Early Life is Associated with a Lower Risk of Inflammatory Bowel Disease: A Population-Based Inception and Birth Cohort Study. Am J Gastroenterol. 2017 Jul 25.
429. Chaparro M, Ramas M, Benítez JM, et al. **Extracolonic Cancer** in Inflammatory Bowel Disease: Data from the **GETECCU** Eneida Registry. Am J Gastroenterol. 2017 Jul;112(7):1135-1143.
430. de Jong MJ, van der Meulen-de Jong AE, Romberg-Camps MJ, et al. **Telemedicine** for management of **inflammatory bowel disease** (mylBDcoach): a pragmatic, multicentre, randomized controlled trial. Lancet 2017 July 14.
431. Feuerstein JD et al. **Therapeutic drug monitoring** in inflammatory bowel disease. Gastroenterology 2017Aug 02.
432. Health Canada Sep/17: **SOLU-MEDROL ACT-O-VIAL 40 mg** is the only formulation of methylprednisolone in Canada that contains bovine-sourced **lactose** as an excipient.
433. Narula N, Kassam Z, Yuan Y, et al. Systematic Review and Meta-analysis: **Fecal Microbiota Transplantation** for Treatment of Active **Ulcerative Colitis**. Inflamm Bowel Dis. 2017 Oct;23(10):1702-1709.
434. Olén O, Askling J, Sachs MC, et al. **Childhood onset inflammatory bowel disease and risk of cancer**: a Swedish nationwide cohort study 1964-2014. BMJ 2017;358:j3951.
435. Bonovas S, Nikolopoulos GK, Lytras T, et al. Comparative **safety of systemic and low-bioavailability steroids** in inflammatory bowel disease: Systematic review and network meta-analysis. Br J Clin Pharmacol. 2017 Oct 22.
436. Ng SC, Shi HY, Hamidi N, et al. **Worldwide incidence and prevalence of inflammatory bowel disease** in the 21st century: a systematic review of population-based studies. Lancet 2017; online Oct 16.
437. Römkens TEH, Te Morsche R, Peters W, et al. **Urinalysis of MMX-mesalazine** as a tool to monitor 5-ASA adherence in daily IBD practice. Br J Clin Pharmacol. 2017 Oct 26.
438. Yoon HM, Suh CH, Kim JR, et al. Diagnostic Performance of **Magnetic Resonance Enterography** for Detection of Active Inflammation in Children and adolescents With **Inflammatory Bowel Disease**: A Systematic Review and Diagnostic Meta-analysis. JAMA Pediatr. 2017 Oct 9.
439. Charlton R;Green A;Shaddick G;Snowball J;Nightinga **Risk of uveitis and inflammatory bowel disease in people with psoriatic arthritis**: a population-based cohort study**.** Ann Rheum Dis. 2017 Nov 1.
440. Desai RJ, Gagne JJ, Lii J, et al. Comparative risk of incident **venous thromboembolism in patients with inflammatory bowel disease initiating tumour necrosis factor-α inhibitors or nonbiologic agents**: a cohort study. CMAJ. 2017 Nov 27;189(47):E1438-E1447.
441. Lemaitre M, Kirchgesner J, Rudnichi A, et al. Association Between Use of **Thiopurines or Tumor Necrosis Factor Antagonists Alone or in Combination and Risk of Lymphoma** in Patients With Inflammatory Bowel Disease. JAMA. 2017 Nov 7;318(17):1679-1686.
442. Charlton R, Green A, Shaddick G, et al; **PROMPT** study group. **Risk of uveitis and inflammatory bowel disease** in people **with psoriatic arthritis**: a population-based cohort study. Ann Rheum Dis. 2017 Nov 1.
443. Colombel JF, Panaccione R, Bossuyt P, et al. Effect of **tight control management on Crohn's disease** (**CALM**): a multicentre, randomised,controlled phase 3 trial. Lancet. 2017 Oct 31
444. Ng SC, Shi HY, Hamidi N, et al. **Worldwide incidence and prevalence of inflammatory bowel disease** in the 21st century: a systematic review of population-based studies. Lancet. 2017 Oct 13
445. Castelli AA, Estrada JJ, Kaminski JP. Patient With **Ulcerative Colitis and Abdominal Pain**. JAMA Surg. 2018 Jan 3.
446. Charlton R, Green A, Shaddick G, et al. Risk of **uveitis and inflammatory bowel disease in people with psoriatic arthritis**: a population-based cohort study. Ann Rheum Dis. 2018 Feb;77(2):277-280.
447. Ergen EN, Stratton MS, Granada CP. Intertriginous Condyloma-like Plaques and Ulcers (**Metastatic Crohn disease**). JAMA Dermatol. 2018 Jan 10.
448. Burisch J, Kiudelis G, Kupcinskas L, et al. **Natural disease course of Crohn`s disease** during the first 5 years after diagnosis in a European population-based inception cohort: an Epi-IBD study. Gut. 2018 Jan 23.
449. Mukherjee A, Hazra A, Smith MK, et al. Exposure-response characterisation of **tofacitinib** efficacy in moderate to severe ulcerative colitis: results from a dose-ranging phase 2 trial. Br J Clin Pharmacol. 2018 Jan 28.
450.Ponsioen CY, de Groof EJ, Eshuis EJ, et al; LIR!C study group. **Laparoscopic ileocaecal resection versus infliximab for terminal ileitis in Crohn's disease**: a randomised controlled, open-label, multicentre trial. Lancet Gastroenterol Hepatol. 2017 Nov;2(11):785-792.
451. Abrahami D, Douros A, Yin H, et al. **Dipeptidyl peptidase-4 inhibitors and incidence of inflammatory bowel disease** among patients with type 2 diabetes: population based cohort study. BMJ. 2018 Mar 21;360:k872.
452. Papadopoulos M, Patel D, Korologou-Linden R, et al. Safety and efficacy of **parenteral iron in** children with inflammatory bowel disease. Br J Clin Pharmacol. 2018 Apr;84(4):694-699.
453. Pinnell J, Potter T. A **rare reaction to sulfasalazine**. BMJ 2017 Nov 30; 359:j5189.
454. Lichtenstein GR, Loftus EV, Isaacs KL, et al. **ACG Clinical Guideline: Management of Crohn's Disease** in Adults. Am J Gastroenterol. 2018 Apr;113(4):481-517.

455. Brennan GT, Ha I, Hogan C, et al. Does preoperative **enteral or parenteral nutrition reduce postoperative complications in Crohn's disease** patients: a meta-analysis. Eur J Gastroenterol Hepatol. 2018 May 7.
456. Diamond CE, Hennessey C, Meldau J, et al. **Catheter-Related Venous Thrombosis** in Hospitalized Pediatric Patients **with Inflammatory Bowel Disease**: Incidence, Characteristics, and Role of Anticoagulant Thromboprophylaxis with Enoxaparin. J Pediatr. 2018 Apr 5.
457. Ordás I, Domènech E, Mañosa M, et al; ENEIDA registry of GETECCU. Post-operative morbidity and mortality of a cohort of **steroid refractory acute severe ulcerative colitis**: Nationwide multicenter study of the GETECCU ENEIDA Registry. Am J Gastroenterol. 2018 May 1.
458. Ponsioen CY, de Groof EJ, Eshuis EJ, et al. **Laparoscopic ileocaecal resection versus infliximab for terminal ileitis in Crohn's disease**: a randomised controlled, open-label, multicentre trial. Lancet Gastroenterol Hepatol. 2017 Nov;2(11):785-792.
459. Komaki Y, Komaki F, Micic D, et al. Risk of **Fractures in Inflammatory Bowel Diseases**: A Systematic Review and Meta-Analysis. J Clin Gastroenterol. 2018 Apr 18.
460. Matro R et al. Exposure concentrations of **infants breastfed by women receiving biologic therapies for inflammatory bowel diseases** and effects of breastfeeding on infections and development. Gastroenterology 2018 May 29.
461. Villumsen M, Aznar S, Pakkenberg B, et al. **Inflammatory bowel disease increases the risk of Parkinson's** disease: a Danish nationwide cohort study 1977-2014. Gut. 2018 May 21**.**
462. Bernstein CN, Hitchon CA, Walld Ret al. **Increased Burden of Psychiatric Disorders in Inflammatory Bowel Disease**. Inflamm Bowel Dis. 2018 Jul 7.
463. Herfarth H et al. **Methotrexate is not superior to placebo** in maintaining steroid-free response or **remission in ulcerative colitis**. Gastroenterology 2018 Jun 29
464. Shi HY, Ng SC. The state of the art on **treatment of Crohn's disease**. J Gastroenterol. 2018 Jul 6.
465. Axelrad JE, Joelson A, Green PHR, et al. **Enteric Infections** Are Common in Patients with Flares of Inflammatory Bowel Disease. Am J Gastroenterol. 2018 Aug 3.
466. Kirchgesner J, Lemaitre M, Carrat F, et al. Risk of **Serious and Opportunistic Infections** Associated With Treatment of Inflammatory Bowel Diseases. Gastroenterology. 2018 Aug;155(2):337-346.e10.
467. Morita T, Fujimoto K, Shima Y, et al. Minimal **neonatal transfer of certolizumab pegol** in a Japanese patient with **rheumatoid arthritis**. Ann Rheum Dis. 2018 Sep;77(9):e56.
468. Perricone G, Vangeli M. **Pyoderma Gangrenosum** in Ulcerative Colitis. N Engl J Med. 2018 Jul 26;379(4):e7.
469. Lindoso L, Mondal K, Venkateswaran S, et al. The **Effect of Early-Life Environmental Exposures on Disease Phenotype and Clinical Course of Crohn's Disease in** Children. Am J Gastroenterol. 2018 Sep 28.
470. Nelson SM, Nguyen TM, McDonald JW, et al. **Natalizumab for induction of remission in Crohn`s disease**. Cochrane Database Syst Rev. 2018 Aug 1;8:CD006097. High quality data suggest that natalizumab is effective for induction of clinical remission and response in some patients with moderately to severely active CD. However, none of the included studies had the power to detect rare but serious adverse events such as PML. Due to the association with PML, and the availability of alternative agents that are not associated with PML, natalizumab is not likely to be used in patients who fail currently available medical therapy. The use of natalizumab in select patients (e.g. patients allergic to different biologics) needs to be carefully considered against the potential risk of developing PML.
471. Siegel CA. **Refocusing IBD Patient Management**: Personalized, Proactive, and Patient-Centered Care. Am J Gastroenterol. 2018 Oct 4.
472. Alexakis C, Saxena S, Chhaya V, et al. **Smoking** Status at Diagnosis and Subsequent Smoking Cessation: Associations With Corticosteroid Use and Intestinal Resection in **Crohn's Disease**. Am J Gastroenterol. 2018 Oct 15.
473. Frolkis AD, Vallerand IA, Shaheen AA, et al. **Depression** increases the risk of inflammatory bowel disease, which may be mitigated by the use of **antidepressants** in the treatment of depression. Gut. 2018 Oct 18.
474. Kurnool S, Nguyen NH, Proudfoot J, et al. **High body mass index** is associated with increased risk of treatment failure and surgery in **biologic-treated** patients with **ulcerative colitis**. Aliment Pharmacol Ther. 2018 Jun;47(11):1472-1479.
475. Luu M, Benzenine E, Doret M, et al. **Continuous anti-TNFα use throughout pregnancy**: possible complications for the mother but not for the fetus. A retrospective cohort on the French national health insurance database (EVASION). Am J Gastroenterol 2018. https://doi.org/10.1038/ s41395-018-0176-7.
476. Bye WA, Ma C, Nguyen TM, et al. **Strategies for Detecting Colorectal Cancer in Patients with Inflammatory Bowel Disease:** A Cochrane Systematic Review and Meta-Analysis**.** Am J Gastroenterol. 2018 Oct 23.
477. Fu Y, Lee CH, Chi CC. Association of **Psoriasis With Inflammatory Bowel Disease**: A Systematic Review and Meta-analysis. JAMA Dermatol. 2018 Oct 24.
478. Shen B, Kochhar G, Hull TL; Global International Inflammatory Bowel Disease (Gi-IBD) Working Group**. Bridging Medical and Surgical Treatment of Inflammatory Bowel Disease**: The Role of Interventional IBD. Am J Gastroenterol. 2018 Nov 21.
479. **Crohn's Disease**. Am Fam Physician. 2018 Dec 1;98(11):Online.
480. Meyer A, Rudant J, Drouin J, et al. Effectiveness and safety of **reference infliximab and biosimilar in Crohn disease**. A French equivalence study. Ann Intern Med. 2018. [Epub ahead of print]. doi:10.7326/M18-1512
481. Veauthier B, Hornecker JR. **Crohn's Disease: Diagnosis and Management**. Am Fam Physician. 2018; 98(11): 661-669.
482. Costello SP, Hughes PA, Waters O, et al. Effect of **fecal microbiota transplantation on 8-week remission** in patients with ulcerative colitis: a randomized clinical trial [published Jan 15, 2018]. JAMA. doi:10.1001/jama.2018.20046
483. Dreesen E, Faelens R, Van Assche Get al. **Optimising infliximab induction dosing** for patients with ulcerative colitis. Br J Clin Pharmacol. 2019 Jan 11.
484. Ko CW, Singh S, Feuerstein JD, et al; **AGA** Institute Clinical Guidelines Committee. American Gastroenterological Association Institute **Guideline on the Management of Mild-to-Moderate Ulcerative Colitis**. Gastroenterology. 2018 Dec 18.
485. Nemoz B, Ternant D, Bailly S, et al. **New steps in infliximab therapeutic drug monitoring** in patients with inflammatory bowel diseases. Br J Clin Pharmacol. 2018 Dec 21.
486. George L, Cross R. Telemedicine platform **myIBDcoach reduces hospitalisations and outpatient gastroenterology visits** in patients with IBD. BMJ Evid Based Med. 2019 Feb;24(1):37-38.
487. Örtqvist AK, Lundholm C, Halfvarson J, et al. **Fetal and early life antibiotics exposure** and very early onset inflammatory bowel disease: a population-based study. Gut. 2019 Feb;68(2):218-225.
488. Townsend CM, Parker CE, MacDonald JK, et al. **Antibiotics for induction and maintenance of remission** in Crohn`s disease. Cochrane Database Syst Rev. 2019 Feb 7;2:CD012730.
489. Chanchlani N, Russell RK. Inflammatory bowel **disease in children and adolescents**. CMAJ. 2019 Feb 11;191(6):E164.
490. Ludvigsson JF, Mahl M, Sachs MC, et al. **Fracture Risk** in Patients With Inflammatory Bowel disease: A Nationwide Population-Based Cohort Study From 1964 to 2014. Am J Gastroenterol. 2019 Feb;114(2):291-304.
491. Mahadevan U, Robinson C, Bernasko N, et al. **Inflammatory Bowel Disease in Pregnancy** Clinical Care Pathway: A Report From the American Gastroenterological Association (AGA) IBD Parenthood Project Working Group. Inflamm Bowel Dis. 2019 Mar 1.
492. Walker GJ, Harrison JW, Heap GA, et al; IBD Pharmacogenetics Study Group. Association of **Genetic Variants in NUDT15 With Thiopurine-Induced Myelosuppression in Patients With Inflammatory Bowel Disease**. JAMA. 2019 Feb 26;321(8):773-785.
493. Bar-Gil Shitrit A, Ben Ya'acov A, Livovsky DM, et al. Exposure to **Vedolizumab in IBD Pregnant Women** Appears of Low Risk for Mother and Neonate: A First Prospective Comparison Study. Am J Gastroenterol. 2019 Mar 5.
494. Berends SE, D'Haens GR, Schaap J, et al**. Dried blood samples can support monitoring of infliximab concentrations** in patients with inflammatory bowel disease: a clinical validation. Br J Clin Pharmacol. 2019 Mar 30.
495. Rubin DT, Ananthakrishnan AN, Siegel CA, et al. **ACG Clinical Guideline**: Ulcerative Colitis in Adults. Am J Gastroenterol. 2019 Mar;114(3):384-413.
496. Schreiber S, Colombel JF, Feagan BG, et al. Incidence **rates of inflammatory bowel disease in patients with psoriasis, psoriatic arthritis and ankylosing spondylitis treated with secukinumab**: a retrospective analysis of pooled data from 21 clinical trials. Ann Rheum Dis. 2019 Apr;78(4):473-479.
497. Tewari A, Mahmood A, Harland C. **Multiple eruptive ulcers** in a patient with quiescent ulcerative colitis. BMJ. 2019 Mar 28;364:l847
498. Masnadi Shirazi K, Nikniaz Z, Masnadi Shirazi A, Rohani M. **Vitamin A supplementation decreases disease activity** index in patients with ulcerative colitis: A randomized controlled clinical trial. Complement Ther Med. 2018 Dec;41:215-219.
499. Sandborn WJ, Cyrille M, Hansen MB, et al. **Efficacy and Safety of Abrilumab** in a Randomized, Placebo-Controlled Trial for Moderate-to-Severe Ulcerative Colitis. Gastroenterology. 2019 Mar;156(4):946-957.e18.
500. Ungaro R, Colombel JF, Lissoos T, Peyrin-Biroulet L. A **Treat-to-Target Update** in Ulcerative Colitis: A Systematic Review. Am J Gastroenterol. 2019 Mar 22.
501. McIntyre RS, Subramaniapillai M, Lee Y, et al. **Efficacy of Adjunctive Infliximab vs Placebo in the Treatment of Adults With Bipolar I/II Depression**: A Randomized Clinical Trial. JAMA Psychiatry. 2019 May 8.
502. Singh S, Proudfoot JA, Dulai PS, et al. No Benefit of **Concomitant 5-Aminosalicylates in Patients With Ulcerative Colitis Escalated to Biologic Therapy**: Pooled Analysis of Individual Participant Data From Clinical Trials. Am J Gastroenterol. 2018 Aug;113(8):1197-1205.
503. Singh S, Proudfoot J, Xu R, Sandborn WJ. **Obesity and Response to Infliximab in Patients with Inflammatory Bowel Diseases**: Pooled Analysis of Individual Participant Data from Clinical Trials. Am J Gastroenterol. 2018 Jun;113(6):883-889.
504. Lloyd-Price J, Arze C, Ananthakrishnan AN, et al. **Multi-omics of the gut microbial ecosystem** in inflammatory bowel diseases. Nature. 2019 May;569(7758):655-662.
505. Olen O, Askling J, Sachs MC, et al. **Mortality** in adult-onset and elderly-onset IBD: a nationwide register-based cohort study 1964-2014. Gut. 2019 May 15.
506. Piovani D, Danese S, Peyrin-Biroulet L, et al. **Environmental Risk Factors** for Inflammatory Bowel Diseases: an Umbrella Review of Meta-analyses. Gastroenterology. 2019 Apr 20.
507. Bonovas S, Nikolopoulos GK, Piovani D, et al. Comparative assessment of **budesonide-MMX and mesalamine in active, mild-to-moderate ulcerative colitis**: a systematic review and network meta-analysis. Br J Clin Pharmacol. 2019 Jul 3.
508. Chen WT, Chi CC. Association of H**idradenitis Suppurativa** With Inflammatory Bowel Disease: A Systematic Review and Meta-analysis. JAMA Dermatol. 2019 Jul 10.
509. Khan R, Nugent CM, Scaffidi MA, et al. Association of **Biologic Prescribing for Inflammatory Bowel Disease With Industry Payments to Physicians**. JAMA Intern Med. 2019 Jul 8.
510. Murthy SK, Begum J, Benchimol EI, et al. Introduction of **anti-TNF therapy has not yielded expected declines** in hospitalisation and intestinal resection rates in inflammatory bowel diseases: a population-based interrupted time series study. Gut. 2019 Jun 12.
511. Faye AS, Wen T, Ananthakrishnan AN, et al. **Acute Venous Thromboembolism Risk Highest Within 60 Days** After Discharge From the Hospital in Patients With Inflammatory Bowel Diseases. Clin Gastroenterol Hepatol. 2019 Jul 20. pii: S1542-3565(19)30772-4.
512. Feuerstein JD, Moss AC, Farraye FA. **Ulcerative Colitis**. Mayo Clin Proc. 2019 Jul;94(7):1357-1373.
513. Levine A, Wine E, Assa A, et al. Crohn's Disease **Exclusion Diet Plus Partial Enteral Nutrition Induces Sustained Remission** in a Randomized Controlled Trial. Gastroenterology. 2019 Aug;157(2):440-450.e8.
514. Butwicka A, Olén O, Larsson H, et al. Association of Childhood-Onset Inflammatory Bowel Disease With **Risk of Psychiatric Disorders and Suicide Attempt**. JAMA Pediatr. 2019 Aug 19.
515. Jess T, Jensen BW, Andersson M, et al. Inflammatory Bowel Disease Increases **Risk of Type 2 Diabetes** in a Nationwide Cohort Study. Clin Gastroenterol Hepatol. 2019 Aug 5.
516. Kennedy ST, Maddux MH; IMPROVECARENOW PEDIATRIC IBD LEARNING HEALTH SYSTEM. Patient-Clinician Collaboration in the Development of an **IBD Transfer Toolkit**. Pediatrics. 2019 Aug 7.
517. Mack DR, Benchimol EI, Critch J, et al. Canadian Association of Gastroenterology Clinical Practice Guideline for the Medical Management of **Pediatric Luminal Crohn's Disease**. Gastroenterology. 2019 Aug;157(2):320-348.
518. Panaccione R, Steinhart AH, Bressler B, et al. Canadian Association of Gastroenterology Clinical Practice Guideline for the Manage ment of **Luminal Crohn's Disease**. J Can Assoc Gastroenterol. 2019 Aug;2(3):e1-e34.
519. Shergill AK, Lightdale JR, Bruining DH, Acosta RD, Chandrasekhara V, Chathadi KV, Decker GA, Early DS, Evans JA, Fanelli RD, Fisher DA. The role of endoscopy in inflammatory bowel disease. Gastrointestinal Endoscopy. 2015 May 1;81(5):1101-21.
520. Tools for Practice #236. Danielle Perry, Joey Ton, Michael R Kolber. Accessed Sept 4, 2019 from https://gomainpro.ca/wp-content/uploads/tools-for-practice/1559165324_1558969328_tfp236biosimilarsfv.pdf
521. Cohen ER, Salem M, Ha C. **Managing Immunosuppressed Patients** With Inflammatory Bowel Disease During a Measles Outbreak. Am J Gastroenterol. 2019 Sep 6.
522. Sands BE, Peyrin-Biroulet L, Loftus EV Jr, et al. **Vedolizumabversus adalimumab** for moderate-to-severe ulcerative colitis. (VARSITY) N Engl J Med 2019; 381: 1215-26.
523. Sands BE, Sandborn WJ, Panaccione R, et al. **Ustekinumab as induction and maintenance therapy** for ulcerative colitis. (UNIFI) N Engl J Med 2019; 381: 1201-14.

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References:

1. Veldhuyzen van Zanten SJ, Flook N, Chiba N, Armstrong D, Barkun A, Bradette M, et al. An evidence-based approach to the management of uninvestigated dyspepsia in the era of Helicobacter pylori. Canadian Dyspepsia Working Group. CMAJ 2000;162(12 Suppl):S3-S23.
2. CADTH. Scientific Report: Evidence for PPIs use in Gastroesophageal Reflux Disease, Dyspepsia and Peptic Ulcer Disease (Mar 2007) www.cadth.ca
3. Inadomi JM, et al. Step-down from multiple- to single-dose PPIs: a prospective study of patients with heartburn or acid regurgitation completely relieved with PPIs. Am J Gastroenterol. 2003 Sep;98(9):1940-4.
4. Armstrong A, et al. Canadian Consensus Conference on the management of GERD in adults – update 2004. Can J Gastroenterol 2005;19(1):15-35.
5. Reid M, Keniston A, Heller JC, Miller M, Medvedev S, Albert RK. Inappropriate prescribing of proton pump inhibitors in hospitalized patients. J Hosp Med. 2012 May-Jun;7(5):421-5.
6. Mastronarde JG, Anthonisen NR, Castro M, Holbrook JT, Leone FT, Teague WG, Wise RA. American Lung Association Asthma Clinical Research Centers. Efficacy of esomeprazole for treatment of poorly controlled asthma. N Engl J Med. 2009 Apr 9;360(15):1487-99.
7. Chey et al; Practice Parameters Committee of the American College of Gastroenterology. American College of Gastroenterology guideline on the management of Helicobacter pylori infection. Am J Gastroenterol. 2007 Aug;102(8):1808-25.
   Hunt RH, et al. Canadian Helicobacter Study Group. Consensus Conference Update: Infections in Adults. Can J Gastroenterol 1999;13(3): 213-217.
   Hunt R, Thomson ABR. Canadian Helicobacter pylori Consensus Conference. Can J. Gasteroenterol 1998;12(1):31-41.
   Preventing NSAID-Induced Ulcers.. Pharmacist's Letter/Prescriber's Letter 2002; 18(3):180306.
8. Chan FKL, et al Clopidogrel versus Aspirin and Esomeprazole to Prevent Recurrent Ulcer Bleeding. N Engl J Med 2005;352:238-44. n=320 1yr (InfoPOEMs: For patients with a history of bleeding peptic ulcer, **aspirin and a proton pump inhibitor** twice a day was safer in terms of bleeding side effects than clopidogrel. While esomeprazole was used in this study, generic omeprazole 20 mg give twice a day provides nearly the same degree of acid suppression at a much lower cost. This study calls into question the overall safety of clopidogrel, which has been promoted as not increasing the risk of bleeding significantly. (LOE = 1b))
9. Lai KC, et al. Esomeprazole 20mg/d + ASA (100mg/d) vs clopidogrel 75mg od for prevention of recurrent gastrointestinal ulcer complications. Clin Gastroenterol Hepatol. 2006 Jul;4(7):860-5. Epub 2006 Jun 22. n=170 1yr 0 $^{\text{esomeprazole + ASA}}$ vs 13.6% $^{\text{clopidogrel}}$ recurrent ulcer complications)
10. Luo JC, Huang KW, Leu HB, et al. Randomised clinical trial: **rabeprazole plus aspirin is not inferior to rabeprazole plus clopidogrel** for the healing of aspirin-related peptic ulcer. Aliment Pharmacol Ther. 2011 Sep;34(5):519-25.
11. Leontiadis GI, Sharma VK, et al. Systematic review & meta-analysis of proton pump inhibitor therapy in peptic ulcer bleeding. BMJ. 2005 Jan 31; [Epub ahead of print] (InfoPOEMs: Neither oral nor intravenous use of proton pump inhibitors decreases the risk of dying as the result of peptic ulcer bleeding. The likelihood of rebleeding or the need for surgery is reduced, with 1 episode of rebleeding avoided in every 10 pts treated & 1 surgery avoided for every 25 patients who received treatment. (LOE = 1a))
    Leontiadis GI, Sharma VK, Howden CW. WITHDRAWN: Proton pump inhibitor treatment for acute peptic ulcer bleeding. Cochrane Database Syst Rev. 2010 May 12;(5):CD002094.
    Sung JJ, Suen BY, Wu JC, et al. Effects of **Intravenous and Oral Esomeprazole** in the Prevention of Recurrent Bleeding from Peptic Ulcers after Endoscopic Therapy. Am J Gastroenterol. 2014 Apr 29.
12. Sachar H, Vaidya K, Laine L. Intermittent vs Continuous Proton Pump Inhibitor Therapy for High-Risk Bleeding Ulcers: A Systematic Review and Meta-analysis. JAMA Intern Med. 2014 Sep 8.
13. Giacomo CD, Bawa P, Franceschi M et al. Omeprazole for severe reflux esophagitis in children. J Ped Gastroent Nutr 1997;24:528-532.
14. van der Pol, Rachel J., Smits, Marije J., van Wijk, Michiel P., et al. Efficacy of Proton-Pump Inhibitors in Children With Gastroesophageal Reflux Disease: A Systematic Review. Pediatrics 2011 0: peds.2010-2719.
15. Larson JD, Patatanian E, Miner PB, et al. Double-blind, placebo controlled study of ranitidine for gastroesophageal reflux symptoms during pregnancy. Obstet Gynecol 1997;90:83-7.
16. Gill SK, O`Brien L, Einarson TR, et al. The safety of proton pump inhibitors (PPIs) in pregnancy: a meta-analysis. Am J Gastroenterol. 2009 Jun;104(6):1541-5; quiz 1540, 1546. Epub 2009 Apr 28. On the basis of these results, PPIs are not associated with an increased risk for major congenital birth defects, spontaneous abortions, or preterm delivery. The narrow range of 95% CIs is further reassuring, suggesting that PPIs can be safely used in pregnancy.
17. Pasternak Björn, Hviid Anders, Use of Proton-Pump Inhibitors in Early Pregnancy and the Risk of Birth Defects. N Engl J Med 2010; 363:2114-2123. In this large cohort, exposure to PPIs during the first trimester of pregnancy was not associated with a significantly increased risk of major birth defects.
18. Briggs GG, Freeman RK, Sumner JY. Drugs in Pregnancy and Lactation 9th Edition. Williams & Wilkins, Baltimore, 2011.

Additional references:

e-therapeutics www.e-therapeutics.ca

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Bredenoord AJ, Pandolfino JE, Smout AJ. **Gastro-oesophageal reflux disease**. Lancet. 2013 Mar 7.

Bhatt DL, Scheiman J, Abraham NS, et al. ACCF/ACG/AHA 2008 expert consensus document on reducing the gastrointestinal risks of **antiplatelet therapy and NSAID** use: a report of the American College of Cardiology Foundation Task Force on Clinical Expert Consensus Documents. *J Am Coll Cardiol***.** 2008; *Circulation*. 2008; DOI: DOI: 10.1161/CIRCULATIONAHA.108.191087. Available at: http://circ.ahajournals.org

Devitt J, Lyon C, Swanson SB, DeSanto K. What are the **risks of long-term PPI use for GERD symptoms in patients > 65 years**? J Fam Pract. 2019 Apr;68(3):E18-E19.

Giannini EG, Zentilin P, Dulbecco P, Vigneri S, Scarlata P, Savarino V. Management strategy for patients with gastroesophageal reflux disease: a comparison between empirical treatment with esomeprazole and endoscopy-oriented treatment. Am J Gastroenterol. 2008 Feb;103(2):267-75. Early endoscopy for patients with gastroesophageal reflux disease (GERD) without alarm symptoms does not improve symptoms or quality of life, but increases costs. (LOE = 1b)

Gisbert JP, Calvet X, Cosme A, et al. H. pylori Study Group of the Asociación Española de Gastroenterología (Spanish Gastroenterology Association). Long-term follow-up of 1,000 patients **cured of Helicobacter pylori infection following an episode of peptic ulcer bleeding**. Am J Gastroenterol. 2012 Aug;107(8):1197-204.

Gonzalez Ayerbe JI, Hauser B, Salvatore S, Vandenplas Y. **Diagnosis and Management of Gastroesophageal Reflux Disease in Infants and Children**: from Guidelines to Clinical Practice. Pediatr Gastroenterol Hepatol Nutr. 2019 Mar;22(2):107-121.

Graham DY, Agrawal NM, Campbell DR, et al. NSAID-Associated Gastric Ulcer Prevention Study Group. Ulcer prevention in long-term users of nonsteroidal anti-inflammatory drugs: results of a double-blind, randomized, multicenter, active- and placebo-controlled study of **misoprostol vs lansoprazole**. Arch Intern Med. 2002 Jan 28;162(2):169-75.

Hsu PI, Lai KH, Liu CP. **Esomeprazole with clopidogrel reduces peptic ulcer recurrence, compared with clopidogrel alone**, in patients with atherosclerosis. Gastroenterology. 2011 Mar;140(3):791-8.

Hudson N, Taha AS, Russell RI, et al. **Famotidine** for healing and maintenance in nonsteroidal anti-inflammatory drug-associated gastroduodenal ulceration. Gastroenterology. 1997 Jun;112(6):1817-22.

Jaynes M, Kumar AB. The **risks of long-term use of proton pump inhibitors**: a critical review. Ther Adv Drug Saf. 2018 Nov 19;10:2042098618809927.

Katz PO, Gerson LB, Vela MF. **ACG**-Guidelines for the diagnosis and management of **gastroesophageal reflux disease**. Am J Gastroenterol. 2012 Mar;108(3):308-28.

Kyaw MH, Otani K, Ching JYL, et al. **Misoprostol Heals Small Bowel Ulcers in Aspirin Users** With Small Bowel Bleeding. Gastroenterology. 2018 Oct;155(4):1090-1097.e1.

Lin KJ, Hernández-Díaz S, García Rodríguez LA. **Acid suppressants reduce risk of gastrointestinal bleeding in patients on antithrombotic** or anti-inflammatory therapy. Gastroenterology. 2011 Jul;141(1):71-9.

Liu CP, Chen WC, Lai KH, et al. **Esomeprazole Alone Compared with Esomeprazole Plus Aspirin** for the Treatment of Aspirin-Related Peptic Ulcers. Am J Gastroenterol. 2012 Apr 17.

Moayyedi P, Lacy BE, Andrews CN, Enns RA, Howden CW, Vakil N. **ACG and CAG Clinical Guideline: Management of Dyspepsia**. Am J Gastroenterol. 2017 Jul;112(7):988-1013

Oakland K, Chadwick G, East JE, et al. **Diagnosis and management of acute lower Gastrointestinal bleeding**: guidelines from the British Society of Gastroenterology. Gut. 2019 Feb 12.

Peery AF, Dellon ES, Lund J, et al. **Burden of Gastrointestinal Disease in the United States**: 2012 Update. Gastroenterology. 2012 Aug 8.

Shaheen NJ, Weinberg DS, Denberg TD, Chou R, Qaseem A, Shekelle P; for the Clinical Guidelines Committee of the American College of Physicians. **Upper endoscopy for gastroesophageal**

reflux disease: best practice advice from the Clinical Guidelines Committee of the American College of Physicians. Ann Intern Med. 2012;157:808-16.
Srygley FD, Gerardo CJ, Tran T, Fisher DA. Does this **patient have a severe upper gastrointestinal bleed**? JAMA. 2012 Mar 14;307(10):1072-9. . Melena, nasogastric lavage with blood or coffee grounds, or serum urea nitrogen:creatinine ratio of more than 30 increase the likelihood of a UGIB. Blood clots in the stool make a UGIB much less likely. The Blatchford clinical prediction score, which does not require nasogastric lavage, is very efficient for identifying patients who do not require urgent intervention.
Taha AS, McCloskey C, Prasad R, Bezlyak V. **Famotidine** for the prevention of peptic ulcers and oesophagitis in patients taking low-dose aspirin (**FAMOUS**): a phase III, randomised, double-blind, placebo-controlled trial. Lancet. 2009 Jul 11;374(9684):119-25.

Taha AS, Hudson N, Hawkey CJ, et al. **Famotidine** for the prevention of gastric and duodenal ulcers caused by nonsteroidal antiinflammatory drugs. N Engl J Med. 1996 May 30;334(22):1435-9.
Treatment Guidelines: Drugs for **Peptic Ulcers & GERD**. **The Medical Letter**: February, **2004**; 2(18) pp. 9-12. New & Updated August 2008. **New & Updated Sept 2011**
van Marrewijk CJ, Mujakovic S, Fransen GA, Numans ME. Effect and cost-effectiveness of step-up versus step-down treatment with antacids, H2-receptor antagonists, and proton pump inhibitors in patients with new onset dyspepsia (DIAMOND study): a primary-care-based randomised controlled trial. Lancet. 2009 Jan 17;373(9659):215-25.
Villegas K, Meier JL, Long M, et al. The Effect of **Proton Pump Inhibitors on Glycemic Control in Patients with Type 2 Diabetes**. Metab Syndr Relat Disord. 2019 Feb 7.
Wilkinson JM, Cozine EW, Loftus CG. **Gas, Bloating, and Belching**: Approach to Evaluation and Management. Am Fam Physician. 2019; 99(5): 301-309.

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References

1. AHFS 2018; Micromedix 2018
2. Armstrong D, Marshall JK, Chiba N, et al.; Canadian Association of Gastroenterology GER Consensus Group. Canadian Consensus Conference on the management of **gastroesophageal reflux disease in adults** - update 2004. Can J Gastroenterol. 2005 Jan;19(1):15-35.
3. Laheij RJ, Sturkenboom MC, Hassing RJ, Dieleman J, Stricker BH, Jansen JB. Risk of community-acquired **pneumonia** and use of gastric acid-suppressive drugs. JAMA. 2004 Oct 27;292(16):1955-60. (Dial S, Delaney JA, Barkun AN, Suissa S. Use of gastric acid-suppressive agents and the risk of community-acquired **Clostridium difficile**-associated disease. JAMA. 2005 Dec 21;294(23):2989-95. Dial S, Delaney JA, Schneider V, Suissa S. Proton pump inhibitor use and risk of community-acquired **Clostridium difficile**-associated disease defined by prescription for oral vancomycin therapy. CMAJ. 2006 Sep 26;175(7):745-8.) (Lowe DO, Mamdani MM, Kopp A, Low DE, Juurlink DN. Proton pump inhibitors and hospitalization for **Clostridium difficile**-associated disease: a population-based study. Clin Infect Dis. 2006 Nov 15;43(10):1272-6. Epub 2006 Oct 13. Among community-dwelling older patients, PPI use is not a risk factor for hospitalization with CDAD.) [CAG Clinical Affairs Committee. Community-acquired **pneumonia** and acid-suppressive drugs: position statement. Can J Gastroenterol. 2006 Feb;20(2):119-21, 123-5.] (Gulmez SE, Holm A, Frederiksen H, et al. Use of proton pump inhibitors and the risk of community-acquired **pneumonia**: a population-based case-control study. Arch Intern Med. 2007 May 14;167(9):950-5. The use of PPIs, especially when recently begun, is associated with an increased risk of community-acquired pneumonia.)
4. Pham C, Sadowski-Hayes L, Regal R. Prevalent Prescribing of Proton Pump Inhibitors: Prudent or Pernicious. P&T 2006;31(3):159-165.
   Yang YX, Lewis JD, Epstein S, Metz DC. Long-term proton pump inhibitor therapy and risk of **hip fracture**. JAMA. 2006 Dec 27;296(24):2947-53. Long-term PPI therapy, particularly at high doses, is associated with an increased risk of hip fracture. InfoPOEMs: Long-term use (greater than one year) of proton pump inhibitors (PPIs) is associated with an increased risk of hip fracture in adults over age 50 years. Risk is also higher among individuals taking higher doses of PPIs and increases with duration of use. Appropriate use, dose, and duration of therapy should be carefully assessed on an individual basis. (LOE = 3b)
   Vestergaard P, Rejnmark L, Mosekilde L. Proton pump inhibitors, histamine H2 receptor antagonists, and other antacid medications and the risk of fracture. Calcif Tissue Int. 2006 Aug;79(2):76-83. Epub 2006 Aug 15.] Targownik, L. E., Lix, L. M., Metge, C. J. et al. Use of proton pump inhibitors and risk of osteoporosis-related fractures. Can Med Assoc J 2008 179: p. 319-326.
   Sarkar M, Hennessy S, Yang YX. Proton-pump inhibitor use and the risk for community-acquired pneumonia. Ann Intern Med. 2008 Sep 16;149(6):391-8. Proton-pump inhibitor therapy started within the past 30 days was associated with an increased risk for CAP, whereas longer-term current use was not.
   Aseeri M, Schroeder T, Kramer J, Zackula R. Gastric acid suppression by proton pump inhibitors as a risk factor for clostridium difficile-associated diarrhea in hospitalized patients. Am J Gastroenterol. 2008 Sep;103(9):2308-13. Epub 2008 Aug 12. This study showed elevated risk of developing CDAD in hospitalized patients with acid suppressive therapy, especially when PPIs were used. Sultan N, Nazareno J, Gregor J. Association between proton pump inhibitors and respiratory infections: A systematic review and meta-analysis of clinical trials. Can J Gastroenterol. 2008 Sep;22(9):761-6.
   Herzig Shoshana J.; Howell Michael D.; Ngo Long H.; et al. Acid-Suppressive Medication Use and the Risk for Hospital-Acquired Pneumonia. JAMA. 2009;301(20):2120-2128.
   Herzig SJ, Vaughn BP, Howell MD, Ngo LH, Marcantonio ER. Acid-suppressive medication use and the risk for **nosocomial gastrointestinal tract bleeding**. Arch Intern Med. 2011 Jun 13;171(11):991-7.
   Laine L. Proton pump inhibitors and bone fractures? Am J Gastroenterol 2009;104:S21-S26.
   Miano TA, Reichert MG, Houle TT, et al. Nosocomial pneumonia risk and stress ulcer prophylaxis: a comparison of pantoprazole vs ranitidine in cardiothoracic surgery patients. Chest. 2009 Aug;136(2):440-7.
   Targownik LE, Lix LM, Leung S, Leslie WD. Proton Pump Inhibitor Use Is Not Associated With Osteoporosis or Accelerated Bone Mineral Density Loss. Gastroenterology. 2009 Nov 18.
   Eurich DT, Sadowski CA, Simpson SH, et al. Recurrent community-acquired pneumonia in patients starting acid-suppressing drugs. Am J Med. 2010 Jan;123(1):47-53.
   Linsky Amy; Gupta Kalpana; Lawler Elizabeth V.; et al. Proton Pump Inhibitors and Risk for Recurrent **Clostridium difficile** Infection. Arch Intern Med. 2010;170(9):772-778. Proton pump inhibitor use during incident CDI treatment was associated with a 42% increased risk of recurrence. Our findings warrant further studies to examine this association and careful consideration of the indications for prescribing PPIs during treatment of CDI.
   Gray Shelly L.; LaCroix Andrea Z.; Larson Joseph; et al. Proton Pump Inhibitor Use, **Hip Fracture**, and Change in Bone Mineral Density in Postmenopausal Women: Results From the Women's Health Initiative. Arch Intern Med. 2010;170(9):765-771. Use of PPIs was not associated with hip fractures but wasmodestly associated with clinical spine, forearm or wrist, and total fractures.
   Howell Michael D.; Novack Victor; Grgurich Philip; et al. Iatrogenic Gastric Acid Suppression and the Risk of **Nosocomial Clostridium difficile** Infection. Arch Intern Med. 2010;170(9):784-790. Increasing levels of pharmacologic acid suppression are associated with increased risks of nosocomial C difficile infection. This evidence of a dose-response effect provides further support for the potentially causal nature of iatrogenic acid suppression in the development of nosocomial C difficile infection.
   FDA May/10: Proton-Pump Inhibitors Might Increase Risk for Wrist, Hip, and Spine Fractures http://www.fda.gov/Safety/MedWatch/SafetyInformation/SafetyAlertsforHumanMedicalProducts/ucm213321.htm
   Redelmeier D, McAlister FA, Kandel CE, Lu H, Daneman N. Postoperative pneumonia in elderly patients receiving acid suppressants: retrospective cohort analysis. BMJ 2010;340:c2608.
   Eom CS, Jeon CY, Lim JW, et al. Use of acid-suppressive drugs and **risk of pneumonia**: a systematic review and meta-analysis. CMAJ. 2011 Feb 22;183(3):310-9.
   Herzig Shoshana J.; Vaughn Byron P.; Howell Michael D.; et al. Acid-Suppressive Medication Use and the **Risk for Nosocomial Gastrointestinal Tract Bleeding**. *Arch Intern Med*. 2011;0(2011):archinternmed.2011.14.
   Abrahamsen Bo; Eiken Pia; Eastell Richard. Proton Pump Inhibitor Use and the **Antifracture Efficacy of Alendronate**. *Arch Intern Med*. 2011 Jun 13;171(11):998-1004.
   Furlanetto Tania Weber; Faulhaber Gustavo Adolpho Moreira. **Hypomagnesemia** and Proton Pump Inhibitors: Below the Tip of the Iceberg. Arch Intern Med. 2011;0(2011):archinternmed.2011.199.
   Eom CS, Park SM, Myung SK, et al. Use of Acid-Suppressive Drugs and **Risk of Fracture**: A Meta-analysis of Observational Studies. Ann Fam Med. 2011 May-Jun;9(3):257-67.
   Langan RC, Zawistoski KJ. Update on **Vitamin B12 Deficiency**. Am Fam Physician. 2011 Jun 15;83(12):1425-1430.
   Khalili H, Huang ES, Jacobson BC, et al. Use of proton pump inhibitors and risk of **hip fracture** in relation to dietary and lifestyle factors: a prospective cohort study. BMJ. 2012 Jan 30;344:e372.
   Kwok CS, Arthur AK, Anibueze CI, et al. Risk of **Clostridium difficile** Infection With Acid Suppressing Drugs and Antibiotics: Meta-Analysis. Am J Gastroenterol. 2012 Apr 24.
   de Jager CP, Wever PC, Gemen EF, et al. Proton pump inhibitor therapy **predisposes to community-acquired Streptococcus pneumoniae pneumonia**. Aliment Pharmacol Ther. 2012 Nov;36(10):941-9.
   Janarthanan S et al. **Clostridium difficile**-associated diarrhea **and proton pump inhibitor** therapy: A meta-analysis. Am J Gastroenterol 2012 Jul; 107:1001.
   Bajaj JS, Ratliff SM, Heuman DM, Lapane KL. Proton pump inhibitors are associated with a high rate of **serious infections** in veterans with decompensated cirrhosis. Aliment Pharmacol Ther. 2012 Sep 11.
   Chitnis AS, Holzbauer SM, Belflower RM, et al. Epidemiology of **Community-Associated Clostridium difficile Infection**, 2009 Through 2011. JAMA Intern Med. 2013 Jul 22;173(14):1359-67.
   Bateman BT, Bykov K, Choudhry NK, et al. Type of **stress ulcer prophylaxis** (**PPIs** vs H2) and risk of nosocomial pneumonia in cardiac surgical patients: cohort study. BMJ. 2013 Sep 19;347:f5416.
   Lam JR, Schneider JL, Zhao W, et al. Proton pump inhibitor and histamine 2 receptor antagonist use and vitamin B12 deficiency. JAMA. 2013 Dec 11;310(22):2435-42.
   Nylund CM, Eide M, Gorman GH. Association of **Clostridium difficile** Infections with Acid Suppression Medications in Children. J Pediatr. 2014 Aug 8.
   Herzig SJ, Doughty C, Lahoti S, et al. **Acid-Suppressive** Medication **Use in Acute Stroke and Hospital-Acquired Pneumonia**. Ann Neurol. 2014 Aug 28.
   McDonald EG, Milligan J, Frenette C, et al. Continuous Proton Pump Inhibitor Therapy and the Associated Risk of Recurrent **Clostridium difficile** Infection. JAMA Intern Med. 2015 Mar 2.
   Lambert AA, Lam JO, Paik JJ, et al. Risk of **community-acquired pneumonia** with outpatient proton-pump inhibitor therapy: a systematic review and meta-analysis. PLoS One. 2015 Jun 4;10(6):e0128004.
   Begley J, Smith T, Barnett K, et al. **Proton Pump Inhibitor Associated Hypomagnasaemia** - A Cause for Concern? Br J Clin Pharmacol. 2015 Nov 27.

Lazarus B, Yuan C, Wilson FP, et al. Proton pump inhibitor use and the risk of **chronic kidney disease** [online January 11, 2016].JAMA Intern Med. doi:10.1001/jamainternmed.2015.7193.
Gomm W, von Holt K, Thomé F, et al. Association of proton pump inhibitors with risk of **dementia**: a pharmacoepidemiological claims data analysis [online February 15, 2016].JAMA Neurol. doi:10.1001/jamaneurol.2015.4791.
Xie Y, Bowe B, Li T, Xian H, Balasubramanian S, Al-Aly Z. Proton Pump Inhibitors and **Risk of Incident CKD** and Progression to ESRD. J Am Soc Nephrol. 2016 Apr 14.
Verhaegh BPM et al. High risk of drug-induced **microscopic colitis** with concomitant use of NSAIDs and proton pump inhibitors. Aliment Pharmacol Ther 2016 Mar 9.
Antoniou T, Macdonald EM, Hollands S, et al. Proton pump inhibitors and the risk of **acute kidney injury** in older patients: a population-based cohort study. CMAJ Open. 2015 Apr 2
McCaleb RV, Gandhi AS, Clark SM, et al. Clinical Outcomes of Acid Suppressive Therapy Use in Hematology/Oncology Patients at an Academic Medical Center. (HAP & CDAD) Ann Pharmacother. 2016 Jul;50(7):541-7.
Arj A, Razavi Zade M, Yavari M, et al. **Proton pump inhibitors use and change in bone mineral density**. Int J Rheum Dis. 2016 May 31.
Othman F, Crooks C, Card T. Community acquired pneumonia incidence before and after proton pump inhibitor prescription: population based study. BMJ 2016;355:i5813.
Targownik LE, Goertzen AL, Luo Y, Leslie WD. Long-Term Proton Pump Inhibitor Use Is **Not** Associated With Changes in **Bone Strength and Structure**. Am J Gastroenterol. 2016 Nov 15.
Tsai CF, Chen MH, Wang YP et al. Proton Pump Inhibitors Increase Risk for **Hepatic Encephalopathy** In Patients with Cirrhosis in a Population Study. Gastroenterology. 2017;152:134-141.
Wei L, Ratnayake L, Phillips G, et al. Acid suppression medications and **bacterial gastroenteritis**: a population-based cohort study. Br J Clin Pharmacol. 2017 Jan 5.
Kvistholm Jensen A, Simonsen J, Ethelberg S. Use of **proton pump inhibitors and the risk of listeriosis**. A nationwide registry-based case-control study. Clin Infect Dis. 2016 Dec 24.
Chen Y, Liu B, Glass K, et al. Use of **Proton Pump Inhibitors and the Risk of Hospitalization for Infectious Gastroenteritis**. PLoS One. 2016 Dec 20;11(12):e0168618.
Freedberg DE, Kim LS, Yang YX. The **Risks and Benefits of Long-term Use of Proton Pump Inhibitors**: Expert Review and Best Practice Advice From the American Gastroenterological Association (**AGA**). Gastroenterology. 2017 Mar;152(4):706-715.
Tariq R, et al. Association of **gastric acid suppression with recurrent Clostridium difficile infection**: systematic review and meta-analysis [online Mar 27/17].JAMA Intern Med. . doi:10.1001 /jamainternmed.2017.0212
Yu LY, Sun LN, Zhang XH, et al. A Review of the **Novel Application** and Potential **Adverse Effects of Proton Pump Inhibitors**. Adv Ther. 2017 May;34(5):1070-1086.
Xie Y, Bowe B, Li T, et al. **Long-term kidney outcomes** among users of proton pump inhibitors without intervening acute kidney injury. Kidney Int. 2017 Jun;91(6):1482-1494.
Wang YF, Chen YT, Luo JC, et al. **Proton-Pump Inhibitor Use and the Risk of First-Time Ischemic Stroke** in the General Population: A Nationwide Population-Based Study. Am J Gastroenterol. 2017 Apr 11.
Klatte DCF et al. Association between **proton pump inhibitor use and risk of progression of chronic kidney disease**. Gastroenterology 2017 Jun 2.
Vaezi MF, Yang YX, Howden CW. **Complications of Proton Pump Inhibitor Therapy**. Gastroenterology. 2017 May 19. pii: S0016-5085(17)35623-8.
Goldstein FC, Steenland K, Zhao L, et al. Proton Pump Inhibitors and Risk of **Mild Cognitive Impairment and Dementia**. J Am Geriatr Soc. 2017 Jun 7.
Taipale H, Tolppanen AM, Tiihonen M, et al. No Association Between Proton Pump Inhibitor Use and Risk of **Alzheimer's** Disease. Am J Gastroenterol. 2017 Jul 11.
Xie Y, Bowe B, Li T, et al. Risk of **death** among users of Proton Pump Inhibitors: a longitudinal observational cohort study of United States veterans. BMJ Open. 2017 Jul 4;7(6):e015735.
Eusebi LH et al. Proton pump inhibitors: **risks of long-term use**. J Gastroenterol Hepatol 2017; 32:1295.
Zhou B et al. Proton-pump inhibitors and risk of **fractures**: an update meta-analysis. Osteoporos Int 2016; 27:339.
Lochhead P, Hagan K, Joshi AD, et al. Association Between Proton Pump Inhibitor Use and **Cognitive** Function in Women. Gastroenterology. 2017 Jul 17.
Cheung KS, Chan EW, Wong AYS, et al. **Long-term proton pump inhibitors and risk of gastric cancer development** after treatment for Helicobacter pylori: a population-based study. Gut. 2017 Oct 31
Landi SN et al. No increase in risk of acute **myocardial infarction** in privately insured adults prescribed proton pump inhibitors vs histamine-2 receptor antagonists (2002–2014). Gastroenterology 2017 Nov 6.
Brusselaers N, Engstrand L, Lagergren J. Maintenance proton pump inhibition therapy and risk of **oesophageal cancer**. Cancer Epidemiol. 2018 Feb 21;53:172-177.
Lai T, Wu M, Liu J, et al. **Acidsuppressive drug use during pregnancy** and the **risk of childhood asthma**: a meta-analysis. Pediatrics. 2018;141(2):e20170889
Nguyen LH, Lochhead P, Joshi AD, et al. No Significant Association Between Proton Pump Inhibitor Use and **Risk of Stroke** After Adjustment for Lifestyle Factors and Indication. Gastroenterology. 2017 Dec 18.
Nehra AK, Alexander JA, Loftus CG, Nehra V. **Proton Pump Inhibitors**: Review of Emerging Concerns. Mayo Clin Proc. 2018 Feb;93(2):240-246.
Targownik L. **Discontinuing Long-Term PPI Therapy**: Why, With Whom, and How? Am J Gastroenterol. 2018 Mar 20.
Mitre E, Susi A, Kropp LE, et al. Association Between Use of **Acid-Suppressive Medications and Antibiotics During Infancy and Allergic Diseases** in Early Childhood. JAMA Pediatr. 2018 Apr 2:e180315.
Tergast TL, Wranke A, Laser H, et al. Dose Dependent Impact of **Proton Pump Inhibitors on the Clinical Course of Spontaneous Bacterial Peritonitis**. Liver Int. 2018 Apr 19.
Zirk-Sadowski J, Masoli JA, Delgado J, et al. **Proton-Pump Inhibitors and Long-Term Risk of Community-Acquired Pneumonia** in Older Adults. J Am Geriatr Soc. 2018 Apr 20.
Malhotra K, Katsanos AH, Bilal M, et al.**Cerebrovascular Outcomes** With **Proton Pump Inhibitors and Thienopyridines**: A Systematic Review and Meta-Analysis. Stroke. 2018 Feb;49(2):312-318.
Varallo FR, de Nadai TR, de Oliveira ARA, et al. Potential Adverse Drug Events and Nephrotoxicity Related to Prophylaxis With Omeprazole for Digestive Disorders: A Prospective Cohort Study. Clin Ther. 2018 Jun;40(6):973-982.
Xie Y, Bowe B, Yan Y, et al. Estimates of **all cause mortality** and cause specific mortality associated with proton pump inhibitors among US veterans: cohort study. BMJ. 2019 May 29;365:l1580.
5. P. Moayyedi, J.W. Eikelboom, J. Bosch, et al.**Safety of proton pump inhibitors based on a large, multi-year, randomized trial of patients receiving rivaroxaban or aspirin** Gastroenterology, 157 (2019), pp. 682-691

COXIB/NSAID

Chan FK, Hung LC, Suen BY, et al. Celecoxib versus diclofenac and omeprazole in reducing the risk of recurrent ulcer bleeding in patients with arthritis. N Engl J Med. 2002 Dec 26;347(26):2104-10. Among patients with a recent history of ulcer bleeding, treatment with celecoxib was as effective as treatment with diclofenac plus omeprazole, with respect to the prevention of recurrent bleeding.
(Agrawal NM, Campbell DR, Safdi MA, et al. Superiority of **lansoprazole vs ranitidine in healing** nonsteroidal anti-inflammatory drug-associated gastric ulcers: results of a double-blind, randomized, multicenter study. NSAID-Associated Gastric Ulcer Study Group. Arch Intern Med. 2000 May 22;160(10):1455-61. In patients who require continuous treatment with NSAIDs, lansoprazole is superior to ranitidine for healing of NSAID associated gastric ulcers. Healing is not delayed by the presence of H pylori infection.)(Yeomans ND, Tulassay Z, et al. A comparison of omeprazole with ranitidine for ulcers associated with nonsteroidal antiinflammatory drugs. Acid Suppression Trial: Ranitidine versus Omeprazole for NSAID-associated Ulcer Treatment (ASTRONAUT) Study Group. N Engl J Med. 1998 Mar 12;338(11):719-26. In patients with regular use of NSAIDs, omeprazole healed & prevented ulcers more effectively than did ranitidine.)

(Goldstein JL, Johanson JF, et al. Healing of gastric ulcers with **esomeprazole versus ranitidine** in patients who continued to receive NSAID therapy: a randomized trial. Am J Gastroenterol. 2005 Dec;100(12):2650-7.) (Hawkey CJ, et al. Omeprazole compared with misoprostol for ulcers associated with nonsteroidal antiinflammatory drugs. Omeprazole versus Misoprostol for NSAID-induced Ulcer Management (OMNIUM) Study Group. N Engl J Med. 1998 Mar 12;338(11):727-34. The overall rates of successful treatment of ulcers, erosions, and symptoms associated with NSAIDs were similar for the two doses of omeprazole and misoprostol. Maintenance therapy with omeprazole was associated with a lower rate of relapse than misoprostol. Omeprazole was better tolerated than misoprostol.) (Chan FK, Wong VW, Suen BY, et al. Combination of a cyclo-oxygenase-2 inhibitor (celecoxib 200mg bid) and a proton-pump inhibitor (esomeprazole 20mg bid) for prevention of recurrent ulcer bleeding in patients at very high risk: a double-blind, randomised trial. Lancet. 2007 May 12;369(9573):1621-6. The 13-month cumulative incidence of the primary endpoint was 0% in the combined-treatment group and 12 (8.9%) in the controls (95% CI difference, 4.1 to 13.7; p=0.0004). n=441 12months. Patients at very high risk for recurrent ulcer bleeding who need anti-inflammatory analgesics should receive combination treatment with a COX 2 inhibitor and a PPI. Our findings should encourage guideline committees to review their recommendations for patients at very high risk of recurrent ulcer bleeding.

Chan FK, Hung LC, Suen BY, Wong et al. Celecoxib versus diclofenac plus omeprazole in high-risk arthritis patients: results of a randomized double-blind trial. Gastroenterology. 2004 Oct;127(4):1038-43. Among patients with previous ulcer bleeding, neither celecoxib nor diclofenac plus omeprazole adequately prevents ulcer recurrence. Treatment-induced significant dyspepsia is an indication for endoscopic evaluation..

PEPTI C ULCER BLEEDING

Leontiadis GI, Sharma VK, et al. Systematic review & meta-analysis of proton pump inhibitor therapy in peptic ulcer bleeding. BMJ. 2005 Jan 31; [Epub ahead of print] (InfoPOEMs: Neither oral nor intravenous use of proton pump inhibitors decreases the risk of dying as the result of peptic ulcer bleeding. The likelihood of rebleeding or the need for surgery is reduced, with 1 episode of rebleeding avoided in every 10 pts treated & 1 surgery avoided for every 25 patients who received treatment. (LOE = 1a)) Leontiadis GI, Sharma VK, Howden CW. WITHDRAWN: Proton pump inhibitor treatment for acute peptic ulcer bleeding. Cochrane Database Syst Rev. 2010 May 12;(5):CD002094.

Sung JJ, Suen BY, Wu JC, et al. Effects of **Intravenous and Oral Esomeprazole** in the Prevention of Recurrent Bleeding from Peptic Ulcers after Endoscopic Therapy. Am J Gastroenterol. 2014 Apr 29.

Sachar H, Vaidya K, Laine L. **Intermittent vs Continuous Proton Pump Inhibitor** Therapy for **High-Risk Bleeding Ulcers**: A Systematic Review and Meta-analysis. JAMA Intern Med. 2014 Sep 8.

Additional References:

Abrahamsen Bo; Eiken Pia; Eastell Richard. Proton Pump Inhibitor Use and the **Antifracture Efficacy of Alendronate**. *Arch Intern Med*. 2011;0(2011):archinternmed.2011.20.

ACCF/ACG/AHA 2008 expert consensus document on reducing the gastrointestinal risks of antiplatelet therapy and NSAID use: a report of the American College of Cardiology Foundation Task Force on Clinical Expert Consensus Documents. *J Am Coll Cardiol***.** 2008; *Circulation*. 2008; DOI: DOI: 10.1161/CIRCULATIONAHA.108.191087. Available at: http://circ.ahajournals.org http://circ.ahajournals.org/cgi/reprint/CIRCULATIONAHA.108.191087

ACCF/ACG/AHA 2010 expert consensus document on the concomitant use of proton pump inhibitors and thienopyridines: A focused update of the ACCF/ACG/AHA 2008 expert consensus document on reducing the gastrointestinal risks of antiplatelet therapy and NSAID use. *J Am Coll Cardiol* 2010; DOI:10.1016/j.jacc2010.09.010. http://content.onlinejacc.org/cgi/reprint/j.jacc.2010.09.010v1.pdf

Agostino JA, Passarella M, Martin AE, et al. Use of **Gastroesophageal Reflux Medications in Premature Infants after NICU Discharge**. Pediatrics. 2016;138(6):e20161977

Ajmera AV, Shastri GS, Gajera MJ, Judge TA. **Suboptimal response to ferrous sulfate** in iron-deficient patients taking omeprazole. Am J Ther. 2012 May;19(3):185-9.

Albeldawi M, Qadeer MA, Vargo JJ. Managing **acute upper GI bleeding**, preventing recurrences. Cleve Clin J Med. 2010 Feb;77(2):131-42.

Alhazzani W, Alshamsi F, Belley-Cote E, et al. Efficacy and safety of **stress ulcer prophylaxis** in critically ill patients: a network meta-analysis of randomized trials. Intensive Care Med. 2017 Dec 4.

Ament PW, Dicola DB, James ME. Reducing adverse effects of **proton pump inhibitors**. Am Fam Physician. 2012 Jul 1;86(1):66-70.

American College of Cardiology Foundation, , American Heart Association Task Force on Practice Guidelines, , Society for Cardiovascular Angiography and Interventions, , Levine, Glenn N., Bates, Eric R., Blankenship, Et al. **2011 ACCF/AHA/SCAI Guideline for Percutaneous Coronary Intervention**: Executive Summary. J Am Coll Cardiol 2011 0: j.jacc.2011.08.006. http://content.onlinejacc.org/cgi/reprint/j.jacc.2011.08.006v1.pdf

American College of Cardiology Foundation, , American Heart Association Task Force on Practice Guidelines, , American Association for Thoracic Surgery, , Society of Cardiovascular Anesthesiologists, , Society of Thoracic Surgeons, Hillis, L. David, Smith, Peter K., Anderson, Jeffrey L., et al. **2011 ACCF/AHA Guideline for Coronary Artery Bypass Graft Surgery**: Executive Summary. J Am Coll Cardiol 2011 0: j.jacc.2011.08.008. http://content.onlinejacc.org/cgi/reprint/j.jacc.2011.08.008v1.pdf

American Gastroenterological Association (**AGA**), Spechler SJ, Sharma P, Souza RF, Inadomi JM, Shaheen NJ. American Gastroenterological Association medical position statement on the management of **Barrett's esophagus**. Gastroenterology 2011 Mar;140(3):1084-91.

Andriulli A, Annese V, Caruso N, et al. Proton-pump inhibitors and outcome of endoscopic hemostasis in bleeding peptic ulcers: a series of meta-analyses. Am J Gastroenterol 2005; 100:207-19. (InfoPOEMs: In all groups, proton pump inhibitors reduce rebleeding and the need for surgery, particularly when used in combination with endotherapy, but do not affect mortality. (LOE = 1a))

Andriulli A, Loperfido S, Focareta R, et al. High- versus low-dose proton pump inhibitors after **endoscopic hemostasis** in patients with peptic ulcer bleeding: a multicentre, randomized study. Am J Gastroenterol. 2008 Dec;103(12):3011-8. Intensive regimen (pant or omep (80 mg bolus followed by 8 mg/h as continuous infusion for 72 h) or a standard regimen (40 mg bolus daily followed by saline infusion for 72 h). After the infusion, all pts were given 20 mg PPI bid po. N=238. Following endoscopic hemostasis of bleeding ulcers, standard-dose PPIs infusion was as effective as a high-dose regimen in reducing risk of recurrent bleeding.

Angelidou A, Bell K, Gupta M, et al. Implementation of a **Guideline to Decrease Use of Acid-Suppressing Medications in the NICU**. Pediatrics. 2017 Nov 21.

Anheyer D, Frawley J, Koch AK, et al. **Herbal Medicines for Gastrointestinal Disorders** in **Children and Adolescents**: A Systematic Review. Pediatrics. 2017;139(6):e20170062

Antoniou T, Macdonald EM, Hollands S, et al. Proton pump inhibitors and the risk of **acute kidney injury** in older patients: a population-based cohort study. CMAJ Open. 2015 Apr 2

Arj A, Razavi Zade M, Yavari M, et al. **Proton pump inhibitors use and change in bone mineral density**. Int J Rheum Dis. 2016 May 31.

ASGE Standards of Practice Committee, Wani S, Qumseya B, Sultan S, et al. **Endoscopic eradication therapy for patients with Barrett's esophagus**-associated dysplasia and intramucosal cancer. Gastrointest Endosc. 2018 Apr;87(4):907-931.e9.

Attwood SE et al. **Long-term safety of proton pump inhibitor therapy** assessed under controlled, randomised clinical trial conditions: Data from the SOPRAN and LOTUS studies. Aliment Pharmacol Ther 2015 Apr 10.

Aumar M, Lalanne A, Guimber D,et al. Influence of **Percutaneous Endoscopic Gastrostomy on Gastroesophageal Reflux Disease in Children**. J Pediatr. 2018 Apr 11.

Bajaj JS, Zadvornova Y, et al. Association of proton pump inhibitor therapy with **spontaneous bacterial peritonitis** in cirrhotic patients with ascites. Am J Gastroenterol. 2009 May;104(5):1130-4. Epub 2009 Mar 31.

Bajaj JS, Ratliff SM, Heuman DM, Lapane KL. Proton pump inhibitors are associated with a high rate of **serious infections** in veterans with **decompensated cirrhosis**. Aliment Pharmacol Ther. 2012 Sep 11.

Baird DC, Harker DJ, Karmes AS. Diagnosis and Treatment of **Gastroesophageal Reflux in Infants and Children**. Am Fam Physician. 2015;92(8):705-714.

Barkun AN, Bardou M, Kuipers EJ, et al. and for the **International Consensus** Upper Gastrointestinal Bleeding Conference Group. Management of Patients With **Nonvariceal Upper Gastrointestinal Bleeding**. *Ann Intern Med* January 19, 2010 152:101-113.

Barkun AN, Bhat M, Armstrong D, et al. Effectiveness of **disseminating consensus management recommendations for ulcer bleeding**: a cluster randomized trial. CMAJ. 2013 Feb 19;185(3):E156-66.

Barletta JF. **Histamine-2-receptor antagonist** administration & gastrointestinal bleeding when used for **stress ulcer prophylaxis** in patients with severe sepsis or septic shock. Ann Pharmacother. 2014 Oct;48(10):1276-81

Bateman BT, Bykov K, Choudhry NK, et al. Type of **stress ulcer prophylaxis** (**PPIs** vs H2) and risk of nosocomial pneumonia in cardiac surgical patients: cohort study. BMJ. 2013 Sep 19;347:f5416.

Beaumont H, Boeckxstaens GE. Does the Presence of a Hiatal Hernia Affect the Efficacy of the Reflux Inhibitor Baclofen During Add-On Therapy? Am J Gastroenterol. 2009 Jul;104(7):1764-1771. Epub 2009 Jun 2.This study shows that **baclofen** is also effective in patients with GERD with +HH, further underscoring the potential of reflux inhibitors as treatment of GERD.

Begley J, Smith T, Barnett K, et al. **Proton Pump Inhibitor Associated Hypomagnasaemia** - A Cause for Concern? Br J Clin Pharmacol. 2015 Nov 27.

Bell JC, Schneuer FJ, Harrison C, et al. **Acid suppressants for managing gastro-oesophageal reflux** and gastro-oesophageal reflux disease **in infants**: a national survey. Arch Dis Child. 2018 Jul;103(7):660-664.

Bell RC, Lipham JC, Louie BE, et al. **Laparoscopic magnetic sphincter augmentation versus double-dose proton pump inhibitors** for management of **moderate-to-severe regurgitation in GERD**: a randomized controlled trial. Gastrointest Endosc. 2018 Jul 18.

Benmassaoud A, McDonald EG, Lee TC. Potential **harms of proton pump inhibitor therapy**: rare adverse effects of commonly used drugs. CMAJ. 2016 Jun 14;188(9):657-62.

Bennett C, Vakil N, Bergman J, et al. Consensus Statements for Management of **Barrett's Dysplasia** and Early-Stage Esophageal Adenocarcinoma, Based on a Delphi Process. Gastroenterology. 2012 Aug;143(2):336-46.

Bennett C, Moayyedi P, Corley DA, et al; BOB CAT Consortium. BOB CAT: A Large-Scale Review and **Delphi Consensus for Management of Barrett's Esophagus** With No Dysplasia, Indefinite for, or Low-Grade Dysplasia. Am J Gastroenterol. 2015 May;110(5):662-82; quiz 683.

Bhat Shivaram, Coleman Helen G., Yousef Fouad, et al. Risk of Malignant Progression in **Barrett's Esophagus** Patients: Results from a Large Population-Based Study JNCI J Natl Cancer Inst (2011) first published online June 16, 2011 doi:10.1093/jnci/djr203. (Risk only 0.13%)

Bhatt DL et al. for the **COGENT** Investigators. **Clopidogrel with or without omeprazole** in coronary artery disease. N Engl J Med 2010 Oct 6; [e-pub ahead of print].

Bird-Lieberman EL, Dunn JM, Coleman HG, et al. Population-Based Study Reveals New Risk-Stratification **Biomarker Panel for Barrett's Esophagus**. Gastroenterology. 2012 Oct;143(4):927-935.e3.

Björnsson E, Abrahamsson H, Simrén M, et al. **Discontinuation of proton pump inhibitors** in patients on long-term therapy: a double-blind, placebo-controlled trial. Aliment Pharmacol Ther. 2006 Sep 15;24(6):945-54.

Blume H, Donath F, Warnke A, Schug BS. Pharmacokinetic **drug interaction** profiles of proton pump inhibitors. Drug Saf. 2006;29(9):769-84.

Boeckxstaens GE, Zaninotto G, Richter JE. **Achalasia**. Lancet. 2013 Jul 16.

Boghossian TA, Rashid FJ, Thompson W, et al. **Deprescribing versus continuation of chronic proton pump inhibitor use in adults**. Cochrane Database Syst Rev. 2017 Mar 16;3:CD011969. In people with mild GERD, on-demand deprescribing may lead to an increase in GI symptoms (e.g. dyspepsia, regurgitation) and probably a reduction in pill burden. There was a decline in participant satisfaction, although heterogeneity was high. There were insufficient data to make a conclusion regarding long-term benefits and harms of PPI discontinuation, although two trials (one on-demand trial and one abrupt discontinuation trial) reported endoscopic findings in their intervention groups at study end.

Bour B, et al. Long-term treatment of gastro-oesophageal reflux disease patients with frequent symptomatic relapses using rabeprazole: **on-demand** treatment compared with continuous treatment. Aliment Pharmacol Ther. 2005 Apr 1;21(7):805-12.

Bredenoord AJ, Pandolfino JE, Smout AJ. **Gastro-oesophageal reflux disease**. Lancet. 2013 Mar 7.

Brisebois S, Merati A, Giliberto JP. **Proton pump inhibitors**: Review of reported risks and controversies. Laryngoscope Investig Otolaryngol. 2018 Oct 19;3(6):457-462.

Brusselaers N, Engstrand L, Lagergren J. Maintenance proton pump inhibition therapy and risk of **oesophageal cancer**. Cancer Epidemiol. 2018 Feb 21;53:172-177.

Bull-Henry K, Al-Kawas FH. **Evaluation of Occult Gastrointestinal Bleeding**. Am Fam Physician. 2013;87(6):430-436.

Bulsiewicz WJ, Madanick RD. **Antireflux surgery** in the proton pump inhibitor era. Cleve Clin J Med. 2012 Apr;79(4):273-81.

Calvet X, Gomollon F. What is potent acid inhibition, and how can it be achieved? Drugs. 2005;65 Suppl 1:13-23.

Camilleri M, Parkman HP, Shafi MA, et al. Clinical guideline: management of **gastroparesis**. Am J Gastroenterol. 2013 Jan;108(1):18-37.

Canani RB, et al. Working Group on Intestinal Infections of the Italian Society of Pediatric Gastroenterology, Hepatology and Nutrition (SIGENP). Therapy with gastric acidity inhibitors increases the risk of acute **gastroenteritis and community-acquired pneumonia** in children. Pediatrics. 2006 May;117(5):e817-20. (InfoPOEMs: In this weak study, treatment of gastroesophageal reflux disease (GERD) with gastric acid suppressants increased the likelihood of pneumonia compared with the rate in healthy children. It's not known whether the treatment, the presence of GERD, or some other factor caused the pneumonia. Watch for confirmation in randomized research. (LOE = 4))

Caos A, Breiter J, Perdomo C, Barth J. Long-term prevention of erosive or ulcerative gastro-oesophageal reflux disease relapse with **rabeprazole** 10 or 20 mg vs. placebo: results of a 5-year study in the United States. Aliment Pharmacol Ther. 2005 Aug 1;22(3):193-202.

Cardoso RN, Benjo AM, DiNicolantonio JJ, et al. Incidence of cardiovascular events and gastrointestinal bleeding in patients receiving **clopidogrel with and without proton pump inhibitors**: an updated meta-analysis. Open Heart. 2015 Jun 30;2(1):e000248.

Castro REV, Sousa CDC, de Magalhães-Barbosa MCet al. **Ranitidine-Induced Delirium in a 7-Year-Old Girl**: A Case Report. Pediatrics. 2019 Jan 11.

Centanni M, Gargano L, Canettieri G, Viceconti N, Franchi A, Delle Fave G, Annibale B. **Thyroxine** in goiter, Helicobacter pylori infection, and chronic gastritis. N Engl J Med. 2006 Apr 27;354(17):1787-95.

Chan FK, et al. Preventing recurrent upper gastrointestinal bleeding in patients with Helicobacter pylori infection who are taking low-dose aspirin or naproxen. N Engl J Med. 2001 Mar 29;344(13):967-73. CONCLUSIONS: Among patients with H. pylori infection and a history of upper gastrointestinal bleeding who are taking low-dose aspirin, the eradication of H. pylori is equivalent to treatment with omeprazole in preventing recurrent bleeding. Omeprazole is superior to the eradication of H. pylori in preventing recurrent bleeding in patients who are taking other NSAIDs.

Chan FK, Leung WK. **Peptic-ulcer disease**. Lancet. 2002 Sep 21;360(9337):933-41.

Chan FK, Kyaw M, Tanigawa T, et al. **Similar** Efficacy of **Proton-Pump Inhibitors vs H2-Receptor Antagonists** in Reducing Risk of Upper Gastrointestinal **Bleeding or Ulcers** in High-Risk Users of Low-Dose Aspirin. Gastroenterology. 2017 Jan;152(1):105-110.e1.

Chan FKL, Kyaw MH, Hsiang JC, et al. Risk of **Postpolypectomy Bleeding With Uninterrupted Clopidogrel Therapy** in an Industry-Independent, Double-Blind, Randomized Trial. Gastroenterology. 2019 Mar;156(4):918-925.e1.

Chan Walter W.; Chiou Eric; Obstein Keith L.; et al. The Efficacy of Proton Pump Inhibitors for the **Treatment of Asthma** in Adults: A Meta-analysis. *Arch Intern Med*. 2011;171(7):620-629.

Chang AB, et al. Systematic review and meta-analysis of randomised controlled trials of gastro-oesophageal reflux interventions for **chronic cough** associated with gastro-oesophageal reflux. BMJ. 2005 Dec 5; [Epub] CONCLUSION: Use of a proton pump inhibitor to treat cough associated with GORD has some effect in some adults. The effect, however, is less universal than suggested in consensus guidelines on chronic cough and its magnitude of effect is uncertain. (InfoPOEMs: Treatment for gastroesophageal reflux disease (GERD) in patients with chronic cough may be effective in some patients, but the effect is not universal or consistent. It might be worth a try, but don't expect many patients to improve. (LOE = 1a))

Chang AB, Lasserson TJ, Gaffney J, et al. Gastro-oesophageal reflux treatment for prolonged **non-specific cough** in children and adults. Cochrane Database Syst Rev. 2011 Jan 19;1:CD004823. PPI is not efficacious for cough associated with GORD symptoms in very young children (including infants) and should not be used for cough outcomes. There is insufficient data in older children to draw any valid conclusions. In adults, there is insufficient evidence to conclude definitely that GORD treatment with PPI is universally beneficial for cough associated with GORD.

Chang AB, Oppenheimer JJ, Kahrilas PJ, et al; CHEST Expert Cough Panel. **Chronic cough and gastroesophageal reflux** in children - CHEST Guideline and Expert Panel Report. Chest. 2019 Apr 16.

Charlot M, Ahlehoff O, et al. Proton-pump inhibitors are associated with **increased cardiovascular risk** independent of clopidogrel use: a nationwide cohort study. Ann Intern Med. 2010 Sep 21;153(6):378-86.

Charlot M, Grove EL, Hansen PR, et al. Proton pump inhibitor use and **risk of adverse cardiovascular events in aspirin treated patients** with first time myocardial infarction: nationwide propensity score matched study. BMJ. 2011 May 11;342:d2690. doi: 10.1136/bmj.d2690.

Chen CB, Lin M, Eurich DT, Johnson JA. Safety of Concomitant **Metformin and Proton Pump Inhibitor Use**: A Population Retrospective Cohort Study. Clin Ther. 2016 Apr 6.

Chen JW, Kao JY. **Eosinophilic esophagitis**: update on management and controversies. BMJ. 2017 Nov 13;359:j4482.

Chen Y, Liu B, Glass K, et al. Use of **Proton Pump Inhibitors and the Risk of Hospitalization for Infectious Gastroenteritis**. PLoS One. 2016 Dec 20;11(12):e0168618.

Cheng HC, Wu CT, et al. **Double oral esomeprazole after a 3-day intravenous** esomeprazole infusion reduces recurrent peptic ulcer bleeding in high-risk patients: a randomised controlled study. Gut. 2014 Mar 21.

Cheung KS, Chan EW, Wong AYS, et al. **Long-term proton pump inhibitors and risk of gastric cancer development** after treatment for Helicobacter pylori: a population-based study. Gut. 2017 Oct 31

Chiba N. Proton pump inhibitors in acute healing and maintenance of erosive or worse esophagitis: a systematic overview. Can J Gastroenterol. 1997 Sep;11 Suppl B:66B-73B.
Chitnis AS, Holzbauer SM, Belflower RM, et al. Epidemiology of **Community-Associated Clostridium difficile Infection**, 2009 Through 2011. JAMA Intern Med. 2013 Jul 22;173(14):1359-67.
Chu MP, et al. Association of Proton Pump Inhibitors & **Capecitabine** Efficacy in Advanced Gastroesophageal Cancer: Secondary Analysis of the TRIO-013/LOGiC Randomized Clinical Trial. JAMA Oncol. 2016 Oct 13.
Cohen S, Bueno de Mesquita M, Mimouni FB. **Adverse effects** reported in the **use of gastroesophagal reflux disease treatments** in children: a 10 years literature review. Br J Clin Pharmacol. 2015 Mar 5.
Cojutti PG, Candoni A, Lazzarotto D, et al. **Co-administration of proton pump inhibitors and/or of steroids** may be a risk factor for low trough concentrations of posaconazole delayed-released tablets in adult patients with **hematological malignancies**. Br J Clin Pharmacol. 2018 Jul 5.
Cook D, Guyatt G. **Prophylaxis against Upper Gastrointestinal Bleeding** in Hospitalized Patients. N Engl J Med. 2018 Jun 28;378(26):2506-2516.
Cook MB, Shaheen NJ, Anderson LA, et al. **Cigarette Smoking Increases Risk of Barrett's Esophagus**: An Analysis of the Barrett's and Esophageal Adenocarcinoma Consortium. Gastroenterology. 2012 Jan 11.
Cook MB, Coburn SB, Lam JR, et al. **Cancer incidence** and mortality risks in a large US **Barrett**`s oesophagus cohort. Gut. 2017 Jan 4.
Cooke PA, Gormley GJ, Gilliland A, Cupples ME. **Dyspepsia**. BMJ. 2011 Sep 30;343:d6234.
Corley DA, Mehtani K, Quesenberry C, et al. Impact of Endoscopic Surveillance on Mortality From Barrett's Esophagus-Associated Esophageal Adenocarcinomas. Gastroenterology. 2013 Aug;145(2):312-319.e1.
Coronel E, Bassi N, et al. Evaluation of a Trainee-Led Project to **Reduce Inappropriate Proton Pump Inhibitor Infusion** in Patients With Upper Gastrointestinal Bleeding: Skip the Drips. JAMA Intern Med. 2017 Oct 9
Cremonini F, Wise J, Moayyedi P, Talley N. Diagnostic and therapeutic use of proton pump inhibitors in non-cardiac chest pain. Am J Gastroenterol 205; 100:1226-32. (InfoPOEMs: The use of a proton pump inhibitor (PPI) is useful in the diagnosis of gastroesophageal reflux disease (GERD) and an effective treatment for patients with noncardiac chest pain. Because some smaller studies with negative results may not have been published, the estimate of the degree of benefit of PPIs in this study may be on the high side. (LOE = 1a))
Curvers WL, ten Kate FJ, Krishnadath KK, et al. **Low-grade dysplasia in Barrett`s esophagus**: overdiagnosed and underestimated. Am J Gastroenterol. 2010 Jul;105(7):1523-30.
Davies I, Burman-Roy S, Murphy MS; Guideline Development Group. **Gastro-oesophageal reflux disease in children: NICE guidance**. BMJ. 2015 Jan 14;350:g7703.
Davila RE, Rajan E, Adler DG, Egan J, et al. Standards of Practice Committee. ASGE Guideline: the role of **endoscopy** in the patient with lower-GI bleeding. Gastrointest Endosc. 2005 Nov;62(5):656-60.
de Bortoli N, Martinucci I, Piaggi P, et al. Randomised clinical trial: **twice daily esomeprazole 40 mg** vs. pantoprazole 40mg bid in **Barrett's esophagus** for 1year. Aliment Pharmacol Ther. 2011 Mar 8.
de Jager CP, Wever PC, Gemen EF, et al. Proton pump inhibitor therapy **predisposes to community-acquired Streptococcus pneumoniae pneumonia**. Aliment Pharmacol Ther. 2012 Nov;36(10):941-9.
Delaney B, Ford A, Forman D, Moayyedi P, Qume M, Delaney B. Initial management strategies for **dyspepsia**. Cochrane Database Syst Rev. 2005 Oct 19;(4):CD001961& ACP Journal Club. AUTHORS' CONCLUSIONS: Proton pump inhibitor drugs (PPIs) are effective in the treatment of dyspepsia in these trials which may not adequately exclude patients with gastro-oesophageal reflux disease (GORD). The relative efficacy of histamine H2-receptor antagonists (H2RAs) and PPIs is uncertain early investigation by endoscopy or H. pylori testing may benefit some patients with dyspepsia but is not cost effective as part of an overall management strategy.
Dellon ES, Gonsalves N, Hirano I, Furuta GT, Liacouras CA, Katzka DA. **ACG** clinical guideline: evidenced based approach to the diagnosis and management of **esophageal eosinophilia and eosinophilic esophagitis** (EoE). Am J Gastroenterol. 2013 May;108(5):679-92.
Dekel R, Morse C, Fass R. The role of proton pump inhibitors in gastro-oesophageal reflux disease. Drugs. 2004;64(3):277-95.
Deprescribing Guideline and Algorithms (Benzodiazepine receptor agonits, Proton pump inhibitors, Antipsychotics, Antihyperglycemic) http://deprescribing.org/resources/deprescribing-guidelines-algorithms/
DeVault KR, Castell DO. Updated guidelines for the diagnosis and treatment of gastroesophageal reflux disease (**GERD**) . Am J Gastroenterol **2005**; 100:190-200. (InfoPOEMS:This guideline provides recommendations for management of gastroesophageal reflux disease. Endoscopy is recommended only for patients with alarm symptoms, poor response to therapy, or severe or long-term symptoms. H2 blockers or PPIs are effective in most patient, and many can be tapered to low doses or off treatment all together. (LOE =))
Devine RE, McCleary N, Sheikh A, et al. **Acid-suppressive medications during pregnancy and risk of asthma and allergy in children**: A systematic review and meta-analysis. J Allergy Clin Immunol. 2016 Dec 20.
Devitt J, Lyon C, Swanson SB, DeSanto K. What are the **risks of long-term PPI use for GERD symptoms in patients > 65 years**? J Fam Pract. 2019 Apr;68(3):E18-E19.
Diamond DA, Mattoo TK. **Endoscopic treatment of primary vesicoureteral reflux**. N Engl J Med. 2012 Mar 29;366(13):1218-26.
Dickman R, Schiff E, Holland A, et al. Clinical trial: **acupuncture** vs. doubling the proton pump inhibitor dose in refractory heartburn. Aliment Pharmacol Ther. 2007 Oct 30;26(10):1333-1344. Epub 2007 Sep 17.
Adding acupuncture is more effective than doubling the proton pump inhibitor dose in controlling gastro-oesophageal reflux disease-related symptoms in patients who failed standard-dose proton pump inhibitors. (InfoPOEMs: In this small, short-term study, adding twice weekly acupuncture to standard-dose proton pump inhibitor (PPI) treatment was more effective in controlling symptoms than doubling the PPI dose. Acupuncture may be useful for some patients, but the long-term benefits, if any, have not been established. (LOE = 1b))
Dial S, Delaney JA, Barkun AN, Suissa S. Use of gastric acid-suppressive agents and the risk of community-acquired **Clostridium difficile**-associated disease. JAMA. 2005 Dec 21;294(23):2989-95.
Dial S, Delaney JA, Schneider V, Suissa S. Proton pump inhibitor use and risk of community-acquired **Clostridium difficile**-associated disease defined by prescription for oral vancomycin therapy. CMAJ. 2006 Sep 26;175(7):745-8.
Dodd JM, Crowther CA, Robinson JS. Oral **misoprostol** for induction of labour at term: randomised controlled trial. BMJ. 2006 Mar 4;332(7540):509-13. Epub 2006 Feb 2.
Douglas IJ, Evans SJW, Hingorani A, et al. **Clopidogrel and interaction with proton pump inhibitors**: comparison between cohort and within person study designs. BMJ 2012;345:e4388.
Drug and Therapeutics Bulletin. Managing **gastro-oesophageal reflux in infants**. BMJ. 2010 Aug 27;341:c4420. doi: 10.1136/bmj.c4420.
Duncan DR, Mitchell PD, Larson K, et al. Association of **Proton Pump Inhibitors With Hospitalization Risk in Children With Oropharyngeal Dysphagia**. JAMA Otolaryngol Head Neck Surg. 2018 Oct 11.
Dunbar KB, Agoston AT, Odze RD, et al. Association of **acute gastroesophageal reflux disease with esophageal histological changes**.JAMA. doi:10.1001/jama.2016.5657
Dupree CE, Blair K, Steele SR, et al. **Laparoscopic Sleeve Gastrectomy** in Patients With Preexisting **Gastroesophageal Reflux Disease** : A National Analysis. JAMA Surg. 2014 Feb 5.
Dworzynski K, Pollit V, Kelsey A, et al; on behalf of the Guideline Development Group. Management of **acute upper gastrointestinal bleeding**:summary of **NICE** guidance. BMJ. 2012 Jun 13;344:e3412.
Earnshaw Stephanie R.; Scheiman James; Fendrick A. Mark; et al. **Cost-Utility of Aspirin and Proton Pump Inhibitors for Primary Prevention**. *Arch Intern Med*. 2011;171(3):218-225.
Elati A, Weeks A. **Misoprostol for the management of postpartum haemorrhage**. BMJ. 2011 May 13;342:d2877. doi: 10.1136/bmj.d2877.
Epstein M, McGrath S, Law F. Proton-pump inhibitors and hypomagnesemic hypoparathyroidism. N Engl J Med. 2006 Oct 26;355(17):1834-6.
Epstein David, et al. **REFLUX** trial group. Laparoscopic **fundoplication** compared with medical management for gastro-oesophageal reflux disease: cost effectiveness study. BMJ 2009;339:b2576, doi:10.1136/bmj.b2576
Erichsen R, Robertson D, Farkas DK, et al. **Erosive reflux disease increases risk for esophageal adenocarcinoma**, compared with nonerosive reflux. Clin Gastroenterol Hepatol. 2012 May;10(5):475-480.e1.
Eichenwald EC; Committee on Fetus and Newborn. Diagnosis and Management of **Gastroesophageal Reflux in Preterm Infants**. Pediatrics. 2018 Jun 18.
Eisa N, Bazerbachi F, Alraiyes AH, et al. Q: do all hospitalized patients need **stress ulcer prophylaxis**? Cleve Clin J Med. 2014 Jan;81(1):23-5.
European Rabeprazole Study Group. A randomized, double-blind trial of the efficacy and safety of 10 or 20 mg **rabeprazole** compared with 20 mg omeprazole in the maintenance of gastro-oesophageal reflux disease over 5 years. Aliment Pharmacol Ther. 2003 Feb;17(3):343-51.
Falk GW, Buttar NS, Foster NR, et al; Cancer Prevention Network. A Combination of **Esomeprazole and Aspirin Reduces** Tissue Concentrations of Prostaglandin E(2) in Patients With **Barrett's** Esophagus. Gastroenterology. 2012 Oct;143(4):917-926.e1.
Farrell B, Pottie K, Thompson W, et al. **Deprescribing proton pump inhibitors**: Evidence-based clinical practice guideline. Can Fam Physician. 2017 May;63(5):354-364.
Fashner J, Gitu AC. **Diagnosis and Treatment of Peptic Ulcer Disease and H. pylori Infection**. Am Fam Physician. 2015;91(4):236- 242.
FDA Mar/11 Proton Pump Inhibitor drugs (PPIs): Drug Safety Communication - **Low Magnesium Levels** Can Be Associated With Long-Term Use.
FDA Apr/11: Teva's lansoprazole **delayed-release orally disintegrating tablet has clogged** and blocked oral syringes and feeding tubes, including both gastric and jejunostomy types, when administered as a suspension.
FDA Feb/12 notified the public that the use of stomach acid drugs known as **proton pump inhibitors** (PPIs) may be associated with an increased risk of **Clostridium difficile**–associated diarrhea (CDAD).

FDA Mar/12 **LINX Reflux Management System** is a surgically-placed string of magnetic titanium beads that is placed at the lower esophageal sphincter. When a person swallows, the device expands to accommodate the liquid or food. Once the food passes, the device keeps a weak lower esophageal sphincter closed, thus preventing material from flowing back into the esophagus.

Feld L, Cifu AS. Management of Dyspepsia. JAMA. 2018 May 1;319(17):1816-1817.

Fernando HC, Murthy SC, Hofstetter W, et al. Society of Thoracic Surgeons. The Society of Thoracic Surgeons practice guideline series: guidelines for the management of **Barrett's esophagus with high-grade dysplasia**. Ann Thorac Surg 2009 Jun;87(6):1993-2002.

Filion KB, Chateau D, et al. CNODES Investigators. Proton pump inhibitors & the risk of hospitalisation for **community-acquired pneumonia**: replicated cohort studies with meta-analysis. Gut. 2013 Jul 15.

Fiocca R, Mastracci L, Engström C, et al. Long-Term Outcome of Microscopic Esophagitis in Chronic GERD Patients Treated With Esomeprazole or Laparoscopic Antireflux Surgery in the **LOTUS** Trial. Am J Gastroenterol. 2009 Nov 10.

Fitzgerald RC, di Pietro M, Ragunath K, et al. **British** Society of Gastroenterology. British Society of Gastroenterology guidelines on the diagnosis and **management of Barrett's** oesophagus. Gut. 2014 Jan;63(1):7-42.

Fletcher J, Derakhshan MH, Jones GR, et al. **BMI** is superior to symptoms in predicting response to proton pump inhibitor: randomised trial in patients with upper gastrointestinal symptoms and normal endoscopy. Gut. 2011 Apr;60(4):442-8.

Flook NW, Moayyedi P, Dent J, et al. Acid-suppressive therapy with **esomeprazole for relief of unexplained chest pain** in primary care: a randomized, double-blind, placebo-controlled trial. Am J Gastroenterol. 2013 Jan;108(1):56-64.

Flory J, Haynes K, Leonard CE, et al. **Proton Pump Inhibitors** Do **Not Impair** the Effectiveness of **Metformin** in Diabetic Patients. Br J Clin Pharmacol. 2014 Sep 9.

Fock KM, Teo EK, Ang TL, et al. **Rabeprazole** vs esomeprazole in non-erosive gastro-esophageal reflux disease: a randomized, double-blind study in urban Asia. World J Gastroenterol. 2005 May 28;11(20):3091-8.

Focks JJ, Brouwer MA, van Oijen MG, et al. Concomitant use of **clopidogrel and proton pump inhibitors**: impact on platelet function and clinical outcome- a systematic review. Heart. 2013 Apr;99(8):520-7.

Ford AC, Qume M, Moayyedi P, et al. Helicobacter pylori "**test & treat**" or endoscopy for managing dyspepsia: an individual patient data meta-analysis. Gastroenterology. 2005 Jun;128(7):1838-44 & ACP Journal Club.

Freedberg DE, Salmasian H, Abrams JA, Green RA. Orders for **Intravenous Proton Pump Inhibitors After Implementation of an Electronic Alert**. JAMA Intern Med. 2015 Jan 19.

Freedberg DE, et al. The **Risks and Benefits of Long-term Use of Proton Pump Inhibitors**: Expert Review and Best Practice Advice: American Gastroenterological Association (AGA). Gastro 2017 Mar;152(4):706-715.

Frelinger AL 3rd, Lee RD, Mulford DJ, et al. A randomized, 2-period, crossover design study to assess the effects of **dexlansoprazole, lansoprazole, esomeprazole, and omeprazole** on the steady-state pharmacokinetics and pharmacodynamics of **clopidogrel** in healthy volunteers. J Am Coll Cardiol. 2012 Apr 3;59(14):1304-11.

Furlanetto Tania Weber; Faulhaber Gustavo Adolpho Moreira. **Hypomagnesemia** and Proton Pump Inhibitors: Below the Tip of the Iceberg. Arch Intern Med. 2011;0(2011):archinternmed.2011.199.

Furuta GT, Katzka DA. **Eosinophilic Esophagitis**. N Engl J Med. 2015 Oct 22;373(17):1640-8.

Fyhn TJ, Knatten CK, Edwin B, et al. Randomized Controlled Trial of **Laparoscopic and Open Nissen Fundoplication in Children**. Ann Surg. 2015 Jun;261(6):1061-7.

Gaddam S, Singh M, et al. **Persistence of nondysplastic Barrett's esophagus** identifies patients at lower risk for esophageal adenocarcinoma: results from a large multicenter cohort. Gastroenterology 2013;145:548–553.

Galmiche JP, Hatlebakk J, Attwood S, Laparoscopic antireflux surgery vs esomeprazole treatment for chronic GERD: **LOTUS** randomized clinical trial. JAMA. 2011 May 18;305(19):1969-77.

Ganz RA, Peters JH, Horgan S, et al. **Esophageal sphincter device** for gastroesophageal reflux disease. N Engl J Med. 2013 Feb 21;368(8):719-27.

Garbis H, et al. Pregnancy outcome after exposure to ranitidine and other H2-blockers A collaborative study of the European Network of Teratology Information Services. Reprod Toxicol. 2005 Mar-Apr;19(4):453-8.

Garcia Rodriguez LA, Lagergren J, Lindblad M. Gastric acid suppression and risk of **oesophageal and gastric adenocarcinoma**: a nested case control study in the UK. Gut. 2006 Nov;55(11):1538-44. Epub 2006 Jun 19.

Gasparini R, Lai PL, Casabona F, et al. Do the **omeprazole** family compounds exert a protective effect against **influenza**-like illness? BMC Infect Dis. 2014 Jun 2;14(1):297.

Gatta L, Vaira D, Sorrenti G, et al. Meta-analysis: the efficacy of proton pump inhibitors for **laryngeal symptoms** attributed to gastro-oesophageal reflux disease.Aliment Pharmacol Ther. 2007 Feb 15;25(4):385-92. Therapy with a high-dose proton pump inhibitor is no more effective than placebo in producing symptomatic improvement or resolution of laryngo-pharyngeal symptoms. Further studies are necessary to identify the characteristics of patients that may respond to proton pump inhibitor therapy.

Gawron AJ, Pandolfino JE, Miskevics S, Lavela SL. **Proton Pump Inhibitor Prescriptions and Subsequent Use in US Veterans** Diagnosed with Gastroesophageal Reflux Disease. J Gen Intern Med. 2013 Feb 12.

Gee DW, Andreoli MT, Rattner DW. Measuring the effectiveness of **laparoscopic antireflux surgery**: long-term results. Arch Surg. 2008 May;143(5):482-7. Contrary to the medical literature, our results demonstrate that patients undergoing primary LF by an experienced surgical team have near-normal GERD-HRQL scores at long-term follow-up and low reoperation rates and are satisfied with their decision to undergo surgery. Results following redo LF are not as good, highlighting the importance of proper patient selection and surgical technique when performing primary LF.

Ghebremariam YT, Lependu P, Lee JC, et al. Unexpected effect of proton pump inhibitors: elevation of the **cardiovascular risk factor asymmetric dimethylarginine**. Circulation. 2013 Aug 20;128(8):845-53.

Giannini EG, Zentilin P, Dulbecco P, Vigneri S, Scarlata P, Savarino V. Management strategy for patients with gastroesophageal reflux disease: a comparison between empirical treatment with esomeprazole and endoscopy-oriented treatment. Am J Gastroenterol. 2008 Feb;103(2):267-75. **Early endoscopy** for patients with gastroesophageal reflux disease (GERD) without alarm symptoms does **not** improve symptoms or quality of life, but increases costs. (LOE = 1b)

Gieruszczak-Bialek D, Konarska Z, Skorka A, et al. **No Effect of Proton Pump Inhibitors on Crying and Irritability in Infants**: Systematic Review of Randomized Controlled Trials. J Pediatr. 2014 Dec 30.

Gill SK, O`Brien L, Einarson TR, et al. The safety of proton pump inhibitors **(PPIs) in pregnancy**: a meta-analysis. Am J Gastroenterol. 2009 Jun;104(6):1541-5; quiz 1540, 1546. Epub 2009 Apr 28. On the basis of these results, PPIs are not associated with an increased risk for major congenital birth defects, spontaneous abortions, or preterm delivery. The narrow range of 95% CIs is further reassuring, suggesting that PPIs can be safely used in pregnancy.

Gillessen A, Beil W, Modlin IM, Gatz G, Hole U. **40 mg pantoprazole and 40 mg esomeprazole** are equivalent in the healing of esophageal lesions & relief from gastroesophageal reflux disease-related symptoms. J Clin Gastroenterol. 2004 Apr;38(4):332-40. (n=227) In patients with gastroesophageal reflux disease, 40 mg pantoprazole daily and 40 mg esomeprazole daily are equally effective for healing of esophageal lesions and relieving gastroesophageal reflux disease-related symptoms.

Gisbert JP, Calvet X, Cosme A, et al. H. pylori Study Group of the Asociación Española de Gastroenterología (Spanish Gastroenterology Association). Long-term follow-up of 1,000 patients **cured of Helicobacter pylori infection following an episode of peptic ulcer bleeding**. Am J Gastroenterol. 2012 Aug;107(8):1197-204.

Goldman RD. **Bismuth salicylate** for diarrhea in children. Can Fam Physician. 2013 Aug;59(8):843-4.

Gomm W, von Holt K, Thomé F, et al. Association of **proton pump inhibitors** with risk of **dementia**: a pharmacoepidemiological claims data analysis [online Fe 15, 16].JAMA Neurol. doi:10.1001/jamaneurol.2015.4791.

Gomollon F, Calvet X. Optimising acid inhibition treatment. Drugs. 2005;65 Suppl 1:25-33.

Gonzalez Ayerbe JI, Hauser B, Salvatore S, Vandenplas Y. **Diagnosis and Management of Gastroesophageal Reflux Disease in Infants and Children**: from Guidelines to Clinical Practice. Pediatr Gastroenterol Hepatol Nutr. 2019 Mar;22(2):107-121.

Goodman SG, Clare R, Pieper KS, et al. Association of Proton Pump Inhibitor Use on Cardiovascular Outcomes With **Clopidogrel and Ticagrelor**: Insights From the Platelet Inhibition and Patient Outcomes Trial. (PLATO) Circulation. 2012 Feb 28;125(8):978-986.

Graham DY, Agrawal NM, Campbell DR, et al. NSAID-Associated Gastric Ulcer Prevention Study Group. Ulcer prevention in long-term users of nonsteroidal anti-inflammatory drugs: results of a double-blind, randomized, multicenter, active- and placebo-controlled study of **misoprostol vs lansoprazole**. Arch Intern Med. 2002 Jan 28;162(2):169-75.

Graham DY and Tansel A.**Interchageable use of proton pump inhibitors based on relative potency**. Clin Gastroenterol Hepatol 2017 Sep 27.

Gralnek IM, Barkun AN, Bardou M. **Management of acute bleeding from a peptic ulcer**. N Engl J Med. 2008 Aug 28;359(9):928-37.

Gralnek IM, Dumonceau JM, et al. Diagnosis & management of **nonvariceal upper gastrointestinal hemorrhage: European** Society of Gastrointestinal Endoscopy (**ESGE**) Guideline. Endoscopy. 2015 Oct;47(10):a1-a46.

Gralnek IM, Neeman Z, Strate LL. **Acute Lower Gastrointestinal Bleeding**. N Engl J Med. 2017 Mar 16;376(11):1054-1063.

Grant AM, Wileman SM, Ramsay CR, Mowat NA, Krukowski ZH, Heading RC, Thursz MR, Campbell MK; **REFLUX** Trial Group. Minimal access surgery compared with medical management for chronic gastro-

oesophageal reflux disease: UK collaborative randomised trial. BMJ. 2008 Dec 15;337:a2664. doi: 10.1136/bmj.a2664. At least up to 12 months after surgery, **laparoscopic fundoplication** significantly increased measures of health status in patients with GORD.

Grant AM, Cotton SC, Boachie C, et al. Minimal access **surgery compared with medical** management for gastro-oesophageal reflux disease: five year follow-up of a randomised controlled trial (**REFLUX**). BMJ 2013;346:f1908.

Grant AM, Boachie C, Cotton SC, et al. Clinical and economic evaluation of **laparoscopic surgery compared with medical** management for gastro-oesophageal reflux disease: 5-year follow-up of multicentre randomised trial (the **REFLUX** trial). Health Technol Assess. 2013 Jun;17(22):1-167.

Guillet R, et al.; National Institute of Child Health and Human Development Neonatal Research Network. Association of H2-blocker therapy and higher incidence of necrotizing **enterocolitis** in very low birth weight infants. Pediatrics. 2006 Feb;117(2):e137-42. Epub 2006 Jan 3.

Haastrup P, Paulsen MS, Begtrup LM, et al. Strategies for **discontinuation of proton pump inhibitors**: a systematic review. Fam Pract. 2014 Sep 5.

Hansen KE, Nieves JW, Nudurupati S, et al. **Dexlansoprazole and Esomeprazole Do Not Affect Bone Homeostasis** in Healthy Postmenopausal Women. Gastroenterology. 2018 Nov 13.

Harnik IG. **In the Clinic: Gastroesophageal Reflux Disease**. Ann Intern Med. 2015 Jul 7;163(1):ITC1.

Hashimoto R, Matsuda T, Chonan A. **Iron-deficiency anemia** caused by a proton pump inhibitor. Intern Med. 2014;53(20):2297-9.

Hata KW, Yi F. **Repeated Lower Gastrointestinal Bleeding**. JAMA Surg. 2017 Mar 15.

Health Canada **Aug/07** is advising consumers that it is currently reviewing new preliminary safety information regarding **serious cardiac events** in patients using Losec (omeprazole) and Nexium (esomeprazole), two prescription drugs used to treat acid-related stomach disorders. (**Feb 27, 2008** Health Canada Completes Safety Review of Losec (omeprazole) and Nexium (esomeprazole) OTTAWA - Further to its Information Update dated August 9, 2007, Health Canada is informing Canadians of the results of its review of safety information for Losec (omeprazole) and Nexium (esomeprazole), two prescription drugs used to treat conditions where a reduction of gastric acid secretion is required, such as ulcers and reflux. In Canada, omeprazole is also sold in generic form as Apo-omeprazole, Ratio-omeprazole and Sandoz-omeprazole. Esomeprazole is only sold under the trade name Nexium. Nexium (esomeprazole) Based on its review of the data available at this time, Health Canada has concluded that there is no evidence supporting an increased cardiovascular risk associated with the long-term use of esomeprazole. The Department will continue to monitor safety issues related to esomeprazole by conducting further analysis of ongoing long-term studies as this data becomes available. Losec (omeprazole) After a thorough analysis, based on the data available to us at this time, we are unable to definitively conclude if there is a potential for increased cardiovascular risk associated with the long-term use of omeprazole. We will continue to evaluate should more conclusive data become available, and will advise Canadians if any further regulatory actions are required.)

Health Canada Aug/09 **Plavix & PPI Interaction** http://www.hc-sc.gc.ca/dhp-mps/alt_formats/pdf/medeff/advisories-avis/prof/2009/plavix_hpc-cps-eng.pdf

Health Canada Feb/12 is informing Canadians of a possible association between the use of prescription stomach antacids known as proton pump inhibitors (PPIs) and an increased risk of **Clostridium difficile**-associated diarrhea (CDAD).

Health Canada Oct/12 is informing Canadians that the labelling for **methotrexate and Proton Pump Inhibitors** is being updated to include information on a potential interaction between these products.

Health Canada Apr/13 is informing Canadians and Canadian health care professionals of the potential risk of **bone fractures** associated with the use of drugs known as **proton pump inhibitors**.

Heidelbaugh JJ, Inadomi JM. Magnitude and Economic Impact of **Inappropriate** Use of **Stress Ulcer Prophylaxis** in Non-ICU Hospitalized Patients. Am J Gastroenterol. 2006 Oct;101(10):2200-5. Epub 2006 Sep 4.

Heidelbaugh JJ, Goldberg KL, Inadomi JM.**Overutilization of proton pump inhibitors**: a review of cost-effectiveness and risk in PPI. Am J Gastroenterol 2009;104:S27-S32.

Herzig Shoshana J.; Vaughn Byron P.; Howell Michael D.; et al. Acid-Suppressive Medication Use and the **Risk for Nosocomial Gastrointestinal Tract Bleeding**. *Arch Intern Med*. 2011;0(2011):archinternmed.2011.14.

Herzig SJ, Rothberg MB, Feinbloom DB, et al. Risk Factors for **Nosocomial Gastrointestinal Bleeding** and Use of Acid-Suppressive Medication in Non-Critically Ill Patients. J Gen Intern Med. 2013 Jan 5.

Herzig SJ, Doughty C, Lahoti S, et al. **Acid-Suppressive** Medication **Use in Acute Stroke and Hospital-Acquired Pneumonia**. Ann Neurol. 2014 Aug 28.

Hinson AM, Wilkerson BM, et al. **Hyperparathyroidism Associated with Long-Term Proton Pump Inhibitors** Independent of Concurrent Bisphosphonate Therapy in Elderly Adults. J Am Geriatr Soc. 2015 Sep 29.

Hirano I, Richter JE; Practice Parameters Committee of the American College of Gastroenterology. ACG practice guidelines: **esophageal reflux testing**. Am J Gastroenterol. 2007 Mar;102(3):668-85.

Ho PM et al. Risk of adverse outcomes associated with concomitant use of **clopidogrel** and proton pump inhibitors following acute coronary syndrome. JAMA 2009 Mar 4; 301:937.

Ho T, Dukhovny D, Zupancic JA, et al. **Choosing Wisely in Newborn Medicine**: Five Opportunities to Increase Value. Pediatrics. 2015 Jul 20. (**avoid routine use of antireflux meds for symptomatic GERD**)

Holtmann G, et al. A placebo-controlled trial of **itopride** in functional dyspepsia. N Engl J Med. 2006 Feb 23;354(8):832-40. (InfoPOEMs: Itopride was somewhat effective for functional dyspepsia, with a number needed to treat of 6 for global improvement but only a small 2-point benefit on a 40-point symptom scale (essentially, an improvement from 12 to 8 with placebo and from 12 to 6 with itopride). The drug appears to be safe on the basis of this small, short study. (LOE = 1b))

Hong MT, Monye LC, Seifert CF. **Acid Suppressive Therapy for Stress Ulcer Prophylaxis** in Noncritically Ill Patients. Ann Pharmacother. 2015 Sep;49(9):1004-8.

Hooper L, Brown TJ, Elliott R, et al. The effectiveness of five strategies for the prevention of gastrointestinal toxicity induced by non-steroidal anti-inflammatory drugs: systematic review. BMJ. 2004 Oct 23;329(7472):948. Epub 2004 Oct 8. CONCLUSIONS: Misoprostol, COX-2 specific and selective NSAIDs, and probably proton pump inhibitors significantly reduce the risk of symptomatic ulcers, and misoprostol and probably COX-2 specifics significantly reduce the risk of serious gastrointestinal complications, but data quality is low. More data on H2 receptor antagonists and proton pump inhibitors are needed, as is better reporting of rare but important outcomes.

Hsu PI, Lai KH, Liu CP. **Esomeprazole with clopidogrel reduces peptic ulcer recurrence, compared with clopidogrel alone**, in patients with atherosclerosis. Gastroenterology. 2011 Mar;140(3):791-8.

Hsu PI, Wu DC, Tsay FW, et al. **Histamine-2 Receptor Antagonist Cannot Prevent Recurrent Peptic Ulcers in Patients With Atherosclerotic Diseases Who Receive Platelet ADP Receptor Antagonist Monotherapy**: Randomized-Controlled, Double-Blind, and Double-Dummy Trial. (**famotidine** 40mg daily) Am J Gastroenterol. 2016 Dec 6.

Huang J, Cao Y, Liao C, Wu L, Gao F. Effect of histamine-2-receptor antagonists versus sucralfate on **stress ulcer prophylaxis** in mechanically ventilated patients: a meta-analysis of 10 randomized controlled trials. Crit Care. 2010;14(5):R194. Epub 2010 Oct 29.

Hudson N, Taha AS, Russell RI, et al. **Famotidine** for healing and maintenance in nonsteroidal anti-inflammatory drug-associated gastroduodenal ulceration. Gastroenterology. 1997 Jun;112(6):1817-22.

Hulot JS, Collet JP, Silvain J, et al. Cardiovascular risk in **clopidogrel-treated** patients according to **cytochrome P450 2C19*2 loss-of-function** allele or proton pump inhibitor co-administration. A systematic meta-analysis. J Am Coll Cardiol 2010; 56:134-143.

Hungin APS, Molloy-Bland M, Scarpignato C. Revisiting Montreal: New Insights into Symptoms and Their Causes, and Implications for the Future of GERD. Am J Gastroenterol. 2018 Oct 15.

Hunt R, Fallone C, Veldhuyzan van Zanten S, et al. CHSG 2004 participants. Canadian Helicobacter Study Group Consensus Conference: Update on the management of Helicobacter pylori--an evidence-based evaluation of six topics relevant to clinical outcomes in patients evaluated for H pylori infection. Can J Gastroenterol. 2004 Sep;18(9):547-54.

Hvid-Jensen F, Pedersen L, Drewes AM, et al. Incidence of **adenocarcinoma among patients with Barrett's esophagus**. N Engl J Med 2011;365:1375-83. (Risk only 0.12%)

Hawwa AF, Westwood PM, Collier PS, et al. Prophylactic ranitidine treatment in **critically ill children** - a population pharmacokinetic study. Br J Clin Pharmacol. 2012 Sep 28

Jacobson BC, Somers SC, Fuchs CS, Kelly CP, Camargo CA Jr. **Body-mass index** and symptoms of gastroesophageal reflux in women. N Engl J Med. 2006 Jun 1;354(22):2340-8.

Jacobson BC, Moy B, Colditz GA, Fuchs CS. **Postmenopausal hormone** use & symptoms of gastroesophageal reflux. Arch Intern Med. 2008 Sep 8;168(16):1798-804. Postmenopausal use of estrogens, selective estrogen receptor modulators, or OTC hormone preparations is associated with a greater likelihood of symptoms of GERD.

Janarthanan S et al. **Clostridium difficile**-associated diarrhea **and proton pump inhibitor** therapy: A meta-analysis. Am J Gastroenterol 2012 Jul; 107:1001.

Jankowski J, Barr H, Wang K, Delaney B. Diagnosis and management of **Barrett's oesophagus**. BMJ. 2010 Sep 10;341:c4551. doi: 10.1136/bmj.c4551.

Jankowski JAZ, de Caestecker J, Love SB, et al. **Esomeprazole and aspirin in Barrett's esophagus (AspECT)**: a randomised factorial trial. Lancet. 2018 Jul 26.

Jarbol DE, et al. Proton pump inhibitor or testing for **Helicobacter pylori** as the first step for patients presenting with dyspepsia? A cluster-randomized trial. Am J Gastroenterol. 2006 Jun;101(6):1200-8. (InfoPOEMs:

A test-and-treat strategy is the most cost-effective approach to dyspepsia in the primary care setting. (LOE = 1b))
Jaspers Focks J, Brouwer MA, van Oijen MG, et al. Concomitant use of **clopidogrel and proton pump inhibitors**: impact on platelet function and clinical outcome- a systematic review. Heart. 2012 Jul 31.
Jaynes M, Kumar AB. The **risks of long-term use of proton pump inhibitors**: a critical review. Ther Adv Drug Saf. 2018 Nov 19;10:2042098618809927.
Jeyalingam T, Grover SC. Eosinophilic esophagitis. CMAJ. 2018 Apr 30;190(17):E542.
Jian Z, Li H, Race NS, et al. Is the Era of **intravenous proton pump inhibitors coming to an end** in patients with bleeding peptic ulcers? meta-analysis of the published literature. Br J Clin Pharmacol. 2015 Dec 18.
Johansen ME, Huerta TR, Richardson CR. National use of proton pump inhibitors from 2007 to 2011. JAMA Intern Med. 2014 Nov 1;174(11):1856-8.
Johnson DA, Katz PO, Armstrong D, et al. The **Safety of Appropriate Use of Over-the-Counter Proton Pump Inhibitors**: An Evidence-Based Review and Delphi Consensus. Drugs. 2017 Apr;77(5):547-561.
Jones EK, Mingioni N, Lee JB. Widespread **Scaly Eruption** in a Patient With Multiple Comorbidities. (**pantoprazole**) JAMA. 2015 Oct 27;314(16):1740-1741.
Jones EK, Mingioni N, Lee JB. **Widespread Scaly Eruption** in a Patient With Multiple Comorbidities (**pantoprazole induced**). JAMA. 2015 Oct 27;314(16):1740-1.
Jones MG, Tsega S, Cho HJ. Inappropriate Prescription of Proton Pump Inhibitors in the **Setting of Steroid Use**: A Teachable Moment. JAMA Intern Med. 2016 Apr 11.
Jones R, Charlton J, Latinovic R, Gulliford MC. **Alarm symptoms** and identification of non-cancer diagnoses in primary care: cohort study. BMJ. 2009 Aug 13;339:b3094. doi: 10.1136/bmj.b3094. Clinically relevant diagnoses are made in a high proportion of patients presenting with alarm symptoms. For every four to seven patients evaluated for haematuria, haemoptysis, dysphagia, or rectal bleeding, relevant diagnoses will be identified in one patient within 90 days.
Jordakieva G, Kundi M, Untersmayr E, et al. Country-wide medical records infer **increased allergy risk of gastric acid inhibition**. Nat Commun. 2019 Jul 30;10(1):3298.
Juurlink DN, Gomes T, Ko D, et al. A population-based study of the drug interaction between **proton pump inhibitors and clopidogrel**. CMAJ 2009;180(7). DOI:10.1503/cmaj.082001.
Kahrilas PJ, Shaheen NJ, Vaezi MF; American Gastroenterological Association Institute; Clinical Practice and Quality Management Committee. AGA Institute technical review on the management of **gastroesophageal reflux disease**. Gastroenterology. 2008 Oct;135(4):1392-1413, 1413.e1-5. Epub 2008 Sep 16.http://download.journals.elsevierhealth.com/pdfs/journals/0016-5085/PIIS0016508508016065.pdf
Kahrilas PJ. Clinical practice. **Gastroesophageal reflux disease**. N Engl J Med. 2008 Oct 16;359(16):1700-7.
Kahrilas PJ, Howden CW, Hughes N. Response of **regurgitation** to proton pump inhibitor therapy in clinical trials of gastroesophageal reflux disease. Am J Gastroenterol. 2011 Aug;106(8):1419-25.
Kahrilas PJ, Howden CW, Hughes N, et al. Response of **chronic cough to acid-suppressive therapy** in patients with gastroesophageal reflux disease. Chest. 2013 Mar;143(3):605-12.
Kahrilas PJ, Altman KW, Chang AB, et al; CHEST Expert Cough Panel*. **Chronic Cough due to Gastroesophageal Reflux** in Adults: CHEST Guideline and Expert Panel Report. Chest. 2016 Sep 7.
Kaltenbach T, Crockett S, Gerson LB. Are **lifestyle** measures effective in patients with gastroesophageal reflux disease? An evidence-based approach. Arch Intern Med. 2006 May 8;166(9):965-71. Neither tobacco nor alcohol cessation was associated with improvement in esophageal pH profiles or symptoms (evidence B). Head of bed elevation and left lateral decubitus position improved the overall time that the esophageal pH was less than 4.0 (evidence B). Weight loss improved pH profiles and symptoms (evidence B). Weight loss and head of bed elevation are effective lifestyle interventions for GERD. There is no evidence supporting an improvement in GERD measures after cessation of tobacco, alcohol, or other dietary interventions. (InfoPOEMs: Decreasing gastroesophageal reflux disease (GERD) symptoms with lifestyle changes requires an empirical approach; the research literature gives very little guidance regarding nondrug approaches. Neither smoking cessation, alcohol avoidance, nor any food avoidances have been shown to make, on average, a difference in symptoms, although existing studies are small and of poor quality. Elevating the head of the bed may be effective. Weight loss may also be effective. Of course, if patients find something that works, encourage them to continue doing it. (LOE = 3a-))
Kandil TS, Mousa AA, El-Gendy AA, Abbas AM. The potential therapeutic effect of **melatonin** in Gastro-Esophageal Reflux Disease. BMC Gastroenterol. 2010 Jan 18;10:7.
Kapoor N, Bassi A, Sturgess R, Bodger K. Predictive value of alarm features in a rapid access upper gastrointestinal cancer service. Gut 2005; 54:40-5.
Katz PO, Gerson LB, Vela MF. **ACG**-Guidelines for the diagnosis and management of **gastroesophageal reflux disease (GERD).** Am J Gastroenterol. 2012 Mar;108(3):308-28.
Katz PO, Le Moigne A, Pollack C. Analysis of **2-Week Data** from Two Randomized, Controlled Trials Conducted in Subjects with **Frequent Heartburn** Treated with **Esomeprazole** 20 mg. Clin Ther. 2017 Apr 18.
Kekilli M, Tanoglu A, Ocal S, et al. **Rabeprazole-Induced Tinnitus**. Ann Pharmacother. 2014 Jun 10;48(7):943.
Khan M, Santana J, Donnellan C, Preston C, Moayyedi P. Medical treatments in the short term management of **reflux oesophagitis**. Cochrane Database Syst Rev. 2007 Apr 18;(2):CD003244. PPI therapy is the most effective therapy in oesophagitis but H2RA therapy is also superior to placebo. There is a paucity of evidence on prokinetic therapy but no evidence that it is superior to placebo.
Khouri C, Revol B, Cracowski JL, et al. **Proton pump inhibitors and Raynaud's phenomenon**: is there a link? Br J Clin Pharmacol. 2018 Jul 12.
Kiljander TO, et al. Effects of esomeprazole 40 mg twice daily on **asthma**: a randomized placebo-controlled trial. Am J Respir Crit Care Med. 2006 May 15;173(10):1091-7. Epub 2005 Dec 15. (InfoPOEMs: In this study, esomeprazole (Nexium) was no better than placebo in improving peak expiratory flow, asthma symptoms, or quality of life in patients with stable asthma. Furthermore, esomeprazole was no better than placebo in patients with reflux, either. (LOE = 2b-))
Kiljander TO, et al. Effects of esomeprazole 40 mg twice daily on **asthma**: a randomized placebo-controlled trial. Am J Respir Crit Care Med. 2006 May 15;173(10):1091-7. Epub 2005 Dec 15. Esomeprazole improved PEF in subjects with asthma who presented with both GERD and nocturnal respiratory symptoms (NOC). In subjects without both GERD and NOC, no improvement could be detected. N=770 16weeks
Kinoshita Y, Hongo M. Efficacy of **Twice-Daily Rabeprazole** for **Reflux Esophagitis** Patients Refractory to Standard Once-Daily Administration of PPI: The Japan-Based TWICE Study. Am J Gastroenterol. 2012Mar20.
Klassen S, Krepinsky JC, Prebtani AP. **Pantoprazole-induced acute interstitial nephritis**. CMAJ. 2013 Jan 8;185(1):56-9.
Klatte DCF et al. Association between **proton pump inhibitor use and risk of progression of chronic kidney disease**. Gastroenterology 2017 Jun 2.
Klok RM, Postma MJ, van Hout BA, Brouwers JR. Meta-analysis: comparing the efficacy of proton pump inhibitors in short-term use. Aliment Pharmacol Ther. 2003 May 15;17(10):1237-45. (InfoPOEMs: There is no significant difference between equivalent doses of proton pump inhibitors, including equivalent doses of esomeprazole (Nexium) and omeprazole (Prilosec OTC). The decision to choose one over another should be based first on cost and second on individual patient response. (LOE = 1a))
Koek GH, Sifrim D, Lerut T, et al. Effect of the GABA(B) agonist **baclofen** in patients with symptoms and duodeno-gastro-oesophageal reflux refractory to proton pump inhibitors. Gut. 2003 Oct;52(10):1397-402.
Krag M, Marker S, Perner A, et al. **Pantoprazole in Patients at Risk for Gastrointestinal Bleeding in the ICU**. (SUP-ICU) N Engl J Med. 2018 Oct 24.
Krishnan K, et al. Increased Risk for Persistent Intestinal Metaplasia in Patients With Barrett's Esophagus and Uncontrolled Reflux Exposure Before **Radiofrequency Ablation**. Gastroenterology. 2012 Sep;143(3):576-81.
Kurlander JE, Kolbe M, Scheiman JM,et al. The Right Idea for the Wrong Patient: Results of a **National Survey on Stopping PPIs**. Clin Gastroenterol Hepatol. 2017 Apr 6.
Kvistholm Jensen A, Simonsen J, Ethelberg S. Use of **proton pump inhibitors and the risk of listeriosis**. A nationwide registry-based case-control study. Clin Infect Dis. 2016 Dec 24.
Kwok CS, Arthur AK, Anibueze CI, et al. Risk of **Clostridium difficile** Infection With Acid Suppressing Drugs and Antibiotics: Meta-Analysis. Am J Gastroenterol. 2012 Apr 24.
Kwok TC, Ojha S, Dorling J. **Feed thickener for infants** up to six months of age with gastro-oesophageal reflux. Cochrane Database Syst Rev. 2017 Dec 5;12:CD003211. Gastro-oesophageal reflux is a physiological self resolving phenomenon in infants that does not necessarily require any treatment. However, we found moderate-certainty evidence that feed thickeners should be considered if regurgitation symptoms persist in term bottle-fed infants. The reduction of two episodes of regurgitation per day is likely to be of clinical significance to caregivers. Due to the limited information available, we were unable to assess the use of feed thickeners in infants who are breastfeeding or preterm nor could we conclude which type of feed thickener is superior.
Lai KC, Lam SK, Chu KM, et al. **Lansoprazole** for the prevention of recurrences of ulcer complications from long-term **low-dose aspirin** use. N Engl J Med. 2002 Jun 27;346(26):2033-8.
Lai KC, Chu KM, Hui WM, et al. Celecoxib compared with lansoprazole and naproxen to prevent gastrointestinal ulcer complications. Am J Med. 2005 Nov;118(11):1271-8. CONCLUSIONS: Celecoxib was as effective as lansoprazole co-therapy in the prevention of recurrences of ulcer complications in subjects with a history of NSAID-related complicated peptic ulcers. However, celecoxib, similar to lansoprazole co-therapy, was still associated with a significant proportion of ulcer complication recurrences. In addition, more patients receiving celecoxib developed dyspepsia than patients receiving lansoprazole and naproxen.
Lai T, Wu M, Liu J, et al. **Acidsuppressive drug use during pregnancy** and the **risk of childhood asthma**: a meta-analysis. Pediatrics. 2018;141(2):e20170889
Laine L, Shah A, Bemanian S. Intragastric pH With **Oral vs Intravenous** Bolus Plus Infusion Proton Pump Inhibitor Therapy in Patients With Bleeding Ulcers. Gastroenterology. 2008 Mar 10. [Epub ahead of print]

Frequent oral PPI may be able to replace the currently recommended intravenous bolus plus infusion PPI {intravenous lansoprazole (90-mg bolus followed by 9-mg/h infusion) or oral lansoprazole (120-mg bolus followed by 30 mg every 3 hours)}therapy in patients with bleeding ulcers, although the possibility that intravenous PPIs are superior cannot be definitively excluded given our relatively wide confidence intervals. Intravenous PPI provides more rapid increase in pH, reaching mean pH of 6 approximately 1 hour sooner than oral PPI.

Laine L. Proton pump inhibitors and bone fractures? Am J Gastroenterol 2009;104:S21-S26.

Laine L, Kivitz AJ, et al. Double-blind randomized trials of single-tablet **ibuprofen/high-dose famotidine vs. ibuprofen** alone for reduction of gastric and duodenal ulcers. Am J Gastroenterol. 2012 Mar;107(3):379-86.

Laine L, Yang H, Chang SC, Datto C. Trends for Incidence of **Hospitalization and Death Due to GI Complications** in the United States From 2001 to 2009. Am J Gastroenterol. 2012 Aug;107(8):1190-5.

Laine L, Jensen DM. **Management of patients with ulcer bleeding**. (ACG) Am J Gastroenterol 2012 Mar;107(3):345-60.

Laine L.**NSAID-associated gastrointestinal bleeding**: Assessing the role of concomitant medications. Gastroenterology 2014 Oct; 147:730.

Laine L. **Upper Gastrointestinal Bleeding Due to a Peptic Ulcer**. N Engl J Med. 2016 Jun 16;374(24):2367-2376.

Lam JR, Schneider JL, Zhao W, et al. Proton pump inhibitor and histamine 2 receptor antagonist use and **vitamin B12 deficiency**. JAMA. 2013 Dec 11;310(22):2435-42.

Lam JR et al. **Proton pump inhibitor and histamine-2 receptor antagonist use** and **iron deficiency**.Gastroenterology 2016 Nov 24.

Lambert AA, Lam JO, Paik JJ, et al. Risk of **community-acquired pneumonia** with outpatient proton-pump inhibitor therapy: a systematic review and meta-analysis. PLoS One. 2015 Jun 4;10(6):e0128004.

Lanas A, Chan FK. **Peptic ulcer disease**. Lancet. 2017 Feb 23.

Landi SN, et al. No Increase in Risk of Acute **Myocardial Infarction** in Privately Insured Adults Prescribed Proton Pump Inhibitors vs Histamine-2 Receptor Antagonists (2002-2014). Gastroenterology. 2018 Mar;154(4):861-873.

Langan, RC, Goodgred AJ, **Vitamin B12 Deficiency**: Recognition and Management. Am Fam Physician. 2017;96(6):384-389.

Langtry HD, Wilde MI. Lansoprazole: An update of its pharmacological properties and clinical efficacy in the management of acid-related disorders. Drugs 1997;54(3):473-500.

Lanza FL, Chan FK, Quigley EM; Practice Parameters Committee of the **American College of Gastroenterology. Guidelines** for **prevention of NSAID-related ulcer complications**. Am J Gastroenterol. 2009 Mar;104(3):728-38. Epub 2009 Feb 24.

Lau JY, Sung JJ, Lee KK, et al. Effect of intravenous omeprazole on **recurrent bleeding after endoscopic treatment** of bleeding peptic ulcers.N Engl J Med. 2000 Aug 3;343(5):310-6.

Lau JY, Leung WK, Wu JC, et al. **Omeprazole before endoscopy** in patients with gastrointestinal bleeding. N Engl J Med. 2007 Apr 19;356(16):1631-40. Infusion of high-dose omeprazole before endoscopy accelerated the resolution of signs of bleeding in ulcers and reduced the need for endoscopic therapy. (InfoPOEMs: An overnight infusion of omeprazole prior to endoscopy in patients with acute upper GI hemorrhage reduces the need for intervention and speeds discharge from the hospital. (LOE = 1b))

Lau JY, Barkun A, Fan DM, et al. Challenges in the management of **acute peptic ulcer bleeding**. Lancet. 2013 Jun 8;381(9882):2033-43.

Law R, Maltepe C, Bozzo P, Einarson A. Treatment of **heartburn and acid reflux** associated with nausea and vomiting during **pregnancy**. Can Fam Physician. 2010 Feb;56(2):143-4.

Lebwohl B, Spechler SJ, Wang TC, et al. Use of proton pump inhibitors and subsequent **risk of celiac disease**. Dig Liver Dis. 2014 Jan;46(1):36-40.

Lee C, Lo A, Ubhi K, et al. **Outcome after Discontinuation of Proton Pump Inhibitors** at a Residential Care Site: Quality Improvement Project. Can J Hosp Pharm. 2017 May-Jun;70(3):215-223. Epub 2017 Jun 30.

Lee SJ, Shin DH, Hwang HJ et al. **Bleeding Risk and Major Adverse Events in Patients With Previous Ulcer on Oral Anticoagulation** Therapy. Am J Cardiol. 2012 Apr 18.

Lee TJ, Fennerty MB, Howden CW. Systematic review: Is there excessive use of proton pump inhibitors in gastro-oesophageal reflux disease? Aliment Pharmacol Ther. 2004 Dec;20(11-12):1241-51.

Leontiadis GI, Sharma VK, Dr. Howden CW. Proton pump inhibitor for **acute peptic ulcer bleeding**. The Cochrane Database of Systematic Reviews 2006, Issue 1.

Leung WK, et al. Initial treatment with lansoprazole in young dyspeptic patients with negative urea breath test result: a randomized controlled trial with 12-month follow-up. Am J Gastroenterol. 2007 Jul;102(7):1483-8. Lansoprazole is not effective in the initial management of young dyspeptic patients without H. pylori infection.

Li L,Geraghty OC, Mehta Z, Rothwell PM, on behalf of the Oxford Vascular Study. **Age-specific risks, severity, time course, and outcome of bleeding on long-term antiplatelet treatment after vascular events**: a population-based cohort study. Lancet 2017; online June 5. (consider PPI use with aspirin in secondary prevention)

Li Y, Fang M, Niu L, et al. Associations among **gastroesophageal reflux disease, mental disorders, sleep and chronic temporomandibular disorder**: a case-control study. CMAJ. 2019 Aug 19;191(33):E909-E915.

Lightdale JR, Gremse DA; Section on Gastroenterology, Hepatology and Nutrition. **Gastroesophageal Reflux: Management Guidance for the Pediatrician**. Pediatrics. 2013 Apr 29.

Lilly CM, Aljawadi M, Badawi O, et al. Comparative Effectiveness of **Proton Pump Inhibitors vs. Histamine type-2 receptors** blockers for preventing Clinically Important Gastrointestinal Bleeding during Intensive Care: A population-based study. Chest. 2018 May 29.

Lima JJ, Lang JE, Mougey EB, et al. Association of **CYP2C19 Polymorphisms and Lansoprazole**-Associated Respiratory Adverse Effects in Children. J Pediatr. 2013 Sep;163(3):686-91.

Lin KJ, Hernández-Díaz S, García Rodríguez LA. **Acid suppressants reduce risk of gastrointestinal bleeding in patients on antithrombotic** or anti-inflammatory therapy. Gastroenterology. 2011 Jul;141(1):71-9.

Littman J, Halil R. Potential effects of **rational prescribing** on national **health care spending**: More than half a billion dollars in annual savings (escitalopram, **esomeprazole**, perindoril). Can Fam Physician. 2016 Mar;62(3):235-44.

Littner MR, Leung FW, et al. **Lansoprazole Asthma** Study Group. Effects of 24 weeks of lansoprazole therapy on asthma symptoms, exacerbations, quality of life, and pulmonary function in adult asthmatic patients with acid reflux symptoms. Chest. 2005 Sep;128(3):1128-35.

Liu CP, Chen WC, Lai KH, et al. **Esomeprazole Alone Compared with Esomeprazole Plus Aspirin** for the Treatment of Aspirin-Related Peptic Ulcers. Am J Gastroenterol. 2012 Apr 17.

Liu X, Wong A, Kadri SR, et al. Gastro-Esophageal Reflux Disease Symptoms and Demographic Factors as a **Pre-Screening Tool for Barrett's Esophagus**. PLoS One. 2014 Apr 15;9(4):e94163.

Lo EA, Wilby KJ, Ensom MH. Use of **Proton Pump Inhibitors in the Management of Gastroesophageal Varices**: A Systematic Review. Ann Pharmacother. 2015 Feb;49(2):207-219.

Lødrup AB, Reimer C, Bytzer P. Systematic review: symptoms of **rebound acid hypersecretion following proton pump inhibitor treatment**. Scand J Gastroenterol. 2013 May;48(5):515-22.

Long AN, Atwell CL, Yoo W, Solomon SS. **Vitamin B(12) deficiency** associated with concomitant **metformin and proton pump inhibitor** use. Diabetes Care. 2012 Dec;35(12):e84.

Lowe DO, Mamdani MM, Kopp A, Low DE, Juurlink DN. Proton pump inhibitors and hospitalization for **Clostridium difficile**-associated disease: a population-based study. Clin Infect Dis. 2006 Nov 15;43(10):1272-6. Epub 2006 Oct 13. Among community-dwelling older patients, PPI use is not a risk factor for hospitalization with CDAD.

Loyd R, McClennan DA. Update on the Evaluation and Management of **Functional Dyspepsia**. Am Fam Physician. 2011 Mar 1;83(5):547-552.

Lucendo AJ, Molina-Infante J, Arias Á, et al. **Guidelines on eosinophilic esophagitis**: evidence-based statements and recommendations for diagnosis and management in children and adults. United European Gastroenterol J. 2017 Apr;5(3):335-358.

Luk CP, Parsons R, Lee YP, Hughes JD. Proton pump inhibitor-associated **hypomagnesemia**: what do FDA data tell us? Ann Pharmacother. 2013 Jun;47(6):773-80.

Lundell L, et al. Continued (5-year) followup of a randomized clinical study comparing **antireflux surgery and omeprazole** in gastroesophageal reflux disease. J Am Coll Surg. 2001 Feb;192(2):172-9; discussion 179-81.

Lundell L, Attwood S, Ell C, Fiocca R, Galmiche JP, Hatlebakk J, Lind T, et al. **LOTUS** trial collaborators. Comparing laparoscopic antireflux surgery with esomeprazole in the management of patients with chronic gastro-oesophageal reflux disease: a 3-year interim analysis of the LOTUS trial. Gut. 2008 Sep;57(9):1207-13. Epub 2008 May 9. Over the first 3 years of this long-term study, both laparoscopic total fundoplication and continuous ESO treatment were similarly effective and well-tolerated therapeutic strategies for providing effective control of GORD.

Lundell L, Miettinen P, Myrvold HE, et al. **Nordic GERD** study group. Comparison of outcomes **12 years** after anti-reflux surgery or omeprazole maintenance therapy for reflux esophagitis. Clin Gastroenterol Hepatol. 2009 May 30. [Epub ahead of print] As long-term therapeutic strategies for chronic GERD, surgery and omeprazole are effective and well-tolerated. Anti-reflux surgery is superior to omeprazole in controlling overall disease manifestations but post-fundoplication complaints continue after surgery.

Luo JC, Huang KW, Leu HB, et al. Randomised clinical trial: **rabeprazole plus aspirin is not inferior to rabeprazole plus clopidogrel** for the healing of aspirin-related peptic ulcer.

Aliment Pharmacol Ther. 2011 Sep;34(5):519-25
Maclaren R, et al. **Histamine-2 Receptor Antagonists vs Proton Pump Inhibitors** on Gastrointestinal Tract Hemorrhage and Infectious Complications in the **Intensive Care Unit**. JAMA Intern Med. 2014 Feb 17.
Maggio M, Corsonello A, Ceda GP, et al. Proton pump inhibitors and risk of **1-year mortality and rehospitalization** in older patients discharged from acute care hospitals. online March 4, 2013. JAMA Intern Med.
Mahadevan U, Kane S. AGA-**American gastroenterological association** institute technical review on the use of gastrointestinal medications in **pregnancy**. Gastroenterology. 2006 Jul;131(1):283-311. http://download.journals.elsevierhealth.com/pdfs/journals/0016-5085/PIIS001650850600864X.pdf
Mahon D, et al. Randomized clinical trial of **laparoscopic Nissen fundoplication compared with proton-pump inhibitors** for treatment of chronic gastro-oesophageal reflux. Br J Surg. 2005 Jun;92(6):695-9.
Malchodi L, Wagner K, Susi A, et al. **Early acid suppression therapy exposure and fracture** in young children. Pediatrics. 2019;144(1): e20182625
Malhotra K, Katsanos AH, Bilal M, et al.**Cerebrovascular Outcomes** With Proton Pump Inhibitors and Thienopyridines: A Systematic Review and Meta-Analysis. Stroke. 2018 Feb;49(2):312-318.
Moayyedi P, Eikelboom JW, Bosch J, et al. **Pantoprazole to Prevent Gastroduodenal Events** in Patients Receiving Rivaroxaban and/or Aspirin in a Randomized, Double-Blind, Placebo-Controlled Trial. Gastroenterology. 2019 May 2.
Maret-Ouda J, Brusselaers N, Lagergren J. What is the **most effective treatment for severe gastro-oesophageal reflux disease**? BMJ. 2015 Jun 24;350:h3169.
Maret-Ouda J, Konings P, Lagergren J, et al. **Antireflux Surgery and Risk of Esophageal Adenocarcinoma**: A Systematic Review and Meta-analysis. Ann Surg. 2015 Oct 22.
Maret-Ouda J, Yanes M, Konings P, et al. **Mortality from laparoscopic antireflux surgery** in a nationwide cohort of the working-age population. Br J Surg. 2016 Mar 21
Maret-Ouda J, Wahlin K, El-Serag HB, Lagergren J. Association between **laparoscopic antireflux surgery and recurrence of gastroesophageal reflux**. JAMA. doi:10.1001/jama .2017.10981
Maret-Ouda J, Wahlin K, Artama M, et al. Risk of **Esophageal Adenocarcinoma After Antireflux Surgery in Patients** With Gastroesophageal Reflux Disease in the Nordic Countries. JAMA Oncol. 2018 Nov 1;4(11):1576-1582.
Marmo R, Rotondano G, Piscopo R, et al. Combination of age and sex improves the ability to predict upper gastrointestinal malignancy in patients with uncomplicated dyspepsia: a prospective multicentre database study. Am J Gastroenterol 2005; 100:784-91. (InfoPOEMs: A cutoff age of over 35 years old for men and 56 years old for women would detect more upper gastrointestinal cancers among patients with uncomplicated dyspepsia than a single cutoff of 45 years for both sexes. Presumably the cost of more endoscopies among younger men would be balanced by the need to do fewer among women aged 45 to 56 years. However, whether this sort of differential sex-based screening is politically possible is another matter. (LOE = 1b))
Martin FC et al. Systematic review with meta-analysis: **Fundic gland polyps and proton pump inhibitors**.Aliment Pharmacol Ther 2016 Sep 15.
Martín Merino E, Johansson S, Nagy P, García Rodríguez LA. Effect of Baseline **Gastrointestinal Risk and Use of Proton Pump Inhibitors** on Frequency of **Discontinuation of Aspirin** for Secondary Cardiovascular Prevention in United Kingdom Primary Care. Am J Cardiol. 2013 Jul 4.
Masclee GMC et al. Risk of upper gastrointestinal **bleeding from different drug combinations**. Gastroenterology 2014 Oct; 147:784. (http://dx.doi.org/10.1053/j.gastro.2014.06.007)
Masclee GM, Coloma PM, Kuipers EJ, et al. Increased risk of **microscopic colitis** with use of **proton pump inhibitors and non-steroidal anti-inflammatory drugs**. Am J Gastroenterol. 2015 May;110(5):749-59.
Mastronarde JG, Anthonisen NR, Castro M, et al. Efficacy of **esomeprazole** for treatment of **poorly controlled asthma**. (**SARA**) N Engl J Med. 2009 Apr 9;360(15):1487-99. Despite a high prevalence of asymptomatic gastroesophageal reflux among patients with poorly controlled asthma, treatment with proton-pump inhibitors does not improve asthma control. Asymptomatic gastroesophageal reflux is not a likely cause of poorly controlled asthma.
Mayor S. Proton pump inhibitors match **surgery** in gastroesophageal reflux. BMJ. 2006 Jan 7;332(7532):10.
McDonald EG, Milligan J, Frenette C, et al. Continuous Proton Pump Inhibitor Therapy and the Associated Risk of Recurrent **Clostridium difficile** Infection. JAMA Intern Med. 2015 Mar 2.
McCaleb RV, Gandhi AS, Clark SM, et al. Clinical Outcomes of **Acid Suppressive Therapy Use in Hematology/Oncology Patients** at an Academic Medical Center. Ann Pharmacother. 2016 Jul;50(7):541-7.
Melinder C et al. Decreased **stress resilience** in young men significantly increases the risk of subsequent peptic ulcer disease -a prospective study of 233 093 men in Sweden. Aliment Pharmacol Ther 2015 May; 41:1005.
Melloni C, Washam JB, Jones WS, et al. Conflicting results between randomized trials and observational studies on the impact of **proton pump inhibitors** on cardiovascular events when coadministered with **dual antiplatelet therapy**. *Circ Cardiovasc Qual Outcomes* 2015; 8: 47-55.
Messori A, Trippoli S, Vaiani M, et al. Bleeding and pneumonia in intensive care patients given ranitidine and sucralfate for prevention of **stress ulcer: meta-analysis** of randomised controlled trials. BMJ 2000;321:1103.
Metz DC, Inadomi JM, Howden CW, van Zanten SJ, Bytzer P. **On-demand therapy** for gastroesophageal reflux disease. Am J Gastroenterol. 2007 Mar;102(3):642-53. The available data support the use of on-demand therapy for GERD in uninvestigated reflux disease, nonerosive reflux disease, and possibly mild esophagitis as well. On-demand therapy should not be considered for patients with severe esophagitis.
Mezoff EA, Cohen MB. Acid Suppression and the Risk of **Clostridium difficile** Infection. J Pediatr. 2013 Jun 4.
Mitre E, Susi A, Kropp LE, et al. Association Between Use of **Acid-Suppressive Medications and Antibiotics During Infancy and Allergic Diseases** in Early Childhood. JAMA Pediatr. 2018 Apr 2:e180315.
Miura M, Inoue K, Kagaya H, Satoh S, et al. Influence of rabeprazole and lansoprazole on the pharmacokinetics of tacrolimus in relation to CYP2C19, CYP3A5 and MDR1 polymorphisms in renal transplant recipients. Biopharm Drug Dispos. 2007 May;28(4):167-75.
Moayyedi P, Eikelboom JW, Bosch J, et al; COMPASS investigators. Safety of Proton Pump Inhibitors Based on a Large, Multi-year, Randomized **Trial of Patients Receiving Rivaroxaban or Aspirin**. Gastroenterology. 2019 May 29.
Moayyedi P, Soo S, Deeks J, et al. Eradication of Helicobacter pylori for non-ulcer dyspepsia. Cochrane Database Syst Rev. 2005 Jan 25;(1):CD002096.
Moayyedi P, Yuan Y, Leontiadis G; CAG Clinical Affairs. CAG position statement: **hip fracture and proton pump inhibitor therapy** – a 2013 update. www.cag-acg.org/uploads/position/cag_position_ppi_hip_fracture_2013_rev.pdf (accessed September 10, 2013).
Moayyedi PM, Lacy BE, Andrews CN, et al. **ACG (American) and CAG (Canadian) clinical guideline: management of dyspepsia**. Am J Gastroenterol 2017; advance online publication June 20, 2017. http://gi.org/wp-content/uploads/2017/06/ajg2017154a.pdf (accessed June 22, 2017).
Molina-Infante J, Lucendo AJ. **Proton Pump Inhibitor Therapy for Eosinophilic Esophagitis**: A Paradigm Shift. Am J Gastroenterol. 2017 Oct 31.
Munson JC, Bynum JPW, Bell J-E, et al. Patterns of **prescription drug use before and after fragility fracture** [online August 22, 2016].JAMA Intern Med. doi:10.1001/jamainternmed.2016.4814
Nabi Z, Reddy DN. **Endoscopic Management of Gastroesophageal Reflux Disease**: Revisited. Clin Endosc. 2016 Sep;49(5):408-416.
Nason KS, Wichienkuer PP, Awais O, et al. Gastroesophageal reflux disease symptom severity, proton pump inhibitor use, and **esophageal carcinogenesis.** Arch Surg. 2011 Jul;146(7):851-8.
Nava-Ocampo AA, Velazquez-Armenta EY, Han JY, Koren G. Use of proton pump inhibitors during **pregnancy** and breastfeeding. Can Fam Physician. 2006 Jul;52:853-4.
Nehra AK, Alexander JA, Loftus CG, Nehra V. **Proton Pump Inhibitors**: Review of Emerging Concerns. Mayo Clin Proc. 2018 Feb;93(2):240-246.
Neumann I, Letelier LM, Rada G, Claro JC, et al. Comparison of **different regimens of proton pump inhibitors** for **acute peptic ulcer bleeding**. Cochrane Database Syst Rev. 2013 Jun 12;6:CD007999. There is insufficient evidence for concluding superiority, inferiority or equivalence of high dose PPI treatment over lower doses in peptic ulcer bleeding.
Ng FH, Wong SY, Lam KF, et al. **Famotidine 40mg bid is inferior to pantoprazole 20mg od** in preventing recurrence of **aspirin-related** peptic ulcers or erosions. Gastroenterology. 2010 Jan;138(1):82-8. n=160.
Ng FH, Tunggal P, Chu WM, et al. **Esomeprazole compared with famotidine** in the prevention of upper gastrointestinal bleeding in patients with acute coronary syndrome or myocardial infarction. Am J Gastroenterol. 2012 Mar;107(3):389-96.
Nguyen DM, El-Serag HB, Henderson L, et al. Medication usage and the risk of neoplasia in patients with **Barrett's** esophagus. Clin Gastroenterol Hepatol. 2009 Dec;7(12):1299-304. Epub 2009 Jun 10.
Nguyen LH, Lochhead P, Joshi AD, et al. No Significant Association Between Proton Pump Inhibitor Use and **Risk of Stroke** After Adjustment for Lifestyle Factors and Indication. Gastroenterology. 2017 Dec 18.
Nguyen PV, Tamaz R. **Inappropriate Prescription of Proton Pump Inhibitors** in a Community Setting. Can J Hosp Pharm. 2018 Jul-Aug;71(4):267-271.

NICE: National Institute for Health and Clinical Excellence (**NICE**). **Acute upper gastrointestinal bleeding**: management. London (UK): National Institute for Health and Clinical Excellence (NICE); 2012 Jun. http://www.nice.org.uk/nicemedia/live/13762/59549/59549.pdf

Nice: **Dyspepsia and gastro-oesophageal reflux** disease-Investigation and management of dyspepsia, symptoms suggestive of gastro-oesophageal reflux disease, or both. Sept 2014. https://www.nice.org.uk/guidance/cg184

NICE: National Institute for Health and Care Excellence. **Gastro-oesophageal reflux disease**: recognition, diagnosis and management in children and young people. (Clinical Guideline 193.) 2015. www.nice.org.uk/guidance/NG1.

Niklasson A, Lindström L, Simrén M, et al. **Dyspeptic Symptom Development After Discontinuation** of a Proton Pump Inhibitor: A Double-Blind Placebo-Controlled Trial. Am J Gastroenterol. 2010 Mar 23.

Oakland K, Chadwick G, East JE, et al. **Diagnosis and management of acute lower Gastrointestinal bleeding**: guidelines from the British Society of Gastroenterology. Gut. 2019 May;68(5):776-789.

Obszynska, Jolanta, Atherfold, Paul A, Nanji, Manoj, et al. **Long term proton pump** induced hypergastrinaemia does induce lineage-specific restitution but not clonal expansion in benign Barrett's Esophagus in vivo. Gut 2009 0: gut.2009.186775 While the short term effects of gastrin enhance epithelial restitution in BE (but not squamous mucosa) there is no clinical evidence that BE length expands over time. This study, which is the largest and longest term randomised controlled trial of gastrin biology in BE, is further proof of the clinical safety of PPI therapy.

O'Donoghue ML, et al. Pharmacodynamic effect and clinical efficacy of **clopidogrel and prasugrel** with or without a proton-pump inhibitor: An analysis of two randomised trials. (**TRITON-TIMI 38 & PRINCIPLE-TIMI 44)** Lancet 2009; DOI:10.1016/S0140-6736(09)61525-7.

Oelschlager BK, Quiroga E, Parra JD, et al. CA. Long-Term Outcomes After **Laparoscopic Antireflux Surgery**. Am J Gastroenterol. 2007 Oct 26; [Epub ahead of print] Seven patients (2%) developed a new onset of dysphagia; 32 patients (11%) developed new or increased diarrhea and 27 patients (9%) developed bloating postoperatively. One hundred nineteen patients (41%) were taking some form of antacid medication; 66 (23%) patients were using PPIs and 10 (3%) had undergone reoperation. LARS provides effective long-term relief of GERD. Younger patients, men, and those without dysphagia are predictors of superior outcomes.

Ong AM et al. **Diaphragmatic breathing** reduces belching and proton pump inhibitor refractory gastroesophageal reflux symptoms. Clin Gastroenterol Hepatol 2017 Nov 2.

Oregon Health Sciences University. Drug class review on PPIs (July 2006) http://www.ohsu.edu/drugeffectiveness/reports/documents/PPIs%20Final%20Report%20u4%20Unshaded.pdf

Pace F, et al. *Systematic review: maintenance treatment of gastro-oesophageal reflux disease with proton pump inhibitors taken `**on-demand**`* Aliment Pharmacol Ther. 2007 Jul;26(2):195-204. On the basis of the analysis of 17 studies, we can conclude that on-demand therapy with currently available PPI appears to be effective in the long-term management of patients with NERD or mild and uninvestigated forms of GERD, but not in patients with (severe) erosive oesophagitis.

Pape E, Michel D, Scala-Bertola J, et al. Effect of **esomeprazole on the oral absorption of dasatinib** in a patient with Philadelphia-positive acute lymphoblastic leukemia. Br J Clin Pharmacol. 2016 Feb 1.

Parks T, Ragland KL, Steiner MA, et al. Ménétrier Mimicker Complicating Ulcerative Colitis: **Proton-Pump Inhibitor-Induced Hyperplastic Polyps**. J Pediatr. 2015 Jul 21.

Pasternak Björn, Hviid Anders, Use of **Proton-Pump Inhibitors** in **Early Pregnancy and the Risk of Birth Defects**. N Engl J Med 2010; 363:2114-2123. In this large cohort, exposure to PPIs during the first trimester of pregnancy was not associated with a significantly increased risk of major birth defects.

Patel A, Gyawali CP. **Gastroesophageal Reflux Monitoring**. JAMA. 2018 Mar 27;319(12):1271-1272. (replace esomeprazole with nortriptyline)

Patel A, Posner S, Gyawali CP. **Esophageal High-Resolution Manometry in Gastroesophageal Reflux Disease**. JAMA. 2018 Aug 16.

Patel DA, Sharda R, Choksi YA, et al. Model to Select On-Therapy vs Off-Therapy Tests for Patients With **Refractory Esophageal or Extraesophageal Symptoms**. Gastroenterology. 2018 Dec;155(6):1729-1740.e1.

Patti MG, Allaix ME, Fisichella PM. Analysis of the **Causes of Failed Antireflux Surgery** and the Principles of Treatment: A Review. JAMA Surg. 2015 Apr 8.

Pauwels A, Broers C, et al. A Randomized Double-Blind, Placebo-Controlled, Cross-Over Study Using **Baclofen in the Treatment of Rumination Syndrome**. Am J Gastroenterol. 2017 Dec 5.

Peery AF, Dellon ES, Lund J, et al. **Burden of Gastrointestinal Disease in the United States**: 2012 Update. Gastroenterology. 2012 Aug 8.

Peghini PL, Katz PO, Castell DO. Ranitidine controls nocturnal acid breakthrough on omeprazole: a controlled study in normal subjects. Gastroenterology 1998;115:1335-9.

Pessaux P, Arnaud JP, Delattre JF, Meyer C, Baulieux J, Mosnier H. Laparoscopic **antireflux surgery**: five-year results and beyond in 1340 patients. Arch Surg. 2005 Oct;140(10):946-51.

Pham H, Yang WH. A 34-year-old man with refractory heartburn and **intermittent dysphagia** to solids. CMAJ. 2016 Sep 6;188(12):893-5.

Pharmacist's Letter Feb 2007. PPI and risk of **hip fracture**.

Pharmacist's Letter Mar 2007. **Update** on PPIs.

Phoa KN, van Vilsteren FGI,Weusten BLAM, et al. **Radiofrequency ablation vs endoscopic surveillance for patients with Barrett esophagus** and low-grade dysplasia: a randomized trial. *JAMA*. doi:10.1001/jama.2014.2511.

Phupong V, Hanprasertpong T. **Interventions for heartburn in pregnancy**. Cochrane Database Syst Rev. 2015 Sep 19;9:CD011379. There are no large-scale RCTs to assess heartburn relief in pregnancy. This review of nine small studies (which involved data from only four small studies) indicates that there are limited data suggesting that heartburn in pregnancy could be completely relieved by pharmaceutical treatment. Three outcomes were assessed and assigned a quality rating using the GRADE methods. Evidence from two trials for the outcome of complete relief of heartburn was assessed as of moderate quality. Evidence for the outcomes of partial heartburn relief and side effects was graded to be of very low quality.

Pinto-Sanchez MI, Yuan Y, Bercik P, et al. **Proton pump inhibitors for functional dyspepsia**. Cochrane Database Syst Rev. 2017 Mar 8;3:CD011194. There is evidence that PPIs are effective for the treatment of FD, independent of the dose and duration of treatment compared with placebo. PPIs may be slightly more effective than H2RAs for the treatment of FD; however, the evidence is scarce. The trials evaluating PPIs versus prokinetics are difficult to interpret as they are at risk of bias. Although the effect of these drugs seems to be small, the drugs are well tolerated.

Pittayanon R, Yuan Y, Bollegala NP, et al. **Prokinetics for Functional Dyspepsia**: A Systematic Review and Meta-analysis of Randomized Control Trials. Am J Gastroenterol. 2018 Oct 18.

Pluta RM, Perazza GD, Golub RM. JAMA **patient page. Gastroesophageal reflux disease**. JAMA. 2011 May 18;305(19):2024.

Pohl H, Robertson D, Welch HG. **Repeated upper endoscopy** in the Medicare population. A retrospective analysis. Ann Intern Med. 2014;160:154-60.

Pophali P, Halland M. **Barrett's oesophagus**: diagnosis and management. BMJ. 2016 May 11;353:i2373.

Powell J, O'Hara J, Wilson JA. Are **persistent throat symptoms** atypical features of gastric reflux and should they be treated with proton pump inhibitors? BMJ. 2014 Oct 9;349:g5813.

Prasad Kerlin M, Tokar JL. In the Clinic: **Acute gastrointestinal bleeding**. Ann Intern Med. 2013 Aug 6;159(3):ITC2-1.

Quitadamo P, Zenzeri L, Mozzillo E, et al. Gastric Emptying Time, Esophageal pH-Impedance Parameters, Quality of Life, and Gastrointestinal **Comorbidity in Obese Children and Adolescents**. JPediatr. 2017 Dec 8.

Qumseya BJ et al. **Disease progression in Barrett's low-grade dysplasia with radiofrequency ablation compared with surveillance**: Systematic review and meta-analysis. Am J Gastroenterol 2017 Apr 4.

Ray WA et al. Association of **proton pump inhibitors with reduced risk of warfarin-related serious upper gastrointestinal bleeding**. Gastroenterology 2016 Sep 14.

Ray WA, Chung CP, Murray KT, et al. Association of **Oral Anticoagulants and Proton Pump Inhibitor Cotherapy** With Hospitalization for Upper Gastrointestinal Tract Bleeding. JAMA. 2018 Dec 4;320(21):2221-2230.

Rees JR, Lao-Sirieix P, Wong A, Fitzgerald RC. Treatment for **Barrett's oesophagus**. Cochrane Database Syst Rev. 2010 Jan 20;(1):CD004060.

Reeves DJ, Moore ES, Bascom D, et al. Retrospective evaluation of **methotrexate elimination** when co-administered with proton pump inhibitors. Br J Clin Pharmacol. 2014 Mar 20.

Reeve E, Andrews JM, Wiese MD, et al. Feasibility of a **patient-centered deprescribing process** to reduce inappropriate use of proton pump inhibitors. Ann Pharmacother. 2015 Jan;49(1):29-38.

Regula J, et al. Prevention of **NSAID-associated** gastrointestinal lesions: a comparison study **pantoprazole versus omeprazole**. Am J Gastroenterol. 2006 Aug;101(8):1747-55. Epub 2006 Jun 30. (InfoPOEMs: This study confirms many other study results (all nicely summarized in Aliment Pharmacol Ther 2003;17:1237-1245) that have found no clinically important differences between proton pump inhibitors. Begin with omeprazole 20 mg per day and, if necessary, increase to 40 mg per day before switching to a much more expensive nongeneric alternative. (LOE = 1b))

Reid M, Keniston A, Heller JC, Miller M, Medvedev S, Albert RK. **Inappropriate prescribing** of proton pump inhibitors in hospitalized patients. J Hosp Med. 2012 May-Jun;7(5):421-5.

Reimer C, Søndergaard B, et al. Proton-pump inhibitor therapy **induces acid-related symptoms in healthy** volunteers after withdrawal of therapy. Gastroenterology. 2009 Jul;137(1):80-7, 87.e1. Epub 2009 Apr 10.
Richardson P, Hawkey CJ, Stack WA. Proton Pump Inhibitors: Pharmacology and rationale for use in gastrointestinal disorders. Drugs 1998;56(3)307-335.
Richter JE. Review article: the management of **heartburn in pregnancy**. Aliment Pharmacol Ther. 2005 Nov 1;22(9):749-57.
Richter JE, Kumar A, Lipka S, et al. Efficacy of **Laparoscopic Nissen Fundoplication vs Transoral Incisionless Fundoplication or Proton Pump Inhibitors in Patients With Gastroesophageal Reflux Disease**: A Systematic Review and Network Meta-analysis. Gastroenterology. 2018 Apr;154(5):1298-1308.e7.
Rindi G, Fiocca R, Morocutti A, et al.European Rabeprazole Study Group. Effects of **5 years** of treatment with rabeprazole or omeprazole on the gastric mucosa. Eur J Gastroenterol Hepatol. 2005 May;17(5):559-66. This study has confirmed the link between ECL cell hyperplasia and elevated serum gastrin concentrations, but has found no evidence that this progresses to high grades of hyperplasia during 5 years of treatment with rabeprazole or omeprazole.
Rissling O, Glander P, Hambach P, et al. No relevant pharmacokinetic interaction between **pantoprazole and mycophenolate** in renal transplant patients: a randomized crossover study. Br J Clin Pharmacol. 2015 Apr 24.
Rodgers C, van Zanten SV. A meta-analysis of the success rate of **Helicobacter pylori therapy in Canada**. Can J Gastroenterol. 2007 May;21(5):295-300. Both triple therapies consisting of a proton pump inhibitor (PPI), clarithromycin and either amoxicillin or metronidazole performed well, achieving a success rate of 84% and 82%, respectively. The cure rate of PPI-amoxicillin + metronidazole was 76%. Quadruple therapy consisting of a PPI, bismuth, metronidazole and tetracycline, given for seven to 10 days, achieved a success rate of 87%.
Rohss K, Lind T, Wilder-Smith C. Esomeprazole 40 mg provides more effective intragastric acid control than lansoprazole 30 mg, omeprazole 20 mg, pantoprazole 40 mg and rabeprazole 20 mg in patients with gastro-oesophageal reflux symptoms. Eur J Clin Pharmacol. 2004 Oct;60(8):531-9. Epub 2004 Sep 2.
Roman S, Kahrilas PJ. The diagnosis and management of hiatus hernia. BMJ. 2014 Oct 23;349:g6154.
Ronkainen J, et al. Prevalence of **Barrett's esophagus** in the general population: an endoscopic study. Gastroenterology. 2005 Dec;129(6):1825-31.
Rosen R. **Gastroesophageal Reflux in Infants**: More Than Just a pHenomenon. JAMA Pediatr. 2013 Nov 25.
Rosen R, Amirault J, Liu H, et al. **Changes in Gastric and Lung Microflora With Acid Suppression**: Acid Suppression and Bacterial Growth. JAMA Pediatr. 2014 Aug 18.
Rosen R, Hu L, Amirault J, et. al. 16S Community Profiling Identifies Proton Pump Inhibitor Related **Differences in Gastric, Lung, and Oropharyngeal Microflora**. J Pediatr. 2015 Feb 4. pii: S0022-3476(14)01236-0.
Rosen R, Vandenplas Y, Singendonk M, et al. **Pediatric Gastroesophageal Reflux Clinical Practice Guidelines**: Joint Recommendations of the North American Society for Pediatric Gastroenterology, Hepatology, and Nutrition and the European Society for Pediatric Gastroenterology, Hepatology, and Nutrition. J Pediatr Gastroenterol Nutr. 2018 Mar;66(3):516-554.
RxFiles Jan/09 PPIs May Reduce Effectiveness Of **Clopidogrel**
Sachar H, Vaidya K, Laine L. **Intermittent vs Continuous Proton Pump Inhibitor** Therapy for **High-Risk Bleeding Ulcers**: A Systematic Review and Meta-analysis. JAMA Intern Med. 2014 Sep 8.
Sadowski DC, van Zanten SV. **Dyspepsia**. CMAJ. 2015 Feb 9. pii: cmaj.141606.[Epub ahead of print]
SAGES: Society of American Gastrointestinal and Endoscopic Surgeons. Guidelines for **surgical treatment of gastroesophageal reflux disease**. Los Angeles (CA): Society of American Gastrointestinal and Endoscopic Surgeons (SAGES); 2010 Feb.
Sanabria A, Morales C, Villegas M. **Laparoscopic repair** for perforated peptic ulcer disease. Cochrane Database Syst Rev. 2005 Oct 19;4:CD004778. This systematic review suggests that a decrease in septic abdominal complications may exist when laparoscopic surgery is used to correct perforated peptic ulcer. However, it is necessary to develop more randomised controlled trials that include a greater number of patients to confirm such an assumption, guaranteeing a long learning curve for participating surgeons. With the information provided by the available clinical trials it could be said that laparoscopic surgery results are not clinically different from those of open surgery.
Sandhu DS, Fass R. Current Trends in the **Management of Gastroesophageal Reflux Disease**. Gut Liver. 2017 Apr 24.
Sandström M, Davidson G, Tolia V, et al. Phase I, multicenter, randomized, open-label study evaluating the pharmacokinetics and safety profile of repeated once-daily doses of **intravenous esomeprazole** in **children** 0 to 17 years of age. Clin Ther. 2012 Aug;34(8):1828-38.
Scheiman JM, et al. Prevention of Ulcers by Esomeprazole in At-Risk Patients Using Non-Selective NSAIDs and COX-2 Inhibitors. (**Venus** & **Pluto**) Am J Gastroenterol. 2006 Feb 22; [Epub ahead of print] CONCLUSIONS: For at-risk patients, esomeprazole was effective in preventing ulcers in long-term users of NSAIDs, including COX-2 inhibitors.
Schjerning Olsen AM, Lindhardsen J, Gislason GH, et al. Impact of **proton pump inhibitor** treatment on **gastrointestinal bleeding associated with non-steroidal anti-inflammatory drug** use among post-myocardial infarction patients taking antithrombotics: nationwide study. BMJ. 2015 Oct 19;351:h5096.
Scholl S, Dellon ES, Shaheen NJ. Treatment of **GERD and proton pump inhibitor use in the elderly**: practical approaches and frequently asked questions. Am J Gastroenterol. 2011 Mar;106(3):386-92.
Sehested TSG, Carlson N, Hansen PW, et al. Reduced **risk of gastrointestinal bleeding** associated with proton pump inhibitor therapy in patients treated with dual antiplatelet therapy after myocardial infarction. Eur Heart J. 2019 Jun 21;40(24):1963-1970.
Selvanderan SP, Summers MJ, Finnis ME, et al. **Pantoprazole or Placebo for Stress Ulcer Prophylaxis** (**POP-UP**): Randomized Double-Blind Exploratory Study. Crit Care Med. 2016 Oct;44(10):1842-50.
Shaheen N, Ransohoff DF. Gastroesophageal reflux, **Barrett** esophagus, and esophageal cancer: clinical applications. JAMA. 2002 Apr 17;287(15):1982-6.
Shaheen NJ et al. **Radiofrequency ablation in Barrett's** esophagus with dysplasia. *N Engl J Med* 2009 May 28; 360:2277.
Shaheen NJ, Weinberg DS, Denberg TD, Chou R, Qaseem A, Shekelle P; for the Clinical Guidelines Committee of the American College of Physicians. Upper **endoscopy for gastroesophageal reflux disease**: best practice advice from the Clinical Guidelines Committee of the American College of Physicians. Ann Intern Med. 2012;157:808-16.
Shaheen NJ et al. ACG clinical guideline: Diagnosis and management of **Barrett's esophagus**. Am J Gastroenterol 2015 Nov 3.
Shamliyan TA, Middleton M, Borst C. **Patient-centered Outcomes** with Concomitant Use of **Proton Pump Inhibitors** and Other Drugs. Clin Ther. 2017 Feb 9
Shannon C, et al. Regimens of misoprostol with mifepristone for early medical **abortion**: a randomised trial. BJOG. 2006 Jun;113(6):621-8. (group I) 400 micrograms of **oral** misoprostol, (group II) 600 micrograms of **oral** misoprostol, and (group III) 800 micrograms of **vaginal** misoprostol. (Neilson J, et al. Medical treatment for early fetal death (less than 24 weeks). Cochrane Database Syst Rev. 2006 Jul 19;3:CD002253.)
Sharma, Prateek. **Barrett's Esophagus**. N Engl J Med 2009 361: 2548-2556.
Sheikh I, Waghray A, Waghray N, et al. **Consumer Use of Over-the-Counter Proton Pump Inhibitors** in Patients With Gastroesophageal Reflux Disease. Am J Gastroenterol. 2014 Jun;109(6):789-94.
Sikkema M, Looman CW, Steyerberg EW, et al. Predictors for **neoplastic progression in patients with Barrett's Esophagus**: a prospective cohort study. Am J Gastroenterol. 2011 Jul;106(7):1231-8.
Silverstein FE, et al. Misoprostol reduces serious gastrointestinal complications in patients with rheumatoid arthritis receiving nonsteroidal anti-inflammatory drugs. A randomized, double-blind, placebo-controlled trial. Ann Intern Med. 1995 Aug 15;123(4):241-9.
Singh S, Garg SK, Singh PP, Iyer PG, et al. **Acid-suppressive** medications and risk of **oesophageal adenocarcinoma** in patients with Barrett's oesophagus: a systematic review and meta-analysis. Gut. 2013 Nov 12.
Siple JF, Morey JM, Gutman TE, et al. Proton Pump Inhibitor Use and Association with **Spontaneous Bacterial Peritonitis** in Patients with Cirrhosis and Ascites (October). Ann Pharmacother. 2012 Oct 2.
Smith CH, Israel DM, Schreiber R, Goldman RD. Proton pump inhibitors for **irritable infants**. Can Fam Physician. 2013 Feb;59(2):153-6.
Smith PB. Use of **Reflux Medications in Premature Infants** After Hospital Discharge. Pediatrics.2016;138(6):e20162849
Solana MJ, López-Herce J, Sánchez A, et al. 0.5 mg/kg versus 1 mg/kg of Intravenous **Omeprazole** for the Prophylaxis of Gastrointestinal Bleeding in Critically Ill **Children**: A Randomized Study. J Pediatr. 2012 Nov 10.
Solaymani-Dodaran M, Card TR, West J. Cause-Specific Mortality of People With **Barrett's Esophagus** Compared With the General Population: A Population-Based Cohort Study. Gastroenterology. 2013 Apr 9.
Song H, Zhu J, Lu D. Long-term **proton pump inhibitor** (PPI) use and the development of **gastric pre-malignant lesions**. Cochrane Database Syst Rev. 2014 Dec 2;12:CD010623. There is presently no clear evidence that the long-term use of PPIs can cause or accelerate the progression of corpus gastric atrophy or intestinal metaplasia, although results were imprecise. People with PPI maintenance treatment may have a higher possibility of experiencing either diffuse (simple) or linear/micronodular (focal) ECL cell hyperplasia. However, the clinical importance of this outcome is currently uncertain.

Søreide K, Thorsen K, Harrison EM, et al. **Perforated peptic ulcer**. Lancet. 2015 Sep 26;386(10000):1288-98.
Spechler SJ, Long-term outcome(~10yrs) of **medical and surgical therapies for gastroesophageal reflux disease**: follow-up of a randomized controlled trial. JAMA. 2001 May 9;285(18):2331-8.
Spechler SJ. Clinical practice. **Barrett's Esophagus**. N Engl J Med. 2002 Mar 14;346(11):836-42.
Spechler SJ. **Barrett esophagus and risk of esophageal cancer**: a clinical review. JAMA. 2013 Aug 14;310(6):627-36.
Spechler SJ, Souza RF. **Barrett's esophagus**. N Engl J Med. 2014 Aug 28;371(9):836-45.
Sreedharan A, Martin J, Leontiadis GI, Dorward S, Howden CW, Forman D, Moayyedi P. Proton pump inhibitor treatment initiated **prior to endoscopic diagnosis in upper gastrointestinal bleeding**. Cochrane Database Syst Rev. 2010 Jul 7;7:CD005415. PPI treatment initiated before endoscopy for upper gastrointestinal bleeding might reduce the proportion of participants with SRH at index endoscopy and significantly reduces requirement for endoscopic therapy during index endoscopy. However, there is no evidence that PPI treatment affects clinically important outcomes, namely mortality, rebleeding or need for surgery.
Srygley FD, Gerardo CJ, Tran T, Fisher DA. Does this **patient have a severe upper gastrointestinal bleed**? JAMA. 2012 Mar 14;307(10):1072-9.
Stanley AJ, Ashley D, Dalton HR, et al. Outpatient management of patients with low-risk upper-gastrointestinal haemorrhage: multicentre validation and prospective evaluation. (**Glasgow-Blatchford** vs Rockall score) Lancet. 2009 Jan 3;373(9657):42-7. Epub 2008 Dec 16.
Stark CM, Susi A, Emerick J, Nylund CM. **Antibiotic and acid-suppression medications during early childhood are associated with obesity**. Gut. 2018 Oct 30.
Strand DS, Kim D, Peura DA. **25 Years of Proton Pump Inhibitors**: A Comprehensive Review. Gut Liver. 2016 Nov 14.
Stavropoulos SN, Friedel D, Modayil R, et al. Diagnosis and management of **esophageal achalasia**. BMJ. 2016 Sep 13;354:i2785.
Strate LL and Gralnek IM.**ACG (American)** clinical guideline: Management of patients with **acute lower gastrointestinal bleeding**. Am J Gastroenterol 2016 Apr; 111:459
Stretta Procedure for GERD. Medical Letter Dec 4/18,2006
Sugerman DT. JAMA **patient page. Gastroesophageal reflux disease**. JAMA. 2014 Jun 18;311(23):2452.
Sung JJ, Barkun A, Kuipers EJ,et al.; for the Peptic Ulcer Bleed Study Group*. Intravenous Esomeprazole for Prevention of Recurrent Peptic Ulcer Bleeding: A Randomized Trial. Ann Intern Med. 2009 Feb 16. [Epub ahead of print] High-dose intravenous esomeprazole given after successful endoscopic therapy to patients with high-risk peptic ulcer bleeding reduced recurrent bleeding at 72 hours and had sustained clinical benefits for up to 30 days.
Sung JJ, Suen BY, Wu JC, et al. Effects of **Intravenous and Oral Esomeprazole** in the Prevention of Recurrent Bleeding from Peptic Ulcers after Endoscopic Therapy. Am J Gastroenterol. 2014 Apr 29.
Sung JJ, Chiu PC, Chan FKL, et al. Asia-Pacific working group consensus on **non-variceal upper gastrointestinal bleeding**: an update 2018. Gut. 2018 Apr 24.
Sverdén E, Markar SR, Agreus L, Lagergren J. **Acute upper gastrointestinal bleeding**. BMJ. 2018 Oct 25;363:k4023.
Sverdén E, Mattsson F, Lindström D, et al. **Transcatheter Arterial Embolization** Compared With Surgery for Uncontrolled Peptic Ulcer Bleeding: A Population-based Cohort Study. Ann Surg. 2019 Feb;269(2):304-309.
Taha AS, et al. **Famotidine** for the prevention of peptic ulcers and oesophagitis in patients taking low-dose aspirin (**FAMOUS**): a phase III, randomized, double-blind, placebo-controlled trial. Lancet 2009; 374:119-125.
Taha AS, Hudson N, Hawkey CJ, et al. **Famotidine** for the prevention of gastric and duodenal ulcers caused by nonsteroidal antiinflammatory drugs. N Engl J Med. 1996 May 30;334(22):1435-9.
Talley NJ, Moore MG, Sprogis A, Katelaris P. Randomised controlled trial of pantoprazole versus ranitidine for the treatment of uninvestigated heartburn in primary care. Med J Aust. 2002 Oct 21;177(8):423-7. Pantoprazole was associated with significantly higher rates of complete control of GORD symptoms than ranitidine at four weeks (40% v 19%; P < 0.001), eight weeks (55% v 33%; P < 0.001), six months (71% v 56%; P = 0.007) and **12 months (77% v 59%; P = 0.001).** CONCLUSIONS: Low-dose pantoprazole is an effective alternative to standard-dose ranitidine for initial and maintenance treatment of patients with symptomatic GORD.
Talley NJ, Vakil NB, Moayyedi P. **American gastroenterological association** technical review on the evaluation of **dyspepsia**. Gastroenterology. 2005 Nov;129(5):1756-80. (Talley NJ; American Gastroenterological Association. AGA medical position statement: evaluation of dyspepsia. Gastroenterology. 2005 Nov;129(5):1753-5.) Talley NJ, Vakil N; Practice Parameters Committee of the American College of Gastroenterology. Guidelines for the management of dyspepsia. Am J Gastroenterol. 2005 Oct;100(10):2324-37. (InfoPOEMs: Patients with dyspepsia may have gastroesophageal reflux disease (GERD), peptic ulcer, functional (nonulcer) dyspepsia, or (rarely) malignancy. The authors reviewed the world's literature and based their recommendations on the results of the best available evidence. Patients with the onset of dyspepsia at age 56 or older or those with alarm symptoms (bleeding, anemia, early satiety, unexplained weight loss, dysphagia or odynophagia, persistent vomiting, family history of gastrointestinal malignancy, previous documented peptic ulcer, abdominal mass, or lymphadenopathy) at any age should undergo immediate upper endoscopy. Patients with reflux predominant symptoms should be treated as if they have GERD. If the prevalence of Helicobacter pylori (HP) infection in your community is less than 10%, a trial of a proton pump inhibitor (PPI) is recommended. If that fails, a test for HP infection followed by eradication if positive should be pursued. When HP is more common, the test-and-treat strategy should be pursued first, followed by a trial of a PPI. If these strategies fail, upper endoscopy should be considered according to the clinician's judgment. However, the prevalence of ulcer or malignancy in HP- negative patients is quite low in this group.)
Talley NJ, Ford AC. **Functional Dyspepsia**. N Engl J Med. 2015 Nov 5;373(19):1853-63.
Talley NJ. **Functional Dyspepsia**: Advances in Diagnosis and Therapy. Gut Liver. 2017 May 15;11(3):349-357.
Tanaka M, Kataoka H, Yagi T. **Proton-pump inhibitor-induced fundic gland polyps with hematemesis**. Clin J Gastroenterol. 2019 Apr; 12(2):193-195.
Tang RS, Chan FK. Therapeutic **management of recurrent peptic ulcer disease**. Drugs. 2012 Aug 20;72(12):1605-16.
Targownik LE, Leslie WD, Davison KS, et al. CaMos Research Group. The relationship between **proton pump inhibitor** use and longitudinal change in **bone mineral density**: a population-based from the Canadian Multicentre Osteoporosis Study (CaMos). Am J Gastroenterol. 2012 Sep;107(9):1361-9.
Targownik LE, Goertzen AL, Luo Y, Leslie WD. **Long-Term Proton Pump Inhibitor Use Is Not Associated With Changes in Bone** Strength and Structure. Am J Gastroenterol. 2016 Nov 15.
Targownik L. **Discontinuing Long-Term PPI Therapy**: Why, With Whom, and How? Am J Gastroenterol. 2018 Mar 20.
Tariq R, et al. Association of **gastric acid suppression with recurrent Clostridium difficile infection**: systematic review and meta-analysis [online Mar 27/17].JAMA Intern Med. . doi:10.1001 /jamainternmed.2017.0212
Tasaka CL, Burg C, et al. An interprofessional approach to reducing the **overutilization of stress ulcer prophylaxis** in adult medical and surgical intensive care units. Ann Pharmacother. 2014 Apr;48(4):462-9.
Tergast TL, Wranke A, Laser H, et al. Dose Dependent Impact of **Proton Pump Inhibitors on the Clinical Course of Spontaneous Bacterial Peritonitis**. Liver Int. 2018 Apr 19.
Terrin G et al. **Ranitidine** is Associated With **Infections, Necrotizing Enterocolitis, and Fatal Outcome in Newborns**. Pediatrics. 2011 Dec 12.
Thakkar K, Boatright RO, Gilger MA, et al. **Gastroesophageal reflux and asthma in children: a systematic review.** Pediatrics. 2010 Apr;125(4):e925-30. Epub 2010 Mar 29.
Thjodleifsson B, Rindi G, Fiocca R, et al.; Tofts RPH, Ferrer G, Oliveira E. How should one investigate a **chronic cough**? *Cleveland Clinic Journal of Medicine 2011; 78(2):84-85, 89; doi:10.3949/ccjm.77a.10033.*
Thomas T, Abrams KR, De Caestecker JS, Robinson RJ. Meta analysis: cancer risk in Barrett's oesophagus. Aliment Pharmacol Ther 2007;26(11-12):1465-1477. Approximately 7 per 1000 (0.7%) patients with Barrett's esophagus will develop **esophageal cancer per year**. The low incidence of Barrett's, followed by this low incidence of esophageal cancer, may make routine evaluation of patients with chronic gastroesophageal reflux less important. (LOE = 1b-)
Thrift AP et al. **Nonsteroidal anti-inflammatory drug use** is not associated with reduced risk of **Barrett's esophagus**. Am J Gastroenterol 2016 Aug 30.
Tighe M, Afzal NA, Bevan A, et al. Pharmacological **treatment of children with gastro-oesophageal reflux**. Cochrane Database Syst Rev. 2014 Nov 24;11:CD008550. Moderate evidence was found to support the use of PPIs, along with some evidence to support the use of H antagonists in older children with GORD, based on improvement in symptom scores, pH indices and endoscopic/histological appearances. However, lack of independent placebo-controlled and head-to-head trials makes conclusions as to relative efficacy difficult to determine. Further RCTs are recommended. No robust RCT evidence is available to support the use of domperidone, and further studies on prokinetics are recommended, including assessments of erythromycin. Pharmacological treatment of infants with reflux symptoms is problematic, as many infants have GOR, and little correlation has been noted between reported symptoms and endoscopic and pH findings. Better evidence has been found to support the use of PPIs in infants with GORD, but heterogeneity in outcomes and in study design impairs interpretation of placebo-controlled data regarding efficacy. Some evidence is available to support the use of Gaviscon Infant® , but further studies with longer follow-up times are recommended. Studies of omeprazole and lansoprazole in infants with functional GOR have demonstrated variable benefit, probably because of differences in inclusion criteria. No robust RCT evidence has been found regarding treatment of preterm babies with GOR/GORD or children with neurodisabilities. Initiation of RCTs with common endpoints is recommended, given the frequency of treatment and the use of multiple antireflux agents in these children.
Tleyjeh IM, Abdulhak AA, Riaz M, et al. The Association between **Histamine 2 Receptor Antagonist Use and Clostridium difficile** Infection: A Systematic Review and Meta-analysis. PLoS One. 2013;8(3):e56498.

Tolia V, Boyer K. Long-Term Proton Pump Inhibitor Use in **Children**: A Retrospective Review of Safety.Dig Dis Sci. 2008 Feb;53(2):385-393. Epub 2007 Aug 4. Long-term proton pump inhibitor (PPI) therapy (median treatment duration = 35.2 months) appears to be safe for children. Serum gastrin levels remained elevated in nearly 75% of children, but there was no evidence of an increased risk of carcinoid tumor, abnormal vitamin B12 absorption, or any other concerning outcome. (LOE = 1b-)

Torpy JM, Lynm C, Golub RM. JAMA **patient page**. **Peptic ulcer disease**. JAMA. 2012 Mar 28;307(12):1329.

Tosetti C, Nanni I. Use of **proton pump inhibitors in general practice**. World J Gastrointest Pharmacol Ther. 2017 Aug 6;8(3):180-185.

Treatment Guidelines: Drugs for **Peptic Ulcers & GERD**. **The Medical Letter**: February, **2004**; 2(18) pp. 9-12. Updated August 2008. Updated Sep 2011. **New & Updated Apr 2014.**

Trikudanathan G, Israel J, Cappa J, O'Sullivan DM. Association between proton pump inhibitors and **spontaneous bacterial peritonitis** in cirrhotic patients – a systematic review and meta-analysis. Int J Clin Pract. 2011 Jun;65(6):674-8.

Tringali A, et al. Comparing **intravenous and oral proton pump inhibitor** therapy for **bleeding peptic ulcers** following endoscopic management. A systematic review and meta-analysis. Br J Clin Pharmacol. 2017 Feb 9.

Tsai JJ, Hsu YC, Perng CL, Lin HJ. **Oral or intravenous proton pump** inhibitor in patients with peptic ulcer bleeding after successful endoscopic epinephrine injection. Br J Clin Pharmacol. 2009 Mar;67(3):326-32. Epub 2008 Dec 10. **Oral** rabeprazole and i.v. regular-dose omeprazole are **equally effective** in preventing rebleeding in patients with high-risk bleeding peptic ulcers after successful endoscopic injection with epinephrine.

Tsai CF, Chen MH, Wang YP et al. Proton Pump Inhibitors Increase Risk for **Hepatic Encephalopathy** In Patients with Cirrhosis in a Population Study. Gastroenterology. 2017;152:134-141.

Tsoi KKF et al. Meta-analysis: Comparison of **oral vs. intravenous proton pump inhibitors in patients with peptic ulcer bleeding**. Aliment Pharmacol Ther 2013 Aug 5; [e-pub ahead of print].

Vaduganathan M, Bhatt DL, Cryer BL, et al. **Proton-pump inhibitors** reduce **gastrointestinal events regardless of aspirin dose** in patients requiring dual antiplatelet therapy. *J Am Coll Cardiol* 2016.

Vaezi MF, Hagaman DD, Slaughter JC, et al. Proton pump inhibitor therapy **improves symptoms in postnasal drainage**. Gastroenterology. 2010 Dec;139(6):1887-1893.

Vaezi MF, Yang YX, Howden CW. **Complications of Proton Pump Inhibitor Therapy**. Gastroenterology. 2017 May 19. pii: S0016-5085(17)35623-8.

Vakil N, Moayyedi P, et al. Limited value of **alarm features** in the diagnosis of upper gastrointestinal malignancy: systematic review and meta-analysis. Gastroenterology. 2006 Aug;131(2):390-401; quiz 659-60.

Valle PC, et al. "Test, score and scope": a selection strategy for safe reduction of upper gastrointestinal endoscopies in young dyspeptic patients referred from primary care. Scand J Gastroenterol. 2006 Feb;41(2):161-9. (InfoPOEMs: For men younger than 45 years, the endoscopic yield is very low for those without Helicobacter pylori infection, nonsteroidal anti-inflammatory drug (NSAID) use, unintended weight loss, or anemia. (LOE = 2b))

van der Pol, Rachel J., Smits, Marije J., van Wijk, Michiel P., et al. Efficacy of **Proton-Pump Inhibitors in Children With Gastroesophageal Reflux Disease:** A Systematic Review. Pediatrics 2011 0: peds.2010-2719

van der Pol RJ, Smits MJ, Venmans L, et al. **Diagnostic Accuracy of Tests in Pediatric Gastroesophageal Reflux Disease**. J Pediatr. 2012 Dec 7.

van der Pol R, Langendam M, Benninga M, et al. **Efficacy and Safety** of **Histamine-2 Receptor Antagonists**. JAMA Pediatr. 2014 Aug 18. Evidence to support the efficacy and safety of H2RAs in infants and children is limited and of poor quality.

van Marrewijk CJ, Mujakovic S, Fransen GA, et al. Effect and cost-effectiveness of step-up versus step-down treatment with antacids, H(2)-receptor antagonists, and proton pump inhibitors in patients with new onset dyspepsia (DIAMOND study): a primary-care-based randomised controlled trial. Lancet. 2009 Jan 17;373(9659):215-225. Although treatment success with either step-up or step-down treatment is similar, the **step-up strategy is more cost effective** at 6 months for initial treatment of patients with new onset dyspeptic symptoms in primary care.

van Pinxteren B, Numans ME, Bonis PA, Lau J. Short-term treatment with proton pump inhibitors, H2-receptor antagonists and prokinetics for gastro-oesophageal reflux disease-like symptoms and endoscopy negative reflux disease. Cochrane Database Syst Rev. 2004 Oct 18;(4):CD002095.

Varallo FR, de Nadai TR, de Oliveira ARA, et al. Potential **Adverse Drug Events and Nephrotoxicity Related to Prophylaxis With Omeprazole** for Digestive Disorders: A Prospective Cohort Study. Clin Ther. 2018 Jun;40(6):973-982.

Vazquez-Elizondo G, Ngamruengphong S, et al. The outcome of patients with **oesophageal eosinophilic** infiltration after an eight-week trial of a proton pump inhibitor. Aliment Pharmacol Ther. 2013 Nov;38(10):1312-9.

Veldhuyzen van Zanten SJ, Chiba N, Armstrong D, et al. A randomized trial comparing omeprazole, ranitidine, cisapride, or placebo in Helicobacter pylori negative, primary care patients with dyspepsia: The CADET-HN study. Am J Gastroenterol 2005; 100:1477-88. (InfoPOEMs: Omeprazole (and to a lesser extent, ranitidine) are somewhat effective for patients with Helicobacter pylori (HP) negative dyspepsia, even if patients with a primary complaint of heartburn or reflux are excluded.

Verhaegh BPM et al. High risk of drug-induced microscopic **colitis** with concomitant use of **NSAIDs and proton pump inhibitors**. Aliment Pharmacol Ther 2016 Mar 9.

Verhoef TI, Zuurhout MJ, van Schie RM, et al. The effect of omeprazole and esomeprazole on the maintenance dose of **phenprocoumon**. Br J Clin Pharmacol. 2012 Apr 12.

Villanueva C, Colomo A, Bosch A, et al. **Transfusion strategies** for acute upper gastrointestinal bleeding. N Engl J Med 2013;368:11-21.

Villegas K, Meier JL, Long M, et al. The Effect of **Proton Pump Inhibitors on Glycemic Control in Patients with Type 2 Diabetes**. Metab Syndr Relat Disord. 2019 Feb 7.

Visrodia K et al. Magnitude of **missed esophageal adenocarcinoma** after **Barrett's esophagus diagnosis**: A systematic review and meta-analysis. Gastroenterology 2016 Mar; 150:599.

Visrodia K et al. Systematic review with meta-analysis: Prevalent vs. incident **oesophageal adenocarcinoma and high-grade dysplasia in Barrett's** oesophagus. Aliment Pharmacol Ther 2016 Oct;44:775.

Vita R et al. Switching levothyroxine from the tablet to the oral solution formulation corrects the impaired absorption of levothyroxine induced by proton-pump inhibitors. *J Clin Endocrinol Metab 2014 Dec; 99:4481*.

Wallace JL, Syer S, Denou E, et al. **Proton Pump Inhibitors Exacerbate NSAID-Induced Small Intestinal Injury** by Inducing Dysbiosis. Gastroenterology. 2011 Jul 13.

Wang Chih-Hung; Ma Matthew Huei-Ming; Chou Hao-Chang; et al. **High-Dose vs Non-High-Dose Proton Pump Inhibitors** After Endoscopic Treatment in Patients With Bleeding Peptic Ulcer: A Systematic Review and Meta-analysis of Randomized Controlled Trials. Arch Intern Med. 2010;170(9):751-758. Compared with non–high-dose PPIs, highdose PPIs do not further reduce the rates of rebleeding, surgical intervention, or mortality after endoscopic treatment in patients with bleeding peptic ulcer.

Wang H, Shao F, Liu X, et al. Efficacy, safety and pharmacokinetics of **ilaprazole infusion** in healthy subjects and patients with esomeprazole as positive control. Br J Clin Pharmacol. 2019 Jul 23.

Wang J, Yang K, Ma B, et al. Intravenous pantoprazole as an adjuvant therapy following successful **endoscopic** treatment for peptic ulcer bleeding. Can J Gastroenterol. 2009 Apr [cited 2010 May 19];23(4):287-99.

Wang KK, Sampliner RE, **Updated guidelines 2008** for the diagnosis, surveillance and therapy of **Barrett's esophagus**. Am J Gastroenterol 2008;103:788-97. (American College of Gastroenterology)

Wang WH, Huang JQ, Zheng GF, et al. Is proton pump inhibitor testing an effective approach to diagnose gastroesophageal reflux disease in patients with noncardiac chest pain?: a meta-analysis. Arch Intern Med. 2005 Jun 13;165(11):1222-8. CONCLUSION: The use of PPI treatment as a diagnostic test for detecting GERD in patients with NCCP has an acceptable sensitivity and specificity and could be used as an initial approach by primary care physicians to detect GERD in selected patients with NCCP. (InfoPOEMs: In patients with chest pain known NOT to be cardiac in origin, response to treatment with an stomach-acid reducing proton pump inhibitor will identify most patients with gastroesophageal reflux (GERD) and can be the first step in explaining the chest pain. (LOE = 1b))

Wang YF, Chen YT, Luo JC, et al. **Proton-Pump Inhibitor Use and the Risk of First-Time Ischemic Stroke** in the General Population: A Nationwide Population-Based Study. Am J Gastroenterol. 2017 Apr 11.

Warlé-van Herwaarden MF, Koffeman AR, Valkhoff VE, et al. Time-trends in the **prescribing of gastroprotective agents** to primary care patients initiating low-dose **aspirin or non-steroidal anti-inflammatory drugs**: a population based cohort study. Br J Clin Pharmacol. 2015 Mar 16.

Weersink RA, Bouma M, Burger DM, et al. Safe use of **proton pump inhibitors in patients with cirrhosis**. Br J Clin Pharmacol. 2018 Apr 24.

Wei L, Ratnayake L, Phillips G, et al. Acid suppression medications and **bacterial gastroenteritis**: a population-based cohort study. Br J Clin Pharmacol. 2017 Jan 5.

Wildschut H, Both MI, Medema S, et al. **Medical methods for mid-trimester termination of pregnancy**. Cochrane Database Syst Rev. 2011 Jan 19;1:CD005216. (mifepristone and misoprostol)

Wilkerson PM, et al. A poor response to proton pump inhibition is not a contraindication for laparoscopic **antireflux surgery** for gastro esophageal reflux disease. Surg Endosc. 2005 Sep;19(9):1272-7. Epub 2005 Jul 14.

Wilkinson JM, Cozine EW, Loftus CG. **Gas, Bloating, and Belching**: Approach to Evaluation and Management. Am Fam Physician. 2019; 99(5): 301-309.

Wileman SM, McCann S, Grant AM, Krukowski ZH, Bruce J. **Medical versus surgical** management for **gastro-oesophageal reflux disease** (GORD) in adults. Cochrane Database Syst Rev. 2010 Mar 17;3:CD003243. There is evidence that laparoscopic fundoplication surgery is more effective than medical management for the treatment of GORD at least in the short to medium term. Surgery does carry some risk and whether the benefits of surgery are sustained in the long term

remains uncertain. Treatment decisions for GORD should be based on patient and surgeon preference.
Wilkins T, Khan N, Nabh A et al. Diagnosis and Management of Upper **Gastrointestinal Bleeding**. *Am Fam Physician.* 2012 Mar 1;85(5):469-476.
Wong GLH, Lau LHS, Ching JYL, et al. **Prevention of recurrent idiopathic gastroduodenal ulcer bleeding**: a double-blind, randomised trial. Gut. 2019 Jun 22.
Writing Committee for the American Lung Association Asthma Clinical Research Centers. **Lansoprazole** for children with poorly controlled asthma: a randomized controlled trial. JAMA. 2012;307(4):373-381. PPIs does not improve symptom control in children with asthma.
Xie Y, Bowe B, Li T, Xian H, Balasubramanian S, Al-Aly Z. Proton Pump Inhibitors and **Risk of Incident CKD** and Progression to ESRD. J Am Soc Nephrol. 2016 Apr 14.
Xie Y, Bowe B, Li T, et al. **Long-term kidney outcomes** among users of proton pump inhibitors without intervening acute kidney injury. Kidney Int. 2017 Jun;91(6):1482-1494.
Xie Y, Bowe B, Yan Y, et al. Estimates of **all cause mortality** and cause specific mortality associated with proton pump inhibitors among US veterans: cohort study. BMJ. 2019 May 29;365:l1580.
Yachimski Patrick S.; Farrell Elizabeth A.; Hunt Daniel P.; et al. Proton Pump Inhibitors for **Prophylaxis of Nosocomial Upper Gastrointestinal Tract Bleeding**: Effect of Standardized Guidelines on Prescribing Practice. Arch Intern Med. 2010;170(9):779-783.
Yadlapati R, Vaezi MF, Vela MF, et al. Management options for patients with **GERD and persistent symptoms on proton pump inhibitors**: recommendations from an **expert panel**. Am J Gastroenterol. 2018 Apr 24.
Yates TA, et al. **Lansoprazole use and tuberculosis incidence** in the United Kingdom Clinical Practice Research Datalink: A population based cohort. PLoS Med. 2017 Nov 21;14(11):e1002457.
Yeomans N, Lanas A, Labenz J, van Zanten SV, et al. Efficacy of esomeprazole (20 mg once daily) for reducing the risk of gastroduodenal ulcers associated with continuous use of low-dose aspirin. Am J Gastroenterol. 2008 Oct;103(10):2465-73. Epub 2008 Jul 12. Twenty-seven patients (5.4%) in the placebo group developed a gastric or duodenal ulcer during 26 weeks' treatment compared with eight patients (1.6%) in the esomeprazole group (life-table estimates: 6.2%vs 1.8%; P= 0.0007). **Esomeprazole 20 mg** once daily reduces the risk of developing gastric and/or duodenal ulcers and symptoms associated with the continuous use of low-dose aspirin in patients aged > or =60 yr without preexisting gastroduodenal ulcers.
Yu EW, Bauer SR, Bain PA, et al. **Proton pump inhibitors and risk of fractures**: a meta-analysis of 11 international studies. Am J Med. 2011 Jun;124(6):519-26.
Yu LY, Sun LN, Zhang XH, et al. A Review of the **Novel Application** and Potential **Adverse Effects of Proton Pump Inhibitors**. Adv Ther. 2017 May;34(5):1070-1086.
Zacny J, Zamakhshary M, Sketris I, et al. Systematic review: the efficacy of intermittent and on-demand therapy with histamine H2-receptor antagonists or proton pump inhibitors for gastro-oesophageal reflux disease patients. Aliment Pharmacol Ther. 2005 Jun 1;21(11):1299-312. CONCLUSIONS: Intermittent proton pump inhibitor or H2-receptor antagonist therapy is not effective in maintaining control in oesophagitis patients. H2-receptor antagonists are effective for relief of heartburn episodes. On-demand proton pump inhibitor therapy may work in a proportion of non-erosive gastro-oesophageal reflux disease patients excluded. The benefit did not persist through the next 5 months when patients could use medications as needed rather than in a scheduled manner. Ranitidine was more cost-effective than omeprazole. It still makes sense to try ranitidine first for these patients, then stepping up to omeprazole if their symptoms are not improved adequately, particularly since this is a benign, self-limited condition. (LOE = 1b))
Zalvan CH, Hu S, Greenberg B, Geliebter J. A comparison of **alkaline water and Mediterranean diet vs proton pump inhibition for treatment of laryngopharyngeal reflux** [online September 7, 2017]. JAMA Otolaryngol Head Neck Surg. doi:10.1001/jamaoto.2017.1454
Zimmerman TG. Common questions about **barrett esophagus**. Am Fam Physician. 2014 Jan 15;89(2):92-8
Zirk-Sadowski J, Masoli JA, Delgado J, et al. **Proton-Pump Inhibitors and Long-Term Risk of Community-Acquired Pneumonia** in Older Adults. J Am Geriatr Soc. 2018 Apr 20.

PPIs & Feeding Tubes:
Detail-Document #241204. PHARMACIST'S LETTER / PRESCRIBER'S LETTER. December 2008 ~ Volume 24 ~ Number 241204.
William NT. Medication administration through enteral feeding tubes. Am J Health-Syst Pharm—Vol 65 Dec 15, 2008; 237-2357.
CSHP – PSN email communication.

Web Sites:
American College of Physicians: ACP Special Report: Understanding and Treating Heartburn http://www.acponline.org/patients_families/pdfs/health/heartburn_report.pdf
National Digestive Diseases Information Clearinghouse: Heartburn, Hiatal Hernia, and GERD http://digestive.niddk.nih.gov/ddiseases/pubs/gerd/index.htm

RxFILES: HELICOBACTER PYLORI TESTING & ERADICATION

Complete Abbreviation List

☎=Exception Drug Status SK ✘ =non-formulary SK ✆=prior approval required for NIHB ⊗=not covered by NIHB ▼=covered by NIHB **ABX**=antibiotic(s) **ac**=before meals **AE**=adverse events **ASA**=acetylsalicyclic acid **BID**=twice daily **CA**=cancer **Ca^{++}**=calcium **cc**=with meals **CDN**=Canadian **CI**=contraindication **CrCl**=creatinine clearance **d**=day(s) **DI**=drug interaction **EtOH**=ethanol/alcohol **g**=generic **g**=gram **GERD**=gastroesophageal reflux disease **H_2RA**=H_2-receptor antagonist **H.pylori**=Helicobacter pylori **hx**=history **ITT**=intention to treat **MALT**=mucosa associated lymphoid tissue **mins**=minutes **NSAID**=non-steroidal anti-inflammatory drugs **OBMT**=omeprazole, bismuth, metronidazole, tetracycline **OTC**=over the counter **PRN**=as needed **po**=oral **PPI**=proton pump inhibitor **PUD**=peptic ulcer disease **QID**=four times daily **sx**=symptom(s) **tx**=treatment **UBT**=urea breath test **VBAD**=vomiting, bleeding, abdominal mass, dysphagia **wks**=week(s) **yrs**=years

Extras &/or Historical Note

Quadruple 1 day regimen: PPI double dose + bismuth 2 tab QID + metronidazole 500mg QID + amoxicillin 2gm QID[10]

References

[1] Jones NL. A review of current guidelines for the management of Helicobacter pylori infection in **children** and adolescents. Paediatr Child Health 2004;9(10):709-713.

[2] Duck WM, et al. Antimicrobial resistance incidence & risk factors among Helicobacter pylori-infected persons, United States. Emerg Infect Dis. 2004 Jun;10(6):1088-94.

[3] Fuccio L, Laterza L, Zagari RM, Cennamo V, Grilli D, Bazzoli F. **Treatment of Helicobacter pylori** infection. BMJ. 2008 Sep 15;337:a1454. doi: 10.1136/bmj.a1454.

[4] Liu CC, Lee CL, Chan CC, et al. Maintenance treatment is not necessary after Helicobacter pylori eradication and healing of bleeding peptic ulcer: a 5-year prospective, randomized, controlled study. Arch Intern Med. 2003 Sep 22;163(17):2020-4.

[5] Gottrand F, Kalach N, Spyckerelle C, et al. Omeprazole combined with amoxicillin and clarithromycin in the eradication of Helicobacter pylori in **children** with gastritis: A prospective randomized double-blind trial. J Pediatr. 2001 Nov;139(5):664-8.

[6] Van Zanten V, Lauritsen K, Delchier JC, Labenz J, De Argila CM, Lind T. One-week triple therapy with esomeprazole provides effective eradication of Helicobacter pylori in duodenal ulcer disease. Aliment Pharmacol Ther. 2000 Dec;14(12):1605-11.

[7] Wong BC, Wong WM, Yee YK, et al. Rabeprazole-based 3-day and 7-day triple therapy vs. omeprazole-based 7-day triple therapy for the treatment of Helicobacter pylori infection. Aliment Pharmacol Ther. 2001 Dec;15(12):1959-65.

[8] Lind T, Veldhuyzen van Zanten S, Unge P. Eradication of Helicobacter pylori using one-week triple therapies combining omeprazole with two antimicrobials: the MACH I Study. Helicobacter 1996;1(3):138-44.

[9] Treiber G, Wittig J, Ammon S, Walker S, van Doorn LJ, Klotz U. Clinical outcome and influencing factors of a new short-term quadruple therapy for Helicobacter pylori eradication: a randomized controlled trial (**MACLOR** study). Arch Intern Med. 2002 Jan 28;162(2):153-60.

[10] Lara LF, Cisneros G, Gurney M, Van Ness M, Jarjoura D, Moauro B, Polen A, Rutecki G, Whittier F. One-day quadruple therapy compared with 7-day triple therapy for Helicobacter pylori infection. Arch Intern Med. 2003 Sep 22;163(17):2079-84.

[12] Hunt R, Thomson AB. Canadian Helicobacter pylori consensus conference. Canadian Association of Gastroenterology. Can J Gastroenterol. 1998 Jan-Feb;12(1):31-41.

[13] Hunt R, Fallone C, Veldhuyzan van Zanten S, et al.; CHSG 2004 participants. Canadian Helicobacter Study Group Consensus Conference: Update on the management of Helicobacter pylori--an evidence-based evaluation of six topics relevant to clinical outcomes in patients evaluated for H pylori infection. Can J Gastroenterol. 2004 Sep;18(9):547-54.

[14] Iacopini F, et al. One-week once-daily triple therapy with esomeprazole, levofloxacin and azithromycin compared to a standard therapy for Helicobacter pylori eradication. Dig Liver Dis. 2005 Aug;37(8):571-6.

Federico A, Nardone G, Gravina AG, et al. Efficacy of 5-day **levofloxacin**- containing concomitant therapy in eradication of Helicobacter pylori infection. Gastroenterology 2012;142:000–000.

Liou JM, et al. **Levofloxacin Sequential Therapy vs Levofloxacin Triple Therapy** in the Second-Line Treatment of Helicobacter pylori: A Randomized Trial. Am J Gastroenterol. 2016 Mar;111(3):381-7.

[15] Best L, Cooper-Lesins G, Haldane D, et al. Helicobacter pylori antibiotic resistance in Canadian populations. (Abstr) Gastroenterology 2004;126:S1293.

Eng NF, Ybazeta G, Chapman K, Fraleigh NL, Letto R, Altman E, Diaz-Mitoma F. Antimicrobial susceptibility of Canadian isolates of Helicobacter pylori in **Northeastern Ontario**. Can J Infect Dis Med Microbiol. 2015 May-Jun;26(3):137-44.

Fallone CA, Chiba N, van Zanten SV, et al. The **Toronto Consensus** for the Treatment of **Helicobacter pylori Infection in Adults**. Gastroenterology. 2016 Apr 18.

Optimal treatment of H. pylori requires careful attention to local antibiotic resistance and eradication patterns. Quadruple therapies PAMC or PBMT should play a more prominent role in H. pylori eradication and all treatments should be given for 14 days.

[16] Yang J, Zhang Y, Fan L, et al. **Eradication Efficacy of Modified Dual Therapy Compared with Bismuth-Containing Quadruple Therapy** as a First-Line Treatment of Helicobacter pylori. Am J Gastroenterol. 2019 Feb 25.

Additional sources:

Ables AZ, Simon I, Melton ER. **Update on Helicobacter pylori treatment**. Am Fam Physician. 2007 Feb 1;75(3):351-8.

Albrecht P, Kotowska M, Szajewska H. **Sequential therapy** compared with standard triple therapy for helicobacter pylori eradication in **children**: a double-blind, randomized, controlled trial. J Pediatr. 2011 Jul;159(1):45-9.

Anti-infective Review Panel. **Anti-infective Guidelines for Community-acquired Infections**. Canadian - New-**2012**. Toronto: MUMS Guideline Clearinghouse. http://www.mumshealth.com/

BC 2010 Guidelines.

Bentur Y, Matsui D, Koren G. Safety of **14C-UBT** for diagnosis of Helicobacter pylori infection in **pregnancy**. Can Fam Physician. 2009 May;55(5):479-80.

Best LM, Takwoingi Y, Siddique S, et al. Non-invasive diagnostic tests for Helicobacter pylori infection. Cochrane Database Syst Rev. 2018 Mar 15;3:CD012080. In people without a history of gastrectomy and those who have not recently had antibiotics or proton ,pump inhibitors, urea breath tests had high diagnostic accuracy while serology and stool antigen tests were less accurate for diagnosis of Helicobacter pylori infection.This is based on an indirect test comparison (with potential for bias due to confounding), as evidence from direct comparisons was limited or unavailable. The thresholds used for these tests were highly variable and we were unable to identify specific thresholds that might be useful in clinical practice.

Boltin D, Levi Z, Gingold-Belfer R, et al. Impact of **Previous Exposure to Macrolide Antibiotics on Helicobacter pylori Infection** Treatment Outcomes. Am J Gastroenterol. 2019 Apr 25.

Bourke B, Ceponis P, Chiba N, et al.; Canadian Helicobacter Study Group. Canadian Helicobacter Study Group Consensus Conference: Update on the approach to Helicobacter pylori infection in children and adolescents--an evidence-based evaluation. Can J Gastroenterol. **2005** Jul;19(7):399-408.

Braden B. **Diagnosis** of Helicobacter pylori infection. BMJ. 2012 Feb 24;344:e828.

Briggs GG, Freeman RK, Sumner JY. Drugs in Pregnancy and Lactation 9th Edition. Williams & Wilkins, Baltimore, 2011.

Buonavolontà R, Miele E, Russo D, Vecchione R, et al. Helicobacter pylori **Chronic Gastritis in Children**: To Eradicate or Not to Eradicate? J Pediatr. 2011 Jul;159(1):50-6.

CADTH. Scientific Report: Evidence for PPIs use in Gastroesophageal Reflux Disease, Dyspepsia and Peptic Ulcer Disease (Mar 2007) www.cadth.ca

Centanni M, et al. **Thyroxine** in goiter, Helicobacter pylori infection, and chronic gastritis. N Engl J Med. 2006 Apr 27;354(17):1787-95.

Cheng HC, Chang WL, Chen WY, et al. Levofloxacin-Containing Triple Therapy to Eradicate the Persistent H. pylori after a Failed Conventional Triple Therapy. Helicobacter. 2007 Aug;12(4):359-63. n=124. One-week levofloxacin 500 mg daily-based triple therapy is effective for eradicating the persistent H. pylori after a failed triple therapy with amoxicillin, clarithromycin, and omeprazole.

Chey WD, Moayyedi P. Review article: uninvestigated dyspepsia and non-ulcer dyspepsia-the use of endoscopy and the roles of Helicobacter pylori eradication and antisecretory therapy. Aliment Pharmacol Ther. 2004 Feb;19 Suppl 1:1-8.

Chey WD, Wong BC; Practice Parameters Committee of the **American** College of Gastroenterology (**ACG**). American College of Gastroenterology Guideline on the Management of **Helicobacter pylori Infection**. Am J Gastroenterol. 2007 Aug;102(8):1808-25. Epub 2007 Jun 29.

Chey WD, Leontiadis GI, et al. **ACG (American College of Gastroenterology) Clinical Guideline**: Treatment of Helicobacter pylori Infection. Am J Gastroenterol. **2017** Jan 10.

Chiba N, Van Zanten SJ, Sinclair P, Ferguson RA, Escobedo S, Grace E. Treating Helicobacter pylori infection in primary care patients with uninvestigated dyspepsia: the Canadian adult dyspepsia empiric treatment-Helicobacter pylori positive (CADET-Hp) randomised controlled trial. BMJ. 2002 Apr 27;324(7344):1012-6.

Choi IK, Sung HJ, Lee JH, Kim JS, Seo JH. The relationship between Helicobacter pylori infection and the effects of chemotherapy in patients with advanced or metastatic **gastric cancer**. Cancer Chemother Pharmacol. 2012 Oct;70(4):555-8.

Choi IJ, Kook M-C, Kim Y-I, et al. Helicobacter pylori therapy for the **prevention of metachronous gastric cancer**. N Engl J Med 2018; 378: 1085-95.

Colmers-Gray IN, et al. Helicobacter pylori status among patients undergoing **gastroscopy in rural northern Alberta**. Can Fam Physician. 2016 Sep;62(9):e547-54

Crowe SE. **Helicobacter pylori Infection**. N Engl J Med. 2019 Mar 21;380(12):1158-1165.

Czinn SJ. Helicobacter pylori infection: detection, investigation, and management. J Pediatr. 2005 Mar;146(3 Suppl):S21-6.

Deguchi R, et al. Effect of Pretreatment with **Lactobacillus gasseri OLL2716** on First-line Helicobacter pylori Eradication Therapy. J Gastroenterol Hepatol. 2011 Nov 18.

Delaney BC, Qume M, Moayyedi P, et al. **Helicobacter pylori test and treat versus proton pump inhibitor** in initial management of dyspepsia in primary care: multicentre randomised controlled trial (MRC-CUBE trial). BMJ. 2008 Feb 29; [Epub ahead of print] Test and treat and acid suppression are equally cost effective in the initial management of dyspepsia. Empirical acid suppression is an appropriate initial strategy. As costs are similar overall, general practitioners should discuss with patients at which point to consider H pylori testing.

Efrati C, Nicolini G, et al. Helicobacter pylori eradication: **Sequential therapy and Lactobacillus reuteri** supplementation. World J Gastroenterol. 2012 Nov 21;18(43):6250-4.

El-Serag HB, Kao JY, Kanwal F, et al. Houston Consensus Conference on **testing for Helicobacter pylori infection** in the United States. Clin Gastroenterol Hepatol. March 17, 2018.

Fabis Pedrini MJ, Seewann A, et al. Helicobacter pylori infection as a **protective factor against multiple sclerosis risk** in females. J Neurol Neurosurg Psychiatry. 2015 Jan 19.

Fallone CA, Barkun AN, Szilagyi A, Herba KM, Sewitch M, Martel M, Fallone SS. **Prolonged treatment duration** is required for successful Helicobacter pylori eradication with proton pump inhibitor triple therapy in **Canada**. Can J Gastroenterol. 2013 Jul;27(7):397-402.

Fallone CA, Chiba N, van Zanten SV, et al. The **Toronto Consensus** for the Treatment of **Helicobacter pylori Infection in Adults**. Gastroenterology. 2016 Apr 18.
Optimal treatment of H. pylori requires careful attention to local antibiotic resistance and eradication patterns. Quadruple therapies PAMC or PBMT should play a more prominent role in H. pylori eradication and all treatments should be given for 14 days.

Fashner J, Gitu AC. **Diagnosis and Treatment of Peptic Ulcer Disease and H. pylori Infection**. Am Fam Physician. 2015;91(4):236- 242.

FDA has announced approval of a breath test for *Helicobacter pylori* for use in children aged 3 to 17 years. **BreathTek UBT** was previously approved for adult use. The first breath test for use in children ages 3 to 17 years to detect *Helicobacter pylori* (*H. pylori*) bacterial infections, responsible for chronic stomach inflammation (gastritis) and ulcers, was approved by the U.S. Food and Drug Administration (FDA) on Feb. 22, 2012.

Federico A, Nardone G, Gravina AG, et al. Efficacy of 5-day **levofloxacin**- containing concomitant therapy in eradication of Helicobacter pylori infection. Gastroenterology 2012;142:000–000.

Fischbach W, Goebeler ME, et al.; EGILS (European Gastro-Intestinal Lymphoma Study) Group. Most patients with minimal histological residuals of gastric **MALT lymphoma** after successful eradication of Helicobacter pylori can be managed safely by a watch and wait strategy: experience from a large international series. Gut. 2007 Dec;56(12):1685-7. Epub 2007 Jul 16.

Fletcher EH, Johnston DE, Fisher CR, et al. Systematic review: Helicobacter **pylori and the risk of upper gastrointestinal bleeding** risk in patients taking aspirin. Aliment Pharmacol Ther. 2010 Oct;32(7):831-9. doi: 10.1111/j.1365-2036.2010.04415.x.

Ford A, Delaney B, Forman D, Moayyedi P. Eradication therapy for peptic ulcer disease in Helicobacter pylori positive patients. Cochrane Database Syst Rev. 2004 Oct 18;(4):CD003840.

Ford AC, Forman D, Hunt RH, et al. Helicobacter pylori eradication therapy to **prevent gastric cancer** in healthy asymptomatic infected individuals: systematic review and meta-analysis of randomised controlled trials. BMJ. 2014 May 20;348:g3174.

Ford AC, Moayyedi P. **Whom should we "test and treat"** for Helicobacter pylori? BMJ. 2014 May 20;348:g3320.

Ford AC, Forman D, Hunt R, et al. Helicobacter pylori eradication for the **prevention of gastric neoplasia**. Cochrane Database Syst Rev. 2015 Jul 22;7:CD005583.
We found limited, moderate-quality evidence that searching for and eradicating H. pylori reduces the incidence of gastric cancer in healthy asymptomatic infected Asian individuals, but we cannot necessarily extrapolate this data to other populations.

Francavilla R, et al. Improved efficacy of 10d **sequential** treatment for Helicobacter pylori eradication in children:a randomized trial. Gastroenterology.2005 Nov;129(5):1414-9.

Fuccio L, Minardi ME, Zagari RM, Grilli D, Magrini N, Bazzoli F. Meta-analysis: duration of first-line proton-pump inhibitor based triple therapy for Helicobacter pylori eradication. Ann Intern Med. 2007 Oct 16;147(8):553-62.
Available data suggest that extending triple therapy beyond 7 days is unlikely to be a clinically useful strategy. {InfoPOEMs Dec 2007: Seven days of treatment with triple therapy -- a proton pump inibitor (PPI) + clarithromycin (Biaxin) + amoxicillin or metronidazole -- produces rates of eradication that are nearly as good as 10 days to 14 days of treatment, and are equally good if only high-quality research is considered. (LOE = 1a-)}

Fuccio L, Laterza L, Zagari RM, Cennamo V, Grilli D, Bazzoli F. **Treatment of Helicobacter pylori** infection. BMJ. 2008 Sep 15;337:a1454. doi: 10.1136/bmj.a1454.

Fuccio L, Zagari RM, Eusebi LH, et al. Meta-analysis:can Helicobacter pylori eradication treatment reduce the risk for **gastric cancer**? Ann Intern Med. 2009 Jul21;151(2):121-8.

Fukase K, Kato M, Kikuchi S,et al. Japan Gast Study Group. Effect of **eradication of Helicobacter pylori** on incidence of metachronous gastric carcinoma after endoscopic resection of early gastric cancer: an open-label, randomised controlled trial. Lancet. 2008 Aug 2;372(9636):392-7. Prophylactic eradication of H pylori after endoscopic resection of early gastric cancer should be used to prevent the development of metachronous gastric carcinoma.

Furuta T, et al. Effect of **dosing schemes of amoxicillin** on eradication rates of Helicobacter pylori with amoxicillin-based triple therapy. J Clin Pharmacol 2014; 54: 258–66.

Gatta L, Vakil N, Leandro G, Di Mario F, Vaira D. **Sequential Therapy or Triple Therapy** for Helicobacter pylori Infection: Systematic Review and Meta-Analysis of Randomized Controlled Trials in Adults and Children. Am J Gastroenterol. 2009 Oct 20.

Gatta L, Vakil N, Vaira D, et al. **Global eradication rates** for Helicobacter pylori infection: systematic review and meta-analysis of **sequential therapy**. BMJ. **2013** Aug 7;347:f4587.

Gene E, Calvet X, et al. Triple vs quadruple therapy for treating Helicobacter pylori infection: an updated meta-analysis. Aliment Pharmacol Ther. 2003 Sep 1;18(5):543-4. Giannini EG, et al. Can Helicobacter pylori eradication regimens be shortened in clinical practice? An open-label, randomized, pilot study of 4 and 7-day triple therapy with rabeprazole, high-dose levofloxacin, and tinidazole. J Clin Gastroenterol. 2006 Jul;40(6):515-20.

Giannini EG, et al. A study of **4- and 7-day** triple therapy with rabeprazole, high-dose levofloxacin and tinidazole rescue treatment for Helicobacter pylori eradication. Aliment Pharmacol Ther. 2006 Jan 15;23(2):281-7.

Gisbert JP, Pajares JM. Systematic review and meta-analysis: is 1-week proton pump inhibitor-based triple therapy sufficient to heal peptic ulcer? Aliment Pharmacol Ther. 2005 Apr 1;21(7):795-804. CONCLUSION: In pts with peptic ulcer & H. pylori infection, prolonging therapy with proton pump inhibitor after a triple therapy for 7 days with a PPI & two antibiotics is not necessary to induce ulcer healing.

Gisbert JP. Potent gastric acid inhibition in Helicobacter pylori eradication. Drugs. 2005;65 Suppl 1:83-96.

Gisbert JP, et al. Systematic review & meta-analysis: **levofloxacin**-based rescue regimens after H. pylori treatment failure. Aliment Pharmacol Ther. 2006 Jan 1;23(1):35-44.

Gisbert JP, et al.; The H. pylori Study Group of the Asociacion Espanola de Gastroenterologia. Third-line rescue therapy with levofloxacin after two H. pylori treatment failures. Am J Gastroenterol. 2006 Feb;101(2):243-7.

Gisbert JP, Abraira V. Accuracy of Helicobacter pylori Diagnostic Tests in Patients with Bleeding Peptic Ulcer: A Systematic Review and Meta-analysis. Am J Gastroenterol. 2006 Feb 22; [Epub ahead of print]

Gisbert JP, Calvet X. Review article: the effectiveness of **standard triple therapy for Helicobacter pylori has not changed over the last decade**, but it is not good enough. Aliment Pharmacol Ther. 2011 Oct 21. doi:10.1111/j.1365-2036.2011.04887.x.

Gisbert JP, Calvet X, Cosme A, et al. H. pylori Study Group of the Asociación Española de Gastroenterología (Spanish Gastroenterology Association). Long-term follow-up of 1,000 patients **cured of Helicobacter pylori infection following an episode of peptic ulcer** bleeding. Am J Gastroenterol. 2012 Aug;107(8):1197-204.

Graham DY, Lu H, Yamaoka Y. Therapy for Helicobacter pylori Infection Can be Improved : **Sequential Therapy and Beyond**. Drugs. 2008;68(6):725-36.
Graham DY, Fischbach L. Helicobacter pylori treatment in the era of **increasing antibiotic resistance**. Gut. 2010 Aug;59(8):1143-53.
Greenberg ER, Anderson GL, Morgan DR, et al. **14-day triple**, 5-day concomitant, and 10-day sequential therapies for Helicobacter pylori infection in seven Latin American sites: a randomised trial. Lancet 2011; published online July 20.
Harb AH et al. Systematic review and meta-analysis: **Full- vs. half-dose anti-microbials in clarithromycin-based regimens** for Helicobacter pylori eradication. Aliment Pharmacol Ther 2015 May 24.
Harvey RF, Lane JA, Nair P, Egger M, Harvey I, Donovan J, et al. Clinical trial: **prolonged beneficial effect of Helicobacter pylori eradication on dyspepsia** consultations—the Bristol Helicobacter Project. Aliment Pharmacol Ther 2010;32:394-400.
Hassan-Alin M, et al.Studies on drug interactions between **esomeprazole**, amoxicillin and **clarithromycin** in healthy subjects. Int J Clin Pharmacol Ther. 2006 Mar;44(3):119-27.
Hsu PI, et al. A prospective randomized trial of **esomeprazole**-versus pantoprazole-based triple therapy for H. pylori eradication. Am J Gastroenterol. 2005 Nov;100(11):2387-92.
Hsu PI, Lai KH, Lin CK, et al. A Prospective Randomized Trial of **Esomeprazole**- versus Pantoprazole-Based Triple Therapy for Helicobacter pylori Eradication. Am J Gastroenterol. 2005 Nov;100(11):2387-92.
Hsu PI; Tsai FW; Kao SS;et al. **Ten-Day Quadruple** Therapy Comprising Proton Pump Inhibitor, Bismuth, Tetracycline, and Levofloxacin is **More Effective** than Standard **Levofloxacin Triple Therapy** in the Second-Line Treatment of Helicobacter pylori Infection: A Randomized Controlled Trial. Am J Gastroenterol. 2017 Jul 18.
Jafri NS, Hornung CA, Howden CW. Meta-analysis: **Sequential Therapy** Appears Superior to Standard Therapy for Helicobacter pylori Infection in Patients Naive to Treatment. Ann Intern Med. 2008 May 19. [Epub ahead of print] Sequential therapy appears superior to standard triple therapy for eradication of H. pylori infection. If RCTs in other countries confirm these findings, 10-day sequential therapy could become a standard treatment for H. pylori infection in treatment-naive patients.
Jarbol DE, et al. **Proton pump inhibitor or testing** for Helicobacter pylori as the first step for patients presenting with dyspepsia? A cluster-randomized trial. Am J Gastroenterol. 2006 Jun;101(6):1200-8. (InfoPOEMs: A test-and-treat strategy is the most cost-effective approach to dyspepsia in the primary care setting. (LOE = 1b))
Jones NL, Sherman P, et al. Canadian Helicobacter Study Group Consensus Conference: Update on the approach to Helicobacter pylori infection in **children** and adolescents - An evidence-based evaluation. Can J Gastroenterol. 2005 Jul;19(7):399-408.
Kale-Pradhan PB, Mihaescu A, Wilhelm SM. **Fluoroquinolone Sequential Therapy** for Helicobacter pylori: A Meta-analysis. Pharmacotherapy. 2015 Jul 15.
Kavitt RT, Cifu AS. **Management of Helicobacter pylori Infection**. JAMA. 2017 Apr 18;317(15):1572-1573.
Khan S, Sharrack B, Sewell WA. **Metronidazole-induced aseptic meningitis** during Helicobacter pylori eradication therapy. Ann Intern Med 146 (5): 395-6, 2007.
Kuo SH, Yeh KH, Wu MS, et al. Helicobacter pylori eradication therapy is effective in the treatment of early-stage H pylori-positive gastric diffuse large **B-cell lymphomas**. Blood. 2012 May 24;119(21):4838-44.
Laine L, Estrada R, Trujillo M, et al. Effect of proton-pump inhibitor therapy on diagnostic testing for Helicobacter pylori. Ann Intern Med. 1998 Oct 1;129(7):547-50.
Lane JA, Murray LJ, Noble S, et al. Impact of Helicobacter pylori eradication on **dyspepsia**, health resource use, and quality of life in the Bristol helicobacter project: randomised controlled trial. BMJ. 2006 Jan 28;332(7535):199-204. Epub 2006 Jan 20.
Lender N, Talley NJ, Enck P, et al. Review article: associations between **Helicobacter pylori and obesity** - an ecological study. Aliment Pharmacol Ther. 2014 Jul;40(1):24-31.
Levenstein S, Rosenstock S, Jacobsen RK, Jorgensen T. **Psychological Stress** Increases Risk for Peptic Ulcer, Regardless of Helicobacter pylori Infection or Use of Nonsteroidal Anti-inflammatory Drugs. Clin Gastroenterol Hepatol. 2014 Aug 9.
Li B-Z, Threapleton DE, Wang J-Y, et al. **Comparative effectiveness and tolerance of treatments for Helicobacter pylori**: systematic review and network meta-analysis. BMJ 2015;351:h4052.
Liang X, Xu X, Zheng Q, et al. Efficacy of **Bismuth-Containing Quadruple** Therapies for Clarithromycin-, Metronidazole-, and Fluoroquinolone-Resistant Helicobacter pylori Infections in a Prospective Study. Clin Gastroenterol Hepatol. 2013 Jul;11(7):802-807.e1.
Liou JM, Lin JT, Chang CY, et al. **Levofloacin-based and clarithromycxin-based** triple therapies as first-line and second-line treatments for Helicobacter pylori infection: a randomised comparative trial with crossover design. Gut. 2010 May;59(5):572-8.
Liou JM, Chen CC, Chen MJ, et al. Empirical modified sequential therapy containing **levofloxacin and high-dose esomeprazole** in second-line therapy for Helicobacter pylori infection: a multicentre clinical trial. J Antimicrob Chemother. 2011 May 31.
Liou J-M, Chen C-C, Chen MJ, et al, for the Taiwan Helicobacter Consortium. **Sequential versus triple therapy** for the first-line treatment of Helicobacter pylori: a multicentre, open-label, randomised trial. Lancet 2012; online Nov 16.
Liou JM, Chen PY, Luo JC, et al. Efficacies of **Genotypic Resistance-Guided vs Empirical Therapy** for Refractory Helicobacter pylori Infection. Gastroenterology. 2018 Oct;155(4):1109-1119.
Liou JM, et al. **Levofloxacin Sequential Therapy vs Levofloxacin Triple Therapy** in the Second-Line Treatment of Helicobacter pylori: A Randomized Trial. Am J Gastroenterol. 2016 Mar;111(3):381-7.
Liou J-M, Fang Y-J, Chen C-C, et al, for the Taiwan Gastrointestinal Disease and Helicobacter Consortium. Concomitant, **bismuth quadruple**, and 14-day triple therapy in the first-line treatment of Helicobacter pylori: a multicentre, open-label, randomised trial. Lancet 2016; online Oct 18.
Liu KS, Hung IF, Seto WK, et al. **Ten day sequential versus 10 day modified bismuth quadruple** therapy as empirical firstline and secondline treatment for Helicobacter pylori in Chinese patients: an open label, randomised, crossover trial. Gut. 2013 Dec 2.

Luther J, Higgins PD, Schoenfeld PS, Moayyedi P, et al. Empiric **Quadruple vs. Triple** Therapy for Primary Treatment of Helicobacter pylori Infection: Systematic Review and Meta-Analysis of Efficacy and Tolerability. Am J Gastroenterol. 2009 Sep 15.

Luther J, Higgins PD, Schoenfeld PS, et al. Empiric **quadruple vs. triple** therapy for primary treatment of Helicobacter pylori infection: Systematic review and meta-analysis of efficacy and tolerability. Am J Gastroenterol. 2010 Jan;105(1):65-73.

Malfertheiner P, Bazzoli F, Delchier JC, et al. for Pylera Study Group. Helicobacter pylori eradication with a capsule containing **bismuth subcitrate potassium, metronidazole, and tetracycline given with omeprazole versus clarithromycin-based triple therapy**: a randomised, open-label, non-inferiority, phase 3 trial. Lancet. 2011 Feb 22.

Malfertheiner P, Megraud F, O'Morain CA, et al. European Helicobacter Study Group. Management of Helicobacter pylori infection—the **Maastricht IV/ Florence Consensus** Report. Gut. 2012 May;61(5):646-64.

Malfertheiner P, Megraud F, O'Morain CA, et al; **European** Helicobacter and Microbiota Study Group and Consensus panel.. Management of **Helicobacter pylori infection** -the **Maastricht V/Florence Consensus Report**. Gut. 2016 Oct 5.

Mayerle J, den Hoed CM, Schurmann C, et al. Identification of **genetic loci** associated with Helicobacter pylori serologic status. JAMA. 2013;309(18):1912-1920.

Mazzoleni LE, Sander GB, Francesconi CFM, et al. Helicobacter pylori eradication in **functional dyspepsia**: **HEROES** Trial. Arch Intern Med. 2011;171 (21):1929-1936.
For every 8 patients treated with eradication therapy instead of placebo, one additional patient will have a 50% improvement in symptoms 1 year later. However, the range of this estimate is quite large (4.6 - 38.8).

Mazzoleni LE, Francesconi CF, Sander GB. **Mass eradication** of Helicobacter pylori: feasible and advisable? Lancet. 2011 Aug 6;378(9790):462-4.

McColl, Kenneth E.L. **Helicobacter pylori Infection**. N Engl J Med 2010 362: 1597-1604.

McNicholl AG, Linares PM, Nyssen OP, Calvet X, Gisbert JP. Meta-analysis: esomeprazole or rabeprazole vs. first-generation pump inhibitors in the treatment of Helicobacter pylori infection. Aliment Pharmacol Ther. 2012 Sep;36(5):414-25.

Miehlke S, Krasz S, Schneider-Brachert W, et al. Randomized Trial on 14 versus 7 days with esomeprazole, moxifloxacin and amoxicillin for Second-line or Rescue Treatment of Helicobacter pylori Infection. Helicobacter. 2011 Dec;16(6):420-426. doi: 10.1111/j.1523-5378.2011.00867.x.

Micromedex 2013

Moayyedi P, Soo S, Deeks J, et al. Eradication of Helicobacter pylori for **non-ulcer dyspepsia**. Cochrane Database Syst Rev 2006 Apr 19;(2):CD002096.

Molina-Infante J, Romano M, Fernandez-Bermejo M, et al. **Optimized nonbismuth quadruple therapies** cure most patients with Helicobacter pylori infection in populations with **high rates of antibiotic resistance**. Gastroenterology. 2013 Jul;145(1):121-128.e1.

Molina-Infante J, Lucendo AJ, Angueira T, et al; European Registry on H. pylori management(Hp-EuReg); European Registry on H pylori management Hp-EuReg. Optimised empiric **triple and concomitant therapy** for Helicobacter pylori eradication in clinical practice: the **OPTRICON** study. Aliment Pharmacol Ther. 2015 Mar;41(6):581-9.

Morgan DR, al. Risk of **recurrent Helicobacter pylori** infection 1 year after initial eradication therapy in 7 Latin American communities. JAMA. 2013 Feb 13;309(6):578-86.

Murakami K, Sakurai Y, Shiino M, et al. **Vonoprazan**, a novel potassium-competitive acid blocker, as a component of first-line and second-line triple therapy for Helicobacter pylori eradication: a phase III, randomised, double-blind study. Gut. 2016 Mar 2.

Nam SY et al. Effect of **Helicobacter pylori eradication and high-density lipoprotein** on the risk of de novo gastric cancer development. Gastrointest Endosc 2019 Apr 26; [e-pub].

Nam SY, Choi IJ, Ryu KH, et al. Effect of Helicobacter pylori Infection and Its Eradication on **Reflux Esophagitis and Reflux Symptoms**. Am J Gastroenterol. 2010 Jun 22.

Nista EC, et al. **Levofloxacin**-Based Triple Therapy in First-Line Treatment for Helicobacter pylori Eradication. Am J Gastroenterol. 2006 Sep;101(9):1985-90.

Nyssen OP, McNicholl AG, et al. **Sequential versus standard triple first-line therapy** for Helicobacter pylori eradication. Cochrane Database of Systematic Reviews 2016, Issue 6. Art. No.: CD009034. Our meta-analysis indicates that prior to 2008 SEQ was more effective than STT, especially when STT was given for only seven days. Nevertheless, the apparent advantage of sequential treatment has decreased over time, and more recent studies do not show SEQ to have a higher efficacy versus STT when STT is given for 10 days. Based on the results of this meta-analysis, although SEQ offers an advantage when compared with STT, it cannot be presented as a valid alternative, given that neither SEQ nor STT regimens achieved optimal efficacy (≥ 90% eradication rate).

O'Connor A, Gisbert JP, O'Morain C, et al. **Treatment of Helicobacter pylori Infection 2015**. Helicobacter. 2015 Sep;20 Suppl 1:54-61.

Oderda G, Rapa A, Bona G. A systematic review of Helicobacter pylori eradication treatment schedules in **children**. Aliment Pharmacol Ther. 2000 Oct;14 Suppl 3:59-66.

Ozdil K, Calhan T, Sahin A, et al. **Levofloxacin** based sequential and triple therapy compared with standart plus probiotic combination for helicobacter pylori eradication. Hepatogastroenterology. 2011 Jul-Aug;58(109):1148-52.

Pan KF, Zhang L, Gerhard M, et al. A large randomised controlled intervention trial to **prevent gastric cancer by eradication of Helicobacter pylori** in Linqu County, China: baseline results and factors affecting the eradication. Gut. 2015 May 18.

Park CS, Lee SM, Park CH, et al. Pretreatment Antimicrobial **Susceptibility-Guided Vs. Clarithromycin-Based** Triple Therapy for Helicobacter pylori Eradication in a Region With High Rates of Multiple Drug Resistance. Am J Gastroenterol. 2014 Aug 5.

Pierantozzi M, et al. Helicobacter pylori eradication and l-dopa absorption in patients with PD and motor fluctuations. Neurology. 2006 Jun 27;66(12):1824-9.

Prasertpetmanee S, Mahachai V, Vilaichone RK. Improved Efficacy of Proton Pump Inhibitor - Amoxicillin - Clarithromycin Triple Therapy for Helicobacter pylori Eradication in Low Clarithromycin Resistance Areas or for Tailored Therapy. Helicobacter. 2013 Jan 29. (14 days treatment)

Raju D, Hussey S, Ang M, et al. **Vacuolating cytotoxin and variants in Atg16l1** that disrupt autophagy promote Helicobacter pylori infection in humans. Gastroenterology 2012;142:1160–1171.

Ramakrishnan K, Salinas RC. Peptic ulcer disease. Am Fam Physician. 2007 Oct 1;76(7):1005-12.

Rees K, Stowe R, Patel S, et al. Helicobacter pylori eradication for **Parkinson's disease**. Cochrane Database Syst Rev. 2011 Nov 9;(11):CD008453. There is currently a lack of evidence on the effects of screening and treating H pylori in patients with Parkinson'sdisease. There is limited evidence to suggest that H Pylori eradication improves the absorption of levodopa and

improves motor symptoms.

Ren Q, Yan X, Zhou Y, et al. **Periodontal therapy** as adjunctive treatment for gastric Helicobacter pylori infection. Cochrane Database Syst Rev. 2016 Feb 7;2:CD009477.
Overall, periodontal therapy could increase the efficiency of H. pylori eradication and the non-recurrence rate of gastricH. pylori. In view of the limited number and quality of included studies, it will be necessary to conduct more well-designed, multicenter, and large-scale RCTs to determine the effects of periodontal therapy in eradicating gastric H. pylori and suppressing the recurrence of this bacterium in the stomach.

Rokkas T, Sechopoulos P, Robotis I, Margantinis G, Pistiolas D. Cumulative H. pylori eradication rates in clinical practice by adopting first and second-line regimens proposed by the **Maastricht III consensus** and a third-line empirical regimen. Am J Gastroenterol. 2009 Jan;104(1):21-5. A sequence of 3 strategies was successful in eradicating H. pylori in 89% of patients by intention-to-treat analysis and in 98% of patients by per-protocol analysis. (LOE = 2b)

Ruggiero F, Elena L, Stefania C et al. **Clarithromycin-Resistant Genotypes** and Eradication of Helicobacter Pylori, The Journal of Pediatrics, Vol 157, Issue 2, Aug10, 228-232.

Sabbi T, et al. Efficacy of noninvasive tests in the diagnosis of Helicobacter pylori infection in **pediatric** patients. Arch Pediatr Adolesc Med 2005; 159:238-41. (InfoPOEMs: In children with significant & persistent or recurrent symptoms of upper gastrointestinal disease, fecal antigen testing for Helicobacter pylori is more reliable than serology. Although not part of this study (since serology is unreliable for monitoring response to treatment), direct testing of the stool also provides a more reliable means of evaluating treatment response.(LOE = 1c-))

Saad RJ, et al. **Levofloxacin**-based triple therapy versus bismuth-based quadruple therapy for persistent Helicobacter pylori infection: a meta-analysis. Am J Gastroenterol. 2006 Mar;101(3):488-96. (InfoPOEMs: A 10-day regimen of levofloxacin, amoxicillin, and a proton pump inhibitor (PPI) is more effective and better tolerated than the traditional 7-day 4-drug bismuth-based regimen for patients who have persistent Helicobacter pylori (HP) infection despite previous treatment. (LOE = 1a)) (see also Pharmacist's Letter: Levofloxacin for Persistent H. Pylori Infection, May 2006)

Saad AM, Choudhary A, Bechtold ML. Effect of Helicobacter **pylori treatment on gastroesophageal reflux disease** (GERD): meta-analysis of randomized controlled trials. Scand J Gastroenterol 2012;47:129-35

Sarker SA, Mahmud H, et al. Causal relationship of Helicobacter pylori with iron-deficiency anemia or failure of iron supplementation in children. Gastroenterology. 2008 Nov;135(5):1534-42. Epub 2008 Aug 5. H pylori is neither a cause of IDA/ID nor a reason for treatment failure of iron supplementation in young Bangladeshi children.

Scaccianoce G, et al. Helicobacter pylori eradication with either 7day or 10day triple therapies, and with a 10-day **sequential** regimen. Can J Gastroenterol. 2006 Feb;20(2):113-7.

Spee, Leo A. A., Madderom, MB., Pijpers, M, et al. Association Between Helicobacter pylori and **Gastrointestinal Symptoms** in **Children**. Pediatrics 2010 125: e651-e669.

Sugano K, et al; faculty members of Kyoto Global Consensus Conference. **Kyoto global consensus report** on Helicobacter pylori gastritis. Gut. 2015 Sep;64(9):1353-67.

Szajewska H, Horvath A, Piwowarczyk A. Meta-analysis: the effects of **Saccharomyces boulardii** supplementation on Helicobacter pylori eradication rates and side effects during treatment. Aliment Pharmacol Ther. 2010 Nov;32(9):1069-79. doi: 10.1111/j.1365-2036.2010.04457.x.

Talbert M, Close E, Cooke A, Garrett W, Nashelsky J. **H. pylori Screening Before Initiation of Long-term NSAIDs**. Am Fam Physician. 2019 Jun 15;99(12):783-784.

Talley NJ, Fock KM, Moayyedi P. Gastric Cancer Consensus conference recommends Helicobacter pylori screening and treatment in asymptomatic persons from high-risk populations to prevent **gastric cancer**. Am J Gastroenterol. 2008 Mar;103(3):510-4.

Tay CY, Windsor HM, Thirriot F, Lu W, Conway C, Perkins TT, Marshall BJ. Helicobacter pylori eradication in Western Australia using **novel quadruple therapy combinations**. Aliment Pharmacol Ther. 2012 Oct 16.

Tepes B, O'Connor A, Gisbert JP, O'Morain C. **Treatment of Helicobacter pylori infection 2012**. Helicobacter. 2012 Sep;17 Suppl 1:36-42.

Treatment Guidelines: Drugs for **Peptic Ulcers & GERD**. **The Medical Letter**: February, **2004**; 2(18) pp. 9-12. New & Updated August 2008. **New & Updated Sept 2011**

Treatment Guidelines: Drugs for **Helicobacter pylori infection**. **The Medical Letter**: July, **2017.**

Vaira D, et al. **Sequential** therapy versus standard triple-drug therapy for Helicobacter pylori eradication: a randomized trial. Ann Intern Med. 2007 Apr 17;146(8):556-63. n=300
Sequential therapy is statistically significant compared with standard therapy for eradicating H. pylori infection and is statistically significantly more effective in patients with clarithromycin-resistant strains. Side effects are similar with both treatment regimens and are rarely severe enough to cause discontinuation of therapy.

Valle PC, et al. "Test, score and scope": a selection strategy for safe reduction of upper gastrointestinal endoscopies in young dyspeptic patients referred from primary care. (InfoPOEMs: For men younger than 45 years, the endoscopic yield is very low for those without Helicobacter pylori infection, nonsteroidal anti-inflammatory drug (NSAID) use, unintended weight loss, or anemia. (LOE = 2b))

Veldhuyzen van Zanten SJ, Chiba N, Armstrong D, Barkun A, Thomson A, et al. A randomized trial comparing omeprazole, ranitidine, cisapride, or placebo in helicobacter pylori negative, primary care patients with dyspepsia: the CADET-HN Study. Am J Gastroenterol. 2005 Jul;100(7):1477-88. Treatment with omeprazole provides superior symptom relief compared to ranitidine, cisapride, and placebo in the treatment of H. pylori negative primary care dyspepsia patients.

Vergara M, Vallve M, Gisbert JP, Calvet X. Meta-analysis: comparative efficacy of different proton-pump inhibitors in triple therapy for Helicobacter pylori eradication. Aliment Pharmacol Ther. 2003 Sep 15;18(6):647-54. The efficacy of various proton-pump inhibitors seems to be similar when used for H. pylori eradication in standard triple therapy.

Vergara M, Catalán M, Gisbert JP, Calvet X. Meta-analysis: role of Helicobacter **pylori eradication in the prevention of peptic ulcer in NSAID** users. Aliment Pharmacol Ther. 2005 Jun 15;21(12):1411-8.

Villoria A, Garcia P, Calvet X, Gisbert JP, Vergara M. Meta-analysis: high-dose proton pump inhibitors vs. standard dose in triple therapy for Helicobacter pylori eradication. Aliment Pharmacol Ther. 2008 Oct 1;28(7):868-77.

Wang C, Yuan Y, Hunt RH. Helicobacter pylori infection and **Barrett's esophagus**: a systematic review and meta-analysis. Am J Gastroenterol. 2009 Feb;104(2):492-500.

Wang Z, Shaheen NJ, Whiteman DC, et al. Helicobacter pylori infection is **associated with reduced risk of Barrett's esophagus**: an analysis of the Barrett's and esophageal adenocarcinoma consortium. Am J Gastroenterol. 2018

Wilhelm SM, Johnson JL, Kale-Pradhan PB. Treating bugs with bugs: the role of **probiotics** as adjunctive therapy for Helicobacter pylori.

Ann Pharmacother. 2011 Jul;45(7-8):960-6.
Wong AY, Wong IC, et al. Association Between Acute **Neuropsychiatric Events** and Helicobacter pylori Therapy Containing **Clarithromycin**. JAMA Intern Med. 2016 May 2
Wong BC, Lam SK, et al. Helicobacter pylori eradication to **prevent gastric cancer** in a high-risk region of China: a randomized controlled trial. JAMA 2004; 291: 187–94.
Wündisch T, Dieckhoff P, Greene B, et al. Second Cancers and Residual Disease in Patients Treated for Gastric Mucosa-Associated Lymphoid Tissue Lymphoma by Helicobacter pylori Eradication and Followed for 10 Years. Gastroenterology. 2012 Oct;143(4):936-42.
Yang J, Zhang Y, Fan L, et al. Eradication Efficacy of **Modified Dual Therapy Compared with Bismuth-Containing Quadruple Therapy** as a First-Line Treatment of Helicobacter pylori. Am J Gastroenterol. 2019 Feb 25.
Yang JC, Lin CJ, Wang HL, et al. **High-dose Dual Therapy** Is Superior to **Standard First-line or Rescue Therapy** for Helicobacter pylori Infection. Clin Gastroenterol Hepatol. 2014 Nov 14.
Yeo YH, et al. First-line Helicobacter pylori eradication therapies in countries with **high and low clarithromycin resistance**: a systematic review and network meta-analysis. Gut. 2016 Sep 26.
Yuan Y, Ford AC, Khan KJ, Gisbert JP, Forman D, Leontiadis GI, Tse F, Calvet X, Fallone C, Fischbach L, Oderda G, Bazzoli F, Moayyedi P. Optimum duration of regimens for Helicobacter pylori eradication. Cochrane Database Syst Rev. 2013 Increasing the duration of PPI-based triple therapy increases H. pylori eradication rates. For PCA, prolonging treatment duration from 7 to 10 or from 10 to 14 days is associated with a significantly higher eradication rate. The optimal duration of therapy for PCA and PAN is at least 14 days. More data are needed to confirm if there is any benefit of increasing the duration of therapy for PCN therapy. Information is limited for regimens other than PPI triple therapy; more studies are needed to draw meaningful conclusions for optimal duration of other H. pylori eradication regimens.
Zapata-Colindres JC,et al. The association of **Helicobacter pylori infection and nonsteroidal anti-inflammatory drugs** in peptic ulcer disease. Can J Gastroenterol. 2006 Apr;20(4):277-80. The development of PUD was observed earlier in the combined H pylori and NSAID group than in patients with only NSAID use. This suggests a synergic effect between the two risks factors in the development of PUD.
Zagari RM, et al. Comparison of **one and two weeks** of omeprazole, amoxicillin and clarithromycin treatment for Helicobacter pylori eradication: the HYPER study. Gut. 2006 Oct 6; [Epub ahead of print] n=909 One-week and two-week PPI-based triple therapies (omeprazole, amoxicillin and clarithromycin) for H. pylori eradication are similar in terms of efficacy, safety and patient compliance.
Zagari RM, Bianchi-Porro G, et al. Comparison of 1 and 2 weeks of omeprazole, amoxicillin and clarithromycin treatment for Helicobacter pylori eradication: the HYPER Study. Gut. 2007 Apr;56(4):475-9. Epub 2006 Oct 6. n=909. CONCLUSIONS: 1-week and 2-week triple treatments for H pylori eradication are similar in terms of efficacy, safety and patient compliance. (InfoPOEMs: One week of omeprazole, amoxicillin, and clarithromyin given twice daily is as effective at eradicating Helicobacter pylori (HP) as 2 weeks of treatment. It also costs less and is less burdensome for patients. (LOE = 1b))
Zeng M, Mao Z-H, Li J-X, et al. Efficacy, safety, and immunogenicity of an **oral recombinant Helicobacter pylori vaccine** in children in China: a randomised, double-blind, placebo-controlled, phase 3 trial. Lancet 2015; online July 1.
Zhang W, Chen Q, Liang X, et al. **Bismuth, lansoprazole, amoxicillin and metronidazole or clarithromycin** as first-line Helicobacter pylori therapy. Gut. 2015 Sep 2.
Zhang YW, Hu WL, Cai Y, et al. Outcomes of **furazolidone- and amoxicillin-based quadruple therapy** for Helicobacter pylori infection and predictors of failed eradication. World J Gastroenterol. 2018 Oct 28;24(40):4596-4605.
Zojaji H, Talaie R, Mirsattari D, et al. The efficacy of Helicobacter pylori eradication regimen with and without **vitamin C** supplementation. Dig Liver Dis. 2009 Jun 1. [Epub ahead of print] Addition of vitamin C to H. pylori treatment regimen of amoxicillin, metronidazole and bismuth can significantly increases H. pylori eradication rate.
Zullo A, et al. High rate of H. pylori eradication with **sequential therapy** in elderly pts with peptic ulcer:a prospective controlled study.Aliment Pharmacol Ther.2005;21:1419-24.
Zullo A, Hassan C, Andriani A, et al.. Eradication Therapy for Helicobacter pylori in Patients With Gastric **MALT Lymphoma**: A Pooled Data Analysis. Am J Gastroenterol. 2009 Jun 16. [Epub ahead of print] This was the first comprehensive (approximately 1,300 patients) analysis of the therapeutic management of H. pylori in gastric lymphoma patients. Data suggest that this infection is easily managed in these patients, being cured in nearly all cases.

USA for IBS-C: Lubiprostone AMITIZA 8-24ug po BID cc, ♀ ≥18yr, AE: anorexia, N/D, dyspnea; **Plecanatide TRULANCE** 3mg po daily & **Tenapanor IBSRELA** 50mg po tab bid ac, AE: diarrhea, CI: GI obstruction.

Extras: IRRITABLE BOWEL SYNDROME (IBS)

Legend
ς =scored tablet χ =Non-formulary SK ☎=EDS in SK ✆=prior approval NIHB ⊗=not NIHB ▼=covered NIHB ⌂= NIHB Palliative Care Formulary **BBB**=blood brain barrier **BP**=blood pressure **CBT**=cognitive behaviour therapy **CD**=crohn's disease **CIC**=chronic idiopathic constipation **CV**=cardiovascular **FIT**=fecal immunochemical test **hx**=history **IBD**=irritable bowel disease **mo**=months **SJW**=St. John's Wort **sx**=symptom **UC**=ulcerative colitis

Discontinued Drugs: Alosetron LOTRONEX (2000 -severe constipation & ischemic colitis) 0.5-1mg bid, avail. in USA for women only. Not avail. in Canada.

Tegaserod ZELNORM: Mar07- suspended due to CV ischemic events; but Apr08-FDA for Emergency IND situations only use in IBS-constipation & chronic idiopathic constipation in ♀<55yr with no hx of heart problems. 6 mg po bid $160 (NNT=14) 5HT4 agonist
Not avail in Canada. Oct/18: FDA panel agrees to approve. **Apr/19: FDA approved for women <65yrs with IBS-C, but CI: if history of MI, stroke, TIA or angina**.

Acupuncture: no difference in IBS symptom severity or IBS-related quality of life when compared to sham-acupuncture.[81]

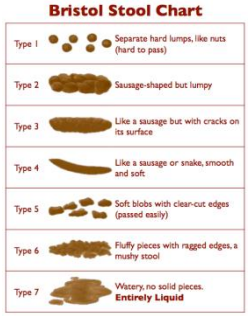
Patient Handout https://www.nice.org.uk/guidance/cg61/ifp/chapter/managing-irritable-bowel-syndrome#diet

FODMAPs: fermentable oligosaccharides, disaccharides, monosaccharides, and polyols (FODMAPs) may be effective in reducing some IBS symptoms. FODMAPs are poorly absorbed, rapidly fermented short-chain carbohydrates that can increase gas production and induce osmosis in the intestinal lumen, causing bloating and abdominal pain. Some common sources of FODMAPs are apples, cherries, onions, garlic, milk, yogurt, wheat, and high fructose corn syrup. Medical Letter 2016

FMT: Fecal Microbiota Transplantation restore the gut endocrine cells to the level of healthy subjects.

Notes:

- Children with IBS or functional abdominal pain: probiotic Lactobacillus rhamnosus GG 3 billion colony forming units twice daily reduced # of pain episodes & pain intensity by ≥50% more in tx vs Pl group (8wks; ave age 6).[53]
- A high-fibre diet and increased frequency of bowel movements may not protect against diverticulosis.[72]



References – IBS – www.RxFiles.ca {Originally prepared by Lynette Kolodziejak for the RxFiles Academic Detailing Program}

1. Micromedex. 2018.
2. Association CP. *Compendium of Pharmaceuticals and Specialties*; 2010.
3. Briggs G, Freeman, Roger, Yaffe, Sumner, ed. *Drugs in **Pregnancy** and Lactation.* 9th ed: TechBooks 2011.
   Weinberg DS, Smalley W, Heidelbaugh JJ, Sultan S. American gastroenterological association (**AGA**) institute guideline on the pharmacological management of irritable bowel syndrome. Gastroenterology. 2014 Nov;147(5):1146-8.
4. Kumar A KN, Vij JC, Sarin SK, Anand BS. Optimum dosage of ispaghula husk in patients with irritable bowel syndromw: correlation of symptom relief with whole gut transit time and stool weight. *Gut.* 1987;28(2):150-155.
5. Zuckerman MJ. The role of **fibre** in the treatment of irritable bowel syndrome: therapeutic recommendations. *J Clin Gastroenterol.* Feb 2006;40(2):104-108.
6. Efskind PS BT, Vatn MH. A double-blind placebo-controlled trial with **loperamide** in irritable bowel syndrome. *Scandanvian Journal of Gastroenterology.* 1996;31:463-468.
7. Cann PA RN, Holdsworth CD et al. Role of **loperamide** and placebo in management of irritable bowel syndrome (IBS). *Digestive diseases and sciences.* 1984;29:239-247.
8. Hadley SK, Gaarder SM. **Treatment** of irritable bowel syndrome. *Am Fam Physician.* Dec 15 2005;72(12):2501-2506.

9. Wald A. **Psychotropic** Agents in Irritable Bowel Syndrome. *J Clin Gastroenterol.* 2002;35(Suppl):S53-S57.

10. Abramowicz M. **Treatment** Guidelines: Drugs for Irritable Bowel Syndrome. *The Medical Letter.* Mar 2006;4(43):11-16.(also July 2011, & **Sep 2016**)

11. Tabas G BM, Wang J, Friday P, Mardini H, Arnold G. **Paroxetine** to treat Irritable Bowel Syndrome not responding to high-fibre diet: a double-blind, placebo-controlled trial. *American Journal of Gastroenterology.* 2004;99(5):914-920.

12. Vahedi H, Merat S, Rashidioon A, Ghoddoosi A, Malekzadeh R. The effect of **fluoxetine** in patients with pain and constipation-predominant irritable bowel syndrome: a double-blind randomized-controlled study. *Aliment Pharmacol Ther.* Sep 1 2005;22(5):381-385.

13. Talley NJ KJ, Boyce P, Tennant C, Huskie S, Jones M. **Antidepressant** Therapy (Imipramine and Citalopram) for Irritable Bowel Syndrome: A double-blind, randomized, placebo-controlled trial. *Digestive diseases and sciences*; 2007.

14. DiPiro, ed. **Pharmacotherapy***: A Pathophysiologic Approach.* 6th ed. New York: McGraw-Hill Companies; 2005.

15. Paterson WG, Thompson WG, Vanner SJ, et al. Recommendations for the **management** of irritable bowel syndrome in family practice. IBS Consensus Conference Participants. *Cmaj.* Jul 27 1999;161(2):154-160.

16. Evidence-based position statement on the **management** of irritable bowel syndrome in North America. *Am J Gastroenterol.* Nov 2002;97(11 Suppl):S1-5.

17. American Gastroenterological Association medical **position** statement: irritable bowel syndrome. *Gastroenterology.* Dec 2002;123(6):2105-2107.

December 18, 2008 -- The **American College of Gastroenterology (ACG)** has today published a new evidence-based systematic review on the management of Irritable Bowel Syndrome (IBS) as a supplement to the **January 2009** issue of *The American Journal of Gastroenterology*. "For the gastroenterologist seeing patients with IBS, the new ACG recommendations specify whether or not the range of potential therapies are better than placebo for resolving IBS symptoms," said Lawrence J. Brandt, MD, ACG IBS Task Force, Bethesda, Maryland. The ACG Evidence-Based Systematic Review on IBS can be accessed here: **http://www.acg.gi.org/media/releases/ajg_ibs_supp_0109.pdf**

American College of Gastroenterology (ACG) Task Force on Irritable Bowel Syndrome, Brandt LJ, Chey WD, Foxx-Orenstein AE, et al. An evidence-based position statement on the management of irritable bowel syndrome. Am J Gastroenterol. 2009 Jan;104 Suppl 1:S1-35.

18. Pharmacist's Letter. FDA Permits restricted use of **Zelnorm** for Qualifying patients. Sept 2007.

April/08 FDA: Zelnorm for Emergency use only http://www.fda.gov/cder/drug/infopage/zelnorm/default.htm

19. Wilson, J. Irritable Bowel Syndrome: In the clinic. Annals of Int Med. 2007, July.

20. Jailwala J, et al. Pharmacologic treatment of IBS: a systematic review of randomized, controlled trials. Ann Intern Med. 2000 Jul 18;133(2):136-47.

21. Irritable bowel syndrome in adults: diagnosis and management of irritable bowel syndrome in primary care **NICE** Guidelines Feb/08 http://www.nice.org.uk/guidance/index.jsp?action=byID&o=11927#summary

22. Heaton KW, Radvan J, Cripps H, Mountford RA, Braddon FE, Hughes AO. Defecation frequency and timing, and stool form in the general population: a prospective study. Gut. 1992 Jun;33(6):818-24. (Type 1: separate hard lumps, like nuts, Type 2: sausage shaped but lumpy, Type 3: Like sausage or snake but with cracks on its surface, Type 4: Like sausage or snake, smooth and soft, Type 5: Soft blobs with clear cut edges, Type 6: Fluffy pieces with ragged edges, a mushy stool , Type 7: Watery, no solid pieces, entirely liquid)

23. Vahedi H, et al. Clinical trial: the effect of amitriptyline in patients with diarrhoea-predominant irritable bowel syndrome. Aliment Pharmacol Ther. 2008 Apr;27(8):678-84. Epub 2008 Jan 30. **Amitriptyline 10mg** daily may be effective in the treatment of diarrhoea-predominant irritable bowel syndrome and at low dose is well tolerated.

24. Mayer EA. Clinical practice. **Irritable bowel syndrome**. N Engl J Med. 2008 Apr 17;358(16):1692-9.

25. Drossman DA. The functional gastrointestinal disorders and **Rome III** process. Gastroenterology. 2006 Apr;130(5):1377-90. http://www.romecriteria.org

26. Drossman DA, Toner BB, Whitehead WE, et al. **Cognitive-behavioral therapy** versus education and desipramine versus placebo for moderate to severe functional bowel disorders. Gastroenterology. 2003 Jul;125(1):19-31.

27. Spiller R, Aziz Q, Creed F, et al. Clinical Services Committee of The **British** Society of Gastroenterology. **Guidelines** on the irritable bowel syndrome: mechanisms and practical management. Gut. 2007 Dec;56(12):1770-98. Epub 2007 May 8.

28. Wilhelm SM, Brubaker CM, Varcak EA, Kale-Pradhan PB. Effectiveness of probiotics in the treatment of irritable bowel syndrome. Pharmacotherapy. 2008 Apr;28(4):496-505. As probiotics have shown benefit and possess a favorable adverse-effect profile, their use may represent an option for symptom relief in patients with IBS. However, additional data are necessary before probiotics can become a standard of care in the treatment of IBS.

Additional References (post Feb 2008)

29. Bahar RJ, Collins BS, Steinmetz B, Ament ME. Double-blind placebo-controlled trial of amitriptyline for the treatment of irritable bowel syndrome in adolescents. J Pediatr 2008;152:685-9.

30. Vahedi H, Merat S, Momtahen S, Kazzazi AS, et al. Clinical trial: the effect of amitriptyline in patients with diarrhoea-predominant irritable bowel syndrome. Aliment Pharmacol Ther. 2008;27:678-84.

31. Camilleri M, Kerstens R, Rykx A, Vandeplassche L. A placebo-controlled trial of prucalopride for severe chronic constipation. N Engl J Med. 2008 May 29;358(22):2344-54. n=620. Over 12 weeks, prucalopride 2-4mg po daily x 12 weeks significantly improved bowel function and reduced the severity of symptoms in patients with severe chronic constipation. Larger and longer trials are required to further assess the risks and benefits of the use of prucalopride for chronic constipation.

32. Ford AC, Talley NJ, et al. Effect of **fibre, antispasmodics, and peppermint oil** in the treatment of irritable bowel syndrome: systematic review and meta-analysis. BMJ. 2008 Nov 13;337:a2313. doi: 10.1136/bmj.a2313. Fibre, antispasmodics, & peppermint oil were all more effective than placebo in treatment of irritable bowel syndrome. Fibre provides minimal likelihood of benefit in patients with irritable bowel syndrome (IBS). Antispasmodics, particularly scopolamine (hyoscine) and otilonium, are effective in 50% to 70% of patients. Peppermint oil is also effective, with approximately 75% of patients responding (number needed to treat = 2.5). (LOE = 1a-)
33. Moayyedi P, Ford AC, Talley NJ, et al. The efficacy of **probiotics** in the therapy of irritable bowel syndrome: a systematic review. Gut. 2008 Dec 17. [Epub ahead of print]
    Probiotics appear to be efficacious in IBS but the magnitude of benefit and the most effective species and strain are uncertain.
34. Nikfar S, Rahimi R, Rahimi F, Derakhshani S, Abdollahi M. Efficacy of **probiotics** in irritable bowel syndrome: a meta-analysis of randomized, controlled trials. Dis Colon Rectum. 2008 Dec;51(12):1775-80. Epub 2008 May 9. This systematic review/meta-analysis of randomized trials found a significant benefit of probiotics (number needed to treat [NNT] = 12) for improving symptoms of irritable bowel syndrome (IBS). Given the frequent difficulty in adequately treating this illness and the generally benign effects of probiotics, clinicians should strongly consider them for their patients with IBS. (LOE = 1a)b
35. Jones R. Treatment of irritable bowel syndrome in **primary care**. BMJ. 2008 Nov 13;337:a2213. doi: 10.1136/bmj.a2213.
36. Ford AC, Talley NJ, Schoenfeld PS, Quigley EM, Moayyedi P. Efficacy of **Antidepressants** and Psychological Therapies in Irritable Bowel Syndrome: Systematic Review and Meta-analysis. Gut. 2008 Nov 10. [Epub ahead of print]
37. Zijdenbos IL, de Wit NJ, van der Heijden GJ, Rubin G, Quartero AO. **Psychological treatments** for the management of irritable bowel syndrome. Cochrane Database Syst Rev. 2009 Jan 21;(1):CD006442. Psychological interventions may be slightly superior to usual care or waiting list control conditions at the end of treatment although the clinical significance of this is debatable. Except for a single study, these therapies are not superior to placebo and the sustainability of their effect is questionable. The meta-analysis was significantly limited by issues of validity, heterogeneity, small sample size and outcome definition. Future research should adhere to current recommendations for IBS treatment trials and should focus on the long-term effects of treatment.
38. Ford AC, Talley NJ, Veldhuyzen van Zanten SJ, Vakil NB, Simel DL, Moayyedi P. Will the **history and physical** examination help establish that irritable bowel syndrome is causing this patient's lower gastrointestinal tract symptoms? JAMA. 2008 Oct 15;300(15):1793-805.
39. Agrawal A, Whorwell PJ. **Irritable bowel syndrome**: diagnosis and management. BMJ. 2006 Feb 4;332(7536):280-3.
40. Ford AC, et al. Efficacy of **5-HT3 antagonists** and **5-HT4 agonists** in IBS: systematic review and meta-analysis. Am J Gastroenterol. 2009 Jul;104(7):1831-43; quiz 1844.
41. Jones R, Rubin G. Acute **diarrhoea** in adults (Post Infective IBS). BMJ. 2009 Jun 15;338:b1877. doi: 10.1136/bmj.b1877.
42. 1) Bijkerk C J, de Wit N J, Muris J W M, et al. Soluble or insoluble fibre in irritable bowel syndrome in primary care? Randomised placebo controlled trial. BMJ 2009;339:b3154,
    doi: 10.1136/bmj.b3154 (Published 27 August 2009).
    2) Luther J, Chey WD. ACP Journal Club. Psyllium increased symptom relief in patients with the irritable bowel syndrome more than bran or placebo. Ann Intern Med. 2010 Jan 19;152(2):JC1-11. PubMed PMID: 20083814.
43. Saps M, Youssef N, Miranda A, Nurko S, et al. Multicenter, Randomized, Placebo-Controlled Trial of **Amitriptyline in Children** With Functional Gastrointestinal Disorders. Gastroenterology. 2009 Jul 30. [Epub ahead of print] Both amitriptyline and placebo were associated with excellent therapeutic response.
44. **WGO Practice Guidelines** Irritable bowel syndrome: a global perspective - April 2009
    http://www.worldgastroenterology.org/assets/downloads/en/pdf/guidelines/20_irritable_bowel_syndrome.pdf
45. Saito YA, Rey E, Almazar-Elder AE, et al. A randomized, double-blind, placebo-controlled trial of **St John's wort** for treating irritable bowel syndrome. Am J Gastroenterol. 2010 Jan;105(1):170-7.Epub 2009 Oct 6. SJW was a less effective treatment for IBS than placebo.
46. Chey WD, Nojkov B, Rubenstein JH, et al. The Yield of **Colonoscopy** in Patients With Non-Constipated Irritable Bowel Syndrome: Results From a Prospective, Controlled US Trial. Am J Gastroenterol. 2010 Feb 23. The prevalence of structural abnormalities of the colon is no higher in suspected non-constipation IBS patients than in healthy controls. Microscopic colitis can be identified in a small proportion of persons with IBS sx.
47. Jung HK et al. Diarrhea-predominant irritable bowel syndrome is associated with **diverticular** disease: A population-based study. Am J Gastroenterol 2010 Mar; 105:652. These results indicate that the association between diverticulosis and IBS is real and that it is stronger for diarrhea-predominant IBS and mixed or alternating IBS than for constipation-predominant IBS.
48. Wedlake L, A'Hern R, Russell D, Thomas K, Walters JR, Andreyev HJ. Systematic review: the prevalence of idiopathic **bile acid malabsorption** as diagnosed by SeHCAT scanning in patients with **diarrhoea-predominant** irritable bowel syndrome. Aliment Pharmacol Ther. 2009 Oct;30(7):707-17.
49. Primavera G, Amoroso B, et al. Clinical utility of Rome criteria managing functional gastrointestinal disorders in **pediatric** primary care. Pediatrics. 2010 Jan;125(1):e155-61.
50. Friedrich M, Grady SE, Wall GC. Effects of **antidepressants** in patients with irritable bowel syndrome and comorbid depression. Clin Ther. 2010 Jul;32(7):1221-1233.
51. Zhou Q, Souba WW, Croce CM, et al. **MicroRNA-29a** regulates intestinal membrane permeability in patients with irritable bowel syndrome. Gut. 2010 Jun;59(6):775-84.

52. Moayyedi P, Ford AC, Talley NJ, et al. The efficacy of **probiotics** in the treatment of irritable bowel syndrome: a systematic review. Gut. 2010 Mar;59(3):325-32. Epub 2008 Dec 17. Probiotics appear to be efficacious in IBS, but the magnitude of benefit and the most effective species and strain are uncertain.
53. Francavilla R, Miniello V, Magistà AM, et al. A Randomized Controlled Trial of **Lactobacillus GG** in Children With Functional Abdominal Pain. Pediatrics. 2010 Nov 15.
54. Pimentel Mark, Lembo Anthony, Chey William D. et al.. for the **TARGET** Study Group. **Rifaximin** Therapy for Patients with Irritable Bowel Syndrome without Constipation. N Engl J Med 2011; 364:22-32.
55. Ford AC, Suares NC. Effect of laxatives and pharmacological therapies in **chronic idiopathic constipation**:systematic review and meta-analysis.Gut.2011Feb;60(2):209-18.
56. Crowe Sheila E. In the Clinic: **Celiac Disease**. *Ann Intern Med* May 3, 2011 154:ITC5-1.
57. Smith Janette, Humes David J, Spiller Robin C. Uncertainties Page: Should we treat uncomplicated symptomatic **diverticular disease with fibre**? BMJ 2011;342.
58. Tabbers Merit M., Chmielewska Ania, Roseboom Maaike G., et al. Fermented Milk Containing **Bifidobacterium lactis DN-173 010** in Childhood Constipation: A Randomized, Double-Blind, Controlled Trial. Pediatrics 2011; 127:6 e1392-e1399; published ahead of print May 23, 2011, doi:10.1542/peds.2010-2590
59. Liu JP, Yang M, Liu Y, et al. **Herbal medicines** for treatment of irritable bowel syndrome. Cochrane Database of Systematic Reviews 2006, Issue 1. Art. No.: CD004116. DOI: 10.1002/14651858.CD004116.pub2.
60. Crowe FL, Appleby PN, Allen NE, Key TJ. Diet and risk of **diverticular disease** in Oxford cohort of European Prospective Investigation into Cancer and Nutrition (EPIC): prospective study of British vegetarians and non-vegetarians. BMJ 2011;343:d4131. (**Vegetarian and high-fibre diets** are each associated with lower risk for hospitalization or death from diverticular disease)
61. Kaminski A, Kamper A, Thaler K, et al. **Antidepressants for the treatment of abdominal pain-related functional gastrointestinal disorders in children and adolescents**. Cochrane Database Syst Rev. 2011 Jul 6;7:CD008013. Clinicians must be aware that for the majority of antidepressant medications no evidence exists that supports their use for the treatment of abdominal pain-related FGIDs in children and adolescents. The existing randomised controlled evidence is limited to studies on amitriptyline and revealed no statistically significant differences between amitriptyline and placebo for most efficacy outcomes. Amitriptyline does not appear to provide any benefit for the treatment of FGIDs in children and adolescents.
62. Lembo AJ, Schneier HA, Shiff SJ, et al. Two randomized trials of **linaclotide** for chronic constipation. N Engl J Med. 2011 Aug 11;365(6):527-36.
63. Ruepert L, Quartero AO, de Wit NJ, et al. **Bulking agents, antispasmodics and antidepressants** for the treatment of irritable bowel syndrome. Cochrane Database Syst Rev. 2011 Aug 10;(8):CD003460. There is no evidence that bulking agents are effective for treating IBS. There is evidence that antispasmodics are effective for the treatment of IBS. The individual subgroups which are effective include: cimetropium/dicyclomine, peppermint oil, pinaverium and trimebutine. There is good evidence that antidepressants are effective for the treatment of IBS. The subgroup analyses for SSRIs and TCAs are unequivocal and their effectiveness may depend on the individual patient.
64.Tabbers Merit M., Boluyt Nicole, Berger Marjolein Y.,et al. **Nonpharmacologic Treatments for Childhood Constipation**: Systematic Review. Pediatrics 2011; peds.2011-0179; published ahead of print September 26, 2011, doi:10.1542/peds.2011-0179
65.Ljotsson B, Hedman E, Andersson E, et al. **Internet-delivered exposure-based treatment vs. stress management** for irritable bowel syndrome: a randomized trial. Am J Gastroenterol. 2011 Aug;106(8):1481-91.
66. Guglielmetti S, Mora D, Gschwender M, Popp K. Randomised clinical trial: **Bifidobacterium bifidum MIMBb75** significantly alleviates irritable bowel syndrome and improves quality of life--a double-blind, placebo-controlled study. Aliment Pharmacol Ther. 2011 May;33(10):1123-32. doi: 10.1111/j.1365-2036.2011.04633.x.
67. Gaylord SA et al. **Mindfulness training** reduces the severity of irritable bowel syndrome in women: Results of a randomized controlled trial. Am J Gastroenterol 2011 Sep;106:1678.
68. Torpy JM, Golub RM. JAMA **patient page**. Irritable bowel syndrome. JAMA. 2011 Oct 5;306(13):1501.
69. Cash BD, Rubenstein JH, Young PE, et al. The **prevalence of celiac disease** among patients with nonconstipated irritable bowel syndrome is similar to controls. Gastroenterology. 2011 Oct;141(4):1187-93.
70. Zucchelli Marco, Camilleri Michael, et al. Association of **TNFSF15 polymorphism** with irritable bowel syndrome. Gut 2011;60:1671-1677 2 June 2011.
71. Park JM, Choi MG, Cho YK. **Cannabinoid receptor 1 gene polymorphism** and irritable bowel syndrome in the Korean population: a hypothesis-generating study. J Clin Gastroenterol 2011;45:45–49.
72. Peery AF, Barrett PR, Park D, et al. A **high-fibre diet** does not protect against asymptomatic diverticulosis. Gastroenterology. 2012 Feb;142(2):266-272.e1.
73. Menees SB, Maneerattannaporn M, Kim HM et al. The efficacy and safety of **rifaximin** for the irritable bowel syndrome: a systematic review and meta-analysis. Am J Gastroenterol. 2012 Jan;107(1):28-35.
74. Gallegos-Orozco JF, Foxx-Orenstein AE, Sterler SM, et al. **Chronic constipation in the elderly**. Am J Gastroenterol. 2012 Jan;107(1):18-25.
75. Vlieger AM, Rutten JM, Govers AM, et al. Long-Term Follow-Up of **Gut-Directed Hypnotherapy** vs. Standard Care in Children With Functional Abdominal Pain or Irritable Bowel Syndrome. Am J Gastroenterol. 2012 Apr;107(4):627-31.
76. Storr M, Storr M. **Chronic constipation**: current management and challenges. Can J Gastroenterol. 2011 Oct;25 Suppl B:5B-6B.
77. Peery AF, Barrett PR, Park D, et al. A **high-fibre diet does not protect against asymptomatic diverticulosis**. Gastroenterology. 2012 Feb;142(2):266-72.e1.
78. Shah E, Kim S, Chong K, et al. Evaluation of **harm in the pharmacotherapy** of irritable bowel syndrome. Am J Med. 2012 Apr;125(4):381-93.
79. Quitadamo P, Coccorullo P, Giannetti E, et al. A Randomized, Prospective, Comparison Study of a Mixture of **Acacia Fibre, Psyllium Fibre, and Fructose** vs **Polyethylene Glycol 3350 with Electrolytes** for the Treatment of Chronic Functional Constipation in Childhood. J Pediatr. 2012 Jun 5.
80. Wilkins T, Pepitone C, Alex B, et al. **Diagnosis and Management of IBS** in Adults. Am Fam Physician. 2012;86(5):419-426.

81. Manheimer E, Wieland LS, Cheng K, et al. **Acupuncture** for irritable bowel syndrome: systematic review and meta-analysis. Am J Gastroenterol. 2012 Jun;107(6):835-47.
82. Ford AC, Talley NJ. **Irritable bowel syndrome**. BMJ. 2012 Sep4;345:e5836.
83. Rao S, Lembo AJ, Shiff SJ, et al. A 12-Week, Randomized, Controlled Trial With a 4-Week Randomized Withdrawal Period to Evaluate the Efficacy and Safety of **Linaclotide** in Irritable Bowel Syndrome With Constipation. Am J Gastroenterol. 2012 Sep 18.
84. Chey WD, Lembo AJ, Lavins BJ, et al. **Linaclotide** for Irritable Bowel Syndrome With Constipation: A 26-Week, Randomized, Double-blind, Placebo-Controlled Trial to Evaluate Efficacy and Safety. Am J Gastroenterol. 2012 Sep 18.
85. Camilleri M. **Peripheral mechanisms** in irritable bowel syndrome. N Engl J Med. 2012 Oct 25;367(17):1626-35.
86. Tan E, Smith CH, Goldman RD. **Antidepressants** (eg. SSRIs) for functional gastrointestinal disorders in children. Can Fam Physician. 2013 Mar;59(3):263-4.
87. Le Nevé B, Posserud I, Böhn L, et al. A Combined Nutrient and **Lactulose Challenge Test** Allows Symptom-Based Clustering of Patients With Irritable Bowel Syndrome. Am J Gastroenterol. 2013 Apr 16.
88. Vazquez-Roque MI, Camilleri M, Smyrk T, et al. A controlled trial of **gluten-free** diet in patients with irritable bowel syndrome-diarrhea: effects on bowel frequency and intestinal function. Gastroenterology. 2013 May;144(5):903-911.e3.
89. Shekhar C, Monaghan PJ, Morris J, et al. **Rome III Functional Constipation and Irritable Bowel Syndrome With Constipation** Are Similar Disorders Within a Spectrum of Sensitization, Regulated by Serotonin. Gastroenterology. 2013 Oct;145(4):749-57.
90. Ford AC, Bercik P, Morgan DG, et al. Validation of the **Rome III Criteria** for the Diagnosis of Irritable Bowel Syndrome in Secondary Care. Gastroenterology. 2013 Dec;145(6):1262-1270.e1.
91. Parkman HP, Van Natta ML, Abell TL, et al. Effect of **nortriptyline** on symptoms of **idiopathic gastroparesis**: the NORIG randomized clinical trial. JAMA. 2013 Dec 25;310(24):2640-9.
92. Garsed K, Chernova J, Hastings M, et al. A randomised trial of **ondansetron** for the treatment of irritable bowel syndrome with diarrhoea. Gut. 2013 Dec 12.
93. Halmos EP, Power VA, Shepherd SJ, et al. A Diet Low in **FODMAPs** Reduces Symptoms of Irritable Bowel Syndrome. Gastroenterology. 2014 Jan;146(1):67-75.
94. Simrén M. **Diet** as a therapy for irritable bowel syndrome: progress at last. Gastroenterology. 2014 Jan;146(1):10-2
95. Waugh N, Cummins E, Royle P, et al. **Faecal calprotectin** testing for differentiating amongst inflammatory and non-inflammatory bowel diseases: systematic review and economic evaluation. Health Technol Assess. 2013;17:xv-xix, 1-211.
96. Ford AC, Bercik P, Morgan DG, et al. The **Rome III Criteria for the Diagnosis of Functional Dyspepsia** in Secondary Care Are Not Superior to Previous Definitions. Gastroenterology. 2014 Apr.
97. Bundeff AW, Woodis CB. **Selective serotonin reuptake inhibitors** for the treatment of irritable bowel syndrome. Ann Pharmacother. 2014 Jun;48(6):777-84.
98. Giannetti E, De'angelis G, Turco R. **Subtypes** of **irritable bowel syndrome** in **children**: prevalence at diagnosis and at follow-up. J Pediatr. 2014 May;164(5)
99. Cristofori F, Fontana C, Magistà A, et al. Increased **prevalence** of **celiac disease** among pediatric patients with **irritable bowel syndrome**: a 6-year prospective cohort study [published online April 21, 2014]. JAMA Pediatr. doi:10.1001/jamapediatrics.2013.4984.
100. Shin A, Camilleri M, Vijayvargiya P, et al. Bowel functions, **fecal unconjugated primary and secondary bile acids**, and colonic transit in patients with irritable bowel syndrome. Clin Gastroenterol Hepatol. 2013 Oct;11(10):1270-1275.e1.
101. Ford AC, Moayyedi P, Lacy BE, et al. American college of gastroenterology (**ACG**) monograph on the management of irritable bowel syndrome and **chronic idiopathic constipation**. Am J Gastroenterol. 2014 Aug;109 Suppl 1:S2-S26.
102. Moayyedi P, Quigley EM, Lacy BE, et al. The Effect of **Fiber Supplementation** on Irritable Bowel Syndrome: A Systematic Review and Meta-analysis. Am J Gastroenterol. 2014 Jul 29.
103. Ford AC, Quigley EM, Lacy BE, et al. Efficacy of **Prebiotics, Probiotics, and Synbiotics** in Irritable Bowel Syndrome and Chronic Idiopathic Constipation: Systematic Review and Meta-analysis. Am J Gastroenterol. 2014 Jul 29. :Probiotics are effective treatments for IBS, although which individual species and strains are the most beneficial remains unclear. Further evidence is required before the role of prebiotics or synbiotics in IBS is known. The efficacy of all three therapies in CIC is also uncertain.
104. Ford AC, Quigley EM, Lacy BE, et al. Effect of **antidepressants and psychological therapies**, including hypnotherapy, in irritable bowel syndrome: systematic review and meta-analysis. Am J Gastroenterol. 2014 Sep;109(9):1350-65; quiz 1366.
105. Weinberg DS, Smalley W, Heidelbaugh JJ, Sultan S. American gastroenterological association (AGA) institute guideline on the pharmacological management of irritable bowel syndrome. Gastroenterology. 2014 Nov;147(5):1146-8.
106. Hookway C, Buckner S, Crosland P, et al. **Irritable bowel syndrome in adults in primary care**: summary of updated **NICE** guidance. BMJ. 2015 Feb 25;350:h701.
107. Chey WD, Eswaran S, Kurlander J. JAMA **patient page. Irritable bowel syndrome**. JAMA. 2015 Mar 3;313(9):982.
108. Chey WD, Kurlander J, Eswaran S. **Irritable bowel syndrome**: a clinical review. JAMA. 2015 Mar 3;313(9):949-58.

109. Menees SB, Powell C, Kurlander J, et al. A Meta-Analysis of the Utility of **C-Reactive Protein, Erythrocyte Sedimentation Rate, Fecal Calprotectin, and Fecal Lactoferrin** to Exclude Inflammatory Bowel Disease in Adults With IBS. Am J Gastroenterol. 2015 Mar;110(3):444-54.
110. Rutten JM, Korterink JJ, Venmans LM, et al. **Nonpharmacologic** Treatment of Functional Abdominal Pain Disorders: A Systematic Review. Pediatrics. 2015 Mar;135(3):522-535.
111. Halland M, Saito YA. **Irritable bowel syndrome**: new and emerging treatments. BMJ. 2015 Jun 18;350:h1622.
112. **NICE**: National Collaborating Centre for Nursing and Supportive Care. **Irritable bowel syndrome in adults**: diagnosis and management of irritable bowel syndrome in primary care. London (UK): National Institute for Health and Care Excellence (NICE); 2015 Feb.
113. Spence MM, Karim FA, Lee EA, et al. Risk of **Injury in Older Adults** Using **Gastrointestinal Antispasmodic and Anticholinergic Medications**. J Am Geriatr Soc. 2015 Jun;63(6):1197-202.
114. Bohn L, Storsrud S, Liljebo T, et al. **Diet Low in FODMAPs** Reduces Symptoms of Irritable Bowel Syndrome as Well as Traditional Dietary Advice: A Randomized Controlled Trial. Gastroenterology. 2015 Nov;149(6):1399-1407
115. Does a low **FODMAP** diet help IBS? Drug Ther Bull. 2015 Aug;53(8):93-6.
116. Hackett C, Kolber MR. **Low FODMAP diet**. Can Fam Physician. 2015 Aug;61(8):691.
117. Rao VL, Cifu AS, Yang LW. **Pharmacologic Management** of Irritable Bowel Syndrome. JAMA. 2015 Dec 22-29;314(24):2684-5
118. Tazzyman S, Richards N, Trueman AR, et al. **Vitamin D** associates with improved quality of life in participants with irritable bowel syndrome: outcomes from a pilot trial. BMJ Open Gastroenterol. 2015 Dec 21;2(1):e000052.
119. Laird KT, Tanner-Smith EE, Russell AC, et al. Short- and Long-Term Efficacy of **Psychological Therapies** for Irritable Bowel Syndrome: A Systematic Review and Meta-analysis. Clin Gastroenterol Hepatol. 2015 Dec 22.
120. Lembo AJ, Lacy BE, Zuckerman MJ, et al. **Eluxadoline** for Irritable Bowel Syndrome with Diarrhea. N Engl J Med. 2016 Jan 21;374(3):242-53.
121. Fukudo S, Kinoshita Y, Okumura T, et al. **Ramosetron** Reduces Symptoms of Irritable Bowel Syndrome With Diarrhea and Improves Quality of Life in Women. Gastroenterology. 2016 Feb;150(2):358-366.e8.
122. Farup PG, Rudi K, Hestad K. **Faecal short-chain fatty acids** - a diagnostic biomarker for irritable bowel syndrome? BMC Gastroenterol. 2016 Apr 27;16(1):51.
123. Lebwohl B, Green PH. **Dietary therapy** for irritable bowel syndrome. BMJ. 2016 Jul 22;354:i3902.
124. Wouters MM, Balemans D, Van Wanrooy S, et al. **Histamine Receptor H1**-Mediated Sensitization of TRPV1 Mediates Visceral Hypersensitivity and Symptoms in Patients With Irritable Bowel Syndrome. Gastroenterology. 2016 Apr;150(4):875-887.e9.
125. Bonilla S, Flores A. A New Piece in the Puzzle of **Pediatric** Irritable Bowel Syndrome. J Pediatr. 2016 Oct 24.
126. Bonnert M, Olen O, Lalouni M, et al. **Internet-Delivered Cognitive Behavior Therapy** for Adolescents With Irritable Bowel Syndrome: A Randomized Controlled Trial. Am J Gastroenterol. 2016 Nov 15.
127. Eswaran SL, Chey WD, Han-Markey T, et al. A Randomized Controlled Trial Comparing the Low **FODMAP Diet vs. Modified NICE Guidelines** in US Adults with IBS-D. Am J Gastroenterol. 2016 Oct 11.
128. Giannetti E, Maglione M, Sciorio E, et al. Do **Children Just Grow Out** of Irritable Bowel Syndrome? J Pediatr. 2017 Jan 18.
129. Kumar S, Shukla R, Ranjan P, et al. **Interleukin-10**: A Compelling Therapeutic Target in Patients With Irritable Bowel Syndrome. Clin Ther. 2017 Feb 23.
130. MHRA Feb/17 **Hyoscine butylbromide (Buscopan) injection**: risk of serious adverse effects in patients with underlying cardiac disease including tachycardia, hypotension, and anaphylaxis.
131. Miner PB Jr, Koltun WD, Wiener GJ, et al. A Randomized Phase III Clinical Trial of **Plecanatide**, a Uroguanylin Analog, in Patients With Chronic Idiopathic Constipation. Am J Gastroenterol. 2017 Feb 7
132. FDA Mar/17 is warning that Viberzi (**eluxadoline**), a medicine used to treat irritable bowel syndrome with diarrhea (IBS-D), should not be used in patients who do not have a gallbladder.
133. Chey WD, Lembo AJ, Rosenbaum DP. **Tenapanor** Treatment of Patients With Constipation-Predominant Irritable Bowel Syndrome: A Phase 2, Randomized, Placebo-Controlled Efficacy and Safety Trial. Am J Gastroenterol. 2017 Feb 28.
134. Pinto-Sanchez MI, Hall GB, Ghajar K, et al. **Probiotic Bifidobacterium longum NCC3001** Reduces Depression Scores and Alters Brain Activity: a Pilot Study in Patients With Irritable Bowel Syndrome. Gastroenterology. 2017 May 5.
135. Sultan S, Malhotra A. **Irritable Bowel Syndrome-In the Clinic**. Ann Intern Med. 2017 Jun 6;166(11):ITC81-ITC96.
136. Donnachie E, Schneider A, Mehring M, et al. Incidence of irritable bowel syndrome and **chronic fatigue** following GI infection: a population-level Study using routinely collected claims data. Gut. 2017 Jun 10.
137. Fabisiak A, Włodarczyk J, Fabisiak N, et al. **Targeting Histamine Receptors** in Irritable Bowel Syndrome: A Critical Appraisal. J Neurogastroenterol Motil. 2017 Jul 30;23(3):341-348.
138. Ford AC, Lacy BE, Talley NJ. **Irritable Bowel Syndrome**. N Engl J Med. 2017 Jun 29;376(26):2566-2578.
139. MHRA Dec/17: **Eluxadoline** (Truberzi ▼: risk of **pancreatitis**; do not use in patients who have undergone cholecystectomy or in those with biliary disorders.

140. Schoenfeld P;Lacy BE;Chey WD;Lembo AJ;Kurtz CB;Rea Low-Dose **Linaclotide** (72 mug) for Chronic Idiopathic Constipation: A 12-Week, Randomized, Double-Blind, Placebo-Controlled Trial. Am J Gastroenterol. 2017 Aug 22.
141. Staudacher HM, Lomer MCE, Farquharson FM, et al. A **Diet Low in FODMAPs** Reduces Symptoms in Patients With Irritable Bowel Syndrome and A **Probiotic** Restores Bifidobacterium Species: A Randomized Controlled Trial. Gastroenterology. 2017 Oct;153(4):936-947.
142. Dai YK, Li DY, Zhang YZ, et al. Efficacy and safety of **Modified Tongxie Yaofang** in diarrhea-predominant irritable bowel syndrome management: A meta-analysis of randomized, positive medicine-controlled trials. PLoS One. 2018 Feb 6;13(2):e0192319.
143. Shah ED, Kim HM, Schoenfeld P. Efficacy and Tolerability of **Guanylate Cyclase-C Agonists** for Irritable Bowel Syndrome with Constipation and Chronic Idiopathic Constipation: A Systematic Review and Meta-Analysis. Am J Gastroenterol. 2018 Jan 30.
144. Williams CE, Williams EA, Corfe BM. **Vitamin D status** in irritable bowel syndrome and the impact of supplementation on symptoms: what do we know and what do we need to know? Eur J Clin Nutr. 2018 Jan 25.
145. Brenner DM, Fogel R, Dorn SD, et al. Efficacy, safety, and tolerability of plecanatide in patients with irritable bowel syndrome with constipation: results of two phase 3 randomized clinical trials. Am J Gastroenterol. 2018 Mar 15.
146. Johnsen PH, Hilpüsch F, Cavanagh JP, et al. Faecal microbiota transplantation versus placebo for moderate-to-severe irritable bowel syndrome: a double-blind, randomised, placebo-controlled, parallel-group, single-centre trial. Lancet Gastroenterol Hepatol. 2018 Jan;3(1):17-24.
147. Schiller LR. Evaluation of chronic diarrhea and irritable bowel syndrome with diarrhea in adults in the era of precision medicine. Am J Gastroenterol. 2018 May 1.
148. Dionne J, Ford AC, Yuan Y, et al A Systematic Review and Meta-Analysis Evaluating the Efficacy of a **Gluten-Free Diet and a Low FODMAPs Diet** in Treating Symptoms of Irritable Bowel Syndrome. Am J Gastroenterol. 2018 Jul 26
149. Ford AC, Lacy BE, Harris LA, et al. Effect of **Antidepressants and Psychological Therapies in Irritable Bowel Syndrome**: An Updated Systematic Review and Meta-analysis. Am J Gastroenterol. 2018 Sep 3.
150. Schnabel L, Buscail C, Sabate JM, et al. Association Between **Ultra-Processed Food Consumption and Functional Gastrointestinal Disorders**: Results From the French NutriNet-Santé Cohort. Am J Gastroenterol. 2018 Jun 15.
151. Zhou Q, Verne ML, Fields JZ, et al. Randomised placebo-controlled trial of dietary **glutamine supplements for postinfectious irritable bowel syndrome**. Gut. 2018 Aug 14.
152. Lackner JM, Jaccard J, Radziwon CD, et al. Durability and Decay of Treatment **Benefit of Cognitive Behavioral Therapy** for Irritable Bowel Syndrome: 12-Month Follow-Up. Am J Gastroenterol. 2018 Nov 14.
153. Scarlata K. **Low FODMAP Diet**: What Your Patients Need to Know. Am J Gastroenterol. 2018 Oct 24.
154. Zhou Q, Verne ML, Fields JZ, et al. Randomised placebo-controlled trial of **dietary glutamine supplements for postinfectious** irritable bowel syndrome. Gut. 2018 Aug 14.
155. Black CJ, Burr NE, Quigley EMM, et al. Efficacy of **Secretagogues** in Patients With Irritable Bowel Syndrome With Constipation: Systematic Review and Network Meta-analysis. Gastroenterology. 2018 Dec;155(6):1753-1763.
156. Lackner JM, Jaccard J, Radziwon CD, et al. Durability and Decay of Treatment Benefit of **Cognitive Behavioral Therapy** for Irritable Bowel Syndrome: 12-Month Follow-Up. Am J Gastroenterol. 2018 Nov 14.
157. Moayyedi P, Andrews CN, MacQueen G, et al. **Canadian Association of Gastroenterology clinical practice guideline** for the management of irritable bowel syndrome (IBS). J Can Assoc Gastroenterol 2019. https://www.cag-acg.org/images/publications/CAG_CPG_for_Management_of_IBS_JCAG_Jan2019.
158. Basnayake C. **Treatment of irritable bowel syndrome**. Aust Prescr. 2018 Oct;41(5):145-149.
159. Saito YA, Almazar AE, Tilkes KE, et al. Randomised clinical trial: **pregabalin vs placebo** for irritable bowel syndrome. Aliment Pharmacol Ther. 2019 Feb;49(4):389-397.
160. Xu D, Chen VL, Steiner CA, et al. Efficacy of **Fecal Microbiota Transplantation** in Irritable Bowel Syndrome: A Systematic Review and Meta-Analysis. Am J Gastroenterol. 2019 Mar 20.
161. Black C, Burr N, Quigley E, et al. Efficacy of secretagogues in patients with irritable bowel syndrome with constipation: systematic review and network meta-analysis. Gastroenterology. 2018;155:1753-63.
162. Shaukat A, Brenner D. Fecal microbiota transplant for irritable bowel syndrome: panacea or placebo? Am J Gastroenterol. 2019;00:1-2.
163. Kovacic K, Hainsworth K, Sood M, et al. Neurostimulation for abdominal pain-related functional gastrointestinal disorders in adolescents: a randomised, double-blind, sham-controlled trial. The Lancet. Gastroenterology and Hepatology. 2017;2(10):727-37.
164. Smalley W, Falck-Ytter C, Carrasco-Labra A, et al. AGA Guideline on the laboratory evaluation of functional diarrhea and diarrhea-predominant irritable bowel syndrome in adults (IBS-D). Gastroenterology. 2019 Aug 1. pii: S0016-5085(19)41150-5. doi: 10.1053/j.gastro.2019.07.053. [Epub ahead of print].

165. American Gastroenterolical Association. AGA Guidelines on the laboratory evaluation of functional diarrhea and diarrhea-predominant irritable bowel syndrome in adults (IBS-D): Patient Summary. Gastroenterology. 2019 Jul 29. pii: S0016-5085(19)41135-9. doi: 10.1053/j.gastro.2019.07.038. [Epub ahead of print]
166. Schulson M, Chiu-Ugalde J, Saez-Rios A, et al. Efficacy of the combination of pinaverium bromide 100mg plus simethicone 300mg in abdominal pain and bloating in irritable bowel syndrome: a randomized, placebo-controlled trial. J Clin Gastroetneterol 2019 Aug 2. doi: 10.1097/MCG.0000000000001242. [Epub ahead of print]
167. El-Salhy M, Hatlebakk J, Hausken T. Diet in irritable bowel syndrome (IBS): Interaction with gut microbiota and gut hormones. Nutrients. 2019;11(8):pii: E1824. doi: 10.3390/nu11081824.
168. Qin D, Yue L, Xue B, et al. Pharmacological treatments for patients with irritable bowel syndrome: an umbrella review of systematic reviews and meta-analyses. Medicine (Baltimore). 2019;98(32):e15920. doi: 10.1097/MD.0000000000001590.
169. Dale H, Rasmussen S, Asiller O, et al. Probiotics in Irritable Bowel Syndrome: An Up-to-Date Systematic Review. Nutrients 2019;11:2048; doi:10.3390/nu11092048
170. Bhargava A, Kolber M. Antispasmodics and peppermint oil: Old news or a breath of fresh air in managing irritable bowel syndrome. Tools for Practice. 2019; February 19. https://gomainpro.ca/wp-content/uploads/tools-for-practice/1554135748_tfp229anti-spasmodicibsfv.pdf, accessed September 6, 2019
171. Brenner DM, Sayuk GS, Gutman CR, et al. Efficacy and Safety of **Eluxadoline** in Patients With Irritable Bowel Syndrome With Diarrhea Who Report Inadequate Symptom Control With Loperamide: RELIEF Phase 4 Study. Am J Gastroenterol. 2019 Jul 26.
172. Everitt HA, Landau S, O'Reilly G, et al. **Cognitive behavioural therapy** for irritable bowel syndrome: 24-month follow-up of participants in the ACTIB randomised trial. Lancet Gastroenterol Hepatol. 2019 Sep 3.
173. Shaukat A, Brenner DM. **Fecal Microbiota Transplant** for Irritable Bowel Syndrome: Panacea or Placebo? Am J Gastroenterol. 2019 May 1.
174. Smalley W, Falck-Ytter C, Carrasco-Labra A, et al. **AGA Clinical Practice Guidelines** on the Laboratory Evaluation of Functional Diarrhea and Diarrhea-Predominant Irritable Bowel Syndrome in Adults (IBS-D). Gastroenterology. 2019 Sep;157(3):851-854.

N/V EXTRAS:

Alarm signs - "Red Flags" for more severe GI disease:

- age >55, unintended ↓ weight, progressive dysphasia, persistent vomiting, evidence for GI bleed, family hx of GI cancer, altered mental status, abdom pain, feculent vomiting, hematochezia, melena, focal neurologic deficit.

Considerations:

-Study of 215 ER patients randomized to 1.25mg of IV droperidol vs. 8mg of IV ondansetron vs. placebo. Both antiemetics reduced nausea similarly to placebo. However, this study was stopped early and more patient centered metrics such as "experienced desired effect" and need for rescue medications were lower than in the placebo group (ondansetron > droperidol > placebo)[38]

-Evidence for Isopropyl alcohol: "Two trials with about 200 nonpregnant adults presenting to the ED found inhaled (smelling) isopropyl alcohol improved mild to moderate nausea and vomiting. For example, after 30 minutes the nausea score improved from 50 out of 100 to 20 with inhaled isopropyl alcohol versus 40 with oral ondansetron. Only 1 study reported adverse events and found none."[39]

Links:

NHS – CKS: Nausea and Vomiting in Pregnancy - management: http://www.cks.library.nhs.uk/nausea_vomiting_in_pregnancy ; NGC: ACCC Netherlands: http://www.guideline.gov/summary/summary.aspx?doc_id=11793
CINV Guidelines: 1) MASCC: http://www.mascc.org/content/1.html ; 2) ASCO: http://www.asco.org/portal/site/ASCO/
BWH-Overtreatment of PONV: 1) low doses of ondansetron, 1mg iv q6h, adequate ; 2) allow for onset, 30 minutes http://www.brighamandwomens.org/pharmacoepid/Research/EduMaterials/antiemetics3.05.04-web.pdf

Other:

- Fosapreitant: Injectible form of EMEND, 150mg vial in Canada.

Hyperemesis gravidarum

- N/V in pregnancy common, but hyperemesis gravidarum likely affects <1%
- Tx: fluids & electrolytes, thiamine (or IV if prolonged & unable to take po), antiemetics. Reserve corticosteroids for severe/refractory cases (limited evidence, conflicting efficacy e.g., re-hospitalizations).

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Adapted from Timmins Palliative Care (P. Critchley MD, T. Dolanjski Pharmacist) Prepared by: *L. Regier* BSP, BA, B. *Jensen* BSP

Deleted product (historical record only).

Droperidol INAPSINE 5mg/2ml amp	0.625-2.5mg IM/IV slow; ?ECG prior $8/amp ✗ ⊗	As above (esp. akathisia); ↑QT ? interval & sudden death (controversial) 22

Other Links:

Info SOGC: https://www.pregnancyinfo.ca/your-pregnancy/healthy-pregnancy/nausea-and-vomiting/
HER(hyperemesis-gravidarum): http://helpher.org/hyperemesis-gravidarum/
CFP Motherisk: http://www.cfp.ca/cgi/reprint/53/12/2109.pdf.
N/V Links: AFP PONV Prediction: http://www.aafp.org/afp/20070515/poc.html
AFP Evaluation n&v: http://www.aafp.org/afp/20070701/76.html
Australia FP: http://www.racgp.org.au/afp/200709

References:

Abas MN, Tan PC, Azmi N, Omar SZ. **Ondansetron compared with metoclopramide** for hyperemesis gravidarum: a randomized controlled trial. Obstet Gynecol. 2014 Jun;123(6):1272-9.
ACOG- Practice Bulletin No. 153: **Nausea and Vomiting of Pregnancy**. Obstet Gynecol. 2015 Sep;126(3):e12-24.
Adrion C, Fischer CS, Wagner J, et al; **BEMED** study group. Efficacy and safety of **betahistine** treatment in patients **with Meniere's disease**: primary results of a long term, multicentre, double blind, randomised, placebo controlled, dose defining trial (BEMED trial). BMJ. 2016 Jan 21;352:h6816.
Alame MM, Chamsy DJ, Zaraket H. **Pityriasis rosea-like eruption** associated with **ondansetron use in pregnancy**. Br J Clin Pharmacol. 2018 Mar 9.
Allan M, Wilson E, Ivers N. Can **ondansetron** help children with vomiting due to **gastroenteritis**? Canadian Family Physician February 2012 **vol. 58** no. 2167.
Allan GM, Finley CR, Ton J, et al. Systematic review of systematic reviews for medical cannabinoids: Pain, nausea and vomiting, spasticity, and harms. Can Fam Physician. 2018 Feb;64(2):e78-e94.
Allan GM, Ramji J, Perry D, et al. Simplified **guideline for prescribing medical** cannabinoids in primary care. **Can** Fam Physician. 2018 Feb;64(2):111-120.
Anderson WD, Strayer SM. Evaluation of **Nausea and Vomiting in Adults**: A Case-Based Approach. Am Fam Physician. 2013;88(6):371-379.
April MD, Oliver JJ, Davis WT, et al. **Aromatherapy Versus Oral Ondansetron** for Antiemetic Therapy Among Adult Emergency Department Patients: A Randomized Controlled Trial. Ann Emerg Med. 2018 Feb 17.
Badihian N;Saneian H;Badihian S;Yaghini O. **Prophylactic** Therapy of **Cyclic Vomiting** Syndrome in **Children**: Comparison of **Amitriptyline** and **Cyproheptadine**: A Randomized Clinical Trial. Am J Gastroenterol. 2017 Jul 18.
Basch E, Prestrud AA, Hesketh PJ, et al. **Antiemetics**: American Society of Clinical Oncology (**ASCO**) Clinical Practice Guideline Update. J Clin Oncol. 2011 Sep 26. http://jco.ascopubs.org/content/early/2011/09/25/JCO.2010.34.4614.full.pdf
Beadle KL, Helbling AR, Love SL, et al. **Isopropyl Alcohol Nasal Inhalation** for Nausea in the Emergency Department: A Randomized Controlled Trial. Ann Emerg Med. 2015 Nov 21.
Bell GC, Caudle KE, Whirl-Carrillo M, et al. Clinical Pharmacogenetics Implementation Consortium (**CPIC) guideline for CYP2D6 genotype and use of ondansetron and tropisetron**. Clin Pharmacol Ther. 2017 Aug;102(2):213-218.
Benevides ML, Oliveira SS, de Aguilar-Nascimento JE. The Combination of **Haloperidol, Dexamethasone, and Ondansetron** for Prevention of Postoperative Nausea and Vomiting in Laparoscopic Sleeve Gastrectomy: a Randomized Double-Blind Trial. Obes Surg. 2013 Mar 26.
Billio A, Morello E, Clarke MJ. **Serotonin receptor antagonists** for highly emetogenic chemotherapy in adults. Cochrane Database Syst Rev. 2010 Jan 20;(1):CD006272.
Boelig RC, Barton SJ, Saccone G, Kelly AJ, Edwards SJ, Berghella V. **Interventions for treating hyperemesis gravidarum.** Cochrane Database of Systematic Reviews 2016, Issue 5. Art. No.: CD010607. DOI: 10.1002/14651858.CD010607.pub2. On the basis of this review, there is little high-quality and consistent evidence supporting any one intervention, which should be taken into account when making management decisions. There was also very limited reporting on the economic impact of hyperemesis gravidarum and the impact that interventions may have.
Brainard A, Gresham C. Prevention and treatment of **motion sickness**. Am Fam Physician. 2014 Jul 1;90(1):41-6.
Camilleri M, Parkman HP, Shafi MA, et al. Clinical guideline: management of **gastroparesis**. Am J Gastroenterol. 2013 Jan;108(1):18-37.
Campbell-Yeo, Marsha L., Allen, Alexander C., Joseph, K. S., et al. Effect of **Domperidone** on the Composition of Preterm Human **Breast Milk**. Pediatrics 2010 125: e107-e114 .
Carstairs SD. **Ondansetron Use in Pregnancy and Birth Defects**: A Systematic Review. Obstet Gynecol. 2016 May;127(5):878-83. The overall risk of birth defects associated with ondansetron exposure appears to be low. There may be a small increase in the incidence of cardiac abnormalities in ondansetron-exposed neonates. Therefore, ondansetron use for nausea and vomiting of pregnancy should be reserved for those women whose symptoms have not been adequately controlled by other methods.
Cavero-Redondo I, Alvarez-Bueno C, Pozuelo-Carrascosa DP, et al. Risk of **extrapyramidal side effects comparing continuous vs. bolus intravenous metoclopramide** administration: a systematic review and meta-analysis of randomised controlled trials. J Clin Nurs. 2015 Sep 15.
Cheng A. Emergency department use of oral **ondansetron for acute gastroenteritis-related vomiting in infants and children**. Paediatr Child Health 2011;16:177-9.
Chou DE, Tso AR, Goadsby PJ. **Aprepitant** for the management of nausea with inpatient IV **dihydroergotamine**. Neurology. 2016 Sep 14.
Clary PL, Lawson P. Pharmacologic Pearls for **End-of-Life Care**. Am Fam Physician. 2009 Jun 15;79(12):1059-65.
Collis E, Mather H. **Nausea and vomiting in palliative care**. BMJ. 2015 Dec 3;351:h6249.
DREAMS Trial Collaborators and West Midlands Research Collaborative. **Dexamethasone versus standard treatment** for postoperative nausea and vomiting in gastrointestinal surgery: randomised controlled trial (DREAMS Trial). BMJ. 2017 Apr 18;357:j1455.
Duval, Arnaud, Dubertret, Louis. **Aprepitant** as an Antipruritic Agent? N Engl J Med 2009 361: 1415-1416

Dupuis LL, Boodhan S, Holdsworth M, et al. **POGO** Guideline for the **prevention of acute nausea and vomiting due to antineoplastic medication in pediatric cancer** patients. Pediatr Blood Cancer 2013;60:1073-82. http://onlinelibrary.wiley.com/doi/10.1002/pbc.24508/pdf (accessed July 9, 2013).

Dupuis LL, Robinson PD, Boodhan S, et al. **POGO** Guideline for the prevention and treatment of **anticipatory nausea and vomiting due to chemotherapy in pediatric cancer patients**. Toronto (ON): Pediatric Oncology Group of Ontario (POGO); **2014** Apr 23.

Dychter SS, Harrigan R, Bahn JD, et al. Tolerability and Pharmacokinetic Properties of **Ondansetron Administered Subcutaneously** With Recombinant Human **Hyaluronidase** in Minipigs and Healthy Volunteers. Clin Ther. 2014 Jan 30.

Egerton-Warburton D, Meek R, Mee MJ, et al. Antiemetic Use for Nausea and Vomiting **in Adult Emergency Department Patients**: Randomized Controlled Trial Comparing **Ondansetron, Metoclopramide, and Placebo**. Ann Emerg Med. 2014 May 9. pii: S0196-0644(14)00223-6.

Enarson Paul, Gouin Serge, Goldman Ran D. **Dimenhydrinate use for children** with vomiting Can Fam Physician April 2011 57: 431-432.

FDA Warning regarding metoclopramide & tardive dyskinesia (Feb 2009): http://www.fda.gov/bbs/topics/NEWS/2009/NEW01963.html

FDA Sep/09 notified healthcare professionals that a Boxed Warning is being added to the prescribing information for **Promethazine** Hydrochloride products, describing the risks of severe tissue injury, including gangrene, requiring amputation following intravenous administration of promethazine.

FDA Dec/09 The Texas Department of State Health Services and FDA notified healthcare professionals and consumers, especially pregnant or breastfeeding women, to avoid consuming a product called "**Nzu**", taken as a traditional remedy for morning sickness,because of the potential health risks from high levels of lead and arsenic, noted on laboratory analysis by Texas DSHS. Nzu, which is sold at African specialty stores is also called Calabash clay, Calabar stone, Mabele, Argile and La Craie. It generally resembles balls of clay or mud and is usually sold in small plastic bags with a handwritten label identifying it as "Nzu" or "Salted Nzu."

FDA Dec/10 The injectable form of **dolasetron** mesylate (Anzemet) should not be used to prevent nausea or vomiting related to chemotherapy because the drug increases the risk for torsade de pointes. The FDA recommends against using Anzemet injections in patients with congenital long-QT syndrome. The warning does not apply to Anzemet tablets because the risks for developing an abnormal heart rhythm are not as high as with the injections. FDA MedWatch alert (Free)

FDA Sep/11 The U.S. Food and Drug Administration (FDA) is informing the public of an ongoing safety review of the anti-nausea drug Zofran (**ondansetron**, ondansetron hydrochloride and their generics). Ondansetron may increase the risk of developing abnormal changes(QT prolongation & torsades) in the electrical activity of the heart

FDA Dec/12 is working with the manufacturers of all **32 mg dose Ondansetron Injectable** Products (brand and generic) to voluntarily recall them from the market due to QT serious cardiac toxicity.

FDA Jan/18: Anaphylaxis, anaphylactic shock and other serious **hypersensitivity reactions** have been reported in the postmarketing setting, some requiring hospitalization. These reactions have occurred during or soon after the infusion of Varubi (**rolapitant**) injectable emulsion. Most reactions have occurred within the first few minutes of administration. Symptoms of anaphylaxis can include wheezing or difficulty breathing; swelling of the face or throat; hives or flushing; itching; abdominal cramping, abdominal pain or vomiting; back pain or chest pain; hypotension or shock.

Flake ZA, Linn BS, Hornecker JR. Practical **Selection of Antiemetics in the Ambulatory Setting**. Am Fam Physician. 2015;91(5):293-296.

Fujii Y, Itakura M. Comparison of **propofol, droperidol**, and metoclopramide for prophylaxis of postoperative nausea and vomiting after breast cancer surgery: a prospective, randomized, double-blind, placebo-controlled study in Japanese patients. Clin Ther. 2008 Nov;30(11):2024-9.

Furyk JS, Meek R, McKenzie S. Drug treatment of **adults with nausea and vomiting in primary care**. BMJ. 2014 Aug 7;349:g4714.

Freedman SB, Finkelstein Y. **Route** of **ondansetron** administration and ventricular **arrhythmias**. J Pediatr. 2017 May 22.

Freedman SB, Parkin PC, Willan AR, Schuh S. **Rapid versus standard intravenous rehydration in paediatric gastroenteritis**: pragmatic, blinded, randomised clinical trial. BMJ 2011;343:d6976.

Furyk JS, Meek RA, Egerton-Warburton D. Drugs for the treatment of **nausea and vomiting in adults in the emergency department setting**. Cochrane Database Syst Rev. 2015 Sep 28;9:CD010106. In an ED population, there is no definite evidence to support the superiority of any one drug over any other drug, or the superiority of any drug over placebo. Participants receiving placebo often reported clinically significant improvement in nausea, implying general supportive treatment such as intravenous fluids may be sufficient for the majority of people. If a drug is considered necessary, choice of drug may be dictated by other considerations such as a person`s preference, adverse-effect profile and cost. The review was limited by the paucity of clinical trials in this setting. Future research should include the use of placebo and consider focusing on specific diagnostic groups and controlling for factors such as intravenous fluid administered.

Gouin S, Vo TT, Roy M, et al. Oral **Dimenhydrinate** Versus Placebo in Children With Gastroenteritis: A Randomized Controlled Trial. Pediatrics. 2012 May 14.

Graham J, Barberio M, Wang GS. **Capsaicin Cream for Treatment of Cannabinoid Hyperemesis Syndrome** in Adolescents: A Case Series. Pediatrics. 2017 Nov 9.

He H, Yin JY, Xu YJ, et al. Association of **ABCB1 Polymorphisms** With the Efficacy of **Ondansetron** on Chemotherapy-Induced Nausea and Vomiting. Clin Ther. 2014 Jul 7.

Health Canada May/11 ANZEMET (**dolasetron** mesylate) - Withdrawal of **20 mg/mL Intravenous** Injection Due to Potential Risk of Arrhythmias. New data suggest that intravenous administration of the injectable form of ANZEMET (dolasetron mesylate) may result in serious arrhythmias.

Health Canada July/11 is informing health professionals and consumers that the labelling information for the drug **metoclopramide** is being updated to include stronger warnings on the risk of a movement disorder known as "**tardive dyskinesia**."

Health Canada Mar/12: **Domperidone** should be used at the lowest possible dose. The risk of serious ventricular arrhythmias (QT) and sudden cardiac death may be higher in patients taking daily doses greater than 30 mg, and in patients over 60 years old.

Health Canada Oct/12: Ondansetron can cause a dose-dependent prolongation of the electrocardiographic-corrected QT interval (QTc), which can lead to Torsade de Pointes, a potentially life-threatening heart rhythm abnormality. The new maximum recommended single intravenous (IV) dose of ZOFRAN®is 16 mg infused over 15 minutes.

Health Canada May/14 has completed a safety review of the serotonin blocking drugs **dolasetron** (ANZEMET), **granisetron** (KYTRIL and generics), **ondansetron** (ZOFRAN and generics) and palonosetron (ALOXI), which are used for treating nausea and vomiting. This review identified a potential risk of **serotonin syndrome**.

Health Canada Jan/15 **Metoclopramide** - Abnormal Involuntary Movements (**Extrapyramidal** Symptoms) in **Children** - Sandoz Canada Inc., Apotex Inc., Omega Laboratories Limited and Pendopharm Division of Pharmascience Inc.

Health Canada Jan/15 **Domperidone** Maleate - Association with Serious **Abnormal Heart Rhythms and Sudden Death** (Cardiac Arrest). Domperidone may be associated with a small increased risk of serious abnormal heart rhythms and sudden death. Prescribing information changes include a new recommended maximum daily dose, new restrictions of use and stronger warnings.

Health Canada. Summary safety review – **Zofran (ondansetron)** – assessing the potential harm to the fetus. November 16, 2016. www.hc-sc.gc.ca/dhp-mps/medeff/reviews-examens/zofran-eng.php (accessed November 24, 2016).

Herrell HE. **Nausea and Vomiting of Pregnancy**. Am Fam Physician. 2014;89(12):965-970.

Hesketh PJ, Kris MG, Basch E, et al. **ASCO-Antiemetics**: American Society of Clinical Oncology clinical **practice guideline** update. J Clin Oncol. 2017 Oct 1;35(28):3240-61.

Hinkle SN, Mumford SL, Grantz KL, et al. Association of **nausea and vomiting during pregnancy with pregnancy loss**: a secondary analysis of a randomized clinical trial [online September 26, 2016].JAMA Intern Med. doi: 10.1001/jamainternmed.2016.5641

Jarvis Sheba, Nelson-Piercy Catherine. Management of nausea and vomiting in **pregnancy**. BMJ 2011;342:doi:10.1136/bmj.d3606 (Published 17 June 2011)

Jin J. **Treatments for Nausea and Vomiting During Pregnancy** (Patient information). JAMA. 2016 Oct 4;316(13):1420.

Kang HJ, Loftus S, Taylor A, DiCristina C, Green S, Zwaan CM. **Aprepitant** for the prevention of **chemotherapy-induced** nausea and vomiting in **children**: a randomised, double-blind, phase 3 trial. Lancet Oncol. 2015 Apr; 16(4):385-94.

Kim HS, Anderson JD, Saghafi O, et al. **Cyclic vomiting** presentations following **marijuana** liberalization in Colorado. Acad Emerg Med. 2015 Jun;22(6):694-9.

Kleine-Brueggeney M, Greif R, Brenneisen R, et al. Intravenous **Delta-9-Tetrahydrocannabinol** to Prevent Postoperative Nausea and Vomiting: A Randomized Controlled Trial. Anesth Analg. 2015 Nov;121(5):1157-1164.

Koren G, Clark S, Hankins GD, et al. Effectiveness of delayed-release **doxylamine and pyridoxine** (**Diclectin**) for nausea and vomiting of pregnancy: a randomized placebo controlled trial. Am J Obstet Gynecol. 2010 Sep 13.

Koren G. Is **ondansetron** safe for use during pregnancy? Can Fam Physician. 2012 Oct;58(10):1092-3.

Koren G. **Treating morning sickness PRN**? Can Fam Physician. 2013 Feb;59(2):150-1.

Kovac AL. Update on the management of **postoperative nausea and vomiting**. Drugs. 2013 Sep;73(14):1525-47.

Kovacic K, Miranda A, Chelimsky G, et al. **Chronic Idiopathic Nausea of Childhood**. J Pediatr. 2014 Mar 4.

Lacy BE, Parkman HP, Camilleri M. **Chronic nausea and vomiting**: evaluation and **treatment**. Am J Gastroenterol. 2018 Mar 15.

Lavecchia M, Chari R, Campbell S, et al. **Ondansetron in pregnancy** and the risk of **congenital malformations**: a systematic review. J Obstet Gynaecol Can 2018;40:910-8.

Levin DN, Dulberg Z, Chan AW, et al. A randomized controlled trial of **nabilone** for the prevention of acute **postoperative nausea** and **vomiting** in elective surgery. Can J Anaesth. 2017 Apr;64(4):385-95.

Lindblad AJ, Koppula S. **Ginger** for nausea and vomiting of pregnancy. Can Fam Physician. 2016 Feb;62(2):145.

Matsuzaki K, Ito Y, Fukuda M, et al. Placebo-controlled phase III study comparing **dexamethasone** on day 1 to on day 1-3 with **NK1 receptor antagonist and palonosetron** in high emetogenic chemotherapy. J Clin Oncol 2016;34:Suppl:10019.

Matthews A, Dowswell T, Haas DM, Doyle M, O'Mathúna DP. Interventions for **nausea and vomiting in early pregnancy**. Cochrane Database of Systematic Reviews 2010, Issue 9. Art. No.: CD007575. DOI: 10.1002/14651858.CD007575.pub2. There is a lack of high-quality evidence to support advice.

Matthews A, Haas DM, O`Mathuna DP, et al. Interventions for **nausea and vomiting in early pregnancy**. Cochrane Database Syst Rev. 2015 Sep 8;9:CD007575. Given the high prevalence of nausea and vomiting in early pregnancy, women and health professionals need clear guidance about effective and safe interventions, based on systematically reviewed evidence. There is a lack of high-quality evidence to support any particular intervention. This is not the same as saying that the interventions studied are ineffective, but that there is insufficient strong evidence for any one intervention. The difficulties in interpreting and pooling the results of the studies included in this review highlight the need for specific, consistent and clearly justified outcomes and approaches to measurement in research studies.

Matok I, Gorodischer R, Koren G, Sheiner E, Wiznitzer A, Levy A. The safety of metoclopramide use in the first trimester of pregnancy. N Engl J Med. 2009 Jun, 11;360(24):2528-35.

McCracken G, Houston P, Lefebvre G, Society of Obstetricians and Gynecologists of Canada (**SOGC**). Guideline for the management of **postoperative** nausea and vomiting. J Obstet Gynaecol Can 2008 Jul;30(7):600-7. http://www.sogc.org/guidelines/documents/gui209CPG0807.pdf

McParlin C, O'Donnell A, Robson SC, et al. **Treatments for Hyperemesis Gravidarum and Nausea and Vomiting in Pregnancy**: A Systematic Review. JAMA. 2016 Oct 4;316(13):1392-1401

Meltzer AC, Mazer-Amirshahi M. For **Adults With Nausea and Vomiting in the Emergency Department**, What Medications Provide Rapid Relief? Ann Emerg Med. 2016 Apr 26.

MHRA Aug/12 The new maximum single intravenous dose of **ondansetron** for the management of chemotherapy-induced nausea and vomiting (CINV) in adults is now 16 mg (infused over at least 15 minutes). This restriction follows a review of new study data, which showed that there is a greater risk of prolongation of the electrocardiographic-corrected **QT** interval (QTc).

Moeller JR, Gummin DD, Nelson TJ, et al. Risk of **Ventricular Arrhythmias and Association with Ondansetron**. J Pediatr. 2016 Sep 21.

Murdin L, Golding J, Bronstein A. **Managing motion sickness**. BMJ. 2011 Dec 2;343:d7430.

Narjoux G, Clarenne J, Azzouz B, et al. **Nightmares and hallucinations with aprepitant and opium powder**: a suspected drug-drug interaction. Br J Clin Pharmacol. 2018 Nov 26.

Navari RM, Aapro M. **Antiemetic Prophylaxis for Chemotherapy-Induced** Nausea and Vomiting. N Engl J Med. 2016 Apr 7

Navari RM, Qin R, Ruddy KJ, et al. **Olanzapine** for the Prevention of Chemotherapy-Induced Nausea and Vomiting. N Engl J Med. 2016 Jul 14;375(2):134-42.

Niebyl JR. Clinical practice. **Nausea and vomiting in pregnancy**. N Engl J Med. 2010 Oct 14;363(16):1544-50.
Okumura LM, Rodrigues FA, Ferreira MA, et al. **Aprepitant** in pediatric patients using moderate and highly emetogenic protocols: a systematic review and meta-analyses of randomized controlled trials. Br J Clin Pharmacol. 2016 Nov 20.
Oliveira LG, Capp SM, You WB, et al. **Ondansetron compared with doxylamine and pyridoxine** for treatment of nausea in pregnancy: a randomized controlled trial. Obstet Gynecol. 2014 Oct;124(4):735-42. d
Pasternak B, Svanstrom H, Molgaard-Nielsen D, et al. **Metoclopramide in pregnancy** and risk of major congenital malformations and fetal death. JAMA 2013;310:1601-11.
Pasternak B et al. **Ondansetron in pregnancy** and risk of adverse fetal outcomes. N Engl J Med 2013 Feb 28; 368:814.
Patel P, Leeder JS, Piquette-Miller M, et al. **Aprepitant and Fosaprepitant Drug Interactions**: A Systematic Review. Br J Clin Pharmacol. 2017 May 4.
Patel P, Robinson PD, Thackray J, et al. Guideline for the prevention of **acute chemotherapy-induced nausea and vomiting in pediatric cancer patients**: a focused update. Pediatr Blood Cancer. 2017 (**Pediatric Oncology Group of Ontario**)
Persaud N, Chin J, Walker M. Should **doxylamine-pyridoxine** be used for nausea and vomiting of **pregnancy**? J Obstet Gynaecol Can. 2014 Apr;36(4):343-8.
Persaud N, Meaney C, El-Emam K, et al. **Doxylamine-pyridoxine** for **nausea and vomiting of pregnancy** randomized placebo controlled trial: Prespecified analyses and reanalysis. PLoS One. 2018 Jan 17;13(1):e0189978.
Pham A, Liu G. **Dexamethasone** for antiemesis in **laparoscopic gynecologic surgery**: a systematic review and meta-analysis. Obstet Gynecol. 2012 Dec;120(6):1451-8.
Phillips RS, Gopaul S, Gibson F, et al. **Antiemetic medication for prevention and treatment of chemotherapy induced nausea and vomiting in childhood**. Cochrane Database of Systematic Reviews 2010, Issue 9. Art. No.: CD007786. DOI: 10.1002/14651858.CD007786.pub2. Our overall knowledge of themost effective antiemetics to prevent chemotherapy-induced nausea and vomiting in childhood is incomplete. This review suggests that 5-HT3 antagonists with dexamethasone added are effective in patients who are to receive highly emetogenic chemotherapy although the risk-benefit profile of additional steroid remains uncertain.
POGO Antineoplastic-Induced Nausea and Vomiting Guideline Development Panel. Guideline for classification of the acute **emetogenic potential of antineoplastic** medication in pediatric cancer patients. Toronto (ON): Pediatric Oncology Group of Ontario (POGO); 2010 Aug 11.
Powell CV, Priestley SJ, Young S, et al. Randomized clinical trial of **rapid versus 24-hour rehydration** for **children** with **acute gastroenteritis**. Pediatrics. 2011 Oct;128(4):e771-8.
Public Health Agency of Canada. Canada Communicable Disease Report. Committee to Advise on Tropical Medicine and Travel (CATMAT) statement. Statement on **pregnancy and travel**. Mar 2010.
http://www.phac-aspc.gc.ca/publicat/ccdr-rmtc/10vol36/acs-2/index-eng.php
Rapoport BL, Chasen MR, Gridelli C, et al. Safety and efficacy of **rolapitant** for prevention of chemotherapy-induced nausea and vomiting after administration of **cisplatin-based highly emetogenic** chemotherapy in patients with cancer: two randomised, active-controlled, double-blind, phase 3 trials. Lancet Oncol 2015; online Aug 11.
Ravi K, Sweetser S. **Persistent nausea and vomiting in pregnancy**. Gastroenterology. 2014 Jan;146(1):33-323
Rawlinson A, Kitchingham N, Hart C, et al. Mechanisms of **reducing postoperative pain, nausea and vomiting**: a systematic review of current techniques. Evid Based Med. 2012 Jun;17(3):75-80.
Renoux C, Dell'Aniello S, Khairy P, et al. Ventricular tachyarrhythmia and sudden cardiac death with **domperidone** use in Parkinson's Disease. Br J Clin Pharmacol. 2016 Apr
Royal College of Obstetricians and Gynaecologists (**RCOG**) , 2016. The management of nausea and vomiting of pregnancy and hyperemesis gravidarum [online]. Available: https://www.rcog.org.uk/globalassets/documents/guidelines/green-top-guidelines/gtg69-hyperemesis.pdf [Accessed 17 August 2016]
Ruhlmann CH, et al. Efficacy and safety of **fosaprepitant** for the prevention of nausea and emesis during 5 weeks of chemoradiotherapy for cervical cancer (the GAND-emesis study): a multinational, randomised, placebo-controlled, double-blind, phase 3 trial. Lancet Oncol 2016; online March 4
Santini D, Vincenzi B, Guida FM, et al. **Aprepitant** for management of severe pruritus related to biological cancer treatments: a pilot study. Lancet Oncol 2012; online Sept 18.
Schwartzberg LS, Modiano MR, Rapoport BL, et al. Safety and efficacy of **rolapitant** for prevention of chemotherapy-induced nausea and vomiting after administration of **moderately emetogenic chemotherapy or anthracycline and cyclophosphamide** regimens in patients with cancer: a randomised, active-controlled, double-blind, phase 3 trial. Lancet Oncol 2015; online Aug 11.
Simonetto DA, Oxentenko AS, Herman ML, Szostek JH. **Cannabinoid hyperemesis**: a case series of 98 patients. Mayo Clin Proc. 2012 Feb;87(2):114-9.
Shoemaker LK. Estfan B Induru R et al. **Symptom management**: An important part of cancer care. Cleveland Clinic Journal of Medicine 2011; 78(1):25-34; doi:10.3949/ccjm.78a.10053.
Slaughter SR, Hearns-Stokes R, van der Vlugt T, et al. **FDA approval of doxylamine-pyridoxine** therapy for use in pregnancy. N Engl J Med. 2014 Mar 20;370(12):1081-3.
Sturm JJ, Hirsh DA, Schweickert A, et al. **Ondansetron use in the pediatric emergency** department and effects on hospitalization and return rates: are we masking alternative diagnoses?. Ann Emerg Med. 2010 May;55(5):415-22. Epub 2010 Jan 19.
Tan PC, Khine PP, Vallikkannu N, Omar SZ. **Promethazine compared with metoclopramide** for hyperemesis gravidarum: a randomized controlled trial. Obstet Gynecol. 2010 May;115(5):975-81.
Tang DH, Malone DC. A network meta-analysis on the efficacy of **serotonin type 3 receptor antagonists** used in adults during the first 24 hours for **postoperative** nausea and vomiting prophylaxis. Clin Ther. 2012 Feb;34(2):282-94.
Tarbell SE, Li BU. Health-related quality of life in children and adolescents with **cyclic vomiting syndrome**: a comparison with published data on youth with irritable bowel syndrome and organic gastrointestinal disorders. J Pediatr. 2013 Aug;163(2):493-7.
Tarbell SE, Li BU. **Anxiety Measures** Predict Health-Related Quality of Life in Children and Adolescents with **Cyclic Vomiting Syndrome**. J Pediatr. 2015 Jun 18.
Taylor, Tricia. Treatment of **nausea and vomiting in pregnancy**. Australian Prescriber. AN INDEPENDENT REVIEW (2014): 42.
Tricco AC, Soobiah C, Blondal E, et al. Comparative safety of **serotonin (5-HT3) receptor antagonists** in patients undergoing **surgery**: a systematic review and network meta-analysis. BMC Med. 2015 Jun 18;13:142.
Trimas SJ, Trimas MD. Use of **Aprepitant** and Factors Associated With Incidence of **Postoperative Nausea and Vomiting** in Patients Undergoing **Facial Plastic Surgery**. JAMA Facial Plast Surg. 2015 May 14.
Vikanes Åse, Skjærven Rolv, Grjibovski Andrej M, et al. Recurrence of **hyperemesis gravidarum** across generations: population based cohort study. BMJ 2010;340:c2050, doi: 10.1136/bmj.c2050 (Published 29 April 2010)
Vincenzi B, Tonini G, Santini D. **Aprepitant for erlotinib-induced pruritus**. N Engl J Med. 2010 Jul 22;363(4):397-8.
Warusevitane A, Karunatilake D, Sim J, et al. Safety and Effect of **Metoclopramide to Prevent Pneumonia** in Patients With Stroke Fed via Nasogastric Tubes Trial. Stroke. 2015 Feb;46(2):454-60.
Weimer K, Horing B, Muth ER, et al. Different Disclosed Probabilities to Receive an Antiemetic Equally Decrease Subjective Symptoms in an Experimental **Placebo Study**: To Be or Not to Be Sure. Clin Ther. 2016 Dec 20.
Wilbur MB, Birrer MJ, Spriggs DR. CLINICAL DECISIONS. **Chemotherapy-Induced Nausea and Vomiting**. N Engl J Med. 2016 Jul 14;375(2):177-9.
Yang T, Liu Q, Lu M, et al. Efficacy of **olanzapine for the prophylaxis of chemotherapy-induced nausea and vomiting**: A meta-analysis. Br J Clin Pharmacol. 2017 Jan 23.
Young-Wolff KC, Sarovar V, Tucker LY, et al. Association of Nausea and Vomiting **in Pregnancy With Prenatal Marijuana Use**. JAMA Intern Med. 2018 Aug 20.
Zhang R, Persaud N. 8-Way Randomized Controlled Trial of **Doxylamine, Pyridoxine and Dicyclomine** for Nausea and Vomiting during Pregnancy: Restoration of **Unpublished** Information. PLoS One. 2017 Jan 4;12(1):e0167609.
Zic JA, Straka BT, McGirt LY, et al. **Aprepitant for the Treatment of Pruritus in Sézary Syndrome**: A Randomized Crossover Clinical Trial. JAMA Dermatol. 2018 Aug 15.

[1] Nuttall GA, Eckerman KM, Jacob KA, Pawlaski EM, et al. Does low-dose droperidol administration increase the risk of drug-induced QT prolongation and torsade de pointes in the general surgical population? Anesthesiology. 2007 Oct;107(4):531-6. [Health Canada: http://www.hc-sc.gc.ca/dhp-mps/medeff/advisories-avis/prof/_2010/index-eng.php]

References: RxFiles Nausea & Vomiting – Management / Treatment Chart www.rxfiles.ca

[1] General references:

a) Mannix KA. Palliation of nausea and vomiting. Oxford Text Palliative Med. Third ed. 2004. Doyle D, Hanks G, Cherney N, Calman K (Eds). Oxford: Oxford. U. Press, 459-468.
b) Quigley EM, Hasler WL, Parkman HP. AGA Technical Review on Nausea and Vomiting. *Gastroenterolgy* 2001; 120(1):263-286
c) Weissman, D. Fast Fact and Concepts #05: Treatment of Nausea and Vomiting. June, 2000. End-of-Life Physician Education Resource Center www.eperc.mcw.edu.
d) Neron A (Ed). Care Beyond Cure: A Pharmacotherapeutic Guide to Palliative Care Pharmacy. 2000. Specialty Group on Palliative Care. 73-81
e) Symptom Management Guidelines. Kingston, Frontenac, Lennox and Addington Palliative Care Integration Project. August 2003 57-61
f) MacLean C. Nausea. Therapeutic Choices. Fifth ed. 2007. Gray J (Ed). Canadian Pharmacists Association
g) Compendium of Pharmaceuticals and Specialties. 2015. Canadian Pharmacists Association
h) Scorza K, Williams A, Phillips DJ, Shaw J. Evaluation of Nausea and Vomiting. AFP 2007;76;76-84. Accessed online:
I) Micromedex Drug Database 2017 (Thomson Healthcare)
j) Dunsfield L, Fitsimmons. CADTH Health Technology Inquiry Service (HTIS): Serotonin (5-HT3) antagonists as anti-emetics. Systematic Review. Feb 6, 2007. www.cadth.ca , htis@cadth.ca .
k) Australian Family Physician September 2007 - Nausea & vomiting collection. http://www.racgp.org.au/afp/200709 {e.g. Hyperemesis gravidarum http://www.racgp.org.au/afp/200709/18538 ; The vomiting **child** http://www.racgp.org.au/afp/200709/18542 ; Diagnostic Approach http://www.racgp.org.au/afp/200709/18541 }

[2] Jewell D, Young G. Interventions for nausea and vomiting in early pregnancy. **Cochrane** Database Syst Rev. 2003;(4):CD000145.
Niebyl JR. Clinical practice. **Nausea and vomiting in pregnancy**. N Engl J Med. 2010 Oct 14;363(16):1544-50.
Matthews A, Haas DM, O'Mathúna DP, Dowswell T. Interventions for nausea and vomiting in early pregnancy. Cochrane Database Syst Rev. 2015 Sep 8;(9):CD007575.

[3] Czeizel AE, Vargha P. A case-control study of congenital abnormality and dimenhydrinate usage during pregnancy. Arch Gynecol Obstet. 2005 Feb;271(2):113-8. Epub 2004 Oct 23.

[4] Briggs Pregnancy & Lactation 11th Edition 2017; {CPP= Collaborative Perinatal Project}

[5] Einarson A, Maltepe C, Navioz Y, Kennedy D, et al. The safety of ondansetron for nausea and vomiting of pregnancy: a prospective comparative study. BJOG. 2004 Sep;111(9):940-3.

[6] Evidence link: http://clinicalevidence.bmj.com/ceweb/conditions/pac/1405/1405_l2.jsp; P6 Picture link: http://www.pyroenergen.com/articles07/images/neiguan-acupressure-point.jpg
[7] Carlisle JB, Stevenson CA. Drugs for preventing postoperative nausea and vomiting. **Cochrane** Database Syst Rev. 2006 Jul 19;3:CD004125 - Withdrawn 2017.
Tang DH, Malone DC. A network meta-analysis on the efficacy of serotonin type 3 receptor antagonists used in adults during the first 24 hours for postoperative nausea and vomiting prophylaxis. Clin Ther. 2012 Feb;34(2):282-94.
[8] Lee A, Done ML. Stimulation of the wrist acupuncture point P6 for preventing postoperative nausea and vomiting. **Cochrane** Database Syst Rev. 2004;(3):CD003281.
[9] Golembiewski, J; Chernin E; Chopra T. Prevention and Treatment of **Postoperative** Nausea and Vomiting. Am J Health-Syst Pharm. 2005;62(12):1247-1260. ©2005 ASHSP Posted 06/27/2005. http://www.medscape.com/viewarticle/506997_print
[10] Kranke P, Morin AM, Roewer N, Eberhart LH. Dimenhydrinate for prophylaxis of postoperative nausea and vomiting: a meta-analysis of randomized controlled trial s. Acta Anaesthesiol Scand. 2002 Mar;46(3):238-44.
[11] Lee Y, Wang PK, Lai HY, Yang YL, Chu CC, Wang JJ. Haloperidol is as effective as ondansetron for preventing postoperative nausea and vomiting. Can J Anaesth. 2007 May;54(5):349-54.
[12] www.Cancercare.on.ca : **Hesketh Classification of Emetogenic Potentia**l; www.cancercare.on.ca/pdfchemo/NVFIGURE%20II.pdf
Hesketh PJ, Kris MG, Basch E, et al. **ASCO-Antiemetics**: American Society of Clinical Oncology clinical **practice guideline** update. J Clin Oncol. 2017 Oct 1;35(28):3240-61.
[15b] Hesketh PJ, **Chemotherapy-Induced Nausea and Vomiting**. N Engl J Med 2008;358:2482-94.
[13] Peterson K, McDonagh M, Carson S, Lopez S. Drug class review on newer antiemetics: final report. Portland (OR): **Oregon Evidence-based** Practice Centre, 2006 Jan. Available: http://www.ohsu.edu/drugeffectiveness/reports/documents/Antiemetics%20Final%20Report.pdf (Updated by Alison Little, Feb 2009 in a P&T Committee Brief)
[14] Kovac AL. Benefits and risks of newer treatments for chemotherapy-induced and postoperative nausea and vomiting. Drug Saf. 2003;26(4):227-59.
[15] Gan TJ, Meyer TA, Apfel CC, Chung F,et al; Society for Ambulatory Anesthesia. Society for Ambulatory Anesthesia **guidelines** for the management of **postoperative** nausea and vomiting. Anesth Analg. 2007 Dec;105(6):1615-28,
[16] Koivuranta M, Läärä E, Snåre L, Alahuhta S. A survey of postoperative nausea and vomiting. Anaesthesia. 1997 May;52(5):443-9.
[17] Apfel CC, Läärä E, Koivuranta M, Greim CA, Roewer N. A simplified risk score for predicting postoperative nausea and vomiting: conclusions from cross-validations between two centers. Anesthesiology. 1999 Sep;91(3):693-700.
[18] Szajewska H, Gieruszczak-Białek D, Dylag M. Meta-analysis: ondansetron for vomiting in acute gastroenteritis in children. Aliment Pharmacol Ther. 2007 Feb 15;25(4):393-400.
Alhashimi D, Al-Hashimi H, Fedorowicz Z. Antiemetics for reducing vomiting related to acute gastroenteritis in children and adolescents. Cochrane Database Syst Rev. 2009 Apr 15;(2):CD005506. The small number of included trials provided some limited evidence favouring the use of ondansetron and metoclopramide over placebo to reduce the number of episodes of vomiting due to gastroenteritis in children. The increased incidence of diarrhea with both ondansetron and metoclopramide was considered to be as a result of retention of fluids and toxins that would otherwise have been eliminated through the process of vomiting.
Uhlig, Ulrike, Pfeil, Nicole, Gelbrich, Gotz, et al. **Dimenhydrinate** in Children With Infectious Gastroenteritis: A Prospective, RCT. Pediatrics 2009 0: peds.2008-1650.
Gouin S, Vo TT, Roy M, et al. Oral **Dimenhydrinate** Versus Placebo in Children With Gastroenteritis: A Randomized Controlled Trial. Pediatrics. 2012 May 14. (dimenhydrinate did not decrease frequency of vomiting)
[19] Leung AK, Robson WL. Acute gastroenteritis in **children**: role of anti-emetic medication for gastroenteritis-related vomiting. Paediatr Drugs. 2007;9(3):175-84. {also: http://www.racgp.org.au/afp/200709/18542}
[20] Freedman SB, Adler M, Seshadri R, Powell EC. Oral ondansetron for gastroenteritis in a pediatric emergency department. N Engl J Med. 2006 Apr 20;354(16):1698-705.
Fedorowicz Z, Jagannath VA, Carter B. Antiemetics for reducing vomiting related to acute gastroenteritis in children and adolescents. Cochrane Database of Systematic Reviews 2011, Issue 9. Art. No.: CD005506. DOI: 10.1002/14651858.CD005506.pub5. Oral ondansetron increased the proportion of patients who had ceased vomiting and reduced the number needing intravenous rehydration and immediate hospital admission. Intravenous ondansetron and metoclopramide reduced the number of episodes of vomiting and hospital admission, and dimenhydrinate as a suppository reduced the duration of vomiting.
[21] 2006-2007 Drug Handbook & Formulary 25th Ed. SickKids – The Hospital for Sick Children, Toronto, ON, Canada.
[22] Nuttall GA, Eckerman KM, Jacob KA, Pawlaski EM, et al. Does low-dose droperidol administration increase the risk of drug-induced QT prolongation and torsade de pointes in the general surgical population? Anesthesiology. 2007 Oct;107(4):531-6. [Health Canada: http://www.hc-sc.gc.ca/dhp-mps/medeff/advisories-avis/prof/_2010/index-eng.php]
Systematic Treatment Disease Site Group. Use of 5-HT3 receptor antagonists in patients receiving moderately or highly emetogenic chemotherapy [Practice guideline; no 12-3].Toronto(ON):Cancer Care Ontario (CCO);2003. Available:http://www.cancercare.on.ca/pdf/pebc12_3f.pdf (Accessed 2008, Jan 22).
Geling O, Eichler HG. Should 5-hydroxytryptamine-3 receptor antagonists be administered beyond 24 hours after chemotherapy to prevent delayed emesis? Systematic re-evaluation of clinical evidence and drug cost implications. J Clin Oncol. 2005 Feb 20;23(6):1289-94.
Spinks AB, Wasiak J, Villanueva EV, Bernath V. Scopolamine (hyoscine) for preventing and treating motion sickness. Cochrane Database Syst Rev. 2007 Jul 18;(3):CD002851.
Apfel Christian C., Zhang Kun, Georgeet Elizabeth al. Transdermal scopolamine for the prevention of postoperative nausea and vomiting: A systematic review and meta-analysis, Clinical Therapeutics, Volume 32, Issue 12, November 2010.
Motherisk website: nausea and vomiting in pregnancy. Including video tutorial. Accessed Dec 10, 2007. http://www.motherisk.org/prof/morningSickness.jsp
Richter J. "Heartburn, Nausea, Vomiting during pregnancy" in Pregnancy in Gastrointestinal Disorders. American College of Gastroenterology 2007. Accessed online Dec 10, 2007 at http://www.acg.gi.org/physicians/pdfs/PregnancyMonograph.pdf .
Arsenault MY, Lane CA, MacKinnon CJ, Bartellas E, Cargill YM, Klein MC, Martel MJ et al. The management of nausea and vomiting of pregnancy. J Obstet Gynaecol Can. 2002 Oct;24(10):817-31; quiz 832-3.
Nulman, Irena, Koren, Gideon. Diclectin for morning sickness: Long-term neurodevelopment. Can Fam Physician 2011 57: 193-194.
Jarvis Sheba, Nelson-Piercy Catherine. Management of nausea and vomiting in pregnancy. BMJ 2011;342:doi:10.1136/bmj.d3606 (Published 17 June 2011)
Koren G. Treating morning sickness PRN? Can Fam Physician. 2013 Feb;59(2):150-1.
Pasternak B et al. Ondansetron in pregnancy and risk of adverse fetal outcomes. N Engl J Med 2013 Feb 28; 368:814.
Royal College of Obstetricians and Gynaecologists (RCOG) , 2016. The management of nausea and vomiting of pregnancy and hyperemesis gravidarum [online]. Available: https://www.rcog.org.uk/globalassets/documents/guidelines/green-top-guidelines/gtg69-hyperemesis.pdf [Accessed 17 August 2016]
SOGC 2016: Campbell K, Rowe H, Azzam H, Lane CA. The Management of Nausea and Vomiting of Pregnancy. J Obstet Gynaecol Can. 2016 Dec;38(12):1127-1137.

Holmgren C, Aagaard-Tillery KM, Silver RM, Porter TF, Varner M. Hyperemesis in pregnancy: an evaluation of treatment strategies with maternal and neonatal outcomes. Am J Obstet Gynecol. 2008 Jan;198(1):56.e1-4. Maternal complications associated with PICC line placement are substantial despite no difference in neonatal outcomes, suggesting that the use of PICC lines for treatment of HEG patients should not be routinely used.
32b Matok I et al. The safety of metoclopramide use in the first trimester of pregnancy. N Engl J Med 2009 Jun 11; 360:2528.
Cyclic Vomiting Syndrome. The National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK), NIH. http://digestive.niddk.nih.gov/ddiseases/pubs/cvs/index.htm#6
Talley NJ. Functional nausea and vomiting. Aust Fam Physician. 2007 Sep;36(9):694-7. Accessed online: http://www.racgp.org.au/Content/NavigationMenu/Publications/AustralianFamilyPhys/2007issues/afp200709/200709tally.pdf
Badihian N;Saneian H;Badihian S;Yaghini O. Prophylactic Therapy of Cyclic Vomiting Syndrome in Children: Comparison of Amitriptyline and Cyproheptadine: A Randomized Clinical Trial. Am J Gastroenterol. 2017 Jul 18.
35 Czarnetzki C, Elia N, Lysakowski C, Dumont L, Landis BN, Giger R, Dulguerov P, Desmeules J, Tramèr MR. Dexamethasone and risk of nausea and vomiting and postoperative bleeding after tonsillectomy in children: a randomized trial. JAMA. 2008 Dec 10;300(22):2621-30.
36 DeCamp LR, Byerley JS, Doshi N, Steiner MJ. Use of antiemetic agents in acute gastroenteritis: a systematic review and meta-analysis. Arch Pediatr Adolesc Med. 2008 Sep;162(9):858-65.
37 Lacrolx R, Eason E, Melzack R. Nausea and vomiting during pregnancy: A prospective study of its frequency, intensity, and patterns of change. Am J Obstet Gynecol 2000;192:9331-7

See also: **Sexual Dysfunction Chart:** http://www.rxfiles.ca/rxfiles/uploads/documents/members/CHT-Sexual-Dysfx-Drugs-Overview.pdf

Erectile Dysfunction Comparison Chart (ED) Treatment Chart

[1] Fazio L, Brock G. Erectile dysfunction: management update. CMAJ. **2004** Apr 27;170(9):1429-37.
[2] Therapeutic Choices 5rd Edition, 2007
[3] Micromedex 2018
[4] Basu A, Ryder RE. New treatment options for erectile dysfunction in patients with diabetes mellitus. Drugs. 2004;64(23):2667-88.
[5] Anderson PC, Gommersall L, Hayne D, Arya M, Patel HR. New phosphodiesterase inhibitors in the treatment of erectile dysfunction. Expert Opin Pharmacother. 2004 Nov;5(11):2241-9.
[6] Viera AJ, Clenney TL, et al. Newer pharmacologic alternatives for erectile dysfunction. Am Fam Physician. 1999 Sep 15;60(4):1159-66, 1169, 1172. Review. Erratum in: Am Fam Physician 2000 Apr 15;61(8):2344.
[7] Montague DK, Barada JH, Belker AM, Levine LA, Nadig PW, Roehrborn CG, Sharlip ID, Bennett AH. Clinical guidelines panel on erectile dysfunction: summary report on the treatment of organic erectile dysfunction. The American Urological Association. J Urol. 1996 Dec;156(6):2007-11.
[8] Canadian Urological Association Guidelines Committee. Erectile dysfunction practice guidelines. Can J Urol. 2002 Aug;9(4):1583-7. 2006 Guidelines: http://www.cua.org/guidelines/ed_2006_en.asp
Bella AJ, Lee JC, Carrier S, et al. **2015 CUA** Practice guidelines for **erectile dysfunction**. Can Urol Assoc J 2015;9(1-2):23-9.
https://www.cua.org/themes/web/assets/files/guidelines/en/erectile_dysfunction_feb_2015.pdf (accessed April 6, 2015)
[9] Viagra and Loss of Vision. Medical Lett Drugs Ther. 2005 June 20;47(1211):49. FDA July/05 http://www.fda.gov/bbs/topics/NEWS/2005/NEW01201.html ; Health Canada July/05 http://www.hc-sc.gc.ca/ahc-asc/media/advisories-avis/2005/2005_83_e.html June/06 (**5 CDN cases as of Oct/05**) http://www.hc-sc.gc.ca/dhp-mps/medeff/advisories-avis/prof/2006/cialis_levitra_viagra_hpc-cps_e.html
[10] Jain P, Rademaker AW, McVary KT. Testosterone supplementation for erectile dysfunction: results of a meta-analysis. J Urol. 2000 Aug;164(2):371-5.
[11] Ernst E, Pittler MH. Yohimbine for erectile dysfunction: a systematic review and meta-analysis of randomized clinical trials. J Urol. 1998 Feb;159(2):433-6.
BAUS Section of Andrology Genitourethral Surgery, Muneer A, Brown G, Dorkin T, et al. **BAUS** consensus document for the management of male genital emergencies: **priapism**. BJU Int. 2018 Jan 22.
Montague DK, Jarow J, Broderick GA, et al; Members of the Erectile Dysfunction Guideline Update Panel; Americal Urological Association. **American** Urological Association guideline on the management of **priapism**. J Urol. 2003 Oct;170(4 Pt 1):1318-24.
[12] Milbank AJ, Montague DK. Surgical management of erectile dysfunction. Endocrine. 2004 Mar-Apr;23(2-3):161-5.
[36] Erectile Dysfuntion Guideline Update Panel. The management of ED: an Update. **American** Urological Association, **2005**. (Updated **2006**) http://www.auanet.org/content/guidelines-and-quality-care/clinical-guidelines.cfm?sub=ed
AUA American Guideline: Burnett AL, Nehra A, Breau RH, et al. Erectile Dysfunction: **American Urological Association Guideline**. J Urol. **2018** May 7.

[37] Barada James. Clinical Perspectives on ED. Medscape Conference Coverage – International Society for Sexual and Impotence Research 11th World Congress, 2005
[38] Basson R. Chapter 78: Male Sexual Dysfunction. Therapeutic Choices. CPhA; 2003.
[39] Wespes E et al. Guidelines on Erectile Dysfunction. European Urology 2002; 41:1-5.
[40] Brock GB et al. Efficacy and safety of tadalafil for treatment of erectile dysfunction: results of integrated analysis. J Urol 2002;168:1332-36.
[41] Anderson P et al. New phosphodiesterases inhibitors in the treatment of erectile dysfunction. Expert Opin Pharmacother 2004;5(11):2241-49.
[42]

[43] Hatzimouratidis K, Hatzichristou DG. A comparative review of the options for treatment of erectile dysfunction: which treatment for which patient? Drugs. 2005;65(12):1621-50.
[44] Chung E, Brock GB. Emerging and novel therapeutic approaches in the treatment of male erectile dysfunction. Curr Urol Rep 2011;12: 432–43.
Babaev A, Jhaveri RR. Angiography and endovascular revascularization of pudendal artery atherosclerotic disease in patients with medically refractory erectile dysfunction. J Invasive Cardiol 2012; 24: 236–40.

Apomorphine (CR sublingual tabs) **ApoKyn** (USA)	Centrally acting agent stimulates dopamine sites in the hypothalamus C	SE: nausea (↓with time, CR SL tabs);headache, dizziness, sedation, yawning Not affected by food or alcohol	Onset <30min Peak ~1h Duration ~1-2h Safe with nitrates so may be preferred in select cardiac patients Can be used in combination with PDE5 inhibitors for increased effect Limited efficacy compared to PDE5 inhibitors generally [39]	2-3mg 6mg	

New References

1. Fazio L, Brock G. Erectile dysfunction: management update. CMAJ. 2004 Apr 27;170(9):1429-37.
2. Therapeutic Choices 5rd Edition, 2007
3. Micromedex 2017
4. Basu A, Ryder RE. New treatment options for erectile dysfunction in patients with diabetes mellitus. Drugs. 2004;64(23):2667-88.
5. Anderson PC, Gommersall L, Hayne D, Arya M, Patel HR. New phosphodiesterase inhibitors in the treatment of erectile dysfunction. Expert Opin Pharmacother. 2004 Nov;5(11):2241-9.
6. Viera AJ, Clenney TL, et al. Newer pharmacologic alternatives for erectile dysfunction. Am Fam Physician. 1999 Sep 15;60(4):1159-66, 1169, 1172. Review. Erratum in: Am Fam Physician 2000 Apr 15;61(8):2344.
7. Montague DK, Barada JH, Belker AM, Levine LA, Nadig PW, Roehrborn CG, Sharlip ID, Bennett AH. Clinical guidelines panel on erectile dysfunction: summary report on the treatment of organic erectile dysfunction. The American Urological Association. J Urol. 1996 Dec;156(6):2007-11.
8. Canadian Urological Association Guidelines Committee. Erectile dysfunction practice guidelines. Can J Urol. 2002 Aug;9(4):1583-7. 2006 Guidelines: http://www.cua.org/guidelines/ed_2006_en.asp
Bella AJ, Lee JC, Carrier S, et al. 2015 CUA Practice guidelines for erectile dysfunction. Can Urol Assoc J 2015;9(1-2):23-9.
https://www.cua.org/themes/web/assets/files/guidelines/en/erectile_dysfunction_feb_2015.pdf (accessed April 6, 2015)
9. Briggs GG, Freeman RK, Sumner JY. Drugs in Pregnancy and Lactation 9th Edition. Williams & Wilkins, Baltimore, 2011.

10. Fink HA, Mac Donald R, Rutks IR, Nelson DB, Wilt TJ. Sildenafil for male erectile dysfunction: a systematic review and meta-analysis. Arch Intern Med. 2002 Jun 24;162(12):1349-60.
11. Carson CC, et al. Erectile response with vardenafil in sildenafil nonresponders: a multicentre, double-blind, 12-week, flexible-dose, placebo-controlled erectile dysfunction clinical trial. BJU Int. 2004 Dec;94(9):1301-9.
12. Raina R, Lakin MM, Agarwal A, Sharma R, et a.. Long-term effect of sildenafil citrate on erectile dysfunction after radical prostatectomy: 3-year follow-up. Urology. 2003 Jul;62(1):110-5.
13. Galie N, Ghofrani HA, Torbicki A, et al. Sildenafil citrate Therapy for Pulmonary Arterial Hypertension. N Engl J Med 2005;353:2148-57.(InfoPOEMs: Sildenafil improves the 6-minute walking distance by approximately 15% & leads to an improvement in functional status for between 28% & 42% of patients with pulmonary arterial hypertension (number needed to treat = 2.5 - 4). It is reasonable to begin with 20 mg TID & only increase that dose if the drug is well tolerated & there is no clear response. (LOE = 1b))
14. Fries R, Shariat K, von Wilmowsky H, Bohm M. Sildenafil in the treatment of Raynaud's phenomenon resistant to vasodilatory therapy. Circulation. 2005 Nov 8;112(19):2980-5.
15. Viagra and Loss of Vision. Medical Lett Drugs Ther. 2005 June 20;47(1211):49. FDA July/05 http://www.fda.gov/bbs/topics/NEWS/2005/NEW01201.html ; Health Canada July/05 http://www.hc-sc.gc.ca/ahc-asc/media/advisories-avis/2005/2005_83_e.html June/06 (5 CDN cases as of Oct/05) http://www.hc-sc.gc.ca/dhp-mps/medeff/advisories-avis/prof/2006/cialis_levitra_viagra_hpc-cps_e.html
16. Brock GB, McMahon CG, Chen KK, et al. Efficacy and safety of tadalafil for the treatment of erectile dysfunction: results of integrated analyses. J Urol. 2002 Oct;168(4 Pt 1):1332-6.
17. Tadalafil (cialis) for erectile dysfunction. Med Lett Drugs Ther. 2003 Dec 22;45(1172):101-2.
Arif SA, Poon H. Tadalafil: A Long-Acting Phosphodiesterase-5 Inhibitor for the Treatment of Pulmonary Arterial Hypertension. Clin Ther. 2011 Jul 13
18. Crowe SM, Streetman DS. Vardenafil treatment for erectile dysfunction. Ann Pharmacother. 2004 Jan;38(1):77-85.
19. Keating GM, Scott LJ. Vardenafil: a review of its use in erectile dysfunction. Drugs. 2003;63(23):2673-703.
20. Hellstrom WJ, Gittelman M, et al. Vardenafil Study Group. Sustained efficacy and tolerability of vardenafil, a highly potent selective phosphodiesterase type 5 inhibitor, in men with erectile dysfunction: results of a randomized, double-blind, 26-week placebo-controlled pivotal trial. Urology. 2003 Apr;61(4 Suppl 1):8-14.
21. Stark S, Sachse R, Liedl T, Hensen J, et al. Vardenafil increases penile rigidity and tumescence in men with erectile dysfunction after a single oral dose. Eur Urol. 2001 Aug;40(2):181-8; discussion 189-90.
22. Goldstein I, Young JM, et al. Vardenafil Diabetes Study Group. Vardenafil, a new phosphodiesterase type 5 inhibitor, in the treatment of erectile dysfunction in men with diabetes: a multicenter double-blind placebo-controlled fixed-dose study. Diabetes Care. 2003 Mar;26(3):777-83.
23. Brock G, Nehra A, Lipshultz LI, Karlin GS, et al. Safety and efficacy of vardenafil for the treatment of men with erectile dysfunction after radical retropubic prostatectomy. J Urol. 2003 Oct;170(4 Pt 1):1278-83.
24. Markou S, Perimenis P, Gyftopoulos K, Athanasopoulos A, Barbalias G. Vardenafil (Levitra) for erectile dysfunction: a systematic review and meta-analysis of clinical trial reports. Int J Impot Res. 2004 Dec;16(6):470-8.
25. Vardenafil (Levitra) for erectile dysfunction. Med Lett Drugs Ther. 2003 Sep 29;45(1166):77-8.
26. Valiquette L, et al.; Vardenafil Study Group. Sustained efficacy and safety of vardenafil for treatment of erectile dysfunction: a randomized, double-blind, placebo-controlled study. Mayo Clin Proc. 2005 Oct;80(10):1291-7.
27. van Ahlen H, Wahle K, Kupper W, Yassin A, Reblin T, Neureither M. Safety and efficacy of vardenafil, a selective phosphodiesterase 5 inhibitor, in patients with erectile dysfunction and arterial hypertension treated with multiple antihypertensives. J Sex Med. 2005;2:856-864.
28. Raina R, Agarwal A, Ausmundson S, et al. Long-term efficacy and compliance of MUSE for erectile dysfunction following radical prostatectomy: SHIM (IIEF-5) analysis. Int J Impot Res. 2005 Feb;17(1):86-90.
29. Steidle C, Padma-Nathan H, Salem S, Tayse N, et al. Topical alprostadil cream for the treatment of erectile dysfunction: a combined analysis of the phase II program. Urology. 2002 Dec;60(6):1077-82.
30. Sommer F, Engelmann U. Future options for combination therapy in the management of erectile dysfunction in older men. Drugs Aging. 2004;21(9):555-64.
31. Jaffe JS, Antell MR, Greenstein M, Ginsberg PC, Mydlo JH, Harkaway RC. Use of intraurethral alprostadil in patients not responding to sildenafil citrate. Urology. 2004 May;63(5):951-4.
32. Urciuoli R, Cantisani TA, CarliniI M, Giuglietti M, Botti FM. Prostaglandin E1 for treatment of erectile dysfunction. Cochrane Database Syst Rev. 2004;(2):CD001784.

33. Jain P, Rademaker AW, McVary KT. Testosterone supplementation for erectile dysfunction: results of a meta-analysis. J Urol. 2000 Aug;164(2):371-5.
34. Ernst E, Pittler MH. Yohimbine for erectile dysfunction: a systematic review and meta-analysis of randomized clinical trials. J Urol. 1998 Feb;159(2):433-6. BAUS Section of Andrology Genitourethral Surgery, Muneer A, Brown G, Dorkin T, et al. BAUS consensus document for the management of male genital emergencies: priapism. BJU Int. 2018 Jan 22.Montague DK, Jarow J, Broderick GA, et al; Members of the Erectile Dysfunction Guideline Update Panel; Americal Urological Association. American Urological Association guideline on the management of priapism. J Urol. 2003 Oct;170(4 Pt 1):1318-24.
35. Milbank AJ, Montague DK. Surgical management of erectile dysfunction. Endocrine. 2004 Mar-Apr;23(2-3):161-5.
36. Erectile Dysfuntion Guideline Update Panel. The management of ED: an Update. American Urological Association, 2005. (Updated 2006) http://www.auanet.org/content/guidelines-and-quality-care/clinical-guidelines.cfm?sub=ed AUA American Guideline: Burnett AL, Nehra A, Breau RH, et al. Erectile Dysfunction: American Urological Association Guideline. J Urol. 2018 May 7.
37. Barada James. Clinical Perspectives on ED. Medscape Conference Coverage – International Society for Sexual and Impotence Research 11th World Congress, 2005
38. Basson R. Chapter 78: Male Sexual Dysfunction. Therapeutic Choices. CPhA; 2003.
39. Wespes E et al. Guidelines on Erectile Dysfunction. European Urology 2002; 41:1-5.
40. Brock GB et al. Efficacy and safety of tadalafil for treatment of erectile dysfunction: results of integrated analysis. J Urol 2002;168:1332-36.
41. Anderson P et al. New phosphodiesterases inhibitors in the treatment of erectile dysfunction. Expert Opin Pharmacother 2004;5(11):2241-49.
42. Hatzimouratidis K, Hatzichristou DG. A comparative review of the options for treatment of erectile dysfunction: which treatment for which patient? Drugs. 2005;65(12):1621-50.
43. Chung E, Brock GB. Emerging and novel therapeutic approaches in the treatment of male erectile dysfunction. Curr Urol Rep 2011;12: 432–43. Babaev A, Jhaveri RR. Angiography and endovascular revascularization of pudendal artery atherosclerotic disease in patients with medically refractory erectile dysfunction. J Invasive Cardiol 2012; 24: 236–40.
44. Shenfeld O, Hanani J, Shalhav A, Vardi Y, Goldwasser B. Papaverine-phentolamine and prostaglandin E1 versus papaverine-phentolamine alone for intracorporeal injection therapy: a clinical double-blind study. J Urol. 1995. Sep;154(3):1017-9.
45. CHEN JK, HWANG TI, YANG CR. Comparison of effects following the intracorporeal injection of papaverine and prostaglandin E1. British journal of urology. 1992 Apr;69(4):404-7.

Additional sources:

Abman SH, Kinsella JP, et al; Pediatric Pulmonary Hypertension Network (PPHNet). Implications of the FDA Warning Against the Use of **Sildenafil** for the Treatment of **Pediatric Pulmonary Hypertension**. Am J Respir Crit Care Med. 2012 Dec 6.
Abman SH, Hansmann G, Archer SL, et al. **Pediatric Pulmonary Hypertension: Guidelines** From the American Heart Association (AHA) and American Thoracic Society (ATS). Circulation. 2015 Nov 3.
Alemozaffar M, Regan MM, Cooperberg MR, et al. Prediction of erectile function **following treatment for prostate cancer**. JAMA. 2011;306(11):1205-1214.
Almuhtaseb H, Kanavati O, Lotery A. Branch retinal vein occlusion secondary to sildenafil. BMJ. 2017 Mar 23;356:j753
Andersen MJ, et al. **Sildenafil** & Diastolic Dysfunction After Acute Myocardial Infarction in Patients With Preserved Ejection Fraction: Sildenafil & Diastolic Dysfunction After Acute Myocardial Infarction(SIDAMI) Trial. Circulation.2013Mar19;127(11):1200-1208.
Andersson DP, Trolle Lagerros Y, Grotta A, et al. Association between treatment for **erectile dysfunction and death or cardiovascular outcomes after myocardial infarction**. Heart. 2017 Mar 9.
Archer, Stephen L., Michelakis, Evangelos D. Phosphodiesterase Type 5 Inhibitors for **Pulmonary Arterial Hypertension**. N Engl J Med 2009 361: 1864-1871.
Arif SA, Poon H. Tadalafil: A Long-Acting Phosphodiesterase-5 Inhibitor for the Treatment of **Pulmonary Arterial Hypertension**. Clin Ther. 2011 Jul 13
AUA Guideline: Burnett AL, Nehra A, Breau RH, et al. Erectile Dysfunction: **American Urological Association Guideline**. J Urol. 2018 May 7.
Australian Therapeutic Goods May/15: **Maxman Cialis** tablets contains undeclared sildenafil.

Badesch DB, Hill NS, Burgess G, et al. SUPER Study Group. Sildenafil for **pulmonary arterial hypertension** associated with connective tissue disease. J Rheumatol. 2007 Dec;34(12):2417-22. Epub 2007 Nov 1.

Barnes H, Brown Z, Burns A, et al. **Phosphodiesterase 5 inhibitors for pulmonary hypertension**. Cochrane Database Syst Rev. 2019 Jan 31;1:CD012621. PDE5 inhibitors appear to have clear beneficial effects in group 1 PAH. Sildenafil, tadalafil and vardenafil are all efficacious in this clinical setting, and clinicians should consider the side-effect profile for each individual when choosing which PDE5 inhibitor to prescribe.While there appears to be some benefit for the use of PDE5 inhibitors in PH-left-heart disease, it is not clear based on the mostly small, short-term studies, which type of left-heart disease stands to benefit.

Barst RJ, et al. A randomized, double-blind,placebo-controlled, dose-ranging study of oral **sildenafil** citrate in treatment-naive children with **pulmonary arterial hypertension**. Circulation. 2012 Jan 17;125(2):324-34.

Bärtsch P, Swenson ER. Clinical practice: **Acute high-altitude illnesses**. N Engl J Med. 2013 Jun 13;368(24):2294-302.

Barst RJ, Beghetti M, Pulido T, et al; STARTS-2 Investigators. STARTS-2: Long-Term Survival With Oral **Sildenafil** Monotherapy in Treatment-Naive **Pediatric Pulmonary Arterial Hypertension**. Circulation. 2014 May 13;129(19):1914-23.

Basson R. Clinical practice. Sexual desire and arousal disorders in **women**. N Engl J Med. 2006 Apr 6;354(14):1497-506.

Baumhakel M, Schlimmer N, Kratz M, et al. **Cardiovascular risk, drugs and erectile function** - a systematic analysis. Int J Clin Pract. 2011 Mar;65(3):289-98. doi: 10.1111/j.1742-1241.2010.02563.x.

Begot I, Peixoto TC, Gonzaga LR, et al. A **home-based walking program** improves erectile dysfunction in men with an acute myocardial infarction. Am J Cardiol. 2015 Mar 1;115(5):571-5.

Bella AJ, Lee JC, Carrier S, et al. **2015 CUA Practice guidelines for erectile dysfunction**. Can Urol Assoc J 2015;9(1-2):23-9.https://www.cua.org/themes/web/assets/files/guidelines/en/erectile_dysfunction_feb_2015.pdf (accessed April 6, 2015)

Berkseth KE, Thirumalai A, Amory JK. Pharmacologic Therapy in Men's Health: Hypogonadism, **Erectile Dysfunction**, and Benign Prostatic Hyperplasia. Med Clin North Am. 2016 Jul;100(4):791-805.

Bermejo J, Yotti R, García-Orta R, et al. **Sildenafil for improving outcomes in patients with corrected valvular heart disease and persistent pulmonary hypertension**: a multicenter, double-blind, randomized clinical trial. Eur Heart J. 2018 Apr 14;39(15):1255-1264.

Blum A. Treating **heart failure** with sildenafil. Congest Heart Fail. 2009 Jul-Aug;15(4):181-5.

Böhm M, Baumhäkel M, Teo K, et al. for the **ONTARGET/TRANSCEND** Erectile Dysfunction Substudy Investigators. Erectile Dysfunction Predicts Cardiovascular Events in High-Risk Patients Receiving Telmisartan, Ramipril, or Both. The ONgoing Telmisartan Alone and in combination with Ramipril Global Endpoint Trial/Telmisartan Randomized AssessmeNt Study in ACE iNtolerant subjects with cardiovascular Disease (ONTARGET/TRANSCEND) Trials. Circulation. 2010 Mar 15.

Brader HS, Athappilly GK, Loewenstein J. **Retinal Toxicity** Associated With Excessive Sildenafil Ingestion. JAMA Ophthalmol. 2019 Jan 10.

Burton TD, Liday C. The comparison of combination **SSRI and PDE-5 inhibitor** therapy to SSRI monotherapy in men with **premature ejaculation**. Ann Pharmacother. 2011 Jul;45(7-8):1000-4.

Cannon JE, Pepke-Zaba J. Contemporary diagnosis and management of **pulmonary hypertension**. Heart. 2016 Oct 15;102(20):1680-91.

Carson CC 3rd. **Cardiac safety** in clinical trials of phosphodiesterase 5 inhibitors. Am J Cardiol. 2005 Dec 26;96(12B):37M-41M. Epub 2005 Dec 5.

Casabé A, Roehrborn CG, et al. Efficacy and safety of the coadministration of **tadalafil once daily with finasteride** for 6 months in men with lower urinary tract symptoms and prostatic enlargement secondary to benign prostatic hyperplasia. J Urol.2014 Mar.

Cassidy A, Franz M, Rimm EB. **Dietary flavonoid intake** and incidence of erectile dysfunction. Am J Clin Nutr. 2016 Jan 13.

Chen Y, Li J, Li T, et al. Association between **homocysteine, vitamin B (12) , folic acid** and erectile dysfunction: a cross-sectional study in China. BMJ Open. 2019 May 22;9(5):e023003.

Chen YF, Lin HH, Lu CC, et al. **Gout and a Subsequent Increased Risk of Erectile Dysfunction** in Men Aged 64 and Under: A Nationwide Cohort Study in Taiwan. J Rheumatol. 2015 Jun 15.

Chiurlia E, D'Amico R, Ratti C, et al. Subclinical coronary artery **atherosclerosis** in patients with erectile dysfunction. J Am Coll Cardiol. 2005 Oct 18;46(8):1503-6. Epub 2005 Sep 28.

Chong J, Poole P, Leung B, Black PN. Phosphodiesterase 4 inhibitors for **chronic obstructive pulmonary disease**. Cochrane Database of Systematic Reviews 2011, Issue 5. Art. No.: CD002309. DOI: 10.1002/14651858.CD002309.pub3. In people with COPD, PDE4 inhibitors offered benefit over placebo in improving lung function and reducing likelihood of exacerbations, however, they had little impact on quality of life or symptoms. Gastrointestinal adverse effects and weight loss were common.

Coghlan JG et al. Initial combination therapy with **ambrisentan and tadalafil** in connective tissue disease-associated **pulmonary arterial hypertension (CTD-PAH):** subgroup analysis from AMBITION trial. Ann Rheum Dis. 2017 Jul;76(7):1219-1227.

Cohen PA, Maller G, DeSouza R, et al. Presence of **banned drugs in dietary supplements following FDA recalls**. JAMA. 2014 Oct 22 29;312(16):1691-3.

Coralic Z, Lenhoff T, Kanzaria HK, et al. A 120-Hour Case of Priapism from an Over-the-Counter Herbal Supplement (**African Black Ant: sildenafil**). Ann Pharmacother. 2013 Feb;47(2):289-90.

Cordell WH, Maturi RK, et al.; ERG Testing During Chronic PDE5 Inhibitor Administration (ERG-PDE5i) Consortium. **Retinal effects** of 6 months of daily use of tadalafil or sildenafil. Arch Ophthalmol. 2009 Apr;127(4):367-73. No abnormalities in ERG or visual function and no treatment-related findings suggestive of drug toxicity are associated with daily administration of tadalafil or sildenafil for 6 months.

De Rose AF, et al. Combined oral therapy with **sildenafil and doxazosin** for the treatment of non-organic erectile dysfunction refractory to sildenafil monotherapy. Int J Impot Res. 2002 Feb;14(1):50-3.

Deyo RA, Smith DH, Johnson ES, et al. Prescription **Opioids for Back Pain** and Use of Medications for Erectile Dysfunction. Spine (Phila Pa 1976). 2013 Mar 1.

Dimitriadis F, Tsambalas S, Tsounapi P, et al. Effects of **phosphodiesterase-5 inhibitors** on **Leydig cell secretory** function in oligoasthenospermic infertile men: a randomized trial. BJU Int. 2010 Feb 22.

Do C, Huyghe E, Lapeyre-Mestre M, et al. **Statins** and Erectile Dysfunction: Results of a Case/Non-Case Study using the French Pharmacovigilance System Database. Drug Saf. 2009;32(7):591-7. doi: 10.2165/00002018-200932070-00005. Despite some methodological limitations, the present study suggests that statins may induce or worsen ED in accordance with other data.

Doggrell SA. Comparison of clinical trials with sildenafil, vardenafil and tadalafil in erectile dysfunction. Expert Opin Pharmacother. 2005 Jan;6(1):75-84.

Dowswell G, Ismail T, Greenfield S, Clifford S, Hancock B, Wilson S. Men's experience of **erectile dysfunction after treatment for colorectal cancer**: qualitative interview study. BMJ 2011;343:d5824.

Drug-induced Male Sexual Dysfunction. Pharmacist's Letter Sept 2006.

Elgendy AY, Elgendy IY, Mahmoud AN, et al. **Statin Use in Men and New Onset of Erectile Dysfunction**: A Systematic Review and Meta-Analysis. Am J Med. 2017 Nov 13

Fava M, et al. Efficacy and safety of sildenafil in men with **serotonergic antidepressant-associated erectile dysfunction**: results from a randomized, double-blind, placebo-controlled trial. J Clin Psychiatry. 2006 Feb;67(2):240-6.

FDA May 2007 FDA chemical analysis revealed that **Energy Max** contains thione analog of sildenafil, a substance with a structure similar to sildenafil, the active ingredient in Viagra, an FDA-approved drug for ED.Substances like this are called analogs because they have a structure similar to another drug and may cause similar side effects and drug interactions. **True Man** contains a thione analog of sildenafil or piperadino vardenafil, an analog of vardenafil, the active ingredient in Levitra, another FDA-approved prescription drug for ED. Neither the thione analog of sildenafil nor piperadino vardenafil are components of approved drug products.

FDA: Sept 21, 2007 -- TWC Global LLC, Inc., issued nationwide recall of **Axcil** and **Desirin**, both marketed as dietary supplements, because they contain potentially harmful, undeclared ingredients. FDA laboratory analysis of **Axcil and Desirin** found that the lot of 02B07 contained 3mg/g of sildenafil, the active ingredient of a FDA approved drug used for erectile dysfunction (ED).

FDA Feb/08 Palo Alto Labs and FDA notified consumers and healthcare professionals of a voluntary nationwide recall of two dietary supplements, **Aspire36** and **Aspire Lite**. The products were recalled because they were found to contain Aildenafil in trace amounts and Dimethyl sildenafil thione, an analog of Sildenafil, a drug used to treat erectile dysfunction.

FDA May/08 The U.S. Food and Drug Administration is advising consumers not to purchase or use "**Blue Steel**" or "**Hero**" products, marketed nationally as dietary supplements, because these products contain undeclared ingredients similar to sildenafil.

FDA May/08 is requesting that the manufacturer of **Xiadafil** — an "all natural" dietary supplement sold to treat erectile dysfunction — recall all its stock from natural food stores & discontinue marketing it on the Web since it contains an analog of sildenafil.

FDA May/08 notified consumers and healthcare professionals that supplement products sold under the brand name of **Viril-ity Power** (VIP) Tablets is being recalled because one lot was found to contain a potentially harmful undeclared ingredient, hydroxyhomosildenafil, an analog of sildenafil.

FDA July/08 Jack Distribution, LLC issued a voluntary nationwide recall of selected lots of **Rize 2 The Occasion Capsules** and **Rose 4 Her Capsules**, marketed as dietary supplements. The products were recalled because certain lots contained thiomethisosildenafil, an undeclared analog of sildenafil, a FDA-approved drug used for Erectile Dysfunction.

FDA July/08 not to buy or use **Viapro** 375mg Capsules because one lot of the product was found to contain a potentially harmful undeclared ingredient, thio-methisosildenafil, an analog of sildenafil.

FDA Aug/08 chemical analysis of **Xiadafil VIP** tablet lots 6K029 and 6K029-SEI found that the product contained an undeclared ingredient, hydroxyhomosildenafil

FDA Mar/09- Bodee LLC and FDA notified consumers and healthcare professionals of a nationwide recall of all the company's supplement product sold under the name **Zencore Plus**. FDA lab analysis of Zencore Plus samples found the product contains benzamidenafil, an undeclared drug product and a PDE5 inhibitor.

FDA Apr/09 Nature & Health Co. and FDA notified healthcare professionals of a recall of a supplement product, **Libimax**. FDA analysis found the product contains tadalafil.

FDA July/09 and Haloteco notified healthcare professionals and consumers of a nationwide voluntary recall of Libipower Plus. Lab analysis of **Libipower Plus** samples were found to contain undeclared Tadalalafil.

FDA July/09 found **Steam** (Nutracoastal Trading LLC's dietary supplement) product contains sulfoaildenafil, an analog of sildenafil.

FDA Nov/09 notified consumers that **Stiff Nights**, a product sold as a dietary supplement, contains sulfoaildenafil, a chemical similar to sildenafil (Viagra).

FDA Nov/09 & RockHard Laboratories notified consumers that **RockHard Weekend**, a product sold as a dietary supplement, contains sulfoaildenafil, an analogue of sildenafil.

FDA Dec/09 warned that **Atlas Operations, Inc**. notified consumers of a nationwide recall of the company's dietary supplements for sexual enhancement. These products are sold as dietary supplements throughout the USA. FDA lab analyses found that the products tested from certain batches contain Sulfoaildenafil.

FDA Mar/10 & Natural Wellness notified consumers that **MasXtreme**, a product sold as a dietary supplement contains aildenafil close in structure to sildenafil and is expected to possess a similar pharmacological and adverse event profile as well as the drug phentolamine which is an alpha-adrenergic blocker.

FDA Apr/10 & Kanec USA notified healthcare professionals of a nationwide recall of **Stud Capsule For Men** [Lot #060607-01/060108-01, Exp 6-2013], after being informed by FDA that laboratory analysis of a sample found the product to be adulterated with sildenafil, an FDA approved drug.

FDA June/10 **Magic Power Coffee**: Product marketed as a dietary supplement for sexual enhancement contains the drug ingredient hydroxythiohomosildenafil.

FDA Aug/10 lab analysis of **Revivexxx Extra Strength** was found to contain undeclared tadalafil.
FDA Aug/10 notified Novacare LLC that certain products appear to contain sulfoaildenafil: **Stiff Nights, Aziffa, Size Matters, Erex, Mojo, Hard Drive, Eyeful, Red Magic, Straight Up, Zotrex, Monster Excyte, WOW, Xaitrex, Verect, Prolatis, Xytamax, Maxyte, Libidinal, OMG, OMG45, and Zilex (with Golden Spear) summers.**
FDA July/10 & Good Health, Inc. is conducting a voluntary recall after FDA lab analyses found that the product tested from certain batches of **Vialipro** contain Sulfoaildenafil.
FDA July/10 notified consumers that lab analysis of lots of ejaculoid **XXTREME** and **stimuloid II** found that the products, sold as dietary supplements, contain sulfoaildenafil
FDA Aug/10 had Lab analysis of **Mr. Magic** to contain hydroxythiohomosildenafil and sulfoaildenafil.
FDA Aug/10 analyzed **TimeOut** and determined that it contains hydroxythiohomosildenafil.
FDA Nov/10 ISSUE: Lab analysis has found **Duro Extend Capsules for Men** to contain Sulfoaidenafil, an analogue of Sildenafil
FDA Dec/10 warned consumers not to use **Man Up Now** capsules, marketed as a dietary supplement for sexual enhancement, because FDA analysis determined that the product contains sulfoaildenafil
FDA Dec/10 notified the public that testing determined that **RockHard Weekend** Lot Numbers 100159 and 100260 sold as blister packs, 3ct bottles and 8ct bottles & **Pandora** Lot Numbers 100378 sold as blister packs & **Passion Coffee** contain an analogue of sildenafil.
FDA Mar/11 notified Biotab Nutraceuticals, Inc. that two lots of counterfeit product purporting to be **Extenze** contain undeclared drug ingredients. Specifically, lot 0709241 contains tadalafil and sildenafil, and lot 0509075 contains tadalafil and sibutramine.
FDA Mar/11 laboratory analysis confirmed that **Black Ant** contains sildenafil.
FDA Mar/11 ISSUE: FDA lab analysis of **X-Hero** found the product contains sulfosildenafil, the analogue of the active ingredient of an FDA-approved drug. In addition, FDA analysis of **Male Enhancer** sample found the product contains tadalafil.
FDA Apr/11 Lab analyses of **Best Enhancer** found that the products to contain Sulfoaildenafil.
FDA May/11 **Regenerect**: Recall - Undeclared Drug Ingredient of lab confirmed the presence of Sulfoaildenafil.
FDA June/11 lab analyses found Via **Xtreme Ultimate Sexual Enhancer Dietary** Supplement for Men to contain sulfoaildenafil methanesulfonate.
FDA Nov/11 lab analysis for Lot 10090571 found **Virility Max** to contain sulfoaildenafil.
FDA Feb/12 Healthy People Co. notified the public of a recall of the company's dietary supplements sold under the brand names Healthy People Co. FDA lab confirmed presence of Sibutramine & Tadalafil, making these products unapproved new drugs. (Mince Belle Dietary Supplement, PERFECT Men Dietary Supplement , EVERLAX Dietary Supplement, EVER Slim Dietary Supplement, Herbal Drink Acai-man Mangosteen Dietary Supplement, EVER SLIM Shake Mix Dietary Supplement)
FDA Feb/12 Regeneca, Inc. notifed the public of a nationwide recall of **RegenArouse**, Lot Number 130100. FDA lab analysis confirmed the presence of Tadalafil.
FDA Feb/12 is advising consumers not to purchase or use "**Hard Ten Days**," & "**Man King**" a product for sexual enhancement sold on various websites. FDA laboratory analysis confirmed that "Hard Ten Days" contains sildenafil
FDA Apr/12 laboratory analysis confirmed that "**France T253**" contains sildenafil.
FDA Apr/12 is advising consumers not to purchase or use "**X-Rock**," a product for sexual enhancement manufactured by CRM Laboratories and sold on various websites, including www.xrockme.com. FDA laboratory analysis confirmed that "X-Rock" contains sildenafil and hydroxythiohomosildenafil.
FDA Apr/12 laboratory analysis confirmed that "**Instant Hard Rod**" contains aminotadalafil. FDA laboratory analysis confirmed that "**ZenMaxx**" contains aminotadalafil. FDA laboratory analysis confirmed that "**RigiRx Plus**" contains aminotadalafil.
FDA May/12 is advising consumers not to purchase or use "**VMaxx Rx**," a product for sexual enhancement sold on various websites, including www.vmaxxrx.com. FDA laboratory analysis confirmed that "VMaxx Rx" contains the undeclared ingredient sulfoaildenafil. FDA is also advising consumers not to purchase or use "**Boost — Ultra Sexual Enhancement Formula**." This product is promoted and sold on various websites, includingwww.boostultra.biz. FDA laboratory analysis confirmed that "Boost—Ultra Sexual Enhancement Formula" contains sildenafil. FDA is also advising consumers not to purchase or use "**Firminite**," a product for sexual enhancement sold on various websites, including **www.firminite.com.** FDA laboratory analysis confirmed that "Firminite" contains tadalafil.
FDA May/12 West Coast Nutritionals, Ltd. is conducting a recall of all lots of their dietary supplements **Firminite, Extra Strength Instant Hot Rod, & Libidron** to the consumer. FDA lab analysis of Firminite was found to contain undeclared Tadalafil.
FDA May/12 is advising consumers not to purchase or use "**EreXite**," a product for sexual enhancement sold on various websites, including www.amazon.com. FDA laboratory analysis confirmed that "EreXite" contains tadalafil.
FDA Aug/12 CRM Laboratories is conducting a consumer/user level recall of all **X-ROCK 3 Day Pill For Men and Z-ROCK** products sold between October, 2011 and April, 2012. Finished product of X-ROCK 3 Day Pill for Men and Z-ROCK was tested and found to contain an analogue of an ingredient in an FDA-approved drug. Analytical tests conducted by the FDA concluded that the products contained sildenafil and hydroxythiohomosildenafil.
FDA Aug/12 Revatio (**sildenafil**) should **not be prescribed to children and adolescents** with pulmonary arterial hypertension, according to an FDA MedWatch alert. The warning is based on the results of a trial published in Circulation that showed increased mortality at medium and high doses of Revatio, compared with low-*dose treatment, among patients aged 1 to 17 years. Low-dose Revatio did not improve exercise capacity.*
FDA Sep/12: Body Basics Inc. announced that it is conducting a voluntary nationwide recall of **ACTRA-Sx 500 Dietary Supplement** Capsules, Lot 008-A, Expiration December 2013. The Company, through independent lab analysis, has confirmed the presence of Sildenafil Citrate.
FDA Sep/12 Evol Nutrition Associates, Inc./Red Dawn ("Evol Nutrition") notified the public of a nationwide recall of all lots of two dietary supplement products distributed by the company under the names **Mojo Nights and Mojo Nights for Her** to the consumer level. Testing by the FDA revealed the presence of undeclared tadalafil and sildenafil in Mojo Nights (Evol Nutrition is also recalling Mojo Nights for Her).
FDA Dec/12: **Libigrow, Libigrow XXXtreme, Blue Diamond, Blue Diamond Platinum, Mojo Nights, Mojo Nights Supreme, And Casanova**: Recall - Undeclared Ingredients Sulfoaildenafil and Thioaildenafil.
FDA Jan/13 Freedom Trading is conducting a voluntary consumer recall of a product sold as a dietary supplement under the brand name of **Super Power**. This product was sold between August 2012 and January 2013 nationwide & the products contained trace amounts of sildenafil.
FDA Mar/13 Green Planet, Inc. notified the public of a recall of its dietary supplement product **Night Bullet**. Analytical tests conducted by the FDA found that the product contains trace amounts of Sulfohydroxyhomosildenafil and Aminotadalafil, which are analogues of sildenafil.
FDA Apr/13 laboratory analysis confirmed that "**Ninja Mojo"& "Love Rider**" contains tadalafil. FDA also confirmed that "**AFFIRM XL**" contains the undeclared ingredient sulfoaildenafil.
FDA Apr/13 Consumer Concepts, Inc. notified the public of a consumer/user level recall of all **ROCK-It MAN** Male Enhancement Capsules sold between October, 2012 and April, 2013. Analytical tests conducted by the FDA concluded that the product contained hydroxythiohomosildenafil.
FDA Apr/13 **Affirm XL**, Inc. is conducting a voluntary recall to the consumer level after FDA lab analysis testing found the product to contain an analogue of sildenafil.
FDA Apr/13 laboratory analysis confirmed that "**Sex Plus**" contains undeclared sildenafil, tadalafil, sulfosildenafil and dimethylacetildenafil. FDA laboratory analysis confirmed that "**Zoom-Zooma-Zoom**" contains sildenafil, the active ingredient in the FDA-approved prescription drug Viagra.
FDA May/13 American Lifestyle is announcing that it is conducting a voluntary recall of all lots of **Vicerex** UPC 893490820087 and **Black Ant** UPC 4026666142546. Laboratory analysis conducted by the FDA has determined the Vicerex product contains undeclared tadalafil and the Black Ant product contains undeclared sildenafil.
FDA May/13 is advising consumers not to purchase or use "**Bullet Proof**," a product promoted and sold for sexual enhancement on various websites and in some retail stores. FDA laboratory analysis confirmed that "Bullet Proof" contains tadalafil. Plus Chang Kwung announced today that it is conducting a voluntary nationwide recall of the company's dietary supplements sold under the brand name **Lightning Rod** (500 mg per capsule packaged in 3-count, UPC 6 89076 20257 2 and 12-count bottles, UPC 6 89076 20297 8), because FDA testing found the Lightning Rod Capsules to contain an analogue of Sildenafil.
FDA May/13: BeaMonstar Products notified the public that it is recalling its **SexVoltz, Velextra, and Ameriect** capsules. Laboratory analysis conducted by the FDA on SexVoltz and Velextra has determined these products contain undeclared tadalafil.
FDA Jun/13 laboratory analysis confirmed that "**Reload**" , "**Cave Diver**" , "**Super Cheetah**", "**Nights to Remember**" , & "**X Zen Platinum**", contains sildenafil.
FDA Jun/13 A sample of **Royal Dragon Herbal Tonic Balls** contains vardenafil.
FDA July/13 **Clalis, Exten 1300 & MaxTreme Zen** contains sildenafil, while **MVP Mega** contains talalafil.
FDA July/13 **Silver Sword** & **Clalis** contains sildenafil.
FDA Aug/13 Volcano Company is recalling all lots of **Volcano Male Enhancement Liquid and Volcano Male Enhancement Capsules** to the consumer level. FDA test results revealed the Volcano Male Enhancement Liquid has been found to contain undeclared Desmethyl Carbodenafil, Dimethylsildenafil, and Dapoxetine.
FDA Aug/13: Jack Rabbit Inc. announced that it is conducting a voluntary nationwide recall of one lot of the company's dietary supplement product sold under the name **Jack Rabbit**. FDA lab analysis of the product was found to contain Sildenafil and Tadalafil.
FDA Aug/13 Hardmenstore.com is voluntarily recalling 1000 lots of **72HP, Evil Root and Pro Power Max** at the consumer level. According to representatives of the FDA, 72HP, Evil Root and Pro Power Max have reportedly been found to contain amounts of the PDE-5 Inhibitor, sildenafil.
FDA Sep/13 is advising consumers not to purchase or use **XZone Premium**, a product promoted and sold for sexual enhancement. FDA laboratory analysis confirmed that XZone Premium contains sildenafil, tadalafil, and dapoxetine.
FDA Sep/13 is advising consumers not to purchase or use **Wood-E**, a product promoted and sold for sexual enhancement. FDA laboratory analysis confirmed that Wood-E contains sildenafil.
FDA Sep/13 is advising consumers not to purchase or use **Xzen 1200, Xzen Gold or Xzen XPress,** products promoted and sold for sexual enhancement. FDA laboratory analysis confirmed that it contains either sildenafil & tadalafil.
FDA Sep/13 Haute Health, LLC is voluntarily recalling all lots of **Virilis Pro, PHUK and Prolifta** at the retail and consumer level. Virilis Pro, PHUK and Prolifta have been found to contain amounts of the PDE-5 Inhibitor sildenafil.
FDA Nov/13: Fossil Fuel Products, LLC is recalling lots OL110714A102 and OL110408B046 of "**BezzRX**." Laboratory analysis conducted by the FDA determined the BezzRX lot OL110714A102 contains undeclared hydroxythiohomosildenafil and

aminotadalafil and RezzRX lot QL110408B046 contains undeclared hydroxylthiohomosildenafil.

FDA Nov/13: Jobbers Wholesale is recalling Lot No. KWAKPMC030505175957019 of **Rhino 5 Plus**, Lot No. JBP-L-1270-70 of **Maxtremezen** and Lot No. KWAKPMC03050517 of **Extenzone**. FDA analysis found these products to contain undeclared desmethylcarbondenafil and dapoxetine, making these products unapproved new drugs.

FDA Nov/13 Vitality Research Labs is recalling lots K58Q and F50Q of **VitaliKOR Fast Acting**. FDA laboratory analysis on VitaliKOR has determined that this product contains undeclared Vardenafil and Tadalafil.

FDA Nov/13: Tendex is voluntarily recalling Lot# F51Q of P-Boost and Lot # F51Q of NatuRECT to the consumer level. FDA laboratory analysis on Lot# F51Q of **P-Boost**, which the firm also labels as **NatuRECT**, has determined that this product contains undeclared tadalafil.

FDA Nov/13 **Alpha Male** contains sildenafil & other analogs.

FDA Jan/14 Midwest Wholesale is voluntarily recalling the following products Boost**: Ultra, XZone Gold, Sexy Monkey, Triple MiracleZen Platinum, Magic for Men, "New" Extenze, and New XZen Platinum**. FDA analysis found these products to contain undeclared Sildenafil and/or Tadalafil.

FDA Jan/14: **JINQIANGBUDOR Red Dragon** & **Tiger King** contains sildenafil; **Bali Mojo** & **Vimax** contains tadalafil; SexRx Contains both sildenafil and tadalafil.

FDA Mar/14 is clarifying its previous recommendation related to prescribing Revatio (**sildenafil**) for children with pulmonary arterial hypertension (PAH). Revatio is FDA-approved only to treat PAH in adults, not in children; however, health care professionals must consider whether the benefits of treatment with the drug are likely to outweigh its potential risks for each patient.

FDA Mar/14: Nova Products, Inc. issued a voluntary recall of the following products: **African Black Ant (Lot# 2006-000926), Black Ant (Lot# 2006-3627878), XZen Gold (Lot# 130310GL), ZXen Platinum (Lot# 130520PL), XZen 1200 (Lot# 13051012), XZone Gold (Lot# 131110GL), and XZone 1200 (Lot# 13071012)** at the retail level. FDA laboratory analysis on these products has determined that they contain undeclared amounts of sildenafil and tadalafil.

FDA apr/14 is advising consumers not to purchase or use **S.W.A.G**, a product promoted and sold for sexual enhancement. FDA laboratory analysis confirmed that S.W.A.G contains sildenafil.

FDA May/14: Eugene Oregon, Inc. is voluntarily conducting this recall because FDA analysis of **African Black Ant, Black Ant, and Mojo Risen** distributed to a third party revealed that the distributed products contained undeclared amounts of the active pharmaceutical ingredients sildenafil and tadalafil.

FDA May/14 is advising consumers not to purchase or use **MV5 Days**, a product promoted and sold for sexual enhancement. FDA laboratory analysis confirmed that MV5 Days contains sildenafil,

FDA Jun/14: advising consumers not to purchase or use **Eyeful** contains hydroxythiohomosildenafil; **Liu Bian Li** contains sildenafil; **Dick's Hard Up** contains tadalafil; **3 Hard Knights** contains sildenafil and thiosildenafil; **Full Throttle On Demand** contains propoxyphenyl sildenafil; GoldReallas contains sildenafil and thiosildenafil.

FDA June/14 laboratory analysis confirmed that **Zhen Gong Fu** contains sildenafil.

FDA Jun/14 laboratory analysis confirmed that **Gold Vigra & Miraculous Evil Root** contains sildenafil.

FDA July/14: **Lian Zhan Qi Tian capsules & Weekend Warrior** contains thiosildenafil.

FDA Aug/14 is advising consumers not to purchase or use **Arize**, a product promoted and sold for sexual enhancement. FDA laboratory analysis confirmed that Arize contains sulfoaildenafil; and **Herbal Vigor Quick Fix** contains tadalafil.

FDA Nov/14 is advising consumers not to purchase or use **Black Storm**. FDA laboratory analysis confirmed that Black Storm contains sildenafil.

FDA Jan/15 is alerting consumers and health care professionals that **counterfeit versions of Cialis 20 mg tablets** were found in the mail on its way to a U.S. consumer.

FDA Jan/15 laboratory analysis confirmed that **Happy Passengers** contains sildenafil.

FDA Feb/15 laboratory analysis confirmed that **Black King Kong, Germany Niubian, Tibet Babao, 72HP, Night Man, & Libigrow XXX Treme** contains sildenafil.

FDA Mar/15 laboratory analysis confirmed that **Santi Scalper, Vigra, Vigour 300, Sex Men, Super Hard, Plant Vigra, MME MAXMAN, Hard Wang & FX3000** contains sildenafil.

FDA Mar/15 laboratory analysis confirmed that **Bigger Longer More Time More Sperms (sic), Black Ant King, African Superman & Black Mamba Premium** contains sildenafil.

FDA May/15 laboratory analysis confirmed that **Black Panther** contains sildenafil.

FDA May/15 laboratory analysis confirmed that **Viagra 007c**ontains sildenafil.

FDA May/15 laboratory analysis confirmed that **King of Romance** contains sildenafil.

FDA Apr/15 laboratory analysis confirmed that **Fatloss Slimming Beauty** contains sildenafil.

FDA Apr/15 laboratory analysis confirmed that **Extreme Diamond 3000** contains desmethyl carbodenafil and dapoxetine.

FDA May/15 **Samurai-X, Happy Passengers, & AMPD Gold Bee Pollen** contains undeclared sildenafil.

FDA May/15: **Black King Kong, Tibet Babao, Vigour 300, Hard Wang**, **FX3000, Sex Men, Vigra, Plant Vigra, Santi Scalper, Baolong, Rhino Blitz Gold 3000, Vim-25, Black Mamba Premium, Bigger Longer More Time More Sperms (sic), Herb Viagra, & La Pepa Negra** contains undeclared sildenafil.

FDA May/15: **Male Silkworm Moth Nourishing Oral Liquid** contains undeclared vardenafil.

FDA May/15: **Lean Body Extreme** contains undeclared sibutramine, desmethyl sibutramine, phenolphthalein & sildenafil.

FDA May/15: **Diablos Eca Fire Caps** contains undeclared sildenafil, phenolphthalein, sibutramine & deisobutylbenzylsibutramine.

FDA July 15: **Extreme Diamond 3000** contains Undeclared desmethyl carbodenafil and dapoxetine.

FDA July 15:**Natural Max Slimming** contains Undeclared sildenafil, fluoxetine, andsibutramine.

FDA Aug/15 R Thomas Marketing, through its websites www.herbviagra.com and www.herbsviagra.com, sold the supplements under the names **Black Ant, Herb Viagra, Real Skill and Stree Overlord**. All four items contain undeclared sildenafil.

FDA Oct/15 **Kaboom Action Strips** 12 Pack contains undeclared sulfoaildenafil.

FDA Sep/15: **Miracle Rock 48** has been found to contain undeclared thiosildenafil.

FDA Oct/15 laboratory analysis confirmed that **Wild Sexx Capsules** contains sildenafil and tadalafil.

FDA Oct/15 laboratory analysis confirmed **Ultra SX Capsules, Super Dragon 6000 Capsules, Sex-Love Secret Code Capsules, Paradise Suplemento Natural Ultra Plus Capsules, APEXXX, & S.W.A.G.G.E.R Extreme Capsules** contains sildenafil.

FDA Oct/15 laboratory analysis confirmed that **Fuel Up High Octane, & Fuel Up Plus** contains hydroxythiohomosildenafil.

FDA Nov/15 laboratory analysis confirmed that **Rhino X, Effective Viagra, Sex Drive Capsules, XForMan Plus & Australia Kangaroo Essence** contains sildenafil.

FDA Dec/15 laboratory analysis confirmed that **Rhino Big Horn 3000** contains desmethyl carbodenafil and sildenafil.

FDA Dec/15 laboratory analysis confirmed that **OrgaZen 3000, OrgaZen 3500, & Rhino 7 Blue 9000** contains tadalafil.

FDA Dec/15 laboratory analysis confirmed that **Triple Power Zen Gold 2000, Triple Power Zen Plus 2000, Xtra Zone 2200, Xtra Zone 2400, Xtra Zone 2600, & Diamond 3500** contains sildenafil and tadalafil.

FDA Dec/15 laboratory analysis confirmed that **Triple MiracleZen Extreme 1750 mg, MiracleZen Gold 1750 mg & Triple MiracleZen Plus 1500 mg** contains sildenafil, tadalafil and dapoxetine.

FDA Dec/15 laboratory analysis confirmed that **Eros Power Zone 1900** contains desmethyl carbodenafil and dapoxetine.

FDA Dec/15 laboratory analysis confirmed that **X Again Platinum** contains sildenafil, tadalafil and dapoxetine.

FDA Dec/15: Nuway Distributors llc is voluntarily recalling all lots of **Apexxx** tablets to the consumer level. FDA analysis found Apexxx to contain amounts of the PDE-5 Inhibitor, sildenafil.

FDA Dec/15 laboratory analysis confirmed that **Power Tiger-X c**ontains sulfoaildenafil.

FDA laboratory analysis confirmed that Ginseng Power-X contains sildenafil and sulfoaildenafil.

FDA Feb/16 laboratory analysis confirmed that **Ninja-X** contains sildenafil and thiosildenafil.

FDA Feb/16 aboratory analysis confirmed that **Golden Night** contains sildenafil and hydroxythiohomosildenafil.

FDA laboratory analysis confirmed that **Boss Number #Six** contains tadalafil.

FDA Feb/16 laboratory analysis confirmed that **Mamba is Hero** contains sildenafil, desmethyl carbodenafil, and dapoxetine

FDA Jan/16 laboratory analysis confirmed that **Wonder-Erect Male Gum & Wonder-Erect Male Pills** contains vardenafil.

FDA Feb/16 laboratory analysis confirmed that **Zhong Hua Niu Bian, Weekend Prince, Bull & Bull's Genital** contains sildenafil.

FDA Mar/16 laboratory analysis confirmed that **Sextra** contains sildenafil.

FDA May/16 laboratory analysis confirmed that **Black Label X** contains sildenafil.

FDA May/16: SOS Telecom, Inc. is voluntarily recalling all lots of the following products (**Tiger-X, Ninja-X, Ginseng Power-X, & Super Samurai-X**) to the consumer level because these products were tested by the FDA and found to contain sildenafil.

FDA July/16 laboratory analysis confirmed that **Xcelerated Weight Loss Ultra Max** contains phenolphthalein and sildenafil.

FDA July 16 laboratory analysis confirmed **Super Shangai, Shangai Ultra X & Power Spring (XXX) Oral Liquid** contains sildenafil.

FDA July/16: FDA laboratory analysis confirmed that **Dream Body Advanced + Acai Weight Loss & Cleanse** contains sibutramine, fluoxetine and sildenafil.

FDA July/16: FDA laboratory analysis confirmed that **Dream Body Extreme Gold** contains sibutramine, fluoxetine and sildenafil.

FDA Jul/16 laboratory analysis confirmed that **Ziyinzhuangyang** contains sildenafil.

FDA Aug/16 laboratory analysis confirmed that **One More Knight 1750** contains tadalfil and dapoxetine.
FDA Aug/16 laboratory analysis confirmed that **Master Zone 1500** contains sildenafil and tadalfil.
FDA Aug/16 laboratory analysis confirmed that L**ove4Long** contains sildenafil.
FDA Aug/16 laboratory analysis confirmed that **De Guo Hei Bei (德国黑啤), Boss-Rhino Gold X-tra Strength, & Anaconda Strong Formula** contains sildenafil.
FDA Aug/16 laboratory analysis confirmed that **Kopi Jantan Tradisional Natural Herbs Coffee** contains desmethyl carbodenafil.
FDA Dec/16 laboratory analysis confirmed that **Triple Green Capsules, Rhino 9 Premium 3500, Rhino 8 Platinum 8000, Rhino 7K 9000 Male Performance Booster, Duramaxxx, Rhino 5 1500, Lang Yi Hao, Bl4ck 4K capsules, Big Penis Male Sexual Stimulant, Power Male Sexual Stimulant, 90° Jiushidu capsules, Black Mamba 2 Premium, Black 3K Plus Male Sexual Enhancement Capsules & African Viagra** contains sildenafil.
FDA Jan/17: **Supreme Slim 5.7** has undeclared phenolphthalein and sildenafil.
FDA Jan/17: **Ready Man!** Has undeclared sildenafil.
FDA Feb/17 laboratory analysis confirmed that **Goldreallas XXX, Goldreallas Original, Ginseng for Reinforcing Kidney, Old Chinese, & Shenjingpian** contains sildenafil.
FDA Mar/17 laboratory analysis confirmed that **Arouse-Plus** contains tadalafil.
FDA Mar/17 laboratory analysis confirmed that **Bazook Bullet** contains aminotadalafil.
FDA Mar/17 **A&H Focal Inc**. is voluntarily recalling all lots marketed as dietary supplements for male sexual enhancement from January 2014 to present. These products have been historically tested by the FDA and found to contain PDE-5 Inhibitors (i.e.sildenafil, tadalafil, vardenafil, etc.).
FDA Apr/17 Organic Herbal Supply Supplement Products: Recall - Undeclared Drug Ingredients: Including **Uproar, Cummor, Zrect, LabidaMAX, Monkey Business, Xrect, Rectalis, Tornado, Zdaily, BigNHard, Enhancerol Natural Male Enhancement capsules-** found the products to contain Tadalafil.
FDA May/17 laboratory analysis confirmed that Big N Hard contains tadalafil.
FDA May/17 laboratory analysis confirmed that **Cummor & Monkey Business** contains N-desmethyl tadalafil.
FDA May/17 laboratory analysis confirmed that **Xrect** contains tadalafil and descarbonsildenafil.
FDA May/17 laboratory analysis confirmed that **Tornado** contains nortadalafil.
FDA May/17 laboratory analysis confirmed that **Z Daily** contains homosildenafil.
FDA May/17 Caverflo.com is voluntarily recalling all lots of **Caverflo Natural Herbal Coffee**, 25 grams to the consumer level. FDA laboratory analysis confirmed the presence of Sildenafil and Tadalafil.
FDA Jun/17 laboratory analysis confirmed that **XXX Zone Platinum & Triple Premium Zen Gold 1300mg** contains sildenafil, tadalafil and dapoxetine.
FDA Jun/17 laboratory analysis confirmed that **Triple X 2000** contains tadalafil and dapoxetine.
FDA Jun/17 laboratory analysis confirmed that **Macho Man 3000, Monster X 1350, Royal Master, & Love Zen 3000** contains tadalafil.
FDA Jun/17 laboratory analysis confirmed that **Own the Knight 1750** contains tadalafil and dapoxetine.
FDA Jun/17 laboratory analysis confirmed that **Xzone Gold, Super Panther 7K & Triple Miracle Zen Plus 1200mg** contains sildenafil and tadalafil.
FDA Jun/17 laboratory analysis confirmed that **Man of Steel 2 & Man of Steel** contains sildenafil.
FDA Jul/17 laboratory analysis confirmed that **Kingdom Honey for Her, Kingdom Honey for Him, & Royal Honey VIP** contains tadalafil.
FDA Jul/17 laboratory analysis confirmed that **Rhino 7 Platinum 5000** contains sildenafil.
FDA Jul/17:**Bestherbs Coffee LLC** is voluntarily recalling all lots of **New of Kopi Jantan Tradisional Natural Herbs Coffee**, 13 grams to the consumer level. FDA laboratory analysis confirmed the presence of desmethyl carbodenafil.
FDA Aug/17: warning consumers not to drink **Longjack Coffee**, in addition to other instant coffee products that have been recalled recently – **Kopi Jantan Tradisional Natural Herbs Coffee, CaverFlo Coffee, and AMPT Coffee**. These products are made in Malaysia, and promoted and sold online for sexual enhancement. These products are labeled to contain instant coffee, non-dairy creamer, and other ingredients. However, FDA laboratory analysis confirmed: **CaverFlo Coffee and AMPT Coffee** contain undeclared sildenafil and tadalafil; **Longjack Coffee and Kopi Jantan Tradisional Natural Herbs Coffee** contain undeclared desmethyl carbodenafil, an analogue of sildenafil; and All of these products contain undeclared milk.
FDA Aug/17: Man of Steel is voluntarily recalling 175 lots of **Man of Steel 1 and Man of Steel 2**, 4000mg at the retail level. The products have been found to contained undeclared Sildenafil.
FDA Sep/17: **Rhino 7, Papa Zen, Fifty Shades, and Grande X** Dietary Supplements by Gadget Island: Recall - Undeclared Drug Ingredients.The products have been found to contain undeclared Active Pharmaceutical Ingredients sildenafil, desmethyl carbodenafil and tadalafil.
FDA Sep/17: Natures Supplement, Inc. is voluntarily recalling 260 bottles of **Vegetable Vigra**, **200 mg capsules** to the consumer level. FDA analysis found this product to be tainted with Sidenafil.
FDA Oct/17 laboratory analysis confirmed that **Tiger 5000** contains sildenafil and tadalafil.
FDA Nov/17 laboratory analysis confirmed that **Hard Times for Men** contains sildenafil.
FDA Dec/17 laboratory analysis confirmed that **Chao Jimengnan** contains sildenafil.
FDA Dec/17: Nutra Labs Inc. is voluntarily recalling lots sold by their firm of the male enhancement supplements **Bull 1800 mg Capsules** with the production date of 05/08/2016, and **Chao Jimengnan 150 mg Tablets** with Lot # 20151018 to the consumer level. FDA analysis found the products to be tainted with sildenafil, 0.026mg/capsule for Bull, and 70.46mg/tablet for Chao Jimengnan respectively.
FDA Dec/17: Marmex Corp is voluntarily recalling all lots of **Blue Pearl All Natural Male Enhancement Supplement**, 500mg to the consumer level. FDA analysis has found the products to contain sildenafil.
FDA Mar/18: laboratory analysis confirmed **that Black Lion Pill contains sildenafil**.
FDA Mar/18: laboratory analysis confirmed that **Red Zone Xtreme 3000 & Rhino 69 Extreme 50000 contains tadalafil**.
FDA Apr/18: Overland Park, KS, Epic Products, LLC is voluntarily recalling all lots of Euphoric capsules, packaged in 1 count blister cards, 3 count bottles, and 12 count bottles to the consumer level. FDA analysis found samples of Euphoric to be tainted with undeclared **sildenafil and tadalafil**,
FDA Apr/18: AMA Wholesale Inc. (Distributor/Re-seller), is voluntarily recalling **Rhino 69 Extreme 50000 capsules** to the consumer level. FDA analysis found the product to be tainted with undeclared **tadalafil.**
FDA May/18: laboratory analysis confirmed that **Best Candy contains nortadalafil**.
FDA May/18: **7K and Poseidon 4500 by Shoreside Enterprises: Voluntary Recall - Due to Presence of Undeclared Sildenafil and Tadalafil.**
FDA July/18: laboratory analysis confirmed that Maximum Powerful contains sildenafil.
FDA Jul/18: laboratory analysis confirmed that Grakcu Capsule, C.U. Plus, Dale Mas contains sildenafil and tadalafil.
FDA Aug/18: laboratory analysis confirmed that XXXPlosion Ultra, Ding Ji Wei Ge, 5K & Panther Power Platinum 11000 contains sildenafil.
FDA Sep/18: laboratory analysis confirmed that Extenze Nutritional Supplement, Extenze Plus, PremierZen Gold 4000 contains sildenafil.
FDA Oct/18: laboratory analysis confirmed that ProSolution, V-Max, USA for Women, Strong Horses & FX75000 contains sildenafil.
FDA Dec/18: laboratory analysis confirmed **that MOB Candy & Willy Go Wild** contains sildenafil and tadalafil,
FDA Dec/18: E-Cialis HelloCig E-Liquid by HelloCig Electronic Technology Co: Warning - Contains the **Undeclared Drugs** Sildenafil and Tadalafil.
FDA Dec/18: E-Rimonabant HelloCig E-Liquid by HelloCig Electronic Technology Co: Warning - **Contains the Undeclared Drug** Sildenafil.
FDA Jan/19: laboratory analysis confirmed that **The Silver Bullet** contains sildenafil and tadalafil.
FDA Jan/19: laboratory analysis confirmed that **Red Stallion** Extra Strong contains tadalafil.
FDA Jan/19: laboratory analysis confirmed that **Natural V=GRA, Yong Gang, Silver Bullet 10x & Black King Kong** contains sildenafil and tadalafil.
FDA Jan/19: laboratory analysis confirmed that **Golden Ant, Instinct Best Sexual Enjoyment & Nectar Del Amor** contains sildenafil.
FDA Jan/19: laboratory analysis confirmed that **Slim Bio Capsules** contain sibutramine, N-desmethylsibutramine, sildenafil, tadalafil, benproperine and diphenhydramine.
FDA Apr/19: **Aphrodisiac Capsules by SD Import: Recall** - Due to Presence of Undeclared Sildenafil

FDA May/19: The Beast Capsules by **STIFF BOY: Recall -** Due to Presence of Undeclared Sildenafil
FDA May/19: laboratory analysis confirmed that **Man Fuel Shooter (Tropical Fruit Flavor**) contains tadalafil and desmethyl carbodenafil.
FDA May/19: laboratory analysis confirmed that **Man Fuel Xtreme Edition** contains sildenafil, dithiodesmethyl carbodenafil and desmethyl carbodenafil.
FDA Jun/19: laboratory analysis confirmed that **Peru Maca & Germany Black Gorilla** contains sildenafil.
FDA July/19: laboratory analysis confirmed that **Black Storm, Big Penis, Boss Lion 9000, De Guo Heijin Gang, Herb Viagra, La Pepa Negra, Odimafo Powerful Tablet 200 mg, Plant Vigra, Shengjingpian, & Vigour 800mg** contains sildenafil.
FDA Sep/19: laboratory analysis confirmed that **Mero Macho** contains tadalafil.
FDA Sep/19: laboratory analysis confirmed that **LOBO** contains sildenafil.
FDA Sep/19: laboratory analysis confirmed that **Anaconda Strong Formula, La Pepa Negra, & Lung Leader** contains sildenafil
Galiè N, Ghofrani HA, Torbicki A, Barst RJ, et al.; Sildenafil Use in Pulmonary Arterial Hypertension (**SUPER**) Study Group. Sildenafil citrate therapy for pulmonary arterial hypertension. N Engl J Med. 2005 Nov 17;353(20):2148-57.
Galiè N, Brundage BH, Ghofrani HA, Oudiz RJ, et al.; on behalf of the Pulmonary Arterial Hypertension and Response to Tadalafil (**PHIRST**) Study Group. Tadalafil Therapy for Pulmonary Arterial Hypertension. Circulation. 2009 May 26. [Epub ahead of print]. In patients with **pulmonary arterial hypertension, tadalafil 40 mg** was well tolerated and improved exercise capacity and quality of life measures and reduced clinical worsening.
Galiè N, Barberà JA, Frost AE, et al; **AMBITION** Investigators. Initial Use of **Ambrisentan plus Tadalafil** in **Pulmonary Arterial Hypertension**. N Engl J Med. 2015 Aug 27;373(9):834-44.
Gazzaruso C, Solerte SB, Pujia A, et al. Erectile dysfunction as a **predictor of cardiovascular events** and death in diabetic patients with angiographically proven asymptomatic coronary artery disease a potential protective role for statins and 5-phosphodiesterase inhibitors. J Am Coll Cardiol. 2008 May 27;51(21):2040-4.
Giannetta E, et al. Chronic Inhibition of Cyclic GMP Phosphodiesterase 5A **Improves Diabetic Cardiomyopathy**: A Randomized, Controlled Clinical Trial using Magnetic Resonance Imaging with Myocardial Tagging. Circulation. 2012 Apr 11.
Gianetta E, Feola T, Gianfrilli D, et al. Is **chronic inhibition of phosphodiesterase type 5 cardioprotective and safe**? A meta-analysis of randomized controlled trial. *BMC Medicine* 2014; 12:185.
Gleason JM, Slezak JM, Jung H, et al. Regular Nonsteroidal Anti-Inflammatory Drug (**NSAIDs**) Use and Erectile Dysfunction. J Urol. 2011 Feb 18.
Goldstein I, Stecher V, Carlsson M. Treatment response to **sildenafil** in men with erectile dysfunction relative to **concomitant comorbidities and age**. Int J Clin Pract. 2017 Mar;71(3-4).
Gopalakrishnan R, et al. **Sildenafil** in the treatment of antipsychotic-induced erectile dysfunction: a randomized, double-blind, placebo-controlled, flexible-dose,two-way crossover trial.Am J Psychiatry.2006Mar;163(3):494-9.
Grimm RH Jr, Grandits GA, Prineas RJ, et al. Long-term effects on **sexual function of five antihypertensive drugs** and nutritional hygienic treatment in hypertensive men and women. Treatment of Mild Hypertension Study (TOMHS). Hypertension. 1997 Jan;29(1 Pt 1):8-14. (chlorthalidone higher rates of erectile dysfunction)
Grover SA, Lowensteyn I, Kaouache M, et al. The prevalence of erectile dysfunction in the primary care setting. Importance of risk factors for diabetes and vascular disease. Arch Intern Med 2006; 166:213-219.
Giuliano F, et al.; Vardenafil Study Group. Efficacy and safety of vardenafil in men with erectile dysfunction caused by **spinal cord injury**. Neurology. 2006 Jan 24;66(2):210-6.
Giuliano F, Sanchez-Ramos A, Lochner-Ernst D, et al. Efficacy and Safety of Tadalafil in Men With Erectile Dysfunction Following **Spinal Cord Injury**. Arch Neurol. 2007 Sep 10; [Epub ahead of print] Tadalafil (10 mg and 20 mg) improved erectile function and was well tolerated by men with ED secondary to traumatic SCI.
Goldstein I, Lue TF, Padma-Nathan H, et al.; Sildenafil Study Group. Oral sildenafil in the treatment of erectile dysfunction. *N Engl J Med* 1998;338:1397-404. (**low 25mg dose effective**)
Gonzalez D, Laughon MM, Smith PB, et al. **Population Pharmacokinetics of Sildenafil in Extremely Premature Infants**. Br J Clin Pharmacol. 2019 Sep 2.
Gandhi NG, Lin LK, O'Hara M. **Sildenafil for Pediatric Orbital Lymphangioma**. JAMA Ophthalmol. 2013 Jul 4.
Grashow R, Weisskopf MG, Miller KK, et al. Association of **Concussion Symptoms With Testosterone Levels and Erectile Dysfunction** in Former Professional US-Style Football Players. JAMA Neurol. 2019 Aug 26.
Guazzi M, Vicenzi M, Arena R, et al. **Pulmonary hypertension** in heart failure with preserved ejection fraction: a target of phosphodiesterase-5 inhibition (sildenafil) in a 1-year study. Circulation. 2011 Jul 12;124(2):164-74.
Gulati G, Grandin EW, Kennedy K, et al. Preimplant Phosphodiesterase-5 Inhibitor Use Is Associated With **Higher Rates of Severe Early Right Heart Failure** After Left Ventricular Assist Device Implantation. Circ Heart Fail. 2019 Jun;12(6):e005537.
Gupta BP, Murad MH, et al. The effect of **lifestyle modification and cardiovascular risk factor reduction** on erectile dysfunction: a systematic review and meta-analysis [Sept 12, 2011]. Arch Intern Med. 2011
Hachulla E, Hatron PY, Carpentier P, et al; **SEDUCE** study group. Efficacy of **sildenafil on ischaemic digital ulcer healing** in systemic sclerosis: the placebo-controlled SEDUCE study. Ann Rheum Dis. 2016 Jun;75(6):1009-15.
Hackett G, Kirby M. **Erectile dysfunction and testosterone deficiency** as **cardiovascular risk factors**? Int J Clin Pract. 2018 Jan 30.
Hagberg KW, Divan HA, Persson R, et al. Risk of erectile dysfunction associated with use of **5-α reductase inhibitors for benign prostatic hyperplasia** or alopecia: population based studies using the Clinical Practice Research Datalink. BMJ. 2016 Sep 22;354:i4823
Hambly N, Alawfi F, Mehta S. **Pulmonary hypertension**: diagnostic approach and optimal management. CMAJ. 2016 Aug 9;188(11):804-12
Health Canada Jan/06 Natural health product **Libidfit** may pose health risks (promoted for sexual enhancement and erectile dysfunction, but contains an undeclared amount of a pharmaceutical ingredient similar to sildenafil) http://www.hc-sc.gc.ca/ahc-asc/media/advisories-avis/2006/2006_02_e.html
Health Canada May/06 is warning consumers not to use the product **Nasutra** because it has been found to contain the undeclared ingredient sildenafil (chemical name for Viagra) that could lead to serious health risks, especially for patients with existing medical conditions such as heart problems, those who may be taking heart medications, or those who may be at risk for strokes.
Health Canada Feb/07 is advising consumers not to use the following product listed in the table below due to concerns about possible side-effects. More info **Power 58; Platinum Power 58; Ehanix; Jolex; Onyo; Deguozonghengtianxia** because they contained acetildenafil. Acetildenafil is an analogue of sildenafil, a prescription medication indicated for treatment of erectile dysfunction.
Health Canada Mar/07 is warning consumers not to use the unauthorized natural health product **XOX For Men**, because it contains an undeclared pharmaceutical ingredient, tadalafil, an ingredient found in the prescription drug Cialis. The use of XOX For Men could pose serious health risks, especially for patients with existing medical conditions such as heart problems, those taking heart medication, or those at risk of stroke.
Health Canada Mar/07 is warning consumers not to use the unauthorized product **Vigorect** Oral Gel Shooter, because it contains an undeclared drug substance tadalafil, which should only be available by prescription.
Health Canada Apr/07 is warning consumers from the United States FDA found **V.MAX and Rhino Max (Rhino V Max) to contain undeclared amounts of aminotadalafil**, an analogue of tadalafil, used to treat erectile dysfunction.
Health Canada May/07 is warning consumers **Urat Madu** capsules are marketed for the treatment of erectile dysfunction. The product is adulterated with **sildenafil**, a prescription drug that has been associated with serious side effects including sudden vision loss, penile tissue damage and urinary tract infection.
Health Canada May/07 is advising consumers that **HS Joy of Love** product is marketed as a dietary supplement and was found to contain piperadino **vardenafil**.
Health Canada May/07 is advising consumers not to use 6 foreign health products due to concerns about possible side-effects: **Power 58 Extra, Platinum Power 58 Extra, Enhanix New Extra Men's Formula, Valentino, King Power Oral Solution, and Stretch Up** Capsules are marketed as treatments for erectile dysfunction. The products contain analogues of **sildenafil** and **vardenafil**, which are prescription drugs used for the treatment of erectile dysfunction.
Health Canada June/07 is warning consumers not to use the product **Encore Tabs for Men**, because it contains an undeclared pharmaceutical ingredient similar to the approved drug tadalafil.
Health Canada July/07 is warning consumers not to use **Zencore** Tabs, a product advertised as a dietary supplement for sexual enhancement, because it contains an undeclared pharmaceutical ingredient similar to the approved drug tadalafil.
Health Canada July/07 & the US Food and Drug Administration (FDA) found ***Liviro3*** to contain tadalafil, a prescription drug that should only be taken under the guidance of a health professional.
Health Canada Aug/07 via Medsafe, the New Zealand health regulatory authority, advised the public not to use the products **Darling Capsules, Dali Capsules, Spanish Fly** Capsules, and an unnamed product, because they were found to contain sildenafil.
Health Canada Aug/07 Consumers who use **Excite for women or Ultimates for men** may be at risk of serious side effects similar to those associated with sildenafil.
Health Canada Sept/07 is advising consumers not to use **Satis 60 Hours Ever Lasting Formula** is used for the treatment of erectile dysfunction/sexual enhancement. It was found to contain piperidenafil an analogue of vardenafil.. **True Man** and **Energy Max** are used as sexual enhancement/ erectile dysfunction products and were found to contain an analogue of sildenafil or vardenafil.
Health Canada Sept/07 is advising consumers not to use 5 foreign health products due to concerns about possible side-effects: **Top Gun for Men Herbal Extracts** has been found to contain a substance similar to tadalafil. **Oyster Plus** has been found to contain tadalafil. **Deguozhanjiang** contains sildenafil and tadalafil, prescription drugs used for the treatment of erectile dysfunction. **Chongcaoliubian Jiaonang** and **Santi Scalper Penis Erection** Capsule contain sildenafil.
Health Canada Nov/07 is advising consumers not to use **Axcil** and **Desirin**, are promoted as natural sexual enhancement/ erectile dysfunction products. Consumers are warned not to use Axcil and Desirin because both products were found to contain the prescription drug sildenafil.
Health Canada Mar/08 is warning consumers not to use **ADAM**, an unauthorized product that contains an undeclared pharmaceutical ingredient similar to the prescription drug sildenafil.
Health Canada Mar/08 is warning consumers not to use **Libidus**, an unauthorized product promoted on the web site of the manufacturer for the treatment of erectile dysfunction. The product may pose serious health risks, as it was found to contain the undeclared prescription drug sildenafil.
Health Canada April//08 warns that Singapore's Health Sciences Authority (HSA) advised the public not to use the product **Power 1 Walnut**, because it was found to contain the prescription drugs sildenafil and glibenclamide
Health Canada April//08 is advising consumers not to use 2 foreign health products, **Aspire 36** and **Aspire Lite**, because they were found to contain undeclared sildenafil analogues.
Health Canada April/08 is warning consumers not to use **Vigoureux**, an unauthorized product promoted for the treatment of erectile dysfunction. The product may pose serious health risks, as it was found to contain the prescription drug sildenafil
Health Canada April/08 is advising consumers not to use 2 foreign health products due to concerns about possible side-effects: **Tian Li** was found to contain tadalafil and hydroxyhomosildenafil. Xian Zhi Wei II was found to contain sibutramine and phenolphthalein, which are not meant for self-care and may cause serious side effects.

Health Canada May/08 is warning consumers not to use **Desire**, an unauthorized product promoted to enhance male sexual performance as this product may pose serious health risks in certain patients. Lot 0070263 of the product was found to contain the prescription drug phentolamine.

Health Canada June/08 **Nangen Zengzhangsu** (may also be known as Nangen or Nangeng), Sanbianwan, Jiu Bian Wang, Tian Huang Gu Shen Dan, Zui Xian Dan Gong Shi Zi, and Power Up. The Hong Kong Department of Health has warned consumers not to use these herbal/proprietary Chinese medicine products promoted for erectile dysfunction because they have been found to contain sildenafil and/or glibenclamide.

Health Canada June/08 **Zhong Hua Niu Bian**. Zhong Hua Niu Bian is an herbal/proprietary Chinese medicine product promoted for erectile dysfunction. Singapore's Health Sciences Authority has warned against the use of this product because it has been found to contain sildenafil, glibenclamide, tadalafil and sibutramine

Health Canada July/08 Foreign Product Alerts: **Super Shangai,Strong Testis, Shangai Ultra, Shangai Ultra X, Lady Shangai, Shangai Regular (also known as Shangai Chaojimengnan), Actra-Sx, An unknown product containing the plant Lycium barbarum L., Adam Free, NaturalUp, Erextra, Yilishen, Blue Steel, Hero, & Naturalë Super Plus.** These products have been found to contain sildenafil or an unapproved substance similar to sildenafil.

Health Canada July/08 is advising consumers not to use foreign health products due to concerns about possible side-effects: Wodibo. **Wodibo** is promoted as an all-natural Chinese potency-enhancing product for the treatment of erectile dysfunction. The Danish Medicines Agency has warned against the use of Wodibo because it was found to contain sildenafil and tadalafil, prescription drugs authorized for treatment of erectile dysfunction. **Viril-Ity-Power** (VIP) Tabs. The U.S. Food and Drug Administration has warned consumers not to use Viril-Ity-Power (VIP) Tabs because it was found to contain an undeclared ingredient similar to the prescription drug sildenafil.

Health Canada Aug/08 is warning consumers not to use **Rize 2 The Occasion** capsules (Rize2), an unauthorized product promoted for the treatment of erectile dysfunction, because it may pose serious health risks. Rize 2 contains an undeclared pharmaceutical ingredient similar to the prescription drug sildenafil.

Health Canada Aug/08 is advising consumers not to use 5 foreign health products due to concerns about possible side-effects: **Oyster Extract** Caps. The Hong Kong Department of Health has recalled Oyster Extract Caps because they were found to contain an undeclared ingredient similar to the prescription drug sildenafil. **Xiadafil** VIP Tabs. At the request of the U.S. Food and Drug Administration, U.S. federal authorities seized all Xiadafil VIP Tabs sold in 8 tablet bottles (Lot #6K029) and blister cards of 2 tablets (Lot #6K029-SEI) because they were found to contain an undeclared ingredient similar to the prescription drug sildenafil. **Herb Vigour, Natural Vigour and China Vigour**. The Netherlands Health Care Inspectorate, the U.K. Medicines and Healthcare Products Regulatory Agency, and the Danish Medicines Agency has warned against the use of Herb Vigour, Natural Vigour and China Vigour because they were found to contain undeclared pharmaceutical ingredients used for the treatment of erectile dysfunction that should only be taken under the supervision of a health care professional.

Health Canada Aug/08 is advising consumers not to use 9 foreign health products due to concerns about possible side-effects: **Armstrong Natural Herbal Supplement, Enhanix New Extra Men's Formula, Power 58 Extra, and Platinum Power 58 Extra** were adulterated with tadalafil or unapproved substances with structures similar to tadalafil and vardenafil.

Health Canada Sep/08 is advising consumers not to use 3 foreign health products due to concerns about possible side-effects: The Hong Kong Department of Health warned consumers not to buy or use **Lover Liquid Nutriment Herbal Supplement and Onyo** because they were found to contain undeclared pharmaceutical ingredients. Lover Liquid Nutriment Herbal Supplement was found to contain sildenafil while Onyo was found to contain sildenafil, as well as unapproved substances with structures similar to sildenafil and vardenafil. The U.S. Food and Drug Administration warned consumers not to use the product **Rose 4 Her** because it was found to contain an undeclared ingredient similar to the prescription drug sildenafil.

Health Canada Sep/08 is advising consumers not to use 6 foreign health products due to concerns about possible side-effects: The Hong Kong Department of Health warned consumers not to buy or use **Dr. Life or Chong Cao Ju Wang** because they were found to contain undeclared pharmaceutical ingredients. Dr. Life contains an unauthorised substance similar in structure to tadalafil while Chong Cao Ju Wang contains sildenafil.

Health Canada Oct/08 is advising consumers not to use 2 foreign health products due to concerns about possible side-effects: Swissmedic warned consumers not to buy or use the product **Powertabs** because it contains an unauthorised substance similar in structure to sildenafil. The Hong Kong Department of Health warned consumers not to buy or use **Sweet Energizer Vitality** Candy because it was found to contain an unauthorised substance similar in structure to tadalafil.

Health Canada Oct/08 is warning consumers not to use **Eros Fire**, a product promoted to enhance sexual performance, as this product may pose serious health risks. The product was found to contain xanthoanthrafil (also known as benzamidenafil), which is not indicated on the label.

Health Canada Nov/08 is advising consumers not to use 5 foreign health products due to concerns about possible side-effects: The Hong Kong Department of Health warned consumers not to buy or use **Lu Quan** because it contains undeclared glibenclamide and sildenafil. The Hong Kong Department of Health warned consumers not to buy or use **Fat Killer, Carbohydrate Cut and Sugar-Carbohydrate Cut** because they contain sibutramine and an unauthorised substance similar in structure to sibutramine, and **Zhuang Yao Gu Shen** Capsule because it contains sildenafil.

Health Canada Nov/08 is warning consumers not to use **Firm Dose** and **Granite Rooster**, two products promoted to enhance male sexual performance, as these products may pose serious health risks. Firm Dose was found to contain an undeclared pharmaceutical ingredient similar to sildenafil, while the product Granite Rooster was found to contain an undeclared pharmaceutical ingredient similar to tadalafil.

Health Canada Jan 2009 is advising consumers not to use 4 foreign products: **Zhuang Tjar Gere** because it contains the undeclared prescription drugs sildenafil & tadalafil, **Zhixhue** Capsules manufactured by Vital Pharmaceutical Holdings Ltd. due to concerns of serious side- effects including liver dysfunction, **Tonik Warisan Banjar** because it contains undeclared dexamethasone & **Healthily Slim** because it contains the undeclared prescription drug sibutramine.

Health Canada Mar/09 Foreign Product Alerts: 68 Weight Loss Products; Best-life Fat Burning Capsules; Bevidan;Huiji Yin Chiao Chieh Tu Pien; Relacore
http://www.hc-sc.gc.ca/ahc-asc/media/advisories-avis/_fpa-ape_2009/index-eng.php

Health Canada June/09 Foreign Product Alerts: **Jia Yi Jian** (undeclared sibutramine & tadalafil); **Zencore Plus** (undeclared benzamidenafil) & **Zhong Guo Shen Fang** (undeclared med like sildenafil).

Health Canada July/09 is warning that the Singapore Health Sciences Authority (HSA) warned consumers to not buy or use **XP Tongkat Ali Supreme** after it was found to contain undeclared tadalafil.

Health Canada Oct/09: **Dynasty Worldwide Jinglida So Young Formula**- The Singapore Health Sciences Authority (HSA) warned consumers to not buy or use since contained undeclared aminotadalafil.
STEAM lot#80214, 90260 -The U.S. FDA informed consumers of a voluntary manufacturer recall of two lots of STEAM after FDA testing found these lots to contain undeclared sulfoaildenafil (lot# 80214) & undeclared tadalafil (lot# 90260).
Syntrax Fyre (contained Yohimbine), **Kam Yuen Brand Wan Ying Yang Gan Wan (contained sildenafil)** - The Hong Kong Department of Health warned consumers not to buy or use these products.

Health Canada Nov/09 is warning consumers not to use Herblex "**Once More**"since it was found to contain sildenafil.

Health Canada Dec/09 is advising Canadians not to use certain Acai Berry products after a large number of shipments of adulterated products were stopped at the border. The product names include: **Anti-Aging Acai Berry, Guarana Blast, Brazillian Pure, Anti-aging Vital Rez V, Weight Loss VitalAcai, Dietary Supplement Acai Power Blast and Muscle Mass**. These products advertised for anti-aging and weight loss were found to contain undeclared sildenafil.

Health Canada Dec/09 is advising consumers not to use the following foreign health products: 1. **Power-Plus P**: The Singapore Health Sciences Authority issued a recall notice for Power-Plus P (expiry date 03/03/2011) after it was found to contain undeclared tadalafil. 2. **Zeng Da Yan Shi Wan**: The Hong Kong Department of Health warned consumers not to buy or use after it was found to contain undeclared sildenafil.

Health Canada Jan/10 informs that Finish Food Safety Authority: **Full Contact Max Potency** contains thio-sildenafil and thio-homosildenafil; Singapore Health Sciences Authority: **M-Action** contains desmethylacetildenafil and acetilacid. U.S. FDA: **RockHard Weekend** contains sulfoaildenafil.

Health Canada Jan/10 is advising consumers not to use the unauthorized product "**Stiff Nights**" after the U.S Food and Drug Administration (FDA) found that this product contains an undeclared substance similar to the prescription drug sildenafil.

Health Canada Feb/10: **2H & 2D**- Hong Kong Department of Health (HKDH) warned consumers not to buy or use 2H & 2Dafter it was found to contain undeclared tadalafil. Products distributed by **Atlas Operations Inc**. The FDA informed consumers of a voluntary recall by Atlas Operations Inc. of certain lots of some products that were found to contain undeclared sulfoaildenafil, which is an unauthorized substance similar to sildenafil. **STRO Emperor** Capsules The Irish Medicines Board warned consumers not to buy or use STRO Emperor Capsules after it was found to contain undeclared tadalafil.

Health Canada Mar/10 is warning Canadians that an unapproved health product, **POWER-MAX** that contains sildenafil.

Health Canada May/10 is advising consumers not to use the following foreign health products due to concerns about possible adverse reactions: 1. **Man Power** The Hong Kong Department of Health warned consumers not to buy or use Man Power product after it was found to contain undeclared tadalafil.

Health Canada June/10 is warning Canadians that the unauthorized health products "**Vigofit**" and "**Once More**," which are promoted to enhance male sexual performance, have been seized by Health Canada inspectors from retail stores in Abbotsford and Surrey, British Columbia. These two products contain sildenafil.

Health Canada July/10 is advising consumers not to use the following foreign health product(s) due to concerns about possible adverse reactions: 1. **Stud Capsule For Men** The U.S. FDA informed consumers of a voluntary recall of one lot (Lot #060607-01/060108-01 Exp 6-2013) after it was found to contain undeclared Sildenafil.

Health Canada July/10 is advising Canadians about "**UP Ultimate Performance for Men**", an unauthorized health product containing undeclared sildenafil.

Health Canada July/10 is advising consumers not to use the following foreign health products due to concerns about possible adverse reactions: **1 Body Beautiful** The Hong Kong Department of Health warned consumers not to buy or consume 1. **Atlas Operations Inc. expands its U.S. recall of over 30 sexual enhancement supplements** The U.S. FDA informed consumers of an expanded recall of certain lots of products after some were found to contain undeclared sulfoaildenafil. The products are being voluntarily recalled nationwide in the U.S. by the company Atlas Operations Inc. 2. **Stallion, SZM Formula for Men, Tomcat Ali and Volcanic** New Zealand's Medsafe warned consumers not to buy or use these four products after they were found to contain undeclared tadalafil. 3. **Vitalex for men and Vitalex for women** The U.S. FDA informed consumers that the *Vitalex*products were found to contain acetildenafil, which is an unauthorized substance similar to sildenafil.

Health Canada Aug/10 is advising **Magic Power Coffee** The U.S. FDA warned consumers not to buy or use Magic Power Coffee after it was found to contain undeclared hydroxythiohomosildenafil.

Health Canada Aug/10: "**SeXXX DRIVE**", promoted as a herbal supplement to enhance male sexual performance, was tested by Health Canada and found to contain undeclared hydroxyhomosildenafil.

Health Canada Aug/10 has seized the unauthorized sexual enhancement supplements "**Male Enhancement ExtenZe**" and "**Women ExtenZe**" imported and sold by the Happy Paradise Adult Store in Burnaby, British Columbia. The labels of each of these unauthorized products list the prescription ingredient pregnenolone and the controlled drug, DHEA dehydroepiandrosterone). The labels of the unauthorized "Male Enhancement ExtenZe Nutritional Supplements" list the ingredient yohimbe extract (bark).

Health Canada Sep/10 **E.O.D. Erection on Demand**" being promoted as a herbal to enhance male sexual performance, the product was tested by Health Canada and found to contain tadalafil.

Health Canada Sep/10 is advising consumers not to use : 1. **Golden aryuru, Baisheng wei ge, Zhonghua niubian, Ten ka dai 1 bou, Kuai gan bei zeng chao yue zi wo (Happy felling doubly increase [sic]), Ling tou lang, SkyFruit, Chu bi ho ken, Jinbolang, Suika Koso, Lov, I ka ou (2009 nen sin hoso) &/or I ka ou (saisinsui shutsu hoso)** The Japanese Ministry of Health, Labour and Welfare warned consumers not to buy or use the 12 products listed above because they were found to contain undeclared sildenafil and/or other unauthorized substances similar to sildenafil that may pose similar health risks (norhongdenafil, acetil acid, and tioqinapiperifil). 2. **Vialipro** The U.S. FDA informed consumers of a recall of certain lots of Vialipro after FDA tests found product samples to contain undeclared sulfoaildenafil, which is an unauthorized substance similar to sildenafil and may pose similar health risks.

Health Canada Nov/10 **Amana Care Seven Slim Herbal Capsules**: The Israel Ministry of Health informed consumers that it found the product Amana Care Seven Slim Herbal Capsules to contain undeclared sibutramine and residue of sildenafil.

Health Canada Nov/10 is advising consumers not to use the following foreign health products due to concerns about possible adverse reactions: **1. MasXtreme** contains undeclared aminotadalafil while the other (#911035) contains undeclared aildenafil and phentolamine **2. Mr. Magic Male Enhancer from Don Wands** contained hydroxythiohomosildenafil and sulfoaildenafil **3. So Hard for Men - Pulse8 for Women - The Rock - Tonic 66** contained the undeclared pharmaceutical substances tadalafil, sildenafil, and/or hydroxyhomosildenafil **4. TimeOut** contained undeclared hydroxythiohomosildenafil.

Health Canada Nov/10 "**Fat Burner No. 1**" (labelled in Chinese characters translated as "**Qian Mei Yin Zi**", an unauthorized Chinese herbal weight loss medicine, is being voluntarily recalled by Ying Tai TCM Supplying Ltd. after Health Canada lab tests revealed the product contains two pharmaceutical ingredients: a chemical similar to sibutramine (N,N- didesmethylsibutramine), and sildenafil.

Health Canada Dec/10 "**Durazest**" and "**Once More**": Certain lots of two male sex enhancement products recalled as they may pose serious health risks. Certain lots (listed below) of two health products promoted for male sexual enhancement, "Durazest for Men" and "Once More," have been voluntarily recalled by Natural Performance Products Ltd. Health Canada laboratory tests identified the presence of a chemical similar to tadalafil (nortadalafil) in one lot of each product.

Health Canada Dec/10 is informing Canadians that NorthRegentRx has begun to voluntarily recall its product, **ResurreXX** from Canadian market. NorthRegentRx is requesting that wholesalers, distributors and retailers stop sale of this product since contained an undeclared substance "hydroxyhomosildenafil".

Health Canada Dec/10 is advising consumers not to use the following foreign health products due to concerns about possible adverse reactions: 1. **Shaguar, Signature Signergy, VIGRX (green capsule), VIGRX (white capsule), VigRx, VigRX Plus** New Zealand's MedSafe warned consumers to not buy or use these products after they were found to contain undeclared sildenafil, hydroxyhomosildenafil, thiosildenafil, and/or tadalafil. .

Health Canada Feb/11 is advising consumers not to use the following foreign health products promoted for sexual enhancement due to the presence of unauthorized substances (PDE5 derivatives eg. sildenafil): **1. Aziffa, Erex, Eyeful, Hard Drive, Libidinal, Maxyte, Mojo, Monster Excyte, OMG, OMG45, Prolatis, Red Magic, Size Matters, Stiff Nights, Straight Up, Verect, WOW, Xaitrex, Xytamax, Zilex (with Golden Spear), Zotrex 2. Prolatis' Duro Extend Capsules For Men 3. Tiger King 4. Vigor-25, Man Up Now**

Health Canada Feb/11 is advising consumers not to use the following foreign health product **RockHard Weekend (lots 100159 and 100260 sold as blister packs, 3-count bottles and 8-count bottles)** The US FDA informed consumers of a nationwide voluntary recall of certain lots (see above) of RockHard Weekend and Pandora after lab tests confirmed the products contain an unauthorized substance similar to sildenafil.

Health Canada Mar/11 is advising consumers not to use the following foreign health products due to concerns about possible adverse reactions: **1. Nite Rider Maximum Sexual Enhancer for Men - STUD Capsule for Men:** The U.S. FDA informed consumers of a company recall of these products after they were found to contain undeclared sildenafil.

Health Canada May/11 is advising consumers not to use the following foreign health products due to concerns about possible adverse reactions: **1. Gold Seagull Long Zhi Wan, Venergy** The Hong Kong Department of Health advised consumers not to buy or use these products after Gold Seagull Long Zhi Wan was found to contain undeclared glibenclamide, while Venergy was found to contain undeclared sildenafil. **2. Rock Hard Extreme, Passion Coffee** The U.S. FDA advised consumers not to buy or use these products after they were found to contain undeclared sulfoaildenafil, which is an unauthorized substance similar to sildenafil and may pose similar health risks.

Health Canada July/11 "**Man Up Now**" Removed From Sale at Delta and Surrey Stores: May Pose Serious Health Risks to Canadians, was removed from sale at "O! Behave" retail stores in Delta and Surrey, B.C. after Health Canada's testing identified undeclared sildenafil.

Health Canada July/11 is advising Canadians that we have updated our list of unauthorized health products. These products were also removed from sale at Male and Female Harmony retail stores in Richmond and Burnaby, B.C., along with the Happy Paradise Adult Store in Burnaby. {**Sildenafil: in BAOLONG Switzerland Rolex 168 Prolong Time, BAOLONG Yilishen, Black Gold, Herbal Viagra, "Jin Chong Chao – Golden Cordyceps", Lubiangaowansu, MAGNA-RX, MAXMAN II capsules, Shenrong dabuwan, Traditional Chinese Medicine Viagra, V100, VIGER, VigRX for Men, VINIX capsules, Wolf, "XiongBaTian", Zang Gong Mi Lian Nan Bao} & Zeng Bei Jiu Zhan-Tadalafil.**

Health Canada July/11 is advising consumers not to use the following foreign health products due to concerns about possible adverse reactions: **1. Black Ant** The U.S. Food and Drug Administration warned consumers to immediately stop using *Black Ant* after it was found to contain undeclared sildenafil at an amount three times the starting dosage for the approved prescription drug product. **2. Natural Vigra VIAGRA Tablets and Satibo Capsules** The Australian Therapeutic Goods Administration (TGA) advised consumers to stop using *Natural Vigra VIAGRA Tablets* after it was found to contain undeclared sildenafil, and *Satibo Capsules* after it was found to contain undeclared tadalafil and hydroxyhomosildenafil. **3. X-Hero and Male Enhancer** The U.S. Food and Drug Administration informed consumers of a voluntary recall after *X-Hero* was found to contain undeclared sulfosildenafil while *Male Enhancer* was found to contain undeclared tadalafil.

Health Canada July/11 is advising Canadians that we have updated our list of unauthorized health products to include a new product, **Tibet Babao**, which was found to contain undeclared sildenafil, a prescription erectile dysfunction drug. This product and several others have been removed from sale at the **Happy Paradise Adult Store in Burnaby, B.C**.

Health Canada Aug/11 is advising consumers not to use the following foreign health products due to concerns about possible adverse reactions: **1. Pink Lady for Women Capsules, St Nirvana Herbal Slimming Capsules** The Australian TGA warned consumers not to use these products after Pink Lady for Women Capsules was found to contain undeclared tadalafil while St Nirvana Herbal Slimming Capsules was found to contain undeclared sibutramine and phenolphthalein. According to the TGA advisories, these products are sold over the Internet.

Health Canada Oct/11 is advising Canadians not to use these foreign health products as they may pose a health risk. **SXL Sexcellence sachets**- The Australian Therapeutic Goods Administration warned that this sexual enhancement product contains an unauthorized drug (sulfosildenafil).

Health Canada Nov/11 is advising Canadians not to use these foreign health products as they may pose a health risk. **1. Maxidus capsules, Chao Jimengnan SuperPowerful Man tablets, Fu Yuan Chun capsules, and Qing Tian Zhu tablets** The Australian Therapeutic Goods Administration warned that these sexual enhancement products contain prescription drugs (sildenafil, tadalafil) and/or unauthorized drugs (sulfohydroxyhomosildenafil, sulfosildenafil).

Health Canada Nov/11: An unauthorized health product, "**Stiff One Hard 169**" is being voluntarily recalled from the Canadian market after Health Canada's testing identified an undeclared prescription medication in the product (thiodimethylsildenafil, an undeclared substance similar to the prescription medication sildenafil).

Health Canada Dec/11 is advising "**Yanshiwang**", "**Jin Kong Fu**" and "**Chong Cao She Bian Zhuang Yang Dan**". These products were removed from sale at Male and Female Harmony retail stores in Richmond & Burnaby, B.C., along with the Happy Paradise Adult Store in Burnaby. These contained sildenafil.

Health Canada Jan/12 advises: **1. Get Stiff, Maxi Mize** New Zealand's Medsafe warned that these sexual enhancement products contain prescription drugs (tadalafil, vardenafil, yohimbine) and/or unauthorized drugs (hydroxyhomosildenafil, hydroxythiohomosildenafil). **2. Ying Da Wang tablets** The Australian Therapeutic Goods Administration warned that this sexual enhancement product contains sildenafil.

safety of Canadians. Health Canada tested the Stiff4Ever products, advertised as male sexual stimulants, and identified sildenafil. The labels of the PurePillz products (see below) state that they contain BZP and TFMPP.

Health Canada Mar/12 **Power-X**" has been removed from a Canadian retail location after Health Canada's testing identified undeclared thiodimethylsildenafil which is similar to the prescription medication sildenafil.

Health Canada May/12: Unauthorized health products, **"X-Rock", "Kaboom" and "One For Her"** have been removed from sale from various retail outlets in British Columbia and Saskatchewan. Health Canada's testing identified undeclared prescription drugs sildenafil and tadalafil, and an undeclared substance, hydroxythiohomosildenafil, which is similar to sildenafil.

Health Canada May/12 **1. AdvanceMen capsules; Miraculous Evil Root tablets** The Australian Therapeutic Goods Administration warned that these sexual enhancement products contain either a prescription drug (sildenafil) or an unauthorized drug (sulfoaildenafil).

Health Canada June/12 **1. African Black Ant; France T253; Hard Ten Days; Man King; Stree Overlord** : The U.S. Food and Drug Administration warned that these sexual enhancement products contain prescription drugs (sildenafil. One product also contains tadalafil). **2. RegenArouse; RegenErect:** The U.S. Food and Drug Administration informed of a recall because these sexual enhancement products contain a prescription drug (tadalafil). **3. Mince Belle; Everlax; Ever Slim; Ever Slim Shake Mix (Strawberry); Ever Slim Shake Mix (Chocolate); Acai-Man Mangosteen Herbal Drink; Perfect Men:** The U.S. Food and Drug Administration informed of a recall because these weight loss and sexual enhancement products contain prescription drugs (sibutramine or tadalafil).

Health Canada June/12 **Natural Vigor Maximum** (Exemption Number: 138273) has been removed from sale from various retail outlets in Ontario after testing by Health Canada identified a hidden ingredient (dimethylhomosildenafil).

Health Canada July/12 **Lightning Rod**, an unauthorized sexual enhancement product, has been removed from sale from various retail outlets in Ontario, British Columbia and Saskatchewan after testing by Health Canada identified a hidden ingredient (hydroxythiohomosildenafil).

Health Canada Aug/12 These products are not authorized for sale in Canada and have not been found on the Canadian market, but they may have been brought into the country by travellers or purchased over the Internet.
1. Boost – Ultra Sexual Enhancement Formula; EreXite; Mojo Nights: The U.S. Food and Drug Administration advised consumers not to buy or use these products after they were found to contain one or more of the following undeclared drug ingredients: tadalafil, sildenafil, and unauthorized substances similar to sildenafil that may pose similar health risks. **2. Firminite; Extra Strength Instant Hot Rod; Libidron:** The U.S. Food and Drug Administration informed consumers of a company recall after these products were found to contain undeclared tadalafil. **3. Instant Hard Rod; RigiRx Plus; ZenMaxx**: The U.S. Food and Drug Administration advised consumers not to buy or use these products after they were found to contain undeclared aminotadalafil, which is similar to tadalafil and may pose similar health risks. **4. VMaxx Rx:** The U.S. Food and Drug Administration informed consumers of a company recall of certain lots of *VMaxx Rx* after found to contain undeclared sulfoaildenafil.

Health Canada Dec/12 Three unauthorized health products -- "**Man Up Now", "Black Ant", "Triple Power Zen Gold 1200mg**"-- are being recalled by DVDXPRO after testing by Health Canada identified undeclared ingredients-sildenafil and/or tadalafil.

Health Canada Dec/12 is advising Four unauthorized natural health products have been removed from sale as they may pose serious risks to the health of Canadians. The "**ExtenZe**" products are promoted as sexual enhancement products and contain ingredients that legally require they be sold with a prescription in Canada. ExtenZe Max Strength Gelcaps, ExtenZe Original Tablets, ExtenZe Natural Female Tablets, and ExtenZe Big Cherry Flavour Liquid: Three of these unauthorized products list the prescription ingredient pregnenolone and the controlled drug DHEA (dehydroepiandrosterone) & three of these unauthorized products contain the prescription medication yohimbine (either as yohimbine HCl or as yohimbe extract).

Health Canada Feb/13: Two unauthorized health products "**18 Again" and "Stiff 4 Hours**" were tested by Health Canada and were found to contain hidden ingredients (sildenafil or tadalafil) that may pose serious risks to the health of Canadians.

Health Canada Feb/13 A Toronto retail outlet (Handy Variety, 591 Sherbourne St.) has voluntarily handed over **counterfeit Viagra and Cialis** to Health Canada following a compliance and enforcement action by the Department. The counterfeit Viagra product is labelled as 100mg tablets (lot number 314833021), and has 11 blister packs of 4 tablets and one incomplete blister of 2 tablets per package. The counterfeit Cialis product is labelled as 20mg tablets (lot number 05668) and contains five blister packs of 2 tablets.

Health Canada Mar/13: An unauthorized natural health product, "**Libigrow**" was tested by Health Canada and found to contain hidden ingredients (sildenafil and tadalafil) that may pose serious risks to the health of Canadians. "Libigrow" was being sold at two retail locations in the province of Québec: Boutique Sexie folie Inc. (Sainte-Catherine) and at Boutique Érotique 5ième avenue Inc. (Valleyfield).

Health Canada Apr/13 **Shan Dian Shou** The Hong Kong Department of Health has advised it contains the undeclared prescription drug sildenafil.

Health Canada May/13 Two unauthorized health products — "**Stiff Nights" and "Stiff 4 Hours**" — were tested by Health Canada & were found to contain hidden ingredients (sildenafil and/or tadalafil) that may pose serious risks to the health of Canadians. The products were being sold at Saints N Sinners Ltd, 1715 Centre Street N.W., Calgary, Alberta.

Health Canada June/13 is advising Canadians not to use these foreign health products as they may pose a health risk. **1. Flutulang, Kapsul Gaut (Asam Urat), and True ProLife Vegrow** The Health Science Authority of Singapore advised consumers not to use these products after they were found to contain phenylbutazone, chlorpheniramine, dexamethasone, and a chemical compound similar to the prescription drug sildenafil. **2. Jinmaoshiwang tablets, Naturally Kouxan Best Slim capsules, and Majestic Slimming capsules** The Australian Therapeutic Goods Administration advised consumers not to use these products after they were found to contain sildenafil, sibutramine and phenolphthalein. **3. WOW, Super Power and SLIMDIA Revolution** The U.S. Food and Drugs Administration (FDA) warned consumers not to use these products after they were found to contain diclofenac sodium, methocarbamol, dexamethasone, sildenafil and sibutramine.
4. Libigrow XXXtreme, Blue Diamond, Blue Diamond Platinum, Mojo Nights Supreme, and Casanova The U.S. Food and Drugs Administration warned consumers not to use these products after they were found to contain sildenafil, sulfoaildenafil and thioaildenafil.

Health Canada Aug/13 **2. Steelman Capsules 2** The Hong Kong Department of Health has advised consumers not to use this product after it was found to contain undeclared aminotadalafil. **6. Libigirl capsules** The Australian Therapeutic Goods Administration warned consumers not to use this product after it was found to contain the undeclared prescription drugs sildenafil and tadalafil

Health Canada Aug/13 **Prema G** (Granules packaged in tea packets, NPN: 80035944) was tested by Canada Border Services Agency and found to contain a hidden ingredient (hydroxyhomosildenafil thione).

Health Canada Oct/13 wishes to inform Canadians that seized natural health products being sold by Lion King Health Enterprises Group Ltd., 1328-8368 Capstan Way, Richmond, BC. were tested and found to contain hidden ingredients and unauthorized substances similar to the prescription drug, sildenafil. (**North America Dami Ana 600mg, South America Maca 600mg, Ashwagandha 600mg, Optimusman 350mg, Superman 350mg, Innerget Instant Erection (NPN#80041194), Innerget Prolonged Performance (NPN#80041194), Innerget Everlasting Strength (NPN#80041194), Megaton 2080**.)

Health Canada Nov/13 is advising Canadians not to use these foreign health products as they may pose a health risk.
1. **14 sexual enhancement products** http://healthycanadians.gc.ca/recall-alert-rappel-avis/hc-sc/2013/36233a-eng.php ; SexVoltz (Regular and Maximum Strength); Velextra (Regular and Maximum Strength); Amerect* (Regular and Maximum Strength); Night Bullet; Bullet Proof; Vicerex; Zoom-Zooma-Zoom; Sex Plus; Affirm XL; Ninja Mojo; Love Rider; Stiff Days; ROCK-IT MAN; Libido Sexual
Enhancer.
2. **Ziyinzhuangyang tablets, Maxman III, and Mojo Risen** http://healthycanadians.gc.ca/recall-alert-rappel-avis/hc-sc/2013/36519a-eng.php.

Health Canada Dec/13 has updated the list of natural health products seized from **Lion King Health Enterprises Group** Ltd., 1328 - 8638 Capstan Way, Richmond, B.C. that have been tested and found to contain hidden ingredients and unauthorized substances similar to the prescription drug tadalafil.

Health Canada Dec/13 testing of an unauthorized natural health product, **MaxHIMize**, found it to contain bacteria (Enterococcus durans and Bacillus spp) and undeclared caffeine that could present a risk to health. MaxHIMize is being promoted as a dietary supplement and for erectile dysfunction.

Health Canada Feb/14: 1. **Li Long Mei Guo Mo Bang, and Ginseng Tu chong Wan Lin Heong** The Singapore Health Sciences Authority warned consumers not to use this product after it was found to contain sildenafil.

Health Canada Mar/14 is advising Canadians not to use these foreign health products as they may pose a health risk. 1. **Xiang Gang Tian Long Sheng Wu Ke Ji Di Qi Dai Chi Jiu Zhan Shen** http://www.healthycanadians.gc.ca/recall-alert-rappel-avis/hc-sc/2014/38599a-eng.php was found to contain sildenafil. 2. **Various Sexual Enhancement Products** http://www.healthycanadians.gc.ca/recall-alert-rappel-avis/hc-sc/2014/38577a-eng.php was found to have sildenafil andtadalafil. 3. **Majestic Slim Perfect and Yixiu L-Carnitine Slimming Capsules** http://www.healthycanadians.gc.ca/recall-alert-rappel-avis/hc-sc/2014/38609a-eng.php was found to contain sildenafil andphenolphthalein.

Health Canada Apr/14: **Volcano Male Enhancement** liquid & caps: The U.S. Food and Drug Administration warned consumers not to use these products after they were found to contain desmethyl

Health Canada May/14 **Blue Stinger** contains sulfoaildenafil**; 72 HP, Evil root and Pro Power Max** contains sildenafil**; Jack Rabbit** contains sildenafil and tadalafil.

Health Canada May/14: 1. **VitaliKOR**: FDA found vardenafil and tadalafil**;** 2. **Vigor Tea sachets:** Australian Therapeutic Goods Administration found sulfoaildenafil**;** 3. **Prolifta capsules, PHUK and Virilis Pro:** FDA found **sildenafil;** 4. **Wood-E, Xzen Gold, Xzen XPress, XZen 1200, and XZone Premium**: FDA found Wood-E contains sildenafil, Xzen Gold and Xzen XPress contain sildenafil and tadalafil, & XZen 1200 contains tadalafil.

Health Canada June/14: **Bali Mojo & Vimax** contains tadalafil., **LOVher capsule**s contains tadalafil, sildenafil and diclofenac. **Erec-Bull,** contains yohimbine. **Best Whips & JINQIANGBUDOR Red Dragon** contains sildenafil. **Super Hard t**ablets contains sildenafil. **CONTROL All Natural Sexual Enhancement** contains sulfoaildenafil and dimethylsildenafil.

Health Canada July/14: **MME Naturally Maxman capsules, Blue Fantasy capsules, African Superman tablets, and MosKa** – energy for adults: The Australian Therapeutic Goods Administration (TGA) warned consumers not to use these products after they were found to contain sildenafil.

Heath Canada Aug/14: The United States Food and Drug Administration (FDA) warned consumers not to use the products **MV5 Days and S.W.A.G**., and the Australian Therapeutic Goods Administration (TGA) warned consumers not to use the product **Zhansheng Weige Cahoyue Xilishi tablets**, after they were found to contain sildenafil. The Australian Therapeutic Goods Administration (TGA) warned consumers not to use **Robust** tablets contained aminotadalafil.

The Singapore Health Sciences Authority warned consumers not to use **Herbal Health V+** after it was found to contain sildenafil and tadalafil. The Singapore Health Sciences Authority warned consumers not to use **Herbal Health Backplus 500mg** after it was found to contain tadalafil.

Health Canada Sep/14: **Gold Vigra, Liu Bian Li, GoldReallas, Black Ant Strong, My Man His Enhancer 12 Pack, Top Man 3 and Vigour 800**: The United States Food and Drug Administration (FDA) warned consumers not to use the products **Gold Vigra, Liu Bian Li and GoldReallas**, and the Australian Therapeutic Goods Administration (TGA) warned consumers not to use the products **Black Ant Strong, My Man His Enhancer 12 Pack, Top Man 3 and Vigour 800**, after they were found to contain sildenafil.

Dick's Hard Up, P-Boost, and NatuRECT: United States Food and Drug Administration (FDA) warned consumers not to use these products after they were found to contain tadalafil.

3 Hard Knights: The United States Food and Drug Administration (FDA) warned consumers not to use this product after it was found to contain sildenafil andthiosildenafil.

Germany Niubian: The Australian Therapeutic Goods Administration (TGA) warned consumers not to use the product after it was found to contain sildenafil and zopiclone.

Alpha Male: The United States Food and Drug Administration (FDA) warned consumers not to use this product after it was found to contain sildenafil,aminotadalafil, sulfosildenafil, sulfoaildenafil, hydroxythiohomosildenafil, and dimethylsildenafil.

REDDES (or REDDIES) and **The Rock**: The Australian Therapeutic Goods Administration (TGA) warned consumers not to use these products after they were found to containsulfosildenafil and hydroxyhomothiosildenafil.

Full Throttle On Demand: The United States Food and Drug Administration warned consumers not to use this product after it was found to contain propoxyphenyl sildenafil.

RezzRX: The United States Food and Drug Administration warned consumers not to use this product after it was found to containhydroxythiohomosildenafil and/or aminotadalafil.

Play Hard for Men: The Australian Therapeutic Goods Administration (TGA) warned consumers not to use this product after it was found to contain yohimbine andhydroxyhomothiosildenafil.

Rhino 5 Plus, Maxtremezen, and Extenzone: The United States Food and Drug Administration warned consumers not to use these products after they were found to containdesmethylcarbondenafil and dapoxetine.

Health Canada Nov/14: An unauthorized health product, **Gra-MaxX Gold**, was seized by Health Canada as it contains an undeclared drug: N-Ethyl Tadalafil.

Health Canada Dec/14 is following up with Rapha Biotech Inc. **Gra-MaxX Gold** (yellow label) -- undeclared ingredient: N-ethyl tadalafil.

Health Canada Dec/14: "**Herberex**" (NPN 80041180) is being recalled nationwide after Health Canada testing confirmed it contains an undeclared drug: tadalafil.

Health Canada Dec/14: The Australian Therapeutic Goods Administration (TGA) warned consumers not to use the products **Zhansheng Weige Chaoyue Xilishi, Chong Cao Zhag Bian Bao, Night Man, and MMC Sex Men capsules** and the United Stated Food and Drug Administration (FDA) warned consumers not to use the product **O.M.G.** after they were found to contain sildenafil. **Arize**: The United Stated Food and Drug Administration (FDA) warned consumers not to use the product Arize after it was found to containsulfoaildenafil. **Herbal Vigor Quick Fix**: The United Stated Food and Drug Administration (FDA) warned consumers not to use the product **Herbal Vigor Quick Fix** after it was found to contain tadalafil.

Health Canada Dec/14: "**Forta for Men**" (NPN 80045132) is being recalled after Health Canada testing confirmed it contains an undeclared drug: homosildenafil.

Health Canada Dec/14: Samson's Supplements stores in Calgary that pose a risk to health. **Nutrex Research Lipo6 Black, Nutrex Research Lipo6 Black Hers, Nutrex Research Lipo6 Unlimited, Nutrex Research Lipo6 Black Ultra Concentrate, West Pharm Yohimbe** Extract (bottle of 50 and 100 capsules), **West Pharm Yohimbe Extract** (bottle of 50 and 100 capsules), **NutraKey Yohimbine** HCl contains Yohimbine. **West Pharm Xtra Lean, West Pharm ThermaLean, West Pharm ThermoMAXXX** (bottle of 80 and 160 capsules), **Twinlab Ripped Fuel** contains Ephedrine and Caffeine. None of the products are approved for sale. The products are promoted for body building purposes, including for weight loss and increased energy, or for sexual enhancement.

Health Canada Mar/15 advises- FDA Mar/15 **Black Storm**: undeclared sildenafil. Australian Therapeutic Goods Administration **Max Hard**: undeclared sildenafil & aminotadalafil.

Rock Hard: undeclared tadalafil. Singapore Health Sciences Authority Mar/15: **SPARTA X**: undeclared hydroxyhomosildenafil & hydroxythiohomosildenafil. Singapore Health Sciences Authority Mar/15:

MAGIC PENIS undeclared sildenafil. Singapore Health Sciences Authority Mar/15

MR ZACK POWERBRO: undeclared propoxyphenyl hydroxyhomosildenafil, propoxyphenyl aildenafil, propoxyphenyl thiohydroxyhomosildenafil & propoxyphenyl thioaildenafil.

Health Canada Apr/15 testing has found that two unauthorized health products, "**Enhance" and "Natural-Power**," contain undeclared sildenafil.

Health Canada May/15 is warning consumers that an unauthorized drug, "**Stiff Rock**" promoted for male sexual performance enhancement was seized from Boutique Érotique 5ième avenue (also known as Boutique Érotique Liberté), 507 Gande-Île, Valleyfield, QC after Health Canada testing confirmed that the product contained drug ingredients: sildenafil; aminotadalafil; and hydroxythiohomosildenafil.

Health Canada Jun/15 requests quarantine of drugs linked to **Zhejiang Hisun Pharma** due to data integrity concerns.

Health Canada Aug/15-Australian Therapeutic Goods Administration has **Golden Root Complex Capsules & Bushen Famous Men Capsules & Laopiaoke Capsules** with undeclared sildenafil.

Health Canada Nov/15:**Dragon** Power, an unauthorized product sold at The Herb Depot, 407-409 Dundas Street West, Toronto, Ontario, was found to contain an undeclared sildenafil.

Health Canada Dec/15: **Mega Power** contains tadalafil .

Health Canada Feb/16: "**Forta for Men**", is being recalled after testing confirmed one lot contains an undeclared drug: tadalafil.

Health Canada Mar/16: Forta for **Men Daily, Forta Xpload and Durazest For Men Volume**- may contain an undeclared drug: sildenafil.

Health Canada Mar/16 says **S Lion Juice Orange 10 gm by Singapore Health Science Authority** undeclared propoxyphenyl thioaidenafil.

Health Canada Mar/16 says **S Lion Juice 20 gm** by Singapore Health Science Authority undeclared thiodimethylsildenafil.

Health Canada Mar/16 says **S Lion Juice 10 gm** by Singapore Health Science Authority undeclared thiodimethylsildenafil and tadalafil.

Health Canada Mar/16 says **S Lion Juice 1** by Singapore Health Science Authority undeclared aminotadalafil and thiodimethylsildenafil

Health Canada Mar/16 says **Rhino 7 3000 & Rhino 7 Platinum 3000 Capsules** by FDA contains undeclared desmethyl carbondenafil and dapoxetine.

Health Canada Mar/16 says **Power Khan** by FDA contains undeclared sildenafil and thiosildenafil.

Health Canada Mar/16 says Australian Therapeutic Goods Administration: **Hongkong Tianli Biological 'Power' tablets, Longue Jambe Frères (Brother Long Legs) tablets** contains undeclared sildenafil.

Health Canada Apr/16: Australian Therapeutic Goods Administration says **100% healthy food for men tablets, & V-MAX Herbal Tablets** contains undeclared sildenafil.

Health Canada June/16: FDA says **Boss Number #Six** contains undeclared tadalafil; **Bull & Bull's Genital** contains undeclared sildenafil; **Ginseng Power-X** contains undeclared sildenafil and sulfoaildenafil; **Golden Night** contains undeclared sildenafil and hydroxythiohomosildenafil; **Neophase Natural Sex Enhancer** contains undeclared hydroxyacetildenafil; **Weekend Prince** contains undeclared sildenafil; & **Wonder-Erect Male Gum** contains undeclared vardenafil.

Health Canada June/16: Australian Therapeutic Goods Administration- **Half Quite** tablets contains undeclared sildenafil; contains undeclared sildenafil and oxytetracycline; **Maxagra** capsules contains undeclared sildenafil and oxytetracycline; **Ninja-X** contains undeclared sildenafil and thiosildenafil; **Sextra** capsules contains undeclared sildenafil and yohimbine & **Zhong Hua Niu Bian** tablets contains undeclared chloramphenicol and sildenafil.

Health Canada July/16: FDA says **Sextra, & Zlimxter Capsules** contains undeclared sildenafil.

Health Canada July/16: FDA says **Salute Capsules** undeclared sildenafil, thiosildenafil, and sulfoaildenafil.

Health Canada July/16: Australian Therapeutic Goods Administration says **MMC Zang Ba Bao tablets, Super Bull 6000 Herbal capsules, & U.S. Black Gold tablets** undeclared sildenafil.

Health Canada July/16: **Wonderblue & B-Hard on Demand** has undeclared sildenafil as well as thiodimethylsildenafil and/or thiomethisosildenafil.

Health Canada July/16 **DR's Secret Bio Herbs Coffee** undeclared tadalafil

Health Canada Aug/16: Australian Therapeutic Goods Administration-**King-Wolf Tablets** undeclared sildenafil.

Health Canada Aug/16: Australian Therapeutic Goods Administration- **MAGNA-RX Capsules** undeclared sildenafil & acetaminophen.

Health Canada Aug/16: FDA-**My Steel Woody** undeclared sildenafil.

Health Canada Aug/16: Australian Therapeutic Goods Administration- **Black Storm** tablets undeclared sildenafil and vardenafil.

Health Canada Aug/16: FDA- **Dream Body Advanced + Acai Weight Loss & Cleanse, & Dream Body Extreme Gold** undeclared sibutramine, fluoxetine, and sildenafil.

Health Canada Oct/16: **Anaconda Strong Formula, Boss-Rhino Gold X-tra Strength, De Guo Hei Bei (德国黑倍), Libigirl, Power Spring (XXX) Oral Liquid, Shangai Ultra X, Super Shangai, The Golden Root, Weili (一炮到天亮 or Yi Pao Dao Tian Liang) , Ziyinzhuangyang**, -Undeclared sildenafil by United States Food and Drug Administration.

Health Canada Oct/16: **Ant Power tablets, Man King capsules**, -Undeclared sildenafil by Australian Therapeutic Goods Administration.

Health Canada Oct/16: **Golden Ant tablets**-Undeclared sildenafil and chloramphenicol byAustralian Therapeutic Goods Administration.

Health Canada Oct/16: **Xcelerated Weight Loss Ultra Max**- Undeclared phenolphthalein and sildenafil by United States Food and Drug Administration.

Health Canada Nov/16: **One More Knight 1750** has undeclared tadalafil and dapoxetine by the United States Food and Drug Administration.

Health Canada Nov/16: **Love4Long** has undeclared sildenafil by the United States Food and Drug Administration.

Health Canada Nov/16: **Kopi Jantan Tradisional Natural Herbs Coffee** has undeclared desmethyl carbodenafil by the United States Food and Drug Administration.

Health Canada Dec/16 reports: Singapore Health Sciences Authority: **LONGRED Oyster-x**-undeclared sildenafil; FDA: **Stiff Bull Herbal Coffee**-undeclared desmethyl carbodenafil; & Australian Therapeutic Goods Administration: **Wolfish Shark Viagra** tablets-undeclared sildenafil.

Health Canada Mar/17: 90° **Jiushidu Capsules, African Viagra, Big Penis Male Sexual Stimulant, Black Mamba 2 Premium, Black 3K Plus Male Sexual Enhancement Capsules, Bl4ck 4K Capsules, Duramaxxx, Power Male Sexual Stimulant, Rhino 5 1500 Capsules, Rhino 7K 9000 Male Performance Booster, Rhino 8 Platinum 8000, Rhino 9 Premium 3500 & Triple Green Capsules** contains undeclared sildenafil.

Health Canada Mar/17: **Megajex Natural Male Sex Enhancer Dietary Supplement** contains undeclared sildenafil & tadalafil.

Health Canada Mar/17: **Chao Jimengnan Super Powerful Man Tablets & Zhen Gongfu** capsules has undeclared sildenafil by the Australian Therapeutic Goods Administration.

Health Canada Mar/17: **GoldReallas Original & GoldReallas XXX** has undeclared sildenafil & thiosildenafil by the FDA.

Health Canada Mar/17: **Impeous Man capsules** has undeclared sildenafil & phenolphthalein by the Australian Therapeutic Goods Administration.

Health Canada Mar/17: **Old Chinese & Shenjingpian** has undeclared sildenafil by the FDA.

Health Canada Mar/17 is advising Canadians that it has seized multiple unauthorized health products from three retailers in Ontario (see table below). The products are promoted for sexual enhancement and were found to contain, or are labelled to contain, prescription drugs that may pose serious risks to the health of Canadians. Hespeler Road Adult SuperStore (261 Hespeler Road, Cambridge ON): **LipsTenZen, Super Panther 7K & Thunder Bull 7K contains Yohimbe. One More Knight contains tadalafil and dapoxetine. MV7 Days 2000** contains sildenafil and tadalafil. Naughty Shop (330 Wellington Rd. S, London ON): **LipsTenZen, Super Panther 7K & Triple Green** contains Yohimbe. VXI Multimedia (800 Petrolia Road, Unit 18, Toronto, ON): **Opti-Sildenafil** 100 mg contains sildenafil, **Opti-Tadalafil** 20 mg contains tadalafil.

Health Canada Apr/17 is advising Canadians that the unauthorized health product "**Rhino Blitz Gold**" may pose serious health risks, after testing confirmed it contains an undeclared prescription drug (sildenafil).

Health Canada Apr/17 laboratory tests have confirmed that two additional unauthorized products seized from **24 Hour Adult Mart in Toronto** contain undeclared tadalafil.

Health Canada May/17: **Africa Black Ant capsules & Australia Kangaroo Essence** by Australia Therapeutic Goods Administration has undeclared sildenafil.

Health Canada May/17: **Arouse-Plus & Bazook Bullet** by FDA has undeclared tadalafil.

Health Canada May/17 is advising Canadians that multiple unauthorized health products seized from **two retailers in Scarborough, ON**, may pose serious risks to health. Products seized include "poppers" and products promoted for sexual enhancement. Adult Store 2365 Eglinton Ave E Scarborough ON had Rochfort 10mL-Isobutyl nitrite; Finegra-100-Sildenafil; Super Panther 7K-Yohimbe; Premium X Pulse 2000-Yohimbe; Premium Pro Power 3500-Yohimbe bark extract; Hard Rock 3800-Yohimbe bark extract; XXL Ant 3000-Yohimbe bark extract; Black Mamba 2 Premium-Yohimbe; Mamba is Hero-Yohimbe, sildenafil, desmethyl carbodenafil and dapoxetine; Master Zone 1500- Sildenafil and tadalafil. Homerama Adult Video 2524 Eglinton Ave E Scarborough had ONWet XXX-Yohimbe; 7K-Yohimbe; Super Panther 7K-Yohimbe; Passion Classic- Yohimbe; Titanium 4000-Sildenafil and tadalafil. Adult Store 2365 Eglinton Ave E Scarborough ON had Zhen Gongfu-previous testing of product with similar packaging, identified as containing undeclared sildenafil; Stiff Rock- previous testing of product with similar packaging, identified as containing undeclared sildenafil; One For Her- Previous testing of product with similar packaging, identified as containing undeclared tadalafil; Rush 10mL, Super Rush 10mL & Blue Boy 10mL-previously seized products with similar packaging were labelled to contain alkyl nitrites. Homerama Adult Video 2524 Eglinton Ave E Scarborough ON had Rush 10mL, Super Rush 10ml, Jungle Juice Gold Label 10mL, Jungle Juice Gold Label 30mL, Jungle Juice Platinum 10mL, & Jungle Juice Platinum 30mL previously seized products with similar packaging were labelled to contain alkyl nitrites.

Health Canada June/17: **VENERGY Capsule** 100mg has undeclared sildenafil by the Hong Kong Department of Health.

Health Canada June/17: **Nangen Zengzhangsu** undeclared sildenafil by Australia Therapeutic Goods Administration.

Health Canada June/17: **Slim-Vie Slimming Capsules** has undeclared sibutramine, sildenafil, and phenolphthalein by Australia Therapeutic Goods Administration.

Health Canada Jul/17: **Big N Hard** has undeclared tadalafil by the United States Food and Drug Administration.

Health Canada Jul/17: **Black Gorilla, Maxman IV, Maxman Premium, Maxman V, MMC Maxman XI, New Advanced Technological, V9 Male Sexual Stimulant, Real Skill Male Sexual Stimulant, & Rize N Shine** has undeclared sildenafil by the Australia Therapeutic Goods Administration.

Health Canada Jul/17: **Cummor & Monkey Business** has undeclared N-desmethyl tadalafil by the United States Food and Drug Administration.

Health Canada Jul/17: **Dragon Max, Oh Baby!, & XXXL Penis Enlarging Ointment** has undeclared tadalafil by the Australia Therapeutic Goods Administration.

Health Canada Jul/17: **Tornado** has undeclared nortadalafil by the United States Food and Drug Administration.

Health Canada Jul/17: **Xrect** has undeclared tadalafil and descarbonsildenafil by the United States Food and Drug Administration.

Health Canada Jul/17: **Z Daily** has undeclared homosildenafil by the United States Food and Drug Administration.

Health Canada Mar/18: is advising Canadians that two versions of the sexual enhancement product "**Leopard Miracle of Honey**" may pose serious health risks. Both versions are labelled as being approved by Health Canada, with NPN 80073650. Health Canada's testing found that both versions of the product contain the undeclared prescription drug sildenafil.

Hedelin H, Stroberg P. Treatment for Erectile Dysfunction Based on Patient-Reported Outcomes: To Every Man the PDE5 Inhibitor that He Finds Superior. Drugs. 2005;65(16):2245-51.

Heidelbaugh JJ. Management of erectile dysfunction. Am Fam Physician. 2010 Feb 1;81(3):305-12.

Hellstrom WJ, Kaminetsky J, Belkoff LH, et al. Efficacy of **Avanafil** 15 Minutes after Dosing in Men with Erectile Dysfunction: A Randomized, Double-Blind, Placebo Controlled Study. J Urol. 2015 Aug;194(2):485-92.

Herrick AL, van den Hoogen F, Gabrielli A, et al. Modified-release **sildenafil** reduces Raynaud's phenomenon attack frequency in limited **cutaneous systemic sclerosis**. Arthritis Rheum. 2011 Mar;63(3):775-82.

Huang W, Sundquist J, Sundquist K, Ji J. Use of Phosphodiesterase 5 Inhibitors Is Associated With Lower Risk of Colorectal Cancer in Men With Benign Colorectal Neoplasms. Gastroenterology. 2019 Sep;157(3):672-681.e4.

Idiopathic Pulmonary Fibrosis Clinical Research Network, Zisman DA, Schwarz M, Anstrom KJ, et al. A controlled trial of **sildenafil** in advanced **idiopathic pulmonary fibrosis**. N Engl J Med. 2010 Aug 12;363(7):620-8.

Jena, Anupam B. Goldman, Dana P. Kamdar, Amee et al. **Sexually Transmitted Diseases** Among Users of Erectile Dysfunction Drugs: Analysis of Claims Data. *Ann Intern Med* July 6, 2010 153:1-7; doi:10.1059/0003-4819-153-1-201007060-00003

Joseph P, Lonn E, Bosch J, et al; **HOPE-3** Investigators. Long-term Effects of Statins, **Blood Pressure-Lowering, and Both on Erectile Function** in Persons at Intermediate Risk for Cardiovascular Disease: A Substudy of the Heart Outcomes Prevention Evaluation-3 (HOPE-3) Randomized Controlled Trial. Can J Cardiol. 2018 Jan;34(1):38-44.

Kao SL, Chan CL, Tan B, Lim CC, Dalan R, Gardner D, Pratt E, Lee M, Lee KO. An unusual outbreak of hypoglycemia. N Engl J Med. 2009 Feb 12;360(7):734-6. No abstract available. Hypoglycaemia outbreak linked to contamination of illegal **sexual-enhancement drugs with glyburide**.

Katz A, Katz A. **Erectile dysfunction**. CMAJ. 2010 Feb 8.

Klinger JR, Elliott CG, Levine DJ, et al. **Therapy for Pulmonary Arterial Hypertension in Adults**: Update of the CHEST Guideline and Expert Panel Report. Chest. 2019 Mar;155(3):565-586.

Kloner RA. Pharmacology and **Drug Interaction** Effects of the Phosphodiesterase 5 Inhibitors: Focus on alpha-Blocker Interactions. Am J Cardiol. 2005 Dec 26;96(12 Suppl 2):42-6. Epub 2005 Dec 5.

Kloner RA, Henderson L. **Sexual Function in Patients With Chronic Angina Pectoris**. Am J Cardiol. 2013 Apr 1.

Köhler TS, Kim J, Faja K, et al. Prevalence of **androgen deficiency** in men with erectile dysfunction. Urology. 2008 Apr;71(4):693-7. Epub 2008 Mar 3. Androgen deficiency was quite common in men presenting with ED and correlated

significantly with age, uncontrolled diabetes, hypercholesteremia, and anemia. Although additional prospective studies evaluating the effect of testosterone supplementation in this population are needed, clinicians, including urologists, should be keenly aware of the large overlap of patients with ED who might also have the entity, androgen deficiency in the aging male.

Kostis JB, Jackson G, Rosen R, et al. Sexual dysfunction and cardiac risk (the Second Princeton Consensus Conference). Am J Cardiol. 2005 Jul 15;96(2):313-21.

Kostis JB, Dobrzynski JM. The Effect of **Statins on Erectile Dysfunction**: A Meta-Analysis of Randomized Trials. J Sex Med. 2014 Mar 29.

Kouidrat Y, Pizzol D, Cosco T, et al. High prevalence of **erectile dysfunction in diabetes**: a systematic review and meta-analysis of 145 studies. Diabet Med. 2017 Jul 18.

Ledda A, Belcaro G, Cesarone MR, et al. Investigation of a complex plant extract for mild to moderate erectile dysfunction in a randomized, double-blind, placebo-controlled, parallel-arm study. BJU Int. 2010 Feb 22.
Prelox, contains pine bark extract and the amino acid L-arginine aspartate; was given as two tablets of Prelox twice daily.

Lian Y, Yin H, Pollak MN, et al. **Phosphodiesterase Type 5 Inhibitors** and the Risk of **Melanoma Skin Cancer**. Eur Urol. 2016 May 10.

Loeb S, Folkvaljon Y, Robinson D, et al. **Phosphodiesterase Type 5 Inhibitor** Use and Disease Recurrence **After Prostate Cancer Treatment**. Eur Urol. 2015 Dec 29.

Levine GN, Steinke EE, Bakaeen FG, et al. **Sexual activity and cardiovascular disease**. A scientific statement from the American Heart Association (**AHA**). Circulation 2012.
http://circ.ahajournals.org/content/early/2012/01/19/CIR.0b013e3182447787.full.pdf?sid=8d962f06-2506-473d-aaaf-5761032aed2b

Leung DG, Herzka DA, Thompson WR, et al. **Sildenafil** does **not** improve cardiomyopathy in **Duchenne/Becker muscular dystrophy**. Ann Neurol. 2014 Jul 4.

Li T, Wu C, Fu F, et al. Association between use of **aspirin or non-aspirin non-steroidal anti-inflammatory drugs and erectile dysfunction**: A systematic review. Medicine (Baltimore). 2018 Jul;97(28):e11367.

LiWQ, Qureshi AA, Robinson KC, Han J. **Sildenafil** use and increased risk of **incident melanoma** in US men: a prospective cohort study [published online April 7, 2014]. JAMA Intern Med.

Lindman BR et al. Effects of Phosphodiesterase Type 5 Inhibition on Systemic and Pulmonary Hemodynamics and Ventricular Function in Patients with Severe Symptomatic **Aortic Stenosis**. Circulation. 2012 Mar 25.

Loeb S, Folkvaljon Y, Lambe M, et al. Use of **Phosphodiesterase Type 5 Inhibitors for Erectile Dysfunction and Risk of Malignant Melanoma**. JAMA. 2015 Jun 23-30;313(24):2449-55.

Loeb S, Ventimiglia E, Salonia A, et al. Meta-analysis of the association between **phosphodiesterase inhibitors (PDE5Is) and risk of melanoma**. J Natl Cancer Inst. 2017;109(8): djx086.

Lopez DS, Wang R, Tsilidis KK, et al. Role of **Caffeine Intake** on Erectile Dysfunction in US Men: Results from NHANES 2001-2004. PLoS One. 2015 Apr 28;10(4)

Lopez DS, Liu L, Rimm EB, et al. **Coffee Intake** and Incidence of Erectile Dysfunction. Am J Epidemiol. 2018 May 1;187(5):951-959.

Ma RC, So WY, Yang X, et al.Erectile dysfunction **predicts coronary heart disease** in type 2 diabetes.J Am Coll Cardiol. 2008 May 27;51(21):2045-50.

Maggiorini M, et al. Both **tadalafil and dexamethasone** may reduce the incidence of **high-altitude pulmonary edema**: a randomized trial. Ann Intern Med. 2006 Oct 3;145(7):497-506.

Maher MA, Sayyed TM, El-Khadry SW. Nifedipine alone or combined with sildenafil citrate for management of threatened preterm labour: a randomised trial. BJOG. 2018 Oct 13.

Maher MA, Sayyed TM, Elkhouly N. Sildenafil Citrate Therapy for Oligohydramnios: A Randomized Controlled Trial. Obstet Gynecol. 2017 Apr;129(4):615-620.

Mandel J, Poch D. In the Clinic: **Pulmonary hypertension**. Ann Intern Med. 2013 May 7;158(9):ITC5-1.

Matthews A, Langan SM, et al. **Phosphodiesterase Type 5 Inhibitors** and **Risk of Malignant Melanoma**: Matched Cohort Study Using Primary Care Data from the UK Clinical Practice Research Datalink. PLoS Med. 2016 Jun 14;13(6):e1002037.

McGwin G Jr, Vaphiades MS, Hall TA, Owsley C. **Non-arteritic anterior ischaemic optic neuropathy** and the treatment of erectile dysfunction. Br J Ophthalmol. 2006 Feb;90(2):154-7.

McGwin G Jr. Phosphodiesterase type 5 inhibitor use and **hearing impairment**. Arch Otolaryngol Head Neck Surg. 2010 May;136(5):488-92.

McLaughlin VV, Archer SL, Badesch DB, et al.; ACCF/AHA. ACCF/**AHA 2009** expert consensus document on **pulmonary hypertension**: a report of the American College of Cardiology Foundation Task Force on Expert Consensus Documents and the American Heart Association: developed in collaboration with the American College of Chest Physicians, American Thoracic Society, Inc., and the Pulmonary Hypertension Association. Circulation. 2009 Apr 28;119(16):2250-94. Epub 2009 Mar 30. Review. Erratum in: Circulation. 2009 Jul 14;120(2):e13.

McMahon CN, Smith CJ, Shabsigh R. Treating erectile dysfunction when **PDE5 inhibitors fail**. BMJ. 2006 Mar 11;332(7541):589-92.

McVary KT. **Erectile dysfunction**. N Engl J Med. **2007** Dec 13;357(24):2472-81.

Medical Letter, Sildenafil (Revatio) for **Pulmonary Arterial Hypertension**. Vol 47 (Issue 1215/1216) Aug 15/29,2005. p.65-67.

Melnik T, Soares B, Nasselo A. **Psychosocial interventions** for erectile dysfunction. Cochrane Database Syst Rev. 2007 Jul 18;(3):CD004825. There was evidence that group psychotherapy may improve erectile function. Treatment response varied between patient subgroups, but focused sex-group therapy showed greater efficacy than control group (no treatment). In a meta-analysis that compared group therapy plus sildenafil citrate versus sildenafil, men randomised to receive group therapy plus sildenafil showed significant improvement of successful intercourse, and were less likely than those receiving only sildenafil to drop out. Group psychotherapy also significantly improved ED compared to sildenafil citrate alone. Regarding the effectiveness of psychosocial interventions for the treatment of ED compared to local injection, vacuum devices and other psychosocial techniques, no differences were found.

MHRA Feb/12 has received advice from AGES PharmMed in Austria and the Danish Medicines Agency, warning that these unlicensed products have been tested and found to contain Tadalafil and/or Sildenafil:
AH Free/Reflexit, Stree Overlord, Man King, VigRX, Maxman, Maxman III, Viriya, & Imbiza for Men.

MHRA: Austrian Sep/12 authorities have issued a warning for **Ramlostan Forte** manufactured by SC Parapharm, Romania. Ramlostan comes in white and blue packaging, with a picture of a ram at the top. Inside, there are ten blue capsules. The Austrian authority (AGES) has issued a warning for this product after finding it to contain Tadalafil.

MHRA Nov/12 has received advice from the Ministry of Health, Jerusalem warning that this unlicensed product, **Shark Essence** has been tested and found to contain Tadalafil and Sildenafil.

MHRA May/14: Singapore Health Sciences Department **Li Long Mei Guo Mo Bang** because it contains sildenafil.

MHRA Sep/17 investigators raided **Antley's** property and seized more than 13,900 doses of unlicensed erectile dysfunction medicines worth more than £40,000. Antley pleaded guilty to the charges and was sentenced to 20 weeks imprisonment (concurrent to all counts). Gurinder Bharaj, of Southall, West London, was sentenced on Friday at Isleworth Crown Court on eight counts of possession and supply of significant quantities of unauthorised and unlicensed medication. Investigators from the Medicines and Healthcare products Regulatory Agency (MHRA) raided a property belonging to Mr Bharaj in Ealing where more than 100,000 individual doses of unlicensed erectile dysfunction medicines worth more than £30,000 were uncovered and seized. A smaller quantity of prescription medication was also seized.

Min JK, Williams KA, Okwuosa TM, et al. Prediction of **coronary heart disease** by erectile dysfunction in men referred for nuclear stress testing. *Arch Intern Med* 2006; 166:201-206.

Mittleman MA, Maclure M, Glasser DB. Evaluation of acute risk for myocardial infarction in men treated with sildenafil citrate. Am J Cardiol. 2005 Aug 1;96(3):443-6.

Molina-Leyva A, Salvador-Rodriguez L, Martinez-Lopez A, et al. Association Between **Psoriasis and Sexual and Erectile Dysfunction in Epidemiologic Studies**: A Systematic Review. JAMA Dermatol. 2018 Oct 10.

Moon RE, Martina SD, Peacher DF, et al. **Swimming-Induced Pulmonary Edema**: Pathophysiology and Risk Reduction With **Sildenafil**. Circulation. 2016 Feb 16.

Morrison Deborah, Aitchison Michael, Connelly Derek T, et al. **10-Minute Consultation: Sexual dysfunction in cardiovascular disease**. BMJ 2011;343:doi:10.1136/bmj.d4437 (Published 26 July 2011)

Muller A, Smith L, Parker M, Mulhall JP. Analysis of the efficacy and safety of sildenafil citrate in the **geriatric population**. BJU Int. 2007 Jul;100(1):117-21. From these data, sildenafil is an effective agent in elderly men, but had a lower efficacy rate with increasing age, especially in men aged >80 years.

Muneer A, Kalsi J, Nazareth I, Arya M. **Erectile dysfunction**. BMJ. 2014 Jan 27;348:g129.

Namachivayam P, et al. Sildenafil **prevents** rebound **pulmonary hypertension** after withdrawal of nitric oxide in children. Am J Respir Crit Care Med. 2006 Nov 1;174(9):1042-7. Epub 2006 Aug 17.

Najari BB, Kashanian JA. **Erectile Dysfunction**. JAMA. 2016 Nov 1;316(17):1838

Nelson MD, Rader F, Tang X, et al. **PDE5 inhibition** alleviates functional **muscle ischemia** in boys with **Duchenne muscular dystrophy**. Neurology. 2014 May 7.

Nickel M, et al. **Cabergoline** treatment in men with psychogenic erectile dysfunction: a randomized, double-blind, placebo-controlled study. Int J Impot Res. 2006 May 18; [Epub ahead of print]

Nurnberg HG, Hensley PL, Heiman JR, Croft HA, Debattista C, Paine S. Sildenafil treatment of women with antidepressant-associated sexual dysfunction: a randomized controlled trial.JAMA. 2008 Jul 23;300(4):395-404.
In this study population, **sildenafil treatment of sexual dysfunction in women** taking SRIs was associated with a reduction in adverse sexual effects.

Oh EG, Yoo JY. Progression of erectile function in men with **chronic obstructive pulmonary disease**: a cohort study. BMC Pulm Med. 2019 Sep 2;19(1):139.

Omland T, Randby A, Hrubos-Strøm H, et al. Relation of **Erectile Dysfunction to Subclinical Myocardial Injury**. Am J Cardiol. 2016 Dec 15;118(12):1821-1825.

Osondu CU, Vo B, Oni ET, et al. The relationship of **erectile dysfunction and subclinical cardiovascular disease**: A systematic review and meta-analysis. Vasc Med. 2017 Dec 1:1358863X17725809.

Padma-Nathan H, Yeager JL. An integrated analysis of **alprostadil topical cream** for the treatment of erectile dysfunction in 1732 patients. Urology. 2006 Aug;68(2):386-91.

Palm P, Zwisler AO, Svendsen JH, et al. **Sexual rehabilitation for cardiac patients** with erectile dysfunction: a randomised clinical trial. Heart. 2018 Oct 31.

Park K, Ku JH, Kim SW, Paick JS. Risk factors in predicting a poor response to sildenafil citrate in elderly men with erectile dysfunction. BJU Int. 2005 Feb;95(3):366-70.

Compared to placebo, PDEI likely leads to a small reduction in IPSS-total and BPHII sores, with a possible increase in AEs. There may be no differences between PDEI and AB with regards to improvement in IPSS-total, BPHII, and incidence of AEs. There appears to be no added benefit of PDEI combined with AB compared to PDEI or AB alone or PDEI combined with 5-ARI compared to ARI alone with regards to urinary symptoms. Most evidence was limited to short-term treatment up to 12 weeks and of moderate or low certainty.

Pennisi G, Vacante M, Russo C, Malaguarnera M. Rhabdomyolysis Induced by **Rosuvastatin and Sildenafil**. South Med J. 2010 Sep 2.

Penson DF, McLerran D, Feng Z, Li L, et al. 5-year urinary and sexual outcomes **after radical prostatectomy**: results from the Prostate Cancer Outcomes Study. J Urol. 2008 May;179(5 Suppl):S40-4. Urinary and sexual dysfunction were common 5 years following radical prostatectomy in this large, community based cohort of prostate cancer survivors. While a small minority of subjects experienced changes in urinary or sexual function between years 2 and 5 after prostatectomy, functional outcomes remained relatively stable in the majority of participants.

Pharmacist's Letter Oct 2006. **Alternative or Off-label** Routes of Drug Administration. (**Vaginal & sublingual** administration of: sildenafil)

Philip A, Ramchandani S, Dorrance K, Dorrance C. **Sildenafil-induced thrombocytopenia**. Ann Intern Med. 2008 Sep 16;149(6):437-9.

Piazza G, Goldhaber SZ. Chronic **Thromboembolic Pulmonary Hypertension**. N Engl J Med. 2011 Jan 27;364(4):351-360.

Pisansky TM, Pugh SL, et al. **Tadalafil** for prevention of erectile dysfunction **after radiotherapy for prostate cancer**: Radiation Therapy Oncology Group [0831] randomized clinical trial. JAMA. 2014 Apr 2;311(13):1300-7.

Porst H, et al. Evaluation of the Efficacy and Safety of **Once-a-Day** Dosing of Tadalafil 5mg and 10mg in the Treatment of Erectile Dysfunction: Results of a Multicenter, Randomized, Double-Blind, Placebo-Controlled Trial. Eur Urol. 2006 Aug;50(2):351-9. Epub 2006 Mar 20. 12-week study enrolled 268 men

Pryor JL, et al.; Dapoxetine Study Group. Efficacy and tolerability of **dapoxetine** in treatment of premature ejaculation: an integrated analysis of two double-blind, randomised controlled trials. Lancet. 2006 Sep 9;368(9539):929-37. (InfoPOEMs: In this study, dapoxetine (an investigational new short-acting selective serotonin reuptake inhibitor) taken 1 to 3 hours before sexual activity delayed ejaculation in men with moderate-to-severe premature ejaculation. The net improvement due to medication was less than 2 minutes compared with baseline, but patients and partners were satisfied with this small amount of improvement. (LOE = 2b))

Qaseem A., Snow V., Denberg T. D., et al and for the Clinical Efficacy Assessment Subcommittee of the American College of Physicians. **Hormonal Testing and Pharmacologic Treatment of Erectile Dysfunction**: A Clinical Practice Guideline From the American College of Physicians. *Ann Intern Med* 2009; 60520-151.

Recommendation 1: The American College of Physicians recommends that clinicians initiate therapy with a PDE-5 inhibitor in men who seek treatment for erectile dysfunction and who do not have a contraindication to PDE-5 inhibitor use (Grade: strong recommendation; high-quality evidence).
Recommendation 2: The American College of Physicians recommends that clinicians base the choice of a specific PDE-5 inhibitor on the individual preferences of men with erectile dysfunction, including ease of use, cost of medication, and adverse effects profile (Grade: weak recommendation; low-quality evidence).
Recommendation 3: The American College of Physicians does not recommend for or against routine use of hormonal blood tests or hormonal treatment in the management of patients with erectile dysfunction (Grade: insufficient evidence to determine net benefits and harms).

Raina R, Pahlajani G, Agarwal A, Zippe CD. The early use of transurethral alprostadil after radical prostatectomy potentially facilitates an earlier return of erectile function and successful sexual activity. BJU Int. 2007 Dec;100(6):1317-21. Epub 2007 Sep 11. Initiating **MUSE** shortly after RP is safe and tolerable, and appears to shorten the recovery time to reagin erectile function.

Redfield MM, et al. Effect of phosphodiesterase-5 inhibition (**sildenafil**) on exercise capacity & clinical status in heart failure with preserved ejection fraction: randomized clinical trial. (RELAX) JAMA 2013.

Reece JC, Dangerfield DC, Coombs CJ. End-to-side Somatic-to-autonomic **Nerve Grafting to Restore Erectile Function** and Improve Quality of Life After Radical Prostatectomy. Eur Urol. 2019 Apr 4.

Rees J, Patel B. **Erectile dysfunction**. BMJ. 2006 Mar 11;332(7541):593.

Reffelmann T, Kloner RA. Pharmacotherapy of erectile dysfunction: focus on cardiovascular safety. Expert Opin Drug Saf. 2005 May;4(3):531-40.

Rew KT, Heidelbaugh JJ. **Erectile Dysfunction**. Am Fam Physician. 2016;94(10):820-827.

Roehrborn CG et al. Effects of tadalafil once daily on maximum urinary flow rate in men with lower urinary tract symptoms suggestive of **benign prostatic hyperplasia**. J Urol 2014 Apr; 191:1045.

Roizenblatt S, et al. A double-blind, placebo-controlled, crossover study of sildenafil in **obstructive sleep apnea**. Arch Intern Med. 2006 Sep 18;166(16):1763-7. In patients with severe obstructive sleep apnea, a single 50-mg dose of sildenafil at bedtime worsens respiratory and desaturation events.

Rosen R, et al.; Vardenafil Study Site Investigators. Efficacy and tolerability of vardenafil in men with mild **depression** and erectile dysfunction: the depression-related improvement with vardenafil for erectile response study. Am J Psychiatry. 2006 Jan;163(1):79-87.

Rosenthal BD, et al.Adjunctive use of AndroGel(testosterone gel) with sildenafil to treat erectile dysfunction in men with acquired androgen deficiency syndrome after failure using sildenafil alone.Urology.2006Mar;67(3):571-4.

Rosman L, Cahill JM, McCammon SL, Sears SF. **Sexual health** concerns in patients with cardiovascular disease. Circulation. 2014 Feb 4;129(5):e313-6.

Roustit M, Blaise S, et al. **Phosphodiesterase-5 inhibitors for the treatment of secondary Raynaud's phenomenon**: systematic review and meta-analysis of randomised trials. Ann Rheum Dis. 2013 Oct 1;72(10):1696-9.

Roustit M, Giai J, Gaget O, et al. **On-Demand Sildenafil as a Treatment for Raynaud Phenomenon**: A Series of n-of-1 Trials. Ann Intern Med. 2018 Oct 30.

Rubin LJ, Badesch DB, Fleming TR, et al; the **SUPER-2** Study Group. Long-term Treatment With **Sildenafil** Citrate in **Pulmonary Arterial Hypertension**: The SUPER-2 Study. Chest. 2011 Nov;140(5):1274-1283.

Russo GI, Milenkovic U, Hellstrom W, et al. Clinical **Efficacy of Injection and Mechanical Therapy for Peyronie`s Disease**: A Systematic Review of the Literature. Eur Urol. 2018 Sep 17.

Saigal CS, Wessells H, Pace J, et al. **Predictors and prevalence** of erectile dysfunction in a racially diverse population. *Arch Intern Med* 2006; 166:207-212.

Scaglione F, Donde S, Hassan TA, et al. **Phosphodiesterase Type 5 Inhibitors for the Treatment of Erectile Dysfunction**: Pharmacology and Clinical Impact of the Sildenafil Citrate Orodispersible Tablet Formulation. Clin Ther. 2017 Jan 27.

Schwartz BG, Kloner RA. **Drug interactions with phosphodiesterase-5 inhibitors** used for the treatment of erectile dysfunction or pulmonary hypertension. Circulation. 2010 Jul 6;122(1):88-95.

Schwartz Bryan G., Kloner Robert A.. **Cardiovascular Implications** of Erectile Dysfunction. **Patient Page**. Circulation 123: e609-611e, doi:10.1161/CIRCULATIONAHA.110.017681

Setter SM, Iltz JL, Fincham JE, Campbell RK, Baker DE. Phosphodiesterase 5 inhibitors for erectile dysfunction. Ann Pharmacother. 2005 Jul;39(7):1286-95.

Shah SJ. **Pulmonary hypertension**. JAMA. 2012 Oct 3;308(13):1366-74.

Shamloul R, Ghanem H. **Erectile dysfunction**. Lancet. 2012 Oct 4.

Sharma RK, Prasad N, Gupta A, Kapoor R. Treatment of erectile dysfunction with sildenafil citrate in **renal allograft** recipients: a randomized, double-blind, placebo-controlled, crossover trial. Am J Kidney Dis. 2006 Jul;48(1):128-33.

SharpA, CornforthC, JacksonR, etal . Maternal **sildenafil for severe growth restriction (STRIDER**): a multicentre randomised placebo-controlled double-blind trial. Lancet Child Adolesc Health 2018;2:93-102. 10.1016/S2352-4642(17)30173-6.

Sheets NC, Goldin GH, Meyer AM, et al. **Intensity-modulated radiation therapy**, **proton therapy, or conformal radiation therapy** and morbidity and disease control in localized **prostate cancer**. JAMA. 2012 Apr 18;307(15):1611-20. (more erectile dysfunction)

Sidharta PN, van Giersbergen PL, et al. Investigation of mutual pharmacokinetic interactions between **macitentan**, a novel endothelin receptor antagonist, and **sildenafil** in healthy subjects. Br J Clin Pharmacol. 2014 Jun 24.

Simon RM, Howard L, Zapata D, et al. The Association of **Exercise** with Both Erectile and Sexual Function in Black and White Men. J Sex Med. 2015 Mar 20.

Simonneau G, Rubin LJ, Galiè N, et al. PACES Study Group. Addition of sildenafil to long-term intravenous epoprostenol therapy in patients with **pulmonary arterial hypertension**: a randomized trial. Ann Intern Med. 2008 Oct 21;149(8):521-30. Summary for patients in: Ann Intern Med. 2008 Oct 21;149(8):I-38.

Skeldon SC, Detsky AS, Goldenberg SL, Law MR. **Erectile Dysfunction and Undiagnosed Diabetes, Hypertension, and Hypercholesterolemia**. Ann Fam Med. 2015 Jul;13(4):331-5.

Small D, Ferguson-Sells L, Dahdah N, et al. Pharmacokinetics and safety of **tadalafil in a paediatric population** with pulmonary arterial hypertension: a multiple ascending-dose study. Br J Clin Pharmacol. 2019 Jun 20.

Spitzer M, Basaria S, Travison TG, et al. Effect of **testosterone replacement on response to sildenafil** citrate in men with erectile dysfunction: a parallel, randomized trial. Ann Intern Med. 2012 Nov 20;157(10):681-91.

Striano P, Zara F, Minetti C, Striano S. **Epileptic seizures** can follow high doses of oral vardenafil. BMJ. 2006 Oct 14;333(7572):785.

Stringham R, Shah NR. **Pulmonary arterial hypertension**: an update on diagnosis and treatment. Am Fam Physician. 2010 Aug 15;82(4):370-7.

Thenappan T, Ormiston ML, Ryan JJ, et al. **Pulmonary arterial hypertension**: pathogenesis and clinical management. BMJ. 2018 Mar 14;360:j5492.

Thompson IM, Tangen CM, Goodman PJ, Probstfield JL, Moinpour CM, Coltman CA. Erectile dysfunction and **subsequent cardiovascular disease**. JAMA. 2005 Dec 21;294(23):2996-3002.

Trapani A Jr, Gonçalves LF, Trapani TF, et al. Perinatal and Hemodynamic Evaluation of **Sildenafil Citrate for Preeclampsia** Treatment: A Randomized Controlled Trial. Obstet Gynecol. 2016 Aug;128(2):253-9.

Trivedi D, Wellsted DM, Collard JB, et al. Simvastatin **improves the sexual health-related quality of life** in men aged 40 years and over with erectile dysfunction: additional data from the erectile dysfunction and statin trial. BMC Urol. 2014 Mar 5;14:24.

Tsertsvadze A, Yazdi F, Fink HA, et al. Oral **Sildenafil** Citrate (Viagra) for Erectile Dysfunction: A Systematic Review and Meta-analysis of Harms. Urology. 2009 Jul 8. [Epub ahead of print]

Oral PDE-5 inhibitors improved erectile functioning and had similar efficacy and safety profiles. Results on the efficacy of hormonal treatments and the value of hormone testing in men with ED were inconclusive.

Tsertsvadze A., Fink H. A., Yazdi F., et al. **Oral Phosphodiesterase-5 Inhibitors** and **Hormonal Treatments** for Erectile Dysfunction: A Systematic Review and Meta-analysis. Ann Intern Med 2009; 60520-150.
Uddin SMI, Mirbolouk M, Dardari Z, et al. **Erectile Dysfunction as an Independent Predictor of Future Cardiovascular Events**: The Multi-Ethnic Study of Atherosclerosis. Circulation. 2018 Jun 11.
Unegbu C, Noje C, Coulson JD, et al. **Pulmonary Hypertension Therapy** and a Systematic Review of Efficacy and Safety of **PDE-5 Inhibitors**. Pediatrics. 2017 Feb 24.
van Iersel L, Li Z, Chemaitilly W, et al. **Erectile Dysfunction in Male Survivors of Childhood Cancer**. JAMA Oncol. 2018 Oct 4.
Veale D, Miles S, Bramley S, et al. Am I normal? A systematic review and construction of **nomograms for flaccid and erect penis length and circumference** in up to 15 521 men. BJU Int. 2014 Dec 8.
Venhuis BJ, de Voogt P, Emke E, Causanilles A, Keizers PH. Success of **rogue online pharmacies: sewage study of sildenafil in the Netherlands**. BMJ. 2014 Jul 2;349:g4317.
Victor RG, Sweeney HL, Finkel R, et al. A phase 3 randomized placebo-controlled trial of **tadalafil for Duchenne muscular dystrophy**. Neurology. 2017 Oct 24;89(17):1811-1820.
Vlachopoulos CV, Printzios-Terentes DG, Ioakeimidis NK, et al. Prediction of **cardiovascular events** and all-cause mortality with erectile dysfunction. Circ Cardiovasc Qual Outcomes 2013.
Wilkins MR, Paul GA, Strange JW, et al. Sildenafil versus endothelin receptor antagonist for pulmonary hypertension (SERAPH) study. Am J Respir Crit Care Med 2005;171:1292-97. (InfoPOEMs: Is sildenafil (Viagra) more effective than bosentan (Tracleer) in patients with class III pulmonary hypertension? In this small study, sildenafil and bosentan had similar effects on patients with moderately severe pulmonary hypertension. (LOE = 1b))
Wirostko BM, Tressler C, Hwang LJ et al. **Ocular safety of sildenafil** citrate when administered chronically for pulmonary arterial hypertension: results from phase III, randomised, double masked, placebo controlled trial and open label extension. BMJ. 2012 Feb 21;344:e554.
Witting N, Kruuse C, Nyhuus B, et al. Effect of **sildenafil** on skeletal and cardiac muscle in **Becker muscular dystrophy**. Ann Neurol. 2014 Jul 4.
Yuan J, Zhang R, Yang Z, et al. **Comparative Effectiveness** and Safety of **Oral Phosphodiesterase Type 5 Inhibitors** for Erectile Dysfunction: A Systematic Review and Network Meta-analysis. Eur Urol. 2013 Jan 31.

Web Links:

American Academy of Family Physicians Web site: http://familydoctor.org
American Urological Association Foundation Web site: http://www.urologyhealthorg/adult/index.cfm?cat=11&topic=174
National Institutes of Health Web site: http://www.nlm.nih.gov/medlineplus/erectiledysfunction.html

Reviewers: Dr. K. Knox (SHR Rehabilitation), C Bell (UofS-SDIS), A Kuntz (SK Health), M Jin (PharmD, Hamilton), & the RxFiles Advisory Committee.

Extras:
Europe/Australia: dapoxetine *Priligy* (30-60mg po taken 1-3 hours prior to intercourse) has official indication for Premature Ejaculation. {short acting SSRI}
Sex and Chronic Pain: link to Mayo Clinic newsletter: http://www.mayoclinic.org/chronic-pain/art-20044369/?utm_source=newsletter&utm_medium=email&utm_campaign=pain-management&pg=2
Five things to know about ...: Superficial dyspareunia: http://www.cmaj.ca/content/189/24/E836.full
Treatment of Vulvovaginal Atrophy – JAMA Sept 2019: https://jamanetwork.com/journals/jama/fullarticle/2752418

Additional references: **Sexual Dysfunction**: Overview & Drug Considerations (www.RxFiles.ca)

Amiaz R, Pope HG Jr, Mahne T, et al. Testosterone gel replacement improves sexual function in depressed men taking serotonergic antidepressants: a randomized, placebo-controlled clinical trial. J Sex Marital Ther. 2011;37:243-254.
American College of Obstetricians and Gynecologists (**ACOG**). **Female sexual dysfunction**. Washington (DC): American College of Obstetricians and Gynecologists (ACOG); 2011 Apr. 12 p. (ACOG practice bulletin; no. 119).
Aro AL, Rusinaru C, Uy-Evanado A, et al. **Sexual Activity as a Trigger for Sudden Cardiac Arrest**. J Am Coll Cardiol.2017 Oct 30.
Baumgart J, Nilsson K, Evers AS, Kallak TK, Poromaa IS. Sexual dysfunction in women on adjuvant endocrine therapy after breast cancer (aromatase inhibitors). Menopause. 2012 Sep 17.
Boeri L, Capogrosso P, Ventimiglia E, et al. **Undiagnosed prediabetes is highly prevalent in primary infertile men** -results from a cross-sectional study. BJU Int. 2018 Oct 16.
Boothby CA, Dada BR, Rabi DM, et al. The **effect of cardiac rehabilitation attendance on sexual activity outcomes** in cardiovascular disease patients: a systematic review. Can J Cardiol 2018;34:1590-9.
Brown CS, Bachmann GA, Wan J, Foster DC; Gabapentin (GABA) Study Group. **Gabapentin for the Treatment of Vulvodynia**: A Randomized Controlled Trial. Obstet Gynecol. 2018 Jun;131(6):1000-1007.
Burton TD, Liday C. The comparison of combination **SSRI and PDE-5 inhibitor** therapy to SSRI monotherapy in men with **premature ejaculation**. Ann Pharmacother. 2011 Jul;45(7-8):1000-4.
Castiglione F, Albersen M, Hedlund P, et al. Current Pharmacological **Management of Premature Ejaculation**: A Systematic Review and Meta-analysis. Eur Urol. 2015 Dec 31.
Coady D, Kennedy V. Sexual Health in Women **Affected by Cancer**: Focus on Sexual Pain. Obstet Gynecol. 2016 Oct;128(4):775-91.
Committee on Adolescence. **Condom use** by adolescents. Pediatrics. 2013 Nov;132(5):973-81.
Cooper K, Martyn-St James M, Kaltenthaler E, et al. Interventions to **treat premature ejaculation**: a systematic review short report. Health Technol Assess. 2015 Mar;19(21):1-180.
Copeland KL, Brown JS, Creasman JM, Van Den Eeden SK, Subak LL, Thom DH, Ferrara A, Huang AJ. **Diabetes mellitus** and sexual function in middle-aged and older women. Obstet Gynecol. 2012 Aug;120(2 Pt 1):331-40.
Dapoxetine for premature ejaculation. Drug Ther Bull. 2014 Mar;52(3):30-3.
Deepmala, Agrawal M. Use of **propranolol for hypersexual behavior** in an adolescent with autism. Ann Pharmacother. 2014 Oct;48(10):1385-8.
Deyo RA, Smith DH, Johnson ES, et al. **Prescription Opioids for Back Pain** and Use of Medications for **Erectile Dysfunction**. Spine (Phila Pa 1976). 2013 Mar 1.
Drake T, Hanna L, Davies M. **Haematospermia**. BMJ. 2016 Nov 10;355:i5124.
Faubion SS, Rullo JE. **Sexual Dysfunction in Women**: A Practical Approach. Am Fam Physician. 2015 Aug 15;92(4):281-8.
FDA: Apr/12 The labels of the alopecia drug Propecia (**finasteride** 1 mg) and the benign prostatic hyperplasia drug Proscar (finasteride 5 mg) are being updated with an expanded list of adverse **sexual effects**, the FDA has announced. Propecia label will include libido, ejaculation, and orgasm disorders that persist after treatment ends; Proscar label will include decreased libido that persists posttreatment & both labels will note reports of male infertility or poor semen quality that improved after drug discontinuation.
FDA Dec/13 is warning that **methylphenidate products**, one type of stimulant drug used to treat attention deficit hyperactivity disorder (ADHD), may in rare instances cause prolonged and sometimes painful erections known as **priapism**.
FDA Apr/19 has determined that changes must be made to **Addyi's** labeling to clarify that there is still a concern about consuming alcohol close in time to taking Addyi but that it does not have to be avoided completely.
Field N, Mercer CH, Sonnenberg P, et al. Associations between **health and sexual lifestyles** in **Britain**: findings from the third National Survey of Sexual Attitudes and Lifestyles (Natsal-3). Lancet. 2013 Nov 30;382(9907):1830-44
Foran T. Managing Postmenopausal Symptoms in Australian Prescriber Nov 2010. Accessed at: http://www.australianprescriber.com/magazine/33/6/171/5 . Link to RxFiles Postmenopausal chts: http://www.rxfiles.ca/rxfiles/uploads/documents/members/CHT-Postmenopausal-RxandHerbal.pdf
Gass M, Larson J, Cochrane B, et al. **Sexual activity and vaginal symptoms** in the postintervention phase of the Women's Health Initiative Hormone Therapy Trials. Menopause. 2017 Nov 13.
Gellad WF, Flynn KE, Alexander GC. Evaluation of **Flibanserin**: Science and Advocacy at the FDA. JAMA. 2015 Jul 6.
Gordijn R, Teichert M, Nicolai MPJ, Elzevier HW, Guchelaar HJ. Adverse drug reactions on sexual functioning: a systematic overview. Drug Discov Today. 2019 Mar;24(3):890-897.
Graham CA, Mercer CH, et al. What factors are associated with **reporting lacking interest in sex and how do these vary by gender**? Findings from the third British national survey of sexual attitudes and lifestyles. BMJ Open. 2017 Sep 13;7(9):e016942.
Gregston M. Teen survival in a sex crazed culture. Parenting Today's Teens. Accessed online 04 Aug 2011 at: http://www.heartlightministries.org/blogs/markgregston/2011/07/29/teen-sexual-promiscuity/
Gupta BP, Murad MH, Clifton MM, et al. The Effect of Lifestyle Modification and Cardiovascular Risk Factor Reduction on Erectile Dysfunction: A Systematic Review and Meta-analysis. Arch Intern Med. 2011 Nov 14;171(20):1797-803. Epub 2011 Sep 12.
Hagberg KW, Divan HA, et al. Risk of erectile dysfunction associated with use of **5-α reductase inhibitors** for benign prostatic hyperplasia or alopecia: population based studies using the Clinical Practice Research Datalink. BMJ. 2016 Sep 22;354:i4823
Jaspers L, Feys F, Bramer WM, et al. Efficacy and safety of **flibanserin** for the treatment of hypoactive sexual desire disorder in women: a systematic review and meta-analysis [online February 29, 2016].JAMA Intern Med. doi:10.1001 /jamainternmed.2015.8565.
Jayasena CN, Alkaabi FM, Liebers CS, et al. A systematic review of randomised controlled trials investigating the efficacy and safety of **testosterone therapy for female** sexual dysfunction in postmenopausal women. Clin Endocrinol (Oxf). 2018 Nov 29.
Jin J. JAMA Patient Page. **Flibanserin** for Treating Low Sexual Desire in Women. JAMA. 2015 Sep 22-29;314(12):1312.
Johnson-Agbakwu C, Brown L, Yuan J, et al. Effects of **Flibanserin** on the Pharmacokinetics of a **Combined Ethinylestradiol/Levonorgestrel** Oral Contraceptive in Healthy Premenopausal Women: A Randomized Crossover Study. Clin Ther. 2017 Nov 30.
Kellogg ND. **Sexual behaviors in children**: evaluation and management. Am Fam Physician. 2010 Nov 15;82(10):1233-8.
Kling JM, Manson JE, Naughton MJ, et al. Association of **sleep disturbance** and sexual function in postmenopausal women. Menopause. 2017 Jan 30.
Kostis JB, Dobrzynski JM. The Effect of **Statins on Erectile Dysfunction**: A Meta-Analysis of Randomized Trials. J Sex Med. 2014 Mar 29.
Kumar K, Robertson D. **Superficial dyspareunia**. CMAJ. 2017;189:E836.
Labrie F, Archer DF, Koltun W, et al; members of the VVA Prasterone Research Group. Efficacy of **intravaginal dehydroepiandrosterone (DHEA)** on moderate to severe **dyspareunia** and vaginal dryness, symptoms of vulvovaginal atrophy, and of the genitourinary syndrome of menopause. Menopause. 2015 Dec 28.
Lee NMW, Jakes AD, Lloyd J, et al. **Dyspareunia**. BMJ. 2018 Jun 19;361:k2341.
Lehmann V, Tuinman MA, Keim MC, et al. Psychosexual development and satisfaction in **long-term survivors of childhood cancer**: Neurotoxic treatment intensity as a risk indicator. Cancer. 2017 Feb 6
Levine GN, Steinke EE, Bakaeen FG, et al. **Sexual activity and cardiovascular disease**. A scientific statement from the American Heart Association (**AHA**). Circulation 2012. http://circ.ahajournals.org/content/early/2012/01/19/CIR.0b013e3182447787.full.pdf?sid=8d962f06-2506-473d-aaaf-5761032aed2b
Lindau, Stacy Tessler, Schumm, L. Philip, Laumann, Edward O., et al. A Study of Sexuality and Health among Older Adults in the United States. N Engl J Med 2007 357: 762-774.
Lindau Stacy Tessler, Gavrilova Natalia.Sex, health, and years of sexually active life gained due to good health: evidence from two US population based cross sectional surveys of ageing. BMJ 2010;340:c810, doi: 10.1136/bmj.c810 (Published 9 March 2010)
Liu KE, Case A. No. 346-**Advanced Reproductive Age and Fertility**. J Obstet Gynaecol Can. 2017 Aug;39(8):685-695.
Lorenz T, Rullo J, Faubion S. **Antidepressant-Induced Female Sexual Dysfunction**. Mayo Clin Proc. 2016 Sep;91(9):1280-6.
Macdowall W, Gibson LJ, Tanton C, et al. Lifetime prevalence, associated factors, and circumstances of **non-volitional sex in women** and men in Britain: findings from the third National Survey of Sexual Attitudes and Lifestyles (Natsal-3).

Lancet. 2013 Nov 30;382(9907):1845-55
Martin SA, Atlantis E, Lange K, et al; Florey Adelaide Male Ageing Study (FAMAS). **Predictors of sexual dysfunction** incidence and remission in **men**. J Sex Med. 2014 May;11(5):1136-47.
McDonald E, Gartland D, Small R, Brown S. **Dyspareunia and childbirth**: a prospective cohort study. BJOG. 2015 Jan 21.
Melnik T, Althof S, Atallah ÁN, Puga MEDS, Glina S, Riera R. **Psychosocial interventions for premature ejaculation**. Cochrane Database of Systematic Reviews 2011, Issue 8. Art. No.: CD008195. DOI: 10.1002/14651858.CD008195.pub2.
Mercer CH, Tanton C, Prah P, et al. Changes in **sexual attitudes and lifestyles in Britain** through the life course and over time: findings from the National Surveys of Sexual Attitudes and Lifestyles (Natsal). Lancet. 2013 Nov 30;382(9907):1781-94.
Mitchell KJ et al. Use of social networking sites in online sex crimes against minors: An examination of national incidence and means of utilization. J Adolesc Health 2010 Apr 25
Mitchell KR, Prah P, Mercer CH, et al. **Medicated sex in Britain**: evidence from the third National Survey of Sexual Attitudes and Lifestyles. Sex Transm Infect. 2015 Jun 19.
Morrison Deborah, Aitchison Michael, Connelly Derek T, et al. **10-Minute Consultation: Sexual dysfunction in cardiovascular disease**. BMJ 2011;343:doi:10.1136/bmj.d4437 (Published 26 July 2011)
Moynihan R. Evening the score **on sex drugs: feminist** movement or marketing masquerade? BMJ. 2014 Oct 17;349:g6246.
Nackers LM, Appelhans BM, Segawa E, et al. Associations between **body mass index and sexual functioning** in midlife women: the Study of Women's Health Across the Nation. Menopause. 2015 Mar 23.
Nappi RE, Palacios S, Bruyniks N, et al; EVES Study investigators. **The burden of vulvovaginal atrophy** on women's daily living: implications on quality of life from a face-to-face real-life survey. Menopause. 2018 Nov 12.
Palm P, Zwisler AO, Svendsen JH, et al. **Sexual rehabilitation for cardiac patients** with erectile dysfunction: a randomised clinical trial. Heart. 2018 Oct 31.
Pipon JC, Williams-Jones B. Preparing for the arrival of "**pink Viagra**": strengthening Canadian direct-to-consumer information regulations. CMAJ. 2016 Mar 15;188(5):319-20.
Ramaraju GA, Teppala S, Prathigudupu K, et al. Association between **obesity and sperm quality**. Andrologia. 2017 Sep 19.
Reed SD, Guthrie KA, Joffe H, et al. **Sexual function in nondepressed women using escitalopram** for vasomotor symptoms: a randomized controlled trial. Obstet Gynecol. 2012 Mar;119(3):527-38.
Robinson K, Cutler JB, Carris NW. First Pharmacological Therapy for Hypoactive Sexual Desire Disorder in Premenopausal Women: **Flibanserin**. Ann Pharmacother. 2015 Dec 20.
Rosman L, Cahill JM, McCammon SL, Sears SF. **Sexual health concerns in patients with cardiovascular disease**. Circulation. 2014 Feb 4;129(5):e313-6.
Sarwer DB, Spitzer JC, Wadden TA, et al. Changes in Sexual Functioning and Sex Hormone Levels in Women Following **Bariatric Surgery**. JAMA Surg. 2013 Nov 4.
Seehusen DA, Baird DC, Bode DV. **Dyspareunia in Women**. Am Fam Physician. 2014;90(7):465-470.
Smith L, Yang L, Veronese N, et al. Sexual Activity is Associated with **Greater Enjoyment of Life** in Older Adults. Sex Med. 2018 Dec 12.
Steinke EE, Jaarsma T, Barnason SA, et al. on behalf of the Council on Cardiovascular and Stroke Nursing of the American Heart Association and the ESC Council on Cardiovascular Nursing and Allied Professions (CCNAP).
Sexual Counseling for Individuals With Cardiovascular Disease and Their Partners: A Consensus Document From the American Heart Association and the ESC Council on Cardiovascular Nursing and Allied Professions (CCNAP). Circulation. 2013 Jul 29.
Steinke E, Palm Johansen P, Fridlund B, et al. Determinants of sexual dysfunction and interventions for patients with **obstructive sleep apnoea**: a systematic review. Int J Clin Pract. 2015 Nov 30.
Steptoe, A, Jackson SE, Wardle J. **Sexual activity and concerns in people with coronary heart disease** from a population-based study. *Heart* 2016; 102:1095-9.
Taylor HS, Tal A, Pal L, et al. **Effects of Oral vs Transdermal Estrogen Therapy on Sexual Function in Early Postmenopause**: Ancillary Study of the Kronos Early Estrogen Prevention Study (KEEPS). JAMA Intern Med. 2017 Aug 28
Thomas HN, Chang CC, Dillon S, et al. **Sexual activity in midlife women**: importance of sex matters. JAMA Intern Med. 2014 Apr 1;174(4):631-3.
Thomas HN, Hess R, Thurston RC. **Correlates of Sexual Activity and Satisfaction in Midlife and Older Women**. Ann Fam Med. 2015 Jul;13(4):336-42.
Trivedi D, Wellsted DM, Collard JB, et al. **Simvastatin improves the sexual health**-related quality of life in men aged 40 years and over with erectile dysfunction: additional data from the erectile dysfunction and statin trial. BMC Urol. 2014 Mar 5;14:24.
Twenge JM, Sherman RA, Wells BE. **Declines in Sexual Frequency** among American Adults, 1989-2014. Arch Sex Behav. 2017 Mar 6.
Wespes E, Amar E, Eardley F, et al. Guidelines on male sexual dysfunction: erectile dysfunction and premature ejaculation. Arnhem, The Netherlands: European Association of Urology (EAU); 2009 Mar.
Wespes E, Eardley I, Giuliano F, Hatzichristou D, et al. Guidelines on **male sexual dysfunction**: erectile dysfunction and premature ejaculation. Arnhem (The Netherlands): European Association of Urology (EAU); 2013 Mar.
Wright H, Jenks RA. Sex on the brain! Associations between sexual activity and cognitive function in older age. Age Ageing. 2016 Jan 28.
Wylie K, Rees M, Hackett G, et al. Androgens, health and sexuality in women and men. Hum Fertil (Camb). 2010 Dec;13(4):277-97.
Zhang C, Cui L, Zhang L, et al. **Sexual activity and function assessment in middle-aged Chinese women** using the female sexual function index. Menopause 2017. 24;6:00

References: Sexual Dysfunction: Overview & Drug Considerations (www.RxFiles.ca)

[1] Shifren J. UpToDate: Sexual dysfunction in women. Sept 30, 2009.
[2] Frank JE, Mistretta P, Will J. Diagnosis and treatment of female sexual dysfunction. Am Fam Physician. 2008 Mar 1;77(5):635-42. Review. Erratum in: Am Fam Physician. 2009 Feb 1;79(3):180.
[3] Stimmel GL, Gutierrez MA. Sexual dysfunction and psychotropic medications. CNS Spectr. 2006 Aug;11(8 Suppl 9):24-30.
[4] Gray, J. Editor. Therapeutic choices – 5th Edition. Canadian Pharmacists Association. 2007.
[5] Labbate LA. Psychotropics and sexual dysfunction: the evidence and treatments. Adv Psychosom Med. 2008;29:107-30.
[6] Hordern A. Intimacy and sexuality after cancer: a critical review of the literature. Cancer Nurs. 2008 Mar-Apr;31(2):E9-17.
[7] Stilos K, Doyle C, Daines P. Addressing the sexual health needs of patients with gynecologic cancers. Clin J Oncol Nurs. 2008 Jun;12(3):457-63.
[8] Ayaz S, Kubilay G. Effectiveness of the PLISSIT model for solving the sexual problems of patients with stoma. J Clin Nurs. 2009 Jan;18(1):89-98.
[9] Drugs for female sexual dysfunction. Med Lett Drugs Ther. 2007 Apr 23;49(1259):33-5. PubMed PMID: 17450112.
[10] Goldstein I. Current management strategies of the postmenopausal patient with sexual health problems. J Sex Med. 2007 Mar;4 Suppl 3:235-53.
[11] RxFiles Postmenopausal Chart. http://www.rxfiles.ca/rxfiles/uploads/documents/members/CHT-Postmenopausal-RxandHerbal.pdf
[12] RxFiles Androgen Chart: http://www.rxfiles.ca/rxfiles/uploads/documents/members/cht-Androgens.pdf
[13] RxFiles Q&A: Can *Zyban*® (bupropion / *Wellbutrin*®) be given with SSRIs Accessed online 19 Mar, 2010 at http://www.rxfiles.ca/rxfiles/uploads/documents/zyban-ssri-QandA.pdf
[14] Segraves RT, Clayton A, Croft H, Wolf A, Warnock J. Bupropion sustained release for the treatment of hypoactive sexual desire disorder in premenopausal women. J Clin Psychopharmacol. 2004 Jun;24(3):339-42.
[15] RxFiles Erectile Dysfunction Chart: http://www.rxfiles.ca/rxfiles/uploads/documents/members/Cht-erectile-dysfx.pdf
[16] Sprunk E, Alteneder RR. The impact of an ostomy on sexuality. Clin J Oncol Nurs. 2000 Mar-Apr;4(2):85-8.
[17] Hatzimouratidis K, Amar E, Eardley I, Giuliano F, Hatzichristou D, Montorsi F, Vardi Y, Wespes E. Guidelines on Male Sexual Dysfunction: Erectile Dysfunction and Premature Ejaculation. Eur Urol. 2010 Feb 20.
[18] Stimmel GL, Gutierrez MA. Counseling patients about sexual issues. Pharmacotherapy. 2006 Nov;26(11):1608-15.
[19] Albright JM. Sex in America online: an exploration of sex, marital status, and sexual identity in internet sex seeking and its impacts. J Sex Res. 2008. Apr-Jun;45(2):175-86. Other (AU-ABC): http://www.abc.net.au/religion/articles/2011/06/14/3243186.htm?topic1=home&t
[20] Giuliano F, Hellstrom WJ. The pharmacological treatment of premature ejaculation. BJU Int. 2008 Sep;102(6):668-75. Epub 2008 May 15.
[21] Palmer B, Henrich W, Snyder P. Sexual dysfunction in uremic men. UpToDate. Sep 30, 2009.
[22] Higgins A. Impact of psychotropic medication on sexuality: literature review. Br J Nurs. 2007 May 10-23;16(9):545-50.
[23] Tessler S, Gavrilova N. Sex, health, and years of sexually active life gained due to good health: evidence form two population based cross sectional surveys of ageing. BMJ 2010;340c810. Accessed online 11 Mar, 2010 at http://www.bmj.com/cgi/content/full/340/mar09_2/c810 .

[24] Willhite LA, O'Connell MB. Urogenital atrophy: prevention and treatment. Pharmacotherapy. 2001 Apr;21(4):464-80. Accessed online 11 Mar 2010 at http://www.medscape.com/viewarticle/409697_4
[25] Harden CL. Sexuality in men and women with epilepsy. CNS Spectr. 2006 Aug;11(8 Suppl 9):13-8.
[26] Gil-Nagel A, López-Muñoz F, Serratosa JM, Moncada I, García-García P, Alamo C. Effect of lamotrigine on sexual function in patients with epilepsy. Seizure. 2006 Apr;15(3):142-9.
[27] RxFiles Q&A. Updated Sep 2006. Can bupropion (Zyban) be added to SSRIs? http://www.rxfiles.ca/rxfiles/uploads/documents/zyban-ssri-QandA.pdf
Sayuk GS, Gott BM, Nix BD, Lustman PJ. Improvement in sexual functioning in patients with type 2 diabetes and depression treated with **bupropion**. Diabetes Care. 2011 Feb;34(2):332-4.
[28] Segraves RT. Sexual dysfunction associated with antidepressant therapy. Urol Clin North Am. 2007 Nov;34(4):575-9, vii.
[29] Clayton A, Kornstein S, Prakash A, Mallinckrodt C, Wohlreich M. Changes in sexual functioning associated with duloxetine, escitalopram, and placebo in the treatment of patients with major depressive disorder. J Sex Med. 2007 Jul;4(4 Pt 1):917-29.
[30] RxFiles Antidepressant Chart. http://www.rxfiles.ca/rxfiles/uploads/documents/members/cht-Psyc-Antidepressant.pdf
[31] Herzog AG, Drislane FW, Schomer DL, Pennell PB, Bromfield EB, Dworetzky BA,Farina EL, Frye CA. Differential effects of antiepileptic drugs on sexual function and hormones in men with epilepsy. Neurology. 2005 Oct 11;65(7):1016-20.
[32] Berner MM, Hagen M, Kriston L. Management of sexual dysfunction due to antipsychotic drug therapy. Cochrane Database Syst Rev. 2007 Jan 24;(1):CD003546.
[33] RxFiles Antipsychotics Chart: http://www.rxfiles.ca/rxfiles/uploads/documents/members/Cht-Psyc-Neuroleptics.pdf
[34] Mortimer JE. Managing the toxicities of the aromatase inhibitors. Curr OpinObstet Gynecol. 2010 Feb;22(1):56-60.
[35] Palha AP, Esteves M. Drugs of abuse and sexual functioning. Adv Psychosom Med.2008;29:131-49.
[36] Bang-Ping J. Sexual dysfunction in men who abuse illicit drugs: a preliminary report. J Sex Med. 2009 Apr;6(4):1072-80.
[37] Gades NM, Nehra A, Jacobson DJ, McGree ME, Girman CJ, Rhodes T, Roberts RO, Lieber MM, Jacobsen SJ. Association between smoking and erectile dysfunction: a population-based study. Am J Epidemiol. 2005 Feb 15;161(4):346-51.
[38] Natural Medicines Comprehensive Database 2010. (www.naturaldatabase.com)

RxFiles Urinary Incontinence On-Line Extras:

Other Medications:

1) ACh, Other: **propantheline** - less effective & ↑ AE than flavoxate & oxybutynin. [11] NICE states not to use[1]; Adult: 7.5mg TID, 7.5-30mg 3-5x/day, 60mg QID; Geriatric: 7.5mg TID; Peds: 7.5-15mg q4-6h.
2) Adrenoreceptor agonists (**phenylpropanolamine** predominantly studied but use extended to **ephedrine**, **pseudoephedrine**): studied for SUI. But cardiac arrhythmias & HTN outweigh benefits.[31]
3) **Belladonna & opium suppositories:** used to relieve **pain of uretal spasms** & pain associated with bladder tenesmus that can occur post-op.[32] Some report use in nocturnal diuresis.[11]
Dicyclomine - insufficient data to recommend over other agents, dose 20-40mg QID.[11]
4) **Flavoxate**: Not used for OAB currently[1] but may be used in discomfort associated with BPH. Efficacy might be comparable to propantheline according to older, short-term studies.[11]
Dose: Adult: 100-200mg TID-QID. May reduce dose with sx improvement. One trial found 1200mg to be superior to 600mg/day. May be effective in children from 6-12 yrs experiencing nocturnal enuresis (33% vs 17% response in placebo).[11] Pediatrics > 12 yr: 100-200mg TID-QID. May reduce dose with sx improvement.[11]
5) **Phenazopyridine:**[11] used strictly as a **urinary analgesic**. Limited availability, some pharmacies can compound product ▼ . The necessity of this medication would suggest pathology different from UI. Dose: Adult: 200mg TID after meals. If renal CrCl or GFR > 50mL/min 200mg q8-16h. Avoid if GFR < 50mL/min. Geriatrics: ↑risk of accumulation & toxicity. AE: discolor urine
6) **Propiverine:**[53] tertiary amine with ACh & calcium channel antagonist activity; has active metabolites; dose: 15mg IR BID or 30mg ER daily; available United Kingdom.[2006]

Oxybutynin (OXY) vs Tolterodine (TOLT) in OAB

- OBJECT: OXY ER 10mg daily vs TOLT IR 2mg BID; 12 week; ♂ & ♀; Oxy ER slightly more effective (e.g. total incontinence episodes/wk: NNT=45); no difference in overall AEs (dry mouth, CNS effects).[52]
- OPERA: OXY ER 10mg vs TOLT ER 4mg daily; 12 week; ♀ only with severe symptoms; OXY ER somewhat more effective (e.g. 23 vs 16.8% no UI; NNT=16); but also more dry mouth (Any 29.7% vs 22.3%; NNH=13; mod-severe 7.4% vs 5.0%, NS).[50]
- ACET: OXY ER 5 or 10mg vs TOLT ER 2 or 4mg daily; 8 week; ♂ & ♀; TOLT 4mg more effective than OXY 10 70 vs 60% improvement; but lower doses efficacy still ~60% & less dry mouth but similar for TOLT 4mg vs OXY 5mg ; open label trial & subjective assessments subject to bias.[51]

Other Urinary Incontinence Patient Resources:

- General information: www.simonfoundation.org, www.womensbladderhealth.com; www.continence-foundation.org.uk; www.mypelvichealth.org
- Bladder Retraining: http://www.fmpe.org/en/documents/doc_aids/UI-Patient-Handout-4.pdf ; or http://www.fmpe.org/en/documents/handouts/handout_ui_retraining.pdf
- Pelvic Muscle Exercises (Kegel Exercises): http://www.fmpe.org/en/documents/doc_aids/UI-Patient-Handout-3.pdf
- Voiding Diary: http://www.fmpe.org/en/documents/doc_aids/UI-Patient-Handout-2.pdf
- Patient Information - Urinary Incontinence: http://www.fmpe.org/en/documents/doc_aids/UI-Patient-Handout-1.pdf
- CFPC: www.cfpc.ca/English/cfpc/programs/patient%20education/urinary%20incontinence
- American (ACOG): www.acog.com/publications/patient_education/bp081.cfm

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References – RxFiles Urinary Incontinence Treatment Chart - www.RxFiles.ca

1. Urinary Incontinence: The management of urinary incontinence in women. www.nice.org.uk/nicemedia/pdf/CG40fullguideline.pdf National Institute for Health and Clinical Excellence (**NICE**) clinical guideline 40; October 2006:1-14.
2. Hashim H, Abrams P. How should patients with an overactive bladder manipulate their fluid intake? BJU Int. 2008 Feb 18; [Epub ahead of print] Fluid manipulation is a cheap, noninvasive and easy way to help control the symptoms of OAB. Patients have difficulty in either decreasing or increasing their fluid input by 50%. Patients can now be told to expect a significant improvement in urgency, frequency and nocturia episodes if they reduce their fluid input by 25%.
3. Glazener C, Boachie C, Buckley B, et al. Urinary incontinence in men after formal one-to-one pelvic-fl oor muscle training following radical prostatectomy or transurethral resection of the prostate (MAPS): two parallel randomised controlled trials. Lancet 2011; published online July 12. DOI:10.1016/S0140-6736(11)60751-4.
4. Shamliyan T, Wyman JF, Ramakrishnan R, Sainfort F, Kane RL. Systematic Review: **Benefits and Harms of Pharmacologic Treatment for Urinary Incontinence** in Women. Ann Intern Med. 2012 Apr 9.
5. Gormley EA, Lightner DJ, Burgio KL, Chai TC, et al. Diagnosis and treatment of **overactive bladder** (non-neurogenic) in adults: **AUA/SUFU guideline**. Linthicum (MD): American Urological Association (AUA); **2012** May. (J Urol. 2012 Oct 19. pii: S0022-5347(12)04959-2.)
Gormley EA, Lightner DJ, Burgio KL, et al. Diagnosis and treatment of overactive bladder (non-neurogenic) in adults: **AUA/SUFU guideline**. Linthicum (MD): American Urological Association Education and Research, Inc.; 2014.
6. Ouslander JG. Management of Overactive Bladder. NEJM 2004;350:786-99.
7. Nygaard I, Barber MD, Burgio KL, et al. Pelvic Floor Disorders Network. Prevalence of symptomatic pelvic floor disorders in US women. JAMA. 2008 Sep 17;300(11):1311-6.
8. Nygaard Ingrid. Idiopathic Urgency Urinary Incontinence. N Engl J Med 2010; 363:1156-1162.
9. Kilicarlslan H, Ayan S, et al. Treatment of detrusor sphincter dyssynergia with baclofen and doxazosin. Int Urol Nephrol 2006;38:537-541.
10. Hay-Smith EJC, Dumoulin C. Pelvic floor muscle training versus no treatment, or inactive control treatments, for urinary incontinence in women. Cochrane Database of Systematic Reviews 2006, Issue 1.
Dumoulin C, Hay-Smith J. Pelvic floor muscle training versus no treatment, or inactive control treatments, for urinary incontinence in women. Cochrane Database of Systematic Reviews 2010, Issue 1. Art. No.: CD005654.
Dumoulin C, Cacciari LP, Hay-Smith EJC. Pelvic floor muscle training versus no treatment, or inactive control treatments, for urinary incontinence in women. Cochrane Database Syst Rev. 2018 Oct 4;10 No.: CD005654
11. Corcos J, Gajewski J, Heritz D, Patrick A, Reid I, Schick E, Stothers L; Canadian Urological Association. **Canadian Urological Association guidelines** on urinary incontinence. Can J Urol. 2006 Jun;13(3):3127-38.
Bettez M, Tu LM, Carlson K, et al. 2012 update: guidelines for **adult urinary incontinence**. Collaborative consensus document for the **Canadian Urological Association**. Can Urol Assoc J **2012**;6:354-63. www.ncbi.nlm.nih.gov/pmc/articles/PMC3478335/pdf/cuaj-5-354.pdf
Corcos J, Przydacz M, Campeau L, et al. **CUA guideline on adult overactive bladder**. Can Urol Assoc J **2017**;11(5):E142-73. www.cua.org/themes/web/assets/files/4586.pdf (accessed May 15, 2017)
Nickel JC, Aaron L, Barkin J, et al. **Canadian Urological Association (CUA)** guideline on male lower urinary tract symptoms/benign prostatic hyperplasia (**MLUTS/BPH**): **2018 update**. Can Urol Assoc J 2018;12:303-12
12. Thüroff, J et al. Guidelines on urinary incontinence. European Association of Urology 2006: 1-12. www.uroweb.org/fileadmin/user_upload/Guidelines/16%20Urinary%20Incontinence.pdf
13. Ancelin, ML et al. Non-degenerative mild cognitive impairment in elderly people and use of anticholinergics drugs: Longitudinal cohort study. BMJ 2006;332:455-459. www.bmj.com/cgi/content/full/332/7539/455
14. Siegler, EL et al. Treatment of urinary incontinence with anticholinergics in patients taking cholinesterase inhibitors for dementia. Clin Pharmacol Ther 2004;75:484-8.
15. Edwards, KR et al. Risk of delirium with concomitant use of tolterodine and acetylcholinesterase inhibitors. Editorial Letter. JAGS 2002;50:1165-1166.
16. Donnellan, CA et al. Oxybutynin and cognitive dysfunction. BMJ 1997;315:1363-1364.
17. Madhuvrata P,Cody JD, EllisG,HerbisonGP,Hay-Smith EJC. Which anticholinergic drug for overactive bladder symptoms in adults. *Cochrane Database of Systematic Reviews* 2012, Issue 1. Art. No.: CD005429. DOI: 10.1002/14651858.CD005429.pub2.

18. Kay G, Crook T, Rekeda L, Lima R, et al. Darifenacin has theoretical cognitive advantages. Some preliminary placebo controlled trials have results supporting this claim. At first glance this trial by Key et al. appears to support these advantages based on the *name-face association test*. However when trial design issues (e.g. high oxybutinin dose for elderly, early drop outs), discussion bias, adverse event rates and overall limitations are considered, this study does not prove a definite advantage for darifenacin over oxybutynin. Further study is needed (especially with a more rational dose comparator) in elderly with urinary incontinence and at high risk for cognitive impairment. Darifenacin may offer a relative advantage or disadvantage to other anticholinergics depending on dose used and individual patient response. Currently, darifenacin offers a cost advantage over some comparators. {Cost/month[SK]: Enablex 7.5-15mg/day= $59; Ditropan XL 5-10mg/day= $84,15-20mg/day=$159; Uromax10-15mg/day=$50-53; Detrol LA 2-4mg/day= $72.} See http://www.rxfiles.ca/acrobat/UI-Darifenacin-Kay-Trial-Q&A.pdf }
19. CPS 2013 online edition
20. Briggs GG et al. Drugs in Pregnancy and lactation, 9th ed, 2011.
21. CEDAC final recommendation and reasons for recommendation: Trospium Chloride. (Trosec -Oryx Pharm) CADTH 24/8/2006. http://cadth.ca/media/cdr/complete/cdr_complete_Trosec_August24-06.pdf
22. CEDAC final recommendation Darifenacin. (Enablex –Novartis) CADTH 16/04/2009. http://cadth.ca/media/cdr/complete/cdr_complete_Enablex_Oct-19-06.pdf http://www.cadth.ca/media/cdr/complete/cdr_complete_Enablex%20Resubmission-1_April-17-2009.pdf
23. CEDAC final recommendation and reasons for recommendation: Solifenacin. (Vesicare –Astellas) CADTH 24/1/2006. http://cadth.ca/media/cdr/complete/cdr_complete_Vesicare_Jan-24-2007.pdf
CADTH Resubmission June/09 http://www.cadth.ca/media/cdr/complete/cdr_complete_Vesicare-Resubmisson_1_June-17-2009.pdf

CADTH= Canadian Agency for Drugs and Technology in Health (www.CADTH.ca)
CDR=Common Drug Review (http://cadth.ca//index.php/en/cdr)
CEDAC= Canadian Expert Drug Advisory Committee

24. Micromedex 2012. Thompson Healthcare.
25. Hay-Smith J et al. Which anticholinergics drug for overactive bladder symptoms in adults. Cochrane Database of Systematic Reviews 2005, Issue 3.
26. Nabi G, Cody JD, Ellis G, Herbison P, Hay-Smith J. Anticholinergic drugs versus placebo for overactive bladder syndrome in adults. **Cochrane** Database Syst Rev. 2006 Oct 18;(4):CD003781. {Also: Herbison P et al. Effectiveness of anticholinergics drugs compared with placebo in the treatment of overactive bladder: systematic review. BMJ 2003;326:841-844.}
27. Chapple CR et al. A comparison of the efficacy and tolerability of solifenacin succinate and extended release tolterodine at treating overactive bladder syndrome: Results of the **STAR** trial. European Urology 2005;48:464-470.
28. Lipton RB et al. Assessment of cognitive function of the elderly population: Effects of darifenacin. J of Urology 2005;173:493-498.
29. Abrams P et al. Muscarinic receptor antagonists for overactive bladder. BJU int 2007;100:987-1006.
30. Hendrix SL et al. Effects of estrogen with and without progestin on urinary incontinence. JAMA 2005;293:935-948.
31. Moehrer B et al. Oestrogens for urinary incontinence in women. **Cochrane** database of systematic reviews 2003, Issue 2.
32. Cody JD, Richardson K, Moehrer B, et al. Oestrogen therapy for urinary incontinence in post-menopausal women. Cochrane Database Syst Rev. 2009 Oct 7;(4):CD001405. Local oestrogen treatment for incontinence may improve or cure it, but there was little evidence from the trials on the period after oestrogen treatment
33. had finished and none about long-term effects. However, systemic hormone replacement therapy, using conjugated equine oestrogen, may make incontinence worse. There were too few data to reliably address other aspects of oestrogen therapy, such as oestrogen type and dose, and no direct evidence on route of
34. administration. The risk of endometrial and breast cancer after long-term use suggests that oestrogen treatment should be for limited periods, especially in those women with an intact uterus.
35. Cody JD, Jacobs ML, Richardson K, et al. **Oestrogen therapy for urinary incontinence** in post-menopausal women. Cochrane Database Syst Rev. 2012 Oct 17;10:CD001405. doi: 10.1002/14651858.CD001405.pub3. Urinary incontinence may be improved with the use of local oestrogen treatment. However, there was little
36. evidence from the trials on the period after oestrogen treatment had finished and no information about the long-term effects of this therapy was given. Conversely, systemic hormone replacement therapy using conjugated equine oestrogen may worsen incontinence.
37. Bélisle S et al. **Canadian Consensus** conference on **menopause** 2006 update. JOGC 2006;171:S7-S10. **SOGC 2009 Menopause and Osteoporosis** Update 2009-SOGC Jan 2009. http://www.sogc.org/media/pdf/advisories/Meno-Osteo-Update_JOGC-Jan_09.pdf
38. Scottish Intercollegiate Guidelines Network. Management of urinary incontinence in primary care. 2004;December. www.sign.ac.uk/pdf/sign79.pdf
39. Haueusler G et al. Drug therapy of urinary urge incontinence: A systematic review. Obstet Gynecol 2002;100:1003-16.
40. Zinner NR et al. Pharmacotherapy for stress urinary incontinence: Present and future options. Drugs 2004;64:1503-1519.
41. Hashim H et al. Pharmacological management of women with mixed urinary incontinence. Drugs 2006;66:591-606.
42. Alhasso A et al. Adrenergic drugs for urinary incontinence in adults. **Cochrane** Database of Systematic Reviews 2005, Issue 3.
43. University of Maryland medical center website. Accessed 14/11/07. www.umm.edu/altmed/drugs/belladonna-opium-012800.htm#Use.
44. Johnson TM 2nd, Burgio KL, Redden DT, Wright KC, Goode PS. Effects of behavioral and drug therapy on nocturia in older incontinent women. J Am Geriatr Soc. 2005 May;53(5):846-50.
45. (**Physiotherapy**- especially if pt can't isolate or exercising wrong muscles, or if stops breathing during Kegels; Saskatoon Health Region: **Pelvic Floor Rehab Program** 655-8208, typically sees females q1-2weeks x 8 times, waiting list ~6months; **Private Clinics** in Saskatoon also treat, quicker access, 3rd party coverage?: Bourassa & Daniels Kimber) **Nurse Continence Advisor**: Eliza Meggs RN,NCA (Nightingale Nursing Group) Phone: 306-652-3314
Hagen S, Stark D, Glazener C, et al. Individualised **pelvic floor muscle training** in women with pelvic organ prolapse (**POPPY**): a multicentre randomised controlled trial. Lancet. 2013 Nov 27.
Hagen S, Glazener C, McClurg D, et al. **Pelvic floor muscle training** for secondary prevention of pelvic organ prolapse (**PREVPROL**): a multicentre randomised controlled trial. Lancet. 2016 Dec 20.
46. Braekken IH, Majida M, Engh ME, et al. Can pelvic floor muscle training reverse pelvic organ prolapse and reduce prolapse symptoms? An assessor-blinded, randomized, controlled trial. Am J Obstet Gynecol. 2010 Aug;203(2):170.e1-7. Epub 2010 May 1.
47. Glazener C, Boachie C, Buckley B, et al. Urinary incontinence in men after formal one-to-one pelvic-fl oor muscle training following radical prostatectomy or transurethral resection of the prostate (MAPS): two parallel randomised controlled trials. Lancet 2011; published online July 12. DOI:10.1016/S0140-6736(11)60751-4.
48. Boyle R, Hay-Smith EJ, Cody JD, et al. Pelvic floor muscle training for prevention and treatment of urinary and faecal incontinence in antenatal and postnatal women. Cochrane Database Syst Rev. 2012 Oct 17;10:CD007471. There is some evidence that for women having their first baby, PFMT can prevent urinary incontinence up to six months after delivery. There is support for the widespread recommendation that PFMT is an appropriate treatment for women with persistent postpartum urinary incontinence.
49. Schurch B, de Sèze M, Denys P, et al.; Botox Detrusor Hyperreflexia Study Team. Botulinum toxin type a is a safe and effective treatment for neurogenic urinary incontinence: results of a single treatment, randomized, placebo controlled 6-month study. J Urol. 2005 Jul;174(1):196-200.
50. Karsenty G, Denys P, Amarenco G, et al. Botulinum Toxin A (Botox((R))) Intradetrusor Injections in Adults with Neurogenic Detrusor Overactivity/Neurogenic Overactive Bladder: A Systematic Literature Review. Eur Urol. 2007 Oct 16; [Epub ahead of print]
51. Schurch B. **Botulinum** toxin for the management of bladder dysfunction.Drugs. 2006;66(10):1301-18.
Chapple C, Sievert KD, MacDiarmid S, et al. OnabotulinumtoxinA 100 U significantly improves all idiopathic overactive bladder symptoms and quality of life in patients with overactive bladder and urinary incontinence: a randomised, double-blind, placebo-controlled trial. Eur Urol. 2013 Aug;64(2):249-56.
52. Naumann M, So Y, Argoff CE, Childers MK, Dykstra DD, Gronseth GS, Jabbari B, Kaufmann HC, Schurch B, Silberstein SD, Simpson DM; Therapeutics and Technology Assessment Subcommittee of the American Academy of Neurology. Assessment: Botulinum neurotoxin in the treatment of autonomic disorders and pain (an evidence-based review): report of the Therapeutics and Technology Assessment Subcommittee of the American Academy of Neurology. Neurology. 2008 May 6;70(19):1707-14. Botulinum neurotoxin (BoNT) should be offered as a treatment option for the treatment of axillary hyperhidrosis and detrusor overactivity (Level A), should be considered for palmar hyperhidrosis, drooling, and detrusor sphincter dyssynergia after spinal cord injury (Level B), and may be considered for gustatory sweating and low back pain (Level C). BoNT is probably ineffective in episodic migraine and chronic tension-type headache (Level B). There is presently no consistent or strong evidence to permit drawing conclusions on the efficacy of BoNT in chronic daily headache (mainly transformed migraine) (Level U). While clinicians' practice may suggest stronger recommendations in some of these indications, evidence-based conclusions are limited by the availability of data.
53. Dmochowski R, Chapple C, Nitti VW, et al. Efficacy and Safety of **OnabotulinumtoxinA** for Idiopathic Overactive Bladder: A Double-Blind, Placebo Controlled, Randomized, Dose Ranging Trial. J Urol. 2010 Dec;184(6):2416-22.
54. Duthie JB, Vincent M, Herbison GP, et al. **Botulinum toxin injections** for adults with overactive bladder syndrome. Cochrane Database Syst Rev. 2011 Dec 7;12:CD005493. Intravesical botulinum toxin appears to be an effective therapy for refractory OAB symptoms, but as yet little controlled trial data exist on benefits and safety compared with other interventions, or with placebo.
55. Visco AG, Brubaker L, Richter HE, et al; the Pelvic Floor Disorders Network. Anticholinergic Therapy vs. **OnabotulinumtoxinA** for **Urgency Urinary Incontinence**. N Engl J Med. 2012 Oct 4.
56. Ayan S, Topsakal K, Gokce G, Gultekin EY. Efficacy of combined anticholinergic treatment and behavioral modification as a first line treatment for nonneurogenic and nonanatomical voiding dysfunction in children: a randomized controlled trial. J Urol. 2007 Jun;177(6):2325-8; discussion 2328-9.
57. Kilic N, Balkan E, Akgoz S, Sen N, Dogruyol H. Comparison of the effectiveness and side-effects of tolterodine and oxybutynin in children with detrusor instability. Int J Urol. 2006 Feb;13(2):105-8.
58. Nijman RJ, Borgstein NG, et al. Tolterodine treatment for children with symptoms of urinary urge incontinence suggestive of detrusor overactivity: results from 2 randomized, placebo controlled trials. J Urol. 2005 Apr;173(4):1334-9.
59. Siami P, Seidman LS, Lama D. A multicenter, prospective, open-label study of tolterodine extended-release 4 mg for overactive bladder: the speed of onset of therapeutic assessment trial (STAT). Clin Ther. 2002 Apr;24(4):616-28.
60. Sand PK, Goldberg RP, Dmochowski RR, McIlwain M, Dahl NV. The impact of the overactive bladder syndrome on sexual function: a preliminary report from the Multicenter Assessment of Transdermal Therapy in Overactive Bladder with Oxybutynin trial. Am J Obstet Gynecol. 2006 Dec;195(6):1730-5.
61. Feinberg M. The problems of anticholinergic adverse effects in older patients.Drugs Aging. 1993 Jul-Aug;3(4):335-48.

62. Tune LE. Anticholinergic effects of medication in elderly patients. J Clin Psychiatry. 2001;62 Suppl 21:11-4.
63. Rudolph JL, Salow MJ, Angelini MC, McGlinchey RE. The anticholinergic risk scale and anticholinergic adverse effects in older persons. Arch Intern Med. 2008 Mar 10;168(5):508-13.
64. Sink KM, Thomas J 3rd, Xu H, Craig B, et al. Dual Use of Bladder Anticholinergics and Cholinesterase Inhibitors: Long-Term Functional and Cognitive Outcomes. J Am Geriatr Soc. 2008 Apr 1. [Epub ahead of print] In higher-functioning NH residents, dual use of ChIs and bladder anticholinergics may result in greater rates
65. of functional decline than use of ChIs alone. The MDS-COGS may not be sensitive enough to detect differences in cognition due to dual use.
66. Lackner TE, Wyman JF, McCarthy TC, Monigold M, Davey C. Randomized, placebo-controlled trial of the cognitive effect, safety, and tolerability of oral extended-release oxybutynin 5mg/day in cognitively impaired nursing home residents with urge urinary incontinence. J Am Geriatr Soc. 2008 May;56(5):862-70. Epub 2008 Apr 9. n=50. 4 weeks. Short-term treatment using oral extended-release oxybutynin 5 mg once daily was safe and well tolerated, with no delirium, in older female nursing home participants with mild to severe dementia. Future research should investigate different dosages and long-term treatment.
67. Han L, Agostini JV, Allore HG. Cumulative anticholinergic exposure is associated with poor memory and executive function in older men. J Am Geriatr Soc. 2008 Dec;56(12):2203-10. Cumulative anticholinergic exposure across multiple medications over 1 year may negatively affect verbal memory and executive function in older men. Prescription of drugs with anticholinergic effects in older persons deserves continued attention to avoid deleterious adverse effects.
68. Carrière I, Fourrier-Reglat A, Dartigues JF, et al. Drugs with anticholinergic properties, cognitive decline, and dementia in an elderly general population: the 3-city study. Arch Intern Med. 2009 Jul 27;169(14):1317-24.
69. Campbell NL, Boustani MA, Lane KA, et al. Use of anticholinergics and the risk of cognitive impairment in an African American population. Neurology. 2010 Jul 13;75(2):152-9.
70. Teramura-Grönblad Mariko, Muurinen Seija, Soini Helena, et al. Use of Anticholinergic Drugs and Cholinesterase Inhibitors and Their Association with Psychological Well-Being Among Frail Older Adults in Residential Care Facilities. Ann Pharmacother ;45:596-602.
71. Stephenson Anne; Seitz Dallas; Bell Chaim M.; et al. Inhaled Anticholinergic Drug Therapy and the Risk of Acute Urinary Retention in Chronic Obstructive Pulmonary Disease: A Population-Based Study. Arch Intern Med. 2011;171(10):914-920.
72. Anticholinergic Cognitive Burden (ACB) scale http://www.indydiscoverynetwork.org/AnticholinergicCognitiveBurdenScale.html
73. Fox C, Richardson K, Maidment ID, et al. **Anticholinergic Medication Use** and Cognitive Impairment in the Older Population: The Medical Research Council Cognitive Function and Ageing Study. J Am Geriatr Soc. 2011 Jun 24
74. Torjesen I. Anticholinergic effects of common drugs are associated with increased **mortality** in over 65s. BMJ. 2011 Jun 28;342:d4037.
75. Abrams P, Andersson KE. **Muscarinic** receptor antagonists for overactive bladder. BJU Int. **2007** Nov;100(5):987-1006.
76. Waine E, Hashim H, Abrams P. **Management of the overactive bladder: a review** of pharmacological therapies and methods used by the urological specialist. Can J Urol. **2007** Apr;14(2):3478-88.
77. Irwin DE, Milsom I, Hunskaar S, Reilly K, Kopp Z, Herschorn S, Coyne K, Kelleher C, Hampel C, Artibani W, Abrams P. Population-based survey of urinary incontinence, overactive bladder, and other lower urinary tract symptoms in five countries (Canada, Germany, Italy, Sweden, and the United Kingdom): results of the EPIC study. Eur Urol. 2006 Dec;50(6):1306-14; discussion 1314-5. Epub 2006 Oct 2.
78. Dmochowski RR, Sanders SW, Appell RA, Nitti VW, Davila GW. Bladder-health diaries: an assessment of 3-day vs 7-day entries. BJU Int. 2005 Nov;96(7):1049-54.
79. Anderson RU, Mobley D, Blank B, Saltzstein D, Susset J, Brown JS. Once daily controlled versus immediate release oxybutynin chloride for urge urinary incontinence. **OROS** Oxybutynin Study Group. J Urol. 1999 Jun;161(6):1809-12.
80. Diokno A, Sand P, Labasky R, et al. Long-term safety of extended-release oxybutynin chloride in a community-dwelling population of participants with overactive bladder: a one-year study. Int Urol Nephrol. 2002;34(1):43-9.
81. Diokno AC, Appell RA, Sand PK, Dmochowski RR, et al.; **OPERA** Study Group. Prospective, randomized, double-blind study of the efficacy and tolerability of the extended-release formulations of oxybutynin and tolterodine for overactive bladder: results of the OPERA trial. Mayo Clin Proc. 2003 Jun;78(6):687-95.
82. Sussman D, Garely A. Treatment of overactive bladder with once-daily extended-release tolterodine or oxybutynin: the antimuscarinic clinical effectiveness trial (**ACET**). Curr Med Res Opin. 2002;18(4):177-84.
83. Appell RA, Sand P, et al. Overactive Bladder: Judging Effective Control and Treatment Study Group. Prospective randomized controlled trial of extended-release oxybutynin chloride and tolterodine tartrate in the treatment of overactive bladder: results of the **OBJECT** Study.Mayo Clin Proc. 2001 Apr;76(4):358-63.
84. Jünemann KP, Halaska M, Rittstein T, et al. Propiverine versus tolterodine: efficacy and tolerability in patients with overactive bladder. Eur Urol. 2005 Sep;48(3):478-82.
85. Albo ME, Richter HE, Brubaker L, et al; Urinary Incontinence Treatment Network. Burch colposuspension versus fascial sling to reduce urinary stress incontinence. N Engl J Med. 2007 May 24;356(21):2143-55. Epub 2007 May 21.
86. Schulz JA, Chan MC, Farrell SA, Sub-Committee on Urogynaecology (**SGOC**) . Midurethral minimally invasive sling procedures for stress urinary incontinence. J Obstet Gynaecol Can 2008 Aug;30(8):728-33. http://www.sogc.org/guidelines/documents/gui213TU0808.pdf
87. **AUA** –American Urological Association, **Surgical Management of Female Stress Urinary Incontinence** Update 2009 http://www.auanet.org/content/guidelines-and-quality-care/clinical-guidelines/main-reports/stress2009/chapter1.pdf
88. De Vocht TF, Chrzan R, Dik P, et al. Long-Term Results of Bulking Agent Injection for Persistent Incontinence in Cases of Neurogenic Bladder Dysfunction. J Urol. 2009 Dec 16.
89. Richter, Holly E., Albo, Michael E., Zyczynski, Halina M. et al, the Urinary Incontinence Treatment Network, **Retropubic versus Transobturator Midurethral Slings for Stress Incontinence** N Engl J Med 2010 0: NEJMoa0912658
90. **SOGC**: **Transvaginal Mesh procedures for Pelvic Organ Prolapse** Feb 2011. http://www.sogc.org/guidelines/documents/gui254TU1102E.pdf
91. Lovatsis D, Easton W, Wilkie D, Urogynaecology Committee. **SOGC** Guidelines for the evaluation and **treatment of recurrent urinary incontinence following pelvic floor surgery**. J Obstet Gynaecol Can 2010 Sep;32(9):894-99. http://www.sogc.org/guidelines/documents/gui248CPG1009E_000.pdf
92. Altman Daniel, Väyrynen Tapio, Engh Marie Ellström, et al. for the Nordic Transvaginal Mesh Group. Anterior Colporrhaphy versus Transvaginal Mesh for Pelvic-Organ Prolapse. N Engl J Med 2011; 364:1826-1836.
93. Walter JE, Lovatsis D, Easton W, Epp A, Farrell SA, Girouard L, Gupta CK, Harvey MA, Larochelle A, et al. **SOGC**: Transvaginal mesh procedures for pelvic organ prolapse. J Obstet Gynaecol Can 2011 Feb;33(2):168-74.
Brubaker L, Cundiff GW, Fine P, et al. **Abdominal sacrocolpopexy with Burch colposuspension** to reduce urinary stress incontinence. (CARE) N Engl J Med 2006;354:1557-66.
Nygaard I, Brubaker L, Zyczynski HM, et al. **Long-term outcomes (up to 7 years) following abdominal sacrocolpopexy for pelvic organ prolapse**. (CARE) JAMA. 2013;309(19):2016-2024.
Labrie J, Berghmans BL, Fischer K, et al. **Surgery versus physiotherapy** for stress urinary incontinence. N Engl J Med. 2013 Sep 19;369(12):1124-33.
94. Chapple C, Khullar V, Gabriel Z, et al. The effects of antimuscarinic treatments in overactive bladder: a **systematic review** & meta-analysis. Eur Urol. 2005 Jul;48(1):5-26. Epub 2005 Mar 22. Review. Erratum: Eur Urol. 2005 Nov;48(5):875.
95. Haab F, Stewart L, Dwyer P. Darifenacin, an M3 selective receptor antagonist, is an effective and well-tolerated once-daily treatment for overactive bladder. Eur Urol. 2004 Apr;45(4):420-9; discussion 429.
96. Cardozo L, Chapple CR, Toozs-Hobson P, et al. Efficacy of trospium chloride in patients with detrusor instability: a placebo-controlled, randomized, double-blind, multicentre clinical trial. BJU Int. 2000 Apr;85(6):659-64.
97. Zinner N, Gittelman M, Harris R, et al; Trospium Study Group. Trospium chloride improves overactive bladder symptoms: a multicenter phase III trial. J Urol. 2004 Jun;171(6 Pt 1):2311-5, quiz 2435.
98. Staskin D, et al.; Trospium Study Group. Once daily 60mg trospium chloride is effective and well tolerated for the treatment of overactive bladder: results from a multicenter phase III trial. J Urol. 2007 Sep;178(3 Pt 1):978-83.
99. Cardozo L, Lisec M, Millard R, et al. Randomized, double-blind placebo controlled trial of the once daily antimuscarinic agent solifenacin succinate in patients with overactive bladder. J Urol. 2004 Nov;172(5 Pt 1):1919-24.
100. Layton D, Pearce GL, Shakir SA. Safety profile of tolterodine as used in general practice in England: results of prescription-event monitoring. Drug Saf. 2001;24(9):703-13.
101. a) Hussain RM, Hartigan-Go K, Thomas SH, Ford GA. Effect of oxybutynin on the QTc interval in elderly patients with urinary incontinence. Br J Clin Pharmacol. 1996 Jan;41(1):73-5. b) Layton D, Pearce GL, Shakir SA. Safety profile of tolterodine as used in general practice in England: results of prescription-event monitoring. Drug Saf. 2001;24(9):703-13. {See also www.torsades.org }
102. Kaplan SA, Roehrborn CG, Rovner ES, et al. Tolterodine and tamsulosin for treatment of men with lower urinary tract symptoms and overactive bladder: a randomized controlled trial. JAMA. 2006 Nov 15;296(19):2319-28. Erratum in: JAMA. 2007 Mar 21:297(11):1195. JAMA. 2007 Oct 24;298(16):1864.
103. Tsao JW, Heilman KM. Transient memory impairment and hallucinations associated with tolterodine use. N Engl J Med. 2003 Dec 4;349(23):2274-5.
104. Womack KB, Heilman KM. Tolterodine and memory: dry but forgetful. Arch Neurol. 2003 May;60(5):771-3.
105. **3rd International Consultation on Incontinence**. Evaluation and Treatment of Urinary Incontinence, Pelvic Organ Prolapse and Faecal Incontinence. 2005 http://www.icsoffice.org/documents/ici_pdfs_3/v2.pdf/summary.pdf
106. Mitterberger M, Marksteiner R, et al. Autologous myoblasts and fibroblasts for female stress incontinence: a 1-year follow-up in 123 patients. BJU Int. 2007 Nov;100(5):1081-5. Epub 2007 Aug 30.
107. Robinson D, Cardozo L, Terpstra G, Bolodeoku J; Tamsulosin Study Group. A randomized double-blind placebo-controlled multicentre study to explore the efficacy and safety of tamsulosin and **tolterodine** in women with overactive bladder syndrome. BJU Int. 2007 Oct;100(4):840-5.
108. Pharmacist's Letter. Alpha-Blockers for Urinary Problems in Women. Oct 2010.
109. FDA Dec/07 Certain patients taking desmopressin are at risk for developing severe hyponatremia that can result in seizures and death. Children treated with desmopressin intranasal formulations for primary nocturnal enuresis (PNE) are particularly susceptible to severe hyponatremia and seizures. As such, **desmopressin intranasal formulations** are **no longer indicated** for the **treatment** of **primary nocturnal enuresis** and should not be used in hyponatremic patients or patients with a history of hyponatremia. PNE treatment with desmopressin tablets should be interrupted during acute illnesses that may lead to fluid and/or electrolyte imbalance. All desmopressin formulations should be used cautiously in patients at risk for water intoxication with hyponatremia. http://www.fda.gov/cder/drug/infopage/desmopressin/default.htm Health Canada July 2008 http://www.hc-sc.gc.ca/dhp-mps/medeff/advisories-avis/prof/_2008/desmopressin_hpc-cps-eng.php
110. Steers WD, Herschorn S, Kreder KJ, et al. Duloxetine OAB Study Group. Duloxetine compared with placebo for treating women with symptoms of overactive bladder. BJU Int. 2007 Aug;100(2):337-45. Epub 2007 May 19.
111. Ghoniem GM, Van Leeuwen JS, et al. Duloxetine/Pelvic Floor Muscle Training Clinical Trial Group. A randomized controlled trial of duloxetine alone, pelvic floor muscle training alone, combined treatment and no active treatment in women with stress urinary incontinence. J Urol. 2005 May;173(5):1647-53.
112. van Kerrebroeck P, Abrams P, Lange R, et al. Duloxetine Urinary Incontinence Study Group. Duloxetine versus placebo in the treatment of European and Canadian women with stress urinary incontinence. BJOG. 2004 Mar;111(3):249-57.
113. Millard RJ, Moore K, Rencken R, et al. Duloxetine UI Study Group. Duloxetine vs placebo in the treatment of stress urinary incontinence: a four-continent randomized clinical trial. BJU Int. 2004 Feb;93(3):311-8.
114. Norton PA, Zinner NR, Yalcin I, Bump RC; Duloxetine Urinary Incontinence Study Group. Duloxetine versus placebo in the treatment of stress urinary incontinence. Am J Obstet Gynecol. 2002 Jul;187(1):40-8.
115. Dmochowski RR, Miklos JR, Norton PA, et al. Duloxetine Urinary Incontinence Study Group. Duloxetine versus placebo for the treatment of North American women with stress urinary incontinence. J Urol. 2003 Oct;170(4 Pt 1):1259-63.
116. Pharmacotherapy of BPH with overactive bladder. Pharmacist's Letter/Prescriber's Letter Feb 2007;23 (2): 230205.

117. Athanasopoulos A, Perimenis P. Efficacy of the combination of an alpha1-blocker with an anticholinergic agent in the treatment of lower urinary tract symptoms associated with bladder outlet obstruction. Expert Opin Pharmacother. 2005 Nov;6(14):2429-33.
118. Athanasopoulos AA, Perimenis PS. Comparison of doxazosin with or without tolterodine in men with symptomatic bladder outlet obstruction and an overactive bladder. BJU Int. 2005 May;95(7):1117-8.
119. Athanasopoulos A, Gyftopoulos K, Giannitsas K, et al. Combination treatment with an alpha-blocker plus an anticholinergic for bladder outlet obstruction: a prospective, randomized, controlled study. J Urol. 2003 Jun;169(6):2253-6.
120. Wagg AS, Cardozo L, Chapple C, De Ridder D, Kelleher C, Kirby M, Milsom I, Vierhout M. Overactive bladder syndrome in older people. BJU Int. 2007 Mar;99(3):502-9.
121. Chapple C, Khullar V, Gabriel Z, Dooley JA. The effects of antimuscarinic treatments in overactive bladder: a systematic review and meta-analysis. Eur Urol. 2005 Jul;48(1):5-26. Epub 2005 Mar 22. Review. Erratum in: Eur Urol. 2005 Nov;48(5):875.
122. Abrams P, Kaplan S, De Koning Gans HJ, Millard R. Safety and tolerability of tolterodine for the treatment of overactive bladder in men with bladder outlet obstruction (**BOO**). J Urol. 2006 Mar;175(3 Pt 1):999-1004.
123. Gill SS, Mamdani M, Naglie G, Streiner DL, Bronskill SE, Kopp A, Shulman KI, Lee PE, Rochon PA. A prescribing cascade involving cholinesterase inhibitors and anticholinergic drugs. Arch Intern Med. 2005 Apr 11;165(7):808-13.
124. Hashimoto M, Imamura T, Tanimukai S, Kazui H, Mori E. Urinary incontinence: an unrecognised adverse effect with donepezil. Lancet. 2000 Aug 12;356(9229):568.
125. Hogan DB, Bailey P, Carswell A, et al. Management of mild to moderate Alzheimer's disease and dementia. Alzheimer's & Dementia 3 (2007) 355-384.
126. DeBeau K. American Geriatrics: Urinary Incontinence (Ch 20). Accessed at: http://www.americangeriatrics.org/staging/products/ui/incon5.m.htm
127. Alhasso AA, McKinlay J, Patrick K, Stewart L. Anticholinergic drugs versus non-drug active therapies for overactive bladder syndrome in adults. Cochrane Database Syst Rev. 2006 Oct 18;(4):CD003193.
Rai BP, Cody JD, Alhasso A, Stewart L. Anticholinergic drugs versus non-drug active therapies for non-neurogenic overactive bladder syndrome in adults. Cochrane Database of Systematic Reviews 2012, Issue 12. Art. No.: CD003193. DOI: 10.1002/14651858.CD003193.pub4.
128. Armitage J, Emberton M. The role of anticholinergic drugs in men with lower urinary tract symptoms. Curr Opin Urol. 2008 Jan;18(1):11-5.
129. **CAU (Canadian Urological Association) 2010 Update: Guidelines for the management of benign prostatic Hyperplasia** http://www.cua.org/guidelines/bph_2009_en__v2a.pdf
130. Nickel JC, Méndez-Probst CE, Whelan TF, Paterson RF, Razvi H. 2010 Update: Guidelines for the management of **benign prostatic hyperplasia**. **Canadian** Urol Assoc J. 2010 Oct;4(5):310-6.
Morlock R, Goodwin B, Gomez Rey G, Eaddy M. Clinical Progression, Acute Urinary Retention, Prostate-Related Surgeries, and Costs in Patients with Benign Prostatic Hyperplasia Taking **Early Versus Delayed Combination 5α-Reductase Inhibitor Therapy and α-Blocker** Therapy: A Retrospective Analysis. Clin Ther. 2013 Apr 12.
Fullhase C, Chapple C, Cornu JN, et al. Systematic review of combination drug therapy for non-neurogenic male lower urinary tract symptoms. Eur Urol. 2013 Aug;64(2):228-43.
131. Goode PS, Burgio KL, Johnson TM 2nd, et al. **Behavioral therapy** with or without biofeedback and pelvic floor electrical stimulation for persistent **postprostatectomy incontinence**: a randomized controlled trial. JAMA. 2011 Jan 12;305(2):151-9.
132. **Benign prostatic hyperplasia** (BPH): **American** Urological Association (**AUA**) Guidelines **2011**. http://www.auanet.org/content/guidelines-and-quality-care/clinical-guidelines/main-reports/bph-management/chap_1_GuidelineManagementof(BPH).pdf
133. Roehrborn CG, Siami P, et al; on behalf of the **CombAT** Study Group. The Effects of Dutasteride, Tamsulosin and Combination Therapy on Lower Urinary Tract Symptoms in Men With Benign Prostatic Hyperplasia & Prostatic Enlargement: **2-Year** Results From the **CombAT** Study. J Urol. 2007 Dec 12; [Epub ahead of print]
134. Roehrborn CG, Siami P, Barkin J, et al. on behalf of the CombAT Study Group. The Effects of Combination Therapy with Dutasteride and Tamsulosin on Clinical Outcomes in Men with Symptomatic Benign Prostatic Hyperplasia: **4-Year** Results from the **CombAT** Study. Eur Urol. 2010 Jan;57(1):123-131.
135. Keam SJ, Scott LJ. Dutasteride: a review of its use in the management of prostate disorders. Drugs. 2008;68(4):463-85. (Dutasteride is being investigated for its efficacy in reducing the risk of prostate cancer in at-risk men in the 4-year REDUCE study and as treatment to extend the time to progression in men with low-risk
136. localized prostate cancer who would otherwise undergo watchful waiting in the 3-year REDEEM study)
137. Kramer BS, Hagerty KL, Justman S, et al. Use of 5alpha-Reductase Inhibitors for **Prostate Cancer Chemoprevention**: American Society of Clinical Oncology/American Urological Association 2008 Clinical Practice Guideline. J Urol. 2009 Feb 24. [Epub ahead of print] Asymptomatic men with a prostate-specific antigen (PSA) </=3.0 ng/mL who are regularly screened with PSA or are anticipating undergoing annual PSA screening for early detection of prostate cancer may benefit from a discussion of both the benefits of 5-ARIs for 7 years for the prevention of prostate cancer and the potential risks (including the possibility of high-grade prostate cancer). Men who are taking 5-ARIs for benign conditions such as lower urinary tract [obstructive] symptoms (LUTS) may benefit from a similar discussion, understanding that the improvement of LUTS relief should be weighed with the potential risks of high-grade prostate cancer from 5-ARIs (although the majority of the Panel members judged the latter risk to be unlikely). A reduction of approximately 50% in PSA by 12 months is expected in men taking a 5-ARI; however, because these changes in PSA may vary across men, and within individual men over time, the Panel cannot recommend a specific cut point to trigger a biopsy for men taking a 5-ARI. No specific cut point or change in PSA has been prospectively validated in men taking a 5-ARI. http://jco.ascopubs.org/cgi/reprint/27/9/1502
138. Redman MW, Tangen CM, Goodman PJ, Lucia MS, Coltman CA Jr, Thompson IM. Finasteride does not increase the risk of high-grade prostate cancer: a bias-adjusted modeling approach. Cancer Prev Res (Phila Pa). 2008 Aug;1(3):174-81. Epub 2008 May 18.
139. Elliott CS, Shinghal R, Presti JC Jr. The Influence of Prostate Volume on Prostate-Specific Antigen Performance: Implications for the Prostate Cancer Prevention Trial Outcomes. Clin Cancer Res. 2009 Jul 7. [Epub ahead of print]
140. Pharmacist's Letter. Controversies in Prostate Cancer: Role of PSA Testing and 5-Alpha-Reductase Inhibitors. July, 2009.
141. Lebdai S, Bigot P, Azzouzi AR. High-grade prostate cancer and finasteride. BJU Int. 2009 Nov 20. [Epub ahead of print]
142. Vickers AJ, Savage CJ, Lilja H. Finasteride to Prevent Prostate Cancer: Should All Men or Only a High-Risk Subgroup Be Treated? J Clin Oncol. 2010 Feb 16.
143. Andriole, Gerald L., Bostwick, David G., Brawley, Otis W., et al. the **REDUCE** Study Group, Effect of Dutasteride on the Risk of Prostate Cancer. N Engl J Med 2010 362: 1192-1202.
144. Tacklind J, Fink HA, MacDonald R, Rutks I, Wilt TJ. **Finasteride** for benign prostatic hyperplasia. Cochrane Database of Systematic Reviews 2010, Issue 10. Art. No.: CD006015. DOI: 10.1002/14651858.CD006015.pub3.
145. Wilt TJ, Macdonald R, Hagerty K, Schellhammer P, Tacklind J, Somerfield MR, Kramer BS. 5-α-Reductase inhibitors for prostate cancer chemoprevention: an updated Cochrane systematic review. BJU Int. 2010 Nov;106(10):1444-51. doi: 10.1111/j.1464-410X.2010.09714.x.
146. CAU (Canadian Urological Association) 2010 Update: Guidelines for the management of benign prostatic Hyperplasia http://www.cua.org/guidelines/bph_2009_en__v2a.pdf
147. Nickel JC, Méndez-Probst CE, Whelan TF, Paterson RF, Razvi H. 2010 Update: **Guidelines** for the management of **benign prostatic hyperplasia**. **Can** Urol Assoc J. 2010 Oct;4(5):310-6.
148. Andriole GL, Bostwick D, Brawley OW, et al. REDUCE Study Group. The Effect of **Dutasteride** on the Usefulness of Prostate Specific Antigen for the Diagnosis of High Grade and Clinically Relevant Prostate Cancer in Men With a Previous Negative Biopsy: Results From the REDUCE Study. J Urol. 2011 Jan;185(1):126-31.
149. FDA June/11 notified that the Warnings and Precautions section of the labels for the 5-alpha reductase inhibitor (5-ARI) class of drugs has been revised to include new safety information about the **increased** risk of being diagnosed with a more serious form of prostate cancer **(high-grade prostate cancer)**. {PCPT & Reduce FDA reviewed data from two prostate cancer prevention trials. In one, finasteride (given daily for 7 years) was associated with a higher frequency of prostate cancers with Gleason scores between 8 and 10, compared with placebo (1.8% vs. 1.1%). In the other, dutasteride (given daily for 4 years) was also associated with more high-grade cancers relative to placebo (1% vs. 0.5%)}.
150. Theoret Marc R., Ning Yang-Min, Zhang Jenny J., et al. The **Risks and Benefits of 5α-Reductase Inhibitors** for Prostate-Cancer Prevention. June 15, 2011 (10.1056/NEJMp1106783)
151. Fleshner NE, Lucia MS, Egerdie B, et al. **Dutasteride** in localised prostate cancer management: the **REDEEM** randomised, double-blind, placebo-controlled trial. Lancet 2012; published online January 25.
Toren P, Margel D, et al. Effect of **dutasteride** on clinical progression of **benign prostatic hyperplasia** in asymptomatic men with enlarged prostate: a post hoc analysis of the **REDUCE** study. BMJ. 2013 Apr 15;346:f2109.
Robinson D, Garmo H, et al. Use of 5α-reductase inhibitors for lower urinary tract symptoms and risk of **prostate cancer** in Swedish men: nationwide, population based case-control study. BMJ. 2013 Jun 18;346:f3406.
Thompson IM Jr, Goodman PJ, Tangen CM, et al. Long-term survival of participants (**finasteride**) in the **Prostate Cancer Prevention Trial. (PCPT)** N Engl J Med 2013;369:603-10.
Preston MA, Wilson KM, Markt SC, et al. **5α-Reductase Inhibitors and Risk of High-Grade or Lethal Prostate Cancer**. JAMA Intern Med. 2014 Jun 2.
152. Carson CC. Combination of phosphodiesterase-5 inhibitors and alpha-blockers in patients with benign prostatic hyperplasia: treatments of lower urinary tract symptoms, erectile dysfunction, or both?BJU Int. 2006 Apr;97 Suppl 2:39-43; discussion 44-5.
153. Klausner AP, Steers WD. Antimuscarinics for the treatment of overactive bladder: a review of central nervous system effects.Curr Urol Rep. 2007 Nov;8(6):441-7.
Wagg A, Dale M, Tretter R, Stow B, Compion G. Randomised, Multicentre, Placebo-controlled, Double-blind Crossover Study Investigating the Effect of **Solifenacin and Oxybutynin** in Elderly People with Mild Cognitive Impairment: The SENIOR Study. Eur Urol. 2013 Jan 11.
154. Sahai A, Mallina R, Dowson C, Larner T, Khan MS. Evolution of transdermal oxybutynin in the treatment of overactive bladder. Int J Clin Pract. 2008 Jan;62(1):167-70.
155. Farrell SA, Baydock S, Amir B, Fanning C. Effectiveness of a new self-positioning pessary for the management of urinary incontinence in women. Am J Obstet Gynecol. 2007 May;196(5):474.e1-8.
156. Wallace SA, Roe B, Williams K, Palmer M. **Bladder training** for urinary incontinence in adults. **Cochrane** Database Syst Rev. 2004;(1):CD001308.
157. McConnell JD, Roehrborn CG, Bautista OM, Andriole GL Jr, et al; Medical Therapy of Prostatic Symptoms (**MTOPS**) Research Group. The long-term effect of doxazosin, finasteride, and combination therapy on the clinical progression of benign prostatic hyperplasia. N Engl J Med. 2003 Dec 18;349(25):2387-98.
158. Wilt TJ, N'Dow J. Benign prostatic hyperplasia. Part 2-Management. BMJ. 2008 Jan 26;336(7637):206-10.
159. Nix JW, Carson CC. Medical management of benign prostatic hypertrophy. Can J Urol. 2007 Dec;14 Suppl 1:53-7.
160. **American** Urological Assoc 2006 Kaplan et al. www.auanet.org/guidelines/bph.cfm ;
161. **European** 2004 Madersbacher et al. http://www.uroweb.org/fileadmin/user_upload/Guidelines/11%20BPH.pdf
Fullhase C, Chapple C, Cornu JN, et al. Systematic review of combination drug therapy for non-neurogenic male lower urinary tract symptoms. Eur Urol. 2013 Aug;64(2):228-43.

Preston MA, Wilson KM, Markt SC, et al. 5α-Reductase Inhibitors and Risk of High-Grade or Lethal Prostate Cancer. JAMA Intern Med. 2014 Jun 2.
Morales EE, Grill S, Svatek RS, et al. **Finasteride** Reduces **Risk of Bladder Cancer** in a Large Prospective Screening Study. Eur Urol. 2016 Mar;69(3):407-10.
Azoulay L, Eberg M, Benayoun S, et al. **5α-Reductase Inhibitors** and the Risk of Cancer-Related Mortality in Men With **Prostate Cancer**. JAMA Oncol. 2015 Jun;1(3):314-20
Welk B, McArthur E, Ordon M, et al. Association of **Suicidality and Depression With 5alpha-Reductase Inhibitors (eg. Finasteride)**. JAMA Intern Med. 2017 Mar 20.
Goodman Goodman PJ, Tangen CM, Darke AK, et al. **Long-Term Effects of Finasteride** on Prostate Cancer Mortality. N Engl J Med. 2019 Jan 24;380(4):393-394.
Wallerstedt A, Strom P, Gronberg H, et al. Risk of **Prostate Cancer in Men Treated With 5α-Reductase Inhibitors**-A Large Population-Based Prospective Study. J Natl Cancer Inst. 2018 Nov 1;110(11):1216-1221.
Unger JM, Hershman DL, Till C, et al. Using Medicare Claims to Examine **Long-term Prostate Cancer Risk of Finasteride** in the Prostate Cancer Prevention Trial. J Natl Cancer Inst. 2018 Nov 1;110(11):1208-1215.
Sarkar RR, Parsons JK, Bryant AK, et al. Association of Treatment With **5α-Reductase Inhibitors With Time to Diagnosis and Mortality in Prostate Cancer**. JAMA Intern Med. 2019 May 6

162. Singh A, Alter HJ, Littlepage A. A systematic review of medical therapy to facilitate passage of **ureteral calculi**. Ann Emerg Med. 2007 Nov;50(5):552-63. Epub 2007 Aug 3. Our results suggest that "medical expulsive therapy," using either alpha-antagonists or calcium channel blockers, augments the stone expulsion rate compared to standard therapy for moderately sized distal ureteral stones. This meta-analysis of low-quality studies shows that ureteral stone passage can be enhanced by treating patients with an alpha-blocker such as tamsulosin (Flomax) or the calcium channel blocker nifedipine (Procardia). Better studies may refute these findings, but for now either approach is an option. (LOE = 1a-).
163. Ferre RM et al. Tamsulosin for ureteral stones in the emergency department: A randomized, controlled trial. Ann Emerg Med 2009 Sep; 54:432. (not useful)
164. John TT, Razdan S. Adjunctive tamsulosin improves stone free rate after ureteroscopic lithotripsy of large renal and ureteric calculi: a prospective randomized study. Urology. 2010 May;75(5):1040-2.
165. Medical Letter. **Drugs for Kidney Stones**. Nov 29, 2010. (Tamsulosin or long aciting nifedipine +/- corticosteroid) Medical Letter. **Drugs for Kidney Stones**. Nov 29, 2010. (Tamsulosin or long acting nifedipine +/- corticosteroid)
166. Vincendeau Sebastien; Bellissant Eric; Houlgatte Alain; et al.; for the Tamsulosin Study Group. **Tamsulosin** Hydrochloride vs Placebo for Management of Distal Ureteral Stones: A Multicentric, Randomized, Double-blind Trial. Arch Intern Med. 2010;170(22):2021-2027.
Berger DA, Ross MA, Hollander JB, et al. **Tamsulosin** does not increase 1-week passage rate of **ureteral stones** in ED patients. Am J Emerg Med. 2015 Dec;33(12):1721-4.
Furyk JS, Chu K, Banks C, et al. **Distal Ureteric Stones** and **Tamsulosin**: A Double-Blind, Placebo-Controlled, Randomized, Multicenter Trial. Ann Emerg Med. 2016 Jan;67(1):86-95.e2.
Wang RC et al. Effect of **tamsulosin** on stone passage for **ureteral stones**: A systematic review and meta-analysis. Ann Emerg Med 2016 Sep 8.
Meltzer AC, Burrows PK, Wolfson AB, et al. Effect of **tamsulosin on passage of symptomatic ureteral stones**: a randomized clinical trial [online June 18, 2018]. JAMA Intern Med. doi:10.1001/jamainternmed.2018.2259

167. Shamliyan TA, Kane RL, Wyman J, Wilt TJ. Systematic Review: Randomized, Controlled Trials of Nonsurgical Treatments for Urinary Incontinence in Women. Ann Intern Med. 2008 Feb 11; [Epub ahead of print]
168. Society of Obstetricians and Gynaecologists of Canada, Robert M, Ross S, Farrel SA, et all. Conservative management of urinary incontinence. J Obstet Gynaecol Can 2006 Dec;28(12):1113-8. http://www.sogc.org/guidelines/documents/186E-CPG-Decembre2006.pdf
169. Landefeld CS, Bowers BJ, Feld AD, Hartmann KE, Hoffman E, Ingber MJ, et al. National Institutes of Health State-of-the-Science Statement: Prevention of Fecal and Urinary Incontinence in Adults. Ann Intern Med. 2008 Feb 11; [Epub ahead of print].
170. Wilt TJ, Mac Donald R, Rutks I. Tamsulosin for benign prostatic hyperplasia. **Cochrane** Database Syst Rev. 2003;(1):CD002081.
171. Desmopressin monitoring to prevent harm: ISMP bulletin Mar2008: http://infonet.sktnhr.ca/pharmaceutical_services/documents/ISMPCndSafetyBulletin2008-01DDAVP.pdf
172. Thomas LH, et al. Treatment of urinary incontinence **after stroke** in adults. Cochrane Database Syst Rev. 2008 Jan 23;(1):CD004462. Data from the available trials are insufficient to guide continence care of adults after stroke. However, there was suggestive evidence that professional input through structured assessment and management of care and specialist continence nursing may reduce urinary incontinence and related symptoms after stroke.
173. Cantrell MA, Bream-Rouwenhorst HR, Steffensmeier A, et al.Intraoperative Floppy Iris Syndrome Associated with {alpha}1-Adrenergic Receptor Antagonists (April). Ann Pharmacother. 2008 Mar 25; [Epub ahead of print] Other alpha1AR antagonists, including terazosin, doxazosin, and alfuzosin, have also been linked to IFIS; however, their relationship to the syndrome is not as definitive. **IFIS** is a clinical syndrome observed during cataract surgery reported in patients taking systemic alpha1AR antagonists. It has been most strongly linked to use of tamsulosin. Medication washout periods of up to 2 weeks and specific surgical procedures have been attempted to reduce risk of complications from alpha1AR antagonists in the setting of cataract surgery.
174. Wilt T, et al. **Five-alpha-reductase Inhibitors for prostate cancer prevention**. Cochrane Database Syst Rev. 2008 Apr 16;(2):CD007091. 5ARI reduce prostate cancer risk but may increase risk of high-grade disease in men who are undergoing regular screening for prostate cancer using prostate specific antigen & digital rectal examination. Effects are consistent across race, family history and age and possibly 5ARI but were limited to men with baseline PSA values <4.0 ng/mL.
175. Chapple CR, Khullar V, Gabriel Z, Muston D, Bitoun CE, Weinstein D. The Effects of **Antimuscarinic** Treatments in Overactive Bladder: An Update of a **Systematic Review** and Meta-Analysis. Eur Urol. 2008 Jun 20. [Epub ahead of print] Antimuscarinics are efficacious, safe, and well-tolerated treatments that improve HRQL. Profiles of each drug and dosage differ and should be considered in making treatment choices.
176. Burgio KL, Kraus SR, Menefee S, et al. Urinary Incontinence Treatment Network. Behavioral therapy to enable women with urge incontinence to discontinue drug treatment: a randomized trial. Ann Intern Med. 2008 Aug 5;149(3):161-9.
177. Brubaker L, Nygaard I, Richter HE, et al. Two-year outcomes after sacrocolpopexy with and without **burch** to prevent stress urinary incontinence. Obstet Gynecol. 2008 Jul;112(1):49-55. The early advantage of prophylactic Burch colposuspension for stress incontinence that was seen at 3 months remains at 2 years. Apical anatomic success rates are high and not affected by concomitant Burch.
178. Dimitrakov J, Kroenke K, Steers WD, Berde C, Zurakowski D, Freeman MR, Jackson JL. Pharmacologic management of painful bladder syndrome/interstitial cystitis: a systematic review. Arch Intern Med. 2007 Oct 8;167(18):1922-9. Review. Erratum in: Arch Intern Med. 2007 Dec 10-22;167(22):2452.
179. Jacobsen SJ, Cheetham TC, Haque R, Shi JM, Loo RK. Association between **5-alpha reductase inhibition and risk of hip fracture**. JAMA. 2008 Oct 8;300(14):1660-4. Exposure to 5-alpha reductase inhibitors was not associated with increased risk of hip fracture. The reduction in risk observed with exposure to 5-alpha reductase inhibitors and the modest increase in risk associated with exposure to alpha-blockers require replication and warrant further investigation.
180. Bauer R, Kaufman R, Mian BM. Use of **anticholinergic therapy in men**. Can J Urol. 2008 Dec;15(6):4359-62.
181. De E. Management of **refractory overactive bladder** in adults. Can J Urol. 2008 Dec;15(6):4388-98.
182. Nickel JC, Krieger JN, McNaughton-Collins M, Anderson RU, Pontari M, Shoskes et al.; Chronic Prostatitis Collaborative Research Network. **Alfuzosin** and symptoms of **chronic prostatitis**-chronic pelvic pain syndrome. N Engl J Med. 2008 Dec 18;359(25):2663-73. Our findings do not support the use of alfuzosin to reduce the symptoms of chronic prostatitis-chronic pelvic pain syndrome in men who have not received prior treatment with an alpha-blocker.
183. Gopal M, Haynes K, Bellamy SL, Arya LA. **Discontinuation rates** of anticholinergic medications used for the treatment of lower urinary tract symptoms. Obstet Gynecol. 2008 Dec;112(6):1311-8. The median time for overall anticholinergic drug discontinuation was 4.76 months. The 6-month unadjusted cumulative incidence of discontinuation was 58.8% (95% confidence interval [CI] 58.4-59.3). The percentage of episodes in which women switched to another medication was 15.8% (95% CI 15.4-16.1). At 6 months, the adjusted cumulative incidence of discontinuation was as follows: oxybutynin 71% (95% CI 68.4-73.5), tolterodine tartrate 61% (59.4,64.3), extended-release oxybutynin 57% (95% CI 55.1-59.4), and extended-release tolterodine tartrate 54% (95% CI 52.3-57.7).Discontinuation rates for anticholinergic medications are high regardless of the class of medication used.
184. Subak LL, Wing R, West DS, et al. **PRIDE** Investigators. Weight loss to treat urinary incontinence in overweight and obese women. N Engl J Med. 2009 Jan 29;360(5):481-90. A 6-month behavioral intervention targeting **weight loss reduced the frequency of self-reported urinary-incontinence** episodes among overweight and obese women as compared with a control group. A decrease in urinary incontinence may be another benefit among the extensive health improvements associated with moderate weight reduction.
185. Herbison GP, Arnold EP. Sacral **neuromodulation** with implanted devices for urinary storage and voiding dysfunction in adults. Cochrane Database Syst Rev. 2009 Apr 15;(2):CD004202.
186. Bell Chaim M.; Hatch; Wendy V. et al. Association Between **Tamsulosin and Serious Ophthalmic Adverse** Events in Older Men Following Cataract Surgery. JAMA. 2009;301(19):1991-1996. Exposure to tamsulosin within 14 days of cataract surgery was significantly associated with serious postoperative ophthalmic adverse events. There were no significant associations with exposure to other alpha-blocker medications used to treat BPH.
187. Iliadou A, Milsom I, Pedersen NL, Altman D. Risk of urinary incontinence symptoms in **oral contraceptive** users: a national cohort study from the Swedish Twin Register. Fertil Steril. 2009 Aug;92(2):428-33. Epub 2008 Aug 15.
188. Hartmann KE, McPheeters ML, Biller DH, et al. Treatment of Overactive Bladder in Women. Evid Rep Technol Assess (2008): 187, 1-11.
189. Ogah J, Cody JD, Rogerson L. Minimally invasive synthetic suburethral sling operations for stress urinary incontinence in women. Cochrane Database Syst Rev. 2009 Oct 7;(4):CD006375.
190. Zeif HJ, Subramonian K. **Alpha blockers** prior to removal of a catheter for acute urinary **retention** in adult men. Cochrane Database Syst Rev. 2009 Oct 7;(4):CD006744.
191. Robson WL. Clinical practice. Evaluation and management of **enuresis**. N Engl J Med. 2009 Apr 2;360(14):1429-36.
192. Glazener CM, Evans JH, Peto RE. Tricyclic and related drugs for nocturnal **enuresis** in children. Cochrane Database Syst Rev. 2003;(3):CD002117.
193. Glazener CM, Evans JH. Desmopressin for nocturnal enuresis in children. Cochrane Database Syst Rev. 2002;(3):CD002112.
194. Brown JS, Bradley CS, Subak LL, et al. Diagnostic Aspects of Incontinence Study (DAISy) Research Group. The sensitivity and specificity of a simple test to distinguish between urge and stress urinary incontinence. Ann Intern Med. 2006 May 16;144(10):715-23.
195. Management of **neurogenic bladder in children**. In: Tekgül S, Riedmiller H, Gerharz E, Hoebeke P, Kocvara R, Nijman R, Radmayr Chr, Stein R. Guidelines on paediatric urology. Arnhem, The Netherlands: **European** Association of Urology, European Society for Paediatric Urology; 2009 Mar. p. 31-41.

196. **Monosymptomatic enuresis**. In: Tekgül S, Riedmiller H, Gerharz E, Hoebeke P, Kocvara R, Nijman R, Radmayr Chr, Stein R. Guidelines on paediatric urology. Arnhem, The Netherlands: **European** Association of Urology, European Society for Paediatric Urology; 2009 Mar. p. 29-31.
197. Daniel R, Mallen CD, Cooper J. **Female stress urinary incontinence**-10minute Consultation. BMJ. 2010 Feb 1;340:b5533. doi: 10.1136/bmj.b5533.
198. Feb/10 Health Canada is informing health care professionals of complications associated with the transvaginal implantation of **surgical mesh** for the treatment of stress urinary incontinence and pelvic organ prolapse.
199. Dumoulin C, Hay-Smith J. **Pelvic floor muscle training** versus no treatment, or inactive control treatments, for urinary incontinence in women. Cochrane Database Syst Rev. 2010 Jan 20;(1):CD005654.
200. Frithsen IL, Simpson WM Jr. Recognition and management of acute medication poisoning. Am Fam Physician. 2010 Feb 1;81(3):316-23.
201. Ostaszkiewicz J, Johnston L, Roe B. **Habit retraining** for the management of urinary incontinence in adults. Cochrane Database Syst Rev. 2004;(2):CD002801.
202. Solans-Domenech M, Sanchez E, Espuna-Pons M. Urinary and anal **incontinence during pregnancy** and postpartum: incidence, severity, and risk factors. Obstet Gynecol. 2010 Mar;115(3):618-28.
203. Kuncharape I, Maeroni B, Johnson D, **Pelvic Organ Prolapse**. Am Fam Physician. 2001 May 1;81(9):1111-1117. (Good **Pessary** overview)
204. Heliovaara-Peippo S, Halmesmaki K, Hurskainen R, et al. The effect of **hysterectomy or levonorgestrel-releasing intrauterine system** on lower urinary tract symptoms: a 10-year follow-up study of a randomised trial. BJOG. 2010 Apr;117(5):602-9. Epub 2010 Feb 15.
205. Anger JT, Weinberg A, Suttorp MJ, Litwin MS, Shekelle PG. Outcomes of **Intravesical Botulinum Toxin** for Idiopathic Overactive Bladder Symptoms: A Systematic Review of the Literature. J Urol. 2010 Apr 16.
206. Goode Patricia S.; Burgio Kathryn L.; Holly E. Richter; Alayne D. Markland. **Incontinence in Older Women**, JAMA. 2010;303(21):2172-2181.
207. Nix D, Haugen V. Prevention and management of **incontinence-associated dermatitis**. Drugs Aging. 2010 Jun 1;27(6):491-6.
208. Ahmad M, McCallum IJ, Mercer-Jones M. Management of **faecal incontinence** in adults. BMJ. 2010 Jun 15;340:c2964.
209. Thirugnanasothy S. Managing **urinary incontinence in older people**. BMJ 2010;341:c3835, doi: 10.1136/bmj.c3835 (Published 9 August 2010)
210. Sand PK, Johnson Ii TM, Rovner ES, Ellsworth PI, Oefelein MG, Staskin DR. **Trospium** chloride once-daily extended release is efficacious and tolerated in elderly subjects (aged >/=75 years) with overactive bladder syndrome. BJU Int. 2010 Aug 6.
211. Lordêlo P, Teles A, Veiga ML, Correia LC, Barroso U Jr. Transcutaneous electrical nerve stimulation (**TENS**) in children with overactive bladder: a randomized clinical trial. J Urol. 2010 Aug;184(2):683-9.
212. American Urological Association Education and Research. Guideline for the **surgical management of female stress urinary incontinence**: 2009 update. Linthicum (MD): American Urological Association Education and Research, Inc.; 2009.
213. Pharmacist's Letter. **Alpha-Blockers for Urinary Problems in Women**. Oct 2010.
214. Nieminen K, Hiltunen R, Takala T, et al. Outcomes after **anterior vaginal wall repair with mesh**: a randomized, controlled trial with a 3 year follow-up. Am J Obstet Gynecol. 2010 Sep;203(3):235.e1-8. Epub 2010 May 21.
215. Afonso AS, Verhamme KM, Stricker BH, et al. **Inhaled anticholinergic drugs** and risk of acute urinary retention. BJU Int. 2010 Sep 29. doi: 10.1111/j.1464-410X.2010.09600.x. Current use of inhaled anticholinergic drugs increases the risk of AUR, especially in patients with BPH or if administered via a nebulizer.
216. **NICE** guideline Oct/10: **Nocturnal enuresis** - the management of bedwetting in **children and young people**. http://www.nice.org.uk/nicemedia/live/13246/51367/51367.pdf
217. Kwak KW, Lee YS, Park KH, Baek M. Efficacy of **Desmopressin and Enuresis Alarm** as First and Second Line Treatment for Primary Monosymptomatic Nocturnal Enuresis: Prospective Randomized Crossover Study. J Urol. 2010 Oct 18.
218. Homma Y, Kakizaki H, Yamaguchi O, et al. Assessment of Overactive Bladder Symptoms: Comparison of **3-Day Bladder Diary and the Overactive Bladder Symptoms Score**. Urology. 2010 Oct 14.
219. Frank, Christopher, Szlanta, Agata. Office management of urinary incontinence among **older patients**. Can Fam Physician 2010 56: 1115-1120.
220. Anothaisintawee T, Attia J, Nickel JC, et al.. Management of **chronic prostatitis/chronic pelvic pain syndrome**: a systematic review and network meta-analysis. JAMA. 2011 Jan 5;305(1):78-86.
221. Wang CJ, Lin YN, Huang SW, Chang CH. Low dose oral **desmopressin for nocturnal polyuria** in patients with **benign prostatic hyperplasia**: a double-blind, placebo controlled, randomized study. J Urol. 2011 Jan;185(1):219-23.
222. Allan GM, Ivers N, Kolber M. **Medical management of renal stones**: More than analgesia? Can Fam Physician. 2011 Feb;57(2):198.
223. Lovatsis D, Easton W, Wilkie D, Urogynaecology Committee. **SOGC** Guidelines for the evaluation and **treatment of recurrent urinary incontinence following pelvic floor surgery**. J Obstet Gynaecol Can 2010 Sep;32(9):894-99. http://www.sogc.org/guidelines/documents/gui248CPG1009E_000.pdf
224. French LM, Bhambore N. **Interstitial cystitis**/painful bladder syndrome. Am Fam Physician. 2011 May 15;83(10):1175-81.
225. Friedman Bat-Chen, Friedman Boris, Goldman Ran D.. **Oxybutynin for treatment of nocturnal enuresis in children**. Canadian Family Physician. May 2011.
226. Stephenson Anne; Seitz Dallas; Bell Chaim M.; et al. Inhaled **Anticholinergic Drug Therapy and the Risk of Acute Urinary Retention** in Chronic Obstructive Pulmonary Disease: A Population-Based Study. Arch Intern Med. 2011;171(10):914-920.
227. Glazener C, Boachie C, Buckley B, et al. Urinary incontinence in men after formal one-to-one **pelvic-fl oor muscle training following radical prostatectomy or transurethral resection of the prostate** (**MAPS**): two parallel randomised controlled trials. Lancet 2011; online July 12. (unlikely to be effective))
228. FDA July/11 **Surgical placement of mesh to repair pelvic organ prolapse poses risks.** In treating pelvic organ prolapse, use of mesh, especially if placed transvaginally, "may expose patients to greater risk than other surgical options," the FDA warned this week. The agency estimates there were at least 100,000 prolapse repairs done with mesh last year, most done transvaginally. The FDA reports that the most frequent complications resulting from mesh include protrusion of the mesh out of vaginal tissue, pain, infection, bleeding, and pain during intercourse. http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm262752.htm
229. Health Canada Aug/11 is informing healthcare practitioners and patients of a labelling update for **finasteride drugs to add safety information on rare reports of breast cancer in men**.
230. FDA Aug/11 Botox (onabotulinumtoxinA) has been approved to treat urinary incontinence in patients with overactive bladder due to neurologic conditions (e.g., multiple sclerosis).
231. Paquette A, Gou P, Tannenbaum C. Systematic review and meta-analysis: do clinical trials testing **antimuscarinic agents for overactive bladder adequately measure central nervous system adverse events**?. J Am Geriatr Soc. 2011 Jul;59(7):1332-9. (More-detailed standardized measurement required)
232. Varilla V, Samala RV, Galindo D, Ciocon J. **Nocturia** in the elderly: A wake-up call. Cleve Clin J Med. 2011 Nov;78(11):757-64.
233. Nelken RS, Ozel BZ, Leegant AR, Felix JC, Mishell DR Jr. Randomized trial of **estradiol vaginal ring versus oral oxybutynin** for the treatment of overactive bladder. Menopause. 2011 Sep;18(9):962-6.
234. Duthie JB, Vincent M, Herbison GP, et al. **Botulinum toxin injections** for adults with overactive bladder syndrome. Cochrane Database Syst Rev. 2011 Dec 7;12:CD005493. Intravesical botulinum toxin appears to be an effective therapy for refractory OAB symptoms, but as yet little controlled trial data exist on benefits and safety compared with other interventions, or with placebo.
235. Pannek J, Stöhrer M, Blok B, Castro-Diaz D, Del Popolo G, Kramer G, Radziszewski P, Reitz A, Wyndaele J-J. Guidelines on **neurogenic lower urinary tract dysfunction**. Arnhem, The Netherlands: European Association of Urology (**EAU**); 2011 Mar.
236. Chung SD, Chen YK, Chen YH et al. **Hyperthyroidism** and female urinary incontinence: a population-based cohort study. Clin Endocrinol (Oxf). 2011 Nov;75(5):704-8.
237. Brazzelli M, Griffiths PV, Cody JD, et al. Behavioural and cognitive interventions with or without other treatments for the management of **faecal incontinence** in children. Cochrane Database Syst Rev. 2011 Dec 7;12:CD002240
238. Sengupta G et al. Comparison of **Murraya koenigii- and Tribulus terrestris**-Based Oral Formulation **Versus Tamsulosin** in the Treatment of Benign Prostatic Hyperplasia in Men Aged >50 Years: A Double-Blind, Double-Dummy, Randomized Controlled Trial. Clin Ther. 2011 Dec; 33(12):1943-52.
239. Madhuvrata P, Cody JD, Ellis G, et al. Which **anticholinergic drug for overactive bladder symptoms in adults**. Cochrane Database Syst Rev. 2012 Jan 18;1:CD005429. Where the prescribing choice is between oral immediate release oxybutynin or tolterodine, tolterodine might be preferred for reduced risk of dry mouth. With tolterodine, 2 mg twice daily is the usual starting dose, but a 1 mg twice daily dose might be equally effective, with less risk of dry mouth. If extended release preparations of oxybutynin or tolterodine are available, these might be preferred to immediate release preparations because there is less risk of dry mouth. Between solifenacin and immediate release tolterodine, solifenacin might be preferred for better efficacy and less risk of dry mouth. Solifenacin 5 mg once daily is the usual starting dose, this could be increased to 10 mg once daily for better efficacy but with increased risk of dry mouth. Between fesoterodine and extended release tolterodine, fesoterodine might be preferred for superior efficacy but has higher risk of withdrawal due to adverse events and higher risk of dry mouth.There is little or no evidence available about quality of life, costs, or long-term outcome in these studies. There were insufficient data from trials of other anticholinergic drugs to draw any conclusions.
240. Burgio KL, Goode PS, Johnson TM, et al. **Behavioral versus drug treatment** for overactive bladder in **men**: the Male Overactive Bladder Treatment in Veterans (MOTIVE) Trial. J Am Geriatr Soc. 2011 Dec;59(12):2209-16.
241. Campbell SE, Glazener CM, Hunter KF, et al. Conservative management for **postprostatectomy urinary incontinence**. Cochrane Database Syst Rev. 2012 Jan 18;1:CD001843. The value of the various approaches to conservative management of postprostatectomy incontinence after radical prostatectomy remains uncertain. It seems unlikely that men benefit from one-to-one pelvic floor muscle training therapy after transurethral resection of the prostate (TURP). Long-term incontinence may be managed by external penile clamp, but there are safety problems.
242. Health Canada Mar/12 is informing health professionals and the public that the prescription drugs **finasteride and dutasteride** may be associated with an increased risk of developing a serious form of prostate cancer known as **high-grade prostate cancer**.
243. FDA: Apr/12 The labels of the alopecia drug Propecia (**finasteride** 1 mg) and the benign prostatic hyperplasia drug Proscar (finasteride 5 mg) are being updated with an expanded list of adverse **sexual effects**, the FDA has announced. Propecia label will include libido, ejaculation, and orgasm disorders that persist after treatment ends; Proscar label will include decreased libido that persists posttreatment & both labels will note reports of male infertility or poor semen quality that improved after drug discontinuation.
244. Gacci M, Corona G, Salvi M, et al. A Systematic Review and Meta-analysis on the Use of **Phosphodiesterase 5 Inhibitors** Alone or in Combination with α-Blockers for Lower Urinary Tract Symptoms Due to Benign Prostatic Hyperplasia. Eur Urol. 2012 May;61(5):994-1003.
245. Marinkovic SP, Rovner ES, Moldwin RM, et al. The **management of overactive bladder syndrome**. BMJ. 2012 Apr 17;344:e2365.

246. Robinson D, Cardozo L. **Antimuscarinic drugs** to treat overactive bladder. BMJ. 2012 Mar 27;344:e2130.
247. Nager CW, Brubaker L, Litman HJ, et al; the Urinary Incontinence Treatment Network. A Randomized Trial of **Urodynamic Testing before Stress-Incontinence Surgery**. N Engl J Med. 2012 May 2.
248. Kiddoo DA. **Nocturnal enuresis**. CMAJ. 2012 Apr 23.
249. Shamliyan T, Wyman JF, Ramakrishnan R, Sainfort F, Kane RL. Systematic Review: **Benefits and Harms of Pharmacologic Treatment for Urinary Incontinence** in Women. Ann Intern Med. 2012 Apr 9.
250. Huang AJ, Hess R, Arya LA, et al. Pharmacologic treatment for urgency-predominant urinary incontinence in women diagnosed using a **simplified algorithm**: a randomized trial. Am J Obstet Gynecol. 2012 May;206(5):444.e1-444.e11.
251. Brubaker L, Cundiff GW, Fine P, et al. **Abdominal sacrocolpopexy with Burch colposuspension** to reduce urinary stress incontinence. (CARE) N Engl J Med 2006;354:1557-66.
252. Wei JT, Nygaard I, Richter HE, et al. A **midurethral sling** to reduce incontinence **after vaginal prolapse repair**. (**OPUS**) N Engl J Med 2012;366:2358-67.
253. Wagg A, Compion G, Fahey A, Siddiqui E. **Persistence with prescribed antimuscarinic** therapy for overactive bladder: a UK experience. BJU Int. 2012 Mar 12.
254. Gormley EA, Lightner DJ, Burgio KL, Chai TC, et al. Diagnosis and treatment of **overactive bladder** (non-neurogenic) in adults: **AUA/SUFU guideline**. Linthicum (MD): American Urological Association (AUA); **2012** May. (J Urol. 2012 Oct 19. pii: S0022-5347(12)04959-2.)
Gormley EA, Lightner DJ, Burgio KL, et al. Diagnosis and treatment of overactive bladder (non-neurogenic) in adults: **AUA/SUFU guideline**. Linthicum (MD): American Urological Association Education and Research, Inc.; **2014**.
255. Sarma AV, Wei JT. Clinical practice. **Benign prostatic hyperplasia** and lower urinary tract symptoms. N Engl J Med. 2012 Jul 19;367(3):248-57.
256. **NICE**: National Institute for Health and Clinical Excellence. Management of **urinary incontinence in neurological disease**: management of lower urinary tract dysfunction in neurological disease (Clinical guideline CG148.) 2012. http://guidance.nice.org.uk/CG148.
257. Stafne S, Salvesen K, Romundstad P, et al. Does regular exercise including **pelvic floor muscle** training prevent urinary and anal incontinence during **pregnancy**? A randomised controlled trial. BJOG. 2012 Sep;119(10):1270-1280.
258. Wilson S, Broders J. **Dutasteride/Tamsulosin (Jalyn)** for Benign Prostatic Hyperplasia. Am Fam Physician. 2012;85(12):1159-1200.
259. O'Halloran T, Bell RJ, Robinson PJ, Davis SR. Urinary Incontinence in **Young Nulligravid Women**: A Cross-sectional Analysis. Ann Intern Med. 2012 Jul 17;157(2):87-93.
260. Vande Griend JP, Linnebur SA. Inhaled Anticholinergic Agents and Acute Urinary Retention in Men with Lower Urinary Tract Symptoms or Benign Prostatic Hyperplasia (September). Ann Pharmacother. 2012 Jul 31.
261. Wolosker N, de Campos JR, Kauffman P, et al. A randomized placebo-controlled trial of **oxybutynin** for the initial treatment of palmar and axillary **hyperhidrosis**. J Vasc Surg. 2012 Jun;55(6):1696-700.
262. Cañete P, Ortiz E, Domingo S, Cano A. **Transobturator suburethral tape** in the treatment of stress urinary incontinence: Efficacy and quality of life after 5 year follow up. Maturitas. 2012 Dec 3.
263. King AB, Wolters JP, Klausner AP, Rapp DE. Vaginal Symptoms and Sexual Function After **Tension-free Vaginal Tape**-obturator Placement: Minimum 12-Month Follow-up. Urology. 2012 Nov 29.
264. Deshpande AV, Caldwell PH, Sureshkumar P. Drugs for **nocturnal enuresis in children (other than desmopressin and tricyclics).** Cochrane Database Syst Rev. 2012 Dec 12;12:CD002238. doi: 10.1002/14651858.CD002238.pub2. There was not enough evidence to judge whether or not the included drugs cured bedwetting when used alone.
265. Tacklind J, Macdonald R, Rutks I, et al. **Serenoa repens (Saw palmetto)** for benign prostatic hyperplasia. Cochrane Database Syst Rev. 2012 Dec 12;12:CD001423. doi: 10.1002/14651858.CD001423.pub3. Serenoa repens, at double and triple doses, did not improve urinary flow measures or prostate size in men with lower urinary tract symptoms consistent with BPH.
266. Wagg A, Dale M, Tretter R, Stow B, Compion G. Randomised, Multicentre, Placebo-controlled, Double-blind Crossover Study Investigating the Effect of **Solifenacin and Oxybutynin in Elderly People with Mild Cognitive Impairment: The SENIOR** Study. Eur Urol. 2013 Jan 11.
267. Khandelwal C, Kistler C. **Diagnosis of Urinary Incontinence**. Am Fam Physician. 2013;87(8):543-550.
268. Carlson JJ, Hansen RN, Dmochowski RR, et al. Estimating the Cost-Effectiveness of **OnabotulinumtoxinA** for Neurogenic Detrusor Overactivity in the United States. Clin Ther. 2013 Mar 20.
269. Society of Obstetricians and Gynaecologists of Canada (**SOGC**). SOGC clinical practice guidelines: treatments for **overactive bladder**: focus on pharmacotherapy. J Obstet Gynaecol Can2012 Nov;34(11):1092-101.
270. Toren P, Margel D, et al. Effect of **dutasteride** on clinical progression of **benign prostatic hyperplasia** in asymptomatic men with enlarged prostate: a post hoc analysis of the **REDUCE** study. BMJ. 2013 Apr 15;346:f2109.
271. Wagg A, Khullar V, Marschall-Kehrel D, et al. Flexible-dose **fesoterodine in elderly** adults with overactive bladder: results of the randomized, double-blind, placebo-controlled study of fesoterodine in an aging population trial. J Am Geriatr Soc. 2013 Feb;61(2):185-93.
272. Hersh L, Salzman B. Clinical **Management of Urinary Incontinence in Women**. Am Fam Physician. 2013;87(9):634-640.
273. Morlock R, Goodwin B, Gomez Rey G, Eaddy M. Clinical Progression, Acute Urinary Retention, Prostate-Related Surgeries, and Costs in Patients with Benign Prostatic Hyperplasia Taking **Early Versus Delayed Combination 5α-Reductase Inhibitor Therapy and α-Blocker** Therapy: A Retrospective Analysis. Clin Ther. 2013 Apr 12.
274. Weiss JP, Jumadilova Z, Johnson TM 2nd, et al. Efficacy and safety of **flexible dose fesoterodine** in men and women with overactive bladder symptoms including nocturnal urinary urgency. J Urol. 2013 Apr;189(4):1396-401.
275. van Leijsen SA, Kluivers KB, Mol BW, et al. Value of **urodynamics** before stress urinary incontinence surgery: a randomized controlled trial. Obstet Gynecol. 2013 May;121(5):999-1008.
276. Nitti VW, Auerbach S, Martin N, Calhoun A, Lee M, Herschorn S. Results of a randomized phase III trial of **mirabegron** in patients with overactive bladder. J Urol. 2013 Apr;189(4):1388-95.
277. Berghmans B, Hendriks E, Bernards A, et al. **Electrical stimulation with non-implanted electrodes for urinary incontinence in men**. Cochrane Database Syst Rev. 2013 Jun 6;6:CD001202. There was some evidence that electrical stimulation enhanced the effect of PFMT in the short term but not after six months. There were, however, more adverse effects (pain or discomfort) with electrical stimulation.
278. Nguyen K, Hunter KF, Wagg A. **Knowledge and understanding of urinary incontinence**: Survey of family practitioners in northern Alberta. Can Fam Physician. 2013 Jul;59(7):e330-7.
279. Caldwell PH, Nankivell G, Sureshkumar P. Simple behavioural interventions for **nocturnal enuresis in children**. Cochrane Database Syst Rev. 2013 Jul 19;7:CD003637. Simple behavioural methods may be superior to no active treatment but appear to be inferior to enuresis alarm therapy and some drug therapy (such as imipramine and amitriptyline). Simple behavioural therapies could be tried as first line treatment before considering enuresis alarm therapy or drug therapy, which may be more demanding and have adverse effects, although evidence supporting their efficacy is lacking.
280. FDA Sep/13 has approved a new device to treat urinary symptoms in men ages 50 and older with benign prostatic hyperplasia. The **UroLift system** is the first permanent implant on the market and relieves blocked or low urine flow by preventing enlarged prostate tissue from blocking the urethra.
281. **NICE**: National Institute for Health and Care Excellence. **Urinary incontinence in women**: the management of urinary incontinence in women. (Clinical guideline 171.) 2013. http://guidance.nice.org.uk/CG171.
282. Chancellor MB, Patel V, Leng WW, et al. **OnabotulinumtoxinA** improves quality of life in patients with neurogenic detrusor overactivity. Neurology. 2013 Aug 27;81(9):841-8.
283. Chancellor MB, Migliaccio-Walle K, Bramley TJ, et al. **Long-Term Patterns of Use and Treatment Failure With Anticholinergic Agents** for Overactive Bladder. Clin Ther. 2013 Sep 30.
284. Labrie J, Berghmans BL, Fischer K, et al. **Surgery versus physiotherapy** for stress urinary incontinence. N Engl J Med. 2013 Sep 19;369(12):1124-33.
285. Agur W, Riad M, Secco S, et al. **Surgical treatment of recurrent stress urinary incontinence** in women: a systematic review and meta-analysis of randomised controlled trials. Eur Urol. 2013 Aug;64(2):323-36.
286. van Kerrebroeck P, Chapple C, Drogendijk T, et al. Combination Therapy with **Solifenacin and Tamsulosin** Oral Controlled Absorption System in a Single Tablet for Lower Urinary Tract Symptoms in Men: Efficacy and Safety Results from the Randomised Controlled NEPTUNE Trial. Eur Urol. 2013 Aug 3.
287. Bird ST, Delaney JAC, Brophy JM, Etminam M, Skeldon SC, Hartzema AG. **Tamsulosin** treatment for benign prostatic hyperplasia and risk of severe hypotension in men aged 40-85 years in the United States: risk window analyses using between and within patient methodology. BMJ 2013 347:f6320.
288. Caldwell PH, Deshpande AV, Gontard AV. Management of **nocturnal enuresis**. BMJ. 2013 Oct 29;347:f6259.
289. Hagen S, Stark D, Glazener C, et al. Individualised **pelvic floor muscle training** in women with pelvic organ prolapse (POPPY): a multicentre randomised controlled trial. Lancet. 2013 Nov 27.
290. Rudnicki M, Laurikainen E, Pogosean R, et al. **Anterior colporrhaphy compared with collagen-coated transvaginal mesh** for anterior vaginal wall prolapse: a randomised controlled trial. BJOG. 2013 Oct 1. Our
291. Ayeleke RO, Hay-Smith EJ, Omar MI. **Pelvic floor muscle training** added to another active treatment versus the same active treatment alone for urinary incontinence in women. Cochrane Database Syst Rev. 2013 Nov 20;11:CD010551. This systematic review found insufficient evidence to state whether or not there were additional effects of adding PFMT to other active treatment when compared with the same active treatment alone for urinary incontinence (SUI, UUI or MUI) in women.
292. Robert M, Schulz JA, Harvey MA. Technical update on **pessary** use. J Obstet Gynaecol Can. 2013 Jul;35(7 eSuppl):S1-11.
293. Liem S, Schuit E, Hegeman M, Bais J, et al. **Cervical pessaries** for prevention of preterm birth in women with a multiple pregnancy (ProTWIN): a multicentre, open-label randomised controlled trial. Lancet. 2013 Oct 19;382(9901):1341-9
294. Mangera A, Apostolidis A, Andersson KE, et al. An Updated Systematic Review and Statistical Comparison of Standardised Mean Outcomes for the Use of **Botulinum Toxin** in the Management of Lower Urinary Tract Disorders. Eur Urol. 2013 Nov 1. pii: S0302-2838(13)01109-3.
295. National Institute for Health and Care Excellence (**NICE**). **Mirabegron** for treating symptoms of overactive bladder. London (UK): National Institute for Health and Care Excellence (NICE); 2013 Jun.
296. Hilde G, Stær-Jensen J, Siafarikas F, Ellström Engh M, Bø K. **Postpartum pelvic floor muscle training** and urinary incontinence: a randomized controlled trial. Obstet Gynecol. 2013 Dec;122(6):1231-8.

297. Nam RK, Cheung P, Herschorn S, et al. Incidence of complications other than urinary incontinence or erectile dysfunction after radical prostatectomy or radiotherapy for **prostate cancer**: a population-based cohort study. Lancet Oncol. 2014 Jan 16
298. Chang SR, Chen KH, Lin HH, et al. Association of **mode of delivery** with urinary incontinence and changes in urinary incontinence over the first year **postpartum**. Obstet Gynecol. 2014 Mar;123(3):568-77.
299. Robert M, Girard I, Brennand E, et al. **Absorbable mesh augmentation compared with no mesh** for anterior prolapse: a randomized controlled trial. Obstet Gynecol. 2014 Feb;123(2 Pt 1):288-94.
300. Rai BP, Cody JD, Alhasso A, Stewart L. **Anticholinergic drugs versus non-drug** active therapies for non-neurogenic overactive bladder syndrome in adults. Cochrane Database of Systematic Reviews 2012, Issue 12. Art. No.: CD003193. DOI: 10.1002/14651858.CD003193.pub4.
301. Casabé A, Roehrborn CG, et al. Efficacy and safety of the coadministration of **tadalafil once daily with finasteride** for 6 months in men with lower urinary tract symptoms and prostatic enlargement secondary to benign prostatic hyperplasia. J Urol.2014 Mar.
302. Barber MD, Brubaker L, Burgio KL, et al. Comparison of **2 transvaginal surgical approaches and perioperative behavioral therapy** for apical **vaginal prolapse**: the OPTIMAL randomized trial. JAMA. 2014 Mar 12;311(10):1023-34.
303. Laurikainen E, Valpas A, Aukee P, et al. Five-year Results of a Randomized Trial Comparing **Retropubic and Transobturator Midurethral Slings** for Stress Incontinence. Eur Urol. 2014 Jan 31.
304. Park C, Park J, Choo MS, et al. A randomised, prospective double-blind, **propiverine-controlled trial of imidafenacin** in patients with overactive bladder. Int J Clin Pract. 2014 Feb;68(2):188-96
305. Cho HJ, Shin SC, Seo DY, et al. Comparison of **alfuzosin 10 mg with or without propiverine** 10 mg, 20 mg in men with lower urinary tract symptom and an overactive bladder: randomised, single-blind, prospective study. Int J Clin Pract. 2014 Jan 29.
306. Anger JT, Mueller ER, Tarnay C, et al. **Robotic compared with laparoscopic sacrocolpopexy**: a randomized controlled trial.Obstet Gynecol. 2014 Jan;123(1):5-12
307. Hung KJ et al. **Urinary incontinence, depression, and economic outcomes** in a cohort of women between the ages of 54 and 65 years. Obstet Gynecol 2014 Apr; 123:822.
308. Pisansky TM, Pugh SL, Greenberg RE, et al. **Tadalafil** for prevention of erectile dysfunction **after radiotherapy for prostate cancer**: the Radiation Therapy Oncology Group [0831] randomized clinical trial. JAMA. 2014 Apr 2;311(13):1300-7.
309. Roehrborn CG et al. Effects of **tadalafil** once daily on maximum urinary flow rate in men with lower urinary tract symptoms suggestive of **benign prostatic hyperplasia**. J Urol 2014 Apr; 191:1045.
310. Abrams P, Kelleher C, Staskin D, et al. Combination Treatment with **Mirabegron and Solifenacin** in Patients with Overactive Bladder: Efficacy and Safety Results from a Randomised, Double-blind, Dose-ranging, Phase 2 Study (Symphony). Eur Urol. 2014 Feb 19.
311. Drug treatment. In: Lucas MG, Bedretdinova D, Bosch JLHR, Burkhard F, Cruz F, Nambiar AK, de Ridder DJMK, Tubaro A, Pickard RS. **Guidelines on urinary incontinence**. Arnhem (The Netherlands): **European** Association of Urology (EAU); 2013 Mar.
312. Dmochowski RR, Staskin DR, Duchin K, et al. Clinical safety, tolerability and efficacy of **combination tolterodine/pilocarpine** in patients with overactive bladder. Int J Clin Pract. 2014 Mar 25.
313. Elterman DS, Kaplan SA. **Lower urinary tract symptoms** in a 66-year-old man. CMAJ. 2014 Apr 15;186(7):525-7.
314. Boyd K, Hilas O**. α-Adrenergic Blockers** for the Treatment of Lower-Urinary-Tract Symptoms and Dysfunction in **Women**. Ann Pharmacother. 2014 Jun;48(6):711-22.
315. Health Canada May/14 **Surgical Mesh** - Complications Associated with Transvaginal Implantation for the Treatment of Stress Urinary Incontinence and Pelvic Organ Prolapse.
316. Kim S, Liu S, Tse V. **Management of urinary incontinence** in adults. Australian Prescriber 37.1. 2014.
317. Sturm RM, Guralnick ML, Stone AR, et al. Comparison of clinical outcomes between "**ideal**" and "**nonideal**" **transobturator male sling** patients for treatment of postprostatectomy incontinence. Urology. 2014 May;83(5):1186-9.
318. van der Ploeg JM, van der Steen A, Oude Rengerink K, et al. **Prolapse surgery** with or without stress incontinence surgery for **pelvic organ prolapse**: a systematic review and meta-analysis of randomised trials. BJOG. 2014 Apr;121(5):537-47.
319. Myers DL. **Female Mixed Urinary Incontinence**-A Clinical Review. JAMA. 2014;311(19):2007-2014. doi:10.1001/jama.2014.4299.
320. Preston MA, Wilson KM, Markt SC, et al. **5α-Reductase Inhibitors and Risk of High-Grade or Lethal Prostate Cancer**. JAMA Intern Med. 2014 Jun 2.
321. Rees J, Bultitude M, Challacombe B. The management of **lower urinary tract symptoms in men**. BMJ. 2014 Jun 24;348:g3861.
322. Wu JM, Matthews CA, Conover MM, et al. **Lifetime risk of stress urinary incontinence or pelvic organ prolapse surgery**. Obstet Gynecol. 2014 Jun;123(6):1201-6.
323. Gravas S, Bachmann A, Descazeaud A, et al. Guidelines on the management of **non-neurogenic male lower urinary tract symptoms (LUTS), including benign prostatic obstruction (BPO).** Arnhem (The Netherlands): European Association of Urology (EAU); 2014 Apr.
324. D'Silva KA, Dahm P, Wong CL. Does this **man** with lower urinary tract symptoms have **bladder outlet obstruction**?: The Rational Clinical Examination: a systematic review. JAMA. 2014 Aug 6;312(5):535-42.
325. Hollingsworth JM, Wilt TJ. **Lower urinary tract symptoms in men**. BMJ. 2014 Aug 14;349:g4474.
326. Qaseem A, Dallas P, Forciea MA, et al; Clinical Guidelines Committee of the American College of Physicians. **Nonsurgical management** of urinary incontinence in women: a clinical practice guideline from the american college of physicians. (**ACP**) Ann Intern Med. 2014 Sep 16;161(6):429-40.
327. Wood LN, Anger JT. **Urinary incontinence in women**. BMJ. 2014 Sep 15;349:g4531.
328. Prieto J, Murphy CL, Moore KN, et al. **Intermittent catheterisation** for long-term bladder management. Cochrane Database Syst Rev. 2014 Sep 10;9:CD006008. Despite a total of 31 trials, there is still no convincing evidence that the incidence of UTI is affected by use of aseptic or clean technique, coated or uncoated catheters, single (sterile) or multiple-use (clean) catheters, self-catheterisation or catheterisation by others, or by any other strategy. Results from user-reported outcomes varied. The current research evidence is weak and design issues are significant. More well-designed trials are strongly recommended. Such trials should include analysis of cost-effectiveness because there are likely to be substantial differences associated with the use of different catheter designs, catheterisation techniques and strategies.
329. American Urogynecologic Society and American College of Obstetricians and Gynecologists. Committee opinion: **evaluation of uncomplicated stress urinary incontinence in women before surgical treatment**. Female Pelvic Med Reconstr Surg. 2014 Sep-Oct;20(5):248-51.
330. Baird DC, Seehusen DA, Bode DV, **Enuresis in Children**: A Case-Based Approach. Am Fam Physician. 2014;90(8):560-568.
331. Ebell MH, Radke T, Gardner J. A systematic review of the efficacy and safety of **desmopressin for nocturia in adults**. J Urol. 2014 Sep;192(3):829-35.
332. Pearson R, Williams PM. Common Questions About the Diagnosis and **Management of Benign Prostatic Hyperplasia**. Am Fam Physician. 2014;90(11):769-774.
333. Liao CH, Kuo HC. How to choose first-line treatment for **men with predominant storage lower urinary tract symptoms**: a prospective randomised comparative study. Int J Clin Pract. 2014 Dec 11.
334. Prieto J, Murphy CL, Moore KN, Fader M. **Intermittent catheterisation for long-term bladder management**. Cochrane Database Syst Rev. 2014 Sep 10;9:CD006008. Despite a total of 31 trials, there is still no convincing evidence that the incidence of UTI is affected by use of aseptic or clean technique, coated or uncoated catheters, single (sterile) or multiple-use (clean) catheters, self-catheterisation or catheterisation by others, or by any other strategy. Results from user-reported outcomes varied. The current research evidence is weak and design issues are significant. More well-designed trials are strongly recommended. Such trials should include analysis of cost-effectiveness because there are likely to be substantial differences associated with the use of different catheter designs, catheterisation techniques and strategies.
335. Rahn DD, Carberry C, Sanses TV, et al. Society of Gynecologic Surgeons Systematic Review Group. **Vaginal estrogen for genitourinary syndrome** of **menopause**: a systematic review. Obstet Gynecol. 2014 Dec;124(6):1147-56.
336. Nassau D, Avulova S, Friedman FM, et al. Prediction of **Nocturia Severity in Men**: Nocturnal Urine Overproduction vs Race or Metabolic Risk Factors. JAMA Surg. 2014 Dec 10.
337. Wiegersma M, Panman CM, Kollen BJ, Berger MY, Lisman-Van Leeuwen Y, Dekker JH. Effect of **pelvic floor muscle training compared** with **watchful waiting** in older women with symptomatic mild **pelvic organ prolapse**: randomised controlled trial in primary care. BMJ 2014;349:g7378.
338. Garely AD, Noor N. Diagnosis and surgical treatment of **stress urinary incontinence**. Obstet Gynecol. 2014 Nov;124(5):1011-27 **.**
339. Nankivell G, Caldwell P. **Paediatric urinary incontinence**. Aust Prescr. 2014;37:192-5.
340. van Kerrebroeck PE. Experience with the long-term use of **desmopressin for nocturnal enuresis** in children and adolescents. BJU Int. 2002 Mar;89(4):420-5.
341. Anderson CA, Omar MI, Campbell SE, et al. Conservative **management for postprostatectomy urinary incontinence**. Cochrane Database Syst Rev. 2015 Jan 20;1:CD001843. The value of the various approaches to conservative management of postprostatectomy incontinence after radical prostatectomy remains uncertain. The evidence is conflicting and therefore rigorous, adequately powered randomised controlled trials (RCTs) which abide by the principles and recommendations of the CONSORT statement are still needed to obtain a definitive answer. The trials should be robustly designed to answer specific well constructed research questions and include outcomes which are important from the patient`s perspective in decision making and are also relevant to the healthcare professionals. Long-term incontinence may be managed by an external penile clamp, but there are safety problems.

342. Hsu A, Nakagawa S, Walter LC, et al. The **burden of nocturia among middle-aged and older women**. Obstet Gynecol. 2015 Jan;125(1):35-43.
343. Garely AD, Noor N. Diagnosis and **Surgical Treatment** of Stress Urinary Incontinence. Obs&Gyn Nov 2014;124(5):1011-1027.
344. Wong AS, Cheung CW, Yeung SW, et al. **Transcervical intralesional vasopressin injection** compared with placebo in hysteroscopic myomectomy: a randomized controlled trial. Obstet Gynecol. 2014 Nov;124(5):897-903.
345. Al-Abri M, Wong BM, Leis JA. A **urinary catheter left in place for slightly too long**: a teachable moment. JAMA Intern Med. 2015 Feb 1;175(2):163.
346. Chughtai B, Mao J, Buck J, et al. Use and risks of **surgical mesh for pelvic organ prolapse** surgery in women in New York state: population based cohort study. BMJ. 2015 Jun 2;350:h2685.
347. Gill JD, Biyani CS. **Frequent urination** causing **sleepless nights** in a 64-year-old man. CMAJ. 2015 Mar 17;187(5):348-9.
348. Pickard R, Starr K, MacLennan G, et al. **Medical expulsive therapy** in adults with ureteric colic: a multicentre, randomised, placebo-controlled trial. Lancet 2015; online May 19.
349. van der Ploeg J, Oude Rengerink K, van der Steen A, et al. **Transvaginal prolapse repair** with or without the addition of a **midurethral sling** in women with genital prolapse and stress urinary incontinence: a randomised trial. BJOG. 2015 Mar 9.
350. Ford AA, Rogerson L, Cody JD, Ogah J. **Mid-urethral sling operations for stress urinary incontinence in women**. Cochrane Database Syst Rev 2015;7:CD006375, doi:10.1002/ 14651858.CD006375.pub3. Mid-urethral sling operations have been the most extensively researched surgical treatment for stress urinary incontinence (SUI) in women and have a good safety profile. Irrespective of the routes traversed, they are highly effective in the short and medium term, and accruing evidence demonstrates their effectiveness in the long term. This review illustrates their positive impact on improving the quality of life of women with SUI. With the exception of groin pain, fewer adverse events occur with employment of a transobturator approach. When comparing transobturator techniques of a medial-to-lateral versus a lateral-to-medial insertion, there is no evidence to support the use of one approach over the other. However, a bottom-to-top route was more effective than top-to-bottom route for retropubic tapes.A salient point illustrated throughout this review is the need for reporting of longer-term outcome data from the numerous existing trials. This would substantially increase the evidence base and provide clarification regarding uncertainties about long-term effectiveness and adverse event profile.
351. Oelke M, Becher K, Castro-Diaz D, et al. **Appropriateness of oral drugs for long-term treatment** of lower urinary tract symptoms in **older persons**: results of a systematic literature review and international consensus validation process (LUTS-FORTA 2014). Age Ageing. 2015 Jun 23
352. Shin DC, Shin SH, Lee MM, et al. **Pelvic floor muscle training** for urinary incontinence in female stroke patients: A randomized, controlled and blinded trial. Clin Rehabil. 2015 Apr 10.
353. Spence MM, Karim FA, Lee EA, et al. **Risk of Injury in Older Adults** Using **Gastrointestinal Antispasmodic and Anticholinergic Medications**. J Am Geriatr Soc. 2015 Jun;63(6):1197-202.
354. Subak LL, King WC, Belle SH, et al. Urinary **Incontinence Before and After Bariatric Surgery**. JAMA Intern Med. 2015 Jun 22.
355. Oelke M, Becher K, Castro-Diaz D, et al. Appropriateness of **oral drugs for long-term treatment of lower urinary tract symptoms in older persons**: results of a systematic literature review and international consensus validation process (LUTS-FORTA 2014). Age Ageing. 2015 Jun 23.
356. Detollenaere RJ, den Boon J, Stekelenburg J, et al. **Sacrospinous hysteropexy versus vaginal hysterectomy** with suspension of the uterosacral ligaments in women with uterine prolapse stage 2 or higher: multicentre randomised non-inferiority trial. BMJ. 2015 Jul 23;351:h3717.
357. Furyk JS, Chu K, Banks C, et al. **Distal Ureteric Stones and Tamsulosin**: A Double-Blind, Placebo-Controlled, Randomized, Multicenter Trial. Ann Emerg Med. 2015 Jul 13.
358. Huang W, Xue P, Zong H, et al. Efficacy and safety of **silodosin** in the **medical expulsion therapy** for distal ureteral calculi: a systematic review andmeta-analysis. Br J Clin Pharmacol. 2015 Aug 10.
359. Pickard R, Starr K, MacLennan G, et al. Use of drug therapy in the management of symptomatic **ureteric stones** in hospitalised adults: a multicentre, placebo-controlled, randomised controlled trial and cost-effectiveness analysis of a calcium channel blocker (**nifedipine**) and an alpha-blocker (**tamsulosin**) (the **SUSPEND** trial). Health Technol Assess. 2015 Aug;19(63):1-172.
360. Stenzelius K, Molander U, Odeberg J, et al. The effect of **conservative treatment of urinary incontinence among older and frail older people**: a systematic review. Age Ageing. 2015 Jun 25.
361. Knowles CH, Horrocks EJ, Bremner SA, et al; **CONFIDeNT** study group. **Percutaneous tibial nerve stimulation versus sham electrical stimulation** for the treatment of **faecal incontinence** in adults (CONFIDeNT): a double-blind, multicentre, pragmatic, parallel-group, randomized controlled trial. Lancet. 2015 Aug 17.
362. Setty P, Redekal L, et al. **Vaginal estrogen** use and effects on **quality of life and urogenital morbidity** in postmenopausal women after publication of the Women's Health Initiative in New York City. Menopause. 2015 Aug 8.
363. Welk B, Al-Hothi H, Winick-Ng J. **Removal or Revision of Vaginal Mesh** Used for the Treatment of Stress Urinary Incontinence. JAMA Surg. 2015 Sep 9:1-9.
364. Welk B, McArthur E, Fraser L-A, et al. The risk of **fall and fracture with the initiation of a prostate-selective α antagonist (tamsulosin...)**: a population based cohort study. BMJ 2015;351:h5398.
365. **NICE**: National Clinical Guideline Centre for Acute and Chronic Conditions. **Lower urinary tract symptoms in men: assessment and management**. London (UK): National Institute for Health and Care Excellence (NICE); 2015 Jun.
366. Shaw C, Tansey R, Jackson C, Hyde C, Allan R. **Barriers to help seeking** in people with urinary symptoms. Fam Pract. 2001 Feb;18(1):48-52.
367. Caldwell PH, Sureshkumar P, Kerr MI, et al. A randomised controlled trial of a **code-word enuresis alarm**. Arch Dis Child. 2015 Dec 8. pii: archdischild-2015-308564.
368. Hajiha M, Elterman D. **Urinary urgency and frequency** in a 53-year-old woman. CMAJ. 2016 Jan 5;188(1):59-60.
369. Imamura M, Williams K, Wells M, et al. **Lifestyle interventions** for the treatment of **urinary incontinence in adults**. Cochrane Database Syst Rev. 2015 Dec 2;12:CD003505. Evidence for the effect of weight loss on urinary incontinence is building and should be a research priority. Generally, there was insufficient evidence to inform practice reliably about whether lifestyle interventions are helpful in the treatment of urinary incontinence.
370. Rudnicki M, Laurikainen E, et al. A 3-year follow-up after **anterior colporrhaphy compared with collagen-coated transvaginal mesh** for anterior vaginal wall prolapse: a randomised controlled trial. BJOG. 2015 Sep 30.
371. Wang RC. **Managing Urolithiasis**. Ann Emerg Med. 2015 Nov 23.
372. Coker TJ, Dierfeldt DM. **Acute Bacterial Prostatitis**: Diagnosis and Management. Am Fam Physician. 2016;93(2):114-120.
373. Pickard R, Starr K, MacLennan G, et al. Use of drug therapy in the management of **symptomatic ureteric stones** in hospitalised adults: a multicentre, placebo-controlled, randomised controlled trial and cost-effectiveness analysis of a calcium channel blocker (**nifedipine**) and an alpha-blocker (**tamsulosin**) (the **SUSPEND** trial). Health Technol Assess 2015;19:1–172.
374. Schollhammer M et al. **Oxybutynin** as a treatment for **generalized hyperhidrosis**: A randomized, placebo-controlled trial. Br J Dermatol 2015 Nov; 173:1163.
375. Azoulay L, Eberg M, Benayoun S, et al. **5α-Reductase Inhibitors** and the Risk of Cancer-Related Mortality in Men With **Prostate Cancer**. JAMA Oncol. 2015 Jun;1(3):314-20
376. Morgan MS, Pearle MS. Medical **management of renal stones**. BMJ. 2016 Mar 14;352:i52.
377. Panman C, Wiegersma M, Kollen BJ, et al. Two-year effects and cost-effectiveness of **pelvic floor muscle training** in mild pelvic organ prolapse: a randomised controlled trial in primary care. BJOG. 2016 Mar 21.
378. Tahtinen RM, Cartwright R, Tsui JF, et al. Long-term Impact of **Mode of Delivery on Stress Urinary Incontinence and Urgency** Urinary Incontinence: A Systematic Review and Meta-analysis. Eur Urol. 2016 Feb 10.
379. Cheung RYK et al. **Vaginal pessary** in women with symptomatic **pelvic organ prolapse**: A randomized controlled trial. Obstet Gynecol 2016 Jun 6; [e-pub].
380. Chua ME, Silangcruz JM, Chang SJ, et al. **Desmopressin Withdrawal** Strategy for **Pediatric Enuresis**: A Meta-analysis. Pediatrics. 2016 Jun 24.
381. Hsu LF, Liao YM, et al. Beneficial effects of **biofeedback-assisted pelvic floor muscle training** in patients with urinary incontinence **after radical prostatectomy**: systematic review & metaanalysis. Int J Nur Stud. 2016 Aug;60:99-111.
382. Brasure M, MacDonald R, Dahm P, et al. **Newer medications for lower urinary tract symptoms attributed to benign prostatic hyperplasia**: A review. Comparative Effectiveness Review No. 178. Rockville (MD): Agency for Healthcare Research and Quality (US); 2016 May. AHRQ Publication No. 16-EHC024-EF
383. Olivera CK, Meriwether K, El-Nashar S, et al. **Nonantimuscarinic treatment for overactive** bladder: a systematic review. Am J Obstet Gynecol. 2016 Jul;215(1):34-57.
384. Wang RC et al. Effect of **tamsulosin** on stone passage for **ureteral stones**: A systematic review and meta-analysis. Ann Emerg Med 2016 Sep 8.
385. Amundsen CL, Richter HE, Menefee SA, et al. **OnabotulinumtoxinA vs Sacral Neuromodulation** on Refractory Urgency Urinary Incontinence in Women: A Randomized Clinical Trial. JAMA. 2016 Oct 4;316(13):1366-1374.
386. Carbone A, Fuschi A, Al Rawashdah SF, et al. Management of lower urinary tract symptoms associated with **benign prostatic hyperplasia** in elderly patients with a new diagnostic, therapeutic and care pathway. Int J Clin Pract. 2016 Sep;70(9):734-43.
387. Lier D, Robert M, Tang S, et al. **Surgical** treatment of stress urinary **incontinence-trans-obturator tape compared with tension-free vaginal tape**-5-year follow up: an economic evaluation. BJOG. 2016 Aug 10.
388. Prieto J, Murphy CL, Moore KN, Fader M. **Intermittent catheterisation** for long-term bladder management. Cochrane Database Syst Rev. 2014 Sep 10;(9):CD006008. Despite a total of 31 trials, there is still no convincing evidence that the incidence of UTI is affected by use of aseptic or clean technique, coated or uncoated catheters, single (sterile) or multiple-use (clean) catheters, self-catheterisation or catheterisation by others, or by any other strategy. Results from user-reported outcomes varied. The current research evidence is weak and design issues are significant. More well-designed trials are strongly recommended. Such trials should include analysis of cost-effectiveness because there are likely to be substantial differences associated with the use of different catheter designs, catheterisation techniques and strategies.
389. Chughtai B, Barber MD, et al. Association Between the Amount of **Vaginal Mesh Used** With Mesh Erosions and Repeated Surgery After Repairing Pelvic Organ Prolapse and Stress Urinary Incontinence. JAMA Surg. 2016 Nov 30.

390. Dahm P, Brasure M, MacDonald R, et al. **Comparative Effectivenes of Newer Medications** for Lower Urinary Tract Symptoms Attributed to **Benign Prostatic Hyperplasia**: A Systematic Review and Meta-analysis. Eur Urol. 2016 Oct 4.
391. Hollingsworth JM, Canales BK, Rogers MA, et al. **Alpha blockers for treatment of ureteric stones**: systematic review and meta-analysis. BMJ. 2016 Dec 1;355:i6112.
392. Newgreen D, Bosman B, Hollestein-Havelaar A, et al. **Solifenacin** in **Children and Adolescents** with Overactive Bladder: Results of a Phase 3 Randomised Clinical Trial. Eur Urol. 2016 Sep 26.
393. Brincat C, Brubaker L. **Mesh, graft, or standard repair for prolapse surgery**? Lancet. 2016 Dec 20.
394. Dekker JH. **Pelvic organ prolapse**: prevention by training? Lancet. 2016 Dec 20.
395. Glazener CM, Breeman S, Elders A, et al. **Mesh, graft, or standard repair** for women having primary transvaginal anterior or posterior compartment **prolapse surgery**: two parallel-group, multicentre, randomised, controlled trials (PROSPECT). Lancet. 2016 Dec 20.
396. Hagen S, Glazener C, McClurg D, et al. **Pelvic floor muscle training** for secondary prevention of pelvic organ prolapse (**PREVPROL**): a multicentre randomised controlled trial. Lancet. 2016 Dec 20.
397. McAchran SE, Goldman HB. **Synthetic midurethral slings redeemed**. Lancet. 2016 Dec 20.
398. Morling JR, McAllister DA, Agur W, et al. Adverse events after first, **single, mesh and non-mesh surgical procedures** for stress urinary incontinence and pelvic organ prolapse in Scotland, 1997-2016: a population-based cohort study. Lancet. 2016 Dec 20.
399. Stewart F, Gameiro LF, El Dib R, et al. **Electrical stimulation with non-implanted electrodes** for overactive bladder in adults. Cochrane Database Syst Rev. 2016 Dec 9;12:CD010098.
400. Suskind AM, Cawthon PM, Nakagawa S, et al. **Urinary Incontinence in Older Women**: The Role of Body Composition and Muscle Strength: From the Health, Aging, and Body Composition Study. J Am Geriatr Soc. 2016 Dec 5
401. Culbertson S, Davis AM. **Nonsurgical Management of Urinary Incontinence** in Women. JAMA. 2017 Jan 3;317(1):79-80.
402. Maund E, Schow Guski L, Gotzsche PC. Considering **benefits and harms of duloxetine** for treatment of **stress urinary incontinence**: a meta-analysis of clinical study reports. CMAJ . Online. Nov 14, 2016.
403. Berkseth KE, Thirumalai A, Amory JK. Pharmacologic Therapy in Men's Health: **Hypogonadism, Erectile Dysfunction, and Benign Prostatic Hyperplasia**. Med Clin North Am. 2016 Jul;100(4):791-805.
404. Shepshelovich D, Schechter A, Calvarysky B, et al. **Medication-induced SIADH**: distribution and characterization according to medication class. Br J Clin Pharmacol. 2017 Feb 7.
405. Welk B, McArthur E, Ordon M, et al. Association of **Suicidality and Depression With 5alpha-Reductase Inhibitors (eg. Finasteride)**. JAMA Intern Med. 2017 Mar 20.
406. Drake MJ, MacDiarmid S, Chapple CR, et al. **Cardiovascular safety** in refractory incontinent patients with overactive bladder receiving **add-on mirabegron therapy to solifenacin** (BESIDE). Int J Clin Pract. 2017 Apr 16.
407. Jun JEJ, Kinkade A, Tung ACH, et al. **5α-Reductase Inhibitors** for Treatment of **Benign Prostatic Hyperplasia**: A Systematic Review and Meta-Analysis. Can J Hosp Pharm. 2017 Mar-Apr;70(2):113-119.
408. Vedanayagam M, Kumar A, Madaan S. **Lower urinary tract symptoms in an older man**. BMJ. 2017 Apr 18;357:j1493.
409. Cho S, Kwon SS, Lee KW, et al. A multicenter real-life study of the efficacy of an **alpha-blocker with or without anticholinergic agent (imidafenacin)** treatment in patients with **lower urinary tract symptoms**/benign prostatic hyperplasia and storage symptoms. Int J Clin Pract. 2017 May;71(5).
410. Fralick M, Kesselheim AS. FDA Approval of **Desmopressin for Nocturia**. JAMA. 2017 May 23;317(20):2059-2060.
411. MHRA May/17 **Finasteride: rare reports of depression and suicidal thoughts**.
412. **Nice**: **Hyperhidrosis- oxybutynin** Mar 2017. https://www.nice.org.uk/advice/es10/chapter/key-points
413. Fusco F, Abdel-Fattah M, Chapple CR, et al. Updated Systematic Review and Meta-analysis of the Comparative Data on **Colposuspensions, Pubovaginal slings, and Midurethral tapes** in the Surgical Treatment of Female **Stress Urinary Incontinence**. Eur Urol. 2017 May 4.
414. Health Canada Jul/17 recently examined the risk of serious muscle-related side effects with **finasteride**, including **rhabdomyolysis**, myopathy and muscle disorders such as pain, weakness, atrophy or stiffness. The safety review was undertaken following 11 Canadian reports of serious muscle-related events in patients treated with oral finasteride 1 mg (Propecia, generics) and finasteride 5 mg (Proscar, generics).
415. Liu Z, Liu Y, Xu H, et al. Effect of **electroacupuncture** on urinary leakage among women with **stress urinary incontinence**: a randomized clinical trial. JAMA. doi:10.1001/jama .2017.7220
416. Carvalhais A, Natal JR, Bø K. **Performing high-level sport** is strongly associated with urinary incontinence in elite athletes: a comparative study of 372 elite female athletes and 372 controls. Br J Sports Med. 2017 Jun 22.
417. Iglesia CB, Smithling KR. **Pelvic Organ Prolapse**. Am Fam Physician. 2017;96(3):179-185.
418. Sakalis VI;Karavitakis M;Bedretdinova D;Bach T;Bos. **Medical Treatment of Nocturia in Men with Lower Urinary Tract Symptoms**: Systematic Review by the European Association of Urology Guidelines Panel for Male Lower Urinary Tract Symptoms. Eur Urol. 2017 Jun 27.
419. Kobashi KC, Albo ME, Dmochowski RR, et al. **Surgical treatment of female stress urinary incontinence: AUA/SUFU guideline**. Linthicum (MD): American Urological Association Education and Research, Inc.; 2017 Mar.
420. Lukacz ES, Santiago-Lastra Y, Albo ME, Brubaker L. **Urinary Incontinence in Women**: A Review. JAMA. 2017 Oct 24;318(16):1592-1604.
421. Muth CC. **Urinary Incontinence in Women (patient information).** JAMA. 2017 Oct 24;318(16):1622.
422. Jung JH, Kim J, MacDonald R, et al. **Silodosin** for the treatment of lower urinary tract symptoms in men with **benign prostatic hyperplasia**. Cochrane Database Syst Rev. 2017 Nov 22;11:CD012615. Silodosin may reduce urologic symptom scores in an appreciable number of men compared to placebo. Quality of life and treatment withdrawals for any reason appears similar. Its efficacy appears similar to that of other alpha blockers (tamsulosin, naftopidil and alfuzosin) but the rate of sexual side effects is likely higher. Our certainty in the estimates of effect was lowered due to study limitations, inconsistency and imprecision.
423. Tsai J-D et al. Association between **allergic disease, sleep-disordered breathing, and childhood nocturnal enuresis**: A population-based case-control study. Pediatr Nephrol 2017 Dec; 32:2293.
424. Stewart F, Berghmans B, Bø K, Glazener CMA. **Electrical stimulation with non-implanted devices for stress urinary incontinence in women**. Cochrane Database of Systematic Reviews 2017, Issue 12. Art. No.: CD012390. The current evidence base indicated that electrical stimulation is probably more effective than no active or sham treatment, but it is not possible to say whether ES is similar to PFMT or other active treatments in effectiveness or not. Overall, the quality of the evidence was too low to provide reliable results.Without sufficiently powered trials measuring clinically important outcomes, such as subjective assessment of urinary incontinence, we cannot draw robust conclusions about the overall effectiveness or cost-effectiveness of electrical stimulation for stress urinary incontinence in women.
425. Geoffrion R. **SOGC No. 283-Treatments for Overactive Bladder: Focus on Pharmacotherapy**. J Obstet Gynaecol Can. 2018 Jan;40(1):e22-e32.
426. Geoffrion R. **SOGC No. 353-Treatments for Overactive Bladder: Focus on Pharmacotherapy - An Addendum**. J Obstet Gynaecol Can. 2017 Dec;39(12):1221-1229.
427. Heneghan C, Aronson JK, Goldacre B, et al. **Transvaginal mesh failure**: lessons for regulation of implantable devices. BMJ. 2017 Dec 7;359:j5515.
428. Chughtai B, Thomas D, Sun T, et al. **Failures of Sacral Neuromodulation** for Incontinence. JAMA Surg. 2018 Feb 14.
429. Franco JV, Turk T, Jung JH, et al. **Non-pharmacological interventions for treating chronic prostatitis/chronic pelvic pain syndrome**. Cochrane Database Syst Rev. 2018 Jan 26;1:CD012551. Some of the interventions can decrease prostatitis symptoms in an appreciable number without a greater incidence of adverse events. The QoE was mostly low.
430. Hubb AJ, Stachowicz AM, Wood SC. **OnabotulinumtoxinA Injections** for Urge Incontinence. Am Fam Physician. 2018 Feb 1;97(3):Online.
431. Komesu YM, Amundsen CL, Richter HE, et al. **Refractory urgency urinary incontinence treatment in women**: impact of age on outcomes and complications. Am J Obstet Gynecol. 2018 Jan;218(1):111.e1-111.e9.
432. Trabuco EC, Linder BJ, Klingele CJ, et al. Two-Year Results of **Burch Compared With Midurethral Sling With Sacrocolpopexy**: A Randomized Controlled Trial. Obstet Gynecol. 2018 Jan;131(1):31-38.
433. Warsi QA, Huang AJ, Hess R, et al. Association of Pharmacologic **Treatment of Urgency Urinary Incontinence With Sleep Quality** and Daytime Sleepiness. Obstet Gynecol. 2018 Feb;131(2):204-211.
434. Welk B, McArthur E, Ordon M, et al. **Association of suicidality and depression with 5α-reductase inhibitors.** JAMA Intern Med. 2017;177:683-91.
435. Stewart F, Berghmans B, Bø K, Glazener CM. **Electrical stimulation withnon-implanted devices for stress urinary incontinence in women**. Cochrane Database Syst Rev. 2017 Dec 22;12:CD012390.
436. Heneghan Carl, Aronson Jeffrey K, Goldacre Ben, Mahtani Kamal R, Plüddemann Annette, Onakpoya Igho et al. **Transvaginal mesh failure: lessons for regulation of implantable devices** BMJ 2017; 359 :j5515
437. Kallner HK, Christensson AA, Elmér C, Flam B, Altman D. **Safety and efficacy of mirabegron in daily clinical practice: a prospective observational study**. Eur J Obstet Gynecol Reprod Biol. 2016 Aug;203:167-72.
438. Katoh T, Kuwamoto K, Kato D, Kuroishi K. **Real-world cardiovascular assessment of mirabegron treatment in patients with overactive bladder and concomitant cardiovascular disease: Results of a Japanese post-marketing study**. Int J Urol. 2016 Sep 13.
439. Rosa GM, Ferrero S, Nitti VW, Wagg A, et al. **Cardiovascular Safety of β3-adrenoceptor Agonists for the Treatment of Patients with Overactive Bladder Syndrome**. Eur Urol. 2016 Feb;69(2):311-23.
440. Altman D, Rogers RG, Yin L, et al. **Cancer Risk After Midurethral Sling Surgery Using Polypropylene Mesh**. Obstet Gynecol. 2018 Mar;131(3):469-474
441. Golding JF, et al. The Effects of the **Selective Muscarinic M3 Receptor Antagonist Darifenacin, and of Hyoscine (scopolamine), on Motion Sickness, Skin Conductance & Cognitive Function**. Br J Clin Pharmacol. 2018 Mar 9.

442. Tutolo M, Ammirati E, Heesakkers J, et al. Efficacy and Safety of **Sacral and Percutaneous Tibial Neuromodulation in Non-neurogenic Lower Urinary Tract Dysfunction and Chronic Pelvic Pain**: A Systematic Review of the Literature. Eur Urol. 2018 Jan 11.
443. Amundsen CL, Komesu YM, Chermansky C, et al. Two-Year Outcomes of **Sacral Neuromodulation Versus OnabotulinumtoxinA** for Refractory Urgency Urinary Incontinence: A Randomized Trial. Eur Urol. 2018 Feb 23.
444. Yoshida M, Takeda M, Gotoh M, et al. **Vibegron**, a Novel Potent and Selective beta3-Adrenoreceptor Agonist, for the Treatment of Patients with Overactive Bladder: A Randomized, Double-blind, Placebo-controlled Phase 3 Study. Eur Urol. 2018 Jan 20.
445. Hagan KA, Erekson E, Austin A, et al. A prospective study of the natural history of urinary incontinence in women. Am J Obstet Gynecol. 2018 May;218(5):502.e1-502.e8.
446. Smith TJ, Loprinzi CL, Deville C. Oxybutynin for Hot Flashes Due to Androgen Deprivation in Men. N Engl J Med. 2018 May 3;378(18):1745-1746.
447. Drake MJ, Chapple C, Esen AA, et al. **Efficacy and Safety of Mirabegron Add-on Therapy** to Solifenacin in Incontinent Overactive Bladder Patients with an Inadequate Response to Initial 4-Week Solifenacin Monotherapy: A Randomised Double-blind Multicentre Phase 3B Study (BESIDE). Eur Urol. 2016 Jul;70(1):136-145.
448. Franco JVA, Turk T, Jung JH, Xiao YT, Iakhno S, Garrote V, Vietto V. **Non-pharmacological** interventions for **treating chronic prostatitis/chronic pelvic pain** syndrome. Cochran e Database of Systematic Reviews 2018, Issue 5. Art. No. : CD012551. Based on the findings of moderate quality evidence, this review found that some non-pharmacological interventions such as acupuncture and extracorporeal shockwave therapy are likely to result in a decrease in pr ostatitis symptoms and may not be associated with a greater incidence of adverse event.
449. Herschorn S, Chapple CR, Abrams P, et al. Efficacy and **safety of combinations of mirabegron and solifenacin** compared with monotherapy and placebo in patients with overactive bladder (SYNERGY study). BJU Int. 2017 Oct;120(4):562-575.
450. Fernandes L, Martin D, Hum S. A case of the giggles: **Diagnosis and management of giggle incontinence**. Can Fam Physician. 2018 Jun;64(6):445-447.
451. Foster HE, Barry MJ, Dahm P, et al. **Surgical Management of Lower Urinary Tract Symptoms** Attributed to Benign Prostatic Hyperplasia: AUA (American Urological Association) Guideline. J Urol. 2018 Jun 11.
452. Meltzer AC, Burrows PK, Wolfson AB, et al. Effect of **tamsulosin on passage of symptomatic ureteral stones**: a randomized clinical trial [online June 18, 2018]. JAMA Intern Med. doi:10.1001/jamainternmed.2018.2259
453. Gratzke C, van Maanen R, Chapple C, et al. **Long-term Safety and Efficacy of Mirabegron and Solifenacin in Combination Compared with Monotherapy in Patients with Overactive Bladder: A Randomised, Multicentre Phase 3 Study (SYNERGY II).** Eur Urol. 2018 Jun 1.
454. Nelson HD, Cantor A, Pappas M, et al. **Screening** for Urinary Incontinence in Women: A Systematic Review for the Women's Preventive Services Initiative. Ann Intern Med. 2018 Aug 14.
455. Tullman M, Chartier-Kastler E, Kohan A, et al. Low-dose **onabotulinumtoxin A** improves urinary symptoms in noncatheterizing patients with MS. Neurology. 2018 Aug 14;91(7):e657-e665.
456. Balk E, Adam GP, Kimmel H, et al. **Nonsurgical Treatments for Urinary Incontinence in Women**: A Systematic Review Update. AHRQ Publication No. 18-EHC016-EF. PCORI Publication No. 2018-SR-03. Rockville, MD: Agency for Healthcare Research and Quality; August 2018.
457. Diokno AC, Newman DK, Low LK, et al. Effect of **Group-Administered Behavioral Treatment** on Urinary Incontinence in Older Women: A Randomized Clinical Trial. (GLADIOLUS) JAMA Intern Med. 2018 Sep 4.
458. Nickel JC, Aaron L, Barkin J, et al. Canadian Urological Association (CUA) guideline on **male lower urinary tract symptoms/benign prostatic hyperplasia** (MLUTS/BPH): 2018 update. Can Urol Assoc J 2018;12:303-12.
459. Xu D, Huang L, Gao J, Li J, et al. Effects of an education program on **toileting behaviors and bladder symptoms in overactive bladder patients with type 2 diabetes**: A randomized clinical trial. Int J Nurs Stud. 2018 Jul 8;87:131-139.
460. Amundsen CL, Richter HE, Menefee SA, Komesu YM, Arya LA, Gregory WT, Myers DL, Zyczynski HM, Vasavada S, Nolen TL, Wallace D, Meikle SF. **OnabotulinumtoxinA vs Sacral Neuromodulation on Refractory Urgency Urinary Incontinence in Women**: A Randomized Clinical Trial. JAMA. 2016 Oct 4;316(13):1366-1374.
461. Chughtai B, Thomas D, Sun T, Sedrakyan **A. Failures of Sacral Neuromodulation for Incontinence.** JAMA Surg. 2018 May 1;153(5):493-494
462. Dumoulin C, Cacciari LP, Hay-Smith EJC **Pelvic floor muscle training versus no treatment**, or inactive control treatments, for urinary incontinence in women. Cochrane Database Syst Rev. 2018 Oct 4;10:CD005654. Based on the data available, we can be confident that PFMT can cure or improve symptoms of SUI and all other types of UI. It may reduce the number of leakage episodes, the quantity of leakage on the short pad tests in the clinic and symptoms on UI-specific symptom questionnaires. The authors of the one economic evaluation identified for the Brief Economic Commentary reported that the cost-effectiveness of PFMT looks promising. The findings of the review suggest that PFMT could be included in first-line conservative management programmes for women with UI. The long-term effectiveness and cost-effectiveness of PFMT needs to be further researched.
463. Lamerton TJ, Torquati L, Brown WJ. **Overweight and obesity** as major, modifiable risk factors for urinary incontinence in young to mid-aged women: a systematic review and meta-analysis. Obes Rev. 2018 Sep 19.
464. Serlin DC, Heidelbaugh JJ, Stoffel JT. **Urinary Retention in Adults**: Evaluation and Initial Management Am Fam Physician. 2018;98(8):496-503.
465. Gurol-Urganci I, Geary RS, Mamza JB, et al. Long-term **Rate of Mesh Sling Removal** Following Midurethral Mesh Sling Insertion Among Women With Stress Urinary Incontinence. JAMA. 2018 Oct 23;320(16):1659-1669.
466. O'Reilly N, Nelson HD, Conry JM, Frost J, et al; Women's Preventive Services Initiative. **Screening for Urinary Incontinence in Women**: A Recommendation From the Women's Preventive Services Initiative. Ann Intern Med. 2018 Sep 4;169(5):320-328.
467. Serati M, Andersson KE, Dmochowski R, et al. Systematic Review of **Combination Drug Therapy** for Non-neurogenic Lower Urinary Tract Symptoms**.** Eur Urol. 2018 Oct 4.
468. Pattanaik S, Mavuduru RS, Panda A, et al**. Phosphodiesterase inhibitors** for lower urinary tract symptoms consistent with benign prostatic hyperplasia. Cochrane Database Syst Rev. 2018 Nov 16;11:CD010060. Compared to placebo, PDEI likely leads to a small reduction in IPSS-total and BPHII sores, with a possible increase in AEs. There may be no differences between PDEI and AB with regards to improvement in IPSS-total, BPHII, and incidence of AEs. There appears to be no added benefit of PDEI combined with AB compared to PDEI or AB alone or PDEI combined with 5-ARI compared to ARI alone with regards to urinary symptoms. Most evidence was limited to short-term treatment up to 12 weeks and of moderate or low certainty.
469. Yeowell G, Smith P, Nazir J, et al. Real-world persistence and **adherence to oral antimuscarinics and mirabegron in patients with overactive bladder** (OAB): a systematic literature review. BMJ Open. 2018 Nov 21;8(11):e021889.
470. Wagg A, Khullar V, Marschall-Kehrel D, et al. Flexible-dose **fesoterodine in elderly adults with overactive bladder**: results of the randomized, double-blind, placebo-controlled study of fesoterodine in an aging population trial. J Am Geriatr Soc. 2013 Feb;61(2):185-93.
471. Blomquist JL, Muñoz A, Carroll M, et al. Association of **Delivery Mode With Pelvic Floor Disorders After Childbirth**. JAMA. 2018 Dec 18;320(23):2438-2447.
472. Unger JM, Hershman DL, Till C, et al. Using Medicare Claims to **Examine Long-term Prostate Cancer Risk of Finasteride** in the Prostate Cancer Prevention Trial. J Natl Cancer Inst. 2018 Nov 1;110(11):1208-1215.
473. Wallerstedt A, Strom P, Gronberg H, et al. Risk of **Prostate Cancer in Men Treated With 5α-Reductase Inhibitors**-A Large Population-Based Prospective Study. J Natl Cancer Inst. 2018 Nov 1;110(11):1216-1221.
474. Herdman M, Nazir J, Hakimi Z, et al. **Assessing preference-based outcome measures for overactive bladder**: an evaluation of patient reported outcome data from the BESIDE clinical trial. Patient 2017;10:677–86
475.] Drake MJ, MacDiarmid S, Al-Shukri S, et al. **Adding mirabegron to solifenacin** to treat overactive bladder has little impact on postvoid residual volume or urinary retention risk. Urology 2017;104:1–4.
476. Gibson W, MacDiarmid S, Huang M, et al. **Treating overactive bladder in older patients with a combination of mirabegron and solifenacin**: a prespecified analysis from the BESIDE study. Eur Urol Focus 2017;3:629–38
477. Roehrborn C, Casabé A, Glina S, Sorsaburu S, Henneges C, Viktrup L. Treatment satisfaction and clinically meaningful symptom improvement in men with lower urinary tract symptoms and prostatic enlargement secondary to benign prostatic hyperplasia: secondary results from a 6-month, randomized, double-blind study comparing finasteride plus tadalafil with finasteride plus placebo. Int J Urol 2015;22:582–7.
478. Ghuman A, de Jonge SW, Dryden SD, et al**. Prophylactic use of alpha-1 adrenergic blocking agents** for prevention of postoperative urinary retention: A review & meta-analysis of randomized clinical trials. Am J Surg. 2018 May;215(5):973-979.
479. Jiwrajka M, Yaxley W, Ranasinghe S, et al. **Drugs for benign prostatic hypertrophy**. Aust Prescr. 2018 Oct;41(5):150-153.
480. Mitcheson HD, Samanta S, Muldowney K, et al. **Vibegron** (RVT-901/MK-4618/KRP-114V) Administered **Once Daily as Monotherapy or Concomitantly with Tolterodine** in Patients with an Overactive Bladder: A Multicenter, Phase IIb, Randomized, Double-blind, Controlled Trial. Eur Urol. 2019 Feb;75(2):274-282.
481. Cerruto MA, D'Elia C, Aloisi A, Fabrello M, Artibani W. **Prevalence, incidence and obstetric factors' impact on female urinary incontinence in Europe: a systematic review**. Urol Int. 2013;90(1):1-9.
482. Balk EM, Rofeberg VN, Adam GP, et al. Pharmacologic and Nonpharmacologic **Treatments for Urinary Incontinence in Women**: A Systematic Review and Network Meta-analysis of Clinical Outcomes. Ann Intern Med. 2019 Mar 19.
483. Wieland LS, Shrestha N, Lassi ZS, et al**. Yoga for treating** urinary incontinence in women. Cochrane Database Syst Rev. 2019 Feb 28;2:CD012668. We identified few trials on yoga for incontinence, and the existing trials were small and at high risk of bias. In addition, we did not find any studies of economic outcomes related to yoga for urinary incontinence. Due to the lack of evidence to answer the review question, we are uncertain whether yoga is useful for women with urinary incontinence. Additional, well-conducted trials with larger sample sizes are needed.

484. Health Canada Mar/19: Summary safety review – **Proscar and Propecia** (finasteride). Assessing the potential risk of suicidal thoughts and/or behaviour (suicidal ideation). February 26, 2019. https://hpr-rps.hres.ca/reg-content/summary-safety-review-detail.php?lang=en&linkID=SSR00218 (accessed March 11, 2019).
485. Karavitakis M, Kyriazis I, Omar MI, et al. Management of **Urinary Retention in Patients with Benign Prostatic Obstruction**: A Systematic Review and Meta-analysis. Eur Urol. 2019 Feb 14.
486. Wei L, Lai EC, Kao-Yang YH, et al. Incidence **of type 2 diabetes mellitus in men receiving steroid 5α-reductase inhibitors**: population based cohort study. BMJ. 2019 Apr 10;365:l1204.
487. Brazzelli M, Javanbakht M, Imamura M, et al. **Surgical treatments for women with stress urinary incontinence**: **the ESTER** systematic review and economic evaluation. Health Technol Assess. 2019 Mar;23(14):1-306.
488. Jelovsek JE, Ploeg JMV, Roovers JP, et al. **Validation of a Model Predicting De Novo Stress Urinary Incontinence** in Women Undergoing Pelvic Organ Prolapse Surgery. Obstet Gynecol. 2019 Apr;133(4):683-690.
489. Murphy C, Cowan A, Moore K, Fader M. **Managing long term indwelling urinarycatheters**. BMJ. 2018 Oct 11;363:k3711.
490. Balk EM, Adam GP, Corsi K, et al. **Adverse Events Associated with Nonsurgical Treatments** for Urinary Incontinence in Women: a Systematic Review. J Gen Intern Med. 2019 May 6.
491. Imamura M, Hudson J, Wallace SA, et al. **Surgical interventions for women** with stress urinary incontinence: systematic review and network meta-analysis of randomised controlled trials. BMJ. 2019 Jun 5;365:l1842.
492. Kaplan SA, Chughtai BI. **Safety of Tamsulosin**: A Systematic Review of Randomized Trials with a Focus on Women and Children. Drug Saf. 2018 Sep;41(9):835-842.
493. Taranto-Montemurro L, Messineo L, Sands SA, et al. The Combination of **Atomoxetine and Oxybutynin Greatly Reduces Obstructive Sleep Apnea Severity**. A Randomized, Placebo-controlled, Double-Blind Crossover Trial. Am J Respir Crit Care Med. 2019 May 15;199(10):1267-1276.
494. **Health Canada July/19**: has completed a safety review of **non-absorbable synthetic surgical mesh** for the transvaginal (implanted through the vagina) repair of pelvic organ prolapse (POP) in Canada. The review found that non-absorbable synthetic transvaginal mesh should no longer be used for a certain type of POP repair, and that it should only be used in specific patient groups for other types of POP repair.
495. Sandhu JS, Breyer B, Comiter C, et al. Incontinence **after Prostate Treatment**: AUA/SUFU Guideline. J Urol. 2019 May 6:101097JU0000000000000314.
496. Tadrous M, Matta R, Greaves S, et al. Association of **Mirabegron With the Risk of Arrhythmia** in Adult Patients 66 Years or Older-A Population-Based Cohort Study. JAMA Intern Med. 2019 Jul 15.
497. Brown HW, Braun EJ, Wise ME, et al. **Small-Group, Community-Member Intervention** for Urinary and Bowel Incontinence: A Randomized Controlled Trial. Obstet Gynecol. 2019 Aug 7.
498. Kondo K, Noonan KM, Freeman M, et al. **Efficacy of Biofeedback for Medical Conditions**: an Evidence Map. J Gen Intern Med. 2019 Aug 14.
499. Martin J, Chandler W, Speakman M**. Investigating chronic urinary retention**. BMJ. 2019 Jul 25;366:l4590.
500. Gray SL, Semla TP. **Post-finasteride syndrome**. BMJ. 2019 Aug 9;366:l5047.
501. Hu JS, Pierre E; **Urinary Incontinence in Women**: Evaluation and Management. Am Fam Physician. 2019; 100(6):339-348.
502. Schulten SFM, Detollenaere RJ, Stekelenburg J, et al. **Sacrospinous hysteropexy versus vaginal hysterectomy** with uterosacral ligament suspension in women with uterine prolapse stage 2 or higher: observational follow-up of a multicentre randomised trial. BMJ. 2019 Sep 10;366:l5149.
503. Sung VW, Borello-France D, Newman DK, et al. Effect of Behavioral and **Pelvic Floor Muscle Therapy Combined With Surgery vs Surgery Alone** on Incontinence Symptoms Among Women With Mixed Urinary Incontinence: The ESTEEM Randomized Clinical Trial. JAMA. 2019 Sep 17;322(11):1066-1076.
504.

Saskatchewan Ministry of Health: Publicly Funded Vaccines for Selected Special Populations [1]

[Excerpted from Saskatchewan Immunization Manual (Chapter 7; Appendix 7.1, Revised **May 2016**)]

Condition [2]	H. influenzae b **(Hib)**	Hepatitis A **(HA)***	Hepatitis B **(HBV)***	Meningococcal	Pneumococcal	MMR	Vari-cella **(Var)**
Bleeding disorders		X	X				
Cerebrospinal fluid leak, including hydrocephaly				X[14]	X[12]		
Children under grade 6 whose families immigrated to Canada from regions of intermediate or high HBV prevalence			X				
Chronic heart or lung disease					X[12]		
Chronic kidney disease (hemo or peritoneal) dialysis, pre-dialysis [3, 4]			X		X[12]	C [6]	C [6]
Chronic liver disease including alcoholism, Hep C, Hep B, cirrhosis		X	X		X[12]		
Cochlear implant candidate or [5, 11]	X			X[14]	X[12]		
Congenital immunodeficiency (e.g., complement, properidin, factor D deficiency). Rotavirus CI	X			X[14]	X[12]	C [6]	C [6]
Cystic fibrosis					X[12]		
Diabetes mellitus					X[12]		
Hematopoietic stem cell transplant (HSCT) recipient [5, 7]	X	X	X	X[14]	X	C [6]	C[6]
HIV	X		X[13]	X[15]	X[12]	C [6]	C[6]
Homelessness					X		
Immunosuppression related to disease or medical therapy	X			X[14]	X[12]	C [6]	C[6]
Individuals living in facilities for the developmentally challenged			X		X		
Infants at high risk of HBV infection at birth related to mother's status or risk of infection [8]	X		X	X	X		
Illicit drug users (all methods of use) [9]		X	X		X		
Males and females with multiple sexual partners [9]			X				
Men who have sex with men		X	Not funded in SK				
Meningococcal disease case contacts				X			
Percutaneous or mucosal blood and body fluid exposure [9]			X				
Sexual assault (when presenting within 14 days of incident) [9]			X				
Splenic disorders [5, 10, 11]	X			X[14]	X[12]		
Solid organ transplant, including islet cell candidates or recipients [5]	X	X liver	X liver, kidney	X	X[12]	C [6]	C[6]
Malignancies	X				X[12]	C [6]	C [6]
Sickle Cell disease	X			X[14]	X[12]		

* Pre-immunization serology is strongly recommended if lifestyle and behavioural risks are factors.

C – CONTRAINDICATED

Footnotes **Saskatchewan** Immunization Manual Chapter 7 – **Immunization of Special Populations Jan. 2015 (Parts updated May 2016)** http://www.health.gov.sk.ca/sim-chapter7
The Saskatchewan Immunization Manual (amended 2012 - 2016) http://www.ehealthsask.ca/services/manuals/pages/sim.aspx

1 For more information on specific vaccines, refer to SIM, Chapter 10, Biological Products.
2 For more information about specific conditions, refer to the specific condition in SIM, Chapter 7, Immunization of Special Populations.
3 Refer in SIM, Chapter 7, Immunization of Special Populations, Appendix 7.4: Hepatitis B Immunization Algorithm for Clients with Chronic Kidney Disease.
4 Refer to Appendix 7.4: Hepatitis B Immunization Algorithm for Clients with Chronic Kidney Disease for appropriate dosages and products appropriate for client's age.
5 Province of surgery transplant physician/team or specialist and SK MHO to determine immunizations.
6 Medical consultations are required; refer to Appendix 7.2: Varicella Immunization Referral Form and Appendix 7.3 MMR Immunization Referral Form. Refer to the specific immune-suppressing condition in SIM, Chapter 7, Special Populations and specific vaccine in SIM, Chapter 10, Biological Products.
7 HSCT recipients require re-immunization due to the ablation of hematopoietic cells in the bone marrow pre-transplant.
8 Refer to SIM, Chapter 7, Special Populations, Section 4.2, Infants Born to HBsAg Positive Mother or High Risk for HB≥ 2000g.
9 Refer to Saskatchewan Guidelines for the Management of Potential Exposures to Hepatitis B, Hepatitis C, HIV, and Recommendations for Post-Exposure Prophylaxis, available at: http://www.ehealthsask.ca/services/manuals/Pages/default.aspx
10 Vaccination with the age-appropriate primary series should be completed for children less than 5 years who have a splenic disorder. 1 Hib dose is required for those 5 years and older regardless of previous Hib immunization history.
11 Includes sickle cell disease, thalassemia major, essential thrombocytopenia, other hemoglobinopathies, celiac disease, and inflammatory bowel disease.
12 1 dose for Pneu-C-13 naïve children 60 months up to and including 17 years of age
13 40ug for those ≥18 years; double dose for those birth up to and including 17 years of age.
14 a high-risk child 12 months of age or older, or an adult who is cohort eligible for a Men-C-C, does not required Men-C-C vaccine when they are eligible to receive Men-C-ACYW-135 vaccine
15 Children up to and including 17 years of age only.
16 eHealth Saskatchewan Panorama Information Bulletin 0022. Quick Reference: *Publicly Funded Vaccine Eligibility and Panorama Risk Factor Category*. Rev. 2016-04-18. http://www.ehealthsask.ca/services/panorama/immun/Documents/Bulletin%200022%20Publicly%20Funded%20Vaccine%20Eligibility%20and%20Risk%20Factor%20Category.doc Accessed June 28 2016.

↓Genital wart age 9-26 NACI;ACIP→yes ♀; ♂routine age 11-12, age 13-26 ok.
Anal Cancer Prevention ♀& ♂, FDA approved Gardasil age 9-45. Cervarix: not ♂ approved.
Also in CDN in ♀ age 27-45, to ↓genital warts & cervical/vulvar cancer.
Cervarix ♀ age 9-14yr & Gardasil ♀ ♂ age 9-13yr: CDN 2 dose option@ 0 & 6-12mos.

1) Breaking the "cold chain"

Canadian Guidelines: Refrigerated vaccines should be stored between +2°C and +8°C. Frozen vaccines should be stored at -15°C or colder. Store light sensitive vaccines away from light. Follow manufacturer recommendations for storage & transport. Administration requires someone trained to give im/sc injections.

Fridges:

-Fridge used should be dedicated to the storage of vaccines only.
-****Use of bar fridges for vaccine storage is the leading cause of cold chain breaks in Canada. Bar fridges are not recommended for the purpose of storing vaccines.**
- Keeping temperature of fridge stable **(2-8° C)**: Avoid opening refrigerator door unnecessarily, store containers of water in refrigerators, or ice packs in the freezer
NEVER store vaccines in the vegetable bin section of the refrigerator. Ideal storage location for vaccine: In the middle compartment, away from floor, coils, walls, and venting for the freezer or cold air.
-Temperature of the compartments of the refrigerator where the vaccine is stored should be checked and logged at least twice a day. Fridge temperatures outside of the 2 to 8 degree C range must be reported immediately to obtain recommendation on the stability of the affected product.
- Fridge temperature recording logs should be retained for 2 years.
- Min-Max thermometer batteries should be routinely changed twice a year: December 1 and June 1 and the date of changing noted on the device.

Transporting Refrigerated Vaccines: Avoid breaking the cold chain

1) Transport vaccines in insulated containers at all times. Hard sided plastic insulated containers, or Styrofoam containers with walls at least 2 inch thick walls should be used. Icepacks should be placed inside the transport container to maintain the cold chain. To prevent freezing the vaccine should never be placed directly onto an ice pack. Instead an insulating barrier (i.e. bubble wrap, Styrofoam peanuts) should be placed between vaccine and ice pack.
2) Make sure vaccine is never placed in trunk of vehicle, or in direct contact with sunlight. Also the vaccine should not be placed in line with the air from the vehicles heater or air conditioner. Vaccine should never be left in a vehicle unattended.
3) If a break in the cold chain identified prior to administration of the vaccine, contact your local public health authority about the appropriate course of action. While waiting for a decision, ensure that the vaccine is stored in appropriate cold chain conditions. The vaccine should not be administered until a decision has been reached.
4) If a break in the cold chain is identified after administration of the vaccine, contact your local public health authority. The type of vaccine, duration and temperature of the exposure will be taken into account in order to determine the course of action. Serological testing or revaccination may be suggested.

Further information: available from the Public Health Agency of Canada's Website. References:

1) Vaccine Storage and Handling Guidelines. Pharmacists letter/Prescriber's letter. May 2008-Volume 24-Number 240517.
2) Canadian Immunization Guide 2006.
3) National Vaccine Storage and Handling Guidelines for immunization providers (2007). Public Health Agency of Canada. http://www.phac-aspc.gc.ca/publicat/2007/nvshglp-ldemv/index-eng.php (Good link for additional information); Other: http://www.vaccineinformation.org/;

References

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[1] Therapeutic Choices 5rd Edition
[2] Micromedex 2018
[3] Advisory Committee on Immunization Practices (**ACIP**). Recommended adult immunization schedule: USA, 2009*. Ann Intern Med. 2009 Jan 6;150(1):40-4. Also accessible via : http://www.cdc.gov/mmwr/preview/mmwrhtml/mm5753a6.htm
Committee on Infectious Diseases, Recommended **Childhood and Adolescent** Immunization Schedules--United States, **2010**. Pediatrics 2010 125: 195-196.
Advisory Committee on Immunization Practices. Recommended **Adult Immunization** Schedule: United States, **2010**. Ann Intern Med January 5, 2010 152:36-39.
http://www.annals.org/content/152/1/36.full.pdf+html ; http://www.cdc.gov/mmwr/preview/mmwrhtml/mm5901a5.htm?s_cid=mm5901a5_x
ACIP: Advisory Committee on Immunization Practices. Recommended **Adult Immunization** Schedule: **United States, 2011**. Ann Intern Med February 1, 2011 154:168-173.
CDC. **General recommendations on immunization practices**; by ACIP. MMWR Recomm Rep. 2011;60(RR-02):1–60 http://www.cdc.gov/mmwr/pdf/rr/rr6002.pdf
ACIP: Recommended **Adult Immunization Schedule**: United States, 2012. Advisory Committee on Immunization Practices. Ann Intern Med E-388 ahead of print January 31, 2012.
AAP/ACIP: Recommended **Childhood and Adolescent** Immunization Schedules—United States, 2012. Committee on Infectious Diseases. Pediatrics 2012; 129:2 385-386.
ACIP: Recommended **Adult Immunization Schedule**: United States, **2014**. Advisory Committee on Immunization Practices. Ann Intern Med Feb 2014.
AAP/ACIP: Recommended **Childhood and Adolescent** Immunization Schedules—United States, **2014**. Committee on Infectious Diseases. Pediatrics **2014**; 133:2 Feb, 2014.
Committee on Infectious Diseases. Recommended **Childhood and Adolescent Immunization Schedule-United States, 2015**. Pediatrics. 2015 Jan 26.
ACIP: Committee on Infectious Diseases. Recommended **Childhood and Adolescent Immunization** Schedule-United States, **2016**. Pediatrics. 2016 Feb 1.
Kim DK, Bridges CB, Harriman KH; Advisory Committee on Immunization Practices. Advisory Committee on Immunization Practices recommended immunization schedule for **adults aged 19 Years or older, United States, 2015**. Ann Intern Med. 2015;162:214-23.
Kim DK, Bridges CB, Harriman KH; Advisory Committee on Immunization Practices. (ACIP) Advisory Committee on Immunization Practices Recommended Immunization Schedule for **Adults Aged 19 Years or Older: United States, 2016.** Ann Intern Med. 2016 Feb 2;164(3):184-94.
ACIP: Committee on Infectious Diseases. Recommended **Childhood and Adolescent Immunization Schedules:** United States, 2018. Pediatrics. 2018 Feb 6.
ACIP Kim DK, Riley LE, Hunter P, et al. Recommended Immunization Schedule for **Adults Aged 19 Years or Older**, United States, 2018. Ann Intern Med. 2018 Feb 6;168(3):210-220.

2) Anaphylaxis Management with vaccine administration:

1) Patients should be kept under supervision for 15 minutes (JE-VAX: 30 minutes) following administration.
2) In order to treat anaphylaxis perform the following steps (note steps a-d should be performed rapidly or simultaneously, however the priority is to complete step a):
   a) **Promptly administer 0.01 mL/kg (maximum 0.5 mL) of aqueous epinephrine 1:1000 by intramuscular (or subcutaneous) injection in the opposite limb to that in which the vaccination was given (or the vastus lateralis). Prompt administration is essential**.
   b) Call for an ambulance
   c) Place the patient in a recumbent position, and elevate their feet.
   d) If necessary, establish an oral airway.
   e) Patients with severe reactions such as cyanosis, dyspnea, should be given oxygen if it is available. Pulse oximetry can be used to monitor if available.
   f) If the vaccine was administered subcutaneously, an additional dose of 0.005 mL/kg (maximum 0.3 mL) of aqueous epinephrine 1:1000, can be injected into the vaccination site to slow down absorption. This should be done shortly after administration of the first dose of epinephrine in moderate to severe cases, and generally should not be repeated. Local injection of epinephrine into an intramuscular vaccination site is contraindicated, as it speeds up absorption of the vaccine.
   g) A dose of diphenhydramine hydrochloride (Benadryl®) can be given as an adjunct to epinephrine. The oral route of diphenhydramine is preferred for conscious patients who are not seriously ill (as the intramuscular injection is painful). Oral dose: 1-2 mg/kg to a maximum single dose of 50 mg.
   h) An inhaled β-agonist should be considered if there is a bronchospasm resistant to an adequate dose of epinephrine (e.g., nebulized salbutamol 2.5-5.0 mg in 3 mL of saline or 1 puff per 3 kg to a maximum of 10 puffs by metered dose inhalers).
   i) Vital signs should be monitored continuously.
   j) Patient should be transported to emergency department for long term monitoring.

◆Epinephrine dosing can be repeated twice at 5-minute intervals if necessary, for a total of three doses. The limb in which the vaccination was given should be avoided. A different limb is preferred for each dose to maximize drug absorption.

3) **Breastfeeding and Vaccinations**: Immunizations for actively breastfeeding women are considered safe, with the exception of smallpox vaccine and yellow fever, by both the CDC and the American academy of pediatrics. Breastfeeding does not appear to influence the maternal immune response. Vaccines do not appear to affect the safety of breast milk for infants.[10,11]

[4] *Public Health Agency of Canada, http://www.phac-aspc.gc.ca/im/q_a_thimerosal-eng.php*
[5] Canadian Coalition for Immunization Awareness and Promotion, http://www.immunize.cpha.ca/en/publications-resources/questions/autism.aspx)
[6] Lancet retracts Wakefield paper linking MMR vaccine to autism (01Feb, 2010). http://www.thelancet.com/journals/lancet/article/PIIS0140-6736(10)60175-7/fulltext
Price, CS., Thompson, WW., Goodson, B, et al. Prenatal and Infant Exposure to Thimerosal From Vaccines and Immunoglobulins and Risk of Autism. Pediatrics 2010 0: peds.2010-0309.
[7] a) Ascherio A, Zhang SM, Hernán MA, Olek MJ, et al. Hepatitis B vaccination and the risk of multiple sclerosis. *N Engl J Med*. 2001 Feb 1;344(5):327-32). b) Demicheli V, Rivetti A, Di Pietrantonj C, Clements CJ, Jefferson T. *J Viral Hepat*. 2003 Sep;10(5):343-4. *Hepatitis B vaccination and multiple sclerosis: evidence from a systematic review.*
[8] Canadian Immunization Guide 2006
[9] Public Health Agency of Canada PHAC. Statement on recommended use of herpes zoster vaccine. Jan 2010. (NACI) Accessed online 03Feb10 at http://www.phac-aspc.gc.ca/publicat/ccdr-rmtc/10vp03/acs-1/index-eng.php .
[10] Kroger AT, Atkinson WL, Marcuse EK, Pickering LK, Advisory Committee on Immunization Practices (ACIP) Centers for Disease Control and Prevention (CDC). General recommendations on immunization: recommendations of the Advisory Committee on Immunization Practices (ACIP). MMWR Recomm Rep. 2006;55(RR-15): 1-48.
[11] Pickering LK, Baker CJ, Long SS, McMillan JA, eds. Red Book: 2006 Report of the Committee on Infectious Diseases. 27th ed. Elk Grove Village, IL: American Academy of Pediatrics.

Additional references:

Gerber JS, Offit PA. Vaccines and Autism: A Tale of Shifting Hypotheses. Clin Infect Dis. 2009 Jan 7. [Epub ahead of print]
Gruslin A, Steben M, Halperin S, et al. Immunization in pregnancy. J Obstet Gynaecol Can. 2008 Dec;30(12):1149-54.
Health Canada: HPV It's your health. Sept 2010: http://hc-sc.gc.ca/hl-vs/iyh-vsv/diseases-maladies/hpv-vph-eng.php
Hsu HE, Shutt KA, Moore MR, et al. Effect of pneumococcal conjugate vaccine on pneumococcal meningitis. N Engl J Med. 2009 Jan 15;360(3):244-56.
Huss A, Scott P, Stuck AE, Trotter C, Egger M. Efficacy of pneumococcal vaccination in adults: a meta-analysis. CMAJ. 2009 Jan 6;180(1):48-58. {InfoPOEMs Mar 2009. The evidence to support the efficacy of pneumococcal polysaccharide vaccine (PPV) in adults is limited at best. The best studies have not shown a consistent benefit, particularly in the most vulnerable populations that we currently target. The impact of increasing herd immunity due to infant vaccination using conjugate vaccines is another factor, although that is not addressed by this analysis. An accompanying editorial argues that some studies excluded for methodologic limitations should have been included, and vice versa, and called for additional well-designed studies in relevant populations rather than a cessation of the vaccination. {LOE = 1a-}.}
Juurlink DN, et al. Guillain-Barre syndrome after influenza vaccination in adults: a population-based study. Arch Intern Med. 2006 Nov 13;166(20):2217-21.
Kim JJ, et al. Cost-Effectiveness of Human Papillomavirus Vaccination & Cervical Cancer Screening in Women Older Than 30 Years in the USA. Ann Intern Med 2009; 538-545.
Medical Letter, Treatment Guidelines. **Adult Immunization**. Apr, 2009;7:27-36. Dec, 2011; 9(112):75-82. **Updated June 2014.**
Omer SB et al. Vaccine refusal, mandatory immunization, and the risks of vaccine-preventable diseases. N Engl J Med 2009 May 7; 360:1981.

Thompson WW, Vaccine Safety Datalink Team. Early thimerosal exposure and neuropsychological outcomes at 7 to 10 years.N Engl J Med. 2007 Sep 27;357(13):1281-92.
Tozzi AE, Bisiacchi P, Tarantino V, et al. Neuropsychological performance 10 years after immunization in infancy with thimerosal-containing vaccines. Pediatrics. 2009 Feb;123(2):475-82.

Canadian Pediatric Info: NACI:CIG Online Canadian Guidelines: www.naci.gc.ca

USA Pediatric Info: AAP/ACIP: Recommended **Childhood and Adolescent** Immunization Schedules—United States, **2018**. Committee on Infectious Diseases. Pediatrics 2018.
USA Catch-up Schedule for Aged 4Months Through 18Yrs who start late or who are more than 1 month behind-**2015**
http://www.cdc.gov/vaccines/schedules/downloads/child/catchup-schedule-pr.pdf

Additional references:

Aaby P, Whittle H, Stabell Benn C. Vaccine programmes must consider their effect on general **resistance**. BMJ. 2012 Jun 14;344:e3769.
AAP Policy Statement--**Prevention of Varicella**: Update of Recommendations for Use of Quadrivalent and Monovalent Varicella Vaccines in Children. Pediatrics. 2011 Aug 28.
AAP: American Academy of Pediatrics.Medical versus nonmedical immunization exemptions for child care and school attendance. Pediatrics 2016 Aug 29.
AAP Committee on Infectious Diseases. Recommendations for Serogroup B **Meningococcal** Vaccine for Persons 10 Years and Older. Pediatrics. 2016:138(3):e20161890
AAP Committee on Practice and Ambulatory Medicine, AAP Committee on Infectious Diseases, AAP Committee on State Government Affairs, AAP Council on School Health, AAP Section on Administration and Practice Management. Medical Versus Nonmedical Immunization **Exemptions** for Child Care and School Attendance. Pediatrics.2016:138(3):e20162145
AAP: Committee on Infectious Diseases. Recommendations for Prevention and Control of **Influenza in Children**, 2016-2017. Pediatrics. 2016 Sep 6.
AAP Committee on Infectious. Recommendations for Prevention and Control of **Influenza** in Children, 2017-2018. Pediatrics. 2017;140(4):e20172550
AAP Committee on Infectious Diseases and AAP Committee on Fetus and Newborn Elimination of **Perinatal Hepatitis B**: Providing the First Vaccine Dose Within 24 Hours of Birth. Pediatrics. 2017;140(3):e20171870
Abraham S, Juel HB, Bang P, et al. Safety and immunogenicity of the **chlamydia vaccine candidate CTH522** adjuvanted with CAF01 liposomes or aluminium hydroxide: a first-in-human, randomised, double-blind, placebo-controlled, phase 1 trial. Lancet Infect Dis. 2019 Aug 12.
Abu-Raya B, Edwards KM. **Optimizing the Timing of Vaccine Administration During Pregnancy**. JAMA. 2019 Feb 25.
Abu Raya B, Edwards KM, Scheifele DW, Halperin SA. **Pertussis** and **influenza** immunisation during pregnancy: a landscape review. Lancet Infect Dis 2017; online April 19.
ACIP: Committee on Infectious Diseases. Recommended **Childhood and Adolescent Immunization Schedules:** United States, 2018. Pediatrics. 2018 Feb 6.
ACIP Kim DK, Riley LE, Hunter P, et al. Recommended Immunization Schedule for **Adults Aged 19 Years or Older**, United States, 2018. Ann Intern Med. 2018 Feb 6;168(3):210-220.
ACOG Committee Opinion No. 741: **Maternal Immunization**. Obstet Gynecol. 2018 Jun;131(6):e214-e217.
ACOG Committee Opinion No. 732: Influenza **Vaccination During Pregnancy**. Obstet Gynecol. 2018 Apr;131(4):e109-e114.
Acosta A, Debolt C, Tasslimi A, et al. **Tdap vaccine** effectiveness among adolescents during the 2012 Washington State **pertussis** epidemic. Pediatrics. 2015
Ackerman LK, Serrano JL. **Update on Routine Childhood and Adolescent Immunizations**. Am Fam Physician. 2015 Sep 15;92(6):460-8.
ACOG-American College of Obstetricians and Gynecologists Committee on Obstetric Practice. ACOG Committee Opinion No. 608: **Influenza vaccination during pregnancy**. Obstet Gynecol. 20114 Sept..
Agénor M, Peitzmeier S, Gordon AR, et al. **Sexual Orientation Identity Disparities** in Awareness and Initiation of the **Human Papillomavirus Vaccine** Among U.S. Women and Girls: A National Survey. Ann Intern Med. 2015 Jul 21:1-11.
Ahmed AS, Khan NZ, Hussain M, et al. Follow-Up of Cases of **Haemophilus influenzae Type b** Meningitis to Determine Its Long-Term Sequelae. J Pediatr. 2013 Jul;163(1 Suppl):S44-9.
Ahmed T, Bhuiyan TR, Zaman K, et al. Vaccines for preventing enterotoxigenic **Escherichia coli (ETEC)** diarrhoea. Cochrane Database of Systematic Reviews 2013, Issue 7. Art. No.: CD009029. DOI: 10.1002/14651858.CD009029.pub2.
Ahuka-Mundeke S, Casey RM, Harris JB, et al. Immunogenicity of Fractional-Dose Vaccine during a **Yellow Fever** Outbreak -Preliminary Report. N Engl J Med. 2018 Feb 14.
Alexander K, Lacy TA, Myers AL, et al. Should Pediatric Practices Have Policies to Not Care for Children With **Vaccine-Hesitant Parents**? Pediatrics. 2016 Sep 2
Ali H, Donovan B, et al. Genital warts in young Australians five years into national **human papillomavirus vaccination** programme: national surveillance data. BMJ 2013;346:f2032.
Ali M, Nelson A, Luquero FJ, et al. Safety of a killed oral **cholera** vaccine (Shanchol) in pregnant women in Malawi: an observational cohort study. Lancet Infect Dis 2017; online Feb 1.
Aliabadi N, Wikswo ME, Tate JE, et al.Factors Associated With **Rotavirus Vaccine Coverage.** Pediatrics. 2019 Jan 17.
Allison MA et al. Primary care physicians' perspectives about HPV vaccine. Pediatrics 2016 Feb; 137:e20152488.
Allan, G. Michael, Ivers, Noah. The **autism-vaccine story**: fiction and deception? Can Fam Physician 2010 56: 1013.
American Academy of Pediatrics (AAP). Committee on Infectious Diseases. Recommendations for **prevention and control of influenza in children, 2011-2012**. Pediatrics. 2011 Oct;128(4):813-25.
Ames HMR, Glenton C, Lewin S. **Parents' and informal caregivers' views** and experiences of communication about routine childhood vaccination: a synthesis of qualitative evidence. Cochrane Database of Systematic Reviews 2017, Issue 2. Art. No.: CD011787. We have high or moderate confidence in the evidence contributing to several review findings. Further research, especially in rural and low- to middle-income country settings, could strengthen evidence for the findings where we had low or very low confidence. Planners should consider the timing for making vaccination information available to parents, the settings where information is available, the provision of impartial and clear information tailored to parental needs, and parents' perceptions of health workers and the information provided.
Amirthalingam G, Andrews N, Campbell H, et al. Effectiveness of **maternal pertussis vaccination** in England: an observational study. Lancet 2014;online July 16.
Amirthalingam G, et al. Evaluation of effect of the **herpes zoster** vaccination programme 3 years after its introduction in England: population-based study. Lancet Public Health. 2017Dec21.
Anderson, Evan J., Rupp, Angela, Shulman, Stanford T., et al. Impact of **Rotavirus Vaccination** on Hospital-Acquired Rotavirus Gastroenteritis in Children. Pediatrics 2011 127: e264-e270.
Anderson EJ, Shippee DB, Weinrobe MH, et al. Indirect Protection of Adults From **Rotavirus** by Pediatric Rotavirus Vaccination. Clin Infect Dis. 2013 Jan 23.
Anderson LJ, Shekelle P, Keeler E, et al. The Cost of Interventions to **Increase Influenza Vaccination**: A Systematic Review. Am J Prev Med. 2018 Feb;54(2):299-315.
Andrews SM, Pollard AJ. A vaccine against **serogroup B Neisseria meningitidis**: dealing with uncertainty. Lancet Infect Dis. 2014 Mar 24.
Andrews NJ, Waight PA, Burbidge P, et al. Serotype-specific effectiveness and correlates of protection for the **13-valent pneumococcal conjugate vaccine**: a postlicensure indirect cohort study. Lancet Infect Dis. 2014 Sep;14(9):839-46.
Angelo KM et al. Spread of **measles in Europe and implications** for US travelers. Pediatrics 2019 Jul 1; 144:e20190414
Angoulvant F, Levy C, Grimprel E, et al. Early impact of **13-valent pneumococcal conjugate** vaccine on community-acquired pneumonia in children. Clin Infect Dis 2014; 58:918–24.
Arie S. Compulsory **vaccination** and growing **measles** threat. BMJ. 2017 Jul 20;358:j3429.
Armah GE, et al. Efficacy, immunogenicity, and safety of two doses of a tetravalent **rotavirus** vaccine RRV-TV in Ghana with the first dose administered during the neonatal period. J Infect Dis. 2013 Aug 1;208(3):423-31.
Arnheim-Dahlström L, Pasternak B, et al. Autoimmune, neurological, and venous thromboembolic adverse events after vaccination of adolescent girls with **quadrivalent human papillomavirus** in Denmark and Sweden: cohort study. BMJ 2013;347:f5906.
Arbyn M, Xu L, Simoens C, Martin-Hirsch PP. **Prophylactic vaccination against human papillomaviruses to prevent cervical cancer and its precursors**. Cochrane Database Syst Rev . 2018 May 9;5:CD009069. There is high-certainty evidence that HPV vaccines protect against cervical precancer in adolescent girls and young women aged 15 to 26. The effect is higher for lesions associated with HPV16/18 than for lesions irrespective of HPV type. The effect is greater in those who are negative for hrHPV or HPV16/18 DNA at enrolment than those unselected for HPV DNA status. There is moderate-certainty evidence that HPV vaccines reduce CIN2+ in older women who are HPV16/18 negative, but not when they are unselected by HPV DNA status.We did not find an increased risk of serious adverse effects. Although the number of deaths is low overall, there were more deaths among women older than 25 years who received the vaccine. The deaths reported in the studies have been judged not to be related to the vaccine. Increased risk of adverse pregnancy outcomes after HPV vaccination cannot be excluded, although the risk of miscarriage and termination are similar between trial arms.
Asghar Z, Coupland C, Siriwardena N. **Influenza vaccination and risk of stroke**: Self-controlled case-series study. Vaccine. 2015 Oct 5;33(41):5458-63.
Atkins KE, Lafferty EI, Deeny SR, et al. Use of mathematical modelling to assess the impact of **vaccines on antibiotic resistance**. Lancet Infect Dis. 2017 Nov 13.
Atwell JE, Van Otterloo J, Zipprich J, et al. **Nonmedical Vaccine Exemptions** and **Pertussis** in California, 2010. Pediatrics. 2013 Oct;132(4):624-630.
Atwell JE, Salmon DA. **Pertussis resurgence** and vaccine uptake: implications for reducing vaccine hesitancy. Pediatrics. 2014 Sep;134(3):602-4.
Auger KA, Patrick SW, Davis MM. Infant Hospitalizations for **Pertussis Before and After Tdap Recommendations** for Adolescents. Pediatrics. 2013 Oct 21.
Aw B, Boraston S, Botten D, et al. **Travel medicine**: What's involved? When to refer? Can Fam Physician. 2014 Dec;60(12):1091-1103.
Aylward Bruce, Yamada Tadataka. The **Polio Endgame**. N Engl J Med 2011; 364:2273-2275.
Badurdeen S, Marshall A, Daish H, et al. Safety and Immunogenicity of **Early Bacillus Calmette-Guérin Vaccination in Infants Who Are Preterm** and/or Have Low Birth Weights: A Systematic Review and Meta-analysis. JAMA Pediatr. 2018 Nov 26.
Bancsi A, Houle SKD, Grindrod KA. **Shoulder injury related to vaccine administration** and other injection site events. Can Fam Physician. 2019 Jan;65(1):40-42.
Bar-Zeev N, Kapanda L, Tate JE, et al. Effectiveness of monovalent **rotavirus** vaccine in infants in Malawi after programmatic roll-out: an observational and case-control study. Lancet Infect Dis 2014; online Jan 29.
Bar-Zeev N, King C, Phiri T, et al. Impact of **monovalent rotavirus vaccine on diarrhoea-associated post-neonatal infant mortality** in rural communities in Malawi: a population-based birth cohort study. Lancet Glob Health. 2018 Sep;6(9):e1036-e1044.
Barker CI, Snape MD. Pandemic influenza A **H1N1 vaccines and narcolepsy**: vaccine safety surveillance in action. Lancet Infect Dis. 2013 Dec 18.
Barrett AD. **Yellow Fever** in Angola and Beyond - The Problem of Vaccine Supply and Demand. N Engl J Med. 2016 Jun 8.
Barskey AE, Schulte C, Rosen JB, et al. **Mumps** outbreak in Orthodox Jewish communities in the United States. N Engl J Med. 2012 Nov;367(18):1704-13.
BarteH, Horvath TH, RutherfordGW. **Yellow fever vaccine** for patients with HIV infection. Cochrane Database of Systematic Reviews 2014, Issue 1. Art. No.: CD010929.
Basta NE, Mahmoud AAF, Wolfson J, et al. Immunogenicity of a **meningococcal** B vaccine during a university outbreak. N Engl J Med 2016; 375:220-8.
Bastidas A, de la Serna J, El Idrissi M, et al. Effect of **Recombinant Zoster Vaccine** on Incidence of Herpes Zoster After Autologous Stem Cell Transplantation: A Randomized Clinical Trial. JAMA. 2019 Jul 9;322(2):123-133.
Bayefsky MJ, Gostin LO. Requiring **Human Papilloma Virus Vaccination for School Entry**. JAMA Pediatr. 2018 Dec 28.
Baxter R, Lewis N, Bakshi N, et al. CISA Network. **Recurrent Guillain-Barre syndrome following vaccination**. Clin Infect Dis. 2012 Mar;54(6):800-4. (not find evidence of risk)
Baxter R, Ray P, Tran TN, et al. Long-term Effectiveness of **Varicella Vaccine**: A **14-Year**,Prospective Cohort Study. Pediatrics. 2013 Apr 1.
Baxter R, Bakshi N, Fireman B, et al. Lack of Association of **Guillain-Barre Syndrome with Vaccinations**. Clin Infect Dis. 2013 Apr 11.
Baxter R, Bartlett J, Rowhani-Rahbar A, et al. Effectiveness of **pertussis** vaccines for adolescents and adults: case-control study. BMJ. 2013 Jul 17;347:f4249.
Baxter R, Reisinger K, Block SL, et al. Antibody Persistence and Booster Response of a Quadrivalent **Meningococcal** Conjugate Vaccine in Adolescents. J Pediatr. 2014 Mar 20.
Baxter R, Tran TN, Ray P, et al. Impact of Vaccination on the Epidemiology of **Varicella**: 1995-2009. Pediatrics. 2014 Jun 9.
Baxter R, Bartlett J, Fireman B, et al. Effectiveness of **Vaccination During Pregnancy** to Prevent Infant **Pertussis**. Pediatrics. 2017;139(5):e20164091
Baxter R, Bartlett J, Fireman B, et al. Long-Term Effectiveness of the **Live Zoster Vaccine** in Preventing Shingles: A Cohort Study. Am J Epidemiol. 2018 Jan 1;187(1):161-169.
Bazemore A, Huntington M. The **Pretravel Consultation**. Am Fam Physician. 2009;80 (6):583-590.
Beals CR, Railkar RA, Schaeff er AK, et al. Immune response and reactogenicity of **intradermal** administration versus **subcutaneous** administration of **varicella-zoster** virus vaccine: an exploratory, randomised, partly blinded trial. Lancet Infect Dis 2016; online April 6.
Beaulieu Andrée-Anne, Boggild Andrea K.. Cases: **Enteric fever** in two vaccinated travellers to Latin AmericaCMAJ October 18, 2011 183:1740-1745; published June 20, 2011.
Becerra-Culqui TA, Getahun D, Chiu V, et al. Prenatal **Tetanus, Diphtheria, Acellular Pertussis Vaccination and Autism Spectrum Disorder**. Pediatrics. 2018 Aug 13.
Bednarczyk RA, Davis R, Ault K, et al. Sexual Activity-Related Outcomes After **Human Papillomavirus Vaccination** of 11- to 12-Year-Olds. Pediatrics. 2012 Oct 15.
Bégué RE, Perrin K. Reduction in gastroenteritis with the use of **pentavalent rotavirus** vaccine in a primary practice. Pediatrics. 2010 Jul;126(1):e40-5.
Behrman A, Offley W. Should **influenza vaccination be mandatory** for healthcare workers? BMJ. 2013 Nov 12;347:f6705
Beirne PV, Hennessy S, Cadogan SL, et al. **Needle size for vaccination procedures in children and adolescents**. Cochrane Database of Systematic Reviews 2018, Issue 8. Art. No.: CD010720. Using 25 mm needles (either 23 G or 25 G) for intramuscular vaccination procedures in the anterolateral thigh of infants using the WHO injection technique probably reduces the occurrence of local reactions whil e achieving a comparable immune response to 25 G 16 mm needle s. These findings are applicable to healthy infants aged two to six months receiving combination DTwP vaccines with a reactogenic whole-cell pertussis antigen component. These vaccines are predominantly used in low- and middle-income countries. The applicability of the findings to vaccines with acellular pertussis components and other vaccines with different reactogenicity profiles is uncertain.
Benard VB, Castle PE, Jenison SA, et al. Population-Based Incidence Rates of Cervical Intraepithelial Neoplasia in the **Human Papillomavirus** Vaccine Era. JAMA Oncol. 2016 Sep 29.
Beirne PV, Hennessy S, Cadogan SL, et al. **Needle size for vaccination procedures in children and adolescents**. Cochrane Database Syst Rev. 2015 Jun 18;6:CD010720. Using 25 mm needles (either 23 G or 25 G) for intramuscular vaccination procedures in the anterolateral thigh of infants using the WHO injection technique probably reduces the occurrence of local reactions while achieving a comparable immune response to 25 G 16 mm needles.
Belongia EA, Simpson MD, et al. Variable **influenza** vaccine eff ectiveness by subtype: a systematic review and meta-analysis of test-negative design studies. Lancet Infect Dis 2016.
Belshe RB, Frey SE, Graham IL, et al. Immunogenicity of avian influenza A/Anhui/01/2005 (H5N1) vaccine with MF59 adjuvant: a randomized clinical trial. JAMA. Oct, 2014.
Ben-Shimol S, Givon-Lavi N, et al. Cocontribution of **Rotavirus** and **Pneumococcal** Conjugate Vaccines to the Reduction of Pediatric Hospital Visits in Young Children. J Pediatr. 2016 Dec 8
Benefits Payments: The Australian "**No Jab, No Pay**" Legislation. JAMA. 2017 Feb 28;317(8):803-804.
Bennett NM. **The Role of the Advisory Committee** on Immunization Practices (ACIP) in Ensuring Optimal Use of Vaccines. JAMA. 2019 Jan 4.
Berenson AB, Hirth JM, Chang M. Change in **Human Papillomavirus** Prevalence Among U.S. Women Aged 18-59 Years, 2009-2014. Obstet Gynecol. 2017 Sep 5.
Bernstein HH, Bocchini JA Jr. Practical Approaches to **Optimize Adolescent Immunization**. Pediatrics. 2017 Feb 6.
Bernstein HH, Monty M, Yang P, et al. Increasing **Tdap Coverage Among Postpartum Women**: A Quality Improvement Intervention. Pediatrics. 2017 Feb 8.
Bernstein HH, Bocchini JA Jr. The Need to **Optimize Adolescent Immunization**. Pediatrics. 2017 Feb 6.
Bester JC. **Measles** and Measles Vaccination: A Review. JAMA Pediatr. 2016 Oct 3.
Bhandari N, Rongsen-Chandola T, Bavdekar A, et al; for the India Rotavirus Vaccine Group. Efficacy of a **monovalent human-bovine (116E) rotavirus** vaccine in Indian infants: a randomised, double-blind, placebo-controlled trial. Lancet. 2014 Mar 11.
Bhatt AS, DeVore AD, Hernandez AF, et al. Can **Vaccinations Improve Heart Failure** Outcomes?: Contemporary Data and Future Directions. JACC Heart Fail. 2017 Jan 28.
Bhattacharya SK, et al. 5 year efficacy of a bivalent killed whole-cell oral **cholera vaccine** in Kolkata, India: cluster-randomised, double-blind, placebo-controlled. Lancet Infect Dis.2013Oct17.
Bi Q, Ferreras E, Pezzoli L, et al. Protection against **cholera** from killed whole-cell oral cholera vaccines: a systematic review and meta-analysis. Lancet Infect Dis. 2017 July 17.
Bialek SR, Perella D, Zhang J, et al. Impact of a Routine **Two-Dose Varicella** Vaccination Program on Varicella Epidemiology. Pediatrics. 2013 Oct 7.
Bielicki JA, Achermann R, Berger C. Timing of **Measles Immunization** and Effective Population Vaccine Coverage. Pediatrics. 2012 Aug 20.
Bihan K, Weiss N, Théophile H, et al. **drug-induced aseptic meningitis**: 329 cases from the French Pharmacovigilance Database Analysis. Br J Clin Pharmacol. 2019 Jul 18.
Bijlsma MW, Bekker V, Brouwer MC, Spanjaard L, van de Beek D, van der Ende A. Epidemiology of **invasive meningococcal disease** in the Netherlands, 1960–2012: an analysis of national surveillance data. Lancet Infect Dis 2014; online Aug 5.
Bines JE, Danchin M, Jackson P, et al; RV3 Rotavirus Vaccine Program. Safety and immunogenicity of RV3-BB human neonatal **rotavirus** vaccine administered at birth or in infancy: a randomised, double-blind, placebo-controlled trial. Lancet Infect Dis. 2015 Aug 26.
Bingham CO 3rd, et al. Immunization responses in rheumatoid arthritis patients treated with **rituximab**: Results from a controlled clinical trial. Arthritis Rheum. 2009 Dec 28;62(1):64-74.
Bingham CO 3rd, Rizzo W, Kivitz A, Hassanali A, Upmanyu R, et al. Humoral immune response to vaccines in patients with rheumatoid arthritis treated with **tocilizumab**: results of a randomised controlled trial (VISARA). Ann Rheum Dis. 2014 Jan 21.
Bitoun S, Nocturne G, Ly B, et al**. Methotrexate and BAFF interaction prevents immunization against TNF inhibitors**. Ann Rheum Dis. 2018 Oct;77(10):1463-1470.
Blake IM, Pons-Salort M, Molodecky NA, et al. **Type 2 Poliovirus Detection after Global Withdrawal of Trivalent Oral Vaccine**. N Engl J Med. 2018 Aug 30;379(9):834-845.
Blanton L, Peacock G, Cox C, et al. **Neurologic disorders** among pediatric deaths associated with the 2009 pandemic **influenza**. Pediatrics. 2012 Sep;130(3):390-6.
Bleser WK, Elewonibi BR, Miranda PY, et al. **Complementary and Alternative Medicine and Influenxa Vaccine Uptake** in US Children. Pediatrics. 2016:138(5):e20154664.
Blyth CC, Jacoby P, Effler PV, et al; on behalf of the WAIVE Study Team. Effectiveness of Trivalent Flu Vaccine in Healthy Young Children. Pediatrics. 2014 Apr 21.
Bogaards JA, Wallinga J, Brakenhoff RH, et al. Direct benefit of **vaccinating boys along with girls** against oncogenic human **papillomavirus**: bayesian evidence synthesis. BMJ 2015;350:h2016.
Boikos C, De Serres G, Lands LC, et al. Safety of **Live-Attenuated Influenza** Vaccination in Cystic Fibrosis. Pediatrics. 2014 Sep 15.
Bombardier C, Hazlewood GS, Akhavan P, et al. Canadian Rheumatology Association recommendations for the pharmacological management of rheumatoid arthritis with traditional and **biologic** disease-modifying antirheumatic drugs: Part II **safety**. J Rheumatol First Release June 15 2012. http://www.irheum.org/content/early/2012/06/11/irheum.120165.full.pdf
Bonaldo G, Vaccheri A, D'Annibali O, et al. Safety profile of **HPV vaccines: an analysis of the USA Vaccine Adverse Event Reporting System (VAERS**) from 2007-2017. Br J Clin Pharmacol. 2018 Dec 20.
Bonaldo G, Vaccheri A, D'Annibali O, Motola D. **Safety profile of human papilloma virus vaccines**: an analysis of the US Vaccine Adverse Event Reporting System from 2007 to 2017. Br J Clin Pharmacol. 2018 Dec 20.
Bonten MJ, Huijts SM, Bolkenbaas M, et al. Polysaccharide conjugate vaccine against **pneumococcal** pneumonia in adults. N Engl J Med. 2015 Mar 19;372(12):1114-25.
Bonwitt J et al. Absence of asymptomatic mumps virus shedding among vaccinated college students during a **mumps outbreak** — Washington, February–June 2017. MMWR Morb Mortal Wkly Rep 2017 Dec 1; 66:1307.
Bortolussi R, Salvadori M; Canadian Paediatric Society, Immunization and infectious diseases committee. a **new meningococcal conjugate vaccine**: What should physiciansknow and do? Paediatr child health 2009;14(8):515-517. http://www.cps.ca/english/statements/ID/ID09-02.pdf
Bottino CJ, Cox JE, Kahlon PS, et al. **Improving immunization rates in a hospital-based primary care** practice. Pediatrics. 2014 Apr;133(4):e1047-54.
Bozzo P, Narducci A, Einarson A. **Vaccination during pregnancy**. Can Fam Physician. 2011 May;57(5):555-7.
Braeckman T, Van Herck K, Meyer N et al; on behalf of the RotaBel Study Group. Effectiveness of **rotavirus** vaccination in prevention of hospital admissions for rotavirus gastroenteritis among young children in Belgium: case-control study. BMJ. 2012 Aug 8;345:e4752.
Breakwell L, Kelso P, Finley C, et al. Pertussis Vaccine Effectiveness in the Setting of Pertactin-Deficient Pertussis. Pediatrics. 2016 May;137(5).
Breuer J, Pacou M, Gauthier A, et al. **Herpes zoster** as a risk factor for **stroke and TIA**: A retrospective cohort study in the UK. Neurology. 2014 Jan 8.
Brewer NT, Hall ME, Malo TL, et al. **Announcements Versus Conversations** to Improve HPV Vaccination Coverage: A Randomized Trial. Pediatrics. 2016 Dec 5.
Bridges CB, Coyne-Beasley T; Immunization Services Division, National Center for Immunization and Respiratory Diseases, CDC. Advisory committee on immunization practices recommended immunization schedule for **adults aged 19 years or older - United States, 2014**. MMWR Morb Mortal Wkly Rep. 2014 Feb 7;63(5):110-2.
Bridges CB, Thompson WW, et al. Effectiveness and cost-benefit of **influenza vaccination of healthy working adults**: A randomized controlled trial. JAMA. 2000 Oct 4;284(13):1655-63.
Briere EC, Jackson M, Shah SG, et al. **Haemophilus influenzae** Type b Disease and Vaccine Booster Dose Deferral, United States, 1998-2009. Pediatrics. 2012 Sep;130(3):414-20.
Briggs GG, Freeman RK, Sumner JY. Drugs in Pregnancy and Lactation 9th Edition. Williams & Wilkins, Baltimore, 2011
Baldur-Felskov B, et al. Early Impact of **Human Papillomavirus** Vaccination on Cervical Neoplasia--Nationwide Follow-up of Young Danish Women. J Natl Cancer Inst. 2014 Feb 19.
Broniatowski DA, Jamison AM, Qi S, et al. Weaponized Health Communication**: Twitter Bots and Russian Trolls Amplify the Vaccine Debate**. Am J Public Health. 2018 Oct;108(10):1378-1384.
Brotherton JML, Fridman M, et al. **Early eff ect of the HPV vaccination** programme on cervical abnormalities in Victoria, Australia: an ecological study. Lancet 2011; 377: 2085–92.
Brunson EK. The Impact of **Social Networks** on Parents' Vaccination Decisions. Pediatrics. 2013 Apr 15.
Bryant, KA., Block, SL., Baker, SA. for the PCV13 Infant Study Group, et al. Safety and Immunogenicity of a **13-Valent Pneumococcal Conjugate Vaccine**. Pediatrics 2010 125: 866-875
Byington CL, Clayton EW, Edwards KM. **Childhood Vaccine Exemptions**: A Broader Perspective Is Required. Pediatrics. 2016 Mar 18.
Buchan SA, Kwong JC. **Influenza** immunization among Canadian health care personnel: a cross-sectional study. CMAJ Open. 2016 Sep 7;4(3):E479-E488
Buchan SA, Rosella LC, Finkelstein M, et al; Public Health Agency of Canada/Canadian Institutes of Health Research Influenza Research Network (PCIRN) Program Delivery and Evaluation Group. Impact of pharmacist administration of **influenza** vaccines on uptake in Canada. CMAJ 2017;189:E146-52.
Buchan SA, Chung H, Campitelli MA, et al. Vaccine effectiveness against laboratory-confirmed **influenza** hospitalizations among young children during the 2010-11 to 2013-14 influenza seasons in Ontario, Canada. PLoS One 2017;359:e0187834.
Buchan SA, Booth S, Scott AN, et al. Effectiveness of **Live Attenuated vs Inactivated Influenza Vaccines in Children** During the 2012-2013 Through 2015-2016 Influenza Seasons in Alberta, Canada: A Canadian Immunization Research Network (CIRN) Study. JAMA Pediatr. 2018 Jul 2:e181514.
Bugenske E, Stokley S, Kennedy A, Dorell C. **Middle School Vaccination Requirements** and Adolescent Vaccination Coverage. Pediatrics. 2012 May 7.
Bundy DG, Solomon BS, Kim JM et al. Accuracy and Usefulness of the **HEDIS Childhood Immunization Measures**. Pediatrics. 2012 Apr;129(4):648-56.
Buxton JA, McIntyre CC, Tu AW, et al. Who **knows more** about immunization?: Survey of **public health nurses and physicians**. Can Fam Physician. 2013 Nov;59(11):e514-21.
Campitelli MA, Inoue M, Calzavara AJ, et al. Low Rates of **Influenza** Immunization in Young Children Under Ontario's Universal Influenza Immunization Program. Pediatrics. 2012 May 14.
Canfell K, Caruana M, Gebski V, et al. Cervical screening with primary HPV testing or cytology in a population of women in which those aged 33 years or younger had previously been offered **HPV vaccination**: Results of the Compass pilot randomised trial. PLoS Med. 2017 Sep 19;14(9):e1002388.

Cantor JD. **Mandatory Measles Vaccination** in New York City - Reflections on a Bold Experiment. N Engl J Med. 2019 Jun 5.

Capeding MR, Tran NH, Hadinegoro SRS, et al, and the CYD14 Study Group. Clinical efficacy and safety of a novel tetravalent **dengue vaccine** in healthy children in Asia: a phase 3, randomised, observer-masked, placebocontrolled trial. Lancet 2014; online July 11.

Cardemil CV, Cortese MM, Medina-Marino A, et al; the Rotavirus Investigation Team. Two **Rotavirus** Outbreaks Caused by Genotype G2P[4] at Large Retirement Communities: Cohort Studies. Ann Intern Med. 2012 Nov 6;157(9):621-631.

Cardemil CV, Dahl RM, James L, et al. Effectiveness of a **Third Dose of MMR Vaccine** for Mumps Outbreak Control. N Engl J Med. 2017 Sep 7;377(10):947-956

Carlin JB, Macartney K, et al. **Intussusception** risk and disease prevention associated with **rotavirus** vaccines in Australia's national immunisation program. Clin Infect Dis. 2013 Aug 30.

Casado I, Cet al. **Repeated influenza** vaccination for preventing severe and fatal influenza infection in older adults: a multicentre case-control study. CMAJ. 2018 Jan 8;190(1):E3-E12.

Casillas SM, Bednarczyk RA. Missed Opportunities for **Hepatitis A** Vaccination, National Immunization Survey-Child, 2013. J Pediatr. 2017 May 5.

Castelblanco RL, Lee M, Hasbun R. Epidemiology of **bacterial meningitis** in the USA from 1997 to 2010: a population observation-based study. Lancet Infect Dis 2014; online Aug 5.

Castle PE, Rodríguez AC, Burk RD, et al.; Proyecto Epidemiológico Guanacaste (PEG) Group. Short term persistence of human papillomavirus and risk of cervical precancer and cancer: population based cohort study. BMJ. 2009 Jul 28;339:b2569. doi: 10.1136/bmj.b2569.

Cates CJ, Rowe BH. Vaccines for preventing **influenza in people with asthma**. Cochrane Database Syst Rev. 2013 Feb 28;2:CD000364. doi: 10.1002/14651858.CD000364.pub4.

CATMAT: Canadian Committee to Advise on Tropical medicine and Travel. **Statement on older travellers**. CCDR 2011;37(ASC2):1-24. www.phac-aspc.gc.ca/publicat/ccdr-rmtc/11vol37/acs-2/index-eng.php

Centers for Disease Control and Prevention (CDC). Updated interim recommendations — HIV-infected adults and adolescents: Considerations for clinicians regarding 2009 **H1N1** influenza. Oct 21 , 2009. (http://www.cdc.gov/h1n1flu/guidance_HIV.htm)

Centers for Disease Control and Prevention (CDC). Pneumonia hospitalizations among young children before and after introduction of **pneumococcal conjugate vaccine**--United States, 1997-2006. MMWR Morb Mortal Wkly Rep. 2009 Jan 16;58(1):1-4.

Centers for Disease Control June 24, 2010 — The US Centers for Disease Control and Prevention (CDC)'s Advisory Committee on Immunization Practices (ACIP) has voted to eliminate precautionary language regarding the risk for **Guillain-Barré syndrome** (GBS) after meningococcal vaccination. In addition, countering current recommendations, ACIP also recommended children aged 6 months to 9 years who have not been immunized with the 2009 H1N1 monovalent vaccine receive 2 rather than 1 dose of seasonal influenza vaccine.

CDC: **Yellow Fever Vaccine** Recommendations of the Advisory Committee on Immunization Practices (ACIP) 2010 http://www.cdc.gov/mmwr/pdf/rr/rr5907.pdf

CDC: Updated Recommendations for Prevention of Invasive Pneumococcal Disease Among Adults Using the **23-Valent Pneumococcal Polysaccharide Vaccine** (PPSV23) MMWR September 3, 2010 / 59(34);1102-1106 http://www.cdc.gov/mmwr/preview/mmwrhtml/mm5934a3.htm?s_cid=mm5934a3_x

CDC: **Vaccination Coverage** among Adolescents Aged 13--17 Years --- United States, 2009 http://www.cdc.gov/mmwr/pdf/wk/mm5932.pdf

CDC : Centers for Disease Control and Prevention (CDC). National and state vaccination coverage among children aged 19--35 months --- United States, 2010. MMWR Morb Mortal Wkly Rep. 2011 Sep 2;60:1157-63. http://www.cdc.gov/mmwr/preview/mmwrhtml/mm6034a2.htm?s_cid=mm6034a2_x

CDC: Nov/11 **Immunization of Health-Care Personnel**. Recommendations of the Advisory Committee on Immunization Practices (ACIP). Recommendations and Reports. http://www.cdc.gov/mmwr/pdf/rr/rr6007.pdf

CDC **Adult Vaccination Coverage -** United States, 2010. *Weekly*. February 3, **2012** / 61(04);66-72 http://www.cdc.gov/mmwr/preview/mmwrhtml/mm6104a2.htm?s_cid=mm6104a2_w

CDC: FDA approval of an extended period for administering **VariZIG** for postexposure prophylaxis of varicella. MMWR Morb Mortal Wkly Rep. 2012 Mar 30;61(12):212.

CDC July/12 has updated its 1991 recommendations for the management of hepatitis B virus (HBV)–infected healthcare providers and students to prevent HBV transmission.

CDC: Prevention and Control of Influenza with Vaccines: Recommendations of the Advisory Committee on Immunization Practices (ACIP) — United States, **2012–13 Influenza** Season. http://www.cdc.gov/mmwr/preview/mmwrhtml/mm6132a3.htm

CDC: Centers for Disease Control and Prevention (CDC). **Human papillomavirus-associated cancers** - United States, 2004-2008. MMWR Morb Mortal Wkly Rep. 2012 Apr 20;61:258-61.

CDC: Centers for Disease Control and Prevention (CDC). Updated CDC recommendations for the management of hepatitis B virus-infected health-care providers and students. MMWR Recomm Rep 2012 Jul 6;61(RR-3):1-12.

CDC: Centers for Disease Control and Prevention (CDC). **Influenza** vaccination coverage among health-care personnel - 2011-12 influenza season, United States. MMWR Morb Mortal Wkly Rep. 2012 Sep 28;61:753-7.

CDC Interim Guidelines for Vaccine **Storage and Handling** Frequently Asked Questions. http://www.cdc.gov/vaccines/recs/storage/interim-faqstorage-handling.pdf (Accessed Nov 2012).

CDC Centers for Disease Control & Prevention. **Noninfluenza vaccination coverage** among adults -United States, 2011. MMWR Morb Mortal Wkly Rep. 2013 Feb 1;62(4):66-72.

Chandler RE. Modernising vaccine **surveillance systems to improve detection of rare or poorly defined adverse events**. BMJ. 2019 May 31;365:l2268.

Chaturvedi AK, Engels EA, Pfeiffer RM, et al. **Human Papillomavirus** and Rising Oropharyngeal Cancer Incidence in the United States. J Clin Oncol. 2011 Oct 3.

Chaturvedi AK, Graubard BI, Broutian T, et al. **Prevalence of Oral HPV Infection** in Unvaccinated Men and Women in the United States, 2009-2016. JAMA. 2019 Sep 10;322(10):977-979.

Chaves SS, Lopez AS, Watson TI, et al. **Varicella in infants after implementation of the US varicella vaccination program**. Pediatrics. 2011;128(6):1071–1077.

Chehab G, Richter JG, Brinks R, et al. **Vaccination coverage in systemic lupus erythematosus**-a cross-sectional analysis of the German long-term study (LuLa cohort). Rheumatology (Oxford). 2018 May 10.

Chen N, Li Q, Zhang Y, et al. Vaccination for preventing **postherpetic neuralgia**. Cochrane Database Syst Rev. 2011 Mar 16;3:CD007795. There is insufficient direct evidence from specialised trials to prove the efficacy of vaccine for preventing postherpetic neuralgia beyond its effect on reducing herpes zoster, although vaccination may be efficacious and safe for preventing herpes zoster and thus reduce the incidence of postherpetic neuralgia in adults aged 60 years or older.

Chen HL, Lin LH, Hu FC et al. Effects of Maternal Screening and Universal Immunization to Prevent Mother-To-Infant Transmission of **HBV**. Gastroenterology. 2011 Dec 23.

Chen SC, Toy M, Yeh JM, et al. Cost-effectiveness of Augmenting Universal **Hepatitis B Vaccination With Immunoglobin** Treatment. Pediatrics. 2013 Mar 25.

Chen Q, Griffin MR, Nian H, et al. **Influenza Vaccine** Prevents Medically Attended Influenza-Associated Acute Respiratory Illness in Adults Aged ≥50 Years. J Infect Dis. 2014 Oct 21.

Cherry JD. Why do **pertussis vaccines fail**? Pediatrics. 2012 May;129(5):968-70.

Chit A, Becker DL, DiazGranados CA, et al. Cost-effectiveness of **high-dose versus standard-dose inactivated infl uenza vaccine** in adults aged 65 years and older: an economic evaluation of data from a randomised controlled trial. Lancet Infect Dis 2015; online Sept 9.

Chong CR et al. Safety of inactivated **Influenza vaccine in cancer patients receiving immune checkpoint inhibitors** (ICI). Clin Infect Dis 2019 Mar 15.

Chong PP, et al. A Comprehensive Review of Immunization Practices in **Solid Organ Transplant** and Hematopoietic **Stem Cell** Transplant Recipients. Clin Ther. 2017 Aug;39(8):1581-1598.

Chouliaras, Giorgos, Spoulou, Vana, Quinlivan, Mark, et al. Vaccine-Associated Herpes **Zoster** Opthalmicus and Encephalitis in an Immunocompetent Child. Pediatrics 2010 125: e969-e972.

Chow EP, Danielewski JA, Fehler G, et al. **Human papillomavirus** in young women with **Chlamydia trachomatis** infection 7 years after the Australian human papillomavirus vaccination programme: a cross-sectional study. Lancet Infect Dis 2015; online July 20.

Chow EP, Machalek DA, Tabrizi SN, et al. Quadrivalent vaccine-targeted **human papillomavirus** genotypes in heterosexual men after the Australian female human papillomavirus vaccination programme: a retrospective observational study. Lancet Infect Dis. 2016 Jun 6. pii: S1473-3099(16)30116-5.

Christensen H, Trotter CL, Hickman M, et al. Re-evaluating cost effectiveness of **universal meningitis vaccination (Bexsero)** in England: modeling study. BMJ. 2014 Oct 9;349:g5725.

Chu DK, Abdurrahman Z. **Vaccine allergy**. CMAJ. 2019 Apr 8;191(14):E395.

Chung EY, Huang L, Schneider L. Safety of **influenza vaccine** administration in **egg-allergic** patients. Pediatrics. 2010 May;125(5):e1024-30. Epub 2010 Apr 5.

Chung JR, Flannery B, Ambrose CS, et al; Influenza Clinical Investigation for Children Study Team; Influenza Incidence Surveillance Project; US Influenza Vaccine Effectiveness Network. **Live attenuated and inactivated influenza vaccine effectiveness**. Pediatrics. 2019;143(2): e20182094

Chung JR, Flannery B, Thompson MG, et al. **Seasonal Effectiveness** of Live Attenuated and Inactivated **Influenza** Vaccine. Pediatrics. 2016 Jan 5.

Churchill L, Rizzuti FA, Fonseca K, et al. **Vaccine-associated measles** in a healthy 40-year-old woman. CMAJ. 2018 Sep 4;190(35):E1046-E1048.

Cifu AS, Davis AM. Use of **HPV Vaccine** in Males and Females. JAMA. 2014 Nov 12;312(18):1920-1921

Clarke E, Saidu Y, Adetifa JU, et al.Safety and immunogenicity of inactivated **poliovirus** vaccine when given with measles-rubella combined vaccine and yellow fever vaccine and when given via different administration routes: a phase 4, randomised, non-inferiority trial in The Gambia. Lancet Glob Health. 2016 Aug;4(8):e534-47.

Clark SJ, Butchart A, Kennedy A, et al. Parents' experiences with and preferences for **immunization reminder/recall technologies**. Pediatrics. 2011 Nov;128(5):e1100-5.

Clark Z, Maurer DM. **Pneumococcal Vaccines in Chronic Obstructive Pulmonary Disease**. Am Fam Physician. 2018 Apr 1;97(7):463-464.

Clemmons NS, Wallace GS, Patel M, Gastañaduy PA. **Incidence of Measles** in the United States, 2001-2015. JAMA. 2017 Oct 3;318(13):1279-1281.

Cobb JE, Cohen LL. A randomized controlled trial of the **ShotBlocker** for children`s immunization distress. Clin J Pain. 2009 Nov-Dec;25(9):790-6. (Data not support effectiveness)

Cohen ER, Salem M, Ha C. **Managing Immunosuppressed Patients With Inflammatory Bowel Disease** During a Measles Outbreak. Am J Gastroenterol. 2019 Sep 6.

Cohen Steven A., Chui Kenneth K.H., Naumova Elena N.. **Influenza** Vaccination in **Young Children Reduces Influenza-Associated Hospitalizations in Older Adults**, 2002–2006. Journal of the American Geriatrics Society. Article first published online: 28 JAN 2011. DOI: 10.1111/j.1532-5415.2010.03271.x.

Cohen, Arlan, Maschopoulos, Panagis, et al. **Congenital varicella syndrome**: the evidence for secondary prevention with **varicella-zoster immune globulin**. CMAJ 2011 0: cmaj.100615.

Cohn AC, MacNeil JR, Harrison LH, et al. Effectiveness and Duration of Protection of One Dose of a **Meningococcal** Conjugate Vaccine. Pediatrics. 2017 Jan 18.

Cohen J. **Waning immunity**. Science. 2019 Apr 19;364(6437):224-227.

Colgrove J. **Vaccine Refusal Revisited** - The Limits of Public Health **Persuasion and Coercion**. N Engl J Med. 2016 Oct 6;375(14):1316-1317.

Colin De Verdiere N, Durier C, Samri A, et al; and the ANRS EP46 NOVAA Group. Immunogenicity and safety of **yellow fever vaccine in HIV-1-infected patients**: ANRS EP46 NOVAA. AIDS. 2018 Aug 8.

Committee on Infectious Diseases, Prevention of **Rotavirus Disease**: Updated Guidelines for Use of Rotavirus Vaccine. Pediatrics 2009 123: 1412-1420.

Committee on Infectious Diseases, **Rabies**-Prevention Policy Update: New Reduced-Dose Schedule. Pediatrics 2011 127: 785-787.

Committee on Practice and Ambulatory Medicine and Council on Community Pediatrics, **Increasing Immunization Coverage**, Pediatrics 2010 125: 1295-1304

Committee on Infectious Diseases. Additional recommendations for use of **tetanus toxoid, reduced-content diphtheria toxoid, and acellular pertussis** vaccine (tdap). Pediatrics. 2011 Oct;128(4):809-12.

Committee on Infectious Diseases. Recommendations for administering **hepatitis a** vaccine to contacts of international adoptees. Pediatrics. 2011 Oct;128(4):803-4.

Committee on Infectious Diseases. **Meningococcal conjugate vaccines** policy update: booster dose recommendations. Pediatrics. 2011 Dec;128(6):1213-8.

Committee on Infectious Diseases Updated recommendations on the use of **meningococcal vaccines**. Pediatrics. 2014 Aug;134(2):400-3.

Committee on Infectious Diseases. Recommendations for Prevention and Control of **Influenza** in Children, **2014-2015**. Pediatrics. 2014 Sep 22.

Committee on Infectious Disease; Immunization for **Streptococcus pneumoniae** Infections in High-Risk Children. Pediatrics. 2014 Dec;134(6):1230-3.

Committee on Infectious Diseases. Recommended **Childhood and Adolescent Immunization Schedule-United States, 2015**. Pediatrics. 2015 Jan 26.

Committee on Infectious Diseases. **Influenza Immunization for All Health Care Personnel**: Keep It Mandatory. Pediatrics. 2015 Sep 7.

Committee on Infectious Diseases. Recommendations for Prevention and Control of **Influenza in Children**, 2015-2016. Pediatrics. 2015 Sep 7.

Committee on Infectious Disease. Recommendations for Prevention and Control of **Influenza** in Children, 2016-2017. Pediatrics. 2016 Oct;138(4).

Committee on Infectious Diseases. Recommendations for Prevention and Control of **Influenza in Children, 2018-2019**. Pediatrics. 2018 Sep 3. pii: e20182367.

COMMITTEE ON INFECTIOUS DISEASES. Recommendations for Prevention and Control of **Influenza in Children, 2019-2020**. Pediatrics. 2019 Sep 2.

Committee to Advise on Tropical Medicine and Travel. Interim Canadian recommendations for the use of fractional dose of **yellow fever** during a vaccine shortage: now in effect. Can Commun Dis Rep 2017;43(2):59. (accessed February 9, 2017).

Committee to Advise on Tropical Medicine and Travel (**CATMAT**). Statement on the use of booster doses of **yellow fever** vaccine. An Advisory Committee Statement (ACS). January 17, 2018(accessed January 18, 2017).

Cook EE, Venkataramani AS, Kim JJ, et al. Legislation to **Increase Uptake of HPV Vaccination and Adolescent Sexual Behaviors**. Pediatrics. 2018 Aug 13.

Cook SJ, Flaherty DK. Review of the Persistence of **Herpes Zoster** Vaccine Efficacy in Clinical Trials. Clin Ther. 2015 Nov 1;37(11):2388-97.

Cooper LZ, Katz SL. Ban on **Thimerosal in Draft Treaty on Mercury**: Why the AAP's Position in 2012 Is So Important. Pediatrics. 2013 Jan;131(1):152-3.

Coulson E, Saravanan V, Hamilton J, et al. **Pneumococcal antibody** levels after **pneumovax** in patients with rheumatoid arthritis on **methotrexate**. Ann Rheum Dis. 2011 Jul;70(7):1289-91.

Cortes JE, Curns AT, Tate JE, et al. **Rotavirus** Vaccine and Health Care Utilization for Diarrhea in U.S. Children. N Engl J Med 2011;365:1108-17.

Cortese MM, LeBlanc J, White KE, et al. Leveraging state immunization **information systems** to measure the effectiveness of **rotavirus** vaccine. Pediatrics. 2011;128(6).

Corti D, Voss J, Gamblin SJ, et al. A **neutralizing antibody** selected from plasma cells that binds to group 1 and group 2 **influenza** A hemagglutinins. Science 2011;333:850-6.

CPS: Canadian Paediatric Society Sep/11. Two shots are better than one to ward off **chickenpox**.

Crowcroft NS, Schwartz KL, Chen C, et al. Pertussis vaccine effectiveness in a frequency matched population-based case-control Canadian Immunization Research Network study in Ontario, Canada 2009-2015. Vaccine. 2019 May 1;37(19):2617-2623.

Crowcroft NS, Thampi N. The prevention and management of **rabies**. BMJ. 2015 Jan 14;350:g7827.

Crowcroft NS, Deeks SL, Upshur RE. Do we need a **new approach to making vaccine recommendations**? BMJ. 2015 Jan 30;350:h308.

Crowe SR, Merrill JT, Vista ES, Dedeke AB, et al. Influenza vaccination responses in human systemic **lupus erythematosus**: impact of clinical and demographic features. Arthritis Rheum. 2011 May 19. doi: 10.1002/art.30388.

Crowe E, Pandeya N, Brotherton JM, et al. Effectiveness of quadrivalent human papillomavirus vaccine for the prevention of cervical abnormalities: case-control study nested within a population based screening programme in Australia. BMJ. 2014 Mar 4;348:g1458.

Crosbie EJ, Einstein MH, Franceschi S, Kitchener HC. **Human papillomavirus** and cervical cancer. Lancet. 2013 Apr 22.

Cunningham AL, Lal H, Kovac M, et al. Efficacy of the **herpes zoster** subunit vaccine in adults 70 years of age or older. N Engl J Med 2016;375:1019-32.

Cyrus N, Blechman AB, Leboeuf M, et al. Effect of Quadrivalent **Human Papillomavirus Vaccination** on Oral Squamous Cell Papillomas. JAMA Dermatol. 2015 Sep 2.

D'Souza G, Westra WH, Wang SJ, et al. Differences in the prevalence of human papillomavirus (HPV) in head and neck squamous cell **cancers** by sex, race, anatomic tumor site, and HPV detection method [online De 8, 2016].JAMA Oncol. doi:10.1001/jamaoncol.2016.3067

Dabestani NM, Leidner AJ, Seiber EE, et al. A review of the **cost-effectiveness of adult influenza vaccination** and other preventive services. Prev Med. 2019 May 29;126:105734.

Dagan R, Pelton S, et al. Prevention of early episodes of otitis media by **pneumococcal** vaccines might reduce progression to complex disease. Lancet Infect Dis. 2016 Apr;16(4):480-92.

Dalcin D, Kwong JC**. High-dose influenza vaccination**. CMAJ. 2019 Mar 18;191(11):E313.

Daley E, Thompson E, Zimet G. **Human Papillomavirus Vaccination and School Entry Requirements**: Politically Challenging, But Not Impossible. JAMA Pediatr. 2018 Nov 5.

Darden PM, Thompson DM, Roberts JR, et al. **Reasons for Not Vaccinating Adolescents**: National Immunization Survey of Teens, 2008-2010. Pediatrics. 2013 Mar 18.

Daugla D, Gami J, Gamougam K, et al. Effect of a **serogroup A meningococcal** conjugate vaccine (PsA-TT) on serogroup A meningococcal meningitis and carriage in Chad: a community trial. Lancet. 2013 Sep 11.

Darvishian M, Bijlsma MJ, Hak E, van den Heuvel ER. **Seasonal influenza** vaccine effectiveness among the community-dwelling elderly: a metaanalysis of test-negative design case-control studies. Lancet Infect Dis 2014; online Nov 6. http://dx.doi.org/10.1016/S1473-3099(14)70960-0.

Darvishian M, van den Heuvel ER, Bissielo A, et al. Effectiveness of seasonal **influenza** vaccination in community-dwelling **elderly** people: an individual participant data meta-analysis of test-negative design case-control studies. Lancet Respir Med. 2017 Feb 8.

de Sanjose S, Quint WG, Alemany L, et al. on behalf of the Retrospective International Survey and **HPV** Time Trends Study Group. Human papillomavirus genotype attribution in invasive cervical cancer: a retrospective cross-sectional worldwide study. Lancet Oncol. 2010 Oct 15. (HPV types 16, 18, 31, 33, 35, 45, 52, and 58 should be given priority)

de St Maurice A, Grijalva CG, Fonnesbeck C, et al. Racial and Regional Differences in Rates of Invasive **Pneumococcal** Disease. Pediatrics. 2015 Oct 12.

de Sanjosé S et al. Primary Prevention of **Cervical Cancer**: American Society of Clinical Oncology (**ASCO**) Resource-Stratified Guideline Summary. J Oncol Pract. 2017 May.

De Wals P, Deceuninck G, Toth E, et al. Risk of **Guillain-Barré syndrome** following **H1N1 influenza 3 vaccination** in Quebec. JAMA. 2012;308(2):175- 181. (GBS cases attributable to vaccine was 2 per 1 million doses.)

DeAngelis H, Scarpino SV, Fitzpatrick MC, et al. Epidemiological and economic effects of priming with the **whole-cell Bordetella pertussis vaccine**. JAMA Pediatr. 2016 Mar 28.

Deeks SL, Lim GH, Simpson MA, et al. An assessment of **mumps** vaccine effectiveness by dose during an outbreak in Canada. CMAJ. 2011 May 16.

Deeks SL, Tunis MC, Ismail S; National Advisory Committee on Immunization. Advisory Committee Statement. Summary of the NACI update on the recommended use of human papillomavirus (**HPV**) vaccine: nine-valent HPV vaccine two-dose immunization schedule and the use of HPV vaccines in immunocompromised populations. CCDR 2017;43-6:138-42. www.phac-aspc.gc.ca/publicat/ccdr-rmtc/17vol43/dr-rm43-6/assets/pdf/17vol43_6-ar-04-eng.pdf (accessed June 2, 2017).

Defay F, De Serres G, Skowronski DM, et al. **Measles in Children Vaccinated** With 2 Doses of MMR. Pediatrics. 2013 Oct 21.

Dekhtyar S, Marseglia A, Xu W, et al. **Genetic risk of dementia risk mitigated by cognitive reserve**: a cohort study. Ann Neurol. 2019 May 8.

Delamater PL, Leslie TF, Yang YT. Change in **Medical Exemptions** From Immunization in California After Elimination of Personal Belief Exemptions. JAMA. 2017 Sep 5;318(9):863-864.

Delamater PL, Pingali SC, Buttenheim AM, et al. **Elimination of Nonmedical Immunization Exemptions** in California and School-Entry Vaccine Status. Pediatrics. 2019 May 21.

Domenech de Cellès M, Magpantay FMG, King AA, et al. The impact of **past vaccination coverage and immunity on pertussis resurgence**. Sci Transl Med. 2018 Mar 28;10(434).

Demicheli V, Rivetti A, Debalini MG, et al. Vaccines for **measles, mumps and rubella** in children. Cochrane Database Syst Rev. 2012 Feb 15;2:CD004407. The design and reporting of safety outcomes in MMR vaccine studies, both pre- and post-marketing, are largely inadequate.

Demicheli V, Jefferson T, Al-Ansary LA, et al. Vaccines for preventing **influenza** in healthy adults. Cochrane Database Syst Rev. 2014 Mar 13;3:CD001269.

Demicheli V, Jefferson T, Di Pietrantonj C, et al. **Vaccines for preventing influenza in the elderly**. Cochrane Database Syst Rev. 2018 Feb 1;2:CD004876. Older adults receiving the influenza vaccine may have a lower risk of influenza (from 6% to 2.4%), and probably have a lower risk of ILI compared with those who do not receive a vaccination over the course of a single influenza season (from 6% to 3.5%). We are uncertain how big a difference these vaccines will make across different seasons. Very few deaths occurred, and no data on hospitalisation were reported. No cases of pneumonia occurred in one study that reported this outcome. We do not have enough information to assess harms relating to fever and nausea in this population. The evidence for a lower risk of influenza and ILI with vaccination is limited by biases in the design or conduct of the studies.

Demicheli V, Jefferson T, Ferroni E, et al. Vaccines for preventing **influenza** in healthy adults. Cochrane Database Syst Rev. 2018 Feb 1;2:CD001269. Healthy adults who receive inactivated parenteral influenza vaccine rather than no vaccine probably experience less influenza, from just over 2% to just under 1% (moderate-certainty evidence). They also probably experience less ILI following vaccination, but the degree of benefit when expressed in absolute terms varied across different settings. Variation in protection against ILI may be due in part to inconsistent symptom classification. Certainty of evidence for the small reductions in hospitalisations and time off work is low.

Dempsey AF, Schaffer S, Singer D, et al. **Alternative Vaccination Schedule** Preferences Among Parents of Young Children. Pediatrics. 2011 Oct 3.

Dempsey AF, Pyrznawoski J, Lockhart S, et al. Effect of a Health Care Professional Communication Training Intervention on Adolescent **Human Papillomavirus** Vaccination: A Cluster Randomized Clinical Trial. JAMA Pediatr. 2018 Mar 5:e180016.

Deng L, Gidding H, Macartney K, et al. Postvaccination **Febrile Seizure Severity** and Outcome. Pediatrics. 2019 Apr 19.

Desai R, Curns AT, Patel MM, Parashar UD. Trends in **Intussusception-Associated Deaths** among US Infants from 1979-2007. J Pediatr. 2011 Sep 16.

Desai S, Shane A, Lewis R. **Measles**. CMAJ. 2012 May 28.

Desai R, Haberling D, Holman RC et al. Impact of **Rotavirus** Vaccine on Diarrhea-Associated Disease Burden Among American Indian and Alaska Native Children. Pediatrics. 2012 Mar 19.

Desai SP, Lu B, Szent-Gyorgyi LE, et al. Increasing **pneumococcal vaccination** for immunosuppressed patients: A cluster quality improvement trial. Arthritis Rheum. 2012 Oct 8.

DeSilva M, Vazquez-Benitez G, et al. Tdap Vaccination During Pregnancy and Microcephaly and Other Structural Birth Defects in Offspring. JAMA. 2016 Nov 1; 316 (17) :1823-1825.

Destefano F, Price CS, Weintraub ES. Increasing Exposure to Antibody-Stimulating Proteins and Polysaccharides in Vaccines Is **Not** Associated with Risk of **Autism**. J Pediatr. 2013 Mar 29.

DeVries Aaron S., Harper Jane, Murray Andrew, et al. **Vaccine-Derived Poliomyelitis** 12 Years after Infection in Minnesota. N Engl J Med 2011; 364:2316-2323.

DiazGranados CA, Dunning AJ, Kimmel M, et al. Efficacy of high-dose versus standard-dose influenza vaccine in older adults. N Engl J Med. 2014 Aug 14;371(7):635-45.

Dixon BE, Zimet GD, Xiao S, et al. An **educational intervention to improve HPV vaccination**: a cluster randomized trial. Pediatrics. 2019;143(1):e20181457

Do VA et al. Effect of an Early Dose of **Measles** Vaccine on Morbidity Between 18 Weeks and 9 Months of Age: A Randomized, Controlled Trial in Guinea-Bissau. J Infect Dis. 2017 Jan 10.

Dobson SRM, et al. Immunogenicity of **2 doses of HPV vaccine** in younger adolescents vs 3 doses in young women: a randomized clinical trial. JAMA. 2013;309(17):1793-1802.

Dodd KE, Mazurek JM. **Pneumococcal** Vaccination Among Adults With Work-related Asthma. Am J Prev Med. 2017 Sep 22.

Domenech de Cellès M, Rohani P, King AA. Duration of Immunity and Effectiveness of **Diphtheria-Tetanus-Acellular Pertussis Vaccines** in Children. JAMA Pediatr. 2019 Apr 22.

Dommasch ED, Joyce CJ, Mostaghimi A. Trends in Nationwide **Herpes Zoster Emergency Department Utilization** From 2006 to 2013. JAMA Dermatol. 2017 Jun 21.

Donahue JG, et al. Association of spontaneous **abortion** with receipt of inactivated **influenza** vaccine containing H1N1pdm09 : 2010-11 & 2011-12. Vaccine. 2017 Sep 25;35(40):5314-5322.

Donegan K, King B, Bryan P. Safety of **pertussis vaccination in pregnant women** in UK: observational study. BMJ. 2014 Jul 11;349:g4219. doi: 10.1136/bmj.g4219.

Donovan B et al. Quadrivalent **human papillomavirus vaccination** and trends in genital warts in Australia: Analysis of national sentinel surveillance data. Lancet Infect Dis 2010 Nov 9

Dorell CG, Yankey D, Santibanez TA, Markowitz LE. **Human Papillomavirus Vaccination Series Initiation and Completion**, 2008 -2009. Pediatrics. 2011 Oct 17.

Dorell CG, Yankey D, Byrd KK, Murphy TV. **Hepatitis A Vaccination Coverage** Among Adolescents in the United States. Pediatrics. 2012 Jan 23.

Dores GM, Bryant-Genevier M, Perez-Vilar S. **Adverse Events Associated With the Use of Sipuleucel-T** Reported to the US Food and Drug Administration's Adverse Event Reporting System, 2010-2017. JAMA Netw Open. 2019 Aug 2;2(8):e199249.

Doshi P. The **unofficial vaccine educators: are CDC funded non-profits sufficiently independent**? BMJ. 2017 Nov 7;359:j5104.

Doshi P. **Pandemrix vaccine: why was the public not told of early warning signs**? BMJ. 2018 Sep 20;362:k3948.

Draeger E, Bedford HE, Elliman DAC. **Should measles vaccination be compulsory**? BMJ. 2019 Jun 5;365:l2359.

Dransfield MT, Nahm MH, Han MK, et al.; COPD Clinical Research Network. Superior immune response to protein-**conjugate** versus free **pneumococcal** polysaccharide vaccine in chronic obstructive pulmonary disease. Am J Respir Crit Care Med. 2009 Sep 15;180(6):499-505. Epub 2009 Jun 25.

Drolet, M, Brisson, M, Schmader, KE., et al. The impact of **herpes zoster** and postherpetic neuralgia on health-related quality of life: a prospective study. CMAJ 2010 0: cmaj.091711

Drolet M, Bénard É, Boily M-C, et al. Population-level impact and herd effects following **human papillomavirus** vaccination programs: a systematic review and meta-analysis. Lancet Infect Dis 2015; online March 3.

Drolet M, Bénard É, Pérez N, et al. Population-level impact and herd effects following the introduction of human papillomavirus vaccination programmes: updated systematic review and meta-analysis. Lancet. 2019 Jun 26.

Drolet M, Zhou Z, Sauvageau C, et al. Effectiveness and cost-effectiveness of vaccination against **herpes zoster** in Canada: a modelling study. CMAJ. 2019 Aug 26;191(34):E932-E939.

Drozd EM, Miller L, Johnsrud M. Impact of **Pharmacist Immunization** Authority on Seasonal **Influenza** Immunization Rates Across States. Clin Ther. 2017 Aug 3

Dubé E, MacDonald NE. Addressing **vaccine hesitancy** and refusal in Canada. CMAJ. 2016 Jan 5;188(1):E17-8.

Dubey V, MacFadden D. Disseminated **varicella zoster virus infection after vaccination** with a live attenuated vaccine. CMAJ. 2019 Sep 16;191(37):E1025-E1027.

Duffy J, Weintraub E, et al; Vaccine Safety Datalink. **Narcolepsy and influenza A(H1N1)** pandemic 2009 vaccination in the United States. Neurology. 2014 Nov 11;83(20):1823-30.

Duffy J, Weintraub E, Hambidge SJ, et al; **Vaccine Safety Datalink. Febrile Seizure** Risk After Vaccination in Children 6 to 23 Months. Pediatrics. 2016 Jun 6.

Dunkle LM, Izikson R, Patriarca P, et al. Efficacy of Recombinant **Influenza Vaccine in Adults 50 Years of Age** or Older. N Engl J Med. 2017 Jun 22;376(25):2427-2436.

Dunkle LM, Izikson R, Patriarca PA, et al. Safety and Immunogenicity of a **Recombinant Influenza Vaccine**: A Randomized Trial. Pediatrics. 2018 Apr 2.

Dunn AC, Black CL, Arnold J, et al. Childhood Vaccination Coverage Rates Among **Military Dependents** in the United States. Pediatrics. 2015 Apr 13.

Edwards KM, Maldonado Y, Byington CL, et al. Is the **timing of recommended childhood vaccines** evidence based? BMJ. 2016 Feb 23;352:i867.

Edwards KM, Hackell JM, AAP The Committee on Infectious Diseases, Committee on Practice and Ambulatory Medicine. **Countering Vaccine Hesitancy**. Pediatrics.2016;138(3):e20162146

ElSherif MS, Brown C, Mackinnon-Cameron D, et al. Assessing the safety and immunogenicity of recombinant vesicular stomatitis virus **Ebola vaccine** in healthy adults: a randomized clinical trial. CMAJ. June 19, 2017;189:E819-27.

Einstein MH, Baron M, Levin MJ, et al. Comparison of the immunogenicity and safety of **Cervarix and Gardasil** (human papillomavirus (HPV) cervical cancer vaccines in healthy women aged 18-45 years. Hum Vaccin. 2009 Oct;5(10):705-19. Epub 2009 Oct 14.

Elding Larsson H, et al. **Pandemrix®** vaccination is not associated with increased risk of islet autoimmunity or type 1 diabetes in the TEDDY study children. Diabetologia. 2017 Oct 9.

Erickson BK, Landers EE, Huh WK. Update on Vaccination Clinical Trials for **HPV**-Related Disease. Clin Ther. 2014 Jan 1

Erlewyn-Lajeunesse M et al. Anaphylaxis as an adverse event following immunisation in the UK and Ireland. Arch Dis Child [Epub ahead of print] 23 January 2012

Estíváriz CF, Anand A, Gary HE Jr, et al. Immunogenicity of three doses of bivalent, trivalent, or type 1 monovalent oral **poliovirus** vaccines with a 2 week interval between doses in Bangladesh: an open-label, non-inferiority, randomised, controlled trial. Lancet Infect Dis. 2015 Jun 17.

Fadel CW, Colson ER, Corwin MJ, et al. **Maternal Attitudes** and Other Factors Associated with Infant Vaccination Status in the United States, 2011-2014. J Pediatr. 2017 Mar 3.

Farmar AM, Love-Osborne K, Chichester K et al. Achieving High Adolescent **HPV** Vaccination Coverage. Pediatrics. 2016 ;138(5) :e20152653

Farnham AC, Zimmerman CM, Papadouka V, et al. Invasive **pneumococcal** disease following the introduction of **13-valent conjugate vaccine** in children in New York City from 2007 to 2012 [onlineMay 4, 2015]. JAMA Pediatr. doi:10.1001/jamapediatrics.2015.0612.

Farez MF, Correale J. Yellow Fever Vaccination and Increased Relapse Rate in Travelers With Multiple Sclerosis. Arch Neurol. 2011 Jun 13.

Farez MF, Correale J, Armstrong MJ, et al. Practice guideline update summary: **Vaccine-preventable infections and immunization in multiple sclerosis**: Report of the Guideline Development, Dissemination, and Implementation Subcommittee of the American Academy of Neurology. Neurology. 2019 Aug 28.

FDA Oct/10 Rotarix: The risk of intussusception with Rotarix has been evaluated in a hospital-based Postmarketing Active Surveillance Study (PASS) in a birth cohort of infants in Mexico. An interim analysis of this study suggests an increased risk of intussusception in the 31-day period following administration of the first dose of Rotarix[Relative Risk: 1.8 (99% CI: 1.0, 3.1)]. In this study, within the 31-day period after the first dose, most cases of intussusception occurred in the first 7 days.

FDA May/19 has approved the **first vaccine to prevent dengue disease**. Dengvaxia is already approved in 19 other countries and the European Union.

Fefferman NH, Naumova EN. **Dangers of vaccine refusal** near the herd immunity threshold: a modelling study. Lancet Infect Dis. 2015 May 14.

Feldman AG, et al. Hospitalizations for **Respiratory Syncytial Virus** and Vaccine-Preventable Infections in the First 2 Years After Pediatric Liver Transplant. J Pediatr. 2017 Jan 11.

Feldman AG, Beaty BL, Curtis D, et al. Incidence of Hospitalization for **Vaccine-Preventable Infections in Children Following Solid Organ Transplant** and Associated Morbidity, Mortality, and Costs. JAMA Pediatr. 2019 Jan 14.

Feldman AG, Feudtner C, Kempe A. Reducing the **Underimmunization of Transplant Recipients**. JAMA Pediatr. 2017 Dec 4.

Feldman AG, Feudtner C, Kempe A. Reducing the **Underimmunization of Transplant Recipients**. JAMA Pediatr. 2018 Feb 1;172(2):111-112.

Fell D, Platt R, Lanes A, et al. **Fetal death** and **preterm birth** associated with maternal **influenza vaccination**: systematic review. BJOG. 2014 Jul 10.

Ferdinands JM, Olsho LE, Agan AA, et al; on behalf of the Pediatric Acute Lung Injury and Sepsis Investigators (PALISI) Network. Effectiveness of **influenza** vaccine against life-threatening RT-PCR-confirmed influenza illness in US children, 2010-2012. J Infect Dis. 2014 Mar 26.

Ferdinands JM, Fry AM, Reynolds S, et al. **Intraseason waning** of **influenza** vaccine protection: Evidence from the US Influenza Vaccine Effectiveness Network, 2011-12 through 2014-15. Clin Infect Dis. 2016 Dec 29.

Ferrini W, Aubert V, Balmer A, et al. **Anterior Uveitis and Cataract After Rubella** Vaccination: A Case Report of a 12-Month-Old Girl. Pediatrics. 2013 Sep 2.

Ferreira I, Isenberg D. **Vaccines and biologics**. Ann Rheum Dis. 2014 Aug;73(8):1446-1454.

Ferris D, Samakoses R, Block SL, et al. Long-term Study of a **Quadrivalent Human Papillomavirus Vaccine**. Pediatrics. 2014 Aug 18.

Ferris DG, Samakoses R, Block SL, et al. 4-Valent Human **Papillomavirus** (**4vHPV**) Vaccine in Preadolescents and Adolescents After 10 Years. Pediatrics. 2017 Nov 22.

Fiks AG, Grundmeier RW, Mayne S, et al. Effectiveness of Decision Support for Families, Clinicians, or Both on **HPV** Vaccine Receipt. Pediatrics. 2013 May 6.

Fiks AG, Luan X, Mayne SL. Improving **HPV** Vaccination Rates Using Maintenance-of-Certification Requirements. Pediatrics. 2016 Feb 3.

Fiks AG, Luan X, Mayne SL. Improving **HPV Vaccination** Rates Using Maintenance-of-Certification Requirements. Pediatrics. 2016 Feb 3.

Fischer M, Lindsey N, Staples JE, Hills S, Centers for Disease Control and Prevention (CDC). Japanese encephalitis vaccines: recommendations of the Advisory Committee on Immunization Practices (ACIP). MMWR Recomm Rep 2010 Mar 12;59(RR-1):1-27.

Fishman J, Taylor L, Kooker P, et al. Parent and Adolescent Knowledge of **HPV** and Subsequent Vaccination. Pediatrics. 2014 Sep 15.

Fishman J, Taylor L, Frank I. Awareness of **HPV** and Uptake of Vaccination in a High-Risk Population. Pediatrics. 2016 Aug;138(2)

Fitzpatrick MC, Hampson K, Cleaveland S, et al. Cost-effectiveness of canine vaccination to prevent **human rabies** in rural Tanzania. Ann Intern Med. 2014 Jan 21;160(2):91-100.

Flacco ME, Manzoli L, Rosso A, et al. Immunogenicity and safety of the **multicomponent meningococcal B vaccine (4CMenB)** in children and adolescents: a systematic review and meta-analysis. Lancet Infect Dis 2018; online Jan 19

Flannery B, Reynolds SB, Blanton L et al. **Influenza** Vaccine Effectiveness **Against Pediatric Deaths**:201-2014. Pediatrics. 2017;139(5):e20164244

Fooks AR, Banyard AC, Horton DL, et al. Current status of **rabies** and prospects for elimination. Lancet. 2014 May 9.

Forinash Alicia B, Yancey Abigail M, Pitlick Jamie M, et al. Safety of the HPV Bivalent and Quadrivalent Vaccines During Pregnancy. Articles Ahead of Print published on 1 February 2011, DOI 10.1345/aph.1P396. Ann Pharmacother ;45:258-262.

Forsyth K, Plotkin S, Tan T, et al. Strategies to **Decrease Pertussis Transmission** to Infants. Pediatrics. 2015 May 11.

Fowler VG, Allen KB, Moreira ED, et al. Effect of an investigational **vaccine for preventing Staphylococcus aureus** infections after cardiothoracic surgery: a randomized trial. JAMA. 2013 Apr 3;309(13):1368-78.

Franck L, Gay CL, Lynch M, Lee KA. Infant sleep following immunization: a randomized controlled trial of prophylactic acetaminophen. Pediatrics. 2011;128(6):1100 –1108.

Freed, Gary L., Clark, Sarah J., Butchart, Amy T., et al. Parental Vaccine Safety Concerns in 2009. Pediatrics 2010 0: peds.2009-1962.

Freedman JL, Reilly AF, Powell SC, et al. Quality Improvement Initiative to Increase **Influenza Vaccination** in Pediatric Cancer Patients. Pediatrics. 2015 Jan 12.

Freedman DO, Chen LH, Kozarsky PE. Medical Considerations before **International Travel**. N Engl J Med. 2016 Jul 21;375(3):247-60

French, Neil, Gordon, Stephen B., Mwalukomo, Thandie, et al. A Trial of a 7-Valent Pneumococcal Conjugate Vaccine (Prevnar) in HIV-Infected Adults. N Engl J Med 2010 362: 812-822.

Friedman, Bat-Chen, Goldman, Ran D. Influenza vaccination for children with asthma. Can Fam Physician 2010 56: 1137-1139.

Fu LY, Zook K, Gingold JA, et al. Strategies for **Improving Vaccine Delivery**: A Cluster-Randomized Trial. Pediatrics. 2016 May 10.

Fu C, Dong Z, Shen J, et al. **Rotavirus Gastroenteritis Infection Among Children Vaccinated and Unvaccinated With Rotavirus Vaccine** in Southern ChinaA Population-Based Assessment. JAMA Netw Open. 2018;1(4):e181382.

Fukuda W, Hanyu T, Katayama M, et al. Incidence of **hepatitis B virus reactivation** in patients with resolved infection on immunosuppressive therapy for rheumatic disease: a multicentre, prospective, observational study in Japan. Ann Rheum Dis. 2017 Jun;76(6):1051-1056.

Fullerton HJ, et al; **VIPS** Investigators. **Infection, vaccination, and childhood arterial ischemic stroke**: Results of the VIPS study. Neurology. 2015 Oct 27;85(17):1459-66.

Fulton TR, Phadke VK, Orenstein WA, et al. Protective Effect of Contemporary **Pertussis** Vaccines: A Systematic Review and Meta-analysis. Clin Infect Dis. 2016 May 1

Furer V, Rondaan C, Heijstek MW, et al. 2019 update of **EULAR recommendations for vaccinatio**n in adult patients with autoimmune inflammatory rheumatic diseases. Ann Rheum Dis. 2019 Aug 14.

FUTURE II Study Group. Quadrivalent vaccine against human papillomavirus (HPV) to prevent high-grade cervical lesions. N Engl J Med. 2007 May 10;356(19):1915-27.

FUTURE I/II Study Group. Four year efficacy of prophylactic human papillomavirus quadrivalent vaccine (HPV) against low grade cervical, vulvar, and vaginal intraepithelial neoplasia and anogenital warts: randomised controlled trial. BMJ 2010;341:c3493, doi: 10.1136/bmj.c3493.

Gagliardi AMZ, Gomes Silva BN, Torloni MR, et al. Vaccines for preventing **herpes zoster** in older adults. Cochrane Database of Systematic Reviews 2012, Issue 10. Art. No.: CD008858.

Gagliardi AM, Andriolo BN, Torloni MR, et al. Vaccines for preventing **herpes zoster** in older adults. Cochrane Database Syst Rev. 2016 Mar 3;3:CD008858. doi: 10.1002/14651858.CD008858.pub3. Herpes zoster vaccine is effective in preventing herpes zoster disease and this protection can last three years. In general, zoster vaccine is well tolerated; it produces few systemic adverse events and injection site adverse events of mild to moderate intensity.There are studies of a new vaccine (with a VZV glycoproteic fraction plus adjuvant), which is currently not yet available for clinical use.

Gagnon R, Primeau MN, Roches AD, et al. on behalf of the PHAC-CIHR influenza Research Network (PCIRN). Safe vaccination of patients with egg allergy with an adjuvanted pandemic H1N1 vaccine. J Allergy Clin Immunol. 2010 Jun 23.

Gahr P, DeVries AS, Wallace G, et al. An Outbreak of **Measles** in an Undervaccinated Community. Pediatrics. 2014 Jun 9.

Gai Y, Feng L. Relationship between **pharmacist density and adult influenzavaccination** after controlling for individual and neighborhood effects. *J Am Pharm Assoc (2003).* 2017 May 4.

Galloway JB, Mercer LK, Moseley A, et al. Risk of skin and soft tissue infections (including **shingles**) in patients exposed to **anti-tumour necrosis factor therapy**: results from the British Society for Rheumatology Biologics Register. Ann Rheum Dis. 2012 Apr 24.

Gardam M, Lemieux C. **Mandatory influenza vaccination**? First we need a better vaccine. CMAJ. 2013 May 14;185(8):639-40.

Gargano LM, Pazol K, Sales JM, et al. Multicomponent interventions to enhance influenza vaccine delivery to adolescents. Pediatrics. 2011 Nov;128(5):e1092-9.

Garland SM. The Australian experience with the human papillomavirus (**HPV**) vaccine. Clin Ther. 2014;1:17–23. 15.

Garland SM. The Australian experience with the **human papillomavirus vaccine**. Clin Ther. 2014 Jan 1

Garland SM, et al. Impact and Effectiveness of the **Quadrivalent Human Papillomavirus Vaccine**: A Systematic Review of 10 Years of Real-world Experience. Clin Infect Dis. 2016 May 26.

Gastañaduy PA, Sánchez-Uribe E, Esparza-Aguilar M, et al. Effect of **Rotavirus Vaccine** on Diarrhea Mortality in Different Socioeconomic Regions of Mexico. Pediatrics. 2013 Mar 4.

Gastañaduy PA, Curns AT, Parashar UD, Lopman BA. Gastroenteritis hospitalizations in older children and adults in the United States before and after implementation of infant **rotavirus** vaccination. JAMA. 2013 Aug 28;310(8):851-3.

Gastañaduy PA, Budd J, Fisher N, et al. A **Measles Outbreak** in an Underimmunized Amish Community in Ohio. N Engl J Med. 2016 Oct 6;375(14):1343-1354.

Gatrad AR, Sheikh A. The hajj. BMJ. 2011 Sep 15;343:d5593. doi:10.1136/bmj.d5593.

Georgousakis M, Jayasinghe S, Brotherton J, et al. Population-wide vaccination against human papillomavirus in adolescent boys: Australia as a case study. Lancet Infect Dis. 2012 Mar 22.

Gerber JS, Offit PA. **Vaccines and autism**: a tale of shifting hypotheses. Clin Infect Dis. 2009 Feb 15;48(4):456-61.

Gilkey MB, Dayton AM, Moss JL, et al. Increasing **Provision of Adolescent Vaccines in Primary Care**: A Randomized Controlled Trial. Pediatrics. 2014 Jul 7.

Gilkey MB, Malo TL, et al. Quality of Physician Communication about Human **Papillomavirus** Vaccine: Findings from a National Survey. Cancer Epidemiol Biomarkers Prev. 2015 Oct 22.

Gilkey MB, Parks MJ, Margolis MA, McRee AL, Terk JV. Implementing evidence-based **strategies to improve HPV vaccine delivery**. Pediatrics. 2019; 144(1):e20182500

Glanz, Jason M., McClure, et al. Parental Refusal of Pertussis Vaccination Is Associated With an Increased Risk of Pertussis Infection in Children Pediatrics 2009 123: 1446-1451 "Children whose parents refuse their pertussis vaccinations are at 23-fold higher risk for pertussis relative to vaccinated controls"

Glanz JM, McClure DL, Magid DJ, et al. Parental refusal of varicella vaccination and the associated risk of varicella infection in children. Arch Pediatr Adolesc Med. 2010 Jan;164(1):66-70. Children of parents who refuse varicella immunizations are at high risk of varicella infection relative to vaccinated children. (odds ratio, 8.6; 95% confidence interval, 2.2-33.3)

Glanz JM, Newcomer SR, et al. A Population-Based Cohort Study of **Undervaccination** in 8 Managed Care Organizations Across the United States. JAMA Pediatr. 2013 Jan 21:1-8.

Glanz JM, Narwaney KJ, Newcomer SR, et al. Association Between **Undervaccination With Diphtheria, Tetanus Toxoids, and Acellular Pertussis** (DTaP) Vaccine and Risk of Pertussis Infection in Children 3 to 36 Months of Age. JAMA Pediatr. 2013 Sep 9.

Glanz JM, Wagner NM, Narwaney KJ, et al. **Web-based Social Media Intervention** to Increase Vaccine Acceptance: A Randomized Controlled Trial. Pediatrics. 2017; 140 (6):e20171117.

Glanz JM, Newcomer SR, Daley MF, et al. Association between estimated **cumulative vaccine antigen exposure through the first 23 months of life** and non–vaccine-targeted infections from 24 through 47 months of age [March 6, 2018]JAMA. doi:10.1001/jama.2018.0708

Glass Roger I., Patel Manish, Parashar Umesh. Lessons From the US Rotavirus Vaccination Program. JAMA. 2011;306(15):1701-1702.doi:10.1001/jama.2011.1475

GlaxoSmithKline Vaccine HPV-007 Study Group, Romanowski B, de Borba PC, Naud PS, et al. Sustained efficacy and immunogenicity of the human papillomavirus (HPV)-16/18 AS04-adjuvanted vaccine (Cervarix): analysis of a randomized placebo-controlled trial up to 6.4 years. Lancet. 2009 Dec 12;374(9706):1975-85.

Glickman G, Harrison E, Dobkins K. **Vaccination Rates** among Younger Siblings of Children with **Autism**. N Engl J Med. 2017 Sep 14;377(11):1099-1101

Goldblatt D, Southern J, Andrews NJ, et al. **Pneumococcal conjugate vaccine 13** delivered **as one primary and one booster dose (1+1)** compared with two primary doses and a booster (2+1) in UK infants: a multicentre, parallel group randomised controlled trial. Lancet Infect Dis 2017; online Nov 22.

Goldman RD. Effectiveness of rotavirus vaccine in preventing severe acute gastroenteritis in children. Can Fam Physician. 2012 Mar;58(3):270-1.

Gosselin Boucher V, Colmegna I, Gemme C, et al. Interventions to improve **vaccine acceptance among rheumatoid arthritis patients**: a systematic review. Clin Rheumatol. 2019 Jan 15.

Gossger N, Snape MD, et al; for the European MenB Vaccine Study Group. Immunogenicity and tolerability of recombinant serogroup B meningococcal vaccine administered with or without routine infant vaccinations according to different immunization schedules: a randomized controlled trial. JAMA. 2012; 307(6):573-582.

Gostin LO, Ratzan SC, Bloom BR. **Safe Vaccinations for a Healthy Nation**: Increasing US Vaccine Coverage Through Law, Science, and Communication. JAMA. 2019 Apr 19.

Gostin Lawrence O.. Mandatory HPV Vaccination and Political Debate. JAMA. 2011;306(15):1699-1700.Published online October 6, 2011.doi:10.1001/jama.2011.1525

Gould PL, Leung J, Scott C, et al. Outbreak of varicella in elementary school children with two-dose varicella vaccine recipients-Arkansas, 2006. Pediatr Infect Dis J. 2009 Aug;28(8):678-81.

Graham BS, Mascola JR, Fauci AS. **Novel Vaccine Technologies**: Essential Components of an Adequate Response to Emerging Viral Diseases. JAMA. 2018 Apr 10;319(14):1431-1432.

Grandjean P, Andersen EW, Budtz-Jørgensen E, et al. Serum vaccine antibody concentrations in children exposed to perfluorinated compounds (PFCs). JAMA. 2012 Jan 25;307(4):391-7.

Gravenstein S, Davidson HE, Taljaard M, et al. Comparative effectiveness of **high-dose versus standard-dose influenza vaccination** on numbers of US nursing home residents admitted to hospital: a cluster-randomised trial. Lancet Respir Med. 2017 Jul 20.

Greenaway C, Schofield S, Henteleff A, et al; on behalf of CATMAT. Summary of the statement on **international travellers and typhoid** by the Committee to Advise on Tropical Medicine and Travel CATMAT. CCDR 2014;40-4. www.phac-aspc.gc.ca/publicat/ccdr-rmtc/14vol40/dr-rm40-04/dr-rm40-04-tropmed-eng.php (accessed February 25, 2014).

Greenberg Harry B., Rotavirus Vaccination and Intussusception — Act Two. N Engl J Med 2011; 364:2354-2355.

Greene MT, Fowler KE, Ratz D, et al. Changes in **influenza vaccination requirements for health care personnel in US hospitals**.JAMA Netw Open. 2018;1(2):e180143.

Greenhawt M, Turner PJ, et al. Administration of **influenza vaccines to egg allergic recipients**: A practice parameter update 2017. Ann Allergy Asthma Immunol. 2018 Jan;120(1):49-52.

Gray GE, Moodie Z, Metch B, et al; on behalf of the HVTN 503/Phambili study team. Recombinant adenovirus type 5 HIV gag/pol/nef vaccine in South Africa: unblinded, long-term follow-up of the phase 2b HVTN 503/Phambili study. Lancet Infect Dis. 2014 Feb 19.

Greenhow TL et al. Bacteremia in children 3 to 36 months old after introduction of conjugated **pneumococcal** vaccines. Pediatrics 2017 Apr; 139:e20162098.

Griffin MR et al. U.S. hospitalizations for pneumonia after a **decade of pneumococcal vaccination**. N Engl J Med 2013 Jul 11; 369:155.

Griffiths PD. Burden of disease associated with human **cytomegalovirus** and prospects for elimination by universal immunisation. Lancet Infect Dis. 2012 Oct;12(10):790-8.

Griffiths UK, Clark A, Hajjeh R. Cost-Effectiveness of **Haemophilus influenzae Type b** Conjugate Vaccine in Low- and Middle-Income Countries: Regional Analysis and Assessment of Major Determinants. J Pediatr. 2013 Jul;163(1Suppl):S50-S59.e9.

Grohskopf LA, Alyanak E, Broder KR, et al. Prevention and Control of **Seasonal Influenza** with Vaccines: Recommendations of the Advisory Committee on Immunization Practices - United States, 2019-20 Influenza Season. MMWR Recomm Rep. 2019 Aug 23;68(3):1-21

Grohskopf LA, Olsen SJ, Sokolow LZ, et al; Influenza Division, National Center for Immunization and Respiratory Diseases, **CDC**. Prevention and Control of Seasonal Influenza with Vaccines:
Recommendations of the Advisory Committee on Immunization Practices (ACIP) - United States**, 2014-15 Influenza Season**. MMWR Morb Mortal Wkly Rep. 2014;63:691-697.

Groom HC, Irving SA, Koppolu P, et al. Uptake and safety of **Hepatitis B vaccination during pregnancy**: A Vaccine Safety Datalink study. Vaccine. 2018 Oct 1;36(41):6111-6116.

Groom AV, Santibanez TA, Bryan RT. Vaccination Coverage Among **American Indian and Alaska** Native Children, 2006-2010. Pediatrics. 2012 Nov 19.

Groome MJ, Page N, Cortese MM, et al. Eff ectiveness of monovalent human **rotavirus** vaccine against admission to hospital for acute rotavirus diarrhoea in South African children: a case-control study. Lancet Infect Dis 2014; online Oct 8.

Groome MJ, Koen A, Fix A, et al. Safety and immunogenicity of a parenteral P2-VP8-P[8] subunit **rotavirus** vaccine in toddlers and infants in South Africa: a randomised, double-blind, placebo-controlled trial. Lancet Infect Dis 2017; online May 5.

Gruben V, Siemieniuk RA, McGeer A. Health care workers, mandatory **influenza** vaccination policies and the law. CMAJ. 2014 Oct 7;186(14):1076-1080. Epub 2014 May 26.

Gruslin A, Steben M, Halperin S, et al.. Immunization in pregnancy. J Obstet Gynaecol Can. 2008 Dec;30(12):1149-54. Erratum in: J Obstet Gynaecol Can. 2009 Mar;31(3):209.
1. All women of childbearing age should be evaluated for the possibility of pregnancy before immunization. (III-A) 2. Health care providers should obtain an immunization history from all women accessing prenatal care. (III-A) 3. In general, live and/or live-attenuated virus vaccines are contraindicated during pregnancy, as there is a, largely theoretical, risk to the fetus. (II-3) 4. Women who have inadvertently received immunization with live or live-attenuated vaccines during pregnancy should not be counselled to terminate the pregnancy because of a teratogenic risk. (II-2) 5. Non-pregnant women immunized with a live or live-attenuated vaccine should be counselled to delay pregnancy for at least four weeks. (III) 6. Inactivated viral vaccines, bacterial vaccines, and toxoids are considered safe in pregnancy. (II-1) 7. Women who are breastfeeding can still be immunized (passive-active immunization, live or killed vaccines). (II-1) 8. Pregnant women should be offered the influenza vaccine when pregnant during the influenza season. (II-1).
http://www.sogc.org/guidelines/documents/gui220CPG0812.pdf

Gruslin A, Steben M, Halperin S, Money DM, Yudin MH. Immunization in pregnancy. J Obstet Gynaecol Can 2009 Nov;31(11):1085-92.
1. All women of childbearing age should be evaluated for the possibility of pregnancy before immunization. (III-A) 2. Health care providers should obtain an immunization history from all women accessing prenatal care. (III-A) 3. In general, live and/or live-attenuated virus vaccines should not be administered during pregnancy, as there is a, largely theoretical, risk to the fetus. (II-3B) 4. Women who have inadvertently received immunization with live or live-attenuated vaccines during pregnancy should not be counselled to terminate the pregnancy because of teratogenic risk. (II-2A) 5. Non-pregnant women immunized with a live or live-attenuated vaccine should be counselled to delay pregnancy for at least four weeks. (III-B) 6. Inactivated viral vaccines, bacterial vaccines, and toxoids are considered safe in pregnancy. (II-1A) 7. Women who are breastfeeding can still be immunized (passive-active immunization, live or killed vaccines). (II-1A) 8. Pregnant women should be offered the influenza vaccine when pregnant during the influenza season. (II-1). Pregnant women should be offered the influenza vaccine (including H1N1 vaccine, when it is available) when they are pregnant during the influenza season. (II-1A) 9. Pregnant women with suspected or documented H1N1 infection should be treated with oseltamivir (Tamiflu, 75 milligrams twice daily for 5 days) within 48 hours of onset of symptoms. (III-B)
http://www.sogc.org/guidelines/documents/gui236CPG0911.pdf

Giuliano Anna R., Palefsky Joel M., Goldstone Stephen, et al. Efficacy of Quadrivalent HPV Vaccine against HPV Infection and Disease in Males. N Engl J Med 2011; 364:401-411.

Haban H, Benchekroun S, Sadeq M,et al. Seroprevalence of **measles vaccine antibody response in vertically HIV-infected children**, in Morocco. BMC Infect Dis. 2018 Dec 19;18(1):680.

Haber P, Sejvar J, Mikaeloff Y, DeStefano F. Vaccines and Guillain-Barré syndrome. Drug Saf. 2009;32(4):309-23. doi: 10.2165/00002018-200932040-00005.

Haber P, Patel M, Pan Y, et al. Intussusception After **Rotavirus** Vaccines Reported to US VAERS,2006-2012. Pediatrics. 2013 May 13.

Håberg SE, Trogstad L, Gunnes N, et al. Risk of **fetal death after pandemic influenza virus infection or vaccination**. N Engl J Med. 2013 Jan 24;368(4):333-40.

Håberg SE, Aaberg KM, Surén P, et al. **Epilepsy in Children After Pandemic Influenza** Vaccination. Pediatrics. 2018 Feb 15.

Haidara FC, Tapia MD, Sow SO, et al. Evaluation of a **Booster Dose of Pentavalent Rotavirus Vaccine Co-Administered with Measles, Yellow Fever and Meningitis A Vaccines** in 9-month-old Malian Infants. J Infect Dis. 2018 Apr 12.

Hales CM, Harpaz R, Joesoef MR, et al Examination of links between **herpes zoster incidence and childhood varicella** vaccination. Ann Intern Med. 2013 Dec 3;159(11):739-45.

Hamaluba M, Kandasamy R, Upreti SR, et. al. Comparison of **two-dose priming plus 9-month booster with a standard three-dose priming schedule for a ten-valent pneumococcal** conjugate vaccine in Nepalese infants: a randomised, controlled, open-label,non-inferiority trial. Lancet Infect Dis. 2015 Feb 17.

Hambidge SJ, Newcomer SR, Narwaney KJ, et al. **Timely Versus Delayed** Early Childhood Vaccination and **Seizures**. Pediatrics. 2014 May 19.

Hamiel U, Kvenstel I, Youngster I. **Recurrent Immune Thrombocytopenia** After **Influenza** Vaccination: A Case Report. Pediatrics. 2016:138(6):e20160124.

Hammarlund E, Thomas A, et al. Durability of Vaccine-Induced Immunity Against **Tetanus and Diphtheria Toxins**: A Cross-sectional Analysis. Clin Infect Dis. 2016 May 1;62(9):1111-8.

Hammarlund E, Thomas A, Poore EA, et al. **Durability of Vaccine-Induced Immunity Against Tetanus and Diphtheria** Toxins: A Cross-sectional Analysis. Clin Infect Dis. 2016 May 1;62(9):1111-1118.

Hammarlund E et al. **Durability of vaccine-induced immunity against tetanus and diphtheria toxins**: A cross-sectional analysis. Clin Infect Dis 2016 May 1; 62:1111.

Han F, Lin L, Warby SC, Faraco J, Li J, et al. **Narcolepsy** onset is seasonal and increased following the 2009 H1N1 pandemic in china. Ann Neurol. 2011 Sep;70(3):410-7.

Han F, Lin L, Li J, et al. Decreased incidence of **childhood narcolepsy** 2 years after the 2009 H1N1 winter flu pandemic. Ann Neurol. 2012 Nov 9.

Han JJ, Beltran TH, Song JW, et al. Prevalence of Genital Human Papillomavirus Infection and **Human Papillomavirus Vaccination** Rates Among US Adult Men: National Health and Nutrition Examination Survey (NHANES) 2013-2014. JAMA Oncol. 2017 Jan 19

Hapfelmeier A, Gasperi C, Donnachie E, Hemmer B. A large case-control study on **vaccination as risk factor for multiple sclerosis**. Neurology 2019;93:e908–e916.

Harris JG, Maletta KI, Ren B, et al. Improving **Pneumococcal** Vaccination in Pediatric Rheumatology Patients. Pediatrics. 2015 Aug 24.

Hariri S, Johnson ML, Bennett NM, Bauer et al; HPV-IMPACT Working Group. Population-based trends in high-grade cervical lesions in the early **human papillomavirus vaccine** era in the United States. Cancer. 2015 Jun 22.

Harrington JW, Logan S, Harwell C, et al. Effective **Analgesia** Using Physical Interventions for **Infant Immunizations**. Pediatrics. 2012 Apr 16.

Haug Charlotte. The Risks and Benefits of **HPV** Vaccination. JAMA. 2009;302(7):795-796.

He D, Zhang H, Xiao J, et al. Molecular and clinical relationship between **live-attenuated Japanese encephalitis vaccination and childhood onset myasthenia gravis**. Ann Neurol. 2018 Sep;84(3):386-400.

Health Canada Childhood Vaccination Information http://hc-sc.gc.ca/hl-vs/iyh-vsv/med/immuniz-eng.php

Health Canada May/10 is advising Canadians and Canadian healthcare practitioners that we are currently reviewing new information regarding the presence of porcine circovirus (PCV-1 and PCV-2) DNA in rotavirus vaccines. Porcine circovirus is a single stranded DNA virus, and is considered a contaminant in these vaccines.

Health Canada Dec/15: After reviewing Canadian and international information regarding the safety of the HPV vaccine **Gardasil**, Health Canada is informing Canadians that the benefits of using this vaccine continue to outweigh the risks. The overall evidence continues to demonstrate that this vaccine can be safely used and that there are no new safety risks.

Health Canada Oct/16 An increased risk of hemolysis or low hemoglobin has been observed when patients already being treated with SOLIRIS (**eculizumab**) were vaccinated against serogroup B **meningococcal** infection with Bexsero.

Health Canada May/18: Several **GlaxoSmithKline Inc. vaccines: Potential Risk of Underdosing**- There have been reports of leakage from ceramic coated tip syringes used for several GlaxoSmithKline Inc. vaccines during vaccine preparation or administration. Although the leakage does not pose a concern for the vaccine sterility, there is a potential risk of underdosing associated with administration of a vaccine from a leaking syringe that may leave patients inadequately protected from disease after vaccination.

Healy CM, Rench MA, et al. Association Between **Third-Trimester Tdap Immunization and Neonatal Pertussis Antibody Concentration**. JAMA. 2018 Oct 9;320(14):1464-1470.

Heath PT, Culley FJ, Jones CE, et al. Group B streptococcus and **respiratory syncytial virus** immunisation during pregnancy. Lancet Infect Dis 2017; online April 19.

Heijstek MW, Ott de Bruin LM, Bijl M, et al. EULAR recommendations for vaccination in paediatric patients with rheumatic diseases. Ann Rheum Dis. 2011 Oct;70(10):1704-12.

Heijstek MW, van Gageldonk PG, et al. Differences in persistence of measles, mumps, rubella, diphtheria and tetanus antibodies between children with rheumatic disease and healthy controls: a retrospective cross-sectional study. Ann Rheum Dis. 2012 Jun;71(6):948-54. (lower antibody rates in: mumps, rubella, diphtheria and tetanus)

Heijstek MW, Kamphuis S, Armbrust W, et al. Effects of the live attenuated **measles-mumps-rubella booster vaccination** on disease activity in patients with **juvenile idiopathic arthritis**: a randomized trial. JAMA. 2013 Jun 19;309(23):2449-56.

Heijstek MW, et al. Immunogenicity of the bivalent **human papillomavirus vaccine** in adolescents with juvenile systemic lupus erythematosus or juvenile dermatomyositis. J Rheumatol. 2013 Sep;40(9):1626-7.

Heinonen Santtu, Silvennoinen Heli, Lehtinen Pasi, et al. Effectiveness of inactivated influenza vaccine in children aged 9 months to 3 years: an observational cohort study, The Lancet Infectious Diseases, Volume 11, Issue 1, January 2011

Henao-Restrepo AM, Longini IM, Egger M, et al. Efficacy and effectiveness of an rVSV-vectored vaccine expressing **Ebola** surface glycoprotein: interim results from the Guinea ring vaccination cluster-randomised trial. Lancet. 2015 Aug 3.

Hendrix KS, Finnell SM, Zimet GD, et al. Vaccine Message **Framing and Parents' Intent to Immunize** Their Infants for MMR. Pediatrics. 2014 Aug 18.

Heneghan C, Onakpoya I. Editors' response to **concerns over the publication of the Cochrane HPV vaccine review** was incomplete and ignored important evidence of bias. BMJ Evid Based Med. 2019 Feb;24(1):1-4.

Henrikson NB, Opel DJ, Grothaus L, et al. Physician Communication Training and **Parental Vaccine Hesitancy**: A Randomized Trial. Pediatrics. 2015 Jun 1. pii: peds.2014-3199.

Heppner DG Jr, Kemp TL, Martin BK, et al, for the V920-004 study team. Safety and immunogenicity of the **rVSVΔG-ZEBOV-GP Ebola virus vaccine** candidate in healthy adults: a phase 1b randomised, multicentre, double-blind, placebo-controlled, dose-response study. Lancet Infect Dis 2017; online June 9. http

Herrero R, Quint W, Hildesheim A, et al; CVT Vaccine Group. Reduced Prevalence of Oral Human Papillomavirus (**HPV**) 4 Years after Bivalent HPV Vaccination in a Randomized Clinical Trial in Costa Rica. PLoS One. 2013 Jul 17;8(7):e68329.

Herweijer E, Leval A, Ploner A, et al. Association of varying number of doses of quadrivalent human papillomavirus vaccine with incidence of condyloma. JAMA. 2014 Feb 12;311(6):597-603

Hersh AL, Fleming-Dutra KE. **Vaccines** and **Outpatient Antibiotic Stewardship**. Pediatrics. 2017;140(3):e20171695

Hesse EM, Shimabukuro TT, Su JR, et al. Postlicensure **Safety Surveillance of Recombinant Zoster Vaccine** (Shingrix) - United States, October 2017-June 2018. MMWR Morb Mortal Wkly Rep. 2019 Feb 1;68(4):91-94.

Hill HA, Elam-Evans LD, Yankey D, et al. **Vaccination Coverage** Among Children Aged 19-35 Months - United States, 2017. MMWR Morb Mortal Wkly Rep. 2018 Oct 12;67(40):1123-1128

Higgins JPT, Soares-Weiser K, López-López JA, et al. Association of **BCG, DTP, and measles** containing vaccines with **childhood mortality**: systematic review. BMJ 2016;355:i5170.

Hirth JM, Tan A, Wilkinson GS, Berenson AB. Completion of the human papillomavirus vaccine series among insured females between 2006 and 2009. Cancer. 2012 Apr 27.

Hochman M, Cohen PA. Reconsidering Guidelines on the Use of **Pneumococcal** Vaccines in Adults 65 Years or Older. JAMA Intern Med. 2015 Oct 26:1-2.

Hofstetter AM, Jacobson EN, deHart MP, Englund JA. Early Childhood **Vaccination Status of Preterm Infants**. Pediatrics. 2019 Aug 7.

Hofstetter AM, Jakob K, Klein NP, et al. **Live Vaccine** Use and Safety in **DiGeorge Syndrome**. Pediatrics. 2014 Apr;133(4):e946-54.

Hofstetter AM, Ompad DC, et al. **Human Papillomavirus Vaccination** and Cervical Cytology Outcomes Among Urban Low-Income Minority Females. JAMA Pediatr. 2016 Mar 14.

Hofstetter AM, Lacombe K, Klein EJ, et al. Risk of **nosocomial spread after inpatient pentavalent rotavirus vaccine**. Pediatrics. 2018;141(1):e20171110

Holman DM, Benard V, Roland KB, et al. Barriers to **Human Papillomavirus Vaccination** Among US Adolescents: A Systematic Review of the Literature. JAMA Pediatr. 2013 Nov 25.

Horne Z, Powell D, Hummel JE, et al. **Countering antivaccination attitudes**. Proc Natl Acad Sci U S A. 2015 Aug 3.

Hough-Telford C, Kimberlin DW, Aban I, et al. **Vaccine Delays, Refusals, and Patient Dismissals**: A Survey of Pediatricians. Pediatrics. 2016:138(3):e20162127

Huang, Susan, Hinrichsen, Virginia L., et al. Continued Impact of Pneumococcal Conjugate Vaccine on Carriage in Young Children.Pediatrics 2009 124: e1-e11. The virtual disappearance of vaccine serotypes in S pneumoniae carriage has occurred in young children, with rapid replacement with penicillin-nonsusceptible nonvaccine serotypes, particularly 19A and 35B. Except for the age group at highest risk, previous predictors of carriage, such as child care attendance and the presence of young siblings, have not been changed by the vaccine.

Huang WT, Gargiullo PM, et al.; for the Vaccine Safety Datalink Team. Lack of Association Between Acellular Pertussis Vaccine and Seizures in Early Childhood. Pediatrics. 2010 Jul 19.

Huh WK, Joura EA, Giuliano, AR, et al. Final efficacy, immunogenicity, and safety analyses of a **nine-valent human papillomavirus** vaccine in women aged 16–26 years: a randomised, double-blind trial. Lancet 2017; online Sept 5.

Huh WK, et al. Final efficacy, immunogenicity, and safety analyses of a **nine-valent human papillomavirus vaccine** in women aged 16-26 years: a randomised, double-blind trial. Lancet. 2017 Sep 5.

Hung IF, Zhang AJ, To KK, et al. Topical **imiquimod before intradermal trivalent influenza** vaccine for protection against heterologous non-vaccine and antigenically drifted viruses: a single-centre, double-blind, randomised, controlled phase 2b/3 trial. Lancet Infect Dis. 2015 Nov 6.

Huttner A, Agnandji ST, Combescure C, et al. Determinants of antibody persistence across doses and continents after single-dose **rVSV-ZEBOV** vaccination: an observational cohort study. Lancet Infect Dis 2018; online April 4.

Hurley LP, Bridges CB, Harpaz R, et al. U.S. physicians' perspective of **adult vaccine delivery**. Ann Intern Med. 2014 Feb 4;160(3):161.

Hurst FP, Lee JJ, Jindal RM, et al. Outcomes Associated with Influenza Vaccination in the First Year after Kidney Transplantation. Clin J Am Soc Nephrol. 2011 Apr 28. April 28 Immunization Work Group of the National and Global Public Health Committee of the Infectious Diseases Society of America. Actions to strengthen adult and adolescent immunization coverage in the United States: policy principles of the Infectious Diseases Society of America. Clin Infect Dis. 2007;44: e104-8.

Huston P. Emerging clone of **meningococcal bacterium** affecting middle-aged and older adults. Canadian Family Physician. 2017 August:62;614

Huttner A, Hatz C, van den Dobbelsteen G, et al. Safety, immunogenicity, and preliminary clinical efficacy of a vaccine against extra-intestinal pathogenic **Escherichia coli** in women with a history of recurrent urinary tract infection: a randomised, placebo-controlled trial. Lancet Infect Dis 2017; online Feb 23.

Hviid A, et al. Association Between **Pandemic Influenza A(H1N1) Vaccination in Pregnancy** and Early Childhood Morbidity in Offspring. JAMA Pediatr. 2016 Nov 28

Hviid A, Hansen JV, Frisch M, Melbye M. **Measles, mumps, rubella vaccination and autism**. A nationwide cohort study. Ann Intern Med. 2019. [Epub ahead of print]. doi:10.7326/M18-2101

Hyle EP, Rao SR, Jentes ES, et al. Missed opportunities for **measles, mumps, rubella** vaccination among departing U.S. adult travelers receiving pretravel health consultations. Ann Intern Med. 2017. [Epub ahead of print]. doi:10 .7326/M16-2249

Imdad A, Tserenpuntsag B, Blog DS, et al. **Religious Exemptions** for Immunization and Risk of Pertussis in New York State, 2000-2011. Pediatrics. 2013 Jun 3.

Influenza **A/H1N1 MF59 adjuvanted vaccine in pregnant** women and adverse perinatal outcomes: multicentre study. BMJ. 2013 Feb 13;346:f990.

IOM Aug 2011: Adverse Effects of Vaccines: Evidence and Causality www.iom.edu/Reports/2011/Adverse-Effects-of-Vaccines-Evidence-and-Causality.Aspx

Iorio A, Basileo M, Marcucci M, et al. Influenza vaccination and vitamin K antagonist treatment: a placebo-controlled, randomized, double-blind crossover study. Arch Intern Med. 2010 Apr 12;170(7):609-16.

Institute of Medicine's Immunization Safety Committee Reports www.iom.edu/imsafety

In the Clinic. Management of Newly Diagnosed HIV Infection. (& Vaccinations) Annals of Internal Medicine 4 October 2011.

Information from your family doctor. **Vaccinations**. Am Fam Physician. 2017 June.

Ipp M, Parkin PC, Lear N, et al. Order of vaccine injection and infant pain response. Arch Pediatr Adolesc Med. 2009 May;163(5):469-72. Pain was reduced when the DPTaP-Hib vaccine was administered before the PCV in infants undergoing routine vaccination. We recommend that the order of vaccine injections be the DPTaP-Hib vaccine followed by the PCV.

Iqbal S, et al. Preparation for global introduction of inactivated **poliovirus** vaccine: safety evidence from the US Vaccine Adverse Event Reporting System, 2000-12. Lancet Inf Dis. 2015 Aug 14.

Irwin MR, Levin MJ, Laudenslager ML, et al. Varicella Zoster Virus-Specific Immune Responses to a **Herpes Zoster** Vaccine in Elderly Recipients With Major Depression and the Impact of Antidepressant Medications. Clin Infect Dis. 2013 Feb 13.

Iro MA, Khatami A, Marshall ASJ, et al. Immunological effect of administration of sequential doses of **Haemophilus influenzae** type b and **pneumococcal** conjugate vaccines in the same versus alternating limbs in the routine infant immunisation schedule: an open-label randomized controlled trial. Lancet Infect Dis 2015; published online Jan 8.

Isanaka S et al. Efficacy of a low-cost, **heat-stable oral rotavirus vaccine** in Niger. N Engl J Med 2017Mar 23; 376:1121.

Ismail SJ, Deeks SL. **Human papillomavirus vaccines** (Five things to know about). CMAJ. 2017 Sep 25;189(38):E1212.

Iversen OE, et al. Immunogenicity of **the 9-valent HPV vaccine** using 2-dose regimens in girls and boys vs a 3-dose regimen in women.JAMA. doi:10.1001 /jama.2016.17615

Ixiaro- A new Japanese Encephalitis Vaccine. Medical Letter. Aug,2009.

Izurieta HS, Thadani N, Shay DK, et al. Comparative effectiveness of **high dose versus standard-dose influenza vaccines** in US residents aged 65 years and older from 2012 to 2013 using Medicare data: a retrospective cohort analysis. Lancet Infect Dis 2014; online Feb 9.

Izurieta HS, Wernecke M, Kelman J, et al. Effectiveness and Duration of Protection Provided by the Live-attenuated **Herpes Zoster Vaccine** in the Medicare Population Ages 65 Years and Older. Clin Infect Dis. 2017 Mar 15;64(6):785-793.

Jackson LA, Janoff EN. Pneumococcal vaccination of elderly adults: new paradigms for protection. Clin Infect Dis. 2008 Nov 15;47(10):1328-38.

JacksonLA., Yu O, et al. Vaccine Safety Datalink Team, Fifth Dose of Diphtheria and Tetanus Toxoids and Acellular Pertussis Vaccine. (DTaP) Pediatrics 2011 0: peds.2010-1886.

Jackson LA, Yu O, Nelson JC, et al; for the Vaccine Safety Datalink Team. Injection Site (Thish less SE than arm)and Risk of Medically Attended Local Reactions to Acellular Pertussis Vaccine. Pediatrics. 2011 Mar;127(3):e581-e587.

Jackson LA, Peterson D, Nelson JC, et al. **Vaccination Site** and Risk of Local Reactions in Children 1 Through 6 Years of Age. Pediatrics. 2013 Jan 14. (DTaP in thigh less rx than arm)

Jackson LA, Campbell JD, Frey SE, et al. Effect of Varying Doses of a **Monovalent H7N9 Influenza** Vaccine With and Without AS03 and MF59 Adjuvants on Immune Response: A Randomized Clinical Trial. JAMA. 2015 Jul 21;314(3):237-46.

Jackson ML, Chung JR, Jackson LA, et al. **Influenza** Vaccine **Effectiveness** in the United States during the **2015-2016** Season. N Engl J Med. 2017 Aug 10;377(6):534-543.

Jacob JA. "**Vaccine hesitant" parents** affect vaccination rates in some communities. BMJ. 2014 Feb 4;348:g1211.

Jacobson Vann JC, Jacobson RM, Coyne-Beasley T, Asafu-Adjei JK, Szilagyi PG. **Patient reminder and recall interventions** to improve immunization rates. Cochrane Database of Systematic Reviews 2018, Issue 1. Art. No.: CD003941. Patient reminder and recall systems, in primary care settings, are likely to be effective at improving the proportion of thetarget population who receive immunizations.

Jain VK, Rivera L, Zaman K, et al. Vaccine (**quadrivalent**) for prevention of mild and moderate-to-severe **influenza** in children. N Engl J Med. DOI: 10.1056/NEJMoa1215817.

Jain VK, Rivera L, Zaman K, et al. Vaccine for Prevention of Mild and **Moderate-to-Severe Influenza in Children**. N Engl J Med. 2013 Dec 11. (**QIV** was efficacious)

Jain A, Marshall J, Buikema A, et al. **Autism Occurrence by MMR Vaccine** Status Among US Children With Older Siblings With and Without Autism. JAMA. 2015 Apr 21;313(15):1534-1540.

Jansen AG, Hak E, Veenhoven RH, et al. Pneumococcal conjugate vaccines for preventing otitis media. Cochrane Database Syst Rev. 2009 Apr 15;(2):CD001480. Based on current evidence of the effectiveness of PCVs for the prevention of AOM, the currently licensed 7-valent PCV administered during infancy has marginal beneficial effects. Discrete reductions of 6% to 7% may mean substantial reductions from a public health perspective. Administering PCV7 in older children with a history of AOM appears to have no benefit in preventing further episodes.

Jefferson T, Di Pietrantonj C, Rivetti A, et al. Vaccines for preventing influenza in healthy adults. Cochrane Database Syst Rev. 2010 Jul 7;7:CD001269. Influenza vaccines have a modest effect in reducing influenza symptoms and working days lost. There is no evidence that they affect complications, such as pneumonia, or transmission.

Jefferson T, Rivetti A, Di Pietrantonj C, et al. Vaccines for preventing **influenza** in healthy children. Cochrane Database Syst Rev. 2012 Aug 15;8:CD004879. : Influenza vaccines are efficacious in preventing cases of influenza in children older than two years of age, but little evidence is available for children younger than two years of age. There was a difference between vaccine efficacy and effectiveness, partly due to differing datasets, settings and viral circulation patterns. No safety comparisons could be carried out, emphasising the need for standardisation of methods and presentation of vaccine safety data in future studies. In specific cases, influenza vaccines were associated with serious harms such as narcolepsy and febrile convulsions.

Jefferson T, Rivetti A, Di Pietrantonj C, et al. Vaccines for preventing **influenza in healthy children**. Cochrane Database Syst Rev. 2018 Feb 1;2:CD004879. In children aged between 3 and 16 years, live influenza vaccines probably reduce influenza (moderate-certainty evidence) and may reduce ILI (low-certainty evidence) over a single influenza season. In this population inactivated vaccines also reduce influenza (highcertainty evidence) and may reduce ILI (low-certainty evidence).

Jenkins, Helen E., Aylward, R. Bruce, Gasasira, Alex, et al. Implications of a Circulating **Vaccine-Derived Poliovirus in Nigeria**. N Engl J Med 2010 362: 2360-2369.

Jena AB, Goldman DP, Seabury SA. Incidence of **sexually transmitted infections after human papillomavirus vaccination** among adolescent females [online February 9, 2015]. J AMA Intern Med. doi:10.1001/jamainternmed.2014.7886.

Jentes ES, Poumerol G, Gershman MD, et al. Informal WHO Working Group on Geographic Risk for **Yellow Fever**. The revised global yellow fever risk map and recommendations for vaccination, 2010: consensus of the Informal WHO Working Group on Geographic Risk for Yellow Fever. Lancet Infect Dis. 2011 Aug;11(8):622-32.

Jeudin P, Liveright E, Del Carmen MG, et al. Race, Ethnicity, and Income Factors Impacting **Human Papillomavirus Vaccination** rates. Clin Ther. 2014 Jan 1.

Jhaveri R, Allyne K. A Feasibility Trial of Home Administration of **Intranasal** Vaccine by Parents to Eligible Children. Clin Ther. 2016 Dec 6.

Jiménez S, Schiller JT, Lowy DR, et al. for the CVT Vaccine Group. Efficacy of a bivalent **HPV** 16/18 vaccine against anal HPV 16/18 infection among young women: a nested analysis within the Costa Rica Vaccine Trial. Lancet Oncol. 2011 Sep;12(9):862-870.

Jin C, Gibani MM, Moore M, et al. Efficacy and immunogenicity of a Vi-tetanus toxoid conjugate vaccine in the prevention of **typhoid** fever using a controlled human infection model of Salmonella Typhi: a randomised controlled, phase 2b trial. Lancet. 2017 Sep 28.

Jin J. JAMA patient page. **Pneumococcal** vaccination. JAMA. 2015 Feb 17;313(7):758.

Jin XW, Lipold L, Sikon A, Rome E. **Human papillomavirus vaccine** (HPV): Safe, effective, underused. Cleve Clin J Med. 2013 Jan;80(1):49-60.

Jit M, Chapman R, Hughes O, Choi YH. Comparing **bivalent and quadrivalent human papillomavirus vaccines**: economic evaluation based on transmission model. BMJ 2011;343:d5775.

Jit M, et al. Comparison of **two** dose and **three dose human papillomavirus** vaccine schedules: cost effectiveness analysis based on transmission model. BMJ. 2015 Jan 6;350:g7584.

Johansen HK, Gotzsche PC. Vaccines for preventing infection with **Pseudomonas** aeruginosa in cystic fibrosis. Cochrane Database Syst Rev. 2013 Jun 17;6:CD001399. doi: 10.1002/14651858.CD001399.pub3. Vaccines against Pseudomonas aeruginosa cannot be recommended.

John J, Giri S, Karthikeyan AS, et al. Effect of a single inactivated **poliovirus vaccine** dose on intestinal immunity against poliovirus in children previously given oral vaccine: an open-label, randomised controlled trial. Lancet 2014;online July 11.

Johnson HC, Lafferty EI, Eggo RM, et al. Effect of **HPV** vaccination and cervical cancer screening in England by ethnicity: a modelling study. Lancet Public Health. 2018 Jan;3(1):e44-e51.

Johnson MG, Bradley KK, Mendus S et al. Vaccine-preventable disease among **homeschooled** children: two cases of tetanus in oklahoma. Pediatrics. 2013 Dec;132(6):e1686-9.

Johnston JA, Tincher LB, Lowe DK. Booster and Higher Antigen Doses of Inactivated **Influenza Vaccine in HIV**-Infected Patients. Ann Pharmacother. 2013 Dec;47(12):1712-6

Johnstone J, Loeb M, Teo KK, et al. **Influenza Vaccination** and Major Adverse Vascular Events in High Risk Patients. Circulation. 2012 Jun 19.

Jolley D, Douglas KM. The effects of **anti-vaccine conspiracy theories** on vaccination intentions. PLoS One. 2014 Feb 20;9(2)

Joura EA, Garland SM, Paavonen J, et al. Effect of the human papillomavirus (**HPV**) quadrivalent vaccine in a subgroup of women with **cervical and vulval disease**: retrospective pooled analysis of trial data. BMJ 2012;344:e1401.

Joura EA, Giuliano AR, Iversen O-E, et al. A **9-valent HPV vaccine** against infection and intraepithelial neoplasia in women. N Engl J Med 2015;372:711-23.

Ju AC. **What I Learned From the Antivaccine Movement**. Pediatrics. 2019 Sep 16.

Juckett G, Hartman-Adams H. **Human papillomavirus**: clinical manifestations and prevention. Am Fam Physician. 2010 Nov 15;82(10):1209-13.

Junewicz A, Brateanu A, Nielsen C. Q: Do patients who received only two doses of **hepatitis B** vaccine need a booster? Cleve Clin J Med. 2014 Jun;81(6):346-8.

Kahn, Jessica A.HPV Vaccination (**HPV**) for the Prevention of Cervical Intraepithelial Neoplasia. N Engl J Med 2009 361: 271-278.

Kahn JA, Brown DR, Ding L, et al. Vaccine-Type **Human Papillomavirus** and Evidence of Herd Protection After Vaccine Introduction. Pediatrics. 2012 Jul 9.

Kamerow D. **HPV vaccine**: effective but underused in the US. BMJ. 2016 Apr 14

Kandasamy R, Voysey M, McQuaid F, et al. **Non-specific immunological effects of selected routine childhood immunisations**: systematic review. BMJ 2016;355:i5225.

Kang LW, Crawford N, Tang ML, et al. Hypersensitivity reactions to **human papillomavirus vaccine** in Australian schoolgirls: retrospective cohort study. BMJ. 2008 Dec 2;337:a2642. doi: 10.1136/bmj.a2642.

Kang JH, Ho JD, Chen YH, Lin HC. Increased Risk of **Stroke** After a **Herpes Zoster** Attack. A Population-Based Follow-Up Study. Stroke. 2009 Oct 8. [Epub ahead of print]

Kapetanovic MC, Roseman C, Jönsson G, et al. **Methotrexate** but not TNF-blockers reduces antibody response following **pneumococcal vaccination** using 7-valent conjugate pneumococcal vaccine in adult patients with established arthritis. Arthritis Rheum. 2011 Aug 10.

Kaplan SL, Barson WJ, Lin PL, et al. **Invasive Pneumococcal Disease** in Children's Hospitals: 2014-2017. Pediatrics. 2019 Aug 16.

Kaplan, SL., Barson, WJ., Lin, Philana L., et al. **Serotype 19A** Is the Most Common Serotype Causing Invasive **Pneumococcal** Infections in Children. Pediatrics 2010 125: 429-436.

Kardas-Nelson M. Despite high rates of vaccination, **pertussis cases are on the rise**. Is a new vaccination strategy needed? BMJ. 2019 Jul 9;366:l4460.

Kardas-Nelson M. Vaccine uptake and **prevalence of HPV related cancers** in US men. BMJ. 2019 Mar 18;364:l1210.

Kashangura R, Jullien S, Garner P, et al. **MVA85A vaccine to enhance BCG for preventing tuberculosis**. Cochrane Database Syst Rev. 2019 Apr 30;4:CD012915.

Kaufman J, Ryan R, Walsh L, Horey D, Leask J, Robinson P, Hill S. Face-to-face interventions for informing or educating parents about **early childhood vaccination**. Cochrane Database of Systematic Reviews 2018, Issue 5. Art. No.: CD010038. There is low- to moderate-certainty evidence suggesting that face-to-face information or education may improve or slightly improve children's vaccination status, parents' knowledge, and parents' intention to vaccinate.

Kaufman J, Synnot A, et al. **Face to face interventions for informing** or educating **parents** about early childhood vaccination. Cochrane Database of Systematic Reviews 2013, Issue 5.

Kaur R, Morris M, Pichichero ME. Epidemiology of **Acute Otitis Media** in the **Postpneumococcal Conjugate** Vaccine Era. Pediatrics. 2017; 140(3):e20170181

Kavanagh K et al. Changes in the prevalence of human papillomavirus following a national bivalent **human papillomavirus vaccination** programme in Scotland: a 7-year cross-sectional study. Lancet Infectious Diseases [ePub ahead of print] 28 Sept 2017.

Keating GM. Shingles (**herpes zoster**) vaccine (zostavax(®)): a review of its use in the prevention of herpes zoster and postherpetic neuralgia in adults aged ≥50 years. Drugs. 2013 Jul;73(11):1227-44.

Kelly RS, Walker P, Kitchener H, et al. Incidence of cervical intraepithelial neoplasia grade 2 or worse in colposcopy-negative/**human papillomavirus**-positive women with low-grade cytological abnormalities. BJOG. 2012 Jan;119(1):20-5.

Kelso JM, Li JT, Nicklas RA, et al. Joint Task Force on Practice Parameters. **Adverse reactions to vaccines**. Ann Allergy Asthma Immunol. 2009 Oct;103(4 Suppl 2):S1-14.

Kempe A, Allison MA, MacNeil JR, et al. **Adoption of Serogroup B Meningococcal Vaccine Recommendations**. Pediatrics. 2018 Aug 20.

Kempe A, Barrow J, Stokley S, et al. Effectiveness and Cost of Immunization **Recall at School-Based Health Centers**. Pediatrics. 2012 May 7.

Kempe A, O'Leary ST, Markowitz LE, et al. **HPV Vaccine Delivery Practices** by Primary Care Physicians. Pediatrics. 2019 Sep 16.

Kempe A, Saville AW, Dickinson LM, et. al, Collaborative Centralized **Reminder/Recall Notification** to Increase Immunization Rates Among Young Children: A Comparative Effectiveness Trial. JAMA Pediatr. 2015 Feb 23.

Kempe A, O'Leary ST, Kennedy A, et al. Physician Response to **Parental Requests to Spread Out the Recommended Vaccine Schedule**. Pediatrics. 2015 Mar 2. pii: peds.2014-3474.

Kemper AR, Barnett ED, Walter EB, et al. **Drinking Water to Prevent Postvaccination Presyncope** in Adolescents: A Randomized Trial. Pediatrics. 2017 Oct 23.

Kent A, Ladhani SN, Andrews NJ, Matheson M,et al. **Pertussis Antibody** Concentrations in Infants Born **Prematurely to Mothers** Vaccinated in Pregnancy. Pediatrics. 2016 Jun 2.

Kent A, Ladhani SN, Andrews NJ, et al Schedules for **pneumococcal** vaccination of preterm infants: an RCT. Pediatrics. 2016;138(3):e20153945

Kent A, Ladhani SN, Andrews NJ, et al. Schedules for **Pneumococcal** Vaccination of Preterm Infants: An RCT. Pediatrics. 2016 Sep;138(3).

Khan S, Stimec J, Kitai I. Nonresponding osteomyelitis in a two-year-old boy. (**BCG osteomyelitis**) CMAJ. 2015 Apr 27.

Kharbanda EO, Vazquez-Benitez G, Lipkind HS, et al. Evaluation of the Association of **Maternal Pertussis Vaccination** With Obstetric Events and Birth Outcomes. JAMA. 2014 Nov 12;312(18):1897-1904.

Kharbanda EO, Vazquez-Benitez G, Lipkind HS, et al. Risk of **Spontaneous Abortion After Inadvertent Human Papillomavirus Vaccination in Pregnancy**. Obstet Gynecol. 2018 Jul;132(1):35-44.

Khazeni N, Hutton DW, Collins CI, et al. Health and Economic Benefits of Early Vaccination and Nonpharmaceutical Interventions for a Human **Influenza** A (H7N9) Pandemic: A Modeling Study. Ann Intern Med. 2014 May 20;160(10):684-94.

Kim DK, Bridges CB, Harriman KH; Advisory Committee on Immunization Practices. Advisory Committee on Immunization Practices recommended immunization schedule for **adults aged 19 Years or older, United States, 2015.** Ann Intern Med. 2015;162:214-23.

Kim DK, Bridges CB, Harriman KH; Advisory Committee on Immunization Practices. (**ACIP**) Advisory Committee on Immunization Practices Recommended Immunization Schedule for **Adults Aged 19 Years or Older**: **United States**, **2016**. Ann Intern Med. 2016 Feb 2;164(3):184-94.

Kim DK, Hunter P; Advisory Committee on Immunization Practices. Recommended **Adult Immunization Schedule**, United States, 2019. Ann Intern Med. 2019 Feb 5;170(3):182-92.

Kim JJ, Targeted **human papillomavirus vaccination** of men who have sex with men in the USA: cost-effectiveness modelling analysis, Lancet Infectious Diseases, Vol10, Issue 12, Dec'10

Kim J, Bell C, Sun M, et al. Effect of human **papillomavirus** vaccination on cervical cancer screening in Alberta. CMAJ. 2016 Jul 4.

Kim JJ, Burger EA, Sy S, et al. Optimal Cervical Cancer Screening in Women Vaccinated Against **Human Papillomavirus**. J Natl Cancer Inst. 2017 Feb;109(2).

Kim M, Juern AM, Paley S, et al. **Vaccine-Associated Herpes Zoster**. J Pediatr. 2015 May 8.

Kitchener HC, Denton K, Soldan K, Crosbie EJ. Developing role of **HPV** in cervical cancer prevention. BMJ. 2013 Aug 7;347:f4781.

Kivitz AJ, Schechtman J, Texter M, et al. **Vaccine responses** in patients with rheumatoid arthritis treated with **certolizumab** pegol: results from a single-blind randomized phase IV trial. J Rheumatol. 2014 Apr;41(4):648-57.

Klein NP, Fireman B, Yih WK et al; Vaccine Safety Datalink. **Measles-mumps-rubella-varicella** combination vaccine and the risk of **febrile seizures**. Pediatrics. 2010 Jul;126(1):e1-8.

Klein NP, Lewis E, Baxter R et al. **Measles-Containing Vaccines and Febrile Seizures** in Children Age 4 to 6 Years. Pediatrics. 2012 Apr 2.

Klein NP, Bartlett J, Rowhani-Rahbar A, Fireman B, Baxter R. Waning protection after fifth dose of acellular **pertussis vaccine** in children. N Engl J Med. 2012 Sep 13;367(11):1012-9.

Klein NP, Hansen J, Chao C, et al. Safety of **Quadrivalent Human Papillomavirus** Vaccine Administered Routinely to Females. Arch Pediatr Adolesc Med. 2012 Oct 1:1-9.

Klein NP, Bartlett J, Fireman B, Rowhani-Rahbar A, Baxter R. Comparative Effectiveness of Acellular Versus Whole-Cell **Pertussis Vaccines** in Teenagers. Pediatrics. 2013 May 20.

Klein NP, Lewis E, Fireman B, et al. Safety of **Measles**-Containing Vaccines in 1-Year-Old Children. Pediatrics. 2015 Jan 5.

Klein NP, Bartlett J, Fireman B, et al. Waning **Tdap** Effectiveness in Adolescents. Pediatrics. 2016 Feb 5.

Kolber MR, Korownyk C, Nickonchuk T. **Zoster vaccine**. Can Fam Physician. 2013 Feb;59(2):157.

Kolber MR, Lau D, Eurich D, Korownyk C. **Effectiveness of the trivalent influenza vaccine**. Can Fam Physician. 2014 Jan;60(1):50.

Koskimaa HM, Waterboer T, Pawlita M, et al. **Human Papillomavirus** Genotypes Present in the Oral Mucosa of Newborns and their Concordance with Maternal Cervical Human Papillomavirus Genotypes. J Pediatr. 2012 May;160(5):837-43.

Kraemer MUG, et al. Spread of **yellow fever** virus outbreak in Angola and the Democratic Republic of the Congo 2015–16: a modelling study. Lancet Infect Dis 2016; online Dec 22.

Kreimer AR, Rodriguez AC, et al; CVT Vaccine Group. Proof-of-Principle Evaluation of the Efficacy of Fewer Than Three Doses of a Bivalent **HPV**16/18 Vaccine.J Natl Cancer Inst. 2011Sep9.

Kreimer AR, González P, Katki HA, et al. for the CVT Vaccine Group. Efficacy of a bivalent HPV 16/18 vaccine against **anal HPV 16/18** infection among young women: a nested analysis within the Costa Rica Vaccine Trial. Lancet Oncol. 2011 Sep;12(9):862-870.

Kreimer AR, Johansson M, Waterboer T, et al. Evaluation of **human papillomavirus antibodies** and risk of subsequent head and neck cancer. J Clin Oncol. 2013 Jul 20;31(21):2708-15.

Kreimer AR, Struyf F, Del Rosario-Raymundo MR, et al; Costa Rica Vaccine Trial and the PATRICIA study groups. Efficacy of **fewer than three doses of an HPV**-16/18 AS04-adjuvanted vaccine: combined analysis of data from the Costa Rica Vaccine and PATRICIA trials. Lancet Oncol. 2015 Jun 9.

Kreijtz JHCM, Goeijenbier M, Moesker FM, et al. Safety and immunogenicity of a Modified-**Vaccinia-virus-Ankara-based infl uenza** A H5N1 vaccine: a randomised phase 1/2a clinical trial. Lancet Infect Dis 2014; online Oct 30. http://dx.doi.org/10.1016/S1473-3099(14)70963-6.

Kriner P, Lopez K, Leung J, et al; Centers for Disease Control and Prevention (CDC). Notes from the field: **varicella-associated death** of a vaccinated child with leukemia - California, 2012. MMWR Morb Mortal Wkly Rep. 2014 Feb 21;63(7):161.

Kuhn S , Twele-Montecinos L, MacDonald J, et al**.** Case report: probable transmission of vaccine strain of **yellow fever virus to an infant via breast milk**. **CMAJ 2011 0: cmaj.100619.**

Kuncio DE, Middleton M, Cooney MG, et al. Health Care Worker Exposures to **Pertussis**: Missed Opportunities for Prevention. Pediatrics. 2013 Dec 16

Kuter BJ, Brown M, Wiedmann RT, et al. Safety and Immunogenicity of **M-M-R®II** (Combination Measles-Mumps-Rubella Vaccine) in Clinical Trials of Healthy Children Conducted Between 1988 and 2009. Pediatr Infect Dis J. 2016 May 31.

Kwok TSH, Libman M, Lake SL. Vaccination in **adults with autoimmune rheumatic diseases**. CMAJ. 2019 Sep 9;191(36):E1005

Kwong JC, Vasa PP, Campitelli MA, et al. Risk of **Guillain-Barré syndrome after seasonal influenza vaccination** and influenza health-care encounters: a self-controlled study. Lancet Infect Dis 2013; online June 28.

Ladhani S, Collins S, Djennad A, et al. Rapid increase in non-vaccine serotypes causing invasive **pneumococcal disease** in England and Wales, 2000–17: a prospective national observational cohort study. Lancet Infect Dis 2018; online Jan 25.

Lal H, Cunningham AL, Godeaux O, et al; ZOE-50 Study Group. Efficacy of an **Adjuvanted Herpes Zoster** Subunit Vaccine in Older Adults. N Engl J Med. 2015 Apr 28.

Lamontagne, Francois, Garant, Marie-Pierre, Carvalho, Jean-Christophe, et al. **Pneumococcal** vaccination and risk of **myocardial infarction** CMAJ 2008 179: 773-777

Lan J , Chen Y , Hsieh TC , et al. Kinetics of viral loads and risk of **HBV** reactivation in HBcAbpositive RA patients undergoing **anti-TNF-α therapy** . Ann Rheum Dis 2011 ; 70:1719–25 .

Langan SM, Smeeth L, Margolis DJ, Thomas SL. **Herpes zoster vaccine** effectiveness against incident herpes zoster and post-herpetic neuralgia in an older US population: a cohort study. PLoS Med 2013;10:e1001420.

Langer-Gould A, Qian L, Tartof SY, et al. **Vaccines and the Risk of Multiple Sclerosis** and Other Central Nervous System Demyelinating Diseases. JAMA Neurol. 2014 Oct 20.

Larson HJ, Smith DMD, Paterson P, et al. Measuring **vaccine confidence**: analysis of data obtained by a media surveillance system used to analyse public concerns about vaccines. Lancet Infect Dis 2013; online May 13.

Lateef TM, Johann-Liang R, Kaulas H, et al. **Seizures, Encephalopathy, and Vaccines**: Experience in the National Vaccine Injury Compensation Program. J Pediatr. 2014 Dec 2.

Lau D, Hu J, Majumdar SR, et al. **Interventions to improve influenza and pneumococcal** vaccination rates among community-dwelling adults: a systematic review and meta-analysis. Ann Fam Med. 2012 Nov;10(6):538-46.

Lau D, Eurich DT, Majumdar SR, et al. Effectiveness of **influenza vaccination** in working-age adults with **diabetes**: a population-based cohort study. Thorax. 2013 Jul;68(7):658-63.

Launay Odile, van der Vliet Diane, Rosenberg Arielle R., et al. Safety and Immunogenicity of 4 Intramuscular Double Doses and 4 Intradermal Low Doses vs Standard **Hepatitis B Vaccine** Regimen in Adults With **HIV-1**: A Randomized Controlled Trial. for the ANRS HB03 VIHVAC-B Trial. *JAMA.* 2011;305(14):1432-1440.doi:10.1001/jama.2011.351

Launay O, Rosenberg AR, Rey D, et al. Long-term Immune Response to **Hepatitis B Virus Vaccination** Regimens in Adults With Human Immunodeficiency Virus 1 (**HIV**): Secondary Analysis of a Randomized Clinical Trial. JAMA Intern Med. 2016 Apr 11.

Lauren CT, et al. Case Report- Subcutaneous Nodules and Sterile Absesses Due to Delayred Type **Hypersensitivity to Aluminum**-Containing Vaccines. Pediatrics. 2016;138(a):e20141690.

Lavallée PC, Labreuche J, Fox KM, et al; PERFORM, OPTIC, and AMISTAD Investigators. **Influenza** vaccination and cardiovascular risk in patients with recent TIA and stroke. Neurology. 2014 May 27;82(21):1905-13.

Lazarus R et al. A randomized study comparing combined **pneumococcal conjugate and polysaccharide vaccination in adults**. Clin Infect Dis. 2011;52:736-42.

Le DP, Vega J, Johnson LA. Notes from the Field: Hospital Contact Investigation for a Patient Who Developed a **Zoster Vaccine-Related Rash** - Maryland, February 2015. MMWR Morb Mortal Wkly Rep. 2017 Jul 21;66(28):763-764.

Le P, Rothberg MB. Cost-effectiveness of the adjuvanted **herpes zoster subunit vaccine** in older adults [online Jan 2, 2017].JAMA Intern Med. doi:10.1001/jamainternmed.2017.7431

Le P, Rothberg M. **Herpes zoster infection**. BMJ. 2019 Jan 10;364:k5095.

Le Saux N; Canadian Paediatric Society, Infectious Diseases and Immunization Committee. Position statement. Recommendations for the use of **rotavirus** vaccines in infants. Posted online September 22, 2016. www.cps.ca/en/documents/position/rotavirus-vaccines (accessed October 12, 2016).

Le Saux N. Recommendations for the use of **rotavirus** vaccines in infants. Paediatr Child Health. 2017;22(5):290-294

LeBras MH, Barry AR. **Influenza Vaccination for Secondary Prevention of Cardiovascular Events**: A Systematic Review. Can J Hosp Pharm. 2017 Jan-Feb;70(1):27-34.

Lee GM, Kleinman K, Pelton S, et al. **Immunization, antibiotic use, and pneumococcal colonization over a 15-year** period. Pediatrics. 2017; 140(5):e20170001

Legge A, Dodds L, Macdonald NE, et al. Rates and determinants of **seasonal influenza vaccination in pregnancy** and association with neonatal outcomes. CMAJ. 2014 Jan 6.

Lehtinen M, Paavonen J, Wheeler CM, et al. Overall effi cacy of **HPV-16/18** AS04-adjuvanted vaccine against grade 3 or greater **cervical intraepithelial neoplasia**: 4-year end-of-study analysis of the randomised, double-blind PATRICIA trial. Lancet Oncol 2011; published online Nov 9. DOI:10.1016/ S1470-2045(11)70286-8.

Leonardi S, et al. Hepatitis B vaccination failure in **celiac** disease: is there a need to reassess current immunization strategies? Vaccine. 2009 Oct 9;27(43):6030-3. Epub 2009 Aug 12.

Leonardi M, Bromberg K, Baxter R, et al. **Immunogenicity and safety of MMRV and PCV-7 vaccines** administered **concomitantly** in healthy children. Pediatrics. 2011;128(6).

Leshem E, Moritz RE, Curns AT, et al. **Rotavirus** Vaccines and Health Care Utilization for Diarrhea in the United States(2007-2011). Pediatrics. 2014 Jun 9.

Leshem E, Lopman B, Glass R, et al. Distribution of **rotavirus** strains and strain-specific effectiveness of the rotavirus vaccine after its introduction: a systematic review and meta-analysis. Lancet Infect Dis. 2014 Sep;14(9):847-56.

Leshem E, Parashar U. Use of Surveillance Data to Assess the Impact of Vaccination on Circulating **Rotavirus** Strains. J Pediatric Infect Dis Soc. 2015 Dec;4(4):e90-2

Leshem E, Tate JE, Steiner CA, et al. Acute gastroenteritis hospitalizations among US children following implementation of the **rotavirus** vaccine. JAMA. 2015 Jun 9;313(22):2282-4.

Leung DT, LaRocque RC, Ryan ET. **Travel Medicine**. Ann Intern Med. 2018 Jan 2;168(1):ITC1-ITC16.

Levandoski KA, Quesenberry CP, et al. **Herpes Zoster** Rates in a Large Cohort of Patients With Systemically Treated Psoriasis. JAMA Dermatol. 2017 Dec 20.

Leung DY, Jepson B, Beck LA, et al. A clinical trial of **intradermal and intramuscular seasonal influenza** vaccination in patients with atopic dermatitis. J Allergy Clin Immunol. 2017 Jan 31.

Leung V, Mapletoft J, Zhang A, et al. Thermal Stabilization of Viral Vaccines in Low-Cost Sugar Films. Sci Rep. 2019 May 21;9(1):7631.

Lewnard JA, Grad YH. Vaccine waning and **mumps re-emergence** in the United States. Sci Transl Med. 2018 Mar 21;10(433).

Li R, Liu L, Mo Z, et al. An inactivated **enterovirus 71** vaccine in healthy children. N Engl J Med. 2014 Feb 27;370(9):829-37.

Liao MT, Chang MH, Lin FG, et al. Universal **Hepatitis B Vaccination Reduces Childhood Hepatitis B Virus-Associated Membranous Nephropathy**. Pediatrics. 2011 Aug 22.

Libster R, McNeal M, Walter E, et al. Safety and immunogenicity of sequential **rotavirus** vaccine schedules. Pediatrics. 2015;137(2):e20152603

Lieu TA, Ray GT, Klein NP, Chung C, Kulldorff M. **Geographic Clusters in Underimmunization** and Vaccine Refusal. Pediatrics. 2015 Jan 19.

Limper HM, Burns JL, Lloyd LM, et al. Challenges to **school-located vaccination**: lessons learned. Pediatrics. 2014 Oct;134(4):803-8.

Lin CJ, Nowalk MP, Pavlik VN, et al. Using **the 4 pillars™ practice transformation** program to increase adult influenza vaccination and reduce missed opportunities in a randomized cluster trial. BMC Infect Dis.2016 Nov 3;16(1):623.

Lin C, Franceschi S, Clifford G. Human **papillomavirus** types from infection to cancer in the anus: a systematic review and meta-analysis, according to gender and HIV status. Lancet Infect Dis 2017; online Nov 17.

Lindley MC., Lorick SA., Spinner JR., et al. **Student Vaccination Requirements** of U.S. Health Professional Schools: A Survey. *Ann Intern Med* March 15, 2011 154:391-400

Lindstrand A, Bennet R, Galanis I, et al. Sinusitis and Pneumonia Hospitalization After Introduction of **Pneumococcal Conjugate** Vaccine. Pediatrics. 2014 Nov 10.

Lipkind HS, Vazquez-Benitez G, Nordin JD, et al. Maternal and Infant Outcomes After Human **Papillomavirus** Vaccination in the Periconceptional Period or During Pregnancy. Obstet Gynecol. 2017 Sep;130(3):599-608.

Liu EY, Smith LM, Ellis AK, et al. Quadrivalent **human papillomavirus vaccination in girls and the risk of autoimmune disorders**: the Ontario Grade 8 HPV Vaccine Cohort Study. CMAJ. 2018 May 28;190(21):E648-E655.

Liyanage SS, Rahman B, Ridda I, et al. The aetiological role of **human papillomavirus** in oesophageal squamous cell carcinoma: a meta-analysis. PLoS One. 2013 Jul 24;8(7):e69238.

Lo NC, Hotez PJ. Public Health and Economic Consequences of **Vaccine Hesitancy** for **Measles** in the United States. JAMA Pediatr. 2017 Jul 24

Lofters A, Vahabi M. Self-sampling for **HPV** to enhance uptake of cervical cancer screening: Has the time come in Canada? CMAJ. 2016 Sep 6;188(12):853-4.

Long MD, Martin C, Sandler RS, et al. Increased risk of **herpes zoster** among 108 604 patients with **inflammatory bowel disease**. Aliment Pharmacol Ther. 2013 Feb;37(4):420-9.

Löbermann M, et al. Vaccination and multiple sclerosis. Nervenarzt. 2009 Oct 17. Some vaccines, for example against yellow fever, are not indicated in MS due to the risk of MS exacerbation.

Loeb M; Russell ML.; Moss L; et al. Effect of **Influenza Vaccination** of Children on Infection Rates in Hutterite Communities: A Randomized Trial. JAMA. 2010;303(10):943-950.

Loeb M, Russell ML, Manning V, et al. Live Attenuated Versus Inactivated **Influenza** Vaccine in Hutterite Children: A Cluster Randomized Blinded Trial. Ann Intern Med. 2016 Aug 16

Loehr J, Savoy M. Strategies for Addressing and **Overcoming Vaccine Hesitancy**. Am Fam Physician. 2016 Jul 15;94(2):94-6.

Lopez, Adriana S., Zhang, John, Brown, Cedric, et al. Varicella-Related Hospitalizations in the United States, 2000-2006: The **1-Dose Varicella Vaccination Era**. Pediatrics 2011.

Lopman BA, Curns AT, Yen C, et al. Infant **rotavirus** vaccination may provide indirect protection to older children and adults in the United States. J Infect Dis. 2011 Oct 1;204(7):980-6.

Lessin HR, Edwards KM; the Committee on Practice and Ambulatory Medicine and the Committee on Infectious Diseases. **Immunizing Parents and Other Close Family Contacts** in the Pediatric Office Setting. Pediatrics. 2012 Jan;129(1):e247-e253.

Leung J, Harpaz R. Impact of the Maturing Varicella Vaccination Program on **Varicella** and Related Outcomes in the United States: 1994-2012. J Pediatric Infect Dis Soc. 2015 Aug 12.

Lodolce AE. Shortened interval between **tetanus vaccines**. Ann Pharmacother. 2012 Jun;46(6):884-8.

Long JE, Drayson MT, Taylor AE, et al. **Morning vaccination** enhances antibody response over afternoon vaccination: A cluster-randomised trial. Vaccine. 2016 Apr 21

Low N et al. A randomized, controlled trial of an **aerosolized** vaccine against **measles**. N Engl J Med 2015 Apr 16; 372:1519.

Lu PJ, Yankey D, Jeyarajah J, et al. **HPV** Vaccination Coverage of Male Adolescents in the United States. Pediatrics. 2015 Oct 26.

Lu Y, Chillarige Y, Izurieta HS, et al. Effect of age on **relative effectiveness of high-dose versus standard-dose influenza vaccines** among US Medicare beneficiaries ages 65 years and older. J Infect Dis. 2019 Jul 9.

Lucey DR, Donaldson H. **Yellow Fever** Vaccine Shortages in the United States and Abroad: A Critical Issue. Ann Intern Med. 2017 Sep 26.

Ludvigsson JF, et al. Maternal vaccination against **H1N1 influenza** and offspring mortality: population based cohort study and sibling design. BMJ. 2015 Nov 16;351:h5585.

Ludvigsson JF, Ström P, Lundholm C, et al. Risk for **Congenital Malformation With H1N1** Influenza Vaccine: A Cohort Study With Sibling Analysis. Ann Intern Med. 2016 Sep 20.

Lujan-Zilbermann J, Warshaw MG, Williams PL, et al. International Maternal Pediatric Adolescent AIDS Clinical Trials Group P1065 Protocol Team. Immunogenicity and Safety of 1 vs 2 Doses of **Quadrivalent Meningococcal Conjugate Vaccine** in Youth Infected with Human Immunodeficiency Virus. J Pediatr. 2012 Oct;161(4):676-681.e2.

Luquero FJ, Grout L, Ciglenecki I, et al. Use of **Vibrio cholerae** vaccine in an outbreak in Guinea. N Engl J Med. 2014 May 29;370(22):2111-20.

Ma L, Du X, Dong Y, et al. First Case of **Stevens-Johnson Syndrome After Rabies** Vaccination. Br J Clin Pharmacol. 2018 Jan 15.

Macartney K, Gidding HF, Trinh L, et al. Evaluation of Combination **Measles-Mumps-Rubella-Varicella** Vaccine Introduction in Australia. JAMA Pediatr. 2017 Aug 14.

Macartney K, Heywood A, McIntyre P. Vaccines for **post-exposure prophylaxis against varicella** (chickenpox) in children and adults. Cochrane Database Syst Rev. 2014 Jun 23;6:CD001833.

MacDonald SE, Dover DC, Simmonds KA, et al. Risk of febrile **seizures** after first dose of **measles-mumps-rubella-varicella** vaccine: a population-based cohort study. CMAJ. 2014 Jun 9.

MacDonald N E. Maternal infectious diseases, antimicrobial therapy or **immunizations**: Very few contraindications to **breastfeeding**. Canadian Paediatric Society. 2014 Jun 17. http://www.cps.ca/documents/position/maternal-infectious-diseases-breastfeeding

MacDougall H, Monnais L. Vaccinating in the age of apathy: **measles vaccination in Canada**, 1963–1998. CMAJ. 2018;190(13):E399-E401.

Machalek DA, Chow EP, et al. **Human papillomavirus prevalence in unvaccinated heterosexual males** following a national female vaccination program. J Infect Dis. 2016 Nov 3.

MacIntyre CR, Heywood AE, Kovoor P, et al. **Ischaemic heart disease**, influenza and **influenza** vaccination: a prospective case control study. Heart 21 Aug 2013

Macneil JR, Cohn AC, Farley M, et al. Current Epidemiology and Trends in **Invasive Haemophilus influenzae** Disease--United States, 1989-2008. Clin Infect Dis. 2011 Dec;53(12):1230-6.

MacNeil JR, Bennett N, Farley MM, et al. Epidemiology of Infant **Meningococcal** Disease in the United States, 2006-2012. Pediatrics. 2015 Jan 12.

Madhi, Shabir A., Cunliffe, Nigel A., Steele, Duncan, et al. Effect of Human **Rotavirus** Vaccine on Severe Diarrhea in African Infants. N Engl J Med 2010 362: 289-298.

Madhi SA, Cutland CL, Kuwanda L, et al; Maternal Flu Trial (Matflu) Team. **Influenza vaccination of pregnant** women and protection of their infants. N Engl J Med. 2014 Sep 4;371(10):918-31.

Madhivanan P, Pierre-Victor D, et al. **Human Papillomavirus Vaccination** and Sexual Disinhibition in Females: A Systematic Review. Am J Prev Med. 2016 Sep;51(3):373-83.

Maglione M, Lopamudra D, Raaen L, et al. **Safety of vaccines** used for routine immunization of U.S. children: a systematic review. Pediatrics. 2014.

Majumder MS, Cohn EL, Mekaru SR, et al. Substandard Vaccination Compliance and the 2015 **Measles** Outbreak. JAMA Pediatr. 2015 Mar 16.

Mackenzie GA, Hill PC, Sahito SM, et al. Effect of the introduction of **pneumococcal conjugate vaccination** on pneumonia in The Gambia: population-based surveillance and case-control studies. Lancet Infect Dis 2017; online June 7.

Malagón T, Drolet M, Boily MC, et al. Cross-protective efficacy of two **human papillomavirus vaccines**: a systematic review and meta-analysis. Lancet Infect Dis. 2012 Oct;12(10):781-9.

Manoff SB, Liss C, Caulfield MJ, et al. Revaccination with a 23-valent **pneumococcal polysaccharide** vaccine induces elevated and persistent functional antibody responses in adults aged 65 > or = years. J Infect Dis. 2010 Feb 15;201(4):525-33.

Manzoli L, Flacco ME, D'Addario M, Capasso L, De Vito C, Marzuillo C, et al. **Non-publication and delayed publication** of randomized **trials** on vaccines: survey. BMJ 2014;348:g3058.

Marchant A, Sadarangani M, Garand M, et al. **Maternal immunisation**: collaborating with mother nature. Lancet Infect Dis 2017; online April 19.

Markowitz LE, Hariri S, Lin C, et al. Reduction in Human Papillomavirus (HPV) Prevalence Among Young Women Following **HPV Vaccine** Introduction in the United States, National Health and Nutrition Examination Surveys, 2003-2010. J Infect Dis. 2013 Jun 19.

Marks JS, Halpin TJ. **Guillain-Barré syndrome** in recipients of A/New Jersey influenza vaccine. JAMA. 1980 Jun 27;243(24):2490-4.

Marin M, Leung J, Gershon AA. Transmission of **Vaccine-Strain Varicella-Zoster Virus**: A Systematic Review. Pediatrics. 2019 Aug 30.

Marin M, Marti M, Kambhampati A, et al. Global **Varicella** Vaccine Effectiveness: A Meta-analysis. Pediatrics. 2016 Feb 16.

Marin M, Zhang JX, Seward JF. Near elimination of **varicella deaths** in the US after implementation of the vaccination program. Pediatrics. 2011 Aug;128(2):214-20.

Markowitz LE, Liu G, Hariri S, et al. Prevalence of **HPV** After Introduction of the Vaccination Program in the United States. Pediatrics. 2016 Feb 22.

Marin M, Zhang JX, Seward JF. Near **elimination of varicella deaths** in the US after implementation of the vaccination program. Pediatrics. 2011;128:214-220.

Marshall GS, Adams GL, Leonardi ML, et al. Immunogenicity, Safety, and Tolerability of a **Hexavalent Vaccine in Infants**. Pediatrics. 2015 Jul 27.

Marshall HS, Richmond PC, Beeslaar J, et al; 6108A12001 Study Investigators. **Meningococcal** serogroup B-specifi c responses after vaccination with **bivalent** rLP2086: 4 year follow-up of a randomised, single-blind, placebo-controlled, phase 2 trial. Lancet Infect Dis 2016; online Oct 10

Martin NG, Sadarangani M, Pollard AJ, Goldacre MJ. Hospital admission rates for **meningitis and septicaemia** caused by Haemophilus infl uenzae, Neisseria meningitidis, and Streptococcus pneumoniae in children in England over five decades: a population-based observational study. Lancet Infect Dis 2014; 14: 397–405.

Martins CL, Benn CS, Andersen A, et al. A Randomized Trial of a Standard Dose of Edmonston-Zagreb **Measles** Vaccine Given at 4.5 Months of Age: Effect on Total Hospital Admissions. J Infect Dis. 2014 Jan 16.

Martinón-Torres F, Czajka H, Center KJ, et al. 13-Valent **Pneumococcal** Conjugate Vaccine (PCV13) in Preterm Versus Term Infants. Pediatrics. 2015 Mar 16.

Martinón-Torres F, Bernatowska E, Shcherbina A, et al. **Meningococcal B vaccine immunogenicity in children with defects in complement and splenic function**. Pediatrics. 2018;141(6):e20174250

Maruyama T, Taguchi O, Niederman MS, et al. Efficacy of **23-valent pneumococcal** vaccine in preventing pneumonia and improving survival in nursing home residents: double blind, randomised and placebo controlled trial. BMJ. 2010 Mar 8

Matlow JN, Pupco A, Bozzo P, Koren G. **Tdap vaccination during pregnancy** to reduce pertussis infection in young infants. Can Fam Physician. 2013 May;59(5):497-8.

Mayhew A, Mullins TL, Ding L et al. Risk Perceptions and Subsequent Sexual Behaviors After HPV Vaccination in Adolescents. Pediatrics. 2014 Feb 2.

Mbaeyi S, Joseph S, Blain A, Wang X, Hariri S, MacNeil J. **Meningococcal disease among college-aged young adults**: 2014-2016. Pediatrics. 2019;143(1):e20182130

McAllister L, Anderson J, Werth K, et al. **Needle-free jet injection** for administration of **influenza** vaccine: a randomised non-inferiority trial. Lancet 2014; 384: 674–81.

McCarthy M. **California ends vaccine exemptions** on grounds of belief-will other states follow? BMJ. 2015 Jul 2;351:h3635.

McCarthy NL, Gee J, Sukumaran L, et al. Vaccination and 30-Day **Mortality** Risk in Children, Adolescents, and Young Adults. Pediatrics. 2016 Feb 1.

McClenathan BM, Edwards KM. **Vaccine Safety**: An Evolving Evidence-based Science. Br J Clin Pharmacol. 2019 Aug 2.

McCormack PL, Joura EA. Quadrivalent human papillomavirus (types 6, 11, 16, 18) recombinant vaccine (**Gardasil®**): a review of its use in the prevention of premalignant genital lesions, genital cancer and genital warts in women. Drugs. 2010 Dec 24;70(18):2449-74. doi: 10.2165/11204920-000000000-00000.

McElhaney JE, Beran J, Devaster J-M, et al. **AS03-adjuvanted** versus non-adjuvanted inactivated trivalent **influenza** vaccine against seasonal influenza in elderly people: a phase 3 randomised trial. Lancet Infect Dis 2013; online March 19.

McElligott, James T., Darden, Paul M. Are **Patient-Held Vaccination Records** Associated With Improved Vaccination Coverage Rates? Pediatrics 2010 125: e467-e472.

McGirr A, Fisman DN. Duration of **Pertussis Immunity** After DTaP Immunization: A Meta-analysis. Pediatrics. 2015 Jan 5.

McIntyre PB, O'Brien KL, Greenwood B, van de Beek D. Effect of vaccines on **bacterial meningitis** worldwide. Lancet. 2012 Nov 10;380(9854):1703-11.

McIntosh AM, McMahon J, Dibbens LM et al. Effects of vaccination on onset and outcome of **Dravet syndrome**: a retrospective study. Lancet Neurol. 2010 May 4.

McKee M, Middleton J. **Information wars**: tackling the threat from disinformation on vaccines. BMJ. 2019 May 13;365:l2144.
McLaughlin JM, Swerdlow DL, et al. Rethinking **number-needed-to-vaccinate** for **pneumococcal conjugate** vaccines in older adults: Current and future implications. Vaccine. 2017 Aug 29.
McLean HQ, et al. Association of **prior vaccination** with **influenza vaccine effectiveness** in **children** receiving live attenuated or inactivated vaccine. JAMA Netw Open. 2018;1(6):e183742.
McNamara LA, Shumate AM, Johnsen P, et al. First Use of a **Serogroup B Meningococcal Vaccine** in the US in Response to a University Outbreak. Pediatrics. 2015 Apr 27.
McNeil MM, Weintraub ES, Duffy J, et al. **Risk of anaphylaxis after vaccination** in children and adults. J Allergy Clin Immunol. 2015 Sep 28.
McQuaid F, Snape MD, John TM, et al. Persistence of specific bactericidal antibodies at 5 years of age after vaccination against serogroup **B meningococcus** in infancy and at 40 months. CMAJ. 2015 Mar 23.
Measles and Rubella Elimination Working Group (MREWG). Guidelines for the prevention and control of measles outbreaks in Canada. CCDR 2013;39(ACS-3):1-52. www.phac-aspc.gc.ca/publicat/ccdr-rmtc/13vol39/acs-dcc-3/assets/pdf/meas-roug-eng.pdf (accessed October 2, 2013).
Medford RJ, Salit IE. **Anal cancer and intraepithelial neoplasia**: epidemiology, screening and prevention of a sexually transmitted disease. CMAJ. 2015 Feb 3;187(2):111-115.
Medical Letter. Treatment Guidelines: **Advice for Travelers**. Nov 2009. Updated **May 2012**.
Medical Letter: **Vaccines for travelers**. Med Lett Drugs Ther. 2014 Nov 24;56(1456):115-20 Updated **Nov 2018**.
Mehanna H, Jones TM, Gregoire V, Ang KK. **Oropharyngeal carcinoma** related to **human papillomavirus**. BMJ. 2010 Mar 25;340:c1439. doi: 10.1136/bmj.c1439.
Meissner HC. Immunization Policy and the Importance of **Sustainable Vaccine Pricing**. JAMA. 2016 Feb 8.
Meissner HC, Farizo K, Pratt D, et al. Understanding **FDA-Approved Labeling and CDC Recommendations for Use of Vaccines**. Pediatrics. 2018 Sep;142(3). pii: e20180780.
Meissner HC, Nair N, Plotkin SA. The National Vaccine Injury Compensation Program: Striking a Balance Between **Individual Rights and Community Benefit**. JAMA. 2019 Jan 4.
Meites E, Kempe A, Markowitz LE. Use of a 2-Dose Schedule for **Human Papillomavirus Vaccination** - Updated Recommendations of the Advisory Committee on Immunization Practices. MMWR Morb Mortal Wkly Rep. 2016 Dec 16;65(49):1405-1408
Meites E, Szilagyi PG, Chesson HW, et al**. Human Papillomavirus** Vaccination for Adults: Updated Recommendations of the Advisory Committee on Immunization Practices. MMWR Morb Mortal Wkly Rep. 2019 Aug 16;68(32):698-702.
Mello MM, Studdert DM, Parmet WE. Shifting Vaccination Politics - The **End of Personal-Belief Exemptions** in California. N Engl J Med. 2015 Jul 22.
Menge T, Cree B, Saleh A, et al. Neuromyelitis Optica Following **Human Papillomavirus Vaccination**. Neurology. 2012 Jun 20.
Merten M. **Polio**: getting ready for the day after eradication. BMJ. 2019 Aug 23;366:l5235.
Mesher D, Panwar K, Thomas SL, et al. The Impact of the **National HPV Vaccination Program in England** Using the Bivalent HPV Vaccine: Surveillance of Type-Specific HPV in Young Females, 2010-2016. J Infect Dis. 2018 Jun 18.
Metlay Joshua P.; Lautenbach Ebbing; Li Yimei; et al. Exposure to Children as a Risk Factor for Bacteremic **Pneumococcal** Disease: Changes in the **Post-Conjugate Vaccine Era**. Arch Intern Med. 2010;170(8):725-731.
Middleman, Amy B., Anding, Roberta, Tung, Celestine. Effect of **Needle Length** When Immunizing Obese Adolescents With Hepatitis B Vaccine. Pediatrics 2010 0: peds.2009-1592
Middleman AB, Baker CJ, Kozinetz CA, et al. Duration of Protection After Infant **Hepatitis B** Vaccination Series. Pediatrics. 2014 May 19.
Miller E, Andrews NJ, Waight PA, Slack MPE, George RC.Herd immunity and serotype replacement 4 years after seven-valent **pneumococcal** conjugate vaccination in England and Wales: an observational cohort study. Lancet Infect Dis 2011; published online May 27. DOI:10.1016/S1473-3099(11)70090-1.
Miller E, Andrews N, Stellitano L, et al. Risk of **narcolepsy in children and young people receiving AS03 adjuvanted pandemic A/H1N1** 2009 influenza vaccine: retrospective analysis. BMJ. 2013 Feb 26;346:f794.
Mina MJ, Metcalf CJ, de Swart RL, et al. Vaccines. Long-term **measles**-induced immunomodulation increases overall childhood infectious disease mortality. Science. 2015 May 8;348(6235):694-9.
Minassian C, Thomas SL, Smeeth L, et al. Acute Cardiovascular Events after **Herpes Zoster**: A Self-Controlled Case Series Analysis in Vaccinated and Unvaccinated Older Residents of the United States. PLoS Med. 2015 Dec 15;12(12):e1001919.
Mir F, Quadri F, Mach O, et al. Monovalent type-1 oral **poliovirus** vaccine given at short intervals in Pakistan: a randomised controlled, four-arm, open-label, non-inferiority trial. Lancet Infect Dis. 2015 Jun 17.
Mirdamadi K, Einarson A. **H1N1** and influenza viruses: Why **pregnant** women might be hesitant to be vaccinated. Can Fam Physician. 2011 Sep;57(9):1003-4.
Misegades LK, et al. Association of childhood **pertussis** with receipt of 5 doses of pertussis vaccine by time since last vaccine dose, California, 2010. JAMA. 2012;308(20):2126-2132.
Moberley SA, Holden J, Tatham DP, Andrews RM. Vaccines for **preventing pneumococcal** infection in adults. Cochrane Database Syst Rev. 2008 Jan 23;(1):CD000422.
Moberley S, Holden J, Tatham DP, et al. Vaccines for **preventing pneumococcal** infection in adults. Cochrane Database Syst Rev. 2012 Jun 22;1:CD000422. DOI: 10.1002/14651858.CD000422.pub3. This meta-analysis provides evidence supporting the recommendation for PPV to prevent IPD in adults. The evidence from RCTs is less clear with respect to adults with chronic illness.
Moberly T. UK doctors re-examine case for mandatory vaccination. BMJ. 2017 Jul 18;358:j3414.
Modin D, Jørgensen ME, Gislason G, et al**. Influenza Vaccine in Heart Failure**: Cumulative Number of Vaccinations, Frequency, Timing, and Survival: A Danish Nationwide Cohort Study. Circulation. 2018 Dec 10.
Mohanty S, Buttenheim A, Joyce C, et al. **Elimination of nonmedical vaccine exemptions in California**: experiences with medical exemptions. Pediatrics. 2018;142(5):e20181051
Mok CC, Ho LY, Fong LS, To CH. Immunogenicity and safety of a **quadrivalent human papillomavirus vaccine** in patients with **systemic lupus erythematosus**: a case-control study. Ann Rheum Dis. 2012 May 15.
Monfries N, Goldman RD. **Prophylactic antipyretics for prevention of febrile seizures** following vaccination. Can Fam Physician 2017;63:128-30.
Monk HM, Motsney AJ, Wade KC. Safety of **Rotavirus** Vaccine in the NICU. Pediatrics. 2014 May 19.
Moore DL; **Canadian Paediatric Society**, Infectious Diseases and Immunization Committee. **Influenza vaccine** recommendations for children and youth for the 2013/2014 season. Paediatr Child Health. 2013;18(8):e51-2.
Moore DL. Vaccine recommendations for children and youth for the 2017/2018 **influenza** season. Paediatr Child Health. 2018 Feb;23(1):e10-e13.
Moore MR, Link-Gelles R, Schaff ner W, et al. Eff ect of use of 13-valent **pneumococcal conjugate vaccine** in children on invasive pneumococcal disease in children and adults in the USA: analysis of multisite, population based surveillance. Lancet Infect Dis 2015; online Feb 3.
Moreira ED Jr, Block SL, Ferris Det al. Safety Profile of the 9-Valent **HPV** Vaccine: A Combined Analysis of 7 Phase III Clinical Trials. Pediatrics. 2016 Aug;138(2)
Mori S, Ueki Y, Hirakata N, et al. Impact of **tocilizumab** therapy on antibody response to **influenza vaccine** in patients with rheumatoid arthritis. Ann Rheum Dis. 2012 Dec;71(12):2006-10.
Mori S, Ueki Y, Akeda Y, et al. **Pneumococcal polysaccharide vaccination** in rheumatoid arthritis patients receiving **tocilizumab** therapy. Ann Rheum Dis. 2013 Aug;72(8):1362-6. T
Moro P, Perez Vilar S, Lewis P, et al. Safety surveillance of **diphtheria and tetanus toxoids and acellular pertussis (DTaP) vaccines**. Pediatrics. 2018;142(1):e20174171
Moro PL, Arana J, Cano M, et al. Deaths Reported to the **Vaccine Adverse Event Reporting System**, United States, 1997-2013. Clin Infect Dis. 2015 Sep 15;61(6):980-7.
Morrison VA, Johnson GR, Schmader KE, et al; Shingles Prevention Study Group. **Longterm persistence of zoster vaccine** efficacy. Clin Infect Dis 2015; 60:900–9.
Moro PL, Harrington T, et al. events after **Fluzone ® Intradermal** vaccine reported to the Vaccine Adverse Event Reporting System (VAERS), 2011-2013. Vaccine. 2013 Oct 9;31(43):4984-7.
Moss JL, Reiter PL, Truong YK, et al. **School entry requirements** and coverage of nontargeted adolescent vaccines. Pediatrics. 2016;138(6):e20161414
Moss WJ, Griffin DE. **Measles**. Lancet. 2011 Aug 17.
Mullane KM, Winston DJ, Wertheim MS, et al. Safety and immunogenicity of heat-treated **zoster** vaccine (ZVHT) in immunocompromised adults. J Infect Dis. 2013 Nov 1;208(9):1375-85.
Mulligan MJ, Bernstein DI, et al. Serological responses to an avian **influenza A/H7N9** vaccine mixed at the point-of-use with MF59 adjuvant: a randomized clinical trial. Jama Oct 2014.
Mulpuru S, Li L, Ye L, et al. **Effectiveness of Influenza Vaccination** on Hospitalizations and Risk Factors for Severe Outcomes in Hospitalized Patients With COPD. Chest. 2019 Jan;155(1):69-78.
Muñoz N, Manalastas R Jr, Pitisuttithum P, et al. Safety, immunogenicity, and efficacy of quadrivalent **human papillomavirus** (types 6, 11, 16, 18) recombinant vaccine in women **aged 24-45 years**: a randomised, double-blind trial. Lancet. 2009 Jun 1. [Epub ahead of print]
Munoz FM, Bond NH, et al. Safety and immunogenicity of **tetanus diphtheria and acellular pertussis (Tdap) immunization during pregnancy** in mothers and infants: a randomized clinical trial. JAMA. doi:10.1001/jama.2014.3633.
Murdoch J, Shroff A, Brooks A, et al. **Peri-splenectomy** vaccination at tertiary-care facilities in Hamilton, Ontario. JAMMI 2017;2(1):41-6. http://jammi.utpjournals.press/doi/abs/10.3138/jammi.2.1.006 (accessed October 4, 2017).
Musher DM, Manof SB, Liss C, et al. Safety and antibody response, including antibody persistence for 5 years, after primary vaccination or revaccination with **pneumococcal polysaccharide** vaccine in middle-aged and older adults. J InfectDis. 2010 Feb 15;201(4):516-24.
Myléus A, Stenlund H, Hernell O, et al. Early Vaccinations Are Not Risk Factors for **Celiac Disease**. Pediatrics. 2012 Jun 25.
Nabel GJ. Designing **tomorrow's vaccines**. N Engl J Med. 2013 Feb 7;368(6):551-60.
Nace DA, Lin CJ, Ross TM, et al. Randomized, Controlled Trial of **High-Dose Influenza Vaccine** Among Frail Residents of Long-Term Care Facilities. J Infect Dis. 2014 Dec17.
NACI Jan/12: National Advisory Committee on Immunization. Update human papillomavirus **HPV vaccines**.www.phac-aspc.gc.ca/publicat/ccdr-rmtc/11vol37/acs-dcc-8/index-eng.php
NACI Oct/13 National Advisory Committee on Immunization. Statement on the use of **conjugate pneumococcal vaccine-13 valent in adults** (Pneu-C-13). CCDR 2013;39(ACS-5). www.phac-aspc.gc.ca/publicat/ccdr-rmtc/13vol39/acs-dcc-5/index-eng.php (accessed Nov 14, 2013).
NACI Feb/14 National Advisory Committee on Immunization, Public Health Agency of Canada. Update on **pertussis vaccination** in pregnancy. http://publications.gc.ca/collections/collection_2014/aspc-phac/HP40-93-2014-eng.pdf (accessed February 18, 2014).
NACI: National Advisory Committee on Immunization, Public Health Agency of Canada. Update on the use of **herpes zoster vaccine**. An Advisory Committee Statement. January 2014.http://publications.gc.ca/collections/collection_2014/aspc-phac/HP40-92-2014-eng.pdf (accessed February 12, 2014).
NACI: National Advisory Committee on Immunization (NACI). Update on the use of **pneumococcal** vaccines: addition of asthma as a high-risk condition. February 2014. http://publications.gc.ca/collections/collection_2014/aspc-phac/HP40-94-2014-eng.pdf (accessed April 2, 2014).
NACI: Meningococcal B Pilot Project Task Group; National Advisory Committee on Immunization; Pan-Canadian Public Health Network. Recommended use of the multicomponent **meningococcal B (4CMenB)** vaccine in Canada: common guidance statement. April 2014.http://publications.gc.ca/collections/collection_2014/aspc-phac/HP40-103-2014-eng.pdf (accessed May 12, 2014).
NACI: Meningococcal B Pilot Project Task Group; National Advisory Committee on Immunization, Pan-Canadian Public Health Network. The recommended use of the multicomponent **meningococcal B (4CMenB)** vaccine in Canada. www.phac-aspc.gc.ca/naci-cni/mening-4cmenb-exec-resum-eng.php (accessed May 12, 2014).
NACI: National Advisory Committee on Immunization. Statement on **seasonal influenza vaccine for 2014-2015**. http://publications.gc.ca/collections/collection_2014/aspc-phac/HP40-114-2014-eng.pdf(accessed August 12, 2014).
NACI: National Advisory Committee on Immunization. An Advisory Committee Statement. Update on **quadrivalent meningococcal vaccines** available in Canada. April 2015. http://publications.gc.ca/collections/collection_2015/aspc-phac/HP40-125-2014-eng.pdf (accessed May 7, 2015).
NACI: National Advisory Committee on Immunization (NACI). Addendum – **LAIV use in children and adolescents**. Advisory Committee Statement (ACS). Canadian Immunization Guide chapter on **influenza** and statement on seasonal influenza vaccine for **2016-2017**.
NACI: National Advisory Committee on Immunization. Update on the use of 13-valent **pneumococcal conjugate vaccine** (PNEU-C-13) in addition to 23-valent pneumococcal polysaccharide vaccine (PNEU-P-23) in **immunocompetent adults 65 years of age and older** – interim recommendation. www.healthycanadians.gc.ca/publications/healthy-living-vie-saine/update-pneu- c-13-and-pneu-p-23-mise-a-jour-2016/index-eng.php (accessed October 26, 2016).
NACI: Henry B, Baclic O; on behalf of the National Advisory Committee on Immunization (NACI). Summary of the NACI update on the recommended use of **hepatitis B** vaccine. CCDR 2017;43-5:104-6. www.phac-aspc.gc.ca/publicat/ccdr-rmtc/17vol43/dr-rm43-5/assets/pdf/17vol43_5-eng.pdf (accessed May 9, 2017).
NACI: National Advisory Committee on Immunization (**NACI**). Canadian Immunization Guide Chapter on Influenza and Statement on **Seasonal Influenza Vaccine 2017-2018**. Public Health Agency of Canada. May 2017.
NACI: National Advisory Committee on Immunization. An Advisory Committee Statement (ACS). Update on immunization in **pregnancy with tetanus toxoid, reduced diphtheria toxoid** and reduced acellular **pertussis** (Tdap) vaccine. February 2018. https://www.canada.ca/content/dam/phac-aspc/documents/services/publications/healthy-living/update-immunization- pregnancy-tdap-vaccine/update-immunization-pregnancy-tdap-vaccine-eng.pdf (accessed March 6, 2018).
NACI: National Advisory Committee on Immunization (NACI). Canadian immunization guide chapter on influenza and statement on seasonal influenza vaccine for 2019–2020. An Advisory Committee Statement (ACS). https://www.canada.ca/content/dam/phac-aspc/documents/services/publications/healthy-living/canadian-immunization-guide-statement-seasonal-influenza-vaccine-2019-2020/NACI_Stmt_on_Seasonal_Influenza_Vaccine_2019-2020_v12.3_EN.pdf .
Nadeau JA, Bednarczyk RA, Masawi MR, et al. Vaccinating my way-use of **alternative vaccination schedules** in new york state. J Pediatr. 2015 Jan;166(1):151-156.e1.
Nakafero G, Grainge MJ, Myles PR, et al. Association between **inactivated influenza vaccine and primary care consultations for autoimmune rheumatic disease flares**: a self-controlled case series study using data from the Clinical Practice Research Datalink. Ann Rheum Dis. 2019 Apr 29.
Naleway AL, Mittendorf KF, Irving SA, et al. **Primary Ovarian Insufficiency and Adolescent Vaccination**. Pediatrics. 2018 Sep;142(3).
Natori Y et al. A double-blind, randomized trial of **high-dose vs standard-dose influenza vaccine in adult solid-organ transplant recipients**. Clin Infect Dis 2018 May 17; 66:1698.
Nayakwadi Singer M, Heath C, Muinde J, et al. **Pneumococcal Vaccine** Response After Exposure to Parasites in Utero, in Infancy, or Mid-Childhood. Pediatrics. 2017 Mar 16.
Neidich SD, Green WD, Rebeles J, et al. Increased risk of **influenza** among vaccinated adults who are **obese**. Int J Obes (Lond). 2017 Jun 6.
Nemes E, Geldenhuys H, Rozot V, et al. Prevention of M. tuberculosis Infection with H4:IC31 Vaccine or BCG Revaccination. N Engl J Med. 2018 Jul 12;379(2):138-149.
Nielsen C. Keeping up with **immunizations for adults**. Cleve Clin J Med. 2014 Oct;81(10):608-12.
Neuzil Kathleen M., Canh Do Gia, Thiem Vu Dinh, et al. Immunogenicity and Reactogenicity of **Alternative Schedules of HPV** Vaccine in Vietnam: A Cluster Randomized Noninferiority Trial. *JAMA*. 2011;305(14):1424-1431.doi:10.1001/jama.2011.407
Ng TWY, Cowling BJ, Gao HZ, et al. **Comparative Immunogenicity of Enhanced Seasonal Influenza Vaccines** in Older Adults: A Systematic Review and Meta-analysis. J Infect Dis. 2019 Apr 19;219(10):1525-1535.
Nguyen MTT;Lindegaard H;Hendricks O;Jorgensen CS;K. Initial Serological Response after Prime-boost **Pneumococcal** Vaccination in **Rheumatoid Arthritis** Patients: Results of a Randomized Controlled Trial. J Rheumatol. 2017 Oct 1. (rituximab lower response rate)
Nguipdop-Djomo P, Heldal E, Rodrigues LC, et al. Duration of **BCG** protection against tuberculosis and change in effectiveness with time since vaccination in Norway: a retrospective population-based cohort study. Lancet Infect Dis. 2015 Nov 18.
Niccolai LM, Pettigrew MM. The Role of Cognitive Bias in Suboptimal **HPV** Vaccine Uptake. Pediatrics. 2016 Sep 9.
Nichols AJ, Gonzalez A, Clark ES, et al. **Combined Systemic and Intratumoral Administration of Human Papillomavirus Vaccine** to Treat Multiple Cutaneous Basaloid Squamous Cell Carcinomas. JAMA Dermatol. 2018 Jul 3.
Nickonchuk T, Lindblad AJ, Kolber MR. Oral **cholera** vaccine for traveler's diarrhea prophylaxis. Can Fam Physician. 2014 May;60(5):451.
Nolan T, Roy-Ghanta S, Montellano M, et al. **Relative Efficacy of AS03-Adjuvanted Pandemic Influenza A(H1N1) Vaccine in Children: Results of a Controlled, Randomized Efficacy Trial.** J Infect Dis. 2014 May 2.
Nordin JD, Kharbanda EO, Benitez GV, Nichol et al. Maternal safety of trivalent inactivated influenza vaccine in pregnant women. Obstet Gynecol. 2013 Mar;121(3):519-25.
Nordin JD, Vazquez-Benitez G, Olsen A, et al. Safety of **guidelines recommending live attenuated influenza vaccine** for routine use in children and adolescents with asthma. Vaccine. 2019 Jul 9;37(30):4055-4060.
Norhayati MN, Ho JJ, Azman MY. **Influenza** vaccines for preventing acute otitis media in infants and children. Cochrane Database of Systematic Reviews 2015, Issue 3. Art. No.: CD010089. DOI: 10.1002/14651858.CD010089.pub2. Influenza vaccine results in a small reduction in AOM. The observed reduction with the use of antibiotics needs to be considered in the light of current recommended practices aimed at avoiding antibiotic overuse. Safety data from these trials are limited. The benefits may not justify the use of influenza vaccine without taking into account the vaccine efficacy in reducing influenza and safety data. The quality of the evidence was high to moderate. Additional research is needed.
Norhayati MN;Ho JJ;Azman MY. **Influenza vaccines for preventing acute otitis media** in infants and children. Cochrane Database Syst Rev. 2017 Oct 17;10:CD010089. Influenza vaccine results in a small reduction in AOM. The observed reduction in the use of antibiotics needs to be considered in light of current recommended practices aimed at avoiding antibiotic overuse. Safety data from these trials were limited. The benefits may not justify the use of influenza vaccine without taking into account the vaccine efficacy in reducing influenza and safety data. We judged the quality of the evidence to be low to moderate.
Noronha AS, Markowitz LE, Dunne EF. Systematic review of **human papillomavirus vaccine coadministration**. Vaccine. 2014 Jan 8. pii: S0264-410X(13)01768-4.
Novak RT, Kambou JL, Diomandé FVK, et al. **Serogroup A meningococcal** conjugate vaccination in Burkina Faso: analysis of national surveillance data. Lancet Infect Dis 2012; July 18.
Novakovic D, Cheng ATL, Zurynski Y, et al. A Prospective Study of the Incidence of Juvenile-Onset Recurrent Respiratory **Papillomatosis** After Implementation of a National **HPV** Vaccination Program. J Infect Dis. 2017 Nov 9.
Nunes MC, Cutland CL, Jones S, et al; Maternal Flu Trial Team. Duration of infant protection against influenza illness conferred by **maternal immunization**: secondary analysis of a randomized clinical trial [online July 5, 2016]. JAMA Pediatr. doi:10.1001/jamapediatrics.2016.0921. Nyhan B, Reifler J, Richey S, et al. Effective **Messages in Vaccine Promotion**: A Randomized Trial. Pediatrics. 2014 Mar 3.
Nunes MC, Cutland CL, Madhi SA. **Influenza Vaccination during Pregnancy** and Protection against Pertussis. N Engl J Med. 2018 Mar 29;378(13):1257-1258.
O'Brien, Megan A., Prosser, Lisa A., et al. New Vaccines Against Otitis Media: Projected Benefits and Cost-effectiveness Pediatrics 2009 123: 1452-1463
O'Brien KL, Hochman M, et al. Combined schedule of **pneumococcal conjugate and polysaccharide vaccines**: is hyporesponsiveness an issue? Lancet Infect Dis. 2007 Sep;7(9):597-606.
Ochoa-Gondar O, Vila-Corcoles A, Rodriguez-Blanco T, et al. Effectiveness of **the 23-valent pneumococcal polysaccharide** vaccine against community-acquired pneumonia in the general population aged ≥60 years: 3 years of follow-up in the CAPAMIS study. Clin Infect Dis 2014; 58:909–17.
O'Leary ST, Glanz JM, et al. The Risk of **Immune Thrombocytopenic Purpura** (ITP) After Vaccination in Children and Adolescents. Pediatrics. 2012 Jan 9 (**MMR** risk in early childhood)
O'Leary ST et al. Effectiveness and cost of bidirectional **text messaging** for adolescent vaccines and well care. Pediatrics 2015 Oct 5; peds.2015-1089.
O'Leary ST, Allison MA, Fisher A, et al. Characteristics of **Physicians Who Dismiss Families for Refusing Vaccines**. Pediatrics. 2015 Nov 2.
O'Leary ST, Lee M, Lockhart S, et al. Effectiveness and Cost of **Bidirectional Text Messaging** for Adolescent Vaccines and Well Care. Pediatrics. 2015 Nov;136(5):e1220-7.
O'Leary ST, Riley LE, Lindley MC, et al. **Immunization Practices** of U.S. Obstetrician/Gynecologists for **Pregnant Patients**. Am J Prev Med. 2017 Dec 12.
O'Leary ST, Riley LE, Lindley MC, et al. **Obstetrician-Gynecologists' Strategies to Address Vaccine Refusal Among Pregnant Women**. Obstet Gynecol. 2019 Jan;133(1):40-47.
O'Reilly KM, Durry E, Ul Islam O, et al. The effect of mass immunisation campaigns and new **oral poliovirus vaccines** on the incidence of poliomyelitis in Pakistan and Afghanistan, 2001-11: a retrospective analysis. Lancet. 2012 Jul 3.
Oberste MS, Lipton HL. Global **polio** perspective. Neurology. 2014 May 20;82(20):1831-2.
Offit PA. Should childhood **vaccination be mandatory**? **Yes**. BMJ. 2012 May 15;344:e2434.
Ogbuanu IU, Kutty PK, Hudson JM, et al. Impact of a **Third Dose of Measles-Mumps-Rubella Vaccine** on a Mumps Outbreak. Pediatrics. 2012 Nov 5.
Ogilvie G, et al. Immunogenicity **of 2 vs 3 Doses of the Quadrivalent Human Papillomavirus** Vaccinein Girls Aged 9 to 13 Years After 60 Months. JAMA. 2017 Apr 25;317(16):1687-1688.
Ogilvie GS, Phan F, Pedersen HN, et al. Population-level **sexual behaviours in adolescent girls before and after introduction of the human papillomavirus vaccine** (2003-2013). CMAJ. 2018 Oct 15;190(41):E1221-E1226.
Okasha O, Rinta-Kokko H, Palmu AA, et al. **Population-level impact of infant 10-valent pneumococcal** conjugate vaccination on adult pneumonia hospitalisations in Finland. Thorax. 2018 Mar;73(3):262-269.
Olarte L, Ampofo K, Stockmann C, et al. Invasive Pneumococcal Disease in Infants Younger Than 90 Days Before and After Introduction of **PCV7**. Pediatrics. 2013 Jun 3.
Olarte L, Barson WJ, Barson RM, et al. Impact of the **13-Valent Pneumococcal** Conjugate Vaccine on Pneumococcal Meningitis in US Children. Clin Infect Dis. 2015 May 13.
Omeñaca Félix, Merino Jose Manuel, et al. Immunization of Preterm Infants With **10-Valent Pneumococcal** Conjugate Vaccine. Pediatrics 2011; peds.2010-1184; July 4, 2011.
Omer SB, Richards JL, Ward M, Bednarczyk RA. Vaccination policies and rates of **exemption** from immunization, 2005-2011. N Engl J Med. 2012 Sep 20;367(12):1170-1.
Omer SB, Orenstein WA, Koplan JP. Go big and go fast--**vaccine refusal and disease eradication**. N Engl J Med. 2013 Apr 11;368(15):1374-6.
Omer SB, Peterson D, Curran EA, et al. **Legislative challenges to school immunization** mandates, 2009-2012. JAMA. 2014 Feb 12;311(6):620-1
Omer SB. **Maternal Immunization**. N Engl J Med. 2017 Mar 30;376(13):1256-1267.
Omer SB, Allen K, Chang DH, et al. **Exemptions From Mandatory Immunization** After Legally Mandated Parental Counseling. Pediatrics. 2017 Dec 18.
Omura J, Buxton J, Kaczorowski J, et al. **Immunization delivery in British Columbia**: Perspectives of primary care physicians. Can Fam Physician. 2014 Mar;60(3):e187-93.
Opel DJ, et al. The Relationship Between **Parent Attitudes** About **Childhood Vaccines** Survey Scores and Future Child Immunization Status: A Validation Study. JAMA Pediatr.2013Sep 23.
Opel DJ, Heritage J, Taylor JA, et al. The architecture of **provider-parent vaccine discussions** at health supervision visits. Pediatrics. 2013 Dec;132(6):1037-46.
Opel DJ, Feemster KA, Omer SB, et al. A 6-month-old with **vaccine-hesitant parents**. Pediatrics. 2014 Mar;133(3):526-30.
Opel DJ, Schwartz JL, Omer SB, et al. Achieving an **Optimal Childhood Vaccine Policy**. JAMA Pediatr. 2017 Jul 3.
Opel DJ, Sonne JA, Mello MM. **Vaccination without Litigation** – Addressing Religious Objections to Hospital Influenza-Vaccination Mandates. N Engl J Med. 2018 Jan 31.
Orenstein WA, Paulson JA, Brady MT, et al. Global vaccination recommendations and **thimerosal**. Pediatrics. 2013 Jan;131(1):149-51.
Orenstein W, Seib K. Mounting a good offense against **measles**. N Engl J Med. 2014 Oct 30;371(18):1661-3.
Orenstein WA;Committee on Infectious Disease. **Eradicating Polio**: How the World's Pediatricians Can Help Stop This Crippling Illness Forever. Pediatrics. 2015 Jan;135(1):196-202.
Osorio JE, Velez ID, Thomson C, et al. Safety and immunogenicity of a recombinant live attenuated tetravalent **dengue vaccine** (DENVax) in flavivirus-naive healthy adults in Colombia: a randomised, placebo-controlled, phase 1 study. Lancet Infect Dis. 2014 Sep;14(9):830-8.

Ostergaard L et al. A bivalent **meningococcal B vaccine** in adolescents and young adults. N Engl J Med 2017 Dec 14; 377:2349.

Osterholm MT, Kelley NS, Sommer A, Belongia EA. Efficacy and effectiveness of **influenza vaccines**: a systematic review and meta-analysis. Lancet Infect Dis. 2012;12:36-44.

Otsuka SH, Tayal NH, Porter K, et al. Improving **herpes zoster** vaccination rates through use of a clinical **pharmacist** and a personal health record. Am J Med. 2013 Sep;126(9):832.e1-6.

Ouldali N, Levy C, Minodier Pet al. Long-term Association of **13-Valent Pneumococcal Conjugate Vaccine Implementation** With Rates of Community-Acquired Pneumonia in Children. JAMA Pediatr. 2019 Feb 4.

Oyo-Ita A, Wiysonge CS, Oringanje C, et al. Interventions for **improving coverage of childhood immunisation** in low- and middle-income countries.Cochrane Database of Systematic Reviews 2016, Issue 7. Art. No.: CD008145. Providing parents and other community members with information on immunisation, health education at facilities in combination with redesigned immunisation reminder cards, regular immunisation outreach with and without household incentives, home visits, and integration of immunisation with other services may improve childhood immunisation coverage in LMIC. Most of the evidence was of low certainty, which implies a high likelihood that the true effect of the interventions will be substantially different. There is thus a need for further well-conducted RCTs to assess the effects of interventions for improving childhood immunisation coverage in LMICs.

Paavonen J, Naud P, Salmerón J, Wheeler C, et al. for the HPV PATRICIA Study Group. Efficacy of human papillomavirus (**HPV**)-16/18 AS04-adjuvanted vaccine against cervical infection and precancer caused by oncogenic HPV types (PATRICIA): final analysis of a double-blind, randomised study in young women. Lancet. 2009 Jul 6

Pace D, Khatami A, McKenna J, et al. Immunogenicity of reduced dose **priming schedules** of **serogroup C meningococcal** conjugate vaccine followed by booster at 12 months in infants: open label randomised controlled trial. BMJ. 2015 Apr 1;350:h1554.

Palefsky JM et al. **HPV vaccine** against anal HPV infection and anal intraepithelial neoplasia. N Engl J Med 2011 Oct 27; 365:1576.

Palmer T, Wallace L, Pollock KG, et al. Prevalence of **cervical disease at age 20 after immunisation** with bivalent HPV vaccine at age 12-13 in Scotland: retrospective population study. BMJ. 2019 Apr 3;365:l1161

Palmu AA, Jokinen J, Borys D, et al. Eff ectiveness of the ten-valent pneumococcal Haemophilus influenzae protein D conjugate vaccine (**PHiD-CV10**) against invasive pneumococcal disease: a cluster randomised trial. Lancet 2012; online Nov 16.

Palmu AA, Kilpi TM, Rinta-Kokko H, et al. **Pneumococcal Conjugate Vaccine** and Clinically Suspected Invasive Pneumococcal Disease. Pediatrics. 2015 Jun 15.

Panagiotou OA, Befano BL, Gonzalez P, et al; on behalf of the Costa Rica HPV Vaccine Trial (CVT) Group. Effect of bivalent **human papillomavirus (HPV) vaccination** on pregnancy outcomes: long term observational follow-up in the Costa Rica HPV Vaccine Trial. BMJ 2015;351:h4358..

PapaniaMJ,Wallace GS, Rota PA, et al. **Elimination of endemic measles, rubella**, and congenital rubella syndrome from theWestern hemisphere: the US experience [online December 5, 2013]. JAMA Pediatr.doi:10.1001/jamapediatrics.2013.4342.

Parashar UD, Nelson EA, Kang G. Diagnosis, management, and prevention of **rotavirus** gastroenteritis in children. BMJ. 2013 Dec 30;347:f7204.

Parez N, Giaquinto C, Du Roure C, et al. **Rotavirus** vaccination in Europe: drivers and barriers. Lancet Infect Dis. 2014 May;14(5):416-425.

Parikh SR, et al. Eff ectiveness and impact of a reduced infant schedule of **4CMenB** vaccine against group B **meningococcal** disease in England: a national observational cohort study. Lancet 2016; online Oct 27.

Parikh SR, Lucidarme J, Bingham C, et al. **Meningococcal B Vaccine** Failure With a **Penicillin-Resistant Strain** in a Young Adult on Long-Term **Eculizumab**. Pediatrics. 2017;140(3):e20162452

Parikh SR, Newbold L, Slater S, et al. **Meningococcal** serogroup B strain coverage of the multicomponent 4CMenB vaccine with corresponding regional distribution and clinical characteristics in England, Wales, and Northern Ireland, 2007–08 and 2014–15: a qualitative and quantitative assessment. Lancet Infect Dis 2017; online Mar 30.

Park JK, Choi Y, Winthrop KL, et al. Optimal time between the last **methotrexate administration and seasonal influenza vaccination** in rheumatoid arthritis: post hoc analysis of a randomised clinical trial. Ann Rheum Dis. 2019 Sep;78(9):1283-1284.

Park JK, Lee MA, Lee EY, et al. Effect of **methotrexate discontinuation** on efficacy of seasonal **influenza** vaccination in patients with rheumatoid arthritis: a randomised clinical

Park JK, Lee YJ, et al. Impact of **temporary methotrexate discontinuation for 2 weeks on immunogenicity of seasonal influenza** vaccination in patients with rheumatoid arthritis: a randomised clinical trial. Ann Rheum Dis. 2018 Mar 23.

Parker LA, et al. Adapting to the global shortage of **cholera** vaccines: targeted single dose cholera vaccine in response to an outbreak in South Sudan. Lancet Infect Dis. 2017 Jan 18.

Partinen M, Kornum BR, Plazzi G, et al. Narcolepsy as an autoimmune disease: the role of H1N1 infection and vaccination. Lancet Neurol. 2014 Jun;13(6):600-613.

Pasternak B, Svanström H, et al. Vaccination against **pandemic A/H1N1 2009 influenza in pregnancy** and risk of fetal death: cohort study in Denmark. BMJ 2012;344:e2794.

Pasternak B, Svanstro¨m H, Mølgaard-Nielsen D, Krause TG, et al. Risk of adverse fetal outcomes following administration of a **pandemic influenza A(H1N1) vaccine** during pregnancy. JAMA. 2012;308(2):165-174.

Patel M, et al. Association between pentavalent rotavirus vaccine and severe **rotavirus** diarrhea among children in Nicaragua. JAMA. 2009 Jun 3;301(21):2243-51.

Patel MM., López-Collada VR, Bulhões MM, et al. **Intussusception Risk** and Health Benefits of **Rotavirus** Vaccination (Rotarix) in Mexico and Brazil. N Engl J Med 2011; 364:2283-2292.

Patel MM, Glass R, Desai R, et al. Fulfilling the promise **of rotavirus vaccines**: how far have we come since licensure? Lancet Infect Dis. 2012 Jul;12(7):561-70.

Patel M, Pedreira C, De Oliveira LH, et al. Duration of protection of pentavalent **rotavirus** vaccination (RV 5) in nicaragua. Pediatrics. 2012 Aug;130(2):e365-72.

Patel MM, Clark AD, Sanderson CF, et al. Removing the age restrictions for **rotavirus** vaccination: a benefit-risk modeling analysis. PLoS Med. 2012 Oct;9(10):e1001330.

Patel MM, Patzi M, Pastor D, et al. Effectiveness of monovalent **rotavirus** vaccine in Bolivia: case-control study. BMJ. 2013 Jun 19;346:f3726.

Patel MK, Orenstein WA. Classification of **global measles cases in 2013-17 as due to policy or vaccination failure**: a retrospective review of global surveillance data. Lancet Glob Health. 2019 Mar;7(3):e313-e320.

Paules CI, Fauci AS. **Yellow Fever -** Once Again on the Radar Screen in the Americas. N Engl J Med. 2017 Mar 8.

Paules C, Subbarao K. **Influenza**. Lancet. 2017 Mar 10.

Pavia, Maria, Bianco, Aida, et al. Efficacy of **Pneumococcal Vaccination** in Children Younger Than 24 Months: A Meta-Analysis Pediatrics 2009 123: e1103-e1110.

Payne DC, Sulemana I, et al. New Vaccine Surveillance Network. Evaluation of Effectiveness of Mixed **Rotavirus** Vaccine Course for Rotavirus Gastroenteritis. JAMA Pediatr. 2016May 31.

Pead PJ. **Vaccination's Forgotten Origins**. Pediatrics. 2017 Mar 7.

Peña MT, et al.. Orbital complications of acute sinusitis: changes in the **post-pneumococcal vaccine** era. JAMA Otolaryngol Head Neck Surg. 2013 Mar 1;139(3):223-7.

Perkins RB, et al. Impact of Number of **Human Papillomavirus Vaccine Doses** on Genital Warts Diagnoses Among a National Cohort of U.S. Adolescents. Sex Transm Dis. 2017 Jun;44(6):365-370.

Perrett KP, Jachno K, Nolan TM, Harrison LC. Association of **Rotavirus Vaccination With the Incidence of Type 1 Diabetes** in Children. JAMA Pediatr. 2019 Jan 22.

Petousis-Harris H, Paynter J, Morgan J, et al. Efficacy of a group B outer membrane vesicle **meningococcal** vaccine against **gonorrhoea** in New Zealand: a retrospective case-control study. Lancet 2017; online July 10.

Pezzotti P, Miglietta A, Neri A, et al. **Meningococcal C conjugate vaccine effectiveness** before and during an outbreak of invasive meningococcal disease due to Neisseria meningitides serogroup C/cc11, Tuscany, Italy. Vaccine. 2018 Jun 9.

Phadke VK, Bednarczyk RA, Salmon DA, Omer SB. Association between **vaccine refusal** and vaccine preventable diseases in the United States: a focus on **measles and pertussis**. JAMA. doi:10.1001 /jama.2016.1353

Pharmacist Letter Detail-Document, Flu Vaccines 2014-2015. Pharmacist's Letter/Prescriber's Letter. September 2014.

Phrommintikul A, Kuanprasert S, et al. **Influenza vaccination reduces cardiovascular events** in patients with acute coronary syndrome. Eur Heart J. 2011 Jul;32(14):1730-5.

Pichichero ME, Casey JR. Emergence of a multiresistant serotype **19A pneumococcal** strain not included in the 7-valent conjugate vaccine as an otopathogen in children. JAMA. 2007 Oct 17;298(15):1772-8. In the years following introduction of PCV7, a strain of S pneumoniae has emerged in the United States as an otopathogen that is resistant to all FDA-approved antibiotics for treatment of AOM in children.

Pickering LK, Baker CJ, Freed GL, et al. Infectious Diseases Society of America-**IDSA**. Immunization programs for **infants, children, adolescents, and adults**: clinical practice guidelines by the Infectious Diseases Society of America. Clin Infect Dis. 2009 Sep 15;49(6):817-40.

Pilishvili T, Zell ER, Farley MM, et al. Risk factors for **invasive pneumococcal disease** in children in the era of conjugate vaccine use. Pediatrics. 2010 Jul;126(1):e9-17.

Pillai Riddell R, Taddio A, et al. **Process Interventions for Vaccine Injections**: Systematic Review of Randomized Controlled Trials and Quasi-Randomized Controlled Trials. Clin J Pain. 2015 Oct;31(10 Suppl):S99-S108.

Pingali SC, Delamater PL, Buttenheim AM, et al. Associations of Statewide Legislative and Administrative **Interventions With Vaccination Status** Among Kindergartners in California. JAMA. 2019 Jul 2;322(1):49-56.

Piram M, Gonzalez Chiappe S, Madhi F, et al. **Vaccination and Risk of Childhood IgA Vasculitis**. Pediatrics. 2018 Oct 30.

Pisano J, Cifu AS. Use of **pneumococcal** vaccine in adults. JAMA. 2015 Feb 17;313(7):719-20.

Pitisuttithum P, Boonnak K, Chamnanchanunt S, et al. Safety and immunogenicity of a live attenuated **influenza H5 candidate** vaccine strain A/17/turkey/Turkey/05/133 **H5N2** and its priming effects for potential pre-pandemic use: a randomised, double-blind, placebo-controlled trial. Lancet Infect Dis; 2017; online May 19.

Plotkin SA, Mahmoud AA, Farrar J. Establishing a **Global Vaccine-Development Fund**. N Engl J Med. 2015 Jul 23;373(4):297-300.

Plotkin SA. How to Prepare for **Expert Testimony on the Safety of Vaccination**. Pediatrics. 2019 Mar 6.

Poehling KA et al. New Vaccine Surveillance Network. Impact of **maternal immunization on influenza** hospitalizations in infants. Am J Obstet Gynecol. 2011 Jun;204(6 Suppl 1):S141-8.

Politi MC, Jones KM, Philpott SE. The Role of **Patient Engagement** in Addressing Parents' Perceptions About Immunizations. JAMA. 2017 Jun 22.

Pop-Vicas A, Rahman M, Gozalo PL, et al. Estimating the Effect of **Influenza Vaccination on Nursing Home Residents'** Morbidity and **Mortality**. J Am Geriatr Soc. 2015 Aug 17.

Pottie K, Greenaway C, Feightner J, et al. coauthors of the Canadian Collaboration for Immigrant and Refugee Health. Evidence-based clinical guidelines for **immigrants and refugees**. CMAJ. 2011 Sep 6;183(12):E824-925.

Powell B, Ford C. **Risks of travel,** benefits of a specialist consult. Cleve Clin J Med. 2010 Apr;77(4):246-54.

Prather AA, Hall M, Fury JM, et al. Sleep and antibody response to **hepatitis B** vaccination. Sleep. 2012 Aug 1;35(8):1063-9**.**

Prevnar 13: December 22, 2009 -- Health Canada has approved a pneumococcal 13-valent conjugate vaccine (Diphtheria CRM197 Protein [Prevnar 13] for children aged 6 weeks through 5 years for active immunisation against invasive pneumococcal disease. The 13-valent vaccine is designed to provide the broadest coverage of any pneumococcal conjugate vaccine. The new vaccine includes strains 1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F, and 23F -- responsible for the greatest remaining burden of invasive disease in young children worldwide.

Price, CS., Thompson, WW., Goodson, B, et al. Prenatal and Infant Exposure to **Thimerosal** From Vaccines and Immunoglobulins and Risk of **Autism**. Pediatrics 2010 0: peds.2010-0309.

Prosser LA, Harpaz R, Rose AM, et al. A cost-**effectiveness analysis of vaccination for prevention of herpes zoster and related complications**: input for national recommendations. Ann Intern Med. 2019. [Epub ahead of print].doi:10.7326/M18-2347

Prymula R, Siegrist CA, Chlibek R, et al. Effect of prophylactic **paracetamol/acetaminophen** administration at time of vaccination on febrile reactions and antibody responses in children: two open-label, randomised controlled trials. Lancet. 2009 Oct 17;374(9698):1339-50.

Prymula R, Bergsaker MR, Esposito S, et al. Protection against **varicella** with **two doses** of combined measles-mumps-rubella-varicella vaccine versus one dose of monovalent varicella vaccine: a multicentre, observer-blind, randomised, controlled trial. Lancet 2014; online Jan 29. http://dx.doi.org/10.1016/S0140-6736(12)61461-5.

Public Health Agency of Canada. Canada Communicable Disease Report. Committee to Advise on Tropical Medicine and Travel (CATMAT) statement. Statement on **pregnancy and travel**. http://www.phac-aspc.gc.ca/publicat/ccdr-rmtc/10vol36/acs-2/index-eng.php Mar 2010.

Public Health Agency of Canada. **Canadian Immunization Guide–**evergreen edition. www.phac-aspc.gc.ca/publicat/cig-gci/index-eng.php (accessed December 17, 2012).

Public Health Agency of Canada. **Yellow fever vaccination** in Canada. E-learning module for health care professionals advising travellers. www.phac-aspc.gc.ca/tmp-pmv/el-mf-eng.php

Public Health Agency of Canada). Canadian Immunization Guide chapter on **influenza** and statement on seasonal influenza vaccine for **2016-2017**. www.phac-aspc.gc.ca/naci-ccni/assets/pdf/flu-2016-grippe-eng.pdf (accessed July 14, 2016).

Pupco Anna, Bozzo Pina, Koren Gideon. **Herpes zoster** during pregnancy. Can Fam Physician October 2011 57: 1133.

Qadri F, Ali M, Chowdhury F, et al. Feasibility and eff ectiveness of **oral cholera vaccine** in an urban endemic setting in Bangladesh: a cluster randomised open-label trial. Lancet 2015; online July 9.

Qadri F, Wierzba TF, Ali M, et al. Efficacy of a Single-Dose, Inactivated **Oral Cholera** Vaccine in Bangladesh. N Engl J Med. 2016 May 5;374(18):1723-32.

Qian J, Heywood AE, Karki S, et al. Risk of **Herpes Zoster Prior to and Following Cancer Diagnosis** and Treatment: A Population-Based Prospective Cohort Study. J Infect Dis. 2018 Dec 13.

Quadri-Sheriff M, Hendrix KS, Downs SM, Sturm LA, Zimet GD, Finnell SM. The role of **herd immunity** in parents' decision to vaccinate children: a systematic review. Pediatrics. 2012 Sep;130(3):522-30.

Quah YL. Aggarwal IM. Discussing **human papilloma virus vaccination**. BMJ. 2017 Jun 22;357:j2730.

Queenan AM, Cassidav PK, Evancelista A. **Pertactin-negative variants of Bordetella pertussis** in the United States. N Engl J Med. 2013 Feb 7;368(6):583-4.

Quinn HE, Snelling TL, Habig A, et al. Parental Tdap Boosters and Infant **Pertussis**: A Case Control Study. Pediatrics. 2014 Sep 15.

Quinn S, Goldman RD. **Human papillomavirus** vaccination for boys. Can Fam Physician. 2015 Jan;61(1):43-6.

Rabies CDC recommendations Mar/2010 : Mar/10 Routine **rabies post-exposure prophylaxis** will now entail a total of five shots — four of vaccine and one of rabies immune globulin — according to an article in MMWR Recommendations and Reports. The change to fewer doses was made based on studies showing that the fifth vaccine shot did not improve outcomes. The Advisory Committee on Immunization Practices recommends: Two shots — one of vaccine and one of rabies immune globulin — given as soon as possible after exposure. Taking the day of the first shots as Day 0, the other vaccine shots should be administered on Days 3, 7, and 14. If immune globulin is not given on Day 0, it should be given by Day 7. Immunocompromised patients should continue to receive all five vaccine shots, with the fifth on Day 28. Vaccine shots may be delivered to the outer aspect of the thigh in younger children and to the deltoid in older children and adults. The gluteal region should never be used.The authors note that their recommendations will differ from vaccine label instructions into the foreseeable future.MMWR Recommendations and Reports: http://cdc.gov/mmwr/preview/mmwrhtml/rr5902a1.htm

Ramsauer K, Schwameis M, Firbas C, et al. Immunogenicity, safety, and tolerability of a recombinant **measles-virus-based chikungunya** vaccine: a randomised, double-blind, placebo-controlled, active comparator, first-in-man trial. Lancet Infect Dis 2015; online March 2.

Ramsay ME. Measles: the legacy of **low vaccine coverage**. Arch Dis Child. 2013 Oct;98(10):752-4.

Rand CM, Schaffer SJ, Dhepyasuwan N, et al. **Provider Communication**, Prompts, and Feedback to Improve **HPV Vaccination** Rates in Resident Clinics. Pediatrics. 2018 Mar 14.

Rashid M, Greenaway C. **Hepatitis B virus screening** and vaccination in a family from Nigeria. CMAJ. 2013 Nov 5;185(16):1417-8

Rasmussen TA, Jørgensen MR, Bjerrum S, et al. Use of **population based background rates** of disease to assess vaccine safety in childhood and mass immunisation in Denmark: nationwide population based cohort study. BMJ. 2012 Sep 17;345:e5823.

Read RC, Baxter D, Chadwick DR, et al. Effect of a **quadrivalent meningococcal ACWY glycoconjugate or a serogroup B meningococcal vaccine** on meningococcal carriage: an observer-blind, phase 3 randomised clinical trial. Lancet 2014; online Aug 19.

Rebolj M, Rimmer J, Denton K, et al. **Primary cervical screening with high risk human papillomavirus testing**: observational study. BMJ. 2019 Feb 6;364:l240.

Regan AK, Bloomfield L, Peters I, et al. Randomized Controlled Trial of **Text Message** Reminders for Increasing **Influenza** Vaccination. Ann Fam Med. 2017 Nov;15(6):507-514.

Reisinger EC, Tschismarov R, Beubler E, et al**. Immunogenicity, safety, and tolerability** of the measles-vectored chikungunya virus vaccine **MV-CHIK**: a double-blind, randomised, placebo-controlled and active-controlled phase 2 trial. Lancet. 2018 Nov 5.

Reisinger KS, Block SL, et al. Safety, Tolerability, & Immunogenicity of **Gardasil Given Concomitantly With Menactra and Adacel**. Pediatrics. 2010 Jun;125(6):1142-1151.

Resik S, Tejeda A, Sutter RW, et al. Priming after a fractional dose of inactivated **poliovirus vaccine**. N Engl J Med. 2013 Jan 31;368(5):416-24.

Rey D, Piroth L, Wendling M-J, et al. Safety and immunogenicity of **doubledose versus standard-dose hepatitis B revaccination** in non-responding adults with **HIV-1** (ANRS HB04 B-BOOST): a multicentre, open-label, randomised controlled trial. Lancet Infect Dis 2015; online Aug 7.

Reyes IS, Hsieh DT, Laux LC, Wilfong AA. **Alleged Cases of Vaccine Encephalopathy Rediagnosed Years Later as Dravet Syndrome**. Pediatrics. 2011 Aug 15.

Ribeiro AC, Guedes LK, Moraes JC, et al. **Reduced seroprotection after pandemic H1N1** influenza adjuvant-free vaccination in patients with **rheumatoid arthritis**: implications for clinical practice. Ann Rheum Dis. 2011 Dec;70(12):2144-7.

Richardson V, Hernandez-Pichardo J, Quintanar-Solares M, et al. Effect of **Rotavirus** Vaccination on Death from Childhood Diarrhea in Mexico. N Engl J Med 2010 362: 299-305

Richmond PC, Marshall HS, Nissen MD, et al. Safety, immunogenicity, and tolerability of **meningococcal serogroup B** bivalent recombinant lipoprotein 2086 vaccine in healthy adolescents: a randomised, singleblind, placebo-controlled, phase 2 trial. Lancet Infect Dis 2012; online May 7.

Riley M, Morrison L, McEvoy A. Health Maintenance in School-Aged Children: Part I. History, Physical Examination, Screening, and Immunizations. Am Fam Physician. 2019 Aug 15;100(4):213-218

Rivera L, et al. Immunogenicity and safety of three aluminium hydroxide adjuvanted vaccines with reduced doses of **inactivated polio vaccine** (IPV-Al) compared with standard IPV in young infants in the Dominican Republic: a phase 2, non-inferiority, observerblinded, randomised, and controlled dose investigation trial. Lancet Infect Dis 2017; online April 25.

Robinson JL. Update on invasive **meningococcal** vaccination for Canadian children and youth. Paediatr Child Health. 2018 Feb;23(1):e1-e4.

Robinson JL; Canadian Paediatric Society, Infectious Diseases and Immunization Committee. Position statement. Potential **strategies to improve childhood immunization rates in Canada**. Paediatr Child Health 2018;23:353-6. https://www.cps.ca/en/documents/position/strategies-to-improve-childhood-immunization (accessed August 2, 2018).

Robison SG, Groom H, Young C. Frequency of **Alternative Immunization Schedule** Use in a Metropolitan Area. Pediatrics. 2012 Jun 18.

Robison SG, Liko J. The Timing of **Pertussis** Cases in Unvaccinated Children in an Outbreak Year: Oregon 2012. J Pediatr. 2017 Jan 11.

Robison SG, Osborn AW. The **Concordance of Parent and Child Immunization**. Pediatrics. 2017;139(5):e20162883

Robison SG, Dunn Ag, Richards DL, et al. Changes in **Influenza** Vaccination Rates After Withdrawal of Live Vaccine. Pediatrics. 2017;140(5):e20170516

Robl Imoto R Dr, Uber M, de Carvalho VO. **Papular crusted rash** in a child after immunisation. Arch Dis Child. 2019 Jul;104(7):706

Rodenburg GD, van Gils EJ, Veenhoven RH, et al. Lower Immunoglobulin G Antibody Responses to **Pneumococcal Conjugate** Vaccination at the Age of 2 Years after Previous Nasopharyngeal Carriage of Streptococcus pneumoniae. J Pediatr. 2011 Dec;159(6):965-970.e1.

Rolfe A, Sheikh A. **Measles, mumps, and rubella vaccination in a child with suspected egg allergy**. BMJ. 2011 Aug 3;343:d4536.

Rondaan C, de Haan A, Horst G, et al. Altered cellular and humoral immunity to **varicella zoster** virus in patients with autoimmune diseases. Arthritis Rheumatol. 2014 Sep 15.

Rothman Sheila M.; Rothman David J. Marketing HPV Vaccine: Implications for Adolescent Health and Medical Professionalism. JAMA. 2009;302(7):781-786.

Rosen JB, Arciuolo RJ, Khawja AM, et al. **Public health consequences of a 2013 measles outbreak in New York** City [online July 30, 2018]. JAMA Pediatr. doi:10.1001/jamapediatrics.2018.1024

Roukens AHE, van Halem K, de Visser AW, Visser LG. Long-Term **Protection After Fractional-Dose Yellow Fever Vaccination**: Follow-up Study of a randomized, Controlled, Noninferiority Trial. Ann Intern Med. 2018 Nov 27.

Rouphael NG, Paine M, Mosley R, et al, for the TIV-MNP 2015 Study Group. The safety, immunogenicity, and acceptability of inactivated **influenza vaccine** delivered by microneedle **patch** (TIV-MNP 2015): a randomised, partly blinded, placebo-controlled, phase 1 trial. Lancet 2017; online June 27.

Rowhani-Rahbar A, Fireman B, et al. Effect of Age on the Risk of **Fever and Seizures** Following Immunization With **Measles-Containing** Vaccines in Children. JAMA Pediatr. 2013 Oct 14.

Rozenbaum Mark H, Sanders Elisabeth A M, van Hoek Albert Jan et al. Cost effectiveness of **pneumococcal** vaccination among Dutch infants: economic analysis of the seven valent pneumococcal conjugated vaccine and forecast for the 10 valent and 13 valent vaccines. BMJ 2010;340:c2509, doi: 10.1136/bmj.c2509

Rozenbaum MH, van Hoek AJ, Fleming D, et al. Vaccination of risk groups in England using **13 valent pneumococcal conjugate** vaccine: economic analysis. BMJ. 2012Oct 26;345:e6879.

Rubin LG, Levin MJ, Ljungman P, et al. 2013 **IDSA Clinical Practice Guideline for Vaccination of the Immunocompromised Host.** Clin Infect Dis. 2013 Dec 4

Rubin LG, Schaffner W. Clinical practice. Care of the **asplenic patient**. N Engl J Med. 2014 Jul 24;371(4):349-56.

Rubin L, Landsman K. The Importance of **Social Networking** in a National **Polio** Vaccine Campaign. Pediatrics. 2016 Aug;138(2)

Rupprecht CE, Briggs D, Brown CM, et al., Centers for Disease Control and Prevention (CDC). Use of a reduced (4-dose) vaccine schedule for postexposure prophylaxis to prevent human **rabies**: recommendations of the Advisory Committee on Immunization Practices. MMWR Recomm Rep 2010 Mar 19;59(RR-2):1-9.

Russell KL, Baker CJ, Hansen C, et al. Lack of eff ectiveness of the 23-valent polysaccharide **pneumococcal** vaccine in reducing all-cause pneumonias among healthy young military recruits: a randomized, double-blind, placebo-controlled trial. Vaccine 2015; 33: 1182–87.

Rutter PD, Donaldson LJ. Mandatory **polio** vaccination for travellers: protecting global public health. Lancet. 2014 May 8.

Sacre K, Goulenok T, Bahuaud M, et al. **Impaired long-term immune protection following pneumococcal 13-valent/23-valent polysaccharide vaccine in systemic lupus erythematosus** (SLE). Ann Rheum Dis. 2018 Oct;77(10):1540-1542.

Sadarangani M, et al. Persistence of immunity after vaccination witha capsular group B **meningococcal** vaccine in 3 different toddler schedules. CMAJ. 2017 Oct 16;189(41):E1276-E1285

Saeterdal I, Lewin S, Austvoll-Dahlgren A,GlentonC,Munabi-Babigumira S. Interventions aimed at communities to inform and/or **educate about early childhood vaccination**. Cochrane Database of Systematic Reviews 2014, Issue 11. Art.No.: CD010232. DOI: 10.1002/14651858.CD010232.pub2. This review provides limited evidence that interventions aimed at communities to informand educate about early childhood vaccination may improve attitudes towards vaccination and probably increase vaccination uptake under some circumstances. However, some of these interventions may be resource intensive when implemented on a large scale and further rigorous evaluations are needed. These interventions may achieve most benefit when targeted to areas or groups that have low childhood vaccination rates.'

Sáez-Llorens X, Tricou V, Yu D, et al. Safety and immunogenicity of one versus two doses of Takeda's tetravalent **dengue** vaccine in children in Asia and Latin America: interim results from a phase 2, randomised, placebo-controlled study. Lancet Infect Dis 2017; 17: 615–25.

Safaeian M, Porras C, Pan Y, et al. CVT Group. Durable antibody responses following **one dose of the bivalent human papillomavirus** l1 virus-like particle vaccine in the costa rica vaccine trial. Cancer Prev Res (Phila). 2013 Nov;6(11):1242-50.

Sahni LC, Tate JE, Payne DC, et al. Variation in **Rotavirus** Vaccine Coverage by Provider Location and Subsequent Disease Burden. Pediatrics. 2015 Jan 12.

Salmon DA, Proschan M, Forshee R, et al; the H1N1 GBS Meta-Analysis Working Group. Association between **Guillain-Barré syndrome and influenza A (H1N1)** 2009 monovalent

inactivated vaccines in the USA: a meta-analysis. Lancet. 2013 Mar 12. (1.6 excess cases of GBS per million people vaccinated)

Salisbury DM. Should childhood **vaccination be mandatory? No**. BMJ. 2012 May 15;344:e2435.

Sammons JS. Ready or Not: Responding to **Measles in the Postelimination Era**. Ann Intern Med. 2014 Apr 24.

Sanford C, McConnell A, Osborn J. The **Pretravel Consultation**. Am Fam Physician. 2016;94(8):620-627.

Santibanez TA, Grohskopf LA, Zhai Y, et al. Complete **Influenza** Vaccination Trends for Children Six to Twenty-Three Months. Pediatrics. 2016 Feb 2. peds.2015-3280.

Santolaya ME, O´Ryan ML, Valenzuela MT, et al. Immunogenicity and tolerability of a multicomponent **meningococcal serogroup B** (4CMenB) vaccine in healthy adolescents in Chile: a phase 2b/3 randomised, observer-blind, placebo-controlled study. Lancet. 2012 Jan 17.

Saskatchewan Immunization Manual Chapter 7 – **Immunization of Special Populations** May **2012** http://www.health.gov.sk.ca/sim-chapter7

Saso A, Kampmann B. Vaccination against **respiratory syncytial virus** in pregnancy: a suitable tool to combat global infant morbidity and mortality? Lancet Infect Dis. 2016 Jun 14.

Sauerbrei, Andreas. **Preventing congenital varicella syndrome with immunization**. CMAJ 2011 0: cmaj.110055.

Sawyer MH, Simon G, Byington C. **Vaccines and Febrile Seizures**: Quantifying the Risk. Pediatrics. 2016 Jun 6.

Sawyer MH, Rathore M. **Pneumococcal** Vaccines in Preterm Infants: Are More Doses Better? Implications for Other Vaccines. Pediatrics. 2016 Aug 8.

Schaltz-Buchholzer F, Biering-Sorensen S, Lund N, et al. **Early Bacille Calmette-Guerin vaccination, hospitalizations and hospital deaths**: Analysis of a secondary outcome in three randomized trials from Guinea-Bissau. J Infect Dis. 2018 Sep 18

Schauner S, Lyon C. Bivalent HPV Recombinant Vaccine (**Cervarix**) for the Prevention of Cervical Cancer. Am Fam Physician. 2010 Dec 15;82(12):1541-2.

Schauer SL, et al. The use of an **immunization information system** to establish baseline childhood immunization rates and measure contract objectives. J Public Health Manag Pract. 2009.

Schechter NL, Bernstein BA, Zempsky WT, Bright NS, Willard AK. **Educational Outreach to Reduce Immunization Pain** in Office Settings. Pediatrics. 2010 Nov 15.

Scheller NM, Pasternak B, Svanström H, et al. Quadrivalent **human papillomavirus vaccine** and the risk of venous thromboembolism. JAMA. 2014 Jul;312(2):187-8.

Scheller NM, et al. **Quadrivalent HPV** vaccination and risk of **multiple sclerosis** and other demyelinating diseases of the central nervous system. JAMA. 2015 Jan 6;313(1):54-61

Scheller NM, Pasternak B, Mølgaard-Nielsen D, et al. **Quadrivalent HPV** vaccination and the risk of adverse pregnancy outcomes. N Engl J Med 2017;376:1223-33.

Schenkein JG, Nahm MH, Dransfield MT. Pneumococcal vaccination for patients with COPD: current practice and future directions. Chest. 2008 Mar;133(3):767-74. Epub 2007 Sep 21.

Schilling A, Parra MM, Gutierrez M, et al. **Coadministration of a 9-Valent Human Papillomavirus Vaccine With Meningococcal and Tdap Vaccines**. Pediatrics. 2015 Aug 3.

Schmader K. **Herpes Zoster.** Ann Intern Med. 2018 Aug 7;169(3):ITC19-ITC31.

Schmader KE, Levin MJ, Gnann JW Jr, et al. Efficacy, safety, and tolerability of **herpes zoster vaccine** in persons aged 50-59 years. Clin Infect Dis. 2012 Apr;54(7):922-8.

Schmader KE, Oxman MN, Levin MJ, et al. Shingles Prevention Study Group. Persistence of the efficacy of **zoster vaccine** in the shingles prevention study and the short-term persistence substudy. Clin Infect Dis. 2012 Nov 15;55(10):1320-8.

Schwameis M, Roppenser B, Firbas C, et al. Safety, tolerability, and immunogenicity of a **recombinant toxic shock syndrome toxin** (rTSST)-1 variant vaccine: a randomised, double-blind, adjuvant-controlled, dose escalation first-in-man trial. Lancet Infect Dis. 2016 Jun 10.

Schwartz BS, Larocque RC, Ryan ET. **Travel medicine**. Ann Intern Med. 2012 Jun 5;156(11):ITC61.

Schwartz JL, Mahmoud A. A **half-century of prevention**--the Advisory Committee on Immunization Practices. N Engl J Med. 2014 Nov 20;371(21):1953-6.

Schwartz JL, Easterling LA. **State Vaccination Requirements for HPV** and Other Vaccines for Adolescents, 1990-2015. JAMA. 2015 Jul 14;314(2):185-186.

Schwartz JL, Easterling LA. State Vaccination Requirements for **HPV** and Other Vaccines for Adolescents, 1990-2015. JAMA. 2015 Jul 14;314(2):185-186.

Schwartz KL, Kwong JC, Deeks SL, et al.Effectiveness of **pertussis** vaccination and duration of immunity. CMAJ. 2016 Sep 26.

Scott VP, Opel DJ, Reifler J, et al. Office-Based **Educational Handout for Influenza Vaccination**: A Randomized Controlled Trial. Pediatrics. 2019 Jul 10.

Secondary and Tertiary Transmission of Vaccinia Virus After Sexual Contact with a **Smallpox Vaccinee** — San Diego, California, 2012.Weekly.**March 1, 2013 / 62(08);145-147.**

Sederdahl BK, Orenstein WA, Yi J, et al. Missed Opportunities for **Rotavirus Vaccination**. Pediatrics. 2019 Apr 25

Seth R, Akinboyo I, Chhabra A, et al. **Mobile Phone** Incentives for **Childhood Immunizations** in Rural India. Pediatrics. 2018 Mar 14.

Sha BE. **Adult Immunization Update**. JAMA. 2019 Aug 19.

Shah PD, Calo WA, Gilkey MB, et al. Questions and Concerns About **HPV Vaccine**: A Communication Experiment. Pediatrics. 2019 Jan 22.

Shakib JH, Korgenski K, Sheng X, et al. **Tetanus, Diphtheria, Acellular Pertussis Vaccine during Pregnancy**: Pregnancy and Infant Health Outcomes. J Pediatr. 2013 Jul 26.

Shakib JH, Korgenski K, Presson AP, et al. **Influenza** in Infants Born to Women Vaccinated During **Pregnancy**. Pediatrics. 2016 Jun;137(6).

Shapiro ED, Vazquez M, Esposito D, et al. Effectiveness of **2 doses of varicella vaccine** in children. J Infect Dis. 2011 Feb;203(3):312-5.

Shapiro Marla, Kvern Brent, Watson Peter, et al. Update on **herpes zoster vaccination**: A family practitioner's guideCan Fam Physician October 2011 57: 1127-1131.

Shapiro GK, Perez S, Rosberger Z. Including males in Canadian **human papillomavirus** vaccination programs: a policy analysis. CMAJ. 2016 Sep 6;188(12):881-6.

Shaw J, Tserenpuntsag B, et al. United States Private Schools Have Higher Rates of **Exemptions to School Immunization Requirements** than Public Schools. J Pediatr. 2014 Apr 29.

Shay LA, Baldwin AS, Betts AC, et al. **Parent-Provider Communication of HPV Vaccine Hesitancy**. Pediatrics. 2018 May 15.

Shearer FM, Moyes CL, Pigott DM, et al. Global **yellow fever** vaccination coverage from **1970** to **2016**: an adjusted retrospective analysis. Lancet Infect Dis 2017; online Aug 16.

Sheffield JS, Greer LG, Rogers VL, et al. Effect of **influenza vaccination** in the **first trimester of pregnancy**. Obstet Gynecol. 2012 Sep;120(3):532-7.

Shen AK, Sobczyk E, Simonsen L, Kahn F, Esber A, Andreae MC. **Financial impact to providers** using pediatric combination vaccines. Pediatrics. 2011;128(6):1087–1093.

Shen SC, Dubey V. **Addressing vaccine hesitancy**: Clinical guidance for primary care physicians working with parents. Can Fam Physician. 2019 Mar;65(3):175-181. Review.

Shi Z, Yang Y, et al. **Breastfeeding** of Newborns by Mothers Carrying **Hepatitis B** Virus: A Meta-analysis and Systematic Review. Arch Pediatr Adolesc Med. 2011 Sep;165(9):837-46.

Shimabukuro TT, Miller ER, Strikas RA, et al. Notes from the field: **vaccine administration errors involving recombinant zoster vaccine** — United States, 2017-2018. MMWR Morb Mortal Wkly Rep. 2018;67:585-586.

Shui IM, Baggs J, Patel M, et al. Risk of **intussusception** following administration of a pentavalent **rotavirus** vaccine (RV5) in US infants. JAMA. 2012 Feb 8;307(6):598-604. (not increased)

Sidikou F, Zaneidou M, et al. Emergence of epidemic **Neisseria meningitidis serogroup C** in Niger, 2015: an analysis of national surveillance data. Lancet Infect Dis 2016; online Aug 22.

Silverman RD, Opel DJ, Omer SB. **Vaccination over Parental Objection** – Should Adolescents Be Allowed to Consent to Receiving Vaccines? N Engl J Med. 2019 Jun 5

Simberkoff MS, Arbeit RD, Johnson GR, et al. Shingles Prevention Study Group. **Safety of herpes zoster vaccine** in the shingles prevention study: a randomized trial. Ann Intern Med. 2010 May 4;152(9):545-54.

Simonsen L, Reichert TA, Viboud C, et al. Impact of **influenza vaccination of seasonal mortality** in the U.S. elderly population. Arch Intern Med. 2005;165:265-272.

Simpson CR, Ritchie LD, Robertson C, et al. Effectiveness of **H1N1 vaccine** for the prevention of pandemic influenza in Scotland: a retrospective observational cohort study. Lancet Infect Dis 2012; published online June 26.

Sinclair D, Abba K, Zaman K, Qadri F, Graves PM. **Oral vaccines for preventing cholera**. Cochrane Database Syst Rev. 2011 Mar 16;3:CD008603.

Sinclair DR, Grefenstette JJ, Krauland MG, et al. Forecasted Size of Measles Outbreaks Associated With Vaccination Exemptions for Schoolchildren. JAMA Netw Open. 2019 Aug 2;2(8):e199768.

Singanayagam A, Zambon M, Lalvani A, et al. Urgent challenges in implementing **live attenuated influenza** vaccine. Lancet Infect Dis. 2017 Aug 2.

Singh JA, Saag KG, Bridges SL Jr, et al. 2015 American College of Rheumatology Guideline for the Treatment of **Rheumatoid Arthritis**. Arthritis Rheumatol. 2015 Nov 6. (**HPV** live vaccine)

Siriwardena AN, Gwini SM, Coupland C. Influenza vaccination, pneumococcal vaccination and **risk of AMI**: Matched case-control study. CMAJ 2010; DOI:10.1503/cmaj.091891.

Sissoko MS, Healy SA, Katile A, et al. Safety and efficacy of PfSPZ Vaccine against **Plasmodium falciparum** via direct venous inoculation in healthy malaria-exposed Malian adults: a randomised, double-blind phase 1 trial. Lancet Infect Dis 2017; online Feb 15.

Skinner SR, Szarewski A, Romanowski B, et al, for the VIVIANE Study Group. Efficacy, safety, and immunogenicity of the **human papillomavirus 16/18 AS04-adjuvanted** vaccine in women older than 25 years: 4-year interim follow-up of the phase 3, double-blind, randomised controlled **VIVIANEstudy**. Lancet 2014; published online Sept 2.

Skoff TH, Kenyon C, Cocoros N, et al. Sources of Infant **Pertussis Infection** in the United States. Pediatrics. 2015 Sep 7.

Skoff TH et al. Impact of the US **maternal tetanus, diphtheria, and acellular pertussis vaccination** program on preventing pertussis in infants <2 months of age: A case-control evaluation. Clin Infect Dis2017 Sep 28;

Skowronski Danuta M, Janjua Naveed Z, De Serres Gaston, et al. Effectiveness of **AS03 adjuvanted pandemic H1N1 vaccine**: case-control evaluation based on sentinel surveillance system **in Canada**, autumn 2009. BMJ 2011;342:doi:10.1136/bmj.c7297 (Published 3 February 2011)

Slade Barbara A.; Leidel Laura; Vellozzi Claudia; et al. Postlicensure Safety Surveillance for Quadrivalent Human Papillomavirus Recombinant Vaccine (**HPV**). JAMA. 2009;302(7):750-757. {The overall adverse event rate was 53.9 per 100,000 doses; some 94% were considered "nonserious." The most common events were syncope, injection site reactions, dizziness, nausea, and headache. Rates of syncope and venous thromboembolic events were higher than expected (8.2 and 0.2, respectively, per 100,000 doses).}

Smith EA, Jacques-Carroll L, Walker TY, et al. The national perinatal **hepatitis B** prevention program, 1994-2008. Pediatrics. 2012 Apr;129(4):609-16.

Smith J. When **free is not fair**: the case of vaccine donations. Lancet Infect Dis. 2017 Feb;17(2):128-130.

Smith KJ, Wateska AR, Nowalk MP, et al. Cost-effectiveness of adult vaccination strategies using **pneumococcal** conjugate vaccine compared with pneumococcal polysaccharide vaccine. JAMA. 2012 Feb 22;307(8):804-12.

Smith LM, Kaufman JS, Strumpf EC, Lévesque LE. Effect of **human papillomavirus** (HPV) vaccination on clinical indicators of sexual behaviour among adolescent girls: the Ontario Grade 8 HPV Vaccine Cohort Study. CMAJ. 2015 Feb 3;187(2):E74-81.

Smith LM, Strumpf EC, Kaufman JS, et al. The **Early Benefits of Human Papillomavirus Vaccination** on Cervical Dysplasia and Anogenital Warts. Pediatrics. 2015 Apr 27.

Smith M, Peacock G, Uyeki TM, et al. **Influenza vaccination** in children with **neurologic** or neurodevelopmental **disorders**. Vaccine. 2015 Mar 30.

Snape MD, Saroey P, John TM, et al. Persistence of bactericidal antibodies following early infant vaccination with a serogroup B **meningococcal vaccine** and immunogenicity of a preschool booster dose. CMAJ. 2013 Sep 23.

Soares-Weiser K, Maclehose H, Ben-Aharon I, et al. Vaccines for preventing **rotavirus** diarrhoea: vaccines in use. Cochrane Database Syst Rev. 2010 May 12;5:CD008521.

Soares-Weiser K, Maclehose H, Bergman H, et al. Vaccines for preventing **rotavirus** diarrhoea: vaccines in use. Cochrane Database Syst Rev. **2012** Nov 14;11:CD008521

Soares-Weiser K, Bergman H, Henschke N, et al. **Vaccines for preventing rotavirus diarrhoea**: vaccines in use. Cochrane Database Syst Rev. 2019 Mar 25;3:CD008521. RV1, RV5, and Rotavac prevent episodes of rotavirus diarrhoea. Whilst the relative effect estimate is smaller in high-mortality than in low-mortality countries, there is a greater number of episodes prevented in these settings as the baseline risk is much higher. We found no increased risk of serious adverse events.

SOGC: Castillo E, Poliquin V. No. 357-**Immunization in Pregnancy**. J Obstet Gynaecol Can. 2018 Apr;40(4):478-489.

Sohn M-W, Yoo J, Oh EH, Amsden LB, Holl JL. **Welfare, maternal work,** and on-time childhood vaccination rates. Pediatrics. 2011; 128(6):1109 –1116.

Solverson KJ, Doig CJ. A fatal case of **pneumococcal sepsis years after splenectomy**. CMAJ. 2017 Jun 12;189(23):E800-E802.

Sonawane K, Suk R, Chiao EY, et al. Oral human **papillomavirus** infection: differences in prevalence between sexes and concordance with genital human papillomavirus infection, NHANES 2011 to 2014. Ann Intern Med. 2017. [Epub ahead of print]. doi:10.7326/M17-1363

Sørup S, et al. Live vaccine against **measles, mumps, and rubella and the risk of hospital admissions for nontargeted infections**. JAMA. doi:10.1001/jama.2014.470.

Sow Samba O., Okoko Brown J., Diallo Aldiouma, et al. Immunogenicity and Safety of a **Meningococcal** A Conjugate Vaccine in Africans. N Engl J Med 2011; 364:2293-2304.

Spencer JP, Trondsen Pawlowski RH, Thomas S. **Vaccine Adverse Events: Separating Myth from Reality**. Am Fam Physician. 2017;95(12):786-794.

Spijkerman J, Veenhoven RH, Wijmenga-Monsuur AJ, et al. Immunogenicity of **13-valent pneumococcal** conjugate vaccine administered according to 4 different primary immunization schedules in infants: a randomized clinical trial. JAMA. doi:10.1001/jama.2013.228052.

Spinner C, Ding L, Bernstein DI, et al. **Human papillomavirus vaccine effectiveness and herd protection in young women**. Pediatrics. 2019;143(2):e20181902

Sricharoenchai S, Sirivichayakul C, Chokephaibulkit K, et al. A genetically inactivated two-component **acellular pertussis vaccine**, alone or combined with tetanus and reduced-dose diphtheria vaccines, in adolescents: a phase 2/3, randomised controlled non-inferiority trial. Lancet Infect Dis. 2017 Oct 20.

Sridhar S, Greenwood B, Head C, et al. Global incidence of **serogroup B invasive meningococcal** disease: a systematic review. Lancet Infect Dis. 2015 Oct 6.

Sridhar S, Luedtke A, Langevin E, et al. Effect of **Dengue Serostatus on Dengue Vaccine Safety and Efficacy**. N Engl J Med. 2018 Jun 13.

Sridhar S, Luedtke A, Langevin E, et al. Effect of **Dengue Serostatus on Dengue Vaccine Safety and Efficacy**. N Engl J Med. 2018 Jul 26;379(4):327-340.

Staat MA, Payne DC, et al. New Vaccine Surveillance Network (NVSN). Effectiveness of **pentavalent rotavirus vaccine** against severe disease. Pediatrics. 2011 Aug;128(2):e267-75.

Stankiewicz Karita HC, Hauge K, Magaret A, et al. Effect of **Human Papillomavirus Vaccine** to Interrupt Recurrence of Vulvar and Anal Neoplasia (VIVA): A Trial Protocol. JAMA Netw Open. 2019 Apr 5;2(4):e190819.

Staples JE, Bocchini JA Jr, Rubin L, Fischer M. **Yellow Fever Vaccine Booster** Doses: Recommendations of the Advisory Committee on Immunization Practices, 2015. MMWR Morb Mortal Wkly Rep. 2015 Jun 19;64(23):647-50.

Starr M. **Paediatric Travel Medicine**: vaccines and medications. Br J Clin Pharmacol. 2012 Nov 16.

SteelFisher GK, Blendon RJ, Guirguis S, et al. Threats to **polio** eradication in high-conflict areas in Pakistan and Nigeria: a polling study of caregivers of children younger than 5 years. Lancet Infect Dis. 2015 Jul 10.

SteelFisher GK, Blendon RJ, Guirguis S, et al. Understanding threats to **polio** vaccine commitment among caregivers in high-priority areas of **Afghanistan**: a polling study. Lancet Infect Dis 2017; online Aug 14.

Steinhoff MC, Omer SB, Roy E, Arifeen et al. Neonatal outcomes after **influenza immunization during pregnancy**: a randomized controlled trial. CMAJ. 2012 Apr 3;184(6):645-53.

Steinhoff MC, Katz J, Englund JA, et al. Year-round **influenza immunisation during pregnancy** in Nepal: a phase 4, placebo-controlled trial. Lancet Infect Dis 2017; online May 15.

Stensballe LG, Sørup S, Aaby P, et al. **BCG vaccination** at birth and early childhood hospitalisation: a randomised clinical multicentre trial. Arch Dis Child. 2017 Mar;102(3):224-231.

Stockwell MS, Kharbanda EO, Martinez RA, et al. Effect of a **text messaging** intervention on influenza vaccination in an urban, low income pediatric and adolescent population: a randomized controlled trial. JAMA. 2012;307(16):1702-1708.

Stockwell MS, Broder K, et al. Risk of **Fever After** Pediatric Trivalent Inactivated **Influenza Vaccine and 13-Valent Pneumococcal** Conjugate Vaccine. JAMA Pediatr. 2014 Jan 6.

Stockwell MS, Catallozzi M, Camargo S, et al. Registry-linked electronic **influenza vaccine** provider **reminders**: a cluster-crossover trial. Pediatrics. 2015 Jan;135(1):e75-82.

Stockwell MS, Hofstetter AM, DuRivage N, et al. **Text message reminders** for second dose of influenza vaccine: a randomized controlled trial. Pediatrics. 2015 Jan;135(1):e83-91.

Stoecker C, Hampton LM, Link-Gelles R, et al. Cost-Effectiveness of Using 2 vs 3 Primary Doses of 13-Valent **Pneumococcal** Conjugate Vaccine. Pediatrics. 2013 Aug;132(2):e324-32.

Stokley S, Cohn A, Dorell C, et al. **Adolescent vaccination coverage levels in the United States**: 2006 –2009. Pediatrics. 2011;128(6): 1078 –1086.

Stone CA Jr, Rukasin CRF, Beachkofsky TM, Phillips EJ. **Immune Mediated Adverse Reactions** to Vaccines. Br J Clin Pharmacol. 2019 Aug 31.

Stoof SP, Heijstek MW, Sijssens KM, et al. Kinetics of the long-term antibody response after **meningococcal C vaccination** in patients with juvenile idiopathic arthritis: a retrospective cohort study. Ann Rheum Dis. 2014 Apr 1;73(4):728-34.

Strebel PM, Orenstein WA. **Measles**. N Engl J Med. 2019 Jul 10.

Stumpf KA, Thompson T, Sánchez PJ. **Rotavirus** Vaccination of Very Low Birth Weight Infants at Discharge From the NICU. Pediatrics. 2013 Sep;132(3):e662-5.

Su JR, Leroy Z, Lewis PW, et al. Safety of Second-Dose Single-Antigen **Varicella** Vaccine. Pediatrics. 2017 Feb 7.

Su Q, Zhang Y, Ma Y, Zheng X, et al. **Measles** Imported to the United States by Children Adopted From China. Pediatrics. 2015 Mar 2. pii: peds.2014-1947.

Sugerman, David E., Barskey, Albert E., Delea, Maryann G., et al. **Measles Outbreak** in a Highly Vaccinated Population, San Diego, 2008: Role of the Intentionally Undervaccinated. Pediatrics 2010 125: 747-755.

Suh CA, Saville A, Daley MF, et al. Effectiveness and Net **Cost of Reminder/Recall** for Adolescent Immunizations. Pediatrics. 2012 May 7.

Suk R, Montealegre JR, Nemutlu GS, et al. Public Knowledge of **Human Papillomavirus** and Receipt of Vaccination Recommendations. JAMA Pediatr. 2019 Sep 16.

Sukumaran L, McCarthy NL, Kharbanda EO, et al. Association of **Tdap Vaccination** With Acute Events and Adverse Birth Outcomes Among **Pregnant Women** With Prior Tetanus-Containing Immunizations. JAMA. 2015 Oct 20;314(15):1581-7.

Sukumaran L, McCarthy NL, Kharbanda EO, et al. Infant Hospitalizations and Mortality After **Maternal Vaccination**. Pediatrics. 2018 Feb 20.

Sull M, Eavey J, Papadouka V, et al. **Adolescent Vaccine Co-administration and Coverage** in New York City: 2007-2013. Pediatrics. 2014 Nov 10.

Sullender WM, Fowler KB, Gupta V, et al. Efficacy of **inactivated trivalent influenza vaccine** in rural India: a 3-year cluster-randomised controlled trial. Lancet Glob Health. 2019 Jul;7(7):e940-e950.

Sun Y, Christensen J, Hviid A, et al. Risk of **febrile seizures** and epilepsy after vaccination with **diphtheria, tetanus, acellular pertussis, inactivated poliovirus, and Haemophilus** influenzae type B. JAMA. 2012 Feb 22;307(8):823-31.

Suragh TA, Lewis P, et al. Safety of **bivalent human papillomavirus vaccine in the US vaccine adverse event reporting system (VAERS)**, 2009-2017. Br J Clin Pharmacol. 2018 Sep 19.

Suryadevara M, Bonville CA, Ferraioli F, et al. Community-centered **education** improves vaccination rates in children from low-income households. Pediatrics. 2013 Aug;132(2):319-25.

Sutcliffe CG, Moss WJ. Do children infected with **HIV receiving HAART need to be revaccinated**? Lancet Infect Dis. 2010 Sep;10(9):630-42.

Sutter RW, Bahl S, et al. Immunogenicity of a new routine vaccination schedule for global **poliomyelitis** prevention: an open-label, randomized controlled trial. Lancet. 2015 Sep 17.

Suzuki M, Dhoubhadel BG, Ishifuji T, et al. Serotype-specific eff ectiveness of 23-valent **pneumococcal** polysaccharide vaccine against pneumococcal pneumonia in adults aged 65 years or older: a multicentre, prospective, test-negative design study. Lancet Infect Dis 2017; online Jan 23.

Swamy GK and Heine RP.**Vaccinations for pregnant women**. Obstet Gynecol 2015 Jan; 125:212.

Swedish KA, Factor SH, Goldstone SE. Prevention of recurrent high-grade anal neoplasia with quadrivalent **human papillomavirus vaccination** of men who have sex with men: a nonconcurrent cohort study. Clin Infect Dis. 2012 Apr;54(7):891-8.

Sykes A, Gerhardt E, Tang L, et al. The Effectiveness of **Trivalent Inactivated Influenza** Vaccine in Children with Acute **Leukemia**. J Pediatr. 2017 Dec;191:218-224.e1.

Szakács A, Darin N, Hallböök T. Increased childhood incidence of **narcolepsy** in western Sweden after **H1N1** influenza vaccination. Neurology 2013;80:1315–1321.

Szarewski A, Skinner SR, Garland SM, et al. Efficacy of the HPV-16/18 AS04-adjuvanted vaccine against low-risk **HPV** types (PATRICIA randomized trial): an unexpected observation. J Infect Dis. 2013 Nov 1;208(9):1391-6.

Szilagyi PG, Schaffer S, Rand CM et al. **School-Located Influenza Vaccinations**: A Randomized Trial. Pediatrics.2016;138(5):e20161746

Tabrizi SN, Brotherton J, Kaldor JM. Assessment of herd immunity and cross-protection after a **human papillomavirus vaccination** programme in Australia: a repeat cross-sectional study. Lancet Infect Dis 2014; online Aug 6.

Taddio A, McMurtry CM, Shah V, et al. **Reducing pain during vaccine injections**: clinical practice guideline. CMAJ. 2015 Aug 24.

Taddio A, Pillai Riddell R, Ipp M, et al. Relative effectiveness of **additive pain interventions** during vaccination in **infants**. CMAJ.2016 Dec 12.

Tak CR, Marciniak MW, Savage A, Ozawa S. The essential role of pharmacists facilitating vaccination in older adults: the case of **Herpes Zoster**. Hum Vaccin Immunother. 2019 Aug 1:1-6.

Taksler GB, Rothberg MB, Cutler DM. Association of **Influenza** Vaccination **Coverage** in **Younger Adults With Influenza-Related Illness in the Elderly**. Clin Infect Dis. 2015 Sep 9.

Talbot TR, Talbot HK. Influenza Prevention Update: Examining **Common Arguments Against Influenza Vaccination**. JAMA. 2013 Jan 18:1-2.

Tam PY, Madoff LC, Coombes B, et al. Invasive **Pneumococcal** Disease After Implementation of 13-Valent Conjugate Vaccine. Pediatrics. 2014 Jul 7.

Tam P-YI et al. Invasive pneumococcal disease after implementation of **13-valent conjugate vaccine**. Pediatrics 2014 Jul 7.

Tan, Lionel K.K., Carlone, George M., Borrow, Ray. Advances in the Development of Vaccines against **Neisseria meningitides**. N Engl J Med 2010 362: 1511-1520.

Taniuchi M, Famulare M, Zaman K, et al. Community transmission of type 2 **poliovirus** after cessation of trivalent oral polio vaccine in Bangladesh: an open-label cluster-randomised trial and modelling study. Lancet Infect Dis 2017; online July 7.

Tapia MD, Sow SO, Tamboura B, et al. **Maternal** immunisation with trivalent inactivated **influenza vaccine** for prevention of influenza in infants in Mali: a prospective, active-controlled, observer-blind, randomised phase 4 trial. Lancet Infect Dis. 2016 May 31.

Tartof SY, Lewis M, Kenyon C, et al. **Waning Immunity to Pertussis** Following 5 Doses of DTaP. Pediatrics. 2013 Mar 11.

Tartof SY, Qian L, Liu IA, et al. Safety of **Influenza Vaccination Administered During Hospitalization**. Mayo Clin Proc. 2019 Jan 3.

Tartof SY, Qian L, Rieg GK, et al. **Safety of Seasonal Influenza Vaccination in Hospitalized Surgical Patients**: A Cohort Study. Ann Intern Med. 2016 Mar 15.

Task Force on Sudden Infant Death Syndrome. **SIDS** & Other Sleep-Related Infant Deaths: Expansion of Recommendations for a Safe Infant Sleeping Environment. Pediatrics. 2011 Oct 17.

Tate JE, Mutuc JD, Panozzo CA, et al. Sustained decline in rotavirus detections in the United States following the introduction of **rotavirus vaccine** in 2006. Pediatr Infect Dis J. 2011 Jan;30(1 Suppl):S30-4.

Tate JE, Burton AH, Boschi-Pinto C, et al. 2008 estimate of worldwide **rotavirus-associated mortality** in children younger than 5year before the introduction of universal rotavirus vaccination programmes: a systematic review and meta-analysis. Lancet Infect Dis 2011; published online Oct 25.

Tate JE, Yen C, Steiner CA, et al. Intussusception Rates Before and After the Introduction of **Rotavirus** Vaccine. Pediatrics. 2016 Aug 24.

Tate JE, Mwenda JM, Armah G, et al. Evaluation of **Intussusception after Monovalent Rotavirus** Vaccination in Africa. N Engl J Med. 2018 Apr 19;378(16):1521-1528.

Terranella A, Asay GR, Messonnier ML, et al. **Pregnancy Dose Tdap** and Postpartum Cocooning to Prevent Infant Pertussis: A Decision Analysis. Pediatrics. 2013 May 27.

Tessmer A, Welte T, Schmidt-Ott R et al. for CAPNETZ study group. **Influenza vaccination** is associated with reduced severity of community acquired pneumonia. Eur Respir J. 2010 Dec 9.

Tetanus and Pertussis Vaccination Coverage Among Adults Aged ≥18 Years --- United States, 1999 and 2008 Weekly MMWR. October 15, 2010 / 59(40);1302-1306. http://www.cdc.gov/mmwr/preview/mmwrhtml/mm5940a3.htm

Thomas RE, Jefferson T, Lasserson TJ. **Influenza vaccination** for **healthcare workers** who work with the elderly. Cochrane Database Syst Rev. 2010 Feb 17;(2):CD005187.

Thomas RE, Jefferson T, Lasserson TJ. **Influenza vaccination for healthcare workers** who care for people aged 60 or older living in long-term care institutions. Cochrane Database Syst Rev. 2013 Jul 22;7:CD005187.

Thomas RE, Lorenzetti DL. **Interventions to increase influenza vaccination rates of those 60 years** and older in the community. Cochrane Database Syst Rev. 2014 Jul 7;7:CD005188. doi: 10.1002/14651858.CD005188.pub3. There are interventions that are effective for increasing community demand for vaccination, enhancing access and improving provider/system response. Heterogeneity limited pooling of trials.

Thomas RE, Lorenzetti DL. Interventions to increase influenza vaccination rates of those 60 years and older in the community. Cochrane Database of Systematic Reviews 2018, Issue 5. Art. No.: CD005188. We identified interventions that demonstrated significant positive effects of low (postcards), medium (personalised phone calls), and high (home visits, facilitators) intensity that increase community demand for vaccination, enhance access, and improve provider/system response.

Thompson MG, Kwong JC, Regan AK, et al; PREVENT Workgroup. **Influenza Vaccine Effectiveness in Preventing Influenza-associated Hospitalizations During Pregnancy**: A Multi-country Retrospective Test Negative Design Study, 2010-2016. Clin Infect Dis. 2018 Oct 11.

Tielemans SMAJ, et al. Non-specific effects of **measles, mumps, and rubella (MMR) vaccination** in high income setting: population based cohort study in the Netherlands. BMJ. 2017 Aug 30;358:j3862.

Ting DSJ, Ghosh N, Ghosh S. **Herpes zoster ophthalmicus**. BMJ. 2019 Jan 17;364:k5234.

Tiwari TS, Baughman AL, et al. First **Pertussis** Vaccine Dose and Prevention of Infant Mortality. Pediatrics. 2015 May 4.

Top KA, MacDonald NE. **Combination measles-mumps-rubella-varicella vaccination and the risk of febrile seizure**. CMAJ. 2014 Aug 5;186(11):812-3.

Toft L, Storgaard M, Muller M, et al. Comparison of the Immunogenicity and Reactogenicity of **Cervarix and Gardasil** Human Papillomavirus Vaccines in **HIV**-Infected Adults: A Randomized, Double-Blind Clinical Trial. J Infect Dis. 2013 Dec 26.

Treanor JJ. **Influenza Vaccination**. N Engl J Med. 2016 Sep 29;375(13):1261-8.

Trentini F, Poletti P, Merler S, et al. **Measles immunity gaps** and the progress towards elimination: a multi-country modelling analysis. Lancet Infect Dis. 2017 Aug 11.

Tricco AC, et al. Efficacy, effectiveness, and safety of **herpes zoster vaccines in adults aged 50 and older**: systematic review and network meta-analysis. BMJ. 2018 Oct 25;363:k4029.

Trieu MC, Zhou F, Lartey S, et al. Long-term Maintenance of the Influenza-Specific Cross-Reactive Memory CD4+ T-Cell Responses Following **Repeated Annual Influenza Vaccination**. J Infect Dis. 2017 Mar1;215(5):740-749.

Trimble CL, Morrow MP, Kraynyak KA, et al. Safety, efficacy, and immunogenicity of VGX-3100, a therapeutic synthetic **DNA vaccine** targeting **human papillomavirus** 16 and 18 E6 and E7 proteins for cervical intraepithelial neoplasia 2/3: a randomised, double-blind, placebo-controlled phase 2b trial. Lancet. 2015 Sep 16.

Troeger C, Khalil IA, Rao PC, et al. **Rotavirus Vaccination and the Global Burden of Rotavirus Diarrhea** Among Children Younger Than 5 Years. JAMA Pediatr. 2018 Aug 13.

Trotta F, Da Cas R, Spila Alegiani S, et al. Evaluation of the safety of **A/H1N1 pandemic vaccine during pregnancy**: cohort study. BMJ 2014;348:g3361.

Trotter C, Lingani C, et al. Effect of **MenAfriVac** in nine countries of the African meningitis belt, 2010–15: an analysis of surveillance data. Lancet Infect Dis 2017; online May 22.

Troy SB, Kouiavskaia D, Siik J, et al. Comparison of the Immunogenicity of Various Booster Doses of Inactivated **Polio Vaccine** Delivered **Intradermally** Versus Intramuscularly to HIV-Infected Adults. J Infect Dis. 2015 Jan 7.

Tsai T, Giudice GD, Crucitti A, et al. Is the **adjuvant** (**AS03**) solely to blame? BMJ. 2013 Apr 17;346:f2375.

Tseng Hung Fu; Slezak Jeffrey M.; Quinn Virginia P.; et al. **Pneumococcal** Vaccination and Risk of Acute **Myocardial Infarction** and Stroke in Men. JAMA. 2010;303(17):1699-1706.

Tseng Hung Fu, Smith Ning, Harpaz Rafael, et al. **Herpes Zoster Vaccine** in Older Adults and the Risk of Subsequent Herpes Zoster Disease. *JAMA*. 2011;305(2):160-166.

Tseng HF, Liu A, Sy L, et al; for the Vaccine Safety Datalink (VSD) Team. **Safety of zoster vaccine** in adults from a large managed-care cohort: a Vaccine Safety Datalink study. J Intern Med. 2012 May;271(5):510-520.

Tseng HF, Chi M, Smith N, et al. **Herpes Zoster Vaccine** and the Incidence of Recurrent Herpes Zoster in an Immunocompetent Elderly Population. J Infect Dis. 2012 Jun 4.

Tseng HF, Sy LS, Qian L, et al; for the Vaccine Safety Datalink (VSD) Team. Safety of a **Tetanus-Diphtheria-Acellular Pertussis** Vaccine When Used Off-Label in an **Elderly** Population. Clin Infect Dis. 2012 Nov 28.

Tseng HF, Tartof S, Harpaz R, et al. Vaccination Against **Zoster** Remains Effective in Older Adults Who Later Undergo **Chemotherapy**. Clin Infect Dis. 2014 Aug 4.

Tseng HF, Schmid DS, Harpaz R, et al. Herpes **zoster caused by vaccine-strain** varicella zoster virus in an immunocompetent recipient of zoster vaccine. Clin Infect Dis. 2014 Apr;58(8):1125-8.

Tseng HF, Lewin B, Hales CM, et al. **Zoster Vaccine and the Risk of Postherpetic Neuralgia** in Patients Who Developed Herpes Zoster Despite Having Received the Zoster Vaccine. J Infect Dis. 2015 Jun 1.

Tseng HF, Sy LS, Ackerson BK, et al. Safety of Quadrivalent **Meningococcal** Conjugate Vaccine in 11- to 21-Year-Olds. Pediatrics. 2016 Dec 26.

Tuerlinckx D, Florkin B, Ferster A, et al. **Pneumococcal** Antibody Levels in Children With PID Receiving Immunoglobulin. Pediatrics. 2014 Jan;133(1):e154-62.

Tung J, Carlisle E, Smieja M, Kim PT, Lee CH. A randomized clinical trial of immunization with combined **hepatitis A and B** versus hepatitis B alone for hepatitis B seroprotection in **hemodialysis patients**. Am J Kidney Dis. 2010 Oct;56(4):713-9. Epub 2010 Jul 13.

Tunis MC, Deeks SL; National Advisory Committee on Immunization. Summary of the National Advisory Committee on Immunization's updated recommendations on human papillomavirus (**HPV**) vaccines: nine-valent HPV vaccine and clarification of minimum intervals between doses in the HPV immunization schedule. Can Comm Dis Rep 2016;42:149-51. *http://www.phac-aspc.gc.ca/publicat/ccdr-rmtc/16vol42/dr-rm42-7/ar-03-eng.php (accessed July 14, 2016).*

Turner PJ, Southern J, Andrews NJ, et al; SNIFFLE-2 Study Investigators. Safety of **live attenuated influenza vaccine in young people with egg allergy**: multicentre prospective cohort study. BMJ. 2015 Dec 8;351:h6291.

Udell JA, Zawi R, Bhatt DL, et al. Association between **influenza vaccination & cardiovascular outcomes** in high-risk patients: ameta-analysis. JAMA.2013.

USPSTF: US Preventive Services Task Force. Screening for **cervical cancer**: US Preventive Services Task Force recommendation statement [August 21, 2018]. JAMA.

USPSTF: Melnikow J, Henderson JT, Burda BU, Senger CA, Durbin S, Weyrich MS. Screening for **cervical cancer with high-risk human papillomavirus testing**: updated evidence report and systematic review for the US Preventive Services Task Force [August 21, 2018]. JAMA.

USPSTF: Kim JJ, Burger EA, Regan C, Sy S. **Screening for cervical cancer** in primary care: a decision analysis for the US Preventive Services Task Force [August 21, 2018]. JAMA.

Uyeki TM. **Influenza**. Ann Intern Med. 2017 Sep 5;167(5):ITC33-ITC48

Uyeki TM, Fowler RA, Fischer WA 2nd. **Gaps in the Clinical Management of Influenza**: A Century Since the 1918 Pandemic. JAMA. 2018 Jul 30.

Vaccine refusal and measles. Can Fam Physician. 2015 Jul;61(7):613.

Vajo Z, et al. **Dose sparing** & the lack of a dose-response relationship with **influenza vaccine** in adult & elderly - randomized, double-blind clinical trial. Br J Clin Pharmacol. 2017 Apr 5.

Vamos EP, Pape UJ, Curcin V, et al. Effectiveness of the **influenza** vaccine in preventing admission to hospital and death in people with type 2 diabetes. CMAJ. 2016 Jul 25.

van Assen S, et al. Humoral responses after influenza vaccination are severely reduced in patients with **rheumatoid arthritis** treated with rituximab. Arthritis Rheum. 2009 Dec28;62(1):75-81.

van Assen S, Agmon-Levin N, Elkayam O, et al. EULAR recommendations for vaccination in adult patients with **autoimmune inflammatory rheumatic diseases**. Ann Rheum Dis 2011;70:414-422. Online: 3 Dec 2010 doi:10.1136/ard.2010.137216

Van Damme P, Olsson SE, Block S, et al. Immunogenicity and Safety of **a 9-Valent HPV** Vaccine. Pediatrics. 2015 Jun 22.

Van Der Meeren O, Hatherill M, Nduba V, et al. **Phase 2b controlled trial of M72/AS01E vaccine to prevent tuberculosis**. N Engl J Med.

van Gils Elske J. M.; Veenhoven Reinier H.; Hak Eelko; et al. **Pneumococcal Conjugate Vaccination** and Nasopharyngeal Acquisition of **Pneumococcal Serotype 19A Strains**. JAMA. 2010;304(10):1099-1106.

Van Trang N, Le Nguyen NT, Dao HT, et al. Incidence and Epidemiology of **Intussusception** among Infants in Ho Chi Minh City, Vietnam. J Pediatr. 2013 Nov 14.

Vannice K, Wilder-Smith A, Hombach J. Fractional-Dose **Yellow Fever Vaccination**- Advancing the Evidence Base. N Engl J Med. 2018 Jul 11.

Vaughn JA, Miller RA. **Update on immunizations in adults**. Am Fam Physician. 2011 Nov 1;84(9):1015-20.

Veerasingam P, Grant CC, Chelimo C, et al. **Vaccine Education During Pregnancy** and Timelines of Infant Immunization. Pediatrics. 2017;140(3):e20163727.

Verbeek NE, Jansen FE, Vermeer-de Bondt PE, et al. Etiologies for **Seizures** Around the Time of **Vaccination**. Pediatrics. 2014 Sep 15.

Verbeek NE, van der Maas NA, Sonsma AC, et al. Effect of **vaccinations on seizure risk** and disease course in Dravet syndrome. Neurology. 2015 Aug 18;85(7):596-603.

Verboon C, Doets AY, Galassi G, et al; IGOS Consortium. Current treatment practice of **Guillain-Barré syndrome**. Neurology. 2019 Jul 2;93(1):e59-e76.

Verity C, Stellitano L, et al. **Pandemic A/H1N1 2009 influenza** vaccination, preceding infections and clinical findings in UK children with Guillain-Barre syndrome. Arch Dis Child. 2014 Feb 28.

Veselsky SL, Walker TY, Fenlon N, et al. Discrepant **hepatitis B** surface antigen results in pregnant women screened to identify hepatitis B virus infection. J Pediatr. 2014 Oct;165(4):773-8.

Vesikari T et al. Oil-in-water emulsion **adjuvant with influenza vaccine** in young children. N Engl J Med 2011 Oct 13; 365:1406. (has MF59 contains squalene)

Vesikari T, Esposito S, Prymula R, et al; for the EU Meningococcal B Infant Vaccine Study group. Immunogenicity and safety of an investigational multicomponent, recombinant, **meningococcal serogroup B** vaccine (4CMenB) administered concomitantly with routine infant and child vaccinations: results of two randomised trials. Lancet. 2013 Jan 11.

Villar L, Dayan GH, Arredondo-Garcia JL, et al. Efficacy of a tetravalent **dengue** vaccine in children in Latin America. N Engl J Med. DOI: 10.1056/NEJMoa1411037.

Voelker R. Increasing Cases of **Shingles in the Eye** Raise Key Questions. JAMA. 2019 Aug 7.

Vogel U, et al. Predicted strain coverage of a meningococcal multicomponent vaccine (**4CMenB**) in Europe: a qualitative and quantitative assessment. Lancet Infect Dis. 2013 Feb 12.

Vogt H, Bråbäck L, Kling AM, et al. **Pertussis** Immunization in Infancy and Adolescent Asthma Medication. Pediatrics. 2014 Sep 22.

von Gottberg A, de Gouveia L, Tempia S, et al. GERMS-SA Investigators. Effects of vaccination on **invasive pneumococcal disease** in South Africa. N Engl J Med. 2014 Nov 13;371(20):1889-99.

Wacholder Sholom, Chen Bingshu Eric, Wilcox Allen, et al. for the CVT group. Risk of **miscarriage** with bivalent vaccine against human papillomavirus (**HPV**) types 16 and 18: pooled analysis of two randomised controlled trials. BMJ 2010;340:c712, doi: 10.1136/bmj.c712 (Published 2 March 2010)

Waight PA, Andrews NJ, Ladhani SN, et al. Effect of the 13-valent **pneumococcal** conjugate vaccine on invasive pneumococcal disease in England and Wales 4 years after its introduction: an observational cohort study. Lancet Infect Dis 2015; online March 20.

Walker UA, Hoffman HM, Williams R, et al. Brief Report: Severe Inflammation Following Vaccination **Against Streptococcus pneumoniae** in Patients With Cryopyrin-Associated Periodic Syndromes. Arthritis Rheumatol. 2016 Feb;68(2):516-20.

Walling EB, Benzoni N, Dornfeld J, et al. Interventions to Improve **HPV Vaccine** Uptake: A Systematic Review. Pediatrics. 2016 Jun 13.

Walsh LK, Donelle J, Dodds L, et al. Health outcomes of young children born to **mothers who received 2009 pandemic H1N1 influenza vaccination during pregnancy**: retrospective cohort study. BMJ. 2019 Jul 10;366:l4151.

Walter EB, Clements DA. **Pneumococcal** conjugate vaccine: are 3 doses equal to 4 doses? Pediatrics. 2013 Aug;132(2):e498-9.

Walter EB et al. **Pain in adolescent girls receiving HPV vaccine** with concomitantly administered vaccines. Pediatr Infect Dis J 2014 Aug 28.

Walter EB, Staat MA. **Rotavirus** Vaccine and Intussusception Hospitalizations. Pediatrics. 2016 Sep;138(3).

Wang K, Fry NK, Campbell H, et al. **Whooping cough** in school age children presenting with persistent cough in UK primary care after introduction of the preschool **pertussis** booster vaccination: prospective cohort study. BMJ. 2014 Jun 24;348:g3668.

Warshaw MG, Siberry GK, Williams P, et al. Immunogenicity of a **Booster Dose of Quadrivalent Meningococcal** Conjugate Vaccine in Previously Immunized HIV-Infected Children and Youth. J Pediatric Infect Dis Soc. 2017 Feb 18.

Warren-Gash C et al. Laboratory-confirmed **respiratory infections as triggers for acute myocardial infarction** and stroke: A self-controlled case series analysis of national linked datasets from Scotland. Eur Respir J 2018 Mar; 51:1701794. (suggests influenza and pneumococcal vaccines useful)

Wasan SK, Baker SE, Skolnik PR, Farraye FA. A Practical Guide to Vaccinating the **Inflammatory Bowel Disease Patient**. Am J Gastroenterol. 2010 Jan 26. [Epub ahead of print]

Weaver T, Metrebian N, Hellier J, et al. Use of contingency management incentives to improve completion of **hepatitis B** vaccination in people undergoing treatment for heroin dependence: a cluster randomised trial. Lancet 2014; online April 8

Weinberg A, Kroehl ME, Johnson MJ, et al. Comparative **Immune Responses to Licensed Herpes Zoster Vaccines**. J Infect Dis. 2018 Sep 22;218(suppl_2):S81-S87.

Weinberger Daniel M, Malley Richard, Lipsitch Marc. **Serotype replacement in disease after pneumococcal vaccination**. www.thelancet.com Published online April 13, 2011.

Weinberger DM, Pitzer VE, Regev-Yochay G, et al. Association Between the **Decline in Pneumococcal Disease in Unimmunized Adults and Vaccine-Derived Protection Against Colonization** in Toddlers and Preschool-Aged Children. Am J Epidemiol. 2018 Nov 20.

Weinmann S, Naleway AL, Koppolu P, et al. **Incidence of herpes zoster among children**: 2003–2014. Pediatrics. 2018; 144(1):e20182917

Weintraub ES, Baggs J, Duffy J, et al. Risk of intussusception after monovalent **rotavirus** vaccination. N Engl J Med. DOI:10.1056/NEJMoa1311738.

Weiser J, et al.. Low Prevalence of **Hepatitis B Vaccination Among Patients Receiving Medical Care for HIV** Infection in the United States, 2009 to 2012. Ann Intern Med. 2017 Dec 26.

Wen SY, Liu WL. Epidemiology of pediatric **herpes zoster** after varicella infection: a population-based study. Pediatrics. 2015 Mar; 135(3):e565-71.

Werner JM, Abdalla A, et al. The **hepatitis B vaccine** protects re-exposed health care workers, but does not provide sterilizing immunity. Gastroenterology. 2013 Nov;145(5):1026-34.

Wheeler CM, Castellsagué X, Garland SM, et al. Cross-protective efficacy of HPV-16/18 AS04-adjuvanted vaccine against **cervical** infection and precancer caused by non-vaccine oncogenic **HPV** types: 4-year end-ofstudy analysis of the randomised, double-blind PATRICIA trial. Lancet Oncol 2011; published online Nov 9. DOI:10.1016/S1470-2045(11)70287-X.

Wheeler CM, Skinner SR, Del Rosario-Raymundo MR, et al; VIVIANE Study Group. Efficacy, safety, and immunogenicity of the human **papillomavirus** 16/18 AS04-adjuvanted vaccine in women older than 25 years: 7-year follow-up of the phase 3, double-blind, randomised controlled VIVIANE study. Lancet Infect Dis. 2016 Jun 28.

WHO: Recommendation of **WHO** Strategic Advisory Group of Experts **(SAGE) on Immunization**. Pediatrics. 2013 Jan;131(1):e343.

Wiggers JB, Chan T, Gold WL, et al. **Mumps** in a 27-year-old man. CMAJ. 2017 Apr 18;189(15):E569-E571.

Wigham S, Ternent L, Bryant A, et al. Parental Financial Incentives for Increasing Preschool **Vaccination Uptake**: Systematic Review. Pediatrics. 2014 Sep 15.

Wightman A, Opel DJ, Marcuse EK, Taylor JA.Washington State pediatricians' attitudes toward **alternative childhood immunization schedules**. Pediatrics. 2011;128(6):1094 –1099

Williams JTB, Nussbaum AM. Minister to Their Instruction: **Revisiting the Minister-Vaccinator Rowland Hill**. Pediatrics. 2018 Dec;142(6).

Williams JTB, Nussbaum AM, O'Leary ST. Building Trust: Clergy and the Call to Eliminate **Religious Exemptions**. Pediatrics. 2019 Sep 9.

Williams SE, Edwards KM, Baxter RP, et al. **Comprehensive Assessment of Serious Adverse Events** Following Immunization by Health Care Providers. J Pediatr. 2013 Feb 26.

Williamson G, Ahmed B, Kumar PS, et al. **Vaccine-Preventable** Diseases Requiring **Hospitalization**. Pediatrics. 2017;140(3):e20170298

Wilson Jennifer F.. In the Clinic: **Herpes Zoster**. *Ann Intern Med* March 1, 2011 154:ITC3-1.

Wilson SE, Deeks SL, Hatchette TF, Crowcroft NS. The role of **seroepidemiology** in the comprehensive surveillance of vaccine-preventable diseases. CMAJ. 2012 Jan 10;184(1):E70-6.

Wilson SE, Rosella LC, Wang J,et al. Population-Level Impact of Ontario's Infant **Rotavirus** Immunization Program: Evidence of Direct and Indirect Effects. PLoS One. 2016 May 11;11(5).

Winter K et al. Effectiveness of **prenatal versus postpartum Tdap** vaccination in preventing infant pertussis. Clin Infect Dis 2016 Sep 13.

Winthrop KL, Baddley JW, Chen L, et al. Association between the initiation of anti-tumor necrosis factor therapy and the risk of **herpes zoster**. JAMA. 2013 Mar 6;309(9):887-95.

Winthrop KL, Silverfield J, Racewicz A, et al. The effect of **tofacitinib on pneumococcal** and influenza vaccine responses in rheumatoid arthritis. Ann Rheum Dis. 2015 Mar 20.

Winthrop KL, Curtis JR, Lindsey S, et al. **Herpes Zoster and Tofacitinib**: Clinical Outcomes and the Risk of Concomitant Therapy. Arthritis Rheumatol. 2017 Aug 28.

Winthrop KL, Wouters A, Choy E, et al. The Safety and Immunogenicity of **Live Zoster** Vaccination in Rheumatoid Arthritis Patients Before Starting **Tofacitinib**: A Randomized Phase II Trial. Arthritis Rheumatol. 2017 Aug 28

Wiggers JB, Leis JA, Gold WL. The resurgence of **pertussis**. CMAJ. 2015 Jul 14;187(10):755.

Wolf E, Rowhani-Rahbar A, Tasslimi A, et al. **Parental Country of Birth** and Childhood Vaccination Uptake in Washington State. Pediatrics. 2016 Jul;138(1).

Wong KK, Burdette E, Mahon BE, Mintz ED, Ryan ET, Reingold AL. Recommendations of the Advisory Committee on Immunization Practices for Use of **Cholera** Vaccine. MMWR Morb Mortal Wkly Rep. 2017 May 12;66(18):482-485.

Wood N, Nolan T, Marshall H, et al. **Immunogenicity and Safety of Monovalent Acellular Pertussis Vaccine at Birth**: A Randomized Clinical Trial. JAMA Pediatr. 2018 Sep 10.

Wu JT, Peak CM, Leung GM, et al. Fractional dosing of **yellow fever** vaccine to extend supply: a modelling study. Lancet. 2016 Nov 9.

Wylie KM, Weinstock GM, Storch GA. Emergence of **Rotavirus** G12P[8] in St. Louis During the 2012-2013 Rotavirus Season. J Pediatric Infect Dis Soc. 2015 Dec;4(4):e84-9.

Wyman MJ, Stabi KL. **Concomitant administration of pneumococcal-23 and zoster** vaccines provides adequate herpes zoster coverage. Ann Pharmacother. 2013 Jul;47(7-8):1064-8.

Wysocki J, Center KJ, Brzostek J, et al. A randomized study of **fever prophylaxis and the immunogenicity of routine pediatric vaccinations**. Vaccine. 2017 Apr 4;35(15):1926-1935.

Yamada M, Kamberos N, Grose C. Breakthrough Varicella in a Cancer Patient with Persistent Varicella Antibody after One **Varicella** Vaccination. J Pediatr. 2013 Aug 6.

Yang DY, Bracken K. Update on the new **9-valent vaccine for human papillomavirus** prevention. Can Fam Physician. 2016 May;62(5):399-402.

Yang YT, Colgrove J. New York City **Childcare Influenza Vaccine Mandate**. JAMA Pediatr. 2018 Dec 3.

Yang YT, Delamater PL, Leslie TF, et al. Sociodemographic Predictors of **Vaccination Exemptions** on the Basis of **Personal Belief in California**. Am J Public Health. 2015 Nov 12:e1-e6.

Yates TA, Paranthaman K, Yu LM, et al. UK vaccination schedule: **persistence** of immunity to **hepatitis B** in children vaccinated after perinatal exposure. Arch Dis Child. 2013 Mar 9.

Yawn BP, Wollan PC, Kurland MJ, St Sauver JL, Saddier P. **Herpes zoster recurrences** more frequent than previously reported. Mayo Clin Proc. 2011 Feb;86(2):88-93.

Yellow Fever Working Group1 on behalf of the Committee to Advise on Tropical Medicine and Travel (CATMAT). Interim Canadian recommendations for the use of a fractional dose of yellow fever vaccine during a vaccine shortage. www.phac-aspc.gc.ca/publicat/ccdr-rmtc/16vol42/dr-rm42-8/assets/pdf/16vol42_8-ar-02-eng.pdf (accessed February 9, 2017).

Yen C, Tate JE, Wenk JD, et al. Diarrhea-associated hospitalizations among US children over 2 **rotavirus** seasons after vaccine introduction. Pediatrics. 2011 Jan;127(1):e9-e15.

Yen C, Tate JE, Steiner CA, Cortese MM, Patel MM, Parashar UD, et al. Trends in **intussusception** hospitalizations among US infants before and after implementation of the **rotavirus** vaccination program, 2000— 2009. Clin Infect Dis 2012; 206:41–8.

Yen C, Hyde TB, Costa AJ, et. al. The development of **global vaccine stockpiles**. Lancet Infect Dis. 2015 Feb 5. pii: S1473-3099(14)70999-5.

Yeung KHT, Duclos P, Nelson EAS, Hutubessy RCW. An update of global burden of pertussis in children younger than 5 years: a modelling study. Lancet Infect Dis 2017; online June 13.

Yih WK, Lieu TA, Kulldorff M, et al. Intussusception risk after **rotavirus** vaccination in U.S. infants. N Engl J Med. DOI:10.1056/NEJMoa1303164.

Yildirim I, Shea KM, Little BA, Silverio AL, Pelton SI; on behalf of the Members of the Massachusetts Department of Public Health. Vaccination, Underlying Comorbidities, and Risk of Invasive **Pneumococcal** Disease. Pediatrics. 2015 Feb 2.

Young MK, Nimmo GR, Cripps AW, Jones MA. Post-exposure passive immunisation for preventing **measles**. Cochrane Database of Systematic Reviews 2014, Issue 4. Art. No.: CD010056.

Young-Xu Y et al. Relative vaccine effectiveness of **high-dose versus standard-dose influenza vaccines among Veterans** Health Administration patients. J Infect Dis 2018 May 5; 217:1718.

Zafack JG, et al; Canadian Immunization Research Network . **Risk of Recurrence of Adverse Events Following Immunization**: A Systematic Review. Pediatrics. 2017 Sep;140(3).

Zakrzewski L, Sur D. **Immunizations in pregnancy**. Am Fam Physician. 2013 Jun 15;87(12):828-30.

Zaman K, et al. Effectiveness of a **live oral human rotavirus** vaccine after programmatic introduction in Bangladesh: A cluster-randomized trial. PLoS Med. 2017 Apr 18;14(4):e1002282.

Zerbo O, Bartlett J, Goddard K, Fireman B, Lewis E, Klein NP. **Acellular pertussis vaccine effectiveness over time**. Pediatrics. 2019;144(1):20183466

Zerbo O, Modaressi S, Goddard K, et al. **Vaccination Patterns in Children After Autism Spectrum Disorder** Diagnosis and in Their Younger Siblings. JAMA Pediatr. 2018 Mar 26.

Zerbo O, Qian Y, Yoshida C, et al. Association Between **Influenza Infection and Vaccination During Pregnancy and Risk of Autism** Spectrum Disorder. JAMA Pediatr. 2016 Nov 28.

Zhang L, Prietsch SO, Axelsson I, et al. **Acellular vaccines** for preventing **whooping cough** in children. Cochrane Database Syst Rev. 2012 Mar 14;3:CD001478.

Zhang J et al. Association between vaccination for **herpes zoster** and risk of herpes zoster infection among older patients with selected **immune-mediated diseases**. JAMA 2012 Jul 4; 308:43.

Zhang J et al. Long-term efficacy of a **hepatitis E** vaccine. N Engl J Med 2015 Mar 5; 372:914.

Zhou F, Shefer A, Wenger J, et al. **Economic** Evaluation of the **Routine Childhood Immunization Program** in the United States, 2009. Pediatrics. 2014 Mar 3.

Zhu F-C, Meng F-Y, Li J-X, et al. Efficacy, safety, and immunology of an inactivated alum-adjuvant **enterovirus** 71 vaccine in children in China: a multicentre, randomised, double-blind, placebo-controlled, phase 3 trial. Lancet 2013; online May 29.

Zhu F, Xu W, Xia J, et al. Efficacy, safety, and immunogenicity of an **enterovirus 71** vaccine in China. N Engl J Med. 2014 Feb 27;370(9):818-28.

Zimmer R. Truth and direct-to-consumer advertising in Canada of **DUKORAL for traveler's diarrhea prevention**. Can Fam Physician. 2019 Mar;65(3):171-173.

Zou H, Tabrizi SN, et al. Site-specific **human papillomavirus** infection in adolescent men who have sex with men (HYPER): observational cohort study. Lancet Infect Dis 2014; online Nov 28.

References: Antifungal Treatment Chart

[1] CPS 2018
[2] Micromedex 2017
[3] Hansten and Horn. Drug interactions
[4] Medical letter. Treatment guidelines : Antifungal drugs. The Medical Letter 2008(Jan);6(65):1-8. (Updated **Dec, 2009 & Aug 2012**.)
[5] Mohr J, Johnson M, Cooper T, et al. Current options in antifungal pharmacotherapy. Pharmacotherapy 2008;28(5):614–645
[6] Pappas PG, Kauffman CA, Andes D, et al: Clinical practice guidelines for the management of candidiasis: 2009 update by the Infectious Diseases Society of America. Clin Infect Dis 2009; 48(5):503-535
[7] Sanford's Guide to Antimicrobial Therapy 2017.
Limper Andrew H., Knox Kenneth S., Sarosi George A., et al. and on behalf of the American Thoracic Society (ATS) Fungal Working Group. An Official American Thoracic Society Statement: Treatment of Fungal Infections in Adult Pulmonary and Critical Care Patients. Am. J. Respir. Crit. Care Med. 183: 96-128. January 3, 2011
[8] Crawford F, Hollis S. Topical treatments for fungal infections of the skin skin and nails of the foot. Cochrane Database Syst Rev 2007; (3) CD001434.
[9] Goldstein AO, Goldstein BG. Onychomycosis. Up-to-date. Accessed 18 August 2009
Westerberg DP, Voyack MJ. Onychomycosis: Current Trends in Diagnosis and Treatment. Am Fam Physician. 2013;88(11):762-770.
Gupta AK, Sibbald RG, Andriessen A, et al. **Toenail onychomycosis—a Canadian** approach with a new transungual treatment: development of a clinical pathway. J Cutan Med Surg 2015;April 9:1-10. [Epub ahead print].http://cms.sagepub.com/content/early/2015/04/09/1203475415581310.full.pdf+html (accessed April 16, 2015).
Muth CC. Fungal Nail Infection. JAMA. 2017 Feb 7;317(5):546.

[10] Olde Hartman TC, van Rijswick E. Fungal Nail Infection. BMJ 2008 Jul 10; 337: a429.
[11] Chang CH, Young-Xu Y, Kurth T et al. The Safety of oral antifungal treatments for superficial dermatophytosis and onychomycosis : a meta-analysis. Am J Med 2007 Sep; 120(9):791-8
[12] Crawford F, Young P, Godfrey C, Bell-Syer SE et al. Oral Treatments for toenail onychomycosis: a systematic review. Arch Dermatol 2002 Jun; 138(6):811-6
[13] Hart R, Bell-Syer SE, Crawford F, Torgerson DJ, Young P, Russell I. Systematic review of topical treatments for fungal infections of the skin and nails of the feet. BMJ. 1999 Jul 10;319(7202):79-82
Eisman S, Sinclair R. **Fungal nail infection**: diagnosis and management. BMJ.2014 Mar 24
[14] Gupta AK; Jain HC; Lynde CW; Macdonald P; Cooper EA, et al. Prevalence and epidemiology of onychomycosis in patients visiting physicians' offices: a multicenter canadian survey of 15,000 patients. J Am Acad Dermatol 2000 Aug;43(2 Pt 1):244-8
[15] Sigurgeirsson B; Steingrimsson O. Risk factors associated with onychomycosis. J Eur Acad Dermatol Venereol 2004 Jan;18(1):48-51
[16] Pierard GE; Pierard-Franchimont C. The nail under fungal siege in patients with type II diabetes mellitus. Mycoses 2005 Sep;48(5):339-42
[17] Sigurgeirsson B, Olaffsson JH, Steinson JB, et al. Long-term effectiveness of treatment of treatment of terbinafine vs itraconazole in onychomycosis : a 5-year blinded prospective follow-up study. Arch Dermat 2002;138:353-7
Piraccini BM, Sisti A, Tosti A. Long-term follow-up of toenail onychomycosis caused by dermatophytes after successful treatment with systemic antifungal agents. J Am Acad Dermatol. 2010 Mar;62(3):411-4.
[18] Evans EG, Sigurgeirsson B. Double blind, randomized study of continuous terbinafine compared with intermittent itraconazole in treatment of toenail onychomycosis. BMJ 1999;318:1031-35
[19] Warshaw EM; Fett DD; Bloomfield HE, et al. Pulse versus continuous terbinafine for onychomycosis: a randomized, double-blind, controlled trial. J Am Acad Dermatol 2005 Oct;53(4):578-84
[20] Natural Medicine Comprehensive Database. Tea tree oil monograph. Accessed 2 October, 2009. (http://www.naturaldatabase.com/)
[21] Pappas PG, Kauffman CA, Andes D, et al: Clinical practice guidelines for the management of candidiasis: 2009 update by the Infectious Diseases Society of America. Clin Infect Dis 2009; 48(5):503-535
[22] Kauffman CA. Treatment of oropharyngeal and esophageal candidiasis. Up-to-date Accessed 7August 2009
[23] Gonsalves WC, Stevens Wrightson A, Henry RG. Common oral conditions in older persons. Am Fam Physician. 2008;78(7):845-852
[24] Kulak Y, Arikan A, Delibalta N. Comparison of three different treatment methods for generalized denture stomatitis. J Prosthet Dent. 1994 Sep;72(3):283-8
[25] Su CW, Jamieson B. Clinical Inquiries. What is the best treatment for oral thrush in healthy infants? J Fam Pract. 2008 Jul;57(7):484-5.
[26] Goins RA, Ascher D, Waecker N, et al. Comparison of fluconazole and nystatin oral suspensions for treatment of oral thrush in infants. Pediatric Infect Dis J. 2002;21:1165-67.
[27] Leung AK. Gentian violet in the treatment of oral candidiasis. Pediatr Infect Dis J. 1988 Apr;7(4):304-5
[28] Walker M Conquering Common Breast-feeding Problems. J Perinat Neonat Nurs 2007;22:267-274
[29] Hoddinott P, Tappin D, Wright C. Breast feeding. BMJ 2008;336:881-7
[30] Naldi L, Rebora A. Seborrheic dermatitis. N Engl J Med 2009;360:387-96.
[31] Korting HC, Kiencke P, Nelles S, Rychlik R. Comparable efficacy and safety of various topical formulations of terbinafine in Tinea pedis irrespective of the treatment regimen. Results of a mata-analysis. Am J Clin Dermat 2007;8(6):357-364
[32] Schwartx A. Superficial fungal infections. Lancet 2004;364:1173-82
[33] Goldstein AO, Goldstein BG. Tinea versicolor. Up-to-date. Accessed 21August 2009
[34] Leeming JP; Sansom JE; Burton JL. Susceptibility of Malassezia furfur subgroups to terbinafine. Br J Dermatol 1997 Nov;137(5):764-7
[35] Janniger CK, Schwartz RA, Szepietowski JC, et al. Intertrigo and common secondary skin infections. Am Fam Physician 2005; 72:833-8,840
[36] Gupta AK, Chow M, Daniel CR, Aly R. Treatments of tinea pedis. Dermatol Clin. 2003 Jul;21(3):431-62.
[37] Gupta AK, Chaudhry M, Elewski B. Tinea corporis, tinea cruris, tinea nigra, and piedra. Dermatol Clin. 2003 Jul;21(3):395-400
[38] Andrews MD, Burns, M. Common Tinea infections in children. Am Fam Physician. 2008;77(10):1415-1420
[39] Sobel JD. Vulvovaginal candidosis. Lancet 2007; 369:1961-1971
[40] Treatment of complicated vaginal yeast infections. Pharmacist's Letter/Prescriber's Letter 2010;26(8):260806
van Schalkwyk J, Yudin MH; Society of Obstetricians & Gynaecologists of Canada. **SOGC clinical practice guideline. Vulvovaginitis**: screening for and management of trichomoniasis, vulvovaginal candidiasis, and bacterial vaginosis. http://sogc.org/wp-content/uploads/2015/03/gui320CPG1503E.pdf (accessed March, 2015).
Pappas PG, Kauffman CA, Andes DR, et al. Clinical Practice Guideline for the **Management of Candidiasis: 2016 Update** by the Infectious Diseases Society of America. (**IDSA**) Clin Infect Dis. 2015 Dec 16.

[41] Watson MC, Grimshaw JM, Bond CM, Mollison J, Ludbrook A. Oral Therapy for Recurrent Vulvovaginal Candidiasis. N Engl J Med. 2004 Aug 26;351(9):876-83.
[41] Carter TC, Druschel CM, Romitti PA, et al. Antifungal drugs and the risk of selected birth defects. Am J Obstet Gynecol 2008; 198:191.e1-191.e7
[42] Sobel JD., Wiesenfeld HC., et al. Maintenance Fluconazole Therapy for Recurrent Vulvovaginal Candidiasis. N Engl J Med. 2004 Aug 26;351(9):876-83
Fischer G, Bradford J. Persistent vaginitis. BMJ 2011;343:d7314 doi: 10.1136/bmj.d7314 (Published 28 November 2011)
Belayneh M, Sehn E, Korownyk C. Recurrent vulvovaginal candidiasis. Can Fam Physician. 2017 Jun;63(6):455.

[43] Canadian STI guidelines 2008 http://www.phac-aspc.gc.ca/std-mts/sti-its/guide-lignesdir-eng.php
[44] Stary A, Soeltz-Szoets J, Ziegler C et al. Comparison of the efficacy and safety of oral fluconazole and topical clotrimazole in patients with candida balanitis. Genitourin Med. 1996 Apr;72(2):98-102.
[45] Edwards, SK. European guideline for the management of balanoposthitis. Int J STD AIDS 2001; 12 Suppl 3:68.
[46] Carter TC, Druschel CM, Romitti PA, et al. Antifungal drugs and the risk of selected birth defects. Am J Obstet Gynecol 2008; 198:191.e1-191.e7
[47] Sobel Jd, Chaim W, Nagappan V, Leaman D. Treatment of vaginitis caused by Candida Glabrata: use of topical boric acid and flucytosine. Am J Obstet Gynecol 2003; 189:1297-1300
[48] Pirotta M. et al. Effect of lactobacillus in preventing post-antibiotic vulvovaginal candidiasis: a randomised controlled trial. BMJ. 2004 Sep 4; 329 (7465): 548.
[49] Das Neves J, Pinto E, Teixera B, et al. Local treatment of vulvovaginal candidosis. Drugs 2008;68(13):1787-1802.
[50] Scheinfeld N. Diaper dermatitis. A Review and Brief Survey of Eruptions of the Diaper Area. Am J Clin Dermat 2005; 6(5):273-81
[51]Chambers WM, Millar A, Jain S, Burroughs AK. Terbinafine-induced hepatic dysfunction. Eur J Gastroenterol Hepatol. 2001 Sep;13(9):1115-8
Stolmeier DA, Stratman HB, McIntee TJ, Stratman EJ. Utility of Laboratory Test Result Monitoring in Patients Taking Oral Terbinafine or Griseofulvin for Dermatophyte Infections. JAMA Dermatol. 2018 Oct 17.

[52] Joseph Mo, Pope E. Dermatology, Dipchand A, Friedman J, Bismilla Z, Gupta S, Lam C. The hospital for sick children: Handbook of pediatrics. Elsevier Canada 2009 p.194-207
[53] Lau, E. Pediatric drug dosing guidelines. In: Dipchand A, Friedman J, Bismilla Z, Gupta S, Lam C. The hospital for sick children: Handbook of pediatrics. Elsevier Canada 2009. p883-996
[54] Brown,SJ. Efficacy of fluconazole for the treatment of onychomycosis. Ann Pharmcother 2009;43:1684-91
[55] Garey KW, Pai MP, Suda KJ, et al. Inadequacy of fluconazole dosing in patients with candidemia based on Infectious Diseases Society of America (IDSA) guidelines. Pharmacoepidemiol Drug Saf 2007;16:919–27.
[56] Janssen Pharmaceutical Products LP. Sporanox (itraconazole) oral solution prescribing information. Titusville, NJ; 2004.
[57] Hickman JG. A double-blind, randomized, placebo-controlled evaluation of short-term treatment with oral itraconazole in patients with tinea versicolor. J Am Acad Dermatol 1996 May;34(5 Pt 1):785-7
[58] Kose O; Bulent Tastan H; Riza Gur A, et al. Comparison of a single 400 mg dose versus a 7-day 200 mg daily dose of itraconazole in the treatment of tinea versicolor. J Dermatolog Treat 2002 Jun;13(2):77-9
[59] Feranandez-Nava HD, Laya-Cuadra B, Tianco EAV. Comparison of single dose 400mg versus 10-day 200mg daily dose ketoconazole in the treatment of tinea versicolor. Int J Dermatol 1997;36:64-66
[60] Goodless DR, Ramos-caro Fa, Flowers FP. Ketoconazole in the treatment of pityriasis versicolor: International review of clinical trial. DICP1991;25:395
[61] Mohr J, Johnson M, Cooper T, et al. Current Options in Antifungal Therapy. Pharmacotherapy 2008;28(5):614–645
[62] Smith J,Safdar N, Knasinski V, et al. Voriconazole therapeutic drug monitoring. Antimicrob Agents Chemother. 2006 Apr;50(4):1570-2
[63] Balian JD, Sukhova N, Harris JW, et al. The hydroxylation of omeprazole correlates with S-mephenytoin metabolism: a population study. Clin Pharmacol Ther 1995; 57:662–9.
[64] Spriafil (posaconazole). Pharmacist's Letter/Prescriber's Letter 2007;23(7):230714.
[65] Zonios DI, Bennett JE. Update on azole antifungals. Semin Respir Crit Care Med. 2008 Apr;29(2):198-210
[66] Krishna G, Moton A, Ma L, Savant I, et al. of oral posaconazole on the pharmacokinetic properties of oral and intravenous midazolam: a phase I, randomized, open-label, crossover study in healthy volunteers. Clin Ther. 2009 Feb;31(2):286-98
[67] Pappas PG, Kauffman CA, Andes D, et al: Clinical practice guidelines for the management of candidiasis: 2009 update by the Infectious Diseases Society of America (**IDSA**). Clin Infect Dis 2009; 48(5):503-535
[68] Alexander BD, Johnson MD, Pfeiffer CD, et al. Increasing echinocandin resistance in Candida glabrata: clinical failure correlates with presence of FKS mutations and elevated minimum inhibitory concentrations Clin Infect Dis. 2013;56:1724-1732. doi:10.1093/cid/cit136.
[69] Goodwin SD, Cleary JD, Walawander CA, Taylor JW, Grasela TH Jr. Pretreatment regimens for adverse events related to infusion of amphotericin B. Clin Infect Dis 1995;20:755–61
[70] Burks LC, Aisner J, Fortner CL, Wiernik PH. Meperidine for the treatment of shaking chills and fever. Arch Intern Med 1980;140:483–4
[71]

Other useful reading :

Abdalla M, Sax PE, Mostaghimi A, et al. Clinical Problem Solving. On the Nose (**Blastomycosis**). N Engl J Med. 2015 Sep 3;373(10):955-61.

Abdel-Rahman SM, Farrand N, Schuenemann E, et al. The Prevalence of Infections With **Trichophyton tonsurans** in Schoolchildren: the **CAPITIS** Study. Pediatrics. 2010 Apr 19.

Abdullah, Lina, Abbas, Ossama. **Common nail changes and disorders in older people**: Diagnosis and management. Can Fam Physician 2011 57: 173-181.

Abraham AO, Panda PK. **Itraconazole induced congestive heart failure**, a case study. Curr Drug Saf. 2017 Oct 3.

Adimadhyam S, Schumock GT, Calip GS, et al. Increased risk of mycotic infections associated with **sodium-glucose co-transprter 2 inhibitors**- a prescription sequence symmetry analysis. Br J Clin Pharmacol. 2018 Oct 7.

Agarwal SK, DiNardo CD, Potluri J, et al. Management of **Venetoclax-Posaconazole Interaction** in Acute Myeloid Leukemia Patients: Evaluation of Dose Adjustments. Clin Ther. 2017 Feb 1.

Agarwal R, Dhooria S, Sehgal IS, et al. A randomized trial of **itraconazole versus prednisolone** in **acute-stage ABPA** (allergic bronchopulmonary aspergillosis) complicating asthma. Chest. 2018 Jan 10.

Aitken SL, Beyda ND, Shah DN, et al. Clinical practice patterns in **hospitalized patients at risk for invasive candidiasis**: role of antifungal **stewardship** programs in an era of rapid diagnostics. Ann Pharmacother. 2014 Jun;48(6):683-90.

Aldulaimi S, Lyttle M. Swelling and Erythema of the Scalp on a Teenager. (kerion) Am Fam Physician. 2016 Nov 15;94(10):836-842.

Allegra S, Fatiguso G, De Francia S, et al. Therapeutic drug monitoring of **voriconazole** for treatment and prophylaxis of invasive fungal infection in children. Br J Clin Pharmacol. 2017 Aug 14.

Andrews E, Damle BD, Fang A, Foster G, Crownover P, LaBadie R, Glue P. Pharmacokinetics and tolerability of voriconazole and a combination oral contraceptive co-administered in healthy female subjects. Br J Clin Pharmacol. 2008 Apr;65(4):531-9. Epub 2008 Feb 21

Andrew EC, Curtis N, Coghlan B, et al. Adverse effects of amphotericin B in children; a retrospective comparison of conventional and liposomal formulations. Br J Clin Pharmacol. 2018 Jan 19.

Anti-infective Review Panel. **Anti-infective Guidelines for Community-acquired Infections**. Canadian - New-**2012**. Toronto: MUMS Guideline Clearinghouse. http://www.mumshealth.com/

Armstrong-James D, Brown GD, Netea MG, et al. **Immunotherapeutic** approaches to treatment of fungal diseases. Lancet Infect Dis. 2017 Jul 31.

Beardsley J, Wolbers M, Kibengo FM, et al; CryptoDex Investigators. Adjunctive **Dexamethasone in HIV-Associated Cryptococcal Meningitis**. N Engl J Med. 2016 Feb 11;374(6):542-554.

Beikert FC, Anastasiadou Z, Fritzen B, et al. Topical Treatment of Tinea Pedis Using 6% **Coriander Oil** in Unguentum Leniens: A Randomized, Controlled, Comparative Pilot Study. Dermatology. 2013 Mar 1.

Belayneh M, Sehn E, Korownyk C. **Recurrent vulvovaginal candidiasis**. Can Fam Physician. 2017 Jun;63(6):455.

Bell-Syer SE, Khan SM, Torgerson DJ. Oral treatments for fungal infections of the skin of the foot. Cochrane Database Syst Rev. 2012 Oct 17;10:CD003584. The evidence suggests that **terbinafine is more effective than griseofulvin**, and terbinafine and itraconazole are more effective than no treatment.

Benedict K, Richardson M, Vallabhaneni S, et al. Emerging issues, challenges, and changing epidemiology of **fungal disease outbreaks**. Lancet Infect Dis. 2017 Jul 31.

Benjamin DK Jr, Hudak ML, Duara S, et al; Fluconazole Prophylaxis Study Team. Effect of **fluconazole prophylaxis** on candidiasis and mortality in **premature infants**: a randomized clinical trial. JAMA. 2014 May 7;311(17):1742-9.

Bérard A, Sheehy O, Zhao J-P, et al. Associations between **low- and high-dose oral fluconazole and pregnancy** outcomes: 3 nested case-control studies. CMAJ 2019;191:E179-87.

Berger FA, Monadian N, de Groot NMS, et al. **QTc-prolongation during ciprofloxacin and fluconazole** combination therapy: prevalence and associated risk factors. Br J Clin Pharmacol. 2017 Oct 22.

Bernardo VA, Cross SJ, Crews KR, et al. **Posaconazole therapeutic drug monitoring in pediatric** patients and young adults with cancer. Ann Pharmacother. 2013 Jul;47(7-8):976-83.

Blanco-Dorado S, Marques Afonso AT, Bandín-Vilar EJ, et al. **Voriconazole hepatotoxicity as a result of steroid withdrawal in a patient with allergic bronchopulmonary aspergillosis**. Br J Clin Pharmacol. 2018 Dec 9.

Blot SI, Taccone FS, Van den Abeele AM, et al; the AspICU Study Investigators. A Clinical **Algorithm** to Diagnose Invasive **Pulmonary Aspergillosis** in Critically Ill Patients. Am J Respir Crit Care Med. 2012 Apr 19.

Bow EJ, Evans G, Fuller J, et al. **Canadian clinical practice guidelines for invasive candidiasis in adults**. Can J Infect Dis Med Microbiol 2010;21(4):e122-e150.

Bortolussi R, Martin S; **Canadian Paediatric Society**, Infectious Diseases and Immunization Committee. Practice point. **Antifungal agents** for common paediatric infections. www.cps.ca/en/documents/position/antifungal-agents-common-infections (accessed August 3, 2012).

Brander EPA, McQuillan SK. **Prepubertal vulvovaginitis**. CMAJ. 2018 Jul 3;190(26):E800.

Breazzano MP, Day HR Jr, Bloch KC, et al. Utility of **Ophthalmologic Screening for Patients With Candida Bloodstream Infections**: A Systematic Review. JAMA Ophthalmol. 2019 Apr 18.

Brown JM, Hess KL, Brown S, et al. **Intravaginal practices and risk of bacterial vaginosis and candidiasis** infection among a cohort of women in the United States. Obstet Gynecol. 2013 Apr;121(4):773-80.

Burns C, Valentine J. **Tinea Imbricata** (griseofulvin-terbinafine-image). N Engl J Med. 2016 Dec 8;375(23):2272.

Canadian Sexually Transmitted Infections -STI guidelines 2008 http://www.phac-aspc.gc.ca/std-mts/sti-its/guide-lignesdir-eng.php

Carrel T, Eberle B. **Candida Endocarditis** after TAVR. N Engl J Med. 2019 Jan 3;380(1):e1.

Casadevall A, Kontoyiannis DP, Robert V. On the **Emergence of Candida auris**: Climate Change, Azoles, Swamps, and Birds. MBio. 2019 Jul 23;10(4).

Che D, Zhou H, Li T, Wu B. Duration and intensity of **fluconazole for prophylaxis in preterm neonates**: a meta-analysis of randomized controlled trials. BMC Infect Dis. 2016 Jun 27;16:312.

Chen IW, Lin CW. **Rhino-orbital-cerebral mucormycosis**. CMAJ. 2019 Apr 23;191(16):E450.

Chen X, Jiang X, Yang M, et al. **Systemic antifungal therapy for tinea capitis** in children. Cochrane Database Syst Rev. 2016 May 12;5:CD004685. Newer treatments including terbinafine, itraconazole and fluconazole are at least similar to griseofulvin in children with tinea capitis caused by Trichophyton species. Limited evidence suggests that terbinafine, itraconazole and fluconazole have similar effects, whereas ketoconazole may be less effective than griseofulvin in children infected with Trichophyton. With some interventions the proportion achieving complete clinical cure was in excess of 90% (e.g. one study of terbinafine or griseofulvin for Trichophyton infections), but in many of the comparisons tested, the proportion cured was much lower.New evidence from this update suggests that terbinafine is more effective than griseofulvin in children with T. tonsurans infection.However, in children with Microsporum infections, new evidence suggests that the effect of griseofulvin is better than terbinafine. We did not find any evidence to support a difference in terms of adherence between four weeks of terbinafine versus eight weeks of griseofulvin. Not all treatments for tinea capitis are available in paediatric formulations but all have reasonable safety profiles.

Chiller TM et al. Clinical findings for **fungal infections caused by methylprednisolone injections**. N Engl J Med 2013 Oct 24; 369:1610.

Cojutti PG, Candoni A, Lazzarotto D, et al. Co-administration of **proton pump inhibitors and/or of steroids** may be a risk factor for **low trough concentrations of posaconazole delayed-released tablets** in adult patients with hematological malignancies. Br J Clin Pharmacol. 2018 Jul 5.

Cojutti PG, Merelli M, Allegri L, et al. Successful and safe **long-term treatment of cerebral aspergillosis with high-dose voriconazole guided by therapeutic drug monitoring**. Br J Clin Pharmacol. 2018 Nov 9.

Cole DC, Govender NP, Chakrabarti A, Sacarlal J, Denning DW. Improvement of fungal disease identification and management: combined health systems and public health approaches. Lancet Infect Dis. 2017 Jul 31.

Colombo AL, de Almeida Júnior JN, Slavin MA, et al. **Candida** and **invasive mould** diseases in non-neutropenic critically ill patients and patients with **haematological cancer**. Lancet Infect Dis. 2017 Jul 31.

Cortegiani A, Russotto V, Giarratano A. Associations of Antifungal Treatments With **Prevention of Fungal Infection in Critically Ill Patients Without Neutropenia**. JAMA. 2017 Jan 17;317(3):311-312.

Cullingham K, Hull PR. **Atrophying pityriasis versicolor**. CMAJ. 2014 Jul 8;186(10):776. doi: 10.1503/cmaj.131846. Epub 2014 Apr 14.

Day JN, Chau TTH, Wolbers M, et al. Combination (**amphotericin & flucytosine**) antifungal therapy for cryptococcal meningitis. N Engl J Med 2013;368: 1291-302.

De Berker D. Fungal nail disease. N Engl J Med. 2009;360:2108-16

Denning DW, Chakrabarti A. **Pulmonary** and **sinus fungal diseases** in non-immunocompromised patients. Lancet Infect Dis. 2017 Jul 31.

Dirix L, Swaisland H, Verheul HM, et al. Effect of **Itraconazole and Rifampin on the Pharmacokinetics of Olaparib** in Patients With Advanced Solid Tumors: Results of Two Phase I Open-Label Studies. Clin Ther. 2016 Oct 10.

Dodds-Ashley E. Management of **drug and food interactions with azole antifungal agents** in transplant recipients. Pharmacotherapy. 2010 Aug;30(8):842-54.

Donders G, Bellen G, Byttebier G, et al. Individualized decreasing-dose maintenance fluconazole regimen for recurrent vulvovaginal candidiasis (ReCiDiF trial). Am J Obstet Gynecol. 2008 Dec;199(6):613.e1-9. Epub 2008 Oct 30.

Elewski BE, Cáceres HW, DeLeon L, et al. Terbinafine hydrochloride oral granules versus oral griseofulvin suspension in children with tinea capitis: results of two randomized, investigator-blinded, multicenter, international, controlled trials. J Am Acad Dermatol. 2008 Jul;59(1):41-54

Elewski BE et al. **Efinaconazole** 10% solution in the treatment of toenail onychomycosis: Two phase III multicenter, randomized, double-blind studies. J Am Acad Dermatol 2013 Apr; 68:600.

El-Gohary M, van Zuuren EJ, Fedorowicz Z, Burgess H, Doney L, Stuart B, Moore M, Little P. **Topical antifungal treatments for tinea cruris and tinea corporis**. Cochrane Database of Systematic Reviews 2014, Issue 8. Art. No.: CD009992. DOI: 10.1002/14651858.CD009992.pub2. The pooled data suggest that the individual treatments terbinafine and naftifine are effective. Adverse effects were generally mild and reported infrequently. A substantial number of the studies were more than 20 years old and of unclear or high risk of bias; there is however, some evidence that other topical antifungal treatments also provide similar clinical and mycological cure rates, particularly azoles although most were evaluated in single studies.There is insufficient evidence to determine if Whitfield's ointment, a widely used agent is effective. Although combinations of topical steroids and antifungals are not currently recommended in any clinical guidelines, relevant studiesincluded in this review reported higher clinical cure rates with similar mycological cure rates at the end of treatment, but the quality of evidence for these outcomes was rated very low due to imprecision, indirectness and risk of bias. There was insufficient evidence to confidently assess relapse rates in the individual or combination treatments. Although there was little difference between different classes of treatment in achieving cure, some interventions may be more appealing as they require fewer applications and a shorter duration of treatment. Further, high quality, adequately powered trials focusing on patient-centred outcomes, such as patient satisfaction with treatment should be considered.

Eisman S, Sinclair R. **Fungal nail infection**: diagnosis and management. BMJ.2014 Mar 24

Elewski BE, Aly R, Baldwin SL, et al. Efficacy and safety of **tavaborole** topical solution, 5%, a novel boron-based antifungal agent, for the treatment of toenail onychomycosis: Results from 2 randomized phase-III studies. J Am Acad Dermatol. 2015 Jul;73(1):62-9. Two studies found minimal benefit to the treatment of toenail onychomycosis with tavaborole topical solution (Kerydin). At best, 1 in 11 patients can expect completely clear nails and a negative fungal culture after 1 full year of treatment. (LOE = 2b)

Ely JW, Rosenfeld S, Stone MS. Diagnosis and Management of **Tinea Infections**. Am Fam Physician. 2014;90(10):702-710.

Epaulard O et al. A multistep **voriconazole-related phototoxic** pathway may lead to **skin carcinoma**: Results from a French nationwide study. Clin Infect Dis 2013 Dec 15; 57:e182.

Evans JD, Morris PJ, Knight SR. **Antifungal prophylaxis in liver transplantation**: a systematic review and network meta-analysis. Am J Transplant. 2014 Dec;14(12):2765-76.

Eyre DW, Sheppard AE, Madder H, et al. A **Candida auris Outbreak** and Its Control in an Intensive Care Setting. N Engl J Med. 2018 Oct 4;379(14):1322-1331.

Ferwerda B, Ferwerda G, Plantinga TS, et al.. Human dectin-1 deficiency and mucocutaneous fungal infections. N Engl J Med. 2009 Oct 29;361(18):1760-7.

FDA Mar/12 has received reports of fungal endophthalmitis (eye infections) in patients who were given **Brilliant Blue G (BBG) during eye** surgeries. Clinicians in several states reported the adverse events. FDA, along with CDC and local and state public health agencies, are actively investigating these adverse events.

FDA Oct/12: The FDA and the CDC are recommending that clinicians stop using *all* products from the New England Compounding Center, which is a suspected source in an outbreak of fungal meningitis. To date, 105 people in nine states have been infected following injections of the company's epidural steroid, and eight people have died.

FDA Jan/16 is cautioning that differences in dosing regimens between the **two oral formulations of the antifungal Noxafil (posaconazole) have resulted in dosing errors**. To help prevent additional medication errors, the drug labels were revised to indicate that the two oral formulations cannot be directly substituted for each other but require a change in dose. Direct mg for mg substitution of the two formulations can result in drug levels that are lower or higher than needed to effectively treat certain fungal infections.

Formanek PE, Dilling DF, Formanek PE. Advances in the Diagnosis and Management of **Invasive Fungal Disease**. Chest. 2019 Jul 24.

Forrestel AK, Modi BG, Longworth S, et al. Primary Cutaneous **Cryptococcus** in a Patient With Multiple Sclerosis Treated With **Fingolimod**. JAMA Neurol. 2016 Jan 11:1-2.

Fremerey C, Nenoff P. **Tinea Capitis** in a **Newborn**. N Engl J Med. 2018 May 24;378(21):2022.

Fuller LC, Barton RC, Mohd Mustapa MF, et al. **British Association of Dermatologists'** guidelines for the management of **tinea capitis** 2014. Br J Dermatol. 2014 Sep;171(3):454-63.

Galgiani JN, Ampel NM, Blair JE, et al. **2016 Infectious Diseases Society of America (IDSA)** Clinical Practice Guideline for the Treatment of **Coccidioidomycosis**. Clin Infect Dis. 2016 Jul 27

Garcia-Doval I, Cabo F, Monteagudo B, et al. **Clinical diagnosis of toenail onychomycosis** is possible in some patients: cross-sectional diagnostic study and development of a diagnostic rule. Br J Dermatol. 2010 Oct;163(4):743-51. doi: 10.1111/j.1365-2133.2010.09930.x.

Gesquiere I, Hens B, der Van Schueren B, et al. Drug disposition before and after **gastric bypass: fenofibrate and posaconazole**. Br J Clin Pharmacol. 2016 Jul 1.

Giglio M, Caggiano G, Dalfino L, et al. Oral **nystatin prophylaxis** in **surgical/trauma ICU patients**: a randomised clinical trial. Crit Care. 2012 Apr 10;16(2):R57.

Glocker EO, Hennigs A, Nabavi M, et al. A homozygous CARD9 mutation in a family with susceptibility to fungal infections. N Engl J Med. 2009 Oct 29;361(18):1727-35.

Glushko T, Colmegna I. **Voriconazole-induced periostitis**. CMAJ. 2015 Oct 6;187(14):1075.

Gregg KS, Kauffman CA. **Invasive Aspergillosis**: Epidemiology, Clinical Aspects, and Treatment. Semin Respir Crit Care Med. 2015 Oct;36(5):662-72.

Grijsen ML, de Vries HJC. **Kerion**. CMAJ. 2017 May 23;189(20):E725.

Gupta AK, Paquet M, Simpson F, Tavakkol A. **Terbinafine** in the treatment of dermatophyte toenail onychomycosis: a meta-analysis of efficacy for **continuous** and intermittent regimens. J Eur Acad Dermatol Venereol. 2012 May 28.

Gupta AK, Bluhm R, Summerbell R. Pityriasis versicolor. J Eur Acad Dermatol Venereol. 2002 Jan;16(1):19-33

Gupta AK, Foley KA, Mays RR, et al. **Monotherapy for toenail onychomycosis**: a systematic review and network meta-analysis. Br J Dermatol. 2019 May 23.

Gupta AK, Sibbald RG, Andriessen A, et al. **Toenail onychomycosis-a Canadian** approach with a new transungual treatment: development of a clinical pathway. J Cutan Med Surg 2015;April 9:1-10. [Epub ahead print] http://cms.sagepub.com/content/early/2015/04/09/1203475415581310.full.pdf+html (accessed April '15)

Hage CA, Carmona EM, Epelbaum O, et al. **Microbiological Laboratory Testing** in the Diagnosis of Fungal Infections in Pulmonary and Critical Care Practice. An Official American Thoracic Society Clinical Practice Guideline. Am J Respir Crit Care Med. 2019 Sep 1;200(5):535-550.
Hall SR, Mecham JC, Lott DG. **Airway Obstruction in a Patient After Kidney Transplant**. JAMA Otolaryngol Head Neck Surg. 2019 May 9.
Health Canada Jun/19 warns Canadians of potential cancer risk associated with gentian violet.
Hanna SA, Kirchhof MG. **Mycosis fungoides mimicking tinea pedis**. CMAJ. 2016 Dec 6;188(17-18):E539.
Haydour Q, Hage CA, Carmona EM, et al**. Diagnosis of Fungal Infections**. A Systematic Review and Meta-Analysis Supporting American Thoracic Society Practice Guideline. Ann Am Thorac Soc. 2019 Sep;16(9):1179-1188.
Health Canada Jun/13 **Ketoconazole** use has been associated with liver damage including cases of death.
Health Canada June/14 TERAZOL 7 Vaginal Cream 0.4% (**terconazole**); TERAZOL 3 Dual-Pak - Vaginal Cream 0.8%/Vaginal Ovules 80 mg (terconazole) - Risk of Anaphylaxis and Toxic Epidermal Necrolysis - Janssen Inc.
Health Canada June/17: **PHQ 1001 Khasiat Penawar Herba Qaseh Serata Herb** has undeclared dexamethasone, piroxicam, **griseofulvin** and paracetamol by Singapore Health Sciences Authority.
Health Canada Aug/18: testing of Jian Pai Natural Skin Care Cream, also called ''Yikangshuang," found that it contains two antifungal drugs (fluconazole and miconazole) that are not listed on the product label.
Health Canada Jun/19 warns Canadians of potential cancer risk associated with **gentian violet**.
Hillier SL, Nyirjesy P, Waldbaum AS, et al. **Secnidazole** Treatment of Bacterial Vaginosis: A Randomized Controlled Trial. Obstet Gynecol. 2017 Aug;130(2):379-386.
Hotta M, Ota M. **Alopecia** in a Boy With Nephrotic Syndrome (**Tinea capitis**). JAMA. 2016 Jan 19;315(3):295-296.
Howley MM, Carter TC, Browne ML, et al; National Birth Defects Prevention Study. **Fluconazole** use and **birth defects** in the National Birth Defects Prevention Study. Am J Obstet Gynecol. 2015 Nov 27.
Huang D. **Disseminated cryptococcosis** in a patient with multiple sclerosis treated with **fingolimod**. Neurology. 2015 Sep 15;85(11):1001-3.
Hudson A, Sturgeon A, Peiris A. **Tinea Versicolor**. JAMA. 2018 Oct 2;320(13):1396.
Hussaini T, Rüping MJ, Farowski F, Vehreschild JJ, Cornely OA. Therapeutic drug **monitoring of voriconazole and posaconazole**. Pharmacotherapy. 2011 Feb;31(2):214-25.
Ingen-Housz-Oro S, Foulet F, Chosidow O. Atypical psoriasis. (**Tinea corporis**) BMJ. 2015 Nov 4;351:h5510.
Jansman FG, Reyners AK, van Roon EN, et al; Scientific Institute for Dutch Pharmacists (WINAp), the Dutch Society for Medical Oncology (NVMO); Dutch Society of Clinical Pharmacology and Biopharmacy (NVKF&B). Consensus-Based Evaluation of Clinical Significance and Management of **Anticancer Drug Interactions**. Clin Ther. 2011 Apr 1.
Jørgensen KJ, Gøtzsche PC, Dalbøge CS, Johansen HK. **Voriconazole versus amphotericin B or fluconazole in cancer patients with neutropenia**. Cochrane Database Syst Rev. 2014;(2):CD004707.
Kao WY, Su CW, Huang YS, et al. Risk of Oral Anti-fungal Agent-Induced **Liver Injury** in Taiwanese. Br J Clin Pharmacol. 2013 Jun 10. (especially **ketoconazole**)
Kaplan YC, Koren G, Bozzo P. **Fluconazole** exposure during **pregnancy**. Can Fam Physician. 2015 Aug;61(8):685-6
Kaufman DA, Cuff AL, Wamstad JB, et al. **Fluconazole prophylaxis in extremely low birth weight infants** and neurodevelopmental outcomes and quality of life at 8 to 10 years of age. J Pediatr. 2011 May;158(5):759-765.e1.
Kempsford R, Allen A, Bal J, et al. The effect of **ketoconazole on the pharmacokinetics and pharmacodynamics of inhaled fluticasone furoate and vilanterol** trifenatate in healthy subjects. Br J Clin Pharmacol. 2012 Nov 1.
Kenyon C, Bonorchis K, Corcoran C, et al. A **dimorphic fungus** causing disseminated infection in South Africa. N Engl J Med 2013;369:1416-24.
Kondo T, Terada K. **Candida Esophagitis**. N Engl J Med. 2017 Apr 20;376(16):1574.
Kreijkamp-Kaspers S, Hawke K, Guo L, et al. **Oral antifungal medication for toenail onychomycosis**. Cochrane Database of Systematic Reviews 2017, Issue 7. Art. No.: CD010031. We found high-quality evidence that compared to placebo, terbinafine and azoles are effective treatments for the mycological and clinical cure of onychomycosis, with moderate-quality evidence of excess harm. However, terbinafine probably leads to better cure rates than azoles with the same risk of adverse events (moderate-quality evidence). Azole and griseofulvin were shown to probably have a similar effect on cure, but more adverse events appeared to occur with the latter (moderate-quality evidence). Terbinafine may improve cure and be associated with fewer adverse effects when compared to griseofulvin (low-quality evidence). Only four comparisons assessed recurrence rate: low-quality evidence found that terbinafine or azoles may lower the recurrence rate when compared to placebo, but there may be no difference between them. Only a limited number of studies reported adverse events, and the severity of the events was not taken into account
Kreijkamp-Kaspers S, Hawke KL, van Driel ML. **Oral Medications to Treat Toenail Fungal Infection**. JAMA. 2018 Jan 23;319(4):397-398.
Kullberg BJ, Arendrup MC. **Invasive Candidiasis**. N Engl J Med. 2015 Oct 8;373(15):1445-56.
Ladizinski B, Piette W. **Disseminated Cutaneous Blastomycosis**. N Engl J Med. 2018 Jul 5;379(1):74.
Laties Alan M., Fraunfelder Frederick T., Tomaszewski Konrad, et al, Long-term **visual safety of voriconazole** in adult patients with paracoccidioidomycosis, Clinical Therapeutics, Volume 32, Issue 13, December 2010, Pages 2207-2217, ISSN 0149-2918, DOI: 10.1016/S0149-2918(10)80024-4.
Laudenbach JM, Epstein JB. Treatment strategies for oropharyngeal candidiasis. Expert Opin. Pharmacother. 2009; 10(9):1413-1421
Le T, Kinh NV, Cuc NTK, et al. A Trial of **Itraconazole or Amphotericin B for HIV-Associated Talaromycosis**. N Engl J Med. 2017 Jun 15;376(24):2329-2340.
León C, Ruiz-Santana S, Saavedra P, et al. EPCAN Study Group. A bedside scoring system ("**Candida score**") for early antifungal treatment in nonneutropenic critically ill patients with Candida colonization. Crit Care Med. 2006 Mar;34(3):730-7.
Leonart LP, Tonin FS, Ferreira VL, et al. **Fluconazole Doses** Used for **Prophylaxis** of Invasive Fungal Infection in **Neonatal** Intensive Care Units: A Network Meta-Analysis. J Pediatr. 2017 Mar 10.
Leroux S, Jacqz-Aigrain E, Elie V, et al. Pharmacokinetics and safety of **fluconazole and micafungin in neonates with systemic candidiasis**: a randomized, open-label clinical trial. Br J Clin Pharmacol. 2018 May 10.
Lestner JM, Smith PB, Cohen-Wolkowiez M, et al. Antifungal Agents and Therapy for **Infants and Children** with Invasive Fungal Infections: A Pharmacological Perspective. Br J Clin Pharmacol. 2012 Nov 6.
Limper AH, Adenis A, Le T, et al. Fungal infections in **HIV/AIDS**. Lancet Infect Dis. 2017 Jul 31.
Limper Andrew H., Knox KS., Sarosi GA., et al. and on behalf of the **American Thoracic Society** (**ATS**) Fungal Working Group. An Official American Thoracic Society Statement: Treatment of **Fungal Infections in Adult Pulmonary and Critical Care Patients**. Am. J. Respir. Crit. Care Med. 183: 96-128. January 3, **2011**
Lin XB, Li ZW, Yan M, et al. Population pharmacokinetics of **voriconazole and CYP2C19 polymorphisms** for optimizing dosing regimens in **renal transplant** recipients. Br J Clin Pharmacol. 2018 Apr 1.
Lipner SR, Scher RK. **Long-standing Onychodystrophy** in a Young Woman. JAMA.2016 Nov 8;316(18):1915-1916.
Liu W, Guan X, Yu Z, et al. **A Drug-drug Interaction Between Cyclosporine and Nystatin**. Clin Ther. 2018 Mar 15.
Lo Re V 3rd, Carbonari DM, Lewis JD, et al **Oral Azole Antifungal** Medications and Risk of **Acute Liver Injury**, Overall and by Chronic Liver Disease Status. Am J Med. 2016 Mar;129(3):283-291.e5.
Lockhart SR et al. Simultaneous emergence of **multidrug-resistant Candida auris** on 3 continents confirmed by whole-genome sequencing and epidemiological analyses. Clin Infect Dis 2017 Jan 15; 64:134.
Maertens JA, Raad II, Marr KA, et al. **Isavuconazole** versus voriconazole for primary treatment of invasive mould disease caused by Aspergillus and other fi lamentous fungi (SECURE): a phase 3, randomised-controlled, non-inferiority trial. Lancet 2015; online Dec 9.
Malani AN et al. **Magnetic resonance imaging** screening to identify spinal and paraspinal infections associated with injections of **contaminated methylprednisolone** acetate. JAMA 2013 Jun 19; 309:2465.
Manzoni P et al. on behalf of the Italian Task Force for the Study and Prevention of Neonatal Fungal Infections–the Italian Society of Neonatology. **Bovine Lactoferrin** Prevents Invasive Fungal Infections in Very Low Birth Weight Infants: A Randomized Controlled Trial. Pediatrics. 2012 Jan;129(1):116-123.
Marr KA, Schlamm HT, Herbrecht R, et al. **Combination antifungal therapy for invasive aspergillosis**: a randomized trial. Ann Intern Med. 2015 Jan 20;162(2):81-9.
McClelland RS et al. Randomized trial of periodic presumptive treatment with high-dose **intravaginal metronidazole and miconazole to prevent vaginal infections** in HIV-negative women. J Infect Dis 2015 Jun 15; 211:1875.
McClelland RS, Balkus JE, Lee J, et al. Randomized Trial of Periodic Presumptive Treatment With **High-Dose Intravaginal Metronidazole and Miconazole** to Prevent Vaginal Infections in HIV-negative Women. J Infect Dis. 2015 Jun 15;211(12):1875-82.
MHRA June/16 **Topical miconazole**, including oral gel: reminder of potential for serious **interactions with warfarin**.
Miceli Marisa H, Diaz Jose A, Lee Samuel A. **Emerging opportunistic yeast infections**, The Lancet Infectious Diseases, Volume 11, Issue 2, February 2011, Pages 142-151, ISSN 1473-3099, DOI: 10.1016/S1473-3099(10)70218-8.
Miceli MH, Kauffman CA. **Aspergillus Galactomannan** for Diagnosing Invasive **Aspergillosis**. JAMA. 2017 Sep 26;318(12):1175-1176.
Mikailov A, Cohen J, Joyce C, Mostaghimi A. Cost-effectiveness of **Confirmatory Testing Before Treatment of Onychomycosis**. JAMA Dermatol. 2016 Mar;152(3):276-81.
Milam EC, Meehan SA, Ramachandran S. Well-Demarcated, Scaly Plaques. (**tinea**) JAMA. 2016 Feb 2;315(5):508-509.
Mølgaard-Nielsen D, Pasternak B, Hviid A. Use of oral **fluconazole during pregnancy and the risk of birth defects**. N Engl J Med. 2013 Aug 29;369(9):830-9.
Mølgaard-Nielsen D, Svanström H, Melbye M, et al. Association Between Use of Oral **Fluconazole** During **Pregnancy and Risk of Spontaneous Abortion and Stillbirth**. JAMA. 2016 Jan 5;315(1):58-67.
Molina I, Gómez i Prat J, Salvador F, et al. Randomized trial of **posaconazole** and benznidazole for chronic **Chagas disease**. N Engl J Med 2014;370:1899-908.
Molloy SF, Kanyama C, Heyderman RS, et al. **Antifungal Combinations for Treatment of Cryptococcal Meningitis** in Africa. N Engl J Med. 2018 Mar 15;378(11):1004-1017.
Moriarty B, Hay R, Morris-Jones R. The diagnosis and management of **tinea**. BMJ. 2012 Jul 10;345:e4380.
Morillo CA, Waskin H, Sosa-Estani S, et al; **STOP-CHAGAS** Investigators.. **Benznidazole and Posaconazole** in Eliminating Parasites in Asymptomatic T. Cruzi Carriers: The STOP-CHAGAS Trial. J Am Coll Cardiol. 2017 Feb 28;69(8):939-947.
Morrissey C Orla, Chen Sharon C-A, Sorrell Tania C, et al, for the Australasian Leukaemia Lymphoma Group and the Australia and New Zealand Mycology Interest Group. **Galactomannan and PCR** versus culture and histology for directing use of antifungal treatment for invasive aspergillosis in high-risk haematology patients: a randomised controlled trial. Lancet Infect Dis 2013; online April 30.
Muth CC. **Fungal Nail Infection**. JAMA. 2017 Feb 7;317(5):546.
Nalla P, Dacruz TA, Obuobie K. **Tiredness** in a patient treated with **itraconazole**. BMJ. 2017 Jan 26;356:i6819.
Nemer KM, Denny G, Mann CM. Crusted Papules and Pustules on the Leg After a **Trout** Fishing Trip. (**Trichophyton**- **Majocchi granuloma**) JAMA Dermatol. 2017 Jul 1;153(7):705-706.
Neoh CF, Leung L, Vajpayee RB, et al. Treatment of alternaria keratitis with **intrastromal and topical caspofungin** in combination with **intrastromal, topical, and oral voriconazole**. Ann Pharmacother. 2011 May;45(5):e24.
Nishimoto M, Koh H, Tokuwame A, et al. **Drug interactions** and safety profiles with concomitant use of **caspofungin and calcineurin inhibitors** in allogeneic hematopoietic cell transplantation. Br J Clin Pharmacol. 2017 Apr 13.
Nucci M, Nouér SA, Esteves P, et al. **Discontinuation** of empirical **antifungal therapy** in ICU patients **using 1,3-β-d-glucan**. J Antimicrob Chemother. 2016 Jun 10.
Nurbhai M, Grimshaw J, Watson M, Bond C, Mollison J, Ludbrook A. Oral versus intra-vaginal imidazole and triazole anti-fungal treatment of uncomplicated vulvovaginal candidiasis (thrush). Cochrane Database Syst Rev. 2007 Oct 17;(4):CD002845. No statistically significant differences were observed in clinical cure rates of anti-fungals administered by the oral and intra-vaginal routes for the treatment of uncomplicated vaginal candidiasis.
Okada N, Azuma M, Imanishi M, et al. Potential Usefulness of Early **Potassium Supplementation for Preventing Severe Hypokalemia Induced by Liposomal Amphotericin B** in Hematologic Patients: A Retrospective Study. Clin Ther. 2018 Jan 2.
Pai MP, Lodise TP. Steady-state plasma pharmacokinetics of oral **voriconazole in obese adults**. Antimicrob Agents Chemother 2011;55:2601-5.
Pappas PG, Kauffman CA, Andes DR, et al. Clinical Practice Guideline for the **Management of Candidiasis: 2016 Update** by the Infectious Diseases Society of America. (**IDSA**) Clin Infect Dis. 2015 Dec 16.
Parajuli S, Wick A, Pandeya S, et al. The feared **five fungal infections in kidney transplant recipients**: A single-center 20-year experience. Clin Transplant. 2018 May 21:e13289.
Pasternak B, Wintzell V, Furu K, et al. **Oral Fluconazole in Pregnancy** and Risk of Stillbirth and Neonatal Death. JAMA. 2018 Jun 12;319(22):2333-2335**.**
Pasquier E, Kunda J, De Beaudrap P, et al. Long-term Mortality and Disability in **Cryptococcal Meningitis**: A Systematic Literature Review. Clin Infect Dis. 2018 Mar 19;66(7):1122-1132.
Patterson TF, Thompson GR 3rd, Denning DW, et al. Practice Guidelines for the Diagnosis and Management of **Aspergillosis**: 2016 Update by the **Infectious Diseases Society of America (IDSA)** . Clin Infect Dis. 2016 Jun 29.
Paudyal S, Battu P, Taylor S, et al. Fluffy **Periostitis Induced by Voriconazole**. Arthritis Rheumatol. 2015 Aug 5.
Pennington KM, Yost KJ, Escalante P, et al. **Antifungal prophylaxis in lung transplant**: A survey of United States' transplant centers. Clin Transplant. 2019 Jun 7:e13630.
Perfect JR, Dismukes WE, Dromer F, et al. Clinical practice guidelines for the management of **cryptococcal** disease: 2010 update by the Infectious Diseases Society of America. Clin Infect Dis 2010 Feb 1;50(3):291-322.
Perlin DS, Rautemaa-Richardson R, Alastruey-Izquierdo A. The global problem of **antifungal resistance**: prevalence, mechanisms, and management. Lancet Infect Dis. 2017 Jul 31.
Pharmacist's Letter. Treatment of Uncomplicated Vaginal Yeast Infections. May 2010.
Pienaar ED, Young T, Holmes H. Interventions for the prevention and management of **oropharyngeal candidiasis associated with HIV infection** in adults and children. Cochrane Database Syst Rev. 2010 Nov 10;11:CD003940.
Prajna NV, Krishnan T, Mascarenhas J, et al; Mycotic Ulcer Treatment Trial Group. The **mycotic ulcer** treatment trial: a randomized trial comparing **natamycin vs voriconazole**.JAMA Ophthalmol. 2013;131(4):422-429.
Prajna NV, Krishnan T, Rajaraman R, et al; Mycotic Ulcer Treatment Trial II Group. Effect of **oral voriconazole on fungal keratitis** in the Mycotic Ulcer Treatment Trial II (**MUTT II**): a randomized clinical trial [online October 27, 2016].JAMA Ophthalmol. doi:10.1001/jamaophthalmol.2016.4096
Queiroz-Telles F, Fahal AH, Falci DR, et al. Neglected endemic **mycoses**. Lancet Infect Dis. 2017 Jul 31.
Rajasingham R, Smith R, Park B, et al. **Global burden of disease of HIV-associated cryptococcal meningitis**: an updated analysis. Lancet Infect Dis 2017; online May 5.
Relhan N, Schwartz SG, Flynn HW Jr. Endogenous **Fungal Endophthalmitis**: An Increasing Problem Among Intravenous Drug Users. JAMA. 2017 Aug 22;318(8):741-742.

Riley TT, Muzny CA, Swiatlo E, et al. Breaking the Mold: A Review of **Mucormycosis** and Current Pharmacological **Treatment** Options. Ann Pharmacother. 2016 Jun 15.

Rose-Nussbaumer J, Prajna NV, Krishnan KT, et al. **Mycotic Ulcer Treatment** Trial I Group. **Vision**-Related Quality-of-Life Outcomes in the Mycotic Ulcer Treatment Trial I: A Randomized Clinical Trial. JAMA Ophthalmol. 2015 Mar 12.

Rossier C, Dunet V, Tissot F, et al.**Voriconazole-induced periostitis**. Eur J Nucl Med Mol Imaging. 2012 Feb;39(2):375-6.

Rotem R, Fishman B, Daniel S, et al. Risk of **major congenital malformations following first-trimester exposure to vaginal azoles used for treating vulvovaginal candidiasis**: a population-based retrospective cohort study. BJOG. 2018 May 22.

Safdar A, Ma J, Saliba F, et al. Drug-induced **nephrotoxicity caused by amphotericin B lipid complex and liposomal amphotericin B**: a review and meta-analysis. Medicine (Baltimore) 89 (4): 236-244, 2010.

Salam AP, Pozniak AL. Disseminated **aspergillosis** in an **HIV**-positive cannabis user taking steroid treatment. Lancet Infect Dis. 2017 Aug;17(8):882

Samaranayake LP, Keung Leung W & Jin L. Oral mucosal fungal infections. Periodontology 2000 2009; 49:39–59

Schauwvlieghe AFAD, Rijnders BJA, Philips N, et al. **Invasive aspergillosis** in patients admitted to the intensive care unit with severe influenza: a retrospective cohort study. Lancet Respir Med 2018; online July 31

Schelenz S, Barnes RA, Barton RC, et al. **British Society for Medical Mycology**. British Society for Medical Mycology best practice recommendations for the diagnosis of **serious fungal diseases**. Lancet Infect Dis. 2015 Apr;15(4):461-474.

Schwartz IS, Dingle TC. **Candida auris**. CMAJ. 2019 Aug 6;191(31):E865.

Schwartz S, Kontoyiannis DP, Harrison T, et al. Advances in the **diagnosis and treatment of fungal infections of the CNS**. Lancet Neurol. 2018 Feb 21.

Schwebke JR, Morgan FG Jr, Koltun W, et al. A phase-3, double-blind, placebo-controlled study of the effectiveness and safety of single oral doses of **secnidazole** 2 g for the treatment of women with bacterial vaginosis. Am J Obstet Gynecol. 2017 Dec;217(6):678.e1-678.e9.

Smith RJ, Boos MD, Burnham JM, et al. Atypical Cutaneous **Blastomycosis** in a Child With Juvenile Idiopathic Arthritis on Infliximab. Pediatrics. 2015 Nov;136(5):e1386-9.

Smith RM et al. Fungal infections associated with **contaminated methylprednisolone injections**. N Engl J Med 2013 Oct 24; 369:1598.

Sohn GK, Kwon GP, Bailey-Healy I, et al. **Topical Itraconazole** for the Treatment of Basal Cell Carcinoma in Patients With Basal Cell Nevus Syndrome or High-Frequency Basal Cell Carcinomas: A Phase 2, Open-Label, Placebo-Controlled Trial. JAMA Dermatol. 2019 Jul 24.

Song Y, Qiao J, Giovanni G, et al. **Mucormycosis in renal transplant** recipients: review of 174 reported cases. BMC Infect Dis. 2017 Apr 18;17(1):283

Spec A, Olsen MA, Raval K, et al. Impact of Infectious Diseases Consultation on Mortality of **Cryptococcal** Infection in Patients Without HIV. Clin Infect Dis. 2017 Feb 9.

Sundar S, Chakravarty J, Agarwal D, Rai M, Murray HW. Single-dose liposomal amphotericin B for visceral leishmaniasis in India. N Engl J Med. 2010 Feb 11;362(6):504-12. RA, Gallagher JC. Drug Fever. Pharmacotherapy. 2010 Jan;30(1):57-69.

Subissi A, Monti D, Togni G, Mailland F. **Ciclopirox**: recent nonclinical and clinical data relevant to its use as a topical antimycotic agent. Drugs 70 (16): 2133-52, 2010.

Timsit J-F, Azoulay E, Schwebel C, et al. Empirical **micafungin** treatment and survival without invasive fungal infection in adults with **ICU-acquired sepsis**, Candida colonization, and multiple organ failure: the **EMPIRICUS** randomized clinical trial.JAMA. doi:10.1001/jama.2016.14655.

Topical treatment of superficial fungal infections. Pharmacist's letter/Prescriber's letter. 2009; (8):250806

Uno T, Wada K, Matsuda S, et al. **Clotrimazole troches** can alter everolimus pharmacokinetics in post-transplant patients: A case report. Br J Clin Pharmacol. 2019 Jun 26.

Uprety S, Sharma R. **Images** in Clinical Medicine. **Kerion** - A Boggy Lump. N Engl J Med. 2016 Sep 8;375(10):980.

Vallabhaneni S, Baggs J, Tsay S, Srinivasan AR, Jernigan JA, Jackson BR. **Trends in antifungal use in US hospitals**, 2006-12. J Antimicrob Chemother. 2018 Oct 1;73(10):2867-2875.

Vallabhaneni S, Jackson BR, Chiller TM. **Candida auris**: An Emerging Antimicrobial Resistance Threat. Ann Intern Med. 2019 Jul 30.

van Schalkwyk J, Yudin MH; Society of Obstetricians & Gynaecologists of Canada. **SOGC** clinical practice guideline. **Vulvovaginitis**: screening for and management of trichomoniasis, vulvovaginal candidiasis, and bacterial vaginosis. http://sogc.org/wp-content/uploads/2015/03/gui320CPG1503E.pdf (accessed Mar, 2015).

Verma S. **Steroid modified tinea**. BMJ. 2017 Mar 8;356:j973

Verweij PE, Zhang J, Debets AJ, et al. In-host adaptation and acquired **triazole resistance in Aspergillus fumigatus**: a dilemma for clinical management. Lancet Infect Dis. 2016 Nov;16(11):e251-e260.

Vethanayagam D, Saad E, Yehya J. **Aspergillosis** spores and **medical marijuana**. CMAJ. 2016 Feb 16;188(3):217.

Vishwanathan K, Dickinson PA, So K, et al. The effect of **itraconazole and rifampicin** on the pharmacokinetics of **osimertinib**. Br J Clin Pharmacol. 2018 Jan 30.

Walker-Smith PK, Wlodek C, Sansom J. **Tinea faciei caused by Arthroderma benhamiae**. BMJ. 2017 May 18;357:j2007

Wan L, Zhang Y, Lai Y, et al. Effect of **Granulocyte-Macrophage Colony-Stimulating Factor** on Prevention and Treatment of Invasive Fungal Disease in Recipients of Allogeneic Stem-Cell **Transplantation**: A Prospective Multicenter Randomized Phase IV Trial. J Clin Oncol. 2015 Sep 21.

Wang JL, Chang CH, Young-Xu Y, Chan KA. Systematic review and meta-analysis of the **tolerability and hepatotoxicity of antifungals** in empirical and definitive therapy for invasive fungal infection. Antimicrob Agents Chemother. 2010 Jun;54(6):2409-19. Epub 2010 Mar 22.

Warkentien T et al. Invasive mold infections **following combat-related injuries**. Clin Infect Dis 2012 Dec 1; 55:1441.

Watson MC, Grimshaw JM, Bond CM, Mollison J, Ludbrook A. Oral versus intra-vaginal imidazole and triazole anti-fungal agents for the treatment of uncomplicated vulvovaginal candidiasis (thrush): a systematic review. BJOG. 2002 Jan;109(1):85-95.

Welsh O, Vera-Cabrera L, Welsh E. Onychomycosis. Clin Dermatol 28 (2): 151-9, 2010.

Wermers RA, Cooper K, Razonable RR, Deziel PJ, Whitford GM, Kremers WK, Moyer TP. **Fluoride excess** and periostitis in transplant patients receiving long-term **voriconazole** therapy. Clin Infect Dis 52 (5): 604-11, 2011.

Westerberg DP, Voyack MJ. **Onychomycosis: Current Trends in Diagnosis and Treatment**. Am Fam Physician. 2013;88(11):762-770.

Wheat CM, Bickley RJ, Hsueh YH, et al. Current Trends in the Use of Two Combination Antifungal/Corticosteroid Creams. J Pediatr. 2017 Jul;186:192-195.

Wiesinger H, Berse M, Klein S, et al. Pharmacokinetic interaction between the **CYP3A4 inhibitor ketoconazole and the hormone drospirenone in combination with ethinylestradiol or estradiol**. Br J Clin Pharmacol. 2015 Aug 14.

Williams K, Mansh M, Chin-Hong P, et al. **Voriconazole-associated cutaneous malignancy**: a literature review on photocarcinogenesis in organ transplant recipients. Clin Infect Dis. 2014 Apr;58(7):997-1002.

Williamson PR, Jarvis JN, Panackal AA, et al. **Cryptococcal meningitis**: epidemiology, immunology, diagnosis and therapy. Nat Rev Neurol. 2017 Jan;13(1):13-24.

Wingard JR, White MH, Anaissie E, Raffalli J, Goodman J, Arrieta A. A randomized, double-blind comparative trial evaluating the safety of **liposomal amphotericin B versus amphotericin B lipid complex** in the empirical treatment of febrile neutropenia. Clin Infect Dis 31 (5): 1155-63, 2000.

Worthington HV, Clarkson JE, Khalid T, et al. Interventions for treating **oral candidiasis for patients with cancer** receiving treatment. Cochrane Database of Systematic Reviews 2010, Issue 7. Art. No.: CD001972. There is insufficient evidence to claim or refute a benefit for any antifungal agent in treating candidiasis.

Xie HY, Feng D, Wei DM, et al. **Probiotics for vulvovaginal candidiasis** in non-pregnant women. Cochrane Database Syst Rev. 2017 Nov 23;11:CD010496. Low and very low quality evidence shows that, compared with conventional treatment, the use of probiotics as an adjuvant therapy could increases the rate of short-term clinical and mycological cure and decrease the relapse rate at one month but this did not translate into a higher frequency of long-term clinical or mycological cure. Probiotics use does not seem to increase the frequency of serious or non-serious adverse events. There is a need for well-designed RCTs with standardized methodologies, longer follow-up and larger sample size.

Zampella JG, Kwatra SG, Blanck J, et al. **Tinea in Tots**: Cases and Literature Review of Oral Antifungal Treatment of Tinea Capitis in Children under 2 Years of Age. J Pediatr. 2017 Jan 12.

Ziakas PD, Kourbeti IS, Voulgarelis M, et al. Effectiveness of systemic **antifungal prophylaxis in patients with neutropenia** after chemotherapy: a meta-analysis of randomized controlled trials. Clin Ther. 2010 Dec;32(14):2316-36.

Ziakas PD, Kourbeti IS, Mylonakis E. Systemic **Antifungal Prophylaxis After Hematopoietic Stem Cell Transplantation**: A Meta-Analysis. Clin Ther. 2014 Jan 16.

Oral Antibiotics: Online Extras

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Rifampin: Monotherapy for treatment for latent TB and prophylaxis for meningococcal disease. Risk of developing resistance if used as monotherapy. Many significant number of drug interactions.

Compounding of Nitrofurantoin Pediatric Suspension, 10mg/mL, 50mL

Nitrofurantoin 50mg/tablet	10 tablets
ORA-Plus	25mL
ORA-Sweet	qs to 50mL

1. Crush ten 50mg nitrofurantoin tablets in a glass mortar to create a fine powder.
2. Add a small amount of ORA-Plus and triturate to a thick, smooth paste. Add the remainder of ORA-Plus by geometric dilution.
3. Bring the suspension to a final volume using ORA-Sweet. Mix briefly with mortar and pestle until a uniform suspension is formed.
4. Dispense in a light-resistant, sealed amber bottle. Product is stable for 91 days with or without refrigeration. Label "Shake Well Before Using".

Reference: Ensom, Mary H.H.; Decarie, Diane. Stability of Nitrofurantoin in Extemporaneously Compounded Suspensions. The Canadian Journal of Hospital Pharmacy, v. 59, n. 1 (Feb 2006).

Note: For kids who dislike the taste of antibiotics – may consider a chocolate syrup chaser. See: https://www.sciencedirect.com/science/article/pii/S0011393X00800399

Oral Antibiotics - References

1. Cohen SH, Gerding DN, Johnson S, Kelly CP, Loo VG, McDonald LC, Pepin J, Wilcox MH; Society for Healthcare Epidemiology of America; Infectious Diseases
2. Society of America. Clinical practice guidelines for Clostridium difficile infection in adults: 2010 update by the society for healthcare epidemiology of America (SHEA) and the infectious diseases society of America (IDSA). Infect Control Hosp Epidemiol. 2010 May;31(5):431-55.
3. Bax R. Development of a twice daily dosing regimen of amoxicillin/clavulanate. Int J Antimicrob Agents. 2007 Dec;30 Suppl 2:S118-21. Epub 2007 Nov 5. Review
4. Gillies M, Ranakusuma A, Hoffmann T, et al. Common harms from amoxicillin: a systematic review and meta-analysis of randomized placebo-controlled trials for any indication. *CMAJ : Canadian Medical Association Journal*. 2015;187(1):E21-E31.
5. Antibiotic resistance in Canada (updated 2015). Retrieved from http://healthycanadians.gc.ca/publications/drugs-products-medicaments-produits/antibiotic-resistance-antibiotique/antimicrobial-surveillance-antimicrobioresistance-eng.php Sept 30, 2016.
6. STI Guidelines in Canada. Retrieved from http://www.phac-aspc.gc.ca/std-mts/sti-its/cgsti-ldcits/index-eng.php Sept 30, 2016.
7. Chan H, Stern RS, Arndt KA, et al. The Incidence of Erythema Multiforme, Stevens-Johnson Syndrome, and Toxic Epidermal Necrolysis: A Population-Based Study With Particular Reference to Reactions Caused by Drugs Among Outpatients. *Arch Dermatol.*1990;126(1):43-47.
8. Brown KA, Khanafer N, Daneman N, Fisman DN. Meta-analysis of antibiotics andthe risk of community-associated Clostridium difficile infection. AntimicrobAgents Chemother. 2013 May;57(5):2326-32. doi: 10.1128/AAC.02176-12. Epub 2013.Mar 11.
9. Arredondo-García JL, Figueroa-Damián R, Rosas A, et al; uUTI Latin American Study Group. Comparison of short-term treatment regimen of ciprofloxacin versus long-term treatment regimens of trimethoprim/sulfamethoxazole or norfloxacin for uncomplicated lower urinary tract infections: a randomized, multicentre, open-label, prospective study. J Antimicrob Chemother. 2004 Oct;54(4):840-3.
10. Auquer F, Cordón F, Gorina E, Caballero JC, Adalid C, Batlle J; Urinary Tract Infection Study Group.Single-dose ciprofloxacin versus 3 days of norfloxacin in uncomplicated urinary tract infections in women. Clin Microbiol Infect. 2002 Jan;8(1):50-4.
11. Iravani A, Tice AD, McCarty J, et al; The Urinary Tract Infection Study Group. Short-course ciprofloxacin treatment of acute uncomplicated urinary tract infection in women. The minimum effective dose. Arch Int Med 1995;155(5):485-94.
12. Camilleri M, Parkman HP, Shafi MA, Abell TL, Gerson L; American College of Gastroenterology. Clinical guideline: management of gastroparesis. Am J Gastroenterol. 2013 Jan;108(1):18-37;
13. van der Ven AJ, Vree TB, Koopmans PP, van der Meer JW. Adverse reactions to co-trimoxazole in HIV infection: a reappraisal of the glutathione-hydroxylamine hypothesis. J Antimicrob Chemother. 1996 May;37 Suppl B:55-60.
14. Fralick M, Macdonald EM, Gomes T, Antoniou T, Hollands S, Mamdani MM, Juurlink DN; Canadian Drug Safety and Effectiveness Research Network. Co-trimoxazole and sudden death in patients receiving inhibitors of renin-angiotensin system: population based study. BMJ. 2014 Oct 30;349:g6196.
15. Antoniou T, Hollands S, Macdonald EM, Gomes T, Mamdani MM, Juurlink DN; Canadian Drug Safety and Effectiveness Research Network. Trimethoprim-sulfamethoxazole and risk of sudden death among patients taking spironolactone. CMAJ. 2015 Mar 3;187(4):E138-43.
16. Sutherland L, Singleton J, Sessions J, Hanauer S, Krawitt E, Rankin G, Summers R, Mekhjian H, Greenberger N, Kelly M, et al. Double blind, placebo controlled trial of metronidazole in Crohn's disease. Gut. 1991 Sep;32(9):1071-5.
17. Trac MH, McArthur E, Jandoc R, et al. **Macrolide antibiotics and the risk of ventricular arrhythmia** in older adults. CMAJ. 2016 Feb 22.
18. Mortensen EM, Halm EA, Pugh MJ, et al. Association of **azithromycin with mortality** and cardiovascular events among older patients hospitalized with pneumonia. JAMA. 2014 Jun 4;311(21):2199-208.
19. Svanström H, Pasternak B, Hviid A, et al. Use of **azithromycin and death from cardiovascular causes**. N Engl J Med 2013; 368:1704-1712.
20. Ray WA, Murray KT, Hall K, et al. **Azithromycin and the risk of cardiovascular death**. N Engl J Med 2012; 366:1881-90.

21. D'Souza AL, Rajkumar C, Cooke J, Bulpitt CJ. Probiotics in prevention of antibiotic associated diarrhoea: meta-analysis. BMJ. 2002;324:1361.
22. **Probiotics for the prevention of Clostridium difficile**–associated diarrhea: a systematic review and meta-analysis.
23. Lee B, Bhuta T, Craig J, Simpson J. Methenamine hippurate for preventing urinary tract infections. Cochrane Database Syst Rev. 2002;(1):CD003265.
24. Grayson ML, McDonald M, Gibson K, et al**. Once-daily intravenous cefazolin plus oral probenecid is equivalent to once-daily intravenous ceftriaxone plus oral placebo** for the treatment of **moderate-to-severe cellulitis in adults**. Clin Infect Dis. 2002 Jun 1;34(11):1440-8
25. Ganjizadeh-Zavareh S, Sodhi M, Spangehl T, et al. **Oral Fluoroquinolones and Risk of Fibromyalgia**. Br J Clin Pharmacol. 2018 Sep 14.
26. Gupta A, Cifu AS, Khanna S. **Diagnosis and Treatment of Clostridium difficile Infection**. JAMA. 2018 Sep 11;320(10):1031-1032.
27. Hamad Y, Warren DK. **Black Hairy Tongue. (minocycline)** N Engl J Med. 2018 Sep 6;379(10):e16.
28. Kulaylat AS, Buonomo EL, Scully KW, et al. Development and Validation of a **Prediction Model for Mortality and Adverse Outcomes** Among Patients With **Peripheral Eosinopenia on Admission for Clostridium difficile Infection**. JAMA Surg. 2018 Sep 12.
29. Lefkowitz A, Shadowitz S. **Reversible cerebellar neurotoxicity induced by metronidazole**. CMAJ. 2018 Aug 13;190(32):E961.
30. Lovegrove MC, Geller AI, Fleming-Dutra KE, et al. US Emergency Department Visits for Adverse Drug Events From Antibiotics in Children, 2011-2015. J Pediatric Infect Dis Soc. 2018 Aug 23.
31. Mullish BH, Quraishi MN, Segal JP, et al. The use of **faecal microbiota transplant** as treatment for **recurrent or refractory Clostridium difficile infection** and other potential indications: joint British Society of Gastroenterology (BSG) and Healthcare Infection Society (HIS) guidelines. Gut. 2018 Aug 28.
32. Salminen P, Tuominen R, Paajanen H, et al. Five-year follow-up of **antibiotic therapy for uncomplicated acute appendicitis** in the APPAC randomized clinical trial [Sept 25,2018]. JAMA.
33. Taplitz RA, Kennedy EB, Bow EJ, et al. **Antimicrobial Prophylaxis for Adult Patients With Cancer-Related Immunosuppression**: ASCO and IDSA Clinical Practice Guideline Update. J Clin Oncol. 2018 Sep 4:JCO1800374.
34. van Dijk ST et al. **Long-term effects of omitting antibiotics in uncomplicated acute diverticulitis**. Am J Gastroenterol 2018 Jul; 113:1045.
35. Guh AY, Kutty PK. **Clostridioides difficile Infection**. Ann Intern Med. 2018 Oct 2;169(7):ITC49-ITC64.
36. Major G, Bradshaw L, Boota N, et al. Follow-on **RifAximin for the Prevention** of recurrence following standard treatment of Infection with **Clostridium Difficile** (**RAPID**): a randomised placebo controlled trial. Gut. 2018 Sep 25.
37. Martinez KA, Rood M, Jhangiani N, et al. **Antibiotic Prescribing for Respiratory Tract Infections** and Encounter Length: An Observational Study of Telemedicine. Ann Intern Med. 2018 Oct 2.
38. Subtil D, Brabant G, Tilloy E, et al. **Early clindamycin for bacterial vaginosis in pregnancy** (**PREMEVA**): a multicentre, double-blind, randomised controlled trial. Lancet 2018; online Oct 12.
39. Toh JWT, Phan K, Hitos K, et al. Association of mechanical bowel preparation and oral **antibiotics before elective colorectal surgery** with surgical site infection: a network meta-analysis. JAMA Netw Open. 2018;1(6):e183226.
40. Chang KL, Guarderas JC. **Allergy Testing**: Common Questions and Answers. Am Fam Physician. 2018 Jul 1;98(1):34-39.
41. Cheon E, Horowitz HW. New avenues for antimicrobial stewardship: the case for **penicillin skin testing by pharmacists**. Clin Infect Dis. 2018 Oct 3.
42. Hassoun A. **Clostridium difficile associated disease**. BMJ. 2018 Oct 29;363:k4369.
43. Revolinski SL, Munoz-Price LS. **Clostridium difficile in Immunocompromised Hosts**: A Review of Epidemiology, Risk Factors, Treatment, and Prevention. Clin Infect Dis. 2018 Oct 3.
44. Shi C, Xiao Y, Zhang Q, et al. **Efficacy and safety of cefazolin versus antistaphylococcal penicillins for the treatment of methicillin-susceptible Staphylococcus aureus bacteremia**: a systematic review and meta-analysis. BMC Infect Dis. 2018 Oct 11;18(1):508.
45. Stark CM, Susi A, Emerick J, Nylund CM. **Antibiotic and acid-suppression medications during early childhood are associated with obesity**. Gut. 2018 Oct 30.
46. Zhang HL, Tan M, Qiu AM, Tao Z, Wang CH. Antibiotics for treatment of **acute exacerbation of chronic obstructive pulmonary disease**: a network meta-analysis. BMC Pulm Med. 2017 Dec 12;17(1):196.
47. Herath SC, Normansell R, Maisey S, et al. **Prophylactic antibiotic therapy** for chronic obstructive pulmonary disease (**COPD**). Cochrane Database Syst Rev. 2018 Oct 30;10:CD009764. Use of continuous and intermittent prophylactic antibiotics results in a clinically significant benefit in reducing exacerbations in COPD patients. All studies of continuous and intermittent antibiotics used macrolides, hence the noted benefit applies only to the use of macrolide antibiotics prescribed at least three times per week. The impact of pulsed antibiotics remains uncertain and requires further research.The studies in this review included mostly participants who were frequent exacerbators with at least moderate-severity COPD. There were also older individuals with a mean age over 65 years. The results of these studies apply only to the group of participants who were studied in these studies and may not be generalisable to other groups.Because of concerns about antibiotic resistance and specific adverse effects, consideration of prophylactic antibiotic use should be mindful of the balance between benefits to individual patients and the potential harms to society created by antibiotic overuse. Monitoring of significant side effects including hearing loss, tinnitus, and long QTc in the community in this elderly patient group may require extra health resources.
48. Meier MA, Branche A, Neeser OL, et al. **Procalcitonin-guided antibiotic treatment** in patients with positive blood cultures: A patient-level meta-analysis of randomized trials. Clin Infect Dis. 2018 Oct 25.
49. Taylor SN, Marrazzo J, Batteiger BE, et al. **Single-Dose Zoliflodacin** (ETX0914) for Treatment of Urogenital Gonorrhea. N Engl J Med. 2018 Nov 8;379(19):1835-1845.
50. Vollenweider DJ, Frei A, Steurer-Stey CA, et al. Antibiotics for **exacerbations of chronic obstructive pulmonary disease**. Cochrane Database Syst Rev. 2018 Oct 29;10:CD010257. Researchers have found that antibiotics have some effect on inpatients and outpatients, but these effects are small, and they are inconsistent for some outcomes (treatment failure) and absent for other outcomes (mortality, length of hospital stay). Analyses show a strong beneficial effect of antibiotics among ICU patients. Few data are available on the effects of antibiotics on health-related quality of life or on other patient-reported symptoms, and data show no statistically significant increase in the risk of adverse events with antibiotics compared to placebo.
51. Warrington R, Silviu-Dan F, Wong T**. Drug allergy**. Allergy Asthma Clin Immunol. 2018 Sep 12;14(Suppl 2):60.
52. Goyal V, Grimwood K, Byrnes CA, et al. Amoxicillin-clavulanate versus azithromycin for respiratory exacerbations in children with bronchiectasis (BEST-2): a multicentre, double-blind, non-inferiority, randomised controlled trial. Lancet. 2018 Oct 6;392(10154):1197-1206.
53. Janszky I, Gémes K, Ahnve S, Asgeirsson H, Möller J. Invasive Procedures Associated With the Development of Infective Endocarditis. J Am Coll Cardiol. 2018 Jun 19;71(24):2744-2752.
54. King LM, Fleming-Dutra KE, Hicks LA. Advances in optimizing the prescription of antibiotics in outpatient settings. BMJ. 2018 Nov 12;363:k3047.
55. Thornhill MH, Gibson TB, Cutler E, et al. Antibiotic Prophylaxis and Incidence of Endocarditis Before and After the 2007 AHA Recommendations. J Am Coll Cardiol. 2018 Oct 30.
56. Bhargava A, Ralph R, Chatterjee B, Bottieau E. Assessment and initial **management of acute undifferentiated fever** in tropical and subtropical regions. BMJ. 2018 Nov 29;363:k4766.
57. Kabbani S, Palms D, Bartoces M, et al. Outpatient **Antibiotic Prescribing for Older Adults** in the United States: 2011 to 2014. J Am Geriatr Soc. 2018 Oct;66(10):1998-2002.
58. Wittekamp BH, Plantinga NL, Cooper BS, et al. **Decontamination strategies and bloodstream infections with antibiotic-resistant microorganisms** in ventilated patients: a randomized clinical trial [online Oct 22, 2018]. JAMA.
59. Kronman MP, Hersh AL, Newland JG, Gerber JS. Getting Over Our **Inpatient Oral Antibiotic Aversion**. Pediatrics. 2018 Dec;142(6).
60. Moran R, Devchand M, Smibert O, Trubiano JA. **Antibiotic allergy labels in hospitalised and critically ill adults**: a review of current impacts of inaccurate labelling. Br J Clin Pharmacol. 2018 Dec 6.
61. Schranz AJ, Fleischauer A, Chu VH, Wu LT, Rosen DL. Trends in drug use–associated **infective endocarditis and heart valve surgery**, 2007 to 2017: a study of statewide discharge data. Ann Intern Med. 2018. [Epub ahead of print]. doi:10.7326/M18-2124
2. Blumenthal KG, Peter JG, Trubiano JA, Phillips EJ. **Antibiotic allergy**. Lancet. 2018 Dec 14.
3. Ibrahim LF, Hopper SM, Donath S, et al. Development and Validation of a **Cellulitis Risk Score**: The Melbourne ASSET Score. Pediatrics. 2019 Jan 3.
4. Kotloff KL, Shirley DT, Creech CB, et al. **Mupirocin for Staphylococcus aureus Decolonization** of Infants in Neonatal Intensive Care Units. Pediatrics. 2018 Dec 26.
5. Li X, Zoller M, Fuhr U, et al. **Ciprofloxacin in critically ill subjects**: considering hepatic function, age and sex to choose the optimal dose. J Antimicrob Chemother. 2018 Nov 29.
6. Paavonen J, Brunham RC. **Bacterial Vaginosis and Desquamative Inflammatory Vaginitis**. N Engl J Med. 2018 Dec 6;379(23):2246-2254.
7. Sartelli M, Guirao X, Hardcastle TC, et al. 2018 WSES/SIS-E consensus **conference: recommendations for the management of skin and soft-tissue infections**. World J Emerg Surg. 2018 Dec 14;13:58.
8. Tamma PD, Miller MA, Cosgrove SE. Rethinking How Antibiotics Are Prescribed: Incorporating the **4 Moments of Antibiotic Decision Making** Into Clinical Practice. JAMA. 2018 Dec 27.

69. Yahav D, Franceschini E, Koppel F, et al; Bacteremia Duration Study Group. **Seven versus fourteen Days of Antibiotic Therapy** for uncomplicated Gram-negative Bacteremia: a Non-inferiority Randomized Controlled Trial. Clin Infect Dis. 2018 Dec 11.
70. Iversen K, Ihlemann N, Gill SU, et al. **Partial Oral versus Intravenous Antibiotic Treatment of Endocarditis**. (**POET**) N Engl J Med. 2018 Aug 28.
71. Li H-K, Rombach I, Zambellas R, et al. Oral versus intravenous antibiotics for **bone and joint infection**. (OVIVA) N Engl J Med 2019;380: 425-36.
72. Örtqvist AK, Lundholm C, Halfvarson J, et al. Fetal and early life antibiotics exposure and very **early onset inflammatory bowel disease**: a population-based study. Gut. 2019 Feb;68(2):218-225.
73. Wald-Dickler N, Spellberg B. **Short Course Antibiotic Therapy-Replacing Constantine Units** with "Shorter Is Better". Clin Infect Dis. 2019 Jan 7.
74. Tamma PD, Conley AT, Cosgrove SE, et al; Antibacterial Resistance Leadership Group. Association of 30-Day Mortality With Oral Step-Down vs Continued Intravenous Therapy in Patients Hospitalized With **Enterobacteriaceae Bacteremia**. JAMA Intern Med. 2019 Jan 22.
75. Papenburg J, Fontela PS, Freitas RR, Burstein B. Inappropriate Antibiotic Prescribing for **Acute Bronchiolitis** in US Emergency Departments, 2007-2015. J Pediatric Infect Dis Soc. 2019 Jan 17.
76. Persson R, Jick S. Clinical implications of the association between **fluoroquinolones and tendon rupture**: the magnitude of the effect with and without corticosteroids. Br J Clin Pharmacol. 2019 Jan 25.
77. Coughlin K, Flibotte J, Cahill AM, et al. Methemoglobinemia in an Infant After **Sclerotherapy With High-Dose Doxycycline**. Pediatrics. 2019 Jan 17.
78. Bomers MK, van Doorn-Schepens MLM, van der Valk P, Peters EJG. **Poststreptococcal Myalgia and Myositis**. Ann Intern Med. 2019 Jan 22.
79. Chandramohan D, Dicko A, Zongo I, et al. Effect of Adding **Azithromycin to Seasonal Malaria Chemoprevention**. N Engl J Med. 2019 Jan 30.
80. Pickens CI, Wunderink RG, Pickens CI. Principles and Practice of **Antibiotic Stewardship in the ICU**. Chest. 2019 Jan 25.
81. Singh AE, Labbé AC, Auguste U. **Mycoplasma genitalium infection**. CMAJ. 2019 Jan 28;191(4):E103.
82. Stefan MS, Shieh MS, Spitzer KA, et al. Association of Antibiotic Treatment With Outcomes in Patients Hospitalized for an **Asthma Exacerbation Treated With Systemic Corticosteroids**. JAMA Intern Med. 2019 Jan 28.
83. de Kraker ME, Stewardson AJ, Harbarth S. Will 10 Million People Die a Year due to Antimicrobial Resistance by 2050? PLoS Med. 2016 Nov 29;13(11):e1002184.
84. Hvas CL, Jørgensen SMD, Jørgensen SP, et al. Fecal Microbiota Transplantation is Superior to Fidaxomicin for Treatment of Recurrent Clostridium difficile Infection.
85. Gastroenterology. 2019 Jan 2
86. Musher DM, Abers MS, Corrales-Medina VF. Acute Infection and Myocardial Infarction. N Engl J Med. 2019 Jan 10;380(2):171-176.
87. Poole NM, Shapiro DJ, Fleming-Dutra KE, et al. Antibiotic prescribing for children in United States emergency departments: 2009–2014. Pediatrics. 2019;143(2):e20181056
88. Paez-Canro C, Alzate JP, Gonzalez LM, et al. Antibiotics for treating urogenital Chlamydia trachomatis infection in men and non-pregnant women. Cochrane Database Syst Rev. 2019 Jan 25;1:CD010871. In men, regimens with azithromycin are probably less effective than doxycycline for microbiological failure, however, there might be little or no difference for clinical failure. For women, we are uncertain whether azithromycin compared to doxycycline increases the risk of microbiological failure. Azithromycin probably slightly reduces adverse events compared to doxycycline in men and women together but may have little difference in men alone. We are uncertain whether doxycycline compared to ofloxacin reduces microbiological failure in men or women alone, or men and women together, nor if it reduces clinical failure or adverse events in men or women.Based on the fact that women suffer mainly asymptomatic infections, and in order to test the effectiveness and safety of the current recommendations (azithromycin, doxycycline and ofloxacin), for CT infection, especially in low and middle income countries, future RCTs should be designed and conducted to include a large enough sample size of women, and with low risk of bias
89. Ding G, Vinturache A, Lu M. Addressing **inappropriate antibiotic prescribing** in China. CMAJ. 2019 Feb 11;191(6):E149-E150.
90. Gulliford MC, Prevost AT, Charlton J, et al. **Effectiveness and safety of electronically delivered prescribing feedback and decision support** on antibiotic use for respiratory illness in primary care: REDUCE cluster randomised trial. BMJ. 2019 Feb 12;364:l236.
91. Hamilton KW, Cifu AS. Diagnosis and Management of **Infectious Diarrhea**. JAMA. 2019 Feb 14.
92. Hopman J, Meijer C, Kenters N, et al. Risk Assessment After a Severe Hospital-Acquired Infection Associated With **Carbapenemase-Producing Pseudomonas aeruginosa**. JAMA Netw Open. 2019 Feb 1;2(2):e187665.
93. Huang SS, Singh R, McKinnell JA, et al; Project CLEAR Trial. **Decolonization to Reduce Postdischarge Infection Risk among MRSA Carriers**. N Engl J Med. 2019 Feb 14;380(7):638-650.
94. O`Riordan W, Green S, Overcash JS, et al. **Omadacycline** for Acute Bacterial Skin and Skin-Structure Infections. N Engl J Med. 2019 Feb 7;380(6):528-538.
95. Chien AL, Tsai J, Leung S, et al. Association of **systemic antibiotic treatment of acne with skin microbiota characteristics** [online Feb 13, 2019]. JAMA Dermatol. \
96. Ding G, Vinturache A, Lu M. Addressing inappropriate antibiotic prescribing in China. CMAJ. 2019 Feb 11;191(6):E149-E150.
97. Francois Watkins LK, McGee L, Schrag SJ, et al. Epidemiology of invasive **group B streptococcal infections** among nonpregnant adults in the United States, 2008-2016 [online Feb 18, 2019]. JAMA Intern Med.
98. Gulliford MC, Prevost AT, Charlton J, et al. Effectiveness and safety of electronically delivered **prescribing feedback** and decision support on antibiotic use for respiratory illness in primary care: REDUCE cluster randomised trial. BMJ. 2019 Feb 12;364:l236.
99. Hamilton KW, Cifu AS. Diagnosis and Management of **Infectious Diarrhea**. JAMA. 2019 Feb 14.
100. Hopman J, Meijer C, Kenters N, et al. Risk Assessment After a Severe Hospital-Acquired Infection Associated With **Carbapenemase-Producing Pseudomonas aeruginosa**. JAMA Netw Open. 2019 Feb 1;2(2):e187665.
101. Huang SS, Singh R, McKinnell JA, et al; Project CLEAR Trial. **Decolonization** to Reduce Postdischarge Infection Risk among **MRSA Carriers**. N Engl J Med. 2019 Feb 14;380(7):638-650.
102. O`Riordan W, Green S, Overcash JS, et al. **Omadacycline for Acute Bacterial Skin and Skin-Structure Infections**. N Engl J Med. 2019 Feb 7;380(6):528-538.
103. Peltan ID, Brown SM, Bledsoe JR, Sorensen J, Samore MH, Allen TL, Hough CL. **Emergency department door-to-antibiotic time and long-term mortality in sepsis**. Chest. 2019 Feb 16.
104. Ting JY, Roberts A, Sherlock R, et al. Duration of initial empirical antibiotic therapy and outcomes in very low birth weight infants. Pediatrics. 2018;143(3): e20182286
105. Barbieri JS, Etzkorn JR, Margolis DJ. Use of **Antibiotics for Dermatologic Procedures** From 2008 to 2016. JAMA Dermatol. 2019 Mar 2.
106. Fisher JM, Feng JY, Tan SY, Mostaghimi A. Analysis **of Readmissions Following Hospitalization for Cellulitis** in the United States. JAMA Dermatol. 2019 Feb 27.
107. Lefebvre B, Martin I, Demczuk W, et al. **Ceftriaxone-Resistant Neisseria gonorrhoeae**, Canada, 2017. Emerg Infect Dis. 2018 Feb;24(2).
108. McCullagh DJ, Chu DK. **Penicillin allergy**. CMAJ. 2019 Feb 25;191(8):E231.
109. Pouwels KB, Hopkins S, Llewelyn MJ, Walker AS, McNulty CAM, Robotham JV. **Duration of antibiotic treatment for common infections** in English primary care: cross sectional analysis and comparison with guidelines. BMJ 2019;364:l440.
110. Thabit AK, Fatani DF, Bamakhrama MS, et al. **Antibiotic penetration into bone and joints**: An updated review. Int J Infect Dis. 2019 Feb 14;81:128-136.
111. Vijh R, Shah R, Andany N. A 60-year-old woman with **recurrent cellulitis**. CMAJ.2019 Mar 4;191(9):E257-E259.
112. Bundgaard H, Ihlemann N, Gill SU, et al. Long-Term Outcomes of **Partial Oral Treatment of Endocarditis**. N Engl J Med. 2019 Mar 17.
113. Huang SS, Septimus E, Kleinman K, et al. **Chlorhexidine versus routine bathing** to prevent multidrug-resistant organisms and all-cause bloodstream infections in general medical and surgical units (ABATE Infection trial): a cluster-randomised trial. Lancet. 2019 Mar 4.
114. Lissauer D, Wilson A, Hewitt CA, et al. A Randomized Trial of **Prophylactic Antibiotics for Miscarriage Surgery**. N Engl J Med. 2019 Mar 14;380(11):1012-1021.
115. Tarakji KG, Mittal S, Kennergren C, et al; WRAP-IT Investigators. Antibacterial Envelope to **Prevent Cardiac Implantable Device Infection**. N Engl J Med. 2019 Mar 17.
116. Biondi EA, Lee B, Ralston SL, et al. Prevalence of **Bacteremia and Bacterial Meningitis in Febrile Neonates and Infants** in the Second Month of Life: A Systematic Review and Meta-analysis. JAMA Netw Open. 2019 Mar 1;2(3):e190874.
117. Berende A, Ter Hofstede HJM, Vos FJ, et al. Effect of prolonged antibiotic treatment on **cognition in patients with Lyme borreliosis.** Neurology. 2019 Mar 26;92(13):e1447-e1455

118. Hamilton D, Lipscomb K. **A man with fever and breathlessness**. BMJ. 2019 Mar 21;364:l1085.
119. Schlapbach LJ, Weiss SL, Wolf J. Reducing Collateral Damage From Mandates for Time to **Antibiotics in Pediatric Sepsis-Primum Non Nocere**. JAMA Pediatr. 2019 Mar 18.
120. Science M, Timberlake K, Morris A, et al;(GAP Can ASAP). **Quality Metrics for Antimicrobial Stewardship Programs**. Pediatrics. 2019 Mar 29.
121. Gulliford MC, Juszczyk D, Prevost AT, et al. **Electronically delivered interventions to reduce antibiotic prescribing** for respiratory infections in primary care: cluster RCT using electronic health records and cohort study. Health Technol Assess. 2019 Mar;23(11):1-70.
122. Jeong R, Quinn RR, Lentine KL, et al. Outcomes Following **Macrolide Use in Kidney Transplant Recipients**. Can J Kidney Health Dis. 2019 Feb 21;6:2054358119830706.
123. Ray KN, Shi Z, Gidengil CA, et al. Antibiotic Prescribing During **Pediatric Direct-to-Consumer Telemedicine Visits**. Pediatrics. 2019 Apr 8.
124. Traeger MW, Cornelisse VJ, Asselin J, et al. Association of **HIV Preexposure Prophylaxis With Incidence of Sexually Transmitted Infections** Among Individuals at High Risk of HIV Infection. JAMA. 2019 Apr 9;321(14):1380-1390.
125. Branch-Elliman W, O'Brien W, Strymish J, et al. Association of Duration and Type of **Surgical Prophylaxis With Antimicrobial-Associated Adverse Events**. JAMA Surg. 2019 Apr 24
126. Breithaupt L, Köhler-Forsberg O, Larsen JT, et al. Association of **Exposure to Infections in Childhood With Risk of Eating Disorders** in Adolescent Girls. JAMA Psychiatry. 2019 Apr 24.
127. Czepiel J, Dróżdż M, Pituch H, et al. **Clostridium difficile infection**: review. Eur J Clin Microbiol Infect Dis. 2019 Apr 3.
128. Geriak M, Haddad F, Rizvi K, et al. Clinical Data on **Daptomycin Plus Ceftaroline** Versus Standard of Care Monotherapy in the Treatment of **Methicillin-Resistant Staphylococcus aureus Bacteremia**. Antimicrob Agents Chemother. 2019 Mar 11.
129. Golan Y. Current Treatment Options for **Acute Skin and Skin-structure Infections**. Clin Infect Dis. 2019 Apr 8;68(Supplement_3):S206-S212.
130. Hirotsu K, Dang TM, Li S, et al. Association of **Antibiotic Resistance With Antibiotic Use** for Epidermal Growth Factor Receptor Inhibitor-Related Papulopustular Eruption. JAMA Dermatol. 2019 Apr 24.
131. van der Heijden CDCC, Duizer ML, Fleuren HWHA, et al**. Intravenous flucloxacillin treatment** is associated with a high incidence of hypokalemia. Br J Clin Pharmacol. 2019 Apr 26.
132. Weis S, Kesselmeier M, Davis JS, et al. **Cefazolin versus anti-staphylococcal penicillins** for the treatment of patients **with Staphylococcus aureus bacteremia**: a systematic review and meta-analysis. Clin Microbiol Infect. 2019 Mar 27.
133. Guo Q, Goldenberg JZ, Humphrey C, El Dib R, Johnston BC. Probiotics for the **prevention of pediatric antibiotic-associated diarrhea**. Cochrane Database Syst Rev. 2019 Apr 30;4:CD004827. The overall evidence suggests a moderate protective effect of probiotics for preventing AAD (NNTB 9, 95% CI 7 to 13). Using five criteria to evaluate the credibility of the subgroup analysis on probiotic dose, the results indicate the subgroup effect based on high dose probiotics (≥ 5 billion CFUs per day) was credible. Based on high-dose probiotics, the NNTB to prevent one case of diarrhea is 6 (95% CI 5 to 9). The overall certainty of the evidence for the primary endpoint, incidence of AAD based on high dose probiotics was moderate due to the minor issues with risk of bias and inconsistency related to a diversity of probiotic agents used. Evidence also suggests that probiotics may moderately reduce the duration of diarrhea, a reduction by almost one day. The benefit of high dose probiotics (e.g. Lactobacillus rhamnosus orSaccharomyces boulardii) needs to be confirmed by a large well-designed multi-centered randomized trial. It is premature to draw firm conclusions about the efficacy and safety of 'other' probiotic agents as an adjunct to antibiotics in children. Adverse event rates were low and no serious adverse events were attributable to probiotics.
134. Morales D, Pacurariu A, Slattery J, et al. Association between **peripheral neuropathy and exposure to oral fluoroquinolone or amoxicillin-clavulanate therapy** [online April 29, 2019]. JAMA Neurol. doi:10.1001/jamaneurol.2019.0887
135. Welte T. **Azithromycin,** the Holy Grail to Prevent Exacerbations in Chronic Respiratory Disease. Am J Respir Crit Care Med. 2019 Apr 15.
136. Garg P, Ko DT, Bray Jenkyn KM, et al. **Infective Endocarditis Hospitalizations and Antibiotic Prophylaxis** Rates Before and After the 2007 American Heart Association Guidelines Revision. Circulation. 2019 Apr 26.
137. Gjika E, Beaulieu JY, Vakalopoulos K, et al. **Two weeks versus four weeks of antibiotic therapy after surgical drainage** for native joint bacterial arthritis: a prospective, randomised, non-inferiority trial. Ann Rheum Dis. 2019 Apr 16.
138. Knight M, Chiocchia V, Partlett C, et al. Prophylactic **antibiotics in the prevention of infection after operative vaginal delivery (ANODE**): a multicentre randomised controlled trial. Lancet 2019; online May 13.
139. Nguyen MH, Clancy CJ, Pasculle AW, et al. Performance of the **T2Bacteria Panel for diagnosing bloodstream infections**. A diagnostic accuracy study. Ann Med. 2019. [Epub ahead of print]. doi:10.7326/M18-2772
140. Oppelaar MC, Zijtveld C, Kuipers S, et al. **Evaluation of Prolonged vs Short Courses of antibiotic Prophylaxis** Following **Ear, Nose, Throat, and Oral and Maxillofacial Surgery:** A Systematic Review and Meta-analysis. JAMA Otolaryngol Head Neck Surg. 2019 May 9.
141. Bar-Zeev N, Moss WJ. Hope and Humility for **Azithromycin**. N Engl J Med. 2019 Jun 6;380(23):2264-2265.
142. Doan T, Arzika AM, Hinterwirth A, et al. **Macrolide Resistance in MORDOR I** - A Cluster-Randomized Trial in Niger. N Engl J Med. 2019 Jun 6;380(23):2271-2273.
143. Keenan JD, Arzika AM, Maliki R, et al. Longer-Term Assessment of **Azithromycin for Reducing Childhood Mortality** in Africa. N Engl J Med. 2019 Jun 6;380(23):2207-2214.
144. Krensky C, Poutanen SM, Hota SS. Diarrhea after fecal microbiota transplantation for recurrent **Clostridioides difficile infection**. CMAJ. 2019 May 21;191(20):E559-E561.
145. Miller JO, Taylor J, Goldman JL. Severe Acute **Respiratory Failure** in Healthy Adolescents Exposed to **Trimethoprim-Sulfamethoxazole**. Pediatrics. 2019 May 29.
146. Moore DL, Allen UD, Mailman T; Canadian Paediatric Society, Infectious Diseases and Immunization Committee. Practice Point. **Invasive group A streptococcal disease**: management and chemoprophylaxis. April 15, 2019. https://www.cps.ca/en/documents/position/invasive-group-a-streptococcal-disease (accessed June 4, 2019).
147. Oh N, Downey P, Ardehali A. A **Febrile, Hypotensive Patient With Bilateral Lung Crackles**. JAMA. 2019 May 20.
148. Sander SD, Andersen AMN, Murray JA, et al. Association between **antibiotics in the first year of life and celiac disease**. Gastroenterology 2019;156:2217-29
149. Brindle R, Williams OM, Barton E, Featherstone P. Assessment of Antibiotic Treatment of **Cellulitis and Erysipelas**: A Systematic Review and Meta-analysis. JAMA Dermatol. 2019 Jun 12.
150. Montanha MC, Magon TFDS, Alcantara CDS, et al. Reduced bioavailability of **oral amoxicillin tablets compared to suspensions in RYGB bariatric subjects**. Br J Clin Pharmacol. 2019 Jun 19.
151. Nielsen TB, Brass EP, Gilbert DN, et al. **Sustainable Discovery and Development** of Antibiotics - Is a Nonprofit Approach the Future? N Engl J Med. 2019 Jun 19.
152. Rajan M B, Budania A, Bohra GK. **Ceftriaxone induced aplastic anaemia**: A deadfall trap for bone marrow. Br J Clin Pharmacol. 2019 Jun 18.
153. van der Heijden CDCC, Duizer ML, Fleuren HWHA, et al. Intravenous **flucloxacillin treatment is associated with a high incidence of hypokalaemia**. Br J Clin Pharmacol. 2019 Apr 26.
154. Edwards JM, Watson N, Focht C, et al. Group B Streptococcus (GBS) Colonization and Disease among Pregnant Women: A Historical Cohort Study. Infect Dis Obstet Gynecol. 2019 Feb 3;2019:5430493.
155. Heianza Y, Zheng Y, Ma W, et al. Duration and life-stage of antibiotic use and **risk of cardiovascular events in women**. Eur Heart J. 2019 Apr 24.
156. Juo YY, Sanaiha Y, Jabaji Z, Benharash P. Trends in Diverting Loop Ileostomy vs Total Abdominal Colectomy as Surgical Management for Clostridium Difficile Colitis. JAMA Surg. 2019 Jul 3.
157. O'Byrne P, MacPherson P. Syphilis. BMJ. 2019 Jun 28;365:l4159.
158. Puopolo KM, Lynfield R, Cummings JJ, et al. Management of Infants at Risk for Group B Streptococcal Disease. Pediatrics. 2019 Jul 8.
159. Rogers Van Katwyk S, Grimshaw JM, Nkangu M, et al. Government policy interventions to reduce human antimicrobial use: A systematic review and evidence map. PLoS Med. 2019 Jun 11;16(6):e1002819.
160. Sartelli M, Di Bella S, McFarland LV, et al. 2019 update of the **WSES guidelines for management of Clostridioides (Clostridium) difficile** infection in surgical patients. World J Emerg Surg. 2019 Feb 28;14:8.
161. Suda KJ, Calip GS, Zhou J, et al. Assessment of the **appropriateness of antibiotic prescriptions for infection prophylaxis before dental procedures**, 2011 to 2015. JAMA Netw Open. 2019;2(5):e193909. doi:10.1001/jamanetworkopen.2019.3909
162. Vaughn VM, Flanders SA, Snyder A, et al. Excess Antibiotic Treatment **Duration and Adverse Events in Patients Hospitalized With Pneumonia**: A Multihospital Cohort Study. Ann Intern Med. 2019 Jul 9.
163. Bihan K, Weiss N, Théophile H, et al. **Drug-induced aseptic meningitis**: 329 cases from the French Pharmacovigilance Database Analysis. Br J Clin Pharmacol. 2019 Jul 18.
164. Grigoryan L, Germanos G, Zoorob R, et al. **Use of Antibiotics Without a Prescription** in the U.S. Population: A Scoping Review. Ann Intern Med. 2019 Jul 23.
165. Hoofnagle JH, Björnsson ES. **Drug-Induced Liver Injury** - Types and Phenotypes. N Engl J Med. 2019 Jul 18;381(3):264-273.
166. Health Canada. Summary Safety Review – **Fluoroquinolones** – assessing the potential risk of aneurysm (a balloon-like bulge) and dissection (a separation or tear in the layers of the wall) of the aorta (a major blood vessel). June 27, 2019. https://hpr-rps.hres.ca/reg-content/summary-safety-review-detail.php?lang=en&linkID=SSR00226 (accessed July 12, 2019).

167. Ihm C, Sutton JD, Timbrook TT, Spivak ES. Treatment Duration and Associated Outcomes for **Skin and Soft Tissue Infections in Patients With Obesity or Heart Failure**. Open Forum Infect Dis. 2019 May 7;6(6):ofz217.
168. Peterson GE, Crowley AL. Antibiotic Prophylaxis for **Infective Endocarditis**. Circulation. 2019 Jul 16;140(3):181-183.
169. Achten NB, Klingenberg C, Benitz WE, et al. Association of Use of the **Neonatal Early-Onset Sepsis Calculator With Reduction in Antibiotic** Therapy and Safety: A Systematic Review and Meta-analysis. JAMA Pediatr. 2019 Sep 3.
170. Ahluwalia T, Jain S, Norton L, et al. **Reducing Streptococcal Testing** in Patients <3 Years Old in an Emergency Department. Pediatrics. 2019 Sep 11.
171. Anderson DJ, Watson S, Moehring RW; (ARLG). Feasibility of Core **Antimicrobial Stewardship Interventions** in Community Hospitals. JAMA Netw Open. 2019 Aug 2;2(8):e199369.
172. Babich T, Naucler P, Valik JK, et al. **Ceftazidime, carbapenems, or piperacillin-tazobactam** as single definitive therapy for Pseudomonas aeruginosa bloodstream infection – a multi-site retrospective study. Clin Infect Dis.2019 Jul 17.
173. Bai AD, Morris AM. Management of **Staphylococcus aureus bacteremia in adults**. CMAJ. 2019 Sep 3;191(35):E967.
174. Billick M, Gold WL. **Group B streptococcal endocarditis** following elective surgical abortion. CMAJ. 2019 Aug 19;191(33):E916-E918.
175. Daniel S, Doron M, Fishman B, et al. The safety of **amoxicillin and clavulanic acid use during the first trimester of pregnancy**. Br J Clin Pharmacol. 2019 Sep 5.
176. Foster CB, Martinez KA, Sabella C, et al. Patient Satisfaction and **Antibiotic Prescribing for Respiratory Infections** by Telemedicine. Pediatrics. 2019 Aug 1.
177. Gjika E, Beaulieu JY, Vakalopoulos K, et al. **Two weeks versus four weeks of antibiotic therapy** after surgical drainage for native joint bacterial arthritis: a prospective, randomised, non-inferiority trial. Ann Rheum Dis. 2019 Aug;78(8):1114-1121.
178. Guery B, Galperine T, Barbut F. **Clostridioides difficile:** diagnosis and treatments. BMJ. 2019 Aug 20;366:l4609.Pdf Laska IF, Chalmers JD. Treatment to prevent exacerbations in bronchiectasis: macrolides as first line? Eur Respir J. 2019 Jul 18;54(1).
179. Lamagni T, Guy R, Chand M, et al. Resurgence **of scarlet fever in England**, 2014-16: a population-based surveillance study. Lancet Infect Dis. 2018 Feb;18(2):180-187.
180. Leggit JC, Saguil A**. Secnidazole (Solosec) for Bacterial Vaginosis**. Am Fam Physician. 2019 Aug 15;100(4):242-243.
181. Liu Y, Chan TC, Yap LW, et al. Resurgence of **scarlet fever in China**: a 13-year population-based surveillance study. Lancet Infect Dis. 2018 Aug;18(8):903-912.
182. Lynskey NN, Jauneikaite E, Li HK, et al. **Emergence of dominant toxigenic M1T1 Streptococcus pyogenes clone** during increased scarlet fever activity in England: a population-based molecular epidemiological study. Lancet Infect Dis 2019; published online Sept 10.
183. Nielsen TB, Brass EP, Gilbert DN, et al**. Sustainable Discovery and Development of Antibiotics** - Is a Nonprofit Approach the Future? N Engl J Med. 2019 Aug 8;381(6):503-505
184. Mitchell R, Taylor G, Rudnick W, et al.; Canadian Nosocomial Infection Surveillance Program. **Trends in health care–associated infections** in acute care hospitals in Canada: an analysis of repeated point-prevalence surveys. CMAJ 2019;191:E981-8.
185. Morales D, Pacurariu A, Slattery J, et al. Association Between **Peripheral Neuropathy and Exposure to Oral Fluoroquinolone or Amoxicillin-Clavulanate Therap**y. JAMA Neurol. 2019 Jul 1;76(7):827-833.
186. Niu KY, Lin YK. Generalized tetanus. CMAJ. 2019 Aug 26;191(34):E944.
187. Pepper DJ, Sun J, Cui X, et al. **Antibiotic- and Fluid-Focused Bundles** Potentially Improve Sepsis Management, but High-Quality Evidence Is Lacking for the Specificity Required in the Centers for Medicare and Medicaid Service's Sepsis Bundle (SEP-1). Crit Care Med. 2019 Jul 31
188. Rimmler C, Lanckohr C, Akamp C, et al. Physiologically Based **Pharmacokinetic Evaluation of Cefuroxime in Perioperative Antibiotic Prophylaxis**. Br J Clin Pharmacol. 2019 Sep 5.
189. Smyczek P, Chu A, Berenger B. Emerging international strain of **multidrug-resistant Neisseria gonorrhoeae**: Infection in a man with urethral discharge. Can Fam Physician. 2019 Aug;65(8):552-554.
190. Sosnin N, Curtis N, Cranswick N, et al. **Vancomycin is commonly under-dosed in** critically ill children and neonates. Br J Clin Pharmacol. 2019 Aug 4.
191. Stall NM, Fischer HD, Fung K, et al. Sex-Specific Differences in End-of-Life Burdensome **Interventions and Antibiotic Therapy in Nursing Home Residents** With Advanced Dementia. JAMA Netw Open. 2019 Aug 2;2(8):e199557.
192. Sun Y, Gao Y, Chen J, et al. Evidence mapping of recommendations on **diagnosis and therapeutic strategies for diabetes foot**: an international review of 22 guidelines. Metabolism. 2019 Aug 5;100:153956.
193. Tessier L, Guilcher SJT, Bai YQ, et al. The impact of hospital harm on **length of stay, costs of care and length of person-centred episodes of care**: a retrospective cohort study. CMAJ 2019;191:E879-85.
194. Willekens R, Puig-Asensio M, Ruiz-Camps I, et al. **Early oral switch to linezolid** for low-risk patients with Staphylococcus aureus bloodstream infections: a propensity-matched cohort study. Clin Infect Dis. 2018 Oct 23.
195. Yende S, Kellum JA, Talisa VB, et al. **Long-term Host Immune Response Trajectories** Among Hospitalized Patients With Sepsis. JAMA Netw Open. 2019 Aug 2;2(8):e198686.
196. Zhang J, Haines C, Watson AJM, et al. **Oral antibiotic use and risk of colorectal cancer** in the United Kingdom, 1989-2012: a matched case-control study. Gut. 2019 Aug 19.
197. Curry A, Williams T, Penny ML. **Pelvic Inflammatory Disease**: Diagnosis, Management, and Prevention. Am Fam Physician. 2019 Sep 15;100(6):357-364.
198. Etminan M, Sodhi M, Ganjizadeh-Zavareh S, et al. **Oral Fluoroquinolones and Risk of Mitral and Aortic Regurgitation**. J Am Coll Cardiol. 2019 Sep 17;74(11):1444-1450.
199. Jacobs K, Vu DM, Mony V, et al. **Congenital Syphilis Misdiagnosed** as Suspected Nonaccidental Trauma. Pediatrics. 2019 Sep 19.
200. Kadri AN, Wilner B, Hernandez AV, et al. Geographic Trends, Patient Characteristics, and Outcomes of **Infective Endocarditis Associated With Drug Abuse** in the United States From 2002 to 2016. J Am Heart Assoc. 2019 Oct;8(19):e012969.
201. Cheng MP, Stenstrom R, Paquette K, et al. **Blood culture results before and after antimicrobial administration** in patients with severe manifestations of sepsis. A diagnostic study. Ann Intern Med. 17 September 2019. [Epub ahead of print]. doi:10.7326/M19-1696.
202. Dreucean D, Beres K, McNierney-Moore A, Gravino D. Use of **meropenem to treat valproic acid overdose**. Am J Emerg Med. 2019 Sep 4:158426.
203. Manley Alice, Sansom Jane**. Phototoxic reaction to ciprofloxacin** BMJ 2019 Jun 27; 365 :l2413
204. Stravitz RT, Lee WM. **Acute liver failure**. Lancet. 2019 Sep 7;394(10201):869-881. (acetaminophen, antibiotics etc…)
205. Blanco N, Harris AD, Magder LS, et al. Sample Size Estimates for **Cluster-Randomized Trials in Hospital Infection Control** and Antimicrobial Stewardship. JAMA Netw Open. 2019 Oct 2;2(10):e1912644.
206. Hamad AF, Alessi-Severini S, Mahmud SM, et al. Antibiotic **Exposure in the First Year of Life and the Risk of Attention-Deficit/Hyperactivity Disorder**: A Population-based Cohort Study. Am J Epidemiol. 2019 Sep 5. doi: 10.1093/aje/kwz178.
207. Hedrick J, Droz N**. Voriconazole-Induced Periostitis**. N Engl J Med. 2019 Oct 10;381(15):e30.
208. Quinn KL, Campitelli MA, Diong C, et al. Association between **Physician Intensity of Antibiotic Prescribing** and the Prescription of Benzodiazepines, Opioids and Proton-Pump Inhibitors to Nursing Home Residents: a Population-Based Observational Study. J Gen Intern Med. 2019 Oct 1. doi:10.1007/s11606-019-05333-8.
209. Ropper AH. **Neurosyphilis**. N Engl J Med. 2019 Oct 3;381(14):1358-1363
210. Skoog Ståhlgren G, Tyrstrup M, Edlund C, et al. **Penicillin V** four times daily for five days versus three times daily for 10 days in patients with pharyngotonsillitis caused by group A streptococci: randomised controlled, open label, non-inferiority study. BMJ. 2019 Oct 4;367:l5337.
211. Van Boeckel TP, Pires J, Silvester R, et al. Global trends in **antimicrobial resistance in animals** in low- and middle-income countries. Science. 2019 Sep 20;365(6459).
212. Vermeersch K, Gabrovska M, Aumann J, et al. **Azithromycin during Acute Chronic Obstructive Pulmonary Disease** Exacerbations Requiring Hospitalization (BACE). A Multicenter, Randomized, Double-Blind, Placebo-controlled Trial. Am J Respir Crit Care Med. 2019 Oct 1;200(7):857-868.
213. Bilal J, Berlinberg A, Riaz IB, et al. Risk of **Infections and Cancer** in Patients With Rheumatologic Diseases Receiving Interleukin Inhibitors: A Systematic Review and Meta-analysis. JAMA Netw Open. 2019 Oct 2;2(10):e1913102.
214. Mustafa SS, Conn K, Ramsey A. Comparing **Direct Challenge to Penicillin Skin Testing** for the Outpatient Evaluation of Penicillin Allergy: A Randomized Controlled Trial. J Allergy Clin Immunol Pract. 2019 Sep - Oct;7(7):2163-2170.

215. Neal EFG, Nguyen C, Ratu FT, et al. A Comparison of **Pneumococcal Nasopharyngeal Carriage** in Very Young Fijian Infants Born by Vaginal or Cesarean Delivery. JAMA Netw Open. 2019 Oct 2;2(10):e1913650.
216. O'Connor CT, O'Rourke S, Buckley A, et al. **Infective endocarditis**: a retrospective cohort study. QJM. 2019 Sep 1;112(9):663-667
217. Olds C, Spataro E, Li K, et al. **Postoperative Antibiotic Use** Among Patients Undergoing Functional Facial Plastic and Reconstructive Surgery. JAMA Facial Plast Surg. 2019 Oct 24. doi: 10.1001/jamafacial.2019.1027.
218. Pinto-Sander N, Soni S. **Mycoplasma genitalium infection**. BMJ. 2019 Oct 18;367:l5820.
219. Rockenschaub P, Jhass A, Freemantle N, et al. Opportunities to **reduce antibiotic prescribing for patients with COPD** in primary care: a cohort study using electronic health records from the Clinical Practice Research Datalink (CPRD). J Antimicrob Chemother. 2019 Oct 9. doi: 10.1093/jac/dkz411
220.

1. CDC. Get Smart Fact Sheet: is it really a penicillin allergy? https://www.cdc.gov/getsmart/week/downloads/getsmart-penicillin-factsheet.pdf (Accessed March 15, 2017).
2. Joint Task Force on Practice Parameters representing the American Academy of Allergy, Asthma and Immunology; American College of Allergy, Asthma and Immunology; Joint Council of Allergy, Asthma and Immunology. Drug allergy: an updated practice parameter. Ann Allergy Asthma Immunol. 2010 Oct;105(4):259-273
3. American Academy of Allergy Asthma & Immunology. Cephalosporin administration to patients with a history of penicillin allergy.
www.aaaai.org/Aaaai/media/MediaLibrary/PDF%20Documents/Practice%20and%20Parameters/Cephalosporin-administration-2009.pdf. (Accessed March 15, 2017).
4. Allergic reactions to long-term benzathine penicillin prophylaxis for rheumatic fever. International Rheumatic Fever Study Group. Lancet. 1991 Jun 1;337(8753):1308-10.
5. Forrest DM, Schellenberg R, Thien VV, et al. Introduction of a practice guideline for penicillin skin testing improves the appropriateness of antibiotic therapy. Clin Infect Dis 2001;32:1685-90.
6. DiPiro JT. Allergic and pseudoallergic drug reactions. *Pharmacotherapy: A Pathophysiologic Approach*. 7th ed. Dipiro JT, Talbert RL, Yee GC, et al, eds. New York, NY: McGraw-Hill; 2008;1447-1482
7. Solensky R, Banerji A, Bloomberg GR, et al. Cephalosporin administration to patients with a history of penicillin allergy. May 1, 2009.
http://www.aaaai.org/Aaaai/media/MediaLibrary/PDF%20Documents/Practice%20and%20Parameters/Cephalosporin-administration-2009.pdf (Accessed March 15, 2017).
8. Salkind AR, Cuddy PG, Foxworth JW. The rational clinical examination. Is this patient allergic to penicillin? An evidence-based analysis of the likelihood of penicillin allergy. JAMA 2001;285:2498-505.
9. Rochester Regional Health. Penicillin skin testing. February 2016. https://www.rochesterregional.org/-/media/files/air/penicillinbrochure.pdf?la=en (Accessed March 15, 2017).
10. Gonzalez-Estrada A, Radojicic C. Penicillin allergy: a practical guide for clinicians. *Cleve Clin J Med* 2015;82:295-300.
11. Spacek LA, Adkinson NF. Johns Hopkins Medicine. Johns Hopkins antibiotic (abx) guide: beta-lactam allergy. January 2014.
https://www.hopkinsguides.com/hopkins/view/Johns_Hopkins_ABX_Guide/540622/all/Beta_lactam_allergy (Accessed March 15, 2017).
12. Macy E and Ngor E. Recommendations for the Management of Beta-Lactam Intolerance. Clinic Rev Allerg Immunol 2014; 47:46-55
13. Blondel-Hill and Fryters. B-Lactam Allergy. Bugs and Drugs: An antimicrobial/infectious disease reference. 2012:87-90.
14. PL Detailed-document, Allergic Cross-reactivity Among Beta-lactam Antibiotics: An Update. Pharmacist's Letter/Prescriber's Letter. October 2013
15. Terico AT and Gallagher JC. Beta-lactam allergy and cross-reactivity. J Pharm Pract. 2014 Dec;27(6):530-44.
16. Romano A, Viola M, Gueant-Rodriguez RM, et al. Imipenem in patients with immediate hypersensitivity to penicillins. N Engl J Med 2006;354:2835-7. Solensky R, Banerji A, Bloomberg GR, et al. Cephalosporin administration to patients with a history of penicillin allergy. May 1, 2009.
17. Brennan PJ, Bouza TR, Hsu FI, et al. Hypersensitivity reactions to mAbs: 105 desensitizations in 23 patients, from evaluation to treatment. J Allerg Clin Immunol 2009; 124:1259.

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References

1. Shehab N, Patel PR, Srinivasan A, Budnitz DS. Emergency department visits for antibiotic-associated adverse events. Clin Infect Dis. 2008 Sep 15;47(6):735-43.
2. Lemiengre MB, van Driel ML, Merenstein D, Young J, De Sutter AI. Antibiotics for clinically diagnosed acute rhinosinusitis in adults. Cochrane Database Syst Rev 2012;10:CD006089.
3. Smith SM, Fahey T, Smucny J, et al. Antibiotics for acute bronchitis. Cochrane Database of Systematic Reviews 2014, Issue 3.
4. Venekamp, Roderick P., et al. "Antibiotics for acute otitis media in children." *The Cochrane Library* (2013).
5. Rosenfeld, Richard M. "Acute Sinusitis in Adults." *New England Journal of Medicine* 375.10 (2016): 962-970.
6. Gillies M, Ranakusuma A, Hoffmann T, et al. Common harms from amoxicillin: a systematic review and meta-analysis of randomized placebo-controlled trials for any indication. CMAJ : Canadian Medical Association Journal. 2015;187(1):E21-E31. doi:10.1503/cmaj.140848.
7. Lee CE, Zembower TR, Fotis MA, Postelnick MJ, Greenberger PA, Peterson LR, Noskin GA. The incidence of antimicrobial allergies in hospitalized patients: implications regarding prescribing patterns and emerging bacterial resistance. Arch Intern Med. 2000 Oct 9;160(18):2819-22.
8. Joint Task Force on Practice Parameters; American Academy of Allergy, Asthma and Immunology; American College of Allergy, Asthma and Immunology; Joint Council of Allergy, Asthma and Immunology. Drug allergy: an updated practice parameter. Ann Allergy Asthma Immunol. 2010 Oct;105(4):259-273.
9. Johansson SG, Bieber T, Dahl R, Friedmann PS, Lanier BQ, Lockey RF, Motala C, Ortega Martell JA, Platts-Mills TA, Ring J, Thien F, Van Cauwenberge P, Williams HC. Revised nomenclature for allergy for global use: Report of the Nomenclature Review Committee of the World Allergy Organization, October 2003. J Allergy Clin Immunol. 2004 May;113(5):832-6.
10. Bhattacharya S. The facts about penicillin allergy: A review. Journal of Advanced Pharmaceutical Technology & Research. 2010;1(1):11-17.
11. Idsoe O, Guthe T, Willcox RR, de Weck AL. Nature and extent of penicillin side-reactions, with particular reference to fatalities from anaphylactic shock. Bull World Health Organ. 1968;38(2):159-88.
12. Allergic reactions to long-term benzathine penicillin prophylaxis for rheumatic fever. International Rheumatic Fever Study Group. Lancet. 1991 Jun 1;337(8753):1308-10.
13. Smieja M. Current indications for the use of clindamycin: A critical review. *The Canadian Journal of Infectious Diseases*. 1998;9(1):22-28.
14. Brown, Kevin A., et al. "Meta-analysis of antibiotics and the risk of community-associated Clostridium difficile infection." *Antimicrobial agents and chemotherapy* 57.5 (2013): 2326-2332.
15. Slimings C, Riley TV. Antibiotics and hospital-acquired Clostridium difficile infection: update of systematic review and meta-analysis. J Antimicrob Chemother 2014;69:881-891.
16. Chan HL, Stern RS, Arndt KA, Langlois J, Jick SS, Jick H, Walker AM. The incidence of erythema multiforme, Stevens-Johnson syndrome, and toxic epidermal necrolysis. A population-based study with particular reference to reactions caused by drugs among outpatients. Arch Dermatol. 1990 Jan;126(1):43-7.
17. Mockenhaupt M, Viboud C, Dunant A, et al. Stevens-Johnson syndrome and toxic epidermal necrolysis: assessment of medication risks with emphasis on recently marketed drugs. The EuroSCAR-study. J Invest Dermatol 2008;128:35e44.
18. Daneman, Nick, Hong Lu, and Donald A. Redelmeier. "Fluoroquinolones and collagen associated severe adverse events: a longitudinal cohort study." *BMJ open* 5.11 (2015): e010077.
19. Fralick M, Macdonald EM, Gomes T, Antoniou T, Hollands S, Mamdani MM, Juurlink DN; Canadian Drug Safety and Effectiveness Research Network.. Co-trimoxazole and sudden death in patients receiving inhibitors of renin-angiotensin system: population based study.
20. Antoniou T, Hollands S, Macdonald EM, Gomes T, Mamdani MM, Juurlink DN; Canadian Drug Safety and Effectiveness Research Network. Trimethoprim-sulfamethoxazole and risk of sudden death among patients taking spironolactone. CMAJ. 2015 Mar 3;187(4):E138-43.
21. Antibiotic Resistance Threats in the United States, 2013. Centre for Disease Control. Retrieved from http://www.cdc.gov/drugresistance/pdf/ar-threats-2013-508.pdf October 6, 2016.
22. Souli, Maria, I. Galani, and H. Giamarellou. "Emergence of extensively drug-resistant and pandrug-resistant Gram-negative bacilli in Europe." *Euro surveillance: bulletin Europeen sur les maladies transmissibles= European communicable disease bulletin* 13.47 (2008): 5437-5453.
23. Seppälä, Helena, et al. "The effect of changes in the consumption of macrolide antibiotics on erythromycin resistance in group A streptococci in Finland." *New England Journal of Medicine* 337.7 (1997): 441-446.
24. Mölstad, Sigvard, et al. "Sustained reduction of antibiotic use and low bacterial resistance: 10-year follow-up of the Swedish Strama programme." *The Lancet infectious diseases* 8.2 (2008): 125-132.

25. Lovegrove MC, Geller AI, Fleming-Dutra KE, et al. US Emergency Department Visits for Adverse Drug Events From Antibiotics in Children, 2011-2015. J Pediatric Infect Dis Soc. 2018 Aug 23.

References – RxFiles Acute Otitis Media (AOM):

Guidelines

CPS 2016: Le Saux N, Robinson JL; Canadian Paediatric Society, Infectious Diseases and Immunization Committee. Management of acute otitis media in children six months of age and older. Paediatr Child Health. 2016 Jan-Feb;21(1):39-50.

NICE 2018: Otitis media (acute): antimicrobial prescribing. NICE Guidelines published March 28 2018. Available from: https://www.nice.org.uk/guidance/ng91/chapter/Recommendations

AAP 2013: Lieberthal AS, Carroll AE, Chonmaitree T, Ganiats TG, Hoberman A, Jackson MA, Joffe MD, Miller DT, Rosenfeld RM, Sevilla XD, Schwartz RH, Thomas PA, Tunkel DE. The diagnosis and management of acute otitis media. Pediatrics. 2013 Mar;131(3):e964-99. doi: 10.1542/peds.2012-3488. Epub 2013 Feb 25. Erratum in: Pediatrics. 2014 Feb;133(2):346. Dosage error in article text. PubMed PMID:23439909.

Sanfords 2019

Bugs & Drugs 2012/2017

MUMS 2013/2016: Anti-infective Guidelines for Community Acquired Infections

Pain Management

Sjoukes A, Venekamp RP, van de Pol AC, Hay AD, Little P, Schilder AG, Damoiseaux RA. Paracetamol (acetaminophen) or non-steroidal anti-inflammatory drugs, alone or combined, for pain relief in acute otitis media in children. Cochrane Database Syst Rev. 2016 Dec 15;12:CD011534

Foxlee R, Johansson A, Wejfalk J, Dawkins J, Dooley L, Del Mar C. Topical analgesia for acute otitis media. Cochrane Database Syst Rev. 2006 Jul 19;(3):CD005657. Review. PubMed PMID: 16856108. Review updated in 2011.

Hoberman A, Paradise JL, Reynolds EA, Urkin J. Efficacy of Auralgan for treating ear pain in children with acute otitis media. Arch Pediatr Adolesc Med. 1997 Jul;151(7):675-8.

Chonmaitree T, Saeed K, Uchida T, Heikkinen T, Baldwin CD, Freeman DH Jr, McCormick DP. A randomized, placebo-controlled trial of the effect of antihistamine or corticosteroid treatment in acute otitis media. J Pediatr. 2003 Sep;143(3):377-85.

Bonney AG, Goldman RD. Antihistamines for children with otitis media. Can Fam Physician. 2014 Jan;60(1):43-6 Ranakusuma RW, Pitoyo Y, Safitri ED, Thorning S, Beller EM, Sastroasmoro S, Del Mar CB. Systemic corticosteroids for acute otitis media in children. Cochrane Database Syst Rev. 2018 Mar 15;3:CD012289. doi: 10.1002/14651858.CD012289.pub2. Review. PubMed PMID: 29543327; PubMed Central PMCID: PMC6492450.

Chonmaitree T, Saeed K, Uchida T, Heikkinen T, Baldwin CD, Freeman DH Jr, McCormick DP. A randomized, placebo-controlled trial of the effect of antihistamine or corticosteroid treatment in acute otitis media. J Pediatr. 2003 Sep;143(3):377-85.

Diagnosis & Etiology

Heikkinen T, Thint M, Chonmaitree T. Prevalence of various respiratory viruses in the middle ear during acute otitis media. N Engl J Med. 1999 Jan 28;340(4):260-4. PubMed PMID: 9920949.

Ruohola A, Meurman O, Nikkari S, et al. Microbiology of acute otitis media in children with tympanostomy tubes: prevalences of bacteria and viruses. Clin Infect Dis. 2006 Dec 1;43(11):1417-22. Epub 2006 Oct 31. PubMed PMID: 17083014.

Marom T, Tan A, Wilkinson GS, Pierson KS, Freeman JL, Chonmaitree T. Trends in otitis media-related health care use in the United States, 2001-2011. JAMA Pediatr. 2014 Jan;168(1):68-75.

Norhayati MN, Ho JJ, Azman MY. Influenza vaccines for preventing acute otitis media in infants and children. Cochrane Database Syst Rev. 2015 Mar 24;(3):CD010089

Intakorn P, Sonsuwan N, Noknu S, Moungthong G, Pirçon JY, Liu Y, Van Dyke MK, Hausdorff WP. Haemophilus influenzae type b as an important cause of culture-positive acute otitis media in young children in Thailand: a tympanocentesis-based, multi-center, cross-sectional study. BMC Pediatr. 2014 Jun 20;14:157

Sakulchit T, Goldman RD. Antibiotic therapy for children with acute otitis media. Can Fam Physician. 2017 Sep;63(9):685-687. Review. PubMed PMID: 28904032; PubMed Central PMCID: PMC5597011.

Watchful Waiting & Antibiotic Regimen

Emergency Medicine. Canadian Association of Emergency Physicians. Last updated March 2018. https://choosingwiselycanada.org/emergency-medicine/

Venekamp RP, Sanders SL, Glasziou PP, Del Mar CB, Rovers MM. Antibiotics for acute otitis media in children. Cochrane Database Syst Rev. 2015 Jun 23;(6):CD000219.

Le Saux N, Gaboury I, Baird M, Klassen TP, MacCormick J, Blanchard C, Pitters C, Sampson M, Moher D. A randomized, double-blind, placebo-controlled noninferiority trial of amoxicillin for clinically diagnosed acute otitis media in children 6 months to 5 years of age. CMAJ. 2005 Feb 1;172(3):335-41

Spurling GK, Del Mar CB, Dooley L, Foxlee R, Farley R. Delayed antibiotic prescriptions for respiratory infections. Cochrane Database Syst Rev. 2017 Sep 7;9:CD004417. doi: 10.1002/14651858.CD004417.pub5. Review. PubMed PMID: 28881007;PubMed Central PMCID: PMC6372405.

McCormick DP, Chonmaitree T, Pittman C, et al. Nonsevere acute otitis media: a clinical trial comparing outcomes of watchful waiting versus immediate antibiotic treatment. Pediatrics. 2005;115(6): 1455–1465

Tähtinen PA, Laine MK, Huovinen P, Jalava J, Ruuskanen O, Ruohola A. A placebocontrolled trial of antimicrobial treatment for acute otitis media. N Engl J Med. 2011;364(2):116–126

Spiro DM, Tay KY, Arnold DH, Dziura JD, Baker MD, Shapiro ED. Wait-and-see prescription for the treatment of acute otitis media: a randomized controlled trial. JAMA. 2006;296(10):1235–1241.

Malhotra-Kumar S, Lammens C, Coenen S, Van Herck K, Goossens H. Effect of azithromycin and clarithromycin therapy on pharyngeal carriage of macrolide-resistant streptococci in healthy volunteers: a randomised, double-blind, placebo-controlled study. Lancet. 2007 Feb 10;369(9560):482-90.

Vanderkooi OG, Low DE, Green K, Powis JE, McGeer A; Toronto Invasive Bacterial Disease Network. Predicting antimicrobial resistance in invasive pneumococcal infections. Clin Infect Dis. 2005 May 1;40(9):1288-97.

Garrison GD, Sorum PC, Hioe W, Miller MM. High-dose versus standard-dose amoxicillin for acute otitis media. Ann Pharmacother. 2004 Jan;38(1):15-9.

Thompson PL, Gilbert RE, Long PF, Saxena S, Sharland M, Wong IC. Effect of antibiotics for otitis media on mastoiditis in children: a retrospective cohort study using the United Kingdom general practice research database. Pediatrics. 2009; 123(2):424–430.

Marchetti F, Ronfani L, Nibali SC, Tamburlini G; Italian Study Group on Acute Otitis Media. Delayed prescription may reduce the use of antibiotics for acute otitis media: a prospective observational study in primary care. Arch Pediatr Adolesc Med. 2005 Jul;159(7):679-84.

Treatment Duration

Hoberman A, Paradise JL, Rockette HE, et al. Shortened Antimicrobial Treatment for Acute Otitis Media in Young Children. N Engl J Med. 2016 Dec 22;375(25):2446-2456. doi: 10.1056/NEJMoa1606043. PubMed PMID: 28002709; PubMed Central PMCID: PMC5319589.

Kozyrskyj A, Klassen TP, Moffatt M, Harvey K. Short-course antibiotics for acute otitis media. Cochrane Database Syst Rev. 2010 Sep 8;(9):CD001095. doi:10.1002/14651858.CD001095.pub2. Review. PubMed PMID: 20824827. (Treatment duration: Block 2000 x 5 days; Block 2004 x 5 days; Catania 2004x 5 days; Ingvarsson 1982 x 5 days; Pessey 1999x 5 days; Ploussard 1984 x 5 days)

Pichichero ME, Marsocci SM, Murphy ML, Hoeger W, Francis AB, Green JL. A prospective observational study of 5-, 7-, and 10-day antibiotic treatment for acute otitis media. Otolaryngol Head Neck Surg. 2001 Apr;124(4):381-7.
Kozyrskyj AL, Hildes-Ripstein GE, Longstaffe SE, Wincott JL, Sitar DS, Klassen TP, Moffatt ME. Treatment of acute otitis media with a shortened course of antibiotics: a meta-analysis. JAMA. 1998 Jun 3;279(21):1736-42.
Leibovitz E, Piglansky L, Raiz S, Press J, Leiberman A, Dagan R. Bacteriologic and clinical efficacy of one day vs. three day intramuscular ceftriaxone for treatment of nonresponsive acute otitis media in children. Pediatr Infect Dis J. 2000 Nov;19(11):1040-5.

Treatment Failure

American Academy of Otolaryngology-Head and Neck Surgery 2016: Rosenfeld RM, Shin JJ, Schwartz SR, Coggins R, Gagnon L, Hackell JM, Hoelting D, Hunter LL, Kummer AW, Payne SC, Poe DS, Veling M, Vila PM, Walsh SA, Corrigan MD. Clinical Practice Guideline: Otitis Media with Effusion (Update). Otolaryngol Head Neck Surg. 2016 Feb;154(1 Suppl):S1-S41. doi: 10.1177/0194599815623467.
PubMed PMID: 26832942.

Recurrence

Azarpazhooh A, Lawrence HP, Shah PS. Xylitol for preventing acute otitis media in children up to 12 years of age. Cochrane Database Syst Rev. 2016 Aug 3;(8):CD007095

Clinical Q&A

Thanaviratananich S, Laopaiboon M, Vatanasapt P. Once or twice daily versus three times daily amoxicillin with or without clavulanate for the treatment of acute otitis media. Cochrane Database Syst Rev. 2013 Dec 13;(12):CD004975.

References – Acute Bronchitis - RxFiles.ca

Guidelines:

2019 Sanfords

2012Bugs & Drugs

2013 Anti-infective Guidelines for Community-acquired Infections. Anti-infective Review Panel.

Braman SS. Chronic cough due to acute bronchitis: ACCP evidence-based clinical practice guidelines. Chest. 2006 Jan;129(1 Suppl):95S-103S.

General:

Albert RH. Diagnosis and treatment of acute bronchitis. Am Fam Physician. 2010 Dec 1;82(11):1345-50. Review.

Gadomski AM. Potential interventions for preventing pneumonia among young children: lack of effect of antibiotic treatment for upper respiratory infections. Pediatr Infect Dis J. 1993 Feb;12(2):115-20.

Gonzales R, Anderer T, McCulloch CE, et al. A cluster randomized trial of decision support strategies for reducing antibiotic use in acute bronchitis. JAMA Intern Med. 2013 Feb 25;173(4):267-73.

Macfarlane J, Holmes W, Gard P, et al. Reducing antibiotic use for acute bronchitis in primary care: blinded, randomized controlled trial of patient information leaflet. BMJ. 2002 Jan 12;324(7329):91-4.

Mainous AG 3rd, Zoorob RJ, Hueston WJ. Current management of acute bronchitis in ambulatory care: The use of antibiotics and bronchodilators. Arch Fam Med. 1996 Feb;5(2):79-83.

Metlay JP, Kapoor WN, Fine MJ. Does this patient have community-acquired pneumonia? Diagnosing pneumonia by history and physical examination. JAMA. 1997 Nov 5;278(17):1440-5.

Pavesi L, Subburaj S, Porter-Shaw K. Application and validation of a computerized cough acquisition system for objective monitoring of acute cough: a meta-analysis. Chest. 2001 Oct;120(4):1121-8.

Petersen I, Johnson AM, Islam A, Duckworth G, Livermore DM, Hayward AC. Protective effect of antibiotics against serious complications of common respiratory tract infections: retrospective cohort study with the UK General Practice Research Database. BMJ. 2007 Nov 10;335(7627):982.

Roberts RM, Hicks LA, Bartoces M. Variation in US outpatient antibiotic prescribing quality measures according to health plan and geography. Am J ManagCare. 2016 Aug;22(8):519-23. PubMed PMID: 27541698.

Antibiotics:

Evans AT, Husain S, Durairaj L, Sadowski LS, Charles-Damte M, Wang Y. Azithromycin for acute bronchitis: a randomised, double-blind, controlled trial. Lancet. 2002 May 11;359(9318):1648-54.

Gonzales R, Bartlett JG, Besser RE, Cooper RJ, Hickner JM, Hoffman JR, Sande MA; Centers for Disease Control and Prevention. Principles of appropriate antibiotic use for treatment of uncomplicated acute bronchitis: background. Ann Emerg Med. 2001 Jun;37(6):720-7

King DE, Williams WC, Bishop L, Shechter A. Effectiveness of erythromycin in the treatment of acute bronchitis. J Fam Pract. 1996 Jun;42(6):601-5.

Little P, Stuart B, Moore M, Coenen S, et al; GRACE consortium. Amoxicillin for acute lower-respiratory-tract infection in primary care when pneumonia is not suspected: a 12-country, randomised, placebo-controlled trial. Lancet Infect Dis.2013 Feb;13(2):123-9.

Llor C, Moragas A, Bayona C, et al. Efficacy of anti-inflammatory or antibiotic treatment in patients with non-complicated acute bronchitis and discoloured sputum: randomised placebo controlled trial. BMJ. 2013 Oct 4;347:f5762.

Smith SM, Fahey T, Smucny J, et al. Antibiotics for acute bronchitis. Cochrane Database of Systematic Reviews 2014, Issue 3.

Smith SM, Fahey T, Smucny J, Becker LA. Antibiotics for acute bronchitis. Cochrane Database Syst Rev. 2017 Jun 19;6:CD000245.

Smucny JJ, Becker LA, Glazier RH, McIsaac W. Are antibiotics effective treatment for acute bronchitis? A meta-analysis. J Fam Pract. 1998 Dec;47(6):453-60.

Symptom Management:

Barker SJ. **Honey** for acute cough in children. Paediatr Child Health. 2016 May;21(4):199-200

Becker LA, Hom J, Villasis-Keever M, van der Wouden JC. **Beta2-agonists** for acute cough or a clinical diagnosis of acute bronchitis. Cochrane Database SystRev. 2015 Sep 3;(9):CD001726. doi: 10.1002/14651858.CD001726.pub5. Review. PubMed PMID: 26333656.

Guppy MP, Mickan SM, Del Mar CB. "Drink plenty of **fluids**": a systematic review of evidence for this recommendation in acute respiratory infections. BMJ. 2004 Feb 28;328(7438):499-500.

Holmes PW, Barter CE, Pierce RJ. Chronic persistent cough: use of **ipratropium** bromide in undiagnosed cases following upper respiratory tract infection. Respir Med. 1992 Sep;86(5):425-9

Hueston WJ. A comparison of **albuterol** and **erythromycin** for the treatment of acute bronchitis. J Fam Pract. 1991 Nov;33(5):476-80.

Hueston WJ. **Albuterol** delivered by metered-dose inhaler to treat acute bronchitis. J Fam Pract. 1994 Nov;39(5):437-40.

Melbye H, Aasebø U, Straume B. Symptomatic effect of inhaled **fenoterol** in acute bronchitis: a placebo-controlled double-blind study. Fam Pract. 1991 Sep;8(3):216-22.

Oduwole O, Meremikwu MM, Oyo-Ita A, Udoh EE. **Honey** for acute cough in children. Cochrane Database Syst Rev. 2014 Dec 23;(12):CD007094.

Saketkhoo K, Januszkiewicz A, Sackner MA. Effects of drinking **hot water, cold water, and chicken soup** on nasal mucus velocity and nasal airflow resistance. Chest. 1978 Oct;74(4):408-10.

Smith SM, Schroeder K, Fahey T. **Over-the-counter** (OTC) medications for acute cough in children and adults in community settings. Cochrane Database Syst Rev. 2014 Nov 24;(11):CD001831.

Zanasi A, Lecchi M, Del Forno M, Fabbri E, et al. A randomized, placebo-controlled, double-blind trial on the management of post-infective cough by inhaled **ipratropium** and **salbutamol** administered in combination. Pulm Pharmacol Ther. 2014 Dec;29(2):224-32.

References – Pharyngitis - RxFiles.ca

Guidelines:

2019 Sanfords

2018 NICE Sore throat (acute): antimicrobial prescribing (published January 2018). Available at: https://www.nice.org.uk/guidance/ng84

Aertgeerts B, Agoritsas T, Siemieniuk RAC, et al. Corticosteroids for sore throat: a clinical practice guideline. BMJ. 2017 Sep 20;358:j4090.

2012Bugs & Drugs

2013 Anti-infective Guidelines for Community-acquired Infections. Anti-infective Review Panel.

Shulman ST, Bisno AL, Clegg HW, et al. Clinical practice guideline for the diagnosis and management of group A streptococcal pharyngitis: 2012 update by the Infectious Diseases Society of America. Clin Infect Dis. 2012 Nov 15;55(10):1279-82.

General:

Centor RM. Expand the pharyngitis paradigm for adolescents and young adults. Ann Intern Med. 2009 Dec 1;151(11):812-5.

Cohen JF, Cohen R, Levy C, et al. Selective testing strategies for diagnosing group A streptococcal infection in children with pharyngitis: a systematic review and prospective multicentre external validation study. CMAJ. 2015 Jan 6;187(1):23-32.

Dooling KL, Shapiro DJ, Van Beneden C, et al. Overprescribing and inappropriate antibiotic selection for children with pharyngitis in the United States, 1997-2010. JAMA Pediatr. 2014 Nov;168(11):1073-4.

Ebell MH. Diagnosis of streptococcal pharyngitis. Am Fam Physician. 2014 Jun 15;89(12):976-7.

Fine AM, Nizet V, Mandl KD. Large-scale validation of the Centor and McIsaac scores to predict group A streptococcal pharyngitis. Arch Intern Med. 2012 Jun 11;172(11):847-52.

Kalra MG, Higgins KE, Perez ED. Common Questions About Streptococcal Pharyngitis. Am Fam Physician. 2016 Jul 1;94(1):24-31. Diagnosis of Streptococcal Pharyngitis MARK H. EBELL, MD, MS, University of Georgia, Athens, Georgia.

Kociolek LK, Shulman ST. In the clinic. Pharyngitis. Ann Intern Med. 2012 Sep 4;157(5):ITC3-1- ITC3-16.

Norton LE, Lee BR, Harte L, et al. Improving Guideline-Based Streptococcal Pharyngitis Testing: A Quality Improvement Initiative. Pediatrics. 2018 Jun 20.

Science M, Bitnun A, McIsaac W. Identifying and treating group A streptococcal pharyngitis in children. CMAJ. 2015 Jan 6;187(1):13-4.

Antibiotics:

Casey JR, Pichichero ME. Metaanalysis of short course antibiotic treatment for group a streptococcal tonsillopharyngitis. Pediatr Infect Dis J. 2005 Oct;24(10):909-17.

Casey JR, Pichichero ME. Higher dosages of azithromycin are more effective in treatment of group A streptococcal tonsillopharyngitis. Clin Infect Dis. 2005 Jun 15;40(12):1748-55.

Clegg HW, Ryan AG, Dallas SD, Kaplan EL, Johnson DR, Norton HJ, Roddey OF, Martin ES, Swetenburg RL, Koonce EW, Felkner MM, Giftos PM. Treatment of streptococcal pharyngitis with once-daily compared with twice-daily amoxicillin: a noninferiority trial. Pediatr Infect Dis J. 2006 Sep;25(9):761-7.

Feder HM Jr, Gerber MA, Randolph MF, Stelmach PS, Kaplan EL. Once-daily therapy for streptococcal pharyngitis with amoxicillin. Pediatrics. 1999 Jan;103(1):47-51.

Gerber MA, Randolph MF, Chanatry J, Wright LL, De Meo K, Kaplan EL. Five vs ten days of penicillin V therapy for streptococcal pharyngitis. Am J Dis Child. 1987 Feb;141(2):224-7
Lennon DR, Farrell E, Martin DR, Stewart JM. Once-daily amoxicillin versus twice-daily penicillin V in group A beta-haemolytic streptococcal pharyngitis. Arch Dis Child. 2008 Jun;93(6):474-8.
Logan LK, McAuley JB, Shulman ST. Macrolide treatment failure in streptococcal pharyngitis resulting in acute rheumatic fever. Pediatrics. 2012 Mar;129(3):e798-802. doi: 10.1542/peds.2011-1198. Epub 2012 Feb 6. Review. PubMed PMID: 22311996.
Kaplan EL, Gooch III WM, Notario GF, Craft JC. Macrolide therapy of group A streptococcal pharyngitis: 10 days of macrolide therapy (clarithromycin) is more effective in streptococcal eradication than 5 days (azithromycin). Clin Infect Dis. 2001 Jun 15;32(12):1798-802.
Shvartzman P, Tabenkin H, Rosentzwaig A, Dolginov F. Treatment of streptococcal pharyngitis with amoxycillin once a day. BMJ. 1993 May 1;306(6886):1170-2
van Driel ML, De Sutter AIM, Keber N, Habraken H, Christiaens T. Different antibiotic treatments for group A streptococcal pharyngitis. Cochrane Database of Systematic Reviews 2016, Issue 9. Art. No.: CD004406. DOI: 10.1002/14651858.CD004406.pub3.
Venuta A, Laudizi L, Beverelli A, Bettelli F, Milioli S, Garetti E. Azithromycin compared with clarithromycin for the treatment of streptococcal pharyngitis in children. J Int Med Res. 1998 Jun-Jul;26(3):152-8.

Rheumatic Fever:

Brusselen DV, Vleighe E, Schelstraete P et al. Streptococcal pharyngitis in children: to treat or not to treat? Eur J Pediatr 2014;173:1275–1283
Carapetis JR, Steer A, Mulholland E, et al. The global burden of group A streptococcal diseases. Lancet Infect Dis 2005;5:685-94.
Catanzaro FJ, Stetson CA, Morris AJ, Chamovitz R, et al. The role of the streptococcus in the pathogenesis of rheumatic fever. Am J Med. 1954 Dec;17(6):749-56. PubMed PMID: 13207156.
Denny FW, Wannamaker LW, Brink WR, Rammelkamp CH Jr, et al. Landmark article May 13, 1950: Prevention of rheumatic fever. Treatment of the preceding streptococci infection. By Floyd W. Denny, Lewis W. Wannamaker, William R. Brink, Charles H. Rammelkamp Jr. and Edward A. Custer. JAMA. 1985 Jul 26;254(4):534-7
Gagnall EM, Ho MG, McCormick IA. A 39-year-old man with recurrent rheumatic fever. CMAJ 2015;187:50-54.
Gerber MA, Baltimore RS, Eaton CB, Gewitz M,et al. Prevention of rheumatic fever and diagnosis and treatment of acute Streptococcal pharyngitis: a scientific statement from the American Heart Association Rheumatic Fever, Endocarditis, and Kawasaki Disease Committee of the Council on Cardiovascular Disease in the Young, the Interdisciplinary Council on Functional Genomics and Translational Biology, and the Interdisciplinary Council on Quality of Care and Outcomes Research: endorsed by the American Academy of Pediatrics. Circulation. 2009 Mar 24;119(11):1541-51.
Herath VCK, Carapetis J. Sore thorat: is it such a big deal anymore? Journal of Infection 2015;71: S101-S105.
Madden S, Kelly L. Update on acute rheumatic fever:It still exists in remote communities.Can Fam Physician 2009;55:475-8.
Robertson KA, Volmink JA, Mayosi BM. Antibiotics for the primary prevention of acute rheumatic fever: a meta-analysis. BMC Cardiovascular Disorders 2005;5:11.
Schams SC, Goldman RD. Steroids as adjuvant treatment of sore throat in acute bacterial pharyngitis. Can Fam Physician. 2012 Jan;58(1):52-4.
Science M, Bitnun A, McIsaac W. Identifying and treating group A streptococcal pharyngitis in children. CMAJ 2015;187:13-4.
Spinks A, Glasziou PP, Del Mar CB. Antibiotics for sore throat. Cochrane Database of Systematic Reviews 2013, Issue 11. Art. No.: CD000023.
Wannamaker LW, Rammelkamp CH Jr, Denny FW, Brink WR, et al. Prophylaxis of acute rheumatic fever by treatment of the preceding streptococcal infection with various amounts of depot penicillin. Am J Med. 1951 Jun;10(6):673-95
Webb RH. Acute rheumatic fever. BMJ 2015;351:h3443.
Wodu B, Bloomfiled GS. Rheumatic Heart Disease in the Twenty-First Century. Curr Cardiol Rep 2016;18:96.
van Driel ML, De Sutter AI, Habraken H, Thorning S, Christiaens T. Different antibiotic treatments for group A streptococcal pharyngitis. Cochrane Database Syst Rev. 2016 Sep 11;9:CD004406.

Symptom Management

Bertin L, Pons G, d'Athis P, Lasfargues G, et al. Randomized, double-blind, multicenter, controlled trial of ibuprofen versus acetaminophen (paracetamol) and placebo for treatment of symptoms of tonsillitis and pharyngitis in children. J Pediatr. 1991 Nov;119(5):811-4.
Chrubasik S, Beime B, Magora F. Efficacy of a benzocaine lozenge in the treatment of uncomplicated sore throat. Eur Arch Otorhinolaryngol. 2012 Feb;269(2):571-7.

Hayward GN, Hay AD, Moore MV, et al. Effect of Oral Dexamethasone Without Immediate Antibiotics vs Placebo on Acute Sore Throat in Adults: A Randomized Clinical Trial. JAMA. 2017 Apr 18;317(15):1535-1543.

Kagan G, Huddlestone L, Wolstencroft P. Two lozenges containing benzocaine assessed in the relief of sore throat. J Int Med Res. 1982;10(6):443-6.

Little P, Stuart B, Wingrove Z, et al. Probiotic capsules and xylitol chewing gum to manage symptoms of pharyngitis: a randomized controlled factorial trial. CMAJ. 2017 Dec 18;189(50):E1543-E1550.

McNally D, Simpson M, Morris C, Shephard A, Goulder M. Rapid relief of acute sore throat with AMC/DCBA throat lozenges: randomised controlled trial. Int J Clin Pract. 2010 Jan;64(2):194-207.

Pierce CA, Voss B. Efficacy and safety of ibuprofen and acetaminophen in children and adults: a meta-analysis and qualitative review. Ann Pharmacother. 2010 Mar;44(3):489-506.

Ruperto N, Carozzino L, Jamone R, Freschi F, et al. A randomized, double-blind, placebo-controlled trial of paracetamol and ketoprofren lysine salt for pain control in children with pharyngotonsillitis cared by family pediatricians. Ital J Pediatr. 2011 Sep 29;37:48.

Schachtel BP, Fillingim JM, Thoden WR, Lane AC, Baybutt RI. Sore throat pain in the evaluation of mild analgesics. Clin Pharmacol Ther. 1988 Dec;44(6):704-11. PubMed PMID: 3197368.

Weckx LL, Ruiz JE, Duperly J, Mendizabal GA, et al. Efficacy of celecoxib in treating symptoms of viral pharyngitis: a double-blind, randomized study of celecoxib versus diclofenac. J Int Med Res. 2002 Mar-Apr;30(2):185-94.

References – Sinusitis - RxFiles.ca

Guidelines:

Rosenfeld RM, Piccirillo JF, Chandrasekhar SS, Brook I, et al. **2015 AAO-HNS Clinical practice guideline** (update): adult sinusitis. Otolaryngol Head Neck Surg. 2015 Apr;152(2 Suppl):S1-S39. PubMed PMID: 25832968.

Rosenfeld RM. CLINICAL PRACTICE. Acute Sinusitis in Adults. N Engl J Med. 2016 Sep 8;375(10):962-70. doi: 10.1056/NEJMcp1601749. Review. PubMed PMID: 27602668.

Kaplan A. Canadian guidelines for acute bacterial rhinosinusitis: clinical summary. Can Fam Physician. 2014 Mar;60(3):227-34. Review. PubMed PMID: 24627376;

2013 Anti-infective Guidelines for Community-acquired Infections. Anti-infective Review Panel.

2012/2017 Bugs & Drugs

2019 Sanfords

Chow AW, Benninger MS, Brook I, Brozek JL, Goldstein EJ, Hicks LA, Pankey GA, Seleznick M, Volturo G, Wald ER, File TM Jr; Infectious Diseases Society of America**. IDSA clinical practice guideline** for acute bacterial rhinosinusitis in children and adults. Clin Infect Dis. 2012 Apr;54(8):e72-e112.

Desrosiers M, Evans GA, Keith PK, Wright ED, et al. **2011 Canadian clinical practice guidelines** for acute and chronic rhinosinusitis. J Otolaryngol Head Neck Surg. 2011 May;40 Suppl 2:S99-193. Review. English, French. PubMed PMID: 21658337.

Wald ER, Applegate KE, Bordley C, Darrow DH, Glode MP, Marcy SM, Nelson CE, Rosenfeld RM, Shaikh N, Smith MJ, Williams PV, Weinberg ST; **American Academy of Pediatrics. Clinical practice guideline** for the diagnosis and management of acute bacterial sinusitis in children aged 1 to 18 years. Pediatrics. 2013 Jul;132(1):e262-80. PubMed PMID: 23796742.

Antibiotics:

Adelglass J, Bundy JM, Woods R. Efficacy and tolerability of cefprozil versus amoxicillin/clavulanate for the treatment of adults with severe sinusitis. Clin Ther. 1998 Nov-Dec;20(6):1115-29.

Ahovuo-Saloranta A, Rautakorpi UM, Borisenko OV, et al. Antibiotics for acute maxillary sinusitis in adults. Cochrane Database of Systematic Reviews 2014, Issue 2. Art. No.: CD000243.

Brook I, Foote PA, Hausfeld JN. Eradication of pathogens from the nasopharynx after therapy of acute maxillary sinusitis with low- or high-dose amoxicillin/clavulanic acid. Int J Antimicrob Agents. 2005 Nov;26(5):416-9.

Del Mar C. Acute sinusitis and sore throat in primary care. Australian Prescriber. August 2016; 39(4).

Falagas ME, Karageorgopoulos DE, Grammatikos AP, Matthaiou DK. Effectiveness and safety of short vs. long duration of antibiotic therapy for acute bacterial sinusitis: a meta-analysis of randomized trials. Br J Clin Pharmacol. 2009 Feb;67(2):161-71.

Gwaltney JM Jr, Savolainen S, Rivas P, Schenk P, Scheld WM, Sydnor A, Keyserling C, Leigh A, Tack KJ. Comparative effectiveness and safety of cefdinir and amoxicillin-clavulanate in treatment of acute community-acquired bacterial sinusitis. Cefdinir Sinusitis Study Group. Antimicrob Agents Chemother. 1997 Jul;41(7):1517-20. PubMed PMID: 9210677

Gwaltney JM Jr, Scheld WM, Sande MA, Sydnor A. The microbial etiology and antimicrobial therapy of adults with acute community-acquired sinusitis: a fifteen-year experience at the University of Virginia and review of other selected studies. J Allergy Clin Immunol. 1992 Sep;90(3 Pt 2):457-61

Hadley JA. The Microbiology and Management of Acute and Chronic Rhinosinusitis. Curr Infect Dis Rep. 2001 Jun;3(3):209-216.

MacKenzie A. Balancing the benefits and risks of empirical antibiotics for sinusitis: a teachable moment. JAMA Intern Med. 2014 Aug;174(8):1221-2

Klapan I, Culig J, Oresković K, Matrapazovski M, Radosević S. Azithromycin versus amoxicillin/clavulanate in the treatment of acute sinusitis. Am J Otolaryngol. 1999 Jan-Feb;20(1):7-11.

Wald ER, Chiponis D, Ledesma-Medina J. Comparative effectiveness of amoxicillin and amoxicillin-clavulanate potassium in acute paranasal sinus infections in children: a double-blind, placebo-controlled trial. Pediatrics. 1986 Jun;77(6):795-800.

Worrall G. Acute sinusitis. Can Fam Physician. 2011 May;57(5):565-7

Symptom Management:

Chong LY, Head K, Hopkins C, Philpott C, et al. **Saline irrigation** for chronic rhinosinusitis. Cochrane Database Syst Rev. 2016 Apr 26;4:CD011995. doi: 10.1002/14651858.CD011995.pub2. Review. PubMed PMID: 27115216.

Little P, Stuart B, Mullee M, Thomas T, et al; **SNIFS Study** Team. Effectiveness of **steam inhalation and nasal irrigation** for chronic or recurrent sinus symptoms in primary care: a pragmatic randomized controlled trial. CMAJ. 2016 Sep 20;188(13):940-9. PubMed PMID: 27431306.

Shaikh N, Wald ER. **Decongestants, antihistamines and nasal irrigation** for acute sinusitis in children. Cochrane Database Syst Rev. 2014 Oct 27;(10):CD007909. doi: 10.1002/14651858.CD007909.pub4. Review. PubMed PMID: 25347280.

Venekamp RP, Thompson MJ, Rovers MM. **Systemic corcosteroid** therapy for acute sinusitis. JAMA. 2015 Mar 24-31;313(12):1258-9.

Zalmanovici Trestioreanu A, Yaphe J. **Intranasal steroids** for acute sinusitis. Cochrane Database Syst Rev. 2013 Dec 2;(12):CD005149.

RxFiles Skin & Soft Tissue Infections References:

GUIDELINES

Stevens DL, Bisno AL, Chambers HF, Dellinger EP, et al; Infectious Diseases Society of America (**IDSA**). Practice guidelines for the diagnosis and management of skin and soft tissue infections: 2014 update by the Infectious Diseases Society of America. Clin Infect Dis. 2014 Jul 15;59(2):e10-52.

Liu C, Bayer A, Cosgrove SE, Daum RS, et al; Infectious Diseases Society of America (**IDSA**). Clinical practice guidelines by the infectious diseases society of america for the treatment of methicillin resistant Staphylococcus aureus infections in adults and children. Clin Infect Dis. 2011 Feb1;52(3):e18-55.

Golan Y. Current Treatment Options for Acute Skin and Skin-structure Infections (**IDSA**). Clin Infect Dis. 2019 Apr 8;68(Supplement_3):S206-S212. doi:10.1093/cid/ciz004.

Bugs and Drugs – App Accessed 2016

Anti-infective Review Panel. **Anti-infective Guidelines for Community Acquired Infections**. Toronto: MUMS Guideline Clearinghouse; 2013.

Sanford Guide Committee. The **Sanford** Guide to Antimicrobial Therapy, 47th Edition. Antimicrobial Therapy, INC; 2017.

Sartelli M, Guirao X, Hardcastle TC, et al. 2018 **WSES/SIS-E** consensus conference: recommendations for the management of skin and soft-tissue infections. World J Emerg Surg. 2018 Dec 14;13:58.

SASKATCHEWAN DOCUMENTS

Saskatoon Health Region 2015 Antibiogram. Available at: https://www.saskatoonhealthregion.ca/locations_services/Services/antimicrobial-stewardship/Pages/Resouces.aspx. Accessed April 4th, 2017.

Regina Qu'Appelle Health Region Antibiogram. Available at: http://www.rqhealth.ca/rqhr-service-lines-files/rqhr-antibiogram-2015. Accessed April 4th, 2017.

Irvine J, Cholin B, Kryzanowski J, Laubscher T, Shevchuk Y. 2014 Northern Saskatchewan Guidelines for Skin & Soft Tissue Infections including suspected MRSA in the Community Setting. December 2013.

MRSA

Cadena J, Nair S, Henao-Martinez A, Jorgensen J, et al. Dose of trimethoprim-sulfamethoxazole to treat skin and skin structure infections caused by methicillin-resistant Staphylococcus aureus. Antimicrob Agents Chemother. 2011;55(12):5430-5432

Center for Disease Control (**CDC**). MRSA. Available at: https://www.cdc.gov/mrsa/. Accessed April 4th, 2017.

Daum RS. Clinical practice. Skin and soft-tissue infections caused by methicillin-resistant Staphylococcus aureus [published correction appears in N Engl J Med. 2007;357(13):1357]. N Engl J Med. 2007;357(4):380–390.

Fridkin SK, Hageman JC, Morrison M, et al Methicillin-resistant Staphylococcus aureus disease in three communities. N Engl J Med 2005;352: 1436-44.

Gilani SJ, Gonzalez M, Hussain I, Finlay AY, Patel GK. Staphylococcus aureus re-colonization in atopic dermatitis: beyond the skin. Clin Exp Dermatol. 2005 Jan; 30(1):10-3.

King MD, Humphrey BJ, Wang YF, Kourbatova EV, Ray SM, Blumberg HM Emergence of community-acquired methicillin-resistant Staphylococcus aureus USA 300 clone as the predominant cause of skin and soft-tissue infections. Ann Intern Med 2006;144:309-17.

Liu C, Bayer A, Cosgrove SE, Daum RS, et al; Infectious Diseases Society of America (IDSA). Clinical practice guidelines by the infectious diseases society of america for the treatment of methicillin resistant Staphylococcus aureus infections in adults and children. Clin Infect Dis. 2011 Feb1;52(3):e18-55.

Miller LG, Perdreau-Remington F, Bayer AS, et al. Clinical and epidemiologic characteristics cannot distinguish community-associated methicillin-resistant Staphylococcus aureus infection from methicillin-susceptible S. aureus infection: a prospective investigation. Clin Infect Dis. 2007;44(4):471–482.

Moran GJ, Krishnadasan A, Gorwitz RJ, Fosheim GE et al; EMERGEncy ID Net Study Group. Methicillin-resistant S. aureus infections among patients in the emergency department. N Engl J Med 2006;355: 666-74.

Singer AJ, Talan DA. Management of skin abscesses in the era of methicillin-resistant Staphylococcus aureus. N Engl J Med. 2014 Mar 13; 370(11):1039-47.

IMPETIGO

Hartman-Adams H, Banvard C, Juckett G. Impetigo: diagnosis and treatment. Am Fam Physician. 2014 Aug 15;90(4):229-35.

Koning S, van der Sande R, Verhagen AP, van Suijlekom-Smit LW, Morris AD, Butler CC, Berger M, van der Wouden JC. Interventions for impetigo. **Cochrane** Database Syst Rev. 2012 Jan 18;1:CD003261.

ABSCESS

Halilovic J, Heintz B, Brown J. Risk factors for clinical failure in patients hospitalized with cellulitis and cutaneous abscess. J Infect. 2012;65(2):128-134.
Talan DA, Mower WR, Krishnadasan A, Abrahamian FM, Lovecchio F, Karras DJ,Steele MT, Rothman RE, Hoagland R, Moran GJ. Trimethoprim-Sulfamethoxazole versus Placebo for Uncomplicated Skin Abscess. N Engl J Med. 2016 Mar 3;374(9):823-32.
Wang W, Chen W, Liu Y, et al. Antibiotics for uncomplicated skin abscesses: systematic review and network meta-analysis. BMJ Open. 2018;8(2):e020991. doi:10.1136/bmjopen-2017-020991.

CELLULITIS

Bowen AC, Liliebridge RA, Tong SY, et al. Is streptococcu pyogenes resistant or susceptible to trimthoprim-sulfamethoxazole? J Clin icrobiol 2012; 50:4067-72
Halilovic J, Heintz B, Brown J. Risk factors for clinical failure in patients hospitalized with cellulitis and cutaneous abscess. J Infect. 2012;65(2):128-134.
Hepburn MJ, Dooley DP, Skidmore PJ, Ellis MW, Starnes WF, Hasewinkle WC. Comparison of short-course (5 days) and standard (10 days) treatment for uncomplicated cellulitis. Arch Intern Med. 2004 Aug 9-23;164(15):1669-74.
Miller LG, Daum RS, Creech CB, Young D, Downing MD, Eells SJ, Pettibone S,Hoagland RJ, Chambers HF; DMID 07-0051 Team. Clindamycin versus trimethoprim-sulfamethoxazole for uncomplicated skin infections. N Engl J Med. 2015 Mar 19;372(12):1093-103.
Pallin DJ, Binder WD, Allen MB, Lederman M, et al. Clinical trial: comparative effectivenss of cephalexin plus trimethoprim-sulfamethoxazole versus cephalexin alone for treatment of uncomplicated cellulitis: a randomized controlled trial. Clin Infect Dis. 2013 Jun;56(12):1754-62.
Weng QY, Raff AB, Cohen JM, Gunasekera N, et al. Costs and Consequences Associated With Misdiagnosed Lower Extremity Cellulitis. JAMA Dermatol. 2016 Nov 2.
Dall L, Peterson S, Simmons T, Dall A. Rapid resolution of cellulitis in patients managed with combination antibiotic and anti-inflammatory therapy.Cutis. 2005 Mar;75(3):177-80.

SKIN INFECTIONS – GENERAL

Chen AE, Carroll KC, Diener-West M, Ross T, Ordun J, Goldstein MA, Kulkarni G,Cantey JB, Siberry GK. Randomized controlled trial of cephalexin versus clindamycin for uncomplicated pediatric skin infections. Pediatrics. 2011Mar;127(3):e573-80. doi: 10.1542/peds.2010-2053.
Esposito S, Bassetti M, Bonnet E, Bouza E, Chan M, et al. Hot topics in the diagnosis and management of skin and soft tissue infections. Int J Antimicrob Agents. 2016 Jul;48(1):19-26.
Hurley HJ, Knepper BC, Price CS, Mehler PS, et al. Avoidable antibiotic exposure for uncomplicated skin and soft tissue infections in the ambulatory care setting. Am J Med. 2013 Dec;126(12):1099-106.
Miller LG. Physician antibiotic prescriptions for skin infections in the outpatient setting are often unnecessarily long and include unnecessary antibiotics. Evid Based Med. 2014 Aug;19(4):160.
Ramakrishnan K, Salinas RC, Agudelo Higuita NI. Skin and Soft Tissue Infections. Am Fam Physician. 2015 Sep 15;92(6):474-83.
Shi C, Xiao Y, Zhang Q, et al. Efficacy and safety of cefazolin versus antistaphylococcal penicillins for the treatment of methicillin-susceptible Staphylococcus aureus bacteremia: a systematic review and meta-analysis. BMC Infect Dis. 2018 Oct 11;18(1):508.

Aabenhus R, Jensen JUS, Jørgensen KJ, Hróbjartsson A, Bjerrum L. **Biomarkers as point-of-care** tests to guide prescription of antibiotics in patients with acute respiratory infections in primary care. Cochrane Database of Systematic Reviews 2014, Issue 11. Art. No.: CD010130. DOI: 10.1002/14651858.CD010130.pub2. A point-of-care biomarker (e.g. C-reactive protein) to guide antibiotic treatment of ARIs in primary care can reduce antibiotic use, although the degree of reduction remains uncertain. Used as an adjunct to a doctor's clinical examination this reduction in antibiotic use did not affect patient-reported outcomes, including recovery fromand duration of illness.However, a possible increase in hospitalizations is of concern. A more precise effect estimate is needed to assess the costs of the intervention and compare the use of a point-of-care biomarker to other antibiotic-saving strategies.

Abrams EM, Khan DA. Diagnosing and managing **drug allergy**. CMAJ. 2018 Apr 30;190(17):E532-E538.

Achten NB, Klingenberg C, Benitz WE, et al. Association of Use of the **Neonatal Early-Onset Sepsis Calculator** With Reduction in Antibiotic Therapy and Safety: A Systematic Review and Meta-analysis. JAMA Pediatr. 2019 Sep 3.

Achiam CC, Fernandes CM, McLeod SL, et al. **Methicillin-resistant Staphylococcus aureus in skin** and soft tissue infections presenting to the Emergency Department of a Canadian Academic Health Care Center. Eur J Emerg Med. 2010 Feb 17.

Acree M, Davis AM. **Acute Diarrheal Infections** in Adults. JAMA. 2017 Sep 12;318(10):957-958.

Adams DJ, Eberly MD, Rajnik M, et al. Risk Factors for Community-Associated **Clostridium difficile Infection** in Children. J Pediatr. 2017 Apr 7.

Adefurin A, Sammons H, Jacqz-Aigrain E, Choonara I. **Ciprofloxacin safety in paediatrics**: a systematic review. Arch Dis Child. 2011 Sep;96(9):874-80.

Aertgeerts B, Agoritsas T, Siemieniuk RAC, et al. **Corticosteroids for sore throat**: a clinical practice guideline. BMJ 2017;358:j4090

Ahluwalia T, Jain S, Norton L, et al. **Reducing Streptococcal Testing in Patients <3 Years Old** in an Emergency Department. Pediatrics. 2019 Sep 11.

Ahovuo-Saloranta A, Borisenko OV, Kovanen N, et al. Antibiotics for acute maxillary **sinusitis**. Cochrane Database Syst Rev. 2008 Apr 16;(2):CD000243. Antibiotics have a small treatment effect in patients with uncomplicated acute sinusitis in a primary care setting with symptoms for more than seven days. However, 80% of participants treated without antibiotics improve within two weeks. Clinicians need to weigh the small benefits of antibiotic treatment against the potential for adverse effects at both the individual and general population level.

Ahovuo-Saloranta A, Rautakorpi UM, Borisenko OV, et al. Antibiotics for acute maxillary **sinusitis** in adults. Cochrane Database Syst Rev. 2014 Feb 11;2:CD000243. There is moderate evidence that antibiotics provide a small benefit for clinical outcomes in immunocompetent primary care patients with uncomplicated acute sinusitis. However, about 80% of participants treated without antibiotics improved within two weeks. Clinicians need to weigh the small benefits of antibiotic treatment against the potential for adverse effects at both the individual and general population levels.

Ah-See KL, Mackenzie J, Practitioner G, Ah-See KW. Management of **chronic rhinosinusitis**. BMJ. 2012 Oct 30;345:e7054.

Aring AM, Chan MM. Current Concepts in Adult Acute **Rhinosinusitis**. Am Fam Physician. 2016 Jul 15;94(2):97-105.

Albert RH. Diagnosis and treatment of **acute bronchitis**. Am Fam Physician. 2010 Dec 1;82(11):1345-50.

Albert RK, Connett J, Bailey WC, et al. **Azithromycin** (up to 1yr) for prevention of exacerbations of COPD. N Engl J Med 2011;365: 689-98.

Albrich WC, Dusemund F, Bucher B, et al. Effectiveness and Safety of **Procalcitonin-Guided Antibiotic Therapy in Lower Respiratory Tract Infections** in "Real Life": An International, Multicenter Poststudy Survey (ProREAL). Arch Intern Med. 2012 May 14;172(9):715-22.

Aliberti S, Reyes LF, Faverio P, Sotgiu et al. **Global initiative for meticillin-resistant Staphylococcus aureus pneumonia** (GLIMP): an international, observational cohort study. Lancet Infect Dis. 2016 Sep 1.

Allegranzi B, Zayed B, Bischoff P, et al; **WHO Guidelines** Development Group.. New WHO recommendations on **intraoperative and postoperative** measures for **surgical site infection prevention**: an evidence-based global perspective. Lancet Infect Dis. 2016 Nov 1.

Allegranzi B, Bischoff P, de Jonge S, et al; **WHO Guidelines** Development Group.. New WHO recommendations on **preoperative measures for surgical site infection prevention**: an evidence-based global perspective. Lancet Infect Dis. 2016 Nov 1.

Allen SJ, Martinez EG, Gregorio GV, Dans LF. **Probiotics for treating acute infectious diarrhoea**. Cochrane Database of Systematic Reviews 2010, Issue 11. Art. No.: CD003048. DOI: 10.1002/14651858.CD003048.pub3. Used alongside rehydration therapy, probiotics appear to be safe and have clear beneficial effects in shortening the duration and reducing stool frequency in acute infectious diarrhoea. However, more research is needed to guide the use of particular probiotic regimens in specific patient groups.

Allen SJ, Wareham K, et al. **Lactobacilli and bifidobacteria in the prevention of antibiotic-associated diarrhoea and Clostridium difficile diarrhoea** in older inpatients (PLACIDE): a randomised, double-blind, placebo-controlled, multicentre trial. Lancet 2013; online Aug 8. (NS)

Allen VG, Mitterni L, Seah C, et al. Neisseria gonorrhoeae treatment failure and susceptibility to cefixime in Toronto, Canada. JAMA. 2013;309(2):163-170.

Alrwisan A, Antonelli PJ, Winterstein AG. **Quinolone Ear Drops After Tympanostomy Tubes** and the Risk of Eardrum Perforation: A Retrospective Cohort Study. Clin Infect Dis. 2017 Feb 27.

Andreoni F, Zürcher C, Tarnutzer A, et al. **Clindamycin Affects Group A Streptococcus Virulence Factors** and Improves Clinical Outcome. J Infect Dis. 2017 Jan 15;215(2):269-277.

Altamimi S, Khalil A, Khalaiwi KA, et al. Short versus standard duration antibiotic therapy for **acute streptococcal pharyngitis in children**. Cochrane Database Syst Rev. 2009 Jan 21;(1):CD004872. Three to six days of oral antibiotics had comparable efficacy compared to the standard duration 10 day oral penicillin in treating children with acute GABHS pharyngitis. In countries with low rates of rheumatic fever, it appears safe and efficacious to treat children with acute GABHS pharyngitis with short duration antibiotics. In areas where the prevalence of rheumatic heart disease is still high, our results must be interpreted with caution.

Altamimi S, Khalil A, Khalaiwi KA, et al. Short-term late-generation antibiotics versus longer term penicillin for **acute streptococcal pharyngitis** in children. Cochrane Database Syst Rev. 2012 Aug 15;8:CD004872. Three to six days of oral antibiotics had comparable efficacy compared to the standard duration 10-day course of oral penicillin in treating children with acute GABHS pharyngitis.

Altenburg J, de Graaff CS, Stienstra Y, et al. Effect of **azithromycin maintenance treatment on infectious exacerbations** among patients with non–cystic fibrosis bronchiectasis: the BAT randomized controlled trial. JAMA. 2013;309(12):1251-1259.

American Academy of Pediatric Dentistry Clinical Affairs Committee, American Academy of Pediatric Dentistry Council on Clinical Affairs. Guideline on antibiotic **prophylaxis for dental patients** at risk for infection. Pediatr Dent 2008-2009;30(7 Suppl):215-8. http://www.aapd.org/media/Policies_Guidelines/G_AntibioticProphylaxis.pdf

American Academy of Pediatrics (AAP) Committee on Infectious Diseases. The Use of **Systemic and Topical Fluoroquinolones**. Pediatrics. 2011 Oct;128(4):e1034-e1045.

Amaya-Guio J, Viveros-Carreno DA, Sierra-Barrios EM, et al. **Antibiotic treatment for the sexual partners of women with bacterial vaginosis**. Cochrane Database Syst Rev. 2016 Oct 1;10:CD011701. High quality evidence shows that antibiotic treatment for sexual partners of women with BV, compared with placebo, does not increase the rate of clinical or symptomatic improvement during the first, between the first and fourth or after the fourth week into the women. Low quality evidence suggests that antibiotic treatment does not led to a lower recurrence rate during the first and fourth or after the fourth week of treatment into the women, but increases the frequency of adverse events reported by sexual partners. Finally, compared with no intervention, antibiotic treatment does not decrease the recurrence rate after the fourth week and does not increase the frequency of clinical or symptomatic improvement between the first and fourth or after the fourth week into the women, respectively.

Anderson DJ, Chen LF, Weber DJ, et al; for the CDC Prevention Epicenters Program. Enhanced **terminal room disinfection** and acquisition and infection caused by multidrug-resistant organisms and Clostridium difficile (the Benefi ts of Enhanced Terminal Room Disinfection study-**BETR**): a clusterrandomised, multicentre, crossover study. Lancet 2017; online Jan 16.

Anderson DJ, Watson S, Moehring RW; (ARLG). Feasibility of **Core Antimicrobial Stewardship Interventions** in Community Hospitals. JAMA Netw Open. 2019 Aug 2;2(8):e199369.

Anti-infective Review Panel. **Anti-infective Guidelines for Community-acquired Infections**. Canadian - New-**2013**. Toronto: MUMS Guideline Clearinghouse. http://www.mumshealth.com/

Anthonisen NR, Manfreda J, Warren CP, et al. Antibiotic therapy in **exacerbation** of chronic obstructive pulmonary disease. Ann Intern Med 1987;106(2):196-204.

Antoniou T, Gomes T, Mamdani MM, et al. **Trimethoprim-sulfamethoxazole induced hyperkalaemia** in elderly patients receiving **spironolactone**: nested case-control study. BMJ. 2011 Sep 12;343:d5228.

Antoniou T, Hollands S, Macdonald EM, et al; for the Canadian Drug Safety and Effectiveness Research Network. **Trimethoprim-sulfamethoxazole** and risk of sudden **death** among patients taking **spironolactone**. CMAJ. 2015 Feb 2.

Arcilla MS, van Hattem JM, Haverkate MR, et al. Import and **spread of extended-spectrum β-lactamase-producing Enterobacteriaceae** by **international travellers** (**COMBAT** study): a prospective, multicentre cohort study. Lancet Infect Dis. 2016 Oct 14.

Årdal C, Outterson K, Hoff man SJ, et al. **International cooperation to improve access** to and sustain eff ectiveness of antimicrobials. Lancet 2015; online Nov 18.

Arias CA, Panesso D, McGrath DM, et al. Genetic basis for in vivo **daptomycin resistance** in enterococci. N Engl J Med. 2011 Sep 8;365(10):892-900.

Arias CA, Murray BE. A new antibiotic (**teixobactin**) and the evolution of resistance. N Engl J Med. 2015 Mar 19;372(12):1168-70.

Aring AM, Chan MM. **Acute rhinosinusitis in adults**. Am Fam Physician. 2011 May 1;83(9):1057-63.

Arshad J, Sayegh R. **Scleral Discoloration from Minocycline** Treatment. N Engl J Med. 2018 Apr 19;378(16):1537.

Asbell PA, Sanfilippo CM, Pillar CM, et al. **Antibiotic Resistance Among Ocular Pathogens** in the United States: Five-Year Results From the Antibiotic Resistance Monitoring in Ocular Microorganisms (ARMOR) Surveillance Study. JAMA Ophthalmol. 2015 Oct 22:1-10.

Ashiru-Oredope D, Sharland M, et al; ARHAI Antimicrobial Stewardship Group. Improving the quality of antibiotic prescribing in the **NHS by developing a new Antimicrobial Stewardship Programme**: Start Smart—Then Focus. J Antimicrob Chemother. 2012 Jul;67 Suppl 1:i51-63

Atkins KE, Lafferty EI, Deeny SR, et al. Use of mathematical modelling to assess the **impact of vaccines on antibiotic resistance**. Lancet Infect Dis. 2017 Nov 13.

Azari AA, Barney NP. **Conjunctivitis**: a systematic review of diagnosis and treatment. JAMA. 2013 Oct 23;310(16):1721-9.

Azarian T, Daum RS, Petty LA, et al. Intra-host evolution of methicillin-resistant Staphylococcus aureus USA300 among individuals with reoccurring skin and soft tissue infections. J Infect Dis. 2016 Jun 10.

Babich T, Naucler P, Valik JK, et al. **Ceftazidime, carbapenems, or piperacillin-tazobactam** as single definitive therapy for Pseudomonas aeruginosa bloodstream infection – a multi-site retrospective study. Clin Infect Dis. 2019 Jul 17.

Backes M, et al. Effect of **Antibiotic Prophylaxis on Surgical Site Infections Following Removal of Orthopedic Implants** Used for Treatment of Foot, Ankle, and Lower Leg Fractures: A Randomized Clinical Trial. JAMA. 2017 Dec 26;318(24):2438-2445

Bader MS, McKinsey DS. **Postexposure Prophylaxis** for Common Infectious Diseases. Am Fam Physician. 2013;88(1):25-32.

Bafeta A, Yavchitz A, Riveros C, Batista R, Ravaud P. Methods and reporting studies **assessing fecal microbiota transplantation**. A systematic review. Ann Intern Med. 2017. [Epub ahead of print]. doi:10 .7326/M16-2810

Bagdasarian N, Rao K, Malani PN. **Diagnosis and treatment of Clostridium difficile in adults**: a systematic review. JAMA. 2015 Jan 27;313(4):398-408.

Baggs J, Fridkin SK, et al. Estimating **National Trends in Inpatient Antibiotic Use Among US Hospitals** From 2006 to 2012. JAMA Intern Med. 2016 Sep 19.

Bai AD, Morris AM. **Management of Staphylococcus** aureus bacteremia in adults. CMAJ. 2019 Sep 3;191(35):E967.

Baker KS, Dallman TJ, Ashton PM, et al. Intercontinental dissemination of **azithromycin-resistant shigellosis through sexual transmission**: a crosssectional study. Lancet Infect Dis 2015; online April 28.

Balkus JE, Manhart LE, Lee J, et al. **Periodic Presumptive Treatment for Vaginal Infections** May Reduce the Incidence of Sexually Transmitted Bacterial Infections. J Infect Dis. 2016 Feb 4.

Balter M, La Forge J, Low D, Mandell L, Grossman R. Canadian guidelines for the management of acute **exacerbations of chronic bronchitis**. Can Respir J 2003;10(Suppl B):3B-32B.

Banach DB, Bearman G, Barnden M, et al. Duration of **Contact Precautions for Acute-Care Settings**. Infect Control Hosp Epidemiol. 2018 Jan 11:1-18.

Bar-Zeev N, Moss WJ. Hope and Humility for **Azithromycin**. N Engl J Med. 2019 Jun 6;380(23):2264-2265.

Barbieri JS, Bhate K, Hartnett KP, Fleming-Dutra KE, Margolis DJ. Trends in **oral antibiotic prescription in dermatology**, 2008 to 2016 [online Jan 16, 2019]. JAMA Dermatol. doi:10.1001/jamadermatol.2018.4944

Barbieri JS, Etzkorn JR, Margolis DJ. Use of **Antibiotics for Dermatologic Procedures** From 2008 to 2016. JAMA Dermatol. 2019 Mar 2.

Barnett ML, Linder JA. **Antibiotic Prescribing to Adults With Sore Throat** in the United States, 1997-2010. JAMA Intern Med. 2013 Oct 3.

Barnett ML, Linder JA. **Antibiotic prescribing for adults with acute bronchitis** in the United States, 1996-2010. JAMA. 2014 May 21;311(19):2020-2.

Barlam TF, Cosgrove SE, Abbo LM, et al. Executive Summary: I**mplementing an Antibiotic Stewardship Program**: Guidelines by the **Infectious Diseases Society of America (IDSA)** and the Society for Healthcare Epidemiology of America. Clin Infect Dis. 2016 May 15;62(10):1197-202.

Barlam TF, Cosgrove SE, Abbo LM, et al. Implementing an **antibiotic stewardship program**: guidelines by the Infectious Diseases Society of America (**IDSA**) and Society for Healthcare Epidemiology of America. Clin Iinfect Dis. 2016;62:e51-e77.
Barrett J, Brown M. **Travellers' diarrhoea**. BMJ. 2016 Apr 19;353:i1937.
Bates JE, Almast J, Augustine EF. Neonatal dentate nucleus **T2 hyperintensity after in utero metronidazole** exposure. Neurology. 2015 Sep 15;85(11):1006.
Baur D, Gladstone BP, Burkert F, et al. Effect of **antibiotic stewardship** on the incidence of infection and colonisation with **antibiotic-resistant bacteria and Clostridium difficile infection**: a systematic review and meta-analysis. Lancet Infect Dis 2017; online June 16.
Bayer AS, Xiong YQ. **Redeploying β-Lactams Against Staphylococcus aureus**: Repurposing With a Purpose. J Infect Dis. 2017 Jan 1;215(1):11-13.
Beaton A, Aliku T, Dewyer A, et al. **Latent rheumatic heart disease**: identifying the children at highest risk of unfavorable outcome. Circulation.2017;136:2233–2244.
Beaudoin AL, Torso L, Richards K, et al. **Invasive group A Streptococcus** infections associated with **liposuction surgery** at outpatient facilities not subject to state or federal regulation [onlineMay 26, 2014]. JAMA Intern Med. doi:10.1001/jamainternmed.2014.1875.
Beck AF, Florin TA, Campanella S, Shah SS. **Geographic Variation in Hospitalization** for **Lower Respiratory Tract Infections** Across One County. JAMA Pediatr. 2015 Jul 20.
Beinortas T, Burr NE, Wilcox MH, Subramanian V. **Comparative efficacy of treatments for Clostridium difficile infection:** a systematic review and network meta-analysis. Lancet Infect Dis. 2018 Jul 16. pii: S1473-3099(18)30285-8.
Belshe RB et al. Efficacy results of a trial of a **herpes simplex vaccine**. N Engl J Med 2012 Jan 5; 366:34
Bérard A, Sheehy O, Zhao JP, et al. Use of **macrolides during pregnancy** and the risk of birth defects: a population-based study. Pharmacoepidemiol Drug Saf. 2015 Oct 29.
Berende A, Ter Hofstede HJM, Vos FJ, et al. Effect of prolonged antibiotic treatment on **cognition in patients with Lyme borreliosis**. Neurology. 2019 Mar 26;92(13):e1447-e1455
Berende A, ter Hofstede HJM, Vos FJ, et al. Randomized trial of longer-term therapy for symptoms attributed to **Lyme disease**. (**PLEASE**) N Engl J Med 2016; 374:1209-20.
Bergmark RW, Pynnonen M. Diagnosis and First-Line **Treatment of Chronic Sinusitis**. JAMA. 2017 Dec 19;318(23):2344-2345
Bergroth E, Remes S, Pekkanen J, et al. Respiratory Tract Illnesses During the First Year of Life: Effect of **Dog and Cat Contacts**. Pediatrics. 2012 Jul 9.
Berkman ND, Wallace IF, Steiner MJ, et al. **Otitis Media With Effusion**: Comparative Effectiveness of Treatments. AHRQ Comparative Effectiveness Review. Rockville (MD): Agency for Healthcare Research and Quality (US); 2013 May. Report No.: 13-EHC091-EF There is evidence that both TT and adenoid reduce OME and improve hearing in the short term, but both treatments also have associated harms.
Bernaola Aponte G, Bada Mancilla CA, Carreazo Pariasca NY, Rojas Galarza RA. **Probiotics for treating persistent diarrhoea** in children. Cochrane Database of Systematic Reviews 2010, Issue 11. Art. No.: CD007401. DOI: 10.1002/14651858.CD007401.pub2. There is limited evidence suggesting probiotics may be effective in treating persistent diarrhoea in children.
Beyerlein A, Donnachie E, Jergens S, et al. **Infections in Early Life** and Development of **Type 1 Diabetes**. JAMA. 2016 May 3;315(17):1899-901.
Bezáková N et al. Recurrence up to 3.5 years after antibiotic treatment of acute **otitis media** in very young Dutch children: Survey of trial participants. BMJ 2009 Jun 30; 338:b2525. BMJ. 2007 Nov 10;335(7627):991.
Bhargava A, Ralph R, Chatterjee B, Bottieau E. Assessment and initial management of **acute undifferentiated fever in tropical and subtropical regions**. BMJ. 2018 Nov 29;363:k4766.
Bhattacharyya S, Darby RR, Raibagkar P, et al. **Antibiotic-associated encephalopathy**. Neurology. 2016 Feb 17.
Biedenbach DJ, Bouchillon SK, Johnson SA, et al. Susceptibility of **Staphylococcus aureus to Topical Agents** in the United States: A Sentinel Study. Clin Ther. 2014 May 14.
Bielicki JA, Barker CI, Saxena S, et al. Not too little, not too much: problems of selecting oral **antibiotic dose for children**. BMJ. 2015 Nov 3;351:h5447.
Bihan K, Weiss N, Théophile H, et al. **drug-induced aseptic meningitis**: 329 cases from the French Pharmacovigilance Database Analysis. Br J Clin Pharmacol. 2019 Jul 18.
Billick M, Gold WL. Group B **streptococcal endocarditis following elective surgical abortion**. CMAJ. 2019 Aug 19;191(33):E916-E918.
Biondi EA, Lee B, Ralston SL, et al. Prevalence of **Bacteremia and Bacterial Meningitis in Febrile Neonates and Infants** in the Second Month of Life: A Systematic Review and Meta-analysis. JAMA Netw Open. 2019 Mar 1;2(3):e190874.
Bird ST, Etminan M, Brophy JM, et al. Risk of **acute kidney injury** associated with the use of **fluoroquinolones**. CMAJ. 2013 Jun 3.
Bird J, Biggs T, Thomas M, Salib R. **Adult acute rhinosinusitis**. BMJ. 2013 May 10;346:f2687.
Blumenthal KG, Lu N, Zhang Y, et al. Risk of **methicillin resistant Staphylococcus aureus and Clostridium difficile in patients with a documented penicillin allergy**: population based matched cohort study. BMJ. 2018 Jun 27;361:k2400.
Blumenthal KG, Peter JG, Trubiano JA, Phillips EJ**. Antibiotic allergy**. Lancet. 2018 Dec 14.
Blumenthal KG, Ryan EE, Li Y, et al. The Impact of a **Reported Penicillin Allergy on Surgical Site Infection Risk**. Clin Infect Dis. 2018 Jan 18;66(3):329-336.
Blumenthal KG, Shenoy ES. **Am I Allergic to Penicillin**? JAMA. 2019 Jan 15;321(2):216.
Bomers MK, van Doorn-Schepens MLM, van der Valk P, Peters EJG. **Poststreptococcal Myalgia and Myositis.** Ann Intern Med. 2019 Jan 22.
Bonomo RA, Burd EM, Conly J, et al. **Carbapenemase-Producing Organisms**: A Global Scourge! Clin Infect Dis. 2017 Oct 16.
Boucher HW et al. Once-weekly **dalbavancin** versus daily conventional therapy for skin infection. N Engl J Med 2014 Jun 5; 370:2169.
Boucher HW, Bakken JS, Murray BE. The **United Nations** and the Urgent Need for Coordinated Global Action in the Fight Against **Antimicrobial Resistance**. Ann Intern Med. 2016 Sep 20.
Bowen AC, Tong SY, Andrews RM, et al. Short-course oral co-**trimoxazole versus intramuscular benzathine benzylpenicillin** for **impetigo** in a highly endemic region: an open-label, randomised, controlled, non-inferiority trial. Lancet. 2014 Aug 26.
Bowen A, Eikmeier D, Talley P, et al; Centers for Disease Control and Prevention (CDC). Notes from the Field: Outbreaks of **Shigella** sonnei Infection with **Decreased Susceptibility to Azithromycin** Among Men Who Have Sex with Men -Chicago and Metropolitan Minneapolis-St. Paul, 2014. MMWR Morb Mortal Wkly Rep.2015 Jun 5;64(21):597-8.
Bradley JS, Kauffman RE, Balis DA, et al. Assessment of **Musculoskeletal Toxicity 5 Years After Therapy With Levofloxacin**. Pediatrics. 2014 Jun 2.
Bradley J, Glasser C, Patino H, et al. **Daptomycin for Complicated Skin Infections**: A Randomized Trial. Pediatrics. 2017 Feb 15.
Bradshaw CS, Pirotta M, De Guingand D, et al. Efficacy of **oral metronidazole with vaginal clindamycin or vaginal probiotic for bacterial vaginosis**: randomised placebo-controlled double-blind trial. PLoS One. 2012;7(4):e34540.
Branch-Elliman W, O'Brien W, Strymish J, et al. Association of Duration and Type of **Surgical Prophylaxis With Antimicrobial-Associated Adverse Events**. JAMA Surg. 2019 Apr 24
Branch-Elliman W, Ripollone JE, O'Brien WJ, et al. Risk of surgical site infection, acute kidney injury, and Clostridium difficile infection following antibiotic prophylaxis with **vancomycin plus a beta-lactam versus either drug alone**: A national propensity-score-adjusted retrospective cohort study. PLoS Med. 2017 Jul 10;14(7):e1002340.
Braykov NP, Morgan DJ, Schweizer ML, et al. **Assessment of empirical antibiotic** therapy optimisation in six hospitals: an observational cohort study. Lancet Inf Dis 2014; 14: 1220–27.
Breda L, Marzetti V, Gaspari S, et al. Population-based study of incidence and clinical characteristics of **rheumatic Fever** in abruzzo, central Italy, 2000-2009. J Pediatr. 2012 May;160(5):832-836.e1.
Breen JO. **Skin and soft tissue infections** in immunocompetent patients. Am Fam Physician. 2010 Apr 1;81(7):893-9.
Breithaupt L, Köhler-Forsberg O, Larsen JT, et al. Association of Exposure to **Infections in Childhood With Risk of Eating Disorders** in Adolescent Girls. JAMA Psychiatry. 2019 Apr 24.
Bremond-Gignac D, Nezzar H, Bianchi PE, et al; for the AZI Study Group. Efficacy and safety of **azithromycin 1.5% eye drops** in paediatric population with purulent bacterial conjunctivitis. Br J Ophthalmol. 2014 Feb 13.
Brendish NJ, Malachira AK, Armstrong L, et al. Routine molecular **point-of-care testing for respiratory viruses** in adults presenting to hospital with acute respiratory illness (ResPOC): a pragmatic, open-label, randomised controlled trial. Lancet Respir Med 2017; 5: 401–11.
Breslin K, Tuchman L, Hayes KL, et al. Sensitivity and Specificity of Empiric Treatment for **Sexually Transmitted Infections** in a Pediatric Emergency Department. J Pediatr. 2017 Jun 16.
Brichacek M, Strazar R, Murray KA, et al. Necrotizing fasciitis after scalpel injury sustained during postmortem examination. CMAJ. 2017 May 23;189(20):E721-E723.
Brindle R, Williams OM, Barton E, Featherstone P. Assessment of Antibiotic Treatment of **Cellulitis and Erysipelas**: A Systematic Review and Meta-analysis. JAMA Dermatol. 2019 Jun 12.
Brinker A. **Scarlet Fever**. N Engl J Med. 2017 May 18;376(20):1972 (Streptococcal pharynitits)
Brill JR. Diagnosis and treatment of **urethritis in men**. Am Fam Physician. 2010 Apr 1;81(7):873-8.
Briggs GG, Freeman RK, Sumner JY. Drugs in Pregnancy and Lactation 9th Edition. Williams & Wilkins, Baltimore, 2011.
Brown K, Valenta K, Fisman D, Simor A, Daneman N. Hospital ward antibiotic prescribing and the **risks of Clostridium difficile** infection [online February 23, 2015]. JAMA Intern Med. doi:10.1001/jamainternmed.2014.8273.
Brown R, Vyas S. **Pelvic pain**. BMJ. 2015 Nov 12;351:h5637.
Brunham RC, Gottlieb SL, Paavonen J. **Pelvic inflammatory disease**. N Engl J Med. 2015 May 21;372(21):2039-48.
Bryan AD, Magnan RE, Gillman AS, et al. Effect of Including **Alcohol and Cannabis Content in a Sexual Risk-Reduction Intervention on the Incidence of Sexually Transmitted Infections** in Adolescents: A Cluster Randomized Clinical Trial. JAMA Pediatr. 2018 Feb 12:e175621.
Bryant PA, Katz NT. **Inpatient versus outpatient parenteral antibiotic therapy** at home for acute infections in children: a systematic review. Lancet Infect Dis. 2017 Aug 16
Budhram A, Silverman M, Burneo JG. **Neurosyphilis** mimicking autoimmune encephalitis in a 52-year-old man. CMAJ. 2017 Jul 24;189(29):E962-E965.
Bundgaard H, Ihlemann N, Gill SU, et al. Long-Term Outcomes of **Partial Oral Treatment of Endocarditis**. N Engl J Med. 2019 Mar 17.
Butler CC, Simpson SA, Dunstan F, Rollnick S, Cohen D, Gillespie D, et al. Effectiveness of multifaceted **educational programme** to reduce antibiotic dispensing in primary care: practice based randomised controlled trial. BMJ 2012.344:d8173.
Butler M, Olson A, Drekonja D, et al. Early Diagnosis, Prevention, and Treatment of **Clostridium difficile**: Update AHRQ Comparative Effectiveness Review No. 172. AHRQ Publication No. 16-EHC012-EF.
Butler M, Olson A, Drekonja D, et al. Early Diagnosis, Prevention, and Treatment of **Clostridium difficile**: Update [Internet]. Rockville (MD): Agency for Healthcare Research and Quality (US); 2016 Mar.
Bystritsky R, Chambers H. **In the Clinic: Cellulitis and Soft Tissue Infections**. Ann Intern Med. 2018 Feb 6;168(3):ITC17-ITC32.
Cabana MD, McKean M, Caughey AB, et al. Early **Probiotic Supplementation for Eczema and Asthma Prevention**: A Randomized Controlled Trial. Pediatrics. 2017 Sep;140(3). pii: e20163000.
Cadena J et al. Dose of **trimethoprim-sulfamethoxazole** to treat skin and skin structure infections caused by **methicillin-resistant Staphylococcus aureus**. Antimicrob Agents Chemother 2011: 55: 5430-2.
Caffarini EM, DeMott J, Patel G, Lat I. Determining the clinical utility of an absolute **procalcitonin value** for predicting a positive culture result. Antimicrob Agents Chemother. 2017 Feb 13.
Cahill TJ, Dayer M, Prendergast B, et al. Do patients at risk of **infective endocarditis need antibiotics before dental procedures**? BMJ. 2017 Sep 7;358:j3942.
Cals JW, Butler CC, Hopstaken RM, et al. Effect of point of care testing for C reactive protein (**CRP**) and training in communication skills on antibiotic use in lower respiratory tract infections: cluster randomised trial. BMJ. 2009
Campagna JD, Bond MC, Schabelman E, Hayes BD. The use of **cephalosporins in penicillin-allergic** patients. J Emerg Med. 2012;42(5):612-620.
Cantey JB, Wozniak PS, Pruszynski JE, Sánchez PJ. **Reducing unnecessary antibiotic** use in the **neonatal intensive care unit (SCOUT):** a prospective interrupted time-series study. Lancet Infect Dis 2016; online July 21.
Cantor AG, Pappas M, Daeges M, Nelson HD. **Screening for syphilis**: updated evidence report and systematic review for the US Preventive Services Task Force. (**USPTSF**) JAMA. doi:10.1001/jama.2016.4114
Cao J, Min L, Lansing B, Foxman B, Mody L. **Multidrug-Resistant Organisms on Patients' Hands**: A Missed Opportunity. JAMA Intern Med. 2016 Mar 14.
Cao Y, Wu K, Mehta R, et al. Long-term use of antibiotics and **risk of colorectal adenoma**. Gut. 2017 Apr 4.
Carignan A et al. Efficacy of secondary **prophylaxis with vancomycin for preventing recurrent Clostridium difficile** infections. Am J Gastroenterol 2016 Dec; 111:1834.

Carter GP, Schultz MB, Baines SL, et al. **Topical Antibiotic Use Coselects for the Carriage of Mobile Genetic Elements Conferring Resistance** to Unrelated Antimicrobials in Staphylococcus aureus. Antimicrob Agents Chemother. 2018 Jan 25;62(2). pii: e02000-17.

Carter MJ, Tingley-Kelley K, Warriner RA 3rd. Silver treatments and **silver-impregnated** dressings for the healing of leg wounds and ulcers: a systematic review and meta-analysis. J Am Acad Dermatol. 2010 Oct;63(4):668-79. Epub 2010 May 14.

Castanheira M, Griffin MA, Deshpande LM, et al. Detection of **mcr-1 among Escherichia coli** clinical isolates collected worldwide as part of the SENTRY Antimicrobial Surveillance Program during 2014-2015.Antimicrob Agents Chemother. 2016 Jul 11.

CATMAT-Committee to Advise on Tropical Medicine and Travel. Statement on **travellers' diarrhea**. www.phac-aspc.gc.ca/tmp-pmv/catmat-ccmtmv/assets/pdfs/diarrhea-diarrhee-eng.pdf (accessed December 3, 2015).

CCDR. Treatment and prevention of **traveler's diarrhea**. Can Fam Physician. 2015 Nov;61(11):976.

CDC July/11 **Cephalosporin Susceptibility Among Neisseria gonorrhoeae** Isolates --- United States, 2000--2010 http://www.cdc.gov/mmwr/pdf/wk/mm6026.pdf

CDC Sep/11 Office-Related **Antibiotic Prescribing for Persons Aged ≤14 Years** --- United States, 1993--1994 to 2007—2008. http://www.cdc.gov/mmwr/preview/mmwrhtml/mm6034a1.htm?s_cid=mm6034a1_x

CDC: Centers for Disease Control and Prevention (CDC). Update to CDC's sexually transmitted diseases treatment guidelines, 2010: oral **cephalosporins no longer a recommended treatment for gonococcal** infections. MMWR Morb Mortal Wkly Rep 2012 Aug 10;61:590-4.

CDC. Sexually Transmitted Diseases Treatment Guidelines, 2015. MMWR Morb Mortal Wkly Rep. 2015;64:1-137.

Centor Robert M. Expand the **Pharyngitis** Paradigm for Adolescents and Young Adults.Ann Intern Med December 1, 2009 151:812-815; doi:10.1059/0003-4819-151-11-200912010-00011.

Centor RM, Atkinson TP, Ratliff AE, et al. The clinical presentation of **Fusobacterium–positive pharyngitis and streptococcal–positive pharyngitis** in a university health clinic. A cross-sectional study. Ann Intern Med. 2015;162:241-7.

Chalmers JR, Wojnarowska F, Kirtschig G, et al. A randomized controlled trial to compare the safety, effectiveness and cost-effectiveness of **doxycycline** (200 mg/day) with that of oral **prednisolone** (0.5 mg/kg/day) for initial treatment of **bullous pemphigoid**: the Bullous Pemphigoid Steroids and Tetracyclines (**BLISTER**) trial. Health Technol Assess. 2017 Mar;21(10):1-90.

Chambers HF.Pharmacology and treatment of **complicated skin and skin-structure infections**. N Engl J Med 2014 Jun 5; 370:2238.

Chan T, Bunce PE. **Fluoroquinolone antimicrobial drugs**. CMAJ. 2017 May 1;189(17):E638.

Chan WY, Clark AB, Wilson AM, et al. The Effect of **Co-Trimoxazole on Serum Potassium** Concentration: Safety Evaluation of a Randomised Controlled Trial. Br J Clin Pharmacol. 2017 Feb 13

Chandramohan D, Dicko A, Zongo I, et al. Effect of Adding **Azithromycin to Seasonal Malaria Chemoprevention**. N Engl J Med. 2019 Jan 30.

Chang KL, Guarderas JC. **Allergy Testing**: Common Questions and Answers. Am Fam Physician. 2018 Jul 1;98(1):34-39.

Chau K, Lau E, Greenberg S, Jacobson S, et al. **Probiotics for Infantile Colic**: A Randomized, Double-Blind, Placebo- Controlled Trial Investigating Lactobacillus reuteri DSM 17938. J Pediatr. 2014 Oct 23.

Chen AE, Carroll KC, Diener-West M, et al. Randomized controlled trial of **cephalexin versus clindamycin for uncomplicated pediatric skin infections**. Pediatrics. 2011 Mar;127(3):e573-80.

Chen N, Li Q, Yang J, et al. **Antiviral** treatment for preventing **postherpetic neuralgia**. Cochrane Database Syst Rev. 2014 Feb 6;2:CD006866. There is high quality evidence that oral aciclovir does not reduce the incidence of PHN significantly. In addition, there is insufficient evidence to determine the effect of other antiviral treatments; therefore, further well-designed RCTs are needed to investigate famciclovir or other new antiviral agents in preventing PHN.

Chen TT, Yeh YC, Chien KL, et al. Risk of **Infective Endocarditis After Invasive Dental Treatments**: A Case-Only Study. Circulation. 2018 Apr 19.

Chen X-S. Challenges in responses to **syphilis** epidemic. Lancet Infect Dis 2017; online July 9.

Cheng MP, Stenstrom R, Paquette K, et al. **Blood culture results before and after antimicrobial administration** in patients with severe manifestations of sepsis. A diagnostic study. Ann Intern Med. 17 September 2019. [Epub ahead of print]. doi:10.7326/M19-1696.

Cheng YJ, Nie XY, Chen XM, et al. The Role of **Macrolide Antibiotics in Increasing Cardiovascular Risk**. J Am Coll Cardiol. 2015 Nov 17;66(20):2173-84.

Cheon E, Horowitz HW. New avenues for antimicrobial stewardship: the case for **penicillin skin testing by pharmacists**. Clin Infect Dis. 2018 Oct 3.

Chiappini E, Regoli M, Bonsignori F, et al. Analysis of different recommendations from international guidelines for the management of **acute pharyngitis in adults and children**. Clin Ther. 2011 Jan;33(1):48-58.

Chiappini E, Bortone B, Di Mauro G, et al. **Choosing Wisely**: The Top-5 Recommendations from the Italian Panel of the National Guidelines for the Management of **Acute Pharyngitis** in Children. Clin Ther. 2017 Feb 6.

Chien AL, Tsai J, Leung S, et al. Association of **systemic antibiotic treatment of acne with skin microbiota characteristics** [online Feb 13, 2019]. JAMA Dermatol.

Chiriac A, Murgu A, Coroș MF, et al. **Intertrigo Caused by Streptococcus pyogenes**. J Pediatr. 2017 Feb 22.

Chitnis AS, Holzbauer SM, Belflower RM, et al. Epidemiology of **Community-Associated Clostridium difficile** Infection, 2009 Through 2011. JAMA Intern Med. 2013 Jun 17:1-9.

Choby BA. Diagnosis and treatment of **streptococcal pharyngitis**. Am Fam Physician. 2009 Mar 1;79(5):383-90.

Chong LY, Head K, Hopkins C, et al. **Intranasal steroids** versus placebo or no intervention for chronic **rhinosinusitis**. Cochrane Database Syst Rev. 2016 Apr 26;4:CD011996. Most of the evidence available was from studies in patients with chronic rhinosinusitis with nasal polyps. There is little information about quality of life (very low quality evidence). For disease severity, there seems to be improvement for all symptoms (low quality evidence), a moderate-sized benefit for nasal blockage and a small benefit for rhinorrhoea (moderate quality evidence). The risk of epistaxis is increased (high quality evidence), but these data included all levels of severity; small streaks of blood may not be a major concern for patients. It is unclear whether there is a difference in the risk of local irritation (low quality evidence).

Chonmaitree T, Trujillo R, Jennings K, et al. **Acute Otitis Media** and Other Complications of **Viral Respiratory Infection**. Pediatrics. 2016 Mar 28.

Chovel-Sella A, Ben Tov A, Lahav E, et al. Incidence of **Rash After Amoxicillin Treatment in Children With Infectious Mononucleosis**. Pediatrics. 2013 Apr 15.

Chou HW, Wang JL, Chang CH, et al. Risk of Severe **Dysglycemia Among Diabetic Patients Receiving Levofloxacin, Ciprofloxacin, or Moxifloxacin** in Taiwan. Clin Infect Dis. 2013 Aug 14.

Chow AW, Benninger MS, Brook I et al. **IDSA** Clinical Practice Guideline for Acute Bacterial **Rhinosinusitis in Children and Adults**. Clin Infect Dis. 2012Apr;54(8):e72-e112.

Chow EP, Danielewski JA, Fehler G, et al. **Human papillomavirus in young women with Chlamydia trachomatis** infection 7 years after the Australian human papillomavirus vaccination programme: a cross-sectional study. Lancet Infect Dis 2015; online July 20.

Chow EP, Howden BP, Walker S, et al. **Antiseptic mouthwash against pharyngeal Neisseria gonorrhoeae**: a randomised controlled trial and an in vitro study. Sex Transm Infect. 2016 Dec 20.

Chow EPF, Cornelisse VJ, Williamson DA, et al. **Kissing may be an important and neglected risk factor for oropharyngeal gonorrhoea**: a cross-sectional study in men who have sex with men. Sex Transm Infect. 2019 May 9.

Chua KP, Fischer MA, Linder JA. **Appropriateness of outpatient antibiotic prescribing** among privately insured US patients: ICD-10-CM based cross sectional study. BMJ. 2019 Jan 16;364:k5092.

Chui CS, Chan EW, Wong AY, et al. Association between oral **fluoroquinolones and seizures**: A self-controlled case series study. Neurology. 2016 May 3;86(18):1708-15.

Church JA, Fitzgerald F, Walker AS, et al. The **expanding role of co-trimoxazole** in developing countries. Lancet Infect Dis. 2015 Jan 21.

Clarke S, Murphy E, et al. **Exercise and associated dietary extremes impact on gut microbial diversity**. Gut 2014. doi:10.1136/gutjnl-2013-306541

Clegg HW, Giftos PM, Anderson WE, Kaplan EL, Johnson DR. Clinical **Perineal Streptococcal Infection** in Children: Epidemiologic Features, Low Symptomatic Recurrence Rate after Treatment, and Risk Factors for Recurrence. J Pediatr. 2015 Jun 19.

Clement ME, Okeke NL, Hicks CB. **Treatment of Syphilis**: A Systematic Review. JAMA. 2014 Nov 12;312(18):1905-1917.

Clement ME, Hicks CB. RPR and the **Serologic Diagnosis of Syphilis**. JAMA. 2014 Nov 12;312(18):1922-1923.

Coco, Andrew, Vernacchio, Louis, Horst, Michael, Anderson, Angela. Management of **Acute Otitis Media** After Publication of the 2004 AAP and AAFP Clinical Practice Guideline. Pediatrics 2010 0: peds.2009-1115.

Cohen SH, Gerding DN, Johnson S, Kelly CP, Loo VG, McDonald LC, Pepin J, Wilcox MH. Clinical practice guidelines for **Clostridium difficile** infection in adults: 2010 update by the society for healthcare epidemiology of America (SHEA) and the infectious diseases society of America (**IDSA**). Infect Control Hosp Epidemiol. 2010 May;31(5):431-55.

Cohen, Arlan, Maschopoulos, Panagis, Stiehm, Richard E., Koren, Gideon. **Congenital varicella syndrome**: the evidence for secondary prevention with **varicella-zoster immune globulin**. CMAJ 2011 0: cmaj.100615.

Cohen JI. Clinical practice: **Herpes zoster**. N Engl J Med. 2013 Jul 18;369(3):255-63.

Cohen JF, Cohen R, Levy C, et al. **Selective testing strategies for diagnosing group A streptococcal** infection in children with **pharyngitis**: a systematic review and prospective multicentre external validation study. CMAJ. 2014 Dec 8.

Cohen JF, Bertille N, Cohen R, Chalumeau M. **Rapid antigen detection test for group A streptococcus in children with pharyngitis**. Cochrane Database of Systematic Reviews 2016, Issue 7. Art. No.: CD010502. In a population of 1000 children with a GAS prevalence of 30%, 43 patients with GAS will be missed. Whether or not RADT can be used as a stand-alone test to rule out GAS will depend mainly on the epidemiological context. The sensitivity of EIA and OIA tests seems comparable. RADT specificity is sufficiently high to ensure against unnecessary use of antibiotics. Based on these results, we would expect that amongst 100 children with strep throat, 86 would be correctly detected with the rapid test while 14 would be missed and not receive antibiotic treatment.

Coia JE, Leanord AT, Reilly J. **Screening for meticillin resistant Staphylococcus aureus (MRSA):** who, when, and how? BMJ. 2014 Feb 27

Coker TJ, Dierfeldt DM. **Acute Bacterial Prostatitis**: Diagnosis and Management. Am Fam Physician. 2016;93(2):114-120.

Colantonio S, Kirshen C. Severe **allergic contact dermatitis** due to **Polysporin**. CMAJ. 2017 Aug 8;189(31):E1018

Cole MJ, Spiteri G, Jacobsson S, et al; Euro-GASP Network. Is the tide turning again for **cephalosporin resistance in Neisseria gonorrhoeae** in Europe? Results from the 2013 European surveillance. BMC Infect Dis. 2015 Aug 11;15(1):321.

Collins S, RamsayM, Slack MPE, et al. Risk of invasive **Haemophilus influenzae infection during pregnancy** and association with adverse fetal outcomes. JAMA. doi:10.1001/jama.2014.1878.

Committee on Adolescence and Society for Adolescent Health and Medicine. **Screening for nonviral sexually transmitted infections** in adolescents and young adults. Pediatrics. 2014 Jul;134(1):e302-11.

Confino-Cohen R et al. **Oral challenge without skin testing safely excludes clinically significant delayed-onset penicillin hypersensitivity**. J Allergy Clin Immunol Pract 2017 May/Jun; 5:669.

Conway EL, Lin K, et al.Impact of **Penicillin Allergy** on Time to First Dose of Antimicrobial Therapy and Clinical Outcomes. Clin Ther. 2017 Oct 9. pii: S0149-2918(17)30986-4.

Copp HL, Shapiro DJ, et al. National Ambulatory Antibiotic Prescribing Patterns for Pediatric **Urinary Tract Infection**,1998-2007.*Pediatrics*, 2011; DOI: 10.1542/peds.2010-3465

Cordoba G, Siersma V, Lopez-Valcarcel B, et al. **Prescribing style and variation** in antibiotic prescriptions for **sore throat**: cross-sectional study across six countries. BMC Fam Pract. 2015 Jan 29;16(1):7.

Corey GR et al. Single-dose **oritavancin** in the treatment of acute bacterial skin infections. N Engl J Med 2014 Jun 5; 370:2180.

Cornia PB, Hersh AL, Lipsky BA, et al. Does this coughing adolescent or adult patient have **pertussis**?. JAMA. 2010 Aug 25;304(8):890-6.

Costelloe Céire, Metcalfe Chris, Lovering Andrew, et al. Effect of **antibiotic prescribing** in primary care on **antimicrobial resistance** in individual patients: systematic review and meta-analysis. BMJ 2010;340:c2096

Coughlin K, Flibotte J, Cahill AM, et al. **Methemoglobinemia in an Infant After Sclerotherapy With High-Dose Doxycycline**. Pediatrics. 2019 Jan 17.

Coxeter P, Del Mar CB, McGregor L, Beller EM, Hoffmann TC. Interventions to facilitate **shared decision making to address antibiotic use** for acute respiratory infections in primary care. Cochrane Database Syst Rev. 2015 Nov 12;11:CD010907. Interventions that aim to facilitate shared decision making reduce antibiotic prescribing in primary care in the short term. Effects on longer-term rates of prescribing are uncertain and more evidence is needed to determine how any sustained reduction in antibioticprescribing affects hospital admission, pneumonia and death.

Coxeter PD, Del Mar C, Hoffman TC. **Parent's Expectations and Experiences of Antibiotics for Acute Respiratory Infections** in Primary Care. Ann Fam Med 2017; 15:149-154

Crellin E, Mansfield KE, Leyrat C, et al. **Trimethoprim use for urinary tract infection** and risk of adverse outcomes in older patients: cohort study. BMJ. 2018 Feb 9;360:k341.

Cronin MJ, Khan S, Saeed S. The role of antibiotics in the treatment of acute **rhinosinusitis in children**: a systematic review. Arch Dis Child. 2013 Apr;98(4):299-303.

Crotty MP, Meyers S, Hampton N, et al. Impact of **antibacterials on subsequent resistance** and clinical outcomes in adult patients with **viral pneumonia**: an opportunity for stewardship. Crit Care. 2015 Nov 18;19:404.

Cruickshank M, O'Flynn N, Faust SN; Guideline Committee. **Lyme disease: summary of NICE guidance**. BMJ. 2018 Apr 12;361:k1261.

Cunha BA, Burillo A, Bouza E. **Legionnaires' disease**. Lancet. 2015 Jul 28.

Currie CJ, Berni E, Jenkins-Jones S, et al. **Antibiotic treatment failure in four common infections in UK** primary care 1991-2012: longitudinal analysis. BMJ. 2014 Sep 23;349:g5493.

Curry A, Williams T, Penny ML. **Pelvic Inflammatory Disease**: Diagnosis, Management, and Prevention. Am Fam Physician. 2019 Sep 15;100(6):357-364.

Czepiel J, Dróżdż M, Pituch H, et al. **Clostridium difficile infection**: review. Eur J Clin Microbiol Infect Dis. 2019 Apr 3.

Dalager-Pedersen M, Søgaard M, Schønheyder HCC, et al. Risk for **myocardial infarction and stroke after community-acquired bacteremia**: A 20-year population-based cohort study. **Circulation** 2014.

Dalal A, Eskin-Schwartz M, Mimouni D, et al. Interventions for the **prevention of recurrent erysipelas and cellulitis**. Cochrane Database Syst Rev. 2017 Jun 20;6:CD009758.
In terms of recurrence, incidence, and time to next episode, antibiotic is probably an effective preventive treatment for recurrent cellulitis of the lower limbs in those under prophylactic treatment, compared with placebo or no treatment (moderate-certainty evidence). However, these preventive effects of antibiotics appear to diminish after they are discontinued (low-certainty evidence). Treatment with antibiotic does not trigger any serious adverse events, and those associated are minor, such as nausea and rash (low-certainty evidence). The evidence is limited to people with at least two past episodes of leg cellulitis within a time frame of up to three years, and none of the studies investigated other common interventions such as lymphoedema reduction methods or proper skin care. Larger, high-quality studies are warranted, including long-term follow-up and other prophylactic measures.

Daneman N, Bronskill SE, Grunier A, et al. Variability in **antibiotic use across nursing homes** and the risk of antibiotic-related adverse outcomes for individual residents [online June 29, 2015].JAMA Intern Med. doi:10.1001 /jamainternmed.2015.2770.

Daneman N, Campitelli MA, Giannakeas V, et al. Influences on the start**, selection and duration of treatment with antibiotics in long-term care facilities**. CMAJ. 2017 Jun 26;189(25):E851-E860.

Daniel S, Doron M, Fishman B, et al. The safety of **amoxicillin and clavulanic acid use during the first trimester of pregnancy**. Br J Clin Pharmacol. 2019 Sep 5.

Daniels JM, Snijders D, de Graaff CS, et al. Antibiotics in Addition to Systemic **Corticosteroids for Acute Exacerbations** of COPD. Am J Respir Crit Care Med. 2009 Oct 29. While equivalent to placebo on clinical success at day 30, doxycycline showed superiority on clinical success and clinical cure at day 10, microbiological success, the use of open label antibiotics and symptoms.

Daniels L, Unlu C, de Korte N, et al. Randomized clinical trial of **observational versus antibiotic treatment** for a first episode of CT-proven uncomplicated acute **diverticulitis**. Br J Surg. 2016 Sep 30.

Dantes R et al. National burden of invasive **methicillin-resistant Staphylococcus aureus** (MRSA) infections, United States, 2011. JAMA Intern Med 2013 Sep 16; [e-pub ahead of print].

Dar OA, Hasan R, Schlundt J, et al. Exploring the evidence base for **national and regional policy interventions to combat resistance**. Lancet 2015; online Nov 18.

Datta Rupak; Platt Richard; Yokoe Deborah S.; et al. **Environmental Cleaning Intervention** and Risk of Acquiring Multidrug-Resistant Organisms From Prior Room Occupants. Arch Intern Med. 2011;171(6):491-494.

Daum RS, Miller LG, Immergluck L, et al. A Placebo-Controlled Trial of **Antibiotics for Smaller Skin Abscesses**. N Engl J Med. 2017 Jun 29;376(26):2545-2555

Davies L, Angus RM, Calverley PM. Oral **corticosteroids** in patients admitted to hospital with **exacerbations** of chronic obstructive pulmonary disease: a prospective randomised controlled trial. Lancet 1999;354(9177):456-60.

Davenport RJ. ACP Journal Club. Review: Adding **antiviral drugs to steroids did not improve facial muscle recovery in Bell palsy**. Ann Intern Med. 2010 Feb 16;152(4):JC-210.

Davey P, Brown E, Charani E, Fenelon L,Gould IM,Holmes A, Ramsay CR,Wiffen PJ,WilcoxM. **Interventions to improve antibiotic prescribing** practices for hospital inpatients. Cochrane Database of Systematic Reviews 2013, Issue 4. Art. No.: CD003543. DOI: 10.1002/14651858.CD003543.pub3. The results show that interventions to reduce excessive antibiotic prescribing to hospital inpatients can reduce antimicrobial resistance or hospital-acquired infections, and interventions to increase effective prescribing can improve clinical outcome.

Davey P, Marwick CA, Scott CL, et al. Interventions to **improve antibiotic prescribing** practices for **hospital inpatients**. Cochrane Database of Systematic Reviews 2017, Issue 2. Art. No.: CD003543. We found high-certainty evidence that interventions are effective in increasing compliance with antibiotic policy and reducing duration of antibiotic treatment. Lower use of antibiotics probably does not increase mortality and likely reduces length of stay. Additional trials comparing antibiotic stewardship with no intervention are unlikely to change our conclusions. Enablement consistently increased the effect of interventions, including those with a restrictive component. Although feedback further increased intervention effect, it was used in only a minority of enabling interventions. Interventions were successful in safely reducing unnecessary antibiotic use in hospitals, despite the fact that the majority did not use the most effective behaviour change techniques. Consequently, effective dissemination of our findings could have considerable health service and policy impact. Future research should instead focus on targeting treatment and assessing other measures of patient safety, assess different stewardship interventions, and explore the barriers and facilitators to implementation. More research is required on unintended consequences of restrictive interventions.

Davies KA, Longshaw CM, Davis GL, et al. **Underdiagnosis of Clostridium diffi cile** across **Europe**: the European, multicentre, prospective, biannual, point-prevalence study of Clostridium diffi cile infection in hospitalised patients with diarrhoea (EUCLID). Lancet Infect Dis 2014.

Dawson-Hahn EE, Mickan S, Onakpoya I, et al. **Short-course versus long-course oral antibiotic treatment for infections treated in outpatient settings**: a review of systematic reviews. Fam Pract. 2017 Sep 1;34(5):511-519.

Dayer MJ, Jones S, Prendergast B, et al. Incidence of **infective endocarditis** in England, 2000-13: a secular trend, interrupted time-series analysis. Lancet. 2014 Nov 18. pii: S0140-6736(14)62007-9.

Dayer MJ, Jones S, Prendergast B, Baddour LM, Lockhart PB, Thornhill MH. Incidence of **infective endocarditis** in **England**, 2000–13: a secular trend, interrupted time-series analysis. Lancet 2014; online Nov 18.

de Bont EG, Alink M, Falkenberg FC, et al. **Patient information leaflets to reduce antibiotic us**e and reconsultation rates in general practice: a systematic review. BMJ Open. 2015 Jun 3;5(6):e007612.

de Jong E, van Oers JA, Beishuizen A, et al. Efficacy and safety of **procalcitonin guidance** in reducing the duration of antibiotic treatment in critically ill patients: a randomised, controlled, open-label trial. Lancet Infect Dis. 2016 Feb 29

de Kraker ME, Stewardson AJ, Harbarth S. Will 10 Million People Die a Year due to **Antimicrobial Resistance by 2050**? PLoS Med. 2016 Nov 29;13(11):e1002184.

de la Poza Abad M, Mas Dalmau G, Moreno Bakedano M, et al; **Delayed Antibiotic Prescription** (DAP) Group. Prescription Strategies in Acute Uncomplicated Respiratory Infections: A Randomized Clinical Trial. JAMA Intern Med. 2016 Jan 1;176(1):21-9.

De Silva D, Peters J, Cole K, et al. Whole-genome sequencing to determine transmission of **Neisseria gonorrhoeae**: an observational study. Lancet Infect Dis 2016; online July 11.

de Smet AM, Kluytmans JA, Blok HE, et al. **Selective digestive tract decontamination and selective oropharyngeal decontamination** and antibiotic resistance in patients in intensive-care units: an open-label, clustered group-randomised, crossover study. Lancet Infect Dis. 2011 Mar 18.

Deleo FR, Otto M, Kreiswirth BN, Chambers HF. Community-associated **methicillin-resistant Staphylococcus aureus**. Lancet. 2010 May 1;375(9725):1557-68.

den Heijer CDJ, van Bijnen EME, Paget WJ, et al, and the APRES Study Team. **Prevalence and resistance of commensal Staphylococcus aureus**, including meticillin-resistant S aureus: a European cross-sectional study. Lancet Infect Dis 2013; online March 6.

Deplanque G, Gervais R, Vergnenegre A, et al. **Doxycycline** for prevention of **erlotinib-induced rash** in patients with non-small-cell lung cancer (NSCLC) after failure of first-line chemotherapy: A randomized, open-label trial. J Am Acad Dermatol. 2016 Jun;74(6):1077-85.

Derde LPG, Cooper BS, Goosens H, et al. Interventions to **reduce colonisation and transmission of antimicrobial-resistant bacteria** in intensive care units: an interrupted time series study and cluster randomised trial. Lancet Infect Dis 2013; online Oct 23.

Desai RJ, Bateman BT, Huybrechts KF, et al. Risk of **serious infections associated with use of immunosuppressive agents in pregnant women** with autoimmune inflammatory conditions: cohort study. BMJ. 2017 Mar 6;356:j895.

Deshpande A, Pasupuleti V, Thota P, et al. **Community-associated Clostridium difficile infection and antibiotics**: a meta-analysis. J Antimicrob Chemother. 2013 Sep;68(9):1951-61.

Desrosiers M, Evans GE, Keith PK, et al. **Canadian clinical practice guidelines for acute and chronic rhinosinusitis**. Allergy Asthma Clin Immunol 2011;7:2. www.aacijournal.com/content/pdf/1710-1492-7-2.pdf

Dhar A, Manoila I, Dugay MH, Sellal F. Mystery Case: **Metronidazole-induced encephalopathy**. Neurology. 2016 Aug 30;87(9):e89-90.

Dhiman RK, Rana B, Agrawal S, et al. **Probiotic VSL#3** Reduces **Liver Disease** Severity and Hospitalization in Patients With Cirrhosis: A Randomized, Controlled Trial. Gastroenterology. 2014 Dec;147(6):1327-1337.e3.

Dhiwakar M, Clement WA, Supriya M, McKerrow W. Antibiotics to reduce **post-tonsillectomy** morbidity. Cochrane Database Syst Rev. 2010 Jul 7;7:CD005607. The present systematic review, including meta-analyses for select outcomes, suggests that although individual studies vary in their findings, there is no evidence to support a consistent, clinically important impact of antibiotics in reducing the main morbid outcomes following tonsillectomy (i.e. pain, need for analgesia and secondary haemorrhage rates). Limited benefit apparent with antibiotics may be a result of positive bias introduced by several important methodological shortcomings in the included trials. Based on existing evidence therefore, we would advocate against the routine prescription of antibiotics to patients undergoing tonsillectomy. Whether a subgroup of patients who might benefit from selective administration of antibiotics exists is unknown and needs to be explored in future trials.

Dholaria BR, Pant S, Lavender RC, et al. The great imitator: **Psychosis** that responded to **penicillin**. Can Fam Physician. 2014 Sep;60(9):818-21.

Di Pentima MC, Chan S, Hossain J. Benefits of a **Pediatric Antimicrobial Stewardship Program** at a Children's Hospital. Pediatrics. 2011 Dec;128(6):1062-70.

Ding G, Vinturache A, Lu M. Addressing **inappropriate antibiotic prescribing in China**. CMAJ. 2019 Feb 11;191(6):E149-E150.

Dingle KE, Didelot X, Quan T P, et al. Effects of control interventions on **Clostridium difficile infection** in England: an observational study. Lancet Infect Dis 2017; online Jan 24.

Dixon JM, Khan LR. Treatment of **breast infection**. BMJ. 2011 Feb 11;342:d396. doi: 10.1136/bmj.d396.

Doan T, Arzika AM, Hinterwirth A, et al. **Macrolide Resistance in MORDOR I** - A Cluster-Randomized Trial in Niger. N Engl J Med. 2019 Jun 6;380(23):2271-2273.

Dooling KL, Shapiro DJ, Van Beneden C, et al. **Overprescribing and Inappropriate Antibiotic Selection for Children With Pharyngitis** in the United States, 1997-2010. JAMA Pediatr. 2014 Sep 29.

Doshi P. **Defining antibiotic effectiveness and resistance**: how a private party may soon rule judgments over susceptibility testing. BMJ. 2016 Jan 6;352:h6849.

Dowlati E, Dovico J, Unwin B. **Skin Hyperpigmentation** and Melanonychia From Chronic **Doxycycline** Use. Ann Pharmacother. 2015 Oct;49(10):1175-6.

Drekonja DM, Butler M, MacDonald R, Bliss D, Filice GA, Rector TS, Wilt TJ. Comparative effectiveness of Clostridium difficile treatments: a systematic review. Ann Intern Med. 2011 Dec 20;155(12):839-47.

Dreucean D, Beres K, McNierney-Moore A, Gravino D. Use of **meropenem to treat valproic acid overdose**. Am J Emerg Med. 2019 Sep 4:158426.

Drug and Therapeutics Bulletin. **Penicillin allergy**-getting the label right.BMJ. 2017 Aug 4;358:j3402

Dumville JC, Gray TA, Walter CJ, et al. **Dressings** for the prevention of **surgical site infection**. Cochrane Database Syst Rev. 2016 Dec 20;12:CD003091.

Dumville JC, Lipsky BA, Hoey C, et al. **Topical antimicrobial agents for treating foot ulcers in people with diabetes**. Cochrane Database Syst Rev. 2017 Jun 14;6:CD011038. The randomised controlled trial data on the effectiveness and safety of topical antimicrobial treatments for diabetic foot ulcers is limited by the availability of relatively few, mostly small, and often poorly designed trials. Based on our systematic review and analysis of the literature, we suggest that: 1) use of an antimicrobial dressing instead of a non-antimicrobial dressing may increase the number of diabetic foot ulcers healed over a medium-term follow-up period (low-certainty evidence); and 2) there is probably little difference in the risk of adverse events related to treatment between systemic antibiotics and topical antimicrobial treatments based on the available studies (moderate-certainty evidence). For each of the other outcomes we examined there were either no reported data or the available data left us uncertain as to whether or not there were any differences between the compared treatments. Given the high, and increasing, frequency of diabetic foot wounds, we encourage investigators to undertake properly designed randomised controlled trials in this area to evaluate the effects of topical antimicrobial treatments for both the prevention and the treatment of infection in these wounds and ultimately the effects on wound healing.

Ebell, M. H. **Diagnosis of Streptococcal Pharyngitis**. American Family Physician. 2014.

Ebell MH, Marchello C, Callahan M. Clinical **Diagnosis of Bordetella Pertussis** Infection: A Systematic Review. J Am Board Fam Med. 2017 May-Jun;30(3):308-319.

Eberly MD, Eide MB, Thompson JL, et al. **Azithromycin in Early Infancy and Pyloric Stenosis**. Pediatrics. 2015 Feb 16.

Edelstein C, Daw JR, Kassam Z. **Seeking safe stool**: Canada needs a universal donor model. CMAJ. 2016 Dec 6;188(17-18):E431-E432

Edmonds M, Lázaro-Martínez JL, et al. **Sucrose octasulfate dressing** versus control dressing in patients with neuroischaemic **diabetic foot ulcers** (**Explorer**): an international, multicentre, double-blind, randomised, controlled trial. Lancet Diabetes Endocrinol 2017; online Dec 20.

Edmonson MB, Eickhoff JC. **Weight gain and obesity in infants** and young children exposed to **prolonged antibiotic prophylaxis** [online Dec 27, 2016].JAMA Pediatr. doi:10.1001 /jamapediatrics.2016.3349

Edwards J, Stapley S. **Debridement of diabetic foot ulcers**. Cochrane Database Syst Rev. 2010 Jan 20;(1):CD003556. There is evidence to suggest that hydrogel increases the healing rate of diabetic foot ulcers compared with gauze dressings or standard care and larval therapy resulted in significantly greater reduction in wound area than hydrogel.

Edwards JM, Watson N, Focht C, et al. **Group B Streptococcus (GBS) Colonization** and Disease among Pregnant Women: A Historical Cohort Study. Infect Dis Obstet Gynecol. 2019 Feb 3;2019:5430493.

Elias, Jackie, Bozzo, Pina, Einarson, Adrienne. Are **probiotics safe for use during pregnancy and lactation**? Can Fam Physician 2011 57: 299-301.

Emerging risk of **untreatable gonorrhea** and what to do about it. Can Fam Physician. 2017 Mar;63(3):214.

Erdener SE, Kansu T, Arsava EM, Dericioglu N. Brain MRI evolution of **metronidazole intoxication**. Neurology. 2013 May 7;80(19):1816-7.

Ericson JE, Popoola VO, Smith PB, et al. Burden of **invasive Staphylococcus aureus infections in hospitalized infants** [online October 19, 2015].JAMA Pediatr. doi:10.1001/jamapediatrics .2015.2380.

Etminan M, Forooghian F, Brophy JM, Bird ST, Maberley D. Oral **Fluoroquinolones and the Risk of Retinal** Detachment. **JAMA**. 2012;307:1414-1419

Etminan M, Brophy JM, Samii A. Oral **fluoroquinolone** use and risk of **peripheral neuropathy**: A pharmacoepidemiologic study. Neurology. 2014 Sep 30;83(14):1261-3.

Etminan M, Sodhi M, Ganjizadeh-Zavareh S, et al. **Oral Fluoroquinolones and Risk of Mitral and Aortic Regurgitation**. J Am Coll Cardiol. 2019 Sep 17;74(11):1444-1450.

European Respiratory Society. **COPD guidelines**. Lausanne, Switz: European Respiratory Society; 2004. Available from: www.ersnet.org/ers/default. aspx?id=1418. Accessed 2008 Oct 31.

Evans AT, Husain S, Durairaj L, et al. Azithromycin for **acute bronchitis**: a randomized, double-blind, controlled trial. Lancet 2002;359(9318):1648-54.

Evensen AE. **Management of COPD Exacerbations**. Am Fam Physician. 2010 Mar 1;81(5):607-13.

Faden, Howard, Lesse, Alan J., Trask, Jennifer, et al. Importance of **Colonization** Site in the Current Epidemic of **Staphylococcal Skin Abscesses**. Pediatrics 2010 125: e618-e624.

Fang L, Oliver A, Jayaraman GC, Wong T. Trends in age disparities between younger and middle-age adults among reported rates of **chlamydia, gonorrhea, and infectious syphilis** infections in Canada: findings from 1997 to 2007. Sex Transm Dis. 2010 Jan;37(1):18-25.

Farmakiotis D, Zeluff B. **Metronidazole-Associated Encephalopathy**. N Engl J Med. 2016 Apr 14

Fatheree NY, Liu Y, Taylor CM, et al. **Lactobacillus reuteri** for **infants with colic**: a double-blind, placebo-controlled, randomized clinical trial. J Pediatr 2017;191:170-8.

Fauchier L, Pericart L, Bourguignon T, et al. Comparison of Outcome of Possible vs Definite Infective **Endocarditis** Involving Prosthetic or Bioprosthetic Heart Valves. Am J Cardio. 2017

FDA Mar/13 is warning the public that **azithromycin (Zithromax or Zmax)** can cause abnormal changes in the electrical activity of the heart that may lead to a potentially fatal irregular heart rhythm. Patients at particular risk for developing this condition include those with known risk factors such as existing **QT interval prolongation**, low blood levels of potassium or magnesium, a slower than normal heart rate, or use of certain drugs used to treat abnormal heart rhythms, or arrhythmias.

FDA May/16 is advising that the **serious side effects associated with fluoroquinolone antibacterial drugs generally outweigh** the benefits for patients with sinusitis, bronchitis, and uncomplicated urinary tract infections who have other treatment options. For patients with these conditions, fluoroquinolones should be reserved for those who do not have alternative treatment options.

FDA Jul/16 has updated the labels of systemic **fluoroquinolones** (e.g., ciprofloxacin, levofloxacin) to emphasize that they're associated with numerous serious and potentially irreversible adverse effects that can occur simultaneously. For patients with sinusitis, bronchitis, or uncomplicated urinary tract infections, the agency says, these antibacterials should be used only when there are no alternative options. Disabling side effects may include **tendinitis, tendon rupture, muscle pain, muscle weakness, joint pain, joint swelling, peripheral neuropathy, and central nervous system effects** (e.g., depression, psychosis). Adverse reactions may begin within hours or weeks of treatment initiation; data suggest that such reactions last, on average, 14 months after stopping treatment.

FDA Jan/18: AuroMedics Pharma LLC is voluntarily **recalling** one lot of **Levofloxacin** in 5% Dextrose Injection 250mg/50mL in a Single-Use flexible container NDC 55150-243-46, Lot CLF160003, Expiry date May 2018, to the hospital level. The product has been found to contain visible particulate matter tentatively identified as mold. This problem was discovered as a result of a product complaint in which the contents of one flexible bag was found to contain white particulate matter.

FDA Mar/18 : FDA is advising caution before prescribing the antibiotic **clarithromycin** (Biaxin) to patients **with heart disease** because of a potential increased risk of heart problems or death that can occur years later. FDAs recommendation is based on a review of the results of a 10-year follow-up study of patients with coronary heart disease from a large clinical trial that first observed this safety issue.

FDA Jul/18: FDA is strengthening the current warnings in the prescribing information that **fluoroquinolone antibiotics may cause significant decreases in blood sugar and certain mental health side effects**. The new label changes will add that low blood sugar levels, also called hypoglycemia, can lead to coma and the new label will also make the mental health side effects more prominent and more consistent across the systemic fluoroquinolone drug class. The mental health side effects to be added to or updated across all the fluoroquinolones are: disturbances in attention, disorientation, agitation, nervousness, memory impairment, serious disturbances in mental abilities called delirium.

FDA Aug/18: **Zithromax, Zmax (azithromycin): FDA Warning** - Increased **Risk of Cancer Relapse** With Long-Term Use After Donor Stem Cell Transplant.

FDA Dec/18: review found that **fluoroquinolone antibiotics can increase the occurrence of rare but serious events of ruptures or tears in the main artery of the body, called the aorta**.

Feltner C, Grodensky C, Ebel C, et al. Serologic **Screening for Genital Herpes**: An Updated Evidence Report and Systematic Review for the US Preventive Services Task Force. JAMA. 2016 Dec 20;316(23):2531-2543.

Fifer H, Natarajan U, Jones L, Alexander et al. **Failure of Dual Antimicrobial Therapy in Treatment of Gonorrhea**. N Engl J Med.2016 Jun 23;374(25):2504-6.

Fifer H, Cole M, Hughes G, et al. Sustained transmission of **high-level azithromycin-resistant Neisseria gonorrhoeae** in England: an observational study. Lancet Infect Dis 2018; online March 6.

Fine AM, Nizet V, Mandl KD. Participatory medicine: a **home score for streptococcal pharyngitis** enabled by real-time biosurveillance. A cohort study. Ann Intern Med. 2013;159:577-83.

Finkelstein Y, Macdonald EM, Li P, et al. Recurrence and mortality following **severe cutaneous adverse reactions**. JAMA. 2014 Jun 4;311(21):2231-2.

Finkelstein JA, Raebel MA, Nordin JD, et al. Trends in **Outpatient Antibiotic Use in 3 Health Plans**. Pediatrics. 2018 Dec 17.

Fisher JM, Feng JY, Tan SY, Mostaghimi A. Analysis of **Readmissions Following Hospitalization for Cellulitis** in the United States. JAMA Dermatol. 2019 Feb 27.

FitzGerald M; on behalf of the British Association of Sexual Health and HIV Clinical Effectiveness Group. **Gonorrhoea treatment**—suggested changes. 2011. www.bashh.org/documents/3256 .

Fleming-Dutra KE, Shapiro DJ, Hicks LA, Gerber JS, Hersh AL. **Race**, **otitis media**, and antibiotic selection. Pediatrics. 2014 Dec;134(6):1059-66.

Fleming-Dutra KE, Hersh AL, Shapiro DJ, et al. Prevalence of **inappropriate antibiotic prescriptions among US ambulatory care visits**, 2010-2011.JAMA. doi:10.1001/jama.2016.4151.

Fleming-Dutra KE, Mangione-Smith R, Hicks LA. How to **Prescribe Fewer Unnecessary Antibiotics**: Talking Points That Work with Patients and Their Families. Am Fam Physician. 2016 Aug 1;94(3):200-2

Fletcher-Lartey S, Yee M, Gaarslev C, et al. **Why do general practitioners prescribe antibiotics for upper respiratory tract infections** to meet patient expectations: a mixed methods study. BMJ Open. 2016 Oct 24;6(10):e012244.

Fokkens WJ, Hoffmans R, Thomas M. **Avoid prescribing antibiotics in acute rhinosinusitis**. BMJ. 2014 Oct 17;349:g5703.

Ford AC, Quigley EM, Lacy BE, et al. Efficacy of **Prebiotics, Probiotics, and Synbiotics** in **Irritable Bowel Syndrome and Chronic Idiopathic Constipation**: Systematic Review and Meta-analysis. Am J Gastroenterol. 2014 Jul 29.

Forster AJ, Taljaard M, Oake N, et al. The effect of **hospital acquired** infection with **Clostridium dificile** on length of stay in hospital. CMAJ 2012;184:37-42.

Foster CB, Martinez KA, Sabella C, et al. Patient Satisfaction and **Antibiotic Prescribing for Respiratory Infections** by Telemedicine. Pediatrics. 2019 Aug 1.

Fralick M, Mandonald EM, Gomes T, Antoniou T, Hollands S, Mamdani MM, et al. **Co-trimoxazole and sudden death in patients receiving inhibitors of renin-angiotensin system**: population based study. BMJ 2014;349:g6196.

Francis NA, Ridd MJ, Thomas-Jones E, et al. **Oral and Topical Antibiotics** for Clinically Infected Eczema in Children: A Pragmatic Randomized Controlled Trial in Ambulatory Care. Ann Fam Med. 2017 Mar;15(2):124-130.

Francois Watkins LK, McGee L, Schrag SJ, et al. Epidemiology of invasive **group B streptococcal infections** among nonpregnant adults in the United States, 2008-2016 [online Feb 18, 2019]. JAMA Intern Med.

Franklin M, Wailoo A, Dayer MJ, et al. The Cost-Effectiveness of **Antibiotic Prophylaxis for Patients at Risk of Infective Endocarditis**. Circulation. 2016 Nov 13.

Fraser CL, Biousse V, Newman NJ. **Minocycline-Induced Fulminant Intracranial Hypertension**. Arch Neurol. 2012 Apr 9.

Freedberg DE, Salmasian H, Cohen B, Abrams et al. **Receipt of Antibiotics** in Hospitalized Patients and Risk for **Clostridium difficile Infection** in Subsequent Patients Who Occupy the Same Bed. JAMA Intern Med. 2016 Oct 10

Frieder J, Mouabbi JA, Zein R, et al. **Autoimmune hemolytic anemia associated with trimethoprim-sulfamethoxazole** use. Am J Health Syst Pharm. 2017 Jun 15;74(12):894-897

Fritz SA, Hogan PG, Hayek G, et al. **Household versus individual approaches to eradication of community-associated Staphylococcus aureus in children**: a randomized trial. Clin Infect Dis. 2012 Mar;54(6):743-51.

Gandhi S, Fleet JL, Bailey DG, et al. **Calcium-channel blocker-clarithromycin** drug interactions and acute kidney injury. JAMA. 2013 Dec 18;310(23):2544-53. (esp. nifedipine)

Ganjizadeh-Zavareh S, Sodhi M, Spangehl T, et al. **Oral Fluoroquinolones and Risk of Fibromyalgia**. Br J Clin Pharmacol. 2018 Sep 14.

Ganske CM, Horning KK. **Levofloxacin-induced tendinopathy** of the hip. Ann Pharmacother. 2012 May;46(5):e13.

Garbutt Jane M, Banister Christina, Spitznagel E, et al. **Amoxicillin for Acute Rhinosinusitis**: A Randomized Controlled Trial. *JAMA*. 2012;307(7):685-692. (not effective)

Garcia Miguel Sanchez; Maria Torre Angeles De la; Morales Gracia et al; Clinical Outbreak of **Linezolid-Resistant Staphylococcus aureus** in an Intensive Care Unit, JAMA. 2010;303(22):2260-2264.

Garg P, Ko DT, Bray Jenkyn KM, et al. **Infective Endocarditis Hospitalizations and Antibiotic Prophylaxis** Rates Before and After the 2007 American Heart Association Guidelines Revision. Circulation. 2019 Apr 26.

Gaydos CA, Ako MC, Lewis M, et al. Use of a **Rapid Diagnostic for Chlamydia trachomatis and Neisseria gonorrhoeae** for **Women in the Emergency Department** Can Improve Clinical Management: Report of a Randomized Clinical Trial. Ann Emerg Med. 2018 Nov 1.

Gebre T, Ayele B, Zerihun M, et al. Comparison of **annual versus twice-yearly mass azithromycin treatment for hyperendemic trachoma** in Ethiopia: a cluster-randomised trial. Lancet 2011; published online Dec 21.

Geisler WM, Uniyal A, Lee JY, et al. **Azithromycin versus doxycycline for urogenital Chlamydia trachomatis** infection. N Engl J Med 2015;373:2512-21.

Gerber MA, Baltimore RS, Eaton CB, et al. Prevention of Rheumatic Fever and Diagnosis and Treatment of Acute **Streptococcal Pharyngitis**. A Scientific Statement From the American Heart Association Rheumatic Fever, Endocarditis, and Kawasaki Disease Committee of the Council on Cardiovascular Disease in the Young, the Interdisciplinary Council on Functional Genomics and Translational Biology, and the Interdisciplinary Council on Quality of Care and Outcomes Research. Circulation. 2009 Feb 26.

Gerber JS, Prasad PA, Fiks AG, et al. Effect of an **outpatient antimicrobial stewardship** intervention on broad-spectrum antibiotic prescribing by primary care pediatricians: a randomized trial. JAMA. 2013 Jun 12;309(22):2345-52.

Gerber JS, Bryan M, Ross RK, et al. **Antibiotic Exposure** During the First 6 Months of Life and **Weight Gain** During Childhood. JAMA. 2016 Mar 22-29;315(12):1258-65.

Gerber JS, Ross RK, Bryan M, et al. Association of **Broad- vs Narrow-Spectrum Antibiotics** With Treatment Failure, Adverse Events, and Quality of Life in Children With Acute Respiratory Tract Infections. JAMA. 2017 Dec 19;318(23):2325-2336

Geriak M, Haddad F, Rizvi K, et al. Clinical Data on **Daptomycin Plus Ceftaroline** Versus Standard of Care Monotherapy in the Treatment of **Methicillin-Resistant Staphylococcus aureus Bacteremia**. Antimicrob Agents Chemother. 2019 Mar 11.

Gibson PG, Yang IA, Upham JW, et al. Effect of **azithromycin on asthma exacerbations** and quality of life in adults with persistent uncontrolled asthma (**AMAZES**): a randomised, double-blind, placebo-controlled trial. Lancet 2017; online July 4.

Gjika E, Beaulieu JY, Vakalopoulos K, et al. **Two weeks versus four weeks of antibiotic therapy** after surgical drainage for native joint bacterial arthritis: a prospective, randomised, non-inferiority trial. Ann Rheum Dis. 2019 Apr 16.

Gillies M, Ranakusuma A, Hoffmann T, et al. Common **harms from amoxicillin**: a systematic review and meta-analysis of randomized placebo-controlled trials for any indication. CMAJ. 2014 Nov 17.

Gjika E, Beaulieu JY, Vakalopoulos K, et al. **Two weeks versus four weeks of antibiotic therapy** after surgical drainage for native joint bacterial arthritis: a prospective, randomised, non-inferiority trial. Ann Rheum Dis. 2019 Aug;78(8):1114-1121.

Golan Y. Current Treatment Options for Acute **Skin and Skin-structure Infections**. Clin Infect Dis. 2019 Apr 8;68(Supplement_3):S206-S212.

Guery B, Galperine T, Barbut F. **Clostridioides difficile**: diagnosis and treatments. BMJ. 2019 Aug 20;366:l4609.Pdf Laska IF, Chalmers JD. Treatment to prevent exacerbations in bronchiectasis: macrolides as first line? Eur Respir J. 2019 Jul 18;54(1).

Gulliford MC, Prevost AT, Charlton J, et al. Effectiveness and safety of electronically delivered **prescribing feedback and decision support on antibiotic use for respiratory illness** in primary care: REDUCE cluster randomised trial. BMJ. 2019 Feb 12;364:l236.

Gillison ML, Broutian T, Pickard R, et al. Prevalence of **oral HPV infection** in the United States, 2009-2010. JAMA. doi:10.1001/jama.2012.101.

Giudicessi JR, Ackerman MJ. **Azithromycin and risk of sudden cardiac death**: Guilty as charged or falsely accused? Cleve Clin J Med. 2013 Sep;80(9):539-44.

Giufrè M, Monaco M, Accogli M, et al; PAMURSA Study Group. Emergence of the **colistin resistance mcr-1** determinant in commensal **Escherichia coli** from residents of **long-term-care facilities** in Italy. J Antimicrob Chemother. 2016 Jun 3. [Epub ahead of print]

Gnann JW Jr, Whitley RJ. Clinical Practice. **Genital Herpes**. N Engl J Med. 2016 Aug 18;375(7):666-74.

Goff DA, Kullar R, Goldstein EJ, et al. A **global** call from five countries to collaborate in **antibiotic stewardship**: united we succeed, divided we might fail. Lancet Infect Dis. 2016 Nov 17.

Goff DA, Kullar R, Bauer KA, File TM Jr. **Eight Habits of Highly Effective Antimicrobial Stewardship Programs** to Meet the Joint Commission Standards for Hospitals. Clin Infect Dis. 2017 Apr 15;64(8):1134-1139.

GOLD Initiative. Guidelines. **GOLD COPD** Initiative; 2008. Available from: www.goldcopd. com/GuidelineList.asp. Accessed 2008 Oct 31.

Goldenberg JZ, Mertz D, Johnston BC. **Probiotics to Prevent Clostridium difficile Infection** in Patients Receiving Antibiotics. JAMA. 2018 Jul 19.

Goldenberg JZ, Yap C, Lytvyn L, et al. **Probiotics for the prevention of Clostridium difficile-associated diarrhea** in adults and children. Cochrane Database Syst Rev. 2017 Dec 19;12:CD006095. Based on this systematic review and meta-analysis of 31 randomized controlled trials including 8672 patients, moderate certainty evidence suggests that probiotics are effective for preventing CDAD (NNTB = 42 patients, 95% CI 32 to 58). Our post hoc subgroup analyses to explore heterogeneity indicated that probiotics are effective among trials with a CDAD baseline risk >5% (NNTB = 12; moderate certainty evidence), but not among trials with a baseline risk ≤5% (low to moderate certainty evidence). Although adverse effects were reported among 32 included trials, there were more adverse events among patients in the control groups. The short-term use of probiotics appears to be safe and effective when used along with antibiotics in patients who are not immunocompromised or severely debilitated. Despite the need for further research, hospitalized patients, particularly those at high risk of CDAD, should be informed of the potential benefits and harms of probiotics.

Goldman JL, Jackson MA, Herigon JC, et al. Trends in **adverse reactions to trimethoprim-sulfamethoxazole**. Pediatrics. 2013 Jan;131(1):e103-8.

Goldman JL, Jackson MA. Tip of the Iceberg: Understanding the **Unintended Consequences of Antibiotics**. Pediatrics. 2015 Aug;136(2):e492-3.

Gonzales R, Anderer T, McCulloch CE, et al. A cluster randomized trial of **decision support strategies for reducing antibiotic use** in acute bronchitis [published online January 14, 2013]. JAMA Intern Med. doi:10.1001/jamainternmed .2013.1984.

Goodman DM, Lynm C, Livingston EH. JAMA **patient page. Ear problems in children**. JAMA. 2013 Jun 5;309(21):2284.

Gottesman BS, Carmeli Y, Shitrit P, Chowers M. Impact of **quinolone restriction on resistance** patterns of Escherichia coli isolated from urine by culture in a community setting. Clin Infect Dis. 2009 Sep 15;49(6):869-75.

Gottlieb M, DeMott JM, Hallock M, et al. Systemic Antibiotics for the Treatment **of Skin and Soft Tissue Abscesses**: A Systematic Review and Meta-Analysis. Ann Emerg Med. 2018 Mar 9.

Goyal V, Grimwood K, Byrnes CA, et al. **Amoxicillin-clavulanate versus azithromycin for respiratory exacerbations in children with bronchiectasis** (**BEST-2**): a multicentre, double-blind, non-inferiority, randomised controlled trial. Lancet. 2018 Oct 6;392(10154):1197-1206.

Grabe M, Bishop MC, Bjerklund-Johansen TE, et al. **Epididymitis and orchitis**: Guidelines on urological infections. Arnhem, The Netherlands: **European** Association of Urology (EAU); 2009 Mar. http://www.uroweb.org/fileadmin/tx_eauguidelines/2009/Full/Urological_Infections.pdf

Grabe M, Bishop MC, Bjerklund-Johansen TE, et al. **Sexually transmitted infections**: Guidelines on urological infections. Arnhem, The Netherlands: **European** Association of Urology (EAU); 2009 Mar.

Grabe M, Bishop MC, Bjerklund-Johansen TE, et al. **Urethritis**: Guidelines on urological infections. Arnhem, The Netherlands: **European** Association of Urology (EAU); 2009 Mar.

Grad YH, Kirkcaldy RD, Trees D, et al. Genomic epidemiology of Neisseria **gonorrhoaea with reduced susceptibility to cefixime** in the USA: a retrospective observational study. Lancet Infect Dis 2014; online Jan 22

Gradison M. **Pelvic inflammatory disease**. Am Fam Physician. 2012 Apri15;85(8):791-6.

Grigoryan L, Germanos G, Zoorob R, et al**. Use of Antibiotics Without a Prescription** in the U.S. Population: A Scoping Review. Ann Intern Med. 2019 Jul 23.

Grijalva Carlos G.; Nuorti J. Pekka; Griffin Marie R.. **Antibiotic Prescription Rates** for Acute Respiratory Tract Infections in US Ambulatory Settings. JAMA. 2009;302(7):758-766.

Groves MJ. **Genital Herpes**: A Review. Am Fam Physician. 2016;93(11):928-934.

Gu D, Dong N, Zheng Z, et al. A fatal outbreak of ST11 **carbapenem resistant hypervirulent Klebsiella pneumoniae** in a Chinese hospital: a molecular epidemiological study. Lancet Infect Dis 2017; online August 29.

Guery B, Menichetti F, Anttila V-J, et al. Extended-pulsed **fidaxomicin versus vancomycin for Clostridium difficile** infection in patients 60 years and older (**EXTEND**): a randomised, controlled, open-label, phase 3b/4 trial. Lancet Infect Dis 2017; online Dec 19.

Guh AY, Kutty PK. **Clostridioides difficile** Infection. Ann Intern Med. 2018 Oct 2;169(7):ITC49-ITC64.

Gulliford MC, Moore MV, Little P, et al. Safety of reduced antibiotic prescribing for self limiting respiratory tract infections in primary care: cohort study using electronic health records. BMJ 2016;254:i3410.

Guo Q, Goldenberg JZ, Humphrey C, El Dib R, Johnston BC. Probiotics for the prevention of pediatric antibiotic-associated diarrhea. Cochrane Database Syst Rev. 2019 Apr 30;4:CD004827. The overall evidence suggests a moderate protective effect of probiotics for preventing AAD (NNTB 9, 95% CI 7 to 13). Using five criteria to evaluate the credibility of the subgroup analysis on probiotic dose, the results indicate the subgroup effect based on high dose probiotics (≥ 5 billion CFUs per day) was credible. Based on high-dose probiotics, the NNTB to prevent one case of diarrhea is 6 (95% CI 5 to 9). The overall certainty of the evidence for the primary endpoint, incidence of AAD based on high dose probiotics was moderate due to the minor issues with risk of bias and inconsistency related to a diversity of probiotic agents used. Evidence also suggests that probiotics may moderately reduce the duration of diarrhea, a reduction by almost one day. The benefit of high dose probiotics (e.g. Lactobacillus rhamnosus orSaccharomyces boulardii) needs to be confirmed by a large well-designed multi-centered randomized trial. It is premature to draw firm conclusions about the efficacy and safety of 'other' probiotic agents as an adjunct to antibiotics in children. Adverse event rates were low and no serious adverse events were attributable to probiotics.

Gupta A, Cifu AS, Khanna S. **Diagnosis and Treatment of Clostridium difficile Infection**. JAMA. 2018 Sep 11;320(10):1031-1032.

Gupta A, Mody P, Pandey A. Inappropriate Antibiotic Therapy in a Patient With Heart Failure and Prolonged **QT** Interval: A Teachable Moment. JAMA Intern Med. 2015 Nov 1;175(11):1748-9. (**quetiapine** & **moxifloxacin**)

Gupta A, Khanna S. **Repeat Clostridium difficile Testing**. JAMA. 2016 Dec 13;316(22):2422-2423

Gurnee EA et al. Gut colonization of **healthy children and their mothers with pathogenic ciprofloxacin-resistant Escherichia coli**. J Infect Dis 2015 Dec 15; 212:1862.

Gutiérrez-Gutiérrez B, Salamanca E, de Cueto M, et al, for the REIPI/ESGBIS/ INCREMENT Investigators. Effect of appropriate combination therapy on mortality of patients with bloodstream infections due to **carbapenemaseproducing Enterobacteriaceae (INCREMENT):** a retrospective cohort study. Lancet Infectious Dis 2017; online April 22.

Ha NB, Yang K, Hanigan S, et al. Impact of a Guideline for the Management of **Antimicrobial/Warfarin Interactions** in the Inpatient Setting and Across Transition of Care. Ann Pharmacother. 2016 Jun 16

Habib G, Hoen B, Tornos P, et al. Guidelines on the prevention, diagnosis, and treatment of **infective endocarditis** (new version **2009**). Eur Heart J 2009; DOI:10.1093/eurheartj/ehp285. http://www.escardio.org/guidelines-surveys/esc-guidelines/GuidelinesDocuments/guidelines-IE-FT.pdf

Hainer BL, Gibson MV. **Vaginitis**: Diagnosis and Treatment.Am Fam Physician. 2011 Apr 1;83(7):807-815.

Hallsworth M, Chadborn T, Sallis A, et al. Provision of **social norm feedback** to high **prescribers of antibiotics** in general practice: a pragmatic national randomised controlled trial. Lancet 2016; online Feb 18.

Hamad Y, Warren DK. **Black Hairy Tongue. (minocycline)** N Engl J Med. 2018 Sep 6;379(10):e16.

Hamilton D, Lipscomb K. **A man with fever and breathlessness**. BMJ. 2019 Mar 21;364:l1085.

Hamilton KW, Cifu AS. Diagnosis and Management of **Infectious Diarrhea**. JAMA. 2019 Feb 14.

Han JH, Sullivan N, Leas BF, et al. **Cleaning Hospital Room Surfaces** to Prevent Health Care-Associated Infections: A Technical Brief. Ann Intern Med. 2015 Aug 11.

Han MK, Tayob N, Murray S, et al. Predictors of **chronic obstructive pulmonary disease exacerbation** reduction in response to daily **azithromycin** therapy. Am J Respir Crit Care Med. 2014 Jun 15;189(12):1503-8.

Handley N, Unger A. **Antibiotic Overuse and Paronychia**: A Teachable Moment. JAMA Intern Med. 2015 Nov 16:1-2.

Hanet MS, Jamart J, Pinheiro Chaves A. **Fluoroquinolones or fortified antibiotics for treating bacterial keratitis**: systematic review and meta-analysis of comparative studies. Can J Ophthalmol. 2012 Dec;47(6):493-9.

Hanretty AM, Gallagher JC. **Shortened courses** of antibiotics for bacterial infections: A systematic review of randomized controlled trials. Pharmacotherapy. 2018 Apr 20.

Hansen V, Oren E, Dennis LK, et al. **Infectious Disease Mortality Trends in the United States**, 1980-2014. JAMA. 2016 Nov 22;316(20):2149-2151.

Hanson AL, Crosby RD, Basson MD. Patient Preferences for **Surgery or Antibiotics for the Treatment of Acute Appendicitis**. JAMA Surg. 2018 Jan 10.

Hao Q, Dong BR, Wu T. **Probiotics** for preventing acute upper respiratory tract infections. Cochrane Database Syst Rev. 2015 Feb 3;2:CD006895. Probiotics were better than placebo in reducing the number of participants experiencing episodes of acute URTI, the mean duration of an episode of acute URTI, antibiotic use and cold-related school absence. This indicates that probiotics may be more beneficial than placebo for preventing acute URTIs. However, the quality of the evidence was low or very low.

Harbarth S et al. Randomized non-inferiority trial to compare **trimethoprim/sulfamethoxazole plus rifampicin versus linezolid** for the treatment of MRSA infection. *J Antimicrob Chemother* 2014 Sep 10.

Harmes KM, Blackwood RA, Burrows HL et al. **Otitis Media**: Diagnosis and Treatment. Am Fam Physician. 2013 Oct 1;88(7):435-440.

Harnden Anthony .**Whooping cough**. BMJ 2009;338:b1772, doi: 10.1136/bmj.b1772 (Published 21 May 2009)

Harris AD, Pineles L, Belton B, et al; and the **BUGG** Investigators. **Universal glove and gown** use and acquisition of antibiotic resistant bacteria in the ICU: a randomized trial (BUGG). JAMA. doi:10.1001/JAMA.2013.277815.

Harris AM, Hicks LA, Qaseem A; High Value Care Task Force of the American College of Physicians and for the Centers for Disease Control and Prevention. **Appropriate Antibiotic Use for Acute Respiratory Tract Infection in Adults**: Advice for High-Value Care From the American College of Physicians and the Centers for Disease Control and Prevention. Ann Intern Med. 2016 Jan 19.

Harris PN, Tambyah PA, Paterson DL. **β-lactam and β-lactamase inhibitor combinations in the treatment of extended-spectrum β-lactamase producing Enterobacteriaceae**: time for a reappraisal in the era of few antibiotic options? Lancet Infect Dis. 2015 Feb 20. pii: S1473-3099(14)70950-8.

Hart T, Milner R, Cifu A. Management of a **Diabetic Foot**. JAMA. 2017 Oct 10;318(14):1387-1388.

Härtel C, Pagel J, Rupp J, et al; German Neonatal Network. Prophylactic Use of **Lactobacillus acidophilus/Bifidobacterium infantis Probiotics** and Outcome in Very Low Birth Weight Infants. J Pediatr. 2014 Aug;165(2):285-289.e1.

Hassoun A. **Clostridium difficile associated disease**. BMJ. 2018 Oct 29;363:k4369.

Havers FP, Hicks LA, Chung JR, et al. Outpatient **Antibiotic Prescribing for Acute Respiratory Infections** During Influenza Seasons. **JAMA Network Open.** 2018;1(2):e180243.

Hawker JI, Smith S, Smith GE, et al. **Trends in antibiotic prescribing in primary care** for clinical syndromes subject to national recommendations to reduce antibiotic resistance, **UK** 1995-2011: analysis of a large database of primary care consultations. J Antimicrob Chemother. 2014 Dec;69(12):3423-30.

Hay AD, Redmond NM, Turnbull S, et al. Development and internal validation of a **clinical rule** to improve antibiotic use in children presenting to primary care with acute **respiratory tract infection and cough**: a prognostic cohort study. Lancet Respir Med 2016; online Sept 1.

Hay AD, Little P, Harnden A, et al. Effect of Oral **Prednisolone on Symptom Duration and Severity in Nonasthmatic Adults With Acute Lower Respiratory Tract Infection**: A Randomized Clinical Trial. JAMA. 2017 Aug 22;318(8):721-730.

Hayward G, Thompson MJ, Perera R, et al. **Corticosteroids** as standalone or add-on treatment for **sore throat**. Cochrane Database Syst Rev. 2012 Oct 17;10:CD008268. doi: 10.1002/14651858.CD008268.pub2. Oral or intramuscular corticosteroids, in addition to antibiotics, increase the likelihood of both resolution and improvement of pain in participants with sore throat.

Hayward GN, Hay AD, Moore MV, et al. Effect of Oral **Dexamethasone** Without Immediate Antibiotics vs Placebo on **Acute Sore Throat** in Adults: A Randomized Clinical Trial. JAMA. 2017 Apr 18;317(15):1535-1543.

Head K, Chong LY, Piromchai P, et al. **Systemic and topical antibiotics** for chronic **rhinosinusitis**. Cochrane Database Syst Rev. 2016 Apr 26;4:CD011994. We found very little evidence that systemic antibiotics are effective in patients with chronic rhinosinusitis. We did find moderate quality evidence of a modest improvement in disease-specific quality of life in adults with chronic rhinosinusitis without polyps receiving three months of a macrolide antibiotic. The size of improvement was moderate (0.5 points on a five-point scale) and only seen at the end of the three-month treatment; by three months later no difference was found.Despite a general understanding that antibiotics can be associated with adverse effects, including gastrointestinal disturbances, the results in this review were very uncertain because the studies were small and few events were reported.No RCTs of topical antibiotics met the inclusion criteria.More research in this area, particularly evaluating longer-term outcomes and adverse effects, is required.

Health Canada Nov/11 **Fluoroquinolone** antibiotics: patients with **myasthenia gravis** may risk increased muscle weakness.

Health Canada May/13: Zithromax/Zmax SR (**azithromycin**) - Risk of Potentially Fatal Irregular (**QT**) Heart Beats - Pfizer Canada Inc.

Health Canada. Notice – antimicrobials product labelling. November 16, 2015. www.hc-sc.gc.ca/dhp-mps/prodpharma/activit/announce-annonce/notice-amr-avis-ram-eng.php (accessed November 27, 2015). (Health Canada is mandating the inclusion of precautionary statements in **antimicrobial product labelling to encourage prudent prescribing and use of antimicrobial drugs**.)
Health Canada Dec/15: **Biseptol 480** contains sulfamethoxazole & trimethoprim.
Health Canada Dec/15: **Oxycort** contains oxytetracycline & hydrocortisone.
Health Canada's Jan/17 recent safety review of oral and injectable **fluoroquinolones**, a class of antibiotics, found that in rare cases some known side effects may be persistent or disabling. This includes muscular issues such as tendonitis and Achilles tendon rupture, nerve damage such as peripheral neuropathy, and central nervous system issues such as anxiety, dizziness and confusion.
Health Canada Aug/18 is warning Canadians of the potential **risk of cancer relapse in patients with cancer of the blood and lymph nodes who have undergone stem cell transplant and are taking long-term azithromycin** (Zithromax). **HealthMap** http://www.healthmap.org/en/
Health Canada. Summary Safety Review – Fluoroquinolones – assessing the potential risk of aneurysm (a balloon-like bulge) and dissection (a separation or tear in the layers of the wall) of the aorta (a major blood vessel). June 27, 2019. https://hpr-rps.hres.ca/reg-content/summary-safety-review-detail.php?lang=en&linkID=SSR00226 (accessed July 12, 2019).
Heianza Y, Zheng Y, Ma W, et al. Duration and life-**stage of antibiotic use and risk of cardiovascular events in women**. Eur Heart J. 2019 Apr 24.
Hemkens LG, Saccilotto R, Reyes SL, et al. **Personalized Prescription Feedback** Using Routinely Collected Data to **Reduce Antibiotic Use** in Primary Care: A Randomized Clinical Trial. JAMA Intern Med. 2016 Dec 27.
Hensgens MPM et al. Diarrhoea in general practice: When should a **Clostridium difficile** infection be considered? Results of a nested case control study. Clin Microbiol Infect 2014 Jul 7.
Herath SC, Normansell R, Maisey S, et al. **Prophylactic antibiotic therapy** for chronic obstructive pulmonary disease (COPD). Cochrane Database Syst Rev. 2018 Oct 30;10:CD009764. Use of continuous and intermittent prophylactic antibiotics results in a clinically significant benefit in reducing exacerbations in COPD patients. All studies of continuous and intermittent antibiotics used macrolides, hence the noted benefit applies only to the use of macrolide antibiotics prescribed at least three times per week. The impact of pulsed antibiotics remains uncertain and requires further research.The studies in this review included mostly participants who were frequent exacerbators with at least moderate-severity COPD. There were also older individuals with a mean age over 65 years. The results of these studies apply only to the group of participants who were studied in these studies and may not be generalisable to other groups.Because of concerns about antibiotic resistance and specific adverse effects, consideration of prophylactic antibiotic use should be mindful of the balance between benefits to individual patients and the potential harms to society created by antibiotic overuse. Monitoring of significant side effects including hearing loss, tinnitus, and long QTc in the community in this elderly patient group may require extra health resources.
Herath SC, Poole P. **Prophylactic antibiotic therapy** for chronic obstructive pulmonary disease (COPD). Cochrane Database of Systematic Reviews 2013, Issue 11. Art. No.: CD009764. DOI: 10.1002/14651858.CD009764.pub2. Use of continuous prophylactic antibiotics results in a clinically significant benefit in reducing exacerbations in COPD patients. All trials of continuous antibiotics used macrolides hence the noted benefit applies only to the use of continuous macrolide antibiotics. The impact of pulsed antibiotics remains uncertain and requires further research. The trials in this review included patients who were frequent exacerbators and needed treatment with antibiotics or systemic steroids, or who were on supplemental oxygen. There were also older individuals with a mean age of 66 years. The results of these trials apply only to the group of patients who were studied in these trials and may not be generalisable to other groups. Because of concerns about antibiotic resistance and specific adverse effects, consideration of prophylactic antibiotic use should be mindful of the balance between benefits to individual patients and the potential harms to society created by antibiotic overuse.
Herath SC, Poole P. **Prophylactic antibiotic therapy in chronic obstructive pulmonary disease**. JAMA. 2014 Jun 4;311(21):2225-6.
Herberg JA, Kaforou M,Wright VJ, et al; IRIS Consortium. Diagnostic test accuracy of a 2-transcript host **RNA signature** for discriminating **bacterial vs viral** infection in febrile children. JAMA. doi:10.1001/jama.2016.11236.
Hersh AL et al. **Antibiotic prescribing in ambulatory pediatrics** in the United States. Pediatrics. 2011 Dec;128(6):1053-61.
Hersh AL, Jackson MA, Hicks LA et al. Principles of **judicious antibiotic prescribing for upper respiratory tract infections in pediatrics**. Pediatrics. 2013 Dec;132(6):1146-54.
Hersh AL, Kronman MP. **Inappropriate Antibiotic Prescribing**: Wind at Our Backs or Flapping in the Breeze? Pediatrics. 2017 Mar 7.
Hersh AL, Fleming-Dutra KE. **Vaccines** and Outpatient Antibiotic Stewardship. Pediatrics. 2017;140(3):e20171695
Hingorani A, LaMuraglia GM, et al. The management of **diabetic foot**: A clinical practice guideline by the Society for Vascular Surgery in collaboration with the **American** Podiatric Medical Association and the Society for Vascular Medicine. J Vasc Surg. 2016 Feb;63(2 Suppl):3S-21S.
Hirotsu K, Dang TM, Li S, et al. Association of **Antibiotic Resistance With Antibiotic Use** for Epidermal Growth Factor Receptor Inhibitor-Related Papulopustular Eruption. JAMA Dermatol. 2019 Apr 24.
Ho JM, Juurlink DN. Considerations when prescribing **trimethoprim-sulfamethoxazole**. CMAJ. 2011 Oct 11.
Hoberman A, Paradise JL, Rockette HE, et al. **Shortened** Antimicrobial **Treatment for Acute Otitis Media in Young Children**. N Engl J Med. 2016 Dec 22;375(25):2446-2456.
Hocking JS, Temple-Smith M, Guy R, et al; ACCEPt Consortium. Population effectiveness of **opportunistic chlamydia testing in primary care in Australia**: a cluster-randomised controlled trial. Lancet. 2018 Oct 20;392(10156):1413-1422.
Hollis A, Ahmed Z. **Preserving antibiotics**, rationally. N Engl J Med. 2013 Dec 26;369(26):2474-6
Hollm-Delgado MG, Stuart EA, Black RE. Acute Lower Respiratory Infection Among **Bacille Calmette-Guerin** (BCG)-Vaccinated Children. Pediatrics. 2014 Jan;133(1):e73-81.
Holmes AH, Moore LSP, Sundsfj ord A, et al. Understanding the **mechanisms and drivers of antimicrobial resistance**. Lancet 2015; online Nov 18.
Holmes A, Holmes M, Gottlieb T, et al. **End non-essential use of antimicrobials in livestock**. BMJ. 2018 Jan 29;360:k259.
Holt PG, Sly PD. **Environmental Microbial Exposure** and Protection against **Asthma**. N Engl J Med. 2015 Dec 24;373(26):2576-8.
Honkila M, Wikström E, Renko M, et al. Probability of **vertical transmission** of **Chlamydia trachomatis** estimated from national registry data. Sex Transm Infect. 2017 Feb 21.
Hoofnagle JH, Björnsson ES. **Drug-Induced Liver Injury** - Types and Phenotypes. N Engl J Med. 2019 Jul 18;381(3):264-273.
Hook EW Rd. **Syphilis**. Lancet. 2016 Dec 16. pii: S0140-6736(16)32411-4
Hook EW 3rd. Continued Evolution of **Gonococcal Antimicrobial Resistance**. Clin Infect Dis. 2017 May 26.
Hopman J, Meijer C, Kenters N, et al. Risk Assessment After a Severe **Hospital-Acquired Infection Associated With Carbapenemase-Producing Pseudomonas aeruginosa**. JAMA Netw Open. 2019 Feb 1;2(2):e187665.
Hornik CP, Benjamin DK Jr, Smith PB, Pencina et al. Electronic Health Records and Pharmacokinetic Modeling to Assess the Relationship between Ampicillin Exposure and Seizure Risk in Neonates. J Pediatr. 2016 Nov;178:125-129.e1
Hota SS, Poutanen SM. **Fecal microbiota transplantation for recurrent Clostridium difficile** infection. CMAJ. 2018 Jun 18;190(24):E746.
Hota SS, Sales V, Tomlinson G, et al. Oral **Vancomycin Followed by Fecal Transplantation** Versus Tapering Oral Vancomycin Treatment for Recurrent **Clostridium difficile Infection**: An Open-Label, Randomized Controlled Trial. Clin Infect Dis. 2017 Feb 1;64(3):265-271.
Horton DB, Scott FI, Haynes K, et al.. **Antibiotic Exposure and Juvenile Idiopathic Arthritis**: A Case-Control Study. Pediatrics. 2015 Jul 20.
Huang DT, Yealy DM, Filbin MR, et al. **Procalcitonin-Guided Use of Antibiotics** for Lower Respiratory Tract Infection. N Engl J Med. 2018 May 20.
Huang HB, et al. **Procalcitonin-guided antibiotic therapy in intensive care unit patients**: a systematic review and meta-analysis. Ann Intensive Care. 2017 Nov 22;7(1):114.
Huang L, Yin Y, Yang L, et al. Comparison of antibiotic therapy and appendectomy for acute uncomplicated appendicitis in children: a meta-analysis [online Mar 27, 2017].JAMA Pediatr. doi:10.1001/jamapediatrics.2017.0057
Huang SS, Septimus E, Kleinman K, et al. **Chlorhexidine versus routine bathing** to prevent multidrug-resistant organisms and all-cause bloodstream infections in general medical and surgical units (ABATE Infection trial): a cluster-randomised trial. Lancet. 2019 Mar 4.
Huang SS, Septimus E, Kleinman K, et al. **Targeted versus universal decolonization** to prevent ICU infection. N Engl J Med 2013. DOI: 10.1056/NEJMoa1207290.
Huang SS, Singh R, McKinnell JA, et al; Project CLEAR Trial. **Decolonization** to Reduce Postdischarge Infection Risk among **MRSA Carriers**. N Engl J Med. 2019 Feb 14;380(7):638-650.
Huang DT, Yealy DM, Filbin MR, et al. **Procalcitonin-Guided Use of Antibiotics for Lower Respiratory Tract Infection**. N Engl J Med. 2018 Jul 19;379(3):236-249.
Hui CPS; Canadian Paediatric Society, Infectious Diseases and Immunization Committee. Practice point. **Acute otitis externa**. Paediatr Child Health 2013;18:96-8. http://www.cps.ca/en/documents/position/acute-otitis-externa (accessed February 19, 2013).
Hurley HJ et al. **Avoidable antibiotic exposure for uncomplicated skin and soft tissue** infections in the ambulatory care setting. Am J Med 2013 Dec; 126:1099.
Hurst JR, Wedzicha JA. Management and prevention of chronic obstructive pulmonary disease **exacerbations**: a state of the art review. BMC Med. 2009 Aug 7;7:40.
Huskins WC et al. **Intervention to reduce transmission of resistant bacteria** in intensive care. N Engl J Med 2011 Apr 14; 364:1407.
Hvas CL, Jørgensen SMD, Jørgensen SP, et al. Fecal Microbiota Transplantation is Superior to Fidaxomicin for **Treatment of Recurrent Clostridium difficile Infection**. Gastroenterology. 2019 Jan 2
Ibrahim LF, Hopper SM, Donath S, et al. **Development and Validation of a Cellulitis Risk Score**: The Melbourne ASSET Score. Pediatrics. 2019 Jan 3.
Ihm C, Sutton JD, Timbrook TT, Spivak ES. Treatment Duration and Associated Outcomes for **Skin and Soft Tissue Infections in Patients With Obesity** or Heart Failure. Open Forum Infect Dis. 2019 May 7;6(6):ofz217.
Inghammar M, Svanström H, Melbye M, et al. Oral **fluoroquinolone use and serious arrhythmia**: bi-national cohort study. BMJ. 2016 Feb 26;352:i843.
Iredell J, Brown J, Tagg K. **Antibiotic resistance in Enterobacteriaceae**: mechanisms and clinical implications. BMJ. 2016 Feb 8;352:h6420.
Isanaka S, Langendorf C, Berthé F, et al. Routine **Amoxicillin** for Uncomplicated Severe Acute **Malnutrition** in Children. N Engl J Med. 2016 Feb 4;374(5):444-53.
Ison C, Town K, Obi C, et al, GRASP collaborative group. **Decreased susceptibility** to **cephalosporins** among **gonococci**: data from Gonococcal Resistance to Antimicrobials Surveillance Programme (GRASP) in England and Wales, 2007–2011. Lancet Infect Dis 2013; online June 11.
Imamura H, KurokawaY, Tsujinaka T, et al. **Intraoperative versus extended antimicrobial prophylaxis** after gastric cancer surgery: a phase 3, open-label, randomised controlled, non-inferiority trial. Lancet Infect Dis 2012; published online Jan 31.
Ivers Noah, Arroll Bruce, Allan G. Michael. **Delayed antibiotic prescriptions** for URTIs. Can Fam Physician November 2011 57: 1287.
Iversen K, Ihlemann N, Gill SU, et al. **Partial Oral versus Intravenous Antibiotic Treatment** of **Endocarditis**. (**POET**) N Engl J Med. 2018 Aug 28.
Iyer PG, Murphy TF. **Chronic obstructive pulmonary disease**: role of **bacteria** and updated guide to antibacterial selection in the older patient. Drugs Aging. 2009;26(12):985-95. doi: 10.2165/11315700-000000000-00000. Penicillin, amoxicillin, cotrimoxazole (trimethoprim/sulfamethoxazole) and doxycycline should not be used as an initial antibacterial because of resistance patterns. We recommend second-/third-generation cephalosporins, amoxicillin/clavulanic acid, azithromycin and respiratory fluoroquinolones as initial choices.
Jackson MA, Schutze GE. The Use of **Systemic and Topical Fluoroquinolones**. Pediatrics.2016;138(5):e20162706
Jacobs K, Vu DM, Mony V, et al. **Congenital Syphilis Misdiagnosed** as Suspected Nonaccidental Trauma. Pediatrics. 2019 Sep 19.
Jahanfar S, Ng CJ, Teng CL. Antibiotics for **mastitis** in breastfeeding women. Cochrane Database of Systematic Reviews 2009, Issue 1. Art. No.: CD005458.
Jain SR, Hosseini-Moghaddam SM, Dwek P, et al. **Infectious diseases specialist management** improves outcomes for outpatients diagnosed with **cellulitis** in the emergency department: a double cohort study. Diagn Microbiol Infect Dis. 2017 Apr;87(4):371-375.
Jain R et al. Veterans Affairs initiative to **prevent methicillin-resistant Staphylococcus aureus infections**. N Engl J Med 2011 Apr 14; 364:1419.
Janszky I, Gémes K, Ahnve S, Asgeirsson H, Möller J. **Invasive Procedures Associated With the Development of Infective Endocarditis**. J Am Coll Cardiol. 2018 Jun 19;71(24):2744-2752.
Jarlier Vincent; Trystram David; Brun-Buisson Christian; et al.; for the Collegiale de Bacteriologie-Virologie-Hygiene des Hopitaux Universitaires de l'Ile de France **Curbing Methicillin-Resistant Staphylococcus** aureus in 38 French Hospitals Through a 15-Year Institutional Control Program. Arch Intern Med. 2010;170(6):552-559.
Jenkins Timothy C.; Knepper Bryan C.; Sabel Allison L.; et al. **Decreased Antibiotic Utilization After Implementation of a Guideline for Inpatient Cellulitis and Cutaneous Abscess**. Arch Intern Med. 2011;171(12):1072-1079.
Jensen JS. **Mycoplasma genitalium**: yet another challenging STI. Lancet Infect Dis 2017; online July 9.
Jerschow E, Lin RY, Scaperotti MM, et al. **Fatal anaphylaxis** in the United States, 1999-2010: Temporal patterns and demographic associations. J Allergy Clin Immunol. 2014 Sep 26.

Jevsevar DS, Abt E. The New **AAOS-ADA** Clinical Practice Guideline on **Prevention of Orthopaedic Implant Infection** in Patients Undergoing **Dental Procedures**. J Am Acad Orthop Surg. 2013 Mar;21(3):195-7.

Jin J. JAMA patient page. **Clostridium difficile infection**. JAMA. 2014 Nov 5;312(17):1818.

Jin J. JAMA **Patient Page. Screening for Syphilis**. JAMA. 2016 Jun 7;315(21):2367.

Joachim L, Campos D Jr, Smeesters PR. Pragmatic **Scoring System for Pharyngitis in Low-Resource Settings**. Pediatrics. 2010 Aug 9. [Epub ahead of print]

Johnson AP, Hughes G. The prospect of **untreatable gonorrhoea**. BMJ. 2017 Aug 25;358:j3973

Johnston BC, Ma SSY, Goldenberg JZ, et al. **Probiotics Meta-analysis**. Ann Intern Med 2012; 157(12):878-888. {20 RCTs, n=3818, mostly adult; ↓ CDAD incidence vs placebo 2.0% vs 5.9%, NNT=26$_{/14\ days}$; ↓ ABX associated diarrhea NNT=13. May ↓ cancer mortality risk. Avoid in immunocompromised.}

Johnston BC, Goldenberg JZ, et al. **Probiotics** and the **Prevention of Antibiotic-Associated Diarrhea** in Infants and Children. JAMA. 2016 Oct 11;316(14):1484-1485.

Johnston C, Saracino M, Kuntz S, et al. **Standard-dose and high-dose daily antiviral** (aciclovir, valaciclovir) therapy for short episodes of **genital HSV-2 reactivation**: three randomised, open-label, cross-over trials. Lancet 2012; published online Jan.

Johnstone J, Patel SN; Provincial Infectious Diseases Advisory Committee – Infection Prevention and Control (PIDAC-IPC). An **emerging multidrug-resistant bacteria (CPE)**. CMAJ. 2017 Sep 5;189(35):E1115

Johnston SL, Szigeti M, Cross M, et al; **AZALEA** Trial Team. **Azithromycin** for acute exacerbations of **asthma**: the AZALEA randomized clinical trial [online Sept 19, 2016].JAMA Intern Med. doi:10.1001/jamainternmed.2016.5664.

Jones BE, Sauer B, Jones MM, et al. **Variation in Outpatient Antibiotic Prescribing for Acute Respiratory Infections** in the Veteran Population: A Cross-sectional Study. Ann Intern Med. 2015 Jul 21;163(2):73-80.

Juo YY, Sanaiha Y, Jabaji Z, Benharash P. Trends in Diverting Loop Ileostomy vs Total Abdominal Colectomy as **Surgical Management for Clostridium Difficile Colitis**. JAMA Surg. 2019 Jul 3.

Juul FE, Garborg K, Bretthauer M, et al. **Fecal Microbiota Transplantation** for Primary Clostridium difficile Infection.N Engl J Med. 2018 Jun 2.

Kabbani S, Hersh AL, Shapiro DJ, et al. Opportunities to **Improve Fluoroquinolone Prescribing in the United States** for Adult Ambulatory Care Visits. Clin Infect Dis. 2018 Jun 18;67(1):134-136.

Kabbani S, Palms D, Bartoces M, et al. **Outpatient Antibiotic Prescribing for Older Adults** in the United States: 2011 to 2014. J Am Geriatr Soc. 2018 Oct;66(10):1998-2002.

Kacker S, Frick KD, Gaydos CA, Tobian AA. Costs and Effectiveness of Neonatal Male **Circumcision**. Arch Pediatr Adolesc Med. 2012 Aug 20:1-9.

Kadri AN, Wilner B, Hernandez AV, et al. Geographic Trends, Patient Characteristics, and Outcomes of **Infective Endocarditis Associated With Drug Abuse** in the United States From 2002 to 2016. J Am Heart Assoc. 2019 Oct;8(19):e012969.

Kaforou M, Herberg JA, Wright VJ, et al. Diagnosis of Bacterial Infection Using **a 2-Transcript Host RNA Signature** in Febrile Infants 60 Days or Younger. JAMA. 2017 Apr 18;317(15):1577-1578.

Kalra MG, Higgins KE, Perez ED. Common Questions About **Streptococcal Pharyngitis**. Am Fam Physician. 2016;94(1):24-31.

Kalwij Sebastian, Macintosh Mary, Baraitser Paula. **Screening** and treatment of **Chlamydia** trachomatis infections. BMJ 2010;340:c1915, doi: 10.1136/bmj.c1915 (Published 21 April 2010)

Kantar A, Chang AB, Shields MD, et al. **ERS statement on protracted bacterial bronchitis** in children. Eur Respir J. 2017 Aug 24;50(2).

Kao D, Roach B, Silva M, et al. Effect of oral **capsule– vs colonoscopy-delivered fecal microbiota transplantation on recurrent Clostridium difficile** infection: a randomized clinical trial.JAMA. doi:10.1001/jama.2017.17077

Kaplan A. **Canadian guidelines for chronic rhinosinusitis**: Clinical summary. Can Fam Physician. 2013 Dec;59(12):1275-81

Kaplan A. **Canadian** guidelines for acute bacterial **rhinosinusitis**: Clinical summary. Can Fam Physician. 2014 Mar;60(3):227-34.

Kaplan YC, Koren G. Use of **ciprofloxacin during breastfeeding** Canadian Family Physician April 2015 **vol. 61** (4). 343-344.

Karageorgopoulos DE, Giannopoulou KP, Grammatikos AP, et al. Fluoroquinolones compared with beta-lactam antibiotics for the treatment of **acute bacterial sinusitis**: a meta-analysis of randomized controlled trials. CMAJ. 2008 Mar 25;178(7):845-54. In the treatment of acute bacterial sinusitis, newer fluoroquinolones conferred no benefit over beta-lactam antibiotics. The use of fluoroquinolones as first-line therapy cannot be endorsed. The authors found no benefit to fluoroquinolones over beta-lactams for acute bacterial rhinosinusitis (ABRS). The more important and relevant questions are whether we can distinguish ABRS from viral sinusitis (not very well) and whether antibiotics are needed at all (probably not for most patients). If you decide to prescribe an antibiotic because of severity of illness or duration of symptoms, a beta-lactam will work as well as a fluoroquinolone. (LOE = 1a)

Karppinen S, Teräsjärvi J, Auranen K, et al. **Acquisition and Transmission of Streptococcus pneumoniae is Facilitated During Rhinovirus** Infection in Families with Children. Am J Respir Crit Care Med. 2017 May 10.

Karthikeyan G, Guilherme L. **Acute rheumatic fever**. Lancet. 2018 Jul 14;392(10142):161-174.

Katz AR et al. **Neisseria gonorrhoeae** with high-level **resistance to azithromycin**: Case report of the first isolate identified in the United States. Clin Infect Dis 2012 Mar 15; 54:841.

Katz KC, Golding GR, Choi KB, et al. The evolving epidemiology of **Clostridium difficile infection in Canadian hospitals** during a postepidemic period (2009-2015). CMAJ. 2018 Jun 25;190(25):E758-E765.

Kaur R, Morris M, Pichichero ME. Epidemiology of **Acute Otitis Media** in the Postpneumococcal Conjugate Vaccine Era. Pediatrics. 2017; 140(3):e20170181

Kaushik V, Malik T, Saeed SR. Interventions for acute **otitis externa**. Cochrane Database Syst Rev. 2010 Jan 20;(1):CD004740.

Keenan JD, Arzika AM, Maliki R, et al. Longer-Term Assessment of **Azithromycin for Reducing Childhood Mortality** in Africa. N Engl J Med. 2019 Jun 6;380(23):2207-2214.

Keller EC, Tomecki KJ, Chadi Alraies M. Distinguishing **cellulitis** from its mimics. Cleve Clin J Med. 2012 Aug;79(8):547-52.

Keller K, von Bardeleben RS, Ostad MA, et al. Temporal **Trends in the Prevalence of Infective Endocarditis** in Germany Between 2005 and 2014. The American Journal of Cardiology (2016).

Kelly CR, Khoruts A, Staley C, et al. Effect of **Fecal Microbiota Transplantation** on Recurrence in Multiply Recurrent Clostridium difficile Infection: A Randomized Trial. Ann Intern Med. 2016 Aug 23.

Kelly C, Chalmers JD, Crossingham I, et al. **Macrolide antibiotics for bronchiectasis**. Cochrane Database Syst Rev. 2018 Mar 15;3:CD012406. Long-term macrolide therapy may reduce the frequency of exacerbations and improve quality of life, although supporting evidence is derived mainly from studies of azithromycin, rather than other macrolides, and predominantly among adults rather than children. However, macrolides should be used with caution, as limited data indicate an associated increase in microbial resistance. Macrolides are associated with increased risk of cardiovascular death and other serious adverse events in other populations, and available data cannot exclude a similar risk among patients with bronchiectasis.

Keenan JD, Emerson PM, Gaynor BD, et al. Adult **Mortality in a Randomized Trial of Mass Azithromycin** for Trachoma. JAMA Intern Med. 2013 Apr 1:1-3.

Keenan JD, Klugman KP, McGee L, et al. Evidence for **Clonal Expansion** After **Antibiotic Selection Pressure**: Pneumococcal Multilocus Sequence Types Before and After Mass Azithromycin Treatments. J Infect Dis. 2014 Oct 6.

Keenan JD, Bailey RL, West SK, et al. **Azithromycin** to **Reduce Childhood Mortality in Sub-Saharan Africa**. N Engl J Med. 2018 Apr 26;378(17):1583-1592.

Kelly R, Zoubiane G, Walsh D, Ward R, Goossens H. Public funding for **research on antibacterial resistance** in the JPIAMR countries, the **European** Commission, and related European Union agencies: a systematic observational analysis. Lancet Infect Dis 2015; online Dec 18.

Kemppainen KM, Vehik K, Lynch KF, et al. Association Between Early-Life Antibiotic Use and the **Risk of Islet or Celiac Disease Autoimmunity**. JAMA Pediatr. 2017 Oct 9.

Kemppainen KM, Vehik K, Lynch KF, et al. Association Between **Early-Life Antibiotic Use and the Risk of Islet or Celiac Disease** Autoimmunity. JAMA Pediatr. 2017 Oct 9.

Keren R, Shah SS, Srivastava R, et al; for the Pediatric Research in Inpatient Settings Network. Comparative Effectiveness of **Intravenous vs Oral Antibiotics** for Postdischarge Treatment of **Acute Osteomyelitis** in Children. JAMA Pediatr. 2014 Dec 15.

Keren R, Shah SS, Srivastava R, et al; Pediatric Research in Inpatient Settings Network. Comparative effectiveness of **intravenous vs oral antibiotics for postdischarge treatment of acute osteomyelitis** in children. JAMA Pediatr. 2015 Feb;169(2):120-8.

Khan O, Shafi AM, Timmis A. International guideline changes and the **incidence of infective endocarditis**: a systematic review. Open Heart. 2016 Aug 25;3(2):e000498.

Khan S, Stimec J, Kitai I. **Nonresponding osteomyelitis** in a two-year-old boy. CMAJ. 2015 Apr 27.

Kim DY, Nassiri N, Saltzman DJ, et al. **Postoperative antibiotics** are not associated with decreased wound complications among patients undergoing **appendectomy** for complicated appendicitis. Am J Surg. 2015 Sep 12.

Kim Nak-Hyun, Kim Moonsuk, Lee Shinwon, et al. Effect of Routine **Sterile Gloving on Contamination Rates** in Blood Culture: A Cluster Randomized Trial. *Ann Intern Med* February 1, 2011 154:145-151.

Kim SJ, Toma HS. **Antimicrobial resistance and ophthalmic antibiotics**: 1-year results of a longitudinal controlled study of patients undergoing intravitreal injections. Arch Ophthalmol. 2011 Sep;129(9):1180-8.

Kimberlin DW et al. Oral **acyclovir suppression** and neurodevelopment after **neonatal herpes**. N Engl J Med 2011 Oct 6; 365:1284.

King LM, Fleming-Dutra KE, Hicks LA. **Advances in optimizing the prescription of antibiotics in outpatient settings**. BMJ. 2018 Nov 12;363:k3047.

King LM, Sanchez GV, Bartoces M, et al. **Antibiotic Therapy Duration in US Adults With Sinusitis**. JAMA Intern Med. 2018 Mar 26.

Kinkade S, Long NA. **Acute Bronchitis**. Am Fam Physician. 2016;94(7):560-565.

Kinlaw AC, Sturmer T, Lund JL, et al. Trends in **Antibiotic Use by Borth Season and Birth Year**. Pediatrics. 2017;140(3):e20170441

Kirkcaldy RD, Hook EW 3rd, Soge OO, et al. Trends in **Neisseria gonorrhoeae Susceptibility to Cephalosporins in the United States**, 2006-2014. JAMA. 2015 Nov 3;314(17):1869-1871.

Kirkcaldy RD, Harvey A, Papp JR, et al.**Neisseria gonorrhoeae Antimicrobial Susceptibility** Surveillance - The Gonococcal Isolate Surveillance Project, 27 Sites, **United States**, 2014. MMWR Surveill Summ. 2016 Jul 15;65(7):1-19.

Klein EY, Van Boeckel TP, Martinez EM, et al. **Global increase and geographic convergence in antibiotic consumption** between 2000 and 2015. Proc Natl Acad Sci U S A. 2018 Mar 26.

Klotz SA, Ianas V, Elliott SP. **Cat-scratch Disease**. Am Fam Physician. 2011 Jan 15;83(2):152-155.

Kluytmans J, Struelens M. **Meticillin resistant Staphylococcus** aureus in the hospital. BMJ. 2009 Feb 12;338:b364. doi: 10.1136/bmj.b364.

Knight M, Chiocchia V, Partlett C, et al. **Prophylactic antibiotics in the prevention of infection after operative vaginal delivery** (ANODE): a multicentre randomised controlled trial. Lancet 2019; online May 13.

Ko LN, Garza-Mayers AC, St John J, et al. Effect of **Dermatology Consultation on Outcomes for Patients With Presumed Cellulitis**: A Randomized Clinical Trial. JAMA Dermatol. 2018 May 1;154(5):529-536.

Ko LN, Garza-Mayers AC, St John J, et al. Clinical Usefulness of **Imaging and Blood Cultures in Cellulitis** Evaluation. JAMA Intern Med. 2018 Apr 2.

Kociolek LK, Shulman ST. **In the Clinic: Pharyngitis**. Ann Intern Med Sep 4, 2012. ITC3-2.

Kociolek LK, Palac HL, Patel SJ, et al. Risk Factors for Recurrent **Clostridium difficile** Infection in Children: A Nested Case-Control Study. J Pediatr. 2015 May 19.

Koning S, van der Sande R, Verhagen AP, et al. **Interventions for impetigo**. Cochrane Database Syst Rev. 2012 Jan 18;1:CD003261. There is good evidence that topical mupirocin and topical fusidic acid are equally, or more, effective than oral treatment. Due to the lack of studies in people with extensive impetigo, it is unclear if oral antibiotics are superior to topical antibiotics in this group. Fusidic acid and mupirocin are of similar efficacy. Penicillin was not as effective as most other antibiotics. There is a lack of evidence to support disinfection measures to manage impetigo.

Koppen L, Suda KJ, Rowan S, et al. **Dentists' prescribing of antibiotics and opioids** to Medicare Part D beneficiaries: Medications of high impact to public health. J Am Dent Assoc. 2018 Aug;149(8):721-730.

Korb K, Scherer M, Chenot JF. **Steroids** as adjuvant therapy for acute pharyngitis in ambulatory patients: a systematic review. Ann Fam Med. 2010 Jan-Feb;8(1):58-63.

Korbila IP, Manta KG, Siempos II, et al. Penicillins vs trimethoprim-based regimens for acute bacterial **exacerbations of chronic** bronchitis: meta-analysis of randomized controlled trials. Can Fam Physician. 2009 Jan;55(1):60-7.

Korpela K, Salonen A, Virta LJ, et al. Association of **Early-Life Antibiotic Use and Protective Effects of Breastfeeding**: Role of the Intestinal Microbiota. JAMA Pediatr. 2016 Jun 13.

Kotloff KL, Shirley DT, Creech CB, et al**. Mupirocin for Staphylococcus aureus** Decolonization of Infants in Neonatal Intensive Care Units. Pediatrics. 2018 Dec 26.

Kozyrskyj A, Klassen TP, Moffatt M, et al. **Short-course antibiotics for acute otitis media**. Cochrane Database Syst Rev. 2010 Sep 8;9:CD001095. Clinicians need to evaluate whether the minimal short-term benefit from longer treatment of

Krensky C, Poutanen SM, Hota SS. Diarrhea after fecal microbiota transplantation for recurrent **Clostridioides difficile infection**. CMAJ. 2019 May 21;191(20):E559-E561.

Kronman MP, Hersh AL, Newland JG, Gerber JS. Getting Over Our **Inpatient Oral Antibiotic Aversion**. Pediatrics. 2018 Dec;142(6).

Kronman MP, Zhou C, Mangione-Smith R. **Bacterial Prevalence** and **Antimicrobial Prescribing Trends for Acute Respiratory Tract Infections**. Pediatrics. 2014 Sep 15.

Kronman MP et al. **Extended- versus narrower-spectrum antibiotics for appendicitis**. Pediatrics 2016 Jul;138:e20154547.

Kuehn Bridget M. FDA Targets Antibiotic Use in **Livestock**. JAMA. 2010;304(4):396.

Kulaylat AS, Buonomo EL, Scully KW, et al. Development and Validation of a **Prediction Model for Mortality and Adverse Outcomes** Among Patients With Peripheral Eosinopenia on Admission for **Clostridium difficile Infection**. JAMA Surg. 2018 Sep 12.

Kumar C, Salzman B, Colburn JL. **Preoperative Assessment in Older Adults:** A Comprehensive Approach Am Fam Physician. 2018;98(4):214-220.

Lahra MM, Ryder N, Whiley DM. A new **multidrug-resistant strain of Neisseria gonorrhoeae** in Australia. N Engl J Med. 2014 Nov 6;371(19):1850-1.

Lai NM, Lai NA, O'Riordan E, et al. **Skin antisepsis** for reducing central venous catheter-related infections. Cochrane Database Syst Rev. 2016 Jul 13;7

Lamagni T, Guy R, Chand M, et al. **Resurgence of scarlet fever** in England, 2014-16: a population-based surveillance study. Lancet Infect Dis. 2018 Feb;18(2):180-187.

Lamont RF, Nhan-Chang CL, Sobel JD, et al. Treatment of abnormal vaginal flora in early pregnancy with clindamycin for the prevention of spontaneous preterm birth: a systematic review and metaanalysis. Am J Obstet Gynecol. 2011 Sep;205(3):177-90.

Laopaiboon M, Panpanich R, Swa Mya K. **Azithromycin** for **acute lower respiratory tract infections**. Cochrane Database Syst Rev. 2015 Mar 8;3:CD001954. There is unclear evidence that azithromycin is superior to amoxycillin or amoxyclav in treating acute LRTI. In patients with acute bronchitis of a suspected bacterial cause, azithromycin tends to be more effective in terms of lower incidence of treatment failure and adverse events than amoxycillin or amoxyclav. However, most studies were of unclear methodological quality and had small sample sizes; future trials of high methodological quality and adequate sizes are needed.

Laursen RP, Larnkjar A, Ritz C, et al. Effect of **probiotics** on **absence from daycare due to infections**: a randomized controlled trial. Pediatrics. 2017;140(2):e20170735.

Laursen RP, Larnkjaer A, Ritz C, et al. **Probiotics** and Child Care Absence Due to Infections: A Randomized Controlled Trial. Peds. 2017;140(2):e20170735

Lautz AJDA, Denson AR, O'Connor KA, Chilutti MR, Ross RK, Gerber JS, et al. Value of **procalcitonin measurement** for early evidence of **severe bacterial** infections in the pediatric intensive care. J Pediatr 2016;doi:10.1016/j.jpeds.2016.07.045.

Lawes T, Lopez-Lozano J-M, Nebot CA, et al. Effect of a **national 4C antibiotic stewardship intervention** on the clinical and molecular epidemiology of **Clostridium difficile** infections in a region of Scotland: a non-linear time-series analysis. Lancet Infect Dis 2016; online Nov 4

Laxminarayan R, Duse A, Wattal C, et al. **Antibiotic resistance**-the need for global solutions. Lancet Infect Dis. 2013 Dec;13(12):1057-98

Laxminarayan R, Matsoso P, Pant S, et al. **Access to eff ective antimicrobials**: a worldwide challenge. Lancet 2015; online Nov 18.

Lázaro-Martínez JL, Aragón-Sánchez J, García-Morales E. **Antibiotics versus conservative surgery for treating diabetic foot osteomyelitis**: a randomized comparative trial. Diabetes Care. 2014 Mar;37(3):789-95.

Le Cleach L, Trinquart L, Do G, et al. Oral antiviral therapy for **prevention of genital herpes outbreaks** in immunocompetent and nonpregnant patients. Cochrane Database Syst Rev. 2014 Aug 3;8:CD009036. Owing to risk of bias and inconsistency, there is low quality evidence that suppressive antiviral therapy with acyclovir, valacyclovir or famciclovir in pacients experiencing at least four recurrences of genital herpes per year decreases the number of pacients with at least one recurrence as compared with placebo. Network meta-analysis of the few direct comparisons and the indirect comparisons did not show superiority of one drug over another.

Lefkowitz A, Shadowitz S. Reversible **cerebellar neurotoxicity induced by metronidazole**. CMAJ. 2018 Aug 13;190(32):E961.

LeMaire SA, Zhang L, Luo W, et al. Effect of **ciprofloxacin on susceptibility to aortic dissection** and rupture in mice [online July 25, 2018]. JAMA Surg. doi:10.1001/jamasurg.2018.1804.

Le Saux N; **Canadian Paediatric Society**, Infectious Diseases and Immunization Committee. **Antimicrobial stewardship** in daily practice: managing an important resource. Paediatr Child Health 2014;19:261-5. www.cps.ca/en/documents/position/antimicrobial-stewardship (accessed May 7, 2014).

Le Saux N, Robinson JL; **Canadian Paediatric Society,** Infectious Diseases and Immunization Committee. **Uncomplicated pneumonia in healthy Canadian children and youth:** practice points for management. Paediatr Child Health 2015;20:441-5. www.cps.ca/en/documents/position/pneumonia-management-children-youth (accessed December 14, 2015).

Le Saux N, Robinson JL; **Canadian Paediatric Society**, Infectious Diseases and Immunization Committee. Position statement. **Management of acute otitis media in children six months of age and older**. Paediatr Child Health 2016;21:39-44. www.cps.ca/en/documents/position/acute-otitis-media(accessed February 5, 2016).

Lean WL, Arnup S, Danchin M, et al. **Rapid Diagnostic Tests** for **Group A Streptococcal Pharyngitis**: A Meta-analysis. Pediatrics. 2014 Oct;134(4):771-781.

Lee CC, Lee MG, Chen YS, et al. Risk of **Aortic Dissection and Aortic Aneurysm in Patients Taking Oral Fluoroquinolone**. JAMA Intern Med. 2015 Oct 5:1-9.

Lee CH, Steiner T, Petrof EO, et al. **Frozen vs Fresh Fecal Microbiota Transplantation** and Clinical Resolution of Diarrhea in Patients With Recurrent Clostridium difficile Infection: A Randomized Clinical Trial. JAMA. 2016 Jan 12;315(2):142-9.

Lee Dong Heun; Vielemeyer Ole. Analysis of Overall **Level of Evidence Behind Infectious Diseases Society of America (IDSA) Practice Guidelines**. Arch Intern Med. 2011;171(1):18-22.

Lee AS, Macedo-Vinas M, François P, et al. Impact of combined low-level **mupirocin** and genotypic **chlorhexidine resistance** on persistent methicillin-resistant Staphylococcus aureus carriage after decolonization therapy: case-control study. Clin Infect Dis. 2011 Jun 15;52(12):1422-30.

Lee GM, Kleinman K, Pelton S, et al. **Immunization, antibiotic use, and pneumococcal colonization over a 15-year period**. Pediatrics. 2017; 140(5):e20170001

Lee KC, Ngo-Metzger Q, Wolff T, et al. **Sexually Transmitted Infections**: Recommendations from the U.S. Preventive Services Task Force. Am Fam Physician. 2016;94(11):907-915.

Lefebvre B et al. **Ceftriaxone-resistant Neisseria gonorrhoeae**, Canada, 2017. Emerg Infect Dis 2018 Feb 15; 24: [e-pub].

LeFevre ML; on behalf of the U.S. Preventive Services Task Force*. **Behavioral Counseling** Interventions to Prevent Sexually Transmitted Infections: U.S. Preventive Services Task Force (USPSTF) Recommendation Statement. Ann Intern Med. 2014 Sep 23.

LeFevre ML. **Screening for Chlamydia and Gonorrhea**: U.S. Preventive Services Task Force (USPSTF) Recommendation Statement. Ann Intern Med. 2014 Sep 23.

Lefebvre B, Martin I, Demczuk W, et al. **Ceftriaxone-Resistant Neisseria gonorrhoeae**, Canada, 2017. Emerg Infect Dis. 2018 Feb;24(2).

Leffler DA, Lamont JT. Treatment of **Clostridium difficile**-associated disease. Gastroenterology. 2009 May;136(6):1899-912. Epub 2009 May 7.

Leffler DA, Lamont JT. **Clostridium difficile** infection. N Engl J Med. 2015 Apr 16;372(16):1539-48.

Légaré F, Labrecque M, Cauchon M, et al. Training family physicians in **shared decision-making** to reduce the overuse of antibiotics in acute respiratory infections: a cluster randomized trial. CMAJ. 2012 Sep 18;184(13):E726-34.

Leggit JC, Saguil A. **Secnidazole (Solosec) for Bacterial Vaginosis**. Am Fam Physician. 2019 Aug 15;100(4):242-243.

Leis JA, Evans GA, Ciccotelli W, et al. ***Choosing* Wisely Canada – top five list in infectious dis**ease: an official position statement of the Association of Medical Microbiology and Infectious Disease (AMMI) Canada**.** J Assoc Med Microbiol Infect Dis Can 2016;1(1):8-12.

Leis JA, Palmay L, Ho G, et al. Point-of-care **Beta-lactam Allergy Skin Testing** by Antimicrobial Stewardship Programs: A Pragmatic Multicenter Prospective Evaluation. Clin Infect Dis. 2017 Jun 1.

LemiengreMB, van Driel ML,Merenstein D, Young J, De Sutter AIM. **Antibiotics for clinically diagnosed acute rhinosinusitis** in adults. Cochrane Database of Systematic Reviews 2012, Issue 10. Art. No.: CD006089. DOI: 10.1002/14651858.CD006089.pub4. The potential benefit of antibiotics in the treatment of clinically diagnosed acute rhinosinusitis needs to be seen in the context of a high prevalence of adverse events. Taking into account antibiotic resistance and the very low incidence of serious complications, we conclude that there is no place for antibiotics for the patient with clinically diagnosed, uncomplicated acute rhinosinusitis. This review cannot make recommendations for children, patients with a suppressed immune system and patients with severe disease, as these populations were not included in the available trials.

Lennon DR Fracp, Farrell E Mhsc, et al. Once-daily Amoxicillin versus Twice-daily Penicillin V in Group A {beta}-Hemolytic **Streprococcus Pharyngitis**. Arch Dis Child. 2008 Mar 12; [Epub ahead of print] In this adequately-powered study, once-daily oral amoxicillin is not inferior to twice-daily penicillin V for the treatment and eradication of GABHS in children with pharyngitis.

Lessa FC, Mu Y, Bamberg WM, et. al. Burden of **Clostridium difficile** infection in the United States. N Engl J Med. 2015 Feb 26;372(9):825-34.

Leung DT, LaRocque RC, Ryan ET. **Travel Medicine**. Ann Intern Med. 2018 Jan 2;168(1):ITC1-ITC16.

Li DG, Xia FD, Khosravi H, et al. Outcomes of **Early Dermatology Consultation for Inpatients Diagnosed With Cellulitis**. JAMA Dermatol. 2018 May 1;154(5):537-543.

Li DQ, Kim R, McArthur E, et al. Risk of adverse events among older adults following co-prescription of **clarithromycin and statins** not metabolized by cytochrome P450 3A4. CMAJ. 2014 Dec 22.

Li DK, Chen H, Ferber J, et al. Infection and **antibiotic use in infancy** and risk of **childhood obesity**: a longitudinal birth cohort study. Lancet Diabetes Endocrinol. 2016 Nov 1.

Li H, Liu DH, Chen LL, Zhao Q, et al. Meta-analysis of the adverse effects of long-term **azithromycin** use in patients with chronic lung diseases. Antimicrob Agents Chemother. 2014 Jan;58(1):511-7

Li H-K, Rombach I, Zambellas R, et al. **Oral versus intravenous antibiotics for bone and joint infection**. (**OVIVA)** N Engl J Med 2019;380: 425-36.

Li J, Echevarria KL, Traugott KA. **β-Lactam Therapy** for Methicillin-Susceptible **Staphylococcus aureus Bacteremia**: A Comparative Review of Cefazolin versus Antistaphylococcal Penicillins. Pharmacotherapy. 2016 Dec 30.

Li M, Al-Sarraf A, Sinclair G, Frohlich J. **Fish odour syndrome**. CMAJ. 2011 Mar 21.

Li X, Zoller M, Fuhr U, et al**. Ciprofloxacin in critically ill subjects**: considering hepatic function, age and sex to choose the optimal dose. J Antimicrob Chemother. 2018 Nov 29.

Liao JM, Schapira MS, et al. The Effect of Emphasizing Patient, Societal, and Institutional Harms of **Inappropriate Antibiotic Prescribing** on Physician Support of **Financial Penalties**: A Randomized Trial. Ann Intern Med. 2017 Aug 1;167(3):215-216.

Libman M; Committee to Advise on Tropical Medicine and Travel. Summary of the Committee to Advise on Tropical Medicine and Travel (**CATMAT**) statement on **travellers' diarrhea**. CCDR 2015; 41(11). www.phac-aspc.gc.ca/publicat/ccdr-rmtc/15vol41/dr-rm41-11/ar-03-eng.php (accessed December 3, 2015).

Libman H, Brockmeyer DM, Gold HS. **Should We Prescribe Antibiotics to This Patient With Persistent Upper Respiratory Symptoms**?: Grand Rounds Discussion From Beth Israel Deaconess Medical Center. Ann Intern Med. 2017 Feb 7;166(3):201-208

Lin JS, Whitlock E, O'Connor E, Bauer V. **Behavioral counseling to prevent sexually transmitted infections**: a systematic review for the U. S. Preventive Services Task Force. Ann Intern Med. 2008;149(7):497–508.

Linden JA. Clinical practice. Care of the adult patient **after sexual assault**. N Engl J Med. 2011 Sep 1;365(9):834-41.

Linder JA, Doctor JN, Friedberg MW, et al. **Time of Day and the Decision to Prescribe Antibiotics**. JAMA Intern Med. 2014 Oct 6.

Linder JA, et al. Effects of **Behavioral Interventions on Inappropriate Antibiotic Prescribing in Primary Care** 12 Months After Stopping Interventions. JAMA. 2017 Oct 10;318(14):1391-1392

Lindgren C, Neuman MI, Monuteaux MC, et al. **Patient and Parent-Reported Signs and Symptoms for Group A Streptococcal Pharyngitis**. Pediatrics. 2016 Jun 8.

Liu Catherine, Bayer Arnold, Cosgrove Sara E., et al. Clinical Practice Guidelines by the Infectious Diseases Society of America (IDSA) for the Treatment of **Methicillin-Resistant Staphylococcus Aureus Infections in Adults and Children.** Clin Infect Dis. ciq146 Jan 4, 2011.

Liu Y, Chan TC, Yap LW, et al. Resurgence of **scarlet fever in China**: a 13-year population-based surveillance study. Lancet Infect Dis. 2018 Aug;18(8):903-912.

Lipsky BA, Berendt AR, Cornia PB, et al. 2012 Infectious Diseases Society of America-**IDSA** clinical practice guideline for the diagnosis and treatment of **diabetic foot infections**. Clin Infect Dis. 2012 Jun;54(12):e132-73.

Lissauer D, Wilson A, Hewitt CA, et al. A Randomized Trial of **Prophylactic Antibiotics for Miscarriage Surgery**. N Engl J Med. 2019 Mar 14;380(11):1012-1021.

Little P, Stuart B, Moore M, et al, on behalf of the GRACE consortium. **Amoxicillin for acute lower-respiratory-tract infection** in primary care when pneumonia is not suspected: a 12-country, randomised, placebo-controlled trial. Lancet Infect Dis 2012; online Dec 19.

Little P, Hobbs FD, Moore M, et al; on behalf of the **PRISM** investigators. **Clinical score and rapid antigen detection test to guide antibiotic use for sore throats**: randomised controlled trial of PRISM (primary care streptococcal management). BMJ. 2013 Oct 10;347:f5806.

Little P, Stuart B, et al. Predictors of **suppurative complications for acute sore throat in primary care**: prospective clinical cohort study. BMJ. 2013 Nov 25;347:f6867.

Little P, Stuart B, Hobbs FDR, et al, for the DESCARTE investigators. **Antibiotic prescription strategies for acute sore throat**: a prospective observational cohort study. Lancet Infect Dis 2014; online Jan 17.

Little P, Moore M, Kelly J, et al. **Delayed antibiotic prescribing** strategies for respiratory tract infections in primary care: pragmatic, factorial, randomized controlled trial. BMJ. 2014 Mar 6.

Little P, Stuart B, Hobbs FD, et al. An **internet-delivered handwashing intervention** to modify influenza-like illness and respiratory infection transmission (PRIMIT): a primary care randomised trial. Lancet. 2015 Aug 6.

Little P, Stuart B, Smith S, et al. **Antibiotic prescription strategies and adverse outcome for uncomplicated lower respiratory tract infections**: prospective cough complication cohort (3C) study. BMJ 2017;357:j2148.

Little P, Stuart B, Wingrove Z, et al. **Probiotic capsules and xylitol chewing gum** to manage symptoms of pharyngitis: a randomized controlled factorial trial. CMAJ. 2017 Dec 18;189(50):E1543-E1550.

Liu VX, Fielding-Singh V, Greene JD, et al. The Timing of **Early Antibiotics and Hospital Mortality in Sepsis**. Am J Respir Crit Care Med. 2017 Mar 27.

Liu Y-Y, Wang T, Walsh TR, et al. Emergence of **plasmid-mediated colistin resistance mechanism MCR-1** in animals and human beings in China: a microbiological and molecular biological study. Lancet Infect Dis 2015; online Nov 18.

Liu Z, Dumville JC, Norman G, et al. **Intraoperative interventions for preventing surgical site infection**: an overview of Cochrane Reviews. Cochrane Database of Systematic Reviews 2018, Issue 2. Art. No.: CD012653. This overview provides the most up-to-date evidence on use of intraoperative treatments for the prevention of SSIs from all currently published Cochrane Reviews. There is evidence that some interventions are useful in reducing SSI risk for people undergoing surgery, such as antibiotic prophylaxis for caesarean section and hernia repair, and also the timing of prophylactic intravenous antibiotics administered before caesarean incision. Also, there is evidence that adhesive drapes increase SSI risk. Evidence for the many other treatment choices is largely of low or very low certainty and no quality-of-life or cost-effectiveness data were reported.

Llewelyn MJ, Fitzpatrick JM, Darwin E, et al. The **antibiotic course has had its day**. BMJ. 2017 Jul 26;358:j3418.

Llor C, Moragas A, Hernández S, et al. Efficacy of antibiotic therapy for acute exacerbations of mild to moderate chronic obstructive pulmonary disease. Am J Respir Crit Care Med. 2012 Oct 15;186(8):716-23.

Llor C, Moragas A, Bayona C, et al. Efficacy of **anti-inflammatory or antibiotic treatment** in patients with non-complicated acute **bronchitis** and discoloured sputum: randomised placebo controlled trial. BMJ. 2013 Oct 4;347:f5762.

Loewen K, Schreiber Y, Kirlew M, et al. **Community-associated methicillin-resistant Staphylococcus aureus infection**: Literature review and clinical update. Can Fam Physician. 2017 Jul;63(7):512-520.

Logan LK, McAuley JB, Shulman ST. **Macrolide treatment** failure in streptococcal pharyngitis resulting in acute **rheumatic fever**. Pediatrics. 2012 Mar;129(3):e798-802.

Logan LK, Gandra S, Mandal S, et al. **Multidrug- and Carbapenem-Resistant Pseudomonas aeruginosa** in Children, United States, 1999-2012. J Pediatric Infect Dis Soc. 2016 Nov 16.

Loo VG, Davis I, Embil J, et al. Association of Medical Microbiology and Infectious Disease Canada treatment practice guidelines for **Clostridium difficile infection**. JAMMI 2018;3(2). Published online: June 29, 2018. https://jammi.utpjournals.press/doi/pdf/10.3138/jammi.2018.02.13 (accessed July 19, 2018).

Lovegrove MC, Geller AI, Fleming-Dutra KE, et al. US **Emergency Department** Visits for **Adverse Drug Events From Antibiotics in Children**, 2011-2015. J Pediatric Infect Dis Soc. 2018 Aug 23.

Low N, Redmond S, Uusküla A, et al. **Screening for genital chlamydia infection**. Cochrane Database of Systematic Reviews 2016, Issue 9. Art. No.: CD010866. Evidence about the effects of screening on C. trachomatis transmission is of low quality because of directness and risk of bias. There is moderate quality evidence that detection and treatment of chlamydia infection can reduce the risk of PID in women at individual level. There is an absence of RCT evidence about the effects of chlamydia screening in pregnancy. Future RCTs of chlamydia screening interventions should determine the effects of chlamydia screening in pregnancy, of repeated rounds of screening on the incidence of chlamydia-associated PID and chlamydia reinfection in general and high risk populations.

Lowy, IM, DC., Leav, BA., et al. Treatment with Monoclonal Antibodies against **Clostridium difficile** Toxins.N Engl J Med 2010 362: 197-205.

Luby SP, Agboatwalla M, Feikin DR, et al. Effect of **handwashing** on child health: a randomised controlled trial. Lancet. 2005 Jul 16-22;366(9481):225-33.

Luce H, Schrager S, Gilchrist V. **Sexual assault of women**. Am Fam Physician. 2010 Feb 15;81(4):489-95.

Lucet J-C et al. Carriage of **methicillin-resistant Staphylococcus aureus** in home care settings: Prevalence, duration, and transmission to household members. Arch Intern Med 2009 Aug 10/24; 169:1372.

Lund M, Pasternak B, Davidsen RB, et al. Use of **macrolides** in mother and child and risk of **infantile hypertrophic pyloric stenosis**: nationwide cohort study. BMJ. 2014 Mar 11.

Lund-Sørensen H, Benros ME, Madsen T, et al. A Nationwide Cohort Study of the Association Between Hospitalization With Infection and Risk of **Death by Suicide**. JAMA Psychiatry. 2016 Aug 10

Lurie I, Yang YX, Haynes K, et al. **Antibiotic exposure and the risk for depression, anxiety, or psychosis**: a nested case-control study. J Clin Psychiatry. 2015 Nov;76(11):1522-8.

Lynskey NN, Jauneikaite E, Li HK, et al. **Emergence of dominant toxigenic M1T1 Streptococcus pyogenes** clone during increased scarlet fever activity in England: a population-based molecular epidemiological study. Lancet Infect Dis 2019; published online Sept 10.

Ma GK, Brensinger CM, Wu Q, Lewis JD. **Increasing incidence** of **multiply recurrent Clostridium difficile infection in the United States**. A cohort study. Ann Intern Med. [Epub ahead of print]. doi:10.7326/ M16-2733

Ma GK, Brensinger CM, Wu Q, et al. Increasing Incidence of Multiply **Recurrent Clostridium difficile** Infection in the United States: A Cohort Study. Ann Intern Med. 2017 Aug 1;167(3):152-158.

MacDonald N E. **Maternal infectious diseases, antimicrobial therapy or immunizations**: Very few contraindications to **breastfeeding**. Canadian Paediatric Society. 2014 Jun 17. http://www.cps.ca/documents/position/maternal-infectious-diseases-breastfeeding

Macy E and Contreras R. Health care use and serious infection prevalence associated with **penicillin ''allergy'' in hospitalized patients**: A cohort study. J Allergy Clin Immunol 2014 Mar; 133:790.

MacFadden DR et al. **Impact of reported beta-lactam allergy on inpatient outcomes**: A multicenter prospective cohort study. Clin Infect Dis 2016 Oct 1; 63:904.

Macfarlane J, Holmes W, Gard P, et al. Reducing antibiotic use for **acute bronchitis** in primary care: blinded, randomized controlled trial of patient information leaflet. BMJ. 2002 Jan 12;324(7329):91-4.

MacKenzie A. Balancing the Benefits and Risks of Empirical Antibiotics for **Sinusitis**: A Teachable Moment. JAMA Intern Med. 2014 Jun 2.

Macy E, Contreras R. Health care use and serious infection prevalence associated with **penicillin "allergy"** in hospitalized patients: a cohort study. J Allergy Clin Immunol. 2014;133:790-796.

Macy E and Contreras R.**Adverse reactions** associated with oral and parenteral use of **cephalosporins**: A retrospective population-based analysis. J Allergy Clin Immunol 2015 Mar; 135:745.

Madden-Fuentes RJ, Arshad M, Ross SS, et al. Efficacy of **Fluoroquinolone/Probiotic Combination** Therapy for Recurrent **Urinary Tract Infection** in Children: A Retrospective Analysis. Clin Ther. 2015 Jul 29.

Major G, Bradshaw L, Boota N, et al. Follow-on **RifAximin for the Prevention of recurrence** following standard treatment of Infection with **Clostridium Difficile (RAPID)**: a randomised placebo controlled trial. Gut. 2018 Sep 25.

Mahajan P, Kuppermann N, Mejias A, et al; Pediatric Emergency Care Applied Research Network (PECARN). Association of **RNA biosignatures** with bacterial infections in febrile infants aged 60 days or younger. JAMA. doi:10.1001/jama.2016.9207.

Mangione-Smith R, Zhou C, Robinson JD, et al. **Communication practices and antibiotic use** for acute respiratory tract infections in children. Ann Fam Med. 2015 May-Jun;13(3):221-7.

Maness DL, Martin M, Mitchell G. **Poststreptococcal Illness**: Recognition and Management. Am Fam Physician. 2018;97(8):517-522.

Manley Alice, Sansom Jane. **Phototoxic reaction to ciprofloxacin** BMJ 2019 Jun 27; 365 :l2413

Marchant JM, Petsky HL, Morris PS, Chang AB. **Antibiotics for prolonged wet cough in children**. Cochrane Database of Systematic Reviews 2018, Issue 7. Art. No.: CD004822. Evidence suggests antibiotics are efficacious for the treatment of children with chronic wet cough (greater than four weeks) with an NNTB of three. However, antibiotics have adverse effects and this review reported only uncertainty as to the risk of increased adverse effects when they were used in this setting. The inclusion of a more robust study strengthened the previous Cochrane review and its results.

Maria de Benedictis F, Bush A. **Recurrent lower respiratory tract infections** in children. BMJ. 2018 Jul 12;362:k2698.

Marie Trotti L, Saini P, Bliwise DL, et al. **Clarithromycin in GABA-related Hypersomnolence**: A Randomized, Crossover Trial. Ann Neurol. 2015 Jun 10.

Marom T, Tan A, Wilkinson GS, et al. **Trends in Otitis Media**-Related Health Care Use in the United States, 2001-2011. JAMA Pediatr. 2013 Nov 25.

Marston HD, Dixon DM, Knisely JM, et al. **Antimicrobial Resistance**. JAMA. 2016 Sep 20;316(11):1193-1204.

Martin I, Sawatzky P, Liu G, et al. Decline in **decreased cephalosporin susceptibility and increase in azithromycin resistance** in **Neisseria gonorrhoeae**, Canada. Emerg Infect Dis 2016;22(1).http://dx.doi.org/10.3201/eid2201.151247 (accessed January 4, 2016).

Martinez KA, Rood M, Jhangiani N, et al. Antibiotic Prescribing for **Respiratory Tract Infections** and Encounter Length: An Observational Study of Telemedicine. Ann Intern Med. 2018 Oct 2.

Mattei PL, Beachkofsky TM, Gilson RT, and Wisco OJ. **Syphilis**: A Reemerging Infection. Am Fam Physician. 2012;86(5):433-440.

Mawhirt SL, Fonacier LS, Calixte R, Davis-Lorton M, Aquino MRet al. **Skin testing and drug challenge outcomes in antibiotic-allergic patients** with immediate-type hypersensitivity. Ann Allergy Asthma Immunol. 2017 Jan;118(1):73-79.

McClain SL, Bohan JG, Stevens DL. Advances in the **medical management of skin and soft tissue infections**. BMJ. 2016 Dec 14;355:i6004

McClelland RS, Balkus JE, Lee J, et al. Randomized Trial of Periodic Presumptive Treatment With **High-Dose Intravaginal Metronidazole and Miconazole** to Prevent Vaginal Infections in HIV-negative Women. J Infect Dis. 2015 Jun 15;211(12):1875-82.

McConaghy JR, Panchal B. **Epididymitis**: An Overview. Am Fam Physician. 2016;94(9):723-726.

McCullagh DJ, Chu DK. **Penicillin allergy**. CMAJ. 2019 Feb 25;191(8):E231.

McDanel JS et al. Comparative effectiveness of **cefazolin versus nafcillin** or oxacillin for treatment of methicillin-susceptible **Staphylococcus aureus** infections complicated by bacteremia: A nationwide cohort study. Clin Infect Dis 2017 Mar 31.

McDonald LC, Gerding DN, Johnson S, et al. Clinical Practice Guidelines for **Clostridium difficile Infection in Adults and Children: 2017 Update** by the Infectious Diseases Society of America (**IDSA**) and Society for Healthcare Epidemiology of America (SHEA). Clin Infect Dis. 2018 Mar 19;66(7):987-994.

McGann P, Snesrud E, Maybank R, et al. **Escherichia coli Harboring mcr-1 and blaCTX-M** on a Novel IncF Plasmid: First report of mcr-1 in the USA. Antimicrob Agents Chemother. 2016 May 26.

McIvor A, Little P. **Chronic obstructive pulmonary disease**. BMJ 2007;334(7597):798.

McMullan BJ, Andresen D, Blyth CC, et al. **Antibiotic duration and timing of the switch from intravenous to oral route** for bacterial infections in children: systematic review and guidelines. Lancet Infect Dis. 2016 Jun 16.

Medical Letter. Treatment Guidelines. **Drugs for Bacterial Infections** In Adults. June 2010, July 2013 & Updated **Oct 2017**.

Medical Letter-Treatment Guidelines. **Drugs for Sexually Transmitted Diseases**. July 2010, Sept 2013 & Updated July 2017.

Medical Letter-Treatment Guidelines: Drugs for Some **Common Eye Disorders**. January 2007;5(53):1-3 ⇒ **Oct 2012**.

Medical Letter. Treatment Guidelines. **Antiviral Drugs**. Mar 2013.

Meeker D, Linder JA, Fox CR, et al. Effect of **behavioral interventions on inappropriate antibiotic prescribing** among primary care practices: a randomized clinical trial.JAMA. doi:10.1001/jama .2016.0275.

Mehrotra A. Reducing Unnecessary Antibiotics Prescribed to Children: What Next? Pediatrics. 2014 Feb 2.

Meier MA, Branche A, Neeser OL, et al. **Procalcitonin-guided antibiotic treatment** in patients with positive blood cultures: A patient-level meta-analysis of randomized trials. Clin Infect Dis. 2018 Oct 25.

Melese M, Alemayehu W, Lakew T, et al. Comparison of annual and biannual mass antibiotic administration for elimination of infectious trachoma. JAMA 2008; 299: 778–84.

Melia MT, Auwaerter PG. Time for a Different Approach to **Lyme Disease** and Long-Term Symptoms. N Engl J Med. 2016 Mar 31

Meltzer JA, Kunkov S, Crain EF. Identifying children at low risk for bacterial **conjunctivitis**. Arch Pediatr Adolesc Med. 2010 Mar;164(3):263-7. Age 6 years or older, presentation in April through November, no or watery discharge, and no glued eye in the morning were the clinical factors found to be independently associated with a negative conjunctival culture.

Mendelson M, Røttingen J-A, Gopinathan U, et al. Maximising access to achieve **appropriate human antimicrobial use** in low-income and middle-income countries. Lancet 2015; online Nov 18.

Mercer CH, Jones KG, Geary RS, et al. Association of **timing of sexual partnerships and perceptions of partners' concurrency with reporting of sexually transmitted infection diagnosis**. JAMA Netw Open. 2018;1(8):e185957. doi:10.1001/jamanetworkopen.2018.5957

Meropol SB, Votruba ME. Decision-Making and the **Barriers to Judicious Antibiotic Use**. Pediatrics. 2015 Aug;136(2):387-8.

Meropol SB, Haupt AA, Debanne SM. Incidence and Outcomes of Infections Caused by **Multidrug-Resistant Enterobacteriaceae** in Children, 2007-2015. J Pediatric Infect Dis Soc. 2017 Feb 22.

Metz LM, Li DKB, Traboulsee AL, et al. Trial of **minocycline** in a **clinically isolated syndrome of multiple sclerosis**. N Engl J Med 2017;376:2122-33.

Meyer Sauteur PM, Huizinga R, Tio-Gillen AP, et al. **Mycoplasma** pneumoniae triggering the **Guillain-Barré syndrome**: A case-control study. Ann Neurol. 2016 Aug 4.

Mikkelsen KH, Knop FK, Frost M, Hallas J, et al. Use of **Antibiotics and Risk of Type 2 Diabetes**: A Population-Based Case-Control Study. J Clin Endocrinol Metab. 2015 Aug 27:jc20152696.

Mill C, Primeau M-N, Medoff E, et al. Assessing the diagnostic properties of a graded **oral provocation** challenge for the diagnosis of immediate and nonimmediate **reactions to amoxicillin** in children [online April 4, 2016].JAMA Pediatr. doi:10.1001/jamapediatrics .2016.0033.

Miller JO, Taylor J, Goldman JL. Severe Acute **Respiratory Failure** in Healthy Adolescents Exposed to **Trimethoprim-Sulfamethoxazole**. Pediatrics. 2019 May 29.

Miller LG, Daum RS, Creech CB, et al. **Clindamycin versus trimethoprim–sulfamethoxazole** for uncomplicated **skin infections**. (DMID 07-0051) N Engl J Med 2015;372:1093-103.

Milstone AM, Elward A, Song X, et al, for the Pediatric SCRUB Trial Study Group. **Daily chlorhexidine bathing** to reduce bacteraemia in critically ill children: a multicentre, cluster-randomised, crossover trial. Lancet 2013

Mintegi S, Gomez B, Martinez-Virumbrales L, et al. **Outpatient management of selected young febrile infants without antibiotics**. Arch Dis Child. 2017 Mar;102(3):244-249

Mishra SC, Chhatbar KC, Kashikar A, Mehndiratta A. **Diabetic foot**. BMJ. 2017Nov 16;359:j5064.

Mishra SC, Chhatbar KC, Kashikar A, et al. **Diabetic foot**. BMJ 2017;359:j5064

Mitchell R, Taylor G, Rudnick W, et al.; Canadian **Nosocomial Infection Surveillance Program**. Trends in health care–associated infections in acute care hospitals in Canada: an analysis of repeated point-prevalence surveys. CMAJ 2019;191:E981-8.

Mitjà O, Hays R, Ipai A, et al. Single-dose **azithromycin versus benzathine benzylpenicillin for treatment of yaws** in children in Papua New Guinea: an open-label, non-inferiority, randomised trial. Lancet 2012; published online Jan 11

Moellering Robert C. **NDM-1** — A Cause for Worldwide Concern. . N Engl J Med 2010; 363:2377-2379.

Mmeje O, Wallett S, Kolenic G, et al. Impact of **expedited partner therapy (EPT) implementation** on **chlamydia** incidence in the USA. Sex Transm Infect. 2017 May 17.

Molina JM, Charreau I, Chidiac C, et al. **Post-exposure prophylaxis with doxycycline to prevent sexually transmitted infections in men who have sex with men**: an open-label randomised substudy of the ANRS IPERGAY trial. Lancet Infect Dis 2017; online Dec 8.

Money D, Steben M, Wong T, et al. Infectious Disease Committee, Executive and Council of the Society of Obstetricians and Gynaecologists of Canada. **Genital herpes: gynaecological aspects**. J Obstet Gynaecol Can 2008 Apr;30(4):347-53. http://www.sogc.org/guidelines/documents/gui207CPG0804_000.pdf

Montanha MC, Magon TFDS, Alcantara CDS, et al. Reduced bioavailability of **oral amoxicillin tablets compared to suspensions in RYGB bariatric subjects**. Br J Clin Pharmacol. 2019 Jun 19.

Moore DL, Allen UD, Mailman T; Canadian Paediatric Society, Infectious Diseases and Immunization Committee. Practice Point**. Invasive group A streptococcal disease**: management and chemoprophylaxis. April 15, 2019. https://www.cps.ca/en/documents/position/invasive-group-a-streptococcal-disease (accessed June 4, 2019)

Moore M, Stuart B, Coenen S, et al. **GRACE** consortium. **Amoxicillin for acute lower respiratory tract infection** in primary care: subgroup analysis of potential high-risk groups. Br J Gen Pract. 2014 Feb;64(619):e75-80.

Mor A, Antonsen S, Kahlert J, et al. **Prenatal exposure to systemic antibacterials and overweight** and obesity in Danish schoolchildren: a prevalence study. Int J Obes (Lond). 2015 Oct;39(10):1450-5.

Morales D, Pacurariu A, Slattery J, et al. Association Between **Peripheral Neuropathy and Exposure to Oral Fluoroquinolone or Amoxicillin-Clavulanate Therapy**. JAMA Neurol. 2019 Jul 1;76(7):827-833.

Moran GJ, Fang E, Corey GR, Das AF, De Anda C, Prokocimer P. **Tedizolid** for 6 days versus **linezolid** for 10 days for acute bacterial skin and skin-structure infections (ESTABLISH-2): a randomised, double-blind, phase 3, non-inferiority trial. Lancet Infect Dis 2014; online June 6.

Moran GJ, Krishnadasan A, Mower WR, et al. Effect of **cephalexin plus trimethoprim sulfamethoxazole vs cephalexin alone** on clinical cure of **uncomplicated cellulitis**: a randomized clinical trial.JAMA. doi:10.1001/jama.2017.5653

Moralejo D, El Dib R, Prata RA, Barretti P, Corrêa I. **Improving adherence to Standard Precautions for the control of health care-associated infections**. Cochrane Database of Systematic Reviews 2018, Issue 2. Art. No.: CD010768. Considerable variation in interventions and in outcome measures used, along with high risk of bias and variability in the certainty of evidence, makes it difficult to draw conclusions about effectiveness of the interventions. This review underlines the need to conduct more robust studies evaluating similar types of interventions and using similar outcome measures.

Morales G, Picazo JJ, Baos E, Candel FJ, Arribi A, Pelaez B, Andrade R, de la Torre MA, Fereres J, Sanchez-Garcia M. **Resistance to linezolid** is mediated by the cfr gene in the first report of an outbreak of linezolid-resistant Staphylococcus aureus. Clin Infect Dis 50 (6): 821-5, 2010.

Morgan DJ, Okeke IN, Laxminarayan R, et al. **Non-prescription (OTC) antimicrobial use worldwide**: a systematic review. Lancet Infect Dis. 2011 Jun 7.

Moran GJ, Talan DA. **Cellulitis**: Commonly Misdiagnosed or Just Misunderstood? JAMA. 2017 Feb 21;317(7):760-761.

Moran R, Devchand M, Smibert O, Trubiano JA. **Antibiotic allergy labels** in hospitalised and critically ill adults: a review of current **impacts of inaccurate labelling**. Br J Clin Pharmacol. 2018 Dec 6.

Moreau R, Elkrief L, Bureau C, et al; NORFLOCIR Trial Investigators. Effects of **Long-term Norfloxacin Therapy in Patients With Advanced Cirrhosis**. Gastroenterology. 2018 Dec;155(6):1816-1827.e9.

Mortensen EM, Halm EA, Pugh MJ, et al. Association of **azithromycin with mortality** and cardiovascular events among older patients hospitalized with pneumonia. JAMA. 2014 Jun 4;311(21):2199-208.

Mosholder AD, Mathew J, Alexander JJ, et al. **Cardiovascular risks with azithromycin** and other antibacterial drugs, N Engl J Med2013; 368; 18:1665-1668.

Muanda FT, Sheehy O, Bérard A. Use of **antibiotics during pregnancy and risk of spontaneous abortion**. CMAJ. 2017 May 1;189(17):E625-E633

Muanda FT, Sheehy O, et al. Use of **antibiotics during pregnancy** and the risk of major congenital malformations: A population based cohort study. Br J Clin Pharmacol. 2017 Jul 19.

Muanda FT, et al. Use of **trimethoprim-sulfamethoxazole during pregnancy and risk of spontaneous abortion**: a nested case control study. Br J Clin Pharmacol. 2018 Feb 8.

Mullish BH, Quraishi MN, Segal JP, et al. The use of **faecal microbiota transplant as treatment for recurrent or refractory Clostridium difficile** infection and other potential indications: joint British Society of Gastroenterology (BSG) and Healthcare Infection Society (HIS) guidelines. Gut. 2018 Aug 28.

Murdoch DR, Corey GR, Hoen B, et al. International Collaboration on Endocarditis-Prospective Cohort Study (ICE-PCS) Investigators. Clinical presentation, etiology, and outcome of **infective endocarditis** in the 21st century: the International Collaboration on Endocarditis-Prospective Cohort Study. Arch Intern Med. 2009 Mar 9;169(5):463-73.

Musher DM, Abers MS, Corrales-Medina VF. **Acute Infection and Myocardial Infarction**. N Engl J Med. 2019 Jan 10;380(2):171-176.

Nadimpalli M, Stewart JR, Pierce E, et al. **Livestock-Associated**, **Antibiotic-Resistant Staphylococcus aureus** Nasal Carriage and Recent Skin and Soft Tissue Infection among Industrial Hog Operation Workers. PLoS One. 2016 Nov 16;11(11):e0165713.

Nakhoul GN, Hickner J. Management of **adults with acute streptococcal pharyngitis**: minimal value for backup strep testing and overuse of antibiotics. J Gen Intern Med. 2013 Jun;28(6):830-4.

Navarro-López V, Ramírez-Boscá A, et al. Effect of Oral Administration of a Mixture of **Probiotic Strains on SCORAD Index and Use of Topical Steroids** in Young Patients With Moderate **Atopic Dermatitis**: A Randomized Clinical Trial. JAMA Dermatol. 2017 Nov 8.

Nelson RL, Suda KJ, Evans CT. **Antibiotic treatment for Clostridium difficile-associated diarrhoea in adults**. Cochrane Database of Systematic Reviews 2017, Issue 3. Art. No.: CD004610. No firm conclusions can be drawn regarding the efficacy of antibiotic treatment in severe CDI as most studies excluded patients with severe disease. The lack of any 'no treatment' control studies does not allow for any conclusions regarding the need for antibiotic treatment in patients with mild CDI beyond withdrawal of the initiating antibiotic. Nonetheless, moderate quality evidence suggests that vancomycin is superior to metronidazole and fidaxomicin is superior to vancomycin. The differences in effectiveness between these antibiotics were not too large and the advantage of metronidazole is its far lower cost compared to the other two antibiotics. The quality of evidence for teicoplanin is very low. Adequately powered studies are needed to determine if teicoplanin performs as well as the other antibiotics. A trial comparing the two cheapest antibiotics, metronidazole and teicoplanin, would be of interest.

Nguyen MH, Clancy CJ, Pasculle AW, et al. **Performance of the T2Bacteria Panel for diagnosing bloodstream infections**. A diagnostic accuracy study. Ann Med. 2019. [Epub ahead of print]. doi:10.7326/M18-2772

NICE Mar 2011 Clinical Guideline 119. **Diabetic foot** - inpatient management of people with diabetic foot ulcers and infection. http://www.nice.org.uk/nicemedia/live/13416/53556/53556.pdf

NICE National Institute for Health and Clinical Excellence. Surgical management of children with **otitis media with effusion (OME**). (Clinical guideline 60.) 2008. www.nice.org.uk/CG060

NICE: National Institute for Health and Care Excellence. **Sore throat (acute): antimicrobial prescribing NICE guideline**. January 2018. www.nice.org.uk/guidance/ng84 (use acetaminophen, ibuprofen)

Nielsen TB, Brass EP, Gilbert DN, et al. **Sustainable Discovery and Development of Antibiotics** - Is a Nonprofit Approach the Future? N Engl J Med. 2019 Aug 8;381(6):503-505

Niland ML, Bonsu BK, Nuss KE, Goodman DG. A pilot study of 1 versus 3 days of **dexamethasone** as add-on therapy in children with **streptococcal pharyngitis**. Pediatr Infect Dis J 2006;25(6):477-81.

Nishimura RA, Carabello BA, Faxon DP, et al. **ACC/AHA 2008** Guideline update on valvular heart disease: focused update on **infective endocarditis**: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines endorsed by the Society of Cardiovascular Anesthesiologists, Society for Cardiovascular Angiography and Interventions, & Society of Thoracic Surgeons.J Am Coll Cardiol. 2008 Aug 19;52(8):676-85.

Nissen JL et al. Effectiveness of **penicillin, dicloxacillin and cefuroxime for penicillin susceptible Staphylococcus aureus** bacteraemia: A retrospective, propensity-score-adjusted case–control and cohort analysis. J Antimicrob Chemother 2013 Apr 18.

Nitschke M, Sayk F, Härtel C et al. Association between **azithromycin** therapy and duration of bacterial shedding among patients with Shiga toxin-producing enteroaggregative **Escherichia coli O104:H4**. JAMA. 2012 Mar 14;307(10):1046-52. (lower carriage)

Niu KY, Lin YK. **Generalized tetanus**. CMAJ. 2019 Aug 26;191(34):E944.

Noble J, Lloyd JC. The **red eye**. CMAJ. 2010 Oct 4.

Nordqvist M, Jacobsson B, Brantsæter AL, et al. Timing of **probiotic milk consumption during pregnancy** and effects on the incidence of preeclampsia and preterm delivery: a prospective observational cohort study in Norway. BMJ Open. 2018 Jan 23;8(1):e018021.

Norhayati MN;Ho JJ;Azman MY. **Influenza vaccines for preventing acute otitis** media in infants and children. Cochrane Database Syst Rev. 2017 Oct 17;10:CD010089. Influenza vaccine results in a small reduction in AOM. The observed reduction in the use of antibiotics needs to be considered in light of current recommended practices aimed at avoiding antibiotic overuse. Safety data from these trials were limited. The benefits may not justify the use of influenza vaccine without taking into account the vaccine efficacy in reducing influenza and safety data. We judged the quality of the evidence to be low to moderate.

Norton AE, Konvinse K, Phillips EJ, et al. **Antibiotic Allergy in Pediatrics**. Pediatrics. 2018 Apr 26.

Norton LE, Lee BR, Harte L, et al. Improving **Guideline-Based Streptococcal Pharyngitis Testing**: A Quality Improvement Initiative. Pediatrics. 2018 Jun 20.

Nouira S, Marghli S, Besbes L, et al. **Standard versus newer antibacterial agents** (SMX/TMP vs Cipro) in the treatment of severe acute exacerbation of chronic obstructive pulmonary disease: a randomized trial of trimethoprim-sulfamethoxazole versus ciprofloxacin. Clin Infect Dis. 2010 Jul 15;51(2):143-9.

Nylund CM, Eide M, Gorman GH. Association of **Clostridium difficile** Infections with **Acid Suppression** Medications in Children. J Pediatr. 2014 Aug 8.

Oake Natalie; Taljaard Monica; van Walraven Carl; et al. The Effect of **Hospital-Acquired Clostridium** difficile Infection on In-Hospital Mortality. Arch Intern Med. 2010;170(20):1804-1810.

Obel N, Dessau RB, Krogfelt KA, etal . Long term **survival, health, social functioning, and education** in patients with **European Lyme neuroborreliosis:** nationwide population based cohort study. BMJ 2018;361:k1998.

O'Byrne P, MacPherson P. **Syphilis**. BMJ. 2019 Jun 28;365:l4159.

O'Connor EA, Lin JS, Burda BU, et al. **Behavioral Sexual Risk-Reduction Counseling** in Primary Care to Prevent Sexually Transmitted Infections: An Updated Systematic Evidence Review for the U.S. Preventive Services Task Force. (USPSTF) Ann Intern Med. 2014 Sep 23.

O'Donnell DE, Aaron S, Bourbeau J, Hernandez P, et al. **Canadian** Thoracic Society recommendations for management of **chronic obstructive pulmonary disease**—2007 update. Can Respir J 2007;14(Suppl B):5B-32B.

O`Riordan W, Green S, Overcash JS, et al. **Omadacycline for Acute Bacterial Skin and Skin-Structure Infections**. N Engl J Med. 2019 Feb 7;380(6):528-538.

O'Sullivan JW, Harvey RT, Glasziou PP, et al. **Written information for patients** (or parents of child patients) to reduce the use of antibiotics for acute upper respiratory tract infections in primary care. Cochrane Database Syst Rev. 2016 Nov 25;11:CD011360. Review.

Oehler RL, Velez AP, Mizrachi M, Lamarche J, Gompf S. **Bite-related** and septic syndromes caused by **cats and dogs**. Lancet Infect Dis. 2009 Jul;9(7):439-47.

Oh N, Downey P, Ardehali A. A **Febrile, Hypotensive Patient With Bilateral Lung Crackles**. JAMA. 2019 May 20.

Olek A, Woynarowski M, Ahren IL, et al. Efficacy and Safety of **Lactobacillus plantarum DSM 9843 (LP299V) in the Prevention of Antibiotic-Associated Gastrointestinal Symptoms** in Children-Randomized, Double-Blind, Placebo-Controlled Study. J Pediatr. 2017 Apr 21.

Olesen SW, Barnett ML, MacFadden DR, et al. Trends in **outpatient antibiotic use and prescribing practice among US older** adults, 2011-15: observational study. BMJ. 2018 Jul 27;362:k3155.

Oluwalana C, Camara B, Bottomley C, et al. **Azithromycin** in Labor Lowers Clinical Infections in **Mothers and Newborns**: A Double-Blind Trial. Pediatrics. 2017 Feb;139(2).

Ooi C, Lewis D. **Updating the management of sexually transmitted infections**. Aust Prescr. 2015 Dec;38(6):204-8. Epub 2015 Dec 1. Review.

Oppelaar MC, Zijtveld C, Kuipers S, et al. Evaluation of **Prolonged vs Short Courses of antibiotic Prophylaxis Following Ear, Nose, Throat, and Oral and Maxillofacial Surgery**: A Systematic Review and Meta-analysis. JAMA Otolaryngol Head Neck Surg. 2019 May 9.

Olympia RP, Khine H, Avner JR. Effectiveness of oral **dexamethasone** in the treatment of moderate to **severe pharyngitis** in children. Arch Pediatr Adolesc Med 2005;159(3):278-82.

Orlovska S, Vestergaard CH, Bech BH, et al. Association of **Streptococcal Throat Infection With Mental Disorders**: Testing Key Aspects of the **PANDAS** Hypothesis in a Nationwide Study. JAMA Psychiatry. 2017 May 24.

Örtqvist AK, Lundholm C, Halfvarson J, et al. **Fetal and early life antibiotics exposure and very early onset inflammatory bowel disease**: a population-based study. Gut. 2019 Feb;68(2):218-225.

Osthoff M et al. **Low-dose acetylsalicylic acid** treatment and impact on short-term mortality in **Staphylococcus aureus bloodstream infection**: A propensity score–matched cohort study. Crit Care Med 2016 Jan 6.

Ortqvist AK, Lundholm C, Kieler H, et al. **Antibiotics in fetal and early life and subsequent childhood asthma**: nationwide population based study with sibling analysis. BMJ. 2014 Nov 28;349:g6979. doi: 10.1136/bmj.g6979.

Ota KV, Jamieson F, Fisman DN, et al. Prevalence of and risk factors for **quinolone-resistant Neisseria gonorrhoeae** infection in Ontario. CMAJ. 2009 Feb 3;180(3):287-90.

Ovetchkine P, Rieder MJ; Canadian Paediatric Society, Drug Therapy and Hazardous Substances Committee. **Azithromycin use in paediatrics**: a practical overview. Paediatr Child Health 2013;18:311-3. www.cps.ca/en/documents/position/azithromycin-use-in-paediatrics

Paavonen J, Brunham RC. **Bacterial Vaginosis and Desquamative Inflammatory Vaginitis**. N Engl J Med. 2018 Dec 6;379(23):2246-2254.

Paez-Canro C, Alzate JP, Gonzalez LM, et al. Antibiotics for treating urogenital Chlamydia trachomatis infection in men and non-pregnant women . Cochrane Database Syst Rev. 2019 Jan 25;1:CD010871. In men, regimens with azithromycin are probably less effective than doxycycline for microbiological failure, however, there might be little or no difference for clinical failure. For women, we are uncertain whether azithromycin compared to doxycycline increases the risk of microbiological failure. Azithromycin probably slightly reduces adverse events compared to doxycycline in men and women together but may have little difference in men alone. We are uncertain whether doxycycline compared to ofloxacin reduces microbiological failure in men or women alone, or men and women together, nor if it reduces clinical failure or adverse events in men or women.Based on the fact that women suffer mainly asymptomatic infections, and in order to test the effectiveness and safety of the current recommendations (azithromycin, doxycycline and ofloxacin), for CT infection, especially in low and middle income countries, future RCTs should be designed and conducted to include a large enough sample size of women, and with low risk of bias

Page M, Macbeth A. A rash that appeared on holiday. BMJ 2017 Oct 5; 359:j4338. (**doxycycline photosensitivity**)

Pal A, Matzneller P, Gautam A, et al. Target site **pharmacokinetics of doxycycline for rosacea in healthy volunteers is independent of food-effect** (PI Markus Zeitlinger). Br J Clin Pharmacol. 2018 Jul 22.

Paladine HL, Desai UA. **Vaginitis**: Diagnosis and Treatment. Am Fam Physician. 2018;97(5):321-329.

Pallin DJ, Binder WD, Allen MB, et al. Clinical trial: comparative effectiveness of **cephalexin plus trimethoprim-sulfamethoxazole versus cephalexin** alone for treatment of uncomplicated **cellulitis**: a randomized controlled trial. Clin Infect Dis. 2013 Jun;56(12):1754-62.

Palms DL, Hicks LA, Bartoces M. Comparison of **antibiotic prescribing in retail clinics, urgent care centers, emergency departments**, and traditional ambulatory care settings in the United States, 2014 [online July 9, 2018]. JAMA Intern Med. doi:10.1001/jamainternmed.2018.1632

Palms DL, Hicks LA, Bartoces M, et al. Comparison of **Antibiotic Prescribing in Retail Clinics, Urgent Care Centers, Emergency Departments**, and Traditional Ambulatory Care Settings in the United States. JAMA Intern Med. 2018 Jul 16.

Pankhania Miran, Judd Owen, Ward Andy. Practice: 10-Minute Consultation: **Otorrhoea**. (otitis externa) BMJ 2011;342:doi:10.1136/bmj.d2299 (Published 20 May 2011)

Papenburg J, Fontela PS, Freitas RR, Burstein B. **Inappropriate Antibiotic Prescribing for Acute Bronchiolitis** in US Emergency Departments, 2007-2015. J Pediatric Infect Dis Soc. 2019 Jan 17.

Parameswaran GI, Sethi S. **Long-term macrolide therapy** in chronic obstructive pulmonary disease. CMAJ. 2014 Oct 21;186(15):1148-1152.

Parekh TM, Raji M, Lin Y-L, Tan A, Kuo Y-F, Goodwin JS. **Hypoglycemia after antimicrobial drug prescription** for older patients using sulfonylureas [published online September 1, 2014]. JAMA Intern Med. doi:10.1001/jamainternmed.2014.3293.

Park JW, Curtis JR, Moon J, et al. Prophylactic effect of **trimethoprim-sulfamethoxazole for pneumocystis pneumonia** in patients with rheumatic diseases exposed to prolonged high-dose glucocorticoids. Ann Rheum Dis. 2018 May;77(5):644-649.

Pasternak B, Hviid A. Use of **acyclovir**, valacyclovir, and famciclovir in the **first trimester of pregnancy** and the risk of birth defects. JAMA. 2010 Aug 25;304(8):859-66.

Pasternak B, Svanström H, Melbye M, Hviid A. Association between oral **fluoroquinolone use and retinal detachment**. JAMA. doi: 10.1001/jama.2013.280500. (not associated)

Pasternak B, Inghammar M, Svanström H. **Fluoroquinolone use and risk of aortic aneurysm** and dissection: nationwide cohort study. BMJ 2018;360:k678.

Patel RA, Gallagher JC. **Drug Fever**. Pharmacotherapy. 2010 Jan;30(1):57-69.

Paul I. M., Maselli J. H., Hersh A. L., et al. Antibiotic Prescribing During Pediatric Ambulatory Care **Visits for Asthma**. *Pediatrics*, 2011; DOI: 10.1542/peds.2011-0218

Paul M, Bishara J, Yahav D, et al. **Trimethoprim-sulfamethoxazole versus vancomycin** for severe infections caused by meticillin resistant Staphylococcus aureus: randomised controlled trial. BMJ. 2015 May 14;350

Paulson JA, Zaoutis TE; Council on Environmental Health; Committee on Infectious Diseases, Nontherapeutic Use of **Antimicrobial Agents in Animal Agriculture**: Implications for Pediatrics. Pediatrics. 2015 Nov 16.

Pedersen TM, Stokholm J, Thorsen J, et al. **Antibiotics in Pregnancy Increase Children's Risk of Otitis Media and Ventilation Tubes**. J Pediatr. 2017 Jan 11.

Pegler S, Healy B. In patients **allergic to penicillin**, consider second and third generation cephalosporins for life threatening infections. BMJ. 2007 Nov 10;335(7627):991.

Pegues DA et al. Impact of **ultraviolet germicidal irradiation** for no-touch terminal room disinfection on **Clostridium difficile** infection incidence among hematology-oncology patients. Infect Control Hosp Epidemiol 2017 Jan; 38:39.

Peltan ID, Brown SM, Bledsoe JR, Sorensen J, Samore MH, Allen TL, Hough CL.**Emergency department door-to-antibiotic time and long-term mortality in sepsis**.Chest. 2019 Feb 16.

Peña MT, Preciado D, Orestes M, Choi S. Orbital complications of **acute sinusitis**: changes in the post-pneumococcal vaccine (PCV7) era. JAMA Otolaryngol Head Neck Surg. 2013 Mar 1;139(3):223-7. (S aureus more common now)

Pepper DJ, Sun J, Cui X, et al. **Antibiotic- and Fluid-Focused Bundles** Potentially Improve Sepsis Management, but High-Quality Evidence Is Lacking for the Specificity Required in the Centers for Medicare and Medicaid Service's Sepsis Bundle (SEP-1). Crit Care Med. 2019 Jul 31

Pereira JB, Farragher TM, Tully MP, et al. Association between **Clostridium difficile infection and antimicrobial usage** in a large group of English hospitals. Br J Clin Pharmacol. 2014 May;77(5):896-903.

Persson R, Jick S. Clinical implications of the association between **fluoroquinolones and tendon rupture**: the magnitude of the effect with and without corticosteroids. Br J Clin Pharmacol. 2019 Jan 25.

Peterson GE, Crowley AL. Antibiotic **Prophylaxis for Infective Endocarditis**. Circulation. 2019 Jul 16;140(3):181-183.

Pettitt DA, Molajo A, McArthur P. A **human bite**. BMJ. 2012 Jul 17;345:e4798.

Pham Thanh D, Thanh Tuyen H, et al. Inducible **colistin resistance** via a disrupted plasmid-borne **mcr-1 gene** in a **2008 Vietnamese** Shigella sonnei isolate. J Antimicrob Chemother. 2016 May 30. [Epub ahead of print]

Phoenix G, Das S, Joshi M. Diagnosis and management of **cellulitis**. BMJ. 2012 Aug 7;345:e4955.

Pichichero ME, Zagursky R. **Penicillin and Cephalosporin allergy.** Ann Allergy Asthma Immunol. 2014 May;112(5):404-412

Pickens CI, Wunderink RG, Pickens CI. Principles and Practice of **Antibiotic Stewardship in the ICU**. Chest. 2019 Jan 25.

Pierson-Marchandise M, Gras V, Moragny J, et al. The **drugs that mostly frequently induce acute kidney injury**: a case - non-case study of a pharmacovigilance database. Br J Clin Pharmacol. 2016 Dec 21. The most frequently implicated drug classes were antibacterials for systemic use (29.5%), diuretics (18.5%), agents acting on the renin-angiotensin system (16.3%), antineoplastic agents (10.2%) and anti-inflammatory agents (5.4%). Gentamicin, eplerenone, spironolactone, candesartan, cisplatin and acyclovir had the highest RORs (>10).

Pillai, Dylan R., McGeer, Allison, Low, Donald E. New Delhi metallo-{beta}-lactamase-1 (**NDM-1**) in Enterobacteriaceae: emerging resistance. CMAJ 2011 183: 59-64.

Pilmann Laursen R, Larnkjaer A, Ritz C, et al. **Probiotics and child care absence** due to infections: a randomized controlled trial. Pediatrics 2017;140(2):e20170735.

Pinninti SG, Angara R, Feja KN, et al. **Neonatal Herpes Disease following Maternal Antenatal Antiviral Suppressive Therapy**: A Multicenter Case Series. J Pediatr. 2012 Feb 14.

Pinto-Sanchez MI, Hall GB, Ghajar K, et al. Probiotic **Bifidobacterium longum NCC3001 Reduces Depression Scores** and Alters Brain Activity: a Pilot Study in Patients With Irritable Bowel Syndrome. Gastroenterology. 2017 May 5.

Pitts SI, Maruthur NM, Langley GE, et al. **Obesity, Diabetes, and the Risk of Invasive Group B Streptococcal Disease in Nonpregnant Adults in** the United States. Open Forum Infect Dis. 2018 Jun 8;5(6):ofy030.

Planche TD, Davies KA, Coen PG, et al. Differences in outcome according to **Clostridium difficile testing method**: a prospective multicentre diagnostic evaluation study of C difficile infection. Lancet Infect Dis 2013; online Sept 3.

Plitt S, Boyington C, Sutherland K, et al. Antimicrobial **Resistance in Gonorrhea**: Influence of Epidemiologic and Laboratory Surveillance Data on Treatment Guidelines: Alberta, Canada 2001-2007. Sex Transm Dis. 2009 Aug 21.

Podolsky SH, Powers JH 3rd. **Regulating Antibiotics in an Era of Resistance**: The Historical Basis and Continued Need for Adequate and Well-Controlled Investigations. Ann Intern Med. 2015 Sep 1;163(5):386-388.

Podolsky SH. Historical Perspective on the Rise and Fall and Rise of **Antibiotics and Human Weight Gain**. Ann Intern Med. 2017 Jan 17;166(2):133-138

Pogany L, Romanowski B, Robinson J, et al. Management of **gonococcal infection** among adults and youth: New key recommendations. **Can Fam Physician**. 2015 Oct;61(10):869-73.

Polage CR, Gyorke CE, Kennedy MA, et al. **Overdiagnosis of Clostridium difficile** Infection in the Molecular Test Era. JAMA Intern Med. 2015 Sep 8:1-10.

Poole NM, Shapiro DJ, Fleming-Dutra KE, et al. Antibiotic prescribing for **children in United States emergency departments**: 2009–2014. Pediatrics. 2019;143(2):e20181056

Poropat F, Pastore S, Gesuete V, et al. A boy with fever and arthralgia (**acute rheumatic fever**). BMJ. 2017 Mar 29;356:j1347

Postenrieder NR, Reed JL, Hesse E, et al. **Rapid Antigen Testing for Trichomoniasis** in an Emergency Department. Pediatrics. 2016 May 20.

Pouwels KB, Hopkins S, Llewelyn MJ, Walker AS, McNulty CAM, Robotham JV. **Duration of antibiotic treatment for common infections** in English primary care: cross sectional analysis and comparison with guidelines. BMJ 2019;364:l440.

Power M, Wigglesworth N, Donaldson E, et al. **Reducing Clostridium difficile** infection in acute care by using an improvement collaborative. BMJ. 2010 Jul 21

Public Health Agency of Canada. Important notice – public health information update on the treatment for **gonococcal infection**. Public Health Agency of Canada issued important notice on gonococcal infection. December 21, 2011. www.phac-aspc.gc.ca/std-mts/sti-its/alert/2011/alert-gono-eng.php (accessed December 21, 2011).

Public Health Agency of Canada. **Interim syphilis treatment guidelines** during the benzathine penicillin G (Bicillin L-A) shortage 2016. www.phac-aspc.gc.ca/std-mts/sti-its/cgsti-ldcits/section-5-10-itg-ldi-eng.php (accessed April 25, 2016).

Puopolo KM, Lynfield R, Cummings JJ, et al. Management of **Infants at Risk for Group B Streptococcal Disease**. Pediatrics. 2019 Jul 8.

Quan J, Li X, Chen Y, et al. Prevalence of **mcr-1 in Escherichia coli and Klebsiella pneumoniae** recovered from bloodstream infections in China: a multicentre longitudinal study. Lancet Infect Dis. 2017 Apr;17(4):400-410.

Rademacher WMH, et al. **Antibiotic prophylaxis** is not indicated prior to **dental procedures** for prevention of periprosthetic joint infections. Acta Orthop. 2017 Jun 22:1-7.

Raff AB, Kroshinsky D. **Cellulitis**: A Review. JAMA. 2016 Jul 19;316(3):325-37.

Raguideau F, Dray-Spira R, Zureik M. Oral **fluoroquinolone** use and **retinal detachment**-reply. JAMA Ophthalmol. 2016;134:1448-1449.

Ranakusuma RW, Pitoyo Y, Safitri ED, et al. **Systemic corticosteroids for acute otitis media in children.** Cochrane Database Syst Rev. 2018 Mar 15;3:CD012289. : The evidence for the effect of systemic corticosteroids on AOM is of low to very low quality, meaning the effect of systemic corticosteroids on important clinical outcomes in AOM remains uncertain. Large, high-quality studies are required to resolve the question.

Rao GA, Mann JR, Shoaibi A, et al. **Azithromycin** and **levofloxacin** use and increased risk of **cardiac arrhythmia** and death. Ann Fam Med 2014; 12: 121-127.

Rao SC, Athalye-Jape GK, Deshpande GC, et al. **Probiotic Supplementation** and Late-Onset **Sepsis** in Preterm Infants: A Meta-analysis. Pediatrics. 2016 Feb 12.

Rajan M B, Budania A, Bohra GK. **Ceftriaxone induced aplastic anaemia**: A deadfall trap for bone marrow. Br J Clin Pharmacol. 2019 Jun 18.

Rajan S**. Skin and soft-tissue infections**: Classifying and treating a spectrum. Cleve Clin J Med. 2012 Jan;79(1):57-66.

Ramakrishnan K, Salinas RC, Agudelo Higuita NI. **Skin and Soft Tissue Infections**. Am Fam Physician. 2015 Sep 15;92(6):474-83.
Raven KE et al. Complex routes of **nosocomial vancomycin-resistant Enterococcus faecium transmission** revealed by genome sequencing. Clin Infect Dis 2017 Apr 1; 64:886.
Ray WA, Murray KT, Hall K, et al. **Azithromycin and the risk of cardiovascular death**. N Engl J Med 2012; 366:1881-90.
Ray KJ, Prajna L, Srinivasan M, et al. **Fluoroquinolone** Treatment and Susceptibility of Isolates From **Bacterial Keratitis**. JAMA Ophthalmol. 2013 Jan 10:1-4.
Rebnord IK, Sandvik H, Batman Mjelle A, et al. **Out-of-hours antibiotic prescription** after screening with **C reactive protein**: a randomised controlled study. BMJ Open. 2016 May 12;6(5).
Rekart ML, Ndifon W, Brunham RC, et al. A double-edged sword: does highly active **antiretroviral therapy contribute to syphilis** incidence by impairing immunity to Treponema pallidum? Sex Transm Infect. 2017 Jan 16.
Revolinski SL, Munoz-Price LS. **Clostridium difficile in Immunocompromised Hosts**: A Review of Epidemiology, Risk Factors, Treatment, and Prevention. Clin Infect Dis. 2018 Oct 3.
Riddle MS, DuPont HL, Connor BA. ACG Clinical Guideline: Diagnosis, Treatment, and Prevention of Acute Diarrheal Infections in Adults. Am J Gastroenterol. 2016 Apr 12.
Rimmler C, Lanckohr C, Akamp C, et al. Physiologically Based **Pharmacokinetic Evaluation of Cefuroxime** in Perioperative Antibiotic Prophylaxis. Br J Clin Pharmacol. 2019 Sep 5.
Rindone JP, Mellen CK. Meta-analysis of trials comparing **cefazolin to antistaphylococcal penicillins in the treatment** of methicillin-sensitive **Staphylococcus aureus bacteraemia**. Br J Clin Pharmacol. 2018 Mar 30.
Rioux J, Edwards J, Bresee L, et al. **Nasal-Swab Results for Methicillin-Resistant Staphylococcus** aureus and Associated Infections. Can J Hosp Pharm. 2017 Mar-Apr;70(2):107-112.
Roberts JA, Abdul-Aziz MH, Davis JS, et al. **Continuous versus Intermittent β-Lactam Infusion in Severe Sepsis**. A Meta- analysis of Individual Patient Data from Randomized Trials. Am J Respir Crit Care Med. 2016 Sep 15;194(6):681-91.
Roberts RM, Bartoces M, Thompson SE, Hicks LA. **Antibiotic prescribing by general dentists** in the United States, 2013. J Am Dent Assoc. 2017;148:172.e1-178.e1.
Robertsson O, Thompson O, W-Dahl A, et al. **Higher risk of revision for infection using systemic clindamycin prophylaxis than with cloxacillin**. Acta Orthop. 2017 May 11:1-6.
Rogers Van Katwyk S, Grimshaw JM, Nkangu M, et al. Government policy **interventions to reduce human antimicrobial use**: A systematic review and evidence map. PLoS Med. 2019 Jun 11;16(6):e1002819.
Rogozinska E, Kara-Newton L, Zamora JR, et al. **On-site test to detect syphilis** in pregnancy: a systematic review of test accuracy studies. BJOG. 2016 Dec 28.
Rollins KE, Varadhan KK, Neal KR, et al. **Antibiotics Versus Appendicectomy** for the Treatment of Uncomplicated Acute Appendicitis: An Updated Meta-Analysis of Randomised Controlled Trials. World J Surg. 2016 May 19.
Romøren M, Lindbaek M, Nordeng H. Pregnancy outcome after **gestational exposure to erythromycin**-a population-based register study from Norway. Br J Clin Pharmacol. 2012 Mar 30.
Root AA, Wong AY, Ghebremichael-Weldeselassie Y, et al. Evaluation of the risk of **cardiovascular events with clarithromycin** using both propensity score and self-controlled study designs. Br J Clin Pharmacol. 2016 Apr 19.
Rosen T, Albareda N, Rosenberg N, et al. Efficacy and Safety of **Ozenoxacin Cream for Treatment of Adult and Pediatric Patients With Impetigo**: A Randomized Clinical Trial. JAMA Dermatol. 2018 Jun 13.
Rosenfeld RM, Brown L, Cannon CR, et al. American Academy of Otolaryngology--Head and Neck Surgery Foundation. Clinical practice guideline: **acute otitis externa**. Otolaryngol Head Neck Surg. 2006 Apr;134(4 Suppl):S4-23. http://www.entnet.org/Practice/upload/AOE-cpg.pdf
Rosenfeld RM, Piccirillo JF, Chandrasekhar SS, et al. Clinical practice guideline (**AAO-HNSF**) update): **adult sinusitis executive summary**. Otolaryngol Head Neck Surg. 2015 Apr;152(4):598-609.
Rosenfeld RM, Shin JJ, Schwartz SR, et al. (**AAO-HNSF**) **Clinical Practice Guideline**: **Otitis Media with Effusion** Executive Summary (Update). Otolaryngol Head Neck Surg. 2016 Feb;154(2):201-14.
Ross AG, Olds GR, Cripps AW, et al. **Enteropathogens** and chronic illness in returning **travelers**. N Engl J Med. 2013 May 9;368(19):1817-25.
Ross JD, Harding J, Duley L, et al. **Gentamicin as an alternative to ceftriaxone in the treatment of gonorrhoea:** the G-TOG non-inferiority RCT**.** Health Technol Assess. 2019 May;23(20):1-104.
Ross JDC, Brittain C, Cole M, et al. **Gentamicin compared with ceftriaxone for the treatment of gonorrhoea (G-ToG**): a randomised non-inferiority trial. Lancet 2019; published online May 2.
Rossen NG, Fuentes S, van der Spek MJ, et al. Findings From a Randomized Controlled Trial of **Fecal Transplantation** for Patients With Ulcerative Colitis. Gastroenterology. 2015 Jul;149(1):110-118.e4.
Rothberg Michael B.; Pekow Penelope S.; Lahti Maureen; et al. Antibiotic Therapy and Treatment Failure in Patients Hospitalized for Acute Exacerbations of **Chronic Obstructive Pulmonary Disease**. JAMA. 2010;303(20):2035-2042.
Rubin G, Orbach H, Rinott M, et al. The use of **prophylactic antibiotics in treatment of fingertip amputation**: a randomized prospective trial. Am J Emerg Med. 2015 May;33(5):645-7.
Rubin MA, et al. The Importance of **Contact Precautions** for Endemic **Methicillin-Resistant Staphylococcus** aureus and **Vancomycin-Resistant Enterococci**. JAMA. 2018 Feb 12.
Saari A, Virta LJ, Sankilampi U, et al. Antibiotic Exposure in Infancy and **Risk of Being Overweight** in the First 24 Months of Life. Pediatrics. 2015 Mar 30.
Sabhaney V, Goldman RD. Management of **dog bites** in children. Can Fam Physician. 2012 Oct;58(10):1094-6.
Sadeghirad B, Siemieniuk RAC, Brignardello-Petersen R, et al. **Corticosteroids for treatment of sore throat**: systematic review and meta-analysis of randomised trials. BMJ. 2017 Sep 20;358:j3887.
Sager R, Kutz A, Mueller B, Schuetz P. **Procalcitonin-guided** diagnosis and antibiotic stewardship revisited. BMC Med. 2017 Jan 24;15(1):15.
Sahnan K, Adegbola SO, Tozer PJ, et al. **Perianal abscess**. BMJ. 2017 Feb 21;356:j475.
Sakulchit T, Goldman RD. Antibiotic therapy for children with **acute otitis media**. Can Fam Physician. 2017 Sep;63(9):685-687
Saint S, Bent S, Vittinghoff E, Grady D. Antibiotics in chronic obstructive pulmonary disease **exacerbations**. A meta-analysis. JAMA 1995;273(12):957-60.
Sallinen V, Akl EA, You JJ, et al. Meta-analysis of **antibiotics versus appendicectomy** for non-perforated acute appendicitis. Br J Surg. 2016 Mar 17.
Salminen P, Paajanen H, Rautio T, et al. **Antibiotic therapy vs appendectomy** for treatment of **uncomplicated acute appendicitis**: the APPAC randomized clinical trial. JAMA. doi:10.1001/jama.2015.6154.
Salminen P, Tuominen R, et al. Five-year follow-up of **antibiotic therapy for uncomplicated acute appendicitis** in the APPAC randomized clinical trial [Sept 25,2018]. JAMA.
Sammons JS, Toltzis P, Zaoutis TE. **Clostridium difficile Infection in Children**. JAMA Pediatr. 2013 Jun 1;167(6):567-73.
Sanchez GV, Fleming-Dutra KE, Roberts RM, et al. **Core Elements of Outpatient Antibiotic Stewardship**. MMWR Recomm Rep. 2016 Nov 11;65(6):1-12.
Sander SD, Andersen AMN, Murray JA, et al. Association between **antibiotics in the first year of life and celiac disease**. Gastroenterology 2019;156:2217-29
Sandhu HS, Brucker AJ, Ma L, VanderBeek BL. Oral **fluoroquinolones and the risk of uveitis** [online October 29, 2015].JAMA Ophthalmol. doi:10.1001/jamaophthalmol.2015.4092.
Santos JM, Batech M, Pelter MA, et al. Evaluation of the Risk of **Nitrofurantoin Lung** Injury and Its Efficacy in Diminished **Kidney** Function in Older Adults in a Large Integrated Healthcare System: A Matched Cohort Study. J Am Geriatr Soc. 2016 Apr;64(4):798-805.
Saito M, Hatakeyama S. **Acute Rheumatic Fever** with Erythema Marginatum. N Engl J Med. 2016 Dec 22;375(25):2480.
Sartelli M, Di Bella S, McFarland LV, et al. 2019 update of the **WSES guidelines for management of Clostridioides (Clostridium) difficile** infection in surgical patients. World J Emerg Surg. 2019 Feb 28;14:8.
Sartelli M, Guirao X, Hardcastle TC, et al. 2018 WSES/SIS-E consensus **conference: recommendations for the management of skin and soft-tissue infections**. World J Emerg Surg. 2018 Dec 14;13:58.
Sauerbrei, Andreas. **Preventing congenital varicella syndrome with immunization**. CMAJ 2011 0: cmaj.110055.
Savaris RF, Fuhrich DG, Duarte RV, et al. **Antibiotic therapy for pelvic inflammatory disease**. Cochrane Database Syst Rev. 2017 Apr 24;4:CD010285. We found no conclusive evidence that one regimen of antibiotics was safer or more effective than any other for the cure of PID, and there was no clear evidence for the use of nitroimidazoles (metronidazole) compared to use of other drugs with activity over anaerobes. Moderate-quality evidence from a single study at low risk of bias suggested that a macrolide (azithromycin) may be more effective than a tetracycline (doxycycline) for curing mild-moderate PID. Our review considered only the drugs that are currently used and mentioned by the CDC.
Sawleshwarkar S, Dwyer DE. **Antivirals for herpes simplex viruses**. BMJ. 2015 Jul 9;351:h3350.
Schaefer P, Baugh RF. **Acute Otitis Externa**: An Update. Am Fam Physician. 2012;86(11):1055-1061.
Schembri S, Williamson PA, Short PM, et al. **Cardiovascular events after clarithromycin** use in lower respiratory tract infections: analysis of two prospective cohort studies. BMJ. 2013 Mar 20;346:f1235.
Schlapbach LJ, Weiss SL, Wolf J. Reducing Collateral Damage From **Mandates for Time to Antibiotics in Pediatric Sepsis-Primum Non Nocere**. JAMA Pediatr. 2019 Mar 18.
Schmitz GR, Bruner D, Pitotti R, et al. Randomized controlled trial of **trimethoprim-sulfamethoxazole for uncomplicated skin abscesses** in patients at risk for community-associated methicillin-resistant Staphylococcus aureus infection. Ann Emerg Med. 2010 Sep;56(3):283-7.
Schranz AJ, Fleischauer A, Chu VH, Wu LT, Rosen DL. Trends in **drug use–associated infective endocarditis** and heart valve surgery, 2007 to 2017: a study of statewide discharge data. Ann Intern Med. 2018. [Epub ahead of print]. doi:10.7326/M18-2124
Schuetz P; Christ-Crain M; Thomann R; et al. Effect of **Procalcitonin-Based** Guidelines vs Standard Guidelines on Antibiotic Use in Lower Respiratory Tract Infections: ProHOSP RCT. JAMA. 2009;302(10):1059-1066.
Schuetz P, Chiappa V, Briel M, et al. **Procalcitonin algorithms** for antibiotic therapy decisions: a systematic review of randomized controlled trials and recommendations for clinical algorithms. Arch Intern Med. 2011 Aug 8;171(15):1322-31.
Schuetz P, Briel M, Mueller B. Clinical outcomes associated with **procalcitonin algorithms** to guide antibiotic therapy in respiratory tract infections. JAMA. 2013 Feb 20;309(7):717-8.
Schuetz P, Wirz Y, Sager R, et al. Effect of **procalcitonin-guided antibiotic treatment on mortality in acute respiratory infections**: a patient level meta-analysis. Lancet Infect Dis 2017; online Oct 13.
Schuetz P;Wirz Y;Sager R;et al. **Procalcitonin to initiate or discontinue antibiotics in acute respiratory tract infections.** Cochrane Database Syst Rev. 2017 Oct 13;10:CD007498. This updated meta-analysis of individual participant data from 12 countries shows that the use of procalcitonin to guide initiation and duration of antibiotic treatment results in lower risks of mortality, lower antibiotic consumption, and lower risk for antibiotic-related side effects. Results were similar for different clinical settings and types of ARIs, thus supporting the use of `procalcitonin in the context of antibiotic stewardship in people with ARIs.`
Schuetz P, et al. **Procalcitonin Testing to Guide Antibiotic Therapy** in Acute Upper and Lower Respiratory Tract Infections. JAMA. 2018 Mar 6;319(9):925-926.
Schuler CL, Courter JD, et al. **Decreasing Duration** of Antibiotic Prescribing for **Uncomplicated Skin and Soft Tissue Infections**. Pediatrics. 2016 Jan 18.
Schwameis M, Kündig T, Huber G, et al. Topical **azithromycin** for the prevention of **Lyme borreliosis**: a randomised, placebo-controlled, phase 3 efficacy trial. Lancet Infect Dis. 2016 Dec 19.
Schwartz RH, Kim D, Martin M, et al. A Re-appraisal of the **Minimum Duration of Antibiotic Treatment Before Approval of Return to school** for Children with **Streptococcal Pharyngitis**. Pediatr Infect Dis J. 2015 Aug 20.
Science M, Timberlake K, Morris A, et al;(GAP Can ASAP). **Quality Metrics for Antimicrobial Stewardship Programs**. Pediatrics. 2019 Mar 29.
Scott FI, Horton DB, Mamtani R, et al. Administration of **Antibiotics** to Children Before Age 2 Years Increases Risk for **Childhood Obesity**. Gastroenterology. 2016 Mar 18.
Sedaghat AR. **Chronic Rhinosinusitis**. Am Fam Physician. 2017;96(8):500-506.
Seemungal TA, Wilkinson TM, Hurst JR, et al. **Long-term erythromycin** therapy is associated with decreased chronic obstructive pulmonary disease **exacerbations**. Am J Respir Crit Care Med. 2008 Dec 1;178(11):1139-47.
Seltz LB, Smith J, Durairaj VD, Enzenauer R, Todd J. Microbiology and antibiotic management of **orbital cellulitis**. Pediatrics. 2011 Mar;127(3):e566-72.
Selva Olid A, Sola I, Barajas-Nava LA, et al. **Systemic antibiotics for treating diabetic foot infections**. Cochrane Database Syst Rev. 2015 Sep 4;9:CD009061. The evidence for the relative effects of different systemic antibiotics for the treatment of foot infections in diabetes is very heterogeneous and generally at unclear or high risk of bias. Consequently it is not clear if any one systemic antibiotic treatment is better than others in resolving infection or in terms of safety. One non-inferiority trial suggested that ertapenem with or without vancomycin is more effective in achieving clinical resolution of infection than tigecycline. Otherwise the relative effects of different antibiotics are unclear. The quality of the evidence is low due to limitations in the design of the included trials and important differences between them in terms of the diversity of antibiotics assessed, duration of treatments, and time points at which outcomes were assessed. Any further studies in this area should have a blinded assessment of outcomes, use standardised criteria to classify severity of infection, define clear outcome measures, and establish the duration of treatment.
Semic-Jusufagic A, Belgrave D, Pickles A, et al. Assessing the association of **early life antibiotic prescription with asthma exacerbations**, impaired antiviral immunity, and genetic variants in 17q21: a population-based birth cohort study. Lancet Respir Med. 2014 May 14.
Seña AC et al. **Sexual assault and sexually transmitted infections in adults, adolescents, and children**. Clin Infect Dis 2015 Dec 15; 61:S856.

Serisier DJ, Martin ML, McGuckin MA, et al. Effect of **long-term, low-dose erythromycin on pulmonary exacerbations** among patients with non–cystic fibrosis bronchiectasis: the BLESS randomized controlled trial. JAMA. 2013;309(12):1260-1267.

Shaikh N, Wald ER, Jeong JH, et al. Predicting response to antimicrobial therapy in children with acute **sinusitis**. J Pediatr. 2014 Mar;164(3):536-41.

Shaikh N, Dando EE, Dunleavy ML, et al. A Cost-Utility Analysis of 5 Strategies for the **Management of Acute Otitis Media** in Children. J Pediatr. 2017 Jun 28.

Shane AL, Mody RK, Crump JA, et al. **2017 IDSA**: Infectious Diseases Society of America Clinical Practice Guidelines for the Diagnosis and Management of **Infectious Diarrhea**. Clin Infect Dis. 2017 Oct 19.

Shannon-Lowe J, Matheson N J, Cooke F J, Aliyu S H. Prevention and medical management of **Clostridium difficile** infection. BMJ 2010;340:c1296, doi: 10.1136/bmj.c1296

Shapiro DJ, Gonzales R, Cabana MD, Hersh AL. National Trends in Visit Rates and Antibiotic Prescribing for Children With **Acute Sinusitis**. Pediatrics. 2010 Dec 27.

Shapiro DJ, Hicks LA, Pavia AT, Hersh AL. **Antibiotic prescribing for adults in ambulatory care** in the USA, 2007-09. J Antimicrob Chemother. 2013 Jul 25.

Shapiro DJ, Lindgren CE, Neuman MI, et al. **Viral Features** and Testing for **Streptococcal Pharyngitis**. Pediatrics. 2017;139(5):e20163403

Sheikh A, Hurwitz B, van Schayck CP, et al. Antibiotics versus placebo for **acute bacterial conjunctivitis**. Cochrane Database Syst Rev. 2012 Sep 12;9:CD001211.

Shekhawat NS, Shtein RM, Blachley TS, et al. **Antibiotic Prescription Fills for Acute Conjunctivitis** among Enrollees in a Large United States Managed Care Network. Ophthalmology. 2017 Jun 14.

Sheldon T. **Saving antibiotics** for when they are really needed: the Dutch example. BMJ. 2016 Aug 3;354:i4192

Shen NT et al. Timely use of **probiotics** in hospitalized adults **prevents clostridium difficile infection**: A systematic review with meta-regression analysis. Gastroenterology 2017 Feb 10.

Shen NT, Maw A, Tmanova LL, et al. Timely Use of **Probiotics in Hospitalized Adults Prevents Clostridium difficile Infection**: A Systematic Review With Meta-Regression Analysis. Gastroenterology. 2017 Jun;152(8):1889-1900.e9

Shenoy ES, Macy E, Rowe T, Blumenthal KG. **Evaluation and Management of Penicillin Allergy**: A Review. JAMA. 2019 Jan 15;321(2):188-199.

Shepherd JP, Frampton GK, Harris P. Interventions for encouraging **sexual behaviours intended to prevent cervical cancer**. Cochrane Database of Systematic Reviews 2011, Issue 4. Art. No.: CD001035. DOI: 10.1002/14651858.CD001035.pub2.

Shi C, Xiao Y, Zhang Q, et al. Efficacy and safety of **cefazolin versus antistaphylococcal penicillins for the treatment of methicillin-susceptible Staphylococcus aureus bacteremia**: a systematic review and meta-analysis. BMC Infect Dis. 2018 Oct 11;18(1):508.

Shoham S, Antar AA, Auwaerter PG, et al. Antimicrobial Access in the 21st Century: **Delays and Critical Shortages**. Ann Intern Med. 2016 Mar 22.

Shorr AF, Sun X, Johannes RS, et al. Validation of a Novel **Risk Score** for Severity of Illness in **Acute Exacerbations of COPD**. (**BAP-65**) Chest. 2011 Nov;140(5):1177-83.

Shulman ST, Bisno AL, Clegg HW, et al. Clinical Practice Guideline for the Diagnosis and Management of **Group A Streptococcal Pharyngitis**: 2012 Update by the Infectious Diseases Society of America (**IDSA**). Clin Infect Dis. 2012 Sep 9.

SIGN-Scottish Intercollegiate Guidelines Network. Diagnosis and management of **childhood otitis media** in primary care. (Guideline 66.) 2003. www.sign.ac.uk/guidelines/fulltext/66/index.html .

Silverman M, Povitz M, Sontrop JM, et al. **Antibiotic Prescribing for Nonbacterial Acute Upper Respiratory Infections in Elderly** Persons. Ann Intern Med. 2017 May 9.

Singer AJ, Thode HC Jr. Systemic **antibiotics after incision and drainage of simple abscesses**: a meta-analysis. Emerg Med J. 2013 May 18.

Singer AJ, Taira BR, Chale S, et al. **Primary versus secondary closure of cutaneous abscesses** in the emergency department: a randomized controlled trial. Acad Emerg Med. 2013 Jan;20(1):27-32.

Singer AJ, Talan DA. Management of **skin abscesses** in the era of methicillin-resistant Staphylococcus aureus. N Engl J Med. 2014 Mar 13.

Singh AE, Labbé AC, Auguste U. **Mycoplasma genitalium infection**. CMAJ. 2019 Jan 28;191(4):E103.

Singh S;Nautiyal A. **Aortic Dissection and Aortic Aneurysms Associated with Fluoroquinolones**: a Systematic Review and Meta-Analysis of Observational Studies. Am J Med. 2017 Jul 21.

Sinnott SJ, Bhate K, Margolis DJ, et al. **Antibiotics and acne**: an emerging iceberg of antibiotic resistance? Br J Dermatol. 2016 Dec;175(6):1127-1128.

Siqueira MBP et al. **Chronic suppression of periprosthetic joint infections with oral antibiotics** increases infection-free survivorship. J Bone Joint Surg Am 2015 Aug 5; 97:1220.

Skalet AH, Cevallos V, Ayele B, Gebre T, Zhou Z, et al. 2010 Antibiotic Selection Pressure and **Macrolide Resistance (azithromycin)** in Nasopharyngeal Streptococcus pneumoniae: A Cluster-Randomized Clinical Trial. PLoS Med 7(12): e1000377. doi:10.1371/journal.pmed.1000377

Skhirtladze-Dworschak K, Hutschala D, Reining G, et al. **Cefuroxime Plasma and Tissue concentrations in Patients Undergoing Elective Cardiac Surgery**: Continuous versus Bolus Application A Pilot Study. Br J Clin Pharmacol. 2019 Jan 12.

Smith JD, MacDougall CC, Johnstone J, et al. Effectiveness of **N95 respirators** versus surgical masks in protecting health care workers from acute respiratory infection: a systematic review and meta-analysis. CMAJ. 2016 May 17;188(8):567-74.

Smith MJ. Evidence for the Diagnosis and Treatment of Acute **Uncomplicated Sinusitis in Children**: A Systematic Review. Pediatrics. 2013 Jun 24.

Smith SM, Fahey T, Smucny J, et al. **Antibiotics for acute bronchitis**. Cochrane Database Syst Rev. 2014 Mar 1;3:CD000245. There is limited evidence to support the use of antibiotics in acute bronchitis. Antibiotics may have a modest beneficial effect in some patients such as frail, elderly people with multimorbidity who may not have been included in trials to date. However, the magnitude of this benefit needs to be considered in the broader context of potential side effects, medicalisation for a self-limiting condition, increased resistance to respiratory pathogens and cost of antibiotic treatment.

Smith SM, Smucny J, Fahey T. **Antibiotics for acute bronchitis**. JAMA. 2014 Dec 24-31;312(24):2678-9.

Smith SM, Fahey T, Smucny J, Becker LA. **Antibiotics for acute bronchitis**. Cochrane Database Syst Rev. 2017 Jun 19;6:CD000245. There is limited evidence of clinical benefit to support the use of antibiotics in acute bronchitis. Antibiotics may have a modest beneficial effect in some patients such as frail, elderly people with multimorbidity who may not have been included in trials to date. However, the magnitude of this benefit needs to be considered in the broader context of potential side effects, medicalisation for a self limiting condition, increased resistance to respiratory pathogens, and cost of antibiotic treatment.

Smith SR, Montgomery LG, Williams JW Jr. Treatment of **mild to moderate sinusitis**. Arch Intern Med. 2012 Mar 26;172(6):510-3. Antibiotics should not be prescribed for mild to moderate sinusitis within the first week of the illness.

Smyczek P, Chu A, Berenger B. Emerging international strain of **multidrug-resistant Neisseria gonorrhoeae**: Infection in a man with urethral discharge. Can Fam Physician. 2019 Aug;65(8):552-554.

So-Hee Kang, Angela Chua-Gocheco, Pina Bozzo, et al. Safety of antiviral **medication for the treatment of herpes during pregnancy** Can Fam Physician April 2011 57: 427-428.

Sodhi M;Sheldon CA;Carleton B;Etminan M. **Oral fluoroquinolones and risk of secondary pseudotumor cerebri syndrome:** Nested case-control study. Neurology. 2017 Jul 28.

Solverson KJ, Doig CJ. A fatal case of **pneumococcal sepsis years after splenectomy**. CMAJ. 2017 Jun 12;189(23):E800-E802.

Sonnenberg P, Clifton S, Beddows S, et al. Prevalence, risk factors, and uptake of interventions for **sexually transmitted infections in Britain**: findings from the National Surveys of Sexual Attitudes and Lifestyles (Natsal). Lancet. 2013 Nov 30;382(9907):1795-806.

Soper DE. **Pelvic inflammatory disease**. Obstet Gynecol. 2010 Aug;116(2 Pt1):419-28.

Sosnin N, Curtis N, Cranswick N, et al. **Vancomycin is commonly under-dosed** in critically ill children and neonates. Br J Clin Pharmacol. 2019 Aug 4.

Spinks A, Glasziou PP, DelMar CB. **Antibiotics for sore throat**. Cochrane Database of Systematic Reviews 2013, Issue 11. Art. No.: CD000023. DOI: 10.1002/14651858.CD000023.pub4. Antibiotics confer relative benefits in the treatment of sore throat. However, the absolute benefits are modest. Protecting sore throat sufferers against suppurative and non-suppurative complications in high-income countries requires treating many with antibiotics for one to benefit. This NNTB may be lower in low-income countries. Antibiotics shorten the duration of symptoms by about 16 hours overall.

Spurling GK, Del Mar CB, Dooley L, et al. **Delayed antibiotics** for respiratory infections. Cochrane Database Syst Rev. 2013 Apr 30;4:CD004417. doi: 10.1002/14651858.CD004417.pub4. Most clinical outcomes show no difference between strategies. Delay slightly reduces patient satisfaction compared to immediate antibiotics (87% versus 92%) but not compared to none (87% versus 83%). In patients with respiratory infections where clinicians feel it is safe not to prescribe antibiotics immediately, no antibiotics with advice to return if symptoms do not resolve is likely to result in the least antibiotic use, while maintaining similar patient satisfaction and clinical outcomes to delayed antibiotics.

Spurling GKP, Del Mar CB, Dooley L, et al. **Delayed antibiotic prescriptions for respiratory infections**. Cochrane Database of Systematic Reviews 2017, Issue 9. Art. No.: CD004417. For many clinical outcomes, there were no differences between prescribing strategies. Symptoms for acute otitis media and sore throat were modestly improved by immediate antibiotics compared with delayed antibiotics. There were no differences in complication rates. Delaying prescribing did not result in significantly different levels of patient satisfaction compared with immediate provision of antibiotics (86%versus 91%) (moderate quality evidence). However, delay was favoured over no antibiotics (87%versus 82%). Delayed antibiotics achieved lower rates of antibiotic use compared to immediate antibiotics (31% versus 93%) (moderate quality evidence). The strategy of no antibiotics further reduced antibiotic use compared to delaying prescription for antibiotics (14% versus 28%).

Staicu ML, Soni D, Conn KM, et al. A survey of inpatient **practitioner knowledge of penicillin allergy** at 2 community teaching hospitals. Ann Allergy Asthma Immunol. 2017 Jul;119(1):42-47.

Staley C, Vaughn BP, Graiziger CT, et al. **Gut-sparing treatment of urinary tract infection in patients at high risk of Clostridium difficile infection**. J Antimicrob Chemother. 2017 Feb;72(2):522-528. (gentamicin)

Stall NM, Fischer HD, Fung K, et al. Sex-Specific Differences in End-of-Life Burdensome Interventions and **Antibiotic Therapy in Nursing Home Residents** With Advanced Dementia. JAMA Netw Open. 2019 Aug 2;2(8):e199557.

Stark CM, Susi A, Emerick J, Nylund CM. **Antibiotic and acid-suppression medications during early childhood are associated with obesity**. Gut. 2018 Oct 30.

Stefan MS et al. Association between **antibiotic treatment and outcomes in patients hospitalized with acute exacerbation of COPD** treated with systemic steroids. Chest 2013 Jan; 143:82.

Stefan MS, Shieh MS, Spitzer KA, et al. Association of **Antibiotic Treatment With Outcomes in Patients Hospitalized for an Asthma Exacerbation** Treated With Systemic Corticosteroids. JAMA Intern Med. 2019 Jan 28.

Steinberg MB, Akincigil A, Kim EJ, et al. **Tobacco Smoking** as a Risk Factor for Increased Antibiotic Prescription. Am J Prev Med. 2016 Jun;50(6):692-8.

Stern A, Carrara E, Bitterman R, et al. **Early discontinuation of antibiotics for febrile neutropenia versus continuation until neutropenia resolution in people with cancer**. Cochrane Database Syst Rev. 2019 Jan 3;1:CD012184. We could make no strong conclusions on the safety of antibiotic discontinuation before neutropenia resolution among people with cancer with febrile neutropenia based on the existing evidence and its low certainty.

Stevens DL, Bisno AL, Chambers HF, et al;Infectious Diseases Society of America (**IDSA**) . Practice guidelines for the diagnosis and **management of skin and soft-tissue infections**. Clin Infect Dis. 2005 Nov 15;41(10):1373-406. Epub 2005 Oct 14.

Stevens DL, Bryant AE. **Necrotizing Soft-Tissue Infections**. N Engl J Med. 2017 Dec 7;377(23):2253-2265.

Stevens R, Moll H, Lakhanpaul M, et al. **Diagnostic value of laboratory tests** in identifying serious infections in febrile children: systematic review. BMJ 2011;342:d3082.

Stevens VW, Nelson RE, Schwab-Daugherty EM, et al. **Comparative Effectiveness of Vancomycin and Metronidazole** for the Prevention of Recurrence and Death in Patients With **Clostridium difficile** Infection. JAMA Intern Med. 2017 Feb 6.

Stewardson AJ, Sax H, et al. Enhanced performance feedback and patient participation to **improve hand hygiene** compliance of health-care workers in the setting of established multimodal promotion: a single-centre, cluster randomised controlled trial.Lancet Infect Dis. 2016 Sep 2.

Stewart CM, Schoeman SA, Booth RA, et al. Assessment of **self taken** swabs versus clinician taken **swab cultures for diagnosing gonorrhoea** in women: single centre, diagnostic accuracy study. BMJ. 2012 Dec 12;345:e8107. doi: 10.1136/bmj.e8107.

Stringham JD, Relhan N, Miller D, et al. Trends in **Fluoroquinolone Nonsusceptibility** Among Coagulase-Negative Staphylococcus Isolates Causing **Endophthalmitis**, 1995-2016. JAMA Ophthalmol. 2017 Jul 1;135(7):814-815.

Stocker M, van Herk W, el Helou S, et al. **Procalcitonin-guided** decision making for duration of **antibiotic therapy in neonates** with suspected early-onset **sepsis**: a multicentre, randomised controlled trial (NeoPIns). Lancet 2017; online July 12.

Stravitz RT, Lee WM. **Acute liver failure**. Lancet. 2019 Sep 7;394(10201):869-881. (acetaminophen, antibiotics etc…)

Strykowski DF, Nielsen AB, Llor C, et al. An intervention with access to **C-reactive protein rapid test reduces antibiotic overprescribing** in acute exacerbations of chronic bronchitis and COPD. Fam Pract. 2015 Aug;32(4):395-400.

Su JR, Beltrami JF, Zaidi AA, Weinstock HS. **Primary and secondary syphilis among black and Hispanic men who have sex with men**: case report data from 27 States. Ann Intern Med. 2011 Aug 2;155(3):145-51.

Subtil D, Brabant G, Tilloy E, et al. Early **clindamycin for bacterial vaginosis** in **pregnancy** (**PREMEVA**): a multicentre, double-blind, randomised controlled trial. Lancet 2018; online Oct 12.

Suda KJ, Calip GS, Zhou J, et al. Assessment of the appropriateness of antibiotic **prescriptions for infection prophylaxis before dental procedures**, 2011 to 2015. JAMA Netw Open. 2019;2(5):e193909. doi:10.1001/jamanetworkopen.2019.3909

Sugerman DT. JAMA **patient** page. **Antibiotic resistance**. JAMA. 2013 Nov 27;310(20):2212.

Sullivan SB et al. Reduced **vancomycin susceptibility** of methicillin-susceptible Staphylococcus aureushas no significant impact on mortality but results in an **increase in complicated infection**. Antimicrob Agents Chemother 2017 Jul; 61:e00316.

Sun D, McCarthy TJ, Liberman DB. Cost-Effectiveness of **Watchful Waiting in Acute Otitis Media**. Pediatrics. 2017 Mar 3.

Sun Y, Gao Y, Chen J, et al. Evidence mapping of recommendations on **diagnosis and therapeutic strategies for diabetes foot**: an international review of 22 guidelines. Metabolism. 2019 Aug 5;100:153956.

Surawicz CM, Brandt LJ, Binion DG, et al. Guidelines for diagnosis, treatment, and prevention of **Clostridium difficile** infections. Am J Gastroenterol 2013;108:478-98.
Sutter R, Rüegg S, Tschudin-Sutter S. **Seizures as adverse events of antibiotic drugs**: A systematic review. Neurology. 2015 Sep 23.
Sutter DM, Chukwuma U, Dzialowy N, et al. Changing **susceptibility of Staphylococcus aureus** in a US pediatric population. Pediatrics. 2016;137(4):e20153099
Svanström H, Pasternak B, Hviid A, et al. Use of **azithromycin and death from cardiovascular** causes. N Engl J Med 2013; 368:1704-1712.
Svanström H, Pasternak B, Hviid A. Use of **clarithromycin and roxithromycin and risk of cardiac death**: cohort study. BMJ. 2014 Aug 19;349:g4930.
Tabaka ME, Quinn JV, Kohn MA, et al. Predictors of infection from **dog bite wounds**: which patients may benefit from prophylactic antibiotics? Emerg Med J. 2015 Jan 29.
Tacconelli E, Carrara E, Savoldi A, et al. **Discovery, research, and development of new antibiotics**: the WHO priority list of antibiotic-resistant bacteria and tuberculosis. Lancet Infect Dis. 2017 Dec 21.
Tahtinen PA, Laine MK, Ruohola A. **Prognostic Factors for Treatment Failure in Acute Otitis Media**. Pediatrics. 2017; 140(3):e20170072
Tasian GE, Jemielita T, Goldfarb DS, et al. Oral Antibiotic Exposure and **Kidney Stone Disease**. J Am Soc Nephrol. 2018 May 10.
Talan DA, Mower WR, Krishnadasan A, et al. **Trimethoprim-Sulfamethoxazole** versus Placebo for **Uncomplicated Skin Abscess**. N Engl J Med. 2016 Mar 3;374(9):823-32.
Talan DA et al. Subgroup analysis of **antibiotic treatment for skin abscesses**. Ann Emerg Med 2017 Oct5; [e-pub].
Tam VH, Hirsch EB, Lasco TM, et al. Correlation of hospital **carbapenem consumption and resistance** trends in selected gram-negative bacteria. Ann Pharmacother. 2012 Jul;46(7-8):1120-2.
Tamma PD, Cosgrove SE. Addressing the **Appropriateness of Outpatient Antibiotic Prescribing in the United States**: An Important First Step. JAMA. 2016 May 3;315(17):1839-41
Tamma PD, Avdic E, Li DX, et al. Association of **Adverse Events With Antibiotic Use** in Hospitalized Patients. JAMA Intern Med. 2017 Jun 12.
Tamma PD, Miller MA, Cosgrove SE. Rethinking How Antibiotics Are Prescribed: Incorporating the **4 Moments of Antibiotic Decision Making** Into Clinical Practice. JAMA. 2018 Dec 27.
Tamma PD, Conley AT, Cosgrove SE, et al; Antibacterial Resistance Leadership Group. Association of **30-Day Mortality With Oral Step-Down vs Continued Intravenous Therapy** in Patients Hospitalized With Enterobacteriaceae Bacteremia. JAMA Intern Med. 2019 Jan 22.
Tan T, Little P, Stokes T; Guideline Development Group. **Antibiotic prescribing** for **self limiting respiratory tract infections** in primary care: summary of NICE guidance. BMJ. 2008 Jul 23;337:a437. doi: 10.1136/bmj.a437.
Tandan M, Cormican M, Vellinga A. **Adverse events of fluoroquinolones vs. other antimicrobials prescribed in primary care**: A systematic review and meta-analysis of randomized controlled trials. Int J Antimicrob Agents. 2018 Nov;52(5):529-540.
Tang KL, Caffrey NP, Nóbrega DB, et al. **Restriction in the use of antibiotics in food-producing animals** and its associations with antibiotic resistance in food-producing animals and human beings: a systematic review and meta-analysis. Lancet Plan Health 2017; 1: e316–27.
Tanizaki R et al. **High-dose oral amoxicillin plus probenecid** is highly effective for **syphilis** in patients with HIV infection. Clin Infect Dis 2015 Jul 15; 61:177.
Tanksley A, Cifu AS. **Screening for Gonorrhea, Chlamydia, and Hepatitis B**. JAMA. 2016 Mar 22-29;315(12):1278-9.
Taplitz RA, Kennedy EB, Bow EJ, et al. **Antimicrobial Prophylaxis for Adult Patients With Cancer-Related Immunosuppression**: ASCO and IDSA Clinical Practice Guideline Update. J Clin Oncol. 2018 Sep 4:JCO1800374.
Tapiainen T, Kujala T, Renko M, et al. Effect of **Antimicrobial Treatment of Acute Otitis Media on the Daily Disappearance of Middle Ear Effusion**: A Placebo-Controlled Trial. JAMA Pediatr. 2014 May 5.
Tarakji KG, Mittal S, Kennergren C, et al; WRAP-IT Investigators. Antibacterial Envelope to Prevent **Cardiac Implantable Device Infection**. N Engl J Med. 2019 Mar 17.
Task Force on **Circumcision**. Male circumcision. Pediatrics. 2012 Sep;130(3):e756-85.
Taylor SN, Marrazzo J, Batteiger BE, et al. **Single-Dose Zoliflodacin** (ETX0914) for Treatment of Urogenital Gonorrhea. N Engl J Med. 2018 Nov 8;379(19):1835-1845.
Teillant A, Gandra S, Barter D, et al Potential burden of **antibiotic resistance on surgery and cancer chemotherapy** antibiotic prophylaxis in the USA: a literature review and modelling study. Lancet Infect Dis. 2015 Oct 15.
Teltsch Dana Y.; Hanley James; Loo Vivian; et al. Infection Acquisition Following Intensive Care Unit **Room Privatization**. Arch Intern Med. 2011;171(1):32-38.
Tessier L, Guilcher SJT, Bai YQ, et al. The impact of hospital harm on **length of stay, costs of care and length of person-centred episodes of care**: a retrospective cohort study. CMAJ 2019;191:E879-85.
Thabit AK, Fatani DF, Bamakhrama MS, et al. **Antibiotic penetration into bone and joints**: An updated review. Int J Infect Dis. 2019 Feb 14;81:128-136.
Thanaviratananich S, Laopaiboon M, Vatanasapt P. **Once or twice daily versus three times daily amoxicillin with or without clavulanate for the treatment of acute otitis media**. Cochrane Database Syst Rev. 2013 Dec 13;12:CD004975.
This review showed that the results of using once or twice daily doses of amoxicillin, with or without clavulanate, were comparable with three doses for the treatment of AOM.
Thibault LP, Rousseau E. **Dog bites.** CMAJ. 2018 Jan 29;190(4):E113.
Thomas KS et al. **Penicillin to prevent recurrent leg cellulitis**. N Engl J Med 2013 May 2; 368:1695.
Thomas Z, Bandali F, Sankaranarayanan J, Reardon T, Olsen KM; Critical Care Pharmacotherapy Trials Network. A Multicenter Evaluation of Prolonged **Empiric Antibiotic Therapy in Adult ICUs in the United States**. Crit Care Med. 2015 Dec;43(12):2527-34.
Thompson PL, Gilbert RE, Long PF, et al. Effect of antibiotics for **otitis media on mastoiditis** in children: a retrospective cohort study using the United kingdom general practice research database. Pediatrics. 2009 Feb;123(2):424-30.
Thompson M, Vodicka TA, Blair PS, et al; TARGET Programme Team. **Duration of symptoms of respiratory tract infections in children**: systematic review. BMJ. 2013 Dec 11;347
Thornhill Martin H, Dayer Mark J, Forde Jamie M, et al. Impact of the NICE guideline recommending **cessation of antibiotic prophylaxis for prevention of infective endocarditis**: before and after study. BMJ 2011;342:doi:10.1136/bmj.d2392 (Published 3 May 2011)
Thornhill MH, Gibson TB, Cutler E, et al. **Antibiotic Prophylaxis and Incidence of Endocarditis Before and After the 2007 AHA Recommendations**. J Am Coll Cardiol. 2018 Oct 30.
Ting JY, Synnes A, Roberts A, et al. Association Between **Antibiotic Use and Neonatal Mortality and Morbidities in Very Low-Birth-Weight Infants Without Culture-Proven Sepsis or Necrotizing Enterocolitis**. JAMA Pediatr. 2016 Oct 24.
Ting JY, Roberts A, Sherlock R, et al. Duration of initial **empirical antibiotic therapy** and outcomes in **very low birth weight infants**. Pediatrics. 2018;143(3): e20182286
Tita ATN, Szychowski JM, Boggess K, et al. Adjunctive **azithromycin prophylaxis for cesarean delivery**. N Engl J Med 2016;375:1231-41.
Tobian AA, Serwadda D, Quinn TC, et al. Male **circumcision** for the prevention of HSV-2 and HPV infections and syphilis. N Engl J Med. 2009;360(13):1298- 1309.
Todd DC, McIvor RA, Pugsley SO, Cox G. Approach to **chronic obstructive pulmonary disease** in primary care. Can Fam Physician 2008;54:7-11.
Todd SR, Dahlgren FS, Traeger MS, et al. No Visible **Dental Staining in Children Treated with Doxycycline** for Suspected Rocky Mountain Spotted Fever. J Pediatr. 2015 Mar 14.
Toh JWT, Phan K, Hitos K, et al. Association of mechanical **bowel preparation and oral antibiotics before elective colorectal surgery** with surgical site infection: a network meta-analysis. JAMA Netw Open. 2018;1(6):e183226
Tonkin-Crine SKG, Tan PS, van Hecke O, et al. **Clinician-targeted interventions to influence antibiotic prescribing behaviour for acute respiratory infections in primary care**: an overview of systematic reviews. Cochrane Database of Systematic Reviews 2017, Issue 9. Art. No.: CD012252. We found evidence that CRP testing, shared decision making, and procalcitonin-guided management reduce antibiotic prescribing for patients with ARIs in primary care. These interventions may therefore reduce overall antibiotic consumption and consequently antibiotic resistance. There do not appear to be negative effects of these interventions on the outcomes of patient satisfaction and reconsultation, although there was limited measurement of these outcomes in the trials. This should be rectified in future trials.
Toyofuku M, Morozumi M, Hida M, et al. Effects of **Intrapartum Antibiotic Prophylaxis on Neonatal Acquisition of Group B Streptococci**. JPed. 2017;190:169-73.
Trac MH, McArthur E, Jandoc R, et al. **Macrolide antibiotics** and the risk of **ventricular arrhythmia** in older adults. CMAJ. 2016 Feb 22.
Tran-Dien A, Le Hello S, Bouchier C, Weill F-X. Early transmissible **ampicillin resistance in zoonotic Salmonella enterica serotype Typhimurium in the late 1950s**: a retrospective, whole-genome sequencing study. Lancet Infect Dis 2017; online Nov 29.
Trivedi S, Williams C, Torrone E, Kidd S. National **Trends and Reported Risk Factors Among Pregnant Women With Syphilis in the United States**, 2012-2016.Obstet Gynecol. 2019 Jan;133(1):27-32.
Trifirò G, de Ridder M, Sultana J, et al. Use of **azithromycin and risk of ventricular arrhythmia**. CMAJ. 2017 Apr 18;189(15):E560-E568.
Tronstein Elizabeth, Johnston Christine, Huang Meei-Li, et al. **Genital Shedding of Herpes Simplex Virus (HSV)** Among Symptomatic and Asymptomatic Persons With HSV-2 Infection. *JAMA.* 2011;305(14):1441-1449.doi:10.1001/jama.2011.420.
Trubiano JA, Adkinson NF, Phillips EJ. **Penicillin Allergy Is Not Necessarily Forever**. JAMA. 2017 Jul 4;318(1):82-83.
Tsuji Y, Holford NH, Kasai H, Ogami C, Heo YA, Higashi Y, Mizoguchi A, To H, Yamamoto Yet al. Population pharmacokinetics and pharmacodynamics of **linezolid-induced thrombocytopenia** in hospitalized patients. Br J Clin Pharmacol. 2017 Feb 10.
Tubiana S, Blotière PO, Hoen B, et al. **Dental procedures, antibiotic prophylaxis, and endocarditis** among people with prosthetic heart valves: nationwide population based cohort and a case crossover study. BMJ. 2017 Sep 7;358:j3776.
Tucker MH et al. **Amoxicillin challenge without penicillin skin testing in evaluation of penicillin allergy** in a cohort of Marine recruits. J Allergy Clin Immunol Pract 2017 May/Jun; 5:813.
Unemo M, Bradshaw CS, Hocking JS, et al. **Sexually transmitted infections**: challenges ahead. Lancet Infect Dis. 2017 Aug;17(8):e235-e279.
Ursu A, Sen A, Ruffin M. Impact of **Cervical Cancer Screening Guidelines on Screening for Chlamydia**. Ann Fam Med. 2015 Jul;13(4):361-3.
Uscher-Pines L, Mulcahy A, Cowling D, et al. Antibiotic Prescribing for Acute Respiratory Infections in **Direct-to-Consumer Telemedicine** Visits. JAMA Intern Med. 2015 May 26.
USPSTF-US Preventive Services Task Force. **Screening for syphilis** infection in nonpregnant adults and adolescents: US Preventive Services Task Force Recommendation Statement.JAMA. doi:10.1001 /jama.2016.5824.
Uzun S, Djamin RS, Kluytmans JA, et al. **Azithromycin maintenance** treatment in patients with frequent exacerbations of chronic obstructive pulmonary disease (COLUMBUS): a randomised, double-blind, placebo-controlled trial. Lancet Respir Med. 2014 May;2(5):361-8.
Valent AM, DeArmond C, Houston JM, et al. Effect of **post–cesarean delivery oral cephalexin and metronidazole on surgical site infections** among obese women: a randomized clinical trial.JAMA. doi:10.1001/jama.2017.10567
Van Boeckel TP, Gandra S, Ashok A, et al. **Global antibiotic consumption 2000 to 2010**: an analysis of national pharmaceutical sales data. Lancet Infect Dis 2014; online July 10.
van den Aardweg MT, Boonacker CW, Rovers MM, Hoes AW, Schilder AG. Effectiveness of **adenoidectomy** in children with recurrent upper respiratory tract infections: open randomised controlled trial. BMJ. 2011 Sep 6;343:d5154.
Van den Bruel A, Thompson M, Haj-Hassan T,
van der Heijden CDCC, Duizer ML, Fleuren HWHA, et al**. Intravenous flucloxacillin treatment** is associated with a high incidence of hypokalemia. Br J Clin Pharmacol. 2019 Apr 26.
van der Linden MMD, van Ratingen AR, van Rappard DC, et al. **DOMINO, doxycycline 40 mg vs. minocycline 100 mg** in the treatment of **rosacea**: a randomized, single-blinded, noninferiority trial, comparing efficacy and safety. Br J Dermatol. 2017 Jun;176(6):1465-1474.
van Dijk ST, Daniels L, Unlu C, et al. Long-Term Effects of Omitting Antibiotics in **Uncomplicated Acute Diverticulitis**. Am J Gastroenterol. 2018 Apr 27.
van Dijk ST et al. **Long-term effects of omitting antibiotics in uncomplicated acute diverticulitis**. Am J Gastroenterol 2018 Jul; 113:1045.
van Dongen TMA et al. A trial of treatment for acute otorrhea in children with **tympanostomy tubes**. N Engl J Med 2014 Feb 20; 370:723.
van Driel ML, De Sutter AI, Keber N, Habraken H, Christiaens T. Different antibiotic treatments for **group A streptococcal pharyngitis**. Cochrane Database Syst Rev. 2010 Oct 6;10:CD004406. Evidence is insufficient for clinically meaningful differences between antibiotics for GABHS tonsillopharyngitis. Limited evidence in adults suggests cephalosporins are more effective than penicillin for relapse, but the NNTB is high.
van Driel ML, De Sutter AI, Keber N, et al. Different antibiotic treatments for **group A streptococcal pharyngitis**. Cochrane Database Syst Rev. 2013 Apr 30;4:CD004406. doi: 10.1002/14651858.CD004406.pub3. Evidence is insufficient to show clinically meaningful differences between antibiotics for GABHS tonsillopharyngitis. Limited evidence in adults suggests cephalosporins are more effective than penicillin for relapse, but the NNTB is high. Limited evidence in children suggests carbacephem is more effective for symptom resolution. Data on complications are too scarce to draw conclusions. Based on these results and considering the low cost and absence of resistance, penicillin can still be recommended as first choice.
van Driel ML, De Sutter AI, Habraken H, et al. **Different antibiotic treatments for group A streptococcal pharyngitis**. Cochrane Database Syst Rev. 2016 Sep 11;9:CD004406. There were no clinically relevant differences in symptom resolution when comparing cephalosporins and macrolides with penicillin in the treatment of GABHS tonsillopharyngitis. Limited evidence in adults suggests cephalosporins are more effective than penicillin for relapse, but the NNTB is high. Limited evidence in children suggests carbacephem is more effective than penicillin for symptom resolution. Data on complications are too scarce to draw conclusions. Based on these results and considering the low cost and absence of resistance, penicillin can still be regarded as a first choice treatment for both adults and children. All studies were in high-income countries with low risk of streptococcal complications, so there is need for trials

in low-income countries and Aboriginal communities where risk of complications remains high.
van Houdt R, Ma B, Bruisten SM, et al. **Lactobacillus iners-dominated vaginal microbiota** is associated with **increased susceptibility to Chlamydia trachomatis infection** in Dutch women: a case-control study. Sex Transm Infect. 2017 Sep 25.
van Houten CB, de Groot JA, Klein A, et al. A **host-protein based assay** to **differentiate between bacterial and viral infections** in preschool children (**OPPORTUNITY**): a double-blind, multicentre, validation study. Lancet Infect Dis. 2017 Apr;17(4):431-440.
van Panhuis WG, Grefenstette J, Jung SY,et al. **Contagious diseases** in the United States from 1888 to the present. N Engl J Med. 2013 Nov 28;369(22):2152-8.
van Schalkwyk J, Yudin MH; Society of Obstetricians & Gynaecologists of Canada. **SOGC** clinical practice guideline. **Vulvovaginitis**: screening for and management of trichomoniasis, vulvovaginal candidiasis, and bacterial vaginosis. http://sogc.org/wp-content/uploads/2015/03/gui320CPG1503E.pdf (accessed Mar, 2015).
van Velzen P, ter Riet G, Bresser P, et al. **Doxycycline for outpatient-treated acute exacerbations of COPD**: a randomised double-blind placebo-controlled trial. Lancet Respir Med 2017; 5: 492–99.
van Vught LA, Klein Klouwenberg PMC, Spitoni C, et al; MARS Consortium. Incidence, risk factors, and attributable **mortality** of **secondary infections in the intensive care unit** after admission for **sepsis**. JAMA. doi:10.1001/jama.2016.2691.
VanderBeek BL. Oral **fluoroquinolones, retinal detachments**, and claims database studies. JAMA Ophthalmol. 2016;134:422-423.
Vardakas KZ, Trigkidis KK, Boukouvala E, Falagas ME. **Clostridium difficile infection following systemic antibiotic administration** in randomised controlled trials: a systematic review and meta-analysis. Int J Antimicrob Agents. 2016 Jul;48(1):1-10.
Vardakas KZ, Voulgaris GL, Maliaros A, et al. **Prolonged intravenous infusion of antipseudomonal s-lactams** for patients with sepsis: a systematic review and meta-analysis of randomized trials. Lancet Infect Dis 2017; online Oct 25.
Vaughn VM, Flanders SA. Annals for Hospitalists Inpatient Notes - **Mindfulness and Antibiotic Appropriateness**-How Point-of-Care Stewardship Begins With Hospitalists. Ann Intern Med. 2016 Nov 15;165(10):HO2-HO3.
Vaughn VM, Flanders SA, Snyder A, et al. Excess Antibiotic Treatment Duration and Adverse **Events in Patients Hospitalized With Pneumonia**: A Multihospital Cohort Study. Ann Intern Med. 2019 Jul 9.
Vaz LE, Kleinman KP, Raebel MA, et al. Recent Trends in **Outpatient Antibiotic Use in Children**. Pediatrics. 2014 Feb 2.
Vaz LE, Kleinman KP, Lakoma MD, et al. Prevalence of **Parental Misconceptions About Antibiotic Use**. Pediatrics. 2015 Jul 20.
Venekamp RP, Sanders S, Glasziou PP, et al. Antibiotics for acute otitis media in children. Cochrane Database Syst Rev. 2013 Jan 31;1:CD000219. doi: 10.1002/14651858.CD000219.pub3. Antibiotic treatment led to a statistically significant reduction of children with AOM experiencing pain at two to seven days compared with placebo but since most children (82%) settle spontaneously, about 20 children must be treated to prevent one suffering from ear pain at two to seven days. Additionally, antibiotic treatment led to a statistically significant reduction of tympanic membrane perforations (NNTB 33) and contralateral AOM episodes (NNTB 11). These benefits must be weighed against the possible harms: for every 14 children treated with antibiotics, one child experienced an adverse event (such as vomiting, diarrhoea or rash) that would not have occurred if antibiotics had been withheld. Antibiotics appear to be most useful in children under two years of age with bilateral AOM, or with both AOM and otorrhoea. For most other children with mild disease, an expectant observational approach seems justified. We have no trials in populations with higher risks of complications.
Venekamp RP, et al. Are **topical antibiotics** an alternative to oral antibiotics for children with **acute otitis media and ear discharge**? BMJ. 2016 Feb 4;352:i308.
Venekamp RP, Burton MJ, van Dongen TMA, van der Heijden GJ, van Zon A, Schilder AGM. **Antibiotics for otitis media with effusion in children**. Cochrane Database of Systematic Reviews 2016, Issue 6. Art. No.: CD009163. DOI: 10.1002/14651858.CD009163.pub3. This review presents evidence of both benefits and harms associated with the use of oral antibiotics to treat children up to 16 years with OME. Although evidence indicates that oral antibiotics are associated with an increased chance of complete resolution of OME at various time points, we also found evidence that these children are more likely to experience diarrhoea, vomiting or skin rash. The impact of antibiotics on short-term hearing is uncertain and low quality evidence did not show that oral antibiotics were associated with fewer ventilation tube insertions. Furthermore, we found no data on the impact of antibiotics on other important outcomes such as speech, language and cognitive development or quality of life. Even in situations where clear and relevant benefits of oral antibiotics have been demonstrated, these must always be carefully balanced against adverse effects and the emergence of bacterial resistance. This has specifically been linked to the widespread use of antibiotics for common conditions such as otitis media.
Verbakel JY, Lemiengre MB, De Burghgraeve et al. **Should all acutely ill children** in primary care be **tested with point-of-care CRP**: a cluster randomized trial. BMC Med. 2016 Oct 6;14(1):131.
Vermandere M, Aertgeerts B, Agoritsas Tet al. **Antibiotics after incision and drainage for uncomplicated skin abscesses**: a clinical practice guideline. BMJ. 2018 Feb 6;360:k243.
Venekamp RP, Mick P, Schilder AG, et al. Grommets (ventilation tubes) for recurrent acute **otitis media in children**. Cochrane Database Syst Rev. 2018 May 9;5:CD012017.
Verbakel JY, Lemiengre MB, De Burghgraeve T, et al**. Point-of-care C reactive protein** to identify serious infection in acutely ill **children** presenting to hospital: prospective cohort study. Arch Dis Child. 2018 May;103(5):420-426.
Vernacchio L, Corwin MJ, Vezina RM, et al. **Xylitol Syrup** for the Prevention of Acute Otitis Media. Pediatrics. 2014 Jan 6.
Versporten A, Bolokhovets G, Ghazaryan L, et al. **Antibiotic use in eastern Europe**: a cross-national database study in coordination with the WHO Regional Office for Europe. Lancet Infect Dis 2014.
Versporten A, Bielicki J, Drapier N, et al; ARPEC project group. The **Worldwide Antibiotic Resistance and Prescribing** in **European** Children (**ARPEC**) point prevalence survey: developing hospital-quality indicators of antibiotic prescribing for children. J Antimicrob Chemother. 2016 Apr;71(4):1106-17.
Vickers RJ, Tillotson GS, Nathan R, et al. Efficacy and safety of **ridinilazole compared with vancomycin** for the treatment of **Clostridium difficile infection**: a phase 2, randomised, double-blind, active-controlled, non-inferiority study. Lancet Infect Dis 2017; online April 28.
Vijh R, Shah R, Andany N. A 60-year-old woman **with recurrent cellulitis**. CMAJ.2019 Mar 4;191(9):E257-E259.
Vincent JL, Bassetti M, François B, et al. **Advances in antibiotic therapy in the critically ill**. Crit Care. 2016 May 17;20(1):133.
Vindigni SM, Surawicz CM. Managing **Clostridium difficile**: an old bug with new tricks. Am J Gastroenterol. 2018 Apr 24.
Visapää JP, Tillonen JS, Kaihovaara PS, et al. **Lack of disulfiram-like reaction with metronidazole** and ethanol. Ann Pharmacother. 2002 Jun;36(6):971-4.
Vivas LL, Gold WL, Mandell DM, et al. An 82-year-old man with ataxia and dysarthria. (**metronidazole encephalopathy**) CMAJ. 2016 Dec 6;188(17-18):1251-1254.
Vo E, Massarweh NN, Chai CY, et al. Association of the addition of **oral antibiotics to mechanical bowel preparation for left colon and rectal cancer resections** with surgical site infections [online Oct 18, 2017]. JAMA Surg. doi:10.1001 /jamasurg.2017.3827
Vollenweider DJ, Frei A, Steurer-Stey CA, et al. Antibiotics for **exacerbations of chronic obstructive pulmonary disease**. Cochrane Database Syst Rev. 2018 Oct 29;10:CD010257. Researchers have found that antibiotics have some effect on inpatients and outpatients, but these effects are small, and they are inconsistent for some outcomes (treatment failure) and absent for other outcomes (mortality, length of hospital stay). Analyses show a strong beneficial effect of antibiotics among ICU patients. Few data are available on the effects of antibiotics on health-related quality of life or on other patient-reported symptoms, and data show no statistically significant increase in the risk of adverse events with antibiotics compared to placebo.
Vollenweider DJ, Jarrett H, Steurer-Stey CA, et al. **Antibiotics for exacerbations of chronic obstructive pulmonary disease**.Cochrane Database Syst Rev. 2012 Dec 12;12:CD010257. doi: 10.1002/14651858.CD010257. Antibiotics for COPD exacerbations showed large and consistent beneficial effects across outcomes of patients admitted to an ICU.
Vorobeichik L, Weber EA, Tarshis J. **Misconceptions Surrounding Penicillin Allergy**: Implications for Anesthesiologists. Anesth Analg. 2018 May 10.
Vyles D, Adams J, Chiu A, et al. **Allergy Testing in Children with Low-Risk Penicillin Allergy Symptoms**. Pediatrics. 2017;140(2):e20170471
Vyles D, Chiu A, Routes J, et al. **Antibiotic Use After Removal of Penicillin Allergy Label**. Pediatrics. 2018 Apr 20.
Wachholz PA, Nunes VDS, Polachini do Valle A, et al. Effectiveness of **probiotics** on the occurrence of infections in older people: systematic review and meta-analysis. Age Ageing. 2018 Feb 3.
Wald A, Corey L, Timmler B, et al. Helicase–primase inhibitor **pritelivir for HSV2** –herpes simplex virus 2- infection. N Engl J Med 2014;370:20110.
Wald-Dickler N, Spellberg B. **Short Course Antibiotic Therapy-Replacing Constantine Units with "Shorter Is Better**". Clin Infect Dis. 2019 Jan 7.
Walkty A, Karlowsky JA, Adam HJ, et al. Frequency of **MCR-1-mediated colistin resistance** among Escherichia coli clinical isolates obtained from patients in **Canadian** hospitals (CANWARD 2008-2015). CMAJ Open. 2016 Oct 26;4(4):E641-E645.
Wallace SS, Brown DN, Cruz AT. Prevalence of Concomitant Acute Bacterial **Meningitis in Neonates with Febrile Urinary Tract Infection**: A Retrospective Cross-Sectional Study. J Pediatr. 2017 Feb 6
Wallinga D, Burch DG. Does adding routine **antibiotics to animal feed** pose a serious risk to human health? BMJ. 2013 Jul 9;347:f4214.
Walsh Edward E.; Greene Linda; Kirshner Ronald. Sustained Reduction in **Methicillin-Resistant Staphylococcus aureus** Wound Infections After Cardiothoracic Surgery. Arch Intern Med. 2010;0(2010):archinternmed.2010.326. This MRSA intervention program, in which all patients receive intranasal mupirocin and patients colonized with MRSA receive vancomycin prophylaxis, has resulted in a near-complete and sustained elimination of MRSA wound infections after cardiac surgery.
Walsh TR, Weeks J, Livermore DM. Dissemination of **NDM-1** positive bacteria in the New Delhi environment and its implications for human health: an environmental point prevalence study. www.thelancet.com/infection Online April 7, 2011 DOI:10.1016/S1473-3099(11)70059-7
Wang J, Wang P, Wang X, et al. Use and **Prescription of Antibiotics in Primary Health Care Settings** in China. JAMA Intern Med. 2014 Oct 6.
Wang W, Chen W, Liu Y, et al. **Antibiotics for uncomplicated skin abscesses**: systematic review and network meta-analysis. BMJ Open. 2018 Feb 6;8(2):e020991.
Wang Y, Tian GB, Zhang R, et al. Prevalence, risk factors, outcomes, and molecular epidemiology of **mcr-1-positive Enterobacteriaceae** in patients and healthy adults from China: an epidemiological and clinical study. Lancet Infect Dis. 2017 Apr;17(4):390-399.
Warrington R, Silviu-Dan F, Wong T. **Drug allergy**. Allergy Asthma Clin Immunol. 2018 Sep 12;14(Suppl 2):60.
Wasserman RC, Gerber JS. **Acute Otitis Media in the 21st Century**: What Now? Pediatrics. 2017;140(3):e20171966
Watson T, Hickok J, Fraker S, et al. Evaluating the **risk factors for hospital-onset Clostridium difficile infections** in a large healthcare system. Clin Infect Dis. 2017 Dec 20.
Weis S, Kesselmeier M, Davis JS, et al. **Cefazolin versus anti-staphylococcal penicillins** for the treatment of patients with **Staphylococcus aureus bacteremia**: a systematic review and meta-analysis. Clin Microbiol Infect. 2019 Mar 27.
Weiss K, Blais R, Fortin A, Lantin S, Gaudet M. Impact of a Multipronged **Education Strategy on Antibiotic Prescribing** in Quebec, Canada. Clin Infect Dis. 2011 Jul 25.
Weizman Z, Abu-Abed J, Binsztok M. **Lactobacillus reuteri** DSM 17938 for the Management of **Functional Abdominal Pain** in Childhood: A Randomized, Double-Blind, Placebo-Controlled Trial. J Pediatr. 2016 May 4.
Wellbery C. Curbing **Inappropriate Antibiotic Prescribing**: What Works? Am Fam Physician. 2016 Aug 1;94(3):203-4
Wellington EM, Boxall AB, Cross P, et al. The role of the **natural environment in the emergence of antibiotic resistance** in Gram-negative bacteria. Lancet Infect Dis. 2013 Feb;13(2):155-65.
Welte T. **Azithromycin, the Holy Grail to Prevent Exacerbations in Chronic Respiratory Disease**. Am J Respir Crit Care Med. 2019 Apr 15.
Weng QY, Raff AB, Cohen JM, et al. Costs and consequences associated with **misdiagnosed lower extremity cellulitis** [online November 9, 2016].JAMA Dermatol. doi:10.1001 /jamadermatol.2016.3816
Wessels Michael R, **Streptococcal Pharyngitis**. N Engl J Med 2011; 364:648-655.
Westgarth C, Brooke M, Christley RM. How many people have been **bitten by dogs**? A cross-sectional survey of prevalence, incidence and factors associated with dog bites in a UK community. J Epidemiol Community Health. 2018 Apr;72(4):331-336.
Westwood M, Ramaekers B, Whiting P, et al. **Procalcitonin testing to guide antibiotic therapy** for the treatment of **sepsis** in intensive care settings and for suspected bacterial infection in emergency department settings: a systematic review and cost-effectiveness analysis. Health Technol Assess. 2015 Nov;19(96):1-236.
Whiles BB, Deis AS, Simpson SQ. **Increased Time to Initial Antimicrobial Administration** Is Associated With Progression to **Septic Shock** in Severe Sepsis Patients. Crit Care Med. 2017 Feb 6.
Whittles LK, White PJ, Didelot X. Estimating the **fitness cost and benefit of cefixime resistance in Neisseria gonorrhoeae to inform prescription policy**: A modelling study. PLoS Med. 2017 Oct 31;14(10):e1002416.
WHO-Global action plan to control the spread and impact of antimicrobial resistance in **Neisseria gonorrhoeae**. 2012 http://whqlibdoc.who.int/publications/2012/9789241503501_eng.pdf
Wiesenfeld HC. **Screening for Chlamydia trachomatis** Infections in Women. N Engl J Med. 2017 Feb 23;376(8):765-773.
Wilcox MH, Gerding DN, Poxton IR, et al. **Bezlotoxumab** for prevention of recurrent **Clostridium difficile** infection. N Engl J Med 2017;376:305-17.
Wilkin T. CLINICAL PRACTICE. Primary Care for **Men Who Have Sex with Men**. N Engl J Med. 2015 Aug 27;373(9):854-62.
Wilkins T, Sequoia J. **Probiotics for Gastrointestinal Conditions**: A Summary of the Evidence. Am Fam Physician. 2017;96(3):170-178.
Willekens R, Puig-Asensio M, Ruiz-Camps I, et al. **Early oral switch to linezolid** for low-risk patients with Staphylococcus aureus bloodstream infections: a propensity-matched cohort study. Clin Infect Dis. 2018 Oct 23.

Williams DJ, Cooper WO, Kaltenbach LA, et al. Comparative Effectiveness of Antibiotic Treatment Strategies for Pediatric **Skin and Soft-Tissue Infections**. Pediatrics. 2011 Aug 15.
Williams DJ, Edwards KM, Self WH, et al. Antibiotic Choice for **Children Hospitalized With Pneumonia** and Adherence to National Guidelines. Pediatrics. 2015 Jun 22.
Williams HC, Wojnarowska F, Kirtschig G, et al. **Doxycycline versus prednisolone** as an initial treatment strategy for **bullous pemphigoid**: a pragmatic, non-inferiority, randomised controlled trial. Lancet 2017; online Mar 6.
Williams L, Malhotra Y, Murante B, et al. A Single-Blinded Randomized Clinical Trial Comparing **Polymyxin B-Trimethoprim and Moxifloxacin** for Treatment of Acute **Conjunctivitis** in Children. J Pediatr. 2012 Oct 20. pii: S0022-3476(12)01027-X.
Wilson BT, Strong A, O'Kelly S, et al. **Metronidazole** Toxicity in **Cockayne Syndrome**: A Case Series. Pediatrics. 2015 Aug 24.
Wilson E, Free C, Morris TP, et al. **Internet-accessed sexually transmitted infection (e-STI) testing** and results service: A randomised, single-blind, controlled trial. PLoS Med. 2017 Dec 27;14(12):e1002479.
Wilson Jennifer F. In the Clinic: **Acute Sinusitis**. *Ann Intern Med* September 7, 2010 153:ITC3-1. September 7, 2010
Wind CM et al. **Decreased azithromycin susceptibility of *Neisseria gonorrhoeae*** isolates in patients recently treated with azithromycin. *Clin Infect Dis* 2017 Mar 24.
Wise BL et al. Impact of age, sex, obesity, and steroid use on **quinolone-associated tendon disorders**. Am J Med 2012 Dec; 125:1228.e23.
Wittekamp BH, Plantinga NL, Cooper BS, et al. **Decontamination strategies and bloodstream infections** with antibiotic-resistant microorganisms in ventilated patients: a randomized clinical trial [online Oct 22, 2018]. JAMA.
Wojcieszek AM, Stock OM, Flenady V. **Antibiotics for prelabour rupture of membranes** at or near term. Cochrane Database Syst Rev. 2014 Oct 29;10:CD001807. doi: 10.1002/14651858.CD001807.pub2. This updated review demonstrates no convincing evidence of benefit for mothers or neonates from the routine use of antibiotics for PROM at or near term. We are unable to adequately assess the risk of short- and long-term harms from the use of antibiotics due to the unavailability of data. Given the unmeasured potential adverse effects of antibiotic use, the potential for the development of resistant organisms, and the low risk of maternal infection in the control group, the routine use of antibiotics for PROM at or near term in the absence of confirmed maternal infection should be avoided.
Wojtyniak K, Horvath A, Dziechciarz P, et al. **Lactobacillus casei rhamnosus** Lcr35 in the Management of Functional **Constipation in Children**: A Randomized Trial. J Pediatr. 2017 Mar 8
Wong AY, Root A, Douglas IJ, et al. **Cardiovascular outcomes associated with use of clarithromycin**: population based study. BMJ. 2016 Jan 14;352:h6926.
Worrall, Graham, Kettle, Angela, Graham, Wendy, et al. **Postdated versus usual delayed antibiotic prescriptions** in primary care: Reduction in antibiotic use for acute respiratory infections? Can Fam Physician 2010 56: 1032-1036.
Worrall Graham. **Acute sinusitis**. Canadian Fam Physician. 2011 May.
Wortham JM, Hansen NI, Schrag SJ, et al; Eunice Kennedy Shriver NICHD Neonatal Research Network. **Chorioamnionitis** and Culture-Confirmed, **Early-Onset Neonatal Infections**. Pediatrics. 2016 Jan;137(1):1-11.
Wu HM, Harcourt BH, Hatcher CP, et al. Emergence of **ciprofloxacin-resistant Neisseria meningitidis** in North America. N Engl J Med. 2009 Feb 26;360(9):886-92.
Ya W, Reifer C, Miller LE. Efficacy of **vaginal probiotic** capsules for recurrent bacterial vaginosis: a double-blind, randomized, placebo-controlled study. Am J Obstet Gynecol. 2010 Aug;203(2):120.e1-120.
Yahav D, Franceschini E, Koppel F, et al; Bacteremia Duration Study Group. **Seven versus fourteen Days of Antibiotic Therapy** for uncomplicated Gram-negative Bacteremia: a Non-inferiority Randomized Controlled Trial. Clin Infect Dis. 2018 Dec 11.
Yefet E, Schwartz N, Chazan B, et al. The safety of **quinolones and fluoroquinolones in pregnancy**: a meta-analysis. BJOG. 2018 Jan 10.
Yende S, Kellum JA, Talisa VB, et al. **Long-term Host Immune Response Trajectories** Among Hospitalized Patients With Sepsis. JAMA Netw Open. 2019 Aug 2;2(8):e198686.
Yeung EYH, Alexander M. Use of junior doctor-led peer education to improve **antibiotic stewardship**. Br J Clin Pharmacol. 2017.
Yoshikawa TT, Norman DC. **Geriatric Infectious Diseases**: Current Concepts on Diagnosis and Management. J Am Geriatr Soc. 2017 Jan 31.
Young J, De Sutter A, Merenstein D, et al. Antibiotics for adults with clinically diagnosed **acute rhinosinusitis**: a meta-analysis of individual patient data. Lancet. 2008 Mar 15;371(9616):908-14. Common clinical signs and symptoms cannot identify patients with rhinosinusitis for whom treatment is clearly justified. Antibiotics are not justified even if a patient reports symptoms for longer than 7-10 days.
Young P, Saxena M, Bellomo R, et al; **HEAT** Investigators and the Australian and New Zealand Intensive Care Society Clinical Trials Group. **Acetaminophen for Fever** in Critically Ill Patients with Suspected Infection. N Engl J Med. 2015 Oct 5.
Young Ryan C.; Hodge David O.; Liesegang Thomas J.; et al. Incidence, Recurrence, and Outcomes of **Herpes Simplex Virus Eye Disease** in Olmsted County, Minnesota, 1976-2007: The Effect of Oral Antiviral Prophylaxis. Arch Ophthalmol. 2010;128(9):1178-1183.
Youngster I, Sauk J, Pindar C, et al. **Fecal microbiota transplant** for relapsing Clostridium difficile infection using a frozen inoculum from unrelated donors: a randomized, open-label, controlled pilot study. Clin Infect Dis. 2014 Jun;58(11):1515-22.
Yue J, Dong BR, Yang M, Chen X,Wu T, Liu GJ. **Linezolid versus vancomycin** for skin and soft tissue infections. Cochrane Database of Systematic Reviews 2013, Issue 7. Art. No.: CD008056. DOI: 10.1002/14651858.CD008056.pub2. Linezolid seems to be more effective than vancomycin for treating people with SSTIs, including SSTIs caused by MRSA. The available evidence is at high risk of bias and is based on studies that were supported by the pharmaceutical company that makes linezolid.
Yun JM, Shin DW, Hwang SS, et al. Effect of **public disclosure** on **antibiotic prescription rate** for upper respiratory tract infections. JAMA Intern Med. 2015 Mar 1;175(3):445-7.
Zakher B, Cantor AG, Pappas M, et al. **Screening for Gonorrhea and Chlamydia**: An Update for the U.S. Preventive Services Task Force. (USPSTF) Ann Intern Med. 2014 Sep 23.
Zhang Yuting; Lee Bruce Y.; Donohue Julie M.. **Ambulatory** Antibiotic Use and Prescription Drug Coverage in Older Adults. Arch Intern Med. 2010;170(15):1308-1314.
Zhang HL, Tan M, Qiu AM, Tao Z, Wang CH. Antibiotics for treatment of **acute exacerbation of chronic obstructive pulmonary disease**: a network meta-analysis. BMC Pulm Med. 2017 Dec 12;17(1):196.
Zhang J, Haines C, Watson AJM, et al. **Oral antibiotic use and risk of colorectal cancer** in the United Kingdom, 1989-2012: a matched case-control study. Gut. 2019 Aug 19.
Zhong NS, Sun T, Zhuo C, et al. **Ceftaroline fosamil versus ceftriaxone** for the treatment of Asian patients with community-acquired **pneumonia**: a randomised, controlled, double-blind, phase 3, non-inferiority with nested superiority trial. Lancet Infect Dis. 2014 Dec 19.
Zoorob R, Sidani M, Murray J. **Croup**: an overview. Am Fam Physician. 2011 May 1;83(9):1067-73.
Zoorob R, Sidani MA, Fremont RD, Kihlberg C. Antibiotic Use in **Acute Upper Respiratory Tract Infections**. Am Fam Physician. 2012;86(9):817-822. C
Zoorob R et al. **Nonprescription antimicrobial use** in a primary care population in the United States. Antimicrob Agents Chemother 2016 Sep; 60:5527.
Zuhlke L, Karthikeyan G, Engel ME, et al. Clinical outcomes in 3343 children and adults with **rheumatic heart disease** from 14 low and middle income countries: 2-year follow-up of the Global Rheumatic Heart Disease Registry (the **REMEDY** study). *Circulation* 2016.

NNTs:
www.thennt.com: Antibiotics for Acute Otitis Media: http://www.thennt.com/antibiotics-for-otitis-media

References

[1] **Bugs and Drugs** 2006; Capital Health Region, Edmonton, AB. Accessed Jan 2010 at: http://www.bugsanddrugs.ca/ . **Bugs and Drugs 2012**; Capital Health Region, Edmonton, AB. Accessed Feb 2013.
[2] Anti-infective Review Panel. **Anti-infective Guidelines for Community-acquired Infections**. Canadian - New-**2012**. Toronto: MUMS Guideline Clearinghouse. http://www.mumshealth.com/
[3] Pharmacist's Letter. September 2009, volume 22, number 220915; Update: Pharmacist's Letter April 2011, Volume 27, number 270423: Recurrent Bacterial vaginosis: Consider longer treatment duration 500mg po BID x 10-14 days or topical metronidazole gel x 10 days , then suppressive therapy with gel twice weekly x 4-6 months. "Clindamycin cream found to be as effective as metronidazole regimens; but is oil-based and may cause failure of latex condoms or diaphragms." Clindamycin cream contains mineral oil.
[4] **Sanford's Guide** to Antimicrobial Therapy 2016.
Vollenweider DJ, Jarrett H, Steurer-Stey CA, et al. Antibiotics for exacerbations of chronic obstructive pulmonary disease.Cochrane Database Syst Rev. 2012 Dec 12;12:CD010257. doi: 10.1002/14651858.CD010257. Antibiotics for COPD exacerbations showed large and consistent beneficial effects across outcomes of patients admitted to an ICU.
[5] Thirion JG (Editor). Snippets for Snappy Antimicrobial Therapy. A concise Canadian Guide 2007. Publications PRISM inc. Dorval QC.
[6] **Medical Letter**: Handbook of Antimicrobial Therapy, 18th Ed. 2008. (Medical Letter. Treatment Guidelines. **Drugs for Bacterial Infections**. June 2010).
Medical Letter-Treatment Guidelines. **Drugs for Sexually Transmitted Diseases**. July 2010.
[7] **Bugs and Drugs** 2006; Capital Health Region, Edmonton, AB. Accessed Jan 2010 at: http://www.bugsanddrugs.ca/ . **Bugs and Drugs 2012**; Capital Health Region, Edmonton, AB. Accessed Feb 2013.
[8] Anti-infective Review Panel. **Anti-infective Guidelines for Community-acquired Infections**. Canadian - New-**2012**. Toronto: MUMS Guideline Clearinghouse. http://www.mumshealth.com/
[9] Pharmacist's Letter. September 2009, volume 22, number 220915; Update: Pharmacist's Letter April 2011, Volume 27, number 270423: Recurrent Bacterial vaginosis: Consider longer treatment duration 500mg po BID x 10-14 days or topical metronidazole gel x 10 days , then suppressive therapy with gel twice weekly x 4-6 months. "Clindamycin cream found to be as effective as metronidazole regimens; but is oil-based and may cause failure of latex condoms or diaphragms." Clindamycin cream contains mineral oil.
[10] **Sanford's Guide** to Antimicrobial Therapy 2016.
Vollenweider DJ, Jarrett H, Steurer-Stey CA, et al. Antibiotics for exacerbations of chronic obstructive pulmonary disease.Cochrane Database Syst Rev. 2012 Dec 12;12:CD010257. doi: 10.1002/14651858.CD010257. Antibiotics for COPD exacerbations showed large and consistent beneficial effects across outcomes of patients admitted to an ICU.
[11] Thirion JG (Editor). Snippets for Snappy Antimicrobial Therapy. A concise Canadian Guide 2007. Publications PRISM inc. Dorval QC.
[12] **Medical Letter**: Handbook of Antimicrobial Therapy, 18th Ed. 2008. (Medical Letter. Treatment Guidelines. **Drugs for Bacterial Infections**. June 2010).
Medical Letter-Treatment Guidelines. **Drugs for Sexually Transmitted Diseases**. July 2010.
[13] Fang L, Oliver A, Jayaraman G, Wong T, et al. Trends in age disparities between younger and middle-age adults among reported rates of Chlamydia, gonorrhea, and infectious syphilis infections in Canada: Findings from 1997 to 2007. *Sexually Transmitted Infections*. 2010 Jan;37(1):18-25. {Canadian data: STIs increasing in middle age group (age 40-59yrs); Chlamydia ↑ 66%; gonorrhea ↑ 210%; syphilis ↑ 11x.}
[14] Ota KV, Jamieson F, Fisman DN, et al. Prevalence of and risk factors for quinolone-resistant Neisseria gonorrhoeae infection in Ontario. CMAJ. 2009 Feb 3;180(3):287-90.
[15] Stone, S. **RxFiles Antifungal** Treatment Chart. Accessed 25 January, 2010 at: http://www.rxfiles.ca/rxfiles/uploads/documents/members/cht-antifungal.pdf

Virological Response (VR) - Definitions

- **Sustained VR SVR:** undetectable HCV-RNA at least 12-24wks after treatment
- **Rapid VR RVR:** undetectable HCV-RNA at TW4 → best predictor of SVR
- **Early VR EVR:** ≥ $2\log_{10}$ ↓ in HCV-RNA at week 12 compared to baseline
- **Delayed VR DVR:** ≥ $2\log_{10}$ ↓ in HCV-RNA but still ≥ 50IU/mL at TW12, then <50IU/mL from TW24 until therapy completed
- **Null Response NR:** < $2\log_{10}$ ↓ in HCV-RNA level at TW12 vs baseline
- **Partial Response PR:** ≥ $2\log_{10}$ ↓ in HCV-RNA but still detectable at week 24
- **Breakthrough:** reappearance of HCV-RNA any time on tx after VR achieved
- **Relapse:** reappearance of HCV-RNA post-treatment after VR achieved
- **End of Treatment Response ETR:** undetectable at completion of therapy

☎=Exception Drug Status SK ✆=prior approval for NIHB Φ=SAIL SK Program ✓=approved indication =↓ dose for renal dysfx =↓ dose for hepatic dysfx ♂=male ♀=female **ALT/AST**=alanine/aspartate transaminase **ANC**=absolute neutrophil count **BMI**=body mass index **CBC**=complete blood count **CDR**=Common Drug Review **CrCl**=creatinine clearance **CV**=cardiovascular **D/C**=discontinue **DRESS**=drug reaction eosinophilia & systemic symptoms **dx**=disease **dysfx**=dysfunction **ESA**=erythropoiesis stimulating agent **GT**=genotype **HD-CKD**=hemodialysis end-stage renal disease **Hgb**=hemoglobin **HIV**=human immunodeficiency virus **hx**=history **IU**=international units **IDU**=intravenous drug user **IL28B**=interleukin 28B **LFT**=liver function test **mos**=months **MSM**=men who have sex with men **PI**=protease inhibitor **pt**=patient **SC**=subcutaneous injection **SCr**=serum creatinine **sx**=symptom **TG**=triglyceride **TSH**=thyroid-stimulating hormone **TW**=treatment week **tx**=treatment/therapy **ULN**=upper limit of normal **WBC**=white blood cell **wk**=week

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Additional articles: Hepatitis

Abbas Z, Khan MA, Salih M, et al. **Interferon alpha for chronic hepatitis D**. Cochrane Database Syst Rev. 2011 Dec 7;12:CD006002. Interferon alpha does not seem to cure hepatitis D in most patients. The agent seems effective in suppressing viral and liver disease activity in some patients, but this improvement is not sustained in the majority of patients.

Arora S, Thornton K, Murata G, et al. Outcomes of **treatment for hepatitis C infection by primary care providers**. N Engl J Med 2011;364:2199-2207

Bouts AH, Schriemer PJ, Zaaijer HL. Chronic **Hepatitis E** Resolved by Reduced Immunosuppression in Pediatric Kidney Transplant Patients. Pediatrics. 2015 Mar 9.

Chayama K, Takahashi S, Toyota J, et al. Dual therapy with the **NS5A inhibitor BMS-790052 and the NS3 protease inhibitor BMS-650032** in HCV genotype 1b-infected null responders. Hepatology 2011;55:742–748.

Chaudhry SA, Verma N, Koren G. **Hepatitis E** infection during pregnancy. Can Fam Physician. 2015 Jul;61(7):607-8.

Collier MG, Tong X, Xu F. **Hepatitis a hospitalizations** in the United States, 2002 - 2011. Hepatology. 2014 Sep 29.

El-Serag Hashem B., **Hepatocellular Carcinoma**. N Engl J Med 2011;365:1118-27.

Friedman LS, Lee SR, Nelson SB, Masia R. Case 36-2016: A 50 year old Man with Acute Liver Injury (**Hepatitis E**). N Engl J Med. 2016 Nov 24;375(21):2082-2092.

Hewitt PE, Ijaz S, Brailsford SR, et al. **Hepatitis E** virus in blood components: a prevalence and transmission study in southeast England. Lancet. 2014 Jul 26.

Hoofnagle JH, Nelson KE, Purcell RH. **Hepatitis E**. N Engl J Med. 2012 Sep 27;367(13):1237-44.

Kamar N, Bendall R, Legrand-Abravanel F, et al. **Hepatitis E**. Lancet. 2012 Apr 27.

Kamar N, Izopet J, Tripon S, et al. **Ribavirin** for chronic **hepatitis E** virus infection in transplant recipients. N Engl J Med 2014;370:1111-20.

Koh C, Canini L, Dahari H, et al. Oral prenylation inhibition with **lonafarnib in chronic hepatitis D** infection: a proof-of-concept randomised, double-blind, placebo-controlled phase 2A trial. Lancet Infect Dis. 2015 Jul 16.

Kwo PY, Cohen SM, Lim JK. ACG Clinical Guideline: **Evaluation of Abnormal Liver Chemistries**. Am J Gastroenterol. 2016 Dec 20.

Liao MT, Chang MH, Lin FG, et al. **Universal Hepatitis B Vaccination** Reduces Childhood Hepatitis B Virus-Associated Membranous Nephropathy. Pediatrics. 2011 Aug 22.

Lin ZH, Xin YN, et al. Performance of the **aspartate aminotransferase-to-platelet ratio index** for the staging of hepatitis C-related fibrosis: an updated meta-analysis. Hepatology 2011;53:726-736

Lo Re V 3rd, Teal V, Localio AR, et al. Relationship between **adherence to hepatitis C virus therapy** and virologic outcomes: a cohort study. Ann Intern Med. 2011 Sep 20;155(6):353-60.

Ly KN, Klevens RM. Trends in Disease and Complications of **Hepatitis A Virus Infection in the United States**, 1999-2011: A New Concern for Adults. J Infect Dis. 2015 Jan 29.

Matheny SC, Kingery JE. **Hepatitis A**. Am Fam Physician. 2012 Dec 1;86(11):1027-1034.

Schaefer EA, Anderson MA, Kim AY, et al. **Case 15-2019: A 55-Year-Old Man with Jaundice. (hepatitis B & C**) N Engl J Med. 2019 May 16;380(20):1955-1963.

Starr SP, Raines D. **Cirrhosis**: diagnosis, management, and prevention. Am Fam Physician. 2011 Dec 15;84(12):1353-9.

Tapper EB, Parikh ND. **Mortality due to cirrhosis and liver cancer** in the United States, 1999-2016: observational study. BMJ. 2018 Jul 18;362:k2817.

Tejada-Strop A, Costafreda MI, et al. Evaluation of potencies of immune globulin products against hepatitis A [online Jan 9, 2017].JAMA Intern Med. doi:10.1001/jamainternmed.2016.9057

The Medical Letter. Treatment Guidelines: **Drugs for Chronic Hepatitis B and C**. March 2013; 11(127): 23-27.

Tseng TC, Liu CJ, Yang HC, et al. High levels of **hepatitis B surface antigen increase risk of hepatocellular carcinoma** in patients with low HBV load. Gastroenterology 2012;142:1140–1149.

van Eijk JJJ, Dalton HR, Ripellino P, et al. Clinical **phenotype and outcome** of **hepatitis E** virus-associated neuralgic amyotrophy. Neurology. 2017 Aug 29;89(9):909-917.
Wai CT, Greenson JK, Fontana RJ, et al. A **simple noninvasive index** can predict both significant fibrosis and cirrhosis in patients with chronic hepatitis C. Hepatology2003;38:518-526 (**APRI** scores)
Wang Y, Zhou X, Debing Y, et al. **Calcineurin Inhibitors** Stimulate and **Mycophenolic** Acid Inhibits Replication of **Hepatitis E** Virus. Gastroenterology. 2014 Feb 26.
Zhang J et al. Long-term efficacy of a **hepatitis E vaccine**. N Engl J Med 2015 Mar 5; 372:914.

HEPATITIS B REFERENCES:

1. Sherman M, Shafran S, Burak K, et al. Management of chronic hepatitis B: **consensus guidelines**. Can J Gastroenterol. 2007 Jun;21 Suppl C:5C-24C. Coffin CS, Fung SK, Ma MM, Canadian Association for the Study of the Liver. Management of chronic hepatitis B: Canadian Association for the Study of the Liver consensus guidelines. Can J Gastroenterol. 2012 Dec;26(12):917-38.
2. Lok AS, McMahon BJ. **American Association for the Study of Liver Diseases**. Chronic hepatitis B: update 2009. Hepatology. 2009 Sep;50(3):661-2.
   Terrault NA, Bzowej NH, Chang KM, et al. **AASLD guidelines** for treatment of chronic hepatitis B. Hepatology. **2016** Jan;63(1):261-83
3. European Association For The Study Of The Liver. EASL **Clinical Practice Guidelines**: management of chronic hepatitis B. J Hepatol. 2009 Feb;50(2):227-42. European Association For The Study Of The Liver. EASL clinical practice guidelines: Management of chronic hepatitis B virus infection. J Hepatol. 2012 Jul;57(1):167-85. doi: 10.1016/j.jhep.2012.02.010. Epub 2012 Mar 20. Erratum in: J Hepatol. 2013 Jan;58(1):201. Janssen, Harry [corrected to Janssen, Harry L A]. PubMed PMID: 22436845.
4. Yang HI, Yuen MF, Chan HL, et al; REACH-B Working Group. Risk estimation for hepatocellular carcinoma in chronic hepatitis B (REACH-B): development and validation of a predictive score. Lancet Oncol. 2011 Jun;12(6):568-74.
5. Launay O, van der Vliet D, Rosenberg AR, et al; ANRS HB03 VIHVAC-B Trial. Safety and immunogenicity of 4 intramuscular double doses and 4 intradermal low doses vs standard hepatitis B vaccine regimen in adults with HIV-1: a randomized controlled trial. JAMA. 2011 Apr 13;305(14):1432-40.
6. Rapti IN, Hadziyannis SJ. Treatment of **special populations with chronic hepatitis B infection**. Expert Rev Gastroenterol Hepatol. 2011 Jun;5(3):323-39.
   Reddy KR, Beavers KL, Hammond SP, Lim JK, Falck-Ytter YT; American Gastroenterological Association (AGA) Institute. American Gastroenterological Association Institute guideline on the **prevention and treatment of hepatitis B virus reactivation during immunosuppressive drug therapy**. Gastroenterology. 2015 Jan;148(1):215-9; quiz e16-7.
7. Lange CM, Bojunga J, Hofmann WP, et al. Severe lactic acidosis during treatment of chronic hepatitis B with entecavir in patients with impaired liver function. Hepatology. 2009 Dec;50(6):2001-6.

Pregnancy References:

8. Pan CQ, Duan ZP, Bhamidimarri KR, Zou HB, Liang XF, Li J, Tong MJ. An algorithm for risk assessment and intervention of mother to child transmission of hepatitis B virus. Clin Gastroenterol Hepatol. 2012 May;10(5):452-9.
9. Bzowej NH. Optimal Management of the Hepatitis B Patient Who Desires Pregnancy or Is Pregnant. Curr Hepat Rep. 2012 Jun;11(2):82-89.
10. Lam NC, Gotsch PB, Langan RC. Caring for pregnant women and newborns with hepatitis B or C. Am Fam Physician. 2010 Nov 15;82(10):1225-9.
11. Dusheiko G. Interruption of mother-to-infant transmission of hepatitis B: time to include selective antiviral prophylaxis? Lancet. 2012 May 26;379(9830):2019-21.
12. Xu WM, Cui YT, Wang L, et al. Lamivudine in late pregnancy to prevent perinatal transmission of hepatitis B virus infection: a multicentre, randomized, double-blind, placebo-controlled study. J Viral Hepat. 2009 Feb;16(2):94-103.
13. van Zonneveld M, van Nunen AB, Niesters HG, de Man RA, Schalm SW, Janssen HL. Lamivudine treatment during pregnancy to prevent perinatal transmission of hepatitis B virus infection. J Viral Hepat. 2003 Jul;10(4):294-7.
14. ter Borg MJ, Leemans WF, de Man RA, Janssen HL. Exacerbation of chronic hepatitis B infection after delivery. J Viral Hepat. 2008 Jan;15(1):37-41
15. Han GR, Cao MK, Zhao W, et al. A prospective and open-label study for the efficacy and safety of telbivudine in pregnancy for the prevention of perinatal transmission of hepatitis B virus infection. J Hepatol. 2011 Apr 15.
16. Lee C, Gong Y, Brok J, et al. Hepatitis B immunisation for newborn infants of hepatitis B surface antigen-positive mothers. Cochrane Database of Systematic Reviews 2006, Issue 2. Art. No.: CD004790. DOI: 10.1002/14651858.CD004790.pub2
    Jourdain G, Ngo-Giang-Huong N, Harrison L, et al. Tenofovir versus Placebo to Prevent Perinatal Transmission of Hepatitis B. N Engl J Med. 2018 Mar 8;378(10):911-923.
17. Yang J, Zeng XM, Men YL, Zhao LS. Elective caesarean section versus vaginal delivery for preventing mother to child transmission of hepatitis B virus—a systematic review. Virol J. 2008 Aug 28;5:100.

Pediatric References:

18. Haber BA, Block JM, Jonas MM, et al; Hepatitis B Foundation. Recommendations for screening, monitoring, and referral of pediatric chronic hepatitis B. Pediatrics. 2009 Nov;124(5):e1007-13.
19. Lim SG, Ng TM, Kung N, et al; Emtricitabine FTCB-301 Study Group. A double-blind placebo-controlled study of emtricitabine in chronic hepatitis B. Arch Intern Med. 2006 Jan 9;166(1):49-56.

Other References:

20. Canadian Liver Foundation. LIVERight: Healthy Living With Viral Hepatitis. March 2010. Accessed via http://www.liver.ca/files/PDF/Eng_Viral_Hep_WEB.pdf on August 9, 2011.
21. Cholongitas E, Goulis J, Akriviadis E, Papatheodoridis GV. Hepatitis B immunoglobulin and/or nucleos(t)ide analogue(s) for prophylaxis from hepatitis B virus recurrence after liver transplantation: A systematic review. Liver Transpl. 2011 Jun 7. doi: 10.1002/lt.22354.
22. Cooke GS, Main J, Thursz MR. Treatment for hepatitis B. BMJ. 2010 Jan 5;340:b5429. doi: 10.1136/bmj.b5429. Review.
23. Dienstag JL. Hepatitis B virus infection. N Engl J Med. 2008 Oct 2;359(14):1486-500. Review. Erratum in: N Engl J Med. 2010 Jul 15;363(3):298.
24. e-CPS. 2011.
25. Gish RG. Hepatitis B treatment: Current best practices, avoiding resistance. Cleve Clin J Med. 2009 May;76 Suppl 3:S14-9.
26. Holness G, Carriero DC, Dieterich DT. Hepatitis B therapies and antiviral resistance detection and management. Expert Rev Gastroenterol Hepatol. 2009 Dec;3(6):693-9. Review.
27. Janssen HL, van Zonneveld M, Senturk H, et al; HBV 99-01 Study Group; Rotterdam Foundation for Liver Research. Pegylated interferon alfa-2b alone or in combination with lamivudine for HBeAg-positive chronic hepatitis B: a randomised trial. Lancet. 2005 Jan 8-14;365(9454):123-9.
28. Janssen HL, Buster EH. Comments on the EASL practice guidelines for the management of chronic hepatitis B: controversies in interferon-based therapy. J Hepatol. 2009 Jul;51(1):224-6.
29. Keeffe EB, Dieterich DT, Han SH, et al. A treatment algorithm for the management of chronic hepatitis B virus infection in the United States: 2008 update. Clin Gastroenterol Hepatol. 2008 Dec;6(12):1315-41; quiz 1286. Epub 2008 Aug 23. Review.
30. Kumar M, Sarin SK. Systematic review: combination therapies for treatment-naïve chronic hepatitis B. Aliment Pharmacol Ther. 2008 Jun;27(12):1187-209. Review.
31. Lai CL, Yuen MF. Chronic hepatitis B--new goals, new treatment. N Engl J Med. 2008 Dec 4;359(23):2488-91.
32. Lai CL, Gane E, Hsu CW, et al. Two-year results from the **GLOBE trial** in patients with hepatitis B: greater clinical and antiviral efficacy for telbivudine (LdT) vs. lamivudine. [Abstract] HEPATOLOGY 2006;44:222A

33. Liaw YF, Sheen IS, Lee CM, et al. Tenofovir disoproxil fumarate (TDF), emtricitabine/TDF, and entecavir in patients with decompensated chronic hepatitis B liver disease. Hepatology. 2011 Jan;53(1):62-72. doi: 10.1002/hep.23952.
34. Lok AS, McMahon BJ. American Association for the Study of Liver Diseases. Chronic hepatitis B. Hepatology. 2007 Feb;45(2):507-39. Erratum in: Hepatology. 2007 Jun;45(6):1347.
35. Lam NC, Gotsch PB, Langan RC. Caring for pregnant women and newborns with hepatitis B or C. Am Fam Physician. 2010 Nov 15;82(10):1225-9. Review.
36. Martín-Carbonero L, Teixeira T, Poveda E, et al. Clinical and virological outcomes in HIV-infected patients with chronic hepatitis B on long-term nucleos(t)ide analogues. AIDS. 2011 Jan 2;25(1):73-9.
37. Pascarella S, Negro F. Hepatitis D virus: an update. Liver Int. 2011 Jan;31(1):7-21. doi: 10.1111/j.1478-3231.2010.02320.x. Review.
38. Paul N, Han SH. Combination Therapy for Chronic Hepatitis B: Current Indications. Curr Hepat Rep. 2011 Jun;10(2):98-105.
39. Public Health Agency of Canada: Hepatitis G Fact Sheet. 2003. Accessed via http://www.phac-aspc.gc.ca/hcai-iamss/bbp-pts/hepatitis/hep_g-eng.php on August 9, 2011.
40. Roque-Afonso AM, Desbois D, Dussaix E. Hepatitis A Virus: Serology and Molecular Diagnostics. Future Virology. 2010;5(2):233-242. Accessed via http://www.medscape.com/viewarticle/719977 on Aug 8, 2011.
41. Shamliyan TA, MacDonald R, Shaukat A, et al. Antiviral therapy for adults with chronic hepatitis B: a systematic review for a National Institutes of Health Consensus Development Conference. Ann Intern Med. 2009 Jan 20;150(2):111-24.
42. Singh AE, Plitt SS, Osiowy C, et al. Factors associated with vaccine failure and vertical transmission of hepatitis B among a cohort of Canadian mothers and infants. J Viral Hepat. 2011 Jul;18(7):468-73. doi: 10.1111/j.1365-2893.2010.01333.x.
43. Sorrell MF, Belongia EA, Costa J, et al. **National Institutes of Health consensus development conference statement: management of hepatitis B.** Hepatology. 2009 May;49(5 Suppl):S4-S12.
44. Standring DN, Seifer M, Patty A, et al. HBV resistance determination from the telbivudine globe registration trial. J Hepatol 2006;44:S191.
45. Sung JJ, Tsoi KK, Wong VW, Li KC, Chan HL. Meta-analysis: Treatment of hepatitis B infection reduces risk of hepatocellular carcinoma. Aliment Pharmacol Ther. 2008 Nov 1;28(9):1067-77.
46. Tenney DJ, Rose RE, Baldick CJ, et al. Long-term monitoring shows hepatitis B virus resistance to entecavir in nucleoside-naïve patients is rare through 5 years of therapy. Hepatology. 2009 May;49(5):1503-14.
47. Tong MJ, Hsu L, Chang PW, Blatt LM. Evaluation of current treatment recommendations for chronic hepatitis B: a 2011 update. J Gastroenterol Hepatol. 2011 May;26(5):829-35. doi: 10.1111/j.1440-1746.2011.06623.x.
48. Wakim-Fleming J. Hepatic encephalopathy: Suspect it early in patients with cirrhosis. Cleveland Clinic Journal of Medicine 2011; 78(9):597-605.
49. WHO. Hepatitis E Fact Sheet No. 280(Revised January 2005). Accessed via http://www.who.int/mediacentre/factsheets/fs280/en/ on August 9, 2011.
50. Wilkins T, Zimmerman D, Schade RR. Hepatitis B: diagnosis and treatment. Am Fam Physician. 2010 Apr 15;81(8):965-72.
51. Gish R, Jia JD, Locarnini S et al. Selection of chronic hepatitis B therapy with high barrier to **resistance**. Lancet Infect Dis. 2012 Feb 8.
52. Lok AS, Ward JW, Perrillo RP, et al. **Reactivation of hepatitis B** during immunosuppressive therapy: potentially fatal yet preventable. Ann Intern Med. 2012 May 15;156(10):743-5.
53. Lai MW, Lin TY, Tsao KC, et al. Increased seroprevalence of HBV DNA with mutations in the s gene among individuals greater than 18 years old after complete **vaccination**. Gastroenterology. 2012 Aug;143(2):400-7.
54. Hadziyannis SJ, Sevastianos V, Rapti I, et al. Sustained Responses and Loss of HBsAg in HBeAg-Negative Patients With Chronic Hepatitis B Who Stop Long-term Treatment With **Adefovir**. Gastroenterology. 2012 May 31.
55. Lok AS, Trinh H, Carosi G, et al. Efficacy of **Entecavir With or Without Tenofovir** Disoproxil Fumarate for Nucleos(t)ide-Naïve Patients With Chronic Hepatitis B. Gastroenterology. 2012 May 27.
56. Lampertico P, Viganò M, Di Costanzo GG, et al; on behalf of the PegBeLiver Study Group. Randomised study comparing 48 and 96 weeks **peginterferon α-2a** therapy in genotype D HBeAg-negative chronic hepatitis B. Gut. 2012 Aug 2.
57. Wu C-Y, Chen Y-J, Ho HJ, et al. Association between nucleoside analogues and risk of hepatitis B virus–related **hepatocellular carcinoma** recurrence following liver resection [online November 12, 2012]. JAMA. 2012;308(18):1906-1913
58. Whitaker JA, Rouphael NG, Edupuganti S, et al. Strategies to increase responsiveness to **hepatitis B vaccination in adults with HIV-1.** Lancet Infect Dis. 2012 Dec;12(12):966-76.
59. Marcellin P, Gane E, et al. **Regression of cirrhosis** during treatment with **tenofovir** disoproxil fumarate for chronic hepatitis B: a 5-year open-label follow-up study. Lancet 2012; online Dec 10.
60. Stone JH, Murali MR. Case records of the Massachusetts General Hospital. Case 10-2013. A 30-year-old man with fever, myalgias, arthritis, and rash. (**Acute Hepatitis B**) N Engl J Med. 2013 Mar 28;368(13):1239-45.
61. Wong GL, Chan HL, Chan HY, et al. Accuracy of **risk scores** for patients with chronic hepatitis B receiving entecavir treatment. Gastroenterology. 2013 May;144(5):933-44.
62. Wiens A, Lenzi L, Venson R, et al. Comparative efficacy of oral **nucleoside or nucleotide analog** monotherapy used in chronic hepatitis B: a mixed-treatment comparison meta-analysis. Pharmacotherapy. 2013 Feb;33(2):144-51. (tenofovir)
63. Zoutendijk R et al. Virological response to **entecavir** is associated with a better clinical outcome in chronic hepatitis B patients with cirrhosis. Gut 2013 May; 62:760.
64. Gatanaga H et al. **Prophylactic** effect of antiretroviral therapy on hepatitis B virus infection. Clin Infect Dis 2013 Jun 15; 56:1812.
65. **NICE**: National Institute for Health and Care Excellence. Hepatitis B (chronic): **diagnosis and management of chronic hepatitis B in children, young people and adults**. (Clinical guideline 165.) 2013. http://guidance.nice.org.uk/CG165.
66. NICE: National Institute for Health and Care Excellence. Hepatitis B and C: ways to **promote and offer testing** to people at increased risk of infection. (Public health guideline 43.) 2012. http://guidance.nice.org.uk/PH43.
67. Sarri G, Westby M, Bermingham S, Hill-Cawthorne G, Thomas H; Guideline Development Group. Diagnosis and management of chronic hepatitis B in children, young people, and adults: summary of NICE guidance. BMJ. 2013 Jun 26;346:f3893.
68. Huang YH, Hsiao LT, Hong YC et al. Randomized Controlled Trial of Entecavir Prophylaxis for Rituximab-Associated Hepatitis B Virus Reactivation in Patients With Lymphoma and Resolved Hepatitis B. J Clin Oncol. 2013 Jun 17.
69. Damme PV, Leuridan E, Hendrickx G, et al. Should Europe have a **universal hepatitis B vaccination** programme? BMJ. 2013 Jul 10;347:f4057.
70. Xu Y, Liu H, Wang Y, et al. The next step in **controlling HBV in China**. BMJ. 2013 Jul 16;347:f4503.
71. Huang YH, Hsiao LT, Hong YC, et al. Randomized Controlled Trial of **Entecavir Prophylaxis for Rituximab-Associated** Hepatitis B Virus Reactivation in Patients With Lymphoma and Resolved Hepatitis B. J Clin Oncol. 2013 Jun 17.
72. Sarri G, Westby M, Bermingham S, et al; on behalf of the Guideline Development Group. **Diagnosis and management of chronic hepatitis B in children, young people, and adults**: summary of **NICE** guidance. BMJ. 2013 Jun 26;346:f3893.
73. Chiang CJ, Yang YW, You SL, et al. **Thirty-year outcomes of the national hepatitis B immunization program** in Taiwan. JAMA. 2013 Sep 4;310(9):974-6.

74. FDA Sep/13 approved changes to the prescribing information of the immune-suppressing and anti-cancer drugs **Arzerra (ofatumumab) and Rituxan (rituximab)** to add new Boxed Warning information about the risk of **reactivation of hepatitis B** virus (HBV) infection.
75. Yu HC, Lin KH, Hsu PI, et al. Real-world application of the roadmap model in chronic hepatitis B patients with **telbivudine** therapy. Clin Ther. 2013 Sep;35(9):1386-99.
76. Lai CL, Ahn SH, Lee KS, et al. Phase IIb multicentred randomised trial of **besifovir (LB80380)** versus **entecavir** in Asian patients with chronic hepatitis B. Gut. 2013 Aug 31.
77. Huang ZB, Zhao SS, Huang Y, et al. Comparison of the Efficacy of **Lamivudine Plus Adefovir Versus Entecavir** in the Treatment of Lamivudine-Resistant Chronic Hepatitis B: A Systematic Review and Meta-Analysis. Clin Ther. 2013 Nov 13.
78. Barbosa C, Smith EA, Hoerger TJ, et al. **Cost-effectiveness** Analysis of the National Perinatal Hepatitis B Prevention Program. Pediatrics. 2014 Jan 6.
79. Gane EJ, Deray G, Liaw YF, et al. **Telbivudine** improves renal function in patients with chronic hepatitis B. Gastroenterology. 2014 Jan;146(1):138-146
80. Health Canada Jan/14 ARZERRA (**ofatumumab**) - Recommendations to Screen, Monitor and to Manage Hepatitis B Virus Reactivation - GlaxoSmithKline Inc. The use of ARZERRA has been shown to be associated with recurrence of Hepatitis B virus infection in patients who show evidence of a previous infection with the Hepatitis B virus, in a blood test.
81. Hamnvik OP, Becker CB, Levy BD, et al. Clinical problem-solving. Wasting away. (**tenofovir: Fanconi** syndrome) N Engl J Med. 2014 Mar 6;370(10):959-66.
82. Yang YJ, Shim JH, Kim KM, et al. Assessment of current criteria for **primary nonresponse** in chronic hepatitis B patients receiving **entecavir** therapy. Hepatology. 2014 Apr;59(4):1303-10.
83. Davison SA, Strasser SI. **Ordering and interpreting hepatitis B serology**. BMJ. 2014 Apr 17;
84. Chan HL, Chan CK, Hui AJ, et al. Effects of **Tenofovir** Disoproxil Fumarate in Hepatitis B e Antigen-Positive Patients With Normal Levels of Alanine Aminotransferase and High Levels of Hepatitis B Virus DNA. Gastroenterology. 2014 May;146(5):1240-8.
85. Lim YS, Han S, Heo NY, et al. Mortality, Liver Transplantation, and Hepatocellular Carcinoma Among Patients with Chronic Hepatitis B Treated with **Entecavir** vs **Lamivudine**. Gastroenterology. 2014 Feb 25.
86. Wu CY, Lin JT, Ho HJ, et al. Association of **Nucleos(t)ide Analogue Therapy with Reduced Risk of Hepatocellular Carcinoma** in Patients with Chronic Hepatitis B-a Nationwide Cohort Study. Gastroenterology. 2014 Apr 1.
87. Fung S, Kwan P, Fabri M, et al. Randomized Comparison of **Tenofovir Disoproxil Fumarate vs Emtricitabine and Tenofovir** Disoproxil Fumarate in Patients With Lamivudine-Resistant Chronic Hepatitis B. Gastroenterology. 2014 Apr;146(4):980-988
88. Chou R, Dana T, Bougatsos C, et al. **Screening for Hepatitis B** Virus Infection in **Adolescents and Adults**: A Systematic Review to Update the U.S. Preventive Services Task Force Recommendation. (USPSTF) Ann Intern Med. 2014 May 27.
89. Kubo A, Shlager L, Marks AR, et al. **Prevention of Vertical Transmission of Hepatitis B:** An Observational Study. Ann Intern Med. 2014 May 27.
90. LeFevre ML; U.S. Preventive Services Task Force. (USPSTF) **Screening for hepatitis B virus infection in nonpregnant adolescents and adults**: U.S. Preventive Services Task Force recommendation statement. Ann Intern Med. 2014;161.
91. Trépo C, Chan HL, Lok A. **Hepatitis B** virus infection. Lancet. 2014 Jun 18.
92. Bouazza N, Tréluyer JM, Ghosn J, et al. Evaluation of **Impaired Renal Function on Lamivudine** Pharmacokinetics. Br J Clin Pharmacol. 2014 Apr 21.
93. Collier MG, Khudyakov YE, Selvage D, et al, for the Hepatitis A Outbreak Investigation Team. Outbreak of **hepatitis A in** the USA associated with frozen pomegranate arils imported from Turkey: an epidemiological case study. Lancet Infect Dis 2014; published online Sept 4.
94. Huang H, Li X, Zhu J, et al. **Entecavir vs lamivudine** for prevention of **hepatitis B** virus reactivation among patients with untreated diffuse large B-cell lymphoma receiving R-CHOP chemotherapy: a randomized clinical trial. JAMA. 2014 Dec 17;312(23):2521-30.
95. Liu J, Tseng T, Yang H, et al. **Predicting Hepatitis B Virus (HBV) Surface Antigen Seroclearance** in HBV e Antigen-Negative Patients With Chronic Hepatitis B: External Validation of a **Scoring System**. J Infect Dis. 2014 Nov 27.
96. Schillie S, Walker T, Veselsky S, et al. **Outcomes of Infants Born to Women Infected With Hepatitis B**. Pediatrics. 2015 Apr 20.
97. Iqbal K, Klevens RM, Kainer MA, et al. The Epidemiology of **Acute Hepatitis B in the United States** from Population-Based Surveillance, 2006-2011. Clin Infect Dis. 2015 Apr 22.
98. Reddy KR, Beavers KL, Hammond SP, Lim JK, Falck-Ytter YT; American Gastroenterological Association (**AGA**) Institute. American Gastroenterological Association Institute guideline on the prevention and treatment of **hepatitis B virus reactivation during immunosuppressive drug therapy**. Gastroenterology. 2015 Jan;148(1):215-9; quiz e16-7.
99. Jhaveri R. Prevention of **hepatitis B virus vertical transmission**: time for the next step. Pediatrics. 2015 May;135(5):e1286-7.
100. Park JH, Jung SW, Park NH, et al. Efficacy of **Tenofovir**-Based Rescue Therapy in Lamivudine-Resistant Chronic Hepatitis B Patients With Failure of **Lamivudine and Adefovir** Combination. Clin Ther. 2015 May 5.
101. Ly KN, Klevens RM. Trends in Disease and Complications of **Hepatitis A Virus Infection in the United States**, 1999-2011: A New Concern for Adults. J Infect Dis. 2015 Jul 15;212(2):176-82.
102. Thio CL, Guo N, Xie C, et al. **Global elimination of mother-to-child transmission** of **hepatitis B**: revisiting the current strategy. Lancet Infect Dis. 2015 Jul 2. pii: S1473-3099(15)00158-9.
103. Liu J, Zhang S, et al. Seroepidemiology of **hepatitis B** virus infection in 2 million men aged 21-49 years in rural China: a population-based, cross-sectional study. Lancet Infect Dis. 2015 Aug 7.
104. Rey D, Piroth L, Wendling M-J, et al. Safety and immunogenicity of **doubledose versus standard-dose hepatitis B** revaccination in non-responding adults with **HIV-1** (ANRS HB04 B-BOOST): a multicentre, open-label, randomised controlled trial. Lancet Infect Dis 2015; online Aug 7.
105. Schweitzer A, Horn J, Mikolajczyk R, et al. Estimations of **worldwide prevalence of chronic hepatitis B** virus infection: a systematic review of data published between 1965 and 2013. Lancet 2015; online July 28.
106. Wu Q, Huang H, Sun X, et al. **Telbivudine prevents vertical transmission of hepatitis B virus from women** with high viral loads: a prospective long-term study. Clin Gastroenterol Hepatol. 2015 Jun;13(6):1170-6.
107. Martin P, Lau DT, et al. A **Treatment Algorithm** for the Management of Chronic Hepatitis B Virus Infectionin the **United States: 2015 Update**. Clin Gastroenterol Hepatol. 2015 Jul 15.
108. Schwarz KB, Cloonan YK, Ling SC, et al; Hepatitis B Research Network. **Children with Chronic Hepatitis B in the United States and Canada**. J Pediatr. 2015 Sep 7.
109. Collins JM et al. **Hepatitis B virus reactivation** during successful treatment of hepatitis C virus with **sofosbuvir and simeprevir**. Clin Infect Dis 2015 Oct 15; 61:1304.
110. Falade-Nwulia O, Seaberg EC, Snider AE, et al. **Incident Hepatitis B Virus Infection in HIV-Infected** and HIV-Uninfected Men Who Have Sex With Men From Pre-HAART to HAART Periods: A Cohort Study. Ann Intern Med. 2015 Oct 13.
111. Sundaram V, Kowdley K. **Management of chronic hepatitis B** infection. BMJ. 2015 Oct 21;351:h4263.
112. Paul S, Saxena A, Terrin N, et al. Hepatitis B Virus **Reactivation and Prophylaxis During Solid Tumor Chemotherapy**: A Systematic Review and Meta-analysis. Ann Intern Med. 2015 Nov 24.
113. Liaw YF, Kao JH, Piratvisuth T, et al. **APASL: Asian-Pacific consensus** statement on the management of chronic **hepatitis B**: a 2012 update. Hepatol Int 2012;6:531– 61.
114. Han SH, Tran TT. Management of Chronic Hepatitis B: An **Overview of Practice Guidelines for Primary Care Providers**. J Am Board Fam Med. 2015 Nov-Dec;28(6):822-37.
115. Hughes E, Bassi S, Gilbody S, et al. Prevalence of HIV, hepatitis B, and hepatitis C in people with severe mental illness: a systematic review and meta-analysis. Lancet Psychiatry. 2015 Nov 24.
116. Marcellin P, Ahn SH, Ma X, et al. Combination of **Tenofovir** Disoproxil Fumarate and **Peginterferon** alpha-2a Increases Loss of **Hepatitis B** Surface Antigen in Patients With Chronic Hepatitis B. Gastroenterology. 2016 Jan;150(1):134-144.e10.
117. Chaudhry SA, Koren G. **Hepatitis A** infection during **pregnancy**. Can Fam Physician. 2015 Nov;61(11):963-4.

118. Health Canada May/16: BCR-ABL **Tyrosine Kinase Inhibitors** [GLEEVEC (imatinib mesylate), TASIGNA (nilotinib), BOSULIF (bosutinib), SPRYCEL (dasatinib), ICLUSIG (ponatinib hydrochloride)] - Risk of **Hepatitis B Reactivation** - Novartis Pharmaceuticals Canada Inc., Pfizer Canada Inc. Canada, Bristol-Myers Squibb, ARIAD Pharmaceuticals, Inc. Cases of reactivation of hepatitis B virus (HBV) have occurred in patients who are chronic carriers of HBV after they received BCR-ABL tyrosine kinase inhibitors. Some cases of HBV reactivation resulted in acute hepatic failure or fulminant hepatitis leading to liver transplantation or a fatal outcome.
119. Terrault NA, Bzowej NH, Chang KM, et al. **AASLD guidelines for treatment of chronic hepatitis B.** Hepatology. 2016 Jan;63(1):261-83.
120. Pan CQ et al. **Tenofovir to prevent hepatitis B transmission in mothers** with high viral load. *N Engl J Med*2016 Jun 16; 374:2324. With its large size and rigorous design, this study confirms that HBeAg-positive HBV-infected pregnant women with high viral loads who receive antiviral treatment — specifically, TDF — during the third trimester have significantly lower rates of vertical transmission to their infants, with an excellent safety profile. Accordingly, this practice should be considered the standard of care.
121. Buckley GJ, Strom BL. What Stands in the Way of **Making Hepatitis B and C Rare** Diseases in the United States? Ann Intern Med. 2016 Aug 16;165(4):284-5
122. Gounder PP, Bulkow LR, Snowball M, et al. **Hepatocellular Carcinoma Risk** in Alaska Native Children and Young Adults with **Hepatitis B** Virus: Retrospective Cohort Analysis. J Pediatr. 2016 Nov;178:206-213.
123. Wang L, Wiener J, Bulterys M, et al. Hepatitis B Virus (HBV) **Load Response** to 2 Antiviral Regimens, **Tenofovir/Lamivudine and Lamivudine, in HIV/ HBV-Coinfected Pregnant Women** in Guangxi, China: The Tenofovir in Pregnancy (TiP) Study. J Infect Dis. 2016 Dec 1;214(11):1695-1699.
124. Loomba R, Liang TJ. **Hepatitis B reactivation associated with immune suppressive and biological modifier therapies**: current concepts, management strategies and future directions. Gastroenterology. 2017 Feb 17.
125. Yan G, Hu C, et al. A **different inhibitor** is required for **overcoming entecavir resistance**: a comparison of four rescue therapies in a retrospective study. Br J Clin Pharmacol. 2017 May 16.
126. Carrillo-Santisteve P, et al. **Seroprevalence and susceptibility to hepatitis A** in the **European** Union and European Economic Area: a systematic review. Lancet Infect Dis. 2017 Jun 20
127. Chen J, Zhao SS, Liu XX, et al. Comparison of the Efficacy of **Tenofovir** Versus **Tenofovir plus Entecavir** in the Treatment of Chronic **Hepatitis B** in Patients with Poor Efficacy of Entecavir: A Systematic Review and Meta-analysis. ClinTher.2017.
128. Ben-Yakov G, Devika K, Etzion O, et al. A **Misleading Pattern of Serologic Findings** During Hepatitis B Virus Infection. Ann Intern Med. 2017 Aug 29.
129. van Eijk JJJ, Dalton HR, Ripellino P, et al. Clinical **phenotype and outcome** of **hepatitis E** virus-associated neuralgic amyotrophy. Neurology. 2017 Aug 29;89(9):909-917.
130. Polish Group of Experts for HBV, Flisiak R, Halota W, Jaroszewicz J, et al. Recommendations for the treatment of **hepatitis B in** 2017. Clin Exp Hepatol. 2017 Jun;3(2):35-46.
131. Tseng TC, Liu CJ, Su TH, et al. **Fibrosis-4 Index Helps Identify HBV Carriers** With the Lowest Risk of Hepatocellular Carcinoma. Am J Gastroenterol. 2017 Aug 29.
132. Wu T;Li J;Shao L;Xin J;Jiang L;et al. **Development of diagnostic criteria and a prognostic score for hepatitis B** virus-related acute-on-chronic liver failure. Gut. 2017 Sep 19.
133. Abara WE, Qaseem A, Schillie S, et al. **Hepatitis B Vaccination, Screening, and Linkage to Care**: Best Practice Advice From the American College of Physicians and the Centers for Disease Control and Prevention. Ann Intern Med. 2017 Nov 21.
134. Kushel M. **Hepatitis A Outbreak in California** - Addressing the Root Cause. N Engl J Med. 2017 Dec 6.
135. Pan CQ, Duan Z, Dai E, et al. **Tenofovir** to **prevent hepatitis B transmission** in mothers with high viral load. N Engl J Med 2016;374:2324-34.
136. Tang LSY, Covert E, Wilson E, et al. Chronic Hepatitis B Infection: A Review. JAMA. 2018 May 1;319(17):1802-1813.
137. Huang G, Li PP, Lau WY, et al. **Antiviral Therapy Reduces Hepatocellular Carcinoma Recurrence in Patients With Low HBV-DNA Levels**: A Randomized Controlled Trial. Ann Surg. 2018 Mar 8.
138. Li Z, Lei Z, Xia Y, et al. Association of **preoperative antiviral treatment with incidences of microvascular invasion and early tumor recurrence in hepatitis B virus**–related hepatocellular carcinoma [online August 1, 2018]. JAMA Surg. doi:10.1001/jamasurg.2018.2721
139. Choi J, Kim HJ, Lee J, et al. Risk of **Hepatocellular Carcinoma** in Patients Treated With **Entecavir vs Tenofovir for Chronic Hepatitis B**: A Korean Nationwide Cohort Study. JAMA Oncol. 2018 Sep 27.
140. Kusari A, Ahluwalia J. **Lichen Planus**. N Engl J Med. 2018 Aug 9;379(6):567.
141. Lee JGH, Carruthers M, Ko HH. **Reactivation of hepatitis B virus** associated with immunosuppression therapy. CMAJ. 2018 Oct 29;190(43):E1284.
142. Seto WK, Lo YR, Pawlotsky JM, Yuen MF. **Chronic hepatitis B virus infection**. Lancet. 2018 Nov 24;392(10161):2313-2324.
143. Wilkins T, Sams R, Carpenter M. Hepatitis B: **Screening, Prevention, Diagnosis, and Treatment.** Am Fam Physician. 2019;99(5):314-323.
144. Fox RK, Taddei TH, Kaplan DE. **Aspirin Use and Risk of Hepatocellular Carcinoma** in Hepatitis B. JAMA Intern Med. 2019 Mar 18.
145. Lee TY, Hsu YC, Tseng HC, et al. **Association of Daily Aspirin Therapy With Risk of Hepatocellular Carcinoma** in Patients With Chronic Hepatitis B. JAMA Intern Med. 2019 Mar 18.
146. Health Canada Apr/19: Important Safety Information on DARZALEX (daratumumab) and Hepatitis B Virus reactivation.
147. Kim AY. Hepatitis B Virus and **HIV Coinfection**: Fibrosis, Fat, and Future Directions. Am J Gastroenterol. 2019 Apr 12
148. Li T, Qu Y, Wang Y, et al. **Entecavir and Low Genetic Barrier Antiviral Agents for Hepatocellular Carcinoma** in Hepatitis B Viral Cirrhosis: Propensity Score Matching. J Coll Physicians Surg Pak. 2019 Apr;29(4):317-323.
149. Thomas DL. **Global Elimination of Chronic Hepatitis**. N Engl J Med. 2019 May 23;380(21):2041-2050.
150. Song C, Lv J, Liu Y, et al. Associations Between Hepatitis B Virus Infection and **Risk of All Cancer Types**. JAMA Netw Open. 2019 Jun 5;2(6):e195718.
151. Pdf USPSTF: US Preventive Services Task Force. Screening for hepatitis B virus **infection in pregnant women**: US Preventive Services Task Force recommendation statement [July 23, 2019]. JAMA. doi:10.1001/jama.2019.9365
152. USPSTF: Henderson JT, Webber EM, Bean SI. Screening for hepatitis B infection in pregnant women: updated evidence report and systematic review for the US Preventive Services Task Force [July 23, 2019]. JAMA. doi:10.1001/jama.2019.1655
153.

REFERENCES –HEPATITIS C

1. Myers RP, Ramji A, Bilodeau M, Wong S et al. An update on the management of hepatitis C: **Consensus guidelines from the Canadian Association for the Study of the Liver**. (**CASL**) Can J Gastroenterol. 2012 Jun;26(6):359-75.
   Myers RP, Shah H, Burak KW, et al. An update on the management of chronic hepatitis C: 2015 consensus guidelines from the Canadian Association for the Study of the Liver. (**CASL**) Can J Gastroenterol Hepatol 2015;29:19-34.
   http://www.pulsus.com/journals/pdf_frameset.jsp?jnlKy=2&atlKy=13233&isArt=t&jnlAdvert=Gastro&adverifHCTp=&sTitle=An%20update%20on%20the%20management%20of%20chronic%20hepatitis%20C%3A%202015%20Consensus%20guidelines%20from%20the%20Canadian%20Association%20for%20the%20Study%20of%20the%20Liver%2C%20Pulsus%20Group%20Inc&VisitorType
   Shah H, Bilodeau M, Burak KW, et al. The management of **chronic hepatitis C: 2018 guideline update from the Canadian Association for the Study of the Liver**. (**CASL**) CMAJ 2018;190:E677-87
2. European Association for the Study of the Liver. **EASL Clinical Practice Guidelines: Management of hepatitis C virus infection.** J Hepatol. 2011 Aug;55(2):245-64. European Association for Study of Liver. EASL Clinical Practice Guidelines: management of hepatitis C virus infection. J Hepatol. 2014 Feb;60(2):392-420. doi: 10.1016/j.jhep.2013.11.003. Epub 2013 Dec 9. Erratum in: J Hepatol. 2014 Jul;61(1):183-4. PubMed PMID: 24331294.

EASL:European Association for the Study of the Liver. Electronic address: easloffice@easloffice.eu. **EASL Recommendations on Treatment of Hepatitis C 2016**. J Hepatol. 2016 Sep 12.
EASL:European Association for the Study of the Liver. Electronic address: easloffice@easloffice.eu. **EASL Recommendations on Treatment of Hepatitis C 2018**. J Hepatol. 2018 Apr 9.

3. Ghany MG, Strader DB, Thomas DL, Seeff LB; **American Association for the Study of Liver Diseases. Diagnosis, management, and treatment of hepatitis C: an update.** Hepatology. 2009 Apr;49(4):1335-74. Ghany MG, Nelson DR, Strader DB, Thomas DL, Seeff LB, American Association for Study of Liver Diseases (**AASLD**). An update on treatment of **genotype 1 chronic hepatitis C** virus infection: 2011 practice guideline by the American Association for the Study of Liver Diseases. Hepatology 2011 Oct;54(4):1433-44. American Association for the Study of Liver Diseases (AASLD) – Infectious Disease Society of America (IDSA). AASLD-IDSA Recommendations for the Testing, Managing, and Treating Hepatitis C. Accessed from http://www.hcvguidelines.org on April 26, 2016.
4. Sulkowski MS, Cooper C, Hunyady B, et al. Management of adverse effects of Peg-IFN and ribavirin therapy for hepatitis C. Nat Rev Gastroenterol Hepatol. 2011 Apr;8(4):212-23
5. Koirala J, Gandotra SD, Rao S, et al. Granulocyte colony-stimulating factor dosing in pegylated interferon alpha-induced neutropenia and its impact on outcome of anti-HCV therapy. J Viral Hepat. 2007 Nov;14(11):782-7.
6. FDA Drug Safety Communication: Modified dosing recommendations to improve the safe use of Erythropoiesis-Stimulating Agents (ESAs) in chronic kidney disease. 2011 June 24. Accessed via http://www.fda.gov/Drugs/DrugSafety/ucm259639.htm#table on August 10, 2011.
7. Bloom RD, Lake JR. Emerging issues in hepatitis C virus-positive liver and kidney transplant recipients. Am J Transplant. 2006 Oct;6(10):2232-7.
8. Guitard J, Rostaing L, Kamar N. New-onset diabetes and nephropathy after renal transplantation. Contrib Nephrol. 2011;170:247-55.
9. Fabrizi F, Messa P, Martin P, et al. Hepatitis C virus infection and post-transplant diabetes mellitus among renal transplant patients: a meta-analysis. Int J Artif Organs. 2008 Aug;31(8):675-82.
10. Awad T, Thorlund K, Hauser G, Stimac D, Mabrouk M, Gluud C. Peginterferon alpha-2a is associated with higher sustained virological response than peginterferon alfa-2b in chronic hepatitis C: systematic review of randomized trials. Hepatology. 2010 Apr;51(4):1176-84.
11. Afdhal NH, Dieterich DT, Pockros PJ, et al; Proactive Study Group. Epoetin alfa maintains ribavirin dose in HCV-infected patients: a prospective, double-blind, randomized controlled study. Gastroenterology. 2004 May;126(5):1302-11.
12. Aghemo A, Rumi MG, Colombo M. Pegylated interferons alpha2a and alpha2b in the treatment of chronic hepatitis C. Nat Rev Gastroenterol Hepatol. 2010 Sep;7(9):485-94. Review.
13. Albeldawi M, Ruiz-Rodriguez E, Carey WD. Hepatitis C virus: Prevention, screening, and interpretation of assays. Cleve Clin J Med. 2010 Sep;77(9):616-26. Review.
14. Alberti A, Clumeck N, Collins S, et al; ECC Jury. Short statement of the first European Consensus Conference on the treatment of chronic hepatitis B and C in HIV co-infected patients. J Hepatol. 2005 May;42(5):615-24. Review. Erratum in: J Hepatol. 2005 Dec;43(6):1098.
15. Ascione A, De Luca M, Tartaglione MT, et al. **Peginterferon alfa-2a plus ribavirin is more effective than peginterferon alfa-2b plus ribavirin for treating chronic hepatitis C virus infection.** Gastroenterology. 2010 Jan;138(1):116-22.
16. Bacon BR, Gordon SC, Lawitz E, et al; **HCV RESPOND-2 Investigators. Boceprevir for previously treated chronic HCV genotype 1 infection.** N Engl J Med. 2011 Mar 31;364(13):1207-17.
17. Buxton JA, Kim JH. Hepatitis A and hepatitis B vaccination responses in persons with chronic hepatitis C infections: A review of the evidence and current recommendations. Can J Infect Dis Med Microbiol. 2008 Mar;19(2):197-202.
18. e-CPS. 2016.
19. Ferguson MC. Current therapies for chronic hepatitis C. Pharmacotherapy. 2011 Jan;31(1):92-111. Review.
20. Freedman ND, Curto TM, Lindsay KL, et al; **HALT-C** TRIAL GROUP. Coffee consumption is associated with response to peginterferon and ribavirin therapy in patients with chronic hepatitis C. Gastroenterology. 2011 Jun;140(7):1961-9.
21. Freedman ND, Everhart JE, Lindsay KL et al; **HALT-C** Trial Group. Coffee intake is associated with lower rates of liver disease progression in chronic hep C. Hepatology. 2009 Nov;50(5):1360-9.
22. Hadigan C, Kottilil S. Hepatitis C virus infection and coinfection with human immunodeficiency virus: challenges and advancements in management. JAMA. 2011 Jul 20;306(3):294-301.
23. Jacobson IM, McHutchison JG, Dusheiko G, et al; **ADVANCE Study Team. Telaprevir for previously untreated chronic hepatitis C virus infection.** N Engl J Med. 2011 Jun 23;364(25):2405-16.
24. Jou JH, Muir AJ. **In the clinic**. Hepatitis C. Ann Intern Med. **2008** Jun 3;148(11):ITC6-1-ITC6-16. Hou JH, Muir AJ. **In the Clinic**: Hepatitis C. Ann Intern Med. Dec 4, **2012**. ITC6-2. Review.
25. Mauss S, Hueppe D, John C, et al. Estimating the likelihood of sustained virological response in chronic hepatitis C therapy. J Viral Hepat. 2011 Apr;18(4):e81-90. doi: 10.1111/j.1365-2893.2010.01372.x.
26. McHutchison JG, Lawitz EJ, Shiffman ML, et al; **IDEAL Study Team. Peginterferon alfa-2b or alfa-2a with ribavirin for treatment of hepatitis C infection.** N Engl J Med. 2009 Aug 6;361(6):580-93. Erratum in: N Engl J Med. 2009 Sep 3;361(10):1027.
27. Muir AJ, Hu KQ, Gordon SC, et al. Hepatitis C treatment among racial and ethnic groups in the IDEAL trial. J Viral Hepat. 2011 Apr;18(4):e134-43. doi: 10.1111/j.1365-2893.2010.01402.x.
28. Nash KL, Bentley I, Hirschfield GM. Managing hepatitis C virus infection. BMJ. 2009 Jun 26;338:b2366. doi: 10.1136/bmj.b2366. Review.
29. Poordad F, McCone J Jr, Bacon BR, et al; **SPRINT-2 Investigators. Boceprevir for untreated chronic HCV genotype 1 infection.** N Engl J Med. 2011 Mar 31;364(13):1195-206.
30. Rosen HR. Clinical practice. Chronic hepatitis C infection. N Engl J Med. 2011 Jun 23;364(25):2429-38. Review.
31. Rosenberg P, Hagen K. Serum B12 levels predict response to treatment with interferon and ribavirin in patients with chronic HCV infection. J Viral Hepat. 2011 Feb;18(2):129-34. doi: 10.1111/j.1365-2893.2010.01288.x.
32. Rumi MG, Aghemo A, Prati GM, et al. Randomized study of peginterferon-alpha2a plus ribavirin vs peginterferon-alpha2b plus ribavirin in chronic hepatitis C. Gastroenterology. 2010 Jan;138(1):108-15.
33. Sherman M, Cohen L, Cooper MA, et al. Clinical recommendations for the use of recombinant human erythropoietin in patients with hepatitis C virus being treated with ribavirin. Can J Gastroenterol. 2006 Jul;20(7):479-85. Review.
34. Sherman M, Shafran S, Burak K, et al. **Management of chronic hepatitis C: consensus guidelines.** Can J Gastroenterol. 2007 Jun;21 Suppl C:25C-34C.
35. Sockalingam S, Abbey SE. Managing depression during hepatitis C treatment. Can J Psychiatry. 2009 Sep;54(9):614-25. Review.
36. Sockalingam S, Links PS, Abbey SE. Suicide risk in hepatitis C and during interferon-alpha therapy: a review and clinical update. J Viral Hepat. 2011 Mar;18(3):153-60. doi: 10.1111/j.1365-2893.2010.01393.x.
37. Soriano V, Puoti M, Sulkowski M, et al. Care of patients with hepatitis C and HIV co-infection. AIDS. 2004 Jan 2;18(1):1-12. Review.
38. Spradling PR, Richardson JT, Buchacz K, et al; HIV Outpatient Study Investigators. Trends in hepatitis C virus infection among patients in the HIV Outpatient Study, 1996-2007. J Acquir Immune Defic Syndr. 2010 Mar 1;53(3):388-96.
39. Stravitz RT, Chung H, Sterling RK, et al. Antibody-mediated pure red cell aplasia due to epoetin alfa during antiviral therapy of chronic hepatitis C. Am J Gastroenterol. 2005 Jun;100(6):1415-9.
40. Sulkowski MS. Anemia in the treatment of hepatitis C virus infection. Clin Infect Dis. 2003;37 Suppl 4:S315-22.
41. Teshale EH. Hepatitis B. CDC Yellow Book. Accessed via <http://wwwnc.cdc.gov/travel/yellowbook/2012/chapter-3-infectious-diseases-related-to-travel/hepatitis-b.htm> on August 29, 2011.

42. Vellozzi C, Buchacz K, Baker R, et al; HOPS Investigators. Treatment of hepatitis C virus (HCV) infection in patients coinfected with HIV in the HIV Outpatient Study (HOPS), 1999-2007. J Viral Hepat. 2011 May;18(5):316-24. doi: 10.1111/j.1365-2893.2010.01299.x.
43. Vezali E, Aghemo A, Colombo M. A review of the treatment of chronic hepatitis C virus infection in cirrhosis. Clin Ther. 2010 Dec;32(13):2117-38. Review.
44. Vezali E, Aghemo A, Colombo M. Interferon in the treatment of chronic hepatitis C: a drug caught between past and future. Expert Opin Biol Ther. 2011 Mar;11(3):301-13.
45. Wakim-Fleming J. Hepatic encephalopathy: Suspect it early in patients with cirrhosis. Cleveland Clinic Journal of Medicine 2011; 78(9):597-605.
46. Zeuzem S, Andreone P, Pol S, et al; **REALIZE** Study Team. **Telaprevir** for retreatment of HCV infection**.** N Engl J Med. 2011 Jun 23;364(25):2417-28.
47. Sherman KE, Flamm SL, Afdhal NH, et al. **ILLUMINATE** Study Team. Response-guided **telaprevir** combination treatment for hepatitis C virus infection. N Engl J Med. 2011 Sep 15;365(11):1014-24.
48. Di Bisceglie AM, Stoddard AM, Dienstag JL, et al. **HALT-C** Trial Group. Excess mortality in patients with advanced chronic hepatitis C treated with long-term peginterferon. Hepatology. 2011 Apr;53(4):1100-8. doi:10.1002/hep.24169.
49. Morgan TR, Ghany MG, Kim HY, et al. **HALT-C** Trial Group. Outcome of sustained virological responders with histologically advanced chronic hepatitis C. Hepatology. 2010 Sep;52(3):833-44.
50. Di Bisceglie AM, Shiffman ML, Everson GT, et al. **HALT-C** Trial Investigators. Prolonged therapy of advanced chronic hepatitis C with low-dose peginterferon. N Engl J Med. 2008 Dec 4;359(23):2429-41.
51. Foote BS, Spooner LM, Belliveau PP. **Boceprevir**: a protease inhibitor for the treatment of chronic hepatitis C. Ann Pharmacother. 2011 Sep;45(9):1085-93.
52. Rowe IA, Mutimer DJ. **Protease inhibitors** for treatment of genotype 1 hepatitis C virus infection. BMJ. 2011 Nov 10;343:d6972. doi: 10.1136/bmj.d6972.
53. Lok AS et al. Preliminary study of two antiviral agents for hepatitis C genotype 1. N Engl J Med 2012 Jan 19; 366:216. (60 mg daily of daclatasvir (an NS5A replication complex inhibitor) and 600 mg twice daily of asunaprevir (an NS3 protease inhibitor)).
54. FDA Feb/12 notified healthcare professionals and patients that drug interactions between the hepatitis C virus (HCV) protease inhibitor Victrelis (**boceprevir**) and certain **ritonavir-boosted** human immunodeficiency virus (HIV) protease inhibitors (atazanavir, lopinavir, darunavir) can potentially reduce the effectiveness of these medicines when they are used together.
55. Centers for Disease Control and Prevention (CDC). Transmission of hepatitis C virus through **transplanted organs and tissue**--Kentucky and Massachusetts, 2011. MMWR Morb Mortal Wkly Rep. 2011 Dec 23;60(50):1697-700.
56. FDA Mar/12 notified healthcare professionals of updates to the prescribing information concerning interactions between protease inhibitors (HIV & HCV) and certain **statin drugs**. Protease inhibitors and statins taken together may raise the blood levels of statins and increase the risk for muscle injury (myopathy/ rhabdomyolysis).
57. Alkhouri N, Zein NN. **Protease inhibitors**: Silver bullets for chronic hepatitis C infection? Cleve Clin J Med. 2012 Mar;79(3):213-22.
58. Ly KN, Xing J, Klevens RM et al. The increasing burden of **mortality** from viral **hepatitis** (**esp C**) in the United States between 1999 and 2007. Ann Intern Med. 2012 Feb 21;156(4):271-8.
59. Liu S, Cipriano LE, Holodniy M, Owens et al. New **protease inhibitors** for the treatment of chronic hepatitis C: a **cost-effectiveness** analysis. Ann Intern Med. 2012 Feb 21;156(4):279-90.
60. Rein DB, Smith BD, Wittenborn JS, et al. The cost-effectiveness of **birth-cohort screening** for hepatitis C antibody in U.S. primary care settings. Ann Intern Med. 2012;156:263-70.
61. Hoofnagle JH, Seeff LB. **Peginterferon and ribavirin** for chronic hepatitis C. N Engl J Med. 2006;355:2444-51.
62. Hadigan C, Kottilil S. **Hepatitis C** virus infection **and** coinfection with **human immunodeficiency virus (HIV)**: challenges and advancements in management. JAMA. 2011 Jul 20;306(3):294-301.
63. Sterling RK, Wright EC, et al. Frequency of elevated hepatocellular carcinoma-HCC **biomarkers** (AFP-fetoprotein) in patients with advanced hepatitis C. Am J Gastroenterol. 2012 Jan;107(1):64-74.
64. FDA notified healthcare professionals that the Victrelis drug label has been revised to state that co-administration of Victrelis (**boceprevir**), a hepatitis C virus (HCV) protease inhibitor, along with certain **ritonavir**-boosted human immunodeficiency virus (HIV) protease inhibitors, is not recommended. The findings of a drug-drug interaction study and clinical trial showed that co-administration increased of the possibility of reducing the effectiveness of the medicines, permitting the amount of HCV or HIV virus in the blood to increase. Ritonavir-boosted HIV protease inhibitors include ritonavir-boosted Reyataz (atazanavir), ritonavir-boosted Prezista (darunavir), and Kaletra (lopinavir/ritonavir).
65. Spaulding AC, Thomas DL. **Screening for HCV infection in jails**. JAMA. 2012 Mar 28;307(12):1259-60.
66. McGilvray I, et al. **Hepatic Cell-Type Specific Gene Expression** Better Predicts HCV Treatment Outcome Than **IL28B Genotype**. Gastroenterology. 2012 May;142(5):1122-1131.e1.
67. Levitsky J, Fiel MI, Norvell JP, et al. Risk for immune-mediated **graft dysfunction in liver transplant** recipients with recurrent HCV infection treated with pegylated interferon. Gastroenterology. 2012 May;142(5):1132-1139.e1.
68. El-Serag HB. Epidemiology of viral hepatitis and **hepatocellular carcinoma (HCC)**. Gastroenterology. 2012 May;142(6):1264-1273.e1.
69. Naggie S, et al. Management of Patients **Coinfected With HCV and HIV**: A Close Look at the Role for Direct-Acting Antivirals. Gastroenterology. 2012 May;142(6):1324-1334.e3.
70. Crespo G, Mariño Z, Navasa M, Forns X. Viral hepatitis in **liver transplantation**. Gastroenterology. 2012 May;142(6):1373-1383.e1.
71. Grebely J, Prins M, Hellard M, et al. on behalf of the International Collaboration of Incident HIV and Hepatitis C in Injecting Cohorts (InC(3)). Hepatitis C virus clearance, reinfection, and persistence, with insights from studies of **injecting drug users**: towards a vaccine. Lancet Infect Dis. 2012 May;12(5):408-414.
72. CDC: All baby boomers should be tested for hepatitis C, according to draft guidelines proposed by the CDC. The CDC estimates that 1 in 30 boomers, those born from 1945 through 1965, is infected with hepatitis C and most are unaware of their infection status. http://www.cdc.gov/nchhstp/newsroom/HepTestingRecsPressRelease2012.html
73. Coffin PO, Scott JD, Golden MR, Sullivan SD. Cost-effectiveness and population outcomes of **general population screening for hepatitis C**. Clin Infect Dis. 2012 May;54(9):1259-71.
74. Pearlman BL. **Protease inhibitors** for the treatment of chronic hepatitis C genotype-1 infection: the new standard of care. Lancet Infect Dis. 2012 May 28.
75. Pol S, Ghalib RH, Rustgi VK, et al. **Daclatasvir** for previously untreated chronic hepatitis C genotype-1 infection: a randomised, parallel-group, double-blind, placebo-controlled, dose-finding, phase 2a trial. Lancet Inf Dis 2012.
76. Lok A, Gardiner D, Hézode C, et al. Confirmation that quadruple therapy with **daclatasvir** (NS5A inhibitor), **asunaprevir** (NS3 inhibitor) and peginterferon/ribavirin results in a high rate of SVR4 in HCV genotype 1 null responders. J Hepatol 2012; 56 (suppl 2): S557.
77. Suzuki F, Ikeda K, Toyota J, et al. Dual oral therapy with the NS5A inhibitor **daclatasvir** (BMS-790052) and NS3 protease inhibitor **asunaprevir** (BMS-650032) in HCV genotype 1b-I infected null responders or ineligible/ intolerant to peginterferon/ribavirin. J Hepatol 2012; 56 (suppl 2): S7–S8.
78. Clark PJ, Muir AJ. Overcoming barriers to care for hepatitis C. N Engl J Med. 2012 Jun 28;366(26):2436-8.
79. Rumi M, Aghemo A, Prati GM. Comparative trials of **peginterferon α2a and peginterferon α2b** for chronic hepatitis C. J Viral Hepat. 2012 Jan;19 Suppl 1:37-41.
80. Brennan BJ, Xu ZX, Grippo J. Effect of **peginterferon alfa-2a** (40KD) on cytochrome P450 isoenzyme activity. Br J Clin Pharmacol. 2012 Jul 6.
81. Centers for Disease Control and Prevention. Updated recommendations on managing **HBV-infected** providers, students.. MMWR 2012;61(No. RR-3):pg1-10.
82. Pol S, Ghalib RH, Rustgi VK, et al. Daclatasvir for previously untreated chronic hepatitis C genotype-1 infection:a randomised, parallel-group, double-blind, placebo-controlled, dose-finding,phase 2a trial. Lancet Infect Dis. 2012 Jun 15.
83. Welzel TM, Zeuzem S. **NS5A inhibitors** to treat hepatitis C virus infection. Lancet Infect Dis. 2012 Jun 15.
84. Limketkai BN, Mehta SH, Sutcliffe CG, et al. Relationship of **liver disease stage** and antiviral therapy with liver-related events and death in adults **coinfected with HIV/HCV**. JAMA. 2012 Jul 25;308(4):370-8.

85. Schaefer M, Sarkar R, Knop V, et al. **Escitalopram** for the Prevention of Peginterferon-α2a-Associated Depression in Hepatitis C Virus-Infected Patients Without Previous Psychiatric Disease: A Randomized Trial. Ann Intern Med. 2012 Jul 17;157(2):94-103.
Ehret M, Sobieraj DM. Prevention of interferon-alpha-associated depression with antidepressant medications in patients with hepatitis C virus: a systematic review and meta-analysis. Int J Clin Pract. 2014 Feb;68(2):255-61.
86. Ghany MG, Nelson DR, Strader DB, Thomas DL, Seeff LB, American Association for Study of Liver Diseases (**AASLD**). An update on treatment of **genotype 1 chronic hepatitis C** virus infection: 2011 practice guideline by the American Association for the Study of Liver Diseases. Hepatology 2011 Oct;54(4):1433-44.
87. CDC Aug/12 is recommending one-time testing for hepatitis C in patients born between **1945 and 1965**, regardless of the patients' risk for hepatitis, according to finalized guidelines in *MMWR*.
88. Poordad F, Bronowicki JP, Gordon SC, et al; SPRINT-2 and RESPOND-2 Investigators. Factors that predict response of patients with hepatitis C virus infection to **boceprevir**. Gastroenterology. 2012 Sep;143(3):608-618.e5.
89. Smith BD, Morgan RL, Beckett GA, Falck-Ytter Y, Holtzman D, Ward JW. Hepatitis C Virus **Testing of Persons Born During 1945 to 1965**: Recommendations From the Centers for Disease Control and Prevention. Ann Intern Med. 2012 Aug 16.
90. National Institute for Health and Clinical Excellence (NICE). **Telaprevir** for the treatment of genotype 1 chronic hepatitis C. London (UK): 2012 Apr.
91. National Institute for Health and Clinical Excellence (NICE). **Boceprevir** for the treatment of genotype 1 chronic hepatitis C. London (UK): 2012 Apr.
92. Matthews SJ, Lancaster JW. **Telaprevir**: A Hepatitis C NS3/4A Protease Inhibitor. Clin Ther. 2012 Aug 27.
93. Rocco A, Compare D, Coccoli P, et al. **Vitamin B12** supplementation improves rates of sustained viral response in patients chronically infected with hepatitis C virus. Gut. 2012 Jul 17.
94. Chang M, Gordon L, and Fung H. **Boceprevir**: a Protease Inhibitor for the treatment of Hepatitis C. Clin Ther 2012; Aug 17
95. Falade-Nwulia O et al. Comparative risk of **liver-related mortality** from chronic **hepatitis B versus chronic hepatitis C virus** infection. Clin Infect Dis 2012 Aug 15; 55:507.
96. Furusyo N, Ogawa E, Sudoh M, et al. **Raloxifene** hydrochloride is an adjuvant antiviral treatment of postmenopausal women with chronic hepatitis C: A randomized trial. J Hepatol. 2012 Aug 10.
97. Bachmeyer C, Pellen JC. **Tongue hyperpigmentation** during hepatitis C treatment (interferon & ribavirin). CMAJ. 2012 Sep 18;184(13):1498.
98. Deuffic-Burban S, Deltenre P, Buti M, et al. Predicted effects of treatment for HCV infection vary among **European countries**. Gastroenterology. 2012 Oct;143(4):974-985.e14.
99. Shivkumar S, Peeling R, Jafari Y, et al. Accuracy of **Rapid and Point-of-Care Screening** Tests for Hepatitis C: Systematic Review & Meta-analysis. Ann Intern Med. 2012 Oct 16;157(8):558-66.
100. Kimer N, Dahl EK, Gluud LL, Krag A. Antiviral therapy for **prevention of hepatocellular carcinoma** (HCC) in chronic hepatitis C: systematic review and meta-analysis of randomised controlled trials. BMJ Open. 2012 Oct 22;2(5).
101. Delgado-Borrego A, Smith L, Jonas MM, et al. Expected and Actual Case Ascertainment and Treatment Rates for Children Infected with Hepatitis C in Florida and the United States: Epidemiologic Evidence from Statewide and Nationwide Surveys. J Pediatr. 2012 Jul 3.
102. Chou R, Cottrell EB, Wasson N, et al. **Screening for Hepatitis C Virus** Infection in Adults: A Systematic Review to Update the 2004 U.S. Preventive Services Task Force Recommendation. (**USPSTF**) Ann Intern Med. 2012 Nov 27.
103. FDA Dec/12received reports of **serious skin reactions**, some fatal, in patients taking the hepatitis C drug **Incivek** (**telaprevir**) in combination with the drugs peginterferon alfa and ribavirin (Incivek combination treatment).
104. Druyts E, Thorlund K, Wu P, et al. Efficacy and Safety of **Pegylated Interferon** Alfa-2a or Alfa-2b Plus **Ribavirin** for the Treatment of Chronic Hepatitis C in **Children and Adolescents**: A Systematic Review and Meta-analysis. Clin Infect Dis. 2012 Dec 27.
105. Poordad F, Lawitz E, Kowdley KV, et al. Exploratory study of oral combination (**ABT-450/r + ABT-333 + ribavirin**) antiviral therapy for hepatitis C. N Engl J Med. 2013 Jan 3;368(1):45-53.
106. Gane EJ, Stedman CA, Hyland RH, et al. Nucleotide polymerase inhibitor **sofosbuvir** plus ribavirin for hepatitis C. N Engl J Med. 2013 Jan 3;368(1):34-44.
107. van der Meer AJ, Veldt BJ, Feld JJ, et al. Association between sustained virological response and all-cause mortality among patients with chronic hepatitis C and advanced **hepatic fibrosis**. JAMA. 2012 Dec 26;308(24):2584-93.
108. Terrier B, Karras A, Cluzel P, et al. Presentation and Prognosis of **Cardiac Involvement** in Hepatitis C Virus-Related Vasculitis. Am J Cardiol. 2012 Oct 29.
109. Mack CL, Gonzalez-Peralta RP, Gupta N, Leung D, Narkewicz MR, Roberts EA, Rosenthal P, Schwarz KB. **NASPGHAN** practice guidelines: diagnosis and management of hepatitis C infection in **infants, children, and adolescents**. J Pediatr Gastroenterol Nutr 2012 Jun;54(6):838-55.
110. Koretz RL, Pleguezuelo M, Arvaniti V, et al. **Interferon for interferon nonresponding and relapsing** patients with chronic hepatitis C. Cochrane Database of Systematic Reviews 2013, Issue 1. Art. No.: CD003617. DOI: 10.1002/14651858.CD003617.pub2. The clinical data were limited to patients with histologic evidence of severe fibrosis who were retreated with pegylated interferon. In this scenario, retreatment with interferon did not appear to provide significant clinical benefit and, when only the trials at low risk of bias were considered, retreatment for several years may even have increased all-cause mortality.
111. Health Canada Feb/13 IncivekTM (**telaprevir**) Combination Treatment - Serious Skin Reactions Reported - Vertex Pharmaceuticals (Canada) Incorporated.
112. Chou R, Hartung D, Rahman B, et al. Treatment for Hepatitis C Virus Infection in Adults [Internet]. Rockville (MD): Agency for Healthcare Research and Quality (US); 2012 Nov. Available from http://www.ncbi.nlm.nih.gov/books/NBK115347/
113. Sitole M, Silva M, Spooner L, et al. Telaprevir Versus Boceprevir in Chronic Hepatitis C: A Meta-Analysis of Data From Phase II and III Trials. Clin Ther. 2013 Jan 29.
114. World Health Organization. Guidance on prevention of viral hepatitis B and C among people who inject drugs. Geneva (Switzerland): World Health Organization (WHO); 2012.
115. Duggal P, et al. Genome-wide association study of spontaneous resolution of hepatitis C virus infection: data from multiple cohorts. Ann Intern Med. 2013 Feb 19;158(4):235-45. (iL-28B & DQB1*03:01)
116. Roujeau JC, Mockenhaupt M, Tahan SR, et al. Telaprevir-Related Dermatitis. Arch Dermatol. 2012 Nov 19:1-7.
117. Cottrell EB, Chou R, et al. Reducing risk for mother-to-infant transmission of hepatitis C virus: a systematic review for the U.S. Preventive Services Task Force. (USPSTF) Ann Intern Med. 2013 Jan 15;158(2):109-13.
118. Morgan RL, Baack B, Smith BD, et al. Eradication of Hepatitis C Virus Infection and the Development of Hepatocellular Carcinoma (HCC): A Meta-analysis of Observational Studies. Ann Intern Med. 2013 Mar 5;158(5 Pt 1):329-37.
119. Kirk GD, Mehta SH, Astemborski J, et al. HIV, Age, and the Severity of Hepatitis C Virus-Related Liver Disease: A Cohort Study. Ann Intern Med. 2013 Feb 26.
120. Lawitz E, Lalezari JP, Hassanein T, et al. Sofosbuvir in combination with peginterferon alfa-2a and ribavirin for non-cirrhotic, treatment-naïve patients with genotypes 1, 2, and 3 hepatitis C infection: a randomised, double-blind, phase 2 trial. Lancet Infect Dis 2013; online March 15.
121. Kowdley KV, Lawitz E, Crespo I, et al. Sofosbuvir with peginterferon alfa-2a and ribavirin for treatment-naive patients with hepatitis C genotype-1 infection (ATOMIC): an open-label, randomised, multicentre phase 2 trial. Lancet 2013; online March 15.
122. Chou R, Hartung D, Rahman B, Wasson N, Cottrell EB, Fu R. Comparative effectiveness of antiviral treatment for hepatitis C virus infection in adults: a systematic review. Ann Intern Med. 2013 Jan 15;158(2):114-23.

123. Deterding K, Grüner N, Buggisch P, et al, for The Hep-Net Acute HCV-III Study Group. Delayed versus immediate treatment for patients with acute hepatitis C: a randomised controlled non-inferiority trial. Lancet Infect Dis 2013; online March 22.
124. Janssen HLA, Reesink HW, Lawitz EJ, et al. Treatment of HCV infection by targeting microRNA. N Engl J Med 2013. DOI: 10.1056/NEJMoa1209026.
125. Jacobson IM, Gordon SC, Kowdley KV, et al. Sofosbuvir for hepatitis C genotype 2 or 3 in patients without treatment options. (POSITRON and FUSION) N Engl J Med 2013.
126. Lawitz E, Mangia A, Wyles D, et al. Sofosbuvir for previously untreated chronic hepatitis C infection. (FISSION and NEUTRINO) N Engl J Med 2013. DOI:10.1056/NEJMoa1214853.
127. Sulkowski M, Pol S, Mallolas J, et al, for the P05411 study investigators. Boceprevir versus placebo with pegylated interferon alfa-2b and ribavirin for treatment of hepatitis C virus genotype 1 in patients with HIV: a randomised, double-blind, controlled phase 2 trial. Lancet Infect Dis 2013; online June 12.
128. Sulkowski MS, Sherman KE, Dieterich DT, et al. Combination therapy with telaprevir for chronic hepatitis c virus genotype 1 infection in patients with HIV: a randomized trial. Ann Intern Med 2013; online May 17.
129. Chou R, Wasson N. Blood tests to diagnose fibrosis or cirrhosis in patients with chronic hepatitis C virus infection: a systematic review. Ann Intern Med. 2013 Jun 4;158(11):807-20.
130. Liang TJ, Ghany MG. Current and future therapies for hepatitis C virus infection. N Engl J Med. 2013 May 16;368(20):1907-17.
131. NICE: National Institute for Health and Care Excellence. Hepatitis B and C: ways to promote and offer testing to people at increased risk of infection. (Public health guideline 43.) 2012. http://guidance.nice.org.uk/PH43.
132. Smith BD, Morgan RL, Beckett GA, et al. CDC: Centers for Disease Control and Prevention. Recommendations for the identification of chronic hepatitis C virus infection among persons born during 1945-1965. MMWR Recomm Rep. 2012 Aug 17;61(RR-4):1-32.
133. Holmberg SD, Spradling PR, Moorman AC, Denniston MM. Hepatitis C in the United States. N Engl J Med. 2013;368:1859-61.
134. Moyer VA, on behalf of the U.S. Preventive Services Task Force (USPSTF). Screening for hepatitis C virus infection in adults: U.S. Preventive Services Task Force recommendation statement. Ann Intern Med. 2013.
135. Slayter K. Hepatitis C: new antivirals are helping move toward erradication. Pharmacy Practice. October 2012; 41-52.
136. van der Helm J, Geskus R, Sabin C, et al; CASCADE Collaboration in EuroCoord. Effect of HCV Infection on Cause-Specific Mortality After HIV Seroconversion, Before and After 1997. Gastroenterology. 2013 Apr;144(4):751-760.e2.
137. Zeuzem S et al. **Faldaprevir and deleobuvir** for HCV genotype 1 infection. N Engl J Med 2013 Aug 15; 369:630.
138. Indolfi G, Azzari C, Resti M. **Perinatal Transmission** of Hepatitis C Virus. J Pediatr. 2013 Aug 3.
139. Asrani SK, Larson JJ, Yawn B, et al. **Underestimation of liver-related mortality** in the United States. Gastroenterology. 2013 Aug;145(2):375-382.e2.
140. Chou R, Wasson N. **Blood tests to diagnose fibrosis or cirrhosis** in patients with chronic hepatitis C virus infection: a systematic review. Ann Intern Med. 2013 Jun 4;158(11):807-20.
141. Dammacco F, Sansonno D. Therapy for hepatitis C virus-related **cryoglobulinemicvasculitis**. N Engl J Med. 2013 Sep 12;369(11):1035-45.
142. Osinusi A, Meissner EG, Lee YJ, et al. **Sofosbuvir** and ribavirin for hepatitis C genotype 1 in patients with unfavorable treatment characteristics: a randomized clinical trial. JAMA. 2013 Aug 28;310(8):804-11.
143. FDA Oct/13 along with the Centers for Disease Control and Prevention (CDC) and the Hawaii Department of Health (DOH), are investigating a growing number of reports of acute non-viral hepatitis in Hawaii. The Hawaii DOH has reported that 24 of these cases share a common link to a dietary supplement product labeled as **OxyElite Pro**.
144. Marcellin P, Cooper C, Balart L, et al. Randomized controlled trial of danoprevir plus peginterferon alfa-2a and ribavirin in treatment-naïve patients with hepatitis C virus genotype 1 infection. Gastroenterology. 2013 Oct;145(4):790-800.e3.
145. McCombs J, Matsuda T, Tonnu-Mihara I, et al. The Risk of **Long-term Morbidity and Mortality in Patients With Chronic Hepatitis C**: Results From an Analysis of Data From a Department of Veterans Affairs Clinical Registry. JAMA Intern Med. 2013 Nov 5.
146. Lawitz E, Poordad FF, Pang PS, et al. **Sofosbuvir and ledipasvir** fixed-dose combination with and without ribavirin in treatment-naive and previously treated patients with genotype 1 hepatitis C virus infection (**LONESTAR**): an open-label, randomised, phase 2 trial. Lancet 2013; online Nov 5.
147. Poordad F, Lawitz E, Reddy KR, et al. Effects of **ribavirin dose reduction vs erythropoietin for boceprevir-related anemia** in patients with chronic Hepatitis C Virus genotype 1 infection—a randomized trial. Gastroenterology 2013;145:1035–1044
148. Koziel MJ, Peters MG. Viral hepatitis in **HIV infection**. N Engl J Med 2007;356:1445-1454.
Wang Q, De Luca A, Smith C, et al; The Hepatitis Coinfection and Non Hodgkin Lymphoma project team for the Collaboration of Observational HIV Epidemiological Research Europe (COHERE) in EuroCoord. **Chronic hepatitis B and C virus infection and risk for non-Hodgkin lymphoma in HIV infected patients**. A cohort study. Ann Intern Med. 2016. [Epub ahead of print]. doi:10.7326/M16-0240
149. Kim AY, Wu RI. Case records of the Massachusetts General Hospital. **Case** 37-2013. A 41-year-old woman with malaise and chest and abdominal pain. N Engl J Med. 2013 Nov 28;369(22):2138-45. (Hepatitis C)
150. Liu CH, Huang CF, Liu CJ, et al. **Pegylated Interferon-α2a With or Without Low-Dose Ribavirin** for Treatment-Naive Patients With Hepatitis C Virus Genotype 1 Receiving **Hemodialysis**: A Randomized Trial. Ann Intern Med. 2013 Dec 3;159(11):729-38.
151. Shah HA, Heathcote J, Feld JJ. A **Canadian screening** program for hepatitis C: Is now the time? CMAJ. 2013 Sep 30.
152. Au JS, Pockros PJ. **Novel therapeutic** approaches for hepatitis C. Clin Pharmacol Ther. 2013 Jan;95(1):78-88
153. Sulkowski MS et al. **Daclatasvir plus sofosbuvir** for previously treated or untreated chronic HCV infection. N Engl J Med 2014 Jan 16; 370:211.
154. Kowdley KV et al. Phase 2b trial of **interferon-free** therapy (ABT-450, ABT-333, ABT-267) for hepatitis C virus genotype 1. N Engl J Med 2014 Jan 16; 370:222.
155. Sulkowski M, Pol S, Mallolas J, et al; P05411 study investigators. **Boceprevir versus placebo with pegylated interferon alfa-2b and ribavirin** for treatment of hepatitis C virus genotype 1 in patients with **HIV**: a randomised, double-blind, controlled phase 2 trial. Lancet Infect Dis. 2013 Jul;13(7):597-605
156. Afdhal NH, Dusheiko GM, Giannini EG, et al. **Eltrombopag** increases **platelet** numbers in thrombocytopenic patients with HCV infection and cirrhosis, allowing for effective antiviral therapy. Gastroenterology. 2014 Feb;146(2):442-452.
157. Zeuzem S, Berg T, Gane E, et al. **Simeprevir** increases rate of sustained virologic response among treatment-experienced patients with HCV genotype-1 infection: a phase IIb trial. Gastroenterology. 2014 Feb;146(2):430-441
158. Everson GT, Sims KD, Rodriguez-Torres M, et al. Efficacy of an Interferon- and Ribavirin-Free Regimen of **Daclatasvir, Asunaprevir, and BMS-791325** in Treatment-Naive Patients With HCV Genotype 1 Infection. Gastroenterology. 2014 Feb;146(2):420-9
159. Hauser G, Awad T, Thorlund K, et al. **Peginterferon alpha-2a versus peginterferon alpha-2b** for chronic hepatitis C. Cochrane Database of Systematic Reviews 2014, Issue 2. Art. No.: CD005642. DOI:10.1002/14651858.CD005642.pub3. There is lack of evidence on patient-important outcomes and paucity of evidence on adverse events.Moderate quality evidence suggests that peginterferon alpha-2a is associated with a higher sustained virological response in serum than with peginterferon alpha-2b.

160. Gane EJ, Stedman CA, Hyland RH, et al. Efficacy of Nucleotide Polymerase Inhibitor **Sofosbuvir** Plus the NS5A Inhibitor **Ledipasvir** or the NS5B Non-Nucleoside Inhibitor GS-9669 Against HCV Genotype 1 Infection. Gastroenterology. 2014 Mar;146(3):736-743.
161. Buti M, Agarwal K, Horsmans Y, et al. **Telaprevir twice daily** is noninferior to telaprevir every 8 hours for patients with chronic hepatitis C. Gastroenterology. 2014 Mar;146(3):744-753.
162. Scottish Intercollegiate Guidelines Network (**SIGN**). **Management of hepatitis C**. A national clinical guideline. Edinburgh (Scotland): Scottish Intercollegiate Guidelines Network (SIGN); 2013 Jul.
163. Dugum M, O'Shea R. Hepatitis C virus: here comes **all oral treatment**. Cleve Clin J Med 2014; 81:159–172.
164. ***CIHR Canadian HIV*** *Trials Network HIV/Hepatitis C Management and Treatment Guidelines Working Group.* ***Canadian guidelines*** *for management and treatment of* ***HIV/hepatitis C coinfection*** *in adults (2013). www.pulsus.com/pdfs/15871_hull.pdf (accessed January 10, 2014).*
Hull M, Shafran S, Tseng A, et al. CIHR Canadian HIV Trials Network Co-Infection and Concurrent Diseases Core: Updated Canadian guidelines for the treatment of hepatitis C infection in HIV-hepatitis C coinfected adults. Can J Infect Dis Med Microbiol. 2014 Nov-Dec;25(6):311-20.
165. National Institute for Health and Care Excellence (NICE). **Peginterferon alfa and ribavirin** for treating chronic **hepatitis C in children and young people**. London (UK): National Institute for Health and Care Excellence (**NICE**); 2013 Nov.
166. Ehret M, Sobieraj DM. Prevention of **interferon-alpha-associated depression with antidepressant medications** (SSRIs) in patients with hepatitis C virus: a systematic review and meta-analysis. Int J Clin Pract. 2014 Feb;68(2):255-61.
167. Afdhal N, Zeuzem S, Kwo P, et al. Ledipasvir and sofosbuvir for untreated HCV genotype 1 infection. N Engl J Med. DOI:10.1056/NEJMoa1402454.
168. El-Serag HB, Kanwal F, Davila JA, et al. A new laboratory-based **algorithm to predict development of hepatocellular carcinoma** in patients with hepatitis C and cirrhosis. Gastroenterology. 2014 May;146(5):1249-1255.
169. Feld JJ, Kowdley KV, Coakley E, et al. Treatment of HCV with **ABT-450/r-Ombitasvir and Dasabuvir with Ribavirin**. N Engl J Med. 2014 Apr 10.
170. Kowdley KV, Gordon SC, Reddy KR, et al. **Ledipasvir and sofosbuvir** for 8 or 12 weeks for chronic HCV without cirrhosis. N Engl J Med. DOI: 10.1056/NEJMoa1402355.
171. Pawlotsky JM. **New Hepatitis C Therapies**: The Toolbox, Strategies, and Challenges. Gastroenterology. 2014 May;146(5):1176-1192.
172. Poordad F, Hezode C, Trinh R, et al. **ABT-450/r-Ombitasvir and Dasabuvir with Ribavirin** for Hepatitis C with **Cirrhosis**. (**Turquoise-II**) N Engl J Med. 2014 Apr 11.
173. Saadoun D, Resche Rigon M, Thibault V, et al. Peg-IFNα/ribavirin/protease inhibitor combination in **hepatitis C virus associated mixed cryoglobulinemia vasculitis**: results at week 24. Ann Rheum Dis. 2014 May 1;73(5):831-7.
174. Strazzula L, Pratt DS, Zardas J, et al. Widespread **Morbilliform Eruption** Associated With **Telaprevir**: Use of Dermatologic Consultation to Increase Tolerability. JAMA Dermatol. 2014 Apr 9.
175. Wei L, Lok AS. Impact of **new** hepatitis C treatments in **different regions of the world**. Gastroenterology. 2014 May;146(5):1145-1150.
176. Zeuzem S, Jacobson IM, Baykal T, et al. Retreatment of HCV with **ABT-450/r-Ombitasvir and Dasabuvir with Ribavirin**. N Engl J Med. 2014 Apr 10.
177. Ferenci P, Bernstein D, Lalezari J, et al. **ABT-450/r–ombitasvir and dasabuvir** with or without **ribavirin** for HCV. (Pearl III-IV) N Engl J Med. DOI: 10.1056/NEJMoa1402338.
178. Zeuzem S, Dusheiko GM, Salupere R, et al. **Sofosbuvir** and **ribavirin** in HCV genotypes 2 and 3. (**Valence**) N Engl J Med. DOI: 10.1056/ NEJMoa1316145.
179. Forns X, Lawitz E, Zeuzem S, et al. **Simeprevir With Peginterferon and Ribavirin** Leads to High Rates of SVR in Patients With HCV Genotype 1 Who Relapsed After Previous Therapy: A Phase 3 Trial. Gastroenterology. 2014 Mar 3.
180. Hezode C, Fontaine H, Dorival C, et al; the cupic study group. Effectiveness of **Telaprevir or Boceprevir** in Treatment-experienced Patients with HCV Genotype 1 Infection and **Cirrhosis**. Gastroenterology. 2014 Apr 3.
181. Denniston MM, Jiles RB, Drobeniuc J, et al. **Chronic hepatitis C virus infection in the United States**, National Health and Nutrition Examination Survey 2003 to 2010. Ann Intern Med. 2014 Mar 4;160(5):293-300.
182. Lo Re V 3rd, Kallan MJ, Tate JP, et al. **Hepatic Decompensation** in Antiretroviral-Treated Patients Co-Infected With **HIV and Hepatitis C** Virus Compared With Hepatitis C Virus-Monoinfected Patients: A Cohort Study. Ann Intern Med. 2014 Mar 18;160(6).
183. Lim JK, Tate JP, Fultz SL, et al. Relationship Between **Alcohol** Use Categories and Noninvasive Markers of Advanced Hepatic Fibrosis in **HIV-Infected, Chronic Hepatitis C** Virus-Infected, and Uninfected Patients. Clin Infect Dis. 2014 May;58(10):1449-58.
184. Jacobson IM, Dore GJ, Foster GR, et al. **Simeprevir with pegylated interferon alfa 2a plus ribavirin** in treatment-naive patients with chronic hepatitis C virus genotype 1 infection (**QUEST-1**): a phase 3, randomised, double-blind, placebo-controlled trial. Lancet. 2014 Jun 3. pii: S0140-6736(14)60494-3.
185. Johnson M, Borland J, Chen S, et al. Effects of **boceprevir and telaprevir** on the pharmacokinetics of **dolutegravir**. Br J Clin Pharmacol. 2014 May 16.
186. Manns M, Marcellin P, Poordad F, et al. **Simeprevir with pegylated interferon alfa 2a or 2b plus ribavirin** in treatment-naive patients with chronic hepatitis C virus genotype 1 infection (**QUEST-2):** a randomised, double-blind, placebo-controlled phase 3 trial. Lancet 2014; online June 4.
187. Rich JD, Allen SA, Williams BA. Responding to hepatitis C through the **criminal justice system**. N Engl J Med. 2014 May 15;370(20):1871-4.
188. van der Meer AJ, Hansen BE, Fattovich G, et al. Reliable prediction of clinical outcome in patients with **chronic HCV infection and compensated advanced hepatic fibrosis**: a validated model using objective and readily available clinical parameters. Gut. 2014 May 9.
189. Abdel-Hady M, Bansal S, Davison SM, et al. Treatment of chronic viral **hepatitis C in children and adolescents**: UK experience. Arch Dis Child. 2014 Jun;99(6):505-10.
190. Aronsohn A, Reau N, Jensen D. Preparing for the uncertain yet inevitable: **off-label combinations of antiviral agents in hepatitis C** virus. Hepatology. 2014 May;59(5):1688-91.
191. Young J, Potter M, Cox J, et al. Variation between Canadian centres in the **uptake of treatment for hepatitis C by patients coinfected with HIV**: a prospective cohort study. Canadian Medical Association Open Access Journal 1.3 (2013): E106-E114.
192. Feeney ER, Chung RT. **Antiviral treatment of hepatitis C**. BMJ. 2014 Jul 7;349:g3308.
193. Hull M, Klein M, Shafran S, et al. **CIHR Canadian HIV Trials Network Coinfection** and Concurrent Diseases Core: Canadian guidelines for management and treatment of **HIV/hepatitis C coinfection** in adults. Can J Infect Dis Med Microbiol. 2013 Winter;24(4):217-38
194. Konerman MA, Lok AS. **Diagnostic challenges of hepatitis C**. JAMA. 2014 Jun 25;311(24):2536-7.
195. Ollendorf DA, Tice JA, Pearson SD. The comparative clinical effectiveness and value of **simeprevir and sofosbuvir** for chronic hepatitis C virus infection. JAMA Intern Med. 2014 Jul 1;174(7):1170-1.
196. Kohli A, Shaffer A, Sheman A et a. **Treatment of Hepatitis C**-A Systematic Review. JAMA. 2014;312(6):631-640. doi:10.1001/jama.2014.7085.
197. Lawitz E, Sulkowski MS, Ghalib R, et al. **Simeprevir plus sofosbuvir**, **with or without ribavirin**, to treat chronic infection with hepatitis C virus genotype 1 in non-responders to pegylated interferon and ribavirin and treatment-naïve patients: the COSMOS randomised study. Lancet. 2014 Jul 26.
198. Manns M, Pol S, Jacobson IM, et al; on behalf of the **HALLMARK-DUAL** Study Team. All-oral **daclatasvir plus asunaprevir** for hepatitis C virus genotype 1b: a multinational, phase 3, multicohort study. Lancet. 2014 Jul 26.
199. Rose L, Bias TE, Mathias CB, et al. **Sofosbuvir**: A Nucleotide NS5B Inhibitor for the Treatment of Chronic Hepatitis C Infection. Ann Pharmacother. 2014 May 8;48(8):1019-1029.
200. Kabiri M, Jazwinski AB, Roberts MS, et al. The **changing burden** of hepatitis C virus infection in the United States: model-based predictions. Ann Intern Med. 2014 Aug 5;161(3):170-80.

201. Smith MA, Johnson HJ, Chopra KB, et al. Incidence and Management of **Rash in Telaprevir**-Treated Patients. Ann Pharmacother. 2014 Jun 17;48(9):1166-1171.
202. Sulkowski MS, Naggie S, Lalezari J, et al. **Sofosbuvir and ribavirin** for hepatitis C in patients with HIV coinfection. JAMA. doi:10.1001/jama.2014 .7734.
203. Ahmad T, Yin P, Saffitz J, et al. **Cardiac dysfunction** associated with a nucleotide polymerase inhibitor (**BMS-986094**) for treatment of hepatitis C. *Hepatology* 2014.
204. Hézode C, Hirschfield GM, Ghesquiere W, et al. **Daclatasvir plus peginterferon alfa and ribavirin** for treatment-naive chronic hepatitis C genotype 1 or 4 infection: a randomised study. Gut. 2014 Jul 30.
205. Muir AJ, Gong L, Johnson SG, Lee MT, Williams MS, Klein TE, Caudle KE, Nelson DR, Clinical Pharmacogenetics Implementation Consortium (CPIC). Clinical Pharmacogenetics Implementation Consortium (CPIC) guidelines for **IFNL3 (IL28B) genotype and PEG interferon-alpha-based regimens**. Clin Pharmacol Ther. 2014 Feb;95(2):141-6.
206. Rahimi RS, Singal AG, Cuthbert JA, Rockey DC. **Lactulose vs polyethylene glycol** 3350-electrolyte solution for treatment of overt hepatic encephalopathy: the HELP randomized clinical trial [online September 22, 2014]. JAMA Intern Med. doi:10.1001/jamainternmed.2014.4746.
207. Sugerman DT. JAMA **patient page. Hepatitis C**. JAMA. 2014 Aug 13;312(6):664.
208. Zhang F, Zhu H, Wu Y, et al. **HIV, hepatitis B virus, and hepatitis C virus co-infection** in patients in the China National Free Antiretroviral Treatment Program, 2010–12: a retrospective observational cohort study. Lancet Infect Dis 2014; onine Oct 8.
209. Jonas MM, Schwarz KB, Gonzalez-Peralta R, et al. **Long-Term Growth Outcomes in Children** Treated for Chronic Hepatitis C. J Pediatr. 2014 Sep 17.
210. Liu S, Watcha D, Holodniy M, et al. **Sofosbuvir**-based treatment regimens for chronic, genotype 1 hepatitis C virus infection in u.s. **Incarcerated populations**: a cost-effectiveness analysis. Ann Intern Med. 2014 Oct 21;161(8):546-53.
211. Pernet C, Pageaux GP, Guillot B, et al. **Telaprevir** Induced Acquired Perforating **Dermatosis**. JAMA Dermatol. 2014 Sep 24.
212. Schanzer DL, Paquette D, et al. **Historical trends and projected hospital admissions** for chronic hepatitis C infection in **Canada**: a birth cohort analysis. CMAJ Open. 2014 Jul 22;2(3):E139-44.
213. Sugerman DT. JAMA **patient page. Hepatitis C**. JAMA. 2014 Aug 13;312(6):664.
214. Kwo PY, Mantry PS, Coakley E, et al. An **Interferon-free Antiviral Regimen for HCV after Liver Transplantation**. N Engl J Med. 2014 Nov 11.
215. Tsui JI, Evans JL, et al. Association of **Opioid Agonist Therapy** With Lower Incidence of Hepatitis C Virus Infection in Young Adult **Injection Drug Users**. JAMA Intern Med. 2014 Oct 27.
216. van der Meer AJ, Wedemeyer H, et al. **Life Expectancy** in Patients With Chronic **HCV Infection** and **Cirrhosis** Compared With a General Population. JAMA. 2014 Nov 12;312(18):1927-1928.
217. Osinusi A, Kohli A, Marti MM, et al. **Re-treatment** of Chronic Hepatitis C Virus Genotype 1 Infection **After Relapse**: An Open-Label Pilot Study. Ann Intern Med. 2014 Nov 4;161(9):634-8.
218. Butt AA, Yan P, Lo Re V III, et al; ERCHIVES (Electronically Retrieved Cohort of HCV Infected Veterans) Study Team. **Liver fibrosis progression** in hepatitis C virus infection after seroconversion [online December 8, 2014]. JAMA Intern Med. doi:10.1001/jamainternmed.2014.6502.
219. Hull M, Shafran S, Tseng A, et al. CI**HR Canadian HIV** Trials Network **Co-Infection** and Concurrent Diseases Core: updated Canadian guidelines for the treatment of hepatitis C infection in **HIV-hepatitis C coinfected adults**. Can J Infect Dis Med Microbiol 2014;25:311-20. (accessed December 19, 2014).
Hull M, Shafran S, Wong A, et al. **CIHR Canadian HIV Trials Network Coinfection** and Concurrent Diseases Core Research Group: **2016 updated** Canadian HIV/hepatitis C adult guidelines for management and treatment. Can J Infect Dis Med Microbiol 2016.
220. Pothineni NV, Delongchamp R, Vallurupalli S, et al. Impact of hepatitis C seropositivity on the **risk of coronary heart disease events**. Am J Cardiol. 2014 Dec 15;114(12):1841-5.
221. Reddy KR, Zeuzem S, Zoulim F, et al. **Simeprevir versus telaprevir** with **peginterferon and ribavirin** in previous null or partial responders with chronic hepatitis C virus genotype 1 infection: a randomised, double-blind, phase 3 trial. Lancet Infect Dis 2014; online Dec 5. http://dx.doi.org/10.1016/S1473-3099(14)71002-3.
222. Solomon SS, Mehta SH, Srikirishnan AK, et al. High burden of HCV disease and poor access to HCV services among people who **inject drugs in India**: A crosssectional study among 14,481 drug users across India. Lancet Infect Dis 2014; online Dec 3.
223. Kohli A, Osinusi A, Sims Z, et al. Virological response **after 6 week triple-drug regimens for hepatitis C**: a proof-of-concept phase 2A cohort study. Lancet 2014; online Jan 13.
224. Koretz RL, Lin KW, Ioannidis JP, et al. Is **widespread screening** for hepatitis C justified? BMJ. 2015 Jan 13;350:g7809.
225. Messina JP, Humphreys I, Flaxman A, et al. **Global distribution and prevalence** of hepatitis C virus genotypes. Hepatology. 2015 Jan;61(1):77-87.
226. Molina J-M, Orkin C, Iser DM, et al, for the PHOTON-2 study team. **Sofosbuvir plus ribavirin** for treatment of **hepatitis C virus in patients co-infected with HIV** (PHOTON-2): a multicentre, open-label, non-randomised, phase 3 study. Lancet 2015; online Feb 4.
227. Charlton M et al. **Sofosbuvir and ribavirin for treatment** of compensated **recurrent hepatitis C virus infection after liver transplantation**. *Gastroenterology* 2015 Jan; 148:108.
228. Curry MP et al. **Sofosbuvir and ribavirin prevent recurrence of HCV infection after liver transplantation**: An open-label study. *Gastroenterology* 2015 Jan; 148:100.
229. Butt AA, Yan P, Lo Re V 3rd, et al; ERCHIVES (Electronically Retrieved Cohort of HCV Infected Veterans) Study Team. **Liver fibrosis progression** in hepatitis C virus infection after seroconversion. JAMA Intern Med. 2015 Feb 1;175(2):178-85.
230. Sulkowski MS, Eron JJ,Wyles D, et al. **Ombitasvir, paritaprevir co-dosed with ritonavir, dasabuvir, and ribavirin for hepatitis C in patients co-infected with HIV-1**: a randomized trial. (Tourquoise-I) JAMA. doi:10.1001/jama.2015.1328.
231. Osinusi A, Townsend K, Kohli A, et al. Virologic response following combined **ledipasvir and sofosbuvir administration in patients with HCV genotype 1 and HIV co-infection**. JAMA. doi:10.1001/jama.2015.1373.
232. Mina MM, Luciani F, Cameron B, et al. **Resistance to hepatitis C** virus: potential genetic and immunological determinants. Lancet Infect Dis. 2015 Feb 18. pii: S1473-3099(14)70965-X.
233. Rolland S, Vachon ML. **Sofosbuvir** for the treatment of hepatitis C virus infection. CMAJ. 2015 Feb 17;187(3):203-4. doi: 10.1503/cmaj.140151.
234. Wong WW, Tu HA, Feld JJ, et al. Cost-effectiveness of **screening for hepatitis C in Canada**. CMAJ. 2015 Feb 17;187(3):E110-21.
235. FDA Mar/15 is warning that serious slowing of the heart rate can occur when the antiarrhythmic drug **amiodarone** is taken together with either the hepatitis C drug Harvoni (ledipasvir/sofosbuvir) or with Sovaldi (sofosbuvir) taken in combination with another direct acting antiviral for the treatment of hepatitis C infection.
236. Wu S, Kanda T, Nakamoto S, et al.. Hepatitis C virus **protease inhibitor-resistance** mutations: our experience and review. World J Gastroenterol. 2013 Dec 21;19(47):8940-8.
237. Poveda E, Wyles DL, Mena A, et al. Update on hepatitis **C virus resistance** to direct-acting antiviral agents. Antiviral Res. 2014 Aug;108:181-91.
238. Bourlière M, Bronowicki JP, de Ledinghen V, et al. **Ledipasvir-sofosbuvir** with or without **ribavirin** to treat patients with HCV **genotype 1 infection and cirrhosis** non-responsive to previous protease-inhibitor therapy: a randomised, double-blind, phase 2 trial (**SIRIUS**). Lancet Infect Dis. 2015 Mar 12.
239. Chhatwal J, Kanwal F, Roberts MS, Dunn MA. **Cost-effectiveness** and budget impact of hepatitis C virus treatment with **sofosbuvir and ledipasvir** in the United States. Ann Intern Med. 2015 Mar 17;162(6):397-406.
240. Health Canada Apr/15: Amiodarone - Slow Heart Rate in Patients Taking **Amiodarone** Together with **Harvoni or Sovaldi** and a Direct Acting Antiviral - Gilead Sciences Canada Inc.
241. Hézode C, Asselah T, Reddy KR, et al. **Ombitasvir plus paritaprevir plus ritonavir with or without ribavirin** in treatment-naive and treatmentexperienced patients with genotype 4 chronic hepatitis C virus infection **(PEARL-I):** a randomised, open-label trial. Lancet 2015; online March 31.
242. Lawitz E, Gane E, Pearlman B, et al. Efficacy and safety of 12 weeks versus 18 weeks of treatment with **grazoprevir** (MK-5172) and **elbasvir** (MK-8742) with or without ribavirin for hepatitis C virus genotype 1 infection in previously untreated patients with cirrhosis and patients with previous null response with or without cirrhosis (**C-WORTHY**): a randomised, open-label phase 2 trial. Lancet 2014; online Nov 11.
243. Linas BP, Barter DM, Morgan JR, et al. The **Cost-Effectiveness** of **Sofosbuvir**-Based Regimens for Treatment of Hepatitis C Virus Genotype 2 or 3 Infection. Ann Intern Med. 2015 Mar 30.
244. Najafzadeh M et al. **Cost-effectiveness** of novel regimens for the treatment of hepatitis C virus. Ann Intern Med 2015 Mar 17; 162:407.

245. Sulkowski M, Hezode C, Gerstoft J, et al. Efficacy and safety of 8 weeks versus 12 weeks of treatment with **grazoprevir** (MK-5172) and **elbasvir** (MK- 8742) with or without ribavirin in patients with hepatitis C virus genotype 1 monoinfection and HIV/hepatitis C virus coinfection (**C-WORTHY**): a randomised, open-label phase 2 trial. Lancet 2014; online Nov 11.
246. Webster DP, Klenerman P, Dusheiko GM. **Hepatitis C**. Lancet. 2015 Mar 21;385(9973):1124-35.
247. Mizokami M, Yokosuka O, Takehara T, et al. **Ledipasvir and sofosbuvir** fixed-dose combination with and without ribavirin for 12 weeks in treatment-naive and previously treated Japanese patients with genotype 1 hepatitis C: an open-label, randomised, phase 3 trial. Lancet Infect Dis. 2015 Apr 8.
248. Zeuzem S, Ghalib R, Reddy KR, et al. **Grazoprevir-Elbasvir Combination** Therapy for Treatment-Naive Cirrhotic and Noncirrhotic Patients With Chronic HCV Genotype 1, 4, or 6 Infection: A Randomized Trial. Ann Intern Med. 2015 Apr 24.
249. Etzion O, Ghany MG. A cure for the **high cost** of hepatitis C virus treatment. Ann Intern Med. 2015 May 5;162(9):660-1.
250. Muir AJ, Poordad F, Lalezari J; et al. **Daclatasvir** in combination with **asunaprevir** and **beclabuvir** for hepatitis C virus genotype 1 infection with compensated cirrhosis. JAMA. doi:10.1001/jama.2015.3868.
251. Poordad F, SievertW, Mollison L, et al. Fixed-dose combination therapy with **daclatasvir, asunaprevir, and beclabuvir** for noncirrhotic patients with HCV genotype 1 infection. JAMA. doi:10.1001/jama.2015.3860.
252. Burgess S, Partovi N, Yoshida EM, et al. **Drug Interactions With Direct-Acting Antivirals for Hepatitis C**: Implications for HIV and Transplant Patients. Ann Pharmacother. 2015 Jun;49(6):674-687. Epub 2015 Mar 13.
253. Rao VB, Johari N, du Cros P, et al. **Hepatitis C seroprevalence and HIV co-infection** in sub-Saharan Africa: a systematic review and meta-analysis. Lancet Infect Dis. 2015 May 5.
254. Wray CM, Davis AM. **Screening for hepatitis C**. JAMA. 2015 May 12;313(18):1855-6.
255. Athanasakis K, Ferrante SA, Kyriopoulos II, et al. **Boceprevir** for Chronic Genotype 1 Hepatitis C Virus in the Current Health Care Setting in Greece: A Cost-Effectiveness Analysis. Clin Ther. 2015 May 29.
256. Wilkins T, Akhtar M, Gititu E, et al. **Diagnosis and Management of Hepatitis C**. *Am Fam Physician.* 2015 Jun 15;91(12):835-842.
257. Onofrey S, Aneja J, Haney GA, et al. **Underascertainment** of Acute Hepatitis C Virus Infections in the **U.S. Surveillance System**: A Case Series and Chart Review. Ann Intern Med. 2015 Jun 30.
258. Kohli A, Kapoor R, Sims Z, et al. **Ledipasvir and sofosbuvir** for hepatitis C genotype 4: a proof-of-concept, single-centre, open-label phase 2a cohort study. Lancet Infect Dis 2015; July 15.
259. Naggie S, Cooper C, Saag M, et al.; **ION-4** Investigators. **Ledipasvir and Sofosbuvir** for HCV in Patients **Coinfected with HIV-1.** N Engl J Med. 2015 Jul 21.
260. Reese PP, Abt PL, Blumberg EA, Goldberg DS. **Transplanting Hepatitis C-Positive Kidneys**. N Engl J Med. 2015 Jul 23;373(4):303-5.
261. Wyles DL, Ruane PJ, Sulkowski MS, et al; **ALLY-2** Investigators. **Daclatasvir plus Sofosbuvir** for HCV in Patients **Coinfected with HIV-1**. N Engl J Med. 2015 Jul 21.
262. Barua S, Greenwald R, Grebely J, et al. **Restrictions for Medicaid Reimbursement of Sofosbuvir** for the Treatment of Hepatitis C Virus Infection in the United States. Ann Intern Med. 2015 Aug 4;163(3):215-23.
263. Canary LA, Klevens RM, Holmberg SD. **Limited Access to New Hepatitis C Virus Treatment** Under State Medicaid Programs. Ann Intern Med. 2015 Aug 4;163(3):226-8.
264. McCance-Katz EF, Valdiserri RO. **Hepatitis C Virus Treatment and Injection Drug Users**: It Is Time to Separate Fact From Fiction. Ann Intern Med. 2015 Aug 4;163(3):224-5.
265. White DA, Anderson ES, Pfeil SK, et al. Results of a Rapid Hepatitis C Virus **Screening and Diagnostic** Testing Program in an Urban **Emergency Department**. Ann Emerg Med. 2015 Jul 29.
266. MHRA Aug/15: Simeprevir with sofosbuvir: risk of severe bradycardia and heart block when taken with amiodarone.
267. Gordon SC, Lamerato LE, Rupp LB, et al. **Prevalence of Cirrhosis in Hepatitis C Patients** in the Chronic Hepatitis Cohort Study (CHeCS): A Retrospective and Prospective Observational Study. Am J Gastroenterol. 2015 Aug;110(8):1169-77.
268. Toussaint-Miller KA, Andres J. Treatment Considerations for **Unique Patient Populations With HCV Genotype 1 Infection**. Ann Pharmacother. 2015 Sep;49(9):1015-30.
269. Liao JM, Fischer MA. Early Patterns of **Sofosbuvir Utilization** by State Medicaid Programs. N Engl J Med. 2015 Sep 24;373(13):1279-81.
270. Simmons B, Saleem J, Heath K, et al. **Long-Term Treatment Outcomes of Patients Infected With Hepatitis C Virus**: A Systematic Review and Meta-analysis of the Survival Benefit of Achieving a Sustained Virological Response. Clin Infect Dis. 2015 Sep 1;61(5):730-40.
271. Collins JM et al. **Hepatitis B virus reactivation** during successful treatment of hepatitis C virus with **sofosbuvir and simeprevir**. Clin Infect Dis 2015 Oct 15; 61:1304.
272. Falade-Nwulia O, Seaberg EC, Snider AE, et al. **Incident Hepatitis B Virus Infection in HIV-Infected** and HIV-Uninfected Men Who Have Sex With Men From Pre-HAART to HAART Periods: A Cohort Study. Ann Intern Med. 2015 Oct 13.
273. Roth D, Nelson DR, Bruchfeld A, et al. **Grazoprevir plus elbasvir** in treatment-naive and treatment-experienced patients with hepatitis C virus genotype 1 infection and stage 4–5 **chronic kidney disease** (the **C-SURFER** study): a combination phase 3 study. Lancet 2015; online Oct 6.
274. FDA Oct/15 is warning that hepatitis C treatments **Viekira Pak and Technivie can cause serious liver injury** mostly in patients with underlying advanced liver disease. As a result, FDA is requiring the manufacturer to include information about serious liver injury adverse events to the Contraindications, Warnings and Precautions, Postmarketing Experience, and Hepatic Impairment sections of the Viekira Pak and Technivie drug labels.
275. Lawitz E et al. Efficacy and safety of **ombitasvir, paritaprevir, and ritonavir** in an open-label study of patients with **genotype 1b** chronic hepatitis C virus infection with and without cirrhosis. Gastroenterology 2015 Oct; 149:971.
276. Fralick M, Feld JJ. **Hepatitis C virus infection**. (Five things to know about) CMAJ. 2015 Oct 20;187(15):1159.
277. Smyth D, Webster D. Hepatitis C virus infection: **accessing drug treatment**. CMAJ. 2015 Oct 20;187(15):1113-4.
278. Tyndall M. Misplaced advocacy: What does **better hepatitis C treatment really mean**? CMAJ. 2015 Oct 20;187(15):1111-2.
279. Curry MP, O'Leary JG, Bzowej N, et al. **Sofosbuvir and velpatasvir** for HCV in patients with decompensated cirrhosis. (**Astral-4**)N Engl J Med. DOI: 10.1056/NEJMoa1512614.
280. Everson GT, Towner WJ, Davis MN, et al. **Sofosbuvir With Velpatasvir** in Treatment-Naive Noncirrhotic Patients With Genotype 1 to 6 Hepatitis C Virus Infection: A Randomized Trial. Ann Intern Med. 2015 Nov 10.
281. Feld JJ, Jacobson IM, Hézode C, et al. **Sofosbuvir and velpatasvir** for HCV genotypes 1, 2, 4, 5, and 6 infection. (**Astral-1**) N Engl J Med. DOI: 10.1056/NEJMoa1512610.
282. Fontaine H, Lazarus A, Pol S, et al; Cochin Hepatology and Cardiology Group. **Bradyarrhythmias** Associated with **Sofosbuvir** Treatment. N Engl J Med. 2015 Nov 5;373(19):1886-8.
283. Foster GR, Afdhal N, Roberts SK, et al. **Sofosbuvir and velpatasvir** for HCV genotype 2 and 3 infection. (**Astral-2, Astral-3**) N Engl J Med. DOI: 10.1056/NEJMoa1512612.
284. Pianko S, Flamm SL, Shiffman ML, et al. **Sofosbuvir Plus Velpatasvir** Combination Therapy for Treatment-Experienced Patients With Genotype 1 or 3 Hepatitis C Virus Infection: A Randomized Trial. Ann Intern Med. 2015 Nov 10.
285. Chahal HS, Marseille EA, Tice JA, et al. **Cost-effectiveness** of **Early** Treatment of Hepatitis C Virus Genotype 1 by **Stage of Liver Fibrosis** in a US **Treatment-Naive** Population. JAMA Intern Med. 2015 Nov 23:1-9.
286. He T, Li K, Roberts MS, et al. Prevention of Hepatitis C by **Screening** and Treatment in **U.S. Prisons**. Ann Intern Med. 2015 Nov 24.
287. Kohli A, Kattakuzhy S, Sidharthan S, et al. **Four-Week Direct-Acting** Antiviral Regimens in Noncirrhotic Patients With Hepatitis C Virus Genotype 1 Infection: An Open-Label, Nonrandomized Trial. Ann Intern Med. 2015 Nov 24:899-907.
288. Hughes E, Bassi S, Gilbody S, et al. **Prevalence of HIV, hepatitis B, and hepatitis C** in people with severe mental illness: a systematic review and meta-analysis. Lancet Psychiatry. 2015Nov 24.
289. Tsai HH, Liou HH, Muo CH, et al. Hepatitis C virus infection as a **risk factor for Parkinson disease**: A nationwide cohort study. Neurology. 2015 Dec 23.

290. Abergel A, Asselah T, Metivier S, et al. **Ledipasvir plus sofosbuvir** in patients with hepatitis C virus genotype 5 infection: an open-label, multicentre, single-arm, phase 2 study. Lancet Infec Dis 2016; online Jan 20.
291. Joy JB, McCloskey RM, Nguyen T, et al. The spread of **hepatitis C** virus **genotype 1a in North America**: a retrospective phylogenetic study. Lancet Infect Dis 2016; online March 30.
292. Lyons MS et al. Prevalence of **diagnosed and undiagnosed hepatitis C** in a Midwestern urban emergency department. Clin Infect Dis 2016 Feb 21.
293. Saab S et al. Safety and efficacy of **ledipasvir/sofosbuvir** for the treatment of genotype 1 hepatitis C in subjects aged 65 years or older. Hepatology 2016 Apr; 63:1112.
294. Swallow E, Song J, Yuan Y, et al. **Daclatasvir and Sofosbuvir Versus Sofosbuvir and Ribavirin** in Patients with Chronic Hepatitis C Coinfected with HIV: A Matching-adjusted Indirect Comparison. Clin Ther. 2016 Jan 30.
295. Mahale P, Sturgis EM, Tweardy DJ, et al. Association Between **Hepatitis C Virus and Head and Neck Cancers**. J Natl Cancer Inst. 2016 Apr 13;108(8).
296. Reig M, Mariño Z, Perelló C, et al. **Unexpected early tumor recurrence** in patients with hepatitis C virus -related hepatocellular carcinoma undergoing **interferon-free therapy**: a note of caution. J Hepatol. 2016 Apr 12.
297. Shiffman ML et al. Safety and efficacy of **ombitasvir/paritaprevir/ritonavir plus dasabuvir** with or without **ribavirin** in HCV-infected patients taking **concomitant acid-reducing agents**. Am J Gastroenterol 2016 Apr 5.
298. Hynicka LM, Khambaty M. **Angioedema** Secondary to **Sofosbuvir/Ledipasvir**. Ann Pharmacother. 2016 Apr 7.
299. Jayasekera CR, Arora S, et al. Hepatitis C Treatment Delivery Mandates Optimizing Available Health Care Human Resources: A Case for **Task Shifting**. JAMA. 2016 May 10;315(18):1947-8.
300. Urrutia J, Porteny T, Daniels N. What does it mean to put new **hepatitis C** drugs on a **list of essential medicines**? BMJ. 2016 Apr 22
301. Rockstroh JK, Nelson M, Katlama C, et al. Efficacy and safety of **grazoprevir (MK-5172) and elbasvir (MK-8742)** in patients with **hepatitis C virus and HIV co-infection** (**C-EDGE CO-INFECTION**): a non-randomised, open-label trial. Lancet HIV. 2015;2(8):e319-e327.
302. Taylor AL, Denniston MM, Klevens RM, et al. Association of Hepatitis C Virus **With Alcohol Use** Among U.S. Adults: NHANES 2003-2010. Am JPrev Med. 2016 May 2.
303. Freiman JM, Tran TM, et al. **Hepatitis C Core Antigen Testing** for Diagnosis of Hepatitis C Virus Infection: A Systematic Review and Meta-analysis. Ann Intern Med. 2016 Jun 21.
304. Manns M, Samuel D, Gane EJ, et al. **Ledipasvir and sofosbuvir** plus ribavirin in patients with **genotype 1 or 4** hepatitis C virus infection and advanced liver disease: a multicentre, open-label, randomised, phase 2 trial (**Solar-2**). Lancet Infect Dis. 2016 Jun;16(6):685-97.
305. Asselah T, Hezode C, Qaquish RB, et al. **Ombitasvir, Paritaprevir, and Ritonavir Plus Ribavirin** in Adults with Hepatitis C Virus **Genotype 4 Infection** and Cirrhosis (**AGATE-I**): A Multicentre, Phase 3, Randomized Open-Label Trial.2016:1:25-35
306. Clinical Management of Cirrhotic Patient With HCV **Genotype 5** Treated With **Simeprevir, Sofosbuvir, and Ribavirin**. Ann Pharmacother. 2016 Jun 15.
307. Dore GJ, Altice F, et al. **Elbasvir-Grazoprevir** to Treat Hepatitis C Virus Infection in Persons Receiving **Opioid Agonist Therapy**: A Randomized Trial. Ann Intern Med. 2016 Aug 9.
308. Fernandez N, Towers CV, Wolfe L, et al. Sharing of **Snorting Straws** and Hepatitis C Virus Infection in Pregnant Women. Obstet Gynecol. 2016 Aug;128(2):234-7.
309. Ge PS, Runyon BA. **Treatment of Patients with Cirrhosis**. N Engl J Med. 2016 Aug 25;375(8):767-77.
310. Hull M, Shafran S, Wong A, et al. CIHR Canadian HIV Trials Network Coinfection and Concurrent Diseases Core Research Group: 2016 updated Canadian **HIV/hepatitis C adult guidelines** for management and treatment. Can J Infect Dis Med Microbiol 2016.
311. Stanaway JD, Flaxman AD, Naghavi M, et al. The **global burden of viral hepatitis** from 1990 to 2013: findings from the Global Burden of Disease Study 2013. Lancet. 2016 Jul 6.
312. Talavera Pons S, Boyer A, Lamblin G, Chennell et al. Managing **drug-drug interactions** with new direct-acting antiviral agents in chronic hepatitis C. Br J Clin Pharmacol. 2016 Aug 16.
313. von Aesch Z, Steel LS, Shah H. **Primary Care Flow** Sheet for Hepatitis C Virus. Can Fam Physician.2016;62:e384-92
314. EASL:European Association for the Study of the Liver. Electronic address: easloffice@easloffice.eu. **EASL Recommendations on Treatment of Hepatitis C 2016**. J Hepatol. 2016 Sep 12.
315. FDA Oct/16 is warning about the risk of **hepatitis B virus (HBV) becoming an active infection again** in any patient who has a current or previous infection with HBV and is treated with certain direct-acting antiviral (DAA) medicines for hepatitis C virus. In a few cases, HBV reactivation in patients treated with DAA medicines resulted in serious liver problems or death. HBV reactivation usually occurred within 4-8 weeks.
316. Kim A. **In the Clinic: Hepatitis C Virus**. Ann Intern Med. 2016 Sep 6;165(5):ITC33-ITC48.
317. Deterding K, Spinner CD, Schott E, et al. **Ledipasvir plus sofosbuvir** fi xed-dose combination for 6 weeks in patients with **acute hepatitis C** virus genotype 1 monoinfection (HepNet Acute HCV IV): an open-label, single-arm, phase 2 study. Lancet Infect Dis 2016; online Oct 28.
318. Jaeckel E, Cornberg M, Wedemeyer et al. German Acute Hepatitis C Therapy Group. Treatment of acute hepatitis C with **interferon alfa-2b**. N Engl J Med. 2001 Nov 15;345(20):1452-7.
319. Marshall AD, Saeed S, Barrett L, et al. **Restrictions for reimbursement** of direct-acting antiviral treatment for hepatitis C virus infection in **Canada**: a descriptive study. CMAJ Open.2016 Oct 14;4(4):E605-E614.
320. Maciocia N, O'Brien A, Ardeshna K. **Remission of Follicular Lymphoma after Treatment for Hepatitis C** Virus Infection. N Engl J Med. 2016 Oct 27;375(17):1699-1701.
321. Su F et al. The association between **race/ethnicity** and the effectiveness of direct antiviral agents for hepatitis C virus infection. Hepatology 2016 Oct 24.
322. Wijdicks EF. **Hepatic Encephalopathy**. N Engl J Med. 2016 Oct 27;375(17):1660-1670.
323. Zhou K, Fitzpatrick T, Walsh N, et al. **Interventions to optimise the care continuum for chronic viral hepatitis**: a systematic review and meta-analyses. Lancet Infect Dis. 2016 Sep 5.
324. Cadieux G, Campbell J, Dendukuri N. Systematic review of the **accuracy of antibody tests** used to screen asymptomatic adults for hepatitis C infection. CMAJ Open. 2016 Dec 2;4(4):E737-E745.
325. Stepanova M, Sayiner M, de Avila L, et al. **Long-term outcomes of liver transplantation** in patients with hepatitis C infection are not affected by HCV positivity of a donor. BMC Gastroenterol. 2016 Nov 15;16(1):137.
326. Taylor J, Carr-Lopez S, Robinson A, et al. Determinants of **Treatment Eligibility** in Veterans With Hepatitis C Viral Infection. Clin Ther. 2016 Dec 15.
327. Younossi ZM, Stepanova M, Feld J, et al. **Sofosbuvir and Velpatasvir** Combination Improves Outcomes Reported by Patients With HCV Infection, Without or with Compensated or **decompensated Cirrhosis**. Clin Gastroenterol Hepatol. 2016 Nov 12.
328. Colombo M, Aghemo A, Liu H, et al. Treatment With **Ledipasvir-Sofosbuvir for 12 or 24 Weeks in Kidney Transplant Recipients** With Chronic Hepatitis C Virus Genotype 1 or 4 Infection: A Randomized Trial. Ann Intern Med. 2016 Nov 15.
329. Ghinea N, Lipworth W, Day R, et al. **Importation of generic hepatitis C therapies**: bridging the gap between price and access in high-income countries. Lancet. 2016 Nov 3.
330. Health Canada Dec/16: safety review found that patients infected with both hepatitis B and hepatitis C viruses who are being **treated for hepatitis C with direct-acting antivirals** may experience a **reactivation of their hepatitis B.**
331. Levitsky J, Verna EC, O'Leary JG, et al. **Perioperative Ledipasvir-Sofosbuvir for HCV in Liver-Transplant Recipients**. N Engl J Med. 2016 Nov 24;375(21):2106-2108
332. MHRA Jan/17: **Direct-acting antiviral interferon-free regimens to treat chronic hepatitis C: risk of hepatitis B reactivation**.All patients should be screened for hepatitis B before starting treatment for chronic hepatitis C with direct-acting antiviral interferon-free regimens.
333. Borgia F, Cacciola I, Filomia R, et al. **Mucocutaneous toxicity during simeprevir** treatment for hepatitis C. A single institution, retrospective case series. Br J Clin Pharmacol. 2017 Jan 24.
334. Jefferson AA, Pearson SD. **Conflict of Interest** in Seminal **Hepatitis C Virus and Cholesterol Management Guidelines**. JAMA Intern Med. 2017 Jan 17.
335. Van der Ree MH, de Vree JM, Stelma F, et al. Safety, tolerability, and antiviral effect of **RG-101 in patients with chronic hepatitis C**: a phase 1B, double-blind, randomised controlled trial. Lancet 2017; online Jan 10.
336. Kleefeld F, Heller S, Jessen H, et al. Effect of **interferon-free therapy on cognition in HCV and HCV/HIV infection**: A pilot study. Neurology. 2017 Feb 14;88(7):713-715.

337. di Biase L, Picillo M, et al. Hepatitis C Virus-Related **Hepatic Myelopathy After Treatment With Sofosbuvir and Ribavirin**: A Case Report. Ann Intern Med. 2017 Mar 7;166(5):379-380.
338. Falade-Nwulia O, Suarez-Cuervo C, Nelson DR, et al. **Oral Direct-Acting Agent Therapy for Hepatitis C Virus Infection: A Systematic Review.** Ann Intern Med. 2017 Mar 21.
339. Jemal A, Fedewa SA. Recent Hepatitis C Virus **Testing Patterns Among Baby Boomers**. Am J Prev Med. 2017 Mar 1.
340. Medsafe (New Zealand) Mar/17: Medsafe was recently alerted to a case of a type 2 **diabetic** who started hepatitis C treatment with **Viekira Pak**. Eight weeks after starting Viekira Pak, the patient's blood glucose control had improved (**HbA1c almost halved**).
341. Barocas JA, Beiser M, León C, et al. Experience and Outcomes of Hepatitis C Treatment in a Cohort of **Homeless and Marginally Housed Adults**. JAMA Intern Med. 2017 Apr 10.
342. Bersoff-Matcha SJ, Cao K, Jason M, et al. **Hepatitis B reactivation** associated with **direct-acting antiviral therapy for chronic hepatitis C** virus: a review of cases reported to the U.S. Food and Drug Administration Adverse Event Reporting System. Ann Intern Med. 2017. [Epub ahead of print]. doi:10.7326/ M17-0377
343. Kullak-Ublick GA, Andrade RJ, Merz M, et al. **Drug-induced liver injury**: recent advances in diagnosis and risk assessment. Gut. 2017 Mar 23.
344. Pakpoor J, Noyce A, Goldacre R, et al. **Viral hepatitis (B & C) and Parkinson disease**: A national record-linkage study. Neurology. 2017 Mar 29.
345. Cadieux G, Sachdeva H. **Toward ending hepatitis C** virus infection: What are the next steps? CMAJ. 2017 Apr 24;189(16):E583-E584.
346. **CTFPHC**: **Canadian** Task Force on Preventive Health Care. Recommendations on **Hepatitis C Screening for Adults**. CMAJ.2017 April 24;189:E594-604
347. Talal AH, Thomas DL, Reynolds JL, et al. **Toward Optimal Control of Hepatitis C** Virus Infection in Persons **With Substance Use Disorders**. Ann Intern Med. 2017 Apr 25.
348. Falade-Nwulia O, Suarez-Cuervo C, Nelson DR, et al. **Oral Direct-Acting Agent Therapy** for Hepatitis C Virus Infection: A Systematic Review. Ann Intern Med. 2017 May 2;166(9):637-648.
349. Goldberg DS, Abt PL, Blumberg EA, et al. Trial of **Transplantation of HCV-Infected Kidneys into Uninfected Recipients**. N Engl J Med. 2017 Apr 30.
350. Campbell CA, Canary L, Smith N, et al. **State HCV Incidence and Policies** Related to HCV Preventive and Treatment Services for Persons **Who Inject Drugs** - United States, 2015-2016. MMWR Morb Mortal Wkly Rep. 2017 May 12;66(18):465-469.
351. Ly KN, Jiles RB, Teshale EH, et al. Hepatitis C virus infection among **reproductive-aged women and children** in the United States, 2006 to 2014. Ann Intern Med. 2017.
352. Smolders EJ, Colbers A, de Kanter CTMM, et al. **Metformin and daclatasvir**: absence of a pharmacokinetic-pharmacodynamic drug interaction in healthy volunteers. Br J Clin Pharmacol. 2017 May 5.
353. Bourlière M, Gordon SC, Flamm SL, et al. **Sofosbuvir, Velpatasvir, and Voxilaprevir** for **Previously Treated HCV Infection**. N Engl J Med. 2017 Jun 1;376(22):2134-2146.
354. Jakobsen JC, Nielsen EE, Feinberg J, et al. **Direct-acting antivirals for chronic hepatitis C**. Cochrane Database of Systematic Reviews 2017, Issue 6. Art. No.: CD012143. Overall, DAAs on the market or under development do not seem to have any effects on risk of serious adverse events. Simeprevir may have beneficial effects on risk of serious adverse event. In all remaining analyses we could neither confirm nor reject that DAAs had any clinical effects. DAAs seemed to reduce the risk of no sustained virological response. The clinical relevance of the effects of DAAs on no sustained virological response is questionable, as it is a non-validated surrogate outcome. All trials and outcome results were at high risk of bias so our results presumably overestimate benefit and underestimate harm. The quality of the evidence was very low.
355. Buckley GJ, Strom BL. A **National Strategy for the Elimination** of Viral Hepatitis Emphasizes **Prevention, Screening, and Universal Treatment** of Hepatitis C. Ann Intern Med. 2017 Jun 20;166(12):895-896.
356. Falade-Nwulia O, Suarez-Cuervo C, Nelson DR, et al. **Oral Direct-Acting Agent Therapy for Hepatitis C Virus Infection**: A Systematic Review. Ann Intern Med. 2017 May 2;166(9):637-648.
357. Ahmad J. **Hepatitis C**. BMJ. 2017 Jul 6;358:j2861
358. Hawkes N. **Are new hepatitis C drugs all they're cracked up to be**? BMJ. 2017 Jun 21;357:j2961
359. Saadoun D, Pol S, et al. Efficacy and Safety of **Sofosbuvir Plus Daclatasvir** for Treatment of HCV-Associated **Cryoglobulinemia Vasculitis**. Gastroenterology. 2017 Jul;153(1):49-52.e5.
360. Ti L, Lima V, Hull M, et al. **Hepatitis C testing in Canada: don't leave baby boomers behind**. CMAJ. 2017 Jun 26;189(25):E870-E871.
361. Ahmad J. Hepatitis C. BMJ. 2017 Jul 6;358:j2861
362. Forns X, Lee SS, Valdes J, et al. **Glecaprevir** plus **pibrentasvir** for chronic hepatitis C virus **genotype 1, 2, 4, 5, or 6** infection in adults with compensated cirrhosis (**EXPEDITION**-1): a single-arm, open-label, multicentre phase 3 trial. Lancet Infect Dis 2017; online August 14.
363. Kattakuzhy S, Gross C, Emmanuel B, et al. **Expansion of Treatment for Hepatitis C** Virus Infection by Task Shifting to Community-Based Nonspecialist Providers: A Nonrandomized Clinical Trial. Ann Intern Med. 2017 Aug 8.
364. Lok AS, Chung RT, Vargas HE, et al. **Comments on Cochrane Review** on Direct-Acting Antivirals for Hepatitis C. Hepatology. 2017 Jul 16.
365. Marrero JA, Singal AG. **Direct-acting antivirals** and recurrence of **hepatocellular carcinoma**. Liver Transpl. 2017 Jul 19. [
366. Reilley B, Leston J. A Tale of **Two Epidemics - HCV Treatment among Native Americans and Veterans**. N Engl J Med. 2017 Aug 31;377(9):801-803.
367. AAP Committee on Infectious Diseases and **AAP Committee on Fetus and Newborn Elimination of Perinatal Hepatitis B**: Providing the First Vaccine Dose Within 24 Hours of Birth. Pediatrics. 2017;140(3):e20171870
368. Jacobson IM, Lawitz E, Gane EJ, et al. Efficacy of **8 Weeks of Sofosbuvir, Velpatasvir, and Voxilaprevir** in Patients With Chronic HCV Infection: 2 Phase 3 Randomized Trials. Gastroenterology. 2017 Jul;153(1):113-122.
369. Siemieniuk RA, Foroutan F, Mirza R, et al. **Antiretroviral therapy for pregnant women living with HIV or hepatitis B**: a systematic review and meta-analysis. BMJ Open. 2017 Sep 11;7(9):e019022
370. Belperio PS, Chartier M, Ross DB, et al. **Curing Hepatitis C** Virus Infection: Best Practices From the U.S. Department of **Veterans Affairs**. Ann Intern Med. 2017 Oct 3;167(7):499-504.
371. Jakobsen JC;Nielsen EE;Feinberg J;Katakam KK;Fobia. **Direct-acting antivirals for chronic hepatitis C.** Cochrane Database Syst Rev. 2017 Sep 18;9:CD012143. The evidence for our main outcomes of interest come from short-term trials, and we are unable to determine the effect of long-term treatment with DAAs. The rates of hepatitis C morbidity and mortality observed in the trials are relatively low and we are uncertain as to how DAAs affect this outcome. Overall, there is very low quality evidence that DAAs on the market or under development do not influence serious adverse events. There is insufficient evidence to judge if DAAs have beneficial or harmful effects on other clinical outcomes for chronic HCV. Simeprevir may have beneficial effects on risk of serious adverse event. In all remaining analyses, we could neither confirm nor reject that DAAs had any clinical effects. DAAs may reduce the number of people with detectable virus in their blood, but we do not have sufficient evidence from randomised trials that enables us to understand how SVR affects long-term clinical outcomes. SVR is still an outcome that needs proper validation in randomised clinical trials.
372. Gane E, Lawitz E, Pugatch D, et al. **Glecaprevir and Pibrentasvir** in Patients with HCV and Severe Renal Impairment. N Engl J Med. 2017 Oct 12;377(15):1448-1455.
373. Solas C, Bregigeon S, Faucher-Zaegel O, et al. **Ledipasvir and Tenofovir drug interaction** in HIV-HCV co-infected patients: Impact on Tenofovir C(trough) and Renal Safety. Br J Clin Pharmacol. 2017 Oct 13
374. Barritt AS 4th, Lee B, Runge T, et al. Increasing Prevalence of Hepatitis C among Hospitalized Children Is Associated with an **Increase in Substance Abuse**. J Pediatr. 2017 Oct 26
375. Gordon J, Bocking N, Pouteau K, et al. First Nations hepatitis C virus infections: Six-year retrospective study of on-reserve rates of newly reported infections in northwestern Ontario. Can Fam Physician. 2017 Nov;63(11):e488-e494.
376. Zelenev A, Li J, Mazhnaya A, Basu S, Altice FL. Hepatitis C virus treatment as prevention in an extended network of people who inject drugs in the USA: a modelling study. Lancet Infect Dis 2017; online Nov 15.
377. Kwo PY, Shiffman ML, Bernstein DE. The Cochrane Review Conclusion for Hepatitis C DAA Therapies is Wrong. Am J Gastroenterol. 2017 Nov 14.
378. Enomoto M, Tateishi C, Tsuruta D, et al. Remission of Psoriasis After Treatment of Chronic Hepatitis C Virus Infection With Direct-Acting Antivirals. Ann Intern Med. 2018 Jan 16.

379. Kanwal F et al. Risk of hepatocellular cancer in HCV patients treated with direct acting antiviral agents. Gastroenterology 2017 Jun 19.
380. Marra F, et al. Clinical impact of pharmacokinetic interactions between the HCV protease inhibitor Simeprevir and frequently used concomitant medications. Br J Clin Pharmacol. 2018 Jan 18.
381. Zeuzem S, Foster GR, Wang S, et al. Glecaprevir-Pibrentasvir for 8 or 12 Weeks in HCV Genotype 1 or 3 Infection. N Engl J Med. 2018 Jan 25;378(4):354-369.
382. Durand CM, Bowring MG, Brown DM, et al. Direct-Acting Antiviral Prophylaxis in Kidney Transplantation From Hepatitis C Virus-Infected Donors to Noninfected Recipients: An Open-Label Nonrandomized Trial. Ann Intern Med. 2018 Mar 6.
383. Kronfli N, Cox J. Care for people with hepatitis C in **provincial and territorial prisons**. CMAJ. 2018 Jan 29;190(4):E93-E94.
384. Lim JK, Liapakis AM, Shiffman ML, et al. Safety and Effectiveness of **Ledipasvir and Sofosbuvir, With or Without Ribavirin**, in Treatment-Experienced Patients with Genotype 1 Hepatitis C Virus Infection and **Cirrhosis**. Clin Gastroenterol Hepatol. 2018 Jan 3.
385. Sullivan EV, Zahr NM, Sassoon SA, et al. The role of aging, drug dependence, and **hepatitis C comorbidity** in **alcoholism** cortical compromise [online Mar 14, 2018]. JAMA Psychiatry. doi:10.1001/jamapsychiatry.2018.0021
386. Liang TJ, Ward JW. **Hepatitis C in Injection-Drug Users** - A **Hidden Danger of the Opioid Epidemic**. N Engl J Med. 2018 Mar 29;378(13):1169-1171.
387. Marcus JL et al. No difference in effectiveness of **8 vs 12 weeks of ledipasvir and sofosbuvir** for treatment of hepatitis C in black patients. Clin Gastroenterol Hepatol 2018 Mar 10.
388. Zamor PJ, Vierling J, Ghalib R, et al. **Elbasvir/grazoprevir** in **black adults** with hepatitis C virus infection: a pooled analysis of phase 2/3 clinical trials. Am J Gastroenterol. 2018 Apr 26.
389. Chappell CA, Hillier SL, Crowe D, et al. Hepatitis C Virus Screening Among **Children Exposed During Pregnancy**. Pediatrics. 2018 May 2.
390. Cheung TT, Yan Chiu JW, Yuen MF, et al. A Phase I, Single- and Multiple-Dose Study to Evaluate the Pharmacokinetics of **Elbasvir and Grazoprevir** in Healthy Chinese Participants. Clin Ther. 2018 Apr 30.
391. **EASL**: European Association for the Study of the Liver. EASL Recommendations on Treatment of Hepatitis C 2018. J Hepatol. 2018 Apr 9.
392. Nakamura H, Fujieda Y, Yasuda S, et al. Remission of **Nephrotic Syndrome** After Therapy for Chronic Hepatitis C Virus Infection in a Patient With **Systemic Lupus Erythematosus**. Ann Intern Med. 2018 May 1.
393. Shiha G, Esmat G, Hassany M, et al. **Ledipasvir/sofosbuvir** with or without ribavirin for 8 or 12 weeks for the treatment of HCV genotype 4 infection: results from a randomised phase III study in Egypt. Gut. 2018 Apr 17.
394. Grebely J, Dalgard O, Conway B, et al. **Sofosbuvir and velpatasvir** for hepatitis C virus infection in people with **recent injection drug use (SIMPLIFY)**: an open-label, single-arm, phase 4, multicentre trial. Lancet Gastroenterol Hepatol. 2018 Jan 5.
395. Jakobsen JC, Nielsen EE, Koretz RL, et al. **Do direct acting antivirals cure chronic hepatitis C**? BMJ. 2018 May 10;361:k1382.
396. Mücke MM, Backus LI, Mücke VT, et al. Hepatitis B virus reactivation during direct-acting antiviral therapy for hepatitis C: a systematic review and meta-analysis. Lancet Gastroenterol Hepatol. 2018 Jan 19.
397. Yeh WW, Fraser IP, Jumes P, et al. Antiviral Activity, Safety, and Tolerability of Multiple Ascending Doses **of Elbasvir or Grazoprevir** in Participants Infected With Hepatitis C Virus Genotype-1 or -3. Clin Ther. 2018 Apr 24.
398. Eckman MH, Woodle ES, Thakar CV, et al. **Transplanting hepatitis C virus–infected versus uninfected kidneys into hepatitis C virus–infected recipients**. A cost-effectiveness analysis. Ann Intern Med. 2018. [Epub ahead of print].
399. Lamoury FMJ, Bajis S, Hajarizadeh B, et al. Evaluation of the Xpert **HCV Viral Load Finger-Stick Point-of-Care Assay**. J Infect Dis. 2018 May 25;217(12):1889-1896.
400. Sood N, Ung D, Shankar A, et al. A Novel Strategy for **Increasing Access to Treatment for Hepatitis C Virus Infection** for Medicaid Beneficiaries. Ann Intern Med. 2018 May 15.
401. Mashiba T, Joko K, Kurosaki M, et al. Does **interferon-free direct-acting antiviral therapy for hepatitis C after curative treatment for hepatocellular carcinoma** lead to unexpected recurrences of HCC? A multicenter study by the Japanese Red Cross Hospital Liver Study Group. PLoS One. 2018 Apr 16;13(4):e0194704.
402. Redman JS, Sterling RK. **Treating HCV in a Captive Audience**: Eradication Efforts in the Prison Microenvironment. Am J Gastroenterol. 2018 Jul 24.
403. Reese PP, Abt PL, Blumberg EA, et al. Twelve-month **outcomes after transplant of hepatitis C–infected kidneys** into uninfected recipients. A single-group trial. Ann Intern Med. 2018. [Epub ahead of print]. doi:10.7326/M18-0749
404. Tung CH, Lai NS, Li CY, et al. **Risk of rheumatoid arthritis in patients with hepatitis C virus infection** receiving interferon-based therapy: a retrospective cohort study using the Taiwanese national claims database. BMJ Open. 2018 Jul 23;8(7):e021747.
405. Schütz A, Moser S, Schwanke C, et al. Directly observed therapy of **chronic hepatitis C with ledipasvir/sofosbuvir in people who inject drugs at risk of nonadherence to direct-acting antivirals**. J Viral Hepat. 2018 Jul;25(7):870-873.
406. Trusheim MR, Cassidy WM, Bach PB. **Alternative State-Level Financing for Hepatitis C Treatment-The "Netflix Model".** JAMA. 2018 Oct 29.
407. Ciancio A, et al. Significant improvement of glycemic control in diabetic patients with HCV infection responding to direct-acting antiviral agents. J Med Virol 2018; 90: 320–27.
408. Hum J, et al. Improvement in Glycemic Control of Type 2 Diabetes After Successful Treatment of Hepatitis C Virus. Diabetes Care 2017; 40: 1173–80.
409. Pavone P, et al. Improving of Glycaemic Control Associated with DAAs HCV Treatment Persists at SVR12. HIV Drug Therapy conference; Glasgow, UK; 28–31 October 2016. Poster P273.
410. Dawood AA, et al. Factors Associated with Improved Glycemic Control by Direct-Acting Antiviral Agent Treatment in Egyptian Type 2 Diabetes Mellitus Patients with Chronic Hepatitis C Genotype 4. Diabetes Metab J 2017; 41: 316–31.
411. Lyman A, et al. The Impact of Achieving Virologic Response from Hepatitis C Direct-Acting Antivirals on Diabetes Control. 2016 Fall Meeting of the Ohio College of Clinical Pharmacy (OCCP). Cleveland, OH, USA; 18 November 2016. Abstract 53.
412. Benitez-Gutierrez LM, et al. Rapid drop in serum glucose and hypoglycemia in chronic hepatitis C patients with diabetes during oral HCV therapy. AASLD 2016: The Liver Meeting; San Francisco, CA, USA; 13–17 November 2015. Abstract 1180.
413. LeClerc SB, et al. Viral response to hepatitis C direct-acting antivirals significantly improves diabetes control. AASLD 2016: The Liver Conference; Boston, MA, USA; 11–15 November 2016. Abstract 964.
414. Grennan D. **Treating Hepatitis C**. JAMA. 2018 Dec 4;320(21):2280.
415. Rosenberg ES, Rosenthal EM, Hall EW, et al. Prevalence of **Hepatitis C Virus Infection in US States and the District of Columbia**, 2013 to 2016. JAMA Netw Open. 2018;1(8):e186371.
416. Li W, Jia L, Zhao X, et al. Efficacy and safety of **tenofovir** in preventing mother-to-infant transmission of **hepatitis B virus**: a meta-analysis based on 6 studies from China and 3 studies from other countries. BMC Gastroenterol. 2018 Aug 2;18(1):121.
417. Powell D, Alpert A, Pacula RL. A Transitioning Epidemic: How The **Opioid Crisis Is Driving The Rise In Hepatitis C**. Health Aff (Millwood). 2019 Feb;38(2):287-294.
418. Ramsey SD, Unger JM, Baker LH, et al. Prevalence of Hepatitis B Virus, Hepatitis C Virus, and HIV Infection Among Patients With Newly Diagnosed Cancer From Academic and Community Oncology Practices. JAMA Oncol. 2019 Jan 17.
419. Carrat F, Fontaine H, Dorival C, et al; French ANRS CO22 Hepather cohort. Clinical outcomes in patients with chronic hepatitis C after **direct-acting antiviral treatment**: a prospective cohort study. Lancet. 2019 Feb 11.
420. da Fonseca EM, Shadlen K, Bastos FI. **Brazil's Fight against Hepatitis C** - Universalism, Local Production, and Patents. N Engl J Med. 2019 Feb 14;380(7):605-607.
421. Padidam S, Burke MT, Apple DB, et al. **Association of Ledipasvir-Sofosbuvir Treatment With Uveitis** in Patients Treated for Hepatitis C. JAMA Ophthalmol. 2019 Mar 28.

422. Akiyama MJ, Norton BL, Arnsten JH, et al. Intensive Models of Hepatitis C **Care for People Who Inject Drugs Receiving Opioid Agonist Therapy**: A Randomized Controlled Trial. Ann Intern Med. 2019 Apr 9.
423. Woolley AE, Singh SK, Goldberg HJ, et al. **Heart and lung transplants from HCV-infected donors** to uninfected recipients. N Engl J Med. DOI: 10.1056/NEJMoa1812406.
424. Chhatwal J, Chen Q, Wang X, et al. Assessment of the **Feasibility and Cost of Hepatitis C Elimination in Pakistan**. JAMA Netw Open. 2019 May 3;2(5):e193613.
425. Huang CF, Hung CH, Cheng PN, et al. An open-label, randomized, active control trial of **8 versus 12 weeks of elbasvir/grazoprevir for treatment-naive chronic hepatitis C genotype** 1b patients with mild fibrosis (EGALITE): Impact of baseline viral loads and NS5A resistance-associated substitution. J Infect Dis. 2019 Apr 8.
426. Chen YM, Huang WN, Liao TL, et al. Comparisons of hepatitis C **viral replication in patients with rheumatoid arthritis** receiving tocilizumab, abatacept and tofacitinib therapy. Ann Rheum Dis. 2019 Jun;78(6):849-850.
427. Marks K, Naggie S. **Management of Hepatitis C in 2019**. JAMA. 2019 May 17.
428. Thomas DL. **Global Elimination of Chronic Hepatitis**. N Engl J Med. 2019 May 23;380(21):2041-2050.
429. Lin WY, Lin MS, Weng YH, et al. Association of **Antiviral Therapy With Risk of Parkinson Disease** in Patients With Chronic Hepatitis C Virus Infection. JAMA Neurol. 2019 Jun 5.
430. Marks K, Naggie S. **Management of Hepatitis C in 2019**. JAMA. 2019 May 17.
431. McGlynn AE, Adams JL, Kramer J, et al. Assessing the **safety of direct-acting antiviral agents for hepatitis C.**JAMA Netw Open. 2019;2(6):e194765. doi:10.1001/jamanetworkopen.2019.4765
432. FDA Aug/19 has received reports that the use of **Mavyret, Zepatier, or Vosevi** to treat chronic Hepatitis C in patients with moderate to severe liver impairment has resulted in rare cases of **worsening liver function or liver failure**.
433. Simon TG, Duberg AS, Aleman S, et al. **Lipophilic Statins and Risk for Hepatocellular Carcinoma and Death** in Patients With Chronic Viral Hepatitis: Results From a Nationwide Swedish Population. Ann Intern Med. 2019 Aug 20.
434. Singal AG, Rich NE, Mehta N, et al. **Direct-Acting Antiviral Therapy for HCV Infection** is Associated with Increased Survival in Patients With a History of Hepatocellular Carcinoma. Gastroenterology. 2019 Jul 30.
435. Schwarz KB, Rosenthal P, Murray KF, Honegger JR, Hardikar W, Hague R, Mittal N, Massetto B, Brainard DM, Hsueh CH, Shao J. Ledipasvir− Sofosbuvir for 12 Weeks in Children 3 to< 6 Years Old With Chronic Hepatitis C. Hepatology. 2019 Jun 20.

References – HIV Drug Treatment – www.RxFiles.ca

Other articles of interest:

1. McCabe S, Ma Q, Slish J, Catanzaro L, Sheth N, DiCenzo R, et al. Antiretroviral Therapy Pharmacokinetic Considerations in Patients with Renal or Hepatic Impairment. Clin Pharmacokinet 2008; 47(3)153-172.
2. Spray J, Willett K, Chase D, Sindelar R, Connelly S; Dosage adjustment for hepatic dysfunction based on Child-Pugh score. Am J Health-Syst Pharm 2007; 64: Apr; 690,692
3. Kovacs JA, Masur H. Prophylaxis against opportunistic infections in patients with human immunodeficiency virus infection.N Engl J Med. 2000 May 11;342(19):1416-29.
4. Lopez Bernaldo de Quiros JC, Miro JM, et al. Grupo de Estudio del SIDA 04/98. A randomized trial of the discontinuation of primary and secondary prophylaxis against Pneumocystis carinii pneumonia after highly active antiretroviral therapy in patients with HIV infection. Grupo de Estudio del SIDA 04/98. N Engl J Med. 2001 Jan 18;344(3):159-67.
5. Feldman, Charles. Pneumonia associated with HIV infection. Curr Opin Infect Dis 18:165–170
6. Croxtall JD, Lyseng-Williamson KA, Perry CM. Raltegravir. Drugs 2008: 68(1):131-138
7. Dhasmana DJ, et al. Immune reconstitution inflammatory syndrome in HIV-infected patients receiving antiretroviral therapy: Pathogenesis, clinical manifestations and management. Drugs;68(2)191-208.
8. Deeks SG, Phillips AN. HIV infection, antiretroviral treatment, ageing, and non-AIDS related morbidity. BMJ. 2009 Jan 26;338:a3172. doi: 10.1136/bmj.a3172.
9. Kitahata MM, Gange SJ, Abraham AG, et al.; the NA-ACCORD Investigators. Effect of Early versus Deferred Antiretroviral Therapy for HIV on Survival. N Engl J Med. 2009 Apr 1. [Epub ahead of print]
10. Health Canada June/09 is Warning Canadians Not to Use Clean Testing **HIV Home Test Kit,** or Any Home HIV Test Kit
11. Kovacs JA, Masur H. Evolving health effects of **Pneumocystis**: one hundred years of progress in diagnosis and treatment. JAMA. 2009 Jun 24;301(24):2578-85.
12. Health Canada July/09: Association of TELZIR (fosamprenavir) with a potential increased risk of myocardial infarction. http://www.hc-sc.gc.ca/dhp-mps/medeff/advisories-avis/prof/_2009/telzir_hpc-cps-eng.php
13. Gutiérrez-Valencia A, et al. for the Sociedad Andaluza de Enfermedades Infecciosas. **Stepped-Dose** vs. Full-Dose **Efavirenz** for HIV Infection and Neuropsychiatric Adverse Events: A Randomized Trial. Ann Intern Med. 2009 Jul 6. [Epub ahead of print]
14. Kredo T, Van der Walt JS, Siegfried N, et al. **Therapeutic drug monitoring** of antiretrovirals for people with HIV. Cochrane Database Syst Rev. 2009 Jul 8;(3):CD007268.
15. Rerks-Ngarm S et al. **Vaccination** with ALVAC and AIDSVAX to prevent HIV-1 infection in Thailand. N Engl J Med 2009 Oct 20; [e-pub ahead of print].
16. Aslangul E, Assoumou L, Bittar R, et al. **Rosuvastatin** versus pravastatin in dyslipidemic HIV-1-infected patients (n=88) receiving protease inhibitors: a randomized trial. AIDS. 2009 Oct 15.
17. Landovitz, Raphael J., Currier, Judith S. **Postexposure Prophylaxis** for HIV Infection. N Engl J Med 2009 361: 1768-1775.
18. Centers for Disease Control and Prevention (CDC). Updated interim recommendations — HIV-infected adults and adolescents: Considerations for clinicians regarding 2009 **H1N1** influenza. Oct 21 , 2009. (http://www.cdc.gov/h1n1flu/guidance_HIV.htm)
19. Silverberg MJ, Leyden W, Hurley L, et al. Response to Newly Prescribed Lipid-Lowering Therapy in Patients With and Without HIV Infection. Ann Intern Med. 2009;150:301-313.
20. Pollack TM, McCoy C, Stead W. Clinically significant adverse events from a drug interaction between quetiapine and atazanavir-ritonavir in two patients. Pharmacotherapy. 2009 Nov;29(11):1386-91.
21. Romanelli F, Matheny SC. HIV infection: the role of **primary care**. Am Fam Physician. 2009 Nov 1;80(9):946-52.
22. Bera E, McCausland K, Nonkwelo R, et al. **Birth defects** following exposure to efavirenz-based antiretroviral therapy during pregnancy: a study at a regional South African hospital. AIDS. 2009 Oct 27.
23. Sax PE, Tierney C, et al. the AIDS Clinical Trials Group Study A5202. Abacavir-Lamivudine vs Tenofovir-Emtricitabine for Initial HIV-1 Therapy. N Engl J Med. 2009 Dec 3;361(23):2230-2240. Epub 2009 Dec 1.
24. WHO Guidelines 2009: Adults & adolescents http://www.who.int/hiv/pub/arv/rapid_advice_art.pdf Pregnant women and preventing HIV Infection in infants http://www.who.int/hiv/pub/mtct/rapid_advice_mtct.pdf
    HIV and infant feeding http://www.who.int/child_adolescent_health/documents/hiv_if_principles_recommendations_112009.pdf
25. . Panel on Antiretroviral Guidelines for Adults and Adolescents. Guidelines for the use of antiretroviral agents in HIV-1-infected adults and adolescents. Department of Health and Human Services. December 1, 2009; 1-161. Available at http://aidsinfo.nih.gov/contentfiles/AdultandAdolescentGL.pdf Accessed 7December, 2009
26. French, Neil, Gordon, Stephen B., Mwalukomo, Thandie, et al. A Trial of a **7-Valent Pneumococcal Conjugate Vaccine (Prevnar) in HIV**-Infected Adults. N Engl J Med 2010 362: 812-822
27. Lingappa JR, Baeten JM, Wald A, et al. Partners in Prevention HSV/HIV Transmission Study Team. Daily **aciclovir** for HIV-1 disease progression in people dually infected with HIV-1 and **herpes simplex** virus type 2: a randomised placebo-controlled trial. Lancet. 2010 Mar 6;375(9717):824-33. (acyclovir)
28. Mathers BM, Degenhardt L, Ali H, et al. for the 2009 Reference Group to the UN on HIV and **Injecting Drug Use**. HIV prevention, treatment, and care services for people who inject drugs: a systematic review of global, regional, and national coverage. Lancet. 2010 Feb 26.
29. Hill A, Sawyer W, Gazzard B. Effects of first-line use of nucleoside analogues, efavirenz, and ritonavir-boosted protease inhibitors on lipid levels. HIV Clin Trials 2009;10(1):1-12.
30. Sturt AS, Dokubo EK, Sint TT. Antiretroviral therapy (ART) for treating HIV infection in ART-eligible **pregnant women**. Cochrane Database Syst Rev. 2010 Mar 17;3:CD008440. In ART-eligible pregnant women with HIV infection, ART is a safe and effective means of providing maternal virologic suppression, decreasing infant mortality, and reducing MTCT. Specifically, AZT/3TC/NVP, AZT/3TC/LPV-r, and AZT/3TC/ABC have been shown to decrease MTCT.
31. Del Romero J, Castilla J, Hernando V, et al. Combined antiretroviral treatment and **heterosexual** transmission of HIV-1: cross sectional and prospective cohort study. BMJ. 2010 May 14.
32. Shapiro RL et al. Antiretroviral regimens in pregnancy and **breast-feeding** in Botswana. N Engl J Med 2010 Jun 17; 362:2282.
33. Chasela CS et al. **Maternal or infant antiretroviral drugs** to reduce HIV-1 transmission. N Engl J Med 2010 Jun 17; 362:2271.
34. Perry CM. **Maraviroc**: a review of its use in the management of CCR5-tropic HIV-1 infection. Drugs. 2010 Jun 18;70(9):1189-213.
35. Severe, Patrice, Jean Juste, Marc Antoine, et al. **Early versus** Standard Antiretroviral Therapy for HIV-Infected Adults in Haiti N Engl J Med 2010 363: 257-265.
36. Mar Pujades-Rodriguez; Suna Balkan; Line Arnould; et al.; for the AIDS Working Group of MSF. Treatment Failure and Mortality Factors in Patients Receiving Second-Line HIV Therapy in Resource-Limited Countries JAMA. 2010;304(3):303-312.
37. Thompson MA, Aberg JA, Cahn P, et al. **International AIDS Society-USA**. Antiretroviral treatment of adult HIV infection: **2010** recommendations of the International AIDS Society-USA panel. JAMA. 2010 Jul 21;304(3):321-33.
38. Bateganya M, Abdulwadud OA, Kiene SM. **Home-based HIV voluntary counselling and testing** (VCT) for improving uptake of HIV testing. Cochrane Database Syst Rev. 2010 Jul 7;7:CD006493. Although home-based HIV VCT has the potential to enhance VCT uptake in developing countries, insufficient data exist to recommend large-scale implementation of home-based HIV testing. Further studies are needed to determine if home-based VCT is better than facility-based VCT in improving VCT uptake.
39. Welz T, Childs K, Ibrahim F, Poulton M, Taylor CB, Moniz CF, Post FA. **Efavirenz** is associated with severe **vitamin D deficiency** and increased alkaline phosphatase. AIDS. 2010 Jul 31;24(12):1923-8.
40. Lang S, Mary-Krause M, Cotte L, et al. Impact of Individual Antiretroviral Drugs on the **Risk of Myocardial Infarction** in Human Immunodeficiency Virus-Infected Patients: A Case-Control Study Nested Within the French Hospital Database on HIV ANRS Cohort CO4. Arch Intern Med. 2010 Jul 26;170(14):1228-1238.
41. Spaulding A, Rutherford GW, Siegfried N. Stavudine or zidovudine in **three-drug combination therapy** for initial treatment of HIV infection in antiretroviral-naive individuals. Cochrane Database Syst Rev. 2010 Aug 4;8:CD008651. While ideally future research would focus on direct comparison of standard therapeutic combinations of d4T+3TC+an NNRTI and AZT+3TC+an NNRTI to compare these regimens more directly,

it is unlikely that additional trials will be mounted. Observational studies should focus on understanding outcomes, including toxicity and tolerability, in low- and middle-income countries.
42. O`Brien K, Nixon S, Tynan AM, et al. **Aerobic exercise** interventions for adults living with HIV/AIDS. Cochrane Database Syst Rev. 2010 Aug 4;8:CD001796. Aerobic exercise appears to be safe and may be beneficial for adults living with HIV.
43. Altice FL, Kamarulzaman A, Soriano VV, et al. Treatment of **medical, psychiatric, and substance-use comorbidities** in people infected with HIV who use drugs. Lancet. 2010 Jul 31;376(9738):367-87.
44. Lockman S, Hughes MD, McIntyre J, et al. OCTANE A5208 Study Team. Antiretroviral therapies in **women after single-dose nevirapine exposure**. N Engl J Med. 2010 Oct 14;363(16):1499-509.
45. Palumbo P, Lindsey JC, Hughes MD, et al. Antiretroviral treatment for children with **peripartum nevirapine** exposure. N Engl J Med. 2010 Oct 14;363(16):1510-20.
46. Lavae-Mokhtari M, Mohammad-Khani S, Schmidt RE, Stoll M. [Acute renal failure and hypercalcemia in an AIDS patient on **tenofovir and low-dose vitamin D** therapy with immune reconstitution inflammatory syndrome]. Med Klin (Munich). 2009 Oct 15;104(10):810-3. Epub 2009 Oct 25.
47. Grant Robert M., Lama Javier R., Anderson Peter L., et al. for the iPrEx Study Team. **Preexposure** Chemoprophylaxis for HIV Prevention in **Men Who Have Sex with Men**. Nov, 2010 (10.1056/NEJMoa1011205)
48. WHO-Guidelines for intensified **tuberculosis** case finding and **isoniazid preventive therapy for people living with HIV** in resource constrained setting-WHO-2010 http://whqlibdoc.who.int/publications/2011/9789241500708_eng.pdf
49. Pienaar ED, Young T, Holmes H. Interventions for the prevention and management of **oropharyngeal candidiasis associated with HIV infection** in adults and children. Cochrane Database Syst Rev. 2010 Nov 10;11:CD003940.
50. Spaulding A, Rutherford GW, Siegfried N. **Tenofovir or zidovudine in three-drug combination** therapy with one nucleoside reverse transcriptase inhibitor & one non-nucleoside reverse transcriptase inhibitor for initial treatment of HIV infection in antiretroviral-naïve individuals. Cochrane Database Syst Rev. 2010 Oct 6;10:CD008740. We conclude that for the critical outcomes of virologic response and serious adverse events, initial ART regimens containing TDF are equivalent to those containing AZT. However, TDF is superior to AZT in terms of immunologic response and adherence and less frequent emergence of resistance.
51. ACOG Committee on Practice Bulletins--Gynecology. ACOG Practice Bulletin No. 117: Gynecologic care for women with human immunodeficiency virus. Obstet Gynecol. 2010 Dec;116(6):1492-509.
52. Allers K, Hütter G, Hofmann J, Loddenkemper C, Rieger K, Thiel E, Schneider T. Evidence for the **cure of HIV infection by CCR5{Delta}32/{Delta}32 stem cell transplantation**. Blood. 2010 Dec 8.
53. Humphrey JH, Marinda E, Mutasa K, et al. on behalf of the ZVITAMBO study group. **Mother to child transmission** of HIV among Zimbabwean women who seroconverted postnatally: prospective cohort study. BMJ. 2010 Dec 22;341:c6580. doi: 10.1136/bmj.c6580.
54. Grant Robert M., Lama JR., Anderson PL., et al. for the **iPrEx** Study Team. **Preexposure Chemoprophylaxis for HIV Prevention in Men Who Have Sex with Men**. N Engl J Med 2010; 363:2587-2599.
55. Long EF, Brandeau ML, Owens DK. Cost-Effectiveness and Population Outcomes of Expanded **HIV Screening** and Antiretroviral Treatment in the United States. Ann Intern Med. 2010 Dec 21;153(12):778-89.
56. Singh S, Willig JH, Mugavero MJ, et al. Comparative Effectiveness and Toxicity of **Statins** Among HIV-Infected Patients. Clin Infect Dis. 2011 Feb;52(3):387-95.
57. Wawer MJ, Tobian AA, Kigozi G, et al. Effect of **circumcision of HIV-negative men** on transmission of human papillomavirus to HIV-negative women: a randomised trial in Rakai, Uganda. Lancet. 2011 Jan 6.
58. Jones CE., Naidoo S, De Beer C, et al. Maternal HIV Infection and **Antibody Responses Against Vaccine-Preventable Diseases** in Uninfected Infants. JAMA. 2011;305(6):576-584.doi:10.1001/jama.2011.100.
59. Chu C, Selwyn PA. Diagnosis and initial **management of acute HIV infection**. Am Fam Physician. 2010 May 15;81(10):1239-44.
60. Chu C, Selwyn PA. **Complications of HIV Infection**: A Systems-Based Approach. Am Fam Physician. 2011 Feb 15;83(4):395-406.
61. Taege A. Seek and treat: **HIV update 2011**. *Cleveland Clinic Journal of Medicine* 2011; 78(2):95-100; doi:10.3949/ccjm.78gr.10003
62. Kaufmann GR, Elzi L, Weber R, et al. Swiss HIV Cohort Study. Interruptions of cART limits CD4 T-cell recovery and increases the risk for opportunistic complications and death. AIDS.2011Feb 20;25(4):441 451.
63. FDA Mar/11: serious health problems that have been reported in premature babies receiving Kaletra (lopinavir/ritonavir) oral solution. **Kaletra** oral solution contains alcohol & propylene glycol.
64. Garvey L, Winston A, Walsh J, et al; For the UK Collaborative HIV Cohort (CHIC) Study. Antiretroviral therapy **CNS penetration** and HIV-1-associated CNS disease. Neurology. 2011 Feb 22;76(8):693-700.
65. Young B, Dao CN, Buchacz K, Baker R, Brooks JT; the HIV Outpatient Study (HOPS) Investigators. **Increased Rates of Bone Fracture** among HIV-Infected Persons in the HIV Outpatient Study (HOPS) Compared with the US General Population, 2000-2006. Clin Infect Dis. 2011 Mar 10.
66. McComsey GA, Tebas P, Shane E, et al. **Bone disease in HIV infection**: a practical review and recommendations for HIV care providers. Clin Infect Dis. 2010 Oct 15;51(8):937-46.
67. Koblic, Paul M., Gold, Wayne L., la Porte, Charles J.L., Lee, Todd C. Medication-based **urolithiasis and atazanavir**. CMAJ 2011 0: cmaj.100019
68. Daar Eric S., Tierney Camlin, Fischl Margaret A., et al. and for the AIDS Clinical Trials Group Study A5202 Team. Atazanavir Plus Ritonavir or Efavirenz as Part of a 3-Drug Regimen for Initial Treatment of HIV Type-1: A Randomized Trial. Ann Intern Med E-316published ahead of print February 14, 2011.
69. Launay Odile, van der Vliet Diane, Rosenberg Arielle R., et al. Safety and Immunogenicity of 4 Intramuscular Double Doses and 4 Intradermal Low Doses vs Standard **Hepatitis B Vaccine** Regimen in Adults With HIV-1: A Randomized Controlled Trial. for the ANRS HB03 VIHVAC-B Trial. JAMA. 2011;305(14):1432-1440.doi:10.1001/jama.2011.351
70. Jansman FG, Reyners AK, van Roon EN, et al; Scientific Institute for Dutch Pharmacists (WINAp), the Dutch Society for Medical Oncology (NVMO); Dutch Society of Clinical Pharmacology and Biopharmacy (NVKF&B). Consensus-Based Evaluation of Clinical Significance and Management of **Anticancer Drug Interactions**. Clin Ther. 2011 Apr 1.
71. Mussini C, Cossarizza A, Sabin C, et al, of CASCADE Collaboration. **Decline of CD4+ T cell count before** start of therapy and immunological response to treatment in antiretroviral-naive individuals. AIDS. 2011 Mar 15.
72. Kalichman SC, Cherry C, Kalichman MO, et al. **Integrated behavioral intervention** to improve HIV/AIDS treatment adherence and reduce HIV transmission. Am J Public Health. 2011 Mar;101(3):531-8.
73. El-Bassel Nabila; Jemmott III John B., Landis J Richard; et al. for the National Institute of Mental Health Multisite HIV/STD Prevention Trial for African-American Couples Group. **Intervention to Influence Behaviors** Linked to Risk of Chronic Diseases: A Multisite Randomized Controlled Trial With African-American HIV-Serodiscordant Heterosexual Couples. Arch Intern Med. 2011;171(8):728-736.
74. Butt AA.; Chang Chung-Chou; Kuller L; et al. **Risk of Heart Failure** With Human Immunodeficiency Virus in the Absence of Prior Diagnosis of Coronary Heart Disease. Arch Intern Med. 2011;171(8):737-743.
75. Rudek MA, Flexner C, Ambinder RF. Use of **antineoplastic agents in patients with cancer who have HIV**/AIDS. Lancet Oncol. 2011 May 12.
76. Cohen Myron S, Shaw George M., McMichaelet Andrew J. al. **Acute HIV-1 Infection**. N Engl J Med 2011; 364:1943-1954.
77. Zhang F, Dou Z, Ma Y, et al. Effect of **earlier initiation of antiretroviral treatment** and increased treatment coverage on HIV-related mortality in China: a national observational cohort study. Lancet Infect Dis 2011: published online May 19. DOI:10.1016/S1473-3099(11)70097-4.
78. Venter W.D. Francois, Ndung'u Thumbi, Karim QA. Case 15-2011 — A 19-Year-Old South African Woman with Headache, Fatigue, and Vaginal Discharge. (Acute HIV & SDT) N Engl J Med 2011; 364:1956-1964.
79. Sutcliffe CG, Moss WJ. Do children infected with **HIV receiving HAART need to be revaccinated**? Lancet Infect Dis. 2010 Sep;10(9):630-42.
80. Dieffenbach CW, Fauci AS. **Thirty Years of HIV** and AIDS: Future Challenges and Opportunities. Ann Intern Med. 2011 May 31.
81. Anglemyer A, et al. Antiretroviral therapy for **prevention of HIV transmission in HIV discordant couples**. Cochrane Database of Systematic Reviews 2011, Issue 5. Art.No.:CD009153.
82. Reust CE. **Common Adverse Effects** of Antiretroviral Therapy for HIV Disease. Am Fam Physician. 2011 Jun 15;83(12):1443-1451.
83. Bhattacharya Sangeeta Das, Bhattacharyya Subhasish, Do children receiving **HAART need to be revaccinated**?, The Lancet Infectious Diseases, Volume 11, Issue 6, June 2011.
84. Costello Daniel J., Gonzalez R. Gilberto, Frosch Matthew P.. Case 18-2011 — A 35-Year-Old HIV-Positive Woman with Headache and Altered Mental Status. (**Neuro-IRIS: Immune reconstitution Inflammatory syndrome**). N Engl J Med 2011; 364:2343-2352.
85. **WHO 2011**: Prevention and Treatment of HIV and Other Sexually Transmitted Infections (STIs) among **Men who have Sex with Men and Transgender** People: Recommendations for a Public Approach is at www.who.int/hiv/pub/guidelines/msm_guidelines2011/en . http://whqlibdoc.who.int/publications/2011/9789241501750_eng.pdf
86. Flateau Clara, Le Loup Guillaume, Pialoux Gilles. Consequences of **HIV infection on malaria** and therapeutic implications: a systematic review. Lancet Infect Dis 2011; 11: 541–56.
87. Simon Albane, Warszawski Josiane, Kariyawasam Dulanjalee, et al., for the ANRS French Perinatal Cohort Study Group. Association of Prenatal and Postnatal Exposure to

Lopinavir-Ritonavir and Adrenal Dysfunction Among Uninfected Infants of HIV-Infected Mothers. JAMA. 2011;306(1):70-78.doi:10.1001/jama.2011.915
88. de BM, Viechtbauer W, Schaalma HP, Kok G, Abraham C, Hospers HJ. Standard care impact on effects of highly active antiretroviral therapy **adherence interventions**: A meta-analysis of randomized controlled trials. Arch Intern Med. 2010 Feb 8;170(3):240-50.
89. Cohen MS, Chen YQ, McCauley M, et al. **Prevention** of HIV-1 infection with early antiretroviral therapy (**HPTN 052**). N Engl J Med 2011. DOI: 10.1056/NEJMoa1105243.
90. Molina J-M, Cahn P, Grinsztejn B, et al, on behalf of the ECHO study group. **Rilpivirine** versus efavirenz with tenofovir and emtricitabine in treatment-naive adults infected with HIV-1 (**ECHO**): a phase 3 randomised double-blind active-controlled trial. Lancet 2011; 378: 238–46.
91. Cohen CJ, Andrade-Villanueva J, Clotet B, et al, on behalf of the THRIVE study group. **Rilpivirine** versus efavirenz with two background nucleoside or nucleotide reverse transcriptase inhibitors in treatment-naive adults infected with HIV-1 (**THRIVE**): a phase 3, randomised, non-inferiority trial. Lancet 2011; 378: 229–37.
92. Allers K, Hütter G, Hofmann J, et al. Evidence for the cure of HIV infection by **CCR5Δ32/Δ32 stem cell transplantation**. Blood. 2011 Mar 10;117(10):2791-9.
Hütter G, Nowak D, Mossner M, et al. Long-term control of HIV by CCR5 Delta32/Delta32 stem-cell transplantation. N Engl J Med. 2009 Feb 12;360(7):692-8.
93. Tanser F, Bärnighausen T, Hund L, et al. Effect of **concurrent sexual partnerships** on rate of new HIV infections in a high-prevalence, rural South African population: a cohort study. Lancet. 2011 Jul 16;378(9787):247-55.
94. Powers KA, Ghani AC, Miller WC, et al. The role of **acute and early HIV infection** in the spread of HIV and implications for transmission prevention strategies in Lilongwe, Malawi: a modelling study. Lancet. 2011 Jul 16;378(9787):256-68.
95. Abdool Karim SS, Kashuba A, Werner L, Abdool Karim Q. Drug concentrations after topical and oral antiretroviral pre-exposure prophylaxis: implications for HIV prevention in women. Lancet 2011; 378: 279–81.
96. Rackal JM, Tynan AM, Handford CD, et al. **Provider training and experience for people living with HIV/AIDS**. Cochrane Database Syst Rev. 2011 Jun 15;6:CD003938. The results demonstrate improved medical outcomes when treated by a provider with more training/expertise in HIV/AIDS care in the outpatient (clinic) setting.
97. Sigaloff KC, Calis JC, Geelen SP, et al. **HIV-1-resistance**-associated mutations after failure of first-line antiretroviral treatment among **children** in resource-poor regions: a systematic review. Lancet Infect Dis. 2011 Aug 25.
98. Royal College of Obstetricians and Gynaecologists (RCOG). Management of **HIV in pregnancy**. London (UK): Royal College of Obstetricians and Gynaecologists (RCOG); 2010 Jun. http://www.rcog.org.uk/files/rcog-corp/GT39HIVPregnancy0610.pdf
99. Health Canada Sep/11 **ACCU-METRICS, has been advertising HIV home test kits** for sale via their website, Health Canada would like to remind Canadians that there are currently no HIV test kits that have been authorized for home use in Canada.
100. Sacktor N, Miyahara S, Deng L, et al. On behalf of ACTG A5235 team. Minocycline treatment for HIV-associated cognitive impairment: Results from a randomized trial. Neurology. 2011 Sep 7.
101. Marine L, Castro P, Enriquez A, et al. **Four-limb acute ischemia induced by ergotamine** in an AIDS patient treated with protease inhibitors. Circulation. 2011 Sep 20;124(12):1395-7.
102. Libman H. **Screening for HIV** infection: a healthy, "low-risk" 42-year-old man. JAMA. 2011 Aug 10;306(6):637-44.
103. Eron JJ Jr, Rockstroh JK, Reynes J, et al, for the QDMRK Investigators. **Raltegravir once daily or twice daily** in previously untreated patients with HIV-1: a randomised, active-controlled, phase 3 non-inferiority trial. Lancet Infect Dis 2011; published online Sept 19.
104. Writing Committee for the **CASCADE** Collaboration. **Timing of HAART initation** and clinical outcomes in human immunodeficiency virus type 1 seroconverters. Arch Intern Med. 2011;171(17):1560-1569.
105. Laurent C, Kouanfack C, Laborde-Balen G, et al, for the Stratall ANRS 12110/ESTHER study group. **Monitoring of HIV viral loads, CD4 cell counts, and clinical assessments versus** clinical **monitoring alone** for antiretroviral therapy in rural district hospitals in Cameroon (Stratall ANRS 12110/ESTHER): a randomised non-inferiority trial. Lancet Infect Dis 2011
106. Jani IV, Sitoe NE, Alfai ER, et al. Effect of **point-of-care CD4 cell count tests** on retention of patients and rates of antiretroviral therapy initiation in primary health clinics: an observational cohort study. Lancet. 2011 Sep 23.
107. In the Clinic. **Management of Newly Diagnosed HIV Infection**. Annals of Internal Medicine 4 October 2011. **Updated July 2017.**
108. Heffron R, Donnell D, Rees H, et al. Use of **hormonal contraceptives** (esp injectables) **& risk of HIV-1 transmission**: a prospective cohort study. Lancet Infect Dis 2011; online Oct 4, 2011.
109. Wainberg MA, Zaharatos GJ, Brenner BG. Development of **antiretroviral drug resistance**. N Engl J Med. 2011 Aug 18;365(7):637-46.
110. Hamers RL, Wallis CL, Kityo C, et al.for PharmAccess African Studies to Evaluate Resistance (PASER). **HIV-1 drug resistance** in antiretroviral-naive individuals in sub-Saharan Africa after rollout of antiretroviral therapy: a multicentre observational study. Lancet Infect Dis. 2011 Oct;11(10):750-9.
111. Burgard M, Blanche S, Jasseron C, et al. Agence Nationale de Recherche sur le SIDA et les Hepatites virales French Perinatal Cohort. Performance of HIV-1 DNA or HIV-1 RNA Tests for **Early Diagnosis of Perinatal** HIV-1 Infection during Anti-Retroviral Prophylaxis. J Pediatr. 2011 Aug 23.
112. Mills EJ, Bakanda C, Birungi J, et al. **Life expectancy** of persons receiving combination antiretroviral therapy in low-income countries: a cohort analysis from Uganda. Ann Intern Med. 2011 Aug 16;155(4):209-16.
113. HIV services--what role for **primary care**? Drug Ther Bull. 2011 Aug;49(8):85.
114. May M, Gompels M, Delpech V, et al. Impact of **late diagnosis** and treatment on life expectancy in people with HIV-1: UK Collaborative HIV Cohort (UK CHIC) Study. BMJ 2011;343:d6016.
115. Berretta Massimiliano, Garlassi Elisa, Cacopardo Bruno,et al. **Hepatocellular Carcinoma** in HIV-Infected Patients: Check Early, Treat Hard. The Oncologist 2011; 16:1258-1269.
116. Parkes-Ratanshi R, Wakeham K, Levin J, et al, on behalf of the **Cryptococcal** Trial Team. Primary prophylaxis of cryptococcal disease with fl uconazole in HIV-positive Ugandan adults: a double-blind, randomised, placebo-controlled trial. Lancet Infect Dis 2011; published online Oct 7. DOI:10.1016/S1473-3099(11)70245-6.
117. Pursuing Later Treatment Options II (**PLATO II**) project team for the Collaboration of Observational HIV Epidemiological Research Europe (COHERE). Risk of **triple-class virological failure** in children with HIV: a retrospective cohort study. Lancet 2011; 377: 1580–87.
118. van Lunzen J, Maggiolo F, Arribas JR, et al. Once daily dolutegravir (S/GSK1349572) in combination therapy in antiretroviral-naive adults with HIV: planned interim 48 week results from SPRING-1, a dose-ranging, randomised, phase 2b trial. Lancet Infect Dis 2011; online Oct 21/11.
119. Abdool Karim SS et al. Integration of antiretroviral therapy with **tuberculosis** treatment. N Engl J Med 2011 Oct 20; 365:1492.
120. Havlir DV et al. Timing of antiretroviral therapy for HIV-1 infection and **tuberculosis**. (A5221) N Engl J Med 2011 Oct 20; 365:1482.
121. Blanc F-X et al. Earlier versus later start of antiretroviral therapy in HIV-infected adults with **tuberculosis**. (**Camelia**) N Engl J Med 2011 Oct 20; 365:1471.
122. Török ME and Farrar JJ. When to start antiretroviral therapy in HIV-associated **tuberculosis**. N Engl J Med 2011 Oct 20; 365:1538.
123. Rekart ML, Macintosh J. **Acute primary HIV** infection. CMAJ. 2011 Aug 9;183(11):1280.
124. Abdool Karim SS, Naidoo K, Grobler A, et al. Timing of initiation of antiretroviral drugs during tuberculosis therapy. (**SAPIT**) N Engl J Med 2010;362:697-706.
125. Ng Marie, Gakidou Emmanuela, Levin-Rector Alison, et al, Assessment of **population-level effect of Avahan**, an HIV-prevention initiative in India, The Lancet, Available online 10 October 2011
126. Marti-Carvajal AJ, Sola I, Pena-Marti GE, et al. Treatment for **anemia** in people with **AIDS**. Cochrane Database Syst Rev. 2011 Oct 5;(10):CD004776.
127. Panel on Antiretroviral Therapy and Medical Management of HIV-Infected Children. **Guidelines** for the use of antiretroviral agents in **pediatric HIV** infection. Bethesda (MD): U.S. Department of Health and Human Services; 2011 Aug 11. http://aidsinfo.nih.gov/contentfiles/PediatricGuidelines.pdf

Panel on Antiretroviral Therapy and Medical Management of HIV-Infected Children. Guidelines for the use of antiretroviral agents in **pediatric HIV** infection. Nov 5 , **2012**. (http://aidsinfo.nih.gov/contentfiles/lvguidelines/pediatricguidelines.pdf)

128. Panel on Treatment of HIV-Infected Pregnant Women and Prevention of Perinatal Transmission. Recommendations for use of **antiretroviral drugs in pregnant HIV-1-infected women** for maternal health & interventions to reduce perinatal HIV-1 transmission in United States. Rockville: Public Health Service Task Force; 2011Sep14. http://aidsinfo.nih.gov/contentfiles/PerinatalGL.pdf
Panel on Treatment of HIV-Infected Pregnant Women and Prevention of Perinatal Transmission. Recommendations for use of antiretroviral drugs in pregnant HIV-1-infected women for maternal health and interventions to reduce perinatal HIV transmission in the United States. Rockville (MD): Public Health Service Task Force; 2012 Jul 31. http://aidsinfo.nih.gov/contentfiles/lvguidelines/perinatalgl.pdf
129. Hazra R, Cohen RA, Gonin R, et al. for the NISDI **Pediatric** Study Group 2011. **Lipid Levels** in the Second Year of Life among HIV-infected and HIV-exposed Uninfected Latin American Children. AIDS. 2011 Oct 15.
130. Mermin J, Ekwaru JP, Were W, et al. **Utility of routine viral load, CD4 cell count, and clinical monitoring** among adults with HIV receiving antiretroviral therapy in Uganda: randomised trial. BMJ. 2011 Nov 9
131. Kahn JG, Marseille E, Moore D, et al. **CD4 cell count and viral load monitoring** in patients undergoing antiretroviral therapy in Uganda: cost effectiveness study. BMJ. 2011 Nov 9;343:d6884.
132. Bärnighausen T, Chaiyachati K, Chimbindi N, et al. Interventions to **increase antiretroviral adherence** in sub-Saharan Africa: a systematic review of evaluation studies. Lancet Infect Dis. 2011 Oct 24.
133. Uyei J, Coetzee D, Macinko J, et al. **Integrated delivery of HIV and tuberculosis** services in sub-Saharan Africa: a systematic review. Lancet Infect Dis. 2011 Nov;11(11):855-67.
134. Committee on Pediatric AIDS. Adolescents and HIV Infection: The Pediatrician's Role in Promoting **Routine Testing**. Pediatrics. 2011 Nov;128(5):1023-9.
135. Kakalia S, Sochett EB, Stephens D, et al. **Vitamin d supplementation** and CD4 count in children infected with human immunodeficiency virus. J Pediatr. 2011 Dec;159(6):951-7.
136. Hamers RL, Schuurman R, Sigaloff KCE, et al. Effect of **pretreatment HIV-1 drug resistance** on immunological, virological, and drug-resistance outcomes of first-line antiretroviral treatment in sub-Saharan Africa: a multicentre cohort study. Lancet Infect Dis 2011 online Oct 28.
137. Whitmore SK et al. Correlates of **Mother-to-Child Transmission** of HIV in the United States and Puerto Rico. Pediatrics. 2011 Dec 5.
138. Ota E, Wariki WM, Mori R, et al. Behavioral interventions to reduce the transmission of **HIV infection among sex workers** and their clients in high-income countries. Cochrane Database Syst Rev. 2011 Dec 7;12:CD006045. There is limited evidence from randomised controlled trials for the effectiveness of behavioural interventions to reduce the transmission of HIV infection among sex workers and their clients in high-income countries.
139. Coovadia HM, Brown ER, Fowler MG, et al. Efficacy and safety of an extended nevirapine regimen in infant children of breastfeeding mothers with HIV-1 infection for prevention of postnatal HIV-1 transmission (HPTN 046): a randomised, double-blind, placebo-controlled trial. Lancet. 2011 Dec 22.
140. d'Almeida KW, Kierzek G, de Truchis P, et al. Modest public health impact of nontargeted human immunodeficiency virus screening in 29 emergency departments [published online October 24, 2011]. Arch Intern Med. 2012;172(1):12-20.
141. Birbeck GL, French JA, Perucca E, et al. Evidence-based guideline: **Antiepileptic drug selection for people with HIV/AIDS**: Report of the Quality Standards Subcommittee of the American Academy of Neurology (**AAN**) and the Ad Hoc Task Force of the Commission on Therapeutic Strategies of the International League Against Epilepsy.Neurology. 2012 Jan 10;78(2):139-45.
142. Pant Pai N, Balram B, Shivkumar S, et al. Head-to-head comparison of accuracy of a **rapid point-of-care HIV test** with oral versus whole-blood specimens: a systematic review and meta-analysis. Lancet Infect Dis 2012.
143. Henderson DK. Management of **needlestick injuries**: a house officer who has a needlestick. JAMA. 2012 Jan 4;307(1):75-84.
144. Wawer MJ, Makumbi F, Kigozi G, et al. **Circumcision** in HIV-infected men and its effect on HIV transmission to female partners in Rakai, Uganda: a randomised controlled trial. Lancet. 2009;374(9685):229-237.
145. Tobian AA, Kong X, Wawer MJ, et al. **Circumcision** of HIV-infected men and transmission of human papillomavirus to female partners: analyses of data from a randomised trial in Rakai, Uganda. Lancet Infect Dis. 2011;11(8):604-612.
146. Patel SM, Patel SS, Myers R. A 37-year-old man with a chronic cough. **(HIV & Coccidioides**). Cleveland Clinic Journal of Medicine 2012; 79(2):141-150;doi:10.3949/ccjm.79a.11010.
147. Berg K, Litwin A, Li X, et al. Lack of sustained improvement in **adherence** or viral load following a directly observed antiretroviral therapy intervention. Clin Infect Dis. 2011Nov;53(9):936-43.
148. FDA Feb/12 notified healthcare professionals and patients that drug interactions between the hepatitis C virus (HCV) protease inhibitor Victrelis (**boceprevir**) and certain **ritonavir-boosted** human immunodeficiency virus (HIV) protease inhibitors (atazanavir, lopinavir, darunavir) can potentially reduce the effectiveness of these medicines when they are used together.
149. Spooner LM, Olin JL. **Tesamorelin**: A Growth Hormone-Releasing Factor Analogue for HIV-Associated Lipodystrophy (February). Ann Pharmacother. 2012 Jan 31.
150. WHO 2012: **Hormonal contraceptivion** & HIV http://www.who.int/reproductivehealth/topics/family_planning/Hormonal_contraception_and_HIV.pdf
151. Mugo NR et al. Increased risk of HIV-1 transmission in pregnancy: A prospective study among African HIV-1-**serodiscordant couples**. *AIDS* 2011 Sep 24; 25:1887.
152. Baird SJ, Garfein RS, McIntosh CT, et al. Effect of a **cash transfer** programme for schooling on prevalence of HIV and herpes simplex type 2 in Malawi: a cluster randomised trial. Lancet 2012.
153. Frassetto L, Kohlstadt I. Treatment and prevention of **kidney stones**: an update. Am Fam Physician. 2011 Dec 1;84(11):1234-42.
154. Horvath T, Azman H, Kennedy GE, Rutherford GW. **Mobile phone text messaging** for promoting **adherence** to antiretroviral therapy in patients with HIV infection. *Cochrane Database of Systematic Reviews* 2012, Issue 3. Art. No.: CD009756. DOI: 10.1002/14651858.CD009756. There is high-quality evidence from the two RCTs that mobile phone text-messaging at weekly intervals is efficacious in enhancing adherence to ART, compared to standard care. There is high quality evidence from one trial that weekly mobile phone text-messaging is efficacious in improving HIV viral load suppression.
155. Kuhn L, Coovadia A, Strehlau R, et al. **Switching children** previously exposed to **nevirapine** to nevirapine-based treatment after initial suppression with a protease-inhibitor-based regimen: long-term follow-up of a randomised, open-label trial. Lancet Infect Dis 2012
156. Reynolds SJ, Makumbi F, Newell K, et al. Effect of daily **acyclovir** on HIV disease progression in individuals in Rakai, Uganda, **co-infected with HIV-1 and herpes simplex virus type 2**: a randomised, double-blind placebo-controlled trial. Lancet Infect Dis 2012; online March 19.
157. Ludema C, Cole SR, Poole C, Chu H, Eron JJ. Meta-analysis of randomized trials on the association of prophylactic acyclovir and HIV-1 viral load in individuals coinfected with herpes simplex virus-2. AIDS 2011; 25: 1265–69.
158. Mugwanya K, Baeten JM, Mugo NR, Irungu E, Ngure K, Celum C. High-dose valacyclovir HSV-2 suppression results in greater reduction in plasma HIV-1 levels compared with standard dose acyclovir among HIV-1/HSV-2 coinfected persons: a randomized, crossover trial. J Infect Dis 2011; 204: 1912–17.
159. Mayer KH et al. **Raltegravir, tenofovir DF, and emtricitabine for postexposure prophylaxis** to prevent the sexual transmission of HIV: Safety, tolerability and adherence. J Acquir Immune Defic Syndr 2012 Apr 1; 59:354.
160. Baral S, Beyrer C, et al. Burden of **HIV among female sex workers** in low-income and middle-income countries: systematic review and meta-analysis. Lancet Infect Dis 2012: online March 15
161. Haynes BF, Gilbert PB, McElrath MJ, et al. Immune-correlates analysis of an **HIV-1 vaccine** efficacy trial. N Engl J Med 2012;366:1275-86.
162. Horwood C, Vermaak K, Butler L, et al. Elimination of paediatric HIV in KwaZulu-Natal, South Africa: large-scale assessment of **interventions for the prevention of mother-to-child** transmission. Bull World Health Organ. 2012 Mar 1;90(3):168-75.
163. Grijsen ML, Steingrover R, Wit FWNM, et al. **No Treatment versus 24 or 60 Weeks** of Antiretroviral Treatment during Primary HIV Infection: The Randomized **Primo-SHM** Trial. 2012 PLoS Med 9(3): e1001196.

164. Jamieson DJ, Chasela CS, Hudgens MG, et al, for the **BAN** study team. **Maternal and infant antiretroviral regimens** to prevent postnatal HIV-1 transmission: 48-week follow-up of the BAN randomised controlled trial. Lancet 2012
165. Siberry GK, Williams PL, Mendez H, et al. for the Pediatric HIVAIDS Cohort Study (PHACS). Safety of **tenofovir use during pregnancy**: early growth outcomes in HIV-exposed uninfected infants. AIDS. 2012 Feb 29.
166. Kenyon C, Mfolozi S, Croxford R, et al. Severe **efavirenz-induced vacuolar axonopathy** complicated by fatal aspiration pneumonia. Br J Clin Pharmacol. 2012 Apr 18.
167. Juusola JL, Brandeau ML, Owens DK, Bendavid E. The Cost-Effectiveness of **Preexposure Prophylaxis for HIV** Prevention in the United States in **Men Who Have Sex With Men**. Ann Intern Med. 2012 Apr 17;156(8):541-50.
168. Walker NF, Clark SO, Oni T, et al. **Doxycycline** and HIV Infection Suppress Tuberculosis-induced Matrix Metalloproteinases. Am J Respir Crit Care Med. 2012 May 1;185(9):989-97.
169. Khalili H, Farasatinasab M, et al. **Efavirenz severe hypersensitivity** reaction: case report and rapid desensitization protocol development. Ann Pharmacother. 2012 May;46(5):e12.
170. Nielsen-Saines K, Komarow L, Cu-Uvin S, et al; for the ACTG 5190/PACTG 1054 Study Team. **Infant Outcomes After Maternal** Antiretroviral Exposure in Resource-Limited Settings. Pediatrics. 2012 May 14.
171. Simms V, Higginson IJ, Harding R. **Integration of palliative care** throughout HIV disease. Lancet Infect Dis. 2012 Jun 8.
172. Thompson MA, Mugavero MJ, Amico KR, et al. Guidelines for Improving Entry Into and Retention in Care and Antiretroviral **Adherence** for Persons With HIV: Evidence-Based Recommendations From an International Association of Physicians in AIDS Care Panel. Ann Intern Med. 2012 Jun5;156(11):817-833.
173. Nielsen-Saines K, Komarow L, Cu-Uvin S, et al; for the ACTG 5190/PACTG 1054 Study Team. **Infant Outcomes After Maternal Antiretroviral Exposure** in Resource-Limited Settings. Pediatrics. 2012 Jun;129(6):e1525-e1532.
174. Bogoch II, Scully EP, Zachary KC. Antiretroviral medication for **preventing** HIV infection in **nonoccupational settings**. CMAJ. 2012 May 28. (postexposure, pre-exposure)
175. Bendavid E, Holmes CB, Bhattacharya J, Miller G. **HIV Development Assistance** and Adult Mortality in Africa HIV Aid and Adult Mortality in Africa. JAMA. 2012 May 16;307(19):2060-7.
176. Robb ML, Rerks-Ngarm S, Nitayaphan S, et al. Risk behaviour and time as covariates for efficacy of the **HIV vaccine regimen ALVAC-HIV** (vCP1521) and AIDSVAX B/E: a post-hoc analysis of the Thai phase 3 eff cacy trial RV 144. Lancet Infect Dis 2012; online May 30.
177. Yehia BR et al. Antiretroviral **medication errors** remain high but are quickly corrected among hospitalized HIV-infected adults.Clin Infect Dis 2012 May 31.
178. Hamers RL, Kityo C, Lange JM, et al. Global threat from drug **resistant HIV** in sub-Saharan Africa. BMJ. 2012 Jun 18;344:e4159.
179. Nielsen-Saines K, Watts DH, Veloso VG, et al; NICHD HPTN 040/PACTG 1043 Protocol Team. Three **postpartum antiretroviral regimens** to prevent intrapartum HIV infection. N Engl J Med. 2012 Jun 21;366(25):2368-79.
180. Violari A, Lindsey JC, Hughes MD, et al. **Nevirapine versus ritonavir-boosted lopinavir** for HIV-infected children. N Engl J Med. 2012 Jun 21;366(25):2380-9.
181. Mulligan K, Harris DR, Emmanuel P, et al; for the ATN 021 Protocol team. **Low Bone Mass** in Behaviorally HIV-Infected Young Men on Antiretroviral Therapy: Adolescent Trials Network (ATN) Study 021B. Clin Infect Dis. 2012 May 9.
182. FDA Jul/12: Food and Drug Administration has approved the first over-the-counter HIV test, the **OraQuick** test allows Americans to check themselves in the privacy of their homes for the virus that causes AIDS.
183. Sax PE, DeJesus E, Mills A, et al;GS-US-236-0102 study team. Co-formulated **elvitegravir, cobicistat, emtricitabine, and tenofovir** versus co-formulated efavirenz, emtricitabine, and tenofovir for initial treatment of HIV-1 infection: a randomised, double-blind, phase 3 trial, analysis of results after 48 weeks. Lancet. 2012 Jun 30;379(9835):2439-48.
184. Cohen CR, Lingappa JR, Baeten JM, et al. **Bacterial Vaginosis** Associated with Increased Risk of Female-to-Male HIV-1 Transmission: A Prospective Cohort Analysis among African Couples. PLoS Med. 2012 Jun;9(6):e1001251.
185. Crawford KW, Ripin DH, Levin AD, et al; for the participants of The Conference on Antiretroviral Drug Optimization. **Optimising the manufacture, formulation, and dose** of antiretroviral drugs for more cost-efficient delivery in resource-limited settings: a consensus statement. Lancet Infect Dis. 2012 Jul;12(7):550-560.
186. Sax PE, DeJesus E, Mills A, et al, for the GS-US-236-0102 study team. Co-formulated **elvitegravir, cobicistat, emtricitabine, and tenofovir** versus co-formulated efavirenz, emtricitabine, and tenofovir for initial treatment of HIV-1 infection: a randomised, double-blind, phase 3 trial, analysis of results after 48 weeks. Lancet 2012; 379: 2439–48.
187. DeJesus E, Rockstroh JK, Henry K, et al, for the GS-236-0103 study team. Co-formulated **elvitegravir, cobicistat, emtricitabine, and tenofovir** disoproxil fumarate versus ritonavir-boosted atazanavir plus co-formulated emtricitabine and tenofovir disoproxil fumarate for initial treatment of HIV-1 infection: a randomised, double-blind, phase 3, non-inferiority trial. Lancet 2012; 379: 2429–38.
188. Tan IL, Smith BR, von Geldern G, et al. HIV-associated **opportunistic infections of the CNS**. Lancet Neurol. 2012 Jul;11(7):605-17.
189. Pearce D, Ani C, et al. Comparison of In-Hospital Mortality From Acute **Myocardial Infarction** in HIV Sero-Positive Versus Sero-Negative Individuals. Am J Cardiol. 2012 Jul 2.
190. Canadian HIV Pregnancy Planning Guideline Development Team Core Working Group. **Canadian HIV pregnancy planning guidelines**. J Obstet Gynaecol Can 2012;34:575–90. www.sogc.org/guidelines/documents/gui278CPG1206E.pdf
191. Okwundu CI, Uthman OA, Okoromah CAN. **Antiretroviral pre-exposure prophylaxis (PrEP)** for preventing HIV in high-risk individuals. Cochrane Database of Systematic Reviews 2012, Issue 7. Art. No.: CD007189. Presently there is no reliable evidence to support the use of any antiretroviral agent for HIV chemoprophylaxis.The value of chemoprophylaxis for HIV prevention cannot be assessed on the basis of the included trial. The result was not statistically significant and, moreover, the trial was not completed as planned; therefore, the use of antiretroviral agents for HIV chemoprophylaxis cannot be recommended at present. To assess the value of antiretroviral agents for HIV chemoprophylaxis, we advocate well-conducted trials with the statistical power to answer questions about PrEP efficacy and safety in various populations and risk groups. These trials also should evaluate other important issues of concern, such as drug safety, adherence, drug resistance, and the effect of PrEP on risk behaviour.
Choopanya K, Martin M, Suntharasamai, et al, for the Bangkok Tenofovir Study Group. **Antiretroviral prophylaxis for HIV infection in injecting drug users** (IDU) in Bangkok, Thailand (the Bangkok Tenofovir Study): a randomised, double-blind, placebo controlled phase 3 trial. Lancet 2013; online June 13.
McCormack S, Dunn DT, Desai M, et al. **Pre-exposure prophylaxis to prevent the acquisition of HIV-1** infection (**PROUD**): effectiveness results from the pilot phase of a pragmatic open-label randomised trial. Lancet. 2015 Sep 9.
Tan DHS, Hull MW, Yoong D, et al. Canadian guideline on HIV pre-exposure prophylaxis and nonoccupational postexposure prophylaxis. CMAJ. 2017 Nov 27;189(47):E1448-E1458.
192. Van Damme L, Corneli A, Ahmed K, et al. **Preexposure prophylaxis** for HIV infection among **African women**. (**FEM-PrEP**) N Engl J Med 2012. DOI: 10.1056/NEJMoa1202614.
193. Thigpen MC, Kebaabetswe PM, Paxton LA, et al. Antiretroviral **preexposure prophylaxis** for **heterosexual** HIV transmission in Botswana. (**TDF2)** N Engl J Med 2012.
194. Baeten JM, Donnell D, Ndase P, et al. Antiretroviral **prophylaxis** for HIV prevention in **heterosexual men and women**. (**PrEP**)N Engl J Med 2012. DOI: 10.1056/NEJMoa1108524.
195. Fairall L, Bachmann MO, Lombard C, et al. Task shifting of antiretroviral treatment from doctors to **primary-care nurses** in South Africa (STRETCH): a pragmatic, parallel, cluster-randomised trial. Lancet. 2012 Aug 14.
196. Millett GA, Peterson JL, Flores SA, et al. Comparisons of disparities and risks of HIV infection in black and other men who have **sex with men** in Canada, UK, and USA: a meta-analysis. Lancet. 2012 Jul 28;380(9839):341-8.
197. Beyrer C, Baral SD, van Griensven F, et al. Global epidemiology of HIV infection in men who have **sex with men**. Lancet. 2012 Jul 28;380(9839):367-77.
198. Sullivan PS, Carballo-Diéguez A, Coates T, et al. Successes and challenges of HIV prevention in men who have **sex with men**. Lancet. 2012 Jul 28;380(9839):388-99.
199. Millett GA, Jeffries WL 4th, Peterson JL, et al. Common roots: a contextual review of HIV epidemics in black men who have **sex with men** across the African diaspora. Lancet. 2012 Jul 28;380(9839):411-23.
200. Trapence G, Collins C, Avrett S, et al. From personal survival to public health: community leadership by men who have **sex with men** in the response to HIV. Lancet. 2012 Jul 28;380(9839):400-10.
201. Beyrer C, Sullivan PS, Sanchez J, et al. A call to action for comprehensive HIV services for men who have **sex with men**. Lancet. 2012 Jul 28;380(9839):424-38.

202. Mayer KH, Bekker LG, Stall R, et al. Comprehensive clinical care for men who have **sex with men**: an integrated approach. Lancet. 2012 Jul 28;380(9839):378-87.
203. Boyd MA, Cooper DA. Optimisation of HIV care and service **delivery**: doing more with less. Lancet. 2012 Jul 20.
204. Gupta RK, Jordan MR, Sultan BJ, et al. Global trends in **antiretroviral resistance** in treatment-naive individuals with HIV after rollout of antiretroviral treatment in resource-limited settings: a global collaborative study and meta-regression analysis. Lancet. 2012 Jul 20.
205. Mateen FJ, Mills EJ. Aging and HIV-related **cognitive loss**. JAMA. 2012 Jul 25;308(4):349-50.
206. Subramanian S, Tawakol A, Burdo TH, et al. **Arterial inflammation** in patients with HIV. JAMA. 2012 Jul 25;308(4):379-86.
207. Thompson MA, Aberg JA, Hoy JF, et al. Antiretroviral treatment of adult HIV infection: **2012 recommendations of the International Antiviral Society-USA panel**. JAMA. 2012 Jul 25;308(4):387-402.
208. Centers for Disease Control and Prevention (CDC). HIV infection and **HIV-associated behaviors among injecting drug users** - 20 cities, United States, 2009. MMWR Morb Mortal Wkly Rep. 2012 Mar 2;61(8):133-8.
209. Keller MJ, Burk RD, Xie X, et al. Risk of **cervical precancer and cancer** among HIV-infected women with normal cervical cytology and no evidence of oncogenic HPV infection. JAMA. 2012 Jul 25;308(4):362-9.
210. Steinbrook R. **HIV/AIDS in 1990 and 2012**: from San Francisco to Washington, DC. JAMA. 2012 Jul 25;308(4):345-6.
211. Stevens LM, Lynm C, Glass RM. JAMA **patient page. HIV infection**: the basics. JAMA. 2010 Jul 21;304(3):364.
212. Prosser AT, Tang T, Hall HI. **HIV in persons born outside the United States**, 2007-2010. JAMA. 2012 Aug 8;308(6):601-7.
213. Limketkai BN, Mehta SH, Sutcliffe CG, et al. Relationship of liver disease stage and antiviral therapy with liver-related events and death in adults **coinfected with HIV/HCV**. JAMA. 2012 Jul 25;308(4):370-8.
214. Kabue MM, Buck WC, Wanless SR, et al. Mortality and Clinical Outcomes in **HIV-Infected Children** on Antiretroviral Therapy in Malawi, Lesotho, and Swaziland. Pediatrics. 2012 Aug 13.
215. Paton NI, Goodall RL, Dunn DT, et al; **Hydroxychloroquine** Trial Team. Effects of hydroxychloroquine on immune activation and disease progression among HIV-infected patients not receiving antiretroviral therapy: a randomized controlled trial. JAMA. 2012 Jul 25;308(4):353-61.
216. Yehia BR, Fleishman JA, Metlay JP, et al. **Sustained viral suppression** in HIV-infected patients receiving antiretroviral therapy. JAMA. 2012 Jul 25;308(4):339-42.
217. Jarzebowski W, Caumes E, Dupin N, et al; for the FHDH-ANRS CO4 Study Team. Effect of **Early Syphilis Infection** on Plasma Viral Load and CD4 Cell Count in Human Immunodeficiency Virus-Infected Men: Results From the FHDH-ANRS CO4 Cohort. Arch Intern Med. 2012 Jul 23:1-7.
218. Lodi S, Meyer L, Kelleher AD, et al. **Immunovirologic Control 24 Months After Interruption** of Antiretroviral Therapy Initiated Close to HIV Seroconversion. Arch Intern Med. 2012 Jul 23:1-4.
219. UK Collaborative Group on HIV Drug Resistance. Time trends in drug **resistant HIV-1** infections in the United Kingdom up to 2009: multicentre observational study. BMJ. 2012 Aug 21;345:e5253.
220. Beijer U, Wolf A, Fazel S. Prevalence of tuberculosis, hepatitis C virus and HIV in **homeless** people: a systematic review and meta-analysis. Lancet Infect Dis 2012; online Aug 20.
221. Cutland CL, Schrag SJ, Zell ER, et al; the PoPS trial team. **Maternal HIV Infection and Vertical Transmission** of Pathogenic Bacteria. Pediatrics. 2012 Sep;130(3):e581-e590.
222. Althoff KN, Buchacz K, Hall HI, et al; for the North American AIDS Cohort Collaboration on Research and Design. **U.S. Trends in Antiretroviral Therapy** Use, HIV RNA Plasma Viral Loads, and CD4 T-Lymphocyte Cell Counts Among HIV-Infected Persons, 2000 to 2008. Ann Intern Med. 2012 Sep 4;157(5):325-335.
223. Naidoo K, Yende-Zuma N, Padayatchi N, et al. The **Immune Reconstitution Inflammatory Syndrome** After Antiretroviral Therapy Initiation in Patients With Tuberculosis: Findings From the SAPiT Trial. Ann Intern Med. 2012 Sep 4;157(5):313-24.
224. Wandeler G, Keiser O, Pfeiffer K, et al; SolidarMed ART program and IeDEA-Southern Africa. Outcomes of antiretroviral treatment programs in rural Southern Africa. J Acquir Immune Defic Syndr. 2012 Feb 1;59(2):e9-16.
225. Walson J, Singa B, Sangare L, et al. Empiric **deworming** to delay HIV disease progression in adults with HIV who are ineligible for initiation of antiretroviral treatment (the HEAT study): a multi-site, randomised trial. Lancet Infect Dis 2012; onine Sept 10.
226. Cornell M, Schomaker M, Garone DB, et al; for the International Epidemiologic Databases to Evaluate AIDS Southern Africa (IeDEA-SA) Collaboration. **Gender Differences** in Survival among Adult Patients Starting Antiretroviral Therapy in South Africa: A Multicentre Cohort Study. PLoS Med. 2012 Sep;9(9):e1001304.
227. Gsponer T, Weigel R, Davies MA, et al; for IeDEA Southern Africa. **Variability of Growth** in Children Starting Antiretroviral Treatment in Southern Africa. Pediatrics. 2012 Sep 17.
228. Elzi L, Erb S, Furrer H, et al; Swiss HIV Cohort Study. Choice of **initial combination antiretroviral therapy** in individuals with HIV infection: determinants and outcomes [published online August 13, 2012]. Arch Intern Med. 2012;172(17):1313-1321
229. Loutfy MR, Margolese S, Money DM, Gysler M, Hamilton S, Yudin MH. **Canadian HIV pregnancy planning guidelines**. J Obstet Gynaecol Can 2012 Jun;34(6):575-90.
230. Reshef R, Luger SM, Hexner EO, et al. Blockade of lymphocyte chemotaxis (**maraviroc**) in visceral graft-versus-host disease. N Engl J Med. 2012 Jul 12;367(2):135-45.
231. Koval CE. Home testing for HIV: Hopefully, a step forward. Cleve Clin J Med. 2012 Oct;79(10):713-716.
232. Persson EC, Shiels MS, Dawsey SM, et al. Increased risk of **stomach and esophageal malignancies** in people with AIDS. Gastroenterology. 2012 Oct;143(4):943-950.e2.
233. Krakower D, Mayer KH. What Primary Care Providers Need to Know About **Preexposure Prophylaxis** for HIV Prevention: A Narrative Review. Ann Intern Med. 2012 Jul 22.
234. Pasternak AO, de Bruin M, Jurriaans S, et al. Modest **Nonadherence** to Antiretroviral Therapy Promotes Residual HIV-1 Replication in the Absence of Virological Rebound in Plasma. J Infect Dis. 2012 Sep 11.
235. Gardner LI, Marks G, Craw JA, et al; for the Retention in Care Study Group. A Low-Effort, **Clinic-Wide Intervention** Improves Attendance for HIV Primary Care. Clin Infect Dis. 2012 Oct;55(8):1124-1134.
236. Benjamin LA, Bryer A, Emsley HC, et al. HIV infection and **stroke**: current perspectives and future directions. Lancet Neurol. 2012 Oct;11(10):878-90.
237. MacArthur GJ, Minozzi S, Martin N, et al. **Opiate substitution** treatment and HIV transmission in people who inject drugs: systematic review & meta-analysis. BMJ 2012;345:e5945.
238. Puthanakit T, Saphonn V, Ananworanich J, et al. **Early versus deferred antiretroviral therapy for children** older than 1 year infected with HIV (PREDICT): a multicentre, randomised, open-label trial. Lancet Infect Dis 2012; online Oct 9.
239. Canalejo E, Pacheco MS. Cushing syndrome due to **ritonavir-fluticasone interaction**. CMAJ. 2012 May 14.
240. Simard EP, Fransua M, Naishadham D, Jemal A. The Influence of Sex, **Race**/Ethnicity, and **Educational** Attainment on Human Immunodeficiency Virus Death Rates Among Adults, 1993-2007. Arch Intern Med. 2012 Oct 8:1-8.
241. Lujan-Zilbermann J, Warshaw MG, Williams PL, et al. International Maternal Pediatric Adolescent AIDS Clinical Trials Group P1065 Protocol Team. Immunogenicity and Safety of
1 vs 2 Doses of **Quadrivalent Meningococcal Conjugate Vaccine** in Youth Infected with Human Immunodeficiency Virus. J Pediatr. 2012 Oct;161(4):676-681.e2.
242. Sonneville R, Schmidt M, et al. Neurologic outcomes and adjunctive steroids in HIV patients with severe **cerebral toxoplasmosis**. Neurology. 2012 Oct 23;79(17):1762-1766.
243. Foissac F, et al. **Vitamin D3** supplementation scheme in HIV-infected patients based upon a pharmacokinetic modelling of 25-hydroxycholecalciferol. Br J Clin Pharmacol. 2012Oct17.
244. Gomez GB, Borquez A, Caceres CF, et al. The Potential Impact of **Pre-Exposure Prophylaxis** for HIV Prevention among Men Who Have Sex with Men and Transwomen in Lima, Peru: A Mathematical Modelling Study. PLoS Med. 2012 Oct;9(10):e1001323.
245. Isanaka S, Mugusi F, Hawkins C, et al. Effect of **high-dose vs standard-dose multivitamin** supplementation at the initiation of HAART on HIV disease progression and mortality in Tanzania: a randomized controlled trial. JAMA. 2012 Oct 17;308(15):1535-44.
246. Geng EH, Hare CB, Kahn JO, et al. The Effect of a "**Universal Antiretroviral Therapy**" Recommendation on HIV RNA Levels Among HIV-Infected Patients Entering Care With a CD4 Count Greater Than 500/μL in a Public Health Setting. Clin Infect Dis. 2012 Oct 16.
247. Mateen FJ, Shinohara RT, Carone M, et al; For the Multicenter AIDS Cohort Study (MACS) Investigators. **Neurologic disorders** incidence in HIV+ vs HIV- men: Multicenter AIDS Cohort Study, 1996-2011. Neurology. 2012 Oct 30;79(18):1873-1880.

248. Rengan R, Mitra N, Liao K, et al. Effect of HIV on survival in patients with **non-small-cell lung cancer** in the era of highly active antiretroviral therapy: a population-based study. Lancet Oncol. 2012 Nov 15.
249. Paltiel AD, Walensky RP. **Home HIV Testing**: Good News but Not a Game Changer. Ann Intern Med. 2012 Oct 9.
250. Liedtke MD, Vanguri A, Rathbun RC. A Probable **Interaction Between Warfarin** and the Antiretroviral TRIO Study Regimen. Ann Pharmacother. 2012 Nov;46(11):e34.
251. Chou R, Selph S, Dana T, et al. **Screening for HIV**: Systematic Review to Update the 2005 U.S. Preventive Services Task Force Recommendation. Ann Intern Med. 2012 Nov 20;157(10):706-18.
252. Chou R, Cantor AG, Zakher B, Bougatsos C. **Screening for HIV in Pregnant Women**: Systematic Review to Update the 2005 U.S. Preventive Services Task Force Recommendation. Ann Intern Med. 2012 Nov 20;157(10):719-28.
253. Jia Z, Ruan Y, Li Q, et al. Antiretroviral therapy to prevent HIV transmission in serodiscordant couples in China (2003–11): national observational cohort . Lancet 2012; online Dec 1.
254. Public Health Agency of Canada. Summary: estimates of HIV **prevalence and incidence in Canada,** 2011. www.phac-aspc.gc.ca/aids-sida/publication/survreport/estimat2011-eng.php (accessed December 4, 2012).
255. Panel on Treatment of HIV-Infected Pregnant Women and Prevention of Perinatal Transmission. Recommendations for use of antiretroviral drugs in pregnant HIV-1-infected women for maternal health and interventions to reduce perinatal HIV transmission in the United States. Rockville (MD): Public Health Service Task Force; 2012 Jul 31. http://aidsinfo.nih.gov/contentfiles/lvguidelines/perinatalgl.pdf
256. Raffi F, Rachlis A, Stellbrink H-J, et al, on behalf of the SPRING-2 study group. Once-daily **dolutegravir versus raltegravir** in antiretroviral-naïve adults with HIV-1 infection: 48 week results from the randomised, double-blind, non-inferiority **SPRING-2** study. Lancet 2013.
Raffi F, Jaeger H, Quiros-Roldan E, et al, on behalf of the extended SPRING-2 Study Group. Once-daily dolutegravir versus twice-daily raltegravir in antiretroviral-naive adults with HIV-1 infection (SPRING-2 study): **96 week** results from a randomised, double-blind, non-inferiority trial. Lancet Infect Dis 2013; online Sept 25.
257. Chang LW, Serwadda D, Quinn TC, et al. Combination implementation for **HIV prevention**: moving from clinical trial evidence to population-level effects. Lancet Infect Dis. 2013 Jan;13(1):65-76.
258. Baral SD, Poteat T, Strömdahl S, et al. Worldwide burden of **HIV in transgender women**: a systematic review and meta-analysis. Lancet Infect Dis. 2012 Dec 20.
259. Achan J, Kakuru A, Ikilezi G, et al. **Antiretroviral agents and prevention of malaria** in HIV-infected Ugandan children. N Engl J Med. 2012 Nov 29;367(22):2110-8.
260. Robbins GK, Lester W, Johnson KL, et al. Efficacy of a **Clinical Decision-Support System** in an HIV Practice: A Randomized Trial. Ann Intern Med. 2012 Dec 4;157(11):757-66.
261. Zhao W, Piana C, Danhof M, et al. Population pharmacokinetics of **abacavir in infants**, toddlers and children. Br J Clin Pharmacol. 2012 Nov 5.
262. Phillips SJ, Curtis KM, Polis CB. Effect of **hormonal contraceptive** methods on HIV disease progression: a Systematic Review. AIDS. 2012 Nov 6.
263. Grelotti DJ, Closson EF, Mimiaga MJ. **Pretreatment** antiretroviral exposure from **recreational use**. Lancet Infect Dis. 2013 Jan;13(1):10-2.
264. Walensky RP, Sax PE, Nakamura YM, et al. Economic savings versus health losses: the cost-effectiveness of **generic antiretroviral therapy** in the United States. Ann Intern Med. 2013;158:84-92.
265. McKittrick N, Frank I, Jacobson JM, et al; for the Center for AIDS Research. Improved Immunogenicity With **High-Dose Seasonal Influenza Vaccine** in HIV-Infected Persons: A Single-Center, Parallel, Randomized Trial. Ann Intern Med. 2013 Jan 1;158(1):19-26.
266. Hodder SL, Justman J, Hughes JP, et al; for the HIV Prevention Trials Network 064; the Women's HIV SeroIncidence Study Team. **HIV Acquisition Among Women** From Selected Areas of the United States: A Cohort Study. Ann Intern Med. 2013 Jan 1;158(1):10-18
267. Foissac F, Bouazza N, Frange P, et al. Evaluation of **Nevirapine** Dosing Recommendations in HIV-infected **Children**. Br J Clin Pharmacol. 2012 Dec 28.
268. Ragin AB, Du H, Ochs R, et al. Structural **brain alterations** can be detected early in HIV infection. Neurology. 2012 Dec 11;79(24):2328-34.
269. Le T, Wright EJ, Smith DM, et al. Enhanced CD4+ T-cell recovery with **earlier HIV-1 antiretroviral therapy**. N Engl J Med 2013;368:218-30.
270. SPARTAC Trial Investigators. **Short-course antiretroviral** therapy in primary HIV infection. N Engl J Med 2013;368:207-17.
271. Cressey TR, Best BM, Achalapong J, et al; IMPAACT P1026s team. Reduced **indinavir** exposure during **pregnancy**. Br J Clin Pharmacol. 2013 Jan 11.
272. Nakasujja N, Miyahara S, Evans S, et al. Randomized trial of **minocycline** in the treatment of HIV-associated **cognitive impairment**. Neurology. 2013 Jan 8;80(2):196-202.
273. Shiau S, Arpadi S, Strehlau R, et al. Initiation of Antiretroviral Therapy **Before 6 Months of Age** is Associated with **Faster Growth Recovery** in South African Children Perinatally Infected with Human Immunodeficiency Virus. J Pediatr. 2013 Jan 10.
274. Boyer CB, Hightow-Weidman L, Bethel J, et al. An Assessment of the Feasibility and Acceptability of a **Friendship-Based Social Network** Recruitment Strategy to Screen At-Risk African American and Hispanic/Latina Young Women for HIV Infection. JAMA Pediatr. 2013 Jan 21:1-8.
275. Crum-Cianflone NF, Moore DJ, Letendre S, et al. Low prevalence of **neurocognitive impairment** in early diagnosed and managed HIV-infected persons. Neurology. 2013 Jan 22;80(4):371-379.
276. Helleberg M et al. Mortality attributable to **smoking among HIV-1**–infected individuals: A nationwide, population-based cohort study. Clin Infect Dis 2012 Dec 18.
277. Birrell PJ, Gill ON, Delpech VC, et al. HIV incidence in **men who have sex with men** in England and Wales 2001–10: a nationwide population study. Lancet Infect Dis 2013; published online Feb 1.
278. Bellan SE, Fiorella KJ, Melesse DY, Getz WM, Williams BG, Dushoff J. **Extra-couple HIV transmission** in sub-Saharan Africa: a mathematical modelling study of survey data. Lancet 2013; published online Feb 5.
279. Gross R, Bellamy SL, Chapman J, et al. Managed Problem Solving for Antiretroviral Therapy **Adherence**: A Randomized Trial. JAMA Intern Med. 2013 Jan 28:1-7.
280. Güerri-Fernandez R, Vestergaard P, Carbonell C, et al. "HIV infection is strongly associated with **hip fracture risk**, independently of age, gender and co-morbidities: A population-based cohort study". J Bone Miner Res. 2013 Jan 29.
281. Centner CM, Bateman KJ, Heckmann JM. Manifestations of HIV infection in the **peripheral nervous system**. Lancet Neurol. 2013 Mar;12(3):295-309.
282. Zhang C, Denti P, Decloedt EH, et al. Model-based evaluation of the pharmacokinetic differences between **adults and children for lopinavir and ritonavir** in combination with **rifampicin**. Br J Clin Pharmacol. 2013 Feb 25.
283. Simioni S, Cavassini M, Annoni JM, et al. **Rivastigmine** for HIV-associated **neurocognitive disorders**: A randomized crossover pilot study. Neurology. 2013 Feb 5;80(6):553-60.
284. Centers for Disease Control and Prevention (CDC). HIV infections attributed to **male-to-male sexual contact** - metropolitan statistical areas, United States and Puerto Rico, 2010. MMWR Morb Mortal Wkly Rep. 2012 Nov 30;61(47):962-6.
285. Bonnet M, Bhatt N, Baudin E, et al, for the **CARINEMO** study group. **Nevirapine versus efavirenz** for patients co-infected with **HIV and tuberculosis**: a randomised non-inferiority trial. Lancet Infect Dis 2013; online Feb 20.
286. Freiberg MS, Chang C-CH, Kuller LH, et al. **HIV infection and the risk of acute myocardial infarction** [online March 4, 2013]. *JAMA Intern Med.* doi:10.1001/jamainternmed.2013.3728.
287. WHO. Use of **efavirenz during pregnancy**: a public health perspective. http://whqlibdoc.who.int/publications/2012/9789241503792_eng.pdf (accessed Feb 2, 2013).
288. Ford N, Calmy A, Mofenson L. Safety of **efavirenz in the first trimester of pregnancy**: an updated systematic review and meta-analysis. *AIDS* 2011; **25:** 2301–04.
289. ARROW Trial team. **Routine versus clinically driven laboratory monitoring** and first-line antiretroviral therapy strategies in African children with HIV (ARROW): a 5-year open-label randomised factorial trial. Lancet 2013; online March 7.
290. Kirk GD, Mehta SH, Astemborski J, et al. HIV, Age, and the **Severity of Hepatitis C** Virus-Related Liver Disease: A Cohort Study. Ann Intern Med. 2013 Feb 26.
291. Shubber Z, Calmy A, Andrieux-Meyer I, et al. **Adverse events** associated with **nevirapine and efavirenz**-based first-line antiretroviral therapy: a systematic review and meta-analysis. AIDS. 2013 Jan 22.
292. Shridharani SM, Mohan R. A 51-year-old man with HIV and **cervicodorsal lipodystrophy (buffalo hump).** JAMA. 2013 Mar 27;309(12):1289-90.
293. Greene M, Justice AC, Lampiris HW, Valcour V. Management of human immunodeficiency virus infection in **advanced age**. JAMA. 2013 Apr 3;309(13):1397-405.

294. Fasawe O, Avila C, et al. Cost-Effectiveness Analysis of **Option B+ for HIV Prevention and Treatment of Mothers and Children** in Malawi. PLoS One. 2013;8(3):e57778.
295. Katlama C, Deeks SG, Autran B, et al. **Barriers to a cure for HIV**: new ways to target and eradicate HIV-1 reservoirs. Lancet. 2013 Mar 28.
296. Sáez-Cirión A, Bacchus C, Hocqueloux L, et al; S VISCONTI Study Group. Post-Treatment HIV-1 Controllers with a Long-Term Virological Remission after the **Interruption of Early Initiated Antiretroviral Therapy ANRS VISCONTI** Study. PLoS Pathog. 2013 Mar;9(3):e1003211.
297. Thomas JB, Brier MR, Snyder AZ, et al. Pathways to **neurodegeneration: effects of HIV** and aging on resting-state functional connectivity. Neurology 2013;80:1186–1193.
298. van der Helm J, Geskus R, Sabin C, et al; CASCADE Collaboration in EuroCoord. Effect of HCV Infection on Cause-Specific **Mortality After HIV** Seroconversion, Before and After 1997. Gastroenterology. 2013 Apr;144(4):751-760.e2.
299. Boyer S, March L, Kouanfack C, et al. **Monitoring** of HIV viral load, CD4 cell count, and clinical assessment versus clinical monitoring alone for antiretroviral therapy in low-resource settings (Stratall ANRS 12110/ESTHER): a cost-eff ectiveness analysis. Lancet Infect Dis 2013.
300. Moyer VA, on behalf of the U.S. Preventive Services Task Force (**USPSTF**). **Screening for HIV**: U.S. Preventive Services Task Force recommendation statement. Ann Intern Med. 2013 Apr 30. [Epub ahead of print]
301. Lipshultz SE, Williams PL, Wilkinson JD, et al **Cardiac Status of Children** Infected With Human Immunodeficiency Virus Who Are Receiving Long-term Combination Antiretroviral Therapy: Results From the Adolescent Master Protocol of the Multicenter Pediatric HIV/AIDS Cohort Study. JAMA Pediatr. 2013 Apr 22:1-8. Long
302. Shiau S, Arpadi S, Strehlau R, et al. Initiation of Antiretroviral Therapy Before 6 Months of Age is Associated with Faster **Growth Recovery** in South African Children Perinatally
Infected with Human Immunodeficiency Virus. J Pediatr. 2013 Jan 10.
303. Donker G, Dorsman S, Spreeuwenberg P, et al. **Twenty-two years of HIV-related consultations** in Dutch general practice: a dynamic cohort study. BMJ Open. 2013 Apr 26;3(4).
304. Lorgis L, Cottenet J, Molins G, Benzenine E, et al. Outcomes After **Acute Myocardial Infarction in HIV-Infected** Patients: Analysis of Data From a French Nationwide Hospital Medical Information Database. Circulation. 2013 Apr 30;127(17):1767-74.
305. Pant Pai N, Sharma J, Shivkumar S, et al. Supervised and **Unsupervised Self-Testing for HIV** in High- and Low-Risk Populations: A Systematic Review. PLoS Med. 2013 Apr;10(4):e1001414.
306. Panel on Opportunistic Infections in HIV-Infected Adults and Adolescents. Guidelines for the prevention and treatment of **opportunistic infections** in HIV-infected adults and adolescents: recommendations from the Centers for Disease Control and Prevention, the National Institutes of Health, and the HIV Medical Association of the Infectious Diseases Society of America. Available at http://aidsinfo.nih.gov/contentfiles/lvguidelines/adult_oi.pdf .
307. Eron JJ, Cooper DA, Steigbigel RT, et al, for the **BENCHMRK** Study Teams. Efficacy and safety of **raltegravir** for treatment of HIV for 5 years in the BENCHMRK studies: fi nal results of two randomised, placebo-controlled trials. Lancet Infect Dis 2013; online May 7.
308. Lowenthal ED, Ellenberg JH, Machine E, et al. Association between **efavirenz-based compared with nevirapine**-based antiretroviral regimens and virological failure in HIV-infected **children**. JAMA. 2013 May 1;309(17):1803-9.
309. Bates D, Dalton B, Gilmour J, Kapler J. Venous thromboembolism due to suspected interaction between **rivaroxaban and nevirapine**. Can J Hosp Pharm. 2013 Mar;66(2):125-9.
310. Brandt AM. How **AIDS invented global health**. N Engl J Med. 2013 Jun 6;368(23):2149-52.
311. Piot P, Quinn TC. Response to the AIDS pandemic--a **global health model**. N Engl J Med. 2013 Jun 6;368(23):2210-8.
312. Lipshultz SE, Williams PL, Wilkinson JD, et al; Pediatric HIV/AIDS Cohort Study (PHACS). **Cardiac Status** of Children Infected With Human Immunodeficiency Virus Who Are Receiving Long-term Combination Antiretroviral Therapy: Results From the Adolescent Master Protocol of the Multicenter Pediatric HIV/AIDS Cohort Study. JAMA Pediatr. 2013 Jun 1;167(6):520-7.
313. Redd AD, Quinn TC, Tobian AA. Frequency and implications of **HIV superinfection**. Lancet Infect Dis. 2013 May 30.
314. Zaba B, Calvert C, Marston M, et al. Effect of HIV infection on **pregnancy-related mortality** in sub-Saharan Africa: secondary analyses of pooled community-based data from the network for Analysing Longitudinal Population-based HIV/AIDS data on Africa (ALPHA). Lancet. 2013 May 18;381(9879):1763-71.
315. SECOND-LINE Study Group. Ritonavir-boosted lopinavir plus nucleoside or nucleotide reverse transcriptase inhibitors versus ritonavir-boosted lopinavir plus raltegravir for treatment of HIV-1 infection in adults with virological failure of a standard fi rst-line ART regimen (SECOND-LINE): a randomised, open-label, non-inferiority study. Lancet 2013; 381: 2091–99.
316. Doherty T, Tabana H, Jackson D, et al. Effect of **home based HIV counselling and testing** intervention in rural South Africa: cluster randomised trial. BMJ. 2013 Jun 13;346:f3481.
317. Committee on Pediatric Aids. **Transitioning HIV-Infected Youth Into Adult** Health Care. Pediatrics. 2013 Jun 24.
318. Antiretroviral drugs for treating and preventing HIV infection-**WHO**-2013 http://apps.who.int/iris/bitstream/10665/85321/1/9789241505727_eng.pdf
319. Hall HI, et al. Differences in Human Immunodeficiency Virus Care and Treatment Among **Subpopulations** in the United States. JAMA Intern Med. 2013 Jun 17:1-7.
320. Bader MS, McKinsey DS. **Postexposure Prophylaxis** (Hepatitis B & C, HIV) for Common Infectious Diseases. Am Fam Physician. 2013;88(1):25-32.
321. Grobler L, Siegfried N, Visser ME, Mahlungulu SSN, Volmink J. **Nutritional interventions** for reducing morbidity and mortality in people with HIV. Cochrane Database of Systematic Reviews 2013, Issue 2. Art. No.: CD004536. DOI:10.1002/14651858.CD004536.pub3. Given the current evidence base, which is limited to fourteen relatively small trials all evaluating different macronutrient supplements in different populations at different stages of HIV infection and with varying treatment status, no firm conclusions can be drawn about the effects of macronutrient supplementation on morbidity and mortality in people living with HIV.
322. Cahn P, Pozniak AL, Mingrone H, et al, on behalf of the extended **SAILING** Study Team. **Dolutegravir versus raltegravir** in antiretroviral-experienced, integrase-inhibitor-naive adults with HIV: week 48 results from the randomised, double-blind, non-inferiority SAILING study. Lancet 2013; online July 3.
323. Ryom L, Mocroft A, Kirk O, et al. Association between **antiretroviral exposure and renal impairment** among HIV-positive persons with normal baseline renal function: the D:A:D study. J Infect Dis. 2013 May 1;207(9):1359-69.
324. Ackerman M, Alter G. Mapping the journey to an **HIV vaccine**. N Engl J Med. 2013 Jul 25;369(4):389-91.
325. Kuhar DT, Henderson DK, Struble KA, et al. Updated **US Public Health Service guidelines** for the management of **occupational exposures** to human immunodeficiency virus and
recommendations for postexposure prophylaxis. Infect Control Hosp Epidemiol Sep 2013;34(9):875-92, doi: 10.1086/672271.
326. Polis CB, Curtis KM. Use of **hormonal contraceptives and HIV acquisition** in women: a systematic review of the epidemiological evidence. Lancet Infect Dis. 2013 Jul 18.
327. Gathogo EN, Hamzah L, Hilton R, et al; for the UK HIV/Kidney Transplantation Study Group (see appendix). **Kidney transplantation in HIV-positive adults**: The UK experience. Int J STD AIDS. 2013 Jul 25.
328. Young SD, Cumberland WG, Lee SJ, et al. **Social Networking** Technologies as an Emerging Tool for HIV Prevention: A Cluster Randomized Trial. Ann Intern Med. 2013 Sep 3;159(5):318- 24.
329. Read TR, Hocking JS, Bradshaw CS, et al. Provision of **rapid HIV tests** within a health service and frequency of HIV testing among men who have sex with men: randomised controlled trial. BMJ. 2013 Sep 4;347:f5086.
330. Holloway CJ, Ntusi N, Suttie J, et al. Comprehensive Cardiac Magnetic Resonance Imaging and Spectroscopy Reveal a High Burden of **Myocardial Disease** in HIV Patients. Circulation. 2013 Aug 20;128(8):814-822.
331. Gigerenzer G. **HIV screening**: helping clinicians make sense of test results to patients. BMJ. 2013 Aug 21;347:f5151.
332. Lichterfeld M, Rosenberg ES. **Acute HIV-1 Infection**: A Call to Action. Ann Intern Med. 2013 Sep 17;159(6):425-7.
333. Hayward, P. Patients have **undetectable HIV after coming off treatment**. Lancet Infectious Dise. August 2013
334. Raffii F, Jaeger H, Quiros-Roldan E, et al, on behalf of the extended SPRING-2 Study Group. Once-daily **dolutegravir** versus twice-daily raltegravir in antiretroviral-naive adults with HIV-1 infection (**SPRING-2** study): 96 week results from a randomised, double-blind, non-inferiority trial. Lancet Infect Dis 2013; online Sept 25.
335. Hammer SM et al. Efficacy trial of a **DNA/rAd5 HIV-1 preventive vaccine**. N Engl J Med 2013 Oct 7; [e-pub ahead of print].

336. Sugarman J. HIV Cure Research: Expanding the **Ethical Considerations**. Ann Intern Med. 2013 Aug 13.
337. Nosyk B, Montaner JSG, Colley G, et al, for the STOP HIV/AIDS Study Group. The **cascade of HIV care in British Columbia**, Canada, 1996–2011: a population-based retrospective cohort study. Lancet Infect Dis 2013; published online Sept 27.
338. Haberer JE, Baeten JM, Campbell J, et al. **Adherence to Antiretroviral Prophylaxis for HIV Prevention**: A Substudy Cohort within a Clinical Trial of Serodiscordant Couples in East Africa. PLoS Med. 2013 Sep;10(9):e1001511.
339. Mugwanya KK, Donnell D, Celum C, et al, for the Partners **PrEP** Study Team. Sexual behaviour of heterosexual men and women receiving antiretroviral pre-exposure prophylaxis for **HIV prevention**: a longitudinal analysis. Lancet Infect Dis 2013; online Oct 17
340. Piana C, Zhao W, Adkison K, et al. Covariate effects and population pharmacokinetics of **lamivudine** in HIV-infected **children**. Br J Clin Pharmacol. 2013 Oct 4.
341. Piana C, Zhao W, Adkison K, et al. A model-based approach for the evaluation of once daily dosing of **lamivudine** in HIV-infected **children**. Br J Clin Pharmacol. 2013 Oct 4.
342. Zhang L, Chow EP, Jing J, et al. HIV **prevalence in China**: integration of surveillance data and a systematic review. Lancet Infect Dis. 2013 Oct 4.
343. Heller HM, Wu CC, Pierce VM, Kradin RL. **Case** 31-2013: A 29-year-old man was seen in an outpatient clinic because of abdominal pain, fever, and weight loss. N Engl J Med. 2013 Oct 10;369(15):1453-1461.
344. Lake JE, Currier JS. **Metabolic disease in HIV** infection. Lancet Infect Dis. 2013 Nov;13(11):964-75.
345. Clifford DB, Ances BM. HIV-associated **neurocognitive disorder**. Lancet Infect Dis. 2013 Nov;13(11):976-86.
346. Cohen MS, Smith MK, Muessig KE, et al. Antiretroviral treatment of **HIV-1 prevents transmission of HIV-1**: where do we go from here? Lancet. 2013 Oct 18.
347. Persaud D, Gay H, Ziemniak C, et al. **Absence of detectable HIV-1 viremia after treatment cessation in an infant**. N Engl J Med 2013. DOI: 10.1056/NEJMoa1302976.
348. Metsch LR, Feaster DJ, Gooden L, et al. Effect of **risk-reduction counseling with rapid HIV testing** on risk of acquiring sexually transmitted infections: the AWARE randomized clinical trial. JAMA. doi:10.1001/jama.2013.280034.
349. Anglemyer A, Horvath T, Rutherford G. Antiretroviral therapy for **prevention of HIV transmission in HIV-discordant couples**. JAMA. 2013 Oct 16;310(15):1619-20.
350. Bandaru VVR, Mielke MM, Sacktor N, et al. A **lipid storage-like disorder contributes to cognitive decline** in HIV-infected subjects. Neurology 2013;81:1492–1499.
351. Walensky RP et al. Cost-effectiveness of HIV treatment as **prevention in serodiscordant couples**. N Engl J Med 2013 Oct 31; 369:1715.
352. Giles SL, Lester F. Should women with HIV, or at high risk of contracting **HIV, use progestogen-containing contraception**? BMJ. 2013 Nov 14;347:f6695.
353. Cotton MF, Violari A, Otwombe K, on behalf of the **CHER** Study Team. **Early time-limited antiretroviral therapy versus deferred therapy** in South African infants infected with HIV: results from the children with HIV early antiretroviral (CHER) randomised trial. Lancet 2013; online Aug 22.
354. Aberg JA, Gallant JE, Ghanem KG, et al. **Primary Care Guidelines** for the Management of Persons Infected With HIV: 2013 Update by the HIV Medicine Association of the Infectious Diseases Society of America **(IDSA)**. Clin Infect Dis. 2013 Nov 13.
355. Walmsley SL, Antela A, Clumeck N et al. **Dolutegravir** plus abacavir-lamivudine for the treatment of HIV-1 infection (**SINGLE** Investigators). N Engl J Med. 2013 Nov 7;369(19):1807-18.
356. Piketty C, Selinger-Leneman H, Bouvier AM, et al. **Incidence of HIV-related anal cancer** remains increased despite long-term combined antiretroviral treatment: results from the french hospital database on HIV. J Clin Oncol. 2012 Dec 10;30(35):4360-6.
357. Nardone A, Delpech V, Gill ON, et al. **HIV in the UK: test**, test, and test again. Lancet. 2013 Nov 23;382(9906):1687-8.
358. Baum MK, Campa A, Lai S, et al. Effect of **micronutrient supplementation** on disease progression in asymptomatic, antiretroviral-naive, HIV-infected adults in Botswana: a randomized clinical trial. JAMA. 2013 Nov 27;310(20):2154-63.
359. Centers for Disease Control and Prevention (CDC).HIV testing and risk behaviors among **gay, bisexual and other men who have sex with men** – United States. MMWR Morb Mortal Wkly Rep 2013 Nov 29; 62:958.
360. Bwakura-Dangarembizi M, Kendall L, Bakeera-Kitaka S, et al; Antiretroviral Research for Watoto (ARROW) Trial Team. A randomized trial of **prolonged co-trimoxazole** in HIV-infected children in Africa. N Engl J Med. 2014 Jan 2;370(1):41-53
361. Ibarra-Barrueta O, Palacios-Zabalza I, Mora-Atorrasagasti O, et al. Effect of concomitant use of **montelukast and efavirenz on neuropsychiatric adverse events**. Ann Pharmacother. 2014 Jan;48(1):145-8
362. Johnston JA, Tincher LB, Lowe DK. Booster and Higher Antigen Doses of **Inactivated Influenza Vaccine** in HIV-Infected Patients. Ann Pharmacother. 2013 Dec;47(12):1712-6
363. Lowenthal ED, Bakeera-Kitaka S, Marukutira T, et al. **Perinatally acquired HIV** infection in adolescents from sub-Saharan Africa: a review of emerging challenges. Lancet Infect Dis. 2014 Jan 6
364. Marcus JL, Glidden DV, et al. **No Evidence of Sexual Risk Compensation** in the iPrEx Trial of Daily Oral HIV **Preexposure Prophylaxis**. PLoS One. 2013 Dec 18;8(12)
365. Mateen FJ, Post WS, Sacktor N, Abraham AG, et al; Multicenter AIDS Cohort Study (MACS) Investigators. Long-term predictive value of the **Framingham Risk Score** for Stroke in HIV-positive vs HIV-negative men. Neurology. 2013 Dec 10;81(24):2094-102.
366. Miller L, Arakaki L, Ramautar A, et al. Elevated Risk for **Invasive Meningococcal** Disease Among Persons With HIV. Ann Intern Med. 2013 Oct 29
367. Miller WC, Powers KA, Smith MK, et al. **Community viral load** as a measure for assessment of HIV treatment as prevention. Lancet Infect Dis. 2013 May;13(5):459-64
368. Samji H, Cescon A, Hogg RS, et al; North American AIDS Cohort Collaboration on Research and Design (NA-ACCORD) of IeDEA. Closing the Gap: **Increases in Life Expectancy** among Treated HIV-Positive Individuals in the United States and Canada. PLoS One. 2013 Dec 18;8(12)
369. Toft L, Storgaard M, Muller M, et al. Comparison of the Immunogenicity and Reactogenicity of **Cervarix and Gardasil** Human Papillomavirus Vaccines in HIV-Infected Adults: A Randomized, Double-Blind Clinical Trial. J Infect Dis. 2013 Dec 26.
370. Hudgins S, Wong A. Severe transient neutropenia with fever and abdominal pain in a 30-year-old man. (**Acute HIV**) CMAJ. 2013 Dec 10;185(18):1593-6.
371. Mills KE, Yudin MH. **Intrapartum care** of the HIV-positive woman. CMAJ. 2014 Feb 4;186(2):135.
372. Fauci AS, Marston HD. Ending AIDS--is an **HIV vaccine** necessary? N Engl J Med. 2014 Feb 6;370(6):495-8.
373. ENCORE1 Study Group. Effi cacy of **400 mg efavirenz** versus standard 600 mg dose in HIV-infected, antiretroviral-naive adults (ENCORE1): a randomised, double-blind, placebo-controlled, non-inferiority trial. Lancet 2014; online Feb 10.
374. Pollard RB, Rockstroh JK, Pantaleo G, et al. Safety and effi cacy of the **peptide-based therapeutic vaccine** for HIV-1, Vacc-4x: a phase 2 randomised, double-blind, placebo-controlled trial. Lancet Infect Dis 2014; online Feb 11.
375. Penazzato M, Revill P, Prendergast AJ, et al. **Early infant diagnosis of HIV** infection in low-income and middle-income countries: does one size fit all? Lancet Infect Dis. 2014 Jan 20
376. Mofenson LM, Brady MT, Danner SP, et al. Guidelines for the Prevention and Treatment of **Opportunistic Infections** among HIV-exposed and HIV-infected children: recommendations from CDC, the National Institutes of Health, the HIV Medicine Association of the Infectious Diseases Society of America, the Pediatric Infectious Diseases Society, and the American Academy of Pediatrics. MMWR Recomm Rep. 2009 Sep 4;58(RR-11):1-166
377. Hull M, Klein M, Shafran S, et al. **CIHR Canadian HIV Trials Network Coinfection** and Concurrent Diseases Core: Canadian guidelines for management and treatment of **HIV/hepatitis C coinfection** in adults. Can J Infect Dis Med Microbiol. 2013 Winter;24(4):217-38
378. Health Canada Feb/14: **TELZIR** should not be used with the antiarrhythmic drugs amiodarone, lidocaine (systemic), or quinidine, as this may cause serious and/or life-threatening reactions such as abnormal heart rhythm (arrhythmias). In addition, Telzir should not be used with delavirdine, another antiviral drug to treat HIV, because it may reduce the effectiveness of delavirdine.
379. Moyers BS, Secemsky EA, Vittinghoff E, et al. Effect of **Left Ventricular Dysfunction** and Viral Load on Risk of **Sudden Cardiac Death** in Patients With Human Immunodeficiency Virus. Am J Cardiol. 2014 Jan 16
380. Tebas P, Stein D, Tang WW, et al. **Gene editing of CCR5** in autologous CD4 T cells of persons infected with HIV. N Engl J Med. 2014 Mar 6;370(10):901-10.
381. Kay MA, Walker BD. **Engineering cellular resistance** to HIV. N Engl J Med. 2014 Mar 6;370(10):968-9.
382. Grinsztejn B, Hosseinipour MC, Ribaudo HJ, et al, and the HPTN 052-ACTG Study Team. Effects of **early versus delayed** initiation of antiretroviral treatment on clinical outcomes of HIV-1 infection: results from the phase 3 HPTN 052 randomised controlled trial. Lancet Infect Dis 2014; online March 4. http://dx.doi.org/10.1016/S1473-3099(13)70692-3.

383. Gray GE, Moodie Z, Metch B, et al; on behalf of the HVTN 503/Phambili study team. **Recombinant adenovirus type 5 HIV gag/pol/nef vaccine** in South Africa: unblinded, long-term follow-up of the phase 2b HVTN 503/Phambili study. Lancet Infect Dis. 2014 Feb 19.
384. Hamnvik OP, Becker CB, Levy BD, et al. Clinical problem-solving. Wasting away. (**tenofovir: Fanconi** syndrome) N Engl J Med. 2014 Mar 6;370(10):959-66.
385. Buchbinder SP, Glidden DV, Liu AY, et al. HIV **pre-exposure prophylaxis in men who have sex with men and transgender** women: a secondary analysis of a phase 3 randomised controlled effi cacy trial. Lancet Infect Dis 2014; online March 7.
386. Patel K, Wang J, Jacobson DL, et al; Pediatric HIV/AIDS Cohort Study (PHACS). **Aggregate risk of cardiovascular disease** among adolescents perinatally infected with the human immunodeficiency virus. Circulation. 2014 Mar 18;129(11):1204-12.
387. CIHR **Canadian** HIV Trials Network HIV/Hepatitis C Management and Treatment Guidelines Working Group. Canadian guidelines for management and treatment of **HIV/hepatitis C coinfection** in adults (2013). www.pulsus.com/pdfs/15871_hull.pdf (accessed January 10, 2014).
388. McNairy ML, El-Sadr WM. **Antiretroviral Therapy for the Prevention** of HIV Transmission: What Will It Take? Clin Infect Dis. 2014 Apr;58(7):1003-11.
389. Ellis RJ, Letendre S, Vaida F, et al. Randomized Trial of **Central Nervous System-Targeted Antiretrovirals** for HIV-Associated Neurocognitive Disorder. Clin Infect Dis. 2014 Apr;58(7):1015-22.
390. Sexton DJ, Reule S, Solid C, et al. **End-Stage Renal Disease** From Human Immunodeficiency Virus-Associated Nephropathy in the United States, 2001 Through 2010. JAMA Intern Med. 2014 Mar 3.
391. Kleyn TJ, Liedtke MD, Harrison DL, et al. Incidence of Transmitted **Antiretroviral Drug Resistance** in Treatment-Naive HIV-1-Infected Persons in a Large South Central United States Clinic. Ann Pharmacother. 2014 Apr;48(4):470-5.
392. CDC. Managing **Drug Interactions** in the Treatment of **HIV-Related Tuberculosis** [online]. 2013. Available from URL: http://www.cdc.gov/tb/TB_HIV_Drugs/default.htm
393. Clotet B, Feinberg J, van Lunzen J, et al, on behalf of the ING114915 Study Team. Once-daily **dolutegravir versus darunavir plus ritonavir** in antiretroviral-naive adults with HIV-1 infection (**FLAMINGO**): 48 week results from the randomised open-label phase 3b study. Lancet 2014; online April 1.
394. Meyer JP, Cepeda J,Wu J, Trestman RL, Altice FL, Springer SA. Optimization of human immunodeficiency virus treatment during **incarceration**: viral suppression at the prison gate. online March 31, 2014]. JAMA InternMed. doi:10.1001/jamainternmed.2014.601.
395. Post WS, Budoff M, Kingsley L, et al. Associations between **HIV infection and subclinical coronary atherosclerosis**. Ann Intern Med. 2014;160:458-67.
396. Antoniou T, Zagorski B, Bayoumi AM, et al. Trends in **HIV prevalence, new HIV diagnoses, and mortality** among adults with HIV who entered care in Ontario, 1996/1997 to 2009/2010: a population-based study. Open Medicine. 2013. 7(4), e98
397. Bouazza N, Tréluyer JM, Ghosn J, et al. Evaluation of Impaired **Renal Function on Lamivudine** Pharmacokinetics. Br J Clin Pharmacol. 2014 Apr 21.
398. Bustinduy A, King C, Scott J, et al. **HIV and schistosomiasis** co-infection in African children. Lancet Infect Dis. 2014 Apr 16.
399. Cahn P, Andrade-Villanueva J, Arribas JR, on behalf of GARDEL Study Group. Dual therapy with **lopinavir and ritonavir plus lamivudine versus triple** therapy with lopinavir and ritonavir plus two nucleoside reverse transcriptase inhibitors in antiretroviral-therapy-naive adults with HIV-1 infection: 48 week results of the randomised, open label, non-inferiority **GARDEL** trial. Lancet Infect Dis 2014; online April 28.
400. Grinsztejn B, De Castro N, Arnold V, et al, for the ANRS 12 180 Refl ate TB study group. **Raltegravir** for the treatment of patients co-infected with HIV and **tuberculosis** (ANRS 12 180 Refl ate TB): a multicentre, phase 2, noncomparative, open-label, randomised trial. Lancet Infect Dis 2014; online April 10.
401. Jones A, Cremin I, Abdullah F, et al. Transformation of HIV from **pandemic to low-endemic levels**: a public health approach to combination prevention. Lancet. 2014 Apr 11.
402. Remick J, Georgiopoulou V, Marti C, et al. **Heart failure** in patients with human immunodeficiency virus infection: epidemiology, pathophysiology, treatment, and future research. Circulation. 2014 Apr 29;129(17):1781-9.
403. Macbrayne CE, Blum JD, Kiser JJ. Tenofovir, Emtricitabine, and Darunavir/Ritonavir Pharmacokinetics in an HIV-Infected Patient After **Roux-en-Y Gastric Bypass** Surgery. Ann Pharmacother. 2014 Jun;48(6):816-9.
404. Sgaier SK, Reed JB, Thomas A, et al. Achieving the HIV Prevention Impact of Voluntary Medical **Male Circumcision**: Lessons and Challenges for Managing Programs. PLoS Med. 2014 May 6;11(5).
405. Mfinanga SG, Kirenga BJ, Chanda DM, et al. **Early versus delayed initiation** of highly active antiretroviral therapy for **HIV**-positive adults with newly diagnosed pulmonary **tuberculosis** (TB-HAART): a prospective, international, randomised, placebo-controlled trial. Lancet Infect Dis 2014; online May 6.
406. Sawyer JR, Ma Q, Hsiao CB. Single**-tablet, once-daily treatment regimens** for HIV. Lancet Infect Dis. 2014 Apr;14(4):265-7
407. Lim JK, Tate JP, Fultz SL, et al. Relationship Between **Alcohol** Use Categories and Noninvasive Markers of Advanced Hepatic Fibrosis in **HIV**-Infected, Chronic **Hepatitis C** Virus-Infected, and Uninfected Patients. Clin Infect Dis. 2014 May;58(10):1449-58.
408. Lo Re V 3rd, Kallan MJ, Tate JP, et al. **Hepatic Decompensation** in Antiretroviral-Treated Patients Co-Infected With **HIV** and **Hepatitis C** Virus Compared With Hepatitis C Virus-Monoinfected Patients: A Cohort Study. Ann Intern Med. 2014 Mar 18;160(6).
409. Rangaka MX, Wilkinson RJ, et al. **Isoniazid plus antiretroviral therapy** to prevent tuberculosis: a randomised double-blind, placebo controlled trial. Lancet 2014; online May 14.
410. BarteH, Horvath TH, RutherfordGW. **Yellow fever vaccine** for patients with HIV infection. Cochrane Database of Systematic Reviews 2014, Issue 1. Art. No.: CD010929. DOI: 10.1002/14651858.CD010929.pub2. YF vaccination can produce protective levels of neutralising antibodies in HIV patients. Immunogenicity of YF vaccine is slightly less in HIV-infected patients compared to HIV-uninfected patients. No serious adverse events related to YF vaccine were observed in HIV-infected study participants. At time of immunisation, higher CD4 cell counts and lower HIV RNA levels in patients with HIV infection seem to be key determinants for development of protective titres of neutralising antibodies.
411. Grant I, Franklin DR Jr, Deutsch R, et al; for the CHARTER Group. **Asymptomatic HIV-associated neurocognitive impairment** increases risk for symptomatic decline. Neurology 2014;82:2055–2062.
412. Maartens G, Celum C, Lewin SR. **HIV infection: epidemiology, pathogenesis, treatment, and prevention**. Lancet. 2014 Jun 4.
413. Penazzato M, Prendergast AJ, Muhe LM, et al. Optimisation of antiretroviral therapy in **HIV-infected children under 3 years** of age. Cochrane Database Syst Rev. 2014 May 22;5:CD004772.
414. Johnson M, Borland J, Chen S, et al. Effects of **boceprevir and telaprevir** on the pharmacokinetics of **dolutegravir**. Br J Clin Pharmacol. 2014 May 16.
415. Young J, Potter M, Cox J, et al. Variation between Canadian centres in the **uptake of treatment for hepatitis C by patients coinfected with HIV**: a prospective cohort study. Canadian Medical Association Open Access Journal 1.3 (2013): E106-E114.
416. Belluz J. The **Truvada wars**. BMJ. 2014 Jun 24;348:g3811.
417. Olsen MF, Abdissa A, Kaestel P, et al. Effects of **nutritional supplementation** for HIV patients starting antiretroviral treatment: randomised controlled trial in Ethiopia. BMJ: British Medical Journal 348 (2014).
418. Finn KM, Ginns LC, Robbins GK, et al. Case records of the Massachusetts General Hospital. Case 20-2014. A 65-year-old man with dyspnea and progressively worsening lung disease. N Engl J Med. 2014 Jun 26;370(26):2521-30. (**pneumocystis pneumonia, HIV**)
419. Mollan KR, Smurzynski M, Eron JJ, et al. Association Between **Efavirenz** as Initial Therapy for HIV-1 Infection and Increased Risk for **Suicidal** Ideation or Attempted or Completed Suicide: An Analysis of Trial Data. Ann Intern Med. 2014 Jul 1;161(1):1-10.
420. Celum C, Morrow RA, Donnell D, et al; Partners **PrEP** Study Team. Daily Oral **Tenofovir and Emtricitabine-Tenofovir Preexposure Prophylaxis** Reduces **Herpes Simplex** Virus Type 2 Acquisition Among Heterosexual HIV-1-Uninfected Men and Women: A Subgroup Analysis of a Randomized Trial. Ann Intern Med. 2014 Jul 1;161(1):11-9.
421. Boulware DR, Meya DB, Muzoora C, et al; COAT Trial Team. Timing of **antiretroviral therapy after diagnosis of cryptococcal meningitis**. N Engl J Med. 2014 Jun 26;370(26):2487-98.

422. Torres GW, Heffelfinger JD, Pollack HA, et al. **HIV screening programs in US emergency departments**: a cross-site comparison of structure, process, and outcomes. Ann Emerg Med. 2011 Jul;58(1 Suppl 1):S104-13.
423. Kredo T, Adeniyi FB, Bateganya M, Pienaar ED. **Task shifting** from doctors to non-doctors for **initiation and maintenance of antiretroviral therapy**. Cochrane Database of Systematic Reviews 2014, Issue 7. Art. No.: CD007331. DOI: 10.1002/14651858.CD007331.pub3.
424. Caniglia EC, Cain LE, Justice A, et al. **Antiretroviral penetration into the CNS** and incidence of AIDS defining neurologic conditions. Neurology 2014;83:134–141.
425. Geren KI, Lovecchio F, Knight J, et al. Identification of Acute HIV Infection Using **Fourth-Generation Testing** in an Opt-Out Emergency Department Screening Program. Ann Emerg Med. 2014 Jun 18.
426. Rayment M, Asboe D, Sullivan AK**. HIV testing and management of newly diagnosed HIV**. BMJ. 2014 Jul 8;349:g4275.
427. Smith CJ, Ryom L, Weber R, et al, for the D:A:D Study Group. Trends in **underlying causes of death** in people with HIV from 1999 to 2011: a multicohort collaboration. Lancet 2014; 384: 241–48.
428. Briand N, Jasseron C, Sibiude J, et al. **Cesarean section for HIV**-infected women in the combination antiretroviral therapies era, 2000–2010. Am J Obstet Gynecol 2013;209:335e1–12.
429. Siberry GK, Abzug MJ, Nachman S, et al. ; Panel on Opportunistic Infections in HIV-Exposed and **HIV-Infected Children**. Guidelines for the prevention and treatment of **opportunistic infections** in HIV-exposed and HIV-infected children: recommendations from the National Institutes of Health, Centers for Disease Control and Prevention, the HIV Medicine Association of the Infectious Diseases Society of America, the Pediatric Infectious Diseases Society, and the American Academy of Pediatrics. Pediatr Infect Dis J. 2013 Nov;32 Suppl 2:i-KK4.
430. Fauchet F, Treluyer JM, Valade E, et al. **Maternal and fetal zidovudine** pharmacokinetics during pregnancy and labor: too high dose infused at labor? Br J Clin Pharmacol. 2014 Jul 9.
431. Wood E, Kerr T, Rowell G, et al. Does this adult patient have **early HIV infection**?: The Rational Clinical Examination systematic review. JAMA. 2014 Jul 16;312(3):278-85.
432. Gandhi M, Gandhi RT. **Single-pill combination regimens** for treatment of HIV-1 infection. N Engl J Med. 2014 Jul 17;371(3):248-59.
433. Paton NI, Kityo C, Hoppe A, et al; EARNEST Trial Team. Assessment of **second-line antiretroviral** regimens for HIV therapy in **Africa**. N Engl J Med. 2014 Jul 17;371(3):234-47.
434. Li EH, Foisy MM. Antiretroviral and **Medication Errors in Hospitalized HIV-Positive Patients**. Ann Pharmacother. 2014 May 8;48(8):998-1010.
435. Mathers BM, Cooper DA. Integrating **HIV prevention** into practice. JAMA. 2014 Jul 23-30;312(4):349-50.
436. Günthard HF, Aberg JA, Eron JJ, et al. Antiretroviral treatment of adult HIV infection: **2014 recommendations** of the **International Antiviral Society-USA Panel**. JAMA. 2014 Jul 23-30;312(4):410-25.
437. Johnson AS, Hall HI, Hu X, et al. **Trends in diagnoses of HIV infection in the United States**, 2002-2011. JAMA. 2014 Jul 23-30;312(4):432-4.
438. Jin J. JAMA patient page. Medications to **prevent HIV infection**. JAMA. 2014 Jul 23-30;312(4):452.
439. MacPherson P, Lalloo DG, Webb EL, et al. Effect of optional **home initiation of HIV care** following HIV self-testing on antiretroviral therapy initiation among adults in Malawi: a randomized clinical trial. JAMA. 2014 Jul 23-30;312(4):372-9.
440. Stanley TL, Feldpausch MN, Oh J, et al. Effect of **tesamorelin** on visceral fat and liver fat in HIV-infected patients with abdominal fat accumulation: a randomized clinical trial. JAMA. 2014 Jul 23-30;312(4):380-9.
441. Thirumurthy H, Masters SH, Rao S, et al. Effect of Providing Conditional Economic Compensation on Uptake of Voluntary Medical **Male Circumcision** in Kenya: A Randomized Clinical Trial. JAMA. 2014 Jul 20.
442. Henrich TJ, Hanhauser E, Marty FM, et al. Antiretroviral-Free HIV-1 **Remission and Viral Rebound After Allogeneic Stem Cell Transplantation**: Report of 2 Cases. Ann Intern Med. 2014 Jul 22.
443. Health Canada Aug/14 is informing healthcare professionals about a suspected drug interaction between **efavirenz (Sustiva) and ginkgo biloba**. The report is based on a 2012 published case report involving a Canadian patient with HIV infection.(1)
444. Woods EA, Foisy MM. Antiretroviral-Related **Alopecia** in HIV-Infected Patients. Ann Pharmacother. 2014 Jun 18;48(9):1187-1193.
445. Anderson SJ, Cherutich P, Kilonzo N, et al. **Maximising the effect** of combination HIV prevention through prioritisation of the people and places in greatest need: a modelling study. Lancet. 2014 Jul 19;384(9939):249-56.
446. Baral SD, Friedman MR, Geibel S, et al. **Male sex workers**: practices, contexts, and vulnerabilities for HIV acquisition and transmission. Lancet. 2014 Jul 21.
447. Shannon K, Strathdee SA, Goldenberg SM, et al. Global epidemiology of HIV among **female sex workers**: influence of structural determinants. Lancet. 2014 Jul 21.
448. Bekker LG, Johnson L, Cowan F, et al. Combination HIV prevention for **female sex workers**: what is the evidence? Lancet. 2014 Jul 21.
449. Decker MR, Crago AL, Chu SK, et al. Human rights violations against **sex workers**: burden and effect on HIV. Lancet. 2014 Jul 21.
450. Poteat T, Wirtz AL, Radix A, et al. HIV risk and preventive interventions in **transgender women sex workers**. Lancet. 2014 Jul 21.
451. Murray CJ, Ortblad KF, Guinovart C, et al. **Global, regional, and national incidence and mortality for HIV, tuberculosis, and malaria** during 1990-2013: a systematic analysis for the Global Burden of Disease Study 2013. Lancet. 2014 Jul 21.
452. Kerrigan D, Kennedy CE, Morgan-Thomas R, et al. A **community empowerment** approach to the HIV response among sex workers: effectiveness, challenges, and considerations for implementation and scale-up. Lancet. 2014 Jul 21.
453. Gold J, Goldacre R, Maruszak H, et al. **HIV and lower risk of multiple sclerosis**: beginning to unravel a mystery using a record-linked database study. J Neurol Neurosurg Psychiatry. 2014 Aug 4.
454. Raffi F, Babiker AG, Richert L, et al, for the NEAT001/ARNS143 Study Group. Ritonavir**-boosted darunavir combined with raltegravir or tenofovir-emtricitabine** in antiretroviral-naive adults infected with HIV-1: 96 week results from the NEAT001/ANRS143 randomised non-inferiority trial. Lancet 2014; online Aug 5.
455. US Public Health Service. **Preexposure prophylaxis** for the prevention of HIV infection in the United States–2014: a clinical practice guideline. Centers for disease control and prevention. 2014.
456. Moreno R,NababanHY,Ota E,WarikiWMV, Ezoe S,Gilmour S, Shibuya K. Structural and community-level interventions for increasing **condom use** to prevent the transmission ofHIV and other sexually transmitted infections. Cochrane Database of Systematic Reviews 2014, Issue 7. Art. No.: CD003363. DOI: 10.1002/14651858.CD003363.pub3. There is no clear evidence that structural interventions at the community level to increase condom use prevent the transmission of HIV and other STIs. However, this conclusion should be interpreted with caution since our results have wide confidence intervals and the results for prevalence may be affected by attrition bias. In addition, it was not possible to find RCTs in which extended changes to policies were conducted and the results only apply to general populations in developing nations, particularly to Sub-Saharan Africa, a region which in turn is widely diverse.
457. Panel on Treatment of HIV-Infected Pregnant Women and Prevention of Perinatal Transmission. Recommendations for use of antiretroviral drugs in **pregnant HIV-1-infected women** for maternal health and interventions to reduce perinatal HIV transmission in the United States. Bethesda (MD): Department of Health and Human Services (DHHS); 2014 Mar 28.
458. Marrazzo JM, del Rio C, Holtgrave DR, et al. **HIV prevention** in clinical care settings: 2014 recommendations of the **International Antiviral Society (IAS) –USA Panel**. JAMA. doi:10.1001/jama.2014.7999.

459. Mugo NR, Hong T, Celum C, et al; for the Partners PrEP Study Team. **Pregnancy incidence and outcomes** among women receiving **preexposure prophylaxis for HIV** prevention: a randomized clinical trial. JAMA. doi:10.1001/jama.2014.8735.
460. **SOGC**: Society of Obstetricians and Gynaecologists of Canada. Guidelines for the care of **pregnant women living with HIV** and interventions to reduce perinatal transmission: executive summary. J Obstet Gynaecol Can 2014;36:721-34.www.jogc.com/abstracts/201408_SOGCClinicalPracticeGuidelines_1.pdf (accessed August 25, 2014)
461. Lucas GM, Ross MJ, Stock PG, et al. Clinical Practice Guideline for the Management of **Chronic Kidney Disease in Patients Infected With HIV**: 2014 Update by the HIV Medicine Association of the Infectious Diseases Society of America. Clin Infect Dis. 2014 Sep 17.
462. Kooij KW et al. **Low bone mineral density** in patients with well-suppressed HIV infection is largely explained by body weight, smoking and prior advanced HIV disease. J Infect Dis 2014 Sep 1.
463. Blumental S, Ferster A, Van den Wijngaert S, et al. **HIV Transmission Through Breastfeeding**: Still Possible in Developed Countries. Pediatrics. 2014 Sep;134(3):e875-9.
464. Henrich TJ, Hanhauser E, Marty FM, Sirignano MN, Keating S, Lee TH, et al. Antiretroviral-free HIV-1 remission and viral rebound after **allogeneic stem cell transplantation**: report of 2 cases. Ann Intern Med. 2014;161:319-27. doi:10.7326/M14-1027
465. Grant RM, Anderson PL, McMahan V, et al for the **iPrEx** study team. Uptake of **pre-exposure prophylaxis, sexual practices, and HIV** incidence in **men and transgender** women who have sex with men: a cohort study. Lancet Infect Dis 2014; online July 22.
466. Zhang F, Zhu H, Wu Y, et al. **HIV, hepatitis B virus, and hepatitis C virus co-infection** in patients in the China National Free Antiretroviral Treatment Program, 2010–12: a retrospective observational cohort study. Lancet Infect Dis 2014; onine Oct 8.
467. White AB, Mirjahangir JF, Horvath H, et al. **Antiretroviral interventions for preventing breast milk transmission of HIV**. Cochrane Database Syst Rev. 2014 Oct 4;10:CD011323. Antiretroviral prophylaxis, whether used by the HIV-infected mother or the HIV-exposed infant while breastfeeding, is efficacious in preventing mother-to-child transmission of HIV. Further research is needed regarding maternal resistance and response to subsequent antiretroviral therapy after maternal prophylaxis. An ongoing trial (IMPAACT 1077BF) compares the efficacy and safety of maternal triple antiretroviral prophylaxis versus daily infant nevirapine for prevention of mother-to-child transmission through breastfeeding.
468. Yin DE, Warshaw MG, Miller WC, et al; PENPACT-1 (PENTA 9/PACTG 390) Study Team. Using **CD4 percentage and age to optimize pediatric antiretroviral therapy initiation**. Pediatrics. 2014 Oct;134(4):e1104 16.
469. Hoglund RM, Byakika-Kibwika P, Lamorde M, et al. **Artemether-lumefantrine coadministration with antiretrovirals**; population pharmacokinetics and dosing implications. Br J Clin Pharmacol. 2014 Oct 8.
470. Tseng CY, Su SC, Chiu NC, et al. **Disseminated papular lesions** in an HIV infected patient. BMJ. 2014 Oct 13;349:g6110.
471. Giacomet V, Trabattoni D, Zanchetta N, et al. **No cure** of HIV infection in a child despite early treatment and apparent viral clearance. Lancet. 2014 Oct 4;384(9950):1320.
472. Persaud D, Patel K, Karalius B, et al; for the Pediatric HIV/AIDS Cohort Study. Influence of **Age at Virologic Control** on Peripheral Blood Human Immunodeficiency Virus Reservoir Size and Serostatus in Perinatally Infected Adolescents. JAMA Pediatr. 2014 Oct 6.
473. Lennox JL, Landovitz RJ, Ribaudo HJ, et al; ACTG A5257 Team. Efficacy and Tolerability of **3 Nonnucleoside Reverse Transcriptase Inhibitor-Sparing Antiretroviral Regimens** for Treatment-Naive Volunteers Infected With HIV-1: A Randomized, Controlled Equivalence Trial. Ann Intern Med. 2014 Oct 7;161(7):461-71.
474. Nightingale S, Winston A, Letendre S, et al. Controversies in **HIV-associated neurocognitive disorders**. Lancet Neurol. 2014 Nov;13(11):1139-1151.
475. Sharma M, Tan DH. **HIV pre-exposure prophylaxis**. CMAJ. 2014 Oct 21;186(15):E588.
476. Shet A, DeCosta A, Kumarasamy N, et al. Effect of **mobile telephone reminders** on treatment outcome in HIV: evidence from a randomized controlled trial in India. BMJ 2014;349:g5978.
477. Vieira CS, Bahamondes MV, de Souza RM, et al. Effect of antiretroviral therapy including **lopinavir/ritonavir or efavirenz on etonogestrel**-releasing implant pharmacokinetics in HIV-positive women. J Acquir Immune Defic Syndr. 2014 Aug 1;66(4):378-85.
478. Chen I et al. **Low-level viremia** early in HIV infection. J Acquir Immune Defic Syndr 2014 Dec 1; 67:405.
479. Chow FC, He W, Bacchetti P, Regan S, et al. Elevated rates of **intracerebral hemorrhage** in individuals from a US clinical care HIV cohort. Neurology. 2014 Nov 4;83(19):1705-11.
480. Short WR, Anderson JR. **Caring for women with HIV**: Unique needs and challenges. Cleve Clin J Med. 2014 Nov;81(11):691-701.
481. Young AC, Yiannoutsos CT, Hegde M, et al. **Cerebral metabolite** changes prior to and after antiretroviral therapy in primary HIV infection. Neurology 2014; 83:1592–1600.
482. Money D, Tulloch K, Boucoiran I, Caddy S; Infectious Diseases Committee, Yudin MH, Allen V, Bouchard C, et al. Guidelines for the **care of pregnant women living with HIV** and interventions to reduce perinatal transmission: executive summary. J Obstet Gynaecol Can. 2014 Aug;36(8):721-51.
483. Gandhi RT, Alkasab TK, Nardi V, et al. Case records of the Massachusetts General Hospital. **Case** 40-2014. A 57-year-old man with inguinal pain, lymphadenopathy, and **HIV** infection. N Engl J Med. 2014 Dec 25;371(26):2511-20.
484. Torre P 3rd, Hoffman HJ, Springer G, et al. **Hearing Loss** Among HIV-Seropositive and HIV-Seronegative Men and Women. JAMA Otolaryngol Head Neck Surg. 2014 Dec 26.
485. Zanni MV et al. 2013 American College of Cardiology-American Heart Association and **2004 Adult Treatment Panel III cholesterol guidelines applied to HIV-infected** patients with-without subclinical high-risk coronary plaque. AIDS 2014 Sep 10; 28:2061.
486. Murray CJ. Maximizing **Antiretroviral Therapy** in **Developing Countries**: The Dual Challenge of Efficiency and Quality. JAMA. 2014 Dec 1.
487. Okulicz JF, Le TD, Agan BK, et al. Influence of the **Timing of Antiretroviral Therapy** on the Potential for Normalization of Immune Status in Human Immunodeficiency Virus 1-Infected Individuals. JAMA Intern Med. 2014 Nov 24.
488. Ralph LJ, McCoy SI, Shiu K, Padian NS. **Hormonal contraceptive use** and women's **risk of HIV acquisition**: a meta-analysis of observational studies. Lancet Infect Dis 2015; online Jan 9.
489. Hughes CA, Tseng A, Cooper R. Managing **drug interactions in HIV**-infected adults with comorbid illness. CMAJ. 2015 Jan 6;187(1):36-43.
490. Mugwanya KK, Wyatt C, Celum C, et al. **Changes in Glomerular Kidney Function** Among HIV-1-Uninfected Men and Women Receiving Emtricitabine-Tenofovir Disoproxil Fumarate Preexposure Prophylaxis: A Randomized Clinical Trial. JAMA Intern Med. 2014 Dec 22.
491. Clifford DB, Vaida F, Kao YT, et al. **Absence of neurocognitive effect of hepatitis C infection in HIV-coinfected** people. Neurology 2015;84:241–250.
492. Ford N, Meintjes G, Pozniak A, et al. The future role of **CD4 cell count** for monitoring antiretroviral therapy. Lancet Infect Dis. 2014 Nov 19. pii: S1473-3099(14)70896-5.
493. Katz IT, Leister E, Kacanek D, et al. Factors Associated With **Lack of Viral Suppression at Delivery** Among Highly Active Antiretroviral Therapy-Naive Women With HIV: A Cohort Study. Ann Intern Med. 2015 Jan 20;162(2):90-9.
494. Maki PM, Rubin LH, Valcour V, et al. **Cognitive function** in women with HIV: findings from the Women's Interagency HIV Study. Neurology 2015;84:231–240.
495. Mugwanya KK, Wyatt C, Celum C, et al. for the Partners PrEP Study Team. **Changes in Glomerular Kidney Function Among HIV**-1-Uninfected Men and Women Receiving Emtricitabine-Tenofovir Disoproxil Fumarate Preexposure Prophylaxis: A Randomized Clinical Trial. JAMA Intern Med. 2014 Dec 22.
496. Sinxadi PZ, Leger PD, McIlleron H, et al. **Pharmacogenetics of plasma efavirenz** exposure in HIV-infected adults and children in south Africa. Br J Clin Pharmacol. 2015 Jan 22.
497. Loulergue P, Coriat R, Mir O. **Recurrent Transaminitis Induced by Oral Contraceptives** During HIV Infection. Ann Pharmacother. 2015 Feb;49(2):258-9.
498. Marrazzo JM et al. **Tenofovir-based preexposure prophylaxis** for HIV infection among **African women. (Voice)** N Engl J Med 2015 Feb 5; 372:509.

499. Molina J-M, Orkin C, Iser DM, et al, for the PHOTON-2 study team. **Sofosbuvir plus ribavirin** for treatment of **hepatitis C virus in patients co-infected with HIV** (PHOTON-2): a multicentre, open-label, non-randomised, phase 3 study. Lancet 2015; online Feb 4.
500. Ravimohan S, Tamuhla N, et al. Immunological profiles to distinguish **tuberculosis-associated immune reconstitution inflamatory syndrome** and non-immune reconstitution inflammatory syndrome death in HIV-infected adults with pulmonary tuberculosis starting antiretroviral therapy: prospective observational cohort study. Lancet Infect Dis 2015;online Feb 9.
501. Chéret A, Nembot G, Mélard A, et al, for the OPTIPRIM ANRS Study Group. **Intensive five-drug antiretroviral therapy regimen versus standard triple drug therapy** during primary HIV-1 infection (**OPTIPRIM-ANRS 147**): a randomised, open-label, phase 3 trial. Lancet Infect Dis 2015; online Feb 18.
502. Muller E, Barday Z, Mendelson M, Kahn D. **HIV-positive to HIV-positive kidney transplantation** — results at 3 to 5 years. N Engl J Med 2015;372:613-20.
503. Skarbinski J, Rosenberg E, Paz-Bailey G, et al. **Human immunodeficiency virus transmission at each step of the care continuum in the United States** [online February 23, 2015]. JAMA Intern Med. doi:10.1001/jamainternmed.2014.8180.
504. Mdodo R, Frazier EL, Dube SR, et al. **Cigarette Smoking Prevalence Among Adults With HIV** Compared With the General Adult Population in the United States: Cross-sectional Surveys. Ann Intern Med. 2015 Mar 3;162(5):335-44.
505. Caniglia EC, Cain LE, Justice A, er al. **Antiretroviral penetration into the CNS** and incidence of AIDS-defining neurologic conditions. Neurology. 2014 Jul 8;83(2):134-41.
506. Locke JE, Mehta S, Reed RD, et al. A National Study of Outcomes among **HIV-Infected Kidney Transplant Recipients**. J Am Soc Nephrol. 2015 Mar 19.
507. Lowenthal ED, Marukutira T, Tshume O, et al. **Parental Absence From Clinic** Predicts Human Immunodeficiency Virus Treatment Failure in Adolescents. JAMA Pediatr. 2015 Mar 30.
508. Luzuriaga K, Gay H, Ziemniak C, et al. **Viremic relapse after HIV-1 remission** in a perinatally infected child. N Engl J Med. 2015 Feb 19;372(8):786-8.
509. Troy SB, Kouiavskaia D, Siik J, et al. Comparison of the Immunogenicity of Various Booster Doses of Inactivated **Polio** Vaccine Delivered **Intradermally Versus Intramuscularly** to HIV-Infected Adults. J Infect Dis. 2015 Jan 7.
510. Sawinski D, Forde KA, Eddinger K, et al. Superior outcomes in **HIV-positive kidney transplant** patients compared with HCV-infected or HIV/HCV-coinfected recipients. Kidney Int. 2015 Mar 25.
511. Desai M, Joyce V, Bendavid E, et al. Risk of **Cardiovascular Events Associated with Current Exposure to HIV Antiretroviral Therapies** in a US Veteran Population. Clin Infect Dis. 2015 Apr 22.
512. Gurm J, Sami H, Nophal A, et al. **Suicide mortality** among people accessing **highly active antiretroviral therapy** for HIV/AIDS in British Columbia: a retrospective analysis. CMAJ Open 2015, 3 (2) E140-E148.
513. Kouri V, Khouri R, Alemán Y, et al. **CRF19_cpx** is an evolutionary fit HIV-1 variant strongly associated with **rapid progression to AIDS** in Cuba. EBioMedicine. 2015 Jan 15.
514. Mulligan K, Glidden DV, Anderson PLet al; iPrEx Study Team. Effects of **Emtricitabine/Tenofovir** on **Bone Mineral Density** in HIV-Negative Persons in a Randomized, Double-Blind, Placebo-Controlled Trial: DXA Results from **iPrEx**. Clin Infect Dis. 2015 Apr 23.
515. Feinstein MJ, Achenbach CJ, Stone NJ, et al. A Systematic Review of the Usefulness of **Statin Therapy in HIV-Infected Patients**. Am J Cardiol. 2015 Jun15;115(12):1760-1766.
516. Himes SK, Tassiopoulos K, Yogev R, et al; Pediatric HIV/AIDS Cohort Study (PHACS). **Antiretroviral Drugs in Meconium**: Detection for Different **Gestational** Periods of Exposure. J Pediatr. 2015 May 19.
517. Mfinanga S, Chanda D, Kivuyo SL, et al, on behalf of the REMSTART trial team. **Cryptococcal meningitis** screening and community-based early adherence support in people with advanced HIV infection starting antiretroviral therapy in Tanzania and Zambia: an open-label, randomized controlled trial. Lancet 2015; published online March 10
518. Payne H, Mkhize N, Otwombe K, et al. Poor reactivity of routine 1 **HIV antibody tests** in children who initiate ART in early infancy: a restrospective obervational study of the Children with HIV Early Antiretroviral Therapy (CHER) trial. Lancet Infect Dis 2015; online June 2, 2015.
519. Rajasingham R, Boulware DR. HIV care: **ART adherence** support and **cryptococcal screening**. Lancet. 2015 Mar 9.
520. Rao VB, Johari N, du Cros P, et al. **Hepatitis C seroprevalence and HIV co-infection** in sub-Saharan Africa: a systematic review and meta-analysis. Lancet Infect Dis. 2015 May 5.
521. Richterman A, Sawinski D, Reese PP, et al. An Assessment of **HIV-Infected Patients Dying in Care for Deceased Organ Donation** in a United States Urban Center. Am J Transplant. 2015 May 14.
522. Samuel M, Winston A, Peters B. **Drug treatment for adults with HIV infection**. BMJ. 2015 Apr 23;350:h1555.
523. Arribas JR, Girard PM, Landman R, et al. Dual treatment with **lopinavir and ritonavir plus lamivudine versus triple treatment with lopinavir and ritonavir plus lamivudine** or **emtricitabine** and a second nucleos(t)ide reverse transcriptase inhibitor for maintenance of HIV1 viral suppression (**OLE**): a randomised, open-label, non-inferiority trial. Lancet Infect Dis 2015; online June 1, 2015.
524. Cahn P, Andrade-Villanueva J, Arribas JR, et al. Dual therapy with **lopinavir and ritonavir plus lamivudine versus triple therapy with lopinavir and ritonavir plus** two nucleoside reverse transcriptase inhibitors in antiretroviral-therapy-naive adults with HIV-1 infection: 48 week results of the randomised, open label, non-inferiority **GARDEL** trial. Lancet Infect Dis 2014; 14: 572–80.
525. Perez-Molina JA, Rubio R, Rivero A. Dual treatment with **atazanavir and ritonavir plus lamivudine versus triple treatment with atazanavir and ritonavir plus** two nucleos[t]ides in patients who are HIV1 infected, on antiretroviral treatment, and virologically stable (**SALT**): 48 week results from a randomised, open-label, non-inferiority trial. Lancet Infect Dis 2015; online June 1, 2015.
526. Sico JJ, Chang CC, So-Armah K, et al; Veterans Aging Cohort Study. HIV status and the **risk of ischemic stroke** among men. Neurology. 2015 May 12;84(19):1933-40.
527. Smit M, Brinkman K, Geerlings S, et al, on behalf of the **ATHENA** observational cohort. **Future challenges** for clinical care of an **ageing population infected with HIV**: a modelling study. Lancet Infect Dis 2015; online June 10.
528. Overton ET, Chan ES, Brown TT, et al. **Vitamin D and Calcium Attenuate Bone Loss With Antiretroviral Therapy Initiation**: A Randomized Trial. Ann Intern Med. 2015 Jun16;162(12):815-24.
529. Song IH, Borland J, Chen S, et al. **Dolutegravir** Has No Effect on the Pharmacokinetics of **Oral Contraceptives** With Norgestimate and Ethinyl Estradiol. Ann Pharmacother. 2015 Jul;49(7):784-9.
530. Djawe K, Buchacz K, Hsu L, et al. **Mortality Risk After AIDS-Defining Opportunistic Illness** Among HIV-Infected Persons-San Francisco, 1981-2012. J Infect Dis. 2015 Jun 3.
531. ENCORE1 Study Group. Efficacy and safety of **efavirenz 400 mg daily versus 600 mg daily**: 96-week data from the randomised, double-blind, placebo-controlled, non-inferiority ENCORE1 study. Lancet Infect Dis. 2015 Jul;15(7):793-802.
532. Sax PE, Wohl D, Yin MT, et al, for the GS-US-292-0104/0111 Study Team. **Tenofovir alafenamide** versus **tenofovir disoproxil fumarate, coformulated with elvitegravir, cobicistat, and emtricitabine,** for initial treatment of HIV-1 infection: two randomised, double-blind, phase 3, non-inferiority trials. Lancet 2015; online April 16.
533. Middel A, Arends JE, van Lelyveld SF, et al. Clinical and immunologic effects of **maraviroc in progressive multifocal leukoencephalopathy**. Neurology. 2015 Jul 7;85(1):104-6.
534. Paydar-Darian N, Pursley DM, et al. **Improvement in Perinatal HIV Status Documentation** in a Massachusetts Birth Hospital, 2009-2013. Pediatrics. 2015 Jul;136(1):e234-41.
535. Rich JD, Adashi EY. Ideological Anachronism Involving **Needle and Syringe Exchange Programs**: Lessons From the Indiana HIV Outbreak. JAMA. 2015 Jul 7;314(1):23-4.

536. Uthman OA, Okwundu C, Gbenga K, et al. Optimal Timing of Antiretroviral Therapy Initiation for HIV-Infected Adults With **Newly Diagnosed Pulmonary Tuberculosis**: A Systematic Review and Meta-analysis. Ann Intern Med. 2015 Jul 7;163(1):32-9.
537. Brown TT, Moser C, Currier JS, et al. Changes in **Bone Mineral Density** After Initiation of Antiretroviral Treatment With **Tenofovir** Disoproxil Fumarate/Emtricitabine Plus Atazanavir/Ritonavir, Darunavir/Ritonavir, or Raltegravir. J Infect Dis. 2015 May 5.
538. **INSIGHT START** Study Group. **Initiation of antiretroviral therapy in early asymptomatic HIV infection**. N Engl J Med. DOI: 10.1056/NEJMoa1506816.
539. Klein N, Palma P, Luzuriaga K, et al. **Early antiretroviral therapy in children** perinatally infected with HIV: a unique opportunity to implement immunotherapeutic approaches to prolong viral remission. Lancet Infect Dis. 2015 Jul 14.
540. Margolis DA, Brinson CC, Smith GHR, et al. **Cabotegravir plus rilpivirine**, once daily, maintains virologic suppression following induction with cabotegravir plus NRTIs in antiretroviral-naive adults with HIV-1 infection: 96-week results from the LAI116482 (**LATTE**) study. Lancet Infect Dis 2015; online July 20.
541. Naggie S, Cooper C, Saag M, et al.; **ION-4** Investigators. **Ledipasvir and Sofosbuvir** for **HCV in Patients Coinfected with HIV-1**. N Engl J Med. 2015 Jul 21.
542. TEMPRANO ANRS 12136 Study Group. A trial of **early antiretrovirals and isoniazid preventive therapy** in Africa. N Engl J Med. DOI: 10.1056/NEJMoa1507198.
543. Wyles DL, Ruane PJ, Sulkowski MS, et al; **ALLY-2** Investigators. **Daclatasvir plus Sofosbuvir for HCV in Patients Coinfected with HIV-1.** N Engl J Med. 2015 Jul 21.
544. Rey D, Piroth L, Wendling M-J, et al. Safety and immunogenicity of **doubledose versus standard-dose hepatitis B revaccination** in non-responding adults with **HIV-1** (ANRS HB04 B-BOOST): a multicentre, open-label, randomised controlled trial. Lancet Infect Dis 2015; online Aug 7.
545. Abdool Karim SS, Abdool Karim Q, Kharsany AB, et al; CAPRISA 004 Trial Group. **Tenofovir Gel** for the Prevention of **Herpes Simplex Virus Type 2** Infection. N Engl J Med. 2015 Aug 6;373(6):530-9.
546. Beyrer C, Birx DL, Bekker LG, et al; Vancouver Consensus Signatories. The **Vancouver Consensus**: antiretroviral medicines, medical evidence, and political will. Lancet. 2015 Aug 8;386(9993):505-7
547. Sherman EM, Worley MV, Unger NR, et al. **Cobicistat**: Review of a Pharmacokinetic Enhancer for HIV Infection. Clin Ther. 2015 Aug 25.
548. Dufouil C, Richert L, Thiébaut R, et al; ANRS CO3 Aquitaine Study Group. **Diabetes and cognitive decline** in a French cohort of patients infected with HIV-1. Neurology. 2015 Jul 8.
549. Falade-Nwulia O, Seaberg EC, Snider AE, et al. **Incident Hepatitis B Virus Infection in HIV**-Infected and HIV-Uninfected Men Who Have Sex With Men From Pre-HAART to HAART Periods: A Cohort Study. Ann Intern Med. 2015 Oct 13.
550. Lefkowitz A, Gold WL, Casaubon LK, et al. **Multifocal strokes** in a 56-year-old man with HIV infection. CMAJ. 2015 Oct 6;187(14):1067-70.
551. McCormack S, Dunn DT, Desai M, et al. **Pre-exposure prophylaxis to prevent the acquisition of HIV-1** infection (**PROUD**): effectiveness results from the pilot phase of a pragmatic open-label randomised trial. Lancet. 2015 Sep 9.
552. Mulenga V, Musiime V, Kekitiinwa A, et al. **Abacavir, zidovudine, or stavudine** as paediatric tablets for African HIV-infected children (**CHAPAS-3**): an open-label, parallel-group, randomised controlled trial. Lancet Infect Dis 2015; online Oct 6.
553. Silverberg MJ, Lau B, Achenbach CJ, et al; North American AIDS Cohort Collaboration on Research and Design of the International Epidemiologic databases to Evaluate AIDS. **Cumulative Incidence of Cancer Among Persons With HIV** in North America: A Cohort Study. Ann Intern Med. 2015 Oct 6;163(7):507-18.
554. Ezeanolue EE, Obiefune MC, Ezeanolue CO, et al. Effect of a **congregation-based intervention on uptake of HIV testing** and linkage to care in pregnant women in Nigeria (Baby Shower): a cluster randomised trial. Lancet Glob Health. 2015 Nov;3(11):e692-700.
555. Lam PW, Bunce PE. A 65-year-old HIV-positive man with **acute diarrhea**. CMAJ. 2015 Oct 20;187(15):1153-4.
556. Margolis DA, Brinson CC, Smith GH, et al; LAI116482 Study Team. **Cabotegravir plus rilpivirine**, once a day, after induction with cabotegravir plus nucleoside reverse transcriptase inhibitors in antiretroviral-naive adults with HIV-1 infection (**LATTE**): a randomised, phase 2b, dose-ranging trial. Lancet Infect Dis. 2015 Oct;15(10):1145-55.
557. Coovadia A, Abrams EJ, Strehlau R, et al. **Efavirenz-based** antiretroviral therapy among **nevirapine-exposed HIV-infected children** in South Africa.JAMA. doi:10.1001/jama.2015.13631.
558. White JR, Chang CCH, So-Armah KA, et al. **Depression** and human immunodeficiency virus infection are risk factors for incident **heart failure** among veterans: Veterans Aging Cohort Study. Circulation. 2015;132:1630–1638.
559. Liu AY, Cohen SE, Vittinghoff E, et al. **Preexposure prophylaxis for HIV** infection integrated with municipal- and community-based sexual health services [online November 16, 2015].JAMA Intern Med. doi:10.1001/jamainternmed.2015.4683.
560. Mills A, Arribas J, Andrade-Villanueva J, et al, for the **GS-US-292-0109** team. Switching from **tenofovir disoproxil fumarate to tenofovir alafenamide** in antiretroviral regimens for virologically suppressed adults with HIV-1 infection: a randomised, active-controlled, multicentre, open-label, phase 3, non-inferiority study. Lancet Infect Dis 2015; online Nov 2.
561. Mohabeer Hart M, Boffito M, Pozniak A. Unexpected rapid weight gain in a patient with HIV and anorexia. (**Iatrogenic Cushings-fluticasone-ritonavir**) BMJ. 2015 Oct 29;351:h5551.
562. Khanna AS, Michaels S, Skaathun B, et al; UConnect Study Team. **Preexposure Prophylaxis** Awareness and Use in a Population-Based Sample of Young **Black** Men Who Have Sex With Men. JAMA Intern Med. 2015 Nov 16:1-3.
563. Sidhu VK, Foisy MM, Hughes CA. **Discontinuing Pneumocystis jirovecii Pneumonia Prophylaxis in HIV-Infected** Patients With a **CD4 Cell Count <200** cells/mm3. Ann Pharmacother. 2015 Dec;49(12):1343-8.
564. Tashima KT, Smeaton LM, Fichtenbaum CJ, et al; A5241 Study Team. **HIV Salvage Therapy Does Not Require Nucleoside Reverse Transcriptase Inhibitors**: A Randomized, Controlled Trial. Ann Intern Med. 2015 Nov 24:908-917.
565. Hughes E, Bassi S, Gilbody S, Bland M, Martin F. Prevalence of **HIV, hepatitis B, and hepatitis C in people with severe mental illness**: a systematic review and meta-analysis. Lancet Psychiatry. 2015 Nov 24.
566. Kakaire O, Byamugisha JK, Tumwesigye NM, et al. **Intrauterine Contraception** Among Women Living With Human Immunodeficiency Virus: A Randomized Controlled Trial. Obstet Gynecol. 2015 Nov;126(5):928-34.
567. Molina JM, Capitant C, Spire B, et al. **ANRS IPERGAY** Study Group. **On-Demand Preexposure Prophylaxis** in Men at High Risk for HIV-1 Infection. N Engl J Med. 2015 Dec 1.
568. Frieden TR, Foti KE, Mermin J. Applying **Public Health Principles to the HIV Epidemic** - How Are We Doing? N Engl J Med. 2015 Dec 1.
569. Byrne EH, Anahtar MN, Cohen KE, et al. Association between injectable **progestin-only contraceptives and HIV acquisition** and HIV target cell frequency in the female genital tract in South African women: a prospective cohort study. Lancet Infect Dis. 2015 Dec 23.
570. CCDR Highlights,Therapeutic approach to **noncompliance in HIV care**. Can Fam Physician. 2015 Dec;61(12):1075.
571. Cohen S, Caan MWA, Mutsaerts HJ, et al. **Cerebral injury in perinatally HIV**-infected children compared to matched healthy controls. Neurology 2016;86:19–27.
572. Reynolds EE, Libman H, Mayer KH. **Preexposure Prophylaxis** for HIV Prevention: Grand Rounds Discussion From Beth Israel Deaconess Medical Center. Ann Intern Med. 2015 Dec 15;163(12):941-8.
573. Wilson PA, Kahana SY, Fernandez MI, et al. **Sexual Risk Behavior** Among Virologically Detectable Human Immunodeficiency Virus-Infected Young Men Who Have Sex With Men. JAMA Pediatr. 2015 Dec 7:1-7.
574. Benjamin LA, Corbett EL, Connor MD, et al. HIV, antiretroviral treatment, **hypertension, and stroke** in Malawian adults: a case-control study. Neurology 2016;86:324–333.

575. Ellington SR, Clarke KE, et al. **Cytomegalovirus** Infection in Human Immunodeficiency Virus (HIV)-Exposed and HIV-Infected Infants: A Systematic Review. J Infect Dis. 2015 Nov 23.
576. Montoy JC, Dow WH, Kaplan BC. Patient choice in **opt-in, active choice, and opt-out HIV screening**: randomized clinical trial. BMJ 2016;352: h6895.
577. Sacktor N, Skolasky RL, Seaberg E, et al. Prevalence of **HIV-associated neurocognitive disorders** in the Multicenter AIDS Cohort Study. Neurology. 2016 Jan 26;86(4):334-40.
578. Van Handel M et al. **HIV testing among US high school students and young adults**. Pediatrics 2016 Jan 18; [e-pub].
579. Baden LR, Karita E, Mutua G, et al; B003-IPCAVD004-HVTN091 Study Group. Assessment of the Safety and Immunogenicity of 2 **Novel Vaccine Platforms** for HIV-1 Prevention: A Randomized Trial. Ann Intern Med. 2016 Feb 2.
580. Pierre S, Pape J, McNairy ML, et al. **10-Year Survival** of Patients with AIDS Receiving Antiretroviral Therapy in **Haiti**. N Engl J Med. 2016 Jan 28;374(4):397-8.
581. TenoRes Study Group. Global **epidemiology of drug resistance** after failure of WHO recommended first-line regimens for adult HIV-1 infection: a multicentre retrospective cohort study. Lancet Infect Dis. 2016 Jan 28. (tenofovir resistance increasing)
582. Nagot N, Kankasa C, Tumwine JK, et al, the ANRS 12174 Trial Group. **Extended pre-exposure prophylaxis** with lopinavir–ritonavir versus lamivudine to prevent HIV-1 transmission through **breastfeeding** up to 50 weeks in **infants in Africa (ANRS 12174):** a randomised controlled trial. Lancet 2015; online Nov 18.
583. Baeten JM et al. Use of a **vaginal ring** containing **dapivirine** for HIV-1 prevention in women. N Engl J Med 2016 Feb 22.
584. Beardsley J, Wolbers M, et al; CryptoDex Investigators. Adjunctive **Dexamethasone** in HIV-Associated **Cryptococcal Meningitis**. N Engl J Med. 2016 Feb 11;374(6):542-554.
585. Justice AC, et al. Risk of **mortality** and physiologic injury evident with lower **alcohol exposure** among HIV infected compared with uninfected men. Drug Alcohol Depend. 2016 Jan 29.
586. Mayer KH, Krakower DS, Boswell SL. **Antiretroviral Preexposure Prophylaxis**: Opportunities and Challenges for Primary Care Physicians. JAMA. 2016 Feb 18.
587. O'Byrne P, MacPherson P. HIV treatment as prevention in **men who have sex with men**: examining the evidence. CMAJ. 2016 Feb 16;188(3):198-203.
588. Peters PJ, et al. Screening Yield of **HIV Antigen/Antibody Combination and Pooled HIV RNA Testing** for Acute HIV Infection in a High-Prevalence Population. JAMA. 2016 Feb 16;315(7):682-90.
589. Caniglia EC, Patel K, Huo Y, et al; Pediatric Hivaids cohort study. **Atazanavir exposure in utero and neurodevelopment** in infants: A comparative safety study. AIDS. 2016 Feb 22.
590. Fourati S, Charpentier C, Amiel C, et al. ANRS AC11 Resistance Study Group. **Cross-resistance to elvitegravir and dolutegravir** in 502 patients failing on raltegravir: a French national study of raltegravir-experienced HIV-1-infected patients. J Antimicrob Chemother. 2015 May;70(5):1507-12.
591. Luzuriaga K, Mofenson LM. **Challenges in the Elimination of Pediatric HIV**-1 Infection. N Engl J Med. 2016 Feb 25;374(8):761-70.
592. Peter JG, Zijenah LS, Chanda D, et al. Effect on mortality of point-of-care, **urine-based lipoarabinomannan (LAM) testing** to guide tuberculosis treatment initiation in HIV-positive hospital inpatients: a pragmatic, parallel-group, multicountry, open-label, randomised controlled trial. Lancet 2016; online March 9.
593. Schafer JJ, Gill TK, Sherman EM, McNicholl IR. **ASHP Guidelines on Pharmacist Involvement in HIV** Care. Am J Health Syst Pharm. 2016 Feb 18.
594. Bienczak A, Cook A, Wiesner L, et al. The impact of **genetic polymorphisms** on the pharmacokinetics of **efavirenz** in African children. Br J Clin Pharmacol. 2016 Mar 16.
595. Byrne EB, Anahtar MN, Doherty KE, et al. Association between **injectable progestin-only contraceptives** and HIV acquisition and HIV target cell frequency in the female genital tract in South African women: a prospective cohort study. Lancet Infect Dis 2015; online Dec 23.
596. Cohen C, Moyes J, Tempia S, et al. Epidemiology of **Acute Lower Respiratory Tract Infection** in HIV-Exposed Uninfected Infants. Pediatrics. 2016 Mar 29.
597. Churchill D, Waters L, Ahmed N. **British HIV Association guidelines** for the treatment of HIV-1 positive adults with antiretroviral therapy 2015. London (UK): British HIV Association (BHIVA); 2015 Sep.
598. Evans C, Jones CE, Prendergast AJ. HIV-exposed, **uninfected infants: new global challenges** in the era of paediatric HIV elimination. Lancet Infect Dis. 2016 Mar 31
599. Heiden D, Saranchuk P, Keenan JD, et al. **Eye examination** for early diagnosis of disseminated **tuberculosis** in patients with AIDS. Lancet Infect Dis. 2016 Apr 16
600. Lenzer J. How **Cuba eliminated mother-to-child transmission** of HIV and syphilis. BMJ. 2016 Mar 21
601. Sampath A, Maduro G, Schillinger JA. **Infant Deaths** Due To Herpes Simplex Virus, Congenital Syphilis, and **HIV** in New York City. Pediatrics. 2016 Mar 1.
602. Bernard CL, Brandeau ML, Humphreys K, Bendavid E, Holodniy M, Weyant C, et al. **Cost-effectiveness of HIV preexposure prophylaxis** for people who inject drugs in the United States. Ann Intern Med. [Epub ahead of print] doi:10.7326/M15-2634
603. Launay O, Rosenberg AR, Rey D, et al. Long-term Immune **Response to Hepatitis B Virus Vaccination** Regimens in Adults With Human Immunodeficiency Virus 1: Secondary Analysis of a Randomized Clinical Trial. JAMA Intern Med. 2016 Apr 11.
604. B-Lajoie MR, Drouin O, Bartlett G, et al. **Incidence and Prevalence of Opportunistic and Other Infections** and the Impact of Antiretroviral Therapy Among HIV-infected Children in Low- and Middle-income Countries: A Systematic Review and Meta-analysis. Clin Infect Dis. 2016 Mar 21.
605. Gallitano SM, McDermott L, Brar K, et al. **Use of tumor necrosis factor (TNF) inhibitors** in patients with HIV/AIDS. J Am Acad Dermatol. 2016 May;74(5):974-80
606. Shah M, Hanrahan C, Wang ZY, Dendukuri N, Lawn SD, Denkinger CM, Steingart KR. **Lateral flow urine lipoarabinomannan assay for detecting active tuberculosis in HIV-positive** adults. Cochrane Database of Systematic Reviews 2016, Issue 5. Art. No.: CD011420. DOI: 10.1002/14651858.CD011420.pub2. We found that LF-LAM has low sensitivity to detect TB in adults living with HIV whether the test is used for diagnosis or screening. For TB diagnosis, the combination of LF-LAM with sputum microscopy suggests an increase in sensitivity for TB compared to either test alone, but with a decrease in specificity. In HIV-positive individuals with low CD4 counts who are seriously ill, LF-LAM may help with the diagnosis of TB.
607. Robb ML, Eller LA, Kibuuka H, et al; RV 217 Study Team. Prospective Study of **Acute HIV-1 Infection in Adults in East Africa and Thailand**. N Engl J Med. 2016 May 18.
608. Rosen S, Maskew M, Fox MP, et al. Initiating Antiretroviral **Therapy for HIV at a Patient's First Clinic** Visit: The **RapIT** Randomized Controlled Trial. PLoS Med. 2016 May 10;13(5):e1002015.
609. Suneja G, Lin CC, Simard EP, et al. **Disparities in cancer treatment** among patients infected with the human immunodeficiency virus. Cancer. 2016 May 17.
610. Updated Guidelines for Antiretroviral **Postexposure Prophylaxis after Sexual, Injection-Drug Use, or Other Nonoccupational Exposure to HIV** -United States, 2016. MMWR Morb Mortal Wkly Rep. 2016 May 6;65(17):458.
611. Zanni MV, Toribio M, Robbins GK, et al. Effects of **antiretroviral therapy on immune function and arterial inflammation** in treatment-naive patients with human immunodeficiency virus infection [online May 25, 2016].JAMA Cardiol. doi: 10.1001/jamacardio.2016.0846.
612. Becker M, Cox J, Evans GA, et al. **AMMI Canada position statement: the use of early antiretroviral therapy in HIV**-infected patients. J Assoc Med Microbiol Infect Dis Can 2016;1:79-85.http://www.pulsus.com/journals/abstract.jsp?sCurrPg=abstract&jnlKy=20&atlKy=14057&isuKy=1311&isArt=t&fromfol%20d=Current+Issue&fold=Abstract&utm_source=eTOC&utm_medium=email&utm_content=Article%20title%20link&utm_campaign=JAMMI_1_2(accessed June 16, 2016). AMMI Canada supports the recommendation that ART should be started in every patient living with HIV as soon as the diagnosis of HIV infection is confirmed, regardless of the patient's CD4 count.
613. Tan WS, Chow EP, Fairley CK, et al. Sensitivity of **HIV rapid tests compared to fourth generation** enzyme immunoassays or HIV RNA tests - a systematic review and meta-analysis. AIDS. 2016 Apr 27.
614. Walensky RP, Borre ED, Bekker LG, et al. The **Anticipated Clinical and Economic Effects of 90-90-90 in South Africa**. Ann Intern Med. 2016 May 31.

615. Butler K, Inshaw J, Ford D, et al. **BREATHER (PENTA 16) short-cycle therapy (SCT)** (5 days on/2 days off) in young people with chronic human immunodeficiency virus infection: an open, randomised, parallel-group Phase II/III trial. Health Technol Assess. 2016 Jun;20(49):1-108.
616. Cohen MS, Chen YQ, McCauley M, et al. Antiretroviral Therapy for the **Prevention of HIV-1 Transmission**. N Engl J Med. 2016 Jul 18.
617. Durand CM, Segev D, Sugarman J. Realizing HOPE: The **Ethics of Organ Transplantation** From HIV-Positive Donors. Ann Intern Med. 2016 Jul 19;165(2):138-42.
618. GBD 2015 HIV Collaborators. Estimates of **global, regional, and national incidence, prevalence, and mortality** of HIV, 1980-2015: the Global Burden of Disease Study 2015. Lancet HIV. 2016 Aug;3(8):e361-87.
619. Günthard HF, Saag MS, Benson CA, et al. **Antiretroviral drugs for treatment and prevention of HIV infection in adults: 2016** recommendations of the **International Antiviral Society**–**USA Panel**. JAMA. doi:10.1001/jama.2016.8900.
620. Hellmuth J, Fletcher JLK, Valcour V, et al. **Neurologic signs and symptoms** frequently manifest in acute HIV infection. Neurology 2016;87:148–154.
621. Hoare J, Phillips N, Joska JA, et al. Applying the HIVassociated **neurocognitive disorder** diagnostic criteria to HIV-infected youth. Neurology 2016;87:xx–xx.
622. Jenness SM, Goodreau SM, Rosenberg E, et al. Impact of the Centers for Disease Control's **HIV Preexposure Prophylaxis Guidelines** for Men Who Have Sex With Men in the United States. J Infect Dis. 2016 Jul 14.
623. Limeres Posse J, Scully C. **Oral HPV**-Associated Papillomatosis in AIDS. N Engl J Med. 2016 Jun 30;374(26):2585.
624. Lu PM, Shearer LS, Edelman EJ. Educating the Primary Care Clinician on **Preexposure Prophylaxis** for Human Immunodeficiency Virus: A Teachable Moment. JAMA Intern Med. 2016 Jul 1;176(7):890-891.
625. McNulty M, Cifu AS, Pitrak D. **HIV Screening**. JAMA. 2016 Jul 12;316(2):213-214.
626. Metsch LR, Feaster DJ, Gooden L, et al. Effect of Patient Navigation With or Without **Financial Incentives on Viral Suppression** Among Hospitalized Patients With HIV Infection and Substance Use: A Randomized Clinical Trial. JAMA. 2016 Jul 12;316(2):156-170.
627. Ofotukun I et al. A single-dose **zoledronic acid** infusion prevents antiretroviral therapy–induced bone loss in treatment-naive HIV-infected patients: A phase IIb trial. Clin Infect Dis 2016 May 18.
628. Peters PJ, Pontones P, Hoover KW, et al. **HIV Infection** Linked to Injection Use of **Oxymorphone** in Indiana, 2014-2015. N Engl J Med. 2016 Jul 21;375(3):229-39
629. Riddell J 4th, Cohn JA. Reaching High-Risk Patients for **HIV Preexposure Prophylaxis**. JAMA. 2016 Jul 12;316(2):211-212.
630. Rodger AJ, Cambiano V, Bruun T, et al. **Sexual activity without condoms** and risk of HIV transmission in serodifferent couples when the HIV-positive partner is using suppressive antiretroviral therapy.JAMA. doi:10.1001 /jama.2016.5148.
631. Shenoy MK, Iwai S, Lin DL, et al. Immune Response and Mortality Risk Relate to **Distinct Lung Microbiomes** in HIV-Pneumonia Patients. Am J Respir Crit Care Med. 2016 Jul 22
632. Swain C-A et al. **Postpartum human immunodeficiency virus care** among women diagnosed during pregnancy. Obstet Gynecol 2016 Jul; 128:44.
633. Ibekwe E, Haigh C, Duncan F, et al. Clinical outcomes of routine **opt-out antenatal human immunodeficiency virus screening**: a systematic review. J Clin Nurs. 2016 Jul 19.
634. Kourtis AP, Mirza A, AAP Committee on Pediatric AIDS. **Contraception for HIV-Infected** Adolescents. Pediatrics.2016;138(3):e20161892
635. Andany N, Gold WL. **Single-tablet antiretroviral treatment** (once daily). CMAJ. 2016 Sep 20;188(13):971
636. Polis CB, Curtis KM, et al. Update on **hormonal contraceptive methods and risk of HIV acquisition** in women: a systematic review of epidemiological evidence, 2016. AIDS. 2016 Aug 5.
637. Ravi S, et al. Effect of **Omega-3 Fatty Acids on Depressive Symptoms** in HIV-Positive Individuals: A Randomized, Placebo-Controlled Clinical Trial. Ann Pharmacother. 2016 Oct;50(10):797-807
638. Phillips N, Amos T, Kuo C, et al. HIV-Associated **Cognitive Impairment** iin Perinatally Infected Children : A meta-analysis. Pediatrics.2016 ;138(5) :e20160893
639. Raifman JR, Flynn C, German D. Healthcare Provider Contact and **Pre-exposure Prophylaxis** in Baltimore Men Who Have Sex With Men. Am J Prev Med. 2016 Sep 20.
640. Smith Fawzi MC, Ng L, Kanyanganzi F, et al. **Mental Health** and Antiretroviral Adherence Among Youth Living With HIV in Rwanda. Pediatrics. 2016; 138(4):e20153235.
641. Yan A, Leis JA, Gold WL. **CD4 measurement** in a 54-year-old man with sustained HIV-1 viral suppression. CMAJ. 2016 Oct 4;188(14):1028-1029.
642. Kroidl I, Saathof E, Maganga L, et al. Effect of **Wuchereria bancrofti infection** on HIV incidence in southwest Tanzania: a prospective cohort study. Lancet 2016; online first Aug 2.
643. Nichols BE, Boucher CAB, van der Valk M, et al. Cost-effectiveness analysis of **pre-exposure prophylaxis** for HIV-1 prevention in the Netherlands: a mathematical modelling study. Lancet Infect Dis 2016; online Sept 22.
644. Rhein J, Morawski BM, Hullsiek KH, et al. Efficacy of adjunctive **sertraline** for the treatment of HIV-associated **cryptococcal meningitis**: an open-label dose-ranging study. Lancet Infect Dis 2016; 16: 809–18.
645. Wang Q, De Luca A, Smith C, et al; The Hepatitis Coinfection and Non Hodgkin Lymphoma project team for the Collaboration of Observational HIV Epidemiological Research Europe (COHERE) in EuroCoord. **Chronic hepatitis B and C virus infection and risk for non-Hodgkin lymphoma** in HIVinfected patients. A cohort study. Ann Intern Med. 2016. [Epub ahead of print]. doi:10.7326/M16-0240
646. Bowen LN, Tyagi R, Li W, et al. HIV-associated **motor neuron disease**: **HERV-K activation** and response to antiretroviral therapy. Neurology. 2016 Oct 25;87(17):1756-1762.
647. Gaur AH, Kizito H, Prasitsueubsai W, et al. Safety, efficacy, and pharmacokinetics of a single-tablet regimen containing **elvitegravir, cobicistat, emtricitabine, and tenofovir alafenamide** in treatment-naive, HIV-infected **adolescents**: a single-arm, open-label trial. Lancet HIV. 2016 Oct 17.
648. Kunisaki KM, Niewoehner DE, Collins G, et al, for the **INSIGHT START** Pulmonary Substudy Group. Pulmonary effects of **immediate versus deferred antiretroviral therapy** in HIV-positive individuals: a nested substudy within the multicentre, international, randomised, controlled Strategic Timing of Antiretroviral Treatment (**START**) trial. Lancet Respir Med 2016; online Oct 20.
649. Fowler MG, Qin M, Fiscus SA, et al; IMPAACT 1077BF/1077FF **PROMISE** Study Team.. **Benefits and Risks of Antiretroviral Therapy for Perinatal HIV Prevention**. N Engl J Med. 2016 Nov 3;375(18):1726-1737.
650. Goldschmidt RH, Chu C. Dong BJ. **Initial Management of Patients with HIV Infection**. Am Fam Physician. 2016;94(9):708-716.
651. Ho D, Jagdeo J. Safety and Efficacy of a **Volumizing Hyaluronic Acid Filler** for Treatment of HIV-Associated Facial **Lipoatrophy**. JAMA Dermatol. 2016 Nov 2.
652. Inzaule SC, Ondoa P, Peter T, et al. **Affordable HIV drug-resistance testing for monitoring** of antiretroviral therapy in sub-Saharan Africa. Lancet Infect Dis. 2016 Nov;16(11):e267-e275.
653. Mason-Jones AJ, Sinclair D, Mathews C, et al. **School-based interventions for preventing HIV, sexually transmitted infections, and pregnancy in adolescents**. Cochrane Database of Systematic Reviews 2016, Issue 11. Art. No.: CD006417. There is a continued need to provide health services to adolescents that include contraceptive choices and condoms and that involve them in the design of services. Schools may be a good place in which to provide these services. There is little evidence that educational curriculum-based programmes alone are effective in improving sexual and reproductive health outcomes for adolescents. Incentivebased interventions that focus on keeping young people in secondary school may reduce adolescent pregnancy but further trials are needed to confirm this.
654. Baeten JM, Palanee-Phillips T, Brown ER, et al. Use of a **vaginal ring containing dapivirine** for HIV-1 prevention in women. (**Aspire**) N Engl J Med 2016;375:2121-32.
655. Nel A, van Niekerk N, Kapiga S, et al. Safety and efficacy of a **dapivirine vaginal ring** for HIV prevention in women. (**Ring**) N Engl J Med 2016;375:2133-43.

656. Nichols BE, Boucher CA, van der Valk M, et al. Cost-effectiveness analysis **of pre-exposure prophylaxis for HIV-1 prevention** in the Netherlands: a mathematical modelling study. Lancet Infect Dis. 2016 Sep 22.
657. Tomi AL, Sellam J, Lacombe K, et al. **Increased prevalence and severity of radiographic hand osteoarthritis** in patients with HIV-1 infection associated with metabolic syndrome: data from the cross-sectional METAFIB-OA study. Ann Rheum Dis. 2016 Dec;75(12):2101-2107
658. Cottrell ML, Yang KH, Prince HM, et al. A Translational Pharmacology Approach to Predicting Outcomes of **Preexposure Prophylaxis** Against HIV in **Men and Women** Using **Tenofovir** Disoproxil Fumarate With or Without **Emtricitabine**. J Infect Dis. 2016 Jul 1;214(1):55-64.
659. Gordon LA, Kumar P, Brooks KM, et al. Antiretroviral Boosting Agent **Cobicistat Increases the Pharmacokinetic Exposure and Anticoagulant Effect of Dabigatran** in HIV-Negative Healthy Volunteers. Circulation. 2016 Dec 6;134(23):1909-1911.
660. Gregson J, Kaleebu P, Marconi VC, et al. Occult **HIV-1 drug resistance to thymidine analogues** following failure of first-line **tenofovir** combined with a cytosine analogue and **nevirapine** or **efavirenz** in sub Saharan Africa: a retrospective multi-centre cohort study. Lancet Infect Dis 2016; online Nov 30
661. Crane HM, Paramsothy P, Drozd DR, et al. **Types of Myocardial Infarction** Among Human Immunodeficiency Virus-Infected Individuals in the United States. JAMA Cardiol. 2017 Jan 4.
662. Feinstein MJ. Nance RM, Drozd DR, et al. Assessing and refining **myocardial infarction risk** estimation among patients with human immunodeficiency virus: a study by the Centers for AIDS Research Network of Integrated Clinical Systems [online Dec 21, 2016]. JAMA Cardiol. doi:10.1001/jamacardio.2016.4494
663. Forsmark CE, Swaroop Vege S, Wilcox CM. **Acute Pancreatitis**. N Engl J Med. 2016 Nov 17;375(20):1972-1981 (azathioprine, 6-mercaptopurine, didanosine, valproic acid,angiotensin-converting–enzyme inhibitors, and mesalamine)
664. Gammal RS, Court MH, Haidar CEet al. Clinical Pharmacogenetics Implementation Consortium (CPIC) guideline for **UGT1A1** and **atazanavir** prescribing. Clin Pharmacol Ther. 2016 Apr;99(4):363-9.
665. Hadigan C, Paules CI, Fauci AS. Association Between Human Immunodeficiency Virus Infection and **Cardiovascular Diseases**: Finding a Solution to Double Jeopardy. JAMA Cardiol. 2016 Dec 21.
666. MHRA Dec/16: **Cobicistat, ritonavir and coadministration with a steroid**: risk of systemic corticosteroid adverse effects. Coadministration of a corticosteroid with an HIV-treatment-boosting agent may increase the risk of adrenal suppression due to a pharmacokinetic interaction.
667. Janssen EJ, Bastiaans DE, Välitalo PA, et al. Dose evaluation of **lamivudine in HIV-infected children aged 5 months-18 years** based on a population pharmacokinetic analysis. Br J Clin Pharmacol. 2017 Jan 12.
668. Rekart ML, Ndifon W, Brunham RC, et al. A double-edged sword: does **highly active antiretroviral therapy contribute to syphilis** incidence by impairing immunity to Treponema pallidum? Sex Transm Infect. 2017 Jan 16.
669. Trezza C, Ford SL, Gould E, et al. Lack of Effect of Oral **Cabotegravir** on the Pharmacokinetics of a **Levonorgestrel/Ethinyl Estradiol**-Containing Oral Contraceptive in Healthy Adult Females. Br J Clin Pharmacol. 2017 Jan 14.
670. Kleefeld F, Heller S, Jessen H, et al. Effect of **interferon-free therapy on cognition in HCV** and HCV/HIV infection: A pilot study. Neurology. 2017 Feb 14;88(7):713-715.
671. Knox DC, Anderson PL, Harrigan PR, et al. **Multidrug-Resistant HIV-1 Infection despite Preexposure Prophylaxis**. N Engl J Med. 2017 Feb 2;376(5):501-502.
672. Siddiqi OK, Elafros MA, Bositis CM, et al. **New-onset seizure** in HIV-infected adult Zambians: A search for causes and consequences. Neurology. 2017 Jan 31;88(5):477-482.
673. Waters L, Ahmed N, Angus B, et al. **British HIV Association guidelines** for the treatment of HIV-1-positive adults with antiretroviral therapy 2015 (2016 interim update). London (UK): British HIV Association (BHIVA); 2016 Aug.
674. Van de Perre P, Kankasa C, Nagot N, et al. **Pre-exposure prophylaxis** for infants exposed to HIV **through breast feeding**. BMJ. 2017 Mar 9;356:j1053.
675. Gregson J, Kaleebu P, Marconi VC, et al. Occult HIV-1 drug resistance to thymidine analogues following **failure of first-line tenofovir** combined with a cytosine analogue and **nevirapine** or **efavirenz** in sub Saharan Africa: a retrospective multi-centre cohort study. Lancet Infect Dis. 2016 Nov 30.
676. World Health Organization (WHO), United Nations Children's Fund (UNICEF). Guideline: updates on **HIV and infant feeding**: **the duration of breastfeeding**, and support from health services to improve feeding practices among mothers living with HIV. Geneva (Switzerland): World Health Organization (WHO); 2016. 58 p. [52 references]
677. Freiberg MS, Chang C-CH, Skanderson M, et al. Association between **HIV infection and the risk of heart failure** with reduced ejection fraction and preserved ejection fraction in the antiretroviral therapy era: results from the **Veterans Aging Cohort Study** [online Apr 5, 2017].JAMA Cardiol. doi:10.1001/jamacardio.2017.0264
678. Kirkham D, Bains M. The **offer of an HIV screen for an asymptomatic adult**. BMJ.2017 Jan 19;356:i6656.
679. Taylor AW, Nesheim SR, Zhang X, et al. **Estimated perinatal HIV infection** among infants born in the United States, 2002-2013 [online Mar 20, 2017]. JAMA Pediatr. doi:10.1001 /jamapediatrics.2016.5053 JAMA Pediatr. doi:10.1001 /jamapediatrics.2016.5053
680. van der Heijden I, Abrahams N, Sinclair D. **Psychosocial group interventions** to improve psychological well-being in adults living with HIV. Cochrane Database of Systematic Reviews 2017, Issue 3. Art. No.: CD010806. Group-based psychosocial interventions may have a small effect on measures of depression, but the clinical importance of this is unclear. More high quality evidence is needed to assess whether group psychosocial intervention improve psychological well-being in HIV positive adults.
681. Antiretroviral Therapy Cohort Collaboration. **Survival of HIV-positive patients** starting antiretroviral therapy between 1996 and 2013: a collaborative analysis of cohort studies. Lancet HIV. 2017 May 10.
682. Cillóniz C, Torres A, Manzardo C, et al. **Community-Acquired Pneumococcal Pneumonia** in Virologically Suppressed HIV-Infected Adult Patients: A Matched Case-Control Study. Chest. 2017 Mar 13.
683. Cole JH, Underwood J, Caan MW, et al. **Increased brain-predicted aging** in treated HIV disease. Neurology. 2017 Apr 4;88(14):1349-1357.
684. Liddy AM, McLaughlin G, Schmitz S, et al. The Pharmacokinetic **Interaction between Ivacaftor and Ritonavir** in Healthy Volunteers. Br J Clin Pharmacol. 2017 May 6.
685. **NICE**: National Institute for Health and Care Excellence (NICE), Public Health England. **HIV testing**: increasing uptake among people who may have undiagnosed HIV (joint NICE and Public Health England guideline). London (UK): National Institute for Health and Care Excellence (NICE); 2016 Dec 1.
686. Bonacci RA, Holtgrave DR. U.S. **HIV Incidence and Transmission Goals, 2020 and 2025**. Am J Prev Med. 2017 May 6.
687. Marzolini C, Decosterd L, et al. Free and total plasma concentrations of **elvitegravir/cobicistat during pregnancy** and postpartum: a case report. Br J Clin Pharmacol. 2017 May 16.
688. O'Connor J et al. Durability of viral suppression with first-line antiretroviral therapy in patients with HIV in the UK: An observational cohort study. Lancet HIV 2017 May 4.
689. Onwumeh J, Okwundu CI, Kredo T. **Interleukin-2** as an adjunct to antiretroviral therapy for HIV-positive adults. Cochrane Database of Systematic Reviews 2017, Issue 5. Art. No.: CD009818. There is high certainty evidence that IL-2 in combination with ART increases the CD4 cell count in HIV-positive adults. However, IL-2 does not confer any significant benefit in mortality, there is probably no difference in the incidence of opportunistic infections, and there is probably an increase in grade 3 or 4 adverse effects. Our findings do not support the use of IL-2 as an adjunct to ART in HIV-positive adults. Based on our findings, further trials are not justified.
690. Ciaffi L, Koulla-Shiro S, Sawadogo AB, et al. **Boosted protease inhibitor monotherapy versus boosted protease inhibitor plus lamivudine dual therapy** as second-line maintenance treatment for HIV-1-infected patients in sub-Saharan Africa (ANRS12 286/MOBIDIP): a multicentre, randomised, parallel, open-label, superiority trial. Lancet HIV. 2017 May 26.
691. Petersen M, Balzer L, Kwarsiima D, et al. Association of implementation of a **universal testing and treatment intervention** with HIV diagnosis, receipt of antiretroviral therapy, and HIV viral suppression in **East Africa**. JAMA. doi:10.1001/jama.2017.5705

692. Youn B, Shireman TI, Lee Y, et al. **Ten-year trends in anti-retroviral therapy persistence among US Medicaid beneficiaries**, 2001-2010. AIDS. 2017 May 16.
693. El-Sadr WM, Donnell D, Beauchamp G, et al. **Financial Incentives for Linkage to Care and Viral Suppression** Among HIV-Positive Patients: A Randomized Clinical Trial (HPTN 065). JAMA Intern Med. 2017 Jun 19
694. Le T, Kinh NV, Cuc NTK, et al. A Trial of **Itraconazole or Amphotericin B for HIV-Associated Talaromycosis**. N Engl J Med. 2017 Jun 15;376(24):2329-2340.
695. Visser ME, Durao S, Sinclair D, et al. **Micronutrient supplementation in adults with HIV infection**. Cochrane Database Syst Rev. 2017 May 18;5:CD003650. The analyses of the available trials have not revealed consistent clinically important benefits with routine multiple micronutrient supplementation in people living with HIV. Larger trials might reveal small but important effects.These findings should not be interpreted as a reason to deny micronutrient supplements for people living with HIV where specific deficiencies are found or where the person's diet is insufficient to meet the recommended daily allowance of vitamins and minerals.
696. Chu C., Pollock LC, Selwyn PA. HIV-Associated Complications: A Systems-Based Approach. Am Fam Physician. 2017;96(3):161-169.
697. Daskapan A, Dijkema D, de Weerd DA, et al. Food intake and darunavir plasma concentrations in people living with HIV in an outpatient setting. Br J Clin Pharmacol. 2017 Jul 7.
698. DiNenno EA, Prejean J, Irwin K, et al. **Recommendations** for HIV **Screening** of Gay, Bisexual, and Other Men Who Have Sex with Men - United States, 2017. MMWR Morb Mortal Wkly Rep. 2017 Aug 11;66(31):830-832.
699. Granich R, Williams B, Montaner J, et al. 90-90-90 and ending AIDS: necessary and feasible. Lancet. 2017 Jul 22;390(10092):341-343.
700. Hakim J, Musiime V, Szubert AJ, et al. Enhanced **prophylaxis** plus antiretroviral therapy for **advanced HIV** infection in **Africa**. N Engl J Med 2017;377:233-45.
701. Limper AH, Adenis A, Le T, et al. **Fungal infections** in HIV/AIDS. Lancet Infect Dis. 2017 Jul 31.
702. Margolis DA, Gonzalez-Garcia J, Stellbrink H-J, et al. Long-acting **intramuscular cabotegravir** and **rilpivirine** in adults with HIV-1 infection (LATTE-2): 96-week results of a randomised, open-label, phase 2b, non-inferiority trial. Lancet 2017; published online July 24.
703. Molina JM, Charreau I, Spire B, et al. Efficacy, safety, and effect on sexual behaviour of **on-demand pre-exposure prophylaxis** for HIV in men who have sex with men: an observational cohort study. Lancet HIV. 2017 Jul 21
704. Paton NI, Kityo C, Thompson J, et al. **Nucleoside reverse-transcriptase inhibitor cross-resistance** and outcomes from second-line antiretroviral therapy in the public health approach: an observational analysis within the randomised, open-label, EARNEST trial. Lancet HIV. 2017 Aug;4(8):e341-e348
705. Pressiat C, Mea-Assande V, Yonaba C, et al. Suboptimal **Cotrimoxazole prophylactic concentrations** in HIV-infected children according to the WHO guidelines. Br J Clin Pharmacol. 2017 Aug 11.
706. Saylor D, Nakigozi G, Nakasujja N, et al. **Peripheral neuropathy** in HIV-infected and uninfected patients in Rakai, Uganda. Neurology. 2017 Aug 1;89(5):485-491.
707. Zash R, Jacobson DL, Diseko M, et al. Comparative Safety of **Antiretroviral Treatment** Regimens in **Pregnancy**. JAMA Pediatr. 2017 Aug 7:e172222.
708. Gallant J, Lazzarin A, Mills A, et al. **Bictegravir**, **emtricitabine**, and **tenofovir alafenamide** versus **dolutegravir**, **abacavir**, and **lamivudine** for initial treatment of HIV-1 infection (GS-US-380-1489): a double-blind, multicentre, phase 3, randomised controlled non-inferiority trial. Lancet 2017; online Aug 31
709. Gulick RM, Wilkin TJ, Chen YQ, et al. Safety and Tolerability of **Maraviroc**-Containing Regimens to **Prevent HIV Infection** in Women: A Phase 2 Randomized Trial. Ann Intern Med. 2017 Aug 22:1-10.
710. Hosek SG, Landovitz RJ, Kapogiannis B, et al. Safety and feasibility of antiretroviral **preexposure prophylaxis** for adolescent men who have sex with men aged 15 to 17 years in the United States [online September 5, 2017].JAMA Pediatr. doi:10.1001/jamapediatrics.2017.2007
711. Koenig SP et al. Same-day HIV testing with **initiation** of **antiretroviral therapy** versus standard care for persons living with HIV: A randomized unblinded trial. PLoS Med 2017 Jul 25; 14:e1002357.
712. Looker KJ, Elmes JAR, et al. Effect of **HSV-2 infection** on subsequent **HIV acquisition**: an updated systematic review and meta-analysis. Lancet Infect Dis 2017; online August 23.
713. Moulignier A, Lamirel C, Picard H, et al. **Long**-term **AIDS**-related **PCNSL** outcomes with **HD-MTX** and combined **antiretroviral therapy**. Neurology. 2017 Aug 22;89(8):796-804
714. Mukhtar F, Ilozumba M, Utuama O, et al. Change in Pattern of **Secondary Cancers After Kaposi Sarcoma** in the Era of Antiretroviral Therapy. JAMA Oncol. 2017 Aug 24.
715. World Health Organization (WHO). **Hormonal contraceptive eligibility for women at high risk of HIV**: guidance statement. Geneva (Switzerland): WHO 2017.
716. Siemieniuk RA, et al. **Antiretroviral therapy for pregnant women living with HIV or hepatitis B**: a systematic review and meta-analysis. BMJ Open. 2017 Sep 11;7(9):e019022
717. Siemieniuk RAC, Lytvyn L, Mah Ming J, et al. **Antiretroviral therapy in pregnant women living with HIV**: a clinical practice guideline. BMJ. 2017 Sep 11;358:j3961.
718. Lytvyn L, Siemieniuk RA, Dilmitis S, et al. Values and preferences of women living with **HIV who are pregnant, postpartum or considering pregnancy** on choice of antiretroviral therapy during pregnancy. BMJ Open. 2017 Sep 11;7(9):e019023.
719. Reddy KP, Kong CY, Hyle EP, et al. **Lung cancer mortality** associated with smoking and **smoking** cessation among people living **with HIV** in the United States [online September 18, 2017].JAMA Intern Med. doi:10.1001 /jamainternmed.2017.4349
720. Tavoschi L, Gomes Dias J, Pharris A, on behalf of the EU/EEA Surveillance Network. **New HIV diagnoses among adults aged 50 years or older** in 31 **European** countries, 2004–15: an analysis of surveillance data. Lancet HIV 2017; online Sept 26.
721. Rubin LH, Maki PM, Springer G, et al. **Cognitive trajectories** over 4 years among HIV-infected women with optimal viral suppression. Neurology 2017;89:1594:1603.
722. Tavoschi L, Gomes Dias J, Pharris A. EU/EEA HIV Surveillance Network. New **HIV diagnoses among adults aged 50 years or older** in 31 **European countries**, 2004-15: an analysis of surveillance data. Lancet HIV 2017.
723. Valverde EE et al. **HIV transmission dynamics among foreign-born persons** in the United States. J Acquir Immune Defic Syndr 2017 Sep 7;
724. Veilleux O, Lee TC, et al. **Rebound adrenal insufficiency after withdrawal of ritonavir** in a 65-year-old man using inhaled budesonide. CMAJ. 2017Sep 18;189(37):E1188-E1191.
725. Beyrer C, Pozniak A. **HIV Drug Resistance** - An Emerging Threat to Epidemic Control. N Engl J Med. 2017 Oct 26;377(17):1605-1607.
726. Daskapan A, Stienstra Y, Kosterink JGW, et al. Risk factors contributing to a low **darunavir** plasma concentration. Br J Clin Pharmacol. 2017 Oct 27.
727. Natukunda E, Gaur AH, Kosalaraka P, et al. Safety, efficacy, and pharmacokinetics of single-tablet **elvitegravir, cobicistat, emtricitabine, and tenofovir alafenamide** in virologically suppressed, HIV-infected children: a single-arm, open-label trial. Lancet Child Adolesc Health. 2017;1:27-34
728. Hakim JG, Thompson J, Kityo C, et al. **Lopinavir plus nucleoside reverse-transcriptase inhibitors, lopinavir plus raltegravir, or lopinavir monotherapy** for second-line treatment of HIV (**EARNEST**): 144-week follow-up results from a randomised controlled trial. Lancet Infect Dis 2017; online Nov 3.
729. Hermans LE, Moorhouse M, Carmona S, et al. Effect of **HIV-1 low-level viraemia** during antiretroviral therapy on **treatment outcomes** in WHO-guided South African treatment programmes: a multicentre cohort study. *Lancet Infect Dis* 2017; online Nov 17.
730. Sanford R, Fellows LK, Ances BM, Collins DL. Association of **Brain Structure Changes** and Cognitive Function With Combination Antiretroviral Therapy in HIV-Positive Individuals. JAMA Neurol. 2017 Nov 13.
731. Siemieniuk RAC, Lytvyn L, Mah Ming J, et al. **Antiretroviral therapy in pregnant women living with HIV: a clinical practice guideline.** BMJ. 2017 Sep 11;358:j3961.
732. Zhao Y, Wang Y, Wang A, et al. Median Time to **Antiretroviral Therapy Initiation in a Cohort of Chinese Infants Born With HIV**. JAMA Pediatr. 2017 Nov 13.
733. Gupta RK, Gregson J, Parkin N, et al. **HIV-1 drug resistance before initiation or re-initiation of first-line antiretroviral therapy** in low-income and middle-income countries: a systematic review and meta-regression analysis. Lancet Infect Dis 2017; online Nov 30.

734. Ladapo JA, Richards AK, DeWitt CM, et al. Disparities in the **Quality of Cardiovascular Care Between HIV-Infected Versus HIV-Uninfected Adults** in the United States: A Cross-Sectional Study. J Am Heart Assoc. 2017 Nov 14;6(11).
735. Tan DHS, Hull MW, et al. **Canadian guideline on HIV pre-exposure prophylaxis and nonoccupational postexposure prophylaxis**. CMAJ. 2017 Nov 27;189(47):E1448-E1458.
736. Cambiano V, Miners A, Dunn D, et al.**Cost-effectiveness** of **pre-exposure prophylaxis** for HIV prevention in **men who have sex with men** in the UK: a modelling study and health economic evaluation. Lancet Infect Dis. 2017 Oct 17.
737. Cohen SD, Kopp JB, Kimmel PL. **Kidney Diseases** Associated with Human Immunodeficiency Virus Infection. N Engl J Med. 2017 Dec 14;377(24):2363-2374.
738. Desai M, Field N, Grant R, et al. Recent advances in **pre-exposure prophylaxis** for HIV. BMJ. 2017 Dec 11;359:j5011.
739. Gallant J, Lazzarin A, Mills A, et al. **Bictegravir, emtricitabine, and tenofovir alafenamide** versus dolutegravir, abacavir, and lamivudine for initial treatment of HIV-1 infection (GS-US-380-1489): a double-blind, multicentre, phase 3, randomised controlled non-inferiority trial. Lancet. 2017 Nov 4;390(10107):2063-2072
740. Grabowski MK, Serwadda DM, Gray RH, et al. **HIV Prevention Efforts** and Incidence of HIV in Uganda. N Engl J Med. 2017 Nov30;377(22):2154-2166.
741. Llibre JM, Hung C-C, Brinson C, et al. Efficacy, safety, and tolerability of **dolutegravir-rilpivirine** for the maintenance of virological suppression in adults with HIV-1: phase 3, randomised, non-inferiority **SWORD-1 and SWORD-2** studies. Lancet 2017; online Jan 5.
742. Pannetier P, Ravalihasy A, Lydié N, et al, on behalf of the Parcours study group. Prevalence and circumstances of **forced sex and post-migration HIV acquisition** in sub-Saharan African migrant women in France: an analysis of the **ANRS-PARCOURS** retrospective population-based study. Lancet Public Health 2017; online Nov 22.
743. Ruiz-Perez I, Murphy M, Pastor-Moreno G, et al. The Effectiveness of **HIV Prevention Interventions in Socioeconomically Disadvantaged Ethnic Minority Women**: A Systematic Review and Meta-Analysis. Am J Public Health. 2017 Dec;107(12):e13-e21.
744. Hapgood JP, Kaushic C, Hel Z. **Hormonal Contraception and HIV-1 Acquisition**: Biological Mechanisms. Endocr Rev. 2018 Jan 4.
745. Loutfy M, Kennedy VL, Poliquin V, et al. **No. 354-Canadian HIV Pregnancy Planning Guidelines**. J Obstet Gynaecol Can. 2018 Jan;40(1):94-114.
746. Margolis DM, Garcia JV. **Countering HIV - Three's the Charm**? N Engl J Med. 2018 Jan 18;378(3):295-297.
747. **Can we eliminate HIV**? Can Fam Physician. 2018 Jan;64(1):42-43.
748. Martin EG, Schackman BR. Treating and Preventing **HIV with Generic Drugs -** Barriers in the United States. N Engl J Med. 2018 Jan 25;378(4):316-319.
749. McHenry MS, McAteer CI, Oyungu E, et al. **Neurodevelopment in Young Children Born to HIV-Infected Mothers**: A Meta-analysis. Pediatrics. 2018 Jan 26.
750. Calcagno A, Pinnetti C, et al. **Cerebrospinal Fluid Abacavir Concentrations** in HIV-positive Patients Following Once-daily Administration. Br J Clin Pharmacol. 2018 Feb 14.
751. Cunningham WE,Weiss RE, Nakazono T, et al. Effectiveness of a **peer navigation intervention** to sustain viral suppression among HIV-positive men and transgender women released from jail: the LINK LA randomized clinical trial [online Mar 12, 2018]. JAMA Intern Med. doi:10.1001/jamainternmed.2018.0150
752. Gopalan N, Santhanakrishnan RK, Palaniappan AN, et al. **Daily vs Intermittent Antituberculosis Therapy** for Pulmonary Tuberculosis in Patients With HIV: A Randomized Clinical Trial. JAMA Intern Med. 2018 Mar 5.
753. Labhardt ND, Ringera I, Lejone TI, et al. Effect of offering **same-day ART vs usual health facility referral** during home-based HIV testing on linkage to care and viral suppression among adults with HIV in Lesotho: the CASCADE randomized clinical trial. JAMA. doi:10.1001/jama.2018.1818
754. Weiser J, Perez A, Bradley H, et al. Low Prevalence of **Hepatitis B Vaccination** Among Patients Receiving Medical Care for HIV Infection in the United States, 2009 to 2012. Ann Intern Med. 2018 Feb 20;168(4):245-254.
755. Riddell J 4th, Amico KR, Mayer KH. **HIV Preexposure Prophylaxis**: A Review. JAMA. 2018 Mar 27;319(12):1261-1268.
756. Ryom L, et al. Highlights of the **2017 European AIDS Clinical Society (EACS) Guidelines** for the treatment of **adult HIV-positive persons** version 9.0. HIV Med. 2018 Mar 1.
757. Singh S, Song R, Johnson AS, et al. HIV Incidence, HIV Prevalence, and Undiagnosed HIV Infections in **Men Who Have Sex With Men, United States**. Ann Intern Med. 2018 Mar 20.
758. Yang YT, Underhill K. **Rethinking Criminalization of HIV Exposure** – Lessons from California's New Legislation. N Engl J Med. 2018 Mar 29;378(13):1174-1175.
759. Yarchoan R, Uldrick TS. **HIV-Associated Cancers and Related Diseases**. N Engl J Med. 2018 Mar 15;378(11):1029-1041.
760. Beckman JA, Duncan MS, Alcorn CW, et al. Association of **HIV Infection and Risk of Peripheral Artery Disease**. Circulation. 2018 Mar 13.
761. Bravo I, Álvarez H, Mariño A, et al. **Recurrent coronary disease in HIV-infected patients: role of drug-drug** interactions. Br J Clin Pharmacol. 2018 Apr 16.
762. Katz IT et al. **The global HIV epidemic**: What will it take to get to the finish line? JAMA 2018 Mar 20; 319:1094.
763. Oster AM, France AM, Mermin J. **Molecular Epidemiology and the Transformation of HIV Prevention**. JAMA. 2018 Apr 9.
764. Dalcin D, Bogoch II. **Point-of-care testing** for HIV. CMAJ. 2018 May 7;190(18):E569.
765. Myer L, Phillips TK, Zerbe A, et al. Integration of **postpartum healthcare services** for HIV-infected women and their infants in South Africa: A randomised controlled trial. PLoS Med. 2018 Mar 30;15(3):e1002547.
766. Rough K, Seage GR 3rd, Williams PL, et al. Birth Outcomes for Pregnant Women with HIV Using **Tenofovir-Emtricitabine**. N Engl J Med. 2018 Apr 26;378(17):1593-1603.
767. Shiels MS et al. Projected cancer incidence rates and burden of incident cancer cases in HIV-infected adults in the United States through 2030. Ann Intern Med 2018 May 8; [e-pub].
768. FDA May/18: Juluca, Tivicay, Triumeq (dolutegravir): FDA to Evaluate - Potential Risk of Neural Tube Birth Defects. The FDA and EMA have warned about a possible increased risk for neural tube defects in infants born to women who take dolutegravir for HIV during pregnancy.
769. Justman JE, Mugurungi O, El-Sadr WM. HIV Population Surveys – Bringing Precision to the Global Response. N Engl J Med. 2018 May 17;378(20):1859-1861.
770. Sanford R, Ances BM, Meyerhoff DJ, et al. Longitudinal Trajectories of **Brain Volume and Cortical Thickness in Treated and Untreated Primary HIV Infection**. Clin Infect Dis. 2018 Apr 24.
771. Singh S, Song R, Johnson AS, et al. HIV Incidence, HIV Prevalence, and Undiagnosed HIV Infections in **Men Who Have Sex With M**en, United States. Ann Intern Med. 2018 Mar 20.
772. Triant VA, Perez J, Regan S, et al. **Cardiovascular risk prediction functions underestimate risk in HIV infection**. Circulation. 018;137:2203–2214. doi: 10.1161/CIR-CULATIONAHA.117.028975.
773. Zhao Y, Wu Z, McGoogan JM, et al. Nationwide cohort study of **antiretroviral therapy timing**: treatment dropout and virological failure in China, 2011-2015. Clin Infect Dis. 2018 May 16.
774. Atwine D, Bonnet M, Taburet AM. Pharmacokinetics of efavirenz in patients on antituberculosis treatment in high human immunodeficiency virus and tuberculosis burden countries: A systematic review. Br J Clin Pharmacol. 2018 Apr 6.
775. Fitzpatrick MC, Gray GE, Galvani AP. The Challenge of Vanquishing HIV for the Next Generation-Facing the Future. JAMA Pediatr. 2018 May 21.
776. Shiels MS, Islam JY, Rosenberg PS, et al. Projected Cancer Incidence Rates and **Burden of Incident Cancer Cases in HIV-Infected Adults** in the United States Through 2030. Ann Intern Med. 2018 May 8.
777. Dorward J, Lessells R, Drain PK, et al. Dolutegravir for **first-line antiretroviral therapy in low-income and middle-income countries**: uncertainties and opportunities for implementation and research. Lancet HIV. 2018 Jun 5.

778. Helath Canada Jun/18: **TIVICAY, TRIUMEQ and JULUCA** (dolutegravir containing medicines) – Possible **Risk of Neural Tube Defects**. Early findings from the ongoing Tsepamo study in Botswana suggest a possible increased risk of neural tube defects (NTD) involving the brain, spine and spinal cord in infants born to women being treated with dolutegravir at the time of conception
779. Holt M, Lea T, Mao L, et al. Community-level changes in **condom use and uptake of HIV pre-exposure prophylaxis by gay and bisexual men** in Melbourne and Sydney, Australia: results of repeated behavioural surveillance in 2013–17. Lancet HIV 2018; online June 6.
780. Piyaraj P, van Griensven F, Holtz TH, et al. Finding **casual sex partners** on the internet**, methamphetamine** use for sexual pleasure, and **incident of HIV infection** among men who have sex with men in Bangkok, Thailand: an observational cohort study. Lancet HIV 2018; online May 31.
781. Chang JL, Tsai AC, Musinguzi N, et al. **Depression and Suicidal Ideation** Among HIV-Infected Adults Receiving **Efavirenz Versus Nevirapine** in Uganda: A Prospective Cohort Study. Ann Intern Med. 2018 Jun 26.
782. Hwang SS, Dukhovny D, Gopal D, et al. Health of Infants After **ART-Treated, Subfertile, and Fertile Deliveries**. Pediatrics. 2018 Jul 3.
783. Ribeiro RMP, de Lima Moreira F, Dantas Moisés EC, et al. **Lopinavir/Ritonavir** treatment increases the **placental transfer of bupivacaine enantiomers in HIV-infected** pregnant women. Br J Clin Pharmacol. 2018 Jun 29.
784. Beckman JA, Duncan MS, Alcorn CW, et al. Association of Human Immunodeficiency Virus Infection and **Risk of Peripheral Artery Disease**. Circulation. 2018 Jul 17;138(3):255-265.
785. Alvi RM, Neilan AM, Tariq N, et al. **Protease Inhibitors and Cardiovascular Outcomes in Patients With HIV and Heart Failure**. J Am Coll Cardiol. 2018 Jul 31;72(5):518-530.
786. Bavinton BR, Pinto AN, Phanuphak N, et al; **Opposites Attract Study Group**. **Viral suppression and HIV transmission in serodiscordant male couples**: an international, prospective, observational, cohort study. Lancet HIV. 2018 Jul 16.
787. Ghosn J, Taiwo B, Seedat S, et al. HIV. Lancet. 2018 Jul 23. pii: S0140-6736(18)31311-4.
788. Jichlinski A, Badolato G, Pastor W, et al. **HIV and Syphilis Screening Among Adolescents** Diagnosed With Pelvic Inflammatory Disease. Pediatrics. 2018 Jul 24.
789. Veroniki AA, Antony J, Straus SE, et al. Comparative **safety and effectiveness of perinatal antiretroviral therapies for HIV-infected women** and their children: Systematic review and network meta-analysis including different study designs. PLoS One. 2018 Jun 18;13(6):e0198447.
790. Zash R, Makhema J, Shapiro RL. **Neural-Tube Defects with Dolutegravir Treatment** from the Time of Conception. N Engl J Med. 2018 Jul 24.
791. Abrams EJ, Mellins CA, Bucek A, et al. **Behavioral Health and Adult Milestones in Young Adults With Perinatal HIV Infection or Exposure**. Pediatrics. 2018 Aug 10.
792. Emu B, Fessel J, Schrader S, et al. Phase 3 Study of **Ibalizumab for Multidrug-Resistant HIV-1**. N Engl J Med. 2018 Aug 16;379(7):645-654.
793. Eron JJ, Orkin C, Gallant J, et al. A week-48 randomized phase-3 trial of **darunavir/cobicistat/emtricitabine/tenofovir alafenamide** in treatment-naive HIV-1 patients. AIDS. 2018 Jul 17;32(11):1431-1442.
794. Garofalo R, Kuhns LM, Reisner SL, et al. Efficacy of an **empowerment-based, group-delivered HIV prevention intervention** for young transgender women: the Project LifeSkills randomized clinical trial [online August 13, 2018]. JAMA Pediatr.
795. Ghosn J, Taiwo B, Seedat S, et al. HIV- Seminar. Lancet. 2018 Jul 23.
796. Orkin C, Molina JM, Negredo E, et al. Efficacy and safety of switching from **boosted protease inhibitors plus emtricitabine and tenofovir disoproxil fumarate regimens to single-tablet darunavir, cobicistat, emtricitabine, and tenofovir alafenamide** at 48 weeks in adults with virologically suppressed HIV-1 (EMERALD): a phase 3, randomised, non-inferiority trial. Lancet HIV. 2018 Jan;5(1):e23-e34.
797. Colin De Verdiere N, Durier C, Samri A, et al; and the ANRS EP46 NOVAA Group. Immunogenicity and safety of **yellow fever vaccine in HIV-1-infected patients**: ANRS EP46 NOVAA. AIDS. 2018 Aug 8.
798. Nance RM, Delaney JAC, Simoni JM, et al. **HIV Viral Suppression Trends Over Time Among HIV-Infected Patients Receiving Care in the United States**, 1997 to 2015: A Cohort Study. Ann Intern Med. 2018 Aug 21.
799. Ryom L, Lundgren JD, El-Sadr W, et al. **Cardiovascular disease and use of contemporary protease inhibitors**: the D:A:D international prospective multicohort study. Lancet HIV. 2018 Jun;5(6):e291-e300.
800. Arrington-Sanders R, Wheeler NJ, Matson P, et al. A System-Level Approach to **Improve HIV Screening in an Urban Pediatric Primary Care Setting**. Pediatrics. 2018 Oct 16.
801. Grulich AE, Guy R, Amin J, et al. Population-level effectiveness of **rapid, targeted, high-coverage roll-out of HIV pre-exposure prophylaxis** in men who have sex with men: the EPIC-NSW single-arm prospective cohort study. Lancet HIV 2018; online Oct 17.
802. Salgado M, Kwon M, Galvez C, et al. **Mechanisms that contribute to a profound reduction of the HIV-1 reservoir after allogeneic stem cell transplant**. Ann Intern Med. 2018. [Epub ahead of print].
803. Sundermann EE, Heaton RK, Pasipanodya E, et al; HNRP Group. **Sex differences in HIV-associated cognitive impairment**: an observational cohort study. AIDS. 2018 Oct 4.
804. Coomes EA, Heendeniya A, Bunce PE. **Progressive multifocal leukoencephalopathy unmasked** by antiretroviral therapy for HIV. CMAJ. 2018 Oct 22;190(42):E1260.
805. Hammoud DA, Sinharay S, Steinbach S, et al. Global and regional **brain hypometabolism on FDG-PET** in treated HIV-infected individuals. Neurology. 2018 Oct 23;91(17):e1591-e1601.
806. McMillan JM, Krentz H, Gill MJ, Hogan DB. Managing HIV infection in patients **older than 50 years**. CMAJ. 2018 Oct 22;190(42):E1253-E1258.
807. Cahn P, Madero JS, Arribas JR, et al; GEMINI Study Team. **Dolutegravir plus lamivudine** versus **dolutegravir plus tenofovir disoproxil fumarate and emtricitabine** in antiretroviral-naive adults with HIV-1 infection (GEMINI-1 and GEMINI-2): week 48 results from two multicentre, double-blind, randomised, non-inferiority, phase 3 trials. Lancet. 2018 Nov 9.
808. Elliott R. Ending overly broad **criminalization of nondisclosure** of human immunodeficiency virus infection. CMAJ. 2018 Nov 19;190(46):E1348-E1349.
809. Hsue PY, Waters DD. Time to Recognize HIV Infection as a **Major Cardiovascular Risk Factor**. Circulation. 2018 Sep 11;138(11):1113-1115.
810. Lê MP,Chaix ML,Raffi F, et al; Once-daily **darunavir/ritonavir** 400/100 mg in triple therapy: efficacy and penetration in seminal compartment in ANRS-165 DARULIGHT study. Br J Clin Pharmacol, 2018Nov12.
811. LeMessurier J, Traversy G, Varsaneux O, et al. Risk of sexual transmission of human immunodeficiency virus with antiretroviral therapy, **suppressed viral load and condom use:** a systematic review. CMAJ. 2018 Nov 19;190(46):E1350-E1360.
812. Meintjes G, Stek C, Blumenthal L, et al; PredART Trial Team. Prednisone for the Prevention of Paradoxical **Tuberculosis-Associated IRIS**. N Engl J Med. 2018 Nov 5; 379(20):1915-1925.
813. Tippett Barr BA, van Lettow M, van Oosterhout JJ, et al. National estimates and risk factors associated with **early mother-to-child transmission of HIV** after implementation of option B+: a cross-sectional analysis. Lancet HIV. 2018 Nov 19.
814. Abdullahi ST, Olagunju A, Soyinka JO, et al. Pharmacogenetics of artemether-lumefantrine influence on nevirapine disposition: clinically significant drug-drug interaction? Br J Clin Pharmacol. 2018 Nov 24.
815. Borges AH, Neuhaus J, Sharma S, et al. The effect of interrupted/deferred antiretroviral therapy on disease risk: a SMART & START combined analysis. J Infect Dis. 2018 Jul 19.
816. Siedner MJ, Tumarkin E, Bogoch II. HIV post-exposure prophylaxis (PEP). BMJ. 2018 Nov 29;363:k4928.
817. Grant PM, Li X, Jacobson LP, et al. Effect of Testosterone Use on Bone Mineral Density in HIV-Infected Men. AIDS Res Hum Retroviruses. 2018 Nov 1.
818. Kityo C, Szubert AJ, Siika A, et al. Raltegravir-intensified initial antiretroviral therapy in advanced HIV disease in Africa: A randomised controlled trial. PLoS Med. 2018 Dec 4;15(12):e1002706.
819. Pastori D, Mezzaroma I, Pignatelli P, et al. Atrial fibrillation and Human Immunodeficiency Virus type-1 infection: a systematic review. Implications for anticoagulant and antiarrhythmic therapy. Br J Clin Pharmacol. 2018 Dec 21.
820. Bowles AA, Smirnov B. Erythrodermic Psoriasis and HIV Infection. N Engl J Med. 2019 Jan 3;380(1):80.
821. Haban H, Benchekroun S, Sadeq M,et al. Seroprevalence of measles vaccine antibody response in vertically HIV-infected children, in Morocco. BMC Infect Dis. 2018 Dec 19;18(1):680.
822. Parker CM, Hirsch JS, Hansen HB, et al. Facing. N Engl J Med. 2019 Jan 3;380(1):1-3.
823. ACOG: Committee on Obstetric Practice; HIV Expert Work Group. ACOG Committee Opinion No. 752: **Prenatal and Perinatal Human Immunodeficiency Virus Testing**. Obstet Gynecol. 2018 Sep;132(3):e138-e142.

824. ACOG: Committee on Obstetric Practice; HIV Expert Work Group. ACOG Committee Opinion No. 751: **Labor and Delivery Management of Women With Human Immunodeficiency Virus Infection**. Obstet Gynecol. 2018 Sep;132(3):e131-e137.
825. Braun DL, Turk T, Tschumi F, et al. **Non-inferiority of simplified dolutegravir monotherapy compared to continued combination antiretroviral therapy that was initiated during primary HIV infection**: a randomized, controlled, multi-site, open-label, non-inferiority trial. Clin Infect Dis. 2019 Jan 2.
826. Eisinger RW, Dieffenbach CW, Fauci AS. **HIV Viral Load and Transmissibility of HIV Infection**: Undetectable Equals Untransmittable. JAMA. 2019 Jan 10.
827. Hocqueloux L, Raffi F, Prazuck T, et al; MONCAY study group. **Dolutegravir monotherapy versus dolutegravir/abacavir/lamivudine for virologically suppressed people living with chronic HIV infection**: the randomized non-inferiority MONCAY trial. Clin Infect Dis. 2019 Jan 2.
828. Pastori D, Mezzaroma I, Pignatelli P, et al. **Atrial fibrillation and human immunodeficiency virus type-1 infection**: a systematic review. Implications for anticoagulant and antiarrhythmic therapy. Br J Clin Pharmacol. 2018 Dec 21.
829. Siedner MJ, Tumarkin E, Bogoch II. **HIV post-exposure prophylaxis** (PEP). BMJ. 2018 Nov 29;363:k4928.
830. Tumarkin E, Siedner MJ, Bogoch II. **HIV pre-exposure prophylaxis** (PrEP). BMJ. 2019 Jan 17;364:k4681.
831. Ben-Chetrit E, Shavit L, Tvito A, et al. The Devil Is in the Details. N Engl J Med. 2019 Feb 7;380(6):581-586.
832. Bahr NC, Yarlagadda SG. **Fanconi Syndrome and Tenofovir Alafenamide**: A Case Report. Ann Intern Med. 2019 Jan 29.
833. Marcus JL, Katz KA, Krakower DS, et al. Risk Compensation and Clinical Decision Making - The Case of **HIV Preexposure Prophylaxis**. N Engl J Med. 2019 Feb 7;380(6):510-512.
834. Ramsey SD, Unger JM, Baker LH, et al. Prevalence of Hepatitis B Virus, Hepatitis C Virus, and HIV **Infection Among Patients With Newly Diagnosed Cancer** From Academic and Community Oncology Practices. JAMA Oncol. 2019 Jan 17.
835. Giguère P, Nhean S, Tseng AL, et al. Getting to the Heart of the Matter: A Review of **Drug Interactions Between HIV Antiretrovirals and Cardiology Medications**. Can J Cardiol. 2019 Mar;35(3):326-340.
836. Gupta RK, Abdul-Jawad S, McCoy LE, et al. HIV-1 **remission following CCR5Δ32/Δ32 haematopoietic stem-cell transplantation**. Nature. 2019 Mar 5.
837. Li Z, Purcell DW, Sansom SL, et al. Vital Signs: HIV **Transmission Along the Continuum of Care** - United States, 2016. MMWR Morb Mortal Wkly Rep. 2018 Mar 22;68(11):267-272.
838. Swindells S, Ramchandani R, Gupta A, et al; BRIEF TB/A5279 Study Team. One Month of **Rifapentine plus Isoniazid to Prevent HIV-Related Tuberculosis**. N Engl J Med. 2019 Mar 14;380(11):1001-1011.
839. Dugdale CM, Ciaranello AL, Bekker LG, et al. Risks and Benefits of **Dolutegravir- and Efavirenz-Based Strategies** for South African Women With HIV of Child-Bearing Potential: A Modeling Study. Ann Intern Med. 2019 Apr 2. doi: 10.7326/M18-3358.
840. Jarolimova J, Kabakyenga J, Bennett K, et al. **Contraceptive use following unintended pregnancy** among Ugandan women living with HIV. PLoS One. 2018 Oct 25;13(10):e0206325.
841. Khuder SS, Chen S, Letendre S, et al. **Impaired insulin sensitivity is associated with worsening cognition in HIV**-infected patients. Neurology. 2019 Mar 19;92(12):e1344-e1353.
842. Traeger MW, Cornelisse VJ, Asselin J, et al. Association of **HIV Preexposure Prophylaxis** With Incidence of Sexually Transmitted Infections Among Individuals at High Risk of HIV Infection. JAMA. 2019 Apr 9;321(14):1380-1390.
843. Wojciechowski D, Gandhi RT, Rosales IA. Case 11-2019: A 49-Year-Old Man with **HIV Infection and Chronic Kidney Disease**. N Engl J Med. 2019 Apr 11;380(15):1464-1472.
844. de Monteynard LA, Matheron S, Grabar S, et al. **Influence of geographic origin on AIDS and serious non-AIDS morbidity/mortality** during cART among heterosexual HIV-infected men and women in France. PLoS One. 2018 Oct 31;13(10):e0205385.
845. El-Sadr WM, Mayer KH, Rabkin M, Hodder SL. **AIDS in America** - Back in the Headlines at Long Last. N Engl J Med. 2019 May 1.
846. Rodger AJ, Cambiano V, Bruun T, et al; PARTNER Study Group. Risk **of HIV transmission through condomless sex in serodifferent gay couples** with the HIV-positive partner taking suppressive antiretroviral therapy (PARTNER): final results of a multicentre, prospective, observational study. Lancet. 2019 May 2.
847. Wang CY, Wong WW, Tsai HC, et al. **Effect of Anti-CD4 Antibody UB-421 on HIV-1 Rebound** after Treatment Interruption. N Engl J Med. 2019 Apr 18;380(16):1535-1545.
848. Archary M, Mcllleron H, Bobat R, et al. Population **pharmacokinetics of abacavir and lamivudine in severely malnourished HIV-infected children** in relation to treatment outcomes. Br J Clin Pharmacol. 2019 May29.
849. Courlet P, Guidi M, Glatard A,et al. **Escitalopram population pharmacokinetics in people living with HIV** and in the psychiatric population: drug-drug interactions and probability of target attainment. Br J Clin Pharmacol. 2019 May 29.
850. Du Plessis NM, Muller CJB, Avenant T, Pepper MS, Goga AE. An early **infant HIV risk score for targeted HIV testing at birth**. Pediatrics. 2019;143(6):e20183834
851. Heendeniya A, Tumarkin E, Bogoch II. HIV **preexposure prophylaxis in Canadian primary care** and community settings. Can Fam Physician. 2019 Apr;65(4):271-272.
852. Kassaye SG, Wang C, Ocampo JMF, et al. **Viremia Trajectories of HIV** in HIV-Positive Women in the United States, 1994-2017. JAMA Netw Open. 2019 May 3;2(5):e193822.
853. Feinstein MJ, Hsue PY, Benjamin LA, et al. Characteristics, Prevention, and Management of **Cardiovascular Disease in People Living With HIV**: A Scientific Statement From the American Heart Association. Circulation. 2019 Jun 3:CIR0000000000000695.
854. USPSTF: Chou R, Evans C, Hoverman A, et al. **Preexposure prophylaxis for the prevention of HIV infection**: evidence report and systematic review for the US Preventive Services Task Force [June 11, 2019]. JAMA. doi:10.1001/jama.2019.2591
855. USPSTF: Selph SS, Bougatsos C, Dana T, Grusing S, Chou R. **Screening for HIV infection in pregnant women**: updated evidence report and systematic review for the US Preventive Services Task Force [online June 11, 2019]. JAMA. doi:10.1001/jama.2019.2593v
856. USPSTF: US Preventive Services Task Force. **Screening for HIV infection in asymptomatic, nonpregnant adolescents and adults**: updated evidence report and systematic review for the US Preventive Services Task Force [online June 11, 2019]. JAMA. doi:10.1001/jama.2019.2592
857. USPSTF: US Preventive Services Task Force. **Screening for HIV infection:** US Preventive Services Task Force recommendation statement [published online June 11, 2019]. JAMA. doi:10.1001/jama.2019.6587
858. Dash PK, Kaminski R, Bella R, et al. Sequential **LASER ART and CRISPR Treatments Eliminate HIV-1** in a Subset of Infected Humanized Mice. Nat Commun. 2019 Jul 2;10(1):2753.
859. **ECHO HIV** incidence among women **using intramuscular depot medroxyprogesterone acetate**, a copper intrauterine device, **or a levonorgestrel implant** for contraception: a randomised, multicentre, open-label trial. Lancet. 2019 Jun 13.
860. Mateo-Urdiales A, Johnson S, Smith R, et al. **Rapid initiation of antiretroviral therapy** for people living with HIV. Cochrane Database Syst Rev. 2019 Jun 17;6:CD012962.
861. USPSTF: Owens DK, Davidson KW, Krist AH, et al. **Preexposure Prophylaxis** for the Prevention of HIV Infection: US Preventive Services Task Force Recommendation Statement. JAMA. 2019 Jun 11;321(22):2203-2213.
862. BHIVA/BASHH **British guidelines** on the use of HIV pre-exposure prophylaxis (PrEP) 2018. HIV Med. 2019 Mar;20 Suppl 2:s2-s80.
863. Feng Q, Zhou A, Zou H, et al. Quadruple versus triple combination **antiretroviral therapies for treatment naive people** with HIV: systematic review and meta-analysis of randomised controlled trials. BMJ. 2019 Jul 8;366:l4179.
864. Havlir DV, Balzer LB, Charlebois ED, et al. HIV Testing and Treatment with the Use of a **Community Health Approach in Rural Africa**. N Engl J Med. 2019 Jul 18;381(3):219-229.
865. Hayes RJ, Donnell D, Floyd S, et al; HPTN 071 (PopART) Study Team. Effect of **Universal Testing and Treatment on HIV Incidence** - HPTN 071 (PopART). N Engl J Med. 2019 Jul 18;381(3):207-218.
866. Makhema J, Wirth KE, Pretorius Holme M, et al. Universal **Testing, Expanded Treatment, and Incidence** of HIV Infection in Botswana. N Engl J Med. 2019 Jul 18;381(3):230-242.
867. Raesima MM, Ogbuabo CM, Thomas V, et al. **Dolutegravir Use at Conception** - Additional Surveillance Data from Botswana. N Engl J Med. 2019 Jul 22.
868. Spinelli MA, Glidden DV, Anderson PL, et al. Impact of Estimated Pre-Exposure Prophylaxis (**PrEP) Adherence Patterns on Bone Mineral Density** in a Large PrEP Demonstration Project. AIDS Res Hum Retroviruses. 2019 Jun 19.

869. Spudich S, Robertson KR, Bosch RJ, et al. Persistent **HIV-infected cells in cerebrospinal fluid** are associated with poorer neurocognitive performance. J Clin Invest. 2019 Jul 15;130.
870. Zash R, Holmes L, Diseko M, et al. **Neural-Tube Defects** and Antiretroviral Treatment Regimens in Botswana. N Engl J Med. 2019 Jul 22.
871. NAMSAL ANRS 12313 Study Group. **Dolutegravir-Based or Low-Dose Efavirenz-Based Regimen** for the Treatment of HIV-1. N Engl J Med. 2019 Jul 24.
872. Rubin LH, Gustafson D, Hawkins KL, et al. **Midlife adiposity predicts cognitive decline** in the prospective Multicenter AIDS Cohort Study. Neurology. 2019 Jul 16;93(3):e261-e271.
873. Venter WDF, Moorhouse M, Sokhela S, et al. **Dolutegravir plus Two Different Prodrugs of Tenofovir** to Treat HIV. N Engl J Med. 2019 Jul 24
874. Azoulay É, de Castro N, Barbier F. **Critically Ill Patients** with the HIV: 40 Years Later. Chest. 2019 Aug 14.
875. Coghill AE, Suneja G, Rositch AF, et al. **HIV Infection, Cancer Treatment Regimens, and Cancer Outcomes** Among Elderly Adults in the United States. JAMA Oncol. 2019 Aug 1.
876. Marcy O, Borand L, Ung V, et al; ANRS 12229 PAANTHER 01 Study Group. A **treatment-decision score for HIVinfected children with suspected tuberculosis**. Pediatrics. 2019;144(3): e20182065.
877. McAuley A, Palmateer NE, Goldberg DJ, et al. **Re-emergence of HIV related to injecting drug use** despite a comprehensive harm reduction environment: a cross-sectional analysis. Lancet HIV. 2019 May;6(5):e315-e324.
878. Alvi RM, Neilan AM, Tariq N, et al. The **Risk for Sudden Cardiac Death** Among Patients Living With Heart Failure and Human Immunodeficiency Virus. JACC Heart Fail. 2019 Sep;7(9):759-767.
879. Cook R, Davidson P, Martin R. **Antiretroviral treatment can reduce the risk** of HIV transmission between male partners to 'zero'. BMJ. 2019 Aug 27;366:l4915.
880. Lübke N, Jensen B, Hüttig F, et al. **Failure of Dolutegravir First-Line ART** with Selection of Virus Carrying R263K and G118R. N Engl J Med. 2019 Aug 29;381(9):887-889.
881. Nath S, Nath S, Lazarte S. **Interpreting CD4 Counts** in a Patient With HIV. JAMA Intern Med. 2019 Sep 3.
882. Nizami S, Morales C, Hu K, et al. **Trends in Mortality** From Human Immunodeficiency Virus Infection, 1984-2016: An Autopsy-Based Study. Arch Pathol Lab Med. 2019 Aug 28.
883. Santos GMA, Locatelli I, Métral M, et al. Cross-Sectional and Cumulative Longitudinal Central Nervous System **Penetration Effectiveness Scores** Are Not Associated With Neurocognitive Impairment in a Well Treated Aging Human Immunodeficiency Virus-Positive Population in Switzerland. Open Forum Infect Dis. 2019 Jul 8;6(7):ofz277.
884. Wedderburn CJ, Yeung S, Rehman AM, et al. **Neurodevelopment of HIV-exposed uninfected children** in South Africa: outcomes from an observational birth cohort study. Lancet Child Adolesc Health. 2019 Sep 9.
885. Wong NS, Chan KCW, Wong BCK, et al. **Latent Tuberculosis Infection Testing Strategies** for HIV-Positive Individuals in Hong Kong. JAMA Netw Open. 2019 Sep 4;2(9):e1910960.
886. Xu L, Wang J, Liu Y, et al. **CRISPR-Edited Stem Cells** in a Patient with HIV and Acute Lymphocytic Leukemia. N Engl J Med. 2019 Sep 11.
887.

Guidelines:

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[1] Micromedex. 2018.
[2] Association CP. Compendium of Pharmaceuticals and Specialties; 2017.
[3] Briggs G, Freeman, Roger, Yaffe, Sumner, ed. *Drugs in **Pregnancy** and Lactation.* 11th ed: TechBooks 2017.
[4] Panel on Antiretroviral Guidelines for Adults and Adolescents. Guidelines for the use of antiretroviral agents in HIV-1-infected adults and adolescents. Department of Health and Human Services. January 29, 2008; 1-128. Available at http://aidsinfo.nih.gov/contentfiles/AdultandAdolescentGL.pdf . Accessed Nov 6, 2008
Panel on Antiretroviral Guidelines for Adults and Adolescents. Guidelines for the use of antiretroviral agents in HIV-1-infected adults and adolescents. Department of Health and Human Services. January 10, 2011; 1–166. Available at http://www.aidsinfo.nih.gov/ContentFiles/AdultandAdolescentGL.pdf . Accessed 10 Jan 2011
[5] Hammer SM, Eron JJ, Reiss P, et al. Antiretroviral treatment if adult HIV infection 2008 Recommendations of the International AIDS society-USA panel. JAMA. 2008; 300(5):555-70. ; Thompson MA;. Aberg JA; Cahn P, et al. Antiretroviral Treatment of Adult HIV Infection: 2010 Recommendations of the International AIDS Society-USA Panel JAMA. 2010;304(3):321-333.
Günthard HF, Saag MS, Benson CA, et al. Antiretroviral drugs for treatment and prevention of HIV infection in adults: 2016 recommendations of the International Antiviral Society–USA Panel. JAMA. doi:10.1001/jama.2016.8900.
Saag MS, Benson CA, Gandhi RT, et al. Antiretroviral drugs for treatment and prevention of HIV infection in adults: 2018 recommendations of the International Antiviral Society–USA Panel [July 24, 2018]. JAMA. doi:10.1001/jama.2018.8431

[6] Public Health Service Task Force Recommendations for Use of Antiretroviral Drugs in Pregnant HIV-Infected Women for Maternal Health and Interventions to Reduce Perinatal HIV Transmission in the United States. July 8, 2008. 1-103. Avalaible at http://aidsinfo.nih.gov/contentfiles/PerinatalGL.pdf . Accessed May 29, 2008
Panel on Treatment of HIV-Infected Pregnant Women and Prevention of Perinatal Transmission. Recommendations for use of antiretroviral drugs in pregnant HIV-1-infected women for maternal health and interventions to reduce perinatal HIV transmission in the United States. Rockville (MD): Public Health Service Task Force; 2012 Jul 31. http://aidsinfo.nih.gov/contentfiles/lvguidelines/perinatalgl.pdf
[7] Friis-Medler N, Reiss P, Sabin CA, Weber R et al. Data Collection on Adverse Events of Anti-HIV Drugs (D:A:D) study. Class of antiretroviral drugs and the risk of myocardial infarction. N Engl J Med 2007;356:1723-35.
[8] New HIV drug: Isentress (raltegravir). Pharmacist's Letter/Prescriber's Letter 2008; 24(1):240177.
[9] Friis-Medler N, Reiss P, Sabin CA, Weber R et al. Data Collection on Adverse Events of Anti-HIV Drugs (D:A:D) study. Class of antiretroviral drugs and the risk of myocardial infarction. N Engl J Med 2007;356:1723-35.
[10] The Strategies for Management of Antiretroviral Therapy (SMART) study group. CD4+ count-guided interruption of antiretroviral treatment. N Engl J med 2006;355:2283-96.
[11] Devesh J. Dhasmana,1 Keertan Dheda,2,3 Pernille Ravn,4 Robert J. Wilkinson5, Graeme Meintjes. Immune Reconstitution Inflammatory Syndrome in HIV-Infected Patients Receiving Antiretroviral Therapy: Pathogenesis, Clinical Manifestations and Management. Drugs 2008; 68 (2): 191-208.
[12] Zolopa A, Andersen J, Powderly W, et al. Early antiretroviral therapy reduces AIDS progression/death in individuals with acute opportunistic infections: a multicenter randomized strategy trial. PLoS One 2009;4(5):e5575.
[13] Sheehan NL, Kelly DV, Tseng AL, van Heeswijk RPG, Beique LC, Hughes CA. Evaluation of HIV drug interaction websites. Ann Pharmacoth 2003;37:1577-86

Extras:

1) Clinical Decision Rule for Point of Care Testing of Influenza Patients: *fever* (2 points), *myalgia* (2 points), *symptoms <48hrs* (1 point), *chills/sweats* (1 point). **0-2points** = 8%; **3 points** = 30%; **4-6 points** = 59%.
2) Amantadine Dosing Adjustments for Age and Renal Function

AMANTADINE -*SYMMETREL* Dosage by Age & Renal Function [7,8] { Note, no longer recommended for influenza prophylaxis due to resistance.}

No recognized renal dysfunction	**TREATMENT DOSAGE**	
Children 1-9 yrs [a]	5mg/kg daily or divided BID (total daily dose not to exceed 150mg)	
Children >10 yrs	200mg daily or divided BID [b] (if less than 40 kg, give 5mg/kg per day)	
Adults ≤ 64 yrs	200mg daily (or 100mg BID) [b] (Note: **100mg daily** adequate/better tolerated for **prophylaxis**)	
Adults ≥ 65 yrs	100mg daily	
Renal dysfunction: CrCl * in ml/second (ml/min in brackets)		**Alternate dosing adjustment schedule[2]**
>1.33ml/s (80-99 ml/min)	100mg po daily	100mg Day 1, 100mg/day start Day 2
1.00-1.32 ml/s (60-79 ml/min)	Alternating daily doses of 100mg & 50mg	100mg Day 1, 75mg/day start Day 2
0.67-0.99 ml/s (40-59 ml/min)	100mg every 2 days	100mg Day 1, 50mg/day start Day 2
0.50-0.66 ml/s (30-39 ml/min)	100mg twice weekly	100mg Day 1, 25mg/day start Day 2
0.33-0.49 ml/s (20-29 ml/min)	50mg three times per week	
<0.32 ml/s (10-19 ml/min)	Alternating weekly doses of 100mg & 50mg	If outbreak continues, repeat 100mg dose every 7 days during outbreak.
Hemodialysis	200mg every 7 days	

* **Calculation of creatinine clearance: CrCl** $_{ml/second}$ = {(140-age) x weight (kg)} / {serum creatinine (umol/L) x 50} ◆ Female: CrCl = 0.85 x CrCl (male)

[a] **Use in children** < 1yr old has not been evaluated

[b] **Patients with history of seizures**: consider reduction in amantadine dose (<100mg daily) or use alternate neuraminidase inhibitor

Rx Files – Drugs for Influenza

References

[1] Cooper NJ, Sutton AJ, Abrams KR, Wailoo A, Turner D, Nicholson KG. Effectiveness of neuraminidase inhibitors in treatment and prevention of influenza A and B: systematic review and meta-analyses of randomised controlled trials. BMJ. 2003 Jun 7;326(7401):1235.

[2] Stiver G. The treatment of influenza with antiviral drugs. CMAJ. 2003 Jan 7;168(1):49-56.

[3] Influenza Prevention 2002-2003. Med Lett Drugs Ther. 2002 Sep 2;44(1138):75-6. Anitviral Drugs for Seasonal Influenza 2015-2016. Medical Letter Dec 2015.

[4] Kiso M., Resistant influenza A viruses in children treated with oseltamivir: descriptive study. Lancet 2004; 364: 759-65. (9 of 50 treated kids had resistant gene mutations, but transmissibility unknown)

Physician's First Watch: Feb/08 A common influenza virus has developed a mutation resistant to oseltamivir (Tamiflu) has been found in U.S., Canada, & 4 European nations, the *New York Times* reports. A small percentage of **influenza A/H1N1** — the predominant flu virus infecting people this season — is affected by the **H274Y mutation**. Norway appears to be hardest hit, with 75% (12 of 16) of the isolated viruses showing **resistance to oseltamivir**. In the U.S., Britain, Denmark, and France, roughly 3% to 5% of tested viruses showed resistance (data on Canada were not provided, but reported in Pharmacy Bulletin Board Feb 4/08 at **10%**). "We don't know right now if this is a trend on the upswing or just a small blip," the CDC's chief of epidemiology and prevention told the Associated Press. Officials from the U.S. and World Health Organization told the *Times* they do not currently advise changes in Tamiflu use. In addition, the flu vaccine is still effective against the mutant virus.

Dec/08: Clinicians should remain alert for changes in recommendations that might occur as the 2008--09 influenza season progresses. Recommendations regarding the use of antiviral medications might be revised if surveillance data indicate a substantial and widespread increase in the prevalence of oseltamivir-resistant influenza viruses in the United States. In fact, the interim CDC guidance provides advice for clinicians on how to treat patients with influenza antiviral medications this season. Clinicians can use influenza test results and information, if available, about which viruses are circulating, to help decide which antiviral(s) should be used. If H1N1 viruses are circulating in the community, or it's not clear which viruses are circulating, health care providers are recommended to use an alternative antiviral, zanamivir (Relenza®), or to use combination therapy of oseltamivir and rimantadine. Use of zanamivir or dual therapy with oseltamivir and rimantadine would provide effective treatment against all circulating influenza viruses. In some instances, oseltamivir alone can still be used, such as when influenza B is diagnosed, or H1N1 viruses are not circulating.

Dharan NJ, Gubareva LV, Meyer JJ, et al. for the Oseltamivir-Resistance Working Group. Infections With Oseltamivir-Resistant Influenza A(H1N1) Virus in the United States. JAMA. 2009 Mar 2. [Epub ahead of print] Oseltamivir-resistant A(H1N1) viruses circulated widely in the United States during the 2007-2008 influenza season, appeared to be unrelated to oseltamivir use, and appeared to cause illness similar to oseltamivir-susceptible A(H1N1) viruses. Circulation of oseltamivir-resistant A(H1N1) viruses will continue, with a higher prevalence of resistance, during the 2008-2009 season.

Van der Vries Erhardl Emergence of a **Multidrug-Resistant Pandemic Influenza A (H1N1)** Virus. N Engl J Med 2010; 363:1381-1382.

[5] Orr P; National Advisory Committee on Immunization. An Advisory Committee Statement (ACS). National Advisory Committee on Immunization (NACI). Statement on influenza vaccination for the 2004-2005 season. Can Commun Dis Rep. 2004 Jun 15;30:1-32. (Canada Communicable Disease Report,Volume 31 • ACS-6,15 June **2005** ,An Advisory Committee Statement (ACS), National Advisory Committee on Immunization (NACI)*† , Statement on Influenza Vaccination, for the 2005-2006 Season, http://www.phac-aspc.gc.ca/publicat/ccdr-rmtc/05pdf/acs-dcc3106.pdf)

NACI: National Advisory Committee on Immunization. Statement on seasonal trivalent inactivated influenza vaccine (TIV) for **2010-2011**. CCDR 2010;36(ACS-6):1-49. www.phac-aspc.gc.ca/publicat/ccdr-rmtc/10vol36/acs-6/index-eng.php (accessed August 30, 2010).

NACI: Statement on Seasonal Influenza vaccine for **2011-2012**. CCDR Sept 2011 (ACS-5) Vol 37. http://www.phac-aspc.gc.ca/publicat/ccdr-rmtc/11vol37/acs-dcc-5/index-eng.php

NACI: National Advisory Committee on Immunization (NACI). Addendum – LAIV use in children and adolescents. Advisory Committee Statement (ACS). Canadian Immunization Guide chapter on influenza and statement on seasonal influenza vaccine for **2016-2017**.

Public Health Agency of Canada. National Advisory Committee on Immunization (NACI): Canadian Immunization Guide chapter on influenza and statement on seasonal influenza vaccine for **2016-2017**. www.phac-aspc.gc.ca/naci-ccni/assets/pdf/flu-2016-grippe-eng.pdf (accessed July 14, 2016).

NACI: National Advisory Committee on Immunization. A review of the literature of **high dose seasonal influenza vaccine for adults 65 years and older**. *http://www.phac-aspc.gc.ca/naci-ccni/influenza-vaccine-65-plus-vaccin-contre-la-grippe-65-plus-eng.php* (accessed July 14, 2016).

NACI: National Advisory Committee on Immunization. Canadian Immunization Guide chapter on influenza and **statement on seasonal influenza vaccine for 2017–2018**. https://www.canada.ca/content/dam/phac-aspc/documents/services/publications/healthy-living/canadian-immunization-guide-statement-seasonal-influenza-vaccine/naci-stmt-2017-2018-eng.pdf

NACI: National Advisory Committee on Immunization (NACI). Addendum – **LAIV use in egg allergic individuals**. Advisory Committee Statement (ACS). Canadian Immunization Guide chapter on influenza and statement on seasonal influenza vaccine for 2016-2017. www.phac-aspc.gc.ca/naci-ccni/assets/pdf/final-addendum2016-17-laiv-egg-allergy-eng.pdf (accessed August 1, 2017).

NACI: National Advisory Committee on Immunization (NACI). Canadian immunization guide chapter on influenza and statement on seasonal influenza vaccine for 2019–2020. An Advisory Committee Statement (ACS). https://www.canada.ca/content/dam/phac-aspc/documents/services/publications/healthy-living/canadian-immunization-guide-statement-seasonal-influenza-vaccine-2019-2020/NACI_Stmt_on_Seasonal_Influenza_Vaccine_2019-2020_v12.3_EN.pdf .

6 Schmidt AC. Antiviral therapy for influenza : a clinical and economic comparative review. Drugs. 2004;64(18):2031-46.

Shun-Shin Matthew, Thompson Matthew, Heneghan Carl, et al. Neuraminidase inhibitors for treatment and prophylaxis of influenza in children: systematic review and meta-analysis of randomised controlled trials**.** BMJ 2009;339:b3172, doi: 10.1136/bmj.b3172 (Published 10 August 2009)

Fry AM, Goswami D, Nahar K, et al. Efficacy of oseltamivir treatment started within 5 days of symptom onset to reduce influenza illness duration and virus shedding in an urban setting in Bangladesh: a randomised placebo-controlled trial. Lancet Infect Dis. 2013 Nov 21.

Jefferson T, Jones MA, Doshi P, et al. **Neuraminidase inhibitors for preventing and treating influenza in healthy adults and children.** Cochrane Database Syst Rev. 2014 Apr 10;4:CD008965. Oseltamivir and zanamivir have small, non-specific effects on reducing the time to alleviation of influenza symptoms in adults, but not in asthmatic children. Using either drug as prophylaxis reduces the risk of developing symptomatic influenza. Treatment trials with oseltamivir or zanamivir do not settle the question of whether the complications of influenza (such as pneumonia) are reduced, because of a lack of diagnostic definitions. The use of oseltamivir increases the risk of adverse effects, such as nausea, vomiting, psychiatric effects and renal events in adults and vomiting in children. The lower bioavailability may explain the lower toxicity of zanamivir compared to oseltamivir. The balance between benefits and harms should be considered when making decisions about use of both NIs for either the prophylaxis or treatment of influenza. The influenza virus-specific mechanism of action proposed by the producers does not fit the clinical evidence.

Jefferson T, Jones M, Doshi P, Spencer EA, et al. **Oseltamivir for influenza in adults and children**: systematic review of clinical study reports and summary of regulatory comments. BMJ 2014;348:g2545.

Heneghan CJ, Onakpoya I, Thompson M, et al. **Zanamivir for influenza in adults and children**: systematic review of clinical study reports. BMJ 2014;348:g2547.

[7] Adapted from the National Advisory Committee on Immunization's Statement on Influenza Vaccination for the 2000-2001 Season. Health Protection Branch - Laboratory Centre for Disease Control (Ottawa, Canada), Vol 26 (ACS-2), June 1, 2000.

NACI: National Advisory Committee on Immunization. Statement on seasonal trivalent inactivated influenza vaccine (TIV) for **2010-2011**. CCDR 2010;36(ACS-6):1-49. www.phac-aspc.gc.ca/publicat/ccdr-rmtc/10vol36/acs-6/index-eng.php (accessed August 30, 2010).

NACI: Statement on Seasonal Influenza vaccine for **2011-2012**. CCDR Sept 2011 (ACS-5) Vol 37. http://www.phac-aspc.gc.ca/publicat/ccdr-rmtc/11vol37/acs-dcc-5/index-eng.php

NACI 2011: Recommendations on the use of **intradermal trivalent inactivated influenza vaccine** (TIV-ID). http://www.phac-aspc.gc.ca/publicat/ccdr-rmtc/11vol37/acs-dcc-4/index-eng.php

NACI National Advisory Committee on Immunization. Statement on seasonal influenza vaccine for 2012–2013. www.phac-aspc.gc.ca/publicat/ccdr-rmtc/12vol38/acs-dcc-4/index-eng.php .

NACI National Advisory Committee on Immunization (NACI). Statement on seasonal influenza vaccine for 2013-2014. CCDR 2013. http://www.phac-aspc.gc.ca/naci-ccni/index-eng.php

NACI: National Advisory Committee on Immunization. Statement on seasonal influenza vaccine for **2014-2015**. http://publications.gc.ca/collections/collection_2014/aspc-phac/HP40-114-2014-eng.pdf (accessed August 12, 2014).

NACI: National Advisory Committee on Immunization. **Canadian** Immunization Guide chapter on influenza and statement on **seasonal influenza vaccine for 2017–201**8 (accessed Nov 15, 2017)

AMMI: Association of Medical Microbiology and Infectious Disease Canada https://www.ammi.ca/guidelines/

Since the 2011-12 influenza season, NACI has recommended that egg-allergic individuals may be vaccinated against influenza using TIV, without a prior influenza vaccine skin test, based on an assessment of risk for a severe allergic reaction to guide the method of vaccination. (NACI recommendation Grade A)Footnote bb Details of the vaccine delivery protocols are found below. Because of the lack of data, the use of FluMist® in egg-allergic persons is not recommended at this time. However, ovalbumin concentrations in FluMist® are documented to be very low and a study is currently underway to assess the use of FluMist® in egg-allergic persons. Its use will be re-evaluated when further data become available. Although ovalbumin content in influenza vaccine manufactured in eggs may vary from year to year, between vaccine products or between lots of the same vaccine,Footnote 6363-Footnote 6565 vaccines marketed in Canada are approved under the European specification for ovalbumin content, which is currently <1.2 µg/mL, the level associated with low risks of adverse events.Footnote 6666 An egg-allergic individual is considered to be at higher risk for severe allergic reactions by CSACI if they have had a previous respiratory or cardiovascular reaction or generalized hives when exposed to egg, or have poorly controlled asthma. Two vaccine delivery protocols can be used for egg-allergic individuals, depending on their level of risk for an allergic reaction.Footnote 6767 Egg-allergic individuals at lower risk for severe allergic reaction can be vaccinated for influenza using a single vaccine dose. The two-step graded protocol is recommended for individuals who are at higher risk for severe allergic reaction. These protocols are as follows:

Full dose - A single vaccine dose without the use of a graded challenge. Individuals should be observed for 30 minutes following administration for symptom development.

Two-step graded dosing - A two-step graded process, whereby 10% of the dose is administered followed by 30 minutes of observation. If no symptoms develop, or symptoms are self-resolving, administer the remaining 90% with another 30 minute observation period. If sustained or severe reactions arise after the initial dose, the vaccine is withheld and the individual should be re-evaluated for receipt of the influenza vaccine.

***More recent studies suggest that the absolute risk of GBS in the period following seasonal and A(H1N1)pdm09 influenza vaccination is about one excess case per 1 million vaccines

[8] McGeer A, Sitar D, Tamblyn S, et al. Use of antiviral prophylaxis in influenza outbreaks in long term care facilities. Can J Infect Dis 2000; 11(4): 187-192.

Additional Influenza Chart sources:

ACIP: Recommended **Adult Immunization Schedule**: United States, **2013**. Advisory Committee on Immunization Practices. Ann Intern Med Jan 2013.

Ackerson B, Tseng HF, Sy LS, et al. Severe Morbidity and Mortality Associated With **Respiratory Syncytial Virus Versus Influenza Infection** in Hospitalized Older Adults. Clin Infect Dis. 2018 Nov 19.

Acosta EP, Jester P, Gal P, et al. Oseltamivir dosing for influenza infection in premature neonates. J Infect Dis. 2010 Aug 15;202(4):563-6.

ACOG-American College of Obstetricians and Gynecologists Committee on Obstetric Practice. ACOG Committee Opinion No. 608: **Influenza vaccination during pregnancy**. Obstet Gynecol. 2014 Sept.

ACOG Committee Opinion No. 732: **Influenza Vaccination During Pregnancy**. Obstet Gynecol. 2018 Apr;131(4):e109-e114.

Allen UD, Aoki FY, Evans GA, et al; **AMMI Canada**. **Guidance on use of antiviral drugs given potential low vaccine effectiveness for the 2017-18 influenza season**. Nov 13, 2017 (accessed November 15, 2017).

Alves Galvão MG, et al. **Amantadine and rimantadine for influenza A in children and the elderly**. Cochrane Database Syst Rev. 2008;1:CD002745 Our conclusions about effectiveness of both antivirals for the treatment of influenza A in children were limited to a proven benefit of RMT in the abatement of fever on day three of treatment. Due to the small number of available studies we could not reach a definitive conclusion on the safety of AMT or the effectiveness of RMT in preventing influenza in children and the elderly.

Alves Galvao MG, Rocha Crispino Santos MA, Alves da Cunha AJ. **Amantadine and rimantadine** for influenza A in children and the elderly. Cochrane Database Syst Rev. 2012 Jan 18;1:CD002745. AMT is effective in preventing influenza A in children but the NNTB is high (NNTB: 12 (95% CI 9 to 17). RMT probably helps the abatement of fever on day three of treatment, but the quality of the evidence is poor. Due to the small number of available studies, we could not reach a definitive conclusion on the safety of AMT or the effectiveness of RMT in preventing influenza in children and the elderly.

Alves Galvao MG, Rocha Crispino Santos MA, Alves da Cunha AJ. **Amantadine and rimantadine for influenza A** in children and the elderly. Cochrane Database Syst Rev. 2014 Nov 21;11:CD002745. The quality of the evidence combined with a lack of knowledge about the safety of amantadine and the limited benefits of rimantadine, do not indicate that amantadine and rimantadine compared to control (placebo or paracetamol) could be useful in preventing, treating and shortening the duration of influenza A in children and the elderly.

American Academy of Pediatrics Committee on Infectious Diseases. **Antiviral therapy and prophylaxis for influenza in children. Pediatrics. 2007** Apr;119(4):852-60.

American Academy of Pediatrics Committee on Infectious Diseases. Prevention of influenza: recommendations for influenza immunization of children, 2006-2007. Pediatrics. 2007 Apr;119(4):846-51.

American Academy of Pediatrics Committee on Infectious Diseases. Prevention of influenza: recommendations for influenza immunization of children, 2008-2009. Pediatrics. 2008 Nov;122(5):1135-41. http://pediatrics.aappublications.org/cgi/reprint/122/5/1135

American Academy of Pediatrics (AAP) Committee on Infectious Diseases, Policy Statement--Recommendations for the **Prevention and Treatment of Influenza in Children**, **2009-2010**. Pediatrics 2009 124: 1216-1226 http://pediatrics.aappublications.org/cgi/reprint/124/4/1216

American Academy of Pediatrics. Committee on Infectious Diseases. Policy statement--recommendations for prevention and control of influenza in children, 2010-2011. Pediatrics 2010 Oct;126(4):816-26. http://aappolicy.aappublications.org/cgi/reprint/pediatrics;126/4/816.pdf

American Academy of Pediatrics (AAP). Committee on Infectious Diseases. Recommendations for prevention and control of influenza in children, 2011-2012. Pediatrics. 2011 Oct;128(4):813-25. http://pediatrics.aappublications.org/content/128/4/813.long

American Academy of Pediatrics (AAP): Committee on Infectious Diseases. Recommendations for **Prevention & Control of Influenza in Children, 2016-2017**. Pediatrics. 2016 Sep 6.

American Academy of Pediatrics (AAP): Committee on Infectious. Recommendations for **Prevention and Control of Influenza in Children, 2017-2018**. Pediatrics. 2017;140(4):e20172550

AMMI: Association of Medical Microbiology and Infectious Disease Canada https://www.ammi.ca/guidelines/

Anderson LJ, Shekelle P, Keeler E, et al. The **Cost of Interventions to Increase Influenza Vaccination**: A Systematic Review. Am J Prev Med. 2018 Feb;54(2):299-315.

Anti-infective Review Panel. **Anti-infective Guidelines for Community-acquired Infections**. Canadian - New-**2012**. Toronto: MUMS Guideline Clearinghouse. http://www.mumshealth.com/

Antiviral Drugs for Prophylaxis and Treatment of Influenza. **Med Lett Drugs Ther**. 2005 Novt 21;47(1222):93-5. (Influenza vaccine Oct 9**,2006** & also Updated Oct 23,2006 & **Oct 22, 2007**)

Aoki FY, Allen UD, Stiver HG, et al. The use of antiviral drugs for influenza: **Guidance for practitioners 2012/2013. Can** J Infect Dis Med Microbiol. 2012 Winter;23(4):e79-92

Aoki FY, Allen UD, Stiver HG, et al. **Guidance for practitioners on the use of antiviral drugs to control influenza outbreaks in long-term care facilities in Canada**, 2014-2015 season. Can J Infect Dis Med Microbiol. 2015 Jan-Feb;26(1):e1-4.

Asghar Z, Coupland C, Siriwardena N. **Influenza vaccination and risk of stroke**: Self-controlled case-series study. Vaccine. 2015 Oct 5;33(41):5458-63.

Australia and New Zealand Extracorporeal Membrane Oxygenation (ANZ **ECMO**) Influenza Investigators. Extracorporeal Membrane Oxygenation for 2009 Influenza A(**H1N1**) Acute Respiratory Distress Syndrome. *JAMA*. 2009;0(2009):2009.1535.

Bal C, Herbreteau CH, Buchy P, et al. Safety, potential efficacy, and pharmacokinetics of **specific polyclonal immunoglobulin F(ab')2 fragments** against **avian influenza** A (H5N1) in healthy volunteers: a single-centre, randomised, double-blind, placebo-controlled, phase 1 study. Lancet Infect Dis 2015; online Feb 5.

Bardage C, Persson I, Ortqvist A, et al. **Neurological and autoimmune disorders** after vaccination against pandemic influenza A (**H1N1**) with a monovalent adjuvanted vaccine: population based cohort study in Stockholm, Sweden. BMJ. 2011 Oct 12;343:d5956. doi: 10.1136/bmj.d5956.

Barker CI, Snape MD. Pandemic influenza A **H1N1 vaccines and narcolepsy**: vaccine safety surveillance in action. Lancet Infect Dis. 2013 Dec 18.

Barry M. Anita. A 29-Year-Old Woman With Flu-like Symptoms: Review of Influenza **Diagnosis and Treatment**. JAMA. 2010;304(6):671-678.

Behrman A, Offley W. Should influenza vaccination be **mandatory for healthcare workers**? BMJ. 2013 Nov 12;347:f6705

Belluz J. **Tug of war for antiviral drugs data**. BMJ. 2014 Apr 9;348:g2227.

Benchimol EI, Hawken S, Kwong JC, Wilson K. Safety and Utilization of Influenza Immunization in Children With **Inflammatory Bowel Disease**. Pediatrics. 2013 May 6.

Beigel JH, Farrar J, Han AM, et al.; Writing Committee of the World Health Organization (WHO) Consultation on Human Influenza A/H5. Avian influenza A (H5N1) infection in humans. N Engl J Med. 2005 Sep 29;353(13):1374-85.

Beigel JH, Bao Y, Beeler J, et al. **Oseltamivir, amantadine, and ribavirin combination antiviral therapy versus oseltamivir** monotherapy for the treatment of influenza: a multicentre, double-blind, randomised phase 2 trial. Lancet Infect Dis 2017; online Sept 22.

Bhat N, Wright JG, Broder KR, et al. Influenza-Associated Deaths among Children in the United States, 2003-2004. N Engl J Med. 2005 Dec 15;353(24):2559-2567.

RESULTS: One hundred fifty-three influenza-associated deaths among children were reported by 40 state health departments
Black S, Nicolay U, Del Giudice G, et al. Influence of **Statins** on Influenza Vaccine Response in Elderly Individuals. J Infect Dis. 2015 Oct 28.
Blanton L, Peacock G, Cox C, et al. **Neurologic disorders** among pediatric deaths associated with the 2009 pandemic influenza. Pediatrics. 2012 Sep;130(3):390-6.
Blyth CC, Jacoby P, Effler PV, et al; on behalf of the WAIVE Study Team. Effectiveness of **Trivalent Flu Vaccine** in Healthy Young Children. Pediatrics. 2014 Apr 21.
Bodewes R, Fraaij PL, Kreijtz JH, et al. **Annual influenza** vaccination affects the development of **heterosubtypic immunity**. Vaccine. 2012 Dec 7;30(51):7407-10.
Bradley JS, Blumer JL, Romero JR, et al. Intravenous **Zanamivir** in Hospitalized Patients With Influenza.Pediatrics. 2017 Oct 19.
Bridges CB, t al. Effectiveness and cost-benefit of **influenza vaccination of healthy working adults**: A randomized controlled trial. JAMA. 2000 Oct 4;284(13):1655-63.
Bright RA, Medina MJ, Xu X, et al. Incidence of adamantane resistance among influenza A (H3N2) viruses isolated worldwide from 1994 to 2005: a cause for concern. Lancet. 2005 Oct 1;366(9492):1175-81. Epub 2005 Sep 22. FINDINGS: More than 7000 influenza A field isolates were screened for specific aminoacid substitutions in the M2 gene known to confer drug resistance. During the decade of surveillance a significant increase in drug resistance was noted, from 0.4% in 1994-1995 to 12.3% in 2003-2004. This increase in the proportion of resistant viruses was weighted heavily by those obtained from **Asia** with 61% of resistant viruses isolated since 2003 being from people in Asia. INTERPRETATION: Our data raise concerns about the appropriate use of adamantanes & draw attention to the importance of tracking the emergence and spread of drug-resistant influenza A viruses.
Bright RA, et al. Adamantane resistance among influenza A viruses isolated early during the 2005-2006 influenza season in the United States. JAMA. 2006 Feb 22;295(8):891-4. Epub 2006 Feb 2. RESULTS: A total of 209 influenza A(H3N2) viruses isolated from patients in 26 states were screened, of which 193 (92.3%) contained a change at amino acid 31 (serine to asparagine [S31N]) in the M2 gene known to be correlated with adamantane resistance. Two of 8 influenza A(H1N1) viruses contained the same mutation. Drug-resistant viruses were distributed across the United States. CONCLUSIONS: The high proportion of influenza A viruses currently circulating in the United States demonstrating adamantane resistance highlights the clinical importance of rapid surveillance for antiviral resistance. Our results indicate that these drugs should not be used for the treatment or prophylaxis of influenza in the United States until susceptibility to adamantanes has been reestablished among circulating influenza A isolates.
Briggs GE, et al **Drugs in Pregnancy & Lactation**, 9th Ed. Wilkins; Baltimore, MD.2011.
Brun-Buisson C, Richard JCM, Mercat A, et al. REVA-SRLF A/H1N1v 2009 Registry Group. Early **corticosteroids** in severe influenza A/H1N1 pneumonia and acute respiratory Distress syndrome. Am J Respir Crit Care Med 2011;183:1200–1206.
Buchan SA, Kwong JC. **Influenza immunization among Canadian health care personnel**: a cross-sectional study. CMAJ Open. 2016 Sep 7;4(3):E479-E488
Buchan SA, Rosella LC, Finkelstein M, et al; Public Health Agency of Canada/Canadian Institutes of Health Research Influenza Research Network (PCIRN) Program Delivery and Evaluation Group. Impact of **pharmacist administration** of influenza vaccines on uptake in Canada. CMAJ 2017;189:E146-52.
Buchan SA, Chung H, Campitelli MA, et al. **Vaccine effectiveness against laboratory-confirmed influenza hospitalizations among young children** during the 2010-11 to 2013-14 influenza seasons in Ontario, Canada. PLoS One 2017;359:e0187834.
Buchan SA, Booth S, Scott AN, et al. Effectiveness of **Live Attenuated vs Inactivated Influenza Vaccines in Children** During the 2012-2013 Through 2015-2016 Influenza Seasons in Alberta, Canada: A Canadian Immunization Research Network (CIRN) Study. JAMA Pediatr. 2018 Jul 2:e181514.
Burch J, Corbett M, Stock C, et al.. **Prescription of anti-influenza drugs** for healthy adults: a systematic review and meta-analysis. Lancet Infect Dis. 2009 Sep;9(9):537-45. Epub 2009 Aug 7.
Burks AW, Jones SM, Wood RA, et al. Consortium of Food Allergy Research (CoFAR). **Oral immunotherapy for treatment of egg allergy** in children. N Engl J Med. 2012 Jul 19;367(3):233-43.
Campitelli MA, Inoue M, Calzavara AJ, et al. Low Rates of Influenza Immunization in Young Children Under **Ontario's Universal Influenza** Immunization Program. Pediatrics. 2012 May 14.
Campos MA, Alazemi S, Zhang G, et al. Influenza Vaccination in Subjects With **Alpha-1 Antitrypsin Deficiency**. Chest. 2007 Oct 1; [Epub ahead of print] Subjects with AATD in the United States receive adequate influenza vaccination regardless of age. However, we did not observe a significant impact of the vaccination on disease exacerbations and other respiratory outcomes during the 2003-2004 influenza season.
Canadian Society of Allergy and Clinical Immunology ADMINISTRATION OF H1N1 AND SEASONAL INFLUENZA **VACCINE TO EGG ALLERGIC** INDIVIDUALS http://www.csaci.ca/include/files/CSACI_H1N1_Statement.pdf
Canetta SE, Bao Y, Co MD, et al. Serological Documentation of **Maternal Influenza Exposure** and Bipolar Disorder in Adult Offspring. Am J Psychiatry. 2014 Jan 31.
Casado I, et al. **Repeated influenza vaccination** for preventing severe & fatal influenza infection **in older adults**: multicentre case-control study. CMAJ. 2018 Jan 8;190(1):E3-E12.
Cates CJ, Jefferson TO, Rowe BH. Vaccines for preventing influenza in people with **asthma**. Cochrane Database Syst Rev. 2008 Apr 16;(2):CD000364. Uncertainty remains about the degree of protection vaccination affords against asthma exacerbations that are related to influenza infection. Evidence from recently published trials indicates that there is no significant increase in asthma exacerbations immediately after vaccination (at least with inactivated influenza vaccination). There is concern regarding possible increased wheezing and hospital admissions in infants given live intranasal vaccination.
CDC Jan 2006 CDC Recommends against the Use of Amantadine and Rimantadine for the Treatment or Prophylaxis of Influenza in the United States during the 2005–06 Influenza Season http://www.cdc.gov/flu/han011406.htm (Recommendations against amantadine for influenza in 2005-06. Pharmacist's Letter/Prescriber's Letter 2006;22(2):220216)
CDC July 2009 Prevention and Control of Seasonal Influenza with Vaccines: Recommendations of the Advisory Committee on Immunization Practices (ACIP), **2009** http://www.cdc.gov/mmwr/preview/mmwrhtml/rr58e0724a1.htm ; http://www.cdc.gov/flu/
CDC Centers for Disease Control and Prevention. Updated interim recommendations — **HIV**-infected adults and adolescents: Considerations for clinicians regarding 2009 **H1N1** influenza. Oct 21 , 2009. (http://www.cdc.gov/h1n1flu/guidance_HIV.htm)
CDC data strengthen the evidence that the risk for **Guillain-Barré syndrome (GBS)** associated with the 2009 H1N1 vaccine is similar to the risk seen with seasonal flu vaccines, according to an *MMWR* report. The CDC's analysis of data from October 2009 through March 2010 found that the incidence of GBS was 1.92 per 100,000 person-years among

vaccinated individuals and 1.21 per 100,000 person-years among the unvaccinated. If final data confirm this finding, the CDC says, then this would translate to 0.8 excess GBS cases for every 1 million vaccinations — a rate comparable to that found with seasonal flu vaccination. *MMWR* article (Free)

CDC **Prevention and Control of Influenza with Vaccines**. Recommendations of the Advisory Committee on Immunization Practices (ACIP), **2010**. http://www.cdc.gov/mmwr/pdf/rr/rr59e0729.pdf

CDC Preliminary Results: Surveillance for **Guillain-Barré Syndrome** After Receipt of Influenza A (H1N1) 2009 Monovalent Vaccine — United States, 2009–2010 http://www.cdc.gov/mmwr/preview/mmwrhtml/mm59e0602a1.htm Preliminary results from an analysis in EIP comparing GBS patients hospitalized through March 31, 2010, who did and did not receive 2009 H1N1 vaccination showed an estimated age-adjusted rate ratio of 1.77 (GBS incidence of 1.92 per 100,000 person-years among vaccinated persons and 1.21 per 100,000 person-years among unvaccinated persons). If end-of-surveillance analysis confirms this finding, this would correspond to 0.8 excess cases of GBS per 1 million vaccinations, similar to that found in seasonal influenza vaccines.[2,3] No other federal system to date has detected a statistically significant association between GBS and 2009 H1N1 vaccination. Surveillance and further analyses are ongoing. The 2009 H1N1 vaccine safety profile is similar to that for seasonal influenza vaccines, which have an excellent safety record. Vaccination remains the most effective method to prevent serious illness and death from 2009 H1N1 influenza infection; illness from the 2009 H1N1 influenza virus has been associated with a hospitalization rate of 222 per 1 million and a death rate of 9.7 per 1 million population.

CDC Aug/10 Estimates of **Deaths** Associated with Seasonal Influenza --- United States, 1976—2007 http://www.cdc.gov/mmwr/pdf/wk/mm5933.pdf

CDC: Interim Guidance on the Use of Influenza Antiviral Agents During the **2010-2011 Influenza Season** Nov 2010. **http://www.cdc.gov/flu/professionals/antivirals/guidance/**

CDC: Antiviral Agents for Treatment and **Chemoprophylaxis of Influenza Recommendations** of the Advisory Committee on Immunization Practices (ACIP) Recommendations and Reports **January 21, 2011** / 60(RR01);1-24 **http://www.cdc.gov/mmwr/preview/mmwrhtml/rr6001a1.htm?s_cid=rr6001a1_x**

CDC: Update: Influenza Activity — United States, **2010–11 Season, and Composition of the 2011–12 Influenza Vaccine** http://www.cdc.gov/mmwr/pdf/wk/mm6021.pdf

CDC: Recommendations for Obstetric Health Care Providers Related to Use of Antiviral Medications in the Treatment and Prevention of Influenza 2016-2017. Https://www.cdc.gov/flu/professionals/antivirals/avrec_ob.htm

CDC Sep/11 Maternal and Infant Outcomes Among Severely Ill **Pregnant and Postpartum Women with 2009 Pandemic Influenza A (H1N1)** --- United States, April 2009—August 2010 http://www.cdc.gov/mmwr/preview/mmwrhtml/mm6035a2.htm

CDC: Centers for Disease Control and Prevention (CDC). Influenza vaccination coverage among **pregnant women** - 29 States and New York City, 2009-10 season. MMWR Morb Mortal Wkly Rep. 2012 Feb 24;61(7):113-8.

CDC: Prevention and Control of Influenza with Vaccines: Recommendations of the Advisory Committee on Immunization Practices (ACIP) — United States, **2012–13** Influenza Season**.** http://www.cdc.gov/mmwr/preview/mmwrhtml/mm6132a3.htm

CDC: Centers for Disease Control and Prevention (CDC). Influenza vaccination coverage **among health-care personnel** - 2011-12 influenza season, United States. MMWR Morb Mortal Wkly Rep. 2012 Sep 28;61:753-7.

Chairat K, Jittamala P, et al. Population pharmacokinetics of **oseltamivir** and oseltamivir carboxylate in **obese** and **Non-obese** volunteers. Br J Clin Pharmacol. 2016 Jan 26.

Chan TY, Chao TF, Liu CJ, et al. The association between influenza infection, vaccination and **atrial fibrillation**: A nationwide case-control study.*Heart Rhythm* 2016.

Chartrand C, Leeflang MM, Minion J, et al. **Accuracy of Rapid Influenza Diagnostic Tests**: A Meta-analysis. Ann Intern Med. 2012 Feb 27.

Chaves SS, Pérez A, Miller L, et al. Impact of Prompt **Influenza Antiviral Treatment** on Extended Care Needs After Influenza Hospitalization Among **Community-Dwelling Older Adults.** Clin Infect Dis. 2015 Sep 2.

Chen XY, Wu TX, Liu GJ, et al. **Chinese medicinal herbs** for influenza. Cochrane Database Syst Rev. 2007 Oct 17;(4):CD004559. The present evidence is too weak to support or reject the use of Chinese medicinal herbs for preventing and treating influenza.

Chen Mark I. C.; Lee Vernon J. M.; Lim Wei-Yen; et al. 2009 Influenza A(H1N1) **Seroconversion** Rates and Risk Factors Among Distinct Adult Cohorts in Singapore. JAMA. 2010;303(14):1383-1391.

Chen Y, Liang W, Yang S, et al. Human infections with the emerging avian influenza A **H7N9** virus from wet market poultry: clinical analysis and characterisation of viral genome. Lancet. 2013 Apr 25.

Chen Y, Liang W, Yang S, et al. Human infections with the emerging avian infl uenza A **H7N9** virus from wet market poultry: clinical analysis and characterisation of viral genome. Lancet 2013; 381: 1916–25.

Chen H, Yuan H, et al. Clinical and epidemiological characteristics of a fatal case of avian infl uenza A **H10N8** virus infection: a descriptive study. *Lancet* 2014; online Feb 5.

Chen Q, Griffin MR, et al. Influenza **Vaccine** Prevents Medically Attended Influenza-Associated Acute Respiratory Illness in **Adults Aged ≥50 Years**. J Infect Dis. 2014 Oct 21.

Chertow DS, Memoli MJ. **Bacterial coinfection** in influenza: a grand rounds review. JAMA. 2013 Jan 16;309(3):275-82.

Chit A, Becker DL, DiazGranados CA, et al. Cost-eff ectiveness of **high-dose versus standard-dose** inactivated influenza vaccine in adults aged 65 years and older: an economic evaluation of data from a randomised controlled trial. Lancet Infect Dis 2015; online Sept 9.

Chong CR et al. Safety of inactivated Influenza vaccine **in cancer patients receiving immune checkpoint inhibitors (ICI**). Clin Infect Dis 2019 Mar 15.

Chung, Erica Y., Huang, Lin, Schneider, Lynda. Safety of Influenza Vaccine Administration in **Egg-Allergic** Patients. Pediatrics 2010 125: e1024-e1030.

Chung JR, Flannery B, Ambrose CS, et al; Influenza Clinical Investigation for Children Study Team; Influenza Incidence Surveillance Project; US Influenza Vaccine Effectiveness Network. **Live attenuated and inactivated influenza vaccine effectiveness**. Pediatrics. 2019;143(2): e20182094

Chung JR, Flannery B, Thompson MG, et al. **Seasonal Effectiveness** of Live Attenuated and Inactivated Influenza Vaccine. Pediatrics. 2016 Jan 5.

Ciszewski A, Bilinska ZT, Brydak LB, et al. Influenza vaccination in secondary prevention from **coronary ischaemic events** in coronary artery disease: FLUCAD study. Eur Heart J. 2008 Jun;29(11):1350-8. Epub 2008 Jan 10. In optimally treated CAD patients influenza vaccination improves the clinical course of CAD and reduces the frequency of coronary ischaemic events. Large-scale studies are warranted to evaluate the effect of influenza vaccination on cardiovascular mortality.

Coffin SE, Leckerman K, Keren R, et al. **Oseltamivir** shortens **hospital stays of critically ill children** hospitalized with seasonal influenza: a retrospective cohort study. Pediatr Infect Dis J. 2011 Nov;30(11):962-6.

Cohen D. Complications: tracking down the **data on oseltamivir**. BMJ 2009;339:b5387.

Cohen Steven A., Chui Kenneth K.H., Naumova Elena N. Influenza Vaccination in Young **Children Reduces Influenza-Associated Hospitalizations in Older Adults**, 2002–2006. Journal of the American Geriatrics Society. Article first published online: 28 JAN 2011. DOI: 10.1111/j.1532-5415.2010.03271.x.

Cohen D. **Oseltamivir**: another case of **regulatory failure**?. BMJ: British Medical Journal . 348. 2014.

Committee on Infectious Diseases. Recommendations for Prevention and Control of Influenza in Children, 2012-2013. Pediatrics. 2012 Sep 10.

Committee on Infectious Diseases. Recommendations for Prevention and Control of **Influenza in Children**, **2013-2014**. Pediatrics. 2013 Sep 2.

Committee on Infectious Diseases. Influenza **Immunization for All Health Care Personnel**: Keep It Mandatory. Pediatrics. 2015 Sep 7.

Committee on Infectious Diseases. Recommendations for **Prevention and Control of Influenza in Children**, 2015-2016. Pediatrics. 2015 Sep 7.

Committee on Infectious Diseases. Recommendations for **Prevention and Control of Influenza in Children**, 2018-2019. Pediatrics. 2018 Sep 3. pii: e20182367.

COMMITTEE ON INFECTIOUS DISEASES. **Recommendations for Prevention and Control of Influenza in Children**, 2018-2019. Pediatrics. 2018 Oct;142(4).

COMMITTEE ON INFECTIOUS DISEASES. **Recommendations for Prevention and Control of Influenza in Children**, 2019-2020. Pediatrics. 2019 Sep 2.

Corti D, Voss J, Gamblin SJ, et al. A **neutralizing antibody** selected from plasma cells that binds to group 1 and group 2 **influenza** A hemagglutinins. Science 2011;333:850-6.

Cowling BJ, Chan KH, et al. **Facemasks and hand hygiene** to prevent influenza transmission in households: a cluster randomized trial. Ann Intern Med. 2009 Oct 6;151(7):437-46.

Cowling, BJ., Chan, KH, Fang, VJ. et al; Comparative **Epidemiology of Pandemic and Seasonal Influenza A** in Households N Engl J Med 2010 362: 2175-2184.

Cowling BJ, Jin L, Lau EHY, et al. Comparative epidemiology of human infections with avian infl uenza A **H7N9 and H5N1** viruses in China: a population-based study of laboratory-confi rmed cases. Lancet 2013; online June 24.

Crowe SR, Merrill JT, Vista ES, Dedeke AB, et al. Influenza vaccination responses in human systemic **lupus erythematosus**: impact of clinical and demographic features. Arthritis Rheum. 2011 May 19. doi: 10.1002/art.30388.

Dalcin D, Kwong JC**. High-dose influenza vaccination**. CMAJ. 2019 Mar 18;191(11):E313.

Dalziel SR, Thompson JM, Macias CG, et al; Pediatric Emergency Research Networks (PERN) H1N1 working group. **Predictors of severe H1N1 infection in children** presenting within Pediatric Emergency Research Networks (PERN): retrospective case-control study. BMJ. 2013 Aug 12;347:f4836.

Darvishian M, Bijlsma MJ, Hak E, van den Heuvel ER. Seasonal influenza **vaccine** effectiveness among the **community-dwelling elderly**: a metaanalysis of test-negative design case-control studies. Lancet Infect Dis 2014; online Nov 6.

Darvishian M, van den Heuvel ER, Bissielo A, et al. Effectiveness of **seasonal influenza vaccination in community-dwelling elderly people**: an individual participant data meta-analysis of test-negative design case-control studies. Lancet Respir Med. 2017 Feb 8.

Dawood FS et al. Emergence of a novel swine-origin influenza A (**H1N1**) virus in humans. N Engl J Med 2009 May 7.

Dawood Fatimah S., Kamimoto Laurie, D'Mello Tiffany A., et al. and the Emerging Infections Program Network. Children With **Asthma** Hospitalized With Seasonal or Pandemic Influenza, 2003–2009. Pediatrics 2011; 128:1 e27-e32; ahead of print June 6, 2011

Dawood FS, Iuliano DA, Reed C, et al. Estimated **global mortality associated with the first 12 months of 2009 pandemic influenza A H1N1** virus circulation: a modelling study. Lancet Infect Dis 2012; published online June 26. (Respiratory deaths: ~ 201,200; Cardiovascular deaths: ~ 83,300)

de Jong MD, Tran TT, Truong HK, et al. Oseltamivir resistance during treatment of influenza A (H5N1) infection. N Engl J Med. 2005 Dec 22;353(25):2667-72.

Demicheli V, Jefferson T, Al-Ansary LA, et al. Vaccines for **preventing influenza in healthy adults**. Cochrane Database Syst Rev. 2014 Mar 13;3:CD001269.

Demicheli V, Jefferson T, Ferroni E, et al. Vaccines for **preventing influenza in healthy adults**. Cochrane Database Syst Rev. 2018 Feb 1;2:CD001269.
Healthy adults who receive inactivated parenteral influenza vaccine rather than no vaccine probably experience less influenza, from just over 2% to just under 1% (moderate-certainty evidence). They also probably experience less ILI following vaccination, but the degree of benefit when expressed in absolute terms varied across different settings. Variation in protection against ILI may be due in part to inconsistent symptom classification. Certainty of evidence for the small reductions in hospitalisations and time off work is low.

Des Roches A, Paradis L, Gagnon R, et al; on behalf of the PCIRN (Public Health Agency of Canada/Canadian Institutes of Health Research Influenza Research Network). **Egg-allergic patients** can be safely vaccinated against influenza. J Allergy Clin Immunol. 2012 Sep 26.

De Wals P, Deceuninck G, Toth E, et al. Risk of **Guillain-Barré syndrome following H1N1** influenza 3 vaccination in Quebec. JAMA. 2012;308(2):175- 181.
(GBS cases attributable to vaccine was 2 per 1 million doses.)

Diaz E, Rodriguez A, Martin-Loeches I, Lorente L, del Mar MM, Pozo JC, et al. Impact of **obesity** in patients infected with 2009 influenza A(H1N1). Chest. 2011 Feb;139(2):382-6.

DiazGranados CA, Dunning AJ, Kimmel M, et al. Efficacy of **high-dose versus standard-dose influenza vaccine** in older adults. N Engl J Med. 2014 Aug 14;371(7):635-45.
Dieleman J, Romio S, Johansen K, et al. **Guillain-Barré syndrome** and adjuvanted pandemic influenza A (H1N1) 2009 vaccine: multinational case-control study in Europe. BMJ 2011;343:d3908.
Diggle L, et al. Effect of **needle size** on immunogenicity and reactogenicity of vaccines in infants: randomised controlled trial. BMJ. 2006 Sep 16;333(7568):571. Epub 2006 Aug 4.
Long (25 mm) needles for infant immunisations can significantly reduce vaccine reactogenicity at each dose while achieving comparable immunogenicity to that of short (16 mm) needles. (InfoPOEMs: Using a 25-mm needle to inject the combined diptheria, pertussis, tetanus, and Haemophilus influenzae type B vaccine (ACT-Hib DTP) will result in significantly fewer injection site reactions and those that occur will be of less severe. The World Health organization recommends use of a 25-mm needle, although most physicians in the United States use the shorter 16-mm needle. (LOE = 1b))
Dobson J, Whitley RJ, Pocock S, Monto AS. **Oseltamivir treatment for influenza in adults**: a meta-analysis of randomised controlled trials. Lancet 2014; online Jan 30.
Dominguez-Cherit Guillermo; Lapinsky Stephen E.; Macias Alejandro E.; et al. Critically Ill Patients With 2009 Influenza A(**H1N1**) in **Mexico**. JAMA. 2009;0(2009):2009.1536.
Donahue JG, Kieke BA, King JP, et al. Association of **spontaneous abortion with receipt of inactivated influenza vaccine** containing H1N1pdm09 in 2010-11 and 2011-12. Vaccine. 2017 Sep 25;35(40):5314-5322.
Donner B, Niranjan V, Hoffmann G. Safety of **oseltamivir in pregnancy**: a review of preclinical and clinical data. Drug Saf. 2010 Aug 1;33(8):631-42.
Doshi P, Jefferson T, Del Mar C. The imperative to **share clinical study reports**: recommendations from the **tamiflu** experience. PLoS Med. 2012 Apr;9(4):e1001201.
Doshi P. **Influenza: marketing vaccine by marketing disease**. BMJ. 2013 May 16;346:f3037.
Drozd EM, Miller L, Johnsrud M. Impact of **Pharmacist Immunization Authority** on Seasonal **Influenza Immunization** Rates Across States. Clin Ther. 2017 Aug 3
Duffy J, Weintraub E, Vellozzi C, et al; Vaccine Safety Datalink. **Narcolepsy and influenza A(H1N1)** pandemic 2009 vaccination in the United States. Neurology. 2014 Nov 11;83(20):1823-30.
Dugas AF, Hsieh YH, Lovecchio F, et al. Derivation and Validation of a **Clinical Decision Guideline for Influenza Testing** in Four U.S. Emergency Departments. Clin Infect Dis. 2019 Mar 7.
Dugas AF, Valsamakis A, Atreya MR, et al. Clinical diagnosis of **influenza in the ED**. Am J Emerg Med. 2015 Jun;33(6):770-5.
Dunkle LM, Izikson R, Patriarca P, et al. Efficacy of **Recombinant Influenza Vaccine in Adults 50 Years of Age or Older**. N Engl J Med. 2017 Jun 22;376(25):2427-2436.
Dunkle LM, Izikson R, Patriarca PA, et al. Safety and Immunogenicity of a **Recombinant Influenza Vaccine**: A Randomized Trial. Pediatrics. 2018 Apr 2.
Dunn AG, Arachi D, Hudgins J, et al. **Financial conflicts** of interest and conclusions about **neuraminidase inhibitors** for influenza: an analysis of systematic reviews. Ann Intern Med. 2014 Oct 7;161(7):513-8.
Dunning J, Baillie JK, Cao B, et al; on behalf of the International Severe Acute Respiratory and Emerging Infection Consortium (ISARIC). **Antiviral combinations for severe** influenza. Lancet Infect Dis. 2014 Sep 8.
Dutkowski R, Smith JR, Davies BE. Safety and pharmacokinetics of **oseltamivir** at standard and **high dosages**. Int J Antimicrob Agents. 2010 Feb 26.
Duval X, van der Werf S, Blanchon T, et al; Bivir Study Group. Efficacy of **oseltamivir-zanamivir combination compared to each monotherapy** for seasonal influenza: a randomized placebo-controlled trial. PLoS Med. 2010 Nov 2;7(11):e1000362.
Earn DJ, He D, Loeb MB, Fonseca K, Lee BE, Dushoff J. Effects of **school closure** on incidence of pandemic influenza in Alberta, Canada. Ann Intern Med. 2011;156:173-81.
Ebell MH, Afonso AM, Gonzales R, et al. Development and validation of a **clinical decision rule** for the diagnosis of influenza. J Am Board Fam Med. 2012 Jan-Feb;25(1):55-62.
Ebell MH, Call M, Shinholser J. **Effectiveness of oseltamivir** in adults: a meta-analysis of published and unpublished clinical trials. Fam Pract. 2013 Apr;30(2):125-33.
Ebell MH. **WHO downgrades status of oseltamivir**. BMJ. 2017 Jul 12;358:j3266.
Ehrlich HJ, Müller M, Oh HM, et al.; Baxter H5N1 Pandemic Influenza Vaccine Clinical Study Team. A clinical trial of a whole-virus H5N1 vaccine derived from cell culture. N Engl J Med. 2008 Jun 12;358(24):2573-84.
Elkayam O, et al. The Effect of **Infliximab** and Timing of Vaccination on the Humoral Response to Influenza Vaccination in Patients with Rheumatoid Arthritis and Ankylosing Spondylitis. Semin Arthritis Rheum. 2009 Feb 24. [Epub ahead of print] Influenza virus vaccine generated good humoral response in RA & AS patients treated with infliximab.
Elkin PL, Froehling DA, Wahner-Roedler DL, et al. Comparison of **natural language processing biosurveillance** methods for identifying influenza from encounter notes. Ann Intern Med. 2012 Jan 3;156(1 Pt 1):11-8.
EMA Jul 21// - European regulators have recommended restricting the use of GlaxoSmithKline's pandemic flu vaccine **Pandemrix because of a potential risk of narcolepsy** in children or adolescents. The European Medicines Agency said on Thursday that Pandemrix should only be used in people under 20 years in the absence of seasonal trivalent influenza vaccines, following its link to very rare cases of narcolepsy in young people.
Engler RJ, Nelson MR, Klote MM, et al. Walter Reed Health Care System Influenza Vaccine Consortium. **Half- vs full-dose** trivalent inactivated influenza vaccine (2004-2005): age, dose, and sex effects on immune responses. Arch Intern Med. 2008 Dec 8;168(22):2405-14. Antibody responses to intramuscular half-dose TIV in healthy, previously immunized adults were not substantially inferior to the full-dose vaccine, particularly for ages 18 to 49 years. Significantly higher geometric mean titer responses in women were identified for all ages, regardless of dose or influenza strain. Half-dose vaccination may be an effective strategy for healthy adults younger than 50 years in the setting of an influenza vaccine shortage.
Erlewyn-Lajeunesse M, et al. Recommendations for the administration of influenza vaccine in children **allergic to egg**. BMJ. 2009 Sep 15;339:b3680. doi: 10.1136/bmj.b3680.
Eshaghi A, Shalhoub S, Rosenfeld P, et al. Multiple influenza A (**H3N2**) mutations conferring **resistance to neuraminidase inhibitors** in a bone marrow transplant recipient. Antimicrob Agents Chemother. 2014 Sep 22.
Esposito S, Pugni L, Daleno C, et al. **Influenza A/H1N1 MF59-Adjuvanted Vaccine in Preterm and Term Children** Aged 6 to 23 Months. Pediatrics 2011 0: peds.2010-1920.

Eurich DT, Marrie TJ, Johnstone J, Majumdar SR. Mortality reduction with influenza vaccine in patients with pneumonia outside "flu" season: pleiotropic benefits or residual confounding? Am J Respir Crit Care Med. 2008 Sep 1;178(5):527-33. Epub 2008 Jun 12. The 51% reduction in mortality with vaccination initially observed in patients with pneumonia who did not have influenza was most likely a result of confounding. Previous observational studies may have overestimated mortality benefits of influenza vaccination.

Ewing A, Lee EC, Viboud C, et al. Contact, travel, and transmission: The **impact of winter holidays** on influenza dynamics in the United States. J Infect Dis. 2016 Dec 28.

Farley M, Ryan P, Lynfield R, et al. Emerging Infections Program Network. Children with **asthma hospitalized** with seasonal or pandemic influenza, 2003-2009. Pediatrics. 2011 Jul;128(1):e27-32.

FDA Acts to Protect Public from **Fraudulent Avian Flu Therapies** Dec/05 http://www.fda.gov/bbs/topics/NEWS/2005/NEW01274.html

FDA April /08 GlaxoSmithKline informed healthcare professionals of changes to the WARNINGS AND PRECAUTIONS sections of prescribing information for **Relenza** regarding information from postmarketing reports (mostly from Japan) of **delirium and abnormal behavior** leading to injury in patients with influenza who are receiving neuraminidase inhibitors, including Relenza. These events were reported primarily among pediatric patients and often had an abrupt onset and rapid resolution. The contribution of Relenza to these events has not been established. Influenza can be associated with a variety of neurologic and behavioral symptoms which can include seizures, hallucinations, delirium, and abnormal behavior, in some cases resulting in fatal outcomes. These events may occur in the setting of encephalitis or encephalopathy but can occur without obvious severe disease.

FDA June/10 notified consumers and healthcare professionals about a potentially harmful product represented as "**Generic Tamiflu" sold over the Internet**. FDA tests revealed that the fraudulent product does not contain Tamiflu's active ingredient, oseltamivir, but cloxacillin, an ingredient in the same class of antibiotics as penicillin.

Fell D, Platt R, Lanes A, et al. **Fetal death** and preterm birth associated with maternal influenza vaccination: systematic review. BJOG. 2014 Jul 10.

Ferdinands JM, Fry AM, Reynolds S, et al. **Intraseason waning** of influenza vaccine protection: Evidence from the US Influenza Vaccine Effectiveness Network, 2011-12 through 2014-15. Clin Infect Dis. 2016 Dec 29.

Fineberg HV. **Pandemic preparedness and response**--lessons from the H1N1 influenza of 2009. N Engl J Med. 2014 Apr 3;370(14):1335-42.

Fiore AE, Shay DK, Broder K, Iskander JK, Uyeki TM, Mootrey G, Bresee JS, Cox NJ, Centers for Disease Control and Prevention. Prevention and control of seasonal influenza with vaccines: recommendations of the Advisory Committee on Immunization Practices (**ACIP**), 2009. MMWR Recomm Rep 2009 Jul 31;58(RR-8):1-52.

Flannery AH, Thompson Bastin ML. **Oseltamivir Dosing** in Critically Ill Patients With Severe Influenza. Ann Pharmacother. 2014 May 9;48(8):1011-1018.

Flannery B, Reynolds SB, Blanton L et al. **Influenza Vaccine Effectiveness Against Pediatric Deaths**:201-2014. Pediatrics. 2017;139(5):e20164244

Food and Drug Administration Oct/11 (FDA) isadvising health care professionals **not to use injector devices** to administer influenza vaccines.

Freemantle N, Shallcross LJ, Kyte D, et al. **Oseltamivir**: the **real world data**. BMJ. 2014 Apr 9;348:g2371.

Friedman BC, Goldman RD. **Influenza vaccination for children with asthma**. Can Fam Physician. 2010 Nov;56(11):1137-9.

Fry AM, Goswami D, Nahar K, et al. Efficacy of **oseltamivir treatment started within 5 days** of symptom onset to reduce influenza illness duration and virus shedding in an urban setting in Bangladesh: a randomised placebo-controlled trial. Lancet Infect Dis. 2013 Nov 21.

Fry AM, Goswami D, Nahar K, et al. Effects of **oseltamivir** treatment of index patients with influenza on **secondary household illness** in an urban setting in Bangladesh: secondary analysis of a randomised, placebo-controlled trial. Lancet Infect Dis. 2015 Mar 13.

Gao R, Cao B, Hu Y, et al. Human Infection with a Novel Avian-Origin Influenza A (**H7N9**) Virus. N Engl J Med. 2013 Apr 11.

Gao HN, Lu HZ, Cao B, et al. Clinical Findings in 111 Cases of Influenza A (**H7N9**) Virus Infection. N Engl J Med. 2013 May 22.

Gagnon R, Primeau MN, Des Roches A, Lemire C, Kagan R, Carr S, Ouakki M, Benoît M, De Serres G; PHAC-CIHR Influenza Research Network. Safe vaccination of patients with **egg allergy with an adjuvanted pandemic H1N1 vaccine**. J Allergy Clin Immunol. 2010 Aug;126(2):317-23.

Garcia-Garcia L, Valdespino-Gómez JL, Lazcano-Ponce E, et al. **Partial protection** of seasonal trivalent inactivated vaccine against novel **pandemic** influenza A/H1N1 2009: case-control study in Mexico City. BMJ. 2009 Oct 6;339:b3928. doi: 10.1136/bmj.b3928.

Gelinck LB, van der Bijl AE, Beyer WE, et al. The effect of **anti-tumor necrosis factor** alpha treatment on the antibody response to influenza vaccination. Ann Rheum Dis. 2007 Oct 26; [Epub ahead of print] The antibody response to influenza vaccination in patients treated with anti-TNF is only modestly impaired. The proportion of patients that achieves a protective titer is not significantly diminished by the use of TNF blocking therapies.

Gelinck LB, van den Bemt BJ, Marijt WA, et al. **Intradermal** influenza vaccination in immunocompromized patients is immunogenic and feasible. Vaccine. 2009 Apr 21;27(18):2469-74. Epub 2009 Feb 24.

Ghebrehewet S, MacPherson P, Ho A. **Influenza**. BMJ. 2016 Dec 7;355:i6258.

Gilca R, Deceuninck G, De Serres G, et al. Effectiveness of **Pandemic H1N1 Vaccine** Against Influenza-Related **Hospitalization** in Children. Pediatrics. 2011Nov;128(5):e1084-91.

Gill PJ, Ashdown HF, Wang K, et al. Identification of **children at risk of influenza-related complications in primary and ambulatory care**: a systematic review and meta-analysis. Lancet Respir Med. 2014 Dec 3.

Glezen WP. Clinical practice. **Prevention and treatment of seasonal influenza**. N Engl J Med. 2008 Dec 11;359(24):2579-85.

Godlee F. Open letter to **Roche about oseltamivir trial data**. BMJ. 2012 Oct 29;345:e7305.

Golovyan DM, Mossad SB. **Prevention and treatment** of influenza in the **primary care** office. Cleve Clin J Med. 2014 Mar;81(3):189-99.
Goossen GM, Kremer LC, van de Wetering MD. Influenza vaccination in **children** being treated with **chemotherapy** for cancer. Cochrane Database Syst Rev. 2009 Apr 15;(2):CD006484. Paediatric oncology patients receiving chemotherapy are able to generate an immune response to the influenza vaccine, but it remains unclear whether this immune response protects them from influenza infection or its complications.
Graner S, Svensson T, Beau AB, et al. **Neuraminidase inhibitors during pregnancy** and risk of adverse neonatal outcomes and congenital malformations: population based European register study. BMJ. 2017 Feb 28;356:j629.
Gravenstein S, Davidson HE, Taljaard M, et al. Comparative effectiveness of **high-dose** versus **standard-dose** influenza vaccination on numbers of US **nursing home** residents admitted to hospital: a cluster-randomised trial. Lancet Respir Med. 2017 Jul 20.
Greene MT, Fowler KE, Ratz D, et al. **Changes in influenza vaccination requirements for health care personnel** in US hospitals.JAMA Netw Open. 2018;1(2):e180143.
Greenhawt M, et al. **Administration of influenza vaccines to egg allergic recipients**: A practice parameter update 2017. Ann Allergy Asthma Immunol. 2018 Jan;120(1):49-52.
Greer LG, Sheffield JS, Rogers VL, Roberts SW, McIntire DD, Wendel GD Jr. **Maternal and neonatal outcomes** after antepartum treatment of influenza with antiviral medications. Obstet Gynecol. 2010 Apr;115(4):711-6.
Grohskopf LA, Olsen SJ, Sokolow LZ, et al; Influenza Division, National Center for Immunization and Respiratory Diseases, CDC. Prevention and Control of Seasonal Influenza with Vaccines: Recommendations of the Advisory Committee on Immunization **Practices (ACIP) - United States, 2014-15 Influenza Season**. MMWR Morb Mortal Wkly Rep. 2014;63:691-697.
Grohskopf LA, Sokolow LZ, Broder KR, et al. Prevention and Control of Seasonal Influenza with Vaccines: **Recommendations** of the Advisory Committee on Immunization **Practices (ACIP) — United States, 2017–18 Influenza Season**. MMWR Recomm Rep 2017;66(No. RR-2):1–20. DOI: http://dx.doi.org/10.15585/mmwr.rr6602a1
Håberg SE, Trogstad L, Gunnes N, et al. Risk of fetal death after pandemic influenza virus infection or vaccination. N Engl J Med. 2013 Jan 24;368(4):333-40.
Håberg SE, Aaberg KM, Surén P, et al. **Epilepsy in Children After Pandemic Influenza Vaccination**. Pediatrics. 2018 Feb 15.
Haffi zulla J, Hartman A, Hoppers M, et al. Effect of **nitazoxanide** in adults and adolescents with acute uncomplicated influenza: a double-blind, randomised, placebo-controlled, phase 2B/3 trial. Lancet Infect Dis 2014; online May 20
Hambidge SJ, et al. Vaccine Safety Datalink Team. Safety of trivalent inactivated influenza **vaccine** in **children 6 to 23 months** old. JAMA. 2006 Oct 25;296(16):1990-7.
Hambidge SJ et al. the Vaccine Safety Datalink Team. Trivalent Inactivated Influenza Vaccine Is **Not Associated With Sickle Cell Crises** in Children. Pediatrics. 2011 Dec 12.
Hamiel U, Kvenstel I, Youngster I. **Recurrent Immune Thrombocytopenia** After Influenza Vaccination: A Case Report. Pediatrics. 2016:138(6):e20160124.
Han F, Lin L, Warby SC, Faraco J, Li J, et al. **Narcolepsy onset** is seasonal and increased following the 2009 H1N1 pandemic in china. Ann Neurol. 2011 Sep;70(3):410-7.
Han F, Lin L, Li J, et al. Decreased incidence of **childhood narcolepsy** 2 years after the 2009 H1N1 winter flu pandemic. Ann Neurol. 2012 Nov 9.
Hansen C, Desai S, Bredfeldt C, et al. A Large, Population-Based Study of 2009 Pandemic Influenza A Virus Subtype H1N1 Infection Diagnosis During **Pregnancy** and Outcomes for Mothers and Neonates. J Infect Dis. 2012 Oct;206(8):1260-8.
Harper SA, Bradley JS, Englund JA, File TM, et al. Expert Panel of the Infectious Diseases Society of America. Seasonal influenza in **adults and children**--diagnosis, treatment, chemoprophylaxis, and institutional outbreak management: clinical practice guidelines of the Infectious Diseases Society of America. (**IDSA**) Clin Infect Dis 2009 Apr 15;48(8):1003-32. http://www.journals.uchicago.edu/doi/pdf/10.1086/598513
Hatakeyama S, Sugaya N, Ito M, et al. Emergence of influenza B viruses with reduced sensitivity to neuraminidase inhibitors. JAMA. 2007 Apr 4;297(13):1435-42. In 1 (1.4%) of the 74 children who had received oseltamivir, we identified a variant with reduced drug sensitivity possessing a Gly402Ser neuraminidase substitution. We also identified variants with reduced sensitivity carrying an Asp198Asn, Ile222Thr, or Ser250Gly mutation in 7 (1.7%) of the 422 viruses from untreated patients. In this population, influenza B viruses with reduced sensitivity to neuraminidase inhibitors do not arise as frequently as resistant influenza A viruses. However, they appear to be transmitted within communities and families, requiring continued close monitoring.
Havers F, Thaker S, Clippard JR, et al. Use of **influenza antiviral agents** by ambulatory care clinicians during the 2012–2013 influenza season. Clin Infect Dis 2014.
Havers FP, Hicks LA, Chung JR, et al. Outpatient **Antibiotic Prescribing for Acute Respiratory Infections During Influenza Seasons**. *JAMA Network Open.* 2018;1(2):e180243.
Hayden FG. Antiviral resistance in influenza viruses--implications for management and pandemic response. N Engl J Med. 2006 Feb 23;354(8):785-8.
Hayden FG, Sugaya N, Hirotsu N, et al. **Baloxavir Marboxil for Uncomplicated Influenza in Adults and Adolescents**. N Engl J Med. 2018 Sep 6;379(10):913-923.
Hayward AC, Harling R, Wetten S, et la. Effectiveness of an influenza vaccine programme for **care home staff** to prevent death, morbidity, and health service use among residents: cluster randomized controlled trial. BMJ. 2006 Dec 1; [Epub ahead of print]
Hayward AC, Fragaszy EB, Bermingham A, et al; on behalf of the Flu Watch Group. Comparative community burden and severity of **seasonal and pandemic influenza**: results of the Flu Watch cohort study. Lancet Respir Med. 2014 Mar 17.
Health Canada Nov/06 (Tamiflu warning) Informing Canadians of international reports of hallucinations and abnormal behaviour, including self harm, in patients taking the antiviral drug Tamiflu.http://www.hc-sc.gc.ca/ahc-asc/media/advisories-avis/2006/2006_116_e.html
Heinonen Santtu, Silvennoinen Heli, Lehtinen Pasi, et al. Effectiveness of inactivated **influenza vaccine in children aged 9 months to 3 years**: an observational cohort study, The Lancet Infectious Diseases, Volume 11, Issue 1, January 2011
Heneghan CJ, Onakpoya I, Thompson M, et al. **Zanamivir for influenza in adults and children**: systematic review of clinical study reports. BMJ 2014;348:g2547.
Heneghan CJ, Onakpoya I, Jones MA, et al. **Neuraminidase inhibitors for influenza**: a systematic review and meta-analysis of regulatory and mortality data.

Health Technol Assess. 2016 May;20(42):1-242.
Hernandez Jaime E., Adiga Raghavendra, Armstrong Robert, et al. and on behalf of the eIND Peramivir Investigators. Clinical Experience in Adults and Children Treated with **Intravenous Peramivir** for 2009 Influenza A (H1N1) Under an Emergency IND Program in the United States *Clin Infect Dis.* (2011) 52(6): 695-706 doi:10.1093/cid/cir001
Hessen, Margaret Trexler. **In the Clinic: Influenza**. Ann Intern Med November 3, 2009 151:ITC5-1; doi:10.1059/0003-4819-151-9-200911030-01011.
Hill AT, Gold PM, El Solh AA, et al. Adult Outpatients With **Acute Cough Due to Suspected Pneumonia or Influenza**: **CHEST Guideline** and Expert Panel Report. Chest. 2019 Jan;155(1):155-167.
Hirose R, Nakaya T, Naito Y, et al. Situations Leading to **Reduced Effectiveness of Current Hand Hygiene** against Infectious Mucus from Influenza Virus-Infected Patients. mSphere. 2019 Sep 18;4(5). doi: 10.1128/mSphere.00474-19.
Hoen AG, Buckeridge DL, Charland KML, et al. Effect of expanded US recommendations for seasonal influenza vaccination: comparison of two **pediatric emergency departments** in the United States and Canada. CMAJ 2011;183:E1021-8.
Holodniy M, Penzak SR, et al. Pharmacokinetics and Tolerability of Oseltamivir (Tamiflu(R)) Combined with **Probenecid**. Antimicrob Agents Chemother. 2008 Jun 16. [Epub ahead of print] Alternate day dosing of oseltamivir plus four times daily probenecid achieved trough oseltamivir carboxylate concentrations adequate for neuraminidase inhibition in vitro; and this combination should be studied further.
Holvast A, van Assen S, et al. Studies of cell-mediated immune responses to influenza vaccination in systemic **lupus** erythematosus. Arthritis Rheum. 2009 Aug;60(8):2438-47.
Holvast A, et al. Safety & efficacy of influenza vaccination in systemic **lupus** erythematosus patients with quiescent disease. Ann Rheum Dis. 2006 Jul;65(7):913-8. Epub 2005 Dec1.
In addition to a decreased antibody response, cell-mediated responses to influenza vaccination are diminished in patients with SLE, which may reflect the effects of the concomitant use of immunosuppressive drugs. This may render these patients more susceptible to (complicated) influenza infections.
Hoopes JD, Driebe EM, Kelley E, et al. Triple combination antiviral drug (TCAD) composed of **amantadine, oseltamivir, and ribavirin** impedes the selection of drug-resistant influenza A virus. PLoS One. 2011;6(12):e29778.
Hsu J, Santesso N, et al. **Antivirals for Treatment of Influenza**: A Systematic Review and Meta-analysis of Observational Studies. Ann Intern Med. 2012 Apr 3;156(7):512-24.
Hu Y, Lu S, Song Z, et al. Association between adverse clinical outcome in human disease caused by novel influenza A **H7N9** virus and sustained viral shedding and emergence of antiviral resistance. Lancet. 2013 May 29.
Hughes RA, et al. No association between immunization and **guillain-barre syndrome** in the United kingdom, 1992 to 2000. Arch Intern Med. 2006 Jun 26;166(12):1301-4.
Hung IF, To KK, Chan JF, et al. Efficacy of **clarithromycin-naproxen-oseltamivir** combination in the treatment of patients hospitalized for influenza A(H3N2) infection: an open-label, randomized controlled, phase 2b/3 trial. Chest. 2016 Nov 21.
Hung IFN, To KKW, Chan JFW, et al. Efficacy of **Clarithromycin-Naproxen-Oseltamivir Combination** in the Treatment of Patients Hospitalized for Influenza A(H3N2) Infection: An Open-label Randomized, Controlled, Phase IIb/III Trial. Chest. 2017 May;151(5):1069-1080.
Hurst FP, Lee JJ, Jindal RM, et al. Outcomes Associated with Influenza Vaccination in the First Year **after Kidney Transplantation**. Clin J Am Soc Nephrol. 2011 Apr 28. April 28
Hurt AC, Hardie K, Wilson NJ et al. **Community transmission of oseltamivir-resistant A(H1N1)pdm09 influenza**. N Engl J Med. 2011 Dec 29;365(26):2541-2.
Hurt AC et al. on behalf of the WHO Consultation on Pandemic Influenza A (H1N1) 2009 Virus Resistance to Antivirals. **Antiviral resistance** during the 2009 influenza A H1N1 pandemic: public health, laboratory, and clinical perspectives. Lancet Infect Dis. 2011 Dec 16.
Hviid A, et al. Association Between **Pandemic Influenza A(H1N1) Vaccination in Pregnancy and Early Childhood Morbidity** in Offspring. JAMA Pediatr. 2016 Nov 28
Iuliano AD, Roguski KM, Chang HH, et al. Estimates of **global seasonal influenza-associated respiratory mortality**: a modelling study. Lancet 2017; online Dec 13.
Infectious Diseases and Immunization Committee, Canadian Paediatric Society. **Autistic spectrum disorder**: no causal relationship with vaccines. Paediatrics & Child Health 2007;12(5): 393-5.http://www.cps.ca/english/statements/id/pidnote_jun07.htm (accessed 2007 Dec 4). http://www.cps.ca/english/statements/ID/PIDnote_Jun07.pdf
Influenza vaccine 2005-2006. Med Lett Drugs Ther. 2005 Oct 24;47(1220):85-7
Influenza Vaccination in Children: Missed Second Doses & Use of Antiviral Drugs for Influenza: Canadian Guidelines. Pharmacist's Letter Jan 2007.
Influenza **A/H1N1 MF59 adjuvanted vaccine in pregnant** women and adverse perinatal outcomes: multicentre study. BMJ. 2013 Feb 13;346:f990.
Ip DK, Liao Q, Wu P, et al. Detection of mild to moderate influenza A/**H7N9** infection by China's national sentinel surveillance system for influenza-like illness: case series. BMJ. 2013 Jun 24;346:f3693.
Izurieta HS, Haber P, Wise RP, et al. Adverse events reported following live, cold-adapted, **intranasal influenza** vaccine. JAMA. 2005 Dec 7;294(21):2720-5.
Izurieta HS, Thadani N, Shay DK, et al. Comparative effectiveness of **high dose versus standard-dose influenza vaccines** in US residents **aged 65 years and older** from 2012 to 2013 using Medicare data: a retrospective cohort analysis. Lancet Infect Dis 2014; online Feb 9.
Jack A. **Tamiflu**: "a **nice little earner**." BMJ 2014;348:g2524.
Jack A. Will **Tamiflu recommendations** change this winter? BMJ. 2014 Nov 27;349:g6742.
Jackson LA, Chen WH, Stapleton JT, et al. Immunogenicity and Safety of Varying Dosages of a Monovalent 2009 H1N1 Influenza Vaccine Given With and Without **AS03 Adjuvant** System in Healthy Adults and Older Persons. J Infect Dis. 2012 Jul 20.
Jackson LA, Campbell JD, Frey SE, et al. Effect of Varying Doses of a Monovalent **H7N9 Influenza Vaccine With and Without AS03 and MF59** Adjuvants on Immune

Response: A Randomized Clinical Trial. JAMA. 2015 Jul 21;314(3):237-46.
Jackson ML, Chung JR, Jackson LA, et al. Influenza **Vaccine Effectiveness** in the United States during the **2015-2016** Season. N Engl J Med. 2017 Aug 10;377(6):534-543.
Jackson ML, Nelson JC, Weiss NS, et al. Influenza vaccination and risk of community-acquired pneumonia in immunocompetent elderly people: a population-based, nested case-control study. Lancet. 2008 Aug 2;372(9636):398-405. The effect of influenza vaccination on the risk of pneumonia in elderly people during influenza seasons might be less than previously estimated.
Jagannath VA, Asokan GV, Fedorowicz Z, Lee TW. **Neuraminidase inhibitors** for the treatment of influenza infection in people with **cystic fibrosis**. Cochrane Database Syst Rev. 2016 Feb 24;2:CD008139. We were unable to identify any randomised controlled studies or quasi-randomised controlled studies on the efficacy of neuraminidase inhibitors for the treatment of influenza infection in people with cystic fibrosis. The absence of high level evidence for the effectiveness of these interventions emphasises the need for well-designed, adequately powered, randomised controlled clinical studies.
Jain VK, Rivera L, Zaman K, et al. Vaccine (**quadrivalent**) for prevention of mild and moderate-to-severe **influenza** in children. N Engl J Med. DOI: 10.1056/NEJMoa1215817.
Jain VK, Rivera L, Zaman K, et al. Vaccine for Prevention of Mild and **Moderate-to-Severe Influenza in Children**. N Engl J Med. 2013 Dec 11. (**QIV** was efficacious)
Jamieson DJ, Honein MA, Rasmussen SA, et al. H1N1 2009 influenza virus infection during **pregnancy** in the USA. Lancet. 2009 Jul 28. Pregnant women might be at increased risk for complications from pandemic H1N1 virus infection. These data lend support to the present recommendation to promptly treat pregnant women with H1N1 influenza virus infection with anti-influenza drugs.
Jefferies S, et al, Perrin K; Pi Study Group. Randomized controlled trial of the effect of regular **paracetamol (acetaminophen) on influenza** infection. Respirology. 2015 Dec 6.
Jefferson T, Rivetti D, et al. Efficacy & effectiveness of influenza vaccines in **elderly** people: a systematic review. Lancet. 2005 Oct1;366(9492):1165-74.Epub 2005Sep 22. (InfoPOEMs: Flu shots prevent influenza and influenza-like illness in the elderly. (LOE = 1a-))
Jefferson T, Demicheli V, Rivetti D, Jones M, Di Pietrantonj C, et al. Antivirals for influenza in **healthy adults**: systematic review.Lancet. 2006 Jan 28;367(9507):303-13. (InfoPOEMs: Antiviral agents are only slightly effective in preventing confirmed influenza or flu-like illness. When given in the first few days of illness, the M2 ion blockers and neuraminidase inhibitors reduce the duration of illness by **approximately 1 day**. (LOE = 1a)) (Jefferson T, Demet al. Neuraminidase inhibitors for preventing and treating influenza in healthy adults. Cochrane Database Syst Rev. 2006 Jul 19;3:CD001265.)
Jefferson T, Assessment of the efficacy and effectiveness of influenza vaccines in healthy **children**: systematic review. Lancet. 2005 Feb 26-Mar 4;365(9461):773-80.
Jefferson T, Deeks JJ, Demicheli V, et al. Amantadine and rimantadine for preventing and treating influenza A in adults. Cochrane Database Syst Rev. 2004;(3):CD001169.
Jefferson T, Foxlee R, Del Mar C, et al. **Physical interventions** to interrupt or reduce the spread of respiratory viruses: systematic review. BMJ. 2008 Jan 12;336(7635):77-80.
Jefferson Tom, Mar Chris Del, et al. **Physical interventions** to interrupt or reduce the spread of respiratory viruses: systematic review. BMJ 2009;339:b3675, doi: 0.1136/bmj.b3675 (Published 22 September 2009)
Jefferson T, et al. Vaccines for preventing influenza in **healthy children**. Cochrane Database Syst Rev. 2008 Apr 16;(2):CD004879. Influenza vaccines are efficacious in children older than two but little evidence is available for children under two. There was a marked difference between vaccine efficacy and effectiveness. No safety comparisons could be carried out, emphasizing the need for standardisation of methods and presentation of vaccine safety data in future studies. It was surprising to find only one study of inactivated vaccine in children under two years, given current recommendations to vaccinate healthy children from six months old in the USA and Canada. If immunisation in children is to be recommended as a public health policy, large-scale studies assessing important outcomes and directly comparing vaccine types are urgently required.
Jefferson T, Jones M, Doshi P, Del Mar C. **Possible harms of oseltamivir**—a call for urgent action. Lancet. 2009 Oct 17;374(9698):1312-3.
Jefferson Tom, Jones Mark, Doshi Peter, et al. **Neuraminidase inhibitors** for preventing and treating influenza in healthy **adults**: systematic review and meta-analysis. BMJ 2009;339:b5106, doi: 10.1136/bmj.b5106 (Published 8 December 2009) . Neuraminidase inhibitors have modest effectiveness against the symptoms of influenza in otherwise healthy adults. The drugs are effective postexposure against laboratory confirmed influenza, but this is a small component of influenza-like illness, so for this outcome neuraminidase inhibitors are not effective.
Jefferson T, Di Pietrantonj C, Rivetti A, et al. **Vaccines for preventing influenza** in healthy adults. Cochrane Database Syst Rev. **2010** Jul 7;7:CD001269. Influenza vaccines have a modest effect in reducing influenza symptoms and working days lost. There is no evidence that they affect complications, such as pneumonia, or transmission.
Jefferson T, Jones MA, Doshi P, et al. Neuraminidase inhibitors for preventing and treating influenza in healthy adults and children - a review of clinical study reports. Cochrane Database of Systematic Reviews 2011, Issue 1. Art. No.: CD008965. DOI: 10.1002/14651858.CD008965. We found a high risk of publication and reporting biases in the trial programme of oseltamivir. Sub-population analyses of the influenza infected population in the oseltamivir trial programme are not possible because the two arms are non-comparable due to oseltamivir's apparent interference with antibody production. The evidence supports a direct oseltamivir mechanism of action on symptoms but we are unable to draw conclusions about its effect on complications or transmission. We expect full clinical study reports containing study protocol, reporting analysis plan, statistical analysis plan and individual patient data to clarify outstanding issues. These full clinical study reports are at present unavailable to us.
Jefferson T, Rivetti A, Di Pietrantonj C, et al. **Vaccines for preventing influenza in healthy children**. Cochrane Database Syst Rev. 2012 Aug 15;8:CD004879. : Influenza vaccines are efficacious in preventing cases of influenza in children older than two years of age, but little evidence is available for children younger than two years of age. There was a difference between vaccine efficacy and effectiveness, partly due to differing datasets, settings and viral circulation patterns. No safety comparisons could be carried out, emphasising the need for standardisation of methods and presentation of vaccine safety data in future studies. In specific cases, influenza vaccines were associated with serious harms such as narcolepsy and febrile convulsions.
Jefferson T, Doshi P. **Multisystem failure**: the story of anti-influenza drugs. *BMJ* 2014;348:g2263.
Jefferson T, Jones MA, Doshi P, et al. **Neuraminidase inhibitors for preventing and treating influenza in healthy adults and children.** Cochrane Database Syst Rev. 2014 Apr 10;4:CD008965. Oseltamivir and zanamivir have small, non-specific effects on reducing the time to alleviation of influenza symptoms in adults, but not in asthmatic children. Using either drug as prophylaxis reduces the risk of developing symptomatic influenza. Treatment trials with oseltamivir or zanamivir do not settle the question of whether the complications of influenza (such as pneumonia) are reduced, because of a lack of diagnostic definitions. The use of oseltamivir increases the risk of adverse effects, such as nausea, vomiting, psychiatric effects and renal events in adults and vomiting in children. The lower bioavailability may explain the lower toxicity of zanamivir compared to oseltamivir. The balance between benefits and harms should be considered when making decisions about use of both NIs for either the prophylaxis or treatment of influenza. The influenza virus-specific mechanism of action proposed by the producers does not fit the clinical evidence.
Jefferson T, Jones M, Doshi P, Spencer EA, et al. **Oseltamivir for influenza in adults and children**: systematic review of clinical study reports and summary of regulatory comments. BMJ 2014;348:g2545.
Jefferson T, Jones MA, Doshi P, et al. Risk of **bias in industry-funded oseltamivir trials**: comparison of core reports versus full clinical study reports. BMJ Open. 2014 Sep 30;4(9):e005253.
Jeyanathan T, Overgaard C, McGeer A. **Cardiac complications** of influenza infection in 3 adults. CMAJ. 2013 Apr 16;185(7):581-4.
Jin XW, Mossad SB. **2012-2013 Influenza update**: Hitting a rapidly moving target. Cleve Clin J Med. 2012 Nov;79(11):777-84.
Johnston JA, Tincher LB, Lowe DK. Booster and Higher Antigen Doses of Inactivated Influenza Vaccine **in HIV-Infected** Patients. Ann Pharmacother. 2013 Dec;47(12):1712-6
Johnstone J, Loeb M, Teo KK, et al. Influenza Vaccination and Major **Adverse Vascular Events** in High Risk Patients. Circulation. 2012 Jun 19.
Joseph KS, Liston RM. H1N1 influenza in **pregnant** women. BMJ. 2011 Jun 14;342:d3237.

Jules A, Grijalva CG, Zhu Y, et al. Influenza-Related **Hospitalization and ED** Visits in **Children** Less Than 5 Years: 2000-2011. Pediatrics. 2014 Dec 8.
Juurlink DN, et al. **Guillain-Barre syndrome** after influenza vaccination in adults: a population-based study. Arch Intern Med. 2006 Nov 13;166(20):2217-21.
Kaiser L, Wat C, Mills T, et al. Impact of oseltamivir treatment on influenza-related lower respiratory tract **complications** and hospitalizations. Arch Intern Med 2003;163:1667-72.
Kalil AC, Thomas PG. Influenza **virus-related critical illness**: pathophysiology and epidemiology. Crit Care. 2019 Jul 19;23(1):258.
Kamal MA, Smith PF, Chaiyakunapruk N, et al. **Interdisciplinary Pharmacometrics Linking Oseltamivir** Pharmacology,Influenza Epidemiology, and Health Economics to Inform Antiviral Use in Pandemics. Br J Clin Pharmacol. 2017 Feb 8.
Kandun IN, et al. Three Indonesian Clusters of **H5N1** Virus Infection in 2005. N Engl J Med. 2006 Nov 23;355(21):2186-2194.
Kashiwagi S, Watanabe A, Ikematsu H, et al; **Laninamivir** Prophylaxis Study Group. Long-acting neuraminidase inhibitor laninamivir octanoate as post-exposure prophylaxis for influenza. Clin Infect Dis. 2016 Apr 26.
Kato H, Hagihara M, Kato Y, et al. Adverse events of **prophylactic anti-influenza agents** in medical staffs. J Infect Chemother. 2017 Aug 3.
Kawai N, et al. A comparison of the effectiveness of **oseltamivir** for the treatment of influenza A and influenza B: a Japanese multicenter study of the 2003-2004 and 2004-2005 influenza seasons. Clin Infect Dis. 2006 Aug 15;43(4):439-44. Epub 2006 Jun 26.
Kedia S, Stroud B, Parsons J, et al. **Pediatric Neurological Complications of 2009 Pandemic Influenza A (H1N1)**. Arch Neurol. 2011 Apr;68(4):455-62.
Keitel WA, et al. Safety of **high doses** of **influenza vaccine** and effect on antibody responses in **elderly** persons. Arch Intern Med. 2006 May 22;166(10):1121-7.
Kerzner B, Murray AV, Cheng E, et al. Safety and immunogenicity profile of the concomitant administration of ZOSTAVAX and inactivated influenza vaccine in adults aged 50 and older. J Am Geriatr Soc. 2007 Oct;55(10):1499-507. **ZOSTAVAX and influenza vaccine** given concomitantly are generally well tolerated in adults aged 50 and older. Ab responses were similar whether ZOSTAVAX and influenza vaccine were given concomitantly or sequentially.
Kim SH, Hong SB, Yun SC, et al. Korean Society of Critical Care Medicine H1N1 Collaborative. **Corticosteroid** treatment in critically ill patients with pandemic influenza A/H1N1 2009 infection: analytic strategy using propensity scores. Am J Respir Crit Care Med 2011;183:1207–1214.
Kloepfer KM, Olenec JP, Lee WM, et al. Increased H1N1 Infection Rate in Children with **Asthma**. Am J Respir Crit Care Med. 2012 Jun 15;185(12):1275-9.
Kmietowicz Z. **WHO downgrades oseltamivir on drugs list** after reviewing evidence. BMJ. 2017 Jun 12;357:j2841.
Kohno S et al. Efficacy and safety of intravenous **peramivir** for treatment of seasonal influenza virus infection. *Antimicrob Agents Chemother* 2010 Nov; 54:4568.
Kolber MR, Lau D, Eurich D, Korownyk C. **Effectiveness of the trivalent influenza vaccine**. Can Fam Physician. 2014 Jan;60(1):50.
Korownyk C, Garrison S, Kolber MR. **Antiviral medications for influenza**. Can Fam Physician. 2015 Apr;61(4):351.
Kostova D, Reed C, Finelli L, et al. **Influenza Illness and Hospitalizations Averted by Influenza Vaccination** in United States, 2005-2011. PLoS One. 2013 Jun 19;8(6):e66312.
Kreijtz JHCM, Goeijenbier M, Moesker FM, et al. Safety and immunogenicity of a **Modified-Vaccinia-virus-Ankara-based influenza A H5N1 vaccine**: a randomised phase 1/2a clinical trial. Lancet Infect Dis 2014; online Oct 30.
Kucharski AJ, Lessler J, et al. Estimating the **Life Course of Influenza A(H3N2) Antibody Responses** from Cross-Sectional Data. PLoS Biol. 2015 Mar 3;13(3):e1002082.
Kumar Anand; Zarychanski Ryan; Pinto Ruxandra; et al. for the **Canadian** Critical Care Trials Group H1N1 Collaborative.Critically Ill Patients With 2009 Influenza A(**H1N1**) Infection in Canada. JAMA. 2009;0(2009):2009.1496.
Kwong JC, Stukel TA, Lim J, McGeer AJ, et al. The effect of universal influenza immunization on mortality and health care use. PLoS Med. 2008 Oct 28;5(10):e211. Compared to targeted programs in other provinces, introduction of universal vaccination in Ontario in 2000 was associated with relative reductions in influenza-associated mortality and health care use. The results of this large-scale natural experiment suggest that **universal vaccination** may be an effective public health measure for reducing the annual burden of influenza.
Kwong JC, Maaten S, Upshur RE, Patrick DM, Marra F. The effect of **universal** influenza immunization on antibiotic prescriptions: an ecological study. Clin Infect Dis. 2009 Sep 1;49(5):750-6. Universal influenza immunization is associated with reduced influenza-associated antibiotic prescriptions.
Kwong JC, Schwartz KL, Campitelli MA, et al. **Acute Myocardial Infarction after Laboratory-Confirmed Influenza Infection**. N Engl J Med. 2018 Jan 25;378(4):345-353.
Kelso JM, Li JT, Nicklas RA, et al. Joint Task Force on Practice Parameters. **Adverse reactions to vaccines**. Ann Allergy Asthma Immunol. 2009 Oct;103(4 Suppl 2):S1-14.
Khazeni N, Bravata DM, Holty JE, et al. Safety and Efficacy of **Extended-Duration Antiviral Chemoprophylaxis** Against Pandemic and Seasonal Influenza. Ann Intern Med. 2009 Aug 3. [Epub ahead of print]
Kumar D, Michaels MG, Morris MI, et al. American Society of Transplantation H1N1 Collaborative Study Group. Outcomes from pandemic influenza A H1N1 infection in recipients of **solid-organ transplants**: a multicentre cohort study. Lancet Infect Dis. 2010 Aug;10(8):521-6.
Kwong JC, Vasa PP, Campitelli MA, et al. Risk of **Guillain-Barré** syndrome after seasonal **influenza vaccination** and influenza health-care encounters: a self-controlled study. Lancet Infect Dis 2013; online June 28.
Kytömaa S, Hegde S, Claggett B, et al. Association of **Influenza-like Illness Activity With Hospitalizations for Heart Failure**: The Atherosclerosis Risk in Communities Study. JAMA Cardiol. 2019 Mar 27
Lambert Linda C., Fauci Anthony S., Influenza **Vaccines for the Future**. N Engl J Med 2010; 363:2036-2044.

Lansbury L, Rodrigo C, Leonardi-Bee J, et al. **Corticosteroids as adjunctive therapy in the treatment of influenza**. Cochrane Database Syst Rev. 2019 Feb 24;2:CD010406. We found one RCT of adjunctive corticosteroid therapy for treating people with community-acquired pneumonia, but the number of people with laboratory-confirmed influenza in the treatment and placebo arms was too small to draw conclusions regarding the effect of corticosteroids in this group, and we did not include it in our meta-analyses of observational studies. The certainty of the available evidence from observational studies was very low, with confounding by indication a major potential concern.

Lau D, Eurich DT, Majumdar SR, et al. Effectiveness of influenza vaccination in working-age adults with **diabetes**: a population-based cohort study. Thorax. 2013 Jul;68(7):658-63.

Lavelle TA, Uyeki TM, Prosser LA. **Cost-Effectiveness of Oseltamivir** Treatment for Children with Uncomplicated Seasonal Influenza. J Pediatr. 2011 Sep 12.

Lavallée PC, Labreuche J, Fox KM, et al; PERFORM, OPTIC, and AMISTAD Investigators. **Influenza vaccination and cardiovascular risk** in patients with recent TIA and stroke. Neurology. 2014 May 27;82(21):1905-13.

Le QM, Kiso M, Someya K, et al. Avian flu: isolation of drug-resistant H5N1 virus. Nature. 2005 Oct 20;437(7062):1108.

Lee N, Cockram CS, Chan PK, et al. Antiviral treatment for patients hospitalized with severe influenza infection may affect clinical outcomes. Clin Infect Dis 2008;46:1323-4.

Lee, Vernon J., Yap, Jonathan, Cook, Alex R. et al; **Oseltamivir Ring Prophylaxis** for Containment of 2009 H1N1 Influenza Outbreaks, N Engl J Med 2010 362: 2166-2174.

Legge A, Dodds L, Macdonald NE, et al. Rates and determinants of **seasonal influenza vaccination in pregnancy** and association with neonatal outcomes. CMAJ. 2014 Jan 6.

Lehmann HC, Hartung HP, Kieseier BC, Hughes RA. **Guillain-Barré syndrome** after exposure to influenza virus. Lancet Infect Dis. 2010 Sep;10(9):643-51.

Lenzer J. Why aren't the **US Centers for Disease Control and Food and Drug Administration speaking with one voice on flu**? BMJ. 2015 Feb 5; 350:h658.

Leung DY, et al. A clinical trial of **intradermal and intramuscular seasonal influenza vaccination** in patients with atopic dermatitis. J Allergy Clin Immunol. 2017 Jan 31.

Leung K, Lipsitch M, Yuen KY, Wu JT. **Monitoring the fitness of antiviral-resistant influenza strains** during an epidemic: a mathematical modelling study. Lancet Infect Dis 2016; online Nov 30.

Lewis EN, Griffin MR, Szilagyi PG, Zhu Y, et al. Childhood influenza: **number needed to vaccinate** to prevent 1 hospitalization or outpatient visit. Pediatrics. 2007 Sep;120(3):467-72. With 1 outpatient visit being prevented through vaccination of <50 children, influenza vaccination can reduce influenza-attributable medical visits in children significantly, even in years with modest vaccine efficacy.

Li Q, Zhou L, Zhou M, et al. Preliminary Report: Epidemiology of the Avian Influenza A (**H7N9**) Outbreak in China. N Engl J Med. 2013 Apr 24.

Li Q, Zhou L, Zhou M, et al. Epidemiology of human infections with avian influenza A(**H7N9**) virus in China. N Engl J Med. 2014 Feb 6;370(6):520-32.

Liebowitz D, Lindbloom JD, Brandl JR, et al. High titre neutralising antibodies to **influenza after oral tablet immunisation**: a phase 1, randomised, placebo-controlled trial. Lancet Infect Dis. 2015 Sep;15(9):1041-8.

Lin J, et al. Safety and immunogenicity of an inactivated adjuvanted whole-virion influenza A (**H5N1**) vaccine: a phase I randomised controlled trial. Lancet. 2006 Sep 16;368(9540):991-7.

Lin CJ, Nowalk MP, Pavlik VN, et al. Using the **4 pillars™ practice transformation program** to increase adult influenza vaccination and reduce missed opportunities in a randomized cluster trial. BMC Infect Dis.2016 Nov 3;16(1):623.

Liu D, Shi W, Shi Y, et al. Origin and diversity of novel avian infl uenza A **H7N9** viruses causing human infection: phylogenetic, structural, and coalescent analyses. Lancet 2013; online May 1.

Loeb M; Russell ML.; Moss L; et al. Effect of **Influenza Vaccination** of Children on Infection Rates in **Hutterite** Communities: A Randomized Trial. JAMA. 2010;303(10):943-950.

Loeb M, Russell ML, et al. **Live Attenuated Versus Inactivated Influenza Vaccine in Hutterite Children**: A Cluster Randomized Blinded Trial. Ann Intern Med. 2016 Aug 16

Louie JK, Acosta M, Samuel MC, et al. A novel risk factor for a novel virus: **obesity** and 2009 pandemic influenza A (H1N1). Clin Infect Dis. 2011 Feb 1;52:1-12.

Louie JK, Yang S, Samuel MC, Uyeki et al. **Neuraminidase inhibitors for critically ill children** with influenza. Pediatrics. 2013 ec;132(6):e1539-45.

Lu Y, Chillarige Y, Izurieta HS, et al. Effect of age on relative effectiveness of **high-dose versus standard-dose influenza vaccines** among US Medicare beneficiaries ages 65 years and older. J Infect Dis. 2019 Jul 9.

Ludvigsson JF, et al. **Maternal vaccination against H1N1** influenza and offspring mortality: population based cohort study and sibling design. BMJ. 2015 Nov 16;351:h5585.

Ludvigsson JF, Ström P, et al. Risk for **Congenital Malformation With H1N1** Influenza Vaccine: A Cohort Study With Sibling Analysis. Ann Intern Med. 2016 Sep 20.

Macdonald NE, Riley LE, Steinhoff MC. Influenza Immunization in **Pregnancy**. Obstet Gynecol. 2009 Aug;114(2, Part 1):365-368. PubMed PMID: 19622998.

MacIntyre CR, Heywood AE, Kovoor P, et al. **Ischaemic heart disease**, influenza and influenza vaccination: a prospective case control study. Heart 21 Aug 2013

Madjid M, Miller CC, et al. Influenza epidemics and acute respiratory disease activity are associated with a surge in autopsy-confirmed **coronary heart disease death**: results from 8 Years of autopsies in 34 892 subjects. Eur Heart J. 2007 Apr 17; [Epub ahead of print]

Mahmud SM., Becker M, Keynan Y et al. Estimated cumulative incidence of pandemic (H1N1) influenza among **pregnant women** during the first wave of the 2009 pandemic. CMAJ 2010 182: 1522-1524.

Mak TK, Mangtani P, Leese J, Watson JM, Pfeifer D. Influenza vaccination in **pregnancy**: current evidence and selected national policies. Lancet Infect Dis. 2008 Jan;8(1):44-52.

Martin ST, Torabi MJ, Gabardi S. Influenza in **Solid Organ Transplant Recipients** (February). Ann Pharmacother. 2012 Jan 10.

Mathie RT, Frye J, Fisher P. **Homeopathic Oscillococcinum** for preventing and treating influenza and influenza-like illness. Cochrane Database Syst Rev2012;12:CD001957. There is insufficient good evidence to enable robust conclusions to be made about Oscillococcinum(®) in the prevention or treatment of influenza and influenza-like illness.

Matheson NJ, Harnden AR, Perera R, et al. Neuraminidase inhibitors for preventing and treating influenza in **children**. Cochrane Database Syst Rev 2007;(1):CD002744.

Maxwell SR. Tamiflu and neuropsychiatric disturbance in adolescents. BMJ. 2007 Jun 16;334(7606):1232-3.
Mayor S. Review says oseltamivir and zanamivir should be kept for epidemics of flu. BMJ. 2006 Jan 28;332(7535):196.
McAllister L, Anderson J, Werth K, et al. **Needle-free jet injection** for administration of influenza vaccine: a randomised non-inferiority trial. Lancet 2014; 384: 674–81.
McCartney M. Margaret McCartney: What use is **mass flu vaccination**? BMJ. 2014 Oct 20;349:g6182.
McCartney M. Margaret McCartney: **Don't be bullied into prescribing Tamiflu**. BMJ. 2015 Jan 22;350:h417.
McElhaney JE, Beran J, Devaster J-M, et al. **AS03-adjuvanted** versus non-adjuvanted inactivated trivalent influenza vaccine against seasonal influenza in elderly people: a phase 3 randomised trial. Lancet Infect Dis 2013; online March 19.
McGeer A, Green KA, Plevneshi A, et al. Toronto Invasive Bacterial Diseases Network. Antiviral therapy and outcomes of influenza requiring hospitalization in Ontario, Canada. Clin Infect Dis. 2007 Dec 15;45(12):1568-75. There is a significant burden of illness attributable to influenza in this highly vaccinated population. Treatment with antiviral drugs was associated with a significant reduction in mortality.
McGrath LJ, Kshirsagar AV, et al. Influenza vaccine effectiveness in patients on **hemodialysis**: an analysis of a natural experiment. Arch Intern Med. 2012 Apr 9;172(7):548-54.
McKittrick N, Frank I, Jacobson JM, et al; for the Center for AIDS Research. Improved Immunogenicity With **High-Dose** Seasonal Influenza Vaccine in **HIV-Infected Persons**: A Single-Center, Parallel, Randomized Trial. Ann Intern Med. 2013 Jan 1;158(1):19-26.
McLean HQ, Caspard H, Griffin MR, et al. Association of **prior vaccination with influenza vaccine effectiveness** in children receiving live attenuated or inactivated vaccine. JAMA Netw Open. 2018;1(6):e183742.
Medical Letter. **Antiviral Drugs for Influenza** 2013-2014. Updated Jan 20,2014. Updated Dec 21, 2105. Updated **Jan 14, 2019**.
Merckx J, Wali R, Schiller I, et al. Diagnostic accuracy of **novel and traditional rapid tests for influenza** infection compared with reverse transcriptase polymerase chain reaction. A systematic review and meta-analysis. Ann Intern Med. 2017;167:394-409. doi:10.7326/M17-0848
Mertz D, Kim TH, Johnstone J, et al. Populations at risk for **severe or complicated influenza illness**: systematic review and meta-analysis. BMJ. 2013 Aug 23;347:f5061.
Miller E, Andrews N, Stellitano L, et al. Risk of **narcolepsy in children and young people receiving AS03 adjuvanted pandemic A/H1N1** 2009 influenza vaccine: retrospective analysis. BMJ. 2013 Feb 26;346:f794.
Munoz FM, Bernstein HH. **Influenza Prophylaxis in Children**: Could a Single Dose of One Drug Be an Option? Pediatrics.2016:138(6): e20162371
Mirdamadi K, Einarson A. **H1N1** and influenza viruses: Why **pregnant** women might be hesitant to be vaccinated. Can Fam Physician. 2011 Sep;57(9):1003-4.
Mistry RD, Fischer JB, Prasad PA, et al. **Severe Complications** in Influenza-like Illnesses. Pediatrics. 2014 Aug 4.
Miyakawa R, Barreto NB, Kato RM, et al. Early Use of **Anti-influenza Medications in Hospitalized Children With Tracheostomy**. Pediatrics. 2019 Mar;143(3).
Modin D, Jørgensen ME, Gislason G, et al. **Influenza Vaccine in Heart Failure**: Cumulative Number of Vaccinations, Frequency, Timing, and Survival: A Danish Nationwide Cohort Study. Circulation. 2018 Dec 10.
Monto AS, et al. Detection of Influenza Viruses **Resistant to Neuraminidase Inhibitors** in Global Surveillance during the First 3 Years of Their Use. Antimicrob Agents Chemother. 2006 Jul;50(7):2395-402.
Moore DL; **Canadian Paediatric Society**, Infectious Diseases and Immunization Committee. **Influenza vaccine** recommendations for children and youth for the 2013/2014 season. Paediatr Child Health. 2013;18(8):e51-2.
Moore DL. **Vaccine recommendations for children and youth** for the **2017/2018 influenza season**. Paediatr Child Health. 2018 Feb;23(1):e10-e13.
Morens DM, Taubenberger JK, Fauci AS. **Pandemic Influenza Viruses** - Hoping for the Road Not Taken. N Engl J Med. 2013 Jun 5.
Morens DM, Taubenberger JK. A possible outbreak of **swine influenza, 1892**. Lancet Infect Dis. 2013 Nov 27
Morens DM, Taubenberger JK. **Influenza Cataclysm, 1918**. N Engl J Med. 2018 Dec 13;379(24):2285-2287.
Moscona A. Neuraminidase inhibitors for influenza. N Engl J Med. 2005 Sep 29;353(13):1363-73.
Moscona A. Global transmission of **oseltamivir-resistant** influenza. N Engl J Med. 2009 Mar 5;360(10):953-6. Epub 2009 Mar 2.
Moynihan R. Was the flu drug **zanamivir** a breakthrough or money for old rope? BMJ. 2014 Jun 2;348:g3611
Mulpuru S, Li L, Ye L, et al. Effectiveness of **Influenza Vaccination on Hospitalizations and Risk Factors for Severe Outcomes in Hospitalized** Patients With COPD. Chest. 2019 Jan;155(1):69-78.
Murphy K, et al. Antibody response **after varicella vaccination** in children treated with **budesonide** inhalation suspension or non-steroidal conventional asthma therapy. Int J Clin Pract. 2006 Dec;60(12):1548-57. VZV antibody responses and tolerability to the live varicella vaccine in paediatric asthma patients treated with BIS vs. NSCAT were comparable, demonstrating that young children with asthma receiving nebulised BIS can be immunised effectively with Varivax.
Muthuri SG, Myles PR, Venkatesan S, et al. Impact of **neuraminidase inhibitor treatment** on outcomes of public health importance during the 2009-2010 influenza A(**H1N1**) pandemic: a systematic review and meta-analysis in hospitalized patients. J Infect Dis. 2013 Feb 15;207(4):553-63.
Muthuri SG, Venkatesan S, Myles PR, et al; PRIDE Consortium Investigators, Nguyen-Van-Tam JS. **Effectiveness of neuraminidase inhibitors** in reducing mortality in patients admitted to hospital with influenza A **H1N1pdm09** virus infection: a meta-analysis of individual participant data. Lancet Respir Med. 2014 May;2(5):395-404.
Nace DA, Lin CJ, Ross TM, et al. Randomized, Controlled Trial of **High-Dose Influenza Vaccine Among Frail Residents of Long-Term Care Facilities**. J Infect Dis. 2014 Dec17.

NACI: National Advisory Committee on Immunization. Statement on seasonal trivalent inactivated influenza vaccine (TIV) for **2010-2011**. CCDR 2010;36(ACS-6):1-49. www.phac-aspc.gc.ca/publicat/ccdr-rmtc/10vol36/acs-6/index-eng.php (accessed August 30, 2010).

NACI: Statement on Seasonal Influenza vaccine for **2011-2012**. CCDR Sept 2011 (ACS-5) Vol 37. http://www.phac-aspc.gc.ca/publicat/ccdr-rmtc/11vol37/acs-dcc-5/index-eng.php

NACI 2011: Recommendations on the use of **intradermal trivalent inactivated influenza vaccine** (TIV-ID). http://www.phac-aspc.gc.ca/publicat/ccdr-rmtc/11vol37/acs-dcc-4/index-eng.php

NACI: National Advisory Committee on Immunization (NACI). Addendum – **LAIV use in egg allergic individuals**. Advisory Committee Statement (ACS). Canadian Immunization Guide chapter on influenza and statement on seasonal influenza vaccine for 2016-2017.

Nakafero G, Grainge MJ, Myles PR, et al. Association between inactivated **influenza vaccine and primary care consultations for autoimmune rheumatic disease flares**: a self-controlled case series study using data from the Clinical Practice Research Datalink. Ann Rheum Dis. 2019 Apr 29.

Nakano T, Ishiwada N, Sumitani T, et al. Inhaled **Laninamivir** Octanoate as Prophylaxis for Influenza in Children. Pediatrics.2016;138(6):e20160109.

Napolitano LM, Angus DC, Uyeki TM. **Critically Ill** Patients With Influenza A(**H1N1**)pdm09 Virus Infection in 2014. JAMA. 2014 Feb 24.

Natori Y et al. A double-blind, randomized trial of **high-dose vs standard-dose influenza vaccine in adult solid-organ transplant** recipients. Clin Infect Dis 2018 May 17; 66:1698.

Neidich SD, Green WD, Rebeles J, et al. **Increased risk** of influenza among vaccinated adults who are **obese**. Int J Obes (Lond). 2017 Jun 6.

Neto HB, Farhat CK, Tregnaghi MW, et al.; for the D153-P504 LAIV Study Group. Efficacy and Safety of **1 and 2 Doses of Live Attenuated** Influenza Vaccine in Vaccine-Naive Children. Pediatr Infect Dis J. 2009 May;28(5):365-371.

Neuzil KM, et al. Immunogenicity and reactogenicity of **1 versus 2 doses** of trivalent inactivated influenza vaccine in vaccine-naive 5-8-year-old children. J Infect Dis. 2006 Oct 15;194(8):1032-9. Epub 2006 Sep 11.

Newsome K, Alverson CJ, Williams J, et al. **Outcomes of infants born to women with influenza A**(H1N1)pdm09. Birth Defects Res. 2019 Jan 15;111(2):88-95.

Ng TWY, Cowling BJ, Gao HZ, et al. **Comparative Immunogenicity** of Enhanced Seasonal Influenza Vaccines in Older Adults: A Systematic Review and Meta-analysis. J Infect Dis. 2019 Apr 19;219(10):1525-1535.

Nguyen JT, Smee DF, Barnard DL, et al. Efficacy of combined therapy with **amantadine, oseltamivir, and ribavirin** in vivo against susceptible and amantadine-resistant influenza A viruses. PLoS One. 2012;7(1):e31006.

Nicoll A, Sprenger M. **Low effectiveness** undermines promotion of seasonal influenza vaccine. Lancet Infect Dis. 2013 Jan;13(1):7-9.

Nichol KL, Nordin JD, Nelson DB, Mullooly JP, Hak E. Effectiveness of influenza vaccine in the **community-dwelling elderly**. N Engl J Med. 2007 Oct 4;357(14):1373-81. During 10 seasons, influenza vaccination was associated with significant reductions in the risk of hospitalization for pneumonia or influenza and in the risk of death among community-dwelling elderly persons. Vaccine delivery to this high-priority group should be improved.

Nicholson KG, Abrams KR, Batham S, et al. Immunogenicity and safety of a two-dose schedule of **whole-virion and AS03(A)-adjuvanted** 2009 influenza A (H1N1) vaccines: a randomised, multicentre, age-stratified, head-to-head trial. Lancet Infect Dis. 2011 Feb;11(2):91-101.

Noah MA, Peek GJ, Finney SJ, et al. Referral to an **extracorporeal membrane oxygenation center** and mortality among patients with severe 2009 influenza A(H1N1) [published online October 5, 2011]. JAMA. doi:10.1001/jama.2011.1471.

Nolan T, Bernstein DI, Block SL, et al. for the LAIV Study Group. Safety and Immunogenicity of **Concurrent Administration** of Live Attenuated Influenza Vaccine With Measles-Mumps-Rubella and Varicella Vaccines to Infants 12 to 15 Months of Age.Pediatrics. 2008 Mar;121(3):508-516. Concurrent administration of live attenuated influenza vaccine with measles-mumps-rubella vaccine and varicella vaccine provided equivalent immunogenicity, compared with separate administration, and was well tolerated.

Nolan T, Roy-Ghanta S, Montellano M, et al. Relative Efficacy of **AS03-Adjuvanted Pandemic Influenza A(H1N1) Vaccine in Children**: Results of a Controlled, Randomized Efficacy Trial. J Infect Dis. 2014 May 2.

Nordin JD, Kharbanda EO, Benitez GV, Nichol et al. **Maternal safety of trivalent inactivated influenza** vaccine in pregnant women. Obstet Gynecol. 2013 Mar;121(3):519-25.

Norhayati MN, Ho JJ, Azman MY. Influenza vaccines for **preventing acute otitis media** in infants and children. Cochrane Database of Systematic Reviews 2015, Issue 3. Art. No.: CD010089. DOI: 10.1002/14651858.CD010089.pub2. Influenza vaccine results in a small reduction in AOM. The observed reduction with the use of antibiotics needs to be considered in the light of current recommended practices aimed at avoiding antibiotic overuse. Safety data from these trials are limited. The benefits may not justify the use of influenza vaccine without taking into account the vaccine efficacy in reducing influenza and safety data. The quality of the evidence was high to moderate. Additional research is needed.

Norhayati MN;Ho JJ;Azman MY. **Influenza vaccines for preventing acute otitis media** in infants and children. Cochrane Database Syst Rev. 2017 Oct 17;10:CD010089. Influenza vaccine results in a small reduction in AOM. The observed reduction in the use of antibiotics needs to be considered in light of current recommended practices aimed at avoiding antibiotic overuse. Safety data from these trials were limited. The benefits may not justify the use of influenza vaccine without taking into account the vaccine efficacy in reducing influenza and safety data. We judged the quality of the evidence to be low to moderate.

Noti JD, Blachere FM, McMillen CM, Lindsley, et al. **High humidity** leads to loss of infectious influenza virus from simulated coughs. PLoS One. 2013;8(2):e57485.

Nunes MC, Cutland CL, Jones S, et al; Maternal Flu Trial Team. Duration of infant protection against influenza illness conferred by **maternal immunization**: secondary analysis of a randomized clinical trial [online July 5, 2016]. JAMA Pediatr. doi:10.1001/jamapediatrics.2016.0921.

Nunes MC, Cutland CL, Madhi SA. **Influenza Vaccination during Pregnancy and Protection against Pertussis**. N Engl J Med. 2018 Mar 29;378(13):1257-1258.

Oboho I, Reed C, et al. The benefit of **early influenza antiviral treatment of pregnant women** hospitalized with laboratory-confirmed influenza. J Infect Dis. 2016 Feb 3.
Osterholm MT, Kelley NS, Sommer A, et al. Efficacy and effectiveness of **influenza vaccines**: a systematic review and meta-analysis. Lancet Infect Dis 2011; online Oct 26.
Osterholm MT, Kelley NS, Sommer A, Belongia EA. **Efficacy and effectiveness of influenza vaccines**: a systematic review and meta-analysis. Lancet Infect Dis. 2012;12:36-44.
Omer SB, Phadke VK, Bednarczyk RA, et al. Impact of **Statins** on Influenza Vaccine Effectiveness Against Medically Attended Acute Respiratory Illness. J Infect Dis. 2015 Oct 28.
Oner AF, et al. Avian Influenza A (**H5N1**) Infection in Eastern Turkey in 2006. N Engl J Med. 2006 Nov 23;355(21):2179-85.
Panhwar MS, Kalra A, Gupta T, et al. Effect of **Influenza on Outcomes in Patients with Heart Failure**. JACC Heart Fail. 2019 Jan 2.
Parboosing R, Bao Y, Shen L, et al. Gestational Influenza and **Bipolar Disorder** in Adult Offspring. JAMA Psychiatry. 2013 May 8:1-8.
Park JK, Lee MA, Lee EY, et al. Effect of **methotrexate discontinuation** on efficacy of seasonal influenza vaccination in patients with rheumatoid arthritis: a randomised clinical
Partinen M, Kornum BR, Plazzi G, et al. **Narcolepsy** as an autoimmune disease: the role of **H1N1** infection and vaccination. Lancet Neurol. 2014 Jun;13(6):600-613.
Pasternak B, Svanström H, Mølgaard-Nielsen D, et al. Vaccination against **pandemic A/H1N1 2009 influenza in pregnancy** and risk of fetal death: cohort study in Denmark. BMJ 2012;344:e2794.
Pasternak B, Svanstro¨m H, Mølgaard-Nielsen D, Krause TG, et al. Risk of adverse **fetal outcomes following administration of a pandemic influenza A(H1N1) vaccine** during pregnancy. JAMA. 2012;308(2):165-174.
Patel K, Rayner CR, Giraudon M, et al. Pharmacokinetics and safety of **oseltamivir** in patients with **end-stage renal disease** treated with automated peritoneal dialysis. Br J Clin Pharmacol. 2014 Oct 7.
Paton Nicholas I, Lee Lawrence, Xu Ying, et al. **Chloroquine** for influenza prevention: a randomised, double-blind, placebo controlled trial, Lancet Infectious Diseases, 5 May 2011.
Paules C, Subbarao K. **Influenza**. (Seminar) Lancet. 2017 Mar 10.
Payne D. **Tamiflu: the battle for secret drug data**. BMJ. 2012 Oct 29;345:e7303.
Pham T, Combes A, Rozé H, et al. **Extracorporeal membrane oxygenation** for pandemic influenza A(H1N1)– induced acute respiratory distress syndrome: a cohort study and propensity-matched analysis. AmJ Respir Crit Care Med 2013;187:276–285.
Pharmacist's Letter Detail-Document, Flu Vaccines 2014-2015. Pharmacist's Letter/Prescriber's Letter. September 2014.
Pharmacist's Letter. **Canadian** Influenza update 2006-07. Sept 2006
Phrommintikul A, Kuanprasert S, et al. **Influenza vaccination reduces cardiovascular events** in patients with acute coronary syndrome. Eur Heart J. 2011 Jul;32(14):1730-5.
Piedra PA et al. Effects of **oseltamivir on influenza-related complications in children** with chronic medical conditions. *Pediatrics* 2009 Jul; 124:170.
Pierce M, Kurinczuk JJ, Spark P, et al. UKOSS. **Perinatal outcomes** after maternal 2009/H1N1 infection: national cohort study. BMJ. 2011 Jun 14;342:d3214.
Pillai VC, Han K, Beigi RH, Hankins GD, et al. Population **pharmacokinetics** of **oseltamivir** in **non-pregnant and pregnant women**. Br J Clin Pharmacol. 2015 Jun 3.
Pitisuttithum P, Boonnak K, Chamnanchanunt S, et al. Safety and immunogenicity of a live attenuated **influenza H5 candidate vaccine** strain A/17/turkey/Turkey/05/133 **H5N2** and its priming effects for potential pre-pandemic use: a randomised, double-blind, placebo-controlled trial. Lancet Infect Dis; 2017; online May 19.
Poehling KA, et al. Accuracy and impact of a point-of-care **rapid influenza test** in young children with respiratory illnesses. Arch Pediatr Adolesc Med. 2006 Jul;160(7):713-8.
(InfoPOEMs: Rapid influenza testing is very accurate, but the results don't seem to influence care in a meaningful way other than to decrease testing in those children seen in the emergency department. (LOE = 1b))
Poehling KA, et al.; New Vaccine Surveillance Network. The underrecognized burden of influenza in **young children**. N Engl J Med. 2006 Jul 6;355(1):31-40.
Poehling KA, Szilagyi PG, Staat MA, et al. New Vaccine Surveillance Network. Impact of **maternal immunization** on influenza hospitalizations in infants. Am J Obstet Gynecol. 2011 Jun;204(6 Suppl 1):S141-8.
Poehling KA, Edwards KM, Griffin MR, et al. The **burden of influenza in young children**, 2004-2009. Pediatrics. 2013 Feb;131(2):207-16.
Pop-Vicas A, Rahman M, et al. Estimating the Effect of **Influenza Vaccination on Nursing Home Residents' Morbidity and Mortality**. J Am Geriatr Soc. 2015 Aug 17.
Presanis AM, Pebody RG, Paterson BJ, et al. **Changes in severity of 2009 pandemic A/H1N1** influenza in England: a Bayesian evidence synthesis. BMJ. 2011 Sep 8;343:d5408.
Price, CS., Thompson, WW., et al. Prenatal and Infant Exposure to **Thimerosal** From Vaccines and Immunoglobulins and Risk of **Autism**. Pediatrics 2010 0: peds.2010-0309.
Price D, Chan D, Greaves N. **Physician surveillance of influenza**: Collaboration between primary care and public health. Can Fam Physician. 2014 Jan;60(1):e7-e15
Public Health Agency of Canada Statement on Influenza Vaccination for the 2007-2008 Season http://www.phac-aspc.gc.ca/publicat/ccdr-rmtc/07vol33/acs-07/index_e.html
Public Health Agency of Canada Statement on Influenza Vaccination for the 2008-2009 Season http://www.phac-aspc.gc.ca/publicat/ccdr-rmtc/08vol34/acs-3/index-eng.php
Public Health Agency of Canada. National Advisory Committee on Immunization (**NACI**): Canadian Immunization Guide chapter on influenza and statement on seasonal influenza vaccine for **2016-2017**. www.phac-aspc.gc.ca/naci-ccni/assets/pdf/flu-2016-grippe-eng.pdf (accessed July 14, 2016).
Prymula R, Siegrist CA, Chlibek R, et al. Effect of prophylactic **paracetamol/acetaminophen** administration at time of vaccination on febrile reactions and antibody responses in children: two open-label, randomised controlled trials. Lancet. 2009 Oct 17;374(9698):1339-50.
Qi X, et al. Probable **person to person** transmission of novel avian influenza A (**H7N9**) virus in Eastern China, 2013: epidemiological investigation. BMJ. 2013 Aug 6;347:f4752.
Quach S, Hamid JS, Pereira JA, et al. Influenza vaccination coverage across **ethnic groups** in Canada. CMAJ. 2012 Sep 10.
Radonovich LJ Jr, Simberkoff MS, Bessesen MT, et al. **N95 Respirators vs Medical Masks** for Preventing Influenza Among Health Care Personnel: A Randomized Clinical Trial.

JAMA. 2019 Sep 3;322(9):824-833.
Randolph AG et al. **Critically ill children** during the 2009–2010 influenza pandemic in the United States. Pediatrics 2011 Dec; 128:e1
Regan AK, Moore HC, et al. **Seasonal Trivalent Influenza Vaccination During Pregnancy** and the Incidence of Stillbirth: Population-Based Retrospective Cohort Study. Clin Infect Dis. 2016 Mar 30.
Ribeiro AC, Guedes LK, Moraes JC, et al. **Reduced seroprotection after pandemic H1N1 influenza** adjuvant-free vaccination in patients with rheumatoid arthritis: implications for clinical practice. Ann Rheum Dis. 2011 Dec;70(12):2144-7.
Rivetti D, Vaccines for preventing influenza in the elderly. Cochrane Database Syst Rev. 2006 Jul 19;3:CD004876.
Robison SG, Dunn Ag, Richards DL, et al. **Changes in Influenza Vaccination Rates After Withdrawal of Live Vaccine**. Pediatrics. 2017;140(5):e20170516
Rodrigo C, Leonardi-Bee J, Nguyen-Van-Tam JS, et al. Effect of **Corticosteroid Therapy on Influenza-Related Mortality**: A Systematic Review and Meta-analysis. J Infect Dis. 2015 Jul 15;212(2):183-94.
Rouphael NG, Paine M, Mosley R, et al, for the TIV-MNP 2015 Study Group. The safety, immunogenicity, and acceptability of **inactivated influenza vaccine** delivered by **microneedle patch** (**TIV-MNP 2015**): a randomised, partly blinded, placebo-controlled, phase 1 trial. Lancet 2017; online June 27.
Rubinstein E, Predy G, Sauvé L, et al. The responses of **Aboriginal Canadians to adjuvanted pandemic (H1N1)** 2009 influenza vaccine. CMAJ. 2011 Aug 8.
Rubinstein F, Micone P, Bonotti A, et al. "EVA" Study Research Group (Estudio "Embarazo y Vacuna Antigripal"). Influenza **A/H1N1 MF59 adjuvanted vaccine in pregnant women** and adverse perinatal outcomes: multicentre study. BMJ. 2013 Feb 4;346:f393.
Ruis C, Brown LK, Roy S, et al. **Mutagenesis in Norovirus in Response to Favipiravir Treatment**. N Engl J Med. 2018 Nov 29;379(22):2173-2176.
Sachedina N, Donaldson LJ. **Paediatric mortality** related to pandemic influenza A **H1N1** infection in England: an observational population-based study. Lancet. 2010 Oct 26.
Salmon DA, Proschan M, Forshee R, et al; the **H1N1** GBS Meta-Analysis Working Group. Association between **Guillain-Barré syndrome** and influenza A (H1N1) 2009 monovalent inactivated vaccines in the USA: a meta-analysis. Lancet. 2013 Mar 12. (1.6 excess cases of GBS per million people vaccinated)
Saito S, Minakami H, Nakai A, et al. Outcomes of **infants exposed to oseltamivir or zanamivir in utero** during pandemic (H1N1) 2009. Am J Obstet Gynecol. 2013 Apr 9.
Santibanez TA, Grohskopf LA, Zhai Y, et al. Complete **Influenza Vaccination Trends for Children Six to Twenty-Three Months**. Pediatrics. 2016 Feb 2. peds.2015-3280.
Scharpé J, Evenepoel P, Maes B, et al. Influenza Vaccination Is Efficacious and Safe in **Renal Transplant** Recipients. Am J Transplant. 2007 Dec 19; [Epub ahead of print]
Schauwvlieghe AFAD, Rijnders BJA, Philips N, et al. **Invasive aspergillosis** in patients admitted to the **intensive care unit with severe influenza**: a retrospective cohort study. Lancet Respir Med 2018; online July 31
Schechter R, Grether JK. Continuing increases in **autism** reported to California's developmental services system: mercury in retrograde. Arch Gen Psychiatry. 2008 Jan;65(1):19-24.
Scott VP, Opel DJ, Reifler J, et al. **Office-Based Educational Handout** for Influenza Vaccination: A Randomized Controlled Trial. Pediatrics. 2019 Jul 10.
Shakib JH, Korgenski K, Presson AP, et al. **Influenza in Infants Born to Women Vaccinated During Pregnancy**. Pediatrics. 2016 Jun;137(6).
Shang M, Blanton L, Brammer L, et al. **Influenza-Associated Pediatric Deaths in the United States, 2010-2016**. Pediatrics. 2018 Feb 12.
Sheffield JS, Greer LG, Rogers VL, et al. Effect of influenza vaccination in the **first trimester of pregnancy**. Obstet Gynecol. 2012 Sep;120(3):532-7.
Short KR, Kroeze EJ, Fouchier RA, Kuiken T. Pathogenesis of **influenza-induced acute respiratory distress syndrome**. Lancet Infect Dis. 2013 Nov 12.
Shuler CM, et al. Vaccine effectiveness against medically attended, laboratory-confirmed influenza among children aged 6 to 59 months, 2003-2004. Pediatrics. 2007 Mar;119(3):e587-95. Full vaccination provided measurable protection against laboratory-confirmed influenza among children who were aged 6 to 59 months during a season with suboptimal vaccine match.
Shun-Shin Matthew, Thompson Matthew, Heneghan Carl, et al. **Neuraminidase inhibitors** for treatment and prophylaxis of influenza in **children**: systematic review and meta-analysis of randomised controlled trials**.** BMJ 2009;339:b3172, doi: 10.1136/bmj.b3172 (Published 10 August 2009)
Simonsen L, Taylor RJ, Viboud C, et al. Mortality benefits of influenza vaccination in elderly people: an ongoing controversy. Lancet Infect Dis. 2007 Oct;7(10):658-66. We conclude that frailty selection bias and use of non-specific endpoints such as all-cause mortality have led cohort studies to greatly exaggerate vaccine benefits. The remaining evidence base is currently insufficient to indicate the magnitude of the mortality benefit, if any, that elderly people derive from the vaccination programme.
Simonsen L, Spreeuwenberg P, Lustig R, et al; GLaMOR Collaborating Teams. **Global mortality estimates** for the **2009 Influenza Pandemic** from the GLaMOR project: a modeling study. PLoS Med. 2013 Nov;10(11):e1001558
Simonsen L, Reichert TA, Viboud C, et al. Impact of **influenza vaccination of seasonal mortality in the U.S. elderly** population. Arch Intern Med. 2005;165:265-272.
Simpson CR, Ritchie LD, Robertson C, et al. Effectiveness of **H1N1 vaccine** for the prevention of pandemic influenza in **Scotland**: a retrospective observational cohort study. Lancet Infect Dis 2012; published online June 26.
Singanayagam A, Zambon M, Lalvani A, et al. Urgent challenges in implementing **live attenuated influenza vaccine**. Lancet Infect Dis. 2017 Aug 2.
Siriwardena AN, Gwini SM, Coupland C. Influenza vaccination, pneumococcal vaccination and risk of **AMI**: Matched case-control study. CMAJ 2010; DOI:10.1503/cmaj.091891.
Skowronski, DM., Hottes, TS., Janjua, NZ., et al. Prevalence of **seroprotection against** the pandemic (H1N1) virus after the 2009 pandemic. CMAJ 2010 0: cmaj.100910.
Skowronski Danuta M, Janjua Naveed Z, De Serres Gaston, et al. Effectiveness of **AS03 adjuvanted pandemic H1N1** vaccine: case-control evaluation based on sentinel surveillance system **in Canada**, autumn 2009. BMJ 2011;342:doi:10.1136/bmj.c7297 (Published 3 February 2011)
Skowronski DM, Hottes TS, Chong M, et al. Randomized controlled trial of dose response to influenza vaccine in **children aged 6 to 23 months**. Pediatrics. 2011 Aug;128(2):e276-89.

Skowronski DM, Moser FS, Janjua NZ, et al. **H3N2v and other influenza epidemic risk** based on age-specific estimates of sero-protection and contact network interactions. PLoS One. 2013;8(1):e54015.

Smith S, Demicheli V, Di Pietrantonj C, et al. Vaccines for preventing influenza in healthy children. Cochrane Database Syst Rev. 2006 Jan 25;(1):CD004879.

Smith SC Jr, et al. AHA/ACC guidelines for **secondary prevention** for patients with coronary and other atherosclerotic vascular disease: 2006 update: endorsed by the National Heart, Lung, and Blood Institute. Circulation. **2006** May 16;113(19):2363-72. http://circ.ahajournals.org/cgi/reprint/113/19/2363

Smith JR, Sacks S. Incidence of **neuropsychiatric adverse events** in influenza patients treated with oseltamivir or no antiviral treatment. Int J Clin Pract. 2009 Apr;63(4):596-605.

Smith M, Peacock G, Uyeki TM, et al. **Influenza vaccination in children with neurologic or neurodevelopmental** disorders. Vaccine. 2015 Mar 30.

South East Asia Infectious Disease Clinical Research Network. Effect of **double dose oseltamivir** on clinical and virological outcomes in children and adults admitted to hospital with severe influenza: double blind randomised controlled trial. BMJ. 2013 May 30;346:f3039.

SteelFisher GK, Blendon RJ, Ward JRM, et al. **Public response** to the 2009 infl uenza A H1N1 pandemic: a polling study in five countries. Lancet Infect Dis 2012; online Oct 5.

Steinhoff MC, Omer SB, Roy E, et al. Neonatal outcomes after **influenza immunization during pregnancy**: a randomized controlled trial. CMAJ. 2012 Apr 3;184(6):645-53.

Steinhoff MC, MacDonald N, Pfeifer D, et al. **Influenza vaccine in pregnancy**: policy and research strategies. Lancet. 2014 May 10;383(9929):1611-3.

Steinhoff MC, Katz J, et al. **Year-round influenza immunisation during pregnancy** in Nepal: a phase 4, placebo-controlled trial. Lancet Infect Dis 2017; online May 15.

Stiver HG, Evans GA, Aoki FY, et al. **Guidance on the use of antiviral drugs for influenza in acute care facilities in Canada**, 2014-2015. Can J Infect Dis Med Microbiol. 2015 Jan-Feb;26(1):e5-8.

Stockmann C, Byington CL, Pavia AT, et al. **Limited and Variable Use of Antivirals for Children** Hospitalized With Influenza. JAMA Pediatr. 2017 Jan 23.

Stockwell MS, Kharbanda EO, Martinez RA, et al. Effect of a **text messaging** intervention on influenza vaccination in an urban, lowincome pediatric and adolescent population: a randomized controlled trial. JAMA. 2012;307(16):1702-1708.

Stockwell MS, Broder K, Larussa P, et al. Risk of Fever After Pediatric **Trivalent Inactivated Influenza Vaccine and 13-Valent Pneumococcal Conjugate** Vaccine. JAMA Pediatr. 2014 Jan 6.

Stockwell MS, Catallozzi M, Camargo S, et al. **Registry-linked electronic** influenza vaccine provider **reminders**: a cluster-crossover trial. Pediatrics. 2015 Jan;135(1):e75-82.

Stockwell MS, Hofstetter AM, DuRivage N, et al. **Text message reminders** for second dose of influenza vaccine: a randomized controlled trial. Pediatrics. 2015 Jan;135(1):e83-91.

Sue K. The science behind "**man flu**". BMJ. 2017 Dec 11;359:j5560.

Sullender WM, Fowler KB, Gupta V, et al. Efficacy of **inactivated trivalent influenza vaccine** in rural India: a 3-year cluster-randomised controlled trial. Lancet Glob Health. 2019 Jul;7(7):e940-e950.

Sykes A, Gerhardt E, Tang L, et al. The Effectiveness of Trivalent **Inactivated Influenza Vaccine in Children with Acute Leukemia**. J Pediatr. 2017 Dec;191:218-224.e1.

Szakács A, Darin N, Hallböök T. Increased childhood incidence of **narcolepsy** in western Sweden after **H1N1** influenza vaccination. Neurology 2013;80:1315–1321.

Szilagyi PG, Schaffer S, Rand CM et al. **School-Located Influenza Vaccinations**: A Randomized Trial. Pediatrics.2016;138(5):e20161746

Taksler GB, Rothberg MB, et al. **Association of Influenza Vaccination Coverage in Younger Adults** With Influenza-Related Illness in the Elderly. Clin Infect Dis. 2015 Sep 9.

Talbot TR, Talbot HK. Influenza Prevention Update: Examining Common **Arguments Against Influenza Vaccination**. JAMA. 2013 Jan 18:1-2.

Tanaka, Toshihiro, Nakajima, Ken, et al. Safety of **neuraminidase inhibitors** against novel influenza A (**H1N1) in pregnant** and breastfeeding women. CMAJ 2009 0: cmaj.090866

Tartof SY, Qian L, Rieg GK, et al. **Safety of Seasonal Influenza Vaccination in Hospitalized Surgical Patients**: A Cohort Study. Ann Intern Med. 2016 Mar 15.

Tartof SY, Qian L, Liu IA, et al. Safety of **Influenza Vaccination Administered During Hospitalization**. Mayo Clin Proc. 2019 Jan 3.

Tessmer A, Welte T, Schmidt-Ott R et al. for CAPNETZ study group. **Influenza vaccination** is associated with reduced severity of community acquired pneumonia. Eur Respir J. 2010 Dec 9.

Thomas RE, RussellM, Lorenzetti D. **Interventions to increase influenza vaccination** rates of those 60 years and older in the community. Cochrane Database of Systematic Reviews 2010, Issue 9. Art.No.: CD005188. DOI: 10.1002/14651858.CD005188.pub2.

Thomas RE, Jefferson T, Lasserson TJ. Influenza **vaccination for healthcare workers** who work with the elderly. Cochrane Database Syst Rev. 2010 Feb 17;(2):CD005187.

Thomas RE, Jefferson T, Lasserson TJ. Influenza **vaccination for healthcare workers** who care for people aged 60 or older living in long-term care institutions. Cochrane Database Syst Rev. 2013 Jul 22;7:CD005187. The results for specific OUTCOMES: laboratory-proven influenza or its complications (lower respiratory tract infection, or hospitalisation or death due to lower respiratory tract illness) did not identify a benefit of healthcare worker vaccination on these key outcomes. This review did not find information on co-interventions with healthcare worker vaccination: hand-washing, face masks, early detection of laboratory-proven influenza, quarantine, avoiding admissions, antivirals and asking healthcare workers with influenza or influenza-like-illness (ILI) not to work. This review does not provide reasonable evidence to support the vaccination of healthcare workers to prevent influenza in those aged 60 years or older resident in LTCIs.

Thomas RE, Lorenzetti DL. **Interventions to increase influenza vaccination rates of those 60 years** and older in the community. Cochrane Database Syst Rev. 2014 Jul 7;7:CD005188. doi: 10.1002/14651858.CD005188.pub3. There are interventions that are effective for increasing community demand for vaccination, enhancing access and

improving provider/system response. Heterogeneity limited pooling of trials.
Thomas RE, Lorenzetti DL. **Interventions to increase influenza vaccination rates of those 60 years and older** in the community. Cochrane Database of Systematic Reviews 2018, Issue 5. Art. No.: CD005188. We identified interventions that demonstrated significant positive effects of low (postcards), medium (personalised phone calls), and high (home visits, facilitators) intensity that increase community demand for vaccination, enhance access, and improve provider/system response.
Thompson MG, Kwong JC, Regan AK, et al; PREVENT Workgroup . **Influenza Vaccine Effectiveness in Preventing Influenza-associated Hospitalizations During Pregnancy**: A Multi-country Retrospective Test Negative Design Study, 2010-2016. Clin Infect Dis. 2018 Oct 11.
Thompson WW, Price C, Goodson B, et al.; Vaccine Safety Datalink Team. Early **thimerosal exposure** and neuropsychological outcomes at 7 to 10 years. N Engl J Med. 2007 Sep 27;357(13):1281-92. Our study does not support a causal association between early exposure to mercury from thimerosal-containing vaccines and immune globulins and deficits in neuropsychological functioning at the age of 7 to 10 years.
Thorne-Humphrey LM, Goralski KB, et al. **Oseltamivir pharmacokinetics in morbid obesity** (OPTIMO trial). J Antimicrob Chemother. 2011;66:2083-91
To KK, Chan JF, et al. The emergence of influenza A **H7N9** in human beings 16 years after influenza A **H5N1**: a tale of two cities. Lancet Infect Dis. 2013 Sep;13(9):809-21.
Tran CH, Sugimoto JD, et al. **School-located influenza vaccination** reduces community risk for influenza and influenza-like illness emergency care visits. PLoS One. 2014 Dec 9;9(12):e114479.
Treanor JJ, et al. Safety and immunogenicity of an inactivated subvirion influenza A **(H5N1) vaccine**. N Engl J Med. 2006 Mar 30;354(13):1343-51.
Treanor JJ, et al. Safety & immunogenicity of baculovirus-expressed (non-egg) hemagglutinin influenza vaccine: a randomized controlled trial. JAMA. 2007 Apr11;297(14):1577-82.
Treanor JJ, Talbot HK, Ohmit SE, et al. US Flu-VE Network. **Effectiveness of seasonal influenza vaccines** in the United States during a season with circulation of all three vaccine strains. Clin Infect Dis. 2012 Oct;55(7):951-9.
Treanor JJ. **Influenza Vaccination**. N Engl J Med. 2016 Sep 29;375(13):1261-8.
Trieu MC, Zhou F, Lartey S, et al. **Long-term Maintenance of the Influenza-Specific Cross-Reactive Memory** CD4+ T-Cell Responses **Following Repeated Annual Influenza Vaccination**. J Infect Dis. 2017 Mar1;215(5):740-749.
Trotta F, Da Cas R, Spila Alegiani S, et al. Evaluation of the safety of **A/H1N1 pandemic vaccine during pregnancy**: cohort study. BMJ 2014;348:g3361.
Turner PJ, Southern J, Andrews NJ, et al; SNIFFLE-2 Study Investigators. Safety of **live attenuated influenza vaccine in young people with egg allergy**: multicentre prospective cohort study. BMJ. 2015 Dec 8;351:h6291.
Udell JA, Zawi R, Bhatt DL, et al. Association between **influenza vaccination and cardiovascular outcomes** in high-risk patients: ameta-analysis. JAMA. 2013. doi:10.1001/jama.2013.279206.
Uyeki TM. **Preventing and Controlling Influenza** with Available Interventions. N Engl J Med. 2014 Jan 22
Uyeki TM. **Influenza**. Ann Intern Med. 2017 Sep 5;167(5):ITC33-ITC48
Uyeki TM, Bernstein HH, Bradley JS, et al. IDSA: Clinical Practice Guidelines by the **Infectious Diseases Society of America**: 2018 Update on Diagnosis, Treatment, Chemoprophylaxis, and Institutional Outbreak **Management of Seasonal Influenza**. Clin Infect Dis. 2018 Dec 19.
Uyeki TM, Fowler RA, Fischer WA 2nd. **Gaps in the Clinical Management of Influenza**: A Century Since the 1918 Pandemic. JAMA. 2018 Jul 30.
Vajo Z, Balaton G, Vajo P, et al. **Dose sparing** and the lack of a dose-response relationship with an **influenza vaccine in adult and elderly patients** - a randomized, double-blind clinical trial. Br J Clin Pharmacol. 2017 Apr 5.
Vamos EP, Pape UJ, Curcin V, et al. Effectiveness of the **influenza vaccine in preventing admission to hospital and death in people with type 2 diabetes**.*CMAJ* 2016.
van Assen S, Holvast A, Benne CA, et al. Humoral responses after influenza vaccination are severely reduced in patients with rheumatoid arthritis treated with **rituximab**. Arthritis Rheum. 2009 Dec 28;62(1):75-81. [Epub ahead of print]
Vanhems Philippe; Voirin Nicolas; Roche Sylvain; et al. **Risk of Influenza-Like Illness in an Acute Health Care Setting** During Community Influenza Epidemics in 2004-2005, 2005-2006, and 2006-2007: A Prospective Study. Arch Intern Med. 2011;171(2):151-157.
Vesikari T et al. Oil-in-water emulsion **adjuvant** with influenza vaccine in young children. N Engl J Med 2011 Oct 13; 365:1406. (has MF59 contains squalene)
Viasus D, Paño-Pardo JR, Pachón J, et al. for the Novel Influenza A(H1N1) Study Group of the Spanish Network for Research in Infectious Diseases (REIPI). **Timing of Oseltamivir** Administration and Outcomes in Hospitalized Adults With Pandemic 2009 Influenza A(H1N1) Virus Infection. Chest. 2011 Oct;140(4):1025-1032.
Vij NK, Stryker CC, Esper FP, et al. Influenza A/H1N1/09-10 **Infections in a NICU** During the 2009-2010 H1N1 **Pandemic**. Pediatrics. 2011 Nov;128(5):e1297-301.
Waddington CS, Walker WT, Oeser C, et al. Safety and immunogenicity of AS03B adjuvanted split virion versus non-adjuvanted whole virion H1N1 influenza vaccine in UK children aged 6 months-12 years: open label, randomised, parallel group, multicentre study. BMJ. 2010 May 27;340:c2649. doi: 10.1136/bmj.c2649.
Wagner J, Abdel-Rahman SM. **Oseltamivir-warfarin interaction** in hypoplastic left heart syndrome: case report and review. Pediatrics. 2015 May;135(5):e1333-6.
Walsh LK, Donelle J, Dodds L, et al. Health outcomes of young children born to mothers who received **2009 pandemic H1N1 influenza vaccination during pregnancy**: retrospective cohort study. BMJ. 2019 Jul 10;366:l4151.
Wang C, Cao B, Liu QQ, et al. **Oseltamivir Compared With the Chinese Traditional Therapy Maxingshigan-Yinqiaosan** in the Treatment of H1N1 Influenza: A Randomized

Trial. Ann Intern Med. 2011 Aug 16;155(4):217-225.
Wang X, Jiang H, Wu P, et al. Evolving epidemiology of human infections with avian influenza A **H7N9 virus** across five epidemic waves in mainland China, 2013-17: an epidemiological study of laboratory-confirmed case series. Lancet Infectious Diseases 2017; online June 1.
Wang Z, Tobler S, Roayaei J, Eick A. Live attenuated or **inactivated influenza** vaccines and medical encounters for respiratory illnesses among US military personnel. JAMA. 2009 Mar 4;301(9):945-53. Epub 2009 Mar 2. Vaccination with TIV was associated with fewer medical encounters related to pneumonia and influenza compared with LAIV or no immunization. In this annually immunized population, this effect was less apparent in those vaccinated with LAIV.
Webster, Duncan, Li, Yan, Bastien, Nathalie, et al. **Oseltamivir-resistant pandemic H1N1 influenza**. CMAJ 2011 0: cmaj.100313
Williams Derek J.; Hall Matthew; Brogan Thomas V.; et al. **Influenza Coinfection and Outcomes in Children With Complicated Pneumonia**. Arch Pediatr Adolesc Med. 2011;0(2011):archpediatrics.2010.295.
Winthrop KL, Silverfield J, Racewicz A, et al. The effect of **tofacitinib on pneumococcal and influenza** vaccine responses in rheumatoid arthritis. Ann Rheum Dis. 2015 Mar 20.
WHO Jan 18/07 - Two people who died of bird flu in Egypt last month had a strain of the H5N1 virus that has shown moderate resistance to the frontline antiviral Tamiflu, the World Health Organization (WHO) said on Thursday. http://www.who.int/csr/disease/avian_influenza/en/index.html
WHO May 2007, New data published by the World Health Organization (WHO) has confirmed a low frequency of resistance to the flu drug Tamiflu between 2003 and 2006, Roche announced. The information, published by WHO's Neuraminidase Inhibitor Susceptibility Network, shows that resistance to Tamiflu (oseltamivir) of approximately 0.3 percent was seen during the past three influenza seasons, during which the drug was used extensively in Japan. This level of resistance is extremely low compared with the 65 percent rate seen in Japan with another antiviral, amantadine.
Wollenhaupt M, Chandrasekaran A, et al. The safety of **oseltamivir in pregnancy**: an updated review of post-marketing data. Pharmacoepidemiol Drug Saf. 2014;23:1035-1042.
Wong K, Campitelli MA, Stukel TA, Kwong JC. Estimating influenza vaccine **effectiveness** in **community-dwelling elderly** patients using the instrumental variable analysis method [published online February 27, 2012]. *Arch Intern Med*. 2012.
Wong KK, Jain S, Blanton L, et al. Influenza-associated **pediatric deaths in the United States**, 2004-2012. Pediatrics. 2013 Nov;132(5):796-804.
Writing Committee of the Second World Health Organization Consultation on Clinical Aspects of Human Infection with Avian Influenza A (H5N1) Virus, Abdel-Ghafar AN, Chotpitayasunondh T, Gao Z, Hayden FG, et al. **Update on avian influenza A (H5N1)** virus infection in humans. N Engl J Med. 2008 Jan 17;358(3):261-73.
Writing Committee of the WHO Consultation on Clinical Aspects of **Pandemic (H1N1) 2009 Influenza**, Clinical Aspects of Pandemic 2009 Influenza A (H1N1) Virus Infection. N Engl J Med 2010 362: 1708-1719.
Wu J et al. **Safety and effectiveness of a 2009 H1N1 vaccine** in Beijing. *N Engl J Med* 2010 Dec 16; 363:2416.
Xiao-Feng Liang, Li Li, Da-Wei Liu, et al. Safety of Influenza A (**H1N1**) Vaccine in **Postmarketing Surveillance** in China. February 2, 2011 (10.1056/NEJMoa1008553)
Yan J, Gret alBueno de Mesquita PJ, Albert B, Liu F, Ehrman S, Milton DK; EMIT Consortium. **Infectious virus in exhaled breath** of symptomatic seasonal influenza cases from a college community. Proc Natl Acad Sci U S A. 2018 Jan 18.
Yang Y, Colgrove J. New York City **Childcare Influenza Vaccine Mandate**. JAMA Pediatr. 2018 Dec 3.
Yang Y, Teja S, Baig K. Bilateral **corneal edema associated with amantadine**. CMAJ. 2015 Oct 20;187(15):1155-8.
Young-Xu Y et al. Relative **vaccine effectiveness of high-dose versus standard-dose influenza vaccines** among Veterans Health Administration patients. J Infect Dis 2018 May 5; 217:1718.
Yu H, Cowling BJ, Feng L, et al. Human infection with avian infl uenza A **H7N9** virus: an assessment of clinical severity. Lancet 2013; online June 24.
Yu Hongjie, Liao Qiaohong, Yuan Yuan, et al. Effectiveness of **oseltamivir** on disease progression and viral RNA shedding in patients with mild pandemic 2009 influenza A H1N1: opportunistic retrospective study of medical charts in China. BMJ 341:doi:10.1136/bmj.c4779 (Published 28 Sept 2010).
Yu H, Wu JT, et al. Eff ect of closure of **live poultry markets** on poultry-to-person transmission of avian infl uenza A **H7N9** virus: an ecological study. Lancet 2013; online Oct 31.
Zaman K, Roy E, Arifeen SE, Rahman M, Raqib R, et al.. Effectiveness of **Maternal Influenza Immunization** in Mothers and Infants. N Engl J Med. 2008 Sep 17. [Epub ahead of print] Inactivated influenza vaccine reduced proven influenza illness by 63% in infants up to 6 months of age and averted approximately a third of all febrile respiratory illnesses in mothers and young infants. Maternal influenza immunization is a strategy with substantial benefits for both mothers and infants.
Zerbo O, Qian Y, et al. Association Between **Influenza Infection and Vaccination During Pregnancy and Risk of Autism** Spectrum Disorder. JAMA Pediatr. 2016 Nov 28.

WEBSITES & Updates:

CDC Flu Update:

http://www.cdc.gov/flu/

http://www.cdc.gov/flu/about/season/index.htm

Public Health Agency of Canada- FluWatch:

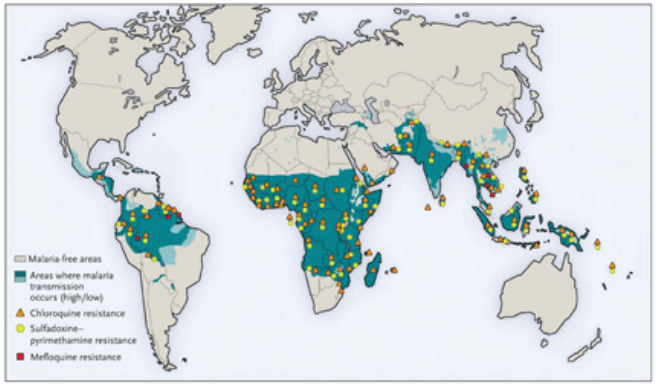
http://www.phac-aspc.gc.ca/fluwatch/

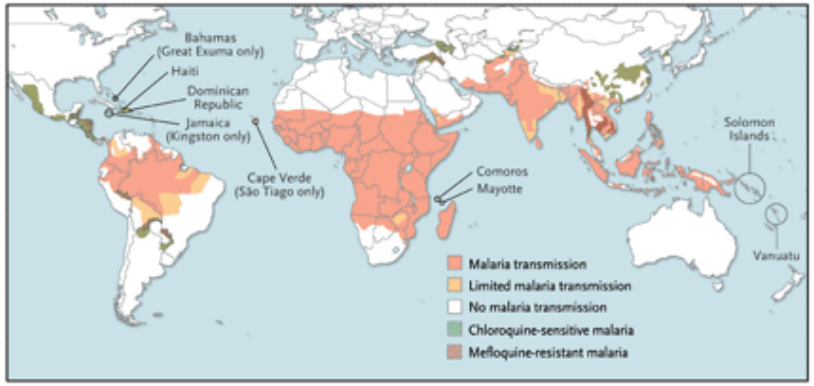
Insecticide Treatment of Clothing and Nets - Tips and Tricks:

1. **Treatment of netting** differs depending on the insecticide. Human error (in measurement, treating for the right length of time, etc.) can decrease efficacy. When possible, buy pre-treated netting. If treating own netting, some products (availability changes over time) include permethrin EC, deltamethrin SC liquid, deltamethrin tablets, lambda-cyhalothrin CS, cyfluthrin EW, and alpha-cypremethrin SC. Follow packet directions to calculate dose of insecticide needed. Dosing is typically dependent on the area of the net and the amount of water the net is able to absorb.
2. **When treating clothing**:
   -wear gloves
   -do not treat underwear
   -some fabrics (e.g. cotton) receive treatment better than others. Permethrin does not adhere well to some synthetic fibres.

References:

[1] WHO. Guidelines for the **treatment of malaria, 2nd edition. 2010**. www.who.int/malaria/publications/atoz/9789241547925/en/index.html
WHO Guidelines for the **treatment of malaria, third edition**. Geneva: World Health Organization, 2015 (http://www.who.int/malaria/publications/atoz/9789241549127/en/).
World Health Organization. (2006). **WHO Guidelines** for the treatment of Malaria. Geneva, Switzerland:. Website: http://www.who.int/malaria/ {**Other websites**: www.iamat.org & www.istm.org }





Thumbnails: Areas of Malaria Transmission and Antimalarial Drug Resistance. Data on malaria transmission are for 2007 and are from the World Health Organization. Data on drug resistance are for 2004 and are from the Roll Back Malaria partnership.**NEJM** June 5,2008. 2nd Map Thumbnail: NEJM Aug 7, 2008. **CDC Map**: http://cdc-malaria.ncsa.uiuc.edu/

[2] **Health Canada** – Malaria Website: http://www.phac-aspc.gc.ca/tmp-pmv/info/pal_mal_e.html#globaldist {Health Canada 2004. Supplement Canadian Recommendations … Prevention & Treatment of Malaria Among International Travelers. CCDR 2004;30SI:I-62}
Canadian Recommendations for the Prevention and Treatment of Malaria Among International Travellers – 2009
http://www.phac-aspc.gc.ca/publicat/ccdr-rmtc/09pdf/35s1-eng.pdf

[3] Baird JK. Effectiveness of antimalarial drugs. New England Journal of Medicine. 352(15):1565-77, 2005 Apr 14.
[4] Malaria in the Dominican Republic: Public Health Agency (n.d.). Retrieved June 15, 2006, from Public Health Agency of Canada Web site: http://www.phac-aspc.gc.ca/tmp-pmv/2006/mal_dr0131_e.html
[5] Gray J (Ed.). (2003). Therapeutic Choices. Ottawa:Canadian Pharmacists Association.
[6] Koda-Kimble MA, et al (Ed.). (2005) Applied Therapeutics: the clinical use of drugs 8th edition. Philadelphia : Lippincott Williams & Wilkins
[7] Recent health advisory: malaria in the Dominican Republic. Parmacist's Letter/Prescriber's Letter 2005;21(1):210122
[8] Hughes C, Tucker R, Bannister B, et al. Malaria prophylaxis for long-term travellers. Commun Dis Public Health. 2003 Sep;6(3):200-8.
[9] **Centers for Disease Control and Prevention (CDC).** Health Information for the International Traveler 2005-2006. Atlanta: US Department of Health and Human Services, Public Health Service, 2005. {"If the switch occurs 4 weeks or more before leaving the risk area, A/P should be taken for the remainder of the stay in the risk area and for one week thereafter. If the switch occurs less than four weeks before leaving the risk area, A/P should be taken for four weeks after the switch."} http://www.cdc.gov/malaria/ Map: http://cdc-malaria.ncsa.uiuc.edu/
[10] Cockburn R, Newton PN, Agyarko EK et al.. The global threat of counterfeit drugs. PLoS Med. 2005 Apr;2(4):e100. http://medicine.plosjournals.org/perlserv/?request=get-document&doi=10.1371/journal.pmed.0020100
[10] Canadian Pharmacists Association. (2015). Compendium of Pharmaceuticals and Specialties. Canada: Webcom Limited
[11] Health Canada. Canadian Immunization Guide 2002. Retrieved 01 August 2006, from http://www.phac-aspc.gc.ca/publicat/cig-gci/pdf/cdn_immuniz_guide-2002-6.pdf

---
[13] Lacy C, Armstrong L, Goldman M, et al. (2004). Lexi-Comp's Drug Information Handbook 12th Edition. Ohio: Lexi-Comp.
[14] Saskatchewan Health. (2016). The Saskatchewan Formulary. Regina.
[15] USP DI (2006). Drug Information for the Healthcare Professional - 26th Ed. Retrieved June 14, 2006, from http://online.statref.com/document.aspx?fxid=6&docid=4023
[16] Canadian Pharmacists Association (2006). Electronic Compendium of Pharmaceuticals and Specialties. Retrieved 17 June 2006, from http://e-cps.pharmacists.ca.cyber.usask.ca/CPHA/main.htm
[17] Gilbert, D. N., R. C. Moellering, G. M. Eliopoulos, and M. A. Sande (eds). (2004). **The Sanford guide** to antimicrobial therapy, 2004. 34th ed. Antimicrobial Therapy, Inc., Hyde Park, VT.
[18]
[19] *Taylor W, Robert J, White, Nicholas J.* Drug Safety. 27(1):25-61, 2004.
[20] van Riemsdijk MM. Sturkenboom MC. Pepplinkhuizen L. Stricker BH. Mefloquine increases the risk of serious psychiatric events during travel abroad: a nationwide case-control study in the Netherlands. Journal of Clinical Psychiatry. 66(2):199-204, 2005 Feb.
[21] van Riemsdijk MM. Sturkenboom MC. Ditters JM. Tulen JH. Ligthelm RJ. Overbosch D. Stricker BH. Low body mass index is associated with an increased risk of neuropsychiatric adverse events and concentration impairment in women on mefloquine. British Journal of Clinical Pharmacology. 57(4):506-12, 2004 Apr.
[22] Croft AM. Clayton TC. World MJ. Side effects of mefloquine prophylaxis for malaria: an independent randomized controlled trial. Transactions of the Royal Society of Tropical Medicine & Hygiene. 91(2):199-203, 1997 Mar-Apr.
[23] Pennie RA. Koren G. Crevoisier C. Steady state pharmacokinetics of mefloquine in long-term travellers. Transactions of the Royal Society of Tropical Medicine & Hygiene. 87(4):459-62, 1993 Jul-Aug.

[24] Overbosch D. Schilthuis H. Bienzle U. Behrens RH. Kain KC. Clarke PD. Toovey S. Knobloch J. Nothdurft HD. Shaw D. Roskell NS. Chulay JD. Malarone International Study Team. Atovaquone-proguanil versus mefloquine for malaria prophylaxis in nonimmune travelers: results from a randomized, double-blind study. Clinical Infectious Diseases. 33(7):1015-21, 2001 Oct 1.
[25] Lobel HO. Miani M. Eng T. Bernard KW. Hightower AW. Campbell CC. Long-term malaria prophylaxis with weekly mefloquine. Lancet. 341(8849):848-51, 1993 Apr 3.
[26] Knobloch J. Long-term malaria prophylaxis for travelers. Journal of Travel Medicine. 11(6):374-8, 2004 Nov-Dec.
[27] Steffen R. Heusser R. Machler R. Bruppacher R. Naef U. Chen D. Hofmann AM. Somaini B. Malaria chemoprophylaxis among European tourists in tropical Africa: use, adverse reactions, and efficacy. Bulletin of the World Health Organization. 68(3):313-22, 1990.
[28] Croft, AMJ, Garner P. **Mefloquine** for preventing malaria in non-immune adult travelers. The **Cochrane Database of Systematic Reviews** 2000, Issue $. Art No.: CD000138. DOI 10.1002/14651858.CD000138.
[29] Saskatoon District Health. International Travel Manual. (M-10) (pp12-24).
[30] Rosser WW, Pennie RA, Pilla NJ and the Anti-infective Review Panel. **Anti-infective Guidelines** for Community-acquired Infections. (Canadian)Toronto: **MUMS** Guideline Clearinghouse;2005. Updated **2012**.
[31] Treatment Guidelines from the Medical Letter: **Advice for Travelers**. May 2006; Vol4 (Issue 45). Updated **May 2012**
[32] Walsh DS. Eamsila C. Sasiprapha T. et al. Efficacy of monthly tafenoquine for prophylaxis of Plasmodium vivax and multidrug-resistant P. falciparum malaria. [Clinical Trial. Journal Article. Randomized Controlled Trial] Journal of Infectious Diseases. 190(8):1456-63, 2004 Oct
[33] Namale L, Burkiwa H. Tafenoquine for preventing malaria. (protocol) The Cochrane Database of Systematic Reviews 2004, Issue 3. Art. No.: CD004911.
[34] Graves P, Gelband H. **Vaccines** for preventing Malaria (SPf66). The **Cochrane Database of Systematic Reviews** 2006, Issue 2. Art. No.: CD005966.
[35] Current malaria risk by country: http://www.cdc.gov/malaria/
36 Juckett G. Malaria prevention in travelers. Am Fam Physician. 1999 May 1;59(9):2523-30, 2535-6. Review. Erratum in: Am Fam Physician 2000 Jan 1;61(1):50, 52.

Additional References:

AAO Task Force in ACP: Do you need to screen for hydroxychlorquine/Chloroquine retinopathy. 2008. Online at: http://www.acponline.org/clinical_information/guidelines/additional_sources/statement.htm
Abba K, Deeks JJ, Olliaro P, et al. **Rapid diagnostic tests** for diagnosing uncomplicated *P. falciparum* malaria in endemic countries. *Cochrane Database of Systematic Reviews* 2011, Issue 7. Art. No.: CD008122. DOI: 10.1002/14651858.CD008122.pub2. The sensitivity and specificity of all RDTs is such that they can replace or extend the access of diagnostic services for uncomplicated *P. falciparum* malaria. HRP-2 antibody types may be more sensitive but are less specific than pLDH antibody-based tests, but the differences are small. The HRP-2 antigen persists even after effective treatment and so is not useful for detecting treatment failures.

Abba K, Kirkham AJ, Olliaro PL, et al. **Rapid diagnostic tests** for diagnosing uncomplicated non-falciparum or Plasmodium vivax malaria in endemic countries. Cochrane Database Syst Rev. 2014 Dec 18;12:CD011431. doi: 10.1002/14651858.CD011431. RDTs designed to detect P. vivax specifically, whether alone or as part of a mixed infection, appear to be more accurate than older tests designed to distinguish P. falciparum malaria from non-falciparum malaria. Compared to microscopy, these tests fail to detect around 5% ofP. vivax cases. This Cochrane Review, in combination with other published information about in vitro test performance and stability in the field, can assist policy-makers to choose between the available RDTs.
Abdullahi ST, Olagunju A, Soyinka JO, et al. **Pharmacogenetics of artemether-lumefantrine influence on nevirapine disposition**: clinically significant drug-drug interaction? Br J Clin Pharmacol. 2018 Nov 24.
Achan J, Kakuru A, Ikilezi G, et al. **Antiretroviral agents and prevention of malaria** in HIV-infected Ugandan children. N Engl J Med. 2012 Nov 29;367(22):2110-8.
Agnandji ST, Lell B, Soulanoudjingar SS, et al.RTS,S Clinical Trials Partnership. First results of phase 3 trial of **RTS,S/AS01 malaria vaccine** in African children. N Engl J Med. 2011 Nov 17;365(20):1863-75.
Amaratunga C, Sreng S, Suon S, et al. **Artemisinin-resistant** Plasmodium falciparum in Pursat province, western Cambodia: a parasite clearance rate study. Lancet Infect Dis. 2012 Aug 29.
Amaratunga C, Lim P, Suon S, et al. **Dihydroartemisinin-piperaquine resistance** in Plasmodium falciparum malaria in Cambodia: a multisite prospective cohort study. Lancet Infect Dis 2016 Jan 7 (Epub).
Amato R, Lim P, Miotto O, et al. **Genetic markers** associated with **dihydroartemisinin–piperaquine failure** in **Plasmodium falciparum malaria** in Cambodia: a genotype–phenotype association study. Lancet Infect Dis 2016; online Nov 3.
Ansah EK, Narh-Bana S, Affran-Bonful H, et al. The impact of providing **rapid diagnostic malaria tests** on fever management in the private retail sector in Ghana: a cluster randomized trial. BMJ. 2015 Mar 4;350:h1019.
Ansah EK, Narh-Bana S, Epokor M, et al. **Rapid testing** for malaria in settings where microscopy is available and peripheral clinics where only presumptive treatment is available: a randomised controlled trial in Ghana. BMJ. 2010 Mar 5;340:c930. doi: 10.1136/bmj.c930.
Anti-infective Review Panel. **Anti-infective Guidelines for Community-acquired Infections**. Canadian - New-**2012**. Toronto: MUMS Guideline Clearinghouse. http://www.mumshealth.com/
Artesunate IV for severe malaria by Special Access Program in Canada.
Asante KP, Abdulla S, Agnandji S, et al. Safety and efficacy of the **RTS,S/AS01(E) candidate malaria vaccine** given with expanded-programme-on-immunisation vaccines: 19 month follow-up of a randomised, open-label, phase 2 trial. Lancet Infect Dis. 2011 Jul 20.
Ashley EA, Dhorda M, Fairhurst RM, et al; Tracking **Resistance to Artemisinin** Collaboration (TRAC). Spread of artemisinin resistance in Plasmodium falciparum malaria. N Engl J Med. 2014 Jul 31;371(5):411-23.
Ashley EA, Pyae Phyo A, Woodrow CJ. Malaria- Seminar. Lancet. 2018 Apr 6.
Batchelor T, Gherardin T. Prevention of malaria in travellers. Aust Fam Physician. 2007;36(5):316-320.
Bazemore A, Huntington M. The **Pretravel Consultation**. Am Fam Physician. 2009;80 (6):583-590.
Bejon P, White MT, Olotu A, et al. Efficacy of **RTS,S malaria vaccines**: individual-participant pooled analysis of phase 2 data. Lancet Infect Dis. 2013 Feb 28.
Bennett A, Bisanzio D, Yukich JO, et al. **Population coverage of artemisinin-based combination treatment** in children younger than 5 years with fever and Plasmodium falciparum infection in Africa, 2003-2015: a modelling study using data from national surveys. Lancet Glob Health. 2017 Apr;5(4):e418-e427.
Bhargava A, Ralph R, Chatterjee B, Bottieau E. Assessment and initial management of **acute undifferentiated fever in tropical and subtropical regions**. BMJ. 2018 Nov 29;363:k4766.
Biai S, Rodrigues A, Gomes M, Ribeiro I, Sodemann M, Alves F, Aaby P. Reduced in-hospital mortality after improved management of children under 5 years admitted to hospital with malaria: randomised trial. BMJ. 2007 Oct 22; [Epub ahead of print]
Biddinger PD, Hooper DC, Shenoy ES, et al.. Case 28-2015. A 32-Year-Old Man with **Fever, Headache, and Myalgias after Traveling from Liberia**. N Engl J Med.2015 Sep 10;373(11):1060-7.
Bigira V, Kapisi J, Clark TD, et al. Protective efficacy and safety of **three antimalarial regimens for the prevention of malaria in young Ugandan children**: a randomized controlled trial. PLoS Med 2014;11:e1001689.
Birbeck Gretchen L, Molyneux Malcolm E, Kaplan Peter W, et al. Blantyre Malaria Project Epilepsy Study (BMPES) of neurological outcomes (**epilepsy**) in retinopathy-positive paediatric **cerebral malaria** survivors: a prospective cohort study, The Lancet Neurology, Volume 9, Issue 12, December 2010
Brady OJ, Slater HC, Pemberton-Ross P, et al. Role of **mass drug administration in elimination of Plasmodium falciparum malaria**: a consensus modelling study. Lancet Glob Health. 2017 Jul;5(7):e680-e687.
Briggs G, Freeman, Roger, Yaffe, Sumner, ed. Drugs in Pregnancy and Lactation. 9th ed: TechBooks
Broderick C, Nadjm B. Smith V, et al. Clinical, geographical, and temporal risk factors associated with presentation and outcome of **vivax malaria imported into the United Kingdom** over 27 years: observational study. BMJ 2015;350:h1703.
Brower V. **Counterfeit and substandard malaria drugs in Africa**. Lancet Infect Dis. 2017 Oct;17(10):1026-1027.
Canadian Recommendations for the Prevention and Treatment of Malaria Among International Travellers – **2009** http://www.phac-aspc.gc.ca/publicat/ccdr-rmtc/09pdf/35s1-eng.pdf
Carias C, Greening Jr B, Campbell C, et al. **Preventive malaria** treatment for contacts of patients with **Ebola** virus disease in the context of the west Africa 2014–15 Ebola response: an economic analysis. Lancet Infect Dis 2015; online Dec 16.
Carroll, Scott P., and Jenella Loye. "PMD, a registered botanical mosquito repellent with deet-like efficacy." ***Journal of the American Mosquito Control Association*** **22.3 (2006): 507-514.**
CDC: Malaria CDC 2008 **Travel Yellow book 2008** information http://wwwn.cdc.gov/travel/ybToc.aspx ; Peds dosing: http://wwwn.cdc.gov/travel/contentMalariaKidsHC.aspx
CDC: Malaria Surveillance — United States, 2011. Surveillance Summaries. November 1, 2013 http://www.cdc.gov/mmwr/preview/mmwrhtml/ss6205a1.htm

CDC: Malaria **Diagnosis & Treatment** in the United States http://www.cdc.gov/malaria/diagnosis_treatment/
Chaccour CJ, Kaur H, Mabey D, Del Pozo JL. **Travel and fake artesunate**: a risky business. Lancet. 2012 Sep 22;380(9847):1120.
Chandramohan D, Dicko A, Zongo I, et al. Effect of **Adding Azithromycin to Seasonal Malaria Chemoprevention**. N Engl J Med. 2019 Jan 30.
Checkley AM, Smith A, Smith V, et al. **Risk factors for mortality from imported** falciparum malaria in the United Kingdom over 20 years: an observational study. BMJ. 2012 Mar 27
Chen LH, Wilson ME, Schulagenhauf P. **Prevention** of malaria in long-term travelers. JAMA 2006;296(18),2234-44.
Chen LH, Wilson ME, Schlagenhauf P. Controversies and misconceptions in malaria **chemoprophylaxis** for travelers. JAMA. 2007 May 23;297(20):2251-63. Despite widespread reports on the adverse effects of mefloquine, controlled studies found that serious neuropsychiatric adverse events occur at rates comparable with or lower than other chemoprophylaxis drugs. Moreover, mefloquine does not appear to impair performance while driving, flying, or diving. Vivax malaria causes significant illness in travelers, but current first-line chemoprophylaxis agents do not prevent relapses of vivax malaria. Although not licensed in most countries as primary prophylaxis, primaquine effectively prevents relapses of vivax malaria.
Chen X, He Y, Miao Y, et al. A young man with severe **acute haemolytic anaemia**. BMJ. 2017 Oct 19;359:j4263. (**primaquine induced**)
Chico RM, Mayaud P, Ariti C, et al. Prevalence of **Malaria and Sexually Transmitted and Reproductive Tract Infections in Pregnancy** in Sub-Saharan Africa: A Systematic Review Malaria and STIs/RTIs in Pregnancy in Africa. JAMA. 2012 May 16;307(19):2079-86.
Chotsiri P, Wattanakul T, Hoglund R, et al. Population pharmacokinetics and **electrocardiographic effects of dihydroartemisinin-piperaquine** in healthy volunteers. Br J Clin Pharmacol. 2017 Jul 11
Clements AC, Reid HL, Kelly GC, Hay SI. Further **shrinking the malaria map**: how can geospatial science help to achieve malaria elimination? Lancet Infect Dis. 2013 Aug;13(8):709-18.
Clinical Knowledge Summaries (CKS) – Malaria. Accessed at: www.cks.nhs.uk
Committee to Advise on Tropical medicine and Travel. **Statement on older travellers**. CCDR 2011;37(ASC2):1-24. http://www.phac-aspc.gc.ca/publicat/ccdr-rmtc/11vol37/acs-2/index-eng.php
Committee to Advise on Tropical Medicine and Travel (**CATMAT**). **Fever in the Returning International Traveller** Initial Assessment Guidelines. July 2011 http://www.phac-aspc.gc.ca/publicat/ccdr-rmtc/11vol37/acs-3/pdf/returningtravellerfever-fievrevoyageurderetour-eng.pdf
Committee to Advise on Tropical Medicine and Travel. Public Health Agency of Canada. Statement on **personal protective measures to prevent arthropod bites**. CCDR 2012;38(ACS-3). www.phac-aspc.gc.ca/publicat/ccdr-rmtc/12vol38/acs-dcc-3/index-eng.php (accessed December 17, 2012).
Corbel V, Akogbeto M, et al. Combination of malaria **vector control interventions in pyrethroid resistance** area in Benin: cluster randomised controlled trial. Lancet Infect Dis; online June 7, 2012.
Cotter C, Sturrock HJ, Hsiang MS, et al. The changing epidemiology of **malaria elimination**: new strategies for new challenges. Lancet. 2013 Apr 15.
Crawley J, Sismanidis C, Goodman T, Milligan P; WHO Advisory Committee on serological responses to vaccines used in the Expanded Programme on Immunization in infants receiving Intermittent Preventive Treatment for malaria. Effect of **intermittent preventive treatment** for malaria during infancy on serological responses to measles and other vaccines used in the Expanded Programme on Immunization: results from five randomised controlled trials. Lancet. 2012 Jul 27.
D'Alessandro U, Hill J, Tarning J, et al. **Treatment of uncomplicated and severe malaria during pregnancy**. Lancet Infect Dis. 2018 Apr;18(4):e133-e146.
Darpo B, Ferber G, Siegl P, et al. Evaluation of the **QT** effect of a combination of **piperaquine and a novel anti-malarial drug candidate OZ439**, for the treatment of uncomplicated malaria. Br J Clin Pharmacol. 2015 May 13.
Desai M, Gutman J, L'lanziva A, et al. **Intermittent screening and treatment or intermittent preventive treatment** with **dihydroartemisinin–piperaquine** versus intermittent preventive treatment with **sulphadoxine–pyrimethamine** for the control of malaria during pregnancy in western Kenya: open-label, three-group, randomised controlled superiority trial. Lancet 2015; online Sept 29.
Desai M, Hill J, Fernandes S, et al. **Prevention of malaria in pregnancy**. Lancet Infect Dis. 2018 Apr;18(4):e119-e132.
Dhalla F, Gulati P, Sreerangaiah D, Abraham SM. A man with **thrombocytopenia**. BMJ. 2012 Feb 16;344:e826.
Dicko A, Doumbo O. Efficacy of **RTS,S malaria vaccine** given with EPI vaccines. Lancet Infect Dis. 2011 Jul 20.
Dicko A, Brown JM, Diawara H, et al. **Primaquine to reduce transmission of Plasmodium falciparum** malaria in Mali: a single-blind, dose-ranging, adaptive randomised phase 2 trial. Lancet Infect Dis. 2016 Jun;16(6):674-84.
Dombrowski JG, Souza RM, Lima FA, et al. Association of Malaria **Infection During Pregnancy** With Head Circumference of Newborns in the Brazilian Amazon. JAMA Netw Open. 2019 May 3;2(5):e193300.
Dondorp AM, Fanello CI, Hendriksen IC, et al. **Artesunate** versus quinine in the treatment of severe falciparum malaria in African children (AQUAMAT): an open-label, randomised trial. Lancet. 2010 Nov 7.
Dondorp Arjen M., Fairhurst Rick M., Slutsker Laurence. The Threat of **Artemisinin-Resistant Malaria**. N Engl J Med 365;12 nejm.org september 22, 2011
Eisele TP, Larsen DA, , et al. Malaria **prevention in pregnancy**, birthweight, and neonatal mortality: a meta-analysis of 32 national cross-sectional datasets in Africa. Lancet Infect Dis 2012; Sept 18.
Enayati A, Hemingway J, Garner P. **Electronic mosquito repellents** for preventing mosquito bites and malaria infection. Cochrane Database Syst Rev. 2007 Apr 18;(2):CD005434. Field entomological studies confirm that EMRs have no effect on preventing mosquito bites. Therefore there is no justification for marketing them to prevent malaria infection.
Esu E, Effa EE, Opie ON, Uwaoma A, Meremikwu MM. **Artemether** for severe malaria. Cochrane Database of Systematic Reviews 2014, Issue 9. Art. No.: CD010678. DOI: 10.1002/14651858.CD010678.pub2. Although there is a lack of direct evidence comparing artemether with artesunate, artemether is probably less effective than artesunate at preventing deaths from severe malaria. In circumstances where artesunate is not available, artemether is an alternative to quinine.
Ezeamama AE, Spiegelman D, Hertzmark E, et al. **HIV infection and the incidence of malaria** among HIV-exposed children from Tanzania. J Infect Dis. 2012 May 15;205(10):1486-94.
Eziefula AC, Bousema T, Yeung S, et al. **Single dose primaquine** for clearance of Plasmodium falciparum gametocytes in children with uncomplicated malaria in Uganda: a randomised, controlled, double-blind, dose-ranging trial. Lancet Infect Dis 2013; published online Nov 11. http://dx.doi. org/10.1016/S1473-3099(13)70268-8.
FDA June /09 approved safety labeling revisions for chloroquine phosphate tablets (Aralen, sanofi-aventis US) to warn of the potential for serious adverse events in **nursing infants**. According to the FDA, a decision should be made whether to discontinue therapy or stop nursing, taking into account the potential clinical benefit of the drug to the mother. In a study of 11 lactating mothers, the maximum daily dose of the drug received by the breast-feeding infant was about 0.7% of the maternal start dose (600 mg base) in malaria chemotherapy. Separate chemoprophylaxis for the infant is required.
Feachem RGA, Chen I, Akbari O, et al. Malaria **eradication within a generation**: ambitious, achievable, and necessary. Lancet 2019; published online Sept 8.
Feder HM, Mansilla-Rivera K. **Fever in Returning Travelers**-A Case-Based Approach- Am Fam Physician. 2013;88(8):524-530.
Flateau Clara, Le Loup Guillaume, Pialoux Gilles. Consequences of **HIV infection on malaria** and therapeutic implications: a systematic review. Lancet Infect Dis 2011; 11: 541–56.
Freedman DO. **Malaria prevention in short-term travelers**. N Engl J Med. 2008 Aug 7;359(6):603-12.
Frosch AE, Laufer MK, Mathanga DP, et al. The return of widespread **chloroquine-sensitive Plasmodium falciparum to Malawi**. J Infect Dis. 2014 Apr 9.
Frosch AE, Ondigo BN, Ayodo GA, et al. **Decline in childhood iron deficiency** after interruption of malaria transmission in highland Kenya. Am J Clin Nutr. 2014 Sep;100(3):968-73.
Galappaththy G, Omari A, Tharyan P. Primaquine for preventing relapses in people with Plasmodium vivax malaria. Cochrane Database Syst Rev. 2007 Jan 24;(1):CD004389.
Gantz VM, Jasinskiene N, Tatarenkova O, et al. Highly efficient **Cas9-mediated gene drive for population modification of the malaria vector mosquito Anopheles stephensi**. Proc Natl Acad Sci U S A. 2015 Nov 23.
Gething PW, Casey DC, Weiss DJ, et al. **Mapping Plasmodium falciparum Mortality** in Africa between 1990 and 2015. N Engl J Med. 2016 Oct 10.
Gogtay N, Kannan S, Thatte UM, et al. **Artemisinin-based combination therapy** for treating uncomplicated Plasmodium vivax malaria. Cochrane Database Syst Rev. 2013 Oct 25;10:CD008492. doi: 10.1002/14651858.CD008492.pub3. ACTs appear at least equivalent to chloroquine at effectively treating the blood stage of P. vivax infection. Even in areas where chloroquine remains effective, this finding may allow for simplified protocols for treating all forms of malaria with ACTs. In areas where chloroquine no longer cures the infection, ACTs offer an effective alternative.Dihydroartemisinin-piperaquine is the most studied ACT. It may provide a longer period of post-treatment prophylaxis than artemether-lumefantrine or artesunate plus amodiaquine. This effect may be clinically important in high transmission settings whether primaquine is also given or not.
Gogtay NJ, Ferner RE. **Mefloquine** for malarial prophylaxis in military personnel. BMJ. 2015 Nov 3;351:h5797.
Gonçalves BP, Huang CY, Morrison R, et al. Parasite burden and **severity of malaria in Tanzanian children**. N Engl J Med. 2014 May 8;370(19):1799-808.
Gonzalez R, Desai M, Macete E, et al. Intermittent Preventive Treatment of Malaria in **Pregnancy with Mefloquine** in HIV-Infected Women Receiving Cotrimoxazole Prophylaxis: A Multicenter Randomized Placebo-Controlled Trial. PLoS Med. 2014 Sep 23;11(9):e1001735.
González R, Pons-Duran C, PiquerasM, et al. **Mefloquine for preventing malaria in pregnant women**. Cochrane Database of Systematic Reviews 2018, Issue 3. Art. No.: CD011444. Mefloquine was more efficacious than sulfadoxine-pyrimethamine in HIV-uninfected women or daily cotrimoxazole prophylaxis in HIV-infected pregnant women for prevention of malaria infection and was associated with lower risk of maternal anaemia, no adverse effects on pregnancy outcomes (such as stillbirths and abortions),

and no effects on low birth weight and prematurity. However, the high proportion of mefloquine-related adverse events constitutes an important barrier to its effectiveness for malaria preventive treatment in pregnant women.
Grazier MR, Armenian P, Vohra R. Illicit Distribution of Prescription Drugs: Report of **Inadvertent Chloroquine Toxicity** and a Market Survey of Businesses Serving Ethnic Minority Populations. Ann Pharmacother. 2014 May 19;48(8):1070-1076.
Griffin JT, Bhatt S, et al. Potential for reduction of burden and local elimination of malaria by **reducing Plasmodium falciparum malaria transmission**: a mathematical modelling study. Lancet Infect Dis 2016; online Jan 19.
Griffith KS, Lewis LS, Mali S, Parise ME. **Treatment of malaria** in the United States: a systematic review. JAMA. 2007 May 23;297(20):2264-77.
Gutman J, Kovacs S, Dorsey G, Stergachis A, et al. The safety, tolerability and efficacy of repeated doses of **dihydroartemisinin piperaquine** for the prevention and treatment of malaria: a systematic review and meta-analysis. Lancet Infec Dis 2016; online Nov 16.
Haakenstad A, Harle AC, Tsakalos G, et al. **Tracking spending** on malaria by source in 106 countries, 2000-16: an economic modelling study. Lancet Infect Dis. 2019 Jul;19(7):703-716.
Hallamaa L, Cheung YB, Maleta K, et al. Child Health Outcomes **After Presumptive Infection Treatment in Pregnant Women**: A Randomized Trial. Pediatrics. 2018 Feb 22.
Hamilton WL, Amato R, van der Pluijm RW, et al. Evolution and expansion of **multidrug-resistant malaria** in southeast Asia: a genomic epidemiology study. Lancet Infect Dis. 2019 Jul 22
Hay SI, Guerra CA, Gething PW, Patil AP, et al. A **world malaria map**: Plasmodium falciparum endemicity in 2007. PLoS Med. 2009 Mar 24;6(3):e1000048.
Health Canada June/17. Summary safety review – **mefloquine** – assessing the potential risk of **rare long-lasting and permanent adverse events** related to the brain and nervous system (neurological) and mental health (psychiatric). June 1, 2017. www.hc-sc.gc.ca/dhp-mps/medeff/reviews-examens/mefloquine-eng.php (accessed June 2, 2017).
Held J, Supan C, Salazar CLO, et al. **Ferroquine and artesunate** in African adults and children with Plasmodium falciparum malaria: a phase 2, multicentre, randomised, double-blind, dose-ranging non-inferiority study. Lancet Infect Dis 2015; online Sept 3.
Hemingway J, Ranson H, Magill A. Averting a malaria disaster: will **insecticide resistance** derail malaria control? Lancet. 2016 Feb 12.
Herc ES, Manthei D, Riddell J 4th. **Fever in a Traveler** Returning From Africa. JAMA. 2017 Apr 4;317(13):1370-1371.
Hopkins H, Bruxvoort KJ, Cairns ME, et al. Impact of introduction of **rapid diagnostic tests** for malaria on antibiotic prescribing: analysis of observational and randomised studies in public and private healthcare settings. BMJ. 2017 Mar 29;356:j1054.
Hidalgo Kathleen, Lyles Adraine, Dean Stacey R. A Potential Interaction between **Warfarin and Atovaquone**. Ahead of Print on 1 January 2011, DOI 10.1345/aph.1P491. Ann Pharmacother ;45:e3.
Hill DR, et al. The practice of travel medicine: guidelines by the Infectious Diseases Society of America. Clin Infect Dis. 2006;43(12):1499-1539.
Hill N, Lenglet A, Arnéz AM, et al. Plant based **insect repellent and insecticide treated bed nets** to protect against malaria in areas of early evening biting vectors: double blind randomised placebo controlled clinical trial in the Bolivian Amazon. BMJ. 2007 Nov 17;335(7628):1023. Epub 2007 Oct 16. Insect repellents can provide protection against malaria. In areas where vectors feed in the early evening, effectiveness of treated nets can be significantly increased by using repellent between dusk and bedtime. This has important implications in malaria vector control programmes outside Africa and shows that the combined use of treated nets and insect repellents, as advocated for most tourists travelling to high risk areas, is fully justified.
Homan T, Hiscox A, Mweresa CK, et al. The effect of mass **mosquito trapping** on malaria transmission and disease burden (SolarMal): a stepped-wedge cluster-randomised trial. Lancet 2016; online Aug 9.
Imwong M, Suwannasin K, Kunasol C, et al. A **molecular epidemiology** observational study of the recent transnational spread of **artemisinin resistant P falciparum** in the Greater Mekong Subregion. Lancet Infect Dis 2017; online Feb 1.
Irvine Marie-Hélène, Einarson Adrienne, Bozzo Pina. Prophylactic use of **antimalarials during pregnancy**. Can Fam Physician November 2011 57: 1279-1281
Jarvis JN, Coltart CE, Pule M, et al. **Artemisinin** therapy and severe delayed haemolysis. Lancet. 2013 Jul 13;382(9887):180.
Johnson BA, Kalra MG. **Prevention of Malaria in Travelers**. Am Fam Physician. 2012 May 15;85(10):973-977.
Johnson TN, Cleary Y, Parrott N, et al. Development of a **PBPK Model for Mefloquine** and its Application alongside a Clinical Effectiveness Model to Select an Optimal Dose for Prevention of Malaria in Young Caucasian Children. Br J Clin Pharmacol. 2018 Sep 10.
Jourde-Chiche N, Mancini J, Dagher N et al. **Antimalarial ototoxicity**: an underdiagnosed complication? A study of spontaneous reports to the French Pharmacovigilance Network. Ann Rheum Dis. 2012 Sep;71(9):1586.
Kabyemela ER, Fried M, Kurtis JD, Duffy PE et al. Decreased susceptibility to Plasmodium falciparum infection in pregnant women with **iron deficiency**. J Infect Dis. 2008 Jul 15;198(2):163-6.
Kajubi R, Ochieng T, Kakuru A, et al. Monthly **sulfadoxine-pyrimethamine versus dihydroartemisinin-piperaquine** for intermittent preventive treatment of malaria in pregnancy: a double-blind, randomised, controlled, superiority trial. Lancet. 2019 Mar 22.
Kakuru A, Jagannathan P, Muhindo MK, et al. **Dihydroartemisinin–piperaquine** for the prevention of malaria in **pregnancy**. N Engl J Med 2016;374:928-39.
Kakuru A, Jagannathan P, Muhindo MK, et al. **Dihydroartemisinin-Piperaquine** for the **Prevention** of Malaria in **Pregnancy**. N Engl J Med. 2016 Mar 10;374(10):928-39.
Katureebe A, Zinszer K, Arinaitwe E, et al. Measures of Malaria Burden after **Long-Lasting Insecticidal Net Distribution** and Indoor Residual Spraying at Three Sites in Uganda: A Prospective Observational Study. PLoS Med. 2016 Nov 8;13(11):e1002167.
Kayentao K, Garner P, van Eijk AM, et al. **Intermittent preventive therapy for malaria during pregnancy** using 2 vs 3 or more doses of sulfadoxine-pyrimethamine and risk of low birth weight in Africa: systematic review and meta-analysis. JAMA. 2013 Feb 13;309(6):594-604.
Kendjo E, Houzé S, Mouri O, et al**. Epidemiologic Trends in Malaria Incidence** Among Travelers Returning to Metropolitan France, 1996-2016. JAMA Netw Open. 2019 Apr 5;2(4):e191691.
Kleinschmidt I, Bradley J, Knox TB, et al. Implications of **insecticide resistance** for malaria vector control with **long-lasting insecticidal nets**: a **WHO**-coordinated, prospective, international, observational cohort study. Lancet Infect Dis 2018; online April 9
Kloprogge F, McGready R, et al. Opposite malaria and **pregnancy effect on oral bioavailability of artesunate** - a population pharmacokinetic evaluation. Br J Clin Pharmacol. 2015 Apr 15.
Koita OA, Sangaré L, et al. **AQ-13,** an investigational antimalarial, versus **artemether plus lumefantrine** for the treatment of uncomplicated Plasmodium falciparum malaria: a randomised, phase 2, non-inferiority clinical trial. Lancet Infect Dis 2017; online Sept 12.
Krey RA, Travassos MA. Severe Malaria **Treatment in the United States at the Precipice**. Ann Intern Med. 2019 Aug 20.
Lacerda MVG, Llanos-Cuentas A, Krudsood S, et al. **Single dose tafenoquine to prevent relapse of Plasmodium vivax malaria**. N Engl J Med 2019; 380: 215-28.
Lalloo DG, Hill DR. **Preventing malaria in travellers**. BMJ. 2008 Jun 14;336(7657):1362-6.
Langfitt JT, McDermott MP, Brim R, et al. **Neurodevelopmental Impairments 1 Year After Cerebral Malaria**. Pediatrics. 2019 Jan 29.
Laufer MK, et al. Return of chloroquine antimalarial efficacy in Malawi. N Engl J Med. 2006 Nov 9;355(19):1959-66.
Leslie T, Mikhail A, Mayan I, et al. **Overdiagnosis and mistreatment** of malaria among febrile patients at primary healthcare level in Afghanistan: observational study. BMJ. 2012 Jul 24;345:e4389.
Leslie T, et al. **Rapid diagnostic tests** to improve treatment of malaria and other febrile illnesses: patient randomized effectiveness trial in primary care clinics in Afghanistan. BMJ. 2014 Jun 19
Llanos-Cuentas A, Lacerda MV, Rueangweerayut R, et al. **Tafenoquine plus chloroquine** for the treatment and relapse prevention of Plasmodium vivax malaria (DETECTIVE): a multicentre, double-blind, randomised, phase 2b dose-selection study. Lancet 2013; online Dec 19.
Llanos-Cuentas A, Lacerda MVG, Hien TT, et al. **Tafenoquine versus primaquine to prevent relapse of Plasmodium** vivax malaria. N Engl J Med 2019; 380: 229-41.
Lobel HO, et al. Use of malaria prevention measures by North American and European travelers to **East Africa**. J Travel Med. 2001;8(4):167-172.
Lobel HO, Kozarsky PE. Update on prevention of malaria for travelers. JAMA. 1997;278(21):1767-1771.
Lu F, Culleton R, Zhang M, et al. Emergence of **Indigenous Artemisinin-Resistant Plasmodium falciparum** in Africa. N Engl J Med. 2017 Feb 22.
Maia MF, Kliner M, Richardson M, et al. **Mosquito repellents for malaria prevention**. Cochrane Database Syst Rev. 2018 Feb 6;2:CD011595. There is insufficient evidence to conclude topical or spatial repellents can prevent malaria. There is a need for better designed trials to generate higher certainty of evidence before well-informed recommendations can be made.
Maitland K. **Severe Malaria in African Children** - The Need for Continuing Investment. N Engl J Med. 2016 Dec 22;375(25):2416-2417.
Manger K, von Streitberg U, Seitz G, et al. **Hard palate hyperpigmentation** - a rare **side effect of antimalarials**. Arthritis Rheumatol. 2017 Sep 21..
Marchant T, Schellenberg D, et al. Assessment of a national voucher scheme to deliver **insecticide-treated mosquito nets** to pregnant women. CMAJ 2010 182: 152-156.
Marmor MF, Kellner U, Lai TY, Lyons JS, Mieler WF; American Academy of Ophthalmology. Revised recommendations on screening for **chloroquine** and **hydroxychloroquine retinopathy**. Ophthalmology. 2011 Feb;118(2):415-22.
Marmor MF, Kellner U, Lai TY, Melles RB, Mieler WF; **American Academy of Ophthalmology**. Recommendations on screening for chloroquine and **hydroxychloroquine retinopathy** (**2016 revision**). Ophthalmology. 2016;123:1386-1394.
Mayor A et al. Changing trends in **P. falciparum** burden, immunity, and disease in **pregnancy**. N Engl J Med 2015 Oct 22; 373:1607.
McCarthy JS, Lotharius J, Rückle T, et al. Safety, tolerability, pharmacokinetics, and activity of the novel **long-acting antimalarial DSM265**: a two-part first-in-human phase 1a/1b randomised study. Lancet Infect Dis 2017; online Mar 28.
McGready R, Lee SJ, Wiladphaingern J, et al. Adverse effects of **falciparum and vivax malaria** and the safety of **antimalarial treatment in early pregnancy**: a population based study. Lancet Infect Dis 2011; published online Dec 13. DOI:10.1016/S1473-3099(11)70339-5.
Medical Letter on Drugs and Therapeutics: **Drugs for Parasitic Infections** 1st Ed. 2007.
Medical Letter. Treatment Guidelines: **Advice for Travelers**. Nov 2009.
Melles RB, Marmor MF. The risk of toxic **retinopathy** in patients on long-term **hydroxychloroquine** therapy. JAMA Ophthalmol. 2014 Dec;132(12):1453-60.
Ménard D, Khim N, Beghain J, et al. A worldwide **map of Plasmodium falciparum** K13-propeller polymorphisms. N Engl J Med 2016;374:2453-64.

Meremikwu M, et al. **Chemoprophylaxis and intermittent treatment** for preventing malaria in children. Cochrane Database Syst Rev. 2008 Apr 16;(2):CD003756. Prophylaxis and intermittent treatment with antimalarial drugs reduce clinical malaria and severe anaemia in preschool children.

Mirza DM, Hashim MJ, Sheikh A. **Malaria**. BMJ. 2011 Mar 15;342:d1149. doi:10.1136/bmj.d1149.

Moonen B, Shiff C. **Should we commit to eradicating malaria worldwide**? BMJ. 2017 Mar 2;356:j916.

Moore BR, Benjamin JM, Auyeung SO, et al. Safety, tolerability and pharmacokinetic properties of co-administered **azithromycin** and **piperaquine** in **pregnant** Papua New Guinean women. Br J Clin Pharmacol. 2016 Feb 17.

Mwangi MN, Roth JM, Smit MR, et al. Effect of **daily antenatal iron supplementation** on Plasmodium infection in Kenyan women: a randomized clinical trial.JAMA. doi:10.1001/jama .2015.9496

Nadjm B, Amos B, Mtove G, et al. WHO guidelines for antimicrobial treatment in children admitted to hospital in an area of intense **Plasmodium falciparum** transmission: prospective study. BMJ. 2010 Mar 30;340:c1350.

Nevin RL, Pietrusiak PP, Caci JB. Prevalence of **contraindications to mefloquine** use among USA military personnel deployed to Afghanistan. Malar J. 2008 Feb 11;7:30.

Nayyar GM, Breman JG, Newton PN, Herrington J. **Poor-quality antimalarial drugs** in southeast Asia and sub-Saharan Africa. Lancet Infect Dis. 2012 Jun;12(6):488-96.

Neafsey DE, Juraska M, Bedford T, et al. Genetic diversity and protective efficacy of the **RTS,S/AS01 malaria vaccine**. N Engl J Med. DOI: 10.1056/NEJMoa1505819

Noor AM, Kinyoki DK, et al. The changing risk of **Plasmodium falciparum malaria infection in Africa**: 2000-10: a spatial and temporal analysis of transmission intensity. Lancet. 2014 Feb 19.

Obaro S, Greenwood B. **Malaria and bacteraemia** in African children. Lancet. 2011 Sep 6.

Ochodo E, Garner P, Sinclair D. Achieving **universal testing** for malaria. BMJ. 2016 Feb 4;352:i107.

Odaga J, Sinclair D, Lokong JA, et al. **Rapid diagnostic tests versus clinical diagnosis** for managing people with fever in malaria endemic settings. Cochrane Database Syst Rev. 2014 Apr 17;4:CD008998.

Okwundu CI, Nagpal S, Musekiwa A, Sinclair D. **Home- or community-based programmes for treating malaria**. Cochrane Database of Systematic Reviews 2013, Issue 5. Art. No.: CD009527. DOI: 10.1002/14651858.CD009527.pub2. Home- or community-based interventions which provide antimalarial drugs free of charge probably improve prompt access to antimalarials, and there is moderate quality evidence from rural Ethiopia that they may impact on childhood mortality when implemented in appropriate settings. Programmes which treat all fevers presumptively with antimalarials lead to overuse antimalarials, and potentially undertreat other causes of fever such as pneumonia. Incorporating RDT diagnosis into home- or community-based programmes formalariamay help to reduce this overuse of antimalarials, and has been shown to be safe under trial conditions.

Olotu A, Lusingu J, Leach A, et al.Efficacy of **RTS,S/AS01E malaria vaccine** and exploratory analysis on anti-circumsporozoite antibody titres and protection in children aged 5-17 months in Kenya and Tanzania: a randomised controlled trial. Lancet Infect Dis. 2011 Feb;11(2):102-9.

Olotu A, Fegan G, Wambua J, et al. **Four-year efficacy of RTS,S/AS01E** and its interaction with malaria exposure. N Engl J Med. 2013 Mar 21;368(12):1111-20.

Olotu A, Fegan G, Wambua J, et al. Seven-year efficacy of **RTS,S/AS01 malaria vaccine** among young African children. N Engl J Med 2016;374:2519-29.

Oniyangi O, Omari AA. Malaria chemoprophylaxis in sickle cell disease. Cochrane Database Syst Rev. 2006 Oct 18;(4):CD003489. It is beneficial to give routine malaria chemoprophylaxis in sickle cell disease in areas where malaria is endemic.

Otieno L, Oneko M, Otieno W, et al. Safety and immunogenicity of **RTS,S/AS01 malaria vaccine** in infants and children with WHO stage 1 or 2 HIV disease: a randomised, double-blind, controlled trial. Lancet Infect Dis 2016; online July 6.

Ouédraogo AL, Bastiaens GJ, Tiono AB, et al. Efficacy and Safety of the **Mosquitocidal Drug Ivermectin** to Prevent Malaria Transmission After Treatment: A Double-Blind, Randomized, Clinical Trial. Clin Infect Dis. 2014 Nov 19.

Packard RM. The origins of **antimalarial-drug resistance**. N Engl J Med. 2014 Jul 31;371(5):397-9.

Pasternak Bjorn; Hviid Anders. **Atovaquone-Proguanil Use in Early Pregnancy** and the Risk of Birth Defects. *Arch Intern Med*. 2011;171(3):259-260.

Penny MA, Veity R, Bever CA, et al. Public health impact and cost-eff ectiveness of the **RTS,S/AS01 malaria vaccine** candidate: a systematic comparison of predictions from four m athematical models. Lancet 2015; online Nov 5.

Penny MA, Verity R, et al. Public health impact and cost-eff ectiveness of the **RTS,S/AS01 malaria vaccine**: a systematic comparison of predictions from four mathematical models. Lancet 2016; published online Nov 5.

Pharmacist's Letter. **Insect Repellants**. July 2010.

Phiri K et al. **Intermittent preventive therapy for malaria** with monthly artemether-lumefantrine for the post-discharge management of severe anaemia in children aged 4-59 months in southern Malawi: a multicentre, randomised, placebo-controlled trial. Lancet Infect Dis. 2011 Dec 13.

Phyo AP, Nkhoma S, Stepniewska K, et al. Emergence of artemisinin-resistant malaria on the western border of Thailand: a longitudinal study. Lancet 2012; 379: 1960–66.

Phyo AP, Jittamala P, Nosten FH, et al. Antimalarial activity of **artefenomel** (OZ439), a novel synthetic antimalarial endoperoxide, in patients with Plasmodium falciparum and Plasmodium vivax malaria: an open-label phase 2 trial. Lancet Infect Dis 2015; online Oct 5.

Pinder M, Jawara M, Jarju LBS, et al. Efficacy of **indoor residual spraying** with dichlorodiphenyltrichloroethane against malaria in Gambian communities with high usage of long-lasting insecticidal mosquito nets: a cluster-randomised controlled trial. Lancet 2014; online Dec 9.

Poirot E, Skarbinski J, Sinclair D, Kachur SP, Slutsker L, Hwang J.**Mass drug administration for malaria**. Cochrane Database of Systematic Reviews 2013, Issue 12. Art. No.: CD008846. DOI: 10.1002/14651858.CD008846.pub2. MDA appears to reduce substantially the initial risk of malaria parasitaemia. However, few studies showed sustained impact beyond six months post-MDA, and those that did were conducted on small islands or in highland settings. To assess whether there is an impact of MDA on malaria transmission in the longer term requires more quasi experimental studies with the intention of elimination, especially in low- and moderate-transmission settings. These studies need to address any long-term outcomes, any potential barriers for community uptake, and contribution to the development of drug resistance.

Postels DG, Taylor TE, Molyneux M, et al. Neurologic outcomes in **retinopathy-negative cerebral malaria** survivors. Neurology. 2012 Sep 18;79(12):1268-72.

Prashanth GP, Maralihalli MB, Bagalkot PS, Joshi SN. **Intravenous Artesunate** for Transfusion-Transmitted Plasmodium vivax Malaria in a Preterm Neonate. Pediatrics. 2012 Sep;130(3):e706-9.

PREGACT Study Group. Four **artemisinin-based treatments in African pregnant women** with malaria. N Engl J Med 2016;374:913-27.

Price RN, von Seidlein L, Valecha N, et al. Prevalence of **chloroquine-resistant Plasmodium vivax:** a systematic review. Lancet Infect Dis 2014; online Sept 9.

Price C, Ashbaugh C, Miller AL, et al. Clinical problem solving. A **chilly fever**. N Engl J Med. 2014 Nov 6;371(19):1833-7.

Protopopoff N, Mosha JF, Lukole E, et al. Effectiveness of a **long-lasting piperonyl butoxide-treated insecticidal net and indoor residual spray interventions**, separately and together, against malaria transmitted by pyrethroid-resistant mosquitoes: a cluster, randomised controlled, two-by-two factorial design trial. Lancet 2018.

Public Health Agency of Canada. Canada Communicable Disease Report. Committee to Advise on Tropical Medicine and Travel (CATMAT) statement. Statement on **pregnancy and travel**. Mar 2010 http://www.phac-aspc.gc.ca/publicat/ccdr-rmtc/10vol36/acs-2/index-eng.php

Pyae Pho A, Nkhoma S, Stepniewska K, et al. Emergence of **artemisinin-resistant** malaria on the western border of Thailand: a longitudinal study. Lancet 2012; online April 5.

Radeva-Petrova D, Kayentao K, Ter Kuile FO, et al. Drugs for **preventing malaria in pregnant women** in endemic areas: any drug regimen versus placebo or no treatment. Cochrane Database Syst Rev. 2014 Oct 10;10:CD000169. Routine chemoprevention to prevent malaria and its consequences has been extensively tested in RCTs, with clinically important benefits on anaemia and parasitaemia in the mother, and on birthweight in infants.

Redditt V, Bogoch I, Rashid M. A 38-year-old man with fever and a history of malaria. CMAJ. 2018 Sep 10;190(36):E1081-E1082.

Riley K, Schwager Z, Stern M, Vleugels RA, Femia A. Assessment of **Antimalarial Therapy in Patients Who Are Hypersensitive to Hydroxychloroquine**. JAMA Dermatol. 2019 Feb 13.

Roestenberg M, Teirlinck AC, McCall MB, et al. Long-term protection against malaria after **experimental sporozoite inoculation**: an open-label follow-up study. Lancet. 2011 Apr 21.

Rogerson SJ, Desai M, Mayor A, et al. **Burden, pathology, and costs of malaria in pregnancy**: new developments for an old problem. Lancet Infect Dis. 2018 Apr;18(4):e107-e118.

Rosenthal Philip J.. Lessons from **Sickle Cell Disease** in the Treatment and Control of Malaria. N Engl J Med 2011; 364:2549-2551.

Royal College of Obstetricians and Gynaecologists (RCOG). The **prevention of malaria in pregnancy**. London (UK): 2010 Apr.

Royal College of Obstetricians and Gynaecologists (RCOG). The **diagnosis and treatment of malaria in pregnancy**. London (UK) 2010 Apr.

RTS,S Clinical Trials Partnership. First results of phase 3 trial of **RTS,S/AS01 malaria vaccine** in African children. N Engl J Med 2011. DOI: 10.1056/NEJMoa1102287

RTS,S Clinical Trials Partnership. A Phase 3 Trial of **RTS,S/AS01 Malaria Vaccine** in African Infants. N Engl J Med. 2012 Nov 9.

RTS,S Clinical Trials Partnership. Efficacy and safety of the **RTS,S/AS01 malaria vaccine** during 18 months after vaccination: a phase 3 randomized, controlled trial in children and young infants at

11 African sites. PLoS Med. 2014 Jul 29;11(7):e1001685
RTS,S Clinical Trials Partnership. Efficacy and safety of **RTS,S/AS01 malaria vaccine** with or without a booster dose in infants and children in Africa: final results of a phase 3, individually randomised, controlled trial. Lancet. 2015 Apr 23.
RTS,S Clinical Trials Partnership. Effi cacy and safety of **RTS,S/AS01 malaria vaccine** with or without a booster dose in infants and children in Africa: final results of a phase 3, individually randomised, controlled trial. Lancet 2015; online April 24.
Rueangweerayut R, Phyo AP, Uthaisin C, et al. **Pyronaridine-artesunate versus mefloquine plus artesunate** for malaria. N Engl J Med. 2012 Apr 5;366(14):1298-309.
Ruiz-Irastorza G, Ramos-Casals M, Brito-Zeron P, Khamashta MA. Clinical efficacy and side effects of antimalarials in systemic lupus erythematosus: a systematic review. Ann Rheum Dis 2010;69(1):20-28.
Sahuguet J, Poulet A, Bou Ali H, et al. **Postmalaria Neurologic Syndrome**-**Autoimmune Encephalitis** With Anti-Voltage-Gated Potassium-Channel Antibodies. Ann Intern Med. 2017 Jul 4;167(1):70-71.
Sandison TG, Homsy J, Arinaitwe E, et al. Protective efficacy of **co-trimoxazole prophylaxis against malaria in HIV exposed** children in rural Uganda: a randomised clinical trial. BMJ. 2011 Mar 31;342:d1617. doi:10.1136/bmj.d1617.
Schwartz BS, Larocque RC, Ryan ET. **Travel medicine**. Ann Intern Med. 2012 Jun 5;156(11):ITC61.
Schwartz E, Lachish T. **Artemisinin-based combination therapy (ACT) versus atovaquone-proguanil**: do not choose between but, rather, combine them. Evid Based Med. 2016 Apr;21(2):64
Scott JA, Berkley JA, Mwangi I, et al. Relation between **falciparum malaria and bacteraemia** in Kenyan children: a population-based, case-control study and a longitudinal study. Lancet. 2011 Sep 6.
Seydel KB, Kampondeni SD, Valim C, et al. Brain swelling and death in children with **cerebral malaria**. N Engl J Med. 2015 Mar 19;372(12):1126-37.
Shah NK, Dhillon GP, Dash AP, Arora U, Meshnick SR, Valecha N. Antimalarial drug **resistance of Plasmodium falciparum in India**: changes over time and space. Lancet Infect Dis. 2011 Jan;11(1):57-64.
Sinclair D, Donegan S, Lalloo DG. **Artesunate versus quinine for treating severe malaria**. Cochrane Database of Systematic Reviews 2011, Issue 3. Art. No.: CD005967.
Sirima SB, Ogutu B, Lusingu JP, et al. Comparison of **artesunate–mefloquine and artemether–lumefantrine** fixed-dose combinations for treatment of uncomplicated Plasmodium falciparum malaria in children younger than 5 years in sub-Saharan Africa: a randomised, multicentre, phase 4 trial. Lancet Infect Dis 2016; online July 15.
Sissoko MS, Healy SA, Katile A, et al. Safety and effi cacy of **PfSPZ Vaccine** against Plasmodium falciparum via direct venous inoculation in healthy malaria-exposed Malian adults: a randomised, double-blind phase 1 trial. Lancet Infect Dis 2017; online Feb 15.
Sluydts V, Durnez L, Heng S, et al. Efficacy of topical **mosquito repellent (picaridin) plus long-lasting insecticidal nets versus long-lasting insecticidal nets** alone for control of malaria: a cluster randomised controlled trial. Lancet Infect Dis. 2016 Jun 29.
Smit MR, Ochomo EO, Aljayyoussi G, et al. Safety and **mosquitocidal efficacy of high-dose ivermectin** when co-administered with dihydroartemisinin-piperaquine in Kenyan adults with uncomplicated malaria (IVERMAL): a randomised, double-blind, placebo-controlled trial. Lancet Infect Dis. 2018 Jun;18(6):615-626.
Spring MD, Lin JW, Manning JE, et al. **Dihydroartemisinin-piperaquine failure** associated with a **triple mutant including kelch13 C580Y in Cambodia**: an observational cohort study. Lancet Infect Dis 2015; online April 13.
Ssenkusu JM,Hodges JS,Opoka RO, et al. **Long-term Behavioural Problems in Children** with Severe Malaria. Pediatrics. 2016 ;138(5) :e20161965
Stanczyk NM, Brookfield JF, Field LM, Logan JG. Aedes aegypti Mosquitoes Exhibit **Decreased Repellency by DEET** following Previous Exposure. PLoS One. 2013;8(2):e54438.
Stanczyk NM, Behrens RH, Chen-Hussey V, et. al, **Mosquito repellents** for travellers. BMJ. 2015 Feb 19;350:h99.
Steinhardt LC, Jean YS, Impoinvil D, et al. Effectiveness of **insecticide-treated bednets** in malaria prevention in Haiti: a case-control study. Lancet Glob Health. 2017 Jan;5(1):e96-e103.
Sulyok M, Rückle T, Roth A, et al. DSM265 for **Plasmodium falciparum chemoprophylaxis**: a randomised, double blinded, phase 1 trial with controlled human malaria infection. Lancet Infect Dis 2017; online Mar 28.
Talisuna AO, Karema C, et al. Mitigating the threat of **artemisinin resistance** in Africa: improvement of drug-resistance surveillance and response systems. Lancet Infect Dis. 2012 Nov;12(11):888-96.
Takwoingi Y, Abba K, Garner P. **Rapid Diagnostic Testing for Plasmodium vivax and Nonfalciparum Malaria** in Endemic Areas. JAMA. 2015 Sep 8;314(10):1065-1066.
Tan IL, Koralnik IJ, Rumbaugh JA, et al. Progressive multifocal leukoencephalopathy in a patient without immunodeficiency. Neurology. 2011 Jul 19;77(3):297-9. (treated with mefloquine)
Tatem, et al. The **geography of imported malaria to non-endemic countries**: a meta-analysis of nationally-reported statistics. Lancet Infect Dis 2016; online Oct 21.
Taylor Steve M.; Molyneux Malcolm E.; Simel David L.; et al. **Does This Patient Have Malaria**? *JAMA.* 2010;304(18):2048-2056.
Taylor SM, Parobek CM, Fairhurst RM. **Haemoglobinopathies** and the clinical epidemiology of malaria: a systematic review and meta-analysis. Lancet Infect Dis. 2012 Jun;12(6):457-68.
ter Kuile FO, van Eijk AM, Filler SJ. Effect of sulfadoxine-pyrimethamine resistance on the efficacy of intermittent preventive therapy for malaria control during **pregnancy**: a systematic review. JAMA. 2007 Jun 20;297(23):2603-16. In areas in which 1 of 4 treatments with sulfadoxine-pyrimethamine fail in children by day 14, the 2-dose IPT with sulfadoxine-pyrimethamine regimen continues to provide substantial benefit to HIV-negative semi-immune pregnant women. However, more frequent dosing is required in HIV-positive women not using cotrimoxazole prophylaxis for opportunistic infections.
Thera MA, Doumbo OK, Coulibaly D, et al. A field trial to assess a blood-stage **malaria vaccine**. N Engl J Med. 2011 Sep 15;365(11):1004-13.
Thompson CA, Boggild AK. **Rapid diagnostic tests** for imported malaria. CMAJ. 2014 Oct 7;186(14):E557.
Tickell-Painter M, Maayan N, Saunders R, Pace C, Sinclair D. **Mefloquine for preventing malaria during travel to endemic areas**. Cochrane Database of Systematic Reviews 2017, Issue 10. Art. No.: CD006491. The absolute risk of malaria during short-term travel appears low with all three established antimalarial agents (mefloquine, doxycycline, and atovaquone-proguanil). The choice of antimalarial agent depends on how individual travellers assess the importance of specific adverse effects, pill burden, and cost. Some travellers will prefer mefloquine for its once-weekly regimen, but this should be balanced against the increased frequency of abnormal dreams, anxiety, insomnia, and depressed mood.
Tougher S, the ACTwatch Group, Ye Y, et al. Effect of the **Affordable Medicines Facility**—**malaria (AMFm)** on the availability, price, and market share of quality-assured artemisinin-based combination therapies in seven countries: a before-and-after analysis of outlet survey data. Lancet 2012; online Oct 31. http://dx.doi.org/10.1016/S0140-6736(12)61732-2.
Tougher S; the ACTwatch Group, Ye Y, Amuasi JH, Kourgueni IA, et al. Effect of the Affordable Medicines Facility-malaria (**AMFm**) on the availability, price, and market share of quality-assured **artemisinin-based combination therapies** in seven countries: a before-and-after analysis of outlet survey data. Lancet. 2012 Oct 30.
Trape JF, Tall A, Diagne N, et al.Malaria morbidity and pyrethroid resistance **after the introduction of insecticide-treated bednets and artemisinin-based combination** therapies: a longitudinal study. Lancet Infect Dis. 2011 Aug 17.
Trape J-F, Tall A, et al. The **rise and fall of malaria in a west African rural community, Dielmo, Senegal**, from 1990 to 2012: a 22 year longitudinal study. Lancet Infect Dis 2014; online May 7.
Tun KM, Imwong M, et al. Spread of **artemisinin-resistant Plasmodium falciparum** in Myanmar: a cross-sectional survey of the K13 molecular marker. Lancet Infect Dis 2015; online Feb 20.
Tusting LS, Willey B, Lucas H, et al. **Socioeconomic development** as an intervention against malaria: a systematic review and meta-analysis. Lancet. 2013 Jun 18.
Twomey PS, Smith BL, McDermott C, et al. **Intravenous Artesunate** for the Treatment of Severe and Complicated Malaria in the United States: Clinical Use Under An Investigational New Drug Protocol. Ann Intern Med. 2015 Aug 25.
van der Pluijm RW, Imwong M, Chau NH, et al. Determinants of **dihydroartemisinin-piperaquine treatment failure** in Plasmodium falciparum malaria in Cambodia, Thailand, and Vietnam: a prospective clinical, pharmacological, and genetic study. Lancet Infect Dis 2019 Sep;19(9):952-961.
van Eijk Anna Maria, Hill Jenny, Alegana Victor A, et al. Coverage of **malaria protection in pregnant women** in sub-Saharan Africa: a synthesis and analysis of national survey data, The Lancet Infectious Diseases, In Press, Corrected Proof, Available online 25 January 2011, ISSN 1473-3099, DOI: 10.1016/S1473-3099(10)70295-4.
van Eijk AM, Hill J, Larsen D, et al. Coverage of **intermittent preventive treatment** and **insecticide-treated nets** for the control of malaria during **pregnancy** in sub-Saharan Africa: a synthesis and meta-analysis of national survey data, 2009–11. Lancet Infect Dis 2013; online Sept 18.
Valliani S, Agasthi P, Westney G, et al. **Transfusion-Transmitted Plasmodium falciparum in a Patient With Sickle Cell Hemoglobinopathy**. Ann Intern Med. 2018 May 8.
Walker P GT, White MT, Griffin JT, et al. **Malaria morbidity and mortality in Ebola**-affected countries caused by decreased health-care capacity, and the potential effect of mitigation strategies: a modelling analysis. Lancet Infect Dis 2015 Apr. 24.
Wang J, Xu C, Liao FL, et al. A Temporizing Solution to "**Artemisinin Resistance**". N Engl J Med. 2019 Apr 24.
Waxman M, Aluisio AR, Rege S, Levine AC. A retrospective cohort study of the characteristics and survival of patients with variable **Ebola virus and malaria parasite infection** states. Lancet Infect Dis 2017; online Feb 28
West African Network for Clinical Trials of Antimalarial Drugs (WANECAM). **Pyronaridine–artesunate or dihydroartemisinin–piperaquine versus current first-line therapies for repeated treatment of uncomplicated malaria**: a randomised, multicentre,

open-label, longitudinal, controlled, phase 3b/4 trial. Lancet 2018; online March 29.
White C. Use **mefloquine for UK troops only as "last resort,"** MPs tell Ministry of Defence. BMJ. 2016 May 24;353:i2946.
White MT, Verity R, Griffi n JT. Immunogenicity of the **RTS,S/AS01 malaria vaccine** and implications for duration of vaccine efficacy: secondary analysis of data from a phase 3 randomised controlled trial. Lancet Infect Dis 2015; online Sept 2
White NJ. **Primaquine to prevent transmission of falciparum malaria**. Lancet Infect Dis. 2012 Nov 22.
White NJ, Pukrittayakamee S, Hien TT, et al. **Malaria**. Lancet. 2013 Aug 14.
White NJ, Pukrittayakamee S, Phyo AP, et al. **Spiroindolone KAE609** for falciparum and vivax malaria. N Engl J Med. 2014 Jul 31;371(5):403-10.
White NJ .Declining malaria transmission and **pregnancy** outcomes in southern Mozambique. N Engl J Med 2015 Oct 22; 373:1672.
White NJ, Duong TT, Uthaisin C, et al. Antimalarial **Activity** of **KAF156** in **Falciparum and Vivax Malaria**. N Engl J Med. 2016 Sep 22;375(12):1152-60.
White NJ. **Does antimalarial mass drug administration increase or decrease the risk of resistance**? Lancet Infect Dis. 2016 Nov 10. pii: S1473-3099(16)30269-9.
Whitty CJ, Chiodini PL, Lalloo DG. **Investigation and treatment of imported malaria** in non-endemic countries. BMJ. 2013 May 21;346:f2900.
WHO: World Health Organization World Malaria Report 2013. http://www.who.int/malaria/en/
WHO: World malaria report **2015**. Geneva: World Health Organization(http://www .who .int/ malaria/ publications/ world-malaria-report-2015/ en/).
WHO Guidelines for the **treatment of malaria, third edition**. Geneva: World Health Organization, 2015 (http://www.who.int/malaria/publications/atoz/9789241549127/en/).
Willcox ML, Mant J, O'Dempsey T. **Imported malaria**. BMJ. 2013 May 30;346:f3214.
Witkowski B, Duru V, Khim N, et al. A **surrogate marker of piperaquine-resistant Plasmodium falciparum malaria**: a phenotype– genotype association study. Lancet Infect Dis 2016; online Nov 3.
Whitty CJM, Ansah E. Malaria **control stalls in high incidence areas**. BMJ. 2019 May 21;365:l2216.
Worldwide Antimalarial Resistance Network (WWARN) AL Dose Impact Study Group. The effect of **dose on the antimalarial efficacy of artemether-lumefantrine**: a systematic review and pooled analysis of individual patient data. Lancet Infect Dis. 2015 Mar 13.
Wylie BJ, Hauptman M, Woolf AD, Goldman RH. **Insect Repellants** During Pregnancy in the Era of the Zika Virus. Obstet Gynecol. 2016 Aug 19.
Yeka A, Kigozi R, Conrad MD, et al. **Artesunate/Amodiaquine Versus Artemether/Lumefantrine** for the Treatment of Uncomplicated Malaria in Uganda: A Randomized Trial. J Infect Dis. 2015 Nov 23.
Zani B, Gathu M, Donegan S, Olliaro PL, Sinclair D. **Dihydroartemisinin-piperaquine** for treating uncomplicated Plasmodium falciparum malaria. Cochrane Database of Systematic Reviews 2014, Issue 1. Art. No.: CD010927. DOI:10.1002/14651858.CD010927. In Africa, dihydroartemisinin-piperaquine reduces overall treatment failure compared to artemether-lumefantrine, although both drugs have PCR-adjusted failure rates of less than 5%. In Asia, dihydroartemisinin-piperaquine is as effective as artesunate plus mefloquine, and is better tolerated.
Zlotkin S, Newton S, Aimone AM, et al. Effect of **iron fortification** on malaria incidence in infants and young children in Ghana: a randomized trial. JAMA. 2013;310(9):JOI130053.
Zurovac D, Sudoi RK, Akhwale WS, et al. The effect of **mobile phone text-message** reminders on Kenyan health workers' adherence to malaria treatment guidelines: a cluster randomised trial. Lancet. 2011 Aug 27;378(9793):795-803.

COMMUNITY ACQUIRED PNEUMONIA – Empiric Antibiotic Selection

References:

1. File TM Jr, Tan JS. **International guidelines** for the treatment of community-acquired pneumonia in adults: the role of macrolides. Drugs. **2003**;63(2):181-205.
2. Mandell LA et al. Canadian guidelines for initial management of community acquired pneumonia: an evidence-based update by the **Canadian** Infectious Diseases Society and the Canadian Thoracic Society. Clin Infec Dis **2000**; 31: 383-421.
3. Bartlett JG et al. **The Infectious Diseases Society of America**. Practice guidelines for management of community acquired pneumonia in adults. Clin Infec Dis **2000**; 31: 347-82.
4. Niederman MS, Mandell LA, Anzueto A, Bass JB, Broughton WA, Campbell GD, Dean N, File T, Fine MJ, Gross PA, Martinez F, Marrie TJ, Plouffe JF, Ramirez J, Sarosi GA, Torres A, Wilson R, Yu VL. The Official Statement of the **American** Thoracic Society. Guidelines for the management of adults with community-acquired pneumonia. Diagnosis, assessment of severity, antimicrobial therapy, and prevention. Am J Respir Crit Care Med. **2001** Jun;163(7):1730-54.
5. Mandell LA, Bartlett JG, Dowell SF, File TM Jr, Musher DM, Whitney C; **Infectious Diseases Society of America**. Update of practice guidelines for the management of community - acquired pneumonia in immunocompetent adults. Clin Infect Dis. **2003** Dec 1;37(11):1405-33. (Mandell LA, Wunderink RG, Anzueto A, Bartlett JG, Campbell GD, Dean NC, Dowell SF, File TM Jr, Musher DM, Niederman MS, Torres A, Whitney CG. **Infectious diseases society of America (IDSA) /American Thoracic Society** consensus guidelines on the management of community-acquired pneumonia in adults. Clin Infect Dis. **2007** Mar 1;44 Suppl 2:S27-72.)
   http://www.journals.uchicago.edu/CID/journal/issues/v44nS2/41620/41620.web.pdf?erFrom=5418644572597678115Guest
6. Medical Letter: **Treatment Guidelines.** Drugs for Pneumonia. September, **2003**; (13) pp. 83-88. (Medical Letter: Treatment Guidelines. **Choice of Antibacterial Drugs**. May 2007) Medical Letter. Treatment Guidelines. **Drugs for Bacterial Infections** In Adults. June 2010, July 2013 & Updated **Oct 2017**.
7. Dunbar LM, Khashab MM, Kahn JB, Zadeikis N, Xiang JX, Tennenberg AM. Efficacy of 750-mg, 5-day levofloxacin in the treatment of community-acquired pneumonia caused by atypical pathogens. Curr Med Res Opin. 2004 Apr;20(4):555-63. Erratum in: Curr Med Res Opin. 2004 Jun;20(6):967.
8. Leophonte P, File T, Feldman C. Gemifloxacin once daily for 7 days compared to amoxicillin/clavulanic acid thrice daily for 10 days for the treatment of community-acquired pneumonia of suspected pneumococcal origin. Respir Med. 2004 Aug;98(8):708-20.
9. Rosser W, Pennie R, Pilla N and the Anti-infective Review Panel (**Canadian**). **Anti-infective Guidelines for Community-acquired Infections** Toronto: **MUMS Guideline** Clearinghouse; 2005, 2010, 2012 & **Revised 2013**.
   Bugs & Drugs: An Antimicrobial / Infectious Diseases Reference 2012. App 2017.
10. Houck PM, Bratzler DW, Nsa W, Ma A, Bartlett JG. Timing of antibiotic administration and outcomes for Medicare patients hospitalized with community-acquired pneumonia. Arch Intern Med. 2004 Mar 22;164(6):637-44. (Kanwar M, Brar N, Khatib R, Fakih MG. Misdiagnosis of community-acquired pneumonia and inappropriate utilization of antibiotics: side effects of the 4-h antibiotic administration rule. Chest. 2007 Jun;131(6):1865-9. Epub 2007 Mar 30. Linking antibiotic administration within 4 h of hospital admission (as a quality indicator) to financial compensation may result in an inaccurate diagnosis of CAP, inappropriate utilization of antibiotics, and thus less than optimal care.)
11. Mills GD, Oehley MR, Arrol B. Effectiveness of {beta} lactam antibiotics compared with antibiotics active against atypical pathogens in non-severe community acquired pneumonia: meta-analysis. BMJ 2005; 330:456-60. (InfoPOEMs: Strange, but true: Oral beta-lactam antibiotics -- amoxicillin, amoxicillin/clavulanate (Augmentin), or a cephalosporin -- are as effective in the treatment of community-acquired pneumonia as antibiotics active against atypical pathogens, even in patients infected with Mycoplasma pneumoniae or Chlamydia pneumoniae. These old standbys can be used instead of the more expensive drugs for most patients. Legionella infection still requires treatment with an antibiotic effective against atypical pathogens, but in these studies only 1.1% of the patients with nonsevere pneumonia had Legionella. These results are backed up by similar findings from clinical practice (Hedlund J, et al. Scand J Infect Dis 2002; 34:887-92). (LOE = 1a))
12. Carratala J, Fernandez-Sabe N, Ortega L, et al. Outpatient care compared with hospitalization for community-acquired pneumonia. Ann Intern Med 2005; 142:165-72. (Aujesky D, Auble TE, et al. Prospective comparison of three validated prediction rules for prognosis in community-acquired pneumonia. Am J Med. 2005 Apr;118(4):384-92.) (Espana PP, et al. Development and Validation of a Clinical Prediction Rule for Severe Community-acquired Pneumonia. Am J Respir Crit Care Med. 2006 Dec 1;174(11):1249-56. Epub 2006 Sep 14.)(**CURB-65**: use of CURB-65 (Confusion, Urea > 7 mmol/L, Respiratory rate ≥ 30/min, systolic blood pressure ≤ 90 mm Hg, and diastolic blood pressure ≥ 60 mm Hg, and age 65 years or older). When calculating the 30-day mortality rate, if the CURB-65 score is greater or equal to 3, the site of care should be the intensive care unit (ICU). If the score is 2, admission to a hospital is sufficient. Outpatient management is warranted when the CURB-65 score is 0 or 1.)
13. Torres OH, Munoz J, et al. Outcome predictors of pneumonia in elderly patients: importance of functional assessment. J Am Geriatr Soc. 2004 Oct;52(10):1603-9. (The PSI may overpredict mortality in older adults. Relying on PSI, without taking into account a patients functional status, may lead to unnecessary and potentially harmful hospitalizations for pts who might otherwise have been safely treated at home ACP 2005)
14. Fuller JD, Low DE. A review of Streptococcus pneumoniae infection treatment failures associated with fluoroquinolone resistance. Clin Infect Dis. 2005 Jul 1;41(1):118-21. Epub 2005 May 26. There were 20 ciprofloxacin and levofloxacin treatment failures reported. Physicians should be aware, when treating pneumococcal respiratory tract infections in older patients with a fluoroquinolone, that clinical failures might occur, especially for patients with comorbid illnesses and a history of recent fluoroquinolone use.
15. Doern GV, Richter SS, Miller A, Miller N, Rice C, Heilmann K, Beekmann S. Antimicrobial resistance among Streptococcus pneumoniae in the United States: have we begun to turn the corner on resistance to certain antimicrobial classes? Clin Infect Dis. 2005 Jul 15;41(2):139-48. Epub 2005 Jun 7.
16. Abraham E, Laterre PF, Garg R, et al.; Administration of Drotrecogin Alfa (Activated) in Early Stage Severe Sepsis (ADDRESS) Study Group. Drotrecogin alfa (activated) for adults with severe sepsis and a low risk of death. N Engl J Med. 2005 Sep 29;353(13):1332-41. CONCLUSIONS: The absence of a beneficial treatment effect, coupled with an increased incidence of serious bleeding complications, indicates that DrotAA should not be used in patients with severe sepsis who are at low risk for death, such as those with single-organ failure or an APACHE II score less than 25.
17. Shefet D, Robenshtok E, Paul M, Leibovici L. Empirical atypical coverage for inpatients with community-acquired pneumonia: systematic review of randomized controlled trials. Arch Intern Med. 2005 Sep 26;165(17):1992-2000. CONCLUSION: Empirical antibiotic coverage of atypical pathogens in hospitalized patients with community-acquired pneumonia showed no benefit of survival or clinical efficacy in this synthesis of randomized trials.
18. D'Ignazio J, Camere MA, et al. Novel, Single-Dose Microsphere Formulation of Azithromycin versus 7-Day Levofloxacin Therapy for Treatment of Mild to Moderate Community-Acquired Pneumonia in Adults. Antimicrob Agents Chemother. 2005 Oct;49(10):4035-41. (InfoPOEMs: Although a single dose of azithromycin in an extended-release formulation was statistically similar to 7 days of levofloxacin, resistance was more common to strep pneumoniae with azithromycin and there was a trend toward worse outcomes with azithromycin using the intention-to-treat analysis. The study was also underpowered to detect clinically important differences based on the author's sample size calculations. (LOE = 1b-))

19. Lexau CA, Lynfield R, Danila R, et al.; Active Bacterial Core Surveillance Team. Changing epidemiology of invasive pneumococcal disease among older adults in the era of pediatric pneumococcal conjugate vaccine. JAMA. 2005 Oct 26;294(16):2043-51.
20. Drehobl MA, et al. **Single-dose azithromycin** microspheres vs clarithromycin extended release for treatment of mild-to-moderate CAP in adults. Chest. 2005 Oct;128(4):2230-7.
21. D'Ignazio J, Camere MA, Lewis DE, Jorgensen D, Breen JD. Novel, **single-dose** microsphere formulation of **azithromycin** versus 7-day levofloxacin therapy for treatment of mild to moderate community-acquired Pneumonia in adults. Antimicrob Agents Chemother. 2005 Oct;49(10):4035-41.
22. Epstein BJ, Gums JG. Optimal pharmacological therapy for community-acquired pneumonia: the role of **dual antibacterial therapy**. Drugs. 2005;65(14):1949-71.
23. Noreddin AM, Hoban DJ, Zhanel GG. Comparison of **gatifloxacin and levofloxacin** administered at various **dosing regimens** to hospitalised patients with community-acquired pneumonia: pharmacodynamic target attainment study using North American surveillance data for Streptococcus pneumoniae. Int J Antimicrob Agents. 2005 Aug;26(2):120-5.
24. Shorr AF, Kollef MH. **Ventilator-associated pneumonia**: insights from recent clinical trials. Chest. 2005 Nov;128(5 Suppl 2):583S-591S.
25. Schito GC, Felmingham D. Susceptibility of Streptococcus pneumoniae to penicillin, azithromycin and telithromycin (PROTEKT 1999-2003). Int J Antimicrob Agents. 2005 Dec;26(6):479-85. Epub 2005 Nov 9. Penicillin non-susceptibility rates were stable over the study period; overall, 21.8% of isolates were resistant. Azithromycin resistance increased from 31.0% in Year 1 to 36.3% in Year 4. Resistance rates for penicillin and azithromycin varied between countries and were highest in France, Spain, South Africa, USA and the Far East. Multidrug resistance in S. pneumoniae did not change significantly over the 4 years, with an overall rate of 38.6%. Telithromycin retained good activity against S. pneumoniae (0.1% of isolates resistant), including multidrug-resistant isolates.
26. Morganroth J, Dimarco JP, Anzueto A, Niederman MS, Choudhri S; CAPRIE Study Group. A randomized trial comparing the cardiac rhythm safety of **moxifloxacin** vs levofloxacin 500mg in elderly patients hospitalized with community-acquired pneumonia. Chest. 2005 Nov;128(5):3398-406.
27. Fry AM, et al. Trends in hospitalizations for pneumonia among persons aged 65 years or older in the United States, 1988-2002. JAMA. 2005 Dec 7;294(21):2712-9.
28. Shefet D, Robenshtok E, Paul M, Leibovici L. Empirical atypical coverage for inpatients with community-acquired pneumonia: systematic review of randomized controlled trials. Arch Intern Med. 2005 Sep 26;165(17):1992-2000.(InfoPOEMs: Treating community-acquired pneumonia with antibiotics effective against atypical organisms is no better and no worse than treating with a penicillin or cephalosporin alone. (LOE = 1a))
29. Yealy DM, et al. Effect of increasing the intensity of **implementing pneumonia guidelines**: a randomized, controlled trial. Ann Intern Med. 2005 Dec 20;143(12):881-94.
30. Anzueto A, Niederman MS, Pearle J, et al.; Community-Acquired Pneumonia Recovery in the Elderly Study Group. Community-Acquired Pneumonia Recovery in the Elderly (**CAPRIE**): efficacy and safety of **moxifloxacin** therapy versus that of levofloxacin therapy. Clin Infect Dis. 2006 Jan 1;42(1):73-81. Epub 2005 Nov 22.
31. CAP Adults ICSI 2006 Outpatient Guidelines http://www.icsi.org/knowledge/detail.asp?catID=29&itemID=160
32. Loeb M, et al Effect of a clinical **pathway** to reduce hospitalizations in nursing home residents with pneumonia: a randomized controlled trial. JAMA. 2006 Jun 7;295(21):2503-10.
33. el Moussaoui R, et al. Effectiveness of discontinuing antibiotic treatment after three days versus eight days in mild to moderate-severe community acquired pneumonia: randomised, double blind study. BMJ. 2006 Jun 10;332(7554):1355. (InfoPOEMs: Dogma successfully challenged: In patients who respond well to initial treatment, stopping antibiotic therapy after 3 days is just as effective as continuing treatment for the standard 8 days. (LOE = 1b))
34. Hoare Z, Lim WS. Pneumonia: update on diagnosis and management. BMJ. 2006 May 6;332(7549):1077-9.
35. Christ-Crain M, et al. Procalcitonin Guidance of Antibiotic Therapy in Community-acquired Pneumonia: A Randomized Trial. Am J Respir Crit Care Med. 2006 Jul 1;174(1): 84-93. Epub 2006 Apr 7.
36. Canani RB, et al. Working Group on Intestinal Infections of the Italian Society of Pediatric Gastroenterology, Hepatology and Nutrition (SIGENP). Therapy with **gastric acidity inhibitors** increases the risk of acute gastroenteritis and community-acquired pneumonia in children. Pediatrics. 2006 May;117(5):e817-20. (InfoPOEMs: In this weak study, treatment of gastroesophageal reflux disease (GERD) with gastric acid suppressants increased the likelihood of pneumonia compared with the rate in healthy children. It's not known whether the treatment, the presence of GERD, or some other factor caused the pneumonia. Watch for confirmation in randomized research. (LOE = 4))
37. Kabra S, Lodha R, Pandey R. Antibiotics for community acquired pneumonia in **children**. Cochrane Database Syst Rev. 2006 Jul 19;3:CD004874.
38 Canadian Bacterial Surveillance Network (**CBSN**) 2005 Canadian Resistance patterns. http://microbiology.mtsinai.on.ca/data/sp/sp_can.shtml
39. Oosterheert JJ, et al. Effectiveness of early switch from IV to oral antibiotics in severe community acquired pneumonia: multicentre randomised trial. BMJ. 2006 Nov 7; [Epub ahead of print] Early switch from intravenous to oral antibiotics in patients with severe community acquired pneumonia is safe and decreases length of hospital stay by 2 days.
40. Barton N, et al. Guidelines for the prevention and management of community-associated **methicillin-resistant Staphylococcus aureus**: A perspective for Canadian health care practionioners. Can J Infect Dis Med Microbiol Vol 17 Suppl C Sept/Oct 2006. (At Risk: young, athletes, inmates, military, Iv drug users & aboriginal population. CMRSA 7 (USA400) from Minnesota; CMRSA10 (USA300) from California & BC. http://www.pulsus.com/infdis/17_SC/Pdf/mrsa_ed.pdf
Liu Catherine, Bayer Arnold, Cosgrove Sara E., et al. Clinical Practice Guidelines by the Infectious Diseases Society of America for the Treatment of Methicillin-Resistant Staphylococcus Aureus Infections in Adults and Children Clin Infect Dis. ciq146 first published online January 4, 2011 doi:10.1093/cid/ciq146
Wunderink RG, Niederman MS, Kollef MH, et al. **Linezolid in methicillin-resistant Staphylococcus aureus nosocomial pneumonia**: a randomized, controlled study. Clin Infect Dis. 2012 Mar 1;54(5):621-9. (vs vancomycin)
41. Gilbert M, MacDonald J, Gregson D, et al. Outbreak in Alberta of community-acquired (**USA300**) **methicillin-resistant Staphylococcus aureus** in people with a history of drug use, homelessness or incarceration. CMAJ. 2006 Jul 18;175(2):149-54. Epub 2006 Jun 27.
42. Majumdar SR, et al. **Statins** and outcomes in patients admitted to hospital with community acquired pneumonia: population based prospective cohort study. BMJ. 2006 Oct 23; [Epub ahead of print]
43. Hazir T, et al. Chest **radiography** in children aged 2-59 months diagnosed with non-severe pneumonia as defined by World Health Organization: descriptive multicentre study in Pakistan. BMJ. 2006 Sep 23;333(7569):629. Epub 2006 Aug 21.
44. Burkhardt O, et al. **Once-daily tobramycin** in cystic fibrosis: better for clinical outcome than thrice-daily tobramycin but more resistance development? J Antimicrob Chemother. 2006 Aug 2; [Epub ahead of print]
45. Metersky ML, et al. Antibiotic timing and **diagnostic uncertainty** in Medicare patients with pneumonia: is it reasonable to expect all patients to receive antibiotics within 4 hours? Chest. 2006 Jul;130(1):16-21.
46. Bergman M, et al. Macrolide and Azithromycin Use Are Linked to Increased **Macrolide Resistance** in Streptococcus pneumoniae. Antimicrob Agents Chemother. 2006 Aug 28;

[Epub ahead of print]
47. Chan EY, Ruest A, Meade MO, Cook DJ. **Oral decontamination** for prevention of pneumonia in mechanically ventilated adults: systematic review and meta-analysis. BMJ. 2007 Apr 28;334(7599):889. Epub 2007 Mar 26. Oral decontamination of mechanically ventilated adults using antiseptics is associated with a lower risk of ventilator associated pneumonia. Neither antiseptic nor antibiotic oral decontamination reduced mortality or duration of mechanical ventilation or stay in the intensive care unit.
48. Arnold FW, Summersgill JT, Lajoie AS, Peyrani P, Marrie TJ, Rossi P, Blasi F, Fernandez P, File TM Jr, et al. Community-Acquired Pneumonia Organization (CAPO) Investigators. A worldwide perspective of **atypical pathogens** in community-acquired pneumonia. Am J Respir Crit Care Med. 2007 May 15;175(10):1086-93. Epub 2007 Mar 1. The significant global presence of atypical pathogens and the better outcomes associated with antimicrobial regimens with atypical coverage support empiric therapy for all hospitalized patients with CAP with a regimen that covers atypical pathogens.
49. Atkinson M, et al. Comparison of **oral amoxicillin** and intravenous benzyl penicillin for community acquired pneumonia in children (PIVOT trial): a multicentre pragmatic randomised controlled equivalence trial. Thorax. 2007 Dec;62(12):1102-6. Epub 2007 Jun 13. Oral amoxicillin is effective for most children admitted to hospital with pneumonia (all but those with the most severe disease who were excluded from this study).
50. Hazir T, Fox LM, Nisar YB, ET AL. New Outpatient Short-Course Home Oral Therapy for Severe Pneumonia Study Group. (NO-SHOTS) Ambulatory short-course high-dose oral amoxicillin for treatment of severe pneumonia in children: a randomised equivalency trial. Lancet. 2008 Jan 5;371(9606):49-56. Home treatment with high-dose oral amoxicillin is equivalent to currently recommended hospitalisation and parenteral ampicillin for treatment of severe pneumonia without underlying complications, suggesting that WHO recommendations for treatment of severe pneumonia need to be revised.
51. Asghar R, Banajeh S, Egas J, et al. for the SPEAR (Severe Pneumonia Evaluation Antimicrobial Research) Study Group. Chloramphenicol versus ampicillin plus gentamicin for community acquired very severe pneumonia among children aged 2-59 months in low resource settings: multicentre randomised controlled trial (SPEAR study). BMJ. 2008 Jan 8 Injectable ampicillin plus gentamicin is superior to injectable chloramphenicol for the treatment of community acquired very severe pneumonia in children aged 2-59 months in low resource settings.
52. Knol W, van Marum RJ, Jansen PA, et al. **Antipsychotic Drug Use** and Risk of Pneumonia in Elderly People. J Am Geriatr Soc. 2008 Feb 7; [Epub ahead of print] Use of antipsychotics in elderly people is associated with greater risk of pneumonia. This risk is highest shortly after the initiation of treatment, with the greatest increase in risk found for atypical antipsychotics.
53. Durrington HJ, Summers C. Recent changes in the management of community acquired pneumonia in adults. BMJ. 2008 Jun 21;336(7658):1429-33.
54. Wunderink RG, Mendelson MH, Somero MS, et al. Early Microbiologic Response to **Linezolid Versus Vancomycin** in Ventilator-Associated Pneumonia (**VAP**) Due to Methicillin-Resistant Staphylococcus aureus (MRSA). Chest. 2008 Aug 21. [Epub ahead of print] Early microbiologic cure rates were not statistically significantly higher with linezolid than with vancomycin despite trends in all secondary clinical outcomes favoring linezolid. These results suggest that any beneficial effect of linezolid may be due to factors other than increased bacterial clearance.
55. Sultan N, Nazareno J, Gregor J. Association between proton pump inhibitors and respiratory infections: A systematic review and meta-analysis of clinical trials. Can J Gastroenterol. 2008 Sep;22(9):761-6.
56. Vardakas KZ Md, Siempos II Md, Grammatikos A Md, Athanassa Z Md, Korbila IP Md, Falagas ME Md Dsc. **Respiratory fluoroquinolones** for the treatment of community-acquired pneumonia: a meta-analysis of randomized controlled trials. CMAJ. 2008 Dec 2;179(12):1269-1277.
57. Bitner-Glindzicz M, Pembrey M, Duncan A, Heron J, Ring SM, Hall A, Rahman S. Prevalence of mitochondrial 1555A-->G mutation in European children. N Engl J Med. 2009 Feb 5;360(6):640-2. (aminoglycoside ototoxicity)
58. Venditti M, Falcone M, Corrao S, Licata G, Serra P; Study Group of the Italian Society of Internal Medicine. Outcomes of patients hospitalized with community-acquired, health care-associated, and hospital-acquired pneumonia. Ann Intern Med. 2009 Jan 6;150(1):19-26.
59. Sjögren P, Nilsson E, Forsell M, Johansson O, Hoogstraate J. A systematic review of the preventive effect of **oral hygiene** on pneumonia and respiratory tract infection in elderly people in hospitals and nursing homes: effect estimates and methodological quality of randomized controlled trials. J Am Geriatr Soc. 2008 Nov;56(11):2124-30. Epub 2008 Sep 15.
60. Yandiola PP, Capelastegui A, Quintana J, et al. Prospective comparison of severity scores for predicting clinically relevant outcomes for patients hospitalized with community-acquired pneumonia. Chest. 2009 Jun;135(6):1572-9. Epub 2009 Jan 13. (Original) The **SCAP score** is as accurate or better than other current scoring systems in predicting adverse outcomes in patients hospitalized with CAP while helping classify patients into different categories of increasing risk for potentially closer monitoring.
61. Dublin Sascha, Jackson Michael L, Nelson Jennifer C, et al. **Statin use** and risk of community acquired pneumonia in older people: population based case-control study. BMJ 2009;338:b2137, doi: 10.1136/bmj.b2137 (Published 16 June 2009)
62. Mills K, Graham AC, Winslow BT, Springer KL. Treatment of **nursing home-acquired pneumonia**. Am Fam Physician. 2009 Jun 1;79(11):976-82.
63. Welker JA, Huston M, McCue JD. **Antibiotic timing** and errors in diagnosing pneumonia. Arch Intern Med. 2008 Feb 25;168(4):351-6.
64. Kaplan V, Clermont G, Griffin MF, et al. Pneumonia: still the old man's friend? Arch Intern Med. 2003 Feb 10;163(3):317-23.
65. Musher DM, Rueda AM, et al. The association between pneumococcal pneumonia and acute **cardiac events**. Clin Infect Dis. 2007 Jul 15;45(2):158-65. Epub 2007 Jun 6.
66. Charles PG, Wolfe R, Whitby M, Fine MJ, et al. Australian Community-Acquired Pneumonia Study Collaboration, Grayson ML. **SMART-COP**: a tool for predicting the need for intensive respiratory or vasopressor support in community-acquired pneumonia. Clin Infect Dis. 2008 Aug 1;47(3):375-84.
67.Ramirez J, Aliberti S, Mirsaeidi M, et al. Acute **myocardial infarction** in hospitalized patients with community-acquired pneumonia. Clin Infect Dis. 2008 Jul 15;47(2):182-7.
68. Shorr AF, Bodi M, Rodriguez A, et al. CAPUCI Study Investigators. Impact of antibiotic **guideline compliance** on duration of mechanical ventilation in critically ill patients with community-acquired pneumonia. Chest. 2006 Jul;130(1):93-100.
69. Mortensen EM, et al. Effects of **guideline-concordant** antimicrobial therapy on mortality among patients with community-acquired pneumonia. Am J Med. 2004 Nov 15;117(10):726-31.
70. Yealy DM, et al. Effect of increasing the intensity of **implementing** pneumonia guidelines: a randomized, controlled trial. Ann Intern Med. 2005 Dec 20;143(12):881-94.
71. Fishbane S, Niederman MS, Daly C, et al. The impact of standardized **order sets** and intensive clinical case management on outcomes in community-acquired pneumonia. Arch Intern Med. 2007 Aug 13-27;167(15):1664-9.
72. Niederman MS. Making sense of **scoring systems** in community acquired pneumonia. Respirology. 2009 Apr;14(3):327-35.
73. Brito V, Niederman MS. Healthcare-associated pneumonia is a heterogeneous disease, and all patients do not need the same broad-spectrum antibiotic therapy as complex nosocomial pneumonia. Curr Opin Infect Dis. 2009 Jun;22(3):316-25.
74. Liapikou A, Ferrer M, Polverino E, et al. Severe Community-Acquired Pneumonia: Validation of the Infectious Diseases Society of America/American Thoracic Society

Guidelines to Predict an **Intensive Care** Unit Admission. Clin Infect Dis. 2009 Jan 13. [Epub ahead of print]
75. Niederman MS. Biological markers to determine eligibility in trials for community-acquired pneumonia: focus on **procalcitonin**. Clin Infect Dis. 2008 Dec 1;47 Suppl 3:S127-32.
76. Lim WS, et al. Defining community acquired pneumonia severity on presentation to hospital: an international derivation and validation study. Thorax. 2003 May;58(5):377-82.
77. Aujesky D, Fine MJ. The **pneumonia severity index**: a decade after the initial derivation and validation. Clin Infect Dis. 2008 Dec 1;47 Suppl 3:S133-9.
78. Aujesky D, Auble TE, Yealy DM, et al. Prospective comparison of three validated prediction rules for prognosis in community-acquired pneumonia. Am J Med. 2005 Apr;118(4):384-92.
79. Valencia M, et al. Pneumonia severity index class v patients with community-acquired pneumonia: characteristics, outcomes, and value of severity scores. Chest. 2007 Aug;132(2):515-22. Epub 2007 May 15.
80. Metersky ML, Ma A, Bratzler DW, Houck PM. Predicting bacteremia in patients with community-acquired pneumonia. Am J Respir Crit Care Med. 2004 Feb 1;169(3):342-7. Epub 2003 Nov 20.
81. Vanderkooi OG, Low DE, Green K, Powis JE, McGeer A; Toronto Invasive Bacterial Disease Network. Predicting antimicrobial resistance in invasive pneumococcal infections. Clin Infect Dis. 2005 May 1;40(9):1288-97. Epub 2005 Mar 31.
82. Yu VL, Chiou CC, Feldman C, et al.; International Pneumococcal Study Group. An international prospective study of pneumococcal bacteremia: correlation with in vitro **resistance**, antibiotics administered, and clinical outcome. Clin Infect Dis. 2003 Jul 15;37(2):230-7. Epub 2003 Jul 7.
83. Baddour LM, Yu VL, Klugman KP, Feldman C, et al. International Pneumococcal Study Group. **Combination antibiotic** therapy lowers mortality among severely ill patients with pneumococcal bacteremia. Am J Respir Crit Care Med. 2004 Aug 15;170(4):440-4. Epub 2004 Jun 7.
84. Leroy O, Saux P, Bédos JP, Caulin E. Comparison of levofloxacin and **cefotaxime combined with ofloxacin** for ICU patients with community-acquired pneumonia who do not require vasopressors. Chest. 2005 Jul;128(1):172-83.
85. Lodise TP, Kwa A, Cosler L, Gupta R, Smith RP. Comparison of beta-lactam and macrolide **combination** therapy versus fluoroquinolone monotherapy in hospitalized Veterans Affairs patients with community-acquired pneumonia. Antimicrob Agents Chemother. 2007 Nov;51(11):3977-82. Epub 2007 Aug 20.
86. Torres A, Garau J, Arvis P, et al.; MOTIV (MOxifloxacin Treatment IV) Study Group. Moxifloxacin monotherapy is effective in hospitalized patients with community-acquired pneumonia: the MOTIV study--a randomized clinical trial. Clin Infect Dis. 2008 May 15;46(10):1499-509.
87. Kovacs JA, Masur H. Evolving health effects of **Pneumocystis**: one hundred years of progress in diagnosis and treatment. JAMA. 2009 Jun 24;301(24):2578-85.
88. Schuetz Philipp; Christ-Crain Mirjam; Thomann Robert; et al.; for the ProHOSP Study Group. Effect of **Procalcitonin**-Based Guidelines vs Standard Guidelines on Antibiotic Use in Lower Respiratory Tract Infections: The ProHOSP Randomized Controlled Trial. JAMA. 2009;302(10):1059-1066.
89 Arnold Forest W.; LaJoie A. Scott; Brock Guy N.; et al.; for the Community-Acquired Pneumonia Organization (CAPO) Investigators. Improving Outcomes in Elderly Patients With Community-Acquired Pneumonia by **Adhering** to National **Guidelines**: Community-Acquired Pneumonia Organization International Cohort Study Results. Arch Intern Med. 2009;169(16):1515-1524.
90. McCabe Caitlin; Kirchner Cheryl; Zhang Huiling; et al. **Guideline-Concordant Therapy** and Reduced Mortality and Length of Stay in Adults With Community-Acquired Pneumonia: Playing by the Rules. Arch Intern Med. 2009;169(16):1525-1531.
91. Miano TA, Reichert MG, Houle TT, et al. Nosocomial pneumonia risk and stress ulcer prophylaxis: a comparison of pantoprazole vs **ranitidine** in cardiothoracic surgery patients. Chest. 2009 Aug;136(2):440-7.
92. Rello J et al. Severity of pneumococcal pneumonia associated with genomic **bacterial load**. Chest 2009 Sep; 136:832.
93. Niederman M. et al. **Community-Acquired Pneumonia**-In the Clinic. Ann Intern Med Oct 6 2009.
94. Bjerre LM, Verheij TJ, Kochen MM. Antibiotics for community acquired pneumonia in **adult outpatients**. **Cochrane** Database Syst Rev. 2009 Oct 7;(4):CD002109. Currently available evidence from RCTs is insufficient to make evidence-based recommendations for the choice of antibiotic to be used for the treatment of CAP in ambulatory patients.
95. Nazarian DJ, Eddy OL, Lukens TW, Weingart SD, Decker WW. Clinical policy: critical issues in the management of adult patients presenting to the **emergency department** with community-acquired pneumonia. Ann Emerg Med. 2009 Nov;54(5):704-31. http://www.acep.org/WorkArea/DownloadAsset.aspx?id=45809
96. Labelle AJ, Arnold H, Reichley RM, et al. A comparison of culture-positive and culture-negative **healthcare-associated** pneumonia. Chest. 2009 Dec 4.
97. Siempos II, Ntaidou TK, Falagas ME. Impact of the administration of **probiotics** on the incidence of ventilator-associated pneumonia: A meta-analysis of randomized controlled trials. Crit Care Med. 2009 Dec 15.
98. Bouadma L, Luyt CE, Tubach F, et al. Use of **procalcitonin** to reduce patients` exposure to antibiotics in intensive care units (PRORATA trial): a multicentre randomised controlled trial. Lancet. 2010 Jan 22.
99. Snijders D, Daniels JM, de Graaff CS, et al. Efficacy of **Corticosteroids** in Community-acquired Pneumonia - A Randomized Double Blinded Clinical Trial. Am J Respir Crit Care Med. 2010 Feb 4.
100. Jung YJ, Koh Y, Hong SB, et al. Effect of vancomycin plus **rifampicin** in the treatment of nosocomial methicillin-resistant Staphylococcus aureus (**MRSA**) pneumonia. Crit Care Med. 2010 Jan;38(1):175-80.
101. Eurich DT, Sadowski CA, Simpson SH, et al. Recurrent community-acquired pneumonia in patients starting **acid-suppressing drugs**. Am J Med. 2010 Jan;123(1):47-53.
102. Lobo LJ, Reed KD, Wunderink RG. Expanded Clinical Presentation of **Community-Acquired MRSA** Pneumonia. Chest. 2010 Feb 19.
103. Ross, JS., Normand, Sharon-Lise T., Wang, Yun, et al. Hospital **Volume** and 30-Day **Mortality** for Three Common Medical Conditions. N Engl J Med 2010 362: 1110-1118.
104. Esayag Y, Nikitin I, Bar-Ziv J, et al. Diagnostic value of **chest radiographs** in bedridden patients suspected of having pneumonia. Am J Med. 2010 Jan;123(1):88.e1-5.
105. Trifirò Gianluca, Gambassi Giovanni, Sen Elif F., et al. Association of **Community-Acquired Pneumonia** With **Antipsychotic** Drug Use in Elderly Patients: A Nested Case–

Control Study.*Ann Intern Med* April 6, 2010.
106. Terragni Pier Paolo; Antonelli Massimo; Fumagalli Roberto; et al. Early vs Late **Tracheotomy** for Prevention of Pneumonia in Mechanically Ventilated Adult ICU Patients: A Randomized Controlled Trial. *JAMA*. 2010;303(15):1483-1489.
107. Gaieski DF et al. Impact of **time to antibiotics** on survival in patients with severe sepsis or septic shock in whom early goal-directed therapy was initiated in the emergency department. *Crit Care Med* 2010 Apr; 38:1045.
108. Cals JW, Schot MJ, de Jong SA, et al. Point-of-care **C-reactive protein** testing and antibiotic prescribing for respiratory tract infections: a randomized controlled trial. Ann Fam Med. 2010 Mar-Apr;8(2):124-33.
109. Kabra SK, Lodha R, Pandey RM. Antibiotics for community-acquired pneumonia in children. Cochrane Database Syst Rev. 2010 Mar 17;3:CD004874.
110. Peleg AY, Hooper DC. **Hospital-acquired** infections due to gram-negative bacteria. N Engl J Med. 2010 May 13;362(19):1804-13.
111. Givens JL.; Jones RN.; Shaffer ML.; et al. Survival and Comfort After Treatment of Pneumonia in **Advanced Dementia**. Arch Intern Med. 2010;170(13):1102-1107.
112. Mulholland S, Gavranich JB, Chang AB. Antibiotics for community-acquired lower respiratory tract infections secondary to **Mycoplasma pneumoniae in children**. Cochrane Database Syst Rev. 2010 Jul 7;7:CD004875. There is insufficient evidence to draw any specific conclusions about the efficacy of antibiotics for this condition in children (although one trial suggests macrolides may be efficacious in some children with LRTI secondary to Mycoplasma). The use of antibiotics has to be balanced with possible adverse events. There is still a need for high quality, double-blinded RCTs to assess the efficacy and safety of antibiotics for LRTI secondary to M. pneumoniae in children.
113. Rotstein C, et al. Clinical practice guidelines for hospital-acquired pneumonia and ventilator-associated pneumonia in adults. **Can** J Infect Dis Med Microbiol 2008Jan;19;1:19-53.
114. Kalil AC, Murthy MH, Hermsen ED, et al. Linezolid versus vancomycin or teicoplanin for nosocomial pneumonia: systematic review & meta-analysis. Crit Care Med.2010Jul 15.
115. FDA Aug/10 reminded healthcare professionals of an **increased mortality** risk associated with the use of the intravenous antibacterial Tygacil (**tigecycline**) compared to that of other drugs used to treat a variety of serious infections. The increased risk was seen most clearly in patients treated for hospital-acquired pneumonia, especially ventilator-associated pneumonia, but was also seen in patients with complicated skin and skin structure infections, complicated intra-abdominal infections and diabetic foot infections.
116. Sorde Roger; Falco Vicenc; Lowak Michael; et al. Current and Potential Usefulness of **Pneumococcal Urinary Antigen** Detection in Hospitalized Patients With Community-Acquired Pneumonia to Guide Antimicrobial Therapy. Arch Intern Med. 2010;0(2010):archinternmed.2010.347.
117. Dalton Bruce R, Zuege Danny J, Shahpori Reza, et al. Concomitant **Ceftriaxone** and High-Concentration Intravenous **Calcium** Therapy in Adult Critical Care Patients: A Matched Cohort Study. Ahead of Print on 1 July 2010, DOI 10.1345/aph.1M745. Ann Pharmacother ;44:1158-1163.
118. Walkey AJ, O'Donnell MR, Wiener RS. Linezolid versus Glycopeptide Antibiotics for the Treatment of Suspected Methicillin-Resistant Staphylococcus Aureus Nosocomial Pneumonia: A Meta-Analysis of Randomized Controlled Trials. Chest. 2010 Sep 23.
119. Lassi ZS, Haider BA, Bhutta ZA. **Zinc supplementation** for the prevention of pneumonia in children aged 2 months to 59 months. Cochrane Database Syst Rev. 2010 Dec 8;12:CD005978.
120. Tessmer A, Welte T, Schmidt-Ott R et al. for CAPNETZ study group. **Influenza vaccination** is associated with reduced severity of community acquired pneumonia. Eur Respir J. 2010 Dec 9.
121. Cai Y, Wang R, Liang B, Bai N, Liu Y. Effectiveness and safety of **tigecycline** for the treatment of infectious disease: a systematic review and meta-analysis. Antimicrob Agents Chemother. 2010 Dec 20.
122. Hazir Tabish, Nisar Yasir Bin, Abbasi Saleem, et al. Comparison of Oral **Amoxicillin** with Placebo for the Treatment of **World Health Organization–Defined** Nonsevere **Pneumonia** in Children Aged 2–59 Months: A Multicenter, Double-Blind, Randomized, Placebo-Controlled Trial in Pakistan. Clin Infect Dis. (2011) 52(3): 293-300.
123. Weiss Anna K., Hall Matthew, Lee Grace E., et al. Adjunct **Corticosteroids in Children** Hospitalized With Community-Acquired Pneumonia. Pediatrics, Jan 2011.
124. Kett DH, Cano E, Quartin AA,et al; Improving Medicine through Pathway Assessment of Critical Therapy of Hospital-Acquired Pneumonia (**IMPACT-HAP**) Investigators. Implementation of guidelines for management of possible multidrug-resistant pneumonia in intensive care: observational, multicentre cohort study. Lancet Infect Dis. 2011 Jan 19.
125. Martín-Loeches I, Sanchez-Corral A, Diaz E, et al; H1N1 SEMICYUC Working Group. Community-Acquired Respiratory **Coinfection in Critically Ill Patients With Pandemic** 2009 Influenza A(H1N1) Virus. Chest. 2011 Mar;139(3):555-62.
126. Yu VL. Guidelines for **hospital-acquired pneumonia and health-care-associated pneumonia**: a vulnerability, a pitfall, & fatal flaw. Lancet Infect Dis. 2011Mar;11(3):248-52.
127. Voiriot G, Dury S, Parrot A, et al. **Nonsteroidal antiinflammatory drugs** may affect the presentation & course of community-acquired pneumonia.Chest.2011Feb;139(2):387-94.
128. Roquilly Antoine, Mahe Pierre Joachim, Seguin Philippe, et al. **Hydrocortisone** Therapy for Patients With Multiple Trauma: The Randomized Controlled HYPOLYTE Study . JAMA. 2011;305(12):1201-1209.doi:10.1001/jama.2011.360 (reduced risk of hospital acquired pneumonia)
129. Edwards P, Arango M, Balica L, Cottingham R, et al. CRASH trial collaborators. Final results of MRC CRASH, a randomized placebo-controlled trial of intravenous **corticosteroid** in adults with head injury-outcomes at 6 months. Lancet. 2005 Jun 4-10;365(9475):1957-9. (higher mortality, but no difference in pneumonia)
130. Ruuskanen O, Lahti E, Jennings LC et al. **Viral pneumonia**. www.thelancet.com Published online March 23, 2011 DOI:10.1016/S0140-6736(10)61459-6.
131. Ruhnke GW, Coca-Perraillon M, Kitch BT, Cutler DM. **Marked reduction in 30-day mortality** among elderly patients with community-acquired pneumonia. Am J Med. 2011 Feb;124(2):171-178.e1.
132. Chen Y, Li K, Pu H, et al. **Corticosteroids for pneumonia**. Cochrane Database Syst Rev. 2011 Mar 16;3:CD007720. In most patients with pneumonia, corticosteroids are generally beneficial for accelerating the time to resolution of symptoms. However, evidence from the included studies was not strong enough to make any recommendations.
133. Douglas I, Evans S, Smeeth L. Effect of **statin** treatment on short term mortality after pneumonia episode: cohort study. BMJ 2011;342:d1642.
134. Tang Karen L.; Eurich Dean T.; Minhas-Sandhu Jasjeet K.; et al. Incidence, Correlates, and **Chest Radiographic Yield of New Lung Cancer** Diagnosis in 3398 Patients With Pneumonia. Arch Intern Med. 2011;0(2011):archinternmed.2011.155.

135. Sun HY, Fujitani S, Quintiliani R, Yu VL. Pneumonia Due to **Pseudomonas aeruginosa**: Part II: Antimicrobial Resistance, Pharmacodynamic Concepts, and Antibiotic Therapy. Chest. 2011 May;139(5):1172-85.
136. Walkey AJ, O'Donnell MR, Wiener RS. **Linezolid vs Glycopeptide** (vancomycin or teicoplanin) Antibiotics for the Treatment of Suspected Methicillin-Resistant Staphylococcus aureus Nosocomial Pneumonia: A Meta-analysis of Randomized Controlled Trials. Chest. 2011 May;139(5):1148-55.
137. Nambiar S, Rellosa N, Wassel RT, et al. **Linezolid-Associated Peripheral and Optic Neuropathy** in Children. Pediatrics. 2011 May 9.
138. Watkins RR, Lemonovich TL. Diagnosis and Management of **Community-Acquired Pneumonia in Adults** . Am Fam Physician. 2011;83(11):1299-1306.
139. Meijvis SC, Hardeman H, Remmelts HH, et al. **Dexamethasone** and length of hospital stay in patients with community-acquired pneumonia: a randomised, double-blind, placebo-controlled trial. Lancet. 2011 May 31.
140. Wilson KC, Schunemann HJ. An Appraisal of the Evidence Underlying **Performance Measures** for Community-acquired Pneumonia. Am J Respir Crit Care Med. 2011 Jun 1;183(11):1454-62.
141. Williams DJ et al. **Influenza coinfection** and outcomes in children with complicated pneumonia. *Arch Pediatr Adolesc Med* 2011 Jun; 165:506.
142. Schuetz P, Chiappa V, Briel M, et al. **Procalcitonin algorithms** for antibiotic therapy decisions: a systematic review of randomized controlled trials and recommendations for clinical algorithms. Arch Intern Med. 2011 Aug 8;171(15):1322-31.
143. Neuman MI et al. **Prediction of pneumonia in a pediatric emergency department**. Pediatrics 2011 Aug; 128:246.
144. Peters J, Singh H, Brooks EG, et al. **Persistence** of Community-Acquired Respiratory Distress Syndrome Toxin-Producing **Mycoplasma pneumoniae** in Refractory Asthma. Chest. 2011 Aug;140(2):401-7.
145. Sandiumenge A, Lisboa T, Gomez F, et al. Effect of **antibiotic diversity on ventilator associated pneumonia (VAP) caused by ESKAPE** organisms. Chest. 2011 Jun 9.
146. Neuman MI, Monuteaux MC, Scully KJ, Bachur RG. **Prediction of pneumonia in a pediatric emergency department**. Pediatrics. 2011 Aug;128(2):246-53.
147. Bradley JS, Byington CL, Shah SS, et al. The management of community-acquired pneumonia in **infants and children older than 3 months of age**: clinical practice guidelines by the pediatric infectious diseases society and the Infectious Diseases Society of America. (IDSA)Clin Infect Dis. 2011 Oct;53(7):e25-76.
148. Anti-infective Review Panel. **Anti-infective Guidelines for Community-acquired Infections**. Canadian - New-**2012. Updated 2019**. Toronto: MUMS Guideline Clearinghouse. http://www.mumshealth.com/
149. Bafadhel M, Clark TW, Reid C, et al. **Procalcitonin and C-reactive protein** in hospitalized adult patients with community-acquired pneumonia or exacerbation of asthma or COPD. Chest. 2011 Jun;139(6):1410-8.
150. Naeije G, Lorent S, Vincent JL, Legros B. Continuous **epileptiform discharges** in patients treated with **cefepime** or meropenem. Arch Neurol. 2011 Oct;68(10):1303-7.
151. Labeau SO, Van de Vyver K, Brusselaers N, et al. Prevention of **ventilator-associated pneumonia** with oral antiseptics: a systematic review and meta-analysis. Lancet Infect Dis. 2011 Jul 26. In intubated patients, oral care with antiseptics reduces the risk of ventilator-associated pneumonia (VAP) as compared with oral care without antiseptics. Current evidence best supports the use of **chlorhexidine** in this population. (LOE = 1a-)
152. Varner TR, Bookstaver PB, Rudisill CN, Albrecht H. Role of **rifampin-based combination therapy** for severe community-acquired Legionella pneumophila pneumonia. Ann Pharmacother. 2011 Jul;45(7-8):967-76.
153. Finlayson O, Kapral M, Hall R, et al. On behalf of the Investigators of the Registry of the Canadian Stroke Network; For the Stroke Outcome Research Canada (SORCan) Working Group. Risk factors, inpatient care, and outcomes of **pneumonia after ischemic stroke**. Neurology. 2011 Oct 4;77(14):1338-1345.
154. Chen D, Restrepo MI, Fine MJ, et al. Observational study of **inhaled corticosteroids on outcomes for COPD patients with pneumonia**. Am J Respir Crit Care Med. 2011 Aug 1;184(3):312-6.
155. **Drugs in Pregnancy & Lactation**, 9th Ed. Briggs GE,et al. Wilkins;Baltimore, MD. 2011.
156. Bailey JL, Yeung SY. **Probiotics** for disease prevention: a focus on **ventilator-associated pneumonia**. Ann Pharmacother. 2011 Nov;45(11):1425-32. (not recommended)
157. Leis JA, Gold WL. Management of community-acquired pneumonia in the **emergency department**. CMAJ. 2012 Jan 23.
158. Haessler S, Schimmel JJ. Managing community-acquired pneumonia **during flu season**. Cleve Clin J Med. 2012 Jan;79(1):67-78.
159. Esposito S et al. **Procalcitonin** measurements for guiding antibiotic treatment in pediatric pneumonia. Respir Med. 2011 Dec;105(12):1939-45.
160. Health Canada Jan/12 Doribax (doripenem for injection) - Higher Mortality Rate and a Lower Clinical Cure Rate Observed During a Comparative Clinical Trial - Janssen Inc. Decreased Clinical Cure Rates and Increased Mortality in an Investigational Ventilator-Associated Pneumonia (VAP) Study. Doribax will be updated to reflect findings of a higher mortality rate and a lower cure rate among patients taking Doribax 1g every 8 hours in a fixed 7-day course vs a fixed 10-day course of imipenem-cilastatin.
161. Harris M, Clark J, Coote N, Fletcher P, Harnden A, McKean M, Thomson A; **British Thoracic Society** Standards of Care Committee. British Thoracic Society-BTS- guidelines for the management of community acquired **pneumonia in children**: update 2011. Thorax. 2011 Oct;66 Suppl 2:ii1-23.
162. Newman RE, Hedican EB, Herigon JC, et al. Impact of a guideline on management of **children hospitalized** with community-acquired pneumonia. Pediatrics. 2012 Mar;129(3):e597-604.
163. Basnet S, Shrestha PS, Sharma A, et al. A Randomized Controlled Trial of **Zinc** as Adjuvant Therapy for Severe Pneumonia in Young Children. Pediatrics. 2012 Mar 5.
164. Lodise TP Jr, Lomaestro B, Drusano GL. **Piperacillin-tazobactam** for Pseudomonas aeruginosa infection: clinical implications of an **extended-infusion** dosing strategy. Clin Infect Dis. 2007 Feb 1;44(3):357-63.
165. Pugh R, Grant C, Cooke RP, et al. **Short-course** versus prolonged-course antibiotic therapy for hospital-acquired pneumonia in critically ill adults. Cochrane Database Syst Rev. 2011;(10): CD007577. We conclude that for patients with VAP not due to NF-GNB, a short fixed-course (seven or eight days) antibiotic therapy may be more appropriate

than a prolonged course (10 to 15 days). Use of an individualised strategy (incorporating clinical features or serum procalcitonin) appears to safely reduce duration of antibiotic therapy for VAP.
166. Tasina E, Haidich AB, Kokkali S, Arvanitidou M. Efficacy and safety of **tigecycline** for the treatment of infectious diseases: a meta-analysis. Lancet Infect Dis. 2011 Jul 22.
167. Zhang Y, Fang C, Dong BR, et al. **Oxygen therapy for pneumonia** in adults. Cochrane Database Syst Rev. 2012 Mar 14;3:CD006607. Non-invasive ventilation can reduce the risk of death in the ICU, endotracheal intubation, shorten ICU stay and length of intubation.
168. Myers EM, Ward SL, Myers JP. Life-threatening respiratory **pasteurellosis associated with palliative pet care**. Clin Infect Dis. 2012 Mar;54(6):e55-7.
169. Bari A, Sadruddin S, Khan A, et al. Community case management of severe pneumonia with oral **amoxicillin in children aged 2–59 months** in Haripur district, Pakistan: a cluster randomised trial. Lancet 2011; 378: 1796–803.
170. Wunderink RG, Niederman MS, Kollef MH, et al. **Linezolid in methicillin-resistant Staphylococcus aureus nosocomial pneumonia**: a randomized, controlled study. Clin Infect Dis. 2012 Mar 1;54(5):621-9. (vs Vancomycin)
171. Manaseki-Holland S, Maroof Z, Bruce J, et al. Effect on the incidence of pneumonia of **vitamin D** supplementation by quarterly bolus dose to infants in Kabul: a randomised controlled superiority trial. Lancet. 2012 Apr 14;379(9824):1419-27.
172. Ray WA, Murray KT, Hall K, et al. **Azithromycin and the risk of cardiovascular death**. N Engl J Med 2012; 366:1881-90.
173. Schuetz P, Amin DN, Greenwald JL. Role of **procalcitonin** in managing adult patients with respiratory tract infections. Chest. 2012 Apr;141(4):1063-73.
174. Novack V, Macfadyen J, Malhotra A, et al. The effect of **rosuvastatin** on incident pneumonia: results from the JUPITER trial. CMAJ. 2012 Mar 19.
175. Lepper PM, Ott S, Nüesch E, et al; on behalf of the German Community Acquired Pneumonia Competence Network (CAPNETZ). **Serum glucose** levels for predicting death in patients admitted to hospital for community acquired pneumonia: prospective cohort study. BMJ. 2012 May 28;344:e3397.
176. Hunter JD. **Ventilator associated pneumonia**. Postgrad Med J. 2006 Mar;82(965):172-8.
177. FDA: Jun/12 There have been cases of a specific type of **seizure** called nonconvulsive status epilepticus associated with the use of **cefepime**, primarily in patients with renal impairment who did not receive appropriate dosage adjustments of cefepime.
178. Nijman RG, Thompson M, van Veen M, et al. Derivation and validation of **age and temperature** specific reference values and centile charts to predict lower respiratory tract infection in children with fever: prospective observational study. BMJ. 2012 Jul 3;345:e4224.
179. Carratalà J, Garcia-Vidal C, Ortega L, et al. Effect of a **3-Step Critical Pathway to Reduce Duration of Intravenous Antibiotic** Therapy and Length of Stay in Community-Acquired Pneumonia: A Randomized Controlled TrialA 3-Step Critical Pathway for CAP. Arch Intern Med. 2012 Jun 25;172(12):922-8.
180. Caldeira D, Alarcão J, et al. Risk of pneumonia associated with use of **angiotensin converting enzyme inhibitors and angiotensin receptor blockers**: systematic review and meta-analysis. BMJ 2012;345:e4260.
181. Albrich WC, Dusemund F, Bucher B, et al. Effectiveness and Safety of **Procalcitonin-Guided Antibiotic Therapy** in Lower Respiratory Tract Infections in "Real Life": An International, Multicenter Poststudy Survey (ProREAL). Arch Intern Med. 2012 May 14;172(9):715-22.
182. Bergroth E, Remes S, Pekkanen J, et al. Respiratory Tract Illnesses During the First Year of Life: Effect of **Dog and Cat Contacts**. Pediatrics. 2012 Jul 9.
183. O'Grady NP, Murray PR, Ames N. Preventing **ventilator-associated pneumonia**: does the evidence support the practice? JAMA. 2012 Jun 20;307(23):2534-9.
184. Institute for Clinical Systems Improvement (**ICSI**). **Prevention of ventilator-associated pneumonia**. Health care protocol. Bloomington (MN): ICSI; 2011 Nov.
185. MHRA Aug/12 The recommended dose of **doripenem** to treat nosocomial pneumonia in patients with augmented renal function and/or infections with pathogens with possible decreased susceptibility has been increased to 1 g every 8 hours given as a 4-hour infusion. Previous dosing regimens for doripenem in such patients were found to be insufficient.
186. Hranjec T, Rosenberger LH, Swenson B, et al. **Aggressive versus conservative initiation** of antimicrobial treatment in critically surgical patients with suspected intensive-care-unit-acquired infection: a quasi-experimental, before-after observational cohort study. Lancet Infect Dis 2012; published online Aug 28.
187. Prasad P, Sun J, Danner RL, Natanson C. Excess **deaths associated with tigecycline** after approval based on noninferiority trials. Clin Infect Dis. 2012 Jun;54(12):1699-709.
188. Choi SH, Hong SB, Ko GB et al. **Viral Infection** in Patients with Severe Pneumonia Requiring Intensive Care Unit Admission. Am J Respir Crit Care Med. 2012 Jun 14.
189. Schuetz P, Müller B, Christ-Crain M, et al. **Procalcitonin** to initiate or discontinue antibiotics in acute respiratory tract infections. Cochrane Database of Systematic Reviews 2012, Issue 9. Art. No.: CD007498. DOI: 10.1002/14651858.CD007498.pub2. Use of procalcitonin to guide initiation and duration of antibiotic treatment in patients with ARI was not associated with higher mortality rates or treatment failure. Antibiotic consumption was significantly reduced across different clinical settings and ARI diagnoses.
190. Ambroggio L, Taylor JA, Tabb LP, et al. Comparative Effectiveness of Empiric β-Lactam Monotherapy and **β-Lactam-Macrolide Combination** Therapy in Children Hospitalized with Community-Acquired Pneumonia. J Pediatr. 2012 Aug 14.
191. Cunha BA, Hamid NS, Krol V, Eisenstein L. Safety of **meropenem in patients reporting penicillin allergy**: lack of allergic cross reactions. J Chemother. 2008 Apr;20(2):233-7.
192. Hawkey PM, Livermore DM. **Carbapenem** antibiotics for serious infections. BMJ. 2012 May 31;344:e3236.
193. Stuckey-Schrock K, Hayes BL, George CM. **Community-Acquired Pneumonia in Children**. Am Fam Physician. 2012;86(7):661-667.
194. Eliakim-Raz N, Robenshtok E, Shefet D, et al. Empiric antibiotic coverage of **atypical pathogens** for community-acquired pneumonia in hospitalized adults. Cochrane Database Syst Rev. 2012 Sep 12;9:CD004418. No benefit of survival or clinical efficacy was shown with empirical atypical coverage in hospitalized patients with CAP. This conclusion relates mostly to the comparison of quinolone monotherapy to beta-lactams. Further trials, comparing beta-lactam monotherapy to the same combined with a macrolide, should be performed.
195. Layios N, Lambermont B, Canivet JL et al. **Procalcitonin** usefulness for the initiation of antibiotic treatment in intensive care unit patients. Crit Care Med.2012Aug;40(8):2304-9.
196. Obiora E, Hubbard R, Sanders RD, Myles PR. The impact of **benzodiazepines** on occurrence of pneumonia and mortality from pneumonia: a nested case-control and survival analysis in a population-based cohort. Thorax. 2012 Dec 5.

197. Reignier J, Mercier E, Le Gouge A, et al; Clinical Research in Intensive Care and Sepsis (CRICS) Group. Effect of not **monitoring residual gastric volume** on risk of ventilator-associated pneumonia in adults receiving mechanical ventilation and early enteral feeding: a randomized controlled trial. JAMA. 2013 Jan 16;309(3):249-56.
198. Corrales-Medina VF, Musher DM, Shachkina S, Chirinos JA. Acute pneumonia and the **cardiovascular system**. Lancet. 2013 Jan 15.
199. Shah VP, Tunik MG, Tsung JW. Prospective Evaluation of **Point-of-Care Ultrasonography** for the Diagnosis of Pneumonia in Children and Young Adults. Arch Pediatr Adolesc Med. 2012 Dec 10:1-7.
200. Corrales-Medina VF, Musher DM, Shachkina S, et al. Acute pneumonia and the **cardiovascular system**. Lancet. 2013 Jan 15.
201. Reissig A, Copetti R, Mathis G, et al. **Lung ultrasound in the diagnosis** and follow-up of community-acquired pneumonia: a prospective, multicenter, diagnostic accuracy study. Chest. 2012 Oct;142(4):965-72.
202. Aparasu RR, Chatterjee S, et al. Risk of pneumonia in elderly nursing home residents using **typical versus atypical antipsychotics**. Ann Pharmacother. 2013 Apr;47(4):464-74.
203. Davydow DS, Hough CL, Levine DA, et al. **Functional Disability, Cognitive Impairment, and Depression** After Hospitalization for Pneumonia. Am J Med. 2013 Mar 14.
204. Sandvall B et al. **Long-term survival** following pneumococcal pneumonia. Clin Infect Dis 2013 Apr 15; 56:1145.
205. Melsen WG, Rovers MM, Groenwold RHH, et al. Attributable **mortality of ventilator-associated pneumonia**: a meta-analysis of individual patient data from randomised prevention studies. Lancet Infect Dis 2013; online April 25.
206. van Vugt SF, Broekhuizen BD, Lammens C, et al; GRACE consortium. Use of serum **C reactive protein and procalcitonin** concentrations in addition to symptoms and signs to predict pneumonia in patients presenting to primary care with acute cough: diagnostic study. BMJ. 2013 Apr 30;346:f2450.
207. Janson C, Larsson K, Lisspers KH, et al. Pneumonia and pneumonia related mortality in patients with COPD treated with **fixed combinations of inhaled corticosteroid and long acting β2 agonist**: observational matched cohort study (PATHOS). BMJ. 2013 May 29;346:f3306.
208. Hemila H, Louhiala P. **Vitamin C** for preventing and treating pneumonia. Cochrane Database Syst Rev. 2013 Aug 8;8:CD005532. The prophylactic use of vitamin C to prevent pneumonia should be further investigated in populations who have a high incidence of pneumonia, especially if dietary vitamin C intake is low. Similarly, the therapeutic effects of vitamin C should be studied, especially in patients with low plasma vitamin C levels. The current evidence is too weak to advocate prophylactic use of vitamin C to prevent pneumonia in the general population.
209. Melsen WG, Rovers MM, Groenwold RH, et al. Attributable mortality of **ventilator-associated pneumonia**: a meta-analysis of individual patient data from randomised prevention studies. Lancet Infect Dis. 2013 Aug;13(8):665-71.
210. Shi Z, Xie H, Wang P, et al. **Oral hygiene care** for critically ill patients to prevent ventilator-associated pneumonia. Cochrane Database of Systematic Reviews 2013, Issue 8. Art. No.: CD008367. DOI: 10.1002/14651858.CD008367.pub2. Effective OHC is important for ventilated patients in intensive care. OHC that includes either chlorhexidine mouthwash or gel is associated with a 40% reduction in the odds of developing ventilator-associated pneumonia in critically ill adults. However, there is no evidence of a difference in the outcomes of mortality, duration of mechanical ventilation or duration of ICU stay
211. FDA Sep/13 notified health professionals and their medical care organizations of a new Boxed Warning describing an increased risk of death when intravenous Tygacil is used for FDA-approved uses as well as for non-approved uses. These changes to the Tygacil Prescribing Information are based on an additional analysis that was conducted for FDA-approved uses after FDA issuing a Drug Safety Communication about this safety concern in September 2010.
212. Raman K, Nailor MD, Nicolau DP, et al. **Early antibiotic discontinuation** in patients with clinically suspected **ventilator-associated pneumonia** and negative quantitative bronchoscopy cultures. Crit Care Med. 2013 Jul;41(7):1656-63.
213. Aliberti S, Cilloniz C, Chalmers JD, et al. **Multidrug-resistant pathogens** in hospitalised patients coming from the community with pneumonia: a European perspective. Thorax. 2013 Jun 17.
214. Singh N, Rogers P, Atwood CW, Wagener MM, Yu VL. **Short-course empiric antibiotic therapy** for patients with pulmonary infiltrates in the intensive care unit. A proposed solution for indiscriminate antibiotic prescription. Am J Respir Crit Care Med 2000; 162:505–511.
215. Li JZ, Winston LG, Moore DH, Bent S. Efficacy of **short-course antibiotic regimens** for community-acquired pneumonia: a meta-analysis. Am J Med 2007; 120:783–790.
216. Papazian L, Roch A, et al. Effect of **Statin** Therapy on Mortality in Patients With **Ventilator-Associated Pneumonia**: A Randomized Clinical Trial. JAMA. 2013 Oct 9.
217. Bateman BT, Bykov K, Choudhry NK, et al. Type of **stress ulcer prophylaxis** (**PPIs** vs H2) and risk of nosocomial pneumonia in cardiac surgical patients: cohort study. BMJ. 2013 Sep 19;347:f5416.
218. Eurich DT, Lee C, Marrie TJ, Majumdar SR. **Inhaled corticosteroids and risk of recurrent pneumonia**: a population-based, nested case-control study. Clin Infect Dis. 2013 Oct;57(8):1138-44.
219. Williams DJ, Hall M, Shah SS, et al. **Narrow Vs Broad-spectrum** Antimicrobial Therapy for **Children Hospitalized With Pneumonia**. Pediatrics. 2013 Nov;132(5):e1141-8.
220. van Vugt SF, Verheij TJ, et al. Diagnosing **pneumonia in patients with acute cough**: clinical judgment compared to chest radiography. Eur Respir J. 2013 Oct;42(4):1076-82.
221. Paul M, Lador A, Grozinsky-Glasberg S, et al. **Beta lactam antibiotic monotherapy versus beta lactam-aminoglycoside antibiotic combination** therapy for sepsis. Cochrane Database Syst Rev. 2014 Jan 7;1:CD003344. The addition of an aminoglycoside to beta lactams for sepsis should be discouraged. All-cause mortality rates are unchanged. Combination treatment carries a significant risk of nephrotoxicity.
222. Queen MA, Myers AL, Hall M, et al. **Comparative Effectiveness of Empiric** Antibiotics for Community-Acquired Pneumonia. Pediatrics. 2013 Dec 9
223. Hollm-Delgado MG, Stuart EA, Black RE. Acute Lower Respiratory Infection Among **Bacille Calmette-Guerin** (BCG)-Vaccinated Children. Pediatrics. 2014 Jan;133(1):e73-81.
224. FDA Mar/14: The U.S. Food and Drug Administration (FDA) has concluded that **Doribax (doripenem),** an antibacterial drug that has been used to treat patients who develop pneumonia while on ventilators, carries an increased risk of death and lower clinical cure rates compared to use of imipenem and cilastatin for injection (marketed in the U.S. under the name Primaxin).

225. Corrales-Medina VF, Taljaard M, Fine MJ, et al. **Risk stratification for cardiac complications** in patients hospitalized for community-acquired pneumonia. Mayo Clin Proc. 2014 Jan;89(1):60-8.
226. Rothberg MB, Pekow PS, Priya A, Lindenauer PK. Variation in **diagnostic coding of patients with pneumonia** and its association with hospital riskstandardized mortality rates. A cross-sectional analysis. Ann Intern Med. 2014; 160:380-8.
227. Angoulvant F, Levy C, et al. Early impact of 13-**valent pneumococcal conjugate vaccine** on community-acquired pneumonia in children. Clin Infect Dis 2014; 58:918–24.
228. Su VY, Liu CJ, Wang HK, et al. **Sleep apnea** and risk of pneumonia: a nationwide population-based study. CMAJ. 2014 Mar 3.
229. Ochoa-Gondar O, Vila-Corcoles A, Rodriguez-Blanco T, et al. Effectiveness of the **23-valent pneumococcal polysaccharide vaccine** against community-acquired pneumonia in the general population aged ≥60 years: 3 years of follow-up in the CAPAMIS study. Clin Infect Dis 2014; 58:909–17.
230. Chang CC, Cheng AC, Chang AB. **Over-the-counter (OTC) medications to reduce cough** as an adjunct to antibiotics for acute pneumonia in children and adults. Cochrane Database Syst Rev. 2014 Mar 10;3:CD006088. There is insufficient evidence to decide whether OTC medications for cough associated with acute pneumonia are beneficial. Mucolytics may be beneficial but there is insufficient evidence to recommend them as an adjunctive treatment for acute pneumonia. This leaves only theoretical recommendations that OTC medications containing codeine and antihistamines should not be used in young children.
231. Wunderink RG, Waterer GW. Clinical practice. **Community-acquired pneumonia**. N Engl J Med. 2014 Feb 6;370(6):543-51.
232. Klompas M, Speck K, Howell MD, et al. Reappraisal of Routine Oral Care With **Chlorhexidine** Gluconate for Patients Receiving **Mechanical Ventilation**: Systematic Review and Meta-Analysis. JAMA Intern Med. 2014 Mar 24.
233. Li N, Zhou X, Yuan J, et al. **Ceftriaxone and acute renal failure** in children. Pediatrics. 2014 Apr;133(4):e917-22.
234. Dimopoulos G, Poulakou G, Pneumatikos IA, et al. **Short- vs long-duration** antibiotic regimens for **ventilator-associated pneumonia**: a systematic review and meta-analysis. Chest. 2013 Dec;144(6):1759-67.
235. Nyboe C, Olsen MS, et al. Risk of Pneumonia in Adults With Closed Versus Unclosed **Atrial Septal Defect** (from a Nationwide Cohort Study). Am J Cardiol. 2014 Apr 18.
236. Qiu H, Tian LW, Pun VC, et al. **Coarse particulate matter** associated with increased risk of emergency hospital admissions for pneumonia in Hong Kong. Thorax. 2014 Aug 27.
237. Lee JS, Nsa W, Hausmann LR, et al. Quality of Care for **Elderly Patients Hospitalized for Pneumonia in the United States**, 2006 to 2010. JAMA Intern Med. 2014 Sep 8.
238. Leyenaar JK, Shieh MS, Lagu T, et al. Variation and Outcomes Associated With **Direct Hospital Admission Among Children** With Pneumonia in the United States. JAMA Pediatr. 2014 Jul 7.
239. Neuman MI, Hall M, Gay JC, et al. **Readmissions Among Children** Previously Hospitalized With Pneumonia. Pediatrics. 2014 Jun 23.
240. Almirall J, Serra-Prat M, Bolíbar I, et al; Study Group of Community-Acquired Pneumonia in Catalan Countries (PACAP). **Passive smoking** at home is a risk factor for community-acquired pneumonia in older adults: a population-based case-control study. BMJ Open. 2014 Jun 13;4(6):e005133.
241. Colin AA, Yousef S, Forno E, et al. Treatment of **Mycoplasma** pneumoniae in Pediatric Lower Respiratory Infection. Pediatrics. 2014 May 26.
242. Biondi E, McCulloh R, Alverson B, et al. Treatment of **Mycoplasma** Pneumonia: A Systematic Review. Pediatrics. 2014 May 26.
243. Garin N, Genne D, Carballo S, et al. **β-Lactam monotherapy vs β-lactam–macrolide combination** treatment in moderately severe community-acquired pneumonia: a randomized noninferiority trial [online October 6, 2014]. *JAMA Intern Med*. doi:10.1001 /jamainternmed.2014.4887.
244. Nie W, Li B, Xiu Q. **β-Lactam/macrolide dual therapy versus β-lactam monotherapy** for the treatment of community-acquired pneumonia in adults: a systematic review and meta-analysis. J Antimicrob Chemother. 2014;69(6):1441-1446.
245. Musher DM, Thorner AR. **Community-acquired pneumonia**. N Engl J Med. 2014 Oct 23;371(17):1619-28.
246. Bo L, Li J, Tao T, Bai Y, Ye X,Hotchkiss RS, KollefMH, Crooks NH,Deng X. **Probiotics for preventing ventilator-associated pneumonia**. CochraneDatabase of Systematic Reviews 2014, Issue 10. Art.No.:CD009066.DOI: 10.1002/14651858.CD009066.pub2. Evidence suggests that use of probiotics is associated with a reduction in the incidence of VAP. However, the quality of the evidence is low and the exclusion of the one study that did not provide a robust definition of VAP increased the uncertainty in this finding. The available evidence is not clear regarding a decrease in ICU or hospital mortality with probiotic use. Three trials reported on the incidence of diarrhoea and the pooled results indicate no clear evidence of a difference. The results of this meta-analysis do not provide sufficient evidence to draw conclusions on the efficacy and safety of probiotics for the prevention of VAP in ICU patients.
247. Lindstrand A, Bennet R, Galanis I, et al. Sinusitis and Pneumonia Hospitalization After Introduction of **Pneumococcal Conjugate Vaccine**. Pediatrics. 2014 Nov 10.
248. Smith SB, Ruhnke GW, Weiss CH, et al. Trends in pathogens among patients **hospitalized for pneumonia from 1993 to 2011**. JAMA Intern Med. 2014 Nov 1;174(11):1837-9.
249. Eccles S, Pincus C, Higgins B, Woodhead M; Guideline Development Group. Diagnosis and management of **community and hospital acquired pneumonia in adults**: summary of **NICE** guidance. BMJ. 2014 Dec 3;349:g6722.

250. N**I**CE: National Institute for Health and Care Excellence. **Pneumonia (including community acquired pneumonia). 2014**. www.nice.org.uk/guidance/cg191.
251. Zhong NS, Sun T, Zhuo C, et al. **Ceftaroline fosamil versus ceftriaxone** for the treatment of Asian patients with community-acquired pneumonia: a randomised, controlled, double-blind, phase 3, non-inferiority with nested superiority trial. Lancet Infect Dis. 2014 Dec 19.
252. Blum CA, Nigro N, Briel M, et al. Adjunct **prednisone therapy for patients with community-acquired pneumonia**: a multicentre, double-blind, randomised, placebo-controlled trial. Lancet 2015; online Jan 19.
253. Corrales-Medina VF, Alvarez KN, et al. Association between hospitalization for pneumonia and subsequent **risk of cardiovascular disease**. *JAMA* 2015; 313:264-274.
254. Warusevitane A, Karunatilake D, Sim J, et al. Safety and Effect of Me**toclopramide to Prevent Pneumonia** in Patients With Stroke Fed via Nasogastric Tubes Trial.

Stroke. 2015 Feb;46(2):454-60.
255. Jain S, Williams DJ, Arnold SR, et. al, **Community-acquired pneumonia requiring hospitalization among U.S. children**. N Engl J Med. 2015 Feb 26;372(9):835-45.
256. Paul KJ, Walker RL, Dublin S. **Anticholinergic Medications** and Risk of Community-Acquired Pneumonia in Elderly Adults: A Population-Based Case-Control Study. J Am Geriatr Soc. 2015 Mar 2.
257. Chan JY, Stern DA, Guerra S, et al. **Pneumonia in Childhood and Impaired Lung Function in Adults**: A Longitudinal Study. Pediatrics. 2015 Mar 2.
258. Torres A, Sibila O, Ferrer M, et al. Effect of **corticosteroids on treatment failure among hospitalized patients with severe community-acquired pneumonia** and high inflammatory response: a randomized clinical trial. JAMA. 2015 Feb 17;313(7):677-86.
259. Chen YX, Li CS. **Lactate** on emergency department arrival as a predictor of mortality and site-of-care in pneumonia patients: a cohort study. Thorax. 2015 Feb 23.
260. Kolditz M, Ewig S, Klapdor B, et al. Community-acquired pneumonia as **medical emergency: predictors of early deterioration**.Thorax. 2015 Mar 17.
261. Postma DF, van Werkhoven CH, van Elden LJ, et al; **CAP-START** Study Group. **Antibiotic Treatment Strategies** for Community-Acquired Pneumonia in Adults. N Engl J Med. 2015 Apr 2;372(14):1312-1323.
262. Polgreen LA, Cook EA, Brooks JM, et al. Increased **statin** prescribing does **not lower pneumonia risk**. Clin Infect Dis. 2015 Mar 10.
263. Park H, Adeyemi AO, Rascati KL. Direct Medical **Costs and Utilization of Health Care Services** to Treat Pneumonia in the United States: An Analysis of the 2007-2011 Medical Expenditure Panel Survey. Clin Ther. 2015 May 19.
264. Pereda MA, Chavez MA, Hooper-Miele CC, et al. **Lung Ultrasound** for the Diagnosis of Pneumonia in Children: A Meta-analysis.Pediatrics. 2015 Apr;135(4):714-722.
265. Rambaud-Althaus C, Althaus F, Genton B, et al. **Clinical features for diagnosis of pneumonia in children younger than 5 years**: a systematic review and meta-analysis. Lancet Infect Dis. 2015 Apr;15(4):439-50. Standard clinical signs and symptoms are minimally useful in accurately diagnosing pneumonia in children younger than 5 years. The most useful signs and symptoms for ruling in pneumonia included a respiratory rate higher than 50 breaths per minute, grunting, chest retractions, and nasal flaring. The most useful signs and symptoms (when absent) for excluding the diagnosis of pneumonia included cough, history of fever, and a respiratory rate higher than 40 breaths per minute.
266. Padilla K, Logan L, Codispoti C, et al. **Persistent Pneumonia in an Infant**. Pediatrics. 2015 Jun 29.
267. Williams DJ, Edwards KM, Self WH, et al. **Antibiotic Choice for Children Hospitalized With Pneumonia** and Adherence to National Guidelines. Pediatrics. 2015 Jun 22.
268. Jain S, Self WH, Wunderink RG, et al; CDC EPIC Study Team. **Community-Acquired Pneumonia Requiring Hospitalization** among U.S. Adults. N Engl J Med. 2015 Jul 14.
269. Shindo Y, Ito R, Kobayashi D, et al, on behalf of the Central Japan Lung Study Group. **Risk factors for 30-day mortality** in patients with pneumonia who receive appropriate initial antibiotics: an observational cohort study. Lancet Infect Dis 2015; online July 3.
270. Chisti MJ, Salam MA, Smith JH, et al. **Bubble continuous positive airway pressure for children** with severe pneumonia and hypoxaemia in Bangladesh: an open, randomized controlled trial. Lancet 2015; published online Aug 19.
271. Prina E, Ranzani OT, Torres A. **Community-acquired pneumonia**. Lancet. 2015 Aug 12.
272. Siemieniuk RA, Meade MO, Alonso-Coello P, et al. **Corticosteroid Therapy** for Patients **Hospitalized With ommunity-Acquired Pneumonia**: A Systematic Review and Meta-analysis. Ann Intern Med. 2015 Aug 11.
273. Lambert AA, Lam JO, Paik JJ, et al. Risk of **community-acquired pneumonia** with outpatient proton-pump inhibitor therapy: a systematic review and meta-analysis. PLoS One. 2015 Jun 4;10(6):e0128004.
274. Bell MM. **Lipoid pneumonia (mineral oil)** : An unusual and preventable illness in elderly patients. Can Fam Physician. 2015 Sep;61(9):775-7.
275. Kalra L, Irshad S, Hodsoll J, et al. **Prophylactic antibiotics after stroke** for reducing pneumonia in patients with dysphagia (**STROKE-INF**): a prospective, cluster-randomised, open-label, masked endpoint, controlled clinical trial. Lancet 2015; online September 4.
276. Ahn A, Edwards KM, et al. **Secondhand Smoke Exposure** and Illness Severity among Children Hospitalized with Pneumonia. J Pediatr. 2015 Oct;167(4):869-874.e1.
277. Casey C, Fullerton MJ, Somerville N. Common Questions About Pneumonia in **Nursing Home Residents**. Am Fam Physician. 2015;92(7):612-620.
278. Grijalva CG, Zhu Y, Williams DJ, et al. Association Between Hospitalization With Community-Acquired Laboratory-Confirmed Influenza Pneumonia and **Prior Receipt of Influenza Vaccination**. JAMA. 2015 Oct 5:1488-1497.
279. Niederman MS. **In the Clinic: Community-Acquired Pneumonia**. Ann Intern Med. 2015 Oct 6;163(7):ITC1.
280. Valley TS, et al. **Association of Intensive Care Unit Admission** With Mortality Among Older Patients With Pneumonia. JAMA. 2015 Sep 22-29;314(12):1272-9.
281. Rhedin S, Lindstrand A, Hjelmgren A, et al. Respiratory viruses (eg. **metapneumovirus**) associated with community-acquired pneumonia in children: matched case-control study. Thorax. 2015 Sep;70(9):847-53.

282. Le Saux N, Robinson JL; **Canadian Paediatric Society**, Infectious Diseases & Immunization Committee. Uncomplicated **pneumonia in healthy Canadian children & youth**: practice points for management. Paediatr Child Health 2015;20:441-5.www.cps.ca/en/documents/position/pneumonia-management-children-youth (accessed Dec 14, 2015).

283. Daniel P, Rodrigo C, Mckeever TM, et al; British Thoracic Society. **Time to first antibiotic and mortality** in adults hospitalized with community-acquired pneumonia: a matched-propensity analysis. Thorax. 2015 Nov 11.
284. Hung GC, Liu HC, Yang SY, et al. **Antipsychotic reexposure and recurrent pneumonia in schizophrenia**: a nested case-control study. J Clin Psychiatry. 2015 Nov 24.
285. Alba GA et al. Diagnostic and prognostic utility of **procalcitonin** in patients presenting to the emergency department with dyspnea. Am J Med 2016 Jan; 129:96.
286. Wan YD, Sun TW, Liu ZQ, et al. Efficacy and Safety of **Corticosteroids** for Community-Acquired Pneumonia: A Systematic Review and Meta-Analysis. Chest. 2015 Oct 22.

287. Barrera CM, Mykietiuk A, Metev H, et al; Efficacy and safety of oral **solithromycin** versus oral moxifloxacin for treatment of community-acquired bacterial pneumonia: a global, double-blind, multicentre, randomised, active-controlled, non-inferiority trial (**SOLITAIRE-ORAL**). Lancet Infect Dis. 2016 Feb 4.
288. Jones BP, Tay ET, Elikashvili I, et al. Feasibility and Safety of **Substituting Lung Ultrasound for Chest X-ray** When Diagnosing Pneumonia in Children: A Randomized Controlled Trial. Chest. 2016 Feb 25.
289. Kulnik ST, Birring SS, Hodsoll J, et al. **Higher cough flow** is associated with lower risk of pneumonia in acute stroke. Thorax. 2016 Feb 1. pii: thoraxjnl-2015-207810.
290. Lee JS, Giesler DL, et al. **Antibiotic Therapy** for **Adults Hospitalized** With Community-Acquired Pneumonia: A Systematic Review. JAMA. 2016 Feb 9;315(6):593-602.
291. Thompson AE. **JAMA Patient page**. Pneumonia. JAMA. 2016 Feb 9;315(6):626.
292. Thomson J, Hall M, Ambroggio L, et al. **Aspiration and Non-Aspiration Pneumonia** in Hospitalized **Children** With **Neurologic Impairment**. Pediatrics. 2016 Jan 19.
293. Valim C, et al. Responses to Bacteria, Virus, and Malaria Distinguish the Etiology of **Pediatric Clinical Pneumonia**. Am J Respir Crit Care Med. 2016 Feb 15;193(4):448-59.
294. Cillóniz C, Gabarrús A, Ferrer M, et al. Community-Acquired Pneumonia due to Multidrug and non-Multidrug resistant **Pseudomonas aeruginosa**. Chest. 2016 Apr 6.
295. Self WH, et al. **Procalcitonin** as an Early Marker of Need for Invasive Respiratory or Vasopressor Support in Adults with Community-Acquired Pneumonia. Chest. 2016 Apr 20.
296. Sharp AL, et al. **CURB-65** Performance among Admitted and Discharged Emergency Department Patients with Community Acquired Pneumonia. Acad Emerg Med. 2016 Jan30.
297. Self WH, Wunderink RG, et al. **Staphylococcus aureus Community-acquired Pneumonia**: Prevalence, Clinical Characteristics, and Outcomes. Clin Infect Dis. 2016 May 8.
298. Ambroggio L, Sucharew H, et al. **Lung Ultrasonography**: A Viable Alternative to Chest Radiography in Children with Suspected Pneumonia? J Pediatr.2016 Jun 15.
299. Kalil AC, Metersky ML, Klompas M, et al. Executive Summary: Management of Adults With **Hospital-acquired and Ventilator-associated Pneumonia**: **2016 Clinical Practice** Guidelines by the **Infectious Diseases Society of America (IDSA)** and the **American Thoracic Society**. Clin Infect Dis. 2016 Sep 1;63(5):575-82.
300. Feldman C, Anderson R. **Corticosteroids** in the adjunctive therapy of community-acquired pneumonia: an appraisal of recent meta-analyses of clinical trials. J Thorac Dis. 2016 Mar;8(3):E162-71.
301. Govindan S, Hyzy RC. The 2016 Guidelines for **Hospital-Acquired and Ventilator-Associated Pneumonia**: A **Selection Correction**? Am J Respir Crit Care Med. 2016 Jul 27
302. Shenoy MK, Iwai S, et al.Immune Response and Mortality Risk Relate to Distinct Lung **Microbiomes in HIV**-Pneumonia Patients. Am J Respir Crit Care Med. 2016 Jul 22
303. Tolppanen AM, Koponen M, et al. **Antipsychotic use** and risk of hospitalisation or death due to pneumonia in persons with and without Alzheimer's disease. Chest. 2016 Jun 10.
304. Uranga A, et al. **Duration of Antibiotic Treatment in Community-Acquired Pneumonia**: A Multicenter Randomized Clinical Trial. JAMA Intern Med. 2016 Jul 25.
305. Dimopoulos G, Matthaiou DK, Karageorgopoulos DE, et al. **Short- versus long-course antibacterial therapy** for community-acquired pneumonia : a meta-analysis. Drugs. 2008;68(13):1841-54.
306. Hua F, Xie H, Worthington HV, Furness S, Zhang Q, Li C. **Oral hygiene care for critically ill** patients to **prevent ventilator-associated pneumonia**. Cochrane Database of Systematic Reviews 2016, Issue 10. Art. No.: CD008367. OHC including chlorhexidine mouthwash or gel reduces the risk of developing ventilator-associated pneumonia in critically ill patients from 25% to about 19%. However, there is no evidence of a difference in the outcomes of mortality, duration of mechanical ventilation or duration of ICU stay. There is no evidence that OHC including both antiseptics and toothbrushing is different from OHC with antiseptics alone, and some weak evidence to suggest that povidone iodine mouthrinse is more effective than saline/placebo, and saline rinse is more effective than saline swab in reducing VAP. There is insufficient evidence to determine whether powered toothbrushing or other oral care solutions are effective in reducing VAP. There is also insufficient evidence to determine whether any of the interventions evaluated in the studies are associated with adverse effects.
307. Jones BP, Tay ET, Elikashvili I, et al. Feasibility and Safety of **Substituting Lung Ultrasonography for Chest Radiography** When Diagnosing **Pneumonia in Children**: A Randomized Controlled Trial. Chest. 2016 Jul;150(1):131-8.
308. Phua J, Dean NC, Guo Q, et al. **Severe community-acquired pneumonia**: timely management measures in the first 24 hours. Crit Care. 2016 Aug 28;20:237.
309. Williams DJ, Zhu Y, Grijalva CG, et al. **Predicting Severe Pneumonia Outcomes in Children**.Pediatrics. 2016 Sep 29.
310. Kaysin A, Viera AJ. **Community-Acquired Pneumonia in Adults: Diagnosis and Management**. Am Fam Physician. 2016;94(9):698-706.
311. Llamas-Álvarez AM, Tenza-Lozano EM, et al. Accuracy of **lung ultrasound** in the **diagnosis** of pneumonia in adults: systematic review and meta-analysis. Chest. 2016 Nov 3.
312. Othman F, Crooks C, Card T. Community acquired **pneumonia** incidence before and after **proton pump inhibitor prescription**: population based study. BMJ 2016;355:i5813.
313. Prina E, Ceccato A, Torres A. **New aspects in the management of pneumonia**. Crit Care. 2016 Oct 1;20(1):267.
314. Lassi ZS, Moin A, Bhutta ZA. **Zinc supplementation** for the prevention of pneumonia in children aged 2 months to 59 months. Cochrane Database Syst Rev. 2016 Dec 4;12:CD005978. Zinc supplementation in children is associated with a reduction in the incidence and prevalence of pneumonia.
315. Metersky ML, Wang Y, Klompas M, et al. Trend in **Ventilator-Associated Pneumonia Rates** Between 2005 and 2013. JAMA. 2016 Dec 13;316(22):2427-2429
316. Mortimer K, Ndamala CB, Naunje AW, et al. A **cleaner burning biomass-fuelled cookstove** intervention to prevent pneumonia in children under 5 years old in rural Malawi (the Cooking and Pneumonia Study): a cluster randomised controlled trial. Lancet. 2016 Dec 6.
317. Shah SS, Srivastava R, We S, et al. **Intravenous Versus Oral Antibiotics** for **Post Discharge** Treatment of Complicated Pneumonia. Pediatrics.2016.138(6):e20161692
318. Shin JY, Eberg M, Ernst P, Filion KB. **Statin Potency** and the Risk of Hospitalization for Community-Acquired **Pneumonia**. Br J Clin Pharmacol. 2016 Dec 9.
319. Canadian Antimicrobial Resistance Alliance (**CARA**). 2015 CANWARD pathogens. Retrieved from http://can-r.com/study.php?study=canw2015&year=2015 on Jan 27, 2017.
320. Ceccato A, Torres A, Cilloniz C, et al. **Invasive Disease versus Urinary Antigen Confirmed Pneumococcal** Community-Acquired Pneumonia. Chest. 2017 Jan 13.
321. Minnaard MC et al. The added value of **C-reactive protein** measurement in diagnosing pneumonia in primary care: a meta-analysis of individual patient data. *Can Med Assoc J* [Epub ahead of print] 19 September 2016; doi:10.1503/cmaj.151163.
322. Parikh K, Biondi E, Nazif J, et al. A Multicenter **Collaborative to Improve Care** of Community Acquired Pneumonia in Hospitalized Children. Pediatrics. 2017 Feb 1.

323. Daniel P, Bewick T, et al. Adults **miscoded and misdiagnosed as having pneumonia**: results from the British Thoracic Society pneumonia audit. Thorax. 2017 Jan 20.
324. Eurich DT, Marrie TJ, et al. **Risk of heart failure after** community acquired pneumonia: prospective controlled study with 10 years of follow-up. BMJ. 2017 Feb 13;356:j413.
325. Haq IJ, Battersby AC, Eastham K, McKean M. **Community acquired pneumonia in children**. BMJ. 2017 Mar 2;356:j686.
326. Handy LK, Bryan M, Gerber JS, et al. **Variability in Antibiotic Prescribing** for Community-Acquired Pneumonia. **Pediatrics**. 2017 Mar 7.
327. Llamas-Alvarez AM, Tenza-Lozano EM, Latour-Perez J. Accuracy of **Lung Ultrasonography** in the Diagnosis of Pneumonia in Adults: Systematic Review and Meta-Analysis. Chest. 2017 Feb;151(2):374-382.
328. Williams DJ, Hall M, Gerber JS, et al. Impact of a National Guideline on **Antibiotic Selection for Hospitalized Pneumonia**. **Pediatrics**. 2017 Mar 8
329. Gorricho J, Garjón J, Alonso A, et al. **Use of oral antidiabetic agents** and risk of community-acquired pneumonia: a nested case-control study. Br J Clin Pharmacol. 2017 Mar 11.
330. Shachor-Meyouhas Y, Ravid S, Hanna S, et al. **Legionella pneumophila Pneumonia** in Two Infants Treated with Adrenocorticotropic Hormone. J Pediatr. 2017 Mar 20.
331. Taipale H, Tolppanen AM, Koponen M, et al. **Risk of pneumonia associated with incident benzodiazepine use** among community-dwelling adults with Alzheimer disease. CMAJ. 2017 Apr 10;189(14):E519-E529
332. Cillóniz C, et al. Community-Acquired Pneumococcal Pneumonia in Virologically Suppressed **HIV-Infected Adult** Patients: Matched Case-Control Study. Chest. 2017 Mar 13.
333. Corrado RE, et al. Burden of Adult **Community-Acquired, Healthcare-Associated, Hospital-Acquired, and Ventilator-Associated Pneumonia - New York City**, 2010-2014. Chest. 2017 Apr 25.
334. Qian CJ, Coulombe J, et al. **Pneumonia Risk in Asthma Patients using Inhaled Corticosteroids**: A Quasi-Cohort Study. Br J Clin Pharmacol. 2017 Mar 28.
335. Gu K, Van Caeseele P, Dust K, et al. **Atypical pneumonia due to human bocavirus** in an immunocompromised patient. CMAJ. 2017 May 15;189(19):E697-E699.
336. Self WH, Balk RA, Grijalva CG, et al. **Procalcitonin** as a Marker of Etiology in Adults Hospitalized with Community-Acquired Pneumonia. Clin Infect Dis. 2017 Apr 12.
337. Eliakim-Raz N, Hellerman M, Yahav D, et al. **Trimethoprim/sulfamethoxazole versus vancomycin** in the treatment of healthcare/ventilator-associated **MRSA pneumonia**: a case-control study. J Antimicrob Chemother. 2017 Mar 1;72(3):882-887.
338. Chen TY, Winkelman JW, Mao WC, et al. The use of **benzodiazepine** receptor agonists and the risk of **pneumonia hospitalization**: a nationwide population-based, nested case control study. Chest. 2017 Aug 4.
339. Schaefer G, El-Kareh R, Quartarolo J,et al. Evaluation of the **Yale New Haven Readmission Risk Score** (YNHRRS) for Pneumonia in a General Hospital Population. Am J Med. 2017 May 22.
340. Schroeder AR, Ralston SL. **Viral** Testing for **Pediatric Respiratory Infections**: Why Precise Diagnoses Do Not Always Translate to Patient Benefit. JAMA. 2017 Aug 1;318(5):472-473.
341. Shah SN, Bachur RG, Simel DL, et al. Does This Child Have Pneumonia?: The Rational Clinical Examination Systematic Review. JAMA. 2017 Aug 1;318(5):462-471.
342. Shah SN, Bachur RG, Simel DL, et al. **Childhood Pneumonia**. JAMA. 2017 Aug 1;318(5):490.
343. Upchurch CP, Grijalva CG, Wunderink RG, et al. Community-acquired Pneumonia Visualized on Computed Tomography but Not Chest X-Ray: Pathogens, Severity, and Clinical Outcomes. Chest. 2017 Aug 9.
344. Wunderink RG, Waterer G. Advances in the causes and management of community acquired pneumonia in adults. BMJ. 2017 Jul 10;358:j2471.
345. Zar HJ, Andronikou S, Nicol MP. Advances in the diagnosis of pneumonia in children. BMJ. 2017 Jul 26;358:j2739.
346. **GBD 2015 LRI Collaborators**. Estimates of the **global, regional, and national morbidity, mortality, and aetiologies of lower respiratory infections** in **195 countries**: a systematic analysis for the Global Burden of Disease Study 2015. Lancet Infect Dis 2017; online August 23.
347. Neuman MI, Hall M, Lipsett SC, Hersh et al. Utility of **Blood Culture Among Children Hospitalized With Community-Acquired Pneumonia**. Pediatrics. 2017 Sep;140(3)
348. Ramakers BP, Heijne M, Lie N, et al. **Zoonotic Chlamydia caviae** Presenting as Community-Acquired Pneumonia. N Engl J Med. 2017 Sep 7;377(10):992-994. (guinea pigs)
349. Breuer O, Picard E, Benabu N, et al. Predictors of Prolonged **Hospitalizations in Pediatric Complicated Pneumonia**. Chest. 2017 Sep 21.
350. Hayes BH, Haberling DL, Kennedy J, et al. **Burden of Pneumonia-Associated Hospitalizations** - United States, 2001-2014. Chest. 2017 Oct 7.
351. Kim B et al. **Bacteremia Prediction Model** for Community-acquired Pneumonia: External Validation in a Multicenter Retrospective Cohort. Acad Emerg Med. 2017 Jul 16.
352. Sakulchit T, Goldman RD. **Zinc supplementation** for pediatric pneumonia. Can Fam Physician. 2017 Oct;63(10):763-765.
353. Leyenaar JK, Shieh MS, Lagu T, et al. Comparative effectiveness of **ceftriaxone in combination with a macrolide compared with ceftriaxone alone** for pediatric patients hospitalized with community-acquired pneumonia. Pediatr Infect Dis J. 2014 Apr;33(4):387-92.
354. Kim B, Choi J, Kim K, et al. **Bacteremia Prediction Model** for Community-acquired Pneumonia: External Validation in a Multicenter Retrospective Cohort. Acad Emerg Med. 2017 Oct;24(10):1226-1234.
355. Williams DJ, Edwards KM, Self WH, et al. Effectiveness of **β-lactam monotherapy vs macrolide combination therapy** for children hospitalized with pneumonia [online October 30, 2017].JAMA Pediatr. doi:10.1001 /jamapediatrics.2017.3225
356. Ranzani OT, Prina E, Menéndez R, et al. New Sepsis Definition (**Sepsis-3**) and Community-acquired Pneumonia **Mortality**. A Validation and Clinical Decision-Making Study. Am J Respir Crit Care Med. 2017 Nov 15;196(10):1287-1297.
357. Shorr AF, Fisher K, Micek ST, Kollef MH. The Burden Of **Viruses in Pneumonia** Associated with Acute Respiratory Failure: An Underappreciated Issue. Chest. 2017 Dec 20.
358. Torres A,Zhong N, Pachl J, et al. **Ceftazidime-avibactam versus meropenem** in nosocomial pneumonia, including ventilator-associated pneumonia (**REPROVE**): a randomised, double-blind, phase 3 non-inferiority trial. Lancet Infect Dis 2017; online Dec 15.
359. Briel M, Spoorenberg SMC, Snijders D, et al. **Corticosteroids** in Patients Hospitalized With Community-Acquired Pneumonia: Systematic Review and Individual Patient Data Metaanalysis. Clin Infect Dis. 2018 Jan 18;66(3):346-354.

360. Maertens B, Blot K, Blot S. Prevention of Ventilator-Associated and Early Postoperative Pneumonia Through **Tapered Endotracheal Tube Cuffs**: A Systematic Review and Meta-Analysis of Randomized Controlled Trials. Crit Care Med. 2018 Feb;46(2):316-323.
361. Stern A, Skalsky K, Avni T, et al. **Corticosteroids for pneumonia**. Cochrane Database Syst Rev. 2017 Dec 13;12:CD007720. Corticosteroid therapy reduced mortality and morbidity in adults with severe CAP; the number needed to treat for an additional beneficial outcome was 18 patients (95% CI 12 to 49) to prevent one death. Corticosteroid therapy reduced morbidity, but not mortality, for adults and children with non-severe CAP. Corticosteroid therapy was associated with more adverse events, especially hyperglycaemia, but the harms did not seem to outweigh the benefits.
362. McKinnell JA, Corman S, Patel D, et al. Effective Antimicrobial Stewardship Strategies for Cost-Effective Utilization of Telavancin for the Treatment of Patients With Hospital-Acquired Bacterial Pneumonia Caused by Staphylococcus aureus. Clin Ther. 2018 Feb 14.
363. Wu WF, Fang Q, He GJ. Efficacy of corticosteroid treatment for severe community-acquired pneumonia: A meta-analysis. Am J Emerg Med. 2018 Feb;36(2):179-184.
364. Zirk-Sadowski J, Masoli JA, Delgado J, et al. Proton-Pump Inhibitors and Long-Term Risk of Community-Acquired Pneumonia in Older Adults. J Am Geriatr Soc. 2018 Apr 20.
365. Burrell A, Huckson S, Pilcher DV; ANZICS. **ICU Admissions for Sepsis or Pneumonia** in Australia and New Zealand in 2017. N Engl J Med. 2018 May 31;378(22):2138-2139.
366. Lee AS, Ryu JH. **Aspiration Pneumonia** and Related Syndromes. Mayo Clin Proc. 2018 May 2.
367. Waterer GW, Self WH, Courtney DM, et al. **In-hospital Deaths** among Adults with Community-Acquired Pneumonia. Chest. 2018 May 30.
368.Ilg A, Moskowitz A, Konanki V, et al. Performance of **the CURB-65 Score** in Predicting **Critical Care Interventions** in Patients Admitted With Community-Acquired Pneumonia. Ann Emerg Med. 2018 Aug 2.
369. Prendki V, Scheffler M, Huttner B, et al. **Low-dose computed tomography for the diagnosis of pneumonia in elderly patients**: a prospective, interventional cohort study. Eur Respir J. 2018 May 30;51(5).
370. Shields RK, Nguyen MH, Chen L, et al. **Pneumonia and Renal Replacement Therapy Are Risk Factors for Ceftazidime-Avibactam Treatment Failures and Resistance among Patients with Carbapenem-Resistant Enterobacteriaceae Infections**. Antimicrob Agents Chemother. 2018 Apr 26;62(5).
371. Stern A, Leibovici L, Paul M. **Corticosteroids Reduce Mortality in Patients with Severe Community Acquired Pneumonia** (CAP). Clin Infect Dis. 2018 Apr 20.
372. Ambroggio L, Mangeot C, Murtagh Kurowski E, et al. **Guideline Adoption for Community-Acquired Pneumonia** in the Outpatient Setting. Pediatrics. 2018 Sep 25.
373. Dragan V, Wei Y, Elligsen M, et al. **Prophylactic Antimicrobial Therapy for Acute Aspiration Pneumonitis**. Clin Infect Dis. 2018 Aug 1;67(4):513-518.
374. Lipsett SC, Monuteaux MC, Bachur RG, Finn N, Neuman MI. **Negative Chest Radiography and Risk of Pneumonia**. Pediatrics. 2018 Sep;142(3).
375. Liu C, Cao Y, Lin J, et al. **Oral care measures for preventing nursing home-acquired pneumonia**. Cochrane Database Syst Rev. 2018 Sep 27;9:CD012416. Although low-quality evidence suggests that professional oral care could reduce mortality due to pneumonia in nursing home residents when compared to usual care, this finding must be considered with caution. Evidence for other outcomes is inconclusive.
376. Ceccato A, Cilloniz C, Martin-Loeches I, et al. Effect of Combined β-Lactam / Macrolide Therapy on Mortality According to the Microbial Aetiology and Inflammatory Status of Patients with Community - Acquired Pneumonia. Chest. 2018 Nov 21.
377. Ginsburg AS, Mvalo T, Nkwopara E, et al. Placebo vs amoxicillin for nonsevere fast-breathing pneumonia in Malawian children aged 2 to 59 months: a double-blind, randomized clinical noninferiority trial [online Nov 12, 2018]. JAMA Pediatr. doi:10.1001/jamapediatrics.2018.3407
378. Leone M, Bouadma L, Bouhemad B, et al; ADARPEF; GFRUP. Brief summary of French guidelines for the prevention, diagnosis and treatment of hospital-acquired pneumonia in ICU. Ann Intensive Care. 2018 Nov 3;8(1):104.
379. Pliakos EE, Andreatos N, Tansarli GS, et al. The Cost-effectiveness of Corticosteroids for the treatment of Community-Acquired Pneumonia. Chest. 2018 Nov 15.
380. Corneli A, Perry B, Collyar D, et al. Assessment of the **perceived acceptability of an early enrollment strategy using advance consent in health care–associated pneumonia**. JAMA Netw Open. 2018;1(8):e185816. doi:10.1001/jamanetworkopen.2018.5816
381. Tribble AC, Ross RK, Gerber JS. Comparison of **Antibiotic Prescribing for Pediatric Community-Acquired Pneumonia** in Children's and Non-Children's Hospitals. JAMA Pediatr. 2018 Dec 10.
382. Wunderink RG, Niederman MS, Kollef MH, et al. **Linezolid in methicillin-resistant Staphylococcus aureus nosocomial pneumonia**: a randomized, controlled study. Clin Infect Dis. 2012 Mar 1;54(5):621-9.
383. Cowley MC, Ritchie DJ, Hampton N, et al. Outcomes Associated With **De-escalating Therapy for Methicillin-Resistant Staphylococcus aureus** in Culture-Negative Nosocomial Pneumonia. Chest. 2019 Jan;155(1):53-59.
384. Edelman EJ, Gordon KS, Crothers K, et al. Association of Prescribed **Opioids With Increased Risk of Community-Acquired Pneumonia** Among Patients With and Without HIV. JAMA Intern Med. 2019 Jan 7.
385. Wadhera RK, Joynt Maddox KE, Wasfy JH, et al. Association of the **Hospital Readmissions Reduction Program with mortality among Medicare beneficiaries hospitalized for heart failure, acute myocardial infarction, and pneumonia** [Dec 25, 2018]. JAMA. doi:10.1001/jama.2018.19232
386. Hill AT, Gold PM, El Solh AA, et al. Adult Outpatients With **Acute Cough Due to Suspected Pneumonia or Influenza**: **CHEST Guideline** and Expert Panel Report. Chest. 2019 Jan;155(1):155-167.
387. Stets R, Popescu M, Gonong JR, et al. **Omadacycline for community-acquired bacterial pneumonia**. N Engl J Med 2019; 380: 517-27.
388. Zilberberg MD, Nathanson BH, Sulham K, Fan W, Shorr AF. A novel algorithm to analyze **epidemiology and outcomes of carbapenem resistance** among patients with hospital-acquired and ventilator-associated pneumonia: A retrospective cohort study. Chest. 2019 Jan 24.
389. Kutty PK, Jain S, Taylor TH, et al. **Mycoplasma pneumoniae Among Children Hospitalized** With Community-acquired Pneumonia. Clin Infect Dis. 2019 Jan 1;68(1):5-12.
390. Mandell LA, Niederman MS. **Aspiration Pneumonia**. N Engl J Med. 2019 Feb 14;380(7):651-663.

391. Ouldali N, Levy C, Minodier Pet al. **Long-term Association of 13-Valent Pneumococcal Conjugate Vaccine** Implementation With Rates of Community-Acquired Pneumonia in Children. JAMA Pediatr. 2019 Feb 4.
392. Ebell MH, Walsh ME, Fahey T, et al. Meta-analysis of **Calibration, Discrimination, and Stratum-Specific Likelihood Ratios for the CRB-65 Score**. J Gen Intern Med. 2019 Apr 16.
393. Webb BJ, Sorensen J, Mecham I, et al. **Antibiotic use and outcomes after implementation of the Drug Resistance in Pneumonia (DRIP) score** in emergency department patients with community-onset pneumonia. Chest. 2019 May 8.
394. Wen J, Chen F, Zhao M, et al. **Solithromycin monotherapy for treatment of community-acquired bacterial pneumonia**: A meta-analysis of randomised controlled trials. Int J Clin Pract. 2019 Feb 27:e13333.
395. Alishlash AS, Atkinson TP, Schlappi C, et al. **Mycoplasma pneumoniae Carriage With De Novo Macrolide-Resistance** and Breakthrough Pneumonia. Pediatrics. 2019 Sep 5.
396. Hong J, Ensom MHH, Lau TTY. What Is the Evidence for **Co-trimoxazole, Clindamycin, Doxycycline, and Minocycline** in the Treatment of Methicillin-Resistant Staphylococcus aureus (MRSA) Pneumonia? Ann Pharmacother. 2019 Jun 10:1060028019856721.
397. Lin JL, Van Haren K, Rigdon J, et al. Pneumonia **Prevention Strategies for Children With Neurologic Impairment**. Pediatrics. 2019 Sep 19.
398. Fritz CQ, Edwards KM, Self WH, et al. Prevalence, Risk Factors, and Outcomes of **Bacteremic Pneumonia in Children**. Pediatrics. 2019 Jun 19.
399. Lloyd M, Karahalios A, Janus E, et al;(IMPROVE-GAP). Effectiveness of a **Bundled Intervention Including Adjunctive Corticosteroids** on Outcomes of Hospitalized Patients With Community-Acquired Pneumonia: A Stepped-Wedge Randomized Clinical Trial. JAMA Intern Med. 2019 Jul 8.
400. Song Y, Yao C, Yao Y, et al. **XueBiJing Injection Versus Placebo** for Critically Ill Patients With Severe Community-Acquired Pneumonia: A Randomized Controlled Trial. Crit Care Med. 2019 Jun 3.
401. Vaughn VM, Flanders SA, Snyder A, et al. **Excess Antibiotic Treatment Duration and Adverse Events** in Patients Hospitalized With Pneumonia: A Multihospital Cohort Study. Ann Intern Med. 2019 Jul 9.
402. Ebell MH. Community-Acquired Pneumonia: Determining **Safe Treatment in the Outpatient Setting**. Am Fam Physician. 2019 Jun 15;99(12):768-769.
403. Gupta NM, Lindenauer PK, Yu P-C, et al. Association between **alcohol use disorders and outcomes of patients hospitalized** with community-acquired pneumonia. JAMA Netw Open. 2019;2(6):e195172. doi:10.1001/jamanetworkopen.2019.5172
404. Song Y, Yao C, Yao Y, et al. **XueBiJing Injection Versus Placebo** for Critically Ill Patients With Severe Community-Acquired Pneumonia: A Randomized Controlled Trial. Crit Care Med. 2019 Jun 3.

Web Sites:

American Lung Association
www.lungusa.org/site/apps/nlnet/content3.aspx?c=dvLUK9O0E&b=2060321&content_id={71CC3CFD-4B3E-49C8-AA88-D76EAE1FB9F5}&notoc=1
National Institute of Allergy and Infectious Diseases
http://www3.niaid.nih.gov/topics/pneumonia/default.htm (English)
Centers for Disease Control and Prevention
www.cdc.gov/vaccines/vpd-vac/pneumo/default.htm (pneumococcal vaccine)
www.cdc.gov/vaccines/vpd-vac/flu/default.htm (influenza vaccine)
National Foundation for Infectious Disease
www.nfid.org/pdf/factsheets/pneuadult.pdf

References – Community-Acquired Pneumonia - RxFiles.ca

Guidelines

2018 Bugs & Drugs

2013 Anti-infective Guidelines for Community-acquired Infections. Anti-infective Review Panel (the "Orange Book").

Mandell LA, Wunderink RG, Anzueto A, et al. **Infectious Diseases Society of America; American Thoracic Society**. Infectious Diseases Society of America/American Thoracic Society consensus guidelines on the management of community-acquired pneumonia in adults. Clin Infect Dis. 2007 Mar 1;44 Suppl 2:S27-72.

CAP

Fine MJ, Stone RA, Singer DE, Coley CM, et al. Processes and outcomes of care for patients with community-acquired pneumonia: results from the Pneumonia Patient Outcomes Research Team (PORT) cohort study. Arch Intern Med. 1999 May 10;159(9):970-80. PubMed PMID: 10326939.

Kutty PK, Jain S, Taylor TH, et al. **Mycoplasma pneumoniae Among Children Hospitalized With Community-acquired Pneumonia**. Clin Infect Dis. 2019 Jan 1;68(1):5-12.

Mandell LA, Niederman MS. **Aspiration Pneumonia**. N Engl J Med. 2019 Feb 14;380(7):651-663.

Postma DF, van Werkhoven CH, van Elden LJ, Thijsen SF, Hoepelman AI, et al. CAP-START Study Group. Antibiotic treatment strategies for community-acquired pneumonia in adults. N Engl J Med. 2015 Apr 2;372(14):1312-23.

Roig J, Casal J, Gispert P, Gea E. 13--Antibiotic therapy of community-acquired pneumonia (CAP) caused by atypical agents. Med Mal Infect. 2006 Nov-Dec;36(11-12):680-9.

Self WH, Wunderink RG, Williams DJ, et al. Staphylococcus aureus Community-acquired Pneumonia: Prevalence, Clinical Characteristics, and Outcomes. Clin Infect Dis. 2016 Aug 1;63(3):300-9.

Immunizations

Andrew C. Berical, Drew Harris, Charles S. Dela Cruz, and Jennifer D. Possick "Pneumococcal Vaccination Strategies. An Update and Perspective", Annals of the American Thoracic Society, Vol. 13, No. 6 (2016), pp. 933-944.

Ouldali N, Levy C, Minodier Pet al. **Long-term Association of 13-Valent Pneumococcal Conjugate Vaccine** Implementation With Rates of Community-Acquired Pneumonia in Children. JAMA Pediatr. 2019 Feb 4.

Canadian Immunization Guide: Pneumococcal Vaccine. Government of Canada. Available from: http://www.phac-aspc.gc.ca/publicat/cig-gci/p04-pneu-eng.php. Updated March 2015.

Fine MJ, Smith MA, Carson CA, et al. Efficacy of pneumococcal vaccination in adults. A meta-analysis of randomized controlled trials. Arch Intern Med. 1994 Dec 12-26;154(23):2666-77.

Potential CAP Risks

Eom CS, Jeon CY, Lim J-W, et al. Use of acid-suppressive drugs and risk of pneumonia: a systematic review and meta-analysis. Can Med Assoc J. 2011 Feb 22;183(3):310–19

Filion KB, Chateau D, Targownik LE, et al. Proton pump inhibitors and the risk of hospitalisation for community-acquired pneumonia: replicated cohort studies with meta-analysis. Gut. 2014 Apr;63(4):552–8

Singh S, Amin AV, Loke YK. Long-term use of inhaled corticosteroids and the risk of pneumonia in chronic obstructive pulmonary disease: a meta-analysis. Arch Intern Med. 2009 Feb 9;169(3):219-29.

Durations of Therapy

Dimopoulos G, Matthaiou DK, Karageorgopoulos DE, Grammatikos AP, Athanassa Z, Falagas ME. Short- versus long-course antibacterial therapy for community-acquired pneumonia : a meta-analysis. Drugs. 2008;68(13):1841-54. PubMed PMID: 18729535.

Ficnar B, Huzjak N, Oreskovic K, Matrapazovski M, Klinar I. Azithromycin:3-day versus 5-day course in the treatment of respiratory tract infections in children. Croatian Azithromycin Study Group. J Chemother. 1997 Feb;9(1):38-43.PubMed PMID: 9106016.

Greenberg D, Givon-Lavi N, Sadaka Y, Ben-Shimol S, Bar-Ziv J, Dagan R. Short-course antibiotic treatment for community-acquired alveolar pneumonia in ambulatory children: a double-blind, randomized, placebo-controlled trial. Pediatr Infect Dis J. 2014 Feb;33(2):136-42.

Li JZ, Winston LG, Moore DH, Bent S. Efficacy of short-course antibiotic regimens for community-acquired pneumonia: a meta-analysis. Am J Med. 2007 Sep;120(9):783-90. PubMed PMID: 17765048.
Schönwald S, Skerk V, Petricevic I, Car V, Majerus-Misic L, Gunjaca M. Comparison of three-day and five-day courses of azithromycin in the treatment of atypical pneumonia. Eur J Clin Microbiol Infect Dis. 1991 Oct;10(10):877-80. PubMed PMID: 1662637.
Uranga A, España PP, Bilbao A, et al. Duration of Antibiotic Treatment in Community-Acquired Pneumonia: A Multicenter Randomized Clinical Trial. JAMA Intern Med. 2016 Jul 25.

Extra references:

Alishlash AS, Atkinson TP, Schlappi C, et al. Mycoplasma pneumoniae Carriage With **De Novo Macrolide-Resistance and Breakthrough Pneumonia**. Pediatrics 2019Sep5.
Daniel P, Bewick T, et al. Adults **miscoded and misdiagnosed as having pneumonia**: results from the British Thoracic Society pneumonia audit. Thorax. 2017 Jan 20.
Ebell MH. Community-Acquired Pneumonia: **Determining Safe Treatment in the Outpatient Setting**. Am Fam Physician. 2019 Jun 15;99(12):768-769.
Ebell MH, Walsh ME, Fahey T, et al. Meta-analysis of **Calibration, Discrimination, and Stratum-**Specific Likelihood Ratios for the **CRB-65 Score**. J Gen Intern Med. 2019 Apr 16.
Eurich DT, Marrie TJ, et al. **Risk of heart failure after** community acquired pneumonia: prospective controlled study with 10 years of follow-up. BMJ. 2017 Feb 13;356:j413.
Fritz CQ, Edwards KM, Self WH, et al. Prevalence, Risk Factors, and Outcomes of **Bacteremic Pneumonia** in Children. Pediatrics. 2019 Jun 19.
Gupta NM, Lindenauer PK, Yu P-C, et al. Association between **alcohol use disorders and outcomes of patients hospitalized** with community-acquired pneumonia. JAMA Netw Open. 2019;2(6):e195172. doi:10.1001/jamanetworkopen.2019.5172
Haq IJ, Battersby AC, Eastham K, McKean M. **Community acquired pneumonia in children**. BMJ. 2017 Mar 2;356:j686.
Hong J, Ensom MHH, Lau TTY. What Is the Evidence for **Co-trimoxazole, Clindamycin, Doxycycline, and Minocycline** in the Treatment of Methicillin-Resistant Staphylococcus aureus (MRSA) Pneumonia? Ann Pharmacother. 2019 Jun 10:1060028019856721.
Lin JL, Van Haren K, Rigdon J, et al. Pneumonia **Prevention Strategies for Children With Neurologic Impairment**. Pediatrics. 2019 Sep 19.
Lloyd M, Karahalios A, Janus E, et al;(IMPROVE-GAP). Effectiveness of a **Bundled Intervention** Including Adjunctive Corticosteroids on Outcomes of Hospitalized Patients With Community-Acquired Pneumonia: A Stepped-Wedge Randomized Clinical Trial. JAMA Intern Med. 2019 Jul 8.
Song Y, Yao C, Yao Y, et al. **XueBiJing Injection Versus Placebo** for Critically Ill Patients With Severe Community-Acquired Pneumonia: A Randomized Controlled Trial. Crit Care Med. 2019 Jun 3.
Vaughn VM, Flanders SA, Snyder A, et al. **Excess Antibiotic Treatment** Duration and Adverse Events in Patients Hospitalized With Pneumonia: A Multihospital Cohort Study. Ann Intern Med. 2019 Jul 9.
Webb BJ, Sorensen J, Mecham I, et al. **Antibiotic use and outcomes** after implementation of the **Drug Resistance in Pneumonia (DRIP) score** in emergency department patients with community-onset pneumonia. Chest. 2019 May 8.
Wen J, Chen F, Zhao M, et al. **Solithromycin monotherapy for treatment of community-acquired bacterial pneumonia**: A meta-analysis of randomised controlled trials. Int J Clin Pract. 2019 Feb 27:e13333.

SEVERE COMMUNITY ACQUIRED PNEUMONIA (SCAP) SCORE OR ESPANA RULE OR PS-CURXO 80

Scoring

Criteria	Points
Major Criteria	
pH <7.3	+13
SBP <90 mmHg	+11
Minor Criteria	
Confusion	+5
B**U**N >10.7 mmol/L	+5
Respiratory rate >30/min	+9
C**X**R multilobar/bilateral infiltrates	+5
Pa**O**$_2$<54 or Pa**O**$_2$/FiO$_2$<250 mmHg	+6
Age ≥ 80 years	+5

Interpretation

Severe CAP: 1 major criterion or 2 minor criteria

Total Points	Risk Class (poor outcome & need for ICU)
<10	Low
10-19	Medium
20-59	High

IDSA/ATS 2007

Scoring

Major Criteria
invasive mechanical ventilation
septic shock with need for vasopressors
Minor Criteria
Respiratory rate ≥ 30 breaths/min PaO_2/FiO_2<250 mmHg
Multilobar infitrates
Confusion/disorientation
BUN ≥ 20 mg/dL
Leukopenia (WBC <4,000 cells/mm^3)
Thrombocytopenia (PLT <100,000 cells/mm^3)
Hypothermia (T <36C)
Hypotension requiring aggressive fluid resuscitation

Interpretation

1 major criterion: direct ICU admission [IDSA 2007 (strong recommendation, LOE II)]

3 minor criteria: direct ICU or high-level monitoring unit [IDSA 2007 (moderate recommendation, LOE II)]

SMART-COP

Scoring

Criteria	Points
Systolic BP <90 mmHg	+2
Multilobar CXR involvement	+1
Albumin <35 g/L	+1
Respiratory rate (age adjusted) ≤ 50 yr: ≥ 25 breaths/min > 50 yr: ≥ 30 breaths/min	+1
Tachycardia ≥ 125 beats/min	+1
Confusion (new onset)	+1
Oxygenation (age adjusted) ≤ 50 yr: PaO_2 < 60 mmHg or O_2sat ≤90% or PaO_2/FiO_2 < 333 > 50 yr: PaO_2 < 70 mmHg or O_2sat ≤93% or PaO_2/FiO_2 < 250	+2
pH <7.35	+2

Interpretation

Total Points	IRVS risk
0-2	Low risk
3-4	Moderate risk (1 in 8)
5-6	High risk (1 in 3)
7-11	Very risk (2 in 3)

Primary Care Pearl: use SMRT-CO (remove albumin, pH, and PaO2, total out of 8) to inform decisions (does not require lab testing):[13]

- 0 Points — Very low risk of needing IRVS
- 1 Point — Low risk (1 in 20) of needing IRVS
- 2 Points — Moderate risk (1 in 10) of needing IRVS
- 3 Points — High risk (1 in 6) of needing IRVS
- ≥4 Points — High risk (1 in 3) of needing IRVS

References: COMMUNITY-ACQUIRED PNEUMONIA (CAP): SEVERITY ASSESSMENT TOOLS

1. Tang CM, Macfarlane JT. Early management of younger adults dying of community-acquired pneumonia. Respir Med 1993;87:289e94.
2. Neill AM, Martin IR, Weir R, et al. Community-acquired pneumonia: aetiology and usefulness of severity criteria on admission. Thorax 1996;51:1010e16.
3. Mandell LA, Wunderink RG, Anzueto A,et al. Infectious Diseases Society of America **(IDSA)**; American Thoracic Society. Infectious DiseasesSociety of America/American Thoracic Society consensus guidelines on the management of community-acquired pneumonia in adults. Clin Infect Dis. 2007 Mar1;44 Suppl 2:S27-72.
4. **NICE**: National Institute for Health and Care Excellence. **Pneumonia** (including community acquired pneumonia). 2014. www.nice.org.uk/guidance/cg191.
5. Chalmers JD, Singanayagam A, et al. **Severity assessment tools** for predicting mortality in hospitalised patients with community-acquired pneumonia. **Systematic review and meta-analysis**. Thorax. 2010 Oct;65(10):878-83.
6. Fang WF, Yang KY, Wu CL, et al. Application and comparison of scoring indices to predict outcomes in patients with healthcare-associated pneumonia. Crit Care. 2011;15(1):R32.
7. Carrabba M, Zarantonello M, Bonara P,et al. Severity assessment of healthcare-associated pneumonia and pneumonia in immunosuppression. Eur Respir J. 2012 Nov;40(5):1201-10.
8. **Fine** MJ, Auble TE, Yealy DM, et al. A prediction rule to identify low-risk patients with community-acquired pneumonia. N Engl J Med. 1997 Jan 23;336(4):243-50.
9. Pereira JM, Paiva JA, Rello J. Assessing severity of patients with community-acquired pneumonia. Semin Respir Crit Care Med. 2012 Jun;33(3):272-83.
10. Lim WS, van der Eerden MM, Laing R, et al. Defining community acquired pneumonia severity on presentation to hospital: an international derivation and validation study. Thorax. 2003 May;58(5):377-82.
11. Bont J, Hak E, Hoes AW, et al. Predicting death in elderly patients with community-acquired pneumonia: a prospective validation study reevaluating the CRB-65 severity assessment tool. Archives of Internal Medicine. 2008; 168(13):1465-1468.
12. Parsonage M, Nathwani D, Davey P, Barlow G. Evaluation of the performance of CURB-65 with increasing age. Clin Microbiol Infect. 2009 Sep;15(9):858-64.
13. Charles PG, Wolfe R, Whitby M, Fine MJ, Fuller AJ, Stirling R, et al. SMART-COP: a tool for predicting the need for intensive respiratory or vasopressor support in community-acquired pneumonia. Clin Infect Dis 2008;47(3):375- 84.
14. Charles PGP, Whitby M, Fuller AJ, et al. The etiology of community- acquired pneumonia in Australia: why penicillin plus doxycycline or a macrolide is the most appropriate therapy. Clin Infect Dis **2008**; 46: 1513–21.
15. Chalmers JD, Singanayagam A, et al. Predicting the need for mechanical ventilation and/or inotropic support for young adults admitted to the hospital with community-acquired pneumonia. Clin Infect Dis 2008;47(12):1571–1574
16. Espana PP, Capelastegui A, Gorordo I, et al. Development and validation of a clinical prediction rule for severe community-acquired pneumonia. Am J Respir Crit Care Med 2006;174:1249e56.
17. Espana PP, Capelastegui A, Quintana J, et al. Prospective comparison severity scores for predicting clinically relevant outcomes for patients hospitalized community-acquired pneumonia. Chest 2009;135:1572e9.
18. Brown SM, Jones BE, Jephson AR, Dean NC; Infectious Disease Society of America/American Thoracic Society 2007. Validation of the Infectious Disease Society of America/American Thoracic Society 2007 guidelines for

severe community-acquired pneumonia. Crit Care Med. 2009 Dec;37(12):3010-6.
19. British Thoracic Society, Myint PK, Kamath AV, Vowler SL, Maisey DN, Harrison BD. Severity assessment criteria recommended by the British Thoracic Society (BTS) for community-acquired pneumonia (CAP) and older patients. Should SOAR (systolic blood pressure, oxygenation, age and respiratory rate) criteria be used in older people? A compilation study of two prospective cohorts. Age Ageing. 2006 May;35(3):286-91.
20. El-Solh AA, Alhajhusain A, Abou Jaoude P, Drinka P. Validity of severity scores in hospitalized patients with nursing home-acquired pneumonia. Chest. 2010 Dec;138(6):1371-6.
21. Subramanian DN, Musonda P, Sankaran P, Tariq SM, Kamath AV, Myint PK. Performance of SOAR (systolic blood pressure, oxygenation, age and respiratory rate) scoring criteria in community-acquired pneumonia: a prospective multi-centre study. Age Ageing. 2013 Jan;42(1):94-7.
22. Ebell MH, Walsh ME, Fahey T, et al. Meta-analysis of Calibration, Discrimination, and Stratum-Specific Likelihood Ratios for the CRB-65 Score. J Gen Intern Med. 2019 Apr 16.
23. Ebell MH. Community-Acquired Pneumonia: Determining Safe Treatment in the Outpatient Setting. Am Fam Physician. 2019 Jun 15;99(12):768-769.

Additional references: **COMMUNITY-ACQUIRED PNEUMONIA (CAP): SEVERITY ASSESSMENT TOOLS**

Arnold Forest W, LaJoie A. Scott, Brock Guy N, et al. for the Community-Acquired Pneumonia Organization (CAPO) Investigators. Improving Outcomes in Elderly Patients With Community-Acquired Pneumonia by Adhering to National Guidelines: Community-Acquired Pneumonia Organization International Cohort Study Results. Arch Intern Med. 2009;169(16):1515-1524.
Aujesky D, Fine MJ. The **pneumonia severity index**: a decade after the initial derivation and validation. Clin Infect Dis. 2008 Dec 1;47 Suppl 3:S133-9.
Aujesky D, Auble TE, Yealy DM, Stone RA, Obrosky DS, Meehan TP, Graff LG, et al. Prospective comparison of **three validated prediction** rules for prognosis in community-acquired pneumonia. Am J Med. 2005 Apr;118(4):384-92.
Bont J, Hak E, Hoes AW, Macfarlane JT, Verheij TJ. Predicting death in elderly patients with community-acquired pneumonia: a prospective validation study reevaluating the **CRB-65** severity assessment tool. Arch Intern Med. 2008 Jul 14;168(13):1465-8.
Brown SM, Jones BE, Jephson AR, et al. **Validation** of the Infectious Disease Society of America/American Thoracic Society 2007 guidelines for severe community-acquired pneumonia. Crit Care Med. 2009 Dec;37(12):3010-6.
Cals JW, Schot MJ, de Jong SA, et al. Point-of-care **C-reactive protein** testing and antibiotic prescribing for respiratory tract infections: a randomized controlled trial. Ann Fam Med. 2010 Mar-Apr;8(2):124-33.
Chen JH, Chang SS, Liu JJ, et al. Comparison of clinical characteristics and performance of **pneumonia severity score** and **CURB-65** among younger adults, **elderly and very old** subjects. Thorax. 2010 Nov;65(11):971-7.
Chen YX, Li CS. **Lactate** on emergency department arrival as a predictor of mortality and site-of-care in pneumonia patients: cohort study. Thorax. 2015 Feb 23.
Christ-Crain M, et al. **Procalcitonin** Guidance of Antibiotic Therapy in Community-acquired Pneumonia: A Randomized Trial. Am J Respir Crit Care Med. 2006 Jul 1;174(1):84-93. Epub 2006 Apr 7.
Daubin C, Parienti JJ, Fradin S, et al. **Procalcitonin** levels and bacterial aetiology among COPD patients admitted to the ICU with severe pneumonia: a prospective cohort study. BMC Infect Dis. 2009 Sep 21;9:157.
España PP, Capelastegui A, Quintana JM, et al. Validation and comparison of SCAP as a predictive score for identifying low-risk patients in community-acquired pneumonia. J Infect. 2010 Feb;60(2):106-13.
Esposito S et al. **Procalcitonin** measurements for guiding antibiotic treatment in pediatric pneumonia. Respir Med. 2011 Dec;105(12):1939-45.
Esayag Y, Nikitin I, Bar-Ziv J, et al. Diagnostic value of **chest radiographs** in bedridden patients suspected of having pneumonia. Am J Med. 2010 Jan;123(1):88.e1-5.
Francis NA, Cals JW, Butler CC, Hood K, Verheij T, Little P et al. Severity assessment for lower respiratory tract infections: potential use and validity of the CRB-65 in primary care. Primary Care Respiratory Journal. 2012; 21(1):65-70
Gomez B, Bressan S, Mintegi S, et al. Diagnostic value of **procalcitonin** in well-appearing young febrile infants. Pediatrics. 2012 Nov;130(5):815-22.
Ilg A, Moskowitz A, Konanki V, et al. Performance of the **CURB-65 Score** in Predicting Critical Care Interventions in Patients Admitted With Community-Acquired Pneumonia. Ann Emerg Med. 2018 Aug 2.
Jones BE, Jones J, Bewick T, et al. **CURB-65** Pneumonia Severity Assessment Adapted for **Electronic** Decision Support. Chest. 2011 Jul;140(1):156-63.
Kett DH, Cano E, Quartin AA,et al; the Improving Medicine through Pathway Assessment of Critical Therapy of Hospital-Acquired Pneumonia (IMPACT-HAP) Investigators. Implementation of guidelines for management of possible multidrug-resistant pneumonia in intensive care: an observational, multicentre cohort study. Lancet Infect Dis. 2011 Jan 19.
Krüger S, Ewig S, Giersdorf S, et al.; CAPNETZ study group. **Cardiovascular and Inflammatory Biomarkers** to Predict Short- and Long-term Survival in Community-acquired Pneumonia. Am J Respir Crit Care Med. 2010 Jul 16.
Layios N, et al. **Procalcitonin** usefulness for the initiation of antibiotic treatment in intensive care unit patients. Crit Care Med. 2012 Aug;40(8):2304-9.
Leis JA, Gold WL. Management of community-acquired pneumonia in the **emergency department**. CMAJ. 2012 Jan 23.
Loke YK, Kwok CS, Niruban A, Myint PK. Value of **severity scales in predicting mortality** from community-acquired pneumonia: systematic review and meta-analysis. Thorax. 2010;65:884-90.
Mathews B, Shah S, Cleveland RH, Lee EY, et al. Clinical predictors of pneumonia among **children with wheezing**. Pediatrics. 2009 Jul;124(1):e29-36.
McCabe Caitlin; Kirchner Cheryl; Zhang Huiling; et al. Guideline-Concordant Therapy and Reduced Mortality and Length of Stay in Adults With Community-Acquired Pneumonia: Playing by the Rules. Arch Intern Med. 2009;169(16):1525-1531.
McNally M, Curtain J, O`Brien KK, et al. Validity of British Thoracic Society guidance (the **CRB-65 rule**) for predicting the severity of pneumonia in general practice: systematic review and meta-analysis. Br J Gen Pract. 2010 Oct;60(579):e423-33.
Musher DM, Thorner AR. **Community-acquired pneumonia**. N Engl J Med. 2014 Oct 23;371(17):1619-28.
NICE: National Institute for Health and Care Excellence. **Pneumonia** (including community acquired pneumonia). 2014. www.nice.org.uk/guidance/cg191.
Niederman MS. Biological markers to determine eligibility in trials for community-acquired pneumonia: focus on **procalcitonin**. Clin Infect Dis. 2008 Dec 1;47 Suppl 3:S127-32.
Niederman MS. Making sense of **scoring systems** in community acquired pneumonia. Respirology. 2009 Apr;14(3):327-35.
Neuman MI et al. Prediction of pneumonia in a **pediatric emergency department**. *Pediatrics* 2011 Aug; 128:246.
Ochoa-Gondar O, Vila-Corcoles A, Rodriguez-Blanco T, et al. Comparison of **three predictive rules** for assessing severity in elderly patients with CAP. Int J Clin Pract. 2011 Nov;65(11):1165-72. Three prediction rules -- the Pneumonia Severity Index (PSI), CURB-65, and the modified CRB-65 -- perform equally well for predicting 30-day mortality among patients 65 years or older with community-acquired pneumonia (CAP). The simpler CRB-65, which does not require laboratory data, is particularly accurate among patients aged 65 years to 74 years. (LOE = 1b)
Ranzani OT, Prina E, Menéndez R, et al. New Sepsis Definition (**Sepsis-3**) and Community-acquired Pneumonia **Mortality**. A Validation and Clinical Decision-Making Study. Am J Respir Crit Care Med. 2017 Nov 15;196(10):1287-1297.
Rello J et al. Severity of pneumococcal pneumonia associated with genomic **bacterial load**. Chest 2009 Sep; 136:832.
Schuetz Philipp, Christ-Crain Mirjam, Thomann Robert, et al. for the ProHOSP Study Group. Effect of **Procalcitonin**-Based Guidelines vs Standard Guidelines on Antibiotic Use in Lower Respiratory Tract Infections: The ProHOSP Randomized Controlled Trial. JAMA. 2009;302(10):1059-1066.
Schuetz P, Amin DN, Greenwald JL. Role of **procalcitonin** in managing adult patients with respiratory tract infections. Chest. 2012 Apr;141(4):1063-73.
Schuetz P, Briel M, Mueller B. Clinical outcomes associated with procalcitonin algorithms to guide antibiotic therapy in respiratory tract infections. JAMA. 2013 Feb 20;309(7):717-8.
Sharp AL, et al. **CURB-65 Performance** among Admitted and Discharged Emergency Department Patients with Community Acquired Pneumonia. Acad Emerg Med. 2016 Jan 30.
Shorr AF, Sun X, Johannes RS, et al. Validation of a Novel **Risk Score** for Severity of Illness in **Acute Exacerbations of COPD**. (**BAP-65**) Chest. 2011 Nov;140(5):1177-83.
Sorde Roger; Falco Vicenc; Lowak Michael; et al. Current and Potential Usefulness of **Pneumococcal Urinary Antigen** Detection in Hospitalized Patients With Community-Acquired Pneumonia to Guide Antimicrobial Therapy. Arch Intern Med. 2010;0(2010):archinternmed.2010.347.

Stolz D, Smyrnios N, Eggimann P, et al. **Procalcitonin** for reduced antibiotic exposure in ventilator-associated pneumonia: randomised study. Eur Respir J. 2009 Dec;34(6):1364-75. Epub 2009 Sep 24.
Valencia M, Badia JR, Cavalcanti M, et al. **Pneumonia severity index class v** patients with community-acquired pneumonia: characteristics, outcomes, and value of severity scores. Chest. 2007 Aug;132(2):515-22. Epub 2007 May 15.
Viasus D, Del Rio-Pertuz G, Simonetti AF, et al. Biomarkers for predicting short-term mortality in community-acquired pneumonia: A systematic review and meta-analysis. J Infect. 2016 Mar;72(3):273-82.
Wacker C, Prkno A, et al. **Procalcitonin** as a diagnostic marker for sepsis: a systematic review and meta-analysis. Lancet Infect Dis 2013; online Feb 1.
Yandiola PP, Capelastegui A, Quintana J, et al. Prospective comparison of severity scores for predicting clinically relevant outcomes for patients hospitalized with community-acquired pneumonia. Chest. 2009 Jun;135(6):1572-9.

References

Guidelines:

IDSA 2017 update c diff

Szajewska H, Canani RB, Guarino A, Hojsak I, Indrio F, Kolacek S, Orel R, Shamir R, Vandenplas Y, van Goudoever JB, Weizman Z; ESPGHAN Working Group for ProbioticsPrebiotics. Probiotics for the Prevention of Antibiotic-Associated Diarrhea in Children. J Pediatr Gastroenterol Nutr. 2016 Mar;62(3):495-506.

van Schalkwyk J, Yudin MH; INFECTIOUS DISEASE COMMITTEE. Vulvovaginitis: screening for and management of trichomoniasis, vulvovaginal candidiasis, and bacterial vaginosis. J Obstet Gynaecol Can. 2015 Mar;37(3):266-274. doi: 10.1016/S1701-2163(15)30316-9.

Workowski KA, Bolan GA; Centers for Disease Control and Prevention. Sexually transmitted diseases treatment guidelines, 2015. MMWR Recomm Rep. 2015 Jun 5;64(RR-03):1-137. Erratum in: MMWR Recomm Rep. 2015 Aug 28;64(33):924.

Epp A, Larochelle A. No. 250-Recurrent Urinary Tract Infection. J Obstet Gynaecol Can. 2017 Oct;39(10):e422-e431. doi: 10.1016/j.jogc.2017.08.017.

American College of Gastroenterology Monograph on Management of Irritable Bowel Syndrome

General:

https://www.canada.ca/en/health-canada/services/food-nutrition/food-labelling/health-claims/accepted-claims-about-nature-probiotic-microorganisms-food.html

Others:

Goldenberg JZ, Yap C, Lytvyn L, Lo CK, Beardsley J, Mertz D, Johnston BC. Probiotics for the prevention of Clostridium difficile-associated diarrhea in adults and children. Cochrane Database Syst Rev. 2017 Dec 19;12:CD006095.

Barker AK, Duster M, Valentine S, Hess T, Archbald-Pannone L, Guerrant R, Safdar N. A randomized controlled trial of probiotics for Clostridium difficile infection in adults (PICO). J Antimicrob Chemother. 2017 Nov 1;72(11):3177-3180.

MakrgeorgouA, Leonardi-BeeJ, Bath-HextallFJ, MurrellDF, TangMLK, RobertsA, BoyleRJ. Probioticsfortreatingeczema. CochraneDatabaseofSystematicReviews2018, Issue11. Art. No.: CD006135. DOI: 10.1002/14651858.CD006135.pub3.

Schnadower D, Tarr PI, Casper TC, et al. Lactobacillus rhamnosus *GG versus placebo for acute gastroenteritis in children.* N Engl J Med. *2018;379(21):2002-2014.*

Ebell MH. Probiotic Ineffective for Treatment of Acute Gastroenteritis in Young Children. Am Fam Physician. 2019 Jun 1;99(11):717-718. PubMed PMID: 31150186.

GuoQ, GoldenbergJZ, HumphreyC, ElDibR, JohnstonBC. Probioticsforthepreventionofpediatricantibiotic-associateddiarrhea. CochraneDatabaseofSystematicReviews2019, Issue4. Art. No.: CD004827. DOI: 10.1002/14651858.CD004827.pub5.

Senok AC, Verstraelen H, Temmerman M, Botta GA. Probiotics for the treatment

of bacterial vaginosis. Cochrane Database Syst Rev. 2009 Oct 7;(4):CD006289. doi: 10.1002/14651858.CD006289.
Xie HY, Feng D, Wei DM, Mei L, Chen H, Wang X, Fang F. Probiotics for vulvovaginal candidiasis in non-pregnant women. Cochrane Database Syst Rev. 2017 Nov 23;11:CD010496. doi: 10.1002/14651858.CD010496.
Schwenger EM, Tejani AM, Loewen PS. Probiotics for preventing urinary tract infections in adults and children. Cochrane Database Syst Rev. 2015 Dec 23;(12):CD008772.
Elias J, Bozzo P, Einarson A. Are probiotics safe for use during pregnancy and lactation? Can Fam Physician. 2011 Mar;57(3):299-301.
Lü M, Yu S, Deng J, Yan Q, Yang C, Xia G, Zhou X. Efficacy of Probiotic Supplementation Therapy for Helicobacter pylori Eradication: A Meta-Analysis of Randomized Controlled Trials. PLoS One. 2016 Oct 10;11(10):e0163743. doi: 10.1371/journal.pone.0163743.
Ko CW, Singh S, Feuerstein JD, Falck-Ytter C, Falck-Ytter Y, Cross RK; American Gastroenterological Association Institute Clinical Guidelines Committee. AGA Clinical Practice Guidelines on the Management of Mild-to-Moderate Ulcerative Colitis. Gastroenterology. 2019 Feb;156(3):748-764. doi: 10.1053/j.gastro.2018.12.009.

Colic

Sung V, D'Amico F, Cabana MD, Chau K, Koren G, Savino F, Szajewska H, Deshpande G, Dupont C, Indrio F, Mentula S, Partty A, Tancredi D. Lactobacillus reuteri to Treat Infant Colic: A Meta-analysis. Pediatrics. 2018 Jan;141(1). pii: e20171811. doi: 10.1542/peds.2017-1811.
20713478

22981952

24690625

25444531
J Pediatr Gastroenterol Nutr 2016 May;62(5):668

URINARY TRACT INFECTIONS (UTI), ABBREVIATION LIST:

💻=online extras ç=scored tab 🫘↓ dose for renal dysfunction; ☎ = Exception Drug Status Sask. ✗ =non-formulary in SK ▼=covered by NIHB ✆=prior NIHB ♀=female ♂=male **ABX**=antibiotic **AE**=adverse events **Alt**=alternate **AMG**=aminoglycoside **cc**=with food **CI**=contraindication **CrCl**=creatinine clearance **C&S**=culture & sensitivity **CEPH**=cephalosporins **CUA**=Canadian Urological Association ***E.coli***= *Escherichia coli* **d**=day(s) **DBW**=dosing body weight **DM**=diabetes mellitus **DS**=double strength (1DS tab= 160/800mg) **ESBL**=extended spectrum beta-lactamases **FQ**=fluoroquinolones **Fx**=function **g**=generic drug available **G6PD**= glucose-6-phosphate dehydrogenase **GI**=gastrointestinal **Gm –ve**= gram negative **HA**=headache **HS**=bedtime **IBW**=ideal body weight **IDSA**=Infectious Diseases Society of America **IV**=intravenous **mos**=month(s) ***P.aeruginosa***= *Pseudomonas aeruginosa* **po**=oral **pt**=patient **q**=every **Rx**= prescription **SAE**=serious advere events **SCI**=spinal cord injury **SK**=Sask **SOGC**=Society of obstetricians and Gynaecologists of Canada **sx**=symptom(s) **tx**=Treatment **TMP/SMX**=trimethoprim/sulfamethoxazole **UTI**=urinary tract infection **wk(s)**=week(s) **yr**=year

URINARY TRACT INFECTIONS (UTI)

Prepared by: Loren Regier; Updated by: Marlys LeBras **May/17**

1. Probable Organisms in UTIs

- **Acute uncomplicated cystitis in otherwise healthy ♀:** *E. coli*$_{(non\text{-}ESBL)}$ 75-95%, other *Enterobacteriaceae* organisms (e.g. *Klebsiella* species, *Proteus mirabilis*), *S. saprophyticus*
  - ≥ 95% of episodes are caused by a single bacterial organism
- **Complicated UTI:** *E. coli,* other *Enterobacteriaceae* organisms (e.g. *Klebsiella* species*, Proteus* specie)*, Enterococci, P. aeruginosa*
  - Episodes may be caused by multiple organisms; increase risk of antibiotic-resistent organsisms due to repeated antimicrobial courses and/or presence of instrumentation.
- **Pyelonephritits:** *E. coli,* other *Enterobacteriaceae* organisms (e.g. *Klebsiella* species, *Proteus mirabilis*), *S. saprophyticus*
- **Prostatitis:** *E. coli,* other *Enterobacteriaceae* organisms (e.g. *Klebsiella* species, *Proteus mirabilis*), *Enterococci, P. Aeruginosa.*
  If risk factors for STI (e.g. sexually active & age <35, or multiple sexual partners) consider treatment for N.gonnorrhoeae, C.trachomatis, trichomonas
- **Note:** Group B *Streptococcus* (*S. agalactiae)* may be present in those with diabetes or pregnancy

2. Oral Antimicrobials Spectrum of Activity for UTIs

Nitrofurantoin (e.g. MACROBID): *E. coli. Klebsiella* species*, S. saprophyticus, Enterococcus faecalis, ESBL*
- No coverage of: *Proteus* species*, Pseudomonas* species, *Enterococcus faecium*

SMX/TMP: *E. coli, Klebsiella* species*, P. mirabilis, S. saprophyticus*
- No coverage of: *Enterococci, Pseudomonas* species

Ciprofloxacin: *E. coli, Klebsiella* species*, P. mirabilis, S. saprophyticus, Pseudomonas* species, *Enterococcus faecalis*
- No coverage of: *Enterococcus faecium*

Fosfomycin: *E. coli, Klebsiella* species*, P. mirabilis, Enterococci, Pseudomonas* species, *ESBLs*

Amoxicillin/Clavulanate: *E. coli, Klebsiella* species*, P. mirabilis, S. saprophyticus, Enterococcus faecalis*
- No coverage of: *Pseudomonas* species, *Enterococcus faecium*

URINARY TRACT INFECTIONS (UTI), ADULT – REFERENCES

References: **1.** Anti-infective Review Panel. Anti-infective Guidelines for Community-acquired infections **2012**, Toronto, ON (Canada). **2.** Sanford Guide to Antimicrobial Therapy 2017.
3. Bugs and Drugs, www.dobugsneeddrugs.org. **4.** Micromedex 2016 drug database. **5.** Walker S, et al. Why are antibiotics prescribed for asymtomatic bacteriuria in institutionalized elderly people? CMAJ 2000;163:273-7. **6.** Nicolle L. Empirical treatment of acute cystitis in women. Int J Antimicrob Agents 2003;22:1-6. **7.** Lummus W, Thompson I. Prostatitis. Emerg Med Clin N America 2001;19:691-707. **8.** Warren J, et al. Guidelines for antimicrobial therapy of uncomplicated acute bacterial cystitis and acute pyelonephritis in women. Clin Infect Dis 1999;29:745-58. **9.** Miller L, Treatment of Uncomplicated Urinary Tract Infections in an Era of Increasing antimicrobial Resistance. Mayo Clin Proc 2004;79:1048-1054. **10.** Sask. resistance data from 2004 Antibiograms – Saskatoon (SHR) & Regina (RQHR). **11**. McConnell JD, et al. The Long-Term Effect of Doxazosin, Finasteride, and Combination Therapy on the Clinical Progression of Benign Prostatic Hyperplasia. N Engl J Med. 2003 Dec 18;349(25):2387-2398. **12**. Vogel T, et al. Optimal duration of antibiotic therapy for uncomplicated urinary tract infection in older women: a double-blind randomized controlled trial. CMAJ. 2004 Feb 17;170(4):469-73.

13. Nicolle LE, Bradley S, Colgan R, Rice JC, et al.; Infectious Diseases Society of America; American Society of Nephrology; American Geriatric Society. Infectious Diseases Society of America guidelines for the diagnosis and treatment of asymptomatic bacteriuria in adults. Clin Infect Dis. 2005 Mar 1;40(5):643-54. Epub 2005 Feb 4. (Colgan R, et al. Asymptomatic bacteriuria in adults. Am Fam Physician. 2006 Sep 15;74(6):985-90. Women who are pregnant should be screened for asymptomatic bacteriuria in the first trimester and treated, if positive. Treating asymptomatic bacteriuria in patients with diabetes, older persons, patients with or without indwelling catheters, or patients with spinal cord injuries has not been found to improve outcomes.)
US Preventive Services Task Force. **Screening** for asymptomatic bacteriuria in adults: U.S. Preventive Services Task Force reaffirmation recommendation statement. Ann Intern Med. 2008 Jul 1;149(1):43-7. Summary for patients in: Ann Intern Med. 2008 Jul 1;149(1):I37. Screen for asymptomatic bacteriuria with urine culture in **pregnant women** at 12 to 16 weeks' gestation or at the first prenatal visit, if later. (Grade A recommendation.) Do not screen for asymptomatic bacteriuria in men and nonpregnant women. (Grade D recommendation.).
Hooton TM, Bradley SF, Cardenas DD, et al. Diagnosis, prevention, and treatment of **catheter-associated** urinary tract infection in adults: 2009 International Clinical Practice Guidelines from the

Infectious Diseases Society of America (IDSA). Clin Infect Dis. 2010 Mar 1;50(5):625-63.

AAP-American Academy of Pediatrics. Urinary Tract Infection: Clinical Practice Guideline for the Diagnosis and Management of the **Initial UTI in Febrile Infants and Children 2 to 24 Months.** Pediatrics. 2011 Aug 28.
Ajayi T, Radhakrishnan R. Urinary tract infection in **older adults** in long-term care facilities. CMAJ. 2016 Sep 6;188(12):899.
Al-Abri M, Wong BM, Leis JA. A **urinary catheter left in place for slightly too long**: a teachable moment. JAMA Intern Med. 2015 Feb 1;175(2):163.
Allan GM, Nicolle L. **Cranberry** for preventing urinary tract infection. Can Fam Physician. 2013 Apr;59(4):367.
Alper BS, Curry SH. Urinary tract infection in **children**. Am Fam Physician. 2005 Dec 15;72(12):2483-8.
American College of Obstetricians & Gynecologists. ACOG Bulletin #91: **Treatment of urinary tract infections in nonpregnant women**. Obstet Gynecol.2008 Mar;111(3):785-94.
American Geriatrics Society **2015 Beers Criteria** Update Expert Panel. American Geriatrics Society 2015 Updated Beers Criteria for Potentially Inappropriate Medication Use in Older Adults. J Am Geriatr Soc. 2015 Oct 8. (Nitrofurantoin on list at CrCl <30mL/min)
AMMI Canada. Symptom-free pee: let it be. **Curbing the use of antibiotics to treat asymptomatic bacteriuria**. https://www.ammi.ca/Update/84.ENG.pdf (accessed Nov 25, 2016).
AMMI Canada. Symptom-free pee: let it be. **Asymptomatic bacteriuria** in **long-term care residents**. https://www.ammi.ca/AntibioticAwareness/ (accessed November 25, 2016).
Anger J, Lee U, Ackerman AL, et al. **Recurrent Uncomplicated Urinary Tract Infections in Women**: AUA/CUA/SUFU Guideline. J Urol. 2019 May 1:101097JU0000000000000296.
Anti-infective Review Panel. **Anti-infective Guidelines for Community-acquired Infections**. Canadian - New-**2013**. Toronto: MUMS Guideline Clearinghouse. http://www.mumshealth.com/
Antoniou T, Gomes T, Mamdani MM, et al. **Trimethoprim-sulfamethoxazole induced hyperkalaemia** in elderly patients receiving **spironolactone**: nested case-control study. BMJ. 2011 Sep 12;343:d5228.
Arnold JJ, Hehn LE, Klein DA. Common Questions About **Recurrent Urinary Tract Infections in Women**. Am Fam Physician. 2016;93(7):560- 569.
Auer S, Wojna A, Hell M. **Oral treatment options** for ambulatory patients with urinary tract infections caused by **extended-spectrum-beta-lactamase-producing Escherichia coli**. Antimicrob Agents Chemother. 2010 Sep;54(9):4006-8. (options: fosfomycin, nitrofurantoin & pivmecillinam)
Bader MS, Loeb M, Brooks AA. An update on the **management of urinary tract infections in the era of antimicrobial resistance**. Postgrad Med. 2016 Oct 7.
Bains A, Buna D, Hoag N. A retrospective review assessing the efficacy and safety of **nitrofurantoin in renal impairment**. Can Pharm J 2009;142:248-252.
Barber AE, Norton JP, Spivak AM, Mulvey MA. Urinary Tract Infections: **Current and Emerging Management Strategies**. Clin Infect Dis. 2013 May 3.
Barbosa-Cesnik C, Brown MB, Buxton M, et al. **Cranberry juice** fails to prevent recurrent urinary tract infection: results from a randomized placebo-controlled trial. Clin Infect Dis. 2011 Jan;52(1):23-30.
Barclay J, Veeratterapillay R, Harding C. **Non-antibiotic options** for recurrent urinary tract infections in women. BMJ. 2017 Nov 23;359:j5193.
Basmaci R, Vazouras K, Bielicki J, et al. Urinary tract infection antibiotic **trial study design**: a systematic review. Pediatrics. 2017;140(6):e20172209
Beahm NP, Nicolle LE, Bursey A, et al. The **assessment and management** of urinary tract infections in adults: Guidelines for pharmacists. Can Pharm J (Ott). 2017 Jul 31;150(5):298-305.
Beahm, N. P., Smyth, D. J., & Tsuyuki, R. T. (2018). **Outcomes of Urinary Tract Infection Management by Pharmacists** (RxOUTMAP): A study of pharmacist prescribing and care in patients with uncomplicated urinary tract infections in the community. Canadian Pharmacists Journal / Revue Des Pharmaciens Du Canada, 151(5), 305–314.
Beerepoot MA, Ter Riet G, Nys S, et al. **Cranberries vs Antibiotics** to Prevent Urinary Tract Infections: A Randomized Double-blind Noninferiority Trial in Premenopausal Women. Arch Intern Med. 2011 Jul 25;171(14):1270-8.
Beerepoot MA, Ter Riet G, Nys S, et al. **Lactobacilli vs Antibiotics** to Prevent Urinary Tract Infections: A Randomized, Double-blind, Noninferiority Trial in Postmenopausal Women. Arch Intern Med. 2012 May 14;172(9):704-12. (L rhamnosus GR-1 and L reuteri RC-14 do not meet the noninferiority criteria)
Bocquet N, Sergent Alaoui A, Jais JP, et al. Randomized Trial of **Oral Versus Sequential IV/Oral Antibiotic** for Acute Pyelonephritis in Children. Pediatrics. 2012 Jan 30.
Bonadio W. Urinary Tract Infection in **Outpatient Febrile Infants Younger than 30 Days of Age**: A 10-Year Evaluation. Pediatr Infect Dis J. 2013 Oct 7.
Bouchillon SK, Badal RE, Hoban DJ, Hawser SP. Antimicrobial **Susceptibility** of Inpatient Urinary Tract Isolates of **Gram-Negative Bacilli in the United States**: Results from the Study for Monitoring Antimicrobial Resistance Trends (SMART) Program: 2009-2011. Clin Ther. 2013 Apr 24.
Brady PW, Conway PH, Goudie A. **Length of intravenous antibiotic therapy** and treatment failure in **infants** with urinary tract infections. Pediatrics. 2010 Aug;126(2):196-203.
Braga LH, Mijovic H, Farrokhyar F, et al. Antibiotic prophylaxis for urinary tract infections in **antenatal hydronephrosis**. Pediatrics. 2013 Jan;131(1):e251-61.
Brandstr.m P, Esbj.rner E, Herthelius M, Swerkersson S, Jodal U, Hansson S. The **Swedish reflux trial in children**. III. Urinary tract infection pattern. J Urol 2010;184:286-91.
Brill JR. Diagnosis and treatment of **urethritis in men**. Am Fam Physician. 2010 Apr 1;81(7):873-8.
Bryce A, Hay AJ, Lane I, et al. **Global prevalence** of antibiotic **resistance** in paediatric urinary tract infections caused by **Escherichia coli** and association with routine use of antibiotics in primary care: systematic review and meta-analysis. BMJ 2016;352:i939
Buetti N, Lo Priore E, Atkinson A, et al; Swiss Centre for Antibiotic Resistance (ANRESIS). **Catheter-related infections**: does the spectrum of microbial causes change over time? A nationwide surveillance study. BMJ Open. 2018 Dec 22;8(12):e023824.
Cai T, Mazzoli S, et al. The role of **asymptomatic bacteriuria** in young women with recurrent urinary tract infections: to treat or not to treat? Clin Infect Dis. 2012 Sep;55(6):771-7.
Cai T et al. **Asymptomatic bacteriuria** treatment is associated with a higher prevalence of antibiotic resistant strains in women with urinary tract infections. Clin Infect Dis 2015 Dec 1; 61:1655.
Caljouw MA, van den Hout WB, Putter H, Achterberg WP, Cools HJ, Gussekloo J. Effectiveness of **cranberry capsules** to prevent urinary tract infections in vulnerable older persons: a double-blind randomized placebo-controlled trial in long-term care facilities. J Am Geriatr Soc. 2014 Jan;62(1):103-10.
Carmeli Y, Armstrong J, Laud PJ, et al. **Ceftazidime-avibactam** or best available therapy in patients with ceftazidime-resistant Enterobacteriaceae and Pseudomonas aeruginosa complicated urinary tract infections or complicated intra-abdominal infections (**REPRISE**): randomised, pathogen-directed, phase 3. Lancet Infect Dis. 2016 Jun;16(6):661-73.
Chaudhari P, Monuteaux M, Bachur R. The optimal **diagnostic threshold of pyuria** for identifying UTI in **young infants**. Pediatrics. 2016;138(5):e20162370.
Chaudhari PP, Monuteaux MC, Bachur RG. **Urine Concentration and Pyuria** for **Identifying UTI in Infants**. Pediatrics. 2016 Nov;138(5). pii: e20162370.
Chaudhari PP, Monuteaux MC, Bachur RG. Emergency Department **Revisits After an Initial Parenteral Antibiotic Dose for UTI**. Pediatrics. 2018 Sep;142(3).
Colgan R, Williams M. Diagnosis and treatment of **acute uncomplicated cystitis**. Am Fam Physician. 2011 Oct 1;84(7):771-6.
Colgan R, Williams M, Johnson JR. Diagnosis and treatment of **acute pyelonephritis in women**. Am Fam Physician. 2011 Sep 1;84(5):519-26.
Conway PH, Cnaan A, Zaoutis T, Henry BV, Grundmeier RW, Keren R. Recurrent urinary tract infections in **children**: risk factors and association with prophylactic antimicrobials. JAMA. 2007 Jul 11;298(2):179-86. Among the children in this study, antimicrobial prophylaxis was not associated with decreased risk of recurrent UTI, but was associated with increased risk of resistant infections.
Copp HL, Shapiro DJ, et al. National Ambulatory Antibiotic Prescribing Patterns for Pediatric **Urinary Tract Infection**,1998-2007.*Pediatrics*, 2011; DOI: 10.1542/peds.2010-3465
Copp HL, Yiee JH, et al.; on behalf of the Urologic Diseases in America Project. Use of **Urine Testing in Outpatients** Treated for Urinary Tract Infection. Pediatrics. 2013 Aug 5.
Cormican M, Murphy AW, Vellinga A. Interpreting **asymptomatic bacteriuria**. BMJ. 2011 Aug 4
Coulthard MG, Verber I, Jani JC, et al. Can **prompt treatment** of childhood UTI prevent kidney **scarring**? Pediatr Nephrol. 2009 Jul 9. [Epub ahead of print]
Coulthard MG et al. Does **prompt treatment** of urinary tract infection in preschool children **prevent renal scarring**: Mixed retrospective & prospective audits. Arch Dis Child 2013Dec 18.
Coussement J, Scemla A, Abramowicz D, et al. **Antibiotics for asymptomatic bacteriuria in kidney transplant recipients**. Cochrane Database of Systematic Reviews 2018, Issue 2. Art. No.: CD011357. Currently, there is insufficient

evidence to support routinely treating kidney transplant recipients with antibiotics in case of asymptomatic bacteriuria after transplantation, but data are scarce. Further studies assessing routine antibiotic treatment would inform practice and we await the results of three ongoing randomised studies, which may help resolve existing uncertainties.

Cowart K, Worley M, Rouby NE, Sando K. Evaluation of FDA Boxed Warning on **Prescribing Patterns of Fluoroquinolones** for Uncomplicated Urinary Tract Infections. Ann Pharmacother. 2019 Jul 18:1060028019865224.

Craig JC, Simpson JM, Williams GJ, et al. **Prevention of Recurrent** Urinary Tract Infection in **Children** with **Vesicoureteric Reflux** and Normal Renal Tracts (**PRIVENT**) Investigators. Antibiotic prophylaxis and recurrent urinary tract infection in children. N Engl J Med. 2009 Oct 29;361(18):1748-59. Antibiotic prophylaxis reduces the likelihood of subsequent urinary tract infection (UTI; number needed to treat [NNT] = 16 for 1 year). However, subsequent infections are more likely to be caused by resistant organisms, and prophylaxis is not effective if the index infection was caused by a resistant organism. (LOE = 1b)

Crellin E, Mansfield KE, Leyrat C, et al. **Trimethoprim use** for urinary tract infection and risk of adverse outcomes in older patients: cohort study. BMJ. 2018 Feb 9;360:k341.

Crider Krista S.; Cleves Mario A.; Reefhuis Jennita; et al. Antibacterial Medication Use During **Pregnancy** and Risk of Birth Defects: National Birth Defects Prevention Study. Arch Pediatr Adolesc Med. 2009;163(11):978-985. Patients may ask about a widely reported, case-control study suggesting that certain antibacterial drugs, including sulfonamides and nitrofurantoins, are associated with increased risk for birth defects.

Cunha BA, Hamid NS, Krol V, Eisenstein L. Safety of **meropenem in patients reporting penicillin allergy**: lack of allergic cross reactions. J Chemother. 2008 Apr;20(2):233-7.

Dahiya A, Goldman RD. Management of **asymptomatic bacteriuria in children**. Can Fam Physician. 2018 Nov;64(11):821-824.

Dai B, Liu Y, Jia J, et al. **Long-term antibiotics for the prevention** of recurrent urinary tract infection in **children**: a systematic review and meta-analysis. Arch Dis Child. 2010 Jul;95(7):499-508. Epub 2010 May 10.

Daniel M, Keller S, Mozafarihashjin M, et al. An Implementation **Guide to Reducing Overtreatment of Asymptomatic Bacteriuria**. JAMA Intern Med. 2017 Dec 11.

Davis A, Obi B, Ingram M. **Investigating urinary tract infections in children**. BMJ. 2013 Jan 30;346:e8654.

Davis GS, Waits K, Nordstrom L, et al. **Intermingled Klebsiella pneumoniae Populations Between Retail Meats** and Human Urinary Tract Infections. Clin Infect Dis. 2015 Jul 22.

Davis KF, Colebaugh AM, Eithun BL, et al. **Reducing catheter-associated urinary tract infections**: a quality-improvement initiative. Pediatrics. 2014 Sep;134(3):e857-64.

Dayan N, Dabbah H, Weissman I et al. Urinary Tract Infections Caused by **Community-Acquired Extended-Spectrum β-Lactamase-Producing** and Nonproducing Bacteria: A Comparative Study. J Pediatr. 2013 Aug 3.

Desai S, Aronson PL, Shabanova V, et al. Parenteral Antibiotic Therapy Duration in **Young Infants With Bacteremic Urinary Tract Infections**. Pediatrics. 2019 Aug 20.

Dore-Bergeron, Marie-Joelle, et al. **Urinary** Tract Infections in 1- to 3-Month-Old **Infants**: **Ambulatory** Treatment With Intravenous Antibiotics. Pediatrics 2009 124: 16-22

Downs SM. UTI and **Watchful Waiting**: The Courage to Do Nothing. Pediatrics. 2014 Mar;133(3):535-6.

Drekonja DM, Rector TS, Cutting A, Johnson JR. **Urinary tract infection in male veterans**: treatment patterns and outcomes [online December 3, 2012]. Arch Intern Med. 2012.

Drekonja DM, Zarmbinski B, Johnson JR. **Preoperative urine cultures** at a Veterans Affairs medical center [online December 3, 2012]. Arch Intern Med. 2012.

Drozdov D, Schwarz S, et al. **Procalcitonin and pyuria**-based algorithm reduces antibiotic use in urinary tract infections: a randomized controlled trial. BMC Med. 2015 May 1;13:104.

Dubrovsky AS, Foster BJ, Jednak R, et al. Visibility of the urethral meatus and risk of urinary tract infections in **uncircumcised** boys. CMAJ. 2012 Jul 9.

Dull RB, Friedman SK, Risoldi ZM, et al. Antimicrobial Treatment of **Asymptomatic Bacteriuria in Noncatheterized Adults**: A Systematic Review. Pharmacotherapy. 2014 May 7.

Durham SH, Stamm PL, Eiland LS. **Cranberry Products** for the Prophylaxis of Urinary Tract Infections in Pediatric Patients. Ann Pharmacother. 2015 Dec;49(12):1349-56.

Ebell MH, Butler CC, Hay AD. **Diagnosis of Urinary Tract Infections in Children**. Am Fam Physician. 2018 Feb 15;97(4):273-274.

Ellison JS, Dy GW, Fu BC, et al. **Neonatal Circumcision and Urinary Tract Infections** in Infants With Hydronephrosis. Pediatrics. 2018 Jun 7.

Emineke S, Cooper AJ, Fouch S, et al. **Diluted honey** inhibits biofilm formation: potential application in urinary catheter management? J Clin Pathol. 2016 Sep 26.

Fadini GP;Bonora BM;Mayur S;et al. **Dipeptidyl peptidase-4 inhibitors moderate the risk of genitourinary tract infections associated with sodium-glucose co-transporter-2 inhibitors**. Diabetes Obes Metab. 2017 Oct 20.

Fakih MG, Watson SR, Greene MT, et al. **Reducing inappropriate urinary catheter use**: a statewide effort. Arch Intern Med. doi:10.1001/archinternmed.2011.627.

Falagas ME, Vouloumanou EK, Samonis G, Vardakas KZ. **Fosfomycin**. Clin Microbiol Rev. 2016 Apr;29(2):321-47.

FDA May/16 is advising that the **serious side effects associated with fluoroquinolone antibacterial drugs generally outweigh** the benefits for patients with sinusitis, bronchitis, and uncomplicated urinary tract infections who have other treatment options. For patients with these conditions, fluoroquinolones should be reserved for those who do not have alternative treatment options.

Ferrara P, et al. **Cranberry juice** for the prevention of recurrent urinary tract infections: a randomized controlled trial in **children**. Scand J Urol Nephrol 2009;43:1-5.

Fisher H, Oluboyede Y, Chadwick T, et al. Continuous **low-dose antibiotic prophylaxis** for adults with repeated urinary tract infections (AnTIC): a randomised, open-label trial. Lancet Infect Dis. 2018 Jun 28.

Fitzgerald A, Mori R, Lakhanpaul M, et al. Antibiotics for treating **lower urinary tract infection in children**. Cochrane Database Syst Rev. 2012 Aug 15;8:CD006857. Although antibiotic treatment is effective for children with UTI, there are insufficient data to answer the question of which type of antibiotic or which duration is most effective to treat symptomatic lower UTI. This review found that 10-day antibiotic treatment is more likely to eliminate bacteria from the urine than single-dose treatments. No differences were observed for persistent bacteriuria, recurrence or re-infection between short and long-course antibiotics where the antibiotic differed between groups. This data adds to an existing Cochrane review comparing short and long-course treatment of the same antibiotic who also reported no evidence of difference between short and long-course antibiotics.

Flower A, Wang LQ, Lewith G, et al. **Chinese herbal medicine** for treating recurrent urinary tract infections in women. Cochrane Database Syst Rev. 2015 Jun 4;6:CD010446.
Evidence from seven small studies suggested that CHM as an independent intervention or in conjunction with antibiotics may be beneficial for treating recurrent UTIs during the acute phase of infection and may reduce the recurrent UTI incidence for at least six months post-treatment. CHM treatments specifically formulated for recurrent UTI may be more effective than herbal treatments designed to treat acute UTI. However, the small number and poor quality of the included studies meant that it was not possible to formulate robust conclusions on the use of CHM for recurrent UTI in women either alone or as an adjunct to antibiotics.

Ford JH 2nd, Vranas L, Coughlin D, et al. Effect of a Standard vs Enhanced Implementation **Strategy to Improve Antibiotic Prescribing in Nursing Homes**: A Trial Protocol of the Improving Management of Urinary Tract Infections in Nursing Institutions Through Facilitated Implementation (IMUNIFI) Study. JAMA Netw Open. 2019 Sep 4;2(9):e199526.

Forster CS, Shaikh N, Hoberman A, et al. **Uropathogens and Pyuria in Children With Neurogenic Bladders**. Pediatrics. 2018 Apr 4.

Fourcroy JL, et al. Efficacy and safety of a novel once-daily extended-release ciprofloxacin tablet formulation for treatment of uncomplicated urinary tract infection in women.
Antimicrob Agents Chemother. 2005 Oct;49(10):4137-43. (InfoPOEMs: A single dose of an extended-release version of ciprofloxacin (Cipro XR) is as effective as the immediate-release version taken twice daily for 3 days. The tiny reduction in the likelihood of gastrointestinal adverse effects (number needed to treat (NNT) = 60 - 80) is likely to be heavily promoted, and must be balanced against the higher cost of this formulation. As we are given more such options, it is important to remember the key elements in choosing a drug: its safety, tolerability, efficacy, price, and simplicity. Although extended-release ciprofloxacin is simpler, it is no more effective and will almost certainly cost more. (LOE = 1b))

Foxman B, Cronenwett AE, Spino C, et al. **Cranberry juice capsules** and urinary tract infection after surgery: results of a randomized trial. Am J Obstet Gynecol. 2015 Apr 13.

Frazee BW, Trivedi T, Montgomery M, et al. Emergency Department Urinary Tract Infections Caused by **Extended-Spectrum β-Lactamase-Producing Enterobacteriaceae**: Many Patients Have No Identifiable Risk Factor and Discordant Empiric Therapy Is Common. Ann Emerg Med. 2018 Jul 3.

Friedman A.Management of **UTI in children: Murky waters**. Pediatrics 2016 Jul; 138:e20161247.

Gágyor I, Bleidorn J, Kochen MG, et al. **Ibuprofen versus fosfomycin** for uncomplicated urinary tract infection in women: randomised controlled trial. BMJ 2015;351: h6544

Gallegos Salazar J, O'Brien W, Strymish J, Itani K,et al. Association of **screening and treatment for preoperative asymptomatic bacteriuria** with postoperative outcomes among US veterans [online Dec 12, 2018]. JAMA Surg. doi:10.1001/jamasurg.2018.4759

Gardiner BJ, Mahony AA, Ellis AG, et al. Is **fosfomycin** a potential treatment alternative for multidrug-resistant gram- negative **prostatitis**? Clin Infect Dis. 2014 Feb;58(4):e101-5.

Garin EH, et al. Clinical significance of **primary vesicoureteral reflux** & urinary antibiotic prophylaxis after acute pyelonephritis: a multicenter, randomized, controlled study.Pediatrics.
2006 Mar;117(3):626-32. (InfoPOEMs: Following treatment of acute pyelonephritis, antibiotic prophylaxis does not prevent further urinary tract infections in children with no documented vesicoureteral reflux (VUR) or in children

with mild to moderate VUR. (LOE = 1b-))
Gauthier M, Gouin S, Phan V, et al. Association of **Malodorous Urine** With Urinary Tract Infection in Children Aged 1 to 36 Months. Pediatrics. 2012 Apr 2.
Geerts AF, Eppenga WL, Heerdink R, et al. Ineffectiveness and adverse events of **nitrofurantoin** in women with urinary tract infection and **renal impairment** in primary care. Eur J Clin Pharmacol. 2013 Sep;69(9):1701-7.
Geerts AFJ, et al. Ineffectiveness and adverse events of **nitrofurantoin** in women with urinary tract infections & **renal impairment** in primary care. Eur J Clin Pharmacol 2013;69:1701-7.
Gharbi M, Drysdale JH, Lishman H, et al. Antibiotic management of urinary tract infection in elderly patients in primary care and its association with **bloodstream infections and all cause mortality**: population based cohort study. BMJ 2019;364:l525.
Ghimire KB, Nepal B. Dyspnea after treatment of recurrent urinary tract infection. Cleve Clin J Med. 2013 Nov;80(11):690-5. (**G6PD: nitrofurantoin** & phenozopyridine)
Glissmeyer EW, Korgenski EK, Wilkes J, et al. **Dipstick Screening** for Urinary Tract Infection in Febrile Infants. Pediatrics. 2014 Apr 28.
Goldberg O, Koren G, et al. Exposure to **nitrofurantoin during the first trimester** of **pregnancy** and the risk for major malformations. J Clin Pharmacol. 2013 Sep;53(9):991-5.
Goudie A, Dynan L, Brady PW, et al. Costs of **Venous Thromboembolism, Catheter-Associated Urinary Tract Infection, and Pressure Ulcer**. Pediatrics. 2015 Aug 10.
Gould CV, Umscheid CA, Agarwal RK, et al., Healthcare Infection Control Practices Advisory Committee (HICPAC). Guideline for **prevention of catheter-associated** urinary tract infections 2009. Atlanta (GA): Centers for Disease Control and Prevention (**CDC**); 2009. http://www.cdc.gov/ncidod/dhqp/pdf/guidelines/CAUTI_Guideline2009final.pdf
Grabe M, Bishop MC, Bjerklund-Johansen TE, et al. **Uncomplicated urinary tract infections in adult**: Guidelines on urological infections. Arnhem, The Netherlands: **European** Association of Urology (EAU); 2009 Mar. http://www.uroweb.org/fileadmin/tx_eauguidelines/2009/Full/Urological_Infections.pdf
Grabe M, Bishop MC, Bjerklund-Johansen TE, et al. **Catheter-associated UTIs**: Guidelines on urological infections. Arnhem, The Netherlands: **European** Association of Urology (EAU); 2009 Mar.
Grabe M, Bishop MC, Bjerklund-Johansen TE, et al. **Complicated URIs** due to urological disorders: Guidelines on urological infections. Arnhem, The Netherlands: **European** Association of Urology (EAU); 2009 Mar.
Grabe M, Bishop MC, Bjerklund-Johansen TE, et al. **Prostatitis and chronic pelvic pain** syndrome: Guidelines on urological infections. Arnhem, The Netherlands: **European** Association of Urology (EAU); 2009 Mar.
Grabe M, Bishop MC, Bjerklund-Johansen TE, et al. **Sepsis syndrome in urology (urosepsis):** Guidelines on urological infections. Arnhem, The Netherlands: **European** Association of Urology (EAU); 2009 Mar.
Grabe M, Bishop MC, Bjerklund-Johansen TE, et al. **Urinary tract infections in children**: Guidelines on urological infections. Arnhem, The Netherlands: **European** Association of Urology (EAU); 2009 Mar.
Grabe M, Bishop MC, Bjerklund-Johansen TE, et al. **UTIs in renal insufficiency, transplant recipients, diabetes mellitus and immunosuppression**: Guidelines on urological infections. Arnhem, The Netherlands: **European** Association of Urology (EAU); 2009 Mar.
Grigoryan L, Trautner BW, Gupta K. **Diagnosis and management of urinary tract infections** in the **outpatient setting**: a review. JAMA. 2014 Oct 22-29;312(16):1677-84.
Guay DR. **Cranberry** and urinary tract infections. Drugs. 2009;69(7):775-807. doi: 10.2165/00003495-200969070-00002. The findings of the Cochrane Collaboration support the potential use of cranberry products in the prophylaxis of recurrent UTIs in young and middle-aged women. However, in light of the heterogeneity of clinical study designs and the lack of consensus regarding the dosage regimen and formulation to use, cranberry products cannot be recommended for the prophylaxis of recurrent UTIs at this time.
Guinto VT, De Guia B, Festin MR, et al. Different antibiotic regimens for treating **asymptomatic bacteriuria in pregnancy**. Cochrane Database Syst Rev. 2010 Sep 8;9:CD007855. We cannot draw any definite conclusion on the most effective and safest antibiotic regimen for the initial treatment of asymptomatic bacteriuria in pregnancy.
Gupta K, Hooton TM, Roberts PL, Stamm WE. Short-course nitrofurantoin for the treatment of acute uncomplicated cystitis in women. Arch Intern Med. 2007 Nov 12;167(20):2207-12. A 5-day course of nitrofurantoin is equivalent clinically and microbiologically to a 3-day course of trimethoprim-sulfamethoxazole and should be considered an effective fluoroquinolone-sparing alternative for the treatment of acute cystitis in women.
Gupta Kalpana, Hooton Thomas M., Naber Kurt G., et al. International Clinical Practice Guidelines for the Treatment of **Acute Uncomplicated Cystitis and Pyelonephritis in Women**: A 2010 Update by the Infectious Diseases Society of America and the European Society for Microbiology and Infectious Diseases (**IDSA/ESCMID**) Clin Infect Dis. (2011) 52(5): e103-e120 doi:10.1093/cid/ciq257
Gupta K, Trautner B. In the Clinic: **Urinary tract infection.** Ann Intern Med. 2012 Mar 6;156(5):ITC31.
Gupta K, Trautner BW. Diagnosis and management of **recurrent urinary tract infections in non-pregnant women**. BMJ. 2013 May 29;346:f3140.
Gupta K, Grigoryan L, Trautner B. **In the Clinic: Urinary Tract Infection**. Ann Intern Med.2017 Oct 3;167(7):ITC49-ITC64.
Hadjipanayis A, Grossman Z, Del Torso S, et al. Current **primary care management of children aged 1-36 months** with urinary tract infections in Europe: large scale survey of paediatric practice. Arch Dis Child. 2014 Nov 5.
Hannula A, Perhomaa M, Venhola M, et al. **Long-term Follow-up of Patients After Childhood** Urinary Tract Infection. Arch Pediatr Adolesc Med. 2012 Oct 15:1-6.
Hawkey PM, Livermore DM. **Carbapenem** antibiotics for serious infections. BMJ. 2012 May 31;344:e3236.
Hay Alastair D, Whiting Penny, Butler Christopher C. Uncertainties Page: How best to **diagnose urinary tract infection in preschool children** in primary care? BMJ 2011;343:doi:10.1136/bmj.d6316 (Published 25 October 2011)
Hay AD, Birnie K, Busby J, et al. The **Diagnosis of Urinary Tract infection in Young children** (**DUTY**): a diagnostic prospective observational study to derive and validate a clinical algorithm for the diagnosis of urinary tract infection in children presenting to primary care with an acute illness. Health Technol Assess. 2016 Jul;20(51):1-294.
Hay AD, Sterne JA, Hood K, et al. Improving the **Diagnosis and Treatment of Urinary Tract Infection in Young Children** in Primary Care: Results from the **DUTY** Prospective Diagnostic Cohort Study. Ann Fam Med. 2016 Jul;14(4):325-36.
Hecker MT, Donskey CJ. Q: **Is antibiotic treatment indicated in a patient with a positive urine culture but no symptoms**? Cleve Clin J Med. 2014 Dec;81(12):721-4.
Heintz BH, Halilovic J, Christensen CL. **Vancomycin-resistant enterococcal** urinary tract infections. Pharmacotherapy. 2010 Nov;30(11):1136-49.
Heliovaara-Peippo S, Halmesmaki K, Hurskainen R, et al. The effect of **hysterectomy or levonorgestrel-releasing intrauterine** system on lower urinary tract symptoms: a 10-year follow-up study of a randomised trial. BJOG. 2010 Apr;117(5):602-9. Epub 2010 Feb 15.
Hewitt IK, Pennesi M, Morello W, et al. **Antibiotic Prophylaxis for Urinary Tract Infection-Related Renal Scarring**: A Systematic Review. Pediatrics. 2017;139(5):e20163145
Hill DM, Wood GC, Hickerson WL. **Linezolid Bladder Irrigation** as Adjunctive Treatment for a Vancomycin-Resistant Enterococcus faecium Catheter Associated Urinary Tract Infection. Ann Pharmacother. 2015 Feb;49(2):250-3.
Hoberman A, Wald ER, Hickey RW, et al. **Oral versus initial intravenous** therapy for urinary tract infections in young **febrile children**. Pediatrics 1999;104:79-86.
Hodson EM, et al. Antibiotics for **acute pyelonephritis in children**. Cochrane Database Syst Rev. 2007 Oct 17;(4):CD003772. These results suggest that children with acute pyelonephritis can be treated effectively with oral antibiotics (cefixime, ceftibuten and amoxycillin/clavulanic acid) or with short courses (2 to 4 days) of IV therapy followed by oral therapy. If IV therapy is chosen, single daily dosing with aminoglycosides is safe and effective.
Hollingsworth JM, Rogers MA, Krein SL, et al. Determining the **Noninfectious Complications of Indwelling Urethral Catheters**: A Systematic Review and Meta-analysis. Ann Intern Med. 2013 Sep 17;159(6):401-10.

Hooton TM, Bradley SF, Cardenas DD, et al. Diagnosis, prevention, and treatment of **catheter-associated urinary tract infection** in adults: 2009 International Clinical Practice Guidelines from the Infectious Diseases Society of America (IDSA). Clin Infect Dis. 2010 Mar 1;50(5):625-63.
Hooton TM, Roberts PL, Stapleton AE. **Cefpodoxime vs ciprofloxacin** for short-course treatment of acute uncomplicated cystitis: a randomized trial. JAMA. 2012 Feb 8;307(6):583-9.
Hooton TM. Clinical practice. **Uncomplicated urinary tract infection**. N Engl J Med. 2012 Mar 15;366(11):1028-37.
Hooton TM et al. **Voided midstream urine culture and acute cystitis in premenopausal women**. N Engl J Med 2013 Nov 14; 369:1883.
Hooton TM, Vecchio M, Iroz A, et al. Effect of **increased daily water intake** in premenopausal women with recurrent urinary tract infections: a randomized clinical trial [online Oct 1, 2018]. JAMA Intern Med.
Huang YY, Chen MJ, Chiu NT, Chou HH, et al. Adjunctive **Oral Methylprednisolone** in Pediatric Acute Pyelonephritis Alleviates **Renal Scarring**. Pediatrics. 2011 Aug 15.
Hudson A, Romao RLP, MacLellan D. **Urinary tract infection in children**. CMAJ. 2017 Apr 24;189(16):E608.
Hunziker M, Mohanan N, D'Asta F, et al. Incidence of Febrile Urinary Tract Infections in Children after **Successful Endoscopic Treatment of Vesicoureteral Reflux**: A Long-Term Follow-Up. J Pediatr. 2012 Jan 25.
Hunziker M, Colhoun E, Puri P. Renal cortical abnormalities in siblings of index patients with **vesicoureteral reflux**. Pediatrics. 2014 Apr;133(4):e933-7.
Huttner A, Hatz C, van den Dobbelsteen G, et al. Safety, immunogenicity, and preliminary clinical efficacy of a **vaccine against extra-intestinal pathogenic Escherichia** coli in women with a history of recurrent urinary tract infection: a randomised, placebo-controlled trial. Lancet Infect Dis 2017; online Feb 23.
Huttner A, Kowalczyk A, et al. Effect of 5-day **nitrofurantoin vs single-dose fosfomycin** on clinical resolution of uncomplicated lower urinary tract infection in women: a randomized clinical trial [online April 22, 2018]. JAMA.
Iravani A, Klimberg I, Briefer C, et al. A trial comparing low-dose, **short-course ciprofloxacin and standard 7 day therapy with co-trimoxazole or nitrofurantoin** in the treatment of uncomplicated urinary tract infection. J Antimicrob Chemother. 1999 Mar;43 Suppl A:67-75.
Jakobsen L, Garneau P, Bruant G, et al. Is Escherichia coli urinary tract infection a **zoonosis**? Proof of direct link with production animals and meat. Eur J Clin Microbiol Infect Dis. 2012 Jun;31(6):1121-9.
Jarvis T, Chan L, and Gottlieb T. Assessment and management of **lower urinary tract infection in adults**. Australian Prescriber. AN INDEPENDENT REVIEW (2014): 7.
Jeffres MN, Shuster JE, Barclay SM. Treatment of **Ciprofloxacin Nonsusceptible Urinary Tract Infections with Ciprofloxacin**. Ahead of Print on 1 June 2011.
Jepson RG, Craig JC. **Cranberries** for preventing urinary tract infections. Cochrane Database Syst Rev. 2008 Jan 23;(1):CD001321. There is some evidence that cranberry juice may decrease the number of symptomatic UTIs over a 12 month period, particularly for women with recurrent UTIs. It's effectiveness for other groups is less certain. The large number of dropouts/withdrawals indicates that cranberry juice may not be acceptable over long periods of time. It is not clear what is the optimum dosage or method of administration (e.g. juice, tablets or capsules).
Jepson RG, Williams G, Craig JC. **Cranberries** for preventing urinary tract infections. Cochrane Database Syst Rev **2012**;(10):CD001321. Prior to the current update it appeared there was some evidence that cranberry juice may decrease the number of symptomatic UTIs over a 12 month period, particularly for women with recurrent UTIs. The addition of 14 further studies suggests that cranberry juice is less effective than previously indicated. Although some of small studies demonstrated a small benefit for women with recurrent UTIs, there were no statistically significant differences when the results of a much larger study were included.
Jepson R, Craig J, Williams G. **Cranberry Products and Prevention** of Urinary Tract Infections. JAMA. 2013 Oct 2;310(13):1395-1396.
Jerardi KE, Elkeeb D, Weiser J, Brinkman WB. Rapid implementation of evidence-based guidelines for **imaging after first urinary tract infection**. Pediatrics. 2013 Sep;132(3):e749-55.
Johnston CL, Johnston MJ, Corke A, et al. A likely urinary tract infection in a **pregnant woman**. BMJ. 2017 Apr 27;357:j1777.
Johnson JR, Russo TA. **Acute Pyelonephritis in Adults**. N Engl J Med. 2018 Jan 4;378(1):48-59.
Juthani-Mehta M, Datunashvili A, Tinetti M. **Tests for urinary tract infection** in nursing home residents. JAMA. 2014 Oct 22-29;312(16):1687-8.
Juthani-Mehta M, Van Ness PH, Bianco L, et al. Effect of **cranberry capsules** on bacteriuria plus pyuria among older women in nursing homes: a randomized clinical trial. JAMA. doi:10.1001/jama.2016.16141
Kahlmeter G, Poulsen HO. Antimicrobial susceptibility of **Escherichia coli** from community-acquired urinary tract infections in **Europe**: the ECO·SENS study revisited. Int J Antimicrob Agents. 2011 Nov 2. In E. coli, resistance to mecillinam, cefadroxil (representing oral cephalosporins), nitrofurantoin, fosfomycin trometamol, gentamicin and the third-generation cephalosporins cefotaxime and ceftazidime was<2%, with the following exceptions: gentamicin in Portugal (2.8%); fosfomycin in Greece (2.9%); and cephalosporins in Austria (2.7-4.1%). Resistance levels were higher for amoxicillin/clavulanic acid (2.0-8.9%) and ciprofloxacin (0.5-7.6%) and much higher to ampicillin (21.2-34.0%), sulfamethoxazole (21.2- 31.3%), trimethoprim (14.9-19.1%) and trimethoprim/sulfamethoxazole (14.4-18.2%). Resistance to quinolones and trimethoprim increased between the ECO·SENS I (1999-2000) and ECO·SENS II (2007-2008): nalidixic acid 4.3% to 10.2%; ciprofloxacin 1.1% to 3.9%; and trimethoprim 13.3% to 16.7%. In the previous study, no isolates with extended-spectrum β-lactamase were found; however, in the present study 11 isolates were identified as having either CTX-M or AmpC.
Karageorgopoulos DE, Wang R, Yu XH, Falagas ME. **Fosfomycin**: evaluation of the published evidence on the emergence of antimicrobial resistance in gram-negative pathogens. J Antimicrob Chemother. 2012;67:255-268.
Kaufman J, Fitzpatrick P, Tosif S, et al. Faster clean catch urine collection (**Quick-Wee method**) from infants: randomised controlled trial. BMJ 2017;357:j1341.
Kazemier BM, Koningstein FN, Schneeberger C, et al. **Maternal and neonatal consequences of treated and untreated asymptomatic bacteriuria in pregnancy**: a prospective cohort study with an embedded randomized controlled trial. Lancet Infect Dis 2015; online Aug 6.
Keating GM. **Fosfomycin** trometamol: a review of its use as a single-dose oral treatment for patients with acute lower urinary tract infections and pregnant women with asymptomatic bacteriuria. Drugs. 2013 Nov;73(17):1951-66.
Keren R, Shaikh N, Pohl H, et al. **Risk Factors** for Recurrent Urinary Tract Infection and **Renal Scarring**. Pediatrics. 2015 Jun 8.
Kiang TK, Ford JA, et al. **Nitrofurantoin**-associated lung and liver toxicity leading to liver transplantation in a middle-aged patient. Can J Hosp Pharm. 2011 Jul;64(4):262-70.
Kallen AJ, et al. Current antibiotic therapy for isolated urinary tract infections in women. Arch Intern Med. 2006 Mar 27;166(6):635-9. CONCLUSIONS: Quinolones have surpassed sulfas as the most common class of antibiotic prescribed for isolated outpatient UTI in women. Few significant predictors of quinolone use exist, suggesting that the increase is not confined to a certain subset of patients. This pervasive growth in quinolone use raises concerns about increases in resistance to this important class of antibiotics.
Kashanian J, Hakimian P, Blute M Jr, et al. **Nitrofurantoin**: the return of an old friend in the wake of growing resistance. BJU Int. 2008 Dec;102(11):1634-7. Epub 2008 Jul 24.
Katchman EA, Milo G, et al. **Three-day** vs longer duration of antibiotic treatment for cystitis in women: systematic review & meta-analysis. Am J Med. 2005 Nov;118(11):1196-207.
Kaye KS, et al. Effect of **Meropenem-Vaborbactam vs Piperacillin-Tazobactam** on Clinical Cure or Improvement and Microbial Eradication in Complicated Urinary Tract Infection: The **TANGO** I Randomized Clinical Trial. JAMA. 2018 Feb 27;319(8):788-799.
Khaw C, Oberle AD, Lund BC, et al. Assessment of **Guideline Discordance With Antimicrobial Prophylaxis** Best Practices for Common Urologic Procedures. JAMA Netw Open. 2018;1(8):e186248.
Kodner CM, Gupton EKT. **Recurrent Urinary Tract Infections in Women**: Diagnosis and Management. Am Fam Physician. 2010 Sep 15;82(6):638-643.
Knottnerus BJ, Grigoryan L, Geerlings SE, et al. **Comparative effectiveness** of antibiotics for uncomplicated urinary tract infections: Network meta-analysis of randomized trials. Fam Pract. 2012 Apr 19.
Knottnerus BJ, Geerlings SE, Moll van Charante EP, Ter Riet G. Toward a **simple diagnostic index** for acute uncomplicated urinary tract infections. Ann Fam Med. 2013 Sep-Oct;11(5):442-51.
Knox K. Women should be able to get **antibiotics for urinary tract infection without a prescription**. BMJ. 2015 Jul 14;351:h3441.
Köves B, Cai T, et al. **Benefits and Harms of Treatment of Asymptomatic Bacteriuria**: A Systematic Review and Meta-analysis by the European Association of Urology Urological Infection Guidelines Panel. Eur Urol. 2017 Jul 25.
Kranjčec B, Papeš D, Altarac S. **D-mannose powder for prophylaxis of recurrent urinary tract infections in women**: a randomized clinical trial. World J Urol. 2014 Feb;32(1):79-84.

Krein SL, Kowalski CP, Harrod M, et al. **Barriers to Reducing Urinary Catheter Use**: A Qualitative Assessment of a Statewide Initiative. JAMA Intern Med. 2013 Mar 25:1-6.
Kronenberg A, Bütikofer L, Odutayo A, et al. **Symptomatic treatment of uncomplicated lower urinary tract infections in the ambulatory setting**: randomised, double blind trial. BMJ 2017;359:j4784
Lavelle JM et al. Two-step process for **ED UTI screening** in febrile young **children**: Reducing catheterization rates. Pediatrics 2016 Jul; 138:e20153023.
Lee BS, Bhuta T, Simpson JM, et al. **Methenamine hippurate** for preventing urinary tract infections. Cochrane Database Syst Rev. 2012 Oct 17;10:CD003265. doi: 10.1002/14651858.CD003265.pub3. Methenamine hippurate may be effective for preventing UTI in patients without renal tract abnormalities, particularly when used for short-term prophylaxis. It does not appear to work in patients with neuropathic bladder or in patients who have renal tract abnormalities. The rate of adverse events was low, but poorly described.
Lee C, Phillips C, Vanstone JR. **Educational intervention to reduce treatment of asymptomatic bacteriuria** in long-term care. BMJ Open Qual. 2018 Dec 1;7(4):e000483.
Lee M, Bozzo P, Einarson A, Koren G. **Urinary tract infections in pregnancy**. Can Fam Physician. 2008 Jun;54(6):853-4.
Lega IC, Bronskill SE, Campitelli MA, et al. **Sodium glucose cotransporter 2 inhibitors and risk** of genital mycotic and urinary tract infection: A population-based study of older women and men with diabetes. Diabetes Obes Metab. 2019 Jul 2
Leis JA, Corpus C, Rahmani A, et al. **Medical Directive for Urinary Catheter Removal** by Nurses on General Medical Wards. JAMA Intern Med. 2015 Nov 16:1-3.
Leroy S, Romanello C, Galetto-Lacour A, et al. **Procalcitonin** is a Predictor for High-Grade Vesicoureteral Reflux in Children: Meta-Analysis of Individual Patient Data. J Pediatr. 2011 Oct;159(4):644-651.e4.
Leroy S, Fernandez-Lopez A, Nikfar R, et al. Association of **Procalcitonin** With Acute Pyelonephritis and Renal Scars in Pediatric UTI. Pediatrics. 2013 Apr 29.
Letica-Kriegel AS, Salmasian H, Vawdrey DK, et al. Identifying the **risk factors for catheter-associated urinary tract infections**: a large cross-sectional study of six hospitals. BMJ Open. 2019 Feb 21;9(2):e022137.
Lewis- de los Angeles WW, Thurm C, Hersh AL, et al. **Trends in Intravenous Antibiotic Duration** for Urinary Tract Infections in Young Infants. Pediatrics. 2017;140(6):e2017021
Li N, Zhou X, Yuan J, et al. **Ceftriaxone and acute renal failure** in children. Pediatrics. 2014 Apr;133(4):e917-22.
Lin E, Bhusal Y, Horwitz D, Shelburne III SA, Trautner BW. **Overtreatment of enterococcal bacteriuria**. Arch Intern Med. 2012;172(1):33-38.
Little P, Moore M V, Turner S, et al. Effectiveness of **five different approaches** in management of urinary tract infection: randomised controlled trial.BMJ 2010;340:c199, doi: 10.1136/bmj.c199 (5 Feb 2010)
Little P, Merriman R, Turner S, et al. Presentation, pattern, and natural course of severe symptoms, and **role of antibiotics and antibiotic resistance** among patients presenting with suspected uncomplicated urinary tract infection in primary care: observational study. BMJ. 2010 Feb 5;340:b5633. doi: 10.1136/bmj.b5633.
Loeb M, Brazil K, Lohfeld L, et al. Effect of a multifaceted intervention on number of antimicrobial prescriptions for suspected urinary tract infections in residents of nursing homes: cluster randomised controlled trial. BMJ. 2005 Sep 24;331(7518):669. Epub 2005 Sep 8.
Los-Arcos I, Pigrau C, Rodríguez-Pardo D, et al. Long-Term **Fosfomycin**-Tromethamine Oral Therapy for Difficult-To-Treat Chronic Bacterial **Prostatitis**. Antimicrob Agents Chemother. 2015 Dec 14;60(3):1854-8.
Lubell TR, Barasch JM, Xu K, et al. **Urinary Neutrophil Gelatinase-Associated Lipocalin** for the Diagnosis of Urinary Tract Infections. Pediatrics. 2017; 140(6):e20171090.
Lumbiganon P, Villar J, Laopaiboon M, et al. One-day compared with **7-day nitrofurantoin** for asymptomatic bacteriuria in pregnancy: a randomized controlled trial. Obstet Gynecol. 2009 Feb;113(2 Pt 1):339-45. A 1-day regimen of nitrofurantoin is significantly less effective than a 7-day regimen. Women with asymptomatic bacteriuria in pregnancy should receive the standard 7-day regimen.
Lutters M, Vogt-Ferrier NB. Antibiotic duration for treating uncomplicated, symptomatic lower urinary tract infections in **elderly women**. Cochrane Database Syst Rev. 2008 Jul 16;(3):CD001535. Short-course treatment (3 to 6 days) could be sufficient for treating uncomplicated UTIs in elderly women, although more studies on specific commonly prescribed antibiotics are needed.
Madden-Fuentes RJ, Arshad M, Ross SS, et al. Efficacy of **Fluoroquinolone/Probiotic Combination** Therapy for Recurrent Urinary Tract Infection in Children: A Retrospective Analysis. Clin Ther. 2015 Jul 29.
Mantadakis E, Plessa E, Vouloumanou EK, et al. Serum **procalcitonin** for prediction of renal parenchymal involvement in children with urinary tract infections: a meta-analysis of prospective clinical studies. J Pediatr. 2009 Dec;155(6):875-881.e1. Epub 2009 Oct 21.
Marshall AD, Dempsey OJ. Is "**nitrofurantoin lung**"on the increase? BMJ. 2013 Jun 18;346:f3897.
Marschall J, Carpenter CR, Fowler S, Trautner BW; CDC Prevention Epicenters Program. **Antibiotic prophylaxis** for urinary tract infections **after removal of urinary catheter**: meta-analysis. BMJ. 2013 Jun 11;346:f3147.
McDaniel CE, Ralston S, Lucas B, Schroeder AR. Association of **Diagnostic Criteria With Urinary Tract Infection** Prevalence in Bronchiolitis: A Systematic Review and Meta-analysis. JAMA Pediatr. 2019 Jan 28.
McIsaac WJ, et al. Validation of a **decision aid** to assist physicians in reducing unnecessary antibiotic drug use for acute cystitis. Arch Intern Med. 2007 Nov 12;167(20):2201-6. A simple 3-item decision aid could significantly reduce unnecessary antibiotic drug prescriptions and urine culture testing in females with symptoms of acute cystitis.
McKinnell JA, Stollenwerk NS, Jung CW, Miller LG. **Nitrofurantoin** compares favorably to recommended agents as empirical treatment of uncomplicated urinary tract infections in a decision and cost analysis. Mayo Clin Proc. 2011 Jun;86(6):480-8.
McKinnell JA, Dwyer JP, Talbot GH, et al; CARE Study Group. **Plazomicin** for Infections Caused by Carbapenem-Resistant Enterobacteriaceae. N Engl J Med. 2019 Feb 21;380(8):791-793
McMurdo ME, Argo I, et al. **Cranberry or trimethoprim** for the prevention of recurrent urinary tract infections? A RCT in older women. J Antimicrob Chemother. 2008 Nov 28. [Epub ahead of print] n=137. Trimethoprim had a very limited advantage over cranberry extract in the prevention of recurrent UTIs in older women and had more adverse effects. Our findings will allow older women with recurrent UTIs to weigh up with their clinicians the inherent attractions of a cheap, natural product like cranberry extract whose use does not carry the risk of antimicrobial resistance or super-infection with C. difficile or fungi.
Medical Letter: Treatment Guidelines. **Choice of Antibacterial Drugs**. May 2007.
Medical Letter. Treatment Guidelines. **Drugs for Bacterial Infections**. June 2010. Updated **July 2013**.
Mehnert-Kay SA. Diagnosis and management of uncomplicated urinary tract infections. Am Fam Physician. 2005 Aug 1;72(3):451-6.
Michels TC, Sands JE. **Dysuria**: Evaluation and Differential Diagnosis in Adults. Am Fam Physician. 2015;92(9):778-786.
Middelkoop SJ, et al. Routine tests and automated urinalysis in patients with suspected urinary tract infection at the ED. Am J Emerg Med. 2016 Aug;34(8):1528-34.
Milo G, Katchman EA, Paul M, et al. Duration of antibacterial treatment for uncomplicated urinary tract infection in women. Cochrane Database Syst Rev. 2005 Apr 18;(2):CD004682.
Mody L, Juthani-Mehta M. JAMA **patient page**. Urinary tract infections in **older women**. JAMA. 2014 Feb 26;311(8):874.
Mody L, Juthani-Mehta M. Urinary tract infections in older women: a clinical review. JAMA. 2014 Feb 26;311(8):844-54.
Mody L, Krein SL, Saint SK, et al. A targeted **infection prevention intervention in nursing home residents with indwelling devices**: a randomized clinical trial [online March 16, 2015]. JAMA Intern Med. doi:10.1001/jamainternmed.2015.132.
Mody L, Greene MT, Meddings J, et al. A **National Implementation Project to Prevent Catheter-Associated Urinary Tract Infection** in Nursing Home Residents. JAMA Intern Med. 2017 May 19.
Montini G, Toffolo A, et al. Antibiotic treatment for pyelonephritis in children: multicentre randomized controlled non-inferiority trial. BMJ. 2007 Jul 4; [Epub ahead of print] Treatment with oral antibiotics is as effective as parenteral then oral treatment in the management of the first episode of clinical pyelonephritis in children.
Montini G, Rigon L, Zucchetta P, et al. IRIS Group. Prophylaxis after first febrile urinary tract infection in children? A multicenter, randomized, controlled, noninferiority trial. Pediatrics. 2008 Nov;122(5):1064-71. Prophylactic antibiotic therapy for 12 months following a febrile urinary tract infection (UTI) in children between the ages of 2 months and 7 years does not reduce the risk of subsequent UTI, even in children with vesicoureteral reflux grades I through III. This is the second trial to find that **prophylaxis is not necessary**. (LOE = 1b-)
Montini Giovanni, Tullus Kjell, Hewitt Ian. **Febrile Urinary Tract Infections in Children**. N Engl J Med 2011;365:239-50.
Moore A, Doull M, Grad R, et al. **Recommendations on screening for asymptomatic bacteriuria in pregnancy**. CMAJ. 2018 Jul 9;190(27):E823-E830.

Mori R, Lakhanpaul M, Verrier-Jones K. Diagnosis and management of urinary tract infection in **children: summary of NICE guidance**. BMJ. 2007 Aug 25;335(7616):395-7.
Mouttalib S, Khan S, Castel-Lacanal E, et al. Risk of urinary tract infection after detrusor **botulinum toxin A injections** for refractory neurogenic detrusor overactivity in patients with no antibiotic treatment. BJU Int. 2010 Jun 29.
Murphy C, Cowan A, Moore K, Fader M. Managing long term indwelling urinary **catheters**. BMJ. 2018 Oct 11;363:k3711.
Naber KG, Llorens L, Kaniga K, et al.. Intravenous **Doripenem** 500 mg Versus Levofloxacin 250 mg With an Option to Switch to Oral Therapy for the Treatment of Complicated Lower Urinary Tract Infection and Pyelonephritis. Antimicrob Agents Chemother. 2009 Jul 6. [Epub ahead of print]
Nagler EV, Williams G, Hodson EM, et al. **Interventions for primary vesicoureteric reflux.** Cochrane Database Syst Rev. 2011 Jun 15;6:CD001532. Compared with no treatment, use of long-term, low-dose antibiotics did not significantly reduce the number of repeat symptomatic and febrile UTIs in children with VUR. Considerable heterogeneity in the analyses and inclusion of only one adequately blinded study, made drawing firm conclusions challenging. Antibiotic prophylaxis significantly reduced the risk of developing new or progressive renal damage, but assuming an 8% baseline risk, 33 children would need long-term antibiotic prophylaxis to prevent one more child developing kidney damage over the course of two to three years.The added benefit of surgical or endoscopic correction of VUR over antibiotic treatment alone remains unclear. Eight children would require combined surgical and antibiotic treatment to prevent one additional child developing febrile UTI by five years, but it would not cause fewer children developing renal damage.
Nelson CP, Hoberman A, Shaikh N, et al. **Antimicrobial Resistance** and Urinary Tract Infection **Recurrence**. Pediatrics. 2016 Mar 11.
Nemetalla M, Frazer K. **Antibiotic Prophylaxis for UTIs in Patients with Neurogenic Bladder**. Am Fam Physician. 2019 Feb 1;99(3):186.
Nicolle LE. Catheter-related urinary tract infection. Drugs Aging. 2005;22(8):627-39.
Nicolle LE. Urinary Tract Infections in the **Older Adult**. Clin Geriatr Med. 2016 Aug;32(3):523-38.
Nicolle LE, Gupta K, Bradley SF, et al. Clinical Practice **Guideline for the Management of Asymptomatic Bacteriuria**: 2019 Update by the Infectious Diseases Society of Americaa. Clin Infect Dis. 2019 Mar 21.
Niel-Weise B, van den Broek P. Antibiotic policies for short-term catheter bladder drainage in adults. Cochrane Database Syst Rev. 2005 Jul 20;(3):CD005428.
Ninan S, Walton C, Barlow G. **Investigation of suspected urinary tract infection in older people**. BMJ. 2014 Jul 3;349:g4070.
Nordeng H, Lupattelli A, Romoren M, et al. **Neonatal outcomes after gestational exposure to nitrofurantoin**. Obstet Gynecol. 2013 Feb;121(2 Pt 1):306-13.
Oplinger M, Andrews CO. **Nitrofurantoin Contraindication** in Patients with a **Creatinine Clearance Below 60 mL/min**: Looking for the Evidence. Ann Pharmacother. 2013 Jan;47(1):106-11.
Paglia M, Peterson J, Fisher AC, et al. Safety and efficacy of **levofloxacin** 750 mg for 2 weeks or 3 weeks compared with levofloxacin 500 mg for 4 weeks in treating chronic bacterial **prostatitis**. Curr Med Res Opin. 2010 Jun;26(6):1433-41.
Paschke AA, Zaoutis T, Conway PH, et al. Previous **Antimicrobial Exposure** Is Associated With Drug-**Resistant** Urinary Tract Infections in Children. Pediatrics. 2010 Mar 1.
Pauchard JY, Chehade H, Kies CZ, et al. **Avoidance of voiding cystourethrography** in infants younger than 3 months with Escherichia coli urinary tract infection and normal renal ultrasound. Arch Dis Child. 2017 Apr 13.
Peleg AY, Hooper DC. **Hospital-acquired** infections due to gram-negative bacteria. N Engl J Med. 2010 May 13;362(19):1804-13.
Percival KM et al. Impact of an **antimicrobial stewardship** intervention on urinary tract infection treatment in the **ED**. Am J Emerg Med 2015 Sep; 33:1129.
Perrotta C, et al. **Oestrogens** for preventing recurrent urinary tract infection in postmenopausal women. Cochrane Database Syst Rev. 2008 Apr 16;(2):CD005131. Based on only two studies comparing vaginal oestrogens to placebo, vaginal oestrogens reduced the number of UTIs in postmenopausal women with RUTI, however this varied according to the type of oestrogen used and the treatment duration. Pharmacist's Letter: Treatment of Uncomplicated UTI June 2006
Petty LA, Vaughn VM, Flanders SA, et al. Risk Factors and Outcomes Associated With **Treatment of Asymptomatic Bacteriuria in Hospitalized Patients**. JAMA Intern Med. 2019 Aug 26.
Pharmacists's Letter. **Cystoplus** (sodium citrate) for Cystitis. Aug 2011.
Pickard R, Lam T, MacLennan G, et al. **Antimicrobial catheters** for reduction of symptomatic urinary tract infection in adults requiring short-term catheterisation in hospital: a multicentre randomised controlled trial. Lancet 2012.
Pohl A. Modes of administration of antibiotics for symptomatic severe urinary tract infections. *Cochrane Database of Systematic Reviews* 2007, Issue 4. Art. No.: CD003237. DOI: 10.1002/14651858.CD003237.pub2. {Cochrane Summary: Severe urinary tract infection (UTI) is a common infection in adults and children, causing acute disease with a variety of symptoms such as fever and flank pain. This may lead to kidney damage, kidney failure or hypertension. Standard therapy involves antibiotics given at least initially by injection. This review identified 15 studies (1743 participants). The results of this review suggest oral therapy is equally effective in treating UTI and preventing long-term damage. This might reduce costs but also inconvenience for the patient.}
Poonai N, Li J, Langford C, et al. **Intraurethral Lidocaine** for Urethral Catheterization in Children: A Randomized Controlled Trial. Pediatrics. 2015 Sep 28.
Price JR, Guran LA, et al. **Nitrofurantoin vs other prophylactic** agents in **reducing recurrent urinary tract infections** in adult women: a systematic review and meta-analysis. Am J Obstet Gynecol. 2016 Nov;215(5):548-560.
Raman G, McMullan B, Taylor P, et al. **Multiresistant E. coli** urine infections in children: a case-control study. Arch Dis Child. 2017 Sep 12.
Richards D, Toop L, Chambers S, Fletcher L. Response to antibiotics of women with symptoms of urinary tract infection but negative dipstick urine test results: double blind randomized controlled trial. BMJ 2005; 331:143-46. (InfoPOEMs: No infection, no antibiotic, right? Maybe not. In women with dysuria and frequency but a negative urine dipstick result for nitrites and leukocytes, 3 of 4 women will respond to antibiotic treatment as compared with 1 of 4 taking placebo. The negative dipstick result correlated with culture 92% of the time. These results imply that some women have microbial infections that are not identified by dipstick or culture. Or, perhaps, the antibiotic is doing something other than killing bacteria. (LOE = 1b))
RIVUR Trial Investigators. Antimicrobial **prophylaxis for children** with **vesicoureteral reflux**. N Engl J Med. DOI: 10.1056/NEJMoa1401811.
Robert KB. Revised **AAP Guideline on UTI in Febrile Infants and Young Children**. Am Fam Physician. 2012;86(10):940-946.
Roberts KB, Wald ER. **The Diagnosis of UTI**: **Colony Count Criteria** Revisited. Pediatrics. 2018 Jan 16.
Robinson JL, Finlay JC, Lang ME, et al; **Canadian Paediatric Society (CPS). Urinary tract infection in infants and children**: diagnosis and management. www.cps.ca/en/documents/position/urinary-tract-infections-in-children (accessed June 24, 2014).
Robinson JL, Finlay JC, Lang ME, et al; **Canadian Paediatric Society**, Community Paediatrics Committee, Infectious Diseases and Immunization Committee. **Prophylactic antibiotics for children with recurrent urinary tract infections**. Paediatr Child Health. 2015 Jan-Feb;20(1):45-51. www.cps.ca/en/documents/position/prophylactic-antibiotics-recurrent-urinary-tract-infections(accessed February 17, 2015).
Rogozinska E, et al. Accuracy of **Onsite Tests to Detect Asymptomatic Bacteriuria in Pregnancy**: A Systematic Review and Meta-analysis. Obstet Gynecol. 2016 Sep;128(3):495-503.
Rotjanapan P; Dosa D; Thomas KS. **Potentially Inappropriate Treatment** of Urinary Tract Infections in Two Rhode Island Nursing Homes. Arch Intern Med. 2011;171(5):438-443.
Saha D, Patel J, Buckingham D, et al. **Urine Culture Follow-up and Antimicrobial Stewardship** in a Pediatric Urgent Care Network. Pediatrics. 2017;139(4):e20162103.
Saint S, Greene MT, Krein SL, et al. A program to **prevent catheter-associated urinary tract infection** in acute care. N Engl J Med 2016;374:2111-9.
Sanchez GV, et al. In vitro antimicrobial **resistance** of urinary **Escherichia coli** isolates among US outpatients from 2000 to 2010. Antimicrob Agents Chemother. 2012Apr;56(4):2181-3. Antimicrobial susceptibility results (n = 12,253,679) showed the greatest increases in E. coli resistance from 2000 to 2010 for ciprofloxacin (3% to 17.1%) and trimethoprim-sulfamethoxazole (TMP-SMX) (17.9% to 24.2%), whereas nitrofurantoin (0.8% to 1.6%) and ceftriaxone (0.2% to 2.3%) showed minimal change.
Saint S, et al. Condom versus indwelling urinary catheters: a randomized trial. J Am Geriatr Soc. 2006 Jul;54(7):1055-61. (InfoPOEMs: After adjusting for other factors, using condom catheters in men older than 40 is associated with fewer complications (bacteriuria, symptomatic urinary tract infection, death) than using indwelling catheters. Since more than 40% of men in each group had complications, I wonder if any kind of catheter is really necessary in most patients. (LOE = 2b))
Saint S, Trautner BW, Fowler KE, et al. A Multicenter Study of Patient-Reported **Infectious and Noninfectious Complications Associated With Indwelling Urethral Catheters**. JAMA Intern Med. 2018 Jul 2.

Salameh A, Mohajer MA, Daroucihe RO. **Prevention of urinary tract infections in patients with spinal cord injury**. CMAJ. 2015 Aug 11;187(11):807-11.
Salo J, Ikäheimo R, Tapiainen T, Uhari M. Childhood Urinary Tract Infections as a **Cause of Chronic Kidney Disease**. Pediatrics. 2011 Oct 10.
Sandberg T, Skoog G, Hermansson AB, et al. **Ciprofloxacin for 7 days versus 14 days in women with acute pyelonephritis**: a randomised, open-label and double-blind, placebo-controlled, non-inferiority trial. Lancet 2012; online June 21. http://dx.doi.org/10.1016/S0140-6736(12)60608-4.
Sanna-Cherchi S, Sampogna RV, Papeta N, et al. **Mutations in DSTYK** and Dominant Urinary Tract Malformations. N Engl J Med.2013 Jul 17.
Santos JM, Batech M, Pelter MA, et al. Evaluation of the Risk of **Nitrofurantoin Lung** Injury and Its Efficacy in Diminished **Kidney Function** in Older Adults in a Large Integrated Healthcare System: A Matched Cohort Study. J Am Geriatr Soc. 2016 Apr;64(4):798-805.
Saskatchewan Guidelines for the Prevention and Treatment of Urinary Tract Infections (UTIs) in **Continuing Care Settings** http://www.health.gov.sk.ca/UTI-guidelines-apr2013
Schaeffer AJ, Nicolle LE. **Urinary Tract Infections in Older Men**. N Engl J Med. 2016 Feb 11;374(6):562-571.
Schneeberger C, Geerlings SE, Middleton P, et al. Interventions for **preventing recurrent urinary tract infection during pregnancy**. Cochrane Database Syst Rev. 2012 Nov 14;11:CD009279. doi: 10.1002/14651858.CD009279.pub2. A daily dose of nitrofurantoin and close surveillance has not been shown to prevent RUTI compared with close surveillance alone. A significant reduction of ASB was found in women with a high clinic attendance rate and who received nitrofurantoin and close surveillance.
Schooff M, Hill K. Antibiotics for **recurrent** urinary tract infections. Am Fam Physician. 2005 Apr 1;71(7):1301-2.
Schroeder AR, Chang PW, Shen MW, et al. **Diagnostic accuracy** of the urinalysis for urinary tract infection in **infants <3 months** of age. Pediatrics. 2015 Jun;135(6):965-71
Selekman RE, Shapiro DJ, Boscardin J, et al. **Uropathogen Resistance and Antibiotic Prophylaxis**: A Meta-analysis. Pediatrics. 2018 Jun 28.
Singh-Grewal D, et al. Circumcision for the prevention of urinary tract infection in boys: a systematic review of randomised trials and observational studies. Arch Dis Child. 2005 Aug; 90(8) :853-8. (InfoPOEMs: Routine circumcision does not provide enough reduction in risk of urinary tract infection (UTI) to justify the surgical complication risk. For boys at high risk of UTI, however, the reduction in risk may justify the procedure. (LOE = 2a-))
Singh N, Gandhi S, McArthur E, et al. **Kidney function** and the use of **nitrofurantoin** to treat urinary tract infections in older women. CMAJ 2015;187:648-56.
Sha SH, Qiu JH, Schacht J. Aspirin to prevent **gentamicin**-induced hearing loss. N Engl J Med. 2006 Apr 27;354(17):1856-7.
Shaikh N. Acute **urinary tract infection** in **infants and young children**. CMAJ. 2010 May 18;182(8):800-1.
Shaikh N et al. Association between **uropathogen and pyuria**. Pediatrics 2016 Jul; 138:e20160087.
Shaikh N et al. Early antibiotic treatment for pediatric febrile urinary tract infection and **renal scarring**. JAMA Pediatr 2016 Jul 25.
Shaikh N, Craig JC, Rovers MM, et al. Identification of Children and Adolescents **at Risk for Renal Scarring** After a First Urinary Tract Infection: A Meta-analysis With Individual Patient Data. JAMA Pediatr. 2014 Aug 4.
Shaikh N, Ewing AL, Bhatnagar S, et al. Risk of **renal scarring in children** with a first urinary tract infection: a systematic review. Pediatrics. 2010 Dec;126(6):1084-91.
Shaikh N, Haralam MA, Kurs-Lasky M, Hoberman A. Association of Renal Scarring With Number of Febrile Urinary Tract Infections in Children. JAMA Pediatr. 2019 Aug 5.
Shaikh N, Hoberman A, Keren R, et al. **Recurrent Urinary Tract Infections in Children With Bladder and Bowel Dysfunction**. Pediatrics. 2016 Jan;137(1):1-7.
Shaikh N, Hoberman A, Hum SW, et al. Development and Validation of a **Calculator** for Estimating the Probability of Urinary Tract Infection in Young Febrile Children. JAMA Pediatr. 2018 Apr 16.
Shaikh N, Morone NE, Lopez J, Chianese J, et al. Does this **child have a urinary tract infection**? JAMA. 2007 Dec 26;298(24):2895-904.
Sharp VJ, Takacs EB, Powell CR. **Prostatitis**: diagnosis and treatment. Am Fam Physician. 2010 Aug 15;82(4):397-406.
Sheffield JS, Cunningham FG. Urinary tract infection in **women**. Obstet Gynecol. 2005 Nov;106(5):1085-92.
Simkins J, Fan J, Camargo JF, et al. **Intravenous Fosfomycin** Treatment for Carbapenem-Resistant Klebsiella pneumoniae in United States. Ann Pharmacother. 2015 Oct;49(10):1177-8.
Singh N, Gandhi S, McArthur E, et al. **Kidney function and the use of nitrofurantoin** to treat urinary tract infections in older women. CMAJ. 2015 Apr 27.
Smith MA, Puckrin R, Lam PW, et al. Association of **Increased Colony-Count Threshold for Urinary Pathogens** in Hospitalized Patients With Antimicrobial Treatment. JAMA Intern Med. 2019 Apr 29.
SOGC 2009 Menopause and Osteoporosis Update 2009-SOGC Jan 2009. http://www.sogc.org/media/pdf/advisories/Meno-Osteo-Update_JOGC-Jan_09.pdf
SOGC 2010 Guideline: Recurrent Urinary Tract Infection http://www.sogc.org/guidelines/documents/gui250CPG1010E.pdf (Epp A, Larochelle A, Lovatsis D, et al. Recurrent urinary tract infection. J Obstet Gynaecol Can 2010 Nov;32(11):1082-90.)
Staley C, Vaughn BP, Graiziger CT, et al. **Gut-sparing treatment of urinary tract infection in patients at high risk of Clostridium difficile infection**. J Antimicrob Chemother. 2017 Feb;72(2):522-528. (gentamicin)
Strohmeier Y, Hodson EM, Willis NS, et al. **Antibiotics for acute pyelonephritis in children**. Cochrane Database Syst Rev. 2014 Jul 28;7:CD003772. This updated review increases the body of evidence that oral antibiotics alone are as effective as a short course (three to four days) of IV antibiotics followed by oral therapy for a total treatment duration of 10 to 14 days for the treatment of acute pyelonephritis in children. When IV antibiotics are given, a short course (two to four days) of IV therapy followed by oral therapy is as effective as a longer course (seven to 10 days) of IV therapy. If IV therapy with aminoglycosides is chosen, single daily dosing is safe and effective. Insufficient data are available to extrapolate these findings to children aged less than one month of age or to children with dilating vesicoureteric reflux (grades III-V). Further studies are required to determine the optimal total duration of antibiotic therapy required for acute pyelonephritis.
Tan IL, Polydefkis MJ, Ebenezer GJ, et al. Peripheral nerve toxic effects of **nitrofurantoin**. Arch Neurol. 2012 Feb;69(2):265-8.
Tekgul S, Riedmiller H, et al. **Guidelines on paediatric urology**. Arnhem, The Netherlands: **European** Association of Urology, European Society for Paediatric Urology; 2013 Mar.
Thomas M. et al. Amoxicillin-Clavulanate vs Ciprofloxacin for the Treatment of Uncomplicated Cystitis in Women -a Randomized Trial. JAMA. 2005;293:949-955.
Torpy JM, Schwartz LA, Golub RM. JAMA **patient page. Urinary tract infection**. JAMA. 2012 May 2;307(17):1877.
Tzimenatos L, Mahajan P, Dayan PS, et al. **Accuracy of the Urinalysis** for Urinary Tract Infections in Febrile Infants 60 Days and Younger. Pediatrics. 2018 Jan 16.
USPSTF: US Preventive Services Task Force. **Screening for asymptomatic bacteriuria** in adults: US Preventive Services Task Force recommendation statement [Sept 24, 2019]. JAMA. doi:10.1001/jama.2019.13069
USPSTF: Henderson JT,Webber EM, Bean SI. **Screening for asymptomatic bacteriuria** in adults: updated evidence report and systematic review for the US Preventive Services Task Force [Sept 24, 2019]. JAMA. doi:10.1001/jama.2019.10060
van den Hout WB, Caljouw MA, Putter H, et al. Cost-effectiveness of **cranberry capsules** to prevent urinary tract infection in long-term care facilities: economic evaluation with a randomized controlled trial. J Am Geriatr Soc. 2014 Jan;62(1):111-6.
van Nieuwkoop C, et al. **Intravesical gentamicin** (80mg od) for recurrent urinary tract infection in patients with intermittent bladder catheterisation. IntJAntimicrob Agents.2010Jun 25.
Vaisman A, Gold WL, Leis JA. A 78-year-old woman with lethargy and a positive urine culture. CMAJ. 2013 May 14;185(8):679-80. (asymptomatic bacteriuria)
Vazquez JC, Abalos E. Treatments for symptomatic urinary tract infections during **pregnancy**. Cochrane Database Syst Rev. 2011 Jan 19;1:CD002256. Although antibiotic treatment is effective for the cure of urinary tract infections, there are insufficient data to recommend any specific drug regimen for treatment of symptomatic urinary tract infections during pregnancy. All the antibiotics studied were shown to be very effective in decreasing the incidence of the different outcomes. Complications were very rare.
Vellinga A, Galvin S, Duane S, et al. **Intervention to improve the quality of antimicrobial prescribing** for urinary tract infection: a cluster randomized trial. CMAJ 2016;188:108-15.
Vik I, Bollestad M, Grude N, et al**. Ibuprofen versus pivmecillinam for uncomplicated urinary tract infection in women**-A double-blind, randomized non-inferiority trial. PLoS Med. 2018 May 15;15(5):e1002569.
Wagenlehner FM, Obiamiwe U, Steenbergen J, Yuan G, Diaruiche RO. **Ceftolozane-tazobactam** compared with **levofloxacin** in the treatment of complicated urinary-tract infections,

including pyelonephritis: a randomised, double-blind, phase 3 trial (**ASPECT-cUTI**). Lancet 2015; online April 28.
Wagenlehner FME, Cloutier DJ, Komirenko AS, et al. Once daily **plazomicin** for complicated urinary tract infections. (EPIC) N Engl J Med 2019; 380: 729-40.
Wallace SS, Brown DN, Cruz AT. Prevalence of Concomitant Acute Bacterial **Meningitis in Neonates with Febrile Urinary Tract Infection**: A Retrospective Cross-Sectional Study. J Pediatr. 2017 Feb 6
Wang CH, Fang CC, Chen NC, et al. **Cranberry-Containing** Products for Prevention of Urinary Tract Infections in Susceptible Populations: A Systematic Review and Meta-analysis of Randomized Controlled Trials. Arch Intern Med. 2012 Jul 9;172(13):988-96.
Welk B, Hickling D. **Frequent** urinary tract infections in a **premenopausal woman**. CMAJ. 2016 Apr 19;188(7):522-3.
White B, Diagnosis and Treatment of **Urinary Tract Infections in Children**. Am Fam Physician. 2011 Feb 15;83(4):409-415.
Williams G, Craig JC. **Long-term antibiotics for preventing recurrent urinary tract infection in children.** Cochrane Database Syst Rev. 2011 Mar 16;3:CD001534. Long-term antibiotics appear to reduce the risk of repeat symptomatic UTI in susceptible children but the benefit is small and must be considered together with the increased risk of microbial resistance.
Wing DA, Rumney PJ, Preslicka CW, Chung JH. Daily **Cranberry Juice** for the Prevention of Asymptomatic Bacteriuria in Pregnancy: A Randomized, Controlled Pilot Study. J Urol. 2008 Aug 14. n=188 These data suggest there may be a protective effect of cranberry ingestion against asymptomatic bacteriuria and symptomatic urinary tract infections in pregnancy. Further studies are planned to evaluate this effect.
Wise GJ, Schlegel PN. **Sterile pyuria**. N Engl J Med. 2015 Mar 12;372(11):1048-54.
Wolfe AJ, Brubaker L. "**Sterile Urine**" and the **Presence of Bacteria**. Eur Urol. 2015 Mar 12.
Zalmanovici Trestioreanu A, Green H, Paul M, et al. Antimicrobial agents for treating **uncomplicated urinary tract infection in women**. Cochrane Database Syst Rev. 2010 Oct 6;10:CD007182. No differences were observed between the classes of antimicrobials included in this review for the symptomatic cure of acute uncomplicated UTI. Fluoroquinolones proved more effective than beta-lactams for the short-term bacteriological outcome, probably with little clinical significance. Individualised treatment should take into consideration the predictable susceptibility of urinary pathogens in local areas, possible adverse events and resistance development, and patient preference.
Zao J, Koren G, Bozzo P. Using **nitrofurantoin while breastfeeding** a newborn. Can Fam Physician. 2014 Jun;60(6):539-40.
Zhanel, George G et al. “Oral Fosfomycin for the Treatment of Acute and Chronic Bacterial Prostatitis Caused by Multidrug-Resistant Escherichia coli” Canadian journal of infectious diseases & medical microbiology = Journal canadien des maladies infectieuses et de la microbiologie medicale vol. 2018 1404813. 30 Jan. 2018, doi:10.1155/2018/1404813
Zhang X, Xu H, Zhou L, et al. Accuracy of Early **DMSA Scan for VUR in Young Children** With Febrile UTI. Pediatrics. 2014 Jan;133(1):e30-8.
Zilberberg MD, Nathanson BH, Sulham K, et al. **Carbapenem resistance**, inappropriate empiric treatment and outcomes among patients hospitalized with **Enterobacteriaceae** urinary tract infection, pneumonia and sepsis. BMC Infect Dis. 2017 Apr 17;17(1):279

References – Acute Uncomplicated Cystitis in Women - RxFiles.ca

1. Anti-infective Review Panel. **Anti-infective Guidelines for Community Acquired Infections**. Toronto: MUMS Guideline Clearinghouse; 2013.
2. Bugs and drugs. Available from: www.bugsanddrugs.ca– App Accessed 2017.
3. Sanford Guide Committee. The **Sanford** Guide to Antimicrobial Therapy, 47th Edition. Antimicrobial Therapy, INC; 2017.
4. Bent S, Nallamothu BK, Simel DL, Fihn SD, Saint S. Does this woman have an acute uncomplicated urinary tract infection? JAMA. 2002 May 22-29;287(20):2701-10.
5. Lindsay E Nicolle, et al. **Clinical Practice Guideline for the Management of Asymptomatic Bacteriuria: 2019 Update by the Infectious Diseases Society of America**, *Clinical Infectious Diseases*, Volume 68, Issue 10, 15 May 2019, Pages e83–e110, https://doi.org/10.1093/cid/ciy1121

Gupta K, Hooton T, Naber K, Wullt B, Colgan R, Miller L, Moran G, et al. Clinical Practice Guidelines for the Treatment of Acute Uncomplicated Cystitis and Pyelonephritis in Women: A **2010 Update by the Infectious Diseases Society of America and the European Society for Microbiology and Infectious Diseases.** Clin Infect Dis. (2011) 52 (5): 103-20.

6. Dason S, Dason JT, Kapoor A. **Guidelines for the diagnosis and management of recurrent urinary tract infection in women. Can Urol Assoc** J. 2011 Oct;5(5):316-22.
7. Cai T, Nesi G, Mazzoli S, et al. Asymptomatic bacteriuria treatment is associated with a higher prevalence of antibiotic resistant strains in women with urinary tract infections. Clin Infect Dis 2015; 61:1655-61.
8. Nicolle LE, Bradley S, Colgan R, et al. **Infectious Diseases Society of America guidelines for the diagnosis and treatment of asymptomatic bacteriuria in adults**. Clin Infect Dis 2005 Mar 1; 40(5):643-654.
9. Saskatoon Health Region 2015 Antibiogram. Available at: https://www.saskatoonhealthregion.ca/locations_services/Services/antimicrobialstewardship/Pages/Resouces.aspx. Accessed April 4th, 2017.
10. Regina Qu'Appelle Health Region 2016 Antibiogram. Unpublished. Regina Qu'Appelle Health Region 2015 Antibiogram Available at: http://www.rqhealth.ca/rqhr-service-lines-files/rqhr-antibiogram-2015. Accessed April 4th, 2017.
11. **American Geriatrics Society 2015 Beers Criteria** Update Expert Panel. American Geriatrics Society 2015 Updated Beers Criteria for Potentially Inappropriate Medication Use in Older Adults. J Am Geriatr Soc. 2015 Oct 8.
12. Choosing Wisely Canada Available from: http://www.choosingwiselycanada.org/recommendations/pathology/. Accessed April 4th, 2017.
    Choosing Wisely IDSA Available form: http://www.choosingwisely.org/wp-content/uploads/2015/03/IDSA-Choosing-Wisely-List.pdf. Accessed Nov.19th, 2018.
13. Christiaens TC, De Meyere M, Verschraegen G, Peersman W, Heytens S, De Maeseneer JM. Randomized controlled trial of nitrofurantoin versus placebo in the treatment of uncomplicated urinary tract infection in adult women. Br J Gen Pract 2002; 52:729–34.
14. Ferry SA, Holm SE, Stenlund H, Lundholm R, Monsen TJ. Clinical and bacteriological outcome of different doses and duration of pivmecillinam compared with placebo therapy of uncomplicated lower urinary tract infection in women: the LUTIW project. Scand J Prim Health Care 2007; 25:49–57.
15. Iravani A, Klimberg I, Briefer C, Munera C, Kowalsky SF, Echols RM. A trial comparing low-dose, short-course ciprofloxacin and standard 7 day therapy with co-trimoxazole or nitrofurantoin in the treatment of uncomplicated urinary tract infection. J Antimicrob Chemother 1999;43(Suppl A):67–75.
16. Stein GE. Comparison of single-dose fosfomycin and a 7-day course of nitrofurantoin in female patients with uncomplicated urinary tract infection. Clin Ther 1999; 21:1864–72.
17. Gupta K, Hooton TM, Roberts PL, Stamm WE. Short-course nitrofurantoin for the treatment of acute uncomplicated cystitis in women. Arch Intern Med 2007; 167:2207–12.
18. Hooton TM , Winter C , Tiu F et al . Randomized comparative trial and cost analysis of 3-day antimicrobial regimens for treatment of acute cystitis in women. JAMA 1995; 273: 41–5.
19. Huttner A, Verhaegh EM, Harbarth S et al. Nitrofurantoin revisited: a systematic review and meta-analysis of controlled trials. J Antimicrob Chemother 2015; 70:2456–2464.
20. Price J, Guran LA, Gregory WT, McDonagh MS. Nitrofurantoin vs other prophylactic agents in reducing recurrent urinary tract infections in adult women: a systematic review and meta-analysis. Am J Obstet Gynecol. 2016 Nov;215(5):548-560.
21. Muller AE, Verhaegh EM, HarbarthS, Mouton JW, Huttner A. Nitrofurantoin's efficacy and safety as prophylaxis for urinary tract infections: a systematic review of the literature and meta-analysis of controlled trials. Clin Microbiol Infect 2016; Aug 17.
22. D'Arcy PF. Nitrofurantoin. Drug Intell Clin Pharm 1985;19(7-8):540-7.
23. Geerts AF, Eppenga WL, Heerdink R, Derijks HJ, Wensing MJ, Egberts TC, De Smet PA. Ineffectiveness and adverse events of nitrofurantoin in women with urinary tract infection and renal impairment in primary care. Eur J Clin Pharmacol. 2013 Sep;69(9):1701-7.
24. Bains, A, Buna D, & Hoag NA. A retrospective review assessing the efficacy and safety of nitrofurantoin in renal impairment. Canadian Pharmacists Journal 2009;142(5), 248-252.
25. Keating GM. Fosfomycin trometamol: a review of its use as a single-dose oral treatment for patients with acute lower urinary tract infections and pregnant women with asymptomatic bacteriuria. Drugs. 2013 Nov;73(17):1951-66.
26. Karageorgopoulos DE, Wang R, Yu XH, Falagas ME. Fosfomycin: evaluation of the published evidence on the emergence of antimicrobial resistance in Gram-negative pathogens. J Antimicrob Chemother. 2012 Feb;67(2):255-68.
27. Oteo J, Bautista V, Lara N, Cuevas O, Arroyo M, Fernández S, Lázaro E, de Abajo FJ, Campos J; Spanish ESBL-EARS-Net Study Group. Parallel increase in community use of fosfomycin and resistance to fosfomycin in extended-spectrum beta-lactamase (ESBL)-producing Escherichia coli. J Antimicrob Chemother. 2010 Nov;65(11):2459-63.
28. Giske CG. Contemporary resistance trends and mechanisms for the old antibiotics colistin, temocillin, fosfomycin, mecillinam and nitrofurantoin. Clin Microbiol Infect. 2015 Oct;21(10):899-905. doi: 10.1016/j.cmi.2015.05.
29. Caron F, et al. The comeback of trimethoprim in France. Med Mal Infect (2016). http://dx.doi.org/10.1016/j.medmal.2016.12.001
30. Andrewes DA, Chuter PJ, Dawson MJ, Eden BW, Moore RM, Freestone DS, Morris CA. Trimethoprim and co-trimoxazole in the treatment of acute urinary tract infections: patient compliance and efficacy. J R Coll Gen Pract. 1981 May;31(226):274-8.
31. Comparison of trimethoprim at three dosage levels with co-trimoxazole in the treatment of acute symptomatic urinary tract infection in general practice. J Antimicrob Chemother. 1981 Feb;7(2):179-83.
32. Spencer RC, Moseley DJ, Greensmith MJ. Nitrofurantoin modified release versus trimethoprim or co-trimoxazole in the treatment of uncomplicated urinary tract infection in general practice. J Antimicrob Chemother. 1994 May;33 Suppl A:121-9.
33. Minassian MA, Lewis DA, Chattopadhyay D, Bovill B, Duckworth GJ, Williams JD. A comparison between single-dose fosfomycin trometamol (Monuril) and a 5-day course of trimethoprim in the treatment of uncomplicated lower urinary tract infection in women. Int J Antimicrob Agents. 1998 Apr;10(1):39-47.
34. Lutters M, Vogt-Ferrier NB. Antibiotic duration for treating uncomplicated, symptomatic lower urinary tract infections in elderly women. Cochrane Database Syst Rev. 2008 Jul 16;(3):CD001535
35. Nitzan O, Elias M, Chazan B, Saliba W. Urinary tract infections in patients with type 2 diabetes mellitus: review of prevalence, diagnosis, and management. Diabetes, Metabolic Syndrome and Obesity: Targets and Therapy. 2015;8:129-136.
36. Geerlings SE. Urinary tract infections in patients with diabetes mellitus: epidemiology, pathogenesis and treatment. Int J Antimicrob Agents. 2008;31:54-57.
37. Fünfstück R, Nicolle LE, Hanefeld M, Naber KG. Urinary tract infection in patients with diabetes mellitus. Clin Nephrol. 2012;77(1):40–48.
38. Epp A, Larochelle A, Lovatsis D, et al. **Society of Obstetricians and Gynaecologists of Canada. Recurrent urinary tract infection**. J Obstet Gynaecol Can. 2010 Nov;32(11):1082-101. retrieved from: http://sogc.org/guidelines/recurrent-urinary-tract-infection/
39. Scholes D, Hooton TM, Roberts PL, Stapleton AE, Gupta K, Stamm WE. Risk factors for recurrent urinary tract infection in young women. J Infect Dis. 2000 Oct;182(4):1177-82.
40. Jepson RG, Williams G, Craig JC. Cranberries for preventing urinary tract infections. Cochrane Database Syst Rev 2012;(10):CD001321.
41. Schwenger EM, Tejani AM, Loewen PS. Probiotics for preventing urinary tract infections in adults and children. Cochrane Database Syst Rev. 2015 Dec 23;(12):CD008772.
42. Albert X, Huertas I, Pereiró II, Sanfélix J, Gosalbes V, Perrota C. Antibiotics for preventing recurrent urinary tract infection in non-pregnant women. Cochrane Database Syst Rev. 2004;(3):CD001209.
43. Dueñas-Garcia OF, Sullivan G, Hall CD, Flynn MK, O'Dell K. Pharmacological Agents to Decrease New Episodes of Recurrent Lower Urinary Tract Infections in Postmenopausal Women. A Systematic Review. Female Pelvic Med Reconstr Surg. 2016 Mar-Apr;22(2):63-9.
44. Perrotta C, Aznar M, Mejia R, et al. Oestrogens for preventing recurrent urinary tract infection in post- menopausal women. Cochrane Database Syst Rev 2008:CD005131.
45. Grigoryan L, Trautner BW, Gupta K. Diagnosis and Management of Urinary Tract Infections in the Outpatient Setting: A Review. JAMA 2014;312(16):1677-84.

A ABX Comparison – Expanded Chart o http://www.rxfiles.ca/rxfiles/uploads/documents/members/CHT-ABX-Expanded.pdf

B What is the risk of peripheral neuropathy with nitrofurantoin (MACROBID)? ⍰
http://www.rxfiles.ca/rxfiles/uploads/documents/Nitrofurantoin-Peripheral-Neuropathy.pdf
What is the risk of pulmonary toxicity with nitrofurantoin (MACROBID)? ⍰
http://www.rxfiles.ca/rxfiles/uploads/documents/Nitrofurantoin-Pulmonary-Toxicity.pdf

Additional References:

1) Jarvis T, Chan L, Gottlieb T. Assessment and management of lower urinary tract infection in adults. Australian Prescriber [serial online]. February 2014;37(1):7-9.
2) Arredondo-García JL, Figueroa-Damián R, Rosas A, et al; uUTI Latin American Study Group. Comparison of short-term treatment regimen of ciprofloxacin versus long-term treatment regimens of trimethoprim/sulfamethoxazole or norfloxacin for uncomplicated lower urinary tract infections: a randomized, multicentre, open-label, prospective study. J Antimicrob Chemother. 2004 Oct;54(4):840-3.

3) Auquer F, Cordón F, Gorina E, Caballero JC, Adalid C, Batlle J; Urinary Tract Infection Study Group.Single-dose ciprofloxacin versus 3 days of norfloxacin in uncomplicated urinary tract infections in women. Clin Microbiol Infect. 2002 Jan;8(1):50-4.
4) Iravani A, Tice AD, McCarty J, et al; The Urinary Tract Infection Study Group. Short-course ciprofloxacin treatment of acute uncomplicated urinary tract infection in women. The minimum effective dose. Arch Int Med 1995;155(5):485-94.
5) Diagnosis and management of urinary tract infections in long term care facilities: clinical practice guideline. Edmonton (AB): Toward Optimized Practice; 2015 [cited 2016 Aug 15]. Available from: http://www.topalbertadoctors.org/download/401/urinary_tract_infection_guideline.pdf.
6) Bent S, Nallamothu BK, Simel DL, Fihn SD, Saint S. Does This Woman Have an Acute Uncomplicated Urinary Tract Infection?. JAMA. 2002;287(20):2701-2710.
7) Arnold JJ, Hehn LE, Klein DA. Common Questions about recurrent urinary tract infections in women. Am Fam Physician. 2016 Apr 1;93(7):560-9.
8) Zhong YH, Fang Y, Zhou JZ, Tang Y, Gong SM, Ding XQ. Effectiveness and safety of patient initiated single-dose versus continuous low-dose antibiotic prophylaxis for recurrent urinary tract infections in postmenopausal women: a randomized controlled study. J Int Med Res. 2011;39(6):2335-43.
9) Melekos MD, Asbach HW, Gerharz E, Zarakovitis IE, Weingaertner K, Naber KG. Post-intercourse versus daily ciprofloxacin prophylaxis for recurrent urinary tract infections in premenopausal women. J Urol. 1997 Mar;157(3):935-9.
10) Eriksen B. A randomized, open, parallel-group study on the preventive effect of an estradiol-releasing vaginal ring (Estring) on recurrent urinary tract infections in postmenopausal women. Am J Obstet Gynecol. 1999 May;180(5):1072-9.
11) Raz R, Stamm WE. A controlled trial of intravaginal estriol in postmenopausal women with recurrent urinary tract infections. N Engl J Med. 1993 Sep 9;329(11):753-6.
12) Stapleton AE, Dziura J, Hooton TM, Cox ME, Yarova-Yarovaya Y, Chen S, et al. Recurrent urinary tract infection and urinary Escherichia coli in women ingesting cranberry juice daily: a randomized controlled trial. Mayo Clin Proc 2012;87(2):143-50.
13) Singh N, Gandhi S, McArthur E, Moist L, Jain AK, Liu AR, Sood MM, Garg AX. Kidney function and the use of nitrofurantoin to treat urinary tract infections in older women. CMAJ. 2015 Jun 16;187(9):648-56.
14) Hoang, Peter, and Rebecca L. Salbu. "Updated Nitrofurantoin Recommendations in the Elderly: A Closer Look at the Evidence." The Consultant Pharmacist® 31.7 (2016): 381-384.
15) Kanji Z, Su VCH, Mainra R. Nitrofurantoin-Induced Pulmonary Reaction Involving Respiratory Symptoms: Case Report. The Canadian Journal of Hospital Pharmacy. 2011;64(5):362-365.
16) Juthani-Mehta, M. Asymptomatic bacteriuria and urinary tract infection in older adults. Clin Geriatr Med 2007 Aug;23(3):585–594.
17) Nicolle LE. Asymptomatic bacteriuria: when to screen and when to treat. Infect Dis Clin North Am 2003; Jun;17(2):367-394.
18) Keating GM. Fosfomycin trometamol: a review of its use as a single-dose oral treatment for patients with acute lower urinary tract infections and pregnant women with asymptomatic bacteriuria. Drugs. 2013 Nov;73(17):1951-66.
19) Huttner A, Kowalczyk A, Turjeman Aet al. Effect of 5-Day Nitrofurantoin vs Single-Dose Fosfomycin on Clinical Resolution of Uncomplicated Lower Urinary Tract Infection in Women: A Randomized Clinical Trial. JAMA. 2018 May 1;319(17):1781-1789.
20) Kranjčec B, Papeš D, Altarac S. D-mannose powder for prophylaxis of recurrent urinary tract infections in women: a randomized clinical trial. World J Urol.2014 Feb;32(1):79-84.
21) Hooton TM, Vecchio M, Iroz A, Tack I, Dornic Q, Seksek I, Lotan Y. Effect of Increased Daily Water Intake in Premenopausal Women With Recurrent Urinary Tract Infections: A Randomized Clinical Trial. JAMA Intern Med. 2018 Nov 1;178(11):1509-1515.
22) Kronenberg A, Bütikofer L, Odutayo A, Mühlemann K, da Costa BR, Battaglia M, Meli DN, Frey P, Limacher A, Reichenbach S, Jüni P. Symptomatic treatment of uncomplicated lower urinary tract infections in the ambulatory setting: randomised, double blind trial. BMJ. 2017 Nov 7;359:j4784.
23) Vik I, Bollestad M, Grude N, Bærheim A, Damsgaard E, Neumark T, Bjerrum L,Cordoba G, Olsen IC, Lindbæk M. Ibuprofen versus pivmecillinam for uncomplicated urinary tract infection in women-A double-blind, randomized non-inferiority trial. PLoS Med. 2018 May 15;15(5):e1002569.
24) Gágyor I, Bleidorn J, Kochen MM, Schmiemann G, Wegscheider K, Hummers-Pradier E. Ibuprofen versus fosfomycin for uncomplicated urinary tract infection in women: randomised controlled trial. BMJ. 2015 Dec 23;351:h6544.
25) Little P, Moore MV, Turner S, Rumsby K, Warner G, Lowes JA, Smith H, Hawke C, Leydon G, Arscott A, Turner D, Mullee M. Effectiveness of five different approaches in management of urinary tract infection: randomised controlled trial.BMJ. 2010 Feb 5;340:c199.

Treatment of Low Back Pain [21, 22]

Red Flags (assessment considerations):

- pain when recumbent
- saddle anesthesia
- pseudoclaudication
- age >55y or <20
- recent UTI
- trauma (major
- pain persisting >1mo

Tx Guidelines:

- symptomatic relief can be accomplished with OTC medication and/or spinal manipulation
- during acute phase, bed rest >4 days may further debilitate the patient
- low-stress aerobic activity & exercise OK in first 2 weeks; may delay trunk muscle exercises
- recommend return to work/normal activities as soon as possible
- if problems persist, reassessment required
- address nonphysical factors (psych/socioeconomic)

Meds: acetaminophen 1st line; NSAIDs option if necessary & not contraindicated; strong opioids may be necessary for some but consider addiction risk, use treatment agreement and set appropriate boundaries; consider referral.

See also Chronic Pain chart – pg 123

Back Pain Treatment Options: REFERENCES

[1] Hasgen KB, Hilde G, Jamtvedt G. Winnem M. Bed rest for acute low back pain and sciatica (Cochrane Review). The Cochrane Library 2001;Issue 3.

[2] Tulder MW van, Malmivaara A, Esmail R, Koes BW. Exercise therapy for low back pain (Cochrane Review). The Cochrane Library 2001;Issue 3.

[3] Staal JB, Hlobil H, Twisk JWR, et al. Graded activity for low back pain in occupational health care. Ann Intern Med 2004; 140:77-84.

[4] Frost H, Lamb SE, Doll HA, et al. Randomised controlled trial of physiotherapy compared with advice for low back pain. BMJ. 2004 Sep 25;329(7468):708.

[5] Hay EM, Mullis R, Lewis M, et al. Comparison of physical treatments versus a brief pain-management programme for back pain in primary care: a randomised clinical trial in physiotherapy practice. Lancet. 2005 Jun 28;365(9476):2024-30. (Kaapa EH, et al. Multidisciplinary group rehabilitation versus individual physiotherapy for chronic nonspecific low back pain: a randomized trial. Spine. 2006 Feb 15;31(4):371-6.)
Fritz JM, Kim M, Magel JS, et al. Cost-Effectiveness of Primary Care Management With or Without Early Physical Therapy for Acute Low Back Pain: Economic Evaluation of a Randomized Clinical Trial. Spine (Phila Pa 1976). 2017 Mar;42(5):285-290.

[6] Childs JD, Fritz JM, et al. A clinical prediction rule to identify patients with low back pain most likely to benefit from spinal manipulation: a validation study. Ann Intern Med 2004; 141:920-28.
Rubinstein SM, Terwee CB, Assendelft WJJ, de Boer MR, van Tulder MW. **Spinal manipulative therapy** for acute low-back pain. Cochrane Database of Systematic Reviews 2012, Issue 9. Art. No.: CD008880. DOI: 10.1002/14651858.CD008880.pub2. SMT is no more effective in participants with acute low-back pain than inert interventions, sham SMT, or when added to another intervention. SMT also appears to be no better than other recommended therapies.
Rubinstein SM, Terwee CB, Assendelft WJ, de Boer MR, van Tulder MW. **Spinal manipulative therapy** for acute low back pain: an update of the cochrane review. Spine (Phila Pa 1976). 2013 Feb 1;38(3):E158-77. The overall quality of the existing research is low, but it appears that spinal manipulation is no better than sham therapy, inactive treatment, or any other intervention for patients with uncomplicated acute low back pain.
Paige NM, Myiake-Lye IM, Booth MS, et al. Association of spinal manipulative therapy with clinical benefit and harm for acute low back pain: systematic review and meta-analysis. JAMA. doi:10.1001/jama.2017.3086
Evans R, Haas M, Schulz C, et al. **Spinal manipulation** and exercise for low back pain in adolescents: a randomized trial. Pain. 2018 Mar 27.
Goertz CM, Long CR, Vining RD, et al. Effect of usual medical care plus **chiropractic care** vs usual medical care alone on pain and disability among US service members with low back pain: a comparative effectiveness clinical trial.JAMA Netw Open. 2018;1(1):e180105.
Rubinstein SM, de Zoete A, van Middelkoop M, et al. Benefits and harms of spinal manipulative therapy for the treatment of chronic low back pain: systematic review and meta-analysis of randomized controlled trials. BMJ. 2019 Mar 13;364:l689.

[7] Keos BW, Assendelft W, Van der Heijden G, et al. Spinal manipulation for low back pain: an updated systematic review of randomized clinical trials. Spine 1996;21:2860-71.
Walker BF, French SD, Grant W, Green S. **Combined chiropractic interventions** for low-back pain. Cochrane Database of Systematic Reviews 2010, Issue 4. Art. No.: CD005427.
Rubinstein SM, van Middelkoop M, Assendelft WJJ, de Boer MR, van Tulder MW. Spinal manipulative therapy for chronic low-back pain. *Cochrane Database of Systematic Reviews* 2011, Issue 2. Art. No.: CD008112. DOI: 10.1002/14651858.CD008112.pub2. High quality evidence suggests that there is no clinically relevant difference between SMT and other interventions for reducing pain and improving function in patients with chronic low-back pain. Determining cost-effectiveness of care has high priority.

[8] Cherkin D, Sherman K, et al. A Review of the Evidence for the effectiveness, safety & cost of acupuncture, message thereapy and spinal manipulation for back pain. Ann Intern Med 2003;138:898-906.

Furlan AD, Imamura M, Dryden T, Irvin E. Massage for low-back pain. Cochrane Database Syst Rev. 2008 Oct 8;(4):CD001929. Massage might be beneficial for patients with subacute and chronic non-specific low-back pain, especially when combined with exercises and education. The evidence suggests that acupuncture massage is more effective than classic massage, but this need confirmation. More studies are needed to confirm these conclusions, to assess the impact of massage on return-to-work, and to determine cost-effectiveness of massage as an intervention for low-back pain.

Sherman KJ, Cherkin DC, Wellman RD, et al. A randomized trial comparing yoga, stretching, and a self-care book for chronic low back pain [published online October 24, 2011]. Arch Intern Med. doi:10.1001/archinternmed.2011.524.

Tilbrook HE, Cox H, Hewitt CE, et al. **Yoga** for chronic low back pain: a randomized trial. Ann Intern Med. 2011 Nov 1;155(9):569-78.

Cramer H, Lauche R, Haller H, et al. A systematic review and meta-analysis of **yoga** for low back pain. Clin J Pain. 2013 May;29(5):450-60.

[9] Guzman J, Esmail R, Karjalainen, et al. Multidisciplinary rehabilitation for chronic low back pain: systematic review. *BMJ* 2001;322:1511-1516

[10] Karjalainene K, Malmivaara A, et al. Multidisciplinary biopsychosocial rehabilitation for subacute low back pain among working age adults (Cochrane Review). The Cochrane Library 2001;Issue 4.

[11] Van Tulder MW, Jellema P, van Poppel MNM,et al. Lumbar supports for prevention and treatment of low back pain (Cochrane Review). The Cochrane Library 2001;Issue 3.

Roelofs PD, Bierma-Zeinstra SM, van Poppel MN, et al. Lumbar supports to prevent recurrent low back pain among home care workers: a randomized trial. Ann Intern Med. 2007 Nov 0;147(10):685-92. Summary for patients in: Ann Intern Med. 2007 Nov 20;147(10):I54. {InfoPOEMs Jan07: A lumbar support belt used by people doing moderately strenuous activity who identify themselves as having back pain decreases the number of days they have pain. However, the overall number of days lost from work is not affected. (LOE = 1b-) }

[12] Cherkin D, Sherman K, et al. A Review of the Evidence for the effectiveness, safety & cost of acupuncture, message thereapy & spinal manipulation for back pain. Ann Intern Med 2003;138:898-906.

[13] Manheimer E, White A, et al. Meta-analysis: **Acupuncture** for low back pain. Ann Intern Med 2005; 142:651-63. (InfoPOEMs: Acupuncture is an effective treatment for decreasing pain in pts with chronic low back pain. It doesn't seem to be a placebo effect; acupuncture produces a significantly greater effect on pain than sham acupuncture. There is not enough research to allow a conclusion for the treatment of acute low back pain. (LOE = 1a)). Thomas KJ, et al. Randomised controlled trial of a short course of traditional acupuncture compared with usual care for persistent non-specific low back pain. BMJ. 2006 Sep 15; [Epub ahead of print] Weak evidence was found of an effect of acupuncture on persistent non-specific low back pain at 12 months, but stronger evidence of a small benefit at 24 months. Referral to a qualified traditional acupuncturist for a short course of treatment seems safe and acceptable to patients with low back pain. (Haake M, Muller HH, Schade-Brittinger C, Basler HD, Schafer H, Maier C, Endres HG, Trampisch HJ, Molsberger A. German Acupuncture Trials (GERAC) for Chronic Low Back Pain: Randomized, Multicenter, Blinded, Parallel-Group Trial With 3 Groups. Arch Intern Med. 2007 Sep 24;167(17):1892-8. Low back pain improved after acupuncture treatment for at least 6 months. Effectiveness of acupuncture, either verum or sham, was almost twice that of conventional therapy.)

Madsen MV, Gøtzsche PC, Hróbjartsson A. **Acupuncture** treatment for pain: systematic review of randomised clinical trials with acupuncture, placebo acupuncture, and no acupuncture groups. BMJ. 2009 Jan 27;338:a3115. doi: 10.1136/bmj.a3115.

Cherkin Daniel C.; et al. A Randomized Trial Comparing Acupuncture, Simulated Acupuncture, & Usual Care for Chronic Low Back Pain Arch Intern Med. 2009;169(9):858-866.

Cho YJ, Song YK, Cha YY, et al. Acupuncture for chronic low back pain: a multicenter, randomized, patient-assessor blind, sham-controlled clinical trial. Spine (Phila Pa 1976). 2013 Apr 1;38(7):549-57.

[14] Van Tulder MW, Scholten RJ, Koes BW, Deyo RA. Non-steroidal anti-inflammatory drugs for low back pain (Cochrane Review). The Cochrane Library 2001;Issue 3.

[15] University of York, Royal Society of Medicine. Acute and chronic low back pain in Effective Health Care 2000;6(5):1-8.

[16] Browning R, Jackson JL, O'Mallery PG. Cyclobenzaprine and back pain; a meta-analysis. Arch Intern Med 2001;161:1613-1620.

[17] Staiger TO, Gaster B, Sullivan MD, Deyo RA. Systematic review of antidepressants in the treatment of chronic low back pain. Spine 2003; 28:2540-45.

[18] a) University of York, Royal Society of Medicine. Acute and chronic low back pain in Effective Health Care 2000;6(5):1-8.

b) Urquhart DM, Wluka AE, van Tulder M, et al. Efficacy of Low-Dose Amitriptyline for Chronic Low Back Pain: A Randomized Clinical Trial. JAMA Intern Med. 2018 Oct 1.PMID: 30285054

[19] Fishbain D. Evidence-based data on pain relief with antidepressants. Ann Med 2000;32:305-316.

[20] Atkinson JH, Slater MA, Williams RA, Zisook S, Patterson TL. A placebo-controlled randomized clinical trial of nortriptyline for chronic low back pain. Pain 1998;76:287-96.

[21] Di Iroio D, Henley E, Doughty A. A survey of Primary Care Physician Practice Patterns and Adherence to Acute Low Back Problem Guidelines. Arch Fam Med 2000;9:1015-1021

[22] Car J, Sheikh A. Acute low back pain. BMJ 2003:327-541.

Additional references:

Abdel Shaheed C, Maher CG, Williams KA, et al. Efficacy, Tolerability, and Dose-Dependent Effects of **Opioid Analgesics for Low Back Pain**: A Systematic Review and Meta-analysis. JAMA Intern Med. 2016 May 23.

Agius S, Gatt D, Rogers M, Borg A. **Back pain** in a young adult. BMJ. 2015 Apr 15;350 :h1752.

Albert HB, Lambert P, Rollason J, et al. Does nuclear tissue infected with **bacteria following disc herniations** lead to Modic changes in the adjacent vertebrae? Eur Spine J 2013;22:690-6.

Albert HB, Sorensen JS, Schiott Christensen B, Manniche C. **Antibiotic treatment in patients with chronic low back pain** and vertebral bone edema (Modic type 1 changes): a double-blind randomized clinical controlled trial of efficacy. Eur Spine J 2013;22:697-707.

Albornoz-Cabello M, Maya-Martin J, Dominguez-Maldonado G, et al. Effect of **interferential current therapy** on pain perception and disability level in subjects with chronic low back pain: A randomized controlled trial. Clin Rehabil. 2016 Mar 14.

Aleksiev AR. Ten-year follow-up of **strengthening versus flexibility exercises with or without abdominal bracing** in recurrent low back pain. Spine (Phila Pa 1976). 2014 Jun 1;39(13):997-1003.

Alford DP. Chronic back pain with possible prescription **opioid misuse**. JAMA. 2013 Mar 6;309(9):919-25.

Allan L, et al. Transdermal fentanyl versus sustained release oral morphine in strong-opioid naive patients with chronic low back pain. Spine. 2005 Nov 15;30(22):2484-90.

Allan G. **X-ray scans** for nonspecific low back pain: A nonspecific pain? Canadian Family Physician. March 2012 vol. 58 no. 3275.

Alsaadi SM, McAuley JH, et al. **Poor sleep quality** is strongly associated with subsequent pain intensity in patients with acute low back pain. Arthritis Rheumatol. 2014 May;66(5):1388-94.

Anheyer D, Haller H, et al. **Mindfulness-Based Stress Reduction** for Treating Low Back Pain: A Systematic Review and Meta-analysis. Ann Intern Med. 2017 Apr 25:1-9.

Arnold E, La Barrie J, DaSilva L, et al. The Effect of **Timing of Physical Therapy** for Acute Low Back Pain on Health Services Utilization: A Systematic Review. Arch Phys Med Rehabil. 2019 Jul;100(7):1324-1338.

Assendelft WJJ, Morton SC, Yu EI, et al. **Spinal manipulative** therapy for low-back pain. Cochrane Database of Systematic Reviews 2004, Issue 1. Art. No.: CD000447.
There is no evidence that spinal manipulative therapy is superior to other standard treatments for patients with acute or chronic low-back pain.

Azevedo DC, Ferreira PH, Santos HO, et al. **Movement System Impairment-Based Classification Treatment Versus General Exercises** for Chronic Low Back Pain: Randomized Controlled Trial. Phys Ther. 2018 Jan 1;98(1):28-39.

Baez S, Hoch MC, Hoch JM. Evaluation of Cognitive Behavioral Interventions and Psychoeducation Implemented by Rehabilitation Specialists to Treat **Fear-Avoidance Beliefs** in Patients With Low Back Pain: A Systematic Review. Arch Phys Med Rehabil. 2018 Nov;99(11):2287-2298.

Balague F, Mannion AF, Pellise F, Cedraschi C. **Clinical update: low back pain**. Lancet. 2007 Mar 3;369(9563):726-8.

Bicket MC, Gupta A, Brown CH 4th, et al. **Epidural injections** for spinal pain: a systematic review and meta-analysis evaluating the ``control`` injections in randomized controlled trials. Anesthesiology. 2013 Oct;119(4):907-31.

Bigos SJ, Holland J, Holland C, et al. High-quality controlled trials on preventing episodes of back problems: systematic literature review in working-age adults. Spine J. 2009 Feb;9(2):147-68. Twenty high-quality controlled trials found strong, consistent evidence to guide prevention of BP episodes in working-age adults. Trials found **exercise interventions** effective and other interventions not effective, including stress management, shoe inserts, back supports, ergonomic/back education, and reduced lifting programs. The varied successful exercise approaches suggest possible benefits beyond their intended physiologic goals.

Bodes Pardo G, Lluch Girbes E, Roussel NA, et al. **Pain Neurophysiology Education and Therapeutic Exercise** for Patients With Chronic Low Back Pain: A Single-Blind Randomized Controlled Trial. Arch Phys Med Rehabil. 2018 Feb;99(2):338-347.

Braschi E, Garrison S, Allan GM. **Cyclobenzaprine** for acute back pain. Can Fam Physician. 2015 Dec;61(12):1074.

Bronfort G, Haas M, Evans RL, Bouter LM. Efficacy of **spinal manipulation and mobilization** for low back pain and neck pain: a systematic review and best evidence synthesis. Spine J. 2004 May-Jun;4(3):335-56.

Bronfort G, Hondras MA, Schulz CA, et al. **Spinal manipulation and home exercise** with advice for subacute and chronic back-related leg pain: a trial with adaptive allocation. Ann Intern Med. 2014 Sep 16;161(6):381-91.

Brox J, Sorensen R, Friis A, Nygaard O, Indahl A, Keller A. Randomized clinical trial of **lumbar instrumented fusion** and cognitive intervention and exercises in patients with chronic low back pain and disc degeneration. Spine 2003;28:1913-21.

Brox JI, et al. Lumbar instrumented fusion compared with cognitive intervention and exercises in patients with chronic back pain after previous surgery for disc herniation: A prospective randomized controlled study. Pain. 2006 May;122(1-2):145-55. Epub 2006 Mar 20.

Brox JI, Nygaard OP, Holm I, et al. Four-year follow-up of **surgical versus non-surgical** therapy for chronic low back pain. Ann Rheum Dis. 2010 Sep;69(9):1643-8.

Calderon-Ospina CA, Nava-Mesa MO, Arbelaez Ariza CE. Effect of **Combined Diclofenac and B Vitamins** (Thiamine, Pyridoxine, and Cyanocobalamin) for Low Back Pain Management: Systematic Review and Meta-analysis. Pain Med. 2019 Sep 16.

Cambron JA, et al. **Shoe Orthotics** for the Treatment of Chronic Low Back Pain: A Randomized Controlled Trial. Arch Phys Med Rehabil. 2017 Sep;98(9):1752-1762.

Campbell J, Colvin LA. **Management of low back pain**. BMJ. 2013 Dec 5

Campbell J, Colvin LA. **Management of low back pain**. BMJ. 2013 Dec 5;347:f3148.

Campbell P, Foster NE, Thomas E, Dunn KM. **Prognostic indicators** of low back pain in primary care: five-year prospective study. J Pain. 2013 Aug;14(8):873-83.

Carey TS, Freburger JK. **Exercise and the Prevention of Low Back Pain**: Ready for Implementation. JAMA Intern Med. 2016 Jan 11:1-2.

Carpenter KM, Stoner SA, Mundt JM, et al. An online **self-help CBT** intervention for chronic lower back pain. Clin J Pain. 2012 Jan;28(1):14-22.

Carragee EJ. Clinical practice. Persistent low back pain. N Engl J Med. 2005 May 5;352(18):1891-8.

Carvalho C, Caetano JM, Cunha L, et al. Open-label **placebo treatment** in chronic low back pain: a randomized controlled trial. Pain. 2016;157(12):2766-2772.

Cerezo-Tellez E, et al. Effectiveness of **dry needling** for chronic nonspecific neck pain: a randomized, single-blinded, clinical trial. Pain. 2016 Sep;157(9):1905-17.

Chaparro LE, Furlan AD, Deshpande A, et al. **Opioids compared with placebo** or other treatments for chronic low back pain: an update of the Cochrane Review. Spine (Phila Pa 1976). 2014 Apr 1;39(7):556-63.

Chaffee DM. **Cyclobenzaprine** in the Treatment of Low Back Pain. Am Fam Physician. 2016 Feb 1;93(3):Online.

Cherkin Daniel C.; et al. A Randomized Trial Comparing **Acupuncture**, Simulated Acupuncture, and Usual Care for Chronic Low Back Pain Arch Intern Med. 2009;169(9):858-866.

Cherkin D, Kovacs FM, Croft P, et al.; International Organizing Committee of the Ninth International Forum for Primary Care Research on Low Back Pain and All the Participants. The **Ninth International Forum** for Primary Care Research on Low Back Pain. Spine (Phila Pa 1976). 2009 Feb 1;34(3):304-7.

Cherkin Daniel C., Sherman Karen J., Kahn Janet, et al. A Comparison of the Effects of 2 Types of **Massage** and Usual Care on Chronic Low Back Pain: A Randomized, Controlled Trial. Ann Intern Med July 5, 2011 155:1-9

Cherkin DC, Sherman KJ, Balderson BH, et al. Effect of **Mindfulness-Based Stress Reduction vs Cognitive Behavioral Therapy** or Usual Care on Back Pain and Functional Limitations in Adults With Chronic Low Back Pain: A Randomized Clinical Trial. JAMA. 2016 Mar 22-29;315(12):1240-9.

Cherkin DC, Anderson ML, Sherman KJ, et al. Two-Year Follow-up of a Randomized Clinical Trial of **Mindfulness-Based Stress Reduction vs Cognitive Behavioral Therapy** or Usual Care for Chronic Low Back Pain. JAMA. 2017 Feb 14;317(6):642-644.

Cherkin DC, Herman PM. **Cognitive and Mind-Body Therapies** for Chronic Low Back Pain and Neck Pain: Effectiveness and Value. JAMA Intern Med. 2018 Mar 5.

Cherkin D, Balderson B, Wellman R, et al. Effect of Low Back Pain Risk**-Stratification Strategy** on Patient Outcomes and Care Processes: the **MATCH** Randomized Trial in Primary Care. J Gen Intern Med. 2018 May 22.

Chilibeck PD, Vatanparast H, Cornish SM, Abeysekara S, Charlesworth S. Evidencebased risk assessment and recommendations for **physical activity**: arthritis, osteoporosis, and low back pain. *Appl Physiol Nutr Metab* 2011;36(Suppl 1):S49-S79.

Cho YJ, Song YK, Cha YY, et al. **Acupuncture** for chronic low back pain: a multicenter, randomized, patient-assessor blind, sham-controlled clinical trial. Spine (Phila Pa 1976). 2013 Apr 1;38(7):549-57.

Choi BK, Verbeek JH, Tam WW, Jiang JY. **Exercises** for prevention of recurrences of low-back pain. Cochrane Database Syst Rev. 2010 Jan 20;(1):CD006555.

Chou R, Huffman LH; American Pain Society; American College of Physicians. **Medications for acute and chronic low back pain**: a review of the evidence for an American Pain Society/American College of Physicians clinical practice guideline. Ann Intern Med. **2007** Oct 2;147(7):505-14. Medications with good evidence of short-term effectiveness for low back pain are NSAIDs, acetaminophen, skeletal muscle relaxants (for acute low back pain), and tricyclic antidepressants (for chronic low back pain). Evidence is insufficient to identify one medication as offering a clear overall net advantage because of complex tradeoffs between benefits and harms. Individual patients are likely to differ in how they weigh potential benefits, harms, and costs of various medications.

Chou R, Huffman LH; American Pain Society; American College of Physicians. **Nonpharmacologic therapies for acute and chronic low back pain**: review of the evidence for an American Pain Society/American College of Physicians clinical practice guideline. Ann Intern Med. **2007** Oct 2;147(7):492-504. Therapies with good evidence of moderate efficacy for chronic or subacute low back pain are cognitive-behavioral therapy, exercise, spinal manipulation, and interdisciplinary rehabilitation. For acute low back pain, the only therapy with good evidence of efficacy is superficial heat.

Chou R, Qaseem A, Snow V, Casey D, Cross JT Jr, Shekelle P, Owens DK; Clinical Efficacy Assessment Subcommittee of the American College of Physicians; American College of Physicians; American Pain Society Low Back Pain Guidelines Panel. **Diagnosis and treatment of low back pain**: a joint clinical practice guideline from the American College of Physicians and the American Pain Society. Ann Intern Med. **2007** Oct 2;147(7):478-91. 1: Clinicians should conduct a focused history and physical examination to help place patients with low back pain into 1 of 3 broad categories: nonspecific low back pain, back pain potentially associated with radiculopathy or spinal stenosis, or back pain potentially associated with another specific spinal cause. The history should include assessment of psychosocial risk factors, which predict risk for chronic disabling back pain (strong recommendation, moderate-quality evidence). RECOMMENDATION 2: Clinicians should not routinely obtain imaging or other diagnostic tests in patients with nonspecific low back pain (strong recommendation, moderate-quality evidence). RECOMMENDATION 3: Clinicians should perform diagnostic imaging and testing for patients with low back pain when severe or progressive neurologic deficits are present or when serious underlying conditions are suspected on the basis of history and physical examination (strong recommendation, moderate-quality evidence). RECOMMENDATION 4: Clinicians should evaluate patients with persistent low back pain and signs or symptoms of radiculopathy or spinal stenosis with magnetic resonance imaging (preferred) or computed tomography only if they are potential candidates for surgery or epidural steroid injection (for suspected radiculopathy) (strong recommendation, moderate-quality evidence). RECOMMENDATION 5: Clinicians should provide patients with evidence-based information on low back pain with regard to their expected course, advise patients to remain active, and provide information about effective self-care options (strong recommendation, moderate-quality evidence). RECOMMENDATION 6: For patients with low back pain, clinicians should consider the use of medications with proven benefits in conjunction with back care information and self-care. Clinicians should assess severity of baseline pain and functional deficits, potential benefits, risks, and relative lack of long-term efficacy and safety data before initiating therapy (strong recommendation, moderate-quality evidence). For most patients, first-line medication options are acetaminophen or nonsteroidal anti-inflammatory drugs. RECOMMENDATION 7: For patients who do not improve with self-care options, clinicians should consider the addition of nonpharmacologic therapy with proven benefits-for acute low back pain, spinal manipulation; for chronic or subacute low back pain, intensive interdisciplinary rehabilitation, exercise therapy, acupuncture, massage therapy, spinal manipulation, yoga, cognitive-behavioral therapy, or progressive relaxation (weak recommendation, moderate-quality evidence).

Chou R, Atlas SJ, Stanos SP, Rosenquist RW. **Nonsurgical interventional therapies for low back pain**: a review of the evidence for an American Pain Society clinical practice guideline. *Spine (Phila Pa 1976)*. 2009;34(10):1078-1093.

Chou R, Fu R, Carrino JA, Deyo RA. **Imaging strategies** for low-back pain: systematic review and meta-analysis. Lancet. 2009 Feb 7;373(9662):463-72. Lumbar imaging for low-back pain without indications of serious underlying conditions does not improve clinical outcomes. Therefore, clinicians should refrain from routine, immediate lumbar imaging in patients with acute or subacute low-back pain and without features suggesting a serious underlying condition.

Chou R, Loeser JD, Owens DK,; American Pain Society (APS) Low Back Pain Guideline Panel. **Interventional therapies, surgery, and interdisciplinary rehabilitation** for low back pain: an evidence-based clinical practice guideline from the American Pain Society. Spine. 2009 May 1;34(10):1066-77. In patients with nonradicular pain: Interdisciplinary rehabilitation emphasizing cognitive-behavioral approaches should be considered for those who don't respond to usual interventions; Provocative discography (injecting material into a disc nucleus in an attempt to reproduce the patient's typical pain) is not recommended; Facet joint corticosteroid injection, prolotherapy (repeated injections of irritant material to stimulate an inflammatory response), and intradiscal corticosteroid injection are not recommended; Persistent disabling symptoms and degenerative spinal changes should prompt discussion and shared decision-making regarding surgery or interdisciplinary rehabilitation (there is insufficient evidence to weigh the use of vertebral disc replacement in these patients. In patients with persistent radiculopathy: Those with herniated discs should be offered discussion about the use of epidural steroid injection; Those with herniated discs and disabling leg pain from spinal stenosis should be offered discussion about surgery; Those with persistent pain after surgery should be offered discussion on the risks and benefits of spinal cord stimulation.

Chou R, Shekelle P. Will this patient develop persistent **disabling low back pain**?. JAMA. 2010 Apr 7;303(13):1295-302.

Chou Roger, Qaseem Amir, Owens Douglas K., et al. and for the Clinical Guidelines Committee of the American College of Physicians. **Diagnostic Imaging for Low Back Pain**: Advice for High-Value Health Care From the American College of Physicians. *Ann Intern Med* February 1, **2011** 154:181-189. Use an initial trial of therapy rather than immediate imaging. However, imaging is warranted when the patient has major risk factors for cancer, or shows severe or progressive neurologic deficits. Risk factors or signs of vertebral infection or the cauda equina syndrome, although rare, also warrant more immediate imaging.

Chou R. **In the Clinic: Low Back Pain**. Ann Intern Med June 3, 2014 ITC6-1-14.

Chou R, Deyo R, Friedly J, et al. **Noninvasive treatments** for low back pain. Comparative Effectiveness Review No. 169. Rockville (MD): Agency for Healthcare Research and Quality (US); 2016 Feb. Report No.:16-EHC004-EF. . A number of pharmacological and nonpharmacological noninvasive treatments for low back pain are associated with small to moderate, primarily short-term effects on pain versus placebo, sham, wait list, or no treatment. Effects on function were generally smaller than effects on pain. More research is needed to understand optimal selection of treatments, effective combinations and sequencing of treatments, effectiveness of treatments for radicular low back pain, and effectiveness on outcomes other than pain and function.

Chou R, Deyo R, Friedly J, Skelly A, et al. **Nonpharmacologic therapies for low back pain**: a systematic review for an American College of Physicians (**ACP**) clinical practice guideline. Ann Intern Med. 2017. [Epub ahead of print]. doi:10.7326/M16 -2459

Chou R, Deyo R, Friedly J, et al. **Systemic pharmacologic therapies for low back pain**: a systematic review for an American College of Physicians(**ACP**) clinical practice guideline. Ann Intern Med. 2017. [Epub ahead of print]. doi:10.7326/M16 -2458

Cohen SP, Argoff CE, Carragee EJ. **Management of low back pain**. BMJ. 2008 Dec 22;337:a2718. doi: 10.1136/bmj.a2718.

Cohen SP, Gupta A, Strassels SA, et al. Effect of **MRI** on treatment results or decision making in patients with lumbosacral radiculopathy referred for **epidural steroid injections**: a multicenter, randomized controlled trial [online Dec 12, 2011]. Arch Intern Med. doi:10.1001 /archinternmed.2011.593. *Arch Intern Med*. 2012;172(2):134-142.

Cohen SP, Hooten WM. Advances in the diagnosis and management of **neck pain**. BMJ. 2017 Aug 14;358:j3221.

Cohen SP, White RL, Kurihara C, et al. Epidural **steroids**, etanercept, or saline in subacute sciatica: a multicenter, randomized trial. Ann Intern Med. 2012 Apr 17;156(8):551-9.

Costa Luciola da C Menezes, Maher Christopher G, et al. **Prognosis** for patients with chronic low back pain: inception cohort study. BMJ 2009;339:b3829, doi: 10.1136/bmj.b3829.

Costa LD, Maher CG, Hancock MJ, et al. The **prognosis of acute and persistent low-back pain**: a meta-analysis. CMAJ. 2012 May 14.

Clarke J, van Tulder M, Blomberg S, et al. Traction for low-back pain with or without sciatica. Cochrane Database Syst Rev. 2005 Oct 19;4:CD003010. AUTHORS' CONCLUSIONS: The evidence suggests that traction is probably not effective.Neither continuous nor intermittent traction by itself was more effective in improving pain, disability or work absence than placebo, sham or other treatments for patients with a mixed duration of LBP, with or without sciatica. Although trials studying patients with sciatica had methodological limitations and inconsistent results, there was moderate evidence that autotraction was more effective than mechanical traction for global improvement in this population.

Cramer H, Lauche R, Haller H, et al. A systematic review and meta-analysis of **yoga** for low back pain. Clin J Pain. 2013 May;29(5):450-60.

Cruz-Diaz D, Romeu M, Velasco-Gonzalez C, et al. The effectiveness of 12 weeks of **Pilates** intervention on disability, pain and kinesiophobia in patients with chronic low back pain: a randomized controlled trial. Clin Rehabil. 2018 Apr 1:269215518768393.

Dahm KT, Brurberg KG, Jamtvedt G, Hagen KB. Advice to rest in bed versus advice to stay active for acute low-back pain and sciatica. Cochrane Database Syst Rev. 2010 Jun 16;6:CD007612. Moderate quality evidence shows that patients with acute LBP may experience small benefits in pain relief and functional improvement from advice to stay active compared to advice to rest in bed; patients with sciatica experience little or no difference between the two approaches. Low quality evidence suggests little or no difference between those who received advice to stay active, exercises or physiotherapy. Further research is very likely to have an important impact on the estimate of effect and is likely to change our confidence in it.

Dario AB, et al. Effectiveness of **telehealth**-based interventions in the management of non-specific low back pain: systematic review with meta-analysis. Spine J. 2017 Sep;17(9):1342-1351.

Dario AB, Moreti Cabral A, Almeida L, et al. Effectiveness of **telehealth-based interventions** in the management of non-specific low back pain: a systematic review with meta-analysis. Spine J. 2017 Sep;17(9):1342-1351.

Darlow B, Stanley J, Dean S, et al. **The Fear Reduction Exercised Early (FREE) approach** to management of low back pain in general practice: A pragmatic cluster-randomised controlled trial. PLoS Med. 2019 Sep 9;16(9):e1002897.

Del Pozo-Cruz B, Adsuar JC, Parraca J, et al. A **web-based intervention** to improve and prevent low back pain among office workers: a randomized controlled trial. J Orthop Sports Phys Ther. 2012;42(10):831-41.

Delitto A, Piva SR, Moore CG, et al. **Surgery versus nonsurgical treatment of lumbar spinal stenosis**. A randomized trial. Ann Intern Med. 2015;162:465-73.

Dengler J, Kools D, Pflugmacher R, et al. Randomized Trial of **Sacroiliac Joint Arthrodesis Compared with Conservative Management for Chronic Low Back Pain** Attributed to the Sacroiliac Joint. J Bone Joint Surg Am. 2019 Mar 6;101(5):400-411.

Deyo RA, Smith DH, Johnson ES, et al. **Prescription Opioids** for Back Pain and Use of Medications for **Erectile Dysfunction**. Spine (Phila Pa 1976). 2013 Mar 1.

Deyo RA, Jarvik JG, Chou R. **Low back pain in primary care**. BMJ. 2014 Jul 16;349:g4266.

Deyo RA, Von Korff M, Duhrkoop D. **Opioids for low back pain**. BMJ. 2015 Jan 5;350:g6380.

Dionne CE, Bourbonnais R, Fremont P, et al. A clinical return-to-work rule for patients with back pain. CMAJ. 2005 Jun 7;172(12):1559-67& ACP Journal Club. (InfoPOEMs: A clinical decision rule can provide guidance regarding a patient's likelihood of successfully returning to work. Patients at high risk for failure may benefit from more intensive follow-up and therapy. Further study is required. (LOE = 1a))

Dubinsky, Richard M., Miyasaki, Janis. Assessment: Efficacy of **transcutaneous electric nerve stimulation** in the treatment of pain in neurologic disorders (an evidence-based review). Report of the Therapeutics and Technology Assessment Subcommittee of the American Academy of Neurology. Neurology 2009 0: WNL.0b013e3181c918fc.

Downie A, Williams CM, Henschke N, et al **Red flags to screen for malignancy and fracture** in patients with low back pain: systematic review. BMJ 2013;347:f7095

Driscoll T, Jacklyn G, Orchard J, et al. The **global burden of occupationally related low back pain**: estimates from the Global Burden of Disease 2010 study. Ann Rheum Dis. 2014 Mar 24.

Dubinsky RM, Miyasaki J. **Assessment: efficacy of transcutaneous electric nerve stimulation in the treatment of pain in neurologic disorders (an evidence-based review): report of the Therapeutics and Technology Assessment Subcommittee of the American Academy of Neurology.** Neurology. 2010 Jan 12;74(2):173-6. Transcutaneous electric nerve stimulation (TENS) is not recommended for the treatment of chronic low back pain (Level A).

el Barzouhi A, Vleggeert-Lankamp CL, et al. **Magnetic resonance imaging** in follow-up assessment of sciatica. N Engl J Med. 2013 Mar 14;368(11):999-1007.

Elder WG, Munk N, Love MM, et al. **Real-World Massage** Therapy Produces Meaningful Effectiveness Signal for Primary Care Patients with Chronic Low Back Pain: Results of a Repeated Measures Cohort Study. Pain Med. 2017 Mar 14.

Eleswarapu AS et al. How effective is **physical therapy for** common low back pain diagnoses? Spine (Phila Pa 1976) 2016 Aug 15; 41:1325.

Engers A, Jellema P, Wensing M, van der Windt D, et al. **Individual patient education** for low back pain. Cochrane Database Syst Rev. 2008 Jan 23;(1):CD004057. For patients with acute or subacute LBP, intensive patient education seems to be effective. For patients with chronic LBP, the effectiveness of individual education is still unclear.

Enke O, New HA, New CH, et al. **Anticonvulsants in the treatment of low back pain** and lumbar radicular pain: a systematic review and meta-analysis. CMAJ. 2018 Jul 3;190(26):E786-E793.

Enthoven WT, Roelofs PD, Deyo RA, et al. **Non-steroidal anti-inflammatory drugs** for chronic low back pain. Cochrane Database Syst Rev. 2016 Feb 10;2:CD012087. Six of the 13 included RCTs showed that NSAIDs are more effective than placebo regarding pain intensity. NSAIDs are slightly more effective than placebo regarding disability. However, the magnitude of the effects is small, and the level of evidence was low. When we only included RCTs at low risk of bias, differences in effect between NSAIDs and placebo were reduced. We identified no difference in efficacy between different NSAID types, including selective versus non-selective NSAIDs. Due to inclusion of RCTs only, the relatively small sample sizes and relatively short follow-up in most included trials, we cannot make firm statements about the occurrence of adverse events or whether NSAIDs are safe for long-term use.

Enthoven WTM, Roelofs PD, Koes BW. **NSAIDs** for Chronic Low Back Pain. JAMA. 2017 Jun 13;317(22):2327-2328.
Ernst E, Lee MS. **Acupuncture** for rheumatic conditions: an overview of systematic reviews**.** Rheumatology (Oxford). 2010 Oct;49(10):1957-61. Epub 2010 Jun 29. European Evidence Based Guidelines: 2005 http://www.backpaineurope.org/web/files/WG2_Guidelines.pdf
Evans R, Haas M, Schulz C, et al. **Spinal manipulation** and exercise for low back pain in adolescents: a randomized trial. Pain. 2018 Mar 27.
Fairbank J, Frost H, et al. Randomised controlled trial to compare **surgical stabilisation of the lumbar spine** with an intensive rehabilitation programme for patients with chronic low back pain: the MRC spine stabilisation trial. BMJ. 2005 May 23; [Epub ahead of print] (InfoPOEMs: Intensive rehabilitation results in a reduction of disability due to chronic low back pain, although it was slightly less effective than spinal fusion surgery. Rehabilitation is more cost-effective and results in fewer complications than surgery. (LOE = 1b-))
Fernandez M, Hartvigsen J, Ferreira ML, et al. **Advice to Stay Active or Structured Exercise** in the Management of Sciatica: A Systematic Review and Meta-analysis. Spine (Phila Pa 1976). 2015 Sep 15;40(18):1457-66. If these authors have found all the relevant studies, patients with uncomplicated sciatica treated with supervised structured exercise have minimally less leg pain in the first 6 weeks, but overall are no better than patients given generic advice to stay active. The data are of good quality but are not very robust. The authors don't report on other important outcomes. The good news is that it's pretty easy to tell patients to stay as active as possible within their comfort level. (LOE = 1a-)
Ferreira ML, Ferreira PH, Latimer J, et al. Comparison of general exercise, motor control exercise and spinal manipulative therapy for chronic low back pain: A randomized trial. Pain. 2007 Sep;131(1-2):31-7. Epub 2007 Jan 23.
Foster NE, Mullis R, Hill JC, et al; IMPaCT Back Study team. Effect of **Stratified Care** for Low Back Pain in Family Practice (**IMPaCT Back**): A Prospective Population-Based Sequential Comparison. Ann Fam Med. 2014 Mar-Apr;12(2):102-11.
Foster NE, Anema JR, Cherkin D, et al. **Prevention and treatment of low back pain**: evidence, challenges, and promising directions. Lancet 2018; online March 21.
Franklin GM. **Opioids for chronic noncancer pain**: A position paper of the American Academy of Neurology (**AAN**) . Neurology. 2014 Sep 30;83(14):1277-84.
French SD, et al. Superficial **heat or cold** for low back pain. Cochrane Database Syst Rev. 2006 Jan 25;(1):CD004750.
Friedly JL, Comstock BA, Turner JA, et al. A randomized trial of **epidural glucocorticoid injections for spinal stenosis**. N Engl J Med 2014;371:11-21.
Friedman BW, Esses D, Solorzano C, et al. A randomized placebo-controlled trial of single-dose im corticosteroid for radicular low back pain. Spine. 2008 Aug 15;33(18):E624-9. This study was a negative study, though there was a suggestion of benefit of methylprednisolone acetate in a population of young adults with acute radicular low back pain.
Friedman BW et al. **One-week and 3-month outcomes** after an emergency department visit for undifferentiated musculoskeletal low back pain. Ann Emerg Med 2012 Feb; 59:128.
Friedman BW et al. Naproxen with **cyclobenzaprine, oxycodone/acetaminophen, or placebo** for treating acute low back pain: A randomized clinical trial. JAMA 2015 Oct 20; 314:1572.
Friedman BW, Irizarry E, Solorzano C, et al. **Diazepam Is No Better Than Placebo When Added to Naproxen** for Acute Low Back Pain. Ann Emerg Med. 2017 Jan 19.
Friedman BW, Irizarry E, Solorzano C, et al. A Randomized, Placebo-Controlled Trial of **Ibuprofen Plus Metaxalone, Tizanidine, or Baclofen for Acute Low Back Pain**. Ann Emerg Med. 2019 Apr 5.
Fritz JM, Magel JS, McFadden M, et al. Early **Physical Therapy vs Usual Care** in Patients With Recent-Onset Low Back Pain: A Randomized Clinical Trial. JAMA. 2015 Oct 13;314(14):1459-67.
Fritz JM, Kim M, Magel JS, et al. Cost-Effectiveness of Primary Care Management With or Without Early **Physical Therapy** for Acute Low Back Pain: Economic Evaluation of a Randomized Clinical Trial. Spine (Phila Pa 1976). 2017 Mar;42(5):285-290.
Frogner BK, Harwood K, Andrilla CHA, et al. **Physical Therapy** as the First Point of Care **to Treat Low Back Pain**: An Instrumental Variables Approach to Estimate Impact on Opioid Prescription, Health Care Utilization, and Costs. Health Serv Res. 2018 May 23.
Furlan AD, Murphy L. A 46-year-old man with **acute low-back pain**. CMAJ. 2016 Apr 5
Furunes H, Storheim K, Brox JI, Jet al. **Total disc replacement versus multidisciplinary rehabilitation** in patients with chronic low back pain and degenerative discs: 8-year follow-up of a randomized controlled multicenter trial. Spine J. 2017 Oct;17(10):1480-1488.
Gagnier JJ, Oltean H, van Tulder MW, et al. **Herbal Medicine** for Low Back Pain: A Cochrane Review. Spine (Phila Pa 1976). 2016 Jan;41(2):116-33. The body of evidence of the effectiveness of herbal products in the treatment of low back pain is limited to a handful of small studies. Topical capsicum (cayenne), which has been studied most frequently, appears to be more effective than placebo in relieving pain. (LOE = 1a-)
Garcia AN, Costa Lda C, da Silva TM, et al. Effectiveness of **back school versus McKenzie exercises** in patients with chronic nonspecific low back pain: a randomized controlled trial. Phys Ther. 2013 Jun;93(6):729-47.
Garra G et al. **Heat or cold packs** for neck and back strain: A randomized controlled trial of efficacy. Acad Emerg Med 2010 May; 17:484.
Genevay S, Finckh A, Zufferey P et al. **Adalimumab** in acute sciatica reduces the long-term need for surgery: a 3-year follow-up of a randomised double-blind placebo-controlled trial. Ann Rheum Dis. 2012 Apr;71(4):560-2.
Gibson J, Waddell G, Gibson JA. Surgery for degenerative lumbar spondylosis. Cochrane Database Syst Rev. 2005 Oct 19;(4):CD001352.
Gimbel JS, Kivitz AJ, Bramson C, et al. Long-term safety and effectiveness of **tanezumab** as treatment for chronic low back pain. Pain. 2014 Jun 14. pii: S0304-3959(14)00279-6.
Godfrey E, Wileman V, Galea Holmes M, et al. **Physical Therapy Informed** by Acceptance and Commitment Therapy (PACT) Versus Usual Care Physical Therapy for Adults With Chronic Low Back Pain: A Randomized Controlled Trial. J Pain. 2019 Jun 5
Goertz CM, Long CR, Vining RD, et al. Effect of usual medical care plus **chiropractic care vs usual medical care alone on pain and disability** among US service members with low back pain. A comparative effectiveness clinical trial. JAMA Network Open 2018;1(1):e180105.
Goforth HW, Preud'homme XA, Krystal AD. A randomized, double-blind, placebo-controlled trial of **eszopiclone for the treatment of insomnia in patients with chronic**

low back pain. Sleep. 2014 Jun 1;37(6):1053-60.
Golden Adam G, Ma Qianli, Nair Vinit, et al. Risk for **Fractures with Centrally Acting Muscle Relaxants**: An Analysis of a National Medicare Advantage Claims Database. Ann Pharmacother 44:1369-1375.
Goodman DM, Burke AE, Livingston EH. JAMA **patient page. Low back pain**. JAMA. 2013 Apr 24;309(16):1738.
Gross A, Forget M, St George K, et al. **Patient education** for neck pain. Cochrane Database Syst Rev. 2012 Mar 14;3:CD005106.
Haas M, Vavrek D, Peterson D, et al. Dose-response and efficacy of **spinal manipulation** for care of chronic low back pain: a randomized controlled trial. Spine J. 2013 Oct 16.
Hagen KB, Jamtvedt G, Hilde G, Winnem MF. The updated Cochrane Review of bed rest for low back pain and sciatica. Spine 2005; 30:542-46. (InfoPOEMs: When they are studied for 3 months, rest in bed for patients with uncomplicated low back pain causes more pain and slows return to function. Similarly, patients with sciatica experience, at best, no benefit with bed rest. (LOE = 1a))
Hall AM, Maher CG, Lam P, et al. **Tai chi exercise** for treatment of pain and disability in people with persistent low back pain: A randomized controlled trial. Arthritis Care Res (Hoboken). 2011 Nov;63(11):1576-83.
Hancock MJ, Maher CG, Latimer J, et al. Assessment of diclofenac or spinal manipulative therapy, or both, in addition to recommended first-line treatment for acute low back pain: a randomised controlled trial. Lancet. 2007 Nov 10;370(9599):1638-1643. Patients with acute low back pain receiving recommended first-line care do not recover more quickly with the addition of diclofenac or spinal manipulative therapy.
Hancock MJ, et al. Is the Number of Different **MRI Findings** More Strongly Associated With Low Back Pain Than Single MRI Findings? Spine (Phila Pa 1976). 2017 Sep 1;42(17):1283-1288.
Heapy AA, Higgins DM, Goulet JL, et al. **Interactive Voice Response-Based Self-management** for Chronic Back Pain: The **COPES** Noninferiority Randomized Trial. JAMA Intern Med. 2017 Apr 3
Hellum C, Johnsen LG, Storheim K, et al. **Surgery with disc prosthesis versus rehabilitation** in patients with low back pain and degenerative disc: two year follow-up of randomised study. BMJ 2011;342:d2786.
Henschke N, Ostelo RWJG, van Tulder MW, et al. **Behavioural treatment** for chronic low-back pain. Cochrane Database of Systematic Reviews 2010, Issue 7. Art. No.: CD002014. For patients with CLBP, there is moderate quality evidence that in the short-term, operant therapy is more effective than waiting list and behavioural therapy is more effective than usual care for pain relief, but no specific type of behavioural therapy is more effective than another. In the intermediate- to long-term, there is little or no difference between behavioural therapy and group exercises for pain or depressive symptoms. Further research is likely to have an important impact on our confidence in the estimates of effect and may change the estimates.
Henschke N, Maher CG, Ostelo RWJG, de Vet HCW, Macaskill P, Irwig L. **Red flags** to screen for malignancy in patients with low-back pain. Cochrane Database of Systematic Reviews 2013, Issue 2. Art. No.: CD008686. DOI:10.1002/14651858.CD008686.pub2. For most "red flags," there is insufficient evidence to provide recommendations regarding their diagnostic accuracy or usefulness for detecting spinal malignancy. The available evidence indicates that in patients with LBP, an indication of spinal malignancy should not be based on the results of one single "red flag" question. Further research to evaluate the performance of different combinations of tests is recommended.
Herman PM, Anderson ML, Sherman KJ, et al. **Cost-effectiveness of Mindfulness-based Stress Reduction Versus Cognitive Behavioral Therapy** or Usual Care Among Adults With Chronic Low Back Pain. Spine (Phila Pa 1976). 2017 Oct 15;42(20):1511-1520.
Heyward J, Jones CM, Compton WM, et al. **Coverage of nonpharmacologic treatments** for low back pain among US public and private insurers. JAMA Netw Open. 2018;1(6):e183044. doi:10.1001/jamanetworkopen.2018.3044
Hill JC, Whitehurst DG, Lewis M, et al. Comparison of **stratified primary care management** for low back pain with current best practice (STarT Back): a randomised controlled trial. Lancet. 2011 Sep 28.
Hill JJ, Keating JL. **Daily exercises and education for preventing** low back pain in children: cluster randomized controlled trial. Phys Ther. 2015 Apr;95(4):507-16.
Hoangmai H. Pham; Bruce E. Landon; et al. Rapidity and Modality of **Imaging** for Acute Low Back Pain in Elderly Patients Arch Intern Med. 2009;169(10):972-981.
Hollinghurst S, Sharp D, Ballard K, et al. Randomised controlled trial of **Alexander technique** lessons, exercise, & massage (ATEAM) for chronic and recurrent back pain: conomic evaluation. BMJ. 2008 Dec 11;337:a2656. doi: 10.1136/bmj.a2656. An exercise prescription and six lessons in Alexander technique alone were both more than 85% likely to be cost effective at values above pound20 000 per QALY, but the Alexander technique performed better than exercise on the full range of outcomes. A combination of six lessons in Alexander technique followed by exercise was the most effective & cost effective option.
Hong AS, Ross-Degnan D, Zhang F, Wharam JF. Clinician-Level Predictors for Ordering **Low-Value Imaging**. JAMA Intern Med. 2017 Sep 25.
Hoy DG, Bain C, Williams G, et al. A systematic review of the **global prevalence of low back pain**. Arthritis Rheum. 2012 Jan 9.
Hoy D, March L, Brooks P, et al. The **global burden of low back pain**: estimates from the Global Burden of Disease 2010 study. Ann Rheum Dis. 2014 Mar 24.
Hsieh LL, et al. Treatment of low back pain by **acupressure** and physical therapy: randomized controlled trial. BMJ. 2006 Feb 17; [Epub ahead of print] (InfoPOEMs: Acupressure was significantly more effective than standard physical therapy modalities and exercise at decreasing disability scores and pain in patients with chronic low back pain. (LOE = 1b))
Hurley DA, Tully MA, Lonsdale C, et al. **Supervised walking in comparison with fitness training** for chronic back pain in physiotherapy: results of the SWIFT single-blinded randomized controlled trial (ISRCTN17592092). Pain. 2015 Jan;156(1):131-47.
Iles R, Taylor N, Davidson M, et al. **Telephone coaching** can increase activity levels for people with non-chronic low back pain: a randomised trial. J Physiother.2011;57(4):231-8.
Imamura M, Imamura ST, al. **Paraspinous Lidocaine Injection** for Chronic Nonspecific Low Back Pain: A Randomized Controlled Clinical Trial. J Pain. 2016 Jan 30.
Iversen T, Solberg T, Romner B, et al. Effect of caudal **epidural steroid or saline injection** in chronic lumbar radiculopathy: multicentre, blinded, randomised controlled trial. BMJ 2011;343:d5278.
Jakes AD, Phillips R, Scales M. **Teenagers with back pain.** BMJ. 2015 Apr 2;350:h1275.
Jarvik JG, Gold LS, Comstock BA, et al. Association of **early imaging for back pain** with clinical outcomes in older adults. JAMA. 2015 Mar 17;313(11):1143-53.
Jena AB, Olenski AR, Molitor D, et al. **Association between rainfall** and diagnoses of joint or back pain: retrospective claims analysis. BMJ. 2017 Dec 13;359:j5326.

Jenkins HJ, Hancock MJ, French SD, et al. Effectiveness of interventions designed to **reduce the use of imaging for low-back pain**: a systematic review. CMAJ. 2015 Apr 7;187(6):401-8.

Juch JNS, Maas ET, Ostelo RWJG, et al. Effect of **Radiofrequency Denervation** on Pain Intensity Among Patients With Chronic Low Back Pain: The **Mint** Randomized Clinical Trials. JAMA. 2017 Jul 4;318(1):68-81.

Jüni P, Battaglia M, Nüesch E, Hämmerle G, Eser P, van Beers R, Vils D, Bernhard J, et al. A randomised controlled trial of **spinal manipulative therapy** in acute low back pain. Ann Rheum Dis. 2008 Sep 5. [Epub ahead of print] **SMT is unlikely to result in relevant early pain reduction** in patients with acute low back pain.

Kamper SJ, Apeldoorn AT, Chiarotto A, Smeets RJ, Ostelo RW, Guzman J, et al. **Multidisciplinary biopsychosocial rehabilitation** for chronic low back pain: Cochrane systematic review and meta-analysis. BMJ 2015;350:h444.

Kapural L, Yu C, Doust MW, et al. **Novel 10-kHz High-frequency Therapy (HF10 Therapy)** Is Superior to Traditional Low-frequency Spinal Cord Stimulation for the Treatment of Chronic Back and Leg Pain: The SENZA-RCT Randomized Controlled Trial. Anesthesiology. 2015 Jul 27.

Kapural L, Yu C, Doust MW, et al. Comparison of 10-kHz High-Frequency and Traditional Low-Frequency **Spinal Cord Stimulation** for the Treatment of Chronic Back and Leg Pain: 24-Month Results From a Multicenter,Randomized, Controlled Pivotal Trial. Neurosurgery. 2016 Nov;79(5):667-677.

Kelle B, Guzel R, Sakalli H. The effect of **Kinesio taping** application for acute non-specific low back pain: A randomized controlled clinical trial. Clin Rehabil. 2015 Aug 27

Kennedy SA, Baerlocher MO. **New and experimental approaches to back pain**. CMAJ. 2014 Jun 10;186(9):E340.

Khadilkar A, et al. **Transcutaneous electrical nerve stimulation** for the treatment of chronic low back pain: a systematic review. Spine. 2005 Dec 1;30(23):2657-66. (InfoPOEMs: These authors only found 2 randomized trials of transcutaneous electrical nerve stimulation (TENS) for managing chronic low back pain. The divergent quality and findings suggest that we cannot draw any reliable conclusions about its efficacy. (LOE = 1a-))

Khadilkar A, Odebiyi DO, Brosseau L, et al. **Transcutaneous electrical nerve stimulation (TENS**) versus placebo for chronic low-back pain. Cochrane Database Syst Rev. 2008 Oct 8;(4):CD003008. At this time, the evidence from the small number of placebo-controlled trials does not support the use of TENS in the routine management of chronic LBP.

Kinkade S. **Evaluation and treatment of acute low back pain**. Am Fam Physician. 2007;75:1181-1188.

Kleine-Borgmann J, Schmidt K, Hellmann A, Bingel U. **Effects of open-label placebo** on pain, functional disability and spine mobility in chronic back pain patients: a randomized controlled trial. Pain. 2019 Aug 30. doi:10.1097/j.pain.0000000000001683.

Kligler B, Teets R, Quick M. **Complementary/Integrative Therapies That Work**: A Review of the Evidence. Am Fam Physician. 2016;94(5):369-374. (acupuncture)

Knezevic NN, Mandalia S, Raasch J, et al. **Treatment of chronic low back pain – new approaches** on the horizon. J Pain Res. 2017 May 10;10:1111-1123.

Koes BW. Evidence-based management of acute low back pain. Lancet. 2007 Nov 10;370(9599):1595-6.

Konno S, Oda N, Ochiai T, et al. Randomized, Double-blind, Placebo-controlled Phase III Trial of **Duloxetine Monotherapy** in Japanese Patients With Chronic Low Back Pain. Spine (Phila Pa 1976). 2016 Nov 15;41(22):1709-1717.

Korhonen T, Karppinen J, Paimela L, et al. The treatment of disc herniation-induced sciatica with infliximab: one-year follow-up results of FIRST II, a randomized controlled trial. Spine. 2006 Nov 15;31(24):2759-66. Although the long-term results of this randomized trial do not support the use of infliximab compared with placebo for lumbar radicular pain in patients with disc herniation-induced sciatica, further study in a subgroup of patients with L4-L5 or L3-L4 herniations, especially in the presence of Modic changes, appears to be warranted.

Krebs EE, Gravely A, Nugent S, et al. Effect of **Opioid vs Nonopioid Medications** on Pain-Related Function in Patients With Chronic Back Pain or Hip or Knee Osteoarthritis Pain: The **SPACE** Randomized Clinical Trial. JAMA. 2018 Mar 6;319(9):872-882.

Kroenke Kurt; Bair Matthew J.; Damush Teresa M.; et al. **Optimized Antidepressant** Therapy and Pain Self-management in Primary Care Patients With Depression and Musculoskeletal Pain: A Randomized Controlled Trial. JAMA. 2009;301(20):2099-2110. Optimized antidepressant therapy followed by a pain selfmanagement program resulted in substantial improvement in depression as well as moderate reductions in pain severity and disability.

Kuijpers T, van Middelkoop M, et al. A systematic review on the effectiveness of **pharmacological interventions** for chronic non-specific low-back pain. Eur Spine J. 2010 Jul 31

Lam OT, Strenger DM, Chan-Fee M, et al. Effectiveness of the **McKenzie Method of Mechanical Diagnosis and Therapy for Treating Low Back Pain**: Literature Review With Meta-analysis. J Orthop Sports Phys Ther. 2018 Jun;48(6):476-490.

Lamb SE, Hansen Z, Lall R, et al. on behalf of the Back Skills Training Trial investigators. Group **cognitive behavioural treatment** for low-back pain in primary care: a randomized controlled trial and cost-effectiveness analysis. Lancet. 2010 Feb 25.

Lamb SE, Gates S, Williams MA, et al. **Emergency department treatments and physiotherapy** for acute whiplash: a pragmatic, two-step, randomised controlled trial. Lancet. 2012 Dec 18.

Lamb SE, Gates S, et al. **Emergency department treatments and physiotherapy for acute whiplash**: a pragmatic, two-step, randomised controlled trial. Lancet 2013;381: 546–56.

Lambeek Ludeke C, van Mechelen Willem, Knol Dirk L, et al. Randomised controlled trial of **integrated care** to reduce disability from chronic low back pain in working and private life. BMJ 2010;340:c1035, doi: 10.1136/bmj.c1035 (Published 16 March 2010)

Lambeek Ludeke C, Bosmans Judith E, Van Royen Barend J, et al. Effect of integrated care for sick listed patients with chronic low back pain: **economic evaluation** alongside a randomised controlled trial. BMJ 341:doi:10.1136/bmj.c6414 (Published 30 Nov 2010)

Langevin P, Peloso PMJ, Lowcock J, et al. **Botulinum toxin for subacute/chronic neck pain**. *Cochrane Database of Systematic Reviews* 2011, Issue 7. Art. No.: CD008626. DOI: 10.1002/14651858.CD008626.pub2. Current evidence fails to confirm either a clinically important or a statistically significant benefit of BoNT-A injection for chronic neck pain associated with or without associated cervicogenic headache. Likewise, there was no benefit seen for disability and quality of life at four week and six months.

Larson AM, et al, and the Acute Liver Failure Study Group. Acetaminophen-Induced Acute Liver Failure: Results of a US Muticenter, Prospective Study. Hepatology; Dec 2005. (Of

662 consecutive acute liver failure pts over 6yrs: 42% from acetaminophen liver injury; 48% were unintentional overdoses; only 65% of pts survived)
Last AR, Hulbert K. **Chronic low back pain**: evaluation and management. Am Fam Physician. 2009 Jun 15;79(12):1067-74.
Lavy C, James A, Wilson-MacDonald J, Fairbank J. **Cauda equina syndrome**. BMJ. 2009 Mar 31;338:b936. doi: 10.1136/bmj.b936.
Leininger B, et al . Cost-effectiveness of **spinal manipulative therapy**, supervised exercise, and home exercise for older adults with chronic neck pain. Spine J. 2016 Jun 23.
Luedtke K, Rushton A, Wright C, et al. Effectiveness of **transcranial direct current stimulation** preceding cognitive behavioural management for chronic low back pain: sham controlled double blinded randomised controlled trial. BMJ. 2015 Apr 16;350 :h1640.
Lewis RA, Williams NH, et al. Comparative clinical effectiveness of management strategies for **sciatica**: systematic review and network meta-analyses. Spine J. 2013 Oct 4.
Licciardone JC, et al. **Osteopathic Manual Treatment & Ultrasound** Therapy for Chronic Low Back Pain: Randomized Controlled Trial. Ann Fam Med. 2013 Mar;11(2):122-129.
Lin DH, Jones CM, Compton WM, et al. **Prescription drug coverage for treatment of low back pain** among US Medicaid, Medicare Advantage, and commercial insurers. JAMA Netw Open. 2018;1(2):e180235.
Little P, et al. RCT trial of Alexander technique lessons, exercise, and massage (**ATEAM**) for chronic and recurrent back pain. BMJ. 2008 Aug 19;337:a884. doi: 10.1136/bmj.a884. One to one lessons in the Alexander technique from registered teachers have long term benefits for patients with chronic back pain. Six lessons followed by exercise prescription were nearly as effective as 24 lessons.
Livshits G, Popham M, Malkin I, et al.. **Lumbar disc degeneration and genetic factors** are the main risk factors for low back pain in women: the UK Twin Spine Study. Ann Rheum Dis. 2011 Oct;70(10):1740-5.
Low Back Pain. Am Fam Physician. 2018 Oct 1;98(7):online.
Lu Y, Guzman JZ, Purmessur D, et al. **Nonoperative management of discogenic back pain**: a systematic review. Spine (Phila Pa 1976). 2014 Jul 15;39(16):1314-24.
Luckhaupt SE, Dahlhamer JM, Gonzales GT, et al. **Prevalence, Recognition of Work-Relatedness, and Effect on Work of Low Back Pain** Among U.S. Workers. Ann Intern Med. 2019 May 14.
Lundqvist LO, Zetterlund C, Richter HO. Effects of **feldenkrais method** on chronic neck/scapular pain in people with visual impairment: a randomized controlled trial with one-year follow-up. Arch Phys Med Rehabil. 2014 Sep;95(9):1656-61.
Maas ET, Ostelo RW, Niemisto L, et al. **Radiofrequency denervation** for chronic low back pain. Cochrane Database Syst Rev. 2015 Oct 23;10:CD008572. The review authors found no high-quality evidence suggesting that RF denervation provides pain relief for patients with CLBP. Similarly, we identified no convincing evidence to show that this treatment improves function. Overall, the current evidence for RF denervation for CLBP is very low to moderate in quality; high-quality evidence is lacking. High-quality RCTs with larger patient samples are needed, as are data on long-term effects.
MacDonald J, Stuart E, Rodenberg R. **Musculoskeletal Low Back Pain in School-aged Children**: A Review. JAMA Pediatr. 2017 Jan 30.
MacPherson H, Tilbrook H, Richmond S, et al. **Alexander Technique Lessons or Acupuncture** Sessions for Persons With Chronic Neck Pain: A Randomized Trial. Ann Intern Med. 2015 Nov 3;163(9):653-62.
Machado LA, Kamper SJ, Herbert RD, et al. **Analgesic effects** of treatments for non-specific low back pain: a meta-analysis of placebo-controlled randomized trials. Rheumatology (Oxford). 2009 May;48(5):520-7. Epub 2008 Dec 24. The overall analgesic effects of most therapeutic interventions in patients with nonspecific low back pain, regardless of duration, are small. The data are limited by small study size and poor study quality. (LOE = 1a-)
MacRae CS, Lewis JS, Shortland AP, et al. Effectiveness of **rocker sole shoes** in the management of chronic low back pain: a randomized clinical trial. Spine (Phila Pa 1976). 2013 Oct 15;38(22):1905-12.
Madsen MV, Gøtzsche PC, Hróbjartsson A. **Acupuncture** treatment for pain: systematic review of randomised clinical trials with acupuncture, placebo acupuncture, and no acupuncture groups. BMJ. 2009 Jan 27;338:a3115. doi: 10.1136/bmj.a3115.
Mafi JN, McCarthy EP, Davis RB, Landon BE. **Worsening Trends in the Management** and Treatment of Back Pain. JAMA Intern Med. 2013 Jul 29.
Maher C, Underwood M, Buchbinder R. **Non-Specific Low Back Pain** Seminar. The Lancet. 2016 Oct 10.
Maiers M, Bronfort G, Evans R, et al. **Spinal manipulative therapy and exercise** for seniors with chronic neck pain. Spine J. 2014 Sep 1;14(9):1879-89.
Marshall PW, Kennedy S, Brooks C, et al. **Pilates exercise or stationary cycling** for chronic nonspecific low back pain: does it matter? a randomized controlled trial with 6-month follow-up. Spine (Phila Pa 1976). 2013 Jul 1;38(15):E952-9.
Martimo K, Verbeek J, et al. **Manual material handling advice and assistive devices** for preventing and treating back pain in workers. Cochrane Database Syst Rev. 2007 Jul 18;(3):CD005958. There is limited to moderate evidence that MMH advice and training with or without assistive devices do not prevent back pain, back pain-related disability or reduce sick leave when compared to no intervention or alternative interventions. There is no evidence available for the effectiveness of MMH advice and training or MMH assistive devices for treating back pain.
Mathieson S, Maher CG, McLachlan AJ, et al. Trial of **pregabalin** for **acute and chronic sciatica**. N Engl J Med 2017;376:1111- 20.
McCullough BJ, Johnson GR, Martin BI, Jarvik JG. **Lumbar MR imaging** and reporting epidemiology: do epidemiologic data in reports affect clinical management? Radiology. 2012 Mar;262(3):941-6.
McCullough BJ, Comstock BA, Deyo RA, et al. Major Medical Outcomes With **Spinal Augmentation vs Conservative Therapy**. JAMA Intern Med. 2013 Sep 9;173(16):1514-21.
McGregor AH, Probyn K, Cro S, Doré CJ, Burton AK, Balagué F, Pincus T, Fairbank J. **Rehabilitation following surgery for lumbar spinal stenosis**. *Cochrane Database of Systematic Reviews* 2013, Issue 12. Art. No.: CD009644. DOI: 10.1002/14651858.CD009644.pub2. Evidence suggests that active rehabilitation is more effective than usual care in improving both short- and long-term (back-related) functional status. Similar findings were noted for secondary outcomes, including short-term improvement in low back pain and longterm improvement in both low back pain and leg pain, although limited impact was observed in relation to improvements in general health status.
Menezes Costa Lda C, Maher CG, Hancock MJ et al. The **prognosis of acute and persistent low-back pain**: a meta-analysis. CMAJ. 2012 Aug 7;184(11):E613-24.
Michaleff Z, Maher CG, Lin C-WC, et al. **Comprehensive physiotherapy** exercise programme or advice for **chronic whiplash** (**PROMISE**): pragmatic randomised controlled trial. Lancet 2014; online April 4.
Moojen WA, Arts MP, Jacobs WCH, et al. **Interspinous process device versus standard conventional surgical decompression** for lumbar spinal stenosis: randomized controlled

trial. BMJ 2013;347:f6415.
Monticone M, Ferrante S, et al. Effect of a **Long-lasting Multidisciplinary Program** on Disability and Fear-Avoidance Behaviors in Patients With Chronic Low Back Pain: Results of a Randomized Controlled Trial. Clin J Pain. 2013 Jan 25.
Morone NE, Greco CM, Moore CG, et al. A **Mind-Body Program** for Older Adults With Chronic Low Back Pain: A Randomized Clinical Trial. JAMA Intern Med. 2016 Feb 22.
Moura CC, Chaves ECL, Chianca TCM, et al. Contribution of Chinese and French **ear acupuncture** for the management of chronic back pain: A randomised controlled trial. J Clin Nurs. 2019 Jun 25.
Natour J, Cazotti LD, Ribeiro LH, et al. **Pilates** improves pain, function and quality of life in patients with chronic low back pain: a randomized controlled trial. Clin Rehabil. 2014 Jun 25.
Naumann M, So Y, Argoff CE, Childers MK, Dykstra DD, Gronseth GS, Jabbari B, Kaufmann HC, Schurch B, Silberstein SD, Simpson DM; Therapeutics and Technology Assessment Subcommittee of the American Academy of Neurology. Assessment: **Botulinum** neurotoxin in the treatment of autonomic disorders and pain (an evidence-based review): report of the Therapeutics and Technology Assessment Subcommittee of the American Academy of Neurology. Neurology. 2008 May 6;70(19):1707-14.
Botulinum neurotoxin (BoNT) should be offered as a treatment option for the treatment of axillary hyperhidrosis and detrusor overactivity (Level A), should be considered for palmar hyperhidrosis, drooling, and detrusor sphincter dyssynergia after spinal cord injury (Level B), and may be considered for gustatory sweating and low back pain (Level C). BoNT is probably ineffective in episodic migraine and chronic tension-type headache (Level B). There is presently no consistent or strong evidence to permit drawing conclusions on the efficacy of BoNT in chronic daily headache (mainly transformed migraine) (Level U). While clinicians' practice may suggest stronger recommendations in some of these indications, evidence-based conclusions are limited by the availability of data.
Navani A, Manchikanti L, Albers SL, et al. **Responsible, Safe, and Effective Use of Biologics** in the Management of Low Back Pain: American Society of Interventional Pain Physicians (ASIPP) Guidelines. Pain Physician. 2019 Jan;22(1S):S1-S74.
Nerland US, Jakola AS, Solheim O, et al. **Minimally invasive decompression versus open laminectomy** for central **stenosis of the lumbar spine**: pragmatic comparative effectiveness study. BMJ 2015;350:h1603.
Ney JP, Difazio et al. Treatment of chronic low back pain with successive injections of **botulinum toxin** a over 6 months: a prospective trial of 60 patients. Clin J Pain. 2006 May;22(4):363-9.
Nguyen C, et al. **Intradiscal Glucocorticoid Injection** for Patients With Chronic Low Back Pain Associated With **Active Discopathy**: Randomized. Ann Intern Med. 2017 Mar 21.
Nice May 2009 Low back guideline summary http://www.nice.org.uk/nicemedia/pdf/CG88QuickRefGuide.pdf
(Savigny P, Watson P, Underwood M; Guideline Development Group. Early management of persistent non-specific low back pain: summary of NICE guidance. BMJ. 2009 Jun 4;338:b1805. doi: 10.1136/bmj.b1805. These guidelines from the United Kingdom's National Institute for Health and Clinical Excellence (NICE) give a nod to exercise, manual therapy, analgesics, acupuncture, and combined physical and psychological therapy for patients with low back pain. They advise against many traditional treatments, including lumbar support, traction, and steroid and other injections, citing either a lack of benefit or a lack of evidence. (LOE = 1a))
NICE: National Institute for Health and Care Excellence. **Low back pain and sciatica**: draft guidance. Mar 2016. www.nice.org.uk/guidance/indevelopment/gid-cgwave0681/ documents.
Okmen K, Okmen BM. The efficacy of **interlaminar epidural steroid administration** in multilevel intervertebral disc disease with chronic low back pain: a randomized, blinded, prospective Study. Spine J. 2016 Aug 20.
Oliveira CB, Franco MR, Maher CG, et al. **Physical Activity Interventions** for Increasing Objectively Measured Physical Activity Levels in Patients With Chronic Musculoskeletal Pain: A Systematic Review. Arthritis Care Res (Hoboken). 2016 Dec;68(12):1832-1842,
Oliveira CB, Maher CG, Pinto RZ, et al. Clinical practice **guidelines** for the management of on-specific low back pain in primary care: an updated overview. Eur Spine J. 2018 Jul 3.
Oltean H, Robbins C, van Tulder MW, et al. **Herbal medicine for low-back pain**. Cochrane Database Syst Rev. 2014 Dec 23;12:CD004504.
C. frutescens (Cayenne) reduces pain more than placebo. Although H. procumbens, S. alba, S. officinale L., S. chilensis, and lavender essential oil also seem to reduce pain more than placebo, evidence for these substances was of moderate quality at best. Additional well-designed large trials are needed to test these herbal medicines against standard treatments. In general, the completeness of reporting in these trials was poor. Trialists should refer to the CONSORT statement extension for reporting trials of herbal medicine interventions.
Oputa TJ, A'Court J. A **woman with lower back pain**. BMJ. 2017 Mar 16;356:j1117.
Overdevest GM, Vleggeert-Lankamp CL, Jacobs WC, et al. **Recovery of motor deficit accompanying sciatica-subgroup** analysis of a randomized controlled trial. Spine J. 2013 Nov 4.
Paige NM, Myiake-Lye IM, Booth MS, et al. Association of **spinal manipulative therapy** with clinical benefit and harm for acute low back pain: systematic review and meta-analysis. JAMA. doi:10.1001/jama.2017.3086
Paolucci T, Attanasi C, Cecchini W, et al. Chronic low back pain and **postural rehabilitation exercise**: a literature review. J Pain Res. 2018 Dec 20;12:95-107.
Pengel LH, Refshauge KM, Maher CG, et al. **Physiotherapist**-directed exercise, advice, or both for subacute low back pain: a randomized trial. Ann Intern Med. 2007 Jun 5;146(11):787-96. In participants with subacute low back pain, physiotherapist-directed exercise and advice were each slightly more effective than placebo at 6 weeks. The effect was greatest when the interventions were combined. At 12 months, the only effect that persisted was a small effect on participant-reported function.
Peul WC, Bredenoord AL, Jacobs WC. **Avoid surgery as first line treatment** for non-specific low back pain. BMJ. 2014 Jul 16;349:g4214.
Phillips FM, et al. **Lumbar spine fusion** for chronic low back pain due to degenerative disc disease: a systematic review. Spine (Phila Pa 1976). 2013 Apr 1;38(7):E409-22.
Pillastrini P, et al. Effectiveness of **Global Postural Re-education** in Patients With Chronic Nonspecific Neck Pain: Randomized Controlled Trial. Phys Ther. 2016 Mar 24.
Pinto RZ, Maher CG, Ferreira ML, Ferreira PH, Hancock M, Oliveira VC, et al. Drugs for relief of pain in patients with **sciatica**: systematic review and meta-analysis. BMJ 2012;344:e497.
Pinto RZ, Verwoerd AJH, Koes BW. Which pain medications are effective for **sciatica (radicular leg pain)?** BMJ. 2017 Oct 12;359:j4248.
Poetscher AW, Gentil AF, Lenza M, et al. **Radiofrequency denervation** for facet joint low back pain: a systematic review. Spine (Phila Pa 1976). 2014 Jun 15;39(14):E842-9.
Pozzobon D, Ferreira PH, Dario AB, et al. Is there an **association between diabetes** and neck and back pain? A systematic review with meta-analyses. PLoS One. 2019 Feb 21;

14(2):e0212030.
Qaseem A, Wilt T, McLean R, Forciea MA. **Noninvasive treatments for acute, subacute, and chronic low back pain**: a clinical practice guideline from the American College of Physicians (**ACP**). Ann Intern Med. 2017. [Epub ahead of print]. doi:10.7326/M16-2367
Qato DM, Ozenberger K, Olfson M. Prevalence of Prescription **Medications With Depression as a Potential Adverse Effect** Among Adults in the United States. JAMA. 2018 Jun 12;319(22):2289-2298. (eg. Gabapentin, **cyclobenzaprine**)
Rasmussen-Barr E, et al. **Nonsteroidal Anti-inflammatory Drugs for Sciatica**: An Updated Cochrane Review. Spine (Phila Pa 1976). 2017 Apr 15;42(8):586-594.
Ribeiro LH, Furtado RN, Konai MS, et al. Effect of **facet joint injection** versus **systemic steroids** in low back pain: a randomized controlled trial. Spine (Phila Pa 1976). 2013 Nov 1;38(23):1995-2002.
Rodríguez-Oviedo P, Ruano-Ravina A, Pérez-Ríos M, et al. School **children's backpacks**, back pain and back pathologies. Arch Dis Child. 2012 Mar 10.
Roelofs PD, Deyo RA, Koes BW, Scholten RJ, van Tulder MW. Nonsteroidal anti-inflammatory drugs for low back pain: an updated cochrane review. Spine. 2008 Jul 15;33(16):1766-74. The evidence from the 65 trials included in this review suggests that **NSAIDs are effective for short-term symptomatic relief** in patients with acute and chronic low back pain without sciatica. However, effect sizes are small. Furthermore, there does not seem to be a specific type of NSAID, which is clearly more effective than others. The selective COX-2 inhibitors showed fewer side effects compared with traditional NSAIDs in the randomized controlled trials included in this review. However, recent studies have shown that COX-2 inhibitors are associated with increased cardiovascular risks in specific patient populations.
Rothberg S, Friedman BW. **Complementary therapies** in addition to medication for patients with nonchronic, nonradicular low back pain: a systematic review. Am J Emerg Med. 2017 Jan;35(1):55-61.
Rubinstein SM, van Middelkoop M, Assendelft WJJ, de Boer MR, van Tulder MW. **Spinal manipulative therapy** for chronic low-back pain. *Cochrane Database of Systematic Reviews* 2011, Issue 2. Art. No.: CD008112. DOI: 10.1002/14651858.CD008112.pub2. High quality evidence suggests that there is no clinically relevant difference between SMT and other interventions for reducing pain and improving function in patients with chronic low-back pain. Determining cost-effectiveness of care has high priority.
Rubinstein SM, de Zoete A, van Middelkoop M, et al. **Benefits and harms of spinal manipulative therapy** for the treatment of chronic low back pain: systematic review and meta-analysis of randomized controlled trials. BMJ. 2019 Mar 13;364:l689.
Rubinstein SM, Terwee CB, Assendelft WJJ, de Boer MR, van Tulder MW. **Spinal manipulative therapy** for acute low-back pain. Cochrane Database of Systematic Reviews 2012, Issue 9. Art. No.: CD008880. DOI: 10.1002/14651858.CD008880.pub2. SMT is no more effective in participants with acute low-back pain than inert interventions, sham SMT, or when added to another intervention. SMT also appears to be no better than other recommended therapies.
Rundell SD, Sherman KJ, Heagerty PJ, et al. The clinical course of **pain and function in older adults** with a new primary care visit for back pain. J Am Geriatr Soc. 2015 Mar;63(3):524-30.
Rutledge T, et al.Randomized Controlled **Telephone-delivered Cognitive Behavioral Therapy** Versus **Supportive** Care for Chronic Back Pain. Clin J Pain.2018Apr;34(4):322-327.
Sands-Lincoln M, Goldmann D. **Acetaminophen** in the Management of Acute and Subacute Low Back and Neck Pain. Am J Med.2016:129(8):806-807
Santilli V, Beghi E, Finucci S. Chiropractic manipulation in the treatment of acute back pain and sciatica with disc protrusion: a randomized double-blind clinical trial of active and simulated spinal manipulations. Spine J. 2006 Mar-Apr;6(2):131-7. Epub 2006 Feb 3.
Saper RB, Lemaster C, Delitto A, et al. **Yoga, Physical Therapy, or Education** for Chronic Low Back Pain: A Randomized Noninferiority Trial. Ann Intern Med. 2017 Jun 20.
Saragiotto BT, Maher CG, Yamato TP, et al. **Motor control exercise** for chronic non-specific low-back pain. Cochrane Database of Systematic Reviews 2016, Issue 1. Art. No.: CD012004. DOI: 10.1002/14651858.CD012004. There is very low to moderate quality evidence that MCE has a clinically important effect compared with a minimal intervention for chronic low back pain. There is very low to low quality evidence that MCE has a clinically important effect compared with exercise plus EPA. There is moderate to high quality evidence that MCE provides similar outcomes to manual therapies and low to moderate quality evidence that it provides similar outcomes to other forms of exercises. Given the evidence that MCE is not superior to other forms of exercise, the choice of exercise for chronic LBP should probably depend on patient or therapist preferences, therapist training, costs and safety.
Saragiotto BT, Machado GC, Ferreira ML, et al. Paracetamol (**acetaminophen**) for low back pain. Cochrane Database Syst Rev. 2016 Jun 7;6:CD012230. We found that paracetamol does not produce better outcomes than placebo for people with acute LBP, and it is uncertain if it has any effect on chronic LBP.
Schneider M, Haas M, Glick R, et al. Comparison of **spinal manipulation methods and usual medical care for acute and subacute low back pain**: a randomized clinical trial. Spine (Phila Pa 1976). 2015 Feb 15;40(4):209-17.
Sears ED, Caverly TJ, et al. Clinicians' Perceptions of **Barriers to Avoiding Inappropriate Imaging** for Low Back Pain-Knowing Is Not Enough. JAMA Intern Med. 2016 Oct 17.
Shanthanna H, Gilron I, Rajarathinam M, et al. Benefits and safety of **gabapentinoids** in **chronic low back pain**: A systematic review and meta-analysis of randomized controlled trials. PLoS Med. 2017 Aug 15;14(8):e1002369.
Sheeran L, van Deursen R, Caterson B, et al. **Classification-guided versus generalized postural intervention** in subgroups of nonspecific chronic low back pain: a pragmatic randomized controlled study. Spine (Phila Pa 1976). 2013 Sep 1;38(19):1613-25.
Sherman KJ, et al. Comparing **yoga**, exercise, and a self-care book for chronic low back pain: a randomized, controlled trial. Ann Intern Med. 2005 Dec 20;143(12):849-56. (InfoPOEMs: A yoga program specifically aimed at patients with chronic low back pain is more effective than either exercise treatment or self-care in decreasing functional disability in patients with chronic low back pain. The style of yoga is called viniyoga and was adapted for use in patients with low back pain. (LOE = 1b))
Sherman KJ, Cherkin DC, Wellman RD, et al. A randomized trial comparing **yoga, stretching, and a self-care book** for chronic low back pain [online October 24, 2011]. Arch Intern Med. doi:10.1001/archinternmed.2011.524.
Simon CB, Riley JL 3rd, et al. Age Group Comparisons of **TENS Response** Among Individuals With Chronic Axial Low Back Pain. J Pain. 2015 Dec;16(12):1268-79.
Song L, Qiu P, Xu J, et al. The Effect of **Combination Pharmacotherapy** on Low Back Pain: A Meta-analysis. Clin J Pain. 2018 Nov;34(11):1039-1046.
Spence MM, Shin PJ, Lee EA, Gibbs NE. Risk of injury associated with **skeletal muscle relaxant** use in older adults. Ann Pharmacother. 2013 Jul;47(7-8):993-8.
Srinivas SV, Deyo RA, Berger ZD. Application of "**Less Is More**" to Low Back Pain Low Back Pain. Arch Intern Med. 2012 Jun 4:1-5.

Staal JB, Nelemans PJ, de Bie RA. **Spinal injection therapy** for low back pain. JAMA. 2013 Jun 19;309(23):2439-40.
Steffens D, Maher CG, Li Q, et al. **Weather** does not affect back pain: Results from a case-crossover study. Arthritis Care Res (Hoboken). 2014 Jul 10.
Steffens D, Ferreira ML, Latimer J, et al. **What triggers an episode of acute low back pain**? A case-crossover study. Arthritis Care Res (Hoboken). 2015 Feb 9.
Steffens D, Maher CG, et al. **Prevention of low back pain**: a systematic review and meta-analysis [online Jan 11, 16]. JAMA Intern Med. doi:10.1001/jamainternmed.2015.7431.
Steger M, Schneemann M, Fox M. Systemic review: the pathogenesis and pharmacological **treatment of hiccups**. Aliment Pharmacol Ther. 2015 Nov;42(9):1037-50.
Su W, Yegappan C, Carlisle EJF, et al. Reduced level of consciousness from **baclofen** in people with low kidney function. BMJ 2009;339:b4559, doi: 10.1136/bmj.b4559 (31Dec09)
Summary for Patients: Steroid Injections for Patients With Low Back Pain. Ann Intern Med. 2017 Apr 18;166(8).
Suri P, Delaney K, Rundell SD, et al. **Predictive Validity of the STarT Back Tool for Risk of Persistent Disabling Back Pain in a U.S. Primary Care Setting.** Arch Phys Med Rehabil. 2018 Aug;99(8):1533-1539.e2.
Suri P, Rainville J, Kalichman L, et al. Does this older adult with lower extremity pain have the clinical syndrome of **lumbar spinal stenosis**? JAMA. 2010 Dec 15;304(23):2628-36.
Tegner H, Frederiksen P, Esbensen BA, et al. **Neurophysiological Pain Education for Patients With Chronic Low Back Pain**: A Systematic Review and Meta-Analysis. Clin J Pain. 2018 Aug;34(8):778-786.
Teut M, Knilli J, Daus D, et al. **Qigong or Yoga Versus No Intervention** in Older Adults With Chronic Low Back Pain-A Randomized Controlled Trial. J Pain. 2016 Mar 30.
Thackeray A, Fritz JM, Childs JD, et al. The Effectiveness of **Mechanical Traction** Among Subgroups of Patients With Low Back Pain and Leg Pain: A Randomized Trial. J Orthop Sports Phys Ther. 2016 Mar;46(3):144-54.
Tilbrook HE, Cox H, Hewitt CE, et al. **Yoga** for chronic low back pain: a randomized trial. Ann Intern Med. 2011 Nov 1;155(9):569-78.
Traeger AC, Hübscher M, Henschke N, et al. Effect of **Primary Care-Based Education on Reassurance in Patients With Acute Low Back Pain**: Systematic Review and Meta-analysis. JAMA Intern Med. 2015 Mar 23.
Traeger AC, Henschke N, Hübscher M, et al. Estimating the **Risk of Chronic Pain**: Development and Validation of a Prognostic Model (**PICKUP**) for Patients with Acute Low Back Pain. PLoS Med. 2016 May 17;13(5):e1002019.
Traeger A, Buchbinder R, Harris I, Maher C. **Diagnosis and management of low-back pain in primary care**. CMAJ. 2017 Nov 13;189(45):E1386-E1395.
Traeger AC, Lee H, Hübscher M, et al. Effect of Intensive **Patient Education vs Placebo Patient Education** on Outcomes in Patients With Acute Low Back Pain: A Randomized Clinical Trial. JAMA Neurol. 2018 Nov 5.
Turner JA, Shortreed SM, Saunders KW, et al. **Optimizing prediction** of **back pain outcomes**. Pain. 2013 Apr 18. pii: S0304-3959(13)00184-X. doi: 10.1016/j.pain.2013.04.029.
UK BEAM Trial Team. United Kingdom back pain exercise and manipulation (UK BEAM) randomised trial: effectiveness of physical treatments for back pain in primary care. BMJ. 2004 Dec 11;329(7479):1377. Epub 2004 Nov 19.
Urits I, Burshtein A, Sharma M, et al. **Low Back Pain, a Comprehensive Review**: Pathophysiology, Diagnosis, and Treatment. Curr Pain Headache Rep. 2019 Mar 11;23(3):23.
Urquhart D, et al. **Antidepressants** for non-specific **low back pain**. Cochrane Database Syst Rev. 2008 Jan 23;(1):CD001703. There is no clear evidence that antidepressants are more effective than placebo in the management of patients with chronic low-back pain.
Urquhart DM, Wluka AE, van Tulder M, et al. Efficacy of Low-Dose Amitriptyline for Chronic Low Back Pain: A Randomized Clinical Trial. JAMA Intern Med. 2018 Oct 1.
VA/DoD: Diagnosis and Treatment of Low Back Pain Work Group. **VA/DoD clinical practice guideline for diagnosis and management of low back pain**. Version 2.0. Washington (DC): Department of Veterans Affairs, Department of Defense; 2017 Sep.Valenza MC, et al. Results of a **Pilates exercise program** in patients with chronic non-specific low back pain: A randomized controlled trial. Clin Rehabil. 2016 Jun 3.
van Wijk RM, Geurts JW, Wynne HJ, et al. Radiofrequency denervation of lumbar facet joints in the treatment of chronic low back pain: a randomized, double-blind, sham lesion-controlled trial. Clin J Pain. 2005 Jul-Aug;21(4):335-44.
Verbeek JH, Martimo KP, Karppinen J, et al. **Manual material handling advice and assistive devices for preventing and treating back pain in workers.** Cochrane Database Syst Rev. 2011 Jun 15;6:CD005958. There is moderate quality evidence that MMH advice and training with or without assistive devices does not prevent back pain or back pain-related disability when compared to no intervention or alternative interventions. There is no evidence available from RCTs for the effectiveness of MMH advice and training or MMH assistive devices for treating back pain.
Verhagen AP, Downie A, Popal N, et al. Red flags presented in current low back pain guidelines: a review. Eur Spine J. 2016 Jul 4.
Wang GS, Le Lait MC, Heard K. **Unintentional pediatric exposures** to central alpha-2 agonists (**clonidine**, guanfacine, tizanidine) reported to the national poison data system. J Pediatr. 2014 Jan;164(1):149-52.
Waseem Z, Boulias C, Gordon A, et al. **Botulinum toxin injections** (Botox) for low-back pain and sciatica. Cochrane Database Syst Rev. 2011 Jan 19;1:CD008257. We identified three studies that investigated the merits of BoNT for LBP, but only one had a low risk of bias and evaluated patients with non-specific LBP (N = 31).
Walker BF, French SD, Grant W, Green S. **Combined chiropractic interventions** for low-back pain. Cochrane Database of Systematic Reviews 2010, Issue 4. Art. No.: CD005427. Combined chiropractic interventions slightly improved pain and disability in the short-term and pain in the medium-term for acute and subacute LBP. However, there is currently no evidence that supports or refutes that these interventions provide a clinically meaningful difference for pain or disability in people with LBP when compared to other interventions. Future research is very likely to change the estimate of effect and our confidence in the results.
Walker BF, Hebert JJ, , et al. Outcomes of **usual chiropractic**. The **OUCH** randomized controlled trial of adverse events. Spine (Phila Pa 1976). 2013 Sep 15;38(20):1723-9.
Wegner I, Widyahening IS, van Tulder MW, et al. **Traction for low-back pain** with or without sciatica. Cochrane Database Syst Rev. 2013 Aug 19;8:CD003010. These findings indicate that traction, either alone or in combination with other treatments, has little or no impact on pain intensity, functional status, global improvement and return to work among people with LBP.
Weinstein JN, et al. Surgical vs Nonoperative Treatment for Lumbar Disk Herniation: The Spine Patient Outcomes Research Trial (SPORT) Observational Cohort. JAMA. 2006 Nov 22;296(20):2451-2459.

Weinstein JN, Tosteson TD, Lurie JD, Tosteson AN, et al. SPORT Investigators. Surgical versus nonsurgical therapy for **lumbar spinal stenosis**. N Engl J Med. 2008 Feb 21;358(8):794-810.

Wieland LS, Skoetz N, Pilkington K, et al. **Yoga** treatment for chronic non-specific low back pain. Cochrane Database of Systematic Reviews 2017, Issue 1. Art. No.: CD010671.
There is low- to moderate-certainty evidence that yoga compared to non-exercise controls results in small to moderate improvements in back-related function at three and six months. Yoga may also be slightly more effective for pain at three and six months, however the effect size did not meet predefined levels of minimum clinical importance. It is uncertain whether there is any difference between yoga and other exercise for back-related function or pain, or whether yoga added to exercise is more effective than exercise alone. Yoga is associated with more adverse events than non-exercise controls, but may have the same risk of adverse events as other back-focused exercise. Yoga is not associated with serious adverse events. There is a need for additional high-quality research to improve confidence in estimates of effect, to evaluate long-term outcomes, and to provide additional information on comparisons between yoga and other exercise for chronic non-specific low back pain.

Wilkens Philip; Scheel Inger B.; Grundnes Oliver; et al. Effect of **Glucosamine** on Pain-Related Disability in Patients With Chronic Low Back Pain and Degenerative Lumbar Osteoarthritis: A Randomized Controlled Trial. JAMA. 2010;304(1):45-52.

Will JS, Bury DC, Miller JA. **Mechanical Low Back Pain**. Am Fam Physician. 2018;98(7):421-428

Williams CM, Latimer J, Maher CG, et al. PACE--the first placebo controlled trial of **paracetamol/acetaminophen** for acute low back pain: design of a randomised controlled trial. BMC Musculoskelet Disord. 2010 Jul 23;11:169.

Williams CM, Maher CG, Hancock MJ, et al. Low back pain and best practice care: A **survey of general practice** physicians. Arch Intern Med. 2010 Feb 8;170(3):271-7.

Williams CM, Maher CG, Latimer J, et al. Efficacy of **paracetamol/acetaminophen** for acute low-back pain: double-blind, randomized controlled trial. (**PACE**) Lancet. 2014 Jul 23.

Woodman JP, Moore NR. Evidence for the effectiveness of **Alexander Technique** lessons in medical and health-related conditions: a systematic review. Int J Clin Pract. 2012 Jan;66(1):98-112.

Wu LC, et al. Literature Review and Meta-Analysis of **Transcutaneous Electrical Nerve Stimulation** in Treating Chronic Back Pain. Reg Anesth Pain Med. 2018 Feb 1.

Wynne-Jones G, Dunn KM. Has there been a change in the **rates of UK sickness certification for back pain** over time? An examination of historical data from 2000 to 2010. BMJ Open. 2016 Apr 25;6(4):e009634.

Yamato TP, Maher CG, Saragiotto BT, et al. **Pilates** for low back pain. Cochrane Database Syst Rev. 2015 Jul 2;7:CD010265. We did not find any high quality evidence for any of the treatment comparisons, outcomes or follow-up periods investigated. However, there is low to moderate quality evidence that Pilates is more effective than minimal intervention for pain and disability. When Pilates was compared with other exercises we found a small effect for function at intermediate-term follow-up. Thus, while there is some evidence for the effectiveness of Pilates for low back pain, there is no conclusive evidence that it is superior to other forms of exercises. The decision to use Pilates for low back pain may be based on the patient's or care provider's preferences, and costs.

Yang JD, et al. Intermittent **Cervical Traction** for Treating **Neck Pain**: A Meta-analysis of Randomized Controlled Trials. Spine (Phila Pa 1976). 2017 Jul 1;42(13):959-965.

Zadro JR, Shirley D, Ferreira M, Carvalho Silva AP, et al. Is **Vitamin D Supplementation Effective for Low Back Pain?** A Systematic Review and Meta-Analysis. Pain Physician. 2018 Mar;21(2):121-145.

Zadro JR, Shirley D, Simic M, et al. **Video-Game-Based Exercises** for Older People With Chronic Low Back Pain: A Randomized Controlledtable Trial (GAMEBACK). Phys Ther. 2019 Jan 1;99(1):14-27.

Web Sites:

American Academy of Family Physicians (information available in English and Spanish) http://familydoctor.org/online/famdoces/home/common/pain/treatment/117.html

MedlinePlus http://www.nlm.nih.gov/medlineplus/backpain.html

National Institutes of Neurological Disorders and Stroke http://www.ninds.nih.gov/disorders/backpain/backpain.htm

The Arthritis Foundation http://ww2.arthritis.org/conditions/DiseaseCenter/back_pain.asp

References: **PAIN: OVERVIEW OF APPROACH & Tx CONSIDERATIONS (RxFiles.ca)**

1) Baumann T, Strickland J, & Herndon C (2011). Chapter 69. Pain Management. In Talber R, Dipiro J, Matzke G, Posey L, Wells B, & Yee C. *Pharmacotherapy: A Pathophysiologic Approach*, 8e. Retrieved November 17, 2012 from http://www.accesspharmacy.com/content.aspx?aID=7986332.
2) Astolfi J (2011). Chaper 12. Palliative Care. In Talber R, Dipiro J, Matzke G, Posey L, Wells B, & Yee C. *Pharmacotherapy: A Pathophysiologic Approach*, 8e. Retrieved November 17, 2012 from http://www.accesspharmacy.com/content.aspx?aID=7967629
3) Shipton E & Tait B. Flagging the pain: preventing the burden of chronic pain by identifying and treating risk factors in acute pain. *European Journal of Anesthesiology.* 2005; 22: 405-12.
4) Blondell RD, Azadfard M, Wisnieeewski AM. Pharmacologic Therapy for Acute Pain. Am Fam Physician. 2013;87(11):766-772.
5) Canadian Guidelines for Safe & Effective Use of Opioids for Chronic Non-Cancer Pain. http://nationalpaincentre.mcmaster.ca/opioid/. Accessed Nov 19, 2012.
Opioid Manager Tool: http://nationalpaincentre.mcmaster.ca/opioidmanager/
6) Wong C, Lau E, Palozzi L, Campbell F. Pain management in children: Part 1 - Pain assessment tools and a brief review of nonpharmacological and pharmacological treatment options. Can Pharm J (Ott). 2012 Sep;145(5):222-5.
7) Regier L, Jensen B, Kessler B. Pediatric Pain: Treatment Considerations. RxFiles, accessed online at http://www.rxfiles.ca/rxfiles/uploads/documents/CHT-Pain-Peds.pdf
8) Klein D, Dumpe M, Katz E, & Bena J. Pain assessment in the intensive care unit: Development and psychometric testing of the nonverbal pain assessment tool. *Heart & Lung.* 2010; 39(6): 521-28.
9) CADTH Rapid Response Report. Pain Assessment Tools for Elderly Patients: Reliability, Validity, and Guidelines for Use. 23 December 2010.
10) Pudas-Tahka S, Axelin A, Aantaa R, Lund V, & Salantera S. Pain assessment tools for unconscious or sedated intensive care patients: a systematic review. *Journal of Advanced Nursing.* 2008; 65(5): 946-56.
11) Geriatric Pain. PACSLAC Pain Assessment Tool. Available online: http://www.geriatricpain.org/Content/Assessment/Impaired/Pages/default.aspx
12) Regier L. Opioid Slow Taper Template. RxFiles. Accessed online at http://www.rxfiles.ca/rxfiles/uploads/documents/Opioid-Taper-Template.pdf
13) Alford D, Compton P, & Samet J. Acute Pain Management for Patients Receiving Maintenance Methadone or Buprenorphine Therapy. *Ann Intern Med*. 2006; 144: 127-34.
14) Quinlan J & Carter K. Acute pain management in patients with persistent pain. *Curr Opin Support Palliat Care.* 2012; 6(2): 188-93.
15) Onsolis (Fentanyl Buccal Film) and BuTrans (Buprenorphine Patch). *Pharmacist's Letter/Prescriber's Letter* Detail-Document #260819 August 2010.
16) Lexicomp Drug Monographs. Accessed November 18, 2012 from http://online.lexi.com/lco/action/home/switch.
17) Smith H & Bruckenthal P. Implications of Opioid Analgesia for Medically Complicated Patients. *Drugs Aging.* 2010; 27(5): 417-33.
18) Karras B, McKee N, Regier L, Stone S. Opioids for chronic noncancer pain in the elderly: an osteoarthritis case. Can Fam Physician. 2011 Aug;57(8):907-11.
19) Stone S, Regier L. *RxFiles Q&A summary: opioids for chronic non-cancer pain (CNCP) management in the elderly*. Saskatoon, SK: RxFiles;2011. Available from:**www.rxfiles.ca/rxfiles/uploads/documents/Opioids-Pain-ELDERLY-QandA.pdf**. Accessed 2013, Dec 11.
20) American Geriatrics Society 2012 Beers Criteria Update Expert Panel. American Geriatrics Society updated Beers Criteria for potentially inappropriate medication use in older adults. J Am Geriatr Soc. 2012 Apr;60(4):616-31.
21) Chandok, N & Watt K. Pain Management in the Cirrhotic Patient: The Clinical Challenge. *Mayo Clin Proc.* 2010; 85(5): 451-58.
22) Nayak-Rao S. Achieving effective pain relief in patients with chronic kidney disease: a review of analgesics in renal failure. *JNephrol.* 2011; 24(01): 35-40.
23) Peterson GM, Randall CT, Paterson J. Plasma levels of morphine and morphine glucuronides in the treatment of cancer pain: relationship to renal function and route of administration. Eur J Clin Pharmacol. 1990;38(2):121-4.
24) Wu C & Raja S. Treatment of acute postoperative pain. *Lancet.* 2011; 377: 2215-25.
25) Pyati S & Gan T. Perioperative Pain Management. *CNS Drugs.* 2007; 21(3): 185-211.
26) American Society of Anesthesiologists Task Force on Acute Pain Management. Practice Guidelines for Acute Pain Management in the Perioperative Setting. *Anesthesiology.* 2012; 116(2): 248-72.
27) Derry S, Derry CJ, Moore RA. Single dose oral ibuprofen plus oxycodone for acute postoperative pain in adults. Cochrane Database Syst Rev. 2013 Jun 26;6:CD010289.
28) Kosar L. Peripregnancy Drug Treatment Considerations. RxFiles. Accessed online 11 Dec, 2013 at http://www.rxfiles.ca/rxfiles/uploads/documents/members/CHT-Peri-Pregnancy-DrugTx.pdf
29) Lam J, Kelly L, Ciszkowski C, Landsmeer M, Nauta, M, Carleton B, Hayden M, Madadi P, & Koren G. Central Nervous System Depression of Neonates Breastfed by Mothers Receiving Oxycodone for Postpartum Analgesia. *Journal of Pediatrics.* 2012; 160: 133-7.
30) Babb M, Koren G, & Einarson A. Motherrisk Update: Treating pain during pregnancy. *Canadian Family Physician.* 2010; 56: 25-26.
31) Hendrickson R & McKeown N. Is maternal opioid use hazardous to breast-fed infants? *Clinical Toxicology.* 2012; 50: 1-14.
32) Bloor M, Paech M, & Kaye R. Tramadol in pregnancy and lactation. *Internation Journal of Obstetric Anesthesia.* 2012; 21: 163-67.
33) Regier L, Butt P, Carter. Pain Approaches: Distinctives for the ACUTE vs PALLIATIVE vs CNCP use of Opioids. RxFiles.ca. Accessed online 11 Dec 2013 at http://www.rxfiles.ca/rxfiles/uploads/documents/members/CHT-Pain-Approaches-Acute-Palliative-CNCP.pdf
34) Regier L. Substance Use Disorders & Addiction. RxFiles.ca. Accessed online 16 Sept 2019 at http://www.rxfiles.ca/rxfiles/uploads/documents/CHT-Substance-Abuse.pdf
35) Alford P, Compton P, & Samet J. Acute pain management for patients receiving maintenance methadone or buprenorphine therapy. *Annals of Internal Medicine* 2006; 144: 127-134.
36) Volkow N & McLellan T. Curtailing Diversion and Abuse of Opioid Analgesics Without Jeopardizing Pain Treatment. *JAMA.* 2011; 305(13): 1346-47.
37) *Veterans Health Administration, Department of Defense: Clinical Practice Guidelines for the Management of Postoperative Pain*, Version 1.2, adapted May 2002. Available online: http://www.healthquality.va.gov/Post_Operative_Pain_Management_POP.asp
38) Corke P. Postoperative Pain Management. Austrailian Prescriber 2013;36(6)202-205.
39) Iedema, J. Cautions with codeine. *Aust Presc.* 2011; 34: 133-35.
40) Codeine Safety in Kids. *Pharmacist's Letter/Prescriber's Letter* Detail Document #280608 June 2012.
41) Chen T & Adamson P. Comparison of ibuprofen & acetaminophen with codeine following cosmetic facial surgery. *Journal of Otolaryngology – Head & Neck Surgery.* 2009; 38 (5): 580-86.
42) Friday J, Kanegaye J, McCaslin I, Zheng A, & Harley J. Ibuprofen provides analgesia equivalent to acetaminophen-codeine in the treatment of acute pain in children with extremity injuries: a randomized clinical trial. *Society for Academic Emergency Medicine*. 2009; 16: 711-16.
43) Nauta M, Landsmeer M, & Koren G. Codeine-acetaminophen versus nonsteroidal anti-inflammatory drugs in the treatment of post-abdominal surgery pain: a systematic reivew of randomized trials. *The American Journal of Surgery.* 2009; 198: 256-61.
44) Common Questions About Ketorolac. *Pharmacist's Letter/Prescriber's Letter* Detail-Document #280607 June 2012.
45) CADTH Rapid Response Report: Summary of Abstracts. Intravenous Ketorolac versus Intravenous Opiates for the Management of Acute Pain in the Emergency Department: Safety. 17 July 2012.
46) *Toradol vs opiates July 2012 CADTH Rapid Response Report*
47) Massey T, Derry S, Moore RA, McQuay HJ. Topical NSAIDs for acute pain in adults. Cochrane Database Syst Rev. 2010 Jun 16;(6):CD007402.
48) Kurmis A, Kurmis T, O'Brien J, & Dalen T. The Effect of Nonsteroidal Anti-Inflammatory Drug Administration on Acute Phase Fracture-Healing: A Review. *J Bone Joint Surg Am.* 2012; 94: 815-23.
49) Regier L. Pain, Chronic Non-cancer – Treatment Considerations. RxFiles Accessed online at http://www.rxfiles.ca/rxfiles/uploads/documents/members/CHT-Pain-Chronic-NonCa.pdf
50) Chang AK, Bijur PE, Esses D, Barnaby DP, Baer J. Effect of a Single Dose of Oral Opioid and Nonopioid Analgesics on Acute Extremity Pain in the Emergency Department: A Randomized Clinical Trial. JAMA. 2017 Nov 7;318(17):1661-1667.
51) Coons C, Regier L. RxFiles Opioid Use Disorder (OUD) Chart. Accessed online 16 Sept 2019 at https://www.rxfiles.ca/rxfiles/uploads/documents/members/CHT-Opioid-Use-Disorder-OUD.pdf
52) MD+CALC. Neuropathy Pain Scale (NPS). Accessed online, 21Oct19 at https://www.mdcalc.com/neuropathy-pain-scale-nps

Additional References

Aiyer R, Gulati A, Gungor S, et al. **Treatment of Chronic Pain With Various Buprenorphine Formulations: A Systematic Review of Clinical Studies.** Anesth Analg. 2018 Aug;127(2):529-538.
Alam A, Gomes T, Zheng H, Mamdani M, Juurlink D, & Bell C. Long-term Analgesic Use After Low-Risk Surgery. *Arch Intern Med.* 2012; 172(5): 425-30.
Boersma K, Sodermark M, Hesser H, et al. Efficacy of a **transdiagnostic emotion-focused exposure treatment** for chronic pain patients with comorbid anxiety and depression: a randomized controlled trial. Pain. 2019 Apr 6.
Boyd C, Crawford C, Berry K, et al. **Conditional Recommendations for Specific Dietary Ingredients** as an Approach to Chronic Musculoskeletal Pain: Evidence-Based Decision Aid for Health Care Providers, Participants, and Policy Makers. Pain Med. 2019 Apr 15.
Cantrill S, Brown M, Russell C, Delaney K, Hays D, Nelson L, O'Connor R, Papa A, Sporer K, Todd K, & Whitson R. Clinical Policy: Critical Issues in Prescribing Opioids for Adult Patients in the Emergency Department. *Ann Emerg Med*. 2012; 60: 499-525.
Clarke H, Soneji N, Ko DT, Yun L, Wijeysundera DN. Rates and risk factors for prolonged opioid use after major surgery: population based cohort study. BMJ. 2014 Feb 11;348:g1251.
Desai M, Bentley A, Keck WA, et al. **Cooled radiofrequency ablation of the genicular nerves** for chronic pain due to osteoarthritis of the knee: a cost-effectiveness analysis based on trial data. BMC Musculoskelet Disord. 2019 Jun 26;20(1):302.
Dodwell E, Latorre J, Parisini E, Zwettler E, Chandra D, Mulpuri K, & Snyder B. NSAID Exposure and Risk of Nonunion: A Meta-Analysis of Case-Control and Cohort Studies. *Calcif Tissue Int.* 2010; 87: 193-202.
Durand Z, Nechuta S, Krishnaswami S, et al. **Prevalence and Risk Factors** Associated With Long-term Opioid Use **After Injury** Among Previously Opioid-Free Workers. JAMA Netw Open. 2019 Jul 3;2(7):e197222.
Lagisetty PA, Healy N, Garpestad C, et al. Access to **Primary Care Clinics for Patients With Chronic Pain Receiving Opioids**. JAMA Netw Open. 2019 Jul 3;2(7):e196928.
Lowenstein M, Grande D, Delgado MK. **Opioid Prescribing Limits for Acute Pain** -Striking the Right Balance. N Engl J Med. 2018 Aug 9;379(6):504-506.
Medical Letter: Treatment Guidelines. Drugs for Pain. *Medical Letter* 2010 92(8): 25-33.
Melby V & colleagues. Acute pain relief in children: use of rating scales and analgesia. *Emergency Nurse.* 2011; 19(6): 32-37.
Mercadante S, Casuccio A, Tirelli W, & Giarratano A. Equipotent doses to switch from high doses of opioids to transdermal buprenorphine. *Support Care Cancer*. 2009. 17: 715-18.
Mooney B. Child-friendly aids in pain management. *WIN.* 2012; 20(6): 37-28.
Subramanian P, Allcock N, James V, & Lathlean J. Challenges faced by nurses in managing pain in a critical care setting. *Journal of Clinical Nursing.* 2011; 21: 1254-62.
McQuay H, Derry S, Eccleston C, Wiffen P, & Moore R. Evidence for analgesic effect in acute pain – 50 yrs on. *Pain.* 2012; 153: 1364-67.
Platts-Mills T, Hunold K, Bortsov A, Soward A, Peak D, Jones J, Swor R, Lee D, Domeier R, Hendry P, Rathlev N, & McLean S. More educated emergency department patients are less likely to receive opioids for acute pain. *Pain.* 2012; 153: 967-73.
Martini C, Olofsen E, Yassen A, Aarts L, & Dahan A. Pharmacokinetic-pharmacodynamic modeling in acute and chronic pain: an overview of the recent literature. *Expert Rev. Clin. Pharmacol.* 2011; 4(6) 719-28.
Macintyre P & Walker S. The scientific evidence for acute pain treatment. *Current Opinion in Anesthesiology.* 2010; 23: 623-28.
Nauta M, Landsmeer M, & Koren G. Codeine-acetaminophen versus nonsteroidal anti-inflammatory drugs in the treatment of post-abdominal surgery pain: a sytematic review of randomized trials. *The American Journal of Surgery.* 2009; 198: 256-61.
RxFiles. Drug Comparison Charts. 9th Ed. pages 69-71
Smith C, Collins T, Crowther C, & Levett K. Intervention Review: Acupuncture or acupressure for pain management in labour. Cochrane Review July 2011. access on 22Nov11 from http://onlinelibrary.whiley.com/doi/10.1002/14651858.CD009232/abstract 13.
Taylor I, Kolber M**. My fracture really hurts, can I use non-steroidal anti-inflammatories? In Tools for Practice, ACFP, May 2014. Accessed online at: http://www.mailoutinteractive.com/Industry/View.aspx?id=572759&q=738814563&qz=10a458**
Thiels CA, Habermann EB, Hooten WM, Jeffery MM. **Chronic use of tramadol after acute pain episode**: cohort study. BMJ 2019;365:l1849.
Victorri-Vigneau C, Verstuyft C, Bouquié R, et al. Relevance of **CYP2B6 and CYP2D6 genotypes to methadone pharmacokinetics** and response in the OPAL study. Br J Clin Pharmacol. 2019 Mar 25.
Watson JA, Ryan CG, Cooper L, et al. **Pain Neuroscience Education** for Adults With Chronic Musculoskeletal Pain: A Mixed-Methods Systematic Review and Meta-Analysis. J Pain. 2019 Mar 1.
Zheng Z, Gibson S, Helme RD, et al. Effects of **Electroacupuncture on Opioid Consumption in Patients with Chronic Musculoskeletal Pain**: A Multicenter Randomized Controlled Trial. Pain Med. 2018 Jun 8.
Zunhammer M, Bingel U, Wager TD; for the Placebo Imaging Consortium. **Placebo effects on the neurologic pain signature**: a meta-analysis of individual participant functional magnetic resonance imaging data [online July 30, 2018]. JAMA Neurol. doi:10.1001/jamaneurol.2018.2017

PQRST Pain Assessment: P=provocation (what causes or relieves); Q=Quality (feel like); R=Region/Radiation (location); S=Severity (0-10 scale); T=Timing (constant or intermittent).

▼on NIHB ☎ =EDS Sask ✆=prior NIHB ✗ =Non Formulary SK ⊗ = not covered by NIHB **#**=fracture **2°** =secondary **5HT**=serotonin activity **ACh**=anticholinergic **ACP**=American College of Physicians **AE**= adverse events **am**=morning **ANRI**=angiotensin-receptor neprilysin inhibitor **BID**=twice daily **BP**=blood pressure **BZ**=benzodiazepine **CBD**=cannabidiol **CBT**= cognitive behavioural therapy **CDN**=Canadian **CNCP**=chronic non-cancer pain **CNS**=central nervous system **COXIB**=selective cyclooxygenase 2 inhibitor **CPS**=Canadian Pain Society **CrCl**=creatinine clearance **CV**=cardiovascular **d**=day **D/C**=discontinue(d) **DI**=drug interaction **ER**=extended release **esp**=especially **EtOH**=alcohol **EULAR**=European League Against Rheumatism **FDA**=Food & Drug Administration **Fx**=function **GI**=gastrointestinal **GFR**=glomerular filtration rate **HF**=heart failure **HR**=heart rate or hazard ratio **HS**=bedtime **Hx**=history **IBS**=irritable bowel syndrome **K+**=potassium **LBP**=low back pain **LFT**=liver function test **MED**=morphine equivalent dose **MMD**=major mood disorder **mo(s)** =month(s)**MS**=multiple sclerosis **MSK**=musculoskeletal **N**=number of studies **n**=number of subjects **NICE**=National Institute for Health & Clinical Excellence **NNH**=number needed to harm **NNT**=number needed to treat **NRS**=numeric rating scale **NS**=non-significant **NSAID**=non-steroidal anti-inflammatory drug **OA**=osteoarthritis **OTC**=over the counter **PDN**=painful diabetic neuropathy **PHN**=post-herpetic neuralgia **PPI**=proton-pump inihibitor **PTSD**=post traumatic stress disorder **QID**=four times daily **RCT**=randomized controlled trial **RD**=risk difference **Rx**= prescription **SCI**=spinal cord injury **SNRI**=serotonin norepinephrine reuptake inhibitor **SR**=sustained release **SSRIs**=selective serotonin reuptake inhibitor(s) **SUD**=substance use disorder **sx**=symptoms **TCA**=tricyclic antidepressant(s) **THC**= delta-9-tetrahydrocannabinol **TID**=three times daily **TN**=trigeminal neuralgia **tx**=treatment **UDS**=urinary drug screen **VAS**= visual analogue scale **wk(s)**=week(s) **Wt**=weight

References – Chronic Pain Outcomes Comparison Chart - www.RxFiles.ca (Duplicates to be removed in future printing)

[1] Busse JW, Craigie S, Juurlink DN, Buckley DN, Wang L, Couban RJ, et al. **Guideline for opioid therapy and chronic noncancer pain. CMAJ. 2017 May 8;189(18):E659-E666**. Also accessible in full online at: http://nationalpaincentre.mcmaster.ca/guidelines.html.

[2] Dowell D, Haegerich TM, Chou R. CDC Guideline for Prescribing Opioids for Chronic Pain--United States, 2016. JAMA. 2016 Apr 19;315(15):1624-45.

[3] CADTH Rapid Response. Opioid Trial Periods in the Treatment of Chronic Non-Cancer Pain: A Review of the Clinical Evidence. June 2012. Accessed online 10Jul17 at https://cadth.ca/opioid-trial-periods-treatment-chronic-non-cancer-pain-review-clinical-evidence.

[4] Qaseem, Amir, et al. "Noninvasive Treatments for Acute, Subacute, and Chronic Low Back Pain: A Clinical Practice Guideline From the American College of Physicians Noninvasive Treatments for Acute, Subacute, and Chronic Low Back Pain." Annals of internal medicine 166.7 (2017): 514-530.

[5] National Guideline Centre (UK). Low Back Pain and Sciatica in Over 16s: Assessment and Management. London: National Institute for Health and Care Excellence (UK); 2016 Nov.

[6] Chou R, Deyo R, Friedly J, Skelly A, Hashimoto R, Weimer M, Fu R, Dana T, Kraegel P, Griffin J, Grusing S, Brodt ED. Nonpharmacologic Therapies for Low Back Pain: A Systematic Review for an American College of Physicians Clinical Practice Guideline. Ann Intern Med. 2017 Apr 4;166(7):493-505.

[7] Chou R, Deyo R, Friedly J, Skelly A, Weimer M, Fu R, Dana T, Kraegel P, Griffin J, Grusing S. Systemic Pharmacologic Therapies for Low Back Pain: A Systematic Review for an American College of Physicians Clinical Practice Guideline. Ann Intern Med. 2017 Apr 4;166(7):480-492.

[8] Mildenberger A, Allan GM. Tools for Practice. Available at: https://www.acfp.ca/wpcontent/uploads/tools-for-practice/1473693475_tfp170exerciseandbackpainfv.pdf.

[9] Williams CM, Maher CG, Latimer J, McLachlan AJ, Hancock MJ, Day RO, et al. Efficacy of paracetamol for acute low-back pain: a double-blind, randomised controlled trial. Lancet. 2014;384:1586-96.

[10] Roelofs PD, Deyo RA, Koes BW, Scholten RJ, van Tulder MW. Non-steroidal anti-inflammatory drugs for low back pain. Cochrane Database Syst Rev. 2008:CD000396.

[11] Saragiotto BT, Machado GC, Ferreira ML, Pinheiro MB, Abdel Shaheed C, Maher CG. Paracetamol for low back pain. Cochrane Database Syst Rev. 2016 Jun 7;(6):CD012230.

[12] Enthoven WT, Roelofs PD, Deyo RA, van Tulder MW, Koes BW. Non-steroidal anti-inflammatory drugs for chronic low back pain. Cochrane Database Syst Rev.2016 Feb 10;2:CD012087.

[13] Skljarevski V, Zhang S, Desaiah D, Alaka KJ, Palacios S, Miazgowski T, Patrick K. Duloxetine versus placebo in patients with chronic low back pain: a 12-week,fixed- dose, randomized, double-blind trial. J Pain. 2010 Dec;11(12):1282-90.

[14] Skljarevski V, Desaiah D, Liu-Seifert H, Zhang Q, Chappell AS, Detke MJ, Iyengar S, Atkinson JH, Backonja M. Efficacy and safety of duloxetine in patients with chronic low back pain. Spine (Phila Pa 1976). 2010 Jun 1;35(13):E578-85.

[15] Skljarevski V, Ossanna M, Liu-Seifert H, Zhang Q, Chappell A, Iyengar S, Detke M, Backonja M. A double-blind, randomized trial of duloxetine versus placebo in the management of chronic low back pain. Eur J Neurol. 2009 Sep;16(9):1041-8.

[16] Shanthanna H, Gilron I, Rajarathinam M, AlAmri R, Kamath S, Thabane L, et al. (2017) Benefits and safety of gabapentinoids in chronic low back pain: A systematic review and metaanalysis of randomized controlled trials. PLoS Med 14(8): e1002369. Available at: https://doi.org/10.1371/journal. pmed.1002369.

[17] Mathieson S, Maher CG, McLachlan AJ, Latimer J, Koes BW, Hancock MJ, Harris I, Day RO, Billot L, Pik J, Jan S, Lin CC. Trial of Pregabalin for Acute and Chronic Sciatica. N Engl J Med. 2017 Mar 23;376(12):1111-1120.

[18] Chaparro LE, Furlan AD, Deshpande A, Mailis-Gagnon A, Atlas S, Turk DC. Opioids compared to placebo or other treatments for chronic low-back pain. Cochrane Database Syst Rev. 2013 Aug 27;(8):CD004959.

[19] O'Donnell JB, Ekman EF, Spalding WM, Bhadra P, McCabe D, Berger MF. The effectiveness of a weak opioid medication versus a cyclo-oxygenase-2 (COX-2) selective non-steroidal anti-inflammatory drug in treating flare-up of chronic low-back pain: results from two randomized, double-blind, 6-week studies. J Int Med Res. 2009 Nov-Dec;37(6):1789-802.

[20] Deyo RA, Von Korff M, Duhrkoop D. Opioids for low back pain. BMJ. 2015 Jan5;350:g6380. doi: 10.1136/bmj.g6380.

[21] Abdel Shaheed C, Maher CG, Williams KA, Day R, McLachlan AJ. Efficacy, Tolerability, and Dose-Dependent Effects of Opioid Analgesics for Low Back Pain: A Systematic Review and Meta-analysis. JAMA Intern Med. 2016 Jul 1;176(7):958-68.doi: 10.1001/jamainternmed.2016.1251.

[22] van Tulder MW, Touray T, Furlan AD, Solway S, Bouter LM. Muscle relaxants for non-specific low back pain. Cochrane Database Syst Rev. 2003;(2):CD004252.

[23] de Rooij M, van der Leeden M, Cheung J, van der Esch M, Häkkinen A, Haverkamp D, Roorda LD, Twisk J, Vollebregt J, Lems WF, Dekker J. Efficacy of Tailored Exercise Therapy on Physical Functioning in Patients With Knee Osteoarthritis and Comorbidity: A Randomized Controlled Trial. Arthritis Care Res (Hoboken). 2017 Jun;69(6):807-816.

[24] Machado GC, Maher CG, Ferreira PH, Pinheiro MB, Lin CW, Day RO, McLachlan AJ, Ferreira ML. Efficacy and safety of paracetamol for spinal pain and osteoarthritis: systematic review and meta-analysis of randomised placebo controlled trials. BMJ. 2015 Mar 31;350:h1225.

[25] Chris Beavington MD, G. Michael Allan MD CCFP. Tools for Practice. AcetaMINophen for Back and Osteoarthritis Pain: Is the effect in the name? Available at: https://www.acfp.ca/wp-content/uploads/tools-for-practice/1473801043_tfp171acetabackandoapainfv.pdf.

[26] Verkleij SP, Luijsterburg PA, Bohnen AM, Koes BW, Bierma-Zeinstra SM. NSAIDs vs acetaminophen in knee and hip osteoarthritis: a systematic review regarding heterogeneity influencing the outcomes. Osteoarthritis Cartilage. 2011 Aug;19(8):921-9. doi: 10.1016/j.joca.2011.04.013.

[27] Derry S, Moore RA, Rabbie R. Cochrane Database System Rev. 2012; 9:CD007400.

[28] da Costa BR, Reichenbach S, Keller N, Nartey L, Wandel S, Jüni P, Trelle S. Effectiveness of non-steroidal anti-inflammatory drugs for the treatment of pain in knee and hip osteoarthritis: a network meta-analysis. Lancet. 2016 May 21;387(10033):2093-2105.

[29] AAOS clinical practice guideline on management of osteoarthritis of the hip 2017. Available from: https://www.aaos.org/uploadedFiles/PreProduction/Quality/Guidelines_and_Reviews/OA%20Hip%20CPG_4.26.17.pdf (accessed July 18/2017).

[30] Singh G, Fort JG, Goldstein JL, et al. Celecoxib versus naproxen and diclofenac in osteoarthritis patients: SUCCESS-I Study. Am J Med. Mar 2006;119(3):255-266.

[31] Ohtori S, Inoue G, Orita S, Takaso M, Eguchi Y, Ochiai N, Kishida S, Kuniyoshi K, Aoki Y, Ishikawa T, Miyagi M, Kamoda H, Suzkuki M, Nakamura J, Kubota G, Sakuma Y, Oikawa Y, Toyone T, Inage K, Sainoh T, Yamauchi K, Takahashi K. Efficacy of combination of meloxicam and pregabalin for pain in knee osteoarthritis. Yonsei Med J. 2013 Sep;54(5):1253-8. doi:10.3349/ymj.2013.54.5.1253.

[32] Cepeda M, Camargo F, Zea C, Valencia L. Tramadol for osteoarthritis: a systematic review and metaanalysis. J Rheumatol. 2007;34(3):543-55.

[33] Cepeda M, Camargo F, Zea C, Valencia L. Tramadol for osteoarthritis. Cochrane Database Syst Rev. 2006;19(3):CD005522.

[34] Santos J, Alarcão J, Fareleira F, Vaz-Carneiro A, Costa J. Tapentadol for chronic musculoskeletal pain in adults. Cochrane Database Syst Rev. 2015 May 27;(5):CD009923.

[35] da Costa B, Nuesch E, Kasteler R, Husni E, Welch V, Rutjes A, et al. Oral or transdermal opioids for osteoarthritis of the knee or hip. Cochrane Database of Systematic Reviews. 2014. September 2014.

[36] Fitzcharles M, Baerwald C, Ablin J, Hauser W. Efficacy, tolerability and safety of cannabinoids in chronic pain associated with rheumatic diseases (fibromyalgia syndrome, back pain, osteoarthritis, rheumatoid arthritis): A systematic review of randomized controlled trials. Schmerz. 2016;30(1):47-61.

[37] McAlindon TE, LaValley MP, Harvey WF, et al. Effect of Intra-articular Triamcinolone vs Saline on Knee Cartilage Volume and Pain in Patients With Knee Osteoarthritis: A Randomized Clinical Trial. JAMA 2017; 317:1967.

[38] Juni P, Hari R, Rutjes A, Fischer R, Silletta M, Reichenbach S, et al. Intra-articular corticosteroid for knee osteoarthritis. Cochrane Database Syst Rev. 2015;22(10):CD005328.

[39] McAlindon TE, LaValley MP, Harvey WF, Price LL, Driban JB, Zhang M, Ward RJ. Effect of Intra-articular Triamcinolone vs Saline on Knee Cartilage Volume and Pain in Patients With Knee Osteoarthritis: A Randomized Clinical Trial. JAMA. 2017 May 16;317(19):1967-1975.

[40] CADTH Rapid Review. Viscosupplementation for Knee Osteoarthritis: A Review of Clinical and Cost-Effectiveness and Guidelines. June 2017. Accessed online 14Jul17 at https://cadth.ca/viscosupplementation-knee-osteoarthritis-review-clinical-and-cost-effectiveness-and-guidelines.

[41] Coigley MH. Comparison of benorylate and indomethacin in the symptomatic control of arthritic disorders. Practitioner 1975;215(1287):348–52.

[42] Towheed TE, Maxwell L, Anastassiades TP, Shea B, Houpt J, Robinson V, Hochberg MC, Wells G. Glucosamine therapy for treating osteoarthritis. Cochrane Database Syst Rev. 2005 Apr 18;(2):CD002946.

[43] Rozendaal RM, Koes BW, van Osch GJ, Uitterlinden EJ, Garling EH, Willemsen SP, Ginai AZ, Verhaar JA, Weinans H, Bierma-Zeinstra SM. Effect of glucosamine sulfate on hip osteoarthritis: a randomized trial. Ann Intern Med. 2008 Feb 19;148(4):268-77.

[44] Wandel S, Jüni P, Tendal B, Nüesch E, Villiger PM, Welton NJ, Reichenbach S, Trelle S. Effects of glucosamine, chondroitin, or placebo in patients with osteoarthritis of hip or knee: network meta-analysis. BMJ. 2010 Sep 16;341:c4675.

[45] Matthews P, Derry S, Moore R, McQuay H. Topical rubefacients for acute and chronic pain in adults. Cochrane Database Syst Rev. 2009 Jul 8;(3):CD007403.

[46] Guedes V, Castro J, Brito I. Topical capsaicin for pain in osteoarthritis: A literature review. Reumatologia Clinica 2016;xxx(xx):xxx-xxx.

[47] Mason L, Moore R, Derry S, Edwards J, McQuay H. Systematic review of topical capsaicin for the treatment of chronic pain. BMJ 2004;328:991.

[48] Pas HI, Winters M, Haisma HJ, et al. Stem cell injections in knee osteoarthritis: a systematic review of the literature Br J Sports Med 2017;51:1125-1133. Accessed online at http://bjsm.bmj.com/content/51/15/1125.

[49] Moulin D, Boulanger A, Clark AJ, Clarke H, Dao T, Finley GA, Furlan A, Gilron I, Gordon A, Morley-Forster PK, Sessle BJ, Squire P, Stinson J, Taenzer P, Velly A, Ware MA, Weinberg EL, Williamson OD; Canadian Pain Society. Pharmacological management of chronic neuropathic pain: revised consensus statement from the Canadian Pain Society. Pain Res Manag. 2014 Nov-Dec;19(6):328-35.

[50] Centre for Clinical Practice at NICE (UK). Neuropathic Pain: The Pharmacological Management of Neuropathic Pain in Adults in Non-specialist Settings [Internet]. London: National Institute for Health and Care Excellence,(UK); 2013 Nov. Updated 2017 Available from: http://guidance.nice.org.uk/CG173.

[51] Finnerup NB, Attal N, Haroutounian S, McNicol E, Baron R, Dworkin RH, Gilron I, Haanpää M, Hansson P, Jensen TS, Kamerman PR, Lund K, Moore A, Raja SN, Rice AS, Rowbotham M, Sena E, Siddall P, Smith BH, Wallace M. Pharmacotherapy for neuropathic pain in adults: a systematic review and meta-analysis. Lancet Neurol. 2015 Feb;14(2):162-73. doi: 10.1016/S1474-4422(14)70251-0.

[52] Moore RA, Derry S, Aldington D, Cole P, Wiffen PJ. Amitriptyline for neuropathic pain in adults. Cochrane Database Syst Rev. 2015 Jul 6;(7):CD008242.

[53] Derry S, Wiffen PJ, Aldington D, Moore RA. Nortriptyline for neuropathic pain in adults. Cochrane Database Syst Rev. 2015 Jan 8;1:CD011209.

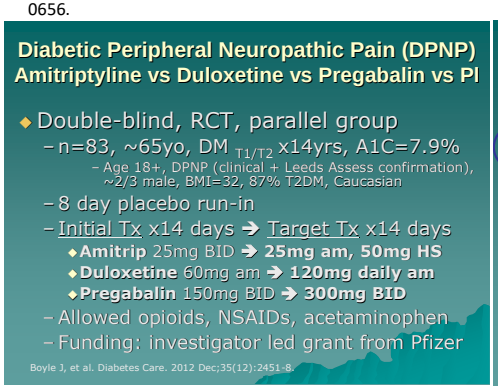
[54] Hearn L, Derry S, Phillips T, Moore RA, Wiffen PJ. Imipramine for neuropathic pain in adults. Cochrane Database Syst Rev. 2014 May 19;(5):CD010769.

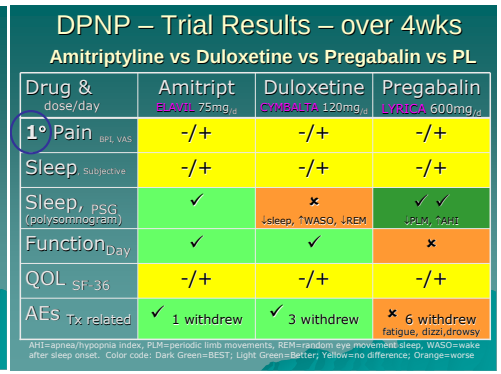
[55] Hearn L, Moore RA, Derry S, Wiffen PJ, Phillips T. Desipramine for neuropathic pain in adults. Cochrane Database Syst Rev. 2014 Sep 23;(9):CD011003.

[56] Max MB, Lynch SA, Muir J, Shoaf SE, Smoller B, Dubner R. Effects of desipramine, amitriptyline, and fluoxetine on pain in diabetic neuropathy. N Engl J Med. 1992 May 7;326(19):1250-6.

[57] Watson CP, Vernich L, Chipman M, Reed K. Nortriptyline versus amitriptyline in postherpetic neuralgia: a randomized trial. Neurology. 1998 Oct;51(4):1166-71.

[58] Boyle J, Eriksson ME, Gribble L, Gouni R, Johnsen S, Coppini DV, Kerr D. Randomized, placebo-controlled comparison of amitriptyline, duloxetine, and pregabalin in patients with chronic diabetic peripheral neuropathic pain: impact on pain, polysomnographic sleep, daytime functioning, and quality of life. Diabetes Care. 2012 Dec;35(12):2451-8. doi: 10.2337/dc12-0656.





[59] Lunn MP, Hughes RA, Wiffen PJ. Duloxetine for treating painful neuropathy, chronic pain or fibromyalgia. Cochrane Database Syst Rev. 2014 Jan 3;(1):CD007115.

[60] Tesfaye S, Wilhelm S, Lledo A, Schacht A, Tölle T, Bouhassira D, Cruccu G,Skljarevski V, Freynhagen R. Duloxetine and pregabalin: high-dose monotherapy or their combination? The "COMBO-DN study"--a multinational, randomized, double-blind, parallel-group study in patients with diabetic peripheral neuropathic pain. Pain. 2013 Dec;154(12):2616-25.

[61] Gallagher HC, Gallagher RM, Butler M, Buggy DJ, Henman MC. Venlafaxine for neuropathic pain in adults. Cochrane Database Syst Rev. 2015 Aug 23;(8):CD011091.

[62] Wiffen PJ, Derry S, Bell RF, Rice ASC, Tölle TR, Phillips T, Moore RA. Gabapentin for chronic neuropathic pain in adults. Cochrane Database of Systematic Reviews 2017, Issue 6. Art. No.: CD007938. DOI: 10.1002/14651858.CD007938.pub4.

[63] Chandra K, Shafiq N, Pandhi P, Gupta S, Malhotra S. Gabapentin versus nortriptyline in post-herpetic neuralgia patients: a randomized, double-blind clinical trial – the GONIP Trial. International Journal of Clinical Pharmacology and Therapeutics 2006;44(8):358–63.

[64] Morello CM, Leckband SG, Stoner CP, Moorhouse DF, Sahagian GA. Randomized double-blind study comparing the efficacy of gabapentin with amitriptyline on diabetic peripheral neuropathy pain. Archives of Internal Medicine 1999;159(16):1931–7.

[65] Moore RA, Straube S, Wiffen PJ, Derry S, McQuay HJ. Pregabalin for acute and chronic pain in adults. Cochrane Database Syst Rev. 2009 Jul 8;(3):CD007076.

[66] Duehmke RM, Derry S, Wiffen PJ, Bell RF, Aldington D, Moore RA. Tramadol for neuropathic pain in adults. Cochrane Database Syst Rev. 2017 Jun 15;6:CD003726.

[67] Wiffen PJ, Derry S, Moore RA, Stannard C, Aldington D, Cole P, Knaggs R. Buprenorphine for neuropathic pain in adults. Cochrane Database Syst Rev. 2015 Sep 30;(9):CD011603.

[68] Cooper TE, Chen J, Wiffen PJ, Derry S, Carr DB, Aldington D, Cole P, Moore RA.Morphine for chronic neuropathic pain in adults. Cochrane Database Syst Rev. 2017 May 22;5:CD011669. doi: 10.1002/14651858.CD011669.pub2.

[69] Gaskell H, Derry S, Stannard C, Moore RA. Oxycodone for neuropathic pain in adults. Cochrane Database Syst Rev. 2016 Jul 28;7:CD010692.

[70] McNicol ED, Ferguson MC, Schumann R. Methadone for neuropathic pain in adults. Cochrane Database of Systematic Reviews 2017, Issue 5. Art. No.: CD012499.

[71] Derry S, Stannard C, Cole P, Wiffen PJ, Knaggs R, Aldington D, Moore RA. Fentanyl for neuropathic pain in adults. Cochrane Database Syst Rev. 2016 Oct 11;10:CD011605.

[72] Stannard C, Gaskell H, Derry S, Aldington D, Cole P, Cooper TE, Knaggs R,Wiffen PJ, Moore RA. Hydromorphone for neuropathic pain in adults. Cochrane Database Syst Rev. 2016 May 24;(5):CD011604. doi: 10.1002/14651858.CD011604.pub2.

[73] Cannabinoid Buccal Spray for Chronic Non-Cancer or Neuropathic Pain: A Review of Clinical Effectiveness, Safety, and Guidelines [Internet]. Ottawa (ON):Canadian Agency for Drugs and Technologies in Health; 2016 Sep 21.

[74] Ware MA, Wang T, Shapiro S, Robinson A, Ducruet T, Huynh T, Gamsa A, Bennett GJ, Collet JP. Smoked cannabis for chronic neuropathic pain: a randomized controlled trial. CMAJ. 2010 Oct 5;182(14):E694-701.

[75] Drug Product Database. Health Canada website. https://health-products.canada.ca/dpd-bdpp/index-eng.jsp.

[76] Cochrane Database of Systematic Reviews, Topical lidocaine for neuropathic pain in adults (Review)Derry S, Wiffen PJ, Moore RA, Quinlan J. Topical lidocaine for neuropathic pain in adults. Cochrane Database of Systematic Reviews 2014, Issue 7. Art. No.: CD010958.DOI: 10.1002/14651858.CD010958.pub2. (Most studies involved lidocaine patch)

[77] Derry S, Wiffen PJ, Kalso EA, Bell RF, Aldington D, Phillips T, Gaskell H, Moore RA. Topical analgesics for acute and chronic pain in adults - an overview of Cochrane Reviews. Cochrane Database of Systematic Reviews 2017, Issue 5. Art. No.: CD008609. DOI: 10.1002/14651858.CD008609.pub2.

[78] Derry S, Rice AS, Cole P, Tan T, Moore RA. Topical capsaicin (high concentration) for chronic neuropathic pain in adults. Cochrane Database Syst Rev. 2017 Jan 13;1:CD007393.

[79] Chaparro LE, Wiffen PJ, Moore RA, Gilron I. Combination pharmacotherapy for the treatment of neuropathic pain in adults. Cochrane Database Syst Rev. 2012 Jul 11;(7):CD008943.

[80] Gilron I, Jensen TS, Dickenson AH. Combination pharmacotherapy for management of chronic pain: from bench to bedside. Lancet Neurol. 2013 Nov;12(11):1084-95.

[81] Macfarlane GJ, Kronisch C, Dean LE, et al EULAR revised recommendations for the management of fibromyalgia. Annals of the Rheumatic Diseases 2017;76:318-328.

[82] Fitzcharles MA, Ste-Marie PA, Goldenberg DL, et al. National Fibromyalgia Guideline Advisory Panel. 2012 Canadian Guidelines for the diagnosis and management of fibromyalgia syndrome: executive summary. Pain Res Manag. 2013 May-Jun;18(3):119-26.

[83] Kodner C. Common questions about the diagnosis and management of fibromyalgia. Am Fam Physician. 2015 Apr 1;91(7):472-8.

[84] Bidonde J, Busch AJ, Schachter CL, Overend TJ, Kim SY, Góes SM, Boden C, Foulds HJ. Aerobic exercise training for adults with fibromyalgia. Cochrane Database Syst Rev. 2017 Jun 21;6:CD012700.

[85] CADTH RAPID RESPONSE REPORT: Physiotherapy Interventions for the Management of Fibromyalgia: Clinical and Cost Effectiveness. June 2017. Accessed online 10Jul17 at https://cadth.ca/sites/default/files/pdf/htis/2017/RB1101%20Physio%20for%20Fibromyalgia%20Final.pdf.

[86] Derry S, Wiffen PJ, Häuser W, Mücke M, Tölle TR, Bell RF, Moore RA. Oral nonsteroidal anti-inflammatory drugs for fibromyalgia in adults. Cochrane Database Syst Rev. 2017 Mar 27;3:CD012332.

[87] Häuser W, Petzke F, Üçeyler N, Sommer C. Comparative efficacy and acceptability of amitriptyline, duloxetine and milnacipran in fibromyalgia syndrome: a systematic review with meta-analysis. Rheumatology (Oxford). 2011 Mar;50(3):532-43.

[88] Heymann RE, Helfenstein M, Feldman D. A double-blind, randomized, controlled study of amitriptyline, nortriptyline and placebo in patients with fibromyalgia. An analysis of outcome measures. Clin Exp Rheumatol. 2001 Nov-Dec;19(6):697-702.

[89] Sayar K, Aksu G, Ak I, Tosun M. Venlafaxine treatment of fibromyalgia. Ann Pharmacother. 2003 Nov;37(11):1561-5.

[90] Walitt B, Urrútia G, Nishishinya MB, Cantrell SE, Häuser W. Selective serotonin reuptake inhibitors for fibromyalgia syndrome. Cochrane Database of Systematic Reviews 2015, Issue 6. Art. No.: CD011735.

[91] Miki K, Murakami M, Oka H, Onozawa K, Yoshida S, Osada K. Efficacy of mirtazapine for the treatment of fibromyalgia without concomitant depression: a randomized, double-blind, placebo-controlled phase IIa study in Japan. Pain. 2016 Sep;157(9):2089-96.

[92] Derry S, Cording M, Wiffen PJ, et al. Pregabalin for pain in fibromyalgia in adults. Cochrane Database Syst Rev. 2016;9:CD011790.

[93] Arnold LM, Emir B, Murphy TK, Zeiher BG, Pauer L, Scott G, Petersel D. Safety profile and tolerability of up to 1 year of pregabalin treatment in 3 open-label extension studies in patients with fibromyalgia. Clin Ther. 2012 May;34(5):1092-102.

[94] Nasser K, Kivitz AJ, Maricic MJ, Silver DS, Silverman SL. Twice daily versus once nightly dosing of pregabalin for fibromyalgia: a double-blind randomized clinical trial of efficacy and safety. Arthritis Care Res (Hoboken). 2014 Feb;66(2):293-300.

[95] Cooper TE, Derry S, Wiffen PJ, Moore RA. Gabapentin for fibromyalgia pain in adults. Cochrane Database Syst Rev. 2017 Jan 3;1:CD012188.

[96] Arnold LM, Goldenberg DL, Stanford SB, Lalonde JK, Sandhu HS, Keck PE Jr, Welge JA, Bishop F, Stanford KE, Hess EV, Hudson JI. Gabapentin in the treatment of fibromyalgia: a randomized, double-blind, placebo-controlled, multicenter trial. Arthritis Rheum. 2007 Apr;56(4):1336-44.

[97] Russell IJ, Kamin M, Bennett RM, Schnitzer TJ, Green JA, Katz WA. Efficacy of tramadol in treatment of pain in fibromyalgia. J Clin Rheumatol. 2000Oct;6(5):250-7.

[98] MacLean AJ, Schwartz TL. Tramadol for the treatment of fibromyalgia. Expert Rev Neurother. 2015 May;15(5):469-75.

[99] Biasi G, Manca S, Manganelli S, Marcolongo R. Tramadol in the fibromyalgia syndrome: a controlled clinical trial versus placebo. Int J Clin Pharmacol Res.1998;18(1):13-9.

[100] Gaskell H, Moore RA, Derry S, Stannard C. Oxycodone for pain in fibromyalgia in adults. Cochrane Database Syst Rev. 2016 Sep 1;9:CD012329.

[101] Painter JT, Crofford LJ. Chronic opioid use in fibromyalgia syndrome: a clinical review. J Clin Rheumatol. 2013 Mar;19(2):72-7.

[102] Goldenberg DL, Clauw DJ, Palmer RE, Clair AG. Opioid Use in Fibromyalgia: A Cautionary Tale. Mayo Clin Proc. 2016 May;91(5):640-8.

[103] FitzcharlesMA, Faregh N, Ste-Marie PA, Shir Y.Opioid use in fibromyalgia is associated with negative health related measures in a prospective cohort study. Pain Res Treat. 2013;2013:898493.

[104] Peng X, Robinson RL, Mease P, et al. Long-term evaluation of opioid treatment in fibromyalgia. Clin J Pain. 2015;31(1):7-13.

[105] Walitt B, Klose P, Fitzcharles MA, Phillips T, Häuser W. Cannabinoids for fibromyalgia. Cochrane Database Syst Rev. 2016 Jul 18;7:CD011694. doi: 10.1002/14651858.CD011694.pub2.

[106] Skrabek RQ, Galimova L, Ethans K, Perry D. Nabilone for the treatment of pain in fibromyalgia. Journal of Pain 2008;**9**:164–73.

[107] Ware MA, Fitzcharles MA, Joseph L, Shir Y. The effects of nabilone on sleep in fibromyalgia: results of a randomized controlled trial. Anesthesia & Analgesia 2010;110:604–10.

[108] Tofferi JK, Jackson JL, O'Malley PG. Treatment of fibromyalgia with cyclobenzaprine: A meta-analysis. Arthritis Rheum. 2004; 51(1): 9-13.

[109] Therapeutics Initiative. Is cyclobenzaprine useful for pain? March-April 2017. Accessed online, July 2017 at http://www.ti.ubc.ca/2017/07/24/105-cyclobenzaprine/.

[110] CADTH Rapid Response. Low-Dose Naltrexone for Chronic Non-Cancer Pain: Clinical Effectiveness. Jun 2017. Access online 10Jul17 at https://cadth.ca/sites/default/files/pdf/htis/2017/RB1102%20Low%20Dose%20Naltrexone%20for%20Pain%20Final.pdf.

[111] Gilron I, Chaparro LE, Tu D, Holden RR, Milev R, Towheed T, DuMerton-Shore D, Walker S. Combination of pregabalin with duloxetine for fibromyalgia: a randomized controlled trial. Pain. 2016 Jul;157(7):1532-40.

[112] Ramzy EA. Comparative Efficacy of Newer Antidepressants in Combination with Pregabalin for Fibromyalgia Syndrome: A Controlled, Randomized Study. Pain Pract.2017 Jan;17(1):32-40.

[113] Goldenberg D, Mayskiy M, Mossey C, Ruthazer R, Schmid C. A randomized, double-blind crossover trial of fluoxetine and amitriptyline in the treatment of fibromyalgia. Arthritis Rheum. 1996 Nov;39(11):1852-9.

[114] Bennett RM, Kamin M, Karim R, Rosenthal N. Tramadol and acetaminophen combination tablets in the treatment of fibromyalgia pain: a double-blind, randomized, placebo-controlled study. Am J Med. 2003 May;114(7):537-45.

[115] CADTH Rapid Response. Physical Therapy Treatments for Chronic Non-Cancer Pain: A Review of Guidelines. Nov 2016. Accessed online 10Jul17 at https://cadth.ca/sites/default/files/pdf/htis/2016/RC0822%20Physical%20Therapy%20for%20Chronic%20Pain%20Final.pdf.

[116] CADTH Rapid Response. Behavioural and Psychological Interventions for Chronic Non-Cancer Pain: A Review of Guidelines. Nov 2016. Accessed online 10Jul17 at https://cadth.ca/sites/default/files/pdf/htis/2016/RC0823_Behavioural%20and%20psychological%20interventions_Final.pdf.

[117] CADTH Rapid Response. Multidisciplinary Treatment Programs for Patients with Chronic Non-Malignant Pain: A Review of Clinical Effectiveness, Cost Effectiveness, and Guidelines. Jun 2017. Accessed online 10Jul17 at https://cadth.ca/sites/default/files/pdf/htis/2017/RC0894-TxProgram-Pain%20Final.pdf.

[118] Sandvik RK, Selbaek G, Seifert R, Aarsland D, Ballard C, Corbett A, Husebo BS. Impact of a stepwise protocol for treating pain on pain intensity in nursing home patients with dementia: a cluster randomized trial. Eur J Pain. 2014 Nov;18(10):1490-500.

[119] Breivik H. A high-quality RCT documents that elderly with dementia, the most neglected pain patients, have effective and safe pain relief from paracetamol alone or with buprenorphine patch. Eur J Pain. 2014 Nov;18(10):1363-4.

[120] Kapusta P, Regier L, Bareham J, Jensen B. Behaviour management in dementia. Can Fam Physician. 2011 Dec;57(12):1420-2.

[121] Leijon G, Boivie J. Central post-stroke pain--a controlled trial of amitriptyline and carbamazepine. Pain. 1989 Jan;36(1):27-36.

[122] Kim JS. Pharmacological management of central post-stroke pain: a practical guide. CNS Drugs. 2014 Sep;28(9):787-97.

[123] Sites BD, Beach ML, Davis MA. Increases in the use of prescription opioid analgesics and the lack of improvement in disability metrics among users. Reg Anesth Pain Med. 2014 Jan-Feb;39(1):6-12.

[124] CADTH Rapid Response. Suboxone for the Treatment of Chronic Non-Cancer Pain: Clinical Effectiveness and Guidelines. Accessed online 10Jul17 at https://cadth.ca/sites/default/files/pdf/htis/jan-2013/RB0556%20Suboxone%20for%20Pain%20Final.pdf.

[125] Nugent SM, Morasco BJ, O'Neil ME, Freeman M, Low A, Kondo K, Elven C, Zakher B, Motu'apuaka M, Paynter R, Kansagara D. The Effects of Cannabis Among Adults With Chronic Pain and an Overview of General Harms: A Systematic Review. Ann Intern Med. 2017 Aug 15. doi: 10.7326/M17-0155.

[126] Nabilone for Chronic Pain Management: A Review of Clinical Effectiveness and Guidelines. Ottawa: CADTH; 2017 Aug. (CADTH rapid response report: summary with critical appraisal).

[127] Vestergaard K, Andersen G, Gottrup H, Kristensen BT, Jensen TS. Lamotrigine for central poststroke pain: a randomized controlled trial. Neurology 2001;**56**(2):184–90.

[128] Kim JS. Pharmacological management of central post-stroke pain: a practical guide. CNS Drugs. 2014 Sep;28(9):787-97.

[129] Wiffen PJ, Derry S, Lunn MP, Moore RA. Topiramate for neuropathic pain and fibromyalgia in adults. Cochrane Database Syst Rev. 2013 Aug 30;(8):CD008314.

[130] Wiffen PJ, Derry S, Moore RA, Kalso EA. Carbamazepine for chronic neuropathic pain and fibromyalgia in adults. Cochrane Database Syst Rev. 2014 Apr 10;(4):CD005451.

[131] Cheatle MD, Foster S, Pinkett A, Lesneski M, Qu D, Dhingra L. Assessing and Managing Sleep Disturbance in Patients with Chronic Pain. Sleep Med Clin. 2016 Dec;11(4):531-541. doi: 10.1016/j.jsmc.2016.08.004. Epub 2016 Oct 27.

[132] Cheatle MD, Foster S, Pinkett A, Lesneski M, Qu D, Dhingra L. Assessing and Managing Sleep Disturbance in Patients with Chronic Pain. Sleep Med Clin. 2016 Dec;11(4):531-541. doi: 10.1016/j.jsmc.2016.08.004. Epub 2016 Oct 27.

[133] Robertson JA, Purple RJ, Cole P, Zaiwalla Z, Wulff K, Pattinson KT. Sleep disturbance in patients taking opioid medication for chronic back pain. Anaesthesia. 2016 Nov;71(11):1296-1307.

[134] Lintzeris N, Moodley R, Campbell G, Larance B, Bruno R, Nielsen S, Degenhardt L. Sleep Quality Among People Living With Chronic Noncancer Pain: Findings From the Pain and Opioids IN Treatment (POINT) Cohort.

[135] Meng H, Johnston B, Englesakis M, Moulin DE, Bhatia A. Selective Cannabinoids for Chronic Neuropathic Pain: A Systematic Review and Meta-analysis. Anesth Analg. 2017 May 19.

[136] Babson KA, Sottile J, Morabito D. Cannabis, Cannabinoids, and Sleep: a Review of the Literature. Curr Psychiatry Rep. 2017 Apr;19(4):23.

[137] Fatal Overdoses with Venlafaxine Extended-Release Capsules. Pharmacist's Letter/Prescriber Letter 2009;25(1):250119.

[138] Martinez C, Assimes TL, Mines D, Dell'aniello S, Suissa S. Use of venlafaxine compared with other antidepressants and the risk of sudden cardiac death or near death: a nested case-control study. BMJ. 2010 Feb 5;340:c249.

[139] Wang GS, Roosevelt G, Heard K. Pediatric marijuana exposures in a medical marijuana state. JAMA Pediatr. 2013 Jul;167(7):630-3.

[140] Emergency visits related to marijuana use at Colorado hospital quadruple. AAP News. Retrieved on August 2, 2017 from www.aappublications.org/news/2017/05/04/PASMarijuana050417.

[141] Claudet I, Mouvier S, Labadie M, Manin C, Michard-Lenoir AP, Eyer D, Dufour D; Marie-Jeanne Study Group. Unintentional Cannabis Intoxication in Toddlers.Pediatrics. 2017 Sep;140(3). pii: e20170017. doi: 10.1542/peds.2017-0017.

[142] Ray WA, Chung CP, Murray KT, Hall K, Stein CM. Prescription of Long-Acting Opioids and Mortality in Patients With Chronic Noncancer Pain. JAMA. 2016 Jun 14;315(22):2415-23.

[143] University of Toronto. Navigating Opioids for Chronic Pain (Infographic). Accessed 10Jul17 online at https://www.cpd.utoronto.ca/opioidprescribing/wp-content/plugins/safe-opioids-infographic//files/navigating-opioids-web.pdf.

[144] Public Health Agency of Canada report, https://www.canada.ca/en/health-canada/services/substance-abuse/prescription-drug-abuse/opioids/national-report-apparent-opioid-related-deaths.html.

[145] National Academies of Sciences, Engineering, and Medicine; Health and Medicine Division; Board on Population Health and Public Health Practice; Committee on the Health Effects of Marijuana: An Evidence Review and Research Agenda. The Health Effects of Cannabis and Cannabinoids: The Current State of Evidence and Recommendations for Research. Washington (DC): National Academies Press (US); 2017 Jan 12. 9, Injury and Death. Available from: https://www.ncbi.nlm.nih.gov/books/NBK425742/.

[146] Mersfelder TL, Nichols WH. Gabapentin: Abuse, Dependence, and Withdrawal. Ann Pharmacother. 2016 Mar;50(3):229-33.

[147] Landsman-Blumberg PB, Katz N, Gajria K, Coutinho AD, Yeung PP, White R. Burden of Alcohol Abuse or Dependence Among Long-Term Opioid Users with Chronic Noncancer Pain. J Manag Care Spec Pharm. 2017 Jul;23(7):718-724.

[148] CADTH Report. Opioid Formulations With Tamper-Resistance or Abuse-Deterrent Features —Products and Policies Mar 2017. Accessed 10Jul17 online at https://cadth.ca/tamper-resistant-formulations-of-opioids.

[149] CADTH Rapid Response. Tamper-Resistant Oxycodone: A Review of the Clinical Evidence and Cost effectiveness. June 2015. Accessed 10Jul17 online at https://cadth.ca/sites/default/files/pdf/htis/june-2015/RC0675%20Tamper%20Resistant%20Drugs%20Final.pdf.

[150] "Weak" opioid analgesics. Codeine, dihydrocodeine and tramadol: no less risky than morphine. Prescrire Int. 2016 Feb;25(168):45-50.

[151] D.M. Bush. The DAWN Report: Emergency Department Visits for Drug Misuse or Abuse Involving the Pain Medication Tramadol.(2015). Substance Abuse and Mental Health Services Administration, Center for Behavioral Health Statistics and Quality. Rockville, MD.

[152] http://www.who.int/medicines/areas/quality_safety/TAPENTADOL_IFPMA_Comments.pdf.

[153] Lopez-Quintero C, Pérez de los Cobos J, Hasin DS, Okuda M, Wang S, Grant BF, Blanco C. Probability and predictors of transition from first use to dependence on nicotine, alcohol, cannabis, and cocaine: results of the National Epidemiologic Survey on Alcohol and Related Conditions (NESARC). Drug Alcohol Depend. 2011 May 1;115(1-2):120-30.

[154] Solomon DH, Rassen JA, Glynn RJ, Lee J, Levin R, Schneeweiss S. The comparative safety of analgesics in older adults with arthritis. Arch Intern Med. 2010 Dec 13;170(22):1968-76.

[155] Ware MA, Wang T, Shapiro S, Collet JP; COMPASS study team. Cannabis for the Management of Pain: Assessment of Safety Study (COMPASS). J Pain. 2015 Dec;16(12):1233-1242.

[156] Acetaminophen general monograph. CPS – RxTx database.

[157] Silverstein F, Faich G, Goldstein J, et al. Gastrointestinal toxicity with celecoxib versus non-steroidal anti-inflammatory drugs for osteoarthritis and rheumatoid arthritis: the CLASS study: A randomized controlled trial. Celecoxib Long-term Arthritis Safety Study. JAMA 2000;284:1247-55.

[158] Choosing Wisely (Canada) – Nephrology. https://choosingwiselycanada.org/nephrology/ Accessed July 7, 2017.

[159] CredibleMeds Available: https://crediblemeds.org/.

[160] PRECISION: CV risk of celecoxib vs ibuprofen vs naproxen N Engl J Med. 2016 Nov 13. DOI: 10.1056/NEJMoa1611593 http://clinicaltrials.gov/ct/show/NCT00346216?order=4.

[161] Chan FKL, et al. Gastrointestinal safety of celecoxib versus naproxen in patients with cardiothrombotic diseases and arthritis after upper gastrointestinal bleeding (CONCERN): an industry independent, double-blind, double-dummy, randomised trial. Lancet 2017; online April 11.

[162] Health Product Infowatch-Product monograph updates. June 2017.

[163] Franz CA, Frishman WH. Marijuana Use and Cardiovascular Disease. Cardiol Rev. 2016 Jul-Aug;24(4):158-62.

[164] American College of Cardiology. Marijuana and Coronary Heart Disease. Retrieved on August 2, 2017 from http://www.acc.org/latest-in-cardiology/articles/2016/09/22/08/58/marijuana-and-coronary-heart-disease.

[165] Page RL 2nd, O'Bryant CL, Cheng D, Dow TJ, Ky B, Stein CM, et al; American Heart Association Clinical Pharmacology and Heart Failure and Transplantation Committees of the Council on Clinical Cardiology; Council on Cardiovascular Surgery and Anesthesia; Council on Cardiovascular and Stroke Nursing; and Council on Quality of Care and Outcomes Research. Drugs That May Cause or Exacerbate Heart Failure: A Scientific Statement From the American Heart Association. Circulation. 2016 Aug 9;134(6):e32-69.

[166] Ponikowski P, Voors AA, Anker SD, Bueno H, Cleland JG, Coats AJ, et al; Authors/Task Force Members; Document Reviewers. 2016 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure: The Task Force for the diagnosis and treatment of acute and chronic heart failure of the European Society of Cardiology (ESC). Eur J Heart Fail. 2016 Aug;18(8):891-975. PubMed PMID: 27207191.

[167] Arnold JM, Liu P, Demers C, Dorian P, Giannetti N, Haddad H, et al; Canadian Cardiovascular Society. Canadian Cardiovascular Society consensus conference recommendations on heart failure 2006: diagnosis and management. Can J Cardiol. 2006 Jan;22(1):23-45. PubMed Central PMCID: PMC2538984.

[168] Yancy CW, Jessup M, Bozkurt B, Butler J, Casey DE Jr, Drazner MH, et al; American College of Cardiology Foundation; American Heart Association Task Force on Practice Guidelines. 2013 ACCF/AHA guideline for the management of heart failure: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. J Am Coll Cardiol. 2013 Oct 15;62(16):e147-239. PubMed PMID: 23747642.

[169] Arfè A, Scotti L, Varas-Lorenzo C, Nicotra F, Zambon A, Kollhorst B, et al; Safety of Non-steroidal Anti-inflammatory Drugs (SOS) Project Consortium. Non-steroidal anti-inflammatory drugs and risk of heart failure in four European countries: nested case-control study. BMJ. 2016 Sep 28;354:i4857. PubMed PMID: 27682515.

[170] Rannou F, Pelletier JP, Martel-Pelletier J. Efficacy and safety of topical NSAIDs in the management of osteoarthritis: Evidence from real-life setting trials and surveys. Semin Arthritis Rheum. 2016 Feb;45(4 Suppl):S18-21. PubMed PMID: 26806189.

[171] Peniston JH, Gold MS, Wieman MS, Alwine LK. Long-term tolerability of topical diclofenac sodium 1% gel for osteoarthritis in seniors and patients with comorbidities. Clin Interv Aging. 2012;7:517-23. PubMed PMID: 23204844.

[172] Baraf HS, Gold MS, Petruschke RA, Wieman MS. Tolerability of topical diclofenac sodium 1% gel for osteoarthritis in seniors and patients with comorbidities. Am J Geriatr Pharmacother. 2012 Feb;10(1):47-60. PubMed PMID: 22264852.

[173] Colucci VJ, Berry BD. Heart failure worsening and exacerbation after venlafaxine and duloxetine therapy. Ann Pharmacother. 2008 Jun;42(6):882-7. PubMed PMID: 18445706.

[174] Ho JM, Gomes T, Straus SE, Austin PC, Mamdani M, Juurlink DN. Adverse cardiac events in older patients receiving venlafaxine: a population-based study. J Clin Psychiatry. 2014 Jun;75(6):e552-8. PubMed PMID: 25004195.

[175] Ho JM, Macdonald EM, Luo J, Gomes T, Antoniou T, Mamdani MM, Juurlink DN. Pregabalin and heart failure: A population-based study. Pharmacoepidemiol Drug Saf. 2017 Jun 16. PubMed PMID: 28620909.

[176] Cheatle MD, Foster S, Pinkett A, Lesneski M, Qu D, Dhingra L. Assessing and Managing Sleep Disturbance in Patients with Chronic Pain. Sleep Med Clin. 2016 Dec;11(4):531-541. doi: 10.1016/j.jsmc.2016.08.004. Epub 2016 Oct 27.

[177] Howlett JG, Chan M, Ezekowitz JA, Harkness K, Heckman GA, Kouz S, et al; Canadian Cardiovascular Society Heart Failure Guidelines Panels. The Canadian Cardiovascular Society Heart Failure Companion: Bridging Guidelines to Your Practice. Can J Cardiol. 2016 Mar;32(3):296-310. PubMed PMID: 26391749.

[178] Delanty N, Vaughan CJ, French JA. Medical causes of seizures. Lancet. 1998 Aug 1;352(9125):383-90.

[179] Hitchings AW, Drugs that lower the seizure threshold. Adverse Drug Reaction Bulletin 2016; 1151.

[180] UpToDate. Medications associated with seizures Available from: https://www.uptodate.com/contents/image?imageKey=NEURO%2F106961&topicKey=NEURO%2F2219&rank=1~150&source=see_link&search=drug%20induced%20seizures (accessed July 7, 2017).

[181] Dynamed. Seizure in adults. Available: http://web.b.ebscohost.com.ezproxy.library.ubc.ca/dynamed/detail?sid=c9723d5c-4924-4a1c-ac94-22bb695459c2%40sessionmgr104&vid=5&bdata=JnNpdGU9ZHluYW1lZC1saXZlJnNjb3BlPXNpdGU%3d#anchor=GenRef10672&AN=114746&db=dme (accessed July 7/2017).

[182] Sanchez-Hernandez MC, Delgado J, Navarro AM, et al. Seizures induced by NSAID. Allergy 1999;54:90–91.

[183] Sanchez Valiente S. Myoclonic encephalopathy induced by diclofenac treatment. Revista de Neurologı´a 1995;23:1226–1227.

[184] Sanchez-Valiente S. EncefalopatõÂa miocloÂ nica originada por el tratamiento con Diclofenac. Rev Neurol 1995;23:1226±1227.

[185] Skowron DM, Stimmel GL. Antidepressants and the risk of seizures. Pharmacotherapy 1992;12(1):18-22.

[186] Johannessen Landmark C, Henning O, Johannessen SI. Proconvulsant effects of antidepressants – what is the current evidence? Epilepsy & Behavior 2016. pii: S1525-5050(16)00050-0. doi: 10.1016/j.yebeh.2016.01.029.

[187] White CM, Gailey RA, Levin GM, Smith T. Seizure resulting from a venlafaxine overdose. Ann Pharmacother. 1997 Feb;31(2):178-80.

[188] Whyte IM, Dawson AH, Buckley NA. Relative toxicity of venlafaxine and selective serotonin reuptake inhibitors in overdose compared to tricyclic antidepressants. QJM: An International Journal of Medicine 2003;96:369–374.

[189] Devinsky O, Cross JH, Laux L, et al. Trial of cannabidiol for drug-resistant seizures in the Dravet syndrome. N Engl J Med 2017;376:2011-20.

[190] Solimini R, Rotolo MC, Pichini S, Pacifici R. Neurological Disorders in Medical Use Of Cannabis: an Update. CNS Neurol Disord Drug Targets. 2017 Apr 13.

[191] Massot-Tarrús A, McLachlan RS. Marijuana use in adults admitted to a Canadian epilepsy monitoring unit. Epilepsy Behav. 2016 Oct;63:73-78.

[192] Zak R, Solomon G, Petito F, Labar D. Baclofen-induced generalized nonconvulsive status epilepticus. Ann Neurol. 1994 Jul;36(1):113-4.

[193] Institute for Safe Medication Practices Canada. Medication Incidents that increase the risk of falls: a multi-incident analysis. ISMP Canada Safety Bulletin 2015; 15(12):1–5.

[194] Saunders KW, Dunn KM, Merrill JO, Sullivan M, Weisner C, Braden JB, Psaty BM, Von Korff M. Relationship of opioid use and dosage levels to fractures in older chronic pain patients. J Gen Intern Med. 2010 Apr;25(4):310-5.

[195] Miller M, Stürmer T, Azrael D, Levin R, Solomon DH. Opioid analgesics and the risk of fractures in older adults with arthritis. J Am Geriatr Soc. 2011 Mar;59(3):430-8.

[196] Solomon DH, Rassen JA, Glynn RJ, Lee J, Levin R, Schneeweiss S. The comparative safety of analgesics in older adults with arthritis. Arch Intern Med. 2010 Dec 13;170(22):1968-76.

[197] Miller M, Sturmer T, Azrael D, Levin R, Solomon DH. Opioid analgesics and the risk of fractures in older adults with arthritis. J Am Geriatr Soc. Mar 2011;59(3):430-438.

[198] American Geriatrics Society 2015 Beers Criteria Update Expert Panel. American geriatrics society 2015 updated beers criteria for potentially inappropriate medication use in older adults. JAGS 2015; 63(11):2227-46.

[199] O'Mahony D, O'Sullivan D, Byrne S, O'Connor MN, Ryan C, Gallagher P. STOPP/START criteria for potentially inappropriate prescribing in order people: version 2. Age and Ageing 2014; 0:1–6.

[200] Hoppmann RA, Peden JG, Ober SK. Central nervous system side effects of nonsteroidal anti-inflammatory drugs. Aseptic meningitis, psychosis, and cognitive dysfunction. Arch Intern Med. 1991 Jul;151(7):1309-13.

[201] Gaynor P, McCarberg B, Zheng W, Shoemaker S, Duenas H. Weight change with long-term duloxetine use in chronic painful conditions: an analysis of 16 clinical studies. Int J Clin Pract. 2011 Mar;65(3):341-9.

[202] Tzellos TG, Toulis KA, Goulis DG, Papazisis G, Zampeli VA, Vakfari A, Kouvelas D. Gabapentin and pregabalin in the treatment of fibromyalgia: a systematic review and a meta-analysis. J Clin Pharm Ther. 2010 Dec;35(6):639-56.

[203] Riediger C, Schuster T, Barlinn K, Maier S, Weitz J, Siepmann T. Adverse Effects of Antidepressants for Chronic Pain: A Systematic Review and Meta-analysis. Front Neurol. 2017 Jul 14;8:307.

[204] University of Toronto. Navigating Opioids for Chronic Pain (Infographic). Accessed 10Jul17 online at https://www.cpd.utoronto.ca/opioidprescribing/wp-content/plugins/safe-opioids-infographic//files/navigating-opioids-web.pdf.

[205] Noble M, Treadwell JR, Tregear SJ, Coates VH, Wiffen PJ, Akafomo C, Schoelles KM. Long-term opioid management for chronic noncancer pain. Cochrane Database Syst Rev. 2010 Jan 20;(1):CD006605.

[206] Nugent SM, Morasco BJ, O'Neil ME, Freeman M, Low A, Kondo K, Elven C, Zakher B, Motu'apuaka M, Paynter R, Kansagara D. The Effects of Cannabis Among Adults With Chronic Pain and an Overview of General Harms: A Systematic Review. Ann Intern Med. 2017 Aug 15. doi: 10.7326/M17-0155.

[207] Salam AP, Pozniak AL. Disseminated aspergillosis in an HIV-positive cannabis user taking steroid treatment. Lancet Infect Dis. 2017 Aug;17(8):882. doi: 10.1016/S1473-3099(17)30438-3. PubMed PMID: 28741551.

[208] Hamadeh R, Ardehali A, Locksley RM, York MK. Fatal aspergillosis associated with smoking contaminated marijuana, in a marrow transplant recipient. Chest. 1988 Aug;94(2):432-3. PubMed PMID: 3293934.

[209] Hoppmann RA, Peden JG, Ober SK. Central nervous system side effects of nonsteroidal anti-inflammatory drugs. Aseptic meningitis, psychosis, and cognitive dysfunction. Arch Intern Med. 1991 Jul;151(7):1309-13.

[210] Murthy, M. What data from 205 million private health insurance claims reveals about America's opioid crisis. Accessed online, 03Jul17 at https://amino.com/blog/opioid-epidemic-data-opioid-use-disorder/.

[211] O'Neil ME, Nugent SM, Morasco BJ, Freeman M, Low A, Kondo K, Zakher B, Elven C, Motu'apuaka M, Paynter R, Kansagara D. Benefits and Harms of Plant-Based Cannabis for Posttraumatic Stress Disorder: A Systematic Review. Ann Intern Med. 2017 Aug 15. doi: 10.7326/M17-0477.

[212] See online: http://www.rxfiles.ca/rxfiles/uploads/documents/ChartsTitlePage-2010-book-index.pdf.

[213] Liew Z, Ritz B, Rebordosa C, Lee PC, Olsen J. Acetaminophen use during pregnancy, behavioral problems, and hyperkinetic disorders. JAMA Pediatr. 2014 Apr;168(4):313-20.

[214] Nakhai-Pour HR et al. Use of nonaspirin nonsteroidal anti-inflammatory drugs during pregnancy and the risk of spontaneous abortion. CMAJ. 2011 Oct 18;183(15):1713-20.

[215] Palacioz K. NSAIDs and Miscarriage. Pharmacist's Letter. October 2003.

[216] Edwards DV, Aldridge T, Baird D et al. Periconceptional OTC NSAID exposure and risk for spontaneous abortion. ObsGyn 2012; 120(1):113-122.

[217] Weston J, Bromley R, Jackson CF, Adab N, Clayton-Smith J, Greenhalgh J, Hounsome J, McKay AJ, Tudur Smith C, Marson AG. Monotherapy treatment of epilepsy in pregnancy: congenital malformation outcomes in the child. Cochrane Database Syst Rev. 2016 Nov 7;11:CD010224.

[218] Fujii H, Goel A, Bernard N, Pistelli A, et al. Pregnancy outcomes following gabapentin use: results of a prospective comparative cohort study. Neurology. 2013 Apr 23;80(17):1565-70.

[219] Cupp M. Analgesics in Pregnancy and Lactation. Pharmacists Letter. February 2012. O'Mara. New pregnancy warnings: opioids, topiramate, and antipsychotics. Pharmacist's Letter. April 2011. Nakhai-Pour HR et al. Use of nonaspirin nonsteroidal anti-inflammatory drugs during pregnancy and the risk of spontaneous abortion. CMAJ. 2011 Oct 18;183(15):1713-20. Palacioz K. NSAIDs and Miscarriage. Pharmacist's Letter. October 2003. Edwards DV, Aldridge T, Baird D et al. Periconceptional OTC NSAID exposure and risk for spontaneous abortion. ObsGyn 2012; 120(1):113-122.

[220] FDA Drug Safety Communication: FDA restricts use of prescription codeine pain and cough medicines and tramadol pain medicines in children; recommends against use in breastfeeding women. Available from (accessed June 28, 2017) Codeine & Tramadol FDA warning lactation: https://www.fda.gov/Drugs/DrugSafety/ucm549679.htm.

[221] Committee Opinion No. 637: Marijuana Use During Pregnancy and Lactation. Obstet Gynecol. 2015 Jul;126(1):234-8.

[222] Gilron I, Bailey JM, Tu D, Holden RR, Jackson AC, Houlden RL. Nortriptyline and gabapentin, alone and in combination for neuropathic pain: a double-blind, randomised controlled crossover trial. Lancet. 2009 Oct 10;374(9697):1252-61.

[223] Gilron I, Bailey JM, Tu D, Holden RR, Weaver DF, Houlden RL. Morphine, gabapentin, or their combination for neuropathic pain. N Engl J Med. 2005;352:1324–1334.

[224] Deyo RA, Smith DH, Johnson ES, Tillotson CJ, Donovan M, Yang X, Petrik A, Morasco BJ, Dobscha SK. Prescription opioids for back pain and use of medications for erectile dysfunction. Spine (Phila Pa 1976). 2013 May 15;38(11):909-15.

[225] Wang ZY, Shi SY, Li SJ, Chen F, Chen H, Lin HZ, Lin JM. Efficacy and Safety of Duloxetine on Osteoarthritis Knee Pain: A Meta-Analysis of Randomized Controlled Trials. Pain Med. 2015 Jul;16(7):1373-85.

[226] Lumley MA, Schubiner H, Lockhart NA, Kidwell KM, Harte SE, Clauw DJ, Williams DA. Emotional awareness and expression therapy, cognitive behavioral therapy, and education for fibromyalgia: a cluster-randomized controlled trial. Pain. 2017 Aug 8.

[227] Uchio et a. A randomized, double-blind, placebo-controlled Phase II trial of duloxetine in Japanese patients with knee pain due to osteoarthritis. Journal of Pain Research 2018;11:809-21.

Additional References:

228 Aiyer R, Gulati A, Gungor S, Bhatia A, Mehta N. Treatment of Chronic Pain With Various Buprenorphine Formulations: A Systematic Review of Clinical Studies. Anesth Analg. 2018 Aug;127(2):529-538.

229 Brutcher RE, Kurihara C, Bicket MC, Moussavian-Yousefi P, Reece DE, Solomon, LM, Griffith SR, Jamison DE, Cohen SP. Compounded Topical Pain Creams to Treat Localized Chronic Pain: A Randomized Controlled Trial. Ann Intern Med. 2019 Feb

230 Han Y, Huang H, Pan J, Lin J, Zeng L, Liang G, Yang W, Liu J. Meta-analysis Comparing Platelet-Rich Plasma vs Hyaluronic Acid Injection in Patients with Knee Osteoarthritis. Pain Med. 2019 Mar 7.

231 Thiels CA, Habermann EB, Hooten WM, Jeffery MM. Chronic use of tramadol after acute pain episode: cohort study. BMJ. 2019 May 14;365:l1849. doi:10.1136/bmj.l1849.

232 Leopoldino AO, Machado GC, Ferreira PH, Pinheiro MB, Day R, McLachlan AJ, Hunter DJ, Ferreira ML. Paracetamol versus placebo for knee and hip osteoarthritis. Cochrane Database Syst Rev. 2019 Feb 25;2:CD013273.

233 Derry S, Bell RF, Straube S, Wiffen PJ, Aldington D, Moore RA. Pregabalin for neuropathic pain in adults. **Cochrane** Database Syst Rev. 2019 Jan 23;1:CD007076. https://www.cochranelibrary.com/cdsr/doi/10.1002/14651858.CD007076.pub3/full

234 Frost DA, Soric MM, Kaiser R, Neugebauer RE. Efficacy of Tramadol for Pain Management in Patients Receiving Strong Cytochrome P450 2D6 Inhibitors. Pharmacotherapy. 2019 Jun;39(6):724-729.

235 Frost Schnitzer TJ, Easton R, Pang S, Levinson DJ, Pixton G, Viktrup L, Davignon I, Brown MT, West CR, Verburg KM. Effect of Tanezumab on Joint Pain, Physical Function, and Patient Global Assessment of Osteoarthritis Among Patients With Osteoarthritis of the Hip or Knee: A Randomized Clinical Trial. JAMA. 2019 Jul 2;322(1):37-48. https://jamanetwork.com/journals/jama/fullarticle/2737173

236 Bendtsen L, Zakrzewska JM, Abbott J, et al. European Academy of Neurology guideline on trigeminal neuralgia. Eur J Neurol.2019 Jun;26(6):831-849.

References: Gout Chart – www.RxFiles.ca

1 Choi HK, Mount DB, Reginato AM; American College of Physicians; American Physiological Society. **Pathogenesis of gout**. Ann Intern Med. 2005 Oct 4;143(7):499-516.

2 Teng GG, Nair R, Saag KG. Pathophysiology, Clinical Presentation and **Treatment of Gout**. Drugs 2006; 66(12):1547-63.

Fam AG, Dunne SM, Iazzetta J, Paton TW. Efficacy and safety of **desensitization to allopurinol** following cutaneous reactions. Arthritis Rheum. 2001 Jan;44(1):231-8.

3 Zhang W, Doherty M, Pascual E, Bardin T, et al.; **EULAR** Standing Committee for International Clinical Studies Including Therapeutics. EULAR evidence based recommendations for gout. **Part I: Diagnosis**. Report of a task force of the Standing Committee for International Clinical Studies Including Therapeutics (ESCISIT). Ann Rheum Dis. **2006** Oct;65(10):1301-11. Epub 2006 May 17. http://ard.bmj.com/cgi/reprint/65/10/1301

4 Canadian Rheumatology Association Handbook

5 Hak AE, Curhan G, Grodstein FD, Choi HK. Menopause, postmenopausal hormone use and risk of incident gout. Ann Rheum Dis. 2009 Jul 9.

6 Gurwitz JH et al. Thiazide diuretics and the initiation of anti-gout therapy. Journal of Clinical Epidemiology; 1997 50:953-57.

7 Gurwitz JH, Kalish SC, Bohn RL et al. Thiazide Diuretics and the Initiation of Anti-Gout Therapy. Journal of Clinical Epidemiology. 1997 Aug;50(8):953-9

8 Choi HK, Curhan G. Soft drinks, fructose consumption, and the risk of gout in men: prospective cohort study. BMJ. 2008 Feb 9;336(7639):309-12. Epub 2008 Jan 31

9 Choi HK, Atkinson K, Karlson EW, et al. Alcohol intake and risk of incident gout in men: a prospective study. Lancet. 2004 Apr 17;363(9417):1251-2.

10 Zhang W, Doherty M, Bardin T, et al. **EULAR** Standing Committee for International Clinical Studies Including Therapeutics. EULAR evidence based recommendations for gout. **Part II: Management**. Report of a task force of the EULAR Standing Committee for International Clinical Studies Including Therapeutics (ESCISIT). Ann Rheum Dis. **2006** Oct;65(10):1312-24. Epub 2006 May 17. http://ard.bmj.com/cgi/reprint/65/10/1312

11 Fox R. Management of recurrent gout. BMJ. 2008 Feb 9;336(7639):329.

12 Peterson GM, Sugden JE. Educational program to improve the dosage prescribing of allopurinol. Med J Aust. 1995 Jan 16;162(2):74-7.

13 Willacy H; Gout; Clinical Knowledge Summary, 5 Jan 2008

14 Wheeler JG, Juzwishin KD, Eiriksdottir G, et al. Serum uric acid and coronary heart disease in 9,458 incident cases and 155,084 controls: prospective study and meta-analysis. PLoS Med. 2005 Mar;2(3):e76. Epub 2005 Mar 29.

15 Feig DI, Kang DH, Johnson RJ. Uric acid and cardiovascular risk. N Engl J Med. 2008 Oct 23;359(17):1811-21.

16 Strasak A, et al. Serum uric Acid and risk of cardiovascular mortality: a prospective long-term study of 83 683 austrian men. Clin Chem. 2008 Feb;54(2):273-84. Epub 2007 Nov 26.

17 Janssens HJ, Lucassen PL, et al. Systemic corticosteroids for acute gout. Cochrane Database Syst Rev. 2008 Apr 16;(2):CD005521.

[18] Rainer TH, Cheng CH, Janssens HJ, et al. Oral **Prednisolone** in the Treatment of Acute Gout: A Pragmatic, Multicenter, Double-Blind, Randomized Trial. (vs indomethacin) Ann Intern Med. 2016 Feb 23.

19 Halevy S, Ghislain PD, Mockenhaupt M, Fagot JP, Bouwes Bavinck JN, Sidoroff A, Naldi L, Dunant A, Viboud C, Roujeau JC; EuroSCAR Study Group. Allopurinol is the most common cause of Stevens-Johnson syndrome and toxic epidermal necrolysis in Europe and Israel. J Am Acad Dermatol. 2008 Jan;58(1):25-32. Epub 2007 Oct 24.

20 Fam AG, Dunne SM, Iazzetta J, Paton TW. Efficacy and safety of desensitization to allopurinol following cutaneous reactions. Arthritis Rheum. 2001 Jan;44(1):231-8.

21 Becker MA, Schumacher HR Jr, Wortmann RL, MacDonald PA, Eustace D, et al. Febuxostat compared with allopurinol in patients with hyperuricemia and gout. N Engl J Med. 2005 Dec 8;353(23):2450-61.

Febuxostat for the management of hyperuricaemia in people with gout. NICE Dec 2008 Guidance http://www.nice.org.uk/TA164

Schumacher HR Jr, Becker MA, Wortmann RL, et al. Effects of febuxostat versus allopurinol and placebo in reducing serum urate in subjects with hyperuricemia and gout: a 28-week, phase III, randomized, double-blind, parallel-group trial. Arthritis Rheum. 2008 Nov 15;59(11):1540-8. Significantly (P < or = 0.05) higher percentages of subjects treated with febuxostat 80 mg (48%), 120 mg (65%), and 240 mg (69%) attained the primary end point of last 3 monthly serum urate levels <6.0 mg/dl compared with allopurinol (22%) and placebo (0%). At all doses studied, febuxostat more effectively lowered and maintained serum urate levels <6.0 mg/dl than did allopurinol (300 or 100 mg) or placebo in subjects with hyperuricemia and gout, including those with mild to moderately impaired renal Function.

Gelber AC. Febuxostat versus allopurinol for gout. N Engl J Med. 2006 Apr 6;354(14):1532-3; author reply 1532-3.

22 Würzner G, Gerster JC, Chiolero A, Maillard M, et al. Comparative effects of losartan and irbesartan on serum uric acid in hypertensive patients with hyperuricaemia and gout. J Hypertens. 2001 Oct;19(10):1855-60.

23 Hare JM, Mangal B, Brown J, ; OPT-CHF Investigators. Impact of oxypurinol in patients with symptomatic heart failure. Results of the OPT-CHF study. J Am Coll Cardiol. 2008 Jun 17;51(24):2301-9. Oxypurinol did not produce clinical improvements in unselected patients with moderate-to-severe heart failure. However, post-hoc analysis suggests that benefits occur in patients with elevated SUA in a manner correlating with the degree of SUA reduction. Serum uric acid may serve as a valuable biomarker to target XO inhibition in heart failure.

[24] Barskova VG, Eliseev MS, Kudaeva FM, Aleksandrova EN, Volkov AV, Nasonova VA, Nasonov EL. [Effect of metformin on the clinical course of gout and insulin resistance]. Klin Med (Mosk). 2009;87(7):41-6.

Milionis HJ, Kakafika AI, Tsouli SG, Athyros VG, Bairaktari ET, Seferiadis KI, Elisaf MS. Effects of statin treatment on uric acid homeostasis in patients with primary hyperlipidemia. Am Heart J. 2004 Oct;148(4):635-40.

[25] Choi HK, Curhan G. Coffee consumption and risk of incident gout in women: the Nurses' Health Study. Am J Clin Nutr. 2010 Oct;92(4):922-7. Epub 2010 Aug 25.

Choi HK, Willett W, Curhan G. Coffee consumption and risk of incident gout in men: a prospective study. Arthritis Rheum. 2007 Jun;56(6):2049-55.

[25] Zhang W, Doherty M, Bardin T, et al. European League Against Rheumatism recommendations for **calcium pyrophosphate deposition (CPPD)**. Part I: terminology and diagnosis. Ann Rheum Dis. 2011 Jan 7.

Zhang W, Doherty M, Pascual E, et al. EULAR recommendations for **calcium pyrophosphate deposition (CPPD)**. Part II: **Management**. Ann Rheum Dis. 2011 Jan 20.

[26] Terkeltaub RA, Furst DE, Bennett K, Kook KA, Crockett RS, Davis MW. High versus low dosing of oral colchicine for early acute gout flare: Twenty-four-hour outcome of the first multicenter, randomized, double-blind, placebo-controlled, parallel-group, dose-comparison colchicine study. Arthritis Rheum. 2010 Apr;62(4):1060-8.

[27] Schlesinger N, De Meulemeester M, Pikhlak A, et al. **Canakinumab** relieves symptoms of acute flares and improves health-related quality of life in patients with difficult-to-treat Gouty Arthritis by suppressing inflammation: results of a randomized, dose-ranging study. Arthritis Research & Therapy. 2011;13(2):R53.

Solomon DH, Glynn RJ, MacFadyen JG, et al. Relationship of Interleukin-1β Blockade With Incident Gout and Serum Uric Acid Levels: Exploratory Analysis of a Randomized Controlled Trial. Ann Intern Med. 2018 Oct 16;169(8):535-542.

Additional References ----------

Aati O, Taylor WJ, Siegert RJ, et al. Development of a **patient-reported outcome measure of tophus burden**: the Tophus Impact Questionnaire (TIQ-20). Ann Rheum Dis. 2015 Dec;74(12):2144-50.

Abe N, Fujieda Y, Amengual O, Atsumi T. Disseminated subcutaneous nodules and **destructive polyarthritis**. BMJ. 2019 Apr 17;365:l1344.

Alabed S, Cabello JB, Irving GJ, Qintar M, Burls A. **Colchicine for pericarditis**. Cochrane Database of Systematic Reviews 2014, Issue 8. Art. No.: CD010652. DOI: 10.1002/14651858.CD010652.pub2. Colchicine, as adjunctive therapy to NSAIDs, is effective in reducing the number of pericarditis recurrences in patients with recurrent pericarditis or acute pericarditis. However, evidence is based on a limited number of small trials. Patients with multiple resistant recurrences were not represented in any published or on-going trials, and it is these patients that are in the most need for treatment.

Alammari YM, Gheta D, Flood RM, et al. Urate-lowering therapy (**ULT) reduces non-episodic foot pain i**n patients who fail to meet ACR/EULAR 2015 gout classification criteria: an effect predicted by ultrasound and potential rationale for reclassification. Ann Rheum Dis. 2019 Apr;78(4):579-580.

Álvarez-Lario B, Macarrón-Vicente J. **Uric acid and evolution**. Rheumatology(Oxford). 2010 Nov;49(11):2010-5.

Andrés M, Bernal JA, Sivera F, et al. **Cardiovascular risk** of patients with gout seen at rheumatology clinics following a structured assessment. Ann Rheum Dis. 2017 Jul;76(7):1263-1268

Ayoub-Charette S, Liu Q, Khan TA, et al. Important **food sources of fructose-containing sugars and incident gout**: a systematic review and meta-analysis of prospective cohort studies. BMJ Open. 2019 May 5;9(5):e024171.

Bao Y, Curhan G, Merriman T, et al. Lack of **gene-diuretic interactions** on the risk of incident gout: the Nurses' Health Study and Health Professionals Follow-up Study. Ann Rheum Dis. 2015 Feb 9.

Bardin T, Keenan RT, Khanna PP, et al. **Lesinurad in combination with allopurinol**: a randomised, double-blind, placebo-controlled study in gout patients with inadequate response to standard of care (the multinational CLEAR 2 study). Ann Rheum Dis 2017;76:811–20.

Bartoli F, Crocamo C, Clerici M, et al. **Allopurinol as add-on treatment for mania symptoms** in bipolar disorder: systematic review and meta-analysis of randomised controlled trials. Br J Psychiatry. 2016 Nov 17.

Batt C, Phipps-Green AJ, Black MA, et al. **Sugar sweetened beverage consumption**: a risk factor for prevalent gout with SLC2A9 genotype-specific effects on serum urate and risk of gout. Ann Rheum Dis. 2014 Dec;73(12):2101-6.

Beattie CJ, Fulton RL, Higgins P, et al. **Allopurinol initiation and change in blood pressure** in older adults with hypertension. Hypertension. 2014;64:1102-1107.

Becker MA, Baraf HS, Yood RA, et al. Long-term safety of **pegloticase** in chronic gout refractory to conventional treatment. Ann Rheum Dis. 2012 Nov 10.

Becker MA, Schumacher HR, Espinoza LR, et al. The Urate-lowering Efficacy and Safety of **Febuxostat** in the Treatment of the Hyperuricemia of Gout: the **CONFIRMS** trial. Arthritis Research and Therapy. 2010; 2:R63

Becker MA, Baraf HS, Yood RA et al. Long-term safety of **pegloticase** in chronic gout refractory to conventional treatment. Ann Rheum Dis. 2013 Sep 1;72(9):1469-74.

Billy CA;Lim RT;Ruospo M;Palmer SC;Strippoli GFM. **Corticosteroid or Nonsteroidal Antiinflammatory** Drugs for the Treatment of Acute Gout: A Systematic Review of Randomized Controlled Trials. J Rheumatol. 2017 Aug 1.

Black E, Sketris I, et al. Adherence to Guidelines and the **Screening Tool of Older Persons' Potentially Inappropriate Prescriptions Criteria for Colchicine Dosing** for Gout Treatment in Beneficiaries of the Nova Scotia Seniors' Pharmacare Program. Clin Ther. 2015 Sep 18.

Blagojevic-Bucknall M, Mallen C, Muller S, et al. The **risk of gout among patients with sleep apnea**: a matched cohort study. Arthritis Rheumatol. 2018 Aug 30.

Bongartz T, Glazebrook KN, Kavros SJ, et al. **Dual-energy CT for the diagnosis** of gout: an accuracy and diagnostic yield study. Ann Rheum Dis. 2014 Mar 25.

Brik R, Butbul-Aviel Y, Lubin S, et al. **Canakinumab** for children with colchicine-resistant familial Mediterranean fever: A 6-month, open-label, single-arm, pilot study. Arthritis Rheumatol. 2014 Jul 21.

Bruderer S, Jick SS, Bodmer M, Meier CR. Use of **diuretics and risk of incident gout**: Population-based case-control study. Arthritis Rheum. 2013 Oct 21.

Bruderer SG, Bodmer M, Jick SS, et al. **Poorly controlled type 2 diabetes** mellitus is associated with a **decreased risk of incident gout**: a population-based case-control study. Ann Rheum Dis. 2015 Sep;74(9):1651-8.

Burns CM, Wortmann RL. Gout therapeutics: **new drugs** for an old disease. Lancet. 2010 Aug 16.

Burns RB, Smith CC, Shmerling RH, Tess A. How Would You Manage This Patient With Gout?: Grand Rounds Discussion From Beth Israel Deaconess Medical Center. Ann Intern Med. 2018 Dec 4;169(11):788-795.

Carnovale C, Venegoni M, Clementi E. **Allopurinol overuse** in asymptomatic hyperuricemia: a teachable moment. JAMA Intern Med. 2014 Jul 1;174(7):1031-2.

Cayley WE Jr. **Gout-10 minute Consultation**. BMJ. 2010 Nov 15;341:c6155. doi: 10.1136/bmj.c6155.

Chamorro Á, Amaro S, et al, for the **URICO-ICTUS** Investigators. Safety and efficacy of **uric acid in patients with acute stroke** (URICO-ICTUS): a randomised, double-blind phase 2b/3 trial. Lancet Neurol 2014; online April 2.

Chen JH, Wen CP, Wu SB, et al. Attenuating the **mortality risk of high serum uric acid**: the role of physical activity underused. Ann Rheum Dis. 2014 Jul 22.

Chen YF, Lin HH, Lu CC, et al. Gout and a Subsequent Increased **Risk of Erectile Dysfunction** in Men Aged 64 and Under: A Nationwide Cohort Study in Taiwan. J Rheumatol. 2015 Jun 15.

Choi HK, Curhan G. Coffee, tea, and caffeine consumption and serum uric acid level: the third national health and nutrition examination survey. Arthritis Rheum. 2007 Jun 15;57(5):816-21. These findings from a nationally representative sample of US adults suggest that **coffee** consumption is associated with lower serum uric acid level and hyperuricemia frequency, but tea consumption is not. The inverse association with coffee appears to be via components of coffee other than caffeine.

Chhana A, Doyle A, Sevao A, et al. Advanced imaging assessment of gout: comparison of **dual-energy CT and MRI** with anatomical pathology. Ann Rheum Dis. 2018 Apr;77(4):629-630.

Choi HK, Gao X, Curhan G. **Vitamin C** intake and the risk of gout in men: a prospective study. Arch Intern Med. 2009 Mar 9;169(5):502-7. Higher vitamin C intake is independently associated with a lower risk of gout. Supplemental vitamin C intake may be beneficial in the prevention of gout.

Choi HK, Soriano LC, Zhang Y, Rodríguez LAG. **Calcium channel blockers, losartan**, and the risk of **incident gout** among patients with hypertension: population based case-control study. BMJ 2012;344:d8190.

Choi HK, Burns LC, Shojania K et al. **Dual energy CT** in gout: a prospective validation study. Ann Rheum Dis. 2012 Sep;71(9):1466-71.

Choi HK, Zhang Y. **Bariatric surgery as urate-lowering therapy** in severe obesity. Ann Rheum Dis. 2014 May;73(5):791-3.

Choi HK, Niu J, Neogi T, et al. **Nocturnal** risk of gout attacks. Arthritis Rheumatol. 2014 Dec 11.

Chowalloor PV, Keen HI. A systematic review of **ultrasonography in gout** and asymptomatic hyperuricaemia. Ann Rheum Dis. 2013 Jan 3.

Chung WH, Chang WC, Stocker SL, et al. Insights into the poor prognosis of **allopurinol-induced severe cutaneous adverse reactions**: the impact of renal insufficiency, high plasma levels of oxypurinol and granulysin. Ann Rheum Dis. 2015 Dec;74(12):2157-64.

Clarson LE, Hider SL, Belcher J, et al. **Increased risk of vascular disease** associated with gout: a retrospective, matched cohort study in the UK Clinical Practice Research Datalink. Ann Rheum Dis. 2015 Apr; 74(4):642-7.

Clemmons AB, Ensley E, Hoge S, et al. Fixed-Dose **Rasburicase** in Overweight and Obese Patients Versus Normal-Weight Patients. Ann Pharmacother. 2014 Jun 17;48(9):1152-1158.

Coburn BW, Michaud K, Bergman DA, et al. **Allopurinol Dose Escalation and Mortality** among Patients with Gout: A National Propensity-Matched Cohort Study. Arthritis Rheumatol. 2018 Mar 7.

Coutsouvelis J, Wiseman M, Hui L, et al. Effectiveness of a single fixed dose of **rasburicase 3mg** in the management of tumour lysis syndrome. Br J Clin Pharmacol. 2012 Jun 11.

Dalal DS, Mbuyi N, Shah I, et al. **Prescription Opioid Use** among Acute Gout Patients Discharged from the Emergency Department. Arthritis Care Res (Hoboken). 2019 Jul 2.

Dalbeth N, Schauer C, MacDonald P, et al. Methods of **tophus assessment** in clinical trials of chronic gout: a systematic literature review and **pictorial** reference guide. Ann Rheum Dis 2011;70:597-604. Online 7 Jan 2011 doi:10.1136/ard.2010.139899

Dalbeth N, Ames R, Gamble GD, et al. Effects of **skim milk powder enriched with glycomacropeptide and G600 milk fat extract** on frequency of gout flares: a proof-of-concept randomised controlled trial. Ann Rheum Dis. 2012 Jun;71(6):929-34.

Dalbeth N, Kalluru R, Aati O et al. **Tendon involvement** in the feet of patients with gout: a dual-energy CT study. Ann Rheum Dis. 2013 Sep 1;72(9):1545-8.

Dalbeth N, Chen P, White M, et al. Impact of **bariatric surgery on serum urate targets** in people with morbid obesity and diabetes: a prospective longitudinal study. Ann Rheum Dis 2014;73:797–802.

Dalbeth N, et al. **Zoledronate** for prevention of bone erosion in tophaceous **gout**: a randomised, double-blind, placebo-controlled trial. Ann Rheum Dis. 2014Jun 1;73(6):1044-51.

Dalbeth N, Stamp L. **Hyperuricaemia and gout: time for a new staging system**? Ann Rheum Dis. 2014 Sep;73(9):1598-600.

Dalbeth N, House ME, Aati O, et al. Urate crystal deposition in **asymptomatic hyperuricaemia** and symptomatic gout: a **dual energy CT** study. Ann Rheum Dis. 2015 Jan 30.

Dalbeth N, Merriman TR, Stamp LK. **Gout**. Lancet. 2016 Apr 21.

Dalbeth N, Jones G, Terkeltaub R, et al. **Lesinurad**, a Selective Uric Acid Reabsorption Inhibitor, in Combination With Febuxostat in Patients With Tophaceous Gout: A Phase III Clinical Trial. Arthritis Rheumatol. 2017 Jun 9

Dalbeth N, Saag KG, Palmer WE, et al. Effects of **Febuxostat** in Early Gout: A Randomized, double-blind, Placebo-controlled Study. Arthritis Rheumatol. 2017 Oct 4.

Dalbeth N, Nicolaou S, Baumgartner S, et al. Presence of monosodium urate crystal deposition by **dual-energy CT in** patients with gout treated with allopurinol. Ann Rheum Dis. 2017 Nov 16. pii: annrheumdis-2017-212046.

Dalbeth N, Phipps-Green A, Frampton C, et al. Relationship between **serum urate concentration and clinically evident incident gout**: an individual participant data analysis. Ann Rheum Dis. 2018 Feb 20.

Dalbeth N, Phipps-Green A, Frampton C, et al. Relationship between **serum urate concentration and clinically evident incident gout**: an individual participant data analysis. Ann Rheum Dis. 2018 Jul;77(7):1048-1052.

Deftereos S, Giannopoulos G, Kossyvakis C, et al. **Colchicine** for prevention of early **atrial fibrillation** recurrence after pulmonary vein isolation. J Am Coll Cardiol 2012.

Deftereos S, Giannopoulos G, Raisakis K, et al. **Colchicine** treatment for prevention of **in-bare-metal-stent restenosis** in diabetics. J Am Coll Cardiol. 2013 Mar 13.

Demarco MA, Maynard JW, Baer AN, et al. **Diuretic use**, increased serum urate and the risk of incident gout in a population-based study of hypertensive adults: The atherosclerosis risk in the communities cohort. Arthritis Rheum. 2011 Sep 27. doi: 10.1002/art.33315.
Thiazide and loop diuretics were associated with increased gout risk, an association mediated by a change in serum urate.

De Vera MA, Rahman MM, Bhole V, et al. Independent impact of gout on the risk of acute **myocardial infarction** among elderly women: a population-based study. Ann Rheum Dis 2010; DOI:10.1136/ard.2009.1227701.

De Vera MA, Marcotte G, Rai S, et al. **Medication adherence** in gout: a systematic review. Arthritis Care Res (Hoboken). 2014 Oct;66(10):1551-9.

Deftereos S, Giannopoulos G, Angelidis C, et al. Anti-Inflammatory Treatment With **Colchicine** in **Acute Myocardial Infarction**: A Pilot Study. Circulation. 2015 Aug 11.

Diav-Citrin O, Shechtman S, Schwartz V, et al. **Pregnancy outcome** after in utero exposure to colchicine. Am J Obstet Gynecol. 2010 Jun 24.

Dion M, et al. **CUA guideline** on the evaluation and medical management of the **kidney stone** patient – 2016 update. www.cua.org/themes/web/assets/files/cua_guideline_on_the_evaluation_and_medical_management_of_the_kidney_stone_patient.pdf (accessed Nov 18, 2016).

Doherty M, Jenkins W, Richardson H, et al. **Efficacy and cost-effectiveness of nurse-led care involving education and engagement of patients and a treat-to-target urate-lowering strategy** versus usual care for gout: a randomised controlled trial. Lancet. 2018 Oct 20;392(10156):1403-1412.

Duarte-García A, Zamore R, Wong JB. The **Evidence Basis for the American College of Rheumatology Practice Guidelines**. JAMA Intern Med. 2017 Nov 27.

Dubreuil M, Zhu Y, Zhang Y, et al. **Allopurinol** initiation and **all-cause mortality** in the general population. Ann Rheum Dis. 2014 Mar 24.

Eason A, House ME, Vincent Z, et al. Factors associated with change in **radiographic damage scores in gout:** a prospective observational study. Ann Rheum Dis. 2016 Dec;75(12):2075-2079

El-Zawawy H, Mandell BF. Managing **gout**: How is it different in patients with **chronic kidney disease**? Cleveland Clinic Journal of Medicine 2010; 77(12):919-928; doi:10.3949/ccjm.77a.09080

FDA Nov/17 is alerting the public that preliminary results from a safety clinical trial show an **increased risk of heart-related death with febuxostat (Uloric)** compared to another gout medicine called allopurinol. The safety trial was conducted in over 6,000 patients with gout treated with either febuxostat or allopurinol. The primary outcome was a combination of heart-related death, non-deadly heart attack, non-deadly stroke, and a condition of inadequate blood supply to the heart requiring urgent surgery. The preliminary results show that overall, febuxostat did not increase the risk of these combined events compared to allopurinol. However, when the outcomes were evaluated separately, febuxostat showed an increased risk of heart-related deaths and death from all causes.

FDA Feb/19 has concluded there is an **increased risk of death with Uloric (febuxostat**) compared to another gout medicine, allopurinol.

Feig DI, Soletsky B, Johnson RJ. Effect of allopurinol (200mg bid) on blood pressure of **adolescents with newly diagnosed essential hypertension**: a randomized trial. JAMA. 2008 Aug 27;300(8):924-32. In this short-term, crossover study of adolescents (n=30) with newly diagnosed hypertension, treatment with allopurinol resulted in **reduction of BP (by 6.9/5.1).** The results represent a new potential therapeutic approach, although not a fully developed therapeutic strategy due to potential adverse effects.

Feig DI, Madero M, Jalal DI, et al. Uric Acid and the Origins of **Hypertension**. J Pediatr. 2013 Feb 9.

Finetti M, Insalaco A, Cantarini L, et al. Long-Term Efficacy of Interleukin-1 Receptor Antagonist (**Anakinra**) in Corticosteroid-Dependent and Colchicine-Resistant Recurrent Pericarditis. J Pediatr. 2014 Mar 12.

Fink HA, Wilt TJ, Eidman KE, et al. Medical management to prevent recurrent **nephrolithiasis** in adults: a systematic review for an american college of physicians clinical guideline. Ann Intern Med. 2013 Apr 2;158(7):535-43. (Thiazide, citrate or allopurinol reduced risk)

Fisher MC, Rai SK, Lu N, et al. The unclosing **premature mortality gap** in gout: a general population-based study. Ann Rheum Dis. 2017 Jul;76(7):1289-1294.

FitzGerald JD, Neogi T, Choi HK. Do **Not Let Gout Apathy Lead to Gouty Arthropathy**. Arthritis Rheumatol. 2016 Dec 21.

Fontenelle LF, Sarti TD. **Kidney Stones: Treatment and Prevention**. Am Fam Physician. 2019;99(8):490-496.

Forman JP, Scheven L, de Jong PE, et al. Association between **sodium intake and change in uric acid**, urine albumin excretion and risk of developing hypertension. Circulation 2012.

Frassetto L, Kohlstadt I. Treatment and prevention of **kidney stones**: an update. Am Fam Physician. 2011 Dec 1;84(11):1234-42. Gaffo AL, Saag KG. Management of hyperuricemia and **gout in CKD**. Am J Kidney Dis. 2008 Nov;52(5):994-1009.

Freund J. **Risk of Gout with the Use of Thiazide Diuretics**. Am Fam Physician. 2015;92(7):622-623.
Gaffo AL, Jacobs DR Jr, Sijtsma F, et al. **Serum urate association with hypertension** in young adults: analysis from the Coronary Artery Risk Development in Young Adults cohort. Ann Rheum Dis. 2013 Aug;72(8):1321-7.
Gaffo AL, Dalbeth N, Saag KG, et al. **Validation of a definition for flare** in patients with established gout. Arthritis Rheumatol. 2017 Nov 21.
Gamala M, Jacobs JWG, van Laar JM The diagnostic performance of **dual energy CT for diagnosing gout**: a systematic literature review and meta-analysis. Rheumatology (Oxford). 2019 May 14.
Givertz MM, Anstrom KJ, Redfield MM, et al; NHLBI Heart Failure Clinical Research Network*. Effects of **Xanthine Oxidase Inhibition in Hyperuricemic Heart Failure Patients**: The Xanthine Oxidase Inhibition for Hyperuricemic Heart Failure Patients (EXACT-HF) Study. Circulation. 2015 May 19;131(20):1763-71.
Glazebrook KN et al. Identification of intraarticular and periarticular uric acid crystals with **dual-energy CT**: Initial evaluation. Radiology 2011 Nov; 261:516.
Goicoechea M, Vinuesa SG, Verdalles U, et al. Effect of Allopurinol in **Chronic Kidney Disease** Progression and **Cardiovascular Risk**. Clin J Am Soc Nephrol. 2010 Jun 10.
Goicoechea M, Garcia de Vinuesa S, Verdalles U, et al. **Allopurinol and Progression of CKD and Cardiovascular Events**: Long-term Follow-up of a Randomized Clinical Trial. Am J Kidney Dis. 2015 Jan 13.
Goldfien RD, Ng MS, Yip G, et al. Effectiveness of a **pharmacist-based gout care management** programme in a large integrated health plan: results from a pilot study. BMJ Open. 2014 Jan 10
Gooch K, Culleton BF, Manns BJ, et al. **NSAID use** and progression of **chronic kidney disease**. Am J Med. 2007 Mar;120(3):280.e1-7.
Gout patient information (including **purine** content of food) http://www.niams.nih.gov/Health_Info/Gout/
Gratton SB, Scalapino KJ, Fye KH. Case of **anakinra** as a steroid-sparing agent for gout inflammation. Arthritis Rheum. 2009 Sep 15;61(9):1268-70.
Grayson PC, Kim SY, Lavalley M, Choi HK. Hyperuricemia and **incident hypertension**: a systematic review and meta-analysis. Arthritis Care Res (Hoboken) 2011;63:102-10.
Grimaldi-Bensouda L, Alpérovitch A, Aubrun E, et al; the PGRx MI Group. Impact of **allopurinol** on risk of **myocardial infarction**. Ann Rheum Dis. 2014 Jan 6.
Habib G, Khazin F, Chernin M. Continuous blood **glucose** monitoring in a patient with type-2 diabetes treated with **intra-articular betamethasone** injection at the knee joint. Arthritis Rheum. 2013 Oct 7.
Hainer BL, Matheson E, Wilkes RT, **Diagnosis, Treatment, and Prevention of Gout.** Am Fam Physician. 2014;90(12):831-836.
Han B, Xue L, Yang C. **Giant gouty tophi** in the hands. Lancet Diabetes Endocrinol. 2016 Feb 19.
Hashkes PJ, Spalding SJ, Giannini EH, et al. **Rilonacept** for colchicine-resistant or -intolerant familial mediterranean Fever: a randomized trial. Ann Intern Med. 2012 Oct 16;157(8):533-41.
Hemkens LG, Ewald H, Gloy VL, et al. Cardiovascular effects and safety of long-term **colchicine** treatment: Cochrane review and meta-analysis. Heart. 2016 Feb 1.
Hemkens LG, Ewald H, Briel M. **Colchicine and Prevention of Cardiovascular Events**. JAMA. 2016 Sep 13;316(10):1106-1107.
Hill-McManus D, Soto E, Marshall S, et al. **Impact of non-adherence** on the safety and efficacy of uric acid lowering therapies in the treatment of gout. Br J Clin Pharmacol. 2017 Sep 9.
Hoffman HM, Throne ML, Amar NJ, et al. Long-Term Efficacy and Safety Profile of **Rilonacept** in the Treatment of Cryopryin-Associated Periodic Syndromes: Results of a 72-Week Open-Label Extension Study. Clin Ther. 2012 Sep 29.
Holeggen A, Alderman MH, Kjeldsen SE, Julius S, Devereux RB, De Faire U, et al. The impact of serum uric acid on **cardiovascular outcomes** in **LIFE** study. Kidney Int 2004;65:1041-9.
Horsfall LJ, Nazareth I, Petersen I. Serum uric acid and the risk of **respiratory disease**: a population-based cohort study. Thorax. 2014 Jun 5.
Howard Scott C., Jones Deborah P., Pui Ching-Hon. The **Tumor Lysis Syndrome**. N Engl J Med 2011; 364:1844-1854.
Hui M, Carr A, Cameron S, et al. The **British Society for Rheumatology Guideline** for the **Management of Gout.** Rheumatology (Oxford). 2017 Jun 12.
Hunter DJ, York M, Chaisson CE, Woods R, Niu J, Zhang Y. **Recent diuretic use and the risk of recurrent gout attacks**: the online case-crossover gout study. J Rheumatol 2006;33:1341-1345.
Hyon K. Choi; Walter Willett; Gary Curhan. **Fructose-Rich Beverages** and Risk of Gout in Women. JAMA. 2010;0(2010):jama.2010.1638.
Imazio Massimo, Trinchero Rita, Brucato Antonio, et al. **Colchicine** for the Prevention of the **Post-pericardiotomy Syndrome** (**COPPS**): a multicentre, randomized, double-blind, placebo-controlled trial Eur Heart J (2010) 31(22): 2749-2754.
Imazio M, Brucato A, Cemin R, et al. **Colchicine for Recurrent Pericarditis** (**CORP**) A Randomized Trial. Ann Intern Med. 2011 Oct 4;155(7):409-414.
Imazio M, Brucato A, Ferrazzi P, et al. Colchicine reduces **postoperative atrial fibrillation**. Results of the colchicine for the prevention of **postperiocardiotomy symdrome (COPPS)** atrial fibrillation substudy. Circulation 2011; 124:2290-2295.
Imazio M, Brucato A, Cemin R, et al. the ICAP Investigators. A Randomized Trial of **Colchicine for Acute Pericarditis**. N Engl J Med. 2013 Aug 31.
Imazio M, Belli R, Brucato A, et al. Efficacy and safety of **colchicine** for treatment of multiple **recurrences of pericarditis (CORP-2):** a multicentre, double-blind, placebo-controlled, randomised trial. Lancet. 2014 Mar 28.
Imazio M, Brucato A, Ferrazzi P, et al; for the **COPPS-2** Investigators. **Colchicine** for Prevention of **Postpericardiotomy Syndrome and Postoperative Atrial Fibrillation**: The COPPS-2 Randomized Clinical Trial. JAMA. 2014 Aug 30.
Imazio M, Gaita F, LeWinter M. Evaluation and **Treatment of Pericarditis**: A Systematic Review. JAMA. 2015 Oct 13;314(14):1498-506.
Indraratna PL, Virk S, Gurram D, et al. Use of **colchicine in pregnancy**: a systematic review and meta-analysis. Rheumatology (Oxford). 2017 Sep 23.
Is **fracture risk linked** to gout or urate-lowering therapy? Drug Ther Bull. 2019 Apr;57(4):54.
Janssen CA, Oude Voshaar MAH, Vonkeman HE, et al. **Anakinra** for the treatment of acute gout flares: a randomized, double-blind, placebo-controlled, active-comparator, non-inferiority trial. Rheumatology (Oxford). 2019 Jan 2.
Janssens Hein J. E. M.; Fransen Jaap; van de Lisdonk Eloy H.; et al. A **Diagnostic Rule for Acute Gouty Arthritis** in Primary Care Without Joint Fluid Analysis Arch Intern Med. 2010;170(13):1120-1126.
Clinical calculator http://www.umcn.nl/goutcalc
Jinno S, Hasegawa K, Neogi T, et al. **Trends in Emergency Department Visits** and Charges for Gout in the United States between 2006 and 2012. J Rheumatol. 2016 Jun 1.
Juraschek SP, McAdams-Demarco M, Gelber AC, et al. Effects of **Lowering Glycemic Index of Dietary Carbohydrate** on Plasma Uric Acid: The OmniCarb Randomized Clinical Trial. Arthritis Rheumatol. 2015 Dec 4.
Juraschek SP, Gelber AC, Choi HK, et al. Effects of the **Dietary Approaches To Stop Hypertension (DASH) Diet** and Sodium Intake on Serum Uric Acid. Arthritis Rheumatol. 2016 Aug 14.
Jutkowitz E, Choi HK, Pizzi LT, et al. **Cost-effectiveness of allopurinol and febuxostat** for the management of gout. Ann Intern Med. 2014 Nov 4;161(9):617-26.
Kang EH, Choi HK, Shin A, et al. Comparative **cardiovascular risk of allopurinol versus febuxostat** in patients with gout: a nation-wide cohort study. Rheumatology (Oxford). 2019 May 16
Kannangara DRW, Graham GG, Wright DFB, et al. **Individualising the Dose of Allopurinol** in Patients with Gout. Br J Clin Pharmacol. 2017 Apr 18.
Kawamura Y, Nakaoka H, Nakayama A, et al. Genome-wide association study revealed **novel loci which aggravate asymptomatic hyperuricaemia into gout**. Ann Rheum Dis. 2019 Jul 8.
Kaya MG, Uyarel H, Akpek M et al. Prognostic Value of Uric Acid in Patients With ST-Elevated **Myocardial Infarction** Undergoing Primary Coronary Intervention. Am J Cardiol. 2011 Nov 17.
Keenan T, Blaha MJ, Nasir K, et al. Relation of **Uric Acid** to Serum Levels of High-Sensitivity **C-Reactive Protein**, **Triglycerides, and High-Density Lipoprotein Cholesterol and to Hepatic Steatosis**. Am J Cardiol. 2012 Sep 10.
Kekre N, Djordjevic B, Touchie C. Spontaneous **tumour lysis syndrome**. CMAJ. 2012 Apr 10.
Keller SF, Lu N, Blumenthal KG, et al. Racial/ethnic variation and risk factors for **allopurinol-associated severe cutaneous adverse reactions**: a cohort study. Ann Rheum Dis. 2018 Apr 13.
Keenan RT. Limitations of the Current **Standards of Care for Treating Gout and Crystal Deposition in the Primary Care** Setting: A Review. Clin Ther. 2017 Jan 11.
Khanna D, Khanna PP, Fitzgerald JD, et al. 2012 American College of Rheumatology (**ACR**) guideline for management of gout. Part 2: **Therapy and antiinflammatory prophylaxis of acute gouty arthritis**. Arthritis Care Res (Hoboken). 2012 Oct;64(10):1447-61.
Khanna D, Fitzgerald JD, et al. 2012 American College of Rheumatology (**ACR**) guideline for gout management. Part 1: Systematic **nonpharmacologic and pharmacologic therapeutic approaches to hyperuricemia**. Arthritis Care Res (Hoboken). 2012 Oct;64(10):1431-46.
Kia DA, Noyce AJ, White J, et al. Mendelian randomization study shows no causal **relationship between circulating urate levels and Parkinson's** disease. Ann Neurol. 2018 Jul 16.
Kienhorst LB, Janssens HJ, Fransen J, Janssen M. The **validation of a diagnostic rule for gout without joint fluid analysis**: a prospective study. Rheumatology (Oxford). 2015 Apr;54(4):609-14.
Kiltz U, Smolen J, Bardin T, et al. **Treat-to-target (T2T)** recommendations for gout. Ann Rheum Dis. 2016 Apr;76(4):632-638.
Kim HR et al. Detection of gouty arthritis of atlantoaxial joint using **dual-energy CT**. Arthritis Rheum. 2011 Dec 2.
Kim SC, Liu J, Solomon DH. Risk of **incident diabetes** in patients with gout: A cohort study. Arthritis Rheumatol. 2014 Oct 20.
Kim SC, Liu J, Solomon DH. Risk of incident **atrial fibrillation** in gout: a cohort study. Ann Rheum Dis. 2016 Aug;75(8):1473-8.
Kim SC, Neogi T, Kang EH, et al. **Cardiovascular Risks** of **Probenecid Versus Allopurinol** in Older Patients With Gout. J Am Coll Cardiol. 2018 Mar 6;71(9):994-1004.
Kimura K, Hosoya T, Uchida S, et al. **Febuxostat Therapy for Patients With Stage 3 CKD and Asymptomatic Hyperuricemia**: A Randomized Trial. Am J Kidney Dis. 2018 Aug 31.
Kivity S, Kopel E, Maor E, et al. Association of Serum Uric Acid and **Cardiovascular Disease** in Healthy Adults. Am J Cardiol. 2013 Jan 23.
Klauser AS, Halpern EJ, Strobl S, et al. Dual-Energy Computed Tomography **Detection of Cardiovascular Monosodium Urate Deposits** in Patients With Gout. JAMA Cardiol. 2019 Sep 11.
Ko T, Tsai C, Chen S, et al. Use of **HLA-B*58:01 genotyping** to prevent **allopurinol** induced severe cutaneous adverse reactions in Taiwan: national prospective cohort study. BMJ 2015;351:h4848
Kobylecki CJ, Nordestgaard BG, Afzal S. **Plasma urate and risk of Parkinson's disease**: a Mendelian randomization study. Ann Neurol. 2018 Jul 16.
Kobylecki CJ, Vedel-Krogh S, Afzal S, et al. **Plasma urate, lung function and chronic obstructive pulmonary disease**: a Mendelian randomisation study in 114 979 individuals from the general population. Thorax. 2017 Nov 29.
Krasnokutsky S, Oshinsky C, Attur M, et al. **Serum Urate Levels** Predict Joint Space Narrowing in Non-gout Patients with Medial **Knee Osteoarthritis**. Arthritis Rheumatol. 2017 Feb 19
Krishnan E, Svendsen K, et al. MRFIT Research Group. Long-term cardiovascular mortality among middle-aged men with gout. Arch Intern Med. 2008 May 26;168(10):1104-10. Among middle-aged men, a diagnosis of gout accompanied by an elevated uric acid level imparts significant independent CVD mortality risk.
Krishnan E. Hyperuricemia and **incident heart failure**. Circ Heart Fail. 2009;2:556 –562.
Krishnan E, Lingala B, Bhalla V. **Low-level lead exposure** and the prevalence of gout: an observational study. Ann Intern Med. 2012 Aug 21;157(4):233-41.
Krishnan E. **Chronic kidney disease and the risk for incident gout** among middle aged men: A seven-year prospective observational study. Arthritis Rheum. 2013 Aug 27.
Kuo CF, Chou IJ, See LC, et al. **Urate-lowering treatment and risk of total joint replacement in patients with gout**. Rheumatology (Oxford). 2018 Jul 27.
Kuo CF, Grainge MJ, See LC, et al. **Familial aggregation** of gout and relative **genetic and environmental contributions**: a nationwide population study in Taiwan. Ann Rheum Dis. 2013 Nov 21

Kuo CF, Grainge MJ, Mallen C, et al. **Rising burden of gout in the UK** but continuing suboptimal management: a nationwide population study. Ann Rheum Dis. 2014 Jan 15.

Kuo CF, Grainge MJ, Mallen C, et al. Eligibility for and **prescription of urate-lowering treatment** in patients with incident gout in England. JAMA. 2014 Dec 24-31;312(24):2684-6.

Kuo CF, Grainge MJ, Mallen C, et al. **Rising burden of gout in the UK** but continuing suboptimal management: a nationwide population study. Ann Rheum Dis. 2015 Apr; 74(4):661-7.

Kuo CF, Grainge MJ, Mallen C, et al. Effect of **allopurinol on all-cause mortality** in adults with incident gout: propensity score-matched landmark analysis. Rheumatology (Oxford). 2015 Jul 12.

Kuo CF, Grainge MJ, Mallen C, et al. **Comorbidities** in patients with gout prior to and following diagnosis: case-control study. Ann Rheum Dis. 2016 Jan;75(1):210-7.

Kydd AS, Seth R, Buchbinder R, et al. **Uricosuric medications for chronic gout**. Cochrane Database Syst Rev. 2014 Nov 14;11:CD010457. There was moderate-quality evidence that there is probably no important difference between benzbromarone and allopurinol at achieving serum urate normalisation, but that benzbromarone is probably more successful than probenecid at achieving serum urate normalisation in people with gout. There is some uncertainty around the effect estimates, based on low-quality evidence from only one or two trials, on the number of acute gout attacks, the number of withdrawals due to adverse events or the total number of participants experiencing adverse events when comparing benzbromarone with allopurinol. However, when compared with probenecid, benzbromarone resulted in fewer withdrawals due to adverse events and fewer participants experiencing adverse events. Low-quality evidence from one small study indicated uncertain effects in the incidence of acute gout attacks when comparing probenecid with allopurinol therapy. We downgraded the evidence because of a possible risk of performance and other biases and imprecision.

Larsen KS, Pottegård A, Lindegaard HM, et al. Effect of **Allopurinol on Cardiovascular Outcomes** in Hyperuricemic patients A Cohort Study. Am J Med. 2015 Nov 14.

Larsson SC, Carlström M. **Coffee consumption and gout**: a Mendelian randomisation study. Ann Rheum Dis. 2018 Oct;77(10):1544-1546.

Latourte A, Soumaré A, Bardin T, et al. **Uric acid and incident dementia** over 12 years of follow-up: a population-based cohort study. Ann Rheum Dis. 2017 Jul 28.

Lessing JN, Mathias PC, Pierce RG. A Tincture of **Time-Latent Crystal Formation** and Clinical Decision-Making in Acute Gout: A Teachable Moment. JAMA Intern Med. 2015 Dec 14:1-2.

Levy GD, Rashid N, Niu F, Cheetham TC. Effect of **urate-lowering therapies on renal disease** progression in patients with hyperuricemia. J Rheumatol 2014; Apr 1.

LeWinter MM. Clinical practice. **Acute pericarditis**. N Engl J Med. 2014 Dec 18;371(25):2410-6.

Li X, Meng X, Timofeeva M, et al. **Serum uric acid levels** and **multiple health outcomes**: umbrella review of evidence from observational studies, randomised controlled trials, and Mendelian randomisation studies. BMJ. 2017 Jun 7;357:j2376.

Li X, Meng X, Spiliopoulou A, et al. MR-PheWAS: exploring the causal effect of **SUA level on multiple disease outcomes** by using genetic instruments in UK Biobank. Ann Rheum Dis. 2018 Jul;77(7):1039-1047.

Lilly LS. Treatment of **acute and recurrent idiopathic pericarditis**. Circulation. 2013 Apr 23;127(16):1723-6.

Lim SY, Lu N, Choi HK. **Septic arthritis** in gout patients: a population-based cohort study. Rheumatology (Oxford). 2015 Jul 12.

Lim SY, Lu N, Oza A, et al. **Trends in Gout and Rheumatoid Arthritis** Hospitalizations in the United States, 1993-2011. JAMA. 2016 Jun 7;315(21):2345-7.

Lin CW, Huang WI, Chao PH, et al. Risk **of cutaneous adverse reactions associated with allopurinol or febuxostat** in real-world patients: A nationwide study. Int J Clin Pract. 2019 Jan 25:e13316.

Lin TM, Chi JE, Chang CC, et al. Do **etoricoxib and indometacin** have similar effects and safety for gouty arthritis? A meta-analysis of randomized controlled trials. J Pain Res. 2018 Dec 19;12:83-91.

Liu P, Chen Y, Wang B, Zhang F, Wang D, Wang Y. **Allopurinol** treatment **improves renal function** in patients with type 2 diabetes and asymptomatic hyperuricemia: a three years of randomized parallel-controlled study. Clin Endocrinol (Oxf). 2014 Nov 17.

Lotrionte M, Biondi-Zoccai G, Imazio M, et al. International collaborative systematic review of controlled clinical trials on pharmacologic treatments for **acute pericarditis** and its recurrences. Am Heart J. 2010 Oct;160(4):662-70.

Lu N, Dubreuil M, Zhang Y, et al. **Gout and the risk of Alzheimer's disease**: a population-based, BMI-matched cohort study. Ann Rheum Dis. 2015 Mar 4.

Major TJ, Gow P, Topless RK, et al. **Evaluation of the diet wide contribution to serum urate levels**: meta-analysis of population based cohorts. BMJ 2018;363:k3951.

Mack Diana R, Cahoon William D, Jr, Lowe Denise K. Colchicine for the **Primary Prevention of the Postpericardiotomy Syndrome**. Articles Ahead of Print published on 1 June 2011, DOI 10.1345/aph.1Q112. Ann Pharmacother ;45:803-806.

Makam AN, John Boscardin W, Miao Y, et al. Risk of **Thiazide-Induced** Metabolic Adverse Events in Older Adults. J Am Geriatr Soc. 2014 May 13.

Mandell BF. Q: Should patients with gout avoid **thiazides** for hypertension? Cleve Clin J Med. 2014 Feb;81(2):83-6.

Matsuo H, Yamamoto K, Nakaoka H, et al. **Genome-wide association study** of clinically defined gout identifies multiple risk loci and its association with clinical subtypes. Ann Rheum Dis. 2016 Apr;75(4):652-9.

McAdams DeMarco MA et al. **Diuretic use**, increased serum urate levels, and risk of incident gout in a population-based study of adults with hypertension: The Atherosclerosis Risk in Communities cohort study. Arthritis Rheum 2012 Jan; 64:121.

McAdams-Demarco MA, Maynard JW, Baer AN, et al. A **urate gene-by-diuretic interaction** and gout risk in participants with hypertension: results from the ARIC study. Ann Rheum Dis. 2012 Jun 29.

McAlindon TE, LaValley MP, Harvey WF, et al. Effect of **intra-articular triamcinolone vs saline** on knee cartilage volume and pain in patients with knee osteoarthritis. A randomized clinical trial. JAMA 2017;317:1967-75.

Medical Letter. **Drugs for Gout**. Volume 56, Issue 1438. March 17, 2014. Page 22-24. Updated **Mar 2019**.

Medsafe Feb/18: is highlighting a possible risk of gout or **gout-like symptoms with the use of dabigatran**. In September 2017 a report of aggravation of gout after starting treatment with dabigatran was received by the Centre for Adverse Reactions Monitoring (CARM). The patient experienced a marked increase in episodes of gout after starting dabigatran and improved after treatment with dabigatran was stopped, without other intervention.

Merola JF, Wu S, Han J. et al. **Psoriasis, psoriatic arthritis** and risk of gout in US men and women. Ann Rheum Dis. 2015 Aug;74(8):1495-500.

Meurin P, Lelay-Kubas S, Pierre B, et al; French Society of Cardiology. **Colchicine for postoperative pericardial effusion**: a multicentre, double-blind, randomised controlled trial. Heart. 2015 Jun 15.

Miao Yan, et al. Effect of a Reduction in Uric Acid on Renal Outcomes During **Losartan** Treatment: A Post Hoc Analysis of the Reduction of Endpoints in Non-Insulin-Dependent Diabetes Mellitus With the Angiotensin II Antagonist Losartan Trial (Renaal). Hypertension. 2011

Miao Y, Ottenbros SA, Laverman GD, et al. Effect of a reduction in uric acid on renal outcomes during losartan treatment: a post hoc analysis of the reduction of endpoints in non-insulin-dependent diabetes mellitus with the Angiotensin II Antagonist Losartan Trial. (RENAAL) Hypertension. 2011 Jul;58(1):2-7.

Mogensen UM, Køber L, Jhund PS, et al; **PARADIGM-HF** Investigators and Committees. **Sacubitril/valsartan reduces serum uric acid** concentration, an independent predictor of adverse outcomes in PARADIGM-HF. Eur J Heart Fail. 2017 Nov 30.

Moon KW, Kim J, Kim JH, et al. Risk factors for acute kidney injury by **non-steroidal anti-inflammatory drugs** in patients with hyperuricaemia. Rheumatology (Oxford). 2011 Oct 22.

Naredo E, Uson J, Jiménez-Palop M, et al. **Ultrasound**-detected musculoskeletal urate crystal deposition: which joints and what findings should be assessed for diagnosing gout? Ann Rheum Dis. 2014 Aug;73(8):1522-8.

Ndrepepa G, Braun S, Haase HU et al. Prognostic Value of Uric Acid in Patients With **Acute Coronary Syndromes**. Am J Cardiol. 2012 Feb 9.

Neogi Tuhina, **Gout**. N Engl J Med 2011; 364:443-452.

Neogi T, George J, Rekhraj S, et al. Are either or both hyperuricemia and xanthine oxidase directly **toxic to the vasculature**? A critical appraisal. Arthritis Rheum. 2011 Sep 27. doi: 10.1002/art.33369.

Neogi T, Jansen TL, Dalbeth N, et al. 2015 **Gout classification criteria: an American College of Rheumatology (ACR) /European League Against Rheumatism (EULAR)** collaborative initiative. Ann Rheum Dis. 2015 Oct;74(10):1789-98.

Neogi T. **Gout**. Ann Intern Med. 2016 Jul 5;165(1):ITC1-ITC16.

Neogi T, Dalbeth N, Stamp L, et al. **Renal dosing of allopurinol** results in suboptimal gout care. Ann Rheum Dis. 2016 Aug 31.

Newberry SJ, FitzGerald JD, Motala A, et al. **Diagnosis of gout**: a systematic review in support of an American College of Physicians (**ACP**) clinical practice guideline. Ann Intern Med. 2016. [Epub ahead of print]. doi:10.7326/M16-0462

NICE: National Institute for Health and Care Excellence (**NICE**). **Pegloticase** for treating severe debilitating chronic tophaceous gout. London (UK): National Institute for Health and Care Excellence (NICE); 2013 Jun.

Nidorf SM, Eikelboom JW, Budgeon CA, et al. Low-dose **colchicine for secondary prevention of cardiovascular disease**. J Am Coll Cardiol. 2013 Jan 29;61(4):404-10.

Nielsen SM, Bartels EM, Henriksen M, et al. **Weight loss** for overweight and obese individuals with gout: a systematic review of longitudinal studies. Ann Rheum Dis. 2017 Nov;76(11):1870-1882.

Noel N, Wechsler B, Nizard J, et al. **Behcet's disease** and pregnancy. Arthritis Rheum. 2013 Jun 18. (**colchicine** seems safe)

Noman A, Ang DS, Ogston S, et al. Effect of high-dose allopurinol on exercise in patients with **chronic stable angina**: a randomised, placebo controlled crossover trial. Lancet. 2010 Jun 7.

Noone DG, Marks SD. **Hyperuricemia** is Associated with Hypertension, Obesity, and Albuminuria in Children with Chronic Kidney Disease. J Pediatr. 2012 Jul 17.

Norrid SE, Oliphant CS. **Colchicine** for the Treatment of Acute and Recurrent **Pericarditis**. Ann Pharmacother. 2014 May 19;48(8):1050-1054.

Noss MR, Saguil A. Gout: **Diagnosis and Management**. Am Fam Physician. 2017 Nov 15;96(10):668-670.

Ogdie A, Taylor WJ, et al. **Imaging modalities for the classification of gout**: systematic literature review and meta-analysis. Ann Rheum Dis. 2015 Oct;74(10):1868-74.

Ogdie A, Taylor WJ, Neogi T, et al. Performance of **Ultrasound in the Diagnosis** of Gout in a Multi-Center Study: Comparison with Monosodium Urate Crystal Analysis as the Gold Standard. Arthritis Rheumatol. 2016 Oct 16.

Opstelten W, Klaasen R. **A swollen red finger**. BMJ. 2017 Feb 16;356:j734.

Ozen S, Demirkaya E, Erer B, et al. **EULAR** recommendations for the management of **familial Mediterranean fever**. Ann Rheum Dis. 2016 Apr;75(4):644-51.

Paik JM, Kim SC, Feskanich D, et al. **Gout and Risk of Fracture** in Women: A Prospective Cohort Study. Arthritis Rheumatol. 2016 Sep 2

Palmer TM, Nordestgaard BG, Benn M, et al. Association of plasma **uric acid with ischaemic heart disease** and **blood pressure**: mendelian randomisation analysis of two large cohorts. BMJ. 2013 Jul 18;347:f4262.

Papanicolas LE, Hakendorf P, Gordon DL. **Concomitant septic arthritis** in crystal monoarthritis. J Rheumatol. 2012 Jan;39(1):157-60.

Park B, Lee HA, Lee SH, et al. Association Between Serum Levels of **Uric Acid and Blood Pressure** Tracking in Childhood. Am J Hypertens. 2017 Mar 14.

Pascual E, Andrés M, Vela P. Gout treatment: should we aim for **rapid crystal dissolution**? Ann Rheum Dis. 2013 Jan 15.

Pascual E, Sivera F, Andrés M. **Managing Gout in the Patient with Renal Impairment**. Drugs Aging. 2018 Feb 13.

Pearle MS, Goldfarb DS, Assimos DG, et al; **American Urological Assocation. Medical management of kidney stones**: AUA guideline. J Urol. 2014 Aug;192(2):316-24.

Perez-Ruiz F, Jansen TL, Tausche AK, et al. Reassessing the Safety Profile of **Lesinurad in Combination with Xanthine Oxidase Inhibitor** Therapy. Rheumatol Ther. 2019 Mar;6(1):101-108.

Perez-Ruiz F, Martínez-Indart L, Carmona L, et al. **Tophaceous gout** and high level of hyperuricaemia are both associated with increased risk of **mortality** in patients with gout. Ann Rheum Dis. 2014 Jan 1;73(1):177-82

Perez-Ruiz F, Sundy JS, Miner JN, et al; RDEA594-203 Study Group. **Lesinurad in combination with allopurinol**: results of a phase 2, randomised, double-blind study in patients with gout with an inadequate response to allopurinol. Ann Rheum Dis. 2016 Jun;75(6):1074-80.

Pharmacist's Letter. **Febuxostat** (Uloric). Nov, 2010.

Phipps-Green AJ, Merriman ME, Topless R, et al. **Twenty-eight loci** that influence serum urate levels: analysis of association with gout. Ann Rheum Dis. 2016 Jan;75(1):124-30.

Pluta RM, Shmerling RH, Burke AE, Livingston EH. JAMA **patient page. Gout**. JAMA. 2012 Nov 28;308(20):2161.

Poiley J, Steinberg AS, Choi YJ, et al. A Randomized, Double-Blind, Active- and Placebo-Controlled Efficacy and Safety Study of **Arhalofenate** for Reducing Flare in Patients With Gout. Arthritis Rheumatol. 2016 Aug;68(8):2027-34.

Pottecher P, Martz P, Ornetti P. **Paraparesis revealing tophaceous gout**. Arthritis Rheumatol. 2018 Feb 6.

Prasad P, Krishnan E. The Filipino **Gout-** A Review. Arthritis Care Res (Hoboken). 2013 Aug 27.

Pyo JY, Ha YJ, Song JJ, et al. **Delta neutrophil index** contributes to the differential diagnosis between acute gout attack and cellulitis within 24 hours after hospitalization. Rheumatology (Oxford). 2017 Jan 23.

Qaseem A, Dallas P, Forciea MA, et al; Clinical Guidelines Committee of the American College of Physicians. Dietary and pharmacologic management to **prevent recurrent nephrolithiasis** in adults: a clinical practice guideline from the american college of physicians. Ann Intern Med. 2014 Nov 4;161(9):659-67.

Qaseem A, McLean R, et al; Clinical Guidelines Committee of the American College of Physicians. **Diagnosis of acute gout**: a clinical practice guideline from the American College of Physicians (**ACP**) . Ann Intern Med. 2016. [Epub ahead of print]. doi:10 .7326/M16-0569 3.

Qaseem A, et al; Clinical Guidelines Committee of the American College of Physicians. **Management of acute and recurrent gout**: a clinical practice guideline from the American College of Physicians (**ACP**). Ann Intern Med. 2016. [Epub ahead of print]. doi:10.7326/M16-0570 4.

Rai SK, Fung TT, Lu N, et al. The **Dietary Approaches to Stop Hypertension** (**DASH**) diet, Western diet, and risk of gout in men: prospective cohort study. BMJ. 2017 May 9;357:j1794

Rainer TH, Cheng CH, Janssens HJ, et al. Oral **Prednisolone** in the Treatment of Acute Gout: A Pragmatic, Multicenter, Double-Blind, Randomized Trial. (vs indomethacin) Ann Intern Med. 2016 Feb 23.

Rees F, Jenkins W, Doherty M. Patients with gout **adhere to curative treatment if informed** appropriately: proof-of-concept observational study. Ann Rheum Dis. 2012 Jun 7.

Rho YH, Lu N, Peloquin CE, et al. Independent impact of **gout on the risk of diabetes** mellitus among women and men: a population-based, BMI-matched cohort study. Ann Rheum Dis. 2016 Jan;75(1):91-5.

Richette P, Bardin T. **Gout. Lancet. 2009** Aug 17. [Epub ahead of print]

Richette P, Bardin T. **Purine-rich foods**: an innocent bystander of gout attacks? Ann Rheum Dis. 2012 Sep;71(9):1435-6.

Richette P, Clerson P, Périssin L, et al. **Revisiting comorbidities** in gout: a cluster analysis. Ann Rheum Dis. 2015 Jan;74(1):142-7.

Richette P, Clerson P, Bouée S, et al. Identification of patients with gout: **elaboration of a questionnaire** for epidemiological studies. Ann Rheum Dis. 2015 Sep;74(9):1684-90.

Richette P, Doherty M, Pascual E, et al. **2016 updated EULAR** evidence-based recommendations for the **management of gout**. Ann Rheum Dis. 2016 Jul 25

Richette P, Doherty M, Pascual E, et al. **2018 updated** European League Against Rheumatism evidence-based recommendations for the diagnosis of gout. Ann Rheum Dis. 2019 Jun 5.

Robbins RC, Edison JD. Images in Clinical Medicine. **Milk of Urate Bulla**. N Engl J Med. 2016 Jul 14;375(2):162.

Roddy E, Mallen CD Doherty M. **Gout**. BMJ. 2013;347:f5648.

Rosenthal AK, Ryan LM. **Calcium Pyrophosphate** Deposition Disease. N Engl J Med.2016 Jun 30;374(26):2575-2584.

Saag KG, Whelton A, Becker MA, et al. Impact of **Febuxostat** on Renal Function in Gout Subjects with Moderate-to-Severe Renal Impairment. Arthritis Rheumatol. 2016 Feb 19.

Saag KG, Fitz-Patrick D, Kopicko J, et al. **Lesinurad Combined With Allopurinol**: Randomized,Double-Blind, Placebo-Controlled Study in Gout Subjects With Inadequate Response to Standard of Care Allopurinol (A US-based Study). Arthritis Rheumatol. 2016 Aug 26.

SampsonAL, Singer RF,WaltersGD.**Uric acid lowering therapies for preventing or delaying the progression of chronic kidney disease**. Cochrane Database of Systematic Reviews 2017, Issue 10. Art. No.: CD009460. There is limited data which suggests uric acid lowering therapy may prevent progression of chronic kidney disease but the conclusion is very uncertain. Benefits were not observed at all time points and study quality was generally low. Larger studies are required to study the effect of uric acid lowering therapy on CKD progression. Three ongoing studies will hopefully provide much needed high quality data

Schlesinger N, Mysler E, Lin HY, et al. **Canakinumab** reduces the risk of acute gouty arthritis flares during initiation of allopurinol treatment: results of a double-blind, randomised study. Ann Rheum Dis. 2011 Jul;70(7):1264-71.

Schlesinger N, Alten RE, Bardin T, et al. **Canakinumab** for acute gouty arthritis in patients with limited treatment options: results from two randomised, multicentre, active-controlled, double-blind trials and their initial extensions. Ann Rheum Dis. 2012 Nov;71(11):1839-48.

Seth R, Kydd AS, Buchbinder R, et al. **Allopurinol for chronic gout**. Cochrane Database Syst Rev. 2014 Oct 14;10:CD006077. Our review found low- to moderate-quality evidence indicating similar effects on withdrawals due to AEs and SAEs and incidence of acute gout attacks when allopurinol (100 to 600 mg daily) was compared with placebo, benzbromarone (100 to 200 mg daily) or febuxostat (80 mg daily). There was moderate-quality evidence of little or no difference in the proportion of participants achieving target serum urate when allopurinol was compared with benzbromarone. However, allopurinol seemed more successful than placebo and may be less successful than febuxostat (80 mg daily) in achieving a target serum urate level (6 mg/dL or less; 0.36 mmol/L or less) based on moderate- to low-quality evidence. Single studies reported no difference in pain reduction when allopurinol (300 mg daily) was compared with placebo over 10 days, and no difference in tophus regression when allopurinol (200 to 300 mg daily) was compared with febuxostat (80 mg daily). None of the trials reported on function, health-related quality of life or participant global assessment of treatment success, where further research would be useful.

Shahinfar S, Simpson RL, Carides AD, et al. Safety of **losartan in hypertensive patients with thiazide-induced hyperuricemia**. Kidney Int 1999;56:1879-1885.

Shekelle PG, Newberry SJ, FitzGerald JD, Motala A, O'Hanlon CE, Tariq A, et al. **Management of gout**: a systematic review in support of an American College of Physicians (**ACP**) clinical practice guideline. Ann Intern Med. 2016. [Epub ahead of print]. doi:10.7326/M16-0461

Shmerling RH. **Management of gout**: a 57-year-old man with a history of podagra, hyperuricemia, and mild renal insufficiency. JAMA. 2012 Nov 28;308(20):2133-41.

Sigurdardottir V, Drivelegka P, Svärd A, et al. **Work disability in gout**: a population-based case-control study. Ann Rheum Dis. 2017 Nov 23.

Singh JA, Yang S, Strand V, et al. **Validation of pain and patient global scales** in chronic gout: data from two randomised controlled trials. Ann Rheum Dis. 2011 Jul;70(7):1277-81.

Singh JA. When gout goes to the **heart**: does gout equal a **cardiovascular disease risk factor**? Ann Rheum Dis. 2015 Apr; 74(4):631-4.

Singh JA, Yu S. **Allopurinol and the risk of stroke** in older adults receiving medicare. BMC Neurol. 2016 Sep 7;16(1):164.

Singh JA, Yu S. **Allopurinol and the risk of atrial fibrillation** in the elderly: a study using Medicare data. Ann Rheum Dis. 2016 May 10.

Singh JA, Yu S. Are **allopurinol** dose and duration of use **nephroprotective** in the elderly? A Medicare claims study of allopurinol use and incident renal failure. Ann Rheum Dis. 2016 Jun 13.

Singh JA, Cleveland JD. Comparative effectiveness of **allopurinol versus febuxostat** for **preventing incident renal disease** in older adults: an analysis of Medicare claims data. Ann Rheum Dis. 2017 Oct;76(10):1669-1678.

Singh JA, Cleveland JD. Gout and healthcare utilization and **complications after hip arthroplasty**: a cohort study using the US National Inpatient Sample (NIS). Clin Rheumatol. 2019 Jan 22.

Singh JA, Cleveland JD. Gout is associated with **increased healthcare utilization after knee arthroplasty**. Ann Rheum Dis. 2019 Aug;78(8):1146-1148.

Singh JA, Cleveland JD. Use of **urate-lowering therapies** is **not associated** with an increase in **the risk of incident dementia** in older adults. Ann Rheum Dis. 2018 Aug;77(8):1243-1245.

Sivera F, Andrés M, et al. **Multinational evidence-based recommendations** for the diagnosis & management of gout: integrating systematic literature review and expert opinion of a broad panel of rheumatologists in the 3e initiative. Ann Rheum Dis. 2014 Feb 1;73(2):328-35

Sircar D, Chatterjee S, Waikhom R, et al. Efficacy of **Febuxostat** for **Slowing the GFR Decline** in Patients With CKD and Asymptomatic Hyperuricemia: A 6-Month, Double-Blind, Randomized, Placebo-Controlled Trial. Am J Kidney Dis. 2015 Jul 30.

Slobodnick A, Shah B, Krasnokutsky S, et al. **Update on colchicine**, 2017. Rheumatology (Oxford). 2018 Jan 1;57(suppl_1):i4-i11.

Smith E, Hoy D, Cross M, et al. The **global burden of gout**: estimates from the Global Burden of Disease 2010 study. Ann Rheum Dis. 2014 Aug;73(8):1470-6

Snyder MJ, Bepko J, White M. **Acute pericarditis**: diagnosis and management. Am Fam Physician. 2014 Apr 1;89(7):553-60.

Solomon DH, Liu CC, Kuo IH, et al. Effects of **colchicine** on risk of **cardiovascular** events and mortality among patients with gout: a cohort study using electronic medical records linked with Medicare claims. Ann Rheum Dis. 2016 Sep;75(9):1674-9.

Solomon DH, Glynn RJ, MacFadyen JG, et al. Relationship of **Interleukin-1β Blockade With Incident Gout and Serum Uric Acid Levels**: Exploratory Analysis of a Randomized Controlled Trial. (Canakinumab) Ann Intern Med. 2018 Sep 18:1-8.

Spencer K, Carr A, Doherty M. **Patient and provider barriers** to effective management of gout in general practice: a qualitative study. Ann Rheum Dis. 2012 Sep;71(9):1490-5.

Sriranganathan MK, Vinik O, Bombardier C, et al. **Interventions for tophi in gout**. Cochrane Database Syst Rev. 2014 Oct 20;10:CD010069. This study showed pegloticase is probably beneficial in the management of tophi in gout, in terms of resolution of tophi, but with a high risk of adverse infusion reactions. However, there is a need for more RCT data considering other interventions, including surgical removal of tophi.

Stamp LK, O'Donnell JL, Zhang M, et al. Using **allopurinol above the dose based on creatinine clearance** is effective and safe in patients with chronic gout, including those with renal impairment. Arthritis Rheum. 2011 Feb;63(2):412-21.

Stamp LK, Taylor WJ, Jones PB, et al. **Starting dose** is a risk factor for **allopurinol hypersensitivity syndrome**: A proposed safe starting dose of allopurinol. Arthritis Rheum. 2012 Apr 5.

Stamp LK, O'Donnell JL, Frampton C, Drake J, Zhang M, Chapman PT. Clinically insignificant effect of **supplemental vitamin C** on serum urate in patients with gout; A pilot randomised controlled trial. Arthritis Rheum. 2013 May 16.

Stamp LK, Chapman PT, Barclay ML, et al. A randomised controlled trial of the efficacy and safety of **allopurinol dose escalation to achieve target serum urate** in people with gout. Ann Rheum Dis. 2017 Mar 17.

Stamp LK, Chapman PT, Barclay M, et al. **Allopurinol dose escalation** to achieve serum urate below 6 mg/dL: an open-label extension study. Ann Rheum Dis. 2017 Dec;76(12):2065-2070.

Stamp LK, Barclay ML. How to **prevent allopurinol hypersensitivity** reactions? Rheumatology (Oxford). 2018 Jan 1;57(suppl_1):i35-i41.

Stamp LK, Merriman T, Frampton C, et al. **Plasma oxypurinol as a measure of adherence** in clinical trials. Ann Rheum Dis. 2018 Feb;77(2):313-314.

Sultan AA, Muller S, Whittle R, Roddy E, Mallen C, Clarson L. **Venous thromboembolism** in patients with gout and the impact of hospital admission, disease duration and urate-lowering therapy. CMAJ. 2019 Jun 3;191(22):E597-E603

Sultan AA, Whittle R, Muller S, et al. **Risk of fragility fracture among patients with gout and the effect of urate-lowering therapy**. CMAJ. 2018 May 14;190(19):E581-E587.

Sundy JS, Baraf HS, Yood RA, et al. Efficacy and tolerability of **pegloticase** for the treatment of chronic gout in patients refractory to conventional treatment: two randomized controlled trials. JAMA. 2011 Aug 17;306(7):711-20.

Talwar S, Selvam MS, Makhija N, et al. Effect of administration of **allopurinol** on postoperative outcomes in patients undergoing **intracardiac repair of tetralogy of Fallot**. J Thorac Cardiovasc Surg. 2018 Jan;155(1):335-343.

Tamariz L, Agarwal S, Soliman EZ, et al. Association of Serum **Uric Acid With Incident Atrial Fibrillation** (from the Atherosclerosis Risk in Communities [ARIC] Study). Am J Cardiol. 2011 Aug 17.

Tausche AK, Panzner I, Aust D; et al. **Disabling gout**. Lancet. 2010 Sep 25;376(9746):1093.

Tausche AK, Alten R, Dalbeth N, et al. **Lesinurad monotherapy** in gout patients **intolerant to a xanthine oxidase inhibitor**: a 6 month phase 3 clinical trial and extension study. Rheumatology (Oxford). 2017 Dec 1;56(12):2170-2178.

Taylor TH, Mecchella JN, Larson RJ, et al. Initiation of **allopurinol at first medical contact for acute attacks** of gout: a randomized clinical trial. Am J Med. 2012 Nov;125(11):1126-1134.e7.

Taylor WJ, Fransen J, Dalbeth N, et al. **Performance of classification criteria for gout in early and established disease**. Ann Rheum Dis. 2016 Jan;75(1):178-82.

Teng GG, Ang LW, Saag KG, et al. **Mortality due to coronary heart disease and kidney disease** among middle-aged and elderly men and women with gout in the Singapore Chinese Health Study. Ann Rheum Dis. 2012 Jun;71(6):924-8.

Teng GG, Pan A, Yuan JM, Koh WP. Food sources of **protein** and risk of incident gout in the Singapore Chinese Health Study. Arthritis Rheumatol. 2015 Mar 25.

Terkeltaub RA, Furst DE, Digiacinto JL, et al. Evidence basis of a novel **colchicine dose reduction algorithm** to predict & prevent colchicine toxicity in the presence of **P-gp/CYP P450 3A4 inhibitors**. Arthritis Rheum. 2011 Apr 7. doi: 10.1002/art.30389.

Terkeltaub RA, Furst DE, Bennett K, et al. High-vs **low-dosing of oral colchicine** for early acute gout flare: Twenty-four hour outcome results of the first randomized, placebo-controlled, dose comparison colchicine trial. Arthritis Rheum. 2010 Jan 21.
Thanassoulis George; Brophy James M.; Richard Hugues; et al. Gout, Allopurinol Use, and **Heart Failure** Outcomes. Arch Intern Med. 2010;170(15):1358-1364.
Thomson S, Urbanski S, MacMullan P. **Gouty tophus** as an unusual cause of talus fracture. Arthritis Rheumatol. 2017 Mar 21.
Trifirò G, Morabito P, Cavagna L, et al. **Epidemiology of gout and hyperuricaemia in Italy** during the years 2005-2009: a nationwide population-based study. Ann Rheum Dis. 2012 Jun 26.
Turak O, Canpolat U, Ozcan F, et al. Usefulness of **Preprocedural Serum Uric Acid** Level to Predict **Restenosis of Bare Metal Stents**. Am J Cardiol. 2013 Oct 2.
Vaduganathan M, Greene SJ, Ambrosy AP, et al; **EVEREST** trial investigators. Relation of **Serum Uric Acid Levels** and Outcomes Among Patients Hospitalized for Worsening **Heart Failure** With Reduced Ejection Fraction (from the Efficacy of Vasopressin Antagonism in Heart Failure Outcome Study With Tolvaptan Trial). Am J Cardiol. 2014 Sep 16.
Valbusa F, Bertolini L, Bonapace S, et al. Relation of Elevated Serum Uric Acid Levels to Incidence of **Atrial Fibrillation** in Patients With Type 2 Diabetes Mellitus. Am J Cardiol. 2013 May 11.
Vazirpanah N, Ottria A, van der Linden Met al. **mTOR inhibition by metformin** impacts monosodium urate crystal-induced inflammation and cell death in gout: a prelude to a new add-on therapy? Ann Rheum Dis. 2019 May;78(5):663-671.
Viazzi F, Antolini L, Giussani M, et al. **Serum Uric Acid and Blood Pressure** in Children at Cardiovascular Risk. Pediatrics. 2013 Jun 17.
Waldman B, Ansquer JC, Sullivan DR, et al. Effect of **fenofibrate on uric acid** and gout in type 2 diabetes: a post-hoc analysis of the randomised, controlled **FIELD** study. Lancet Diabetes Endocrinol. 2018 Feb 26.
Wang JY, Chen YL, Hsu CH, et al. Predictive Value of Serum Uric Acid Levels for the **Diagnosis of Metabolic Syndrome** in Adolescents. J Pediatr. 2012 May 9.
Wang HR, Fu Q, Liu Z, Li ML, Zhai SQ. A systematic review and meta-analysis of randomized controlled trials: Skin-patch of Chinese **herbal medicine for patients with acute gouty arthritis**. J Adv Nurs. 2018 Mar 25.
Wason S, Digiacinto JL, Davis MW. Effects of Grapefruit and Seville Orange Juices on the Pharmacokinetic Properties of **Colchicine** in Healthy Subjects. Clin Ther. 2012 Aug 30.
Watkins JW 4th, Seupaul RA. Are **Corticosteroids Superior to Nonsteroidal Anti-inflammatory Drugs** in the Treatment of Acute Gout? Ann Emerg Med. 2018 Mar 23.
White WB, Saag KG, Becker MA, et al. **Cardiovascular Safety** of **Febuxostat or Allopurinol** in Patients with Gout. (**CARES**) N Engl J Med. 2018 Mar 12.
Wilson JF. **Gout-In the Clinic.** Ann Intern Med. 2010 Feb 2;152(3):ITC21.
Worcester EM, Coe FL. Clinical practice. **Calcium kidney stones**. N Engl J Med. 2010 Sep 2;363(10):954-63.
Wright DF, Duffull SB, Merriman TR, et al. **Predicting allopurinol response** in patients with gout. Br J Clin Pharmacol. 2015 Oct 9.
Wright DFB, Dalbeth N, Phipps-Green AJ, et al. The impact of **diuretic use and ABCG2 genotype** on the predictive performance of a published **allopurinol dosing** tool. Br J Clin Pharmacol. 2018 Jan 17.
van Durme CM, Wechalekar MD, Buchbinder R, et al. **Non-steroidal anti-inflammatory drugs for acute gout**. Cochrane Database Syst Rev. 2014 Sep 16;9:CD010120. Limited evidence supported the use of NSAIDs in the treatment of acute gout. One placebo-controlled trial provided evidence of benefit at 24 hours and little or no harm. We downgraded the evidence due to potential selection and reporting biases, and imprecision. While these data were insufficient to draw firm conclusions, they did not conflict with clinical guideline recommendations based upon evidence from observational studies, other inflammatory arthritis and expert consensus, which support the use of NSAIDs in acute gout.Moderate-quality evidence suggested that selective COX-2 inhibitors and non-selective NSAIDs are probably equally beneficial although COX-2 inhibitors are likely to be associated with significantly fewer total and gastrointestinal adverse events. We downgraded the evidence due to an unclear risk of selection and reporting biases. Moderate-quality evidence indicated that systemic glucocorticoids and NSAIDs were also equally beneficial in terms of pain relief. There were no withdrawals due to adverse events and total adverse events were similar between groups. We downgraded the evidence due to unclear risk of selection and reporting bias. There was low-quality evidence that there was no difference in function. We downgraded the quality due to unclear risk of selection bias and imprecision.
van Durme CM, Wechalekar MD, Landewé RB. **Nonsteroidal anti-inflammatory drugs for treatment of acute gout**. JAMA. 2015 Jun 9;313(22):2276-7.
van Echteld I, Wechalekar MD, Schlesinger N, et al. **Colchicine for acute gout**. Cochrane Database Syst Rev. 2014 Aug 15;8:CD006190. Based upon only two published trials, there is low-quality evidence that low-dose colchicine is likely to be an effective treatment for acute gout. We downgraded the evidence because of a possible risk of selection and reporting biases and imprecision. Both high and low-dose colchicine improve pain when compared to placebo. While there is some uncertainty around the effect estimates, compared with placebo, high-dose but not low-dose colchicine appears to result in a statistically significantly greater number of adverse events. Therefore low-dose colchicine may be the preferred treatment option. There are no trials about the effect of colchicine in populations with comorbidities or in comparison with other commonly used treatments, such as NSAIDs and glucocorticoids.
Vargas-Santos AB, Neogi T. Management of **Gout and Hyperuricemia in CKD**. Am J Kidney Dis. 2017 Apr 26.
Vargas-Santos AB, Peloquin C, Zhang Y, Neogi T. Association of **chronic kidney disease with allopurinol use in gout treatment** [online Oct 8, 2018]. JAMA Intern Med.
Vazirpanah N, Kienhorst LBE, Van Lochem E, et al. Patients with gout have **short telomeres** compared with healthy participants: association of telomere length with flare frequency and cardiovascular disease in gout. Ann Rheum Dis. 2017 Jul;76(7):1313-1319.
Vela P, Pascual E. **Images** in clinical medicine. An **unusual tophus**. N Engl J Med. 2015 Jan 29;372(5):e6.
Yamanaka H, Tamaki S, Ide Y, et al. **Stepwise dose increase of febuxostat** is comparable with colchicine prophylaxis for the prevention of gout flares during the initial phase of urate-lowering therapy: results from **FORTUNE-1**, a prospective,multicentre randomised study. Ann Rheum Dis. 2018 Feb;77(2):270-276.
Yang CY, Chen CH, Deng ST, et al. **Allopurinol Use and Risk of Fatal Hypersensitivity Reactions**: A Nationwide Population-Based Study in Taiwan. JAMA Intern Med. 2015 Jul 20.
Zaramella P, De Salvia A, Zaninotto M, et al. **Lethal** effect of a single dose of **rasburicase in a preterm** newborn infant. Pediatrics. 2013 Jan;131(1):e309-12.
Zhang M, Solomon DH, Desai RJ, et al. Assessment of Cardiovascular Risk in Older Patients with **Gout Initiating Febuxostat versus Allopurinol**: A Population-Based Cohort Study. Circulation. 2018 Jun 13.
Zhang T, Pope JE. **Cardiovascular effects of urate-lowering therapies** in patients with chronic gout: a systematic review and meta-analysis. Rheumatology (Oxford). 2017 Mar 30.
Zhang Y, Chen C, Choi H, et al. **Purine-rich foods intake** and recurrent gout attacks. Ann Rheum Dis. 2012 May 30.
Zhang Y, Neogi T, Chen C, et al. **Cherry consumption** and decreased risk of recurrent gout attacks. Arthritis and Rheumatism. December 2012. 6(12);4004-4011.
Zhang Y, Neogi T, Chen C, et al. **Low-dose aspirin** use and recurrent gout attacks. Ann Rheum Dis. 2014 Feb 1;73(2):385-90
Zhang YK, Yang H, Zhang JY, et al. Comparison of intramuscular compound **betamethasone** and oral **diclofenac** sodium in the treatment of acute attacks of gout. Int J Clin Pract. 2014 Jan 29.
Zhang Y, Peloquin C, Dubreuil M, et al. **Sleep Apnea** nd the Risk of Incident Gout: A Population-Based Body Mass Index-Matched Cohort Study. Arthritis Rheumatol. 2015 Oct 19.
Zhao Y, Xu L, Tian D, et al. Effects of **sodium-glucose co-transporter 2 (SGLT2) inhibitors on serum uric acid level**: A meta-analysis of randomized controlled trials. Diabetes Obes Metab. 2017 Aug 28.
Zhu Y, Pandya BJ, Choi HK. Prevalence of **gout and hyperuricemia** in the US general population: The National Health and Nutrition Examination Survey 2007-2008. Arthritis Rheum. 2011 Oct;63(10):3136-41. doi: 10.1002/art.30520.
Zhu Y, Pandya BJ, Choi HK. **Comorbidities of Gout** and Hyperuricemia in the US General Population: NHANES 2007-2008. Am J Med. 2012 May 23.

Web Sites:

American College of Rheumatology: Gout www.rheumatology.org/public/factsheets/diseases_and_conditions/gout.asp?aud=pat

Arthritis Foundation: Gout www.arthritis.org/disease-center.php?disease_id=42

National Institute of Arthritis and Musculoskeletal and Skin Diseases: Questions and Answers About Gout www.niams.nih.gov/Health_Info/Gout/default.asp

Gout and Uric Acid Education Society www.gouteducation.org/

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26 Jordan KM, Cameron JS, Snaith M, et al; British Society for Rheumatology and **British** Health Professionals in Rheumatology Standards Guideline for the **Management of Gout**. Rheumatology (Oxford). **2007** Aug;46(8):1372-4. Epub 2007 May 23. http://rheumatology.oxfordjournals.org/cgi/reprint/kem056av1
27 Underwood M. Sugary drinks, fruit, and increased risk of gout. BMJ. 2008 Feb 9;336(7639):285-6.
Choi Hyon K.; Willett Walter; Curhan Gary. Fructose-Rich Beverages and Risk of Gout in Women. JAMA. 2010;0(2010):jama.2010.1638.
28 Lee MH, Graham GG, Williams KM, Day RO. A benefit-risk assessment of benzbromarone in the treatment of gout. Was its withdrawal from the market in the best interest of patients? Drug Saf. 2008;31(8):643-65.

Peterson GM, Sugden JE. Educational program to improve the dosage prescribing of allopurinol. Med J Aust. 1995 Jan 16;162(2):74-7.
Reinders MK, van Roon EN, et al. Efficacy and tolerability of urate lowering drugs in gout: a randomised controlled trial of benzbromarone versus probenecid after failure of allopurinol. Ann Rheum Dis. 2008 Apr 23. [Epub ahead of print] This study demonstrates a poor efficacy and tolerability profile of allopurinol 300 mg/day to attain a biochemical predefined target level of sUr </=0.30 mmol/l after 2-months treatment. In stage 2, benzbromarone 200 mg/day is more effective and better tolerated than probenecid 2000mg/day.
Reinders MK, Haagsma C, et al.. A randomised controlled trial on the efficacy and tolerability with dose-escalation of allopurinol 300-600 mg/day versus benzbromarone 100-200 mg/day in patients with gout. Ann Rheum Dis. 2008 Jul 16. [Epub ahead of print] Increase of allopurinol dosage from 300 mg to 600 mg/day and benzbromarone dosage from 100 mg to 200 mg/day according to target sUr, gives significantly higher success rates (both 78% success in sUr </=0.30 mmol/l). No significant differences in treatment success between benzbromarone and allopurinol groups were found after dosage escalation combination in relieving pain but is associated with fewer adverse effects.

GENERIC/TRADE (Strengths & formulations)	LOWEST ANTI-INFLAMMATORY, USUAL RANGE & MAXIMUM DOSE	$/30d	Class/Comments
Acetaminophen TYLENOL, g OTC ✗ (=paracetamol) Chewable tablet: 160mg ✗ ▼ Rapid-dissolving tablet: 80, 160mg ✗ ▼ Immediate release caplet/tablet: 160, 325, 500mg ✗ ▼ PL Extended release caplet: **TYLENOL ARTHRITIS** 650mg ✗ ⊗ Gelcap: 500mg ✗ ⊗ Drops: 80mg/mL ✗ ▼ Liquid: 16mg/mL, 80mg/mL, 32mg/mL ✗ ▼ Suppository: 120, 160, 325,650mg ✗ ▼ {IV: 1000mg/100ml bag} ▼ **Max NIHB is 3600mg/day.** **Caution: ingredient of many products! Unintentional duplication of use sometimes with overdose is common!**	**Lowest Anti-inflammatory:** 650mg po QID 1,300mg ER po TID **Usual Range:** 325-1000mg po TID-QID **Maximum:** 4g/day. Consider limiting dose to ≤3250mg/day, especially if elderly or chronic use. Consider limiting to ≤2600mg/day if hepatic/renal disease or chronic alcohol (≥3 drinks/day) use. **Pediatrics:** 10-15mg/kg q4-6hr; **Max**: 75mg/kg/day	$20 $25 $7-18	**NON-ANTI-INFLAMMATORY ANALGESIC** • Compared to NSAIDs/COXIBs, lowest risk for CV events & GI ulcer/bleed • Option in osteoarthritis • DI: warfarin ↑ INR with scheduled chronic use of acetaminophen. Concurrent use of isoniazid, zidovudine, or barbiturates may promote hepatotoxicity. • M: **LFTs** with chronic use & if ↑ alcohol use [Larson'05] • **Acute Overdose: hepatotoxic** (#1 cause of drug-induced transplant) >140mg/kg or >7.5g – Level within 24 hours predictive [Rumack-Matthew Nomogram 36]

Combination Product to Reduce Dyspepsia: ASPIRIN STOMACH GUARD: ASA 325/500mg & Ca^{++} Carbonate 227.5/350mg **OTC ✗** ⊗

New Drugs/Formulations:

- low-dose **diclofenac submicron** particles (**ZORVOLEX**) [Not in Canada] – 18, 35mg capsules. ↓ in particle size ↑'s surface area resulting in faster dissolution & absorption. No comparative evidence.
- low-dose **indomethacin submicron** (**TIVORBEX**) [Not in Canada] – 20, 40mg capsules. ↓ in particle size ↑'s surface area resulting in faster dissolution & absorption. No comparative evidence. Potent NSAID & ↑ AEs.
- low-dose **meloxicam** (**VIVLODEX**) [Not in Canada] – 5, 10mg capsules. ↓ in particle size ↑'s surface area resulting in faster dissolution & absorption. No comparative evidence.
- **disintegrating meloxicam** (**QMIIZ ODT**) [Not in Canada] – 7.5mg, 15mg tablets 15mg ODT bioequivalent to the 15mg conventional oral meloxicam tablet. Disintegrates rapidly; does not require administration with liquid.

Discontinued Products:

NSAIDs: Choline Mg^{++} Trisalicylate **TRILISATE**, Fenoprofen **NALFON**, Piroxicam **BREXIDOL**, Salsalate **DISALCID**, Tolmentin **TOLECTIN**.

COX-2 Inhibitors:

- Lumiracoxib **PREXIGE** 100mg daily. Discontinued October 2007. Rare severe hepatic toxicity at doses ≥200mg/day.
- Rofecoxib **VIOXX** 12.5mg (OA) to 25mg (OA/RA) daily. Discontinued September 2004. VIGOR: CV events NNH=83, GI NNT=129/8 months.
- Valdecoxib **BEXTRA** 10-20mg daily (OA, RA). Discontinued April 2005 in Canada, USA. Rare severe skin reactions e.g. exfoliative dermatitis & Stevens Johnson Syndrome.

Trials:

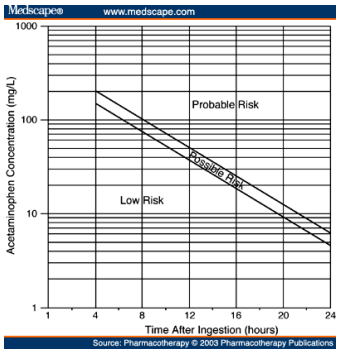
- PRECISION: CV risk of celecoxib vs ibuprofen vs naproxen http://clinicaltrials.gov/ct/show/NCT00346216?order=4 N Engl J Med. 2016 Nov 13. DOI: 10.1056/NEJMoa1611593

NSAIDS, COXIBs & OTHER ANALGESICS: Comparison Chart

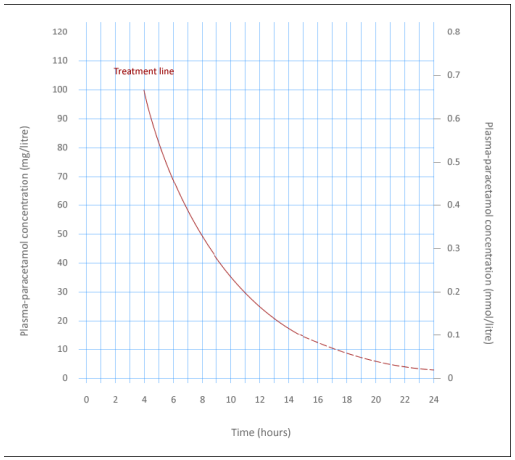
[1] Micromedex 2018
[2] Silverstein F, Faich G, Goldstein J, et al. Gastrointestinal toxicity with celecoxib versus non-steroidal anti-inflammatory drugs for osteoarthritis and rheumatoid arthritis: the **CLASS** study: A randomized controlled trial. Celecoxib Long-term Arthritis Safety Study. JAMA 2000;284:1247-55.
[3] Bombardier C, Laine L, Reicin A, et al. Comparison of upper gastrointestinal toxicity of rofecoxib and naproxen in patients with rheumatoid arthritis. **VIGOR** study group. N Engl J Med 2000;343:1520-8. (Curfman GD, Morrissey S, Drazen JM. Expression of Concern: Bombardier et al., "Comparison of Upper Gastrointestinal Toxicity of Rofecoxib and Naproxen in Patients with Rheumatoid Arthritis," N Engl J Med 2000;343:1520-8. N Engl J Med. 2005 Dec 8; [Epub ahead of print])
[4] Detailed study results for CLASS; FDA Feb 2001 - http://www.fda.gov/ohrms/dockets/ac/01/briefing/3677b1_01_searle.pdf & http://www.fda.gov/ohrms/dockets/ac/01/briefing/3677b1_03_med.pdf Access verified, May 6, 2002.
[5] Detailed study results for VIGOR; FDA Feb, 2001 - http://www.fda.gov/ohrms/dockets/ac/01/briefing/3677b2_01_merck.pdf Access verified, May 6, 2002.
[6] Singh G, Ramey D, Triadafilopoulos G. Early experience with selective COX-2 inhibitors: safety profile in over 340,000 patient years of use [Abstract]. Arthritis Rheum 1999;42(Suppl 9):S296.
[7] Mukherjee D, Nissen SE, Topol EJ. Risk of cardiovascular events associated with selective COX-2 inhibitors. JAMA. 2001;286:954-9.
[8] Singh G, Ramey D. NSAID-induced gastrointestinal complications: the ARAMIS perspective-1997. J Rheumatol 1998;25(suppl 51):8-16.
[9] Wolfe M, Lichtenstein D, Singh G. Gastrointestinal toxicity of non-steroidal anti-inflammatory drugs. N Engl J. Med 1999; 340:1888-99.
[10] Guidelines for the management of rheumatoid arthritis: 2002 Update. Arthritis Rheum. 2002 Feb;46(2):328-46.
[11] Treatment Guidelines: Drugs for Rheumatoid Arthritis. The Medical Letter: January, 2003; (5) pp. 25-32 & **Dec 2005**.
[12] Hawkey C, Kahan A, Steinbruck K, et al. Gastrointestinal tolerability of meloxicam compared to diclofenac in osteoarthritis patients. International MELISSA Study Group. Br J Rheumatol 1998;37:937-45.
[13] Dequeker J, Hawkey C, Kahan A, et al. Improvement in gastrointestinal tolerbility of the selective cyclogenase (COX)-2 inhibitor meloxicam, compared with piroxicam: Results of the Safety and Efficacy Large-scale Evaluation

of COX-inhibiting Therapies (SELECT) trial in osteoarthritis. Br J Rheumatol 1998;37:946-51.
[14] http://www.oregonrx.org/OrgrxPDF/NSAIDS%20review/NSAID%20Update%20Report/5-12-03%20NSAID%20update.pdf
[15] http://www.oregonrx.org/OrgrxPDF/NSAID%20Review.htm
[16] Hunt RH, Barkun AN, Baron D, et al. Recommendations for the appropriate use of anti-inflammatory drugs in the era of the coxibs: defining the role of gastroprotective agents. Can J Gastroenterol. 2002 Apr;16(4):231-40.
[17] Jenkins C, Costello J, Hodge L. Systematic review of prevalence of aspirin induced asthma and its implications for clinical practice. BMJ. 2004 Feb 21;328(7437):434.
[18] **Treatment Guidelines**: Drugs for Rheumatoid Arthritis. **The Medical Letter**: January, **2003**; (5) pp. 25-32 & **Dec 2005**.
Nakhai-Pour HR, Broy P, Sheehy O, Bérard A. Use of nonaspirin nonsteroidal anti-inflammatory drugs during pregnancy and the risk of **spontaneous abortion**. CMAJ. 2011 Sep 6.
Edwards DV, Aldridge T, Baird D et al. Periconceptional OTC NSAID exposure and risk for spontaneous abortion. ObsGyn 2012; 120(1):113-122.
Daniel S, Koren G, Lunenfeld E, et al. Fetal exposure to nonsteroidal anti-inflammatory drugs and **spontaneous abortions**. CMAJ. 2014 Mar 18;186(5) (Concern with indomethacin)
Li DK, Ferber JR, Odouli R, Quesenberry C. Use of **nonsteroidal antiinflammatory drugs during pregnancy** and the risk of miscarriage. Am J Obstet Gynecol. 2018 Sep;219(3):275.e1-275.e8.

[19] Nussmeier NA, Whelton AA, Brown MT, et al. Complications of the COX-2 Inhibitors Parecoxib and Valdecoxib after Cardiac Surgery. N Engl J Med. 2005 Feb 15; [Epub ahead of print]
[20] Bresalier RS, et al. Cardiovascular Events Associated with Rofecoxib in a Colorectal Adenoma Chemoprevention Trial (**APPROVe**). *N Engl J Med 2005; 352:1092-102.* (InfoPOEMs: For every 62 patients who take rofecoxib instead of placebo for 3 years, 1 additional patient will experience a serious cardiovascular event. Remember, there is no greater symptomatic relief with COX-2 inhibitors than with older drugs; acetaminophen is a very safe alternative. The decrease in risk of serious gastrointestinal complications is marginal with COX-2 inhibitors and the cost is high. (LOE = 1b))
[21] Solomon SD, McMurray JJ, Pfeffer MA, et al. Cardiovascular Risk Associated with Celecoxib in a Clinical Trial for Colorectal Adenoma Prevention. (**APC** trial) N Engl J Med 2005; 352:1071-80. (InfoPOEMs: One additional cardiovascular event or cardiovascular death occurs for every 126 patients treated for 1 year with celecoxib. There appears to be a dose response relationship. It is difficult to justify continued use of this and other coxibs, except in the most exceptional circumstances. (LOE = 1b))
(Bertagnolli MM, Eagle CJ, Zauber AG, et al. Celecoxib for the prevention of sporadic colorectal adenomas. (APC study) N Engl J Med 2006; 355:873-884. Follow-up colonoscopies were completed at year 1 in 89.5 percent of randomized patients, and at year 3 in 75.7 percent. The estimated cumulative incidence of the detection of one or more adenomas by year 3 was 60.7 percent for patients receiving **placebo**, as compared with 43.2 percent for those receiving **200 mg of celecoxib twice** a day (risk ratio, 0.67; 95 percent confidence interval, 0.59 to 0.77; P<0.001) and 37.5 percent for those receiving **400 mg of celecoxib twice** a day (risk ratio, 0.55; 95 percent confidence interval, 0.48 to 0.64; P<0.001). Serious adverse events occurred in 18.8 percent of patients in the placebo group, as compared with 20.4 percent of those in the low-dose celecoxib group (risk ratio, 1.1; 95 percent confidence interval, 0.9 to 1.3; P=0.5) and 23.0 percent of those in the high-dose group (risk ratio, 1.2; 95 percent confidence interval, 1.0 to 1.5; P=0.06). As compared with placebo, celecoxib was associated with an increased risk of cardiovascular events (risk ratio for the low dose, 2.6; 95 percent confidence interval, 1.1 to 6.1; and risk ratio for the high dose, 3.4; 95 percent confidence interval, 1.5 to 7.9).) (Arber N, Eagle CJ, Spicak J, et al. Celecoxib for the prevention of colorectal adenomatous polyps. (PreSAP trial) N Engl J Med 2006; 355:885-895. Colonoscopies were performed at year 1 on 88.7 percent of the subjects who had undergone randomization and at year 3 on 79.2 percent. Of the 557 subjects in the **placebo** group and the 840 subjects in the **celecoxib 400mg od** group who were included in the efficacy analysis, 264 and 270, respectively, were found to have at least one adenoma at year 1, at year 3, or both. The cumulative rate of adenomas detected through year 3 was 33.6 percent in the celecoxib group and 49.3 percent in the placebo group (relative risk, 0.64; 95 percent confidence interval, 0.56 to 0.75; P<0.001). The cumulative rate of advanced adenomas detected through year 3 was 5.3 percent in the celecoxib group and 10.4 percent in the placebo group (relative risk, 0.49; 95 percent confidence interval, 0.33 to 0.73; P<0.001). Adjudicated serious cardiovascular events occurred in 2.5 percent of subjects in the celecoxib group and 1.9 percent of those in the placebo group (relative risk, 1.30; 95 percent confidence interval, 0.65 to 2.62). (Kerr DJ, Dunn JA, Langman MJ, Smith JL, Midgley RS, Stanley A, Stokes JC, Julier P, Iveson C, Duvvuri R, McConkey CC; **VICTOR** Trial Group. Rofecoxib and cardiovascular adverse events in adjuvant treatment of colorectal cancer. N Engl J Med. 2007 Jul 26;357(4):360-9. Rofecoxib therapy was associated with an increased frequency of adverse cardiovascular events among patients with a median study treatment of 7.4 months' duration.)
[22] Farkouh ME, Kirshner H., Harrington RA. Comparison of lumiracoxib with naproxen and ibuprofen in the Therapeutic Arthritis Research and Gastrointestinal Event Trial (**TARGET**), cardiovascular outcomes: randomised controlled trial. Lancet 2004;364:675-84. At 1-year follow-up, incidence of the primary endpoint was low, both with lumiracoxib (59 events [0.65%]) and the non-steroidal anti-inflammatory drugs (50 events [0.55%]; hazard ratio 1.14 [95% CI 0.78-1.66], p=0.5074). Incidence of myocardial infarction (clinical and silent) in the overall population in the individual substudies was 0.38% with lumiracoxib (18 events) versus 0.21% with naproxen (ten) and 0.11% with lumiracoxib (five) versus 0.16% with ibuprofen (seven).
[23] Schnitzer TJ., Burmester GR., Mysler E., Comparison of lumiracoxib with naproxen and ibuprofen in the Therapeutic Arthritis Research and Gastrointestinal Event Trial (**TARGET**), reduction in ulcer complications: randomised controlled trial. Lancet 2004;364:665-74. (18325 patients age 50 years or older with osteoarthritis were randomised to lumiracoxib 400 mg once daily (n=9156), naproxen 500 mg twice daily (4754), or ibuprofen 800 mg three times daily (4415) in two substudies of identical design. Randomisation was stratified for low-dose aspirin use and age. In patients not taking aspirin, the cumulative 1-year incidence of ulcer complications was 1.09% (95% CI 0.82-1.36) with non-steroidal anti-inflammatory drugs (64 events) versus 0.25% (95% CI 0.12-0.39) with lumiracoxib (14 events; hazard ratio 0.21 [95% CI 0.12-0.37], p<0.0001). Reductions in ulcer complications were also significant in the overall population (0.34 [0.22-0.52], p<0.0001) but not in those taking aspirin (0.79 [0.40-1.55], p=0.4876). In the overall population, 0.55% (50/9127) of those on non-steroidal anti-inflammatory drugs and 0.65% (59/9117) of those on lumiracoxib reached the cardiovascular endpoint (1.14 [0.78-1.66], p=0.5074).) (see also Pharmacists Letter Dec/06) Hawkey CJ et al. Effect of risk factors on complicated and uncomplicated ulcers in the TARGET lumiracoxib outcomes study. Gastroenterology 2007 Jul; 133:57-64. Lumiracoxib was associated with a reduced risk of ulcer complications compared with NSAIDs in all significant subgroups **except aspirin users**.
[24] Bookman AA, Williams KS, Shainhouse JZ. Effect of a topical diclofenac solution for relieving symptoms of primary osteoarthritis of the knee: a randomized controlled trial. CMAJ. 2004 Aug 17;171(4):333-8.
[25] Roth SH, Shainhouse JZ. Efficacy and safety of a topical diclofenac solution (pennsaid) in the treatment of primary osteoarthritis of the knee: a randomized, double-blind, vehicle-controlled clinical trial. Arch Intern Med. 2004 Oct 11;164(18):2017-23.
28. Bjordal JM, Ljunggren AE, Klovning A, Slordal L. Non-steroidal anti-inflammatory drugs, including cyclo-oxygenase-2 inhibitors, in osteoarthritic knee pain: meta-analysis of randomised placebo controlled trials. BMJ. 2004 Dec 4;329(7478):1317. Epub 2004 Nov 23. **Conclusion** NSAIDs can reduce short term pain in osteoarthritis of the knee slightly better than placebo, but the current analysis does not support long term use of NSAIDs for this condition. As serious adverse effects are associated with oral NSAIDs, only limited use can be recommended.
29. Dieppe PA, Lohmander LS. Pathogenesis and management of pain in osteoarthritis. Lancet. 2005 Mar 12;365(9463):965-73.
30. Savage R. Cyclo-oxygenase-2 inhibitors : when should they be used in the elderly? Drugs Aging. 2005;22(3):185-200.
31. Hippisley-Cox J, Coupland C. Risk of MI in patients taking cyclo-oxygenase-2 inhibitors or conventional non-steroidal anti-inflammatory drugs: population based nested case-control analysis. BMJ.2005 Jun 11;330(7504):1366.
32. Hudson M, et al. Differences in outcomes of patients with congestive heart failure prescribed celecoxib, rofecoxib, or non-steroidal anti-inflammatory drugs: population based study. BMJ. 2005 Jun 11;330(7504):1370.
33. Arrich J, Piribauer F, Mad P, et al. Intra-articular hyaluronic acid for the treatment of osteoarthritis of the knee: systematic review and meta-analysis. CMAJ. 2005 Apr 12;172(8):1039-43. (InfoPOEMs: The evidence that intra-articular hyaluronic acid helps patients with knee osteoarthritis is of poor quality. Improvements in pain at rest and pain during exercise is seen in a minority of studies, and those studies were of lower quality than those showing no benefit. There is no evidence of functional improvement. Injections like this have a potentially powerful placebo effect, so any benefit seen in unblinded studies without concealed allocation is likely represent the placebo effect rather than any effect of the drug. (LOE = 1a-)) Petrella RJ, Petrella M. A prospective, randomized, double-blind, placebo controlled study to evaluate the efficacy of intraarticular hyaluronic acid for osteoarthritis of the knee. J Rheumatol. 2006 May;33(5):951-6.
34. Verhamme KM, Dieleman JP, Van Wijk MA, et al. Nonsteroidal anti-inflammatory drugs and increased risk of acute urinary retention. Arch Intern Med. 2005 Jul 11;165(13):1547-51.
35. Sudbo J, Lee JJ, Lippman SM, et al. Non-steroidal anti-inflammatory drugs and the risk of oral cancer: a nested case-control study. Lancet. 2005 Oct 15-21;366(9494):1359-66.
Long-term use of NSAIDs is associated with a reduced incidence of oral cancer (including in active smokers), but also with an increased risk of death due to cardiovascular disease. These findings highlight the need for a careful risk-benefit analysis when the long-term use of NSAIDs. (Jan/06 The Norwegian daily newspaper Dagbladet reports that a number of **statistical improbabilities** were found in the data set of the cancer trial, published in the Lancet in October last year. Lancet editor Dr Richard Horton told the BBC he would be speaking to the coauthors of the study to seek their permission to retract the paper. One example of the improbabilities" is the fact that of the 908 people in the trial, 250 shared the same birthday.)
36. **Acetaminophen Overdose**: Medscape article: http://www.medscape.com/viewarticle/459187_4 ; Merck Manual's Online Medical Manual: http://www.merck.com/mmpe/sec21/ch326/ch326c.html {Rumack-Matthew nomogram for predicting (Caution with units of measure!) } (10ug/ml = 66.2umol/L) {Acetaminophen level: 4hrs post ingestion & repeat in 4hrs; if ≥150mg/kg and 8hr post, may start **n-acetylcysteine** while awaiting levels; TOXIC levels: 4hr level >993umol/L; 6hr >728umol/L; 8hr >496.5umol/L; 24hr >29.8umol/L } {LFTs: AST usually ↑ first}
Heard KJ. Acetylcysteine for acetaminophen poisoning. N Engl J Med. 2008 Jul 17;359(3):285-92.
Ferner Robin E, Dear James W, Bateman D Nicholas. Management of acetaminophen/paracetamol poisoning. BMJ 2011;342:doi:10.1136/bmj.d2218 (Published 20 April 2011)
Hitchings AW, Wood DM, Dargan PI. Dissemination and uptake of a **new treatment pathway** for paracetamol poisoning in the UK: a survey of healthcare professionals. Br J Clin Pharmacol. 2013 Mar 14.
Bateman DN, Dear JW, Thanacoody HKR, et al. Reduction of adverse events from **intravenous acetylcysteine treatment for paracetamol (acetaminophen) poisoning**: a randomised controlled trial. Lancet 2013; online Nov 28.
This modified acetylcysteine regimen infused a total dose of 300 mg/kg over 12 hours, versus roughly 20 hours; it used a lower initial dose (100 mg/kg over 2 hours, vs. 150 mg/kg over 15 minutes in the U.K. and 1 hour in the U.S.).
Buckley NA, Dawson AH, Isbister GK. Treatments for **paracetamol (acetaminophen) poisoning**. BMJ. 2016 May 18;353:i2579.



MHRA Sept 2012: Paracetamol (acetaminophen) overdose: Simplification of the use of intravenous acetylcysteine



{There is some evidence for the use of **fomepizole** as a **CYP2E1 inhibitor** and for decreased hepatotoxicity in the setting of acetaminophen overdose... To date, the evidence is all animal models but when the patient will otherwise die, the potential benefit outweighs the lack of human evidence.}
Yarema MC, Johnson DW, Berlin RJ, et al. Comparison of the 20-hour intravenous and 72-hour oral **acetylcysteine protocols** for the treatment of acute acetaminophen poisoning. Ann Emerg Med. 2009 Oct;54(4):606-14. Epub 2009 Jun 25. It favored the 20-hour protocol for patients presenting early and favored the 72-hour protocol for patients presenting late after acute acetaminophen overdose. Johnson Michael T, McCammon Craig A, Mullins Michael E, et al. Evaluation of a Simplified N-Acetylcysteine Dosing Regimen for the Treatment of Acetaminophen Toxicity. Articles Ahead of Print published on 1 June 2011, DOI 10.1345/aph.1P613. Ann Pharmacother ;45:713-720.
Blackford MG, Felter T, Gothard MD, Reed MD. Assessment of the Clinical Use of Intravenous and Oral N-Acetylcysteine in the Treatment of Acute Acetaminophen Poisoning in Children: A Retrospective Review. Clin Ther. 2011 Sep 2.
Bateman DN, Carroll R, Pettie J, et al. Effect of the **UK's Revised Paracetamol Poisoning Management** Guidelines on Admissions, Adverse Reactions, and Costs of Treatment. Br J Clin Pharmacol. 2014 Mar 26.

Additional references (NSAID & COXIB chart):

Acheampong P, Thomas SH. Determinants of **hepatotoxicity after repeated supratherapeutic paracetamol (acetaminophen) ingestion**; systematic review of reported cases. Br J Clin Pharmacol. 2016 Jun 4.
ADAPT Research Group. Cognitive Function Over Time in the Alzheimer's Disease Anti-inflammatory Prevention Trial (ADAPT): Results of a Randomized, Controlled Trial of Naproxen and Celecoxib. Arch Neurol. 2008 May 12. [Epub ahead of print] Use of naproxen or celecoxib did not improve cognitive function. There was weak evidence for a detrimental effect of naproxen.
Afshar K, Jafari S, Marks AJ, et al. **Nonsteroidal anti-inflammatory drugs (NSAIDs) and non-opioids for acute renal colic.**Cochrane Database Syst Rev. 2015 Jun 29;6:CD006027. Although due to variability in studies (inclusion criteria, outcome variables and interventions) and the evidence is not of highest quality, we still believe that NSAIDs are an effective treatment for renal colic when compared to placebo or antispasmodics. The addition of antispasmodics to NSAIDS does not result in better pain control. Data on other types of non-opioid, non-NSAID medication was scarce.Major adverse effects are not reported in the literature for the use of NSAIDs for treatment of renal colic.
Ahmed SU, Zhang Y, Chen L, et al. Effect of 1.5% Topical Diclofenac on Clinical Neuropathic Pain. Anesthesiology. 2015 May 8.
Akbar A, Abu Dayyeh BK, Baron TH, et al. **Rectal nonsteroidal** anti-inflammatory drugs are superior to pancreatic duct stents in preventing **pancreatitis after endoscopic retrograde cholangiopancreatography**: a network meta-analysis. Clin Gastroenterol Hepatol 2013;11:778–783.
Al-Sukhun J, Koivusalo A, Tornwall J, Lindqvist C. COX-2 inhibitors and early **failure of free vascular flaps**. N Engl J Med. 2006 Aug 3;355(5):528-9.
Allegaert K, Mian P, Lapillonne A, van den Anker JN. **Maternal paracetamol (acetaminophen) intake and fetal ductus arteriosus constriction** or closure: a case series analysis. Br J Clin Pharmacol. 2018 Oct 9.
Amendolia B, Lynn M, Bhat V, et al. Severe pulmonary hypertension with therapeutic L-lysine **Ibuprofen** in 2 preterm neonates. Pediatrics. 2012 May;129(5):e1360-3.
Amin AK, et al. Does **obesity** influence the clinical outcome at five years following total **knee replacement** for osteoarthritis? J Bone Joint Surg Br. 2006 Mar;88(3):335-40**.** (InfoPOEMs: In this study, obese patients undergoing primary knee arthroplasty had comparable long-term outcomes with nonobese patients. (LOE = 1b-))
Amin SB, Sinkin RA, Glantz JC. Metaanalysis of the effect of antenatal **indomethacin** on **neonatal outcomes**. Am J Obstet Gynecol. 2007 Nov;197(5):486.e1-10. Antenatal indomethacin may be associated with an increased risk of periventricular leukomalacia and necrotizing enterocolitis in premature infants and therefore should be used judiciously for tocolysis.
Ammar H, Ben Fredj N, Ben Fadhel N, et al. **Celecoxib-induced bullous fixed drug eruption**: An unusual presentation. Br J Clin Pharmacol. 2019 Aug 2.
Ananthakrishnan AN, Higuchi LM, Huang ES, et al. Aspirin, Nonsteroidal Anti-inflammatory Drug Use, and **Risk for Crohn Disease and Ulcerative Colitis**: A Cohort Study (NHS). Ann Intern Med. 2012 Mar 6;156(5):350-9.
Andersohn F, et al. Cyclooxygenase-2 Selective Nonsteroidal Anti-Inflammatory Drugs and the **Risk of Ischemic Stroke**. A Nested Case-Control Study. Stroke. 2006 May 25; [Epub ahead of print] Current use of rofecoxib (OR=1.71; 95% CI, 1.33 to 2.18), etoricoxib (OR=2.38; 95% CI, 1.10 to 5.13), but not of celecoxib (OR=1.07; 95% CI, 0.79 to 1.44) was associated with a significantly increased risk of ischemic stroke. For rofecoxib and etoricoxib, ORs tended to increase with higher daily dose and longer duration of use and were also elevated in patients without major stroke risk factors. "From the non-selective NSAIDs, diclofenac, but not ibuprofen or naproxen, was also associated with a slightly increased risk of ischemic stroke," Dr. Andersohn said.
Andersohn F, Suissa S, Garbe E. Use of first- and second-generation cyclooxygenase-2-selective nonsteroidal antiinflammatory drugs & risk of **acute myocardial infarction**. Circulation. 2006 Apr 25;113(16):1950-7. Epub 2006 Apr 17. Current use of etoricoxib was associated with a 2.09-fold (95% confidence interval [CI], 1.10 to 3.97) risk of AMI compared with no use of NSAIDs during the prior year. Current use of rofecoxib (RR=1.29; 95% CI, 1.02 to 1.63), celecoxib (RR=1.56; 95% CI, 1.22 to 2.00), and diclofenac (RR=1.37; 95% CI, 1.17 to 1.59) also significantly increased the AMI risk. For current use of valdecoxib, the RR was 4.60 (95% CI, 0.61 to 34.51). RRs appeared to increase with higher daily doses of COX-2 inhibitors and were also increased in patients without major cardiovascular risk factors.
Andrew T. Chan, MD, MPH; Edward L. et al. Long-term Use of Aspirin and Nonsteroidal Anti-inflammatory Drugs and Risk of Colorectal Cancer JAMA. 2005;294:914-923. CONCLUSIONS: Regular, long-term aspirin use reduces risk of colorectal cancer. Nonaspirin NSAIDs

appear to have a similar effect. However, a significant benefit of aspirin is not apparent until more than a decade of use, with maximal risk reduction at doses greater than 14 tablets per week. These results suggest that optimal chemoprevention for colorectal cancer requires long-term use of aspirin doses substantially higher than those recommended for prevention of cardiovascular disease, but the dose-related risk of gastrointestinal bleeding must also be considered. (InfoPOEMs: Regular use of aspirin and other nonsteroidal anti-inflammatory drugs (NSAIDs), especially more than 14 doses per week for at least 10 years, reduces the risk of colon cancer while also increasing the risk of a major gastrointestinal bleeding event. All-cause mortality is not affected by regular use. We need additional methods (gene testing?) to determine who is at high risk of colorectal cancer before making specific recommendations for prevention. (LOE = 2b))

Antman EM, Bennett JS, Daugherty A, et al. Use of nonsteroidal antiinflammatory drugs. An update for clinicians. A scientific statement from the **American Heart Association**. Circulation 2007; DOI:10.1161/CIRCULATIONAHA.106.181424. Available at: http://circ.ahajournals.org.

Antman EM. **Evaluating the Cardiovascular Safety of Nonsteroidal Anti-Inflammatory Drugs**. Circulation. 2017 May 23;135(21):2062-2072.

Anzellotti P, Capone ML, Jeyam A, et al. Low-dose **naproxen interferes with the antiplatelet effects of aspirin** in healthy subjects: Recommendations to minimize the functional consequences. Arthritis Rheum. 2010 Dec 2.

Are, Chaitanya, Turagam, Mohit, Aucar, John A., Greenberg, Eugene. **Meloxicam-induced enteropathy** of the small bowel. CMAJ 2011 183: 577-580

Aresti N, Kassam J, Bartlett D, et al. Primary care **management of postoperative shoulder, hip, and knee arthroplasty**. BMJ. 2017 Oct 18;359:j4431 (osseointegration concern)

Arfè A, Scotti L, Varas-Lorenzo C, et al. Non-steroidal anti-inflammatory drugs and risk of **heart failure** in four European countries: nested case-control study. BMJ 2016;354:i4857.

Asgari MM, Chren MM, Warton EM, Friedman GD, White E. Association Between Nonsteroidal Anti-inflammatory Drug Use and **Cutaneous Squamous Cell Carcinoma**. Arch Dermatol. 2010 Feb 15.

Ash Z, Gaujoux-Viala C, Gossec L, et al. A systematic literature review of drug therapies for the treatment of **psoriatic arthritis**: current evidence and meta-analysis informing the EULAR recommendations for the management of psoriatic arthritis. Ann Rheum Dis. 2011 Jul 28.

Aspirin for cancer: Rothwell PM, Price JF, Fowkes FGR, et al. Short-term effects of daily aspirin on cancer incidence, mortality, and non-vascular death: analysis of the time course of risks and benefi ts in 51 randomised controlled trials. Lancet 2012; online March 21.

Rothwell PM, Wilson M, Price JF, Belch JFF, Meade TW, Mehta Z. Effect of daily aspirin on risk of cancer metastasis: a study of incident cancers during randomised controlled trials. Lancet 2012; online March 21. DOI:10.1016/S0140-6736(12)60209-8.

Algra AM, Rothwell PM. Effects of regular aspirin on long-term cancer incidence and metastasis: a systematic comparison of evidence from observational studies versus randomised trials. Lancet Oncology 2012; online March 21. DOI:10.1016/S1470-2045(12)70112-2.

Rothwell PM, Wilson M, Elwin CE, et al. Long-term effect of **aspirin on colorectal cancer** incidence and mortality: 20-year follow-up of five randomised trials. Lancet. 2010 Oct 21.

Rothwell PM, Fowkes FG, Belch JF, Ogawa H, Warlow CP, Meade TW. Effect of daily **aspirin on long-term risk of death due to cancer**: analysis of individualpatient data from randomised trials. Lancet. 2011 Jan 1;377(9759):31-41.

Cook NR, Lee IM, Gaziano JM, et al. Low-dose aspirin in the primary prevention of cancer: the Women's Health Study (**WHS**): a randomized controlled trial. JAMA 2005; 294: 47–55. (no effect)

Sturmer T, Glynn RJ, Lee IM, Manson JE, Buring JE, Hennekens CH. Aspirin use and colorectal cancer: post-trial follow-up data from the Physicians' Health Study (**PHS**). Ann Intern Med 1998; 128: 713–20. (no effect)

Atiquzzaman M, Karim ME, Kopec J, et al. Role of Non-Steroidal Anti-Inflammatory Drugs (NSAIDs) in the **Association between Osteoarthritis and Cardiovascular Diseases**: A Longitudinal Study. Arthritis Rheumatol. 2019 Aug 6.

Babb, Malaika, Koren, Gideon, Einarson, Adrienne. Treating **pain during pregnancy**. Can Fam Physician 2010 56: 25-27.

Bäck M, Yin L, Ingelsson E. **Cyclooxygenase-2 inhibitors** and cardiovascular risk in a nationwide cohort study after the withdrawal of rofecoxib. Eur Heart J 2011. (increased risk of developing atrial fibrillation)

Baik CS, Brasky TM, Pettinger M, et al. Nonsteroidal Anti-Inflammatory Drug and Aspirin Use in Relation to **Lung Cancer Risk** among Postmenopausal Women. Cancer Epidemiol Biomarkers Prev. 2015 May;24(5):790-7.

Bandolier. Avocado/soybean unsaponifiables for OA. April 2004;122-23. Web site: http://www.jr2.ox.ac.uk/bandolier/band122/b122-3.html. The limited data to date support the safety and possible efficacy of ASU for osteoarthritis of the knee. More and longer studies are needed before we can recommend this to our patients without hesitation. (LOE = 1b-)

Bannuru RR, Schmid CH, Kent DM, Vaysbrot EE, Wong JB, McAlindon TE. Comparative effectiveness of **pharmacologic interventions for knee osteoarthritis**. A systematic review and network meta- analysis. Ann Intern Med. 2015;162:46-54. doi:10.7326/M14-2636

Barkhuizen A, et al. Celecoxib is efficacious and well tolerated in treating signs and symptoms of **ankylosing spondylitis**. J Rheumatol. 2006 Sep;33(9):1805-12.

Bakkeheim E, Mowinckel P, Carlsen KH, Håland G, Carlsen KC. Paracetamol (**acetaminophen**) in early infancy: the risk of childhood allergy and asthma. Acta Paediatr. 2011 Jan;100(1):90-6. doi: 10.1111/j.1651-2227.2010.01942.x.

Bally M, Dendukuri N, Rich B, et al. **Risk of acute myocardial infarction with NSAIDs in real world use**: Bayesian meta-analysis of individual patient data. BMJ. 2017 May 9;357:j1909 (within 1st month)

Barkin RL, Beckerman M, Blum SL, et al. Should nonsteroidal anti-inflammatory drugs **(NSAIDs) be prescribed to the older adult**? Drugs Aging. 2010 Oct 1;27(10):775-89. Prescribing

Barkun AN, Bardou M, et al. and for the **International Consensus** Upper Gastrointestinal Bleeding Conference Group. Management of Patients With **Nonvariceal Upper Gastrointestinal Bleeding**. Ann Intern Med January 19, 2010 152:101-113.

Baron JA, et al. A randomized trial of **aspirin to prevent colorectal adenomas**. N Engl J Med. 2003 Mar 6;348(10):891-9.

Baron JA, Sandler RS, Bresalier RS, et al. Cardiovascular events associated with **rofecoxib**: final analysis of the **APPROVe** trial. Lancet. 2008 Oct 13. [Epub ahead of print] Use of rofecoxib is associated with increased rates of APTC events. Study data are compatible with an early increase in risk that persists for one year after stopping treatment.

Bateman DN, Carroll R, Pettie J, et al. Effect of the UK's Revised **Paracetamol Poisoning Management** Guidelines on Admissions, Adverse Reactions, and Costs of Treatment. Br J Clin Pharmacol. 2014 Mar 26.

Bateman DN. Changing the Management of **Paracetamol/acetaminophen Poisoning**. Clin Ther. 2015 Jul 29.

Bavbek S, et al. Safety of **Meloxicam** in Aspirin-**Hypersensitive** Patients with Asthma and/or Nasal Polyps. A Challenge-Proven Study. Int Arch Allergy Immunol. 2006 Oct 2;142(1):64-69 [Epub ahead of print]

Bavry AA, Khaliq A, Gong Y, et al. **Harmful effects of NSAIDs** among patients with hypertension and coronary artery disease. Am J Med 2011; 124:614-620.

Bavry AA, Thomas F, Allison M, et al. Nonsteroidal Anti-Inflammatory Drugs and **Cardiovascular Outcomes** in Women: Results From the Women's Health Initiative. Circ Cardiovasc Qual Outcomes. 2014 Jul 8.

Becquet O, Bonnet D, Ville Y, et al. **Paracetamol/Acetaminophen During Pregnancy** Induces Prenatal Ductus Arteriosus Closure. Pediatrics. 2018 Jun 7.

Bellamy N, et al. **Viscosupplementation** for the treatment of osteoarthritis of the knee. Cochrane Database Syst Rev. 2005 Apr 18;(2):CD005321.

Belay ED, Bresee JS, Holman RC, Khan AS, Shahriari A, Schonberger LB. **Reye's syndrome** in the United States from 1981 through 1997. N Engl J Med. 1999 May 6;340(18):1377-82.

Bennell KL, Kyriakides M, Metcalf B, et al. **Neuromuscular versus quadriceps strengthening exercise in people with medial knee osteoarthritis** and varus malalignment: A randomised controlled trial. Arthritis Rheum. 2013 Dec 24.

Berman BM, et al. Effectiveness of **acupuncture** as adjunctive therapy in osteoarthritis of the knee: a randomized, controlled trial. Ann Intern Med. 2004 Dec 21;141(12):901-10. Summary for patients in: Ann Intern Med. 2004 Dec 21;141(12):I20.

Bhatt DL, Scheiman J, Abraham NS, et al. **ACCF/ACG/AHA 2008 expert consensus document on reducing the gastrointestinal risks of antiplatelet therapy and NSAID** use: a report of the American College of Cardiology Foundation Task Force on Clinical Expert Consensus Documents. *J Am Coll Cardiol***.** 2008; *Circulation*. 2008; DOI: DOI: 10.1161/CIRCULATIONAHA.108.191087. Available at: http://circ.ahajournals.org http://circ.ahajournals.org/cgi/reprint/CIRCULATIONAHA.108.191087

Bihan K, Weiss N, Théophile H, et al. **drug-induced aseptic meningitis**: 329 cases from the French Pharmacovigilance Database Analysis. Br J Clin Pharmacol. 2019 Jul 18.

Bijlsma Johannes W J, Berenbaum Francis, Lafeber Floris P J G. **Osteoarthritis**: an update with relevance for clinical practice. Lancet 2011; 377: 2115–26.

Bingham CO 3rd, Eet al. Efficacy and safety of **etoricoxib** 30 mg and celecoxib 200 mg in the treatment of osteoarthritis in two identically designed, randomized, placebo-controlled, non-inferiority studies. Rheumatology (Oxford). 2006 Aug 27.

Biswal S, Medhi B, Pandhi P. Longterm efficacy of **topical nonsteroidal antiinflammatory** drugs in knee osteoarthritis: metaanalysis of randomized placebo controlled clinical trials. J Rheumatol. 2006 Sep;33(9):1841-4.

Blodt S, Pach D, Eisenhart-Rothe SV, et al. Effectiveness of app-based **self-acupressure for women with menstrual pain** compared to usual care: a randomized pragmatic trial. Am J Obstet Gynecol. 2018 Feb;218(2):227.e1-227.e9.

Blouin M, Rhainds M. Use of Nonsteroidal **Anti-inflammatory Drugs** in **Colorectal Surgery**: Do the Risks Cast a Shadow on the Benefits? Ann Pharmacother. 2014 Dec;48(12):1662-4.

Bornehag CG, Reichenberg A, Hallerback MU, et al. **Prenatal exposure to acetaminophen and children's language development** at 30 months. Eur Psychiatry. 2017 Nov 10.

Bouck Z, Mecredy GC, Ivers NM, et al. Frequency and associations of prescription **nonsteroidal anti-inflammatory drug use among patients with a musculoskeletal disorder and hypertension, heart failure, or chronic kidney disease** [online Oct 8, 2018]. JAMA Intern Med. doi:10.1001/jamainternmed.2018.4273

Bourgeois FT, Graham DA, Kesselheim AS, Randolph AG. **Cost Implications of Escalating Intravenous Acetaminophen** Use in Children. JAMA Pediatr. 2019 Mar 11.

Bouroubi A, Donazzolo Y, Donath F, et al. **Pain relief of sore throat** with a new anti- inflammatory throat lozenge, ibuprofen 25 mg: A randomised, double-blind, placebo-controlled, international phase III study. Int J Clin Pract. 2017 Sep;71(9).

Bowers LW, Maximo IX, Brenner AJ, et al. NSAID Use **Reduces Breast Cancer Recurrence** in Overweight and Obese Women: Role of Prostaglandin-Aromatase Interactions. Cancer Res. 2014 Aug 15;74(16):4446-57.

Bowler MA, Raddatz MA, Johnson CL, et al. **Celecoxib Is Associated With Dystrophic Calcification and Aortic Valve Stenosis**. JACC Basic Transl Sci. 2019 Feb 22;4(2):135-143.

Brandlistuen RE, Ystrom E, Nulman I, et al. Prenatal **paracetamol/acetaminophen exposure and child neurodevelopment**: a sibling-controlled cohort study. Int J Epidemiol. 2013 Oct 24

Brass EP, Reynolds KM, Burnham RI, et al. Frequency of **Poison Center Exposures** for Pediatric Accidental Unsupervised Ingestions of **Acetaminophen after the Introduction of Flow Restrictors**. J Pediatr. 2018 Apr 2.

Braun J, van den Berg R, Baraliakos X, et al. **2010 update of the ASAS/EULAR recommendations** for the management of **ankylosing spondylitis**. Ann Rheum Dis 2011;70:896-904 doi:10.1136/ard.2011.151027.

Buckley NA, Dawson AH, Isbister GK. Treatments for **paracetamol (acetaminophen) poisoning**. BMJ. 2016 May 18;353:i2579.

Burmester Gerd, Lanas Angel, Biasucci Luigi, et al. The appropriate use of **non-steroidal anti-inflammatory drugs** (NSAIDs)in rheumatic disease: opinions of a multidisciplinary **European expert panel**. Ann Rheum Dis 2011;70:818-822 Online: 10 Sept 2010.

Burova N, Bychkova V, Shephard A. Improvements in throat function and qualities of sore throat from **locally applied flurbiprofen 8.75 mg in spray or lozenge format**: findings from a randomized trial of patients with upper respiratory tract infection in the Russian Federation. J Pain Res. 2018 Jun 1;11:1045-1055.

Butler GJ, Neale R, Green AC, Pandeya N, Whiteman DC. Nonsteroidal anti-inflammatory drugs and the risk of **actinic keratoses and squamous cell** cancers of the skin. J Am Acad Dermatol. 2005 Dec;53(6):966-72. Epub 2005 Oct 19.

Calder LA, Balasubramanian S, Fergusson D. **Topical nonsteroidal anti-inflammatory drugs** for **corneal abrasions**: meta-analysis of randomized trials. Acad Emerg Med. 2005 May;12(5):467-73.

Cannon CP, et al.; **MEDAL** Steering Committee. Clinical trial design and patient demographics of the Multinational **Etoricoxib and Diclofenac** Arthritis Long-term (MEDAL) study program: cardiovascular outcomes with etoricoxib versus diclofenac in patients with osteoarthritis and rheumatoid arthritis. Am Heart J. 2006 Aug;152(2):237-45.

Cannon CP, Curtis SP, FitzGerald GA, et al. Cardiovascular outcomes with **etoricoxib and diclofenac** in patients with osteoarthritis and rheumatoid arthritis in the Multinational Etoricoxib and Diclofenac Arthritis Long-term (**MEDAL**) programme: a randomised comparison. Lancet 2006: DOI:10.1016/S0140-6736(06)69666-9. Rates of thrombotic cardiovascular events in patients with arthritis on etoricoxib are similar to those in patients on diclofenac with long-term use of these drugs.

Capone ML, Sciulli MG, Tacconelli S, Grana M, Ricciotti E, Renda G, Di Gregorio P, Merciaro G, Patrignani P. Pharmacodynamic interaction of **naproxen with low-dose aspirin** in healthy subjects. J Am Coll Cardiol. 2005 Apr 19;45(8):1295-301.

Cardiovascular and Cerebrovascular Events in the Randomized, Controlled **Alzheimer's** Disease Anti-Inflammatory Prevention Trial (**ADAPT**). PLoS Clin Trials. 2006 Nov 17;1(7):e33 [Epub ahead of print] For celecoxib, ADAPT data do not show the same level of risk as those of the APC trial. The data for **naproxen**, although not definitive, are suggestive of increased cardiovascular and cerebrovascular risk. (Nissen SE. ADAPT: The Wrong Way to Stop a Clinical Trial. PLoS Clin Trials. 2006 Nov 17;1(7):e35 [Epub ahead of print])

Carmo KB, Evans N, Paradisis M. Duration of indomethacin treatment of the **preterm patent ductus arteriosus** as directed by echocardiography. J Pediatr. 2009 Dec;155(6):819-822.e1. Epub 2009 Jul 29.

Carpenter PS, Shepherd HM, McCrary H, et al. Association of **Celecoxib** Use With **Decreased Opioid Requirements After Head and Neck Cancer Surgery** With Free Tissue Reconstruction. JAMA Otolaryngol Head Neck Surg. 2018 Apr 18.

AJ, DeMarco S, Tournier B, Vyas SN, FitzGerald GA. **Cyclooxygenase inhibitors and the antiplatelet effects of aspirin**. N Engl J Med. 2001 Dec 20;345(25):1809-17.

Chan AT, et al. Nonsteroidal Antiinflammatory Drugs, Acetaminophen, and the Risk of **Cardiovascular Events**. Circulation. 2006 Mar 13; [Epub ahead of print]

Chan AT, Ogino S, Fuchs CS. Aspirin use and survival after diagnosis of **colorectal cancer**. JAMA. 2009 Aug 12;302(6):649-58. Regular aspirin use after the diagnosis of colorectal cancer is associated with lower risk of colorectal cancer-specific and overall mortality, especially among individuals with tumors that overexpress COX-2.

Chan FKL, et al Clopidogrel versus **Aspirin and Esomeprazole** to Prevent Recurrent Ulcer Bleeding. N Engl J Med 2005;352:238-44. (InfoPOEMs: For patients with a history of bleeding peptic ulcer, the combination of aspirin and a proton pump inhibitor twice a day was safer in terms of bleeding side effects than clopidogrel. While esomeprazole was used in this study, generic omeprazole 20 mg give twice a day provides nearly the same degree of acid suppression at a much lower cost. This study calls into question the overall safety of clopidogrel, which has been promoted as not increasing the risk of bleeding significantly. **(LOE = 1b)**)

Chan FK, et al. Preventing recurrent upper gastrointestinal bleeding in patients with Helicobacter pylori infection who are taking low-dose aspirin or naproxen. N Engl J Med. 2001 Mar 29;344(13):967-73. CONCLUSIONS: Among patients with H. pylori infection and a history of upper gastrointestinal bleeding who are taking low-dose aspirin, the eradication of H. pylori is equivalent to treatment with omeprazole in preventing recurrent bleeding. Omeprazole is superior to the eradication of H. pylori in preventing recurrent bleeding in patients who are taking other NSAIDs.

Chan FK, Wong VW, Suen BY, et al. Combination of cyclo-oxygenase-2 inhibitor **(celecoxib 200mg bid) and proton-pump inhibitor (esomeprazole 20mg bid)** for prevention of recurrent ulcer bleeding in patients at very high risk: a double-blind, randomised trial. Lancet. 2007 May 12;369(9573):1621-6. The 13-month cumulative incidence of the primary endpoint was 0% in the combined-treatment group and 12 (8.9%) in the controls (95% CI difference, 4.1 to 13.7; p=0.0004). n=441 12months. Patients at very high risk for recurrent ulcer bleeding who need anti-inflammatory analgesics should receive combination treatment with a COX 2 inhibitor and a PPI. Our findings should encourage guideline committees to review their recommendations for patients at very high risk of recurrent ulcer bleeding.

Chan CC, Reid CM, Aw TJ, Liew D, Haas SJ, Krum H. Do COX-2 inhibitors raise blood pressure more than nonselective NSAIDs and placebo? An updated meta-analysis. J Hypertens. 2009 Nov 2. [Epub ahead of print] However, this response was heterogeneous, with markedly raised BP associated with rofecoxib and etoricoxib, whereas celecoxib, valdecoxib and lumiracoxib appeared to have little BP effect.

Chan Francis KL, Lanas Angel, Scheiman James, et al. **Celecoxib versus omeprazole and diclofenac** in patients with osteoarthritis and rheumatoid arthritis (**CONDOR**): a randomised trial, The Lancet, Online 16 June 2010, ISSN 0140-6736, DOI:10.1016/S0140-6736(10)60673-3.

Chan FKL, et al. **Gastrointestinal safety of celecoxib versus naproxen** in patients with cardiothrombotic diseases and arthritis after upper gastrointestinal bleeding (**CONCERN**): an industryindependent, double-blind, double-dummy, randomised trial. Lancet 2017; online April 11.

Chang A, Bijur P, Esses D, et al. Effect of a single dose **of oral opioid and nonopiod analgesics on acute extremity pain in the emergency department**: a randomized clinical trial. JAMA 2017;(Nov). doi:10.1001/jama.2017.16190. (Ibuprofen & acetaminophen good options)

Chang CH, Shau WY, Kuo CW, Chen ST, Lai MS. **Increased Risk of Stroke** Associated With Nonsteroidal Anti-Inflammatory Drugs. A Nationwide Case-Crossover Study. Stroke. 2010 Jul 29.

Chen H, Jacobs E, Schwarzschild MA, McCullough ML, Calle EE, Thun MJ, Ascherio A. **Nonsteroidal antiinflammatory** drug use and the risk for Parkinson's disease. Ann Neurol. 2005 Dec;58(6):963-7.

Chen J, Shen P, Zhang XC, et al. Efficacy and Safety Profile of **Celecoxib for Treating Advanced Cancers**: A Meta-Analysis of 11 Randomized Clinical Trials. Clin Ther. 2014 Jul 9.

Chen W, Janz DR, Bastarache JA, et al. Prehospital **aspirin** use is associated with reduced risk of **acute respiratory distress syndrome** in critically ill patients: a propensity-adjusted analysis. Crit Care Med. 2015 Apr;43(4):801-7.

Chen YF, Jobanputra P, Barton P, Bryan S, Fry-Smith A, Harris G, et al. **Cyclooxygenase-2 selective non-steroidal anti-inflammatory drugs** (etodolac, meloxicam, celecoxib, rofecoxib, etoricoxib, valdecoxib and lumiracoxib) for osteoarthritis and rheumatoid arthritis: a systematic review and economic evaluation. Health Technol Assess. 2008 Apr;12(11):1-278, iii.

Chen YR, Hsieh FI, Chang CC, et al. Effect on Risk of **Stroke and Acute Myocardial Infarction of Nonselective Nonsteroidal Anti-Inflammatory Drugs in Patients** With Rheumatoid Arthritis. Am J Cardiol. 2018 Feb 12.

Chiew AL, Isbister GK, Duffull SB, et al. Evidence for the changing **regimens of acetylcysteine**. Br J Clin Pharmacol. 2015 Sep 19.

Cho E, Curhan G, Hankinson SE, Kantoff P, Atkins MB, Stampfer M, Choueiri TK. Prospective evaluation of analgesic use and **risk of renal cell cancer**. Arch Intern Med. 2011 Sep 12;171(16):1487-93.

Chuang SY, Hsu PF, Lin FJ, et al. Association between **nonsteroidal anti-inflammatory drugs and atrial fibrillation** among a middle-aged population: a nationwide population-based cohort. Br J Clin Pharmacol. 2018 Mar 20.

Cimbollek S, Quiralte J, Avila R. COX-2 inhibitors in patients with **sensitivity to nonselective NSAIDs**. N Engl J Med. 2009 Nov 26;361(22):2197-8.

Claridge LC, Eksteen B, Smith A, Shah T, Holt AP. Acute **liver failure after administration of paracetamol (acetaminophen)** at the maximum recommended daily dose in adults. BMJ. 2010 Dec 2;341:c6764. doi: 10.1136/bmj.c6764.

Clyman R, Wickremasinghe A, Jhaveri N, et al; **Ductus Arteriosus Feed** or Fast with **Indomethacin or Ibuprofen** (DAFFII) Investigators. Enteral Feeding during Indomethacin and Ibuprofen Treatment of a Patent Ductus Arteriosus. J Pediatr. 2013 Mar 5.

Cohen D. **Acetaminophen** for the Treatment of **Pain in Newborns**. Am Fam Physician. 2016 Aug 1;94(3):216-7

Colak T, Ipek T, Kanik A, Ogetman Z, Aydin S. Efficacy of **topical nonsteroidal (diclofenac) antiinflammatory drugs in mastalgia** treatment. J Am Coll Surg. 2003 Apr;196(4):525-30.

Colli A, Conte D, Valle SD, Sciola V, Fraquelli M. Meta-analysis: nonsteroidal anti-inflammatory drugs in **biliary colic**. Aliment Pharmacol Ther. 2012 Jun;35(12):1370-8.

Cook NR, Lee IM, Gaziano JM, et al. Low-dose **aspirin in the primary prevention of cancer**: the Women's Health Study (**WHS**): a randomized controlled trial. JAMA. 2005;294:47-55.

Cooper K, Squires H, Carroll C, et al. **Chemoprevention of colorectal cancer**: systematic review and economic evaluation. Health Technol Assess. 2010 Jun;14(32):1-206. (Especially aspirin & celecoxib reviewed)

Corman SL, Fedutes BA, Ansani NT. Impact of **nonsteroidal antiinflammatory drugs on the cardioprotective effects of aspirin**. Ann Pharmacother. 2005 Jun;39(6):1073-9. Epub 2005 May 3.

Cox-2 inhibitors & NSAIDS: **Drug Class Review Nov 2006** Oregon Health & Science University http://www.ohsu.edu/drugeffectiveness/reports/documents/NSAIDS%20Final%20Report%20Update%203.pdf

Coxib and traditional NSAID Trialists' (**CNT**) Collaboration. **Vascular and upper gastrointestinal effects** of non-steroidal anti-infl ammatory drugs: meta-analyses of individual participant data from randomised trials. Lancet 2013; online May 30.

Craig DG, Bates CM, Davidson JS, et al.. **Staggered overdose pattern and delay** to hospital presentation are associated with adverse outcomes following **paracetamol (acetaminophen)**-induced hepatotoxicity. Br J Clin Pharmacol. 2011 Nov 22.

Cryer B, Li C, Simon LS, et al. GI-REASONS: Novel 6-Month, Prospective, Randomized, Open-Label, Blinded Endpoint (PROBE) Trial. Am J Gastroenterol. 2013 Feb 12. **Celecoxib** was associated with a lower risk of clinically significant upper and/or lower GI events than nsNSAIDs.

Curhan SG, Eavey R, Shargorodsky J, Curhan GC. Analgesic use and the risk of **hearing loss** in men. Am J Med. 2010 Mar;123(3):231-7.

Curhan SG et al. Analgesic use and the risk of hearing loss in women. Am J Epidemiol 2012; 176(6):544-554.

da Costa BR, Reichenbach S, Keller N, et al. Effectiveness of **non-steroidal anti-inflammatory drugs for the treatment of pain in knee and hip osteoarthritis**: a network meta-analysis. Lancet. 2017 Jul 8;390(10090):e21-e33.

da Costa BR, Hari R, Jüni P. **Intra-articular corticosteroids for osteoarthritis** of the knee.JAMA. doi:10.1001/jama.2016.17565

Daniel S, Matok I, Gorodischer R, et al. **Major malformations** following exposure to nonsteroidal antiinflammatory drugs during the first trimester of pregnancy. J Rheumatol. 2012 Nov;39(11):2163-9.

Daniel S, Koren G, Lunenfeld E, et al. **Fetal exposure to nonsteroidal anti-inflammatory drugs and spontaneous abortions**. CMAJ. 2014 Mar 18;186(5)

Daniel S, Koren G, Lunenfeld E, et al. **NSAIDs and spontaneous abortions** - true effect or an indication bias? Br J Clin Pharmacol. 2015 Apr 6.

Dart RC, et al. **Acetaminophen poisoning**: an evidence-based consensus guideline for out-of-hospital management. Washington (DC): American Association of Poison Control Centers; 2005.http://www.aapcc.org/FinalizedPMGdlns/APAP%20-%20final%20guideline%209.9.05.pdf

Davidson BL, Verheijen S, Lensing AW, et al. Bleeding Risk of Patients With Acute Venous Thromboembolism (**on warfarin) Taking Nonsteroidal Anti-Inflammatory Drugs or Aspirin**. JAMA Intern Med. 2014 Apr 14.

Day RO, Graham GG. Non-steroidal anti-inflammatory drugs (**NSAIDs**). BMJ. 2013 Jun 11;346:f3195.

De Caterina Raffaele; Ruigomez Ana; Rodriguez Luis Alberto Garcia. Long-term Use of Anti-inflammatory Drugs (**NSAIDS**) and Risk of **Atrial Fibrillation**. Arch Intern Med. 2010;170(16):1450-1455.

De Silva V, El-Metwally A, Ernst E, et al. Evidence for the efficacy of **complementary and alternative medicines in the management of osteoarthritis**: a systematic review. Rheumatology (Oxford). 2011 May;50(5):911-20.

Dear JW, Antoine DJ, Park BK. Where are we now with **paracetamol/acetaminophen**? BMJ. 2015 Jul 10;351:h3705.

den Hertog HM, van der Worp HB, et al.; on behalf of the PAIS investigators. The Paracetamol (**Acetaminophen**) In **Stroke (PAIS)** trial: a multicentre, randomised, placebo-controlled, phase III trial. Lancet Neurol. 2009 May;8(5):434-440. Epub 2009 Mar 16.

Derry S, Moore RA. Single dose oral **aspirin for acute postoperative pain** in adults. Cochrane Database Syst Rev. 2012 Apr 18;4:CD002067. Aspirin is an effective analgesic for acute pain of moderate to severe intensity. High doses are more effective, but are associated with increased adverse events, including drowsiness and gastric irritation. The pain relief achieved with aspirin was very similar milligram for milligram to that seen with paracetamol.

Derry S, Moore RA, Rabbie R. Topical NSAIDs for chronic musculoskeletal pain in adults. Cochrane Database of Systematic Reviews 2012, Issue 9. Art. No.: CD007400. DOI: 10.1002/14651858.CD007400.pub2. Topical NSAIDs can provide good levels of pain relief; topical diclofenac solution is equivalent to that of oral NSAIDs in knee and hand osteoarthritis, but there is no evidence for other chronic painful conditions. Formulation can influence efficacy. The incidence of local adverse events is increased with topical NSAIDs, but gastrointestinal adverse events are reduced compared with oral NSAIDs.

Derry S, Derry CJ, Moore RA. Single dose oral **ibuprofen plus oxycodone** for acute postoperative pain in adults. Cochrane Database Syst Rev. 2013 Jun 26;6:CD010289. The combination of ibuprofen 400mg + oxycodone 5mg provided analgesia for longer than oxycodone alone, but not ibuprofen alone (at the same dose). There was also a smaller chance of needing additional analgesia over about eight hours, and with no greater chance of experiencing an adverse event.

Derry S, Moore RA, Gaskell H, et al. **Topical NSAIDs for acute musculoskeletal pain in adults**. Cochrane Database Syst Rev. 2015 Jun 11;6:CD007402. Topical NSAIDs provided good levels of pain relief in acute conditions such as sprains, strains and overuse injuries, probably similar to that provided by oral NSAIDs. Gel formulations of diclofenac (as Emugel(R)), ibuprofen, and ketoprofen, and some diclofenac patches, provided the best effects. Adverse events were usually minimal.Since the last version of this review, the new included studies have provided additional information. In particular, information on topical diclofenac is greatly expanded. The present review supports the previous review in concluding that topical NSAIDs are effective in providing pain relief, and goes further to demonstrate that certain formulations, mainly gel formulations of diclofenac, ibuprofen, and ketoprofen, provide the best results. Large amounts of unpublished data have been identified, and this could influence results in updates of this review.

Derry S, Wiffen PJ, Moore RA. **Single dose oral ibuprofen plus caffeine for acute postoperative pain in adults**. Cochrane Database Syst Rev 2015;7:CD011509. For ibuprofen 200 mg + caffeine 100 mg particularly, the low NNT value is among the lowest (best) values for analgesics in this pain model. The combination is not commonly available, but can be probably be achieved by taking a single 200 mg ibuprofen tablet with a cup of modestly strong coffee or caffeine tablets. In principle, this can deliver good analgesia at lower doses of ibuprofen.

Derry S, Wiffen P, Moore A. **Topical Nonsteroidal** Anti-inflammatory Drugs for Acute Musculoskeletal Pain. JAMA. 2016 Feb 23;315(8):813-814.

Derry S, Conaghan P, Da Silva JA, et al. **Topical NSAIDs for chronic musculoskeletal pain in adults**. Cochrane Database Syst Rev. 2016 Apr 22;4:CD007400. Topical diclofenac and topical ketoprofen can provide good levels of pain relief beyond carrier in osteoarthritis for a minority of people, but there is no evidence for other chronic painful conditions. There is emerging evidence that at least some of the substantial placebo effects seen in longer duration studies derive from effects imparted by the NSAID carrier itself, and that NSAIDs add to that.

Derry S, Wiffen PJ, Hauser W, et al. **Oral nonsteroidal anti-inflammatory drugs for fibromyalgia** in adults. Cochrane Database Syst Rev. 2017 Mar 27;3:CD012332. There is only a modest amount of very low-quality evidence about the use of NSAIDs in fibromyalgia, and that comes from small, largely inadequate studies with potential risk of bias. That bias would normally be to increase the apparent benefits of NSAIDs, but no such benefits were seen. Consequently, NSAIDs cannot be regarded as useful for treating fibromyalgia.

Desjardins PJ, Olugemo K, Solorio D, et al. Pharmacokinetic Properties and Tolerability of **Low-dose SoluMatrix Diclofenac**. Clin Ther. 2014 Dec 8.

Diener HC, et al. Efficacy and tolerability of diclofenac potassium sachets in migraine: a randomized, double-blind, cross-over study in comparison with diclofenac potassium tablets and placebo. Cephalagia. 2006 May;26(5):537-47.

Diercks GR, Comins J, Bennett K, et al. Comparison of **Ibuprofen vs Acetaminophen and Severe Bleeding Risk** After Pediatric Tonsillectomy: A Noninferiority Randomized Clinical Trial. JAMA Otolaryngol Head Neck Surg. 2019 Apr 4.

Din Farhat V N, Theodoratou Evropi, Farrington Susan M, Effect of **aspirin and NSAIDs on risk and survival from colorectal cancer**. Gut gut.2009.203000Published Online First: 15 September 2010 doi:10.1136/gut.2009.203000.

Doherty M, Hawkey C, Goulder M, et al.A randomised controlled trial of **ibuprofen, paracetamol or a combination** tablet of ibuprofen/paracetamol in community-derived people with knee pain. Ann Rheum Dis. 2011 Sep;70(9):1534-41.

Donati M, Conforti A, Lenti MC, et al. Risk of **acute and serious liver injury associated to nimesulide and other NSAIDs**: data from drug-induced liver injury case-control study in Italy. Br J Clin Pharmacol. 2016 Mar 18.

Dong YH, Chang CH, Wu LC, et al. Comparative **cardiovascular safety of non-steroidal anti-inflammatory drugs** in patients with hypertension: a population-based cohort study. Br J Clin Pharmacol. 2018 Feb 22.

Dougados M, Baeten D. **Spondyloarthritis**. Lancet. 2011 Jun 18;377(9783):2127-37.

Douglas L, Akil M. Sodium in soluble **paracetamol** may be linked to raised blood pressure. BMJ. 2006 May 13;332(7550):1133. (some forms of acetaminophen may have high sodium content)

Dreischulte T, Donnan P, Grant A, et al. Prescribing--A **Trial of Education, Informatics, and Financial Incentives**. (antiplatelets & NSAIDS) N Engl J Med. 2016 Mar 17;374(11):1053-64.

Drendel AL, Lyon R, Bergholte J, et al. Outpatient pediatric **pain** management practices for **fractures**. Pediatr Emerg Care. 2006 Feb;22(2):94-9. Most children with fractures have the "worst" pain in the first 48 hours after injury and used analgesia for 3 days after injury. There are noteworthy functional limitations for both children and their caregivers. Ibuprofen and acetaminophen with codeine are the analgesics most commonly used, with no clear superiority.

Drendel AL, Gorelick MH, Weisman SJ, Lyon R, Brousseau DC, Kim MK. A randomized clinical trial of **ibuprofen** versus acetaminophen with codeine for acute pediatric arm fracture pain. Ann Emerg Med. 2009 Oct;54(4):553-60.

Driver Jane A, Logroscino Giancarlo, Lu Linda, et al. Use of non-steroidal anti-inflammatory drugs (NSAIDs) and risk of **Parkinson's disease**: nested case-control study. BMJ 2011;342:doi:10.1136/bmj.d198 (20 Jan 2011) –no association found

Drugs in Pregnancy and Lactation. 9th ed. Briggs GE, Freeman RK, Yaffe SJ, editors. Williams and Wilkins; Philadelphia, PA: 2011.

Dubreuil M, Louie-Gao Q, Peloquin CE, et al. Risk of **myocardial infarction** with use of selected non-steroidal anti-inflammatory drugs in patients with **spondyloarthritis and osteoarthritis**. Ann Rheum Dis. 2018 Apr 19. (diclofenac, naproxen)

Eliassen AH, Chen WY, Spiegelman D, Willett WC, Hunter DJ, Hankinson SE. Use of aspirin, other nonsteroidal anti-inflammatory drugs, and acetaminophen and **risk of breast cancer** among premenopausal women in the Nurses' Health Study II. Arch Intern Med. 2009 Jan 26;169(2):115-21; discussion 121. These data **suggest** that the use of aspirin, other NSAIDs, and acetaminophen is not associated with a reduced risk of breast cancer among premenopausal women.

Eljezi V, Biboulet C, Boby H, et al. The **Dose-Dependent Effects of Ketoprofen** on Dynamic Pain after Open Heart Surgery. Pain Physician. 2017 Sep;20(6):509-520.

Elmunzer BJ, Waljee AK, Elta GH, Taylor JR, Fehmi SM, Higgins PD. A meta-analysis of rectal NSAIDs in the **prevention of post-ERCP pancreatitis**. Gut. 2008 Sep;57(9):1262-7.

Elmunzer BJ, Scheiman JM, Lehman GA, et al. U.S. Cooperative for Outcomes Research in Endoscopy (**USCORE**). A randomized trial of rectal **indomethacin** to **prevent post-ERCP pancreatitis**. N Engl J Med. 2012 Apr 12;366(15):1414-22.

Enthoven WT, Roelofs PD, Deyo RA, et al. Non-steroidal anti-inflammatory drugs for **chronic low back pain**. Cochrane Database Syst Rev. 2016 Feb 10;2:CD012087. Six of the 13 included RCTs showed that NSAIDs are more effective than placebo regarding pain intensity. NSAIDs are slightly more effective than placebo regarding disability. However, the magnitude of the effects is small, and the level of evidence was low. When we only included RCTs at low risk of bias, differences in effect between NSAIDs and placebo were reduced. We identified no difference in efficacy between different NSAID types, including selective versus non-selective NSAIDs. Due to inclusion of RCTs only, the relatively small sample sizes and relatively short follow-up in most included trials, we cannot make firm statements about the occurrence of adverse events or whether NSAIDs are safe for long-term use.

Enthoven WTM, Roelofs PD, Koes BW. **NSAIDs for Chronic Low Back Pain**. JAMA. 2017 Jun 13;317(22):2327-2328.

Etminan M, Sadatsafavi M, Jafari S, Doyle-Waters M, Aminzadeh K, Fitzgerald JM. **Acetaminophen** Use and the **Risk of Asthma** in Children and Adults: A Systematic Review and Metaanalysis. Chest. 2009 Aug 20. [Epub ahead of print]

European Medicines Agency (**EMA**), 2012. Agency finalises review of recent published data on **cardiovascular safety of NSAIDs** [online]. Available:http://www.ema.europa.eu/ema/index.jsp?curl=pages/news_and_events/news/2012/10/news_detail_001637.jsp&mid=WC0b01ac058004d5c1

FDA- **Acetaminophen and Liver Injury**: Q & A for Consumers 2009 http://www.fda.gov/downloads/ForConsumers/ConsumerUpdates/UCM172664.pdf

FDA Dec/09 , Endo, & Novartis revised the Hepatic Effects section of the Prescribing Information to add new warnings and precautions about the potential for elevation in liver function tests during treatment with all products (**including diclofenac gel**) on **diclofenac** sodium. In postmarketing reports, cases of drug-induced **hepatotoxicity** have been reported in the first month but can occur at any time during treatment with diclofenac. Postmarketing surveillance has reported cases of severe hepatic reactions, including liver necrosis, jaundice, fulminant hepatitis with and without jaundice, and liver failure. Some of these reported cases resulted in fatalities or liver transplantation.

FDA June/12 cautioned late last week against using **Reumofan Plus**, a dietary supplement marketed as a "natural" pain reliever for arthritis, osteoporosis, and other conditions. The drug, which is made in Mexico but available online, contains unlabeled and potentially harmful pharmaceutical ingredients: diclofenac, methocarbamol & sometimes dexamethasone. (Dec/12 FDA: Reumofan Plus is being relabeled and sold under the name "**WOW**.")

FDA Aug/12 is issuing an updated alert that **Reumofan Plus and Reumofan Plus Premium** contain undeclared active ingredients found in prescription drugs that should be used only under the supervision of a health care professional. It contains Diclofenac Sodium and Methocarbamol.

FDA Aug/13 laboratory analysis confirmed that **Ortiga contains the prescription drug ingredient, diclofenac**.

FDA Jan/14 is recommending health care professionals **discontinue prescribing and dispensing prescription combination drug products that contain more than 325 milligrams (mg) of acetaminophen** per tablet, capsule or other dosage unit.

FDA Feb/14 analysis of **Arth-Q supplement** contains hidden ingredient ibuprofen.

FDA Mar/14: Pain Free By Nature is recalling "**Reumofan Plus**" Tablets purchased through their website at www.painfreebynature.com, after FDA discovered that the product was distributed in packaging that did not reveal the presence of the active pharmaceutical ingredients methocarbamol and **diclofenac**, making it an unapproved drug.

FDA Apr/14: Nano Well-being Health Inc. issued a voluntary recall of **Super Arthgold**, 500 mg capsules to the consumer level. FDA laboratory analysis has found the product to contain chlorzoxazone, diclofenac and indomethacin.

FDA Apr/15 is alerting pet owners, veterinarians, health care providers and pharmacists that pets are at risk of illness and death when exposed to topical pain medications containing the nonsteroidal anti-inflammatory drug (NSAID) **flurbiprofen**. People using these medications should use care when applying them in a household with pets, as even very small amounts could be dangerous to these animals.

FDA Jul/15 is strengthening an existing label warning that non-aspirin nonsteroidal anti-inflammatory drugs (**NSAIDs**) increase the chance of a **heart attack or stroke**.

FDA Dec/15 Lucy's Weight Loss System is voluntarily recalling all lots of **Pink Bikini White powder Capsules**, 30 white (750MG per capsule) to the consumer level. Pink Bikini has been found positive for diclofenac.

Felson DT. Clinical practice. **Osteoarthritis of the knee**. N Engl J Med. 2006 Feb 23;354(8):841-8.

Fidahic M, Jelicic Kadic A, Radic M, Puljak L. **Celecoxib for rheumatoid arthritis**. Cochrane Database Syst Rev. 2017 Jun 9;6:CD012095. Celecoxib may improve clinical symptoms, alleviate pain and contribute to little or no difference in physical function compared with placebo. Celecoxib was associated with fewer numbers of participant withdrawals. Results for incidence of gastroduodenal ulcers (≥ 3 mm) and short-term serious adverse events were uncertain; however, there were few reported events for either.Celecoxib may slightly improve clinical symptoms compared with tNSAIDs. Results for reduced pain and improved physical function were uncertain. Particpants taking celecoxib had lower incidence of gastroduodenal ulcers (≥ 3 mm) and there were fewer withdrawals from trials. Results for cardiovascular events and short-term serious adverse events were also uncertain.Uncertainty about the rate of cardiovascular events between celecoxib and tNSAIDs could be due to risk of bias; another factor is that these were small, short-term trials. Catella-Lawson F, Reilly MP, Kapoor SC, Cucchiara

Floyd CN, Dargan PI. The toxicity of **paracetamol-codeine combination** in overdose is an unresolved issue. Br J Clin Pharmacol. 2017 Jul 30.

Flossmann E, Rothwell PM; British Doctors Aspirin Trial and the UK-TIA Aspirin Trial. Effect of **aspirin on long-term risk of colorectal cancer**: consistent evidence from randomised and observational studies. Lancet. 2007 May 12;369(9573):1603-13. Use of 300 mg or more of aspirin a day for about 5 years is effective in primary prevention of colorectal cancer in randomised controlled trials, with a latency of about 10 years, which is consistent with findings from observational studies. Long-term follow-up is required from other randomised trials to establish the effects of lower or less frequent doses of aspirin.

Forman JP, Rimm EB, Curhan GC. Frequency of analgesic use and risk of hypertension among men. Arch Intern Med 2007; 167:394-399. The frequency of **nonnarcotic analgesic** use is independently associated with a moderate increase in the risk of incident **hypertension**. Given the widespread use of these medications and the high prevalence of hypertension, these results may have important public health implications.

Forestier R, Desfour H, Tessier JM, et al. **Spa therapy** in the treatment of knee osteoarthritis: a large randomised multicentre trial. Ann Rheum Dis. 2010 Apr;69(4):660-5. Epub 2009 Sep 3.

Fosbøl EL, Folke F, Jacobsen S, et al. Cause-Specific Cardiovascular Risk Associated With Nonsteroidal Antiinflammatory Drugs Among Healthy Individuals. Circ Cardiovasc Qual Outcomes. 2010 Jun 8. (**Diclofenac & rofecoxib**)

Foster NE, Thomas E, Barlas P, Hill JC, Young J, Mason E, Hay EM. Acupuncture as an adjunct to exercise based physiotherapy for osteoarthritis of the knee: randomised controlled trial. BMJ. 2007 Sep 1;335(7617):436. Epub 2007 Aug 15. The addition of **acupuncture** to a course of advice and exercise for osteoarthritis of the knee delivered by physiotherapists provided no additional improvement in pain scores.

Fransen M, et al. HIPAID Collaborative Group. Safety and efficacy of routine postoperative ibuprofen for pain and disability related to ectopic bone formation after hip replacement surgery (HIPAID): randomised controlled trial. BMJ. 2006 Sep 9;333(7567):519. Epub 2006 Aug 2. These data do not support the use of routine prophylaxis with NSAIDs in patients undergoing **total hip replacement surgery**.

Friday JH, Kanegaye JT, McCaslin I, Zheng A, Harley JR. **Ibuprofen** provides analgesia equivalent to **acetaminophen-codeine** in the treatment of acute pain in children with extremity injuries: a randomized clinical trial. Acad Emerg Med. 2009 Aug;16(8):711-6. Epub 2009 Jul 14. Acute pain relief from ibuprofen is equivalent to that of acetaminophen-codeine for children presenting to the emergency department with extremity injury. More than half the children in this study were consequently found to have fractures. (LOE = 1b)

Friedman BW, Irizarry E, Solorzano C, et al. **Diazepam Is No Better Than Placebo** When Added to **Naproxen for Acute Low Back Pain**. Ann Emerg Med. 2017 Jan 19.

Friis S, Riis AH, Erichsen R, et al. Low-Dose **Aspirin or Nonsteroidal Anti-inflammatory Drug** Use and **Colorectal Cancer** Risk: A Population-Based, Case-Control Study. Ann Intern Med. 2015 Aug 25.

Frithsen IL, Simpson WM Jr. Recognition and management of acute medication **poisoning**. Am Fam Physician. 2010 Feb 1;81(3):316-23.

Fujiki EN, Netto NA, Kraychete DC, et al. Efficacy and safety of **loxoprofen sodium topical patch for the treatment of pain** in patients with minor acute traumatic limb injuries in Brazil: a randomized, double-blind, noninferiority trial. Pain. 2019 Jul;160(7):1606-1613.

Furyk J, Levas D, Close B, et al. **Intravenous versus oral paracetamol** (acetaminophen) for acute pain in adults in the emergency department setting: a prospective, double-blind, double-dummy, randomised controlled trial. Emerg Med J. 2018 Mar;35(3):179-184.

Gaskell H, Derry S, Wiffen PJ, et al. Single dose oral **ketoprofen or dexketoprofen for acute postoperative pain in adults**. Cochrane Database Syst Rev. 2017 May 25;5:CD007355. Ketoprofen at doses of 25 mg to 100 mg is an effective analgesic in moderate to severe acute postoperative pain with an NNT for at least 50% pain relief of 2.9 with a 50 mg dose. This is similar to that of commonly used NSAIDs such as ibuprofen (NNT 2.5 for 400 mg dose) and diclofenac (NNT 2.7 for 50 mg dose). Dexketoprofen is also effective with an NNT of 4.1 in the dose range 10 mg to 25 mg. Differential efficacy between dental surgery and other types of surgery seen for both drugs is unusual. Both drugs were well tolerated in single doses.

Gatoulis SC, Voelker M, Fisher M. Assessment of the Efficacy and Safety Profiles of **Aspirin 1gm and Acetaminophen With Codeine**: Results From 2 Randomized, Controlled Trials in Individuals With Tension-Type Headache and Postoperative Dental Pain. Clin Ther. 2011 Dec 12.

Gauer RL, Semidey MJ. Diagnosis and Treatment of **Temporomandibular Disorders**. Am Fam Physician. 2015 Mar 15;91(6):378-386.

Gaujoux-Viala C, Dougados M, Gossec L. Efficacy and safety of **steroid injections** for shoulder and elbow tendonitis: a meta-analysis of randomized controlled trials. Ann Rheum Dis. 2009 Dec;68(12):1843-9. Epub 2008 Dec 3. In the first 3 months of tendinitis of either the elbow or shoulder, injected corticosteroids are more effective than placebo or physical therapy, but no more effective than treatment with nonsteroidal anti-inflammatory drugs (NSAIDs). In the longer term they are no more effective than any treatment. What hasn't been studied is the effectiveness of steroid injections in patients for whom NSAID treatment isn't effective, since this is the usual progression of treatment of these painful conditions. (LOE = 1a-)

Gelber AC**. In the Clinic**: **Osteoarthritis**. Ann Intern Med. July1,2014. ITC1-2.

Girard P, Sourdet S, Cantet C, et al. **Acetaminophen Safety: Risk of Mortality and Cardiovascular Events** in Nursing Home Residents, a Prospective Study. J Am Geriatr Soc. 2019 Mar 26

Gislason GH, et al. **Risk of Death or Reinfarction** Associated With the Use of Selective Cyclooxygenase-2 Inhibitors and Nonselective Nonsteroidal Antiinflammatory Drugs After Acute Myocardial Infarction. Circulation. 2006 Jun 19; [Epub ahead of print] For any use of rofecoxib, celecoxib, ibuprofen, diclofenac, and other NSAIDs, the hazard ratios and 95% confidence intervals for death were 2.80 (2.41 to 3.25; for rofecoxib), 2.57 (2.15 to 3.08; for celecoxib), 1.50 (1.36 to 1.67; for ibuprofen), 2.40 (2.09 to 2.80; for diclofenac), and 1.29 (1.16 to 1.43; for other NSAIDS); there were dose-related increases in risk of death for all of the drugs. There were trends for increased risk of rehospitalization for MI associated with the use of both the selective COX-2 inhibitors and the nonselective NSAIDs. CONCLUSIONS: Selective COX-2 inhibitors in all dosages and nonselective NSAIDs in high dosages increase mortality in patients with previous MI and should therefore be used with particular caution in these patients.

Gislason GH, Rasmussen JN, Abildstrom SZ, et al. Increased mortality and cardiovascular morbidity associated with use of nonsteroidal anti-inflammatory drugs (NSAIDs) in chronic **heart failure**. Arch Intern Med. 2009 Jan 26;169(2):141-9.

Gleason JM, Slezak JM, Jung H, et al. Regular Nonsteroidal Anti-Inflammatory Drug (**NSAIDs**) Use and **Erectile Dysfunction**. J Urol. 2011 Feb 18.

Glyn-Jones S, Palmer AJ, Agricola R, et al. **Osteoarthritis**. Lancet. 2015 Mar 3.

Gokmen T, Erdeve O, Altug N, et al. Efficacy and safety of oral versus intravenous Ibuprofen in very low birth weight preterm infants with patent ductus arteriosus. J Pediatr. 2011 Apr;158(4):549-554.e1.

Goldberg DS, Forde KA, Carbonari DM, et al. Population-representative Incidence of **Drug-induced Acute Liver Failure** Based on an Analysis of an Integrated Healthcare System. Gastroenterology. 2015 Feb 27. pii: S0016-5085(15)00299-1. (**acetaminophen, herbal**, antimicrobial etc.)

Goldstein JL, Johanson JF, et al. Healing of gastric ulcers with **esomeprazole versus ranitidine** in patients who continued to receive NSAID therapy: a randomized trial. Am J Gastroenterol. 2005 Dec;100(12):2650-7.

Goldstein JL, Cryer B, Amer F, Hunt B. Celecoxib plus aspirin versus naproxen and lansoprazole plus aspirin: a randomized, double-blind, endoscopic trial. Clin Gastroenterol Hepatol. 2007 Oct;5(10):1167-74. n=854 In patients with osteoarthritis taking low-dose aspirin, the use of celecoxib or naproxen plus lansoprazole resulted in similar rates of gastroduodenal ulceration.

Goldstein LH, Berlin M, Berkovitch M, Kozer E. Effectiveness of oral vs rectal acetaminophen: a meta-analysis. Arch Pediatr Adolesc Med. 2008 Nov;162(11):1042-6. Among 4 small studies, oral and rectal acetaminophen for fever control were comparable in effectiveness. The authors could only find 1 study comparing **oral and rectal acetaminophen** for pain. It appeared that oral administration was more effective, but the effect may not have been clinically meaningful. The authors don't report on adverse effects. (LOE = 1a-)

Goldstein JL, Chan FK, Lanas A, Wilcox CM, Peura D, Sands GH, Berger MF, Nguyen H, Scheiman JM. **Haemoglobin decreases in NSAID** users over time: an analysis of two large outcome trials. Aliment Pharmacol Ther. 2011 Aug 2.

Gong J, Colligan M, Kirkpatrick C, Jones P. **Oral Paracetamol Versus Combination Oral Analgesics** for Acute Musculoskeletal Injuries. Ann Emerg Med. 2019 Aug 1.

González ELM et al. **Variability** among nonsteroidal antiinflammatory drugs in risk of upper **gastrointestinal bleeding**. Arthritis Rheum 2010 Jun; 62:1592.

Gouyon JB, Kibleur Y. Efficacy and tolerability of enteral formulations of **ibuprofen** in the treatment of **patent ductus arteriosus** in preterm infants. Clin Ther. 2010 Sep;32(10):1740-8.

Gossec L, Smolen JS, Gaujoux-Viala C, et al. European League Against Rheumatism (**EULAR**) recommendations for the management of **psoriatic arthritis** with pharmacological therapies. Ann Rheum Dis. 2011 Sep 27.

Graham GG, Scott KF, Day RO. Tolerability of **paracetamol**. Drug Saf. 2005;28(3):227-40.

Graham DJ, et al. Risk of acute myocardial infarction and sudden cardiac death in patients treated with cyclo-oxygenase 2 selective and non-selective non-steroidal anti-inflammatory drugs: nested case-control study. Lancet. 2005 Feb 5-11;365(9458):475-81.

Graham DY, Agrawal NM, Campbell DR, et al. NSAID-Associated Gastric Ulcer Prevention Study Group. Ulcer prevention in long-term users of nonsteroidal anti-inflammatory drugs: results of a double-blind, randomized, multicenter, active- and placebo-controlled study of **misoprostol vs lansoprazole**. Arch Intern Med. 2002 Jan 28;162(2):169-75.

Gulmez SE, Larrey D, Pageaux GP, Lignot S, Lassalle R, Jove J, et al. **Transplantation** for acute liver failure in patients exposed to **NSAIDs or paracetamol acetaminophen**): the multinational case-population SALT study. Drug Saf 2013;36:135-44.

Gulmez SE, Larrey D, Pageaux GP, et al. **Liver transplant associated with paracetamol (acetaminophen) overdose**: results from the seven-country SALT study. Br J Clin Pharmacol. 2015 May 27.

Guo D, Lam JM. **Henoch-Schönlein purpura**. CMAJ. 2016 Oct 18;188(15):E393. (NSAIDs an option for treatment)

Haas DM, Caldwell DM, Kirkpatrick P, McIntosh JJ, Welton NJ. **Tocolytic therapy** for preterm delivery: systematic review and network meta-analysis. BMJ. 2012 Oct 9;345:e6226.

Hakkarainen TW, Steele SR, Bastaworous A, et al. **Nonsteroidal Anti-inflammatory Drugs and the Risk for Anastomotic Failure**: A Report From Washington State's Surgical Care and Outcomes Assessment Program (SCOAP). JAMA Surg. 2015 Jan 21.

Hammerman C et al. **Ductal closure with paracetamol** (acetaminophen): a surprising new approach to patent ductus arteriosus treatment. Pediatrics. 2011 Dec;128(6):e1618-21.

Hammers AL, Sanchez-Ramos L, et al. Antenatal exposure to **indomethacin increases the risk of severe intraventricular hemorrhage, necrotizing enterocolitis, & periventricular leukomalacia**: a systematic review with metaanalysis. Am J Obstet Gynecol. 2015 Apr;212(4):505.e1-13.

Harbin M, Turgeon RD, Kolber MR. **Cardiovascular safety** of NSAIDs. Can Fam Physician. 2014 Mar;60(3):e166.

Harnden A, Takahashi M, Burgner D. **Kawasaki disease**. BMJ. 2009 May 5;338:b1514. doi: 10.1136/bmj.b1514.

Harris RE, Beebe-Donk J, Alshafie GA. Reduction in the risk of human **breast cancer** by selective cyclooxygenase-2 (COX-2) inhibitors. BMC Cancer. 2006 Jan 30;6:27.

Hauser TH, Salastekar N, Schaefer EJ, et al; Targeting Inflammation Using **Salsalate** in **Cardiovascular Disease** (**TINSAL-CVD**) Study Team. Effect of targeting inflammation with salsalate: the TINSAL-CVD randomized clinical trial on progression of coronary plaque in overweight and obese patients using statins [online May 25, 2016]. JAMA Cardiol. doi:10.1001/jamacardio .2016.0605.

Hay EM, et al. Effectiveness of community **physiotherapy** and enhanced **pharmacy review** for knee pain in people aged over 55 presenting to primary care: pragmatic randomized trial. BMJ. 2006 Oct 20; [Epub ahead of print] Evidence based care for older adults with knee pain, delivered by primary care physiotherapists and pharmacists, resulted in short term improvements in health outcomes, reduced use of non-steroidal anti-inflammatory drugs, and high patient satisfaction.

Hay AD, Costelloe C, Redmond NM, et al. Paracetamol plus ibuprofen for the treatment of fever in children (**PITCH**): randomised controlled trial. BMJ. 2008 Sep 2;337:a1302. doi: 10.1136/bmj.a1302. Parents, nurses, pharmacists, and doctors wanting to use medicines to supplement physical measures to maximise the time that children spend without fever should use **ibuprofen first** and consider the relative benefits and risks of using paracetamol plus ibuprofen over 24 hours.

Hayward KL, Powell EE, Irvine KM, et al. Can **Paracetamol (Acetaminophen) be administered to Patients with Liver Impairment**? Br J Clin Pharmacol. 2015 Oct 13.

Hawkey CJ, et al. Omeprazole compared with misoprostol for ulcers associated with nonsteroidal antiinflammatory drugs. **Omeprazole** versus Misoprostol for NSAID-induced Ulcer Management (**OMNIUM**) Study Group. N Engl J Med. 1998 Mar 12;338(11):727-34.

Hawton K, Bergen H, Simkin S, et al. Long term effect of reduced **pack sizes of paracetamol (acetaminophen)** on poisoning deaths and liver transplant activity in England and Wales: interrupted time series analyses. BMJ 2013;346:f403.

Health Canada Prohits sale of Bextra http://www.hc-sc.gc.ca/ahc-asc/media/advisories-avis/2005/2005_134_e.html

Health Canada June/06 two documents as part of its ongoing evaluation of COX-2-selective drugs: its official comments on the advice provided by the COX-2 Expert Advisory Panel and a report on the Department's scientific review of certain COX-2s. http://www.hc-sc.gc.ca/dhp-mps/prodpharma/activit/sci-consult/cox2/index_e.html

Health Canada Aug/07 reports that the Therapeutic Goods Administration (TGA), the federal regulatory authority in Australia, recently withdrew market authorization for **Prexige due to eight reports of serious liver adverse events** in Australia linked to the drug, including two deaths and two liver transplants. These adverse events were primarily with use of 200 mg and 400 mg doses daily.

Health Canada Sept/07 reports that **Qiangli Zhuanggutongbiling** has reportedly been used for joint pain and stiffness. It was found to contain the undeclared prescription drugs prednisolone acetate, cortisone acetate, piroxicam, and diclofenac.

Health Canada Sept/07: **Khun-Phra** is a health product promoted for pain relief that has been found to contain the undeclared drugs dexamethasone, prednisolone, phenylbutazone, diazepam, cyproheptadine and mebhydrolin.. **Asam Urat Flu Tulang, PJ Dewandaru** is a health product promoted to treat joint pain, rheumatism and arthritis. It has been found to contain the undeclared drugs dexamethasone, diclofenac and acetaminophen.

Health Canada Oct/07 Foreign Product Alerts: ***Zhen Feng Da Brand Xi Tong Wan*** is promoted as a pain reliever. Lot #060908 has been found to contain undeclared indomethacin, a prescription anti-inflammatory drug that should only be taken under the guidance of a health professional. ***Wellring Brand Yin Qiao Jie Du*** is a health product promoted to treat cold and flu symptoms. Lot#51005 has been found to contain undeclared acetaminophen. ***Gu Ci Dan*** and ***Xu Log Bou*** are promoted as pain relievers and have been found to contain indomethacin.

Health Canada Oct/07 is advising consumers that it has stopped the sale of the anti-inflammatory drug **Prexige** (lumiracoxib) in Canada and will cancel the drug's market authorization due to the potential for serious liver-related adverse events. (2 new severe cases in Canada)

Health Canada July/08 is advising consumers not to use 2 foreign health products due to concerns about possible side-effects: **3rd Generation In Homoeopathy Arthrit Indica Tablet**. The product is labelled for "intense joint pain." The Health Sciences Authority of Singapore has warned consumers not to use the product because it contains **nimesulide**, a pharmaceutical ingredient that has been associated with liver damage.

Health Canada Aug/08 is advising consumers not to use foreign health products due to concerns against the use of **AA Qu Feng Shu Jin Wan** because it was found to contain the undeclared pharmaceutical ingredient dexamethasone. **Obat Asam Urat** and **Asam Urat** both contained dexamethasone, phenylbutazone and piroxicam.

Health Canada June/09 is informing Canadian health care professionals and consumers of recent restrictions regarding the use of the prescription drug piroxicam. Health Canada has conducted a safety review and concluded that **piroxicam** should no longer be used to treat short-term pain and inflammation due to an increased risk of serious skin reactions and gastrointestinal problems relative to other similar drugs.

Health Canada July/09 is warning consumers not to use the unauthorized health product labelled as **Specific-Formula Arthro-Ace** as it was found to contain undeclared dexamethasone and may cause serious health effects.

Health Canada July/09 is warning that the Singapore Health Sciences Authority (HSA) warned consumers to not buy or use **Air Ikan Haruan** after it was found to contain undeclared dexamethasone. The Hong Kong Department of Health warned consumers not to buy or use the product **Neovidan** after it was found to contain undeclared prednisolone and mefenamic acid.

Health Canada Aug/09 is advising via Singapore Health Sciences Authority (HSA) that **Delima Raja Urat** contains undeclared dexamethasone, chlorpheniramine, pheniramine and sibutramine, while **Cao Gen Bai Lin Wan** contains undeclared dexamethasone and chlorpheniramine.

Health Canada Aug/10 **Huo Luo Jing Dan** The Singapore Health Sciences Authority warned consumers not to buy or consume Huo Luo Jing Dan after it was found to contain undeclared indomethacin, dexamethasone and prednisolone.

Health Canada Oct/11 **Huo Li Bao and Ren Sem Tu Chon Chin Kuo Pill** - The Singapore Health Sciences Authority warned that these Chinese pain-relief products contain prescription and/or over-the-counter drugs (furosemide, piroxicam, chlorpheniramine, and/or dexamethasone).

Health Canada Dec/11 is advising Canadians that Vita Health's product, "**Compliments Muscle and Back Pain Relief Regular Strength**" contains a significant labelling error in the French dosing directions that may pose serious risks to children (less than 12 years of age).

Health Canada Apr/13 **1. Diet Garcinia Forte; Shan Dian Shou; Aulura Energy Dietary Supplement** The Hong Kong Department of Health has advised consumers not to use these products after they were found to contain sibutramine and phenolphthalein, drug ingredients that were not declared on their product label. Shan Dian Shou also contains the undeclared prescription drug sildenafil. **2. Snake Powder Capsule for Rheumatism; Jia Rong Zhuang Gu Tong Bi Jiaonang; Long Ren Tang Fu She Gu Rang Jiao Nang** The Hong Kong Department of Health advised consumers not to use these products after they were found to contain multiple prescription and non-prescription drugs that were not declared on their product label. (prednisone, indomethacin, diclofenac, hydrochlorothiazide, cimetidine, prednisone, theophylline, dexamethasone etc). **3. Tinea Schwartz's; Tiao Jing Bu Xue Pills; Yeung Ng Tong Tin Hee Pills** The Hong Kong Department of Health advised consumers not to use these products after they were found to contain prescription drugs that were not declared on their product label (prednisone, indomethacin, diclofenac). **4. Quan Xie Jin Gu Tong; Xinhuang Pian; Jin Gu Feng Shi Kang Jiao Nang** The Hong Kong Department of Health advised consumers not to use these products after they were found to contain multiple prescription and non-prescription drugs that were not declared on their product label. (prednisone, piroxicam, diclofenac, indomethacin, naproxen).

Health Canada Apr/14: Nano Well-being Health Inc. issued a voluntary recall of **Super Arthgold**, 500 mg capsules to the consumer level. FDA laboratory analysis has found the product to contain chlorzoxazone, diclofenac and indomethacin, making it an unapproved new drug.

Health Canada May/14 **Ortiga** contains diclofenac.

Health Canada June/14: **Pro ArthMax** contains diclofenac, ibuprofen, naproxen, indomethacin, chlorzoxazone.

Health Canada June/14: **Zi Xiu Tang Pollen capsule and Zi Xiu Tang Beauty Face and Figure capsule**: The Australian Therapeutic Goods Administration (TGA) warned consumers not to use these products after they were found to contain undeclared sibutramine, phenolphthalein, diclofenac, and ibuprofen. The product, Zi Xiu Tang Beauty Face and Figure capsule, was also found to contain undeclared glibenclamide, and indomethacin.

Health Canada Sep/14: **JIN LONG Snakes Bones Rheumatic Capsules**- The Singapore Health Sciences Authority warned consumers not to use this product after it was found to contain betamethasone, piroxicam,oxethazaine, paracetamol (also known as acetaminophen) and furosemide.

Health Canada Oct/14 Diclofenac - Update to Heart and Stroke Related Safety Information and Decrease in the Maximum Recommended Daily Dose for Tablets and Suppositories - Novartis Pharma Canada Inc. and Pfizer Canada Inc. Diclofenac at 150 mg per day, is associated with an increased risk of serious cardiovascular adverse events. The maximum recommended daily dose of systemic **diclofenac** is now **100 mg per day**. Diclofenac is not recommended in patients with pre-existing cardiovascular or cerebrovascular disease.

Health Canada Dec/14: **Joint-Soft**: The Singapore Health Sciences Authority warned consumers not to use the product **JOINT-SOFT** after it was found to contain piroxicam anddexamethasone. The Singapore Health Sciences Authority warned consumers not to use the product **KEBIGUTAIJIAONANG** after it was found to contain piroxicam, hydrochlorothiazide, and prednisone. The Singapore Health Sciences Authority warned consumers not to use the product **Pil Raja Urat Asli** after it was found to contain piroxicam and indomethacin.

Health Canada Mar/15 advises- **Feng Shi Ling**: undeclared diclofenac & indomethacin.

Health Canada Apr/15 is working with the Canadian manufacturers of prescription oral **ibuprofen** products to update the safety information regarding the risk of serious **cardiovascular side effects** (e.g., heart attack and stroke) when these products are used at high doses (**at or above 2400 mg/day**). This risk increases with dose and duration of use.

Health Canada Jul/15 is taking additional steps to minimize the risk of **liver damage** and improve **acetaminophen** safety. This action is in light of a Health Canada review that assessed acetaminophen and liver injury in the Canadian context, a summary of which is available on Health Canada's website.

Health Canada Dec/15: **Naproxen Emo** contains naproxen.

Health Canada Feb/16 is informing Canadians that Pfizer Consumer Healthcare has initiated a voluntary **recall of 124 lots of Advil liquid** products for infants and children because of a potential risk of inconsistences in dosing of the product.

Health Canada Mar/16 says **Asia Black, Black Widow 25, Burn Fat Now, Extreme Stack, Fataway Ultimate Stack, MaxOut Body, Metabolic Accelerator, Methyldrene Original 25 Dietary Supplements, ThermoFX, Thermogenic Fat Burner & Thin and Slim Naturall**y by FDA contains undeclared salicylic acid.

Health Canada June/16: Singapore Health Sciences Authority-**Meizitang Botanical Slimming 100% Natural Soft Gel** contains undeclared diclofenac.

Health Canada Aug/16: Hong Kong Department of **Health-4L Slimness and 4L Slimburn Plus** undeclared diclofenac.

Health Canada Sep/16 is releasing an updated **Labelling Standard for over-the-counter acetaminophen** products to help consumers use these products more safely. Product packages will include clearer instructions and stronger warnings to help reduce the potential for liver damage. Improvements to the Labelling Standard include: clearer instructions on packages that emphasize the importance of using the lowest effective dose; not exceeding the recommended daily maximum (which is 4,000 mg for adults) in a 24-hour period; using these products for no more than five days for pain or three days for fever; and not mixing them with alcohol if drinking three or more drinks in a day; displaying the words "contains acetaminophen" in bold, red text in the top right corner of the front of the package to make it easier for consumers to know if a product contains this drug; a new Drug Facts table for packages to provide product instructions, warnings and other safety information in a consistent, quick-reference format; and a recommendation that all children's liquid products include a calibrated dosing device, so parents and caregivers can be sure that they're giving their child the right amount.

Health Canada June/17: **PHQ 1001 Khasiat Penawar Herba Qaseh Serata Herb** has undeclared dexamethasone, piroxicam, griseofulvin and paracetamol by Singapore Health Sciences Authority.

Health Canada June/17: **TONIK TUAN HAJI 1921** has undeclared dexamethasone by Hong Kong Department of Health.

Heard KJ, Green JL, Dart RC. Serum alanine aminotransferase elevation during 10 days of acetaminophen use in nondrinkers. Pharmacotherapy. 2010 Aug;30(8):818-22.

Hedayati H, Parsons J, Crowther CA. **Rectal analgesia for pain from perineal trauma following childbirth**. Cochrane Database Syst Rev. 2003; (3): CD003931.

Hedberg ML, Peyser ND, Bauman JE, et al. Use of nonsteroidal anti-inflammatory drugs predicts **improved patient survival for PIK3CA-altered head and neck cancer**. J Exp Med. 2019 Jan 25.

Helin-Salmivaara A, et al. NSAID use and the risk of hospitalization for first myocardial infarction in the general population: a nationwide case-control study from Finland. Eur Heart J. 2006 Jul;27(14):1657-63. Epub 2006 May 26.

Heppell SP, Isbister GK. **Lack of respiratory depression** in **paracetamol (acetaminophen)-codeine combination** overdoses. Br J Clin Pharmacol. 2016 Dec 30

Hider-Mlynarz K, Cavalié P, Maison P. Trends in **Analgesic Consumption in France Over the last 10 Years and Comparison of Patterns Across Europe**. Br J Clin Pharmacol. 2018 Mar 7.

Hill KP, Ross JS, Egilman DS, Krumholz HM. The **ADVANTAGE seeding trial**: a review of internal documents. (Vioxx marketing trial) Ann Intern Med. 2008 Aug 19;149(4):251-8.

Hinz B, Brune K. **Paracetamol and cyclooxygenase inhibition**: is there a cause for concern? Ann Rheum Dis. 2012 Jan;71(1):20-5.

Hippisley-Cox J, Coupland C, Logan R. Risk of adverse gastrointestinal outcomes in patients taking **cyclo-oxygenase-2 inhibitors or conventional** non-steroidal anti-inflammatory drugs: population based nested case-control analysis. BMJ. 2005 Dec 3;331(7528):1310-6.
CONCLUSION: No consistent evidence was found of enhanced safety against gastrointestinal events with any of the new cyclo-oxygenase-2 inhibitors compared with non-selective non-steroidal anti-inflammatory drugs. The use of ulcer healing drugs reduced the increased risk of adverse gastrointestinal outcomes with all groups of non-steroidal anti-inflammatory drugs, but for diclofenac the increased risk remained significant.

Ho JM, Juurlink DN. Considerations when prescribing **trimethoprim-sulfamethoxazole**. CMAJ. 2011 Oct 11. (NSAID DIs)

Hochberg, M. C., Altman, R. D., April, K. T., et al. **American College of Rheumatology (ACR) 2012** recommendations for the use of nonpharmacologic and pharmacologic therapies in **osteoarthritis of the hand, hip, and knee**. 2012 Arthritis Care Res, 64: 465–474.

Hochberg MC, Martel-Pelletier J, Monfort J, et al. on behalf of the **MOVES** Investigation Group. Combined **chondroitin sulfate and glucosamine** for painful knee osteoarthritis: a multicentre, randomised, double-blind, non-inferiority trial versus celecoxib. Ann Rheum Dis. 2015 Jan 14.

Hoffman HJ, Dobie RA, Losonczy KG, et al. **Declining Prevalence of Hearing Loss** in US Adults Aged 20 to 69 Years. JAMA Otolaryngol Head Neck Surg. 2016 Dec 15.

Holmes, Michelle D., Chen, Wendy Y., Li, Lisa, et al. **Aspirin** Intake and Survival **After Breast Cancer**. J Clin Oncol 2010 0: JCO.2009.22.7918.

Hoofnagle JH, Björnsson ES. **Drug-Induced Liver Injury** - Types and Phenotypes. N Engl J Med. 2019 Jul 18;381(3):264-273.

Hooper L, Brown TJ, Elliott R, et al. The effectiveness of **five strategies for the prevention of gastrointestinal toxicity** induced by non-steroidal anti-inflammatory drugs: systematic review. BMJ. 2004 Oct 23;329(7472):948. Epub 2004 Oct 8. CONCLUSIONS: Misoprostol, COX-2 specific and selective NSAIDs, and probably proton pump inhibitors significantly reduce the risk of symptomatic ulcers, and misoprostol and probably COX-2 specifics significantly reduce the risk of serious gastrointestinal complications, but data quality is low. More data on H2 receptor antagonists and proton pump inhibitors are needed, as is better reporting of rare but important outcomes.

Hoover RM, Hayes VA, Erramouspe J. Association Between **Prenatal Acetaminophen Exposure and Future Risk of Attention Deficit/Hyperactivity Disorder** in Children. Ann Pharmacother. 2015 Dec;49(12):1357-61.

Hou LC, Huang F, Xu HB. Does **celecoxib** improve the efficacy of chemotherapy for advanced non-small cell **lung cancer**? Br J Clin Pharmacol. 2015 Aug 29.

Hudson N, Taha AS, Russell RI, et al. **Famotidine** for healing and maintenance in nonsteroidal anti-inflammatory drug-associated gastroduodenal ulceration. Gastroenterology. 1997 Jun;112(6):1817-22.

Huerta C, Varas-Lorenzo C, Castellsague J, Garcia Rodriguez LA. Non-steroidal anti-inflammatory drugs and risk of first hospital admission for **heart failure** in the general population. Heart. 2006 Nov;92(11):1610-5. Epub 2006 May 22.

Hughes GJ, Patel PN, Saxena N.. Effect of **acetaminophen on international normalized ratio** in patients receiving warfarin therapy. Pharmacotherapy 2011 June;31(6):591–597.

Hurtado-Gonzalez P, Anderson RA, Macdonald J, et al. Effects of Exposure to **Acetaminophen and Ibuprofen on Fetal Germ Cell Development** in Both Sexes in Rodent and Human Using Multiple Experimental Systems. Environ Health Perspect. 2018 Apr 16;126(4):047006.

Husebo BS, Ballard C, Sandvik R, Nilsen OB, Aarsland D. Efficacy of treating **pain to reduce behavioural disturbances** in residents of nursing homes with dementia: cluster randomised clinical trial. BMJ 2011;343;d4065. (**70% on 3g/day acetaminophen**)

Imamura M, Okamoto Y, Nishikawa T, et al. **Celecoxib as a Potential Treatment for Intractable Lymphatic Malformation**. Pediatrics. 2019 Aug 28.

Imazio M, Gaita F, LeWinter M. Evaluation and Treatment of **Pericarditis**: A Systematic Review. JAMA. 2015 Oct 13;314(14):1498-506.

Irwin RS, et al. American College of Chest Physicians (ACCP). **Diagnosis and management of cough** executive summary: ACCP evidence-based clinical practice guidelines. Chest. 2006 Jan;129(1 Suppl):1S-23S. http://www.chestjournal.org/cgi/content/full/129/1_suppl/1S

Iversen MD, Hammond A, Betteridge N. **Self-management** of rheumatic diseases: state of the art and future perspectives. Ann Rheum Dis 2010; 69: 955–63.

Jain A, Shah PS. Diagnosis, Evaluation, and Management of **Patent Ductus Arteriosus in Preterm Neonates**. JAMA Pediatr. 2015 Jul 13.

James LP, et al. Pediatric Acute Liver Failure Study Group. Detection of **acetaminophen** protein adducts in children with acute **liver failure** of indeterminate cause. Pediatrics. 2006 Sep;118(3):e676-81.

James ND, Sydes MR, Mason MD, et al. **Celecoxib plus hormone therapy versus hormone** therapy alone for hormone-sensitive **prostate cancer**: first results from the STAMPEDE multiarm, multistage, randomised controlled trial. Lancet Oncol 2012; online March 26.

Jaturapatporn D, Isaac MG, McCleery J, et al. Aspirin, steroidal and non-steroidal anti-inflammatory drugs for the treatment of **Alzheimer`s disease**. Cochrane Database Syst Rev. 2012 Feb 15;2:CD006378. Based on the studies carried out so far, the efficacy of aspirin, steroid and NSAIDs (traditional NSAIDs and COX-2 inhibitors) is not proven. Therefore, these drugs cannot be recommended for the treatment of AD.

Jensen EA, Dysart KC, Gantz MG, et al. Association between use of **prophylactic indomethacin and the risk for bronchopulmonary dysplasia in extremely preterm infants**. J Pediatr 2017;186:34-40.

Jerschow E, Lin RY, Scaperotti MM, et al. **Fatal anaphylaxis** in the United States, 1999-2010: Temporal patterns and demographic associations. J Allergy Clin Immunol. 2014 Sep 26.

Jevsevar DS. Treatment of osteoarthritis of the knee: evidence-based guideline, 2nd edition. J Am Acad Orthop Surg. 2013 Sep;21(9):571-6.

Jick H, et al. Nonsteroidal antiinflammatory drugs and **acute myocardial infarction** in patients with no major risk factors. Pharmacotherapy. 2006 Oct;26(10):1379-87. Extensive use of rofecoxib, celecoxib, and diclofenac increases the risk of acute myocardial infarction, but similar use of ibuprofen and naproxen does not.

Jickling G, Heino A, Ahmed SN. **Acetaminophen toxicity** with concomitant use of **carbamazepine**. Epileptic Disord. 2009 Dec 9.

Jin J. **Nonsteroidal Anti-inflammatory Drugs (Patient page)**. JAMA. 2015 Sep 8;314(10):1084.

Johannesdottir SA, Chang ET, Mehnert F, et al. Nonsteroidal anti-inflammatory drugs and the risk of **skin cancer**: A population-based case-control study. Cancer. 2012 May 29.

Johnson MT, McCammon CA, Mullins ME, Halcomb SE. Evaluation of a **Simplified N-Acetylcysteine Dosing Regimen** for the Treatment of Acetaminophen Toxicity (June). Ann Pharmacother. 2011 May 17.

Jones P, Dalziel SR, Lamdin R, et al. **Oral non-steroidal anti-inflammatory drugs versus other oral analgesic agents for acute soft tissue injury**. Cochrane Database Syst Rev. 2015 Jul 1;7:CD007789. There is generally low- or very low-quality but consistent evidence of no clinically important difference in analgesic efficacy between NSAIDs and other oral analgesics. There is low-quality evidence of more gastrointestinal adverse effects with non-selective NSAID compared with paracetamol. There is low- or very low-quality evidence of better function and fewer adverse events with NSAIDs compared with opioid-containing analgesics; however, one study dominated this evidence using a now unavailable COX-2 selective NSAID and is of uncertain applicability. Further research is required to determine whether there is any difference in return to function or adverse effects between both non-selective and COX-2 selective NSAIDs versus paracetamol.

Jordan KM, Arden NK, Doherty M, et al. **EULAR** Recommendations 2003: an evidence based approach to the management of knee **osteoarthritis**: report of a Task Force of the Standing Committee for International Clinical Studies Including Therapeutic Trials (ESCISIT). Ann Rheum Dis 2003; 62: 1145–55.

Juhl C et al. Impact of **exercise** type and dose on pain and disability in knee osteoarthritis: A systematic review and meta-regression analysis of randomized controlled trials. Arthritis Rheumatol 2014 Mar; 66:622.

Kai S, Kondo E, Kawaguchi Y, et al. **Flurbiprofen** Concentration in the Soft Tissues Is Higher after **Topical** Application Than after Oral Administration. Br J Clin Pharmacol. 2012 Jul 24.

Kamal A, Akshintala VS, Talukdar R, et al. A Randomized Trial of **Topical Epinephrine and Rectal Indomethacin** for Preventing **Post-Endoscopic Retrograde Cholangiopancreatography Pancreatitis** in High-Risk Patients. Am J Gastroenterol. 2019 Feb;114(2):339-347.

Kamour A, Crichton S, Cooper G, et al. **Central Nervous System toxicity of mefenamic acid overdose** compared to other NSAIDs: an analysis of cases reported to the United Kingdom National Poisons Information Service. Br J Clin Pharmacol. 2016 Oct 26.

Kang EM, Lundsberg LS, Illuzzi JL, Bracken MB. Prenatal exposure to **acetaminophen and asthma** in children. Obstet Gynecol. 2009 Dec;114(6):1295-306.

Kang AM, Brooks DE. **US Poison Control Center Calls** for Infants 6 Months of Age and Younger. Pediatrics. 2016 Jan 13.

Kastelein F et al. Probar-study Group. Nonsteroidal Anti-Inflammatory Drugs and Statins Have **Chemopreventative Effects in Patients With Barrett's Esophagus**. Gastroenterology. 2011 Dec;141(6):2000-8

Kaufman DW, Kelly JP, Battista DR, et al. **Exceeding the daily dosing limit of nonsteroidal anti-inflammatory drugs among ibuprofen users**. Pharmacoepidemiol Drug Saf. 2018 Jan 26.

Kaufman DW, Kelly JP, Battista DR, et al. **Five-year trends in Acetaminophen use** exceeding the recommended daily maximum dose. Br J Clin Pharmacol. 2019 Feb 10.

Kent AP, Brueckmann M, Fraessdorf M, et al. Concomitant **oral anticoagulant and nonsteroidal anti-inflammatory drug therapy in patients with atrial fibrillation**. (RE-LY) J Am Coll Cardiol 2018;72:255–67.

Kearney PM, et al. Do selective cyclo-oxygenase-2 inhibitors and traditional non-steroidal anti-inflammatory drugs increase the risk of **atherothrombosis**? Meta-analysis of randomised trials. BMJ. 2006 Jun 3;332(7553):1302-8. Selective COX 2 inhibitors are associated with a moderate increase in the risk of vascular events, as are high dose regimens of ibuprofen and diclofenac, but high dose naproxen is not associated with such an excess.

Kerry S. Kuehl, Review of the efficacy and tolerability of the **diclofenac epolamine topical** patch 1.3% in patients with acute pain due to soft tissue injuries, Clinical Therapeutics, Volume 32, Issue 6, June 2010, Pages 1001-1014.

Khalaf N, Yuan C, Hamada T, et al. Regular Use of **Aspirin or Non-Aspirin Nonsteroidal Anti-Inflammatory Drugs Is Not Associated With Risk of Incident Pancreatic Cancer** in Two Large Cohort Studies**.** Gastroenterology. 2018

Khan M, Adili A, Winemaker M, et al. **Management of osteoarthritis of the knee in younger patients**. CMAJ. 2018 Jan 22;190(3):E72-E79.

Kim SY, Chang YJ, Cho HM, Hwang YW, Moon YS. Non-steroidal anti-inflammatory drugs for the **common cold**. Cochrane Database Syst Rev. 2009 Jul 8;(3):CD006362.

Kim SY, Chang YJ, Cho HM, et al. **Non-steroidal anti-inflammatory drugs for the common cold**. Cochrane Database Syst Rev. 2015 Sep 21;9:CD006362.
NSAIDs are somewhat effective in relieving the discomfort caused by a cold but there is no clear evidence of their effect in easing respiratory symptoms. The balance of benefit and harms needs to be considered when using NSAIDs for colds.

Kim SY, Shin SH, Kim HS, et al. **Pulmonary Arterial Hypertension after Ibuprofen** Treatment for **Patent Ductus Arteriosus i**n Very Low Birth Weight Infants. J Pediatr. 2016 Sep 28.

Kiriakidou M, Cotton D, Taichman D, Williams S. **Systemic Lupus Erythematosus**. Ann Intern Med. 2013 Oct 1;159(7):ITC4-1.

Kirkley A, et al. A Randomized Trial of **Arthroscopic Surgery** for Osteoarthritis of the Knee. N Engl J Med. 2008 Sep 11;359(11):1097-1107. Arthroscopic surgery for osteoarthritis of the knee provides no additional benefit to optimized physical and medical therapy.

Kirpalani A, Rieder M. Is NSAID use in children associated with the **risk of renal injury**? Paediatr Child Health. 2019 May;24(2):119-121.

Klein M, Gögenur I, Rosenberg J. Postoperative use of non-steroidal anti-inflammatory drugs in patients with **anastomotic leakage** requiring reoperation after colorectal resection: cohort study based on prospective data. BMJ. 2012 Sep 26;345:e6166. (diclofenac concerning)

Köhler O, Benros ME, Nordentoft M, et al. Effect of **Anti-inflammatory Treatment on Depression**, Depressive Symptoms, and Adverse Effects: A Systematic Review and Meta-analysis of Randomized Clinical Trials. JAMA Psychiatry. 2014 Oct 15.

Konrad G, Katz A. Are medication restrictions before **FOBT** necessary?:Practical advice based on a systematic review of the literature. Can Fam Physician. 2012 Sep;58(9):939-48.

Kroon F, Landewe R, Dougados M, et al. Continuous NSAID use reverts the effects of inflammation on radiographic progression in patients with **ankylosing spondylitis**. Ann Rheum Dis 2012.

Konstan MW, Schluchter MD, Xue W, Davis PB. Clinical use of Ibuprofen is associated with slower FEV1 decline in children with **cystic fibrosis**. Am J Respir Crit Care Med. 2007 Dec 1;176(11):1084-9. Epub 2007 Sep 13. Slower rates of FEV(1) decline are seen in children and adolescents with cystic fibrosis who are treated with ibuprofen. The apparent benefits of ibuprofen therapy outweigh the small risk of gastrointestinal bleeding.

Krijthe BP, Heeringa J, Hofman A, et al. Non-steroidal anti-inflammatory drugs and the risk of **atrial fibrillation**: a population-based follow-up study. BMJ Open. 2014 Apr 8

Kristensen DM, Desdoits-Lethimonier C, Mackey AL, et al. **Ibuprofen alters human testicular physiology to produce a state of compensated hypogonadism**. Proc Natl Acad Sci U S A. 2018 Jan 8.

Kuo HW, Tsai SS, Tiao MM, Liu YC, Lee IM, Yang CY. Analgesic use and the **risk for progression of chronic kidney disease**. Pharmacoepidemiol Drug Saf. 2010 Jul;19(7):745-51.

Kurmis AP, Kurmis TP, O'Brien JX, Dalén T. The effect of nonsteroidal anti-inflammatory drug administration on **acute phase fracture-healing**: a review. J Bone Joint Surg Am. 2012 May 2;94(9):815-23.

Kurth T, Hennekens CH, Stürmer T, Sesso HD, Glynn RJ, Buring JE, Gaziano JM. Analgesic use and risk of **subsequent hypertension** in apparently healthy men. Arch Intern Med. 2005 Sep 12;165(16):1903-9.

Lackner JE, et al. Correlation of leukocytospermia with clinical infection and the positive effect of antiinflammatory (**valdecoxib**) treatment on **semen** quality. Fertil Steril. 2006 Sep;86(3):601-5. Epub 2006 Jun 16.

Lai KC, Chu KM, Hui WM, et al. Celecoxib compared with **lansoprazole and naproxen** to prevent gastrointestinal ulcer complications. Am J Med. 2005 Nov;118(11):1271-8. (InfoPOEMs: In patients at high risk for recurrent peptic ulcer with nonsteroidal anti-inflammatory drug therapy, celecoxib was no more effective than the combination of naproxen (Naprosyn) and lansoprazole (Prevacid) in preventing serious adverse effects and was more likely to cause dyspepsia symptoms. The benefit of COX-2 inhibitors in preventing serious gastrointestinal adverse events is likely overstated. (LOE = 1b-))

Lai KC, Lam SK, et al. **Lansoprazole** for the prevention of recurrences of ulcer complications from long-term **low-dose aspirin** use. N Engl J Med. 2002 Jun 27;346(26):2033-8.

Laine L, Kivitz AJ, Bello AE, et al. Double-blind randomized trials of single-tablet **ibuprofen/high-dose famotidine vs. ibuprofen** alone for reduction of gastric and duodenal ulcers. Am J Gastroenterol. 2012 Mar;107(3):379-86.

Laine L.**NSAID-associated gastrointestinal bleeding**: Assessing the role of concomitant medications. Gastroenterology 2014 Oct; 147:730.

Lamberts M, Lip GY, et al. Relation of Nonsteroidal Anti-inflammatory Drugs to **Serious Bleeding and Thromboembolism Risk in Patients With Atrial Fibrillation** Receiving Antithrombotic Therapy: A Nationwide Cohort Study. Ann Intern Med. 2014 Nov 18;161(10):690-8.

Lands LC, Milner R, Cantin AM, Manson D, Corey M. High-dose **ibuprofen in cystic fibrosis**: Canadian safety and effectiveness trial. J Pediatr. 2007 Sep;151(3):249-54. Epub 2007 Jun 26.

Lane NE. Clinical practice. **Osteoarthritis of the hip**. N Engl J Med. 2007 Oct 4;357(14):1413-21.

Lanas A, Boers M, Nuevo J. **Gastrointestinal events** in at-risk patients starting non-steroidal anti-inflammatory drugs (NSAIDs) for rheumatic diseases: the EVIDENCE study of European routine practice. Ann Rheum Dis. 2013 Dec 18.

Lanza FL, Chan FK, Quigley EM; Practice Parameters Committee of the **American College of Gastroenterology. Guidelines** for **prevention of NSAID-related ulcer** complications. Am J Gastroenterol. 2009 Mar;104(3):728-38. Epub 2009 Feb 24.

Lapi F, Azoulay L, Yin H, et al. Concurrent use of **diuretics, angiotensin converting enzyme inhibitors, and angiotensin receptor blockers** with non-steroidal anti-inflammatory drugs (**NSAIDs**) and risk of acute kidney injury: nested case-control study. BMJ 2013;346:e8525.

Larson AM, et al, and the Acute Liver Failure Study Group. **Acetaminophen-Induced Acute Liver Failure**: Results of a US Muticenter, Prospective Study. Hepatology; Dec 2005. (of 662 consecutive acute liver failure pts over 6yrs: 42% from acetaminophen liver injury; 48% were unintentional overdoses; only 65% of pts survived) (Benson GD, Koff RS, Tolman KG. The therapeutic use of acetaminophen in patients **with liver disease**. Am J Ther. 2005 Mar-Apr;12(2):133-41. & Oviedo J, Wolfe MM. Alcohol, acetaminophen, & toxic effects on the liver. Arch Intern Med. 2002 May 27;162(10):1194-5.) (Mahadevan SB, McKiernan PJ, Davies P, Kelly DA. Paracetamol-induced hepatotoxicity in children. Arch Dis Child. 2006 Mar 17; [Epub ahead of print]) (Watkins PB, et al. Aminotransferase elevations in healthy adults receiving 4 grams of acetaminophen daily: a randomized controlled trial. JAMA. 2006 Jul 5;296(1):87-93.) (Kuffner EK, Green JL, Bogdan GM, Knox PC, Palmer RB, Heard K, Slattery JT, Dart RC. The effect of acetaminophen (four grams a day for three consecutive days) on hepatic tests in alcoholic patients--a multicenter randomized study. BMC Med. 2007 May 30;5:13. Alcoholic patients treated with the maximum recommended daily dose of acetaminophen for 3 consecutive days did not develop increases in serum transaminase or other measures of liver injury. Treatment of pain or fever for 3 days with acetaminophen appears safe in newly-abstinent alcoholic patients, such as those presenting for acute medical care.) (Heard K, Green JL, Bailey JE, Bogdan GM, Dart RC. A randomized trial to determine the change in alanine aminotransferase during 10 days of paracetamol (acetaminophen) administration in subjects who consume moderate amounts of alcohol. Aliment Pharmacol Ther. 2007 Jul 15;26(2):283-90. Therapeutic dosing of paracetamol administered for 10 days appears to elevate serum ALT in moderate drinkers, but does not produce clinically evident liver injury.)

Latimer Nicholas, Lord Joanne, Grant Robert L, et al., on behalf of the National Institute for Health and Clinical Excellence Osteoarthritis Guideline Development Group. **Cost effectiveness** of COX 2 selective inhibitors and traditional NSAIDs alone or in combination with a proton pump inhibitor for people with osteoarthritis. BMJ 2009;339:b2538, doi: 10.1136/bmj.b2538

Lavonas, Eric J., Reynolds, Kate M., Dart, Richard C. **Therapeutic Acetaminophen** Is **Not Associated With Liver Injury in Children**: A Systematic Review. Pediatrics 2010 0: peds.2009-3352

Le J, Gales MA, Gales BJ. **Acetaminophen for Patent Ductus Arteriosus**. Ann Pharmacother. 2015 Feb;49(2):241-246.

Lebrun-Vignes B, Guy C, Jean-Pastor MJ, et al. Is **acetaminophen associated with a risk of Stevens Johnson Syndrome and Toxic Epidermal Necrolysis**? Analysis of the French Pharmacovigilance database. Br J Clin Pharmacol. 2017 Sep 30.

Lee K, Cooke J, Cooper G, et a. Move it or Lose it. Is it Reasonable for Older Adults with **Osteoarthritis** to Continue to Use **Paracetamol** (**acetaminophen**) in Order to Maintain Physical Activity? Drugs Aging. 2017 Mar 4.

Lee WM. **Acetaminophen and the U.S. Acute Liver Failure** Study Group: lowering the risks of hepatic failure. Hepatology. 2004 Jul;40(1):6-9.

Lee WM, Larson AM, Stravitz T. AASLD position paper: the management of **acute liver failure**: update 2011. Baltimore (MD): American Association for the Study of Liver Diseases; 2011 Sep. 26 (acetaminophen etc)

Leopoldino AO, Machado GC, Ferreira PH, et al. **Paracetamol versus placebo for knee and hip osteoarthritis**. Cochrane Database Syst Rev. 2019 Feb 25;2:CD013273.

Leverrier-Penna S, Mitchell RT, Becker E, et al. **Ibuprofen** is deleterious for the development of **first trimester human fetal ovary** ex vivo. Hum Reprod. 2018 Feb 2.

Levesque LE, Brophy JM, Zhang B. Time variations in the risk of **myocardial infarction** among elderly users of COX-2 inhibitors. CMAJ. 2006 May 23;174(11):1563-9. Epub 2006 May 2. A small proportion of patients using rofecoxib for the first time had their first MI shortly after starting the drug. This risk did not increase with the length of treatment and returned to baseline shortly after treatment was discontinued. More research is needed to identify those most susceptible to cardiotoxicity mediated by COX-2 inhibitor therapy.

Li L,Geraghty OC, Mehta Z, Rothwell PM, on behalf of the Oxford Vascular Study. **Age-specific risks, severity, time course, and outcome of bleeding on long-term antiplatelet treatment after vascular events**: a population-based cohort study. Lancet 2017; online June 5. (consider PPI use with aspirin in secondary prevention)

Liao LM, Vaughan TL, Corley DA, et al. Nonsteroidal Anti-inflammatory Drug Use **Reduces Risk of Adenocarcinomas of the Esophagus** and Esophagogastric Junction in a Pooled Analysis. Gastroenterology. 2012 Mar;142(3):442-452.e5

Li DK, Liu L, Odouli R. Exposure to non-steroidal anti-inflammatory drugs during **pregnancy and risk of miscarriage**: population based cohort study. BMJ. 2003 Aug 16;327(7411):368.

Liccardi G, et al. Safety of celecoxib in patients with adverse **skin reactions** to acetaminophen (paracetamol) and other non-steroidal anti-inflammatory drugs. J Investig Allergol Clin Immunol. 2005;15(4):249-53.

Liebowitz M, Clyman RI. **Prophylactic Indomethacin** Compared with Delayed Conservative Management of the **Patent Ductus Arteriosus** in **Extremely Preterm** Infants: Effects on Neonatal Outcomes. J Pediatr. 2017 Apr 7.

Liebowitz M, Koo J, Wickremasinghe A, et al. Effects of **Prophylactic Indomethacin** on Vasopressor-Dependent **Hypotension** in Extremely Preterm Infants. J Pediatr. 2016 Dec 1.

Liebowitz M, Koo J, Wickremasinghe A, Allen IE, Clyman RI. Effects of **prophylactic indomethacin** on vasopressor-dependent hypotension in **extremely preterm infants**. J Pediatr 2017;182:21-7, e2

Liebowitz M, Clyman RI. Prophylactic **Indomethacin Compared with Delayed Conservative Management** of the **Patent Ductus Arteriosus** in Extremely Preterm Infants: Effects on Neonatal Outcomes. J Pediatr. 2017 Apr 7.

Liew Z, Ritz B, Rebordosa C, Lee PC, Olsen J. **Acetaminophen use during pregnancy**, behavioural problems, and hyperkinetic disorders [online February 24, 2014]. JAMA Pediatr. doi:10.1001/jamapediatrics.2013.4914.

Lilly LS. Treatment of **acute and recurrent idiopathic pericarditis**. Circulation. 2013 Apr 23;127(16):1723-6.

Lim BX, Lim CHL, Lim DK, et al. **Prophylactic non-steroidal anti-inflammatory drugs for the prevention of macular oedema** after cataract surgery. Cochrane Database of Systematic Reviews 2016, Issue 11. Art. No.: CD006683. Using topical NSAIDs may reduce the risk of developing macular oedema after cataract surgery, although it is possible that current estimates as to the size of this reduction are exaggerated. It is unclear the extent to which this reduction has an impact on the visual function and quality of life of patients. There is little evidence to suggest any important effect on vision after surgery. The value of adding topical NSAIDs to steroids, or using them as an alternative to topical steroids, with a view to reducing the risk of poor visual outcome after cataract surgery is therefore uncertain. Future trials should address the remaining clinical uncertainty of whether prophylactic topical NSAIDs are of benefit, particularly with respect to longer-term follow-up (at least to 12 months), and should be large enough to detect reduction in the risk of the outcome of most interest to patients, which is chronic macular oedema leading to visual loss.

Lin BM, Curhan SG, Wang M, et al. Duration of Analgesic Use and Risk of **Hearing Loss** in Women. Am J Epidemiol. 2016 Dec 14.

Lin J, Zhang W, Jones A, Doherty M. Effi cacy of **topical non-steroidal** anti-infl ammatory drugs in the treatment of osteoarthritis: meta-analysis of randomised controlled trials. BMJ 2004; 329: 324–26.

Lindhardsen J, Gislason GH, Jacobsen S, et al. Non-steroidal anti-inflammatory drugs and risk of **cardiovascular disease** in patients with rheumatoid arthritis: a nationwide cohort study. Ann Rheum Dis. 2013 Jun 8.

Lipman GS, Kanaan NC, Holck PS, et al. **Ibuprofen Prevents Altitude Illness**: A Randomized Controlled Trial for Prevention of Altitude Illness With Nonsteroidal Anti-inflammatories. Ann Emerg Med. 2012 Mar 20.

Little P, Moore M, Kelly J, et al; PIPS investigators. **Ibuprofen, paracetamol, and steam** for patients with respiratory tract infections in primary care: pragmatic randomised factorial trial. BMJ. 2013 Oct 25;347:f6041.

Liu Y, Lu Y, Wang J, et al. Association between non-steroidal anti-inflammatory drug use and **brain tumour risk**: a meta-analysis. Br J Clin Pharmacol. 2013 Dec 17

Llor C, Moragas A, Bayona C, et al. Efficacy of **anti-inflammatory or antibiotic treatment** in patients with non-complicated acute **bronchitis** and discoloured sputum: randomised placebo controlled trial. BMJ. 2013 Oct 4;347:f5762.

Loke YK, Trivedi AN, Singh S. Meta-analysis: Gastrointestinal bleeding due to interaction between **selective serotonin uptake inhibitors** and non-steroidal anti-inflammatory drugs. Aliment Pharmacol Ther. 2007 Oct 5; [Epub ahead of print]

Lotrionte M, Biondi-Zoccai G, Imazio M, et al. International collaborative systematic review of controlled clinical trials on pharmacologic treatments for **acute pericarditis** and its recurrences. Am Heart J. 2010 Oct;160(4):662-70.

Lovecchio F, Derman P, Stepan J, et al. Support for **Safer Opioid Prescribing Practices**: A Catalog of Published Use After Orthopaedic Surgery. J Bone Joint Surg Am. 2017 Nov 15;99(22):1945-1955

Lynde, Carrie B, Pierscianowski, Tadeusz A, Pratt, Melanie D. **Allergic contact dermatitis** caused by diclofenac cream. CMAJ 2009 0: cmaj.081784

Lyrtzis C, Natsis K, Papadopoulos C, et al. Efficacy of **Paracetamol** Versus Diclofenac for Grade II Ankle Sprains. Foot Ankle Int. 2011 Jun;32(6):571-5.

MacDonald TM, Hawkey CJ, Ford I, et al. Randomized trial of **switching from prescribed non-selective non-steroidal anti-inflammatory drugs to prescribed celecoxib**: the Standard care vs. Celecoxib Outcome Trial (**SCOT**). Eur Heart J. 2016 Oct 4.

Machado GC, Maher CG, Ferreira PH, et al. Efficacy and safety of **paracetamol (acetaminophen)** for **spinal pain and osteoarthritis**: systematic review and meta-analysis of randomised placebo controlled trials. BMJ 2015;350:h1225.

Machado GC, Maher CG, Ferreira PH, et al. **Non-steroidal anti-inflammatory drugs for spinal pain**: a systematic review and meta-analysis. Ann Rheum Dis. 2017 Feb 2.

Madden T, Proehl S, Allsworth JE, et al. **Naproxen** or estradiol for bleeding and **spotting with the levonorgestrel intrauterine system**: a randomized controlled trial. Am J Obstet Gynecol. 2012 Feb;206(2):129.e1-8.

Magnus MC, Karlstad Ø, Håberg SE, et al. **Prenatal and infant paracetamol-acetaminophen** exposure and development of **asthma**: the Norwegian Mother and Child Cohort Study. Int J Epidemiol. 2016 Feb 9.

Mamdani M, Warren L, Kopp A, Paterson JM, Laupacis A, Bassett K, Anderson GM. Changes in rates of upper gastrointestinal hemorrhage after the introduction of **cyclooxygenase-2 inhibitors** in British Columbia and Ontario. CMAJ. 2006 Dec 5;175(12):1535-8. (InfoPOEMs: Although COX-2 inhibitors may be slightly less likely to cause gastrointestinal (GI) complications, the overall increase in the use of nonsteroidal anti-inflammatory drugs (NSAIDs) seen after their introduction appears to have led to an overall increase in the number of GI complications in the population (not to mention the thousands of cardiovascular deaths attributed to this class of drugs). Although physicians complain about prescribing restrictions, sometimes for good reason, in this case they seem to be of benefit. (LOE = 2c))

Marjoribanks J, Proctor M, Farquhar C, Derks RS. Nonsteroidal anti-inflammatory drugs for **dysmenorrhoea**. Cochrane Database Syst Rev. 2010 Jan 20;(1):CD001751.

Marjoribanks J, Ayeleke RO, Farquhar C, Proctor M. **Nonsteroidal anti-inflammatory drugs for dysmenorrhoea**. Cochrane Database Syst Rev. 2015 Jul 30;7:CD001751. NSAIDs appear to be a very effective treatment for dysmenorrhoea, though women using them need to be aware of the substantial risk of adverse effects. There is insufficient evidence to determine which (if any) individual NSAID is the safest and most effective for the treatment of dysmenorrhoea. We rated the quality of the evidence as low for most comparisons, mainly due to poor reporting of study methods.

Marks DJ, Dargan PI, Archer JR, et al. Outcomes from massive **paracetamol (acetaminophen) overdose**: a retrospective observational study. Br J Clin Pharmacol. 2016 Dec 21.

Masclee GMC, Valkhoff VE, Coloma PM, et al. Risk of upper **gastrointestinal bleeding from different drug combinations**. Gastroenterology 2014;147:784–792.

Masclee GM, Coloma PM, Spaander MC, et al. **NSAIDs, statins, low-dose aspirin and PPIs, and the risk of oesophageal adenocarcinoma** among patients with Barrett's oesophagus: a population-based case-control study. BMJ Open. 2015 Jan 29;5(1):e006640.

Masclee GM, Coloma PM, Kuipers EJ, Sturkenboom MC. Increased risk of **microscopic colitis** with use of proton pump inhibitors and non-steroidal anti-inflammatory drugs. Am J Gastroenterol. 2015 May;110(5):749-59.

Massey T, Derry S, Moore RA, McQuay HJ. **Topical NSAIDs** for acute pain in adults. Cochrane Database Syst Rev. 2010 Jun 16;6:CD007402. Topical NSAIDs can provide good levels of pain relief, without the systemic adverse events associated with oral NSAIDs, when used to treat acute musculoskeletal conditions. NNT=4.5 (3.9-5.3) for ≥50% reduction in pain.

Masuda I, Matsuo T, Okamoto K, et al. Two cases of corneal perforation after oral administration of nonsteroidal anti-inflammatory drugs: oral NSAID-induced **corneal damage**. Eur J Ophthalmol. 2009 Dec 12. [Epub ahead of print]

Mbeledogu CN, Cecil EV, Millett C, et al. Hospital admissions for **unintentional poisoning** in preschool children in England; 2000-2011. Arch Dis Child. 2014 Aug 28.

McBride John T.. The Association of **Acetaminophen and Asthma** Prevalence and Severity. Pediatrics 2011; peds.2011-1106; published ahead of print November 7, 2011, doi:10.1542/peds.2011-1106

McCormack PL. **Celecoxib**: a review of its use for symptomatic relief in the treatment of osteoarthritis, rheumatoid arthritis and ankylosing spondylitis. Drugs. 2011 Dec 24;71(18):2457-89. doi: 10.2165/11208240-000000000-00000.

McCrae JC, Morrison EE, MacIntyre IM, et al. **Long-term Adverse Effects of Paracetamol (Acetaminophen)** - a Review. Br J Clin Pharmacol. 2018 Jun 4.

McGettigan P, Henry D. Cardiovascular Risk and Inhibition of Cyclooxygenase: A Systematic Review of the Observational Studies of Selective and Nonselective Inhibitors of Cyclooxygenase 2. JAMA. 2006 Sep 12; [Epub ahead of print] A dose-related risk was evident with rofecoxib, summary relative risk with 25 mg/d or less, 1.33 (95% confidence interval [CI], 1.00-1.79) and 2.19 (95% CI, 1.64-2.91) with more than 25 mg/d. The risk was elevated during the first month of treatment. Celecoxib was not associated with an elevated risk of vascular occlusion, summary relative risk 1.06 (95% CI, 0.91-1.23). Among older nonselective drugs, diclofenac had the highest risk with a summary relative risk of 1.40 (95% CI, 1.16-1.70). The other drugs had summary relative risks close to 1: naproxen, 0.97 (95% CI, 0.87-1.07); piroxicam, 1.06 (95% CI, 0.70-1.59); and ibuprofen, 1.07 (95% CI, 0.97-1.18). CONCLUSIONS: This review confirms the findings from randomized trials regarding the risk of cardiovascular events with rofecoxib and suggests that celecoxib in commonly used doses may not increase the risk, contradicts claims of a protective effect of naproxen, and raises serious questions about the safety of diclofenac, an older drug. (InfoPOEMs: Rofecoxib (Vioxx), diclofenac (Voltaren, Cataflam), and indomethacin (Indocin) are associated with a significant increased risk of CVD. It is likely that all NSAIDs carry some risk, but the risks may vary between medicines. Current evidence does not point to an increased risk for low dose (over the counter) ibuprofen and this remains safe to use at recommended doses. (LOE = 2a-))

McGettigan P, Henry D. **Cardiovascular risk with nonsteroidal anti-inflammatory drugs**: systematic review of population-based controlled observational studies. PLoS Med 2011; DOI:10.1371/journal.pmed.1001098. (High CV risk with rofecoxib & diclofenac)

McGettigan P, Henry D (2013) Use of nonsteroidal anti-inflammatory drugs that elevate **cardiovascular risk**: an examination of sales and essential medicines lists in low-, middle-, and high-income countries. (**diclofenac** risk) PLoS Med 10: e1001388. doi:10.1371/journal.pmed.1001388

McInerney KA, Hatch EE, Wesselink AK, et al. **Preconception use** of pain-relievers and time-to-**pregnancy**: a prospective cohort study. Hum Reprod. 2017 Jan;32(1):103-111.

Medical Letter: **Treatment guidelines. Drugs for Pain**. April 2007; April 2010. **April 2013.**

Medical Letter. Off-Label Use of **Ketorolac** for Athletic Injuries (IM into injured muscles). May 14, 2012.

Mehlisch Donald R., Aspley Sue, Daniels Stephen E., et al., Comparison of the analgesic efficacy of concurrent **ibuprofen and paracetamol** with ibuprofen or paracetamol alone in the management of moderate to severe acute postoperative dental pain in adolescents and adults: A randomized, double-blind, placebo-controlled, parallel-group, single-dose, two-center, modified factorial study, Clinical Therapeutics, Volume 32, Issue 5, May 2010, Pages 882-895.

Merry AF, Edwards KE, Ahmad Z, et al. Randomized comparison between the combination of **acetaminophen and ibuprofen** and each constituent alone for analgesia following **tonsillectomy** in children. Can J Anaesth. 2013 Dec;60(12):1180-9.

Messier SP, et al. **Exercise and dietary** weight loss in overweight and obese older adults with knee osteoarthritis: the Arthritis, Diet, and Activity Promotion Trial. Arthritis Rheum. 2004 May;50(5):1501-10.

Meurin Philippe, Tabet JY, Thabut Gabriel, et al. and for the French Society of Cardiology. Nonsteroidal Anti-inflammatory Drug Treatment for Postoperative **Pericardial Effusion**: Multicenter Randomized, Double-Blind Trial (**POPE**). Ann Intern Med Feb 2, 2010 152:137-143.

Miao XP, Li JS, Ouyang Q, et al. Tolerability of selective **cyclooxygenase 2 inhibitors used for the treatment of rheumatological manifestations of inflammatory bowel disease**. Cochrane Database Syst Rev. 2014 Oct 23;10:CD007744. The results for disease exacerbation and AEs between the COX-2 inhibitors celecoxib and etoricoxib and placebo were uncertain. Thus no definitive conclusions regarding the tolerability and safety of the short term use of celecoxib and etoricoxib in patients with IBD can be drawn. The two included studies suggest that celecoxib and etoricoxib do not exacerbate IBD symptoms. However, it should be noted that both studies had relatively small sample sizes and short follow-up durations. Clinicians need to continue to weigh the risks and benefits of these drugs when treating patients IBD patients with rheumatological manifestations in order to avoid disease exacerbation and other adverse effects. Further RCTs are needed to determine the tolerability and safety of celecoxib and etoricoxib in these patients.

Mindikoglu AL, Magder LS, et al. Outcome of **liver transplantation** for drug-induced acute liver failure in the United States: analysis of the united network for organ sharing database. Liver Transpl. 2009 Jul;15(7):719-29. The 4 leading implicated drug groups were acetaminophen (n = 265; **40%**), antituberculosis drugs (n = 50; 8%), antiepileptics (n = 46; 7%), & antibiotics (n = 39; 6%). Being on life support, DIALF due to antiepileptics (at age < 18), and elevated serum creatinine were independent pretransplant predictors of poor survival after LT for DIALF.

Mirza H, Oh W, Laptook A, et al. **Indomethacin Prophylaxis to Prevent Intraventricular Hemorrhage**: Association between Incidence and Timing of Drug Administration. J Pediatr. 2013 Mar 22.

Misurac JM, Knoderer CA, Leiser JD, et al. Nonsteroidal Anti-Inflammatory Drugs Are an Important Cause of **Acute Kidney Injury** in Children. J Pediatr. 2013 Jan 26.

Mitra S, Florez ID, et al. Association of Placebo, **Indomethacin, Ibuprofen, and Acetaminophen** With Closure of Hemodynamically Significant **Patent Ductus Arteriosus in Preterm Infants**: A Systematic Review and Meta-analysis. JAMA. 2018 Mar 27;319(12):1221-1238.

Mohammadinejad P, Arya P, Esfandbod M, et al. **Celecoxib Versus Diclofenac** in Mild to Moderate **Depression** Management Among Breast Cancer Patients: A Double-Blind, Placebo-Controlled, Randomized Trial. Ann Pharmacother. 2015 Sep;49(9):953-61.

Moon KW, Kim J, Kim JH, et al. Risk factors for acute kidney injury by non-steroidal anti-inflammatory drugs in patients with hyperuricaemia. Rheumatology (Oxford). 2011 Oct 22. (Low GFR and **low serum albumin**)

Moore PA, Hersh EV. Combining **ibuprofen and acetaminophen** for acute pain management after third-molar extractions: Translating clinical research to dental practice. J Am Dent Assoc. 2013 Aug;144(8):898-908.

Moore PA, Ziegler KM, Lipman RD, et al. Benefits and harms associated with **analgesic medications used in the management of acute dental pain**: An overview of systematic reviews. J Am Dent Assoc. 2018 Apr;149(4):256-265.e3.

Moore RA, Derry S, Wiffen PJ, Straube S. Effects of **food** on pharmacokinetics of immediate release oral formulations of **aspirin, dipyrone, paracetamol, and NSAIDs** - systematic review. Br J Clin Pharmacol. 2015 Mar 17.

Moore RA, Chi CC, Wiffen PJ, et al. **Oral nonsteroidal anti-inflammatory drugs for neuropathic pain**. Cochrane Database Syst Rev. 2015 Oct 5;10:CD010902. There is no evidence to support or refute the use of oral NSAIDs to treat neuropathic pain conditions.

Moore RA, Moore N. Paracetamol (**acetaminophen**) and pain: the kiloton problem. Eur J Hosp Pharm.2016;0:1-2

Moore PA, Ziegler KM, Lipman RD, et al. Benefits and harms associated with analgesic medications used in the management of **acute dental pain**: An overview of systematic reviews. J Am Dent Assoc. 2018 Apr;149(4):256-265.e3.

Morales DR, Lipworth BJ, Guthrie B, et al. Safety risks for patients with **aspirin-exacerbated respiratory disease** after acute exposure to **selective nonsteroidal anti-inflammatory drugs and COX-2** inhibitors: Meta-analysis of controlled clinical trials. J Allergy Clin Immunol. 2013 Dec 30. pii: S0091-6749(13)01774-0.

Motov S, Fassassi C, Drapkin J, et al. Comparison of intravenous **lidocaine/ketorolac combination to either analgesic alone for suspected renal colic pain** in the ED. Am J Emerg Med. 2019 Jan 30.

Motov S, Masoudi A, Drapkin J, et al. Comparison of **Oral Ibuprofen at Three Single-Dose Regimens** for Treating Acute Pain in the Emergency Department: A Randomized Controlled Trial. Ann Emerg Med. 2019 Aug 2.

Motov S, Yasavolian M, Likourezos A, et al. Comparison of **Intravenous Ketorolac** at Three Single-Dose Regimens for Treating Acute Pain in the Emergency Department: A Randomized Controlled Trial. Ann Emerg Med. 2016 Dec 16. (10mg effective)

Mu DL, Zhang DZ, Wang DX, et al. **Parecoxib Supplementation to Morphine Analgesia Decreases Incidence of Delirium** in Elderly Patients After Hip or Knee Replacement Surgery: A Randomized Controlled Trial. Anesth Analg. 2017 Jun;124(6):1992-2000.

Murata S, Okasora K, Tanabe T, et al. **Acetaminophen and Febrile Seizure Recurrences During the Same Fever Episode**. Pediatrics. 2018 Oct 8. pii: e20181009.

Nakhai-Pour HR, Broy P, Sheehy O, Bérard A. Use of nonaspirin nonsteroidal anti-inflammatory drugs during **pregnancy and the risk of spontaneous abortion**. CMAJ. 2011 Sep 6.

Najafi N, Van de Velde A, Poelaert J. Potential risks of **hemolysis** after short-term administration of analgesics in children with **glucose-6-phosphate dehydrogenase deficiency**. J Pediatr. 2011 Dec;159(6):1023-8.

Nan H, Hutter CM, Lin Y, et al; Colon Cancer Family Registry, Genetics and Epidemiology of Colorectal Cancer Consortium. Association of **aspirin and NSAID use with risk of colorectal cancer** according to genetic variants. JAMA. doi:10.1001/jama.2015.1815.

Nderitu P, Doos L, Jones PW, Davies SJ, Kadam UT. **Non-steroidal anti-inflammatory drugs and chronic kidney disease progression**: a systematic review. Fam Pract. 2013 Jun;30(3):247-55.

Nehus E, Kaddourah A, Bennett M, et al. **Subclinical Kidney Injury** in Children Receiving Nonsteroidal Anti-Inflammatory Drugs After Cardiac Surgery. J Pediatr. 2017 Jul 13.

Nelson DA, Marks ES, Deuster PA, et al. Association of Nonsteroidal Anti-inflammatory Drug Prescriptions With **Kidney Disease** Among Active Young and Middle-aged Adults. JAMA Netw Open. 2019 Feb 1;2(2):e187896.

Nezvalová-Henriksen K, Spigset O, Nordeng H. Effects of **ibuprofen, diclofenac, naproxen and piroxicam on the course of pregnancy** and pregnancy outcome: a prospective cohort study. BJOG 2013;120:948–59.

Ng FH, Wong SY, Lam KF, et al. **Famotidine 40mg bid is inferior to pantoprazole 20mg od** in preventing recurrence of **aspirin-related** peptic ulcers or erosions. Gastroenterology. 2010 Jan;138(1):82-8. n=160 Epub 2009 Nov 11.

Ni X, Ma J, Zhao Y, et al. Meta-analysis on the association between non-steroidal anti-inflammatory drug use and **ovarian cancer**. Br J Clin Pharmacol. 2012 Apr 3.

NICE Guidelines for the care and management of Osteoarthritis in Adults Feb, 2008. Updated Feb 2014. http://www.nice.org.uk/guidance/index.jsp?action=byID&o=11926
NICE Guidelines: National Institute for Health and Care Excellence. **Feverish illness** in children: assessment and initial management in children younger than five years. (Clinical guideline CG160.) 2013. http://guidance.nice.org.uk/CG160).
Nissen SE, Yeomans ND, Solomon DH, et al. Cardiovascular safety of **celecoxib, naproxen, or ibuprofen** for arthritis. (**PRECISION**) N Engl J Med. 2016 Nov 13. DOI: 10.1056/NEJMoa1611593. [Epub ahead of print]
Nyirenda MJ, Tang JI, Padfield PL, Seckl JR. **Hyperkalaemia**. BMJ. 2009 Oct 23;339:b4114. doi: 10.1136/bmj.b4114.
Odom DM, Mladsi DM, Saag KG, et al. Relationship Between **Diclofenac Dose and Risk of Gastrointestinal and Cardiovascular Events**: Meta-Regression Based on Two Systematic Literature Reviews. Clin Ther. 2014 May 23.
Ofori B, et al. Risk of **congenital anomalies** in pregnant users of non-steroidal anti-inflammatory drugs: a nested case-control study. Birth Defects Res B Dev Reprod Toxicol. 2006 Aug 23; [Epub ahead of print] Our study suggests that women prescribed NSAIDs during early pregnancy may be at a greater risk of having children with congenital anomalies, specifically cardiac septal defects.
Ogilvie JD, Rieder MJ, Lim R. **Acetaminophen overdose** in children. CMAJ. 2012 Jun 4.
Oh JH, Seo HJ, Lee YH, et al. **Do Selective COX-2 Inhibitors Affect Pain Control and Healing After Arthroscopic Rotator Cuff Repair**? A Preliminary Study. Am J Sports Med. 2017 Dec 1:363546517744219.
Ohlsson A, Walia R, Shah SS. **Ibuprofen for the treatment of patent ductus arteriosus** in preterm and/or low birth weight infants. Cochrane Database Syst Rev. 2010 Apr 14;4:CD003481. Ibuprofen is effective in closing a PDA. Ibuprofen is as effective as indomethacin in closing a PDA and reduces the risk of NEC and transient renal insufficiency.
Ohlsson A, Shah PS. **Paracetamol (acetaminophen**) for **patent ductus arteriosus** in preterm or low-birth-weight infants. Cochrane Database of Systematic Reviews 2015, Issue 3. Art. No.: CD010061. DOI: 10.1002/14651858.CD010061.pub2. Although a limited number of infants with a PDA have been studied in randomised trials of low to moderate quality according to GRADE, oral paracetamol appears to be as effective in closing a PDA as oral ibuprofen. In view of a recent report in mice of adverse effects on the developing brain from paracetamol, and another report of an association between prenatal paracetamol and the development of autism or autism spectrum disorder in childhood, long-term follow-up to at least 18 to 24 months postnatal age must be incorporated in any studies of paracetamol in the newborn population. Such trials are required before any recommendations for the use of paracetamol in the newborn population can be made.
Ohlsson A, Shah PS. **Paracetamol (acetaminophen)** for **prevention or treatment of pain in newborns**. Cochrane Database Syst Rev 2015;6:CD011219. Paracetamol does not significantly reduce pain associated with heel lance or eye examinations. Paracetamol given after assisted vaginal birth may increase the response to later painful exposures. Paracetamol should not be used for painful procedures given its lack of efficacy and its potential for adverse effects. Paracetamol may reduce the total need for morphine following major surgery, and for this aspect of paracetamol use, further research is needed.
Olsen Anne-Marie Schjerning, Fosbøl Emil L., Lindhardsen Jesper, et al. Duration of Treatment With Nonsteroidal Anti-Inflammatory Drugs and Impact on Risk of Death and Recurrent **Myocardial Infarction** in Patients With Prior Myocardial Infarction: A Nationwide Cohort Study. Circulation published May 9, 2011, doi:10.1161/CIRCULATIONAHA.110.004671
Oncel MY, Yurttutan S, Erdeve O, et al. Oral **Paracetamol (acetaminophen)** versus Oral **Ibuprofen** in the Management of **Patent Ductus Arteriosus** in Preterm Infants: A Randomized Controlled Trial. J Pediatr. 2014 Mar;164(3):510-514.
Orchard J, Kountouris A. The management of **tennis elbow**. BMJ. 2011 May 10;342:d2687. doi: 10.1136/bmj.d2687.
Osayande AS, Mehulic S. Diagnosis and initial management of **dysmenorrhea**. Am Fam Physician. 2014 Mar 1;89(5):341-6.
Patel RA, Gallagher JC. **Drug Fever**. Pharmacotherapy. 2010 Jan;30(1):57-69.
Pathan SA, Mitra B, Straney LD, et al. Delivering safe and eff ective analgesia for **management of renal colic** in the emergency department: a double-blind, multigroup, randomised controlled trial. Lancet 2016; online March 15.
Pathan SA, Mitra B, Cameron PA. A Systematic Review and Meta-analysis Comparing the Efficacy of **Nonsteroidal Anti-inflammatory Drugs, Opioids, and Paracetamol in the Treatment of Acute Renal Colic**. Eur Urol. 2017 Nov 21.
Patrono C, Baigent C. Nonsteroidal anti-inflammatory drugs and the **heart**. Circulation. 2014 Feb 25;129(8):907-16.
Patrono C. **Cardiovascular Effects** of **Cyclooxygenase-2 Inhibitors**: A Mechanistic and Clinical Perspective. Br J Clin Pharmacol. 2016 Jun 17.
Paul IM, Sturgis SA, Yang C, et al. Efficacy of standard doses of **Ibuprofen** alone, **alternating, and combined with acetaminophen** for the treatment of febrile children. Clin Ther. 2010 Dec;32(14):2433-40.
Petersen TG, Liew Z, Andersen AN, et al. Use of paracetamol **(acetaminophen), ibuprofen or aspirin in pregnancy and risk of cerebral palsy** in the child. Int J Epidemiol. 2018 Feb 1;47(1):121-130.
Pharmacist's Letter Oct 2006. Alternative or **Off-label** Routes of Drug Administration. (Oral administration of: N-acetylcysteine Mucomyst)
Pharmacist's Letter Oct 2006. **Cardiovascular Risks** of NSAIDs and Cox-2 Inhibitors.
Pharmacist's Letter. Can Individuals with **Aspirin Sensitivity Take NSAIDs**? Oct 2010.
Pierson-Marchandise M, Gras V, Moragny J, et al. The **drugs that mostly frequently induce acute kidney injury**: a case - non-case study of a pharmacovigilance database. Br J Clin Pharmacol. 2016 Dec 21. The most frequently implicated drug classes were antibacterials for systemic use (29.5%), diuretics (18.5%), agents acting on the renin-angiotensin system (16.3%), antineoplastic agents (10.2%) and anti-inflammatory agents (5.4%). Gentamicin, eplerenone, spironolactone, candesartan, cisplatin and acyclovir had the highest RORs (>10).
Pontes C, Marsal JR, Elorza JM, et al.**Analgesic Use and Risk for Acute Coronary Events in Patients With Osteoarthritis**: A Population-based, Nested Case-control Study. Clin Ther. 2018 Feb 2.
Poddubnyy D, Rudwaleit M, Haibel H, et al. Effect of non-steroidal anti-inflammatory drugs on radiographic spinal progression in patients with axial **spondyloarthritis**: results from the German Spondyloarthritis Inception Cohort. Ann Rheum Dis 2012.
Poonai N, Bhullar G, Lin K, et al. Oral administration of **morphine versus ibuprofen to manage postfracture pain in children**: a randomized trial. CMAJ. 2014 Oct 27.
Poonai N, Datoo N, Ali S, et al. **Oral morphine versus ibuprofen administered at home for postoperative orthopedic pain in children**: a randomized controlled trial. CMAJ.2017 Oct 10;189(40):E1252-E1258.
Psaty BM and Potter JD. Risks and benefits of celecoxib to prevent recurrent **adenomas**. N Engl J Med 2006; 355:950-952.
Psaty BM, Weiss NS. NSAID trials and the **choice of comparators**--questions of public health importance. N Engl J Med. 2007 Jan 25;356(4):328-30.
Prymula R, Siegrist CA, Chlibek R, et al. Effect of prophylactic **paracetamol administration at time of vaccination** on febrile reactions and antibody responses in children: two open-label, randomised controlled trials. Lancet. 2009 Oct 17;374(9698):1339-50.
Puljak L, Marin A, Vrdoljak D, et al. **Celecoxib for osteoarthritis**. Cochrane Database of Systematic Reviews 2017, Issue 5. Art. No.: CD009865. We are highly reserved about results due to pharmaceutical industry involvement and limited data. We were unable to obtain data from three studies, which included 15,539 participants, and classified as awaiting assessment. Current evidence indicates that celecoxib is slightly better than placebo and some tNSAIDs in reducing pain and improving physical function. We are uncertain if harms differ among celecoxib and placebo or tNSAIDs due to risk of bias, low quality evidence for many outcomes, and that some study authors and Pfizer declined to provide data from completed studies with large numbers of participants. To fill the evidence gap, we need to access existing data and new, independent clinical trials to investigate benefits and harms of celecoxib versus tNSAIDs for people with osteoarthritis, with longer follow-up and more direct head-to-head comparisons with other tNSAIDs.
Purssell E. Systematic review of studies comparing **combined treatment with paracetamol (acetaminophen) and ibuprofen**, with either drug alone. Arch Dis Child. 2011 Dec;96(12):1175-9.
Qi DS, May LG, Zimmerman B, et al. A Randomized, Double-Blind, Placebo-Controlled Study of **Acetaminophen 1000 mg Versus Acetaminophen 650 mg** for the Treatment of Postsurgical Dental Pain. Clin Ther. 2012 Dec;34(12):2247-2258.e3.
Rahman NM, Pepperell J, et al. Effect of **Opioids vs NSAIDs and Larger vs Smaller Chest Tube Size on Pain Control and Pleurodesis** Efficacy Among Patients With Malignant Pleural Effusion: The TIME1 Randomized Clinical Trial. JAMA. 2015 Dec 22-29;314(24):2641-53.
Rahme E, Barkun A, Nedjar H, Gaugris S, Watson D. Hospitalizations for Upper and Lower GI Events Associated With Traditional NSAIDs and Acetaminophen Among the Elderly in Quebec, Canada. Am J Gastroenterol. 2008 Apr;103(4):872-82. Epub 2008 Mar 26. Among elderly patients requiring analgesic/anti-inflammatory treatment, use of the combination of a **NSAID and acetaminophen may increase the risk of GI bleeding** compared with either agent alone.
Rangnekar AS, Ellerbe C, Durkalski V, et al. Quality of life is significantly impaired in long-term survivors of **acute liver failure and particularly in acetaminophen-overdose** patients. Liver Transpl. 2013 Jun 18.
Rasmussen-Barr E, Held U, Grooten WJ, et al**. Non-steroidal anti-inflammatory drugs for sciatica**. Cochrane Database Syst Rev. 2016 Oct 15;10:CD012382. This updated systematic review including 10 trials evaluating the efficacy of NSAIDs versus placebo or other drugs in people with sciatica reports low- to very low-level evidence using the GRADE criteria. The efficacy of NSAIDs for pain reduction was not significant. NSAIDs showed a better global improvement compared to placebo. These findings must be interpreted with caution, as the level of evidence according to the GRADE classification was very low for the outcome pain reduction and low for global improvement due to small study samples, inconsistent results, imprecision, and a high risk of bias in the included trials. While the trials included in the analysis were not powered to detect potential rare side effects, we found an increased risk for side effects in the short-term NSAIDs use. As NSAIDs are frequently prescribed, the risk-benefit ratio of prescribing the drug needs to be considered.
Rasmussen-Barr E, Held U, Grooten WJ, et al. **Nonsteroidal Anti-inflammatory Drugs for Sciatica**: An Updated Cochrane Review. Spine (Phila Pa 1976). 2017 Apr 15;42(8):586-594.
Ray WA, Varas-Lorenzo C, Chung CP, et al. **Cardiovascular risks** of nonsteroidal antiinflammatory drugs in patients after hospitalization for serious coronary heart disease. Circ Cardiovasc Qual Outcomes. 2009 May;2(3):155-63. Epub 2009 May 5. (**Naproxen** good CV safety)
Rebordosa C, Kogevinas M, Horváth-Puhó E,et al. **Acetaminophen use during pregnancy**: effects on risk for congenital abnormalities. Am J Obstet Gynecol. 2008 Feb;198(2):178.e1-7. Acetaminophen is not associated with an increased prevalence of congenital abnormalities overall or with any specific group of major abnormalities.
Rechberger T, Mack RJ, McCallum SW, et al. Analgesic Efficacy and Safety of **Intravenous Meloxicam** in Subjects With Moderate-to-Severe Pain After Open Abdominal Hysterectomy: A Phase 2 Randomized Clinical Trial. Anesth Analg. 2019 Jun;128(6):1309-1318.
Reddy KS, Roy A. **Cardiovascular Risk of NSAIDs**: Time to Translate Knowledge into Practice. PLoS Med. 2013 Feb;10(2):e1001389.
Reginster JY, Dudler J, Blicharski T, et al. **Pharmaceutical-grade Chondroitin sulfate** is as effective as **celecoxib** and superior to placebo in symptomatic knee osteoarthritis: the ChONdroitin versus CElecoxib versus Placebo Trial (**CONCEPT**). Ann Rheum Dis. 2017 May 22.
Reuben A et al. Outcomes in adults with **acute liver failure** between 1998 and 2013: An observational cohort study. (**acetaminophen**) Ann Intern Med 2016 Apr 5. ALF has often been viewed as a fatal condition without the availability of a transplant. These data refute that clinical premise in that three fourths of patients survived 21 days, and most without a transplant. Additionally, severe bleeding and need for ventilation and vasopressors were noted in many fewer patients than historically observed. As the authors conclude, it seems obvious that advances in intensive care units are responsible for this improvement in prognosis for patients with ALF.
Ringdahl E, Pandit S. **Treatment of Knee Osteoarthritis**. Am Fam Physician. 2011;83(11):1287-1292.
Risser A, Donovan D, Heintzman J et al. **NSAID Prescribing Precautions**. Am Fam Physician. 2009;80(12):1371–1378.
Roberts E, Delgado Nunes V, Buckner S, et al. **Acetaminophen/Paracetamol: not as safe as we thought**? A systematic literature review of observational studies. Ann Rheum Dis. 2015 Mar 2.
Roddy E, Zhang W, Doherty M. **Aerobic walking or strengthening exercise** for osteoarthritis of the knee? A systematic review. Ann Rheum Dis. 2005 Apr;64(4):544-8 & ACP Journal Club .
Rosekelly M, Wheeler V. **NSAIDs for Postpartum Perineal Pain**. Am Fam Physician. 2018 Jun 1;97(11):Online.
Ross Joseph S.; Madigan David; Hill Kevin P.; et al. Pooled Analysis of **Rofecoxib** Placebo-Controlled Clinical Trial Data: Lessons for Postmarket Pharmaceutical Safety Surveillance. Arch Intern Med. 2009;169(21):1976-1985.
Ross Joseph S.; Madigan David; Konstam Marvin A.; et al. Persistence of **Cardiovascular Risk After Rofecoxib Discontinuation**. Arch Intern Med. 2010;170(22):2035-2036.
Ross JS, Krumholz HM. **Bringing Vioxx back to market**. BMJ. 2018 Jan 25;360:k242.
Rostom A, et al; U.S. Preventive Services Task Force. Nonsteroidal anti-inflammatory drugs and cyclooxygenase-2 inhibitors for **primary prevention of colorectal cancer**: a systematic review prepared for the U.S. Preventive Services Task Force. Ann Intern Med. 2007 Mar 6;146(5):376-89. Review. Summary for patients in: Ann Intern Med. 2007 Mar 6;146(5):I35. Cyclooxygenase-2 inhibitors and NSAIDs reduce the incidence of colonic adenomas. Nonsteroidal anti-inflammatory drugs also reduce the incidence of CRC. However, these agents are associated with important cardiovascular events and gastrointestinal harms. The balance of benefits to risk does not favor chemoprevention in average-risk individuals. (InfoPOEMs: The US Preventive Services Task Force recommends against routine use of aspirin or nonsteroidal anti-inflammatory drugs (NSAIDs) to prevent colorectal cancer. The beneficial decrease in colorectal adenoma, cancer incidence, and possibly cancer-related mortality is more than offset by the harm associated with their use. Ulcers leading to gastrointestinal bleeding, renal impairment, and an increase in cardiovascular events are the main problems. (LOE = 1a))
Rostom A, Muir K, Dube C, Jolicoeur E, Boucher M, Joyce J, Tugwell P, Wells GW. Gastrointestinal safety of cyclooxygenase-2 inhibitors: a Cochrane Collaboration systematic review. Clin Gastroenterol Hepatol. 2007

Jul;5(7):818-28, 828.e1-5; quiz 768. Epub 2007Jun 6. **COX-2s appear to offer greater upper GI safety** and are better tolerated than nonselective NSAIDs. The co-administration of acetylsalicylic acid might reduce the safety advantage of COX-2s over that of nonselective NSAIDs.

Rostom A, Moayyedi P, Hunt R; CAG Consensus Group. **Canadian consensus guidelines** on long-term nonsteroidal anti-inflammatory drug therapy and the need for gastroprotection: benefits versus risks. Aliment Pharmacol Ther. **2009** Mar 1;29(5):481-96 {Recommendations based on personal opinion: *Low GI & low CV risk* ⇨ traditional NSAID; *low GI & high CV risk* ⇨ naproxen; *high GI & low CV risk* ⇨ COXIB plus PPI standard dose; *high GI & high CV risk* ⇨ careful assessment to priorize risks (consider alternatives) ; prescribe lowest dose for shortest time possible.}

Rother M, Conaghan PG. A randomized, double-blind, phase III trial in moderate osteoarthritis knee pain comparing **topical ketoprofen** gel with ketoprofen-free gel. J Rheumatol. 2013 Oct;40(10):1742-8.

Rothwell PM, Wilson M, Elwin CE, et al. Long-term effect of **aspirin on colorectal cancer** incidence and mortality: 20-year follow-up of five randomised trials. Lancet. 2010 Oct 21.

Rothwell PM, Fowkes FG, Belch JF, Ogawa H, Warlow CP, Meade TW. Effect of daily **aspirin on long-term risk of death due to cancer**: analysis of individualpatient data from randomised trials. Lancet. 2011 Jan 1;377(9759):31-41.

Roumie CL, Mitchel EF Jr, Kaltenbach L, Arbogast PG, Gideon P, Griffin MR. Nonaspirin NSAIDs, cyclooxygenase 2 inhibitors, and the risk for stroke. Stroke. 2008 Jul;39(7):2037-45. Epub 2008 Apr 24. Our results indicate an increased risk of stroke with current use of two highly selective coxibs, rofecoxib and valdecoxib, also shown to increase cardiovascular risk. These results also provide some reassurance about other specific NSAIDs regarding stroke risk.

Rubin AK, Burk KS, Staller K, et al. Case 30-2018: A **66-Year-Old Woman with Chronic Abdominal Pain**. N Engl J Med. 2018 Sep 27;379(13):1263-1272. (NSAIDs)

Ruschitzka F, Borer JS, Krum H, et al; **PRECISION-ABPM** Investigators. Differential **blood pressure effects of ibuprofen, naproxen, and celecoxib** in patients with arthritis: the PRECISION-ABPM (Prospective Randomized Evaluation of Celecoxib Integrated Safety Versus Ibuprofen or Naproxen Ambulatory Blood Pressure Measurement) Trial. Eur Heart J. 2017 Aug 28.

Sachs HC; COMMITTEE ON DRUGS. The transfer of drugs and therapeutics into human breast milk: an update on selected topics. Pediatrics. 2013 Sep;132(3):e796-809. doi: 10.1542/peds.2013-1985.

Sahasrabuddhe VV, Gunja MZ, Graubard BI, et al. Non-steroidal antiinflammatory drug use, chronic liver disease, and **hepatocellular carcinoma**. J Natl Cancer Inst. 2012;XX(X):XXX-XXX.

Sakulchit T, Goldman RD. **Acetaminophen use and asthma in children**. Can Fam Physician. 2017 Mar;63(3):211-213

Samadder NJ, Kuwada SK, Boucher KM, et al. Association of **Sulindac and Erlotinib** vs Placebo With Colorectal Neoplasia in **Familial Adenomatous Polyposis**: Secondary Analysis of a Randomized Clinical Trial. JAMA Oncol. 2018 Feb 8.

Samadder NJ, Neklason DW, Boucher KM, et al. Effect of **Sulindac and Erlotinib** vs Placebo on **Duodenal Neoplasia in Familial Adenomatous Polyposis**: A Randomized Clinical Trial. JAMA. 2016 Mar 22-29;315(12):1266-75.

Samii A, Etminan M, Wiens MO, Jafari S. NSAID use and the risk of **Parkinson's disease**: systematic review and meta-analysis of observational studies. Drugs Aging. 2009;26(9):769-79.

Saragiotto BT, Machado GC, Ferreira ML, et al. **Paracetamol (acetaminophen) for low back pain**. Cochrane Database Syst Rev. 2016 Jun 7;6:CD012230. We found that paracetamol does not produce better outcomes than placebo for people with acute LBP, and it is uncertain if it has any effect on chronic LBP.

Savino, Francesco, Lupica, Maria Maddalena, Tarasco, Valentina, et al. Fulminant **Hepatitis After 10 Days of Acetaminophen** Treatment at Recommended Dosage in an Infant. Pediatrics 2011 127: e494-e497.

Sawhney MS, McDougall H, Nelson DB, Bond JH. **Fecal Occult Blood Test** in Patients on Low-Dose Aspirin, Warfarin, Clopidogrel, or Non-steroidal Anti-inflammatory Drugs. Dig Dis Sci. 2010 Mar 3. [Epub ahead of print] Anticoagulants and antiplatelet medications lower the positive-predictive-value of FOBT for advance colonic neoplasia and should be stopped if clinically feasible prior to stool collection.

Sawitzke AD, Shi H, Finco MF, Dunlop DD, et al.. Clinical efficacy and safety of **glucosamine, chondroitin sulphate, their combination, celecoxib or placebo** taken to treat osteoarthritis of the knee: 2-year results from **GAIT**. Ann Rheum Dis. 2010 Jun 4.

Scharf HP, et al. Acupuncture and knee osteoarthritis: a three-armed randomized trial. Ann Intern Med. 2006 Jul 4;145(1):12-20. Compared with physiotherapy and as-needed anti-inflammatory drugs, addition of either TCA or sham acupuncture led to greater improvement in WOMAC score at 26 weeks.

Scheiman JM, et al. Prevention of Ulcers by Esomeprazole in At-Risk Patients Using Non-Selective NSAIDs and COX-2 Inhibitors. (**Venus** & **Pluto**) Am J Gastroenterol. 2006 Feb 22; [Epub ahead of print] CONCLUSIONS: For at-risk patients, esomeprazole was effective in preventing ulcers in long-term users of NSAIDs, including COX-2 inhibitors.

Schjerning Olsen AM, Fosbøl EL, et al. Duration of treatment with nonsteroidal anti-inflammatory drugs and impact on risk of **death and recurrent myocardial infarction** in patients with prior myocardial infarction: a nationwide cohort study. Circulation. 2011;123: 2226-35.

Schjerning Olsen A, Fosbøl L, Lindhardsen J, et al. Long-term **cardiovascular risk of NSAID use** according to time passed after first-time myocardial infarction. A nationwide cohort study. Circulation 2012.

Schjerning Olsen A-M, Gislason GH, McGettigan P, et al. Association of **NSAID use with risk of bleeding and cardiovascular events in patients receiving antithrombotic therapy after myocardial infarction**. JAMA. doi:10.1001/jama.2015.0809.

Schjerning Olsen AM, et al. Impact of proton **pump inhibitor treatment on gastrointestinal bleeding associated with non-steroidal anti-inflammatory drug** use among post-myocardial infarction patients taking antithrombotics: nationwide study. BMJ. 2015 Oct 19;351:h5096.

Schmidt M, Christiansen CF, Mehnert F, Rothman KJ, Sørensen HT. Non-steroidal anti-inflammatory drug use and **risk of atrial fibrillat**ion or flutter: population based case-control study. BMJ 2011;343:d3450.

Schmidt M, Hovath-Puho E, Christiansen CF, et al. **Preadmission use** of nonaspirin nonsteroidal anti-inflammatory drugs and 30-day **stroke mortality**. Neurology. 2014 Nov 5.

Schmidt M, Sørensen HT, Pedersen L. **Diclofenac use and cardiovascular risks**: series of nationwide cohort studies. BMJ. 2018 Sep 4;362:k3426.

Schneider V, Levesque LE, Zhang B, Hutchinson T, Brophy JM. Association of selective and conventional nonsteroidal antiinflammatory drugs with **acute renal failure**: A population-based, nested case-control analysis. Am J Epidemiol. 2006 Nov 1;164(9):881-9. Epub 2006 Sep 27. There was a significant association for both selective and nonselective NSAIDs with acute renal failure, but confirmatory studies are required.

Scott PA, Kingsley GH, Smith CM, et al. Non-steroidal anti-inflammatory drugs and **myocardial infarctions**: comparative **systematic review** of evidence from observational studies and randomized controlled trials. Ann Rheum Dis. 2007 Oct;66(10):1296-304. Epub 2007 Mar 7. {The comparative risk of myocardial infarction (MI) with cyclo-oxygenase-2-specific drugs and traditional non-steroidal anti-inflammatory drugs (NSAIDs) was determined. METHODS: The results of studies of a suitable size in colonic adenoma and arthritis-that had been published in English and from which crude data about MIs could be extracted-were evaluated. Medline, Embase and Cinahl (2000-2006) databases, as well as published bibliographies, were used as data sources. Systematic reviews examined MI risks in case-control and cohort studies, as well as in randomised controlled trials (RCTs). RESULTS: 14 case-control studies (74 673 MI patients, 368 968 controls) showed no significant association of NSAIDs with MI in a random-effects model (OR 1.17; 95% **CI 0.99 to 1.37**) and a small risk of MI in a fixed-effects model (OR 1.32; 95% **CI 1.29 to 1.35**). Sensitivity analyses showed higher risks of MI in large European studies involving matched controls. Six cohort studies (387 983 patient years, 1 120 812 control years) showed no significant risk of MI with NSAIDs (RR 1.03; 95% CI **1.00 to 1.07**); the risk was higher with rofecoxib (RR 1.25; 95% **CI 1.17 to 1.34**) but not with any other NSAIDs. Four RCTs of NSAIDs in colonic adenoma (6000 patients) showed an increased risk of MI (RR 2.68; 95% CI 1.43 to 5.01). Fourteen RCTs in arthritis (45 425 patients) showed more MIs with cyclo-oxygenase-2-specific drugs (Peto OR **1.6**; 95% CI 1.1 to 2.4), but fewer serious upper gastrointestinal events (Peto OR 0.40; 95% CI 0.31 to 0.53). CONCLUSION: The overall risk of MI with NSAIDs and cyclo-oxygenase-2-specific drugs was small; rofecoxib showed the highest risk. There was an increased MI risk with cyclo-oxygenase-2-specific drugs compared with NSAIDs, but less serious upper gastrointestinal toxicity.}

Semberova J, Sirc J, Miletin J,et al. **Spontaneous closure of patent ductus arteriosus in infants** ≤1500 g. Pediatrics. 2017;140(2):e20164258.

Sheehan WJ, Mauger DT, Paul IM, et al. **Acetaminophen versus ibuprofen** in young children with mild persistent **asthma**. (**AVICA**) N Engl J Med 2016; 375: 619-30.

Shephard A, Smith G, Aspley S, et al. Randomised, double-blind, placebo-controlled studies on **flurbiprofen** 8.75 mg lozenges in patients with/without **group A or C streptococcal throat infection**, with an assessment of clinicians` prediction of strep throat. Int J Clin Pract. 2014 Oct 9.

Sherve K, Gerard CJ, Neher JO, et al. **Cardiovascular effects of NSAIDs**. Am Fam Physician. 2014 Aug 15;90(4):Online.

Shiffman S, Battista DR, Kelly JP, et al. **Prevalence of Exceeding Maximum Daily Dose of Acetaminophen, and Seasonal Variations in Cold-Flu Season**. Br J Clin Pharmacol. 2018 Mar 7.

Shin J, Park M, Lee SH, et al. Risk of **intracranial haemorrhage in antidepressant users with concurrent use of non-steroidal anti-inflammatory drugs**: nationwide propensity score matched study. BMJ 2015;351:h3517.

Sieper J, Listing J, et al. Effect of **continuous versus on-demand treatment** of **ankylosing spondylitis** with **diclofenac** over 2 years on radiographic progression of the spine: results from a randomised multicentre trial (ENRADAS). Ann RheumDis. 2016 Aug;75(8):1438-43.

Sih K, Goldman RD. **Nonsteroidal** anti-inflammatory drug administration in children with **history of wheeze**. Can Fam Physician. 2016 Aug;62(8):633-4

Silverstein FE, et al. **Misoprostol** reduces serious gastrointestinal complications in patients with rheumatoid arthritis receiving nonsteroidal anti-inflammatory drugs. A randomized, double-blind, placebo-controlled trial. Ann Intern Med. 1995 Aug 15;123(4):241-9.

Sin B, Wai M, Tatunchak T, et al. The use of **intravenous acetaminophen** for acute pain in the emergency department. Acad Emerg Med. 2016 Jan 29.

Sinusas K. **Osteoarthritis**: diagnosis and treatment. Am Fam Physician. 2012 Jan 1;85(1):49-56.

Skeid MS, Pedersen-Bjergaard U, Kristensen PL, et al. **NSAID-induced** symptomatic **hypophosphataemia**. Br J Clin Pharmacol. 2016 Aug 10

Slaughter JL, Reagan PB, Newman TB, et al. **Comparative Effectiveness of Nonsteroidal Anti-inflammatory Drug Treatment** vs No Treatment for Patent **Ductus Arteriosus** in Preterm Infants. JAMA Pediatr. 2017 Jan 3:e164354.

Smith CA, Zhu X, He L, et al. **Acupuncture for primary dysmenorrhoea**. Cochrane Database Syst Rev. 2011 Jan 19;1:CD007854. Acupuncture may reduce period pain, however there is a need for further well-designed randomised controlled trials.

Smith CH, Goldman RD. **Topical nonsteroidal** anti-inflammatory drugs for **corneal** abrasions in children. Can Fam Physician. 2012 Jul;58(7):748-9.

Smith TO, Zou K, Abdullah N, et al. Does **flare trial design** affect the effect size of non-steroidal anti-inflammatory drugs in symptomatic osteoarthritis? A systematic review and meta-analysis. Ann Rheum Dis. 2016 Feb 16.

Snyder MJ, Bepko J, White M. **Acute pericarditis**: diagnosis and management. Am Fam Physician. 2014 Apr 1;89(7):553-60.

SOGC: Burnett M, Lemyre M. SOGC: Society of Obstetricians and Gynaecologists of Canada. **SOGC** clinical practice guideline No. 345-**Primary Dysmenorrhea Consensus Guideline**. J Obstet Gynaecol Can. 2017 Jul;39(7):585-595.

Soininen H, West C, Robbins J, Niculescu L. Long-Term Efficacy and Safety of **Celecoxib** in **Alzheimer's** Disease. Dement Geriatr Cogn Disord. 2006 Oct 26;23(1):8-21 [Epub ahead of print] Celecoxib 200 mg bid did not slow the progression of AD in this study, and the occurrence of adverse events was as expected for an elderly population with a complex chronic medical condition.

Solomon SD, et al.; APC and **PreSAP** Trial Investigators. Effect of **celecoxib** on cardiovascular events and blood pressure in two trials for the prevention of colorectal adenomas. Circulation. 2006 Sep 5;114(10):1028-35.

Solomon SD, Wittes J, Finn PV, et al.; for the Cross Trial Safety Assessment Group. Cardiovascular Risk of Celecoxib in 6 Randomized Placebo-Controlled Trials. The Cross Trial Safety Analysis. Circulation. 2008 Mar 31; [Epub ahead of print] We observed evidence of differential cardiovascular risk as a function of celecoxib dose regimen and baseline cardiovascular risk. By further clarifying the extent of celecoxib-related cardiovascular risk, these findings may help guide treatment decisions for patients who derive clinical benefit from selective cyclooxygenase-2 inhibition. The risk, which increased with dose regimen (P=0.0005), was lowest for the 400-mg-QD dose (hazard ratio, 1.1; 95% CI, 0.6 to 2.0), intermediate for the 200-mg-BID dose (hazard ratio, 1.8; 95% CI, 1.1 to 3.1), and highest for the 400-mg-BID dose (hazard ratio, 3.1; 95% CI, 1.5 to 6.1).

Solomon Daniel H.; Rassen Jeremy A.; Glynn Robert J.; et al. The Comparative Safety of **Analgesics in Older Adults With Arthritis**. Arch Intern Med. 2010;170(22):1968-1978. The comparative safety of analgesics varies depending on the safety event studied. Opioid use exhibits an increased relative risk of many safety events compared with nsNSAIDs.

Solomon Daniel H.; Rassen Jeremy A.; Glynn Robert J.; et al. The Comparative Safety of **Opioids for Nonmalignant Pain in Older Adults**. Arch Intern Med. 2010;170(22):1979-1986.

Solomon DH, Husni ME, Wolski KE, et al. **Differences in Safety of Nonsteroidal Antiinflammatory Drugs in Patients With Osteoarthritis and Patients With Rheumatoid Arthritis**: A Randomized Clinical Trial. Arthritis Rheumatol. 2018 Apr;70(4):537-546.

Sondergaard KB, Weeke P, Wissenberg M, et al. Non-steroidal anti-inflammatory drug use is associated with increased risk of **out-of-hospital cardiac arrest**: a nationwide case-time-control study. Eur Heart J Cardiovasc Pharmacother. 2016 Dec 26.

Sood BG, Lulic-Botica M, Holzhausen KA, et al. The risk of **necrotizing enterocolitis after indomethacin tocolysis**. Pediatrics. 2011 Jul;128(1):e54-62.

Sotoudehmanesh R, Khatibian M, Kolahdoozan S, Ainechi S, Malboosbaf R, Nouraie M. Indomethacin may reduce the incidence and severity of acute pancreatitis after **ERCP**. Am J Gastroenterol. 2007 May;102(5):978-83. Epub 2007 Mar 13. n=490.

Sperber SJ, et al. Effects of **naproxen on experimental rhinovirus** colds. A randomized, double-blind, controlled trial. Ann Intern Med. 1992 Jul 1;117(1):37-41.

Stergiakouli E, Thapar A, Davey Smith G. Association of **Acetaminophen Use During Pregnancy** With Behavioral Problems in Childhood: Evidence Against Confounding. JAMA Pediatr. 2016 Aug 15.

Strand V. Are COX-2 inhibitors preferable to non-selective non-steroidal anti-inflammatory drugs in patients with risk of cardiovascular events taking low-dose aspirin? Lancet 2007; 370:2138-2151. Mortality associated with gastrointestinal events is less frequent than with cardiovascular events, but asymptomatic ulcers can result in severe complications. Data support the conclusion that COX-2 inhibitors are preferable to non-selective NSAIDs in patients with chronic pain and cardiovascular risk needing low-dose aspirin, but relative risks and benefits should be assessed individually for each patient.

Strate LL, Liu YL, Huang ES, et al. Use of aspirin or nonsteroidal anti-inflammatory drugs increases risk for **diverticulitis and diverticular bleeding**. Gastroenterology. 2011 May;140(5):1427-33.

Stürmer T, Glynn RJ, Lee IM, et al. **Aspirin use and colorectal cancer**: post-trial follow-up data from the Physicians' Health Study (PHS). Ann Intern Med. 1998;128:713-20.

Sudano I, Flammer AJ, Périat D, et al. **Acetaminophen increases blood pressure** in patients with coronary artery disease. Circulation. 2010 Nov 2;122(18):1789-96.

Suissa D, Delaney JA, Dial S, et al. Non-Steroidal Anti-Inflammatory Drugs and The Risk of **Clostridium Difficile**-Associated Disease. Br J Clin Pharmacol. 2012 Jan 29. (diclofenac increased risk of CDAD)

Taggart E, Doran S, Kokotillo A, et al. **Ketorolac** in the Treatment of **Acute Migraine**: A Systematic Review. Headache. 2013 Jan 8.

Taha AS, McCloskey C, Prasad R, Bezlyak V. **Famotidine** for the prevention of peptic ulcers and oesophagitis in patients taking low-dose aspirin (**FAMOUS**): a phase III, randomised, double-blind, placebo-controlled trial. Lancet. 2009 Jul 11;374(9684):119-25. Epub 2009 Jul 3.

Taha AS, Hudson N, Hawkey CJ, et al. **Famotidine** for the prevention of gastric and duodenal ulcers caused by nonsteroidal antiinflammatory drugs. N Engl J Med. 1996 May 30;334(22):1435-9.

Tanaka R, Ozawa J, Kito N, et al. Efficacy of **strengthening or aerobic exercise on pain relief in people with knee osteoarthritis**: a systematic review and meta-analysis of randomized controlled trials. Clin Rehabil. 2013 Jul 4.

Tannenbaum H, Bombardier C, Davis P, Russell AS; **Third Canadian Consensus** Conference Group. An evidence-based approach to prescribing nonsteroidal antiinflammatory drugs. Third Canadian Consensus Conference. J Rheumatol. 2006 Jan;33(1):140-57. Epub 2005 Dec 1.

Tarp S, Bartels EM, Bliddal H, et al. Effect of nonsteroidal antiinflammatory drugs on **C-reactive protein (naproxen**) in rheumatoid arthritis: A meta-analysis of randomized controlled trials. Arthritis Rheum. 2012 Jul 25.

Taylor IC, Lindblad AJ, Kolber MR. **Fracture healing and NSAIDs**. Can Fam Physician. 2014 Sep;60(9):817.

Temple AR, Temple BR, Kuffner EK. Dosing and Antipyretic Efficacy of Oral **Acetaminophen in Children**. Clin Ther. 2013 Aug 22.

The "**Triple Whammy**". Pharmacist's Letter Dec/06 (Impaired renal function while involving an ACE &/or ARB, an NSAID &/or a diuretic)

Thiruvengadam NR et al. **Rectal indomethacin reduces pancreatitis** in high- and low-risk patients undergoing endoscopic retrograde cholangiopancreatography. Gastroenterology 2016 Aug; 151:288.

Thrift AP et al. Nonsteroidal anti-inflammatory drug use is **not associated with reduced risk of Barrett's esophagus**. Am J Gastroenterol 2016 Aug 30.

Thybo KH, Hägi-Pedersen D, Dahl JB, et al. Effect of Combination of **Paracetamol (Acetaminophen) and Ibuprofen vs Either Alone on Patient-Controlled Morphine Consumption** in the First 24 Hours **After Total Hip Arthroplasty**: The PANSAID Randomized Clinical Trial. JAMA. 2019 Feb 12;321(6):562-571.

Towheed TE, et al. Acetaminophen for osteoarthritis (review). *The Cochrane Database of Systematic Reviews* 2006, Issue 1.

Treatment Guidelines from the Medical Letter. Pharmaceutical Drug Overdose. Sept 2006. (**Acetaminophen**: N-acetylcysteine treatment. **Aspirin**: sodium bicarbonate treatment)

Treatment guidelines from the Medical Letter. **Drugs for Pain** April 2007.

Trelle S, Reichenbach S, Wandel S, et al. **Cardiovascular safety of non-steroidal anti-inflammatory drugs: network meta-analysis**. BMJ. 2011 Jan 11;342:c7086. doi: 10.1136/bmj.c7086.

Tsaganos T, Tseti IK, Tziolos N, et al. Randomized controlled multicenter clinical trial of the **antipyretic effect of intravenous paracetamol** in patients admitted to hospital with infection. Br J Clin Pharmacol. 2016 Oct 28.

Ungprasert P, Srivali N, Wijarnpreecha K, et al. Non-steroidal anti-inflammatory drugs and **risk of venous thromboembolism**: a systematic review and meta-analysis. Rheumatology (Oxford). 2014 Sep 24.

Unlu N, Kocaoglan H, Sayin F, et al. Penetration of topically applied **diclofenac and ketorolac into the aqueous humour and subretinal fluid**: randomized clinical trial. Can J Ophthalmol. 2010 Dec 8;45(6):1-6.

Uthman OA, van der Windt DA, Jordan JL, et al. **Exercise for lower limb osteoarthritis**: systematic review incorporating trial sequential analysis and network meta-analysis. BMJ. 2013 Sep 20;347:f5555.

Valkhoff VE, van Soest EM, Mazzaglia G, et al. **Adherence to gastroprotection during cyclooxygenase-2 inhibitor use** and the risk of upper gastrointestinal events: A population-based study. Arthritis Rheum. 2012 Apr 16.

Välitalo PA, Kemppainen H, Kulo A, et al. Body weight, gender, and pregnancy affect enantiomer-specific **ketorolac** pharmacokinetics. Br J Clin Pharmacol. 2017 Apr 21.

van der Heijde D, Ramiro S, Landewé R, et al. **2016 update of the ASAS-EULAR management recommendations for axial spondyloarthritis**. Ann Rheum Dis. 2017 Jun;76(6):978-991.

van Durme CM, Wechalekar MD, Landewé RB. Nonsteroidal anti-inflammatory drugs for treatment of **acute gout**. JAMA. 2015 Jun 9;313(22):2276-7.

Van Marter LJ, Hernandez-Diaz S, Werler MM, et al. Nonsteroidal antiinflammatory drugs in late pregnancy and **persistent pulmonary hypertension** of the newborn. Pediatrics. 2013 Jan;131(1):79-87.

Vasikasin V, Rojdumrongrattana T, Chuerboonchai W, et al. Effect **of standard dose paracetamol versus placebo as antipyretic therapy on liver injury in** adult dengue infection: a multicentre randomised controlled trial. Lancet Glob Health. 2019 May;7(5):e664-e670.

Vergara M, Catalán M, Gisbert JP, Calvet X. Meta-analysis: role of Helicobacter **pylori eradication in the prevention of peptic ulcer in NSAID** users. Aliment Pharmacol Ther. 2005 Jun 15;21(12):1411-8.

Verkleij SP, Luijsterburg PA, Willemsen SP, et al. Effectiveness of **diclofenac versus paracetamol-acetaminophen in knee osteoarthritis**: a randomised controlled trial in primary care. Br J Gen Pract 2015;65:e530–7.

Veys L, Derry S, Moore RA. **Ketoprofen for episodic tension-type headache** in adults. Cochrane Database Syst Rev. 2016 Sep 22;9:CD012190. Ketoprofen 25 mg provided a small benefit compared with placebo in terms of being pain-free at two hours or having mild or no pain at two hours for people with frequent episodic TTH who have an acute headache of moderate or severe intensity. Its use was associated with more people experiencing adverse events. Ketoprofen 25 mg was not superior to paracetamol 1000 mg for any efficacy outcome.

Vik I, Bollestad M, Grude N, et al. **Ibuprofen versus pivmecillinam** for uncomplicated **urinary tract infection** in women-A double-blind, randomized non-inferiority trial. PLoS Med. 2018 May 15;15(5):e1002569.

Viteri OA, England JA, Alrais MA, et al. Association of **Nonsteroidal Antiinflammatory Drugs and Postpartum Hypertension in Women With Preeclampsia** With Severe Features. Obstet Gynecol. 2017 Sep 5.

Voiriot G, Dury S, Parrot A, Mayaud C, Fartoukh M. Nonsteroidal antiinflammatory drugs may affect the presentation and course of **community-acquired pneumonia**. Chest. 2011 Feb;139(2):387-94.

Wahlsten LR, Eckardt H, Lyngbæk S, et al. **Symptomatic venous thromboembolism** following **fractures distal to the knee**: a nationwide Danish cohort study. J Bone Joint Surg Am. 2015 Mar 18;97(6):470-7. (risk with oral contraceptives & NSAIDs)

Wallace JL, Syer S, Denou E, et al. **Proton Pump Inhibitors Exacerbate NSAID-Induced Small Intestinal Injury** by Inducing Dysbiosis. Gastroenterology. 2011 Jul 13.

Walson PD, Halvorsen M, Edge J, et al. Pharmacokinetic Comparison of **Acetaminophen Elixir Versus Suppositories** in Vaccinated Infants (Aged 3 to 36 Months): A Single-Dose, Open-Label, Randomized, Parallel-Group Design. Clin Ther. 2013 Jan 22.

Wang AY, Strand DS, Shami VM. Prevention of **Post-ERCP Pancreatitis**: Medications and Techniques. Clin Gastroenterol Hepatol. 2016 May 26. pii: S1542-3565(16)30215-4.

Wang C, Schmid CH, Iversen MD, et al. Comparative Effectiveness of **Tai Chi Versus Physical Therapy** for **Knee Osteoarthritis**: A Randomized Trial. Ann Intern Med. 2016 May 17.

Wang R, Dasgupta A, Ward MM. **Comparative efficacy of non-steroidal anti-inflammatory drugs in ankylosing spondylitis:** a Bayesian network meta-analysis of clinical trials. Ann Rheum Dis. 2016 Jun;75(6):1152-60.

Wang SY, Olson-Kellogg B, Shamliyan TA, et al. **Physical therapy** interventions for knee pain secondary to osteoarthritis: a systematic review. Ann Intern Med. 2012 Nov 6;157(9):632-44.

Watanabe T, Tanigawa T, Nadatani Y, et al. Risk factors for severe nonsteroidal anti-inflammatory drug-induced **small intestinal damage**. Dig Liver Dis. 2013 Jan 17.

Weisz DE, Mirea L, Resende MHF, et al. Outcomes of **Surgical Ligation after Unsuccessful Pharmacotherapy for Patent Ductus Arteriosus** in Neonates Born Extremely Preterm. J Pediatr. 2018 Jan 3.

Wen YC, Hsiao FY, Chan KA, Lin ZF, Shen LJ, Fang CC. **Acute Respiratory Infection** and Use of Nonsteroidal Anti-Inflammatory Drugs on **Risk of Acute Myocardial Infarction**: A Nationwide Case-Crossover Study. J Infect Dis. 2017 Feb 1.

Wheatley BM, Nappo KE, Christensen DL, et al. Effect of **NSAIDs on Bone Healing Rates**: A Meta-analysis. J Am Acad Orthop Surg. 2019 Apr 1;27(7):e330-e336.

White AA, Stevenson DD. **Aspirin-Exacerbated Respiratory Disease**. N Engl J Med. 2018 Sep 13;379(11):1060-1070.

White WB, et al. Risk of **cardiovascular events in patients receiving celecoxib**: a meta-analysis of randomized clinical trials. Am J Cardiol. 2007 Jan 1;99(1):91-8. Epub 2006 Nov 10. These analyses failed to demonstrate an increased CV risk with celecoxib relative to placebo and demonstrated a comparable rate of CV events with celecoxib treatment compared with nonselective NSAIDs.

Wilasrusmee S, Chittacheron A, Jirasirtum S, Srisangchai P. **Naproxen suppository for perineal pain after vaginal delivery**. Int J Gynaecol Obstet. 2008; 102(1): 19-22.

Wilcox CM, Allison J, Benzuly K, et al. Consensus development conference on the use of nonsteroidal anti-inflammatory agents, including cyclooxygenase-2 enzyme inhibitors and aspirin. Clin Gastroenterol Hepatol. 2006 Sep;4(9):1082-9. Epub 2006 Jul 31.

Williams CM, Latimer J, Maher CG, et al. PACE--the first placebo controlled trial of **paracetamol/acetaminophen** for acute low back pain: design of a randomised controlled trial. BMC Musculoskelet Disord. 2010 Jul 23;11:169.

Williams CM, Maher CG, Latimer J, et al. Efficacy of **paracetamol/acetaminophen** for acute low-back pain: a double-blind, randomized controlled trial. (**PACE**) Lancet. 2014 Jul 23. pii: S0140-6736(14)60805-9.

Wilson DJ, Schutte SM, Abel SR. Comparing the Efficacy of **Ophthalmic NSAIDs** in Common Indications: A Literature Review to Support Cost-effective Prescribing. Ann Pharmacother. 2015 Jun;49(6):727-734. Epub 2015 Feb 27. Review.

Wininger SJ, Miller H, Minkowitz HS, et al. A randomized, double-blind, placebo-controlled, multicenter, repeat-dose study of two **intravenous acetaminophen** dosing regimens for the treatment of pain after abdominal laparoscopic surgery. Clin Ther. 2010 Dec;32(14):2348-69.

Witt CM, et al. **Acupuncture** in patients with osteoarthritis of the knee or hip: A randomized, controlled trial with an additional nonrandomized arm. Arthritis Rheum. 2006 Oct 30;54(11):3485-3493. These results indicate that acupuncture plus routine care is associated with marked clinical improvement in patients with chronic OA-associated pain of the knee or hip.

Wong T, Stang AS, Ganshorn H, Hartling L, Maconochie IK, Thomsen AM, Johnson DW. **Combined and alternating paracetamol and ibuprofen** therapy for febrile children. Cochrane Database of Systematic Reviews 2013, Issue 10. Art. No.: CD009572. DOI: 10.1002/14651858.CD009572.pub2. There is some evidence that both alternating and combined antipyretic therapy may be more effective at reducing temperatures than monotherapy alone.However, the evidence for improvements inmeasures of child discomfort remains inconclusive.

Wuytack F, Smith V, Cleary BJ. Oral non-steroidal anti-inflammatory drugs (single dose) for **perineal pain** in the early postpartum period. Cochrane Database Syst Rev. 2016; (7): CD011352.

Yelland MJ, Nikles CJ, McNairn N, Del Mar CB, Schluter PJ, Brown RM. Celecoxib compared with sustained-release paracetamol for osteoarthritis: a series of n-of-1 trials. Rheumatology (Oxford). 2007 Jan;46(1):135-40. {InfoPOEMs – Feb07: In this short-term study emphasizing individual response, acetaminophen and celecoxib (Celebrex) are virtually indistinguishable in improving pain, stiffness, and function in patients with clinically diagnosed degenerative joint disease (DJD). Since acetaminophen is less expensive and has fewer safety concerns, it should be the drug of first choice. (LOE = 1b).}

Zapata-Colindres JC,et al. The association of Helicobacter pylori infection and nonsteroidal anti-inflammatory drugs in peptic ulcer disease. Can J Gastroenterol. 2006 Apr;20(4):277-80. The development of PUD was observed earlier in the combined H pylori and NSAID group than in patients with only NSAID use. This suggests a synergic effect between the two risks factors in the development of PUD.

Zhang W, Doherty M, Arden N, et al. EULAR Standing Committee for International Clinical Studies Including Therapeutics (ESCISIT). EULAR evidence based recommendations for the management of **hip osteoarthritis**: report of a task force of the EULAR Standing Committee for International Clinical Studies Including Therapeutics (ESCISIT). Ann Rheum Dis. 2005 May;64(5):669-81. Epub 2004 Oct 7 & ACP Journal Club .

Zhang J, Ding EL, Song Y. Adverse Effects of Cyclooxygenase 2 Inhibitors on Renal and Arrhythmia Events: Meta-analysis of Randomized Trials. JAMA. 2006 Sep 12; [Epub ahead of print] In this comprehensive analysis of 114 randomized trials with 116 094 participants, **rofecoxib** was associated with increased renal and arrhythmia risks. A COX-2 inhibitor class effect was not evident.

Zhang W, Doherty M, et al. **EULAR** evidence based recommendations for the management of **hand osteoarthritis**: report of a Task Force of the EULAR Standing Committee for International Clinical Studies Including Therapeutics (ESCISIT). Ann Rheum Dis 2007; 66: 377–88.

Zayat AS, Conaghan PG, Sharif M, et al. Do non-steroidal anti-inflammatory drugs have a significant effect on **detection and grading of ultrasound-detected synovitis** in patients with rheumatoid arthritis? Results from a randomised study. Ann Rheum Dis. 2011 Oct;70(10):1746-51.

Zhou L, Maviglia SM, Mahoney LM, et al. Supratherapeutic dosing of **acetaminophen** among hospitalized patients. Arch Intern Med. 2012 Dec 10;172(22):1721-8.

New coxib - Etoricoxib (ARCOXIA) - NOT approved by FDA (April, 2007)

Lumiracoxib – hepatic toxicity – deregulation in Australia. http://www.medadnews.com/News/index.cfm?articleid=467159

[26] Mazieres B, Rouanet S, Guillon Y, Scarsi C, Reiner V. Topical ketoprofen patch in the treatment of tendinitis: a randomized, double blind, placebo controlled study. J Rheumatol. 2005 Aug;32(8):1563-70.

Underwood M, Ashby D, Cross P, et al; on behalf of the TOIB study team. Advice to use **topical or oral ibuprofen** for chronic knee pain in older people: randomised controlled trial & patient preference study. BMJ. 2007 Dec 4; [Epub ahead of print] Advice to use oral or topical preparations has an equivalent effect on knee pain over one year, and there are more minor side effects with oral NSAIDs. Topical NSAIDs may be a useful alternative to oral NSAIDs.

Massey T, Derry S, Moore RA, McQuay HJ. **Topical NSAIDs** for acute pain in adults. Cochrane Database Syst Rev. 2010 Jun 16;6:CD007402. Topical NSAIDs can provide good levels of pain relief, without the systemic adverse events associated with oral NSAIDs, when used to treat acute musculoskeletal conditions.

Derry S, Moore RA, Rabbie R. Topical NSAIDs for chronic musculoskeletal pain in adults. Cochrane Database of Systematic Reviews 2012, Issue 9. Art. No.: CD007400. DOI: 10.1002/14651858.CD007400.pub2. Topical NSAIDs can provide good levels of pain relief; topical diclofenac solution is equivalent to that of oral NSAIDs in knee and hand osteoarthritis, but there is no evidence for other chronic painful conditions. Formulation can influence efficacy. The incidence of local adverse events is increased with topical NSAIDs, but gastrointestinal adverse events are reduced compared with oral NSAIDs.

[27] Lin J, Zhang W, Jones A, Doherty M. Efficacy of topical non-steroidal anti-inflammatory drugs in the treatment of osteoarthritis: meta-analysis of randomised controlled trials. BMJ. 2004 Aug 7;329(7461):324. (Towheed TE. **Pennsaid** therapy for osteoarthritis of the knee: a systematic review and metaanalysis of randomized controlled trials. J Rheumatol. 2006 Mar;33(3):567-73.)

- **Oral Oxymorphone**
    i. (Opana, Opana ER): **Potency** is about 10x more potent than morphine! Caution!. [Immediate release: 5, 10mg tabs; Extended release; 5, 10, 20, 40 mg tabs]

Additional References & Links:

- **Canadian Guidelines for Safe and Effective Use of Opioids**: http://nationalpaincentre.mcmaster.ca/index.html
- **Responsible Physician Opioid Prescribing Resources (USA) Links:** http://www.responsibleopioidprescribing.org
- Health Canada – Company – Dosage Conversion Guidelines for Fentanyl; Revised Mar 2010: http://www.hc-sc.gc.ca/dhp-mps/alt_formats/pdf/medeff/advisories-avis/prof/2010/fentanyl_2_hpc-cps-eng.pdf
- **Opioid Manager Tool**: Point of care tool summarizing Canadian Guidelines:
    - **From CEP**: http://www.effectivepractice.org/index.cfm?pagePath=CEP_TOOLS/Opioid_Manager&id=23515
    - **From NPC:** http://nationalpaincentre.mcmaster.ca/opioidmanager/
- Tramadol warning (FDA): http://www.fda.gov/Safety/MedWatch/SafetyInformation/SafetyAlertsforHumanMedicalProducts/ucm213264.htm
- **AFP article Aug 2012 - on Rational Use of Opioids for Management of Chronic Nonterminal Pain** http://www.aafp.org/afp/2012/0801/p252.html

Treatment Agreements:

Medscape discussion on use in primary care. http://www.medscape.com/viewarticle/711659?src=mp&spon=30&uac=93517FV
Canadian Guideline sample at http://nationalpaincentre.mcmaster.ca/opioid/cgop_b_app_b05.html
RxFiles 1 page version at http://www.rxfiles.ca/rxfiles/uploads/documents/Pain-CNMP-Opioid-TreatmentAGREEMENT.pdf ; Customizable MS-Word versionhttp://www.rxfiles.ca/rxfiles/uploads/documents/Pain-CNMP-Opioid-TreatmentAGREEMENT.doc
RxFiles 2 page version at: ♦**customizable MS Word**: http://www.rxfiles.ca/rxfiles/uploads/documents/Opiod-Informed-Consent-And-Agreement.docx ♦**pdf**: http://www.rxfiles.ca/rxfiles/uploads/documents/Opiod-Informed-Consent-And-Agreement.pdf

[1] Ballantyne JC, Mao J. Opioid Therapy for Chronic Pain. N Engl J Med. 2003 Nov 13;349(20):1943-1953.
[2] Micromedex 2018
[3] Hansten, PD and Horn JR. Drug Interactions Analysis and Management. Applied Therapeutics Incorporated. Vancouver, WA. 2008.
[4] Drugs in Pregnancy & Lactation 9th edition, 2011.
[5] Morrison, R. Sean, Meier, Diane E., Palliative Care. N Engl J Med 2004 350: 2582-2590.
[6] Gilron I, Bailey JM, Tu D, et al. Morphine, gabapentin, or their combination for neuropathic pain. N Engl J Med. 2005 Mar 31;352(13):1324-34. (InfoPOEMs: The combination of gabapentin & morphine provides a small but clinically unimportant benefit over either drug alone. Tricyclic antidepressants have been shown in other studies to be as effective as gabapentin & much less expensive, but were not studied in this trial. (LOE = 1b))
[7] Health Canada Aug 2005 http://www.hc-sc.gc.ca/ahc-asc/media/advisories-avis/2005/2005_84_e.html (Long-Acting Opioids and a New Type of **Alcohol Warning**. Pharmacit's Letter. Dec 2005).
[8] Other Opioid Conversion (e.g. tramadol): http://databaseinnovationsdraft.com/OpioidConversionChart2007.pdf

Additional references:

AAP Committee on Substance Use and Prevention. **Medication-Assisted Treatment of Adolescents with Opioid Use Disorders**. Pediatrics.2016:138(3):e20161893
Abdel Shaheed C, et al. Efficacy, Tolerability, and Dose-Dependent Effects of **Opioid Analgesics for Low Back Pain**: A Systematic Review and Meta-analysis. JAMA Intern Med. 2016 May 23.
Abou-Karam M, Dubé S, Kvann HS, et al. **Parental Report of Morphine Use at Home after Pediatric Surgery**. J Pediatr. 2015 Jul 20. pii: S0022-3476(15)00673-3.
Abouk R et al. Association between **state laws facilitating pharmacy distribution of naloxone and risk of fatal overdose**. JAMA Intern Med 2019 May 6.
ACOG: Committee Opinion No. 711: **Opioid Use and Opioid Use Disorder in Pregnancy**. Obstet Gynecol. 2017 Aug;130(2):e81-e94.
Ackerman AL, O'Connor PG, Doyle DL, et al. Association of an **Opioid Standard of Practice Intervention** With **Intravenous Opioid Exposure** in Hospitalized Patients. JAMA Intern Med. 2018 May 14.
Acurcio FA, Moura CS, Bernatsky S, et al. Opiod use and risk of non-vertebral fractures in adults with rheumatoid arthritis: A nested case-control study using administrative databases. Arthritis Rheumatol. 2015 Sep 11.
Adams JM. Increasing **Naloxone Awareness and Use:** The Role of Health Care Practitioners. JAMA. 2018 Apr 5.
Admon LK, Bart G, Kozhimannil KB, et al. **Amphetamine- and Opioid-Affected Births**: Incidence, Outcomes, and Costs, United States, 2004-2015. Am J Public Health. 2018 Nov 29:e1-e7.
Agthe AG, Kim GR, Mathias KB, et al. **Clonidine** as an adjunct therapy to opioids for neonatal abstinence syndrome: a randomized, controlled trial. Pediatrics. 2009 May;123(5): e849-56. Epub 2009 Apr 27.
Agito M, Rizk M. Recurrent abdominal pain and vomiting (**narcotic bowel syndrome**). Cleve Clin J Med. 2013 Jul;80(7):436-40.
Aiyer R, Gulati A, Gungor S, et al. **Treatment of Chronic Pain With Various Buprenorphine** Formulations: A Systematic Review of Clinical Studies. Anesth Analg. 2018 Aug;127(2):529-538.
Akiyama MJ, Norton BL, et al. Intensive Models of **Hepatitis C Care for People Who Inject Drugs Receiving Opioid Agonist Therapy**: A Randomized Controlled Trial. Ann Intern Med. 2019 Apr 9.
Alambyan V, Pace J, Miller B, et al. The **Emerging Role of Inhaled Heroin** in the Opioid Epidemic: A Review. JAMA Neurol. 2018 Jul 9.
Al-Huniti N, Chapel S, Xu H, et al. Population pharmacokinetics of **naloxegol** in a population of 1,247 healthy subjects and patients. Br J Clin Pharmacol. 2015 Aug 28.
Allen JD et al. **Prescription opioid exposures among children and adolescents** in the **United States**: 2000–2015. Pediatrics 2017 Mar 20.
Allen B, Nolan ML, Kunins HV, Paone D. **Racial differences in opioid overdose deaths** in New York City, 2017 [online Feb 11, 2019]. JAMA Intern Med.
Alford DP, Livingston EH. JAMA patient page. **Misuse of opioid medication**. JAMA. 2013 May 15;309(19):2055.

Alford DP. **Opioid Prescribing for Chronic Pain**--Achieving the Right Balance through Education. N Engl J Med. 2016 Jan 28;374(4):301-3.

Alford DP, et al. How Would You **Manage Opioid Use in These Three Patients**?: Grand Rounds Discussion From Beth Israel Deaconess Medical Center. Ann Intern Med. 2017 Apr 4;166(7):506-513

Amato L, Minozzi S, Davoli M, Vecchi S, Ferri MM, Mayet S. Psychosocial and pharmacological treatments versus pharmacological treatments for opioid detoxification. Cochrane Database Syst Rev. 2008 Oct 8;(4):CD005031. Psychosocial treatments offered in addition to pharmacological detoxification treatments are effective in terms of completion of treatment, use of opiate, results at follow-up and compliance. Although a treatment, like detoxification, that exclusively attenuates the severity of opiate withdrawal symptoms can be at best partially effective for a chronic relapsing disorder like opiate dependence, this type of treatment is an essential step prior to longer-term drug-free treatment and it is desirable to develop adjunct psychosocial approaches that might make detoxification more effective.

Amato L, Minozzi S, Davoli M, et al. **Psychosocial and pharmacological treatments** versus pharmacological treatments for **opioid detoxification**. Cochrane Database Syst Rev. 2011 Sep 7;9:CD005031. Psychosocial treatments offered in addition to pharmacological detoxification treatments are effective in terms of completion of treatment, use of opiate, participants abstinent at follow-up and clinical attendance.

Analgesic options for patients with **allergic-type opioid** reactions. Pharmacist's Letter/Prescriber's Letter 2006;22(2):220201.

Anand, Kanwaljeet J.S., Willson, Douglas F., Berger, John, et al., for the Eunice Kennedy Shriver National Institute of Child Health and Human Development Collaborative Pediatric Critical Care Research Network, **Tolerance and Withdrawal From Prolonged Opioid** Use in Critically Ill **Children**. Pediatrics 2010 0: peds.2009-0489.

Ansermot Nicolas; Albayrak Ozgur; Schlapfer Jurg; et al. Substitution of **(R,S)-Methadone by (R)-Methadone**: Impact on QTc Interval. Arch Intern Med. 2010;170(6):529-536.

APS-Opioid Treatment Guidelines Clinical Guidelines for the Use of **Chronic Opioid Therapy in Chronic Noncancer Pain** Feb/09 http://download.journals.elsevierhealth.com/pdfs/journals/1526-5900/PIIS1526590008008316.pdf

(Chou R, Fanciullo GJ, Fine PG, et al. **American Pain Society**-American Academy of Pain Medicine Opioids Guidelines Panel. Clinical guidelines for the use of chronic opioid therapy in chronic noncancer pain. J Pain. **2009** Feb;10(2):113-30.)

Armenian P, Olson A, Anaya A, Kurtz Aet al. Fentanyl and a Novel **Synthetic Opioid U-47700** Masquerading as Street "Norco" in Central California: A Case Report. Ann Emerg Med. 2016 Jul 20.

Asadi P, Monsef Kasmaei V, Ziabari SZ, et al. Prevalence of **Tramadol Consumption in First Seizure Patients**; a One-Year Cross-sectional Study. Emerg (Tehran). 2015 Fall;3(4):159-61.

Auger N, Low N, Carrier FM, et al. **Maternal prepregnancy surgery and risk of neonatal abstinence syndrome** in future newborns: a longitudinal cohort study. CMAJ. 2019 Jul 15;191(28):E779-E786.

Australian Prescriber: Caution with **Codeine**: http://www.australianprescriber.com/magazine/34/5/133/5. { Codeine is a weak opioid analgesic. It has to be converted to morphine, but there is significant inter-individual variation in its pharmacokinetics which results in variable effectiveness. Codeine's efficacy in clinical trials is generally modest and while its adverse events are usually mild, serious adverse events, including death, have occurred. Tolerance and drug dependence can occur. There is a risk of toxicity especially if combination products containing codeine and other drugs are misused. Treatment with simple analgesics, or other opioids if required, provides a more predictable response.}

Avouac J, Gossec L, Dougados M. Efficacy and safety of **opioids for osteoarthritis**: a meta-analysis of randomized controlled trials. Osteoarthritis Cartilage 2007; 15: 957–65.

Azam MA, Weinrib AZ, Montbriand J, et al. **Acceptance and Commitment Therapy to Manage Pain and Opioid Use After Major Surgery**: Preliminary Outcomes from the Toronto General Hospital Transitional Pain Service. Canadian Journal of Pain. 2017;1(1):37-49

Azuine RE, Ji Y, Chang HY, et al. **Prenatal Risk Factors and Perinatal and Postnatal Outcomes** Associated With Maternal Opioid Exposure in an Urban, Low-Income, Multiethnic US Population. JAMA Netw Open. 2019 Jun 5;2(6):e196405.

Babb, Malaika, Koren, Gideon, Einarson, Adrienne. Treating **pain during pregnancy**. Can Fam Physician 2010 56: 25-27.

Babu KM, Brent J, Juurlink DN. **Prevention of Opioid Overdose**. N Engl J Med. 2019 Jun 6;380(23):2246-2255.

Bada HS, Sithisarn T, Gibson J, et al. **Morphine Versus Clonidine for Neonatal Abstinence Syndrome**. Pediatrics. 2015 Jan 26.

Baggett TP, Hwang SW, O'Connell JJ, et al. **Mortality Among Homeless** Adults in Boston: Shifts in Causes of Death Over a 15-Year Period. JAMA Intern Med. 2013 Jan 14:1-7.

Bagley SM, Forman LS, Ruiz S, et al. Expanding access to **naloxone for family members**: The Massachusetts experience. Drug Alcohol Rev. 2017 Apr 20.

Bai JW, Bao J, Bhatia A, Chan VWS. A **perioperative approach to the opioid crisis**. CMAJ. 2018 Oct 1;190(39):E1151-E1152.

Bailey AM, Wermeling DP. **Naloxone for opioid overdose prevention**: pharmacists' role in community-based practice settings. Ann Pharmacother. 2014 May;48(5):601-6.

Baillargeon J, Raji MA, Urban RJ, et al. Opioid-Induced **Hypogonadism** in the United States. Mayo Clin Proc Innov Qual Outcomes. 2019 Aug 23;3(3):276-284.

Baker JA, Avorn J, Levin R, Bateman BT. Opioid prescribing **after surgical extraction of teeth** in Medicaid patients, 2000-2010.JAMA. doi:10.1001 /jama.2015.19058.

Banerjee G, Edelman EJ, Barry DT, et al. **Non-medical use of prescription opioids** is associated with **heroin initiation** among US veterans: a prospective cohort study. Addiction. 2016 Aug 23.

Bao Y et al. **Prescription drug monitoring programs** are associated with sustained reductions in opioid prescribing by physicians. Health Aff (Millwood) 2016 Jun 1; 35:1045.

Barash JA, Ganetsky M, Boyle KL, et al. **Acute Amnestic Syndrome Associated with Fentanyl Overdose**. N Engl J Med. 2018 Mar 22;378(12):1157-1158.

Barnett ML et al. **Opioid-prescribing patterns of emergency physicians** and risk of long-term use. N Engl J Med 2017 Feb 16; 376:663.

Barnett ML, Olenski AR, Jena AB. **Opioid-Prescribing Patterns of Emergency Physicians** and Risk of Long-Term Use. N Engl J Med. 2017 Feb 16;376(7):663-673.

Barnett ML, Gray J, Zink A, et al. **Coupling Policymaking with Evaluation - The Case of the Opioid Crisis**. N Engl J Med. 2017 Dec 14;377(24):2306-2309.

Barnett ML, Hicks TR, Jena AB. **Prescription Patterns of Family Members** After Discontinued Opioid or Benzodiazepine Therapy of Users. JAMA Intern Med. 2019 Jul 1.

Bateman BT et al. Patterns of **opioid prescription** and use after **cesarean** delivery. Obstet Gynecol 2017Jul; 130:29.

Bateman BT, Hernandez-Diaz S, et al. Patterns of **Opioid Utilization in Pregnancy** in a Large Cohort of Commercial Insurance Beneficiaries in the United States. Anesthesiology. 2014 Feb 12.

Bateman BT, Choudhry NK. **Limiting the Duration of Opioid Prescriptions**: Balancing Excessive Prescribing and the Effective Treatment of Pain. JAMA Intern Med. 2016 May 1

Bateman BT, Cole NM, Maeda A, et al. **Patterns of Opioid Prescription and Use After Cesarean Delivery**. Obstet Gynecol. 2017 Jun 6.

Baumblatt JA, Wiedeman C, Dunn JR, et al. High-Risk Use by Patients Prescribed Opioids for Pain and Its **Role in Overdose Deaths**. JAMA Intern Med. 2014 Mar 3.

Bawor M, Bami H, Dennis BB, et al. **Testosterone suppression** in opioid users: a systematic review and meta-analysis. Drug Alcohol Depend. 2015 Apr 1;149:1-9

Becker WC, Fiellin DA. **Abuse-Deterrent Opioid Formulations** - Putting the Potential Benefits into Perspective. N Engl J Med. 2017 Jun 1;376(22):2103-2105.

Becker WC, Fiellin DA. Limited evidence, faulty reasoning, and potential for a **global opioid crisis**. BMJ. 2017 Jul 5;358:j3115.

Becker WC, Merlin JS, Manhapra A, et al. Management of patients with issues related to opioid safety, efficacy and/or misuse: a case series from an integrated, interdisciplinary clinic. Addict Sci Clin Pract. 2016 Jan 28;11(1):3

Bedene A, Lijfering WM, Niesters M, et al. Opioid **Prescription Patterns and Risk Factors** Associated With Opioid Use in the Netherlands. JAMA Netw Open. 2019 Aug 2;2(8):e1910223.
Beetham T, Saloner B, Wakeman SE, et al. **Access to office-based buprenorphine treatment** in areas with high rates of opioid-related mortality. An audit study. Ann Intern Med. 2019. [Epub ahead of print]. doi:10.7326/M18-3457
Berterame S, Erthal J, Thomas J, et al. **Use of and barriers to access to opioid analgesics**: a worldwide, regional, and national study. Lancet 2016; online Feb 3.
Bertin C, Delorme J, Riquelme M, et al. Risk assessment of **using off-label morphine sulfate** in a population-based retrospective cohort of opioid-dependent patients. Br J Clin Pharmacol. 2019 Aug 6.
Bicket MC, Long JJ, Pronovost PJ, et al. Prescription Opioid Analgesics Commonly **Unused After Surgery**: A Systematic Review. JAMA Surg. 2017 Aug 2.
Binswanger IA. **Opioid Use Disorder and Incarceration** - Hope for Ensuring the Continuity of Treatment. N Engl J Med. 2019 Feb 27.
Binswanger IA, Blatchford PJ, Mueller SR, et al. **Mortality after prison release: opioid overdose** and other causes of death, risk factors, and time trends from 1999 to 2009. Ann Intern Med. 2013 Nov 5;159(9):592-600.
Blanch B, Pearson S, Haber PS. An overview of the patterns of prescription **opioid use, costs and related harms** in Australia. Br J Clin Pharmacol. 2014 Jun 24.
Blanco C, Wall MM, Okuda M, et al. **Pain as a Predictor of Opioid Use Disorder** in a Nationally Representative Sample. Am J Psychiatry. 2016 Jul 22
Blendon RJ, Benson JM. The **Public and the Opioid-Abuse Epidemic**. N Engl J Med. 2018 Jan 3.
Bohnert Amy S. B., Valenstein Marcia, Bair Matthew J., et al. Association Between **Opioid Prescribing Patterns and Opioid Overdose-Related Deaths**. JAMA. 2011;305(13): 1315-1321.doi:10.1001/jama.2011.370. (Opioid overdose is now the second most common cause of unintentional death in the US, after motor vehicle crashes, write two observers)
Boland JW, Boland EG. Pharmacological therapies for **opioid induced constipation** in adults with cancer. BMJ. 2017 Aug 2;358:j3313
Bohnert ASB, Guy GP Jr, Losby JL. **Opioid Prescribing** in the United States Before and After the Centers for Disease Control and Prevention's **2016 Opioid Guideline**. Ann Intern Med. 2018 Sep 18;169(6):367-375.
Bohnert ASB, Ilgen MA. Understanding **Links among Opioid Use, Overdose, and Suicide**. N Engl J Med. 2019 Jan 3;380(1):71-79.
Bonnie RJ, Kesselheim AS, Clark DJ. Both Urgency and Balance Needed in Addressing Opioid Epidemic: A Report From the National Academies of Sciences, Engineering, and Medicine. JAMA. 2017 Aug 1;318(5):423-424.
Borenstein-Levin L, Synnes A, Grunau RE, et al. **Narcotics and Sedative Use in Preterm Neonates**. J Pediatr. 2016 Sep 7
Borys D, Stanton M, Gummin D, Drott T. **Tapentadol** Toxicity in Children. Pediatrics. 2015 Jan 19.
Bosilkovska M, Walder B, Besson M, Daali Y, Desmeules J. **Analgesics in patients with hepatic impairment**: pharmacology and clinical implications. Drugs. 2012 Aug 20;72(12):1645-69.
Bounthavong M, Harvey MA, Wells DL, et al. Trends in **naloxone prescriptions** prescribed after implementation of a **National Academic Detailing Service** in the Veterans Health Administration: A preliminary analysis. J Am Pharm Assoc (2003). 2017 Jan 11.
Bourne C, Gouraud A, et al; French Association of Regional Pharmacovigilance Centres. **Tramadol and hypoglycaemia**: comparison with other step 2 analgesic drugs. Br J Clin Pharmacol. 012 Sep 4.
Bowers KJ, McAllister KB, Ray M, et al. **Ketamine** as an Adjunct to **Opioids** for **Acute Pain** in the Emergency Department: A Randomized Controlled Trial. Acad Emerg Med. 2017 Jun;24(6):676-685.
Boyer EW. Management of **opioid analgesic overdose**. N Engl J Med. 2012 Jul 12;367(2):146-55.
Braden Jennifer Brennan; Russo Joan; Fan Ming-Yu; et al. **Emergency Department Visits** Among Recipients of Chronic Opioid Therapy. Arch Intern Med. 2010;170(16):1425-1432.
Brands Bruna, Paglia-Boak Angela, Sproule Beth A., et al. **Nonmedical use of opioid** analgesics among Ontario students. Can Fam Physician 2010 56: 256 -262.
Brat GA, Agniel D, Beam A, et al. **Postsurgical prescriptions for opioid naive patients** and association with overdose and misuse: retrospective cohort study. BMJ. 2018 Jan 17;360:j5790.
Brenner DM, Hu Y, Datto C, et al. A Randomized, Multicenter, Prospective, Crossover, Open-Label Study of Factors Associated With Patient Preferences for **Naloxegol or PEG 3350 for Opioid-Induced Constipation**. Am J Gastroenterol. 2019 May 3.
Brent DA, Hur K, Gibbons RD. Association Between **Parental Medical Claims for Opioid Prescriptions and Risk of Suicide Attempt by Their Children**. JAMA Psychiatry. 2019 May 22.
Brogly SB, Saia KA, Walley AY, et al. **Prenatal Buprenorphine Versus Methadone** Exposure and Neonatal Outcomes: Systematic Review and Meta-Analysis. Am J Epidemiol. 2014 Aug 22.
Brooks MJ. **Mitigating the safety risks** of drugs with a focus on opioids: are risk evaluation and mitigation strategies the answer? Mayo Clin Proc. 2014 Dec;89(12):1673-84.
Broussard CS, Rasmussen SA, Reefhuis J, et al. **Maternal treatment with opioid** analgesics and risk for **birth defects**. Am J Obstet Gynecol 2011;204:x.ex-x.ex. PII: S0002-9378(10)02524-X doi:10.1016/j.ajog.2010.12.039.
Brown JD, Doshi PA, et al. Rates of **Neonatal Abstinence Syndrome** Amid Efforts to Combat the Opioid Abuse Epidemic. JAMA Pediatr. 2016 Sep 26.
Brummett CM, Waljee JF, Goesling J, et al. New Persistent **Opioid Use After Minor and Major Surgical Procedures** in US Adults. JAMA Surg. 2017 Apr 12:e170504.
Bruneau J, , et al; CIHR Canadian Research Initiative in Substance Misuse. **Management of opioid use disorders: a national clinical practice guideline**. CMAJ. 2018 Mar 5;190(9):E247-E257.
Buchanich JM, Balmert LC, Williams KE, et al. The Effect of **Incomplete Death Certificates on Estimates of Unintentional Opioid-Related Overdose** Deaths in the United States, 1999-2015. Public Health Rep. 2018 Jan 1:33354918774330.
Busse JW, Juurlink D, Guyatt GH. Addressing the **limitations of the CDC guideline for prescribing opioids** for chronic noncancer pain. CMAJ. 2016 Dec 6;188(17-18):1210-1211.
Busse JW, Craigie S, Juurlink DN, et al. **Guideline for opioid therapy and chronic noncancer pain**. CMAJ 2017;189:E659-66. (**Canadian**)
Busse JW, Wang L, Kamaleldin M, et al. Opioids for **chronic noncancer pain:** a systematic review and meta-analysis. JAMA. doi:10.1001/jama.2018.18472
Buxton JA, Gauthier T, Kinshella MW, et al. A 52-year-old man with **fentanyl-induced muscle rigidity**. CMAJ. 2018 Apr 30;190(17):E539-E541.
Byford S, Barrett B, Metrebian N, et al. Cost-effectiveness of **injectable opioid treatment v. oral methadone** for chronic heroin addiction. Br J Psychiatry. 2013 Nov;203(5):341-9.
Calcaterra SL, Drabkin AD, Leslie SE, et al. The **hospitalist perspective on opioid prescribing**: A qualitative analysis. J Hosp Med. 2016 Aug;11(8):536-42.
Califf RM, Woodcock J, Ostroff S. A **Proactive Response to Prescription Opioid Abuse**. N Engl J Med. 2016 Feb 4.

Cantrill SV, Brown MD, Carlisle RJ, et al. Clinical policy: critical issues in the prescribing of opioids for adult patients in the **emergency department.** Ann Emerg Med 2012 Oct;60(4):499-525.
Cao S, Karmouta R, Li DG, et al. **Opioid Prescribing Patterns and Complications in the Dermatology** Medicare Population. JAMA Dermatol. 2018 Feb 7.
Carey CM, Jena AB, Barnett ML. **Patterns of potential opioid misuse** and subsequent adverse outcomes in Medicare, 2008 to 2012. Ann Intern Med. 2018. [Epub ahead of print]. doi:10.7326/M17-3065
Carico R, Zhao X, Thorpe CT, et al. Receipt of **Overlapping Opioid and Benzodiazepine Prescriptions Among Veterans** Dually Enrolled in Medicare Part D and the Department of Veterans Affairs: A Cross-sectional Study. Ann Intern Med. 2018 Oct 9.
Carise D, Dugosh KL, McLellan AT, et al. Prescription **OxyContin Abuse** Among Patients Entering Addiction Treatment. Am J Psychiatry. 2007 Nov;164(11):1750-6.
Carpenter PS, Shepherd HM, McCrary H, et al. Association of **Celecoxib Use With Decreased Opioid Requirements** After Head and Neck Cancer Surgery With Free Tissue Reconstruction. JAMA Otolaryngol Head Neck Surg. 2018 Apr 18.
Carroll JJ, Marshall BDL, Rich JD, et al. Exposure to **fentanyl-contaminated heroin and overdose risk** among illicit opioid users in Rhode Island: A mixed methods study. Int J Drug Policy. 2017 Jun 1.
CDC June/10 About one fifth of US high school students reported ever having used prescription drugs not prescribed to them, such as OxyContin, Percocet, Vicodin, Adderall, Ritalin, and Xanax. The CDC reports the first assessment of such use within the National Youth Risk Behavior Survey. In addition, prescription drug abuse was more common among white than Hispanic or black students. The agency highlighted these findings from the 2009 survey in the context of an ongoing national trend toward higher rates of nonsuicide-related overdoses and deaths associated with prescription drug abuse. 2009 National Youth Risk Behavior Survey (Free PDF)CDC news release (Free)
2007 *MMWR* article on unintentional poisoning deaths (Free)
CDC: Centers for Disease Control and Prevention (CDC). Emergency department visits involving nonmedical use of selected prescription drugs - United States, 2004-2008. MMWR Morb Mortal Wkly Rep. 2010 Jun 18;59(23):705-9. This report describes the results of that review, which showed that the estimated number of ED visits for nonmedical use of opioid analgesics increased 111% during 2004-2008 (from 144,600 to 305,900 visits) and increased 29% during 2007-2008. The highest numbers of ED visits were recorded for oxycodone, hydrocodone, and methadone, all of which showed statistically significant increases during the 5-year period. The estimated number of ED visits involving nonmedical use of benzodiazepines increased 89% during 2004-2008 (from 143,500 to 271,700 visits) and 24% during 2007-2008.
CDC Grand Rounds: **Prescription Drug Overdoses** — a U.S. Epidemic.Weekly. January 13, 2012 / 61(01);10-13.This is another in a series of occasional MMWR reports titled CDC Grand Rounds. These reports are based on grand rounds presentations at CDC on high-profile issues in public health science, practice, and policy. *http://www.cdc.gov/about/grand-rounds*.
CDC Vital Signs: **Risk for Overdose from Methadone** Used for Pain Relief — United States, 1999–2010. Early Release. July 3, 2012 / 61(Early Release);1-5. http://www.cdc.gov/mmwr/preview/mmwrhtml/mm61e0703a1.htm?s_cid=mm61e0703a1_x
CDC: Centers for Disease Control and Prevention. Emergency department visits and hospitalizations for **buprenorphine ingestion by children**--United States, 2010-2011. MMWR Morb Mortal Wkly Rep. 2013 Jan 25;62(3):56.
CDC: Dowell D, Haegerich TM, Chou R. **CDC guideline** for **prescribing opioids for chronic pain—United States, 2016**. MMWR Recomm Rep. 2016;65(RR-1): 1-49.
Chan F, Koren G. Is **periconceptional opioid use safe**? Can Fam Physician. 2015 May;61(5):431-3.
Chang AK, Bijur PE, Lupow JB, et al. Randomized clinical trial of efficacy and safety of a **single 2-mg intravenous dose of hydromorphone** versus usual care in the management of acute pain. Acad Emerg Med. 2013 Feb;20(2):185-92.
Chang AK, Bijur PE, Holden L, et al. Comparative Analgesic Efficacy of **Oxycodone/Acetaminophen Versus Hydrocodone/Acetaminophen** for Short-term Pain Management in Adults Following ED Discharge. Acad Emerg Med. 2015 Nov;22(11):1254-60.
Chang HY, et al. Impact of **prescription drug monitoring programs and pill mill laws** on high-risk opioid prescribers: Comparative interrupted time series analysis. Drug Alcohol Depend. 2016 May 26..
Chang A, et al. Effect of a **single dose of oral opioid and nonopiod analgesics on acute extremity pain** in the emergency department: a randomized clinical trial. JAMA 2017;(Nov).
Chang HY, Murimi IB, Jones CM, et al. Relationship between **high-risk patients receiving prescription opioids and high-volume opioid prescribers**. Addiction. 2017 Nov 29.
Chapman E, Leipsic J, Satkunam N, Churg A. **Pulmonary alveolar proteinosis** as a reaction to **fentanyl patch smoke**. Chest. 2012 May;141(5):1321-3.
Chaudhary MA, Bhulani N, de Jager EC, et al. Development and Validation of a Bedside Risk Assessment for Sustained Prescription Opioid Use After Surgery. JAMA Netw Open.2019 Jul 3;2(7):e196673
Chaudhary MA, Schoenfeld AJ, et al. Incidence and predictors of **opioid prescription at discharge after traumatic injury** [published online June 21, 2017].JAMA Surg. doi:10.1001/jamasurg .2017.1685
Chen EY, Marcantonio A, Tornetta P III. **Correlation between 24-hour predischarge opioid use and amount of opioids prescribed at hospital discharge** [online Dec 13, 2017]. JAMA Surg. doi:10.1001/jamasurg.2017.4859
Chen JH, Humphreys K, Shah NH, et al. **Distribution** of Opioids by Different **Types of Medicare Prescribers**. JAMA Intern Med. 2015 Dec 14:1-3.
Chen A, Blumenthal DM, Jena AB. Characteristics of **Physicians Excluded From US Medicare and State Public Insurance Programs for Fraud**, Health Crimes, or Unlawful Prescribing of Controlled Substances. JAMA Netw Open. 2018;1(8):e185805.
Chen Q, Larochelle MR, Weaver DT, et al. **Prevention of Prescription Opioid Misuse and Projected Overdose Deaths** in the United States. JAMA Netw Open. 2019 Feb 1;2(2):e187621.
Chen Y, Shiels MS, Thomas D, et al. **Premature Mortality From Drug Overdoses**: A Comparative Analysis of 13 Organisation for Economic Co-operation and Development Member Countries With High-Quality Death Certificate Data, 2001 to 2015. Ann Intern Med. 2018 Nov 13.
Chey WD, Webster L, Sostek M, et al. **Naloxegol** for Opioid-Induced Constipation in Patients with Noncancer Pain. N Engl J Med. 2014 Jun 4.
Chidgey BA, McGinigle KL, McNaull PP. When a Vital Sign Leads a Country Astray-**The Opioid Epidemic**. JAMA Surg. 2019 Aug 14
Chihuri S, Li G. Trends in Prescription Opioids Detected in Fatally **Injured Drivers** in 6 US States: 1995-2015. Am J Public Health. 2017 Jul 20:e1-e6
Chihuri S, Li G. **Use of Prescription Opioids and Initiation of Fatal 2-Vehicle Crashes**. JAMA Netw Open. 2019 Feb 1;2(2):e188081.
Chiu AS, Jean RA, Hoag JR, Freedman-Weiss M, Healy JM, Pei KY. Association of **lowering default pill counts in electronic medical record systems with postoperative opioid prescribing** [online July 18, 2018]. JAMA Surg. doi:10.1001/jamasurg.2018.2083
Choo EK, Feldstein Ewing SW, Lovejoy TI. **Opioids Out, Cannabis In**: Negotiating the Unknowns in Patient Care for Chronic Pain. JAMA. 2016 Nov 1;316(17):1763-1764.
Chou R, et al. Management of suspected **opioid overdose with naloxone in out-of-hospital settings**. A systematic review. Ann Intern Med. [Epub ahead of print 28 Nov 2017] doi:10.7326/M17 -2224

Chou R, Ballantyne J, Lembke A. Rethinking Opioid **Dose Tapering, Prescription Opioid Dependence, and Indications for Buprenorphine**. Ann Intern Med. 2019 Aug 27.
Chou R, Cruciani RA, Fiellin DA, et al. American Pain Society, Heart Rhythm Society. **Methadone safety**: a clinical practice guideline from the American Pain Society and College on Problems of Drug Dependence, in collaboration with the Heart Rhythm Society. J Pain. 2014 Apr;15(4):321-37.
Chou R, Deyo R, Devine B, et al. The **Effectiveness and Risks of Long-Term Opioid Treatment of Chronic Pain**. Evidence Report/Technology Assessment No. 218. AHRQ Comparative Effectiveness Review. Rockville (MD): Agency for Healthcare Research and Quality (US); 2014 Sep. Report No.: 14-E005-EF. Evidence on long-term opioid therapy for chronic pain is very limited but suggests an increased risk of serious harms that appears to be dose-dependent. More research is needed to understand long-term benefits, risk of abuse and related outcomes, and effectiveness of different opioid prescribing methods and risk mitigation strategies.
Chua KP, Harbaugh CM, Brummett CM, et al. Association of Perioperative Opioid Prescriptions With **Risk of Complications After Tonsillectomy** in Children. JAMA Otolaryngol Head Neck Surg. 2019 Aug 8.
Chua K-P, Shrime MG, Conti RM. Effect of **FDA Investigation on Opioid Prescribing to Children After Tonsillectomy/Adenoidectomy**. Pediatrics. 2017;140(6):e20171765
Chung CP, Callahan ST, Cooper WO, et al. Outpatient **Opioid Prescriptions for Children** and **Opioid-Related Adverse Events**. Pediatrics. 2018 Jul 16.
Cicero TJ, Ellis MS, Surratt HL. Effect of **abuse-deterrent formulation of OxyContin**. N Engl J Med. 2012 Jul 12;367(2):187-9.
Cicero TJ, Ellis MS, Harney J. Shifting Patterns of **Prescription Opioid and Heroin Abuse in the United States**. N Engl J Med. 2015 Oct 29;373(18):1789-90.
Ciszkowski C, Madadi P, Phillips MS, Lauwers AE, Koren G. **Codeine, ultrarapid-metabolism** genotype, and postoperative death. N Engl J Med. 2009 Aug 20;361(8):827-8.
Clarke DL, Drobatz KJ, Korzekwa C, et al. Trends in Opioid Prescribing and **Dispensing by Veterinarians** in Pennsylvania. JAMA Netw Open. 2019;2(1):e186950.
Clarke H, Soneji N, Ko DT, et al. Rates and risk factors for **prolonged opioid use after major surgery**: population based cohort study. BMJ. 2014 Feb 11;348:g1251.
Clary PL, Lawson P. Pharmacologic Pearls for **End-of-Life Care**. Am Fam Physician. 2009 Jun 15;79(12):1059-65.
Cleary BJ, Donnelly JM, Strawbridge JD, et al. **Methadone and perinatal outcomes**: a retrospective cohort study. Am J Obstet Gynecol. 2010 Dec 7.
Cleary J, Simha N, Panieri A, et al. Formulary availability and regulatory barriers to accessibility of **opioids for cancer pain in India**: a report from the Global Opioid Policy Initiative (GOPI). Ann Oncol. 2013 Dec.
Clegg A, Young JB. Which medications to avoid in people at risk of delirium: a systematic review. Age Ageing. 2011 Jan;40(1):23-9.
Clemency BM, Eggleston W, Shaw EW, et al. Hospital Observation Upon Reversal (**HOUR) With Naloxone**: A Prospective Clinical Prediction Rule Validation Study. Acad Emerg Med. 2019 Jan;26(1): 7-15.
Cohen JP, Mendoza M, Roland C. Challenges Involved in the **Development and Delivery of Abuse-deterrent Formulations of Opioid Analgesics**. Clin Ther. 2018 Feb 2.
Colvin LA, Bull F, Hales TG. **Perioperative opioid analgesia**-when is enough too much? A review of opioid-induced tolerance and hyperalgesia. Lancet. 2019 Apr 13;393(10180):1558-1568.
Comer SD, Dworkin RH, Strain EC. **Medical Devices to Prevent Opioid Use Disorder**: Innovative Approaches to Addressing the Opioid Crisis. JAMA Psychiatry. 2019 Feb 20.
Compton WM, Jones CM, Baldwin GT. **Relationship between Nonmedical Prescription-Opioid Use and Heroin Use**. N Engl J Med. 2016 Jan 14;374(2):154-63.
Conradt E, Flannery T, Aschner JL, et al. **Prenatal Opioid Exposure**: Neurodevelopmental Consequences and Future Research Priorities. Pediatrics. 2019 Aug 28.
Corli O, Floriani I, et al. **Are strong opioids equally effective and safe** in the treatment of chronic cancer pain? A multicenter randomized phase IV 'real life' trial on the variability of response to opioids. Ann Oncol. 2016 Mar 2
Cornish R, Macleod J, Strang J, et al. Risk of death during and after **opiate substitution treatment** in primary care: prospective observational study in UK General Practice Research Database. BMJ. 2010 Oct 26;341:c5475. doi: 10.1136/bmj.c5475.
Cottler LB, Hu H, et al. **Nonmedical Opioid Pain Relievers and All-Cause Mortality**: A 27-Year Follow-Up From the Epidemiologic Catchment Area Study. Am J Public Health. 2016 Mar;106(3):509-16.
Crabtree A, Rose C, Chong M, Smolina K. **Effects of the new prescribing standards in British Columbia** on consumption of opioids and benzodiazepines and z drugs. Can Fam Physician. 2019 May;65(5):e231-e237.
Cragg A, Hau JP, Woo SA, et al. **Risk Factors for Misuse** of Prescribed Opioids: A Systematic Review and Meta-Analysis. Ann Emerg Med. 2019 Jun 19.
Cressman AM, Mazereeuw G, Guan Q, et al. **Availability of naloxone** in Canadian pharmacies:a population-based survey. CMAJ Open. 2017 Nov 8;5(4):E779-E784.
Crews KR, Gaedigk A, Dunnenberger HM, et al. Clinical Pharmacogenetics Implementation Consortium guidelines for cytochrome **P450 2D6 genotype and codeine** therapy: 2014 update. Clin Pharmacol Ther. 2014 Apr;95(4):376-82.
Crockett SD, Greer KB, Heidelbaugh JJ, et al; AGAICG Committee. American Gastroenterological Association (**AGA**) Institute Guideline on the **Medical Management of Opioid-Induced Constipation**. Gastroenterology. 2018 Oct 16.
Cupp M. **Analgesics in pregnancy and lactation**. Pharmacists Letter. February 2012.
Curfman GD, Beletsky L, Sarpatwari A. Benefits, Limitations, and Value of **Abuse-Deterrent Opioids**. JAMA Intern Med. 2017 Dec 11.
Curtis JR, Xie F, Smith C, et al. **Changing Trends in Opioid Use among U.S. Rheumatoid Arthritis Patients**. Arthritis Rheumatol. 2017 Jun 21.
Cushman PA, Liebschutz JM, Hodgkin JG, et al. **What do providers want to know about opioid prescribing**? A qualitative analysis of their questions. Subst Abus. 2017 Apr 10:1-8.
Czarnecki ML, Hainsworth KR, Simpson PM, et al. **Parent/Nurse-Controlled Analgesia Compared with Intravenous PRN Opioids** for Postsurgical Pain Management in Children with **Developmental Delay**: A Randomized Controlled Trial. Pain Med. 2017 Nov 1.
D'Onofrio G, et al. **Emergency Department-Initiated Buprenorphine** for Opioid Dependence with Continuation in Primary Care: Outcomes During and After Intervention. J Gen Intern Med. 2017 Feb 13.
D'Onofrio G, McCormack RP, Hawk K. **Emergency Departments** - A **24/7/365 Option for Combating the Opioid Crisis**. N Engl J Med. 2018 Dec 27;379(26):2487-2490.
da Costa BR, Nuesch E, Kasteler R, et al. **Oral or transdermal opioids for osteoarthritis** of the knee or hip. Cochrane Database Syst Rev. 2014 Sep 17;9:CD003115. The small mean benefit of non-tramadol opioids are contrasted by significant increases in the risk of adverse events. For the pain outcome in particular, observed effects were of questionable clinical relevance since the 95% CI did not include the minimal clinically important difference of 0.37 SMDs, which corresponds to 0.9 cm on a 10-cm VAS.

Daeninck P, Gagnon B, Gallagher R, et al. **Canadian recommendations** for the management of **breakthrough cancer pain**. Curr Oncol. 2016 Apr;23(2):96-108.
Dalal DS, Mbuyi N, Shah I, et al. Prescription Opioid **Use among Acute Gout Patients** Discharged from the Emergency Department. Arthritis Care Res (Hoboken). 2019 Jul 2.
Daoust R, Paquet J, Moore L, et al. **Recent opioid use and fall-related injury among older patients with trauma**. CMAJ. 2018 Apr 23;190(16):E500-E506.
Darpo B, Zhou M, Bai SA, et al. Differentiating the Effect of an **Opioid Agonist** on Cardiac Repolarization From μ-Receptor-Mediated, Indirect Effects on the **QT Interval**: A Randomized, 3-Way Crossover Study in Healthy Subjects. Clin Ther. 2015 Dec 31.
Dart RC, Surratt HL, Cicero TJ, et al. Trends in **Opioid Analgesic Abuse and Mortality** in the United States. N Engl J Med. 2015 Jan 15;372(3):241-248.
Daubresse M, Saloner B, Pollack HA, et al. **Non-buprenorphine opioid utilization** among patients using buprenorphine. Addiction. 2017 Jan 20.
Davis CS. The **SUPPORT for Patients and Communities Act** - What Will It Mean for the Opioid-Overdose Crisis? N Engl J Med. 2018 Nov 14.
Davis JM, Shenberger J, Terrin N, et al. Comparison of Safety and Efficacy of **Methadone vs Morphine for Treatment of Neonatal Abstinence Syndrome**: A Randomized Clinical Trial. JAMA Pediatr. 2018 Jun 18.
Delgado MK, Huang Y, Meisel Z, et al. National **Variation in Opioid Prescribing and Risk of Prolonged Use for Opioid-Naive Patients** Treated in the Emergency Department for Ankle Sprains. Ann Emerg Med. 2018 Jul 24.
Delgado MK, Shofer FS, Patel MS, et al. Association between **Electronic Medical Record Implementation** of Default Opioid Prescription Quantities and Prescribing Behavior in Two Emergency Departments. J Gen Intern Med. 2018 Jan 16.
Dewan KC, Dewan KS, Idrees JJ, et al. Trends and **Outcomes of Cardiovascular Surgery** in Patients With Opioid Use Disorders. JAMA Surg. 2018 Dec 5.
Deyo RA, et al. Association Between **Initial Opioid Prescribing Patterns** and Subsequent **Long-Term Use** Among Opioid-Naïve Patients: A Statewide Retrospective Cohort Study. J Gen Intern Med. 2016 Aug 2.
Desai RJ, Huybrechts KF, et al. Exposure to **prescription opioid analgesics in utero and risk of neonatal abstinence syndrome**: population based cohort study. BMJ. 2015 May 14;350
Desai RJ, Jin Y, Franklin PD, et al. Association of geography and access to healthcare providers with long term prescription opioid use in Medicare **patients with severe osteoarthritis**: A cohort study. Arthritis Rheumatol. 2019 Jan 28.
Desveaux L, Saragosa M, Kithulegoda N, et al. Understanding the behavioural determinants of opioid prescribing among family physicians: a qualitative study. BMC Fam Pract. 2019 May 10;20(1):59.
Deyo RA, Von Korff M, Duhrkoop D. **Opioids for low back pain**. BMJ. 2015 Jan 5;350:g6380.
Dhalla, Irfan A., Mamdani, et al. Prescribing of opioid analgesics and related **mortality** before and after the introduction of **long-acting oxycodone**. CMAJ 2009 181: 891-896
Dhalla, Irfan A., Mamdani, Muhammad M., Gomes, Tara, et al. Clustering of **opioid prescribing and opioid-related mortality** among family physicians in Ontario. Can Fam Physician 2011 57: e92-96.
Disher T, Gullickson C, Singh B, et al. Pharmacological treatments for **neonatal abstinence syndrome**: a systematic review and network meta-analysis [online Jan 22, 2019]. JAMA Pediatr. doi:10.1001/jamapediatrics.2018.5044
Doctor JN, Nguyen A, Lev R, et al. Opioid prescribing decreases after learning of a patient's fatal overdose. Science. 2018 Aug 10;361(6402):588-590.
Donohue JM, Kennedy J, Seymour CW, et al. Patterns of opioid administration among **opioid-naive inpatients and associations with postdischarge opioid use**. A cohort study. Ann Intern Med. 2019. doi:10.7326/M18-2864
Donroe JH, Holt SR, Tetrault JM. **Caring for patients with opioid use disorder** in the hospital. CMAJ. 2016 Dec 6;188(17-18):1232-1239. Review.
Donroe JH, Tetrault JM. **Narrowing the treatment gap in managing opioid use disorder**. CMAJ. 2018 Mar 5;190(9):E236-E237.
Dooley R, Dooley J, et al. **Narcotic tapering in pregnancy using long-acting morphine**: an 18-month prospective cohort study in northwestern Ontario. Can Fam Physician. 2015 Feb;61(2):e88-95.
Dooley J, Gerber-Finn L, Antone I, et al. **Buprenorphine-naloxone use in pregnancy for treatment of opioid dependence**: Retrospective cohort study of 30 patients. Canadian Family Physician. 2016;62(4):e194-e200.
Dormuth CR, Miller TA, Huang A, et al. Effect of a **centralized prescription network** on inappropriate prescriptions for opioid analgesics and benzodiazepines. CMAJ. 2012 Sep 4.
Doucette ML, Shields WC, Haring RS, et al. Storing and Disposing of Opioid Analgesics: What Does Our Medicine Tell Us? Ann Intern Med. 2018 Apr 17.
Dowell D, Kunins HV, Farley TA. Opioid Analgesics-**Risky Drugs, Not Risky Patients**. JAMA. 2013 May 9:1-2.
Dowell D, Haegerich TM, Chou R. **CDC guideline** for **prescribing opioids for chronic pain—United States, 2016**. MMWR Recomm Rep. 2016;65(RR-1): 1-49.
Dowell D, Haegerich TM, Chou R. **CDC guideline** for **prescribing opioids for chronic pain—United States, 2016**.JAMA. doi:10.1001/jama.2016.1464.
Dowell D, Noonan RK, Houry D. Underlying Factors in **Drug Overdose Deaths**. JAMA. 2017 Oct 11.
Drossman DA, Morris CB, et al. Diagnosis, characterization, and 3-month outcome after detoxification of 39 patients with **narcotic bowel syndrome**. Am J Gastroenterol. 2012 Sep;107(9):1426-40.
Dunn KM., Saunders KW., Rutter CM., et al. **Opioid Prescriptions for Chronic Pain and Overdose**: A Cohort Study. *Ann Intern Med* January 19, 2010 152:85-92.
Dunn KE, Tompkins DA, Bigelow GE, et al. Efficacy of **Tramadol Extended-Release for Opioid Withdrawal**: A Randomized Clinical Trial. JAMA Psychiatry. 2017 Jul 12
Durand CM, et al. The drug **overdose epidemic and deceased donor transplantation** in the United States. A national registry study. Ann Intern Med. 2018. [Epub ahead of print]. doi:10.7326/M17-2451
Durand Z, Nechuta S, Krishnaswami S, et al. Prevalence and Risk Factors Associated With Long-term Opioid **Use After Injury Among Previously Opioid-Free Workers**. JAMA Netw Open. 2019 Jul 3;2(7):e197222.
Duru UB, Pawar G, Barash JA, et al. An Unusual **Amnestic Syndrome** Associated With **Combined Fentanyl and Cocaine Use**. Ann Intern Med. 2018 Jan 30.
Edelman EJ, Gordon KS, Crothers K, et al. Association of **Prescribed Opioids With Increased Risk of Community-Acquired Pneumonia** Among Patients With and Without HIV. JAMA Intern Med. 2019 Jan 7.
Edlund MJ, et al. The role of opioid prescription in incident **opioid abuse and dependence** among individuals with chronic noncancer pain: role of opioid prescription. Clin J Pain. 2014 Jul;30(7):557-64.

Egan TD. **Are opioids indispensable for general anaesthesia**? Br J Anaesth. 2019 Jun;122(6):e127-e135.

Eggerstedt M, Stenson KM, Ramirez EA, et al. Association of Perioperative Opioid-Sparing **Multimodal Analgesia With Narcotic Use** and Pain Control After Head and Neck Free Flap Reconstruction. JAMA Facial Plast Surg. 2019 Aug 8.

Ehret GB, et al. Drug-Induced Long QT Syndrome in Injection Drug Users Receiving **Methadone**: High Frequency in Hospitalized Patients and Risk Factors. Arch Intern Med. 2006 Jun 26;166(12):1280-7.

Eisenberg E, McNicol ED, Carr DB. Efficacy and safety of opioid agonists in the treatment of neuropathic pain of nonmalignant origin: systematic review and meta-analysis of randomized controlled trials. JAMA. 2005 Jun 22;293(24):3043-52. CONCLUSIONS: Short-term studies provide only equivocal evidence regarding the efficacy of opioids in reducing the intensity of neuropathic pain. Intermediate-term studies demonstrate significant efficacy of opioids over placebo for neuropathic pain, which is likely to be clinically important. Reported adverse events of opioids are common but not life-threatening. Further RCTs are needed to establish their long-term efficacy, safety (including addiction

Eisenberg MD, Saloner B, Krawczyk N, et al. Use of Opioid Overdose Deaths Reported in One State's Criminal Justice, Hospital, and Prescription Databases to **Identify Risk of Opioid Fatalities**. JAMA Intern Med. 2019 Apr 15.

Ekström MP, Bornefalk-Hermansson A, et al. Safety of **benzodiazepines and opioids** in very severe respiratory disease: national prospective study. BMJ. 2014 Jan 30;348.

Els C, Jackson TD, Kunyk D, et al. **Adverse events associated with medium- and long-term use of opioids for chronic non-cancer pain**: an overview of Cochrane Reviews. Cochrane Database of Systematic Reviews 2017, Issue 10. Art. No.: CD012509. A number of adverse events, including serious adverse events, are associated with the medium- and long-term use of opioids for CNCP. The absolute event rate for any adverse event with opioids in trials using a placebo as comparison was 78%, with an absolute event rate of 7.5% for any serious adverse event. Based on the adverse events identified, clinically relevant benefit would need to be clearly demonstrated before long-term use could be considered in people with CNCP in clinical practice. A number of adverse events that we would have expected to occur with opioid use were not reported in the included Cochrane Reviews. Going forward, we recommend more rigorous identification and reporting of all adverse events in randomised controlled trials and systematic reviews on opioid therapy. The absence of data for many adverse events represents a serious limitation of the evidence on opioids. We also recommend extending study follow-up, as a latency of onset may exist for some adverse events.

Eldridge WB, Foster C, Wyble L. Neonatal Abstinence Syndrome Due to **Maternal Kratom Use**. Pediatrics. 2018 Nov 7.

Esser MB, Guy GP Jr, Zhang K, Brewer RD. **Binge Drinking and Prescription Opioid Misuse** in the U.S., 2012-2014. Am J Prev Med. 2019 Jun 7.

Evoy KE, Hill LG, Groff L, et al. **Naloxone Accessibility Without a Prescriber** Encounter Under Standing Orders at Community Pharmacy Chains in Texas. JAMA. 2018 Nov 3; 320(18):1934-1937.

Farkas A, Lynch MJ, Westover R, et al. **Pulmonary Complications** of Opioid Overdose Treated With Naloxone. Ann Emerg Med. 2019 Jun 7.

Farley KX, Anastasio AT, Kumar A, et al. Association Between Quantity of Opioids Prescribed After Surgery or Preoperative Opioid Use **Education With Opioid Consumption**. JAMA. 2019 Jun 25;321(24):2465-2467.

Faul M, Dailey MW, et al. Disparity in **Naloxone** Administration by **Emergency Medical Service Providers** and the Burden of Drug Overdose in US Rural Communities. Am J Public Health. 2015 Apr 23:e1-e7.

FDA July/09 notified healthcare professionals that it is taking several actions to reduce the risk of overdose in patients using pain medications that contain propoxyphene because of data linking **propoxyphene and fatal overdoses**. The agency will require manufacturers of propoxyphene-containing products to strengthen the label, including the boxed warning, emphasizing the potential for overdose when using these products and to provide a medication guide to patients stressing the importance of using the drugs as directed.

FDA Nov/10 is requesting that manufacturers of the painkiller **propoxyphene** pull the drug from the market because of concerns over cardiotoxicity. (Propoxyphene is marketed alone as Darvon and combined with acetaminophen as Darvocet.) The agency's request is based on data showing that, even when taken at therapeutic doses, the drug can lead to potentially dangerous changes in the heart's electrical activity, including prolonged PR and QT intervals and widened QRS complex. The FDA advises clinicians to stop prescribing propoxyphene and to ask current users to discontinue the drug. FDA's MedWatch alert (Free)

FDA: July/12 Clinicians who prescribe extended-release and long-acting opioids may receive training as part of an FDA effort to curb misuse. With the **risk evaluation and mitigation strategy**, pharmaceutical companies must develop programs to train clinicians on how to choose patients for opioid therapy appropriately, how to weigh the risks and benefits for a given patient, how to counsel patients against misuse, and how to spot signs of opioid misuse and addiction. The first training programs are expected to be available by March 2013. Currently, this training is optional, but the Obama administration has endorsed a mandatory training plan.

FDA Aug/12 is reviewing reports of children who developed serious adverse effects or died after taking **codeine** for pain relief after tonsillectomy and/or adenoidectomy for obstructive sleep apnea syndrome. Recently, three pediatric deaths and one non-fatal but life-threatening case of respiratory depression were documented in the medical literature.

FDA Sep/13 Extended-release and long-acting (ER/LA) opioid pain relievers are no longer indicated for merely moderate pain, the US Food and Drug Administration (FDA) announced today as part of a sweeping move to stem the deadly misuse and abuse of the drugs. Previously, the labels for ER/LA opioid analgesics stated that they were indicated for "moderate to severe pain in patients requiring continuous, around-the-clock opioid treatment for an extended period of time." The labels now will state that the drugs are indicated "**for the management of pain severe enough to require daily, around-the-clock opioid treatment and for which alternative treatments are inadequate**."

FDA Sep/15 is investigating the use of the pain medicine **tramadol in children aged 17 years and younger**, because of the rare but serious risk of slowed or difficult breathing. This risk may be increased in children treated with tramadol for pain after surgery to remove their tonsils and/or adenoids. FDA is evaluating all available information and will communicate final conclusions and recommendations to the public when the review is complete. In the body, tramadol is converted in the liver to the active form of the opioid, called O-desmethyltramadol. Some people have genetic variations that cause tramadol to be converted to the active form of the opioid faster and more completely than usual.

FDA Jan/16 is warning consumers not to use **Licorice Coughing Liquid**, a cough syrup product sold over-the-counter, because it contains unidentified morphine.

FDA Aug/16 review has found that the growing combined use of **opioid medicines with benzodiazepines** or other drugs that depress the central nervous system (CNS) has resulted in serious side effects, including slowed or difficult breathing and deaths.

FDA Apr/17 is **restricting the use of codeine and tramadol medicines in children**. These medicines carry serious risks, including slowed or difficult breathing and death, which appear to be a greater risk in children younger than 12 years, and should not be used in these children. These medicines should also be limited in some older children. Single-ingredient codeine and all tramadol-containing products are FDA-approved only for use in adults. FDA is also recommending against the use of codeine and tramadol medicines in breastfeeding mothers due to possible harm to their infants.

FDA Sep/17 is advising that the opioid addiction medications **buprenorphine and methadone** should not be withheld from patients taking **benzodiazepines** or other drugs that depress the central nervous system (CNS). The combined use of these drugs increases the risk of serious side effects; however, the harm caused by untreated opioid addiction usually outweighs these risks.

FDA Jan/18 is requiring safety labeling changes for prescription cough and cold medicines containing **codeine or hydrocodone to limit the use of these products to adults 18 years and older** because the risks of these medicines outweigh their benefits in children younger than 18. FDA is also requiring the addition of safety information about the risks of misuse, abuse, addiction, overdose, death, and slowed or difficult breathing to the Boxed Warning, the most prominent warning, of the drug labels for prescription cough and cold medicines containing codeine or hydrocodone.

FDA Apr/19 has received reports of serious harm in patients who are physically dependent on opioid pain medicines suddenly having these medicines discontinued or the dose rapidly decreased. These include serious withdrawal symptoms, uncontrolled pain, psychological distress, and suicide.

FDA Apr/19 Alvogen, Inc. is voluntarily recalling two lots of Fentanyl Transdermal System 12 mcg/h transdermal patches to the consumer level. A small number of cartons labeled 12 mcg/h Fentanyl Transdermal System patches contained 50 mcg/h patches. The 50 mcg/h patches that were included in cartons labeled 12 mcg/h are individually labeled as 50 mcg/h.

Feder KA, Letourneau EJ, Brook J. **Children in the Opioid Epidemic**: Addressing the Next Generation's Public Health Crisis. Pediatrics. 2018 Dec 4.

Feeney Colin, Ani Chizobam, Sharma Naini, et al. Morphine-Induced **Cardiogenic Shock**. Articles Ahead of Print published on 1 June 2011, DOI 10.1345/aph.1Q022. Ann Pharmacother ;45:e30.

Feinstein JA, Rodean J, Hall M, et al. Outpatient Prescription **Opioid Use in Pediatric Medicaid Enrollees** With Special Health Care Needs. Pediatrics. 2019 May 28.

Fiellin DA, et al. Counseling plus **buprenorphine-naloxone maintenance** therapy for opioid dependence. N Engl J Med. 2006 Jul 27;355(4):365-74. (InfoPOEMs: More intensive counseling and more frequent medication dispensing does not improve outcomes for treatment of opioid dependence in the primary care setting. (LOE = 1b))

Fiellin DA, Schottenfeld RS, Cutter CJ, et al. Primary Care-Based **Buprenorphine Taper vs Maintenance** Therapy for Prescription Opioid Dependence: A Randomized Clinical Trial. JAMA Intern Med. 2014 Oct 20.

Fill MA, Miller AM, Wilkinson RH, et al. **Educational Disabilities Among Children Born With Neonatal Abstinence Syndrome**. Pediatrics. 2018 Sep;142(3). pii: e20180562.

Fink DS, Schleimer JP, Sarvet A, et al. Association between **prescription drug monitoring programs** and nonfatal and fatal drug overdoses. A systematic review. Ann Intern Med. 2018. [Epub ahead of print].

Finkel JC, et al. Ketamine as an adjuvant for treatment of cancer pain in children and adolescents. J Pain. 2007 Jun;8(6):515-21. Epub 2007 Apr 16. In many children with advanced stages of cancer, pain control remains inadequate. We used subanesthetic doses of ketamine to treat 11 children & adolescents who were on high doses of opioids and had uncontrolled cancer pain. In the majority of patients, ketamine appeared to improve pain control and to have an opioid-sparing effect.

Finkelstein Y, Macdonald EM, Gonzalez A, et al. **Overdose Risk in Young Children** of Women Prescribed Opioids. Pediatrics. 2017 Feb 20.

Finnell JT, Twillman RK, Breslan SA, et al. The Role of **Continuing Medical Education** in Increasing Enrollment in **Prescription Drug Monitoring Programs**. Clin Ther. 2017 Aug 30.

Finney FT, Gossett TD, Hu HM, et al. Rate of Opioid Prescriptions for Patients With **Acute Ankle Sprain**. Ann Intern Med. 2019 Jul 9.

Fiscella K, Wakeman SE, Beletsky L. Implementing **Opioid Agonist Treatment in Correctional Facilities**. JAMA Intern Med. 2018 Jul 30.

Fiscella K, Wakeman SE, Beletsky L. **Buprenorphine Deregulation and Mainstreaming Treatment** for Opioid Use Disorder: X the X Waiver. JAMA Psychiatry. 2018 Dec 26.

Frank JW, Lovejoy TI, et al. **Patient outcomes in dose reduction or discontinuation of long-term opioid therapy**. A systematic review. Ann Intern Med. [Epub ahead of print]. doi:10.7326/M17-0598

Frank RG, Pollack HA. **Addressing the Fentanyl Threat** to Public Health. N Engl J Med. 2017 Feb 16;376(7):605-607

Finestone HM, Juurlink DN, Power B, et al. **Opioid prescribing is a surrogate for inadequate pain management** resources. Can Fam Physician. 2016 Jun;62(6):465-8.

Fischer B, Rehm J. **Deaths** related to the use of prescription opioids. CMAJ. 2009 Dec 8;181(12):881-2. Epub 2009 Dec 7.

Fischer B, Rehm J, Tyndall M. Effective **Canadian policy to reduce harms from prescription opioids**: learning from past failures. CMAJ. 2016 Dec 6;188(17-18):1240-1244. Review.

Fishbain DA, Pulikal A. Does Opioid **Tapering in Chronic Pain Patients** Result in Improved Pain or Same Pain vs Increased Pain at Taper Completion? A Structured Evidence-Based Systematic Review. Pain Med. 2018 Dec 28.

Follman S, Arora VM, Lyttle C, et al. **Naloxone Prescriptions Among Commercially Insured Individuals** at High Risk of Opioid Overdose. JAMA Netw Open. 2019 May 3;2(5):e193209.

Foral PA, Malesker MA, Huerta G, Hilleman DE. **Nebulized opioids** use in COPD. Chest. 2004 Feb;125(2):691-4.

Ford AC, Brenner DM, Schoenfeld PS. Efficacy of Pharmacological Therapies for the Treatment of **Opioid-Induced Constipation**: Systematic Review and Meta-Analysis. Am J Gastroenterol. 2013 Jun 11.

Fortuna RJ, Robbins BW, Caiola E, et al. Prescribing of **Controlled Medications to Adolescents and Young Adults** in the United States. Pediatrics. 2010 Nov 29.

Fournier J-P, et al. **Tramadol use and the risk of hospitalization for hypoglycemia** in patients with noncancer pain [online Dec 8, 2014]. JAMA Intern Med. doi:10.1001 /jamainternmed.2014.6512.

Frazier W, Cochran G, Lo-Ciganic WH, et al. **Medication-Assisted Treatment and Opioid Use Before and After Overdose** in Pennsylvania Medicaid. JAMA. 2017 Aug 22;318(8):750-752.

Freo U, Romualdi P, Kress HG. **Tapentadol for neuropathic pain**: a review of clinical studies. J Pain Res. 2019 May 16;12:1537-1551. doi: 10.2147/JPR.S190162.eCollection 2019.

Freynhagen R, Geisslinger G, Schug SA. **Opioids for chronic non-cancer pain**. BMJ. 2013 May 29;346:f2937.

Friday JH, Kanegaye JT, McCaslin I, Zheng A, Harley JR. **Ibuprofen** provides analgesia equivalent to acetaminophen-codeine in the treatment of acute pain in children with extremity injuries: a randomized clinical trial. Acad Emerg Med. 2009 Aug;16(8):711-6. Epub 2009 Jul 14. Acute pain relief from ibuprofen is equivalent to that of acetaminophen-codeine for children presenting to the emergency department with extremity injury. More than half the children in this study were consequently found to have fractures. (LOE = 1b)

Frieden TR, Houry D. **Reducing the Risks of Relief** - The **CDC Opioid-Prescribing Guideline**. N Engl J Med. 2016 Mar 15.

Friedman J, Kim D, Schneberk T, et al. Assessment of **racial/ethnic and income disparities in the prescription of opioids and other controlled medications** in California [online Feb 11, 2019]. JAMA Intern Med.

Friedmann PD, Andrews CM, Humphreys K. How **ACA Repeal Would Worsen the Opioid Epidemic**. N Engl J Med. 2017 Mar 9;376(10):e16.

Friesen KJ, Woelk C, Bugden S. Safety of **fentanyl initiation** according to past opioid exposure among patients newly prescribed fentanyl patches. CMAJ. 2016 Apr 4

Frogner BK, Harwood K, Andrilla CHA, et al. **Physical Therapy as the First Point of Care to Treat Low Back Pain**: An Instrumental Variables Approach to Estimate Impact on Opioid Prescription, Health Care Utilization, and Costs. Health Serv Res. 2018 May 23.
Frost DA, Soric MM, Kaiser R, Neugebauer RE. Efficacy of **Tramadol for Pain Management** in Patients Receiving Strong Cytochrome P450 2D6 Inhibitors. Pharmacotherapy. 2019 Jun;39(6):724-729.
Fulda GJ, Giberson F, Fagraeus L. A prospective randomized trial of nebulized morphine compared with patient-controlled analgesia morphine in the management of acute thoracic pain. J Trauma. 2005 Aug;59(2):383-8; discussion 389-90.
Furlan AD, Reardon R, Weppler C; **National Opioid Use Guideline Group**. Opioids for chronic noncancer pain: a new Canadian practice guideline. (**NOUGG**) CMAJ. 2010 Jun 15;182(9):923-30.
Part A Executive summary & background: http://nationalpaincentre.mcmaster.ca/documents/opioid_guideline_part_a_v4_5.pdf
Part B Recommendations for practice: http://nationalpaincentre.mcmaster.ca/documents/opioid_guideline_part_b_v5_6.pdf
Gaeta JM, Racine M. New Strategies Are Needed to Stop Overdose Fatalities: The Case for **Supervised Injection Facilities**. Ann Intern Med. 2018 Feb 6.
Gadkaree SK, Shaye DA, Occhiogrosso J, Lee LN. Association Between **Pain and Patient Satisfaction After Rhinoplasty**. JAMA Facial Plast Surg. 2019 Sep 19.
Gagne JJ, He M, Bateman BT. Trends in **Opioid Prescription** in Children and Adolescents **in a Commercially Insured Population** in the United States, 2004-2017. JAMA Pediatr. 2018 Nov 12.
Gagnon DJ, Jwo K. **Tremors and agitation** following low-dose intravenous hydromorphone administration in a patient with **kidney dysfunction**. Ann Pharmacother. 2013 Jul;47(7-8):e34.
Gaither JR, Leventhal JM, Ryan SA, et al. **National Trends** in **Hospitalizations for Opioid Poisonings Among Children and Adolescents**, 1997 to 2012. JAMA Pediatr. 2016 Oct 31.
Gaither JR, Shabanova V, Leventhal JM. US National **Trends in Pediatric Deaths From Prescription and Illicit Opioids**, 1999-2016. JAMA Netw Open. 2018;1(8):e186558.
Galinkin J, Koh JL; Committee on Drugs; Section On Anesthesiology and Pain Medicine; American Academy of Pediatrics. Recognition and management of **iatrogenically induced opioid dependence and withdrawal in children**. Pediatrics. 2014 Jan;133(1):152-5.
Gallagher R. The use of **opioids for dyspnea** in advanced disease. CMAJ. 2011 Jul 12;183(10):1170.
Gammal RS, Crews KR, Haider CE, et al. Pharmacogenetics for safe **codeine use in sickle cell disease**. Pediatrics. 2016;138(1):e20153497.
Gana TJ, et al. The 023 Study Group. Extended-release **tramadol** in the treatment of osteoarthritis: a multicenter, randomized, double-blind, placebo-controlled clinical trial. Curr Med Res Opin. 2006 Jul;22(7):1391-401.
Garcia-Portilla MP, Bobes-Bascaran MT, et al. Long-term outcomes of pharmacological treatments for opioid dependence: Does **methadone** still lead the pack? Br J Clin Pharmacol. 2012 Nov 12.
Gehrie EA, Keiser A, Haglock-Adler CJ, et al. **Detecting Pharmaceuticals in the Red Blood Cell Inventory** of a Hospital Blood Bank. J Pediatr. 2017 Jun 29.
Gellad WF, Good CB, Shulkin DJ. **Addressing the Opioid Epidemic in the United States**: Lessons From the Department of Veterans Affairs. JAMA Intern Med. 2017 Mar 13.
George R, Haywood A, Good P, et al. Can **Saliva and Plasma Methadone** Concentrations Be Used for Enantioselective Pharmacokinetic and Pharmacodynamic Studies in Patients With Advanced Cancer? Clin Ther. 2017 Aug 18.
Gershman K, Timm K, Frank M, et al. **Deaths** in Colorado Attributed to **Kratom**. N Engl J Med. 2019 Jan 3;380(1):97-98.
Ghazawi FM, Beecker J. **Necrotic leg ulcers** associated with krokodil injection in a 41-year-old man. CMAJ. 2019 Jun 24;191(25):E712.
Gimbel J, Spierings EL, Katz N, et al. Efficacy and tolerability of **buccal buprenorphine** in opioid-experienced patients with moderate to severe chronic low back pain: results of a phase 3, enriched enrollment, randomized withdrawal study. Pain. 2016 Nov;157(11):2517-2526.
Gladstone E, Smolina K, Morgan SG, et al. Sensitivity and specificity of **administrative mortality data for identifying prescription opioid-related deaths**. CMAJ. 2015 Nov 30.
Glanz JM, Binswanger IA, Shetterly SM, et al. Association Between Opioid **Dose Variability and Opioid Overdose** Among Adults Prescribed Long-term Opioid Therapy. JAMA Netw Open. 2019 Apr 5;2(4):e192613.
Glare P, Aubrey KR, Myles PS. Transition from **acute to chronic pain after surgery**. Lancet. 2019 Apr 13;393(10180):1537-1546
Glatstein MM, Garcia-Bournissen F, Finkelstein Y, Koren G. **Methadone exposure during lactation**. Can Fam Physician. 2008 Dec;54(12):1689-90.
Glod SA. The Other **Victims of the Opioid Epidemic**. N Engl J Med. 2017 Jun 1;376(22):2101-2102.
Gomes T, Juurlink DN, Dhalla IA, et al. Trends in **opioid use and dosing among** socio-economically disadvantaged patients. Open Medicine 2011;5(1). www.openmedicine.ca/article/viewArticle/421/373 (Jan 24, 2011).
Gomes Tara; Mamdani Muhammad M.; Dhalla IA.; et al. **Opioid Dose and Drug-Related Mortality** in Patients With Nonmalignant Pain. *Arch Intern Med*. 2011;171(7):686-691.
Gomes T, Redelmeier DA, Juurlink DN, et al. Opioid Dose and **Risk of Road Trauma** in Canada: A Population-Based Study. JAMA Intern Med. 2013 Jan 14:1-6.
Gomes T, Mamdani MM, Dhalla IA, et al. The burden of **premature opioid-related mortality**. Addiction. 2014 Jul 7.
Gomes T, Mamdani MM, Paterson JM, et al. Trends in **high-dose opioid prescribing** in Canada. Can Fam Physician. 2014 Sep;60(9):826-32.
Gomes T, Greaves S, Tadrous M, et al. Measuring the Burden of Opioid-related Mortality in Ontario, Canada. J Addict Med. 2018 Apr 25.
Gomes T, Greaves S, van den Brink W, et al. **Pregabalin and the Risk for Opioid-Related Death**: A Nested Case-Control Study. Ann Intern Med. 2018 Aug 21.
Gomes T, Tadrous M, Mamdani MM, et al. The **burden of opioid-related mortality** in the United States.JAMA Netw Open. 2018;1(2):e180217.
Gomes T, Khuu W, Martins D, et al. Contributions of **prescribed and non-prescribed opioids to opioid related deaths**:population based cohort study in Ontario, Canada. BMJ. 2018 Aug 29;362:k3207.
Gomes T, Greaves S, van den Brink W, et al. **Pregabalin and the Risk for Opioid-Related Death**: A Nested Case-Control Study. Ann Intern Med. 2018 Aug 21.
Goodwin JS, Kuo Y-F, Brown D, et al. Association of **chronic opioid use with presidential voting patterns in US counties** in 2016.JAMA Netw Open. 2016;1(2):e180450.
Gopinath KG, Hewton C, Shibu PK. **Myoclonus** associated with concomitant **Ciprofloxacin and Oxycodone** in an older Patient. Br J Clin Pharmacol. 2013 Jul 23.
Gottlieb S, Woodcock J. **Marshaling FDA Benefit-Risk Expertise** to Address the Current Opioid Abuse Epidemic. JAMA. 2017 Jul 6.
Gowing L, et al. Opioid antagonists under heavy sedation or anaesthesia for **opioid withdrawal**. Cochrane Database Syst Rev. 2006 Apr 19;(2):CD002022. Heavy sedation compared to

light sedation does not confer additional benefits in terms of less severe withdrawal or increased rates of commencement on naltrexone maintenance treatment. Given that the adverse events are potentially life-threatening, the value of antagonist-induced withdrawal under heavy sedation or anaesthesia is not supported. The high cost of anaesthesia-based approaches, both in monetary terms and use of scarce intensive care resources, suggest that this form of treatment should not be pursued.

Gowing L, Farrell M, Ali R, et al. **Alpha(2)-adrenergic** agonists for the management of opioid withdrawal. Cochrane Database Syst Rev. 2009 Apr 15;(2):CD002024. **Clonidine** and lofexidine are **more effective** than placebo for the management of withdrawal from heroin or methadone. No significant difference in efficacy was detected for treatment regimes based on clonidine or lofexidine, and those based on reducing doses of methadone over a period of around 10 days but methadone is associated with fewer adverse effects than clonidine, and lofexidine has a better safety profile than clonidine.

Gowing L, Ali R, White JM. **Buprenorphine** for the management of opioid withdrawal**.** Cochrane Database Syst Rev. 2009 Jul 8;(3):CD002025.

Gowing L, Farrell MF, Ali R, White JM. **Alpha2-adrenergic agonists** for the management of **opioid withdrawal**. Cochrane Database of Systematic Reviews 2014, Issue 3. Art. No.: CD002024. DOI: 10.1002/14651858.CD002024.pub4. Clonidine and lofexidine are more effective than placebo for the management of withdrawal from heroin or methadone. No significant difference in efficacy was detected for treatment regimens based on clonidine or lofexidine, and those based on reducing doses of methadone over a period of around 10 days but methadone is associated with fewer adverse effects than clonidine, and lofexidine has a better safety profile than clonidine.

Gowing L, Ali R, White JM, et al. **Buprenorphine for managing opioid withdrawal**. Cochrane Database Syst Rev. 2017 Feb 21;2:CD002025. Buprenorphine is more effective than clonidine or lofexidine for managing opioid withdrawal in terms of severity of withdrawal, duration of withdrawal treatment, and the likelihood of treatment completion.Buprenorphine and methadone appear to be equally effective, but data are limited. It remains possible that the pattern of withdrawal experienced may differ and that withdrawal symptoms may resolve more quickly with buprenorphine.It is not possible to draw any conclusions from the available evidence on the relative effectiveness of different rates of tapering the buprenorphine dose. The divergent findings of studies included in this review suggest that there may be multiple factors affecting the response to the rate of dose taper. One such factor could be whether or not the initial treatment plan includes a transition to subsequent relapse prevention treatment with naltrexone. Indeed, the use of buprenorphine to support transition to naltrexone treatment is an aspect worthy of further research.Most participants in the studies included in this review were male. None of the studies reported outcomes on the basis of sex, preventing any exploration of differences related to this variable. Consideration of sex as a factor influencing response to withdrawal treatment would be relevant research for selecting the most appropriate type of intervention for each individual.

Grady Deborah; Berkowitz Seth; Katz Mitchell H.. **Opioids for Chronic Pain**. Arch Intern Med. 2011;0(2011):archinternmed.2011.213.

Green R, Bulloch B, Kabani A, Hancock BJ, Tenenbein M. Early analgesia for children with acute abdominal pain. Pediatrics. 2005 Oct;116(4):978-83. (InfoPOEMs: The immediate administration of morphine in children aged 5 years to 16 years with acute abdominal pain does not obscure the diagnosis of appendicitis and does not affect the surgeon's confidence in his or her diagnosis. It also causes a small decrease in pain. As with adults, pain relief should not be withheld in children until the cause of the pain is determined. (LOE = 2b))

Green TC, Clarke J, et al. **Postincarceration Fatal Overdoses** After Implementing Medications for Addiction Treatment in a Statewide Correctional System. JAMA Psychiatry. 2018 Feb 14.

Gregory TB. **Hydromorphone** (**Exalgo** ER OROS) : Evolving to Meet the Challenges of Today's Health Care Environment. Clin Ther. 2013 Nov 27.

Gressler LE, Shah S, Shaya FT. Association of **Criminal Statutes for Opioid Use Disorder** With Prevalence and Treatment Among Pregnant Women With Commercial Insurance in the United States. JAMA Netw Open. 2019 Mar 1;2(3):e190338.

Griesler PC, Hu MC, Wall MM, Kandel DB. **Nonmedical Prescription Opioid Use** by Parents and Adolescents in the US. Pediatrics. 2019 Mar;143(3).

Grissa MH et al. **Acupuncture vs intravenous morphine** in the management of acute pain in the ED. Am J Emerg Med 2016 Jul 20.

Grossman MR, Berkwitt AK, Osborn RR, et al. An Initiative to Improve the **Quality of Care of Infants With Neonatal Abstinence Syndrome**. Peds.2017;139(6):e20163360

Guadamuz JS, Alexander GC, Chaudhri T, et al. **Availability and Cost of Naloxone Nasal Spray** at Pharmacies in Philadelphia, Pennsylvania, 2017. JAMA Netw Open. 2019 Jun 5;2(6):e195388.

Gupta R, Shah ND, Ross JS. The **Rising Price of Naloxone** - Risks to Efforts to Stem Overdose Deaths. N Engl J Med. 2016 Dec 8;375(23):2213-2215

Gupta N, Vujicic M, Blatz A. **Opioid prescribing practices from 2010 through 2015 among dentists** in the United States: What do claims data tell us? J Am Dent Assoc. 2018 Apr;149(4):237-245.e6.

Gupta N, Vujicic M, Blatz A. **Multiple opioid prescriptions among privately insured dental patients** in the United States: Evidence from claims data. J Am Dent Assoc. 2018 Jul;149(7):619-627.e1.

Guy GP Jr, Zhang K, Schieber LZ, et al. **County-level opioid prescribing** in the United States, 2015 and 2017 [online Feb 11, 2019]. JAMA Intern Med.

Habbouche J, Lee J, Steiger R, et al. Association of **Hydrocodone Schedule Change With Opioid Prescriptions Following Surgery**. JAMA Surg. 2018 Aug 22.

Hadland SE, Wharam JF, Schuster MA, et al. **Trends in receipt of buprenorphine and naltrexone for opioid use disorder among adolescents and young adults**, 2001-2014 [published online June 19, 2017].JAMA Pediatr. doi:10.1001/jamapediatrics.2017.0745

Hadland SE, Krieger MS, Marshall BDL. **Industry Payments to Physicians for Opioid Products**, 2013-2015. Am J Public Health. 2017 Sep;107(9):1493-1495

Hadland SE, Cerdá M, Li Y, et al. Association of **Pharmaceutical Industry Marketing of Opioid Products to Physicians** With Subsequent Opioid Prescribing. JAMA Intern Med. 2018 May 14.

Hadland SE, Bagley SM, Rodean J, et al. Receipt of **Timely Addiction Treatment and Association** of Early Medication Treatment With Retention in Care Among Youths With Opioid Use Disorder. JAMA Pediatr. 2018 Sep 10.

Hadland SE, Rivera-Aguirre A, Marshall BDL, Cerdá M. Association of pharmaceutical industry **marketing of opioid products with mortality from opioid-related overdoses**. JAMA Netw Open. 2019;2(1):e186007. doi:10.1001/jamanetworkopen.2018.6007

Hadley G, Derry S, Moore RA, et al. **Transdermal fentanyl for cancer pain**. Cochrane Database Syst Rev. 2013 Oct 5;10:CD010270. The randomised trial literature for effectiveness of transdermal fentanyl is limited, but it is an important medicine. Most studies recruited fewer than 100 participants and did not provide data appropriate for meta-analysis. Only a few reported how many patients had good pain relief but, where data were reported, a majority had no worse than mild pain within a reasonably short time period. The evidence pointed to a useful and significant reduction in complaints about constipation for transdermal fentanyl compared with oral morphine.

Haffajee RL, Frank RG. Making the Opioid Public Health Emergency Effective. JAMA Psychiatry. 2018 Apr 25.

Haffajee RL, Jena AB, Weiner SG. **Mandatory Use of Prescription Drug Monitoring Programs**. JAMA. 2015 Jan 26.

Haffajee RL, Lin LA, Bohnert ASB, et al. Characteristics of US Counties With High Opioid Overdose Mortality and **Low Capacity to Deliver Medications for Opioid Use Disorder**. JAMA Netw Open. 2019 Jun 5;2(6):e196373.

Haffajee RL, Mello MM. **Drug Companies' Liability for the Opioid Epidemic**. N Engl J Med. 2017 Dec 14;377(24):2301-2305.

Hah J, Mackey SC, Schmidt P, et al. Effect of **perioperative gabapentin on postoperative pain resolution and opioid cessation** in a mixed surgical cohort: a randomized clinical trial [online Dec 13, 2017].JAMA Surg. doi:10.1001/jamasurg.2017.4915

Hah JM, Cramer E, Hilmoe H, et al. **Factors Associated With** Acute Pain Estimation, Postoperative Pain Resolution, **Opioid Cessation**, and Recovery: Secondary Analysis of a Randomized Clinical Trial. JAMA Netw Open. 2019 Mar 1;2(3):e190168.

Haider A, Qian Y, Lu Z, et al. Implications of the **Parenteral Opioid Shortage for Prescription Patterns and Pain Control** Among Hospitalized Patients With Cancer Referred to Palliative Care. JAMA Oncol. 2019 Mar 21.

Hall AJ, Logan JE, Toblin RL, et al. Patterns of abuse among **unintentional pharmaceutical overdose** fatalities. JAMA. 2008 Dec 10;300(22):2613-20. The majority of overdose

deaths in West Virginia in 2006 were associated with nonmedical use and diversion of pharmaceuticals, primarily opioid analgesics.
Hall ES, Wexelblatt SL, Crowley M, et al; **CHNAS** Consortium. Implementation of a **Neonatal Abstinence Syndrome Weaning Protocol**: A Multicenter Cohort Study. Pediatrics. 2015 Sep 14.
Hallway A, Vu J, Lee J, et al. Patient Satisfaction and **Pain Control Using an Opioid-Sparing Postoperative Pathway**. J Am Coll Surg. 2019 Sep;229(3):316-322.
Han B, Compton WM, et al. **Nonmedical Prescription Opioid Use and Use Disorders** Among Adults Aged 18 Through 64 Years in the United States, 2003-2013. JAMA. 2015 Oct 13;314(14):1468-78.
Han B, Compton WM, Blanco C, et al. Prescription Opioid Use, Misuse, and Use Disorders in U.S. Adults: 2015 National Survey on Drug Use and Health. Ann Intern Med. 2017 Aug 1.
Harbaugh CM, Lee JS, Hu HM, et al. **Persistent opioid use among pediatric patients after surgery**. Pediatrics. 2018;141(1):e20172439
Harbaugh CM, Lee JS, Chua K-P, et al. Association between **long-term opioid use in family members and persistent opioid use after surgery** among adolescents and young adults [online Feb 27, 2019]. JAMA Surg.
Harbaugh CM, Nalliah RP, Hu HM, et al. Persistent Opioid Use After **Wisdom Tooth Extraction**. JAMA. 2018 Aug 7;320(5):504-506.
Harbaugh CM, Vargas G, Streur CS, et al. **Eliminating Unnecessary Opioid Exposure** After Common Children's Surgeries. JAMA Surg. 2019 Sep 4.
Hauk L. **Management of Chronic Pain and Opioid Misuse**: A Position Paper from the **AAFP**. Am Fam Physician. 2017 Apr 1;95(7):458-459
Hauser W, Schug S, Furlan AD. The opioid epidemic and national guidelines for **opioid** therapy for **chronic noncancer pain**: a perspective from different continents. Pain Reports. 2017:2:e599
Hawkins, Joy L. **Epidural Analgesia** for Labor and Delivery. N Engl J Med 2010 362: 1503-1510.
Hawton Keith, Bergen Helen, Simkin Sue, et al. Effect of withdrawal of co-proxamol (**dextropropoxyphene** & acetaminophen) on prescribing and **deaths from drug poisoning** in England and Wales: time series analysis. BMJ 2009;338:b2270, doi: 10.1136/bmj.b2270 (Published 18 June 2009)
Haymond S, Nagpal G, Heiman H. **Urine Drug Screens to Monitor Opioid Use for Managing Chronic Pain**. JAMA. 2017 Sep 19;318(11):1061-1062.
Health Canada July/10 RELISTOR (methylnaltrexone bromide) Subcutaneous Injection - Association with gastrointestinal perforation - Wyeth Canada Patients with advanced illness being treated with **RELISTOR may be at increased risk of gastrointestinal perforation**.
Health Canada Nov/10 **Darvon-N (dextropropoxyphene) - Recall and Withdrawal in Canada** - Paladin Labs Inc. Paladin Labs Inc. in collaboration with Health Canada would like to inform healthcare professionals of the voluntary recall and withdrawal of the opioid analgesic Darvon-N (dextropropoxyphene) in Canada. (widen the QRS complex, prolong the QT interval and therefore increase the risk of serious abnormal heart rhythms.)
Health Canada's Jun/12 review recommends **codeine be used in patients aged 12 and over**. This recommendation is based on very rare cases of serious side effects and deaths in children that have been attributed to codeine, when given directly to a child, or to babies from breast milk.
Health Canada Oct/13 Reminding Canadians to safely **use and dispose of fentanyl patches** to prevent accidental exposure. A fentanyl patch is an adhesive patch that is placed on the skin. It delivers the drug fentanyl, continuously through the skin and into the blood stream to control pain. Accidental exposure to fentanyl can be very dangerous and even lead to death.
Health Canada Aug/14 is advising healthcare professionals and Canadians that it has implemented labelling changes for the class of drugs known as controlled-release opioid pain medicines, to enhance their safe and appropriate use. The changes provide standardized wording that more clearly outlines the risks and safety concerns associated with controlled-release opioids. The updated guidance also encourages more appropriate patient selection and monitoring.
Health Canada Dec/15: **Herba Pini Syrop** contains codeine.
Health Canada Aug/16 is taking new action to improve the safe use of two prescription opioid drugs, **codeine and hydrocodone**, to help further address the rare but potentially life-threatening risk of breathing problems in children and adolescents. Serious breathing problems known as respiratory depression (slowed breathing) are a known risk with the use of any opioid, particularly when too much is taken. The action is in light of Health Canada safety reviews that identified the need for new warnings and restrictions on prescription codeine and hydrocodone products, to enhance their safe use. Specifically, the reviews determined that: codeine should no longer be used (contraindicated) in patients under 18 years of age to treat pain after surgery to remove tonsils or adenoids, as these patients are more susceptible to the risk of serious breathing problems. Codeine (prescription and non-prescription) is already not recommended for children under the age of 12, for any use. Hydrocodone is no longer recommended in under six years of age. This recommendation is based on rare cases of serious breathing problems including deaths in children in this age group, usually involving higher-than-recommended doses.
Health Canada Jun/17 is advising health care professionals and Canadians that the **Canadian authorized version of NARCAN** will transition onto the market by July 5, 2017.
Health Canada Dec/17 held a Scientific Advisory Panel on Opioid Use and Contraindications, to consider whether the current contraindications for opioid use are sufficient, or whether labelling updates and other actions may be needed to reduce risks to Canadians. After thoroughly assessing the Panel's recommendations, Health Canada is working with manufacturers to update the Canadian labelling of all prescription opioid products. **Recommendation for a daily opioid threshold dose for the management of chronic non-cancer, non-palliative pain (which aims to reduce risks of adverse events and overdoses associated with taking higher doses of opioids); Recommendation to limit the quantity of opioids prescribed for acute pain** (which aims to reduce the duration of use and associated risks of developing dependence and substance use disorder); and Clarification of warnings, including those for special populations such as **pregnant women and patients with a history of dependence or substance use disorder**.
Health Canada Dec/17 is advising Canadians of the potential limitations when using **test strips to detect fentanyl**. A preliminary study undertaken by Health Canada indicated that false negatives could occur when using fentanyl-detection test strips. A false negative would be a test result that does not detect the fentanyl in a drug sample even though it does contain fentanyl
Health Canada June/18: Health Canada reminds Canadians of the **limitations of fentanyl test strips** being used to check street drugs before consumption.
Heitz C, Morgenstern J, Bond C, Milne WK. Hot Off the Press: A Systematic Review And Meta-analysis of **Ketamine as an Alternative to Opioids** for **Acute Pain** in the Emergency Department. Acad Emerg Med. 2018 Nov 27.
Helmich F, Lock G. Burton's Line from Chronic Lead Intoxication. N Engl J Med. 2018 Nov 8;379(19):e35. (**chewing opium**)
Henke RM, Tehrani AB, Ali MM, et al. **Opioid Prescribing to Adolescents** in the United States From 2005 to 2016. Psychiatr Serv. 2018 Jul 9:appips201700562.
Heppell SP, Isbister GK. **Lack of respiratory depression** in **paracetamol (acetaminophen)-codeine** combination overdoses. Br J Clin Pharmacol. 2016 Dec 30
Herder M, Juurlink D. High-strength opioid formulations: **the case for a ministerial recall**. CMAJ. 2018 Dec 3;190(48):E1404-E1405.
Hernandez I, He M, Brooks MM, et al. Exposure-Response Association Between **Concurrent Opioid and Benzodiazepine Use and Risk of Opioid-Related Overdose** in Medicare Part D Beneficiaries. *JAMA Network Open.* 2018;1(2):e180919.
Herzig SJ, et al. **Improving the Safety of Opioid Use for Acute Noncancer Pain in Hospitalized Adults**: A Consensus Statement From the Society of Hospital Medicine.

J Hosp Med. 2018 Apr;13(4):263-271.
Herzig SJ. Web Exclusive. Annals for Hospitalists Inpatient Notes – **Managing Acute Pain in the Hospital in the Face of the Opioid Crisis**. Ann Intern Med. 2018 Sep 18;169(6):HO2-HO3.
Hill MV, McMahon ML, Stucke RS, Barth RJ Jr. Wide Variation and **Excessive Dosage of Opioid Prescriptions for Common General Surgical Procedures**. Ann Surg. 2017 Apr;265(4):709-714.
Hilliard P, Waljee J, Moser S, et al. Prevalence of **preoperative opioid use and characteristics associated with opioid use** among patients presenting for surgery [online July 11, 2018]. JAMA Surg. doi:10.1001/jamasurg.2018.2102
Hippard HK, Govindan K, Friedman EM, et al. Postoperative Analgesic and Behavioral Effects of **Intranasal Fentanyl, Intravenous Morphine, and Intramuscular Morphine** in Pediatric Patients Undergoing Bilateral Myringotomy and Placement of Ventilating Tubes. Anesth Analg. 2012 Jun 5.
Hodgins David C, Stea Jonathan N, Grant Jon E. **Gambling disorders**. www.thelancet.com Published online May 19, 2011 DOI:10.1016/S0140-6736(10)62185-X
Hoffman EM, Watson JC, St Sauver J, et al. Association of **long-term opioid therapy with functional status, adverse outcomes, and mortality** among patients with polyneuropathy [online May 22, 2017].JAMA Neurol. doi:10.1001/jamaneurol.2017.0486
Holbrook TL et al. Morphine use after combat injury in Iraq and **post-traumatic stress disorder**. *N Engl J Med* 2010 Jan 14; 362:110.
Holmes AV, Atwood EC, Whalen B, et al. **Rooming-In to Treat Neonatal Abstinence Syndrome**: Improved Family-Centered Care at Lower Cost. Pediatrics. 2016 May 18.
Honein MA, Boyle C, Redfield RR. Public Health Surveillance of **Prenatal Opioid Exposure** in Mothers and Infants. Pediatrics. 2019 Jan 17.
Hooten WM, St Sauver JL, McGree ME, et al. Incidence and Risk Factors for Progression **From Short-term to Episodic or Long-term Opioid Prescribing**: A Population-Based Study. Mayo Clin Proc. 2015 Jul;90(7):850-6.
Hoppe JA, Nelson LS, Perrone J, et al; Prescribing Opioids Safely in the Emergency Department (**POSED**) Study Investigators. **Opioid Prescribing in a Cross Section of US Emergency Departments**. Ann Emerg Med. 2015 Apr 24.
Howard R, Fry B, Gunaseelan V, et al. Association of **Opioid Prescribing With Opioid Consumption After Surgery** in Michigan. JAMA Surg. 2018 Nov 7:e184234.
Howard R, Hallway A, et al. Optimizing **Postoperative Opioid Prescribing Through Quality-Based Reimbursement**. JAMA Netw Open. 2019 Sep 4;2(9):e1911619.
Howard R, Waljee J, Brummett C, et al. **Reduction in Opioid Prescribing Through Evidence-Based Prescribing Guidelines**. JAMA Surg. 2017 Dec 6.
Hser YI, et al. **Distinctive Trajectories of Opioid Use** Over an Extended Follow-up of Patients in a Multisite Trial on **Buprenorphine + Naloxone & Methadone**. J Addict Med. 2017 Jan/Feb;11(1):63-69.
Hu T, Nijmeh L, Pyle A**. Buprenorphine-naloxone**. CMAJ. 2018 Nov 26;190(47):E1389.
Huang X, Keyes KM, Li G. Increasing **Prescription Opioid and Heroin Overdose Mortality** in the United States, 1999-2014: An Age-Period-Cohort Analysis. Am J Public Health. 2017 Nov 21:e1-e6
Hudak ML, Tan RC et al. **Neonatal Drug Withdrawal**. Pediatrics. 2012 Jan 30.
Hudgins JD, Porter JJ, Monuteaux MC, Bourgeois FT. Trends in opioid **prescribing for adolescents and young adults** in ambulatory care settings. Pediatrics. 2019,143(6):e20181578
Hudson TJ, Painter JT, Martin BC, et al. Pharmacoepidemiologic analyses of **opioid use among OEF/OIF/OND veterans**. Pain. 2017 Mar 25.
Humphreys K. Avoiding globalisation of the prescription opioid epidemic. Lancet. 2017 Jul 29;390(10093):437-439
Huybrechts KF, Bateman BT, Desai RJ, et al. Risk of **neonatal drug withdrawal** after intrauterine co-exposure to **opioids** and **psychotropic** medications: cohort study. BMJ. 2017 Aug 2;358:j3326.
Hwang CS, Turner LW, Kruszewski SP, Kolodny A, Alexander GC. Primary Care Physicians' **Knowledge And Attitudes Regarding Prescription Opioid Abuse & Diversion**. Clin J Pain. 2015 Jun 22.
Hwang CS, Kang EM, Kornegay CJ, Staffa JA, Jones CM, McAninch JK. Trends in the **concomitant prescribing of opioids and benzodiazepines**, 2002-2014. Am J Prev Med. 2016;51:151-160.
Hwang CS, Kang EM, Ding Y, et al. Patterns of **immediate-release and extended-release opioid analgesic use in the management of chronic pain**, 2003-2014.JAMA Netw Open.2018;1(2):e180216.
Ibrahim AM, Obaidi Z, Ruan G, et al. **Nalbuphine for Opioid-Induced Urine Retention**. Ann Intern Med. 2018 Sep 4.
Im YJ, Jeon JY, Kim EY, et al. An Assessment of the **Pharmacokinetics** of a Sustained-Release Formulation of a **Tramadol/Acetaminophen** Combination in Healthy Subjects. Clin Ther. 2015 Jan 21.
Induru RR, Laman RL. Cancer Diagnosis and Management: **Managing cancer pain**: Frequently asked questions. Cleveland Clinic Journal of Medicine 2011; 78(7):449-464.
Irvine MA, Buxton JA, Otterstatter M, et al. Distribution of **take-home opioid antagonist kits** during a synthetic opioid epidemic in British Columbia, Canada: a modelling study. Lancet Public Health. 2018 Apr 17.
Isbister GK, Brown AL, Gill A, et al. **QT interval prolongation in opioid agonist treatment**: analysis of continuous 12-lead electrocardiogram recordings. Br J Clin Pharmacol. 2017 May 9.
Jansson LM, Choo R, Velez ML, et al. et al. **Methadone maintenance and breastfeeding** in the neonatal period. Pediatrics. 2008 Jan;121(1):106-14. (n=8) Results contribute to the recommendation of breastfeeding for methadone-maintained women.
Jarvis M, Williams J, Hurford M, et al. **Appropriate Use of Drug Testing** in Clinical Addiction Medicine. J Addict Med. 2017 May/Jun;11(3):163-173.
Jeffery MM, Hooten WM, Henk HJ, et al. **Trends in opioid use in commercially insured and Medicare Advantage populations in 2007-16**: retrospective cohort study. BMJ. 2018 Aug 1;362:k2833.
Jeffery MM, Hooten WM, Hess EP, et al. **Opioid Prescribing for Opioid-Naive Patients in Emergency Departments and Other Settings**: Characteristics of prescriptions and Association With Long-Term Use. Ann Emerg Med. 2017 Sep 21.
Jeffery MM, Hooten WM, Jena AB, et al. Rates of **Physician Coprescribing of Opioids and Benzodiazepines** After the Release of the Centers for Disease Control and Prevention Guidelines in 2016. JAMA Netw Open. 2019 Aug 2;2(8):e198325.
Jena AB, Goldman D, Weaver L, et al. **Opioid prescribing by multiple Providers in Medicare**: retrospective observational study of insurance claims. BMJ. 2014 Feb 19;348:g1393.
Jena AB, Goldman D, Karaca-Mandic P. **Hospital Prescribing of Opioids to Medicare** Beneficiaries. JAMA Intern Med. 2016 Jun 13.
Jerry JM, Collins GB. Medication-assisted (methadone, buprenorphine)treatment of **opiate dependence** is gaining favor. Cleve Clin J Med. 2013 Jun;80(6):345-9.
Jerschow E, Lin RY, Scaperotti MM, et al. **Fatal anaphylaxis** in the United States, 1999-2010: Temporal patterns and demographic associations. J Allergy Clin Immunol. 2014 Sep 26.
Jiang R, Lee I, Lee TA, et al. The **societal cost of heroin use** disorder in the United States. PLoS One. 2017 May 30;12(5):e0177323.
Jin J. **Risks of Codeine and Tramadol in Children**. JAMA. 2017 Oct 17;318(15):1514

Jones AA, Jang K, Panenka WJ, et al. Rapid Change in **Fentanyl Prevalence** in a Community-Based, High-Risk Sample. JAMA Psychiatry. 2018 Jan 31.
Jones CM. Frequency of **Prescription Pain Reliever Nonmedical Use**: 2002-2003 and 2009-2010. Arch Intern Med. 2012 Jun 25:1-2.
Jones CM, Mack KA, Paulozzi LJ. **Pharmaceutical overdose deaths**, United States, 2010. JAMA. 2013 Feb 20;309(7):657-9.
Jones CM, Paulozzi LJ, Mack KA. **Sources of Prescription Opioid** Pain Relievers by Frequency of Past-Year Nonmedical Use: United States, 2008-2011. JAMA Intern Med. 2014 Mar 3.
Jones CM, Lurie P, Woodcock J. Addressing **prescription opioid overdose**: data support a comprehensive policy approach. JAMA. 2014 Nov 5;312(17):1733 4.
Jones CM, et al. Effect of US Drug Enforcement Administration's **Rescheduling of Hydrocodone Combination Analgesic Products** on Opioid Analgesic Prescribing. JAMA Intern Med. 2016 Jan 25.
Jones HE, Kaltenbach K, Heil SH, et al. Neonatal abstinence syndrome after **methadone or buprenorphine** exposure. N Engl J Med. 2010 Dec 9;363(24):2320-31.
Jones HE, Deppen K, Hudak ML, et al. Clinical care for **opioid-using pregnant and postpartum women**: the role of obstetric providers. Am J Obstet Gynecol. 2014 Apr;210(4):302-10.
Jones CM, Einstein EB, Compton WM. Changes in Synthetic Opioid Involvement in Drug Overdose Deaths in the United States, 2010-2016. JAMA. 2018 May 1;319(17):1819-1821.
Jumah NA, Edwards C, Balfour-Boehm J, et al. Observational study of the safety of **buprenorphine+naloxone in pregnancy** in a rural and remote population. BMJ Open. 2016 Oct 31;6(10):e011774.
Kahan Meldon, Mailis-Gagnon Angela, Wilson Lynn, et al. **Canadian guideline** for safe and effective use of opioids for chronic noncancer pain: Clinical summary for family physicians. **Part 1: general population**. Can Fam Physician November 2011 57: 1257-1266.
Kahan Meldon, Wilson Lynn, Mailis-Gagnon Angela, et al. **Canadian guideline** for safe and effective use of opioids for chronic noncancer pain: Clinical summary for family physicians. **Part 2: special populations**. Can Fam Physician November 2011 57: 1269-1276.
Kaiser S, Asteria-Penaloza R, Vittinghoff E, et al. **National patterns of codeine prescriptions** for children in the emergency department. Pediatrics. 2014;133(5).
Kale N. **Urine Drug Tests**: Ordering and Interpretation. Am Fam Physician. 2019;99(1):33-39.
Kanazi GE, El-Khatib MF, Yazbeck-Karam VG, et al. Effect of **vitamin C on morphine** use after laparoscopic cholecystectomy: a randomized controlled trial. Can J Anaesth. 2012 Jun;59(6):538-43.
Kane JM, Colvin JD, Bartlett AH, et al. **Opioid-Related Critical Care Resource Use in US Children's Hospitals**. Pediatrics. 2018 Mar 5.
Kao D, Bucher Bartelson B, Khatri V, et al. Trends in reporting **methadone-associated cardiac arrhythmia**, 1997-2011: an analysis of registry data. Ann Intern Med. 2013 May 21;158(10):735-40.
Kapil RP, Friedman K, Cipriano A, et al. Effects of **Paroxetine**, a CYP2D6 Inhibitor, on the Pharmacokinetic Properties of **Hydrocodone** After Coadministration With a Single-Entity, Once-Daily, Extended-Release Hydrocodone Tablet. Clin Ther. 2015 Sep 6.
Karamchandani K, Pyati S, Bryan W, et al. **New Persistent Opioid Use After Postoperative Intensive Care** in US Veterans. JAMA Surg. 2019 Jun 5
Karttunen N, Taipale H, Hamina A. **Concomitant use of benzodiazepines and opioids** in community-dwelling older people with or without Alzheimer's disease – A nationwide register-based study in Finland. Int J Geriatr Psychiatry. 2018 Oct 29.
Kelley-Quon LI, Cho J, Strong DR, et al. Association of Nonmedical Prescription Opioid **Use With Subsequent Heroin Use Initiation** in Adolescents. JAMA Pediatr. 2019 Jul 8:e191750.
Kelly L, Guilfoyle J, Dooley J, et al. Incidence of **narcotic abuse during pregnancy** in northwestern Ontario: Three-year prospective cohort study. Can Fam Physician. 2014 Oct;60(10):e493-8.
Kennedy-Hendricks A, Gielen A, McDonald E, et al. **Medication Sharing, Storage, and Disposal** Practices for Opioid Medications Among US Adults. JAMA Intern Med. 2016 Jun 13.
Kennedy-Hendricks A, Levin J, Stone E, et al. **News Media Reporting On Medication Treatment For Opioid Use Disorder** Amid The Opioid Epidemic. Health Aff (Millwood). 2019 Apr;38(4):643-651.
Kennedy-Hendricks A, Richey M, McGinty EE, Stuart EA, et al. Opioid Overdose Deaths and **Florida's Crackdown on Pill Mills**. Am J Public Health. 2015 Dec 21:e1-e8.
Khademi H, Malekzadeh R, Pourshams A, Jafari E, Salahi R, et al. **Opium use and mortality** in Golestan Cohort Study: prospective cohort study of 50 000 adults in Iran. BMJ 2012;344:e2502.
Khan NF, Bateman BT, Landon JE, Gagne JJ. Association of Opioid Overdose With **Opioid Prescriptions to Family Members**. JAMA Intern Med. 2019 Jun 24.
Kiang MV, Basu S, Chen J, Alexander MJ. Assessment of **Changes in the Geographical Distribution of Opioid-Related Mortality** Across the United States by Opioid Type, 1999-2016. JAMA Netw Open. 2019 Feb 1;2(2):e190040.
Kim HK, Smiddy M, Hoffman RS, Nelson LS. **Buprenorphine** (Suboxone) may not be as safe as you think: a pediatric fatality from unintentional exposure. Pediatrics. 2012 Dec;130(6):e1700-3.
Kim SC, Jin Y, Lee YC, et al. Association of **Preoperative Opioid Use With Mortality and Short-term Safety Outcomes** After Total Knee Replacement. JAMA Netw Open. 2019 Jul 3;2(7):e198061.
Kimber J, Copeland L, Hickman M, et al. Survival and cessation in **injecting drug users**: prospective observational study of outcomes and effect of **opiate substitution treatment**. BMJ. 2010 Jul 1;341:c3172. doi: 10.1136/bmj.c3172.
Kimmel PL, Fwu CW, Abbott KC, et al. **Opioid Prescription, Morbidity, and Mortality in United States Dialysis** Patients. J Am Soc Nephrol. 2017 Sep 21.
King NB, Fraser V. **Untreated pain, narcotics regulation, and global health ideologies**. PLoS Med. 2013 Apr;10(4):e1001411.
King NB, Strumpf E, Harper S. Has the Increase in **Disability Insurance** Participation Contributed to **Increased Opioid-Related Mortality**? Ann Intern Med. 2016 Nov 15;165(10):729-730.
Kirschner N, Ginsburg J, Snyder Sulmasy L. **Prescription drug abuse: executive summary of a policy position paper from the American College of Physicians**. Ann Intern Med. 2014;160:198-200.
Klimas J, Gorfinkel L, Fairbairn N, et al. **Strategies to Identify Patient Risks** of Prescription Opioid Addiction When Initiating Opioids for Pain: A Systematic Review. JAMA Netw Open. 2019 May 3;2(5):e193365.
Knight JR, Sherritt L, Gibson EB, et al. Effect of **Computer-Based Substance Use Screening and Brief Behavioral Counseling** vs Usual Care for Youths in Pediatric Primary Care: A Pilot Randomized Clinical Trial. JAMA Netw Open. 2019 Jun 5;2(6):e196258.
Ko JY, Patrick SW, Tong VT, et al. Incidence of **Neonatal Abstinence Syndrome** - 28 States, 1999-2013. MMWR Morb Mortal Wkly Rep. 2016 Aug 12;65(31):799-802.
Kocherlakota P. **Neonatal Abstinence Syndrome**. Pediatrics. 2014 Aug;134(2):e547-e561. Review.
Kokki H, Lintula H, Vanamo K, et al. Oxycodone vs placebo in children with undifferentiated abdominal pain: a randomized, double-blind clinical trial of the effect of analgesia on diagnostic accuracy. Arch Pediatr Adolesc Med 2005;159:320-25. (InfoPOEMs: Giving analgesics to children with abdominal pain does not obscure the surgical diagnosis. We don't need to make kids suffer while waiting for a surgeon to evaluate their abdominal pain. (LOE = 2b))
Kolodny A, Frieden TR. **Ten Steps the Federal Government Should Take Now to Reverse the Opioid Addiction Epidemic**. JAMA. 2017 Oct 12.

Kolomeyer AM, Yu Y, VanderBeek BL. Association of **Opioids With Incisional Ocular Surgery**. JAMA Ophthalmol. 2019 Sep 19.
Koons AL, Rayl Greenberg M, Cannon RD, et al. **Women and the Experience of Pain and Opioid Use Disorder**: A Literature-based Commentary. Clin Ther. 2018 Jan 9.
Koppen L, Suda KJ, Rowan S, et al. **Dentists' prescribing of antibiotics and opioids to Medicare Part D beneficiaries**: Medications of high impact to public health. J Am Dent Assoc. 2018 Aug;149(8):721-730.
Koren G, Cairns J, Chitayat D, et al. Pharmacogenetics of morphine poisoning in a breastfed neonate of a codeine-prescribed mother. Lancet. 2006 Aug 19;368(9536):704.
Korownyk C, Perry D, Ton J, et al. **Managing opioid use disorder in primary care**. PEER simplified guideline. Can Fam Physician 2019;65:321-30. http://www.cfp.ca/content/cfp/65/5/321.full.pdf
Korthuis PT, McCarty D, Weimer M, et al. **Primary care–based models for the treatment of opioid use disorder**. A scoping review. Ann Intern Med. 2016. [Epub ahead of print]. doi:10.7326/M16-2149
Kosten TR, Graham DP, Nielsen DA. Opioid Use Disorder After Self-medicating Pain From **Traumatic Brain Injury**. JAMA Psychiatry. 2018 Apr 25.
Kosten TR, Graham DP, Nielsen DA. Neurobiology of Opioid Use Disorder and Comorbid **Traumatic Brain Injury**. JAMA Psychiatry. 2018 Apr 25.
Kraft WK, Adeniyi-Jones SC, Chervoneva I, et al. **Buprenorphine** for the Treatment of the **Neonatal Abstinence Syndrome**. N Engl J Med. 2017 May 4.
Kral AH, Davidson PJ. Addressing the Nation's Opioid Epidemic: Lessons from an Unsanctioned **Supervised Injection Site** in the U.S. Am J Preventive Med. 2017.
Krane EJ, Weisman SJ, Walco GA. The **National Opioid Epidemic and the Risk of Outpatient Opioids** in Children. Pediatrics. 2018 Jul 16.
Krans EE and Patrick SW. **Opioid use disorder in pregnancy**: Health policy and practice in the midst of an epidemic. Obstet Gynecol 2016 Jul; 128:4.
Krantz MJ, Martin J, et al. QTc Interval Screening in **Methadone** Treatment. Ann Intern Med. 2009 Jan 19. [Epub ahead of print]
Krebs E, Enns B, Evans E, Urada D, et al. **Cost-effectiveness of publicly funded treatment of opioid use disorder** in California. Ann Intern Med. 2017. [Epub ahead of print]. doi: 10.7326/M17-0611
Krebs EE, Gravely A, Nugent S, et al. Effect of **Opioid vs Nonopioid Medications** on Pain-Related Function in Patients With **Chronic Back Pain or Hip or Knee Osteoarthritis Pain: The SPACE** Randomized Clinical Trial. JAMA. 2018 Mar 6;319(9):872-882.
Krupitsky E, Nunes EV, Ling W, Illeperuma A, et al. **Injectable extended-release naltrexone for opioid dependence**: a double-blind, placebo-controlled, multicentre randomised trial. Lancet 2011; published online April 28. DOI:10.1016/S0140-6736(11)60358-9.
Kubica J, Adamski P, Ostrowska M, et al. **Morphine delays and attenuates ticagrelor** exposure and action in patients with myocardial infarction: the randomized, double-blind, placebo-controlled IMPRESSION trial. Eur Heart J. 2016 Jan 14;37(3):245-52.
Kulak JA, Griswold KS. **Adolescent Substance Use and Misuse**: Recognition and Management Am Fam Physician 2019;99(11): 689-696.
Kurdyak P, Jacob B, Zaheer J, et al. Patterns of **methadone maintenance treatment provision in Ontario**: Policy success or pendulum excess? Can Fam Physician. 2018 Feb;64(2):e95-e103.
Kwatra SG, Ständer S, Kang H. PD-1 **Blockade-Induced Pruritus Treated with a Mu-Opioid Receptor Antagonist**. N Engl J Med. 2018 Oct 18;379(16):1578-1579. (naltrexone)
Lacaze T, O'Flaherty P; **Canadian Paediatric Society**, Fetus & Newborn Committee. **Management of infants born to mothers who have used opioids during pregnancy** (accessed Jan 15, 2018).
Ladapo JA, Larochelle MR, Chen A, et al. Physician Prescribing of Opioids to Patients at Increased Risk of Overdose From Benzodiazepine Use in the United States. JAMA Psychiatry. 2018 Apr 12.
Ladha KS, Gagne JJ, Patorno E, et al. Opioid Overdose After **Surgical Discharge**. JAMA. 2018 Aug 7;320(5):502-504.
Ladha KS, Neuman MD, Broms G, et al. Opioid **Prescribing After Surgery** in the United States, Canada, and Sweden. JAMA Netw Open. 2019 Sep 4;2(9):e1910734.
Lagisetty PA, Healy N, Garpestad C, et al. **Access to Primary Care Clinics for Patients** With Chronic Pain Receiving Opioids. JAMA Netw Open. 2019 Jul 3;2(7):e196928.
Lagisetty PA, Ross R, Bohnert A,et al. **Buprenorphine Treatment Divide by Race/Ethnicity and Payment**. JAMA Psychiatry. 2019 May 8.
Lakha, S. Fatima, Yegneswaran, Balaji, Furlan JC, et al. **Referring patients with chronic noncancer pain to pain clinics**: Survey of Ontario family physicians. Can Fam Physician 2011 57: e106-112.
Lalic S, Gisev N, Simon Bell J, et al. **Predictors of persistent prescription opioid analgesic use** among people without cancer in Australia. Br J Clin Pharmacol. 2018 Feb 16.
Lalic S, Ilomäki J, Bell JS, et al. **Prevalence and incidence of prescription opioid analgesic use in Australia**. Br J Clin Pharmacol. 2018 Oct 19.
Lam J, Kelly L, Ciszkowski C, et al. Central Nervous System Depression of Neonates **Breastfed by Mothers Receiving Oxycodone** for Postpartum Analgesia. J Pediatr. 2011 Aug 31.
Lancaster E, Inglis-Arkell C, Hirose K, et al. **Variability in Opioid-Prescribing Patterns** in Endocrine Surgery and Discordance With Patient Use. JAMA Surg. 2019 Aug 14.
Larach DB, Sahara MJ, As-Sanie S, et al. **Patient Factors Associated with Opioid Consumption** in the Month Following Major Surgery. Ann Surg. 2019 Aug 5.
Larance B, Dobbins T, Peacock A, et al. The effects of a potentially **tamperresistant oxycodone formulation** on opioid use and harm: main findings of the National Opioid Medications Abuse Deterrence (NOMAD) study. Lancet Psychiatry 2018; online Jan 11.
Larochelle MR, Bernson D, Land T, et al. **Medication for opioid use disorder after nonfatal opioid overdose** and association with mortality. A cohort study. Ann Intern Med. 2018. [Epub ahead of print]. doi:10.7326/M17-3107
Larochelle MR, Zhang F, Ross-Degnan D, et al. Rates of **Opioid Dispensing and Overdose** After Introduction of **Abuse-Deterrent** Extended-Release **Oxycodone** and Withdrawal of Propoxyphene. JAMA Intern Med. 2015 Apr 20.
Larochelle MR, Liebschutz JM, Zhang F, Ross-Degnan D, Wharam JF. Opioid prescribing after nonfatal overdose and association with **repeated overdose**. A cohort study. Ann Intern Med. 2016;164:1-9.
Larson JJ, Graham DL, Singer LT, et al. Cognitive and Behavioral Impact on Children Exposed to Opioids During Pregnancy. Pediatrics. 2019 Aug;144(2).
LaRue L, Twillman RK, Dawson E, et al. Rate of Fentanyl Positivity Among Urine Drug Test Results Positive for Cocaine or Methamphetamine. JAMA Netw Open. 2019 Apr 5;2(4):e192851.
Lasser KE. Prescription Opioid Use Among U.S. Adults: Our Brave New World. Ann Intern Med. 2017 Aug 1.
Latif ZE, Šaltyte Benth J, Solli KK, et al. **Anxiety, Depression, and Insomnia Among Adults With Opioid Dependence** Treated With Extended-Release Naltrexone vs Buprenorphine-Naloxone: A Randomized Clinical Trial and Follow-up Study. JAMA Psychiatry. 2018 Dec 19.
Lavalley J, Kastor S, Valleriani J, et al. **Reconciliation and Canada's overdose crisis**: responding to the needs of Indigenous Peoples. CMAJ. 2018 Dec 17;190(50):E1466-E1467.
Lavonas EJ, Banner W, Bradt P, et al. **Root Causes, Clinical Effects, and Outcomes of Unintentional Exposures to Buprenorphine** by Young Children. J Pediatr. 2013 Aug 22.

Lee JD et al. Extended-release **naltrexone** to prevent opioid relapse in ex-prisoners (**criminal justice offenders**). N Engl J Med 2016 Mar 31; 374:1232.
Lee JD, Nunes EV, Novo P, et al. Comparative effectiveness of **extended-release naltrexone versus buprenorphine-naloxone for opioid relapse prevention (X:BOT)**: a multicentre, open-label, randomized controlled trial. Lancet 2017; online Nov 14.
Lee JS, et al. **Postoperative Opioid Prescribing and the Pain Scores** on Hospital Consumer Assessment of Healthcare Providers and Systems Survey. JAMA. 2017 May 16;317(19):2013-2015
Leece P, Orkin AM, Kahan M. **Tamper-resistant drugs** cannot solve the opioid crisis. CMAJ. 2015 Jul 14;187(10):717-8.
Lembke A, Humphreys K, Newmark J. **Weighing the Risks and Benefits of Chronic Opioid Therapy**. Am Fam Physician. 2016;93(12):982-990.
Leonard J, Baker DE. **Naloxegol**: Treatment for Opioid-Induced Constipation in Chronic Non-Cancer Pain. Ann Pharmacother. 2015 Mar;49(3):360-365.
Lerner AM, Fauci AS. Opioid Injection in Rural Areas of the United States: A Potential **Obstacle to Ending the HIV Epidemic**. JAMA. 2019 Aug 1.
Leshner AI, Dzau VJ. **Medication-Based Treatment** to Address Opioid Use Disorder. JAMA. 2019 May 2.
Letourneau LM, Ritzo J, Shonk R, et al. **Supporting Physicians and Practice Teams** in Efforts to Address the Opioid Epidemic. Ann Fam Med. 2019 Aug 12;17(Suppl 1):S77-S81.
Leung PTM, Macdonald EM, Stanbrook MB, et al. A **1980 Letter on the Risk of Opioid Addiction**. N Engl J Med. 2017 Jun 1;376(22):2194-2195.
Levy S. **Youth and the Opioid Epidemic**. Pediatrics. 2019 Jan 2.
Li Y,et al. Association of **Preoperative Narcotic Use** With **Postoperative Complications** and Prolonged Length of Hospital Stay in Patients With Crohn Disease. JAMA Surg. 2016 Aug 1;151(8):726-34
Li RJ, Loyo Li M, Leon E, et al. Comparison of **Opioid Utilization Patterns After Major Head and Neck Procedures Between Hong Kong and the United States**. JAMA Otolaryngol Head Neck Surg. 2018 Sep 6.
Liang TJ, Ward JW. **Hepatitis C in Injection-Drug Users - A Hidden Danger of the Opioid Epidemic**. N Engl J Med. 2018 Mar 29;378(13):1169-1171.
Liebschutz JM, Crooks D, Herman D, et al. **Buprenorphine** treatment for hospitalized, opioid-dependent patients: a randomized clinical trial [online June 30, 2014]. JAMA Intern Med.
Liebschutz JM, et al. **Improving Adherence to Long-term Opioid Therapy Guidelines** to Reduce Opioid Misuse in Primary Care: A Cluster-Randomized Clinical Trial. JAMA Intern Med. 2017 Jul 17.
Lin DH, Lucas E, et al. **Financial Conflicts of Interest** and the **Centers for Disease Control and Prevention's 2016 Guideline** for Prescribing Opioids for Chronic Pain. JAMA Intern Med. 2017 Jan 17.
Lind JN, Interrante JD, Ailes ED, et al. Maternal Use of **Opioids During Pregnancy and Congenital Malformations**: A Systematic Review. Peds. 2017;139(6):e20164131
Ling Walter; Casadonte P; Bigelow G, et al. **Buprenorphine Implants** for Treatment of Opioid Dependence: A Randomized Controlled Trial. JAMA. 2010;304(14):1576-1583.
Lisonkova S, Richter LL, Ting J, et al. **Neonatal Abstinence Syndrome** and Associated Neonatal and Maternal Mortality and Morbidity. Pediatrics. 2019 Jul 12.
Lo-Ciganic WH, Huang JL, Zhang HH, et al. Evaluation of Machine-Learning **Algorithms for Predicting Opioid Overdose Risk** Among Medicare Beneficiaries With Opioid Prescriptions. JAMA Netw Open. 2019 Mar 1;2(3):e190968.
Lofwall MR, Walsh SL, Nunes EV, et al. Weekly and Monthly Subcutaneous Buprenorphine Depot Formulations vs Daily Sublingual Buprenorphine With Naloxone for Treatment of Opioid Use Disorder: A Randomized Clinical Trial. JAMA Intern Med. 2018 May 14.
Lovecchio F, Derman P, Stepan J, et al. Support for **Safer Opioid Prescribing Practices**: A Catalog of Published Use After Orthopaedic Surgery. J Bone Joint Surg Am. 2017 Nov 15;99(22):1945-1955.
Lovegrove MC, Mathew J, Hampp C, et al. Emergency Hospitalizations for Unsupervised Prescription Medication **Ingestions by Young Children**. Pediatrics. 2014 Sep 15. (buprenorphine & clonidine concerning)
Lowenstein M, Grande D, Delgado MK. Opioid Prescribing **Limits for Acute Pain** -Striking the Right Balance. N Engl J Med. 2018 Aug 9;379(6):504-506.
Lucyk S, Nelson L. Consequences of **unsafe prescribing of transdermal fentanyl**. CMAJ. 2016 Jun 14;188(9):638-9.
Lukasewycz S, Holman M, Kozlowski P, et al. Does a **perioperative belladonna and opium suppository** improve postoperative pain following robotic assisted laparoscopic radical prostatectomy? Results of a single institution randomized study. Can J Urol. 2010 Oct;17(5):5377-82.
Lutfiyya MN, Gross AJ, Schvaneveldt N, et al. A scoping review exploring the **opioid prescribing practices of US dental professionals**. J Am Dent Assoc. 2018 Dec;149(12):1011-1023.
Luthra P, Burr NE, Brenner DM, et al. Efficacy of **pharmacological therapies for the treatment of opioid-induced constipation**: systematic review and network meta-analysis. Gut. 2018 May 5.
Lynch M. A review of the use of methadone for the treatment of noncancer pain. Pain Res Manage 2005;10(3):133-44.
MacArthur GJ, Minozzi S, Martin N, et al. **Opiate substitution treatment and HIV transmission** in people who inject drugs: systematic review and meta-analysis. BMJ 2012;345:e5945.
MacMillan KDL, Rendon CP, Verma K, et al. Association of **Rooming-in With Outcomes for Neonatal Abstinence Syndrome**: A Systematic Review and Meta-analysis. JAMA Pediatr. 2018 Feb 5.
Madadi P, Moretti M, Djokanovic N, Bozzo P, et al. Guidelines for **maternal codeine** use during breastfeeding. Can Fam Physician. 2009 Nov;55(11):1077-8.
Madadi P, Koren G, et al. Safety of **codeine during breastfeeding**. Canadian Family Physician. Vol 53 Jan 2007 p33-35..
Maeda A, Bateman BT, Clancy CR, Creanga AA, et al. **Opioid Abuse and Dependence during Pregnancy**: Temporal Trends and Obstetrical Outcomes. Anesthesiology. 2014 Dec;121(6):1158-65.
Mailis-Gagnon, Angela, Lakha, S. Fatima, Ou, Ting, et al. Chronic noncancer pain: **Characteristics of patients prescribed opioids** by community physicians and referred to a tertiary pain clinic. Can Fam Physician 2011 57: e97-105.
Manchikanti L, Abdi S, Atluri S, Balog CC, et al. American Society of Interventional Pain Physicians (**ASIPP**) guidelines for **responsible opioid prescribing** in chronic non-cancer pain: part 2 - guidance. Pain Physician 2012 Jul;15(3 Suppl):S67-S116.
Manterola C, Astudillo P, Losada H, Pineda V, Sanhueza A, Vial M. Analgesia in patients with **acute abdominal pain**. In: Cochrane database of systematic reviews [database online]. Malden (MA): Wiley Interscience; 2009. Issue 2. Avail: http://mrw.interscience.wiley.com/cochrane/clsysrev/articles/CD005660/pdf_fs.html
Mark J, Argentieri DM, Gutierrez CA, et al. **Ultrarestrictive opioid prescription protocol** for pain management after gynecologic and abdominal surgery. JAMA Netw Open. 2018;1(8):e185452. doi:10.1001/jamanetworkopen.2018.5452
Mark TL, Parish W, Zarkin GA. Association Between Medicare and FDA Policies and Prior Authorization **Requirements for Buprenorphine Products** in Medicare Part D Plans. JAMA. 2019 Jul 9;322(2):166-167.

Marsch LA, et al. Comparison of pharmacological treatments for **opioid-dependent** adolescents: a randomized controlled trial. Arch Gen Psychiatry. 2005 Oct;62(10):1157-64.
Martin J, Cunliffe J, Décary-Hétu D, et al. Effect of **restricting the legal supply of prescription opioids** on buying through online illicit marketplaces: interrupted time series analysis. BMJ. 2018 Jun 13;361:k2270.
Martins SS, Sarvet A, Santaella-Tenorio J, et al. Changes in **US Lifetime Heroin Use** and Heroin Use Disorder: Prevalence From the 2001-2002 to 2012-2013 National Epidemiologic Survey on Alcohol and Related Conditions. JAMA Psychiatry. 2017 Mar 29.
Martyn JAJ, Mao J, Bittner EA. Opioid **Tolerance in Critical Illness**. N Engl J Med. 2019 Jan 24;380(4):365-378.
Mattick RP, Kimber J, Breen C, Davoli M. **Buprenorphine** maintenance versus placebo or **methadone** maintenance for opioid dependence. Cochrane Database Syst Rev. 2008 Apr 16;(2):CD002207. Buprenorphine is an effective intervention for use in the maintenance treatment of heroin dependence, but it is less effective than methadone delivered at adequate dosages.
Mattick RP, BreenC, Kimber J,DavoliM. **Buprenorphine maintenance versus placebo or methadone** maintenance for opioid dependence. Cochrane Database of Systematic Reviews 2014, Issue 2. Art.No.: CD002207. DOI: 10.1002/14651858.CD002207.pub4.
Maughan BC, Hersh EV, Shofer FS, et al. **Unused opioid analgesics and drug disposal** following outpatient **dental surgery**: A randomized controlled trial. Drug Alcohol Depend. 2016 Sep 16.
Mazer-Amirshahi M, Mullins PM, Rasooly I, et al. **Rising Opioid Prescribing in Adult U.S. Emergency Department Visits**: 2001-2010. Acad Emerg Med. 2014 Mar;21(3):236-243.
McCarthy M. How **inappropriate prescribing prompted the opioid addiction** ravaging small town America. BMJ. 2017 Oct 19;359:j4730.
McCowan C, Kidd B, Fahey T. Factors associated with **mortality** in Scottish patients receiving **methadone** in primary care: retrospective cohort study. BMJ 2009;338:b2225, doi: 10.1136/bmj.b2225 (Published 17 June 2009)
McCoy MS, Kanter GP. Campaign Contributions From **Political Action Committees** to Members of Congressional Committees Responding to the **Opioid Crisis**. JAMA. 2018 Sep 6.
MacDonald N, MacLeod SM. Has the **time come to phase out codeine**? CMAJ. 2010 Nov 23;182(17):1825.
McCabe SE et al. Trends in **medical and nonmedical use of prescription opioids** among **US adolescents**: 1976–2015. Pediatrics 2017 Mar 20.
McDonald DC, Carlson KE. Estimating the **prevalence of opioid diversion** by "doctor shoppers" in the United States. PLoS One. 2013 Jul 17;8(7):e69241.
McDonald EM, Kennedy-Hendricks A, McGinty EE, et al. **Safe Storage of Opioid** Pain Relievers Among Adults Living in Households With Children. Pediatrics. 2017 Feb 20.
McLellan AT. New Department of **Veterans Affairs and Department of Defense Guidelines on Pain Management With Opioids**: Comment and Concern. Ann Intern Med. 2017 May 30
McNicol ED, Midbari A, Eisenberg E. **Opioids for neuropathic pain**. Cochrane Database Syst Rev. 2013 Aug 29;8:CD006146. doi: 10.1002/14651858.CD006146.pub2. Since the last version of this review, new studies were found providing additional information. Data were reanalyzed but the results did not alter any of our previously published conclusions. Short-term studies provide only equivocal evidence regarding the efficacy of opioids in reducing the intensity of neuropathic pain. Intermediate-term studies demonstrated significant efficacy of opioids over placebo, but these results are likely to be subject to significant bias because of small size, short duration, and potentially inadequate handling of dropouts. Analgesic efficacy of opioids in chronic neuropathic pain is subject to considerable uncertainty.
McPherson C, Haslam M, Pineda R, et al. **Brain Injury and Development in Preterm Infants Exposed to Fentanyl**. Ann Pharmacother. 2015 Dec;49(12):1291-7.
McQueen K, Murphy-Oikonen J. **Neonatal Abstinence Syndrome**. N Engl J Med. 2016 Dec 22;375(25):2468-2479.
Meara E, Horwitz JR, Powell W, McClelland et al.State **Legal Restrictions** and Prescription-Opioid Use among **Disabled** Adults. N Engl J Med. 2016 Jun 22.
Medical Letter: **Treatment guidelines. Drugs for Pain**. April 2007; April 2010. **April 2013.**
Medical Letter. A Morphine/Naltrexone Combination (**Embeda**) for pain. Mar 22, 2010.
Megale RZ, Deveza LA, Blyth FM, et al. Efficacy and Safety of Oral and **Transdermal Opioid Analgesics for Musculoskeletal Pain** in Older Adults: A Systematic Review of Randomized, Placebo-Controlled Trials. J Pain. 2018 May;19(5):475.e1-475.e24.
Mehra MR, Jarcho JA, Cherikh W, et al. The **Drug-Intoxication Epidemic and Solid-Organ Transplantation**. N Engl J Med. 2018 May 17;378(20):1943-1945.
Meisel ZF, Lupulescu-Mann N, Charlesworth CJ, et al. **Conversion to Persistent or High-Risk Opioid Use** After a New Prescription From the Emergency Department: Evidence From Washington Medicaid Beneficiaries. Ann Emerg Med. 2019 Jun 20.
Meisenberg BR, Grover J, Campbell C, et al. Assessment of **Opioid Prescribing Practices Before and After Implementation of a Health System Intervention to Reduce Opioid Overprescribing**. *JAMA Netw Open.*2018;1(5):e182908.
Methadone: a focus on safety. Pharmacist's Letter Sept 2006. (FDA Nov/06 warning http://www.fda.gov/cder/drug/InfoSheets/HCP/methadoneHCP.htm)
Michael SS, et al. Effect of a Data-Driven Intervention on **Opioid Prescribing Intensity Among Emergency Department Providers**: A Randomized Controlled Trial. Acad Emerg Med. 2018 Mar 2.
Michna E, Blonsky ER, Schulman S, et al. **Subcutaneous methylnaltrexone** for treatment of opioid-induced constipation in patients with chronic, nonmalignant pain: a randomized controlled study. J Pain. 2011 May;12(5):554-62.
Miech R, Johnston L, O'Malley PM, et al. **Prescription Opioids in Adolescence and Future Opioid Misuse**. Pediatrics. 2015 Oct 26.
Miller M, Sturmer T, Azrael D, et al. Opioid analgesics and the **risk of fractures** in older adults with arthritis. J Am Geriatr Soc. 2011 Mar;59(3):430-8.
Miller M, Barber CW, Leatherman S, et al. **Prescription Opioid Duration of Action** and the Risk of Unintentional Overdose Among Patients Receiving Opioid Therapy. JAMA Intern Med. 2015 Feb 16.
Milloy MJ, Wood E. **Withdrawal from methadone in US prisons**: cruel and unusual? Lancet. 2015 May 28.
Moe-Byrne T, Brown JVE, McGuire W. **Naloxone for opioid-exposed newborn infants**. Cochrane Database Syst Rev. 2018 Oct 12;10:CD003483. The existing evidence from randomised controlled trials is insufficient to determine whether naloxone confers any important benefits to newborn infants with cardiorespiratory or neurological depression that may be due to intrauterine exposure to opioid. Given concerns about the safety of naloxone in this context, it may be appropriate to limit its use to randomised controlled trials that aim to resolve these uncertainties.
Moeller SJ et al. Behavioral preference for viewing drug v. **pleasant images predicts current and future opioid misuse** among chronic pain patients. Psychol Med 2019 Apr 15.
Molero Y, Zetterqvist J, Binswanger IA, et al. Medications for Alcohol and Opioid Use Disorders and Risk of Suicidal Behavior, Accidental Overdoses, and Crime. Am J Psychiatry. 2018 Aug 2:appiajp201817101112.
Monarrez-Espino J, et al. New opioid analgesic use and the risk of injurious **single-vehicle crashes** in drivers aged 50-80 years: population-based matched case-control study. Age Ageing. 2016 Jul 26.

Montandon G, Slutsky AS. Solving the Opioid Crisis: **Respiratory Depression by Opioids as Critical Endpoint**. Chest. 2019 Jun 10.
Moore K, Magee M, Sevinsky H, et al. **Methadone and buprenorphine** pharmacokinetics and pharmacodynamics when coadministered with **fostemsavir** to opioid-dependent, HIV-seronegative participants. Br J Clin Pharmacol. 2019 Apr 13.
Moore PA, et al. Benefits & harms associated with **analgesic medications used in management of acute dental pain**: overview of systematic reviews. J Am Dent Assoc. 2018 Apr;149(4):256-265.e3.
Mora B, et al. Transcutaneous electrical nerve stimulation: an effective treatment for pain caused by renal colic in emergency care. J Urol. 2006 May;175(5):1737-41; discussion 1741. (InfoPOEMs: Local transcutaneous electrical nerve stimulation (TENS) is a rapid and effective nondrug treatment for pain caused by renal colic. TENS may be most useful in the difficult circumstance of out-of-hospital rescue. (LOE = 1b))
Morales KB, Park JN, Glick JL, et al. **Preference for drugs containing fentanyl** from a cross-sectional survey of people who use illicit opioids in three United States cities. Drug Alcohol Depend. 2019 Aug 23;204:107547.
Mordecai L, Reynolds C, Donaldson LJ, et al. **Patterns of regional variation of opioid prescribing in primary care in England**: a retrospective observational study. Br J Gen Pract. 2018 Feb 12.
Morice AH, Menon MS, Mulrennan SA, et al. Opiate therapy in **chronic cough**. Am J Respir Crit Care Med 2007; 175: 312–15.
Morrow RL, Bassett K, Wright JM, et al. Influence of opioid prescribing standards on **drug use among patients with long-term opioid use**: a longitudinal cohort study. CMAJ Open. 2019 Jul 25;7(3):E484-E491.
Moshfegh J, George SZ, Sun E. **Risk and Risk Factors for Chronic Opioid Use Among Opioid-Naive Patients** With **Newly Diagnosed Musculoskeletal** Pain in the Neck, Shoulder, Knee, or Low Back. Ann Intern Med. 2018 Dec 18.
Moyo P, Zhao X, Thorpe CT, et al. **Dual receipt of prescription opioids** from the Department of Veterans Affairs and Medicare Part D and prescription opioid overdoses among veterans. A nested case–control study. Ann Intern Med. 2019. [Epub ahead of print]. doi:10.7326/M18-2574
Munch T, Christiansen CF, Pedersen L, et al. Impact of **Preadmission Opioid Treatment on 1-Year Mortality Following Nonsurgical Intensive Care**. Crit Care Med. 2018 Mar 9.
Murthy VH. Ending the **Opioid Epidemic** - A Call to Action. N Engl J Med. 2016 Nov 9.
Murphy SM, McCollister KE, Leff JA, , et al. Cost-effectiveness of **buprenorphine-naloxone versus extendedrelease naltrexone** to prevent opioid relapse. Ann Intern Med. 2018.[Epub ahead of print].
Muvvala SB, Edens EL, Petrakis IL. **What Role Should Psychiatrists Have** in Responding to the Opioid Epidemic? JAMA Psychiatry. 2018 Nov 28.
Mylonas KS, Reinhorn M, et al. Patient-reported **opioid analgesic requirements after elective inguinal hernia repair**: A call for procedure-specific opioid-administration strategies. Surgery. 2017 Aug 1
Nagpal G, Heiman H, Haymond S. **Interpretation of Urine Drug Screens**: Metabolites and Impurities. JAMA. 2017 Nov 7;318(17):1704-1705.
Narjoux G, Clarenne J, Azzouz B, et al. **Nightmares and hallucinations with aprepitant and opium powder**: a suspected drug-drug interaction. Br J Clin Pharmacol. 2018 Nov 26.
Nee J, Zakari M, Sugarman MA, et al. Efficacy of **Treatments for Opioid-induced Constipation**: A Systematic Review and Meta-Analysis. Clin Gastroenterol Hepatol. 2018 Jan 25.
Neuman MD, Bateman BT, Wunsch H. **Inappropriate opioid prescription after surgery**. Lancet. 2019 Apr 13;393(10180):1547-1557.
Nicholas B. King, Veronique Fraser, et al. Determinants of Increased **Opioid-Related Mortality** in the United States and Canada, 1990–2013: A Systematic Review. *American Journal of Public Health*, 2014; e1-11
NICE: National Institute for Health and Care Excellence. **Controlled drugs**: safe use and management. London (UK): National Institute for Health and Care Excellence (NICE); 2016 Apr 12.
Nicholson B. Morphine sulfate extended-release capsules (Kadian) for the treatment of chronic, moderate-to-severe pain. Expert Opin Pharmacother. 2008 Jun;9(9):1585-94.
Nicholson AB. Methadone for cancer pain. **Cochrane** Database Syst Rev. 2007 Oct 17;(4):CD003971.
Nielsen S, Larance B, Degenhardt L, et al. **Opioid agonist treatment for pharmaceutical opioid dependent people**. Cochrane Database Syst Rev. 2016 May 9;5:CD011117. There was low to moderate quality evidence supporting the use of maintenance agonist pharmacotherapy for pharmaceutical opioid dependence. Methadone or buprenorphine appeared equally effective. Maintenance treatment with buprenorphine appeared more effective than detoxification or psychological treatments.Due to the overall low to moderate quality of the evidence and small sample sizes, there is the possibility that the further research may change these findings.
Nielsen S, Larance B, Lintzeris N. **Opioid Agonist Treatment** for Patients With **Dependence on Prescription Opioids**. JAMA. 2017 Mar 7;317(9):967-968
Nisavic M, Flores EJ, Heng M, et al. Case 26-2019: A 27-Year-Old Woman with Opioid Use Disorder and **Suicidal Ideation**. N Engl J Med. 2019 Aug 22;381(8):763-771.
Noormohammadi A, Forinash A, Yancey A, et al. **Buprenorphine Versus Methadone** for Opioid Dependence in Pregnancy. Ann Pharmacother. 2016 Aug;50(8):666-72.
Nuckols TK, Anderson L, Popescu I, et al. **Opioid Prescribing**: A Systematic Review and Critical Appraisal of Guidelines for Chronic Pain. Ann Intern Med. 2013 Nov 12.
Nüesch E, Rutjes AW, Husni E, Welch V, Jüni P. Oral or transdermal opioids for osteoarthritis of the knee or hip. Cochrane Database Syst Rev. 2009 Oct 7;(4):CD003115. The small to moderate beneficial effects of non-tramadol opioids are outweighed by large increases in the risk of adverse events. Non-tramadol opioids should therefore not be routinely used, even if osteoarthritic pain is severe.
Oei JL, Melhuish E, Uebel H, et al. **Neonatal Abstinence Syndrome** and High School Performance. Pediatrics. 2017 Jan 16.
O'Hara NN, Pollak AN, Welsh CJ, et al. **Factors Associated With Persistent Opioid Use Among Injured Workers' Compensation Claimants**. JAMA Netw Open. 2018;1(6):e184050.
Okie, Susan. A Flood of Opioids, a **Rising Tide of Deaths**. N Engl J Med 2010; 363:1981-1985
Olds C, Spataro E, Li K, et al. Assessment of **Persistent and Prolonged Postoperative Opioid Use** Among Patients Undergoing Plastic and Reconstructive Surgery.JAMA Facial Plast Surg.2019 Mar 7.
Olfson M, Crystal S, Wall M, et al. Causes of **Death After Nonfatal Opioid Overdose**. JAMA Psychiatry. 2018 Jun 20.
Olfson M, Wall MM, Liu SM, Blanco C. **Cannabis Use and Risk of Prescription Opioid Use Disorder** in the United States. Am J Psychiatry. 2017 Sep 26:appiajp201717040413.
Olfson M, Wall M, Wang S, et al. **Service Use Preceding Opioid-Related Fatality**. Am J Psychiatry. 2017 Nov 28:appiajp201717070808.
Oosten AW, Oldenmenger WH, Mathijssen RH, et al. A Systematic Review of Prospective Studies Reporting **Adverse Events of Commonly Used Opioids for Cancer**-Related Pain: A Call for the Use of Standardized Outcome Measures. J Pain. 2015 Oct;16(10):935-46.
Opdal MS, Arnesen M, Müller LD, et al. Effects of **Hemodialysis on Methadone Pharmacokinetics and QTc**. Clin Ther. 2015 May 8.
Opioid Therapy for Chronic Pain Work Group. **VA/DoD** clinical practice guideline for opioid therapy for chronic pain. Version 3.0. Washington (DC): Department of Veterans Affairs, Department of Defense; 2017 Feb.
Orliaguet G, Hamza J, Couloigner Vet al. A Case of Respiratory Depression in a Child With **Ultrarapid CYP2D6 Metabolism After Tramadol**. Pediatrics. 2015 Mar;135(3):e753-5.

Osmundson SS et al. **Postdischarge opioid** use after **cesarean** delivery. Obstet Gynecol 2017 Jul; 130:36.
Oviedo-Joekes, Eugenia, Brissette, Suzanne, Marsh, David C., et al. **Diacetylmorphine** versus Methadone for the Treatment of Opioid Addiction. N Engl J Med 2009 361: 777-786
Oviedo-Joekes E, Guh D, Brissette S, et al. **Hydromorphone compared with diacetylmorphine** for long-term opioid dependence: a randomized clinical trial [online April 6, 2016].JAMA Psychiatry.
Paice JA, Portenoy R, et al. Management of **Chronic Pain in Survivors of Adult Cancers**: American Society of Clinical Oncology (**ASCO**) Clinical Practice Guideline. J Clin Oncol. 2016 Jul 25.
Papaleontiou M, Henderson CR Jr, Turner BJ, et al. Outcomes associated with opioid use in the treatment of chronic **noncancer pain in older adults**: a systematic review and meta-analysis. J Am Geriatr Soc. 2010 Jul;58(7):1353-69.
Parker CM, Hirsch JS, Hansen HB, et al. Facing **Opioids in the Shadow of the HIV Epidemic**. N Engl J Med. 2019 Jan 3;380(1):1-3.
Patanwala AE, Duby J, Waters D, Erstad BL. **Opioid conversions** in acute care. Ann Pharmacother. 2007 Feb;41(2):255-66. Epub 2007 Feb 13. Review. Erratum in: Ann Pharmacother. 2007 Mar;41(3):531. Access online at: http://www.theannals.com/cgi/content/abstract/41/2/255
Patanwala AE, Holmes KL, Erstad BL. Analgesic response to **morphine in obese** and morbidly obese patients in the emergency department. Emerg Med J. 2013 Jan 12.
Patel S, Sturm A, Bobian M, et al. **Opioid Use by Patients After Rhinoplasty**. JAMA Facial Plast Surg. 2017 Nov 9.
Pathan SA, Mitra B, Cameron PA. A Systematic Review and Meta-analysis Comparing the Efficacy of **Nonsteroidal Anti-inflammatory Drugs, Opioids, and Paracetamol** in the Treatment of **Acute Renal Colic**. Eur Urol. 2017 Nov 21.
Patrick SW, Schumacher RE, Benneyworth BD, et al. **Neonatal abstinence syndrome** and associated health care expenditures: United States, 2000-2009 [published online April 30, 2012]. JAMA.
Patrick SW, Dudley J, Martin PR, et al. **Prescription Opioid Epidemic and Infant Outcomes**. Pediatrics. 2015 Apr 13.
Patrick SW, Faherty LJ, Dick AW, et al. Association among county-level economic factors, clinician supply, metropolitan or rural location, and **neonatal abstinence syndrome**.JAMA. doi:10.1001/jama.2018.20851
Patrick SW, Schiff DM; Committee on Substance Use and Prevention. A Public Health Response to **Opioid Use in Pregnancy**. Pediatrics. 2017 Feb 20.
Peltz G, Südhof TC. The **Neurobiology of Opioid Addiction** and the **Potential for Prevention Strategies**. JAMA. 2018 Apr 26.
Pergolizzi J, Aloisi AM, Dahan A, et al. Current knowledge of **buprenorphine** and its unique pharmacological profile. Pain Pract.2010 Sep-Oct;10(5):428-50.
Pergolizzi JV, Varrassi G, Paladini A, LeQuang J. **Stopping or Decreasing Opioid Therapy** in Patients on Chronic Opioid Therapy. Pain Ther. 2019 Aug 3.
Peters PJ, Pontones P, Hoover KW, et al. **HIV Infection** Linked to Injection Use of **Oxymorphone** in Indiana, 2014-2015. N Engl J Med. 2016 Jul 21;375(3):229-39
Pharmacist's Letter Oct 2006. Alternative or Off-label Routes of Drug Administration. (Rectal administration of: Ms Contin, OxyContin; Sublingual administration of: methadone, fentanyl & buprenorphine; Inhalational use of morphine, hydromorphone & fentanyl)
Pharmacist's Letter **Suboxone** (buprenorphine / naloxone 2/0.5mg & 8/2mg sl tabs) Dec 2007.
Pharmacist's Letter. **Onsolis** (Fentanyl Buccal Film) and **BuTrans** (Buprenorphine Patch). Aug 2010.
Phillips RH, Salzman M, Haroz R, et al. **Elective Naloxone-Induced Opioid Withdrawal** for Rapid Initiation of Medication-Assisted Treatment of Opioid Use Disorder. Ann Emerg Med. 2019 Feb 14.
Piirainen P, Kokki H, Hautajärvi H, et al. The analgesic efficacy and pharmacokinetics of **epidural oxycodone after gynaecological laparotomy**: a randomized, double-blind, double-dummy comparison with intravenous administration. Br J Clin Pharmacol. 2018 May 21.
Poelaert J, Koopmans-Klein G, Dioh A, et al. Treatment With Prolonged-Release **Oxycodone/Naloxone** Improves Pain Relief and Opioid-Induced Constipation Compared With Prolonged-Release Oxycodone in Patients With Chronic Severe Pain and Laxative-Refractory Constipation. Clin Ther. 2015 Mar 7.
Podolsky SH, Herzberg D, Greene JA. **Preying on Prescribers (and Their Patients)** - Pharmaceutical Marketing, Iatrogenic Epidemics, and the Sackler Legacy. N Engl J Med. 2019 May 9;380(19):1785-1787.
Pollini RA, Waehrer G, Kelley-Baker T. **Receipt of Warnings Regarding Potentially Impairing Prescription Medications** and Associated Risk Perceptions in a National Sample of U.S. Drivers. J Stud Alcohol Drugs. 2017 Nov;78(6):805-813.
Pontes C, Marsal JR, Elorza JM, et al.**Analgesic Use and Risk for Acute Coronary Events in Patients With Osteoarthritis**: A Population-based, Nested Case-control Study. Clin Ther. 2018 Feb 2.
Poon S, Pupco A, Koren G et al. Motherisk Update: Safety of the newer class of opioid antagonists in pregnancy. Canadian Family Physician. 2014; 60:631-632.
Poonai N, Bhullar G, Lin K, et al. Oral administration of **morphine versus ibuprofen to manage postfracture pain in children**: a randomized trial. CMAJ. 2014 Oct 27.
Poonai N, Paskar D, Konrad SL, et al. Opioid analgesia for **acute abdominal pain** in children: A systematic review and meta-analysis. Acad Emerg Med. 2014 Nov;21(11):1183-92.
Poonai N, et al. **Oral morphine versus ibuprofen** administered at home for **postoperative orthopedic pain in children**: a randomized controlled trial. CMAJ.2017 Oct 10;189(40):E1252-E1258.
Post S, Spiller HA, Casavant MJ, et al. **Buprenorphine Exposures Among Children and Adolescents** Reported to US Poison Control Centers. Pediatrics. 2018 Jun 25.
Prabhu M et al. A shared decision-making intervention to guide **opioid** prescribing after **cesarean** delivery. Obstet Gynecol 2017 Jul; 130:42.
Probst C, Rehm J. Alcohol use, opioid overdose and socioeconomic status in Canada: **A threat to life expectancy**? CMAJ. 2018 Nov 5;190(44):E1294-E1295.
Provenzano AM. Caring for Ms. L. - **Overcoming My Fear of Treating Opioid Use Disorder**. N Engl J Med. 2018 Feb 15;378(7):600-601.
Pryor JR, Maalouf FI, et al. The **opioid epidemic and neonatal abstinence syndrome** in the USA: a review of the continuum of care. Arch Dis Child Fetal Neonatal Ed. 2017 Mar;102(2):F183-F187.
Psaty BM, Merrill JO. **Addressing the Opioid Epidemic - Opportunities in the Postmarketing Setting**. N Engl J Med. 2017 Apr 20;376(16):1502-1504.
Puzantian T, Gasper JJ. Provision of **Naloxone Without a Prescription** by California Pharmacists **2 Years After** Legislation Implementation. JAMA. 2018 Nov 13;320(18):1933-1934.
Quinn PD, et al. Incident & **long-term opioid therapy among patients with psychiatric conditions and medications**: national study of commercial health care claims. Pain. 2017 Jan;158(1):140-148.
Quinn PD, et al. Association of **mental health conditions** & treatments with long-term opioid analgesic receipt among adolescents [Mar 12/18]. JAMA Pediatr. doi:10.1001/jamapediatrics.2017.5641
Qureshi WT, O'Neal WT, Khodneva Y, et al. Association Between **Opioid Use and Atrial Fibrillation**: The Reasons for Geographic and Racial Differences in Stroke (REGARDS) Study. JAMA Intern Med. 2015 Apr 27.

Raebel MA, Newcomer SR, Reifler LM, et al. Chronic use of **opioid medications before and after bariatric surgery**. JAMA. doi:10.1001/jama.2013.278344.
Racoosin JA, Roberson DW, Pacanowski MA et al. New Evidence about an Old Drug - **Risk with Codeine after Adenotonsillectomy**. N Engl J Med. 2013 Apr 24.
Raffa RB, Pergolizzi JV Jr. **Opioid formulations designed to resist/deter abuse**. Drugs. 2010 Sep 10;70(13):1657-75. doi: 10.2165/11537940-000000000-00000.
Raghunathan K, Ray N, Bryan W, et al. Trends in **Chronic Opioid Use Around Inpatient Surgery** Within the Veterans Health Administration. JAMA Surg. 2019 Sep 18.
Rahmati A, Shakeri R, Khademi H, et al. **Mortality from respiratory diseases associated with opium use**: a population-based cohort study. Thorax. 2016 Nov 24.
Raja AS, Miller ES, Flores EJ, et al. Case 37-2017. A 36-Year-Old Man with **Unintentional Opioid Overdose**. N Engl J Med. 2017 Nov 30;377(22):2181-2188.
Rakhman Evgeny, Shmain Dmitri, White Ian, et al. Repeated and Escalating Preoperative **Subanesthetic Doses of Ketamine** for Postoperative Pain Control in Patients Undergoing Tumor Resection: A Randomized, Placebo-Controlled, Double-Blind Trial, Clinical Therapeutics, In Press, Corrected Proof, Available online 1 July 2011
Raleigh MF. **Buprenorphine Maintenance vs. Placebo for Opioid Dependence**. Am Fam Physician. 2017 Mar 1;95(5):Online.
Ranji SR, Goldman LE, Simel DL, Shojania KG. Do opiates affect the clinical **evaluation** of patients with **acute abdominal pain**? JAMA. 2006 Oct 11;296(14):1764-74.
(InfoPOEMs: Opiate analgesia for adults and children presenting with acute abdominal pain may alter the physical examination, but does not increase the risk of management errors. Since most patients prefer pain control, it makes sense to abandon the outdated and incorrect practice of withholding opiate analgesia from patients with acute abdominal pain. (LOE = 1a))
Rauck RL, Potts J, Xiang Q, et al. Efficacy and tolerability of **buccal buprenorphine** in opioid-naive patients with moderate to severe chronic low back pain. Postgrad Med. 2016 Jan;128(1):1-11.
Ray WA, Chung CP, Murray KT, et al. **Out-of-Hospital Mortality Among Patients Receiving Methadone for Noncancer Pain**. JAMA Intern Med. 2015 Jan 19.
Ray WA, Chung CP, Murray KT, et al. Out-of-Hospital **Mortality** Among Patients Receiving **Methadone** for Noncancer Pain. JAMA Intern Med. 2015 Mar 1;175(3):420-7.
Ray WA, Chung CP, Murray KT, et al. **Prescription of Long-Acting Opioids and Mortality** in Patients With Chronic Noncancer Pain. JAMA. 2016 Jun 14;315(22):2415-23.
Redding SE, Liu S, Hung WW, Boockvar KS. Opioid interruptions, pain, and withdrawal symptoms in **nursing home residents**. Clin Ther. 2014 Nov 1;36(11):1555-63.
Reddy RG, Aung T, Karavitaki N, Wass JA. Opioid induced **hypogonadism**. BMJ. 2010 Aug 31;341:c4462. doi: 10.1136/bmj.c4462.
Reddy S, Orenstein LAV, Strunk A, Garg A. Incidence of Long-term Opioid **Use Among Opioid-Naive Patients With Hidradenitis Suppurativa** in the United States. JAMA Dermatol. 2019 Sep 11.
Reid CM, et al. **Oxycodone** for cancer-related pain: meta-analysis of randomized controlled trials. Arch Intern Med. 2006 Apr 24;166(8):837-43.
Reid MC, Eccleston C, Pillemer K. Management of **chronic pain in older adults**. BMJ. 2015 Feb 13;350:h532.
Rennick A, Atkinson T, Cimino NM, et al. **Variability in Opioid Equivalence Calculations**. Pain Med. 2015 Sep 9.
Reuben DB, Alvanzo AA, et al. National institutes of health **pathways to prevention workshop: the role of opioids** in the treatment of chronic pain. Ann Intern Med. 2015 Feb 17;162(4):295-300.
Rahman NM, Pepperell J, Rehal S, et al. Effect of **Opioids vs NSAIDs and Larger vs Smaller Chest Tube Size** on Pain Control and **Pleurodesis** Efficacy Among Patients With Malignant Pleural Effusion: The TIME1 Randomized Clinical Trial. JAMA. 2015 Dec 22-29;314(24):2641-53.
Rich JD, McKenzie M, et al. **Methadone continuation versus forced withdrawal on incarceration** in a combined US **prison** and jail: a randomised, open-label trial. Lancet 2015; online May 29
Ringdahl E, Pandit S. Treatment of **Knee Osteoarthritis**. Am Fam Physician. 2011;83(11):1287-1292.
Rivera OJS, Havens JR, Parker MA, et al. Risk of **Heroin Dependence in Newly Incident Heroin Users**. JAMA Psychiatry. 2018 May 30.
Roan JP, Bajaj N, Davis FA, et al. **Opioids and Chest Wall Rigidity** During Mechanical Ventilation. Ann Intern Med. 2018 Jan 9.
Rolita L, Spegman A, Tang X, et al. Greater number of narcotic analgesic prescriptions for osteoarthritis is associated with **falls and fractures** in elderly adults. J Am Geriatr Soc. 2013 Mar;61(3):335-40.
Rose AJ, McBain R, Schuler MS, et al. **Effect of Age on Opioid Prescribing, Overdose, and Mortality** in Massachusetts, 2011 to 2015. J Am Geriatr Soc. 2019 Jan;67(1):128-132.
Rosen DA and Murray PJ. **Clues to the opioid crisis** in monitoring the future but still looking for solutions. Pediatrics 2017 Mar 20.
Rosic T, et al. The impact of **comorbid psychiatric disorders on methadone maintenance treatment in opioid use disorder**: a prospective cohort study. Neuropsychiatr Dis Treat 2017;13:1399-408.
Roussos-Ross K, Reisfield G, Elliot I, et al. Opioid use in **pregnant women and the increase in neonatal abstinence syndrome**: what is the cost? J Addict Med. 2015 May-Jun;9(3):222-5.
Roydhouse JK, Suzman DL, Menapace LA, et al. Global Variation in **Opioid Use in Prostate Cancer Trials**. JAMA Oncol. 2019 Sep 12:e192971.
Rubin R. Analysis reveals **large increase in hospitalizations** in recent years among older patients prescribed opioids. JAMA. 2014 Oct 22 29;312(16):1621-3.
Rudd RA, Seth P, David F, et al. Increases in **Drug and Opioid-Involved Overdose Deaths** - United States, 2010-2015. MMWR Morb Mortal Wkly Rep. 2016 Dec 30;65(5051):1445-1452.
Ruhm CJ. Geographic Variation in **Opioid** and **Heroin** Involved Drug **Poisoning** Mortality Rates. Am J Preventive Med. 2017.
Russolillo A, Moniruzzaman A, Somers JM. **Association of Methadone Treatment With Substance-Related Hospital Admissions** Among a Population in Canada With a History of Criminal Convictions. JAMA Netw Open. 2019 Mar 1;2(3):e190595.
Rutkow L, Chang HY, Daubresse M, et al. Effect of **Florida's Prescription Drug Monitoring Program** and Pill Mill Laws on Opioid Prescribing and Use. JAMA Intern Med. 2015 Aug 17.
Rutkow L, Vernick JS. **Emergency Legal Authority and the Opioid Crisis**. N Engl J Med. 2017 Dec 28;377(26):2512-2514.
Ruzycki S, Yarema M. **Fentanyl misuse**. CMAJ. 2016 Jun 14;188(9):673.
Ryan SA. Calculating the **Real Costs of the Opioid Crisis**. Pediatrics. 2018 Mar 5.
Safdar B, et al. Intravenous **morphine plus ketorolac** is superior to either drug alone for treatment of acute renal colic. Ann Emerg Med. 2006 Aug;48(2):173-81, 181.e1.
(InfoPOEMs: Intravenous morphine 5 mg combined with ketorolac (Toradol) 15 mg provided greater pain relief than either drug alone. The combination did not increase the likelihood of nausea or vomiting. (LOE = 1b))
Salehi Omran S, Chatterjee A, Chen ML, et al. National Trends in Hospitalizations for **Stroke Associated With Infective Endocarditis** and Opioid Use Between 1993 and 2015. Stroke. 2019 Jan 30:STROKEAHA118024436.
Salili AR, Müller D, Skendaj R, et al. Breakthrough Pain Associated with a Reduction in Serum **Buprenorphine** Concentration during Dialysis. Clin Ther. 2015 Nov 10.
Saloner B, Levin J, Chang H, et al. **Changes in Buprenorphine-Naloxone and Opioid Pain Reliever Prescriptions After the Affordable Care Act Medicaid Expansion**. JAMA Netw Open. 2018;1(4):e181588.
Saloner B, Stoller KB, Alexander GC. Moving Addiction Care to the Mainstream -**Improving the Quality of Buprenorphine Treatment**. N Engl J Med. 2018 Jul 5;379(1):4-6.

Samet JH, Botticelli M, Bharel M. **Methadone in Primary Care** - One Small Step for Congress, One Giant Leap for Addiction Treatment. N Engl J Med. 2018 Jul 5;379(1):7-8.
Samet JH, Kertesz SG. **Suggested Paths to Fixing the Opioid Crisis**: Directions and Misdirections. JAMA Netw Open. 2018 Jun 1;1(2):e180218.
Sandhu H, Underwood M, Furlan AD, et al. What **interventions** are effective **to taper opioids** in patients with chronic pain? BMJ. 2018 Sep 27;362:k2990.
Santos J, Alarcão J, Fareleira F, et al. **Tapentadol** for chronic musculoskeletal pain in adults. Cochrane Database Syst Rev. 2015 May 27;5:CD009923. Tapentadol extended release is associated with a reduction in pain intensity in comparison to placebo and oxycodone. However, the clinical significance of the results is uncertain due to the following reasons: modest difference between interventions in efficacy outcomes, high heterogeneity in some comparisons and outcomes, high withdrawals rates, lack of data for the primary outcome in some studies and impossibility to use BOCF as imputation method. Tapentadol is associated with a more favourable safety profile and tolerability than oxycodone.
Saulle R, Vecchi S, Gowing L. Supervised dosing with a **long-acting opioid medication in the management of opioid dependence**. Cochrane Database of Systematic Reviews 2017, Issue 4. Art. No.: CD011983. Take-home medication strategies are attractive to treatment services due to lower costs, and place less restrictions on clients, but it is unknown whether they may be associated with increased risk of diversion and unsanctioned use of medication. There is uncertainty about the effects of supervised dosing compared with unsupervised medication due to the low and very low quality of the evidence for the primary outcomes of interest for this review. Data on defined secondary outcomes were similarly limited. More research comparing supervised and take-home medication strategies is needed to support decisions on the relative effectiveness of these strategies. The trials should be designed and conducted with high quality and over a longer follow-up period to support comparison of strategies at different stages of treatment. In particular, there is a need for studies assessing in more detail the risk of diversion and safety outcomes of using supervised OST to manage opioid dependence.
Saveland C, Hawker L, Miedema B, et al. **Abuse of family physicians** by patients seeking controlled substances. Can Fam Physician. 2014 Feb;60(2):e131-6.
Schaffer AL, Buckley NA, Degenhardt L, et al. Person-level changes in **oxycodone use after the introduction of a tamper-resistant formulation** in Australia. CMAJ. 2018 Mar 26;190(12):E355-E362.
Sharfstein JM, Olsen Y. **Lessons Learned** From the Opioid Epidemic. JAMA. 2019 Aug 5.
Scherrer JF, Salas J, Lustman PJ, et. al, **Change in opioid dose and change in depression** in a longitudinal primary care patient cohort. Pain. 2015 Feb;156(2):348-55.
Schieber LZ, Guy GP Jr, Seth P, et al. Trends and Patterns of **Geographic Variation in Opioid Prescribing** Practices by State, United States, 2006-2017. JAMA Netw Open. 2019 Mar 1;2(3):e190665.
Schmidt-Hansen M, Bennett MI, Hilgart J. **Oxycodone for Cancer Pain** in Adult Patients. JAMA. 2015 Sep 22-29;314(12):1282-3.
Schneider JP, Matthews M, Jamison RN. **Abuse-deterrent and tamper-resistant opioid formulations**: what is their role in addressing prescription opioid abuse? CNS Drugs. 2010 Oct 1;24(10):805-10. doi: 10.2165/11584260-000000000-00000.
Schoenfeld AJ, Belmont PJ Jr, Blucher JA, et al. Sustained Preoperative **Opioid Use Is a Predictor of Continued Use Following Spine Surgery**. J Bone Joint Surg Am. 2018 Jun 6;100(11):914-921.
Schoenfeld AJ, Jiang W, Chaudhary MA, et al. Sustained Prescription Opioid Use Among Previously **Opioid-Naive** Patients Insured Through TRICARE (2006-2014). JAMA Surg. 2017 Aug 16.
Schroeder AR, Dehghan M, Newman TB, et al. Association of **Opioid Prescriptions From Dental Clinicians** for US Adolescents and Young Adults With Subsequent Opioid Use and Abuse. JAMA Intern Med. 2018 Dec 3.
Schuchat A, Houry D, Guy GP Jr. New Data on **Opioid Use and Prescribing in the United States**. JAMA. 2017 Jul 6.
Schuckit MA. **Treatment of Opioid-Use Disorders**. N Engl J Med. 2016 Jul 28;375(4):357-368.
Schwab T. US opioid prescribing: the federal government **advisers with recent ties to big pharma**. BMJ. 2019 Aug 22;366:l5167.
Schwartz RP, Highfield DA, Jaffe JH, et al. A randomized controlled trial of interim **methadone** maintenance. Arch Gen Psychiatry. 2006 Jan;63(1):102-9.
Scully RE, et al. **Defining optimal length of opioid pain medication prescription after common surgical procedures** [online September 27, 2017].JAMA Surg. doi:10.1001/jamasurg.2017.3132
Seal KH, Shi Y, Cohen G et al. Association of mental health disorders with prescription opioids and high-risk opioid use in **US veterans** of Iraq and Afghanistan. JAMA. 2012 Mar 7;307(9):940-7.
Seamans MJ, Carey TS, Westreich DJ, et al. Association of **Household Opioid Availability** and Prescription Opioid Initiation **Among Household Members**. JAMA Intern Med. 2017 Dec 11.
See also RxFiles Newsletter – Fall, 2005 - Opioids in Chronic Non-Malignant Pain Troubleshooting Drug Therapy Issues www.RxFiles.ca
Segura LE, Mauro CM, Levy NS, et al. Association of **US Medical Marijuana Laws With Nonmedical Prescription Opioid Use** and Prescription Opioid Use Disorder. JAMA Netw Open. 2019 Jul 3;2(7):e197216.
Sethi RKV, Panth N, Puram SV, et al. **Opioid Prescription Patterns Among Patients With Head and Neck Cancer**. JAMA Otolaryngol Head Neck Surg. 2018 Mar 8.
Sethi RKV, Lee LN, Quatela OE, et al. **Opioid Prescription Patterns After Rhinoplasty**. JAMA Facial Plast Surg. 2018 Sep 6.
Shafi S, Collinsworth AW, Copeland LA, et al. Association of **Opioid-Related Adverse Drug Events With Clinical and Cost Outcomes** Among Surgical Patients in a Large Integrated Health Care Delivery System. JAMA Surg. 2018 May 23.
Shah A, Hayes CJ, Martin BC. **Factors Influencing Long-Term Opioid Use Among Opioid Naive Patients**: An Examination of Initial Prescription Characteristics and Pain Etiologies. J Pain. 2017 Jul 13
Sharek PJ, McClead RE Jr, Taketomo C, et al. An **intervention to decrease narcotic**-related adverse drug events in **children's** hospitals. Pediatrics. 2008 Oct;122(4):e861-6.
Shepshelovich D, Schechter A, Calvarysky B, et al. **Medication-induced SIADH**: distribution and characterization according to medication class. Br J Clin Pharmacol. 2017 Feb 7.
Sherry TB, Sabety A, Maestas N. **Documented Pain Diagnoses in Adults Prescribed Opioids**: Results From the National Ambulatory Medical Care Survey, 2006-2015. Ann Intern Med. 2018 Sep 11.
Shiels MS, Freedman ND, Thomas D, et al. **Trends in U.S. Drug Overdose Deaths** in Non-Hispanic Black, Hispanic, and Non-Hispanic White Persons, 2000-2015. Ann Intern Med. 2017 Dec 5.
Shindo M, Lim J, Leon E, et al. **Opioid prescribing practice and needs in thyroid and parathyroid surgery** [online Oct 25, 2018]. JAMA Otolaryngol Head Neck Surg. doi:10.1001/jamaoto.2018.2427
Shiran MR, Lennard MS, Iqbal MZ, et al.et al. Contribution of the activities of CYP3A, CYP2D6, CYP1A2 and other potential covariates to the disposition of methadone in patients undergoing methadone maintenance treatment. Br J Clin Pharmacol. 2009 Jan;67(1):29-37. **CYP3A** activity has a modest influence on **methadone** disposition. Inhibitors and inducers of this enzyme should be monitored in patients taking methadone.
Shirk MB, Donahue KR, Shirvani J. Unlabeled uses of **nebulized** medications. Am J Health Syst Pharm. 2006 Sep 15;63(18):1704-16.
Short TD, Stallings EB, Isenburg J, et al. **Gastroschisis Trends and Ecologic Link** to Opioid Prescription Rates - United States, 2006-2015. MMWR Morb Mortal Wkly Rep. 2019 Jan 18;68(2):31-36.
Sigmon SC, Ochalek TA, Meyer AC, et al. **Interim Buprenorphine vs. Waiting List** for Opioid Dependence. N Engl J Med. 2016 Dec 22;375(25):2504-2505.
Sigurdsson MI, Helgadottir S, Long TE, et al. Association Between **Preoperative Opioid and Benzodiazepine Prescription Patterns** and Mortality After Noncardiac Surgery. JAMA Surg. 2019 Jun

19:e191652.
Sinha M, et al. Evaluation of **nonpharmacologic** methods of pain and anxiety management for laceration repair in the pediatric emergency department. Pediatrics. 2006 Apr;117(4):1162-8.
Sites BD, Harrison J, Herrick MD, et al. **Prescription Opioid Use and Satisfaction With Care Among Adults With Musculoskeletal Conditions**. Ann Fam Med. 2018 Jan;16(1):6-13.
Sloan VS, Sheahan A, Stark JL, Suruki RY. Opioid Use in Patients with **Ankylosing Spondylitis** is Common in the United States: Outcomes of a Retrospective Cohort Study. J Rheumatol. 2019 Jan 15.
Smith J, Owen E, Earis J, Woodcock A. Effect of codeine on objective measurement of **cough** in chronic obstructive pulmonary disease. J Allergy Clin Immunol. 2006 Apr;117(4):831-5. Epub 2006 Feb 7.
Smith JE, Rickett M, Creanor S, et al. PAin SoluTions In the Emergency Setting (**PASTIES**)—**patient controlled analgesia** versus routine care in emergency department patients with non-traumatic abdominal pain: randomised trial. BMJ 2015;350:h3147.
Smith LA, Burns E, Cuthbert A. **Parenteral opioids** for maternal pain management **in labour**. Cochrane Database of Systematic Reviews 2018, Issue 6. Art. No.: CD007396. Though most evidence is of low- or very-low quality, for healthy women with an uncomplicated pregnancy who are giving birth at 37 to 42 weeks, parenteral opioids appear to provide some relief from pain in labour but are associated with drowsiness, nausea, and vomiting in the woman. Effects on the newborn are unclear. Maternal satisfaction with opioid analgesia was largely unreported.
Smith SR, Bido J, Collins JE, et al. Impact of **Preoperative Opioid Use on Total Knee Arthroplasty Outcomes**. J Bone Joint Surg Am. 2017 May 17;99(10):803-808.
Smolina K, Weymann D, Morgan S, et al. Association between **regulatory advisories and codeine prescribing to postpartum women**. JAMA. 2015 May 12;313(18):1861-2.
Snyder DL, Crowell MD, Horsley-Silva J, et al. **Opioid-Induced Esophageal Dysfunction**: Differential Effects of Type and Dose. Am J Gastroenterol. 2019 Aug 13.
Socías ME, Ahamad K. An urgent call to increase access to **evidence-based opioid agonist therapy for prescription opioid use disorders**. CMAJ. 2016 Dec 6;188(17-18):1208-1209.
Socías ME, Wood E. **Evaluating Slow-Release Oral Morphine to Narrow the Treatment Gap for Opioid Use Disorders**. Ann Intern Med. 2018 Jan 16;168(2):141-142.
Sohn M, Talbert JC, Huang Z, et al. Association of **Naloxone Coprescription Laws With Naloxone Prescription Dispensing** in the United States. JAMA Netw Open. 2019 Jun 5;2(6):e196215.
Solomon Daniel H.; Rassen Jeremy A.; Glynn Robert J.; et al. The Comparative Safety of **Analgesics in Older Adults With Arthritis**. Arch Intern Med. 2010;170(22):1968-1978.
The comparative safety of analgesics varies depending on the safety event studied. Opioid use exhibits an increased relative risk of many safety events compared with nsNSAIDs.
Solomon Daniel H.; Rassen Jeremy A.; Glynn RJ.; et al. The Comparative Safety of **Opioids for Nonmalignant Pain in Older Adults**. Arch Intern Med. 2010;170(22):1979-1986.
Song Z. **Mortality** Quadrupled Among **Opioid-Driven Hospitalizations**, Notably Within Lower-Income And Disabled White Populations. Health Aff (Millwood). 2017 Dec;36(12):2054-2061.
Sordo L, Barrio G, Bravo MJ, et al. **Mortality risk during and after opioid substitution treatment**: systematic review and meta-analysis of cohort studies. BMJ 2017;357:j1550
Sproule B, Brands B, Li S, Catz-Biro L. Changing patterns in opioid addiction: characterizing users of **oxycodone** and other opioids. Can Fam Physician. 2009 Jan;55(1):68-9, 69.e1-5.
Srivastava A, Kahan M. **Buprenorphine**: a potential new treatment option for opioid dependence. CMAJ;2006;174(13). http://www.cmaj.ca/cgi/content/full/174/13/1835
Srivastava A, Kahan M, Nader M. **Primary care management of opioid use disorders**: Abstinence, methadone, or buprenorphine-naloxone? Can Fam Physician. 2017 Mar;63(3):200-205. Review.
Staloch DA, Hedley JS. **Pulmonary Foreign-Body Granulomatosis**. N Engl J Med. 2017 Sep 28;377(13):1273. (**inject oral opiates**)
Standridge JB, Adams SM, Zotos AP. **Urine drug screening**: a valuable office procedure. Am Fam Physician. 2010 Mar 1;81(5):635-40.
Starrels JL., Becker WC., Alford DP., et al. Systematic Review: **Treatment Agreements** and Urine Drug Testing to Reduce Opioid Misuse in Patients With Chronic Pain. *Ann Intern Med* June 1, 2010 152:712-720; doi:10.1059/0003-4819-152-11-201006010-00004
Stein BD, Sorbero M, Dick AW, Pacula et al. Physician Capacity to Treat Opioid Use Disorder With **Buprenorphine-Assisted Treatment**. JAMA. 2016 Sep 20;316(11):1211-1212.
Steinhorn R, McPherson C, Anderson PJ, et al. **Neonatal morphine exposure** in very preterm infants-cerebral development and outcomes. J Pediatr. 2015 May;166(5):1200-1207.e4.
Strand MC, Vindenes V, Gjerde H, et al. A clinical trial on the acute effects of **methadone and buprenorphine on actual driving** and cognitive function of healthy volunteers. Br J Clin Pharmacol. 2018 Dec 4.
Strand MC, Vindenes V, Gjerde H, et al. A clinical trial on the **acute effects of methadone and buprenorphine on actual driving and cognitive function** of healthy volunteers. Br J Clin Pharmacol. 2018 Dec 4.
Strang John, Hall Wayne, Hickman Matt, et al Impact of **supervision of methadone consumption** on deaths related to methadone overdose (1993-2008): analyses using OD4 index in England and Scotland. BMJ 341:doi:10.1136/bmj.c4851 (Published 16 September 2010)
Strang J, Bird SM, Dietze P, et al. **Take-home emergency naloxone** to prevent deaths from heroin overdose. BMJ. 2014 Nov 4;349:g6580.
Strømmen M, Helland A, Kulseng B, et al. Bioavailability of **Methadone After Sleeve Gastrectomy**: A Planned Case Observation. Clin Ther. 2016 May 12.
Stonington S, Coffa D. Structural Iatrogenesis - A 43-Year-Old Man with "Opioid Misuse". N Engl J Med. 2019 Feb 21;380(8):701-704.
Stucke RS, Kelly JL, Mathis KA, et al. Association of the Use of a **Mandatory Prescription Drug Monitoring Program** With Prescribing Practices for Patients Undergoing Elective Surgery. JAMA Surg. 2018 Aug 22.
Suda KJ, Durkin MJ, Calip GS, et al. Comparison of **Opioid Prescribing by Dentists** in the United States and England. JAMA Netw Open. 2019 May 3;2(5):e194303.
Sullivan M et al. **Long-acting injectable naltrexone induction**: A randomized trial of outpatient opioid detoxification with naltrexone versus buprenorphine. Am J Psychiatry 2017 Jan 10.
Sullivan MD, Turner JA, DiLodovico C, et al. **Prescription Opioid Taper** Support for Outpatients With Chronic Pain: A Randomized Controlled Trial. J Pain. 2016 Nov 28.
Sullivan M, Bisaga A, Pavlicova M, et al. **Long-Acting Injectable Naltrexone Induction**: A Randomized Trial of Outpatient Opioid Detoxification With Naltrexone Versus Buprenorphine. Am J Psychiatry. 2017 Jan 10:appiajp201616050548.
Sullivan MD, Turner JA, DiLodovico C, et al. **Prescription Opioid Taper** Support for Outpatients With Chronic Pain: A Randomized Controlled Trial. J Pain. 2016 Nov 28.
Sun EC, Darnall B, et al. Incidence of and Risk Factors for Chronic Opioid Use Among Opioid-Naive Patients in the **Postoperative Period**. JAMA Intern Med. 2016 Jul 11.
Sun EC, Dixit A, Humphreys K, et al. Association between **concurrent use of prescription opioids and benzodiazepines and overdose**: retrospective analysis. BMJ 2017;356:j760.

Sun EC, Jena AB. **Distribution of Prescription Opioid Use Among Privately Insured Adults Without Cancer**: United States, 2001-2013. Ann Intern Med. 2017 Sep 12.
Sun E, Moshfegh J, Rishel CA, et al. Association of Early **Physical Therapy With Long-term Opioid Use** Among Opioid-Naive Patients With Musculoskeletal Pain. JAMA Netw Open. 2018;1(8):e185909.
Surmaitis RM, Amaducci A, et al. Perception and Practice Among **Emergency Medicine Health Care Providers Regarding Discharging Patients After Opioid Administration**. Clin Ther. 2018 Jan 19.
Taddio A, et al. Intravenous morphine and topical tetracaine for treatment of pain in preterm neonates undergoing central line placement.JAMA. 2006 Feb 15;295(7):793-800.
Taipale H, Hamina A, Karttunen N, et al. Incident **opioid use and risk of hip fracture among persons with Alzheimer disease**: a nationwide matched cohort study. Pain. 2018 Oct 12.
Taipale H, Hamina A, Lampela P, et al. Is **Alzheimer's Disease Associated with Previous Opioid Use**? Pain Med. 2017 Aug 28.
Tanum L, et al. Effectiveness of Injectable Extended-Release **Naltrexone vs Daily Buprenorphine-Naloxone for Opioid Dependence**: Randomized Noninferiority Trial. JAMA Psychiatry. 2017 Oct 18
Tapentadol-Nucynta-A New Analgesic. Medical Letter Aug 10, 2009.
Taylor RG, Budhram A, Lee DH, Mirsattari SM. Opioid-associated **amnestic syndrome observed with fentanyl patch** use. CMAJ. 2019 Mar 25;191(12):E337-E339.
Tedesco D;Gori D;et al. **Drug-Free Interventions** to Reduce Pain or **Opioid Consumption After Total Knee Arthroplasty**: A Systematic Review and Meta-analysis. JAMA Surg. 2017 Aug 16:e172872.
Tedesco D, Asch SM, Curtin C, et al. **Opioid Abuse And Poisoning: Trends In Inpatient And Emergency Department Discharges**. Health Aff (Millwood). 2017 Oct 1;36(10):1748-1753.
Thakur D, Dickerson S, Kumar Bhutani M, et al. Impact of Prolonged release **Oxycodone/Naloxone** on Outcomes Affecting Patients' Daily Functioning in Comparison With Extended-release Tapentadol: A Systematic Review. Clin Ther. 2015 Jan 1;37(1):212-224.
Thielke SM, Shortreed SM, Saunders K, et al. A Prospective Study of **Predictors of Long-term Opioid Use Among Patients With Chronic Noncancer Pain**. Clin J Pain. 2017 Mar;33(3):198-204.
Thiels CA, Habermann EB, Hooten WM, Jeffery MM. **Chronic use of tramadol after acute pain episode**: cohort study. BMJ 2019;365:l1849.
Thienprayoon R, Porter K, Tate M, et al. **Risk Stratification for Opioid Misuse** in Children, Adolescents, and Young Adults: A Quality Improvement Project. Pediatrics. 2016 Dec 15.
Thomas J, Karver S, Cooney GA, et al. **Methylnaltrexone for opioid-induced constipation** in advanced illness. N Engl J Med. 2008 May 29;358(22):2332-43. Subcutaneous methylnaltrexone rapidly induced laxation in patients with advanced illness and opioid-induced constipation. Treatment did not appear to affect central analgesia or precipitate opioid withdrawal. {InfoPOEMs Aug2008: Methylnaltrexone (Relistor) is effective for the treatment of opioid-induced constipation in hospice patients. However, long-term safety is not known, so it should not be widely used for nonterminally ill patients until longer studies have been performed. (LOE = 1b)}
Thompson JP, Thompson DF. **Nebulized Fentanyl** in Acute Pain: A Systematic Review. Ann Pharmacother. 2016 Oct;50(10):882-91.
Throckmorton DC, Woodcock J. **Combined Gabapentinoid and Opioid Use**: The Consequences of Shifting Prescribing Trends. Ann Intern Med. 2018 Aug 21.
Thybo KH, Hägi-Pedersen D, Dahl JB, et al. Effect of Combination of **Paracetamol (Acetaminophen) and Ibuprofen vs Either Alone** on Patient-Controlled Morphine Consumption in the First 24 Hours After **Total Hip Arthroplasty**: The PANSAID Randomized Clinical Trial. JAMA. 2019 Feb 12;321(6):562-571.
Tilbrook D, Jacob J, Parsons P, Edwards C, Loewen K, Kelly L. **Opioid use disorder and type 2 diabetes mellitus**: Effect of participation in buprenorphine-naloxone substitution programs on glycemic control. Can Fam Physician. 2017 Jul;63(7):e350-e354.
Timm NL. **Maternal Use of Oxycodone** Resulting in Opioid Intoxication in Her Breastfed Neonate. J Pediatr. 2012 Oct 10.
Tobias JD, Green TP, Coté CJ. **Codeine**: Time To **Say "No".** Pediatrics. 2016 Sep 19.
Toce MS, Kim H, Chung S, Krauss BS. **Prolonged central apnoea after intravenous morphine** administration in a 12-year-old male with a UGT1A1 loss-of-function polymorphism. Br J Clin Pharmacol. 2018 Nov 12.
Tomaszewski DM, Arbuckle C, Yang S, Linstead E. Trends **in Opioid Use in Pediatric Patients in US Emergency Departments** From 2006 to 2015. JAMA Netw Open. 2018;1(8):e186161.
Torjesen I. **Fentanyl misuse** in the UK: will we see a surge in deaths? BMJ. 2018 Apr 9;361:k1564. doi: 10.1136/bmj.k1564.
Toupin April K, Bisaillon J, Welch V, et al. **Tramadol for osteoarthritis**. Cochrane Database Syst Rev. 2019 May 27;5:CD005522. Moderate quality evidence indicates that compared to placebo, tramadol alone or in combination with acetaminophen probably has no important benefit on mean pain or function in people with osteoarthritis, although slightly more people in the tramadol group report an important improvement (defined as 20% or more). Moderate quality evidence shows that adverse events probably cause substantially more participants to stop taking tramadol.
Towers C, Hyatt BW, Visconti KC, Chernicky L, Chattin K, Fortner KB. Neonatal head circumference in **newborns with neonatal abstinence syndrome**. Pediatrics. 2019;143(1):e20180541
Treatment Guidelines from the Medical Letter. Pharmaceutical **Drug Overdose**. Sept 2006. (Opiates: naloxone treatment)
Tsutaoka BT, Ho RY, Fung SM, et al. Comparative toxicity of **tapentadol and tramadol** utilizing data reported to the National Poison Data System. Ann Pharmacother 2015. online Sept 14, 2015
Tsutaoka BT, Ho RY, Fung SM, et al. Comparative **Toxicity of Tapentadol and Tramadol** Utilizing Data Reported to the National Poison Data System. Ann Pharmacother. 2015 Dec;49(12):1311-6.
Tuminello S, Schwartz RM, Liu B, et al. **Opioid Use After Open Resection or Video-Assisted Thoracoscopic Surgery for Early-Stage Lung Cancer**. JAMA Oncol. 2018 Sep 24.
Tuminello S, Schwartz RM, Liu B, et al. **Opioid Use After** Open Resection or Video-Assisted **Thoracoscopic Surgery** for Early-Stage **Lung Cancer**. JAMA Oncol. 2018 Sep 24
Turner SD, Gomes T, Camacho X, et al. **Neonatal opioid withdrawal and antenatal opioid prescribing**. CMAJ Open. 2015 Jan 13;3(1):E55-61.
Tyndall M. An **emergency response to the opioid overdose crisis in Canada**: a regulated opioid distribution program. CMAJ. 2018 Jan 15;190(2):E35-E36.
Uyei J, Fiellin DA, Buchelli M et al. Effects of **naloxone distribution alone or in combination with addiction treatment with or without pre-exposure prophylaxis for HIV prevention** in people who inject drugs: a cost-effectiveness modeling study. Lancet Public Health. March 2017;2:e133-40.
Vaduganathan M, Machado SR, DeFilippis EM, et al. **Organ Donation and Drug Intoxication-Related Deaths** in the United States. N Engl J Med. 2019 Feb 7;380(6):597-599.
Vallecillo G et al. Risk of **QTc prolongation** in a cohort of opioid-dependent HIV-infected patients on **methadone** maintenance therapy. Clin Infect Dis 2013 Aug 14.
Van den Brink W, Haasen C. Evidenced-based treatment of **opioid-dependent** patients. Can J Psychiatry. 2006 Sep;51(10):635-46.
van Donge T, Samiee-Zafarghandy S, Pfister M, et al**. Methadone dosing strategies in preterm neonates** can be simplified. Br J Clin Pharmacol. 2019 Feb 25.
Vargas-Schaffer G, Cogan J. Patient therapeutic education: Placing the **patient at the centre of the WHO analgesic ladder**. Can Fam Physician. 2014 Mar;60(3):235-41.

Veliz P, Boyd CJ, McCabe SE. **Nonmedical Prescription Opioid and Heroin Use** Among Adolescents Who Engage in Sports and Exercise. Pediatrics. 2016 Jul 25.
Verberkt CA, van den Beuken-van Everdingen MHJ, et al. **Respiratory adverse effects of opioids for breathlessness**: a systematic review and meta-analysis**.** Eur Respir J. 2017 Nov 22;50(5).
Victorri-Vigneau C, Verstuyft C, Bouquié R, et al. Relevance of **CYP2B6 and CYP2D6 genotypes to methadone pharmacokinetics** and response in the **OPAL study**. Br J Clin Pharmacol. 2019 Mar 25.
Villapiano NL, Winkelman TN, Kozhimannil KB, et al. **Rural and Urban Differences** in Neonatal Abstinence Syndrome and Maternal Opioid Use, 2004 to 2013. JAMA Pediatr. 2016 Dec 12.
Voepel-Lewis T, Wagner D, Tait AR. **Leftover Prescription Opioids After Minor Procedures**: An Unwitting Source for Accidental Overdose In Children. JAMA Pediatr. 2015 Mar 23.
Volkow ND, McLellan AT. Opioid **Abuse** in Chronic Pain--**Misconceptions and Mitigation Strategies**. N Engl J Med. 2016 Mar 31;374(13):1253-63.
Volkow ND, Collins FS. The Role of **Science in Addressing the Opioid Crisis**. N Engl J Med. 2017 May 31.
Volkow ND, Jones EB, Einstein EB, Wargo EM. **Prevention and Treatment of Opioid Misuse** and Addiction: A Review. JAMA Psychiatry. 2018 Dec 5.
Von Korff M, Kolodny A, Deyo RA, Chou R. **Long-term opioid therapy reconsidered**. Ann Intern Med. 2011 Sep 6;155(5):325-8.
Vozoris NT, Wang X, Fischer HD, et al. Incident opioid drug use and **adverse respiratory outcomes among older adults with COPD**. Eur Respir J. 2016 Sep;48(3):683-93.
Vozoris NT, Wang X, Austin PC, et al. Adverse cardiac events associated with incident **opioid drug use among older adults with COPD**. Eur J Clin Pharmacol. 2017 Jun 29.
Waade RB, et al. **Psychotropics and weak opioid analgesics in plasma samples of older hip fracture patients** - detection frequencies & consistency with drug records. Br J Clin Pharm. 2017 Mar 7
Wachman EM, Schiff DM, Silverstein M. **Neonatal Abstinence Syndrome**: Advances in Diagnosis and Treatment. JAMA. 2018 Apr 3;319(13):1362-1374.
Wahawisan Joy, Kolluru Srikanth, Nguyen Tu, et al. **Methadone Toxicity Due to Smoking Cessation**—A Case Report on the Drug-Drug Interaction Involving Cytochrome P450 Isoenzyme 1A2. Articles Ahead of Print published on 1 June 2011, DOI 10.1345/aph.1P759. Ann Pharmacother ;45:e34.
Wakeman SE, Barnett ML. Primary Care and the **Opioid-Overdose Crisis** - **Buprenorphine Myths and Realities**. N Engl J Med. 2018 Jul 5;379(1):1-4.
Wakeman SE, Ladin K, Brennan T, et al. **Opioid Use Disorder, Stigma, and Transplantation**: A Call to Action. Ann Intern Med. 2018 Jul 10.
Walley AY, et al. Opioid overdose rates and implementation of overdose education and nasal **naloxone distribution** in Massachusetts: interrupted time series analysis.BMJ. 2013 Jan 30;346:f174.
Walsh SL, Comer SD, Lofwall MR, et al. Effect of **Buprenorphine Weekly Depot (CAM2038) and Hydromorphone Blockade** in Individuals With Opioid Use Disorder: A Randomized Clinical Trial. JAMA Psychiatry. 2017 Jun 22.
Walsh MC, Crowley M, Wexelblatt S,et al. Ohio Perinatal Quality Collaborative Improves Care of **Neonatal Narcotic Abstinence Syndrome**. Pediatrics. 2018 Mar 7.
Wang GS, Severtson SG, Bau GE, et al. Unit-Dose Packaging and Unintentional **Buprenorphine-Naloxone** Exposures. Pediatrics. 2018 May 3.
Warner M, Trinidad JP, Bastian BA, et al. Drugs Most Frequently Involved in **Drug Overdose Deaths**: United States, 2010-2014. Natl Vital Stat Rep. 2016 Dec;65(10):1-15.
Watkins KE, Paddock SM, Hudson TJ, et al. Association between process measures and **mortality in individuals with opioid use disorders**. Drug Alcohol Depend. 2017 Jun 27.
Watkins KE, Ober AJ, Lamp K, et al. Collaborative Care for **Opioid and Alcohol Use Disorders in Primary Care**: The **SUMMIT** Randomized Clinical Trial. JAMA Intern Med. 2017 Aug 28.
Webster LR, Fine PG. Overdose deaths demand a new paradigm for **opioid rotation**. Pain Med. 2012 Apr;13(4):571-4.
Webster LR, Fine PG. Review and critique of **opioid rotation practices** and associated risks of toxicity. Pain Med. 2012 Apr;13(4):562-70.
Webster LR, Israel RJ. **Oral methylnaltrexone does not negatively impact analgesia in patients with opioid-induced constipation and chronic noncancer pain**. J Pain Res. 2018 Aug 13;11:1503-1510.
Weick J, Bawa H, Dirschl DR, Luu HH. **Preoperative Opioid Use Is Associated with Higher Readmission** and Revision Rates in **Total Knee and Total Hip Arthroplasty**. J Bone Joint Surg Am. 2018 Jul 18;100(14):1171-1176.
Weiner SG, Griggs CA, Mitchell PM, et al. Clinician **impression versus prescription drug monitoring program** criteria in the assessment of drug-seeking behavior in the emergency department. Ann Emerg Med. 2013 Oct;62(4):281-9.
Wen H, Hockenberry JM, Pollack HA. Association of **Buprenorphine-Waivered Physician Supply With Buprenorphine Treatment Use and Prescription Opioid Use** in Medicaid Enrollees. *JAMA Netw Open.*2018;1(5):e182943.
Wenghofer, Elizabeth Francis, Wilson, Lynn, Kahan, et al. Survey of Ontario primary care **physicians' experiences with opioid prescribing**. Can Fam Physician 2011 57: 324-332.
Whitley H, Lindsey W. **Sex-based** differences in drug activity. Am Fam Physician. 2009 Dec 1;80(11):1254-8.
Whittle SL, Richards BL, Husni E, et al. **Opioid therapy** for treating **rheumatoid arthritis pain**. Cochrane Database Syst Rev. 2011 Nov 9;11:CD003113. There is limited evidence that weak oral opioids may be effective analgesics for some patients with RA, but adverse effects are common and may offset the benefits of this class of medications.
Wei YJ, Chen C, Sarayani A, Winterstein AG. Performance of the Centers for Medicare & Medicaid Services' **Opioid Overutilization Criteria for Classifying Opioid Use Disorder or Overdose**. JAMA. 2019 Feb 12;321(6):609-611.
Weick J, Bawa H, Dirschl DR, et al. **Preoperative Opioid Use Is Associated with Higher Readmission and Revision Rates in Total Knee and Total Hip Arthroplasty**. J Bone Joint Surg Am. 2018 Jul 18;100(14):1171-1176.
Wetzel M, Hockenberry J, Raval MV. **Interventions** for **Postsurgical Opioid Prescribing**: A Systematic Review. JAMA Surg. 2018 Oct 1;153(10):948-954.
Wiese AD, Griffin MR, et al. **Opioid analgesic use and risk for invasive pneumococcal diseases**. A nested case–control study. Ann Intern Med. 2018. [Epub ahead of print]. doi:10.7326/M17-1907
Wiffen PJ, Wee B, Moore RA. Oral **morphine for cancer pain**. Cochrane Database Syst Rev. 2013 Jul 22;7:CD003868. doi: 10.1002/14651858.CD003868.pub3. The effectiveness of oral morphine has stood the test of time, but the randomised trial literature for morphine is small given the importance of this medicine. Most trials recruited fewer than 100 participants and did not provide appropriate data for meta-analysis. Only a few reported how many people had good pain relief, but where it was reported, over 90% had no worse than mild pain within a reasonably short time period.
Wiffen PJ, Cooper TE, Anderson AK, et al **Opioids for cancer-related pain in children and adolescents**. Cochrane Database of Systematic Reviews 2017, Issue 7. Art. No.: CD012564. No conclusions can be drawn about efficacy or harm in the use of opioids to treat cancer-related pain in children and adolescents. As a result, there is no RCT evidence to support or refute the use of opioids to treat cancer-related pain in children and adolescents.
Wiles JR, Isemann B, Ward LP, et al. Current Management of **Neonatal Abstinence Syndrome** Secondary to Intrauterine Opioid Exposure. J Pediatr. 2014 Jun 16.

Wiles JR, Isemann B, Mizuno T, et al. Pharmacokinetics of Oral **Methadone** in the Treatment of **Neonatal Abstinence Syndrome**: A Pilot Study. J Pediatr. 2015 Sep 10.
Willsie SK, Evashenk MA, Hamel LG, et al. Pharmacokinetic Properties of Single- and Repeated-Dose **Sufentanil Sublingual Tablets** in Healthy Volunteers. Clin Ther. 2014 Dec 24.
Wilson JF. Strategies to **stop abuse** of prescribed opioid drugs. Ann Intern Med. 2007 Jun 19;146(12):897-900.
Winkelman TNA, Villapiano N, Kozhimannil KB, et al. Incidence and Costs of **Neonatal Abstinence Syndrome** Among Infants With Medicaid: 2004-2014. Pediatrics. 2018 Mar 23.
Wolfe SM. A **morphine-oxycodone combo pill**: toward the "holy grail" for opioids or a justifiably rejected drug? BMJ. 2014 Jun 9;348:g3620.
Wood E. Strategies for Reducing Opioid-Overdose Deaths - Lessons from Canada. N Engl J Med. 2018 Apr 26;378(17):1565-1567.
Woody GE, Poole SA, Subramaniam G, et al. Extended vs short-term buprenorphine-naloxone for treatment of opioid-addicted youth: a randomized trial. JAMA. 2008 Nov 5;300(17):2003-11. Continuing treatment with **buprenorphine-naloxone** improved outcome compared with short-term detoxification. Further research is necessary to assess the efficacy and safety of longer-term treatment with buprenorphine for young individuals with opioid dependence.
Wright AP, Becker WC, Schiff GD. Strategies for **Flipping the Script on Opioid Overprescribing**. JAMA Intern Med. 2015 Nov 2:1-2.
Wright JD, Huang Y, Melamed A, et al. Use and Misuse of **Opioids After Gynecologic Surgical Procedures**. Obstet Gynecol. 2019 Aug;134(2):250-260.
Wu BU, Butler RK, Chen W. Factors Associated With Opioid Use in Patients Hospitalized for **Acute Pancreatitis**. JAMA Netw Open. 2019 Apr 5;2(4):e191827.
Wunsch H, Wijeysundera DN, Passarella MA, Neuman MD. Opioids prescribed **after low-risk surgical procedures** in the United States, 2004-2012.JAMA. doi:10.1001/jama.2016.0130.
Xu J, et al. Effect of **US Food and Drug Administration-Approved Pediatric Labeling** on Dispensing of Extended Release **Oxycodone** in the Outpatient Retail Setting. JAMA Pediatr. 2016 Sep 9.
Yang YT, Chen B, Bennett CL. **FDA Approval** of Extended-Release **Oxycodone for Children With Severe Pain**. Pediatrics. 2016 May;137(5).
Yazdy M, Mitchell A, Tinker S et al. **Periconceptional Use of Opioids** and the Risk of Neural Tube Defects. Obstetrics&Gynecology. September 2013.
Yokell MA, Delgado MK, Zaller ND, et al. Presentation of **Prescription and Nonprescription Opioid Overdoses** to US Emergency Departments. JAMA Intern Med. 2014 Oct 27.
Young JW, Juurlink DN. **Tramadol**. CMAJ. 2013 May 14;185(8):E352.
Young K. US opioid epidemic: it's **harder to get the painkillers I legitimately need**. BMJ. 2017 Feb 15;356:j784.
Zamani N, Hassanian-Moghaddam H**. Ingestion of Lead-Contaminated Packs of Opium**. N Engl J Med. 2018 Nov 8;379(19):1861.
Zecca E, Brunelli C, Centurioni F, et al. **Fentanyl Sublingual Tablets Versus Subcutaneous Morphine** for the Management of Severe Cancer Pain Episodes in Patients Receiving Opioid Treatment: A Double-Blind, Randomized, Noninferiority Trial. J Clin Oncol. 2017 Mar;35(7):759-765.
Zeppetella G, Davies AN. **Opioids for the management of breakthrough pain in cancer** patients. Cochrane Database of Systematic Reviews 2013, Issue 10. Art. No.: CD004311. DOI: 10.1002/14651858.CD004311.pub3. Oral and nasal transmucosal fentanyl is an effective treatment in the management of breakthrough pain.
Zhang H, Kalluri HV, Bastian JR, et al. **Gestational changes in buprenorphine exposure**: A physiologically-based pharmacokinetic analysis. Br J Clin Pharmacol. 2018 Jun 5.
Zhang VS, Olfson M, King M. Opioid and **Benzodiazepine Coprescribing** in the United States Before and After US Food and Drug Administration Boxed Warning. JAMA Psychiatry. 2019 Sep 18.
Zheng Z, Gibson S, Helme RD, et al. Effects of **Electroacupuncture on Opioid Consumption in Patients with Chronic Musculoskeletal Pain**: A Multicenter Randomized Controlled Trial. Pain Med. 2018 Jun 8.
Zhu W, Chernew ME, Sherry TB, Maestas N. **Initial Opioid Prescriptions** among U.S. Commercially Insured Patients, 2012-2017. N Engl J Med. 2019 Mar 14;380(11):1043-1052.
Ziegler L, Mulvey M, Blenkinsopp A, et al. **Opioid prescribing for patients with cancer in the last year of life**: a longitudinal population cohort study. Pain. 2016 Jul 16.
Zwicker JG, Miller SP, Grunau RE, et al. Smaller cerebellar growth and **poorer neurodevelopmental outcomes in very preterm infants exposed to neonatal morphine**. J Pediatr 2016;172:81–7.

Opioid Treatment Agreements

- Useful for:
  - Identifying drug abuse
  - Reducing doctor shopping
  - Outlining how "requests" will be handled
    - E.g. early refills? Running out due to "borrowing from tomorrow"
  - Educating patients on:
    - What to expect?
    - What not too expect?
      - realistic expectations for 30-50% reduction in pain
    - Importance of non-drug interventions
    - Role or lack thereof for "prns" in therapeutic plan
  - Outline responsibilities and expectations
    - monitoring plans, especially functional goals
    - how opioids will be obtained and taken
    - use of concomitant drugs
    - storage and security requirements
    - consequences for non-adherence or aberrant behaviour
  - option of including informed consent components
  - proactive managing of highly functioning, charming and convincing individuals with borderline personality traits – to pre-empt typical conflict that can arise
- The more routine the clinicians use of an agreement, the easier it is!
  - Removes stigma of "suspicion" and any issues of trust
  - Offers best practice protection to all

Education Programs of Interest

- *Inventory of Pain and Addiction Education Programs for Canadian Prescribers*
  - From the National Pain Centre in collaboration with CCSA
  - Link: http://nationalpaincentre.mcmaster.ca/tools.html

References: **Pain Approaches: Acute/Palliative/CNCP chart**

[i] **Canadian Guideline** for Safe and Effective Use of Opioids for Chronic Non-Cancer Pain — Part B: Recommendations for Practice, Version 5.5 April 30, 2010. [NOUGG] Accessed at: http://nationalpaincentre.mcmaster.ca/documents/opioid_guideline_part_b_v5_6.pdf
[ii] Passik SD, Weinreb HJ. Managing chronic nonmalignant pain: overcoming obstacles to the use of opioids. Adv Ther. 2000 Mar-Apr;17:70-83.
[iii] **AFP article Aug 2012 - on Rational Use of Opioids for Management of Chronic Nonterminal Pain** http://www.aafp.org/afp/2012/0801/p252.html
[iv] Miller M, Barber CW, Leatherman S, Fonda J, Hermos JA, Cho K, Gagnon DR. Prescription opioid duration of action and the risk of unintentional overdose among patients receiving opioid therapy. JAMA Intern Med. 2015 Apr 1;175(4):608-15.
[v] Von Korff M, Kolodny A, Deyo RA, Chou R. Long-term opioid therapy reconsidered. Ann Intern Med. 2011 Sep 6;155(5):325-8.
[vi] Gourlay DL, Heit HA, Almahrezi A. Universal precautions in pain medicine: a rational approach to the treatment of chronic pain. Pain Med. 2005;6(2):107-12.
[vii] Passik SD, Heit H, Kirsh KL. Reality and responsibility: a commentary on the treatment of pain and suffering in a drug-using society. J Opioid Manag. 2006 May-Jun;2(3):123-7.

Additional references:

Dowell D, Haegerich TM, Chou R. **CDC guideline** for **prescribing opioids for chronic pain—United States, 2016**. MMWR Recomm Rep. 2016;65(RR-1): 1-49.
Dowell D, Haegerich TM, Chou R. **CDC guideline** for **prescribing opioids for chronic pain—United States, 2016**.JAMA. doi:10.1001/jama.2016.1464.

RxFiles 2017 Pain Management and Opioids Newsletter (& Pain Mini-Book)
http://www.rxfiles.ca/rxfiles/uploads/documents/Opioids-Pain-2017-Newsletter.pdf

See also RxFiles:

- **Pain Approaches - Distinctives for the ACUTE vs PALLIATIVE vs CNCP use of Opioids:**
  - **http://www.rxfiles.ca/rxfiles/uploads/documents/members/CHT-Pain-Approaches-Acute-Palliative-CNCP.pdf**
- **RxFiles Pain & Opioid Links:**
  - **http://www.rxfiles.ca/rxfiles/uploads/documents/RxFiles-Pain-and-Opioid-Resource-Links.pdf**
- **RxFiles PainLinks (for patient resources& support services):**
  - **http://www.rxfiles.ca/rxfiles/uploads/documents/PainLinks.pdf**

Prescribing Opioids Safely – RxFiles Chart - **http://www.rxfiles.ca/rxfiles/uploads/documents/members/Prescribing%20Opioids%20Safely.pdf**

References

1. Busse, Jason. "The 2017 Canadian Guideline for Opioids for Chronic Non-Cancer Pain." National Pain Centre, McMaster University.
2. Ballantyne JC, Mao J. Opioid therapy for chronic pain. N Engl J Med. 2003 Nov 13;349(20):1943-53.
3. Portenoy RK. Opioid therapy for chronic nonmalignant pain: a review of the critical issues.J Pain Symptom Manage. 1996 Apr;11(4):203-17.
4. Finestone HM, Juurlink DN, Power B, et al. Opioid prescribing is a surrogate for inadequate pain management resources. Can Fam Physician 2016;62:465-8.
5. Mildenberger A, Allan GM. Tools for Practice. Available at: www.acfp.ca/wpcontent/uploads/tools-for-practice/1473693475_tfp170exerciseandbackpainfv.pdf
6. Thorson D, Biewen P, Bonte B, Epstein H, Haake B, Hansen C, Hooten M, Hora J, Johnson C, Keeling F, Kokayeff A, Krebs E, Myers C, Nelson B, Noonan MP, Reznikoff C, Thiel M, Trujillo A, Van Pelt S, Wainio J. Institute for Clinical Systems Improvement. Acute Pain Assessment and Opioid Prescribing Protocol. Published January 2014.
7. Harden P., Ahmed S., Ang K., Wiedemer N. Clinical Implications of Tapering Chronic Opioids in a Veteran Population. Pain medicine 2015;16(10):1975-81
8. Barth KS, Becker WC, Wiedemer NL, Mavandadi S., Oslin DW, Meghani SH, Gallagher RM Association between urine drug test results and treatment outcome in high-risk chronic pain patients on opioids. Journal of addiction medicine 2010;4(3):167-73
9. Passik SD, Heit H, Kirsh KL. Reality and responsibility: a commentary on the treatment of pain and suffering in a drug-using society. J Opioid Manag. 2006 May-Jun;2(3):123-7.
10. Gourlay, Douglas L., Howard A. Heit, and Abdulaziz Almahrezi. "Universal precautions in pain medicine: a rational approach to the treatment of chronic pain." *Pain Medicine* 6.2 (2005): 107-112.
11. Johnson SJ. Opioid safety in patients with renal or hepatic dysfunction. Available at: http://www.pain-topics.org. 2007.
12. Cicero, Theodore J., et al. "Factors influencing the selection of hydrocodone and oxycodone as primary opioids in substance abusers seeking treatment in the United States." PAIN 154.12 (2013): 2639-2648.
13. CADTH. Opioid Formulations With Tamper-Resistance or Abuse-Deterrent Features — Products and Policies. Available at: www.cadth.ca/tamper-resistant-formulations-of-opioids
14. 2019 American Geriatrics Society Beers Criteria® Update Expert Panel, Fick DM, Semla TP, Steinman M, Beizer J, Brandt N, Dombrowski R, DuBeau CE, Pezzullo L, Epplin JJ, Flanagan N. American Geriatrics Society 2019 updated AGS Beers Criteria® for potentially inappropriate medication use in older adults. Journal of the American Geriatrics Society. 2019 Apr;67(4):674-94.

Online Extras:

- Fentanyl Patch Taper – Alternate Approach: Limiting matrix patch area in contact with skin (e.g. tape) done anecdotally, but NOT usually recommended. {Fentanyl (Cover ½ of 12mcg/h patch with tape so only ½ patch exposed to skin) x4-8wks then D/C}

Resources

1. BC Centre on Substance Use: Office-Based Induction of Buprenorphine/Naloxone https://www.youtube.com/watch?v=cr-7Nouhzew
2. CPSS Suboxone CME https://www.suboxonecme.ca/
3. RxFiles - http://www.rxfiles.ca/rxfiles/uploads/documents/RxFiles-Pain-and-Opioid-Resource-Links.pdf
    a. Tapering Template (ongoing updates): http://www.rxfiles.ca/rxfiles/uploads/documents/Opioid-Taper-Template.pdf
    b. Tapering Newsletter (2018): http://www.rxfiles.ca/rxfiles/uploads/documents/Opioid-Tapering-Newsletter-Compilation.pdf
    c. Tapering - Patient Q&A Booklet: http://www.rxfiles.ca/rxfiles/uploads/documents/Opioid-Patient-Booklet-Taper-RxFiles.pdf
4. Wellhealth – Opioid Tapering Template: https://cep.health/clinical-products/opioid-tapering-template/

References

1. Frank et al. Patient Outcomes in Dose Reduction or Discontinuation of Long-Term Opioid Therapy: A Systematic Review. Ann Intern Med. 2017;167:181-191.
2. Eccleston et al. Interventions for the reduction of prescribed opioid use in CNCP. Cochrane Database of Systematic Reviews 2017. CD010323
3. Murphy et al. Guidance on opioid tapering in the context of chronic pain: Evidence, practical advice and frequently asked questions. Canadian Pharmacists Journal.Vol 151, Issue 2, pp. 114 – 120.
4. Baron MJ, McDonald PW. Significant pain reduction in chronic pain patients after detoxification from high-dose opioids. Journal of Opioid Management. 2006. DOI: 10.5055/jom.2006.0041
5. Harden P., Ahmed S., Ang K., Wiedemer N. Clinical Implications of Tapering Chronic Opioids in a Veteran Population. Pain medicine 2015;16(10):1975-81
6. Busse et al. The 2017 Canadian Guideline for Opioids for Chronic Non-Cancer Pain.
    a. http://www.cmaj.ca/content/2017-canadian-opioid-guideline-1-already-time-overhaul;
    b. http://www.cmaj.ca/content/re-response-%E2%80%9C-2017-canadian-opioid-guideline-already-time-overhaul%E2%80%9D

References

1 Canadian Guideline for Safe and Effective Use of Opioids for Chronic Non-Cancer Pain — Part B: Recommendations for Practice, Version 5.5 April 30, 2010. [NOUGG] Accessed at: http://nationalpaincentre.mcmaster.ca/documents/opioid_guideline_part_b_v5_6.pdf

2 Opioid withdrawal scales, Saskatoon Health Region, Saskatchewan. http://pauliplace.com/02%20Involuntary%20DSS/03%20YIAP&MA%20hyperlinks/YIDSMAIS%2008%20SHR%20Opiate%20Withdrawal%20Scale.pdf

3 Butt P, McLeod M. Opioid withdrawal protocol, Saskatchewan. http://www.quadrant.net/cpss/pdf/Opioid_Withdrawal_Protocol.pdf

4 Frank JW, Levy C, Matlock DD, Calcaterra SL, Mueller SR, Koester S, et al. Patients' perspectives on tapering of chronic opioid therapy: a qualitative study. Pain Med. 2016;17:1838-47

5 Frank JW, Lovejoy TI, Becker WC, Morasco BJ, Koenig CJ, Hoffecker L, Dischinger HR, Dobscha SK, Krebs EE. Patient Outcomes in Dose Reduction or Discontinuation of Long-Term Opioid Therapy: A Systematic Review. Ann Intern Med. 2017 Jul 18.

6 Merrigan JM, Buysse DJ, Bird JC, Livingston EH. JAMA patient page. Insomnia.JAMA. 2013 Feb 20;309(7):733. Accessed online 21 Oct, 2013 at http://jama.jamanetwork.com/article.aspx?articleid=1653524.

7 Sedative Patient Information Sheet (RxFiles) http://www.rxfiles.ca/rxfiles/uploads/documents/PSYC-Sedative-PtHdout.pdf

8 Chronic Insomnia in Older Adults (RxFiles Q&A) http://www.rxfiles.ca/rxfiles/uploads/documents/Insomnia-Older-Adults-QandA.pdf

9 Gowing L, Farrell MF, Ali R, White JM. Alpha2-adrenergic agonists for the management of opioid withdrawal. Cochrane Database Syst Rev. 2014 Mar 31;3:CD002024.

10 Kowalczyk WJ, Phillips KA, Jobes ML, Kennedy AP, Ghitza UE, Agage DA,et al. Clonidine Maintenance Prolongs Opioid Abstinence and Decouples Stress From Craving in Daily Life: A Randomized Controlled Trial With Ecological Momentary Assessment. Am J Psychiatry. 2015 Aug 1;172(8):760-7.

Additional references:

9 Berna C, Kulich RJ, Rathmell JP. Tapering Long-term Opioid Therapy in Chronic Noncancer Pain: Evidence and Recommendations for Everyday Practice. Mayo Clin Proc. 2015 Jun;90(6):828-42. doi: 10.1016/j.mayocp.2015.04.003.

10 Suttner J, Lovett A, Varnachio K. Best Practices in Tapering Methods in Patients Undergoing Opioid Therapy. Advances in Pharmacology and Pharmacy 2013;1(2)42-57.

Online Extras for RxFiles Peri-Operative Chart

Pasero Opioid-induced Sedation Scale (POSS)

S **= Sleep, easy to arouse**
Acceptable; no action necessary; may increase opioid dose if needed

1. **Awake and alert**
Acceptable; no action necessary; may increase opioid dose if needed

2. **Slightly drowsy, easily aroused**
Acceptable; no action necessary; may increase opioid dose if needed

3. **Frequently drowsy, arousable, drifts off to sleep during conversation**
Unacceptable; monitor respiratory status and sedation level closely until sedation level is stable at less than 3 and respiratory status is satisfactory; decrease opioid dose 25% to 50% or notify prescriber or anaesthesiologist for orders; consider administering a non-sedating, opioid-sparing nonopioid, such as acetaminophen or an NSAID, if not contraindicated.

4. **Somnolent, minimal or no response to verbal or physical stimulation**
Unacceptable; stop opioid; consider administering naloxone; notify prescriber or anesthesiologist; monitor respiratory status and sedation level closely until sedation level is stable at less than 3 and respiratory status is satisfactory

References: Peri-Operative Pain Management Considerations - Type of Surgery (RxFiles.ca)

1) Baumann T, Strickland J, & Herndon C (2011). Chapter 69. Pain Management. In Talber R, Dipiro J, Matzke G, Posey L, Wells B, & Yee C. *Pharmacotherapy: A Pathophysiologic Approach*, 8e. Retrieved November 17, 2012 from http://www.accesspharmacy.com/content.aspx?aID=7986332.
2) Wu C & Raja S. Treatment of acute postoperative pain. *Lancet.* 2011; 377: 2215-25.
3) Pyati S & Gan T. Perioperative Pain Management. *CNS Drugs.* 2007; 21(3): 185-211.
4) American Society of Anesthesiologists Task Force on Acute Pain Management. Practice Guidelines for Acute Pain Management in the Perioperative Setting. *Anesthesiology.* 2012; 116(2): 248-72.
5) Derry S, Derry CJ, Moore RA. Single dose oral ibuprofen plus oxycodone for acute postoperative pain in adults. Cochrane Database Syst Rev. 2013 Jun 26;6:CD010289.
6) Regier L, Butt P, Carter. Pain Approaches: Distinctives for the ACUTE vs PALLIATIVE vs CNCP use of Opioids. RxFiles.ca. Accessed online 11 Dec 2013 at http://www.rxfiles.ca/rxfiles/uploads/documents/members/CHT-Pain-Approaches-Acute-Palliative-CNCP.pdf
7) Alford P, Compton P, & Samet J. Acute pain management for patients receiving maintenance methadone or buprenorphine therapy. *Annals of Internal Medicine* 2006; 144: 127-134.
8) Volkow N & McLellan T. Curtailing Diversion and Abuse of Opioid Analgesics Without Jeopardizing Pain Treatment. *JAMA.* 2011; 305(13): 1346-47.
9) *Veterans Health Administration, Department of Defense: Clinical Practice Guidelines for the Management of Postoperative Pain*, Version 1.2, adapted May 2002. Available online: http://www.healthquality.va.gov/Post_Operative_Pain_Management_POP.asp
10) Corke P. Postoperative Pain Management. Austrailian Prescriber 2013;36(6)202-205.
11) Friday J, Kanegaye J, McCaslin I, Zheng A, & Harley J. Ibuprofen provides analgesia equivalent to acetaminophen-codeine in the treatment of acute pain in children with extremity injuries: a randomized clinical trial. *Society for Academic Emergency Medicine*. 2009; 16: 711-16.
12) Nauta M, Landsmeer M, & Koren G. Codeine-acetaminophen versus nonsteroidal anti-inflammatory drugs in the treatment of post-abdominal surgery pain: a systematic reivew of randomized trials. *The American Journal of Surgery.* 2009; 198: 256-61.
13) Regier L. Pain, Chronic Non-cancer – Treatment Considerations. RxFiles Accessed online at http://www.rxfiles.ca/rxfiles/uploads/documents/members/CHT-Pain-Chronic-NonCa.pdf
14) **Clarke H, Soneji N, Ko DT, Yun L, Wijeysundera DN. Rates and risk factors for prolonged opioid use after major surgery: population based cohort study. BMJ. 2014 Feb 11;348:g1251.**
15) Taylor I, Kolber M. My fracture really hurts, can I use non-steroidal anti-inflammatories? In Tools for Practice, ACFP, May 2014. Accessed online at: **http://www.mailoutinteractive.com/Industry/View.aspx?id=572759&q=738814563&qz=10a458**
16) Paul JE, Nantha-Aree M, Buckley N, Shahzad U, Cheng J, Thabane L, Tidy et al. Randomized controlled trial of gabapentin as an adjunct to perioperative analgesia in total hip arthroplasty patients. Can J Anaesth. 2015 May;62(5):476-484.
17) Sun EC, Darnall B, Baker LC, Mackey S. Incidence of and Risk Factors for Chronic Opioid Use Among Opioid-Naive Patients in the Postoperative Period. JAMA Intern Med. 2016 Jul 11
18) Plunkett A, Haley C, McCoart A, Beltran T, Highland KB, Berry-Caban C, Lamberth S, Bartoszek M. A Preliminary Examination of the Comparative Efficacy of Intravenous vs Oral Acetaminophen in the Treatment of Perioperative Pain. Pain Med. 2016 Dec 29. pii: pnw273. doi: 10.1093/pm/pnw273. http://painmedicine.oxfordjournals.org/content/early/2016/12/07/pm.pnw273
19) Association of Anaesthetists. Guidelines: Controlled drugs in peri-operative care 2019. Accessed online Sept 15, 2019 at https://anaesthetists.org/Home/Resources-publications/Guidelines/Controlled-drugs-in-perioperative-care

Additional References

Alam A, Gomes T, Zheng H, Mamdani M, Juurlink D, & Bell C. Long-term Analgesic Use After Low-Risk Surgery. *Arch Intern Med.* 2012; 172(5): 425-30.

Dodwell E, Latorre J, Parisini E, Zwettler E, Chandra D, Mulpuri K, & Snyder B. NSAID Exposure and Risk of Nonunion: A Meta-Analysis of Case-Control and Cohort Studies. *Calcif Tissue Int.* 2010; 87: 193-202.

Gaskell H, Derry S, Wiffen PJ, et al. Single dose oral **ketoprofen or dexketoprofen for acute postoperative pain in adults**. Cochrane Database Syst Rev. 2017 May 25;5:CD007355. Ketoprofen at doses of 25 mg to 100 mg is an effective analgesic in moderate to severe acute postoperative pain with an NNT for at least 50% pain relief of 2.9 with a 50 mg dose. This is similar to that of commonly used NSAIDs such as ibuprofen (NNT 2.5 for 400 mg dose) and diclofenac (NNT 2.7 for 50 mg dose). Dexketoprofen is also effective with an NNT of 4.1 in the dose range 10 mg to 25 mg. Differential efficacy between dental surgery and other types of surgery seen for both drugs is unusual. Both drugs were well tolerated in single doses.

Hah JM, Cramer E, Hilmoe H, Schmidt P, McCue R, et al. Factors Associated With Acute Pain Estimation, Postoperative Pain Resolution, Opioid Cessation, and Recovery: Secondary Analysis of a Randomized Clinical Trial. JAMA Netw Open. 2019 Mar 1;2(3):e190168.

Hah JM, Bateman BT, Ratliff J, Curtin C, Sun E. Chronic Opioid Use After Surgery: Implications for Perioperative Management in the Face of the Opioid Epidemic. Anesth Analg. 2017;125(5):1733–1740. doi:10.1213/ANE.0000000000002458. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6119469/

Hamilton TW, Strickland LH, Pandit HG. A Meta-Analysis on the Use of Gabapentinoids for the Treatment of Acute Postoperative Pain Following Total Knee Arthroplasty. J Bone Joint Surg Am. 2016 Aug 17;98(16):1340-50.

Hill MV, McMahon ML, Stucke RS, Barth RJ Jr. Wide Variation and Excessive Dosage of Opioid Prescriptions for Common General Surgical Procedures. Ann Surg. 2017 Apr;265(4):709-714.

Kelly LE, Sommer DD, Ramakrishna J, et al. Morphine or Ibuprofen for Post-Tonsillectomy Analgesia: A Randomized Trial. Pediatrics. 2015 Jan 26.

Macintyre P & Walker S. The scientific evidence for acute pain treatment. *Current Opinion in Anesthesiology.* 2010; 23: 623-28.

Martini C, Olofsen E, Yassen A, Aarts L, & Dahan A. Pharmacokinetic-pharmacodynamic modeling in acute and chronic pain: an overview of the recent literature. *Expert Rev. Clin. Pharmacol.* 2011; 4(6) 719-28.

McQuay H, Derry S, Eccleston C, Wiffen P, & Moore R. Evidence for analgesic effect in acute pain – 50 yrs on. *Pain.* 2012; 153: 1364-67.

Medical Letter: Treatment Guidelines. Drugs for Pain. *Medical Letter* 2010 92(8): 25-33.

Melby V & colleagues. Acute pain relief in children: use of rating scales and analgesia. *Emergency Nurse.* 2011; 19(6): 32-37.

Mooney B. Child-friendly aids in pain management. *WIN.* 2012; 20(6): 37-28.

Nauta M, Landsmeer M, & Koren G. Codeine-acetaminophen versus nonsteroidal anti-inflammatory drugs in the treatment of post-abdominal surgery pain: a sytematic review of randomized trials. *The American Journal of Surgery.* 2009; 198: 256-61.

Poonai N, Bhullar G, Lin K, Papini A, Mainprize D, Howard J, et al. Oral administration of morphine versus ibuprofen to manage postfracture pain in children: a randomized trial. CMAJ. 2014 Dec 9;186(18):1358-63.

Subramanian P, Allcock N, James V, & Lathlean J. Challenges faced by nurses in managing pain in a critical care setting. *Journal of Clinical Nursing.* 2011; 21: 1254-62.

Tedesco D;Gori D;Desai KR;Asch S;Carroll IR;Curtin. Drug-Free Interventions to Reduce Pain or Opioid Consumption After Total Knee Arthroplasty: A Systematic Review and Meta-analysis. JAMA Surg. 2017 Aug 16:e172872.

What is a reasonable amount of opioid to prescribe/dispense post-op in opioid naïve patients?

Links to related articles / materials:

- **Michigan Opioid Prescribing Network Michigan OPEN**: https://michigan-open.org/prescribing-recommendations/ https://michigan-open.org/wp-content/uploads/2019/07/Prescribing-Recommendations-Table- -Michigan-OPEN.pdf
- **Lancet article related to Michigan OPEN (see table)**: https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(19)30428-3/fulltext#
- **Bree Collaborative, July 2018: Prescribing Opioids for Post-operative Pain – Supplemental Guidance** http://www.agencymeddirectors.wa.gov/Files/FinalSupBreeAMDGPostopPain091318wcover.pdf
- **Choosing Wisely: Using Opioids Safely After Surgery** http://www.choosingwisely.org/patient-resources/using-opioids-safely-after-surgery/

AAOS- Guideline on the Treatment of Symptomatic Osteoporotic Spinal Compression Fractures- **Vertebroplasty** 2010 Recommendations (Calcitonin for 4 weeks post acute injury) http://www.aaos.org/Research/guidelines/SCFsummary.pdf

Abrahamsen B, Eiken P, Eastell R. **Subtrochanteric and diaphyseal femur fractures** in patients treated with **alendronate**: a register-based national cohort study. J Bone Miner Res 2009; 24:1095-102.

Abrahamsen B. **Bisphosphonate adverse effects**, lessons from large databases. Curr Opin Rheumatol. 2010 Jul;22(4):404-9.

Abrahamsen B. **Adverse effects of bisphosphonates**. Calcif Tissue Int. 2010 Jun;86(6):421-35. Epub 2010 Apr 21.

Abrahamsen Bo; Eiken Pia; Eastell Richard. **Proton Pump Inhibitor Use** and the Antifracture Efficacy of Alendronate. Arch Intern Med. 2011;0(2011):archinternmed.2011.20.

Abrahamsen B, Rubin KH, Eiken PA, Eastell R. Characteristics of patients who suffer major osteoporotic **fractures despite adhering to alendronate** treatment: a National Prescription registry study. Osteoporos Int. 2012 Oct 16.

Abrahamsen B, Eiken P, et al. Risk of hip, **subtrochanteric, and femoral shaft fractures among mid and long term users of alendronate**: nationwide cohort and nested case-control study. BMJ. 2016 Jun 28;353:i3365.

Abou-Setta AM, Beaupre LA, Rashiq S, et al. Comparative effectiveness of pain management interventions for **hip fracture:** a systematic review. Ann Intern Med. 2011 Aug 16;155(4):234-45.

ACCORD Schwartz AV, Margolis KL, Sellmeyer DE, et al. Intensive Glycemic Control Is Not Associated With **Fractures or Falls** in the ACCORD Randomized Trial. Diabetes Care. 2012 Jul;35(7):1525-31.

Ackman JM, Lata PF, Schuna AA, et al. Bone Health Evaluation in a **Veteran Population**: A Need for the Fracture Risk Assessment Tool (**FRAX**). Ann Pharmacother. 2014 Oct;48(10):1288-93.

Adachi JD, Bensen WG, Brown J., et al. Intermittent **etidronate** therapy to prevent corticosteroid-induced osteoporosis. N Engl J Med 1997; 337:382-8.

Adams AL, Adams JL, Raebel MA, et al. **Bisphosphonate Drug Holiday** and Fracture Risk: A Population-Based Cohort Study. J Bone Miner Res. 2018 Mar 12.

Adler RA, Tran MT, et al. Performance of the **Osteoporosis Self-assessment Screening Tool (OST)** for osteoporosis in American men. Mayo Clin Proc. 2003 Jun;78(6):723-7.

Adler RA, El-Hajj Fuleihan G, Bauer DC, et al. **Managing Osteoporosis in Patients on Long-Term Bisphosphonate Treatment**: Report of a Task Force of the **American Society for Bone and Mineral Research**. (**ASBMR**) J Bone Miner Res. 2016 Jan;31(1):16-35.

Akesson K, Marsh D, Mitchell PJ, et al; IOF Fracture Working Group. **Capture the Fracture: a Best Practice Framework** and global campaign to break the fragility fracture cycle. Osteoporos Int. 2013 Aug;24(8):2135-52.

Akram Z, Abduljabbar T, Kellesarian SV, et al. Efficacy of **bisphosphonate as an adjunct to Non-surgical periodontal therapy in the management of periodontal disease**: a systematic review. Br J Clin Pharmacol. 2016 Oct 8.

Adler RA, El-Hajj Fuleihan G, et al. Managing Osteoporosis in Patients on **Long-Term Bisphosphonate Treatment**: Report of a Task Force of the American Society for Bone and Mineral Research (**ASBMR**). J Bone Miner Res. 2016 Jan;31(1):16-35.

Alekel DL, Genschel U, Koehler KJ, et al. **Soy Isoflavones** for Reducing Bone Loss Study: effects of a 3-year trial on hormones, adverse events, and endometrial thickness in postmenopausal women. Menopause. 2014 Jul 7.

Alford SH, Rattan R, Buekers TE, et al. Protective effect of **bisphosphonates on endometrial cancer** incidence in data from the Prostate, Lung, Colorectal and Ovarian (PLCO) cancer screening trial. Cancer. 2014 Dec 22.

Ali SN, Tan T, Meeran K, Wynne K. A man with anxiety, confusion, and red eyes. (**induced by calcium supplements**) BMJ. 2012 Jul 5;345:e4443.

Alibhai SM, Duong-Hua M, et al. Impact of **androgen deprivation therapy** on cardiovascular disease and diabetes. J Clin Oncol. 2009 Jul 20;27(21):3452-8. Epub 2009 Jun 8.

Alibhai SMH, Zukotynski K, Walker-Dilks C, et al. **Bone Health** and Bone-Targeted Therapies for **Nonmetastatic Prostate Cancer**: A Systematic Review and Meta-analysis. Ann Intern Med. 2017 Aug 8.

Alibhai SMH, Zukotynski K, Walker-Dilks C, et al; Cancer Care Ontario Genitourinary Cancer Disease Site Group. Bone Health and Bone-targeted Therapies for Prostate Cancer: a Programme in Evidence-based Care - Cancer Care Ontario Clinical Practice Guideline. Clin Oncol (R Coll Radiol). 2017 Jun;29(6):348-355.

Allen CS, Yeung J HS, Vandermeer B, Homik J. **Bisphosphonates for steroid-induced osteoporosis**. Cochrane Database of Systematic Reviews 2016, Issue 10. Art. No.: CD001347. There was high-certainty evidence that bisphosphonates are beneficial in reducing the risk of vertebral fractures with data extending to 24 months of use. There was low-certainty evidence that bisphosphonates may make little or no difference in preventing nonvertebral fractures. There was moderate-certainty evidence that bisphosphonates are beneficial in preventing and treating corticosteroid-induced bone loss at both the lumbar spine and femoral neck. Regarding harm, there was low-certainty evidence that bisphosphonates may make little or no difference in the occurrence of serious adverse events or withdrawals due to adverse events. We are cautious in interpreting these data as markers for harm and tolerability due to the potential for bias. Overall, our review supports the use of bisphosphonates to reduce the risk of vertebral fractures and the prevention and treatment of steroid-induced bone loss.

Aloia JF, Dhaliwal R, Shieh A, et al. **Calcium and Vitamin D** Supplementation in Postmenopausal Women. J Clin Endocrinol Metab. 2013 Sep 24.

Alonso-Coello P, García-Franco AL, Guyatt G, Moynihan R. Drugs for **pre-osteoporosis**: prevention or disease mongering? BMJ. 2008 Jan 19;336(7636):126-9.

Altkorn D, Cifu AS. **Screening for osteoporosis**. JAMA. 2015 Apr 14;313(14):1467-8.

Amadori D, Aglietta M, Alessi B, et al. Efficacy and safety of **12-weekly versus 4-weekly zoledronic** acid for prolonged treatment of patients with bone metastases from **breast cancer (ZOOM):** a phase 3, open-label, randomised, non-inferiority trial. Lancet Oncol 2013; online May 16.

American Association of Oral and Maxillofacial Surgeons-**AAOMS** Position Paper on **Bisphosphonate-Related Osteonecrosis of the Jaw**—2009 Update http://www.aaoms.org/docs/position_papers/bronj_update.pdf

American College of Obstetricians and Gynecologists (**ACOG**). Osteoporosis. Washington (DC): American College of Obstetricians and Gynecologists (ACOG); 2012 Sep. 17 p. (ACOG practice bulletin; no. 129).

Anastassios G. Pittas, Mei Chung, Thomas Trikalinos, Et al. Systematic Review: **Vitamin D and Cardiometabolic Outcomes**. Ann Intern Med March 2, 2010 152:307-314; doi:10.1059/0003-4819-152-5-201003020-00009.

Anderson GL, Limacher M, Assaf AR, et al. Effects of conjugated equine **estrogen** in postmenopausal women with hysterectomy: the Women's Health Initiative randomized controlled trial. JAMA 2004; 291(14):1701-1712.

Anderson JJ, Roggenkamp KJ, Suchindran CM. **Calcium intakes and femoral and lumbar bone density** of elderly U.S. men and women: National Health and Nutrition Examination Survey 2005-2006 analysis. J Clin Endocrinol Metab. 2012 Dec;97(12):4531-9.

Anderson J, Kruszka B, Delaney JAC, et al. **Calcium intake from Diet and Supplements and the Risk of Coronary Atery Calcification** and its Progression Among Older Adults : 10-Year Follow-Up of the Multi-Ethnic Study of Atherosclerosos (MESA). J Am Heart Assoc.2016 ;5 :e003815.

Anderson JJ, Kruszka B, Delaney JA, et al. **Calcium intake from diet and supplements and the risk of coronary artery calcification** and its progression among older adults: 10-year follow-up of the Multi-Ethnic Study of Atherosclerosis (MESA). J Am Heart Assoc 2016.

Appiah D, Winters SJ, Muldoon SB, et al. **Androgens, Bilateral Oophorectomy, and Cardiovascular Disease Mortality** in Postmenopausal Women With and Without Diabetes: The Study of Osteoporotic Fractures. Diabetes Care. 2015 Oct 12.

Appiah D, Winters SJ, Muldoon SB, et al. **Androgens, Bilateral Oophorectomy, and Cardiovascular Disease Mortality** in Postmenopausal Women With and Without Diabetes: The Study of Osteoporotic Fractures. Diabetes Care. 2015 Dec;38(12):2301-7.

Arai R, Takahashi D, Inoue M, et al. Efficacy of **teriparatide** in the treatment of **nontraumatic osteonecrosis of the femoral head**: a retrospective comparative study with alendronate. BMC Musculoskelet Disord. 2017 Jan 19;18(1):24.

Arj A, Razavi Zade M, Yavari M, et al. **Proton pump inhibitors** use and change in bone mineral density. Int J Rheum Dis. 2016 May 31.

Armingeat T, Brondino R, Pham T et al. Intravenous **pamidronate for pain relief in recent osteoporotic vertebral compression fracture**: a randomized double-blind controlled study.Osteoporosis International 2006;17(11):1659-1665 .

Auais MA, Eilayyan O, Mayo NE. **Extended exercise** rehabilitation after hip fracture improves patients` physical function: a systematic review and meta-analysis. Phys Ther. 2012 Nov;92(11):1437-51.

Avenell A, Gillespie WJ, Gillespie LD, O'Connell D. **Vitamin D** and vitamin D analogues for preventing fractures associated with involutional and post-menopausal osteoporosis. Cochrane Database Syst Rev. 2009 Apr 15;(2):CD000227.

Avenell A, Smith TO, Curtain JP, et al. **Nutritional supplementation for hip fracture** aftercare in older people. Cochrane Database of Systematic Reviews 2016, Issue 11. Art. No.: CD001880. There is low-quality evidence that oral multinutrient supplements started before or soon after surgery may prevent complications within the first 12 months after hip fracture, but that they have no clear effect on mortality. There is very low-quality evidence that oral supplements may reduce 'unfavourable outcome' (death or complications) and that they do not result in an increased incidence of vomiting and diarrhoea. Adequately sized randomised trials with robust methodology are required. In particular, the role of dietetic assistants, and peripheral venous feeding or nasogastric feeding in very malnourished people require further evaluation.

Axelsson KF, et al. Association Between **Alendronate Use** and Hip Fracture Risk in Older Patients **Using Oral Prednisolone**. JAMA. 2017 Jul 11;318(2):146-155.

Axelsson KF, Werling M, Eliasson B, et al. **Fracture Risk After Gastric Bypass Surgery**: A Retrospective Cohort Study. J Bone Miner Res. 2018 Jul 16.

Bachrach LK, Gordon CM; Section on Endocrinology. **Bone Densitometry in Children and Adolescents**. Pediatrics. 2016 Sep 26.

Bacon CJ, Gamble GD, Horne AM, Scott MA, Reid IR. **High-dose oral vitamin D(3) supplementation** in the elderly. Osteoporos Int. 2008 Dec 20.

Balani A, Marda SS. Images in Clinical Medicine. **Paget's Disease** of Bone. N Engl J Med. 2016 Mar 31;374(13):1264.

Banks E, Beral V, Reeves G, et al., for the **Million Women Study** Collaborators. Fracture incidence in relation to the pattern of use of hormone therapy in postmenopausal women. JAMA 2004;291:2212-2220.

Barrett-Connor E, Grady D, Sashegyi A, et al. **Raloxifene** and cardiovascular events in osteoporotic postmenopausal women: four-year results from the **MORE** (Multiple Outcomes of Raloxifene Evaluation) randomized trial. JAMA 2002; 287(7):847- 857.

Barrett-Connor E, Mosca L, Collins P, et al. Effects of **raloxifene** on cardiovascular events and breast cancer in postmenopausal women. (**RUTH**)N Engl J Med 2006; 355(2):125-137.

Barrett-Connor Elizabeth, Nielson Carrie M, Orwoll Eric, et al., for the Osteoporotic Fractures in Men (MrOS) Study Group. Epidemiology of **rib fractures in older men**: Osteoporotic Fractures in Men (MrOS) prospective cohort study. BMJ 2010;340:c1069, doi: 10.1136/bmj.c1069 (Published 15 March 2010).

Barrett-Lee P, Casbard A, Abraham J, et al. **Oral ibandronic acid versus intravenous zoledronic** acid in treatment of bone metastases from breast cancer: a randomised, open label, non-inferiority phase 3 trial. (ZICE) Lancet Oncol 2013; online Dec 11.

Bashutski JD, Eber RM, Kinney JS, et al. **Teriparatide and Osseous Regeneration** in the Oral Cavity. N Engl J Med. 2010 Oct 16. (n=40, 6 weeks, 1yr follow up)

Bauer DC. Clinical practice. **Calcium supplements** and fracture prevention. N Engl J Med. 2013 Oct 17;369(16):1537-43.

Bauer DC, Schwartz A, Palermo L, et al. **Fracture prediction after discontinuation of 4 to 5 years of alendronate** therapy: the **FLEX** study [online May 5, 2014]. JAMA Intern Med. doi:10.1001/jamainternmed.2014.1232.

Bazelier MT, van Staa T-P, Uitdehaag BMJ, et al. Risk of **fractures** in patients with **multiple sclerosis**: a population based cohort study. Neurology 2012;78:1967–1973.

Bazzocchi A, Diano D. **Dual-energy x-ray absorptiometry** in **obesity**. CMAJ. 2014 Jan 7;186(1):48

BC Guideline: Medical Services Commission. **Vitamin D testing protocol**. British Columbia Medical Services Commission; 2010 Oct 1. http://www.bcguidelines.ca/pdf/vitamind.pdf

Bedatsova L, Drake MT. The **Skeletal Impact of Cancer Therapies**. Br J Clin Pharmacol. 2019 Feb 5.

Bejhed RS, Kharazmi M, Hallberg P. Identification of Risk Factors for **Bisphosphonate-Associated Atypical Femoral Fractures** and **Osteonecrosis** of the Jaw in a Pharmacovigilance Database. Ann Pharmacother. 2016 Aug;50(8):616-24.

Bell KJ, Hayen A, Macaskill P, et al. Value of routine monitoring of **bone mineral density** after starting bisphosphonate treatment: secondary analysis of trial data. BMJ. 2009 Jun 23;338:b2266. doi: 10.1136/bmj.b2266.

Berger C, Langsetmo L, Joseph L, et al.; Canadian Multicentre Osteoporosis Study Research Group. Change in **bone mineral density** as a function of age in women and men and association with the use of antiresorptive agents. CMAJ. 2008 Jun 17;178(13):1660-8. The extent of bone loss that we observed in both sexes indicates that, in the absence of additional risk factors or therapy, repeat testing of bone mineral density to diagnose osteoporosis could be delayed to every 5 years.

Berry SD, Kiel DP, Colón-Emeric C. **Hip Fractures** in Older Adults in 2019. JAMA. 2019 Jun 11;321(22):2233-2234.

Berry SD, Samelson EJ, Pencina MJ, et al. **Repeat bone mineral density screening** and prediction of hip and major osteoporotic fracture. JAMA. 2013 Sep 25;310(12):1256-62.

Bertone-Johnson ER et al. Vitamin D supplementation and **depression** in the **Women's Health Initiative** Calcium and Vitamin D Trial. Am J Epidemiol 2012 Jul 1; 176:1.

Bhardwaj A, Swe KM, Sinha NK, et al. Treatment for osteoporosis in people with ss-**thalassaemia**. Cochrane Database Syst Rev. 2016 Mar 10;3:CD010429. There is evidence to indicate an increase in bone mineral density at the femoral neck, lumbar spine and forearm after administration of bisphosphonates and at the lumbar spine and hip after zinc sulphate supplementation. The authors recommend that further long-term randomised control trials on different bisphosphonates and zinc supplementation therapies in people with beta-thalassaemia and osteoporosis are undertaken.

Bhasin S, et al. **Testosterone therapy** in adult men with androgen deficiency syndromes: an endocrine society clinical practice guideline. J Clin Endocrinol Metab. 2006 Jun;91(6):1995-2010. Epub 2006 May 23. Erratum in: J Clin Endocrinol Metab. 2006 Jul;91(7):2688.

Bhuriya R, Singh M, Molnar J, Arora R, et al. Bisphosphonate use in women and the risk of atrial **fibrillation**: A systematic review and meta-analysis. Int J Cardiol. 2010 Jan 3.

Bianchi ML, Colombo C, Assael BM, et al. Treatment of low bone density in young people with **cystic fibrosis**: a multicentre, prospective, open-label observational study of calcium and calcifediol followed by a randomised placebo-controlled trial of alendronate. Lancet Respir Med. 2013 Jul;1(5):377-85

Bilezikian JP, Bandeira L, Khan A, et al. **Hyperparathyroidism**. Lancet.2017 Sep 15.

Bindon B, Adams W, Balasubramanian N, et al. Osteoporotic **fracutes during Bisphosphonate Drug Holiday**. Endocr Pract. 2018 Feb;24(2):163-169.

Bingham CO 3rd, Buckland-Wright JC, Garnero P, et al. **Risedronate** decreases biochemical markers of cartilage degradation but does not decrease symptoms or slow radiographic progression in patients with medial compartment **osteoarthritis** of the knee: results of the two-year multinational knee osteoarthritis structural arthritis study. Arthritis Rheum 2006; 54: 3494–507.

Binkley N et al. Evaluation of **ergocalciferol or cholecalciferol** dosing, 1600 IU daily or 50,000 IU monthly in older adults. *J Clin Endocrinol Metab* 2011 Apr; 96:981.

Bischoff-Ferrari H A, Dawson-Hughes B, Staehelin H B, et al. **Fall prevention** with supplemental and active forms of **vitamin D**: a meta-analysis of randomised controlled trials. BMJ 2009;339:b3692, doi: 10.1136/bmj.b3692 (Published 1 October 2009)

Bischoff-Ferrari HA, Willett WC, Wong JB, et al. Prevention of nonvertebral fractures with oral **vitamin D** and dose dependency: a meta-analysis of randomized controlled trials. Arch Intern Med. 2009 Mar 23;169(6):551-61.

Bischoff-Ferrari Heike A.; Dawson-Hughes Bess; Platz Andreas; et al. Effect of **High-Dosage Cholecalciferol** (2000 vs 800 IU/day) and Extended Physiotherapy on Complications After Hip Fracture: A Randomized Controlled Trial. Arch Intern Med. 2010;170(9):813-820.

Bischoff-Ferrari HA, Willett WC, Oray EJ, et al. A pooled analysis of **vitamin D dose** requirements for fracture prevention. N Engl J Med 2012;367:40-9. {highest actual-intake quartile (792 to 2000 IU daily), there was a 30% reduction in hip fracture incidence}

Bishop N, Adami S, Ahmed SF, et al. **Risedronate in children with osteogenesis imperfecta**: a randomised, double-blind, placebo-controlled trial. Lancet. 2013 Aug 5.

Bjelakovic G, Gluud LL, Nikolova D, et al. **Vitamin D** supplementation for **prevention of mortality in adults**. *Cochrane Database of Systematic Reviews* 2011, Issue 7. Art. No.: CD007470. DOI: 10.1002/14651858.CD007470.pub2. Vitamin D in the form of vitamin D3 seems to decrease mortality in predominantly elderly women who are mainly in institutions and dependent care. Vitamin D2, alfacalcidol, and calcitriol had no statistically significant effect on mortality. Vitamin D3 combined with calcium significantly increased nephrolithiasis. Both alfacalcidol and calcitriol significantly increased hypercalcaemia.

Bjelakovic G, Gluud LL, Nikolova D, Whitfield K, Krstic G, Wetterslev J, Gluud C. Vitamin D supplementation for **prevention of cancer** in adults.

Cochrane Database of Systematic Reviews 2014, Issue 6. Art. No.: CD007469. DOI: 10.1002/14651858.CD007469.pub2. There is currently no firm evidence that vitamin D supplementation decreases or increases cancer occurrence in predominantly elderly community-dwelling women. Vitamin D supplementation decreased cancer mortality and vitamin D supplementation decreased all-cause mortality, but these estimates are at risk of type I errors due to the fact that too few participants were examined, and to risks of attrition bias originating from substantial dropout of participants. Combined vitamin D and calcium supplements increased nephrolithiasis, whereas it remains unclear from the included trials whether vitamin D , calcium, or both were responsible for this effect.

Black DM, Schwartz AV, Ensrud KE, et al. FLEX Research Group. Effects of continuing or **stopping alendronate** after 5 years of treatment: the Fracture Intervention Trial Long-term Extension (**FLEX**): a randomized trial. JAMA. 2006 Dec 27;296(24):2927-38.

Black DM, Reid IR, Boonen S, et al. The effect of **3 versus 6 years of zoledronic acid** treatment in osteoporosis: a randomized extension to the HORIZON-Pivotal Fracture Trial (PFT). J Bone Miner Res 2012;27:243-54.

Black DM, Bauer DC, Schwartz AV, et al. **Continuing Bisphosphonate Treatment for Osteoporosis** - For Whom and for How Long? N Engl J Med. 2012 May 9.

Black DM et al. The effects of parathyroid hormone **(teriparatide) and alendronate alone or in combination** in postmenopausal osteoporosis. N Engl J Med 2003 Sep25;349:1207-15.

Black DM, Rosen CJ. Clinical Practice. **Postmenopausal Osteoporosis**. N Engl J Med. 2016 Jan 21;374(3):254-62.

Blau LA, Hoehns JD. Analgesic efficacy of **calcitonin** for vertebral fracture pain. Ann Pharmacother 2003; 37(4):564-570.

Bolland MJ, Grey AB, Gamble GD, Reid IR. Effect of Osteoporosis Treatment on **Mortality**: A Meta-Analysis. J Clin Endocrinol Metab. 2010 Jan 15.

Bolland MJ, Avenell A, Baron JA, et al, Effect of **calcium** supplements on risk of **myocardial infarction** and cardiovascular events: meta-analysis. BMJ 2010;341:c3691

Bolland MJ, Jackson R, Gamble GD, Grey A. **Discrepancies** in predicted fracture risk in **elderly people**. BMJ 2013;346:e8669.

Bolland ML, Leung W, Tai V, et al. **Calcium intake and risk of fracture**: systematic review. BMJ 2015;351:h4580.

Bolland MJ, Grey A. Ten years too long: **strontium ranelate**, cardiac events, and the European Medicines Agency. BMJ. 2016 Sep 30;354:i5109.

Bolton JM, Morin SN, et al. Association of **Mental Disorders and Related Medication Use** With Risk for Major Osteoporotic Fractures. JAMA Psychiatry. 2017 Apr 19.

Boonen S, Reginster JY, Kaufman JM, et al. Fracture risk and **zoledronic acid therapy in men with osteoporosis**. N Engl J Med. 2012 Nov;367(18):1714-23.

Bone HG, Hosking D, Devogelaer JP, et al. Alendronate Phase III Osteoporosis Treatment Study Group. **Ten years' experience** with **alendronate** for osteoporosis in postmenopausal women. N Engl J Med. 2004 Mar 18;350(12):1189-99.

Bone HG, Chapurlat R, Brandi ML, et al. The Effect of **3 or 6 Years of Denosumab** Exposure in Women With Postmenopausal Osteoporosis: Results From the **FREEDOM** Extension. J Clin Endocrinol Metab. 2013 Aug 26.

Bonnick S, De Villiers T, Odio A, et al. Effects of **Odanacatib** on BMD and Safety in the Treatment of Osteoporosis in Postmenopausal Women Previously Treated With Alendronate: A Randomized Placebo-Controlled Trial. J Clin Endocrinol Metab. 2013 Sep 24.

Bonovas S, Nikolopoulos G, Bagos P. **Bisphosphonate Use and Risk of Colorectal Cancer**: A Systematic Review and Meta-analysis. Br J Clin Pharmacol. 2013 Apr 18.

Boonen S, Sellmeyer DE, Lippuner K, et al. **Renal safety of annual zoledronic** acid infusions in osteoporotic postmenopausal women. Kidney Int 2008; 74(5):641-648.

Bordelon P, Ghetu MV, Langan RC. Recognition and management of **vitamin D deficiency**. Am Fam Physician. 2009 Oct 15;80(8):841-6.

Boucher M, Murphy G, Coyle D, et al. **Bisphosphonates and teriparatide** for the prevention of osteoporotic fractures in postmenopausal women [Technology overview no 22]. 22. 2006. Ottawa, Canadian Agency for Drugs and Technologies in Health.

Boyd C, Moodambail A. Severe **hypercalcaemia in a child secondary to use of alternative therapies**. BMJ Case Rep. 2016 Oct 6;2016.

Bridgeman MB, Pathak R. **Denosumab** for the reduction of bone loss in postmenopausal osteoporosis: a review. Clin Ther. 2011 Nov;33(11):1547-59.

Briggs GE, Freeman RK, Yaffe SJ, editors. **Drugs in Pregnancy and Lactation**. 9th ed. Williams and Wilkins; Philadelphia, PA: 2011

Briot Karine, Legrand Erik, Pouchain Denis, et al. Accuracy of patient-reported **height loss** and risk factors for height loss among postmenopausal women. CMAJ 2010 0: cmaj.090710.

Briot K, Durnez A, Paternotte S, et al. **Bone oedema on MRI** is highly associated with low bone mineral density in patients with early inflammatory back pain: results from the DESIR cohort. Ann Rheum Dis. 2012 Nov 17.

Bristow SM, Horne AM, Gamble GD, et al. **Dietary Calcium Intake and Bone Loss** Over 6 Years in Osteopenic Postmenopausal Women. J Clin Endocrinol Metab. 2019 Aug 1;104(8):3576-3584.

Brown JP, Morin S, Leslie W, et al. **Bisphosphonates** for treatment of osteoporosis: Expected **benefits, potential harms, and drug holidays**. Can Fam Physician. 2014 Apr;60(4):324-33.

Brufsky AM, Harker WG, Beck JT, et al. Final 5-year results of **Z-FAST** trial: **Adjuvant Zoledronic** Acid Maintains Bone Mass in Postmenopausal **Breast Cancer** Patients Receiving Letrozole. Cancer. 2011 Oct 10.

Buchbinder R, Osborne RH, Ebeling, PR., et al. A Randomized Trial of **Vertebroplasty** for Painful Osteoporotic Vertebral Fractures. N Engl J Med 2009 361: 557-568.

Buchbinder R, Johnston RV, Rischin KJ, et al. **Percutaneous vertebroplasty** for osteoporotic vertebral compression fracture. Cochrane Database of Systematic Reviews 2018, Issue 4. Art. No.: CD006349. Based upon high- to moderate-quality evidence, our updated review does not support a role for vertebroplasty for treating acute or subacute osteoporotic vertebral fractures in routine practice. We found no demonstrable clinically important benefits compared with placebo (sham procedure) and subgroup analyses indicated that the results did not differ according to duration of pain ≤ 6 weeks versus > 6 weeks.

Buckley L, Guyatt G, Fink HA, et al. **2017 American College of Rheumatology Guideline for the Prevention and Treatment of Glucocorticoid-Induced Osteoporosis**. Arthritis Care Res (Hoboken). 2017 Jun 6.

Buckley L, Humphrey MB. **Glucocorticoid-Induced Osteoporosis**. N Engl J Med. 2018 Dec 27;379(26):2547-2556.

Buppasiri P, Lumbiganon P, Thinkhamrop J, et al. **Calcium supplementation** (other than for preventing or treating hypertension) for improving pregnancy and infant outcomes. Cochrane Database of Systematic Reviews 2011, Issue 10. Art. No.: CD007079. DOI: 10.1002/14651858.CD007079.pub2. Calcium supplementation is associated with a significant protective benefit in the prevention of **pre-eclampsia**, and should be used for this indication according to a previous review. This review indicates that there are no additional benefits for calcium supplementation in prevention of preterm birth or low infant birth weight.

Burns RB, Rosen H, Berry S, et al. How Would You Manage This Patient With Osteoporosis?: Grand Rounds Discussion From Beth Israel Deaconess Medical Center. Ann Intern Med. 2018 Jun 5;168(11):801-808.

Burt LA, Billington EO, Rose MS, et al. Effect of **High-Dose Vitamin D Supplementation** on Volumetric Bone Density and Bone Strength: A Randomized Clinical Trial. JAMA. 2019 Aug 27;322(8):736-745.

Cadarette SM, Katz JN, Brookhart MA, Sturmer T, Stedman MR, Solomon DH. **Relative effectiveness** of osteoporosis drugs for preventing nonvertebral fracture. Ann Intern Med 2008; 148(9):637-646.

Cai S, Zhu J, Sun L, et al. Association between **urinary triclosan with bone mass density** and osteoporosis in the US adult women, 2005-2010. J Clin Endocrinol Metab. 2019 Jun 25.

Calarge CA, Schlechte JA, Burns TL, et al. The Effect of **Psychostimulants** on **Skeletal Health** in Boys Co-Treated with **Risperidone**. J Pediatr. 2015 Apr 8.

Camacho PM, Petak SM, Binkley N, et al. (**AACE/ACE**) **American Association of Clinical Endocrinologists** and American College of Endocrinology Clinical Practice Guidelines for the **Diagnosis and Treatment of Postmenopausal Osteoporosis** -2016. Endocr Pract. 2016 Sep 2;22(Suppl 4):1-42.

Cameron ID, Murray GR, Gillespie LD, et al. Interventions for **preventing falls** in older people in nursing care facilities and hospitals. Cochrane Database Syst Rev. 2010 Jan 20;(1):CD005465. There is evidence that multifactorial interventions reduce falls and risk of falling in hospitals and may do so in nursing care facilities. Vitamin D supplementation is effective in reducing the rate of falls in nursing care facilities. Exercise in subacute hospital settings appears effective but its effectiveness in nursing care facilities remains uncertain.

Cano A, Chedraui P, Goulis DG, et al.**Calcium** in the prevention of postmenopausal osteoporosis: **EMAS clinical guide**. Maturitas. 2018 Jan;107:7-12.

Cano Porras D, Siemonsma P, Inzelberg R, et al. Advantages of **virtual reality in the rehabilitation of balance and gait**: Systematic review. Neurology. 2018 May 29;90(22):1017-1025.

Capeci CM and Tejwani NC. Bilateral **low-energy** simultaneous or sequential **femoral fractures** in patients on long-term alendronate therapy. *J Bone Joint Surg Am* 2009 Nov; 91:2556.

Caplan L, Hansen KE, Saag KG. **Response to the ACP Osteoporosis Guideline 2017 Revision**. Arthritis Rheumatol. 2017 Sep 7.

Carberry GA et al. Unreported vertebral body compression fractures at **abdominal multidetector CT**. Radiology 2013 Jul; 268:120.

Cass AR, Shepherd AJ. Validation of the **Male Osteoporosis Risk Estimation Score (MORES)** in a primary care setting. J Am Board Fam Med. 2013 Jul-Aug;26(4):436-44.

Cass AR, Shepherd AJ, Asirot R, et al. Comparison of the **Male Osteoporosis Risk** Estimation Score (**MORES**) With FRAX in Identifying Men at Risk for Osteoporosis. Ann Fam Med. 2016 Jul;14(4):365-9.

Castro M, King TS, Kunselman SJ, et al; for the National Heart, Lung, and Blood Institute's AsthmaNet. Effect of Vitamin D3 on **Asthma Treatment** Failures in Adults With Symptomatic Asthma and Lower Vitamin D Levels: The **VIDA** Randomized Clinical Trial. JAMA. 2014 May 18.

Cauley JA, Lacroix AZ, Wu L, et al. Serum **25-hydroxyvitamin D** concentrations and risk for hip fractures. Ann Intern Med. 2008 Aug 19;149(4):242-50.

Cazanave C, Dupon M, Lavignolle-Aurillac V, et al. Groupe d'Epidémiologie Clinique du SIDA en Aquitaine. Reduced bone mineral density in **HIV**-infected patients: prevalence and associated factors. AIDS. 2008 Jan 30;22(3):395-402.

Cerani A, Zhou S, Forgetta V, et al. **Genetic predisposition** to increased serum calcium, bone mineral density, and fracture risk in individuals with normal calcium levels: mendelian randomisation study. BMJ. 2019 Aug 1;366:l4410.

Chatterjee S. **Atypical femoral fractures** associated with long-term bisphosphonate use. CMAJ. 2013 Oct 1;185(14):1248.

Chawla S, Henshaw R, Seeger L, et al. Safety and effi cacy of **denosumab** for adults and skeletally mature adolescents with **giant cell tumour** of bone: interim analysis of an open-label, parallel-group, phase 2 study. Lancet Oncol 2013; online July 16.

Chen CH et al. Alendronate in the **prevention of collapse of the femoral head in non-traumatic osteonecrosis** (a randomized, multicenter, double-blind study). Arthritis Rheum. 2011 Nov 29. (no effect)

Chen F, Du M, Blumberg JB, et al. Association Among **Dietary Supplement Use, Nutrient Intake, and Mortality** Among U.S. Adults: A Cohort Study. Ann Intern Med. 2019 Apr 9. (calcium a concern)

Chen HM, Chen FP, Yang KC, Yuan SS. Association of **Bone Metastasis With Early-Stage Breast Cancer** in Women With and Without Precancer Osteoporosis According to Osteoporosis Therapy Status. JAMA Netw Open. 2019 Mar 1;2(3):e190429.

Chen YL, Weng SF, Shen YC, et al. **Obstructive Sleep Apnea** and Risk of Osteoporosis: A Population-Based Cohort Study in Taiwan. J Clin Endocrinol Metab. 2014 Apr 15

Cheng TT, Yu SF, et al. Differences in **Adherence** to Osteoporosis Regimens: A 2-Year Analysis of a Population Treated Under Specific Guidelines. Clin Ther. 2013 Jul 4.

Cheung AM, Tile l, Cardew S, et al. **Bone density and structure** in healthy postmenopausal women treated with **exemestane** for the primary prevention of breast cancer: a nested substudy of the MAP.3 randomised controlled trial. Lancet Oncol 2012; online February 7.

Chilibeck PD, Vatanparast H, Cornish SM, Abeysekara S, Charlesworth S. Evidencebased risk assessment and recommendations for **physical activity**: arthritis, osteoporosis, and low back pain. *Appl Physiol Nutr Metab* 2011;36(Suppl 1):S49-S79.

Chiu WY, Lee JJ, Tsai KS. **Atypical femoral fractures** shortly after osteonecrosis of the jaw in a postmenopausal woman taking alendronate for osteoporosis. J Clin Endocrinol Metab. 2013 Apr;98(4):E723-6.

Chlebowski RT, Chen Z, Cauley JA, et al. Oral **Bisphosphonate Use and Breast Cancer Incidence** in Postmenopausal Women. J Clin Oncol. 2010 Jun 21.

Christmas C. Hip fracture. Ann Intern Med. 2011 Dec 6;155(11):ITC61.

Chukir T, Liu Y, Farooki A. **Antiresorptive Agents' Bone-protective and Adjuvant Effects in Postmenopausal Women with Early Breast Cancer**. Br J Clin Pharmacol. 2018 Dec 11.

Chung M, Lee J, Terasawa T, et al. **Vitamin D With or Without Calcium** Supplementation for Prevention of Cancer and **Fractures**: An Updated Meta-analysis for the U.S. Preventive Services Task Force (USPSTF). Ann Intern Med. 2011 Dec 20;155(12):827-38.

Chung M, Tang AM, Fu Z, Wang DD, Newberry SJ. **Calcium intake and cardiovascular disease risk**: an updated systematic review and meta-analysis. Ann Intern Med. 2016.

Clark W, Bird P, Gonski P, et al. Safety and efficacy of **vertebroplasty for acute painful osteoporotic fractures (VAPOUR):** a multicentre, randomised, double-blind, placebo-controlled trial. Lancet. 2016 Aug 17.

Coco M. Treating the **renal patient** who has a fracture: opinion vs evidence. Cleve Clin J Med. 2009 Dec;76(12):684-8.

Coleman RE, Marshall H, Cameron D, et al. **AZURE** Investigators. **Breast-cancer adjuvant therapy** with **zoledronic acid**. N Engl J Med. 2011 Oct 13;365(15):1396-405.

Coleman R, Cameron D, Dodwell D, et al; on behalf of the **AZURE** investigators. Adjuvant zoledronic acid in patients with early breast cancer: final efficacy analysis of the AZURE (BIG 01/04) randomised open-label phase 3 trial. Lancet Oncol. 2014 Jul 14.

Collier J. Bone disorders in **chronic liver disease**. HEPATOLOGY 2007;46: 1271-1278.

Collins Gary S, Mallett Susan, Altman Douglas G. Predicting risk of osteoporotic and hip fracture in the United Kingdom: prospective independent and external validation of **QfractureScores**. BMJ 2011;342:doi:10.1136/bmj.d3651 (Published 22 June 2011)

Compston J. **Glucocorticoid-induced osteoporosis**: an update. Endocrine. 2018 Apr 24.

Compston JE, McClung MR, Leslie WD. **Osteoporosis-Seminar**. Lancet. 2019 Jan 26;393(10169):364-376.

Conwell LS, Chang AB. **Bisphosphonates** for osteoporosis in people with **cystic fibrosis**. Cochrane Database Syst Rev. 2012 Apr 18;4:CD002010. Oral and intravenous bisphosphonates increase bone mineral density in people with cystic fibrosis. Severe bone pain and flu-like symptoms may occur with intravenous agents. Additional trials are needed to determine if bone pain is more common or severe (or both) with the more potent zoledronate and if corticosteroids ameliorate or prevent these adverse events. Additional trials are also required to further assess gastrointestinal adverse effects associated with oral bisphosphonates. Trials in larger populations are needed to determine effects on fracture rate and survival.

Cosman F, Nieves JW, Zion M, et al. Retreatment with **teriparatide** one year after the first teriparatide course in patients on continued long-term alendronate. J Bone Miner Res. 2009 Jun;24(6):1110-5.

Cosman F, Nieves J, Zion M, Woelfert L, Luckey M, et al.. Daily and cyclic **parathyroid hormone** in women receiving alendronate. N Engl J Med. 2005 Aug 11;353(6):566-75.

Cosman F, Cauley JA, Eastell R, et al. **Reassessment of Fracture Risk in women** after 3 years of treatment with **Zoledronic** Acid: when is it reasonable to discontinue treatment? J Clin Endocrinol Metab. 2014 Sep 12

Cosman F, Crittenden DB, et al. **Romosozumab** treatment in postmenopausal women with osteoporosis. (**FRAME**) N Engl J Med. DOI: 10.1056/NEJMoa1607948.

Cosman F, de Beur SJ, LeBoff MS, et al. Clinician's Guide to Prevention and Treatment of Osteoporosis. *Osteoporos Int*. 2014;25(10):2359-81.

Cotts KG, Cifu AS. **Treatment of Osteoporosis**. JAMA. 2018 Mar 13;319(10):1040-1041.

Crandall CJ, Newberry SJ, Diamant A, et al. **Comparative Effectiveness of Pharmacologic Treatments to Prevent Fractures**: An Updated Systematic Review. Ann Intern Med. 2014 Sep 9.

Crandall CJ, Larson JC, Watts NB, et al. Comparison of **Fracture Risk Prediction** by the US Preventive Services Task Force (**USPSTF**) Strategy and **Two Alternative** Strategies in Women 50-64 Years Old in the Women's Health Initiative. J Clin Endocrinol Metab. 2014 Oct 16:jc20142332.

Crandall C, Yildiz V, Wactawski-Wenda J, Johnson K, Chen Z, Going S, et al. **Postmenopausal weight change and incidence of fracture**: post hoc findings from the Womens Health Initiative (**WHI**) Observational Study and Clinical Trials. *BMJ* 2015;350:h25.

Cremers S, Drake MT, Ebetino FH, et al. **Pharmacology of Bisphosphonates**. Br J Clin Pharmacol. 2019 Jan 16.

Cummings SR. A 55-year-old woman with **osteopenia**. JAMA. 2006 Dec 6;296(21):2601-10.

Cummings SR et al. **Lasofoxifene** in postmenopausal women with osteoporosis. (**PEARL**) N Engl J Med 2010 Feb 25; 362:686.

Cummings SR, Black DM, Thompson DE, et al. Effect of **alendronate** on risk of fracture in women with low bone density but without vertebral fractures: results from the Fracture Intervention Trial. (**FIT**) JAMA 1998; 280(24):2077-82.

Cummings SR, Eckert S, Krueger KA, et al. The effect of **raloxifene** on risk of breast cancer in postmenopausal women: results from the **MORE** randomized trial. Multiple Outcomes of Raloxifene Evaluation. JAMA 1999; 281(23):2189

Cummings SR, Eastell R, Ensrud K, et al. The effects of **lasofoxifene** on fractures and breast cancer: 3-year results from the PEARL trial. J Bone Miner Res 2008;23 (Suppl 1):S81.

Cummings SR, Ettinger B, Delmas PD, et al. **LIFT** Trial Investigators. The effects of **tibolone** in older postmenopausal women. N Engl J Med. 2008 Aug 14;359(7):697-708.

Cummings SR, Lui LY, Eastell R, et al. Association Between **Drug Treatments for Patients With Osteoporosis and Overall Mortality Rates**: A Meta-analysis. JAMA Intern Med. 2019 Aug 19.

Cummings SR, San Martin J, McClung MR, et al.; **FREEDOM** Trial. **Denosumab** for prevention of fractures in postmenopausal women with osteoporosis. N Engl J Med. 2009 Aug 20;361(8):756-65.
Curtis JR, Carbone L, Cheng H, et al. **Longitudinal trends in use of bone mass measurement** among older Americans, 1999-2005. J Bone Miner Res. 2008;23:1061-7.
Dagan N, Cohen-Stavi C, Leventer-Roberts M, et al. **External validation and comparison of three prediction tools for risk of osteoporotic fractures** using data from population based electronic health records: retrospective cohort study. BMJ. 2017 Jan 19;356:i6755
Dalbeth N, et al. **Zoledronate** for prevention of bone erosion in tophaceous **gout**: a randomised, double-blind, placebo-controlled trial. Ann Rheum Dis. 2014Jun 1;73(6):1044-51.
Dalhousie CME Academic Detailing Service. **Osteoporosis in 2009**. Dalhousie CME Academic Detailing Service. http://cme.medicine.dal.ca/files/AD_Osteo_2009.pdf
Davis S, et al. A systematic review and economic evaluation of **bisphosphonates for the prevention of fragility fractures**. Health Technol Assess. 2016 Oct;20(78):1-406.
Deal CL. Recent recommendations on **steroid-induced osteoporosis**: More targeted, but more complicated. Cleve Clin J Med. 2013 Feb;80(2):117-25.
de Abajo FJ, et al. Risk of Ischemic **Stroke Associated With Calcium Supplements** With or Without Vitamin D: A Nested Case-Control Study. J Am Heart Assoc. 2017 May 18;6(5).
Desai RJ, Mahesri M, Abdia Y, et al. Association of **osteoporosis medication use after hip fracture with prevention of subsequent nonvertebral fractures**: an instrumental variable analysis. JAMA Netw Open. 2018;1(3):e180826. doi:10.1001/jamanetworkopen.2018.0826
de Steenwinkel FD, Hokken-Koelega AC, Hazes JM, et al. Does medication or disease activity during pregnancy in patients with rheumatoid arthritis (RA), Influence bone density of their 7-year-old offspring? Arthritis Rheum. 2013 Nov 18.
de Villiers TJ, Chines AA, Palacios S, et al. Safety and tolerability of **bazedoxifene** in postmenopausal women with osteoporosis: results of a 5-year, randomized, placebo-controlled phase 3 trial. Osteoporos Int. 2010 Jun 10.
Denham JW, Joseph D, Lamb DS, et al. Short-term androgen suppression and radiotherapy versus intermediate-term androgen suppression and radiotherapy, with or without **zoledronic** acid, in men with locally advanced **prostate cancer** (TROG 03.04 RADAR): open-label, randomised, phase 3 factorial trial. Lancet Oncol 2014; online Aug 15.
Dhesy-Thind S, Fletcher GG, Blanchette PS, et al. Use of **Adjuvant Bisphosphonates and Other Bone-Modifying Agents in Breast Cancer**: A Cancer Care Ontario and American Society of Clinical Oncology (ASCO) Clinical Practice-Guideline. J Clin Oncol. 2017; 35.
Diem SJ et al. Rates of **bone loss among women initiating antidepressant** medication use in midlife. J Clin Endocrinol Metab 2013 Sep 3; [e-pub ahead of print].
Diez-Perez A, Adachi JD, Agnusdei D, et al; for the IOF CSA Inadequate Responders Working Group. **Treatment failure in osteoporosis**. Osteoporos Int. 2012 Jul 27.
Diez-Perez, K. E. Naylor, B. Abrahamsen, D. et al. International Osteoporosis Foundation and European Calcified Tissue Society Working Group. Recommendations for the **screening of adherence to oral bisphosphonates**. Osteoporosis International, 2017.
Digiovanna JJ. Fracturing support for the role of systemic **retinoid therapy** as a cause of bone demineralization. Arch Dermatol. 2010 May;146(5):551-3.
DIPART (**Vitamin D** Individual Patient Analysis of Randomized Trials) Group.Patient level pooled analysis of 68 500 patients from seven major vitamin D fracture trials in US and Europe. BMJ. 2010 Jan 12;340:b5463. doi:10.1136/bmj.b5463. This individual patient data analysis indicates that vitamin D given alone in doses of 10-20 microg is not effective in preventing fractures. By contrast, calcium and vitamin D given together reduce hip fractures and total fractures, and probably vertebral fractures, irrespective of age, sex, or previous fractures.
Dore RK. How to prevent glucocorticoid-induced osteoporosis (GIO). Cleve Clin J Med. 2010 Aug;77(8):529-36.
Doshi KB, Khan LZ, Williams SE, Licata AA. **Bone mineral density testing**: Is a T score enough to determine the screening interval? Cleve Clin J Med. 2013 Apr;80(4):234-9.
Dormuth CR, Carney G, Carleton B, Bassett K, Wright JM. **Thiazolidinediones** and fractures in men and women. Arch Intern Med. 2009 Aug 10;169(15):1395-402.
Driessen JH, de Vries F, van Onzenoort H, et al. The use of **incretins and fractures** - a meta-analysis on population-based real life data. Br J Clin Pharmacol. 2016 Oct 25.
Durie BG, Katz M, Crowley J. **Osteonecrosis of the jaws** and bisphosphonates. N Engl J Med 2005;353:99-102.
Dykes Patricia C.; Carroll Diane L.; Hurley Ann; et al. **Fall Prevention** in Acute Care Hospitals: A Randomized Trial. *JAMA*. 2010;304(17):1912-1918. (**Tool kit**)
Eastell R, Hamilton CJ, Cummings SR. **Notice of Retraction**: Jamal SA, et al. Effect of **Nitroglycerin** Ointment on Bone Density and Strength in Postmenopausal Women: A Randomized Trial. JAMA. 2011;305(8):800-807. JAMA. 2015 Dec 28:1.
Eastell R, Rosen CJ, Black DM, et al. Pharmacological Management of **Osteoporosis in Postmenopausal Women**: An Endocrine Society* Clinical Practice Guideline. J Clin Endocrinol Metab. 2019 May 1;104(5):1595-1622.
Ebeling PR, Akesson K, Bauer DC, etal . The efficacy and safety of **vertebral augmentation**: a second **ASBMR task force report**. J Bone Miner Res 2019;34:3-21. 10.1002/jbmr.3653. 30677181
Ebeling PR. Clinical practice. **Osteoporosis in men**. N Engl J Med. 2008 Apr 3;358(14):1474-82.
Edwards BJ, Song J, Dunlop DD, et al. Functional decline after incident **wrist fractures**--Study of Osteoporotic Fractures: prospective cohort study. BMJ. 2010 Jul 8.
Elhakeem A, Frysz M, Tilling K, et al. Association Between **Age at Puberty and Bone Accrual From** 10 to 25 Years of Age. JAMA Netw Open. 2019 Aug 2;2(8):e198918.
EMA: European Medicines Agency. **Calcitonin** and possible **Cancer** Risk. July 2012. http://www.ema.europa.eu/ema/index.jsp?curl=pages/medicines/human/referrals/Calcitonin/human_referral_000319.jsp&mid=WC0b01ac0580024e99
Ensrud K, Lacroix A, Thompson JR, et al. **Lasofoxifene** and Cardiovascular Events in Postmenopausal Women With Osteoporosis: Five-Year Results From the Postmenopausal Evaluation and Risk Reduction With Lasofoxifene (**PEARL**) Trial. Circulation. 2010 Oct 26;122(17):1716-24. Epub 2010 Oct 11.
Ensrud KE, Crandall CJ. **Osteoporosis**. Ann Intern Med. 2017 Aug 1;167(3):ITC17-ITC32.
Ensrud KE, Kats AM, Boyd CM, et al. Association of disease definition, comorbidity burden, and prognosis with **hip fracture probability among late-life women** [online June 17, 2019]. JAMA Intern Med. doi:10.1001/jamainternmed.2019.0682
Ensrud KE, Schousboe JT. Clinical practice. **Vertebral fractures**. N Engl J Med. 2011 Apr 28;364(17):1634-42.
Ensrud KE, Taylor BC, Peters KW, et al. Implications of expanding indications for drug treatment to **prevent fracture in older men** in United States: cross sectional and longitudinal analysis of prospective cohort study. BMJ 2014;349:g4120.
Ensrud Kristine E.; Lui Li-Yung; Taylor Brent C.; et al. for the Study of Osteoporotic Fractures Research Group A Comparison of Prediction Models for Fractures in Older Women: Is More Better? (**FRAX**) Arch Intern Med. 2009;169(22):2087-2094. Simple models based on age and BMD alone or age and fracture history alone predicted 10-year risk of hip, major osteoporotic, and clinical fracture as well as more complex FRAX models.
Early Breast Cancer Trialists' Collaborative Group (EBCTCG). **Adjuvant bisphosphonate treatment in early breast cancer**: meta-analyses of individual patient data from randomised trials. Lancet. 2015 Jul 23.
Etminan M, Forooghian F, Maberley D. Inflammatory **ocular adverse events with the use of oral bisphosphonates**: a retrospective cohort study. CMAJ. 2012 Apr 2.
Favus Murray J., **Bisphosphonates for Osteoporosis**. N Engl J Med 2010; 363:2027-2035.
FDA Oct/10 **Atypical subtrochanteric femur fractures** are fractures in the bone just below the hip joint. Diaphyseal femur fractures occur in the long part of the thigh bone. These fractures are very uncommon and appear to account for less than 1% of all hip and femur fractures overall. Although it is not clear if bisphosphonates are the cause, these unusual femur fractures have been predominantly reported in patients taking bisphosphonates.
FDA Nov/10 has approved **denosumab** (marketed as **Xgeva**) for the prevention of fracture and bone pain in patients with cancer that has metastasized to the bone. FDA news release (Free) Xgeva prescribing information (Free PDF)
FDA July/11 notified healthcare professionals and patients about its ongoing review of data from published studies to evaluate whether use of **oral bisphosphonate** drugs is

associated with an **increased risk of cancer of the esophagus**. FDA has not concluded that taking an oral bisphosphonate drug increases the risk of esophageal cancer. There are insufficient data to recommend endoscopic screening of asymptomatic patients.

FDA Sep/11 notified healthcare professionals and patients of an update to the drug label for **Reclast (zoledronic acid)** regarding the risk of kidney failure. Cases of acute renal failure requiring dialysis or having a fatal outcome following Reclast use have been reported to FDA. The revised label states that Reclast is contraindicated in patients with creatinine clearance less than 35 mL/min or in patients with evidence of acute renal impairment.

FDA. Bisphosphonate Treatment for Osteoporosis- Background document for meeting of Advisory Committee for Reproductive Health Drugs and Drug Safety and Risk Management Advisory Committee. Sept 2011 http://www.fda.gov/downloads/AdvisoryCommittees/CommitteesMeetingMaterials/Drugs/DrugSafetyandRiskManagementAdvisoryCommittee/UCM270958.pdf

FDA Sep/15 The U.S. Food and Drug Administration (FDA) has strengthened the warning for the type 2 diabetes medicine **canagliflozin (Invokana, Invokamet)** related to the increased risk of bone fractures and added new information about **decreased bone mineral density**.

Fenton JJ, Robbins JA, Amarnath AL, et al. **Osteoporosis Overtreatment** in a Regional Health Care System. JAMA Intern Med. 2016 Jan 4:1-3.

Ferrari S, Bianchi ML, Eisman JA, et al. For the **IOF** Committee of Scientific Advisors Working Group on Osteoporosis Pathophysiology. **Osteoporosis in young adults**: pathophysiology, diagnosis, and management. Osteoporos Int. 2012 Jun 9.

Feskanich D, Willett W, Colditz G. **Walking** and leisure-time activity and risk of hip fracture in postmenopausal women. JAMA 2002; 288(18):2300-2306.

Feskanich D, Bischoff-Ferrari HA, Frazier L, WillettWC. **Milk consumption** during teenage years and risk of hip fractures in older adults [online November 18, 2013]. JAMA Pediatr. doi:10.1001/jamapediatrics.2013.3821.

Feuer AJ, Thai A, Demmer RT, et al. Association of **Stimulant Medication Use With Bone Mass** in Children and Adolescents With **Attention-Deficit**/Hyperactivity Disorder. JAMA Pediatr. 2016 Oct 3:e162804.

Fink HA, MacDonald R, Forte ML, et al. **Long-term drug therapy and drug holidays** for osteoporosis fracture prevention: a systematic review. Comparative Effectiveness Review No. 218. AHRQ Publication No. 19-EHC016-EF. Rockville, MD: Agency for Healthcare Research and Quality; April 2019.

Fink HA, MacDonald R, Forte ML, et al. Long-Term Drug Therapy and **Drug Discontinuations and Holidays** for Osteoporosis Fracture Prevention: A Systematic Review. Ann Intern Med. 2019 Apr 23.

Finkelstein JS, Wyland JJ, Lee H, et al. Effects of **Teriparatide, Alendronate, or Both** in Women with Postmenopausal Osteoporosis. J Clin Endocrinol Metab. 2010 Feb 17.

Firanescu CE, de Vries J, Lodder P, etal . **Vertebroplasty versus sham procedure** for painful acute osteoporotic vertebral compression fractures (**VERTOS IV**): randomised sham controlled clinical trial. BMJ 2018;361:k1551.

Fizazi K, Carducci M, Smith M, et al. **Denosumab versus zoledronic** acid for treatment of bone metastases in men with castration-resistant prostate cancer: a randomised, double- blind study. Lancet. 2011 Feb 24.

Follis SL, Bea J, Klimentidis Y, et al. **Psychosocial stress and bone loss** among postmenopausal women: results from the Women's Health Initiative. J Epidemiol Community Health. 2019 Jul 9.

Formoso G, Perrone E, Maltoni S, et al. Short-term and long-term effects of **tibolone in postmenopausal women**. Cochrane Database Syst Rev. 2016 Oct 12;10:CD008536.
Moderate-quality evidence suggests that tibolone is more effective than placebo but less effective than HT in reducing menopausal vasomotor symptoms, and that tibolone is associated with a higher rate of unscheduled bleeding than placebo but with a lower rate than HT.Compared with placebo, tibolone increases recurrent breast cancer rates in women with a history of breast cancer, and may increase stroke rates in women over 60 years of age. No evidence indicates that tibolone increases the risk of other long-term adverse events, or that it differs from HT with respect to long-term safety.Much of the evidence was of low or very low quality. Limitations included high risk of bias and imprecision. Most studies were financed by drug manufacturers or failed to disclose their funding source.

Fraser LA, Liu K, et al. **Falls and fractures with atypical antipsychotic** medication use: a population-based cohort study. JAMA Intern Med. 2015 Mar1;175(3):450-2.

Fraunfelder, Frederick W., Fraunfelder, Frederick T. **Bisphosphonates and Ocular Inflammation**. N Engl J Med 2003 348: 1187-1188.

Frick KD, Kung JY, Parrish JM, et al. Evaluating the cost-effectiveness of **fall prevention programs** that reduce fall-related hip fractures in older adults. J Am Geriatr Soc. 2010 Jan;58(1):136-41. Of single interventions studied, management of psychotropics and tai chi reduces costs the most.

Ftouh Saoussen, Morga Antonia, Swift Cameron. Guidelines: Management of **hip fracture** in adults: summary of **NICE** guidance. BMJ 2011;342:doi:10.1136/bmj.d3304 June/11

Fu AS, Gao KL, Tung AK, et al. Effectiveness of **Exergaming Training** in Reducing Risk and Incidence of Falls in Frail Older Adults With a History of Falls. (Wii Fit) Arch Phys Med Rehabil. 2015 Dec;96(12):2096-102.

Fung V, Kendler D. **Preventing fractures** in postmenopausal women: how to **assess risk**. CMAJ. 2011 Dec 13;183(18):2129-31.

Gabel L, et al. **Physical Activity, Sedentary Time** & Bone Strength From **Childhood** to Early Adulthood: Mixed Longitudinal HR-pQCT study. J Bone Miner Res. 2017 Mar 22

Gajic-Veljanoski O, Phua CW, Shah PS, et al. Effects of Long-Term **Low-Molecular-Weight Heparin on Fractures** and Bone Density in Non-Pregnant Adults: A Systematic Review With Meta-Analysis. J Gen Intern Med. 2016 Feb 19.

Gallagher JC, Levine JP. Preventing osteoporosis in **symptomatic postmenopausal women**. Menopause. 2010 Aug 5.

Gallagher JC, Smith LM, et al. Incidence of **hypercalciuria and hypercalcemia** during vitamin D and calcium supplementation in older women. Menopause. 2014 Jun 16.

Gatti D, Antoniazzi F, Prizzi R, et al. Intravenous **neridronate** in children with **osteogenesis imperfecta**: a randomized controlled study. J Bone Miner Res 2005; 20: 758–63.

George S, et al. Short Term Safety of **Zoledronic Acid in Young Patients** with Bone Disorders: An Extensive Institutional Experience. J Clin Endocrinol Metab. 2015 Aug 26.

Gerber Y, Melton LJ, Weston SA, et al. Association between **myocardial infarction and fractures**. An emerging phenomenon. Circulation 2011;

Geusens P, Hochberg MC, van der Voort DJ, et al. **Performance of risk indices** for identifying low bone density in postmenopausal women. (**OST**) Mayo Clin Proc. 2002 Jul;77(7):629-37. P

Gillespie WJ, Gillespie LD, Parker MJ. **Hip protectors for preventing hip fractures** in older people. Cochrane Database Syst Rev. 2010 Oct 6;10:CD001255. The effectiveness of the provision of hip protectors in reducing the incidence of hip fracture in older people is still not clearly established, although they may reduce the rate of hip fractures if made available to frail older people in nursing care.

Gillespie CW, Morin PE. **Osteoporosis-Related Health Services Utilization** Following First Hip Fracture Among a Cohort of Privately-Insured Women in the United States, 2008-2014: An Observational Study. J Bone Miner Res. 2017 Feb 23.

Gimsing P, Carlson K, Turesson I, et al. Effect of **pamidronate 30 mg** versus 90 mg on physical function in patients with newly diagnosed multiple myeloma (Nordic Myeloma Study Group): a double-blind, randomised controlled trial. Lancet Oncol. 2010 Oct;11(10):973-82.

Glorieux FH, Bishop NJ, Plotkin H, et al. Cyclic administration of **pamidronate** in children with severe **osteogenesis imperfecta**. N Engl J Med 1998; 339: 947–52.

Golden NH, Abrams SA; COMMITTEE ON NUTRITION; Optimizing **bone health in children and adolescents**. Pediatrics. 2014 Oct;134(4):e1229-43.

Goldstein SR, Neven P, Cummings S, et al. Postmenopausal Evaluation and Risk Reduction With Lasofoxifene (Pearl): 5-yr gynecological outcomes. Menopause. 2010 Aug 3.

Gnant M, Mlineritsch B, Schippinger W, et al. **ABCSG-12** Trial Investigators, Marth C. Endocrine therapy plus **zoledronic** acid in premenopausal breast cancer. N Engl J Med. 2009 Feb 12;360(7):679-91.

Gnant M, Mlineritsch B, Stoeger H, et al. on behalf of the Austrian Breast and Colorectal Cancer Study Group, Vienna, Austria. Adjuvant endocrine therapy plus zoledronic acid in premenopausal women with early-stage breast cancer: 62-month follow-up from the **ABCSG-12** randomised trial. Lancet Oncol. 2011 Jun 3.

Gnant M, Mlineritsch B, Luschin-Ebengreuth G, et al. Austrian Breast and Colorectal Cancer Study Group (ABCSG). Adjuvant endocrine therapy plus **zoledronic** acid in premenopausal women with early-stage **breast cancer**: 5-year follow-up of the ABCSG-12 bone-mineral density substudy. Lancet Oncol. 2008 Sep;9(9):840-9.

Gnant M, Pfeiler G, Dubsky PC, et al, on behalf of the Austrian Breast and Colorectal Cancer Study Group. Adjuvant **denosumab** in **breast cancer** (ABCSG-18): a multicentre, randomised, double-blind, placebo-controlled trial. *Lancet* 2015; online June 1.

Gnant M, Pfeiler G, Steger GG, et al; Austrian Breast and Colorectal Cancer Study Group. **Adjuvant denosumab in postmenopausal patients** with hormone receptor-positive breast cancer (ABCSG-18): disease-free survival results from a randomised, double-blind, placebo-controlled, phase 3 trial. Lancet Oncol. 2019 Feb 19.

Goldhahn J, Little D, Mitchell P, et al.; ISFR working group drugs and fracture repair. Evidence for anti-osteoporosis therapy in **acute fracture situations**--recommendations of a multidisciplinary workshop of the International Society for Fracture Repair. Bone. 2010 Feb;46(2):267-71.

Goodall EC, Granados AC, Luinstra K, et al. Vitamin D3 and **gargling for the prevention of upper respiratory tract infections**: a randomized controlled trial. BMC Infect Dis. 2014 May 19;14(1):273.

Gordon PL, Frassetto LA. Management of **osteoporosis in CKD Stages 3 to 5**. Am J Kidney Dis. 2010 May;55(5):941-56.

Goshtasebi A, Subotic Brajic T, Scholes D, et al. Adolescent use of combined **hormonal contraception and peak bone mineral density** accrual: A meta-analysis of international prospective controlled studies. Clin Endocrinol (Oxf). 2019 Jan 7.

Gourlay Margaret L., Fine Jason P., May Ryan C et al. for the Study of Osteoporotic Fractures Research Group. **Bone-Density Testing Interval** and Transition to Osteoporosis in Older Women. N Engl J Med 2012; 366:225-233.

Gourlay ML. **Osteoporosis Screening-2 Steps May Be Too Much** for Women Younger Than 65 Years. JAMA Intern Med. 2018 Jun 26.

Gourlay ML, Overman RA, Fine JP, et al. for the Women's Health Initiative (**WHI**) Investigators. Baseline age and **time to major fracture** in younger postmenopausal women. Menopause. 2014 Oct 27.

Grey A, Bolland MJ, Wattie D, Horne A, Gamble G, Reid IR. The antiresorptive effects of a single dose of **zoledronate persist** for **two years**: a randomized, placebo-controlled trial in osteopenic postmenopausal women. J Clin Endocrinol Metab. 2009 Feb;94(2):538-44.

Gray N, Howard A, Zhu J, et al. Association Between **Inhaled Corticosteroid Use** and Bone Fracture in Children With Asthma. JAMA Pediatr. 2017 Nov 13.

Green JO, Nagaraja S, Diab T, et al. **Age-related changes in human trabecular bone**: Relationship between microstructural stress and strain and damage morphology. J Biomech. 2011 Aug 11;44(12):2279-85.

Greenspan SL, Coates P, Sereika SM, et al. Bone loss after initiation of **androgen deprivation therapy** in patients with prostate cancer. J Clin Endocrinol Metab 2005;90:6410-7.

Greenspan SL, Bone HG, Ettinger MP, et al.; Treatment of Osteoporosis with Parathyroid Hormone Study Group. Effect of recombinant human parathyroid hormone (**1-84**) on vertebral fracture and bone mineral density in postmenopausal women with osteoporosis: a randomized trial. Ann Intern Med. 2007 Mar 6;146(5):326-39.

Greenspan SL, Schneider DL, McClung MR, et al. **Alendronate** improves bone mineral density in **elderly women** with osteoporosis residing in long-term care facilities. A randomized, double-blind, placebo-controlled trial. Ann Intern Med. 2002 May 21;136(10):742-6.

Greenspan SL, Nelson JB, Trump DL, Resnick NM. Effect of once-weekly oral **alendronate** on bone loss in men receiving **androgen deprivation therapy** for prostate cancer: a randomized trial. Ann Intern Med 2007;146:416-24.

Greenspan SL, Perera S, Ferchak MA, Nace DA, Resnick NM. Efficacy and safety of **single-dose zoledronic acid for osteoporosis in frail elderly women**: a randomized clinical trial [online April 13, 2015]. JAMA Intern Med. 10.1001/jamainternmed.2015.0747.

Grey A, Bolland MJ, Horne A, et al. Duration of antiresorptive activity of **zoledronate** in **postmenopausal women with osteopenia**: a randomized, controlled multidose trial. CMAJ. 2017 Sep 11;189(36):E1130-E1136.

Grossman JM, Gordon R, Ranganath VK, et al. American College of Rheumatology (ACR) 2010 recommendations for the prevention and treatment of **glucocorticoid-induced Osteoporosis** (GIO). Arthritis Care Res (Hoboken). 2010 Jul 26.

Gulamhusein H, Yun L, Cheung AM, et al. **Bisphosphonate prescriptions** in men with **androgen deprivation therapy** use. JAMA. 2014 Dec 3;312(21):2285-6.

Gutierrez-Buey G, Restituto P, Botella S, et al. Trabecular bone score and bone remodeling **markers identify perimenopausal women at high risk of bone loss.** Clin Endocrinol (Oxf). 2019 May 29.

Hadji P, Aapro MS, Body JJ, et al. Management of **Aromatase Inhibitor-Associated Bone Loss** (**AIBL**) in postmenopausal women with hormone sensitive breast cancer: Joint position statement of the **IOF**, CABS, ECTS, IEG, ESCEO IMS, and SIOG. J Bone Oncol. 2017 Mar 23;7:1-12.

Haentjens Patrick, Magaziner Jay, Colón-Emeric Cathleen S., Et al. Meta-analysis: Excess **Mortality After Hip Fracture** Among Older Women and Men. *Ann Intern Med* March 16, 2010 152:380-390; doi:10.1059/0003-4819-152-6-201003160-00008.

Hageman K, Patel KC, Mace K, Cooper MR. The role of **denosumab** for prevention of skeletal-related complications in multiple myeloma. Ann Pharmacother. 2013 Jul;47(7-8):1069-74.

Han SL, Wan SL. Effect of **teriparatide** on bone mineral density and fracture in postmenopausal osteoporosis: meta-analysis of randomised controlled trials. Int J Clin Pract. 2012 Feb;66(2):199-209.

Handoll HH, Ollivere BJ, Rollins KE. Interventions for treating **proximal humeral fractures** in adults. Cochrane Database Syst Rev. 2012 Dec 12;12:CD000434. doi: 10.1002/14651858.CD000434.pub3. There is insufficient evidence to inform the management of these fractures. Early physiotherapy, without immobilisation, may be sufficient for some types of undisplaced fractures.

Hanley DA, Cranney A, Jones G, et al. **Vitamin D** in adult health & disease: a review and guideline statement from **Osteoporosis Canada**–summary.CMAJ 2010 0: cmaj.091062.

Haring B, Crandall CJ, Wu C, et al. **Dietary patterns** and fractures in postmenopausal women: results from the Women's Health Initiative [online March 28, 2016]. JAMA Intern Med. doi:10.1001/jamainternmed.2016.0482.

Haring B, Crandall CJ, Carbone L, et al. **Lipoprotein(a) plasma levels, bone mineral density and risk of hip fracture**: a post hoc analysis of the Women's Health Initiative, USA. BMJ Open. 2019 Apr 24;9(4):e027257.

Harper CM, Fitzpatrick SK, Zurakowski D, et al. Distal **radial fractures in older men**: a missed opportunity? J Bone Joint Surg Am. 2014 Nov 5;96(21):1820-7.

Hauser B, Riches PL, Wilson JF, et al. **Prevalence and clinical prediction** of osteoporosis in a contemporary cohort of patients with rheumatoid arthritis. Rheumatology (Oxford). 2014 Apr 24.

Harvey NC, et al. **Falls Predict Fractures Independently of FRAX Probability**: Meta-Analysis of Osteoporotic Fractures in Men (**MrOS**) Study. J Bone Miner Res. 2017 Dec 8.

Hauk L. **Treatment of Low BMD and Osteoporosis to Prevent Fractures**: Updated Guideline from the ACP. Am Fam Physician. 2018 Mar 1;97(5):352-353.

Health Canada Oct/10 & Novartis, is notifying healthcare professionals and the public of reports of renal impairment and renal failure requiring dialysis or with fatal outcome that occurred in patients with history of renal impairment or other risk factors receiving ACLASTA (zoledronic acid).

Health Canada Dec/11 is updating Canadians with respect to its review of bisphosphonate drugs, used to treat osteoporosis, and the risk of a rare but serious type of thigh bone fracture known as an "**atypical femur fracture** <1% ."

Health Canada May/12: Cases of severe, sometimes **fatal, symptomatic hypocalcemia associated with XGEVA (denosumab)** treatment have been reported in cancer patients with bone metastases

Health Canada Nov/12 **PROLIA (denosumab)** - Association with the Risk of **Atypical Femoral Fractures** - Amgen Canada Inc. Cases of atypical femoral fractures associated with PROLIA (denosumab) treatment have been reported in patients participating in an ongoing clinical trial involving postmenopausal women with osteoporosis.

Health Canada Oct /15 **Strontium health products**: New restrictions to address possible heart and circulatory-related risks. At Health Canada's request, companies are strengthening product labels for certain strontium-containing natural health products with new restrictions, to minimize a possible increased risk of cardiovascular-related side effects (e.g., heart attack, stroke, blood clots) in people who are at risk of these types of events.

Health Canada Nov/18: XOFIGO (radium Ra 223 dichloride) – Increased Incidence of Fractures and Trend for Increased Deaths with **XOFIGO** used in combination with **abiraterone and prednisone/prednisolone** - Bayer Inc.

Health Canada. Summary safety review – bisphosphonates – assessing the risk of jaw bone loss (**osteonecrosis of the jaw**). November 25, 2016. www.hc-sc.gc.ca/dhp-mps/medeff/reviews-examens/bisphosphonates-eng.php (accessed November 29, 2016).

Heaney RP et al. **Vitamin D3 is more potent than vitamin D2** in humans. *J Clin Endocrinol Metab* 2011 Mar; 96:E447.

Heckbert SR, Li G, Cummings SR, Smith NL, Psaty BM. Use of alendronate and risk of incident **atrial fibrillation** in women. Arch Intern Med. 2008 Apr 28;168(8):826-31.
Hidayat K, Du X, Shi BM. Risk of fracture with **dipeptidyl peptidase-4 inhibitors, glucagon-like peptide-1 receptor agonists, or sodium-glucose cotransporter-2 inhibitors** in real-world use: systematic review and meta-analysis of observational studies. Osteoporos Int. 2019 May 27.
Hietala, Strandberg, et al. Usefulness of **Troponin T to Predict** Short-and Long-term Mortality in Patients after Hip Fracture. The American Journal of Cardiology. 2014.
Hillier TA, Stone KL, Bauer DC, et al. Evaluating the value of **repeat bone mineral density measurement** and prediction of fractures in older women: the study of osteoporotic fractures. Arch Intern Med 2007; 167:155–160.
Himelstein AL, Foster JC, Khatcheressian JL, et al. Effect of **Longer-Interval vs Standard Dosing of Zoledronic Acid on Skeletal Events** in Patients With **Bone Metastases**: A Randomized Clinical Trial. JAMA. 2017 Jan 3;317(1):48-58.
Hippisley-Cox Julia, Coupland Carol, Predicting risk of osteoporotic fracture in men and women in England and Wales: prospective derivation and validation of **QFractureScores.** BMJ 2009;339:b4229, doi: 10.1136/bmj.b4229 (Published 19 November 2009)
Hippisley-Cox J, Coupland C. Derivation and validation of **updated QFracture algorithm** to predict risk of osteoporotic fracture in primary care in the United Kingdom: prospective open cohort study. BMJ. 2012 May 22;344:e3427.
Hodsman A, Papaioannou A, Ann C. Clinical practice guidelines for the use of **parathyroid hormone** in the treatment of osteoporosis. CMAJ 2006; 175(1):48.
Holick MF. **Vitamin D deficiency**. N Engl J Med. 2007 Jul 19;357(3):266-81.
Hou WH, Chang KC, Li CY, et al. **Dipeptidyl peptidase-4 inhibitor use is associated with decreased risk of fracture** in patients with type 2 diabetes: a population-based cohort study. Br J Clin Pharmacol. 2018 May 16.
Hopewell S, Adedire O, Copsey BJ, et al. Multifactorial and multiple component interventions for preventing falls in older people living in the community. Cochrane Database of Systematic Reviews 2018, Issue 7. Art. No.: CD012221. Multifactorial interventions may reduce the rate of falls compared with usual care or attention control. However, there may be little or no effect on other fall-related outcomes. Multiple component interventions, usually including exercise, may reduce the rate of falls and risk of falling compared with usual care or attention control.
Hopkins RB, Goeree R, Pullenayegum E, et al. The **relative efficacy of nine osteoporosis medications** for reducing the rate of fractures in post-menopausal women. BMC Musculoskelet Disord. 2011 Sep 26;12(1):209. Teriparatide, zoledronic acid & denosumab have the highest probabilities of being most efficacious for non-vertebral & vertebral fractures, & having the greatest effect sizes.
Hortobagyi GN, Van Poznak C, Harker WG, et al. Continued Treatment Effect of **Zoledronic Acid Dosing Every 12 vs 4 Weeks in Women With Breast Cancer Metastatic to Bone**: The **OPTIMIZE-2** Randomized Clinical Trial. JAMA Oncol. 2017 Jan 26.
Hosking D, Chilvers CED, Christiansen C, et al. Prevention of bone loss with **alendronate** in postmenopausal women under 60 years of age. N Engl J Med 1998; 338:485-92.
Howe TE, Shea B, Dawson LJ, et al. **Exercise for preventing and treating osteoporosis** in postmenopausal women. *Cochrane Database of Systematic Reviews* 2011, Issue 7. Art. No.: CD000333. DOI: 10.1002/14651858.CD000333.pub2. Our results suggest a relatively small statistically significant, but possibly important, effect of exercise on bone density compared with control groups. Exercise has the potential to be a safe and effective way to avert bone loss in postmenopausal women.
Huang J, Meixner L, Fernandez S, McCutchan JA. A double-blinded, randomized controlled trial of zoledronate therapy for **HIV**-associated osteopenia and osteoporosis. AIDS. 2009 Jan 2;23(1):51-7.
Huang HK, Lin SM, Loh CH, et al. Association Between **Cataract and Risks of Osteoporosis** and Fracture: A Nationwide Cohort Study. J Am Geriatr Soc. 18Oct03
Huang HT, Kang L, Huang PJ, Fu YC, Lin SY, Hsieh CH, Chen JC, Cheng YM, Chen CH. Successful **teriparatide treatment of atypical fracture** after long-term use of alendronate without surgical procedure in a postmenopausal woman: a case report. Menopause. 2012 Sep 10.
Hue TF, Cummings SR, Cauley JA, et al. Effect of **Bisphosphonate** Use on Risk of Postmenopausal **Breast Cancer**: Results From the Randomized Clinical Trials of Alendronate and Zoledronic Acid. JAMA Intern Med. 2014 Aug 11.
Hung CL, et al. Is Partial or Total **Thyroidectomy Associated with Risk of Long-Term Osteoporosis**: A Nationwide Population-Based Study. World J Surg. 2018 Mar 14.
Hung WW, Egol KA, Zuckerman JD, Siu AL. **Hip fracture management**: tailoring care for the older patient. JAMA. 2012 May 23;307(20):2185-94.
Hung YC, Lin CC, et al. **Severe hypoglycemia and hip fracture** in patients with type 2 diabetes: a nationwide population-based cohort study. Osteoporos Int. 2017 Apr 3.
Hunt LP, Ben-Shlomo Y, Clark EM, et al. **90-day mortality after 409 096 total hip replacements** for osteoarthritis, from the National Joint Registry for England and Wales: a retrospective analysis. Lancet 2013; 382: 1097–104.
ICSI: Institute for Clinical Systems Improvement. Diagnosis and treatment of osteoporosis. Bloomington (MN): Institute for Clinical Systems Improvement (ICSI); 2011 Jul.
ICSI: **Diagnosis and treatment of osteoporosis**. Bloomington (MN): Institute for Clinical Systems Improvement (ICSI); 2017.
Ikegame M, Hattori A, Tabata MJ, et al. **Melatonin** is a potential drug for the prevention of bone loss during space flight. J Pineal Res. 2019 Jul 9:e12594
Ikesue H, Tsuji T, Hata K, et al. Time Course of Calcium Concentrations and Risk Factors for **Hypocalcemia** in Patients Receiving **Denosumab** for the Treatment of Bone Metastases From Cancer. Ann Pharmacother. 2014 Jun 13;48(9):1159-1165.
International Society for Clinical Densitometry http://www.iscd.org/
Ioannidis G, Papaioannou A, Hopman WM, et al. Relation between **fractures and mortality**: results from the Canadian Multicentre Osteoporosis Study. CMAJ. 2009 Sep 1;181(5):265-71. Epub 2009 Aug 4.
Is **fracture risk linked to gout or urate-lowering therapy**? Drug Ther Bull. 2019 Apr;57(4):54.
Ito K, Elkin EB, Girotra M, Morris MJ. Cost-effectiveness of fracture prevention in men who receive **androgen deprivation therapy** for localized prostate cancer. Ann Intern Med. 2010 May 18;152(10):621-9.
Jackson RD, LaCroix AZ, Gass M, et al. Calcium plus vitamin D supplementation and the risk of fractures. N Engl J Med 2006; 354(7):669-683.
Jagpal A, Saag KG. **How to use bisphosphonates safely and optimally**: Using bisphosphonates. Rheumatology (Oxford). 2017 Nov 20.
Jamal SA, Hamilton CJ, Eastell R, et al. Effect of **nitroglycerin** ointment (15mg-1 inch of nitroglycerin 2% ointment) on bone density and strength in postmenopausal women: a randomized trial. JAMA. 2011 Feb 23;305(8):800-7.
Jankowski CM, Wolfe P, Schmiege SJ, et al. **Sex-specific Effects of DHEA on Bone Mineral Density and Body Composition**: A Pooled Analysis of Four Clinical Trials. Clin Endocrinol (Oxf). 2018 Nov 12.
Järvinen TL, Sievänen H, Khan KM, Heinonen A, Kannus P. Shifting the focus in fracture prevention from osteoporosis to **falls**. BMJ. 2008 Jan 19;336(7636):124-6.
Järvinen TL, Jokihaara J, Guy P, et al. **Conflicts at the heart of the FRAX** tool. CMAJ. 2014 Feb 8;186(3):165-7.
Järvinen TL, Michaëlsson K, Jokihaara J, et al. **Overdiagnosis of bone fragility** in the quest to prevent hip fracture. BMJ. 2015 May 26;350
Jeremiah MP, Unwin BK, Greenawald MH, et al. **Diagnosis and Management of Osteoporosis**. Am Fam Physician. 2015 Aug 15;92(4):261-8.
Jette Nathalie; Lix Lisa M; Metge CJ; et al. Association of **Antiepileptic Drugs** With **Nontraumatic Fractures**: Population-Based Analysis. Arch Neurol. 2011;68(1):107-112.
Jha S, Wang Z, Laucis N, Bhattacharyya T. Trends in **Media Reports, Oral Bisphosphonate Prescriptions, and Hip Fractures** 1996-2012: An Ecological Analysis. J Bone Miner Res. 2015 May 27.
Jiang X, Westermann LB, et al. **Age** as a predictor of osteoporotic fracture compared with current **risk-prediction** models. Obstet Gynecol. 2013 Nov;122(5):1040-6.
Jin J. **Vitamin D and Calcium Supplements** for Preventing Fractures. JAMA. 2018 Apr 17;319(15):1630.
Jin J. **Prevention of Falls** in Older Adults. JAMA. 2018 Apr 24;319(16):1734.
Jin J. **Screening for Osteoporosis** to Prevent Fractures. JAMA. 2018 Jun 26;319(24):2566.
Jin YZ, Lee JH, Xu B, Cho M. **Effect of medications on prevention** of secondary osteoporotic vertebral compression fracture, non-vertebral fracture, and discontinuation due to adverse events: a meta-analysis of randomized controlled trials. BMC Musculoskelet Disord. 2019 Aug 31;20(1):399.

Jones S, Restrepo D, Kasowitz A, et al. Risk factors for decreased bone density and effects of **HIV** on bone in the elderly. Osteoporos Int. 2008 Jul;19(7):913-8.
Joseph S, Wang C, Bushby K, et al. Fractures and Linear Growth in a Nationwide Cohort of **Boys With Duchenne Muscular Dystrophy** With and Without Glucocorticoid Treatment: Results From the UK NorthStar Database. JAMA Neurol. 2019 Mar 11.
Jung JW, Kang HR, Kim JY, et al. Are **asthmatic patients prone to bone loss**? Ann Allergy Asthma Immunol. 2014 May;112(5):426-31.
Kallmes, David F., Comstock, Bryan A., Heagerty, Patrick J., et al. A Randomized Trial of **Vertebroplasty** for Osteoporotic Spinal Fractures. N Engl J Med 2009 361: 569-579.
Kaemmerer D, Lehmann G, Wolf G, et al. Treatment of osteoporosis after **liver transplantation** with **ibandronate**. Transpl Int. 2010 Feb 15.
Kammire DE, Walkup MP, Ambrosius WT, et al. Effect of **Weight Change Following Intentional Weight Loss** on Bone Health in Older Adults with Obesity. Obesity (Silver Spring). 2019 Sep 4.
Kane CM, Hoskin P, Bennett MI. **Cancer induced bone pain**. BMJ. 2015 Jan 29;350:h315.
Kanis JA, Johnell O, Black DM, et al. Effect of **raloxifene** on the risk of new vertebral fracture in postmenopausal women with **osteopenia** or osteoporosis: a reanalysis of the multiple outcomes of raloxifene evaluation trial. (**More**) Bone 2003;33:293-300.
Kaplan SJ, Pham TN, Arbabi S, et al. **Association of Radiologic Indicators of Frailty** With 1-Year Mortality in Older Trauma Patients: Opportunistic Screening for Sarcopenia and Osteopenia. JAMA Surg. 2017 Feb 15;152(2):e164604
Kapoor E, Austin PC, Alibhai SMH, et al. Screening and Treatment for **Osteoporosis After Stroke**. Stroke. 2019 Apr 25:STROKEAHA118024685.
Kapral MK, Fang J, Alibhai SM, et al. Risk of **fractures after stroke**: Results from the Ontario Stroke Registry. Neurology. 2017 Jan 3;88(1):57-64.
Karaplis AC, Chouha F, Djandji M, Sampalis JS, Hanley DA. **Vitamin D Status and Response to Daily 400 IU Vitamin D3 and Weekly Alendronate 70 mg** in Men and Women with Osteoporosis. Ann Pharmacother. 2011 May;45(5):561-8.
Karim R, Dell RM, Greene DF, et al. Hip fracture in postmenopausal women **after cessation of hormone therapy**: results from a prospective study in a large health management organization. Menopause. 2011 Nov;18(11):1172-7.
Kaulfers, Anne-Marie D., Bean, Judy A., Inge, Thomas H., Dolan, et al. Bone Loss in Adolescents **After Bariatric Surgery**. Pediatrics 2011 0: peds.2010-0785.
Kavanagh KL, Guo K, Dunford JE, et al. The molecular **mechanism** of nitrogen-containing **bisphosphonates** as antiosteoporosis drugs. Proc Natl Acad Sci U S A. 2006 May 16;103(20):7829-34. Epub 2006 May 9.
Kawahara T, Nishikawa M, Kawahara C, et al. **Atorvastatin, etidronate**, or both in patients at high risk for atherosclerotic **aortic plaques**: a randomized, controlled trial. Circulation. 2013 Jun 11;127(23):2327-35.
KDIGO : Kidney Disease: Improving Global Outcomes (**KDIGO**) **CKD-MBD** Update Work Group. KDIGO 2017 clinical practice guideline update for the diagnosis, evaluation, prevention, and treatment of **chronic kidney disease–mineral and bone disorder** (**CKD-MBD**). Kidney Int Suppl. 2017 Jul;7(1):1-59.
Kemmler Wolfgang; von Stengel Simon; Engelke Klaus; et al. **Exercise** Effects on Bone Mineral Density, Falls, Coronary Risk Factors, and Health Care Costs in Older Women: The Randomized Controlled Senior Fitness and Prevention (**SEFIP**) Study. Arch Intern Med. 2010;170(2):179-185.
Kendler DL, Marin F, Zerbini CAF, et al. Effects of **teriparatide and risedronate** on new fractures in post-menopausal women with **severe osteoporosis (VERO):** a multicentre, double-blind, double-dummy, randomized controlled trial. Lancet 2017; online Nov 9.
Kern J, Kern S, Blennow K, et al. **Calcium supplementation and risk of dementia** in women with cerebrovascular disease. Neurology. 2016 Oct 18;87(16):1674-1680.
Khan AA, Sándor GK, Dore E, et al. **Canadian** Taskforce on Osteonecrosis of the Jaw. Bisphosphonate associated **osteonecrosis** of the **jaw**. J Rheumatol.2009Mar;36(3):478-90.
Khan AA, Sándor GK, Dore E, et al. **Canadian** Association of Oral and Maxillofacial Surgeons. Canadian consensus practice guidelines for bisphosphonate associated **osteonecrosis of the jaw**. J Rheumatol. 2008 Jul;35(7):1391-7. Epub 2008 Jun 1. Erratum in: J Rheumatol. 2008 Oct;35(10):2084. J Rheumatol. 2008 Aug;35(8):1688.
Khan AA, Sandor GK, Dore E, Morrison AD, Alshali M, Amin F, et al. **Bisphosphonate-associated osteonecrosis** of the jaw—literature review. J Rheumatol 2009;36:478-90.
Khan AA, Kaiser S. **Atypical femoral fracture**. CMAJ. 2017 Apr 10;189(14):E542.
Khosla S. Update in **male osteoporosis**. J Clin Endocrinol Metab. 2010 Jan;95(1):3-10.
Khosla S, Melton LJ 3rd. Clinical practice. **Osteopenia**. N Engl J Med. 2007 May 31;356(22):2293-300.
Kirby MW and Spritzer C. **Radiographic detection of hip and pelvic fractures** in the emergency department. *AJR Am J Roentgenol* 2010 Apr; 194:1054.
Kim SK. Identification of **613 new loci associated with heel bone mineral density and a polygenic risk score for bone mineral density, osteoporosis and fracture**. PLoS One. 2018 Jul 26;13(7):e0200785.
Klazen CA, Lohle PN, de Vries J, et al. **Vertebroplasty** versus conservative treatment in acute osteoporotic vertebral compression fractures (Vertos II): an open-label randomised trial. Lancet. 2010 Aug 9.
Klop C, de Vries F, Bijlsma JW, et al. **Predicting the 10-year risk of hip and major osteoporotic fracture in rheumatoid arthritis** and in the general population: an independent validation and update of **UK FRAX** without bone mineral density. Ann Rheum Dis. 2016 Dec;75(12):2095-2100.
Knopp JA, Diner BM, Blitz M, Lyritis GP, Rowe BH. **Calcitonin** for treating **acute pain** of osteoporotic vertebral compression fractures: a systematic review of randomized, controlled trials. Osteoporos Int. 2005 Oct;16(10):1281-90. Epub 2004 Dec 22.
Knopp JA, Diner BM, Blitz M, Lyritis GP, Rowe BH. **Calcitonin for treating acute pain** of osteoporotic vertebral compression fractures: a systematic review of randomized, controlled trials. Osteoporos Int. 2005 Oct;16(10):1281-90.
Koh JH, Myong JP, et al. **Atypical femur fracture** in rheumatoid arthritis patients treated with bisphosphonates: A nested case-control study. Arthritis Rheumatol. 2015 Sep 11.
Kolber MR, Sadowski CA, Korownyk C. **Bisphosphonates: forever or 5 years and stop**? Can Fam Physician. 2015 May;61(5):443.
Komaki Y, Komaki F, Micic D, et al. Risk of Fractures in **Inflammatory Bowel Diseases**: A Systematic Review and Meta-Analysis. J Clin Gastroenterol. 2018 Apr 18.
Kopecky SL, Bauer DC, Gulati M, et al. Lack of Evidence Linking **Calcium With or Without Vitamin D Supplementation to Cardiovascular Disease** in Generally Healthy Adults: A Clinical Guideline From the National Osteoporosis Foundation and the American Society for Preventive Cardiology. Ann Intern Med. 2016 Oct 25.
Korownyk C, McCormack J, Michael Allan G. **Who should receive bone mineral density testing**? Can Fam Physician. 2015 Jul;61(7):612.
Korpelainen Raija; Keinanen-Kiukaanniemi Sirkka; Nieminen Pentti; et al. Long-term Outcomes of **Exercise**: Follow-up of a Randomized Trial in Older Women With Osteopenia. Arch Intern Med. 2010;170(17):1548-1556.
Krantz E, Trimpou P, Landin-Wilhelmsen K. Effect of **Growth Hormone Treatment** on Fractures and Quality of Life in Postmenopausal Osteoporosis: A 10-Year Follow-Up Study. J Clin Endocrinol Metab. 2015 Aug 27:jc20151757.
Krishnan M, Beck S, et al. Predicting outcome after hip fracture: using a **frailty index** to integrate comprehensive geriatric assessment results. Age Ageing. 2013 Jul 5.
Kumar S, Drake MT, Schleck CD, et al. Incidence and predictors of **osteoporotic fractures in patients with Barrett's oesophagus**: a population-based nested case-control study. Aliment Pharmacol Ther.2017 Oct 5.
Kurmis AP, et al. Effect of **nonsteroidal anti-inflammatory drug administration on acute phase fracture-healing**: a review. J Bone Joint Surg Am. 2012 May 2;94(9):815-23.
Kyle RA, Yee GC, Somerfield MR, et al. Society of Clinical Oncology. **American** Society of Clinical Oncology 2007 clinical practice guideline update on the role of **bisphosphonates in multiple myeloma**. J Clin Oncol. 2007 Jun 10;25(17):2464-72.
LaFleur J, Steenhoek CL, Horne J, Meier J, et al. Comparing **Fracture Absolute Risk Assessment** (**FARA**) **Tools**: An Osteoporosis Clinical Informatics Tool to Improve Identification and Care of Men at High Risk of First Fracture. Ann Pharmacother. 2015 May;49(5):506-14.

Lagari V, Gavcovich T, Levis S. The **Good and the Bad About the 2017 American College of Physicians Osteoporosis Guidelines**. Clin Ther. 2017 Nov 28.
Lai CC, Wang SH, et al. Increased risk of osteoporotic **fractures in patients with systemic sclerosis**: a nationwide population-based study. Ann Rheum Dis. 2014 Feb 14.
Lai CL, Kuo RN, Chen HM, et al. Risk of **hip/femur fractures during the initiation period of alpha-blocker** therapy among elderly males: a self-controlled case series study. Br J Clin Pharmacol. 2015 Apr 28.
Laine CM, Joeng KS, Campeau PM, et al. **WNT1 mutations** in early-onset osteoporosis and osteogenesis imperfecta. N Engl J Med. 2013 May 9;368(19):1809-16.
Lalmohamed A, de Vries F, Bazelier MT et al. Risk of **fracture after bariatric surgery** in the United Kingdom: population based, retrospective cohort study. BMJ. 2012 Aug 3;345:e5085.
Lamberg AL, Horvath-Puho E, et al. Use of oral bisphosphonates and risk of venous **thromboembolism**: a population-based case-control study. Osteoporos Int. 2009 Dec 9.
Landfeldt E, Ström O. The comparative gastrointestinal tolerability of **proprietary versus generic alendronate** in patients treated for primary osteoporosis. Bone. 2012 Jul 24;51(4):637-642. No significant difference in the incidence of GIAEs was identified between patients prescribed proprietary and generic alendronates between 2005 and 2009 in Sweden.
Langdahl BL, Libanati C, Crittenden DB, et al. Romosozumab (sclerostin monoclonal antibody) versus teriparatide in postmenopausal women with osteoporosis transitioning **from oral bisphosphonate therapy**: a randomised, open-label, phase 3 trial. Lancet 2017; online July 26.
Langston AL, Campbell MK, Fraser WD, MacLennan GS, Selby PL, Ralston SH; **PRISM** Trial Group. Randomized trial of intensive bisphosphonate treatment versus symptomatic management in **Paget's disease of bone**. J Bone Miner Res. 2010 Jan;25(1):20-31.
Lansang MC, Hustak LK. **Glucocorticoid-induced diabetes and adrenal suppression**: How to detect and manage them. Cleve Clin J Med. 2011 Nov;78(11):748-56.
Langsetmo L, Nguyen TV, Nguyen D, et al. Independent external validation of **nomograms (Dubbo & FRAX) for predicting risk of low-trauma fracture and hip fracture** CMAJ 2010 0: cmaj.100458. Dec 20/10. (BMD not required for Dubbo or Frax. Dubbo: less variables to calculate, formula published & classifies Canadian men better).
Langsetmo L, Berger C, Kreiger N, et al; the **CaMos** Group. **Calcium and Vitamin D Intake and Mortality**: Results from the Canadian Multicentre Osteoporosis Study (CaMos). J Clin Endocrinol Metab. 2013 May 24.
Laroche M, Cantogrel S, Jamard B et al. Comparison of the **analgaesic efficacy of pamidronate and synthetic human calcitonin in osteoporotic vertebral** fractures: a double-blind controlled study. Clin Rheumatol 2006;25:683-686.
Laslett LL, Doré DA, Quinn SJ, et al G. **Zoledronic acid** reduces **knee pain and bone marrow lesions** over 1 year: a randomised controlled trial. Ann Rheum Dis. 2012 Feb 21.
Laslett LL, Kingsbury SR, Hensor EM, et al. Effect of **bisphosphonate** use in patients with symptomatic and radiographic **knee osteoarthritis**: data from the Osteoarthritis Initiative. Ann Rheum Dis. 2014 May 1;73(5):824-30.
Latham NK, Harris BA, Bean JF, et al. Effect of a **home-based exercise program** on functional recovery following rehabilitation after hip fracture: a randomized clinical trial. JAMA. 2014 Feb 19;311(7):700-8.
Lau WC, Chan EW, et al. Association Between **Dabigatran vs Warfarin** and Risk of **Osteoporotic Fractures** Among Patients With Nonvalvular Atrial Fibrillation. JAMA. 2017 Mar 21;317(11):1151-1158.
Leblanc ES, Hillier TA, Pedula KL, et al. **Hip Fracture and Increased Short-term** but Not Long-term **Mortality** in Healthy Older Women. Arch Intern Med. 2011 Sep 26.
Leblanc ES, Perrin N, Johnson JD, et al. Over-the-Counter and **Compounded Vitamin D: Is Potency** What We Expect? JAMA Intern Med. 2013 Feb 11:1-2.
LeBlanc KE, Muncie HL. LeBlanc LL. **Hip Fracture**: Diagnosis, Treatment, and Secondary Prevention. Am Fam Physician. 2014;89(12):945-951.
Leder BZ. Optimizing Sequential and Combined **Anabolic and Antiresorptive Osteoporosis Therapy**. JBMR Plus. 2018 Mar 12; 2(2): 62-68.
Leder BZ, Tsai JN, Uihlein AV, et al. **Denosumab and teriparatide** transitions in postmenopausal osteoporosis (the **DATA-Switch study**): extension of a randomised controlled trial. Lancet 2015; online July 3.
Lee GJ, Birken CS, Parkin PC, et al; for the **TARGet Kids**! Collaboration. Consumption of **non-cow's milk beverages and serum vitamin D levels** in early childhood. CMAJ. 2014 Oct 20.
Lee S, Yin RV, Hirpara H, et al. Increased risk for **atypical fractures associated with bisphosphonate use**. Fam Pract. 2015 Apr 5.
Lekamwasam S, Adachi JD, et al. A framework for the development of guidelines for the management of **glucocorticoid-induced osteoporosis**. Osteoporos Int. 2012 Mar 21.
Lems WF, Dreinhöfer KE, Bischoff-Ferrari H, et al. **EULAR/EFORT** recommendations for management of patients older than 50 years with a **fragility fracture** and prevention of subsequent fractures. Ann Rheum Dis. 2016 Dec 22.
Lems WF, et al. **EULAR/EFORT** recommendations for management of patients **older than 50 years with a fragility fracture** and prevention of subsequent fractures. Ann Rheum Dis. 2017 May;76(5):802-810.
Lems WF. Bisphosphonates: a therapeutic option for knee osteoarthritis? Ann Rheum Dis. 2018 Sep;77(9):1247-1248.
Lenart BA et al. Association of **low-energy femoral fractures** with prolonged bisphosphonate use: A case control study. Osteoporos Int 2009 Aug; 20:1353.
Leslie WD, Tsang JF, Lix LM. Validation of ten-year fracture **risk prediction**: a clinical cohort study from the Manitoba Bone Density Program. Bone 2008; 43(4):667-671.
Leslie WD, Berger C, Langsetmo L, et al. Construction and validation of a simplified fracture risk assessment tool for Canadian women and men: results from the CaMos and Manitoba BMD cohorts. Osteoporos Int. (**CAROC** 2010) In press. http://osteoporosis.bluerush.ca/www/pdf/caroc_oct_2010.pdf
Leslie WD., Morin S, Lix LM. A Before-and-After Study of **Fracture Risk Reporting** and Osteoporosis treatment Initiation. *Ann Intern Med* November 2, 2010 153:580-586.
Leslie WD, LaBine L, Klassen P, et al. Closing the **gap in postfracture care** at the population level: a randomized controlled trial. CMAJ 2012;184:290-6.
Leslie WD, Morin SN, Lix LM; Manitoba Bone Density Program. **Rate of bone density change does not enhance fracture prediction** in routine clinical practice. J Clin Endocrinol Metab 2012; 97:1211–1218.
Leslie WD, Majumdar SR, Morin SN, et al. **Change in Bone Mineral Density** Is an Indicator of Treatment-Related Antifracture Effect in Routine Clinical Practice: A Registry-Based Cohort Study. Ann Intern Med. 2016 Oct 4;165(7):465-472.
Levis S, Strickman-Stein N, Ganjei-Azar P, et al. **Soy isoflavones** in the prevention of menopausal bone loss and menopausal symptoms: a randomized, double-blind trial. (SPARE) Arch Intern Med. 2011;171 (15):1363-1369. (200mg for 2yrs did not prevent bone loss or menopausal symptoms)
Lewerin C, Nilsson-Ehle H, Jacobsson S, et al. **Low holotranscobalamin and cobalamins** predict incident fractures in elderly men: the MrOS Sweden. Osteoporos Int. 2014 Jan;25(1):131-40
Lewiecki EM. **Managing osteoporosis**: challenges and strategies. Cleve Clin J Med. 2009 Aug;76(8):457-66.
Lewiecki E. Michael. **In the Clinic: Osteoporosis**. Ann Intern Med July 5, 2011 155:ITC1-1; doi:10.1059/0003-4819-155-1-201107050-01001.
Li F, Harmer P, Fitzgerald K, et al. Effectiveness of a **Therapeutic Tai Ji Quan Intervention vs a Multimodal Exercise Intervention to Prevent Falls Among Older Adults** at High Risk of Falling: A Randomized Clinical Trial. JAMA Intern Med. 2018 Sep 10.
Li Kuanrong, Kaaks R, Linseisen J, et al. Associations of **dietary calcium intake and calcium supplementation** with **myocardial infarction** and stroke risk and overall cardiovascular mortality in the Heidelberg cohort of the European Prospective Investigation into Cancer and Nutrition study (EPIC-Heidelberg). Heart 2012. (In press)
Li M, Zhang ZL, Liao EY, et al. Effect of **low-dose alendronate** treatment on bone mineral density and bone turnover markers in Chinese postmenopausal women with

osteopenia and osteoporosis. Menopause. 2012 Sep 10.
Liede A, Wade S, et al. An Observational Study of Concomitant Use of Emerging Therapies and **Denosumab or Zoledronic Acid in Prostate Cancer**. Clin Ther. 2018 Jan 24.
Lim LS, Hoeksema LJ, Sherin K; **ACPM** Prevention Practice Committee. **Screening** for osteoporosis in the adult U.S. population: ACPM position statement on preventive practice. Am J Prev Med. 2009 Apr;36(4):366-75. All adult patients aged >or=50 years should be evaluated for risk factors for osteoporosis. Screening with BMD testing for osteoporosis is recommended in women aged >or=65 years and in men aged >or=70 years. Younger postmenopausal women and men aged 50-69 years should undergo screening if they have at least one major or two minor risk factors for osteoporosis. It is also recommended that clinicians consider using an osteoporosis risk-assessment tool to evaluate absolute fracture risk to determine appropriate osteoporosis therapies.
Lim SH, Benseler SM, Tyrrell PN, et al. Low bone mineral density is present in newly diagnosed **paediatric systemic lupus erythematosus** patients. Ann Rheum Dis. 2011 Nov;70(11):1991-4.
Lin SM, Wang JH, Liang CC, et al. **Statin use is associated with decreased osteoporosis** and fracture risks in stroke patients. J Clin Endocrinol Metab. 2018 Jul 2.
Lips P, Bouillon R, van Schoor NM, et al. Reducing fracture risk with **calcium and vitamin D**. Clin Endocrinol (Oxf). 2009 Sep 10. [Epub ahead of print]
Liu JM, Wai-Chee Kung A, et al. Efficacy and safety of 2 g/day of **strontium ranelate** in Asian women with postmenopausal osteoporosis. Bone. 2009 Sep;45(3):460-5.
Liu Y, Liu JP, Xia Y. **Chinese herbal medicines for treating osteoporosis**. Cochrane Database Syst Rev. 2014 Mar 6;3:CD005467.
Current findings suggest that the beneficial effect of Chinese herbal medicines in improving BMD is still uncertain and more rigorous studies are warranted.
Lloyd AA, Gludovatz B, Riedel C, et al. **Atypical fracture** with long-term **bisphosphonate therapy** is associated with altered cortical composition and reduced fracture resistance. Proc Natl Acad Sci U S A. 2017 Jul 31
Lo JC, Hui RL, Grimsrud CD, Chandra M, et al. The association of **race/ethnicity and risk of atypical femur fracture** among older women receiving oral bisphosphonate therapy. Bone. 2016 Apr;85:142-7.
Logan PA, Coupland CA, Gladman JR, et al. Community **falls prevention** for people who call an emergency ambulance after a fall:randomised controlled trial. BMJ. 2010May11
Loke YK, Singh S, Furberg CD. Long-term use of **thiazolidinediones** and fractures in type 2 diabetes: a meta-analysis. CMAJ. 2009 Jan 6;180(1):32-9. Epub 2008 Dec 10.
Loke YK, Jeevanantham V, Singh S. Bisphosphonates and **atrial fibrillation**: systematic review and meta-analysis. Drug Saf. 2009;32(3):219-28. doi: 10.2165/00002018- 200932030-00004.
Lu PY, Hsieh CF, Tsai YW, Huang WF. **Alendronate and raloxifene** use related to **cardiovascular diseases**: differentiation by different dosing regimens of alendronate. Clin Ther. 2011 Sep;33(9):1173-9.
Ma J, Gao S, Ni X, et al. Exposure to **Bisphosphonates** and Risk of **Colorectal Cancer**. Br J Clin Pharmacol. 2013 Mar 4.
Maalouf Naim M.; Sato Alicia H.; Welch Brian J.; et al. **Postmenopausal Hormone Use** and the Risk of **Nephrolithiasis**: Results From the Women's Health Initiative Hormone Therapy Trials. Arch Intern Med. 2010;170(18):1678-1685.
Macherey S, Monsef I, Jahn F, et al. **Bisphosphonates for advanced prostate cancer**. Cochrane Database of Systematic Reviews 2017, Issue 12. Art. No.: CD006250.
Based on low quality evidence, there may be no clinically relevant difference in the proportion of men with pain response between bisphosphonates and control regimens in men with bone metastasesfrom prostate cancer. Bisphosphonates probably decreasethe number of skeletal-related events and disease progression. These benefits need to be weighed against the increased risk of renal impairment and nausea in men receiving bisphosphonates. Future studies should explicitly evaluate patient important outcomes such as quality of life and pain by using standardized and comparable assessment tools.
Maïmoun L, Renard E, Lefebvre P, et al. **Oral contraceptives partially protect** from bone loss in young women with anorexia nervosa. Fertil Steril. 2019 May;111(5):1020-1029.e2.
Majumdar SR, Lix LM, Yogendran M, et al. Population-Based Trends in Osteoporosis Management after **New Initiations of Long-Term Systemic Glucocorticoids** (1998-2008). J Clin Endocrinol Metab. 2012 Feb 1.
Majumdar SR, McAlister FA, Johnson JA, et al. **Interventions to increase osteoporosis treatment in patients with 'incidentally' detected** vertebral fractures. Am J Med. 2012 Sep;125(9):929-36.
Malluche HH, Blomquist G, Monier-Faugere MC, et al. High Parathyroid Hormone Level and Osteoporosis Predict Progression of Coronary Artery Calcification in Patients on **Dialysis**. J Am Soc Nephrol. 2015 Apr 2.
Mammo Z, Guo M, Maberley D, et al. **Oral Bisphosphonates** and Risk of **Wet Age-Related Macular Degeneration**. Am J Ophthalmol. 2016 Aug;168:62-7.
Mannstadt M, Lin AE, Le LP. Case records of the Massachusetts General Hospital. Case 24-2014. A 27-year-old **man with severe osteoporosis** and multiple bone fractures. N Engl J Med. 2014 Jul 31;371(5):465-72.
Maraka S, Kennel KA. **Bisphosphonates** for the prevention and treatment of osteoporosis. BMJ. 2015 Sep 2;351:h3783.
Marques A, Ferreira RJ, et al. The accuracy of **osteoporotic fracture risk prediction tools**: a systematic review and meta-analysis. Ann Rheum Dis. 2015 Nov;74(11):1958-67.
Marrinan S, Pearce MS, Jiang XY, et al. Admission for **osteoporotic pelvic fractures** and predictors of length of hospital stay, mortality and loss of independence. Age Ageing. 2014 Nov 3.
Martino S, Cauley JA, Barrett-Connor E, et al. **CORE** Investigators. Continuing outcomes relevant to Evista: breast cancer incidence in postmenopausal osteoporotic women in a Randomized trial of raloxifene. J Natl Cancer Inst. 2004 Dec 1;96(23):1751-61.
Mavrokokki T, Cheng A, Stein B, Goss A. Nature and frequency of **bisphosphonate-associated osteonecrosis** of the jaws in Australia. J Oral MaxillofacSurg 2007;65:415-23.
Mazziotti G, Canalis E, Giustina A. **Drug-induced osteoporosis**: mechanisms and clinical implications. Am J Med. 2010 Oct;123(10):877-84.
McCarthy J, Davis A. Diagnosis and Management of **Vertebral Compression Fractures**. Am Fam Physician. 2016;94(1):44-50.
McClung MR, Siris E, Cummings S, et al. Prevention of bone loss in postmenopausal women treated with **lasofoxifene** compared with raloxifene. Menopause 2006;13:377-386.
McClung MR, Lewiecki EM, Cohen SB, et al. **Denosumab** in postmenopausal women with low bone mineral density. N Engl J Med 2006;354:821-831.
McClung M, et al. **Zoledronic** acid for the prevention of bone loss in postmenopausal women with **low bone mass**: a randomized controlled trial. Obstet Gynecol. November 2009;114(5):999–1007.
McClung MR, Grauer A, Boonen S, et al. **Romosozumab** in postmenopausal women with low bone mineral density. N Engl J Med. DOI: 10.1056/NEJMoa1305224.
McComsey GA, Kendall MA, Tebas P, et al. Alendronate with calcium and vitamin D supplementation is safe and effective for the treatment of decreased bone mineral density in **HIV**. AIDS. 2007 Nov 30;21(18):2473-82.
McComsey GA, Tebas P, Shane E, et al. Bone disease in **HIV** infection: a practical review and recommendations for HIV care providers.Clin Infect Dis.2010Oct 15;51(8):937-46.
McCormack SE, et al. Association Between **Linear Growth and Bone Accrual** in a Diverse Cohort of **Children and Adolescents**. JAMA Pediatr. 2017 Jul 3:e171769.
McKague M, Jorgenson D, Buxton KA. **Ocular side effects of bisphosphonates**: A case report and literature review. Can Fam Physician. 2010 Oct;56(10):1015-7.
McKinlay CJ, et al. **Mid-Childhood Bone Mass** After Esposure to Repeat Doses of **Antenatal Glucocorticoids**: A Randomized Trial. Pediatrics. 2017;138(5):e20164250
McVeigh JA, Howie EK, Zhu K, et al. **Organized Sport Participation** From Childhood to Adolescence Is **Associated With Bone Mass** in Young Adults From the Raine Study. J Bone Miner Res. 2018 Oct 17.
Mellström D, Yang X, Li Z, et al. Proportion and Characteristics of Patients in Sweden Remaining at **High Risk of Fracture Despite Prior Treatment**. Clin Ther. 2016 Jun 7.
Merriman NA, Putt ME, Metz DC, Yang YX. Hip Fracture Risk in Patients with a Diagnosis of **Pernicious Anemia**. Gastroenterology. 2009 Dec 16.
Meunier PJ, Roux C, Seeman E, et al. The effects of **strontium ranelate** on the risk of vertebral fracture in women with postmenopausal osteoporosis. N Engl J Med. 2004 Jan 29;350(5):459-68.
Meunier PJ, Roux C, Ortolani S, et al. Effects of long-term **strontium ranelate** treatment on vertebral fracture risk in postmenopausal women with osteoporosis. Osteoporos Int. 2009 Oct;20(10):1663-73. Epub 2009 Jan 20.
Mhaskar R, Redzepovic J, Wheatley K, Clark OAC, Miladinovic B, Glasmacher A, Kumar A, Djulbegovic B. **Bisphosphonates** in **multiple myeloma**: a network meta-analysis.
Cochrane Database of Systematic Reviews 2012, Issue 5. Art. No.: CD003188. DOI: 10.1002/14651858.CD003188.pub3. Use of bisphosphonates in patients with MM reduces pathological vertebral fractures, SREs and pain. Assuming a baseline risk of 20% to 50% for vertebral fracture without treatment, between 8 and 20 MM patients should be treated to prevent vertebral fracture(s) in one patient. Assuming a baseline risk of 31% to 76% for pain amelioration without treatment, between 5 and 13 MM patients should be treated to reduce pain in one patient. With a baseline risk of 35% to 86% for SREs without treatment, between 6 and 15 MM patients should be treated to prevent SRE(s) in one patient. Overall, there were no significant adverse effects associated with the administration of bisphosphonates identified in the included RCTs. We found no evidence of superiority of any specific aminobisphosphonate (zoledronate, pamidronate or ibandronate) or nonaminobisphosphonate (etidronate or clodronate) for any outcome. However, zoledronate appears to be superior to placebo and etidronate in improving overall survival.
MHRA Aug/12 There is an increased risk of **cancer associated with the long-term use of calcitonin**. Because of this risk, calcitonin-containing medicines should no longer be

used in the treatment of osteoporosis. All intra-nasal calcitonin sprays, which are the only formulation of calcitonin licensed for osteoporosis, will be withdrawn from the European market.
MHRA Apr/16 **Aflibercept** (Zaltrap▼): minimising the risk of **osteonecrosis of the jaw**. Dental examination and appropriate preventive dentistry should be considered before treatment, especially for patients also treated with an intravenous bisphosphonate. https://www.gov.uk/drug-safety-update/aflibercept-zaltrap-minimising-the-risk-of- osteonecrosis-of-the-jaw
Michaëlsson K, Wolk A, Langenskiöld S, et al. **Milk intake and risk of mortality and fractures in women and men**: cohort studies. BMJ2014;349:g6015.
Miller PD. Fragility fractures in **chronic kidney disease**: an opinion-based approach. Cleve Clin J Med. 2009 Dec;76(12):715-23.
Miller PD, Chines AA, Christiansen C, et al. Effects of **bazedoxifene** on BMD and bone turnover in postmenopausal women: 2-yr results of a randomized, double-blind, placebo-, and active-controlled study. J Bone Miner Res 2008;23:525-535.
Miller PD, Hattersley G, Riis BJ, et al. Effect of **Abaloparatide** vs Placebo on New Vertebral Fractures in Postmenopausal Women With Osteoporosis: A Randomized Clinical Trial. (**Active**) JAMA. 2016 Aug 16;316(7):722-33
Min HK, Ahn JH, Ha KY, et al. Effects of **anti-osteoporosis medications** on radiological and clinical results **after acute osteoporotic spinal fractures**: a retrospective analysis of prospectively designed study. Osteoporos Int. 2019 Aug 17.
Mittan D, Lee S, Miller E, et al. Bone loss following hypogonadism in men with **prostate cancer treated with GnRH analogs**. J Clin Endocrinol Metab 2002;87:3656-61.
Mok Chi Chiu, Ying King Yee, To Chi Hung, et al. **Raloxifene for prevention of glucocorticoid-induced bone loss**: a 12-month randomised double-blinded placebo-controlled trial. Ann Rheum Dis 2011;70:778-784 Published Online First: 27 December 2010 doi:10.1136/ard.2010.143453.
Morgan GJ, Child JA, Gregory WM, et al. National Cancer Research Institute Haematological Oncology Clinical Studies Group. Effects of **zoledronic acid versus clodronic** acid on skeletal morbidity in patients with newly diagnosed **multiple myeloma** (MRC Myeloma IX): secondary outcomes from a randomised controlled trial. Lancet Oncol. 2011 Aug;12(8):743-52.
Mosca L, Grady D, Barrett-Connor E, et al. Effect of **raloxifene** on stroke and venous thromboembolism according to subgroups in postmenopausal women at increased risk of coronary heart disease. Stroke 2009; 40(1):147-155.
Mosca L, Grady D, Barrett-Connor E, et al. Effect of **raloxifene** on stroke and venous thromboembolism according to subgroups in postmenopausal women at increased risk of coronary heart disease. Stroke. 2009 Jan;40(1):147-55.
Mosenzon O, Wei C, Davidson J, et al. Incidence of **Fractures** in Patients With Type 2 **Diabetes** in the **SAVOR-TIMI 53** Trial. Diabetes Care. 2015 Sep 10.
Mueller NJ, Fux CA, Ledergerber B, et al. the Swiss **HIV** Cohort Study. High prevalence of severe vitamin D deficiency in combined antiretroviral therapy-naive and successfully treated Swiss HIV patients. AIDS. 2010 Feb 15.
Nadler M, Alibhai S, Catton P, et al. Osteoporosis knowledge, health beliefs, and healthy bone behaviours in patients on **androgen-deprivation therapy** (ADT) for prostate cancer. BJU Int 2013.
NAMS: North American Menopause Society. Management of osteoporosis in postmenopausal women: **2006** position statement of The North American Menopause Society. Menopause. 2006 May-Jun;13(3):340-67
NAMS: Management of **osteoporosis in postmenopausal women**: **2010** position statement of The North American Menopause Society. Menopause. **2010** Jan-Feb;17(1):25-54.
Mazziotti G, Canalis E, Giustina A. **Drug-induced osteoporosis**: mechanisms and clinical implications. Am J Med. 2010 Oct;123(10):877-84.
MHRA Feb/13 **Atypical femoral fractures** have been reported rarely in patients with postmenopausal osteoporosis receiving long-term (≥2.5 years) treatment with **denosumab** 60 mg (Prolia▼) in a clinical trial.
MHRA – Drug Safety Update July 2015: **Denosumab** (Xgeva▼, Prolia); intravenous bisphosphonates: **osteonecrosis of the jaw**—further measures to minimise risk. Patient reminder cards about the risk of osteonecrosis of the jaw are being introduced; denosumab 120 mg is now contraindicated in patients with unhealed lesions from dental or oral surgery.
Miller-Martinez D, Seeman T, Karlamangla AS, et al. **Marital histories, marital support, and bone density**: findings from the Midlife in the United States Study. Osteoporos Int. 2014 Jan 15
Modi A, Siris ES, Steve Fan CP, et al. **Gastrointestinal Events** Among Patients Initiating Osteoporosis Therapy: A Retrospective Administrative Claims Database Analysis. Clin Ther. 2015 Apr 9.
Moen SM, Celius EG, Sandvik L, et al. **Low bone mass** in newly diagnosed **multiple sclerosis** and clinically isolated syndrome. Neurology. 2011 Jul 12;77(2):151-7.
Morgan Gareth J, Davies Faith E, Gregory Walter M et al.,on behalf of the National Cancer Research Institute Haematological Oncology Clinical Study Group. First-line treatment with **zoledronic** acid as compared with clodronic acid in **multiple myeloma** (MRC Myeloma IX): a randomised controlled trial. The Lancet - 4 Dec 2010.
Moyer VA; U.S. Preventive Services Task Force-USPSTF. **Vitamin D and calcium supplementation to prevent fractures** in adults: U.S. Preventive Services Task Force Recommendation Statement. Ann Intern Med. 2013. [Epub ahead of print] Postmenopausal women should not take supplementary calcium (1000 mg or less) and vitamin D (400 IU or less) to prevent fractures, the U.S. Preventive Services Task Force says in a new recommendation.
Munson JC, et al. Patterns of prescription drug use before and after fragility fracture [online Aug 22, 2016].JAMA Intern Med. doi:10.1001/jamainternmed.2016.4814
Murad MH, Drake MT, Mullan RJ, et al. **Comparative Effectiveness** of Drug Treatments to Prevent Fragility Fractures: A Systematic Review and Network Meta-Analysis. J Clin Endocrinol Metab. 2012 Mar 30. Teriparatide, bisphosphonates, and denosumab are most effective in reducing the risk of fragility fractures.
Murphy-Menezes M. Role of the **Pharmacist in Medication Therapy Management Services** in Patients With Osteoporosis. Clin Ther. 2015 Apr 23.
Nancollas GH, Tang R, Phipps RJ, et al. Novel insights into **actions of bisphosphonates** on bone: differences in interactions with hydroxyapatite. Bone. 2006 May;38(5):617-27.
Naseri C, Haines TP, et al. **Reducing falls in older adults recently discharged from hospital**: a systematic review and meta-analysis. Age Ageing. 2018 Mar 23.
National Osteoporosis Foundation (**NOF**) http://www.nof.org/
Nayak S, Roberts MS, Greenspan SL. **Cost-effectiveness of different screening** strategies for osteoporosis in postmenopausal women. Ann Intern Med. 2011; 155:751-61.
Screening strategies composed of alternative tests (central dual-energy x-ray absorptiometry [DXA], calcaneal quantitative ultrasonography [QUS], and the Simple Calculated Osteoporosis Risk Estimation [SCORE] tool) initiation ages, treatment thresholds, and rescreening intervals. No strategy substantially outperforms another.
Nayak S, Greenspan SL. **Osteoporosis Treatment Efficacy for Men**: A Systematic Review and Meta-Analysis. J Am Geriatr Soc. 2017 Mar;65(3):490-495.
Neer RM, Arnaud CD, Zanchetta JR, et al. Effect of **parathyroid hormone** (1-34) on fractures and bone mineral density in postmenopausal women with osteoporosis. N Engl J Med 2001; 344(19):1434-1441.
Nelson HD, Helfand M, Woolf SH, et al. **Screening** for postmenopausal osteoporosis: a review of the evidence for the U.S. Preventive Services Task Force. (**USPSTF**) Ann Intern Med. 2002 Sep 17;137(6):529-41.
Nelson Heidi D., Haney Elizabeth M., Dana Tracy, et al. **Screening** for Osteoporosis: An Update for the U.S. Preventive Services Task Force (**USPSTF**). Ann Intern Med published ahead of print July 5, **2010**, doi:10.1059/0003-4819-153-2-201007200-00262.
Neogi T;Li S;Peloquin C;Misra D;Zhang Y. Effect of **bisphosphonates on knee replacement surgery**. Ann Rheum Dis. 2017 Oct 7.
Neuner J, Carnahan J. **Dual X-ray absorptiometry** for diagnosis of osteoporosis. JAMA. 2014 Sep 17;312(11):1147-8.
Newberry SJ, Chung M, Shekelle PG, et al. **Vitamin D and Calcium: A** Systematic Review of Health Outcomes (Update). Evidence Report/Technology Assessment No. 217. AHRQ Comparative Effectiveness Review. Rockville (MD): Agency for Healthcare Research and Quality (US); 2014 Sept. Report No.: 14-E004-EF.
Newcomb PA, Trentham-Dietz A, Hampton JM. Bisphosphonates for osteoporosis treatment are associated with reduced **breast cancer risk**. Br J Cancer. 2010 Mar 2;102(5):799-802.
Ni Mhuircheartaigh O, Crowson CS, Gabriel SE, et al. **Fragility Fractures** Are Associated with an Increased **Risk for Cardiovascular Events** in

Women and Men with Rheumatoid Arthritis: A Population-based Study. J Rheumatol. 2017 Jan 15.
NICE: National Institute for Clinical Excellence. Falls: the assessment and prevention of **falls** in older people. (Clinical guideline 21.) 2004. http://guidance.nice.org.uk/CG21 .
NICE: National Institute for Health and Clinical Excellence. **Denosumab** for the prevention of osteoporotic fractures in postmenopausal women. London (UK): 2010 Oct.
NICE:National Institute for Health and Clinical Excellence. **Osteoporosis—secondary prevention** including strontium ranelate. Alendronate, etidronate, risedronate, raloxifene, strontium ranelate and teriparatide for the secondary prevention of osteoporotic fragility fractures in postmenopausal women (amended). (Technology appraisal 161.) 2011 (originally published 2008, amended 2010 and 2011). http://guidance.nice.org.uk/TA161.
NICE: Management of **hip fracture** in adults: summary of NICE guidance June 2011. http://www.nice.org.uk/nicemedia/live/13489/54921/54921.pdf
NICE: National Institute for Health and Clinical Excellence. Osteoporosis: **assessing the risk of fragility fracture**. (Clinical guideline 146.) 2012. www.nice.org.uk/CG146.
NICE technology appraisal guidance TA265. **Denosumab for the prevention of skeletal related events** in adults with bone metastases from solid tumours. October 2012. http://www.nice.org.uk/nicemedia/live/13939/61129/61129.pdf
NICE: National Institute for Health and Care Excellence. **Percutaneous vertebroplasty and percutaneous balloon kyphoplasty** for treating osteoporotic vertebral compression fractures. London (UK): National Institute for Health and Care Excellence (NICE); 2013 Apr.
NICE: National Clinical Guideline Centre. **Fractures (non-complex):** assessment & management. London (UK): National Institute for Health and Care Excellence; 2016 Feb 17.
NICE: National Clinical Guideline Centre. **Fractures (complex):** assessment and management. London (UK): National Institute for Health and Care Excellence; 2016 Feb 17.
NIH Osteoporosis and Related Bone Diseases ~ National Resource Center http://www.niams.nih.gov/Health_info/bone/Osteoporosis/default.asp
Nordström P, Gustafson Y, Michaëlsson K, Nordström A. **Length of hospital stay after hip fracture and short term risk of death after discharge**: a total cohort study in Sweden. BMJ 2015;350:h696.
Nayak S, Greenspan SL. **Osteoporosis Treatment Efficacy for Men**: A Systematic Review and Meta-Analysis. J Am Geriatr Soc. 2017 Mar;65(3):490-495.
Nyandege AN, Slattum PW, Harpe SE. Risk of Fracture and the Concomitant Use of Bisphosphonates With **Osteoporosis-Inducing Medications**. Ann Pharmacother. 2015 Apr;49(4):437-447. Epub 2015 Feb 9. Review.
O'Carrigan B, Wong MHF, Willson ML, Stockler MR, Pavlakis N, Goodwin A. **Bisphosphonates and other bone agents for breast cancer**. Cochrane Database of Systematic Reviews 2017, Issue 10. Art. No.: CD003474. For women with EBC, bisphosphonates reduce the risk of bone metastases and provide an overall survival benefit compared to placebo or no bisphosphonates. There is preliminary evidence suggestive that bisphosphonates provide an overall survival and disease-free survival benefit in postmenopausal women only when compared to placebo or no bisphosphonate. This was not a planned subgroup for these early trials, and we await the completion of new large clinical trials assessing benefit for postmenopausal women. For women with BCBM, bisphosphonates reduce the risk of developing SREs, delay the median time to an SRE, and appear to reduce bone pain compared to placebo or no bisphosphonate.
O'Donnell S, Cranney A, Wells GA, et al. **Strontium ranelate** for preventing and treating postmenopausal osteoporosis. Cochrane Database Syst Rev. 2006 Jul 19;3:CD005326.
O'Hanlon CE, Parthan A, Kruse M, et al. A Model for Assessing the **Clinical and Economic Benefits of Bone-Forming Agents** for Reducing Fractures in Postmenopausal Women at High, Near-Term Risk of Osteoporotic Fracture. Clin Ther. 2017 Jun 16.
Oderda LH, Young JR, Asche CV, Pepper GA. **Psychotropic-related** hip fractures: meta-analysis of first-generation and second-generation antidepressant and antipsychotic drugs. Ann Pharmacother. 2012 Jul;46(7-8):917-28.
Odvina CV, Zerwekh JE, Rao DS, Maalouf N, Gottschalk FA, Pak CY. **Severely suppressed bone turnover**: a potential complication of **alendronate** therapy. J Clin Endocrinol Metab 2005; 90:1294-301.
Ogdie A, Harter L, et al. The **risk of fracture** among patients with **psoriatic arthritis and psoriasis**: a population-based study. Ann Rheum Dis. 2017 May;76(5):882-885.
Olmos JM, Hernández JL, Llorca J, et al. Effects of **25-Hydroxyvitamin D3** Therapy on Bone Turnover Markers and PTH Levels in Postmenopausal Osteoporotic Women Treated with Alendronate. J Clin Endocrinol Metab. 2012 Oct 5.
Olszynski WP, Adachi JD, Davison KS. Differences in In Vitro **Disintegration Time** among Canadian **Brand and Generic Bisphosphonates**. J Osteoporos. 2014;2014:420451.
Orford NR, Lane SE, Bailey M, et al. **Changes in Bone Mineral Density** in the Year **After Critical Illness**. Am J Respir Crit Care Med. 2015 Nov 11.
Orwig Denise L.; Hochberg Marc; Yu-Yahiro Janet; et al. Delivery and Outcomes of a Yearlong Home **Exercise Program** After Hip Fracture: A Randomized Controlled Trial. Arch Intern Med. 2011;171(4):323-331.
Orwoll E, Ettinger M, Weiss S, Miller P, Kendler D, Graham J et al. **Alendronate** for the treatment of osteoporosis in **men**. N Engl J Med 2000; 343(9):604-610.
Orwoll E, Teglbjaerg CS, Langdahl BL, et al. A randomized, placebo-controlled study of the effects of **denosumab for the treatment of men** with low bone mineral density. (**ADAMO**) J Clin Endocrinol Metab 2012;97:3161-9.
Ott SM. What is the optimal **duration of bisphosphonate therapy**? Cleve Clin J Med. 2011 Sep;78(9):619-30.
Ott SM. What should be the **interval between bone density screenings**? Cleve Clin J Med. 2013 Apr;80(4):240-1.
Overman RA, Borse M, Gourlay ML. **Salmon calcitonin** use and associated **cancer** risk. Ann Pharmacother. 2013 Dec;47(12):1675-84
Overton ET, et al. **Vitamin D and Calcium** Attenuate Bone Loss **With Antiretroviral Therapy** Initiation: A Randomized Trial. Ann Intern Med. 2015 Jun16;162(12):815-24.
Paccou J, Edwards MH, Ward KA, et al. **Ischemic heart disease** is associated with lower cortical volumetric bone mineral density of distal radius. Osteoporos Int. 2015 Jul;26(7):1893-901.
Paik JM, Kim SC, Feskanich D, et al. **Gout** and **Risk of Fracture in Women**: A Prospective Cohort Study. Arthritis Rheumatol. 2016 Sep 2
Pallan S, Khan A. **Primary hyperparathyroidism**: Update on presentation, diagnosis, and management in primary care. Can Fam Physician. 2011 Feb;57(2):184-9.
Pallan S, Rahman MO, Khan AA. Diagnosis and management of **primary hyperparathyroidism**. BMJ. 2012 Mar 19;344:e1013.
Palmer SC, McGregor DO, Macaskill P, et al. Meta-analysis: **vitamin D** compounds in chronic kidney disease. Ann Intern Med. 2007;147(12):840–853.
Papadakis G, Hans D, Gonzalez-Rodriguez E, et al. The Benefit of **Menopausal Hormone Therapy on Bone Density** and Microarchitecture Persists **After its Withdrawal**. J Clin Endocrinol Metab. 2016 Nov 17:jc20162695.
Papaioannou A, Santesso N, et al; Scientific Advisory Council of **Osteoporosis Canada**. Recommendations for **preventing fracture in long-term care**. CMAJ. 2015 Sep 14.
Papapoulos S, Chapurlat R, Libanati C, et al. Five years of **denosumab** exposure in women with postmenopausal osteoporosis: results from the first two years of the **FREEDOM** extension. J Bone Miner Res. 2012 Mar;27(3):694-701.
Park-Wyllie LY, Mamdani MM, Juurlink DN, et al. Bisphosphonate use and the risk of **subtrochanteric or femoral shaft fractures** in older women. JAMA. 2011 Feb 23;305(8):783-9.
Paschou SA, Dede AD, Anagnostis PG, et al. **Type** 2 **diabetes** and **osteoporosis**: a guide to optimal management. J Clin Endocrinol Metab. 2017 June 21.
Paskins Z, Warburton L. **Bisphosphonates beyond five years**. BMJ. 2016 Mar 16
Passos-Soares JS, Vianna MI, et al. Association between osteoporosis treatment and **severe periodontitis** in postmenopausal women. Menopause. 2017 Feb 20
Paterson AHG, Anderson SJ, Lembersky BC, et al. Oral **clodronate** for adjuvant treatment of operable **breast cancer** (National Surgical Adjuvant Breast and Bowel Project protocol B-34): a multicentre, placebo-controlled, randomised trial. Lancet Oncol 2012
Pazianas M, Clark EM, Eiken PA, et al. **Inflammatory eye reactions** in patients treated with **bisphosphonates** and other osteoporosis medications - cohort analysis using a

national prescription database. J Bone Miner Res. 2012 Oct 8.
Pearce Simon HS, Cheetham Tim D. Diagnosis and management of **vitamin D** deficiency. BMJ 2010;340:b5664, doi: 10.1136/bmj.b5664 (Published 11 January 2010)
Pedersen AB, Heide-Jørgensen U, Sørensen HT, et al. Comparison of Risk of Osteoporotic Fracture in **Denosumab vs Alendronate** Treatment Within 3 Years of Initiation. JAMA Netw Open. 2019 Apr 5;2(4):e192416.
Peppone LJ, Hebl S, Purnell JQ, et al. The efficacy of **calcitriol** therapy in the management of bone loss and fractures: a qualitative review. Osteoporos Int. 2009 Dec 4.
Peris P, Martínez-Ferrer A, et al. **25 hydroxyvitamin D serum levels** influence adequate response to bisphosphonate treatment in postmenopausal osteoporosis. Bone. 2012Apr 1.
Pham AN, Datta SK, Weber TJ, et al. **Cost-Effectiveness** of Oral **Bisphosphonates** for Osteoporosis at Different **Ages** and Levels of **Life Expectancy**. J Am Geriatr Soc. 2011 Aug 30. doi: 10.1111/j.1532-5415.2011.03571.x.
Pickhardt PJ, Pooler BD, Lauder T, et al. Opportunistic **screening** for osteoporosis using **abdominal computed tomography** scans obtained for other indications. Ann Intern Med. 2013;158: 588-95.
Pimentel A, Ureña-Torres P, Zillikens MC, et al. **Fractures in patients with CKD**-diagnosis, treatment, and prevention: a review by members of the European Calcified Tissue Society and the European Renal Association of Nephrology Dialysis and Transplantation. Kidney Int. 2017 Sep 27.
Piperno-Neumann S, Le Deley MC, Rédini F, et al. **Zoledronate** in combination with chemotherapy and surgery to treat **osteosarcoma**(**OS2006**): a randomised, multicentre, open-label, phase 3 trial. Lancet Oncol. 2016 Jun 17.
Pirruccio K, Yoon YM, Ahn J**. Fractures** in Elderly Americans **Associated With Walking Leashed Dogs**. JAMA Surg. 2019 Mar 6.
Pollock NK, Bernard PJ, Gutin B, et al. **Adolescent** obesity, bone mass, and cardiometabolic risk factors. J Pediatr. 2011 May;158(5):727-34.
Poole KE, Compston JE. **Bisphosphonates in the treatment of osteoporosis**. BMJ. 2012 May 22;344:e3211.
Poolman RW, Agoritsas T, Siemieniuk RA, et al. **Low intensity pulsed ultrasound (LIPUS)** for bone healing: a clinical practice guideline. BMJ. 2017 Feb 21;356:j576.
Popat VB, Calis KA, Kalantaridou SN, et al. Bone Mineral Density in Young Women With Primary Ovarian Insufficiency: Results of a Three-Year Randomized Controlled Trial of Physiological **Transdermal Estradiol and Testosterone** Replacement. J Clin Endocrinol Metab. 2014 Jun 6:jc20134145.
Posen J, Beaton DE, Sale J, Bogoch ER. **Bone mineral density testing after fragility fracture**: Informative test results likely. Can Fam Physician. 2013 Dec;59(12):e564-71
Powles TJ, Paterson AHG. Unproven Efficacy of **Low-Dose Bisphosphonates as a Means of Decreasing Bone Metastases and Death in Early Breast Cancer**. JAMA Oncol. 2018 Jul 26.
Prada D, Zhong J, Colicino E, et al. Association of **air particulate pollution with bone loss** over time and bone fracture risk: analysis of data from two independent studies. Lancet Planet Health 2017; 1: e337–47.
Prasad C, Cummings E. **Rickets presenting as gross motor delay** in twin girls. CMAJ. 2018 May 7;190(18):E565-E568.
Premaor MO, Compston JE. **Testing for secondary causes of osteoporosis**. BMJ. 2010 Dec 16;341:c6959. doi: 10.1136/bmj.c6959.
Prestmo A, Hagen G, Sletvold O, et al. **Comprehensive geriatric care for patients with hip fractures**: a prospective, randomised, controlled trial. Lancet 2015; online Feb 5.
Prieto-Alhambra D, Javaid MK, Judge A, et al. Association between **bisphosphonate use and implant survival** after primary total arthroplasty of the knee or hip: population based retrospective cohort study. BMJ. 2011 Dec 6;343:d7222. doi: 10.1136/bmj.d7222.
Prieto-Alhambra D, Lalmohamed A, Abrahamsen B, et al. Oral **bisphosphonate** use and **total knee/hip implant survival**: validation of results in an external population-based cohort. Arthritis Rheumatol. 2014 Jul 21.
Puar TH, Khoo JJ, Cho LW, Xu Y, Chen YT, Chuo AM, Poh CB, Ng JM. Association between **glycemic control and hip fracture**. J Am Geriatr Soc. 2012 Aug;60(8):1493-7.
Pun KK, Chan LW. **Analgesic** effect of intranasal salmon **calcitonin** in the treatment of osteoporotic vertebral fractures. Clin Ther. 1989 Mar-Apr;11(2):205-9.
Pundole XN, Barbo AG, Lin H, et al. Increased Incidence of Fractures in Recipients of **Hematopoietic Stem-Cell Transplantation**. J Clin Oncol. 2015 Mar 16.
Qaseem A, Snow V, Shekelle P, et al.; Clinical Efficacy Assessment Subcommittee of the American College of Physicians. **ACP Pharmacologic treatment** of low bone density or osteoporosis to prevent fractures:a clinical practice guideline from the American College of Physicians. Ann Intern Med. 2008 Sep 16;149(6):404-15.
Qaseem A, Snow V, Shekelle P, et al.; Clinical Efficacy Assessment Subcommittee of the American College of Physicians. **ACP Screening for osteoporosis in men**: a clinical practice guideline from the American College of Physicians. Ann Intern Med. 2008 May 6;148(9):680-4. Erratum in: Ann Intern Med. 2008 Jun 3;148(11):888.
Qaseem A, Forciea MA, McLean RM, Denberg TD; Clinical Guidelines Committee of the American College of Physicians (**ACP**). Treatment of low bone density or osteoporosis to **prevent fractures in men and women**: a clinical practice guideline update from the **American College of Physicians**. Ann Intern Med. [Epub 9 May 2017].
QFractureScore http://www.qfracture.org/
Quandt SA, Thompson DE, Schneider DL, et al. Effect of **alendronate** on vertebral fracture risk in women with bone mineral density T score of −1.6 to −2.5 at the femoral neck: the fracture intervention trial. Mayo Clin Proc 2005;80:343-9.
Rabar S, Lau R, O'Flynn N, Li L, Barry P; Guideline Development Group. Risk assessment of **fragility fractures**: summary of NICE guidance. BMJ. 2012 Aug 8;345:e3698.
Rachner Tilman D. **Osteoporosis: now and the future**. www.thelancet.com Published online March 29, 2011 DOI:10.1016/S0140-6736(10)62349-5
Rahmani, Poupak, Morin, Suzanne. **Prevention of osteoporosis**-related fractures among postmenopausal women and older men. CMAJ 2009 0: cmaj.080709
Ralston SH. Clinical practice. **Paget's disease** of bone. N Engl J Med. 2013 Feb 14;368(7):644-50.
Ramin C, May BJ, Roden RBS, et al. **Evaluation of osteopenia and osteoporosis in younger breast cancer survivors compared with cancer-free women**: a prospective cohort study. Breast Cancer Res. 2018 Nov 13;20(1):134.
Rao SS, Budhwar N, Ashfaque A. **Osteoporosis in men**. Am Fam Physician. 2010 Sep 1;82(5):503-8.
Recknor C, Czerwinski E, Bone HG, et al. **Denosumab Compared With Ibandronate** in Postmenopausal Women Previously Treated With Bisphosphonate Therapy: A Randomized Open-Label Trial. Obstet Gynecol. 2013 Jun;121(6):1291-1299.
Reddy Munagala VV, Tomar V. **Images** in clinical medicine. **Osteomalacia**. N Engl J Med. 2014 Feb 6;370(6):e10
Reginster JY, Seeman E, De Vernejoul MC, et al. **Strontium ranelate** reduces the risk of nonvertebral fractures in postmenopausal women with osteoporosis: Treatment of Peripheral Osteoporosis (**TROPOS**) study. J Clin Endocrinol Metab. 2005 May;90(5):2816-22.
Reginster JY, Bruyère O, Sawicki A, et al. Long-term treatment of postmenopausal osteoporosis with **strontium ranelate**: results at 8 years. Bone. 2009 Dec;45(6):1059-64.
Reginster JY, Felsenberg D, Boonen S, et al. Effects of long-term **strontium ranelate** treatment on the risk of nonvertebral and vertebral fractures in postmenopausal osteoporosis: Results of a five-year, randomized, placebo-controlled trial. Arthritis Rheum. 2008 Jun;58(6):1687-95.
Reginster JY, Badurski J, Bellamy N, et al. Efficacy and safety of **strontium** ranelate in the treatment of **knee osteoarthritis**: results of a double-blind, randomised placebo-controlled trial. Ann Rheum Dis. 2012 Nov 9.
Reid DM, Devogelaer JP, Saag K, et al. **Zoledronic** acid and risedronate in the prevention and treatment of **glucocorticoid-induced** osteoporosis (**HORIZON**): a multicentre, double-blind, double-dummy, randomised controlled trial. Lancet 2009; 373(9671):1253-1263.
Reid IR, Bolland MJ, Grey A. Effects of **vitamin D supplements** on bone mineral density: a systematic review and meta-analysis. Lancet 2013; online Oct 11.
Reid IR, Horne AM, Mihov B, et al. Fracture prevention with **zoledronate** in older women with osteopenia. N Engl J Med.
Rejnmark L, Avenell A, Masud T, et al. **Vitamin D with Calcium Reduces Mortality**: Patient Level Pooled Analysis of 70,528 Patients from Eight Major Vitamin D Trials. J Clin Endocrinol Metab. 2012 May 17.
Rennert G, Rennert HS, Pinchev M, et al. The effect of **bisphosphonates** on the risk of **endometrial and ovarian malignancies**. Gynecol Oncol. 2014 May;133(2):309-13.

Reyes C, Tebe C, Martinez-Laguna D, et al. **One and two-year persistence** with different anti-osteoporosis medications: retrospective cohort study. Osteoporos Int. 2017 Jul 16.
Richards JB, Papaioannou A, Adachi JD,et al.; Canadian Multicentre Osteoporosis Study Research Group. Effect of selective **serotonin reuptake inhibitors** on the risk of fracture. Arch Intern Med. 2007 Jan 22;167(2):188-94.
Ring Madsen L, Espersen R, Rejnmark L, et al. Effect of **calcium citrate vs calcium carbonate on elevated parathyroid hormone after Roux-en-Y gastric bypass**. A double-blinded, randomized trial. Clin Endocrinol (Oxf). 2018 Aug 14.
Ringe JD, Farahmand P, Faber H, Dorst A. Sustained efficacy of **risedronate in men** with primary and secondary osteoporosis: results of a 2-year study. Rheumatol Int 2009; 29(3):311-315.
Rios LP, Khan A, Sultan M, et al. Approach to diagnosing **celiac disease in patients with low bone mineral density** or fragility fractures: Multidisciplinary task force report. Can Fam Physician. 2013 Oct;59(10):1055-61.
Rizzoli R, Biver E, Bonjour JP, et al. Benefits and safety of **dietary protein** for bone health-an expert consensus paper endorsed by the European Society for Clinical and Economical Aspects of Osteoporororosis, Osteoarthritis, and Musculoskeletal Diseases and by the International Osteoporosis Foundation. Osteoporos Int. 2018 May 8.
Robertson MC, Campbell AJ, Gardner MM, Devlin N. Preventing injuries in older people by **preventing falls**: a meta-analysis of individual-level data. J Am Geriatr Soc 2002; 50(5):905-911
Robinovitch SN, Feldman F, Yang Y, et al. Video capture of the circumstances of falls in elderly people residing in long-term care: an observational study. Lancet. 2012 Oct 16.
Robbins JA, Aragaki A, Crandall CJ, et al. Women's Health Initiative clinical trials: interaction of **calcium and vitamin D** with hormone therapy. Menopause. 2013 Jun 24.
Roca-Ayats N, Balcells S, Garcia-Giralt N, et al. **GGPS1 Mutation and Atypical Femoral Fractures with Bisphosphonates**. N Engl J Med. 2017 May 4;376(18):1794-1795.
Rooks D, Praestgaard J, Hariry S, et al. Treatment of **Sarcopenia** with **Bimagrumab**: Results from a Phase II, Randomized, Controlled, Proof-of-Concept Study. J Am Geriatr Soc. 2017 Jun 27.
Rousing R, Hansen KL, Andersen MO, et al. Twelve-months follow-up in forty-nine patients with acute/semiacute osteoporotic vertebral fractures treated conservatively or with **percutaneous vertebroplasty**: a clinical randomized study. Spine (Phila Pa 1976). 2010 Mar 1;35(5):478-82.
Roux C, Fechtenbaum J, Kolta S, et al. **Strontium ranelate** reduces the risk of vertebral fracture in young postmenopausal women with severe osteoporosis. Ann Rheum Dis. 2008 Dec;67(12):1736-8.
Roux S, Cabana F, Carrier N, et al. The World Health Organization Fracture Risk Assessment Tool (**FRAX**) **Underestimates** Incident and Recurrent Fractures in Consecutive Patients With Fragility Fractures. J Clin Endocrinol Metab. 2014 Apr 29:jc20134507.
Rozental TD, Makhni EC, Day CS, et al. Improving evaluation and treatment for osteoporosis following **distal radial fractures**. A prospective randomized intervention. J Bone Joint Surg Am. 2008 May;90(5):953-61.
Ruggiero SL, Dodson TB, Assael LA, Landesberg R, Marx RE, Mehrotra B; **American** Association of Oral and Maxillofacial Surgeons. American Association of Oral and Maxillofacial Surgeons position paper on **bisphosphonate-related osteonecrosis** of the jaws--2009 update. J Oral Maxillofac Surg. 2009 May;67(5 Suppl):2-12.
Russell RG, Watts NB, Ebetino FH, Rogers MJ. **Mechanisms of action of bisphosphonates**: similarities and differences and their potential influence on clinical efficacy. Osteoporos Int 2008;19:733-59.
Ruzycki SM, Nixon NA. **Bone health after diagnosis of breast cancer**. CMAJ. 2018 Dec 10;190(49):E1452.
Saad F, Gleason DM, Murray R, et al, for the **Zoledronic Acid Prostate Cancer Study Group**. A randomized, placebo-controlled trial of zoledronic acid in patients with hormone-refractory metastatic prostate carcinoma. J Natl Cancer Inst 2002; 94: 1458–68.
Saad F, Abrahamsson PA, Miller K. Preserving bone health in patients with hormone-sensitive **prostate cancer**: the role of **bisphosphonates**. BJU Int. 2009 Dec;104(11):1573-9.
Saag KG, Emkey R., Schnitzer TJ, et al. **Alendronate** for the prevention and treatment of **glucocorticoid-induced** osteoporosis. N Engl J Med 1998; 339:292-9.
Saag KG, Zanchetta JR, Devogelaer JP, et al. Effects of **teriparatide versus alendronate** for treating **glucocorticoid**-induced osteoporosis: Thirty-six-month results of a randomized, double-blind, controlled trial. Arthritis Rheum. 2009 Oct 29;60(11):3346-3355.
Saag KG, Shane E, Boonen S, et al. **Teriparatide or alendronate** in glucocorticoid-induced osteoporosis. N Engl J Med 2007; 357(20):2028-2039.
Saag KG, Petersen J, Brandi ML, et al. **Romosozumab or alendronate** for fracture prevention in women with osteoporosis. N Engl J Med. DOI: 10.1056/NEJMoa1708322.(**ARCH**)
Saarelainen L, Tolppanen AM, Koponen M, et al. **Risk of Hip Fracture in Benzodiazepine Users** With and Without Alzheimer Disease. J Am Med Dir Assoc. 2016 Nov 12.
Sabhaney V, Boutis K, Yang G, et al. **Bone Fractures** in Children: Is There an Association with **Obesity**? J Pediatr. 2014 May 13.
Sadowski CA, Lyder C, Yuksel N. **Bisphosphonates** for Osteoporosis in Patients with **Renal Insufficiency**: Pharmacists' Practices and Beliefs. Can J Hosp Pharm. 2016 Jan-Feb;69(1):14-22.
Sànchez-Riera L, Carnahan E, Vos T, et al. The **global burden** attributable to **low bone mineral density**. Ann Rheum Dis. 2014 Sep;73(9):1635-45.
Sanders Kerrie M.; Stuart Amanda L.; Williamson Elizabeth J.; et al. Annual **High-Dose Oral Vitamin D** (500,000IU x1/yr for 3-5yrs: increased falls & fractures) and Falls and Fractures in Older Women: A Randomized Controlled Trial. JAMA. 2010;303(18):1815-1822.
Sarnes E, Crofford L, Watson M, et al. Incidence and US Costs of **Corticosteroid-Associated Adverse Events**: A Systematic Literature Review. Clin Ther. 2011 Oct 12.
Sawka AM, Ismaila N, Raina P, et al. **Hip fracture prevention strategies in long-term care**: a survey of Canadian physicians' opinions. Can Fam Physician. 2010 Nov;56(11):e392-7.
Schandelmaier S, Kaushal A, Lytvyn L, et al. **Low intensity pulsed ultrasound for bone healing**: systematic review of randomized controlled trials. BMJ 2017;356:j656.
Schilcher J, Koeppen V, Aspenberg P, et al. **Risk of atypical femoral fracture** during and after bisphosphonate use. N Engl J Med. 2014 Sep 4;371(10):974-6.
Schlingmann Karl P., Weber Stefanie, Goos Caroline, et al. **Mutations in CYP24A1 and Idiopathic Infantile Hypercalcemia**. June 15, 2011 (10.1056/NEJMoa1103864).
Schneider JP, Hinshaw WB, Su C, Solow P. **Atypical femur fractures**: 81 individual personal histories. J Clin Endocrinol Metab. 2012 Dec;97(12):4324-8.
Schöttker B, Jorde R, Peasey A, et al; Consortium on Health and Ageing: Network of Cohorts in Europe and the United States **(CHANCES). Vitamin D and mortality**: meta-analysis of individual participant data from a large consortium of cohort studies from Europe and the United States. BMJ. 2014 Jun 17;348:g3656.
Schwartz AV, Bauer DC, Cummings SR, et al. for the **FLEX** Research Group. Efficacy of continued **alendronate** for fractures in women **with and without prevalent vertebral fracture**: The FLEX trial. J Bone Miner Res. 2010 Jan 8.
Schwartz AV, Vittinghoff E, Bauer DC, et al. Study of Osteoporotic Fractures (SOF) Research Group; Osteoporotic Fractures in Men (MrOS) Research Group; Health, Aging, and Body Composition (Health ABC) Research Group. Association of **BMD and FRAX score with risk of fracture in older adults with type 2 diabetes**. JAMA. 2011 Jun 1;305(21):2184-92.
Scott LJ, Muir VJ. **Denosumab**: in the prevention of skeletal-related events in patients with **bone metastases** from solid tumours. Drugs 2011;71:1059-69.
Scully C, Brooke AE. Images in clinical medicine. Halitosis and sensory loss. (**alendronate osteonecrosis** of the jaw image) N Engl J Med. 2012 Aug 9;367(6):551.
Seeman E, Boonen S, Borgström F, et al. Five years treatment with **strontium ranelate** reduces vertebral and nonvertebral fractures and increases the number and quality of remaining life-years in women over 80 years of age. Bone. 2009 Dec 21. [Epub ahead of print]
Seeman E, Devogelaer J, Lorenc R, et al. **Strontium** ranelate reduces the risk of vertebral fractures in patients with **osteopenia**. J Bone Miner Res 2007 Nov 12.
Seeman E, Vellas B, Benhamou C, et al. **Strontium** ranelate reduces the risk of vertebral and nonvertebral fractures in women eighty years of age and older. J Bone Miner Res. 2006 Jul;21(7):1113-20.
Seifert CF, Wiltrout TR. Calcaneal Bone Mineral Density in Young Adults Prescribed Selective **Serotonin Reuptake Inhibitors**. Clin Ther. 2013 Aug 16.
Seton M, **How soon after hip fracture surgery** should a patient **start bisphosphonates**? *Cleveland Clinic Journal of Medicine* 2010; 77(11):751-755; doi:10.3949/ccjm.77a.10045

Seton M. **Paget disease** of bone: Diagnosis and drug therapy. Cleve Clin J Med. 2013 Jul;80(7):452-462.
Seton M. **Breaking from bisphosphonates**. Arthritis Rheumatol. 2016 Oct 27.
Shahinian VB, Kuo Y-F, Freeman JL, Goodwin JS. Risk of fracture after **androgen deprivation for prostate cancer**. N Engl J Med 2005;352:154-64.
Shane E, Burr D, Abrahamsen B, Adler RA, et al. **Atypical subtrochanteric and diaphyseal femoral fractures**: second report of a Task Force of the American Society for Bone and Mineral Research. J Bone Miner Res. 2014 Jan;29(1):1-23. In the absence of a randomized, placebo controlled trial, no definite conclusion can be reached regarding the efficacy of TPTD treatment of patients with AFF. From the low quality evidence available, the recommendations of the ASBMR task force for medical management remain reasonable: discontinuation of BPs, adequate calcium and vitamin D, and consideration of TPTD for those who appear not to heal on conservative therapy.
Sharma A, Chatterjee S, Arbab-Zadeh A, et al. Risk of Serious Atrial Fibrillation and Stroke With Use of Bisphosphonates: Evidence From a Meta-analysis. Chest. 2013 Oct;144(4):1311-22.
Sharma A, Einstein AJ, Vallakati A, et al. Risk of **atrial fibrillation with use of oral and intravenous bisphosphonates**. Am J Cardiol. 2014 Jun 1;113(11):1815-21.
Sharman Moser S, Yu J, Goldshtein I, et al. **Cost and Consequences of Nonadherence** With Oral Bisphosphonate Therapy: Findings From a Real-World Data Analysis. Ann Pharmacother. 2016 Apr;50(4):262-9.
Shepstone L, Lenaghan E, et al. **Screening in the community to reduce fractures** in older women (**SCOOP**): a randomised controlled trial. Lancet 2017; online Dec 15.
Sheu YH, Lanteigne A, Stürmer T, et al. **SSRI use and risk of fractures** among perimenopausal women without mental disorders. Inj Prev. 2015 Jun 25.
Sheu A, Diamond T. **Secondary osteoporosis**. Aust Prescr. 2016 Jun;39(3):85-7.
Shieh A, Han W, Ishii S, et al. Quantifying the Balance Between **Total Bone Formation and Total Bone Resorption**: An **Index** of Net Bone Formation. J Clin Endocrinol Metab. 2016 Jun 23:jc20154262.
Shiek Ahmad B, Hill KD, O'Brien TJ, et al. **Falls and fractures** in patients chronically treated with antiepileptic drugs. Neurology. 2012 Jun 13.
Shin K, Park SH, Park W, et al. Monthly Oral **Ibandronate** Reduces Bone Loss in Korean Women With Rheumatoid Arthritis and Osteopenia Receiving Long-term Glucocorticoids: A 48-week Double-blinded Randomized Placebo-controlled Investigator-initiated Trial. Clin Ther. 2017 Feb 1.
Shumaker SA, Legault C, Rapp SR, et al, for the **WHIMS** Investigators. **Estrogen plus progestin** and the incidence of **dementia** and mild cognitive impairment in postmenopausal women: the Women_s Health Initiative Memory Study: a randomized controlled trial. JAMA 2003;289:2651-2662.
Silva-Fernández L, Rosario MP, Martínez-López JA, et al. **Denosumab** for the treatment of osteoporosis: A systematic literature review. Reumatol Clin. 2012 Sep 1.
Silverman SL, Cummings SR, Watts NB; Consensus Panel of the ASBMR, ISCD, and NOF. Recommendations for the **clinical evaluation** of agents for treatment of osteoporosis: consensus of an expert panel representing the American Society for Bone and Mineral Research (ASBMR), the International Society for Clinical Densitometry (ISCD), and the National Osteoporosis Foundation (NOF). J Bone Miner Res. 2008 Jan;23(1):159-65.
Silverman SL, Christiansen C, Genant HK, et al. Efficacy of **bazedoxifene** in reducing new vertebral fracture risk in postmenopausal women with osteoporosis: results from a 3-year, randomized, placebo-, and active-controlled clinical trial. J Bone Miner Res 2008;23:1923-1934.
Silverman S, Christiansen C. Individualizing osteoporosis therapy. Osteoporos Int. 2012 Jan 5.
Siminoski K, Leslie WD, Frame H, et al. Canadian Association of Radiologists. Recommendations for **bone mineral density** reporting in **Canada**. Can Assoc Radiol J. 2005 Jun;56(3):178-88.
Simunovic N, Devereaux PJ, et al. Effect of **early surgery after hip fracture** on mortality and complications: systematic review and meta-analysis. CMAJ 2010 0: cmaj.092220.
Sing CW, Wong AY, Kiel DP, et al. Association of **Alendronate and Risk of Cardiovascular Events in Patients With Hip Fracture**. J Bone Miner Res. 2018 May 9.
Singer FR, Bone HG 3rd, Hosking DJ, et al. **Paget's Disease** of Bone: An Endocrine Society Clincal Practice Guideline. J Clin Endocrinol Metab. 2014 Dec;99(12):4408-22.
Siris ES, Miller PD, Barrett-Connor E, et al. Identification and fracture outcomes of undiagnosed low bone mineral density in postmenopausal women: results from the National Osteoporosis Risk Assessment (**NORA**). JAMA 2001;286:2815-2822.
Siris ES, Simon JA, Barton IP, et al. Effects of **risedronate** on fracture risk in postmenopausal women with **osteopenia**. Osteoporos Int 2007 Oct 30.
Siu A, Allore H, Brown D, et al. National Institutes of Health Pathways to Prevention Workshop: Research Gaps for Long-Term Drug Therapies for Osteoporotic **Fracture Prevention**. Ann Intern Med. 2019 Apr 23.
Skjødt MK, Frost M, Abrahamsen B. **Side effects of drugs for osteoporosis and metastatic bone disease**. Br J Clin Pharmacol. 2018 Sep 7.
Skversky AL, Kumar J, Abramowitz MK, et al. Association of **Glucocorticoid Use and Low 25-Hydroxyvitamin D Levels**: Results from the National Health and Nutrition Examination Survey (NHANES): 2001-2006. J Clin Endocrinol Metab. 2011 Sep 28.
Slatkovska Lubomira, Alibhai Shabbir M.H., Beyene Joseph, et al. Effect of 12 Months of **Whole-Body Vibration Therapy** on Bone Density and Structure in Postmenopausal Women: A Randomized Trial. Ann Intern Med November 15, 2011 155:668-679.
Smith EE, Fang J, Alibhai SM, et al. Derivation and External Validation of a **Scoring System for Predicting Fracture Risk After Ischemic Stroke** in a Canadian Cohort. JAMA Neurol. 2019 May 13.
Smith MR, Eastham J, Gleason DM, et al. Randomized controlled trial of **zoledronic acid** to prevent bone loss in men receiving **androgen deprivation therapy** for nonmetastatic prostate cancer. J Urol 2003; 169:2008-12.
Smith MR, McGovern FJ, Zietman AL, et al. **Pamidronate** to prevent bone loss during androgen-deprivation therapy for prostate cancer. N Engl J Med 2001;345:948-55.
Smith MR, Lee WC, Brandman J, et al. **Gonadotropin-releasing hormone agonists** and fracture risk: a claims-based cohort study of men with nonmetastatic prostate cancer. J Clin Oncol 2005;23:7897-903.
Smith H, Anderson F, Raphael H, et al. Effect of annual intramuscular **vitamin D** on fracture risk in elderly men and women--a population-based, randomized, double-blind, placebo-controlled trial. Rheumatology (Oxford). 2007 Dec;46(12):1852-7. An **annual i.m. injection of 300 000 IU vitamin D(2)** is not effective in preventing non-vertebral fractures among elderly men and women resident in the general population.
Smith MR, Egerdie B, Hernández Toriz N, et al. **Denosumab HALT** Prostate Cancer Study Group. Denosumab in men receiving androgen-deprivation therapy for prostate cancer. N Engl J Med. 2009 Aug 20;361(8):745-55. Epub 2009 Aug 11.
Smith MR, Fallon MA, Lee H, Finkelstein JS. **Raloxifene** to **prevent gonadotropin-releasing hormone agonist**-induced bone loss in men with prostate cancer: a randomized controlled trial. J Clin Endocrinol Metab 2004;89:3841-6.
Smith MR, Morton RA, Barnette KG, et al. **Toremifene** to reduce fracture risk in men receiving **androgen deprivation therapy** for prostate cancer. J Urol 2010;184:1316-21.
Smith Matthew R.,. Zietman Anthony L, Finkelstein Joel S., et al. Case 16-2011 — A 67-Year-Old Man with Recurrent **Prostate Cancer**. N Engl J Med 2011; 364:2044-2051.
Smith MR, Saad F, Coleman R, et al. **Denosumab and bone-metastasis**-free survival in men with castration-resistant **prostate** cancer: results of a phase 3, randomised, placebo-controlled trial. Lancet 2011; published online Nov 16. DOI:10.1016/S0140-6736(11)61226-9.
Smith MR, Halabi S, Ryan CJ, et al: Randomized controlled trial of early **zoledronic** acid in men with castration-sensitive **prostate cancer** and bone metastases: Results of CALGB 90202 (Alliance). J Clin Oncol 32:1143-1150, 2014.
SOGC Society of Obstetricians and Gynaecologists of **Canada**. **Osteoporosis in menopause**. J Obstet Gynaecol Can 2014;36(9 eSuppl C):S1-S15. http://sogc.org/wp-content/uploads/2014/09/JOGC-Sept2014-CPG-312_Eng_Online-Complete.pdf (accessed September 30, 2014).
Sohn W, Lee E, et al. An open-label study in healthy men to evaluate the **risk of seminal fluid transmission of denosumab** to pregnant partners. Br J Clin Pharmacol. 2015 Oct 8.
Solomon DH, Iversen MD, Avorn J et al. Osteoporosis **Telephonic Intervention** to Improve Medication Regimen Adherence: A Large, Pragmatic, Randomized Controlled Trial.

Arch Intern Med. 2012 Feb 27.
Solomon DH, Kay J, Duryea J, et al. Effects of **Teriparatide on Joint Erosions** in Rheumatoid Arthritis: A Randomized Controlled Trial. Arthritis Rheumatol. 2017 May 23.
Sonneville KR, Gordon CM, Kocher MS, et al. **Vitamin D**, Calcium, & Dairy Intakes and **Stress Fractures** Among Female Adolescents. Arch Pediatr Adolesc Med. 2012 Mar 5.
Sontag A, Krege JH. **First fractures** among postmenopausal women with osteoporosis. (**MORE**) J Bone Miner Metab. 2010 Jan 7. (Spine & radius fractures)
Sophocleous A, Robertson R, et al. **Heavy Cannabis** Use Is Associated With **Low Bone Mineral Density** and an Increased Risk of Fractures. Am J Med. 2016 Sep 2.
Spinelli MA, Glidden DV, Anderson PL, et al. Impact of Estimated Pre-Exposure Prophylaxis (**PrEP) Adherence Patterns on Bone Mineral Density** in a Large PrEP Demonstration Project. AIDS Res Hum Retroviruses. 2019 Jun 19.
Sri-On J, Tirrell GP, Kamsom A, et al. A High-yield Fall Risk and Adverse Events Screening Questions From the Stopping Elderly Accidents, Death, and Injuries (**STEADI)** Guideline for Older Emergency Department Fall Patients. Acad Emerg Med. 2018 Mar 25.
Staples MP, Kallmes DF, Comstock BA, Jarvik JG, Osborne RH, Heagerty PJ, et al. Effectiveness of **vertebroplasty** using individual patient data from two randomised placebo controlled trials: meta-analysis. BMJ 2011;343:d3952.
Stiles VH, Metcalf BS, Knapp KM, et al. A small amount of precisely measured high-intensity habitual physical activity predicts bone health in pre- and post-menopausal women in UK Biobank. Inter J Epidemiol. 2017,1-10.
Stopeck AT, Lipton A, Body JJ, et al. **Denosumab Compared With Zoledronic** Acid for the Treatment of **Bone Metastases** in Patients With Advanced **Breast Cancer**: A Randomized, Double-Blind Study. J Clin Oncol. 2010 Nov 8.
Stoch SA, Saag KG, Greenwald M, et al. Once-weekly oral alendronate 70 mg in patients with **glucocorticoid-induced** bone loss: a 12-month randomized, placebo-controlled clinical trial. J Rheumatol. 2009 Aug;36(8):1705-14.
Stoch SA, Zajic S, Stone JA, et al. **Odanacatib**, a Selective Cathepsin K inhibitor to Treat Osteoporosis: Safety, Tolerability, Pharmacokinetics and Pharmacodynamics – Results from Single Oral Dose Studies in Healthy Volunteers. Br J Clin Pharmacol. 2012 Sep 26.
Stone JA, McCrea J, Witter R, et al. Clinical and translational pharmacology of the **cathepsin K inhibitor odanacatib** studied for osteoporosis. Br J Clin Pharmacol. 2019 Jan 20.
Straube S, Derry S, Moore RA, et al. **Vitamin D** for the treatment of **chronic painful conditions** in adults. Cochrane Database Syst Rev. 2010 Jan 20;(1):CD007771.
Strom T., Thamsborg G., Steiniche T., et al. Effect of intermittent cyclical **etidronate** therapy on bone mass and fracture rate in women with postmenopausal osteoporosis. N Engl J Med 1990; 322:1265-71.
Sugerman DT. JAMA **patient page. Osteoporosis**. JAMA. 2014 Jan 1;311(1):104
Sullivan SD, Lehman A, Nathan NK, et al. Age of **menopause and fracture risk** in postmenopausal women randomized to calcium + vitamin D, hormone therapy, or the combination: results from the Women's Health Initiative Clinical Trials. Menopause. 2016 Oct 31.
Sultan AA, Whittle R, Muller S, et al. **Risk of fragility fracture among patients with gout and the effect of urate-lowering therapy**. CMAJ. 2018 May 14;190(19):E581-E587.
Svanström H, Pasternak B, Hviid A. Use of **strontium** ranelate and **risk of acute coronary syndrome**: cohort study. Ann Rheum Dis. 2014 Jun;73(6):1037-43.
Svejme O, Ahlborg H, et al. **Early menopause** and risk of osteoporosis, fracture and mortality: a 34-year prospective observational study in 390 women. BJOG. 2012 Apr 25.
Symonds C, Kline G. **Warning of an increased risk of vertebral fracture after stopping denosumab**. CMAJ. 2018 Apr 23;190(16):E485-E486.
Tabacco G, Bilezikian JP. **Osteoanabolic and Dual Action Drugs**. Br J Clin Pharmacol. 2018 Sep 15.
Tadrous M, Wong L, Mamdani MM, et al. Comparative **gastrointestinal safety of bisphosphonates** in primary osteoporosis: network meta-analysis. Osteoporos Int. 2013Nov28.
Takeuchi T, Tanaka Y, Soen S, et al. Effects of the **anti-RANKL antibody denosumab** on joint structural damage in patients with rheumatoid arthritis treated with conventional synthetic disease-modifying antirheumatic drugs (DESIRABLE study): a randomised, double-blind, placebo-controlled phase 3 trial. Ann Rheum Dis. 2019 Jul;78(7):899-907.
Tan A, Goodman K, Walker A, et al. Long-Term Randomized Trial of **Intensive Versus Symptomatic Management** in **Paget's Disease** of Bone: The **PRISM-EZ** Study. J Bone Miner Res. 2017 Feb 8.
Targownik LE, Lix LM, Leung S, Leslie WD. **Proton Pump Inhibitor** Use Is Not Associated With Osteoporosis or Accelerated Bone Mineral Density Loss. Gastroenterology. 2009 Nov 18.
Targownik LE, Lix LM, Metge CJ, et al. Use of **proton pump inhibitors** and risk of osteoporosis-related fractures. CMAJ. 2008 Aug 12;179(4):319-26.
Targownik LE, Leslie WD, Davison KS, et al. CaMos Research Group. The relationship between **proton pump inhibitor** use and longitudinal change in bone mineral density: a population-based from the Canadian Multicentre Osteoporosis Study (CaMos). Am J Gastroenterol. 2012 Sep;107(9):1361-9.
Tadrous M, Wong L, Mamdani MM, et al. Comparative **gastrointestinal safety of bisphosphonates** in primary osteoporosis: network meta-analysis. Osteoporos Int. 2013Nov 28
Tai V, Leung W, Grey A. Reid IR, Bolland MJ. **Calcium intake and bone mineral density**: systematic review and meta-analysis. BMJ 2015;351:h4183.
Taipale H, Rysä J, Hukkanen J, et al. **Long-term thiazide use and risk** of low-energy fractures among persons with Alzheimer's disease-nested case-control study. Osteoporos Int. 2019 Apr 16
Taxel P, Dowsett R, Richter L, Fall P, Klepinger A, Albertsen P. Risedronate prevents early bone loss and increased bone turnover in the first 6 months of **luteinizing hormone-releasing hormone-agonist therapy** for prostate cancer. BJU Int. 2010 Apr 30.
Tee Shang-Ian; Yosipovitch Gil; Chan Yuin Chew; et al. **Prevention of Glucocorticoid-Induced Osteoporosis in Immunobullous Diseases** With **Alendronate**: A Randomized, Double-blind, Placebo-Controlled Study. Arch Dermatol. 2011;0(2011):archdermatol.2011.354.
Teng K. Premenopausal osteoporosis, an overlooked **consequence of anorexia nervosa**. Cleve Clin J Med. 2011 Jan;78(1):50-8.
Tejero García S, Giráldez Sánchez MA, et al. Bone health, **daily physical activity**, and exercise tolerance in patients with **cystic fibrosis**. Chest. 2011 Aug;140(2):475-81.
Terpos E, Sezer O, Croucher PI, et al. **European** Myeloma Network. The use of **bisphosphonates in multiple myeloma**: recommendations of an expert panel on behalf of the European Myeloma Network. Ann Oncol. 2009 Aug;20(8):1303-17. Epub 2009 May 22.
Thacher TD, Bommersbach TJ, Pettifor JM, et al. Comparison of **Limestone and Ground Fish** for Treatment of Nutritional Rickets in Children in Nigeria. J Pediatr. 2015 Jul;167(1):148-154.e1.
Thomas D, Henshaw R, Skubitz K, et al. **Denosumab** in patients with **giant-cell tumour** of bone: an open-label, phase 2 study. Lancet Oncol. 2010 Mar;11(3):275-80.
Thomas T, Horlait S, et al. Oral **bisphosphonates** reduce the risk of clinical fractures in **glucocorticoid-induced osteoporosis** in clinical practice. Osteoporos Int. 2012 Jun 27.
Tirosh A, de Souza RJ, Sacks F, et al. **Sex Differences** in the Effects of **Weight Loss** Diets on Bone Mineral Density and Body Composition: **POUNDS LOST** Trial. J Clin Endocrinol Metab. 2015 Mar 31
Toh Sengwee, Hernández-Díaz Sonia, Logan Roger, Et al. Coronary Heart Disease in Postmenopausal Recipients of Estrogen Plus Progestin Therapy: Does the Increased Risk Ever Disappear?: A Randomized Trial. (**WHI**) Ann Intern Med February 16, 2010.
Trajanoska K, Morris JA, Oei L, et al; GEFOS/GENOMOS consortium and the 23andMe research team. Assessment of the **genetic and clinical determinants of fracture risk**: genome wide association and mendelian randomisation study. BMJ. 2018 Aug 29;362:k3225.
Tsai JN, Lee H, David NL, et al. Combination **denosumab and high dose teriparatide** for postmenopausal osteoporosis (DATA-HD): a randomised, controlled phase 4 trial. Lancet Diabetes Endocrinol. 2019 Aug 22.
Tsai JN, Uihlein AV, Lee H, et al. **Teriparatide and denosumab**, alone or combined, in women with postmenopausal osteoporosis: **DATA** study randomised trial. Lancet 2013; online May 15.

Tsai JN, Uihlein AV, Burnett-Bowie SM, et al. Effects of **Two Years of Teriparatide, Denosumab, or Both** on Bone Microarchitecture and Strength (**DATA**-HRpQCT study). J Clin Endocrinol Metab. 2016 May;101(5):2023-30

Tseng VL, Yu F, Lum F, Coleman AL. Risk of fractures following **cataract surgery** in Medicare beneficiaries. JAMA. 2012 Aug 1;308(5):493-501.

Tsourdi E, Rachner TD, Gruber M, Hamann C, Ziemssen T, Hofbauer LC. **Seizures Associated with Zoledronic** Acid for Osteoporosis. J Clin Endocrinol Metab. 2011 Apr 20.

USPSTF- U.S. Preventive Services Task Force. **Hormone therapy** for the prevention of chronic conditions in postmenopausal women: recommendations from the U.S. Preventive Services Task Force. Ann Intern Med. 2005 May 17;142(10):855-60.

USPSTF- U.S. Preventive Services Task Force. **Postmenopausal hormone replacement therapy** for primary prevention of chronic conditions: recommendations and rationale. Ann Intern Med. 2002 Nov 19;137(10):834-9.

USPSTF- U.S. Preventive Services Task Force. **Screening** for osteoporosis in postmenopausal women: recommendations & rationale. Ann Intern Med.2002 Sep 17;137(6):526-8.

USPSTF- U.S. Preventive Services Task Force. **Screening** for Osteoporosis: U.S. Preventive Services Task Force Recommendation Statement. *Ann Intern Med* E-307 Jan 17, 11.
Screen all women aged 65 and older; screen women younger than 65 if their 10-year fracture risk is similar to or greater than that of a 65-year-old white woman without additional risk factors — roughly 9%. (The article recommends using the WHO's FRAX tool to estimate fracture risk.) The USPSTF expanded its review to include men, and concludes that there is not enough evidence to determine whether screening is beneficial or harmful

USPSTF- U.S. Preventive Services Task Force (USPSTF). **Screening** for osteoporosis: U.S. preventive services task force **recommendation statement**. Ann Intern Med. 2011 Mar 1;154(5):356-64.

USPSTF: US Preventive Services Task Force. **Vitamin D, calcium, or combined supplementation for the primary prevention of fractures** in communitydwelling adults: US Preventive Services Task Force recommendation statement [online April 17, 2018].JAMA. doi:10.1001/jama.2018.3185

USPSTF: Kahwati LC, Weber RP, Pan H, et al. **Vitamin D, calcium, or combined supplementation for the primary prevention of fractures** in communitydwelling adults: evidence report and systematic review for the US Preventive Services Task Force [online April 17, 2018].JAMA. doi:10.1001 /jama.2017.21640

USPSTF: US Preventive Services Task Force. **Interventions to prevent falls in community-dwelling older adults**: US Preventive Services Task Force recommendation statement [online April 17, 201].JAMA. doi: 10.1001/jama.2018.3097

USPSTF: Guirguis-Blake JM, Michael YL, Perdue LA, et al. **Interventions to prevent falls in communitydwelling older adults: updated evidence report** and systematic review for the US Preventive Services Task Force [online April 17, 2018].JAMA. doi:10.1001/jama.2017.21962

USPSTF: US Preventive Services Task Force, Curry SJ, Krist AH, Owens DK, et al. **Screening for Osteoporosis to Prevent Fractures**: US Preventive Services Task Force Recommendation Statement. JAMA. 2018 Jun 26;319(24):2521-2531.

USPSTF: Viswanathan M, Reddy S, Berkman N, et al. Screening to Prevent Osteoporotic Fractures: Updated Evidence Report and Systematic Review for the US Preventive Services Task Force. JAMA. 2018 Jun 26;319(24):2532-2551.

Van Poznak CH, Temin S, Yee GC, et al. American Society of Clinical Oncology (**ASCO**) Executive Summary of the Clinical Practice Guideline Update on the Role of **Bone-Modifying Agents in Metastatic Breast Cancer**. J Clin Oncol. 2011 Feb 22.

Van Poznak C, Somerfield MR, Barlow WE, et al. Role of **Bone-Modifying Agents in Metastatic Breast Cancer**: An American Society of Clinical Oncology-Cancer Care Ontario Focused Guideline Update. J Clin Oncol. 2017 Dec 10;35(35):3978-3986.

Van Staa TP, Leufkens HG, Abenhaim L, Zhang B, Cooper C. Use of **oral corticosteroids** and risk of fractures. J Bone Miner Res. 2000 Jun;15(6):993-1000.

Vandenbroucke A, Luyten FP, Flamaing J, Gielen E. Pharmacological **treatment of osteoporosis in the oldest old**. Clin Interv Aging. 2017 Jul 6;12:1065-1077.

Varenna M, Zucchi F, Failoni S, et al. Intravenous **neridronate** in the treatment of **acute painful knee osteoarthritis**: a randomized controlled study. Rheumatology (Oxford). 2015 May 20.

Vatanparast H, Dolega-Cieszkowski JH, Whiting SJ. Many adult Canadians are not meeting current **calcium recommendations from food and supplement** intake. Appl Physiol Nutr Metab. 2009 Apr;34(2):191-6.

Vestergaard P, Rejnmark L, Mosekilde L. High-dose treatment with **vitamin A analogues** and risk of fractures. Arch Dermatol. 2010 May;146(5):478-82. Risk not ↑.

Vimaleswaran KS, Cavadino A, Berry DJ, et al. Association of vitamin D status with **arterial blood pressure and hypertension risk**: A Mendelian randomisation study. *Lancet Diabetes Endocrinol* 2014.

Vinogradova Y, Coupland C, Hippisley-Cox J. Exposure to **bisphosphonates and risk of gastrointestinal cancers**: series of nested case-control studies with QResearch and CPRD data. BMJ. 2013 Jan 16;346:f114.

Virgini VS, Rodondi N, Cawton PM, et al; Osteoporotic Fractures in Men (**MrOS**) Research Group. **Subclinical Thyroid Dysfunction** and Frailty among Older Men. J Clin Endocrinol Metab. 2015 Oct 23:jc20153191.

Viscoli CM et al. **Pioglitazone** and risk for bone fracture: Safety data from a randomized clinical trial. J Clin Endocrinol Metab 2017 Mar; 102:914.

Viswanathan M, Reddy S, Berkman N, et al. Screening to **Prevent Osteoporotic Fractures**: Updated Evidence Report and Systematic Review for the US Preventive Services Task Force. JAMA. 2018 Jun 26;319(24):2532-2551.

Vlachopoulos D, et al. Longitudinal Adaptations of **Bone** Mass, Geometry and Metabolism in **Adolescent Male Athletes**. The **PRO-BONE** Study. J Bone Miner Res. 2017 Jul 7.

Waljee AK, et al. Short term use of **oral corticosteroids** and related harms among adults in the United States: population based cohort study. BMJ. 2017 Apr 12;357:j1415.

Wang CC, Wu CH, Farley JF. Patterns of **Pharmacological Treatment for Osteoporosis** Among Patients Qualified for Pharmacotherapy According to the

Wang, Lu, Manson, JoAnn E. Song, Yiqing et al. Systematic Review: **Vitamin D and Calcium** Supplementation in Prevention of **Cardiovascular Events**. Ann Intern Med March 2, 2010 152:315-323.

Wang Y, Wactawski-Wende J, et al. **Gene-hormone therapy interaction** and fracture risk in postmenopausal women. J Clin Endocrinol Metab. 2017 Mar 6.

Ward L. M., Rauch F., Whyteet M. P. al. Alendronate for the Treatment of **Pediatric Osteogenesis Imperfecta**: A Randomized Placebo-Controlled Study. J. Clin. Endocrinol. Metab. published November 24, 2010, doi:10.1210/jc.2010-0636. (not reduce fractures)

Waterbrook AL, Adhikari S, Stolz U, Adrion C. The accuracy of **point-of-care ultrasound** to diagnose long bone fractures in the ED. Am J Emerg Med. 2013 Sep;31(9):1352-6. Watts NB, Chines A, Olszynski WP, McKeever CD, McClung MR, Zhou X, Grauer A. Fracture risk remains reduced **one year after discontinuation** of risedronate. Osteoporos Int. 2008 Mar;19(3):365-72. Epub 2007 Oct 16.

Watts NB, Grbic JT, Binkley N, et al. **Invasive Oral Procedures and Events** in Women With Postmenopausal Osteoporosis **Treated With Denosumab for up to 10 Years**. J Clin Endocrinol Metab. 2019 Feb 13.

Watts NB, Harris ST, Genant H, et al. Intermittent cyclical **etidronate** treatment of postmenopausal osteoporosis. N Engl J Med 1990; 323:73-79.

Watts NB, Diab DL. **Long-term use** of bisphosphosphonates in osteoporosis. J Clin Endocrinol Metab 2010 February 19 (Epub ahead of print).
Bisphosphonates have demonstrated antifracture efficacy in randomized, placebo-controlled trials of 3 and 4 yr duration and have been widely used since the initial release of alendronate in 1995. For zoledronic acid and risedronate, an early effect (fractures reduced within 6-12 months of starting therapy) has been shown. A sustained effect for risedronate has been shown through 5 yr and suggested through 7 yr. Ten-year data with alendronate and 8 yr data with risedronate indicated good tolerability and safety; it is unlikely that longer-term studies will be done.

Watts NB, Bilezikian JP, Camacho PM, et al. **AACE** Osteoporosis Task Force. American Association of Clinical Endocrinologists medical guidelines for clinical practice for the **diagnosis and treatment of postmenopausal osteoporosis**. Endocr Pract 2010 Nov-Dec;16(Suppl 3):1-37.

Watts NB, Adler RA, Bilezikian JP, et al. **Osteoporosis in men**: an **Endocrine Society** clinical practice guideline. J Clin Endocrinol Metab. 2012 Jun;97(6):1802-22.

Watts NB, Bilezikian JP, Usiskin K, et al. Effects of **canagliflozin on fracture risk** in patients with type 2 diabetes mellitus. J Clin Endocrinol Metab 2016;101:157-66.

Watts NB, Manson JE. Osteoporosis and Fracture Risk Evaluation and Management: **Shared Decision Making** in Clinical Practice. JAMA. 2016 Dec 12.
Weaver CM, Alexander DD, Boushey CJ, et al. **Calcium plus vitamin D supplementation and risk of fractures**: an updated meta-analysis from the National Osteoporosis Foundation. Osteoporos Int. 2016;27:367-376.
Weinstein Robert S. **Glucocorticoid-Induced Bone Disease**. N Engl J Med 2011; 365:62-70.
Welles CC, Schafer AL, Vittinghoff E, et al. **Urine Calcium Excretion**, Cardiovascular Events, and Mortality in Outpatients With Stable Coronary Artery Disease (from the Heart and Soul Study). Am J Cardiol. 2012 Sep 10.
Welles CC, Whooley MA, Karumanchi SA, et al. Vitamin d deficiency and **cardiovascular events in patients with coronary heart disease**: data from the heart and soul study. Am J Epidemiol. 2014 Jun 1;179(11):1279-87.
Wells G, Cranney A, Peterson J, et al. **Risedronate** for the primary and secondary prevention of osteoporotic fractures in postmenopausal women. Cochrane Database Syst Rev. 2008 Jan 23;(1):CD004523.
Wells GA, Cranney A, Peterson J, et al. **Etidronate** for the primary and secondary prevention of osteoporotic fractures in postmenopausal women. Cochrane Database Syst Rev. 2008 Jan 23;(1):CD003376.
Wells GA, Cranney A, Peterson J et al. **Alendronate** for the primary and secondary prevention of osteoporotic fractures in postmenopausal women. Cochrane Database Syst Rev. 2008 Jan 23;(1):CD001155.
Wells GA, Cranney A, Boucher M, et al. **Bisphosphonates** for the primary and secondary prevention of osteoporotic fractures in postmenopausal women: a meta-analysis [Technology report no 69]. Ottawa: Canadian Agency for Drugs and Technologies in Health; 2006.
West H. **Denosumab** for prevention of skeletal-related events in patients with bone metastases from solid tumors: incremental benefit, debatable value. J Clin Oncol. 2011 Mar 20;29(9):1095-8.
Wimalawansa SJ, Grimes JP, Wilson AC, et al. Transdermal **nitroglycerin therapy may not prevent early postmenopausal bone loss**. J Clin Endocrinol Metab. 2009 Sep;94(9):3356-64.
Winser SJ, Tsang WW, Krishnamurthy K, et al. Does **Tai Chi improve balance** and **reduce falls** incidence in neurological disorders? A systematic review and meta-analysis. Clin Rehabil. 2018 May 1:269215518773442.
Winser SJ, Tsang WW, Krishnamurthy K, Kannan P. Does **Tai Chi improve balance and reduce falls incidence in neurological disorders?** A systematic review and meta-analysis. Clin Rehabil. 2018 May 1:269215518773442.
Winzenberg TM, Powell S, Shaw KA, Jones G. **Vitamin D** supplementation for improving bone mineral density in **children**. Cochrane Database of Systematic Reviews 2010, Issue 10. Art. No.: CD006944. DOI: 10.1002/14651858.CD006944.pub2.
These results do not support vitamin D supplementation to improve bone density in healthy children with normal vitamin Dlevels, but suggest that supplementation of deficient children may be clinically useful.
Whitaker M, Guo J, Kehoe T, Benson G. **Bisphosphonates for Osteoporosis – Where Do We Go from Here**? N Engl J Med. 2012 May 9.
Wilson LM, et al. **Benefits and Harms of Osteoporosis Medications in Patients With Chronic Kidney Disease**: A Systematic Review and Meta-analysis. Ann Intern Med. 2017 Apr 11.
Wirth M, Tammela T, Cicalese V, et al. Prevention of Bone Metastases in Patients with High-risk Nonmetastatic **Prostate Cancer** Treated with **Zoledronic** Acid: Efficacy and Safety Results of the Zometa European Study (**ZEUS**). Eur Urol. 2014 Feb 20.
Wren TA, Shepherd JA, Kalkwarf HJ, et al. **Racial Disparity** in Fracture Risk between White and Nonwhite Children in the United States. J Pediatr. 2012 Sep 10.
Wren TA, Kalkwarf HJ, Zemel BS, Lappe JM, Oberfield S, Shepherd JA, et al. Longitudinal tracking of **DXA bone measures over 6 years in children** and adolescents: persistence of low bone mass to maturity. J Pediatr 2014 (in press).
Wren TA, Kalkwarf HJ, Zemel BS, et al; Bone Mineral Density in Childhood Study Group. Longitudinal **Tracking of Dual-Energy X-ray Absorptiometry** Bone Measures Over 6 Years in **Children and Adolescents**: Persistence of Low Bone Mass to Maturity. J Pediatr. 2014 Jan 30.
Wright E, Schofield PT, Seed P, Molokhia M. **Bisphosphonates and Risk of Upper Gastrointestinal Cancer** - A Case Control Study Using the General Practice Research Database (GPRD). PLoS One. 2012;7(10):e47616.
Wu Q, Liu B, Tonmoy S. **Depression and risk of fracture** and bone loss: an updated meta-analysis of prospective studies. Osteoporos Int. 2018 Mar 12.
Wysowski DK. Reports of **esophageal cancer** with oral bisphosphonate use. N Engl J Med. 2009 Jan 1;360(1):89-90.
Yang L, Hu X, Zhang H, et al. Association of **bone mineral density with a first-degree family history of diabetes** in normoglycemic postmenopausal women. Menopause. 2019 Aug 19.
Yang S, Leslie WD, Morin SN, et al. **Antiresorptive Therapy and Newly-Diagnosed Diabetes in Women**: A Historical Cohort Study. Diabetes Obes Metab. 2016 Apr 21.
Yeh JH, Chen HJ, Chen YK, et al. Increased risk of osteoporosis in patients with **myasthenia gravis**: A population-based cohort study. Neurology. 2014 Sep 16;83(12):1075-9.
Yeh MW, Zhou H, Adams AL, et al. The Relationship of **Parathyroidectomy** and Bisphosphonates With Fracture Risk in Primary **Hyperparathyroidism**: An Observational Study. Ann Intern Med. 2016 Apr 5
Yu EW, Bauer SR, Bain PA, et al. **Proton pump inhibitors** and risk of fractures: a meta-analysis of 11 international studies. Am J Med. 2011 Jun;124(6):519-26.
Yu EW, Kim SC, Sturgeon DJ, et al. **Fracture risk after Roux-en-Y gastric bypass vs adjustable gastric banding among Medicare beneficiares** [online May 15, 2019]. JAMA Surg. doi:10.1001/jamasurg.2019.1157
Yu EW, Wewalka M, Ding SA, et al. Effects of Gastric Bypass and **Gastric Banding on Bone Remodeling** in Obese Patients with Type 2 Diabetes. J Clin Endocrinol Metab. 2015 Nov 24:jc20153437.
Zebic L, Patel V. P**reventing medication-related osteonecrosis of the jaw.** BMJ. 2019 May 8;365:l1733.
Zhao R, Zhang M, Zhang Qi. The Effectiveness of **Combined Exercise Interventions** for Preventing Postmenopausal Bone Loss: A Systematic Review and Meta-Analysis. J Orthop Sports Phys Ther. 2017;47(4):214-251.
Zhao JG, Zeng XT, Wang J, et al. Association Between **Calcium or Vitamin D** Supplementation and Fracture Incidence in Community-Dwelling Older Adults: A Systematic Review and Meta-analysis. JAMA. 2017 Dec 26;318(24):2466-2482.
Zhu K, Devine A, Lewis JR, et al. "**Timed Up and Go**" (TUG) test and bone mineral density measurement for fracture prediction. Arch Intern Med. 2011;171(18):1655-1661.
Zhu L, Jiang X, Sun Y, Shu W. Effect of **hormone therapy** on the risk of bone fractures: a systematic review and meta-analysis of randomized controlled trials. Menopause. 2015 Oct 27.

Web Links:

Calculating Bone Mineral Densitometry, BMD fracture risk http://www.halls.md/bone-mineral-densitometry/bmd.htm
National Osteoporosis Foundation (NOF) http://www.nof.org/
Osteoporosis Canada – www.osteoporosis.ca
QFractureScore http://www.qfracture.org/
Simple Calculated Osteoporosis Risk Estimation (SCORE) tool http://osteoed.org/tools.php (sensitivity 91%, specificity 40%)[BMD]

[i] Jackson RD, LaCroix AZ, Gass M, et al. Calcium plus vitamin D supplementation and the risk of fractures. N Engl J Med 2006;354:669-83. (**WHI**)
Manson JE, Allison MA, Carr JJ, et al. for the Women's Health Initiative and Women's Health Initiative-Coronary Artery Calcium Study Investigators. Calcium/vitamin D supplementation and coronary artery calcification in the Women's Health Initiative. Menopause. 2010 Jun 14.
Warensjö Eva, Byberg Liisa, Melhus Håkan, et al. **Dietary calcium intake** and risk of fracture and osteoporosis: prospective longitudinal cohort study. BMJ 2011;342:doi:10.1136/bmj.d1473 (Published 24 May 2011)
Xiao Q, Murphy RA, Houston DK, Harris TB, et al. Dietary and supplemental calcium intake and cardiovascular disease mortality. (NIH-AARP) JAMA Intern Med 2013.
Michaëlsson K, Melhus H, Warensjö Lemming E, et al. Long term calcium intake and rates of all cause and cardiovascular mortality: community based prospective longitudinal cohort study. BMJ. 2013 Feb 12;346:f228.

PEDIATRIC PAIN: Extras, Links & References

◆**AMETOP**: **tetracaine** (amethocaine) **4% Gel** : Adults (including geriatrics) & children over 1 month of age: **Apply** contents of the tube to the skin starting from the centre of the area to be anesthetized & cover with an occlusive dressing. The contents expellable from 1 tube (approximately 1 g) will cover & anesthetize an area of up to 30cm^2 (6×5 cm {~ 3/4 area of a credit card}). Smaller areas of anesthetized skin may be adequate in infants & small children. Adequate anesthesia can usually be achieved for venepuncture following a 30-minute application time, & for venous cannulation following a 45-minute application time; after which the gel should be removed with a gauze swab & the site prepared with an antiseptic wipe in the normal manner. It is not necessary to apply tetracaine gel for longer than the above times & anesthesia is maintained for 4 to 6 hrs in most patients after a single application. [Clinical Trial in progress: Ametop vs Maxilene: http://www.druglib.com/trial/02/NCT00353002.html]

◆ **EMLA (lidocaine and prilocaine)** - for intact skin, requires occlusion, needs to be applied for at least one hour **Dose** — To attain adequate anesthesia, 1 to 2 g of EMLA cream should be applied per 10 sq cm (approximate size of a Canadian "toonie") of skin and covered with an occlusive dressing for 45 to 60 minutes. The maximum application areas recommended for children are Less than 10 kg —100 sq cm {~ 2.5x area of a credit card}; 10 to 20 kg — 600 sq cm; Greater than 20 kg — 2000 sq cm; causes vasoconstriction & ? seizures.

See www.usask.ca/pediatrics/services/pain for information for parents on children's pain

Health Canada Advisory, March 2009: Caution regarding serious adverse events, including fatalities, with excessive application of topical anesthetics in adults & peds!

◆ **acetaminophen use with vaccination:** may ↓ immunogenicity ∴ avoid if possible.
◆ **Benzocaine** –in NG tube placement controversial[10] Causes methemoglobinemia!!! AVOID!
◆ **Lidocaine iontophoresis** {Numby Stuff}: mild electric current penetrates skin more quickly; effective in 10-20min.[43] EMLA similar or slightly better.[44,45] (Tingle may be bothersome.)
◆ **TAC** tetracaine 0.5% / epinephrine 0.05% / cocaine ≤ 11.8%; AE: seizures, arrhythmias, fatal; requires narcotic storage (LET preferred)
◆**Cancer Pain:** Reference [46]
◆**Urethral Catheterization**: lidocaine gel 2 min prior to insertion while setting up then use as the lubricant as well (video: http://www.uihealthcare.com/topics/medicaldepartments/urology/catheterization/index.html)
◆**Acetaminophen vs ibuprofen**: http://www.cps.ca/English/statements/DT/dt98-01.htm For fever:[47]
◆ **SHR Peds Pain Links**: http://www.usask.ca/pediatrics/services/pain/
◆ **CADTH.** Short-Acting Agents for Procedural Sedation and Analgesia in Canadian Emerg.: A Review of Clinical Outcomes and Economic Evaluation http://cadth.ca/media/pdf/O0428_Short-Acting-Procedural-Sedation_to_e.pdf

References {RxFiles Pediatric Pain Chart: Treatment Considerations, Q&As}

[1] Anand KJ, Hickey PR. Pain and its effects in the human neonate and fetus. N Engl J Med. 1987 Nov 19;317(21):1321-9. {Also: Finley, G.A., Franck, L.S., Grunau, R.E., & von Baeyer, C.L. (2005). Why children's pain matters. International Association for the Study of Pain. *Pain: Clinical Updates,* XIII(4), 1-6. Online (PDF) available at http://www.iasp-pain.org/AM/Template.cfm?Section=Resources1&Template=/CM/ContentDisplay.cfm&ContentID=2265 ; Razzaq Q. The underuse of analgesia and sedation in pediatric emergency medicine. Ann Saudi Med. 2006 Sep-Oct;26(5):375-81.}
[2] Taylor EM, Boyer K, Campbell FA. Pain in hospitalized children: A prospective cross-sectional survey of pain prevalence, intensity, assessment and management in a Canadian pediatric teaching hospital. Pain Res Manag. 2008 Jan-Feb;13(1):25-32.}
[3] McHale PM, LoVecchio F. Narcotic analgesia in the acute abdomen--a review of prospective trials. Eur J Emerg Med. 2001 Jun;8(2):131-6.
[4] Ann Emerg Med. 2007 Oct;50(4):371-8. Epub 2007 Jun 27.Efficacy and impact of intravenous morphine before surgical consultation in children with right lower quadrant pain suggestive of appendicitis: a randomized controlled trial. Bailey B, Bergeron S, Gravel J, Bussières JF, Bensoussan A.
[5] Thomas SH, Silen W. Br J Surg 2003;90(1):5-9.& J Fam Pract. 2003;52(6):435-6. Effect on diagnostic efficiency of analgesia for undifferentiated abdominal pain.
[6] Zempsky WT, Cravero JP. Relief of pain and anxiety in pediatric patients in emergency medical systems. Pediatrics. 2004 Nov;114(5):1348-56.
[7] Dlugosz CK, Chater RW, Engle JP. Appropriate use of nonprescription analgesics in pediatric patients. J Pediatr Health Care. 2006;20(5):316-25; quiz 326-8.
[8] Drendel AL, Brousseau DC, Gorelick MH. Pain assessment for pediatric patients in the emergency department. Pediatrics. 2006 May;117(5):1511-8.
[9] von Baeyer CL. Children's self-reports of pain intensity: scale selection, limitations and interpretation. *Pain Research and Management 2006*;11(3):157-62.
[10] Hicks CL, von Baeyer CL, Spafford PA, van Korlaar I, Goodenough B. The **Faces Pain Scale-Revised**: toward a common metric in pediatric pain measurement. *Pain* 2001;93(2):173-83 Available online at: http://www.iasp-pain.org/FPSR See thumbnail of scale at lower right of page.
[11] Merkel SI, Voepel-Lewis T, Shayevitz JR, Malviya S. The FLACC: a behavioral scale for scoring postoperative pain in young children. Pediatr Nurs. 1997 May-Jun;23(3):293-7. Accessible online: http://www.childcancerpain.org/content.cfm?content=assess08
[12] Stinson JN, Kavanagh T, Yamada J, Gill N, Stevens B. Systematic review of the psychometric properties, interpretability and feasibility of self-report pain intensity measures for use in clinical trials in children and adolescents. Pain 2006;125(1-2):143-57.
[13] von Baeyer CL, Spagrud LJ. Systematic review of observational (behavioral) measures of pain for children & adolescents aged 3 to 18 years. Pain 2007;127:140-50.
[14] Stevens B, Yamada J, Ohlsson A. Sucrose for analgesia in newborn infants undergoing painful procedures. **Cochrane** Database Syst Rev. 2004;(3):CD001069.
[15] Acad Emerg Med. 2006 Jun;13(6):617-22. Epub 2006 Apr 24. A randomized, controlled trial of sucrose analgesia in infants younger than 90 days of age who require bladder catheterization in the pediatric emergency department.Rogers AJ, Greenwald MH, Deguzman MA, Kelley ME, Simon HK.
[16] Uman LS, Chambers CT, McGrath PJ, Kisely S. Psychological interventions for needle-related procedural pain and distress in children and adolescents. **Cochrane** Database of Systematic Reviews. 2006 Oct 18;(4):CD005179.0
[17] Shah PS, Aliwalas L, Shah V. Breastfeeding or breastmilk to alleviate procedural pain in neonates: a systematic review. Breastfeed Med. 2007 Jun;2(2):74-82. Shah PS, Aliwalas LI, Shah V. Breastfeeding or breast milk for procedural pain in neonates. **Cochrane** Database Syst Rev. 2006 Jul 19;3:CD004950
[18] Efe E, Ozer ZC. The use of breast-feeding for pain relief during neonatal immunization injections. Appl Nurs Res. 2007 Feb;20(1):10-6.
[19] Lakeside clinic medical staff: {Quote: "I usually tell them I'm going to have to pinch them for a second (again no need to know the pinch is a needle) and that I'm going to put some magic potion on the cut so it doesn't hurt anymore. Parents can read to them from a BIG picture book if the wound is below their eyes, which also blocks their view of what I'm doing. Also, when inserting a needle, the tissue edge of the wound has no pain receptors, so entering the tissue from the wound edge, rather than going through skin is helpful. They still feel the burn of the local, but not the sharpness of the needle. Local kept in a warming cupboard or neutralized with bicarb is less painful too. Kids LOVE to talk about themselves--so asking lots of questions about who they play with, what their favorite things are, etc is a big distraction."}
[20] Bailey B, Bergeron S, Gravel J, Bussières JF, Bensoussan A. Efficacy & impact of intravenous morphine before surgical consultation in children with right lower quadrant pain suggestive of appendicitis: a randomized controlled trial. Ann Emerg Med. 2007 Oct;50(4):371-8.
[21] Singer et al. Management of Local Burns in the ED. The Am J of Emerg Med 2007;25:666-71. Estimation of burn size for PDA: http://www.sagediagram.com/
[22] Moore AJ, Shevell M. Chronic daily headaches in pediatric neurology practice. J Child Neurol. 2004 De c;19(12):925-9.http://www.medscape.com/viewarticle/501997_print
[23] Gunner KB, Smith HD. Practice guideline for diagnosis & management of migraine headaches in children & adolescents: Part 2. J Pediatr Health Care 2008;22:52-9.
[24]Clark E, Plint AC, Correll R, Gaboury I, Passi B. A randomized, controlled trial of acetaminophen, ibuprofen, and codeine for acute pain relief in children with musculoskeletal trauma. Pediatrics. 2007 Mar;119(3):460-7. Comment in: Evid Based Med. 2007;12(5):144. Pediatrics. 2007;120(1):237; author reply 237-8.
[25] Schechter NL, Zempsky WT, Cohen LL, McGrath PJ, McMurtry CM, Bright NS. Pain reduction during pediatric immunizations: evidence-based review and recommendations. Pediatrics. 2007 May;119(5):e1184-98.
[26] Taddio A, Manley J, Potash L, Ipp M, Sgro M, Shah V. Routine immunization practices: use of topical anesthetics & oral analgesics. Pediatrics 2007;120(3):e637-43.
[27] Hatfield LA, Gusic ME, Dyer AM, Polomano RC. Analgesic properties of oral sucrose during routine immunizations at 2 and 4 months of age. Pediatrics. 2008;121.
Harrison D, et al. Efficacy of sweet solutions for analgesia in infants between 1 and 12 months of age: a systematic review. Arch Dis Child. 2010 Jun;95(6):406-13.
[Home made sugar solution: 1 packet or 1 sugar cube mixed into 10ml water. Taddio A. New Clinical Practice Guideline for pain…childhood vaccination. CPJ 2011;144(3):114-115]
[28] O'Sullivan R, Oakley E, Starr M. Wound repair in children. Aust Fam Physician. 2006 Jul;35(7):476-9.
[29] Farion KJ, Osmond MH, Hartling L, Russell KF, Klassen TP, Crumley E, Wiebe N. Tissue adhesives for traumatic lacerations: a systematic review of randomized controlled trials. Acad Emerg Med. 2003 Feb;10(2):110-8. Review.
[30] Taddio A, Soin HK, Schuh S, Koren G, Scolnik D. Liposomal lidocaine to improve procedural success rates and reduce procedural pain among children: a randomized controlled trial. CMAJ. 2005 Jun 21;172(13):1691-5.
[31] Lander JA, Weltman BJ, So SS. **Cochrane** Database 2006;19;3:CD004236.EMLA & amethocaine for reduction of children's pain associated with needle insertion.
[32] Anghelescu DL, Ross CE, Oakes LL, Burgoyne LL. The Safety of Concurrent Administration of Opioids via Epidural and Intravenous Routes for Postoperative Pain in Pediatric Oncology Patients. J Pain Symptom Manage. 2008 Feb 19; [Epub ahead of print] PMID: 18291619
[33] Therapeutic Dilemma Alternating acetaminophen and ibuprofen. *L Shortridge, V Harris* February 2007, Volume 12 Issue 2: 127-128
Mehlisch Donald R., Aspley Sue, Daniels Stephen E., et al., Comparison of the analgesic efficacy of concurrent **ibuprofen and paracetamol** with ibuprofen or paracetamol alone in the management of moderate to severe acute postoperative dental pain in adolescents and adults: A randomized, double-blind, placebo-controlled, parallel-group, single-dose, two-center, modified factorial study, Clinical Therapeutics, Volume 32, Issue 5, May 2010, Pages 882-895.
Paul IM, Sturgis SA, Yang C, et al. Efficacy of standard doses of **Ibuprofen** alone, **alternating, and combined with acetaminophen** for the tx of febrile children. Clin Ther. 2010 Dec;32(14):2433-40.
Purssell E. Systematic review of studies comparing combined treatment with paracetamol and ibuprofen, with either drug alone. Arch Dis Child. 2011 Dec;96(12):1175-9.
[34] Eggleston ST, Lush LW. Understanding allergic reactions to local anesthetics. Ann Pharmacother. 1996 Jul-Aug;30(7-8):851-7.
[35] DeBoard RH, Rondeau DF, Kang CS, et al. Principles of basic wound evaluation & management in the emergency department. Emerg Med Clin North Am. 2007;25:23-39.
[36] Therapeutic Choices 5th ed. Canadian Pharmacists Association 2007. Editor J Gray. (pg 201).
[37] Nasal Midazolam for Sedation in Pediatric Patients Prior to Invasive Procedures. CADTH HTIS. Email: this@cadth.ca
[38] PA protocols - in PA Pearls January 1999. Accessed online at: http://www.erpearls.com/content/publications/01%20PA%20Pearls%20JAN%2099.pdf
[39] Confirmed by Emergency Medicine: A Comprehensive Study Guide – 6th Ed(2004) through StatRef http://online.statref.com.cyber.usask.ca/document.aspx?fxid=80&docid=949
[40] Acute Pain Management And Procedural Sedation In Children - Michael N. Johnston, Erica L. Liebelt (STAT REF)
[41] Birmingham PK, Tobin MJ, Fisher DM, et al. Initial & subsequent dosing of rectal acetaminophen in children: a 24-hour pharmacokinetic study of new dose recommendations. Anesthesiology. 2001;94:385-9. {See also: Kleiber C. Acetaminophen dosing for neonates, infants, & children. J Spec Pediatr Nurs. 2008;13:48-9. }
[42] Emslander HC. Local and topical anesthesia for pediatric wound repair: a review of selected aspects. Pediatr Emerg Care. 1998 Apr;14(2):123-9.
[43] UPTODATE reference on topical anaesthesia (2006) (http://www.uptodate.com/home/index.html)
[44] Eur J Anaesthesiol. 2004 Mar;21(3):210-3.3 Comparison of EMLA and lidocaine iontophoresis for cannulation analgesia.Moppett IK, Szypula K, Yeoman PM
[45] Galinkin JL, Rose JB, Harris K, Watcha MF. Lidocaine iontophoresis versus eutectic mixture of local anesthetics (EMLA) for IV placement in children. Anesth Analg. 2002;94:1484-8.
[46] Pediatric Cancer Pain; Access: http://www.nccn.org/professionals/physician_gls/PDF/pediatric_pain.pdf ; National Comprehensive Cancer Network (NCCN) ; 2006
[47] Sarrell EM, Wielunsky E, Cohen HA. Antipyretic treatment in young children with fever: acetaminophen, ibuprofen, or both alternating in a randomized, double-blind study. Arch Pediatr Adolesc Med. 2006 Feb;160(2):197-202
[64] Farion KJ, Splinter KL, Newhook K, Gaboury I, Splinter WM. The effect of vapocoolant spray on pain due to intravenous cannulation in children: a RCT. CMAJ. 2008;179:31-6.
[65] Wallace DP, Allen KD, Lacroix AE, et al. The "**Cough Trick**," a Brief Strategy to Manage Pediatric Pain From Immunization Injections. Pediatrics. 2010 Jan 11.

Pain Intensity Scoring:

[66] Taddio

- Chose a scale that is age appropriate to patient & become familiar with using!
- Interpret in light of any other pain related physical factors (e.g. heart rate)
- Also interpret according to trends for improvement or worsening of pain control
- Sherbrooke algorithm for acute pain in children (post-op): gave regular analgesic according to pain scale: {0-3: acetaminophen; 3-6: naproxen + acetaminophen; 6-9: morphine + naproxen + acetaminophen; 9-10: notify MD. Overall ↓ in pain scores & a ↓ in opioid requirement.}
- Other links: **Visual Analogue Scale**: suitable for age 7+ {McGrath PA, Seifert CE, Speechley KN, et al. A new analogue scale for assessing children's pain: an initial validation study. Pain. 1996 Mar;64(3):435-43.} **Oucher Scale**: age 3-12: http://www.oucher.org/history.html
BMJ Clinical Review: Pain Management and Sedation for Children in the Emergency Setting: http://www.bmj.com/cgi/content/full/339/oct30_1/b4234

FLACC SCALE – for assessing pain in very young children non-verbal; suitable for cognitively impaired

Face	No particular expression or smile	Occasional grimace or frown, withdrawn, disinterested	Frequent to constant quivering chin, clenched jaw
Legs	Normal position or relaxed	Uneasy, restless, tense	Kicking, or legs drawn up
Activity	Lying quietly, normal position, moves easily	Squirming, shifting back and forth, tense	Arched, rigid or jerking
Cry	No cry (awake or asleep)	Moans or whimpers; occasional complaint	Crying steadily, screams or sobs, frequent complaints
Consolability	Content, relaxed	Reassured by occasional touching, hugging or being talked to, distractible	Difficult to console or comfort

◆Each of the five categories (F) Face; (L) Legs; (A) Activity; (C) Cry; (C) Consolability is scored from 0-2, which results in a total score between zero and ten.
◆From ***The FLACC****: A behavioral scale for scoring postoperative pain in young children*, by S Merkel and others, 1997,

Faces Pain Scale – Revised (FPS-R) – age 4+

This is a thumbnail image. The full-size FPS-R with instructions is available on page 3 at http://www.iasp-pain.org/FPSR Numbers are not shown to children.

From: Hicks CL, von Baeyer CL, Spafford PA, Van Korlaar I, Goodenough B. The *Faces Pain Scale – Revised*. Toward a common metric in pediatric pain measurement. *Pain* 2001;93:173-183. ©2001 International Association for the Study of Pain. Reprinted with permission.

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Vaccination & antipyretic interactions [Wysocki 2017]:

- Acetaminophen may interfere with pneumococcal vaccinations
- Ibuprofen may interfere with pertussis and tetanus vaccinations

Additional references:

Adams Denise, Cheng Florence, Jou Hsing, et al. The Safety of Pediatric **Acupuncture**: A Systematic Review. Pediatrics 2011; peds.2011-1091; November 21, 2011

Ahola Kohut S, Stinson JN, Ruskin D, et al. **iPeer2Peer program**: a pilot feasibility study in adolescents with chronic pain. Pain. 2016 May;157(5):1146-55.

Anghelescu DL, et al. Prospective Randomized Crossover Evaluation: Three Anesthetic Regimens for Painful Procedures in Children with Cancer. J Pediatr.2012Aug 8.

Atkinson Paul, Chesters Adam,Heinz Peter. Pain management and sedation for children in the **emergency** department. BMJ 2009;339:b4234, doi: 10.1136/bmj.b4234

Axelin A, Salantera S, Kirjavainen J, et al. Oral glucose and parental holding preferable to opioid in pain management in preterm infants. Clin J Pain. 2009 Feb;25:138-45. Our study demonstrated that "**facilitated tucking by parents**" is not just equal, but preferable to other pain management methods when both efficacy and safety are considered.

Babl FE, Goldfinch C, et al. Does **nebulized lidocaine** reduce the pain and distress of **nasogastric tube** insertion in young children? A randomized, double-blind, placebo-controlled trial. Pediatrics. 2009 Jun;123(6):1548-55. Nasogastric tube insertion results in very high FLACC scores irrespective of lidocaine use. Nebulized lidocaine cannot be recommended as pain relief for nasogastric tube insertion in children. The delay and distress of nebulization likely outweigh a possible benefit in the postinsertion period.

Belliveau MJ, Jordan DR. **Minimizing injection pain**. CMAJ. 2012 Oct 16;184(15):1715.

Bembich S, Cont G, Baldassi G, et al. **Maternal Holding vs Oral Glucose Administration** as Nonpharmacologic Analgesia in Newborns: A Functional Neuroimaging Study. JAMA Pediatr. 2015 Mar 1;169(3):284-5.

Bembich S, Cont G, Causin E, Paviotti G, Marzari P, Demarini S. **Infant Analgesia** With a Combination of Breast Milk, Glucose, or Maternal Holding. Pediatrics. 2018 Sep;142(3). pii: e20173416

Biran V, Gourrier E, et al. Analgesic Effects of **EMLA Cream and Oral Sucrose** During Venipuncture in Preterm Infants. Pediatrics. 2011 Jul;128(1):e63-70.

Brummelte S, Grunau RE, Chau V, et al Procedural pain and brain development in **premature** newborns. Ann Neurol. 2012 Feb 28.

Bueno M, Stevens B, et al. Breast Milk and **Glucose 25%** for Pain Relief in Preterm Infants: A Noninferiority Randomized Controlled Trial. Pediatrics. 2012 Mar 5.

Bulloch B et al. Reliability of the **color analog scale**: Repeatability of scores in traumatic and nontraumatic injuries. Acad Emerg Med 2009 May; 16:465.

Campbell-Yeo ML, Johnston CC, et al. **Cobedding** and recovery time after heel lance in preterm twins: results of a randomized trial. Pediatrics.2012 Sep;130(3):500-6.

Carbajal R, Rousset A, et al. Epidemiology and treatment of painful procedures in neonates in intensive care units. JAMA. 2008 Jul 2;300(1):60-70. During neonatal intensive care in the Paris region, large numbers of painful and stressful procedures were performed, the majority of which were not accompanied by analgesia.

Chan E, Hovenden M, Ramage E, et al. **Virtual Reality for Pediatric Needle Procedural Pain**: Two Randomized Clinical Trials. J Pediatr. 2019 Jun;209:160-167.e4.

Chester SJ, Tyack Z, De Young A, et al. Efficacy of **hypnosis on pain, wound-healing, anxiety, and stress in children with acute burn** injuries: a randomized controlled trial. Pain. 2018 Sep;159(9):1790-1801.

Chermont, Aurimery Gomes, Falcao, Luis Fabio Magno, et al. Skin-to-Skin Contact and/or Oral 25% Dextrose for Procedural Pain Relief for Term Newborn Infants. Pediatrics 2009 124: e1101-e1107.

Chowdhary S, Bukoye B, Bhansali AM, et al. Risk of Topical **Anesthetic-Induced Methemoglobinemia**: A 10-Year Retrospective Case-Control Study. (benzocaine) JAMA Intern Med. 2013 Apr 1:1-6.

Chua ME, Firaza PNB, Ming JM, et al. **Lidocaine Gel for Urethral Catheterization in Children**: A Meta-Analysis. J Pediatr. 2017 Sep 13.

Cignacco EL, Sellam G, et al. **Oral Sucrose** and "Facilitated Tucking" for Repeated Pain Relief in Preterms: A Randomized Controlled Trial. Pediatrics. 2012 Jan 9.

Cobb JE, Cohen LL. A randomized controlled trial of the **ShotBlocker** for children`s immunization distress. Clin J Pain. 2009 Nov-Dec;25(9):790-6. (Data not support effectiveness)

Codipietro L, et al. **Breastfeeding** or oral sucrose solution in term neonates receiving heel lance: a randomized, controlled trial. Pediatrics. 2008 Sep;122(3):e716-21. This study suggests that breastfeeding provides superior analgesia for heel lance compared with oral sucrose in term neonates.

Cohen D. **Acetaminophen** for the Treatment of Pain in **Newborns**. Am Fam Physician. 2016 Aug 1;94(3):216-7

Committee on Fetus and Newborn and Section on Anesthsiology and Pain Medicine. **Prevention and Management of Procedural Pain in the neonate**: An Update. Pediatrics. 2016 Jan 25.

de Sousa Freire NB, et al. Evaluation of analgesic effect of **skin-to-skin** contact compared to oral glucose in preterm neonates. Pain. 2008 Sep 30;139(1):28-33.

Dilli D, Küçük IZ, Dallar Y. Interventions to Reduce Pain during Vaccination in Infancy. J Pediatr. 2008 Oct 10

Disher T, Cameron C, Mitra S, et al. Pain-Relieving Interventions for **Retinopathy of Prematurity**: A Meta-analysis. Pediatrics. 2018 Jun 1.

Drendel AL, Lyon R, Bergholte J, et al. Outpatient pediatric **pain** management practices for **fractures**. Pediatr Emerg Care. 2006 Feb;22(2):94-9. Most children with fractures have the "worst" pain in the first 48 hours after injury and used analgesia for 3 days after injury. There are noteworthy functional limitations for both children and their caregivers. Ibuprofen and acetaminophen with codeine are the analgesics most commonly used, with no clear superiority.

Drendel AL, Gorelick MH, Weisman SJ, et al. A randomized clinical trial of **ibuprofen** versus acetaminophen with codeine for acute pediatric arm fracture pain. Ann Emerg Med. 2009 Oct;54(4):553-60.

Dulai SK, Firth K, Al-Mansoori K, et al. Does **Topical Anesthetic Reduce Pain During Intraosseous Pin Removal in Children**? A Randomized Controlled Trial. J Pediatr Orthop. 2015 Feb 26.

Ekbom K, Kalman S, Jakobsson J, Marcus C. Efficient Intravenous Access Without Distress: A Double-blind Randomized Study of **Midazolam and Nitrous Oxide** in Children and Adolescents. Arch Pediatr Adolesc Med. 2011 Sep;165(9):785-91.

Eidelman A, Weiss JM, Baldwin CL, et al. **Topical anaesthetics** for repair of dermal laceration. Cochrane Database of Systematic Reviews 2011, Issue 6. Art. No.: CD005364. DOI: 10.1002/14651858.CD005364.pub2. Based on mostly descriptive analysis, topical anaesthetics are possibly an efficacious, non-invasive means of providing analgesia prior to suturing of dermal lacerations.

Falagas ME, Vouloumanou EK, Plessa E, et al. Inaccuracies in **dosing drugs with teaspoons and tablespoons**. Int J Clin Pract. 2010 Aug;64(9):1185-9.

FDA Jan/09 An public health advisory reminds patients and physicians of potentially serious side effects from the improper use of topical anesthetics, including **lidocaine, tetracaine, benzocaine, and prilocaine**. The latest advisory was prompted by a small study that tested whether lidocaine reduced discomfort during breast mammography. No serious adverse events were noted. However, the FDA remains concerned about the potential for seizures, irregular heartbeat, and breathing problems when topical anesthetics are applied over a large area or are covered by plastic wrap or a heating pad. Two deaths were previously reported in women using the anesthetics before laser hair removal.

FDA Aug/12 is reviewing reports of children who developed serious adverse effects or died after taking **codeine** for pain relief after tonsillectomy and/or adenoidectomy for obstructive sleep apnea syndrome. Recently, three pediatric deaths and one non-fatal but life-threatening case of respiratory depression were documented in the medical literature.

FDA Jun/14 warns that prescription **oral viscous lidocaine** 2 percent solution should not be used to treat infants and children with teething pain. We are requiring a new Boxed Warning, FDA's strongest warning, to be added to the drug label to highlight this information. Oral viscous lidocaine solution is not approved to treat teething pain, and use in infants and young children can cause serious harm, including death

FDA May/18 is warning that over-the-counter (OTC) oral drug products containing benzocaine should not be used to treat infants and children younger than 2 years. We are also warning that benzocaine oral drug products should only be used in adults and children 2 years and older if they contain certain warnings on the drug label. These products carry serious risks and provide little to no benefits for treating oral pain, including sore gums in infants due to teething. Benzocaine, a local anesthetic, can cause a condition in which the amount of oxygen carried through the blood is greatly reduced. This condition, called methemoglobinemia, can be life-threatening and result in death.

Fein JA et al. Relief of **pain and anxiety in pediatric patients in emergency** medical systems. Pediatrics 2012 Nov; 130:e1391.

Fortier, Michelle A., MacLaren, Jill E., Martin, Sarah R., et al. Pediatric Pain After **Ambulatory Surgery**: Where's the Medication? Pediatrics 2009 124: e588-e595.

Franck LS, Oulton K, Nderitu S, et al. **Parent Involvement** in Pain Management for NICU Infants: A Randomized Controlled Trial. Pediatrics. 2011 Aug 22.

Frey TM, Florin TA, Caruso M, et al. Effect of **Intranasal Ketamine vs Fentanyl on Pain Reduction for Extremity Injuries in Children**: The PRIME Randomized Clinical Trial. JAMA Pediatr. 2018 Dec 28.

Gao H, Xu G, Gao H, et al. Effect of repeated **Kangaroo Mother Care** on repeated procedural pain in preterm infants: A randomized controlled trial. Int J Nurs Stud. 2015 Jul;52(7):1157-65.

Goldman RD. **Analgesia for lumbar puncture** in infants and children. Can Fam Physician. 2019 Mar;65(3):192-194.

Gray L, Garza E, Zageris D, et al. **Sucrose and Warmth** for Analgesia in Healthy Newborns: An RCT. Pediatrics. 2015 Feb 16.

Groenewald CB, Wright DR, Palermo TM. **Health care expenditures** associated with pediatric pain-related conditions in the USA. Pain 2015;156:951–7.

Harrington JW, Logan S, Harwell C, et al. Effective **Analgesia Using Physical Interventions for Infant Immunizations**. Pediatrics. 2012 Apr 16.

Harman S, Zemek R, Duncan MJ, et al. Efficacy of pain control with topical **lidocaine-epinephrine-tetracaine** (LET) during laceration repair with tissue adhesive in children: a randomized controlled trial. CMAJ. 2013 Aug 6.

Harrison D, Stevens B, et al. Efficacy of **sweet solutions** for analgesia in infants between 1 and 12 months of age: a systematic review. Arch Dis Child. 2010 May 12.

Harrison D, Beggs S, Stevens B. **Sucrose** for Procedural Pain Management in Infants. Pediatrics. 2012 Oct 8.

Harrison D, Reszel J, Bueno M, et al. **Breastfeeding for procedural pain in infants beyond the neonatal period**. Cochrane Database Syst Rev. 2016 Oct 28;10:CD011248. We conclude, based on the 10 studies included in this review, that breastfeeding may help reduce pain during vaccination for infants beyond the neonatal period. Breastfeeding consistently reduced behavioural responses of cry duration and composite pain scores during and following vaccinations. However, there was no evidence that breastfeeding had an effect on physiological responses. No studies included in this review involved populations of hospitalised infants undergoing other skin-breaking procedures. Although it may be possible to extrapolate the review results to this population, further studies of efficacy, feasibility, and acceptability in this population are warranted.

Harrison D, Larocque C, Bueno M, et al. **Sweet Solutions** to Reduce Procedural Pain in Neonates: A Meta-analysis. Pediatrics. 2016 Dec 16.

Hartling L, Newton AS, et al. **Music** to Reduce Pain and Distress in the Pediatric Emergency Department: A Randomized Clinical Trial. JAMA Pediatr. 2013 Jul 15.

Hauer J, Houtrow AJ, AAP Section on Hospice and Palliative Medicine, Council on Children with Disabilities. **Pain Assessment and Treatment in Children With Significant Impairment of the Central Nervous System**. Peds.2017;139(6):e20171002

Hauer JM. **Pain in Children With Severe Neurologic Impairment**: Undoing Assumptions. JAMA Pediatr. 2018 Aug 20.

Hay AD, Redmond NM, Costelloe C, et al. Paracetamol and ibuprofen for the treatment of fever in children: the **PITCH** randomised controlled trial. Health Technol Assess. 2009 May;13(27):iii-iv, ix-x, 1-163. Young children who are unwell with fever should be treated with ibuprofen first, but the relative risks (inadvertently exceeding the maximum recommended dose) and benefits (extra 2.5 hours without fever) of using paracetamol plus ibuprofen over 24 hours should be considered.

Health Canada Apr/12 is informing Canadians that it has requested companies to add new risk statements to the packaging and labelling of licensed benzocaine products. In April 2011, Health Canada reminded Canadians of certain health risks associated with **benzocaine** products, including a very rare but serious blood condition known as **methemoglobinemia** that can affect sensitive individuals.

Hechler T, et al. Systematic Review on **Intensive Interdisciplinary Pain Treatment** of Children With Chronic Pain. Pediatrics. 2015 Jul;136(1):115-27.

Hippard HK, Govindan K, Friedman EM, et al. Postoperative Analgesic and Behavioral Effects of **Intranasal Fentanyl, Intravenous Morphine, and Intramuscular Morphine** in Pediatric Patients Undergoing Bilateral Myringotomy and Placement of Ventilating Tubes. Anesth Analg. 2012 Jun 5.

Hogan ME et al. Systematic review and meta-analysis of the effect of **warming local anesthetics** on injection pain. Ann Emerg Med 2011 Jul; 58:86.

Holsti, Liisa, Grunau, Ruth E. Considerations for Using **Sucrose** to Reduce Procedural Pain in Preterm Infants. Pediatrics 2010 125: 1042-1047.

Jain S, Hegenbarth MA, Humiston SG, et al. Increasing **ED Use** of Jet Injection of **Lidocaine for IV-Related Pain Management**. Pediatrics. 2017 Mar 9

Jalota Leena, Kalira Vicki, George Elizabeth, et a. l on behalf of the Perioperative Clinical Research Core. **Prevention of pain on injection of propofol**: systematic review and meta-analysis. BMJ 342:doi:10.1136/bmj.d1110 (15 Mar 2011)

Johnston CC, Campbell-Yeo M, Filion F. Paternal vs **maternal kangaroo care** for procedural pain in preterm neonates: a randomized crossover trial. Arch Pediatr Adolesc Med 2011;165:792–6.

Johnston C, Campbell-Yeo M, Disher T, et al. **Skin-to-skin care for procedural pain in neonates**. Cochrane Database Syst Rev. 2017;(2):CD008435. SSC appears to be effective as measured by composite pain indicators with both physiological and behavioural indicators and, independently, using heart rate and crying time; and safe for a single painful procedure. Purely behavioural indicators tended to favour SSC but with facial actions there is greater possibility of observers not being blinded. Physiological indicators were mixed although the common measure of heart rate favoured SSC. Two studies compared mother-providers to others, with non-significant results. There was more heterogeneity in the studies with behavioural or composite outcomes.

Kassab M, Foster JP, Foureur M, et al. **Sweet-tasting solutions** for needle-related procedural pain in infants one month to one year of age. Cochrane Database of Systematic Reviews 2012, Issue 12. Art. No.: CD008411. DOI: 10.1002/14651858.CD008411.pub2. There is insufficient evidence to confidently judge the effectiveness of sweet-tasting solutions in reducing needle-related pain in infants (one month to 12 months of age). The treatments do, however, appear promising.

Kelly LE, Sommer DD, Ramakrishna J, et al. **Morphine or Ibuprofen for Post-Tonsillectomy Analgesia**: A Randomized Trial. Pediatrics. 2015 Jan 26.

Klein EJ, Brown JC, Kobayashi A, et al. A randomized clinical trial comparing oral, **aerosolized intranasal, and aerosolized buccal midazolam**. Ann Emerg Med. 2011 Oct;58(4):323-9.

Krauss BS, Krauss BA, Green SM. Videos in clinical medicine. **Procedural sedation and analgesia in children**. N Engl J Med. 2014 Apr 10;370(15):e23.

Krauss BS, Calligaris L, Green SM, et al. Current concepts in management of **pain in children in the emergency department**. Lancet. 2015 Jun 18.

Lambert C, Goldman RD. Pain management for **children needing laceration repair**. Can Fam Physician. 2018 Dec;64(12):900-902.

Le May S, Ali S, Plint AC, et al. **Oral Analgesics Utilization for Children With Musculoskeletal Injury** (**OUCH** Trial): An RCT. Pediatrics. 2017 Oct 11.

Lee J, Lee J, Lim H, et al. Cartoon distraction alleviates anxiety in children during induction of anesthesia. Anesth Analg. 2012 Nov;115(5):1168-73.

Lee GY, Yamada J, Kyololo O, et al. Pediatric clinical practice **guidelines for acute procedural pain**: a systematic review. Pediatrics. 2014 Mar;133(3):500-15.

Li Y, Jackson KA, Slon B, et. al, CYP2B6*6 allele and age substantially reduce steady-state **ketamine** clearance in chronic pain patients: impact on adverse effects. Br J Clin Pharmacol. 2015 Feb 22.

Liossi C, Howard RF. Pediatric **Chronic Pain : Biopsychosocial Assessment and Formulation**. Pediatrics.2016 ;138(5) :e20160331

Meesters N, Simons S, et al. **Waiting 2 minutes after sucrose administration- unnescessary**? Arch Dis Child Fetal Neonatal Ed. Published Online First.2016.

Nabulsi M. Is combining or alternating **antipyretic** therapy more beneficial than **monotherapy** for febrile children? BMJ. 2009Oct 1;339:b3540. doi: 10.1136/bmj.b3540.

NICE Guidelines: National Institute for Health and Care Excellence. **Feverish** illness in children: assessment and initial management in children younger than five years. (Clinical guideline CG160.) 2013. http://guidance.nice.org.uk/CG160).

Palermo TM, et al. **Problem-solving skills training** for parents of children with chronic pain: a pilot randomized controlled trial. Pain. 2016 Jun;157(6):1213-23.

Pillai Riddell RR, Racine NM, Turcotte K, et al. **Non-pharmacological** management of infant and young child procedural pain.Cochrane Database Syst Rev. 2011 Oct 5;10:CD006275. There is evidence that different non-pharmacological interventions can be used with preterms, neonates, and older infants to significantly manage pain behaviors associated with acutely painful procedures.

Poonai N, Paskar D, Konrad SL, et al. **Opioid analgesia for acute abdominal pain** in children: A systematic review and meta-analysis. Acad Emerg Med. 2014 Nov;21(11):1183-92.

Poonai N, Li J, Langford C, et al. **Intraurethral Lidocaine for Urethral Catheterization** in Children: A Randomized Controlled Trial. Pediatrics. 2015 Sep 28.

Poonai N, et al. **Oral morphine versus ibuprofen** administered at home for **postoperative orthopedic pain in children**: a randomized controlled trial. CMAJ.2017 Oct 10;189(40):E1252-E1258.

Prymula R, Siegrist CA, Chlibek R, et al. Effect of prophylactic **paracetamol/acetaminophen** administration at time of vaccination on febrile reactions and antibody responses in children: two open-label, randomised controlled trials. Lancet. 2009 Oct 17;374(9698):1339-50.

Racoosin JA, Roberson DW, Pacanowski MA et al. New Evidence about an Old Drug - **Risk with Codeine after Adenotonsillectomy**. N Engl J Med. 2013 Apr 24.

Rasooly IR, Mullins PM, Mazer-Amirshahi M, van den Anker J, Pines JM. The Impact of **Race on Analgesia** Use among Pediatric Emergency Department Patients. J Pediatr. 2014 Jun 11.
Reinoso-Barbero F, Pascual-Pascual SI, de Lucas R, et al. Equimolar **Nitrous Oxide/Oxygen** Versus Placebo for Procedural Pain in Children: A Randomized Trial. Pediatrics 2011;127:e1464-70.
Savino, Francesco, Lupica, Maria Maddalena, Tarasco, Valentina, et al. Fulminant **Hepatitis After 10 Days of Acetaminophen** Treatment at Recommended Dosage in an Infant. Pediatrics 2011 127: e494-e497.
Schechter NL, Bernstein BA, Zempsky WT, Bright NS, Willard AK. **Educational Outreach to Reduce Immunization Pain** in Office Settings. Pediatrics. 2010 Nov 15.
Shah V, Taddio A, McMurtry CM, et al. **Pharmacological and Combined Interventions to Reduce Vaccine Injection Pain in Children** and Adults: Systematic Review and Meta-Analysis. Clin J Pain. 2015 Oct;31(10 Suppl):S38-63.
Shah SR, Kadage S, Sinn J. Trial of **Music, Sucrose, and Combination Therapy for Pain Relief** during **Heel Prick Procedures** in Neonates. J Ped. 2017;190:153-8
Shahid S, Florez ID, Mbuagbaw L. Efficacy and Safety of **EMLA Cream for Pain Control Due to Venipuncture** in Infants: A Meta-analysis. Pediatrics. 2018 Dec 26
Sharara-Chami R, Lakissian Z, Charafeddine L, et al. **Combination Analgesia for Neonatal Circumcision**: A Randomized Controlled Trial. Pediatrics. 2017 Nov 17.
Sikka K, Ahmed AA, Diaz D, et al. Automated Assessment of Children's **Postoperative Pain Using Computer Vision**. Pediatrics. 2015 Jul;136(1):e124-31.
Simonse E, Mulder PG, et al. Analgesic Effect of **Breast Milk Versus Sucrose** for Analgesia During Heel Lance in Late Preterm Infants. Pediatrics. 2012 Mar 5.
Slater R, Cornelissen L, Fabrizi L, et al. Oral **sucrose** as an analgesic drug for procedural pain in newborn infants: a randomised controlled trial. Lancet. 2010 Sep 1.
Smith D, Cheek H, Denson B, Pruitt CM. **Lidocaine Pretreatment** Reduces the Discomfort of **Intranasal Midazolam** Administration: A Randomized, Double-blind, Placebo-controlled Trial. Acad Emerg Med. 2017 Feb;24(2):161-167.
Stevens, Bonnie J., Abbott, Laura K., Yamada, Janet, et al. Epidemiology and management of **painful procedures** in children in Canadian hospitals. CMAJ 2011 0: cmaj.101341
Strazar R, Lalonde D. **Minimizing injection pain** in local anesthesia. CMAJ. 2012 Apr 30.
Taddio A, Shah V, Katz J. Reduced infant response to a routine care procedure after **sucrose** analgesia. Pediatrics. 2009 Mar;123(3):e425-9.
Taddio A, Shah V, Hancock R, et al. Effectiveness of **sucrose** analgesia in newborns undergoing painful medical procedures. CMAJ. 2008 Jul 1;179(1):37-43.
Taddio, A, Appleton, M, et al. **Reducing the pain of childhood vaccination**: an evidence-based clinical practice guideline (**summary**). CMAJ 2010 0: cmaj.092048.
Taddio, A, Appleton, M, Bortolussi, R, et al. **Reducing the pain of childhood vaccination**: an evidence-based clinical practice guideline. CMAJ 2010 0: cmaj.101720
Taddio, Anna, Shah, Vibhuti, Stephens, Derek, et al. Effect of Liposomal Lidocaine and **Sucrose** Alone and in Combination for Venipuncture Pain in Newborns. Pediatrics 2011 0: peds.2010-2914
Taddio A, McMurtry CM, Shah V, et al. **Reducing pain during vaccine injections**: clinical practice guideline. CMAJ. 2015 Aug 24. http://www.cmaj.ca/content/early/2015/08/24/cmaj.150391.full.pdf (accessed September 16, 2015).
Taddio A, Pillai Riddell R, Ipp M, et al. Relative effectiveness of **additive pain interventions during vaccination** in infants. CMAJ.2016 Dec 12.
Thyr M, Sundholm A, Teeland L, et al. Oral glucose as an analgesic to reduce infant distress following immunization at the age of 3, 5 and 12 months. Acta Paediatr 2007;96(2):233-6.
Tinner EM, Hoesli I, Jost K, et al. **Rectal Paracetamol** in Newborn Infants after Assisted Vaginal Delivery May **Increase Pain Response**. J Pediatr. 2012 Jul 17.
Tomlinson D, von Baeyer CL, Stinson JN, Sung L. A Systematic Review of **Faces Scales** for the Self-report of Pain Intensity in Children. Pediatrics. 2010 Oct 4.
Tsze DS, von Baeyer CL, Bulloch B, Dayan PS. **Validation of Self-Report Pain Scales** in Children. Pediatrics. 2013 Sep 2.
Uman LS, Birnie KA, Noel M, et al. **Psychological interventions** for needle-related procedural pain and distress in children and adolescents. Cochrane Database Syst Rev. 2013;10:CD005179.
van Tilburg MA, et al. **Audio-Recorded Guided Imagery** Treatment Reduces Functional Abdominal Pain in Children: A Pilot Study. Pediatrics. 2009 Oct 12.
Walson PD, Halvorsen M, Edge J, et al. Pharmacokinetic Comparison of **Acetaminophen Elixir Versus Suppositories** in Vaccinated Infants (Aged 3 to 36 Months): A Single-Dose, Open-Label, Randomized, Parallel-Group Design. Clin Ther. 2013 Jan 22.
Wang S, Giannakopoulos H, Lowstetter J, et al. **Lack of Methemoglobin** Elevations After Topical Applications of **Benzocaine Alone or Benzocaine Plus Tetracaine** to the Oral Mucosa. Clin Ther. 2017 Sep 21.
Warren OU, Blackwood B. **Acquired Methemoglobinemia**. N Engl J Med. 2019 Sep 19;381(12):1158
Weissman, Amir, Aranovitch, Michal, Blazer, Shraga, Zimmer, Etan Z. **Heel-Lancing** in Newborns: Behavioral and Spectral Analysis Assessment of Pain Control Methods. Pediatrics 2009 124: e921-e926.
Wong T, Stang AS, Ganshorn H, et al. **Combined and alternating paracetamol and ibuprofen** therapy for febrile children. Cochrane Database of Systematic Reviews 2013, Issue 10. Art. No.: CD009572. DOI: 10.1002/14651858.CD009572.pub2. There is some evidence that both alternating and combined antipyretic therapy may be more effective at reducing temperatures than monotherapy alone.However, the evidence for improvements inmeasures of child discomfort remains inconclusive.
Wysocki J, Center KJ, Brzostek J, et al. A randomized study of **fever prophylaxis and the immunogenicity of routine pediatric vaccinations**. Vaccine. 2017 Apr 4;35(15):1926-1935.
Yang YT, Chen B, Bennett CL. **FDA Approval** of Extended-Release **Oxycodone for Children** With Severe Pain. Pediatrics. 2016 May;137(5).
Zarnegar-Lumley S, Lange KR, Mathias MD, et al. Local Anesthesia With General **Anesthesia for Pediatric Bone Marrow Procedures**. Pediatrics. 2019 Aug;144(2)
Zempsky WT, et al. **Needle-free powder lidocaine** delivery system provides rapid effective analgesia for venipuncture or cannulation pain in children: randomized, double-blind Comparison of Venipuncture and Venous Cannulation Pain After Fast-Onset Needle-Free Powder Lidocaine or Placebo Treatment trial. Pediatrics. 2008 May;121(5):979-87. The needle-free powder lidocaine delivery system was well tolerated and produced significant analgesia within 1 to 3 minutes.
Zimmerman KO, et al. **Sedatives and Analgesics Given to Infants** in Neonatal Intensive Care Units at the End of Life. J Pediatr. 2015 Aug;167(2):299-304.e3.

Rheumatoid Arthritis: Online Extras

ACR/EULAR 2010 RA scoring system for diagnosis of rheumatoid arthritis[48] see calculator at https://www.rheumakit.com/en/calculators/acr_eular2010

	Category	Points
Joint Involvement	1 large joint	0
	2-10 large joints	1
	1-3 small joints (with or without involvement of large joints)	2
	4-10 small joints (with or without involvement of large joints)	3
	>10 joints, including at least one small joint	5
Serology	Negative RF and negative ACPA	0
	Low positive RF or low positive ACPA	2
	High positive RF or high positive ACPA	3
Acute Phase Reactants	Normal CRP and normal ESR	0
	Abnormal CRP or abnormal ESR	1
Duration of Symptoms	< 6 weeks	0
	≥ 6 weeks	1
A total score of 6 or higher is indicative of rheumatoid arthritis.		

Sensitivity of the scoring system[68] (likelihood of correctly diagnosing a true case of rheumatoid arthritis): 82%
Specificity of the scoring system[68] (likelihood of correctly ruling out rheumatoid arthritis): 61%

Rheumatoid Arthritis References:

1. **CRA 2012 Guidelines**. Bykerk VP, Akhavan P, Hazlewood GS, Schieir O, Dooley A, Haraoui B, Khraishi M, Leclercq SA, Légaré J, Mosher DP, Pencharz J, Pope JE, Thomson J, Thorne C, Zummer M, Bombardier C; Canadian Rheumatology Association. Canadian Rheumatology Association recommendations for pharmacological management of rheumatoid arthritis with traditional and biologic disease-modifying antirheumatic drugs. J Rheumatol. 2012 Aug;39(8):1559-82.
2. **CRA 2012 Guidelines Part 2.** Bombardier C, Hazlewood GS, Akhavan P, Schieir O, Dooley A, Haraoui B, Khraishi M, Leclercq SA, Légaré J, Mosher DP, Pencharz J, Pope JE, Thomson J, Thorne C, Zummer M, Gardam MA, Askling J, Bykerk V; Canadian Rheumatology Association. Canadian Rheumatology Association recommendations for the pharmacological management of rheumatoid arthritis with traditional and biologic disease-modifying antirheumatic drugs: part II safety. J Rheumatol. 2012 Aug;39(8):1583-602.
3. **ACR 2015 Guidelines**. Singh JA, Saag KG, Bridges SL Jr, Akl EA, Bannuru RR, Sullivan MC, Vaysbrot E, McNaughton C, Osani M, Shmerling RH, Curtis JR, Furst DE, Parks D, Kavanaugh A, O'Dell J, King C, Leong A, Matteson EL, Schousboe JT, Drevlow B, Ginsberg S, Grober J, St Clair EW, Tindall E, Miller AS, McAlindon T. 2015 American College of Rheumatology Guideline for the Treatment of Rheumatoid Arthritis. Arthritis Rheumatol. 2016 Jan;68(1):1-26.
4. **ACR 2018 Biosimilars White Paper**. Bridges SL Jr, White DW, Worthing AB, Gravallese EM, O'Dell JR, Nola K, Kay J, Cohen SB; American College of Rheumatology. The Science Behind Biosimilars: Entering a New Era of Biologic Therapy. Arthritis Rheumatol. 2018 Mar;70(3):334-344.
5. **EULAR 2016 Guidelines**. Smolen JS, Landewé R, Bijlsma J, Burmester G, Chatzidionysiou K, Dougados M, Nam J, Ramiro S, Voshaar M, van Vollenhoven R, Aletaha D, Aringer M, Boers M, Buckley CD, Buttgereit F, Bykerk V, Cardiel M, Combe B, Cutolo M, van Eijk-Hustings Y, Emery P, Finckh A, Gabay C, Gomez-Reino J, Gossec L, Gottenberg JE, Hazes JMW, Huizinga T, Jani M, Karateev D, Kouloumas M, Kvien T, Li Z, Mariette X, McInnes I, Mysler E, Nash P, Pavelka K, Poór G, Richez C, van Riel P, Rubbert-Roth A, Saag K, da Silva J, Stamm T, Takeuchi T, Westhovens R, de Wit M, van der Heijde D. EULAR recommendations for the management of rheumatoid arthritis with synthetic and biological disease-modifying antirheumatic drugs: 2016 update. Ann Rheum Dis. 2017 Jun;76(6):960-977.
6. **ACR 2017 Perioperative Guidelines**. Goodman SM, Springer B, Guyatt G, Abdel MP, Dasa V, George M, Gewurz-Singer O, Giles JT, Johnson B, Lee S, Mandl LA, Mont MA, Sculco P, Sporer S, Stryker L, Turgunbaev M, Brause B, Chen AF, Gililland J, Goodman M, Hurley-Rosenblatt A, Kirou K, Losina E, MacKenzie R, Michaud K, Mikuls T, Russell L, Sah A, Miller AS, Singh JA, Yates A. 2017 American College of Rheumatology/American Association of Hip and Knee Surgeons Guideline for the Perioperative Management of Antirheumatic Medication in Patients With Rheumatic Diseases Undergoing Elective Total Hip or Total Knee Arthroplasty. Arthritis Rheumatol. 2017 Aug;69(8):1538-1551.
7. Krieckaert CL, Bartelds GM, Lems WF, Wolbink GJ. The effect of immunomodulators on the immunogenicity of TNF-blocking therapeutic monoclonal antibodies: a review. Arthritis Res Ther. 2010;12(5):217.
8. Garcês S, Demengeot J, Benito-Garcia E. The immunogenicity of anti-TNF therapy in immune-mediated inflammatory diseases: a systematic review of the literature with a meta-analysis. Ann Rheum Dis. 2013 Dec;72(12):1947-55.

9. Kalden JR, Schattenkirchner M, Sorensen H, et al. The efficacy and safety of leflunomide in patients with active rheumatoid arthritis: A five-year followup study. Arthritis Rheum 2003;48(6):1513–1520.
10. Finckh A, Dehler S, Gabay C; SCQM doctors. The effectiveness of leflunomide as a co-therapy of tumour necrosis factor inhibitors in rheumatoid arthritis: a population-based study. Ann Rheum Dis. 2009 Jan;68(1):33-9.
11. Kremer JM, Genovese MC, Cannon GW, Caldwell JR, Cush JJ, Furst DE, Luggen ME, Keystone E, Weisman MH, Bensen WM, Kaine JL, Ruderman EM, Coleman P, Curtis DL, Kopp EJ, Kantor SM, Waltuck J, Lindsley HB, Markenson JA, Strand V, Crawford B, Fernando I, Simpson K, Bathon JM. Concomitant leflunomide therapy in patients with active rheumatoid arthritis despite stable doses of methotrexate. A randomized, double-blind, placebo-controlled trial. Ann Intern Med. 2002 Nov 5;137(9):726-33.
12. Osiri M, Shea B, Robinson V, Suarez-Almazor M, Strand V, Tugwell P, Wells G. Leflunomide for treating rheumatoid arthritis. Cochrane Database Syst Rev. 2003;(1):CD002047.
13. Meta-analysis of treatment termination rates among rheumatoid arthritis patients receiving disease-modifying anti-rheumatic drugs. Maetzel A, Wong A, Strand V, Tugwell P, Wells G, Bombardier C. Rheumatology (Oxford). 2000;39(9):975.
14. Garneau KL, Iversen MD, Tsao H, Solomon DH. Primary care physicians' perspectives towards managing rheumatoid arthritis: room for improvement. Arthritis Research & Therapy. 2011;13(6):R189.
15. Proudman SM, James MJ, Spargo LD, Metcalf RG, Sullivan TR, Rischmueller M, Flabouris K, Wechalekar MD, Lee AT, Cleland LG. Fish oil in recent onset rheumatoid arthritis: a randomised, double-blind controlled trial within algorithm-based drug use. Ann Rheum Dis. 2015 Jan;74(1):89-95.
16. Singh JA, Cameron C, Noorbaloochi S, Cullis T, Tucker M, Christensen R, Ghogomu ET, Coyle D, Clifford T, Tugwell P, Wells GA. Risk of serious infection in biological treatment of patients with rheumatoid arthritis: a systematic review and meta-analysis. Lancet. 2015 Jul 18;386(9990):258-65.
17. **NOR-SWITCH.** Jørgensen KK, Olsen IC, Goll GL, Lorentzen M, Bolstad N, Haavardsholm EA, Lundin KEA, Mørk C, Jahnsen J, Kvien TK; NOR-SWITCH study group. Switching from originator infliximab to biosimilar CT-P13 compared with maintained treatment with originator infliximab (NOR-SWITCH): a 52-week, randomised, double-blind, non-inferiority trial. Lancet. 2017 Jun 10;389(10086):2304-2316.
18. **PLANETAS.** Park W, Hrycaj P, Jeka S, Kovalenko V, Lysenko G, Miranda P, Mikazane H, Gutierrez-Ureña S, Lim M, Lee YA, Lee SJ, Kim H, Yoo DH, Braun J. A randomised, double-blind, multicentre, parallel-group, prospective study comparing the pharmacokinetics, safety, and efficacy of CT-P13 and innovator infliximab in patients with ankylosing spondylitis: the PLANETAS study. Ann Rheum Dis. 2013 Oct;72(10):1605-12.
19. **PLANETRA.** Yoo DH, Hrycaj P, Miranda P, Ramiterre E, Piotrowski M, Shevchuk S, Kovalenko V, Prodanovic N, Abello-Banfi M, Gutierrez-Ureña S, Morales-Olazabal L, Tee M, Jimenez R, Zamani O, Lee SJ, Kim H, Park W, Müller-Ladner U. A randomised, double-blind, parallel-group study to demonstrate equivalence in efficacy and safety of CT-P13 compared with innovator infliximab when coadministered with methotrexate in patients with active rheumatoid arthritis: the PLANETRA study.
Ann Rheum Dis. 2013 Oct;72(10):1613-20.
20. **EGALITY.** Griffiths CEM, Thaçi D, Gerdes S, Arenberger P, Pulka G, Kingo K, Weglowska J; EGALITY study group, Hattebuhr N, Poetzl J, Woehling H, Wuerth G, Afonso M. The EGALITY study: a confirmatory, randomized, double-blind study comparing the efficacy, safety and immunogenicity of GP2015, a proposed etanercept biosimilar, vs. the originator product in patients with moderate-to-severe chronic plaque-type psoriasis. Br J Dermatol. 2017 Apr;176(4):928-938.
21. Mason M, Currey HL, Barnes CG, Dunne JF, Hazleman BL, Strickland ID. Azathioprine in rheumatoid arthritis. Br Med J. 1969 Feb 15;1(5641):420-2.
22. Jeurissen ME, Boerbooms AM, van de Putte LB, Doesburg WH, Lemmens AM. Influence of methotrexate and azathioprine on radiologic progression in rheumatoid arthritis. A randomized, double-blind study. Ann Intern Med. 1991 Jun 15;114(12):999-1004.
23. Tugwell P, Pincus T, Yocum D, Stein M, Gluck O, Kraag G, McKendry R, Tesser J, Baker P, Wells G. Combination therapy with cyclosporine and methotrexate in severe rheumatoid arthritis. The Methotrexate-Cyclosporine Combination Study Group. N Engl J Med. 1995 Jul 20;333(3):137-41.
24. Kremer JM, Habros JS, Kolba KS, Kaine JL, Borton MA, Mengle-Gaw LJ, Schwartz BD, Wisemandle W, Mekki QA; Tacrolimus-Methotrexate Rheumatoid Arthritis Study Group. Tacrolimus in rheumatoid arthritis patients receiving concomitant methotrexate: a six-month, open-label study. Arthritis Rheum. 2003 Oct;48(10):2763-8.
25. **DRESS**. van Herwaarden N, van der Maas A, Minten MJ, et al. Disease activity guided dose reduction and withdrawal of adalimumab or etanercept compared with usual care in rheumatoid arthritis: open label, randomised controlled, non-inferiority trial. (DRESS) BMJ. 2015 Apr 9;350:h1389.
26. **BeSt Study.** Klarenbeek NB, Güler-Yüksel M, van der Kooij SM, et al.: The impact of four dynamic, goal-steered treatment strategies on the 5-year outcomes of rheumatoid arthritis patients in the BeSt study. Ann Rheum Dis 2011; 70: 1039–46.
27. **TICORA.** Grigor C, et al. Effect of a treatment strategy of **tight control** for rheumatoid arthritis (the **TICORA study**): a single-blind randomised controlled trial. Lancet. 2004 Jul 17-23;364(9430):263-9.
28. **TEMPO**. Klareskog Lars, van der Heijde Désirée, de Jager Julien P, et al. for the TEMPO (Trial of Etanercept and Methotrexate with Radiographic Patient Outcomes) study investigators. Therapeutic effect of the **combination** of **etanercept** and **methotrexate compared** with each treatment **alone** in patients with rheumatoid arthritis: double-blind randomised controlled trial. The Lancet Volume 363, Number 9410 28 February 2004.
29. **SWEFOT**. van Vollenhoven RF et al. Addition of **infliximab** compared with addition of sulfasalazine and hydroxychloroquine to methotrexate in patients with early rheumatoid arthritis (**Swefot** trial): 1-year results of a randomised trial. *Lancet* 2009 Aug 8; 374:459.

30. **TEAR**. Moreland LW, O'Dell JR, Paulus HE, et al. **TEAR** Investigators. A randomized comparative effectiveness study of **oral triple therapy versus etanercept plus methotrexate** in early, aggressive rheumatoid arthritis. Arthritis Rheum. 2012 Apr 16.
31. **RACAT**. O'Dell JR, Mikuls TR, et al. Therapies for active rheumatoid arthritis **after methotrexate failure**. N Engl J Med 2013. DOI: 10.1056/NEJMoa1303006. (**methotrexate/hydroxychloroquine/sulfasalazine vs etanercept/MTX**)
32. **EXXELERATE**. Smolen JS, Burmester GR, Combe B, et al. Head-to-head comparison of **certolizumab pegol versus adalimumab** in rheumatoid arthritis: 2-year efficacy and safety results from the randomised **EXXELERATE** study. Lancet. 2016 Nov 11.
33. **ATTEST**. Schiff M, Keiserman M, Codding C, et al. Efficacy and safety of abatacept or infliximab vs placebo in ATTEST: a phase III, multi-centre, randomised, double-blind, placebo-controlled study in patients with rheumatoid arthritis and an inadequate response to methotrexate. *Annals of the Rheumatic Diseases*. 2008;67(8):1096-1103.
34. **AMPLE**. Schiff M, Weinblatt ME, Valente R, et al. Head-to-head comparison of **subcutaneous abatacept versus adalimumab** for rheumatoid arthritis: two-year efficacy and safety findings from AMPLE trial. Ann Rheum Dis. 2014 Jan 1;73(1):86-94
35. **CERTAIN**. Smolen JS, Emery P, Ferraccioli GF, et al. **Certolizumab** pegol in rheumatoid arthritis patients with low to moderate activity: the **CERTAIN** double-blind, randomised, placebo-controlled trial. Ann Rheum Dis. 2014 Jan 15.
36. **FIN-RACO**. Mottonen T, Hannonen P, et al. Comparison of **combination** therapy with **single**-**drug** therapy in early rheumatoid arthritis: a randomised trial. **FIN-RACo trial** group. Lancet. 1999 May 8;353(9164):1568-73.
37. **GO-AFTER**. Smolen JS, Kay J, Doyle MK, et al. GO-AFTER study investigators. **Golimumab** in patients with active rheumatoid arthritis after treatment with tumour necrosis factor alpha inhibitors (**GO-AFTER** study): a multicentre, randomised, double-blind, placebo-controlled, phase III trial. Lancet. 2009 Jul 18;374(9685):210-21. Epub 2009 Jun 26.
38. **HOPEFUL**. Takeuchi T, Yamanaka H, Ishiguro N, et al. **Adalimumab**, a human anti-TNF monoclonal antibody, outcome study for the prevention of joint damage in Japanese patients with early rheumatoid arthritis: the **HOPEFUL 1** study. Ann Rheum Dis. 2014 Mar 1;73(3):536-43.
39. **OPTIMA.** Kavanaugh A, Fleischmann RM, Emery P, et al. Clinical, functional and radiographic consequences of achieving stable low disease activity and remission with adalimumab plus methotrexate or methotrexate alone in early rheumatoid arthritis: 26-week results from the randomised, controlled OPTIMA study. Ann Rheum Dis. 2013 Jan;72(1):64-71.
40. **PREMIER.** Breedveld FC, et al. The PREMIER study: A multicenter, randomized, double-blind clinical trial of combination therapy with adalimumab plus methotrexate versus methotrexate alone or adalimumab alone in patients with early, aggressive rheumatoid arthritis who had not had previous methotrexate treatment. Arthritis Rheum. 2005 Dec 29;54(1):26-37
41. **PRESERVE**. Smolen JS, Nash P, Durez P, et al. **Maintenance, reduction, or withdrawal of etanercept** after treatment with etanercept and methotrexate in patients with moderate rheumatoid arthritis (**PRESERVE**): a randomised controlled trial. Lancet 2013; online Jan 17.
42. l'Ami MJ, Krieckaert CL, et al. Successful reduction of overexposure in patients with rheumatoid arthritis with high serum adalimumab concentrations: an open-label, non-inferiority, randomised clinical trial. Ann Rheum Dis 2018;77:484–7.
43. Burmester GR, Landewé R, Genovese MC, Friedman AW, Pfeifer ND, Varothai NA, Lacerda AP. Adalimumab long-term safety: infections, vaccination response and pregnancy outcomes in patients with rheumatoid arthritis. Ann Rheum Dis. 2017 Feb;76(2):414-417.
44. Kremer JM, Weinblatt ME. Quantifying the hepatotoxic risk of alcohol consumption in patients with rheumatoid arthritis taking methotrexate. Ann Rheum Dis. 2018 Jan;77(1):e4.
45. Hazlewood GS, Barnabe C, Tomlinson G, Marshall D, Devoe D, Bombardier C. Methotrexate monotherapy and methotrexate combination therapy with traditional and biologic disease modifying antirheumatic drugs for rheumatoid arthritis: abridged Cochrane systematic review and network meta-analysis. BMJ. 2016 Apr 21;353:i1777.
46. O'Dell JR, Leff R, Paulsen G, Haire C, Mallek J, Eckhoff PJ, Fernandez A, Blakely K, Wees S, Stoner J, Hadley S, Felt J, Palmer W, Waytz P, Churchill M, Klassen L, Moore G. Treatment of rheumatoid arthritis with methotrexate and hydroxychloroquine, methotrexate and sulfasalazine, or a combination of the three medications: results of a two-year, randomized, double-blind, placebo-controlled trial. Arthritis Rheum. 2002 May;46(5):1164-70.
47. Genovese MC, Becker JC, Schiff M, Luggen M, Sherrer Y, Kremer J, Birbara C, Box J, Natarajan K, Nuamah I, Li T, Aranda R, Hagerty DT, Dougados M. Abatacept for rheumatoid arthritis refractory to tumor necrosis factor alpha inhibition. N Engl J Med. 2005 Sep 15;353(11):1114-23.
48. Jonathan Kay, Katherine S. Upchurch; ACR/EULAR 2010 rheumatoid arthritis classification criteria, Rheumatology, Volume 51, Issue suppl_6, 1 December 2012, Pages vi5–vi9.
49. van Everdingen AA, Jacobs JW, Siewertsz Van Reesema DR, Bijlsma JW. Low-dose prednisone therapy for patients with early active rheumatoid arthritis: clinical efficacy, disease-modifying properties, and side effects: a randomized, double-blind, placebo-controlled clinical trial. Ann Intern Med. 2002 Jan 1;136(1):1-12.
50. Bakker MF, Jacobs JW, Welsing PM, Verstappen SM, Tekstra J, Ton E, Geurts MA, van der Werf JH, van Albada-Kuipers GA, Jahangier-de Veen ZN, van der Veen MJ, Verhoef CM, Lafeber FP, Bijlsma JW; Utrecht Rheumatoid Arthritis Cohort Study Group. Low-dose prednisone inclusion in a methotrexate-based, tight control strategy for early rheumatoid arthritis: a randomized trial. Ann Intern Med. 2012 Mar 6;156(5):329-39.
51. The effect of glucocorticoids on joint destruction in rheumatoid arthritis. The Arthritis and Rheumatism Council Low-Dose Glucocorticoid Study Group. Kirwan JR N Engl J Med. 1995;333(3):142.
52. Morris SJ, Wasko MC, Antohe JL, Sartorius JA, Kirchner HL, Dancea S, Bili A. Hydroxychloroquine use associated with improvement in lipid profiles in rheumatoid arthritis patients. Arthritis Care Res (Hoboken). 2011 Apr;63(4):530-4.

53. Gotestam Skorpen C, Hoeltzenbein M, Tincani A, et al. The EULAR points to consider for use of antirheumatic drugs before pregnancy, and during pregnancy and lactation. Ann Rheum Dis. 2016 Feb 17. pii: annrheumdis-2015-208840.
54. Royal College of Ophtalmologists (RCOphth). Hydroxychloroquine and chloroquine retinopathy: recommendations on screening. 2018. Available from https://www.rcophth.ac.uk/wp-content/uploads/2018/03/Hydroxychloroquine-and-Chloroquine-Retinopathy-Screening-Guideline-and-Recommendations.pdf
55. Seideman P, Albertioni F, Beck O, Eksborg S, Peterson C. Chloroquine reduces the bioavailability of methotrexate in patients with rheumatoid arthritis - a possible mechanism of reduced hepatotoxicity. Arthritis Rheum 37 (1994): 830-3.
56. Kerbleski JF, Gottlieb AB. Dermatological complications and safety of anti-TNF treatments. Gut. 2009 Aug;58(8):1033-9.
57. Ciccarelli, Fedra, et al. Psoriasis induced by anti-tumor necrosis factor alpha agents: a comprehensive review of the literature. *Acta Dermatovenerologica Croatica* 24.3 (2016): 169-74.
58. Scheinfeld N. A review of rituximab in cutaneous medicine. Dermatol Online J. 2006 Jan 27;12(1):3.
59. Bird P, Griffiths H, Tymms K, Nicholls D, Roberts L, Arnold M, Burnet S, de Jager J, Scott J, Zochling J, Littlejohn G. The SMILE study -- safety of methotrexate in combination with leflunomide in rheumatoid arthritis. J Rheumatol. 2013 Mar;40(3):228-35.
60. Furst DE, Keystone EC, Braun J, et al Updated consensus statement on biological agents for the treatment of rheumatic diseases, 2011 Annals of the Rheumatic Diseases 2012;71:i2-i45.
61. Tilley BC, Alarcón GS, Heyse SP, Trentham DE, Neuner R, Kaplan DA, Clegg DO, Leisen JC, Buckley L, Cooper SM, Duncan H, Pillemer SR, Tuttleman M, Fowler SE. Minocycline in rheumatoid arthritis. A 48-week, double-blind, placebo-controlled trial. MIRA Trial Group. Ann Intern Med. 1995 Jan 5;122(2):81-9.
62. Lee EB, Daskalakis N, Xu C, Paccaly A, Miller B, Fleischmann R, Bodrug I, Kivitz A. Disease–drug interaction of sarilumab and simvastatin in patients with rheumatoid arthritis. Clinical pharmacokinetics. 2017 Jun 1;56(6):607-15.
63. Silverman E. et al. Leflunomide or Methotrexate for Juvenile Rheumatoid Arthritis. N Engl J Med 2005;352:1655-66.
64. Schiff MH, et al. Safety Analyses of Adalimumab (HUMIRA(R)) in Global Clinical Trials and US Postmarketing Surveillance of Patients With Rheumatoid Arthritis. Ann Rheum Dis. 2006 Feb 13.
65. Gibofsky A, Palmer WR, Keystone EC, Schiff MH, Feng J, McCroskery P, Baumgartner SW, Markenson JA. Rheumatoid arthritis disease-modifying antirheumatic drug intervention and utilization study: safety and etanercept utilization analyses from the RADIUS 1 and RADIUS 2 registries. J Rheumatol. 2011 Jan;38(1):21-8.
66. **ASSURE**. Weinblatt M, Combe B, Covucci A, Aranda R, Becker JC, Keystone E. Safety of the selective costimulation modulator abatacept in rheumatoid arthritis patients receiving background biologic and nonbiologic disease-modifying antirheumatic drugs: A one-year randomized, placebo-controlled study. Arthritis Rheum. 2006 Sep;54(9):2807-16.
67. **NICE 2018 Guidelines**. National Institute for Health and Care Excellence (2018) Rheumatoid arthritis in adults: management. NICE guideline [NG100].
68. Radner H, Neogi T, Smolen JS, et al. Performance of the **2010 ACR/EULAR classification criteria** for rheumatoid arthritis: a systematic literature review. Ann Rheum Dis. 2014 Jan 1;73(1):114-23
69. Aga AB, Lie E, Uhlig T, et al. **Time trends** in disease activity, response and remission rates in rheumatoid arthritis during the past decade: results from the NOR-DMARD study 2000-2010. Ann Rheum Dis. 2015 Feb;74(2):381-8.
70. Barnabe C, Jones CA, Bernatsky S, Peschken CA, Voaklander D, Homik J, Crowshoe LF, Esdaile JM, El-Gabalawy H, Hemmelgarn B. Inflammatory Arthritis Prevalence and Health Services Use in the First Nations and Non-First Nations Populations of Alberta, Canada. Arthritis Care Res (Hoboken). 2017 Apr;69(4):467-474.
71. Whittle SL, Hughes RA. Folate supplementation and methotrexate treatment in rheumatoid arthritis: a review. Rheumatology. 2004 Jan 6;43(3):267-71.
72. Hazlewood GS, Thorne JC, Pope JE, Lin D, Tin D, Boire G, Haraoui B, Hitchon CA, Keystone EC, Jamal S, Bykerk VP. The comparative effectiveness of oral versus subcutaneous methotrexate for the treatment of early rheumatoid arthritis. Annals of the rheumatic diseases. 2016 Jun 1;75(6):1003-8.
73. **tREACH**. De Jong PH, Hazes JM, Han HK, Huisman M, Van Zeben D, Van Der Lubbe PA, Gerards AH, van Schaeybroeck B, de Sonnaville PB, van Krugten MV, Luime JJ. Randomised comparison of initial triple DMARD therapy with methotrexate monotherapy in combination with low-dose glucocorticoid bridging therapy; 1-year data of the tREACH trial. Annals of the rheumatic diseases. 2014 Jul 1;73(7):1331-9.

Additional references:

Abhishek A, Doherty M, Kuo CF, et al. **Rheumatoid arthritis is getting less frequent**-results of a nationwide population-based cohort study. Rheumatology (Oxford). 2017 Jan 7.
Abou-Raya A, Abou-Raya S, Khadrawe T. **Retracted: Methotrexate in the treatment of symptomatic knee osteoarthritis**: randomised placebo-controlled trial. Ann Rheum Dis. 2018 Jul;77(7):e46.
Abou-Raya A, et al. Effect of **low-dose oral prednisolone** on symptoms and systemic inflammation in older adults with moderate to severe knee osteoarthritis: a randomized placebo-controlled trial. J Rheumatol. 2014 Jan;41(1):53-9.
Abou-Raya A, Abou-Raya S, Khadrawe T. **Methotrexate** in the treatment of symptomatic knee **osteoarthritis**: randomised placebo-controlled trial. Ann Rheum Dis. 2014 Mar 27.
Adab P, Jiang CQ, Rankin E, et al. Breastfeeding practice, oral contraceptive use and risk of rheumatoid arthritis among Chinese women: the Guangzhou Biobank Cohort Study. Rheumatology(Oxford). 2014 Jan 6.
Adler BL, Albayda J, Shores JT, et al. **Erosive Rheumatoid Arthritis** After Bilateral **Hand Transplantation**. Ann Intern Med. 2017 Aug 1;167(3):216-218
Agarwal SK, et al. Pattern of **infliximab utilization** in rheumatoid arthritis patients at an academic medical center. Arthritis Rheum. 2005 Dec;53(6):872-8.
Agca R, Heslinga SC, van Halm VP, et al. Atherosclerotic cardiovascular disease in patients with chronic inflammatory joint disorders. Heart. 2016 May 15;102(10):790-5.
Agca R, Heslinga SC, et al. **EULAR** recommendations for **cardiovascular disease risk management** in patients with rheumatoid arthritis and other forms of inflammatory joint disorders: 2015/2016 update. Ann Rheum Dis. 2016 Oct 3.
Ahmed AR, Spigelman Z, Cavacini LA, Posner MR. Treatment of **pemphigus vulgaris** with **rituximab** and intravenous immune globulin. N Engl J Med. 2006 Oct 26;355(17):1772-9.
Ahn CS, Dothard EH, Garner ML, et al. To test or not to test? An updated evidence-based assessment of the value of **screening and monitoring tests when using systemic biologic agents** to treat psoriasis and psoriatic arthritis. J Am Acad Dermatol. 2015 Sep;73(3):420-8.e1.
Ai JW, Zhang S, Ruan QL, et al. The Risk of **Tuberculosis** in Patients with Rheumatoid Arthritis Treated with **Tumor Necrosis Factor-alpha Antagonist**: A Metaanalysis of Both Randomized Controlled Trials and Registry/Cohort Studies.

Ajeganova S, Andersson ML, Frostegard J, et al. Disease Factors in Early Rheumatoid Arthritis Are Associated with Differential **Risks for Cardiovascular Events** and Mortality Depending on Age at Onset: A 10-year Observational Cohort Study. J Rheumatol. 2013 Aug 15.

Akdemir G, Heimans L, Bergstra SA, et al. Clinical and radiological outcomes of **5-year drug-free remission-steered treatment** in patients with early arthritis: **IMPROVED** study. Ann Rheum Dis. 2018 Jan;77(1):111-118.

Aksentijevich I, Masters SL, Ferguson PJ,et al. An Autoinflammatory Disease with Deficiency of the Interleukin-1-Receptor Antagonist. (**DIRA**) N Engl J Med. 2009 Jun 4;360(23):2426-2437.

J Rheumatol. 2015 Oct 15. pii: jrheum.150057.

Alarcon GS, McGwin G, Bertoli AM, et al. Effect of **hydroxychloroquine** on the survival of patients with systemic **lupus** erythematosus: data from LUMINA, a multiethnic US cohort (LUMINA L). Ann Rheum Dis 2007;66:1168-72.

Albrecht K, Callhoff J, Buttgereit F, et al. The association between the use of oral contraceptives and patient-reported outcomes in an early arthritis cohort. Arthritis Care Res (Hoboken). 2015 Aug 14.

Aletaha D, Neogi T, Silman AJ, et al. **2010 rheumatoid arthritis classification criteria**: an American College of Rheumatology (ACR)/European League Against Rheumatism (EULAR) collaborative initiative. Ann Rheum Dis. 2010 Sep;69(9):1580-8. In the new criteria set, classification as 'definite RA' is based on the confirmed presence of synovitis in at least one joint, absence of an alternative diagnosis better explaining the synovitis, and achievement of a total score of 6 or greater (of a possible 10) from the individual scores in four domains: number and site of involved joints (range 0-5), serological abnormality (range 0-3), elevated acute-phase response (range 0-1) and symptom duration (two levels; range 0-1).

Aletaha Daniel, Funovits Julia, Smolen Josef S. **Physical disability** in rheumatoid arthritis is associated with cartilage damage rather than bone destruction. Ann Rheum Dis 2011;70:733-739 Published Online First: 14 February 2011.

Aletaha D, Alasti F, Smolen JS. **Rheumatoid arthritis near remission**: clinical rather than laboratory inflammation is associated with radiographic progression. Ann Rheum Dis. 2011 Nov;70(11):1975-80.

Aletaha D, Alasti F, Smolen JS. **Optimisation of a treat-to-target approach** in rheumatoid arthritis: strategies for the 3-month time point. Ann Rheum Dis. 2016 Aug;75(8):1479-85.

Aletaha D, Bingham CO III, Tanaka Y, et al. Efficacy and safety of **sirukumab** in patients with active rheumatoid arthritis refractory to anti-TNF therapy (SIRROUND-T): a randomised, double-blind, placebo-controlled, parallel-group, multinational, phase 3 study. Lancet 2017; online Feb 15

Aletaha D, Smolen JS. Diagnosis and Management of **Rheumatoid Arthritis**: A Review. JAMA. 2018 Oct 2;320(13):1360-1372.

Alivernini S, Tolusso B, Petricca L, et al. **Synovial features** of patients with rheumatoid arthritis and psoriatic arthritis in clinical and ultrasound remission differ under **anti-TNF therapy**: a clue to interpret different chances of relapse after clinical remission? Ann Rheum Dis. 2017 Jul;76(7):1228-1236.

Almeida C, Choy EHS, Hewlett S, Kirwan JR, Cramp F, Chalder T, Pollock J, Christensen R. Biologic interventions for fatigue in rheumatoid arthritis. Cochrane Database of Systematic Reviews 2016, Issue 6. Art. No.: CD008334. Treatment with biologic interventions in patients with active RA can lead to a small tomoderate improvement in fatigue. Themagnitude of improvement is similar for anti-TNF and non-anti-TNF biologics. However, it is unclear whether the improvement results from a direct action of the biologics on fatigue or indirectly through reduction in inflammation, disease activity or some other mechanism.

Alten R, Kaine J, Keystone E, et al. Long-term safety of **subcutaneous abatacept** in rheumatoid arthritis: Integrated analysis of clinical trial data of up to 4.75 years of treatment. Arthritis Rheumatol. 2014 Apr 29.

Alten R, Kaine J, Keystone E, et al. Long-term safety of **subcutaneous abatacept** in rheumatoid arthritis: integrated analysis of clinical trial data representing more than four years of treatment. Arthritis Rheumatol. 2014 Aug;66(8):1987-97.

Arabelovic S, et al. Preliminary evidence shows that folic acid fortification of the food supply is associated with higher methotrexate dosing in patients with rheumatoid arthritis. J Am Coll Nutr. 2007 Oct;26(5):453-5.This preliminary study suggests that folic acid supplementation may contribute to higher MTX dosing in patients with RA.

Araujo EG, Finzel S, Englbrecht M, et al. **High incidence of disease recurrence after discontinuation of disease-modifying antirheumatic** drug treatment in patients with **psoriatic arthritis** in remission. Ann Rheum Dis. 2015 Apr; 74(4):655-60.

Ardalan ZS, Vasudevan A, Testro AG. **Arthralgia and Fevers** in a Patient With Autoimmune **Hepatitis**. JAMA. 2016 Jul 5;316(1):91-92.

Arkema EV, Neovius M, Joelsson JK, et al. Is there a **sex bias in prescribing anti-tumour necrosis factor** medications to patients with rheumatoid arthritis? A nation-wide cross-sectional study. Ann Rheum Dis. 2012 Apr 13.

Arkema EV, van Vollenhoven RF, Askling J; ARTIS Group. Incidence of **progressive multifocal leukoencephalopathy (PML)** in patients with rheumatoid arthritis: a national population-based study. Ann Rheum Dis. 2012 Nov;71(11):1865-1867.

Arkema EV, Hart JE, Bertrand KA, et al. Exposure to **ultraviolet-B** and risk of developing rheumatoid arthritis among women in the Nurses' Health Study. Ann Rheum Dis. 2013 Apr;72(4):506-11.

Arkema EV, Jonsson J, Baecklund E, et al; ARTIS Study Group. Are patients with rheumatoid arthritis still at an increased risk of **tuberculosis and what is the role of biological treatments**? Ann Rheum Dis. 2015 Jun;74(6):1212-7.

Armbrust W, Bos GJFJ, et al. Internet Program for **Physical Activity and Exercise Capacity in Children With Juvenile Idiopathic Arthritis**: A Multicenter Randomized Controlled Trial. Arthritis Care Res (Hoboken). 2017 Jul;69(7):1040-1049.

Arts E E A, Jansen T L, Broeder A Den, et al. **Statins inhibit the antirheumatic effects of rituximab** in rheumatoid arthritis: results from the Dutch Rheumatoid Arthritis Monitoring (DREAM) registry. Ann Rheum Dis 2011;**70**:877-878 Published Online First: 18 October 2010 doi:10.1136/ard.2010.136093.

Arts EE, Fransen J, den Broeder AA, et al. The effect of disease duration and disease activity on the **risk of cardiovascular disease** in rheumatoid arthritis patients. Ann Rheum Dis. 2014 Jan 23.

Arts EE, Popa C, Den Broeder AA, Semb et al. Performance of **four current risk algorithms in predicting cardiovascular events** in patients with early rheumatoid arthritis. Ann Rheum Dis. 2015 Apr; 74(4):668-74.

Arts EE, Popa CD, Den Broeder AA, et al. **Prediction of cardiovascular risk** in rheumatoid arthritis: performance of original and adapted SCORE algorithms. Ann Rheum Dis. 2016 Apr;75(4):674-80.

Arts EE, Fransen J, et al. Low disease activity (DAS28≤3.2) reduces the **risk of first cardiovascular event** in rheumatoid arthritis: a time-dependent Cox regression analysis in a large cohort study. Ann Rheum Dis. 2017 Oct;76(10):1693-1699

Ash Z, Gaujoux-Viala C, Gossec L, et al. A systematic literature review of drug therapies for the treatment of psoriatic arthritis: current evidence and meta-analysis informing the **EULAR** recommendations for the management of **psoriatic arthritis**. Ann Rheum Dis. 2011 Jul 28.

Askling J, van Vollenhoven RF, Granath F, et al. **Cancer risk** in patients with rheumatoid arthritis treated with anti-tumor necrosis factor alpha therapies: Does the risk change with the time since start of treatment? Arthritis Rheum. 2009 Oct 29;60(11):3180-3189. During the first 6 years after the start of anti-TNF therapy in routine care, no overall elevation of cancer risk and no increase with followup time were observed.

Atsumi T, Yamamoto K, Takeuchi T, et al. The first double-blind, randomised, parallel-group **certolizumab pegol study in methotrexate-naive** early rheumatoid arthritis patients with poor prognostic factors, C-OPERA, shows inhibition of radiographic progression. Ann Rheum Dis. 2016 Jan;75(1):75-83.

Atsumi T, Tanaka Y, Yamamoto K, et al. Clinical benefit of 1-year **certolizumab** pegol (CZP) add-on therapy to methotrexate treatment in patients with early rheumatoid arthritis was observed following CZP discontinuation: 2-year results of the **C-OPERA** study, a phase III randomized trial. Ann Rheum Dis. 2017 Aug;76(8):1348-1356.

Au WY, Ma ES, Choy C, Chung LP, Fung TK, Liang R, Kwong YL. Therapy-related **lymphomas** in patients with autoimmune diseases after treatment with disease-modifying anti-rheumatic drugs. Am J Hematol. 2006 Jan;81(1):5-11.

Avina-Zubieta JA, Thomas J, Sadatsafavi M et al. Risk of incident **cardiovascular events** in patients with rheumatoid arthritis: a meta-analysis of observational studies. Ann Rheum Dis. 2012 Sep;71(9):1524-9.

Aviña-Zubieta JA, Abrahamowicz M, et al. Immediate and past cumulative effects of **oral glucocorticoids on the risk of acute myocardial infarction** in rheumatoid arthritis: a population-based study. Rheumatology. 2013;52:68-75.

Axelsen MB, Eshed I, Hørslev-Petersen K, et al; **OPERA** study group. A treat-to-target strategy with **methotrexate and intra-articular triamcinolone** with or without **adalimumab** effectively reduces MRI synovitis, osteitis and tenosynovitis and halts structural damage progression in early rheumatoid arthritis: results from the OPERA randomised controlled trial. Ann Rheum Dis. 2014 Jan 16.

Bacani AK, Gabriel SE, Crowson CS, et al. Noncardiac vascular disease in rheumatoid arthritis: increase in **venous thromboembolic** events?. Arthritis Rheum. 2012 Jan;64(1):53-61.

Baddley JW, Winthrop KL, Chen L, et al. **Non-viral opportunistic infections** in new users of tumour necrosis factor inhibitor therapy: results of the SAfety Assessment of Biologic ThERapy (SABER) Study. Ann Rheum Dis. 2014 Nov;73(11):1942-8.

Bae SC, Kim J, Choe JY, et al. A phase III, multicentre, randomised, double-blind, active-controlled, parallel-group trial comparing safety and efficacy of **HD203, with innovator etanercept**, in combination with methotrexate, in patients with rheumatoid arthritis: the HERA study. Ann Rheum Dis 2017;76:65–71.

Baker JF, Ostergaard M, Emery P, et al. **Early MRI measures** independently predict 1-year and 2-year radiographic progression in rheumatoid arthritis: secondary analysis from a large clinical trial Ann Rheum Dis. 2014 Nov;73(11):1968-74.

Baker JF, Sauer BC, Cannon GW, et al. **Changes in Body Mass** Related to the Initiation of Disease Modifying Therapies in Rheumatoid Arthritis. Arthritis Rheumatol. 2016 Feb 16.

Bakker MF, Jacobs JW, Welsing PM, et al. the Utrecht Arthritis Cohort Study Group. **Early clinical response to treatment predicts 5-year outcome** in RA patients: follow-up results from the CAMERA study. Ann Rheum Dis. 2011 Mar 15.

Bakker MF, Jacobs JW, Welsing PM, Verstappen SM, Tekstra J, Ton E, et al. **Low-dose prednisone** inclusion into a **methotrexate-based**, tight control strategy for early rheumatoid arthritis. A randomized trial. Ann Intern Med. 2012;156:329-39.

Bachelez H, van de Kerkhof PCM, Strohal R, et al, for the OPT Compare Investigators. **Tofacitinib versus etanercept** or placebo in moderate-tosevere chronic plaque psoriasis: a phase 3 randomised non-inferiority trial. Lancet 2015; online June 5.

Bansback N, Shojania K, Lacaille D. **Improving patient-centred care** for rheumatoid arthritis. CMAJ. 2016 Oct 4;188(14):999-1000.

Bansback N, Phibbs CS, Sun H, et al; CSP 551 **RACAT** Investigators. **Triple therapy (methotrexate, sulfasalazine, hydroxychloroquine) versus biologic therapy (methtotrexate plus etanercept)** for active rheumatoid arthritis. A cost-effectiveness analysis. Ann Intern Med. 2017. [Epub ahead of print]. doi:10.7326/M16-0713

Bansback N, Phibbs CS, Sun H, et al; CSP 551 RACAT Investigators. **Triple therapy versus biologic therapy for active rheumatoid arthritis**. A **cost-effectiveness** analysis. Ann Intern Med. 2017;167:8-16.

Baraliakos X, Haibel H, Listing J, et al. Continuous **long-term anti-TNF therapy** does **not** lead to an increase in the rate of new **bone formation** over 8 years in patients with ankylosing spondylitis. Ann Rheum Dis. 2014 Apr 1;73(4):710-5.

Baranauskaite A, Raffayová H, Kungurov N, et al. **Infliximab plus methotrexate** is superior to methotrexate alone in the treatment of **psoriatic arthritis** in methotrexate-naive patients: the **RESPOND** study. Ann Rheum Dis. 2012 Apr;71(4):541-8.

Barnabe C, Thanh NX, Ohinmaa A, et al. **Healthcare service utilisation costs** are reduced when rheumatoid arthritis patients achieve sustained remission. Ann Rheum Dis. 2013 Oct 1;72(10):1664-8.

Barnes PJ, Adcock IM. **Glucocorticoid resistance** in inflammatory diseases. Lancet. 2009 May 30;373(9678):1905-17.

Barsalou J, Costedoat-Chalumeau N, Berhanu A, et al. Effect of in **utero hydroxychloroquine exposure on the development of cutaneous neonatal lupus erythematosus**. Ann Rheum Dis. 2018 Dec;77(12):1742-1749.

Bartalesi F, Bartoloni A, Bisoffi Z, et al. The emerging problem of **biological treatment in migrant and travelling populations**: it is time to extend guidelines for the screening of infectious diseases. Ann Rheum Dis. 2014 May 1;73(5):794-6.
Bartelds GM, Wijbrandts CA, Nurmohamed MT, et al. **Anti-infliximab and anti-adalimumab antibodies** in relation to response to adalimumab in infliximab switchers and anti-TNF naive patients: a cohort study. Ann Rheum Dis. 2009 Jul 5.
Bartelds Geertje M., Krieckaert Charlotte L. M., Nurmohamed Michael T., et al. Development of **Antidrug Antibodies Against Adalimumab** and Association With Disease Activity and Treatment Failure During Long-term Follow-up. *JAMA.* 2011;305(14):1460-1468.doi:10.1001/jama.2011.406
Baser O, Ganguli A, Roy S, et al. Impact of **Switching From an Initial Tumor Necrosis Factor Inhibitor** on Health Care Resource Utilization and Costs Among Patients With Rheumatoid Arthritis. Clin Ther. 2015 May 18.
Bastida C, Ruíz V, Pascal M, et al. Is there potential for **Therapeutic Drug Monitoring of Biologic Agents** in Rheumatoid Arthritis? Br J Clin Pharmacol. 2016 Dec 19.
Bastida C, Ruiz-Esquide V, Pascal M, et al. Fixed dosing of intravenous **tocilizumab** in rheumatoid arthritis. Results from a population pharmacokinetic analysis. Br J Clin Pharmacol. 2018 Apr;84(4):716-725.
Baszis K, Garbutt J, Toib D, et al. Clinical outcomes after **withdrawal of anti-tumor necrosis factor-alpha therapy in juvenile idiopathic arthritis**: A twelve-year experience. Arthritis Rheum. 2011 Jun 23. doi: 10.1002/art.30502.
Bathon JM, Martin RW, et al A comparison of **etanercept** and **methotrexate** in patients with **early** rheumatoid arthritis. (**ERA trial**) N Engl J Med. 2000 Nov 30;343(22):1586-93.
Bathon J, Robles M, et al. Sustained disease remission and inhibition of radiographic progression in methotrexate-naïve patients with rheumatoid arthritis and poor prognostic factors treated with **abatacept**: 2-year outcomes. (**AGREE**) Ann Rheum Dis. 2011 Nov;70(11):1949-56.
Bathon JM, Giles JT, Solomon DH. TNF Antagonists: **Killing Two "Birds" with one Biologic "Stone**". Arthritis Rheumatol. 2017 Nov 16.
Bejan-Angoulvant T, Ternant D, Daoued F, et al. Relationship Between **Serum Infliximab Concentrations and Risk of Infections** in Patients Treated for Spondyloarthritis. Arthritis Rheumatol. 2016 Nov 28.
Belkhir R, Burel SL, Dunogeant L. Rheumatoid arthritis and polymyalgia rheumatica occurring **after immune checkpoint inhibitor treatment**. Ann Rheum Dis. 2017;76:1747-1750
Ben-Zvi I, Kukuy O, Giat E, et al. **Anakinra for colchicine resistant familial Mediterranean fever** - A randomized, double blind, placebo-controlled trial. Arthritis Rheumatol. 2016 Nov 11.
Bensalem A, Mulleman D, Thibault G, et al. CD4+ count-dependent concentration-effect relationship of **rituximab** in rheumatoid arthritis. Br J Clin Pharmacol. 2019 Aug 27.
Bengtsson C, Padyukov L, Källberg H, et al. **Thyroxin substitution** and the risk of developing rheumatoid arthritis; results from the Swedish population-based EIRA study. Ann Rheum Dis. 2014 Jun 1;73(6):1096-100.
Bérard A, Zhao JP, Shui I, et al. **Leflunomide use during pregnancy** and the risk of adverse pregnancy outcomes. Ann Rheum Dis. 2018 Apr;77(4):500-509.
Berger CT, Rebholz-Chaves B, Recher M, et al. **Serial IL-6 measurements** in patients with tocilizumab-treated large-vessel vasculitis **detect infections and may predict early relapses**. Ann Rheum Dis. 2019 Jul;78(7):1012-1014.
Bergstra SA, Allaart CF, Stijnen T, et al. Meta-Regression of a **Dose-Response Relationship of Methotrexate** in Mono- and Combination Therapy in Disease-Modifying Antirheumatic Drug-Naive Early Rheumatoid Arthritis Patients. Arthritis Care Res (Hoboken). 2017 Oct;69(10):1473-1483.
Bergstra SA, Branco JC, Vega-Morales D, et al. **Inequity in access to DMARD care** and how it influences disease outcomes across countries worldwide: results from the METEOR-registry. Ann Rheum Dis. 2018 Oct;77(10):1413-1420.
Bergstra SA, Winchow LL, Murphy E, et al. How to treat **patients with rheumatoid arthritis when methotrexate has failed**? The use of a multiple propensity score to adjust for confounding by indication in observational studies. Ann Rheum Dis. 2019 Jan;78(1):25-30.
Bernatsky S, Clarke AE, Suissa S. Hematologic **malignant neoplasms** after drug exposure in rheumatoid arthritis. Arch Intern Med. 2008 Feb 25;168(4):378-81. In this large cohort of patients with rheumatoid arthritis, the greatest relative risk for hematologic malignant neoplasms was noted after use of cyclophosphamide.
Bertsias GK, Tektonidou M, Amoura Z, et al. Joint European League Against Rheumatism and European Renal Association-European Dialysis and Transplant Association (EULAR/ERA-EDTA) recommendations for the management of adult and paediatric **lupus nephritis**. Ann Rheum Dis. 2012 Nov;71(11):1771-82.
Best JH, Kong AM, et al. Association Between **Glucocorticoid Exposure and Healthcare Expenditures** for Potential Glucocorticoid-related Adverse Events in Patients with Rheumatoid Arthritis. J Rheumatol. 2018 Mar;45(3):320-328.
Beukelman T, Patkar NM, Saag KG, et al. **2011 American College of Rheumatology** recommendations for the treatment of **juvenile idiopathic arthritis**: Initiation and safety monitoring of therapeutic agents for the treatment of arthritis and systemic features. Arthritis Care Res(Hoboken). 2011 Apr;63(4):465-82. doi: 10.1002/acr.20460. http://www.rheumatology.org/practice/clinical/guidelines/ACR_2011_jia_full_manuscript.pdf
Beukelman T, Haynes K, Curtis JR, et al. Rates of **malignancy associated with juvenile idiopathic arthritis** and its treatment. Arthritis Rheum. 2012 Feb 10.
Beukelman T, Xie F, Chen L, et al; On behalf of the Safety Assessment of Biological ThERapeutics (SABER) Collaboration. Rates of **hospitalized bacterial infection** associated with juvenile idiopathic arthritis and its treatment. Arthritis Rheum. 2012 May 8.
Beukelman T, Xie F, Chen L, et al. Risk of **malignancy associated with paediatric use of tumour necrosis factor inhibitors**. Ann Rheum Dis. 2018 Jul;77(7):1012-1016.
Beukelman T, Xie F, et al; On behalf of the Safety Assessment of Biological ThERapeutics (SABER) Collaboration. Incidence of selected **opportunistic infections** among children with **juvenile idiopathic arthritis**. Arthritis Rheum. 2013 Mar 4.
Bijlsma JW, Welsing PM, Woodworth TG, et al. **Early rheumatoid arthritis** treated with **tocilizumab, methotrexate,** or their **combination (U-Act-Early):** multicentre, randomised, double-blind, double-dummy, strategy trial. Lancet. 2016 Jun 7.
Binder A, Ellis S. When to **order an antinuclear antibody test**. BMJ. 2013 Aug 21;347:f5060.
Bingham CO 3rd, et al. **Immunization** responses in rheumatoid arthritis patients treated with **rituximab**: Results from a controlled clinical trial. Arthritis Rheum. 2009 Dec 28;62(1):64-74.
Bingham CO 3rd, Weinblatt M, Han C, et al. The Effect of Intravenous **Golimumab** on Health-related Quality of Life in Rheumatoid Arthritis: 24-week Results of the Phase III GO-FURTHER Trial. J Rheumatol. 2014 Jun;41(6):1067-76.
Bingham CO 3rd, Rizzo W, Kivitz A, Hassanali A, et al. **Humoral immune response to vaccines** in patients with rheumatoid arthritis treated with **tocilizumab**: results of a randomised controlled trial (VISARA). Ann Rheum Dis. 2014 Jan 21.
Bisset L, et al. Mobilisation with movement and exercise, corticosteroid injection, or wait and see for **tennis elbow**: randomised trial. BMJ. 2006 Nov 4;333(7575):939. Epub 2006 Sep 29.
Bitoun S, Miceli-Richard C, Verstuyft C, et al. Frequency of **tumour necrosis factor alpha receptor superfamily 1A multiple sclerosis-associated variants in patients with rheumatoid arthritis** with anti-tumour necrosis factor therapy-related demyelinating complications. Ann Rheum Dis. 2018 Dec;77(12):1835-1836.
Bitoun S, Nocturne G, Ly B, et al. **Methotrexate and BAFF interaction prevents immunization against TNF inhibitors**. Ann Rheum Dis. 2018 Oct;77(10):1463-1470.
Björnsson ES, Bergmann OM, Björnsson HK, et al. Incidence, presentation, and outcomes in patients with **drug-induced liver injury** in the general population of iceland. Gastroenterology. 2013 Jun;144(7):1419-1425.e3. In a population-based study in Iceland, the incidence of DILI was the highest reported to date. Amoxicillin-clavulanate was the most commonly implicated agent. The highest risk of hepatotoxicity was associated with azathioprine and **infliximab**, but the actual number of cases attributed to these agents was small.
Blanco FJ, Möricke R, Dokoupilova E, et al. **Secukinumab** in active rheumatoid arthritis: A randomized, double-blind placebo and active comparator controlled phase 3 study. Arthritis Rheumatol. 2017 Feb 19.
Bliddal H, et al. A randomized, controlled study of a single **intra-articular** injection of **etanercept** or glucocorticosteroids in patients with rheumatoid arthritis. Scand J Rheumatol. 2006 Sep-Oct;35(5):341-5.
Bluett J, Morgan C, Thurston L, et al; on behalf of BRAGGSS. Impact of **inadequate adherence on response to subcutaneously administered anti-tumour necrosis** factor drugs: results from the Biologics in Rheumatoid Arthritis Genetics and Genomics Study Syndicate cohort. Rheumatology (Oxford). 2014 Sep 10.
Bluett J, Riba-Garcia I, Verstappen SMM, et al. Development and validation of a **methotrexate adherence assay**. Ann Rheum Dis. 2019 Sep;78(9):1192-1197.
Bodar EJ, Kuijk LM, Drenth JP, et al. On-demand **anakinra** treatment is effective in **mevalonate kinase deficiency**. Ann Rheum Dis. 2011 Dec;70(12):2155-8.
Boers M, Verhoeven AC, et al. Randomised comparison of combined step-down **prednisolone**, **methotrexate and sulphasalazine** with **sulphasalazine alone** in early rheumatoid arthritis. Lancet. 1997 Aug 2;350(9074):309-18.
Boers M, van Tuyl L, van den Broek M, et al. Meta-analysis suggests that **intensive non-biological combination therapy with step-down prednisolone** (COBRA strategy) may also 'disconnect' disease activity and damage in rheumatoid arthritis. Ann Rheum Dis. 2013 Mar;72(3):406-9.
Boeters DM, Burgers LE, Toes RE, et al. Does **immunological remission**, defined as disappearance of autoantibodies, occur with current treatment strategies? A long-term follow-up study in rheumatoid arthritis patients who achieved sustained DMARD-free status. Ann Rheum Dis. 2019 Nov;78(11):1497-1504.
Boeters DM, Nieuwenhuis WP, van Steenbergen HW, et al. Are **MRI-detected erosions specific for RA**? A large explorative cross-sectional study. Ann Rheum Dis. 2018 Jun;77(6):861-868.
Bolge SC, Carter CT, Mueller CS, et al. Comparative multidatabase analysis of **dosing patterns and infusion intervals for the first 12 infliximab infusions** in patients with rheumatoid arthritis. Clin Ther. 2012 Dec;34(12):2286-92.
Bombardier C, Hazlewood GS, Akhavan P, et al. **Canadian Rheumatology Association** recommendations for the pharmacological management of rheumatoid arthritis with **traditional and biologic** disease-modifying antirheumatic drugs: Part II **safety**. J Rheumatol First Release June 15 2012. http://www.jrheum.org/content/early/2012/06/11/jrheum.120165.full.pdf .
Bongartz T, et al. Anti-TNF antibody therapy in rheumatoid arthritis and the risk of **serious infections & malignancies**: systematic review & meta-analysis of rare harmful effects in randomized controlled trials. JAMA. 2006 May 17;295(19):2275-85. (see also Pharmacist's Letter July 2006) Malignancies were significantly more common in patients treated with higher doses compared with patients who received lower doses of anti-TNF antibodies. For patients treated with anti-TNF antibodies in the included trials, the number needed to harm was 154 (95% CI, 91-500) for 1 additional malignancy within a treatment period of 6 to 12 months. For serious infections, the number needed to harm was 59 (95% CI, 39-125) within a treatment period of 3 to 12 months. (Health Canada July/06 Possible Association of REMICADE® with hepatosplenic T-cell lymphoma in pediatric and young adult patients with Crohn's disease http://www.hc-sc.gc.ca/dhp-mps/medeff/advisories-avis/prof/2006/remicade_3_hpc-cps_e.html) (Setoguchi S, et al. Tumor necrosis factor alpha antagonist use and cancer in patients with rheumatoid arthritis. Arthritis Rheum. 2006 Aug 31;54(9):2757-2764 [Epub ahead of print] Our results indicate that users of biologic agents are unlikely to have a substantial increase in the risk of hematologic malignancies and solid tumors as compared with MTX users. Despite the use of large combined data sets, studying the effect of an infrequent exposure (biologic DMARDs) on rare diseases (hematologic malignancies) remains a challenge.) (Wolfe F, Michaud K. The effect of methotrexate and anti-tumor necrosis factor therapy on the risk of lymphoma in rheumatoid arthritis in 19,562 patients during 89,710 person-years of

observation. Arthritis Rheum. 2007 May;56(5):1433-9. In a study of lymphoma in 19,591 RA patients over 89,710 person-years of followup, which included exposure to anti-TNF therapy in 10,815 patients, we did not observe evidence for an increase in the incidence of lymphoma among patients who received anti-TNF therapy.)

Bose N, Calabrese LH. Q: Should I **order an anti-CCP antibody test** to diagnose rheumatoid arthritis? Cleve Clin J Med. 2012 Apr;79(4):249-52.

Bouman CA, Herwaarden NV, van den Hoogen FH, et al. Long-term outcomes **after disease activity-guided dose reduction of TNF inhibition in rheumatoid arthritis: 3-year** data of the **DRESS** study - a randomised controlled pragmatic non-inferiority strategy trial. Ann Rheum Dis. 2017 Jun 12.

Bourre-Tessier J, Haraoui B. **Methotrexate drug interactions** in the treatment of rheumatoid arthritis: a systematic review. J Rheumatol. 2010 Jul;37(7):1416-21. Epub 2010 May 1.

Brandt J, Khariouzov A, et al. Six-month results of a double-blind, placebo-controlled trial of **etanercept** treatment in patients with active **ankylosing spondylitis**. Arthritis Rheum. 2003 Jun;48(6):1667-75.

Braschi E, Shojania K, Allan GM. **Anti-CCP**: a truly helpful rheumatoid arthritis test? Can Fam Physician. 2016 Mar;62(3):234.

Braun J, Brandt J, et al. Treatment of active **ankylosing spondylitis** with **infliximab**: a randomised controlled multicentre trial. Lancet. 2002 Apr 6;359(9313):1187-93.

Braun J, et al. Long-term efficacy & safety of **infliximab** in **ankylosing spondylitis**: an open, observational, extension study of a 3month, randomized, placebo-controlled trial. Arthritis Rheum. 2003 Aug;48(8):2224-33.

Braun J, Kästner P, Flaxenberg P, et al; MC-MTX.6/RH Study Group. Comparison of the clinical efficacy and safety of **subcutaneous (15-20mg) versus oral administration of methotrexate** (15mg) in patients with active rheumatoid arthritis: results of a six-month, multicenter, randomized, double-blind, controlled, phase IV trial. Arthritis Rheum. 2008 Jan;58(1):73-81. This 6-month prospective, randomized, controlled trial is the first to examine oral versus SC administration of MTX. We found that SC administration was significantly more effective than oral administration of the same MTX dosage. There was no difference in tolerability.

Braun J, Davis J, Dougados M, et al. First update of the international ASAS consensus statement for the use of anti-TNF agents in patients with **ankylosing spondylitis**. Ann Rheum Dis 2006; 65: 316–20.

Braun J, van den Berg R, Baraliakos X, et al. **2010 update of the ASAS/EULAR recommendations** for the management of **ankylosing spondylitis**. Ann Rheum Dis 2011;70:896-904 doi:10.1136/ard.2011.151027.

Braun J, Deodhar A, Inman RD, van et al. **Golimumab** administered subcutaneously every 4 weeks in **ankylosing spondylitis**: 104-week results of the GO-RAISE study. Ann Rheum Dis. 2011 Nov 11.

Braun J, Baraliakos X, Hermann KG, et al. **Golimumab** reduces spinal inflammation in **ankylosing spondylitis**: MRI results of the randomised, placebo- controlled GO-RAISE study. Ann Rheum Dis. 2012 Jun;71(6):878-84.

Braun J, Baraliakos X, Hermann KG, et al. The effect of two **golimumab** doses on radiographic progression in ankylosing spondylitis: results through 4 years of the GO-RAISE trial. Ann Rheum Dis. 2014 Jun 1;73(6):1107-13.

Braun J, Baraliakos X, Deodhar A, et al. Effect of **secukinumab** on clinical and radiographic outcomes in ankylosing spondylitis: 2-year results from the randomised phase III MEASURE 1 study. Ann Rheum Dis. 2017 Jun;76(6):1070-1077.

Breedveld FC, et al. The PREMIER study: A multicenter, randomized, double-blind clinical trial of combination therapy with adalimumab plus methotrexate versus methotrexate alone or adalimumab alone in patients with early, aggressive rheumatoid arthritis who had not had previous methotrexate treatment. Arthritis Rheum. 2005 Dec 29;54(1):26-37 [Epub ahead of print]

Bresnihan B, Newmark R, Robbins S, Genant HK. Effects of **anakinra** monotherapy on joint damage in patients with rheumatoid arthritis. Extension of a 24-week randomized, placebo-controlled trial. J Rheumatol. 2004 Jun;31(6):1103-11.

Bridges SL Jr., White DW, Worthing AB, et al. The **Science Behind Biosimilars**: Entering a New Era of Biologic Therapy. Arthritis Rheumatol. 2018 Feb 7.

Bronckers IMGJ, Seyger MMB, West DP, et al. **Safety of Systemic Agents (TNFs,MTX…) for the Treatment of Pediatric Psoriasis**. JAMA Dermatol. 2017 Sep 13 (**folic acid 6-7 times per week if on weekly methotrexate** useful)

Brouwer J, Laven JS, Hazes JM, et al. **Miscarriages** in female rheumatoid arthritis patients - associations with serology, disease activity and anti-rheumatic treatment. Arthritis Rheumatol. 2015 Apr 30.

Brouwer J, Hazes JM, Laven JS, et al. **Fertility in women** with rheumatoid arthritis: influence of disease activity and medication. Ann Rheum Dis. 2015 Oct;74(10):1836-41.

Brucato A, Imazio M, Gattorno M, et al. Effect of **Anakinra on Recurrent Pericarditis** Among Patients With Colchicine Resistance and Corticosteroid Dependence: AIRTRIP Randomized Clinical Trial. JAMA. 2016 Nov 8;316(18):1906-1912.

Brunner HI, Ruperto N, Zuber Z, et al; Paediatric Rheumatology International Trials Organisation (PRINTO) and the Pediatric Rheumatology Collaborative Study Group (PRCSG); Paediatric Rheumatology International Trials Organisation PRINTO and the Pediatric Rheumatology Collaborative Study Group PRCSG. Efficacy and safety of **tocilizumab** in patients with polyarticular-course juvenile idiopathic arthritis: results from a phase 3, randomised, double-blind withdrawal trial. Ann Rheum Dis. 2015 Jun;74(6):1110-7.

Brunner HI, Ruperto N, et al. Subcutaneous **golimumab** for children with active polyarticular-course juvenile idiopathic arthritis: results of a multicentre, double-blind, randomised-withdrawal trial. Ann Rheum Dis. 2018 Jan;77(1):21-29.

Brunner HI, Tzaribachev N, Vega-Cornejo G, et al. **Subcutaneous Abatacept** in Patients With Polyarticular-Course Juvenile Idiopathic Arthritis: Results From a Phase III Open-Label Study. Arthritis Rheumatol. 2018 Feb 26.

Buch MH, Smolen JS, Betteridge N, et al. for the **Rituximab Consensus** Expert Committee. Updated consensus statement on the use of rituximab in patients with rheumatoid arthritis. Ann Rheum Dis. 2011 Mar 6.

Buchbinder R, Barber M, Heuzenroeder L, et al. Incidence of **melanoma** and other malignancies among rheumatoid arthritis patients treated with **methotrexate**. Arthritis Rheum. 2008 May 30;59(6):794-799.[Epub ahead of print]Compared with the general population, methotrexate-treated RA patients have an increased incidence of melanoma, non-Hodgkin's lymphoma, and lung cancer.

Buchbinder R, Van Doornum S, Staples M, et al. **Malignancy risk** in Australian rheumatoid arthritis patients treated with **anti-tumour necrosis factor therapy**: analysis of the Australian Rheumatology Association Database (ARAD) prospective cohort study. BMC Musculoskelet Disord. 2015 Oct 20;16(1):309.

Buch MH. **Defining refractory rheumatoid arthritis**. Ann Rheum Dis. 2018 Mar 27.

Buch MH. Defining **refractory rheumatoid arthritis**. Ann Rheum Dis. 2018 Jul;77(7):966-969.

Burggraaf B, van Breukelen-van der Stoep DF, de Vries MA,et al. Effect of a **treat-to-target intervention of cardiovascular risk factors on subclinical and clinical atherosclerosis** in rheumatoid arthritis: a randomised clinical trial. Ann Rheum Dis. 2019 Mar;78(3):335-341.

Bukhari M, Abernethy R, Deighton C, et al. BSR and BHPR Standards, Guidelines and Audit Working Group. **BSR and BHPR guidelines** on the use of **rituximab** in rheumatoid arthritis. London (England): British Society for Rheumatology; 2011.

Bulatović M, Heijstek MW, Verkaaik M, et al. High prevalence of **methotrexate intolerance in juvenile** idiopathic arthritis: Development and validation of a methotrexate intolerance severity score. Arthritis Rheum. 2011 Mar 24. doi: 10.1002/art.30367.

Bulatovic M, Heijstek MW, Van Dijkhuizen EH et al. Prediction of clinical **non-response to methotrexate** treatment in **juvenile** idiopathic arthritis. Ann Rheum Dis. 2012 Sep;71(9):1484-9.

Burmester Gerd R, Feist E, Kellner H, et al. Effectiveness and safety of the interleukin 6-receptor antagonist **tocilizumab** after 4 and 24 weeks in patients with active rheumatoid arthritis: the first phase IIIb real-life study (TAMARA). Ann Rheum Dis 2011;**70**:755-759 Published Online First: 27 December 2010 doi:10.1136/ard.2010.139725.

Burmester Gerd, Lanas Angel, Biasucci Luigi, et al. The appropriate use of **non-steroidal anti-inflammatory drugs** (NSAIDS) in rheumatic disease: opinions of a multidisciplinary **European expert panel**. Ann Rheum Dis 2011;**70**:818-822 Published Online First: 10 September 2010 doi:10.1136/ard.2010.128660.

Burmester GR, Panaccione R, Gordon KB, et al. **Adalimumab: long-term safety (up to 12yrs)** in 23 458 patients from global clinical trials in rheumatoid arthritis, juvenile idiopathic arthritis, ankylosing spondylitis, psoriatic arthritis, psoriasis and Crohn's disease. Ann Rheum Dis. 2012 Jun 26.

Burmester GR, Blanco R, Charles-Schoeman C, et al, on behalf of the **ORAL Step** investigators. **Tofacitinib** (CP-690550) in combination with methotrexate in patients with active rheumatoid arthrtis with an inadequate response to tumour necrosis factor inhibitors: a randomised phase 3 trial. Lancet 2013.

Burmester GR, Panaccione R, Gordon KB, et al. **Adalimumab**:long-term safety in 23 458 patients (nearly 12 years) from global clinical trials in rheumatoid arthritis, juvenile idiopathic arthritis, ankylosing spondylitis, psoriatic arthritis, psoriasis and Crohn's disease. Ann Rheum Dis. 2013 Apr;72(4):517-24.

Burmester GR, Rubbert-Roth A, Cantagrel A, et al. A randomised, double-blind, parallel-group study of the safety and efficacy of **subcutaneous tocilizumab** versus intravenous tocilizumab in combination with traditional disease-modifying antirheumatic drugs in patients with moderate to severe rheumatoid arthritis (SUMMACTA study). Ann Rheum Dis. 2014 Jan 1;73(1):69-74

Burmester GR, Kivitz AJ, Kupper H, et al. Efficacy and safety of **ascending methotrexate** dose in combination with adalimumab: the randomised **CONCERTO** trial. Ann Rheum Dis. 2015 Jun;74(6):1037-44.

Burmester GR, Kremer JM, Van den Bosch F, et al. **Safety and efficacy of upadacitinib** in patients with rheumatoid arthritis and inadequate response to conventional synthetic disease-modifying anti-rheumatic drugs (**SELECT-NEXT**): a randomised, double-blind, placebo-controlled phase 3 trial. Lancet. 2018 Jun 12.

Burmester GR, Rubbert-Roth A, Cantagrel A, et al. Efficacy and safety of **subcutaneous tocilizumab** versus **intravenous tocilizumab** in combination with traditional DMARDs in patients with RA at week 97 (SUMMACTA). Ann Rheum Dis. 2016 Jan;75(1):68-74

Burmester GR, Rigby WF, van Vollenhoven RF, et al. **Tocilizumab** in early progressive rheumatoid arthritis: **FUNCTION**, a randomised controlled trial. Ann Rheum Dis. 2016 Jun;75(6):1081-91.

Burmester GR, Landewé R, Genovese MC, et al. **Adalimumab long-term safety**: infections, vaccination response and pregnancy outcomes in patients with rheumatoid arthritis. Ann Rheum Dis. 2016 Jun 23.

Burmester GR, Lin Y, Patel R, et al. Efficacy and safety of **sarilumab monotherapy versus adalimumab monotherapy** for the treatment of patients with active rheumatoid arthritis (**MONARCH**): a randomised, double-blind, parallel-group phase III trial. Ann Rheum Dis. 2017 May;76(5):840-847.

Burmester GR, Rigby WF, van Vollenhoven RF, et al. **Tocilizumab combination therapy or monotherapy or methotrexate** monotherapy in methotrexate-naive patients with early rheumatoid arthritis: 2-year clinical and radiographic results from the randomised, placebo-controlled **FUNCTION** trial. Ann Rheum Dis. 2017 Jul;76(7):1279-1284.

Burmester GR, Pope JE. **Novel treatment strategies** in rheumatoid arthritis. Lancet. 2017 Jun 10;389(10086):2338-2348.

Burmester GR, Choy E, Kivitz A, et al. Low immunogenicity of **tocilizumab** in patients with rheumatoid arthritis. Ann Rheum Dis. 2017 Jun;76(6):1078-1085

Burns JC, Koné-Paut I, Kuijpers T, et al. Found in Translation: International initiatives pursuing **interleukin-1 blockade** for treatment of acute **Kawasaki** Disease. Arthritis Rheumatol. 2016 Oct 28.

Buscombe CP, Lin S, Wilson-Holt NJ. Blurred vision (**hydroxychloroquine** toxicity): targeting a diagnosis. BMJ. 2013 Sep 12;347:f5209.

Buszewicz M, et al. **Self management** of arthritis in primary care: randomised controlled trial. BMJ. 2006 Oct 13; [Epub ahead of print]

Butchart J, Brook L, Hopkins V, et al. **Etanercept** in Alzheimer disease: A randomized, placebo-controlled, double-blind, phase 2 trial. Neurology. 2015 May 26;84(21):2161-8.

Buttgereit F. Do the treatment with **glucocorticoids** and/or the disease itself drive the impairment in glucose metabolism in patients with rheumatoid arthritis? Ann Rheum Dis. 2011 Nov;70(11):1881-3.

Buttgereit F, Mehta D, Kirwan J, et al. **Low-dose prednisone** chronotherapy for rheumatoid arthritis: a randomised clinical trial (CAPRA-2). Ann Rheum Dis. 2012 May 5.

Buttgereit F, Dejaco C, Matteson EL, et al. **Polymyalgia Rheumatica and Giant Cell Arteritis**: A Systematic Review. JAMA. 2016 Jun 14;315(22):2442-58.

Bykerk VP, Akhavan P, Hazlewood GS, Schieir O, et al. **Canadian Rheumatology Association** Recommendations for Pharmacological Management of **Rheumatoid Arthritis with Traditional and Biologic** Disease-modifying Antirheumatic Drugs. J Rheumatol. **2011** Sep 15.

Bykerk VP, Ostör AJ, Alvaro-Gracia J, et al. **Tocilizumab** in patients with active rheumatoid arthritis and inadequate responses to DMARDs and/or TNF inhibitors: a large, open-label study close to clinical practice. Ann Rheum Dis. 2012 Dec;71(12):1950-4.

CADTH Drugs for the **management of rheumatoid arthritis**: clinical evaluation. Canadian Coordinating Office for Health Technology Assessment (CCOHTA) 2018 Mar;(146)

Calguneri M, Pay S, et al. **Combination therapy** versus **monotherapy** for the treatment of patients with rheumatoid arthritis. Clin Exp Rheumatol. 1999 Nov-Dec;17(6):699-704.

Callhoff J, Weiß A, Zink A, Listing J. Impact of **biologic therapy on functional status** in patients with rheumatoid arthritis--a meta-analysis. Rheumatology (Oxford). 2013 Dec;52(12):2127-35.

Callhoff J, Sieper J, Weiss A, et al. Efficacy of **TNFalpha blockers in patients with ankylosing spondylitis** and non-radiographic axial spondyloarthritis: a meta-analysis. Ann Rheum Dis. 2014 Apr 9.

Callhoff J, Sieper J, Weiß A, et al. Efficacy of **TNFα blockers** in patients with ankylosing spondylitis and non-radiographic axial spondyloarthritis: a meta-analysis. Ann Rheum Dis. 2015 Jun;74(6):1241-8.

Cameron M, Gagnier JJ, Chrubasik S. **Herbal therapy** for treating rheumatoid arthritis. Cochrane Database Syst Rev. 2011 Feb 16;(2):CD002948. Several herbal interventions are inadequately justified by single studies or non-comparable studies in the treatment of rheumatoid arthritis. There is moderate evidence that oils containing GLA (evening primrose, borage, or blackcurrant seed oil) afford some benefit in relieving symptoms for RA, while evidence for Phytodolor® N is less convincing.Tripterygium wilfordii products may reduce some RA symptoms, however, oral use may be associated with several side effects.

Cameron ID, Dyer SM, Panagoda CE, et al. **Interventions for preventing falls in older people in care facilities and hospitals**. Cochrane Database Syst Rev. 2018 Sep 7;9:CD005465.

Campbell L, Chen C, Bhagat SS, et al. Risk of adverse events including **serious infections** in rheumatoid arthritis patients treated with **tocilizumab**: a systematic literature review and meta-analysis of randomized controlled trials. Rheumatology (Oxford). 2011 Mar;50(3):552-62.

Canhão H, Rodrigues AM, Mourão AF, et al. **Comparative effectiveness** and predictors of response to **tumour necrosis factor inhibitor** therapies in rheumatoid arthritis. Rheumatology (Oxford). 2012 Jul 28. Over 1 year, we found no difference in effectiveness between adalimumab, etanercept and infliximab.

Caporali R, Smolen JS. Back to the future: **forget ultrasound and focus on clinical assessment** in rheumatoid arthritis management. Ann Rheum Dis. 2018 Jan;77(1):18-20.

Caporali R, Crepaldi G, Codullo V, Benaglio F, Monti S, Todoerti M, Montecucco C. **20 years of experience with tumour necrosis factor inhibitors**: what have we learned? Rheumatology (Oxford). 2018 Oct 1;57(57 Suppl 7):vii5-vii10.

Cappelli LC, Gutierrez AK, Baer AN, et al. Inflammatory **arthritis and sicca syndrome induced by nivolumab and ipilimumab**. Ann Rheum Dis 2017;76:43–50

Carron P, Varkas G, Cypers H, et al. **Anti-TNF**-induced remission in very **early peripheral spondyloarthritis**: the **CRESPA** study. Ann Rheum Dis. 2017 Aug;76(8):1389-1395.

Carsons SE, et al. Treatment Guidelines for Rheumatologic Manifestations of **Sjögren's Syndrome**: Use of Biologic Agents, Management of Fatigue, and Inflammatory Musculoskeletal Pain. Arthritis Care Res (Hoboken). 2017 Apr;69(4):517-527.

Cassina M, Johnson D, Robinson L, et al. **Pregnancy outcome in women exposed to leflunomide** before or during pregnancy. Arthritis Rheum. 2012 Feb 3. n=45

Cavallo S, Brosseau L, et al. **Ottawa Panel Evidence-Based Clinical Practice Guidelines for Structured Physical Activity in the Management of Juvenile Idiopathic Arthritis.** Arch Phys Med Rehabil. 2017 May;98(5):1018-1041.

Cavallo S, Brosseau L, Toupin-April K, et al. Ottawa Panel Evidence-Based Clinical Practice Guidelines for Structured **Physical Activity in the Management of Juvenile Idiopathic Arthritis**. Arch Phys Med Rehabil. 2017 May;98(5):1018-1041.

Cavone JL, Yang D, Wang A. **Glucarpidase** Intervention for Delayed **Methotrexate** Clearance. Ann Pharmacother. 2014 Apr 17;48(7):897-907.

Chakravarty EF, Michaud K, Wolfe F. **Skin cancer**, rheumatoid arthritis, and tumor necrosis factor inhibitors. J Rheumatol. 2005 Nov;32(11):2130-5. CONCLUSION: In this large, national cohort, RA was associated with an increased risk for development of NMSC. Among patients with RA, use of TNF inhibitors and prednisone were associated with an increased risk of NMSC.

Chakravarty EF, Murray ER, Kelman A, Farmer P. Pregnancy outcomes after maternal exposure to **rituximab**. Blood. 2011 Feb 3;117(5):1499-506.

Chambers CD, Johnson DL, Robinson LK, et al.. Birth outcomes in **pregnant women taking leflunomide**. Arthritis Rheum. 2010 Jan 28.

Chang Z, Spong C, Jesus AA, et al. **Anakinra use during pregnancy** in patients with cryopyrin-associated periodic syndromes (CAPS). Arthritis Rheumatol. 2014 Sep 15.

Charles-Schoeman C, Burmester G, Nash P, et al. Efficacy and safety of **tofacitinib** following inadequate response to conventional synthetic or biological disease-modifying antirheumatic drugs. Ann Rheum Dis. 2016 Jul;75(7):1293-301.

Chatzidionysiou K, Lie E, Nasonov E, et al. Effectiveness of disease-modifying antirheumatic drug **co-therapy with methotrexate and leflunomide in rituximab**-treated rheumatoid arthritis patients: results of a 1-year follow-up study from the CERERRA collaboration. Ann Rheum Dis. 2012 Mar;71(3):374-7.

Chatzidionysiou K, Askling J, Eriksson J, et al; for the ARTIS group. Effectiveness of **TNF inhibitor switch in RA**: results from the national Swedish register. Ann Rheum Dis. 2014 Jan 15.

Chatzidionysiou K, Emamikia S, Nam J, et al. Efficacy of **glucocorticoids, conventional and targeted synthetic disease-modifying antirheumatic drugs**: a systematic literature review informing the 2016 update of the **EULAR** recommendations for the management of rheumatoid arthritis. Ann Rheum Dis. 2017 Mar 29.

Chaudhari U, Romano P, Mulcahy LD, Dooley LT, Baker DG, Gottlieb AB. Efficacy and safety of **infliximab** monotherapy for plaque-type **psoriasis**: a randomised trial. Lancet. 2001 Jun 9;357(9271):1842-7.

Chen DY, Chen YM, et a. Significant associations of **antidrug antibody levels** with serum drug trough levels and therapeutic response of **adalimumab and etanercept** treatment in rheumatoid arthritis. Ann Rheum Dis. 2015 Mar;74(3):e16.

Chen DY, Chen YM, Hung WT, et al. Immunogenicity, **drug trough levels and therapeutic response** in patients with rheumatoid arthritis or ankylosing spondylitis after 24-week **golimumab** treatment. Ann Rheum Dis. 2015 Dec;74(12):2261-4.

Chen HH, Huang N, Chen YM, et al. Association between a history of **periodontitis** and the risk of rheumatoid arthritis: a nationwide, population-based, case-control study. Ann Rheum Dis. 2012 Aug 31.

Chen YF, et al. A systematic review of the effectiveness of **adalimumab**, **etanercept** and **infliximab** for the treatment of rheumatoid arthritis in adults and an economic evaluation of their cost-effectiveness. Health Technol Assess. 2006 Nov;10(42):1-248.

Chen YJ et al. Association between systemic **anti-psoriatic drugs and cardiovascular risk** in patients with psoriasis and psoriatic arthritis: A nationwide cohort study. Arthritis Rheum. 2011 Dec 12.

Chen YM, Huang WN, Liao TL, et al. Comparisons of **hepatitis C viral replication** in patients with rheumatoid arthritis receiving tocilizumab, abatacept and tofacitinib therapy. Ann Rheum Dis. 2019 Jun;78(6):849-850.

Chen YM, Huang WN, Wu YD, et al. Reactivation of **hepatitis B virus infection** in patients with rheumatoid arthritis receiving **tofacitinib**: a real-world study. Ann Rheum Dis. 2018 May;77(5):780-782.

Chevalier X, Ravaud P, Maheu E, et al; French section of osteoarthritis. Adalimumab in patients with hand osteoarthritis refractory to analgesics and NSAIDs: a randomised, multicentre, double-blind, placebo-controlled trial. Ann Rheum Dis. 2015 Sep;74(9):1697-705.

Chilibeck PD, Vatanparast H, Cornish SM, Abeysekara S, Charlesworth S. Evidencebased risk assessment and recommendations for **physical activity**: arthritis, osteoporosis, and low back pain. Appl Physiol Nutr Metab 2011;36(Suppl 1):S49-S79.

Chingcuanco F, Segal JB, Kim SC, Alexander GC. **Bioequivalence of biosimilar tumor necrosis factor- inhibitors** compared with their reference biologics. A systematic review. Ann Intern Med. 2016;165: 565-74.

Choe JY, Prodanovic N, Niebrzydowski J, et al. A randomised, double-blind, phase III study comparing **SB2, an infliximab biosimilar**, **to the infliximab reference product Remicade** in patients with moderate to severe rheumatoid arthritis despite methotrexate therapy. Ann Rheum Dis 2017;76:58–64.

Choi HK, Hernan MA, Seeger JD, Robins JM, Wolfe F. **Methotrexate and mortality** in patients with rheumatoid arthritis: a prospective study. Lancet. 2002 Apr 6;359(9313):1173-7.

Choi HK, Rho YH, Zhu Y, et al. The risk of **pulmonary embolism and deep vein thrombosis** in rheumatoid arthritis: a UK population-based outpatient cohort study. Ann Rheum Dis. 2012 Aug 28.

Chua JR, Jamal S, Riad M, et al. **Disease burden in osteoarthritis (OA)** is similar to rheumatoid arthritis (RA) at initial rheumatology visit and significantly greater 6-months later. Arthritis Rheumatol. 2019 Mar 20.

Chung ES, Packer M, et al. Anti-TNF Therapy Against Congestive Heart Failure Investigators. Randomized, double-blind, placebo-controlled, pilot trial of **infliximab**, a chimeric monoclonal antibody to tumor necrosis factor-alpha, in patients with moderate-to-severe heart failure: results of the anti-TNF Therapy Against Congestive **Heart Failure** (ATTACH) trial. Circulation. 2003 Jul 1;107(25):3133-40.

Chung HY, Machado P, van der Heijde D, et al. **Smokers in early axial spondyloarthritis** have earlier disease onset, more disease activity, inflammation and damage, and poorer function and healthrelated quality of life: results from the DESIR cohort. Ann Rheum Dis. Published Online First: 11 Oct 2011.

Chung WS, Peng CL, Lin CL, et al. Rheumatoid arthritis increases the risk of deep vein thrombosis and pulmonary thromboembolism: a nationwide cohort study. Ann Rheum Dis 2013.

Chung WS, Peng CL, Lin CL, et al. Rheumatoid arthritis increases the **risk of deep vein thrombosis and pulmonary thromboembolism**: a nationwide cohort study. Ann Rheum Dis. 2014 Oct;73(10):1774-80

Ciurea A, Scherer A, Weber U, et al. on behalf of the Rheumatologists of Swiss Clinical Quality Management Program for Axial Spondyloarthritis. **Impaired response to treatment with tumour necrosis factor α inhibitors in smokers** with axial spondyloarthritis. Ann Rheum Dis. 2015 Feb 9.
Ciurea A, Scherer A, Weber U, et al; on behalf of the Rheumatologists of Swiss Clinical Quality Management Program for Axial Spondyloarthritis. **Impaired** response to treatment **with tumour necrosis factor α inhibitors in smokers** with **axial spondyloarthritis**. Ann Rheum Dis. 2015 Feb 9.
Cleynen I, Moerkercke WV, Billiet T, et al. Characteristics of **Skin Lesions** Associated With **Anti-Tumor Necrosis Factor Therapy** in Patients With Inflammatory Bowel Disease: A Cohort Study. Ann Intern Med. 2015 Dec 8:10-22.
Clifford DB, Ances B, Costello C,et al. **Rituximab-Associated Progressive Multifocal Leukoencephalopathy** (PML) in Rheumatoid Arthritis. Arch Neurol. 2011 May 9.
Clowse ME, Förger F, Hwang C, et al. Minimal to no transfer of **certolizumab pegol into breast** milk: results from CRADLE, a prospective, postmarketing, multicentre, pharmacokinetic study. Ann Rheum Dis. 2017 Nov;76(11):1890-1896.
Coates LC, Tillett W, Chandler D, et al; BSR Clinical Affairs Committee & Standards, Audit and Guidelines Working Group and the BHPR. The **2012 BSR and BHPR guideline for the treatment of psoriatic arthritis** with biologics. Rheumatology (Oxford). 2013 Oct;52(10):1754-7.
Cochrane Musculoskeletal Group- **Patient Decision Aids** http://musculoskeletal.cochrane.org/decision-aids
Cohen S, Cannon GW, et al. Two-year, blinded, randomized, controlled trial of treatment of active rheumatoid arthritis with **leflunomide** compared with **methotrexate**. Utilization of Leflunomide in the Treatment of Rheumatoid Arthritis Trial Investigator Group.(**ULTRA**) Arthritis Rheum. 2001 Sep;44(9):1984-92.
Cohen S, Hurd E, et al. Treatment of rheumatoid arthritis with **anakinra**, a recombinant human interleukin-1 receptor antagonist, in combination **with methotrexate**: results of a twenty-four-week, multicenter, randomized, double-blind, placebo-controlled trial. Arthritis Rheum. 2002 Mar;46(3):614-24.
Cohen SB, Moreland LW, Cush JJ, Greenwald MW, Block S, Shergy WJ, Hanrahan PS, Kraishi MM, Patel A, Sun G, Bear MB; 990145 Study Group. A multicentre, double blind, randomised, placebo controlled trial of anakinra (Kineret), a recombinant interleukin 1 receptor antagonist, in patients with rheumatoid arthritis treated with background methotrexate. Ann Rheum Dis. 2004 Sep;63(9):1062-8. Epub 2004 Apr 13.
Cohen SB, Emery P, Greenwald MW, Dougados M, et al. **REFLEX** Trial Group. **Rituximab** for rheumatoid arthritis refractory to anti-tumor necrosis factor therapy: Results of a multicenter, randomized, double-blind, placebo-controlled, phase III trial evaluating primary efficacy and safety at twenty-four weeks. Arthritis Rheum. 2006 Sep;54(9):2793-806.
Cohen SB, et al. **Rituximab** for rheumatoid arthritis refractory to anti-tumor necrosis factor therapy: Results of a multicenter, randomized, double-blind, placebo-controlled, phase III trial evaluating primary efficacy and safety at twenty-four weeks. Arthritis Rheum. 2006 Aug 31;54(9):2793-2806 [Epub ahead of print]
Cohen S, Radominski SC, Gomez-Reino JJ, et al. Analysis of **infections** and all-cause mortality in Phase II, III and long-term extension studies of **tofacitinib** in patients with rheumatoid arthritis. Arthritis Rheumatol. 2014 Jul 21.
Cohen SB, Tanaka Y, Mariette X, et al. Long-term safety of **tofacitinib** for the treatment of rheumatoid arthritis up to 8.5 years: integrated analysis of data from the global clinical trials. Ann Rheum Dis. 2017 Jul;76(7):1253-1262.
Cohen S, et al. Efficacy & safety of the **biosimilar ABP 501** compared with adalimumab in patients with moderate to severe rheumatoid arthritis: a randomised, double-blind, phase III equivalence study. Ann Rheum Dis. 2017 Oct;76(10):1679-1687.
Cohen SB, Alonso-Ruiz A, Klimiuk PA, et al. Similar efficacy, safety and immunogenicity of **adalimumab biosimilar BI 695501 and Humira** reference product in patients with moderately to severely active rheumatoid arthritis: results from the phase III randomised **VOLTAIRE-RA** equivalence study. Ann Rheum Dis. 2018 Mar 7.
Colebatch-Bourn AN, Edwards CJ, Collado P, et al. EULAR-PReS points to consider for the use of **imaging in the diagnosis and mnagement of juvenile iopathic arthritis** in clinical practice. Ann Rheum Dis. 2015 Nov;74(11):1946-57.
Combe B, et al. Etanercept European Investigators Network (Etanercept Study 309 Investigators). **Etanercept and sulfasalazine**, alone and combined, in patients with active rheumatoid arthritis despite receiving sulfasalazine: a double-blind comparison. Ann Rheum Dis. 2006 Oct;65(10):1357-62. Epub 2006 Apr 10.
Combe B, Balsa A, Sarzi-Puttini P, et al. **Efficacy and safety data** based on historical or pre-existing conditions at baseline for patients with active rheumatoid arthritis who were treated with **baricitinib**. Ann Rheum Dis. 2019 Aug;78(8):1135-1138
Combe B, Dasgupta B, Louw I, et al. Efficacy and safety of **golimumab** as add-on therapy to disease-modifying antirheumatic drugs: results of the GO-MORE study. Ann Rheum Dis. 2013 Jun 5.
Combe B, Dasgupta B, Louw I, et al; GO-MORE Investigators. Efficacy and safety of **golimumab** as add-on therapy to disease-modifying antirheumatic drugs: results of the GO-MORE study. Ann Rheum Dis. 2014 Aug;73(8):1477-86.
Combe B, Logeart I, Belkacemi MC, et al. Comparison of the **long-term outcome** for patients with rheumatoid arthritis with **persistent moderate disease activity or disease remission** during the first year after diagnosis: data from the ESPOIR cohort. Ann Rheum Dis. 2014 Jan 7.
Combe B, Furst DE, Keystone EC, et al. **Certolizumab Pegol Efficacy Across Methotrexate Regimens**: A Pre-Specified Analysis of Two Phase III Trials. Arthritis Care Res (Hoboken). 2016 Mar;68(3):299-307.
Combe B, Landewe R, Daien CI, et al. **2016 update of the EULAR** recommendations for the **management of early arthritis**. Ann Rheum Dis. 2016 Dec 15.
Conaghan PG, Emery P, et al. Assessment by MRI of inflammation and damage in rheumatoid arthritis patients with methotrexate inadequate response receiving **golimumab**: results of the **GO-FORWARD** trial. Ann Rheum Dis. 2011 Nov;70(11):1968-74.
Conaghan PG, Durez P, Alten RE, et al. Impact of intravenous abatacept on synovitis, osteitis and structural damage in patients with rheumatoid arthritis and an inadequate response to methotrexate: the ASSET randomised controlled trial. Ann Rheum Dis. 2013 Aug;72(8):1287-94.
Conaghan PG, Peterfy C, Olech E, et al. The effects of **tocilizumab** on osteitis, synovitis and erosion progression in rheumatoid arthritis: results from the ACT-RAY MRI substudy. Ann Rheum Dis. 2014 May 1;73(5):810-6.
Conway R, Low C, Coughlan RJ, et al. **Methotrexate and lung disease** in rheumatoid arthritis - A meta-analysis of randomized controlled trials. Arthritis Rheum. 2013 Dec 24
Conway R, Low C, Coughlan RJ, et al. **Methotrexate use and risk of lung disease** in psoriasis, psoriatic arthritis, and inflammatory bowel disease: systematic literature review and meta-analysis of randomised controlled trials. BMJ. 2015 Mar 13;350:h1269.
Conway R, Low C, Coughlan RJ, et al. **Leflunomide** Use and Risk of **Lung Disease** in Rheumatoid Arthritis: A Systematic Literature Review and Metaanalysis of Randomized Controlled Trials. J Rheumatol. 2016 May;43(5):855-60.
Cooper AM, Horwitz M, Becker ML. Improving the Safety of **Teratogen Prescribing Practices** in a Pediatric Rheumatology Clinic. Pediatrics. 2019 Mar 5.
Cooper WO, Cheetham TC, Li DK et al. Brief report: Risk of adverse fetal outcomes associated with immunosuppressive medications for chronic immune-mediated diseases in pregnancy. Arthritis Rheumatol. 2014 Feb;66(2):444-50.
Cordtz R, Mellemkjaer L, Glintborg B, et al. **Risk of virus-associated cancer in** female arthritis patients treated with **biological DMARDs**-a cohort study. Rheumatology (Oxford). 2016 Feb 24
Cordtz RL, et al. **Predictors of revision, prosthetic joint infection** and mortality following total hip or total knee arthroplasty in patients with rheumatoid arthritis: a nationwide cohort study using Danish healthcare registers. Ann Rheum Dis. 2018 Feb;77(2):281-288.
Cordtz RL, Hawley S, Prieto-Alhambra D, et al. **Incidence of hip and knee replacement in patients with rheumatoid arthritis following the introduction of biological DMARDs**: an interrupted time-series analysis using nationwide Danish healthcare registers. Ann Rheum Dis. 2018 May;77(5):684-689.
Corrales A, Parra JA, González-Juanatey C, et al. **Cardiovascular risk stratification** in rheumatic diseases: carotid ultrasound is more sensitive than Coronary Artery Calcification Score to detect subclinical atherosclerosis in patients with rheumatoid arthritis. Ann Rheum Dis. 2013 Nov 1;72(11):1764-1770
Corrales A, González-Juanatey C, Peiró ME, et al. **Carotid ultrasound is useful for the cardiovascular risk stratification** of patients with rheumatoid arthritis: results of a population-based study. Ann Rheum Dis. 2014 Apr 1;73(4):722-7.
Costantino F, Talpin A, Said-Nahal R, et al. Prevalence of **spondyloarthritis in reference to HLA-B27** in the French population: results of the GAZEL cohort. Ann Rheum Dis. 2013 Dec 18.
Costedoat-Chalumeau N, Galicier L, Aumaître O, et al. **Hydroxychloroquine** in systemic lupus erythematosus: results of a French multicentre controlled trial (PLUS Study). Ann Rheum Dis. 2013 Nov 1;72(11):1786-1792.
Coulson E, Saravanan V, Hamilton J, et al. **Pneumococcal antibody levels after pneumovax** in patients with rheumatoid arthritis on methotrexate. Ann Rheum Dis. 2011 Jul;70(7):1289-91.
Cramer H, Lauche R, Langhorst J, et al. **Yoga** for rheumatic diseases: a systematic review. Rheumatology (Oxford). 2013 Aug 9.
Crowson CS, et al. How much of the increased incidence of **heart failure** in rheumatoid arthritis is attributable to traditional cardiovascular risk factors and ischemic heart disease? Arthritis Rheum. 2005 Oct;52(10):3039-44.
Crowson Cynthia S, Gabriel Sherine E. Towards improving **cardiovascular risk management** in patients with rheumatoid arthritis: the need for accurate risk assessment. Ann Rheum Dis 2011;70:719-721 Published Online First: 22 February 2011 doi:10.1136/ard.2010.145482.
Crowson CS, Gabriel SE, Semb AG, et al; A Trans-Atlantic Cardiovascular Consortium for Rheumatoid Arthritis. **Rheumatoid arthritis-specific cardiovascular risk scores** are not superior to general risk scores: a validation analysis of patients from seven countries. Rheumatology (Oxford). 2017 Mar 8.
Coulson E, Saravanan V, Hamilton J, et al. **Pneumococcal antibody levels after pneumovax** in patients with rheumatoid arthritis on methotrexate. Ann Rheum Dis. 2011 Apr 22.
Cross M, Smith E, Hoy D, et al. The **global burden of rheumatoid arthritis**: estimates from the Global Burden of Disease 2010 study. Ann Rheum Dis. 2014 Jul;73(7):1316-22.
Crowson CS, Gabriel SE, Semb AG, et al; A Trans-Atlantic Cardiovascular Consortium for Rheumatoid Arthritis. **Rheumatoid arthritis-specific cardiovascular risk** scores are not superior to general risk scores: a validation analysis of patients from seven countries. Rheumatology (Oxford). 2017 Mar 8.
Crowson CS, Rollefstad S, Ikdahl E, et al. Impact of risk factors associated with **cardiovascular outcomes** in patients with rheumatoid arthritis. Ann Rheum Dis. 2018 Jan;77(1):48-54.
Cudmore J, Seftel M, Sisler J, et al. **Methotrexate and trimethoprim-sulfamethoxazole**: Toxicity from this combination continues to occur. Can Fam Physician. 2014 Jan;60(1):53-6

Cummins LL, Vangaveti V, Roberts LJ. Rheumatoid arthritis **referrals and rheumatologist scarcity: a prioritization tool**. Arthritis Care Res (Hoboken). 2015;67:326-31.
Curtis JR, Beukelman T, Onofrei A, Cassell S, et al. **Elevated liver enzyme tests** among patients with rheumatoid arthritis or psoriatic arthritis treated with **methotrexate and/or leflunomide**. Ann Rheum Dis [Internet]. 2010 Jan;69(1):43-7.
Curtis JR, Chen L, Luijtens K, et al. **No additional efficacy with dose escalation of certolizumab** pegol from 200 mg to 400 mg every other week: An analysis of individual patient-level data from RAPID 1. Arthritis Rheum. 2011 Apr 11.
Curtis JR, Xie F, Chen L, et al. The comparative risk of **serious infections** among rheumatoid arthritis patients starting or switching biological agents. Ann Rheum Dis. 2011 Aug;70(8):1401-6.
Curtis JR, Zhang J, Xie F, et al. Use of **oral and subcutaneous methotrexate** in rheumatoid arthritis patients in the United States. Arthritis Care Res(Hoboken). 2014 Nov;66(11):1604-11.
Curtis JR, Xie F, Yun H, et al. Risk of **Hospitalized Infection among Biologic-Treated** Rheumatoid Arthritis Patients Concurrently Treated with Denosumab. Arthritis Rheumatol. 2015 Feb 23.
Curtis JR, Lee EB, Kaplan IV, et al. **Tofacitinib**, an oral Janus kinase inhibitor: analysis of malignancies across the rheumatoid arthritis clinical development programme. Ann Rheum Dis. 2015 Apr 22.
Curtis JR, Churchill M, Kivitz A, et al. A Randomized Trial Comparing Disease Activity Measures to Assess and Predict Response in Rheumatoid Arthritis Patients Initiating **Certolizumab** Pegol. Arthritis Rheumatol. 2015 Aug 28.
Curtis JR, Lee EB, Kaplan IV, et al. **Tofacitinib**, an oral Janus kinase inhibitor: analysis of malignancies across the rheumatoid arthritis clinical development programme. Ann Rheum Dis. 2016 May;75(5):831-41.
Curtis JR, Xie F, Yun H, et al. Real-world comparative risks of **herpes virus infections in tofacitinib** and biologic-treated patients with rheumatoid arthritis. Ann Rheum Dis. 2016 Oct;75(10):1843-7.
Curtis JR, Xie F, Mackey D, Gerber et al. Patient's experience with **subcutaneous and oral methotrexate** for the treatment of rheumatoid arthritis. BMC Musculoskelet Disord. 2016 Sep 26;17(1):405
Curtis JR, Xie F, Smith C, et al. Changing Trends in **Opioid Use among U.S. Rheumatoid Arthritis Patients**. Arthritis Rheumatol. 2017 Jun 21.
Curtis JR, Xie F, Yang S, et al. **Risk for Herpes Zoster** in Tofacitinib-Treated Rheumatoid Arthritis Patients With and Without Concomitant Methotrexate and Glucocorticoids. Arthritis Care Res (Hoboken). 2019 Sep;71(9):1249-1254.
Curtis JR, Yang S, Singh JA, et al. Is **Rheumatoid Arthritis a Cardiovascular Risk Equivalent** to Diabetes? Arthritis Care Res (Hoboken). 2018 Feb 6.
Curtis JR, Xie F, Chen L, et al. **Biomarker-related risk for myocardial infarction and serious infections** in patients with rheumatoid arthritis: a population-based study. Ann Rheum Dis. 2017 Dec 21.
D'Agostino MA, Boers M, Wakefield RJ, et al. Is it time to revisit the role of **ultrasound** in rheumatoid arthritis management? Ann Rheum Dis. 2017 Jan;76(1):7-8.
Da Silva JA, et al. Safety of **low dose glucocorticoid** treatment in rheumatoid arthritis: published evidence and prospective trial data.Ann Rheum Dis. 2006 Mar;65(3):285-93. Epub 2005 Aug 17. (InfoPOEMs: Available data are scant, but seem to provide evidence that low-dose glucocorticoids (10 mg or less of prednisolone/equivalent) in the treatment of rheumatoid arthritis do not increase osteoporotic fractures, blood pressure, cardiovascular diseases, or peptic ulcer incidence. Weight gain is common when taking these drugs, as are skin changes. (LOE = 2b))
Dagfi nrud H, Kvien TK, Hagen KB. Physiotherapy interventions for **ankylosing spondylitis**. Cochrane Database Syst Rev 2008; 1: CD002822.
Daïen CI, Duny Y, Barnetche T, et al. Effect of **TNF inhibitors on lipid profile** in rheumatoid arthritis: a systematic review with meta-analysis. Ann Rheum Dis. 2012 Jun;71(6):862-8.
Daïen CI, Tubery A, Cailar GD, et al. Application of the **2015/2016 EULAR recommendations for cardiovascular risk** in daily practice: data from an observational study. Ann Rheum Dis. 2018 Apr;77(4):625-626.
Dalbeth N, Aati O, Gamble GD, et al. **Zoledronate** for prevention of bone erosion in tophaceous gout: a randomised, double-blind, placebo-controlled trial. Ann Rheum Dis. 2014 Jun 1;73(6):1044-51.
Dalbeth N, Aati O, Kalluru R, et al. Relationship between structural joint damage and urate deposition in **gout**: a plain radiography and dual-energy CT study. Ann Rheum Dis. 2015 Jun;74(6):1030-6.
Dalrymple JM, Stamp LK, O'Donnell JL, Chapman PT, Zhang M, Barclay ML. **Pharmacokinetics of oral methotrexate** in patients with rheumatoid arthritis. Arthritis Rheum. 2008 Nov;58(11):3299-308.
Das S, Vital EM, Horton S, et al. **Abatacept or tocilizumab after rituximab** in rheumatoid arthritis? An exploratory study suggests non-response to rituximab is associated with persistently high IL-6 and better clinical response to IL-6 blocking therapy. Ann Rheum Dis. 2014 May 1;73(5):909-12.
Davies HD; Committee on Infectious Diseases. **Infectious Complications** With the Use of **Biologic Response Modifiers** in Infants and Children. Pediatrics. 2016 Aug;138(2)
Davies R, Galloway JB, Watson KD, Lunt M, Symmons DP, Hyrich KL; ; BSRBR Control Centre Consortium, British Society for Rheumatology Biologics Register. **Venous thrombotic events** are not increased in patients with rheumatoid arthritis treated with anti-TNF therapy: results from the British Society for Rheumatology Biologics Register. Ann Rheum Dis. 2011 Jul 22.
De Benedetti F, Brunner H, Ruperto N, et al. Effi cacy and safety of **tocilizumab** in patients with systemic juvenile idiopathic arthritis (sJIA): 12-week data from the phase 3 tender trial. Ann Rheum Dis 2010; 69 (suppl 146): 146.
De Benedetti F et al. Randomized trial of **tocilizumab in systemic juvenile idiopathic arthritis**. N Engl J Med 2012 Dec 20; 367:2385.
De Benedetti F, Brunner H, Ruperto N, et al; the Paediatric Rheumatology International Trials Organisation (PRINTO); Pediatric Rheumatology Collaborative Study Group (PRCSG). Catch-up growth during **tocilizumab** therapy for systemic juvenile idiopathic arthritis: Results from the TENDER trial. Arthritis Rheumatol. 2014 Dec 10.
de Hair MJ, Landewé RB, van de Sande MG, et al. **Smoking and overweight** determine the likelihood of developing rheumatoid arthritis. Ann Rheum Dis. 2013 Oct 1;72(10):1654-8.
de Jong PH, Hazes JM, Barendregt PJ, et al. Induction therapy with a **combination of DMARDs** is better than methotrexate monotherapy: first results of the **tREACH** trial. Ann Rheum Dis. 2013 Jan;72(1):72-8.
de Jong PH, Quax RA, Huisman M, et al. Response to **glucocorticoids at 2 weeks** predicts the effectiveness of DMARD induction therapy at 3 months: post hoc analyses from the tREACH study. Ann Rheum Dis. 2013 Oct 1;72(10):1659-63.
de Jong PH, Hazes JM, Han HK, et al. Randomised comparison of **initial triple DMARD therapy with methotrexate monotherapy** in combination with **low-dose glucocorticoid** bridging therapy; 1-year data of the tREACH trial. Ann Rheum Dis. 2014 Jul;73(7):1331-9.
De Luca G, Campochiaro C, Dinarello CA, et al. **Treatment of Dilated Cardiomyopathy With Interleukin-1 Inhibition (anakinra).** Ann Intern Med. 2018 Jul 31.
De Lucia O, Ravagnani V, Pregnolato F, et al. **Baseline ultrasound examination as possible predictor of relapse in patients affected by juvenile idiopathic arthritis** (JIA). Ann Rheum Dis. 2018 Oct;77(10):1426-1431.
de Moel EC, Derksen VFAM, Trouw LA, et al. **In RA, becoming seronegative over the first year of treatment does not translate to better chances of drug-free remission**. Ann Rheum Dis. 2018 Dec;77(12):1836-1838.
de Rooy DP, van Nies JA, Kapetanovic MC, et al. **Smoking** as a risk factor for the radiological severity of rheumatoid arthritis: a study on six cohorts. Ann Rheum Dis. 2014 Jul;73(7):1384-7.
de Steenwinkel FD, Hokken-Koelega AC, de Ridder MA, et al. Rheumatoid arthritis during **pregnancy and postnatal catch-up growth** in the offspring. Arthritis Rheumatol. 2014 Feb 27.
Deepak P, Sifuentes H, Sherid M, et al. **T-Cell Non-Hodgkin's Lymphomas** Reported to the FDA AERS With **Tumor Necrosis Factor-Alpha**(TNF-α) Inhibitors: Results of the REFURBISH Study. Am J Gastroenterol. 2013 Jan;108(1):99-105.
Del Rincón I, Battafarano DF, Restrepo JF, et al. **Glucocorticoid dose thresholds associated with all-cause and cardiovascular mortality** in rheumatoid arthritis. Arthritis Rheum. 2013 Oct 7.
Del Rincón I, Polak JF, O'Leary DH, et al. Systemic inflammation and **cardiovascular risk factors** predict rapid progression of atherosclerosis in rheumatoid arthritis. Ann Rheum Dis. 2015 Jun;74(6):1118-23.
Demirkaya E, Lanni S, Bovis F, et al; Paediatric Rheumatology International Trials Organisation (PRINTO). A Meta-Analysis to Estimate the **Placebo Effect in Juvenile Idiopathic Arthritis** in Randomized Controlled Trials. Arthritis Rheumatol. 2016 Jan 8.
den Uyl D, van Raalte DH, Nurmohamed MT, et al. Metabolic effects of **high-dose prednisolone** treatment in early rheumatoid arthritis: Diabetogenic effects and inflammation reduction on the balance. Arthritis Rheum. 2011 Sep 27.
den Uyl D, Ter Wee M, Boers M, et al. A non-inferiority trial of an **attenuated combination strategy** ('COBRA-light') compared to the original **COBRA** strategy: clinical results after 26 weeks. Ann Rheum Dis. 2014 Jun 1;73(6):1071-8.
Deodhar AA, Dougados M, et al. Effect of **Secukinumab** on Patient-Reported Outcomes in Patients With Active Ankylosing Spondylitis: A Phase III Randomized Trial (**MEASURE 1**). Arthritis Rheumatol. 2016 Dec;68(12):2901-2910.
Dervieux T, Kremer JM, Weinblatt ME. Differing contribution of **methotrexate polyglutamates to adalimumab blood levels as compared with etanercept**. Ann Rheum Dis. 2019 Sep;78(9):1285-1286.
Desai RJ, Hansen RA, Rao JK, et al. **Mixed treatment comparison of the treatment discontinuations of biologic disease-modifying antirheumatic drugs** in adults with rheumatoid arthritis. Ann Pharmacother. 2012 Nov;46(11):1491-505.
Desai RJ, Huybrechts KF, Bateman BT, et al. Patterns and secular trends in use of **immunomodulatory agents during pregnancy in women with rheumatologic conditions**. Arthritis Rheumatol. 2015 Nov 25.
Desai RJ, et al. Disease-modifying antirheumatic drug use and the **risk of incident hyperlipidemia** (**hydroxychloroquine**) in patients with early rheumatoid arthritis: a retrospective cohort study. Arthritis Care Res (Hoboken). 2015;67:457-66.
Desai RJ, Bateman BT, Huybrechts KF, et al. Risk of **serious infections associated with use of immunosuppressive agents in pregnant women** with autoimmune inflammatory conditions: cohort study. BMJ. 2017 Mar 6;356:j895.
Dessein PH, Semb AG. Could **cardiovascular disease risk stratification** and management in rheumatoid arthritis be enhanced? Ann Rheum Dis. 2013 Nov 1;72(11):1743-1746.
Detert J, Bastian H, Listing J, et al. Induction therapy with **adalimumab plus methotrexate** for 24 weeks followed by methotrexate monotherapy up to week 48 versus methotrexate therapy alone for DMARD-naive patients with early rheumatoid arthritis: HIT HARD, an investigator-initiated study. Ann Rheum Dis. 2012 Jul 10.
Devauchelle-Pensec V, Mariette X, Jousse-Joulin S, et al. Treatment of **primary sjögren syndrome with rituximab**: a randomized trial. Ann Intern Med. 2014 Feb 18;160(4).
Devauchelle-Pensec V, Berthelot JM, Cornec D, et al. Efficacy of first-line **tocilizumab** therapy in early **polymyalgia rheumatica**: a prospective longitudinal study. Ann Rheum Dis. 2016 Aug;75(8):1506-10.
Dhir V, Singla M, Gupta N, et al. Randomized Controlled Trial Comparing 2 Different **Starting Doses of Methotrexate** in Rheumatoid Arthritis. Clin Ther. 2014 Jun 26.
Di Giuseppe D, Alfredsson L, Bottai M, et al. Long term **alcohol intake** and risk of rheumatoid arthritis in women: a population based cohort study. BMJ. 2012 Jul 10;345:e4230.
Di Giuseppe D, Wallin A, Bottai M, et al. **Long-term intake of dietary long-chain n-3 polyunsaturated fatty acids** and risk of rheumatoid arthritis: a prospective cohort study of women. Ann Rheum Dis. 2014 Nov;73(11):1949-53.
Diak P, Siegel J, La Grenade L, Choi L, Lemery S, McMahon A. **Tumor necrosis factor alpha blockers and malignancy in children**: forty-eight cases reported to the Food and Drug Administration. Arthritis Rheum. 2010 Aug;62(8):2517-24.
Diekhoff T, Ulas ST, Poddubnyy D, et al. **Ultra-low-dose CT detects synovitis in patients with suspected rheumatoid arthritis**. Ann Rheum Dis. 2019 Jan;78(1):31-35.
Ding T, Ledingham J, Luqmani R, et al. Standards, Audit and Guidelines Working Group of BSR Clinical Affairs Committee and BHPR. **BSR and BHPR rheumatoid arthritis guidelines on safety of anti-TNF therapies**. London (England): British Society for Rheumatology; 2010.

Dixon WG, et al. Rates of serious infection, including site-specific and bacterial intracellular infection, in rheumatoid arthritis patients receiving **anti-tumor necrosis factor** therapy: Results from the British Society for Rheumatology Biologics Register. Arthritis Rheum. 2006 Jul 25;54(8):2368-2376 [Epub ahead of print]

Dixon WG, Hyrich KL, Watson KD, et al. Drug-specific risk of tuberculosis in patients with rheumatoid arthritis treated with anti-TNF therapy: Results from the British Society for Rheumatology Biologics Register (BSRBR). Ann Rheum Dis. 2009 Oct 22. [Epub ahead of print] The rate of TB in patients with RA treated with anti-TNF therapy was 3-4 fold higher in patients receiving infliximab and adalimumab compared to etanercept.

Dixon WG, Kezouh A, Bernatsky S, et al. The influence of **systemic glucocorticoid** therapy upon the risk of **non-serious infection** in older patients with rheumatoid arthritis: a nested case-control study. Ann Rheum Dis. 2011 Feb1.

Dixon WG, Abrahamowicz M, Beauchamp ME, et al. Immediate and delayed impact of **oral glucocorticoid** therapy on risk of **serious infection** in older patients with rheumatoid arthritis: a nested case-control analysis. Ann Rheum Dis. 2012 Jan 12.

Dommasch ED, Kim SC, Lee MP, et al. Risk of **Serious Infection in Patients Receiving Systemic Medications for the Treatment of Psoriasis**. JAMA Dermatol. 2019 May 10.

Donahue KE, Gartlehner G, Jonas DE, et al. Systematic Review: Comparative Effectiveness and Harms of Disease-Modifying Medications for Rheumatoid Arthritis. Ann Intern Med. 2007 Nov 19; [Epub ahead of print] Limited available comparative evidence does not support one monotherapy over another for adults with rheumatoid arthritis. Although combination therapy is more effective for patients whose monotherapy fails, the evidence is insufficient to draw firm conclusions about whether one combination or treatment strategy is better than another or is the best treatment for early rheumatoid arthritis.

Donahue KE, Gartlehner G, Schulman ER, et al. Drug **Therapy for Early Rheumatoid Arthritis**: A Systematic Review Update. Comparative Effectiveness Review No. 211. AHRQ Publication No. 18-EHC015-EF. PCORI Publication No. 2018-SR-02. Rockville, MD: Agency for Healthcare Research and Quality; July 2018.

Donahue KE, Schulman ER, Gartlehner G, et al. Comparative Effectiveness of **Combining MTX with Biologic Drug Therapy Versus Either MTX or Biologics Alone** for Early Rheumatoid Arthritis in Adults: a Systematic Review and Network Meta-analysis. J Gen Intern Med. 2019 Aug 6.

Dörner T, Strand V, Cornes P, et al. The changing **landscape of biosimilars** in rheumatology.Ann Rheum Dis. 2016 Jun;75(6):974-82. doi: 10.1136/annrheumdis-2016-209166. Epub 2016 Mar 8.

Dougados M, Braun J, Szanto S, et al. Efficacy of **etanercept** on rheumatic signs and pulmonary function tests in advanced **ankylosing spondylitis**: results of a randomised double-blind placebo-controlled study (SPINE). Ann Rheum Dis 2011;**70**:799-804 Published Online First: 13 February 2011 doi:10.1136/ard.2010.139261.

Dougados M, Baeten D. **Spondyloarthritis**. Lancet. (psoriatic arthritis, reactive arthritis, arthritis related to IBD, subgroup of JIA & ankylosing spondylitis) 2011 Jun 18;377(9783):2127-37.

Dougados M, Kissel K, Sheeran T, et al. Adding **tocilizumab** or switching to tocilizumab monotherapy in methotrexate inadequate responders: 24-week symptomatic and structural results of a 2-year randomised controlled strategy trial in rheumatoid arthritis (ACT-RAY). Ann Rheum Dis. 2013 Jan;72(1):43-50.

Dougados M, Kissel K, Conaghan PG, et al. Clinical, radiographic and immunogenic effects after 1 year of **tocilizumab**-based treatment strategies in rheumatoid arthritis: the ACT-RAY study. Ann Rheum Dis. 2014 May 1;73(5):803-9.

Dougados M, van der Heijde D, Sieper J, et al. Symptomatic efficacy of **etanercept** and its effects on objective signs of inflammation in early nonradiographic axial spondyloarthritis: a multicenter, randomized, double-blind, placebo-controlled trial. Arthritis Rheumatol. 2014 Aug;66(8):2091-102.

Dougados M, Maksymowych WP, Landewé RBM, et al. Evaluation of the change in structural radiographic **sacroiliac joint damage after 2 years of etanercept therapy** (**EMBARK** trial) in comparison to a contemporary control cohort (DESIR cohort) in recent onset axial spondyloarthritis. Ann Rheum Dis. 2018 Feb;77(2):221-227.

Dregan A, Matcham F, Harber-Aschan L, et al. Common **mental disorders within chronic inflammatory disorders**: a primary care database prospective investigation. Ann Rheum Dis. 2019 May;78(5):688-695.

Dreyer L, Mellemkjær L, Andersen AR, et al. Incidences of overall and site specific **cancers in TNFα inhibitor treated patients** with rheumatoid arthritis and other arthritides - a follow-up study from the DANBIO Registry. Ann Rheum Dis. 2013 Jan;72(1):79-82.

Dreyer L, Cordtz RL, et al.Risk of **second malignant neoplasm and mortality in patients with rheumatoid arthritis treated with biological DMARDs**: a Danish population-based cohort study. Ann Rheum Dis. 2018 Apr;77(4):510-514.

Duarte-García A, Zamore R, Wong JB. The **Evidence Basis for the American College of Rheumatology Practice Guidelines**. JAMA Intern Med. 2017 Nov 27.

Ducharme J, Pelletier C, Zacharias R. The safety of **infliximab infusions** in the community setting. Can J Gastroenterol. 2010 May;24(5):307-11.

Durán J, Bockorny M, Dalal D, et al. **Methotrexate dosage** as a source of bias in biological trials in rheumatoid arthritis: a systematic review.Ann Rheum Dis. 2016 Sep;75(9):1595-8.

Durcan L, Wilson F, Cunnane G. The Effect of Exercise on **Sleep and Fatigue** in Rheumatoid Arthritis: A Randomized Controlled Study. J Rheumatol. 2014 Aug 15.

Duru N, van der Goes MC, et al. **EULAR** evidence-based and consensus-based recommendations on the management of **medium to high-dose glucocorticoid therapy** (>7.5mg but ≤ 100mg/day) in rheumatic diseases. Ann Rheum Dis. 2013 Jul 19.

Eder L, Thavaneswaran A, et al. **Tumour necrosis factor** α blockers are more effective than **methotrexate** in the inhibition of radiographic joint damage progression among patients with psoriatic arthritis. Ann Rheum Dis. 2014Jun 1;73(6):1007-11.

Edwards JC, et al. Efficacy of B-cell-targeted therapy with **rituximab** in patients with rheumatoid arthritis. N Engl J Med. 2004 Jun 17;350(25):2572-81.

Edwards CJ, Fautrel B, Schulze-Koops H, et al. **Dosing down with biologic therapies**: a systematic review and clinicians' perspective. Rheumatology (Oxford). 2017 Feb 16.

Emery P, et al. DANCER Study Group. The efficacy and safety of **rituximab** in patients with active rheumatoid arthritis despite methotrexate treatment: results of a phase IIB randomized, double-blind, placebo-controlled, dose-ranging trial. Arthritis Rheum. 2006 May;54(5):1390-400.

Emery P, Breedveld FC, Hall S, et al. Comparison of methotrexate monotherapy with a combination of **methotrexate and etanercept** in active, early, moderate to severe rheumatoid arthritis (**COMET**): a randomised, double-blind, parallel treatment trial. Lancet. 2008 Aug 2;372(9636):375-82. Epub 2008 Jul 16.

Emery P, Breedveld F, van der Heijde D, et al. Combination of **Methotrexate and Etanercept** in Early Rheumatoid Arthritis Trial Group. Two-year clinical and radiographic results with combination etanercept-methotrexate therapy versus monotherapy in early rheumatoid arthritis: A two-year, double-blind, randomized study. Arthritis Rheum. 2010 Feb 25;62(3):674-682.

Emery P, Fleischmann R, van der Heijde D, et al. The effect of **golimumab** on radiographic progression in rheumatoid arthritis: Results of the GO-BEFORE and GO-FORWARD randomized, controlled studies. Arthritis Rheum. 2011 Jan 28.

Emery P, Kvien TK, Combe B, et al. Combination **etanercept and methotrexate provides better disease control in very early (≤4 months)** versus early rheumatoid arthritis (>4 months and <2 years): post hoc analyses from the COMET study. *Ann Rheum Dis* 2012; published online March 8. DOI:10.1136/annrheumdis-2011-201066.

Emery P, Smolen JS, Kavanaugh A, et al. **Maintenance of biologic-free disease control** in early rheumatoid arthritis patient after induction of low disease activity with adalimumab plus methotrexate. *Ann Rheum Dis* 2011; **70** (suppl 3)**:** 262–63.

Emery P, Kvien TK, Combe B, et al. Combination **etanercept and methotrexate** provides better disease control in very early (<=4 months) versus early rheumatoid arthritis (>4 months and <2 years): post hoc analyses from the **COMET** study. Ann Rheum Dis. 2012 Jun;71(6):989-92.

Emery P, Sebba A, Huizinga TW. **Biologic and oral disease-modifying antirheumatic drug monotherapy** in rheumatoid arthritis. Ann Rheum Dis. 2013 Aug 10.

Emery P, Hammoudeh M, FitzGerald O, et al. Sustained remission with **etanercept tapering** in early rheumatoid arthritis. N Engl J Med. 2014 Nov 6;371(19):1781-92.

Emery P, Burmester GR, Bykerk VP, et al. Evaluating **drug-free remission** with **abatacept** in early rheumatoid arthritis: results from the phase 3b, multicentre, randomised, active-controlled AVERT study of 24 months, with a 12-month, double-blind treatment period. Ann Rheum Dis. 2015 Jan;74(1):19-26.

Emery P, Gottenberg JE, Rubbert-Roth A, et al. **Rituximab** versus an alternative **TNF inhibitor** in patients with rheumatoid arthritis who failed to respond to a single previous TNF inhibitor: **SWITCH-RA**, a global, observational, comparative effectiveness study. Ann Rheum Dis. 2015 Jun;74(6):979-84.

Emery P, Kavanaugh A, Bao Y, et al. **Comprehensive disease control (CDC):** what does achieving CDC mean for patients with rheumatoid arthritis? Ann Rheum Dis. 2015 Dec;74(12):2165-74.

Emery P, Vencovsky J, et al. A phase III randomised, double-blind, parallel-group study comparing **SB4 with etanercept reference product** in patients with active rheumatoid arthritis despite methotrexate therapy. Ann Rheum Dis 2017;76: 51–7.

Emery P, Bingham CO 3rd, Burmester GR, et al. **Certolizumab** pegol in combination with dose-optimised **methotrexate** in DMARD-naïve patients with early, active rheumatoid arthritis with poor prognostic factors: 1-year results from **C-EARLY**, a randomised, double-blind, placebo-controlled phase III study. Ann Rheum Dis. 2016 May 10.

Emery P, Vencovský J, et al. Long-term efficacy and safety in patients with rheumatoid arthritis continuing on **SB4 or switching from reference etanercept to SB4**. Ann Rheum Dis. 2017 Aug 9. pii: annrheumdis-2017-211591.

Emery P, Vencovský J, Sylwestrzak A, et al. 52-week results of the phase 3 randomized study comparing **SB4 with reference etanercept** in patients with active rheumatoid arthritis. Rheumatology (Oxford). 2017 Aug 19.

England BR, Thiele GM, Anderson DR, et al. **Increased cardiovascular risk in rheumatoid arthritis**: mechanisms and implications. BMJ. 2018 Apr 23;361:k1036.

Eriksson JK, Neovius M, Bratt J, et al. **Biological (infliximab) vs conventional combination (MTX, HCQ & SSZ)** treatment and work loss in early rheumatoid arthritis: a randomized trial. online July 1, 2013. JAMA Intern Med.

Eriksson JK, Johansson K, Askling J, et al. **Costs for hospital care, drugs and lost work days** in incident and prevalent rheumatoid arthritis: how large, and how are they distributed? Ann Rheum Dis. 2015 Apr; 74(4):648-54.

Eriksson JK, Karlsson JA, Bratt J, et al. Cost-effectiveness of **infliximab versus conventional combination treatment in methotrexate-refractory** early rheumatoid arthritis: 2-year results of the register-enriched randomised controlled **SWEFOT** trial. Ann Rheum Dis. 2015 Jun;74(6):1094-101.

Eriksson K, Nise L, Alfredsson L, et al. **Seropositivity combined with smoking is associated with increased prevalence of periodontitis** in patients with rheumatoid arthritis. Ann Rheum Dis. 2017 Oct 6.

Ersoy A, Baran B, Ersoy C, Kahvecioglu S, Akdag I. Calcineurin inhibitors and post-transplant weight gain. Nephrology (Carlton). 2008 Mar 5; [Epub ahead of print] Only pretransplant BMI, creatinine clearance, **cyclosporine A** usage, being hypertensive and dysplipidemic were independent predictors of weight gain at the 12th month. Our results suggested that the type of immunosuppression may affect post-transplant weight gain.

Ertz-Archambault N, Kosiorek H, Taylor GE, et al. Association of Therapy for Autoimmune Disease With **Myelodysplastic Syndromes and Acute Myeloid Leukemia**. JAMA Oncol. 2017 Feb 2. (**azathioprine exposure**)

Estellat C, Ravaud P. **Lack of head-to-head trials and fair control arms**: randomized controlled trials of biologic treatment for rheumatoid arthritis. Arch Intern Med. 2012;172(3):237-244.

Evans S, Moieni M, Lung K, et al. Impact of **Iyengar Yoga** on Quality of Life in Young Women with Rheumatoid Arthritis. Clin J Pain. 2013 Jan 30.

Faber WR, et al. Treatment of recurrent **erythema nodosum leprosum** with **infliximab**. N Engl J Med. 2006 Aug 17;355(7):739.

Fagerli KM, Lie E, van der Heijde D, et al. **Switching between TNF inhibitors in psoriatic arthritis**: data from the NOR-DMARD study. Ann Rheum Dis. 2013 Nov 1;72(11):1840-1844.

Fanouriakis A, Kostopoulou M, Alunno A, et al. 2019 update of the **EULAR recommendations** for the management of **systemic lupus erythematosus**. Ann Rheum Dis. 2019 Mar 29.

Fardet L, Nazareth I, Petersen I. Chronic **hydroxychloroquine/chloroquine exposure for connective tissue diseases and risk of Alzheimer's disease**: a population-based cohort study. Ann Rheum Dis. 2019 Feb;78(2):279-282.

Farrell DF. **Retinal toxicity** to antimalarial drugs: **chloroquine and hydroxychloroquine**: a neurophysiologic study. Clin Ophthalmol. 2012;6:377-83.

Fautrel B, Pham T, Alfaiate T, et al. **Step-down strategy of spacing TNF-blocker injections** for established rheumatoid arthritis in remission: results of the multicentre non-inferiority randomised open-label controlled trial (**STRASS**: Spacing of TNF-blocker injections in Rheumatoid ArthritiS Study). Ann Rheum Dis. 2016 Jan;75(1):59-67.

FDA July/10 will require that the label for the rheumatoid arthritis drug **leflunomide (Arava)** carry an added warning for severe liver injury. The label already warns against the drug's use in pregnant women and those of childbearing potential. The new warning comes after the FDA received **49 reports of severe liver injury**, including 14 instances of fatal liver failure, from 2002 to 2009. Risk for liver injury was higher among patients using other drugs associated with liver injury and patients with liver disease. Clinicians should monitor liver enzymes at least monthly for 3 months after beginning the drug. After that, enzymes should be monitored every quarter. Treatment should be halted if liver enzymes rise to two times the upper limit of normal. http://www.fda.gov/Safety/MedWatch/SafetyInformation/SafetyAlertsforHumanMedicalProducts/ucm218912.htm

FDA Sep/11 notified healthcare professionals that the Boxed Warning for the entire class of **Tumor Necrosis Factor-alpha (TNFα) blockers** has been updated to include the risk of infection from two bacterial pathogens, **Legionella and Listeria**. In addition, the Boxed Warning and Warnings and Precautions sections of the labels for all of the TNFα blockers have been revised so that they contain consistent information about the risk for serious infections and the associated disease-causing pathogens.

FDA Feb/19: **Xeljanz, Xeljanz XR** (tofacitinib): Safety Communication - Safety Trial Finds **Increased Risk of Blood Clots** in the Lungs and Death with Higher Dose in Rheumatoid Arthritis Patients.

FDA July/19: has approved new warnings about an increased risk of blood clots and of death with the 10 mg twice daily dose of **Xeljanz, Xeljanz XR (tofacitinib**), which is used in patients with ulcerative colitis.

Felson David T, Smolen Josef S, Wells George, et al. American College of Rheumatology/European League Against Rheumatism Provisional **Definition of Remission** in Rheumatoid Arthritis for Clinical Trials. Ann Rheum Dis 2011;70:404-413. Pdf

Fent G, Mankia K, Erhayiem B, et al. **First cardiovascular MRI study** in individuals at risk of rheumatoid arthritis detects abnormal aortic stiffness suggesting an anti-citrullinated peptide antibody-mediated role for accelerated atherosclerosis. Ann Rheum Dis. 2019 Aug;78(8):1138-1140.

Fidahic M, Jelicic Kadic A, Radic M, Puljak L. **Celecoxib for rheumatoid arthritis**. Cochrane Database Syst Rev. 2017 Jun 9;6:CD012095. Celecoxib may improve clinical symptoms, alleviate pain and contribute to little or no difference in physical function compared with placebo. Celecoxib was associated with fewer numbers of participant withdrawals. Results for incidence of gastroduodenal ulcers (≥ 3 mm) and short-term serious adverse events were uncertain; however, there were few reported events for either.Celecoxib may slightly improve clinical symptoms compared with tNSAIDs. Results for reduced pain and improved physical function were uncertain. Particpants taking celecoxib had lower incidence of gastroduodenal ulcers (≥ 3 mm) and there were fewer withdrawals from trials. Results for cardiovascular events and short-term serious adverse events were also uncertain.Uncertainty about the rate of cardiovascular events between celecoxib and tNSAIDs could be due to risk of bias; another factor is that these were small, short-term trials.

Filippou G, Filippucci E, Tardella M, et al. Extent and distribution of CPP deposits in patients affected by **calcium pyrophosphate dihydrate deposition** disease: an ultrasonographic study. Ann Rheum Dis. 2013 Nov 1;72(11):1836-1839.

Filippou G, Sakellariou G, Scirè CA, et al. The predictive role of ultrasound-detected **tenosynovitis and joint synovitis** for flare in patients with rheumatoid arthritis in stable remission. Results of an Italian multicentre study of the Italian Society for Rheumatology Group for Ultrasound: the **STARTER study**. Ann Rheum Dis. 2018 Sep;77(9):1283-1289.

Finckh A, Simard JF, Gabay C, Guerne PA; SCQM physicians. Evidence for differential acquired drug resistance to anti-tumour necrosis factor agents in rheumatoid arthritis. Ann Rheum Dis. 2006 Jun;65(6):746-52.

Finckh A Finckh A, Bansback N, et al. Treatment of very early rheumatoid arthritis with symptomatic therapy, **disease-modifying antirheumatic drugs**, or biologic agents: a cost-effectiveness analysis. Ann Intern Med. 2009 Nov 3;151(9):612-21.

Finckh A, Möller B, Dudler J, et al; on behalf of the physicians of the Swiss Clinical Quality Management for Rheumatoid Arthritis; On behalf of the physicians of SCQM-RA.. Evolution of radiographic joint damage in **rituximab**-treated versus TNF-treated rheumatoid arthritis cases with inadequate response to TNF antagonists. Ann Rheum Dis. 2012 Oct;71(10):1680-1685.

Finzel S, Kraus S, Figueiredo CP, et al. Comparison of the effects of **tocilizumab monotherapy and adalimumab in combination with methotrexate** on bone erosion repair in rheumatoid arthritis. Ann Rheum Dis. 2019 Sep;78(9):1186-1191.

Fleischmann R, Cutolo M, Genovese MC, et al. Phase 2B dose-ranging study of the oral JAK inhibitor **tofacitinib** (CP-690,550) or adalimumab monotherapy versus placebo in patients with active rheumatoid arthritis with an inadequate response to DMARDs. Arthritis Rheum. 2011 Sep 27. doi: 10.1002/art.33383.

Fleischmann R, Genovese MC, Lin Y, et al. Long-term **safety of sarilumab** in rheumatoid arthritis: an integrated analysis with up to 7 years' follow-up. Rheumatology (Oxford). 2019 Jul 15.

Fleischmann R, Kremer J, Cush J et al; **ORAL Solo** Investigators. Placebo-controlled trial of **tofacitinib** monotherapy in rheumatoid arthritis. N Engl J Med. 2012 Aug 9;367(6):495-507.

Fleischmann R, van Adelsberg J, Lin Y, et al. **Sarilumab** andNon-Biologic Disease-Modifying Antirheumatic Drugs in Patients With Active RA and Inadequate Response or Intolerance to TNF Inhibitors. Arthritis Rheumatol. 2016 Nov 17.

Fleischmann R, Mysler E, Hall S, et al, on behalf of the **ORAL** Strategy investigators. Efficacy and safety of **tofacitinib** monotherapy, tofacitinib with methotrexate, and adalimumab with methotrexate in patients with rheumatoid arthritis (ORAL Strategy): a phase 3b/4, double-blind, head-to-head, randomised controlled trial. Lancet 2017; online June 16.

Fleischmann R. The American College of Rheumatology White Paper on **Biosimilars**: It Isn't All White-There Is Some Gray and Black. Arthritis Rheumatol. 2018 Feb 7.

Fleischmann R, Pangan AL, Song IH, et al. **Upadacitinib Versus Placebo or Adalimumab** in Patients With Rheumatoid Arthritis and an Inadequate Response to Methotrexate: Results of a Phase III, Double-Blind, Randomized Controlled Trial. Arthritis Rheumatol. 2019

Fleischmann RM, et al. **Anakinra**, a recombinant human interleukin-1 receptor antagonist (r-metHuIL-1ra),in patients with rheumatoid arthritis: A large, international, multicenter, placebo-controlled trial. Arthritis Rheum. 2003 Apr;48(4):927-34.

Fleischmann RM, et al. Safety of extended treatment with **anakinra** in patients with rheumatoid arthritis. Ann Rheum Dis. 2006 Aug;65(8):1006-12. Epub 2006 Jan 5.

Fleischmann RM, Genovese MC, Enejosa JV, et al. Safety and effectiveness of **upadacitinib or adalimumab plus methotrexate** in patients with rheumatoid arthritis over 48 weeks with switch to alternate therapy in patients with insufficient response. Ann Rheum Dis. 2019 Nov;78(11):1454-1462.

Fobelo Lozano MJ, Serrano Giménez R, Sánchez Fidalgo S. **THERAPEUTIC DRUG MONITORING OF INFLIXIMAB IN SPONDYLOARTHRITIS**. A REVIEW OF THE LITERATURE. Br J Clin Pharmacol. 2019 Jul 17.

Foell Dirk; Wulffraat Nico; Wedderburn Lucy R.; et al. for the Paediatric Rheumatology International Trials Organization (PRINTO) **Methotrexate Withdrawal at 6 vs 12 Months in Juvenile** Idiopathic Arthritis in Remission: A Randomized Clinical Trial. JAMA. 2010;303(13):1266-1273.

Foley P, Gordon K, Griffiths CEM, et al. Efficacy of **Guselkumab Compared With Adalimumab** and Placebo for Psoriasis in Specific Body Regions: A Secondary Analysis of 2 Randomized Clinical Trials. JAMA Dermatol. 2018 May 16.

Forrest CB, Crandall WV, Bailey LC, et al. Effectiveness of **Anti-TNFα for Crohn Disease: Research in a Pediatric** Learning Health System. Pediatrics. 2014 Jun 16.

Fournier MR, Klein J, Minuk GY, Bernstein CN. Changes in **Liver Biochemistry** During **Methotrexate** Use for Inflammatory Bowel Disease. Am J Gastroenterol. 2010 Feb 16. Methotrexate is commonly associated with LET abnormalities, but these frequently normalize while still on therapy, and in only 5% will drug discontinuation be necessary. Liver biopsies rarely have substantive abnormalities

França IL, Ribeiro AC, Aikawa NE, et al. **TNF blockers** show distinct patterns of immune response to the **pandemic influenza A H1N1 vaccine** in inflammatory arthritis patients. Rheumatology (Oxford). 2012 Aug 20.

Frisell T, Saevarsdottir S, Askling J. Does a **family history of RA influence the clinical presentation and treatment** response in RA? Ann Rheum Dis. 2016 Jun;75(6):1120-5.

Frisell T, Baecklund E, Bengtsson K, et al. **Patient characteristics influence the choice of biological drug in RA**, and will make non-TNFi biologics appear more harmful than TNFi biologics. Ann Rheum Dis. 2018 May;77(5):650-657.

Fukuda W, et al. Incidence of **hepatitis B virus reactivation** with resolved infection on immunosuppressive therapy for rheumatic disease: multicentre, prospective, observational study in Japan. Ann Rheum Dis. 2017 Jun;76(6):1051-1056.

Furer V, Rondaan C, Heijstek MW, et al. **2019 update of EULAR recommendations for vaccination** in adult patients with autoimmune inflammatory rheumatic diseases. Ann Rheum Dis. 2019 Aug 14.

Furukawa H, Oka S, Shimada K, et al; Rheumatoid Arthritis associated Interstitial Lung Disease (RA-ILD) Study Consortium. **HLA-A*31:01** and **methotrexate**-induced interstitial lung disease in Japanese rheumatoid arthritis patients: a multidrug hypersensitivity marker? Ann Rheum Dis. 2013 Jan;72(1):153-5.

Furst DE, et al. Updated consensus statement on **biological agents**, specifically tumour necrosis factor {alpha} (TNF{alpha}) blocking agents and interleukin-1 receptor antagonist (IL-1ra), for the treatment of rheumatic diseases, 2005. Ann Rheum Dis. 2005 Nov;64 Suppl 4:iv2-14.

Gabay C, Bel M, Combescure C, et al; for the **H1N1** study group. Impact of synthetic and biological disease modifying antirheumatic drugs on antibody responses to the ASO3-adjuvanted pandemic influenza vaccine. Arthritis Rheum. 2011 Mar 7. doi: 10.1002/art.30325.

Gabay C, Emery P, van Vollenhoven R, et al; on behalf of the ADACTA Study Investigators. **Tocilizumab** monotherapy versus adalimumab monotherapy for treatment of rheumatoid arthritis (ADACTA): a randomised, double-blind, controlled phase 4 trial. Lancet. 2013 Mar 18.

Gabay C, Riek M, Hetland ML, et al. Effectiveness of **tocilizumab with and without synthetic disease-modifying antirheumatic drugs** in rheumatoid arthritis: results from a European collaborative study. Ann Rheum Dis. 2016 Jul;75(7):1336-42
Gallitano SM, McDermott L, Brar K, et al. Use of tumor necrosis factor (**TNF) inhibitors in patients with HIV/AIDS**. J Am Acad Dermatol. 2016 May;74(5):974-80
Galloway JB, Hyrich KL, Mercer LK, et al. BSRBR Control Centre Consortium, Symmons DP; on behalf of the British Society for Rheumatology Biologics Register. **Anti-TNF therapy is associated with an increased risk of serious infections** in patients with rheumatoid arthritis especially in the **first 6 months** of treatment: updated results from the British Society for Rheumatology Biologics Register with special emphasis on risks in the elderly. Rheumatology (Oxford). 2010 Jul 31.
Galloway JB, Hyrich KL, Mercer LK, et al. on behalf of the BSR Biologics Register. **Risk of septic arthritis** in patients with rheumatoid arthritis and the effect of anti-TNF therapy: results from the British Society for Rheumatology Biologics Register. Ann Rheum Dis. 2011 Jul 21.
Galloway JB, Mercer LK, Moseley A, et al. Risk of **skin and soft tissue infections (including shingles)** in patients exposed to anti-tumour necrosis factor therapy: results from the British Society for Rheumatology Biologics Register. Ann Rheum Dis. 2012 Apr 24.
Galloway JB, et al. Risk of **skin and soft tissue infections (including shingles)** in patients exposed to **anti-tumour necrosis factor therapy**: results from the British Society for Rheumatology Biologics Register. Ann Rheum Dis. 2012 Apr 24.
Garcês S, Demengeot J, Benito-Garcia E. The **immunogenicity of anti-TNF therapy** in immune-mediated inflammatory diseases: a systematic review of the literature with a meta-analysis. Ann Rheum Dis. 2012 Dec 6.
Garcês S, Antunes M, et al. A preliminary **algorithm** introducing immunogenicity assessment in the management of patients with RA receiving **tumour necrosis factor** inhibitor therapies. Ann Rheum Dis. 2014Jun 1;73(6):1138-43.
Garneau AP, Riopel J, Isenring P. Acute **Methotrexate-Induced Crystal Nephropathy**. N Engl J Med. 2015 Dec 31;373(27):2691-3.
Garzo-Caldas N, Ruiz-Sainz E, Vila-Bedmar S, et al. Enteroviral **T-cell encephalitis** related to immunosuppressive therapy including **rituximab**. Neurology. 2017 Jul 25;89(4):408-409.
Gaujoux-Viala C, Smolen JS, Landewé R, et al. Current evidence for the management of rheumatoid arthritis with **synthetic disease-modifying antirheumatic drugs**: a systematic literature review informing the **EULAR** recommendations for the management of rheumatoid arthritis. Ann Rheum Dis. 2010 Jun;69(6):1004-9. Epub
Gaujoux-Viala C, Nam J, Ramiro S, et al. Efficacy of **conventional synthetic disease-modifying antirheumatic drugs, glucocorticoids and tofacitinib**: a systematic literature review informing the 2013 update of the EULAR recommendations for management of rheumatoid arthritis. Ann Rheum Dis. 2014 Mar 1;73(3):510-5.
Gaujoux-Viala C, et al. **Optimal methotrexate dose** is associated with better clinical outcomes than non-optimal dose in daily practice: results from the **ESPOIR** early arthritis cohort. Ann Rheum Dis. 2017 Dec;76(12):2054-2060.
Geborek P, Bladstrom A, et al.. **Tumour necrosis factor blockers** do not increase overall tumour risk in patients with rheumatoid arthritis, but **may** be associated with an **increased** risk of **lymphomas**. Ann Rheum Dis. 2005 May;64(5):699-703.
Gelfand JM, Bradshaw MJ, Stern BJ, et al. **Infliximab** for the treatment of **CNS sarcoidosis**: A multi-institutional series. Neurology. 2017 Nov 14;89(20):2092-2100
Gelinck LB, van der Bijl AE, Beyer WE, et al. The effect of **anti-tumor necrosis factor** alpha treatment on the antibody response to **influenza vaccination**. Ann Rheum Dis. 2007 Oct 26; [Epub ahead of print] The antibody response to influenza vaccination in patients treated with anti-TNF is only modestly impaired. The proportion of patients that achieves a protective titer is not significantly diminished by the use of TNF blocking therapies.
Gendelman O, Weitzman D, Rosenberg V, et al. Characterization of **adherence and persistence** profile in a real-life population of patients treated with **adalimumab**. Br J Clin Pharmacol. 2017 Dec 22
Genevay S, Finckh A, Zufferey P et al. **Adalimumab** in **acute sciatica** reduces the long-term need for surgery: a 3-year follow-up of a randomised double-blind placebo-controlled trial. Ann Rheum Dis. 2012 Apr;71(4):560-2.
Genovese MC, Bathon JM, et al. **Etanercept** versus **methotrexate** in patients with early rheumatoid arthritis: two-year radiographic and clinical outcomes. Arthritis Rheum. 2002 Jun;46(6):1443-50.
Genovese MC, Cohen S, Moreland L, Lium D, Robbins S, Newmark R, Bekker P; 20000223 Study Group. **Combination** therapy with **etanercept and anakinra** in the treatment of patients with rheumatoid arthritis who have been treated unsuccessfully with methotrexate. Arthritis Rheum. 2004 May;50(5):1412-9.
Genovese MC, Becker JC, Schiff M, et al. **Abatacept** for rheumatoid arthritis refractory to tumor necrosis factor alpha inhibition (**ATTAIN**). N Engl J Med. 2005 Sep 15;353(11):1114-23.
Genovese M, Covarrubias A, Leon G, et al. **Subcutaneous abatacept** versus intravenous abatacept: A phase IIIb non-inferiority study in patients with an inadequate response to methotrexate. Arthritis Rheum. 2011 May 25.
Genovese MC, Kalunian K, Gottenberg J-E, et al. Effect of **filgotinib vs placebo** on clinical response in patients with moderate to severe rheumatoid arthritis refractory to disease-modifying antirheumatic drug therapy: the FINCH 2 randomized clinical trial [July 23, 2019]. JAMA. doi:10.1001/jama.2019.9055
Genovese MC, Kremer J, Zamani O, Ludivico et al. **Baricitinib** in Patients with Refractory Rheumatoid Arthritis. N Engl J Med. 2016 Mar 31;374(13):1243-52.
Genovese MC, Kremer JM, van et al. Transaminase Levels and Hepatic Events During **Tocilizumab** Treatment: Pooled Analysis of Long-Term Clinical Trial Safety Data in Rheumatoid Arthritis. Arthritis Rheumatol. 2017 Jun 8.
George MD, Baker JF, Winthrop K, et al. Risk of **biologics and glucocorticoids in patients with rheumatoid arthritis undergoing arthroplasty**. A cohort study. Ann Intern Med. 2019. [Epub ahead of print]. doi:10.7326/M18-2217
Geraldino-Pardilla L, Dhaduvai S, Giles JT, Bathon JM. Lack of association of oral **calcium supplementation** with coronary artery calcification in rheumatoid arthritis. Arthritis Rheumatol. 2015 Mar 25.
Gerlag DM, Safy M, Maijer KI, et al. Effects of **B-cell directed therapy on the preclinical stage of rheumatoid arthritis**: the **PRAIRI** study. Ann Rheum Dis. 2018 Dec 1.
Girolomoni G, Feldman SR, et al. Comparison of injection site reactions between the **etanercept biosimilar SB4** and the reference etanercept in patients with rheumatoid arthritis from a Phase III study. Br J Dermatol. 2017 Oct 11.
Glace B, Gottenberg JE, , et al. Efficacy of **rituximab** in the treatment of pulmonary rheumatoid nodules: 10 patients from the French AutoImmunity and Rituximab/Rheumatoid Arthritis registry (AIR/PR registry). Ann Rheum Dis. 2012 Apr 13.
Gladman DD, et al. **Adalimumab** improves joint- and skin-related functional impairment in patients with **psoriatic arthritis**: Patient- reported outcomes of the Adalimumab Effectiveness in Psoriatic Arthritis Trial (**ADEPT**). Ann Rheum Dis. 2006 Oct 17; [Epub ahead of print]
Gladman D, Rigby W, Azevedo VF, et al. **Tofacitinib** for psoriatic arthritis in patients with an inadequate response to TNF inhibitors. N Engl J Med 2017;377:1525-36.
Glatt S, Taylor PC, McInnes IB, et al. Efficacy and safety of **bimekizumab as add-on therapy** for rheumatoid arthritis in patients with inadequate response to certolizumab pegol: a proof-of-concept study. Ann Rheum Dis. 2019 Aug;78(8):1033-1040.
Glintborg B, Loft AG, Omerovic E, et al. To switch or not to switch: results of a nationwide guideline of mandatory **switching from originator to biosimilar etanercept**. One-year treatment outcomes in 2061 patients with inflammatory arthritis from the **DANBIO** registry. Ann Rheum Dis. 2019 Feb;78(2):192-200
Glintborg B, Ostergaard M, Krogh NS, et al. Clinical response, drug survival and predictors thereof among 548 **switchers of tumor necrosis factor α inhibitor** therapy in psoriatic arthritis. Results from the Danish nationwide DANBIO registry. Arthritis Rheum. 2013 Mar 4.
Glintborg B, et al. A nationwide non-medical switch from **originator infliximab to biosimilar CT-P13** in 802 patients with inflammatory arthritis: 1-year clinical outcomes from the DANBIO registry. Ann Rheum Dis. 2017 Aug;76(8):1426-1431.
Goekoop-Ruiterman YP, De Vries-Bouwstra JK, Allaart CF, et al. Clinical and radiographic outcomes of **four different treatment strategies in patients with early rheumatoid arthritis (the BeSt study)**: A randomized, controlled trial. Arthritis Rheum. 2005 Nov;52(11):3381-90. CONCLUSION: In patients with early RA, initial combination therapy including either prednisone or infliximab resulted in earlier functional improvement and less radiographic damage after 1 year than did sequential monotherapy or step-up combination therapy. (Goekoop-Ruiterman YP, de Vries-Bouwstra JK, Allaart CF, et al. Comparison of treatment strategies in early rheumatoid arthritis: a randomized trial (BeSt). Ann Intern Med. 2007 Mar 20;146(6):406-15. Currently available antirheumatic drugs can be highly effective in patients with early rheumatoid arthritis in a setting of tight disease control. Initial combination therapies seem to provide earlier clinical improvement and less progression of joint damage, but all treatment strategies eventually showed at 2yrs similar clinical improvements. In addition, combination therapy can be withdrawn successfully and less treatment adjustments are needed than with initial monotherapies.)
Goekoop-Ruiterman YP, de Vries-Bouwstra JK, Allaart CF, et al. **Comparison of treatment strategies** in early rheumatoid arthritis: a randomized trial. Ann Intern Med. 2007 Mar 20;146(6):406-15.
Goldbach-Mansky R, et al. Neonatal-onset multisystem inflammatory disease responsive to interleukin-1beta inhibition. (anakinra) N Engl J Med. 2006 Aug 10;355(6):581-92.
Goldbach-Mansky R., et al. Comparison of **Tripterygium wilfordii Hook F** Versus Sulfasalazine in the Treatment of Rheumatoid Arthritis: A Randomized Trial. Ann Intern Med 2009; 229-240.
Gómez-Reino JJ, Rodríguez-Lozano C, Campos-Fernández Cet al. Change in the **discontinuation pattern of tumour necrosis factor antagonists** in rheumatoid arthritis over 10 years: data from the Spanish registry BIOBADASER 2.0. Ann Rheum Dis. 2012 Mar;71(3):382-385. (inefficacy being the main reason)
Gómez-Reino J. **Biologic monotherapy as initial treatment** in patients with early rheumatoid arthritis. Rheumatology (Oxford). 2012 Jul;51 Suppl 5:v31-v37.
Gomez-Reino JJ, Maneiro JR, Ruiz J, et al; on behalf of the MIRAR Study Group. Comparative effectiveness of **switching to alternative tumour necrosis factor** (TNF) antagonists versus switching to **rituximab** in patients with rheumatoid arthritis who failed previous TNF antagonists: the MIRAR Study. Ann Rheum Dis. 2012 Nov;71(11):1861-1864.
González-Gay MA, Matteson EL, Castañeda S. **Polymyalgia** rheumatica. Lancet. 2017 Jul 31
Goodman SM, Menon I, et al. Management of **perioperative tumour necrosis factor alpha inhibitors** in rheumatoid arthritis patients **undergoing arthroplasty**: a systematic review and meta-analysis. Rheumatology (Oxford). 2015 Oct 7
Goodman SM. **Optimizing perioperative outcomes** for older patients with rheumatoid arthritis undergoing arthroplasty: emphasis on medication management. Drugs Aging. 2015 May;32(5):361-9.
Goodman SM, Springer B, Guyatt G, et al. **2017 American College of Rheumatology**/American Association of Hip and Knee Surgeons Guideline for the **Perioperative Management of Antirheumatic** Medication in Patients With Rheumatic Diseases Undergoing Elective Total Hip or Total Knee Arthroplasty. Arthritis Rheumatol. 2017 Jun 16.
Gordon KB, et al. Clinical response to **adalimumab** in patients with moderate to severe **psoriasis**: double-blind, randomized controlled trial and open-label extension study. J Am Acad Dermatol. 2006 Oct;55(4):598-606. Epub 2006 Aug 10.
Goss SL, Klein CE, Jin Z, et al. **Methotrexate Dose in Patients With Early Rheumatoid Arthritis** Impacts Methotrexate Polyglutamate Pharmacokinetics, **Adalimumab** Pharmacokinetics, and Efficacy: Pharmacokinetic and Exposure-response Analysis of the **CONCERTO** Trial. Clin Ther. 2018 Feb;40(2):309-319.

Gossec L, Smolen JS, Gaujoux-Viala C, et al. European League Against Rheumatism recommendations for the management of **psoriatic arthritis** with pharmacological therapies. Ann Rheum Dis. 2011 Sep 27.

Gossec L, Smolen JS, Ramiro S, et al. European League Against Rheumatism (**EULAR**) recommendations for the **management of psoriatic arthritis** with pharmacological therapies: 2015 update. Ann Rheum Dis. 2015 Dec 7.

Gotestam Skorpen C, Hoeltzenbein M, Tincani A, et al. The **EULAR** points to consider for use of **antirheumatic drugs before pregnancy, and during pregnancy and lactation**. Ann Rheum Dis. 2016 Feb 17. pii: annrheumdis-2015-208840.

Gottenberg J, Ravaud P, Bardin T, et al. on behalf of all the investigators of the AIR registry the French Society of Rheumatology.. Risk factors of severe **infections** in patients with rheumatoid arthritis treated with rituximab in the AutoImmunity And **Rituximab** (AIR) registry. Arthritis Rheum. 2010 May 6.

Gottenberg JE, Ravaud P, Cantagrel A, et al. **Positivity for anti-cyclic citrullinated peptide** is associated with a better response to **abatacept**: data from the 'Orencia and Rheumatoid Arthritis' registry. Ann Rheum Dis. 2012 May 21. Nov;71(11):1815-9.

Gottenberg JE, Ravaud P, Puéchal X, et al. Effects of **hydroxychloroquine** on symptomatic improvement in primary **Sjögren syndrome**: the **JOQUER** randomized clinical trial. JAMA. 2014 Jul 16;312(3):249-58.

Gottenberg JE, Courvoisier DS, et al. **Rheumatoid factor** and **anti-citrullinated protein antibody positivity** are associated with a better effectiveness of **abatacept**: The Pan-European registry analysis. Arthritis Rheumatol. 2016 Jan 27.

Gottenberg JE, et al. **Non-TNF-Targeted Biologic vs Second Anti-TNF Drug** to Treat Rheumatoid Arthritis in Patients With Insufficient Response to a First Anti-TNF Drug: A Randomized Clinical Trial. JAMA. 2016 Sep 20;316(11):1172-1180.

Gottlieb AB, et al. **Infliximab** induction therapy for patients with severe plaque-type **psoriasis**: a randomized, double-blind, placebo-controlled trial.J Am Acad Dermatol. 2004 Oct;51(4):534-42.

Gorman JD, Sack KE, et al. Treatment of **ankylosing spondylitis** by inhibition of tumor necrosis factor alpha **etanercept**. N Engl J Med. 2002 May 2;346(18):1349-56.

Gorter SL, Bijlsma JW, Cutolo M, et al. Current evidence for the management of rheumatoid arthritis with **glucocorticoids**: a systematic literature review informing the **EULAR** recommendations for the management of rheumatoid arthritis. Ann Rheum Dis. 2010 Jun;69(6):1010-4. Epub 2010 May 6.

Griffi ths CE, Reich K, Lebwohl M, et al, for the UNCOVER-2 UNCOVER-3 investigators. Comparison of **ixekizumab with etanercept** or placebo in moderate-to-severe psoriasis (UNCOVER-2 and UNCOVER-3): results from two phase 3 randomised trials. Lancet 2015; online June 10.

Griffiths, Christopher E.M., Strober, Bruce E., van de Kerkhof, Peter, et ak, the ACCEPT Study Group, Comparison of **Ustekinumab** and Etanercept for Moderate-to-Severe Psoriasis. N Engl J Med 2010 362: 118-128.

Grigor C, et al. Effect of a treatment strategy of **tight control** for rheumatoid arthritis (the **TICORA study**): a single-blind randomised controlled trial. Lancet. 2004 Jul 17-23;364(9430):263-9.

Graudal N, Jürgens G. Similar effects of **disease modifying anti rheumatic drugs, glucocorticoids and biologics** on radiographic progression in rheumatoid arthritis: meta-analysis of 70 randomised placebo or drug controlled studies including 112 comparisons. Arthritis Rheum. 2010 Jun 17. DMARDs, glucocorticoids, biologics and combination treatments significantly reduced radiographic progression at one year with a relative effect of 50-80%.

Graudal N, Hubeck-Graudal T, et al. **Combination Therapy With and Without Tumor Necrosis Factor Inhibitors** in Rheumatoid Arthritis: A Meta-Analysis of Randomized Trials. Arthritis Care Res (Hoboken). 2015 Nov;67(11):1487-95.

Greenberg Jeffrey D, Kremer Joel M, Curtis Jeffrey R, et al. , on behalf of the CORRONA Investigators. Tumour necrosis factor antagonist use and associated **risk reduction of cardiovascular events** among patients with rheumatoid arthritis. Ann Rheum Dis 2011;70:576-582

Greenberg JD, Reed G, Decktor D, et al.on behalf of the **CORRONA** Investigators. A comparative effectiveness study of **adalimumab, etanercept and infliximab** in biologically naive and switched rheumatoid arthritis patients: results from the US CORRONA registry. Ann Rheum Dis. 2012 Jan 30.

Greenwald MW, Shergy WJ, Kaine JL, et al. Evaluation of the safety of **rituximab in combination with a tumor necrosis factor inhibitor and methotrexate** in patients with active rheumatoid arthritis: results from a randomized controlled trial. Arthritis Rheum. 2011 Mar;63(3):622-32. doi: 10.1002/art.30194.

Gremese E, Carletto A, et al. the Gruppo Italiano di Studio sulle Early Arthritis (GISEA). **Obesity reduces** the response rate to anti TNFα in rheumatoid arthritis. an approach to a personalized medicine. Arthritis Care Res (Hoboken). 2012 Jun 21.

Gremese E, Salaffi F, Bosello SL, et al. **Very early rheumatoid arthritis** as a predictor of remission: a multicentre real life prospective study. Ann Rheum Dis. 2012 Jul 13.

Grijalva CG, Chen L, Delzell E, et al. Initiation of **tumor necrosis factor-alpha antagonists** and the risk of hospitalization for **infection** in patients with autoimmune diseases. [published online November 6, 2011]. JAMA.

Gron KL, Arkema EV, Glintborg B, et al. **Risk of serious infections** in patients with rheumatoid arthritis treated in routine care **with abatacept, rituximab and tocilizumab** in Denmark and Sweden. Ann Rheum Dis. 2019 Jan 5.

Gronseth GS, et al. Practice advisory: **Etanercept for poststroke disability**: Report of the Guideline Development, Dissemination, and Implementation Subcommittee of the American Academy of Neurology. Neurology. 2016 Jun 7;86(23):2208-11.

Groot N, Graeff N, Avcin T, et al. European evidence-based recommendations for diagnosis and treatment of childhood-onset systemic lupus erythematosus: the SHARE initiative. Ann Rheum Dis. 2017 Jun 19.

Guermazi A, Roemer FW, Felson DT. **Inadequacy of radiographs**: One cause for failure of clinical trials to identify a disease modifying drug for osteoarthritis. Arthritis Rheum. 2013 Jul 16.

Guiddir T, Frémond ML, Triki TB, et al. **Anti-TNF-α Therapy** May Cause Neonatal **Neutropenia**. Pediatrics. 2014 Oct;134(4):e1189-93.

Guillevin L, Pagnoux C, Karras A, et al. **Rituximab versus azathioprine for maintenance in ANCA-associated vasculitis**. N Engl J Med 2014;371:1771-80.

Guyot P, Taylor P, Christensen R, et al. **Abatacept with methotrexate** versus other biologic agents in treatment of patients with active rheumatoid arthritis despite methotrexate: a network meta-analysis. Arthritis Res Ther. 2011;13(6):R204.

Guzman J, Oen K, Tucker LB, et al. The outcomes of **juvenile idiopathic arthritis** in children managed with contemporary treatments: results from the **ReACCh-Out** cohort. Ann Rheum Dis. 2014 May 19. pii: annrheumdis-2014-205372.

Guzman J, Henrey A, Loughin T, et al. Predicting Which Children with **Juvenile Idiopathic Arthritis Will Have a Severe Disease** Course: Results from the **ReACCh-Out** Cohort. J Rheumatol. 2016 Dec 15.

Gwinnutt JM, et al. The **20 year outcome** & association between **early treatment & mortality** and disability in an inception cohort of patients with rheumatoid arthritis: Results from the Norfolk Arthritis Register. Arthritis Rheumatol. 2017 Apr 20.

Haavardsholm EA, Aga AB, Olsen IC, et al. **Ultrasound in management** of rheumatoid arthritis: ARCTIC randomised controlled strategy trial. BMJ. 2016 Aug 16;354:i4205.

Hackmon, Rinat, Sakaguchi, Sachi, Koren, Gideon. Effect of **methotrexate treatment of ectopic pregnancy on subsequent pregnancy**. Can Fam Physician 2011 57: 37-39.

Hadam J, Aoun E, Clarke K, Wasko MC. Managing **risks of TNF inhibitors**: An update for the internist. Cleve Clin J Med. 2014 Feb;81(2):115-27.

Hagel S, Petersson IF, Bremander A, et al. **Trends in the first decade of 21st century** healthcare utilisation in a rheumatoid arthritis cohort compared with the general population. Ann Rheum Dis. 2012 Dec 8.

Hall JJ, Katz SJ, Cor MK. Patient Satisfaction with **Pharmacist-Led Collaborative** Follow-Up Care in an Ambulatory Rheumatology Clinic. Musculoskeletal Care. 2016 Sep 30.

Hambardzumyan K, Bolce R, Saevarsdottir S, et al. **Pretreatment multi-biomarker disease activity score** and radiographic progression in early RA: results from the **SWEFOT** trial. Ann Rheum Dis. 2014 May 8.

Hambardzumyan K, Saevarsdottir S, Forslind K, et al. A **multi-biomarker disease** activity score and the choice of second-line therapy in early rheumatoid arthritis after methotrexate failure. Arthritis Rheumatol. 2016 Dec 19.

Harnden K, Pease C, Jackson A. **Rheumatoid arthritis**. BMJ. 2016 Mar 23;352:i387.

Harrold LR, et al. The comparative effectiveness of **abatacept versus anti-tumour necrosis factor switching** for rheumatoid arthritis patients previously treated with an anti-tumour necrosis factor. Ann Rheum Dis. 2015 Feb;74(2):430-6.

Haschka J, Englbrecht M, Hueber AJ, et. al. **Relapse rates in patients with rheumatoid arthritis in stable remission tapering or stopping antirheumatic therapy**: interim results from the prospective randomised controlled RETRO study. Ann Rheum Dis. 2015 Feb 6. pii: annrheumdis-2014-206439.

Hashkes PJ, Laxer RM. Medical treatment of **juvenile idiopathic arthritis**. JAMA. 2005 Oct 5;294(13):1671-84. (InfoPOEMs: Nonsteroidal anti-inflammatory drugs (NSAIDs), intra-articular injections of corticosteroids, methotrexate, and possibly biologic-modifiers are somewhat beneficial in the management of juvenile idiopathic arthritis (JIA), particularly oligoarthritis. Patients with polyarthritis and a positive rheumatoid factor respond poorly to medications and require aggressive individual management. (LOE = 1a-))

Haraoui B, Cameron L, Ouellet M, White B. **Anti-infliximab antibodies** in patients with rheumatoid arthritis who require higher doses of infliximab to achieve or maintain a clinical response. J Rheumatol. 2006 Jan;33(1):31-6.

Harrison SR, Li D, Jeffery LE, et al. **Vitamin D, Autoimmune Disease and Rheumatoid Arthritis**. Calcif Tissue Int. 2019 Jul 8.

Harrold LR, Harrington JT, Curtis JR, et al. **Prescribing practices** in a US cohort of rheumatoid arthritis patients before and after publication of the ACR treatment recommendations. Arthritis Rheum. 2011 Sep 27. doi: 10.1002/art.33380.

Haroon N, Inman RD, Learch TJ, et al. The Impact of **TNF-inhibitors on radiographic progression** in Ankylosing Spondylitis. Arthritis Rheum. 2013 Jul 1.

Hart JE, Källberg H, Laden F, et al. **Ambient air pollution** exposures and risk of rheumatoid arthritis in the Nurses' Health Study. Arthritis Care Res (Hoboken). 2013 Feb 11.

Hashkes PJ, Becker ML, Cabral DA, Laxer et al. **Methotrexate**: New Uses for an Old Drug. J Pediatr. 2013 Nov 25.

Hatzara C, Hadziyannis E, Kandili A, Koutsianas C, et al. Frequent **conversion of tuberculosis screening tests during anti-tumour necrosis factor therapy** in patients with rheumatic diseases. Ann Rheum Dis. 2015 Oct;74(10):1848-53.

Haynes K, Beukelman T, et al; the Safety Assessment of Biological thERapeutics (SABER) Collaboration. **Tumor necrosis factor alpha inhibitor therapy and cancer** risk in chronic immune mediated diseases. Arthritis Rheum. 2012 Oct 10.

Hazlewood GS, Barnabe C, Tomlinson G, et al. **Methotrexate monotherapy and methotrexate combination therapy** with **traditional and biologic disease modifying antirheumatic drugs** for rheumatoid arthritis: abridged Cochrane systematic review and network meta-analysis. BMJ. 2016 Apr 21;353:i1777.

Hazlewood GS, Thorne JC, Pope JE, et al; **CATCH** Investigators. The comparative effectiveness of **oral versus subcutaneous methotrexate** for the treatment of early rheumatoid arthritis. Ann Rheum Dis. 2016 Jun;75(6):1003-8.

Hazlewood GS, Bombardier C, Tomlinson G, Thorne Cet al. **Treatment preferences** of patients with **early rheumatoid** arthritis: a discrete-choice experiment. Rheumatology (Oxford). 2016 Jul 31.

Hazlewood GS, Barnabe C, Tomlinson G, Marshall D, Devoe DJA, Bombardier C. **Methotrexate monotherapy and methotrexate combination therapy** with traditional and biologic disease modifying anti-rheumatic drugs for rheumatoid arthritis: A network meta-analysis. Cochrane Database of Systematic Reviews 2016, Issue 8. Art. No.: CD010227. We found moderate to high quality evidence that combination therapy with methotrexate + sulfasalazine+ hydroxychloroquine (triple therapy) or methotrexate + most biologic DMARDs or tofacitinib were similarly effective in controlling disease activity and generally well tolerated in methotrexate-naïve patients or after an inadequate response to methotrexate. Methotrexate + some biologic DMARDs were superior to methotrexate in preventing joint damage in methotrexate-naïve patients, but the magnitude of these effects was small over one year.

Health Canada Aug/09 TNF blockers & risk of **cancer** in children and young adults http://www.hc-sc.gc.ca/ahc-asc/media/advisories-avis/_2009/2009_137-eng.php
Health Canada June/11 **RITUXAN (rituximab) - Fatal Infusion Related Reactions** in Patients with Rheumatoid Arthritis
Health Canada Oct/12 is informing Canadians and Canadian health care practitioners that the labelling for **methotrexate and Proton Pump Inhibitors** (eg. Omeprazole) will include information on a potential interaction between these products.
Health Canada Feb/13 Severe skin reactions such as Toxic Epidermal Necrolysis (TEN) and Stevens-Johnson Syndrome (**SJS**) have been reported very rarely in patients who were given **RITUXAN** for the treatment of cancer or disorders of the immune system such as rheumatoid arthritis (RA). Some cases resulted in death.
Health Canada Mar'19: Clinical trial finds an increased **risk of blood clots in the lungs and of death in rheumatoid arthritis patients taking high dose of tofacitinib** (sold as Xeljanz or Xeljanz XR)
Health Canada May/19: **ACTEMRA® (tocilizumab) – Risk of Hepatotoxicity** - Hoffmann-La Roche Limited, serious cases of drug-induced liver injuries (DILI) have been reported in patients treated with ACTEMRA, including cases of acute liver failure requiring a transplant.
Hedström AK, Klareskog L, Alfredsson L. Exposure to **passive smoking and rheumatoid arthritis risk**: results from the Swedish **EIRA study**. Ann Rheum Dis. 2018 Jul;77(7):970-972.
Heijstek MW, Ott de Bruin LM, Bijl M, et al. EULAR recommendations for **vaccination in paediatric patients with rheumatic diseases**. Ann Rheum Dis. 2011 Oct;70(10):1704-12.
Heijstek MW, van Gageldonk PG, et al. Differences in persistence of **measles, mumps, rubella, diphtheria and tetanus antibodies** between children with **rheumatic disease** and healthy controls: a retrospective cross-sectional study. Ann Rheum Dis. 2012 Jun;71(6):948-54. (lower antibody rates in: mumps, rubella, diphtheria and tetanus)
Heijstek MW, Kamphuis S, Armbrust W, et al. Effects of the live attenuated **measles-mumps-rubella booster vaccination** on disease activity in patients with juvenile idiopathic arthritis: a randomized trial. JAMA. 2013 Jun 19;309(23):2449-56.
Heimans L, Wevers-de Boer KV, Visser K, et al. A two-step treatment strategy trial in patients with **early arthritis** aimed at achieving remission: the **IMPROVED** study. Ann Rheum Dis. 2014 Jul;73(7):1356-61.
Hellgren K, Dreyer L, Arkema EV, et al. **Cancer risk in patients with spondyloarthritis treated with TNF inhibitors**: a collaborative study from the ARTIS and DANBIO registers. Ann Rheum Dis. 2016 May 4. pii: annrheumdis-2016-209270.
Henaux S, et al. Risk of losing remission, low disease activity or radiographic progression in case of **bDMARD discontinuation or tapering** in rheumatoid arthritis: systematic analysis of the literature and meta-analysis. Ann Rheum Dis. 2018 Apr;77(4):515-522.
Henes JC, Schedel J, Kanz L, Koetter I. **Rituximab** and concomitant **leflunomide** for the treatment of rheumatoid arthritis. Rheumatol Int. . [Epub ahead of print]
Henness S, Yang LP. **Modified-Release Prednisone**: in Patients with Rheumatoid Arthritis. Drugs. 2013 Nov 19.
Hensvold AH, Frisell T, Magnusson PK, et al. How well do **ACPA discriminate** and predict RA in the general population: a study based on 12 590 population-representative Swedish twins. Ann Rheum Dis. 2016 Apr 28.
Hernández MV et al. **Cutaneous adverse events** during treatment of chronic inflammatory rheumatic conditions with **tumor necrosis factor antagonists**: Study using the Spanish Registry of Adverse Events of Biological Therapies in Rheumatic Diseases. Arthritis Care Res (Hoboken) 2013 Dec; 65:2024.
Hernandez-Molina G, Avila-Casado C, Nunez-Alvarez C, et al. Utility of the American-European Consensus Group and American College of Rheumatology Classification Criteria for **Sjogren`s syndrome** in patients with systemic autoimmune diseases in the clinical setting. Rheumatology (Oxford). 2014 Sep 5.
Hetland ML, Stengaard-Pedersen K, Junker P, et al. **CIMESTRA** study group. **Aggressive combination therapy** with intra-articular glucocorticoid injections and conventional disease-modifying anti-rheumatic drugs in early rheumatoid arthritis: second-year clinical and radiographic results from the CIMESTRA study. Ann Rheum Dis. 2008 Jun;67(6):815-22. Epub 2007 Sep 18.
Hetland ML, Ostergaard M, Ejbjerg B, et al; **CIMESTRA** study group. Short- and long-term efficacy of **intra-articular injections with betamethasone** as part of a treat-to-target strategy in early rheumatoid arthritis: impact of joint area, repeated injections, MRI findings, anti-CCP, IgM-RF and CRP. Ann Rheum Dis. 2012 Jun;71(6):851-6.
Hetta DF, Elawamy AM, Hassanein MM, et al. **Efficacy of Atlantoaxial Joint Glucocorticoid Injection** in Patients with Rheumatoid Arthritis: A Randomized Trial. Pain Physician. 2019 Jul;22(4):E295-E302.
Hewitt RJ, Francis M, Singanayagam A, Kon OM. **Screening tests for tuberculosis before starting biological therapy**. BMJ. 2015 Mar 5;350:h1060.
Hider SL, et al. Comparing the long-term clinical outcome of treatment with **methotrexate or sulfasalazine** prescribed as the first disease-modifying antirheumatic drug in patients with inflammatory polyarthritis. Ann Rheum Dis. 2006 Nov;65(11):1449-55. Epub 2006 Mar 15.
Hilliquin S, Hugues B, Mitrovic S, et al. Ability of **disease-modifying antirheumatic drugs to prevent or delay rheumatoid arthritis onset**: a systematic literature review and meta-analysis. Ann Rheum Dis. 2018 Jun 8.
Hissink Muller P, Brinkman DMC, Schonenberg-Meinema D, et al. **Treat to target (drug-free) inactive disease in DMARD-naive juvenile idiopathic arthritis**: 24-month clinical outcomes of a three-armed randomised trial. Ann Rheum Dis. 2019 Jan;78(1):51-59.
Hjardem E, Ostergaard M, Podenphant J, et al.. Do rheumatoid arthritis patients in clinical practice benefit from **switching from infliximab to a second tumor necrosis factor** alpha inhibitor? Ann Rheum Dis. 2007 Sep;66(9):1184-9. Epub 2007 Mar 27. Lack of efficacy switchers had a better clinical response to the second treatment. Adverse effect switchers responded equally well to both treatments, with a low risk of discontinuing the second drug as a result of AE. Drug survival of the switchers' second biological therapy was higher than of the first, but lower than that of non-switchers. No difference between various sequences of drugs were found. Danish post-marketing data thus support that RA patients may benefit from switching biological therapy.
Hodax JK, Bialo SR, Yalcindag A. SIADH in Systemic JIA Resolving After Treatment With an **IL-6 Inhibitor (tocilizumab).** Pediatrics. 2017 Dec 14.
Hoekstra M, Haagsma C, Neef C, Proost J, Knuif A, van de Laar M. **Bioavailability of higher dose methotrexate comparing oral and subcutaneous** administration in patients with rheumatoid arthritis. J Rheumatol. 2004 Apr;31(4):645-8.
Hoekstra M, et al. **Splitting high-dose oral methotrexate** improves bioavailability: a pharmacokinetic study in patients with rheumatoid arthritis. J Rheumatol. 2006 Mar;33(3):481-5. Epub 2006 Jan 15.
Hoes JN, Jacobs JW, Boers M, et al. EULAR evidence-based recommendations on the management of systemic glucocorticoid therapy in rheumatic diseases. Ann Rheum Dis. 2007 Dec;66(12):1560-7. Epub 2007 Jul 27.
Hoes JN, Jacobs JW, Verstappen SM, Bijlsma JW, Van der Heijden GJ. Adverse events of low- to medium-dose oral **glucocorticoids** in inflammatory diseases: a meta-analysis. Ann Rheum Dis. 2009 Dec;68(12):1833-8. Epub 2008 Dec 9.
Hoes JN, van der Goes MC, et al. Glucose tolerance, insulin sensitivity and {beta}-cell function in patients with rheumatoid arthritis treated with or without low-to-medium dose **glucocorticoids**. Ann Rheum Dis. 2011 Nov;70(11):1887-94.
Højgaard P, Glintborg B, Hetland ML, et al. Association between **tobacco smoking and response to tumour necrosis factor α inhibitor treatment** in psoriatic arthritis: results from the **DANBIO** registry. Ann Rheum Dis. 2015 Dec;74(12):2130-6.
Holle JU, Dubrau C, Herlyn K, et al. **Rituximab** for refractory **granulomatosis with polyangiitis** (**Wegener's granulomatosis**): comparison of efficacy in granulomatous versus vasculitic manifestations. Ann Rheum Dis. 2012 Mar;71(3):327-33.
Holmqvist ME, Neovius M, Eriksson J, et al. **Risk of venous thromboembolism** in patients with rheumatoid arthritis and association with disease duration and hospitalization. JAMA. 2012 Oct 3;308(13):1350-6.
Holmqvist M, Ljung L, Askling J. **Acute coronary syndrome** in new-onset rheumatoid arthritis: a population-based nationwide cohort study of time trends in risks and excess risks. Ann Rheum Dis. 2017 Oct;76(10):1642-1647
Holmqvist M;Ljung L;Askling J **Mortality** following new-onset Rheumatoid Arthritis: has modern Rheumatology had an impact?. Ann Rheum Dis. 2017 Sep 26.
Holmqvist M, et al. **Mortality** following new-onset Rheumatoid Arthritis: has modern Rheumatology had an impact? Ann Rheum Dis. 2018 Jan;77(1):85-91.
Holvast A, et al. Safety & efficacy of influenza vaccination in systemic **lupus** erythematosus patients with quiescent disease. Ann Rheum Dis. 2006 Jul;65(7):913-8. Epub 2005 Dec1.
Horneff G, Ebert A, Fitter S, et al. Safety and effi cacy of once **weekly etanercept** 0.8 mg/kg in a multicentre 12 week trial in active polyarticular course juvenile idiopathic arthritis. Rheumatology (Oxford) 2009; 48: 916–19.
Horneff G, De Bock F, et al. Safety and efficacy of combination of **etanercept and methotrexate** compared to treatment with etanercept only in patients with juvenile idiopathic arthritis (JIA): preliminary data from the German JIA Registry. Ann Rheum Dis 2009; 68: 519–25.
Horneff G, Burgos-Vargas R, Constantin T, et al; Paediatric Rheumatology International Trials Organisation (PRINTO). Efficacy and safety of open-label **etanercept** on extended oligoarticular juvenile idiopathic arthritis, enthesitis-related arthritis and psoriatic arthritis: part 1 (week 12) of the **CLIPPER** study. Ann Rheum Dis. 2014 Jun 1;73(6):1114-22.
Hørslev-Petersen K, Hetland ML, Junker P, et al. **Adalimumab** added to a treat-to-target strategy with **methotrexate and intra-articular triamcinolone** in early rheumatoid arthritis increased remission rates, function and quality of life. The OPERA Study: an investigator-initiated, randomised, double-blind, parallel-group, placebo-controlled trial. Ann Rheum Dis. 2014 Apr 1;73(4):654-61.
Hørslev-Petersen K, Hetland ML, Ørnbjerg LM, et al. Clinical and radiographic outcome of a **treat-to-target strategy** using **methotrexate** and intra-articular **glucocorticoids** with or without **adalimumab** induction: a 2-year investigator-initiated, double-blinded, randomised, controlled trial (**OPERA**). Ann Rheum Dis. 2016 Sep;75(9):1645-53.
Horton DB, Scott FI, Haynes K, et al.. **Antibiotic Exposure and Juvenile Idiopathic Arthritis**: A Case-Control Study. Pediatrics. 2015 Jul 20.
Hu Y, Sparks JA, Malspeis S, et al. **Long-term dietary quality** and risk of developing rheumatoid arthritis in women. Ann Rheum Dis. 2017 Aug;76(8):1357-1364.
Huang F, Gu J, Zhu P, et al Efficacy and safety of **adalimumab** in Chinese adults with active **ankylosing spondylitis**: results of a randomised, controlled trial. Ann Rheum Dis. 2014 Mar 1;73(3):587-94.
Hughes CD, Scott DL, Ibrahim F. **Intensive therapy and remissions in rheumatoid arthritis**: a systematic review. BMC Musculoskelet Disord. 2018 Oct 30;19(1):389.
Huizinga Tom W.J. Pincus Theodore **In the Clinic**: **Rheumatoid Arthritis**. *Ann Intern Med* July 6, 2010 153:ITC1-1; doi:10.1059/0003-4819-153-1-201007060-01001. (**Updated Jan 2019**)
Huizinga TW, Conaghan PG, Martin-Mola E, et al. Clinical and radiographic outcomes at 2 years and the effect of **tocilizumab discontinuation** following sustained remission in the second and third year of the ACT-RAY study. Ann Rheum Dis. 2015 Jan;74(1):35-43.

Humby F, Lewis M, Ramamoorthi N, et al. **Synovial cellular and molecular signatures stratify clinical response to csDMARD** therapy and predict radiographic progression in early rheumatoid arthritis patients. Ann Rheum Dis. 2019 Jun;78(6):761-772.

Humphreys JH, Verstappen SM, Hyrich KL, et al.The incidence of rheumatoid arthritis in the UK: comparisons using the **2010 ACR/EULAR classification criteria and the 1987 ACR** classification criteria. Results from the Norfolk Arthritis Register. Ann Rheum Dis. 2013 Aug;72(8):1315-20.

Humphreys JH, Warner A, Costello R, et al. Quantifying the **hepatotoxic risk** of **alcohol** consumption in patients with rheumatoid arthritis taking **methotrexate**. Ann Rheum Dis. 2017 Mar 23.

Huang Z, Lee PY, Yao X, Zheng S, Li T. **Tofacitinib Treatment of Refractory Systemic Juvenile Idiopathic Arthritis.** Pediatrics. 2019 Apr 4.

Hurkmans E, van der Giesen FJ, Vliet Vlieland TP, et al. Dynamic **exercise programs** (aerobic capacity and/or muscle strength training) in patients with rheumatoid arthritis. Cochrane Database Syst Rev. 2009 Oct 7;(4):CD006853.

Hyldgaard C, Hilberg O, Pedersen AB, et al. A population-based cohort study of **rheumatoid arthritis-associated interstitial lung disease**: comorbidity and mortality. Ann Rheum Dis. 2017 Jun 13.

Hyrich KL, et al. Comparison of the response to **infliximab or etanercept monotherapy with the response to cotherapy with methotrexate or another disease-modifying** antirheumatic drug in patients with rheumatoid arthritis: Results from the British Society for Rheumatology Biologics Register. Arthritis Rheum. 2006 May 30;54(6):1786-1794 [Epub ahead of print]

l'Ami MJ, Krieckaert CL, et al. Successful reduction of overexposure in patients with rheumatoid arthritis with **high serum adalimumab concentrations**: an open-label, non-inferiority, randomised clinical trial. Ann Rheum Dis 2018;77:484–7.

Iacono AT, et al. A randomized trial of inhaled cyclosporine in lung-transplant recipients. N Engl J Med. 2006 Jan 12;354(2):141-50.

Iannone F, Gremese E, et al. **Longterm** Retention of **Tumor Necrosis Factor-α Inhibitor** Therapy in a Large Italian Cohort of Patients with Rheumatoid Arthritis from the GISEA Registry: An Appraisal of Predictors. J Rheumatol. 2012 Apr 1.

Iking-Konert C, Aringer M, Wollenhaupt J, et al. Performance of the new 2011 ACR/EULAR remission criteria with **tocilizumab** using the phase IIIb study **TAMARA** as an example and their comparison with traditional remission criteria. Ann Rheum Dis. 2011 Nov;70(11):1986-90.

Ilar A, Alfredsson L, Wiebert P, et al. **Occupation** and Risk of **Developing Rheumatoid Arthritis**: Results From a Population-Based Case-Control Study. Arthritis Care Res (Hoboken). 2017 Aug 10.

Isaacs JD, Cohen SB, Emery P, et al. Effect of baseline rheumatoid factor and anticitrullinated peptide antibody serotype on **rituximab** clinical response: a meta-analysis. Ann Rheum Dis. 2013 Mar;72(3):329-36.

Izmirly PM, Costedoat-Chalumeau N, Pisoni C, et al. Maternal Use of **Hydroxychloroquine** is Associated with a Reduced Risk of Recurrent Anti-SSA/Ro Associated Cardiac Manifestations of **Neonatal Lupus**. Circulation. 2012 May 24.

Jafarzadeh SR, Felson DT. Updated estimates suggest a much **higher prevalence of arthritis in US** adults than previous ones. Arthritis Rheumatol. 2017 Nov 27.

Jaffe GJ, Dick AD, Brézin AP, et al. **Adalimumab** in Patients with Active Noninfectious **Uveitis**. N Engl J Med. 2016 Sep 8;375(10):932-43.

Jaimes-Hernández J, Meléndez-Mercado CI, et al. Efficacy of **leflunomide 100mg weekly** compared to low dose methotrexate in patients with active rheumatoid arthritis. Double blind,randomized clinical trial. Reumatol Clin. 2012 Jul 2.

Jani M, Chinoy H, Warren RB, et al; BRAGGSS. Clinical utility of **random anti-TNF drug level testing and measurement of anti-drug antibodies** on long-term treatment response in rheumatoid arthritis. Arthritis Rheumatol. 2015 Jun 24.

Jani M, Isaacs JD, Morgan AW, et al; BRAGGSS.. High frequency of antidrug **antibodies** and association of random **drug levels** with efficacy in **certolizumab** pegol-treated patients with rheumatoid arthritis: results from the **BRAGGSS** cohort. Ann Rheum Dis. 2016 May 31.

Jamnitski A et al. Patients **non-responding to etanercept obtain lower etanercept concentrations** compared with responding patients. Ann Rheum Dis. 2012 Jan;71(1):88-91.

Jeimy S, McRae K, Pattani R. A **63-year-old** returned traveller with **fever, rash, hepatitis and eosinophilia**. CMAJ. 2018 Jul 9;190(27):E831-E835. (**sulfasalazine**)

Jensen TW, et al; Periarticular & generalised bone loss in patients with early rheumatoid arthritis: influence of **alendronate** and intra-articular glucocorticoid treatment. Post hoc analyses-**CIMESTRA** trial. Ann Rheum Dis. 2014 Jun 1;73(6):1123-9.

Ji X, Zhu J, Li K, et al. The Bull's Eye of **Antimalarial Toxicity**. Arthritis Rheumatol. 2016 Aug;68(8):2015.

Jiang X, Trouw LA, van Wesemael TJ, et al. **Anti-CarP antibodies** in two large cohorts of patients with rheumatoid arthritis and their relationship to genetic risk factors, cigarette smoking and other autoantibodies. Ann Rheum Dis. 2014 Oct;73(10):1761-8.

Jin Z, Xiang C, Cai Q, et al. **Alcohol consumption** as a preventive factor for developing rheumatoid arthritis: a dose-response meta-analysis of prospective studies. Ann Rheum Dis. 2014 Nov;73(11):1962-7.

Johnsen AK, Schiff MH, Mease PJ, et al. Comparison of 2 Doses of **Etanercept (50 vs 100 mg)** in Active Rheumatoid Arthritis: a Randomized Double Blind Study. J Rheumatol. 2006 Feb 15; [Epub ahead of print]

Jølving LR, Nielsen J, Kesmodel US, et al. **Children born by women with rheumatoid arthritis have increased susceptibility for selected chronic diseases** - a nationwide cohort study. Arthritis Care Res (Hoboken). 2017 Dec 11.

Joly P, Maho-Vaillant M, Prost-Squarcioni C, et al. First-line **rituximab** combined with short-term prednisone versus **prednisone** alone for the treatment of **pemphigus** (**Ritux 3**): a prospective, multicentre, parallel-group, open-label randomised trial. Lancet 2017; online Mar 22.

Jones HJ, Hubbard L, Mitchell RE, et al. Association of **Genetic Risk** for Rheumatoid Arthritis **With Cognitive and Psychiatric Phenotypes** Across Childhood and Adolescence. JAMA Netw Open. 2019 Jun 5;2(6):e196118.

Jørgensen KK, Olsen IC, Goll GL, et al, on behalf of the **NOR-SWITCH** study group. Switching from originator **infliximab to biosimilar CT-P13** compared with maintained treatment with originator infliximab (NOR-SWITCH): 52-week, randomised, double-blind, non-inferiority trial. Lancet 2017; online May 11.

Jung M, Barra L. **Pain and swelling in the hands** and wrists of a 45-year-old woman. CMAJ. 2015 Jan 6;187(1):E53-4.

Just SA, Rostgaard K, Titlestad K, et al. **Transmission of rheumatoid arthritis through blood transfusion**: a retrospective cohort study. Ann Rheum Dis. 2018 Oct;77(10):1536-1537.

Juster-Switlyk K, Smith AG, Kovacsovics T, et al. **MTHFR C677T polymorphism** is associated with **methotrexate-induced myelopathy** risk. Neurology. 2017 Feb 7;88(6):603-604.

Kaine J et al. Evaluation of **abatacept administered subcutaneously** in adults with active rheumatoid arthritis: impact of withdrawal and reintroduction on immunogenicity, efficacy and safety (phase Iiib ALLOW study). Ann Rheum Dis. 2012 Jan;71(1):38-44.

Kalb RE, Fiorentino DF, Lebwohl MG, et al. Risk of **Serious Infection With Biologic and Systemic Treatment of Psoriasis**: Results From the Psoriasis Longitudinal Assessment and Registry (**PSOLAR**). JAMA Dermatol. 2015 May 13.

Kalden JR, Schattenkirchner M, et al. The efficacy and safety of **leflunomide** in patients with active rheumatoid arthritis: a five-year followup study. Arthritis Rheum. 2003 Jun;48(6):1513-20.

Källberg Henrik, Ding Bo, Padyukov Leonid, et al. EIRA Study Group. Concise report: **Smoking** is a major preventable risk factor for rheumatoid arthritis: estimations of risks after various exposures to cigarette smoke. Ann Rheum Dis 2011;70:508-511 Published Online First: 13 December 2010 doi:10.1136/ard.2009.120899.

Källberg H, Ding B, Padyukov L, et al. EIRA Study Group. **Smoking** is a major preventable risk factor for rheumatoid arthritis: estimations of risks after various exposures to cigarette smoke. Ann Rheum Dis. 2010 Dec 13.

Kane S, Ford J, et al. **Placental transport of immunoglobulins**: a clinical review for gastroenterologists who prescribe therapeutic monoclonal antibodies to women during conception and pregnancy. Am J Gastroenterol. 2009;104:228-233.

Kaneko Y, Atsumi T, Tanaka Y, et al. Comparison of adding **tocilizumab** to methotrexate with switching to tocilizumab in patients with rheumatoid arthritis with inadequate response to methotrexate: 52-week results from a prospective, randomised, controlled study (**SURPRISE** study). Ann Rheum Dis. 2016 Jan 5.

Kaneko Y, Kameda H, Ikeda K, et al. **Tocilizumab in patients with adult-onset still's disease refractory to glucocorticoid treatment**: a randomised, double-blind, placebo-controlled phase III trial. Ann Rheum Dis. 2018 Dec;77(12):1720-1729.

Kaneko Y, Kato M, Tanaka Y, et al. **Tocilizumab discontinuation after attaining remission in patients with rheumatoid arthritis** who were treated with tocilizumab alone or in combination with methotrexate: results from a prospective randomised controlled study (the second year of the SURPRISE study). Ann Rheum Dis. 2018 Sep;77(9):1268-1275.

Kapetanovic MC, Roseman C, Jönsson G, et al. **Methotrexate but not TNF-blockers reduces antibody response following pneumococcal vaccination** using 7-valent conjugate pneumococcal vaccine in adult patients with established arthritis. Arthritis Rheum. 2011 Aug 10.

Kaplan YC, Ozsarfati J, Nickel C, et al. **Reproductive Outcomes** Following **Hydroxychloroquine** Use for Autoimmune Diseases: A Systematic Review and Meta-analysis. Br J Clin Pharmacol. 2015 Dec 23.

Kapoor SR, Filer A, Fitzpatrick MA, et al. **Metabolic profiling predicts response** to **anti-TNFα therapy** in patients with rheumatoid arthritis. Arthritis Rheum. 2013 Mar 4.

Karlsson JA, Neovius M, Nilsson JA, et al. **Addition of infliximab** compared with **addition of sulfasalazine and hydroxychloroquine to methotrexate** in early rheumatoid arthritis: 2-year quality-of-life results of the randomised, controlled, **SWEFOT** trial. Ann Rheum Dis. 2012 Nov 29.

Karpouzas GA, Estis J, Rezaeian P, et al. High-sensitivity cardiac **troponin I is a biomarker for occult coronary plaque burden** and cardiovascular events in patients with rheumatoid arthritis. Rheumatology (Oxford). 2018 Mar 14.

Kastbom A, Forslind K, Ernestam S, et al. Changes in the **anticitrullinated peptide antibody response** in relation to therapeutic outcome in early rheumatoid arthritis: results from the SWEFOT trial. Ann Rheum Dis. 2014 Dec 30.

Katchamart W, Bourré-Tessier J, Donka T, Drouin J, Rohekar G, Bykerk VP. **Canadian recommendations for use of methotrexate** in patients with rheumatoid arthritis. J Rheumatol [Internet]. 2010 Jul;37(7):1422-30.

Katchamart W, Trudeau J, Phumethum V, Bombardier C. **Methotrexate monotherapy versus methotrexate combination** therapy with non-biologic disease modifying anti-rheumatic drugs for rheumatoid arthritis. Cochrane Database of Syst Rev [Internet]. 2010 Apr [cited 2011 Apr 11];(4):CD008495.

Katz P, Margaretten M, Gregorich S, Trupin L. **Physical Activity** to Reduce Fatigue in Rheumatoid Arthritis: A Randomized Controlled Trial. Arthritis Care Res (Hoboken). 2018 Jan;70(1):1-10.

Kaur K, Kalra S, Kaushal S. Systematic Review of **Tofacitinib**: A New Drug for the Management of Rheumatoid Arthritis. Clin Ther. 2014 Jul 1;36(7):1074-1086.

Kaur P, Chow V, Zhang N, et al. A randomised, single-blind, single-dose, three-arm, parallel-group study in healthy subjects to demonstrate pharmacokinetic **equivalence** of **ABP 501 and adalimumab**. Ann Rheum Dis. 2017 Mar;76(3):526-533.

Kavanaugh A, et al. The **Infliximab** Multinational **Psoriatic Arthritis** Controlled Trial (**IMPACT**): results of radiographic analyses after 1 year. Ann Rheum Dis. 2006 Aug;65(8):1038-43. Epub 2006 Jan 26.

Kavanaugh A, Husni ME, Harrison DD, et al. Safety and efficacy of intravenous **golimumab** in patients with active **psoriatic arthritis**: Results through week 24 of the **GO-VIBRANT** study. Arthritis Rheumatol. 2017 Aug 13.

Kavanaugh A, van der Heijde D, McInnes I, et al. **Golimumab**, a human TNF-alpha antibody, administered every 4 weeks as a subcutaneous injection in **psoriatic arthritis**: Clinical efficacy, radiographic, and safety findings through 1year of the randomized, placebo-controlled, **GO-REVEAL**® study. Arthritis Rheum. 2012 Feb 29.

Kavanaugh A, Fleischmann RM, Emery P, et al. Clinical, functional and radiographic consequences of achieving stable low disease activity and remission with **adalimumab plus methotrexate** or methotrexate alone in early rheumatoid arthritis: 26-week results from the randomised, controlled OPTIMA study. Ann Rheum Dis. 2013 Jan;72(1):64-71.

Kavanaugh A, McInnes IB, Mease PJ, et al. Clinical efficacy, radiographic and safety findings through **2 years of golimumab** treatment in patients with active psoriatic arthritis: results from a long-term extension of the randomised, placebo-controlled GO-REVEAL study. Ann Rheum Dis. 2013 Nov 1;72(11):1777-1785.

Kavanaugh A, Gladman D, van der Heijde D, et al. Improvements in **productivity at paid work** and within the household, and increased participation in daily activities after 24 weeks of certolizumab pegol treatment of patients with psoriatic arthritis: results of a phase 3 double-blind randomized placebo-controlled study. Ann Rheum Dis. 2015 Jan;74(1):44-51.

Kavanaugh A, Lee SJ, Curtis JR, et al. **Discontinuation of tumour necrosis factor inhibitors** in patients with rheumatoid arthritis in low-disease activity: persistent benefits. Data from the Corrona registry. Ann Rheum Dis. 2015 Jun;74(6):1150-5.

Kavanaugh A, et al. Safety and Efficacy of Intravenous **Golimumab** in Patients With Active Psoriatic Arthritis: Results Through Week Twenty-Four of the GO-VIBRANT Study. Arthritis Rheumatol. 2017 Nov;69(11):2151-2161.

Kavanaugh A, et al. Testing treat-to-target outcomes with initial **methotrexate monotherapy compared** with initial tumour necrosis factor inhibitor **(adalimumab) plus methotrexate** in early rheumatoid arthritis. Ann Rheum Dis. 2018 Feb;77(2):289-292.

Kawai VK et al. The ability of the 2013 **American College of Cardiology/American Heart Association cardiovascular risk score** to identify rheumatoid arthritis patients with high coronary artery calcification scores. Arthritis Rheum (Munch) 2015 Feb; 67:381.

Kay J, Fleischmann R, Keystone E, et al. **Golimumab** 3-year safety update: an analysis of pooled data from the long-term extensions of randomised, double-blind, placebo-controlled trials conducted in patients with rheumatoid arthritis, psoriatic arthritis or ankylosing spondylitis. Ann Rheum Dis. 2015 Mar;74(3):538-46.

Kay J, Fleischmann R, et al. Five-year Safety Data from 5 Clinical Trials of Subcutaneous **Golimumab** in Patients with Rheumatoid Arthritis, Psoriatic Arthritis, and Ankylosing Spondylitis. J Rheumatol. 2016 Dec;43(12):2120-2130.

Kay J, Schoels MM, et al; Task Force on the **Use of Biosimilars** to Treat Rheumatological Diseases. Consensus-based recommendations for the use of biosimilars to treat rheumatological diseases. Ann Rheum Dis. 2018 Feb;77(2):165-174.

Kearsley-Fleet L, Davies R, De Cock D, et al. **Biologic refractory disease in rheumatoid arthritis:** results from the British Society for Rheumatology Biologics Register for Rheumatoid Arthritis. Ann Rheum Dis. 2018 Oct;77(10):1405-1412.

Keeling S, et al. Prospective observational analysis of the efficacy and safety of low-dose (3 mg/kg) infliximab in **ankylosing spondylitis**: 4-year followup. J Rheumatol. 2006 Mar;33(3):558-61. Epub 2006 Feb 1.

Kermani TA, Warrington KJ. **Polymyalgia rheumatica**. Lancet. 2012 Oct 5.

Kerola AM, Kauppi MJ, Kerola T, Nieminen TV. How early in the course of rheumatoid arthritis does the excess **cardiovascular risk** appear? Ann Rheum Dis. 2012 Oct;71(10):1606-15.

Kerola AM, Kerola T, Kauppi MJ, et al. **Cardiovascular comorbidities** antedating the diagnosis of rheumatoid arthritis. Ann Rheum Dis. 2013 Nov 1;72(11):1826-1829.

Keysor JJ, LaValley MP, Brown C, et al. **Efficacy of a Work Disability Prevention Program for People with Rheumatic and Musculoskeletal Conditions: A Single-Blind Parallel-Arm Randomized Controlled Trial.** Arthritis Care Res (Hoboken). 2018 Jul;70(7):1022-1029.

Keystone EC, Schiff MH, et al. **Once-weekly** administration of 50 mg **etanercept** in patients with active rheumatoid arthritis: results of a multicenter, randomized, double-blind, placebo-controlled trial. Arthritis Rheum. 2004 Feb;50(2):353-63.

Keystone EC, Genovese MC, Klareskog L, et al. GO-FORWARD Study. **Golimumab**, a human antibody to tumour necrosis factor {alpha} given by monthly subcutaneous injections, in active rheumatoid arthritis despite methotrexate therapy: the **GO-FORWARD** Study. Ann Rheum Dis. 2009 Jun;68(6):789-96. Epub 2008 Dec 9.

Keystone EC, Kremer JM, Russell A, et al. **Abatacept** in subjects who switch from intravenous to **subcutaneous** therapy: results from the phase IIIb ATTUNE study. Ann Rheum Dis. 2012 Jun;71(6):857-61.

Keystone EC, van der Heijde D, Kavanaugh A, et al. Clinical, Functional, and Radiographic Benefits of **Longterm Adalimumab Plus Methotrexate**: Final 10-year Data in Longstanding Rheumatoid Arthritis. J Rheumatol. 2013 Jul 1.

Keystone E, et al. **Long-term safety and efficacy of certolizumab** pegol in combination with methotrexate in the treatment of rheumatoid arthritis: 5-year results from the RAPID 1 trial and open-label extension. Ann Rheum Dis. 2013 Aug 5.

Keystone E, Landewé R, van Vollenhoven R, et al. Long-term safety and efficacy of **certolizumab** pegol in combination with methotrexate in the treatment of rheumatoid arthritis: 5-year results from the RAPID 1 trial and open label extension. Ann Rheum Dis. 2014 Dec;73(12):2094-100.

Keystone EC, Taylor PC, et al. Patient-reported outcomes from a phase 3 study of **baricitinib versus placebo or adalimumab** in rheumatoid arthritis: secondary analyses from the **RA-BEAM** study. Ann Rheum Dis. 2017 Nov;76(11):1853-1861.

Khan A, Scott DL, Batley M. **Smoking**, rheumatoid factor status and responses to rituximab. Ann Rheum Dis. 2012 Sep;71(9):1587-8.

Khanna D, Park GS, Paulus HE, et al. **Reduction of the efficacy of methotrexate** by the use of **folic acid**: post hoc analysis from two randomized controlled studies. Arthritis Rheum. 2005 Oct;52(10):3030-8.

Khanna D, McMahon M, Furst DE. **Safety of tumour necrosis factor-alpha antagonists**. (Pregnancy) Drug Saf. 2004;27(5):307-24.

Khanna D, Denton CP, Lin CJF, et al. Safety and efficacy of subcutaneous **tocilizumab** in **systemic sclerosis**: results from the open-label period of a phase II randomised controlled trial(faSScinate). Ann Rheum Dis. 2018 Feb;77(2):212-220.

Kiadaliri AA, Felson DT, Neogi T, et al. **Rheumatoid arthritis** as underlying **cause of death** in 31 countries, 1987-2011: Trend analysis of WHO mortality database. Arthritis Rheumatol. 2017 Apr 20.

Kiely P, Busby AD, Nikiphorou E, et al. Is incident **rheumatoid arthritis interstitial lung disease associated with methotrexate treatment**? Results from a multivariate analysis in the ERAS and ERAN inception cohorts. BMJ Open. 2019 May 5;9(5):e028466.

Kievit W, et al. **Disease activity-guided dose optimisation** of **adalimumab and etanercept** is a cost-effective strategy compared with non-tapering tight control rheumatoid arthritis care: analyses of the **DRESS** study. Ann Rheum Dis. 2016 Jan 13.

Kilic L, Erden A, Bingham CO 3rd, et al. The Reporting of Patient-reported Outcomes in Studies of Patients with Rheumatoid Arthritis: A Systematic Review of 250 Articles. J Rheumatol. 2016 Apr 15.

Kim G, Barner JC, et al. Examining **Time to Initiation of Biologic Disease-Modifying Antirheumatic Drugs** and Medication **Adherence** and **Persistence** Among Texas Medicaid Recipients With Rheumatoid Arthritis. Clin Ther. 2016 Feb 18.

Kim SC, Liu J, Solomon DH. The risk of **atrial fibrillation** in patients with rheumatoid arthritis. Ann Rheum Dis. 2014 Jun 1;73(6):1091-5.

Kim SC, Schneeweiss S, Liu J, et al. **Biologic Disease-Modifying Antirheumatic Drugs** and Risk of **High-grade Cervical Dysplasia and Cervical Cancer** in Rheumatoid Arthritis: A Cohort Study. Arthritis Rheumatol. 2016 Mar 25.

Kim SC, Solomon DH, Rogers JR, et al. **Cardiovascular Safety** of **Tocilizumab versus Tumor Necrosis Factor Inhibitors** in Patients with Rheumatoid Arthritis - a Multi-database Cohort Study. Arthritis Rheumatol. 2017 Feb 28.

Kim ST, Tayar J, Trinh VA, et al. Successful treatment of **arthritis induced by checkpoint inhibitors with tocilizumab**: a case series. Ann Rheum Dis. 2017 Dec;76(12):2061-2064.

Kimball AB, Kerdel F, Adams D, et al. **Adalimumab** for the treatment of moderate to severe **hidradenitis suppurativa**: a parallel randomized trial. Ann Intern Med. 2012 Dec 18;157(12):846-55.

Kimball AB, Okun MM, Williams DA, et al. Two Phase 3 Trials of **Adalimumab** for **Hidradenitis Suppurativa**. N Engl J Med. 2016 Aug 4;375(5):422-34.

Kindstedt E, Johansson L, Palmqvist P, et al. **Marginal jawbone loss** is associated with onset of rheumatoid arthritis and is related to plasma level of receptor activator of nuclear factor kappa-B ligand (RANKL). Arthritis Rheumatol. 2017 Dec 1.

Kingsbury SR, Tharmanathan P, Keding A, et al. **Hydroxychloroquine** effectiveness in reducing symptoms of **hand osteoarthritis**. A randomized trial. Ann Intern Med. 2018. [Epub ahead of print]. doi:10.7326/M17-1430

Kiriakidou M, Cotton D, Taichman D, Williams S. **Systemic Lupus Erythematosus**. Ann Intern Med. 2013 Oct 1;159(7):ITC4-1.

Kirwan JR, Bijlsma JW, Boers M, Shea BJ. Effects of **glucocorticoids** on radiological progression in rheumatoid arthritis. Cochrane Database Syst Rev. 2007 Jan 24;(1):CD006356.

Kivitz AJ, Schechtman J, Texter M, et al. **Vaccine responses** in patients with rheumatoid arthritis treated with **certolizumab** pegol: results from a single-blind randomized phase IV trial. J Rheumatol. 2014 Apr;41(4):648-57.

Kivitz A, Olech E, et al. Two-year Efficacy and Safety of **Subcutaneous Tocilizumab** in Combination with Disease-modifying Antirheumatic Drugs Including Escalation to Weekly Dosing in Rheumatoid Arthritis. J Rheumatol. 2017 Dec 15.

Klarenbeek NB, Kerstens PJ, Huizinga TW, et al. **Recent advances in the management of rheumatoid arthritis**. BMJ. 2010 Dec 21;341:c6942. doi: 10.1136/bmj.c6942.

Klarenbeek NB, van der Kooij SM, Güler-Yüksel M, et al. **Discontinuing treatment in patients with rheumatoid arthritis** in sustained clinical remission: exploratory analyses from the BeSt study. Ann Rheum Dis. 2011 Feb;70(2):315-9.

Klareskog Lars, van der Heijde Désirée, de Jager Julien P, et al. for the TEMPO (Trial of Etanercept and Methotrexate with Radiographic Patient Outcomes) study investigators. Therapeutic effect of the **combination** of **etanercept** and **methotrexate compared** with each treatment **alone** in patients with rheumatoid arthritis: double-blind randomised controlled trial. The Lancet Volume 363, Number 9410 28 February 2004.

Klareskog L, Catrina AI, Paget S. **Rheumatoid arthritis**. Lancet. **2009** Jan 19. [Epub ahead of print]

Klein A, Kaul I, et al. Efficacy and safety of **oral and parenteral methotrexate** therapy in children with juvenile idiopathic arthritis. An observational study with patients of the German Methotrexate Registry. Arthritis Care Res. 2012 May 30.

Kloppenburg M, Ramonda R, Bobacz K, et al. **Etanercept in patients with inflammatory hand osteoarthritis (EHOA)**: a multicentre, randomised, double-blind, placebo-controlled trial. Ann Rheum Dis.2018 Dec;77(12):1757-1764.

Klotsche J, Minden K, Niewerth M, et al. **Time spent in inactive disease before MTX withdrawal is relevant** with regard to the flare risk in **patients with JIA**. Ann Rheum Dis. 2018 Jul;77(7):996-1002.

Klotsche J, Niewerth M, Haas JP, et al. **Long-term safety of etanercept and adalimumab compared to methotrexate** in patients with juvenile idiopathic arthritis (JIA). Ann Rheum Dis. 2016 May;75(5):855-61.

Kneepkens EL, Plasencia C, Krieckaert CL, et al. **Golimumab trough levels**, antidrug antibodies and clinical response in patients with rheumatoid arthritis treated in daily clinical practice. Ann Rheum Dis. 2014 Dec;73(12):2217-9.

Kneepkens EL, Wei JC, Nurmohamed MT, et al. Immunogenicity, **adalimumab levels** and clinical response in ankylosing spondylitis patients during 24 weeks of follow-up. Ann Rheum Dis. 2015 Feb;74(2):396-401.

Kneepkens EL, Krieckaert CL, van der Kleij D, et al. **Lower etanercept levels** are associated with high disease activity in ankylosing spondylitis patients at 24 weeks of follow-up. Ann Rheum Dis. 2015 Oct;74(10):1825-9.

Kneepkens EL, Pouw MF, Wolbink GJ, et al. Dried blood spots from finger prick facilitate therapeutic drug monitoring of **adalimumab** and anti-adalimumab in patients with inflammatory diseases. Br J Clin Pharmacol. 2017 Aug 9.

Koike T, Harigai M, Inokuma S, et al. Postmarketing surveillance of **tocilizumab** for rheumatoid arthritis in Japan: interim analysis of 3881 patients. Ann Rheum Dis. 2011 Dec;70(12):2148-51.

Komano Y et al. Incidence and risk factors for **serious infection** in patients with rheumatoid arthritis treated with **tumor necrosis factor inhibitors**: A report from the Registry of Japanese Rheumatoid Arthritis Patients for Longterm Safety. J Rheumatol 2011 Jul; 38:1258. (about double the infection risk)

Koopman FA et al. **Vagus nerve stimulation** inhibits cytokine production and attenuates disease severity in rheumatoid arthritis. Proc Natl Acad Sci U S A 2016 Jul 5; [e-pub].

Korpela M, Laasonen L, Hannonen P, et al.; FIN-RACo Trial Group. Retardation of joint damage in patients with early rheumatoid arthritis by initial aggressive treatment with **disease-modifying antirheumatic drugs**: five-year experience from the FIN-RACo study. Arthritis Rheum. 2004 Jul;50(7):2072-81.

Korswagen LA, Bartelds GM, Krieckaert CL, et al. Venous and arterial **thromboembolic events in adalimumab-treated patients with antiadalimumab antibodies**: a case series and cohort study. Arthritis Rheum. 2011 Apr;63(4):877-83.

Kostine M, et al. **Rheumatic disorders associated with immune checkpoint inhibitors** in patients with cancer-clinical aspects & relationship with tumour response: single-centre prospective cohort study. Ann Rheum Dis. 2018 Mar;77(3):393-398.

Krause ML, Crowson CS, Michet CJ, et al. **Juvenile Idiopathic Arthritis in Olmsted County** 1960-2013. Arthritis Rheumatol. 2015 Aug 28.

Kraut R, Katz S, Cave A. **Back pa**in in a 59-year-old woman with rheumatoid arthritis. CMAJ. 2016 Aug 9;188(11):817-9

Kremer JM, et al. Concomitant **leflunomide** therapy in patients **with** active rheumatoid arthritis despite stable doses of **methotrexate**. A randomized, double-blind, placebo-controlled trial. Ann Intern Med. 2002 Nov 5;137(9):726-33.

Kremer JM, et al. Treatment of rheumatoid arthritis with the selective costimulation modulator **abatacept**: Twelve-month results of a phase iib, double-blind, randomized, placebo-controlled trial. Arthritis Rheum. 2005 Aug;52(8):2263-71.

Kremer JM, et al. Effects of **abatacept** in patients with **methotrexate-resistant** active rheumatoid arthritis: a randomized trial. Ann Intern Med. 2006 Jun 20;144(12):865-76. Summary for patients in: Ann Intern Med. 2006 Jun 20;144(12):I18. (but fair number of pts may have been partial MTX responders)

Kremer JL, Blanco R, Brzosko M, et al. **Tocilizumab** inhibits structural joint damage in rheumatoid arthritis patients with inadequate responses to methotrexate at 1 year: The **LITHE** study. Arthritis Rheum. 2010 Nov 19.

Kremer JM, Russell AS, Emery P, et al. Long-term safety, efficacy and inhibition of radiographic progression with **abatacept** treatment in patients with rheumatoid arthritis and an inadequate response to methotrexate: 3-year results from the AIM trial. Ann Rheum Dis. 2011 Oct;70(10):1826-30.

Kremer J, Li ZG, Hall S, et al. **Tofacitinib** in combination with nonbiologic disease-modifying antirheumatic drugs in patients with active rheumatoid arthritis: a randomized trial. Ann Intern Med. 2013 Aug 20;159(4):253-61.

Krieckaert CL, Jamnitski A, Nurmohamed MT, et al. Comparing the long-term clinical outcome of **etanercept and adalimumab** treatment with respect to **immunogenicity**. Arthritis Rheum. 2012 Aug 29.

Krieckaert CL, Nurmohamed MT, Wolbink GJ. **Methotrexate reduces immunogenicity in adalimumab** treated rheumatoid arthritis patients in a dose dependent manner. Ann Rheum Dis. 2012 Nov;71(11):1914-5.

Krieckaert CL, Nair SC, Nurmohamed MT, et al. Personalised treatment using **serum drug levels of adalimumab** in patients with rheumatoid arthritis: an evaluation of costs and effects. Ann Rheum Dis. 2015 Feb;74(2):361-8.

Krishnan E, Lingala B, Bruce B, Fries JF. **Disability in rheumatoid arthritis in the era of biological treatments**. Ann Rheum Dis. 2012 Feb;71(2):213-8.

Kristensen LE, Englund M, Neovius M, et al. **Long-term work disability** in patients with psoriatic arthritis treated with anti-tumour necrosis factor: a population-based regional Swedish cohort study. Ann Rheum Dis. 2013 Oct 1;72(10):1675-9.

Kroon F, Landewe R, Dougados M, et al. Continuous **NSAID** use reverts the effects of inflammation on radiographic progression in patients with **ankylosing spondylitis**. Ann Rheum Dis 2012.

Kroot EJ, et al. The prognostic value of **anti-cyclic citrullinated peptide antibody** in patients with recent-onset rheumatoid arthritis.Arthritis Rheum. 2000 Aug;43(8):1831-5.

Kuijper TM, et al. Flare Rate in Patients with Rheumatoid Arthritis in Low Disease Activity or Remission When **Tapering or Stopping Synthetic or Biologic DMARD**: A Systematic Review. J Rheumatol. 2015 Nov;42(11):2012-22.

Kuijper TM, Luime JJ, de Jong PH, et al. **Tapering conventional synthetic DMARDs** in patients with early arthritis in sustained remission: 2-year follow-up of the **tREACH** trial. Ann Rheum Dis. 2016 Dec;75(12):2119-2123.

Kuller LH, Mackey RH, Walitt BT, et al. Determinants of **mortality among postmenopausal women** who report rheumatoid arthritis in the Women's Health Initiative. Arthritis Rheum. 2013 Dec 23.

Kumar A, Dhir V, et al. Efficacy of **Methylprednisolone Acetate Versus Triamcinolone Acetonide** Intra-Articular Knee Injection in Patients With Chronic Inflammatory Arthritis: A 24-Week Randomized Controlled Trial. Clin Ther. 2016 Dec 21.

Kung TN, Dennis J, Ma Y, et al. **RFC-1 80G>A is a genetic determinant of methotrexate efficacy** in Rheumatoid Arthritis: A HuGE review and meta-analysis of observational studies. Arthritis Rheum. 2013 Dec 24.

Kuntze G, Nesbitt C, Whittaker JL, et al. **Exercise Therapy in Juvenile Idiopathic Arthritis**: A Systematic Review and Meta-Analysis. Arch Phys Med Rehabil. 2018 Jan;99(1):178-193.e1.

Kuriya B, Hernández-Díaz S, Liu J, Bermas BL, Daniel G, Solomon DH. **Patterns of drug use during pregnancy** in rheumatoid arthritis. Arthritis Care Res (Hoboken). 2011 Jan 4.

Kwok TSH, Libman M, Lake SL. **Vaccination in adults with autoimmune rheumatic diseases**. CMAJ. 2019 Sep 9;191(36):E1005

Kwon HJ, Cote TR, Cuffe MS, Kramer JM, Braun MM. Case reports of **heart failure** after therapy with a **tumor necrosis** factor antagonist. Ann Intern Med. 2003 May 20;138(10):807-11.

Lacaille D, Avina-Zubieta JA, Sayre EC, et al. Improvement in 5-year **mortality in incident rheumatoid arthritis** compared with the general population-closing the mortality gap. Ann Rheum Dis. 2017 Jun;76(6):1057-1063.

l'Ami MJ, Krieckaert CL, et al. Successful reduction of **overexposure in patients with rheumatoid arthritis with high serum adalimumab** concentrations: an open-label, non-inferiority, randomised clinical trial. Ann Rheum Dis. 2017 Sep 22.

Labetoulle R, Roblin X, Paul S. Prolonged Persistence of **Adalimumab** Transferred From Mother to Infant During **Pregnancy**. Ann Intern Med. 2018 Mar 6.

Lahiri M, Luben RN, Morgan C, et al. Using **lifestyle factors** to identify individuals at higher risk of inflammatory polyarthritis (results from the European Prospective Investigation of Cancer-Norfolk and the Norfolk Arthritis Register--the EPIC-2-NOAR Study). Ann Rheum Dis. 2013 Mar 16.

Lamb SE, Williamson EM, Heine PJ, et al; on behalf of the Strengthening and Stretching for Rheumatoid Arthritis of the Hand Trial (SARAH) Trial Team. **Exercises to improve function** of the rheumatoid hand (SARAH): a randomised controlled trial. Lancet. 2014 Oct 9.

Lan J , Chen Y , Hsieh TC , et al. Kinetics of viral loads and risk of **HBV** reactivation in HBcAbpositive RA patients undergoing **anti-TNF-α therapy** . Ann Rheum Dis 2011 ; 70:1719–25.

Landewe R, Sieper J, Mease P, et al. Efficacy and safety of continuing versus withdrawing **adalimumab therapy in maintaining remission in patients with non-radiographic axial spondyloarthritis (ABILITY-3)**: a multicentre, randomised, double-blind study. Lancet. 2018 Jun 28.

Landewé RBM. **Overdiagnosis and overtreatment in rheumatology**: a little caution is in order. Ann Rheum Dis. 2018 Oct;77(10):1394-1396.

Langford CA, Cuthbertson D, Ytterberg SR, et al. A randomized, double-blind trial of **abatacept** (CTLA4-ig) for the treatment of **takayasu's arteritis**. Arthritis Rheumatol. 2017 Jan 30.

Langford CA, Cuthbertson D, Ytterberg SR, et al. A randomized, double-blind trial of **abatacept** (CTLA4-IG) for the treatment of **giant cell arteritis. Arthritis** Rheumatol. 2017 Jan 30.

Lauper K, Nordström DC, Pavelka K, et al. Comparative effectiveness of **tocilizumab versus TNF inhibitors as monotherapy or in combination with conventional synthetic disease-modifying antirheumatic drugs** in patients with rheumatoid arthritis after the use of at least one biologic disease-modifying antirheumatic drug: analyses from the pan-European TOCERRA register collaboration. Ann Rheum Dis. 2018 Sep;77(9):1276-1282.

Lazaros G, Vasileiou P, Koutsianas C, et al. **Anakinra** for the management of resistant idiopathic recurrent **pericarditis**. Initial experience in 10 adult cases. Ann Rheum Dis. 2014 Dec;73(12):2215-7.

Lebwohl M, et al. **No** evidence for increased risk of **cutaneous squamous** cell carcinoma in patients with rheumatoid arthritis receiving **etanercept** for up to 5 years. Arch Dermatol. 2005 Jul;141(7):861-4.

Ledingham J, Snowden N, Ide Z. Diagnosis and early management of **inflammatory arthritis**. BMJ. 2017 Jul 27;358:j3248.

Lee EB, Fleischmann R, Hall S, et al; ORAL Start Investigators. **Tofacitinib** versus methotrexate in rheumatoid arthritis. N Engl J Med. 2014 Jun 19;370(25):2377-86.

Lee WJ, Lee TA, Suda KJ, et al. Risk of **serious bacterial infection associated with tumour necrosis factor-alpha inhibitors** in **children** with **juvenile idiopathic arthritis**. Rheumatology (Oxford). 2017 Apr 18.

Leffers HC, Ostergaard M, Glintborg B, et al. on behalf of all departments of rheumatology in Denmark. Efficacy of **abatacept and tocilizumab** in patients with rheumatoid arthritis treated in clinical practice: results from the nationwide Danish **DANBIO** registry. Ann Rheum Dis. 2011 Jul;70(7):1216-1222.

Lehman AJ, Esdaile JM, Klinkhoff AV, et al.; METGO Study Group. A 48-week, randomized, double-blind, double-observer, placebo-controlled multicenter trial of combination **methotrexate and intramuscular gold** therapy in rheumatoid arthritis: results of the METGO study. Arthritis Rheum. 2005 May;52(5):1360-70.

Leirisalo-Repo M, Kautiainen H, Laasonen L, et al; for the NEO-RACo Study Group. **Infliximab** for 6 months added on **combination therapy** in early rheumatoid arthritis: 2-year results from an investigator-initiated, randomised, double-blind, placebo-controlled study (the NEO-RACo Study). Ann Rheum Dis. 2012 Jun 30.

Lemmey AB, Wilkinson TJ, Clayton RJ, et al. **Tight control of disease activity fails to improve body composition or physical function** in rheumatoid arthritis patients. Rheumatology (Oxford). 2016 Jun 10.

Lems WF, Dreinhofer KE, Bischoff-Ferrari H, et al. **EULAR/EFORT** recommendations for management of patients older than 50 years with a **fragility fracture** and prevention of subsequent fractures. Ann Rheum Dis. 2016 Dec 22.

Lenssinck ML, Burdorf A, Boonen A, et al. Consequences of inflammatory arthritis for **workplace productivity loss and sick leave**: a systematic review. Ann Rheum Dis. 2013 Apr;72(4):493-505.

Leonardi CL, Powers JL, Matheson RT, Goffe BS, Zitnik R, Wang A, Gottlieb AB; **Etanercept Psoriasis** Study Group. Etanercept as monotherapy in patients with psoriasis. N Engl J Med. 2003 Nov 20;349(21):2014-22.

Lequerre T, et al. Management of **Infusion Reactions to Infliximab** in Patients with Rheumatoid Arthritis or Spondyloarthritis: Experience from an Immunotherapy Unit of Rheumatology. J Rheumatol. 2006 Jun 1; [Epub ahead of print]

Lethaby A, Lopez-Olivo MA, Maxwell L, et al. **Etanercept for the treatment of rheumatoid arthritis**. Cochrane Database Syst Rev. 2013 May 31;5:CD004525. doi: 10.1002/14651858.CD004525.pub2. Etanercept 25 mg administered subcutaneously twice weekly together with MTX was more efficacious than either etanercept or MTX monotherapy for ACR50 and it slowed joint radiographic progression after up to three years of treatment for all participants (responders or not). There was no evidence of a difference in the rates of infections between groups.

Li N, Betts KA, Messali AJ, et al. Real-world Effectiveness of Biologic Disease-modifying Antirheumatic Drugs for the Treatment of Rheumatoid Arthritis **After Etanercept Discontinuation** in the United Kingdom, France, and Germany. Clin Ther. 2017 Aug;39(8):1618-1627.
Lie E, van der Heijde D, Uhlig T, et al. Treatment **strategies** in patients with rheumatoid arthritis for whom **methotrexate monotherapy has failed**: data from the NOR-DMARD register. Ann Rheum Dis. 2011 Dec;70(12):2103-10.
Lie E, Kristensen LE, Forsblad-d'Elia H, et al; ARTIS Study Group. The effect of comedication with **conventional synthetic disease modifying antirheumatic drugs on TNF inhibitor** drug survival in patients with ankylosing spondylitis and undifferentiated spondyloarthritis: results from a nationwide prospective study. Ann Rheum Dis. 2015 Jun;74(6):970-8.
Lie E, Lindström U, Zverkova-Sandström T, et al. Tumour necrosis factor inhibitor treatment and occurrence of **anterior uveitis** in **ankylosing spondylitis**: results from the Swedish biologics register. Ann Rheum Dis. 2017 Mar 2.
Lim SY, Lu N, Oza A, et al. **Trends in Gout and Rheumatoid Arthritis** Hospitalizations in the United States, 1993-2011. JAMA. 2016 Jun 7;315(21):2345-7.
Lindhardsen J, Ahlehoff O, Gislason GH, et al. The risk of **myocardial infarction** in rheumatoid arthritis and diabetes mellitus: a Danish nationwide cohort study. Ann Rheum Dis. 2011 Jun;70(6):929-34.
Lindhardsen J, Ahlehoff O, Gislason GH, et al. Risk of **atrial fibrillation** and stroke in rheumatoid arthritis: Danish nationwide cohort study. BMJ. 2012 Mar 8;344:e1257.
*Lindhardsen J, Ahlehoff O, Gislason GH et al. **Initiation and adherence to secondary prevention** pharmacotherapy after myocardial infarction in patients with **rheumatoid arthritis**: a nationwide cohort study. Ann Rheum Dis. 2012 Sep;71(9):1496-501.*
Lioger B, Edupuganti SR, Mulleman D, et al. **Antigenic burden and serum IgG concentrations** influence **rituximab** pharmacokinetics in rheumatoid arthritis patients. Br J Clin Pharmacol. 2017 Feb 23.
Lionetti G, Kimura Y, Schanberg LE, et al. Using **registries to identify adverse events** in rheumatic diseases. Pediatrics. 2013 Nov;132(5):e1384-94.
Lipsky PE, van der Heijde DM, et al. Anti-Tumor Necrosis Factor Trial in Rheumatoid Arthritis with Concomitant Therapy Study Group. **Infliximab and methotrexate** in the treatment of rheumatoid arthritis. Anti-Tumor Necrosis Factor Trial in Rheumatoid Arthritis with Concomitant Therapy Study Group. N Engl J Med. 2000 Nov 30;343(22):1594-602.
Listing J, Strangfeld A, Kary S, et al. **Infections** in patients with rheumatoid arthritis treated with **biologic agents**. Arthritis Rheum. 2005 Nov;52(11):3403-12.
Listing J, Kekow J, Manger B, et al. **Mortality in rheumatoid arthritis**: the impact of disease activity, treatment with glucocorticoids, TNFα inhibitors and rituximab. Ann Rheum Dis. 2015 Feb;74(2):415-21.
Ljung L, Simard JF, Jacobsson L, et al. ARTIS Study Group. Treatment with **tumour necrosis factor-inhibitors and the risk of acute coronary syndromes** in early rheumatoid arthritis. Arthritis Rheum. 2011 Aug 26.doi: 10.1002/art.30654.
Ljung L, Rantapää-Dahlqvist S, Jacobsson LT, Askling J; **ARTIS** Study Group. Response to **biological treatment and subsequent risk of coronary events** in rheumatoid arthritis. Ann Rheum Dis. 2016 Mar 16.
Lopez-Olivo MA, Tayar JH, Martinez-Lopez JA, et al. Risk of **malignancies** in patients with rheumatoid arthritis treated with biologic therapy: a meta-analysis. JAMA. 2012 Sep 5;308(9):898-908.
Lopez-Olivo MA, Amezaga Urruela M, McGahan L, et al. **Rituximab** for rheumatoid arthritis. Cochrane Database Syst Rev. 2015 Jan 20;1:CD007356. Evidence from eight studies suggests that rituximab (two 1000 mg doses) in combination with methotrexate is significantly more efficacious than methotrexate alone for improving the symptoms of RA and preventing disease progression.
Lopez-Olivo MA, Kakpovbia-Eshareturi V, des Bordes JK, et al. **Treating Early Undifferentiated Arthritis**: A Systematic Review and Meta-Analysis of Direct and Indirect Trial Evidence. Arthritis Care Res (Hoboken). 2018 Sep;70(9):1355-1365.
Lovell DJ, Giannini EH, et al. Pediatric Rheumatology Collaborative Study Group. Long-term efficacy and safety of **etanercept** in **children** with polyarticular-course juvenile rheumatoid arthritis: interim results from an ongoing multicenter, open-label, extended-treatment trial. Arthritis Rheum. 2003 Jan;48(1):218-26.
Lovell DJ, Giannini EH, et al. **Etanercept** in **children** with polyarticular juvenile rheumatoid arthritis. Pediatric Rheumatology Collaborative Study Group. N Engl J Med. 2000 Mar 16;342(11):763-9.
Lovell DJ, Reiff A, Ilowite NT, et al. Safety and efficacy of up to **eight years of continuous etanercept** therapy in patients with juvenile rheumatoid arthritis. Arthritis Rheum 2008; 58: 1496–504.
Lovell DJ, Ruperto N, Goodman S, et al. **Adalimumab with or without methotrexate** in juvenile rheumatoid arthritis. N Engl J Med 2008; 359: 810–20.
Lovell DJ, Giannini EH, Reiff AO, et al. Long-Term Safety and Efficacy of **Rilonacept** in Patients with Systemic Juvenile Idiopathic Arthritis(sJIA). Arthritis Rheum. 2013 Jun 10.
Lovell DJ, Ruperto N, Mouy R, et al; Pediatric Rheumatology Collaborative Study Group (PRCSG); Paediatric Rheumatology International Trials Organization (PRINTO). Long-Term Safety, Efficacy, and Quality of Life with Intravenous **Abatacept** in Juvenile Idiopathic Arthritis: Up to 7 Years of Treatment. Arthritis Rheumatol. 2015 Jun 19.
Low AS, Lunt M, Mercer LK, et al. Association between **ischaemic stroke and tumour necrosis factor inhibitor therapy** in patients with rheumatoid arthritis. Arthritis Rheumatol. 2016 Jan 8.
Low AS, Symmons DP, Lunt M, et al. Relationship between exposure to **tumour necrosis factor inhibitor therapy and incidence and severity of myocardial infarction** in patients with rheumatoid arthritis. Ann Rheum Dis. 2017 Jan 10.
Low AS, Symmons DP, et al. Relationship between exposure to **tumour necrosis factor inhibitor therapy and incidence and severity of myocardial infarction** in patients with rheumatoid arthritis. Ann Rheum Dis. 2016 Apr;76(4):654-660.
Lu B, Hiraki LT, Sparks JA, et al. Being **overweight or obese** and risk of developing rheumatoid arthritis among women: a prospective cohort study. Ann Rheum Dis. 2014 Nov;73(11):1914-22.
Lucas CJ, Dimmitt SB, Martin JH. Optimising Low Dose **Methotrexate** for Rheumatoid Arthritis - A Review. Br J Clin Pharmacol. 2019 Jul 5.
Luczak A, Knevel R, Huizinga TW, et al. No impact of **serum uric acid** on the outcome of recent-onset arthritis. Ann Rheum Dis. 2012 Mar 22.
Lukas C, Combe B, Ravaud P, et al. Favorable effect of **very early DMARD treatment** on radiographic progression in early inflammatory arthritis. The ESPOIR cohort study. Arthritis Rheum. 2011 Mar 30. doi:10.1002/art.30371.
Lunt M, Watson KD, Dixon WG, et al; The BSRBR Control Centre Consortium; on behalf of the BSR Biologics Register. **No evidence of association between anti-TNF treatment and mortality** in patients with rheumatoid arthritis: Results from the British Society for Rheumatology Biologics Register. Arthritis Rheum. 2010 Jul 26.
Lutz V, Lipsker D. Acitretin- and tumor necrosis factor inhibitor-resistant acrodermatitis continua of hallopeau responsive to the interleukin 1 receptor antagonist **anakinra**. Arch Dermatol. 2012 Mar;148(3):297-9.
Luqmani R, et al. British Society for Rheumatology and **British Health** Professionals in Rheumatology **Guideline** for the Management of **Rheumatoid Arthritis** (The first 2 years). Rheumatology (Oxford). 2006 Jul 13; [Epub ahead of print]
Luu M, Benzenine E, Doret M, et al. Continuous **anti-TNFα** use throughout **pregnancy**: possible complications for the mother but not for the fetus. A retrospective cohort on the French national health insurance database (EVASION). Am J Gastroenterol 2018. https://doi.org/10.1038/ s41395-018-0176-7.
Lv QW, Zhang W, Shi Q, et al. Comparison of **Tripterygium wilfordii Hook F** with methotrexate in the treatment of active rheumatoid arthritis (TRIFRA): a randomised, controlled clinical trial. Ann Rheum Dis. 2014 Apr 14.
Mackie SL, Pease CT, Fukuba E, et al. **Whole-body MRI** of patients with polymyalgia rheumatica identifies a distinct subset with complete patient-reported response to **glucocorticoids**. Ann Rheum Dis. 2015 Dec;74(12):2188-92.
Mahadevan U, Cucchiara S, Hyams JS, et al. The London position statement of the World Congress of Gastroenterology on **Biological Therapy for IBD with the European Crohn's and Colitis Organisation: Pregnancy and Pediatrics**. Am J Gastroenterol. 2010 Dec 14.
Mahmoud I, Jellouli M, Boukhris I, et al. Efficacy and Safety of **Rituximab** in the Management of **Pediatric Systemic Lupus Erythematosus**: A Systematic Review. J Pediatr. 2017 Jun 8.
Maksymowych WP, Dougados M, van der Heijde D, et al. **Clinical and MRI responses to etanercept** in early non-radiographic axial spondyloarthritis: 48-week results from the **EMBARK** study. Ann Rheum Dis. 2016 Jul;75(7):1328-35.
Maini R, St Clair EW, et al. **Infliximab** (chimeric anti-tumour necrosis factor alpha monoclonal antibody) versus placebo in rheumatoid arthritis patients receiving **concomitant methotrexate**: a randomised phase III trial. **ATTRACT** Study Group. Lancet. 1999 Dec 4;354(9194):1932-9.
Makol A, Davis JM 3rd, Crowson CS, et al. Time **trends in glucocorticoid** use in rheumatoid arthritis: results from a population-based inception cohort, 1980-1994 versus 1995-2007. Arthritis Care Res (Hoboken). 2014 Oct;66(10):1482-8.
Maksymowych WP, et al. Modification of structural lesions on MRI of the sacroiliac joints by **etanercept** in the **EMBARK** trial: a 12-week randomized placebo-controlled trial in patients with non-radiographic axial spondyloarthritis. Ann Rheum Dis. 2018 Jan;77(1):78-84.
Mamtani R, Clark AS, Scott FI, et al. Association between **breast cancer recurrence** with **immunosuppression in rheumatoid arthritis and inflammatory bowel disease**: A cohort study. Arthritis Rheumatol. 2016 May 9.
Mancarella L, Bobbio-Pallavicini F, Ceccarelli F, et al. Good Clinical Response, Remission, and Predictors of Remission in Rheumatoid Arthritis Patients Treated with **Tumor Necrosis Factor-alpha Blockers**: The GISEA Study. J Rheumatol. 2007 Aug;34(8):1670-3. Epub 2007 Jul 1. We show that **only a minority** of patients with longstanding RA achieve a good clinical response or remission at the outpatient community level. Predictors of remission identify characteristics commonly observed in subsets with less severe RA.
Maneiro JR, Salgado E, et al. **Immunogenicity of Monoclonal Antibodies** Against Tumor Necrosis Factor Used in Chronic Immune-Mediated Inflammatory Conditions: Systematic Review and Meta-analysis. JAMA Intern Med. 2013 Jun 24:1-13.
Manning VL, Hurley MV, Scott DL, et al. Education, self-management, and upper extremity **exercise training** in people with rheumatoid arthritis: a randomized controlled trial. Arthritis Care Res (Hoboken). 2014 Feb;66(2):217-27.
Mantel A, Holmqvist M, Andersson DC, et al. Association Between **Rheumatoid Arthritis and Risk of Ischemic and Nonischemic Heart Failure**. J Am Coll Cardiol. 2017 Mar 14;69(10):1275-1285.
Mantel Ä, Holmqvist M, Jernberg T, et al. Long-term outcomes and secondary prevention after **acute coronary events in patients with rheumatoid arthritis**. Ann Rheum Dis. 2017 Dec;76(12):2017-2024.
Mariette X, Tubach F, Bagheri H, et al. **Lymphoma** in patients treated with anti-TNF. Results of the 3-year prospective French RATIO registry. Ann Rheum Dis. 2009 Oct 14.
Mariette X, Matucci-Cerinic M, et al. **Malignancies** associated with **tumour necrosis factor inhibitors** in registries and prospective observational studies: a systematic review and meta-analysis. Ann Rheum Dis. 2011 Nov;70(11):1895-904.
Mariette X, Baron G, et al. Influence of replacing **tuberculin skin test with ex vivo interferon γ release assays** on decision to administer prophylactic antituberculosis antibiotics **before anti-TNF** therapy. Ann Rheum Dis. 2012 No;71(11):1783-90.
Mariette X, Rouanet S, Sibilia J, et al. Evaluation of low-dose **rituximab** for the retreatment of patients with active rheumatoid arthritis: a non-inferiority randomised controlled trial. Ann Rheum Dis. 2014 Aug;73(8):1508-14.
Mariette X, Förger F, Abraham B, et al. Lack of placental transfer of **certolizumab pegol during pregnancy**: results from CRIB, a prospective, postmarketing, pharmacokinetic study. Ann Rheum Dis. 2018 Feb;77(2):228-233.

Mariette X, Criswell LA. **Primary Sjögren's Syndrome**. N Engl J Med. 2018 Mar 8;378(10):931-939.

Markusse IM, Akdemir G, Dirven L, et al. **Long-Term Outcomes** of Patients With **Recent-Onset Rheumatoid Arthritis After 10 Years** of **Tight Controlled Treatment**: A Randomized Trial. (**BeSt**) Ann Intern Med. 2016 Apr 19;164(8):523-31.

Marmor MF, Kellner U, Lai TY, Lyons JS, Mieler WF; American Academy of Ophthalmology. Revised recommendations on screening for **chloroquine** and **hydroxychloroquine retinopathy**. Ophthalmology. 2011 Feb;118(2):415-22.

Marmor MF, Melles RB. **Hydroxychloroquine and the retina**. JAMA. 2015 Feb 24;313(8):847-8.

Marmor MF, Kellner U, Lai TY, Melles RB, Mieler WF, American Academy of O. Recommendations on Screening for **Chloroquine and Hydroxychloroquine Retinopathy** (2016 Revision). Ophthalmology. 2016.

Marmor MF, Kellner U, Lai TY, Melles RB, Mieler WF; **American Academy of Ophthalmology**. Recommendations on screening for **chloroquine and hydroxychloroquine retinopathy** (2016 revision). Ophthalmology. 2016;123:1386-1394.

Marshall JK, Bessette L, Thorne C, et al. Impact of the **Adalimumab Patient Support Program's** Care Coach Calls on Persistence and Adherence in Canada: An Observational Retrospective Cohort Study. Clin Ther. 2018 Mar 5.

Martel-Pelletier J, et al. First-line analysis of the effects of treatment on progression of structural changes in **knee osteoarthritis** over 24 months: data from the osteoarthritis initiative progression cohort. Ann Rheum Dis. 2015 Mar;74(3):547-56.

Matcham F, Galloway J, Hotopf M, et al. The Impact of **Targeted Rheumatoid Arthritis Pharmacologic Treatment on Mental Health**: A Systematic Review and Network Meta-Analysis. Arthritis Rheumatol. 2018 Jun 6.

Matsuno H, Tomomitsu M, Hagino A, et al. Phase III, multicentre, double-blind, randomised, parallel-group study to evaluate the similarities between **LBEC0101 and etanercept reference** product in terms of efficacy and safety in patients with active rheumatoid arthritis inadequately responding to methotrexate. Ann Rheum Dis. 2018 Apr;77(4):488-494.

Mary J, et al. **Triple Oral Therapy Versus Antitumor Necrosis Factor Plus Methotrexate (MTX)** in Patients with Rheumatoid Arthritis and Inadequate Response to MTX: A Systematic Literature Review. J Rheumatol. 2017 Jun;44(6):773-779.

Matcham F, Norton S, Steer S, Hotopf M. Usefulness of the **SF-36 Health Survey** in screening for **depressive and anxiety disorders** in rheumatoid arthritis. BMC Musculoskelet Disord. 2016 May 23;17(1):224.

Matro R et al. Exposure concentrations of **infants breastfed by women receiving biologic therapies for inflammatory bowel diseases** and **effects of breastfeeding on infections and development**. Gastroenterology 2018 May 29.

Matteson EL, Dejaco C. In the Clinic: **Polymyalgia Rheumatica**. Ann Intern Med. 2017 May 2;166(9):ITC65-ITC80.

Maxwell L, Singh JA. **Abatacept** for rheumatoid arthritis. Cochrane Database Syst Rev. 2009 Oct 7;(4):CD007277.

Maya Y, Ota M. **Methotrexate induced labial haemorrhagic erosions**. BMJ 2017 Nov 16; 359:j5063.

McBain H, Shipley M, Olaleye A, et al. A **patient-initiated DMARD self-monitoring service** for people with rheumatoid or psoriatic arthritis onmethotrexate: a randomised controlled trial. Ann Rheum Dis. 2016 Jul;75(7):1343-9.

McCallum C, Johnson B. **Mycobacterium chelonae** bacteremia in a patient **taking infliximab and prednisone**. CMAJ. 2016 Dec 6;188(17-18):E538.

McDougall JA, Ferucci ED, Glover J, et al. **Telerheumatology**: A Systematic Review. Arthritis Care Res (Hoboken). 2017 Oct;69(10):1546-1557.

McInnes IB, Schett G. The **Pathogenesis of Rheumatoid Arthritis**. N Engl J Med 2011; 365:2205-2219

McInnes IB, Mease PJ, Kirkham B, et al, on behalf of the FUTURE 2 Study Group. **Secukinumab**, a human anti-interleukin-17A monoclonal antibody, in patients with psoriatic arthritis (FUTURE 2): a randomised, double-blind, placebo-controlled, phase 3 trial. Lancet 2015; online June 29.

McInnes IB, Schett G. **Pathogenetic insights from the treatment of rheumatoid arthritis**. Lancet. 2017 Jun 10;389(10086):2328-2337.

McInnes IB, Mease PJ, Ritchlin CT, et al. **Secukinumab** sustains improvement in signs and symptoms of **psoriatic arthritis**: 2 year results from the phase 3 **FUTURE 2** study. Rheumatology (Oxford). 2017 Nov 1;56(11):1993-2003.

Md Yusof MY, Shaw D, El-Sherbiny YM, et al. Predicting and managing primary and secondary non-response to **rituximab** using B-cell biomarkers in systemic lupus erythematosus. Ann Rheum Dis. 2017Nov;76(11):1829-1836.

Mease PJ, Goffe BS, et al. **Etanercept** in the treatment of **psoriatic arthritis** and psoriasis: a randomised trial. Lancet. 2000 Jul 29;356(9227):385-90.

Mease PJ, Gladman DD, Collier DH, et al. **Etanercept and Methotrexate** as Monotherapy or in Combination for Psoriatic Arthritis: Primary Results From a Randomized, Controlled Phase III Trial. Arthritis Rheumatol. 2019 Jul;71(7):1112-1124.

Mease PJ, Gladman DD, Ritchlin CT, et al. Adalimumab Effectiveness in Psoriatic Arthritis Trial Study Group. **Adalimumab** for the treatment of patients with moderately to severely active **psoriatic arthritis**: results of a double-blind, randomized, placebo-controlled trial. Arthritis Rheum. 2005 Oct;52(10):3279-89.

Mease PJ, Fleischmann R, Deodhar AA, et al. Effect of certolizumab pegol on signs and symptoms in patients with psoriatic arthritis: 24-week results of a Phase 3 double-blind randomised placebo-controlled study (RAPID-PsA). Ann Rheum Dis. 2013 Oct 16.

Mease P, Sieper J, Van den Bosch F, et al. Randomized Controlled Trial of **Adalimumab** in Patients with **Non Psoriatic Peripheral Spondyloarthritis**. Arthritis Rheumatol. 2014 Dec 29.

Mease PJ, van der Heijde D, Ritchlin CT, et al. **Ixekizumab**, an interleukin-17A specific monoclonal antibody, for the treatment of biologic-naive patients with active psoriatic arthritis: results from the 24-week randomised, double-blind, placebo-controlled and active (adalimumab)-controlled period of the phase III trial SPIRIT-P1. Ann Rheum Dis. 2016 Aug 23.

Mease P, Hall S, FitzGerald O, et al. **Tofacitinib** or **adalimumab** versus placebo for psoriatic arthritis. N Engl J Med 2017; 377:1537-50.

Mease P, van der Heijde D, et al. **Secukinumab** improves active psoriatic arthritis symptoms and inhibits radiographic progression: primary results from the randomised, double-blind, phase III FUTURE 5 study. Ann Rheum Dis. 2018 Mar 17.

Mehta J, Beukelman T. **Biologic Agents** in the Treatment of **Childhood-Onset Rheumatic Disease**. J Pediatr. 2017 Jul 13.

Meissner Y, Richter A, Manger B, et al Serious adverse events and the risk of **stroke** in patients with **rheumatoid** arthritis: results from the German **RABBIT** cohort. Ann Rheum Dis. 2017 May 8.

Mercer LK, Green AC, Galloway JB, et al; **British** Society for Rheumatology **Biologics Register** Control Centre Consortium, Symmons DP, Hyrich KL; on behalf of the British Society for Rheumatology Biologics Register. The influence of anti-TNF therapy upon incidence of **keratinocyte skin cancer** in patients with rheumatoid arthritis: longitudinal results from the British Society for Rheumatology Biologics Register. Ann Rheum Dis. 2012 Jun;71(6):869-874.

Mercer LK, Lunt M, Low AL, et al; BSRBR Control Centre Consortium. **Risk of solid cancer in patients exposed to anti-tumour necrosis factor therapy**: results from the British Society for Rheumatology Biologics Register for Rheumatoid Arthritis. Ann Rheum Dis. 2015 Jun;74(6):1087-93.

Mercer LK, Askling J, Raaschou P, et al. Risk of invasive **melanoma** in patients with rheumatoid arthritis treated with **biologics**: results from a collaborative project of 11 European biologic registers. Ann Rheum Dis. 2016 Jun 15.

Mercer LK, et al. **Risk of lymphoma** in patients exposed to **antitumour necrosis factor therapy**: results from the **British Society for Rheumatology Biologics Register** for Rheumatoid Arthritis. Ann Rheum Dis. 2017 Mar;76(3):497-503.

Mercer LK, Regierer AC, Mariette X, et al. Spectrum of **lymphomas across different drug treatment groups in rheumatoid arthritis**: a European registries collaborative project. Ann Rheum Dis. 2017 Dec;76(12):2025-2030.

Mertens M, Singh JA. **Anakinra** for rheumatoid arthritis. Cochrane Database Syst Rev. 2009 Jan 21;(1):CD005121. Anakinra is a relatively safe and modestly efficacious biologic therapy for rheumatoid arthritis.

Meshkov AD, Novikov PI, Zhilyaev EV, et al. **Tofacitinib in steroid-dependent relapsing polychondritis**. Ann Rheum Dis. 2019 Jul;78(7):e72.

Micha R, Imamura F, Wyler von Ballmoos M, et al. Systematic Review and Meta-Analysis of **Methotrexate Use and Risk of Cardiovascular Disease**. Am J Cardiol. 2011 Aug 17.

Michaud TL, Rho YH, Shamliyan T, Kuntz KM, Choi HK. The comparative **safety of tumor necrosis factor inhibitors** in rheumatoid arthritis: a meta-analysis update of 44 trials. Am J Med. 2014;127:1208-32.

Michelsen B, Uhlig T, Sexton J, et al. Health-related quality of life in patients with psoriatic and rheumatoid arthritis: data from the prospective multicentre NOR-DMARD study compared with Norwegian general population controls. Ann Rheum Dis. 2018 Sep;77(9):1290-1294.

Miettunen PM, Pistorio A, Palmisani E et al; Paediatric Rheumatology International Trials Organisation (PRINTO). Therapeutic approaches for the treatment of renal disease in **juvenile systemic lupus erythematosus**: an international multicentre PRINTO study. Ann Rheum Dis. 2013 Sep 1;72(9):1503-9.

Miloslavsky EM, Naden RP, Bijlsma JW, et al. Development of a **Glucocorticoid Toxicity Index** (**GTI**) using multicriteria decision analysis. Ann Rheum Dis. 2017 Mar;76(3):543-546.

Minden K, Niewerth M, Zink A, et al. **Long-term outcome of patients with JIA treated with etanercept**, results of the biologic register JuMBO. Rheumatology (Oxford). 2012 Mar 24.

Mititelu M, Wong BJ, Brenner M, et al. Progression of **hydroxychloroquine toxic effects** after drug therapy cessation: new evidence from multimodal imaging. JAMA Ophthalmol. 2013 Sep 1;131(9):1187-97.

Modi YS, Singh RP**. Bull's-Eye Maculopathy Associated with Hydroxychloroquine**. N Engl J Med. 2019 Apr 25;380(17):1656.

Mohan C, Assassi S. **Biomarkers in rheumatic diseases**: how can they facilitate diagnosis and assessment of disease activity? BMJ. 2015 Nov 26;351:h5079.

Mok C, Kwok C, Ho L, et al. **Life expectancy**, standardized mortality ratios and causes of death of six rheumatic diseases in Hong Kong, China. Arthritis Rheum. 2011 Mar 9. doi: 10.1002/art.30277.

Mollard E, Pedro S, Chakravarty E, et al. The impact of **menopause on functional status in women with rheumatoid arthritis**. Rheumatology (Oxford). 2018 Jan 29.

Møller-Bisgaard S, Horslev-Petersen K, Ejbjerg B, et al. Effect of **magnetic resonance imaging vs conventional treat-to-target strategies on disease activity remission and radiographic progression in rheumatoid arthritis**: the IMAGINE-RA randomized clinical trial [Feb 5, 2019].

Molnar C, Scherer A, et al. **TNF blockers inhibit spinal radiographic progression in ankylosing spondylitis** by reducing disease activity: results from the Swiss Clinical Quality Management cohort. Ann Rheum Dis. 2018 Jan;77(1):63-69.

Molto A, Granger B, Wendling D, et al. **Non-steroidal anti-inflammatory drug-sparing effect of tumor necrosis alpha inhibitors** in early axial spondyloarthritis: Results from the DESIR cohort. Arthritis Rheumatol. 2015 Jun 24.

Moltó A, Etcheto A, Gossec L, et al. Evaluation of the impact of concomitant **fibromyalgia on TNF alpha blockers' effectiveness in axial spondyloarthritis**: results of a prospective, multicentre study. Ann Rheum Dis. 2018 Apr;77(4):533-540.

Mönch S, Zimmo B, El Helou T, et al. **Methotrexate-Induced Cutaneous Erosions**. Arthritis Rheumatol. 2015 Aug 28.

Moonaz SH, Bingham CO 3rd, Wissow L, Bartlett SJ. **Yoga** in Sedentary Adults with Arthritis: Effects of a Randomized Controlled Pragmatic Trial. J Rheumatol. 2015 Jul;42(7):1194-202.

Moots RJ, Naisbett-Groet B. The efficacy of biologic agents in patients with rheumatoid arthritis and an **inadequate response to tumour necrosis factor inhibitors**: a systematic review. Rheumatology (Oxford). 2012 Sep 1.
Mor A, Bingham CO 3rd, et al. **Methotrexate combined with isoniazid** treatment for latent tuberculosis is well tolerated in patients with rheumatoid arthritis: experience from an urban arthritis clinic. Ann Rheum Dis. 2008 Apr;67(4):462-5.
Moradi-Lakeh M, Forouzanfar MH, et al. **Burden of musculoskeletal disorders in the Eastern Mediterranean Region**, 1990-2013: findings from the Global Burden of Disease Study 2013. Ann Rheum Dis. 2017 Aug;76(8):1365-1373.
Moreland LW, Schiff MH, et al. **Etanercept** therapy in rheumatoid arthritis. A randomized, controlled trial. Ann Intern Med. 1999 Mar 16;130(6):478-86.
Moreland LW, Baumgartner SW, et al. Treatment of rheumatoid arthritis with a recombinant human tumor necrosis factor receptor (p75)-Fc fusion protein **etanercept**. N Engl J Med. 1997 Jul 17;337(3):141-7.
Moreland LW, et al. **Etanercept** treatment in adults with established rheumatoid arthritis: **7 years** of clinical experience. J Rheumatol. 2006 May;33(5):854-61. Epub 2006 Mar 15.
Moreland LW, O'Dell JR, Paulus HE, et al. **TEAR** Investigators. A randomized comparative effectiveness study of **oral triple therapy versus etanercept plus methotrexate** in early, aggressive rheumatoid arthritis. Arthritis Rheum. 2012 Apr 16.
Morgan SL, Baggott JE, et al. Supplementation with **folic acid during methotrexate** therapy for rheumatoid arthritis. A double-blind, placebo-controlled trial. Ann Intern Med. 1994 Dec 1;121(11):833-41.
Mori S, Ueki Y, Hirakata N, Oribe M, Hidaka T, Oishi K. Impact of **tocilizumab** therapy on antibody response to **influenza vaccine** in patients with rheumatoid arthritis. Ann Rheum Dis. 2012 Aug 11.
Mori S, Ueki Y, Hirakata N, et al. Impact of **tocilizumab therapy on antibody response to influenza vaccine** in patients with rheumatoid arthritis. Ann Rheum Dis. 2012 Dec;71(12):2006-10.
Mori S, Ueki Y, Akeda Y, et al. **Pneumococcal polysaccharide vaccination** in rheumatoid arthritis patients receiving **tocilizumab** therapy. Ann Rheum Dis. 2013 Aug;72(8):1362-6. T
Morita T, Fujimoto K, Shima Y, et al**. Minimal neonatal transfer of certolizumab pegol** in a Japanese patient with **rheumatoid arthritis**. Ann Rheum Dis. 2018 Sep;77(9):e56.
Mottonen T, Hannonen P, et al. Comparison of **combination** therapy with **single-drug** therapy in early rheumatoid arthritis: a randomised trial. **FIN-RACo trial** group. Lancet. 1999 May 8;353(9164):1568-73.
Movahedi M, Beauchamp ME, Abrahamowicz M, et al. Risk of **Incident Diabetes** Associated with Dose and Duration of **Oral Glucocorticoid Therapy** in Patients with Peumatoid Arthritis. Arthritis Rheumatol. 2015 Dec 14.
Murase JE, Heller MM, Butler DC. Safety of dermatologic medications in pregnancy and lactation. J Am Acad Dermatol 2014;70:401-14 (part I) and 417-26 (part II).
Myasoedova E, Chandran A, Ilhan B, et al. The role of rheumatoid arthritis (RA) flare and cumulative burden of RA severity in the **risk of cardiovascular disease**. Ann Rheum Dis. 2015 Jan 30.
Myasoedova E, Gabriel SE, Matteson EL, et al. **Decreased Cardiovascular Mortality** in Patients with Incident Rheumatoid Arthritis (RA) in Recent Years: Dawn of a New Era in Cardiovascular Disease in RA?. J Rheumatol. 2017 Apr 1.
Nakagomi D, Ikeda K, Okubo A, et al. **Ultrasound** can improve the accuracy of the 2010 ACR/EULAR classification criteria for rheumatoid arthritis to **predict methotrexate requirement**. Arthritis Rheum. 2013 Jan 17.
Nakaoka Y, et al. Efficacy and safety of **tocilizumab** in patients with refractory **Takayasu arteritis**: results from a randomised, double-blind, placebo-controlled, phase 3 trial in Japan (the TAKT study). Ann Rheum Dis. 2018 Mar;77(3):348-354.
Nam JL, Villeneuve E, Hensor EM, et al. Remission induction comparing **infliximab and high-dose intravenous steroid, followed by treat-to-target**: a double-blind, randomised, controlled trial in new-onset, treatment-naive, rheumatoid arthritis (the IDEA study). Ann Rheum Dis. 2014 Jan 1;73(1):75-85
Nam JL, Ramiro S, Gaujoux-Viala C, et al. Efficacy of **biological disease-modifying antirheumatic drugs**: a systematic literature review informing the 2013 update of the EULAR recommendations for the management of rheumatoid arthritis. Ann Rheum Dis. 2014 Mar 1;73(3):516-28.
Nam JL, Villeneuve E, Hensor EM, et al. A randomized controlled trial of **etanercept** and **methotrexate** to induce remission in early inflammatory arthritis: the EMPIRE trial. Ann Rheum Dis. 2014 Jun 1;73(6):1027-36.
Nam JL, et al. **Efficacy of biological disease-modifying anti rheumatic drugs**: a systematic literature review informing the 2016 update of the EULAR recommendations for the management of rheumatoid arthritis. Ann Rheum Dis. 2017 Mar 10.
Nanda KS, Cheifetz AS, Moss AC. Impact of **Antibodies to Infliximab** on Clinical Outcomes and Serum Infliximab Levels in Patients With Inflammatory Bowel Disease (IBD): A Meta-Analysis. Am J Gastroenterol. 2013 Jan;108(1):40-7.
Nash P, Kirkham B, Okada M, et al, on behalf of the SPIRIT-P2 Study Group. **Ixekizumab** for the treatment of patients with active psoriatic arthritis and an inadequate response to tumour necrosis factor inhibitors: results from the 24-week randomised, double-blind, placebo-controlled period of the **SPIRIT-P2** phase 3 trial. Lancet 2017; online May 24, 2017.
Navarro-Compán V, van der Heijde D, et al. **Measurement error** in the assessment of **radiographic** progression in rheumatoid arthritis (RA) clinical trials: the smallest detectable change (SDC) revisited. Ann Rheum Dis. 2014 Jun 1;73(6):1067-70.
Navarro-Compan V, Plasencia-Rodriguez C, de Miguel E, et al. **Anti-TNF discontinuation and tapering strategies** in patients with axial spondyloarthritis: a systematic literature review. Rheumatology (Oxford). 2016 Mar 21.
Navarro-Millán I, Charles-Schoeman C, Yang S, et al. **Changes in lipoproteins** associated with treatment with **methotrexate** or combination therapy in early rheumatoid arthritis: Results from the TEAR trial. Arthritis Rheum. 2013 Mar 4.
Navarro-Millán I, Sattui SE, Curtis JR. Systematic Review of **Tumor Necrosis Factor Inhibitor Discontinuation** Studies in Rheumatoid Arthritis. Clin Ther. 2013 Oct 22.
Navarro-Sarabia F, Ariza-Ariza R, Hernandez-Cruz B, Villanueva I. **Adalimumab** for treating rheumatoid arthritis. Cochrane Database Syst Rev. 2005 Jul 20;(3):CD005113.
Navarro-Compán V, Plasencia-Rodríguez C, de Miguel E, et al. **Anti-TNF discontinuation and tapering strategies in patients with axial spondyloarthritis**: a systematic literature review. Rheumatology (Oxford). 2016 Jul;55(7):1188-94.
Ndosi M, Lewis M, Hale C, et al. The outcome and cost-effectiveness of **nurse-led care** in people with rheumatoid arthritis: a multicentre randomised controlled trial. Ann Rheum Dis. 2014 Nov;73(11):1975-82.
Neovius M, Simard JF, Klareskog L, Askling J; for the ARTIS Study Group. **Sick leave and disability pension** before and after initiation of antirheumatic therapies in clinical practice. Ann Rheum Dis. 2011 Aug;70(8):1407-1414. Obici L, Meini A,
Neovius M, Arkema EV, Olsson H, et al; ARTIS Study Group. **Drug survival on TNF inhibitors** in patients with rheumatoid arthritis comparison of **adalimumab, etanercept and infliximab**. Ann Rheum Dis. 2015 Feb;74(2):354-60.
Newman ED, Lerch V, Billet J, et al. Improving the quality of care of patients with **rheumatic disease using patient-centric electronic redesign software**. Arthritis Care Res (Hoboken). 2015;67:546-53.
Newton-Cheh Christopher, Lin Angela E., Baggish Aaron L., et al. Case 11-2011 — A 47-Year-Old Man with Systemic Lupus Erythematosus and Heart Failure. N Engl J Med 2011; 364:1450-1460. (Infiltrative cardiomyopathy & possible long-QT syndrome due to **hydroxychloroquine**)
Nguyen MTT;Lindegaard H;et al. Initial Serological Response after Prime-boost **Pneumococcal Vaccination** in Rheumatoid Arthritis Patients: Results of a Randomized Controlled Trial. J Rheumatol. 2017 Oct 1. (**rituximab lower response rate**)
NICE: Ankylosing spondylitis - adalimumab, etanercept and infliximab Adalimumab, etanercept and infliximab for ankylosing spondylitis **May 2008** http://www.nice.org.uk/guidance/index.jsp?action=byID&o=11992
NICE Feb/09 **Rheumatoid Arthritis Guidelines** http://www.nice.org.uk/Guidance/CG79 (Deighton C, O'Mahony R, Tosh J, Turner C, Rudolf M; Guideline Development Group. Management of rheumatoid arthritis: summary of NICE guidance. BMJ. 2009 Mar 16;338:b702. doi: 10.1136/bmj.b702.)
NICE: Rheumatoid arthritis - drugs for treatment **after failure of a TNF inhibitor** Aug/10 http://guidance.nice.org.uk/TA195.)
NICE: National Institute for Health and Clinical Excellence. **Adalimumab, etanercept, infliximab, rituximab and abatacept** for the **treatment of rheumatoid arthritis after the failure of a TNF inhibitor**. London (UK): National Institute for Health and Clinical Excellence (NICE); 2010 Aug. http://www.nice.org.uk/nicemedia/live/13108/50409/50409.pdf
NICE: **Tocilizumab** for rheumatoid arthritis Aug/10 http://guidance.nice.org.uk/TA198
NICE: National Institute for Health and Clinical Excellence (NICE). Etanercept, infliximab and adalimumab for the treatment of **psoriatic arthritis**. London (UK): National Institute for Health and Clinical Excellence (NICE); 2010 Aug. 35 p. (Technology appraisal guidance; no. 199). http://www.nice.org.uk/nicemedia/live/13110/50424/50424.pdf
NICE: National Institute for Health and Clinical Excellence (NICE). **Certolizumab** pegol for the treatment of rheumatoid arthritis. London (UK): National Institute for Health and Clinical Excellence (NICE); 2010 Feb. (Technology appraisal guidance; no. 186). http://www.nice.org.uk/nicemedia/live/12808/47528/47528.pdf
NICE: National Institute for Health and Clinical Excellence (NICE). **Tocilizumab** for the treatment of rheumatoid arthritis. London (UK): National Institute for Health and Clinical Excellence; 2012 Feb. http://www.nice.org.uk/nicemedia/live/13669/58202/58202.pdf
NICE: National Institute for Health and Care Excellence (NICE). **Abatacept** for treating rheumatoid arthritis after the failure of conventional disease-modifying anti-rheumatic drugs (rapid review of technology appraisal guidance 234). London (UK): National Institute for Health and Care Excellence (NICE); 2013 Apr.
NCIE: National Institute for Health and Care Excellence (**NICE**). **Abatacept, adalimumab, etanercept and tocilizumab** for treating **juvenile idiopathic arthritis**. (UK): National Institute for Health and Care Excellence (NICE); 2015 Dec 16.
NICE: National Institute for Health and Care Excellence (**NICE**). **Adalimumab, etanercept, infliximab, certolizumab pegol, golimumab, tocilizumab and abatacept** for rheumatoid arthritis not previously treated with DMARDs or after conventional DMARDs only have failed. London (UK): National Institute for Health and Care Excellence (NICE); 2016 Jan 26.
NICE: National Institute for Health and Care Excellence. **TNF-alpha inhibitors** for **ankylosing spondylitis** and non-radiographic axial spondyloarthritis. London (UK): National Institute for Health and Care Excellence (NICE); 2016 Feb 1.
NICE: National Institute for Health and Care Excellence. **Spondyloarthritis in over 16s**: diagnosis and management (NICE guideline NG65). 2016. www.nice.org.uk/guidance/ng65 .
NICE: National Institute for Health and Care Excellence. **TNF-alpha inhibitors for ankylosing spondylitis** and non-radiographic axial spondyloarthritis (technology appraisal guidance TA383). 2016. www.nice.org.uk/guidance/ta383.
NICE: **Secukinumab for active ankylosing spondylitis** after treatment with non-steroidal anti-inflammatory drugs or TNF-alpha inhibitors (technology appraisal guidance TA407). 2016. www.nice.org.uk/guidance/ta407.
NICE: National Institute for Health and Care Excellence. **Draft for consultation: rheumatoid arthritis in adults: management. 2018**. www.nice.org.uk/guidance/GID-NG10014/ documents/draft-guideline
NICE: National Institute for Health and Care Excellence. **Rheumatoid arthritis in adults: management** NICE guideline.11 July 2018 nice.org.uk/guidance/ng100
NICE: National Institute for Health and Care Excellence. **Rheumatoid arthritis in adults: management** (NICE guideline NG100). **2018**. www.nice.org.uk/guidance/ng100.
Nielsen SF, Bojesen SE, Schnohr P, Nordestgaard BG. Elevated **rheumatoid factor** and long term risk of rheumatoid arthritis: a prospective cohort study. BMJ. 2012 Sep 6;345:e5244.
Nielsen OH, Loftus EV, Jess T. Safety of **TNF-α inhibitors during IBD pregnancy**: a systematic review. BMC Med 2013;11:174.

Nigrovic PA, Mannion M, Prince FH, et al. **Anakinra** as first-line disease-modifying therapy in **systemic juvenile idiopathic arthritis**: report of forty-six patients from an international multicenter series. Arthritis Rheum. 2011 Feb;63(2):545-55. doi: 10.1002/art.30128.

Nikiphorou E, Carpenter L, Morris S, et al. **Hand and Foot Surgery** Rates in Rheumatoid Arthritis Have Declined From 1986 to 2011, but Large-Joint Replacement Rates Remain Unchanged: Results From Two UK Inception Cohorts. Arthritis Rheumatol. 2014 May;66(5):1081-9.

Nishimura K, Sugiyama D, Kogata Y, et al. Meta-analysis: diagnostic accuracy of anti-cyclic citrullinated peptide antibody and rheumatoid factor for rheumatoid arthritis. Ann Intern Med. 2007 Jun 5;146(11):797-808. **Anti-CCP antibodies** are more specific than RF for diagnosing rheumatoid arthritis & may better predict erosivedisease.

Noe A, Howard C, Thuren T, et al. Pharmacokinetic and Pharmacodynamic Characteristics of Single-Dose **Canakinumab** in Patients With Type 2 Diabetes Mellitus. Clin Ther. 2014 Sep 17.

Nordal E, Zak M, Aalto Ket al. **Juvenile idiopathic arthritis**; Ongoing disease activity and changing categories in a long-term Nordic cohort study. Arthritis Rheum. 2011 May 10.

Nørgård BM, Larsen MD, Friedman S, et al J. **Decreased chance of a live born child in women with rheumatoid arthritis after assisted reproduction treatment**: a nationwide cohort study. Ann Rheum Dis. 2019 Mar;78(3):328-334.

Norgeot B, Glicksberg BS, Trupin L, et al. Assessment of a **Deep Learning Model Based on Electronic Health Record Data to Forecast Clinical Outcomes in Patients With Rheumatoid Arthritis**. JAMA Netw Open. 2019 Mar 1;2(3):e190606

Norton S, Sacker A, Dixey J, et al. **Trajectories of functional limitation** in early rheumatoid arthritis and their **association with mortality**. Rheumatology (Oxford). 2013 Nov;52(11):2016-24.

Nozawa T, Imagawa T, Ito S. **Coronary-Artery Aneurysm in Tocilizumab**-Treated Children with Kawasaki's Disease. N Engl J Med. 2017 Nov 9;377(19):1894-1896.

Nuki G, Bresnihan B, et al. European Group Of Clinical Investigators. Long-term safety and maintenance of clinical improvement following treatment with **anakinra** (recombinant human interleukin-1 receptor antagonist) in patients with rheumatoid arthritis: extension phase of a randomized, double-blind, placebo-controlled trial. Arthritis Rheum. 2002 Nov;46(11):2838-46.

Nurmohamed MT. **Treat to target in rheumatoid arthritis**: Good for the joints but also for the **heart**? Arthritis Rheumatol. 2015 Mar 16.

Nyboe Andersen N, Pasternak B, et al. Association between **tumor necrosis factor-α antagonists and risk of cancer in patients with inflammatory bowel disease.** JAMA. 2014 Jun 18;311(23):2406-13.

Nyboe Andersen N, Pasternak B, et al. Association between **tumour necrosis factor-α inhibitors** and risk of **serious infections** in people with inflammatory bowel disease: nationwide Danish cohort study. BMJ. 2015 Jun 5;350:h2809.

Obici L, Meini A, Cattalini M, et al. Favourable and sustained response to **anakinra** in **tumour necrosis factor receptor-associated periodic syndrome (TRAPS)** with or without AA amyloidosis. Ann Rheum Dis. 2011 Aug;70(8):1511-2.

O'Dell JR, Leff R, et al. Treatment of rheumatoid arthritis with **methotrexate and hydroxychloroquine**, **methotrexate and sulfasalazine**, or a **combination** of the **three** medications: results of a two-year, randomized, double-blind, placebo-controlled trial. Arthritis Rheum. 2002 May;46(5):1164-70.

O'Dell JR, Haire CE, et al. Treatment of rheumatoid arthritis with **methotrexate alone**, **sulfasalazine and hydroxychloroquine**, or a **combination** of all **three** medications. N Engl J Med. 1996 May 16;334(20):1287-91.

O'Dell JR, Blakely KW, et al. Treatment of early seropositive rheumatoid arthritis: a two-year, double-blind comparison of **minocycline** and **hydroxychloroquine**. Arthritis Rheum. 2001 Oct;44(10):2235-41.

O'dell JR, Petersen K, Leff R, et al. **Etanercept in Combination with Sulfasalazine, Hydroxychloroquine, or Gold** in the Treatment of Rheumatoid Arthritis. J Rheumatol. 2005 Dec 15; [Epub ahead of print]

O'Dell JR, Curtis JR, Mikuls T, et al; for the TEAR trial investigators. **Validation of methotrexate-first strategy** in early poor prognosis rheumatoid arthritis: Results from a randomized, double-blind, 2-year trial. Arthritis Rheum. 2013 May 17.

O'Dell JR, Mikuls TR, et al. Therapies for active rheumatoid arthritis **after methotrexate failure**. (CSP 551 RACAT) N Engl J Med 2013. DOI: 10.1056/NEJMoa1303006. (**methotrexate/hydroxychloroquine/sulfasalazine vs etanercept/MTX**)

Ojeda-Uribe M, Afif N, Dahan E, Sparsa L, Haby C, Sibilia J, Ternant D, Ardizzone M. Exposure to **abatacept or rituximab in the first trimester of pregnancy in three women** with autoimmune diseases. Clin Rheumatol. 2013 Jan 5.

Okada Y, Eyre S, Suzuki A, et al. **Genetics of rheumatoid arthritis**: 2018 status. Ann Rheum Dis. 2019 Apr;78(4):446-453.

Okuyama A, Nagasawa H, Suzuki K, et al. **Fc{gamma} receptor IIIb polymorphism and use of glucocorticoids** at baseline are associated with **infusion reactions to infliximab** in patients with rheumatoid arthritis. Ann Rheum Dis. 2011 Feb;70(2):299-304.

Olivieri I, Palazzi C, Peruz G, Padula A. Management Issues with Elderly-Onset Rheumatoid Arthritis : An Update. Drugs Aging. 2005;22(10):809-822.

Olofsson T, Petersson IF, Eriksson JK, et al. **Predictors of work disability** during the first 3 years after diagnosis in a national rheumatoid arthritis inception cohort. Ann Rheum Dis. 2014 May 1;73(5):845-53.

Olofsson T, et al. Predictors of **work disability** after start of **anti-TNF therapy** in a national cohort of Swedish patients with rheumatoid arthritis: does early anti-TNF therapy bring patients back to work? Ann Rheum Dis. 2017 Jul;76(7):1245-1252.

Orellana C, Wedrén S, Källberg H, et al. **Parity and the risk of developing rheumatoid arthritis**: results from the Swedish Epidemiological Investigation of Rheumatoid Arthritis study. Ann Rheum Dis. 2014 Apr 1;73(4):752-5.

Orellana C, Saevarsdottir S, Klareskog L, et al. **Oral contraceptives, breastfeeding and the risk** of developing rheumatoid arthritis: results from the Swedish EIRA study. Ann Rheum Dis. 2017 Aug 17.

Ørnbjerg LM, Brahe CH, Askling J, et al. Treatment response and drug retention rates in 24 195 biologic-naïve **patients with axial spondyloarthritis initiating TNFi treatment**: routine care data from 12 registries in the EuroSpA collaboration. Ann Rheum Dis. 2019 Nov;78(11):1536-1544

Ornetti P, Chevillotte H, Zerrak A, Maillefert JF. **Anti-Tumour Necrosis** Factor-alpha Therapy for Rheumatoid and Other Inflammatory Arthropathies : Update on Safety in **Older Patients**. Drugs Aging. 2006;23(11):855-60.

Ornbjerg LM, Ostergaard M, Bøyesen P, et al. Impact of **tumour necrosis factor inhibitor** treatment on **radiographic progression** in rheumatoid arthritis patients in clinical practice: results from the nationwide Danish **DANBIO** registry. Ann Rheum Dis. 2013 Jan;72(1):57-63.

Ortiz-Sanjuán F, Blanco R, Calvo-Rio V, et al. Efficacy of **tocilizumab** in refractory adult-onset still's disease: Multicenter retrospective open-label study of 34 patients. Arthritis Rheumatol. 2014 Feb 10

Osiri M, Shea B, Welch V, Suarez-Almazor ME, Strand V, Tugwell P, et al. **Leflunomide** for the treatment of rheumatoid arthritis. Cochrane Database Syst Rev [Internet]. 2009 [cited 2011 Apr 11];(4):CD002047.

Østergaard M, Emery P, Conaghan PG, et al. Significant improvement in synovitis, osteitis, and bone erosion following **golimumab and methotrexate** combination therapy as compared with methotrexate alone: a magnetic resonance imaging study of 318 methotrexate-naive rheumatoid arthritis patients. Arthritis Rheum. 2011 Dec;63(12):3712-22.

Østergaard M, Jacobsson LT, Schaufelberger C, et al. MRI assessment of early response to **certolizumab** pegol in rheumatoid arthritis: a randomised, double-blind, placebo-controlled phase IIIb study applying MRI at weeks 0, 1, 2, 4, 8 and 16. Ann Rheum Dis. 2015 Jun;74(6):1156-63.

Otten Marieke H., Prince Femke H. M., Armbrust Wineke, et al. Original Contribution Factors Associated With Treatment Response to **Etanercept** in **Juvenile Idiopathic Arthritis**. JAMA. 2011;Published online November 6, 2011.

Otten MH, Prince FH, Anink J, et al. Effectiveness and safety of a **second and third biological agent after failing etanercept** in juvenile idiopathic arthritis: results from the Dutch National ABC Register. Ann Rheum Dis. 2012 Jun 23.

Otten MH, Anink J, Spronk S, et al. Efficacy of **biological agents in juvenile idiopathic arthritis**: a systematic review using indirect comparisons. Ann Rheum Dis. 2013 Nov 1;72(11):1806-1812.

Otten MH, Anink J, Prince FH, et al. **Trends in prescription of biological agents** and outcomes of **juvenile idiopathic arthritis**: results of the Dutch national Arthritis and Biologics in Children Register. Ann Rheum Dis. 2014 Mar 18.

Overman CL, Jurgens MS, Bossema ER, et al. Patients with rheumatoid arthritis nowadays are **less psychologically distressed and physically disabled** than patients two decades ago. Arthritis Care Res (Hoboken). 2013 Dec 3

Overman RA, Yeh JY, Deal CL. Prevalence of **oral glucocorticoid usage in the United States**: a general population perspective. Arthritis Care Res (Hoboken). 2013 Feb;65(2):294-8

Ozen G, Pedro S, Holmqvist ME, et al. **Risk of diabetes mellitus associated with disease-modifying antirheumatic drugs** and statins in rheumatoid arthritis. Ann Rheum Dis. 2017 May;76(5):848-854. (HCQ & abatacept)

Ozen G, Pedro S, Wolfe F, Michaud K. **Medications associated with fracture risk** in patients with rheumatoid arthritis. Ann Rheum Dis. 2019 Aug;78(8):1041-1047.

Paller AS, Siegfried EC, Langley RG, et al.; **Etanercept Pediatric Psoriasis** Study Group. Etanercept treatment for children and adolescents with plaque psoriasis. N Engl J Med. 2008 Jan 17;358(3):241-51.

Papadopoulou C, Kostik M, Böhm M, et al. **Methotrexate Therapy May Prevent the Onset of Uveitis** in Juvenile Idiopathic Arthritis. J Pediatr. 2013 May 9.

Papp KA, Tyring S, Lahfa M, et al.; **Etanercept Psoriasis** Study Group. A global phase III randomized controlled trial of etanercept in psoriasis: safety, efficacy, and effect of dose reduction. Br J Dermatol. 2005 Jun;152(6):1304-12.

Papp K, Thaçi D, et al. Efficacy & safety **adalimumab every other week versus methotrexate once weekly in children and adolescents with severe chronic plaque psoriasis**: a randomised, double-blind, phase 3 trial. Lancet 2017; online May 4.

Paradisi A, Abeni D, Bergamo F, et al. **Etanercept** therapy for **toxic epidermal necrolysis**. J Am Acad Dermatol. 2014 Aug;71(2):278-83.

Paramarta JE, De Rycke L, Heijda TF, et al. Efficacy and safety of **adalimumab** for the treatment of peripheral arthritis in spondyloarthritis patients without ankylosing spondylitis or psoriatic arthritis. Ann Rheum Dis. 2013 Nov 1;72(11):1793-1799.

Park JK, Choi Y, Winthrop KL, et al. Optimal time between the last **methotrexate administration and seasonal influenza vaccination** in rheumatoid arthritis: post hoc analysis of a randomised clinical trial. Ann Rheum Dis. 2019 Sep;78(9):1283-1284.

Park JK, Lee MA, Lee EY, et al. Effect of **methotrexate discontinuation** on efficacy of seasonal influenza vaccination in patients with rheumatoid arthritis: a randomised clinical trial. Ann Rheum Dis. 2017 Sep;76(9):1559-1565.

Park JK, Lee YJ, et al. Impact of **temporary methotrexate discontinuation for 2 weeks on immunogenicity of seasonal influenza vaccination** in patients with rheumatoid arthritis: a randomised clinical trial. Ann Rheum Dis. 2018 Mar 23.

Park JK, Lee YJ, Bitoun S, et al.Interaction between **B-cell activation factor and methotrexate impacts immunogenicity of seasonal influenza vaccination** in patients with rheumatoid arthritis. Ann Rheum Dis. 2019 Feb;78(2):282-284

Park JW, Curtis JR, et al. Prophylactic effect of **trimethoprim-sulfamethoxazole for pneumocystis pneumonia** in patients with rheumatic diseases **exposed to prolonged high-dose glucocorticoids**. Ann Rheum Dis. 2018 May;77(5):644-649.

Partington RJ, Muller S, Helliwell T, et al. **Incidence, prevalence and treatment burden of polymyalgia rheumatica in the UK over two decades**: a population-based study. Ann Rheum Dis. 2018 Dec;77(12):1750-1756

Pasnoor M, He J, et al; Methotrexate in MG Investigators of the Muscle Study Group. A randomized controlled trial of **methotrexate** for patients with generalized **myasthenia gravis**. Neurology. 2016 Jul 5;87(1):57-64. Epub 2016 Jun 15.

Paulshus Sundlisæter N, Aga AB, Olsen IC, et al; ARCTIC study group**. Clinical and ultrasound remission after 6 months of treat-to-target therapy in early rheumatoid arthritis**: associations to future good radiographic and physical outcomes. Ann Rheum Dis. 2018 Oct;77(10):1421-1425.
Pavelka K, Jarosova K, et al. Increasing the **infliximab dose** in rheumatoid arthritis patients: a randomized, double blind study failed to confirm its efficacy. Ann Rheum Dis. 2009 Apr 6. [Epub ahead of print]
Pawar A, Desai RJ, Solomon DH, et al. Risk of serious **infections in tocilizumab versus other biologic drugs** in patients with rheumatoid arthritis: a multidatabase cohort study. Ann Rheum Dis. 2019 Apr;78(4):456-464.
Payet J, Goulvestre C, Biale L, et al. **Anticyclic Citrullinated Peptide Antibodies** in Rheumatoid and Nonrheumatoid Rheumatic Disorders: Experience with 1162 Patients. J Rheumatol. 2014 Oct 1.
Perier A, Savey L, Marcelin AG, et al. De Novo **HHV-8** tumors induced by **rituximab** in autoimmune or inflammatory systemic diseases. Arthritis Rheumatol. 2017 Jul 18.
Perlman EM, Greenberg PB, et al. Solving the **Hydroxychloroquine Dosing** Dilemma With a Smartphone App. JAMA Ophthalmol. 2018 Jan 4.
Persson MSM, Sarmanova A, Doherty M, Zhang W. Conventional and biologic **disease-modifying anti-rheumatic drugs for osteoarthritis**: a meta-analysis of randomized controlled trials. Rheumatology (Oxford). 2018 Jun 16.
Peterfy C, Emery P, Tak PP, et al. MRI assessment of suppression of structural damage in patients with rheumatoid arthritis receiving **rituximab**: results from the randomised, placebo-controlled, double-blind RA-SCORE study. Ann Rheum Dis. 2014 Oct 29.
Peterfy C, Burmester GR, Bykerk VP, et al. Sustained improvements in MRI outcomes with **abatacept** following the withdrawal of all treatments in patients with early,progressive rheumatoid arthritis. Ann Rheum Dis. 2016 Aug;75(8):1501-5.
Peterfy C, et al. Short-term changes on **MRI predict long-term changes** on radiography in rheumatoid arthritis: analysis by an OMERACT Task Force of pooled data from four randomised controlled trials. Ann Rheum Dis. 2017 Jun;76(6):992-997.
Peters MJ, Symmons DP, et al. EULAR evidence-based recommendations for **cardiovascular risk** management in patients with rheumatoid arthritis and other forms of inflammatory arthritis. Ann Rheum Dis. 2009 Sep 22.
Pharmacist's Letter. Selected Issues in the Effective and Safe Use of **Live Vaccines**. Oct 2007.
Pharmacist's Letter Detail-Document, DMARDs in the Treatment of Rheumatoid Arthritis. Pharmacist's Letter/Prescriber's Letter. September 2014.
Pikwer M, Bergström U, et al. **Breast-feeding**, but not oral contraceptives, is associated with a reduced risk of rheumatoid arthritis. Ann Rheum Dis. 2008 May 14. [Epub ahead of print]
Pikwer M, Bergström U, Nilsson JÅ et al. **Early menopause** is an independent predictor of rheumatoid arthritis. Ann Rheum Dis. 2012 Mar;71(3):378-81.
Pikwer M, Giwercman A, Bergström U, et al. Association between **testosterone levels** and risk of future rheumatoid arthritis in men: a population-based case-control study. Ann Rheum Dis. 2014 Mar 1;73(3):573-9.
Pinnell J, Potter T. A **rare reaction to sulfasalazine**. BMJ 2017 Nov 30; 359:j5189.
Pivovarov K, Zipursky JS. **Low-dose methotrexate toxicity**. CMAJ. 2019 Apr 15;191(15):E423.
Plant D, Prajapati R, Hyrich KL, et al. Investigation of established rheumatoid-arthritis (RA) susceptibility genetic markers as predictors of response to **anti-TNF therapy** in a large UK cohort replicates association with the **PTPRC gene**. Arthritis Rheum. 2011 Sep 27. doi: 10.1002/art.33381.
Plasencia C, Pascual-Salcedo D, Nuño L, et al. Influence of **immunogenicity** on the efficacy of longterm treatment of spondyloarthritis with **infliximab**. Ann Rheum Dis. 2012 Dec;71(12):1955-60.
Plosker GL, Croom KF. **Sulfasalazine**: a review of its use in the management of rheumatoid arthritis. Drugs. 2005;65(13):1825-49.
Poddubnyy D, Rudwaleit M, et al. Effect of **non-steroidal anti-inflammatory drugs** on radiographic spinal progression in patients with axial **spondyloarthritis**: results from the German Spondyloarthritis Inception Cohort. Ann Rheum Dis 2012.
Poiroux L, Allanore Y, Kahan A, et al. All-cause **Mortality Associated with TNF-alpha Inhibitors** in Rheumatoid Arthritis: A Meta-Analysis of Randomized Controlled Trials. Am J Med. 2015 Aug 3.
Pollastro S, Klarenbeek PL, Doorenspleet ME, et al. **Non-response to rituximab therapy** in rheumatoid arthritis is associated with incomplete disruption of the B cell receptor repertoire. Ann Rheum Dis. 2019 Jun 19.
Ponchel F, Goëb V, Parmar R, et al. An **immunological biomarker to predict MTX response** in early RA. Ann Rheum Dis. 2014 Nov;73(11):2047-53.
Poor G, Strand V. Efficacy and safety of **leflunomide 10 mg versus 20 mg** once daily in patients with active rheumatoid arthritis: multinational double-blind, randomized trial. Rheumatology (Oxford). 2004 Mar 16 [Epub ahead of print]
Pope JE, Haraoui B, Thorne JC, et al. The **Canadian Methotrexate and Etanercept Outcome Study**: a randomised trial of **discontinuing versus continuing methotrexate** after 6 months of etanercept and methotrexate therapy in rheumatoid arthritis. Ann Rheum Dis. 2013 Aug 26.
Poppelaars PB, van Tuyl LHD, Boers M. **Normal mortality of the COBRA early rheumatoid arthritis** trial cohort after 23 years of follow-up. Ann Rheum Dis. 2019 May;78(5):586-589.
Poropat F, Pastore S, Gesuete V, et al. A boy with fever and arthralgia (**acute rheumatic fever**). BMJ. 2017 Mar 29;356:j1347
Porter D, van Melckebeke J, et al. **Tumour necrosis factor inhibition versus rituximab** patients with rheumatoid arthritis who require biological treatment (**ORBIT**): open-label, randomised controlled, non-inferiority, trial. Lancet. 2016 May 16.
Potikuri D, Dannana KC, Kanchinadam S et al. **Periodontal disease** is significantly higher in non-smoking treatment-naive rheumatoid arthritis patients: results from a case-control study. Ann Rheum Dis. 2012 Sep;71(9):1541-4.
Pouw MF, Krieckaert CL, Nurmohamed MT, et al. Key findings towards optimising **adalimumab** treatment: the **concentration-effect curve**. Ann Rheum Dis. 2015 Mar;74(3):513-8.
Prakken B, Albani S, Martini A. **Juvenile idiopathic arthritis (JIA)**. Lancet 2011; 377: 2138–49.
Prevalence of Doctor-Diagnosed Arthritis and Arthritis-Attributable Activity Limitation --- United States, 2003—2005 http://www.cdc.gov/mmwr/preview/mmwrhtml/mm5540a2.htm?s_cid=mm5540a2_x
Prey S, Paul C. Effect of **folic or folinic acid** supplementation on methotrexate-associated safety and efficacy in inflammatory disease: a systematic review. Br J Dermatol. 2008 Oct 20. [Epub ahead of print] Supplementation with folic acid is an effective measure to reduce hepatic adverse effects associated with methotrexate treatment. There is no difference between folinic acid and folic acid, but the lower cost of the latter promotes its use.
Primdahl J, Clausen J, Hørslev-Petersen K. Results from **systematic screening for cardiovascular risk** in outpatients with rheumatoid arthritis in accordance with the EULAR recommendations. Ann Rheum Dis. 2013 Nov 1;72(11):1771-1776.
Prince FH, Otten MH, van Suijlekom-Smit LW. Diagnosis and management of **juvenile idiopathic arthritis**. BMJ. 2010 Dec 3;341:c6434. doi: 10.1136/bmj.c6434.
Proano C, Kimball GP. **Hydroxychloroquine Retinal Toxicity**. N Engl J Med. 2019 Apr 25;380(17):e27.
Proudman SM, James MJ, Spargo LD, et al. Fish oil in recent onset rheumatoid arthritis: a randomised, double-blind controlled trial within algorithm-based drug use. Ann Rheum Dis. 2013 Sep 30.
Provan SA, Lillegraven S, Sexton J, et al. Trends in **all-cause and cardiovascular mortality** in patients with incident rheumatoid arthritis: a 20-year follow-up matched case-cohort study. Rheumatology (Oxford). 2019 Aug 29. doi:10.1093/rheumatology/kez371.
Putrik P, Ramiro S, et al; Working Group '**Equity in access to treatment** of rheumatoid arthritis in Europe'. Inequities in access to biologic and synthetic DMARDs across 46 European countries. Ann Rheum Dis. 2014 Jan 1;73(1):198-206
Putrik P, Ramiro S, Guillemin F, et al. Patients with rheumatoid arthritis facing **sick leave or work disability** meet varying regulations: a study among rheumatologists and patients from 44 European countries. Ann Rheum Dis. 2019 Nov;78(11):1472-1479.
Putrik P, Ramiro S, Kvien TK, et al; Equity in Clinical Eligibility Criteria for RA treatment Working Group. Variations in criteria regulating treatment with **reimbursed biologic DMARDs across European countries**. Are differences related to country's wealth? Ann Rheum Dis. 2014 Nov;73(11):2010-21
Putrik P, Ramiro S, Keszei AP, et al. **Lower education and living in countries with lower wealth** are associated with higher disease activity in rheumatoid arthritis: results from the multinational COMORA study. Ann Rheum Dis. 2015 Jan 28.
Quartier Pierre, Allantaz Florence, Cimaz Rolando, et al. A multicentre, randomised, double-blind, placebo-controlled trial with the interleukin-1 receptor antagonist **anakinra** in patients with **systemic-onset juvenile** idiopathic arthritis (**ANAJIS** trial). Ann Rheum Dis 2011;70:747-754 Published Online First: 20 December 2010 doi:10.1136/ard.2010.134254.
Quartier P, Baptiste A, Despert V, et al. **ADJUVITE**: a double-blind, randomised, placebo-controlled trial of **adalimumab in early onset, chronic, juvenile idiopathic arthritis-associated anterior uveitis**. Ann Rheum Dis. 2018 Jul;77(7):1003-1011.
Raaschou P, Simard JF, Neovius M, Askling J; Anti-Rheumatic Therapy in Sweden Study Group (ARTIS). Does **cancer** that occurs during or after **anti-tumor necrosis factor therapy** have a worse prognosis? A national assessment of overall and site-specific cancer survival in rheumatoid arthritis patients treated with biologic agents. Arthritis Rheum. 2011 Jul;63(7):1812-22.
Raaschou P, Simard JF, Holmqvist M, et al. Rheumatoid arthritis, **anti-tumour necrosis factor therapy**, & risk of **malignant melanoma**: nationwide population based prospective cohort study from Sweden. BMJ. 2013 Apr 8;346:f1939.
Raaschou P, Simard JF, Asker Hagelberg C, et al; ARTIS Study Group. Rheumatoid arthritis, **anti-tumour necrosis factor treatment**, and **risk of squamous cell and basal cell skin cancer**: cohort study based on nationwide prospectively recorded data from Sweden. BMJ. 2016 Jan 28;352:i262.
Rahman MU, Buchanan J, et al. Changes in **patient characteristics in anti-tumour necrosis factor clinical trials** for rheumatoid arthritis: results of an analysis of the literature over the past 16 years. Ann Rheum Dis. 2011 Sep;70(9):1631-40.
Rahman P, Puig L, Gottlieb AB, et al. Ustekinumab Treatment and Improvement of Physical Function and Health-Related Quality of Life in Patients With Psoriatic Arthritis. Arthritis Care Res (Hoboken). 2016 Dec;68(12):1812-1822.
Rakieh C, Nam JL, Hunt L, et al. Predicting the development of clinical arthritis in **anti-CCP positive individuals** with non-specific musculoskeletal symptoms: a prospective observational cohort study. Ann Rheum Dis. 2014 Apr 12.
Ramanan AV, Dick AD, Jones AP, et al. **Adalimumab plus methotrexate** for **uveitis** in **juvenile idiopathic arthritis**. N Engl J Med 2017;376:1637-46.
Ramiro S, Gaujoux-Viala C, Nam JL, et al. **Safety of synthetic and biological DMARDs**: a systematic literature review informing the 2013 update of the EULAR recommendations for management of rheumatoid arthritis. Ann Rheum Dis. 2014 Mar 1;73(3):529-35.
Ramiro S, Smolen JS, Landewe R, et al. Pharmacological treatment of **psoriatic arthritis**: a systematic literature review for the **2015** update of the **EULAR** recommendations for the management of psoriatic arthritis. Ann Rheum Dis. 2015 Dec 11.

Ramiro S, Sepriano A, et al. **Safety of synthetic and biological DMARDs**: a systematic literature review informing the 2016 update of the EULAR recommendations for management of rheumatoid arthritis. Ann Rheum Dis. 2017 Mar 15.

Rantalaiho VM, Kautiainen H, Korpela M, et al; for the FIN-RACo Trial Group. Changing **sulphasalazine to methotrexate** does not improve the 2-year outcomes of the initial single DMARD treatment in early rheumatoid arthritis: subanalysis of the FIN-RACo trial. Ann Rheum Dis. 2013 Jan 24.

Rantalaiho V, Kautiainen H, Korpela M, et al; NEO-RACo Study Group. **Targeted treatment with a combination of traditional DMARDs** produces excellent clinical and radiographic long term outcomes in early rheumatoid arthritis regardless of initial **infliximab**. The 5-year follow-up results of a randomised clinical trial, the NEO-RACo trial. Ann Rheum Dis. 2014 Nov;73(11):1954-61. (**methotrexate, sulfasalazine, hydroxychloroquine & prednisone**)

Raaschou P, Frisell T, Askling J; **ARTIS** Study Group. **TNF inhibitor therapy and risk of breast cancer recurrence** in patients with rheumatoid arthritis: a nationwide cohort study. Ann Rheum Dis. 2015 Dec;74(12):2137-43.

Raaschou P, Söderling J, Turesson C, et al. **Tumor Necrosis Factor Inhibitors and Cancer Recurrence** in Swedish Patients With Rheumatoid Arthritis: A Nationwide Population-Based Cohort Study. Ann Intern Med. 2018 Aug 14.

Ravelli A, Davì S, et al. **Intra-articular corticosteroids versus intra-articular corticosteroids plus methotrexate** in oligoarticular juvenile idiopathic arthritis: a multicentre, prospective, randomised, open-label trial. Lancet 2016; online Feb 2.

Ravelli A, Consolaro A, Horneff G, et al. Treating **juvenile idiopathic arthritis** to target: recommendations of an international task force. Ann Rheum Dis. 2018 Jun;77(6):819-828.

Ravi B, Croxford R, Austin PC, et al. Increased **surgeon experience** with rheumatoid arthritis reduces the risk of complications following **total joint arthroplasty**. Arthritis Rheumatol. 2014 Mar;66(3):488-96.

Ravindran V, Rachapalli S, Choy EH. Safety of medium- to long-term **glucocorticoid therapy** in rheumatoid arthritis: a meta-analysis. Rheumatology (Oxford). 2009 Jul;48(7):807-11. Epub 2009 May 15.

Ray M, Curtis JR, Baddley JW. A case report of progressive multifocal leucoencephalopathy (**PML**) associated with **adalimumab**. Ann Rheum Dis. 2014 Jul;73(7):1429-30.

Reeves DJ, Moore ES, Bascom D, et al. Retrospective evaluation of **methotrexate elimination** when co-administered with proton pump inhibitors. Br J Clin Pharmacol. 2014 Mar 20.

Reeves D, DiDominick S, Finn S, et al. **Methotrexate Elimination** When Coadministered With **Levetiracetam**. Ann Pharmacother. 2016 Dec;50(12):1016-1022.

Reich K, Nestle FO, Papp K, et al.; **EXPRESS** study investigators. Infliximab induction and maintenance therapy for moderate-to-severe **psoriasis**: a phase III, multicentre, double-blind trial. Lancet. 2005 Oct 15-21;366(9494):1367-74.

Remaeus K, Johansson K, Askling J, et al. **Juvenile onset arthritis and pregnancy** outcome: a population-based cohort study. Ann Rheum Dis. 2017 Nov;76(11):1809-1814.

Rempenault C;Combe B;Barnetche T;et al. Metabolic and cardiovascular benefits of **hydroxychloroquine** in patients with rheumatoid arthritis: a systematic review and meta-analysis. Ann Rheum Dis. 2017 Sep 25. pii: annrheumdis-2017-211836.

Rempenault C, Combe B, Barnetche T, et al. Metabolic and cardiovascular benefits of **hydroxychloroquine** in patients with rheumatoid arthritis: a systematic review and meta-analysis. Ann Rheum Dis. 2018 Jan;77(1):98-103.

Rezaei H, Saevarsdottir S, Forslind K et al. In early rheumatoid arthritis, patients with a good initial response to **methotrexate** have excellent 2-year clinical outcomes, but radiological progression is not fully prevented: data from the methotrexate responders population in the **SWEFOT** trial. Ann Rheum Dis. 2012 Feb;71(2):186-91. (infliximab)

Reveille JD, Deodhar A, Caldron PH, et al. **Safety and Efficacy of Intravenous Golimumab in Adults with Ankylosing Spondylitis**: Results through 1 Year of the GO-ALIVE Study. J Rheumatol. 2019 Mar 1. pii: jrheum.180718.

Ribeiro AC, Guedes LK, Moraes JC, et al. **Reduced seroprotection after pandemic H1N1 influenza** adjuvant-free vaccination in patients with rheumatoid arthritis: implications for clinical practice. Ann Rheum Dis. 2011 Dec;70(12):2144-7.

Richards BL, Whittle SL, Buchbinder R. **Antidepressants for pain management** in rheumatoid arthritis. Cochrane Database Syst Rev. 2011 Nov 9;11:CD008920. There is currently insufficient evidence to support the routine prescription of antidepressants as analgesics in patients with RA as no reliable conclusions about their efficacy can be drawn from eight placebo RCTs.

Richards BL, Whittle SL, Buchbinder R. **Muscle relaxants for pain** management in rheumatoid arthritis. Cochrane Database of Systematic Reviews 2011, Issue 1. Art. No.: CD008922. DOI: 10.1002/14651858.CD008922

Richards BL, Whittle SL, Buchbinder R. **Neuromodulators for pain** management in rheumatoid arthritis. Cochrane Database of Systematic Reviews 2011, Issue 1. Art. No.: CD008921. DOI: 10.1002/14651858.CD008921.

Richards JS, Dowell SM, Quinones ME, et al. **How to use biologic agents** in patients with rheumatoid arthritis who have **comorbid disease**. BMJ. 2015 Aug 17;351:h3658.

Richmond SJ, Gunadasa S, et al. **Copper bracelets and magnetic wrist straps** for rheumatoid arthritis - analgesic and anti-inflammatory effects: a randomised double-blind placebo controlled crossover trial. PLoS One. 2013 Sep16;8(9):e71529.

Richter A, Listing J, Schneider M, et al. Impact of treatment with **biologic DMARDs** on the risk of **sepsis or mortality after serious infection** in patients with rheumatoid arthritis. Ann Rheum Dis. 2016 Sep;75(9):1667-73

Ridker PM, Everett BM, Pradhan A, et al; CIRT Investigators. **Low-Dose Methotrexate for the Prevention of Atherosclerotic Events**. N Engl J Med. 2018 Nov 10.

Rigby W, Ferraccioli G, Greenwald M, et al. **Rituximab** improved physical function and quality of life in patients with rheumatoid arthritis naïve to methotrexate (**IMAGE** study). Arthritis Care Res (Hoboken). 2010 Dec 8.

Ringold S, Weiss PF, Beukelman T, et al. **2013** update of the 2011 american college of rheumatology (**ACR**) recommendations for the treatment of **juvenile idiopathic arthritis**: recommendations for the medical therapy of children with systemic juvenile idiopathic arthritis and tuberculosis screening among children receiving biologic medications. Arthritis Care Res (Hoboken). 2013 Oct;65(10):1551-63.

Ringold S, Nigrovic PA, et al. The **Childhood Arthritis & Rheumatology Research Alliance Consensus Treatment Plans**: Towards Comparative Effectiveness in the Pediatric Rheumatic Diseases. Arthritis Rheumatol. 2018 Jan 15.

Ritchlin CT, Colbert RA, Gladman DD. **Psoriatic Arthritis**. N Engl J Med. 2017 Mar 9;376(10):957-970.

Rituximab (Rituxan) for Rheumatoid Arthritis. Pharmacist's Letter Aug, 2006. (Roche patient Assisance program 1-888-748-8926)

Robert N, Wong GW, Wright JM. Effect of **cyclosporine on blood pressure**. Cochrane Database Syst Rev. 2010 Jan 20;(1):CD007893. There appears to be a dose-related effect with lower doses (1-4 mg/kg/d) increasing mean BP by an average of 5 mmHg and higher doses (>10 mg/kg/d) increasing mean BP by 11 mmHg on average.

Roerink ME, Bredie SJ, Heijnen M, et al. Cytokine Inhibition (**anakinra**) in Patients With **Chronic Fatigue Syndrome**: A Randomized Trial. Ann Intern Med. 2017 Mar 7.

Rom AL, Wu CS, Olsen J, et al. **Fetal growth and preterm birth** in children exposed to maternal or paternal rheumatoid arthritis: a nationwide cohort study. Arthritis Rheumatol. 2014 Dec;66(12):3265-73.

Rom AL, Wu CS, Olsen J, et al. Parental rheumatoid arthritis and childhood **epilepsy**: A nationwide cohort study. Neurology. 2016 Dec 13;87(24):2510-2516.

Rongen-van Dartel SA, Repping-Wuts H, Flendrie M, et al. Effect of **Aerobic Exercise Training** on **Fatigue** in Rheumatoid Arthritis: A Meta-Analysis. Arthritis Care Res (Hoboken). 2015 Aug;67(8):1054-62.

Roodenrijs NMT, de Hair MJH, van der Goes MC, et al; whole EULAR Task Force on development of EULAR recommendations for the comprehensive management of difficult-to-treat rheumatoid arthritis. Characteristics of **difficult-to-treat rheumatoid arthritis**: results of an international survey. Ann Rheum Dis. 2018 Dec;77(12):1705-1709.

Rosenbaum JT, Mount GR, Youssef J, et al. New Perspectives in Rheumatology: **Avoiding Antimalarial Toxicity**. Arthritis Rheumatol. 2016 Aug;68(8):1805-9.

Rossi-Semerano L, Piram M, Chiaverini C, et al. First Clinical Description of an Infant With Interleukin-36-Receptor Antagonist Deficiency Successfully Treated With **Anakinra**. Pediatrics. 2013 Sep 9.

Roubille C, Richer V, Starnino T, et al. The effects of **tumour necrosis factor inhibitors**, **methotrexate**, **non-steroidal anti-inflammatory drugs and corticosteroids on cardiovascular events** in rheumatoid arthritis, psoriasis and psoriatic arthritis: a systematic review and meta-analysis. Ann Rheum Dis. 2015 Mar;74(3):480-489.

Roubille C, Rincheval N, Dougados M, et al. **Seven year tolerability profile of glucocorticoids** use in early rheumatoid arthritis: data from the **ESPOIR** cohort. Ann Rheum Dis 2017:annrheumdis-2016-210135.

Rudwaleit M, van der Heijde D, et al. The development of **Assessment of SpondyloArthritis international Society** classifi cation criteria for axial spondyloarthritis (part II): validation and final selection. Ann Rheum Dis 2009; 68: 777–83.

Ruiz-Argüello MB, Maguregui A, Ruiz Del Agua A, et al. **Antibodies to infliximab** in Remicade-treated rheumatic patients show identical reactivity towards **biosimilars**. Ann Rheum Dis. 2016 Sep;75(9):1693-6

Ruperto N, Brunner HI, Quartier P, et al; Paediatric Rheumatology International Trials Organisation (PRINTO) and the Pediatric Rheumatology Collaborative Study Group (PRCSG). **Canakinumab in patients with systemic juvenile idiopathic arthritis and active systemic features**: results from the 5-year long-term extension of the phase III pivotal trials. Ann Rheum Dis. 2018 Dec;77(12):1710-1719.

Ruperto N, Murray KJ, Gerloni V, et al. A randomized trial of parenteral **methotrexate** comparing an intermediate dose with a higher dose in children with juvenile idiopathic arthritis who failed to respond to standard doses of methotrexate. Arthritis Rheum 2004; 50: 2191–201.

Ruperto N, Lovell DJ, Cuttica R, et al. A randomized, placebo-controlled trial of **infliximab plus methotrexate** for the treatment of polyarticular-course juvenile rheumatoid arthritis. Arthritis Rheum 2007; 56: 3096–106.

Ruperto N, Lovell DJ, Quartier P, et al. **Abatacept** in children with juvenile idiopathic arthritis: a randomised, double-blind, placebo-controlled withdrawal trial. Lancet 2008; 372: 383–91.

Ruperto N, Lovell DJ, et al. Long-term efficacy and safety of **infliximab plus methotrexate** for the treatment of polyarticular-course juvenile rheumatoid arthritis: fi ndings from an open-label treatment extension. Ann Rheum Dis 2010; 69: 718–22.

Ruperto N, Lovell DJ, Quartier P, et al. Long-term safety and efficacy of **abatacept** in children with juvenile idiopathic arthritis. Arthritis Rheum 2010; 62: 1792–802.

Ruperto N, Quartier P, Wulffraat N, et al. for the Paediatric Rheumatology International Clinical Trials Organisation (**PRINTO**). A phase II study to evaluate dosing and preliminary safety and efficacy of **canakinumab** in systemic juvenile idiopathic arthritis with active systemic features. Arthritis Rheum. 2011 Sep 27. doi: 10.1002/art.33342.

Ruperto N et al. Two randomized trials of **canakinumab** in systemic juvenile idiopathic arthritis. N Engl J Med 2012 Dec 20; 367:2396.

Russo PA, Wiese MD, Smith MD, et al. **Leflunomide** for inflammatory arthritis in end-stage renal disease on **peritoneal dialysis**: a pharmacokinetic and pharmacogenetic study. Ann Pharmacother. 2013 Mar;47(3):e15.

Rutherford AI, Subesinghe S, Hyrich KL, et al. Serious infection across biologic-treated patients with rheumatoid arthritis: results from the British Society for Rheumatology Biologics Register for Rheumatoid Arthritis. Ann Rheum Dis. 2018 Jun;77(6):905-910.

Ryu YS, Park SH, Kim JM, et al. A case of **leukoencephalopathy associated with adalimumab**-treated rheumatoid arthritis and a review of literature. Rheumatol Int. 2011 Nov 8.

Saad AA, Symmons DP, Noyce PR, et al. Risks and benefits of 12 tumor necrosis factor-alpha inhibitors in the management of **psoriatic arthritis**: systematic review and meta-analysis of randomized controlled trials. J Rheumatol 2008;35:883-90.

Saag KG, Teng GG, et al. American College of Rheumatology-**ACR 2008** recommendations for the use of **nonbiologic and biologic disease-modifying antirheumatic drugs** in rheumatoid arthritis. Arthritis Rheum 2008 Jun 15;59(6):762-84.

Sadr-Azodi O, Mattsson F, Bexlius TS, et al. Association of Oral **Glucocorticoid** Use With an Increased Risk of **Acute Pancreatitis**: A Population-Based Nested Case-Control Study. JAMA Intern Med. 2013 Feb 25:1-6.

Sadra V, Khabbazi A, Kolahi S, et al. Randomized double-blind study of the effect of **dexamethasone and methylprednisolone pulse** in the control of rheumatoid arthritis flare-up: a preliminary study. Int J Rheum Dis. 2014 Jan 9.

Saevarsdottir S, Rezaei H, Geborek P, et al; SWEFOT study group. **Current smoking status** is a strong predictor of radiographic progression in early rheumatoid arthritis: results from the SWEFOT trial. Ann Rheum Dis. 2015 Aug;74(8):1509-14.

Safiri S, Kolahi AA, Hoy D, et al. **Global, regional and national burden** of rheumatoid arthritis 1990-2017: a systematic analysis of the Global Burden of Disease study 2017. Ann Rheum Dis. 2019 Nov;78(11):1463-1471.

Safy M, Jacobs J, IJff ND, et al; Society for Rheumatology Research Utrecht (SRU).. Long-term outcome is better when a **methotrexate-based treatment strategy is combined with 10 mg prednisone** daily: follow-up after the second Computer-Assisted Management in Early Rheumatoid Arthritis trial. (Camera II) Ann Rheum Dis. 2017 Apr 27.

Safy M, Jacobs J, IJff ND, et al. Long-term outcome is better when a **methotrexate**-based treatment strategy is **combined with 10 mg prednisone daily**: follow-up after the second Computer-Assisted Management in Early Rheumatoid Arthritis trial. Ann Rheum Dis. 2017 Aug;76(8):1432-1435.

Sakai R, Tanaka M, Nanki T, et al; for the REAL Study Group. **Drug retention rates** and relevant risk factors for drug discontinuation due to adverse events in rheumatoid arthritis patients receiving **anticytokine therapy** with different target molecules. Ann Rheum Dis. 2012 Nov;71(11):1820-1826. Reasons for discontinuation are significantly different among biologics. Use of infliximab and tocilizumab was significantly associated with treatment discontinuation due to AE compared with etanercept.

Salgado E, Maneiro JR, Carmona L, et al. Safety profile of **protein kinase inhibitors** in rheumatoid arthritis: systematic review and meta-analysis. Ann Rheum Dis. 2014 May 1;73(5):871-82.

Salliot C, van der Heijde D. **Long-term safety of methotrexate** monotherapy in patients with rheumatoid arthritis: a systematic literature research. Ann Rheum Dis. 2009 Jul;68(7):1100-4. Epub 2008 Dec 5.

Salmon-Ceron D, Tubach F, Lortholary O, for RATIO group. Drug-specific risk of non-tuberculosis **opportunistic infections** in patients receiving anti-TNF therapy reported to the 3-year prospective French RATIO registry. Ann Rheum Dis. 2010 Dec 21. Various and severe OIs, especially those with intracellular micro-organisms, may develop in patients receiving anti-TNF treatment. Monoclonal anti-TNF antibody rather than soluble TNF receptor therapy and steroid use >10 mg/day are independently associated with OI.

Salmon JH, Gottenberg JE, Ravaud P, et al; all the investigators of the ORA registry and the French Society of Rheumatology. Predictive risk factors of **serious infections** in patients with rheumatoid arthritis treated with **abatacept** in common practice: results from the Orencia and Rheumatoid Arthritis (ORA) registry. Ann Rheum Dis. 2016 Jun;75(6):1108-13.

Salt E, Wiggins AT, Rayens MK, et al. Risk Factors for Targeted **Fungal and Mycobacterial Infections in Patients Taking TNF-alpha Inhibitors**. Arthritis Rheumatol. 2015 Oct 16.

Sandberg ME, Wedrén S, Klareskog L, et al. Patients with **regular physical activity** before onset of rheumatoid arthritis present with milder disease. Ann Rheum Dis. 2014 Aug;73(8):1541-4.

Sandberg ME, Bengtsson C, Källberg H, et al. **Overweight** decreases the chance of achieving good response and low disease activity in early rheumatoid arthritis. Ann Rheum Dis. 2014 Nov;73(11):2029-33.

Sandberg ME, Bengtsson C, Klareskog L, et al. **Recent infections are associated with decreased risk of rheumatoid arthritis**: a population-based case-control study. Ann Rheum Dis. 2015 Feb 5. pii: annrheumdis-2014-206493.

Sandborn WJ, Su C, Sands BE, et al. **Tofacitinib** as induction and maintenance therapy for ulcerative colitis. (Octave Sustain) N Engl J Med 2017; 376: 1723-36.

Sarnes E, Crofford L, Watson M, et al. Incidence and US Costs of **Corticosteroid-Associated Adverse Events**: A Systematic Literature Review. Clin Ther. 2011 Oct 12.

Sauer BC, Teng CC, et al. **Persistence With Conventional Triple Therapy Versus a Tumor Necrosis Factor Inhibitor and Methotrexate in US Veterans** With Rheumatoid Arthritis. Arthritis Care Res (Hoboken). 2017 Mar;69(3):313-322.

Savage RL. **Leflunomide in combination** therapy for rheumatoid arthritis. Drug Saf. 2010 Jun 1;33(6):523-6.

Schanz S, Schmalzing M, Guenova E, et al. **Interstitial granulomatous dermatitis** with arthritis responding to **tocilizumab**. Arch Dermatol. 2012 Jan;148(1):17-20

Schenfeld J, Iles J, Trivedi M, et al. **Dose relationship between oral glucocorticoids and tumor necrosis factor inhibitors and the risk of hospitalized infectious events** among patients with rheumatoid arthritis. Rheumatol Int. 2017 Mar 2.

Schett G, Emery P, Tanaka Y, et al. **Tapering biologic and conventional DMARD** therapy in rheumatoid arthritis: current evidence and future directions. Ann Rheum Dis. 2016 Aug;75(8):1428-37.

Scheuern A, Tyrrell PN, Haas JP, Hügle B. Countermeasures against **methotrexate intolerance** in juvenile idiopathic arthritis instituted by parents show no effect. Rheumatology (Oxford). 2017 Jan 24.

Schieir O, Tosevski C, Glazier RH, et al. **Incident myocardial infarction** associated with major types of arthritis in the general population: a systematic review and meta-analysis. Ann Rheum Dis. 2017 Aug;76(8):1396-1404

Schiff MH, et al. Safety Analyses of **Adalimumab** (HUMIRA(R)) in Global Clinical Trials and US Postmarketing Surveillance of Patients With Rheumatoid Arthritis. Ann Rheum Dis. 2006 Feb 13; [Epub ahead of print]

Schiff M, Keiserman M, Codding C, et al. Efficacy and safety of **abatacept or infliximab** vs placebo in ATTEST: a phase III, multi-centre, randomised, double-blind, placebo-controlled study in patients with rheumatoid arthritis and an inadequate response to methotrexate. Ann Rheum Dis. 2008;67:1096-1103.

Schiff M, Pritchard C, Huffstutter JE, et al. The 6-month safety and efficacy of **abatacept** in patients with rheumatoid arthritis who underwent a washout after anti-tumour necrosis factor therapy or were directly switched to abatacept: the ARRIVE trial. Ann Rheum Dis. 2009 Nov;68(11):1708-14. Epub 2008 Dec 15.

Schiff M. **Abatacept** treatment for rheumatoid arthritis. Rheumatology (Oxford). 2011 Mar;50(3):437-49.

Schiff M, Keiserman M, et al. Clinical response & tolerability to **abatacept** in patients with rheumatoid arthritis previously treated with infliximab or abatacept: open-label extension of the **ATTEST** Study. Ann Rheum Dis. 2011 Nov;70(11):2003-7.

Schiff M, Weinblatt ME, Valente R, et al. Head-to-head comparison of **subcutaneous abatacept versus adalimumab** for rheumatoid arthritis: two-year efficacy and safety findings from AMPLE trial. Ann Rheum Dis. 2014 Jan 1;73(1):86-94

Schiff MH, Jaffe JS, Freundlich B. Head-to-head, randomised, crossover study of **oral versus subcutaneous methotrexate** in patients with rheumatoid arthritis: drug-exposure limitations of oral methotrexate at doses ≥15 mg may be overcome with subcutaneous administration. Ann Rheum Dis. 2014 Aug;73(8):1549-51.

Schiff MH, von Kempis J, Goldblum R, et al. Rheumatoid arthritis secondary non-responders to TNF can attain an efficacious and safe response by switching to **certolizumab** pegol: a phase IV, randomised, multicentre, double-blind, 12-week study, followed by a 12-week open-label phase. Ann Rheum Dis. 2014 Dec;73(12):2174-7.

Schipper LG, Vermeer M, Kuper HH, et al. A **tight control** treatment strategy aiming for remission in early rheumatoid arthritis is more effective than usual care treatment in daily clinical practice: a study of two cohorts in the Dutch Rheumatoid Arthritis Monitoring registry. Ann Rheum Dis. 2012 Jun;71(6):845-50.

Schmajuk G, Trivedi AN., Solomon DH., et al. Receipt of **Disease-Modifying Antirheumatic Drugs** Among Patients With Rheumatoid Arthritis in **Medicare Managed** Care Plans. *JAMA.* 2011;305(5):480-486.doi:10.1001/jama.2011.67

Schmeling H, Minden K, Foeldvari I, et al. Efficacy and safety of **Adalimumab** as first and second used biologic agent in **juvenile idiopathic arthritis** - the German Biologics JIA Registry (BiKeR). Arthritis Rheumatol. 2014 Jun 18.

Schmitz S, Adams R, Walsh CD, et al. A **mixed treatment comparison of the efficacy of anti-TNF agents** in rheumatoid arthritis for methotrexate non-responders demonstrates differences between treatments: a Bayesian approach. Ann Rheum Dis. 2012 Feb;71(2):225-30.

Schneeweiss MC, Perez-Chada L, Merola JF. Comparative Safety of **Systemic Immuno-modulatory Medications** in Adults with Atopic Dermatitis. J Am Acad Dermatol. 2019 May 31.

Schoels M, Wong J, Scott DL, et al. **Economic aspects of treatment options in rheumatoid arthritis**: a systematic literature review informing the EULAR recommendations for the management of rheumatoid arthritis. Ann Rheum Dis. 2010 Jun;69(6):995-1003.

Schoels M, Aletaha D, Smolen JS, Wong JB. Comparative effectiveness and safety of **biological treatment options after tumour necrosis factor α inhibitor failure** in rheumatoid arthritis: systematic review and indirect pairwise meta-analysis. Ann Rheum Dis. 2012 Jan 30.

Schoels MM, van der Heijde D, Breedveld FC, et al. Blocking the effects of interleukin-6 (**tocilizumab**) in rheumatoid arthritis and other inflammatory rheumatic diseases: systematic literature review and meta-analysis informing a consensus statement. Ann Rheum Dis. 2013 Apr;72(4):583-9.

Schreiber K, Davies N, Hunt BJ. Using **hydroxychloroquine and protecting the retina**. Lupus. 2018 Jan 1:961203318777113.

Schulman E, et al. **Overweight and Obesity Reduce the Likelihood of Achieving Sustained Remission in Early Rheumatoid Arthritis**: Results from the Canadian Early Arthritis Cohort Study. Arthritis Care Res (Hoboken). 2017 Nov 30.

Schumacher HR, Chen LX. **Injectable corticosteroids** in treatment of arthritis of the knee. Am J Med. 2005 Nov;118(11):1208-14.

Schuna AA. **Rituximab** for the treatment of rheumatoid arthritis. Pharmacotherapy. 2007 Dec;27(12):1702-10.

Scirè CA, Lunt M, Marshall T, et al. **Early remission is associated with improved survival** in patients with inflammatory polyarthritis: results from the Norfolk Arthritis Register. Ann Rheum Disease. Online First: 7 June 2013.

Scott DL, et al. European Leflunomide Study Group. Treatment of active rheumatoid arthritis with **leflunomide**: two year follow up of a double blind, placebo controlled trial **versus sulfasalazine**. Ann Rheum Dis. 2001 Oct;60(10):913-23.

Scott DL, Wolfe F, Huizinga TW. **Rheumatoid arthritis**. Lancet. 2010 Sep 25;376(9746):1094-108.

Scott DL, Kingsley GH. **Tumor necrosis factor inhibitors** for rheumatoid arthritis. N Engl J Med. 2006 Aug 17;355(7):704-12.

Scott DL, Ibrahim F, Farewell V, et al. **Tumour necrosis factor inhibitors versus combination intensive therapy** with conventional disease modifying anti-rheumatic drugs in established rheumatoid arthritis: **TACIT** non-inferiority randomised controlled trial. BMJ. 2015 Mar 13;350:h1046.

Selvaag AM, Aulie HA, Lilleby V, Flatø B. Disease **progression into adulthood** and predictors of long-term active disease in **juvenile idiopathic arthritis**. Ann Rheum Dis. 2016 Jan;75(1):190-5.

Semb AG, Kvien TK, Demicco D, et al. Effect of **intensive lipid lowering** on cardiovascular outcome in patients with and without inflammatory joint disease. Arthritis Rheum. 2012 May 10.

Sengler C, Zink J, Klotsche J, et al. **Vitamin D deficiency** is associated with higher disease activity and the risk for uveitis in juvenile idiopathic arthritis - data from a German inception cohort. Arthritis Res Ther. 2018 Dec 13;20(1):276.

Seror R, Baron G, Hachulla E, et al. **Adalimumab** for steroid sparing in patients with giant-cell arteritis: results of a multicentre randomized controlled trial. Ann Rheum Dis. 2014 Dec;73(12):2074-81.

Setoguchi S, et al. **Tumor necrosis factor** alpha antagonist use and **cancer** in patients with rheumatoid arthritis. Arthritis Rheum. 2006 Sep;54(9):2757-64. Comparing biologic DMARD users with MTX users, the propensity score-adjusted pooled hazard ratio was 1.37 (95% confidence interval 0.71-2.65) for hematologic malignancies and 0.91 (95% confidence interval 0.65-1.26) for solid tumors. Our results indicate that users of biologic agents are unlikely to have a substantial increase in the risk of hematologic malignancies and solid tumors as compared with MTX users.

Sfikakis PP, Arida A, Panopoulos S, et al. Drug-free long-term remission in severe **Behcet's disease following withdrawal of successful anti-TNF treatment**. Arthritis Rheumatol. 2017 Aug 22.

Sieper J, Porter-Brown B, Thompson L, et al. Assessment of short-term symptomatic efficacy of **tocilizumab in ankylosing spondylitis**: results of randomised, placebo-controlled trials. Ann Rheum Dis. 2014 Jan 1;73(1):95-100

Sieper J, Landewé R, Rudwaleit M, van der Heijde D, et al. Effect of **Certolizumab Pegol** over 96 Weeks in Patients with **Axial Spondyloarthritis**: Results from a Phase 3 Randomized Trial. Arthritis Rheumatol. 2014 Dec 2.

Shalom G, Zisman D, Bitterman H, et al. Systemic (**biologic medications**) Therapy for Psoriasis and the Risk of **Herpes Zoster**: A 500 000 Person-year Study. JAMA Dermatol. 2015 Mar 22:1-7.

Shea B, Swinden MV, Ghogomu ET, et al. **Folic Acid and Folinic Acid** for Reducing Side Effects in Patients Receiving **Methotrexate** for Rheumatoid Arthritis. J Rheumatol. 2014 Jun;41(6):1049-1060.

Shi J, van de Stadt LA, Levarht EW, et al. **Anti-carbamylated protein (anti-CarP) antibodies** precede the onset of rheumatoid arthritis. Ann Rheum Dis. 2013 Dec 13.

Shigaki CL, Smarr KL, Siva C, et al. **RAHelp: an online** intervention for individuals with rheumatoid arthritis. Arthritis Care Res (Hoboken). 2013 Oct;65(10):1573-81.

Shin A, Shin S, Kim JH, et al. Association between **socioeconomic status and comorbidities** among patients with rheumatoid arthritis: results of a nationwide cross-sectional survey. Rheumatology (Oxford). 2019 Sep 1;58(9):1617-1622.

Shukla S, Gultekin SH, Saporta M. Pearls & Oy-sters: **Hydroxychloroquine-induced toxic myopathy mimics Pompe disease**: Critical role of genetic test. Neurology. 2019 Feb 12;92(7):e742-e745.

Sibley CH, Chioato A, Felix S, et al. A 24-month open-label study of **canakinumab** in neonatal-onset multisysteminflammatory disease. Ann Rheum Dis. 2015 Sep;74(9):1714-9.

Sieper J, van der Heijde D, Dougados M, et al. Efficacy and safety of **adalimumab** in patients with non-radiographic axial spondyloarthritis: results of a randomised placebo-controlled trial (ABILITY-1). Ann Rheum Dis. 2012 Jul 7

Sieper J, Poddubnyy D. **Axial spondyloarthritis**. Lancet. 2017 Jan 19.

Sieper J, Deodhar A, Marzo-Ortega H, et al. **Secukinumab** efficacy in anti-TNF-naive and anti-TNF-experienced subjects with active ankylosing spondylitis: results from the MEASURE 2 Study. Ann Rheum Dis. 2017 Mar;76(3):571-592

Silva F, Seo P, Schroeder DR, et al; for the **Wegener's Granulomatosis Etanercept Trial Research Group. Solid malignancies** among patients with Wegener's granulomatosis treated with etanercept: Long-term follow-up of a multicenter longitudinal cohort. Arthritis Rheum. 2011 Apr 11.

Silva-Fernández L, Lunt M, Kearsley-Fleet L, et al. British Society for Rheumatology Biologics Register (BSRBR) Control Centre Consortium. The incidence of cancer in patients with rheumatoid arthritis and a prior malignancy who receive TNF inhibitors or rituximab: results from the British Society for Rheumatology Biologics Register-Rheumatoid Arthritis. Rheumatology (Oxford). 2016 Aug 22.

Silva-Fernandez L, et al. The incidence of cancer in patients with rheumatoid arthritis and a **prior malignancy** who receive **TNF inhibitors or rituximab**: results from the British Society for Rheumatology Biologics Register-Rheumatoid Arthritis. Rheumatology. 2016 Aug 22.

Silva-Fernandez L;De Cock D;Lunt M;Low AS;Watson K **Serious infection risk after 1 year between patients with rheumatoid arthritis treated with rituximab or with a second TNFi after initial TNFi failure**: results from The British Society for Rheumatology Biologics Register for Rheumatoid Arthritis. Rheumatology (Oxford). 2017 Aug 16.

Silverman E. et al. **Leflunomide or Methotrexate** for **Juvenile Rheumatoid Arthritis**. N Engl J Med 2005;352:1655-66.

Silverman E, Spiegel L, Hawkins D, et al. Long-term open-label preliminary study of the safety and efficacy of **leflunomide** in patients with polyarticular-course juvenile rheumatoid arthritis. Arthritis Rheum 2005; 52: 554–62.

Simard JF, Neovius M, Hagelberg S, Askling J. **Juvenile idiopathic arthritis and risk of cancer**: a nationwide cohort study. Arthritis Rheum 2010; 62: 3776–82.

Simard JF, Neovius M, Askling J; for the ARTIS study group. **Mortality** in patients with rheumatoid arthritis treated with **TNF inhibitors**: drug-specific comparisons in the swedish biologics register. Arthritis Rheum. 2012 Aug 8.

Simsek I, Erdem H, Pay S, Sobaci G, Dinc A. **Optic neuritis occurring with anti-tumour necrosis factor alpha** therapy.Ann Rheum Dis. 2007 Sep;66(9):1255-8. Epub 2007 Apr 24.

Singh JA. **Tapering Janus kinase inhibitors** in rheumatoid arthritis with low disease activity or remission: reality or dream? Ann Rheum Dis. 2019 Feb;78(2):153-154.

Singh JA, Christensen R, Wells GA, et al. **Biologics for rheumatoid arthritis**: an overview of Cochrane reviews. Cochrane Database Syst Rev. 2009 Oct 7;(4):CD007848.

Singh, Jasvinder A, Christensen, Robin, Wells, George A, et al. A network meta-analysis of randomized controlled trials of **biologics for rheumatoid arthritis**: a Cochrane overview. CMAJ 2009 0: cmaj.091391.

Singh JA, Noorbaloochi S, Singh G. **Golimumab** for rheumatoid arthritis. Cochrane Database Syst Rev. 2010 Jan 20;(1):CD008341.

Singh JA, Beg S, Lopez-Olivo MA. **Tocilizumab** for rheumatoid arthritis. Cochrane Database Syst Rev. 2010 Jul 7;7:CD008331. Tocilizumab is beneficial in decreasing RA disease activity and improving function. Tocilizumab treatment was associated with significant increase in cholesterol levels and in total adverse events. Larger safety studies are needed to address these safety concerns.

Singh JA, Wells GA, Christensen R, et al. **Adverse effects of biologics**: a network meta-analysis and Cochrane overview. Cochrane Database of Systematic Reviews 2011, Issue 2. Art. No.: CD008794. DOI: 10.1002/14651858.CD008794.pub2. Overall, in the short term biologics were associated with significantly higher rates of total adverse events, withdrawals due to adverse events and TB reactivation. Some biologics had a statistically higher association with certain adverse outcomes compared to control, but there was no consistency across the outcomes so caution is needed in interpreting these results.

Singh JA, Furst DE, Bharat A, et al. **2012 update** of the 2008 American College of Rheumatology recommendations for the use of **disease-modifying antirheumatic drugs and biologic agents** in the treatment of rheumatoid arthritis. Arthritis Care Res (Hoboken). 2012 May;64(5):625-39.

Singh JA. **Use of biologics** in a patient with rheumatoid arthritis **refractory to methotrexate**. CMAJ. 2013 Jun 11;185(9):793-5.

Singh JA, Cameron C, Noorbaloochi S, et al. **Risk of serious infection in biological treatment** of patients with rheumatoid arthritis: a systematic review and meta-analysis. Lancet. 2015 May 11.

Singh JA, Saag KG, Bridges SL Jr, et al. **2015 American College of Rheumatology Guideline for the Treatment of Rheumatoid Arthritis**. Arthritis Rheumatol. 2015 Nov 6.

Singh JA, Hossain A, Tanjong Ghogomu E, et al. **Biologics or tofacitinib** for rheumatoid arthritis in **incomplete responders to methotrexate or other traditional** disease-modifying anti-rheumatic drugs: a systematic review and network meta-analysis. Cochrane Database of Systematic Reviews 2016, Issue 5. Art. No.: CD012183. Based primarily on RCTs of 6 months' to 12 months' duration, there is moderate quality evidence that the use of biologic+MTX/ DMARD in people with rheumatoid arthritis who have failed to respond to MTX or other DMARDs results in clinically important improvement in function and higher ACR50 and remission rates, and increased risk of serious adverse events than the comparator (MTX/DMARD/PL; high quality evidence). Radiographic progression is slowed but its clinical relevance is uncertain. Results were inconclusive for whether biologics + MTX/DMARDs are associated with an increased risk of cancer or withdrawals due to adverse events.

Singh JA, Hossain A, Tanjong Ghogomu E, et al. **Biologic or tofacitinib monotherapy** for rheumatoid arthritis in people with **traditional disease-modifying anti-rheumatic drug (DMARD) failure**: a Cochrane Systematic Review and network meta-analysis (NMA). Cochrane Database of Systematic Reviews 2016, Issue 11. Art. No.: CD012437. Based mostly on RCTs of six to 12-month duration in people with RA who had previously experienced and failed treatment with MTX/other DMARDs, biologic monotherapy improved ACR50, function and RA remission rates compared to placebo or MTX/ other DMARDs. Radiographic progression was reduced versus active comparator, although the clinical significance was unclear. Results were inconclusive for whether biologic monotherapy was associated with an increased risk of withdrawals due to adverse events, serious adverse events or cancer, versus placebo (no data on cancer) or MTX/other DMARDs.

Singh JA, Hossain A, Tanjong Ghogomu E, et al. **Biologics or tofacitinib** for people with rheumatoid arthritis **unsuccessfully treated with biologics**: a systematic review and network meta-analysis. Cochrane Database Syst Rev. 2017 Mar 10;3:CD012591. Biologic (with or without MTX) or tofacitinib (with MTX) use was associated with clinically meaningful and statistically significant benefits (ACR50, HAQ, remission) compared to placebo or an active comparator (MTX/other traditional DMARDs) among people with RA previously unsuccessfully treated with biologics.No studies examined radiographic progression. Results were not clinically meaningful or statistically significant for withdrawals due to adverse events and serious adverse events, and were inconclusive for cancer.

Smolen JS, et al. Patient-reported outcomes from a randomised phase III study of **baricitinib** in patients with rheumatoid arthritis and an inadequate response to biological agents (RA-BEACON). Ann Rheum Dis. 2016 Apr;76(4):694-700.

Smolen JS, Agarwal SK, Ilivanova E, et al. A randomised phase II study evaluating the efficacy and safety of **subcutaneously administered ustekinumab and guselkumab** in patients with active rheumatoid arthritis despite treatment with methotrexate. Ann Rheum Dis. 2017 May;76(5):831-839

Smolen JS, Breedveld FC, Burmester GR, et al. **Treating rheumatoid arthritis to target: 2014 update** of the recommendations of an **international task force**. Ann Rheum Dis. 2016 Jan;75(1):3-15.

Smolen JS, Burmester GR, Combe B, et al. Head-to-head comparison of **certolizumab pegol versus adalimumab** in rheumatoid arthritis: 2-year efficacy and safety results from the randomised **EXXELERATE** study. Lancet. 2016 Nov 11.

Smolen JS, Choe JY, Prodanovic N, et al. Safety, immunogenicity and efficacy after switching from reference **infliximab to biosimilar SB2** compared with continuing reference infliximab and SB2 in patients with rheumatoid arthritis: results of a randomised, double-blind, phase III transition study. Ann Rheum Dis. 2018 Feb;77(2):234-240.

Smolen JS, Cohen SB, Tony HP, et al. A randomised, double-blind trial to demonstrate bioequivalence of **GP2013** and reference **rituximab** combined with **methotrexate** in patients with active rheumatoid arthritis. Ann Rheum Dis. 2017 Jun 21.

Smolen JS, Emery P, Fleischmann R, et al. Adjustment of therapy in rheumatoid arthritis on the basis of achievement of stable low disease activity with **adalimumab plus methotrexate or methotrexate** alone: the randomised controlled **OPTIMA** trial. Lancet 2013; online Oct 26.

Smolen JS, Emery P, Keystone EC, et al. Consensus Statement on the Use of **Rituximab** in Patients With Rheumatoid Arthritis. Ann Rheum Dis. 2006 Nov 15; [Epub ahead of print]

Smolen JS, Kalden JR, Scott DL, et al.. Efficacy and safety of **leflunomide** compared with placebo and **sulphasalazine** in active rheumatoid arthritis: a double-blind, randomised, multicentre trial. European Leflunomide Study Group. Lancet. 1999 Jan 23;353(9149):259-66.

Smolen JS, Kay J, Doyle MK, et al. GO-AFTER study investigators. **Golimumab** in patients with active rheumatoid arthritis after treatment with tumour necrosis factor alpha inhibitors (**GO-AFTER** study): a multicentre, randomised, double-blind,

placebo-controlled, phase III trial. Lancet. 2009 Jul 18;374(9685):210-21. Epub 2009 Jun 26.
Smolen JS, Kay J, Landewé RB, et al. **Golimumab** in patients with active rheumatoid arthritis who have previous experience with tumour necrosis factor inhibitors: results of a long-term extension of the randomised, double-blind, placebo-controlled GO-AFTER study through week 160. Ann Rheum Dis. 2012 Oct;71(10):1671-9.
Smolen JS, Kay J, Matteson EL, et al. Insights into the efficacy of **golimumab plus methotrexate** in patients with active rheumatoid arthritis who discontinued prior anti-tumour necrosis factor therapy: post-hoc analyses from the GO-AFTER study. Ann Rheum Dis. 2014 Oct;73(10):1811-8.
Smolen JS, Landewe R, Bijlsma J, et al. **EULAR** recommendations for the management of **rheumatoid arthritis with synthetic and biological disease-modifying antirheumatic drugs**: 2016 update. Ann Rheum Dis. 2017 Mar 6.
Smolen JS, Landewé R, Breedveld FC, et al. **EULAR** recommendations for the management of rheumatoid arthritis with **synthetic and biological disease-modifying antirheumatic drugs**. Ann Rheum Dis. 2010 May 5. [Epub ahead of print]
Smolen JS, Landewé R, Breedveld FC, et al. **EULAR** recommendations for the management of rheumatoid arthritis with **synthetic and biological disease-modifying antirheumatic drugs**: 2013 update. Ann Rheum Dis. 2014 Mar 1;73(3):492-509.
Smolen JS, Nash P, Durez P, et al. **Maintenance, reduction, or withdrawal of etanercept** after treatment with etanercept and methotrexate in patients with moderate rheumatoid arthritis (**PRESERVE**): a randomised controlled trial. Lancet 2013; online Jan 17.
Smolen JS, Pangan AL, Emery P, et al. **Upadacitinib as monotherapy** in patients with active rheumatoid arthritis and inadequate response to methotrexate (SELECT-MONOTHERAPY): a randomised, placebo-controlled, double-blind phase 3 study. Lancet. 2019 May 23.
Smolen JS, Schoels MM, Nishimoto N, et al. Consensus statement on blocking the effects of **interleukin-6** and in particular by interleukin-6 receptor inhibition (**tocilizumab**) in rheumatoid arthritis and other inflammatory conditions. Ann Rheum Dis. 2013 Apr;72(4):482-92.
Smolen JS, van der Heijde D, Machold KP, et al. Proposal for a **new nomenclature of disease-modifying antirheumatic drugs**. Ann Rheum Dis. 2014 Jan 1;73(1):3-5
Snijders GF, van den Ende CH, van Riel PL, et al. on behalf of NOAC study group. The effects of **doxycycline** on reducing symptoms in knee osteoarthritis: results from a triple-blinded randomised controlled trial. Ann Rheum Dis. 2011 Jul;70(7):1191-1196.
Smolen JS, van Vollenhoven RF, Florentinus S, et al. Predictors of disease activity and structural progression after treatment with **adalimumab plus methotrexate** or continued methotrexate monotherapy in patients with early rheumatoid arthritis and suboptimal response to methotrexate. Ann Rheum Dis. 2018 Nov;77(11):1566-1572.
Soliman Moetaza M, Ashcroft Darren M, Watson Kath D, et al. , on behalf of the British Society for Rheumatology Biologics Register. Impact of **concomitant use of DMARDs on the persistence with anti-TNF therapies** in patients with rheumatoid arthritis: results from the British Society for Rheumatology Biologics Register. Ann Rheum Dis 2011;70:583-589
Solomon DH, Avorn J, Katz JN, et al. **Immunosuppressive medications** and hospitalization for **cardiovascular events** in patients with rheumatoid arthritis. Arthritis Rheum. 2006 Nov 29;54(12):3790-3798. Monotherapy with oral glucocorticoids was associated with an increased risk of cardiovascular events (OR 1.5, 95% CI 1.1 - 2.1), and a similar trend in the direction of risk was seen with glucocorticoid combination therapy (OR 1.3, 95% CI 0.8-2.0). Cytotoxic immunosuppressive agents other than MTX (azathioprine, cyclosporine, and leflunomide) were also associated with an increased risk of cardiovascular events (with both monotherapy and combination treatment, OR 1.8, 95% CI 1.1-3.0). When compared with RA patients receiving MTX monotherapy, those receiving biologic immunosuppressive agents had neither an increased nor decreased risk of experiencing a cardiovascular event, whereas use of oral glucocorticoids and cytotoxic immunosuppressive agents was associated with significant increases in the risk of cardiovascular events.
Solomon Daniel H., Massarotti Elena, Garg Rajesh, et al. Association Between **Disease-Modifying Antirheumatic Drugs and Diabetes Risk** in Patients With Rheumatoid Arthritis and Psoriasis. JAMA. 2011;305(24):2525-2531.
Solomon DH, Mercer E, Kavanaugh A. Observational studies on the risk of **cancer associated with TNF-Inhibitors** in RA: A review of their methodologies and results. Arthritis Rheum. 2011 Aug 26. doi: 10.1002/art.30653.
Solomon DH, Rassen JA, Kuriya B, et al. **Heart failure** risk among patients with rheumatoid arthritis starting a **TNF antagonist**. Ann Rheum Dis. 2013 Nov 1;72(11):1813-1818.
Solomon DH, Bitton A, Katz JN, et al. **Treat to target in rheumatoid arthritis**: Fact, fiction or hypothesis? Arthritis Rheum. 2013 Dec 24.
Solomon DH, Kremer JM, Fisher M, et al. Comparative **cancer risk associated with methotrexate**, other non-biologic and biologic disease-modifying anti-rheumatic drugs. Semin Arthritis Rheum. 2014 Feb;43(4):489-97.
Solomon DH, Greenberg J, Curtis JR, et al. Derivation and internal validation of an expanded **cardiovascular risk prediction score for rheumatoid arthritis**: a Consortium of Rheumatology Researchers of North America Registry Study. Arthritis Rheumatol. 2015 May;67(8):1995-2003.
Solomon DH, Husni ME, Wolski KE, et al. Differences in Safety of **Non-Steroidal Anti-Inflammatory Drugs** in Patients with Osteoarthritis and Rheumatoid Arthritis: A Randomized Clinical Trial. Arthritis Rheumatol. 2017 Dec 20.
Smith RJ, Boos MD, Burnham JM, et al. Atypical Cutaneous **Blastomycosis** in a Child With Juvenile Idiopathic Arthritis on **Infliximab**. Pediatrics. 2015 Nov;136(5):e1386-9.
Smolen JS, Emery P, Ferraccioli GF, et al. **Certolizumab** pegol in rheumatoid arthritis patients with low to moderate activity: the **CERTAIN** double-blind, randomised, placebo-controlled trial. Ann Rheum Dis. 2014 Jan 15.
Smolen JS, Aletaha D, McInnes IB. **Rheumatoid arthritis**. Lancet. 2016 May 3. pii: S0140-6736(16)30173-8.
Sokolove J, Schiff M, Fleischmann R, et al. Impact of baseline **anti-cyclic citrullinated peptide-2 antibody concentration** on efficacy outcomes following treatment with subcutaneous abatacept or adalimumab: 2-year results from the AMPLE trial. Ann Rheum Dis. 2016 Apr;75(4):709-14.
Solomon DH, Reed G, Kremer JM, et al. Disease activity in rheumatoid arthritis and the **risk of cardiovascular events**. Arthritis Rheumatol. 2015 Mar 16.
Solomon DH, Kay J, Duryea J, et al. Effects of **Teriparatide on Joint Erosions** in Rheumatoid Arthritis: A Randomized Controlled Trial. Arthritis Rheumatol. 2017 May 23.
Solomon DH, Losina E, Lu B, et al. Implementation of **Treat to Target** in Rheumatoid Arthritis through a Learning Collaborative: Results of the **TRACTION** Randomized Controlled Trial. Arthritis Rheumatol. 2017 May 17.
Song I-H, Hermann KG, Haibel H, et al. Effects of **etanercept versus sulfasalazine** in early axial **spondyloarthritis** on active inflammatory lesions as detected by whole-body MRI (ESTHER): a 48-week randomised controlled trial. Ann Rheum Dis 2011;**70**:590-596 doi:10.1136/ard.2010.139667
Song IH, Althoff CE, Haibel H, et al. Frequency and duration of drug-free remission after 1 year of treatment with **etanercept versus sulfasalazine** in early **axial spondyloarthritis**: 2 year data of the ESTHER trial. Ann Rheum Dis. 2012 Mar 22.
Souto A, Salgado E, et al. **Lipid profile changes** in patients with chronic inflammatory arthritis treated with **biologics and tofacitinib** in randomized clinical trials: A systematic review and meta-analysis. Arthritis Rheumatol. 2014 Oct 9.
Sparks JA.**In the Clinic: Rheumatoid Arthritis**. Ann Intern Med. 2019 Jan 1;170(1):ITC1-ITC16.
Sparks JA, Chang SC, Liao KP, et al. **Rheumatoid arthritis and mortality** among women during 36 years of prospective follow-up: Results from the **Nurses' Health Study**. Arthritis Care Res (Hoboken). 2015 Oct 16.
Sparks JA, Krumme AA, Shrank WH, et al. **Intensification to triple therapy non-biologic disease**-modifying antirheumatic drugs for rheumatoid arthritis in the United States from 2009 to 2014. Arthritis Rheumatol. 2016 Feb 11.
Sparks JA, Chang SC, Nguyen US, et al. **Weight change** in the early rheumatoid arthritis period and risk for subsequent **mortality** among women with RA and matched comparators. Arthritis Rheumatol. 2017 Nov 30.
Sterry W, Ortonne JP, Kikham B, Brocq O, Robertson D, Pederson RD, et al. 1 Comparison of two **etanercept** regimens for treatment of psoriasis and **psoriatic arthritis**: **PRESTA** randomised double blind multicentre trial. BMJ 2010;340:c147.
St Clair EW, van der Heijde DM, Smolen JS, et al.; Active-Controlled Study of Patients Receiving Infliximab for the Treatment of Rheumatoid Arthritis of **Early Onset** Study Group. Combination of **infliximab and methotrexate** therapy for early rheumatoid arthritis: a randomized, controlled trial. Arthritis Rheum. 2004 Nov;50(11):3432-43.
Stohl W, Gomez-Reino J, Olech E, et al. Safety and efficacy of **ocrelizumab** in combination with methotrexate in MTX-naive subjects with rheumatoid arthritis: the phase III FILM trial. Ann Rheum Dis. 2012 Feb 2.
Strand V, Cohen S, et al. Treatment of active rheumatoid arthritis with **leflunomide** compared with placebo and **methotrexate**. Leflunomide Rheumatoid Arthritis Investigators Group. Arch Intern Med. 1999 Nov 22;159(21):2542-50.
Strand V, Smolen JS, van Vollenhoven RF, et al. **Certolizumab pegol plus methotrexate** provides broad relief from the burden of rheumatoid arthritis: analysis of patient-reported outcomes from the RAPID 2 trial. Ann Rheum Dis. 2011 Mar 17.
Strangfeld A, Listing J, Herzer P, Liebhaber A, Rockwitz K, Richter C, Zink A. Risk of **herpes zoster** in patients with rheumatoid arthritis treated with anti-TNF-alpha agents. JAMA. 2009 Feb 18;301(7):737-44. Treatment with monoclonal anti-**TNF-alpha antibodies** may be associated with increased risk of herpes zoster, but this requires further study.
Strangfeld A, Eveslage M, et al. Treatment **benefit or survival** of the fittest: what drives the time-dependent decrease in serious infection rates under TNF inhibition and what does this imply for the individual patient? Ann Rheum Dis. 2011 Nov;70(11):1914-20.
Strangfeld A, Richter A, Siegmund B, et al. Risk for lower intestinal perforations in patients with rheumatoid arthritis treated with **tocilizumab** in comparison to treatment with other biologic or conventional synthetic DMARDs. Ann Rheum Dis. 2017 Mar;76(3):504-510.
Stoffer MA, Schoels MM, Smolen JS, et al. **Evidence for treating rheumatoid arthritis to target**: results of a systematic literature search update. Ann Rheum Dis. 2016 Jan;75(1):16-22.
Stone JH et al. Trial of **tocilizumab** in **giant-cell arteritis**. N Engl J Med 2017 Jul 27; 377:317.
Strehl C, et al. **Defining conditions where long-term glucocorticoid treatment has an acceptably low level of harm** to facilitate implementation of existing recommendations: viewpoints from EULAR task force. Ann Rheum Dis 2016;75:952–7.
Summers KM, Kockler DR. **Rituximab** Treatment of Refractory Rheumatoid Arthritis (December). Ann Pharmacother. 2005 Oct 25; [Epub ahead of print]
Suter Lisa G.; Fraenkel Liana; Braithwaite R. Scott. Cost-effectiveness of Adding **Magnetic Resonance Imaging** (MRI) to Rheumatoid Arthritis Management. Arch Intern Med. 2011;171(7):657-667.
Svanström H, Pasternak B, Hviid A. Use of **strontium** ranelate and risk of **acute coronary syndrome**: cohort study. Ann Rheum Dis. 2014 Jun 1;73(6):1037-43.
Svensson B, Boonen A, Albertsson K, et al. **Low-dose prednisolone** in addition to the initial disease-modifying antirheumatic drug in patients with early active rheumatoid arthritis reduces joint destruction and increases the remission rate: a two-year randomized trial. Arthritis Rheum. 2005 Nov;52(11):3360-70.

Swart JF, van Dijkhuizen EHP, Wulffraat NM, et al. **Clinical Juvenile Arthritis Disease Activity Score** proves to be a useful tool in treat-to-target therapy in juvenile idiopathic arthritis. Ann Rheum Dis. 2018 Mar;77(3):336-342.

Symmons D, et al. Patients with stable long-standing rheumatoid arthritis **continue to deteriorate** despite intensified treatment with traditional disease modifying anti-rheumatic drugs--results of the British Rheumatoid Outcome Study Group Randomized controlled clinical trial. Rheumatology (Oxford). 2006 May;45(5):558-65. Epub 2005 Nov 1.

Tada M, Koike T, Okano T, et al. Comparison of joint destruction between standard- and low-dose **etanercept** in rheumatoid arthritis from the Prevention of Cartilage Destruction by Etanercept (PRECEPT). Rheumatology (Oxford). 2012 Jul 23.

Tak PP, Rigby WF, Rubbert-Roth A, et al. Inhibition of joint damage and improved clinical outcomes with **rituximab plus methotrexate** in early active rheumatoid arthritis: the **IMAGE** trial. Ann Rheum Dis. 2011 Jan;70(1):39-46.

Takashima S, Ota M. **Methotrexate-induced nodulosis**. CMAJ. 2015 Jul 14;187(10):E327.

Takeshita M, Suzuki K, Kondo Y, et al. Multi-dimensional analysis identified rheumatoid arthritis-**driving pathway in human T cell**. Ann Rheum Dis. 2019 Jun 5.

Takeuchi T, Genovese MC, Haraoui B, et al. **Dose reduction of baricitinib** in patients with rheumatoid arthritis achieving sustained disease control: results of a prospective study. Ann Rheum Dis. 2019 Feb;78(2):171-178.

Takeuchi T, Harigai M, Tanaka Y et al.; GO-MONO study group. **Golimumab** monotherapy in Japanese patients with active rheumatoid arthritis despite prior treatment with disease-modifying antirheumatic drugs: results of the phase 2/3, multicentre, randomised, double-blind, placebo-controlled GO-MONO study through 24 weeks. Ann Rheum Dis. 2013 Sep 1;72(9):1488-95.

Takeuchi T, Tanaka Y, Ishiguro N, et al. Effect of **denosumab** on Japanese patients with rheumatoid arthritis: a dose-response study of AMG 162 (Denosumab) in patients with RheumatoId arthritis on methotrexate to Validate inhibitory effect on bone Erosion (**DRIVE**)-a 12-month, multicentre, randomised, double-blind, placebo-controlled, phase II clinical trial. Ann Rheum Dis. 2015 Nov 19.

Takeuchi T, Tanaka Y, Soen S, et al. Effects of the **anti-RANKL antibody denosumab on joint structural damage** in patients with rheumatoid arthritis treated with conventional synthetic disease-modifying antirheumatic drugs (DESIRABLE study): a randomised, double-blind, placebo-controlled phase 3 trial. Ann Rheum Dis. 2019 Jul;78(7):899-907.

Takeuchi T, Yamanaka H, Ishiguro N, et al. **Adalimumab**, a human anti-TNF monoclonal antibody, outcome study for the prevention of joint damage in Japanese patients with early rheumatoid arthritis: the **HOPEFUL 1** study. Ann Rheum Dis. 2014 Mar 1;73(3):536-43.

Takeuchi T, Thorne C, Karpouzas G, et al. **Sirukumab** for rheumatoid arthritis: the phase III SIRROUND-D study. Ann Rheum Dis. 2017 Dec;76(12):2001-2008.

Tan CS, Koralnik IJ. **Progressive multifocal leukoencephalopathy** (PML) and other disorders caused by JC virus: clinical features and pathogenesis. Lancet Neurol. 2010 Apr;9(4):425-37.

Tanaka Y, et al. for the RRR study investigators. **Discontinuation of infliximab** after attaining **low disease activity** in patients with rheumatoid arthritis: RRR (remission induction by Remicade in RA) study. Ann Rheum Dis. 2010 Apr 1.

Tanaka Y, Fautrel B, Keystone EC, et al. Clinical **outcomes in patients switched from adalimumab to baricitinib** due to non-response and/or study design: phase III data in patients with rheumatoid arthritis. Ann Rheum Dis. 2019 Jul;78(7):890-898.

Tanaka Y, Hirata S. Is It Possible to **Withdraw Biologics** From Therapy in Rheumatoid Arthritis? Clin Ther. 2013 Nov 27.

Tanaka Y, Hirata S, Kubo S, et al. **Discontinuation of adalimumab after achieving remission** in patients with established rheumatoid arthritis: 1-year outcome of the HONOR study. Ann Rheum Dis. 2015 Feb;74(2):389-95.

Tanaka Y, Sugiyama N, Toyoizumi S, et al. **Modified- versus immediate-release tofacitinib** in Japanese rheumatoid arthritis patients: a randomized, phase III, non-inferiority study. Rheumatology (Oxford). 2018 Aug 17.

Tanaka Y, Takeuchi T, Tanaka S, et al. Efficacy and safety of **peficitinib (ASP015K)** in patients with rheumatoid arthritis and an inadequate response to conventional DMARDs: a randomised, double-blind, placebo-controlled phase III trial (RAJ3). Ann Rheum Dis. 2019 Jul 26.

Tanaka Y, Yamanaka H, Ishiguro N, et al. **Low disease activity** for up to 3 years after **adalimumab discontinuation** in patients with early rheumatoid arthritis: 2-year results of the **HOPEFUL-3** Study. Arthritis Res Ther. 2017 Mar 14;19(1):56.

Tarp S, Amarilyo G, Foeldvari I, et al. Efficacy and safety of **biological agents for systemic juvenile idiopathic arthritis**: a systematic review and meta-analysis of randomized trials. Rheumatology (Oxford). 2015 Nov 30.

Taurog JD, Chhabra A, Colbert RA. **Ankylosing Spondylitis and Axial Spondyloarthritis**. N Engl J Med. 2016 Jun 30;374(26):2563-2574.

Taylor OA, Brown AL, Brackett J, et al. Disparities in **Neurotoxicity Risk and Outcomes among Pediatric Acute Lymphoblastic Leukemia Patients**. Clin Cancer Res. 2018 Sep 11. (methotrexate)

Taylor PC, Schiff MH, Wang Q, et al. Efficacy and safety of monotherapy with **sirukumab compared with adalimumab** monotherapy in biologic-naïve patients with active rheumatoid arthritis (SIRROUND-H): a randomised, double-blind, parallel-group, multinational, 52-week, phase 3 study. Ann Rheum Dis. 2018 May;77(5):658-666.

Taylor PC, Weinblatt ME, Burmester GR, et al. **Cardiovascular Safety During Treatment With Baricitinib** in Rheumatoid Arthritis. Arthritis Rheumatol. 2019 Jul;71(7):1042-1055.

Tedeschi SK, Bathon JM, Giles JT, et al. The relationship between **fish consumption and disease activity in rheumatoid arthritis**. Arthritis Care Res (Hoboken). 2017 Jun 21.

Tedeschi SK et al. Relationship between **fish consumption** and disease activity in rheumatoid arthritis. Arthritis Care Res (Hoboken) 2018 Mar; 70:327.

Teitsma XM, Jacobs JWG, Welsing PMJ, et al. Inadequate response to treat-to-**target methotrexate therapy in patients with new-onset rheumatoid arthritis**: development and validation of clinical predictors. Ann Rheum Dis. 2018 May 14.

Ter Wee MM, Lems WF, Usan H et al. The effect of **biological agents on work participation** in rheumatoid arthritis patients: a systematic review. Ann Rheum Dis. 2012 Feb;71(2):161-71.

Ter Wee MM, den Uyl D, Boers M, et al. **Intensive combination treatment regimens, including prednisolone**, are effective in treating patients with early rheumatoid arthritis regardless of additional etanercept: 1-year results of the **COBRA**-light open-label, randomised, non-inferiority trial. Ann Rheum Dis. 2015 Jun;74(6):1233-40.

Ternant D, Ducourau E, Perdriger A, et al. Relationship between inflammation and **infliximab pharmacokinetics** in rheumatoid arthritis. Br J Clin Pharmacol. 2013 Dec 19

Tesfa1 D, Ajeganova S, Hägglund1 H, et al. **Late-onset neutropenia following rituximab** therapy in rheumatic diseases: Association with B-lymphocyte depletion and infections. Arthritis Rheum. 2011 May 10. doi: 10.1002/art.30427.

Thompson AE, Rieder SW, Pope JE. **TNF therapy and the risk of serious infection** and malignancy in patients with early rheumatoid arthritis: A meta-analysis of randomized controlled trials. Arthritis Rheum. 2011 Feb 25. doi: 10.1002/art.30310.

Thorlund K, Druyts E, Aviña-Zubieta JA et al. Why the findings of published multiple treatment comparison meta-analyses of **biologic treatments** for rheumatoid arthritis are different: an overview of recurrent methodological shortcomings. Ann Rheum Dis. 2013 Sep 1;72(9):1524-35.

Tjärnlund A, Tang Q, Wick C, et al. **Abatacept** in the treatment of adult **dermatomyositis and polymyositis**: a randomised, phase IIb treatment delayed-start trial. Ann Rheum Dis. 2018 Jan;77(1):55-62.

Tkacz J, Ellis L, Bolge SC, et al **Utilization and Adherence** Patterns of Subcutaneously Administered **Anti-Tumor Necrosis Factor** Treatment Among Rheumatoid Arthritis Patients. Clin Ther. 2014 Mar 21

Too CL, Muhamad NA, et al; MyEIRA Study Group. **Occupational exposure to textile dust** increases the risk of rheumatoid arthritis: results from a Malaysian population-based case-control study. Ann Rheum Dis. 2016 Jun;75(6):997-1002.

Toulemonde G, Scoazec JY, Miossec P. Treatment with **etanercept of autoimmune hepatitis** associated with rheumatoid arthritis: an open label proof of concept study. Ann Rheum Dis. 2012 Mar 8.

Tremoulet AH, Jain S, Jaggi P, et al. **Infliximab** for intensification of primary therapy for Kawasaki disease: a phase 3 randomised, double-blind, placebo-controlled trial. *Lancet* 2014; online Feb 24.

Tsao NW, Sayre EC, et al. **Risk of preterm delivery and small-for-gestational-age births in women with autoimmune disease using biologics before or during pregnancy**: a population-based cohort study. Ann Rheum Dis. 2018 Mar 1.

Tubach F, Salmon D, Ravaud P, et al. Research Axed on Tolerance of Biotherapies Group. **Risk of tuberculosis** is higher with anti-tumor necrosis factor monoclonal antibody therapy than with soluble tumor necrosis factor receptor therapy: The three-year prospective french research axed on tolerance of biotherapies registry. Arthritis Rheum. 2009 Jun 29;60(7):1884-1894.

Tugwell P, Pincus T, et al. Combination therapy with **cyclosporine and methotrexate** in severe rheumatoid arthritis. The Methotrexate-Cyclosporine Combination Study Group. N Engl J Med. 1995 Jul 20;333(3):137-41.

Tugwell P, Singh JA, Wells GA. **Biologicals for rheumatoid arthritis**. BMJ. 2011 Jul 28;343:d4027.

Tung CH, Lai NS, Li CY, et al. **Risk of rheumatoid arthritis in patients with hepatitis C virus infection** receiving interferon-based therapy: a retrospective cohort study using the Taiwanese national claims database. BMJ Open. 2018 Jul 23;8(7):e021747.

Tweehuysen L, van den Ende CH, Beeren FM, et al. Little evidence for prediction of successful **dose reduction or discontinuation of a biologic i**n rheumatoid arthritis: A systematic review. Arthritis Rheumatol. 2016 Oct 1.

Tweehuysen L, van den Bemt BJF, van Ingen IL, et al. Subjective Complaints as Main Reason for **Biosimilar Discontinuation** after Open Label Transitioning from Originator to **Biosimilar Infliximab**. Arthritis Rheumatol. 2017 Oct 18.

Tynjälä P, Vähäsalo P, Tarkiainen M, et al. Aggressive Combination Drug Therapy in **Very Early Polyarticular Juvenile Idiopathic** Arthritis (**ACUTE-JIA**): a multicentre randomised open-label clinical trial. Ann Rheum Dis. 2011 May 28.

Tyring S, Gottlieb A, Papp K, Gordon K, et al. **Etanercept** and clinical outcomes, fatigue, and depression in **psoriasis**: double-blind placebo-controlled randomised phase III trial. Lancet. 2006 Jan 7;367(9504):29-35.

Umicevic Mirkov M, Cui J, Vermeulen SH, et al. **Genome-wide association analysis of anti-TNF drug response** in patients with rheumatoid arthritis. Ann Rheum Dis. 2013 Aug;72(8):1375-81.

Umićević Mirkov M, Janss L, Vermeulen SH, van de Laar MA, et al. Estimation of **heritability** of different **outcomes** for genetic studies of **TNFi response** in patients with rheumatoid arthritis. Ann Rheum Dis. 2015 Dec;74(12):2183-7.

Üsküdar Cansu D, Demirtaş E, Andiç N, et al. Is it required to routinely **check fibrinogen level in patients with rheumatic diseases on tocilizumab**? Case-based review. Rheumatol Int. 2019 Apr;39(4):743-750.

van Aken J, Heimans L, Gillet-van Dongen H, et al. **Five-year outcomes** of probable rheumatoid arthritis treated with **methotrexate** or placebo during the first year (the PROMPT study). Ann Rheum Dis. 2014 Feb 1;73(2):396-400

van Assen S, et al. Humoral responses after **influenza vaccination** are severely reduced in patients with rheumatoid arthritis treated with **rituximab**. Arthritis Rheum. 2009 Dec 28;62(1):75-81.

van Assen S, Agmon-Levin N, Elkayam O, et al. EULAR recommendations for **vaccination in adult patients** with autoimmune inflammatory rheumatic diseases. Ann Rheum Dis 2011;**70**:414-422. Online: 3 Dec 2010 doi:10.1136/ard.2010.137216

van Breukelen-van der Stoep DF, van Zeben D, Klop B, et al. Marked **underdiagnosis and undertreatment of hypertension and hypercholesterolaemia** in rheumatoid arthritis. Rheumatology (Oxford). 2016 Mar 23

van Daalen EE, Rizzo R, Kronbichler A, et al. Effect of **rituximab on malignancy risk in patients with ANCA-associated vasculitis**. Ann Rheum Dis. 2017 Jun;76(6):1064-1069.

van Dartel SA, Fransen J, Kievit W, et al. Difference in the risk of **serious infections** in patients with rheumatoid arthritis treated with adalimumab, infliximab and etanercept: results from the Dutch Rheumatoid Arthritis Monitoring (DREAM) registry. Ann Rheum Dis. 2012 Aug 11.

van Dartel SA, Fransen J, Kievit W, et al. Difference in the **risk of serious infections** in patients with rheumatoid arthritis treated with **adalimumab, infliximab and etanercept**: results from the Dutch Rheumatoid Arthritis Monitoring (DREAM) registry. Ann Rheum Dis. 2012 Aug 11.
van de Stadt LA, van Schaardenburg D. **Alcohol consumption** protects against arthritis development in seropositive arthralgia patients. Ann Rheum Dis. 2012 May 12.
van den Bemt BJ, den Broeder AA, Wolbink GJ, et al. The combined use of **disease activity and infliximab serum trough** levels for early prediction of (non-)response to infliximab in rheumatoid arthritis. Br J Clin Pharmacol. 2013 Apr 19.
van den Broek M, Klarenbeek NB, Dirven L, et al. **Discontinuation of infliximab** and potential predictors of persistent low disease activity in patients with early rheumatoid arthritis and disease activity score-steered therapy: subanalysis of the **BeSt** study. Ann Rheum Dis. 2011 Aug;70(8):1389-94.
van den Broek M, Dirven L, Klarenbeek N, et al. The association of **treatment response and joint damage with ACPA-status** in recent-onset RA: a subanalysis of the 8-year follow-up of the **BeSt study**. Ann Rheum Dis. 2012 Feb;71(2):245-8.
van den Broek M, Dirven L, de Vries-Bouwstra JK et al. **Rapid radiological progression** in the first year of early rheumatoid arthritis is predictive of disability and joint damage progression during 8 years of follow-up. Ann Rheum Dis. 2012 Sep;71(9):1530-3.
van den Oever IA, Sattar N, Nurmohamed MT. **Thromboembolic** and **cardiovascular risk** in rheumatoid arthritis: role of the haemostatic system. Ann Rheum Dis. 2014 Jun 1;73(6):954-7
van der Burg LR, Ter Wee MM, Boonen A. Effect of biological therapy on **work participation in patients with ankylosing spondylitis**: a systematic review. Ann Rheum Dis. 2012 Dec;71(12):1924-33.
van der Heijde D, et al. Comparison of etanercept and methotrexate, alone and combined, in the treatment of rheumatoid arthritis: **Two-year** clinical and radiographic results from the **TEMPO** study, a double-blind, randomized trial. Arthritis Rheum. 2006 Mar 29;54(4):1063-1074 [Epub ahead of print]
van der Heijde D, et al. **Once-weekly** 50-mg dosing of **Etanercept** (Enbrel(R)) is as effective as 25-mg twice-weekly dosing in patients with **ankylosing spondylitis**. Ann Rheum Dis. 2006 Sep 12; [Epub ahead of print]
van der Heijde D, Breedveld FC, Kavanaugh A, et al. Disease Activity, Physical Function, and Radiographic Progression After Longterm Therapy with **Adalimumab** Plus Methotrexate: 5-Year Results of **PREMIER**. J Rheumatol. 2010 Oct 1.
van der Heijde Désirée, Sieper Joachim, Maksymowych Walter P, et al. for the Assessment of SpondyloArthritis international Society. **2010 Update of the international ASAS recommendations** for the use of **anti-TNF agents** in patients with **axial spondyloarthritis**. Ann Rheum Dis 2011;70:905-908 doi:10.1136/ard.2011.151563.
van der Heijde D, Tanaka Y, Fleischmann R, et al; the **ORAL Scan** investigators. **Tofacitinib** (CP-690,550) in patients with rheumatoid arthritis on methotrexate: 12-Month data from a 24-month Phase 3 randomized radiographic study. Arthritis Rheum. 2013 Jan 24.
van der Heijde D, Deodhar A, et al. The Effect of **Golimumab** Therapy on Disease Activity and Health-related Quality of Life in Patients with Ankylosing Spondylitis: 2-year Results of the GO-RAISE Trial. J Rheumatol. 2014 Jun;41(6):1095-103.
van der Heijde D, Ramiro S, Landewé R, et al. **2016** update of the **ASAS-EULAR** management recommendations for **axial spondyloarthritis**. Ann Rheum Dis. 2017 Jun;76(6):978-991.
van der Heijde D, Deodhar A, Wei JC, et al. **Tofacitinib** in patients with **ankylosing spondylitis**: a phase II, 16-week, randomised, placebo-controlled, dose-ranging study. Ann Rheum Dis. 2017 Aug;76(8):1340-1347.
van der Heijde D, et al. Efficacy and safety of **filgotinib**, a selective Janus kinase 1 inhibitor, in patients with active **ankylosing spondylitis** (**TORTUGA**): results from a randomised, placebo-controlled, phase 2 trial. Lancet. 2018 Oct 22.
van der Helm-van Mil AH, Zink A. **What is rheumatoid arthritis**? Considering consequences of **changed classification criteria**. Ann Rheum Dis. 2016 Sep 22.
van der Linden MP, van der Woude D, Ioan-Facsinay A, et al. Value of **anti-modified citrullinated vimentin** and third-generation anti-cyclic citrullinated peptide compared with second-generation anti-cyclic citrullinated peptide and rheumatoid factor in predicting disease outcome in undifferentiated arthritis and rheumatoid arthritis. Arthritis Rheum. 2009 Aug;60(8):2232-41.
van der Linden MP, le Cessie S, Raza K, et al. Long-term **impact of delay in assessment of patients with early arthritis**. Arthritis Rheum. 2010 Dec;62(12):3537-46. doi: 10.1002/art.27692.
van der Maas A, Kievit W, van den Bemt BJ, et al. **Down-titration and discontinuation of infliximab** in rheumatoid arthritis patients with stable low disease activity and stable treatment: an observational cohort study. Ann Rheum Dis. 2012 Nov;71(11):1849-54.
van der Woude D, Young A, Jayakumar K,et al. Prevalence of and predictive factors for sustained disease-modifying antirheumatic drug-free **remission** in rheumatoid arthritis: Results from two large early arthritis cohorts. Arthritis Rheum. 2009 Aug;60(8):2262-71. Sustained DMARD-free remission in RA patients treated with conventional therapy is not uncommon (15%). Symptom duration at presentation and the absence of autoantibodies are associated with sustained DMARD-free remission.
van Everdingen AA, Jacobs JW, et al. **Low-dose prednisone** therapy for patients with early active rheumatoid arthritis: clinical efficacy, disease-modifying properties, and side effects: a randomized, double-blind, placebo-controlled clinical trial. Ann Intern Med. 2002 Jan 1;136(1):1-12.
van Herwaarden N, van der Maas A, Minten MJ, et al. Disease activity guided **dose reduction and withdrawal of adalimumab or etanercept** compared with usual care in rheumatoid arthritis: open label, randomised controlled, non-inferiority trial. (**DRESS**) BMJ. 2015 Apr 9;350:h1389.
van Herwaarden N, Bouman CA, van der Maas A, et al. **Adalimumab and etanercept serum (anti)drug levels** are not predictive for successful dose reduction or discontinuation in rheumatoid arthritis. Ann Rheum Dis. 2015 Dec;74(12):2260-1.
van Lümig PPM et al. Relevance of laboratory investigations in **monitoring patients with psoriasis on etanercept or adalimumab**. Br J Dermatol 2011 Mar 24
van Mens LJJ, de Jong HM, Fluri I, et al. Achieving **remission in psoriatic arthritis by early initiation of TNF inhibition**: a double-blind, randomised, placebo-controlled trial of golimumab plus methotrexate versus placebo plus methotrexate. Ann Rheum Dis. 2019 May;78(5):610-616.
van Mulligen E, de Jong PHP, Kuijper TM, et al. **Gradual tapering TNF inhibitors versus conventional synthetic DMARDs after achieving controlled disease** in patients with rheumatoid arthritis: first-year results of the randomised controlled TARA study. Ann Rheum Dis. 2019 Apr 6.
van Mulligen E, de Jong PHP, Kuijper TM, et al. **Gradual tapering TNF inhibitors versus conventional synthetic DMARDs a**fter achieving controlled disease in patients with rheumatoid arthritis: first-year results of the randomised controlled TARA study. Ann Rheum Dis. 2019 Jun;78(6):746-753.
van Nies JA, Brouwer E, van Gaalen FA, et al. Improved **early identification of arthritis**: evaluating the efficacy of Early Arthritis Recognition Clinics. Ann Rheum Dis. 2013 Aug;72(8):1295-301.
van Nies JA, Krabben A, Schoones JW, et al. What is the evidence for the presence of a **therapeutic window of opportunity in rheumatoid arthritis**? A systematic literature review. Ann Rheum Dis. 2014 May 1;73(5):861-70.
van Nies JA, Tsonaka R, Gaujoux-Viala C, et al. Evaluating relationships between **symptom duration and persistence of rheumatoid arthritis**: does a window of opportunity exist? Results on the Leiden Early Arthritis Clinic and ESPOIR cohorts. Ann Rheum Dis. 2015 Jan 5.
Van Nieuwenhove E, Lagou V, Van Eyck L, et al. **Machine learning** identifies an **immunological pattern associated with multiple juvenile idiopathic arthritis subtypes**. Ann Rheum Dis. 2019 May;78(5):617-628.
van Riel PL, et al. Add **Enbrel or Replace Methotrexate** Study Investigators. Efficacy and safety of combination etanercept and methotrexate versus etanercept alone in patients with rheumatoid arthritis with an inadequate response to methotrexate: the ADORE study. Ann Rheum Dis. 2006 Nov;65(11):1478-83. Epub 2006 Feb 7.
van Rossum MA, et al. **Sulfasalazine** in the treatment of juvenile chronic arthritis: a randomized, double-blind, placebo-controlled, multicenter study. Dutch **Juvenile** Chronic Arthritis Study Group. Arthritis Rheum. 1998 May;41(5):808-16.
van Schie KA, Ooijevaar-De Heer P, Kruithof S, et al. Infusion reactions during infliximab treatment are **not** associated with **IgE anti-infliximab antibodies**. Ann Rheum Dis. 2017 Apr 28.
van Schouwenburg PA, van de Stadt LA, de Jong RN, et al. **Adalimumab** elicits a restricted **anti-idiotypic antibody response** in autoimmune patients resulting in functional neutralisation. Ann Rheum Dis. 2013 Jan;72(1):104-9.
van Schouwenburg PA, et al. Long-term measurement of **anti-adalimumab using pH-shift-anti-idiotype antigen binding** test shows predictive value and transient antibody formation. Ann Rheum Dis. 2013 Oct 1;72(10):1680-6.
van Sijl AM, van den Oever IA, Peters MJ, et al. Subclinical **renal dysfunction** is independently associated with cardiovascular events in rheumatoid arthritis: **the CARRE Study**. Ann Rheum Dis. 2012 Mar;71(3):341-4.
van Sijl AM, van Eijk IC, Peters MJ, et al. **Tumour necrosis factor blocking agents and progression of subclinical atherosclerosis** in patients with ankylosing spondylitis. Ann Rheum Dis. 2015 Jan;74(1):119-23.
van Steenbergen HW, Aletaha D, Beaart-van de Voorde LJ, et al. **EULAR definition of arthralgia** suspicious for progression to rheumatoid arthritis. Ann Rheum Dis. 2017 Mar;76(3):491-496.
van Tuyl LH, Hewlett S, Sadlonova M, Davis B, et al. The **patient perspective on remission in rheumatoid arthritis**: 'You've got limits, but you're back to being you again'. Ann Rheum Dis. 2015 Jun;74(6):1004-10.
van Vollenhoven RF et al. Addition of **infliximab** compared with addition of sulfasalazine and hydroxychloroquine to methotrexate in patients with early rheumatoid arthritis (**Swefot** trial): 1-year results of a randomised trial. *Lancet* 2009 Aug 8; 374:459.
van Vollenhoven RF, Geborek P, Forslind K, et al, for the **Swefot** study group. **Conventional combination treatment versus biological** treatment in methotrexate-refractory early rheumatoid arthritis: 2 year follow-up of the randomised, non-blinded, parallel-group Swefot trial. Lancet 2012; online March 29.
van Vollenhoven RF, Fleischmann R, Cohen S et al; **ORAL Standard** Investigators. **Tofacitinib or adalimumab** versus placebo in rheumatoid arthritis. N Engl J Med. 2012 Aug 9;367(6):508-19.
van Vollenhoven RF, Emery P, Bingham CO 3rd et al. Long-term safety of **rituximab** in rheumatoid arthritis: 9.5-year follow-up of the global clinical trial programme with a focus on adverse events of interest in RA patients. Ann Rheum Dis. 2013 Sep 1;72(9):1496-502.
van Vollenhoven RF, Østergaard M, Leirisalo-Repo M, et al. **Full dose, reduced dose or discontinuation of etanercept** in rheumatoid arthritis. Ann Rheum Dis. 2016 Jan;75(1):52-8.
van Vollenhoven RF, et al. Efficacy and safety of **tregalizumab** in patients with rheumatoid arthritis and an inadequate response to methotrexate: results of a phase IIb, randomised, placebo-controlled trial. Ann Rheum Dis. 2018 Apr;77(4):495-499.
Vastert SJ, de Jager W, Noordman BJ, et al. Effectiveness of first line use of **recombinant IL-1RA treatment in steroid naïve systemic juvenile idiopathic** arthritis: Results of a prospective cohort study. Arthritis Rheum. 2013 Dec 18

Verhoeven MM, de Hair MJ, Tekstra J, et al. **Initiating tocilizumab, with or without methotrexate**, compared with starting methotrexate with prednisone within step-up treatment strategies in early rheumatoid arthritis: an indirect comparison of effectiveness and safety of the U-Act-Early and CAMERA-II treat-to-target trials. Ann Rheum Dis. 2019 Jun 13.

Vermeer M, Kuper HH, Hoekstra M et al. Implementation of a **treat-to-target strategy in very early** rheumatoid arthritis: results of the Dutch Rheumatoid Arthritis Monitoring remission induction cohort study **(DREAM Study).** Arthritis Rheum. 2011 Oct;63(10):2865-72.

Verschueren P, De Cock D, Corluy L, Joos R, et al. **Methotrexate** in **combination with other DMARDs** is not superior to methotrexate alone for remission induction with **moderate-to-high-dose glucocorticoid bridging** in early rheumatoid arthritis after 16 weeks of treatment: the **CareRA** trial. Ann Rheum Dis. 2014 Oct 30.

Verschueren P, De Cock D, Corluy L, et al. Effectiveness of **methotrexate with step-down glucocorticoid** remission induction (**COBRA Slim**) versus other intensive treatment strategies for early rheumatoid arthritis in a treat-to-target approach: 1-year results of CareRA, a randomised pragmatic open-label superiority trial. Ann Rheum Dis. 2017 Mar;76(3):511-520.

Verstappen SM, Bakker MF, et al. Adverse events and factors associated with toxicity in patients with early rheumatoid arthritis treated with **methotrexate** tight control therapy (the CAMERA study). Ann Rheum Dis. 2009 Jul 5.

Verstappen SM, McCoy MJ, Roberts C, et al. The beneficial effects of a **3 week** course of **intramuscular glucocorticoid** injections in patients with very early inflammatory polyarthritis: Results of the STIVEA trial. Ann Rheum Dis. 2009 Oct 12.

Verstappen Suzanne M M, King Yvonne, Watson Kath D, et al. BSRBR Control Centre Consortium, BSR Biologics Register. **Anti-TNF therapies and pregnancy**: outcome of 130 pregnancies in the British Society for Rheumatology Biologics Register. Ann Rheum Dis 2011;**70**:823-826 Published Online First: 28 February 2011 doi:10.1136/ard.2010.140822.

Verstappen SM, Lunt M, Bunn DK, Scott DG, Symmons DP. In patients with **early inflammatory polyarthritis**, ACPA positivity, younger age and inefficacy of the first non-biological DMARD are predictors for receiving biological therapy: results from the Norfolk Arthritis Register. Ann Rheum Dis. 2011 Aug;70(8):1428-32.

Viatte S, Plant D, Han B, et al. Association of **HLA-DRB1 haplotypes** with rheumatoid arthritis severity, mortality, and treatment response. JAMA. doi:10.1001/jama.2015.3435.

Vieira MC, et al. **Tofacitinib Versus Biologic Treatments** With Active Rheumatoid Arthritis Who Have Had an **Inadequate Response to Tumor Necrosis Factor Inhibitors**: Results From Network Meta-analysis. Clin Ther. 2016 Nov 23.

Vincent FB, Morand EF, Murphy K, et al. **Antidrug antibodies (ADAb) to tumour necrosis factor (TNF)-**specific neutralising agents in chronic inflammatory diseases: a real issue, a clinical perspective. Ann Rheum Dis. 2012 Nov 29.

Vinet E, Pineau C, Gordon C, Clarke AE, Bernatsky S. **Biologic therapy and pregnancy** outcomes in women with rheumatic diseases. Arthritis Rheum. 2009 May 15;61(5):587-92.

Villeneuve E, Nam JL, Bell MJ, et al. A systematic literature review of strategies promoting **early referral and reducing delays** in the diagnosis and management of inflammatory arthritis. Ann Rheum Dis. 2013 Jan;72(1):13-22.

Villiger PM, Adler S, Kuchen S, et al. **Tocilizumab** for induction and maintenance of remission in giant cell arteritis: a phase 2, randomised, double-blind, placebo-controlled trial. Lancet. 2016 Mar 4.

Visser K, Katchamart W, Loza E, et al. Multinational **evidence-based recommendations for the use of methotrexate** in rheumatic disorders with a focus on rheumatoid arthritis: integrating systematic literature research and expert opinion of a broad international panel of rheumatologists in the 3E Initiative. Ann Rheum Dis. 2008 Nov 25. [Epub ahead of print]

Visser K, van der Heijde D. Optimal dosage and route of administration of **methotrexate** in rheumatoid arthritis: a systematic review of the literature. Ann Rheum Dis. 2009 Jul;68(7):1094-9. Epub 2008 Nov 25. Starting on methotrexate 15 mg/week orally, escalating with 5 mg/month to 25-30 mg/week, or the highest tolerable dose, with a subsequent switch to subcutaneous administration in the case of an insufficient response, seems to be the optimal evidence-based dosing and routing recommendation for methotrexate in RA.

Vital EM, Dass S, Buch MH, Rawstron AC, Emery P. An extra dose of **rituximab** improves clinical response in rheumatoid arthritis patients with initial incomplete B cell depletion: a randomised controlled trial. Ann Rheum Dis. 2015 Jun;74(6):1195-201.

Vlieland ND, Gardarsdottir H, Bouvy ML, et al. The majority of patients do **not store their biologic disease-modifying antirheumatic drugs** within the recommended temperature range. Rheumatology (Oxford). 2016 Apr;55(4):704-9.

Vo Kevin H, Waddell James Aubrey, Suda Katie J. Rapid Development of Infusion-Related Severe **Hypotension During Rituximab** Therapy. Articles Ahead of Print published on 1 May 2011, DOI 10.1345/aph.1P733. Ann Pharmacother ;45:e29.

Vogelzang EH, Kneepkens EL, Nurmohamed MT, et al. **Anti-adalimumab antibodies** and adalimumab **concentrations** in psoriatic arthritis; an association with disease activity at 28 and 52 weeks of follow-up. Ann Rheum Dis. 2014 Dec;73(12):2178-82.

Vriezekolk JE, van Lankveld WG, Geenen R, et al. Longitudinal association between **coping and psychological distress** in rheumatoid arthritis: a systematic review. Ann Rheum Dis. 2011 Jul;70(7):1243-50.

Vroom F, et al. Disease-modifying antirheumatic drugs in **pregnancy**: current status and implications for the future. Drug Saf. 2006;29(10):845-63.

Wadstrom H, Frisell T, et al. Do RA or **TNF inhibitors increase the risk of cervical neoplasia**, or of recurrence of previous neoplasia? A nationwide study from Sweden. Ann Rheum Dis 2016;75: 1272–8.

Wadström H, Frisell T, Askling J. **Malignant Neoplasms** in Patients With Rheumatoid Arthritis Treated With **Tumor Necrosis Factor Inhibitors, Tocilizumab, Abatacept, or Rituximab** in Clinical Practice: A Nationwide Cohort Study From Sweden. JAMA Intern Med. 2017Sep 18

Wagner C. **Absence of Infliximab in Infant Sera and Breast Milk** From Nursing Mothers Receiving Therapy for Crohn's Disease Before and After Delivery. J Clin Gastroenterol. 2009 Jan 12. [Epub ahead of print]n=3. Infliximab was detected in the mothers' sera, but not in the breast milk of nursing mothers or in the sera of the breast-fed newborns. Data from this small series of patients suggest that infliximab was not transferred from mother to child, either in utero or through breast milk. These data suggest that mothers receiving infliximab should not be discouraged from nursing their children.

Waimann CA, Marengo MF, et al. Electronic Monitoring of Oral Therapies in Ethnically Diverse and Economically Disadvantaged Patients With Rheumatoid Arthritis: Consequences of **Low Adherence**. Arthritis Rheum. 2013 Jun;65(6):1421-1429.

Waljee AK, Rogers MA, Lin P, et al. Short term use of **oral corticosteroids and related harms** among adults in the United States: population based cohort study. BMJ. 2017 Apr 12;357:j1415.

Wallenius M, Lie E, Daltveit AK, et al. **No excess risks in offspring with paternal preconception exposure** to disease modifying anti-rheumatic drugs. Arthritis Rheumatol. 2014 Nov 24.

Wang F, Morris C, Bodet ND, Kim BS. Treatment of Refractory **Chronic Pruritus of Unknown Origin With Tofacitinib** in Patients With Rheumatoid Arthritis. JAMA Dermatol. 2019 Sep 18.

Wang R, Dasgupta A, Ward MM. Comparative efficacy of **non-steroidal anti-inflammatory drugs in ankylosing spondylitis**: a Bayesian network meta-analysis of clinical trials. Ann Rheum Dis. 2016 Jun;75(6):1152-60.

Wang SQ, Zhang LW, Wei P, et al. Is **hydroxychloroquine** effective in treating **primary Sjogren`s syndrome**: a systematic review and meta-analysis. BMC Musculoskelet Disord. 2017 May 12;18(1):186.

Warren RB, et al. An intensified dosing schedule of subcutaneous **methotrexate** with moderate to severe **plaque-type psoriasis** (**METOP**): a 52 week, multicentre, randomised, double-blind, placebo-controlled, phase 3. Lancet 2016; online Dec 21.

Wasko MC, Hubert HB, Lingala VB, et al. **Hydroxychloroquine and risk of diabetes** in patients with rheumatoid arthritis. JAMA. 2007 Jul 11;298(2):187-93.

Wasko MC, Dasgupta A, Hubert H, et al. Propensity-adjusted association of **methotrexate with overall survival** in rheumatoid arthritis. Arthritis Rheum. 2012 Oct 8.

Wasko MC, Hsia EC, Kirkham B, et al. Effect of **golimumab** on carotid atherosclerotic disease measures and cardiovascular events in inflammatory arthritides. J Clin Rheumatol.2014 Jan;20(1):1-10

Wassenberg S, Rau R, Steinfeld P, et al. Very **low-dose prednisolone** in early rheumatoid arthritis retards radiographic progression over two years: a multicenter, double-blind, placebo-controlled trial. Arthritis Rheum. 2005 Nov;52(11):3371-80.

Wasserman AM. **Diagnosis and management of rheumatoid arthritis**. Am Fam Physician. 2011 Dec 1;84(11):1245-52.

Wasserman A. **Rheumatoid Arthritis: Common Questions About Diagnosis and Management**. Am Fam Physician. 2018 Apr 1;97(7):455-462.

Weber-Schoendorfer C, Chambers C, Wacker E, et al. **Pregnancy** outcome after rheumatologic **methotrexate** (MTX) treatment prior to or during early pregnancy: A prospective multicenter cohort study. Arthritis Rheumatol. 2014 Jan 27

Weber-Schoendorfer C, Hoeltzenbein M, Wacker E, et al. No evidence for an increased risk of adverse **pregnancy** outcome after paternal low-dose **methotrexate**: an observational cohort study. Rheumatology (Oxford). 2013 Dec 24.

Weber-Schoendorfer C, Oppermann M, Wacker E, et al. **Pregnancy outcome after TNF-α inhibitor therapy during the first trimester**: a prospective multicentre cohort study. Br J Clin Pharmacol. 2015 Mar 25.

Weiss-Smith S, Deshpande G, Chung S, et al. The **FDA drug safety surveillance program: adverse event reporting** trends. Arch Intern Med 2011;171:591-3. The drugs most frequently cited were biologic agents etanercept, adalimumab and infliximab (the first, third and fourth most frequently reported suspect drugs).

Wegener's Granulomatosis Etanercept Trial (**WGET**) Research Group. **Etanercept** plus standard therapy for **Wegener's** granulomatosis. N Engl J Med. 2005 Jan 27;352(4):351-61. (Stone JH, et al. Solid malignancies among patients in the Wegener's granulomatosis etanercept trial. Arthritis Rheum. 2006 May;54(5):1608-18.)

Weijers JM, et al. Implementation of **EULAR cardiovascular risk management guideline** in patients with rheumatoid arthritis: results of a successful collaboration between primary and secondary care. Ann Rheum Dis. 2018 Apr;77(4):480-483.

Weinblatt ME, Kremer JM, et al. A trial of **etanercept**, a recombinant tumor necrosis factor receptor:Fc fusion protein, in patients with rheumatoid arthritis **receiving methotrexate**. N Engl J Med. 1999 Jan 28;340(4):253-9.

Weinblatt ME, et al. Long term efficacy and safety of **adalimumab plus methotrexate** in patients with rheumatoid arthritis: **ARMADA** 4 year extended study. Ann Rheum Dis. 2006 Jun;65(6):753-9. Epub 2005 Nov 24.

Weinblatt ME, et al.. Adalimumab, a fully human anti-tumor necrosis factor alpha monoclonal antibody, for the treatment of rheumatoid arthritis in patients taking concomitant methotrexate: the ARMADA trial. Arthritis Rheum. 2003 Jan;48(1):35-45. Erratum in: Arthritis Rheum. 2003 Mar;48(3):855. Arthritis Rheum. 2004 Mar-Apr;22(2):144.

Weinblatt ME, et al. Selective co-stimulation modulation using **abatacept** in patients with active rheumatoid arthritis while receiving etanercept: a randomized clinical trial. Ann Rheum Dis. 2006 Aug 25; [Epub ahead of print]

Weinblatt M, et al. Safety of the selective costimulation modulator **abatacept** in rheumatoid arthritis patients receiving background biologic and nonbiologic disease-modifying antirheumatic drugs: A one-year randomized, placebo-controlled study. Arthritis Rheum. 2006 Aug 31;54(9):2807-2816 [Epub ahead of print] Abatacept in combination with synthetic DMARDs was well tolerated and improved physical function and physician- and patient-reported disease outcomes. However, abatacept in combination with biologic background therapies was associated with an increase in the rate of serious adverse events. Therefore, abatacept is not recommended for use in combination with biologic therapy.

Weinblatt ME, Kavanaugh A, Genovese MC, Musser TK, Grossbard EB, Magilavy DB. An **oral spleen tyrosine kinase (Syk) inhibitor** for rheumatoid arthritis. N Engl J Med. 2010 Sep 30;363(14):1303-12.

Weinblatt ME, Schiff M, Valente R, et al. Head-to-head comparison of **subcutaneous abatacept versus adalimumab** for Rheumatoid Arthritis. Arthritis Rheum. 2012 Nov 20.

Weinblatt ME, Bingham CO 3rd, Mendelsohn AM, et al. **Intravenous golimumab** is effective in patients with active rheumatoid arthritis despite methotrexate therapy with responses as early as week 2: results of the phase 3, randomised, multicentre, double-blind, placebo-controlled GO-FURTHER trial. Ann Rheum Dis. 2013 Mar;72(3):381-9.
Weinblatt ME, Genovese MC, Ho M, et al. Effects of **fostamatinib**, an oral spleen tyrosine kinase inhibitor, in rheumatoid arthritis patients with an inadequate response to methotrexate: Results from a phase III, multicenter, randomized, double-blind, placebo-controlled, parallel-group study. Arthritis Rheumatol. 2014 Sep 15.
Weinblatt ME, Westhovens R, Mendelsohn AM, et al; GO-FURTHER investigators. Radiographic benefit and maintenance of clinical benefit with intravenous **golimumab** therapy in patients with active rheumatoid arthritis despite methotrexate therapy: results up to 1 year of the phase 3, randomised, multicentre, double blind, placebo controlled GO-FURTHER trial. Ann Rheum Dis. 2014 Dec;73(12):2152-9.
Weinblatt ME, Bingham CO 3rd, et al. A Phase 3 Study Evaluating **Continuation, Tapering, and Withdrawal** of **Certolizumab** Pegol after 1 Year of Therapy in Early Rheumatoid Arthritis Patients. Arthritis Rheumatol. 2017 Jun 30.
Weinblatt ME, Baranauskaite A, et al. Phase 3 Randomized Study of SB5, an **Adalimumab Biosimilar**, Versus Reference Adalimumab in Patients With Moderate to Severe Rheumatoid Arthritis. Arthritis Rheumatol. 2017 Sep 26.
Weinblatt ME, et al. A Phase III Study Evaluating Continuation, Tapering, and Withdrawal of **Certolizumab** Pegol After One Year of Therapy in Patients With Early Rheumatoid Arthritis. Arthritis Rheumatol. 2017 Oct;69(10):1937-1948.
Weinblatt ME, Baranauskaite A, et al. Switching From Reference Adalimumab to **SB5** (**Adalimumab Biosimilar**) in Patients With Rheumatoid Arthritis: 52-Week Phase 3 Randomized Study Results. Arthritis Rheumatol. 2018 Feb 13.
Wells AF, Curtis JR, Betts KA, et al. Systematic Literature Review and Meta-analysis of **Tumor Necrosis Factor-Alpha Experienced Rheumatoid Arthritis**. Clin Ther. 2017 Aug;39(8):1680-1694.e2
Welsh P, Peters MJ, Sattar N. **Vitamin D** in rheumatoid arthritis: A magic bullet or a mirage? The need to improve the evidence base prior to calls for supplementation. Arthritis Rheum. 2011 Mar 11. doi: 10.1002/art.30341.
Westhovens R, et al. The safety of infliximab, combined with background treatments, among patients with rheumatoid arthritis and various comorbidities: A large, randomized,placebo-controlled trial. Arthritis Rheum. 2006 Mar 29;54(4):1075-1086 [Epub ahead of print] CONCLUSION: The risk of serious infections in patients receiving the approved infliximab dose of 3 mg/kg plus MTX was similar to that in patients receiving MTX alone. Patients receiving the unapproved induction regimen of 10 mg/kg infliximab plus MTX followed by a 10 mg/kg maintenance regimen had an increased risk of serious infections through week 22.
Westhovens R, Robles M, et al. **Maintenance of remission following 2 years of standard treatment then dose reduction** with **abatacept** in patients with early rheumatoid arthritis and poor prognosis. Ann Rheum Dis. 2015 Mar;74(3):564-8.
Westlake SL, Colebatch AN, Baird J, et al.. The effect of **methotrexate on cardiovascular disease** in patients with rheumatoid arthritis: a systematic literature review. Rheumatology (Oxford). 2009 Nov 27. [Epub ahead of print]
Wevers-de Boer K, Visser K, Heimans L et al. Remission induction therapy with **methotrexate and prednisone** in patients with early rheumatoid and undifferentiated arthritis (the IMPROVED study). Ann Rheum Dis. 2012 Sep;71(9):1472-7.
Wevers-de Boer KV, Heimans L, Huizinga TW et al. **Drug therapy in undifferentiated arthritis**: a systematic literature review. Ann Rheum Dis. 2013 Sep 1;72(9):1436-44.
Whiting Penny F., Smidt Nynke, Sterne Jonathan A.C., Et al. Systematic Review: Accuracy of **Anti–Citrullinated Peptide Antibodies** for Diagnosing Rheumatoid Arthritis. *Ann Intern Med* April 6, 2010 152:456-464.
Whittle SL, Richards BL, Husni E, et al. **Opioid therapy** for treating rheumatoid arthritis pain. Cochrane Database Syst Rev. 2011 Nov 9;11:CD003113. There is limited evidence that weak oral opioids may be effective analgesics for some patients with RA, but adverse effects are common and may offset the benefits of this class of medications.
Wiese AD, Griffin MR, Stein CM, et al. **Opioid analgesics and the risk of serious infections** among patients with rheumatoid arthritis: A self-controlled case series study. Arthritis Rheumatol. 2015 Oct 16.
Wiland P, Dudler J, Veale D, et al. The Effect of Reduced or Withdrawn Etanercept-methotrexate Therapy on Patient-reported Outcomes in Patients with Early Rheumatoid Arthritis. J Rheumatol. 2016 Jun 1.
Wilsdon TD, Whittle SL, Thynne TR, et al. **Methotrexate for psoriatic arthritis**. Cochrane Database Syst Rev. 2019 Jan 18;1:CD012722. Low-quality evidence suggests that low-dose (15 mg or less) oral methotrexate might be slightly more effective than placebo when taken for six months; however we are uncertain if it is more harmful. Effects of methotrexate on health-related quality of life, radiographic progression, enthesitis, dactylitis, and fatigue; its benefits beyond six months; and effects of higher-dose methotrexate have not been measured or reported in a randomised placebo-controlled trial.
Winthrop K, Baxter R, Liu L, et al. **Mycobacterial diseases and antitumour necrosis factor therapy** in USA. Ann Rheum Dis. 2013 Jan;72(1):37-42.
Winthrop KL, Baddley JW, Chen L, et al. Association between the initiation of **anti-tumor necrosis factor therapy** and the risk of **herpes zoster**. JAMA. 2013 Mar 6;309(9):887-95.
Winthrop KL, Yamanaka H, Valdez H, et al. **Herpes Zoster and Tofacitinib** Therapy in Patients with Rheumatoid Arthritis. Arthritis Rheumatol. 2014 Jun 18.
Winthrop KL, Silverfield J, Racewicz A, et al. The effect of **tofacitinib** on **pneumococcal and influenza vaccine** responses in rheumatoid arthritis. Ann Rheum Dis. 2015 Mar 20.
Winthrop KL, Park SH, Gul A, et al. **Tuberculosis and other opportunistic infections** in **tofacitinib**-treated patients with rheumatoid arthritis. Ann Rheum Dis. 2016 Jun;75(6):1133-8.
Winthrop KL, Curtis JR, Lindsey S, et al. **Herpes Zoster and Tofacitinib**: Clinical Outcomes and the Risk of Concomitant Therapy. Arthritis Rheumatol. 2017 Aug 28.
Winthrop KL, Wouters A, Choy E, et al. The Safety and Immunogenicity of **Live Zoster Vaccination in Rheumatoid Arthritis Patients Before Starting Tofacitinib**: A Randomized Phase II Trial. Arthritis Rheumatol. 2017 Aug 28
Wolstencroft PW, Casciola-Rosen L, Fiorentino DF. Association Between **Autoantibody Phenotype and Cutaneous Adverse Reactions to Hydroxychloroquine in Dermatomyositis**. JAMA Dermatol. 2018 Aug 22.
Wojciechowski J, Wiese MD, Proudman SM, et al. A Population Model of Early Rheumatoid Arthritis Disease Activity during treatment with **Methotrexate, Sulfasalazine and Hydroxychloroquine**. Br J Clin Pharmacol. 2014 Nov 12.
Wolbink GJ, et al. Development of **antiinfliximab antibodies** and relationship to clinical response in patients with rheumatoid arthritis. Arthritis Rheum. 2006 Mar;54(3):711-5.
Wolf D, Skup M, Yang H, et al. Clinical Outcomes Associated with **Switching or Discontinuation from Anti-TNF Inhibitors** for Nonmedical Reasons. Clin Ther. 2017 Mar 28.
Woo P, Southwood TR, et al. Randomized, placebo-controlled, crossover trial of low-dose oral **methotrexate** in **children** with extended oligoarticular or systemic arthritis. Arthritis Rheum. 2000 Aug;43(8):1849-57.
Wong SP, Chu CM, Kan CH, Tsui HS, Ng WL. Successful treatment of leflunomide-induced acute pneumonitis with **cholestyramine** wash-out therapy. J Clin Rheumatol. 2009 Dec;15(8):389-92.
Wu JJ, Poon KY, Channual JC, Shen AY. Association Between Tumor Necrosis Factor Inhibitor Therapy and **Myocardial Infarction** Risk in Patients With Psoriasis. Arch Dermatol. 2012 Aug 20:1-7.
Wu JJ, Guérin A, Sundaram M, et al. **Cardiovascular event risk** assessment in psoriasis patients treated with **tumor necrosis factor-α inhibitors versus methotrexate**. J Am Acad Dermatol. 2017 Jan;76(1):81-90.
Xie F, Yun H, Bernatsky S, et al. Risk for **Gastrointestinal Perforation** among Rheumatoid Arthritis Patients receiving **Tofacitinib, Tocilizumab, or other Biologics**. Arthritis Rheumatol. 2016 May 23.
Xie W, Huang Y, Xiao S, et al. Impact of **Janus kinase inhibitors on risk of cardiovascular events in patients** with rheumatoid arthritis: systematic review and meta-analysis of randomised controlled trials. Ann Rheum Dis. 2019 May 14.
Yan K, Zhang Y, Han L, et al**. Safety and Efficacy of Methotrexate** for Chinese Adults With Psoriasis With and Without Psoriatic Arthritis. JAMA Dermatol. 2019 Jan 30.
Yang DD, Krasnova A, Nead KT, et al. **Androgen deprivation therapy and risk of rheumatoid arthritis** in patients with localized prostate cancer. Ann Oncol. 2018 Feb 1;29(2):386-391.
Yates M, Watts RA, Bajema IM,et al.**EULAR**/ERA-EDTA recommendations for the management of **ANCA-associated vasculitis**. Ann Rheum Dis. 2016 Sep;75(9):1583-94.
Yazdany J, Schmajuk G, Robbins M, et al. American College of Rheumatology Core Membership Group. **Choosing wisely**: the American College of Rheumatology's **Top 5 list of things physicians and patients should question**. Arthritis Care Res (Hoboken). 2013 Mar;65(3):329-39.
Yazdany J, Dudley RA, Chen R, et al. Coverage for **high-cost specialty drugs for rheumatoid arthritis** in Medicare Part D. Arthritis Rheumatol. 2015;67:1474-80.
Yazici Y, Curtis JR, Ince A, et al. Efficacy of **tocilizumab** in patients with moderate to severe active rheumatoid arthritis and a previous inadequate response to disease-modifying antirheumatic drugs: the ROSE study. Ann Rheum Dis. 2012 Feb;71(2):198-205.
Yokogawa N, Eto H, Tanikawa A, et al. Effects of **hydroxychloroquine** on cutaneous **lupus** erythematosus: A multi-center double-blind randomized parallel-group trial. Arthritis Rheumatol. 2016 Dec 19.
Yokota S, Imagawa T, Mori M, et al. Efficacy and safety of **tocilizumab** in patients with systemic-onset juvenile idiopathic arthritis: a randomised, double-blind, placebo-controlled, withdrawal phase III trial. Lancet 2008; 371: 998–1006.
Yokota S, Imagawa T, Mori M, et al. Long-term treatment of systemic juvenile idiopathic arthritis with **tocilizumab**: results of an open-label extension study in Japan. Ann Rheum Dis. 2013 Apr;72(4):627-8.
Yokota S, Itoh Y, et al. **Tocilizumab** in systemic juvenile idiopathic arthritis in a real-world clinical setting: results from 1 year of postmarketing surveillance follow-up of 417 patients in Japan. Ann Rheum Dis. 2016 Sep;75(9):1654-60
Yoo DH, Suh CH, et al. A multicentre randomised controlled trial to compare the pharmacokinetics, efficacy and safety of **CT-P10 and innovator rituximab** in patients with rheumatoid arthritis. Ann Rheum Dis. 2017 Mar;76(3):566-570
Yoshida K, Sung YK, Kavanaugh A, et al. **Biologic discontinuation studies**: a systematic review of methods. Ann Rheum Dis. 2014 Mar 1;73(3):595-9.
Young JD, McGwire BS. **Infliximab** and reactivation of **cerebral toxoplasmosis**. N Engl J Med. 2005 Oct 6;353(14):1530-1; discussion 1530-1.
therapy: results from the BSRBR-RA. Ann Rheum Dis. 2013 May 5.
Yousaf A. **Rheumatologic Tests**: A Primer for Family Physicians. Am Fam Physician. 2018;98(3):164-170.
Yun H, Xie F, Delzell E, et al. The Comparative Effectiveness of **Biologics among Older Adults** and Disabled Rheumatoid Arthritis Patients in the Medicare Population. Br J Clin Pharmacol. 2015 Jun 30.
Yun H, Xie F, Delzell E, et al. Comparative Risk of **Hospitalized Infection Associated with Biological Agents** among Medicare Rheumatoid Arthritis Patients. Arthritis Rheumatol. 2015 Aug 28.
Yusuf IH, Ledingham JM, MacPhie E, et al. Monitoring for **retinal toxicity in patients taking hydroxychloroquine and chloroquine**. Rheumatology (Oxford). 2018 Feb 26.
Zangi HA, Ndosi M, Adams J, et al. EULAR recommendations for **patient education** for people with inflammatory arthritis. Ann Rheum Dis. 2015 Mar 3.
Závada J, Lunt M, Davies R, et al. on behalf of the British Society for Rheumatology Biologics Register (BSRBR) Control Centre Consortium. The risk of **gastrointestinal perforations** in patients with rheumatoid arthritis treated with anti-**TNF**
Závada J, Uher M, Sisol K, et al. A **tailored approach to reduce dose of anti-TNF drugs** may be equally effective, but substantially less costly than standard dosing in patients with ankylosing spondylitis over 1 year: a propensity score-matched cohort study. Ann Rheum Dis. 2016 Jan;75(1):96-102.
Zhang Y, Lu N, Peloquin C, et al. Improved **survival** in rheumatoid arthritis: a general population-based cohort study. Ann Rheum Dis. 2016 Jun 23.

Zhang J, Xie F, Yun H, Chen et al. Comparative effects of **biologics on cardiovascular risk** among older patients with rheumatoid arthritis. Ann Rheum Dis. 2016 Oct;75(10):1813-8.

Zink A, et al. Effectiveness of tumor necrosis factor inhibitors in rheumatoid arthritis in an observational cohort study: Comparison of patients according to their eligibility for major randomized clinical trials. Arthritis Rheum. 2006 Oct 30;54(11):3399-3407 [Epub ahead of print] Only 21-33% of the patients in the RABBIT register would have been eligible for the major trials.

Zochling J, van der Heijde D, Burgos-Vargas R, et al. ASAS/EULAR recommendations for the management of **ankylosing spondylitis**. Ann Rheum Dis 2006; 65: 442–52.

Zuelgaray E, Domont F, et al. **Tocilizumab**-Induced Drug Reaction With Eosinophilia and Systemic Symptoms Syndrome (**DRESS**) in Adult-Onset Still Disease: A Case Report. Ann Intern Med. 2017 Jul 18;167(2):141-142.

Zulian F, Martini G, Vallongo C, et al. **Methotrexate in juvenile localized scleroderma**: A randomised, double-blind, placebo-controlled trial. Arthritis Rheum. 2011 Jan 28.

Behavioural & Psychological Symptoms of DEMENTIA (BPSD) Treatment Chart

[1] Therapeutic Choices 5rd Edition, 2007
[2] Ontario Guidelines for the Management of Anxiety Disorders in Primary Care Fall 2000 1st Edition
[3] Micromedex 2018
[4] **Treatment Guidelines**: Drugs for Psychiatric Disorders. **The Medical Letter**: August 2010. (July, 2003; p. 69-76). Updated **June 2013.**
[5] Kawas CH. Clinical practice. Early Alzheimer's disease. N Engl J Med. 2003 Sep 11; 349(11): 1056-63.
[6] Ritchie K, Lovestone S. The dementias. Lancet. 2002 Nov 30; 360(9347): 1759-66.
Corrada MM, Brookmeyer R, Berlau D, Paganini-Hill A, Kawas CH. Prevalence of dementia after age 90: results from the 90+ study. Neurology. 2008 Jul 29;71(5):337-43. Epub 2008 Jul 2. In a very large sample of participants aged 90 and older, prevalence of all-cause dementia doubled every 5 years for women but not men. The overall prevalence of all-cause dementia was higher in women (45%, 95% CI = 41.5-49.0) than men (28%, 95% CI = 21.7-34.2).
[7] Doody RS. Current treatments for Alzheimer's disease: **cholinesterase inhibitors**. J Clin Psychiatry. 2003;64 Suppl 9:11-7. s. 2000 Nov;60(5):1095-122.
[8] Cummings JL. Use of **cholinesterase inhibitors** in clinical practice: **evidence-based** recommendations. Am J Geriatr Psychiatry. 2003 Mar-Apr;11(2):131-45.
[9] Gauthier S. Advances in the pharmacotherapy of **Alzheimer's** disease. CMAJ. 2002 Mar 5;166(5):616-23.
[10] DeLaGarza VW. Pharmacologic treatment of **Alzheimer's disease**: an update. Am Fam Physician. 2003 Oct 1; 68(7): 1365-72.
[11] Kindermann SS, Dolder CR, Bailey A, Katz IR, Jeste DV. Pharmacological treatment of **psychosis and agitation** in elderly patients with dementia: four decades of experience. Drugs Aging. 2002; 19(4): 257-76.
[12] Lanctot KL, Herrmann N, Yau KK, et al. Efficacy and safety of **cholinesterase inhibitors** in Alzheimer's disease: a **meta-analysis**. CMAJ. 2003 Sep 16;169(6):557-64.
[13] Trinh NH, Hoblyn J, et al. Efficacy of **cholinesterase inhibitors** in the treatment of neuropsychiatric symptoms and functional impairment in Alzheimer disease: a **meta-analysis**. JAMA. 2003 Jan 8;289(2):210-6.
[14] Wilkinson DG, Passmore AP, et al. A multinational, randomised, 12-week, comparative study of **donepezil** and **rivastigmine** in patients with mild to moderate Alzheimer's disease. Int J Clin Pract. 2002 Jul-Aug;56(6):441-6.
[15] AGS Clinical Practice Committee. Guidelines abstracted from the **American Academy of Neurology's Dementia Guidelines** for Early Detection, Diagnosis, and Management of Dementia. J Am Geriatr Soc. 2003 Jun; 51(6): 869-73.
[16] U.S. Preventive Services Task Force. **Screening for dementia**: recommendation and rationale. Ann Intern Med. 2003 Jun 3; 138(11): 925-6. No abstract available. Summary for patients in: Ann Intern Med. 2003 Jun 3;138(11):I60.
[17] Patterson CJ, Gauthier S, Bergman H, Cohen CA, et al. The recognition, assessment and management of dementing disorders: conclusions from the **Canadian Consensus Conference on Dementia**. (CCCD) CMAJ. 1999 Jun 15; 160(12 Suppl): S1-15.
[18] Bullock R. Cholinesterase inhibitors and **vascular dementia**: another string to their bow? CNS Drugs. 2004; 18(2): 79-92.
[19] Department of Veterans Affairs; Drug Review March 2004 http://www.vapbm.org/reviews/CholinestInh.pdf
[20] Cummings JL. **Alzheimer's disease**. N Engl J Med. **2004** Jul 1;351(1):56-67.
[21] Sink KM, Holden KF, Yaffe K. Pharmacological treatment of **neuropsychiatric** symptoms of dementia: a review of the evidence. **JAMA. 2005** Feb 2;293(5):596-608. (InfoPOEMs: Pharmacologic agents are minimally, if at all, effective in managing the neuropsychiatric symptoms of dementia. The atypical antipsychotics olanzapine (Zyprexa) and risperidone (Risperdal) are the most effective, but these agents may increase the risk of stroke. The decision to use any of these drugs must be made on the basis of individual circumstances. (LOE = 1a-))
[22] Desai AK, Grossberg GT. Diagnosis and treatment of Alzheimer's disease. Neurology. 2005 Jun 28;64(12 Suppl 3):S34-9.
Kales HC, Gitlin LN, Lyketsos CG. **Assessment and management of behavioral and psychological symptoms of dementia**. BMJ. 2015 Mar 2;350:h369.
[23] Clinical **Handbook of Psychotropic Drugs** 13th Edition, Bezchlibnyk-Butler K, Jeffries J. 2003
[24] Bentue-Ferrer D, Tribut O, Polard E, Allain H. Clinically significant drug interactions with cholinesterase inhibitors: a guide for neurologists. CNS Drugs. 2003; 17(13): 947-63.
[25] Birks JS, Harvey R. **Donepezil** for dementia due to Alzheimer's disease. Cochrane Database Syst Rev. 2003;(3):CD001190.
[26] Black S, et al. **Donepezil** 307 **Vascular** Dementia Study Group. Efficacy & tolerability of donepezil in vascular dementia: positive results of a 24-week, multicenter, international, randomized, placebo-controlled clinical trial. Stroke. 2003 Oct;34(10):2323-30.
[27] Geldmacher DS, Provenzano G, McRae T, Mastey V, Ieni JR. **Donepezil** is associated with delayed nursing home placement in patients with Alzheimer's disease. J Am Geriatr Soc. 2003 Jul;51(7):937-44.
[28] Feldman H, Gauthier S, et al. Donepezil MSAD Study Investigators. Efficacy of **donepezil** on maintenance of activities of daily living with moderate to severe Alzheimer's disease & the effect on caregiver burden. J Am Geriatr Soc. 2003 Jun;51(6):737-44.
[29] Wimo A, Winblad B, Engedal K, et al. Donepezil Nordic Study Group. An economic evaluation of **donepezil** in mild to moderate Alzheimer's disease: results of a 1-year, double-blind, randomized trial. Dement Geriatr Cogn Disord. 2003;15(1):44-54.
[30] Winblad B, Engedal K, Soininen H, Verhey F, et al. Donepezil Nordic Study Group. A 1-year, randomized, placebo-controlled study of **donepezil** in patients with mild to moderate AD. Neurology. 2001 Aug 14;57(3):489-95.
[31] Mohs RC, Doody RS, Morris JC, Ieni JR, et al. "312" Study Group. A 1-year, placebo-controlled preservation of function survival study of **donepezil** in AD patients. Neurology. 2001 Aug 14;57(3):481-8. Erratum in: Neurology 2001 Nov 27;57(10):1942.
[32] Homma A, et al. Clinical efficacy & safety of **donepezil** on cognitive & global function in Alzheimer's. A 24-wk, multicenter, double-blind, placebo-controlled study in Japan. E2020 Study Gp. Dement Geriatr Cogn Disord. 2000 Nov-Dec;11(6):299-313.
[33] Rogers SL, Doody RS, et al. Long-term efficacy and safety of **donepezil** in the treatment of Alzheimer's disease: final analysis (**up to 4.9yrs**) of a US multicentre open-label study. Eur Neuropsychopharmacol. 2000 May;10(3):195-203
[34] Wilkinson D, Doody R, Helme R, Taubman K, Mintzer J, Kertesz A, Pratt RD; Donepezil 308 Study Group. **Donepezil** in **vascular** dementia: a randomized, placebo-controlled study. Neurology. 2003 Aug 26; 61(4): 479-86.
[35] Auriacombe S, Pere JJ, Loria-Kanza Y, Vellas B. Efficacy and safety of **rivastigmine** in patients with Alzheimer's disease who failed to benefit from treatment with **donepezil**. Curr Med Res Opin. 2002; 18(3): 129-38.
[36] Courtney C, Farrell D, Gray R, et al.; **AD2000** Collaborative Group. **Long-term donepezil** treatment in 565 patients with Alzheimer's disease (AD2000): randomised double-blind trial. Lancet. 2004 Jun 26;363(9427):2105-15. (Author reply: Oct 2,2004)
[37] Seltzer B, Zolnouni P, Nunez M, Goldman R, Kumar D, Ieni J, Richardson S; Donepezil "402" Study Group. Efficacy of **donepezil** in **early-stage** Alzheimer disease: a randomized placebo-controlled trial. Arch Neurol. 2004 Dec;61(12):1852-6.
[38] Ronald C. Petersen, Ph.D., M.D., Ronald G. Thomas, Ph.D., Michael Grundman, M.D., M.P.H., et al., for the Alzheimer's Disease Cooperative Study Group Vitamin E & Donepezil for the Treatment of **Mild Cognitive Impairment.** N Engl J Med 2005
June 9;352:2379-88. (Conclusions: Vitamin E had no benefit in patients with mild cognitive impairment. Although donepezil therapy was associated with a lower rate of progression to Alzheimer's disease during the first 12 months of treatment, the rate of progression to Alzheimer's disease after three years was not lower among patients treated with donepezil than among those given placebo.) (InfoPOEMs: Vitamin E does not slow progression of mild cognitive impairment to full-fledged Alzheimer's disease. Donepezil provides an early benefit that is gone by 3yr. A secondary analysis found that donepezil appeared more beneficial for pts with the apolipoprotein E4 (APOE) gene. This finding requires prospective confirmation before we begin to test all pts with mild cognitive impairment for APOE & use it to guide therapy.(LOE = 1b)) Lu PH, Edland SD, Teng E, Tingus K, Petersen RC, Cummings JL; Alzheimer's Disease Cooperative Study Group. Donepezil delays progression to AD in MCI subjects with depressive symptoms. Neurology. 2009 Jun 16;72(24):2115-21.
[39] Holmes C, Wilkinson D, Dean C, Vethanayagam S, et al. The efficacy of donepezil in the treatment of **neuropsychiatric** symptoms in Alzheimer disease. Neurology. 2004 Jul 27;63(2):214-9.
[40] Suh DC, Thomas SK, Valiyeva E, Arcona S, Vo L. Drug Persistency of Two Cholinesterase Inhibitors : Rivastigmine versus Donepezil in Elderly Patients with Alzheimer's Disease. Drugs Aging. 2005;22(8):695-707.
[41] Bullock R, Touchon J, Bergman H, Gambina G, He Y, Rapatz G, Nagel J, Lane R. Rivastigmine and donepezil treatment in moderate to moderately-severe Alzheimer's disease over a 2-year period. Curr Med Res Opin. 2005 Aug;21(8):1317-27.
[42] Winblad B,et al.; Severe Alzheimer's Disease Study Group. **Donepezil** in patients with **severe Alzheimer's disease**: double-blind, parallel-group, placebo-controlled study. Lancet. 2006 Apr 1;367(9516):1057-65. INTERPRETATION: Donepezil improves cognition and preserves function in individuals with severe Alzheimer's disease who live in nursing homes. (Editorial: a case of too little, too late & points out the limitations of using last observation carried forward & questions the clinical sig. of the findings.)
[43] Feldman H, Gauthier S, et al. Donepezil MSAD Study Investigators Group. A 24-week, randomized, double-blind study of **donepezil** in **moderate to severe** Alzheimer's disease. Neurology. 2001 Aug 28;57(4):613-20.
[44] Tariot PN, Cummings JL, Katz IR, Mintzer J, et al. A randomized, double-blind, placebo-controlled study of the efficacy and safety of **donepezil** in patients with Alzheimer's disease in the nursing home setting. J Am Geriatr Soc. 2001 Dec;49(12):1590-9.

[45] Kaduszkiewicz H, Zimmermann T, Beck-Bornholdt HP, et al. **Cholinesterase inhibitors** for patients with Alzheimer's disease: **systematic review** of randomised clinical trials. BMJ. **2005** Aug 6;331(7512):321-7. (InfoPOEMs: The evidence supporting the effectiveness of cholinesterase inhibitors is based on exceedingly **small effects found in poorly analyzed studies**. Studies of Alzheimer's drugs need to be carefully scrutinized for methodologic errors that inflate the appearance of benefit. (LOE = 1a))

[46] Wild R, Pettit T, Burns A. Cholinesterase inhibitors for dementia with **Lewy bodies**. Cochrane Database Syst Rev. 2003;(3):CD003672.

[47] McKeith I, Del Ser T, Spano P, et al. Efficacy of **rivastigmine** in dementia with Lewy bodies: a randomised, double-blind, placebo-controlled international study. Lancet. 2000 Dec 16;356(9247):2031-6.

[48] Health Canada Public Advisory April 2005 -Information about Reminyl in patients with mild cognitive impairment (mortality: 1.3% galantamine vs 0.1% placebo group) http://www.hc-sc.gc.ca/hpfb-dgpsa/tpd-dpt/reminyl_hpc_e.html Doody RS et al. Donepezil treatment of patients with MCI: A 48-week randomized, placebo-controlled trial. Neurology 2009 May 5; 72:1555.

Russ TC, Morling JR. **Cholinesterase inhibitors for mild cognitive impairment**. Cochrane Database Syst Rev. 2012 Sep 12;9:CD009132. doi: 10.1002/14651858.CD009132.pub2. There is very little evidence that cholinesterase inhibitors affect progression to dementia or cognitive test scores in mild cognitive impairment. This weak evidence is overwhelmed by the increased risk of adverse events, particularly gastrointestinal. Cholinesterase inhibitors should not be recommended for mild cognitive impairment.

Petersen RC, Lopez O, Armstrong MJ, et al. Practice guideline update summary: Mild cognitive impairment: Report of the Guideline Development, Dissemination, and Implementation Subcommittee of the American Academy of Neurology (AAN). Neurology. 2017 Dec 27

[49] Olin J, Schneider L. **Galantamine** for Alzheimer's disease. Cochrane Database Syst Rev. 2002;(3):CD001747.

[50] Scott LJ, Goa KL. **Galantamine**: a review of its use in Alzheimer's disease. Drugs. 2000 Nov;60(5):1095-122.

[51] Kurz AF, Erkinjuntti T, et al. Long-term safety and cognitive effects of **galantamine** in the treatment of probable vascular dementia or Alzheimer's disease with cerebrovascular disease. Eur J Neurol. 2003 Nov;10(6):633-40.

[52] Small G, Erkinjuntti T, Kurz A, Lilienfeld S. **Galantamine** in the treatment of cognitive decline in patients with vascular dementia or Alzheimer's disease with cerebrovascular disease. CNS Drugs. 2003;17(12):905-14.

[53] Mintzer JE, Kershaw P. The efficacy of **galantamine** in the treatment of Alzheimer's disease: comparison of patients previously treated with acetylcholinesterase inhibitors to patients with no prior exposure. Int J Geriatr Psychiatry. 2003 Apr;18(4):292-7.

[54] Blesa R, Davidson M, Kurz A, Reichman W, et al. **Galantamine** provides sustained benefits in patients with 'advanced moderate' Alzheimer's disease for at least 12 months. Dement Geriatr Cogn Disord. 2003;15(2):79-87.

[55] Erkinjuntti T, Kurz A, Gauthier S, et al. Efficacy of **galantamine** in probable **vascular** dementia and Alzheimer's disease combined with cerebrovascular disease: a randomised trial. Lancet. 2002 Apr 13;359(9314):1283-90.

[56] Wilcock GK, et al. Efficacy & safety of **galantamine** in mild to moderate Alzheimer's disease: multicentre randomised controlled trial. Galantamine International-1 Study Group. BMJ. 2000 Dec 9;321(7274):1445-9. Erratum: BMJ 2001 Feb 17;322(7283):405.

[57] Tariot PN, Solomon PR, Morris JC, Kershaw P, et al. A 5-month, randomized, placebo-controlled trial of **galantamine** in AD. The Galantamine USA-10 Study Group. Neurology. 2000 Jun 27;54(12):2269-76.

[58] Raskind MA, Peskind ER, Wessel T, et al. **Galantamine** in AD: A 6-month randomized, placebo-controlled trial with a 6-month extension. The Galantamine USA-1 Study Group. Neurology. 2000 Jun 27;54(12):2261-8.

[59] Raskind MA, Peskind ER, Truyen L, Kershaw P, Damaraju CV. The cognitive benefits of **galantamine** are sustained for at least 36 months: a long-term extension trial. Arch Neurol. 2004 Feb;61(2):252-6.

[60] Pirttila T, Wilcock G, Truyen L, Damaraju CV. Long-term efficacy and safety of **galantamine** in patients with mild-to-moderate Alzheimer's disease: multicenter trial. Eur J Neurol. 2004 Nov;11(11):734-41.

[61] Health Canada Public Advisory April 2005 -Information about Reminyl in patients with mild cognitive impairment (mortality: 1.3% galantamine vs 0.1% placebo group) http://www.hc-sc.gc.ca/hpfb-dgpsa/tpd-dpt/reminyl_hpc_e.html Winblad B, Gauthier S, Scinto L, Feldman H, Wilcock GK, Truyen L, Mayorga AJ, Wang D, Brashear HR, Nye JS; GAL-INT-11/18 Study Group. Safety and efficacy of galantamine in subjects with mild cognitive impairment. Neurology. 2008 May 27;70(22):2024-35.Doody RS et al. Donepezil treatment of patients with MCI: A 48-week randomized, placebo-controlled trial. Neurology 2009 May 5; 72:1555.

[62] Birks J, Grimley Evans J, Iakovidou V, Tsolaki M. **Rivastigmine** for Alzheimer's disease. Cochrane Database Syst Rev. 2000;(4):CD001191.

[63] Rigaud AS, Andre G, Vellas B, Touchon J, Pere JJ; French Study Group. No additional benefit of **HRT** on response to **rivastigmine** in menopausal women with AD. Neurology. 2003 Jan 14;60(1):148-9.

[64] Farlow M, Anand R, Messina J Jr, Hartman R, Veach J. A 52-week study of the efficacy of **rivastigmine** in patients with mild to moderately severe Alzheimer's disease. Eur Neurol. 2000;44(4):236-41.

[65] Rosler M, Anand R, et al. Efficacy and safety of **rivastigmine** in patients with Alzheimer's disease: international randomised controlled trial. BMJ. 1999 Mar 6;318(7184):633-8. Erratum: BMJ 2001 Jun 16;322(7300):1456.

[66] Moretti R, Torre P, Antonello RM, Cazzato G, Bava A. **Rivastigmine** in subcortical vascular dementia: a randomized, controlled, open 12-month study in 208 patients. Am J Alzheimers Dis Other Demen. 2003 Sep-Oct; 18(5): 265-72.

[67] Aupperle PM, Koumaras B, Chen M, Rabinowicz A, Mirski D. Long-term effects of **rivastigmine** treatment on neuropsychiatric and behavioral disturbances in nursing home residents with moderate to severe Alzheimer's disease: results of a 52-week open-label study. Curr Med Res Opin. 2004 Oct;20(10):1605-12.

[68] Farlow MR, Lilly ML. **Rivastigmine**: An open-label, observational study of safety and effectiveness in treating patients with Alzheimer's Disease for up to **5 years**. BMC Geriatr. 2005 Jan 19;5(1):3 [Epub ahead of print]

[69] Lai MW, Moen M, Ewald MB. Pesticide-like poisoning from a prescription drug. N Engl J Med. 2005 Jul 21;353(3):317-8.

[70] Wilcock GK. **Memantine** for the treatment of dementia. Lancet Neurol. 2003 Aug; 2(8): 503-5.

Wilcock G, Mobius HJ, Stoffler A; MMM 500 group. A double-blind, placebo-controlled multicentre study of **memantine** in mild to moderate vascular dementia. Int Clin Psychopharmacol. 2002 Nov; 17(6): 297-305.

Orgogozo JM, Rigaud AS, Stoffler A, et al. Efficacy and safety of **memantine** in patients with mild to moderate vascular dementia: a randomized, placebo-controlled trial (MMM 300). Stroke. 2002 Jul; 33(7): 1834-9.

Memantine for Alzheimer's disease. Med Lett Drugs Ther. 2003 Sep 15; 45(1165): 73-4.

Areosa SA, Sherriff F. **Memantine** for dementia. Cochrane Database Syst Rev. 2003; (3): CD003154.

Reisberg B, Doody R, Stoffler A, Schmitt F, Ferris S, Mobius HJ; Memantine Study Group. Memantine in moderate-to-severe Alzheimer's disease. N Engl J Med. 2003 Apr 3;348(14):1333-41.

Tariot PN, et al. Memantine Study Group. **Memantine** treatment in patients with moderate to severe Alzheimer disease **already receiving donepezil**: a randomized controlled trial. JAMA. 2004 Jan 21; 291(3): 317-24.

Perras C. Memantine for treatment of moderate to severe Alzheimer's disease. Issues Emerg Health Technol. 2005 Mar;(64):1-4.

Gauthier S, Wirth Y, et al. Effects of memantine on behavioural symptoms in Alzheimer's disease patients: an analysis of the Neuropsychiatric Inventory (NPI) data of two randomised, controlled studies. Int J Geriatr Psychiatry. 2005 May;20(5):459-64.

Hanney M, Prasher V, Williams N, et al, on behalf of the **MEADOWS** trial researchers. **Memantine** for dementia in adults older than 40 years with **Down's syndrome** (MEADOWS): a randomised, double-blind, placebo-controlled trial. Lancet 2012; online Jan 10.

[71] Reisberg B, Doody R, Stöffler A et al. A 24-Week Open-Label Extension Study of Memantine in Moderate to Severe Alzheimer Disease. Archives of Neurology 2006;63:1-6
(Kirby J, et al. A systematic review of the clinical and cost-effectiveness of memantine in patients with moderately severe to severe Alzheimer's disease. Drugs Aging. 2006;23(3):227-40.) (Cummings JL, Schneider E, Tariot PN, Graham SM; Memantine MEM-MD-02 Study Group. Behavioral effects of memantine in Alzheimer disease patients Receiving donepezil treatment. Neurology. 2006 Jul 11;67(1):57-63.)

[72] Herrmann N, Li A, Lanctot K. Memantine in dementia: a review of the current evidence. *Expert Opin Pharmacother* 2011; 12(5): 787-800.

Gauthier S, Loft H, Cummings J. Improvement in behavioural symptoms in patients with moderate to severe Alzheimer's disease by memantine: a pooled data-analysis. *Int J Geriatr Psychiatry* 2008; 23: 537-545.

Maidment I, Fox CG, Boustani M, Rodriguez J, et al. Efficacy of memantine on behavioral and psychological symptoms related to dementia: a systematic meta-analysis. *Ann Pharmacother* 2008; 43:32-38.

Herrmann N, Cappell J, Eryavec GM, Lanctot KL. Changes in nursing burden following memantine for agitation and aggression in LTC residents with moderate-severe Alzheimers' disease. *CNS Drugs* 2011; 25(5): 425-433.

[73] Devanand DP, Marder K, Michaels KS, et al. A randomized, placebo-controlled dose-comparison trial of **haloperidol** for psychosis and disruptive behaviors in Alzheimer's disease. Am J Psychiatry. 1998 Nov; 155(11): 1512-20.
Devanand DP, Pelton GH, Cunqueiro K, Sackeim HA, Marder K. A 6-month, randomized, double-blind, placebo-controlled pilot **discontinuation trial following response to haloperidol** treatment of psychosis and agitation In Alzheimer's disease. Int J Geriatr Psychiatry. 2011 Sep;26(9):937-43.

[74] Schneider LS, Tariot PN, Dagerman KS, et al. **CATIE-AD** Study Group. Effectiveness of atypical antipsychotic drugs in patients with Alzheimer's disease. N Engl J Med. 2006 Oct 12;355(15):1525-38. (n=421 36weeks risperidone 1mg/d, olanzapine 5.5mg/d, & quetiapine 56.5mg/d) Adverse effects offset advantages in the efficacy of atypical antipsychotic drugs for the treatment of psychosis, aggression, or agitation in patients with Alzheimer's disease. There were no significant differences among treatments with regard to the time to the discontinuation of treatment for any reason: olanzapine (median, 8.1 weeks), quetiapine (median, 5.3 weeks), risperidone (median, 7.4 weeks), and placebo (median, 8.0 weeks) (P=0.52). The median time to the discontinuation of treatment due to a lack of efficacy favored olanzapine (22.1 weeks) and risperidone (26.7 weeks) as compared with quetiapine (9.1 weeks) and placebo (9.0 weeks) (P=0.002). The time to the discontinuation of treatment due to adverse events or intolerability favored placebo. Overall, 24% of patients who received olanzapine, 16% of patients who received quetiapine, 18% of patients who received risperidone, & 5% of patients who received placebo discontinued their assigned treatment owing to intolerability (P=0.009). No significant differences were noted among the groups with regard to improvement on the CGIC scale. Improvement was observed in 32% of patients assigned to olanzapine, 26% of patients assigned to quetiapine, 29% of patients assigned to risperidone, and 21% of patients assigned to placebo (P=0.22). (InfoPOEMs: Atypical antipsychotics are minimally, if at all, effective for patients with Alzheimer's disease (AD), and they have significant adverse effects. They should not be routinely used for the treatment of psychosis, agitation, or aggression in these patients. (LOE = 1b))

[75] Hien le TT, Cumming RG, Cameron ID, et al. Atypical antipsychotic medications and **risk of falls** in residents of aged care facilities. J Am Geriatr Soc. 2005 Aug;53(8):1290-5. CONCLUSION: Despite fewer extrapyramidal side effects, atypical antipsychotic medications are not associated with fewer falls than the older, more-established antipsychotics.

[76] Consensus Development Conference on Antipsychotic Drugs and Obesity and **Diabetes**; Diabetes Care.2004; 27: 596-558.

[77] Lee PE, Gill SS, Freedman M, Bronskill SE, Hillmer MP, Rochon PA. **Atypical antipsychotic** drugs in the treatment of behavioural and psychological symptoms of dementia: systematic review. BMJ. 2004 Jul 10;329(7457):75. CONCLUSIONS: Although atypical antipsychotic drugs are being used with increasing frequency, few randomised trials have evaluated their use for BPSD. Limited evidence supports the perception of improved efficacy and adverse event profiles compared with typical antipsychotic drugs.

[78] Herrmann N, Mamdani M, Lanctot KL. Atypical antipsychotics and risk of cerebrovascular accidents. Am J Psychiatry. 2004 Jun;161(6):1113-5.

[79] Cummings JL, Street J, Masterman D, Clark WS. Efficacy of **olanzapine** in the treatment of psychosis in dementia with lewy bodies. Dement Geriatr Cogn Disord. 2002; 13(2): 67-73.

[80] Street JS, Clark WS, Kadam DL, Mitan SJ, et al. A. Long-term efficacy of **olanzapine** in the control of psychotic and behavioral symptoms in nursing home patients with Alzheimer's dementia. Int J Geriatr Psychiatry. 2001 Dec; 16 Suppl 1: S62-70.

[81] Street JS, et al. **Olanzapine** treatment of psychotic & behavioral symptoms in patients with Alzheimer's in nursing care facilities: a double-blind, randomized, placebo-controlled trial. HGEU Study Group. Arch Gen Psychiatry. 2000 Oct; 57(10): 968-76.

[82] De Deyn PP, Carrasco MM, Deberdt W, et al. Olanzapine versus placebo in the treatment of psychosis with or without associated behavioral disturbances in patients with Alzheimer's disease. Int J Geriatr Psychiatry. 2004 Feb;19(2):115-26.

[83] De Deyn PP, Carrasco MM, Deberdt W, Jeandel C, Hay DP, Feldman PD, Young CA, Lehman DL, Breier A. Olanzapine versus placebo in the treatment of psychosis with or without associated behavioral disturbances in patients with Alzheimer's disease. Int J Geriatr Psychiatry. 2004 Feb;19(2):115-26.

[84] Deberdt WG, Dysken MW, Rappaport SA, Feldman PD, et al.. Comparison of olanzapine and risperidone in the treatment of psychosis and associated behavioral disturbances in patients with dementia. Am J Geriatr Psychiatry. 2005 Aug;13(8):722-30. CONCLUSIONS: Patients' neuropsychiatric functioning improved with olanzapine, risperidone, and placebo treatment. There was a substantial response in the placebo group, and no significant differences emerged among treatments.

[85] Kennedy J, Deberdt W, Siegal A, et al. **Olanzapine** does **not** enhance **cognition** in non-agitated and non-psychotic patients with mild to moderate Alzheimer's dementia. Int J Geriatr Psychiatry. 2005 Oct 26;20(11):1020-1027.

[86] Lim CJ, Trevino C, Tampi RR. Can Olanzapine Cause Delirium in the Elderly? (January). Ann Pharmacother. 2005 Dec 20; [Epub ahead of print]

[87] Sajatovic M, Mullen JA, Sweitzer DE. Efficacy of quetiapine and risperidone against depressive symptoms in outpatients with psychosis. J Clin Psychiatry. 2002 Dec; 63(12): 1156-63.

[88] Ballard C, Margallo-Lana M, Juszczak E, et al. **Quetiapine** and **rivastigmine** and **cognitive decline in Alzheimer's disease**: randomised double blind placebo controlled trial. BMJ. 2005 Apr 16;330(7496):874. CONCLUSIONS: Neither quetiapine nor rivastigmine are effective in the treatment of agitation in people with dementia in institutional care. Compared with placebo, quetiapine is associated with significantly greater **cognitive decline**.

[89] Brodaty H, Ames D, Snowdon J, et al. A randomized placebo-controlled trial of **risperidone** for the treatment of aggression, agitation, and psychosis of dementia. J Clin Psychiatry. 2003 Feb; 64(2): 134-43.

[90] Katz IR, Jeste DV, Mintzer JE, et al. Comparison of **risperidone** and placebo for psychosis and behavioral disturbances associated with dementia: a randomized, double-blind trial. Risperidone Study Group. J Clin Psychiatry. 1999 Feb; 60(2): 107-15.

[91] De Deyn PP, Rabheru K, Rasmussen A, et al. A randomized trial of **risperidone**, placebo, and **haloperidol** for behavioral symptoms of dementia. Neurology 1999;53:946-55.

[92] Fontaine CS, Hynan LS, Koch K, et al. A double-blind comparison of **olanzapine versus risperidone** in the acute treatment of dementia-related behavioral disturbances in extended care facilities. J Clin Psychiatry. 2003 Jun; 64(6): 726-30.

[93] De Deyn PP, Katz IR, et al. Management of agitation, aggression, and psychosis associated with dementia: A pooled analysis including three randomized, placebo-controlled double-blind trials in nursing home residents treated with risperidone. Clin Neurol Neurosurg. 2005 May 24; [Epub ahead of print]

Komossa K, Rummel-Kluge C, Schwarz S, et al. Risperidone versus other atypical antipsychotics for schizophrenia. Cochrane Database Syst Rev. 2011 Jan 19;1:CD006626. Risperidone seems to produce somewhat more extrapyramidal side effects and clearly more prolactin increase than most other SGAs. It may also differ from other compounds in efficacy and in the occurrence of other adverse effects such as weight gain, metabolic problems, cardiac effects, sedation and seizures. Nevertheless, the large proportion of participants leaving studies early and incomplete reporting of outcomes makes it difficult to draw firm conclusions.

[94] Therapeutic Choices 5rd Edition, 2007

[95] Ontario Guidelines for the Management of Anxiety Disorders in Primary Care Fall 2000 1st Edition

[96] Micromedex 2014

[97] **Treatment Guidelines**: Drugs for Psychiatric Disorders. **The Medical Letter**: August 2010. (July, 2003; p. 69-76). Updated **June 2013**.

[98] Kawas CH. Clinical practice. Early Alzheimer's disease. N Engl J Med. 2003 Sep 11; 349(11): 1056-63.

[99] Ritchie K, Lovestone S. The dementias. Lancet. 2002 Nov 30; 360(9347): 1759-66.

Corrada MM, Brookmeyer R, Berlau D, Paganini-Hill A, Kawas CH. Prevalence of dementia after age 90: results from the 90+ study. Neurology. 2008 Jul 29;71(5):337-43. Epub 2008 Jul 2. In a very large sample of participants aged 90 and older, prevalence of all-cause dementia doubled every 5 years for women but not men. The overall prevalence of all-cause dementia was higher in women (45%, 95% CI = 41.5-49.0) than men (28%, 95% CI = 21.7-34.2).

[100] Doody RS. Current treatments for Alzheimer's disease: **cholinesterase inhibitors**. J Clin Psychiatry. 2003;64 Suppl 9:11-7. s. 2000 Nov;60(5):1095-122.

[101] Cummings JL. Use of **cholinesterase inhibitors** in clinical practice: **evidence-based** recommendations. Am J Geriatr Psychiatry. 2003 Mar-Apr;11(2):131-45.

[102] Gauthier S. Advances in the pharmacotherapy of **Alzheimer's** disease. CMAJ. 2002 Mar 5;166(5):616-23.

[103] DeLaGarza VW. Pharmacologic treatment of **Alzheimer's disease**: an update. Am Fam Physician. 2003 Oct 1; 68(7): 1365-72.

[104] Kindermann SS, Dolder CR, Bailey A, Katz IR, Jeste DV. Pharmacological treatment of **psychosis and agitation** in elderly patients with dementia: four decades of experience. Drugs Aging. 2002; 19(4): 257-76.

[105] Lanctot KL, Herrmann N, Yau KK, et al. Efficacy and safety of **cholinesterase inhibitors** in Alzheimer's disease: a **meta-analysis**. CMAJ. 2003 Sep 16;169(6):557-64.

[106] Trinh NH, Hoblyn J, et al. Efficacy of **cholinesterase inhibitors** in the treatment of neuropsychiatric symptoms and functional impairment in Alzheimer disease: a **meta-analysis**. JAMA. 2003 Jan 8;289(2):210-6.

[107] Wilkinson DG, Passmore AP, et al. A multinational, randomised, 12-week, comparative study of **donepezil** and **rivastigmine** in patients with mild to moderate Alzheimer's disease. Int J Clin Pract. 2002 Jul-Aug;56(6):441-6.

[108] AGS Clinical Practice Committee. Guidelines abstracted from the **American Academy of Neurology's Dementia Guidelines** for Early Detection, Diagnosis, and Management of Dementia. J Am Geriatr Soc. 2003 Jun; 51(6): 869-73.

[109] U.S. Preventive Services Task Force. **Screening for dementia**: recommendation and rationale. Ann Intern Med. 2003 Jun 3; 138(11): 925-6. No abstract available. Summary for patients in: Ann Intern Med. 2003 Jun 3;138(11):I60.

[110] Patterson CJ, Gauthier S, Bergman H, Cohen CA, et al. The recognition, assessment and management of dementing disorders: conclusions from the **Canadian Consensus Conference on Dementia**. (CCCD) CMAJ. 1999 Jun 15; 160(12 Suppl): S1-15.

[111] Bullock R. Cholinesterase inhibitors and **vascular dementia**: another string to their bow? CNS Drugs. 2004; 18(2): 79-92.

[112] Department of Veterans Affairs; Drug Review March 2004 http://www.vapbm.org/reviews/CholinestInh.pdf

[113] Cummings JL. **Alzheimer's disease**. N Engl J Med. **2004** Jul 1;351(1):56-67.

[114] Sink KM, Holden KF, Yaffe K. Pharmacological treatment of **neuropsychiatric** symptoms of dementia: a review of the evidence. **JAMA. 2005** Feb 2;293(5):596-608. (InfoPOEMs: Pharmacologic agents are minimally, if at all, effective in managing the neuropsychiatric symptoms of dementia. The atypical antipsychotics olanzapine (Zyprexa) and risperidone (Risperdal) are the most effective, but these agents may increase the risk of stroke. The decision to use any of these drugs must be made on the basis of individual circumstances. (LOE = 1a-))

[115] Desai AK, Grossberg GT. Diagnosis and treatment of Alzheimer's disease. Neurology. 2005 Jun 28;64(12 Suppl 3):S34-9.

[116] Clinical **Handbook of Psychotropic Drugs** 13th Edition, Bezchlibnyk-Butler K, Jeffries J. 2003

[117] Bentue-Ferrer D, Tribut O, Polard E, Allain H. Clinically significant drug interactions with cholinesterase inhibitors: a guide for neurologists. CNS Drugs. 2003; 17(13): 947-63.

[118] Pollock BG, et al. Comparison of **citalopram**, perphenazine, and placebo for the acute treatment of psychosis and behavioral disturbances in hospitalized, demented patients. Am J Psychiatry. 2002 Mar;159(3):460-5.

[119] Nyth AL, et al. A controlled multicenter clinical study of **citalopram** and placebo in elderly depressed patients with and without concomitant dementia. Acta Psychiatr Scand. 1992 Aug;86(2):138-45.

[120] Nyth AL, Gottfries CG. The clinical efficacy of **citalopram** in treatment of emotional disturbances in dementia disorders. A Nordic multicentre study. Br J Psychiatry. 1990 Dec;157:894-901.

Seitz DP, Adunuri N, Gill SS, et al. Antidepressants for agitation and psychosis in dementia. Cochrane Database Syst Rev. 2011 Feb 16;2:CD008191. Currently there are relatively few studies of antidepressants for the treatment of agitation and psychosis in dementia. The SSRIs sertraline and citalopram were associated with a reduction in symptoms of agitation when compared to placebo in two studies. Both SSRIs and trazodone appear to be tolerated reasonably well when compared to placebo, typical antipsychotics and atypical antipsychotics.

[121] Modell JG, Katholi CR, Modell JD, et. al. Comparative **sexual side effects** of bupropion fluoxetine, paroxetine, and sertraline. Clin Pharmacol Ther 1997;61(4):476-87.

[122] Gonzalez M, Llorca G, Izquierdo JA, et.al. J Sex Marital Ther 1997;23(3):176-94.

[123] Petracca GM, Chemerinski E, Starkstein SE. A double-blind, placebo-controlled study of **fluoxetine** in depressed patients with Alzheimer's disease. Int Psychogeriatr. 2001 Jun; 13(2): 233-40.
[124] Olafsson K, Jorgensen S, Jensen HV, Bille A, Arup P, Andersen J. **Fluvoxamine** in the treatment of demented elderly patients: a double-blind, placebo-controlled study. Acta Psychiatr Scand. 1992 Jun; 85(6): 453-6.
[125] Katona CL, Hunter BN, Bray J. A double-blind comparison of the efficacy and safely of **paroxetine** and **imipramine** in the treatment of depression with dementia. Int J Geriatr Psychiatry. 1998 Feb; 13(2): 100-8.
[126] Schatzberg AF, Kremer C, Rodrigues HE, Murphy GM Jr; Mirtazapine vs. Paroxetine Study Group. Double-blind, randomized comparison of mirtazapine and paroxetine in elderly depressed patients. Am J Geriatr Psychiatry. 2002 Sep-Oct; 10(5): 541-50.
[127] Lyketsos CG, et al. Randomized, placebo-controlled, double-blind clinical trial of **sertraline** in the treatment of depression complicating Alzheimer's: initial results from the Depression in Alzheimer's Disease study. Am J Psychiatry. 2000 Oct;157(10):1686-9.
[128] Lyketsos CG, DelCampo L, et al. Treating depression in Alzheimer disease: efficacy and safety of **sertraline** therapy, and the benefits of depression reduction: the DIADS. Arch Gen Psychiatry. 2003 Jul; 60(7): 737-46.
[129] Mulsant BH, Pollock BG, Nebes R, et al. A twelve-week, double-blind, randomized comparison of **nortriptyline** and **paroxetine** in older depressed inpatients and outpatients. Am J Geriatr Psychiatry. 2001 Fall; 9(4): 406-14.
[130] Shumaker SA, et al; **Estrogen plus progestin** & the incidence of dementia & mild cognitive impairment in postmenopausal women: Women's Health Initiative Memory Study: randomized controlled trial. JAMA.2003May28;289(20): 2651-62. (WHIMS)
Mulnard RA, et al. **Estrogen replacement** therapy for treatment of mild to moderate Alzheimer disease: a randomized controlled trial. Alzheimer's Disease Cooperative Study. JAMA. 2000 Feb 23; 283(8): 1007-15. Erratum: JAMA 2000 Nov 22-29;284(20):2597.
Shao H, Breitner JCS, Whitmer RA, et al. **Hormone therapy and Alzheimer** disease dementia: new findings from the **Cache County Study**. Neurology 2012;79:1846 –1852.
[131] Etminan M, Gill S, Samii A. Effect of non-steroidal a**nti-inflammatory** drugs on risk of Alzheimer's disease: systematic review and meta-analysis of observational studies. BMJ. 2003 Jul 19; 327(7407): 128.
Ad2000 Collaborative Group. **Aspirin 75mg/d in Alzheimer's disease** (AD2000): a randomised open-label trial. Lancet Neurol. 2007 Dec 6; [Epub ahead of print] n=310. Although aspirin is commonly used in dementia, in patients with typical AD 2 years of treatment with low-dose aspirin has no worthwhile benefit and increases the risk of serious bleeds.
Martyn C. **Anti-inflammatory** drugs and Alzheimer's disease. BMJ. 2003 Aug 16;327(7411):353-4.
Tabet N, Feldmand H. **Ibuprofen** for Alzheimer's disease. Cochrane Database Syst Rev. 2003;(2):CD004031. (Naproxen 220 mg BID and celecoxib 200 mg BID or placebo. do not prevent AD in early results from a randomized controlled trial. **ADAPT** Research Group Neurology. 2007 Apr 25; [Epub ahead of print] These results do not support the hypothesis that celecoxib or naproxen prevent Alzheimer dementia, at least within the early years after initiation of treatment. Masked long-term follow-up of these participants will be essential. Kang JH, Cook N, Manson J, Buring JE, Grodstein F. Low dose aspirin and cognitive function in the **Women's Health Study** cognitive cohort. BMJ. 2007 Apr 27; [Epub ahead of print] n=6377 mean 9.6yr. Long term use of low dose aspirin (100mg on alternate days) does not provide overall benefits for cognition among generally healthy women aged 65 or more.)
ADAPT Research Group. Cognitive Function Over Time in the Alzheimer's Disease Anti-inflammatory Prevention Trial (ADAPT): Results of a Randomized, Controlled Trial of Naproxen and Celecoxib. Arch Neurol. 2008 May 12. [Epub ahead of print] Use of naproxen or celecoxib did not improve cognitive function. There was weak evidence for a detrimental effect of naproxen.
Arvanitakis Z, Grodstein F, Bienias JL, Schneider JA, Wilson RS, Kelly JF, Evans DA, Bennett DA. Relation of NSAIDs to incident AD, change in cognitive function, and AD pathology. Neurology. 2008 Jun 3;70(23):2219-25. These data do not support a strong relation between nonsteroidal anti-inflammatory drugs and Alzheimer disease or cognition. Consistent findings across clinical and pathologic outcomes provide additional confidence in these results.
Price JF, Stewart MC, et al. AAA Trialists. Low dose aspirin and cognitive function in middle aged to elderly adults: randomised controlled trial. BMJ. 2008 Sep 1;337:a1198. doi: 10.1136/bmj.a1198. Low dose aspirin (100 mg daily) or placebo for five years. Low dose aspirin does not affect cognitive function in middle aged to elderly people at increased cardiovascular risk.
Jaturapatporn D, Isaac MG, McCleery J, et al. Aspirin, steroidal and non-steroidal anti-inflammatory drugs for the treatment of Alzheimer`s disease. Cochrane Database Syst Rev. 2012 Feb 15;2:CD006378. Based on the studies carried out so far, the efficacy of aspirin, steroid and NSAIDs (traditional NSAIDs and COX-2 inhibitors) is not proven. Therefore, these drugs cannot be recommended for the treatment of AD.
Meyer PF, Tremblay-Mercier J, Leoutsakos J, Madjar C, Lafaille-Maignan MÉ, Savard M, Rosa-Neto P, Poirier J, Etienne P, Breitner J; PREVENT-AD Research Group. **INTREPAD**: A randomized trial of naproxen to slow progress of presymptomatic Alzheimer disease. Neurology. 2019 Apr 30;92(18):e2070-e2080.

[132] Le Bars PL, Katz MM, Berman N, et al. A placebo-controlled, double-blind, randomized trial of an extract of **Ginkgo** biloba for dementia. North American EGb Study Group. JAMA. 1997 Oct 22-29;278(16):1327-32.
van Dongen MC, et al. The efficacy of **ginkgo** for elderly people with dementia & age-associated memory impairment: new results of a randomized trial. J Am Geriatr Soc. 2000 Oct;48(10):1183-94.
Birks J, Grimley EV, Van Dongen M. **Ginkgo** biloba for cognitive impairment and dementia. Cochrane Database Syst Rev. 2002;(4):CD003120.
Dekosky ST, Williamson JD, Fitzpatrick AL, Kronmal RA, Ives DG, Saxton JA, Lopez OL, Burke G, Carlson MC, Fried LP, Kuller LH, Robbins JA, Tracy RP, Woolard NF, Dunn L, Snitz BE, Nahin RL, Furberg CD; for the Ginkgo Evaluation of memory (**GEM**) Study Investigators. Ginkgo biloba for Prevention of Dementia: A Randomized Controlled Trial. JAMA. 2008 Nov 19;300(19):2253-2262. In this study, G biloba at 120 mg twice a day was not effective in reducing either the overall incidence rate of dementia or AD incidence in elderly individuals with normal cognition or those with MCI.
Snitz Beth E.; O'Meara Ellen S.; Carlson Michelle C.; et al. for the Ginkgo Evaluation of Memory (**GEM**) Study Investigators. Ginkgo biloba for Preventing Cognitive Decline in Older Adults: A Randomized Trial. JAMA. 2009;302(24):2663-2670. Compared with placebo, the use of G biloba, 120 mg twice daily, did not result in less cognitive decline in older adults with normal cognition or with mild cognitive impairment.
Geng J, Dong J, Ni H, et al. **Ginseng** for cognition. Cochrane Database of Systematic Reviews 2010, Issue 12. Art. No.: CD007769. DOI: 10.1002/14651858.CD007769.pub2. Currently, there is a lack of convincing evidence to show a cognitive enhancing effect of Panax ginseng in healthy participants and no high quality evidence about its efficacy in patients with dementia. Randomized, double-blind, placebo-controlled, parallel group trials with large sample sizes are needed to further investigate the effect of ginseng on cognition in different populations, including dementia patients.
Vellas B, Coley N, Ousset P-J, et al, for the GuidAge Study Group. Long-term use of standardised **ginkgo biloba extract** for the prevention of Alzheimer's disease (**GuidAge**): a randomised placebo-controlled trial. Lancet Neurol 2012; online Sept 6
[133] Rockwood K, Kirkland S, Hogan DB, MacKnight C, Merry H, Verreault R, Wolfson C, McDowell I. Use of lipid-lowering agents, indication bias, and the risk of dementia in community-dwelling elderly people. Arch Neurol. 2002 Feb;59(2):223-7.
Scott HD, Laake K. **Statins** for the prevention of Alzheimer's disease. Cochrane Database Syst Rev. 2001;(4):CD003160.
Rea TD, Breitner JC, Psaty BM, et al. **Statin** use and the risk of incident dementia: the cardiovascular health study. Arch Neurol. 2005 Jul;62(7):1047-51. CONCLUSIONS: In this cohort study, statin therapy was not associated with a decreased risk of dementia.
Arvanitakis Z, Schneider JA, Wilson RS, et al. Statins, incident Alzheimer disease, change in cognitive function, and neuropathology. Neurology. 2008 Jan 16; [Epub ahead of print] Overall, **statins were not** related to incident Alzheimer disease (AD) or change in cognition, or continuous measures of AD pathology or infarction.
Feldman HH, Doody RS, Kivipelto M, Sparks DL, Waters DD, Jones RW, Schwam E,Schindler R, Hey-Hadavi J, Demicco DA, Breazna A; On behalf of the **LEADe** Investigators. Randomized controlled trial of atorvastatin in mild to moderate Alzheimer disease. LEADe. Neurology. 2010 Mar 3.
McGuinness B, O`Hare J, Craig D, et al. Statins for the treatment of dementia. Cochrane Database Syst Rev. 2010 Aug 4;8:CD007514. There is insufficient evidence to recommend statins for the treatment of dementia. Analysis from the studies available, including one large RCT, indicate statins have no benefit on the outcome measures ADAS-Cog or MMSE. We need to await full results from CLASP 2008 before we can be certain.
Mielke MM, Zandi PP, Shao H, et al. The 32-year relationship between **cholesterol and dementia** from midlife to late life. Neurology. 2010 Nov 10.
Sano M, Bell KL, Galasko D, et al. A randomized, double-blind, placebo-controlled trial of **simvastatin to treat Alzheimer disease**. Neurology. 2011 Aug 9;77(6):556-63. (no benefit)
[134] Tabet N, Birks J, Grimley Evans J. **Vitamin E** for Alzheimer's disease. Cochrane Database Syst Rev. 2000;(4):CD002854. (Pham DQ, Plakogiannis R. **Vitamin e** supplementation in Alzheimer's disease, Parkinson's disease, tardive dyskinesia, and cataract: part 2. Ann Pharmacother. 2005 Dec;39(12):2065-71. Epub 2005 Nov 15.)
Sano M, Ernesto C, Thomas RG, et al. A controlled trial of selegiline, alpha-tocopherol, or both as treatment for Alzheimer's disease. The Alzheimer's Disease Cooperative Study. N Engl J Med. 1997 Apr 24;336(17):1216-22.
Ronald C. Petersen, Ph.D., M.D., Ronald G. et al., for the Alzheimer's Disease Cooperative Study Group **Vitamin E** and Donepezil for the Treatment of Mild Cognitive Impairment Published at www.nejm.org April 13, 2005
Farina N, Isaac MGEKN, Clark AR, Rusted J, Tabet N. **Vitamin E** for Alzheimer's dementia and mild cognitive impairment.Cochrane Database of Systematic Reviews 2012, Issue 11. Art. No.: CD002854. DOI: 10.1002/14651858.CD002854.pub3. No convincing evidence that vitamin E is of benefit in the treatment of AD or MCI. Future trials assessing vitamin E treatment in AD should not be restricted to alpha-tocopherol.
Dysken MW, Sano M, Asthana S, et al. Effect of **vitamin E 2000IU/d & memantine** on functional decline in Alzheimer disease: **TEAM-AD VA** Cooperative randomized trial. JAMA. doi:10.1001/jama.2013.282834. Dec 31/13.

Kryscio RJ, Abner EL, Caban-Holt A, et al. Association of antioxidant supplement use and dementia in the Prevention of Alzheimer's Disease by Vitamin E and Selenium trial (PREADViSE) [online Mar 20, 2017].JAMA Neurol. doi:10.1001/jamaneurol.2016.5778

Farina N, Llewellyn D, Isaac MGEKN, Tabet N. Vitamin E for Alzheimer's dementia and mild cognitive impairment. Cochrane Database of Systematic Reviews 2017, Issue 4. Art. No.: CD002854.

We found no evidence that the alpha-tocopherol form of vitamin E given to people with MCI prevents progression to dementia, or that it improves cognitive function in people with MCI or dementia due to AD. However, there is moderate quality evidence from a single study that it may slow functional decline in AD. Vitamin E was not associated with an increased risk of serious adverse events or mortality in the trials in this review. These conclusions have changed since the previous update, however they are still based on small numbers of trials and participants and further research is quite likely to affect the results.

[135] Malouf R, Areosa Sastre A. **Vitamin B12** for cognition. Cochrane Database Syst Rev. 2003;(3):CD004326.

Aisen PS, Schneider LS, Sano M, et al. Alzheimer Disease Cooperative Study (ADCS). High-dose B vitamin supplementation and cognitive decline in Alzheimer disease: a randomized controlled trial. JAMA. 2008 Oct 15;300(15):1774-83. This regimen of high-dose B vitamin supplements does not slow cognitive decline in individuals with mild to moderate AD.

Hooshmand B, Solomon A, Kåreholt I, et al. Homocysteine and holotranscobalamin and the risk of Alzheimer disease: A longitudinal study. Neurology. 2010 Oct 19;75(16):1408-14.

van der Zwaluw NL, Dhonukshe-Rutten RA, van Wijngaarden JP, et al. Results **of 2-year vitamin B treatment** on cognitive performance: Secondary data from an RCT. Neurology. 2014 Dec 2;83(23):2158-66.

[136] Forette F, et al. Systolic Hypertension in Europe Investigators. The prevention of dementia with antihypertensive treatment: new evidence from the Systolic Hypertension in Europe (Syst-Eur) study. Arch Intern Med 2002 Oct 14;162(18):2046-52.

Peila R, et al. Reducing the risk of dementia: efficacy of long-term treatment of hypertension. Stroke. 2006 May;37(5):1165-70. Epub 2006 Apr 6.)

[137] Adapted from: Primary Care Management & Pharmacological Management of BPSD, International Psychogeriatric Association, Module 1-8 2002. http://www.ipa-online.org/ipaonlinev3/ipaprograms/bpsdrev/6BPSDfinal.pdf

[138] Hien le TT, Cumming RG, Cameron ID, et al. Atypical antipsychotic medications and risk of falls in residents of aged care facilities. J Am Geriatr Soc. 2005 Aug;53(8):1290-5.

[139] Feldman HH, Ferris S, Winblad B, Sfikas N, Mancione L, He Y, Tekin S, Burns A, Cummings J, del Ser T, Inzitari D, Orgogozo JM, Sauer H, Scheltens P, Scarpini E, Herrmann N, Farlow M, Potkin S, Charles HC, Fox NC, Lane R. Effect of rivastigmine on delay to diagnosis of Alzheimer's disease from mild cognitive impairment: the InDDEx study. Lancet Neurol. 2007 Jun;6(6):501-12.

[140] Massoud F, Belleville S, Bergman H, et al. Mild cognitive impairment and cognitive impairment, no dementia: Part B, therapy. Alzheimers Dement 2007;3:283- 91. Jean L, Bergeron ME, Thivierge S, Simard M. Cognitive intervention programs for individuals with mild cognitive impairment: systematic review of the literature. Am J Geriatr Psychiatry 2010;18:281-96.

Petersen RC, Stevens JC, Ganguli M, Tangalos EG, Cummings JL, DeKosky ST. Practice parameter: early detection of dementia: mild cognitive impairment (an evidence-based review): report of the Quality Standards Subcommittee of the American Academy of Neurology. Neurology 2001;56:1133-42.

[141] Bjerre LM, Farrell B, Hogel M, Graham L, Lemay G, McCarthy L, Raman-Wilms L, Rojas-Fernandez C, Sinha S, Thompson W, Welch V, Wiens A. Deprescribing antipsychotics for behavioural and psychological symptoms of dementia and insomnia: Evidence-based clinical practice guideline. Can Fam Physician. 2018 Jan;64(1):17-27.

Additional references:

Abell JG, Kivimäki M, Dugravot A, et al. Association between **systolic blood pressure and dementia** in the Whitehall II cohort study: role of age, duration, and threshold used to define hypertension. Eur Heart J. 2018 Jun 12.

Abi-Jaoude E, Stall NM, Rochon PA. **Psychotropic drugs for the behavioural and psychological symptoms of dementia**: no free ride. CMAJ. 2018 Nov 26;190(47):E1374-E1375.

Abner EL, Kryscio RJ, Schmitt FA, et al. Outcomes after **diagnosis of mild cognitive impairment in a large autopsy series**. Ann Neurol. 2017 Feb 22.

Acosta-Baena Natalia, Sepulveda-Falla Diego, Lopera-Gomez Carlos Mario, et al. **Pre-dementia** clinical stages in presenilin 1 E280A familial early-onset Alzheimer's disease: a retrospective cohort study, The Lancet Neurology, Vol10, Issue 3, Mar 2011.

Adams DR, Kern DW, Wroblewski KE, et al. **Olfactory Dysfunction** Predicts Subsequent Dementia in Older U.S. Adults. J Am Geriatr Soc. 2017 Sep 25.

Aga VM. When and How to Treat Agitation in Alzheimer's Disease Dementia With **Citalopram and Escitalopram**. Am J Geriatr Psychiatry. 2019 May 10.

Agar MR, Lawlor PG, Quinn S, et al. Efficacy of oral **risperidone, haloperidol, or placebo for symptoms of delirium** among patients in palliative care: a randomized clinical trial [online Dec 5, 2016].JAMA Intern Med. doi:10.1001/jamainternmed.2016.7491

AGS: **American** Geriatrics Society Expert Panel on **Postoperative Delirium in Older Adults**. American Geriatrics Society abstracted clinical practice guideline for postoperative delirium in older adults. J Am Geriatr Soc. 2015 Jan;63(1):142-50.

AHA-ASA-American Heart Association/American Stroke Association. Scientific statement: **Vascular contributions to cognitive impairment and dementia**. *Stroke* 2011; DOI:10.1161/?STR.0b013e3182299496. http://stroke.ahajournals.org/content/early/2011/07/21/STR.0b013e3182299496.full.pdf+html

Ahmadi-Abhari S, et al. **Temporal trend in dementia incidence since 2002 and projections for prevalence in England and Wales to 2040**: modelling study. BMJ 2017;358:j2856.

Ahmed RM, Latheef S, Bartley L, et al. **Eating behavior** in frontotemporal dementia: Peripheral hormones vs hypothalamic pathology. Neurology. 2015 Sep 16.

Akbaraly TN, Singh-Manoux A, Dugravot A, et al. Association of **Midlife Diet With Subsequent Risk** for Dementia. JAMA. 2019 Mar 12;321(10):957-968

Akhlaghi N, Payandemehr P, Yaseri M, et al. **Premedication With Midazolam or Haloperidol to Prevent Recovery Agitation** in Adults Undergoing **Procedural Sedation With Ketamine**: A Randomized Double-Blind Clinical Trial. Ann Emerg Med. 2019

Al-Qadheeb NS, Balk EM, Fraser GL, et al. Randomized ICU Trials Do Not Demonstrate an Association Between Interventions That Reduce **Delirium Duration and Short-Term Mortality**: A Systematic Review and Meta-Analysis. Crit Care Med. 2014 Feb 19.

Alagiakrishnan K, Marrie T, Rolfson D, et al. Gaps in patient care practices to **prevent hospital-acquired delirium**. Can Fam Physician. 2009 Oct;55(10):e41-6.

Albanese E, Lombardo FL, Prince MJ, Stewart R. **Dementia and lower blood pressure** in Latin America, India, and China: A 10/66 cross-cohort study. Neurology. 2013 Jul 16;81(3):228-35.

Albanese E, Matthews KA, Zhang J, et al. **Hostile attitudes** and effortful coping in young adulthood predict cognition 25 years later. Neurology. 2016 Mar 29

Albert MS, DeKosky ST, Dickson D, et al. The diagnosis of mild cognitive impairment due to Alzheimer's disease: recommendations from the National Institute on Aging and Alzheimer's Association workgroup. Alzheimers Dement 2011 April 20 (Epub ahead of print).

Alexopoulos GS, Streim J, et al.; **Expert Consensus Panel** for Using Antipsychotic Drugs in Older Patients. Using antipsychotic agents in older patients. J Clin Psychiatry. 2004;65 Suppl 2:5-99;discussion 100-102;quiz 103-4.

Alhurani RE, Vassilaki M, Aakre JA, et al. **Decline in Weight** and Incident Mild Cognitive Impairment: Mayo Clinic Study of Aging. JAMA Neurol. 2016 Feb 1.

Ali I, Guidone D, Nicolazzo JA, Brouwer KLR. Impact of **Reduced P-glycoprotein Function on Digoxin Concentrations** in Patients with Dementia. Br J Clin Pharmacol. 2019 Jul 3.

Alladi S, Bak TH, Duggirala V, et al. **Bilingualism delays** age at onset of dementia, independent of education and immigration status. Neurology. 2013 Nov 26;81(22):1938-44.

Alladi S, Hachinski V. World dementia: One approach does not fit all. Neurology. 2018 Aug 7;91(6):264-270.

Allan CL, Behrman S, Baruch N, Ebmeier KP. **Driving and dementia**: a clinical update for mental health professionals. Evid Based Ment Health. 2016 Oct 20.

Allen M, Zou F, Chai HS, et al. Novel late-onset Alzheimer disease **loci variants** associate with brain gene expression. Neurology 2012;79:221–228.

Allendorfer JB, Arida RM. Role of **Physical Activity and Exercise** in Alleviating Cognitive Impairment in People With Epilepsy. Clin Ther. 2017 Dec 20

Almaraz AC, Driver-Dunckley ED, Woodruff BK, et al. Efficacy of rivastigmine for cognitive symptoms in **Parkinson** disease with dementia. Neurologist. 2009 Jul;15(4):234-7. Rivastigmine therapy for PDD is associated with significant tradeoffs in efficacy and adverse effects. Carefully monitored trials of rivastigmine may provide meaningful benefits for a minority of PDD patients.

Almeida OP, Hankey GJ, Yeap BB, et al. **Alcohol consumption** and cognitive impairment in older men: A mendelian randomization study. Neurology. 2014 Mar 25;82(12):1038-44.

Alosco ML, Stein TD, Tripodis Y, et al. Association of **White Matter Rarefaction, Arteriolosclerosis, and Tau With Dementia** in Chronic Traumatic Encephalopathy. JAMA Neurol. 2019 Aug 5.

Altmann A, Tian L, Henderson VW, et al; Alzheimer's Disease Neuroimaging Initiative Investigators. **Sex modifies the APOE-related risk** of developing Alzheimer disease. Ann Neurol. 2014 Mar 13.

Amariglio RE, Townsend MK, Grodstein F, et al. **Specific Subjective Memory Complaints** in Older Persons May Indicate Poor Cognitive Function. J Am Geriatr Soc. 2011 Sep 15.

Amariglio RE, Donohue MC, Marshall GA, et al; for the Alzheimer's Disease Cooperative Study. **Tracking Early Decline in Cognitive Function** in Older Individuals at Risk for Alzheimer Disease Dementia: The Alzheimer's Disease Cooperative Study Cognitive Function Instrument. JAMA Neurol. 2015 Feb 23.

Amato MP, Hakiki B, Goretti B, et al. Association of **MRI metrics** and cognitive impairment in radiologically isolated syndromes. Neurology. 2012 Jan 31;78(5):309-314.

Amieva H, Mokri H, Le Goff M, et al. Compensatory mechanisms in **higher-educated** subjects with Alzheimer's disease: a study of 20 years of cognitive decline. Brain. 2014 Apr;137(Pt 4):1167-75.

Amjad H, Roth DL, Samus QM, et al. **Potentially Unsafe Activities and Living Conditions** of Older Adults with Dementia. J Am Geriatr Soc. 2016 Jun 2.

Ancelin ML, et al. Non-degenerative mild **cognitive impairment** in elderly people and use of **anticholinergic** drugs: longitudinal cohort study. BMJ. 2006 Feb 25;332(7539):455-9. Epub 2006 Feb 1.
CONCLUSIONS: Elderly people taking anticholinergic drugs had significant deficits in cognitive functioning and were highly likely to be classified as mildly cognitively impaired, although not at increased risk for dementia. Doctors should assess current use of anticholinergic drugs in elderly people with mild cognitive impairment before considering administration of acetylcholinesterase inhibitors.

Anderson Craig, Teo Koon, Gao Peggy, et al. and for the **ONTARGET and TRANSCEND Investigators, Renin-angiotensin system blockade** and cognitive function in patients at high risk of cardiovascular disease: analysis of data from the ONTARGET and TRANSCEND studies, The Lancet Neurology, Volume 10, Issue 1, January 2011, Pages 43-53, ISSN 1474-4422, DOI: 10.1016/S1474-4422(10)70250-7. (no clear benefits)

Andrieu S, Guyonnet S, Coley N, et al, for the **MAPT** Study Group. Effect of **long-term omega-3 polyunsaturated fatty acid supplementation** with or without multidomain intervention on cognitive function in elderly adults with memory complaints (**MAPT**): a randomised, placebo-controlled trial. Lancet Neurol 2017; online Mar 27.

Andre L, Gallini A, Montastruc F, et al. **Anticholinergic exposure and cognitive decline** in older adults: Effect of anticholinergic exposure definitions in a 3-year analysis of the Multidomain Alzheimer Preventive Trial (MAPT) study. Br J Clin Pharmacol. 2018 Aug 10.

Anticholinergic Cognitive Burden (ACB) scale http://www.indydiscoverynetwork.org/AnticholinergicCognitiveBurdenScale.html

Arenaza-Urquijo EM, Gonneaud J, Fouquet M, et al. Interaction between years of education and APOE ε4 status on frontal and temporal metabolism. Neurology. 2015 Oct 20;85(16):1392-9.

Arendash G, Cao C, Abulaban H, et al. A Clinical Trial of Transcranial Electromagnetic Treatment in Alzheimer's Disease: Cognitive Enhancement and Associated Changes in Cerebrospinal Fluid, Blood, and Brain Imaging. J Alzheimers Dis. 2019;71(1):57-82.

Arevalo-Rodriguez I, Smailagic N, Roque I Figuls M, et al. **Mini-Mental State Examination (MMSE) for** the detection of **Alzheimer**`s disease and other dementias in people with mild cognitive impairment (MCI). Cochrane Database Syst Rev. 2015 Mar 5;3:CD010783. Our review did not find evidence supporting a substantial role of MMSE as a stand-alone single-administration test in the identification of MCI patients who could develop dementia. Clinicians could prefer to request additional and extensive tests to be sure about the management of these patients. An important aspect to assess in future updates is if conversion to dementia from MCI stages could be predicted better by MMSE changes over time instead of single measurements. It is also important to assess if a set of tests, rather than an isolated one, may be more successful in predicting conversion from MCI to dementia.

Arnoldussen IAC, Gustafson DR, Leijsen EMC, et al. **Adiposity is related to cerebrovascular and brain volumetry** outcomes in the RUN DMC study. Neurology. 2019 Aug 27;93(9):e864-e878.

Arvanitakis Z, et al. Relation of **cerebral vessel disease** to Alzheimer's disease dementia and cognitive function in elderly people: cross-sectional study. Lancet Neurol 2016; online June 13.

Arvanitakis Z, Capuano AW, Lamar M, et al. **Late-life blood pressure association with cerebrovascular and Alzheimer disease** pathology. Neurology. 2018 Jul 11.

Aslam RW, Bates V, Dundar Y, et al. **Automated tests for diagnosing and monitoring cognitive impairment**: a diagnostic accuracy review. Health Technol Assess. 2016 Oct;20(77):1-74.

Atri A, Frölich L, Ballard C, et al. Effect of **idalopirdine** as adjunct to cholinesterase inhibitors on change in cognition in patients with Alzheimer disease: three randomized clinical trials. JAMA. doi:10.1001/jama.2017.20373

Aubert CE, et al. The association between **subclinical thyroid dysfunction and dementia**: the Health, Aging and Body Composition (**Health ABC**) Study. Clin Endocrinol (Oxf). 2017 Aug 29.

Avidan MS, Maybrier HR, Ben Abdallah A, et al, on behalf of the PODCAST Research Group. Intraoperative **ketamine** for prevention of postoperative delirium or pain after major surgery in older adults: an international, multicentre, double-blind, randomised clinical trial. Lancet 2017; online May 30.

Axelrud LK, et al. **Polygenic Risk Score** for Alzheimer's Disease: Implications for Memory Performance and Hippocampal Volumes in Early Life. Am J Psychiatry. 2018 Mar 2:appiajp201717050529.

Axley M, Schenning KJ. **Preoperative cognitive and frailty screening in the geriatric surgical patient**: a narrative review. Clin Ther. 2015;37:xxx–xxx

Axona (Accera) Medical Letter June 29, 2009. (Medical food containing medium-chain triglycerides –insufficient evidence.

Baakman AC, Alvarez-Jimenez R, Rissmann R, et al. An **Anti-Nicotinic Cognitive Challenge Model using Mecamylamine** in Comparison with the Anti-Muscarinic Cognitive Challenge using Scopolamine. Br J Clin Pharmacol. 2017 Feb 20.

Bagge CN, Henderson VW, Laursen HB, et al. Risk of **Dementia in Adults With Congenital Heart Disease**: Population-Based Cohort Study. Circulation. 2018 Feb 12.

Baik SH, et al. Risk of Alzheimer's Disease Among Senior Medicare Beneficiaries **Treated With Androgen Deprivation Therapy for Prostate Cancer**. J Clin Oncol. 2017 Oct 20;35(30):3401-3409.

Bak TH, Nissan JJ, Allerhand MM, et al. Does **bilingualism** influence cognitive aging? Ann Neurol. 2014 Jun 2.

Balasa M., Gelpi E., Antonell A., et al. and For the Neurological Tissue Bank/University of Barcelona/Hospital Clínic NTB/UB/HC Collaborative Group. Clinical features and APOE genotype of pathologically proven **early-onset Alzheimer** disease Neurology May 17, 2011 76:1720-1725. (1/3 present with atypical features)

Baldi I et al. Neurobehavioral effects of long-term exposure to **pesticides**: Results from the 4-year follow-up of the PHYTONER Study. Occup Environ Med 2010 Nov 22

Ball J et al. **Mild cognitive impairment** in high-risk patients with **chronic atrial fibrillation**: A forgotten component of clinical management? Heart 2013 Jan 12.

Ballard C, Waite J. The effectiveness of **atypical antipsychotics** for the treatment of **aggression and psychosis in Alzheimer's disease**. Cochrane Database Syst Rev. 2006 Jan 25;(1):CD003476.

Ballard C, Hanney ML, Theodoulou M, et al; the **DART-AD** investigators. The dementia antipsychotic withdrawal trial (DART-AD): long-term follow-up of a randomised placebo-controlled trial. Lancet Neurol. 2009 Jan 8. [Epub ahead of print] There is an increased long-term risk of mortality in patients with AD who are prescribed antipsychotic medication; these results further highlight the need to seek less harmful alternatives for the long-term treatment of neuropsychiatric symptoms in these patients.

Ballard C, Gauthier S, Corbett A, et al. **Alzheimer's** disease. Lancet. 2011 Mar 19;377(9770):1019-31.

Ballard C, Corbett A. Management of **neuropsychiatric symptoms** in people with dementia. CNS Drugs. 2010 Sep 1;24(9):729-39. doi:10.2165/11319240-000000000-00000.

Ballard C, Orrell M, Yong Zhong S, et al. Impact of **Antipsychotic Review and Nonpharmacological Intervention on Antipsychotic Use, Neuropsychiatric Symptoms**, and Mortality in People With Dementia Living in Nursing Homes: A Factorial Cluster-Randomized Controlled Trial by the Well-Being and Health for People With Dementia (**WHELD**) Program. Am J Psychiatry. 2015 Nov 20:appiajp201515010130.

Ballard C, Corbett A, Orrell M, et al. Impact of **person-centred care training and person-centred activities** on quality of life, agitation, and antipsychotic use in people with dementia living in nursing homes: A cluster-randomised controlled trial. PLoS Med. 2018 Feb 6;15(2):e1002500.

Ballard C, Banister C, Khan Z, et al, for the ADP Investigators. Evaluation of the safety, tolerability, and efficacy of **pimavanserin** versus placebo in patients with Alzheimer's disease **psychosis**: a phase 2, randomised, placebo-controlled, double-blind study. Lancet Neurol 2018; 17: 213–22.

Banerjee S, Hellier J, Dewey M, et al. **Sertraline** (150mg/day) **or mirtazapine** (45mg/day) for depression in dementia (**HTA-SADD**): a randomised, multicentre, double-blind, placebo-controlled trial. Lancet 2011; July 18.

Barak Y, Plopski I, Tadger S, et al. **Escitalopram versus risperidone** for the treatment of behavioral and psychotic symptoms associated with Alzheimer's disease: a randomized double-blind pilot study. Int Psychogeriatr. 2011 Apr 15:1-5.

Barnes DE, Covinsky KE, Whitmer RA, Kuller LH, Lopez OL, Yaffe K. Predicting risk of dementia in older adults. The **late-life dementia risk index**. Neurology. 2009 May 13. [Epub ahead of print]

Barnes Deborah E, Yaffe Kristine, The projected effect of **risk factor reduction** on Alzheimer's disease prevalence, The Lancet Neurology, online 19 July 2011

Barnes DE, Yaffe K, Byers AL, et al. **Midlife vs Late-Life Depressive Symptoms** and Risk of Dementia: Differential Effects for Alzheimer Disease and Vascular Dementia. Arch Gen Psychiatry. 2012 May;69(5):493-8.

Barnes DE, Santos-Modesitt W, Poelke G, et al. The **Mental Activity and eXercise (MAX)** Trial: a randomized controlled trial to enhance cognitive function in older adults [online April 1, 2013]. JAMA Intern Med.

Barnes DE, Kaup A, Kirby KA, et al. **Traumatic brain injury** and risk of dementia in older veterans. Neurology. 2014 Jul 22;83(4):312-9.

Barnes DE, Byers AL, Gardner RC, et al. Association of mild **traumatic brain injury** with and without loss of consciousness with dementia in US military veterans [online May 7, 2018]. JAMA Neurol.

Barnes LL, Leurgans S, Aggarwal NT, et al. **Mixed pathology** is more likely in **black than white** decedents with Alzheimer dementia. Neurology. 2015 Aug 11;85(6):528-34.

Bartels C, et al. Impact of **SSRI Therapy on Risk of Conversion From Mild Cognitive Impairment to Alzheimer's** Dementia in Individuals With Previous Depression. Am J Psychiatry. 2017 Nov 28:appiajp201717040404.

Barthel H, Gertz HJ, Dresel S, et al. for the **Florbetaben** Study Group. Cerebral amyloid-β PET with florbetaben ((18)F) in patients with Alzheimer's disease and healthy controls: a multicentre phase 2 diagnostic study. Lancet Neurol. 2011 Apr 8.

Bartorelli L, et al.; Upgrade Study Group. Effects of **switching** from an AChE inhibitor to a dual AChE-BuChE inhibitor in patients with Alzheimer's disease. Curr Med Res Opin. 2005 Nov;21(11):1809-18.

Barzilay Joshua I.; Gao Peggy; O'Donnell Martin; et al. for the ONTARGET and TRANSCEND Investigators. **Albuminuria and Decline in Cognitive Function**: The ONTARGET/TRANSCEND Studies. Arch Intern Med. 2011;171(2):142-150.

Bateman RJ, Xiong C, Benzinger TL, et al; the Dominantly Inherited Alzheimer Network. Clinical and **Biomarker** Changes in Dominantly Inherited Alzheimer's Disease. N Engl J Med. 2012 Jul 11.

Bathula M, Gonzales JP. The pharmacologic **treatment of intensive care unit delirium**: a systematic review. Ann Pharmacother. 2013 Sep;47(9):1168-74.

Bayer-Carter JL, Green PS, Montine TJ, et al. **Diet intervention** and cerebrospinal fluid biomarkers in amnestic mild cognitive impairment. Arch Neurol. 2011 Jun;68(6):743-52.

Beckett TL, Webb RL, Niedowicz DM, et al. Postmortem **Pittsburgh Compound B (PiB)** Binding Increases with Alzheimer's Disease Progression. J Alzheimers Dis. 2012 Jul 5.

Belle SH, et al. Resources for Enhancing Alzheimer's Caregiver Health (**REACH**) II Investigators. Enhancing the quality of life of dementia caregivers from different **ethnic or racial groups**: a randomized, controlled trial. Ann Intern Med. 2006 Nov 21;145(10):727-38.

Bellelli G, Morandi A, Davis DH, et al. **Validation of the 4AT, a new instrument for rapid delirium screening**: a study in 234 hospitalised older people. Age Ageing. 2014 Jul;43(4):496-502.

Bellelli G, Morandi A, Di Santo SG, et al. "**Delirium Day**": a nationwide point prevalence study of delirium in older hospitalized patients using an easy standardized diagnostic tool. BMC Med. 2016 Jul 18;14:106

Belleville S, Hudon C, Bier N, et al. **MEMO+:** Efficacy, Durability and Effect of Cognitive Training and Psychosocial Intervention in Individuals with Mild Cognitive Impairment. J Am Geriatr Soc. 2018 Jan 4.

Benedictus MR, Prins ND, Goos JD, et al. **Microbleeds, Mortality, and Stroke** in Alzheimer Disease: The MISTRAL Study. JAMA Neurol. 2015 Mar 23.

Benito-León J, Romero JP, Louis ED, et al. Faster cognitive decline in elders without dementia and decreased risk of **cancer mortality**: NEDICES Study. Neurology. 2014 Apr 22;82(16):1441-8.

Benito-León J, Louis ED, Villarejo-Galende A, et al. Long sleep duration in elders without dementia increases risk of dementia mortality (NEDICES). Neurology. 2014 Oct 21;83(17):1530-7.

Benn M, Nordestgaard BG, et al. Low LDL cholesterol, PCSK9 and HMGCR genetic variation, and risk of Alzheimer's disease and Parkinson's disease: Mendelian randomisation study. BMJ. 2017 Apr 24;357:j1648.

Benussi A, Di Lorenzo F, Dell'Era V, et al. Transcranial magnetic stimulation distinguishes **Alzheimer** disease from **frontotemporal dementia**. Neurology. 2017 Jul 26.

Berende A, Ter Hofstede HJM, Vos FJ, et al. Effect of **prolonged antibiotic treatment on cognition** in patients with Lyme borreliosis. Neurology. 2019 Mar 26;92(13):e1447-e1455

Bergh S, Selbæk G, Engedal K. **Discontinuation of antidepressants** in people with dementia and neuropsychiatric symptoms (DESEP study): double blind, randomised, parallel group, placebo controlled trial. BMJ. 2012 Mar 9;344:e1566.

Bergman J, Dwolatzky T, Brettholz I, Lerner V. Beneficial effect of **donepezil** in the treatment of elderly patients with **tardive movement** disorders. J Clin Psychiatry. 2005 Jan;66(1):107-10.

Bergeron N, Dubois MJ, Dumont M, Dial S, Skrobik Y. Intensive care **delirium** screening checklist: evaluation of a new **screening tool**. Intensive Care Med 2001;27:859-64.

Bernick C, Cummings J, Raman R, et al. **Age and Rate of Cognitive Decline** in Alzheimer Disease: Implications for Clinical Trials. Arch Neurol. 2012 Mar 19.

Bernier PJ, Gourdeau C, Carmichael P-H, et al. **Validation and diagnostic accuracy of predictive curves for age-associated longitudinal cognitive decline** in older adults. CMAJ 2017;189:1472-80.

Berntsen S, Kragstrup J, Siersma V, et al. Alcohol consumption and mortality in patients with mild Alzheimer's disease: a prospective cohort study. BMJ Open. 2015 Dec 11;5(12):e007851.

Berry SD, Rothbaum RR, Kiel DP, et al. Association of **Clinical Outcomes With Surgical Repair of Hip Fracture vs Nonsurgical Management** in Nursing Home **Residents With Advanced Dementia**. JAMA Intern Med. 2018 May 7.

Berthier ML, et al. A randomized, placebo-controlled study of **donepezil** in **poststroke aphasia**. Neurology. 2006 Nov 14;67(9):1687-9. n=16

Bettens K, Sleegers K, Van Broeckhoven C. **Genetic insights** in Alzheimer's disease. Lancet Neurol. 2013 Jan;12(1):92-104.

Beynel L, Davis SW, Crowell CA, et al. Online repetitive **transcranial magnetic stimulation during working memory in younger and older adults**: A randomized within-subject comparison. PLoS One. 2019 Mar 22;14(3):e0213707.

Biffi A, Bailey D, Anderson CD, et al. Risk Factors Associated With Early vs Delayed Dementia **After Intracerebral Hemorrhage**. JAMA Neurol. 2016 Jun 13.

Billioti de Gage S, Bégaud B, Bazin F, Verdoux H, et al. **Benzodiazepine use** and risk of dementia: prospective population based study. BMJ. 2012 Sep 27;345:e6231.

Birks J, Harvey RJ. **Donepezil** for dementia due to Alzheimer's disease. Cochrane Database Syst Rev 2006; 1: CD001190.

Birks JS, Harvey RJ. **Donepezil for dementia due to Alzheimer's disease**. Cochrane Database of Systematic Reviews 2018, Issue 6. Art. No.: CD001190. There is moderate-quality evidence that people with mild, moderate or severe dementia due to Alzheimer's disease treated for periods of 12 or 24 weeks with donepezil experience small benefits in cognitive function, activities of daily living and clinician-rated global clinical state. There is some evidence that use of donepezil is neither more nor less expensive compared with placebo when assessing total healthcare resource costs. Benefits on 23 mg/day were no greater than on 10 mg/day, and benefits on the 10 mg/day dose were marginally larger than on the 5 mg/day dose, but the rates of withdrawal and of adverse events before end of treatment were higher the higher the dose.

Birks J, Grimley Evans J, Iakovidou V, Tsolaki M, Holt FE. **Rivastigmine** for Alzheimer's disease. Cochrane Database Syst Rev. 2009 Apr 15;(2):CD001191.

Bjerre LM, Farrell B, et al. **Deprescribing antipsychotics for behavioural and psychological symptoms of dementia and insomnia**: Evidence-based clinical practice guideline. Can Fam Physician. 2018 Jan;64(1):17-27.

Black SE, Doody R, Li H, et al. **Donepezil** preserves cognition and global function in patients with **severe Alzheimer disease**. Neurology. 2007 Jul 31;69(5):459-69.

Black BS, Johnston D, Rabins PV, et al. **Unmet needs of community-residing persons** with dementia and their informal caregivers: findings from the maximizing independence at home study. J Am Geriatr Soc. 2013 Dec;61(12):2087-95

Blackwell T, Yaffe K, Ancoli-Israel S, et al; Osteoporotic Fractures in Men Study Group. Associations between sleep architecture and **sleep-disordered breathing** and cognition in older community-dwelling men: the Osteoporotic Fractures in Men Sleep Study. J Am Geriatr Soc. 2011 Dec;59(12):2217-25.

Blennow K, Zetterberg H, Rinne JO, et al. Effect of Immunotherapy With **Bapineuzumab** on Cerebrospinal Fluid Biomarker Levels in Patients With Mild to Moderate Alzheimer Disease. Arch Neurol. 2012 Apr 2.

Blumenthal JA, Smith PJ, Mabe S, et al**. Lifestyle and neurocognition** in older adults with cognitive impairments: A randomized trial. Neurology. 2018 Dec 19.

Blumenthal JA, Smith PJ, Mabe S, et al. **Lifestyle and neurocognition** in older adults with cognitive impairments: A randomized trial. Neurology. 2019 Jan 15;92(3):e212-e223.

Boccardi M et al. Assessment of the incremental diagnostic value of **florbetapir F 18 imaging** in patients with cognitive impairment: The Incremental Diagnostic Value of Amyloid PET With [18F]-Florbetapir (INDIA-FBP) study. JAMA Neurol 2016 Oct 31.

Böhm M, Schumacher H, Leong D, et al. **Systolic blood pressure variation and mean heart rate** is associated with cognitive dysfunction in patients with high cardiovascular risk. *Hypertension* 2015.

Boots EA, Schultz SA, Clark LR, et al. **BDNF Val66Met** predicts cognitive decline in the Wisconsin Registry for Alzheimer's Prevention. Neurology. 2017 May 30;88(22):2098-2106.

Bosch J, O'Donnell M, Swaminathan B, et al; HOPE-3 Investigators. Effects of **blood pressure and lipid lowering on cognition**: Results from the HOPE-3 study. Neurology. 2019 Mar 26;92(13):e1435-e1446.

Bougea A, Gerakoulis S, Anagnostou E, et al. **Donepezil-induced myoclonus** in a patient with Alzheimer disease. Ann Pharmacother. 2014 Dec;48(12):1659-61.

Bove R, Secor E, Chibnik LB, et al. **Age at surgical menopause influences cognitive decline** and Alzheimer pathology in older women. Neurology 2014;82:222–229.

Bowman K, Jones L, Pilling LC, et al. **Vitamin D levels and risk of delirium**: A mendelian randomization study in the UK Biobank. Neurology. 2019 Mar 19;92(12):e1387-e1394.

Boxer AL, Knopman DS, Kaufer DI, et al. **Memantine** in patients with **frontotemporal lobar degeneration**: a multicentre, randomised, double-blind, placebo-controlled trial. Lancet Neurol. 2012 Dec 28.

Boyd CD, Tierney M, Wassermann EM, et al. **Visuoperception test** predicts pathologic diagnosis of Alzheimer disease in corticobasal syndrome. Neurology. 2014 Aug 5;83(6):510

Boyle PA et al. Scam **awareness related to incident Alzheimer dementia and mild cognitive impairment**: A prospective cohort study. Ann Intern Med 2019 Apr 16.

Boyle PA, Buchman AS, Wilson RS, et al. Effect of **purpose in life** on the relation between Alzheimer disease pathologic changes on cognitive function in advanced age. Arch Gen Psychiatry. 2012 May;69(5):499-504.

Boyle PA, Yu L, Schneider JA, et al. **Scam Awareness** Related to Incident Alzheimer Dementia and Mild Cognitive Impairment: A Prospective Cohort Study. Ann Intern Med. 2019 Apr 16.

Brasure M, Desai P, Davila H, et al. **Physical activity interventions** in preventing cognitive decline and Alzheimer-type dementia. A systematic review. Ann Intern Med. 2018;168:30-8.

Brayne C, Matthews FE. **The determinants of cognitive decline and dementia**. BMJ. 2019 Aug 7;366:l4946.

Bredesen DE. **Reversal of cognitive decline**: A novel therapeutic program. Aging(Albany NY). 2014 Sep;6(9):707-17.

Breen DA, Breen DP, Moore JW, Breen PA, O'Neill D. **Driving and dementia**. BMJ. 2007 Jun 30;334(7608):1365-9.

Breitbart W, Alici Y. Agitation and **delirium** at the end of life: "We couldn't manage him". JAMA. 2008 Dec 24;300(24):2898-910, E1.

Breitbart W, et al. A double-blind trial of **haloperidol**, chlorpromazine, and lorazepam in the treatment of **delirium** in hospitalized AIDS patients. Am J Psychiatry. 1996 Feb;153(2):231-7.

Briesacher BA et al. **Antipsychotic use among nursing home residents**. JAMA 2013 Feb 6; 309:440.

Brodaty H, Ames D, Snowdon J, et al. **Risperidone** for psychosis of Alzheimer's disease and mixed dementia: results of a double-blind, placebo-controlled trial. Int J Geriatr Psychiatry. 2005 Dec;20(12):1153-7.

Brodaty H, Arasaratnam C. Meta-analysis of **nonpharmacological interventions** for neuropsychiatric symptoms of dementia.Am J Psychiatry. 2012 Sep 1;169(9):946-53.

Broeders M, de Bie RM, Velseboer DC, et al. Evolution of **mild cognitive impairment in Parkinson** disease. Neurology. 2013 Jul 23;81(4):346-52.

Brown CH, Faigle R, Klinker L, et al. The association of brain **MRI** characteristics and postoperative **delirium** in **cardiac surgery** patients. Clin Ther. 2015;37:xxx–xxx

Brown Jeremy, Pengas George. Self administered cognitive **screening test** (**TYM**) for detection of Alzheimer's disease: cross sectional study. BMJ 2009;338:b2030, doi: 10.1136/bmj.b2030 (Published 9 June 2009) http://www.bmj.com/cgi/data/bmj.b2030/DC1/1

Brookmeyer R, Kawas CH, Abdallah N, et al. **Impact of interventions to reduce Alzheimer's disease pathology** on the prevalence of dementia in the oldest-old. Alzheimers Dement. 2016 Mar;12(3):225-32.

Buchhave P, Minthon L, Zetterberg H, et al. **Cerebrospinal Fluid Levels of β-Amyloid 1-42**, but Not of Tau, Are Fully Changed Already 5 to 10 Years Before the Onset of Alzheimer Dementia. Arch Gen Psychiatry. 2012 Jan;69(1):98-106.

Buchman AS, Boyle PA, Yu L, Shah RC, Wilson RS, Bennett DA. Total **daily physical activity** and the risk of AD and cognitive decline in older adults. Neurology 2012;78: 1323–1329.

Buchman AS, Yu L, Boyle PA, et al. Higher brain **BDNF** gene expression is associated with slower cognitive decline in older adults. Neurology. 2016 Feb 23;86(8):735-741.

Buchman AS, Yu L, Wilson RS, et al. Physical **activity, common brain pathologies, and cognition in community-dwelling older** adults. Neurology. 2019 Jan 16.

Buckley RF, Hanseeuw B, et al. Region-specific association of subjective cognitive decline with **tauopathy** independent of global β-amyloid burden [online October 2, 2017]. JAMA Neurol. doi:10.1001/jamaneurol.2017 .2216

Bullain SS, Corrada MM, Shah BA, et al. Poor **Physical Performance** and Dementia in the Oldest Old: The **90+ Study**. Arch Neurol. 2012 Oct 22:1-7.

Bunch TJ, Bair TL, Crandall BG, et al. **Stroke and dementia risk** in patients with and without atrial fibrillation and carotid arterial disease. Heart Rhythm. 2019 Jul 9.

Burnham SC, Rowe CC, Baker D, et al. Predicting Alzheimer disease from a **blood-based biomarker** profile: A 54-month follow-up. Neurology. 2016 Sep 13;87(11):1093-101.

Burns A, Bernabei R, Bullock R, et al. Safety and efficacy of **galantamine** (Reminyl) in severe Alzheimer's disease (the SERAD study): a randomised, placebo-controlled, double-blind trial. Lancet Neurol. 2008 Nov 28. Galantamine can be started and used safely in elderly patients with severe AD. Galantamine improved cognitive function but failed to significantly improve the co-primary parameter of overall activities of daily living.

Burns A, Iliffe S. **Dementia**. BMJ. **2009 Feb** 5;338:b75. doi: 10.1136/bmj.b75.

Burns A, Iliffe S. **Alzheimer's disease**. BMJ. **2009 Feb** 5;338:b158. doi: 10.1136/bmj.b158.

Burckhardt M, Herke M, Wustmann T, et al. **Omega-3 fatty acids** for the treatment of dementia. Cochrane Database Syst Rev. 2016 Apr 11;4:CD009002. We found no convincing evidence for the efficacy of omega-3 PUFA supplements in the treatment of mild to moderate AD. This result was consistent for all outcomes relevant for people with dementia. Adverse effects of omega-3 PUFAs seemed to be low, but based on the evidence synthesised in this review, we cannot make a final statement on tolerability. The effects on other populations remain unclear.

Burrell JR, Hornberger M, Carpenter RH, et al. **Saccadic abnormalities** in frontotemporal dementia. Neurology. 2012 Jun 5;78(23):1816-23.

Burry L, Hutton B, Williamson DR, et al. **Pharmacological interventions for the treatment of delirium** in critically ill adults. Cochrane Database Syst Rev. 2019 Sep 3;9:CD011749. We identified trials of varying quality that examined six different drug classes for treatment of delirium in critically ill adults. We found evidence that the alpha2 agonist dexmedetomidine may shorten delirium duration, although this small effect (compared with placebo) was seen in pairwise analyses based on a single study and was not seen in the NMA results. Alpha2 agonists also ranked best for duration of mechanical ventilation and length of ICU stay, whereas the CHE inhibitor rivastigmine was associated with longer ICU stay. We found no evidence of a difference between placebo and any drug in terms of delirium-free and coma-free days, days with coma, physical restraint use, length of stay, long-term cognitive outcomes, or mortality. No studies reported delirium relapse, resolution of symptoms, or quality of life. The ten ongoing studies and the six studies awaiting classification that we identified, once published and assessed, may alter the conclusions of the review.

Bush SH, Lawlor PG. **Delirium**. CMAJ. 2015 Feb 3;187(2):129.

Butchart J, Brook L, Hopkins V, et al. **Etanercept** in **Alzheimer** disease: A randomized, placebo-controlled, double-blind, phase 2 trial. Neurology. 2015 May 26;84(21):2161-8.

Butler M, Nelson VA, et al. **Over-the-counter supplement interventions** to prevent cognitive decline, mild cognitive impairment, and clinical Alzheimer-type dementia. A systematic review. Ann Intern Med. 2018;168:52-62.

Butler M, McCreedy E, Nelson VA, et al. **Does cognitive training prevent** cognitive decline? A systematic review. Ann Intern Med. 2018;168:63-8.

Callahan CM, et al. Effectiveness of **collaborative care** for older adults with Alzheimer disease in primary care: a randomized controlled trial.JAMA. 2006 May 10;295(18):2148-57.

Callahan CM, Boustani MA, Schmid AA, et al. **Targeting Functional Decline** in Alzheimer Disease: A Randomized Trial. Ann Intern Med. 2016 Nov 22.

Callisaya ML, Beare R, Moran C, et al. **Type 2 diabetes mellitus, brain atrophy and cognitive decline** in older people: a longitudinal study. Diabetologia. 2018 Dec 13.

Campbell NL, Boustani MA, Lane KA, et al. Use of **anticholinergics** and the risk of **cognitive impairment** in an African American population. Neurology. 2010 Jul 13;75(2):152-9.

Campbell MC, Markham J, Flores H, et al. Principal component analysis of **PiB distribution** in Parkinson and Alzheimer diseases. Neurology 2013;81:520–527.

Canadian Coalition for Seniors' Mental Health (**CCSMH**) National Guidelines for **Delirium & Depression** Mental Health 2006: http://www.ccsmh.ca/en/default.cfm http://www.ccsmh.ca/pdf/final%20supplement.pdf

Canadian Task Force on Preventive Health Care. (**CTFPHC**) Recommendations on **screening for cognitive impairment** in older adults. CMAJ. 2015 Nov 30.

Canessa N, Ferini-Strambi L. **Sleep-disordered breathing** and cognitive decline in older adults. JAMA. 2011 Aug 10;306(6):654-5.

Cannon-Albright LA, Foster NL, Schliep K, et al. **Relative risk for Alzheimer disease based on complete family history**. Neurology. 2019 Apr 9;92(15):e1745-e1753.

Cao B, Rosenblat JD, Brietzke E, et al. Comparative **efficacy and acceptability of antidiabetic agents for Alzheimer`s disease** and mild cognitive impairment: A systematic review and network meta-analysis. Diabetes Obes Metab. 2018 May 23.

Carcaillon L, Brailly-Tabard S, Ancelin ML, et al. High plasma estradiol interacts with diabetes on risk of dementia in older postmenopausal women. Neurology. 2014 Feb 11;82(6):504-11

Cadar D, Lassale C, Davies H, et al. Individual and Area-Based **Socioeconomic Factors Associated With Dementia** Incidence in England: Evidence From a 12-Year Follow-up in the English Longitudinal Study of Ageing. JAMA Psychiatry. 2018 May 16.

Cardarelli R, Kertesz A, Knebl JA. **Frontotemporal dementia**: a review for primary care physicians. Am Fam Physician. 2010 Dec 1;82(11):1372-7.

Cardiovascular and Cerebrovascular Events in the Randomized, Controlled **Alzheimer's** Disease Anti-Inflammatory Prevention Trial (**ADAPT**). PLoS Clin Trials. 2006 Nov 17;1(7):e33 [Epub ahead of print] For celecoxib, ADAPT data do not show the same level of risk as those of the APC trial. The data for **naproxen**, although not definitive, are suggestive of increased cardiovascular and cerebrovascular risk. (Nissen SE. ADAPT: The Wrong Way to Stop a Clinical Trial. PLoS Clin Trials. 2006 Nov 17;1(7):e35 [Epub ahead of print]

Carey IM, Anderson HR, Atkinson RW, et al. Are **noise and air pollution related to the incidence of dementia**? A cohort study in London, England. BMJ Open. 2018 Sep 11;8(9):e022404.

Dudas R, Malouf R, McCleery J, et al. **Antidepressants for treating depression in dementia**. Cochrane Database Syst Rev. 2018 Aug 31;8:CD003944. The available evidence is of variable quality and does not provide strong support for the efficacy of antidepressants for treating depression in dementia, especially beyond 12 weeks. On the only measure of efficacy for which we had high-quality evidence (depression rating scale scores), antidepressants showed little or no effect. The evidence on remission rates favoured antidepressants but was of moderate quality, so future research may find a different result. There was insufficient evidence to draw conclusions about individual antidepressant drugs or about subtypes of dementia or depression. There is some evidence that antidepressant treatment may cause adverse events.

Cannon-Albright LA, Foster NL, Schliep K, et al. **Relative risk** for Alzheimer disease based on complete family history. Neurology. 2019 Apr 9;92(15):e1745-e1753.

Caroli A, Prestia A, Galluzzi S, et al. Alzheimer's Disease Neuroimaging Initiative; Alzheimer's Disease Neuroimaging Initiative. **Mild cognitive impairment with suspected nonamyloid pathology** (SNAP): Prediction of progression. Neurology. 2015 Feb 3;84(5):508-15.

Carrasco MP, Villarroel L, Andrade M, et al. Development and validation of a **delirium predictive score** in older people. Age Ageing. 2013 Sep 24.

Carrière I, Fourrier-Reglat A, Dartigues JF, et al. Drugs with **anticholinergic** properties, cognitive decline, and dementia in an elderly general population: the 3-city study. Arch Intern Med. 2009 Jul 27;169(14):1317-24.

Carson S, McDonagh MS, Peterson K. A systematic review of the efficacy and safety of atypical antipsychotics in patients with psychological and behavioral symptoms of dementia. J Am Geriatr Soc. 2006 Feb;54(2):354-61.

Carvalho DZ, St Louis EK, Knopman DS, et al. Association of **Excessive Daytime Sleepiness** With Longitudinal β-Amyloid Accumulation in Elderly Persons Without Dementia. JAMA Neurol. 2018 Mar 12.

Caselli RJ, Dueck AC, Osborne D, et al. Longitudinal modeling of age-related memory decline and the **APOE epsilon4** effect. N Engl J Med. 2009 Jul 16;361(3):255-63.

Caselli RJ, Dueck AC, Locke DE, et al. Cerebrovascular risk factors and preclinical memory decline in healthy **APOE** {varepsilon}4 **homozygotes**. Neurology. 2011 Mar 22;76(12):1078-84.

Cash DM, Ridgway GR, et al; On behalf of the Dominantly Inherited Alzheimer Network (DIAN). The pattern of atrophy in familial Alzheimer disease: **Volumetric MRI** results from the DIAN study. Neurology. 2013 Sep 18.

Cedeño Laurent JG, Williams A, Oulhote Y, et al. Reduced cognitive function during a heat wave among residents of non-air-conditioned buildings: An observational study of young adults in the summer of 2016. PLoS Med. 2018 Jul 10;15(7):e1002605.

Chaker L, Wolters FJ, Bos D, et al. **Thyroid function** and the risk of dementia: The Rotterdam Study. Neurology. 2016 Oct 18;87(16):1688-1695.

Chan KY, Wang W, Wu JJ, et al; Global Health Epidemiology Reference Group(GHERG). Epidemiology of Alzheimer's disease and other forms of **dementia in China**, 1990-2010: a systematic review and analysis. Lancet. 2013 Jun 8;381(9882):2016-23.

Chandler MJ, Locke DE, Crook JE, et al. Comparative effectiveness of **behavioral interventions on quality of life for older adults with mild cognitive impairment**: a randomized clinical trial. JAMA Netw Open. 2019;2(5):e193016. doi:10.1001/jamanetworkopen.2019.3016

Chang YS, Chu H, Yang CY, et al. The efficacy of **music therapy** for people with dementia: A meta-analysis of randomised controlled trials. J Clin Nurs. 2015 Aug 24. doi: 10.1111/jocn.12976.

Charlesworth G, Burnell K, Crellin N, et al. **Peer support and reminiscence therapy** for people with dementia and their family carers: a factorial pragmatic randomised trial. J Neurol Neurosurg Psychiatry. 2016 Aug 12.

Chatterjee S, Chen H, Johnson ML, et al. Comparative risk of **cerebrovascular adverse events in community-dwelling older adults using risperidone, olanzapine and quetiapine**: a multiple propensity score-adjusted retrospective cohort study. Drugs Aging. 2012 Oct;29(10):807-17.

Chau S, Herrmann N, Ruthirakuhan MT, et al. **Latrepirdine** for Alzheimer`s disease. Cochrane Database Syst Rev. 2015 Apr 21;4:CD009524. Our meta-analysis is limited by the small number of studies, imprecision, inconsistencies between studies and likelihood of bias. Nevertheless, the evidence to date suggests that while not associated with an increased risk of adverse events compared with placebo, there is no effect of latrepirdine on cognition and function in mild-to-moderate AD patients, though there appears to be a modest benefit for behaviour. Further studies should investigate the potential benefit of latrepirdine on neuropsychiatric symptoms in AD.

Chen C, Anderson CS. **Does reducing blood pressure and cholesterol provide any HOPE** for preventing cognitive decline and dementia? Neurology. 2019 Mar 26;92(13):593-594

Chen CC, Li HC, et al. Effect of a **Modified Hospital Elder Life Program on Delirium** and Length of Hospital Stay in Patients Undergoing Abdominal Surgery: A Cluster Randomized Clinical Trial. JAMA Surg. 2017 May 24.

Chen H, Kwong JC, Copes R, et al. **Living near major roads** and the incidence of dementia, Parkinson's disease, and multiple sclerosis: a population-based cohort study. Lancet 2016; online Jan 4.

Chen M-K, Mecca AP, Naganawa M, et al. Assessing **synaptic density in Alzheimer disease** with synaptic vesicle glycoprotein 2A positron emission tomographic imaging [online July 16, 2018]. JAMA Neurol. doi:10.1001/jamaneurol.2018.1836

Chen R, Chan PT, Chu H, et al. Treatment effects between **monotherapy of donepezil versus combination with memantine** for Alzheimer disease: A meta-analysis. PLoS One. 2017 Aug 21;12(8):e0183586.

Cheng HT;Lin FJ;Erickson SR;Hong JL;Wu CH. The Association Between the Use of **Zolpidem and the Risk of Alzheimer`s Disease** Among Older People. J Am Geriatr Soc. 2017 Sep 7.

Chiu HL;Chan PT;Chu H;et al. Effectiveness of **Light Therapy** in Cognitively Impaired Persons: A Metaanalysis of Randomized Controlled Trials. J Am Geriatr Soc. 2017 Jul 22.

Chen Yong; Briesacher Becky A.; Field Terry S.; et al. Unexplained Variation Across US **Nursing Homes in Antipsychotic Prescribing Rates**. Arch Intern Med. 2010;170(1):89-95.

Chen SP, Bhattacharya J, Pershing S. Association of **Vision Loss** With **Cognition** in Older Adults. JAMA Ophthalmol. 2017 Aug 17

Chertkow H. **Diagnosis and treatment of dementia: introduction**. Introducing a series based on the **Third Canadian Consensus** Conference on the Diagnosis and Treatment of Dementia. (**CCCDTD3**) CMAJ. 2008 Jan 29;178(3):316-21.

Chertkow H, Massoud F, Nasreddine Z, et al. Diagnosis and treatment of dementia: 3. **Mild cognitive impairment and cognitive impairment without dementia**. CMAJ. 2008 May 6;178(10):1273-85.

Chew EY, Clemons TE, Agrón E, et al. Effect of **omega-3 fatty acids, lutein/zeaxanthin**, **or other nutrient supplementation** on **cognitive function**: the **AREDS2** randomized clinical trial.JAMA. doi:10 .1001/jama.2015.9677.

Chi NF, Chien LN, Ku HL, et al. Alzheimer disease and **risk of stroke**: A population-based cohort study. Neurology. 2013 Feb 19;80(8):705-711.

Child A, Clarke A, Fox C, Maidment I. A **pharmacy led program** to review **anti-psychotic prescribing for people with dementia**. BMC Psychiatry. 2012 Sep 25;12:155.

Chinthapalli K. Alzheimer's disease: still a **perplexing problem**. BMJ. 2014 Jul 8;349:g4433.

Chiu HL, Chan PT, Chu H, et al. Effectiveness of **Light Therapy** in Cognitively Impaired Persons: A Metaanalysis of Randomized Controlled Trials. J Am Geriatr Soc. 2017 Oct;65(10):2227-2234.

Chiu WC, Ho WC, Liao DL, et al. Progress of **Diabetic Severity and Risk of Dementia**. J Clin Endocrinol Metab. 2015 Jul 9

Cho H, Choi JY, Hwang MS, Lee Jhet al. **Tau PET** in Alzheimer disease and mild cognitive impairment. Neurology. 2016 Jun 29.

Christensen K, Thinggaard M, Oksuzyan A, et al. **Physical and cognitive functioning of people older than 90 years**: a comparison of two Danish cohorts born 10 years apart. Lancet 2013; online July 11.

Christensen KD, Roberts JS, Whitehouse PJ, et al; REVEAL Study Group. Disclosing Pleiotropic Effects During **Genetic Risk Assessment** for Alzheimer Disease: A Randomized, Controlled Trial. Ann Intern Med. 2016 Jan 26.

Clark Christopher M., Schneider Julie A., Bedell Barry J., et al., for the AV45-A07 Study Group. Use of **Florbetapir-PET for Imaging β-Amyloid** Pathology. *JAMA*. 2011;305(3):275-283.doi:10.1001/jama.2010.2008

Clark CM, Pontecorvo MJ, Beach TG, et al; for the AV-45-A16 Study Group. **Cerebral PET with florbetapir** compared with neuropathology at autopsy for detection of neuritic amyloid-β plaques: a prospective cohort study. Lancet Neurol. 2012 Jun 27.

Clark LR, et al. **Age-accelerated cognitive decline in asymptomatic adults with CSF β-amyloid**. Neurology. 2018 Apr 10;90(15):e1306-e1315.

Clegg A, Young JB. Which medications to avoid in people at risk of delirium: a systematic review. Age Ageing. 2011 Jan;40(1):23-9. (opiates and benzos)

Clegg A, Siddiqi N, Heaven A, Young J, Holt R. Interventions for **preventing delirium in older people** in institutional long-term care. Cochrane Database Syst Rev. 2014 Jan 31;1:CD009537.

Clinical **Handbook of Psychotropic Drugs** 22nd Edition, Procyshyn RM, Bezchlibnyk-Butler KZ, Jeffries JJ. 2003

Cohen JP, Dong J, Lu CY, et al. **Restricting access to florbetapir**: Medicare coverage criteria for diagnostics and drugs are inconsistent. BMJ. 2015 Jul 3;351:h3333.

Cohen-Bittan J, Boddaert J, Guettrot-Imbert G, et al. **Atypical dementia**. Lancet. 2010 Aug 21;376(9741):656.

Cook AH et al. Rates of **cortical atrophy** in adults 80 years and older with **superior vs average episodic memory**. JAMA 2017 Apr 4; 317:1373.

Cook M, Baker N, Lanes S, et al. Incidence of **stroke and seizure** in Alzheimer's disease dementia. Age Ageing. 2015 May 24.

Cook Maher A, Kielb S, Loyer E, et al. **Psychological well-being** in elderly adults with extraordinary episodic memory. PLoS One. 2017 Oct 23;12(10):e0186413.

Cook R, Lamont T, Martin R. Steps to better **understanding resistant behaviours in hospitalised patients** with dementia. BMJ. 2019 Aug 23;366:l4912.

Cooper C, Selwood A, Blanchard M, Walker Z, Blizard R, Livingston G. **Abuse of people** with dementia by family carers: representative cross sectional survey. BMJ. 2009 Jan 22;338:b155. doi: 10.1136/bmj.b155.

Cooper C, Katona C, Lyketsos K, et al. A Systematic Review of Treatments for **Refractory Depression in Older People**. Am J Psychiatry. 2011 Mar 31.

Cooper C, Li R, Lyketsos C, et al. Treatment for **mild cognitive impairment**: systematic review**.** Br J Psychiatry. 2013 Oct;203:255-64.

Cooper C, Sommerlad A, Lyketsos CG, et al. **Modifiable Predictors of Dementia in Mild Cognitive Impairment**: A Systematic Review and Meta-Analysis. Am J Psychiatry. 2015 Feb 20.

Corbett A, Burns A, Ballard C. **Don't use antipsychotics routinely to treat agitation and aggression in people with dementia**. BMJ. 2014 Nov 3;349:g6420.

Corrada MM, Hayden KM, Paganini-Hill A, et al. **Age of onset of hypertension** and risk of dementia in the oldest-old: The 90+ Study. Alzheimers Dement. 2017 Jan 6.

Corraini P, Henderson VW, Ording AG, et al. **Long-Term Risk of Dementia Among Survivors of Ischemic or Hemorrhagic Stroke**. Stroke. 2017 Jan;48(1):180-186.

Coughlan G, Coutrot A, Khondoker M, et al. **Toward personalized cognitive diagnostics of at-genetic-risk Alzheimer's disease**. Proc Natl Acad Sci U S A. 2019 May 7;116(19):9285-9292.

Coupland CAC, Hill T, Dening T, et al. **Anticholinergic drug exposure and the risk of dementia**: a nested case-control study. JAMA Intern Med. 2019 June 24.

Cox KL, Flicker L, Almeida OP, et al. The FABS trial: A randomised control trial of the effects of a 6-month **physical activity** intervention on adherence and long-term physical activity and self-efficacy in older adults with memory complaints. Prev Med. 2013 Sep 25. pii: S0091-7435(13)00355-1

Crane PK, Walker R, Hubbard RA, et al. **Glucose levels and risk of dementia**. N Engl J Med. 2013 Aug 8;369(6):540-8.

Creavin ST, Wisniewski S, Noel-Storr AH, et al. **Mini-Mental State Examination** (**MMSE**) for the **detection** of **dementia** in clinically unevaluated people aged 65 and over in community and primary care populations. Cochrane Database Syst Rev. 2016 Jan 13;1:CD011145. The MMSE contributes to a diagnosis of dementia in low prevalence settings, but should not be used in isolation to confirm or exclude disease. We recommend that future work evaluates the diagnostic accuracy of tests in the context of the diagnostic pathway experienced by the patient and that investigators report how undergoing the MMSE changes patient-relevant outcomes.

Creavin S, Fish M, Gallacher J, Bayer A, Ben-Shlomo Y. **Clinical history** for diagnosis of dementia in men: Caerphilly Prospective Study. Br J Gen Pract. 2015 Aug;65(637):e489-99.

Cross AJ, Le VJ, George J, et al. Stakeholder perspectives on **pharmacist involvement in a memory clinic** to review patients' medication management and assist with deprescribing. Res Social Adm Pharm. 2019 Aug 7.

Cummings J, Zhong K. **Biomarker-driven** therapeutic management of Alzheimer's disease: establishing the foundations. Clin Pharmacol Ther. 2013 Jan;95(1):67-77

Cummings JL, Lyketsos CG, Peskind ER, et al. Effect of **dextromethorphan-quinidine** on **agitation** in patients with Alzheimer disease dementia: a randomized clinical trial.JAMA. doi:10.1001/jama .2015.10214.

Cummings-Vaughn LA, Chavakula NN, Malmstrom TK, et al. **Veterans Affairs Saint Louis University Mental Status Examination Compared with the Montreal Cognitive Assessment** and the

Short Test of Mental Status. J Am Geriatr Soc. 2014 Jun 10.
Curhan SG, Willett WC, Grodstein F, Curhan GC. Longitudinal study of **hearing loss and subjective cognitive function decline** in men. Alzheimers Dement. 2019 Jan 21.
Cuyvers E, De Roeck A, Van den Bossche T, et al. **Mutations in ABCA7** in a Belgian cohort of Alzheimer's disease patients: a targeted resequencing study. Lancet Neurol 2015; online July 1.
Cuyvers E, Sleegers K. **Genetic variations underlying Alzheimer's disease**: evidence from genome-wide association studies and beyond. Lancet Neurol. 2016 Jul;15(8):857-68.
da Silva J, Gonçalves-Pereira M, Xavier M, Mukaetova-Ladinska EB. **Affective disorders (depression, bipolar) and risk of developing dementia**: systematic review. Br J Psychiatry. 2013 Mar;202:177-86.
Daffner KR, Gale SA, Barrett AM, et al. **Improving clinical cognitive testing**: Report of the AAN Behavioral Neurology Section Workgroup. Neurology. 2015 Sep 8;85(10):910-8.
Daiello LA, Gongvatana A, Dunsiger S, et al. Alzheimer's Disease Neuroimaging Initiative. Association of **fish oil supplement** use with preservation of brain volume and cognitive function. Alzheimers Dement. 2014 Jun 18.
Dalmases M, Sole-Padulles C, Torres M, et al. Effect of **CPAP on Cognition**, Brain Function, and Structure Among Elderly Patients With OSA: A Randomized Pilot Study. Chest. 2015 Nov 1;148(5):1214-23.
Dangour AD et al. Effect of 2-y n–3 long-chain **polyunsaturated fatty acid supplementation** on cognitive function in older people: A randomized, double-blind, controlled trial. Am J Clin Nutr 2010 Apr 21.
Danthiir V, Hosking DE, Nettelbeck T, et al. An 18-mo randomized, double-blind, placebo-controlled trial of **DHA-rich fish oil to prevent age-related cognitive decline in cognitively normal older adults**. Am J Clin Nutr. 2018 May 1;107(5):754-762.
Dartigues JF, Féart C. **Risk factors** for Alzheimer disease: Aging beyond age? Neurology. 2011 Jul 19;77(3):206-7.
Davies NM, Kehoe PG, Ben-Shlomo T, Martin RM. Associations of anti-hypertensive treatments (**ARBS**) with **Alzheimer's disease**, vascular dementia, and other dementias. J Alzheimer's Dis 2011; 26:699-708.
Daviglus ML, Plassman BL, Pirzada A, et al. **Risk Factors and Preventive Interventions** for Alzheimer Disease: State of the Science. Arch Neurol. 2011 May 9.
Davis DH, Creavin ST, Yip JL, et al. **Montreal Cognitive Assessment** for the diagnosis of Alzheimer`s disease and other dementias. Cochrane Database Syst Rev. 2015 Oct 29;10:CD010775. The overall quality and quantity of information is insufficient to make recommendations on the clinical utility of MoCA for detecting dementia in different settings. Further studies that do not recruit participants based on diagnoses already present (case-control design) but apply diagnostic tests and reference standards prospectively are required. Methodological clarity could be improved in subsequent DTA studies of MoCA by reporting findings using recommended guidelines (e.g. STARDdem). Thresholds lower than 26 are likely to be more useful for optimal diagnostic accuracy of MoCA in dementia, but this requires confirmation in further studies.
Davis DH, Muniz-Terrera G, Keage HA, et al.Association of **Delirium With Cognitive Decline in Late Life**: A Neuropathologic Study of 3 Population-Based Cohort Studies. JAMA Psychiatry. 2017 Jan 18.
Dawson BK, Fereshtehnejad SM, Anang JBM, et al. **Office-Based Screening for Dementia in Parkinson Disease**: The **Montreal Parkinson Risk of Dementia Scale** in 4 Longitudinal Cohorts. JAMA Neurol. 2018 Mar 26.
de Boer C, Echlin HV, et al. **Thinking-While-Moving Exercises May Improve Cognition in Elderly with Mild Cognitive Deficits**: A Proof-of-Principle Study. Dement Geriatr Cogn Dis Extra. 2018 Jul 11;8(2):248-258.
de Brouwer EJM, Kockelkoren R, Claus JJ, et al. **Hippocampal Calcifications**: Risk Factors and Association with Cognitive Function. Radiology. 2018 Jun 12:172588.
de Bruijn RF, Heeringa J, Wolters FJ, et al. Association Between **Atrial Fibrillation and Dementia** in the General Population. JAMA Neurol. 2015 Sep 21:1-7.
De Deyn P, Jeste DV, Swanink R, Kostic D, Breder C, Carson WH, Iwamoto T. **Aripiprazole** for the treatment of psychosis in patients with Alzheimer's disease: a randomized, placebo-controlled study. J Clin Psychopharmacol. 2005 Oct;25(5):463-7.
De Deyn PP, Drenth AF, Kremer BP, Oude Voshaar RC, Van Dam D. **Aripiprazole** in the treatment of Alzheimer's disease. Expert Opin Pharmacother. 2013 Jan 28.
de Jong DLK, de Heus RAA, Rijpma A, et al. **Effects of Nilvadipine** on Cerebral Blood Flow in Patients With Alzheimer Disease. Hypertension. 2019 Jun 17:HYPERTENSIONAHA11912892.
de Jonghe A, van Munster BC, Goslings JC, et al; on behalf of the Amsterdam Delirium Study Group. Effect of **melatonin on incidence of delirium** among patients with hip fracture: a multicentre, double-blind randomized controlled trial. CMAJ. 2014 Sep 2.
de Havenon A, Majersik JJ, Tirschwell DL, et al. **Blood pressure, glycemic control**, and white matter hyperintensity progression in type 2 diabetics(ACCORD MIND). Neurology. 2019 Mar 12; 92(11):e1168-e1175.
De Meyer Geert; Shapiro Fred; Vanderstichele Hugo; et al.; for the Alzheimer's Disease Neuroimaging Initiative. Diagnosis-Independent Alzheimer **Disease Biomarker** Signature in Cognitively Normal Elderly People. Arch Neurol. 2010;67(8):949-956.
de Wilde A, van der Flier WM, Pelkmans W, et al. Association of **Amyloid Positron Emission Tomography** With Changes in Diagnosis and Patient Treatment in an Unselected Memory Clinic Cohort: **The ABIDE Project**. JAMA Neurol. 2018 Jun 11.
Deal JA et al. **Retinal signs** and 20-year cognitive decline in the Atherosclerosis Risk in Communities study. Neurology 2018 Feb 28
DeCarli C. **Blood pressure control** and cognitive performance: something to think about with aging. JAMA. 2015 May 19;313(19):1963-4.
Deckers K, Camerino I, van Boxtel MP, et al. Dementia **risk in renal dysfunction**: A systematic review and meta-analysis of prospective studies. Neurology. 2017 Jan 10;88(2):198-208
Declercq T, Petrovic M, Azermai M, Vander Stichele R, De Sutter AIM, van Driel ML, Christiaens T. **Withdrawal versus continuation of chronic antipsychotic drugs for behavioural and psychological symptoms in older people with dementia**. Cochrane Database of Systematic Reviews 2013, Issue 3. Art. No.: CD007726. DOI: 10.1002/14651858.CD007726.pub2. Our findings suggest that many older people with Alzheimer's dementia and NPS can be withdrawn from chronic antipsychotic medication without detrimental effects on their behaviour. It remains uncertain whether withdrawal is beneficial for cognition or psychomotor status, but the results of this review suggest that discontinuation programmes could be incorporated into routine practice. However, two studies of people whose agitation or psychosis had previously responded well to antipsychotic treatment found an increased risk of relapse or shorter time to relapse after discontinuation. Two other studies suggest that people with more severe NPS at baseline could benefit from continuing their antipsychotic medication. In these people, withdrawal might not be recommended.
Defina LF, Willis BL, Radford NB, et al. The association between **midlife cardiorespiratory fitness** levels and later-life dementia: a cohort study. Ann Intern Med. 2013 Feb 5;158(3):162-8.
Deiner S, Luo X, Silverstein JH, Sano M. Can **intraoperative processed EEG** predict postoperative cognitive dysfunction in the elderly? Clin Ther. 2015;37:xxx–xxx
Deiner S, Luo X, Lin H-M, et al; Dexlirium Writing Group. Intraoperative infusion of **dexmedetomidine** for prevention of postoperative delirium and cognitive dysfunction in elderly patients undergoing major elective noncardiac surgery: a randomized clinical trial [online June 7, 2017].JAMA Surg. doi:10.1001/jamasurg.2017.1505
Dekosky ST, Williamson JD, Fitzpatrick AL, et al.; for the Ginkgo Evaluation of Memory (GEM) Study Investigators. Ginkgo biloba for Prevention of Dementia: A Randomized Controlled Trial. JAMA. 2008 Nov 19;300(19):2253-2262. (n=3,069 6.1yrs) In this study, G biloba at 120 mg twice a day was not effective in reducing either the overall incidence rate of dementia or AD incidence in elderly individuals with normal cognition or those with MCI.
Del Campo N, Payoux P, Djilali A, et al; MAPT/DSA Study Group. Relationship of **regional brain β-amyloid to gait speed**. Neurology. 2016 Jan 5;86(1):36-43.
Delbanco T. A 76-Year-Old Woman With **Delirium Following Surgery**. JAMA. 2012 Jun 6:1-2.
Deprescribing Guideline and Algorithms (Benzodiazepine receptor agonits, Proton pump inhibitors, Antipsychotics, Antihyperglycemic) http://deprescribing.org/resources/deprescribing-guidelines-algorithms/
Deramecourt V, Slade JY, Oakley AE, et al. **Staging and natural history of cerebrovascular pathology** in dementia. Neurology 2012;78:1043–1050.
Derby CA, Burns LC, Wang C, et al. **Screening for predementia AD**: time-dependent operating characteristics of episodic memory tests. Neurology 2013;80:1307–1314.
Derby CA, Katz MJ, et al. Trends in **Dementia Incidence in a Birth Cohort Analysis of the Einstein Aging Study**. JAMA Neurol. 2017 Sep 5.
Deshmukh SR, Holmes J, Cardno A. **Art therapy for people with dementia**. Cochrane Database Syst Rev. 2018 Sep 13;9:CD011073. There is insufficient evidence about the efficacy of art therapy for people with dementia. More adequately-powered and high-quality studies using relevant outcome measures are needed.
Desideri G, Kwik-Uribe C, Grassi D, et al. Benefits in cognitive function, blood pressure, and insulin resistance through **cocoa flavanol consumption** in elderly subjects with mild cognitive impairment: The Cocoa, Cognition, and Aging (CoCoA) study. Hypertension 2012.
Desveaux L, Saragosa M, Rogers J, et al. Improving the **appropriateness of antipsychotic prescribing in nursing homes**: a mixed-methods process evaluation of an **academic detailing** intervention. Implement Sci. 2017 May 26;12(1):71
Devanand DP, Schupf N, Stern Y, et al. Plasma A{beta} and **PET PiB binding** are inversely related in mild cognitive impairment. Neurology. 2011 Jul 12;77(2):125-31.
Devanand DP, Pelton GH, Cunqueiro K, Sackeim HA, Marder K. A 6-month, randomized, double-blind, placebo-controlled pilot **discontinuation trial following response to haloperidol** treatment of psychosis and agitation In Alzheimer's disease. Int J Geriatr Psychiatry. 2011 Sep;26(9):937-43.
Devanand DP et al. **Relapse risk after discontinuation of risperidone** in Alzheimer's disease. N Engl J Med 2012 Oct 18; 367:1497.
Devanand DP, Lee S, Manly J, et al. **Olfactory deficits** predict cognitive decline and Alzheimer dementia in an urban community. Neurology. 2015 Jan 13;84(2):182-9.

Devlin JW, Roberts RJ, Fong JJ, et al. Efficacy and safety of **quetiapine** in critically ill patients with **delirium**: a prospective, multicenter, randomized, double-blind, placebo-controlled pilot study. Crit Care Med. 2010 Feb;38(2):419-27. In ICU patients with delirium, the addition of scheduled quetiapine to as-needed haloperidol results in faster resolution of delirium, decreased time spent in delirium, and less agitation. This study was too small to detect significant differences in adverse events, if they exist. (LOE = 1b)

Devlin JW, Skrobik Y, Gélinas C, et al. Clinical Practice **Guidelines** for the Prevention and Management of Pain, Agitation/Sedation, Delirium, Immobility, and Sleep Disruption in **Adult Patients in the ICU**. Crit Care Med. 2018 Sep;46(9):e825-e873.

Devore EE, Grodstein F, van Rooij FJ, et al. **Dietary antioxidants** and long-term risk of dementia. Arch Neurol. 2010 Jul;67(7):819-25.

Devore EE, Kang JH, Breteler MM, Grodstein F. Dietary intakes of berries and flavonoids in relation to cognitive decline. Ann Neurol. 2012 Apr 26.

Dhamoon MS, Cheung YK, Moon Y, et al. Cerebral white matter disease and functional decline in older adults from the Northern Manhattan Study: A longitudinal cohort study. PLoS Med. 2018 Mar 20;15(3):e1002529.

Dickerson BC, Stoub TR, Shah RC, et al. Alzheimer-signature MRI biomarker predicts AD dementia in cognitively normal adults. Neurology. 2011 Apr 19;76(16):1395-402.

Dickerson BC, Wolk DA. **MRI cortical thickness biomarker** predicts AD-like CSF and cognitive decline in normal adults. Neurology 2012;78:84 –90.

Dichgans M, Markus HS, et al. Donepezil in patients with subcortical vascular cognitive impairment: a randomised double-blind trial in CADASIL. Lancet Neurol. 2008 Feb 22; [Epub ahead of print] Donepezil had no effect on the primary endpoint, the V-ADAS-cog score in CADASIL patients with cognitive impairment. Improvements were noted on several measures of executive function, but the clinical relevance of these findings is not clear.

Diener HC. Does **atrial fibrillation** lead to cognitive decline and dementia? Eur Heart J. 2017 Sep 7;38(34):2619-2620.

Ding J, Sigurðsson S, Jónsson PV, et al. Large Perivascular Spaces Visible on Magnetic Resonance Imaging, **Cerebral Small Vessel Disease** Progression, and Risk **of Dementia**: The Age, Gene/Environment Susceptibility Reykjavik Study. JAMA Neurol. 2017 Jul 17

Dhillon S. Spotlight on **rivastigmine transdermal patch**: in dementia of the Alzheimer's type. Drugs Aging. 2011 Nov 1;28(11):927-30.

Dobbs AR. Accuracy of the **DriveABLE cognitive assessment** to determine cognitive fitness to drive. Can Fam Physician. 2013 Mar;59(3):e156-61.

Dobbs BM, Shergill SS. How effective is the **Trail Making Test (Parts A and B)** in identifying cognitively impaired **drivers**? Age Ageing. 2013 Sep;42(5):577-81.

Dodge HH, Zitzelberger T, Oken BS, et al. A randomized placebo-controlled trial of ginkgo biloba for the prevention of cognitive decline. Neurology. 2008 Feb 27; [Epub ahead of print] n=118 42 month In unadjusted analyses, **ginkgo biloba** extract (GBE) neither altered the risk of progression from normal to Clinical Dementia Rating (CDR) = 0.5, nor protected against a decline in memory function. Secondary analysis taking into account medication adherence showed a protective effect of GBE on the progression to CDR = 0.5 and memory decline.

Dodel R, Rominger A, et al. **Intravenous immunoglobulin** for treatment of mild-to-moderate Alzheimers Disease: a phase 2, randomised, double-blind, placebo-controlled dose-fi nding trial. Lancet Neurol 2013; online Jan 31.

Dodge HH, Mattek NC, Austin D, et al. **In-home walking speeds** and variability trajectories associated with mild cognitive impairment. Neurology. 2012 Jun12;78(24):1946-52.

Dolder Christian R, Davis Lauren Nicole, McKinsey Jonathan. Use of **Psychostimulants in Patients with Dementia** . Ahead of Print on 1 Oct2010, DOI 10.1345/aph.1P341. Ann Pharmacother ;44:1624-1632.

Donadio V, Incensi A, Rizzo G, et al. A new potential biomarker for dementia with **Lewy bodies**: Skin **nerve α-synuclein** deposits. Neurology. 2017 Jul 25;89(4):318-326.

Donohue MC, Sperling RA, Petersen R; et al. Association between **elevated brain amyloid** and subsequent cognitive decline among cognitively normal persons.JAMA. doi:10.1001/jama.2017.6669

Donovan NJ, Okereke OI, Vannini P, et al. Association of higher cortical amyloid burden with **loneliness** in cognitively normal older adults [online November 2, 2016].JAMA Psychiatry. doi:10.1001/jamapsychiatry.2016.2657

Doody RS, Raman R, Farlow M, et al; Alzheimer's Disease Cooperative Study Steering Committee, Siemers E, Sethuraman G, Mohs R; **Semagacestat** Study Group. A phase 3 trial of semagacestat for treatment of Alzheimer's disease. N Engl J Med. 2013 Jul 25;369(4):341-50.

Doody RS, Thomas RG, Farlow M, et al. Phase 3 trials of **solanezumab** for mild-to-moderate Alzheimers disease. N Engl J Med 2014;370:311-21.

Dopper EG, Rombouts SA, Jiskoot LC, et al. Structural and functional **brain connectivity** in presymptomatic familial frontotemporal dementia. Neurology. 2014 Jul 8;83(2):e19-26.

Doraiswamy PM, Sperling RA, Coleman RE, et al; For the AV45-A11 Study Group. Amyloid-β assessed by **florbetapir F 18 PET** and 18-month cognitive decline: A multicenter study. Neurology. 2012 Jul 11.

Dorothée G, Bottlaender M, Moukari E, et al. Distinct **Patterns of Antiamyloid-β Antibodies** in Typical and Atypical Alzheimer Disease Distinct Patterns of Anti-Aβ Antibodies and AD. Arch Neurol. 2012 Jun18:1-5.

Dorsey E. Ray; Rabbani Atonu; Gallagher Sarah A.; et al. Impact of **FDA Black Box Advisory** on Antipsychotic Medication Use. Arch Intern Med. 2010;170(1):96-103.

Dougherty RJ, Schultz SA, Kirby TK, et al. **Moderate Physical Activity** is Associated with Cerebral Glucose Metabolism in Adults at Risk for Alzheimer's Disease. J Alzheimers Dis. 2017 May 17.

Douiri A, McKevitt C, Emmett ES, et al. Long-term effects of **secondary prevention on cognitive function** in stroke patients. Circulation. 2013 Sep 17;128(12):1341-8.

Driver JA, Beiser A, Au R, Kreger BE, Splansky GL, Kurth T, et al. **Inverse association between cancer and Alzheimer's** disease: results from the Framingham Heart Study. BMJ 2012;344:e1442.

Drugs for Cognitive Loss and Dementia. Treatment Guidelines from the Medical Letter. Feb 2007, Mar 2010, Oct 2013 & revised **Sept 2017**.

Drummond N, McCleary L, Freiheit E, et al. **Antidepressant and antipsychotic prescribing** in primary care for people with **dementia**. Can Fam Physician. 2018 Nov;64(11):e488-e497.

Dubois B, Feldman HH, Jacova C, Dekosky ST, Barberger-Gateau P, Cummings J, Delacourte A, Galasko D, Gauthier S, Jicha G, Meguro K, O'brien J, Pasquier F, Robert P, Rossor M, Salloway S, Stern Y, Visser PJ, Scheltens P. Research criteria for the **diagnosis of Alzheimer's disease**: revising the NINCDS-ADRDA criteria. Lancet Neurol. 2007 Aug;6(8):734-46. These new criteria are centred on a clinical core of early and significant episodic memory impairment. They stipulate that there must also be at least one or more abnormal biomarkers among structural neuroimaging with MRI, molecular neuroimaging with PET, and cerebrospinal fluid analysis of amyloid beta or tau proteins.

Dubois B, Feldman HH, Jacova C, Cummings JL, Dekosky ST, et al. Revising the **definition of Alzheimer's disease**: a new lexicon. Lancet Neurol. 2010 Oct 8.

Dubois B, Tolosa E, Katzenschlager R, et al. **Donepezil in Parkinson's disease dementia**: A randomized, double-blind efficacy and safety study. Mov Disord. 2012 Sep 1;27(10):1230-8.

Dubois B, Feldman HH, Jacova C, et al. Advancing research **diagnostic criteria for Alzheimer's** disease: the **IWG-2 criteria**. Lancet Neurol 2014; 13: 614–629.

Dubois B, Epelbaum S, Nyasse F, et al. Cognitive and neuroimaging features and brain β-amyloidosis in individuals at risk of Alzheimer's disease (INSIGHT-preAD): a longitudinal observational study. Lancet Neurol 2018; online Feb 27.

DyskenMW, Sano M, Asthana S, et al. Effect of vitamin E and memantine on functional decline in Alzheimer disease: the TEAM-AD VA Cooperative randomized trial. JAMA. doi:10.1001/jama.2013.282834. Dec. 31, 2013

Ecay-Torres M, Estanga A, Tainta M, et al. Increased CAIDE **dementia risk, cognition, CSF biomarkers, and vascular burden** in healthy adults. Neurology. 2018 Jul 17;91(3):e217-e226.

Egan MF, Kost J, Tariot PN, et al. Randomized Trial of **Verubecestat** for Mild-to-Moderate Alzheimer's Disease. N Engl J Med. 2018 May 3;378(18):1691-1703.

Egeberg A, Hansen PR, Gislason GH, et al. Patients with **rosacea** have increased risk of dementia. Ann Neurol. 2016 Apr 28

Ehlenbach William J.; Hough Catherine L.; Crane Paul K.; et al. Association Between Acute Care and Critical Illness **Hospitalization and Cognitive Function** in Older Adults. JAMA. 2010;303(8):763-770.

Ekström I, Sjölund S, Nordin S, et al. Smell Loss Predicts Mortality Risk Regardless of Dementia Conversion. J Am Geriatr Soc. 2017 Mar 22.

Ely EW, Margolin R, Francis J, May L, Truman B, Dittus R, et al. Evaluation of **delirium** in critically ill patients: validation of the confusion assessment method for the Intensive Care Unit (**CAM-ICU**). Crit Care Med 2001;29:1370-9.

Emre M, Tsolaki M, Bonuccelli Uet al; 11018 Study Investigators. **Memantine** for patients with **Parkinson's disease dementia** or dementia with **Lewy bodies**: a randomised, double-blind, placebo-controlled trial. Lancet Neurol. 2010 Oct;9(10):969-77.

Ennis GE, An Y, Resnick SM, et al. **Long-term cortisol measures** predict Alzheimer disease risk. Neurology. 2017 Jan 24;88(4):371-378

Epperly T. , Dunay MA, Boice JL. **Alzheimer Disease: Pharmacologic and Nonpharmacologic Therapies** for Cognitive and Functional Symptoms. Am Fam Physician. 2017;95(11):771-778.

Espeland MA, Tindle HA, Bushnell CA, et al. for the **Women's Health Initiative Memory Study. Brain Volumes, Cognitive Impairment, and Conjugated Equine Estrogens**. J Gerontol A Biol Sci Med Sci. 2009 Sep 3.

Espeland MA, Luchsinger JA, Baker LD, et al. Effect of a **long-term intensive lifestyle intervention** on prevalence of cognitive impairment. Neurology 2017;88:2026–2035.

Espeland MA, et al; Action for Health in Diabetes Brain Magnetic Resonance Imaging Research Group. **Long Term Effect of Intensive Lifestyle Intervention** on Cerebral Blood Flow. J Am Geriatr Soc. 2017 Oct 30.

Etgen Thorleif; Sander Dirk; Huntgeburth Ulrich; et al. **Physical Activity** and Incident Cognitive Impairment in Elderly Persons: The INVADE Study. Arch Intern Med. 2010;170(2):186-193.

Ewers M, Insel PS, Stern Y, Weiner MW, for the Alzheimer's Disease Neuroimaging Initiative (ADNI). Cognitive reserve associated with **FDG-PET in preclinical Alzheimer** disease. Neurology 2013;80:1194–1201.

Exalto LG, Biessels GJ, Karter AJ, et al. **Risk score for prediction of 10 year dementia** risk in individuals with type 2 **diabetes**: a cohort study. Lancet Diabetes Endocrinol. 2013 Nov;1(3):183-90.

Factora RM, Tousi B. Don't forget **non-Alzheimer dementias**. Cleve Clin J Med. 2014 Apr;81(4):243-54.

Falk N, Cole A, Meredith TJ. **Evaluation of Suspected Dementia**. Am Fam Physician. 2018;97(6):398-405.

Fancourt D, Steptoe A. **Television viewing and cognitive decline** in older age: findings from the English Longitudinal Study of Ageing. Sci Rep. 2019 Feb 28;9(1):2851.

Fancourt D, Steptoe A. **Television viewing and cognitive decline in older** age: findings from the English Longitudinal Study of Ageing. Sci Rep. 2019 Feb 28;9(1):2851.

Fann JR, Ribe AR, Pedersen HS, et al. **Long-term risk of dementia among people with traumatic brain injury** in Denmark: a population-based observational cohort study. Lancet Psychiatry. 2018 Apr 10.

Fardet L, Nazareth I, Petersen I. **Chronic hydroxychloroquine/chloroquine exposure** for connective tissue diseases and risk of Alzheimer's disease: a population-based cohort study. Ann Rheum Dis. 2019 Feb;78(2):279-282.

Farfel JM, Yu L, Buchman AS, Schneider et al. Relation of **genomic variants** for Alzheimer disease dementia to common neuropathologies. Neurology. 2016 Aug 2;87(5):489-96.

Farina N, Llewellyn D, Isaac MG, et al. **Vitamin E** for Alzheimer`s dementia and mild cognitive impairment. Cochrane Database Syst Rev. 2017 Jan 27;1:CD002854. We found no evidence that the alpha-tocopherol form of vitamin E given to people with MCI prevents progression to dementia, or that it improves cognitive function in people with MCI or dementia due to AD. However, there is moderate quality evidence from a single study that it may slow functional decline in AD. Vitamin E was not associated with an increased risk of serious adverse events or mortality in the trials in this review. These conclusions have changed since the previous update, however they are still based on small numbers of trials and participants and further research is quite likely to affect the results.

Farlow M, Salloway S, Tariot P, et al. Effectiveness & tolerability of **high-dose (23 mg/d)** versus standard-dose (10 mg/d) **donepezil** in moderate to severe Alzheimer's disease: 24-week, randomized, double-blind study. Clin Ther. 2010Jul;32(7):1234-1251.

FDA Aug/11 Antidepressant **citalopram** (*Celexa*, Forest Laboratories) should not be used in doses higher than 40 mg per day because of concerns that it can cause potentially fatal changes in heart rhythm (eg. ↑ QT)

FDA Apr/12 approved **Amyvid (florbetapir F 18 injection)** which binds to beta-amyloid plaques in patients' brains, an active diagnostic for detection of the tell-tale sign of Alzheimer's disease.

Féart C, Samieri C, Rondeau V, Amieva H, Portet F, Dartigues JF, Scarmeas N, Barberger-Gateau P. Adherence to a Mediterranean diet, cognitive decline, and risk of dementia. JAMA. 2009 Aug 12;302(6):638-48.

Feldman HH, Jacova C, Robillard A, et al. **Diagnosis and treatment of dementia**: 2. Diagnosis. CMAJ. 2008 Mar 25;178(7):825-36.

Femminella GD, Dani M, Wood M, et al. **Microglial activation** in early Alzheimer trajectory is associated with **higher gray matter volume**. Neurology. 2019 Mar 19;92(12):e1331-e1343.

Ferman TJ, Smith GE, Kantarci K, et al. **Nonamnestic mild cognitive impairment progresses** to dementia with Lewy bodies. Neurology. 2013 Dec 3;81(23):2032-8

Ferrara N, Corbi G, Capuano A, Filippelli A, Rossi F. **Memantine-induced hepatitis** with cholestasis in a very elderly patient. Ann Intern Med. 2008 Apr 15;148(8):631-2.

Ferrari R, Hernandez DG, Nalls MA, et al. **Frontotemporal dementia** and its subtypes: a genome-wide association study. Lancet Neurol 2014; online June 6.

Ferri CP, Prince M, Brayne C, Brodaty H, et al.; Alzheimer's Disease International. **Global prevalence of dementia**: a Delphi consensus study. Lancet. 2006 Dec 17;366(9503):2112-7.

Ferro DA, van den Brink H, Exalto LG, et al. Clinical relevance of acute cerebral microinfarcts in vascular cognitive impairment. Neurology. 2019 Apr 2;92(14):e1558-e1566.

Fetherston AA, Rowley G, Allan CL. **Challenges in end-of-life dementia care**. Evid Based Ment Health. 2018 Aug;21(3):107-111.

Fialova D, et al. R; AdHOC Project Research Group. Potentially **inappropriate medication** use among elderly home care patients in Europe. JAMA. 2005 Mar 16;293(11):1348-58.

Filippi M, Agosta F, Barkhof F, Dubois B, et al. **EFNS** task force: the use of **neuroimaging in the diagnosis of dementia**. Eur J Neurol. 2012 Dec;19(12):e131-40, 1487-501.

Fillit HM, Doody RS, Binaso K, et al. Recommendations for **best practices** in the treatment of Alzheimer's disease in managed care. Am J Geriatr Pharmacother. 2006;4 Suppl A:S9-S24; quiz S25-S28.

Fink HA, Hemmy LS, MacDonald R, et al. Intermediate- and long-term **cognitive outcomes after cardiovascular procedures** in older adults. Ann Intern Med 2015; 163:107-117.

Fink HA, Jutkowitz E, McCarten JR, et al. **Pharmacologic interventions** to **prevent cognitive decline, mild cognitive impairment, and clinical Alzheimer-type dementia**. A systematic review. Ann Intern Med. 2018;168:39-51.

Flaherty JH, Gonzales JP, Dong B. **Antipsychotics in the treatment of delirium** in older hospitalized adults: a systematic review. J Am Geriatr Soc. 2011 Nov;59 Suppl 2:S269-76.

Fleet JL, McArthur E, Patel A, et al. Risk of **rhabdomyolysis with donepezil** compared with rivastigmine or galantamine: a population-based cohort study. CMAJ. 2019 Sep 16;191(37):E1018-E1024.

Fleisher AS, Chen K, et al. Using Positron Emission Tomography and **Florbetapir F 18** to Image Cortical Amyloid in Patients With Mild Cognitive Impairment or Dementia Due to Alzheimer Disease. Arch Neurol. 2011 Jul 11.

Fleisher AS, Truran D, Mai JT, et al. For the Alzheimer's Disease Cooperative Study. Chronic **divalproex** sodium use and brain atrophy in Alzheimer disease. Neurology. 2011 Sep 27;77(13):1263-1271.

Fleisher AS, Chen K, et al. **Florbetapir PET analysis** of amyloid-β deposition in the presenilin 1 E280A autosomal dominant Alzheimers disease kindred: a cross-sectional study. Lancet Neurol 2012; online Nov 6.

Flynn E, Smith CH, Walsh CD, Walshe M. Modifying the consistency of **food and fluids for swallowing difficulties in dementia**. Cochrane Database of Systematic Reviews 2018, Issue 9. Art. No.: CD011077. We are uncertain about the immediate and long-term effects of modifying the consistency of fluid for swallowing difficulties in dementia as too few studies have been completed. There may be differences in outcomes depending on the grade of thickness of fluids and the sequence of interventions trialled in videofluoroscopy for pe ople with dementia. Clinicians should be aware th at while thickening fluids may have an immediate positive effect on swallowing, the long-term impact of thickened fluids on th e health of the person with dementia should be considered. Fur ther high-quality clinical trials are required.

Fong TG et al. **Delirium accelerates** cognitive decline in Alzheimer disease. Neurology 2009 May 5; 72:1570.

Fong Tamara G.; Jones Richard N.; Rudolph James L.; et al. Development and Validation of a Brief **Cognitive Assessment Tool**: **The Sweet 16**. Arch Intern Med. 2010;0(2010):archinternmed.2010.423. http://hospitalelderlifeprogram.org

Fong TG, Jones RN, Marcantonio ER, et al. **Adverse outcomes after hospitalization and delirium** in persons with Alzheimer disease. Ann Intern Med. 2012 Jun 19;156(12):848-56.

Fong TG, Davis D, Growdon ME, et al. The **interface between delirium and dementia** in elderly adults. Lancet Neurol. 2015 Aug;14(8):823-32.

Forlenza OV, Diniz BS, Radanovic M, et al. Disease-modifying properties of long-term **lithium treatment for amnestic mild cognitive impairment**: randomised controlled trial. Br J Psychiatry. 2011 May;198:351-6.

Fortes-Filho SQ, Apolinario D, Melo JA, et al. Predicting **delirium after hip fracture with a 2-min cognitive screen: prospective cohort study (10-CS).** Age Ageing. 2016 May 17.

Fossey J, et al. Effect of enhanced **psychosocial care** on antipsychotic use in nursing home residents with severe dementia: cluster randomised trial. BMJ. 2006 Apr 1;332(7544):756-61. Epub 2006 Mar 16. Erratum in: BMJ. 2006 Apr 1;332(7544):61.

Foster NL, Bondi MW, Das R, et al. Quality improvement in neurology: Mild cognitive impairment quality measurement set. Neurology. 2019 Sep 18.

Fox C, Richardson K, Maidment ID, et al. **Anticholinergic Medication Use** and Cognitive Impairment in the Older Population: The Medical Research Council Cognitive Function and Ageing Study. J Am Geriatr Soc. 2011 Jun 24

Fralick M, Sacks CA, Kesselheim AS. Assessment of Use of Combined **Dextromethorphan and Quinidine** in Patients With Dementia or Parkinson Disease After US Food and Drug Administration Approval **for Pseudobulbar Affect**. JAMA Intern Med. 2019 Jan 7.

Frank Christopher, Feldman Sid, Schulz Mary. Resources for people with dementia: The Alzheimer Society and beyond (**First Link**). Can Fam Physician December 2011 57: 1387-1391.

Frank C, Forbes RF. A **patient's experience** in dementia care: Using the "**lived experience**" to improve care. Can Fam Physician. 2017 Jan;63(1):22-26

Frank CC, Lee L, Molnar F. **Driving assessment** for people with dementia. Can Fam Physician. 2018 Oct;64(10):744.

Freudenberger P, Petrovic K, Sen A, et al. **Fitness and cognition** in the elderly: the Austrian Stroke Prevention Study. Neurology 2016;86:418–424.

Friberg L, Rosenqvist M. **Less dementia with oral anticoagulation** in atrial fibrillation. Eur Heart J. 2017 Oct 24.

Friedman JI, Soleimani L, McGonigle DP, et al. Pharmacological Treatments of **Non-Substance-Withdrawal Delirium**: A Systematic Review of Prospective Trials. Am J Psychiatry. 2013 Dec 20

Frisoni GB. **PET and (18)F ligands** in the diagnosis of Alzheimer's disease. Lancet Neurol. 2011 Apr 8.

Frisoni GB, Boccardi M, Barkhof F, et al, 2017. Strategic roadmap for an **early diagnosis of Alzheimer's Disease based on biomarkers**. Lancet Neurol 2017; 16: 661–76

Fuchs A, Wiese B, Altiner A, Wollny A, Pentzek M. Cued recall and other cognitive tasks to facilitate dementia recognition in primary care (**VAT-Visual Association Test**). J Am Geriatr Soc. 2012 Jan;60(1):130-5.

Furukawa TA. **Prognosis of delirium**. Evid Based Ment Health. 2017 May;20(2):53-54.

Galasko DR, Peskind E, Clark CM, et al. the Alzheimer's Disease Cooperative Study. **Antioxidants** for Alzheimer Disease: A Randomized Clinical Trial With Cerebrospinal Fluid Biomarker Measures. Arch Neurol. 2012 Mar 19.

Galasko D, Bell J, Mancuso JY, et al; Alzheimer's Disease Cooperative Study. Clinical trial of an inhibitor of **RAGE-Aβ interactions** in Alzheimer disease. Neurology. 2014 Apr 29;82(17):1536-42.

Gallacher J, Ilubaera V, Ben-Shlomo Y, et al. **Auditory threshold**, phonologic demand, and incident dementia. Neurology. 2012 Oct 9;79(15):1583-90.

Galvin JE, Roe CM, Powlishta KK, Coats MA, Muich SJ, Grant E, Miller JP, Storandt M, Morris JC. The **AD8**: a brief informant **interview to detect dementia**. Neurology. 2005 Aug 23;65(4):559-64.

Ganguli M, Snitz BE, Saxton JA, et al. Outcomes of **mild cognitive impairment** by definition: a population study. Arch Neurol. 2011 Jun;68(6):761-7.

Ganguli M, Lee CW, Snitz BE, et al. Rates and risk factors for **progression to incident dementia** vary by age in a population cohort. Neurology. 2015 Jan 6;84(1):72-80.

Gao C, Chapagain NY, Scullin MK. **Sleep Duration and Sleep Quality** in Caregivers of Patients With Dementia: A Systematic Review and Meta-analysis. JAMA Netw Open. 2019 Aug 2;2(8):e199891.

Gao Y, O'Caoimh R, Healy L, et al. Effects of **centrally acting ACE inhibitors** on the rate of cognitive decline in dementia. BMJ Open 2013.

Garcia PS, Duggan EW, McCullough IL, et al. **Post-anesthesia care** for the elderly patient. Clin Ther. 2015;37:xxx–xxx

Gardner DM, Baldessarini RJ, Waraich P. Modern antipsychotic drugs: a critical overview. CMAJ. 2005 Jun 21;172(13):1703-11.

Gardener H, Wright CB, Dong C, et al. **Ideal Cardiovascular Health** and Cognitive Aging in the Northern Manhattan Study. J Am Heart Assoc. 2016 Mar 16;5(3).

Gardner RC, Yaffe K. **Traumatic brain injury** may increase risk of young-onset dementia. Ann Neurol. 2014 Feb 18.

Gardner RC, Burke JF, Nettiksimmons J, et al. Dementia Risk **After Traumatic Brain Injury** vs Nonbrain Trauma: The Role of Age and Severity. JAMA Neurol. 2014 Oct 27.

Gasby D. Alzheimer dementia's **other victim: The spouse**. Neurology. 2017 Nov 7;89(19):1934-1937.

Gaster B, Larson EB, Curtis JR. **Advance Directives** for Dementia: Meeting aUnique Challenge. JAMA. 2017 Nov 6.

Gates NJ, Rutjes AW, Di Nisio M, et al. **Computerised cognitive training** for maintaining cognitive function in cognitively healthy people in midlife. Cochrane Database Syst Rev. 2019 Mar 13;3:CD012278.

Gauthier S, et al. International Psychogeriatric Association Expert Conference on mild cognitive impairment. **Mild cognitive impairment**. Lancet. 2006 Apr 15;367(9518):1262-70.

Gauthier S, Herrmann N, Ferreri F, Agbokou C. Use of **memantine** to treat Alzheimer's disease. CMAJ. 2006 Aug 29;175(5):501-2.

Gauthier S, et al. EXTEND Investigators. A large, naturalistic, **community-based** study of **rivastigmine** in mild-to-moderate AD: the **EXTEND** Study. Curr Med Res Opin. 2006 Nov;22(11):2251-65.

Gauthier S, Patterson C, Chertkow H, et al. Soucy JP. Recommendations of the **4th Canadian Consensus Conference on the Diagnosis and Treatment of Dementia (CCCDTD4).** Can Geriatr J. **2012** Dec;15(4):120-6.

Gauthier S, et al. Efficacy & safety of **tau-aggregation inhibitor** therapy in mild or moderate Alzheimer's disease: a randomised, controlled, double-blind, parallel-arm, phase 3 trial. Lancet 2016; online Nov 15. (LMTM)

Geijselaers SL, Sep SJ, Stehouwer CD, et al. **Glucose regulation, cognition, and brain MRI in type 2 diabetes**: a systematic review. Lancet Diabetes Endocrinol. 2014 Aug 22.

Gelber RP, Ross GW, Petrovitch H, et al. **Antihypertensive medication use and risk of cognitive impairment**: The Honolulu-Asia Aging Study. (HAAS) Neurology. 2013 Sep 3;81(10):888-95.

Gerhard T, Huybrechts K, Olfson M, et al. Comparative **mortality risks of antipsychotic** medications in community-dwelling older adults. Br J Psychiatry. 2013 Aug 8.

Gerstein HC, Marcovina S, Akpunonu BE, et al. Association of **Depression With Accelerated Cognitive Decline Among Patients With Type 2 Diabetes in the ACCORD-MIND** Trial. JAMA Psychiatry. 2013 Aug 14.

Gidicsin CM, Maye JE, Locascio JJ, et al. **Cognitive activity relates to cognitive performance** but not to Alzheimer disease biomarkers. Neurology. 2015 Jul 7;85(1):48-55.

Gill Sudeep S; et al. **Syncope** and Its Consequences in Patients With Dementia Receiving Cholinesterase Inhibitors: A Population-Based Cohort Study Arch Intern Med. 2009;169(9):867-873.

Gilsanz P, Albers K, Beeri MS, et al. Traumatic brain injury associated with dementia risk among people with type 1 diabetes. Neurology. 2018 Oct 3; 91(17):e1611-e1618.

Gilsanz P, Lee C, Corrada MM, et al. **Reproductive period and risk of dementia** in a diverse cohort of health care members. Neurology. 2019 Apr 23;92(17):e2005-e2014.

Gilsanz P, Mayeda ER, Glymour MM, et al. Association Between **Birth** in a **High Stroke Mortality State**, Race, and Risk of **Dementia**. JAMA Neurol. 2017 Jul 31.

Gilsanz P, Mayeda ER, Glymour MM, et al. Female sex, early-onset **hypertension, and risk of dementia**. Neurology. 2017 Oct 31;89(18):1886-1893

Gimson A, Schlosser M, Huntley JD, et al. Support for **midlife anxiety diagnosis as an independent risk factor for dementia**: a systematic review. BMJ Open. 2018 Apr 30;8(4):e019399.

Girard TD, Exline MC, Carson SS, et al. **Haloperidol and ziprasidone** for treatment of **delirium** in critical illness. (**MIND-USA**) N Engl J Med. DOI: 10.1056/NEJMoa1808217.

Gitlin Laura N.; Winter Laraine; et al. A **Biobehavioral Home-Based Intervention** and the Well-being of Patients With Dementia and Their Caregivers: The **COPE** Randomized Trial. JAMA. 2010;304(9):983-991.

Gitlin LN, Kales HC, Lyketsos CG. **Nonpharmacologic management of behavioural symptoms in dementia**. JAMA. 2012 Nov 21;308(19):2020-9.

Givens Jane L.; Jones Richard N.; Shaffer Michele L.; et al. Survival and Comfort After **Treatment of Pneumonia** in Advanced Dementia. Arch Intern Med. 2010;170(13):1102-1107.

Gleason LJ, Schmitt EM, Kosar CM, et al. Effect of **Delirium** and Other Major Complications on Outcomes **After Elective Surgery** in Older Adults. JAMA Surg. 2015 Sep 9:1-7.

Godin O, Tzourio C, Maillard P, et al. **Antihypertensive Treatment** and Change in Blood Pressure Are Associated With the Progression of White Matter Lesion Volumes: The Three-City (3C)-Dijon Magnetic Resonance Imaging Study. Circulation. 2011 Jan 25;123(3):266-73.

Goh KL, Bhaskaran K, Minassian C, et al. **Angiotensin receptor blockers** and risk of dementia: cohort study in UK Clinical Practice Research Datalink. Br J Clin Pharmacol. 2014 Sep 16.

Goldberg SE, Bradshaw LE, Kearney FC, et al; Medical Crises in Older People Study Group. Care in **specialist medical and mental health unit compared with standard care** for older people with cognitive impairment admitted to general hospital: randomised controlled trial (NIHR TEAM trial). BMJ. 2013 Jul 2;347:f4132.

Goldfeld Keith S.; Stevenson David G.; Hamel Mary Beth; et al. **Medicare Expenditures Among Nursing Home Residents** With Advanced Dementia. *Arch Intern Med*. 2011;171(9):824-830.

Goldstein FC, Steenland K, Zhao L, et al. **Proton Pump Inhibitors** and **Risk of Mild Cognitive Impairment and Dementia**. J Am Geriatr Soc. 2017 Jun 7.

Gomes-Osman J, Cabral DF, Morris TP, et al. **Exercise for cognitive brain health in aging:** A systematic review for an evaluation of dose. Neurol Clin Pract. 2018 Jun;8(3):257-265.

Gomm W, von Holt K, Thomé F, et al. Association of **proton pump inhibitors with risk of dementia**: a pharmacoepidemiological claims data analysis [online Feb 15, 2016].JAMA Neurol. doi:10.1001/jamaneurol.2015.4791.

Gonzalez BD et al. Course and predictors of cognitive function in patients with **prostate cancer** receiving **androgen-deprivation therapy**: A controlled comparison. J Clin Oncol 2015 May 11.

Goodarzi ZS, Mele BS, Roberts DJ, et al. **Depression Case Finding** in Individuals with Dementia: A Systematic Review and Meta-Analysis. J Am Geriatr Soc. 2017 Feb 2.

Goodwill AM, Szoeke C. A Systematic Review and Meta-Analysis of The Effect of Low **Vitamin D on Cognition**. J Am Geriatr Soc. 2017 Oct;65(10):2161-2168.

Gordon BA, Blazey TM, Su Y, et al. Spatial patterns of **neuroimaging biomarker change** in individuals from families with autosomal dominant Alzheimer's disease: a longitudinal study. Lancet Neurol 2018; online Jan 31.

Gorelick PB, Scuteri A, Black SE et al. **Vascular contributions** to cognitive impairment and dementia: a statement for healthcare professionals from the American Heart Association-AHA/American Stroke Association-ASA.Stroke.2011Sep;42(9):2672-713.

Gottesman RF et al. **Delirium after coronary artery bypass graft surgery** and late mortality. Ann Neurol 2010 Mar; 67:338.

Gottesman RF, Schneider AL, Albert M, et al. **Midlife Hypertension** and 20-Year Cognitive Change: The Atherosclerosis Risk in Communities Neurocognitive Study. JAMA Neurol. 2014 Aug 4.

Gottesman RF, Schneider AL, Zhou Y, et al. Association Between **Midlife Vascular Risk Factors and Estimated Brain Amyloid Deposition**. JAMA. 2017 Apr 11;317(14):1443-1450.

Gow AJ, Bastin ME, Maniega SM, Valdés Hernández MC, Morris Z, Murray C, et al. **Neuroprotective lifestyles** and the aging brain: activity, atrophy, and white matter integrity. Neurology2012;79:1802-8.

Gozalo P, Teno JM, Mitchell SL, et al. **End-of-life transitions** among nursing home residents with cognitive issues. N Engl J Med. 2011 Sep 29;365(13):1212-21.

Graff MJ, Adang EM, Vernooij-Dassen MJ, et al. Community **occupational therapy** for older patients with dementia and their care givers: cost effectiveness study. BMJ. 2008 Jan 19;336(7636):134-8. Epub 2008 Jan 2. Community occupational therapy intervention for patients with dementia and their care givers is successful and cost effective, especially in terms of informal care giving.

Gray SL, Anderson ML, Dublin S, et al. Cumulative use of **strong anticholinergics and incident dementia**: a prospective cohort study [online January 26, 2015]. JAMA Intern Med. doi:10.1001/jamainternmed.2014.7663.

Green R, Lanphear B, Hornung R, et al. Association Between **Maternal Fluoride Exposure During Pregnancy and IQ Scores** in Offspring in Canada. JAMA Pediatr. 2019 Aug 19.

Green RC, Roberts JS, Cupples LA, et al.; REVEAL Study Group. Disclosure of **APOE genotype** for risk of Alzheimer's disease. N Engl J Med. 2009 Jul 16;361(3):245-54.

Green RC.; Schneider LS.; et al. the Tarenflurbil Phase 3 Study Group. Effect of **Tarenflurbil** on Cognitive Decline and Activities of Daily Living in Patients With Mild Alzheimer Disease: A Randomized Controlled Trial. JAMA. 2009;302(23):2557-2564.

Grodstein F, O'Brien J, Kang JH, Dushkes R, Cook NR, Okereke O, et al. Long-term **multivitamin supplementation and cognitive function** in men. A randomized trial. Ann Intern Med. 2013;159:806-14.

Gross AL, Jones RN, Habtemariam DA, et al. Delirium and Long-term **Cognitive Trajectory** Among Persons With Dementia. Arch Intern Med. 2012 Aug 20:1-8.

Grothe MJ, Barthel H, Sepulcre J, et al. In vivo staging of **regional amyloid deposition**. Neurology 2017;89:2031–2038.

Growdon JH, Hyman BT. **Plasma {beta}-Amyloid** Linked to Cognitive Decline. Arch Neurol. 2011 Jun;68(6):799-801.

Growdon ME, Schultz AP, Dagley AS, et al. **Odor identification** and Alzheimer disease biomarkers in clinically normal elderly. Neurology. 2015 May 26;84(21):2153-60.

Gu Y, Schupf N, Cosentino SA, et al. **Nutrient intake** (ω-3 PUFA) and plasma β-amyloid. Neurology. 2012 Jun 5;78(23):1832-40.

Gu Y, Brickman AM, Stern Y, et al. **Mediterranean diet** and brain structure in a multiethnic elderly cohort. Neurology. 2015 Nov 17;85(20):1744-51.

Guerreiro R, Wojtas A, Bras J, et al. **TREM2 variants** in Alz hei mer's disease. N Engl J Med 2012. DOI: 10.1056/NEJMoa1211851.

Guerreiro R, Ross OA, Kun-Rodrigues C, et al. Investigating the **genetic architecture of dementia with Lewy bodies**: a two-stage genome-wide association study. Lancet Neurol 2018; 17: 64–74.

Gupta VB, Laws SM, Villemagne VL,et al; For the AIBL Research Group. Plasma **apolipoprotein E** and Alzheimer disease risk: The **AIBL** study of aging. Neurology. 2011 Mar 22;76(12):1091-1098.

Gurwitz JH, Bonner A, Berwick DM. Reducing **Excessive Use of Antipsychotic Agents in Nursing Homes**. JAMA. 2017 Jun 15.

Guterman EL, Allen IE, Josephson SA, et al. Association Between **Caregiver Depression and Emergency Department Use** Among Patients With Dementia. JAMA Neurol. 2019 Jul 8.

Haan M, Espeland MA, Klein BE, et al. Cognitive function and **retinal** and ischemic **brain** changes: the Women's Health Initiative (WHI). Neurology 2012;78:942–949.

Hachinski V, Einhäupl K, Ganten D, et al. **Preventing dementia by preventing stroke**: The Berlin Manifesto. Alzheimers Dement. 2019 Jul;15(7):961-984.

Haddad P. **Weight** change with atypical antipsychotics in the treatment of schizophrenia. J Psychopharmacol. 2005 Nov;19(6 Suppl):16-27.

Hadjistavropoulos T, Herr K, Prkachin KM, et al. **Pain assessment in elderly** adults with dementia. Lancet Neurol. 2014 Dec;13(12):1216-1227.

Hagger-Johnson G, Sabia S, Brunner EJ, et al. Combined impact of **smoking and heavy alcohol** use on cognitive decline in early old age: Whitehall II prospective cohort study. Br J Psychiatry. 2013 Jul 11.

Hajjar I, Brown L, Mack WJ, Chui H. Impact of **Angiotensin Receptor Blockers** on Alzheimer Disease Neuropathology in a Large Brain Autopsy Series. Arch Neurol. 2012 Sep 10:1-7.

Hakim SM, Othman AI, Naoum DO. Early treatment with **risperidone for subsyndromal delirium** after on-pump cardiac surgery in the elderly: a randomized trial. Anesthesiology. 2012 May;116(5):987-97.

Halladay CW, Sillner AY, Rudolph JL. **Performance of Electronic Prediction Rules for Prevalent Delirium at Hospital Admission**. JAMA Netw Open. 2018;1(4):e181405.

Hamer M, Batty GD. Association of **body mass index and waist-to-hip ratio** with brain structure: UK Biobank study. Neurology. 2019 Feb 5;92(6):e594-e600.

Hamina A, Taipale H, Tanskanen A, et al. Differences in **analgesic use** in **community- dwelling persons with and without Alzheimer's disease**. Eur J Pain. 2016 Nov 14.

Hamina A, Taipale H, et al. Long-term use of **opioids** for non-malignant pain among **community-dwelling persons with and without Alzheimer's** disease in Finland: a nationwide register-based study. Pain. 2016 Nov 4.

Hamina A, Lavikainen P, Tanskanen A, et al. Impact of **opioid initiation on antipsychotic and benzodiazepine and related drug use among persons with Alzheimer's disease**. Int Psychogeriatr. 2018 Mar 21:1-10.

Han JH, Wilson A, et al. **Diagnosing delirium in older emergency department patients**: validity and reliability of the delirium triage screen and the brief confusion assessment method. Ann Emerg Med. 2013 Nov;62(5):457-65.

Han JH, Wilson A, et al. Validation of the **Confusion Assessment Method for the Intensive Care** Unit in Older Emergency Department Patients. Acad Emerg Med. 2014 Feb;21(2):180-187.

Han JH, Vasilevskis EE, Schnelle JF, et al. The Diagnostic Performance of the **Richmond Agitation Sedation Scale for Detecting Delirium** in Older Emergency Department Patients. Acad Emerg Med. 2015 Jul;22(7):878-82.

Han L, Agostini JV, Allore HG. **Cumulative anticholinergic exposure** is associated with poor memory and executive function in older men. J Am Geriatr Soc. 2008 Dec;56(12):2203-10. Cumulative anticholinergic exposure across multiple medications over 1 year may negatively affect verbal memory and executive function in older men. Prescription of drugs with anticholinergic effects in older persons deserves continued attention to avoid deleterious adverse effects.

Hankey GJ, Ford AH, Yi Q, et al. Effect of **B vitamins and lowering homocysteine on cognitive** impairment in patients with previous stroke or transient ischemic attack: a prespecified secondary analysis of a randomized, placebo-controlled trial (VITATOPS) and meta-analysis. Stroke. 2013 Aug;44(8):2232-9.

Hankey GJ. **Public Health Interventions for Decreasing Dementia Risk**. JAMA Neurol. 2017 Nov 20.

Hanlon JT, Aspinall SL, Handler SM, et al. **Potentially suboptimal prescribing** for older veteran nursing home patients with dementia. Ann Pharmacother. 2015 Jan;49(1):20-8.

Hanney M, Prasher V, Williams N, et al, on behalf of the **MEADOWS** trial researchers. **Memantine** for dementia in adults older than 40 years with **Down's syndrome** (MEADOWS): randomised, double-blind, placebo-controlled trial. Lancet 2012; Jan 10.

Hanseeuw BJ, Betensky RA, Jacobs HIL, et al. **Association of Amyloid and Tau With Cognition** in Preclinical Alzheimer Disease: A Longitudinal Study. JAMA Neurol. 2019 Jun 3.

Hanson LC, Ersek M, Gilliam R, et al. **Oral feeding** options for people with dementia: a systematic review. J Am Geriatr Soc. 2011 Mar;59(3):463-72. doi: 10.1111/j.1532-5415.2011.03320.x.

Hara Y, McKeehan N, Fillit HM. Translating **the biology of aging into novel therapeutics** for Alzheimer disease. Neurology. 2019 Jan 8;92(2):84-93.

Haring B, Leng X, Robinson J, et al. **Cardiovascular Disease and Cognitive Decline** in **Postmenopausal** Women: Results From the Women's Health Initiative Memory Study. J Am Heart Assoc. 2013 Dec 18;2(6)

Harrison JK, Fearon P, Noel-Storr AH, et al. **Informant Questionnaire on Cognitive Decline** in the **Elderly** (**IQCODE**) for the diagnosis of dementia within a secondary care setting. Cochrane Database Syst Rev. 2015 Mar 10;3:CD010772. The IQCODE can be used to identify older adults in the general hospital setting who are at risk of dementia and require specialist assessment; it is useful specifically for ruling out those without evidence of cognitive decline. The language of administration did not affect test accuracy, which supports the cross-cultural use of the tool. These findings are qualified by the significant heterogeneity, the potential for bias and suboptimal reporting found in the included studies.

Harrison TM, La Joie R, Maass A, et al. Longitudinal **tau accumulation and atrophy** in aging and Alzheimer's disease. Ann Neurol. 2018 Dec 31

Hashimoto K. Can **Minocycline Prevent** the Onset of Alzheimer's Disease? Annals of Neurology. 2011; 1-4 [online].

Hatta K, Kishi Y, Wada K, et al; for the DELIRIA-J Group. Preventive Effects of **Ramelteon on Delirium**: A Randomized Placebo-Controlled Trial. JAMA Psychiatry. 2014 Feb 19.

Hayden KM, Norton MC, Darcey D, et al. Cache County Study Investigators. Occupational exposure to **pesticides** increases the risk of incident AD: the Cache County study. Neurology. 2010 May 11;74(19):1524-30.

Head D, Bugg JM, Goate AM, et al. **Exercise** Engagement as a Moderator of the Effects of APOE Genotype on Amyloid Deposition. Arch Neurol. 2012 Jan 9.

Health Canada May/10: Novartis, in consultation with Health Canada, is informing healthcare providers and consumers that serious adverse events including **death** were associated with errors/misuse of the **Exelon Patch**.

Health Canada Nov/13 **Risperidone- and paliperidone**-containing products are primarily prescribed for the treatment of schizophrenia; however, the risk of Intraoperative floppy iris syndrome (**IFIS**) applies to all patients undergoing cataract surgery, who have been exposed to these products, irrespective of indication.

Health Canada Nov/14 REMINYL ER (**galantamine** hydrobromide) - New Safety Information Regarding the Risk of **Serious Skin Reactions** - Janssen Inc. Very rare cases of serious skin reactions have been reported in patients taking REMINYL ER.

Health Canada Jan 2015 Alzheimer's drug Aricept (donepezil) - New warnings on the serious risks of muscle breakdown and of a neurological disorder. (Rhabdomyolysis, NMS). http://healthycanadians.gc.ca/recall-alert-rappel-avis/hc-sc/2015/43469a-eng.php

Health Canada Jan/15 Alzheimer's drug **Aricept** (**donepezil**) - New warnings have been added to the prescribing information for the Alzheimer's drug Aricept (donepezil) advising of the risk of two rare but potentially serious conditions: muscle breakdown (**rhabdomyolysis**) and a neurological disorder called **neuroleptic malignant syndrome** (**NMS**).

Health Canada Feb/15 **Risperidone** - Restriction of the Dementia Indication - Janssen Inc. The indication for risperidone in dementia has been restricted to the **short-term symptomatic management of aggression or psychotic symptoms in patients with severe dementia of the Alzheimer type**. The indication no longer includes the treatment of other types of dementia.

Heath L, Gray SL, Boudreau DM, et al. **Cumulative Antidepressant Use and Risk of Dementia** in a Prospective Cohort Study. J Am Geriatr Soc. 2018 Sep 17.

Hebert LE, Weuve J, Scherr PA, Evans DA. **Alzheimer disease in the United States (2010-2050) estimated** using the 2010 census. Neurology. 2013 May 7;80(19):1778-83.

Heister D, Brewer JB, Magda S, et al; For the Alzheimer's Disease Neuroimaging Initiative. **Predicting MCI** outcome with clinically available **MRI and CSF biomarkers**. Neurology. 2011 Oct 25;77(17):1619-1628.

Helmer C et al. **Chronic kidney disease**, cognitive decline, and incident dementia:The 3C Study. Neurology. 2011 Dec 6;77(23):2043-51.

Hernandez RK, Farwell W, Cantor MD, Lawler EV. Cholinesterase Inhibitors and Incidence of **Bradycardia** in Patients with Dementia in the Veterans Affairs New England Healthcare System. J Am Geriatr Soc. 2009 Sep 28.

Henderson VW, St John JA, Hodis HN, et al; For the **WISH** Research Group. Long-term **soy isoflavone** supplementation and cognition in women: A randomized, controlled trial. Neurology. 2012 Jun5;78(23):1841-1848.

Henderson VW, St John JA, Hodis HN, et al. Cognitive effects of **estradiol** after menopause: A randomized trial of the timing hypothesis. Neurology. 2016 Jul 15

Hendry K, Green C, McShane R, et al. **AD-8** for detection of dementia across a variety of healthcare settings. Cochrane Database Syst Rev. 2019 Mar 4;3:CD011121. The high sensitivity of the AD-8 suggests it can be used to identify adults who may benefit from further specialist assessment and diagnosis, but is not a diagnostic test in itself. This pattern of high sensitivity and lower specificity is often suited to a screening test. Test accuracy varies by setting, however data in primary care and acute hospital settings are limited.

Hendry K, Hill E, Quinn TJ, et al. **Single screening questions for cognitive impairment** in older people: a systematic review. Age Ageing. 2014 Nov 10

Heneka MT, Carson MJ, Khoury JE, et al. **Neuroinflammation** in Alzheimer's disease. Lancet Neurol. 2015 Apr;14(4):388-405.

Heneka MT, Fink A, Doblhammer G. Effect of **pioglitazone** medication on the incidence of dementia. Ann Neurol. 2015 May 14.

Herrmann N, Rapoport MJ, Sambrook R, et al. Canadian Outcomes Study in Dementia (COSID) Investigators. Predictors of **driving cessation** in mild-to-moderate dementia. CMAJ. 2006 Sep 12;175(6):591-5.

Herrmann N, Lanctôt KL. Pharmacologic management of **neuropsychiatric symptoms of Alzheimer disease**. Can J Psychiatry. 2007 Oct;52(10):630-46.

Herrmann N Md, Gauthier S Md. Diagnosis and treatment of dementia: 6. Management of **severe Alzheimer disease**. CMAJ. 2008 Dec 2;179(12):1279-1287.

Herrmann N, Black SE, Chow T, Cappell J, Tang-Wai DF, Lanctôt KL. **Serotonergic Function** (citalopram) and Treatment of Behavioral and Psychological Symptoms of **Frontotemporal Dementia**. Am J Geriatr Psychiatry. 2011 Aug 27.

Herrmann N, Black SE, Li A, Lanctôt KL. **Discontinuing cholinesterase inhibitors**: results of a survey of Canadian dementia experts. Int Psychogeriatr 2011;23:539-45.

Herrmann N, Gauthier S, et al. A randomized, double-blind, placebo-controlled trial of **memantine in a behaviorally** enriched sample of patients with moderate-to-severe Alzheimer's disease. Int Psychogeriatr. 2013 Mar 8:1-9.

Herholz Karl, Ebmeier Klaus. Clinical **amyloid imaging** in Alzheimer's disease. The Lancet Neurology 1 July 2011 (Volume 10 Issue 7 Pages 667-670 DOI: 10.1016/S1474-4422(11)70123-5)

Hershey LA, Coleman-Jackson R. Pharmacological Management of **Dementia with Lewy Bodies**. Drugs Aging. 2019 Jan 25.

Hindin SB, Zelinski EM. **Extended practice and aerobic exercise interventions** benefit untrained cognitive outcomes in older adults: a meta-analysis. J Am Geriatr Soc. 2012 Jan;60(1):136-41.

Hithersay R, Startin CM, Hamburg S, et al. Association of **dementia with mortality** among adults with **Down syndrome older than 35 years** [online Nov 21, 2018]. JAMA Neurol. doi:10.1001/jamaneurol.2018.3616

Hoang TD, Reis J, Zhu N, et al. Effect of Early Adult Patterns of **Physical Activity and Television** Viewing on Midlife Cognitive Function. JAMA Psychiatry. 2015 Dec 2:1-8.

Hogan DB, Bailey P, Black S, Carswell A, Chertkow H, Clarke B, Cohen C, Fisk JD, Forbes D, Thorpe L et al. Diagnosis and treatment of dementia: 4. Approach to management of **mild to moderate dementia**. CMAJ. 2008 Oct 7;179(8):787-93.

Hogan DB, Bailey P, Black S, Carswell A, Chertkow H, Clarke B, Cohen C, Fisk JD, Forbes D, Man-Son-Hing M, Lanctôt K, Morgan D, Thorpe L. Diagnosis and treatment of dementia: 5. **Nonpharmacologic and pharmacologic** therapy for **mild to moderate dementia**. CMAJ. 2008 Nov 4;179(10):1019-26.

Hollis AM, Duncanson H, Kapust LR, et al. **Validity of the Mini-Mental State Examination** and the **Montreal Cognitive Assessment** in the Prediction of Driving Test Outcome. J Am Geriatr Soc. 2015 May 4.

Holmes C, Cunningham C, Zotova E, et al. Proinflammatory **cytokines**, sickness behavior, and Alzheimer disease. Neurology. 2011 Jul 19;77(3):212-8.

Holroyd-Leduc JM, Khandwala F, Sink KM. How can **delirium** best be prevented and managed in older patients in hospital? CMAJ. 2009 Aug 17. [Epub ahead of print]

Holmes C, Wilkinson D, Dean C, et al. The efficacy of **donepezil** in the treatment of neuropsychiatric symptoms in Alzheimer disease. Neurology 2004;63:214-9.

Holsinger T, Deveau J, Boustani M, Williams JW Jr. **Does this patient have dementia**? JAMA. 2007 Jun 6;297(21):2391-404.

Holsinger T, Plassman BL, Stechuchak KM, et al. **Screening for cognitive impairment**: comparing the performance of four instruments in primary care. J Am Geriatr Soc. 2012 Jun;60(6):1027-36.

Hong CH, Falvey C, Harris TB, et al. **Anemia** and risk of dementia in older adults: Findings from the Health ABC study. Neurology. 2013 Aug 6;81(6):528-533.

Honig LS, Vellas B, Woodward M, et al. Trial of **solanezumab** for mild dementia due to Alzheimer's disease. (Expedition3) N Engl J Med 2018;378:321-30.

Hörder H, Johansson L, Guo X, et al. **Midlife cardiovascular fitness and dementia**: A 44-year longitudinal population study in women. Neurology. 2018 Apr 10;90(15):e1298-e1305.

Hort J, O'Brien JT, Gainotti G, Pirttila T, Popescu BO, Rektorova I, Sorbi S, Scheltens P, EFNS Scientist Panel on Dementia. **EFNS guidelines** for the **diagnosis and management of Alzheimer's** disease. Eur J Neurol 2010 Oct;17(10):1236-48.

Hosker CM, Bennett MI. **Delirium and agitation at the end of life**. BMJ. 2016 Jun 9;353:i3085.

Hosker C, Ward D. **Hypoactive delirium**. BMJ. 2017 May 25;357:j2047

Howard RJ, et al. **Donepezil** for the treatment of agitation in Alzheimer`s disease. (**CALM-AD**) N Engl J Med. 2007 Oct 4;357(14):1382-92. In this 12-week trial, donepezil was not more effective than placebo in treating **agitation** in patients with Alzheimer's disease.

Howard R et al. **Donepezil and memantine** for moderate-to-severe Alzheimer's disease. (**DOMINO**) *N Engl J Med* 2012 Mar 8; 366:893.

Howard R, Costafreda SG, et al. Baseline characteristics and treatment-emergent risk factors associated with cerebrovascular event and death with **risperidone** in dementia patients. Br J Psychiatry. 2016 Jul 7. (anti-inflammatory)

Howard R et al. **Nursing home placement in the Donepezil and Memantine** in Moderate to Severe Alzheimer's Disease (**DOMINO-AD**) trial: Secondary and post-hoc analyses. Lancet Neurol 2015 Oct 26.

Howes LG. **Cardiovascular effects** of drugs used to treat Alzheimer's disease. Drug Saf. 2014 Jun;37(6):391-5.

Hshieh TT, Yue J, Oh E, et al. Effectiveness of **Multicomponent Nonpharmacological Delirium Interventions**: A Meta-analysis. JAMA Intern Med. 2015 Feb 2.

Hu WT, Holtzman DM, Fagan AM, et al. **Plasma multianalyte profiling** in mild cognitive impairment and Alzheimer disease. Neurology 2012;79:897–905.

Huang TY, Wei YJ, Moyo P, et al. **Treated Behavioral Symptoms and Mortality** in Medicare Beneficiaries in Nursing Homes with Alzheimer`s Disease and Related Dementias. J Am Geriatr Soc. 2015 Aug 27.

Hughes TM, Kuller LH, Barinas-Mitchell EJ, et al. **Pulse wave velocity** is associated with **β-amyloid deposition** in the brains of very elderly adults. Neurology. 2013 Oct 16.

Hughes ME, Peeler J, Hogenesch JB, et al. The **Growth and Impact of Alzheimer** Disease Centers as Measured by Social Network Analysis. JAMA Neurol. 2014 Feb 10.

Hughes TM, Kuller LH, Barinas-Mitchell EJ, et al. **Arterial Stiffness and β-Amyloid Progression** in Nondemented Elderly Adults. JAMA Neurol. 2014 Mar 31.

Hui D, et al. Effect of **lorazepam with haloperidol vs haloperidol alone on agitated delirium** in patients with advanced **cancer receiving palliative care**: a randomized clinical trial. JAMA. doi:10.1001/jama.2017.11468

Hunt LJ, Covinsky KE, Yaffe K, et al. **Pain in Community-Dwelling Older Adults with Dementia**: Results from the National Health and Aging Trends Study. J Am Geriatr Soc. 2015 Jul 22.

Hurd MD, Martorell P, Delavande A, et al. **Monetary costs of dementia** in the United States. N Engl J Med. 2013 Apr 4;368(14):1326-34.

Hui DS, Morley JE, Mikolajczak PC, et al. **Atrial fibrillation**: A major risk factor for cognitive decline. Am Heart J. 2015 Apr;169(4):448-456.

Humeidan M, Otey A, Zuleta-Alarcon A, et al. **Perioperative cognitive protection** - cognitive exercise and cognitive reserve (The **Neurobics** Trial): a single-blinded randomized trial. Clin Ther. 2015;37:xxx–xxx

Hunsberger J, Rao M, Kurtzberg J, et al. Accelerating **stem cell trials** for Alzheimer's disease. Lancet Neurol 2015; published online Dec 15.

Husebo BS, Ballard C, Aarsland D. **Pain treatment of agitation** in patients with dementia: a systematic review. Int J Geriatr Psychiatry. 2011 Oct;26(10):1012-8. doi: 10.1002/gps.2649.

Husebo BS, Ballard C, Sandvik R, Nilsen OB, Aarsland D. Efficacy of **treating pain** to reduce behavioural disturbances in residents of nursing homes with dementia: cluster randomised clinical trial. BMJ 2011;343;d4065.

Huybrechts KF, Rothman KJ, Silliman RA., et al. **Risk of death and hospital admission** for major medical events after initiation of psychotropic medications in older adults admitted to nursing homes. CMAJ 2011 0: cmaj.101406

Hyde C, Peters J, Bond M, et al. Evolution of the evidence on the effectiveness and **cost-effectiveness of acetylcholinesterase inhibitors and memantine** for Alzheimer`s disease: systematic review and economic model. Age Ageing. 2013Jan;42(1):14-20.

Hyman BT. **Amyloid**-Dependent and Amyloid-Independent Stages of Alzheimer Disease. Arch Neurol. 2011 Apr 11.

Iadecola C, Yaffe K, Biller J, et al. Impact of **Hypertension on Cognitive Function** : A Scientific Statement From the American Heart Association. Hypertension. 2016 ;68 :000-000.

Ihara R, Vincent BD, Baxter MR, et al. **Relative neuron loss in hippocampal sclerosis of aging and Alzheimer's disease**. Ann Neurol. 2018 Sep 24.

Ilango SD, McEvoy LK, Laughlin GA, et al**. Pregnancy history and cognitive aging** among older women: the Rancho Bernardo Study. Menopause. 2019 Mar 18.

Iliffe S, Pealing L. **Subjective memory problems**. BMJ. 2010 Mar 19;340:c1425.

Imfeld P, Bodmer M, Schuerch M, et al. **Risk of incident stroke in patients with Alzheimer** disease or vascular dementia. Neurology. 2013 Sep 3;81(10):910-9.

Imtiaz B, Tuppurainen M, Rikkonen T, et al. **Postmenopausal hormone therapy and Alzheimer disease**: A prospective cohort study. Neurology. 2017 Mar 14;88(11):1062-1068.

Inouye SK. **Delirium in older persons**. N Engl J Med. 2006 Mar 16;354(11):1157-65.

Inouye SK, Westendorp RG, Saczynski JS. **Delirium in elderly people**. Lancet. 2013 Aug 27.

Inouye SK, Kosar CM, Tommet D, et al. The **CAM-S**: development and validation of a new scoring system for **delirium** severity in 2 cohorts. Ann Intern Med. 2014;160:526-33.

Inouye SK. **Enhancing Cognitive Aging**: Clinical Highlights of a Report From the Institute of Medicine. Ann Intern Med. 2015 Jun 23.

Inouye SK. **Enhancing Cognitive Aging**: Clinical Highlights of a Report From the **Institute of Medicine**. Ann Intern Med. 2015 Jun 23.

Inouye SK. **Enhancing Cognitive Aging**: Clinical Highlights of a Report From the Institute of Medicine. Ann Intern Med. 2015 Jun 23.

Insel PS, Weiner M, Mackin RS, et al. Determining clinically meaningful **decline in preclinical Alzheimer disease**. Neurology. 2019 Jul 23;93(4):e322-e333.

Inzitari M, Pozzi C, Ferrucci L, Chiarantini D, Rinaldi LA, Baccini M, Pini R, Masotti G, Marchionni N, Di Bari M. **Subtle neurological abnormalities** as risk factors for cognitive and functional decline, cerebrovascular events, and mortality in older community-dwelling adults. Arch Intern Med. 2008 Jun 23;168(12):1270-6. In this sample of older community-dwelling persons without overt neurological diseases, multiple SNAs were associated with cognitive and functional decline and independently predicted mortality and CVEs.

Ir anzo A, Tolosa E, Gelpi E, et al. Neurodegenerative disease status and post-mortem pathology in idiopathic **rapid-eye-movement sleep behaviour disorder**: an observational cohort study. Lancet Neurology 2013.

Irwin DJ, McMillan CT, Toledo JB, et al. Comparison of **Cerebrospinal Fluid Levels of Tau and Aβ 1-42** in Alzheimer Disease and Frontotemporal Degeneration Using 2 Analytical Platforms. Arch Neurol. 2012 Apr 9.

Isik AT, Babacan Yildiz G, Bozoglu E, Yay A, Aydemir E. **Cardiac safety of donepezil** in elderly patients with Alzheimer disease. Intern Med. 2012;51(6):575-8.

Ismail Z, Elbayoumi H, Fischer CE, et al. **Prevalence of Depression** in Patients With Mild Cognitive Impairment: A Systematic Review and Meta-analysis. JAMA Psychiatry.2016 Nov 23.

Iverson DJ, Gronseth GS, Reger MA, et al. Practice parameter update: evaluation and management of **driving risk** in dementia: report of the Quality Standards Subcommittee of the American Academy of Neurology. Neurology. 2010 Apr 20;74(16):1316-24.http://www.neurology.org/cgi/rapidpdf/WNL.0b013e3181da3b0fv1.pdf

Iwashyna Theodore J.; Ely E. Wesley; Smith Dylan M.; et al. Long-term Cognitive Impairment and Functional Disability Among Survivors of **Severe Sepsis**. *JAMA*. 2010;304(16):1787-1794.

Irizarry M, Jin S; He F et al. Incidence of **New-Onset Seizures** in Mild to Moderate Alzheimer Disease Arch Neurol. 2012;69(3):368-372.

Jack CR Jr, et al. Age-specific and sex-specific prevalence of **cerebral β-amyloidosis**, tauopathy, and neurodegeneration in clinically normal individuals aged 50–95 years: cross-sectional study. Lancet Neurol 2017; online Apr 26.

Jack CR Jr, et al. Age-specific population frequencies of **cerebral β-amyloidosis and neurodegeneration among people with normal cognitive function aged 50-89 years**: a cross-sectional study. Lancet Neurol. 2014 Sep 4.

Jack CR Jr, Bennett DA, Blennow K, et al. A/T/N: An unbiased descriptive **classification scheme** for Alzheimer disease biomarkers. Neurology. 2016 Aug 2;87(5):539-47

Jack CR Jr, Knopman DS, Jagust WJ, et al. **Tracking pathophysiological processes** in Alzheimer's disease: an updated hypothetical model of dynamic biomarkers. Lancet Neurol. 2013 Feb;12(2):207-16.

Jack CR Jr, Therneau TM, Weigand SD, et al. Prevalence of Biologically vs Clinically **Defined Alzheimer Spectrum Entities** Using the National Institute on Aging-Alzheimer's Association Research Framework. JAMA Neurol. 2019 Jul 15.

Jack CR Jr, Vemuri P, Wiste HJ, et al. for the Alzheimer's Disease Neuroimaging Initiative. Evidence for Ordering of **Alzheimer Disease Biomarkers**. Arch Neurol. 2011 Aug 8.

Jack CR Jr, Wiste HJ, Weigand SD, et al. **Amyloid-first and neurodegeneration-first** profiles characterize incident amyloid PET positivity. Neurology 2013;81:1732–1740.

Jack CR Jr, Wiste HJ, Knopman DS, et al. Rates of **β-amyloid accumulation** are independent of hippocampal neurodegeneration. Neurology. 2014 Apr 4.

Jacobs V, Woller SC, Stevens S, et al. **Time outside of therapeutic** range in atrial fibrillation patients is associated with long-term risk of **dementia**. Heart Rhythm. 2014 Aug 9.

Jacobs V, Woller SC, Stevens SM, et al. Percent Time With a **Supratherapeutic INR** in Atrial Fibrillation Patients Also Using an Antiplatelet Agent Is Associated With Long-Term Risk of Dementia. J Cardiovasc Electrophysiol. 2015 Aug 13.

Jacobs V, Woller SC, et al. Percent Time With a **Supratherapeutic INR** in Atrial Fibrillation Patients Also Using an Antiplatelet Agent Is Associated With Long-Term Risk of Dementia. J Cardiovasc Electrophysiol. 2015 Aug13.

Jack CR Jr, Therneau TM, Wiste HJ, et al. Transition rates between **amyloid and neurodegeneration biomarker states** and to dementia: a population-based, longitudinal cohort study. Lancet Neurol 2015; online Nov 17.

Jagger C, Matthews FE, Wohland P, et al, on behalf of the Medical Research Council Cognitive Function and Ageing Collaboration. A comparison of **health expectancies** over two decades in England: results of the Cognitive Function and Ageing Study I and II. Lancet 2015; online Dec 8.

Jagust WJ. **Amyloid Imaging**: Liberal or Conservative? Let the Data Decide. Arch Neurol. 2011 Jul 11.

Jagust W. Tracking brain **amyloid-β** in presymptomatic Alzheimer's disease. Lancet Neurol. 2012 Nov 5.

James BD, Leurgans SE, Hebert LE, et al. Contribution of **Alzheimer** disease to **mortality in the United States**. Neurology. 2014 Mar 25;82(12):1045-50.

Jang H, Bae JB, Dardiotis E, et al. Differential effects of **completed and incomplete pregnancies on the risk of Alzheimer disease**. Neurology. 2018 Aug 14;91(7):e643-e651.

Jansen WJ, Ossenkoppele R, Knol DL, et al. Prevalence of **cerebral amyloid pathology** in persons without dementia. JAMA. doi:10.1001/jama.2015.4668.

Jaturapatporn D, Isaac MG, McCleery J, et al. **Aspirin, steroidal and non-steroidal anti-inflammatory** drugs for the treatment of Alzheimer`s disease. Cochrane Database Syst Rev. 2012 Feb 15;2:CD006378. Based on the studies carried out so far, the efficacy of aspirin, steroid and NSAIDs (traditional NSAIDs and COX-2 inhibitors) is not proven. Therefore, these drugs cannot be recommended for the treatment of AD.

Jayadevappa R, Chhatre S, Malkowicz SB, et al. Association Between **Androgen Deprivation Therapy Use and Diagnosis** of Dementia in Men With Prostate Cancer. JAMA Netw Open. 2019 Jul 3;2(7):e196562.

Jefferson AL, Beiser AS, Himali JJ, et al. **Low Cardiac Index** is Associated with Incident Dementia and Alzheimer's Disease: The Framingham Heart Study. Circulation. 2015 Feb 19.

Jefferson AL, Beiser AS, Himali JJ, et al. **Low cardiac index** is associated with incident dementia and Alzheimer disease: the framingham heart study. Circulation. 2015 Apr 14;131(15):1333-9.

Jefferson AL, Liu D, Gupta DK, et al. **Lower cardiac index** levels relate to lower cerebral blood flow in older adults. Neurology. 2017 Nov 8.

Jin J. JAMA patient page. Alzheimer disease. JAMA. 2015 Apr 14;313(14):1488.

Jiskoot LC, Dopper EG, Heijer TD, et al. **Presymptomatic cognitive decline** in familial frontotemporal dementia: A longitudinal study. Neurology. 2016 Jun 29.

Jochemsen HM, Muller M, Visseren FL, et al; for the SMART Study Group. **Blood Pressure** and Progression of Brain Atrophy: The SMART-MR Study. JAMA Neurol. 2013 Jun 10:1-7.

Johansson L, Guo X, Hällström T, et al. Common **psychosocial stressors** in middle-aged women related to longstanding distress and increased risk of Alzheimer's disease: a 38-year longitudinal population study. BMJ Open. 2013 Sep 30;3(9):e003142.

Johansson L, Guo X, Duberstein PR, et al. **Midlife personality** and risk of Alzheimer disease and distress: A 38 year follow-up. Neurology. 2014 Oct 21;83(17):1538-44.

Johnson KA et al. **Tau positron emission tomographic imaging** in aging and early Alzheimer's disease. Ann Neurol 2016 Jan; 79:110.

Jokinen H, Gouw AA, Madureira S, et al. On behalf of the LADIS Study Group. Incident **lacunes** influence cognitive decline: The LADIS study. Neurology. 2011 May 31;76(22):1872-1878.

Jones HE, Joshi A, et al. The effect of treatment with **selective serotonin reuptake inhibitors** in comparison to placebo in the progression of dementia: a systematic review and meta-analysis. Age Ageing. 2016 Jul;45(4):448-56.

Jones RN, Cizginer S, Pavlech L, et al; Better Assessment of Illness (BASIL) Study Group. Assessment of **Instruments for Measurement of Delirium** Severity: A Systematic Review. JAMA Intern Med. 2018 Dec 17.

Jongstra S, van Gool WA, Moll van Charante EP, et al. Improving **Prediction of Dementia in Primary Care**. Ann Fam Med. 2018 May;16(3):206-210.

Jonsson T, Stefansson H, Steinberg S, et al. **Variant of TREM2** associated with the risk of Alz hei mer's disease. N Engl J Med 2012. DOI: 10.1056/NEJMoa1211103.

Ju YE, McLeland JS, Toedebusch CD, et al. **Sleep Quality** and Preclinical Alzheimer Disease. JAMA Neurol. 2013 Mar 11:1-7.

Julayanont P, Brousseau M, Chertkow H, et al. **Montreal Cognitive Assessment Memory Index Score (MoCA-MIS)** as a Predictor of Conversion from Mild Cognitive Impairment to Alzheimer`s Disease. J Am Geriatr Soc. 2014 Mar 17.

Jutkowitz E, Brasure M, Fuchs E, et al. **Care-Delivery Interventions to Manage Agitation and Aggression in Dementia** Nursing Home and Assisted Living Residents: A Systematic Review and Meta-analysis. J Am Geriatr Soc. 2016 Mar;64(3):477-88.

Jutkowitz E, Kane RL, Gaugler JE, et al. **Societal** and **Family** Lifetime **Cost** of **Dementia**: Implications for Policy. J Am Geriatr Soc. 2017 Aug 17.

Kaffashian S, Dugravot A, Elbaz A, et al. Predicting cognitive decline: A **dementia risk score vs the Framingham vascular risk scores**. Neurology. 2013 Apr 2;80(14):1300-6.

Kales HC, Zivin K, Kim HM, Valenstein M, Chiang C, Ignacio R, Ganoczy D, Cunningham F, Schneider LS, Blow FC. Trends in **antipsychotic use in dementia** 1999-2007. Arch Gen Psychiatry. 2011 Feb;68(2):190-7.

Kales HC , Kim HM, Zivin K, Valenstein M, Seyfried LS, Chiang C , Cunningham F, Schneider LS, Blow FC: Risk of **mortality among individual antipsychotics** in patients with dementia. Am J Psychiatry 2011; 168:71–79.

Kales HC, Gitlin LN, Lyketsos CG; Detroit Expert Panel on the Assessment and Management of the Neuropsychiatric Symptoms of Dementia. **Management of neuropsychiatric symptoms of dementia** in clinical settings: recommendations from a **multidisciplinary expert panel**. J Am Geriatr Soc. 2014 Apr;62(4):762-9.

Kales HC, Gitlin LN, Lyketsos CG. **Assessment and management of behavioral and psychological symptoms of dementia**. BMJ. 2015 Mar 2;350:h369.

Kalisch Ellett LM, Pratt NL, Ramsay EN, et al. **Multiple anticholinergic medication** use and risk of hospital admission for confusion or dementia. J Am Geriatr Soc. 2014 Oct;62(10):1916-22.

Kalisvaart KJ, de Jonghe JF, Bogaards MJ, Vreeswijk R, Egberts TC, Burger BJ, Eikelenboom P, van Gool WA. **Haloperidol** prophylaxis for elderly hip-surgery patients at risk for **delirium**: a randomized placebo-controlled study. J Am Geriatr Soc. 2005 Oct;53(10):1658-66. (InfoPOEMs: Low-dose haloperidol was no more effective than placebo in preventing delirium in elderly patients undergoing hip surgery. However, when delirium occurred, it was milder and shorter in patients receiving haloperidol. Furthermore, haloperidol shortened the hospital length of stay among patients who became delirious. (LOE = 1b-))

Kamble P, Chen H, et al. Use of **antipsychotics among elderly nursing home residents** with dementia in US: an analysis of National Survey Data. Drugs Aging.2009;26(6):483-92.doi:10.2165/00002512-200926060-00005.

Kane RL, Butler M, Fink HA, et al. Interventions To **prevent age-related cognitive decline, mild cognitive impairment, and clinical Alzheimer's-type dementia**. Comparative Effectiveness Review No. 188. AHRQ Comparative Effectiveness Reviews. 2017 Mar. No. 189;1-693.

Kantarci K, Lowe V, Przybelski SA, et al. **APOE modifies** the association between **AB load** and cognition in cognitively normal older adults. Neurology 2012;78:232–240.

Kantarci K, Weigand SD, Przybelski SA, et al. **MRI and MRS predictors** of mild cognitive impairment in a population-based sample. Neurology. 2013 Jul 9;81(2):126-33. Quantitative MRI and MRS markers predict progression to MCI & cognitive decline in cognitively normal older adults. MRS may contribute to the assessment of preclinical dementia pathologies by capturing neurodegenerative changes that are not detected by hippocampal volumetry.

Kantarci K, Lowe VJ, Lesnick TG, et al. Early Postmenopausal **Transdermal 17β-Estradiol** Therapy and Amyloid-β Deposition. J Alzheimers Dis. 2016 May 7.

Kantarci K, Lesnick T, Ferman TJ, et al. **Hippocampal volumes** predict risk of dementia with Lewy bodies in mild cognitive impairment. Neurology. 2016 Nov 29;87(22):2317-2323.

Kapusta Peter, Regier Loren, Bareham Julia, et al. **RxFiles**: **Behaviour management in dementia**. Can Fam Physician December 2011 57: 1420-1422.

Karim R, Dang H, Henderson VW, et al. Effect of **Reproductive History and Exogenous Hormone Use on Cognitive** Function in Mid- and Late Life. J Am Geriatr Soc. 2016 Dec;64(12):2448-2456.

Karlamangla AS, Lachman ME, Han W, et al. Evidence for **Cognitive Aging in Midlife Women**: Study of Women's Health Across the Nation. PLoS One. 2017 Jan 3;12(1):e0169008.

Katan M, Moon YP, Paik MC, et al. **Infectious burden** (herpes simplex virus…) and cognitive function: the Northern Manhattan Study. Neurology 2013;80:1209–1215.

Katila H, et al. Randomized, Double-Blind Study of the Efficacy and Tolerability of **Extended Release Quetiapine** Fumarate (Quetiapine XR) Monotherapy in Elderly Patients With Major **Depressive Disorder**. Am J Geriatr Psychiatry. 2012 Jun 7.

Katon W, Pedersen HS, Ribe AR, et al. Effect of **Depression and Diabetes Mellitus** on the Risk for Dementia: A National Population-Based Cohort Study. JAMA Psychiatry. 2015 Apr 15.

Kaup AR, Nettiksimmons J, LeBlanc ES, Yaffe K. **Memory complaints** and risk of **cognitive impairment** after nearly **2 decades** among older women. Neurology. 2015 Nov 24;85(21):1852-8.

Kawas CH, Kim RC, Sonnen JA, et al. **Multiple pathologies** are common and related to dementia in the oldest-old: The 90+ Study. Neurology. 2015 Aug 11;85(6):535-42.

Keenan TD, Goldacre R, Goldacre MJ. Associations Between **Age-Related Macular Degeneration, Alzheimer Disease, and Dementia**: Record Linkage Study of Hospital Admissions. JAMA Ophthalmol. 2013 Nov 14.

Kelley AS, McGarry K, Gorges R, et al. The Burden of **Health Care Costs** for Patients With Dementia in the **Last 5 Years of Life**. Ann Intern Med. 2015 Oct 27.

Kennedy J, Deberdt W, Siegal A, et al. **Olanzapine does not enhance cognition** in non-agitated and non-psychotic patients with mild to moderate Alzheimer's dementia. Int J Geriatr Psychiatry. 2005 Nov;20(11):1020-7.

Kennedy RE, Cutter GR, Fowler ME, et al. Association of **Concomitant Use of Cholinesterase Inhibitors or Memantine With Cognitive Decline in Alzheimer** Clinical TrialsA Meta-analysis. JAMA Netw Open. 2018;1(7):e184080.

Kern S, Skoog I, Östling S, et al. Does low-dose **acetylsalicylic acid prevent cognitive decline** in women with high cardiovascular risk? A 5-year follow-up of a non-demented population-based cohort of Swedish elderly women. BMJ Open 2012.

Kern S, Zetterberg H, Kern J, et al. Prevalence of **preclinical Alzheimer disease**: Comparison of current classification systems. Neurology. 2018 Apr 13.

Kern J, Kern S, Blennow K, et al. **Calcium supplementation** and risk of dementia in women with cerebrovascular disease. Neurology. 2016 Oct 18;87(16):1674-1680.

Kerti L, Witte AV, Winkler A, et al. **Higher glucose levels associated with lower memory** and reduced hippocampal microstructure. Neurology. 2013 Nov 12;81(20):1746-52.

Kessing LV, Gerds TA, Knudsen NN, et al. Association of **lithium** in **drinking water** with the incidence of dementia [published online August 23, 2017].JAMA Psychiatry. doi:10.1001/jamapsychiatry .2017.2362

Khachaturian et al. **Antihypertensive** Medication Use and Incident Alzheimer Disease: The Cache County Study. Arch Neurol. 2006 Mar 13; [Epub ahead of print]

Khanassov V, Vedel I. **Family Physician-Case Manager Collaboration** and Needs of Patients With Dementia and Their Caregivers: A Systematic Mixed Studies Review. Ann Fam Med. 2016 Mar;14(2):166-77.

Khosrow-Khavar F, Rej S, Yin H, et al. **Androgen Deprivation Therapy** and the Risk of Dementia in Patients With Prostate Cancer. J Clin Oncol. 2017 Jan 10;35(2):201-207

Kieboom BCT, Licher S, Wolters FJ, et al. Serum **magnesium** is associated with the risk of dementia. Neurology. 2017 Oct 17;89(16):1716-1722.

Kim DH, Brown RT, Ding EL, et al. Dementia medications and risk of falls, **syncope**, and related adverse events: meta-analysis of randomized controlled trials. J Am Geriatr Soc. 2011 Jun;59(6):1019-31.(syncope for ChEIs)

Kim JP, Seo SW, Shin HY, et al. Effects of **education on aging**-related cortical thinning among cognitively normal individuals. Neurology. 2015 Jul 31.

Kirby J, et al. A systematic review of the clinical and cost-effectiveness of **memantine** in patients with moderately severe to severe Alzheimer's disease. Drugs Aging. 2006;23(3):227-40.

Kirkham J, Sherman C, Velkers C, et al. **Antipsychotic Use** in Dementia. Can J Psychiatry. 2017 Mar;62(3):170-181.

Kishi T, Hirota T, Matsunaga S, et al. **Antipsychotic medications for the treatment of delirium**: a systematic review and meta-analysis of randomised controlled trials. J Neurol Neurosurg Psychiatry. 2015 Sep 4.

Kivimäki M, Luukkonen R, Batty GD, et al. **Body mass index and risk of dementia**: Analysis of individual-level data from 1.3 million individuals. Alzheimers Dement. 2017 Nov 21.

Kivimäki M, Singh-Manoux A, Pentti J, et al**. Physical inactivity, cardiometabolic disease, and risk of dementia**: an individual-participant meta-analysis. BMJ. 2019 Apr 17;365:l1495.

Klassen BT, Hentz JG, Shill HA, et al. **Quantitative EEG** as a predictive biomarker for Parkinson disease dementia. Neurology. 2011 Jul 12;77(2):118-24.

Klein Klouwenberg PMC, Zaal IJ, Spitoni C, et al. The **attributable mortality of delirium in critically ill patients**: prospective cohort study. BMJ 2014;349:g6652.

Klein Klouwenberg PM, Zaal IJ, Spitoni C, et al. The attributable **mortality of delirium** in critically ill patients: prospective cohort study. BMJ. 2014 Nov 24;349:g6652.

Klein LR, Driver BE, Miner JR, et al. **Intramuscular Midazolam, Olanzapine, Ziprasidone, or Haloperidol for Treating Acute Agitation in the Emergency Department**. Ann Emerg Med. 2018 Oct;72(4):374-385

Knapp M, King D, Romeo R, et al. Cost effectiveness of a **manual based coping strategy** programme in promoting the mental health of family carers of people with dementia (the **START** (STrAtegies for RelaTives) study): a pragmatic randomised controlled trial. BMJ. 2013 Oct 25;347:f6342.

Knickmeyer RC, Ross ME. Imaging and rare APOE alleles: Alzheimer disease as a developmental disorder. Neurology. 2016 Aug 9;87(6):558-9.

Knight R, Khondoker M, Magill N, et al. A Systematic Review and Meta-Analysis of the **Effectiveness of Acetylcholinesterase Inhibitors and Memantine** in Treating the Cognitive Symptoms of Dementia. Dement Geriatr Cogn Disord. 2018 May 7;45(3-4):131-151.

Knopman DS, Penman AD, Catellier DJ, et al. **Vascular risk factors** and longitudinal changes on brain MRI: The ARIC study. Neurology. 2011 May 31;76(22):1879-85.

Knopman DS, Jack CR Jr, Wiste HJ, et al. Short-term clinical outcomes for stages of **NIA-AA preclinical Alzheimer disease**. Neurology. 2012 May 15;78(20):1576-82.

Knopman DS, Beiser A, Machulda MM, et al. **Spectrum of cognition short of dementia**: Framingham Heart Study and Mayo Clinic Study of Aging. Neurology. 2015 Nov 10;85(19):1712-21.

Koepsell TD, Monsell SE. **Reversion** from mild cognitive impairment to normal or near-normal cognition: **Risk factors and prognosis**. Neurology. 2012 Oct 9;79(15):1591-8.

Koivunen J, Scheinin N, Virta JR, et al. **Amyloid PET imaging** in patients with mild cognitive impairment: A 2-year follow-up study. Neurology. 2011 Mar 22;76(12):1085-90.

Kolanowski A, Litaker M, Buettner L, et al. A randomized clinical trial of **theory-based activities** for the behavioral symptoms of dementia in nursing home residents. J Am Geriatr Soc. 2011 Jun;59(6):1032-41.

Kongpakwattana K, Sawangjit R, Tawankanjanachot I, et al. **Pharmacological treatments for alleviating agitation in dementia**: a systematic review and network meta-analysis. Br J Clin Pharmacol. 2018 Apr 10.

Köpke S, Mühlhauser I, Gerlach A, et al. Effect of a guideline-based **multicomponent intervention on use of physical restraints** in nursing homes: a randomized controlled trial. JAMA. 2012 May 23;307(20):2177-84.

Kor PPK, Liu JYW, Chien WT. Effects of a modified mindfulness-based **cognitive therapy for family caregivers of people with dementia**: A pilot randomized controlled trial. Int J Nurs Stud. 2019 Mar 8.

Kosar CM, Tabloski PA, Travison TG, et al. Effect of **preoperative pain and depressive symptoms on the development of postoperative delirium**. Lancet Psychiatry. 2014 Nov;1(6):431-436.

Kotagal V, Langa KM, Plassman BL, et al. Factors associated with **cognitive evaluations** in the United States. Neurology. 2015 Jan 6;84(1):64-71.

Kövari E, Herrmann FR, Bouras C, et al. **Amyloid deposition is decreasing in aging brains**: An autopsy study of 1,599 older people. Neurology. 2013 Dec 20

Koyama A, Okereke OI, Yang T, et al. **Plasma Amyloid-β** as a Predictor of Dementia and Cognitive Decline: A Systematic Review and Meta-analysis. Arch Neurol. 2012 Mar 26.

Krause BM, Sabia S, Manning HJ, et al. Association between major **surgical admissions and the cognitive trajectory**: 19 year follow-up of Whitehall II cohort study. BMJ. 2019 Aug 7;366:l4466.

Krell-Roesch J, et al. Association Between **Mentally Stimulating Activities** in Late Life and the Outcome of Incident Mild Cognitive Impairment, With an Analysis of the APOE ε4 Genotype. JAMA Neurol. 2017 Jan 30.

Krell-Roesch J, Syrjanen JA, Vassilaki M, et al. Quantity and quality of **mental activities and the risk of incident mild cognitive impairment**. Neurology. 2019 Aug 6;93(6):e548-e558.

Kröger E, Mouls M, Wilchesky M, et al. **Adverse Drug Reactions Reported With Cholinesterase Inhibitors**: An Analysis of 16 Years of Individual Case Safety Reports From VigiBase. Ann Pharmacother. 2015 Nov;49(11):1197-206.

Krupp LB, Christodoulou C, Melville P, et al. Multicenter randomized clinical trial of **donepezil** for memory impairment in multiple sclerosis. Neurology. 2011 Apr 26;76(17):1500-7. (not work)

Kryscio RJ, Abner EL, Cooper GE, et al. **Self-reported memory complaints**: Implications from a longitudinal cohort with autopsies. Neurology. 2014 Oct 7;83(15):1359 65.

Kryscio RJ, Abner EL, et al. Association of **antioxidant supplement use** and dementia in the Prevention of Alzheimer's Disease by Vitamin E and Selenium trial (**PREADViSE**) [online Mar 20, 2017].JAMA Neurol.

Kuh D, Cooper R, Moore A, et al. Age at **menopause and lifetime cognition**: Findings from a British birth cohort study. Neurology. 2018 Apr 11.

Kuller LH, Lopez OL, Mackey RH, et al. **Subclinical Cardiovascular Disease** and Death, Dementia, and Coronary Heart Disease in Patients 80+ Years. J Am Coll Cardiol. 2016 Mar 8;67(9):1013-22.

Kuźma E, Lourida I, Moore SF, et al. **Stroke and dementia risk**: A systematic review and meta-analysis. Alzheimers Dement. 2018 Aug 25.

Kwok CS, Loke YK, Hale R, et al. **Atrial fibrillation** and incidence of dementia: A systematic review and meta-analysis. Neurology 2011; 76:914-922.

Laakkonen ML, Kautiainen H, Holtta E, et al. Effects of **Self-Management Groups** for People with Dementia and Their Spouses-Randomized Controlled Trial. J Am Geriatr Soc. 2016 Apr 5.

Lafaille-Magnan ME, Poirier J, Etienne P, et al. **Odor identification** as a biomarker of preclinical AD in older adults at risk. Neurology. 2017 Jul 25;89(4):327-335.

LaFerla FM. **Preclinical success** against Alzheimer's disease with an **old drug**. (**bexarotene**) N Engl J Med. 2012 Aug 9;367(6):570-2.

Laforce R Jr, Rabinovici GD. **Amyloid imaging** in atypical dementia. CMAJ. 2014 Jun 10;186(9):695.

Laforce R Jr, Bensaïdane MR. **Amyloid imaging** for dementia in Canada. CMAJ. 2016 May 17;188(8):598-602.

Lam RE, Lam PJ. **Nutrition** in dementia. CMAJ. 2014 Nov 18;186(17):1319.

Lamb SE, Sheehan B, Atherton N, et al. **Dementia And Physical Activity (DAPA) trial of moderate to high intensity exercise training for people with dementia**: randomised controlled trial. BMJ. 2018 May 16;361:k1675.

Lamb SE, Mistry D, Alleyne S, et al. **Aerobic and strength training exercise programme for cognitive impairment** in people with mild to moderate dementia: the DAPA RCT. Health Technol Assess. 2018 May;22(28):1-202.

Lampit A, Hallock H, Valenzuela M. **Computerized cognitive training** in cognitively healthy older adults: a systematic review and meta-analysis of effect modifiers. PLoS Med. 2014 Nov 18;11(11):e1001756.

Lancto KL, Lindsay MP, Smith EE, et al; the Heart & Stroke Canadian Stroke Best Practices and Quality Advisory Committee; in collaboration with the Canadian Stroke Consortium. Canadian Stroke Best Practice Recommendations: mood, cognition and fatigue following stroke, 6th edition update 2019. https://journals.sagepub.com/doi/pdf/10.1177/1747493019847334

Landau Susan M.; Marks Shawn M.; Mormino Elizabeth C.; et al. Association of **Lifetime Cognitive Engagement** and Low {beta}-Amyloid Deposition. Arch Neurol. 2012

Landy KM, Salmon DP, Galasko D, et al. **Motion discrimination in dementia** with Lewy bodies and Alzheimer disease. Neurology. 2015 Oct 20; 85 (16): 1376-82.

Lane CA, Barnes J, Nicholas JM, et al. Associations between **blood pressure across adulthood and late-life brain structure** and pathology in the neuroscience substudy of the 1946 British birth cohort (Insight 46): an Epidemiological study. Lancet Neurol. 2019 Aug 20.

Langa KM et al. A comparison of the **prevalence of dementia in the United States in 2000 and 2012** .JAMA Intern Med 2016 Nov 21; [e-pub].

Largent EA, Terrasse M, Harkins K, et al. **Attitudes Toward Physician-Assisted Death** From Individuals Who Learn They Have an Alzheimer Disease Biomarker. JAMA Neurol. 2019 Apr 29.

Larson EB, Wang L, Bowen JD, McCormick WC, Teri L, Crane P, Kukull W. **Exercise** is associated with reduced risk for incident dementia among persons 65 years of age and older. Ann Intern Med. 2006 Jan 17;144(2):73-81.

Larson EB, Yaffe K, Langa KM. New **Insights into the Dementia Epidemic**. N Engl J Med. 2013 Nov 27.

Larrson SC, Traylor M, Malik R, **CoSTREAM** Consortium. **Modifiable pathways in Alzheimer's disease**: Mendelian randomisation analysis. BMJ2017;359:j5375.

Lautenschlager NT, et al. Effect of **physical activity** on cognitive function in older adults at risk for Alzheimer disease: a randomized trial. JAMA. 2008 Sep 3;300(9):1027-37. In this study of adults with subjective memory impairment, a 6-month program of physical activity provided a modest improvement in cognition over an 18-month follow-up period.

Lavikainen P, Taipale H, Tanskanen A, et al. **Antiepileptic Drugs and Accumulation of Hospital Days Among Persons With Alzheimer's Disease**. J Am Med Dir Assoc. 2019 Jan 7.

Lavoie-Vaughan N. A **Critical Analysis and Adaptation of a Clinical Practice Guideline** for Management of Behavioral Problems in Residents with Dementia in Long-Term Care. Nurs Clin North Am. 2014 Mar;49(1):105-113.

Law LL, Barnett F, Yau MK, et al. Effects of **functional tasks exercise** on older adults with cognitive impairment at risk of Alzheimer`s disease: a randomised controlled trial. Age Ageing. 2014 May 21. pii: afu055.

Lawrence AJ, Zeestraten EA, Benjamin P, et al. Longitudinal **decline in structural networks predicts dementia in cerebral small vessel disease**. Neurology. 2018 Apr 25.

Le Couteur DG, Doust J, Creasey H, Brayne C. Political drive to **screen for pre-dementia**: not evidence based and ignores the harms of diagnosis. BMJ. 2013 Sep 9;347:f5125.

Le Couteur DG, Bateman B, Brayne C. **Idalopirdine**: another disappointment for people with dementia. BMJ. 2018 Feb 21;360:k753.

Le Guennec K, Nicolas G, Quenez O, et al. **ABCA7 rare variants** and Alzheimer disease risk. Neurology 2016;86: 2134–2137.

Leanos S, Kürüm E, Strickland-Hughes CM, et al. The impact of learning multiple **real-world skills on cognitive abilities** and functional independence in healthy older adults. J Gerontol B Psychol Sci Soc Sci. 2019 Jun 14.

Lee AT, Richards M, Chan WC, et al. Lower risk of incident dementia among Chinese older adults having three servings of **vegetables and two servings of fruits** a day. Age Ageing. 2017 Feb 10:1-6.

Lee ATC, Richards M, Chan WC, et al. Association of daily intellectual activities with lower risk of incident dementia among older Chinese adults [online May 30, 2018].JAMA Psychiatry. doi:10.1001 /jamapsychiatry.2018.0657.

Lee JH, Kim SH, Kim GH, et al. Identification of pure **subcortical vascular dementia** using 11C-Pittsburgh compound B. Neurology. 2011 Jul 5;77(1):18-25.

Lee L, Weston WW, Heckman G, et al. **Structured approach to patients with memory difficulties** in family practice. Can Fam Physician. 2013 Mar;59(3):249-54.

Lee L, Molnar F. Driving and dementia: Efficient approach to **driving safety** concerns in family practice. Can Fam Physician. 2017 Jan;63(1):27-31.

Lee L, Patel T, Molnar F, et al. **Optimizing medications in older adults with cognitive impairment**: Considerations for primary care clinicians. Can Fam Physician. 2018 Sep;64(9):646-652.

Leelakanok N, D'Cunha RR. **Association between polypharmacy and dementia** – A systematic review and meta-analysis. Aging Ment Health. 2018 May 10:1-10.

Lefèvre-Arbogast S, Gaudout D, Bensalem J, et al. Pattern of **polyphenol intake and the long-term risk of dementia** in older persons. Neurology. 2018 May 29;90(22):e1979-e1988.

Legere LE, McNeill S, et al. **Nonpharmacological approaches** for behavioural and psychological symptoms of dementia in older adults: A systematic review of reviews. J Clin Nurs. 2018 Apr;27(7-8):e1360-e1376.

Lehallier B, Essioux L, et al; Alzheimer's Disease Neuroimaging Initiative. **Combined Plasma and Cerebrospinal Fluid Signature** for the Prediction of Midterm Progression From Mild Cognitive Impairment to Alzheimer Disease. JAMA Neurol. 2015 Dec 14:1-10.

Leng Y, et al. Association of **Sleep-Disordered Breathing With Cognitive Function** and Risk of Cognitive Impairment: A Systematic Review Meta-analysis. JAMA Neurol. 2017 Aug 28.

Leonard R, Tinetti ME, Allore HG, Drickamer MA. Potentially **modifiable resident characteristics** that are associated with physical or verbal aggression among nursing home residents with dementia. Arch Intern Med. 2006 Jun 26;166(12):1295-300. If the associations we have estimated are causal, then treatment of depression, delusions, hallucinations, and constipation may reduce physical aggression among nursing home residents.

Leonenko G, Shoai M, Bellou E, et al. **Genetic risk for alzheimer** disease is distinct from genetic risk **for amyloid deposition**. Ann Neurol. 2019 Jun 14.

Levine DA, Galecki AT, Langa MK, et al. **Trajectory of cognitive decline after incident stroke**. JAMA. doi:10.1001/jama.2015.6968.

Lewis M, et al. Long-term **home and community-based exercise programs** improve function in community-dwelling older people with cognitive impairment: a systematic review. J Physiother. 2017 Jan;63(1):23-29.

Llewellyn David J.; Lang Iain A.; Langa Kenneth M.; et al. **Vitamin D** and Risk of Cognitive Decline in Elderly Persons Arch Intern Med. 2010;170(13):1135-1141. Conclusion: Low levels of vitamin D were associated with substantial cognitive decline in the elderly population studied over a 6-year period, which raises important new possibilities for treatment and prevention.

Li G, Mayer CL, Morelli D, et al. Effect of **simvastatin on CSF Alzheimer disease biomarkers** in cognitively normal adults. Neurology. 2017 Aug 18.

Li NC, Lee A, Whitmer RA, et al. Use of **angiotensin receptor blockers** and risk of dementia in a predominantly male population: prospective cohort analysis. BMJ. 2010 Jan 12;340:b5465. doi:10.1136/bmj.b5465.

Li J, Wang YJ, Zhang M, et al. On behalf of the Chongqing Ageing Study Group. **Vascular risk factors** promote conversion from mild cognitive impairment to Alzheimer disease. Neurology. 2011 Apr 26;76(17):1485-1491.

Li W, Risacher SL, Huang E, Saykin AJ; for the Alzheimer's Disease **Neuroimaging** Initiative. Type 2 diabetes mellitus is associated with **brain atrophy** and hypometabolism in the ADNI cohort. Neurology 2016;87:595–600.

Licher S, Leening MJG, Yilmaz P, et al. Development and Validation of a **Dementia Risk Prediction Model in the General Population**: An Analysis of Three Longitudinal Studies. Am J Psychiatry. 2018 Dec 11:appiajp201818050566.

Lieb Wolfgang; Beiser Alexa S.; Vasan Ramachandran S.; et al. Association of Plasma **Leptin** Levels With Incident Alzheimer Disease and MRI Measures of Brain Aging. JAMA. 2009;302(23):2565-2572.

Liew TM. **A 4-Item Case-Finding Tool** to Detect Dementia in Older Persons. J Am Med Dir Assoc. 2019 Aug 6.

Liljegren M, Naasan G, Temlett J, et al. **Criminal Behavior** in Frontotemporal Dementia and Alzheimer Disease. JAMA Neurol. 2015 Jan 5.

Lim ASP, Gaiteri C, Yu L, et al. **Seasonal plasticity of cognition** and related biological measures in adults with and without Alzheimer disease: Analysis of multiple cohorts. PLoS Med. 2018 Sep 4;15(9):e1002647.

Lim WS, Gammack JK, Van Niekerk J, Dangour AD. **Omega 3 fatty acid** for the prevention of dementia. Cochrane Database Syst Rev. 2006 Jan 25;(1):CD005379.

Lim YY, Kalinowski P, Pietrzak RH, et al. Association of **β-Amyloid and Apolipoprotein E ε4** With Memory Decline in Preclinical Alzheimer Disease. JAMA Neurol. 2018 Jan 22.

Lin FR, Metter EJ, O'Brien RJ, Resnick SM, Zonderman AB, Ferrucci L. **Hearing loss** and incident dementia. Arch Neurol. 2011 Feb;68(2):214-20.

Lin FR, Yaffe K, Xia J, et al; for the Health ABC Study Group. **Hearing Loss** and Cognitive Decline in Older Adults. JAMA Intern Med. 2013 Jan 21:1-7.

Lin JS, O'Connor E, Rossom RC, et al. **Screening for Cognitive Impairment** in Older Adults: A Systematic Review for the U.S. Preventive Services Task Force (**USPSTF**). Ann Intern Med. 2013 Oct 22.

Lindau ST, Dale W, Feldmeth G, et al. **Sexuality and Cognitive Status**: A U.S. Nationally Representative Study of Home-Dwelling Older Adults. J Am Geriatr Soc. 2018 Sep 12.

Lins S, Hayder-Beichel D, Rücker G, Motschall E, Antes G, Meyer G, Langer G. Efficacy and experiences of **telephone counselling for informal carers of people with dementia**. Cochrane Database of Systematic Reviews 2014, Issue 9. Art. No.: CD009126. DOI: 10.1002/14651858.CD009126.pub2. There is evidence that telephone counselling can reduce depressive symptoms for carers of people with dementia and that telephone counselling meets important needs of the carer. This result needs to be confirmed in future studies that evaluate efficacy through robust RCTs and the experience aspect through qualitative studies with rich data.

Liperoti R, Pedone C, Lapane KL, et al. **Venous Thromboembolism** Among Elderly Patients Treated With **Atypical** and Conventional Antipsychotic Agents. Arch Intern Med. 2005 Dec 12;165(22):2677-2682.

Littlejohns TJ, Henley WE, Lang IA, et al. **Vitamin D** and the risk of **dementia** and **Alzheimer disease**. Neurology. 2014 Sep 2;83(10):920-8.

Liu CM, Lee CT. Association of **Hearing Loss With Dementia**. JAMA Netw Open. 2019 Jul 3;2(7):e198112.

Liu E, Schmidt ME, et al; **Bapineuzumab** 301 and 302 Clinical Trial Investigators. Amyloid-β 11C-PiB-PET imaging results from 2 randomized bapineuzumab phase 3 AD trials. Neurology. 2015 Aug 25;85(8):692-700.

Liu-Ambrose Teresa; Nagamatsu Lindsay S.; Graf Peter; et al. **Resistance Training** and Executive Functions: A 12-Month Randomized Controlled Trial. Arch Intern Med. 2010;170(2):170-178.

Liu-Ambrose T, Best JR, Davis JC, et al. **Aerobic exercise** and vascular cognitive impairment: a randomized controlled trial. Neurology 2016;87:2082–2090.

Liu E,Wang D, Sperling R, et al. **Biomarker pattern of ARIA-E** in phase 3 randomized clinical trials with bapineuzumab. Neurology 2018;90:e877–e886.

Livingston G, et al. Old Age Task Force of the World Federation of Biological Psychiatry. **Systematic review of psychological approaches** to the management of neuropsychiatric symptoms of dementia. Am J Psychiatry. 2005 Nov;162(11):1996-2021.

Livingston G, Barber J, Rapaport P, et al. Clinical effectiveness of a **manual based coping strategy programme (START, STrAtegies for RelaTives)** in promoting the mental health of carers of family members with dementia: pragmatic randomised controlled trial. BMJ. 2013 Oct 25;347:f6276.

Livingston G, Kelly L, Lewis-Holmes E, et al. A systematic review of the clinical effectiveness and cost-effectiveness of **sensory, psychological and behavioural interventions** for managing agitation in older adults with dementia. Health Technol Assess. 2014 Jun;18(39):1-226. Person-centred care, communication skills and DCM (all with supervision), sensory therapy activities, and structured music therapies reduce agitation in care-home dementia residents. Future interventions should change care home culture through staff training and permanently implement evidence-based treatments and evaluate health economics. There is a need for further work on interventions for agitation in people with dementia living in their own homes.

Livingston G, Kelly L, Lewis-Holmes E, et al. **Non-pharmacological interventions** for **agitation in dementia**: systematic review of randomised controlled trials. Br J Psychiatry. 2014 Dec;205(6):436-42.

Livingston G, Barber J, et al. Long-term clinical and cost-effectiveness of **psychological intervention for family carers** of people with dementia: a single-blind, randomised, controlled trial. Lancet Psychiatry. 2014 Dec.

Livingston G, Sommerlad A, Orgeta V, et al. **Dementia prevention, intervention, and care**. Lancet 2017; online July 20.

Lochhead P, Hagan K, Joshi AD, et al. Association Between **Proton Pump Inhibitor** Use and Cognitive Function in Women. Gastroenterology. 2017 Jul 17.

Lo RY, Hubbard AE, Shaw LM, et al. for the Alzheimer's Disease **Neuroimaging Initiative. Longitudinal Change of Biomarkers** in Cognitive Decline. Arch Neurol. 2011 Jun 13.

Lo RY, Jagust WJ, for the Alzheimer's Disease Neuroimaging Initiative. Predicting missing **biomarker data** in a longitudinal study of Alzheimer disease. Neurology 2012;78: 1376–1382.

Loizeau AJ, Shaffer ML, Habtemariam DA, et al. Association of Prognostic Estimates With **Burdensome Interventions** in Nursing Home Residents With Advanced Dementia. JAMA Intern Med. 2018 May 29.

Lonergan E, Luxenberg J, Areosa Sastre A, Wyller TB. **Benzodiazepines** for delirium. Cochrane Database Syst Rev. 2009 Jan 21;(1):CD006379. No adequately controlled trials could be found to support the use of benzodiazepines in the treatment of non-alcohol withdrawal related delirium among hospitalised patients, and at this time benzodiazepines cannot be recommended for the control of this condition. Because of the scarcity of trials with randomization of patients, placebo control, and adequate concealment of allocation of subjects, it is clear that further research is required to determine the role of benzodiazepines in the treatment of non-alcohol withdrawal related delirium.

Lonergan E, Luxenberg J, **Valproate** preparations for agitation in dementia. *Cochrane Database of Systematic Reviews* 2009; Issue 3.

Lopez OL, Becker JT, Chang YF, et al. Incidence of mild cognitive impairment in the Pittsburgh Cardiovascular Health Study-Cognition Study. Neurology. 2012 Oct 9;79(15):1599-606.

Lopez OL, Becker JT, Chang YF, et al. The Long-Term Effects of **Conventional and Atypical Antipsychotics in Patients With Probable Alzheimer**`s Disease. Am J Psychiatry. 2013 Jul 30.

Lopez OL, Becker JT, Chang Y, et al. **Amyloid deposition and brain structure as long-term predictors of MCI, dementia, and mortality**. Neurology. 2018 Apr 25.

Loughrey DG, Kelly ME, Kelley GA, et al. Association of **age-related hearing loss** with cognitive function, cognitive impairment and dementia: a systematic review and meta-analysis [online Dec 7, 2017]. JAMA Otolaryngol Head Neck Surg. doi:10.1001 /jamaoto.2017.2513

Lourida I, Hannon E, Littlejohns TJ, et al. Association of **Lifestyle and Genetic Risk** With Incidence of Dementia. JAMA. 2019 Jul 14.

Lövheim H, Gilthorpe J, Adolfsson R, et al. **Reactivated herpes simplex** infection increases the risk of Alzheimer's disease. Alzheimers Dement. 2014 Jul 17.

Lövheim H, Gilthorpe J, Johansson A, et al. **Herpes simplex infection** and the risk of Alzheimer's disease-A nested case control study. Alzheimers Dement. 2014 Oct 7.

Loveman E, Green C, Kirby J, Takeda A, et al. The **clinical and cost-effectiveness of donepezil, rivastigmine, galantamine and memantine** for Alzheimer's disease. Health Technol Assess. 2006 Jan;10(1):1-176.

Lowe VJ, Peller PJ, Weigand SD, et al. Application of the National Institute on Aging-**Alzheimer's Association AD criteria to ADNI**. Neurology. 2013 May 3.

Loy C, Schneider L. **Galantamine** for Alzheimer's disease and mild cognitive impairment. Cochrane Database Syst Rev 2006; 1: CD001747.

Loy CT, Schofield PR, Turner AM, Kwok JB. **Genetics of dementia**. Lancet. 2013 Aug 5.

Lu D, Song H, Hao Z, Wu T, McCleery J. **Naftidrofuryl** for dementia. Cochrane Database of Systematic Reviews 2011, Issue 12. Art. No.: CD002955. DOI: 10.1002/14651858.CD002955.pub4. Oral administration of naftidrofuryl is well-tolerated by patients with dementia.The low-quality evidence shows that, by use of naftidrofuryl, people with dementia may benefit on performance, behaviour, cognition, and mood. However, the benefit on global impression is inconsistent and unconvincing.

Lu PH, Masterman DA, Mulnard R, et al. Effects of Testosterone on Cognition and Mood in Male Patients With Mild **Alzheimer Disease** and Healthy Elderly Men. Arch Neurol. 2005 Dec 12; [Epub ahead of print]

Lu PH, Edland SD, Teng E, Tingus K, Petersen RC, Cummings JL; Alzheimer's Disease Cooperative Study Group. Donepezil delays progression to AD in MCI subjects with depressive symptoms. Neurology. 2009 Jun 16;72(24):2115-21.

Luck T, Riedel-Heller SG, Roehr S, et al; **AgeCoDe** study group..**Mortality in Incident Cognitive Impairment**: Results of the Prospective AgeCoDe Study. J Am Geriatr Soc. 2016 Dec 19.

Lyall LM, Wyse CA, Graham N, et al. Association of **disrupted circadian rhythmicity with mood disorders, subjective wellbeing, and cognitive function**: a cross-sectional study of 91 105 participants from the UK Biobank. Lancet Psychiatry. 2018 May 15.

Lyketsos CG, et al.; Task Force of **American Association for Geriatric Psychiatry**. Position statement of the American Association for Geriatric Psychiatry regarding principles of care for patients with dementia resulting from **Alzheimer** disease. Am J Geriatr Psychiatry. 2006 Jul;14(7):561-72.

Ma Y, Jun GR, Zhang X, et al. **Analysis of Whole-Exome Sequencing Data** for Alzheimer Disease Stratified by APOE Genotype. JAMA Neurol. 2019 Jun 10.

Machulda MM, Jones DT, Vemuri P, et al. Effect of **APOE {varepsilon}4 Status** on Intrinsic Network Connectivity in Cognitively Normal Elderly Subjects. Arch Neurol. 2011 May 9.

Mackin P, Thomas SH. **Atypical antipsychotic drugs**. BMJ. 2011 Mar 4;342:d1126. doi: 10.1136/bmj.d1126.

MacLullich AM, Shenkin SD, Goodacre S, et al. The **4 'A's test for detecting delirium** in acute medical patients: a diagnostic accuracy study. Health Technol Assess. 2019 Aug;23(40):1-194.

Maher AR, Maglione M, Bagley S, et al. Efficacy and comparative effectiveness of **atypical antipsychotic medications** for **off-label** uses in adults: a systematic review and meta-analysis. JAMA. 2011 Sep 28;306(12):1359-69.

Mahinrad S, Jukema JW, van Heemst D, et al. **10-Second heart rate variability** and cognitive function in old age. Neurology. 2016 Mar 22;86(12):1120-7.

Maillard P, Seshadri S, Beiser A, et al. Effects of **systolic blood pressure on white-matter integrity** in young adults in the Framingham Heart Study: a cross-sectional study. Lancet Neurol 2012.

Malouf R, Grimley Evans J. **Folic acid with or without vitamin B12** for the prevention & treatment of healthy elderly and demented people. Cochrane Database Syst Rev. 2008 Oct 8;(4):CD004514. The small number of studies which have been done provide no consistent evidence either way that folic acid, with or without vitamin B12, has a beneficial effect on cognitive function of unselected healthy or cognitively impaired older people. In a preliminary study, folic acid was associated with improvement in the response of people with Alzheimer`s disease to cholinesterase inhibitors. In another, long-term use appeared to improve the cognitive function of healthy older people with high homocysteine levels. More studies are needed on this important issue.

Mangialasche Francesca, Solomon Alina, Winblad Bengt et al; **Alzheimer's disease: clinical trials and drug development**, The Lancet Neurology, Volume 9, Issue 7, July 2010

Manly JJ, Schupf N, Stern Y, et al. **Telephone-based identification** of mild cognitive impairment and dementia in a multicultural cohort. Arch Neurol. 2011 May;68(5):607-14.

Marcantonio Edward R. In the Clinic: **Delirium**. Ann Intern Med June 7, 2011 154:ITC6-1; doi:10.1059/0003-4819-154-11-201106070-01006.

Marcantonio ER, Ngo LH, O'Connor M, et al. **3D-CAM**: Derivation and Validation of a **3-Minute Diagnostic Interview for CAM-Defined Delirium**: A Cross-sectional Diagnostic Test Study. Ann Intern Med. 2014 Oct 21;161(8):554-61.

Marcantonio ER. **Delirium in Hospitalized Older** Adults. N Engl J Med. 2017 Oct 12;377(15):1456-1466.

Margenfeld F, Klocke C, Joos S. **Manual massage** for persons living with dementia: A systematic review and meta-analysis. Int J Nurs Stud. 2019 Jan 4.

Marsh L. Treatment of **Lewy-body dementias and psychopathology**. Lancet Neurol. 2010 Oct;9(10):943-5. Epub 2010 Aug 20. PubMed PMID: 20729149.

Martinez F, Tobar C, Hill N. **Preventing delirium**: should **non-pharmacological, multicomponent** interventions be used? A systematic review and meta-analysis of the literature. Age Ageing. 2015 Mar;44(2):196-204.

Martinez G, Vernooij RW, Fuentes Padilla P, et al. **18F PET with florbetapir for the early diagnosis of Alzheimer's disease** dementia and other dementias in people with mild cognitive impairment (MCI). Cochrane Database Syst Rev. 2017 Nov 22;11:CD012216. Although sensitivity was good in one included study, considering the poor specificity and the limited data available in the literature, we cannot recommend routine use of 18F-florbetapir PET in clinical practice to predict the progression from MCI to ADD.Because of the poor sensitivity and specificity, limited number of included participants, and the limited data available in the literature, we cannot recommend its routine use in clinical practice to predict the progression from MCI to any form of dementia.Because of the high financial costs of 18F-florbetapir, clearly demonstrating the DTA and standardising the process of this modality are important prior to its wider use.

Martinez-Valbuena I, Valenti-Azcarate R, Amat-Villegas I, et al. Amylin as a **potential link between type 2 diabetes and Alzheimer's** disease. Ann Neurol. 2019 Aug 3.

Mascarenhas Starling F, Medeiros-Souza P, Francisco de Camargos E, et al. **Tablet Splitting of Psychotropic Drugs** for Patients With Dementia: A Pharmacoepidemiologic Study in a Brazilian Sample. Clin Ther. 2015 Sep 14.

Massimo L, Zee J, Xie SX, et al. **Occupational attainment influences survival** in autopsy-confirmed front temporal degeneration. Neurology. 2015 May 19;84(20):2070-5.

Masters MC et al. "**Noncognitive**" **symptoms** of **early Alzheimer** disease: A longitudinal analysis. Neurology 2015 Jan 14;.

Masters MC, Morris JC, Roe CM. "**Noncognitive" symptoms** of early Alzheimer disease: A longitudinal analysis. Neurology. 2015 Jan 14.

Matthews FE, Arthur A, Barnes LE, et al, on behalf of the Medical Research Council Cognitive Function and Ageing Collaboration. A **two-decade comparison of prevalence of dementia** in individuals aged 65 years and older rom three geographical areas of England: results of the Cognitive Function and Ageing Study I and II. Lancet 2013; published online July 16.

Mattsson N, Cullen NC, Andreasson U, et al. Association Between **Longitudinal Plasma Neurofilament Light and Neurodegeneration** in Patients With Alzheimer Disease. JAMA Neurol. 2019 Apr 22.

Mattsson N, Rosén E, Hansson O, et al. Age and diagnostic performance of Alzheimer disease **CSF biomarkers**. Neurology. 2012 Feb 1.

Mattsson N, Schott JM, Hardy J, et al. Selective vulnerability in **neurodegeneration**: insights from clinical variants of Alzheimer's disease. J Neurol Neurosurg Psychiatry. 2016 Sep;87(9):1000-4.

Martin M, Clare L, Altgassen AM, Cameron MH, Zehnder F. **Cognition-based interventions** for healthy older people and people with mild cognitive impairment. Cochrane Database of Systematic Reviews 2011, Issue 1. Art. No.: CD006220. DOI: 10.1002/14651858.CD006220.pub2. There is evidence that cognitive interventions do lead to performance gains but none of the effects observed could be attributable specifically to cognitive training, as the improvements observed did not exceed the improvement in active control conditions. This does not mean that longer, more intense or different interventions might not be effective, but that those which have been reported thus far have only limited effect. We therefore suggest more standardized study protocols in order to maximize comparability of studies and to maximize the possibility of data pooling - also in other cognitive domains than memory.

Marzona I, O'Donnell M, Teo K, et al. Increased risk of cognitive and functional decline in patients with **atrial fibrillation**: results of the **ONTARGET** and **TRANSCEND** studies. CMAJ 2012

Mastroiacovo D, Kwik-Uribe C, Grassi D,et al. **Cocoa flavanol consumption** improves cognitive function, blood pressure control, and metabolic profile in elderly subjects: the Cocoa, Cognition, and Aging (CoCoA) Study-a randomized controlled trial. Am J Clin Nutr. 2015 Mar;101(3):538-48.

Matsuzaki T, Sasaki K, Tanizaki Y, et al. **Insulin resistance** is associated with the pathology of Alzheimer disease. The Hisayama Study. Neurology. 2010 Aug 25.

Matsuzaki T, Sasaki K, Hata J, et al. Association of Alzheimer disease pathology with **abnormal lipid metabolism**: The Hisayama Study. Neurology. 2011 Sep 13;77(11):1068-75.

Mattsson N, Zetterberg H, Hansson O, Andreasen N, Parnetti L, Jonsson M, ET AL. **CSF biomarkers** and incipient Alzheimer disease in patients with mild cognitive impairment. JAMA. 2009 Jul 22;302(4):385-93.

Mattsson N, Zetterberg H, Janelidze S, et al. **Plasma tau** in Alzheimer disease. Neurology. 2016 Oct 25;87(17):1827-1835

Maust DT, Kim HM, Seyfried LS, et al. **Antipsychotics, Other Psychotropics**, and the Risk of **Death** in Patients With **Dementia**: Number Needed to Harm. JAMA Psychiatry. 2015 Mar 18.

Maust DT, Kim HM, Chiang C, et al. Association of the Centers for Medicare & Medicaid Services' **National Partnership to Improve Dementia Care With the Use of Antipsychotics and Other Psychotropics** in Long-term Care in the United States From 2009 to 2014. JAMA Intern Med. 2018 Mar 17.

Mavros Y, Gates N, Wilson GC et al. Mediation of Cognitive Function Improvements by **Strength Gains After Resistance Training** in Older Adults with Mild Cognitive Impairment: Outcomes of the Study of Mental and Resistance Training. J Am Geriatr Soc. 2016. Online. Oct 24, 216.

Mayeux R. Clinical practice. **Early Alzheimer's disease**. N Engl J Med. 2010 Jun 10;362(23):2194-201.

Mazza M, Capuano A, Bria P, Mazza S. **Ginkgo biloba and donepezil**: a comparison in the treatment of Alzheimer's dementia in a randomized placebo-controlled double-blind study. Eur J Neurol. 2006 Sep;13(9):981-5.

McAdams-DeMarco MA, Bae S, Chu N, et al. Dementia and Alzheimer's Disease **among Older Kidney Transplant Recipients**. J Am Soc Nephrol. 2016 Dec 15.

McCarten JR, Anderson P, Kuskowski MA et al. **Screening for cognitive impairment** in an elderly veteran population: acceptability and results using different versions of the Mini-Cog. J Am Geriatr Soc. 2011 Feb;59(2):309-13.

McCartney M. Margaret McCartney: Drugs with **anticholinergic side effects** and cognitive decline-cause or effect? BMJ. 2015 Mar 16;350:h1428.

McCleery J, Cohen DA, Sharpley AL. **Pharmacotherapies for sleep disturbances in Alzheimer's disease**. Cochrane Database Syst Rev. 2014 Mar 21;3:CD009178. We discovered a distinct lack of evidence to help guide drug treatment of sleep problems in AD. In particular, we found no RCTs of many drugs that are widely prescribed for sleep problems in AD, including the benzodiazepine and non-benzodiazepine hypnotics, although there is considerable uncertainty about the balance of benefits and risks associated with these common treatments. From the studies we identified for this review, we found no evidence that melatonin is beneficial to AD patients with moderate to severe dementia and sleep problems. There is some evidence to support the use of a low dose (50 mg) of trazodone, although a larger trial is needed to allow a more definitive conclusion to be reached on the balance of risks and benefits. There was no evidence of any effect of ramelteon on sleep in patients with mild to moderate dementia due to AD. This is an area with a high need for pragmatic trials, particularly of those drugs that are in common clinical use for sleepproblems in AD. Systematic assessment of adverse effects is essential.

McCleery J, Cohen DA, Sharpley AL. **Pharmacotherapies for sleep disturbances in dementia**. Cochrane Database of Systematic Reviews 2016, Issue 11. Art. No.: CD009178. We discovered a distinct lack of evidence to help guide drug treatment of sleep problems in dementia. In particular, we found no RCTs of many drugs that are widely prescribed for sleep problems in dementia, including the benzodiazepine and non-benzodiazepine hypnotics, although there is considerable uncertainty about the balance of benefits and risks associated with these common treatments. From the studies we identified for this review, we found no evidence that melatonin (up to 10mg) helped sleep problems in patients with moderate to severe dementia due to AD. There was some evidence to support the use of a low dose (50 mg) of trazodone, although a larger trial is needed to allow a more definitive conclusion to be reached on the balance of risks and benefits. There was no evidence of any effect of ramelteon on sleep in patients with mild to moderate dementia due to AD. This is an area with a high need for pragmatic trials, particularly of those drugs that are in common clinical use for sleep problems in dementia. Systematic assessment of adverse effects is essential.

McDonagh J. **Statin-Related Cognitive Impairment** in the Real World: You'll Live Longer, but You Might Not Like It. JAMA Intern Med. 2014 Dec 1;174(12):1889.

McEvoy CT, Hoang T, Sidney S, et al. **Dietary patterns during adulthood** and cognitive performance in midlife: The CARDIA study. Neurology. 2019 Apr 2;92(14):e1589-e1599.

McGovern A, Pendlebury ST, Mishra NK, et al. Test Accuracy of **Informant-Based Cognitive Screening Tests** for Diagnosis of Dementia and Multidomain Cognitive Impairment in Stroke. Stroke. 2016 Feb;47(2):329-35.

McGrath ER, Beiser AS, DeCarli C, et al. **Blood pressure from mid- to late life** and risk of incident dementia. Neurology. 2017 Dec 12;89(24):2447-2454.

McGuinness B, Todd S, Passmore P, Bullock R. The effects of blood pressure lowering on development of cognitive impairment & dementia in patients without apparent prior cerebrovascular disease. Cochrane Database Syst Rev. 2006 Apr 19;(2):CD004034. There was no convincing evidence from the trials identified that blood pressure lowering prevents the development of dementia or cognitive impairment in hypertensive patients with no apparent prior cerebrovascular disease. There were significant problems identified with analysing the data, however, due to the number of patients lost to follow-up and the number of placebo patients given active treatment. This introduced bias. More robust results may be obtained by analysing one year data to reduce differential drop-out or by conducting a meta- analysis using individual patient data.

McGuinness B, O`Hare J, Craig D, et al. Statins for the treatment of dementia. Cochrane Database Syst Rev. 2010 Aug 4;8:CD007514. There is insufficient evidence to recommend statins for the treatment of dementia. Analysis from the studies available, including one large RCT, indicate statins have no benefit on the outcome measures ADAS-Cog or MMSE. We need to await full results from CLASP 2008 before we can be certain.

McIntosh EC, Nation DA; Alzheimer's Disease Neuroimaging Initiative. Importance of **Treatment Status in Links Between Type 2 Diabetes and Alzheimer Disease**. Diabetes Care. 2019 Mar 4.

McKeith IG, Boeve BF, Dickson DW, et al. **Diagnosis and management of dementia with Lewy bodies**: Fourth consensus report of the DLB Consortium. Neurology. 2017 Jul 4;89(1):88-100.

McLeod PJ, Huang AR, Tamblyn RM, Gayton DC. Defining **inappropriate** practices in prescribing for elderly people: a national consensus panel. CMAJ. 1997 Feb 1;156(3):385-91.

McMahon JA, Green TJ, Skeaff CM, Knight RG, Mann JI, Williams SM. A controlled trial of **homocysteine** lowering and cognitive performance. N Engl J Med. 2006 Jun 29;354(26):2764-72.

McShane R, Areosa Sastre A, Minakaran N. **Memantine** for dementia. Cochrane Database Syst Rev 2006; 2: CD003154.

McShane R, Westby MJ, Roberts E, et al. **Memantine for dementia**. Cochrane Database Syst Rev. 2019 Mar 20;3:CD003154.

McSorley VE, Bin YS, Lauderdale DS. Associations of **Sleep Characteristics With Cognitive Function and Decline** Among Older Adults. Am J Epidemiol. 2019 Jun 1;188(6):1066-1075.

Medical Letter. Treatment Guidelines. **Drugs for Cognitive Loss and Dementia**. Mar 2010.

Meeuwsen EJ, Melis RJ, Van Der Aa GC, et al. Effectiveness of dementia follow-up care by **memory clinics** or general practitioners: randomised controlled trial. BMJ. 2012 May 15;344:e3086.

Mehlig K, Lapidus L, Thelle DS, et al. Low **fasting serum insulin and dementia in nondiabetic women** followed for 34 years. Neurology. 2018 Jul 31;91(5):e427-e435.

Merkler AE, Iadecola C. Rollercoaster Blood Pressure: An Alzheimer Disease Risk Factor? Circulation. 2017 Aug 8;136(6):526-528

Mesulam MM, Lalehzari N, Rahmani F, et al. **Cortical cholinergic denervation** in primary progressive aphasia with Alzheimer pathology. Neurology. 2019 Apr 2;92(14):e1580-e1588.

Meyer PF, Tremblay-Mercier J, Leoutsakos J, et al; PREVENT-AD Research Group. INTREPAD: A randomized trial of naproxen to slow progress of presymptomatic Alzheimer disease. Neurology. 2019 Apr 30;92(18):e2070-e2080.

Mueller C, Ballard C, Corbett A, et al. The **prognosis of dementia with Lewy bodies**. Lancet Neurol. 2017 May;16(5):390-398.

Michaud CJ, Thomas WL, McAllen KJ. **Early pharmacological treatment of delirium** may reduce physical restraint use: a retrospective study. Ann Pharmacother. 2014 Mar;48(3):328-34

Middleton LE, Manini TM, Simonsick EM, et al. **Activity energy expenditure** and incident cognitive impairment in older adults. (**Health ABC**) Arch Intern Med. 2011 Jul 25;171(14):1251-7.

Middleton LE, Grinberg LT, Miller B, et al. **Neuropathologic features** associated with Alzheimer disease diagnosis: Age matters. Neurology. 2011 Nov 8;77(19):1737-44.

Mielke MM, Zandi PP, Shao H, et al. The 32-year relationship between **cholesterol and dementia** from midlife to late life. Neurology. 2010 Nov 10.

Mielke MM, Bandaru VV, Haughey NJ et al. **Serum ceramides** increase the risk of Alzheimer disease: The Women's Health and Aging Study II. Neurology. 2012 Aug 14;79(7):633-41.

Mielke MM, Wiste HJ, Weigand SD, et al. Indicators of **amyloid burden** in a population-based study of cognitively normal elderly. Neurology. 2012 Oct 9;79(15):1570-7.

Miller BL, Dickerson BC, Lucente DE, et al. Case records of the Massachusetts General Hospital. Case 9-2015. A 31-year-old man with **personality changes and progressive neurologic decline**. N Engl J Med. 2015 Mar 19;372(12):1151-62.

Miller JW, Harvey DJ, Beckett LA, et al. **Vitamin D Status** and Rates of Cognitive Decline in a Multiethnic Cohort of Older Adults. JAMA Neurol. 2015 Sep 14.

Mintzer JE, Tune LE, Breder CD, et al. **Aripiprazole** for the treatment of psychoses in institutionalized patients with Alzheimer dementia: a multicenter, randomized, double-blind, placebo-controlled assessment of three fixed doses. Am J Geriatr Psychiatry. 2007 Nov;15(11):918-31.

Mirza SS, Wolters FJ, Swanson SA, et al. **10-year trajectories of depressive symptoms** and risk of dementia: a population-based study. Lancet Psychiatry. 2016 Jul;3(7):628-35.

Mitchell SL. A **93-year-old man with advanced dementia and eating problems**. JAMA. 2007 Dec 5;298(21):2527-36. Epub 2007 Nov 6.

Mitchell SL et al. The clinical course of **advanced dementia**. N Engl J Med 2009 Oct 15; 361:1529.

Mitchell SL, Shaffer ML, Cohen S, et al. An **Advance Care Planning Video Decision Support Tool** for Nursing Home Residents With Advanced Dementia: A Cluster Randomized Clinical Trial. JAMA Intern Med. 2018 Jun 4.

Mitchell AJ, Shiri-Feshki M. Rate of **progression** of **mild cognitive impairment to dementia**--meta-analysis of 41 robust inception cohort studies. Acta Psychiatr Scand. 2009 Apr;119(4):252-65.

Mitchell SL, Black BS, Ersek M, et al. Advanced Dementia: **State of the Art and Priorities** for the Next Decade. Ann Intern Med. 2012 Jan 3;156(1_Part_1):45-51.

Mintzer J, et al. **Risperidone** in the treatment of psychosis of Alzheimer disease: results from a prospective clinical trial. Am J Geriatr Psychiatry. 2006 Mar;14(3):280-91. (Negative trial)

Mittelman MS, Haley WE, Clay OJ, Roth DL. Improving **caregiver** well-being delays nursing home placement of patients with Alzheimer disease. Neurology. 2006 Nov 14;67(9):1592-9.

Mitchell SL, Kiely DK, Hamel MB, Park PS, Morris JN, Fries BE. **Estimating prognosis** for nursing home residents with advanced dementia. JAMA. 2004 Jun 9;291(22):2734-40.

Mitchell Susan L.; Miller Susan C.; Teno Joan M.; et al. **Prediction of 6-Month Survival** of Nursing Home Residents With Advanced Dementia Using ADEPT vs Hospice Eligibility Guidelines. *JAMA*. 2010;304(17):1929-1935.

Miwa K, Tanaka M, Okazaki S, et al. **Chronic kidney disease** is associated with dementia independent of cerebral small-vessel disease. Neurology. 2014 Mar 25;82(12):1051-7.

Moghekar A, Goh J, Li M, et al. **Cerebrospinal fluid aβ and tau** level fluctuation in an older clinical cohort. Arch Neurol. 2012 Feb;69(2):246-50.

Moghekar A, Li S, Lu Y, et al; BIOCARD Research Team. **CSF biomarker changes** precede symptom onset of mild cognitive impairment. Neurology. 2013 Nov 12;81(20):1753-8.

Molnar, Frank J., Simpson, Christopher S. Approach to assessing **fitness to drive** in patients with cardiac and cognitive conditions. Can Fam Physician 2010 56: 1123-1129. (See also www.mocatest.org)

Moncada LV. Management of **falls in older persons**: a prescription for prevention. Am Fam Physician. 2011 Dec 1;84(11):1267-76.

Moniz Cook ED, Swift K, et al. **Functional analysis-based interventions** for challenging behaviour in dementia. Cochrane Database of Systematic Reviews 2012, Issue 2. Art. No.: CD006929. DOI:10.1002/14651858.CD006929.pub2. The delivery of FA has been incorporated within wide ranging multi-component programmes and study designs have varied according to setting - i.e. family care, care homes and hospital, with surprisingly few studies located in care homes. Our findings suggest potential beneficial effects of multi-component interventions, which utilise FA. Whilst functional analysis for challenging behaviour in dementia care shows promise, it is too early to draw conclusions about its efficacy.

Montine TJ, Koroshetz WJ, Babcock D, et al; For the **ADRD 2013 Conference** Organizing Committee. **Recommendations** of the Alzheimer's Disease-Related Dementias Conference. Neurology. 2014 Aug 26;83(9):851-860.

Montlahuc C, Soumaré A, Dufouil C, et al. **Self-rated health and risk of incident dementia**: a community-based elderly cohort, the 3C Study. Neurology 2011;77:1457–1464

Moore A, Patterson C, Lee L, et al. **Fourth Canadian Consensus Conference** on the **Diagnosis and Treatment of Dementia**: Recommendations for family physicians. Can Fam Physician. 2014 May;60(5):433-438.

Moore EM, Mander AG, Ames D, et al. Increased risk of cognitive impairment in patients with diabetes is associated with **metformin**. Diabetes Care. 2013 Oct;36(10):2981-7.

Moran C, Beare R, Wang W, Callisaya M, Srikanth V; Alzheimer's Disease Neuroimaging Initiative (ADNI). **Type 2 diabetes mellitus, brain atrophy, and cognitive decline**. Neurology. 2019 Feb 19;92(8):e823-e830.

Morandi A, McCurley J, Vasilevskis EE, et al. **Tools to detect delirium** superimposed on dementia: a systematic review. J Am Geriatr Soc. 2012 Nov;60(11):2005-13.

Mori E, Ikeda M, et al. **Donepezil for dementia with Lewy bodies**: A randomized, placebo-controlled trial. Annals of Neurology 2012.

Mokry LE, Ross S, Morris JA, et al. Genetically decreased **vitamin D** and risk of Alzheimer disease. Neurology. 2016 Dec 13;87(24):2567-2574

Mormino EC, Betensky RA, Hedden T, et al. **Amyloid and APOE e4 interact** to influence short-term decline in preclinical Alzheimer disease. Neurology 2014;82: 1760–1767.

Mormino EC, Sperling RA, Holmes AJ, et al. **Polygenic risk** of Alzheimer disease is associated with early- and late-life processes. Neurology. 2016 Aug 2;87(5):481-8

Morrens M, Wezenberg E, Verkes RJ, Hulstijn W, Ruigt GS, Sabbe BG. Psychomotor and memory effects of haloperidol, olanzapine, and paroxetine in healthy subjects after short-term administration. J Clin Psychopharmacol. 2007 Feb;27(1):15-21. Short-term administration of olanzapine, and not of haloperidol, impedes several aspects of psychomotor function and verbal memory in healthy volunteers.

Morris JC, Schindler SE, McCue LM, et al. Assessment of **Racial Disparities in Biomarkers** for Alzheimer Disease. JAMA Neurol. 2019 Jan 7

Morris MC, et al. Associations of **vegetable and fruit consumption** with age-related cognitive change. Neurology. 2006 Oct 24;67(8):1370-6.

Morris MC, Tangney CC, Wang Y, et al. **MIND diet** associated with reduced incidence of Alzheimer's disease. Alzheimers Dement. 2015 Feb 11.

Morris MC, Brockman J, Schneider JA, et al. Association of **seafood consumption**, **brain mercury** level and **APOE ε4 status** with brain neuropathology in older adults.JAMA. doi:10.1001/jama.2015.19451.

Morris MC, Wang Y, Barnes LLet al. **Nutrients and bioactives in green leafy vegetables** and cognitive decline: Prospective study. Neurology. 2017 Dec 20.

Morton RE, St John PD, Tyas SL. **Migraine and the risk** of all-cause dementia, Alzheimer's disease, and vascular dementia: A prospective cohort study in community-dwelling older adults. Int J Geriatr Psychiatry. 2019 Sep 4.

Mosconi L, Berti V, Quinn C, et al. **Sex differences in Alzheimer risk**: Brain imaging of endocrine vs chronologic aging. Neurology. 2017 Sep 26;89(13):1382-1390.

Mosing MA, Lundholm C, Cnattingius S, et al**. Associations between birth characteristics and age-related cognitive impairment and dementia**: A registry-based cohort study. PLoS Med. 2018 Jul 18;15(7):e1002609.

Mossello E, Pieraccioli M, Nesti N, et al. Effects of **Low Blood Pressure in Cognitively Impaired Elderly Patients** Treated With Antihypertensive Drugs. JAMA Intern Med. 2015 Mar 2.

Moulin S, Labreuche J, Bombois S, et al. **Dementia risk after spontaneous intracerebral haemorrhage**: a prospective cohort study. Lancet Neurol 2016; online April 28.

Moyer VA. **Screening for Cognitive Impairment** in Older Adults: U.S. Preventive Services Task Force (**USPSTF**) Recommendation Statement. Ann Intern Med. 2014 Mar 25.

Mueller C, Perera G, et al. Associations of **acetylcholinesterase inhibitor treatment with reduced mortality** in Alzheimer`s disease: a **retrospective** survival analysis. Age Ageing. 2017 Jun 24:1-7.

Mukundan A, Faulkner G, Cohn T, Remington G. **Antipsychotic switching** for people with schizophrenia who have neuroleptic-induced **weight or metabolic problems**. Cochrane Database of Systematic Reviews 2010, Issue 12. Art. No.: CD006629. DOI: 10.1002/14651858.CD006629.pub2. Evidence from this review suggests that switching antipsychotic medication to one with lesser potential for causing weight gain or metabolic problems could be an effective way to manage these side effects, but the data were weak due to the limited number of trials in this area and small sample sizes. Poor reporting of data also hindered using some trials and outcomes. There was no difference in mental state, global state and other treatment related adverse events between switching to another medication and continuing on the previous one. When the three switching strategies were compared none of them had an advantage over the others in their effects on the primary outcomes considered in this review. Better designed trials with adequate power would provide more convincing evidence for using medication switching as an intervention strategy.

Murray ME, Graff-Radford NR, Ross OA, et al. **Neuropathologically defined subtypes of Alzheimer's disease** with distinct clinical characteristics: a retrospective study. Lancet Neurol. 2011 Sep;10(9):785-96.

Murray ME, Ferman TJ, Boeve BF, et al. **MRI and pathology of REM sleep** behavior disorder in dementia with Lewy bodies. Neurology. 2013 Oct 9.

Murray AD. A new **biomarker classification** system for AD, independent of cognition: Agnosticism is a start. Neurology. 2016 Aug 2;87(5):456-7.

Musicco M, Adorni F, Di Santo S, et al. **Inverse occurrence of cancer and Alzheimer disease**: a population-based incidence study. Neurology 2013;81:322–328.

Nägga K, Gustavsson AM, Stomrud E, et al. Increased midlife **triglycerides** predict brain β-amyloid and tau pathology 20 years later. Neurology. 2017 Dec 1.

Najar J, Östling S, Gudmundsson P, et al. **Cognitive and physical activity** and dementia: A 44-year longitudinal population study of women. Neurology. 2019 Mar 19;92(12):e1322-e1330.

Nation DA, Edland SD, Bondi MW, et al. **Pulse pressure** is associated with Alzheimer biomarkers in cognitively normal older adults. Neurology. 2013 Dec 3;81(23):2024-7.

Nation DA, Edmonds EC, Bangen KJ, et al; Alzheimer's Disease Neuroimaging Initiative Investigators. **Pulse Pressure** in Relation to **Tau-Mediated Neurodegeneration**, Cerebral Amyloidosis, and Progression to Dementia in Very Old Adults. JAMA Neurol. 2015 Mar 30.

Naqvi R, Liberman D, Rosenberg J, et al. **Preventing cognitive decline in healthy older adults**. CMAJ. 2013 Jul 9;185(10):881-5.

Naqvi RM, Haider S, et al. Cognitive assessments in **multicultural populations** using the **Rowland Universal Dementia Assessment Scale**: systematic review and meta-analysis. CMAJ. 2015 Feb 17.

Naqvi RM, Haider S, Tomlinson G, Alibhai S. Cognitive assessments in **multicultural** populations using the **Rowland Universal Dementia Assessment Scale**: a systematic review and meta-analysis. CMAJ. 2015 Mar 17;187(5):E169-75.

Nead KT, Gaskin G, Chester C, et al. **Androgen Deprivation** Therapy and Future Alzheimer's Disease Risk. J Clin Oncol. 2015 Dec 7.

Nead KT, Gaskin G, Chester C, et al. Association between **androgen deprivation therapy** and risk of dementia [online October 13, 2016]. JAMA Oncol. doi:10.1001/jamaoncol.2016.3662

Needham DM, Colantuoni E, Dinglas VD, et al. **Rosuvastatin** versus placebo for **delirium** in intensive care and subsequent cognitive impairment in patients with sepsis-associated acute respiratory distress syndrome: an ancillary study to a randomised controlled trial. Lancet Respir Med. 2016 Jan 28.

Needham DM, Colantuoni E, Dinglas VD, et al. **Rosuvastatin** versus placebo for **delirium** in intensive care and subsequent cognitive impairment in patients with sepsis-associated acute respiratory distress syndrome: an ancillary study to a randomised controlled trial. Lancet Respir Med. 2016 Jan 28.

Nelson JC, Devanand DP. A Systematic Review and Meta-Analysis of Placebo-Controlled **Antidepressant** Studies in People with **Depression and Dementia** J Am Geriatr Soc. 2011 Apr;59(4):577-85.

Nelson PT, Dickson DW, Trojanowski JQ, et al. **Limbic-predominant age-related TDP-43 encephalopathy** (LATE): consensus working group report. Brain. 2019 Jun 1;142(6):1503-1527.

Nettiksimmons J, Ayonayon H, et al; Health ABC Study. Development and validation of **risk index for cognitive decline using blood-derived markers**. Neurology. 2015 Feb 17;84(7):696-702.

Neufeld KJ, Needham DM, Oh ES, et al. **Antipsychotics for the prevention and treatment of delirium**. Comparative Effectiveness Review No. 219. AHRQ Publication No. 19-EHC019-EF September 2019

Neufeld KJ, Yue J, et al. **Antipsychotic Medication for Prevention and Treatment of Delirium** in Hospitalized Adults: A Systematic Review and Meta-Analysis. J Am Geriatr Soc. 2016 Mar 23.

Neu SC, Pa J, Kukull WA, et al. **Apolipoprotein** E **genotype** and **sex risk factors** for Alzheimer disease: a meta-analysis [online August 28, 2017]. JAMA Neurol. doi:10.1001/jamaneurol.2017.2188.

Neuvonen E, Rusanen M, Solomon A, et al. **Late-life cynical distrust**, risk of incident dementia, and mortality in a population-based cohort. Neurology. 2014 Jun 17;82(24):2205-12.

Newhouse P, Kellar K, Aisen P, et al. **Nicotine treatment** (transdermal 15mg/day) of mild cognitive impairment: A 6-month double-blind pilot clinical trial. Neurology. 2012 Jan 10;78(2):91-101.

Ng TP, Feng L, Nyunt MS, et al. **Metabolic Syndrome** and the Risk of Mild Cognitive Impairment and Progression to Dementia: Follow-up of the Singapore ongitudinal Ageing Study Cohort. JAMA Neurol. 2016 Feb 29.

Ngandu T, Lehtisalo J, Solomon A, et al. A 2 year multidomain intervention of **diet, exercise, cognitive training, and vascular risk monitoring** versus control to prevent cognitive decline in at-risk elderly people (**FINGER**): a randomized controlled trial. Lancet. 2015 Mar 11.

Nho K, Kueider-Paisley A, Ahmad S, et al. Association of **Altered Liver Enzymes With Alzheimer Disease Diagnosis**, Cognition, Neuroimaging Measures, and Cerebrospinal Fluid Biomarkers. JAMA Netw Open. 2019 Jul 3;2(7):e197978.

NHS CKS Dementia Clinical Knowledge Summary 2010 http://www.cks.nhs.uk/dementia/management/scenario_screening_diagnosis_and_assessment/suspecting_dementia/early_recognition_of_dementia_is_a_challenge

NIA: Jack Clifford R., Albert Marilyn S., Knopman David S.. Introduction to the **recommendations** from the National Institute on Aging and the **Alzheimer's** Association workgroup on diagnostic guidelines for Alzheimer's disease. http://www.alz.org/documents_custom/Intro_Diagnostic_Recommendations_Alz_proof.pdf

NIA:McKhann Guy M, Knopman David S., Chertkow Howard. The **diagnosis of dementia due to Alzheimer's disease**: Recommendations from the National Institute on Aging and the Alzheimer's Association workgroup. http://www.alz.org/documents_custom/Diagnostic_Recommendations_Alz_proof.pdf

NIA: Albert Marilyn S., DeKosky Steven T., Dickson Dennis. The diagnosis of **mild cognitive impairment due to Alzheimer's disease**: Recommendations from the National Institute on Aging and Alzheimer's Association workgroup. http://www.alz.org/documents_custom/Diagnositic_Recommendations_MCI_due_to_Alz_proof.pdf

NIA: Sperling Reisa A., Aisen Paul S., Beckett Laurel A..Toward defining the **preclinical stages of Alzheimer's disease**: Recommendations from the National Institute on Aging and the Alzheimer's Association workgroup. http://www.alz.org/documents_custom/Diagnostic_Recommendations_Alz_Preclinical.pdf

NIH: National Institutes of Health. State-of-the-Science Conference statement: **preventing Alzheimer's disease and cognitive decline**. April 26-28, 2010. National Institutes of Health http://consensus.nih.gov/2010/alzstatement.htm Accessed Aug 24, 2010.

NIH NATIONAL INSTITUTES OF HEALTH STATE-OF-THE-SCIENCE CONFERENCE STATEMENT NIH State-of-the-Science Conference: **Preventing Alzheimer's Disease** and Cognitive Decline April 26–28, 2010 http://consensus.nih.gov/2010/docs/alz/alz_stmt.pdf

NICE National Institute for Health and Clinical Excellence. **Donepezil, galantamine, rivastigmine (review) and memantine** for the treatment of Alzheimer's disease. London (UK): National Institute for Health and Clinical Excellence; 2006 Nov. 64 p. (Technology appraisal guidance; no. 111). http://www.nice.org.uk/guidance/TA111/guidance/pdf/English

NICE: National Collaborating Centre for Acute and Chronic Conditions. **Delirium: diagnosis, prevention and management**. London (UK): National Institute for Health and Clinical Excellence (NICE); 2010 Jul. 29 p. (Clinical guideline; no. 103). http://www.nice.org.uk/nicemedia/live/13060/49913/49913.pdf

NICE- Delirium: diagnosis, prevention and management. (Clinical guidline 103.) **2010**. http://www.nice.org.uk/CG103

NICE: Technical Appraisal Guidance 111 Mar 2011. **Donepezil, galantamine, rivastigmine and memantine** for the treatment of Alzheimer's disease http://www.nice.org.uk/nicemedia/live/13419/53619/53619.pdf **Donepezil, galantamine and rivastigmine** are now recommended as options for managing mild as well as moderate Alzheimer's disease, and **Memantine** is now recommended as an option for managing moderate Alzheimer's disease for people who cannot take acetylcholinesterase (AChE) inhibitors, and as an option for managing severe Alzheimer's disease.

NICE: National Institute for Health and Care Excellence. **Dementia - assessment, management and support for people living with dementia and their carers** (NICE guideline NG97). 2018. www.nice.org.uk/guidance/ng97.

Nikooie R, Neufeld KJ, Oh ES, et al. **Antipsychotics for treating delirium** in hospitalized adults. A systematic review. Ann Intern Med. 3 September 2019 [Epub ahead of print]. doi:10.7326/M19-1860

Nishiguchi S, Yamada M, Tanigawa T, et al. A 12-Week **Physical and Cognitive Exercise Program** Can Improve Cognitive Function and Neural Efficiency in Community-Dwelling Older Adults: Randomized Controlled Trial. J Am Geriatr Soc. 2015 Jun 26.

Noel-Storr AH, McCleery JM, Richard E, et al. Reporting standards for studies of **diagnostic test accuracy** in dementia: The STARDdem Initiative. Neurology. 2014 Jul 22;83(4):364-373.

Nordestgaard LT, Tybjærg-Hansen A, Nordestgaard BG, et al. **Body Mass Index** and Risk of Alzheimer Disease: a Mendelian Randomization Study of 399,536 Individuals. J Clin Endocrinol Metab. 2017 May 9.

Nordström P, Religa D, Wimo A, Winblad B, et al. The use of **cholinesterase inhibitors** and the risk of **myocardial infarction and death**: a nationwide cohort study in subjects with Alzheimers disease. Eur Heart J 4 Jun 2013.

Nordström P, Nordström A, Eriksson M, et al. **Risk Factors in Late Adolescence for Young-Onset Dementia in Men**: A Nationwide Cohort Study. JAMA Intern Med. 2013 Aug 12.

Nordström A, Nordström P. **Traumatic brain injury** and the risk of dementia diagnosis: A nationwide cohort study. PLoS Med. 2018 Jan 30;15(1):e1002496.

Norris DR, Clark MS, Shipley S. The **Mental Status Examination**. (Am Fam Physician. 2016;94(8):635-641.

Northey JM, Cherbuin N, Pumpa KL, et al. **Exercise interventions** for cognitive function in adults older than 50: a systematic review with meta-analysis. Br J Sports Med2017;0:1-9.

Norton DJ, Amariglio R, Protas H, et al. **Subjective memory complaints** in preclinical autosomal dominant Alzheimer disease. Neurology. 2017 Oct 3;89(14):1464-1470.

Norton S, Matthews FE, Barnes DE, et al. Potential for **primary prevention** of Alzheimer's disease: an analysis of population-based data. Lancet Neurol. 2014 Aug;13(8):788-94.

Nourhashemi Fati, Andrieu Sandrine, Gillette-Guyonnet Sophie, et al., on behalf of the **PLASA** Group. Effectiveness of a **specific care plan** in patients with Alzheimer's disease: cluster randomised trial (PLASA study). BMJ 2010;340.

Novak P, Schmidt R, Kontsekova E, et al. The first-in-man **tau vaccine for the treatment of Alzheimer's disease "AADvac1"** displays a favourable safety and tolerability profile and high immunogenicity: a randomised double-blind placebo-controlled Phase I study. Lancet Neurol 2016; online Dec 9.

Nygaard HB. **Current and emerging therapies for Alzheimer's** disease. Clin Ther. 2013 Oct;35(10):1480-9.

O'Bryhim BE, Apte RS, Kung N, et al. Association of **Preclinical Alzheimer Disease With Optical Coherence** Tomographic Angiography Findings. JAMA Ophthalmol. 2018 Aug 23.

O'Kee e E, Mukhtar O, O'Kee e ST. **Orientation to time** as a guide to the presence and severity of cognitive impairment in older hospital patients. J Neurol Neurosurg Psychiatry. 2011;82:500-4.

O'Mahony Rachel, Murthy Lakshmi, Akunne A, et al. , for the Guideline Development Group. Synopsis of the National Institute for Health (**NIH**) and Clinical Excellence Guideline for **Prevention of Delirium**. Ann Intern Med June 7, 2011 154:746-751.

O'Regan NA, Ryan DJ, Boland E, et al. Attention! A good **bedside test for delirium**? J Neurol Neurosurg Psychiatry. 2014 Oct;85(10):1122-31.

Oda H, Ishii K, Terashima A, et al. **Myocardial scintigraphy** may predict the conversion to probable dementia with Lewy bodies. Neurology 2013;81:1741–1745.

Oh ES, Fong TG, Hshieh TT, et al. **Delirium in Older Persons**: Advances in Diagnosis and Treatment. JAMA. 2017 Sep 26;318(12):1161-1174.

Oh ES, Needham DM, Nikooie R, et al. **Antipsychotics for preventing delirium** in hospitalized adults. A systematic review. Ann Intern Med. 3 September 2019 [Epub ahead of print]. doi:10.7326/M19-1859

Oh ES, Rabins PV. **Dementia**. Ann Intern Med. 2019 Sep 3;171(5):ITC33-ITC48.

Ohara T, Doi Y, Ninomiya T, et al. **Glucose tolerance status** and risk of dementia in the community: The Hisayama Study. Neurology. 2011 Sep 20;77(12):1126-34.

Ohara T, Hata J, Yoshida D, et al. Trends in **dementia prevalence, incidence, and survival rate in a Japanese** community. Neurology. 2017 May 16;88(20):1925-1932.

Oishi E, Ohara T, Sakata S, et al. Day-to-Day **Blood Pressure Variability** and Risk of **Dementia** in a General Japanese Elderly Population: The Hisayama Study. Circulation. 2017 Aug 8;136(6):516-525

Okonkwo OC, Xu G, Dowling NM, et al. **Family history of Alzheimer** disease predicts hippocampal atrophy in healthy middle-aged adults. Neurology. 2012 May 29;78(22):1769-76.

Oldenbeuving AW, de Kort PL, Jansen BP, et al. **Delirium in the acute phase after stroke**: Incidence, risk factors, and outcome. Neurology. 2011 Mar 15;76(11):993-9.

Olsson B, Lautner R, Andreasson U,et al. **CSF and blood biomarkers** for the diagnosis of Alzheimer's disease: a systematic review and meta-analysis. Lancet Neurol. 2016 Apr 8

Olsson B, Lautner R, Andreasson U, et al. **CSF and blood biomarkers** for the diagnosis of Alzheimer's disease: a systematic review and meta-analysis. Lancet Neurol 2016; 15: 673–84

Orgeta V, Qazi A, Spector AE, et al. **Psychological treatments for depression and anxiety** in dementia and mild cognitive impairment. Cochrane Database Syst Rev. 2014 Jan 22;1:CD009125. We found evidence that psychological interventions added to usual care can reduce symptoms of depression and clinician-rated anxiety for people with dementia. We conclude that psychological interventions have the potential to improve patient well-being. Further high quality studies are needed to investigate which treatments are most effective and to evaluate the effect of psychological interventions in people with MCI.

Orgeta V, Qazi A, Spector A, et al. **Psychological treatments** for depression and anxiety in dementia and mild cognitive impairment: systematic review and meta-analysisd. Br J Psychiatry. 2015 Oct;207(4):293-8.

Orkaby AR, Cho K, Cormack J, et al. **Metformin vs sulfonylurea use and risk of dementia** in US veterans aged $65 years with diabetes. Neurology 2017;89:1877–1885.

Orrell M, Aguirre E, Spector A, et al. **Maintenance cognitive stimulation therapy** for dementia: single-blind, multicentre, pragmatic randomised controlled trial. Br J Psychiatry. 2014 Mar 27.

Osler M, Rozing MP, Christensen GT, et al. **Electroconvulsive therapy** and risk of dementia in patients with affective disorders: a cohort study. Lancet Psychiatry. 2018 Mar 6.

Ossenkoppele R, JansenWJ, Rabinovici GD, et al. Prevalence of **amyloid PET positivity** in dementia syndromes. JAMA. doi:10.1001/jama.2015.4669.

Ossenkoppele R, Rabinovici GD, Smith R, et al. Discriminative Accuracy of **[18F]flortaucipir Positron Emission Tomography** for Alzheimer Disease vs Other Neurodegenerative Disorders. JAMA 2018 Sep 18;320(11):1151-62

Ossenkoppele R, Smith R, Ohlsson T, et al. Associations between **tau, Aβ, and cortical thickness** with cognition in Alzheimer disease. Neurology. 2019 Feb 5;92(6):e601-e612.

Østergaard SD, Mukherjee S, Sharp SJ, et al. Alzheimer's Disease Genetics Consortium; GERAD1 Consortium; EPIC-InterAct Consortium, Larson EB, Powell JF, Langenberg C, et al. Associations between Potentially Modifiable **Risk Factors and Alzheimer Disease**: A Mendelian Randomization Study. PLoS Med. 2015 Jun 16;12(6):e1001841.

Ostrowitzki S, Deptula D, Thurfjell L, et al. Mechanism of Amyloid Removal in Patients With Alzheimer Disease Treated With **Gantenerumab**. Arch Neurol. 2011 Oct 10.

Ott BR, Daiello LA, Dahabreh IJ, Springate BA, et al. **Do Statins Impair Cognition**? A Systematic Review and Meta- analysis of Randomized Controlled Trials. J Gen Intern Med. 2015 Jan 10.

Ottens TH, Dieleman JM, Sauer AM, et al. Effects of **dexamethasone** on **cognitive decline** after cardiac surgery: a randomized clinical trial. Anesthesiology. 2014 Sep;121(3):492-500.

Oveisgharan S, Hachinski V. **Hypertension**, executive dysfunction, and progression to dementia: the Canadian study of health and aging. Arch Neurol 2010; 67:187-192.

Owusu JE, Islam S, Katumuluwa SS, et al. Cognition and **Vitamin D** in Older African-American Women- Physical performance and Osteoporosis prevention with vitamin D in older African Americans Trial and Dementia. J Am Geriatr Soc. 2018 Oct 25.

Padala PR et al. **Methylphenidate for apathy** in community-dwelling older veterans with mild Alzheimer's disease: A double-blind, randomized, placebo-controlled trial. Am J Psychiatry 2017 Sep 15.

Page VJ, Ely EW, et al. Effect of intravenous **haloperidol** on the **duration of delirium** and coma in critically ill patients (**Hope-ICU**): a randomised, double-blind, placebo-controlled trial Lancet Resp Med. 2013 Sep 1(7) 515-523

Page VJ, Davis D, Zhao XB, et al. Statin Use and **Risk of Delirium** in the Critically Ill. Am J Respir Crit Care Med. 2014 Jan 13

Pagano G, Rengo G, Pasqualetti G, et al. **Cholinesterase inhibitors for Parkinson`s disease**: a systematic review and meta-analysis. J Neurol Neurosurg Psychiatry. 2014 Sep 15.

Palmqvist S, et al; Swedish BioFINDER study group, Detailed comparison of **amyloid PET and CSF biomarkers** for identifying early Alzheimer disease. Neurology. 2015 Oct 6;85(14):1240-9.

Palmqvist S, Janelidze S, Stomrud E, et al. Performance of **Fully Automated Plasma Assays as Screening Tests** for Alzheimer Disease-Related β-Amyloid Status. JAMA Neurol. 2019 Jun 24.

Pandharipande PP, Girard TD, Jackson JC, et al. **Long-term cognitive impairment after critical illness**. N Engl J Med 2013; 369:1306-16.

Pankratz VS, Roberts RO, Mielke MM, et al. Predicting the **risk of mild cognitive impairment** in the Mayo Clinic Study of Aging. Neurology. 2015 Apr 7;84(14):1433-42.

Panza GA, Taylor BA, MacDonald HV, et al. Can **Exercise** Improve Cognitive Symptoms of Alzheimer's Disease? A Meta-Analysis. J Am Geriatr Soc. 2018 Jan 24.

Pariente A, Fourrier-Réglat A, Ducruet T, Farrington P, et al. Antipsychotic use and **myocardial infarction** in older patients with treated dementia [published online Mar 26, 2012]. Arch Intern Med doi:10.1001/archinternmed.2012.28.

Pariente A, Fourrier-Réglat A, Bazin F, et al. Effect of **treatment gaps** in elderly patients with dementia treated with **cholinesterase inhibitors**. Neurology. 2012 Mar 27;78(13):957-63. (not compromise outcome)

Park J, Jeong E, Seomun G. **The clock drawing test**: A systematic review and meta-analysis of diagnostic accuracy. J Adv Nurs. 2018 Jul 25.

Park Y, Bateman BT, Kim DH, et al. Use of **haloperidol versus atypical antipsychotics and risk of in-hospital death in patients with acute myocardial infarction**: cohort study. BMJ. 2018 Mar 28;360:k1218.

Parker C et al. **Antipsychotic drugs and risk of venous thromboembolism**: nested case-control study. BMJ 2010; 341: c4245

Parmar J, Dobbs B, McKay R, Kirwan C, Cooper T, Marin A, Gupta N. **Diagnosis and management of dementia in primary care**: Exploratory study. Can Fam Physician. 2014 May;60(5):457-65.

Parra MA, Baez S, Allegri R, et al. **Dementia in Latin America**: Assessing the present and envisioning the future. Neurology. 2018 Jan 30;90(5):222-231.

Parsons C, Hughes CM, Passmore AP, Lapane KL. **Withholding, discontinuing and withdrawing medications in dementia patients** at the end of life: a neglected problem in the disadvantaged dying? Drugs Aging. 2010 Jun 1;27(6):435-49.

Pase MP, Beiser AS, Himali JJ, et al. Assessment of Plasma Total **Tau Level as a Predictive Biomarker for Dementia** and Related Endophenotypes. JAMA Neurol. 2019 Mar 4.

Pase MP, Davis-Plourde K, Himali JJ, et al. **Vascular risk at younger ages** most strongly associates with **current and future brain volume**. Neurology 2018;91:e1479–e1486.

Passamonti L, Rodríguez PV, Hong YT, etal. [(11)C]**PK11195 binding in Alzheimer disease** and progressive supranuclear palsy. Neurology. 2018 May 29;90(22):e1989-e1996.

Patel BB, Holland NW. **Mild cognitive impairment**: Hope for stability, plan for progression. Cleve Clin J Med. 2012 Dec;79(12):857-64.

Patel T, Slonim K, Lee L. Use of **potentially inappropriate medications among ambulatory home-dwelling elderly patients with dementia**: A review of the literature. Can Pharm J (Ott). 2017 May 1;150(3):169-183.

Patterson C, Feightner JW, Garcia A, Hsiung GY, MacKnight C, Sadovnick AD. Diagnosis and treatment of dementia: 1. **Risk assessment and primary prevention** of Alzheimer disease. CMAJ. 2008 Feb 26;178(5):548-56.

Paul KC, Schulz J, Bronstein JM, et al. Association of **Polygenic Risk Score** With Cognitive Decline and Motor Progression in Parkinson Disease. JAMA Neurol. 2018 Jan 16.

Pauley E, Lishmanov A, Schumann S, et al. **Delirium is a robust predictor of morbidity and mortality** among **critically ill patients** treated in the cardiac intensive care unit. Am Heart J. 2015 Jul;170(1):79-86.e1.

Peltz CB, Corrada MM, Berlau DJ, Kawas CH. **Incidence of dementia in oldest-old** with amnestic MCI and other cognitive impairments. Neurology. 2011 Nov 22;77(21):1906-12.

Pendlebury ST. **Delirium screening in older patients**. Age Ageing. 2018 Jul 11.

Pendlebury ST, Rothwell PM; Oxford Vascular Study. Incidence and prevalence of **dementia associated with transient ischaemic attack and stroke**: analysis of the population-based Oxford Vascular Study. Lancet Neurol. 2019 Mar;18(3):248-258.

Peng M, Chen G, Tang KL, et al. **Blood pressure at age 60-65 versus age 70-75 and vascular dementia**: a population based observational study. BMC Geriatr. 2017 Oct 27;17(1):252.

Perneczky R, Tsolakidou A, Arnold A, et al. **CSF soluble amyloid precursor proteins** in the diagnosis of incipient Alzheimer disease. Neurology. 2011 Jul 5;77(1):35-8.

Penninkilampi R, Eslick GD. A Systematic Review and Meta-Analysis of the **Risk of Dementia Associated with Benzodiazepine Use**, After Controlling for Protopathic Bias. CNS Drugs. 2018 Jun 20.

Perras C, Shukla VK, Lessard C, et al.Cholinesterase Inhibitors for Alzheimer's Disease:A Systematic Review of Randomized Controlled Trials [Technology report no 58]. Ottawa: Canadian Coordinating Office for Health Technology Assessment; Sept 2005. 129pages. CCOHTA https://www.ccohta.ca/publications/pdf/217_cholinesterase_tr_e.pdf

Peters R, Beckett N, Forette F, et al. **HYVET** investigators. Incident dementia and blood pressure lowering in the Hypertension in the Very Elderly Trial cognitive function assessment (**HYVET-COG**): a double-blind, placebo controlled trial. Lancet Neurol. 2008 Aug;7(8):683-9. Epub 2008 Jul 7. Antihypertensive treatment in elderly patients does not statistically reduce incidence of dementia. This negative finding might have been due to the short follow-up, owing to the early termination of the trial, or the modest effect of treatment. Nevertheless, the HYVET findings, when included in a meta-analysis, might support antihypertensive treatment to reduce incident dementia.

Peters ME et al. **Neuropsychiatric symptoms** as **predictors of progression to severe Alzheimer's dementia and death**: The Cache County Dementia Progression Study. Am J Psychiatry 2015 Jan 13 .

Petersen RC, Stevens JC, Ganguli M, Tangalos EG, Cummings JL, DeKosky ST. Practice parameter: early detection of dementia: mild cognitive impairment (an evidence-based review): report of the Quality Standards Subcommittee of the American Academy of Neurology. Neurology 2001;56:1133-42.

Petersen RC. Clinical practice. **Mild cognitive impairment**. N Engl J Med. 2011 Jun 9;364(23):2227-34.

Petersen RC, Aisen P, Boeve BF, et al. Criteria for **mild cognitive impairment** due to alzheimer's disease in the community. Ann Neurol. 2013 May 20.

Petersen RC, Thomas RG, Aisen PS, et al. **Randomized controlled trials in mild cognitive impairment**: Sources of variability. Neurology. 2017 May 2;88(18):1751-1758.

Petersen RC, Lopez O, Armstrong MJ, et al. Practice guideline update summary: **Mild cognitive impairment**: Report of the Guideline Development, Dissemination, and Implementation Subcommittee of the American Academy of Neurology (**AAN**). Neurology. 2017 Dec 27

Petersen RC. **How early can we diagnose Alzheimer disease** (and is it sufficient)? The 2017 Wartenberg lecture. Neurology. 2018 Aug 28;91(9):395-402.

Pharmacist's Letter Oct 2006. **Drug treatment of Dementia** due to Alzheimer's Disease.

Pharmacist's Letter. **Fall prevention in the elderly**. April 2010.

Phelan EA, Borson S, Grothaus L, Balch S, Larson EB. Association of **incident dementia with hospitalizations**. JAMA. 2012;307(2):165-172.

Phillips VL, Diwan S. The incremental effect of dementia-related problem **behaviors** on the time to nursing home placement in poor, frail, demented older people.J Am Geriatr Soc. 2003 Feb;51(2):188-93.

Pieper MJ, Francke AL, van der Steen JT, et al. Effects of a **Stepwise Multidisciplinary Intervention** for Challenging Behavior in Advanced Dementia: A Cluster Randomized Controlled Trial. J Am Geriatr Soc. 2016 Jan 25.

Piguet Olivier, Hornberger Michael, Mioshi Eneida, et al. **Behavioural-variant frontotemporal dementia**: diagnosis, clinical staging, and management, The Lancet Neurology, In Press, Corrected Proof, Available online 10 Dec 2010, ISSN 1474-4422

Pink J, O'Brien J, Robinson L, et al. Dementia: **assessment, management and support**: summary of updated NICE guidance. BMJ. 2018 Jun 20;361:k2438.

Pitkälä KH, Pöysti MM, Laakkonen ML, et al. Effects of the **Finnish Alzheimer Disease Exercise Trial** (**FINALEX**): A Randomized Controlled Trial. JAMA Intern Med. 2013 Apr 15:1-8.

Plassman Brenda L., Williams, Jr John W.., Burke, James R.et al. **NIH Conferences**: Systematic Review: Factors Associated With **Risk for and Possible Prevention of Cognitive Decline in Later Life**. *Ann Intern Med* August 3, 2010 153:182-193.

Poels MM, Ikram MA, van der Lugt A et al. **Cerebral microbleeds** are associated with worse cognitive function: The **Rotterdam** Scan Study. Neurology. 2012 Jan 31;78(5):326-33.

Pointing the way to **primary** preve**n**tion of **dementia**. Lancet Neurol. 2017 Sept;16:677

Pollock BG, Mulsant BH, et al. Double-blind comparison of **citalopram and risperidone** for the treatment of behavioural and psychotics symptoms associated with dementia. *Am J Geriatr Psychiatry* 2007; 15: 942-952.

Pollock, Bruce G., Mulsant, Benoit H. Between Scylla and Charybdis: **antipsychotic and other psychotropic medications** in older nursing home residents CMAJ 2011 183: 778-779.

Pool LR, Weuve J, Wilson RS, et al. **Occupational cognitive requirements** and late-life cognitive aging. Neurology. 2016 Mar 16

Porsteinsson AP, Drye LT, Pollock BG, et al. Effect of **citalopram** on agitation in Alzheimer disease: the **CitAD** randomized clinical trial. *JAMA*. doi:10.1001/jama.2014.93.

Possin KL, Feigenbaum D, Rankin KP, et al. **Dissociable executive functions in behavioral variant frontotemporal** and Alzheimer dementias. Neurology 2013;80:2180–2185.

Pouryamout L, Dams J, Wasem J, Dodel R, Neumann A. Economic Evaluation of Treatment Options in Patients with Alzheimer's Disease: A **Systematic Review of Cost-Effectiveness** Analyses. Drugs. 2012 Apr 5.

Powell MR, et al. Cognitive measures predict pathologic Alzheimer disease. Arch Neurol. 2006 Jun;63(6):865-8. (InfoPOEMs: Baseline scores on the Mayo Cognitive Factor Scales (MCFS) are somewhat predictive of developing Alzheimer disease after 6 years. (LOE = 2b))

Prasad KM et al. Progressive gray matter loss and changes in cognitive functioning associated with exposure to **herpes simplex virus** 1 in schizophrenia: A longitudinal study. Am J Psychiatry2011 Jun 1

Prestia A, Caroli A, van der Flier WM, et al. **Prediction of dementia in MCI patients based on core diagnostic markers** for Alzheimer disease. Neurology 2013;80:1048–1056.

Prince M, Acosta D, Ferri CP, et al. Dementia incidence and mortality in middle-income countries, and associations with **indicators of cognitive reserve**: a 10/66 Dementia Research Group population-based cohort study. Lancet 2012; online May 23.

Prince M. **Progress on dementia**—**leaving no one behind**. Lancet 2017; online July 20.

Prorok JC, Horgan S, Seitz DP. **Health care experiences** of people with dementia and their caregivers: a meta-ethnographic analysis of qualitative studies. CMAJ. 2013 Oct 1;185(14):E669-E680.

Pruss H, Höltje M, Maier N, et al. **IgA NMDA receptor antibodies** are markers of synaptic immunity in slow cognitive impairment. Neurology 2012;78:1743–1753.

Pu L, Moyle W, Jones C, et al. **Psychosocial interventions for pain management** in older adults with dementia: A systematic review of randomized controlled trials. J Adv Nurs. 2018 Dec 10.

Purandare N, Burns A, Morris J, et al. Association of **cerebral emboli with accelerated cognitive deterioration** in Alzheimer's disease and vascular dementia. Am J Psychiatry. 2012 Mar;169(3):300-8.

Qaseem A, Snow V, Cross JT Jr, et al. **American College of Physicians/American Academy of Family Physicians Panel on Dementia**. Current pharmacologic treatment of dementia: a clinical practice guideline from the American College of Physicians and the American Academy of Family Physicians. Ann Intern Med. 2008 Mar 4;148(5):370-8.

Qian ZJ, Wattamwar K, Caruana FF, et al. **Hearing Aid** Use is Associated with Better Mini-Mental State Exam Performance. Am J Geriatr Psychiatry. 2016 Sep;24(9):694-702.

Qin B, Viera AJ, Muntner P, et al. **Visit-to-Visit Variability in Blood Pressure** Is Related to Late-Life Cognitive Decline. Hypertension. 2016 May 23.

Qiu C, von Strauss E, Bäckman L, et al. **Twenty-year changes** in dementia occurrence suggest decreasing incidence in central Stockholm, **Sweden**. Neurology. 2013 May 14;80(20):1888-94.

Querfurth HW, LaFerla FM. **Alzheimer's** Disease-**Mechanism of Disease**. N Engl J Med 2010 362: 329-344

Quinn JF.; Raman R,Thomas RG.; et al. **Docosahexaenoic Acid (DHA) Supplementation** and Cognitive Decline in Alzheimer Disease: A Randomized Trial. JAMA. 2010;304(17):1903-1911.

Quinn TJ, Fearon P, Noel-Storr AH, et al. Informant **Questionnaire on Cognitive Decline** in the Elderly (IQCODE) for the diagnosis of dementia within community dwelling populations. Cochrane Database Syst Rev. 2014 Apr 10;4:CD010079.

Quiroz YT, Sperling RA, et al. Association between **amyloid and tau accumulation** in young adults with autosomal dominant Alzheimer disease [online Feb 12, 2018].JAMA Neurol. doi: 10.1001/jamaneurol.2017 .4907.

Quispel-Aggenbach DWP, Holtman GA, Zwartjes HAHT, et al. **Attention, arousal and other rapid bedside screening instruments for delirium in older patients**: a systematic review of test accuracy studies. Age Ageing. 2018 Sep 1;47(5):644-653.

Qizilbash N, Gregson J, Johnson ME, et al. **BMI and risk of dementia** in two million people over two decades: a retrospective cohort study. Lancet Diabetes Endocrinol. 2015 Jun;3(6):431-6.

Rabin JS, Klein H, Kirn DR, et al. Associations of **Physical Activity and β-Amyloid** With Longitudinal Cognition and Neurodegeneration in Clinically Normal Older Adults. JAMA Neurol. 2019 Jul 16

Rabin JS, Schultz AP, Hedden T, et al. Interactive Associations of **Vascular Risk and β-Amyloid Burden With Cognitive Decline in Clinically Normal Elderly Individuals**: Findings From the Harvard Aging Brain Study. JAMA Neurol. 2018 May 21.

Rabinovici GD, Gatsonis C, Apgar C, et al. Association of **Amyloid Positron Emission Tomography With Subsequent Change in Clinical Management** Among Medicare Beneficiaries With Mild Cognitive Impairment or Dementia. JAMA. 2019 Apr 2;321(13):1286-1294.

Rabinovici GD, Rosen HJ, Alkalay A, et al. Amyloid vs FDG-PET in the differential diagnosis of AD and FTLD. Neurology. 2011 Nov 30.

Rabins PV et al. Practice Guideline for the Treatment of patients with Alzheimer's Disease and other Dementias. APA American 2007 http://www.psych.org/psych_pract/treatg/pg/AlzPG101007.pdf

Rabins PV, Blass DM. In the Clinic: **Dementia**. Ann Intern Med. 2014 Aug 5;161(3):ITC1.

Raffaitin C, Féart C, Le Goff M, et al. **Metabolic syndrome** and cognitive decline in French elders: The Three-City Study. Neurology. 2011 Feb 8;76(6):518-25.

Rafii MS, Walsh S, Little JT, et al. Alzheimer's Disease Cooperative Study. A phase II trial of **huperzine A** in mild to moderate Alzheimer disease. Neurology. 2011 Apr 19;76(16):1389-94. (not benefit)

Rafii MS, et al. **Adeno-associated viral vector (serotype 2)–nerve growth factor** for patients with Alzheimer disease: a randomized clinical trial [online Mar 26, 2018]. JAMA Neurol. doi:10.1001/jamaneurol .2018.0233

Raina P, Santaguida P, Ismaila A, et al. Effectiveness of **cholinesterase inhibitors and memantine** for treating dementia: evidence review for a clinical practice guideline. Ann Intern Med. 2008 Mar 4;148(5):379-97.

Rait G., Walters K., Bottomley C., Petersen I., Iliffe S., Nazareth I. **Survival** of people with clinical diagnosis of dementia in primary care: cohort study. BMJ 2010;341:c3584, doi: 10.1136/bmj.c3584 (Published 5 August 2010)

Raivio MM, Laurila JV, Strandberg TE, et al. **Neither atypical nor conventional antipsychotics increase mortality** or hospital admissions among elderly patients with dementia: a two-year prospective study. Am J Geriatr Psychiatry. 2007 May;15(5):416-24.

Rajan KB, Wilson RS, Weuve J, et al. **Cognitive impairment 18 years before clinical diagnosis of Alzheimer** disease dementia. Neurology. 2015 Sep 8;85(10):898-904.

Rajan KB, Arvanitakis Z, Lynch EB, et al. Cognitive decline following **incident and preexisting diabetes** mellitus in a population sample. Neurology 2016;87:1681–1687.

Rajan KB, Barnes LL, Wilson RS, et al. **Blood pressure and risk of incident Alzheimer's disease dementia by antihypertensive medications and APOE ε4 allele**. Ann Neurol. 2018 Apr 10.

Ramos AR, Gardener H, Rundek T, et al. **Sleep disturbances** and cognitive decline in the Northern Manhattan Study. Neurology. 2016 Oct 4;87(14):1511-1516

Ranson JM, Kuźma E, Hamilton W, et al. Predictors of **dementia misclassification when using brief cognitive assessments**. Neurol Clin Pract. 2019 Apr;9(2):109-117.

Rantalainen V, Lahti J, Henriksson M, et al. **Cognitive ability in young adulthood** predicts **risk of early-onset dementia** in Finnish men. Neurology. 2018 Jul 10;91(2):e171-e179.

Rapp SR, Luchsinger JA, Baker LD, et al. Effect of a **Long-Term Intensive Lifestyle Intervention** on Cognitive Function: Action for Health in Diabetes Study. J Am Geriatr Soc. 2017 Jan 9.

Rappaport SA, Marcus RN, Manos G, McQuade RD, Oren DA. A randomized, double-blind, placebo-controlled tolerability study of **intramuscular aripiprazole** in acutely agitated patients with Alzheimer's, vascular, or mixed dementia. J Am Med Dir Assoc. 2009 Jan;10(1):21-7.

Rapoport MJ, Herrmann N, Molnar FJ, et al. Sharing the responsibility for assessing the risk of the **driver** with dementia. CMAJ. 2007 Sep 11;177(6):599-601.

Raschetti R, Albanese E, Vanacore N, Maggini M. Cholinesterase inhibitors in **mild cognitive impairment**: a systematic review of randomised trials. PLoS Med. 2007 Nov 27;4(11):e338. The use of ChEIs in MCI was not associated with any delay in the onset of AD or dementia. Moreover, the safety profile showed that the risks associated with ChEIs are not negligible.

Rasmussen KL, Tybjaerg-Hansen A, Nordestgaard BG, Frikke-Schmidt R. Plasma levels of **apolipoprotein E** and risk of dementia in the general population. Ann Neurol. 2014 Dec 3.

Rasmussen KL, Tybjærg-Hansen A, Nordestgaard BG, et al. **Absolute 10-year risk of dementia by age, sex and APOE genotyp**e: a population-based cohort study. CMAJ. 2018 Sep 4;190(35):E1033-E1041.

Ravona-Springer R, Schnaider-Beeri M, Goldbourt U. **Body weight variability** in midlife and risk for dementia in old age. Neurology. 2013 Apr 30;80(18):1677-83.

Rawlings AM, Sharrett AR, Schneider AL, et al. **Diabetes in midlife and cognitive change** over 20 years: a cohort study. Ann Intern Med. 2014 Dec 2;161(11):785-93.

Rawlings AM, Juraschek SP, Heiss G, et al. Association of **orthostatic hypotension with incident dementia, stroke, and cognitive decline**. Neurology. 2018 Jul 25.

Ray J, Popli G, Fell G. **Association of Cognition and Age-Related Hearing Impairment** in the English Longitudinal Study of Ageing. JAMA Otolaryngol Head Neck Surg. 2018 Sep 6.

Reade MC, Finfer S. **Sedation and delirium** in the intensive care unit. N Engl J Med. 2014 Jan 30;370(5):444-54

Reade MC, Eastwood GM, Bellomo R, et al; for the **DahLIA** Investigators and the Australian and New Zealand Intensive Care Society Clinical Trials Group. Effect of **dexmedetomidine** added to standard care on ventilator-free time in patients with **agitated delirium**: a randomized clinical trial. JAMA. doi:10.1001/jama.2016.2707.

Rebok GW, Ball K, et al. **Ten-Year Effects of the Advanced Cognitive Training** for Independent & Vital Elderly Cognitive Training Trial on Cognition and Everyday Functioning in Older Adults. J Am Geriatr Soc. 2014 Jan 13

Redelmeier DA, Thiruchelvam D, Daneman N. **Delirium** after elective surgery among elderly patients **taking statins**. CMAJ. 2008 Sep 23;179(7):645-52.

Reese TR, Thiel DJ,Cocker KE. **Behavioral Disorders in Dementia**: Appropriate Nondrug Interventions and Antipsychotic Use. Am Fam Physician. 2016;94(4):276-282.

Reeve E, Farrell B, Thompson W, et al. Evidence-based clinical practice guideline for **deprescribing cholinesterase inhibitors and memantine**. Sydney: University of Sydney/ Bruyère Research Institute (Ottawa); 2018. http://sydney.edu.au/medicine/cdpc/documents/resources/deprescribing-guideline.pdf

Reeve E, Farrell B, Thompson W, et al. Evidence-based clinical practice guideline for **deprescribing cholinesterase inhibitors and memantine**: **recommendations**. Sydney: University of Sydney/ Bruyère Research Institute (Ottawa); 2018. http://sydney.edu.au/medicine/cdpc/documents/resources/deprescribing-recommendations.pdf

Reeve E, Farrell B, Thompson W, et al. Deprescribing **cholinesterase inhibitors and memantine in dementia**: guideline summary. Med J Aust. 2019 Mar;210(4):174-179.

Reilly S, Miranda-Castillo C, Malouf R, Hoe J, Toot S, Challis D, Orrell M. **Case management approaches to home support** for people with dementia. Cochrane Database of Systematic Reviews 2015, Issue 1. Art. No.: CD008345. DOI: 10.1002/14651858.CD008345.pub2. There is some evidence that case management is beneficial at improving some outcomes at certain time points, both in the person with dementia and in their carer. However, there was considerable heterogeneity between the interventions, outcomes measured and time points across the 13 included RCTs. There was some evidence from good-quality studies to suggest that admissions to care homes and overall healthcare costs are reduced in the medium term; however, the results at longer points of follow-up were uncertain. There was not enough evidence to clearly assess whether case management could delay institutionalisation in care homes. There were uncertain results in patient depression, functional abilities and cognition. Further work should be undertaken to investigate what components of case management are associated with improvement in outcomes. Increased consistency in measures of outcome would support future meta-analysis.

Reiman EM, Quiroz YT, Fleisher AS, et al. Brain **imaging and fluid biomarker** analysis in young adults at genetic risk for autosomal dominant Alzheimers disease in the presenilin 1 E280A kindred: a case-control study. Lancet Neurol 2012.

Reiman EM. **Alzheimer's disease and other dementias**: advances in 2013. Lancet Neurol. 2014 Jan;13(1):3-5

Reinhart RMG and Nguyen JA. **Working memory revived** in older adults by **synchronizing rhythmic brain circuits**. Nat Neurosci 2019 Apr 8.

Relkin NR, Thomas RG, Rissman RA, et al. A phase 3 trial of **IV immunoglobulin** for Alzheimer disease. Neurology. 2017 May 2;88(18):1768-1775.

Resnick SM, Matsumoto AM, Stephens-Shields AJ, et al. **Testosterone** treatment and **cognitive function** in older men with low testosterone and age-associated memory impairment. (**TT trials**) JAMA 2017; 317:717-727.

Reston JT, Schoelles KM. **In-facility delirium programs** as a patient safety strategy. A systematic review. Ann Intern Med. 2013;158:375-80.

Reus VI, Fochtmann LJ, et al. American Psychiatric Association (**APA**) Practice Guideline on the Use of **Antipsychotics to Treat Agitation or Psychosis in Patients With Dementia**. Am J Psychiatry. 2016 May 1;173(5):543-6.

Reynolds CF 3rd, Butters MA, Lopez O, et al. Maintenance treatment of depression in old age: a randomized, double-blind, placebo-controlled evaluation of the efficacy and safety of **donepezil** combined with antidepressant Pharmacotherapy. Arch Gen Psychiatry. 2011 Jan;68(1):51-60. (no clear benefit)

Richard E, Reitz C, Honig LH, et al. Late-Life **Depression**, Mild Cognitive Impairment, and Dementia. Arch Neurol. 2012 Dec 31:1-7.

Richardson JR, Roy A, Shalat SL, et al. Elevated serum **pesticide levels** (DDE/DDT) and risk for Alzheimer disease [online January 27, 2014]. JAMA Neurol. doi:10.1001/jamaneurol.2013.6030.

Richardson K, Fox C. Maidment I. **Anticholinergic drugs** and risk of dementia: case-control study. BMJ 2018;361:k1315.

Richardson K, Mattishent K, Loke YK, et al. History of Benzodiazepine Prescriptions and **Risk of Dementia:** Possible Bias Due to Prevalent Users and Covariate Measurement Timing in a Nested Case-Control Study. Am J Epidemiol. 2019 Mar 27

Richter T, Meyer G, Möhler R, Köpke S. **Psychosocial interventions** for reducing antipsychotic medication in **care home residents**. Cochrane Database of Systematic Reviews 2012, Issue 12. Art. No.: CD008634. DOI: 10.1002/14651858.CD008634.pub2. There is evidence to support the effectiveness of psychosocial interventions for reducing antipsychotic medication in care home residents.

Richters A, Melis RJ, Olde Rikkert MG, et al. The International Dementia Alliance Instrument for Feasible and Valid **Staging** of Individuals with Dementia by Informal Caregivers. J Am Geriatr Soc. 2016 Jun 15.

Ridgway GR, Lehmann M, Barnes J, et al. Early-onset Alzheimer disease clinical variants: Multivariate analyses of **cortical thickness**. Neurology. 2012 Jun 20.

Ringman John M. Setting the stage for **prevention of familial Alzheimer's disease**, The Lancet Neurology, Volume 10, Issue 3, March 2011, Pages 200-201, ISSN 1474-4422, DOI: 10.1016/S1474-4422(10)70328-8.

Rinne JO, et al. 11C-PiB PET assessment of change in fibrillar amyloid-β load in patients with Alzheimer's disease treated with **bapineuzumab**: a phase 2, double-blind, placebo-controlled, ascending-dose study. Lancet Neurol 2010; 9: 363–72.

Risacher SL, McDonald BC, Tallman EF, et al. Alzheimer's Disease Neuroimaging Initiative. Association Between **Anticholinergic Medication Use and Cognition**, Brain Metabolism, and Brain Atrophy in Cognitively Normal Older Adults. JAMA Neurol. 2016 Apr 18.

Risacher SL, Anderson WH, Charil A, et al; Alzheimer's Disease Neuroimaging Initiative. Alzheimer disease **brain atrophy subtypes** are associated with cognition and rate of decline. Neurology. 2017 Nov 21;89(21):2176-2186

Rist PM, Capistrant BD, Wu Q, et al. **Dementia and dependenc**e: Do modifiable risk factors delay disability? Neurology. 2014 Apr 29;82(17):1543-50.

Ritchie K., Carrière I., Ritchie C. Wet al. **Designing prevention programmes** to reduce incidence of dementia: prospective cohort study of modifiable risk factors. BMJ 2010;341:c3885, doi: 10.1136/bmj.c3885 (Published 5 August 2010)

Rizzo Matthew. **Impaired Driving From Medical Conditions**: A 70-Year-Old Man Trying to Decide if He Should Continue Driving. JAMA. 2011;305(10):1018-1026.

Roberts HJ, Noble JM. Education Research: Changing **medical student perceptions of dementia**: An arts-centered experience. Neurology. 2015 Aug 25;85(8):739-41.

Roberts RO, Geda YE, Knopman DS, et al. The incidence of **MCI differs by subtype and is higher in men**: the Mayo Clinic Study of Aging. Neurology 2012;78:342–351.

Roberts RO, Knopman DS, Mielke MM, et al. Higher risk of progression to dementia in **mild cognitive impairment** cases who revert to normal. Neurology 2014;82:317–325.

Roberts RO, Knopman DS, Przybelski SA, et al. Association of **type 2 diabetes with brain atrophy** and cognitive impairment. Neurology. 2014 Apr 1;82(13):1132-41.

Roberts RO, Christianson TJ, Kremers WK, et al. Association Between **Olfactory Dysfunction** and **Amnestic Mild Cognitive Impairment and Alzheimer Disease Dementia**. JAMA Neurol. 2015 Nov 16:1-9.

Roberts RO, Cha RH, Mielke MM, et al. **Risk and protective factors** for cognitive impairment in persons **aged 85 years and older**. Neurology. 2015 May 5;84(18):1854-61.

Roberts RO, Aakre JA, Kremers WK, et al. Prevalence and Outcomes of **Amyloid Positivity** Among Persons Without Dementia in a Longitudinal, Population-Based Setting. JAMA Neurol. 2018 Apr 30.

Robinson DM, Keating GM. **Memantine**: a review of its use in Alzheimer's disease. Drugs. 2006;66(11):1515-34.

Robinson L, Tang E, Taylor JP. **Dementia: timely diagnosis and early intervention**. BMJ. 2015 Jun 16;350:h3029.

Rocca WA, Bower JH, Maraganore DM, et al. Increased risk of cognitive impairment or dementia in women who underwent oophorectomy before menopause. Neurology. 2007 Sep 11;69(11):1074-83. Epub 2007 Aug 29. Both unilateral and bilateral **oophorectomy** preceding the onset of menopause are associated with an increased risk of cognitive impairment or dementia. The effect is age-dependent and suggests a critical age window for neuroprotection.

Rochon PA, Gruneir A, Gill SS, et al. **Older men with dementia** are at greater risk than women of **serious events** after initiating antipsychotic therapy. J Am Geriatr Soc. 2013 Jan;61(1):55-61.

Rochon PA, Gruneir A, Gill SS, et al. Initial **Cholinesterase Inhibitor Therapy Dose and Serious Events** in Older Women and Men. J Am Geriatr Soc. 2018 Sep;66(9):1692-1699.

Rodakowski J, Skidmore ER, Reynolds CF 3rd, et al. Can **Performance on Daily Activities** Discriminate Between Older Adults with Normal Cognitive Function and Those with Mild Cognitive Impairment? J Am Geriatr Soc. 2014 Jun 2.

Rodda J, Carter J. **Cholinesterase inhibitors and memantine** for symptomatic treatment of dementia. BMJ. 2012 May 1;344:e2986.

Rodrigue KM, Kennedy KM, Devous MD Sr, et al. **β-Amyloid burden in healthy aging**: Regional distribution and cognitive consequences. Neurology. 2012 Feb 7;78(6):387-95.

Rodrigue KM, Rieck JR, Kennedy KM, et al. **Risk Factors for β-Amyloid Deposition in Healthy Aging**: Vascular and Genetic Effects. JAMA Neurol. 2013 Mar 18:1-7.

Roe CM, Fagan AM, Williams MM, et al. Improving **CSF biomarker** accuracy in predicting prevalent and incident Alzheimer disease. Neurology. 2011 Feb 8;76(6):501-10.

Roe CM, Fagan AM, Grant EA, et al. **Cerebrospinal fluid biomarkers**, **education**, **brain volume**, and future cognition. Arch Neurol. 2011 Sep;68(9):1145-51.

Roe CM, Rentz DM. Alzheimer disease: **Before the diagnosis**. Neurology. 2013 Mar 26;80(13):e148-9.

Roe CM, Fagan AM, Grant EA, et al. **Amyloid imaging and CSF biomarkers** in predicting cognitive impairment up to 7.5 years later. Neurology. 2013 May 7;80(19):1784-1791.

Roe CM, Fagan AM, Grant EA, Holtzman DM, Morris JC. **CSF biomarkers** of Alzheimer disease: "Noncognitive" outcomes. Neurology. 2013 Dec 3;81(23):2028-31.

Rohrer JD, Nicholas JM, Cash DM, et al. **Presymptomatic cognitive and neuroanatomical changes in genetic frontotemporal dementia** in the Genetic Frontotemporal dementia Initiative (GENFI) study: a cross-sectional analysis. Lancet Neurology 2015; online Feb 4.

Rojas-Fernandez C, Mikhail M, Brown SG. **Psychotropic and Cognitive-Enhancing Medication Use** and Its Documentation in Contemporary Long-term Care Practice. Ann Pharmacother. 2014 Apr;48(4):438-46.

Rojas-Fernandez CH, Patel T, Lee L. An interdisciplinary **memory clinic**: a novel practice setting for pharmacists in primary care. Ann Pharmacother. 2014 Jun;48(6):785-95.

Rolland Y, et al. **Exercise program** for nursing home residents with Alzheimer's disease: a 1-year randomized, controlled trial. J Am Geriatr Soc. 2007 Feb;55(2):158-65. A simple exercise program, 1 hour twice a week, led to significantly slower decline in ADL score in patients with AD living in a nursing home than routine medical care.

Roman GC, Salloway S, Black SE, et al. Randomized, placebo-controlled, clinical trial of **donepezil in vascular dementia**: differential effects by **hippocampal size**. Stroke. 2010 Jun;41(6):1213-21. Epub 2010 Apr 15.

Romeo R, Zala D, Knapp M, et al. **Improving the quality of life of care home residents with dementi**a: cost-effectiveness of an optimized intervention for residents with clinically significant agitation in dementia. Alzheimers Dement 2018. 10.1016/j.jalz.2018.08.010.

Rosa RG, Falavigna M, da Silva DB, et al. Effect of Flexible **Family Visitation on Delirium Among Patients in the Intensive Care Unit**: The ICU Visits Randomized Clinical Trial. JAMA. 2019 Jul 16;322(3):216-228.

Rosenberg PB, Drye LT, Martin BK, et al. DIADS-2 Research Group. **Sertraline** for the treatment of **depression in Alzheimer disease**. Am J Geriatr Psychiatry. 2010 Feb;18(2):136-45. CONCLUSIONS: Sertraline not effective.

Rosenberg RN. Treat Alzheimer disease **before it is symptomatic**. Arch Neurol. 2011 Oct;68(10):1237-8.

Rosenberg PB, Mielke MM, Han D, et al. The association of **psychotropic medication use with the cognitive, functional and neuropsychiatric trajectory** of Alzheimer's disease. Int J Geriatr Psychiatry 2012; 27:1248–57.

Rosenheck RA, Leslie DL, Sindelar JL, et al. Clinical Antipsychotic Trial of Intervention Effectiveness-Alzheimer's Disease (**CATIE-AD**) investigators. **Cost-benefit analysis** of second-generation antipsychotics and placebo in a randomized trial of the treatment of psychosis and aggression in Alzheimer disease. Arch Gen Psychiatry. 2007 Nov;64(11):1259-68. There were no differences in measures of effectiveness between initiation of active treatments or placebo (which represented watchful waiting) but the placebo group had significantly lower health care costs. Sultzer DL, Davis SM, Tariot PN, Dagerman KS, Lebowitz BD, Lyketsos CG, Rosenheck RA, Hsiao JK, Lieberman JA, Schneider LS; CATIE-AD Study Group. Clinical Symptom Responses to Atypical Antipsychotic Medications in Alzheimer's Disease: Phase 1 Outcomes From the CATIE-AD Effectiveness Trial. Am J Psychiatry. 2008 Jun 2. [Epub ahead of print] In this descriptive analysis of outpatients with Alzheimer's disease in usual care settings, some clinical symptoms improved with atypical antipsychotics. Antipsychotics may be more effective for particular symptoms, such as anger, aggression, and paranoid ideas. They do not appear to improve functioning, care needs, or quality of life.

Rossetti HC, Lacritz LH, Cullum CM, Weiner MF. **Normative data for the Montreal Cognitive Assessment (MoCA)** in a population-based sample. Neurology. 2011 Sep 27;77(13):1272-5.

Rosso AL, Verghese J, Metti AL, et al. Slowing **gait** and risk for **cognitive impairment**: The hippocampus as a shared neural substrate. Neurology. 2017 Jul 25;89(4):336-342.

Rossom RC, Rector TS, Lederle FA, et al. Are All Commonly Prescribed Antipsychotics Associated with Greater **Mortality** in Elderly Male Veterans with Dementia? J Am Geriatr Soc. 2010 May 7.
Commonly prescribed doses of haloperidol, olanzapine, and risperidone, but not quetiapine, were associated with a short-term increase in mortality.

Rossom RC, Espeland MA, Manson JE, et al. **Calcium and vitamin D supplementation and cognitive impairment** in the women's health initiative (**WHI**). J Am Geriatr Soc. 2012 Dec;60(12):2197-205.

Rovio SP, Pahkala K, Nevalainen J, et al. **Cardiovascular Risk Factors From Childhood and Midlife Cognitive Performance**: The Young Finns Study. J Am Coll Cardiol. 2017 May 9;69(18):2279-2289

Rovner BW, Casten RJ, Hegel MT, et al. **Preventing Cognitive Decline in Black Individuals With Mild Cognitive Impairment**: A Randomized Clinical Trial. JAMA Neurol. 2018 Sep 10.

Rowe CC, Bourgeat P, Ellis KA, et al. Predicting Alzheimer disease with **β-amyloid imaging**: Results from the Australian imaging, biomarkers, and lifestyle study of ageing. Ann Neurol. 2013 Dec;74(6):905-13

Ruiz Vargas E, Sposato LA, Lee SAW, et al. **Anticoagulation Therapy for Atrial Fibrillation in Patients With Alzheimer's Disease**. Stroke. 2018 Dec;49(12):2844-2850.

Rusanen Minna; Kivipelto Miia; Quesenberry Charles P. Jr; et al. Heavy **Smoking in Midlife** and Long-term Risk of Alzheimer Disease and Vascular Dementia. Arch Intern Med. 2011;171(4):333-339.

Russ TC, Morling JR. **Cholinesterase inhibitors for mild cognitive impairment**. Cochrane Database Syst Rev. 2012 Sep 12;9:CD009132. doi: 10.1002/14651858.CD009132.pub2. There is very little evidence that cholinesterase inhibitors affect progression to dementia or cognitive test scores in mild cognitive impairment. This weak evidence is overwhelmed by the increased risk of adverse events, particularly gastrointestinal. Cholinesterase inhibitors should not be recommended for mild cognitive impairment.

Ruthirakuhan MT, Herrmann N, Abraham EH, et al. **Pharmacological interventions for apathy** in Alzheimer`s disease. Cochrane Database Syst Rev. 2018 May 4;5:CD012197. Methylphenidate may demonstrate a benefit for apathy and may have slight benefits for cognition and functional performance in people with AD, but this finding is associated with low-quality evidence. Our meta-analysis is limited by the small number of studies within each drug class, risk of bias, publication bias, imprecision and inconsistency between studies.

Rutjes AW, Denton DA, Di Nisio M, et al. **Vitamin and mineral supplementation** for maintaining cognitive function in cognitively healthy people in mid and late life. Cochrane Database Syst Rev. 2018 Dec 17;12:CD011906.
We did not find evidence that any vitamin or mineral supplementation strategy for cognitively healthy adults in mid or late life has a meaningful effect on cognitive decline or dementia, although the evidence does not permit definitive conclusions. There were very few data on supplementation starting in midlife (< 60 years); studies designed to assess cognitive outcomes tended to be too short to assess maintenance of cognitive function; longer studies often had other primary outcomes and used cognitive measures which may have lacked sensitivity. The only positive signals of effect came from studies of long-term supplementation with antioxidant vitamins.

Ryan NS, Nicholas JM, Weston PSJ, et al. **Clinical phenotype and genetic associations** in autosomal dominant familial Alzheimer's disease: a case series. Lancet Neurol 2016; online Oct 21.

Ryman DC, Acosta-Baena N, Aisen PS, et al; Dominantly Inherited Alzheimer Network. **Symptom onset** in autosomal dominant Alzheimer disease: A systematic review and meta-analysis. Neurology. 2014 Jul 15;83(3):253-60.

Saarelainen L, Tolppanen AM, Koponen M, et al. Risk of death associated with new **benzodiazepine use** among persons with Alzheimer disease: A matched cohort study. Int J Geriatr Psychiatry. 2017 Nov 15.

Sabayan B, Wijsman LW, Foster-Dingley JC, et al. Association of **visit-to-visit variability** in blood pressure with **cognitive function** in old age: prospective cohort study. BMJ. 2013 Jul 29;347:f4600.

Sabayan B, Gussekloo J, de Ruijter W, et al. **Framingham stroke risk score and cognitive impairment** for predicting first-time stroke in the oldest old. Stroke. 2013 Jul;44(7):1866-71.

Sabayan B, Sorond F. **Reducing Risk of Dementia in Older Age**. JAMA. 2017 May 16;317(19):2028.

Sabia S, Elbaz A, Britton A, et al. **Alcohol consumption** and cognitive decline in early old age. Neurology. 2014 Jan 15.

Sabia S, Dugravot A, Dartigues JF, et al. **Physical activity, cognitive decline, and risk of dementia: 28 year** follow-up of **Whitehall II cohort** study. BMJ. 2017 Jun 22;357:j2709

Sabia S, FayosseA, DumurgierJ, etal . **Alcohol consumption and risk of dementia**: 23 year follow-up of Whitehall II cohort study. BMJ 2018;362:k2927.

Sabia S, Fayosse A, Dumurgier J, et al. Association of **ideal cardiovascular health at age 50 with incidence of dementia**- 25 year follow-up of Whitehall II cohort study. BMJ. 2019 Aug 7;366:l4414.

Sacarny A, Barnett ML, Le J, et al. Effect of **peer comparison letters for high-volume primary care prescribers of quetiapine** in older and disabled adults: a randomized clinical trial [online August 1, 2018]. JAMA Psychiatry. doi:10.1001/jamapsychiatry.2018.1867

Sacchetti E, Turrina C, Valsecchi P. **Cerebrovascular accidents in elderly people treated with antipsychotic** drugs: a systematic review. Drug Saf. 2010 Apr 1;33(4):273-88. doi: 10.2165/11319120-000000000-00000.

Sacks CA, Avorn J, Kesselheim AS. The Failure of **Solanezumab** - How the FDA Saved Taxpayers Billions. N Engl J Med. 2017 May 4;376(18):1706-1708

Sachs GA, Carter R, Holtz LR, et al. **Cognitive impairment**: an independent predictor of **excess mortality**: a cohort study. Ann Intern Med. 2011 Sep 6;155(5):300-8.

Saczynski, J.S., Beiser, A., Seshadri, S., et al. **Depressive symptoms** and risk of dementia: The Framingham Heart Study. Neurology 2010 75: 35-41.

Saczynski JS, Marcantonio ER, Quach L, et al. Cognitive trajectories after **postoperative delirium**. N Engl J Med 2012; 367:30-39.

Salloway S, Sperling R, Fox NC, et al. Two phase 3 trials of **bapineuzumab** in mild-to-moderate Alzheimers disease. N Engl J Med 2014;370:322-33.

Salluh JI, Wang H, Schneider EB, et al. Outcome of **delirium** in critically ill patients: systematic review and meta-analysis. BMJ. 2015 Jun 3;350:h2538.

Samieri C, Perier M-C, Gaye B, et al. Association of **cardiovascular health level** in older age with cognitive decline and incident dementia [August 21, 2018]. JAMA.

Sanders AE, Nininger J, Absher J, et al. **Quality improvement in neurology**: Dementia management quality measurement set update. Neurology. 2017 May 16;88(20):1951-1957

Sanders Robert D, Pandharipande Pratik P, Davidson Andrew J, et al. Anticipating and managing **postoperative delirium** and cognitive decline in adults. BMJ 2011;343:doi:10.1136/bmj.d4331 (Published 20 July 2011)

San-Juan-Rodriguez A, Zhang Y, He M, Hernandez I. Association of **Antidementia Therapies With Time to Skilled Nursing Facility Admission and Cardiovascular Events** Among Elderly Adults With Alzheimer Disease. JAMA Netw Open. 2019 Mar 1;2(3):e190213.

Sano M, Bell KL, Galasko D, et al. A randomized, double-blind, placebo-controlled trial of **simvastatin to treat Alzheimer disease**. Neurology. 2011 Aug 9;77(6):556-63. (no benefit)

Saposnik G, Cote R, Rochon PA, et al. On behalf of the Investigators of the Registry of the Canadian Stroke Network and the Stroke Outcome Research Canada (SORCan) Working Group. Care and outcomes in patients with **ischemic stroke** with and without preexisting dementia. Neurology. 2011 Nov 1;77(18):1664-1673.

Sarnak MJ, Tighiouart H, Scott TM, et al. Frequency of and risk factors for poor cognitive performance in **hemodialysis patients**. Neurology. 2013 Jan 29;80(5):471-80.

Satizabal CL, Beiser AS, Chouraki V, et al. Incidence of Dementia over **Three Decades in the Framingham Heart Study**. N Engl J Med. 2016 Feb 11;374(6):523-532.

Savolainen-PeltonenH, Rahkola-SoisaloP, HotiF, etal . Use of **postmenopausal hormone therapy and risk for Alzheimer's disease** in Finland: nationwide case-control study. BMJ 2018;364:l665.

West NA, Windham BG, Knopman DS, et al. **Neuroimaging findings in midlife and risk of late-life dementia** over 20 years of follow-up. Neurology. 2019 Feb 26;92(9):e917-e923.

Scarmeas N, et al. **Physical activity, diet**, and risk of Alzheimer disease. JAMA. 2009 Aug 12;302(6):627-37. In this study, both higher Mediterranean-type diet adherence and higher physical activity were independently associated with reduced risk for AD.

Scarmeas N, Honig LS, Choi H, et al. **Seizures** in Alzheimer disease: who, when, and how common? Arch Neurol. 2009 Aug;66(8):992-7.

Schaare HL, Kharabian Masouleh S, Beyer F, et al. **Association of peripheral blood pressure with gray matter volume** in 19- to 40-year-old adults. Neurology. 2019 Jan 23.

Schafer JH, et al. **Homocysteine** and cognitive function in a population-based study of older adults. J Am Geriatr Soc. 2005 Mar;53(3):381-8.

Scheltens P, Blennow K, Breteler MM, et al. **Alzheimer's disease**. Lancet. 2016 Feb 23.

Scheltens P, Blennow K, Breteler MM, et al. **Alzheimer's disease. (Seminar)** Lancet. 2016 Jul 30;388(10043):505-17.

Schindler SE, Bollinger JG, Ovod V, et al. High-precision **plasma β-amyloid 42/40 predicts current and future brain amyloidosis**. Neurology. 2019 Aug 1.

Schmidt C, Wolff M, Weitz M, et al. **Rapidly progressive Alzheimer disease**. Arch Neurol. 2011 Sep;68(9):1124-30.

Schneider AL, Rawlings AM, Sharrett AR, et al. High-sensitivity **cardiac troponin T** and cognitive function and dementia risk: the atherosclerosis risk in communities study. Eur Heart J. 2014 Jul 14;35(27):1817-24.

Schneider JA, Viswanathan A. The time for **multiple biomarkers** in studies of cognitive aging and dementia is now. Neurology. 2019 Mar 19;92(12):551-552.

Schneider LS, Dagerman K, Insel PS. Efficacy and adverse effects of **atypical antipsychotics** for **dementia**: meta-analysis of randomized, placebo-controlled trials. Am J Geriatr Psychiatry. 2006 Mar;14(3):191-210.

Schneider LS, Dagerman KS, Higgins JP, McShane R. Lack of Evidence for the Efficacy of **Memantine in Mild Alzheimer** Disease. Arch Neurol. 2011 Apr 11.

Schneider LS, Frangakis, C, Drye LT, et al. **Heterogeneity of treatment response** to **citalopram** for patients with Alzheimer's disease with aggression or agitation: the **CitAD** randomized clinical trial. Am J Psychiatry 2016;173:465–72.

Schneider LS, Thomas RG, Hendrix S, et al. **Safety and Efficacy of Edonerpic Maleate** for Patients With Mild to Moderate Alzheimer Disease: A Phase 2 Randomized Clinical Trial. JAMA Neurol. 2019 Jul 8.

Schoonenboom NS, Reesink FE, Verwey NA, et al. **Cerebrospinal fluid markers** for differential dementia diagnosis in a large memory clinic cohort. Neurology. 2012 Jan 3;78(1):47-54.

Schott JM, Warren JD, Barkhof F, Rossor MN, Fox NC. Suspected early dementia. BMJ. 2011 Sep 20;343:d5568. doi: 10.1136/bmj.d5568.

Schrijvers Elisabeth M. C., Koudstaal Peter J., Hofman Albert, et al. **Plasma Clusterin** and the Risk of Alzheimer Disease. JAMA. 2011;305(13):1322-1326.doi:10.1001/jama.2011.381.

Schrijvers EMC, Verhaaren BFJ, Koudstaal PJ, Hofman A, Ikram MA, Breteler MMB. Is **dementia incidence declining**? Trends in dementia incidence since 1990 in the Rotterdam Study. Neurology 2012;78:1456 –1463.

Schrijver EJM, de Vries OJ, et al. **Haloperidol versus placebo for delirium prevention** in acutely hospitalised older at risk patients: a multi-centre double-blind randomised controlled clinical trial. Age Ageing. 2017 Jul 15:1-8.

Schuckit MA. Recognition and management of **withdrawal delirium** (**delirium tremens**). N Engl J Med. 2014 Nov 27;371(22):2109-13.

Schwarzinger M, et al Contribution of **alcohol use disorders** to **burden of dementia** in France 2008-13: nationwide retrospective cohort study. Lancet Public Health10.1016/S2468-2667(18)30022-7.

Scott JC, Slomiak ST, Jones JD, et al. Association of **Cannabis** With Cognitive Functioning in Adolescents and Young Adults: A Systematic Review and Meta-analysis. JAMA Psychiatry. 2018 Apr 18.

Scoralick FM, Louzada LL, Quintas JL, et al. **Mirtazapine** does **not improve sleep** disorders in Alzheimer's disease: results from a double-blind, placebo-controlled pilot study. Psychogeriatrics. 2016 Jan 27.

Seidel K, Bouzrou M, Heidemann N, et al. **Involvement of the cerebellum** in Parkinson's disease and Dementia with Lewy bodies. Ann Neurol. 2017 Apr 25

Seitz DP, Adunuri N, Gill SS, et al. **Antidepressants for agitation and psychosis** in dementia. Cochrane Database Syst Rev. 2011 Feb 16;2:CD008191. Currently there are relatively few studies of antidepressants for the treatment of agitation and psychosis in dementia. The SSRIs sertraline and citalopram were associated with a reduction in symptoms of agitation when compared to placebo in two studies. Both SSRIs and trazodone appear to be tolerated reasonably well when compared to placebo, typical antipsychotics and atypical antipsychotics.

Seo SW, Gottesman RF, Clark JM, et al. **Nonalcoholic fatty liver disease** is associated with cognitive function in adults. Neurology. 2016 Mar 22;86(12):1136-42.

Sepulcre J, Grothe MJ, Sabuncu M, et al. **Hierarchical organization of tau and amyloid deposits** in the cerebral cortex [online May 30, 2017]. JAMA Neurol. doi:10.1001 /jamaneurol.2017.0263

Sessums LL, Zembrzuska H, Jackson JL. Does this patient have **medical decision-making capacity**?. JAMA. 2011 Jul 27;306(4):420-7.

Seshadri Sudha; Fitzpatrick Annette L.; Ikram M. Arfan et al; for the CHARGE, GERAD1, and EADI1 Consortia Genome-wide Analysis of **Genetic Loci Associated With Alzheimer Disease**. *JAMA*. 2010;303(18):1832-1840.

Sha SJ, Deutsch GK, Tian L, et al. Safety, tolerability, and feasibility of **young plasma infusion in the Plasma for Alzheimer Symptom Amelioration** Study: a randomized clinical trial [online Oct 29, 2018]. JAMA Neurol.

Shah RC, Buchman AS, Wilson RS, et al. **Hemoglobin level** in older persons and incident Alzheimer disease: Prospective cohort analysis. Neurology. 2011 Jul 19;77(3):219-26.

Shao H, Breitner JCS, Whitmer RA, et al. **Hormone therapy and Alzheimer** disease dementia: new findings from the **Cache County Study**. Neurology 2012;79:1846 –1852.

Sharma RA, Varga AW, Bubu OM, et al. **Obstructive Sleep Apnea** Severity Affects Amyloid Burden in Cognitively Normal Elderly: A Longitudinal Study. Am J Respir Crit Care Med. 2017 Nov 10.

Sheffrin M, Miao Y, Boscardin WJ, et al. **Weight Loss Associated with Cholinesterase Inhibitors** in Individuals with Dementia in a National Healthcare System. J Am Geriatr Soc. 2015 Aug 3.

Sheldon Tony. Study of **rivastigmine for delirium** in intensive care is stopped after **deaths.** BMJ 2010;340:c2895, doi: 10.1136/bmj.c2895 (Published 28 May 2010)

Shulman MB, Harkins K, Green RC, Karlawish J. Using **AD biomarker research** results for clinical care: a survey of ADNI investigators. Neurology 2013;81:1114–1121.

Sienaert P. **Electroconvulsive therapy does not increase the risk of dementia** in patients with affective disorders. Evid Based Ment Health. 2019 Feb;22(1):e5.

Silverman JM, Schmeidler J, Beeri MS, et al. **C-reactive protein** and familial risk for dementia: A phenotype for successful cognitive aging. Neurology. 2012 Sep 11;79(11):1116-23.

Simmons BB, Hartmann B, Dejoseph D. **Evaluation of Suspected Dementia**. Am Fam Physician. 2011 Oct 15;84(8):895-902.

Singh J, Kour K, Jayaram MB. **Acetylcholinesterase inhibitors for schizophrenia**. Cochrane Database of Systematic Reviews 2012, Issue 1. Art. No.: CD007967. DOI: 10.1002/14651858.CD007967.pub2.
The results seem to favour the use of acetylcholinesterase inhibitors in combination with antipsychotics on a few domains of mental state and cognition, but because of the various limitations in the studies as mentioned in the main text, the evidence is weak.

Singh JA, Cleveland JD. Use of **urate-lowering therapies** is **not associated with an increase in the risk of incident dementia** in older adults. Ann Rheum Dis. 2018 Aug;77(8):1243-1245.

Singh-Manoux A, Kivimaki M, Glymour MM, Elbaz A, Berr C, et al. Timing of **onset of cognitive decline**: results from **Whitehall II** prospective cohort study. BMJ 2012;344:d7622. Evident in **middle age** (age 45-49).

Singh-Manoux A, Dugravot A, Brunner E, et al. **Interleukin-6 and C-reactive protein** as predictors of cognitive decline in late midlife. Neurology 2014;83:486–493.

Singh B, Mielke MM, Parsaik AK, et al. A Prospective Study of **Chronic Obstructive Pulmonary Disease** and the Risk for Mild Cognitive Impairment. JAMA Neurol. 2014 Mar 17.

Sink KM, Thomas J 3rd, Xu H, Craig B, et al. Dual Use of Bladder **Anticholinergics and Cholinesterase Inhibitors**: Long-Term Functional and Cognitive Outcomes. J Am Geriatr Soc. 2008 Apr 1. [Epub ahead of print] In higher-functioning NH residents, dual use of ChIs and bladder anticholinergics may result in greater rates of functional decline than use of ChIs alone. The MDS-COGS may not be sensitive enough to detect differences in cognition due to dual use.

Sink KM, Espeland MA, et al. Effect of a **24-month physical activity intervention vs health education** on cognitive outcomes in sedentary older adults: the LIFE randomized trial.JAMA. doi: 10.1001/jama.2015.9617.

Sinyavskaya L, Gauthier S, Renoux C, et al. Comparative effect of **statins on the risk of incident Alzheimer disease**. Neurology. 2017 Dec 15.

Skrobik Y, Duprey MS, Hill NS, Devlin JW. Low-dose Nocturnal **Dexmedetomidine** Prevents ICU Delirium: A Randomized, Placebo-controlled Trial. Am J Respir Crit Care Med. 2018 Mar 2.

Small GW, Siddarth P, Kepe V, et al. Prediction of cognitive decline by **positron emission tomography** of brain amyloid and tau. Arch Neurol. 2012 Feb;69(2):215-22.

Smart EL, Gow AJ, Deary IJ. **Occupational complexity** and **lifetime cognitive abilities**. Neurology. 2014 Dec 9;83(24):2285-91.

Smyth A, Dehghan M, O'Donnell M, et al; **ONTARGET** and **TRANSCEND** Investigators. **Healthy eating** and reduced risk of cognitive decline: A cohort from 40 countries. Neurology. 2015 Jun 2;84(22):2258-65.

Snowden M, Steinman L, Mochan K, et al. Effect of **Exercise on Cognitive Performance** in Community-Dwelling Older Adults: Review of Intervention Trials and Recommendations for Public Health Practice and Research. J Am Geriatr Soc. 2011 Apr;59(4):704-716.

Snowden JS et al. The **clinical diagnosis of early-onset dementias**: Diagnostic accuracy and clinicopathological relationships. Brain 2011 Aug 11

Soininen H, West C, Robbins J, Niculescu L. Long-Term Efficacy and Safety of **Celecoxib** in Alzheimer's Disease. Dement Geriatr Cogn Disord. 2006 Oct 26;23(1):8-21 [Epub ahead of print] Celecoxib 200 mg bid did not slow the progression of AD in this study, and the occurrence of adverse events was as expected for an elderly population with a complex chronic medical condition.

Soininen H, et al. 24-month intervention with a **specific multinutrient** in people with prodromal Alzheimer's disease (**LipiDiDiet**): a randomised, double-blind, controlled trial. Lancet Neurol 2017; published online Oct 30.

Sojkova J, Zhou Y, An Y, et al. Longitudinal Patterns of {beta}-**Amyloid Deposition in Nondemented Older Adults**. Arch Neurol. 2011 May;68(5):644-9.

Solomon PR, Murphy CA. Should we **screen for Alzheimer's** disease? A review of the evidence for and against screening Alzheimer's disease in primary care practice. Geriatrics. 2005 Nov;60(11):26-31.

Solomon A, et al. Effect of the **Apolipoprotein E Genotype** on Cognitive Change During a Multidomain Lifestyle Intervention: A Subgroup Analysis of a Randomized Clinical Trial. (Finger) JAMA Neurol. 2018 Jan 22.

Sommerlad A, Ruegger J, Singh-Manoux A, et al. **Marriage and risk of dementia**: systematic review and meta-analysis of observational studies. J Neurol Neurosurg Psychiatry. 2017 Nov 28.

Song X, Mitnitski A, Rockwood K. **Nontraditional risk factors** combine to predict Alzheimer disease and dementia. Neurology. 2011 Jul 19;77(3):227-34.

Sorbi S, Hort J, Erkinjuntti T, Fladby T, et al. **EFNS** Scientist Panel on Dementia and Cognitive Neurology. EFNS-ENS guidelines on the **diagnosis and management of disorders associated with dementia**. Eur J Neurol 2012 Sep;19(9):1159-79.

Soysal P, Isik AT, Stubbs B, et al. **Acetylcholinesterase inhibitors** are associated with weight loss in older people with dementia: a systematic review and meta-analysis. J Neurol Neurosurg Psychiatry. 2016 Jun 3.

Spartano NL, Davis-Plourde KL, Himali JJ, et al. Association of **Accelerometer-Measured Light-Intensity Physical Activity With Brain Volume**: The Framingham Heart Study. JAMA Netw Open. 2019 Apr 5;2(4):e192745.

Spartano NL, Himali JJ, Beiser AS, et al. **Midlife exercise blood pressure, heart rate, and fitness** relate to brain volume 2 decades later. Neurology. 2016 Apr 5

Spillantini MG, Goedert M. **Tau pathology** and neurodegeneration. Lancet Neurol. 2013 Jun;12(6):609-22.

Spira AP, Gamaldo AA, An Y, et al. Self-reported **Sleep and β-Amyloid Deposition** in Community-Dwelling Older Adults. JAMA Neurol. 2013 Oct 21.

SPRINT MIND Investigators for the SPRINT Research Group. Effect of **intensive vs standard blood pressure control on probable dementia**: a randomized clinical trial [online Jan 28, 2019]. JAMA. doi:10.1001/jama.2018.21442

Stall NM, Fischer HD, Fung K, et al. Sex-Specific Differences in **End-of-Life Burdensome Interventions and Antibiotic Therapy** in Nursing Home Residents With Advanced Dementia. JAMA Netw Open. 2019 Aug 2;2(8):e199557.

Staubo SC, Aakre JA, Vemuri P, et al. **Mediterranean diet, micronutrients and macronutrients, and MRI** measures of cortical thickness. Alzheimers Dement. 2016 Jul 23.

Stall N, Wong CL. **Hospital-acquired delirium** in older adults. CMAJ. 2014 Jan 7

Stark SL, Roe CM, Grant EA, et al. Preclinical Alzheimer disease and **risk of falls**. Neurology. 2013 Jul 30;81(5):437-43.

Steenland K, Zhao L, Goldstein FC, Levey AI. **Statins and cognitive decline** in older adults with normal cognition or mild cognitive impairment. J Am Geriatr Soc. 2013 Sep;61(9):1449-55.

Steinman MA, Zullo AR, Lee Y, et al. Association of **β-blockers with functional outcomes, death, and rehospitalization in older nursing home residents after acute myocardial infarction** [online Dec 12, 2016]. JAMA Intern Med. doi:10.1001/jamainternmed.2016.7701

Steinberg M, Lyketsos CG. **Atypical antipsychotic use in patients with dementia**: managing safety concerns. Am J Psychiatry. 2012 Sep 1;169(9):900-6.

Strain JF, Smith RX, Beaumont H, et al. **Loss of white matter integrity** reflects tau accumulation **in Alzheimer disease** defined regions. Neurology. 2018 Jul 24;91(4):e313-e318.

Streim JE, Porsteinsson AP, Breder CD, Swanink R, Marcus R, McQuade R, Carson WH. A randomized, double-blind, placebo-controlled study of **aripiprazole** (~9mg/d) for the treatment of psychosis in nursing home patients with Alzheimer disease. Am J Geriatr Psychiatry. 2008 Jul;16(7):537-50. n=256 10weeks. In nursing home residents with AD and psychosis, aripiprazole did not confer specific benefits for the treatment of psychotic symptoms; but psychological and behavioral symptoms, including agitation, anxiety, and depression, were improved with aripiprazole, with a low risk of AEs.

Streit S, Poortvliet RKE, Elzen WPJD, et al. **Systolic Blood Pressure and Cognitive Decline** in Older Adults With Hypertension. Ann Fam Med. 2019 Mar;17(2):100-107.

Streit S, Poortvliet RKE, Gussekloo J. **Lower blood pressure during antihypertensive treatment** is associated with higher all-cause mortality and **accelerated cognitive decline in the oldest-old**-data from the Leiden 85-plus Study. Age Ageing. 2018 May 8.

Stephan BCM, Tzourio C, Auriacombe S, et al. Usefulness of data from **magnetic resonance imaging to improve prediction of dementia**: population based cohort study. BMJ 2015:350:h2863.

Stocks SJ, Kontopantelis E, Webb RT, Avery AJ, Burns A, Ashcroft DM. **Antipsychotic prescribing to patients diagnosed with dementia** without a diagnosis of psychosis in the context of national guidance and drug safety warnings: longitudinal study in UK general practice. Drug Saf 2017;358:679-92. doi:10.1007/s40264-017-0538-x pmid:28439716.

Streit S, Poortvliet RKE, Elzen WPJD, et al. **Systolic Blood Pressure and Cognitive Decline** in Older Adults With Hypertension. Ann Fam Med. 2019 Mar;17(2):100-107.

Su X, Meng ZT, Wu XH, et al. **Dexmedetomidine** for prevention of delirium in elderly patients after non-cardiac surgery: a randomised, double-blind, placebo-controlled trial. Lancet. 2016 Aug 16.

Sudeep S Gill, Paula A Rochon, Nathan Herrmann, et al. Atypical antipsychotic drugs and **risk of ischaemic stroke**: population based retrospective cohort study BMJ, doi:10.1136/bmj.38330.470486.8F (published 24 January 2005) CONCLUSION: Older adults with dementia who take atypical antipsychotics have a similar risk of ischaemic stroke to those taking typical antipsychotics.

Suh GH, Shah A. Effect of **antipsychotics on mortality** in elderly patients with dementia: a 1-year prospective study in a nursing home. Int Psychogeriatr. 2005 Sep;17(3):429-41.

Suh SW, Han JW, Lee JRet al. **Sleep and Cognitive Decline**: A Prospective Non-demented Elderly Cohort Study. Ann Neurol. 2018 Feb 2.

Sultana J, Chang CK, Hayes RD, et al. Associations between risk of **mortality and atypical antipsychotic use in vascular dementia**: a clinical cohort study. Int J Geriatr Psychiatry. 2014 Mar 14. doi: 10.1002/gps.4101.

Sultzer DL, Davis SM, Tariot PN, et al. **CATIE-AD** Group. Clinical **symptom responses** to atypical antipsychotic medications in Alzheimer's disease: phase 1 outcomes from the CATIE-AD effectiveness trial. Am J Psychiatry. 2008 Jul;165(7):844-54.

Sumowski JF, Benedict R, Enzinger C, et al. **Cognition in multiple sclerosis**: State of the field and priorities for the future. Neurology. 2018 Feb 6;90(6):278-288.

Sundbøll J, Horváth-Puhó E, Adelborg K, et al. **Higher risk of vascular dementia in myocardial infarction survivors**. Circulation. 2018;137:567–577.

Supasitthumrong T, Bolea-Alamanac BM, Asmer S, et al. **Gabapentin and pregabalin to treat aggressivity in dementia**: a systematic review and illustrative case reports. Br J Clin Pharmacol. 2018 Dec 21.

Swiger KJ, Manalac RJ, Blumenthal RS et al. **Statins and Cognition**: A Systematic Review and Meta-analysis of Short- and Long-term Cognitive Effects. Mayo Clin Proc. 2013 Sep 27.

Sydenham E, Dangour AD, Lim WS. **Omega 3 fatty acid** for the prevention of cognitive decline and dementia. Cochrane Database of Systematic Reviews 2012, Issue 6. Art. No.: CD005379. Direct evidence on the effect of omega-3 PUFA on incident dementia is lacking. The available trials showed no benefit of omega-3 PUFA supplementation on cognitive function in cognitively healthy older people. Omega-3 PUFA supplementation is generally well tolerated with the most commonly reported side-effect being mild gastrointestinal problems.

Taipale H, Tolppanen AM, Koponen M, et al. Risk of **pneumonia associated with incident benzodiazepine use** among community-dwelling adults with Alzheimer disease. CMAJ. 2017 Apr 10;189(14):E519-E529

Taipale H, Tolppanen AM, Tiihonen M, et al. No Association Between **Proton Pump Inhibitor** Use and Risk of **Alzheimer's Disease**. Am J Gastroenterol. 2017 Jul 11.

Taipale H, Hamina A, Lampela P, et al. Is **Alzheimer's Disease Associated with Previous Opioid Use**? Pain Med. 2017 Aug 28.

Taipale H, Gomm W, Broich K, et al. Use of **Antiepileptic Drugs and Dementia Risk**-an Analysis of Finnish Health Register and German Health Insurance Data. J Am Geriatr Soc. 2018 Mar 22.

Takeda A, Loveman E, Clegg A, et al. A systematic review of the clinical effectiveness of **donepezil, rivastigmine and galantamine** on cognition, quality of life and adverse events in Alzheimer's disease. Int J Geriatr Psychiatry. 2005 Dec 2;21(1):17-28

Tamimi I, Ojea T, Sanchez-Siles JM, et al. **Acetylcholinesterase inhibitors and the risk of hip fracture** in Alzheimer's disease patients: case-control study. J Bone Miner Res. 2012 Jul;27(7):1518-27.

Tan ZS, Spartano NL, Beiser AS, et al. **Physical Activity**, Brain Volume, and Dementia Risk: The Framingham Study. J Gerontol A Biol Sci Med Sci. 2016 Jul 15.

Tang M, Ryman DC, McDade E, et al, for the Dominantly Inherited Alzheimer Network (DIAN). **Neurological manifestations** of autosomal dominant familial Alzheimer's disease: a comparison of the published literature with the Dominantly Inherited Alzheimer Network observational study (**DIAN-OBS**). Lancet Neurol 2016; online Oct 21.

Tangney CC, Aggarwal NT, Li H, et al. **Vitamin B12**, cognition, and brain MRI measures: A cross-sectional examination. Neurology. 2011 Sep 27;77(13):1276-82.

Tangney CC, Li H, Wang Y, et al. Relation of **DASH- and Mediterranean**-like dietary patterns to cognitive decline in older persons. Neurology. 2014 Oct 14;83(16):1410-6.

Tapiainen V, Hartikainen S, et al. **Hospital-treated mental and behavioral disorders and risk of Alzheimer's** disease: A nationwide nested case-control study. Eur Psychiatry. 2017 Mar 9;43:92-98.

Tapiainen V, Taipale H, Tanskanen A, et al. The risk of Alzheimer's disease associated with **benzodiazepines and related drugs**: a nested case-control study. Acta Psychiatr Scand. 2018 May 31.

Tariot PN, Farlow MR, Grossberg GT, Graham SM, McDonald S, Gergel I. **Memantine** treatment in patients with moderate to severe Alzheimer disease already receiving donepezil: a randomized controlled trial. JAMA 2004;291:317-24.

Tariot PN, Schneider L, Katz IR, et al. Quetiapine treatment of psychosis associated with dementia: a double-blind, randomized, placebo-controlled clinical trial. Am J Geriatr Psychiatry. 2006 Sep;14(9):767-76. Epub 2006 Aug 11. Erratum in: Am J Geriatr Psychiatry. 2006 Nov;14(11):988. n=284 All treatment groups showed improvement in measures of psychosis without significant differences between them when planned comparisons were performed. Participants treated with quetiapine or haloperidol showed inconsistent evidence of improvement in agitation. Tolerability was better with quetiapine compared with haloperidol.

Taylor JP, McKeith IG, Burn DJ, et al. New evidence on the **management of Lewy body dementia**. Lancet Neurol. 2019 Sep 10.

Teipel S, Drzezga A, Grothe MJ, et al. **Multimodal imaging** in Alzheimer's disease: validity and usefulness for early detection. Lancet Neurol. 2015 Aug 26.

Teno JM, et al. Association of increasing use of **mechanical ventilation** among nursing home residents with advanced dementia and intensive care unit beds [online Oct 10, 16].JAMA IM. doi:10.1001/jamainternmed.2016.5964

Teramura-Grönblad M, Muurinen S, Soini H, et al. Use of **anticholinergic drugs and cholinesterase inhibitors** and their association with psychological well-being among frail older adults in residential care facilities. Ann Pharmacother. 2011 May;45(5):596-602.

Teri L, Gibbons LE, McCurry SM, et al. **Exercise plus behavioral management** in patients with Alzheimer disease: a randomized controlled trial. JAMA. 2003 Oct 15;290(15):2015-22.

Terracciano A et al. **Personality traits and risk of cognitive impairment** and dementia. J Psychiatr Res 2017 Jun; 89:22.

Terracciano A, An Y, Sutin AR, et al. **Personality Change** in the Preclinical Phase of Alzheimer Disease. JAMA Psychiatry. 2017 Sep 20.

Tess AV, Mattison MLP, et al. **Should This Patient Receive Prophylactic Medication to Prevent Delirium**?: Grand Rounds Discussion From Beth Israel Deaconess Medical Center. Ann Intern Med. 2018 Apr 3;168(7):498-505.

The American Geriatrics Society **2012 Beers Criteria Update** Expert Panel. American Geriatrics Society Updated Beers Criteria for Potentially Inappropriate Medication Use in Older Adults. J Am Geriatr Soc. 2012 Feb 29.

Thacker EL, McKnight B, Psaty BM, et al. **Atrial fibrillation** and **cognitive decline**: A longitudinal cohort study. Neurology. 2013 Jul 9;81(2):119-125.

Thacker EL, Gillett SR, Wadley VG, et al. The American Heart Association **Life's Simple 7 and Incident Cognitive Impairment**: The REasons for Geographic And Racial Differences in Stroke(REGARDS) Study. J Am Heart Assoc. 2014 Jun 11;3(3).

Thambisetty M, Metter EJ, Yang A, et al. **Glucose Intolerance, Insulin Resistance**, and Pathological Features of Alzheimer Disease in the Baltimore Longitudinal Study of Aging. JAMA Neurol. 2013 Jul 29.

Then C-K et al. **Risk** analysis of use of different classes of **antidepressants on subsequent dementia**: A nationwide cohort study in Taiwan. PLoS One 2017 Apr 6; 12:e0175187.

Then FS, Luck T, Luppa M, et al. Differential effects of **enriched environment** at work on cognitive decline in old age. Neurology. 2015 May 26;84(21):2169-76. Epub 2015 Apr 29.

Thielke S, Slatore CG, Banks WA. Association Between **Alzheimer Dementia Mortality Rate and Altitude** in California Counties. JAMA Psychiatry. 2015 Oct. 21:1-2.

Thomas RG, Albert M, Petersen RC, Aisen PS. **Longitudinal decline in mild-to-moderate Alzheimer's** disease: Analyses of placebo data from clinical trials. Alzheimers Dement. 2016 Feb 23.

Thoonsen H, Richard E, Bentham P, Gray R, et al. **Aspirin in Alzheimer's disease: increased risk of intracerebral hemorrhage**: cause for concern? Stroke. 2010 Nov;41(11):2690-2.

Thornton SL, Pchelnikova JL, Cantrell FL. Characteristics of **Pediatric Exposures to Antidementia Drugs Reported to a Poison** Control System. J Pediatr. 2016 May

Thorpe JM, Thorpe CT, Gellad WF, Good CB, Hanlon JT, Mor MK, et al. **Dual health care system use and high-risk prescribing in dementia patients**: a national cohort study. Ann Intern Med. 2016. [Epub ahead of print]. doi:10.7326/M16-0551

Thorpe JM, Thorpe CT, et al. **Dual Health Care System Use and High-Risk Prescribing** in Patients With Dementia: A National Cohort Study. Ann Intern Med.2017 Feb 7;166(3):157-163.

Thyrian JR, Hertel J, Wucherer D, et al. Effectiveness and Safety of **Dementia** Care Management in **Primary Care**: A Randomized Clinical Trial. JAMA Psychiatry. 2017 Jul 26.

Tifratene K, Robert P, Metelkina A, et al. Progression of **mild cognitive impairment to dementia due to AD** in clinical settings. Neurology. 2015 Jul 28;85(4):331-8.

Tilly J, Reed P, editor(s). Dementia care practice recommendations for assisted living residences and nursing homes. Washington (DC): Alzheimer's Association; 2006 Sep. 28 p. http://www.alz.org/documents/national/DementiaCarePracticeRecommendations.pdf

Tiraboschi P, Attems J, Thomas A, et al. Clinicians' ability to **diagnose dementia with Lewy bodies is not affected by β- amyloid load**. Neurology. 2015 Feb 3;84(5):496-9.

Tisher A, Salardini A. A Comprehensive Update on **Treatment of Dementia**. Semin Neurol. 2019 Apr;39(2):167-178.

Tolppanen AM, Lavikainen P, Solomon A, et al. **Incidence of stroke** in people with Alzheimer disease: A national register-based approach. Neurology. 2013 Jan 22;80(4):353-8.

Tomata Y, Sugiyama K, Kaiho Y, et al. **Green Tea Consumption** and the Risk of Incident Dementia in Elderly Japanese: The Ohsaki Cohort 2006 Study. Am J Geriatr Psychiatry. 2016 Oct;24(10):881-9.

Ton J, Ramji J, Allan GM. **Antipsychotics for agitation in dementia**. Can Fam Physician. 2018 May;64(5):369. Ginis KA, Heisz J, Spence JC, et al. Formulation of evidence-based messages to promote the use of physical activity to prevent and manage Alzheimer's disease. BMC Public Health. 2017 Feb 17;17(1):209.

Toots A, Littbrand H, Lindelof N, et al. Effects of a **High-Intensity Functional Exercise** Program on Dependence in Activities of Daily Living and Balance in Older Adults with Dementia. J Am Geriatr Soc. 2016 Jan;64(1):55-64

Tosto G, Bird TD, Tsuang D, et al. **Polygenic risk scores** in familial Alzheimer disease. Neurology. 2017 Mar 21;88(12):1180-1186.

Tosto G, Vardarajan B, Sariya S, et al. **Association of Variants in PINX1 and TREM2 With Late-Onset Alzheimer Disease**. JAMA Neurol. 2019 May 6.

Tricco AC, Soobiah C, Berliner S, et al. Efficacy and safety of **cognitive enhancers for patients with mild cognitive impairment**: a systematic review and meta-analysis. CMAJ. 2013 Sep 16.

Tricco AC, et al. Comparative **Effectiveness and Safety of Cognitive Enhancers** for Treating Alzheimer's Disease: Systematic Review and Network Metaanalysis. J Am Geriatr Soc. 2017 Sep 29.

Trinh J, Guella I, Farrer MJ. **Disease Penetrance of Late-Onset Parkinsonism**: A Meta-analysis. JAMA Neurol. 2014 Oct 20.

Tsivgoulis G, Alexandrov AV, Wadley VG, et al. Association of higher **diastolic blood pressure** levels with cognitive impairment. Neurology 2009; 73:589-595.

Tsoi KK, Chan JY, Chan FC, et al. **Monotherapy Is Good Enough** for Patients with Mild-to-Moderate Alzheimer's Disease: A Network Meta-analysis of 76 Randomized Controlled Trials. Clin Pharmacol Ther. 2018 May 1.

Tsoi KK, Chan JY, Hirai HW, et al. **Cognitive Tests to Detect Dementia: A Systematic Review and Meta-analysis.** JAMA Intern Med. 2015 Jun 8.

Tsivgoulis G, Judd S, Letter AJ, et al. Adherence to a **Mediterranean diet** and risk of incident cognitive impairment. Neurology. 2013 Apr 30;80(18):1684-1692.

Tsuang D, Leverenz JB, Lopez OL, et al. **GBA mutations** increase risk for Lewy body disease with and without Alzheimer disease pathology. Neurology 2012;79:1944–1950.

Tsivgoulis G, Judd S, Letter AJ, et al. Adherence to a **Mediterranean diet** and risk of incident cognitive impairment. Neurology. 2013 Apr 30;80(18):1684-1692.

Tully PJ, Dartigues JF, Debette S, Helmer C, Artero S, Tzourio C. Dementia risk with **antihypertensive use** and blood pressure variability: A cohort study. Neurology. 2016 Aug 9;87(6):601-8.

Tuovinen S, Räikkönen K, Kajantie E, et al. **Hypertensive disorders** in pregnancy and cognitive decline in the offspring up to old age. Neurology. 2012 Oct 9;79(15):1578-1582.

Turner RS, et al; Alzheimer's Disease Cooperative Study. A randomized, double-blind, placebo-controlled trial of **resveratrol** for Alzheimer disease. Neurology. 2015 Oct 20;85(16):1383-91.

Unverzagt FW, McClure LA, Wadley VG, et al. **Vascular risk factors** and cognitive impairment in a stroke-free cohort. Neurology. 2011 Nov 8;77(19):1729-36.

Valls-Pedret C, Sala-Vila A, Serra-Mir M, et al. **Mediterranean Diet** and Age-Related Cognitive Decline: A Randomized Clinical Trial. JAMA Intern Med. 2015 May 11.

Ungar A et al. Etiology of **syncope** and unexplained **falls in elderly adults with dementia**: Syncope and Dementia (SYD) study. J Am Geriatr Soc 2016 Aug; 64:1567.

van Dalen JW, Van Wanrooij LL, Moll van Charante EP, et al. **Apathy** is associated with incident dementia in community-dwelling older people. Neurology. 2017 Dec 1

van de Rest O, Wang Y, Barnes LL, et al. **APOE ε4** and the associations of seafood and long-chain omega-3 fatty acids with cognitive decline. Neurology. 2016 May 31;86(22):2063-70.

Van den Boogaard M, Pickkers P, Slooter AJC, et al. Development and validation of **PRE-DELIRIC** (PREdiction of DELIRium in ICu patients) **delirium prediction model** for intensive care patients: observational multicentre study. BMJ 2012;344:e420.

van den Boogaard M, Schoonhoven L, van Achterberg T, et al. **Haloperidol prophylaxis** in critically ill patients with a high **risk of delirium**. Crit Care. 2013;17:R9.

van den Boogaard M, et al. Effect of **Haloperidol** on Survival Among Critically Ill Adults With a High Risk of **Delirium**: **REDUCE** Randomized Clinical Trial. JAMA. 2018 Feb 20;319(7):680-690.

Van den Bossche T, Sleegers K, Cuyvers E, et al. Phenotypic characteristics of Alzheimer patients carrying an **ABCA7 mutation**. Neurology 2016;86:2126–2133.

van den Elsen GA, Ahmed AI, Verkes RJ, et al. **Tetrahydrocannabinol** for neuropsychiatric symptoms in dementia: A randomized controlled trial. Neurology. 2015 Jun 9;84(23):2338-46.

van der Flier WM, Pijnenburg YA, Fox NC, et al. **Early-onset versus late-onset Alzheimer's disease**: the case of the missing APOE E4 allele. Lancet Neurol. 2010 Dec 22.

van der Lee SJ, Wolters FJ, Ikram MK, et al. The effect of **APOE and other common genetic variants on the onset of Alzheimer's** disease and dementia: a community-based cohort study. Lancet Neurol 2018; online Mar 16

van der Steen JT, Smaling HJA, van der Wouden JC, et al. Music-based therapeutic interventions for people with dementia. Cochrane Database of Systematic Reviews 2018, Issue 7. Art. No.: CD003477.

Providing people with dementia who are in institutional carewith at least five sessions of a music-based therapeutic intervention probably reduces depressive symptoms and improves overall behavioural problems at the end of treatment. It may also improve emotional wellbeing and quality of life and reduce anxiety, but may have little or no effect on agitation or aggression or on cognition. We are uncertain about effects on social behaviour and about long-term effects. Future studies should examine the duration of effects in relation to the overall duration of treatment and the number of sessions.

van der Steen JT, van Soest-Poortvliet MC, van der Wouden JC, et al. **Music-based therapeutic interventions for people with dementia**. Cochrane Database Syst Rev. 2017 May 2;5:CD003477.

Providing people with dementia with at least five sessions of a music-based therapeutic intervention probably reduces depressive symptoms but has little or no effect on agitation or aggression. There may also be little or no effect on emotional well-being or quality of life, overall behavioural problems and cognition. We are uncertain about effects on anxiety or social behaviour, and about any long-term effects. Future studies should employ larger sample sizes, and include all important outcomes, in particular 'positive' outcomes such as emotional well-being and social outcomes. Future studies should also examine the duration of effects in relation to the overall duration of treatment and the number of sessions.

van der Vaart T, Plasschaert E, Rietman AB et al. **Simvastatin for cognitive deficits** and behavioural problems in patients with neurofibromatosis type 1 (NF1-SIMCODA): a randomised, placebo-controlled trial. Lancet Neurol. 2013 Sep 30.

van Dyck CH, Nygaard HB, Chen K, et al. Effect of **AZD0530 on Cerebral Metabolic Decline** in Alzheimer Disease: A Randomized Clinical Trial. JAMA Neurol. 2019 Jul 22.

van Eijk MM, Roes KC, Honing ML, et al. Effect of **rivastigmine** as an adjunct to usual care with **haloperidol** on duration of **delirium** and mortality in critically ill patients: a multicentre, double-blind, placebo-controlled randomised trial.Lancet.2010Nov4.

van Harten AC, Mielke MM, Swenson-Dravis DM, et al. Subjective **cognitive decline and risk of MCI**: the Mayo Clinic Study of Aging. Neurology 2018;91: e300–e312.

van Harten AC, Smits LL, Teunissen CE, et al. **Preclinical AD predicts** decline in memory and executive functions in subjective complaints. Neurology. 2013 Sep 18.

van Himbergen TM, Beiser AS, et al. **Biomarkers for Insulin Resistance and Inflammation** and the Risk for All-Cause Dementia and Alzheimer Disease: Results From the Framingham Heart Study. Arch Neurol. 2012 Jan 2.

Van Leer P. The Risk of Cardiovascular Disease, Fracture, Dementia, and Cancer **After Long-Term Hormone Therapy** in Perimenopausal and Postmenopausal Women. Am Fam Physician. 2018 Jul 15;98(2):117-118.

Van Leeuwen E, Petrovic M, van Driel ML, et al. **Withdrawal versus continuation of long-term antipsychotic drug use for behavioural and psychological symptoms in older people with dementia**. Cochrane Database Syst Rev. 2018 Mar 30;3:CD007726. There is low-quality evidence that antipsychotics may be successfully discontinued in older people with dementia and NPS who have been taking antipsychotics for at least three months, and that discontinuation may have little or no important effect on behavioural and psychological symptoms. This is consistent with the observation that most behavioural complications of dementia are intermittent and often do not persist for longer than three months. Discontinuation may have little or no effect on overall cognitive function. Discontinuation may make no difference to adverse events and quality of life. Based on the trials in this review, we are uncertain whether discontinuation of antipsychotics leads to a decrease in mortality.People with psychosis, aggression or agitation who responded well to long-term antipsychotic drug use, or those with more severe NPS at baseline, may benefit behaviourally from continuation of antipsychotics.

van Loenhoud AC, van der Flier WM, Wink AM, et al. **Cognitive reserve and clinical progression** in Alzheimer disease: A paradoxical relationship. Neurology. 2019 Jul 23;93(4):e334-e346.

van Maurik IS, Zwan MD, et al. **Interpreting Biomarker Results** in Individual Patients With Mild Cognitive Impairment in the Alzheimer's Biomarkers in Daily Practice (ABIDE) Project. JAMA Neurol. 2017 Oct 16.

van Rossum IA, Vos SJ, Burns L, et al. **Injury markers** predict time to dementia in subjects with MCI and **amyloid pathology**. Neurology. 2012 Oct 23;79(17):1809-1816.

van Uden IW, van der Holst HM, van Leijsen EM, et al. **Late-onset depressive symptoms** increase the risk of dementia in small vessel disease. Neurology. 2016 Sep 13;87(11):1102-9.

van Vliet P, Sabayan B, Wijsman LW, et al. **NT-proBNP**, **blood pressure**, and cognitive decline in the oldest old: The Leiden 85-plus Study. Neurology. 2014 Sep 23;83(13):1192-9

Varsaldi F, et al. Impact of the **CYP2D6** polymorphism on steady-state plasma concentrations and clinical outcome of **donepezil** in Alzheimer's disease patients. Eur J Clin Pharmacol. 2006 Jul 15; [Epub ahead of print]

Vassilaki M, Aakre JA, Cha RH, et al. **Multimorbidity and Risk of Mild Cognitive Impairment**. J Am Geriatr Soc. 2015 Sep;63(9):1783-90.

Vasunilashorn SM, Guess J, Ngo L, et al. Derivation and Validation of a Severity Scoring Method for the **3-Minute Diagnostic Interview for Confusion Assessment Method**--Defined Delirium. J Am Geriatr Soc. 2016 Jul 4.

Vellas B, Coley N, Ousset P-J, et al, for the GuidAge Study Group. Long-term use of standardised **ginkgo biloba extract** for the prevention of Alzheimer's disease (**GuidAge**): a randomised placebo-controlled trial. Lancet Neurol 2012; online Sept 6

Vemuri P, Lesnick TG, Przybelski SA, et al. Association of **Lifetime Intellectual Enrichment** With Cognitive Decline in the Older Population. JAMA Neurol. 2014 Jun 23.

Vemuri P, Lesnick TG, Przybelski SA, et al. Effect of **intellectual enrichment on AD biomarker trajectories**: Longitudinal imaging study. Neurology. 2016 Mar 22;86(12):1128-35.

Vercambre MN, Grodstein F, Manson JE, et al. **Physical activity** and cognition in women with vascular conditions. (**WACS**) Arch Intern Med. 2011 Jul 25;171(14):1244-50.

Verdelho A, Madureira S, Ferro JM, et al; on behalf of the LADIS Study. **Physical Activity** Prevents Progression for Cognitive Impairment and Vascular Dementia: Results From the **LADIS** (Leukoaraiosis and Disability) Study. Stroke. 2012 Nov 1.

Verghese PB, Castellano JM, Holtzman DM. **Apolipoprotein E** in Alzheimer's disease and other neurological disorders. Lancet Neurol. 2011 Mar;10(3):241-52.

Verhey FR, Verkaaik M, Lousberg R. **Olanzapine versus Haloperidol** in the Treatment of Agitation in Elderly Patients with Dementia: Results of a Randomized Controlled Double-Blind Trial. Dement Geriatr Cogn Disord. 2005 Oct 21;21(1):1-8

Vernooij-Dassen M, Draskovic I, McCleery J, Downs M. **Cognitive reframing** for carers of people with dementia. Cochrane Database of Systematic Reviews 2011, Issue 11. Art. No.: CD005318. DOI: 10.1002/14651858.CD005318.pub2. Cognitive reframing for family carers of people with dementia seems to reduce psychological morbidity and subjective stress but without altering appraisals of coping or burden. The results suggest that it may be an effective component of individualised, multi-component interventions for carers.

Vickrey BG, et al. The effect of a **disease management intervention** on quality and outcomes of dementia care: a randomized, controlled trial. Ann Intern Med. 2006 Nov 21;145(10):713-26.

Vidal EI, Villas Boas PJ, Valle AP, et al. **Delirium in older adults**. BMJ. 2013 Apr 9;346:f2031.

Vidoni ED, Townley RA, Honea RA, Burns JM; For the Alzheimer's Disease Neuroimaging Initiative. **Alzheimer disease biomarkers** are associated with body mass index. Neurology. 2011 Nov 22;77(21):1913-1920.

Vidoni ED, Johnson DK, Morris JK, et al. Dose-Response of **Aerobic Exercise on Cognition**: A Community-Based, Pilot Randomized Controlled Trial. PLoS One. 2015 Jul 9;10(7):e0131647.

Vigen CL, Mack WJ, Keefe RS, et al. **Cognitive Effects of Atypical Antipsychotic** Medications in Patients With Alzheimer's Disease: Outcomes From **CATIE-AD**. Am J Psychiatry. 2011 May 15.

Villain N, Dubois B. **Alzheimer's Disease Including Focal Presentations**. Semin Neurol. 2019 Apr;39(2):213-226.

Villemagne VL, Pike KE, Chételat G, et al. **Longitudinal assessment of Aβ** and cognition in aging and Alzheimer disease. Ann Neurol. 2011 Jan;69(1):181-92. doi: 10.1002/ana.22248.

Villemagne VL, Okamura N, Pejoska S, et al. In vivo assessment of **vesicular monoamine transporter** type 2 in dementia with lewy bodies and Alzheimer disease. Arch Neurol. 2011 Jul;68(7):905-12.

Villemagne VL, Burnham S, et al, for the Australian Imaging Biomarkers and Lifestyle Research Group. **Amyloid βdeposition**, neurodegeneration, and cognitive decline in sporadic Alzheimers disease: a prospective cohort study. Lancet Neurol 2013.

Villeneuve S, Reed BR, Madison CM, et al. **Vascular risk and Aβ interact** to reduce cortical thickness in AD vulnerable brain regions. Neurology. 2014 Jul 1;83(1):40-7.

Voevodskaya O, Poulakis K, Sundgren P, et al. **Brain myoinositol as a potential marker of amyloid-related pathology**: a longitudinal study. Neurology 2019;92: e395–e405.

Voisin T, Vellas B. Diagnosis and treatment of patients with **severe Alzheimer's disease**. Drugs Aging. 2009;26(2):135-44. doi: 10.2165/0002512-200926020-00005.

Vos SJ, van Rossum IA, Verhey F, et al. **Prediction of Alzheimer** disease in subjects with amnestic and nonamnestic MCI. Neurology. 2013 Mar 19;80(12):1124-1132.

Vos SJB, Xiong C, Visser PJ, et al. **Preclinical Alzheimers disease** and its outcome: a longitudinal cohort study. Lancet Neurol 2013; published online Sept 2.

Vossel KA, Beagle AJ, Rabinovici GD, et al. **Seizures and Epileptiform Activity** in the Early Stages of Alzheimer Disease. JAMA Neurol. 2013 Jul 8:1-9.

Vossel KA, Tartaglia MC, Nygaard HB, et al. **Epileptic activity in Alzheimer's disease**: causes and clinical relevance. Lancet Neurol. 2017 Apr;16(4):311-322.

Wagner M, Helmer C, Tzourio C, et al. Evaluation of the **Concurrent Trajectories of Cardiometabolic Risk Factors in the 14 Years Before Dementia**. JAMA Psychiatry. 2018 Jul 24.

Waldemar G, Dubois B, Emre M, Georges J, McKeith IG, et al. **EFNS**. Recommendations for the **diagnosis and management** of Alzheimer's disease and other disorders associated with dementia: EFNS guideline. Eur J Neurol 2007 Jan;14(1):e1-26.

Waldorff FB, Buss DV, Eckermann A, et al. Efficacy of **psychosocial intervention** in patients with mild Alzheimer's disease: the multicentre, rater blinded, randomised Danish Alzheimer Intervention Study (DAISY). BMJ. 2012 Jul 17;345:e4693.

Walker KA, Gottesman RF, Wu A, et al. **Systemic inflammation during midlife** and cognitive change over 20 years: The ARIC Study. Neurology. 2019 Mar 12;92(11):e1256-e1267.

Wallin AK, Blennow K, Zetterberg H, Londos E, Minthon L, Hansson O. **CSF biomarkers** predict a more malignant outcome in Alzheimer disease. Neurology. 2010 May 11;74(19):1531-7.

Walters K, Hardoon S, Petersen I, et al. **Predicting dementia risk in primary care**: development and validation of the Dementia Risk Score using routinely collected data. BMC Medicine 2016;14:6.

Wang CZ, Du GJ, Zhen Z, Calway T, Yuan CS. Significant dose **differences in donepezil purchased from the United States and Canada**. Ann Intern Med. 2011 Aug 16;155(4):279-80.

Wang DC, Black SE, Zukotynski KA. **Diagnosing dementia**. CMAJ. 2016 May 17;188(8):603.

Wang J, Yu JT, Wang HF, et al. **Pharmacological treatment of neuropsychiatric symptoms** in Alzheimer`s disease: a systematic review and meta-analysis. J Neurol Neurosurg Psychiatry. 2014 May 29. pii: jnnp-2014-308112.

Wang W, Li HL, Wang DX, et al. **Haloperidol prophylaxis decreases delirium** incidence in elderly patients after noncardiac surgery: a randomized controlled trial*. Crit Care Med. 2012 Mar;40(3):731-9. For elderly patients who are admitted to the intensive care unit (ICU) after noncardiac surgery, the use of prophylactic continuous intravenous (0.5mg x 1 then 0.1mg/hr) haloperidol during the first 12 hours decreases the incidence of delirium.

Warren JD, Rohrer JD, Rossor MN. **Frontotemporal dementia**. BMJ. 2013 Aug 6;347:f4827. doi: 10.1136/bmj.f4827.

Warrick N, Prorok JC, Seitz D. Care of **community-dwelling older adults with dementia and their caregivers**. CMAJ. 2018 Jul 3;190(26):E794-E799.

Wassenaar A, Schoonhoven L, Devlin JW, et al. **External Validation of Two Models to Predict Delirium** in Critically Ill Adults Using Either the Confusion Assessment Method-ICU or the Intensive Care Delirium Screening Checklist for Delirium Assessment. Crit Care Med. 2019 Jul 15.

Waszynski CM, Milner KA, et al. Using simulated **family presence** to decrease agitation in older hospitalized delirious patients: A randomized controlled trial. Int J Nurs Stud. 2018 Jan;77:154-161

Watt JA, Gomes T, Bronskill SE, et al. **Comparative risk of harm associated with trazodone** or atypical antipsychotic use in older adults with dementia: a retrospective cohort study. CMAJ 2018 Nov 26 ;190(47):E1376-E1383.

Wayne PM, Walsh JN, Taylor-Piliae RE, et al. Effect of **Tai Chi** on Cognitive Performance in Older Adults: Systematic Review and Meta-Analysis. J Am Geriatr Soc. 2014 Jan 2.

Weden MM, Shih RA, Kabeto MU, et al. Secular Trends in Dementia and Cognitive Impairment of U.S. **Rural and Urban** Older Adults. Am J Prev Med. 2017 Dec 6.

Wei LA, Fearing MA, Sternberg EJ, Inouye SK. The **Confusion Assessment Method (CAM)** : a systematic review of current usage. J Am Geriatr Soc [Internet]. 2008 May [cited 2011 Oct 4];56(5):823-30.

Wei M, Shi J, Li T, et al. Diagnostic Accuracy of the Chinese Version of the **Trail-Making Test** for Screening Cognitive Impairment. J Am Geriatr Soc. 2017 Nov 14.

Weiner MW, Crane PK, Montine TJ, et al. **Traumatic brain injury** may not increase the risk of Alzheimer disease. Neurology. 2017 Oct 31;89(18):1923-1925

Weinstein G, Maillard P, Himali JJ, et al. **Glucose indices** are associated with cognitive and structural brain measures in young adults. Neurology 2015;84:2329–2337.

Weir E, Seitz D. Dementia-friendly communities: where home care and mental health intersect. CMAJ. 2017 Apr 24;189(16):E581-E582.

Wellington H, Paterson RW, Portelius E, et al. Increased **CSF neurogranin concentration** is specific to Alzheimer disease. Neurology. 2016 Mar ;86(9):829-35.

Wergin R, Modrykamien A. **Cognitive impairment in ICU survivors**: Assessment and therapy. Cleve Clin J Med. 2012 Oct;79(10):705-712.

Westlye LT, Reinvang I, Rootwelt H, Espeseth T. Effects of **APOE** on brain white matter microstructure in healthy adults. Neurology. 2012 Nov 6;79(19):1961-9.

Weston PSJ, Poole T, Ryan NS, et al. **Serum neurofilament light** in familial Alzheimer disease: A marker of early neurodegeneration. Neurology. 2017 Nov 21;89(21):2167-2175.

Weston PSJ, Nicholas JM, et al. **Accelerated long-term forgetting** in presymptomatic autosomal dominant Alzheimer's disease: a cross-sectional study. Lancet Neurol 2018; 17: 123–32.

Westwood AJ, Beiser A, Decarli C, et al. **Insulin-like growth factor-1** and risk of Alzheimer dementia and brain atrophy. Neurology. 2014 Apr 4.

Westwood AJ, Beiser A, Jain N, et al. **Prolonged sleep duration** as a marker of early neurodegeneration predicting incident dementia. Neurology. 2017 Mar 21;88(12):1172-1179.

Weuve J, Puett RC, Schwartz J, Yanosky JD, Laden F, Grodstein F. Exposure to **particulate air pollution** and cognitive decline in older women. Arch Intern Med. 2012;172(3):219-227.

Whear R, Coon JT, Bethel A, et al. What Is the Impact of Using **Outdoor Spaces Such as Gardens** on the Physical and Mental Well-Being of Those With Dementia? A Systematic Review of Quantitative and Qualitative Evidence. J Am Med Dir Assoc. 2014 Jul 15.

White LR, Edland SD, Hemmy LS, et al. **Neuropathologic comorbidity** and cognitive impairment in the Nun and Honolulu-Asia Aging Studies. Neurology. 2016 Mar 15;86(11):1000-8.

White RS, Lipton RB, Hall CB, Steinerman JR. **Nonmelanoma skin cancer** is associated with reduced Alzheimer disease risk. Neurology. 2013 May 21;80(21):1966-72.

Whitlock EL, Diaz-Ramirez LG, Glymour MM, et al. Association Between **Persistent Pain and Memory Decline** and Dementia in a Longitudinal Cohort of Elders. JAMA Intern Med. 2017 Jun 5.

Whitwell JL, Dickson DW, Murray ME, et al. **Neuroimaging** correlates of pathologically defined subtypes of Alzheimer's disease: a case-control study. Lancet Neurol. 2012 Aug 31.

Whitmer RA, Karter AJ, Yaffe K, et al. **Hypoglycemic episodes** and risk of dementia in older patients with type 2 diabetes mellitus.JAMA. 2009 Apr 15;301(15):1565-72.

Widera Eric, Steenpass Veronika, Marson Daniel, et al. **Finances in the Older Patient** With Cognitive Impairment: "He Didn't Want Me to Take Over." JAMA. 2011;305(7):698-706.doi:10.1001/jama.2011.164

Wildes TS, Mickle AM, Ben Abdallah A, et al. Effect of **electroencephalography-guided anesthetic administration on postoperative delirium** among older adults undergoing major surgery: the ENGAGES randomized clinical trial [Feb 5, 2019]. JAMA. doi:10.1001/jama.2018.22005

Willem van Dalen J, van Wanrooij LL, Moll van Charante EP, et al. Association of **Apathy With Risk of Incident Dementia** A Systematic Review and Meta-analysis. *JAMA Psychiatry.* 2018 Jul 18.

Willey JZ, Gardener H, Caunca MR, et al. **Leisure-time physical activity** associates with cognitive decline: The Northern Manhattan Study. Neurology. 2016 May 17;86(20):1897-903.

Williams DM, Karlsson IK, Pedersen NL, et al. **Circulating insulin-like growth factors** and Alzheimer disease: A mendelian randomization study. Neurology. 2018 Jan 23;90(4):e291-e297.

Williams JW, Plassman BL, Burke J, et al. **Preventing Alzheimer's disease** and cognitive decline. Evid Rep Technol Assess (Summ). 2010 April;193:1-727.

Williamson JD, Launer LJ, Bryan RN, et al. Cognitive Function and Brain Structure in Persons With Type 2 **Diabetes** Mellitus After Intensive Lowering of Blood Pressure and Lipid Levels: A Randomized Clinical Trial. JAMA Intern Med. 2014 Feb 3.

Williamson W, Lewandowski AJ, Forkert ND, et al. Association **of cardiovascular risk factors with MRI indices of cerebrovascular structure and function and white matter hyperintensities in young adults** [August 21, 2018].JAMA.

Wilkinson D, Windfeld K, Colding-Jorgensen E. Safety and efficacy of **idalopirdine**, a 5-HT6 receptor antagonist, in patients with moderate Alzheimer's disease (LADDER): a randomised, double-blind, placebocontrolled phase 2 trial. Lancet Neurol 2014; online Oct 6.

Wilson RS, Hebert LE, Scherr PA, Barnes LL, Mendes de Leon CF, et al. **Educational attainment** and cognitive decline in old age. Neurology. 2009 Feb 3;72(5):460-5. The results suggest that education is robustly associated with level of cognitive function but not with rate of cognitive decline and that the former association primarily accounts for education's correlation with risk of dementia in old age.

Wilson RS, Hebert LE, Scherr PA, et al. **Cognitive decline after hospitalization** in a community population of older persons. Neurology 2012; 78:950 –956

Wilson RS, Segawa E, Boyle PA, Bennett DA. Influence of **late-life cognitive activity** on cognitive health. Neurology. 2012 Apr 10;78(15):1123-9.

Wilson RS, Boyle PA, Yu L, et al. **Life-span cognitive activity**, neuropathologic burden, and cognitive aging. Neurology 2013;81:314–321.

Wilson RS, Yu L, Lamar M, et al. Education and cognitive reserve in old age. Neurology. 2019 Mar 5;92(10):e1041-e1050.

Winblad B, et al. 3-Year Study of Donepezil Therapy in Alzheimer's Disease: Effects of **Early and Continuous** Therapy. Dement Geriatr Cogn Disord. 2006 Feb 27;21(5-6):353-363 [Epub ahead of print]

Winblad B, Kilander L, Eriksson S, et al. **Severe Alzheimer's** Disease Study Group. **Donepezil** in patients with severe Alzheimer's disease: double-blind, parallel-group, placebo-controlled study. Lancet. 2006 Apr 1;367(9516):1057-65.

Winblad, B, Andreasen N, et al. Safety, tolerability, and antibody response of active **Aβ immunotherapy with CAD106** in patients with Alzheimer's disease: randomised, double-blind, placebo-controlled, fi rst-in-human study. Lancet Neurol 2012.

Winblad B, Amouyel P, Andrieu S, et al. Defeating **Alzheimer's disease and other dementias**: a priority for **European** science and society. Lancet Neurol 2016; 15: 455–532.

Windham BG, Griswold ME, Wilkening SR, et al. Midlife Smaller and Larger Infarctions, White Matter Hyperintensities, and **20-Year Cognitive Decline:** A Study. Ann Intern Med. 2019 Aug 27.

Wingo TS, Cutler DJ, Wingo AP, et al. Association of early-onset Alzheimer disease with **elevated low-density lipoprotein cholesterol levels and rare genetic coding variants of APOB** [online May 28, 2019]. JAMA Neurol. doi:10.1001/jamaneurol.2019.0648

Winslow BT, Onysko MK, Stob CM. **Treatment of Alzheimer Disease**. Am Fam Physician. 2011;83(12):1403-1412.

Witlox J, Eurelings LS, de Jonghe JF, et al.. **Delirium** in elderly patients and the risk of **postdischarge mortality**, institutionalization, and dementia: a meta-analysis. JAMA. 2010 Jul 28;304(4):443-51.

Wolters FJ, Mattace-Raso FU, Koudstaal PJ, et al. **Orthostatic Hypotension** and the Long-Term Risk of Dementia: A Population-Based Study. PLoS Med. 2016 Oct 11;13(10):e1002143.

Wolters FJ, Zonneveld HI, Hofman A, et al. **Cerebral Perfusion** and the Risk of Dementia: A Population-Based Study. Circulation. 2017 Aug 22;136(8):719-728.

Wolters FJ, Zonneveld HI, Licher S, et al. **Hemoglobin and anemia in relation to dementia risk** and accompanying changes on brain MRI. Neurology. 2019 Aug 27;93(9):e917-e926.

Wolz R, Schwarz AJ, Gray KR, et al. Enrichment of clinical trials in MCI due to AD using **markers of amyloid and neurodegeneration**. Neurology. 2016 Sep 20;87(12):1235-1241.

Wong Camilla L.; Holroyd-Leduc Jayna; Simel DL.; Straus SE. **Does This Patient Have Delirium**?: Value of Bedside Instruments. JAMA. 2010;304(7):779-786. The **Confusion Assessment Method** is the most accurate tool for diagnosing delirium in adults that can be performed in less than 5 minutes. The Mini-Mental State Examination (MMSE) was the least useful diagnostic tool for delirium. (LOE = 3a)

Woods DL, Craven RF, Whitney J. The effect of therapeutic **touch** on behavioral symptoms of persons with dementia. Altern Ther Health Med 2005; 11:66-74. (InfoPOEMs: Short-duration therapeutic touch, a specific treatment modality often practiced by nurses, decreases behavioral symptoms in patients with dementia, especially vocalizing and manual manipulation of hands or objects. This simple intervention was administered twice daily for 5 minutes to 7 minutes by a trained practitioner. (LOE = 1b-))

Woods B, Aguirre E, Spector AE,OrrellM. **Cognitive stimulation to** improve cognitive functioning in people with dementia. Cochrane Database of Systematic Reviews 2012, Issue 2. Art. No.: CD005562. DOI: 10.1002/14651858.CD005562.pub2. There was consistent evidence from multiple trials that cognitive stimulation programmes benefit cognition in people with mild to moderate dementia over and above any medication effects.

Woon FL, Dunn CB, Hopkins RO. Predicting Cognitive Sequelae in Survivors of **Critical Illness with Cognitive Screening Tests**. Am J Respir Crit Care Med. 2012 Jun 14.

Wong WB, Lin VW, Boudreau D, et al. **Statins** in the **prevention of dementia** and Alzheimer's disease: a meta-analysis of observational studies and an assessment of confounding. Pharmacoepidemiol Drug Saf. 2013 Apr;22(4):345-58.

Whitwell JL, Shiung MM, Przybelski SA, Weigand SD, Knopman DS, Boeve BF, et al. **MRI** patterns of atrophy associated with progression to AD in amnestic mild cognitive impairment. Neurology. 2007 Sep 26.

Woods SW, Morgenstern H, Saksa JR, et al. Incidence of **tardive dyskinesia with atypical versus conventional antipsychotic** medications: a prospective cohort study. J Clin Psychiatry. 2010 Feb 9.

Wotton CJ, Goldacre MJ. **Age at obesity** and association with subsequent **dementia**: record linkage study. Postgrad Med J. 2014 Oct;90(1068):547 51.

Wright H, Jenks RA. Sex on the brain! Associations between **sexual activity** and cognitive function in older age. Age Ageing. 2016 Jan 28.

Wu Y-C, Tseng P-T, Tu Y-K, et al. Association of **delirium response and safety of pharmacological interventions** for the management and prevention of delirium: a network meta-analysis [online Feb 27, 2019]. JAMA Psychiatry. doi:10.1001/jamapsychiatry.2018.4365

Wu A, Sharrett AR, Gottesman RF, et al. Association of **Brain Magnetic Resonance Imaging Signs With Cognitive Outcomes in Persons With Nonimpaired Cognition** and Mild Cognitive Impairment. JAMA Netw Open. 2019 May 3;2(5):e193359.

Xia C, Makaretz SJ, Caso C, et al. Association of in vivo **18F-AV-1451 tau PET imaging** results with cortical atrophy and symptoms in typical and atypical Alzheimer disease. JAMA Neurol. 2017;74 (4):427-436.

Xie J, Brayne C, Matthews FE; Medical Research Council Cognitive Function and Ageing Study collaborators. **Survival times** in people with dementia: analysis from population based cohort study with 14 year follow-up. BMJ. 2008 Feb 2;336(7638):258-62. Epub 2008 Jan 10. **Men will live a median 4.1 years and women a median of 4.6 years beyond a diagnosis of dementia**. Survival time is shorter in older people and in patients with disability. (LOE = 1b)

Xie W, Zheng F, Yan L, Zhong B. **Cognitive Decline Before and After Incident Coronary Events**. J Am Coll Cardiol. 2019 Jun 25;73(24):3041-3050.

Xiong C, Roe CM, Buckles V, et al. Role of family history for Alzheimer **biomarker abnormalities** in the adult children study. Arch Neurol. 2011 Oct;68(10):1313-9.

Xiong C, Jasielec MS, Weng H, et al. **Longitudinal relationships among biomarkers** for Alzheimer disease in the Adult Children Study. Neurology. 2016 Mar 23.

Xu H, Yang R, Qi X, et al. Association of **Lifespan Cognitive Reserve Indicator** With Dementia Risk in the Presence of Brain Pathologies. JAMA Neurol. 2019 Jul 14

Xu W, Tan L, Wang HF, et al. Meta-analysis of **modifiable risk factors** for Alzheimer's disease. J Neurol Neurosurg Psychiatry. 2015 Aug 20.

Xu W, Wang HF, Wan Y, et al. **Leisure time physical activity** and dementia risk: a dose-response meta-analysis of prospective studies. BMJ Open. 2017 Oct 22;7(10):e014706

Yaffe Kristine, Weston Andrea, Graff-Radford Neill R., et al. Original Contribution Association of **Plasma β-Amyloid Level and Cognitive Reserve** With Subsequent Cognitive Decline. *JAMA*. 2011;305(3):261- 266.

Yaffe K, Middleton LE, Lui LY, et al. **Mild cognitive impairment, dementia**, and their subtypes in **oldest old women**. Arch Neurol. 2011 May;68(5):631-6

Yaffe K, Laffan AM, Harrison SL, et al. **Sleep-disordered breathing**, hypoxia, and risk of mild cognitive impairment and dementia in older women. JAMA. 2011; 306(6):613-619.

Yaffe K, Lindquist K, Schwartz AV, et al. **Advanced glycation end product level**, diabetes, and accelerated cognitive aging. Neurology. 2011 Oct 4;77(14):1351-6.

Yaffe K, Falvey C, Hamilton N, et al. **Diabetes, Glucose Control**, and 9-Year Cognitive Decline Among Older Adults Without Dementia Diabetes and Risk of Cognitive Decline. Arch Neurol. 2012 Jun 18:1-6.

Yaffe K, Falvey CM, Hamilton N, et al; for the Health ABC Study. Association Between **Hypoglycemia and Dementia** in a Biracial Cohort of Older Adults With Diabetes Mellitus. JAMA Intern Med. 2013 Jun 10:1-6.

Yaffe K, Falvey CM, Hamilton N, Harris TB, et al. Association between **hypoglycemia and dementia** in a biracial cohort of older adults with diabetes mellitus. JAMA Intern Med. 2013 Jul 22;173(14):1300-6.

Yaffe K, Falvey C, Harris TB, et al; Health ABC Study. Effect of **socioeconomic disparities** on incidence of dementia among biracial older adults: prospective study. BMJ. 2013 Dec 19

Yaffe K, Vittinghoff E, Pletcher MJ, et al. Early adult to **midlife cardiovascular risk factors and cognitive function**. *Circulation*. 2014;129:1560–1567.

Yaffe K, Falvey CM, Hoang T. Connections between **sleep and cognition** in older adults. Lancet Neurol. 2014 Oct;13(10):1017-1028.

Yaffe K. **Modifiable Risk Factors and Prevention of Dementia**: What Is the Latest Evidence? JAMA Intern Med. 2017 Dec 18.

Yaffe K, Lwi SJ, Hoang TD, et al. **Military-related risk factors in female veterans and risk of dementia**. Neurology 2019;92:e205–e211.

Yan R, Vassar R. Targeting the **β secretase BACE1** for Alzheimer's disease therapy. Lancet Neurol. 2014 Mar;13(3):319-329.

Yang HL, Chan PT, Chang PC, et al. **Memory-focused interventions** for people with cognitive disorders: A systematic review and meta-analysis of randomized controlled studies. Int J Nurs Stud. 2017 Aug 20.

Yang T, Dang Y, Ostaszewski B, et al. Target Engagement in an Alzheimer Trial: **Crenezumab Lowers Aβ Oligomers in CSF**. Ann Neurol. 2019 Jun 5.

Yasar S, Xia J, Yao W, et al. **Antihypertensive drugs decrease** risk of Alzheimer's disease: Ginkgo Evaluation of Memory Study. (GEMS) Neurology 2013;81:896–903.
Yasar S, Whitmer R. **Statin use and risk of Alzheimer disease**: A new view on an old relationship. Neurology. 2017 Dec 15.
Yassine HN, Braskie MN, Mack WJ, et al. Association of **Docosahexaenoic Acid Supplementation** With Alzheimer Disease Stage in Apolipoprotein E ε4 Carriers: A Review. JAMA Neurol.2017 Jan 17.
Yates PA, Desmond PM, Phal PM, et al; AIBL Research Group. Incidence of **cerebral microbleeds in preclinical Alzheimer** disease. Neurology. 2014 Apr 8;82(14):1266-73.
Yau W-YW, Torascu DL, McDade EM, et al. Longitudinal assessment of **neuroimaging and clinical markers in autosomal dominant Alzheimer's** disease: a prospective cohort study. Lancet Neurol 2015; online June 30.
Ye BS, Seo SW, Kim JH, et al. Effects of **amyloid and vascular markers** on cognitive decline in subcortical vascular dementia. Neurology. 2015 Nov 10;85(19):1687-93.
Ying I. **Artificial nutrition and hydration** in advanced dementia. Can Fam Physician. 2015 Mar;61(3):245-8.
Yohanna D, Cifu AS. **Antipsychotics to Treat Agitation or Psychosis in Patients With Dementia**. JAMA. 2017 Sep 19;318(11):1057-1058.
Yokoyama JS, Wang Y, Schork AJ, et al. Alzheimer's Disease Neuroimaging Initiative. Association Between Genetic Traits for Immune-Mediated Diseases and Alzheimer Disease. JAMA Neurol. 2016 Apr 18.
Yoon BK, Chin J, Kim JW, et al. **Menopausal hormone therapy and mild cognitive impairment**: a randomized, placebo-controlled trial. Menopause. 2018 May 29.
Young J, Inouye SK. **Delirium in older people**. BMJ. 2007 Apr 21;334(7598):842-6.
Young John, Meagher David, MacLullich Alasdair. **Cognitive assessment of older people**. BMJ 2011;343:d5042 doi: 10.1136/bmj.d5042.
Yu L, Petyuk VA, Tasaki S, et al. Association of **Cortical β-Amyloid Protein in the Absence of Insoluble Deposits** With Alzheimer Disease. JAMA Neurol. 2019 Apr 22.
Yu TM, Chuang YW, Sun KT, et al. **Polycystic kidney disease** is significantly associated with dementia risk. Neurology. 2017 Oct 3;89(14):1457-1463.
Yuan C, Fondell E, Bhushan A, et al. Long-term **intake of vegetables and fruits and subjective cognitive function** in US men. Neurology. 2019 Jan 1;92(1):e63-e75.
Yunusa I, Alsumali A, Garba AE, et al. Assessment of Reported Comparative Effectiveness and Safety of **Atypical Antipsychotics in the Treatment of Behavioral and Psychological Symptoms** of Dementia: A Network Meta-analysis. JAMA Netw Open. 2019 Mar 1;2(3):e190828.
Zeki Al Hazzouri A, Caunca MR, Nobrega JC, et al. **Greater depressive symptoms, cognition, and markers of brain aging**: Northern Manhattan Study. Neurology. 2018 Jun 5;90(23):e2077-e2085.
Zekry D, Gold G. Management of **mixed dementia**. Drugs Aging. 2010 Sep 1;27(9):715-28. doi: 10.2165/11538250-000000000-00000.
Zeng Y, Feng Q, Hesketh T, et al. **Survival, disabilities in activities of daily living, and physical and cognitive functioning** among the oldest-old in China: a cohort study. Lancet 2017; online Mar 9.
Zenilman ME. **Delirium**: An Important Postoperative Complication. JAMA. 2017 Jan 3;317(1):77-78.
Zhan C, et al. Potentially **inappropriate** medication use in the community-dwelling elderly: findings from the 1996 Medical Expenditure Panel Survey.JAMA. 2001 Dec 12;286(22):2823-9.
Zhan X, Stamova B, Jin LW, et al. **Gram-negative bacterial molecules associate** with Alzheimer disease pathology. Neurology. 2016 Nov 29;87(22):2324-2332.
Zhang YP, Lou Y, Hu J, et al. **DHA supplementation** improves cognitive function via enhancing Abeta-mediated autophagy in Chinese elderly with mild cognitive impairment: a randomised placebo-controlled trial. J Neurol Neurosurg Psychiatry. 2017 Nov 15
Zheng F, Yan L, Yang Z, et al. **HbA(1c), diabetes and cognitive decline**: the English Longitudinal Study of Ageing. Diabetologia. 2018 Jan 25.
Zhong KX, Tariot PN, Mintzer J, et al. **Quetiapine** to treat agitation in dementia: a randomized, double-blind, placebo-controlled study. Curr Alzheimer Res. 2007 Feb;4(1):81-93. n=333. The results of this study suggest that quetiapine 200mg/day was effective and well-tolerated for treating agitation associated with dementia. However, caution should be exercised given the concerns regarding increased mortality with atypical antipsychotics in this vulnerable patient population.
Zhu H, Tao Q, Ang TFA, et al. Association of **Plasma Amylin Concentration With Alzheimer Disease and Brain Structure** in Older Adults. JAMA Netw Open. 2019 Aug 2;2(8):e199826.
Zhu J, Wang Y, Li J, et al. **Intracranial artery stenosis** and progression from mild cognitive impairment to Alzheimer disease. Neurology. 2014 Mar 11;82(10):842-9.
Zhu N, Jacobs DR Jr, Schreiner PJ, et al. **Cardiorespiratory fitness and cognitive** function in middle age: The CARDIA Study. Neurology. 2014 Apr 15;82(15):1339-46.
Zsido RG, Heinrich M, Slavich GM, et al. Association of **Estradiol and Visceral Fat** With Structural Brain Networks and Memory Performance in Adults. JAMA Netw Open. 2019 Jun 5;2(6):e196126.
Zwan MD, Rinne JO, Hasselbalch SG, et al. Use of **amyloid-PET to determine cutpoints for CSF markers**: A multicenter study. Neurology. 2016 Jan 5;86(1):50-8.

Useful Web sites:

Alzheimer Society Canada www.alzheimer.ca
Alzheimer Association USA www.alz.org
Alzheimer Society UK www.alzheimers.org.uk

GERI-RXFILES ANTICHOLINERGIC REFERENCES

[1] Carnahan RM, Lund BC, Perry PJ, et al. The Anticholinergic Drug Scale as a measure of drug-related anticholinergic burden: associations with serum anticholinergic activity. J Clin Pharmacol. 2006 Dec;46(12):1481-6.

[2] National Prescribing Service. Examples of medications with anticholinergic activity. January 2009. Available: http://www.brisbanesouth.com.au/content/Document/Resources/NPS/NPS%20Anticholinergic%20Medications%20200902.pdf

[3] Chew ML, Mulsant BH, Pollock BG, et al. **Anticholinergic** activity of 107 medications commonly used by older adults. J Am Geriatr Soc. 2008 Jul;56(7):1333-41.

[4] Clinical Resource, *Drugs with Anticholinergic Activity*. *Pharmacist's Letter/Prescriber's Letter*. September 2019.

[5] Mintzer J, Burns A. Anticholinergic side-effects of drugs in elderly people. J R Soc Med. 2000 Sep;93(9):457-62.

[6] Feinberg M. The problems of **anticholinergic** adverse effects in older patients. Drugs Aging. 1993 Jul-Aug;3(4):335-48.

[7] Tune LE. Anticholinergic effects of medication in elderly patients. J Clin Psyc. 2001.

[8] Treatment of Dry Mouth. Canadian Pharmacist's Letter 2010; 26(10):261006.

[9] Drugs with Anticholinergic Activity. Canadian Pharmacist's Letter 2011; 27(12):271206.

Clinical Resource. Drugs with **Anticholinergic** Activity. Pharmacist's Letter/Prescriber's Letter. August 2017.

ADDITIONAL REFERENCES

Aldebert G, Faillie JL, Hillaire-Buys D, et al. Association of **Anticholinergic Drug Use With Risk for Late Age-Related Macular Degeneration**. JAMA Ophthalmol. 2018 May 24.

Andre L, Gallini A, Montastruc F, et al. **Anticholinergic exposure** and cognitive decline in older adults: Effect of anticholinergic exposure definitions in a 3-year analysis of the Multidomain Alzheimer Preventive Trial (MAPT) study. Br J Clin Pharmacol. 2018 Aug 10.

Anticholinergic Cognitive Burden Scale http://www.indydiscoverynetwork.org/AnticholinergicCognitiveBurdenScale.html

Beau AB, Montastruc JL, Lacroix I, et al. **Atropinic (anticholinergic) burden** of drugs during pregnancy and psychological development of children: a cohort study in the EFEMERIS database. Br J Clin Pharmacol. 2016 Apr 16.

Boustani MA, Campbell NL, Munger S, Maidment I, Fox GC. Impact of **anticholinergics on the aging brain**: a review and practical application. Aging Heatlh. 2008;4(3):311-320.

Cai X, Campbell N, Khan B, Callahan C, Boustani M. **Long-term anticholinergic use and the aging brain**. Alzheimers Dementia. 2012; epub ahead of print.

Campbell N, Boustani M, Limbil T, et al. The **cognitive impact of anticholinergics**: a clinical review. Clinical Interventions in Aging. 2009;4(1):225-233.

Campbell N, Boustani M, Lane K, et al. Use of **anticholinergics and the risk of cognitive impairment** in an African- American population. Neurology. 2010;75:152-159.

Campbell NL, Boustani MA, Lane KA, et al. Use of anticholinergics and the risk of cognitive impairment in an African American population. Neurology. 2010 Jul 13;75(2):152-9.

Carrière I, Fourrier-Reglat A, Dartigues JF, et al. Drugs with anticholinergic properties, cognitive decline, and dementia in an elderly general population: the 3-city study. Arch Intern Med. 2009 Jul 27;169(14):1317-24.

Clinical Resource. Drugs with Anticholinergic Activity. Pharmacist's Letter/Prescriber's Letter. August 2017.

Coupland CAC, Hill T, Dening T, et al. Anticholinergic drug exposure and the risk of dementia: a nested case-control study [online June 24, 2019]. JAMA Intern Med.

Fox C, Richardson K, Maidment I, et al. **Anticholinergic medication use and cognitive impairment** in the older population: the Medical Research Council Cognitive Function and Ageing Study. Journal of the American Geriatric Society. 2011; 59(8): 1477-1483.

Gomm W, von Holt K, Thomé F, et al. Association of **proton pump inhibitors with risk of dementia**: a pharmacoepidemiological claims data analysis [online Feb 15, 2016]. JAMA Neurol. doi:10.1001/jamaneurol.2015.4791.

Gray SL, Anderson ML, Dublin S, et al. Cumulative use of **strong anticholinergics and incident dementia**: a prospective cohort study [online January 26, 2015]. JAMA Intern Med. doi:10.1001/jamainternmed.2014.7663.

Han L, Agostini JV, Allore HG. Cumulative anticholinergic exposure is associated with poor memory and executive function in older men. J Am Geriatr Soc. 2008 Dec;56(12):2203-10. Cumulative anticholinergic exposure across multiple medications over 1 year may negatively affect verbal memory and executive function in older men. Prescription of drugs with anticholinergic effects in older persons deserves continued attention to avoid deleterious adverse effects.

Heath L, Gray SL, Boudreau DM, et al. Cumulative Antidepressant Use and Risk of Dementia in a Prospective Cohort Study. J Am Geriatr Soc. 2018 Sep 17. (paroxetine)

Kalisch Ellett LM, Pratt NL, et al. Multiple anticholinergic medication use and **risk of hospital admission for confusion or dementia**. J Am Geriatr Soc. 2014 Oct;62(10):1916-22.

Kennedy J, Deberdt W, Siegal A, et al. **Olanzapine does not enhance cognition** in non-agitated and non-psychotic patients with mild to moderate Alzheimer's dementia. Int J Geriatr Psychiatry. 2005 Nov;20(11):1020-7.

Lackner TE, Wyman JF, McCarthy TC, Monigold M, Davey C. Randomized, placebo-controlled trial of the cognitive effect, safety, and tolerability of oral extended-release oxybutynin 5mg/day in cognitively impaired nursing home residents with urge urinary incontinence. J Am Geriatr Soc. 2008 May;56(5):862-70. n=50. 4 weeks. Short-term treatment using oral extended-release oxybutynin 5 mg once daily was safe and well tolerated, with no delirium, in older female nursing home participants with mild to severe dementia. Future research should investigate different dosages and long-term treatment.

Marcum ZA, Perera S, Thorpe JM, et al; Health ABC Study, USA. **Anticholinergic Use and Recurrent Falls** in Community-Dwelling Older Adults: Findings From the Health ABC Study. Ann Pharmacother. 2015 Nov;49(11):1214-21.

McCartney M. Margaret McCartney: **Drugs with anticholinergic side effects** and cognitive decline-cause or effect? BMJ. 2015 Mar 16;350:h1428.

Myint PK, Fox C, Kwok CS, et al. Total **anticholinergic burden and risk of mortality** and cardiovascular disease over 10 years in 21,636 middle-aged and older men and women of **EPIC-Norfolk** prospective population study. Age Ageing. 2014 Nov 27.

NICE: National Institute for Health and Care Excellence. **Dementia** - **assessment, management and support for people living with dementia and their carers** (NICE guideline NG97). 2018. www.nice.org.uk/guidance/ng97.

Page AT, Clifford RM, Potter K, et al. The feasibility and the effect of **deprescribing** in older adults on mortality and health: A systematic review. Br J Clin Pharmacol. 2016 Apr 14.

Paul KJ, Walker RL, Dublin S. Anticholinergic Medications and **Risk of Community-Acquired Pneumonia** in Elderly Adults: A Population-Based Case-Control Study. J Am Geriatr Soc. 2015 Mar 2.

Richardson KFox CMaidment I. **Anticholinergic drugs and risk of dementia**: case-control study. BMJ 2018;361:k1315.

Risacher SL, McDonald BC, Tallman EF, et al. Alzheimer's Disease Neuroimaging Initiative. Association Between **Anticholinergic Medication Use and Cognition**, Brain Metabolism, and Brain Atrophy in Cognitively Normal Older Adults. JAMA Neurol. 2016 Apr 18.

Rudolph JL, Salow MJ, Angelini MC, McGlinchey RE. The anticholinergic risk scale and anticholinergic adverse effects in older persons. Arch Intern Med. 2008 Mar 10;168(5):508-13.

Sink KM, Thomas J 3rd, Xu H, Craig B, et al. Dual Use of Bladder Anticholinergics and Cholinesterase Inhibitors: Long-Term Functional and Cognitive Outcomes. J Am Geriatr Soc. 2008 Apr 1. In higher-functioning NH residents, dual use of ChIs and bladder anticholinergics may result in greater rates of functional decline than use of ChIs alone. The MDS-COGS may not be sensitive enough to detect differences in cognition due to dual use.

Spence MM, Karim FA, Lee EA, et al. **Risk of Injury in Older Adults Using Gastrointestinal Antispasmodic and Anticholinergic Medications**. J Am Geriatr Soc. 2015 Jun;63(6):1197-202.

Tannenbaum C, Paquette A, Hilmer S, et al. A systematic review of **amnestic and non-amnestic mild cognitive impairment** induced by anticholinergic, antihistamine, GABAergic and opioid drugs. Drugs Aging. 2012 Aug 1;29(8):639-58.

Teramura-Grönblad M, Muurinen S, Soini H, et al. Use of anticholinergic drugs and cholinesterase inhibitors and their association with psychological well-being among frail older adults in residential care facilities. Ann Pharmacother. 2011 May;45(5):596-602.

The American Geriatrics Society **2012 Beers Criteria Update** Expert Panel. American Geriatrics Society Updated Beers Criteria for Potentially Inappropriate Medication Use in Older Adults. J Am Geriatr Soc. 2012 Feb 29.

Torjesen I. Anticholinergic effects of common drugs are associated with increased **mortality** in over 65s. BMJ. 2011 Jun 28;342:d4037.

Additional articles:
Abbasi M, Rolfson D, Khera AS, et al. Identification and management of **frailty** in the primary care setting. CMAJ 2018;190:E1134-40.
ACC/AHA 2017 Whelton PK, Carey RM, et al. **2017 ACC/AHA**/AAPA/ABC/ACPM/AGS/APhA/ASH/ASPC/NMA/PCNA **Guideline for the Prevention, Detection, Evaluation, and Management of High Blood Pressure** in Adults: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. Hypertension. 2017 Nov 13.
ADA 2015: Standards of medical care in diabetes--2015: summary of revisions. Diabetes Care. 2015 Jan;38 Suppl:S4.
ADA 2017: American Diabetes Association Guideline Section 11. Older Adults. Diabetes Care. 2017 Jan;40(Suppl 1):S99-S104.
Agmon M, Zisberg A, Gil E, et al. Association Between **900 Steps a Day and Functional Decline** in Older Hospitalized Patients. JAMA Intern Med. 2016 Dec 5.
AGS Choosing Wisely Workgroup. American Geriatrics Society identifies **five things that healthcare providers and patients should question**. J Am Geriatr Soc. 2013 Apr;61(4):622-31.
AGS: American Geriatrics Society 2019 Beers Criteria Update Expert Panel. American Geriatrics Society updated **AGS Beers Criteria for potentially inappropriate medication use in older adults**. J Am Geriatr Soc 2019; doi: 10.1111/jgs.15767.
Aguayo GA, Donneau AF, Vaillant MT, et al. Agreement Between **35 Published Frailty Scores** in the General Population. Am J Epidemiol. 2017 Aug 15;186(4):420-434.

Ailabouni NJ, Nishtala PS, Mangin D, et al. **General practitioners' insight into deprescribing** for the multimorbid older individual: a qualitative study. Int J Clin Pract. 2016 Mar;70(3):261-76.
Aldebert G, Faillie JL, Hillaire-Buys D, et al. Association of **Anticholinergic Drug Use** With Risk for **Late Age-Related Macular Degeneration**. JAMA Ophthalmol. 2018 May 24.
Alderman CP. Saving the Elderly From **Drug-Related Harm**. Ann Pharmacother. 2016 Aug;50(8):685-6.
Aliberti MJR, Cenzer IS, Smith AK, et al. **Assessing Risk for Adverse Outcomes** in Older Adults: The Need to Include Both Physical Frailty and Cognition. J Am Geriatr Soc. 2018 Nov 23.
Alldred DP, Kennedy MC, Hughes C, et al. **Interventions to optimize prescribing for older people in care homes**. Cochrane Database Syst Rev. 2016 Feb 12;2:CD009095. We could not draw robust conclusions from the evidence due to variability in design, interventions, outcomes and results. The interventions implemented in the studies in this review led to the identification and resolution of medication-related problems and improvements in medication appropriateness, however evidence of a consistent effect on resident-related outcomes was not found. There is a need for high-quality cluster-randomised controlled trials testing clinical decision support systems and multidisciplinary interventions that measure well-defined, important resident-related outcomes.
American Geriatrics Society Expert Panel on the **Care of Older Adults with Multimorbidity**. Guiding principles for the care of older adults with multimorbidity: an approach for clinicians. J Am Geriatr Soc 2012 Oct;60(10):E1-25.

American Geriatrics Society 2015 Beers Criteria Update Expert Panel. American Geriatrics Society 2015 Updated Beers Criteria for Potentially Inappropriate Medication Use in Older Adults. J Am Geriatr Soc. 2015 Oct 8.
Ammerman CA, Simpkins BA, Warman N, Downs TN. Potentially Inappropriate Medications in Older Adults: **Deprescribing** with a Clinical Pharmacist. J Am Geriatr Soc. 2019 Jan;67(1):115-118.
Andre L, Gallini A, Montastruc F, et al. **Anticholinergic exposure and cognitive decline in older adults**: Effect of anticholinergic exposure definitions in a 3-year analysis of the Multidomain Alzheimer Preventive Trial (MAPT) study. Br J Clin Pharmacol. 2018 Aug 10.
Andre L, Gallini A, Montastruc F, et al. **Anticholinergic exposure** and cognitive decline in older adults: Effect of anticholinergic exposure definitions in a 3-year analysis of the Multidomain Alzheimer Preventive Trial (MAPT) study. Br J Clin Pharmacol. 2018 Aug 10.

Andrews MA, O'Malley PG. **Diabetes overtreatment** in elderly individuals: risky business in need of better management. JAMA. doi:10.1001 /jama.2014.4563.
Andreotti F, Rocca B, Husted S, et al; ESC Thrombosis Working Group. **Antithrombotic therapy in the elderly**: expert position paper of the European Society of Cardiology Working Group on Thrombosis. Eur Heart J. 2015 Jul 9.
Arrieta H, Rezola-Pardo C, Gil SM, et al. Effects of **Multicomponent Exercise** on Frailty in Long-Term Nursing Homes: A Randomized Controlled Trial. J Am Geriatr Soc. 2019 Mar 19.
Atkinson TJ, Fudin J, Pandula A, Mirza M. **Medication Pain Management in the Elderly**: Unique and Underutilized Analgesic Treatment Options. Clin Ther. 2013 Oct 22.
Barenholtz Levy H, Marcus EL. **Potentially Inappropriate Medications in Older Adults**: Why the Revised Criteria Matter. Ann Pharmacother. 2016 Jul;50(7):599-603.
Barry AR, O'Neill DE, Graham MM. **Primary Prevention of Cardiovascular Disease in Older Adults**. Can J Cardiol. 2016 Apr 19.
Bayoumi I, Dolovich L, Hutchison B, Holbrook A. **Medication-related emergency department visits** and hospitalizations among older adults. Can Fam Physician. 2014 Apr;60(4):e217-22.
Beau AB, Montastruc JL, Lacroix I, et al. **Atropinic (anticholinergic) burden** of drugs during pregnancy and psychological development of children: a cohort study in the EFEMERIS database. Br J Clin Pharmacol. 2016 Apr 16.
Beckett MK, Elliott MN, Ritenour D, et al. **Adapting the Vulnerable Elders Survey-13 to Predict Mortality** Using Responses to the Medicare Health Outcomes Survey. J Am Geriatr Soc. 2017 Apr 3.
Beernaert K, Smets T, Cohen J, et al. **Improving comfort around dying in elderly people**: a cluster randomised controlled trial. (**CAREFul**) Lancet 2017; online May 16.
Bell MM. **Lipoid pneumonia**: An unusual and preventable illness in elderly patients. Can Fam Physician. 2015 Sep;61(9):775-7.
Benetos A, Labat C, Rossignol P, et al. Treatment With **Multiple Blood Pressure Medications**, Achieved Blood Pressure, and Mortality in **Older Nursing Home Residents: The PARTAGE** Study. JAMA Intern Med. 2015 Feb 16.
Benetos A, Rossignol P, Cherubini A, et al. Polypharmacy in the Aging Patient: **Management of Hypertension in Octogenarians**. JAMA. 2015 Jul 14;314(2):170-180.
Benetos A, Bulpitt CJ, Petrovic M, et al. An Expert Opinion From the European Society of Hypertension-European Union Geriatric Medicine Society Working Group on the Management of **Hypertension in Very Old, Frail** Subjects. Hypertension. 2016 May;67(5):820-5.
Beuscart JB, Pont LG, Thevelin S, Boland et al. A systematic review of the outcomes reported in trials of **medication review** in older patients: the need for a core outcome set. Br J Clin Pharmacol.2016 Nov 27.
Birkenhäger-Gillesse EG, den Elzen WP, Achterberg WP, et al. Association Between **Glycosylated Hemoglobin and Cardiovascular Events** and Mortality in Older Adults without Diabetes Mellitus in the General Population: The Leiden 85-Plus Study. J Am Geriatr Soc. 2015 Jun;63(6):1059-66.
Bjerre LM, et al. Potentially inappropriate prescribing (PIP) in **long-term care (LTC) patients**: validation of the **2014 STOPP-START and 2012 Beers** criteria in a LTC population-a protocol for a cross-sectional comparison of clinical and health administrative data. BMJ Open. 2015 Oct 9;5(10):e009715.
Blachman NL, Leipzig RM, Mazumdar M, et al. **High-Risk Medications** in Hospitalized Elderly Adults: Are We Making It **Easy to Do the Wrong Thing**? J Am Geriatr Soc. 2016 Nov 28.

Black E, Sketris I, Skedgel C, et al. Adherence to Guidelines and the Screening Tool of Older Persons' Potentially Inappropriate Prescriptions Criteria for **Colchicine Dosing for Gout** Treatment in Beneficiaries of the Nova Scotia Seniors' Pharmacare Program. Clin Ther. 2015 Sep 18.
Blanco-Reina E, Ariza-Zafra G, Ocaña-Riola R, León-Ortiz M. **2012 American Geriatrics Society Beers criteria**: enhanced applicability for detecting potentially inappropriate medications in European older adults? A comparison with the Screening Tool of Older Person's Potentially Inappropriate Prescriptions. J Am Geriatr Soc. 2014 Jul;62(7):1217-23.
Ble A, Masoli JA, Barry HE, et al. **Any versus long-term prescribing of high risk medications** in older people using **2012 Beers Criteria**: results from three cross-sectional samples of primary care records for 2003/4, 2007/8 and 2011/12. BMC Geriatr. 2015 Nov 5;15:146.
Boeckxstaens P, Vaes B, De Sutter A, et al. A High **Sense of Coherence** as Protection Against Adverse Health Outcomes in Patients Aged 80 Years and Older. Ann Fam Med. 2016 Jul;14(4):337-43.
Boersma MN, Huibers CJA, Drenth-van Maanen AC, et al. The effect of **providing prescribing recommendations** on appropriate prescribing: a cluster-randomized controlled trial in older adults in a preoperative setting. Br J Clin Pharmacol. 2019 May 20.
Boyd M, Armstrong D, Parker J, et al. Do **Gerontology Nurse Specialists Make a Difference** in Hospitalization of Long-Term Care Residents? Results of a Randomized Comparison Trial. J Am Geriatr Soc. 2014 Oct 3.
Boyd PJ, Nevard M, Ford JA, et al. The **electronic frailty index as an indicator** of community healthcare service utilisation in the older population**.** Age Ageing. 2018 Dec 27.
Boye ND, van der Velde N, de Vries OJ, et al. Effectiveness of **medication withdrawal in older fallers**: results from the Improving Medication Prescribing to reduce Risk Of FALLs (IMPROveFALL) trial. Age Ageing. 2016 Sep 10.
Briasoulis A, Agarwal V, Tousoulis D, et al. Effects of **antihypertensive treatment in patients over 65 years of age**: a meta-analysis of randomised controlled studies. Heart. 2013 Jun 27.
Brown JD, Hutchison LC, Li C, et al. **Predictive Validity of the Beers and Screening Tool of Older Persons` Potentially Inappropriate Prescriptions (STOPP) Criteria to Detect Adverse Drug Events, Hospitalizations, and Emergency Department Visits in the United States.** J Am Geriatr Soc. 2016 Jan;64(1):22-30.
Bruin-Huisman L, Abu-Hanna A, van Weert HC, et al. **Potentially inappropriate prescribing** to older patients in primary care in the **Netherlands**: a retrospective longitudinal study. Age Ageing. 2017 Jan 6.
Brummel NE, Bell SP, Girard TD, et al. **Frailty and Subsequent Disability and Mortality** Among Patients With Critical Illness. Am J Respir Crit Care Med. 2016 Dec 6.
Bucholz EM, Butala NM, Normand SL, et al. Association of **Guideline-Based Admission Treatments and Life Expectancy After Myocardial Infarction in Elderly Medicare Beneficiaries**. J Am Coll Cardiol. 2016 May 24;67(20):2378-91.
Buurman BM, Parlevliet JL, Allore HG, et al. **Comprehensive Geriatric Assessment and Transitional Care** in Acutely Hospitalized Patients: The Transitional Care Bridge Randomized Clinical Trial. JAMA Intern Med. 2016 Feb 15.
Cahir C, Moriarty F, Teljeur C, Fahey T, Bennett K. **Potentially inappropriate prescribing** and vulnerability and hospitalization in **older community-dwelling** patients. Ann Pharmacother. 2014 Dec;48(12):1546-54.
Campitelli MA, Maxwell CJ, Maclagan LC, et al. **One-year survival and admission to hospital for cardiovascular events** among older residents of long-term care facilities who were **prescribed intensive- and moderate-dose statins**. CMAJ 2019;191:E32-9.
Cassels A. 'Can I stop even one of these pills?' The development of a **tool to make deprescribing easier**. Eur J Hosp Pharm 2017; 24:3-4.
Chei CL, Lee JM, Ma S, Malhotra R. **Happy older people live longer**. Age Ageing. 2018 Nov 1;47(6):860-866.
Chukwulebe SB, Kim HS, McCarthy DM, et al. Potentially Inappropriate Medication Prescriptions for Older Adults with **Painful Conditions** and Association with Return **Emergency Department Visits**. J Am Geriatr Soc. 2019 Jan 27.
Clegg A, Young J, Iliffe S, et al. **Frailty** in elderly people. Lancet. 2013 Feb 7.
Clegg A, Rogers L, Young J. **Diagnostic test accuracy of simple instruments for identifying** frailty in community-dwelling older people: a systematic review. Age Ageing. 2015 Jan;44(1):148-52.
Clegg A, Bates C, Young J, et al. **Development and validation of an electronic frailty index** using routine primary care electronic health record data. Age Ageing. 2016 Mar 3.
Cool C, Cestac P, McCambridge C, et al. Reducing potentially **inappropriate drug prescribing in nursing home residents**: effectiveness of a geriatric intervention. Br J Clin Pharmacol. 2018 Apr 1
Cooper AL, Kazis LE, Dore DD, et al. **Underreporting high risk prescribing** among Medicare Advantage plans. A cross-sectional analysis. Ann Intern Med. 2013;159:456-62.
Corrada MM, Hayden KM, Paganini-Hill A, et al. Age of **onset of hypertension and risk of dementia** in the oldest-old: The **90+ Study**. Alzheimers Dement. 2017 Jan 6.
Costa AP, Hirdes JP, Bell CM, et al. Derivation and validation of the detection of indicators and vulnerabilities for **emergency room trips scale** for classifying the risk of emergency department use in frail community-dwelling older adults. J Am Geriatr Soc. 2015 Apr;63(4):763-9.
Counter D, Millar JWT, McLay JS. Hospital readmissions, mortality and potentially inappropriate prescribing: A retrospective **study of older adults discharged from hospital**. Br J Clin Pharmacol. 2018 May 9.
Crocker T, Young J, Forster A, et al. The effect of **physical rehabilitation on activities** of daily living in older residents of long-term care facilities: systematic review with meta-analysis. Age Ageing. 2013 Sep 4.
Cruz M, Covinsky K, Widera EW, et al. **Predicting 10-year mortality** for older adults. JAMA. 2013 Mar 6;309(9):874-6.
Dauphinot V, Mouchoux C, Veillard S, et al. **Anticholinergic drugs and functional, cognitive impairment** and behavioral disturbances in patients from a memory clinic with subjective cognitive decline or neurocognitive disorders. Alzheimers Res Ther. 2017 Aug 1;9(1):58.

Davidoff AJ, Miller GE, Sarpong EM, et al. Prevalence of **potentially inappropriate medication use in older adults using the 2012 Beers criteria**. J Am Geriatr Soc. 2015 Mar;63(3):486-500.
Davies EA, O'Mahony MS. **Adverse drug reactions in special populations – the elderly**. Br J Clin Pharmacol. 2015 Jan 24.
De Coninck L, Bekkering GE, Bouckaert L, et al. Home- and Community-Based **Occupational Therapy** Improves Functioning in Frail Older People: A Systematic Review. J Am Geriatr Soc. 2017 Apr 3.
Deprescribing Guideline and Algorithms (Benzodiazepine receptor agonits, Proton pump inhibitors, Antipsychotics, Antihyperglycemic) http://deprescribing.org/resources/deprescribing-guidelines-algorithms/
Doan J, Zakrzewski-Jakubiak H, Roy J, et al. Prevalence and risk of potential cytochrome p450-mediated **drug-drug interactions** in older hospitalized patients with polypharmacy. Ann Pharmacother. 2013 Mar;47(3):324-32.
Dolovich L, Oliver D, Lamarche L, et al. Combining **volunteers and primary care teamwork to support health goals and needs of older adults**: a pragmatic randomized controlled trial. CMAJ. 2019 May 6;191(18):E491-E500.
Dregan A, Ravindrarajah R, Hazra N, et al. Longitudinal Trends in **Hypertension** Management and Mortality Among Octogenarians:Prospective Cohort Study. (ELSA) Hypertension. 2016 May 9.
Drenth-van Maanen ACC, Wilting I, Jansen PPAF**. Prescribing medicines** to older people - How to consider the impact of ageing on human organ and body functions. Br J Clin Pharmacol. 2019 Aug 19.
Early NK, Fairman KA, Hagarty JM, Sclar DA. Joint effects of advancing age and number of potentially inappropriate **medication classes on risk of falls** in Medicare enrollees. BMC Geriatr. 2019 Jul 19;19(1):194
Edmans J, Bradshaw L, Franklin M, et al. **Specialist geriatric medical assessment** for patients discharged from hospital acute assessment units: randomised controlled trial. BMJ. 2013 Oct 8;347:f5874.

El-Sharkawy AM, Watson P, Neal KR, et al. **Hydration** and outcome in older patients admitted to hospital (The HOOP prospective cohort study). Age Ageing. 2015 Aug 26.
Ellam T, Twohig H, Khwaja A. **Chronic kidney disease in elderly people**: disease or disease label? BMJ. 2016 Jan 18;352:h6559.
Evans CJ, Ho Y, Daveson BA, et al; GUIDE_Care project. Place and **cause of death in centenarians**: a population-based observational study in England, 2001 to 2010. PLoS Med. 2014 Jun 3;11(6):e1001653.
Evans CS, Hunold KM, Rosen T, Platts-Mills TF. Diagnosis of **Elder Abuse** in U.S. Emergency Departments. J Am Geriatr Soc. 2016 Oct 18.
Fajardo MA, Weir KR, Bonner C, et al. Availability and readability of **patient education materials for deprescribing**: An environmental scan. Br J Clin Pharmacol. 2019 Mar 8.
Farmer C, Fenu E, O'Flynn N, et al. **Clinical assessment and management of multimorbidity**: summary of **NICE** guidance. BMJ. 2016 Sep 21;354:i4843
Farrell B, Merkley VF, Thompson W. **Managing polypharmacy** in a 77-year-old woman with multiple prescribers. CMAJ. 2013 Jul 15.
Farrell B, Monahan A, Ingar N. Identifying and managing **drug-related causes of common geriatric symptoms**. Can Fam Physician. 2014 Feb;60(2):147-53.
Farrell B, Monahan A, Thompson W. **Revisiting medication use in a frail 93-year-old man** experiencing possible adverse effects. CMAJ. 2014 Apr 1;186(6):445-9.
Farrell B, Eisener-Parsche P, Dalton D. Turning over the rocks: Role of **anticholinergics and benzodiazepines in cognitive decline** and falls. Can Fam Physician. 2014 Apr;60(4):345-50.
Farrell B, Shamji S, Ingar N. **Reducing fall risk** while managing hypotension, pain, and poor sleep in an 83-year-old woman. Can Fam Physician. 2013 Dec;59(12):1300-5
Farrell B, Monahan A, Dore N, et al. **Blood pressure targets in the very old**: Development of a tool in a geriatric day hospital. Can Fam Physician. 2014 Jul;60(7):e350-5.
Farrell B, Shamji S, Ingar N. Reducing fall risk while **managing pain and insomnia**: Addressing polypharmacy in an 81-year-old woman. Can Pharm J (Ott). 2013 Nov;146(6):335-41.
Farrell B, Tsang C, Raman-Wilms L, et al. What are **priorities for deprescribing for elderly patients**? Capturing the voice of practitioners: a modified delphi process. PLoS One. 2015 Apr 7;10(4):e0122246.
Farrell B, Pottie K, Rojas-Fernandez CH, Bjerre LM, Thompson W, Welch V. Methodology for developing **deprescribing guidelines**: using evidence and GRADE to guide recommendations for deprescribing. PLoS One. 2016;11:e0161248.
Farrell B, Black C, Thompson W, et al. **Deprescribing antihyperglycemic agents** in older persons: Evidence-based clinical practice guideline. Can Fam Physician. 2017 Nov;63(11):832-843.
Ferrante LE, Pisani MA, Murphy TE, Gahbauer EA, Leo-Summers LS, Gill TM. **Functional trajectories** among older persons before and after critical illness [online February 9, 2015]. JAMA Intern Med. doi:10.1001/jamainternmed.2014 .7889.
Fried TR, Niehoff KM, Street RL, et al. Effect of the Tool to Reduce **Inappropriate Medications** on Medication Communication and **Deprescribing**. J Am Geriatr Soc. 2017 Aug 14.
Fox C, Smith T, Maidment I, et al. Effect of medications with **anti-cholinergic properties on cognitive** function, delirium, physical function and mortality: a systematic review. Age Ageing. 2014 Jul 19. pii: afu096.
Fragala MS, Cadore EL, Dorgo S, et al. **Resistance Training** for Older Adults: Position Statement From the National Strength and Conditioning Association. J Strength Cond Res. 2019 Aug;33(8):2019-2052.
Frank C. **Deprescribing**: a new word to guide medication review. CMAJ. 2014 Apr 1;186(6):407-8.
Frank C, Weir E. **Deprescribing for older patients**. CMAJ. 2014 Dec 9;186(18):1369-1376.
Frank C, Wilson CR. **Models of primary care for frail patients**. Can Fam Physician. 2015 Jul;61(7):601-6.
Frankenthal D, Lerman Y, et al. Intervention with the **screening tool** of older persons potentially inappropriate prescriptions/screening tool to alert doctors to right treatment criteria in elderly residents of a chronic geriatric facility: a randomized clinical trial. J Am Geriatr Soc. 2014 Sep;62(9):1658-65.
Franklin BA, Brinks J, Sacks R, et al. **Reduced Walking Speed and Distance** as Harbingers of the Approaching Grim Reaper. Am J Cardiol. 2015 Jul 15;116(2):313-7.
Fraser LA, Adachi JD, Leslie WD, et al; for the CaMos Research Group. Effect of **Anticholinergic Medications** on Falls, Fracture Risk, and Bone Mineral Density Over a 10-Year Period. Ann Pharmacother. 2014 May 9;48(8):954-961.
Freak-Poli, De Castro Lima G, Direk N, et al. **Happiness, rather than depression**, is associated with **sexual behaviour** in partnered older adults. Age and Ageing. 2016;0:1-7.
Frenkel WJ, Jongerius EJ, Mandjes-van Uitert MJ, et al. Validation of the **charlson comorbidity index** in acutely hospitalized elderly adults: a prospective cohort study. J Am Geriatr Soc. 2014 Feb;62(2):342-6.
Gaddey HL, Holder K. **Unintentional weight loss** in older adults. Am Fam Physician. 2014 May 1;89(9):718-22.
Gao L, Maidment I, Matthews FE, et al; Medical Research Council Cognitive Function and Ageing Study. **Medication usage change in older people (65+) in England over 20 years: findings from CFAS I and CFAS II.** Age Ageing. 2017 Sep 26:1-6.
George C, Verghese J. **Polypharmacy and Gait Performance** in Community-dwelling Older Adults. J Am Geriatr Soc. 2017 Sep;65(9):2082-2087.
Godwin M, Pike A, McCrate F, et al. The healthy aged: Descriptive analysis by sex of **cognitively functioning** elderly patients 80 years and older living independently in the community. Can Fam Physician. 2015 Mar; 61(3):e142-7.
Goldberg SE, Bradshaw LE, Kearney FC, et al; Medical Crises in Older People Study Group. Care in **specialist medical and mental health unit compared with standard care** for older people with **cognitive impairment** admitted to general hospital: randomised controlled trial (NIHR TEAM trial). BMJ. 2013 Jul 2;347:f4132.
Gomm W, von Holt K, Thomé F, et al. Association of **proton pump inhibitors with risk of dementia**: a pharmacoepidemiological claims data analysis [online Feb 15, 2016].JAMA Neurol. doi:10.1001/jamaneurol.2015.4791.
Grad R, Thériault G, Singh H, et al. Age to stop? **Appropriate screening in older patients**. Can Fam Physician. 2019 Aug;65(8):543-548.
Gray SL, Anderson ML, Dublin S, et al. Cumulative use of **strong anticholinergics and incident dementia**: a prospective cohort study [online January 26, 2015]. JAMA Intern Med. doi:10.1001/jamainternmed.2014.7663.
Guerville F, de Souto Barreto P, Giudici KV, et al. Association of 3-Year Multidomain Intervention and Omega-3 **Supplementation with Frailty Incidence**. J Am Geriatr Soc. 2019 Jun 6.
Guidet B, Vallet H, Boddaert J, et al. **Caring for the critically ill patients over 80**: a narrative review. Ann Intensive Care. 2018 Nov 26;8(1):114.
Gulliford M, Ravindrarajah R, Hamada S, et al. **Inception and deprescribing of statins** in people aged over 80 years: cohort study. Age Ageing. 2017 Nov 1;46(6):1001-1005.
Gutiérrez-Valencia M, Izquierdo M, Cesari M, et al. The relationship between **frailty and polypharmacy** in older people: A systematic review. Br J Clin Pharmacol. 2018 Mar 25.
Haapanen MJ, Perälä MM, Salonen MK, et al. **Early life stress and frailty in old age**: the Helsinki birth cohort study. BMC Geriatr. 2018 Aug 13;18(1):179.
Halli-Tierney AD, Scarbrough C, Carroll D. **Polypharmacy: Evaluating Risks and Deprescribing**. Am Fam Physician. 2019; 100(1): 32-38.
Hamada S, Gulliford MC. Mortality in Individuals Aged 80 and Older with Type 2 Diabetes Mellitus in Relation to **Glycosylated Hemoglobin**, **Blood Pressure**, and **Total Cholesterol**. J Am Geriatr Soc. 2016 Jul;64(7):1425-31.

Hanlon JT, Semla TP, Schmader KE. **Alternative Medications** for Medications in the Use of High-Risk Medications in the Elderly and Potentially Harmful Drug-Disease Interactions in the Elderly Quality Measures. J Am Geriatr Soc. 2015 Oct 8.
Hazra NC, Dregan A, Jackson S, Gulliford MC. Differences in **Health at Age 100 According to Sex**: Population-Based Cohort Study of Centenarians Using Electronic Health Records. J Am Geriatr Soc. 2015 Jun 21.
Heath L, Gray SL, Boudreau DM, et al. **Cumulative Antidepressant Use and Risk of Dementia** in a Prospective Cohort Study. J Am Geriatr Soc. 2018 Sep 17.

Hewitt J, Carter B, McCarthy K, et al. Frailty predicts **mortality in all emergency surgical admissions** regardless of age. An observational study. Age Ageing. 2019 Feb 19.
Hippisley-Cox J, Coupland C. Development and validation of **QMortality risk prediction algorithm** to estimate short term risk of death and assess frailty: cohort study. BMJ 2017;358:j4208. doi:10.1136/bmj.j4208 pmid:28931509.
Hsu WH, Wen YW, Chen LK, Hsiao FY. Comparative Associations Between **Measures of Anti-cholinergic Burden** and Adverse Clinical Outcomes. Ann Fam Med. 2017 Nov;15(6):561-569.
Hu T, Dattani ND, Cox KA, et al. **Effect of comorbidities and medications** on frequency of primary care visits among older patients. Can Fam Physician. 2017 Jan;63(1):45-50.
Huang ES, Davis AM. **Glycemic Control** in Older Adults With Diabetes Mellitus. JAMA. 2015 Oct 13;314(14):1509-10.
Hubbard RE, Peel NM, Samanta M, Gray LC, Mitnitski A, Rockwood K. **Frailty status** at admission to hospital predicts **multiple adverse outcomes**. Age Ageing. 2017 May 22:1-6.
Jamerson BD, Fillenbaum GG, Sloane R, et al. A New Method of Identifying Characteristics of **Needing Help to Take Medications** in an Older Representative Community-Dwelling Population: The Older Adults Medication Assist Scale. J Am Geriatr Soc. 2016 Jun;64(6):1195-202.
James PA, Oparil S, Carter BL, et al. **2014** evidence-based guideline for the management of **high blood pressure in adults**: report from the panel members appointed to the Eighth Joint National Committee (**JNC 8**). JAMA. doi:10.1001/jama.2013.284427.
Jansen J, Naganathan V, Carter SM, et al. **Too much medicine in older people? Deprescribing** through shared decision making. BMJ. 2016 Jun 3;353:i2893.
Jay S, Whittaker P, Mcintosh J, Hadden N. Can consultant geriatrician led comprehensive **geriatric assessment** in the emergency department reduce **hospital admission rates**? A systematic review. Age Ageing. 2016 Dec 9.
Johansson T, Abuzahra ME, Keller S, et al. Impact of strategies to **reduce polypharmacy** on clinically relevant endpoints: a systematic review and meta-analysis. Br J Clin Pharmacol. 2016 Aug;82(2):532-48.
Kahlon S, Pederson J, Majumdar SR, et al. Association between **frailty and 30-day outcomes** after **discharge from hospital**. CMAJ. 2015 May 25.
Kalisch Ellett LM, Pratt NL, Ramsay EN, et al. **Multiple anticholinergic medication** use and risk of hospital admission for confusion or dementia. J Am Geriatr Soc. 2014 Oct;62(10):1916-22.
Kanaan AO, Donovan JL, Duchin NP, et al. **Adverse drug events** after hospital discharge in older adults: types, severity, and involvement of **Beers** Criteria Medications. J Am Geriatr Soc. 2013 Nov;61(11):1894-9.
Khodyakov D, Ochoa A, Olivieri-Mui BL, et al. **Screening Tool of Older Person's Prescriptions/Screening Tools to Alert Doctors** to Right Treatment Medication Criteria Modified for U.S. Nursing Home Setting. J Am Geriatr Soc. 2017 Mar;65(3):586-591.

Kheirbek RE, Fokar A, Shara N, et al. **Characteristics and Incidence of Chronic Illness** in Community-Dwelling Predominantly Male U.S. Veteran **Centenarians**. J Am Geriatr Soc. 2017 Apr 19.
Kirkman MS, Briscoe VJ, Clark N, et al. **Diabetes in older adults**. Diabetes Care. 2012 Dec;35(12):2650-64.
Kobayashi LC, Jackson SE, Lee SJ, et al. The development and validation of an **index to predict 10-year mortality risk** in a longitudinal cohort of older English adults. Age Ageing. 2016 Nov 3.
Kojima G, Iliffe S, Walters K. **Frailty index** as a predictor of mortality: a systematic review and meta-analysis. Age Ageing. 2017 Oct 13:1-8.
Kok RM, Reynolds CF 3rd. Management of Depression in Older Adults: A Review. JAMA. 2017 May 23;317(20):2114-2122.
Kouladjian L, Gnjidic D, Reeve E, et al. Health Care Practitioners' Perspectives on **Deprescribing Anticholinergic and Sedative** Medications in Older Adults. Ann Pharmacother. 2016 Aug;50(8):625-36.
Krishnaswami A, Steinman MA, Goyal P, et al; Geriatric Cardiology Section Leadership Council, American College of Cardiology. **Deprescribing in Older Adults With Cardiovascular Disease**. J Am Coll Cardiol. 2019 May 28;73(20):2584-2595.
Kuhn-Thiel AM, Weiß C, Wehling M; **FORTA** authors/expert panel members. **Consensus validation of the FORTA (Fit fOR The Aged) List**: a clinical tool for increasing the appropriateness of pharmacotherapy in the elderly. Drugs Aging. 2014 Feb;31(2):131-40.

Kulmala J, Ngandu T, Havulinna S, et al. The Effect of **Multidomain Lifestyle Intervention** on Daily Functioning in Older People. J Am Geriatr Soc. 2019 Feb 26.
Kumar C, Salzman B, Colburn JL. **Preoperative Assessment in Older Adults**: A Comprehensive Approach Am Fam Physician. 2018;98(4):214-220.
Kutner JS, Blatchford PJ, Taylor DH, et al. Safety and benefit of **discontinuing statin therapy** in the setting of advanced, life-limiting illness: a randomized clinical trial [online March 23, 2015]. JAMA InternMed. doi:10.1001/jamainternmed.2015.0289.
Lachs MS, Pillemer KA. **Elder Abuse**. N Engl J Med. 2015 Nov 12;373(20):1947-56.
Ladapo JA, Budoff MJ, Sharp D, et al. Utility of a **Precision Medicine Test** in Elderly Adults with Symptoms Suggestive of **Coronary Artery Disease**. J Am Geriatr Soc. 2017 Dec 6
LaMonte MJ, Buchner DM, Rillamas-Sun E, et al.**Accelerometer-Measured Physical Activity** and Mortality in Women Aged 63 to 99. J Am Geriatr Soc. 2017 Nov 16.
Lavan AH, Gallagher P, Parsons C, O'Mahony D. **STOPPFrail** (Screening Tool of Older Persons Prescriptions in Frail adults with limited life expectancy): consensus validation. Age Ageing. 2017 Jul 1;46(4):600-607.
Lee JK, Slack MK, Martin J, et al. Geriatric Patient Care by U.S. Pharmacists in Healthcare Teams: Systematic Review and Meta-Analyses. J Am Geriatr Soc. 2013 Jun 24.
Lee L, Heckman G, Molnar FJ. Frailty: Identifying elderly patients at **high risk of poor outcomes**. Can Fam Physician. 2015 Mar;61(3):227-231.
Lee L, Patel T, Costa A, et al. **Screening for frailty** in primary care: Accuracy of gait speed and hand-grip strength. Can Fam Physician. 2017 Jan;63(1):e51-e57.
Lee LO, James P, Zevon ES, et al. **Optimism is associated with exceptional longevity** in 2 epidemiologic cohorts of men and women. Proc Natl Acad Sci U S A. 2019 Aug 26.
Lee PG, Jackson EA, Richardson CR. **Exercise Prescriptions** in Older Adults. Am Fam Physician. 2017;95(7):425-432.
Lee SWH, Mak VSL, Tang YW. **Pharmacist services in nursing home**: A systematic review and meta-analysis. Br J Clin Pharmacol. 2019 Aug 29.
Leelakanok N, D'Cunha RR. Association between **polypharmacy and dementia** – A systematic review and meta-analysis. Aging Ment Health. 2018 May 10:1-10.
Leung AA, Daskalopoulou SS, Dasgupta K, et al. **Hypertension Canada's 2017 Guidelines for Diagnosis, Risk Assessment, Prevention, and Treatment of Hypertension in Adults**. Can J Cardiol. 2017 May;33(5):557-576 (**CHEP**)
Li Y, Pederson JL, Churchill TA, et al. Impact of **frailty on outcomes after discharge in older surgical patients**: a prospective cohort study. CMAJ 2018;190:E184-90.
Lipska KJ, Ross JS, Miao Y, et al. Potential **Overtreatment of Diabetes Mellitus in Older Adults** With Tight Glycemic Control. JAMA Intern Med. 2015 Jan 12.
Lipska KJ, Krumholz H, Soones T, et al. **Polypharmacy** in the Aging Patient: A Review of Glycemic Control in Older Adults With Type 2 Diabetes. JAMA. 2016 Mar 8;315(10):1034-45.
Lohman MC, Cotton BP, Zagaria AB, et al. **Hospitalization Risk and Potentially Inappropriate Medications** among **Medicare** Home Health Nursing Patients. J Gen Intern Med. 2017 Aug 28.
Lorgunpai SJ, Grammas M, Lee DS, et al. Potential therapeutic competition in community-living older adults in the u.s.: use of **medications that may adversely affect a coexisting condition**. PLoS One. 2014 Feb 25
Lu WH, Wen YW, Chen LK, et al. Effect of **polypharmacy, potentially inappropriate medications and anticholinergic burden** on clinical outcomes: a retrospective cohort study. CMAJ. 2015 Mar 3; 187(4):E130-7.
Lundby C, Graabaek T, Ryg J, et al. Health care professionals' **attitudes towards deprescribing** in older patients with limited life expectancy: a systematic review. Br J Clin Pharmacol. 2019 Jan 10
Luymes CH, Poortvliet RKE, van Geloven N, et al. **Deprescribing preventive cardiovascular medication** in patients with predicted **low cardiovascular disease risk** in general practice – the **ECSTATIC study**: a cluster randomised non-inferiority trial. BMC Med. 2018 Jan 11;16(1):5.
Maclagan LC, Maxwell CJ, Gandhi S, et al. **Frailty and Potentially Inappropriate Medication** Use at Nursing Home Transition. J Am Geriatr Soc. 2017 Oct;65(10):2205-2212.
Makam AN, John Boscardin W, Miao Y, et al. Risk of **Thiazide-Induced Metabolic Adverse Events in Older Adults**. J Am Geriatr Soc. 2014 May 13.
Mallery LH, Allen M, Fleming I, et al. Promoting higher **blood pressure targets for frail older adults**: A consensus guideline from Canada. Cleve Clin J Med. 2014 Jul;81(7):427-437.
Malmstrom TK, Miller DK, Morley JE. A Comparison of **Four Frailty Models**. J Am Geriatr Soc. 2014 Mar 17.
Makris UE, Abrams RC, Gurland B, et al. Management of **persistent pain** in the older patient: a clinical review. JAMA. 2014 Aug 27;312(8):825-36.
Marcum ZA, Perera S, Thorpe JM, et al; Health ABC Study, USA. **Anticholinergic Use and Recurrent Falls** in Community-Dwelling Older Adults: Findings From the Health ABC Study. Ann Pharmacother. 2015 Nov;49(11):1214-21.
Markovitz AA, Hofer TP, Froehlich W, et al. An Examination of **Deintensification Recommendations** in Clinical Practice Guidelines: **Stepping Up or Scaling Back**? JAMA Intern Med. 2017 Dec 18.
Martin P, Tamblyn R, Ahmed S, Tannenbaum C. An **educational intervention to reduce the use of potentially inappropriate medications among older adults (EMPOWER** study): protocol for a cluster randomized trial. Trials. 2013 Mar 20;14:80.
Martin P, Tamblyn R, Benedetti A, et al. Effect of a **Pharmacist-Led Educational Intervention on Inappropriate Medication Prescriptions in Older Adults**: The **D-PRESCRIBE** Randomized Clinical Trial. JAMA. 2018 Nov 13;320(18):1889-1898.
Martinez-Velilla N, Casas-Herrero A, Zambom-Ferraresi F, et al. Effect of **Exercise Intervention on Functional Decline in Very Elderly Patients During Acute Hospitalization**: A Randomized Clinical Trial. JAMA Intern Med. 2018 Nov 12.
Maust DT, Gerlach LB, Gibson A, et al. **Trends in Central Nervous System-Active Polypharmacy** Among Older Adults Seen in Outpatient Care in the United States. JAMA Intern Med. 2017 Feb 13.
McCartney M. Margaret McCartney: Drugs with **anticholinergic side effects** and cognitive decline-cause or effect? BMJ. 2015 Mar 16;350:h1428.
McIntyre C, McQuillan R, Bell C, Battistella M. **Targeted Deprescribing** in an Outpatient **Hemodialysis** Unit: A Quality Improvement Study to Decrease Polypharmacy. Am J Kidney Dis. 2017 Nov;70(5):611-618.
McIsaac DI, Bryson GL, van Walraven C. Association of **Frailty** and 1-Year **Postoperative Mortality** Following **Major Elective Noncardiac Surgery**: A Population-Based Cohort Study. JAMA Surg. 2016 Jan 20.
Meid AD, Lampert A, Burnett A, et al. The impact of **pharmaceutical care interventions for medication underuse in older people**: a systematic review and meta-analysis. Br J Clin Pharmacol. 2015 Apr 13.
Merel SE, Paauw DS. **Common Drug Side Effects and Drug-Drug Interactions** in Elderly Adults in Primary Care. J Am Geriatr Soc. 2017 Jul;65(7):1578-1585.
Metzelthin SF, van Rossum E, de Witte LP, et al. Effectiveness of **interdisciplinary primary care approach** to reduce disability in community dwelling frail older people: cluster randomised controlled trial. BMJ. 2013 Sep 10;347:f5264.
Mieiro L, Beuscart JB, Knol W, et al. **Achieving appropriate medication** for older adults: A multidimensional perspective. Maturitas. 2019 Jun;124:43-47.
Mohanty S, Rosenthal RA, Russell MM, et al. **Optimal Perioperative Management** of the Geriatric Patient: A Best Practices Guideline from the **American** College of Surgeons NSQIP and the American Geriatrics Society. J Am Coll Surg. 2016 Jan 4
Montero-Odasso M, Sarquis-Adamson Y, Song HY, et al. **Polypharmacy, Gait Performance, and Falls** in Community-Dwelling Older Adults. Results from the Gait and Brain Study. J Am Geriatr Soc. 2019 Jun;67(6):1182-1188.

Moonen JE, Foster-Dingley JC, de Ruijter W, et al. Effect of **Discontinuation of Antihypertensive Treatment in Elderly People on Cognitive** Functioning-the DANTE Study Leiden: A Randomized Clinical Trial. JAMA Intern Med. 2015 Aug 24.
Morandi A, Vasilevskis E, Pandharipande PP, et al. **Inappropriate medication prescriptions** in elderly adults surviving an intensive care unit hospitalization. J Am Geriatr Soc. 2013 Jul;61(7):1128-34.

Morgan SG, Weymann D, Pratt B, et al. **Sex differences in the risk of receiving potentially inappropriate prescriptions** among older adults. Age Ageing. 2016 May 5.
Morgan SG, Hunt J, Rioux J, et al. Frequency and cost of potentially **inappropriate prescribing** for older adults: a cross-sectional study. CMAJ Open. 2016 Jun 22;4(2):E346-51.

Moriarty F, Bennett K, Cahir C, et al. Potentially inappropriate prescribing according to **STOPP and START and adverse outcomes in community-dwelling older people**: a prospective cohort study. Br J Clin Pharmacol. 2016 May 2
Morin L, Fastbom J, Laroche ML, et. al, **Potentially inappropriate drug use in older people**: a nationwide comparison of different explicit criteria for population-based estimates. Br J Clin Pharmacol. 2015 Feb 22.
Morin L, Vetrano DL, Rizzuto D, et al. Choosing Wisely? Measuring the **Burden of Medications in Older Adults near the End of Life**: Nationwide, Longitudinal Cohort Study. Am J Med. 2017 Apr 25.
Morin L, Wastesson JW, Laroche ML, et al. How many older adults receive **drugs of questionable clinical benefit near the end of life**? A cohort study. Palliat Med. 2019 Jun 7:269216319854013.
Mortensen MB, Falk E. **Primary Prevention With Statins in the Elderly**. J Am Coll Cardiol. 2018 Jan 2;71(1):85-94.
Mossello E, Pieraccioli M, Nesti N, et al. Effects of **Low Blood Pressure in Cognitively Impaired Elderly Patients Treated With Antihypertensive Drugs**. JAMA Intern Med. 2015 Mar 2.
Mousa A, Savva GM, Mitnitski A, et al. **Is frailty a stable predictor of mortality across time**? Evidence from the Cognitive Function and Ageing Studies. Age Ageing. 2018 Jun 6.

Mrdutt MM, Papaconstantinou HT, Robinson BD, et al. Preoperative **Frailty and Surgical Outcomes** Across Diverse Surgical Subspecialties in a Large Health Care System. J Am Coll Surg. 2019 Apr;228(4):482-490.
Murad MH, Larrea-Mantilla L, Haddad A, et al. **Antihypertensive Agents** in Older Adults: A Systematic Review and Meta-Analysis of Randomized Clinical Trials. J Clin Endocrinol Metab. 2019 May 1;104(5):1575-1584.
Myint PK, Fox C, Kwok CS, et al. Total **anticholinergic burden and risk of mortality and cardiovascular disease** over 10 years in 21,636 middle-aged and older men and women of EPIC-Norfolk prospective population study. Age Ageing. 2014 Nov 27.

Narayan SW, Pearson SA, Litchfield M, et al **Anticholinergic medicines** use among older adults before and after initiating dementia medicines. Br J Clin Pharmacol. 2019 May 2.
Neri SG, Cardoso JR, Cruz L, et al. Do **virtual reality games** improve **mobility skills and balance** measurements in community-dwelling older adults? Systematic review and meta-analysis. Clin Rehabil. 2017 Oct;31(10):1292-1304.

Ng TP, Feng L, Nyunt MS, et al. **Nutritional, Physical, Cognitive, and Combination Interventions and Frailty Reversal** Among Older Adults: A Randomized Controlled Trial. Am J Med. 2015 Jul 6.
Ng TP, Feng L, Nyunt MS, et al. **Nutritional, Physical, Cognitive, and Combination Interventions** and **Frailty** Reversal Among Older Adults: A Randomized Controlled Trial. Am J Med. 2015 Jul 6.
Ní Chróinín D, Ní Chróinín C, Beveridge A. **Factors influencing deprescribing** habits among geriatricians. Age Ageing. 2015 Mar 10.
Nightingale G, Hajjar E, Swartz K, et al. Evaluation of a **Pharmacist-Led Medication Assessment** Used to Identify Prevalence of and Associations With Polypharmacy and Potentially Inappropriate Medication Use Among Ambulatory Senior Adults With Cancer. J Clin Oncol. 2015 Mar 23.
Nijsten JMH, Leontjevas R, Pat-El R, et al. **Apathy**: Risk Factor for Mortality in Nursing Home Patients. J Am Geriatr Soc. 2017 Aug 9.

O'Connell J, Burke E, Mulryan N, et al. **Drug Burden Index** to Define the Burden of Medicines in Older Adults **with Intellectual Disabilities**: An Observational Cross-Sectional Study. Br J Clin Pharmacol. 2017 Nov 29.
O'Mahony D, O'Sullivan D, Byrne S, et al. **STOPP/START** criteria for potentially inappropriate prescribing in older people: **version 2**. Age Ageing. 2014 Oct 16.
Ofori-Asenso R, Chin KL, Mazidi M, et al. Global Incidence of **Frailty and Prefrailty** Among Community-Dwelling Older Adults: A Systematic Review and Meta-analysis. JAMA Netw Open. 2019 Aug 2;2(8):e198398.
Ogliari G, Mahinrad S, Stott DJ, et al. **Resting heart rate, heart rate variability** and functional decline in old age. CMAJ. 2015 Aug 31.
O'Mahony D, O'Sullivan D, Byrne S, O'Connor MN, Ryan C, Gallagher P. **STOPP/START criteria** for potentially inappropriate prescribing in older people: **version 2**. Age Ageing. 2015 Mar;44(2):213-8.
Onder G, Marengoni A. **Polypharmacy. (Patient information)** JAMA. 2017 Nov 7;318(17):1728.
Oresanya LB, Lyons WL, Finlayson E. **Preoperative assessment** of the older patient: a narrative review. JAMA. 2014 May 28;311(20):2110-20.
Page AT, Clifford RM, Potter K, Schwartz D, Etherton-Beer CD. The **feasibility and effect of deprescribing in older adults** on mortality and health: a systematic review and meta-analysis. Br J Clin Pharmacol. 2016;82:583-623.
Parsons C, Hughes CM, Passmore AP, Lapane KL. **Withholding, discontinuing and withdrawing medications in dementia patients** at the end of life: a neglected problem in the disadvantaged dying? Drugs Aging. 2010 Jun 1;27(6):435-49.
Partridge JS, Harari D, Martin FC, et al. Randomized clinical trial of **comprehensive geriatric assessment** and optimization in vascular surgery. Br J Surg. 2017 Feb 15.
Patel T, Slonim K, Lee L. Use of **potentially inappropriate medications among ambulatory home-dwelling elderly patients with dementia**: A review of the literature. Can Pharm J (Ott). 2017 May 1;150(3):169-183.
Patterson SM, Hughes C, Kerse N, Cardwell CR, Bradley MC. Interventions to **improve the appropriate use of polypharmacy** for older people. Cochrane Database of Systematic Reviews 2012, Issue 5. Art. No.: CD008165.
Pérez T, Moriarty F, Wallace E, et al. Prevalence of **potentially inappropriate prescribing in older people in primary care and its association with hospital admission**: longitudinal study. BMJ. 2018 Nov 14;363:k4524.

Pighills A, Drummond A, Crossland S, Torgerson DJ. What type of **environmental assessment and modification prevents falls** in community dwelling older people? BMJ. 2019 Mar 14;364:l880.
Pilotto A, Gallina P, Panza F, et al.Relation of **Statin Use and Mortality** in Community-Dwelling Frail Older Patients With Coronary Artery Disease. Am J Cardiol. 2016 Dec 1;118(11):1624-1630.
Pinto JM, Wroblewski KE, Huisingh-Scheetz M, et al. **Global Sensory Impairment** Predicts Morbidity and Mortality in Older U.S. Adults. J Am Geriatr Soc. 2017 Sep 24.
Ploeg J, Matthew-Maich N, Fraser K, et al. **Managing multiple chronic conditions in the community**: a **Canadian qualitative study of the experiences of older adults**, family caregivers and healthcare providers. BMC Geriatr. 2017;17:40.
Pont LG, Nielen JT, McLachlan AJ, et al. Measuring **anticholinergic drug exposure** in older community-dwelling Australian men: a comparison of four different measures. Br J Clin Pharmacol. 2015 Apr 28.
Potter K, Flicker L, Page A, Etherton-Beer C. **Deprescribing in Frail Older People**: A Randomised Controlled Trial. PLoS One. 2016 Mar 4;11(3):e0149984.
Pottie K, Thompson W, Davies S, et al. **Deprescribing benzodiazepine receptor agonists**: Evidence-based clinical practice guideline. Can Fam Physician. 2018 May;64(5):339-351.
Poudel A, Peel NM, Nissen L, et al. Potentially **inappropriate prescribing** in older patients discharged from **acute care hospitals to residential aged care facilities**. Ann Pharmacother. 2014 Nov;48(11):1425-33.
Poudel A, Peel NM, Mitchell CA, et al. **Geriatrician interventions on medication prescribing for frail** older people in residential aged care facilities. Clin Interv Aging. 2015 Jun 25;10:1043-51.
Price SD, Holman CD, Sanfilippo FM, et al. Association between potentially inappropriate medications from the **beers criteria and the risk of unplanned hospitalization** in elderly patients. Ann Pharmacother. 2014 Jan;48(1):6-16
Qaseem A, Wilt TJ, Rich R, et al. Pharmacologic treatment of **hypertension in adults aged 60 years or older to higher versus lower blood pressure targets**: a clinical practice guideline from the American College of Physicians (**ACP**) and the American Academy of Family Physicians (**AAFP**). Ann Intern Med. 2017. [Epub ahead of print]. doi:10.7326/M16-1785
Qato DM, Wilder J, Schumm LP, et al. **Changes in Prescription and Over-the-Counter Medication and Dietary Supplement Use** Among Older Adults in the United States, 2005 vs 2011. JAMA Intern Med. 2016 Apr 1
Quinn TJ, Mooijaart SP, Gallacher K, Burton JK. **Acute care assessment of older adults living with frailty**. BMJ. 2019 Jan 31;364:l13.
Raimbault-Chupin M, Spiesser-Robelet L, Guir V, et al. Drug related problems and **pharmacist interventions** in a geriatric unit employing electronic prescribing. Int J Clin Pharm 2013. Published online July 16, 2013.
Ramaswamy R. **Complex care: treating an older patient with multiple comorbidities**. Am Fam Physician. 2014 Mar 1;89(5):392-4.

Raschi E, Piccinni C, Signoretta V, et al; Emilia-Romagna elderly poly-treated patients research group. Clinically important **drug-drug interactions in poly-treated elderly outpatients**: a campaign to improve appropriateness in General Practice. Br J Clin Pharmacol. 2015 Aug 25.
Reeve E, Farrell B, Thompson W, et al. **Deprescribing cholinesterase inhibitors and memantine in dementia**: guideline summary. Med J Aust. 2019 Mar;210(4):174-179.
Reeve E, Gnjidic D, Long J, et al. A systematic review of the emerging definition of **'deprescribing'** with network analysis: implications for future research and clinical practice. Br J Clin Pharmacol. 2015 Dec
Reeve E, Low LF, Hilmer SN. **Attitudes of Older Adults and Caregivers in Australia toward Deprescribing**. J Am Geriatr Soc. 2019 Jun;67(6):1204-1210.
Reeve E, Wolff JL, Skehan M, et al. Assessment of Attitudes Toward **Deprescribing in Older Medicare Beneficiaries** in the United States. JAMA Intern Med. 2018 Oct 15.
Reid MC, Eccleston C, Pillemer K. Management of **chronic pain** in older adults. BMJ. 2015 Feb 13;350:h532.
Richardson KFox CMaidment I. **Anticholinergic drugs and risk of dementia**: case-control study. BMJ 2018;361:k1315.
Rippon I, Steptoe A. **Feeling Old vs Being Old**: Associations Between Self-perceived Age and Mortality. JAMA Intern Med. 2014 Dec 15.
Risacher SL, McDonald BC, Tallman EF, et al. Alzheimer's Disease Neuroimaging Initiative. Association Between **Anticholinergic Medication Use and Cognition**, Brain Metabolism, and Brain Atrophy in Cognitively Normal Older Adults. JAMA Neurol. 2016 Apr 18.
Roller-Wirnsberger R, Thurner B, Pucher C, et al. The clinical and **therapeutic challenge of treating older patients** in clinical practice. Br J Clin Pharmacol. 2019 Jul 19.
Ruxton K, Woodman RJ, Mangoni AA. Drugs with **anticholinergic effects and cognitive impairment, falls and all-cause mortality** in older adults: a systematic review and meta-analysis. Br J Clin Pharmacol. 2015 Mar 2.
Salahudeen MS, Duffull SB, Nishtala PS. **Anticholinergic burden quantified by anticholinergic risk scales** and adverse outcomes in older people: a systematic review. BMC Geriatr. 2015 Mar 25;15:31
Savarese G, Gotto AM Jr, Paolillo S, et al. Benefits Of **Statins In Elderly** Subjects Without Established Cardiovascular Disease. A Meta-Analysis. J Am Coll Cardiol. 2013 Aug 14.
Schonberg MA, Li V, Marcantonio ER, Davis RB, McCarthy EP. **Predicting Mortality** up to 14 Years Among Community-Dwelling Adults Aged 65 and Older. J Am Geriatr Soc. 2017 Feb 21.
Scholl S, Dellon ES, Shaheen NJ. Treatment of **GERD and proton pump inhibitor use in the elderly**: practical approaches and frequently asked questions. Am J Gastroenterol. 2011 Mar;106(3):386-92.
Schuster BG, Kosar L, Kamrul R. **Constipation in older adults**: Stepwise approach to keep things moving. Can Fam Physician. 2015 Feb;61(2):152-8.
Scott IA, Gray LC, Martin JH, Pillans PI, Mitchell CA. Deciding when to stop: towards evidence-based **deprescribing** of drugs in older populations. Evid Based Med. 2013 Aug;18(4):121-4.
Scott IA, Hilmer SN, Reeve E, et al. Reducing Inappropriate Polypharmacy: The Process of **Deprescribing**. JAMA Intern Med. 2015 Mar 23.
Shahrokni A, Tin A, Alexander K, et al. Development and evaluation of a **new frailty index for older surgical patients with cancer.** JAMA Netw Open. 2019;2(5):e193545. doi:10.1001/jamanetworkopen.2019.3545
Shimura T, Yamamoto M, Kano S, et al. On behalf of the **OCEAN-TAVI** Investigators. Impact of the **clinical frailty scale on outcomes after transcatheter aortic valve replacement**. Circulation. 2017;135:2013–2024.
Shrestha S, Poudel A, Steadman K, Nissen L. **Outcomes of deprescribing interventions** in older patients with life-limiting illness and limited life expectancy: a systematic review. Br J Clin Pharmacol. 2019 Sep 4.
Simonsick EM, Schrack JA, Santanasto AJ, et al. **Pittsburgh Fatigability Scale:** One-Page Predictor of **Mobility Decline in Mobility-Intact Older Adults.** J Am Geriatr Soc. 2018 Oct 13.
Smith GI, Julliand S, Reeds DN, et al. **Fish oil-derived n-3 PUFA therapy** increases muscle mass and function in healthy older adults. Am J Clin Nutr. 2015 May 20.
Srikanthan P, Karlamangla AS. **Muscle Mass Index** as a Predictor of Longevity in Older-Adults. Am J Med. 2014 Feb 18.
Spence MM, Karim FA, Lee EA, et al. **Risk of Injury in Older Adults Using Gastrointestinal Antispasmodic and Anticholinergic Medications**. J Am Geriatr Soc. 2015 Jun;63(6):1197-202.
St John PD, Tyas SL, Menec V, et al. **Multimorbidity, disability, and mortality in community-dwelling** older adults. Can Fam Physician. 2014 May;60(5):e272-80.
Stall N, Nowaczynski M, Sinha SK. Systematic review of **outcomes from home-based primary care** programs for homebound older adults. J Am Geriatr Soc. 2014 Dec;62(12):2243-51.

Stall NM, Savage RD, Rochon PA. **Loneliness** in older adults. CMAJ. 2019 Apr 29;191(17):E476.
Steffens NK, Cruwys T, Haslam C, et al. **Social group memberships** in retirement are associated with reduced risk of premature death: evidence from a longitudinal cohort study. BMJ Open. 2016 Feb 16;6(2):e010164.
Steffens NM, Tucholka JL, Nabozny MJ, Schmick et al. Engaging Patients, Health Care Professionals, and Community Members to Improve **Preoperative Decision Making** for Older Adults Facing High-Risk Surgery. JAMASurg. 2016 Jun 29

Steinman MA, Beizer JL, DuBeau CE, et al. How to Use the American Geriatrics Society **2015 Beers Criteria-A Guide for Patients**, Clinicians, Health Systems, and Payors. J Am Geriatr Soc. 2015 Oct 8.
Steinman MA, Zullo AR, Lee Y, et al. Association of **β-blockers with functional outcomes, death, and rehospitalization in older nursing home residents after acute myocardial infarction** [online Dec 12, 2016].JAMA Intern Med. doi:10.1001/jamainternmed.2016.7701
Stenzelius K, Molander U, Odeberg J, et al. The effect of **conservative treatment of urinary incontinence among older and frail** older people: a systematic review. Age Ageing. 2015 Jun 25.
Stuck AE, Moser A, Morf U, et al. Effect of **Health Risk Assessment and Counselling** on Health Behaviour and Survival in Older People: A Pragmatic Randomised Trial. PLoS Med. 2015 Oct 19;12(10):e1001889.
Szabo SM, Gooch K, Schermer C, et al. Association between **cumulative anticholinergic burden and falls and fractures in patients with overactive bladder**: US-based retrospective cohort study. BMJ Open. 2019 May 5;9(5):e026391.
Tannenbaum C, Paquette A, Hilmer S, et al. A systematic review of **amnestic and non-amnestic mild cognitive impairment induced by anticholinergic, antihistamine, GABAergic and opioid drugs**. Drugs Aging. 2012 Aug 1;29(8):639-58.
Tannenbaum C, Martin P, Tamblyn R, et al. **Reduction of Inappropriate Benzodiazepine** Prescriptions Among Older Adults Through Direct Patient Education: The **EMPOWER** Cluster Randomized Trial. JAMA Intern Med. 2014 Apr 14.
Tazkarji B, Lam R, Lee S, et al. Approach to **preventive care in the elderly**. Can Fam Physician. 2016 Sep;62(9):717-21.
Tessier DM, Meneilly GS. **Diabetes in an older woman living in a long-term care** residence. CMAJ. 2015 Mar 3; 187(4):269-71.
Theou O, Blodgett JM, Godin J, et al. Association between **sedentary time and mortality across levels of frailty**. CMAJ. 2017 Aug 21;189(33):E1056-E1064
Thevelin S, Spinewine A, Beuscart JB, et al. Development of a Standardized Chart Review Method to Identify Drug-Related Hospital Admissions in Older People. Br J Clin Pharmacol. 2018 Jul 14.
Thio SL, Nam J, van Driel ML, et al. Effects **of discontinuation of chronic medication in primary care**: a systematic review of deprescribing trials. Br J Gen Pract. 2018 Oct;68(675):e663-e672.
Thomas R, Huntley AL, Mann M, et al. **Pharmacist-led interventions** to reduce unplanned admissions for older people: a systematic review and meta-analysis of randomised controlled trials. Age Ageing. 2014 Mar;43(2):174-87.

Thompson W, Lundby C, Graabaek T, et al. Tools for **Deprescribing** in Frail Older Persons and Those with Limited Life Expectancy: A Systematic Review. J Am Geriatr Soc. 2019 Jan;67(1):172-180.
Tignanelli CJ, Napolitano LM. The **Fragility Index** in Randomized Clinical Trials as a Means of **Optimizing Patient Care**. JAMA Surg. 2018 Nov 7
Tjia J, Briesacher BA, Peterson D, Liu Q, Andrade SE,Mitchell SL. Use of medications of **questionable benefit in advanced dementia** [online September 8, 2014]. JAMA Intern Med.
Tjia J, Cutrona SL, Peterson D, et al. **Statin discontinuation** in nursing home residents with advanced **dementia**. J Am Geriatr Soc. 2014 Nov;62(11):2095-101.
Tinetti ME, McAvay G, Trentalange M, et al. Association between guideline recommended drugs and death in older adults with multiple chronic conditions: population based cohort study. BMJ 2015;351:h4984
Tosato M, Landi F, Martone AM, et al. on behalf of Investigators of the **CRIME** Study. **Potentially inappropriate drug use** among hospitalised older adults: results from the CRIME study. Age Ageing. 2014 Mar 17.
Tracy B, Morrison RS. **Pain management** in olderadults. Clin Ther. 2013;35:XXX–XXX. 22.
Trombetti A, Hars M, Hsu FC, et al. Effect of **physical activity on frailty**. Secondary analysis of a randomized controlled trial. Ann Intern Med. 2017.
Tsugawa Y, Newhouse JP, Zaslavsky AM, et al. **Physician age and outcomes in elderly patients** in hospital in the US: observational study. BMJ. 2017 May 16;357:j1797.
Turner JP, Tannenbaum C. **Older Adults' Awareness of Deprescribing**: A Population-Based Survey. J Am Geriatr Soc. 2017 Sep 15.
Umpierrez GE, Pasquel FJ. **Management of Inpatient Hyperglycemia and Diabetes** in Older Adults. Diabetes Care. 2017 Apr;40(4):509-517.
van der Cammen TJ, Rajkumar C, Onder G, et al. **Drug cessation** in complex older adults: time for action. Age Ageing. 2013 Nov 12.
van Walraven C, McAlister FA, Bakal JA, et al. External validation of the **Hospital-patient One-year Mortality Risk (HOMR)** model for predicting death within 1 year after hospital admission. CMAJ. 2015 Jun 8.
Varenne O, Cook S, Sideris G, et al. **Drug-eluting stents in elderly** patients with coronary artery disease (**SENIOR**): a randomised single-blind trial. Lancet. 2017 Oct 31.
Varga S, Alcusky M, Keith SW, et al. **Hospitalization Rates** during Potentially **Inappropriate Medication Use** in a Large Population-Based Cohort of Older Adults. Br J Clin Pharmacol. 2017 Jul 1.
Voukelatos A, Merom D, Sherrington C, et al. The impact of a **home-based walking programme on falls** in older people: the Easy Steps randomised controlled trial. Age Ageing. 2015 May;44(3):377-83.
Wallace E, Salisbury C, Guthrie B, et al. **Managing patients with multimorbidity** in primary care. BMJ. 2015 Jan 20;350:h176.
Wallerstedt SM, Kindblom JM, Nylén K, et al. **Medication reviews** for nursing home residents to reduce mortality and hospitalisation: Systematic review and meta-analysis. Br J Clin Pharmacol. 2014 Feb 18.
Wallis SJ, Wall J, Biram RW, et al. Association of the **clinical frailty scale** with hospital outcomes. QJM. 2015 Mar 15.
Walsh CA, Cahir C, Tecklenborg S, et al. The association between **medication non-adherence and adverse health outcomes** in ageing populations: A systematic review and meta-analysis. Br J Clin Pharmacol. 2019 Sep 4.
Wauters M, Elseviers M, Vaes B, et al. Too many, too few, or too unsafe? Impact of **inappropriate prescribing** on mortality, and hospitalisation in a cohort of community-dwelling oldest old. Br J Clin Pharmacol. 2016 Jul 18.
Wehling M, Burkhardt H, Kuhn-Thiel A, et al. **VALFORTA**: a randomised trial to validate the **FORTA (Fit fOR The Aged)** classification. Age Ageing. 2016 Mar;45(2):262-7.
Weiss J, Freeman M, et al. **Benefits and harms of intensive blood pressure treatment in adults aged 60 years or older**: a systematic review and meta-analysis. Ann Intern Med. 2017. [Epub ahead of print]. doi:10.7326/M16-1754 3.
Werner RM, Coe NB, Qi M, Konetzka RT. Patient outcomes after **hospital discharge to home with home health care vs to a skilled nursing facility** [online Mar 11, 2019]. JAMA Intern Med.doi:10.1001/jamainternmed.2018.7998
Welk B, McArthur E, Fraser L-A, et al. The risk of **fall and fracture with the initiation of a prostate-selective α antagonist (tamsulosin...):** a population based cohort study. BMJ 2015;351:h5398.
Willeboordse F, Schellevis FG, Chau SH, et al. The effectiveness of **optimised clinical medication reviews for geriatric patients: Opti-Med** a cluster randomised controlled trial. Fam Pract. 2017 Feb 23.
Wilson AH, Kidd AC, Skinner J, et al. A simple 5-point scoring system, **NaURSE** (Na+, Urea, Respiratory Rate and Shock Index in the Elderly), **predicts in-hospital mortality in oldest old**. Age Ageing. 2014 Jan 31.
Wilson E, Caswell G, Turner N, Pollock K. **Managing Medicines for Patients Dying at Home**: A Review of Family Caregivers' Experiences. J Pain Symptom Manage.2018 Dec;56(6):962-974.
Wimmer BC, Bell JS, Fastbom J, et al. **Medication Regimen Complexity and Polypharmacy** as Factors Associated With All-Cause Mortality in Older People: A Population-Based Cohort Study. Ann Pharmacother. 2015 Dec 17.
Wolff A, Stuckler D, McKee M. Are patients admitted to hospitals from **care homes dehydrated**? A retrospective analysis of hypernatraemia and in-hospital mortality. J R Soc Med. 2015 Jan 15.
Wood S, Petty D, Glidewell L, Raynor DT. Application of **prescribing recommendations in older people with reduced kidney function**: a cross-sectional study in general practice. Br J Gen Pract. 2018 May;68(670):e378-e387.
Wouters H;Scheper J;Koning H;Brouwer C;Twisk JW;va **Discontinuing Inappropriate Medication Use in Nursing Home Residents**: A Cluster Randomized Controlled Trial**.** Ann Intern Med. 2017 Oct 10. (3MR, STOPP & Beers)
Yudi MB, Jones N, Fernando D, et al. Management of Patients Aged ≥85 Years With ST-Elevation **Myocardial Infarction**. Am J Cardiol. 2016 Jul 1;118(1):44-8.
Zaninotto P, Steptoe A. Association Between **Subjective Well-being and Living Longer Without Disability or Illness**. JAMA Netw Open. 2019 Jul 3;2(7):e196870.

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LTC-Elderly-Pearls Chart: References

[1] Gallagher P, O'Mahony D. STOPP (Screening Tool of Older Persons' potentially inappropriate Prescriptions): application to acutely ill elderly patients and comparison with Beers' criteria. Age Ageing. 2008 Nov;37(6):673-9.
O'Mahony D, O'Sullivan D, Byrne S, O'Connor MN, Ryan C, Gallagher P. STOPP/START criteria for potentially inappropriate prescribing in older people: version 2. Age Ageing. 2015 Mar;44(2):213-8.

[2] The American Geriatrics Society 2012 Beers Criteria Update Expert Panel. American Geriatrics Society Updated Beers Criteria for Potentially Inappropriate Medication Use in Older Adults. J Am Geriatr Soc. 2012 Apr;60(4):616-631.
American Geriatrics Society 2015 Beers Criteria Update Expert Panel. American Geriatrics Society 2015 Updated Beers Criteria for Potentially Inappropriate Medication Use in Older Adults. J Am Geriatr Soc. 2015 Oct 8.
Hanlon JT, Semla TP, et al. Alternative Medications for Medications in the Use of High-Risk Medications in the Elderly and Potentially Harmful Drug-Disease Interactions in the Elderly Quality Measures. J Am Geriatr Soc. 2015 Oct 8.
Steinman MA, Beizer JL, DuBeau CE, et al. How to Use the American Geriatrics Society 2015 Beers Criteria-A Guide for Patients, Clinicians, Health Systems, and Payors. J Am Geriatr Soc. 2015 Oct 8.
2019 American Geriatrics Society Beers Criteria® Update Expert Panel. American Geriatrics Society 2019 Updated AGS Beers Criteria® for Potentially Inappropriate Medication Use in Older Adults. J Am Geriatr Soc. 2019 Jan 29.

[3] Bell AD, Roussin A, Cartier R, Chan WS, Douketis JD, Gupta A, et al. The use of antiplatelet therapy in the outpatient setting: Canadian Cardiovascular Society Guidelines Executive Summary. Can J Cardiol. 2011 Mar-Apr;27(2):208-21.
McNeil JJ, Wolfe R, Woods RL, et al; ASPREE Investigator Group. Effect of Aspirin on Cardiovascular Events and Bleeding in the Healthy Elderly. N Engl J Med. 2018 Oct 18;379(16):1509-1518.
[4] Guyatt GH, Akl EA, Crowther M, Gutterman DD, Schuünemann HJ; American College of Chest Physicians Antithrombotic Therapy and Prevention of Thrombosis Panel. Executive summary: Antithrombotic Therapy and Prevention of Thrombosis, 9th ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines. Chest. 2012 Feb;141(2 Suppl):7S-47S.
[5] RxFiles. Reference List of Drugs with Anticholinergic Effects. Accessed 04 Apr 2012 at http://www.rxfiles.ca/rxfiles/uploads/documents/members/Psyc-anticholinergic-Ref%20List%20SPDP-complete.pdf
[6] Bareham J, Regier L, Jensen B. Behaviour Management in Dementia – RxFiles Newsletter. Accessed 04 Apr 2012 at http://www.rxfiles.ca/rxfiles/uploads/documents/Psych-BPSD-Newsletter.pdf
Declercq T, Petrovic M, Azermai M, Vander Stichele R, De Sutter AIM, van Driel ML, Christiaens T. Withdrawal versus continuation of chronic antipsychotic drugs for behavioural and psychological symptoms in older people with dementia. Cochrane Database of Systematic Reviews 2013, Issue 3. Art. No.: CD007726. DOI: 10.1002/14651858.CD007726.pub2. Our findings suggest that many older people with Alzheimer's dementia and NPS can be withdrawn from chronic antipsychotic medication without detrimental effects on their behaviour. It remains uncertain whether withdrawal is beneficial for cognition or psychomotor status, but the results of this review suggest that discontinuation programmes could be incorporated into routine practice. However, two studies of people whose agitation or psychosis had previously responded well to antipsychotic treatment found an increased risk of relapse or shorter time to relapse after discontinuation. Two other studies suggest that people with more severe NPS at baseline could benefit from continuing their antipsychotic medication. In these people, withdrawal might not be recommended.
[7] Breault R, Regier L, Jensen B. Metformin: Precautions with Renal Impairment, Hepatic Disease and Heart Failure. RxFiles Q&A, Oct 2008. Accessed 04 Apr 2012 at http://www.rxfiles.ca/rxfiles/uploads/documents/Diabetes-Metformin-LacticAcidosis-QandA.pdf
[8] Regier L, Bareham J. Individualizing Glycemic Targets in the Frail Elderly - RxFiles Q&A. Accessed 04 Apr 2012 at http://www.rxfiles.ca/rxfiles/uploads/documents/members/Diabetes-Glucose-Targets-in-Elderly-LTC.pdf {Also see article in CFP jounal: Diabetes in the frail elderly; Individualization of glycemic management http://www.cfp.ca/content/58/5/543.full }
Canadian Diabetes 20013 Guidelines (April 2013): http://guidelines.diabetes.ca/
[9] Ismail-Beigi F, Moghissi E, Tiktin M, Hirsch IB, Inzucchi SE, Genuth S. Individualizing glycemic targets in type 2 diabetes mellitus: implications of recent clinical trials. Ann Intern Med. 2011 Apr 19;154(8):554-9.
[10] Dumont Z. The Gout – RxFiles Q&A & Chart. Accessed 04 Apr 2012 at http://www.rxfiles.ca/rxfiles/uploads/documents/members/CHT-Gout.pdf
Qaseem A, McLean RM, Starkey M, Forciea MA; Clinical Guidelines Committee of the American College of Physicians. Diagnosis of Acute Gout: A Clinical Practice Guideline From the American College of Physicians. Ann Intern Med. 2017 Jan 3;166(1):52-57.
Neogi T, Jansen TL, Dalbeth N, et al. 2015 Gout classification criteria: an American College of Rheumatology/European League Against Rheumatism collaborative initiative. Ann Rheum Dis. 2015 Oct;74(10):1789-98.
[11] Jin M. Heart Failure Treatment – RxFiles Chart. Accessed 04 Apr 2012 at http://www.rxfiles.ca/rxfiles/uploads/documents/members/cht-Heart-Failure.pdf
[12] RxFiles Weight Chart and Furosemide Sliding Scale – RxFiles Q&A. Accessed 04 Apr 2012 at http://www.rxfiles.ca/rxfiles/uploads/documents/HF-FurosemideSlidingScale.pdf
[13] RxFiles ACCORD Lipid & BP Trial Overview. Accessed 04 Apr 2012 at http://www.rxfiles.ca/rxfiles/uploads/documents/ACCORD-BP-Lipid-Trial-Overview.pdf
[14] Rakugi H, Ogihara T, Goto Y, Ishii M; JATOS Study Group. Comparison of strict- and mild-blood pressure control in elderly hypertensive patients: a per-protocol analysis of JATOS. Hypertens Res. 2010 Nov;33(11):1124-8.
Ogihara T, Saruta T, Rakugi H, et al. Valsartan in Elderly Isolated Systolic Hypertension Study Group. Target blood pressure for treatment of isolated systolic hypertension in the elderly: valsartan in elderly isolated systolic hypertension study. (Valish) Hypertension. 2010 Aug;56(2):196-202.
Allen M, Kelly K, Fleming I. Hypertension in elderly patients: Recommended systolic targets are not evidence based. Can Fam Physician. 2013 Jan;59(1):19-21.
[15] RxFiles Lipid Trials. Accessed 04 Apr 2012 at http://www.rxfiles.ca/rxfiles/uploads/documents/members/CHT-lipid%20agents-major%20trials.pdf
[16] RxFiles Lipid Agents. Accessed 04 Apr 2012 at http://www.rxfiles.ca/rxfiles/uploads/documents/members/CHT-lipid%20agents.pdf
Ramos R, Comas-Cufí M, Martí-Lluch R, et al. Statins for primary prevention of cardiovascular events and mortality in old and very old adults with and without type 2 diabetes: retrospective cohort study. BMJ. 2018 Sep 5;362:k3359.

[17] Regier L, Jensen B. Statins in the Media. RxFiles Q&A. May 2012. Accessed 08 May 2012 at http://www.rxfiles.ca/rxfiles/uploads/documents/Lipid-statins-heart-risk-media.pdf
[18] RxFiles Osteoporosis Tx Chart. http://www.rxfiles.ca/rxfiles/uploads/documents/members/Cht-osteoporosis.pdf
Qaseem A, Forciea MA, McLean RM, Denberg TD; Clinical Guidelines Committee of the American College of Physicians (ACP). Treatment of low bone density or osteoporosis to prevent fractures in men and women: a clinical practice guideline update from the American College of Physicians. Ann Intern Med. [Epub ahead of print 9 May 2017].

[19] FRAX Canada – Online Calculator: Accessed 04 Apr 2012 at http://www.sheffield.ac.uk/FRAX/tool.jsp?country=19
[20] Stone S. Vitamin D – RxFiles Q&A Summary. Accessed 04 Apr 2012 at http://www.rxfiles.ca/rxfiles/uploads/documents/Vitamin-D-Overview-QandA.pdf
[21] Stone S, Regier L. Opioids for Chronic Non-Cancer Pain (CNCP) Management in the Elderly – RxFiles Q&A. Accessed 04 Apr 2012 at http://www.rxfiles.ca/rxfiles/uploads/documents/Opioids-Pain-ELDERLY-QandA.pdf
[22] Glass J, Lanctôt KL, Herrmann N, Sproule BA, Busto UE. Sedative hypnotics inolder people with insomnia: meta-analysis of risks and benefits. BMJ. 2005 Nov 19;331(7526):1169.
[23] Herpes Zoster Vaccine – RxFiles Q&A. Accessed April 2014 at http://www.rxfiles.ca/rxfiles/uploads/documents/Zostavax-QandA.pdf
Non-Live Recombinant Herpes Zoster Vaccine (SHINGRIX) June 2018 https://www.rxfiles.ca/RxFiles/uploads/documents/Shingrix_QandA.pdf
[24] Kernan WN, Ovbiagele B, Black HR, et al; American Heart Association Stroke Council, Council on Cardiovascular and Stroke Nursing, Council on Clinical Cardiology, and Council on Peripheral Vascular Disease. Guidelines for the prevention of stroke in patients with stroke and transient ischemic attack: a guideline for healthcare professionals from the American Heart Association/American Stroke Association. Stroke. 2014 Jul;45(7):2160-236.
[25] Wang Y, Wang Y, Zhao X, et al; CHANCE Investigators. Clopidogrel with aspirin in acute minor stroke or transient ischemic attack. N Engl J Med. 2013 Jul 4;369(1):11-9.

[26] Diener HC, Bogousslavsky J, Brass LM, et al; MATCH investigators. Aspirin and clopidogrel compared with clopidogrel alone after recent ischaemic stroke or transient ischaemic attack in high-risk patients (MATCH): randomised, double-blind, placebo-controlled trial. Lancet. 2004 Jul 24-30;364(9431):331-7.

[27] Johnston SC, Easton JD, Farrant M, et al. Platelet-oriented inhibition in new TIA and minor ischemic stroke (POINT) trial: rationale and design. Int J Stroke. 2013 Aug;8(6):479-83.

[28] Hutchison, L.C., & Sleeper, R.B. (2010). Biomedical Principles of Aging. In *Fundamentals of Geriatric Pharmacotherapy: An Evidence-Based Approach* (pp. 56). Bethesda, MD: American Society of Health-System Pharmacists.

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Essential Tremor & Restless Legs: References

1. Zesiewicz TA, et al. **Practice Parameter**: Therapies for **essential tremor**. Report - American Academy of Neurology. Neurology. **2005** Jun 22 http://www.neurology.org/cgi/reprint/64/12/2008.pdf?ck=nck
   Zesiewicz TA, Elble RJ, et al. Evidence-based guideline update: treatment of **essential tremor**: report of the Quality Standards subcommittee of the American Academy of Neurology. (**AAN**) Neurology. **2011** Nov 8;77(19):1752-5. http://www.neurology.org/content/early/2011/10/18/WNL.0b013e318236f0fd.full.pdf
2. Louis ED. **Essential tremor**. Lancet Neurol. 2005 Feb;4(2):100-110.
3. Smaga S. **Tremor**. Am Fam Physician. 2003 Oct 15;68(8):1545-52.
4. Lyons KE, Pahwa R, Comella CL, et al. Benefits and risks of pharmacological treatments for **essential tremor**. Drug Saf. 2003;26(7):461-81.
5. Sullivan KL, Hauser RA, Zesiewicz TA. **Essential tremor**. Epidemiology, diagnosis, and treatment. Neurologist. 2004 Sep;10(5):250-8.
6. Micromedex 2018.
7. Lyons KE, Pahwa R. Pharmacotherapy of **essential tremor** : an overview of existing and upcoming agents. CNS Drugs. 2008;22(12):1037-45.
8. Elble RJ. **Tremor**: clinical features, pathophysiology, and treatment. Neurol Clin. 2009 Aug;27(3):679-95, v-vi.
9. Jensen B. **RxFiles Anticonvulsants** Drug Chart. http://www.rxfiles.ca/rxfiles/uploads/documents/members/Cht-psyc-seizure.pdf (Subscription required)
10. Serrano-Dueñas M. Use of **primidone** in low doses (250 mg/day) versus high doses (750 mg/day) in the management of **essential tremor**. Double-blind comparative study with one-year follow-up. Parkinsonism Relat Disord. 2003 Oct;10(1):29-33.
11. Connor GS. A double-blind placebo-controlled trial of **topiramate** (Mean dose 333mg/d) treatment for **essential tremor**. Neurology. 2002 Jul 9;59(1):132-4.
12. Jensen B. **RxFiles Benzodiazepine** Drug Chart: http://www.rxfiles.ca/rxfiles/uploads/documents/members/Cht-Psyc-Benzodiazepines.pdf
13. Simpson DM, Blitzer A, Brashear A, Comella C, Dubinsky R, Hallett M, Jankovic J, Karp B, Ludlow CL, Miyasaki JM, Naumann M, So Y; Therapeutics and Technology Assessment Subcommittee of the American Academy of Neurology. Assessment: **Botulinum** neurotoxin for the treatment of movement disorders (an evidence-based review): report of the Therapeutics and Technology Assessment Subcommittee of the American Academy of Neurology. Neurology. 2008 May 6;70(19):1699-706.
14. Bushara KO, Malik T, Exconde RE. The effect of **levetiracetam** on **essential tremor**. Neurology. 2005 Mar 22;64(6):1078-80.
15. Thorpy MJ. New paradigms in the treatment of **restless legs** syndrome. Neurology. **2005 Jun** 28;64(12_suppl_3):S28-S33.
16. Allen RP, Picchietti D, Hening WA, et al; **Restless Legs** Syndrome Diagnosis and Epidemiology workshop at the NIH. Sleep Med. 2003 Mar;4:101-19.
17. Chaudhuri KR, Forbes A, Grosset D, et al.. Diagnosing **restless legs** syndrome (RLS) in primary care. Curr Med Res Opin. 2004 Nov;20(11):1785-95.
18. 2004 **Restless Legs** Syndrome Foundation Bulletin. Accessed June 02, 2005 @ http://www.rls.org/literature/bulletin.html
19. Silber MH, Ehrenberg BL, Allen RP, et al. An algorithm for the management of **restless legs** syndrome. Mayo Clin Proc. 2004 Jul;79(7):916-22.
20. Micromedix 2009; and Micromedix Drug Consults – **Restless Legs** Syndrome – Drugs of Choice Dec 2002.
21. Happe S, Trenkwalder C. Role of **dopamine** receptor **agonists** in the treatment of **restless legs** syndrome. CNS Drugs. 2004;18(1):27-36.
22. Pharmacists Letter June 2005 – Treatment of **Restless Legs** Syndrome.
23. Hening WA, Allen RP, Earley CJ, et al. **Restless Legs** Syndrome Task Force of the Standards of Practice Committee of the **American** Academy of Sleep Medicine. An update on the dopaminergic treatment of restless legs syndrome and periodic limb movement disorder. Sleep. 2004May 1;27(3):560-83.
    Winkelman JW, Armstrong MJ, Allen RP, et al. Practice guideline summary (**AAN**): **Treatment of restless legs syndrome in adults**: Report of the Guideline Development, Dissemination, and Implementation Subcommittee of the **American** Academy of Neurology. Neurology. 2016 Nov 16.
24. Earley CJ. Clinical practice. **Restless legs** syndrome. N Engl J Med. 2003 May 22;348(21):2103-9.
25. Manconi M, Govoni V, De Vito A, Economou NT, et al. **Restless legs** syndrome and pregnancy. Neurology. 2004 Sep 28;63(6):1065-9.
26. Jensen B. **RxFiles Parkinson's** Drug Chart: http://www.rxfiles.ca/rxfiles/uploads/documents/members/Cht-Parkinson.pdf (Subscription required.)
27. Regier L. **RxFiles Opioid** Drug Chart. http://www.rxfiles.ca/rxfiles/uploads/documents/members/CHT-Opioid.pdf (Subscription required.);
    Newsletter: http://www.rxfiles.ca/rxfiles/uploads/documents/Pain-Chronic-NonCa-NEWSLETTER-Header.pdf ;
    Opioid Sample Treatment Agreement: http://www.rxfiles.ca/rxfiles/uploads/documents/Pain-CNMP-Opioid-TreatmentAGREEMENT.doc
28. Trenkwalder C, Benes H, Grote L, et al. Prolonged release oxycodone-naloxone for treatment of severe restless legs syndrome after failure of previous treatment: a double-blind, randomised, placebo-controlled trial with an open-label extension. Lancet Neurology 2013; online Oct 18.
29. Allen RP, Chen C, Garcia-Borreguero D, et al. Comparison of **pregabalin with pramipexole** for **restless legs syndrome**. N Engl J Med 2014;370:621-31.

30. Sasso E, Perucca E, Calzetti S. Double-blind comparison of **primidone** and **phenobarbitone** in **essential tremor**. *Neurology* 1988;38:808–810.
31. Yang C, White DP, Winkelman JW. **Antidepressants and periodic leg movements of sleep**. Biol Psychiatry. 2005 Sep 15;58(6):510-4. Epub 2005 Jul 7.
32. Trotti LM, Becker LA. Iron for the treatment of restless legs syndrome. Cochrane Database of Systematic Reviews. 2019(1).

Additional References

AAN **Essential Tremor Guideline**, Neurology Oct 2011. http://www.neurology.org/content/early/2011/10/18/WNL.0b013e318236f0fd.full.pdf
Abboud H, Ahmed A, Fernandez HH. Essential tremor: Choosing the right management plan for your patient. Cleve Clin J Med. 2011 Dec;78(12):821-8.
Ahmed M, Hays R, Steven Poceta J, et al. Effect of **Gabapentin Enacarbil** on Individual Items of the International Restless Legs StudyGroup Rating Scale and Post-Sleep Questionnaire in Adults with Moderate-to-Severe Primary **Restless Legs Syndrome**: Pooled Analysis of 3 Randomized Trials. ClinTher. 2016 Jun 7.
Allen RP, Barker PB, Horská A, Earley CJ. **Thalamic glutamate/glutamine** in restless legs syndrome: increased and related to disturbed sleep. Neurology 2013;80:2028–2034.
Allen RP, Picchietti DL, Garcia-Borreguero D, et al; International Restless Legs Syndrome Study Group. Restless legs syndrome/ Willis-Ekbom disease diagnostic criteria: updated International RestlessLegs Syndrome Study Group (IRLSSG) consensus criteria—history, rationale, description, and significance. Sleep Med. 2014; 15:860-73.
Alty J, Cosgrove J, Thorpe D, Kempster P. How to use **pen and paper tasks to aid tremor diagnosis** in the clinic. Pract Neurol. 2017 Aug 26.
Akpinar S. Treatment of **restless legs syndrome with levodopa** plus benserazide. Arch Neurol 1982;39:739.
Alterman RL. One Step Backward: Magnetic Resonance Guided Focused **Ultrasound Thalamotomy** for the Treatment of Medically **Refractory Tremor**. Ann Neurol. 2017 Feb 13
Aukerman MM, Aukerman D, Bayard M, et al. **Exercise and restless legs syndrome**: a randomized controlled trial. J Am Board Fam Med 2006;19:487-93.
Aurora RN, Kristo DA, Bista SR, et al. The treatment of **restless legs syndrome and periodic limb movement disorder** in adults-an update for 2012: practice parameters with an evidence-based systematic review and meta-analyses: an American Academy of Sleep Medicine clinical practice guideline (**AASM**). Sleep. 2012 Aug 1;35(8):1039-62.
Baizabal-Carvallo JF, Kagnoff MN, et al. The safety and efficacy of **thalamic deep brain stimulation in essential tremor**: 10 years and beyond. J Neurol Neurosurg Psychiatry. 2014 May;85(5):567-72.
Baker WL, White CM, Coleman CI. Effect of nonergot **dopamine agonists** on symptoms of **restless** legs syndrome. Ann Fam Med. 2008 May-Jun;6(3):253-62.
Baran RT, Atar M, Pirgon Ö, et al. **Restless Legs Syndrome and Poor Sleep Quality in Obese Children and Adolescents**. J Clin Res Pediatr Endocrinol. 2018 Jun 1;10(2):131-138.
Barbe MT, Dembek TA, Becker J, et al. Individualized **current-shaping** reduces **DBS-induced dysarthria** in patients with essential tremor. Neurology. 2014 Feb 18;82(7):614-9.
Barbe MT, Reker P, Hamacher S, et al. **DBS of the PSA and the VIM in essential tremor**: A randomized, double-blind, crossover trial. Neurology. 2018 Aug 7;91(6):e543-e550.
Batool-Anwar S, Malhotra A, Forman J, Winkelman J, Li Y, Gao X. **Restless legs syndrome and hypertension** in middle-aged women. Hypertension. 2011;58:791–796.
Bauer A, Cassel W, et al; SP0977 study investigators. **Rotigotine's effect on PLM-associated blood pressure** elevations in restless legs syndrome: An RCT. Neurology. 2016 May 10;86(19):1785-93.
Bayard M, Avonda T, Wadzinski J. **Restless** legs syndrome. Am Fam Physician. 2008 Jul 15;78(2):235-40.
Benito-León J, Louis ED, Sánchez-Ferro A, Bermejo-Pareja F. Rate of **cognitive decline during the premotor phase of essential tremor**: A prospective study. Neurology. 2013 Jul 2;81(1):60-66.
Bertisch S. **In the Clinic: Restless Legs Syndrome**. Ann Intern Med. 2015 Nov 3;163(9):ITC1.
Bhatia KP, Bain P, Bajaj N, et al; Tremor Task Force of the **International Parkinson and Movement Disorder Society**. Consensus Statement on the **classification of tremors**. from the task force on tremor of the International Parkinson and Movement Disorder Society. Mov Disord. 2018 Jan;33(1):75-87.
Bogan RK. From Bench to Bedside: An Overview of **Rotigotine** for the Treatment of **Restless Legs Syndrome**. Clin Ther. 2014 Mar 1;36(3):436-455.
Boghen D, Lamothe L, Elie R, Godbout R, Montplaisir J. The treatment of the **restless legs syndrome** with **clonazepam**: a prospective controlled study. Can J Neurol Sci1986;13:245-247
Bogan RK, et al.; TREAT RLS US Study Group. **Ropinirole** in the treatment of **RLS**: a US-based double-blind, placebo-controlled RCT. Mayo Clin Proc. 2006 Jan;81(1):17-27.(InfoPOEMs Apr/06).
Bogan RK, Cheray JA. **Restless legs syndrome**: a review of diagnosis and management in primary care. Postgrad Med 2013;125:99-111.
Bruno E, Nicoletti A, Quattrocchi G, et al. **Alprazolam for essential tremor**. Cochrane Database Syst Rev. 2015 Dec 6;12:CD009681. Currently available data reveal evidence insufficient for assessment of the efficacy and safety of alprazolam treatment for individuals with ET.
Bruno E, Nicoletti A, Quattrocchi G, et al. **Topiramate for essential tremor**. Cochrane Database Syst Rev. 2017 Apr 14;4:CD009683. This systematic review highlighted the presence of limited data and very low to low quality evidence to support the apparent efficacy and the occurrence of treatment-limiting AEs in people with ET treated with topiramate. Further research to assess topiramate efficacy and safety on ET is needed.
Bushara KO, Malik T, Exconde RE. The effect of **levetiracetam** on essential tremor. Neurology. 2005 Mar 22;64(6):1078-80.
Canadian Adverse Reaction Newsletter. **Quinine sulfate and serious adverse reactions**. April 2011.
Cesnik E, Casetta I, Turri M, Govoni V, Granieri E, Strambi LF, Manconi M. Transient RLS during pregnancy is a risk factor for the chronic idiopathic form. Neurology. 2010 Dec 7;75(23):2117-20.
Chang JW, Park CK, Lipsman N, et al. A Prospective Trial of Magnetic Resonance guided **Focused Ultrasound Thalamotomy for Essential Tremor**: Results at the 2-year Follow-up. Ann Neurol. 2017 Dec 19.
Choe CU, Hidding U, Schaper M, et al. **Thalamic short pulse stimulation** diminishes adverse effects in essential tremor patients. Neurology. 2018 Jul 25.
Cikrikcioglu MA, Sekin Y, Halac G, et al. **Reduced bone resorption** and increased bone mineral density in women with **restless legs syndrome**. Neurology 201
Connor GS, Edwards K, Tarsy D. **Topiramate** in **essential** tremor: findings from double-blind, placebo-controlled, crossover trials. Clin Neuropharmacol. 2008 Mar-Apr;31(2):97-103.
Crawford P, Zimmerman EE. **Differentiation and diagnosis of tremor**. Am Fam Physician. 2011 Mar 15;83(6):697-702.
Crawford P, Zimmerman EE, Tremor: **Sorting Through the Differential Diagnosis**. Am Fam Physician. 2018;97(3):180-186.
Dallapiazza RF, Lee DJ, De Vloo P, et al. Outcomes from stereotactic surgery for essential tremor. J Neurol Neurosurg Psychiatry. 2018 Oct 18.
Deuschl G, Raethjen J, Hellriegel H, et al. **Treatment of patients with essential tremor**. Lancet Neurol. **2011** Feb;10(2):148-61
Di Biase L, Brittain JS, Shah SA, et al. **Tremor stability index**: a new tool for differential diagnosis in tremor syndromes. Brain. 2017 Jul 1;140(7):1977-1986.
Duma SR, Fung VS. **Drug-induced movement disorders**. Aust Prescr. 2019 Apr;42(2):56-61.
Earley CJ, Allen RP. Restless legs syndrome augmentation associated with **tramadol**. Sleep Med 2006;7:592-3.
El-Tawil S, Al Musa T, Valli H, et al. **Quinine for muscle cramps**. Cochrane Database Syst Rev. 2010 Dec 8;12:CD005044. There is moderate quality evidence that quinine significantly reduces cramp frequency, intensity and cramp days in dosages between 200 and 500 mg/day. There is moderate quality evidence that with use up to 60 days, the incidence of serious adverse events is not significantly greater than for placebo in the identified trials. Further research is required on the optimal dose and duration of use, and also on alternative treatments.
Elias WJ et al. A pilot study of focused **ultrasound thalamotomy for essential tremor**. N Engl J Med 2013 Aug 15; 369:640.
Elias WJ, Shah BB. **Tremor**. JAMA. 2014 Mar 5;311(9):948-54.
Elias WJ, Lipsman N, Ondo WG, et al. A randomized trial of **focused ultrasound thalamotomy for essential tremor**. N Engl J Med 2016;375:730-9.
Fardet L, Nazareth I, Petersen I. Association Between Long-term **Quinine Exposure and All-Cause Mortality**. JAMA. 2017 May 9;317(18):1907-1909

Fasano A, Llinas M, Munhoz RP, et al. MRI-guided focused **ultrasound thalamotomy in non-ET tremor syndromes**. Neurology. 2017 Aug 22;89(8):771-775

Gao X, Schwarzschild MA, Wang H, Ascherio A. **Obesity** and **restless legs** syndrome in men and women. Neurology. 2009 Apr 7;72(14):1255-61. Both overall and abdominal adiposity are associated with increased likelihoods of having restless legs syndrome (RLS).

Garcia-Borreguero D, Larrosa O, Williams AM, Albares J, et al. Treatment of restless legs syndrome with **pregabalin**: a double-blind, placebo-controlled study. Neurology. 2010 Jun 8;74(23):1897-904.

Garcia-Borreguero D, Stillman P, Benes H, et al. **Algorithms for the diagnosis and treatment of restless legs syndrome in primary care**. (EURLSSG) BMC Neurol. 2011;11:28.

Garcia-Borreguero D, Ferini-Strambi L, Kohnen R, et al; European Federation of Neurological Societies. **European guidelines on management of restless legs syndrome**: report of a joint task force by the European Federation of Neurological Societies, the **European Neurological Society and the European Sleep Research Society**. Eur J Neurol. 2012;19:1385-96.

Garcia-Borreguero D, Kohnen R, Silber MH, et al. The long-term treatment of **restless legs syndrome/Willis-Ekbom disease**: evidence-based guidelines and clinical consensus best practice guidance: a report from the **International Restless Legs Syndrome Study Group**. Sleep Med. 2013;14:675-84.

Garcia-Borreguero D, Cano-Pumarega I. New concepts in the **management of restless legs syndrome**. BMJ. 2017 Feb 27;356:j104.

Garrison SR, Dormuth CR, Morrow RL, et al. **Nocturnal leg cramps** and prescription use that precedes them: a sequence symmetry analysis. Arch Intern Med. 2012 Jan 23;172(2):120-6.

Garrison SR, Allan GM, Sekhon RK, Musini VM, Khan KM. **Magnesium** for skeletal muscle cramps. Cochrane Database Syst Rev. 2012 Sep 12;9:CD009402. It is unlikely that magnesium supplementation provides clinically meaningful cramp prophylaxis to older adults experiencing skeletal muscle cramps.

Garrison SR, Dormuth CR, Morrow RL, et al. **Seasonal effects on the occurrence of nocturnal leg cramps**: a prospective cohort study. CMAJ. 2015 Jan 26.

Gjerstad MD, Tysnes OB, Larsen JP. Increased risk of **leg motor restlessness but not RLS** in early Parkinson disease. Neurology 2011;77:1941–1946.

Gironell A, Kulisevsky J, Barbanoj M, et al. A randomized placebo-controlled comparative trial of **gabapentin** and **propranolol** in **essential tremor**. Arch Neurol. 1999 Apr;56(4):475-80.

Haba-Rubio J, Marti-Soler H, Marques-Vidal P, et al. Prevalence and Determinants of **Periodic Limb Movements** in the General Population. Ann Neurol. 2015 Dec 24.

Hallegraeff JM, van der Schans CP, et al. **Stretching** before sleep reduces the frequency and severity of **nocturnal leg cramps** in older adults: a randomised trial. J Physiother. 2012;58(1):17-22.

Haubenberger D, McCrossin G, Lungu C, et al. **Octanoic acid** in alcohol-responsive **essential tremor**: A randomized controlled study. Neurology. 2013 Mar 5;80(10):933-940.

Haubenberger D, Hallett M. Essential Tremor. N Engl J Med. 2018 May 10;378(19):1802-1810.

Hay WJ, Lemon MD, Farver DK. **Gabapentin Enacarbil** for Treatment of **Restless Legs Syndrome** in Adults (February). Ann Pharmacother. 2012 Jan 31.

Health Canada Aug/07: Eli Lilly Canada advises Healthcare Professionals that they will **cease sale of Permax** August 30, 2007 due to risk of cardiac valvulopathy.

Heim B, Djamshidian A, Heidbreder A. **Augmentation and impulsive behaviors in restless legs syndrome**: coexistence or association? Neurology 2016;87:xxx–xxx.

Hoque R, Chesson AL Jr. **Pharmacologically induced/exacerbated** restless legs syndrome, periodic limb movements of sleep, and REM behavior disorder/REM sleep without atonia: literature review, qualitative scoring, and comparative analysis. J Clin Sleep Med. 2010 Feb 15;6(1):79-83.

Hornyak M, Kaube H. Long-Term treatment of a patient with severe **restless legs syndrome using intrathecal morphine**. Neurology. 2012 Dec 11;79(24):2361-2.

Hübner A, Krafft A, Gadient S, et al. Characteristics and determinants of **restless legs syndrome in pregnancy**: A prospective study. Neurology. 2013 Feb 19;80(8):738-42.

International Restless Legs Syndrome Study Group. 2012. Accessed at http://irlssg.org/diagnostic-criteria/ on 3 August 2014.

Katzberg, Hans D., Khan, Ahmir H., So, Yuen T. Assessment: Symptomatic treatment for **muscle cramps** (an evidence-based review): Report of the Therapeutics and Technology Assessment Subcommittee of the American Academy of Neurology. Neurology 2010 74: 691-696

Klepitskaya O, Liu Y, Sharma S, et al. **Deep brain stimulation** improves restless legs syndrome in patients **with Parkinson disease**. Neurology. 2018 Sep 11;91(11):e1013-e1021.

Koller WC. **Propranolol** therapy for **essential tremor** of the head. Neurology. 1984;34(8):1077-9.

Koller W, Biary N, Cone S. **Disability in essential tremor**: effect of treatment. Neurology. 1986 Jul;36(7):1001-4.

Koo BB, Blackwell T, Ancoli-Israel S, Stone KL, Stefanick ML, Redline S; for the Osteoporotic Fractures in Men (MrOS) Study Group. Association of Incident Cardiovascular Disease With **Periodic Limb Movements During Sleep** in Older Men: Outcomes of Sleep Disorders in Older Men (**MrOS**) Study. Circulation. 2011 Sep 13;124(11):1223-1231.

Kuhlenbäumer G, Hopfner F, Deuschl G. **Genetics** of essential tremor: Meta-analysis and review. Neurology. 2014 Mar 18;82(11):1000-7.

Kumar H, Jog M. A patient with **tremor**, part 1: making the **diagnosis**. CMAJ. 2011 Aug 2.

Kumar H, Jog M. A patient with **tremor**, part 2: from diagnosis to **treatment**. CMAJ. 2011 Aug 15.

Lee BY, Kim J, Connor JR, Podskalny GD, Ryu Y, Yang QX. Involvement of the **central somatosensory system in restless legs syndrome**: a neuroimaging study. Neurology 2018;90:e1834–e1841.

Leschziner G, Gringras P. **Restless legs syndrome**. BMJ. 2012 May 23;344:e3056.

Lettieri CJ, Eliasson AH. **Pneumatic compression devices** are an effective therapy for restless legs syndrome: a prospective, randomized, double-blinded, sham-controlled trial. Chest. 2009 Jan;135(1):74-80. Epub 2008 Nov 18. PCDs resulted in clinically significant improvements in symptoms of RLS in comparison to the use of sham devices & may be an effective adjunctive or alternative therapy for RLS.

Li Y, Munger KL, Batool-Anwar S, et al. Association of **multiple sclerosis** with **restless legs syndrome** and other sleep disorders in women. Neurology. 2012 May 8;78(19):1500-6.

Li Y, Walters AS, Chiuve SE, et al. Prospective study of restless legs syndrome and **coronary heart disease** among women.Circulation 2012.

Li Y, Wang W, Winkelman JW, et al. Prospective study of **restless legs syndrome and mortality** among men. Neurology. 2013 Jun 12.

Li Y, Li Y, Winkelman JW, et al. Prospective study of restless legs syndrome and **total and cardiovascular mortality** among women.Neurology. 2018 Jan 9;90(2):e135-e141.

Lipsman N, Schwartz ML, Huang Y, et al. **MR-guided focused ultrasound thalamotomy for essential tremor**: a proof-of-concept-study. Lancet Neurol 2013; online March 21.

Liu GJ, Wu L, Lin et al. Efficacy of **Pramipexole** for the Treatment of Primary **Restless Leg Syndrome**: A Systematic Review and Meta-Analysis of Randomized Clinical Trials. Clin Ther. 2015 Nov 11.

Louis ED. **Essential tremor**: evolving clinicopathological concepts in an era of intensive post-mortem enquiry. Lancet Neurol. 2010 May 5. [Epub ahead of print]

Louis ED. **Diagnosis and Management of Tremor**. Continuum (Minneap Minn). 2016 Aug;22 (4 Movement Disorders):1143-58.

Machado A, Fernandez HH, Deogaonkar M. **Deep brain stimulation**: What can patients expect from it? (Essential tremor) Cleveland Clinic Journal of Medicine 2012; 79(2):113-120.

Makumi CW, Paska W, Rolfe K, et al. A Retrospective, Pooled **Suicidality Evaluation of Ropinirole** Immediate Release and Controlled Release for the Treatment of Restless Legs Syndrome. Clin Ther. 2015 Apr 10.

Manconi M, Ferri R, Zucconi M, et al. **Preferential D2 (bromocriptine) or preferential D3 (pramipexole) dopamine agonists in restless legs syndrome**. Neurology. 2011 Jul 12;77(2):110-7.

Medcalf P, Bhatia KP. **Restless legs** syndrome. BMJ. 2006 Sep 2;333(7566):457-8.

Molnar MZ, Novak M, Mucsi I. Management of **restless legs syndrome** in patients on **dialysis**.Drugs. 2006;66(5):607-24.

Monderer RS, Wu WP, Thorpy MJ. **Nocturnal leg cramps**. Curr Neurol Neurosci Rep. 2010 Jan;10(1):53-9.

Muth CC. **Essential Tremor. (Patient page)** JAMA. 2016 Nov 22;316(20):2162.

Muth CC. **Restless Legs Syndrome** (Patient information). JAMA. 2017 Feb 21;317(7):780.

Oertel Wolfgang, Trenkwalder Claudia, Benes Heike, et al. and on behalf of the SP710 study group, Long-term safety and efficacy of **rotigotine** transdermal patch for moderate-to-severe idiopathic **restless legs syndrome**: a 5-year open-label extension study, The Lancet Neurology, In Press, Corrected Proof, Available online 24 June 20116; 86:1235–1241.

Ohayon MM, Bagai K, Roberts LW, et al. Refining duration and **frequency thresholds of restless legs syndrome** diagnosis criteria. Neurology. 2016 Dec 13;87(24):2546-2553

Ondo WG, et al.; Topiramate Essential Tremor Study Investigators. **Topiramate** in **essential tremor**: a double-blind, placebo-controlled trial. Neurology. 2006 Mar 14;66(5):672-7. Epub 2006 Jan 25. (InfoPOEMs: Topiramate (Topamax) is slightly better than placebo in improving tremor and function in patients with essential tremor. In this study, the differences do not appear to be clinically significant. Given the expense and the significant drop-out rate due to side effects, topiramate should not be used as a first-line treatment. (LOE = 1b))

Ondo W, Hunter C, Vuong KD, Schwartz K, Jankovic J. **Gabapentin** for **essential tremor**: a multiple-dose, double-blind, placebo-controlled trial. Mov Disord. 2000 Jul;15(4):678-82.

Oyieng'o DO, Kirwa K, Tong I, et al. **Restless Legs Symptoms and Pregnancy** and Neonatal Outcomes. Clin Ther. 2015 Dec 28.

Pahwa R, Lyons K, Hubble JP, Busenbark K, Rienerth JD, Pahwa A, Koller WC. Double-blind controlled trial of **gabapentin** in **essential tremor**. Mov Disord. 1998 May;13(3):465-7.

Paige C, Hopewell BL, Gamsarian V, et al. Characterizing the **Normative Voice Tremor Frequency in Essential Vocal Tremor**. JAMA Otolaryngol Head Neck Surg. 2018 Oct 25.

Park SJ, Yoon KB, Yoon DM, et al. **Botulinum Toxin Treatment for Nocturnal Calf Cramps** in Patients With Lumbar Spinal Stenosis: A Randomized Clinical Trial. Arch Phys Med Rehabil. 2017 May;98(5):957-963.

Paschen S, Forstenpointner J, Becktepe J, et al. Long-term efficacy of **deep brain stimulation for essential tremor**: An observer-blinded study. Neurology. 2019 Mar 19;92(12):e1378-e1386.

Patel PN, Kabagambe EK, Starkweather JC, et al. Outcomes of **Onabotulinum Toxin A** Treatment for Adductor Spasmodic Dysphonia and Laryngeal Tremor. JAMA Otolaryngol Head Neck Surg. 2018 Feb 8.

Pérez-Díaz H, Iranzo A, Rye DB, Santamaría J. **Restless abdomen**: a phenotypic variant of restless legs syndrome. Neurology. 2011 Sep 27;77(13):1283-6.

Pharmacist's Letter: Mirapex (Pramipexole) for RLS Nov/06.

Pipis M, Dehabadi M, Matthews E, Gould L. **Tremor**. BMJ. 2013 Dec 12;347:f7200

Reccoppa L, Malcolm R, Ware M. **Gabapentin abuse** in inmates with prior history of cocaine dependence. Am J Addict. 2004 May-Jun;13(3):321-3.

Rizek P, Kumar N. **Restless legs syndrome**. CMAJ. 2017 Feb 13;189(6):E245.

Roguin Maor N, Alperin M, Shturman E, et al. Effect of **Magnesium Oxide Supplementation on Nocturnal Leg Cramps**: A Randomized Clinical Trial. JAMA Intern Med. 2017 Feb 20.

Salminen AV, Rimpilä V, Polo O. **Peripheral hypoxia** in restless legs syndrome (Willis-Ekbom disease). Neurology 2014;82:1856–1861.

Sasso E, Perucca E, Calzetti S. Double-blind comparison of **primidone** and **phenobarbitone** in **essential tremor**. *Neurology* 1988;38:808–810.

Sasso E, Perucca E, Fava R, Calzetti S. Quantitative comparison of **barbiturates** in **essential hand** and **head tremor**. Mov Disord. 1991;6(1):65-8.

Satija P, Ondo WG. **Restless legs syndrome** : pathophysiology, diagnosis and treatment. CNS Drugs. 2008;22(6):497-518

Scholz H, Trenkwalder C, Kohnen R, et al. **Dopamine agonists for restless legs syndrome**. Cochrane Database Syst Rev. 2011 Mar 16;3:CD006009. The meta-analyses show the superiority of dopamine agonists over placebo in RCTs up to seven months. Cabergoline and pramipexole showed larger efficacy compared to levodopa in some but not all outcomes.

Schormair B, Zhao C, Bell S, et al. Identification of novel risk **loci for restless legs syndrome** in genome-wide association studies in individuals of European ancestry: a meta-analysis. Lancet Neurol 2017; 16: 898–907.

Schreglmann SR, Bauer R, Hägele-Link S, et al. **Unilateral cerebellothalamic tract ablation in essential tremor by MRI-guided focused ultrasound**. Neurology. 2017 Apr 4;88(14):1329-1333.

Schwindt G, Rezmovitz J. **Essential tremor**. CMAJ. 2017 Nov 6;189(44):E1364.

Sebo P, Cerutti B, Haller DM. Effect of **magnesium** therapy on **nocturnal leg cramps**:systematic review of randomized controlled trials with meta-analysis using simulations. Fam Pract. 2014 Feb;31(1):7-19.

Shen SC, House RA. **Hand-arm vibration syndrome**: What family physicians should know. (calcium channel blocker) Can Fam Physician. 2017 Mar;63(3):206-210.

Silber MH, Becker PM, Earley C, et al; Medical Advisory Board of the **Willis-Ekbom Disease Foundation**. Willis-Ekbom Disease Foundation revised consensus statement on the management of restless legs syndrome. Mayo Clin Proc. 2013;88:977-86.

Silva MA, Duarte GS, Camara R, et al. **Placebo and nocebo responses in restless legs syndrome**: a systematic review and meta-analysis. Neurology 2017;88:2216–2224.

Silver N, Allen RP, Senerth J, Earley CJ. A **10-year, longitudinal** assessment of **dopamine agonists** and methadone in the treatment of **restless legs syndrome**. Sleep Med 2011; 12: 440–44.

Spence D. **Bad medicine: restless legs syndrome**. BMJ. 2013 Dec 19;347:f7615.

Stefansson H, Rye DB, Hicks A, et al. A genetic risk factor for periodic limb movements in sleep.N Engl J Med. 2007 Aug 16;357(7):639-47. Epub 2007 Jul 18. We have discovered a variant associated with susceptibility to periodic limb movements in sleep. The inverse correlation of the variant with iron stores is consistent with the suspected involvement of iron depletion in the pathogenesis of the disease.

Szentkirályi A, Völzke H, Hoffmann W, et al. **Multimorbidity** and the risk of **restless legs syndrome** in 2 prospective cohort studies. Neurology. 2014 Jun 3;82(22):2026-33.

Trenkwalder C, et al. Controlled withdrawal of **pramipexole** after 6 months of open-label treatment in patients with **restless legs** syndrome. Mov Disord. 2006 Jun 5; [Epub ahead of print]

Trenkwalder C, et al; PEARLS Study Group. Efficacy of **pergolide** in treatment of **restless legs** syndrome: the PEARLS Study. Neurology. 2004 Apr 27;62(8):1391-7.

Trenkwalder C, et al.; Therapy with Ropiunirole; Efficacy and Tolerability in RLS 1 Study Group. **Ropinirole** in the treatment of **restless legs** syndrome: results from the TREAT RLS 1 study, a 12 week, randomised, placebo controlled study in 10 European countries. J Neurol Neurosurg Psychiatry. 2004 Jan;75(1):92-7.

Trenkwalder C, Benes H, Grote L, et al. Prolonged release **oxycodone-naloxone** for treatment of severe restless legs syndrome after failure of previous treatment: a double-blind, randomised, placebo-controlled trial with an open-label extension. Lancet Neurology 2013; online Oct 18.

Trenkwalder C, Allen R, Högl B, et al. **Restless legs syndrome associated with major diseases**: A systematic review and new concept. Neurology. 2016 Apr 5

Trotti LM, Becker LA. **Iron for the treatment of restless legs syndrome**. Cochrane Database Syst Rev. 2019 Jan 4;1:CD007834. : Iron therapy probably improves restlessness and RLS severity in comparison to placebo. Iron therapy may not increase the risk of side effects in comparison to placebo. We are uncertain whether iron therapy improves quality of life in comparison to placebo. Iron therapy may make little or no difference to pramipexole in restlessness and RLS severity, as well as in the risk of adverse events.

Vignatelli L, Billiard M, Clarenbach P, et al; EFNS Task Force. **EFNS guidelines** on management of **restless legs** syndrome and periodic limb movement disorder in sleep. Eur J Neurol. 2006 Oct;13(10):1049-65. The following level A recommendations can be offered: for primary RLS, cabergoline, gabapentin, pergolide, ropinirole, levodopa and rotigotine by transdermal delivery (the latter two for short-term use) are effective in relieving the symptoms. Transdermal oestradiol is ineffective for PLMD.

Webb AJS, Fischer U, Rothwell PM. Effects of **beta-blocker selectivity** on blood pressure variability and **stroke**: a systematic review. Neurology 2011;77:731–737.

Wilson SJ, Nutt DJ, Alford C, et al. **British Association for Psychopharmacology** consensus statement on evidence-based treatment of insomnia, parasomnias and circadian rhythm disorders. J Psychopharmacol. 2010 Sep 2.

Wilt TJ, Macdonald R, Ouellette J, et al. Pharmacologic Therapy for **Primary Restless Legs Syndrome**: A Systematic Review and Meta-analysis. JAMA Intern Med. 2013 Mar 4:1-10.

Winkelman JW, Allen RP, Tenzer P, Hening W. **Restless legs** syndrome: nonpharmacologic and pharmacologic treatments. Geriatrics. 2007 Oct;62(10):13-6.

Winkelman JW, et al. Efficacy and safety of **pramipexole** in **restless legs** syndrome. Neurology. 2006 Sep 26;67(6):1034-9. Epub 2006 Aug 23.

Winkelman JW, Shahar E, Sharief I, Gottlieb DJ. Association of **restless legs** syndrome and cardiovascular disease in the Sleep Heart Health Study. Neurology. 2008 Jan 1;70(1):35-42. Restless legs syndrome (RLS) is associated with prevalent coronary artery disease and cardiovascular disease. This association appears stronger in those with greater frequency or severity of RLS symptoms.

Winkelman JW, Armstrong MJ, Allen RP, et al. Practice guideline summary (**AAN**): **Treatment of restless legs syndrome in adults**: Report of the Guideline Development, Dissemination, and Implementation Subcommittee of the **American** Academy of Neurology. Neurology. 2016 Nov 16.

Witjas T, Carron R, Krack P, et al. A prospective single-blind study of **Gamma Knife thalamotomy for tremor**. Neurology. 2015 Nov 3;85(18):1562-8.

Wolkove N, Baltzan M. A 68-year-old woman with **sleep-onset insomnia**. (Restless leg syndrome) CMAJ.2013 Nov 19;185(17):1517-9.

Zesiewicz TA, Ward CL, Hauser RA, et al.. A pilot, double-blind, placebo-controlled trial of **pregabalin** (Lyrica) in the treatment of **essential tremor**. Mov Disord. 2007 Aug 15;22(11):1660-3.

Zesiewicz TA, Elble RJ, et al. Evidence-based guideline update: treatment of **essential tremor**: report of the Quality Standards subcommittee of the American Academy of Neurology. (AAN) Neurology. 2011 Nov 8;77(19):1752-5. http://www.neurology.org/content/early/2011/10/18/WNL.0b013e318236f0fd.full.pdf

Zhang C, Li Y, Malhotra A, et al. Restless legs syndrome status as a predictor for lower **physical function**. Neurology. 2014 Apr 8;82(14):1212-8.

References: Multiple Sclerosis Agents Comparison Chart – www.RxFiles.ca

[1] Micromedex 2018

[2] Calabresi PA. Diagnosis and management of multiple sclerosis. Am Fam Physician. 2004 Nov 15;70(10):1935-44.

[3] Rizvi SA, Agius MA. Current approved options for treating patients with multiple sclerosis. Neurology. 2004 Dec 28;63(12 Suppl 6):S8-14.

[4] Goodin DS, Frohman EM, Garmany GP Jr, et al.; Therapeutics and Technology Assessment Subcommittee of the American Academy of Neurology and the MS Council for Clinical Practice Guidelines. Disease modifying therapies in multiple sclerosis: report of the Therapeutics and Technology Assessment Subcommittee of the American Academy of Neurology and the MS Council for Clinical Practice Guidelines. Neurology. 2002 Jan 22;58(2):169-78. (Goodin DS, Frohman EM, Hurwitz B, O'Connor PW, Oger JJ, Reder AT, Stevens JC. Neutralizing antibodies to interferon beta: assessment of their clinical and radiographic impact: an evidence report: report of the Therapeutics and Technology Assessment Subcommittee of the American Academy of Neurology. Neurology. **2007** Mar 27;68(13):977-84.)

Deisenhammer F. Neutralizing Antibodies to Interferon-beta and other Immunological Treatments for Multiple Sclerosis: Prevalence and Impact on Outcomes. CNS Drugs. 2009;23(5):379-96. doi: 10.2165/00023210-200923050-00003.

Pachner AR, Cadavid D, Wolansky L, Skurnick J. Effect of anti-IFN{beta} antibodies on MRI lesions of MS patients in the BECOME study. Neurology. 2009 Nov 3;73(18):1485-92. PubMed PMID: 19884576. High levels of anti-interferon beta (IFNbeta) antibodies, which result in diminished bioactivity, are correlated with reduced therapeutic efficacy of IFNbeta.

Pachner AR, Warth JD, Pace A, Goelz S; INSIGHT investigators. Effect of neutralizing antibodies on biomarker responses to interferon beta: the INSIGHT study. Neurology. 2009 Nov 3;73(18):1493-500. These data provide evidence that high titers of neutralizing antibodies abolish the in vivo response to interferon beta.

Polman Chris H, Bertolotto A, Deisenhammer F et al; Recommendations for clinical use of data on neutralising antibodies to interferon-beta therapy in multiple sclerosis, The Lancet Neurology, Vol 9, Issue 7, July 2010, P 740-50.

Freedman MS, Patry DG, Grand'Maison F, Myles ML, Paty DW, Selchen DH; Canadian MS Working Group. Treatment optimization in multiple sclerosis. Can J Neurol Sci. 2004 May;31(2):157-68.

Freedman MS, Selchen D, Arnold DL, et al; Canadian Multiple Sclerosis Working Group. **Treatment optimization in MS: Canadian MS Working Group** updated recommendations. Can J Neurol Sci. **2013**;40:307-323.

Recommendations for determining the level of concern when considering treatment modification based on **relapse**:

Criteria		Level of Concern	
	Low	Medium	High
Rate	1 relapse in 2nd year of tx	1 relapse in 1st yr of tx	>1 relapse in the 1st yr of tx
Severity	**Mild**	**Moderate**	**Severe**
	-steroids not required	-steroids required	-steroids/ hospitalization required
	-minimal effect on ADL	-moderate effect on ADL	-severe effect on ADL
	-1 functional domain affected	->1 functional domain affected	->1 functional domain affected
	-no or mild motor/cerebellar involvement	-moderate motor/cerebellar involvement	-severe motor/cerebellar involvement
Recovery	-prompt recovery	-incomplete recovery at 3 months	-incomplete recovery at 6 months
	-no functional deficit	-some functional impairment	-functional impairment

Recommendations for determining the level of concern when considering treatment modification based **disability progression**:

Criteria		Level of Concern	
EDSS score:	Low	Medium	High
≤ 3.5	≤ 1 points	2 points at 6months	>2 points at 6months 2 points at 12months
4-5	<1 point	1 point at 6 months	>1 point at 6months 1 point at 12months
≥5.5		0.5 points at 6months	>0.5 points at 6 months
Clinically Documented Progression	No motor Minor sensory	Some motor, cerebellar or cognitive Multiple EDSS domains affected	Pronounced motor, cerebellar or cognitive Multiple EDSS domains affected
T25FW	≤ 20% confirmed at 6months	>20% and ,100% increase confirmed at 6months	≥ 100% increase confirmed at 6 months

Recommendations for determining the level of concern when considering treatment modification based on annual MRI findings:

Criteria	Level of Concern		
	Low	Medium	High
Activity on MRI: New Gd-enhancing Lesions OR accumulation Of new T2 lesions per year	1 lesion	2 lesion	≥3 lesions

Rae-Grant A, Day GS, Marrie RA, et al. **Practice guideline** recommendations summary: **Disease-modifying therapies for adults with multiple sclerosis**: Report of the Guideline Development, Dissemination, and Implementation Subcommittee of the American Academy of Neurology (**AAN**). Neurology. **2018** Apr 24;90(17):777-788.

Rae-Grant A, Day GS, Marrie RA, et al. **Comprehensive systematic review summary**: Disease-modifying therapies for adults with multiple sclerosis: Report of the Guideline Development, Dissemination, and Implementation Subcommittee of the American Academy of Neurology (**AAN**). Neurology. **2018** Apr 24;90(17):789-800.

[5] Briggs GG, Freeman RK, Sumner JY. Drugs in **Pregnancy** and Lactation **11th Edition**. Williams & Wilkins, Baltimore, 2017.

[6] Filippi M, Rovaris M, Inglese M, et al. Interferon beta-1a for brain tissue loss in patients at presentation with syndromes suggestive of multiple sclerosis: a randomised, double-blind, placebo-controlled trial. Lancet. 2004 Oct 23;364(9444):1489-96.

[7] Andersen O, Elovaara I, Farkkila M, et al. Multicentre, randomised, double blind, placebo controlled, phase III study of weekly, low dose, subcutaneous interferon beta-1a in secondary progressive multiple sclerosis. J Neurol Neurosurg Psychiatry. 2004 May;75(5):706-10.

[8] **PRISMS** Study Group and the University of British Columbia MS/MRI Analysis Group.. PRISMS-4: Long-term efficacy of interferon-beta-1a in relapsing MS. Neurology. 2001 Jun 26;56(12):1628-36. Erratum in: Neurology 2001 Sep 25;57(6):1146.

[9] Li DK, Zhao GJ, Paty DW; University of British Columbia MS/MRI Analysis Research Group. The **SPECTRIMS** Study Group. Randomized controlled trial of interferon-beta-1a in secondary progressive MS: **MRI** results. Neurology. 2001 Jun 12;56(11):1505-13.

[10] Secondary Progressinv Efficacy Clinical Trial of Recombinant Interferon-beta-1a in MS (**SPECTRIMS**) Study Group.. Randomized controlled trial of interferon- beta-1a in secondary progressive MS: **Clinical** results. Neurology. 2001 Jun 12;56(11):1496-504.
[11] Comi G, Filippi M, Barkhof F, et al.; Early Treatment of Multiple Sclerosis Study Group. Effect of early interferon treatment on conversion to definite multiple sclerosis: a randomised study (**ETOMS**). Lancet. 2001 May 19;357(9268):1576-82.
[12] Randomised double-blind placebo-controlled study of interferon beta-1a in relapsing/remitting multiple sclerosis. PRISMS (Prevention of Relapses and Disability by Interferon beta-1a Subcutaneously in Multiple Sclerosis) Study Group. Lancet. 1998 Nov 7;352(9139):1498-504. Erratum in: Lancet 1999 Feb 20;353(9153):678.
[13] Medscape Medical News. www.medscape.com/viewarticle/501540. Last acccessed 17 Mar 2005
[14] Clanet M, Kappos L, Hartung HP, Hohlfeld R; European IFNbeta-1a Dose-Comparison Study Investigators. Interferon beta-1a in relapsing multiple sclerosis: four-year extension of the European IFNbeta-1a Dose-Comparison Study. Mult Scler. 2004 Apr;10(2):139-44.
[15] Galetta SL. The controlled high risk Avonex multiple sclerosis trial (**CHAMPS** Study). J Neuroophthalmol. 2001 Dec;21(4):292-5. Erratum in: J Neuroophthalmol 2002 Mar;22(1):67.
[16] **CHAMPS** Study Group. Interferon beta-1a for optic neuritis patients at high risk for multiple sclerosis. Am J Ophthalmol. 2001 Oct;132(4):463-71.
[17] Jacobs LD, Beck RW, Simon JH, et al. Intramuscular interferon beta-1a therapy initiated during a first demyelinating event in multiple sclerosis. **CHAMPS** Study Group. N Engl J Med. 2000 Sep 28;343(13):898-904.
[18] : Simon JH, Jacobs LD, Campion M, et al. Magnetic resonance studies of intramuscular interferon beta-1a for relapsing multiple sclerosis. The Multiple Sclerosis Collaborative Research Group. Ann Neurol. 1998 Jan;43(1):79-87.
[19] Important Drug Warning. http://www.fda.gov/medwatch/SAFETY/2005/avonex_DHCP.pdf. Last accessed 17 Mar 2005.
[20] Molyneux PD, Barker GJ, Barkhof F, et al.; European Study Group on Interferon Beta-1b in Secondary Progressive MS. Clinical-MRI correlations in a European trial of interferon beta-1b in secondary progressive MS. Neurology. 2001 Dec 26;57(12):2191-7.
[21] Kappos L, Polman C, Pozzilli C, et al.; European Study Group in Interferon beta-1b in Secondary-Progressive MS. Final analysis of the European multicenter trial on IFNbeta-1b in secondary-progressive MS. Neurology. 2001 Dec 11;57(11):1969-75.
[22] Koch-Henriksen N, Sorensen PS. The Danish National Project of interferon-beta treatment in relapsing-remitting multiple sclerosis. The Danish Multiple Sclerosis Group. Mult Scler. 2000 Jun;6(3):172-5.
[23] Miller DH, Molyneux PD, Barker GJ, et al. Effect of interferon-beta1b on magnetic resonance imaging outcomes in secondary progressive multiple sclerosis: results of a European multicenter, randomized, double-blind, placebo-controlled trial. European Study Group on Interferon-beta1b in secondary progressive multiple sclerosis. Ann Neurol. 1999 Dec;46(6):850-9.
Ebers GC, Reder AT, Traboulsee A, et al.; Investigators of the **16-Year Long-Term Follow-Up** Study. Long-term follow-up of the original interferon-beta1b trial in multiple sclerosis: design and lessons from a 16-year observational study. Clin Ther. 2009 Aug;31(8):1724-36.
[24] Filippini G, Munari L, Incorvaia B, et al. Interferons in relapsing remitting multiple sclerosis: a **systematic review. Lancet**. 2003 Feb 15;361(9357):545-52.
[25] MS Therapy Consensus Group J Neurol 2004;251:1329-39
[26] Reess J, Haas J, Gabriel K, Fuhlrott A, Fiola M. Both paracetamol and ibuprofen are equally effective in managing flu-like symptoms in relapsing-remitting multiple sclerosis patients during interferon beta-1a (AVONEX) therapy. Mult Scler. 2002 Feb;8(1):15-8.
[27] Panitch H, Goodin DS, Francis G, et al.; **EVIDENCE** Study Group. Evidence of Interferon Dose-response: European North American Compartative Efficacy; University of British Columbia MS/MRI Research Group. Randomized, comparative study of interferon beta-1a treatment regimens in MS: The EVIDENCE Trial. Neurology. 2002 Nov 26;59(10):1496-506. (Panitch H, Goodin D, Francis G. For the **EVIDENCE** (Evidence of Interferon Dose-response: European North American Comparative Efficacy) Study Group and the University of British Columbia MS/MRI Research Group. Benefits of high-dose, high-frequency interferon beta-1a in relapsing-remitting multiple sclerosis are sustained to 16 months: Final comparative results of the EVIDENCE trial. J Neurol Sci. 2005 Sep 16; [Epub ahead of print])
[28] Durelli L, Verdun E, Barbero P, et al.; Independent Comparison of Interferon (INCOMIN) Trial Study Group. Every-other-day interferon beta-1b versus once-weekly interferon beta-1a for multiple sclerosis: results of a 2-year prospective randomised multicentre study (**INCOMIN**). Lancet. 2002 Apr 27;359(9316):1453-60.
[29] Leary S, Miller D, Stevenson V, Brex P, Chard D, Thompson A. Interferon Beta 1a in PPMS. Neurology 2003;60:44-51
[30] Johnson KP, Brooks BR, Ford CC, et al. Glatiramer acetate (Copaxone): comparison of continuous versus delayed therapy in a six-year organized multiple sclerosis trial. Mult Scler. 2003 Dec;9(6):585-91.
[31] Wolinsky JS, Comi G, Filippi M, et al. European/Canadian Glatiramer Acetate Study Group. Copaxone's effect on MRI-monitored disease in relapsing MS is reproducible and sustained. Neurology. 2002Oct 22;59(8):1284-6.
[32] Wolinsky JS, Narayana PA, Johnson KP; Multiple Sclerosis Study Group and the MRI Analysis Center. United States open-label glatiramer acetate extension trial for relapsing multiple sclerosis: MRI and clinical correlates. Multiple Sclerosis Study Group and the MRI Analysis Center. Mult Scler. 2001 Feb;7(1):33-41.
[33] Comi G, Filippi M, Wolinsky JS. European/Canadian multicenter, double-blind, randomized, placebo-controlled study of the effects of glatiramer acetate on magnetic resonance imaging-measured disease activity and burden in patients with relapsing multiple sclerosis. European/Canadian Glatiramer Acetate Study Group. Ann Neurol. 2001 Mar;49(3):290-7.
[34] Johnson KP, Brooks BR, Ford CC, et al. Sustained clinical benefits of glatiramer acetate in relapsing multiple sclerosis patients observed for 6 years. Copolymer 1 Multiple Sclerosis Study Group. Mult Scler. 2000 Aug;6(4):255-66.
[35] Munari L, Lovati R, Boiko A. Therapy with glatiramer acetate for multiple sclerosis. Cochrane Database Syst Rev. 2004;(1):CD004678. (Rovaris M, et al. Effect of glatiramer acetate on MS lesions enhancing at different gadolinium doses. Neurology. 2002 Nov 12;59(9):1429-32.) & (Comi G, Filippi M, Wolinsky JS. European/Canadian multicenter, double-blind, randomized, placebo-controlled study of the effects of glatiramer acetate on magnetic resonance imaging--measured disease activity and burden in patients with relapsing multiple sclerosis. European/Canadian Glatiramer Acetate Study Group. Ann Neurol. 2001 Mar;49(3):290-7.)
[36] Brenner T, Arnon R, Sela M et al. Humoral and cellular immune responses to Co-polymer 1 in MS patients treated with Copaxone. J Neuroimmunol 2001;115:152-160. (Namaka M, Pollitt-Smith M, Gupta A, et al. The clinical importance of neutralizing antibodies in relapsing-remitting multiple sclerosis. Curr Med Res Opin. 2006 Feb;22(2):223-39.The induction of NAbs in IFN-beta treated patients reduce clinical effect and accelerate disease progression.), (Ure DR, Rodriguez M. Polyreactive antibodies to glatiramer acetate promote myelin repair in murine model of demyelinating disease. FASEB J. 2002 Aug;16(10):1260-2. Epub 2002 Jun 7.) (Goodin DS, Frohman EM, Hurwitz B, O'Connor PW, Oger JJ, Reder AT, Stevens JC. Neutralizing antibodies to interferon beta: assessment of their clinical and radiographic impact: an evidence report: report of the Therapeutics and Technology Assessment Subcommittee of the American Academy of Neurology. Neurology. 2007 Mar 27;68(13):977-84.)
van der Voort Laura F.; Gilli Francesca; Bertolotto Antonio; et al. Clinical Effect of Neutralizing Antibodies to Interferon Beta That Persist Long After Cessation of Therapy for Multiple Sclerosis. Arch Neurol. 2010;0(2010):2010.21.
[37] Cohen, JA., Barkhof F, Comi G, et al., **TRANSFORMS** Study, Oral **Fingolimod** or Intramuscular Interferon for Relapsing Multiple Sclerosis. N Engl J Med 2010 0: NEJMoa0907839 (n=1292, 1yr, 1.25 or 0.5mg po od vs 30ug IM/wk)
Kappos L, Radue EW, O'Connor P et al. **FREEDOMS** Study, A Placebo-Controlled Trial of Oral **Fingolimod** in Relapsing Multiple Sclerosis. N Engl J Med 2010 0: NEJMoa0909494.. (n=1272, 2yr, 1.25 or 0.5mg po od vs placebo)
For fingolimod versus placebo, the relative risk reduction was 54% for the 0.5-mg dose and 60% for the 1.25-mg dose. For fingolimod versus interferon beta-1a, the relative risk reduction was 52% for the 0.5-mg dose and 39% for the 1.25-mg dose. Adverse effects were similar in all three trials of cladribine and fingolimod, and rates of events leading to discontinuation of a study drug were low but still at least twice as frequent with high-dose cladribine (7.9% for the 5.25-mg dose) and fingolimod (10% and 14% for the 1.25-mg dose). Side effects: herpetic infections, ?cancer, macular edema, bradycardia & lymphocytopenia.
Medical Letter. Oral Fingolimod (Gilenya) for Multiple Sclerosis. Dec 13/27, 2010.
Khatri B, Barkhof F, Comi G, et al; Comparison of fingolimod with interferon beta-1a in relapsing-remitting multiple sclerosis: a randomised **extension of the TRANSFORMS** study. Lancet Neurol. 2011 May 13.
Pelletier Daniel, Hafler David A. **Fingolimod** for Multiple Sclerosis. N Engl J Med 2012; 366:339-347.
Jain N, Bhatti MT. Fingolimod-associated **macular edema**: Incidence, detection, and management. Neurology. 2012 Feb 28;78(9):672-80.
Agashivala N, Kim E. **Cost-Effectiveness** of Early Initiation of **Fingolimod** Versus Delayed Initiation After 1 Year of Intramuscular Interferon Beta-1a in Patients with Multiple Sclerosis. Clin Ther. 2012 Jun 27.
Centonze D, R ossi S, Rinaldi F, Gallo P. **Severe relapses** under fingolimod treatment prescribed after natalizumab. Neurology 2012;79:2004 –2006.
Gross CM, Baumgartner A, Rauer S, Stich O. **Multiple sclerosis rebound** following herpes zoster infection and suspension of fingolimod. Neurology 2012;79:2006 –2007.
Visser F, Wattjes MP, Pouwels PJW, Linssen WHJP, van Oosten BW. **Tumefactive multiple sclerosis lesions** under fingolimod treatment. Neurology 2012;79:2000 –2002.
Ratchford JN, Costello K, Reich DS, Calabresi PA. **Varicella-zoster virus encephalitis and vasculopathy** in a patient treated with fingolimod. Neurology 2012;79: 2002–2004.
Calabresi PA, Radue E-W, Goodin D, et al. Safety and efficacy of fingolimod in patients with relapsing-remitting multiple sclerosis (FREEDOMS II): a double-blind, randomised, placebo-controlled, phase 3 trial. Lancet Neurology 2014; online March 28.
Karlsson G, Francis G, Koren G, et al. Pregnancy outcomes in the clinical development program of fingolimod in multiple sclerosis. Neurology 2014;82:674–680.
[38] O'Connor PW, Goodman A, Willmer-Hulme AJ, et al.; Natalizumab Multiple Sclerosis Trial Group. Randomized multicenter trial of natalizumab in acute MS relapses: clinical and MRI effects. Neurology. 2004 Jun 8;62(11):2038-43.

[39] Miller DH, Khan OA, Sheremata WA, et al.; International Natalizumab Multiple Sclerosis Trial Group. A controlled trial of natalizumab for relapsing multiple sclerosis. N Engl J Med. 2003 Jan 2;348(1):15-23.
[40] Tubridy N, Behan PO, Capildeo R, et al. The effect of anti-alpha4 integrin antibody on brain lesion activity in MS. The UK Antegren Study Group. Neurology. 1999 Aug 11;53(3):466-72.
[41] FDA Alert for Healthcare Professionals. Natalizuma (marketed as Tysabri) 02/28/2005; http://www.fda.gov/cder/drug/InfoSheets/HCP/natalizumabHCP.pdf. Last accessed 15 Mar 2005.
[42] Polman CH, O'Connor PW, Havrdova E, et al. AFFIRM Investigators. A randomized, placebo-controlled trial of natalizumab for relapsing multiple sclerosis. N Engl J Med. 2006 Mar 2;354(9):899-910. (InfoPOEMs: Natalizumab reduces the likelihood of relapse and progression of disability in patients with relapsing multiple sclerosis (RMS). Although no cases of progressive multifocal leukoencephalopathy (PML) were seen in this study, and the drug was well tolerated, a meta-analysis estimates the risk at approximately 1 per 1000 patients treated for 18 months. (LOE = 1b))
[43] Rudick RA, Stuart WH, Calabresi PA, et al. **SENTINEL** Investigators. Natalizumab plus interferon beta-1a for relapsing multiple sclerosis. N Engl J Med. 2006 Mar 2;354(9):911-23. (Ransohoff RM. Natalizumab for multiple sclerosis. N Engl J Med. 2007 Jun 21;356(25):2622-9.)
Pucci E, Giuliani G, Solari A, Simi S, Minozzi S, Di Pietrantonj C, Galea I. **Natalizumab** for relapsing remitting multiple sclerosis. Cochrane Database of Systematic Reviews 2011, Issue 10. Art. No.: CD007621. DOI: 10.1002/14651858.CD007621.pub2. Although one trial did not contribute to efficacy results due to its duration, we found robust evidence in favour of a reduction in relapses and disability at 2 years in RRMS patients treated with NTZ. The drug was well tolerated. There are current significant safety concerns due to reporting of an increasing number of PML cases in patients treated with NTZ. This review was unable to provide an up-to-date systematic assessment of the risk due to the maximum 2 year-duration of the trials included. An independent systematic review of the safety profile of NTZ is warranted. NTZ should be used only by skilled neurologists in MS centres under surveillance programs.
Hellwig K, Haghikia A, Gold R. Pregnancy and natalizumab: results of an observational study in 35 accidental pregnancies during natalizumab treatment. Mult Scler. 2011 Aug;17(8):958-63.
Haghikia A, Langer-Gould A, Rellensmann G, et al. Natalizumab Use During the Third Trimester of Pregnancy. JAMA Neurol. 2014 May 12.
[44] Kleinschmidt-Demasters BK, Tyler KL. Progressive Multifocal Leukoencephalopathy Complicating Treatment with Natalizumab and Interferon Beta-1a for Multiple Sclerosis. N Engl J Med. 2005 Jun 9; [Epub ahead of print]
(Yousry TA, Major EO, Ryschkewitsch C, et al. Evaluation of patients treated with natalizumab for progressive multifocal leukoencephalopathy. N Engl J Med. 2006 Mar 2;354(9):924-33.) (May 3, 2007 - Biogen Idec (NASDAQ: BIIB) and Elan Corporation, plc (NYSE: ELN) announced today that new data from the TOUCH Prescribing Programä and TYGRIS safety study confirm the safety profile from previous clinical studies of TYSABRI® (natalizumab). Also presented at the 59th annual meeting of the American Academy of Neurology in Boston, MA were extension study data that showed that TYSABRI has a sustained treatment effect on clinical relapses and the risk of disability progression in multiple sclerosis (MS) patients treated for up to three years. The companies recently reported that as of mid-April 2007 approximately 12,500 patients have been prescribed TYSABRI worldwide. The companies estimate that in both commercial use and clinical trials, there are currently over 10,000 patients on TYSABRI therapy worldwide. No New PML Cases 10 Months After Tysabri Allowed Back on Market. The drug is currently being used by more than 10,00 patients worldwide -- including roughly 6600 in the U.S. -- the manufacturer said.) July 31/08 Biogen, Elan Report Brain Infections in Patients Shares of Biogen Idec Inc. and Elan Corp. fell sharply in late trading Thursday, after the companies said their multiple sclerosis drug Tysabri has been linked to **two new cases** of a rare and often fatal brain inflammation.
Goodin DS, Cohen BA, O'Connor P, Kappos L, Stevens JC; Therapeutics and Technology Assessment Subcommittee of the **American Academy of Neurology**. Assessment: the use of natalizumab (Tysabri) for the treatment of multiple sclerosis (an evidence-based review): report of the Therapeutics and Technology Assessment Subcommittee of the American Academy of Neurology. Neurology. 2008 Sep 2;71(10):766-73. The **PML** risk in a pooled clinical trial cohort has been estimated to be 1 person for every 1,000 patients treated for an average of 17.9 months, although this figure could change in either direction with more experience with the drug.
December 17, 2008 — Biogen Idec and Élan reported to the United States Securities and Exchange Commission (SEC) that "relevant regulatory agencies" had been informed of another case of progressive multifocal leukoencephalopathy (PML) with natalizumab (Tysabri) monotherapy in a patient with multiple sclerosis (MS). The case was found through surveillance, the companies note, and the patient is stable. The male patient is from Germany and had been on natalizumab monotherapy for 26 months. He is reported to be stable and under the care of his physician. The companies released information on their December 11 Form 8-K report to the SEC December 15.
Health Canada Feb/09 New Safety Information Regarding Progressive Multifocal Leukoencephalopathy (PML) Associated with Tysabri (natalizumab) http://www.hc-sc.gc.ca/dhp-mps/medeff/advisories-_avis/prof/_2009/tysabri_2_hpc-cps-eng.php
Biogen http://phx.corporate-ir.net/External.File?item=UGFyZW50SUQ9ODc0MXxDaGlsZElEPS0xfFR5cGU9Mw==&t=1
Chen, Yiping, Bord, Evelyn, Tompkins, Troy, et al. Asymptomatic Reactivation of **JC Virus** in Patients Treated with Natalizumab. N Engl J Med 2009 361: 1067-1074.
Wenning, Werner, Haghikia, Aiden, Laubenberger, Jorg, et al. **Treatment of Progressive Multifocal Leukoencephalopathy** Associated with Natalizumab. N Engl J Med 2009 361: 1075-1080.
Linda, Hans, von Heijne, Anders, Major, Eugene O., et al. **Progressive Multifocal Leukoencephalopathy** after **Natalizumab Monotherapy**. N Engl J Med 2009 361: 1081-1087.
Major, Eugene O.Reemergence of PML in Natalizumab-Treated Patients -- New Cases (=14), Same Concerns. N Engl J Med 2009 361: 1041-1043.
FDA Sep/09 documents 13 PML cases http://www.fda.gov/Drugs/DrugSafety/PostmarketDrugSafetyInformationforPatientsandProviders/ucm107198.htm
October 27, 2009 — The European Medicines Agency (EMEA) disclosed October 23 that it has begun a review of the risk–benefit balance for use of natalizumab (*Tysabri*, Biogen Idec/Elan) in relapsing-remitting multiple sclerosis in light of new cases of progressive multifocal leukoencephalopathy (PML) with treatment. The EMEA notes it started a review of the benefits and risks of natalizumab because reports of PML cases worldwide have climbed now to 23 since the drug was reinstated in the market in 2006. "This review is initiated to discuss any additional measures necessary to ensure the safe use of Tysabri and how to balance the risks to the patients against the benefits of the treatment," a press release from EMEA notes. The release was a round-up of EMEA activities as of October 2009. Natalizumab was taken off the market in February 2005 after the first 3 cases of PML were reported. On September 23, 2009, the US Food and Drug Administration (FDA) reported that the count for confirmed cases of PML worldwide in patients treated with natalizumab as monotherapy had reached 13. They have now confirmed the new total case count at 23.
Jan 21,2010 (Dow Jones)--As of Wednesday, there have been 31 cases of a rare brain infection in multiple sclerosis patients on Tysabri, sold by Biogen Idec Inc. (BIIB) and Elan Corp. (ELN), according to a review by a European regulatory panel. The European Medicines Agency's Committee for Medicinal Products for Human Use, known as CHMP, reported the cases of progressive multifocal leukoencephalopathy, or PML, in a review of the drug that concluded its rewards outweigh its risks and the drug should stay on the market. Of the **31 cases**, 23 of the patients were on the drug for more than two years, which puts the infection rate at about 1 in 1,000 patients for those exceeding that duration.
This assertion is the same held by the company and implied by the drug's label.
FDA Feb/10 notified healthcare professionals and patients that the risk of developing progressive multifocal leukoencephalopathy (PML) increases with the number of Tysabri infusions received. This new safety information, based on reports of 31 confirmed cases of PML received by the FDA as of January 21, 2010, will now be included in the Tysabri drug label and patient *Medication Guide*.
March 18, 2010 9:22 AM EDT Biogen Idec (Nasdaq: BIIB) disclosed that the number of PML cases involving those taking its Tysabri drug has increased to 42 patients with 9 who have died.
May/10 Biogen Idec Canada Inc., has updated the Tysabri product information with new information on Progressive Multifocal Leukoencephalopathy (PML). The risk of PML increases with increasing duration of treatment with Tysabri. After 24 infusions, physicians are to review with their patients, the benefits and risk of continuing Tysabri treatment.
Schröder A, Lee DH, Hellwig K, Lukas C, Linker RA, Gold R. **Successful Management of Natalizumab**-Associated Progressive Multifocal Leukoencephalopathy and Immune Reconstitution Syndrome in a Patient With Multiple Sclerosis. Arch Neurol. 2010 Jul 12.
Oct 22/10 - Two more patients taking Biogen Idec Inc's multiple sclerosis drug Tysabri (natalizumab) have developed progressive multifocal leukoencephalopathy (PML), the company said on Wednesday. The Cambridge, Massachusetts-based biotechnology company said in its latest monthly update that as of Oct. 1, there have been **70 confirmed cases of PML**, up from 68 as of Sept. 2. Of those, 14 have died and 56 are alive with varying degrees of disability ranging from mild to severe. There were no additional deaths in October. As of June 30, about 71,400 patients had received Tysabri since it was launched.
Vermersch P, Kappos L, Gold R, et al. Clinical outcomes of natalizumab-associated progressive multifocal leukoencephalopathy. Neurology. 2011 May 17;76(20):1697-704.
FDA Jan/12 JC virus is common and usually harmless, the agency said, but its presence — along with either of the other two PML risk factors — can be dangerous in patients taking immunomodulating drugs like natalizumab. The other risk factors are treatment with natalizumab for longer than 2 years, and previous treatment with immunosuppressant drugs such as methotrexate or cyclophosphamide. The FDA estimates that patients with all three risk factors face about a 1% risk for PML (11 cases per 1000 patients treated).
Schwab N, Schneider-Hohendorf T, et al. **Natalizumab-associated PML**: challenges with incidence, resulting risk, and risk stratification. Neurology 2017;88:1197–1205.

Bloomgren G, Richman S, Hotermans C, et al. **Risk** of natalizumab-associated **progressive multifocal leukoencephalopathy**. N Engl J Med 2012;366:1870-80.
[45] Filipini G, Brusaferri F, Sibley WA et al. Corticosteroids or ACTH for acute exacerbations in MS. Cochrane DataBase Syst Rev 2000;CD001331.
[46] Wenning GK, Wietholter H, Schnauder G et al. Recovery of the HTPA axis from suppression by short-term, high dose IV prednisolone therapy in patients with MS. Acta Neurol Scand 1994;89:270-273.
[47] Rizvi SA, Bashir K. Other therapy options and future strategies for treating patients with multiple sclerosis. Neurology. 2004 Dec 28;63(12 Suppl 6):S47-54.
[48] Patti F, Amato MP, Filippi M, et al. A double blind, placebo-controlled, phase II, add-on study of cyclophosphamide (CTX) for 24 months in patients affected by multiple sclerosis on a background therapy with interferon-beta study denomination: CYCLIN. J Neurol Sci. 2004 Aug 15;223(1):69-71.
La Mantia L, Milanese C, Mascoli N, et al. Cyclophosphamide for multiple sclerosis. Cochrane Database Syst Rev. 2002;(4):CD002819.
Patti F, Reggio E, Palermo F, et al. A. Stabilization of rapidly worsening multiple sclerosis for 36 months in patients treated with interferon beta plus cyclophosphamide followed by interferon beta. J Neurol. 2004 Dec;251(12):1502-6.

Jeffery DR. The argument against the use of cyclophosphamide and mitoxantrone in the treatment of multiple sclerosis. J Neurol Sci. 2004 Aug 15;223(1):41-6.
Krishnan C, Kaplin AI, Brodsky RA, et al. Reduction of Disease Activity and Disability With High-Dose Cyclophosphamide in Patients With Aggressive Multiple Sclerosis. Arch Neurol. 2008 Jun 9. [Epub ahead of print] Treatment with HiCy (50 mg/kg/d for 4 consecutive days) was safe and well tolerated in our patients with MS. Patients experienced (n=9) a pronounced reduction in disease activity and disability after HiCy treatment. This immunoablative regimen of cyclophosphamide for patients with aggressive MS is worthy of further study and may be an alternative to bone marrow transplantation.
Makhani N, Gorman MP, Branson HM, et al. **Cyclophosphamide** therapy in pediatric multiple sclerosis. Neurology. 2009 May 13. Cyclophosphamide is an option for the treatment of children with aggressive multiple sclerosis refractory to first-line therapies. Recommendations regarding patient selection, treatment administration, and monitoring are discussed.

[49] Casetta I ; Iuliano G ; Filippini G. **Azathioprine** for multiple sclerosis. **Cochrane** Database Syst Rev. 2007; (4):CD003982 (ISSN: 1469-493X) {Azathioprine is an appropriate maintenance treatment for patients with multiple sclerosis who frequently relapse and require steroids. Cumulative doses of 600 g should not be exceeded in relation to a possible increased risk of malignancy. Considering the trade off between the benefits and harms, azathioprine is a fair alternative to interferon beta for treating multiple sclerosis. A logical next step for future trials would seem the direct comparison of azathioprine and interferon beta. In fact the direct comparison between these two widely used treatments in multiple sclerosis has not been made.}

[50] Gray O, McDonnell GV, Forbes RB. Intravenous immunoglobulins for multiple sclerosis. Cochrane Database Syst Rev. 2003;(4):CD002936.
Dudesek A and Zettl U. Intravenous immunoglobulins as therapeutic option in the treatment of MS. J Neurol 2006; 253 (suppl 5):v50-58.
Schwarz S, Meinck HM, Storch-Hagenlocher B. [Intravenous immunoglobulins in multiple sclerosis. An update]. Nervenarzt. 2009 Aug;80(8):918-28. German.

[51] Gray O, McDonnell GV, Forbes RB. Methotrexate for multiple sclerosis. Cochrane Database Syst Rev. 2004;(2):CD003208.

[52] Keegan M, Konig F, McClelland R et al. Relation between humoral pathological changes in multiple sclerosis and response to therapeutic plasma exchange. Lancet. 2005 Aug 13-19;366(9485):579-82.
Stork L, Ellemberger D, Beißbarth T, et al. Differences in responses to **apheresis therapy** of patients with 3 histopathologically classified immunopathological patterns of multiple sclerosis [online Feb 5, 2018]. JAMA Neurol. doi:10.1001/jamaneurol.2017.4842

[53] Muraro PA, Bielekova B. Emerging therapies for multiple sclerosis. Neurotherapeutics. 2007 Oct;4(4):676-92.
Hauser SL, Waubant E, Arnold DL, et al. HERMES Trial Group. B-cell depletion with **rituximab** in relapsing-remitting multiple sclerosis. N Engl J Med. 2008 Feb 14;358(7):676-88. A single course of rituximab reduced inflammatory brain lesions and clinical relapses for 48 weeks.
Hawker K, O'Connor P, Freedman MS, et al. OLYMPUS trial group. Rituximab in patients with primary progressive multiple sclerosis: Results of a randomized double-blind placebo-controlled multicenter trial. Ann Neurol. 2009 Oct;66(4):460-71.
Naismith RT, Piccio L, Lyons JA, et al. **Rituximab** add-on therapy for breakthrough relapsing multiple sclerosis: a 52-week phase II trial. Neurology. 2010 Jun 8;74(23):1860-7.
de Flon P, Gunnarsson M, Laurell K, et al. Reduced inflammation in relapsing-remitting multiple sclerosis after therapy switch to **rituximab**.Neurology. 2016 Jul 12;87(2):141-7.
Salzer J, Svenningsson R, Alping P, et al. **Rituximab** in multiple sclerosis: a retrospective observational study on safety and efficacy. Neurology 2016;87:2074–2081.
Bergman J, Burman J, Gilthorpe JD, et al. **Intrathecal** treatment trial of **rituximab** in progressive MS: An open-label phase 1b study. Neurology. 2018 Nov 13;91(20):e1893-e1901.
Naegelin Y, Naegelin P, von Felten S, et al. Association of Rituximab Treatment With Disability Progression Among Patients With Secondary Progressive Multiple Sclerosis (SPMS). JAMA Neurol. 2019 Jan 7.

[54] Giovannoni G, Comi G, Cook S, et al. the **CLARITY** Study Group, A Placebo-Controlled Trial of Oral Cladribine for Relapsing Multiple Sclerosis. N Engl J Med 2010 0: NEJMoa0902533. (n=1326, 96 weeks, 3.5 or 5.25mg/kg) For cladribine versus placebo, the relative risk reduction in the annualized relapse rate was 57.6% for the group receiving 3.5 mg per kilogram of body weight and 54.5% for those receiving 5.25 mg per kilogram. Adverse effects were similar in all three trials of cladribine and fingolimod, and rates of events leading to discontinuation of a study drug were low but still at least twice as frequent with high-dose cladribine (7.9% for the 5.25-mg dose) and fingolimod (10% and 14% for the 1.25-mg dose). Side effects: herpetic infections, ?cancer & lymphocytopenia.
Giovannoni G, Cook S, Rammohan K, et al; on behalf of the **CLARITY** study group. Sustained disease-activity-free status in patients with relapsing-remitting multiple sclerosis treated with **cladribine** tablets in the CLARITY study: a post-hoc and subgroup analysis. Lancet Neurol. 2011 Mar 10.
June 22/11, Merck Serono announced that, in light of feedback from regulatory authorities, the company would **no longer pursue a global approval process for cladribine tablets (Movectro)** for the treatment of relapsing-remitting MS & indeed would withdraw the drug from Australia and Russia, where it already had achieved approval.
Leist TP, Comi G, Cree BAC, et al, on behalf of the oral cladribine for early MS (ORACLE MS) Study Group. Effect of oral cladribine on time to conversion to clinically defi nite multiple sclerosis in patients with a fi rst demyelinating event (ORACLE MS): a phase 3 randomised trial. *Lancet Neurol* 2014; online Feb 4.

[55] Frohman EM, Goodin DS, Calabresi PA, et al.; Therapeutics and Technology Assessment Subcommittee of the American Academy of Neurology. The utility of MRI in suspected MS: report of the Therapeutics and Technology Assessment Subcommittee of the American Academy of Neurology. Neurology. 2003 Sep 9;61(5):602-11. (Whiting P, et al. Accuracy of magnetic resonance imaging for the diagnosis of multiple sclerosis: systematic review. BMJ. 2006 Mar 24; [Epub ahead of print] (InfoPOEMs: Magnetic resonance imaging (MRI) is not particularly useful in either ruling in or ruling out multiple sclerosis (MS). Relying on it to make the diagnosis will result in overdiagnosis of patients, and using it to rule out MS will cause you to miss approximately half the patients who will eventually be given a clinical diagnosis. (LOE = 1a))
Thompson Alan J, Toosy Ahmed T, Ciccarelli Olga, Pharmacological management of **symptoms in multiple sclerosis**: current approaches and future directions, The Lancet Neurology, Volume 9,Issue 12, Dec 2010, Pages 1182-1199.
Polman C, Reingold S, Banwell B, et al. Diagnostic Criteria for Multiple Sclerosis: 2010 Revisions to the "McDonald Criteria."Annals of Neurology.2011 Jan 11; 3-76.
Thompson AJ, Banwell BL, Barkhof F, et al. **Diagnosis** of multiple sclerosis: **2017 revisions of the McDonald criteria**. Lancet Neurol 2017; published online Dec 21.
Filippi M, et al. Prediction of multiple sclerosis diagnosis with **clinically isolated syndrome** using **2016 MAGNIMS & 2010 McDonald criteria**: retrospective study. Lancet Neurol 2017; online Dec 21.

[56] Crayton H, Heyman RA, Rossman HS. A multimodal approach to managing the symptoms of multiple sclerosis. Neurology. 2004 Dec 14;63(11 Suppl 5):S12-8.

[57] Krupp LB, Christodoulou C, Melville P, Scherl WF, MacAllister WS, Elkins LE. Donepezil improved memory in multiple sclerosis in a randomized clinical trial. Neurology. 2004 Nov 9;63(9):1579-85.

[58] Taus C, Giuliani G, Pucci E, D'Amico R, Solari A. Amantadine for fatigue in multiple sclerosis. Cochrane Database Syst Rev. 2003;(2):CD002818. (Pucci E, Branas P, D'Amico R, Giuliani G, Solari A, Taus C. Amantadine for fatigue in multiple sclerosis. Cochrane Database Syst Rev. 2007 Jan 24;(1):CD002818. The efficacy of amantadine in reducing fatigue in people with MS is poorly documented, as well as its tolerability.)

[59] Stankoff B, Waubant E, Confavreux C, et al.; French Modafinil Study Group. Modafinil for fatigue in MS: a randomized placebo-controlled double-blind study. Neurology. 2005 Apr 12;64(7):1139-43.
Brousil JA, Roberts RJ, Schlein AL. Cladribine: an investigational immunomodulatory agent for multiple sclerosis. Ann Pharmacother. 2006 Oct;40(10):1814-21. Epub 2006 Sep 19.
Yadav V, Bever C Jr, Bowen J, et al. Summary of evidence-based guideline: Complementary and alternative medicine in multiple sclerosis: Report of the Guideline Development Subcommittee of the American Academy of Neurology. Neurology. 2014 Mar 25;82(12):1083-92.

[60] Shakespeare DT, Boggild M, Young C. Anti-spasticity agents for multiple sclerosis. Cochrane Database Syst Rev. 2003;(4):CD001332. (Gallien P, Reymann JM, Amarenco G, Nicolas B, de Seze M, Bellissant E. Placebo controlled, randomised, double blind study of the effects of botulinum A toxin on detrusor sphincter dyssynergia in multiple sclerosis patients. J Neurol Neurosurg Psychiatry. 2005 Dec;76(12):1670-6.)

[61] Goodman AD, Brown TR, Edwards KR, et al. MSF204 Investigators. A phase 3 trial of extended release oral dalfampridine in multiple sclerosis. Ann Neurol. 2010 Oct;68(4):494-502.

[62] Bennett M, Heard R. Hyperbaric oxygen therapy for multiple sclerosis. Cochrane Database Syst Rev. 2004;(1):CD003057.

[63] Brown SJ. The Role of Vitamin D in Multiple Sclerosis (June). Ann Pharmacother. 2006 May 9; [Epub ahead of print]
Munger KL, et al. Serum 25-hydroxyvitamin D levels and risk of multiple sclerosis. JAMA. 2006 Dec 20;296(23):2832-8.
Ascherio A, Munger KL, Simon KC. Vitamin D and multiple sclerosis. Lancet Neurol. 2010 Jun;9(6):599-612.
Bentzen J, Flachs EM, Stenager E, Brønnum-Hansen H, Koch-Henriksen N. Prevalence of multiple sclerosis in Denmark 1950-2005. Mult Scler. 2010 Mar 9.
Stein MS, Liu Y, Gray OM, et al. A randomized trial of high-dose **vitamin D2** in relapsing-remitting multiple sclerosis. Neurology 2011;77:1611–1618.
Sotirchos ES, Bhargava P, Eckstein C, et al. Safety and immunologic effects of **high- vs low-dose cholecalciferol** in multiple sclerosis. Neurology. 2016 Jan 26;86(4):382-90. (10,400 vs 800 IU/daily x 6 months)
Munger KL, Hongell K, Åivo J, et al. **25-Hydroxyvitamin D deficiency** and risk of MS among women in the Finnish Maternity Cohort. Neurology. 2017 Sep 13.
Evans E, Piccio L, Cross AH. Use of Vitamins and Dietary Supplements by Patients With Multiple Sclerosis: A Review. JAMA Neurol. 2018 Apr 23.
Jagannath VA, Filippini G, Di Pietrantonj C, et al. **Vitamin D for the management of multiple sclerosis.** Cochrane Database Syst Rev. 2018 Sep 24;9:CD008422. To date, very low-quality evidence suggests no benefit of vitamin D for patient-important outcomes among people with MS. Vitamin D appears to have no effect on recurrence of relapse, worsening of disability measured by the Expanded Disability Status Scale (EDSS), and MRI lesions. Effects on health-related quality of life and fatigue are unclear. Vitamin D3 at the doses and treatment durations used in the included trials appears to be safe, although available data are limited. Seven ongoing studies will likely provide further evidence that can be included in a future update of this review.

[95] Traboulsee AL, Machan L, Girard JM, et al. Safety and efficacy of venoplasty in MS: a randomized, double-blind, sham-controlled, phase II trial. Neurology 2018;91: e1660–e1668.
[96] Traboulsee AL, Knox KB, Machan L, et al. Prevalence of extracranial venous narrowing on catheter venography in people with multiple sclerosis, their siblings, and unrelated healthy controls: a blinded, case-control study. Lancet 2013; online Oct 9. (CCSVI)
[97]Cortese I, Muranski P, Enose-Akahata Y, et al. **Pembrolizumab Treatment** for Progressive Multifocal Leukoencephalopathy. N Engl J Med. 2019 Apr 10
[98]Kim ES. **Fampridine Prolonged Release: A Review in Multiple Sclerosis Patients with Walking Disability**. Drugs. 2017 Sep;77(14):1593-1602.
[99]Xu Z, Zhang F, Sun F, Gu K, Dong S, He D. **Dimethyl fumarate for multiple sclerosis**. Cochrane Database of Systematic Reviews 2015, Issue 4. Art. No.: CD011076.
[100]Gold, Ralf et al. "**Long-term effects of delayed-release dimethyl fumarate in multiple sclerosis: Interim analysis of ENDORSE, a randomized extension study**." Multiple sclerosis (Houndmills, Basingstoke, England) vol. 23,2 (2017): 253-265.
[101] He D, Zhang C, Zhao X, Zhang Y, Dai Q, Li Y, Chu L. **Teriflunomide for multiple sclerosis**. Cochrane Database of Systematic Reviews 2016, Issue 3. Art. No.: CD009882
[102] Brown JWL, Coles A, Horakov D, et al. Association of initial **disease-modifying therapy with conversion to secondary progressive multiple sclerosis** among patients with relapsing-remitting multiple sclerosis [published Jan 15, 2019]. JAMA.
[103] Burt RK, Balabanov R, Burman J, et al. **Effect of Nonmyeloablative Hematopoietic Stem Cell Transplantation vs Continued Disease-Modifying Therapy on Disease Progression in Patients With Relapsing-Remitting Multiple Sclerosis: A Randomized Clinical Trial**. *JAMA.* 2019;321(2):165–174
[104]McCool R, Wilson K, Arber M, Fleetwood K, Toupin S, Thom H, Bennett I, Edwards S. **Systematic review and network meta-analysis comparing ocrelizumab with other treatments for relapsing multiple sclerosis**. Mult Scler Relat Disord. 2019 Apr;29:55-61
[105]Montalban X, Arnold DL, Weber MS, Staikov I, Piasecka-Stryczynska K, Willmer J, Martin EC, Dangond F, Syed S, Wolinsky JS; **Evobrutinib Phase 2 Study Group. Placebo-Controlled Trial of an Oral BTK Inhibitor in Multiple Sclerosis**. N Engl J Med. 2019 Jun 20;380(25):2406-2417.
[106] Palace J, Duddy M, Lawton M, et al **Assessing the long-term effectiveness of interferon-beta and glatiramer acetate in multiple sclerosis: final 10-year results from the UK multiple sclerosis risk-sharing scheme**. Journal of Neurology, Neurosurgery & Psychiatry 2019;90:251-260.

Additional references:

Abbas M, Lalive PH, Chofflon M, Simon HU, Chizzolini C, Ribi C. **Hypereosinophilia** in patients with multiple sclerosis treated with **natalizumab**. Neurology. 2011 Oct 18;77(16):1561-4.
Absinta M, Sati P, Masuzzo F, et al. Association of Chronic Active Multiple Sclerosis **Lesions With Disability In Vivo**. JAMA Neurol. 2019 Aug 12.
Absinta M, Vuolo L, Rao A, et al. Gadolinium-based **MRI characterization of leptomeningeal inflammation** in multiple sclerosis. Neurology 2015;84:18–28.
Agnihotri SP, Dang X, Carter JL, et al. **JCV GCN** in a **natalizumab**-treated MS patient is associated with mutations of the VP1 capsid gene. Neurology. 2014 Aug 19;83(8):727-32.
Aktas O, Hartung HP. CSI: MS. **Tracing optic nerve involvement** by standardized optical coherence tomography. Ann Neurol. 2019 Mar 22.
Almusalam N, Oh J, Terzaghi M, et al. Comparison of **Physician Therapeutic Inertia** for Management of Patients With Multiple Sclerosis in Canada, Argentina, Chile, and Spain. JAMA Netw Open. 2019 Jul 3;2(7):e197093.
Alping P, Frisell T, Novakova L, Islamet al. **Rituximab versus fingolimod after natalizumab** in multiple sclerosis patients. Ann Neurol. 2016 Mar 31.
Alroughani R, Alowayesh MS, Ahmed SF, et al. **Relapse occurrence in women with multiple sclerosis during pregnancy** in the new treatment era. Neurology. 2018 Mar 6;90(10):e840-e846.
AmatoMP, Razzolini L, Goretti B, et al. **Cognitive reserve** and **cortical atrophy** in multiple sclerosis: a longitudinal study. Neurology 2013;80:1728–1733.
Amato MP, Goretti B, Ghezzi A, et al; MS Study Group of the Italian Neurological Society. **Neuropsychological features in childhood** and juvenile multiple sclerosis: Five-year follow-up. Neurology. 2014 Oct 14;83(16):1432-8.
Andorra M, Nakamura K, Lampert EJ, et al. Assessing Biological and Methodological Aspects of **Brain Volume Loss in Multiple Sclerosis**. JAMA Neurol. 2018 Jul 2.
Androdias G, Bernard E, Biotti D, et al. Multiple sclerosis **broke my heart**. Ann Neurol. 2017 Apr 24.
Antoniol C, Jilek S, Schluep M, et al. Impairment of **JCV-specific T-cell response by corticotherapy**: Effect on PML-IRIS management? Neurology. 2012 Dec 4;79(23):2258-64.
Applebee A, Goodman AD, Mayadev AS, et al. Effects of **Dalfampridine** Extended-Release Tablets on 6-Minute Walk Distance in Patients With Multiple Sclerosis: A Post Hoc Analysis of a Double-Blind, Placebo-Controlled Trial. Clin Ther. 2015 Nov 9.
Arnold DL, Fisher E, et al. Superior MRI outcomes with **alemtuzumab compared with subcutaneous interferon β-1a** (**REBIF**) in MS. Neurology (**Care-MS I & II**). 2016 Oct 4;87(14):1464-1472.
Arntzen EC, Straume B, Odeh F, et al. Group-based, individualized, comprehensive core **stability and balance intervention** provides immediate and long-term improvements in walking in individuals with multiple sclerosis: A randomized controlled trial. Physiother Res Int. 2019 Jul 3:e1798.
Arrambide G, Espejo C, Eixarch H, et al. **Neurofilament light chain level** is a weak risk factor for the development of MS. Neurology. 2016 Sep 13;87(11):1076-84
Arvin AM, Wolinsky JS, et al. **Varicella-Zoster Virus** Infections in Patients Treated With **Fingolimod**: Risk Assessment & Consensus Recommendations for Management. JAMA Neurol. 2014 Nov 24.
Ascherio A, Munger KL, Simon KC. **Vitamin D** and multiple sclerosis. Lancet Neurol. 2010 Jun;9(6):599-612.
Ascherio A, Munger KL, White R, et al. **Vitamin D as an Early Predictor** of Multiple Sclerosis Activity and Progression. JAMA Neurol. 2014 Jan 20
Atkins HL, Bowman M, et al. Immunoablation and autologous **haemopoietic stem-cell transplantation** for aggressive multiple sclerosis: a multicentre single-group phase 2 trial. Lancet. 2016 Jun 8.
Aubert-Broche B, Fonov V, Narayanan S, et al. Canadian Pediatric Demyelinating Disease Network. Onset of multiple sclerosis before adulthood leads to **failure of age-expected brain growth**. Neurology. 2014 Dec 2;83(23):2140-6.
Aubert-Broche B, Weier K, Longoni G, et al. **Monophasic demyelination reduces brain growth** in children. Neurology 2017;88:1744–1750.

Axtell RC, de Jong BA, Boniface K, et al. **T helper type 1 and 17 cells** determine effi cacy of interferon-beta in multiple sclerosis and experimental encephalomyelitis. Nat Med 2010; 16: 406–12.
Azary S, Schreiner T, Graves J, et al. The contribution of **dietary intake** to relapse rate in early pediatric multiple sclerosis. J Neurol Neurosurg Psychiatry 2017. Online First 10.1136/jnnp-2017-315936.
Azary S, et al. Contribution of **dietary intake** to relapse rate in early paediatric multiple sclerosis. J Neurol Neurosurg Psychiatry. 2017 Oct 9. (? decrease saturated fat & increase vegetable intake)
Bagert BA, Marder E, Stüve O. Chronic Cerebrospinal Venous Insufficiency (**CCSVI**) and Multiple Sclerosis. Arch Neurol. 2011 Jul 11.
Balak D, Hajdarbegovic E. **PML** in Patients Treated with Dimethyl **Fumarate**. N Engl J Med. 2015 Aug 6;373(6):582-3.
Balint B, Haas J, Schwarz A, et al. **T-cell homeostasis in pediatric** multiple sclerosis: old cells in young patients. Neurology 2013;81:784–792.
Banwell B, Ghezzi A, Bar-Or A, Mikaeloff Y, Tardieu M. Multiple sclerosis in **children**: clinical diagnosis, therapeutic strategies, and future directions. Lancet Neurol. 2007 Oct;6(10):887-902.
Banwell B, Bar-Or A, Arnold DL, et al. Clinical, environmental, and genetic determinants of multiple sclerosis in **children with acute demyelination**: a prospective national cohort study. Lancet Neurol. 2011 Mar 31.
Bar-Or A, Freedman MS, Kremenchutzky M, et al. **Teriflunomide** effect on immune **response to influenza vaccine** in patients with multiple sclerosis. Neurology. 2013 Aug 6;81(6):552-8.
Bar-Or A, Grove RA, Austin DJ, et al. **Subcutaneous ofatumumab in patients with relapsing-remitting multiple sclerosis**: The MIRROR study. Neurology. 2018 May 15;90(20):e1805-e1814.
Baracchini C, Perini P, Calabrese M, et al. No evidence of chronic cerebrospinal venous insufficiency (**CCSVI**) at multiple sclerosis onset. Ann Neurol. 2011 Jan;69(1):90-9. doi: 10.1002/ana.22228.
Baracchini C, Perini P, Calabrese M, et al. Normal Cerebrospinal Venous Drainage (**CCSVI**) in MS at Onset. Ann Neurol. 2011 March 7.
Baracchini C, Perini P, Causin F, et al. Progressive multiple sclerosis is not associated with chronic cerebrospinal venous insufficiency (**CCSVI**). Neurology. 2011 Aug 17.
Barbin L, Rousseau C, et al. **CFSEP** and **OFSEP** groups. Comparative efficacy of **fingolimod vs natalizumab**: A French multicenter observational study. Neurology. 2016 Feb 23;86(8):771-778.
Baroncini D, Zaffaroni M, Moiola L, et al; iMED Registry and Gruppo di Studio SM-Società Italiana di Neurologia. **Long-term follow-up of pediatric MS patients starting treatment with injectable first-line agents**: A multicentre, Italian, retrospective, observational study. Mult Scler. 2018 Jan 1:1352458518754364.
Bargiela D, Bianchi MT, Westover MB, et al. **Selection of first-line therapy** in multiple sclerosis using risk-benefit decision analysis. Neurology. 2017 Feb 14;88(7):677-684
Barton J, Hardy TA, Riminton S, et al. **Tumefactive demyelination** following treatment for relapsing multiple sclerosis with **alemtuzumab**. Neurology. 2017 Mar 7;88(10):1004-1006.
Batista S, Alves C, d'Almeida OC, et al. **Disconnection as a mechanism for social cognition impairment** in multiple sclerosis. Neurology. 2017 Jul 4;89(1):38-45.
Bazelier MT, van Staa T-P, Uitdehaag BMJ, et al. Risk of **fractures** in patients with multiple sclerosis: a population based cohort study. Neurology 2012;78:1967–1973.
Bazelier MT, van Staa TP, Uitdehaag BM, et al. A **simple score** for estimating the long-term risk of **fracture** in patients with multiple sclerosis. Neurology. 2012 Aug 15.
Beadnall HN, Gill AJ, Riminton S, et al. **Virus-related Merkel cell carcinoma** complicating **fingolimod** treatment for multiple sclerosis. Neurology. 2016 Dec 13;87(24):2595-2597.
Beiki O, Frumento P, Bottai M, et al. Changes in the **Risk of Reaching Multiple Sclerosis Disability Milestones** In Recent Decades: A Nationwide Population-Based Cohort Study in Sweden. JAMA Neurol. 2019 Mar 18.
Bejaoui K, Rolak LA. What is the **risk of permanent disability** from a multiple sclerosis relapse? Neurology. 2010 Mar 16;74(11):900-2.
Belbasis L, Bellou V, Evangelou E, et al. **Environmental risk factors** and multiple sclerosis: an umbrella review of systematic reviews and meta-analyses. Lancet Neurol 2015; online Feb 4.
Belman AL, Krupp LB, Olsen CS, et al; US Network of Pediatric MS Centers. Characteristics of **Children and Adolescents With Multiple Sclerosis**. Pediatrics. 2016 Jul;138(1).
Berger JR, Houff SA, Gurwell J, et al. **JC virus antibody** status underestimates infection rates. Ann Neurol. 2013 Mar 22.
Berger JR, Aksamit AJ, et al. **PML diagnostic criteria**: Consensus statement from the **AAN Neuroinfectious Disease Section**. Neurology. 2013 Apr 9;80(15):1430-1438. (37% false negative)
Berger JR, Cree BA, Greenberg B, et al**. Progressive multifocal leukoencephalopathy after fingolimod treatment**. Neurology. 2018 May 15;90(20):e1815-e1821.
Bergman J, Burman J, Gilthorpe JD, et al. **Intrathecal treatment trial of rituximab in progressive MS**: An open-label phase 1b study. Neurology. 2018 Nov 13;91(20):e1893-e1901.
Bermel R, Weinstock-Guttman B, Bourdette D, Foulds P, You X, Rudick R. Intramuscular **interferon beta-1a** therapy in patients with relapsing-remitting multiple sclerosis: a **15-year follow-up** study. Mult Scler. 2010 Feb 18.
Bermel Robert A, Cohen Jeffrey A, Multiple sclerosis: advances in understanding pathogenesis and emergence of **oral treatment** options, The Lancet Neurology, Volume 10, Issue 1, January 2011, Pages 4-5, ISSN 1474-4422, DOI: 10.1016/S1474-4422(10)70282-9.
Bermel RA, You X, Foulds P, et al. **Predictors of long-term outcome** in multiple sclerosis patients treated with **interferon beta**. Ann Neurol. 2013 Jan;73(1):95-103.
Bevan RJ, Evans R, Griffiths L, et al. **Meningeal Inflammation and Cortical Demyelination** in Acute Multiple Sclerosis. Ann Neurol. 2018 Oct 25.
Bielekova B, Becker BL. **Monoclonal antibodies** in MS: mechanisms of action. Neurology. 2010 Jan 5;74 Suppl 1:S31-40.
Bielekova B, Richert N, Herman ML, et al. Intrathecal effects of **daclizumab** treatment of multiple sclerosis. Neurology 2011;77:1877–1886.
Birnbaum G, Cree B, Altafullah I, Zinser M, Reder AT. Combining beta interferon and **atorvastatin may increase disease** activity in multiple sclerosis. Neurology. 2008 Jun 4. [Epub ahead of print]
Birnbaum G, Iverson J. **Dalfampridine** may activate latent trigeminal neuralgia in patients with multiple sclerosis. Neurology. 2014 Oct 28;83(18):1610-2.
Bittner S, Simon OJ, Göbel K, et al. **Rasmussen encephalitis** treated with **natalizumab**. Neurology. 2013 Jul 23;81(4):395-7.
Blankenbach K, Schwab N, Hofner B, et al. **Natalizumab-associated progressive multifocal leukoencephalopathy** in Germany. Neurology. 2019 May 7;92(19):e2232-e2239.
Block VJ, Bove R, Zhao C, et al. Association of **Continuous Assessment of Step Count** by Remote Monitoring With Disability Progression Among Adults With Multiple Sclerosis. JAMA Netw Open. 2019 Mar 1;2(3):e190570.
Bodini B, Chard D, Altmann DR, et al. **White and gray matter** damage in primary progressive MS: The chicken or the egg? Neurology. 2016 Jan 12;86(2):170-6.
Bonafede MM, Johnson BH, Wenten M, Watson C. **Treatment patterns in disease-modifying therapy** for patients with multiple sclerosis in the United States. Clin Ther. 2013 Oct;35(10):1501-12.
Boster AL, et al. Lessons learned from **fatal progressive multifocal leukoencephalopathy** (PML) in a patient with multiple sclerosis treated with natalizumab. JAMA Neurol. 2013 Mar 1;70(3):398-402.
Bourre B, Marignier R, Zéphir H, et al. **Neuromyelitis optica and pregnancy**. Neurology 2012;78:875– 879.
Bourre B, Gueudry J, Lefaucheur R, et al. Progressive outer **retinal necrosis** in a multiple sclerosis patient on **natalizumab**. Neurology. 2016 Jan 19;86(3):312-3.
Bove R, Alwan S, Friedman JM, et al. Management of **multiple sclerosis during pregnancy and the reproductive years**: a systematic review. Obstet Gynecol. 2014 Dec;124(6):1157-68.
Bove R, Malik MT, Diaz-Cruz C, et al. The **2D:4D ratio**, a proxy for prenatal **androgen levels**, differs in men with and without MS. Neurology. 2015 Oct 6;85(14):1209-13.
Bove R, White CC, Fitzgerald KC, et al. **Hormone therapy** use and physical quality of life in postmenopausal women with multiple sclerosis. Neurology 2016;87:1457–1463.
Bove RM, Hauser SL. **Diagnosing** multiple sclerosis: art and science. Lancet Neurol. 2017 Dec 21.
Boz C, Terzi M, Özer B, et al. Comparative analysis of **fingolimod versus teriflunomide** in relapsing-remitting multiple sclerosis. Mult Scler Relat Disord. 2019 Aug 26;36:101376.
Braley TJ, Segal BM, Chervin RD. **Sleep-disordered breathing** in multiple sclerosis. Neurology. 2012 Aug 15.
Braley TJ, Chervin RD. **Fatigue** in multiple sclerosis: mechanisms, evaluation, and treatment. Sleep. 2010 Aug;33(8):1061-7.

Brickshawana A, Hinson SR, Romero MF, et al. Investigation of the **KIR4.1 potassium channel** as a putative antigen in patients with multiple sclerosis: a comparative study. Lancet Neurol 2014; online July 7.
Brioschi A, Gramigna S, et al. Effect of Modafinil on Subjective Fatigue in Multiple Sclerosis and Stroke Patients. Eur Neurol. 2009 Aug 7;62(4):243-249. [Epub ahead of print]
Brousil JA, Roberts RJ, Schlein AL. Cladribine: an investigational immunomodulatory agent for multiple sclerosis. Ann Pharmacother. 2006 Oct;40(10):1814-21. Epub 2006 Sep 19.
Brown RA, Narayanan S, Stikov N, et al. MTR recovery in brain lesions in the **BECOME** study of **glatiramer acetate vs interferon β-1b**. Neurology. 2016 Aug 30;87(9):905-11.
Browne P, Chandraratna D, Angood C, et al. **Atlas of Multiple Sclerosis 2013**: A growing global problem with widespread inequity. Neurology. 2014 Sep 9;83(11):1022-4.
Brownlee WJ, Hardy TA, Fazekas F, et al. **Diagnosis of multiple sclerosis**: progress and challenges. Lancet. 2016 Nov 23.
Brownlee WJ, Miszkiel KA, Tur C, et al. Inclusion of **optic nerve involvement in dissemination in space criteria for multiple sclerosis**. Neurology. 2018 Sep 18;91(12):e1130-e1134.
Brück W, Gold R, Lund BT, et al. **Therapeutic Decisions** in Multiple Sclerosis: Moving Beyond Efficacy. JAMA Neurol. 2013 Aug 5.
Brunetti L, Wagner ML, Maroney M, et al. **Teriflunomide** for the treatment of relapsing multiple sclerosis: a review of clinical data. Ann Pharmacother. 2013 Sep;47(9):1153-60.
Buck D, Cepok S, Hoffmann S, et al. Influence of the **HLA-DRB1 Genotype on Antibody Development to Interferon Beta** in Multiple Sclerosis. Arch Neurol. 2011 Apr;68(4):480-7.
Burman J, Iacobaeus E, et al. **Autologous haematopoietic stem cell transplantation** for aggressive multiple sclerosis: the Swedish experience. J Neurol Neurosurg Psychiatry. 2014 Feb 19.
Burman J, Zelano J. **Epilepsy** in multiple sclerosis: A nationwide population-based register study. Neurology. 2017 Dec 12;89(24):2462-2468.
Buron MD, Chalmer TA, Sellebjerg F, et al. Comparative effectiveness of **teriflunomide and dimethyl fumarate**: a nationwide cohort study. Neurology 2019;92:e1811–e1820.
Burt RK, Balabanov R, Han X, et al. Association of **nonmyeloablative hematopoietic stem cell transplantation** with neurological disability in patients with relapsing-remitting multiple sclerosis. JAMA. doi:10.1001/jama.2014.17986.
Burton JM, O`Connor PW, Hohol M, et al. **Oral versus intravenous steroids** for treatment of relapses in multiple sclerosis. Cochrane Database Syst Rev. 2012 Dec 12;12:CD006921. The analysis of the five included trials comparing intravenous versus oral steroid therapy for MS relapses do not demonstrate any significant differences in clinical (benefits and adverse events), radiological or pharmacological outcomes. Based on the evidence, oral steroid therapy may be a practical and effective alternative to intravenous steroid therapy in the treatment of MS relapses.
Buttmann M, Seuffert L, Mäder U, et al. **Malignancies after mitoxantrone** for multiple sclerosis: A retrospective cohort study. Neurology. 2016 May 11.
Button J, Al-Louzi O, Lang A, et al. **Disease-modifying therapies** modulate **retinal atrophy** in multiple sclerosis: A retrospective study. Neurology. 2017 Feb 7;88(6):525-532.
CADTH: Recommendations for **Drug Therapies** for **Relapsing-Remitting Multiple Sclerosis**-2013
CADTH: **Comparative Clinical and Cost-Effectiveness** of Drug Therapies for **Relapsing-Remitting Multiple Sclerosis**-CADTH-2013
Calabrese M, Gasperini C, Tortorella C, et al. “Better explanations” in multiple sclerosis **diagnostic workup**: a 3-year longitudinal study. Neurology 2019;92: e2527–e2537.
Calabrese M, Rinaldi F, Mattisi I, et al. The predictive value of **gray matter** atrophy in clinically isolated syndromes. Neurology. 2011 Jul 19;77(3):257-63.
Calabrese M, Romualdi C, Poretto V, et al. The changing clinical course of multiple sclerosis: A matter of **grey matter**. Ann Neurol. 2013 Mar 12.
Calabresi PA, Bohnen NI. Can **PET imaging** tell us what's the matter with the gray matter in multiple sclerosis? Neurology. 2012 Aug 7;79(6):496-7.
Calabresi PA, Giovannoni G, Confavreux C, et al.for the AFFIRM and SENTINEL Investigators. The incidence and significance of **anti-natalizumab antibodies**. Results from AFFIRM and SENTINEL. Neurology. 2007 Aug 29; [Epub ahead of print] The incidence of persistent antibody positivity associated with natalizumab is 6%. Reduced clinical efficacy is apparent in persistently positive patients. Patients with a suboptimal clinical response or persistent infusion-related adverse events should be considered for antibody testing.
Calabresi PA, Radue E-W, Goodin D, et al. Safety and efficacy of **fingolimod** in patients with relapsing-remitting multiple sclerosis (**FREEDOMS II**): a double-blind, randomised, placebo-controlled, phase 3 trial. Lancet Neurology 2014; online March 28.
Calabresi PA, Kieseier BC, Arnold DL, et al; for the **ADVANCE** Study Investigators. **Pegylated interferon beta-1a** for relapsing-remitting multiple sclerosis (ADVANCE): a randomised, phase 3, double-blind study. Lancet Neurol. 2014 Apr 30.
Calabresi PA. **B-Cell Depletion** - A Frontier in Monoclonal Antibodies for Multiple Sclerosis. N Engl J Med. 2016 Dec 21.
Caloyeras JP, Zhang B, et al. **Cost-Effectiveness Analysis of Interferon Beta-1b** for the Treatment of Patients With a First Clinical Event Suggestive of Multiple Sclerosis. Clin Ther. 2012 Apr 26.
CAMMS223 Trial Investigators, Coles AJ, Compston DA, et al. **Alemtuzumab** vs. Interferon beta-1a in early multiple sclerosis. N Engl J Med. 2008 Oct 23;359(17):1786-801. In patients with early, relapsing-remitting multiple sclerosis, alemtuzumab was more effective than interferon beta-1a but was associated with autoimmunity, most seriously manifesting as immune thrombocytopenic purpura. The study was not powered to identify uncommon adverse events.
Cantó E, Barro C, Zhao C, et al. Association Between **Serum Neurofilament Light Chain Levels and Long-term Disease Course** Among Patients With Multiple Sclerosis Followed up for 12 Years. JAMA Neurol. 2019 Aug 12.
Carrá A, Onaha P, Luetic G, et al. Therapeutic outcome 3 years after **switching of immunomodulatory** therapies in patients with relapsing-remitting multiple sclerosis in Argentina. Eur J Neurol. 2008 Apr;15(4):386-93. In conclusion, patients who fail first-line immunomodulatory therapy generally benefit from switching to another class of immunomodulatory therapy.
Carrithers MD. Update on **Disease-Modifying Treatments** for Multiple Sclerosis. Clin Ther. 2014 Sep 10.
Castela E, Lebrun-Frenay C, Laffon M, et al. Evolution of **Nevi** During Treatment With **Natalizumab**: A Prospective Follow-up of Patients Treated With Natalizumab for Multiple Sclerosis. Arch Dermatol. 2010 Sep 20.
Castrop F, Kowarik MC, Albrecht H, et al. Severe **multiple sclerosis relapse under fingolimod** therapy: Incident or coincidence? Neurology. 2012 Mar 20;78(12):928-30.
Chalkias S, Dang X, Bord E, et al. **JC virus Reactivation During Prolonged Natalizumab** Monotherapy for Multiple Sclerosis. Ann Neurol. 2014 Mar 31.
Chan A, Lo-Coco F. **Mitoxantrone-related acute leukemia** in MS: An open or closed book? Neurology. 2013 Apr 16;80(16):1529-33.
Chan D, Binks S, Nicholas JM, et al. Effect of **high-dose simvastatin** on cognitive, neuropsychiatric, and health-related quality-of-life measures in secondary progressive multiple sclerosis: secondary analyses from the **MS-STAT** randomised, placebo-controlled trial. Lancet Neurol. 2017 Aug;16(8):591-600.
Chard DT, Geurts JJ. Predicting the development of multiple sclerosis: Is **gray matter** a missing piece of the puzzle? Neurology. 2011 Jul 19;77(3):210-1.
Chard DT, Benedict RH. Paradoxes in **thalamic function and cognition** in people with multiple sclerosis: Less is more. Neurology. 2015 Feb 24;84(8):764-5.
Chartier N, Epstein J, Soudant M, et al. Clinical follow-up of **411 patients with relapsing and progressive multiple sclerosis 10 years after discontinuing mitoxantrone treatment**: a real-life cohort study. Eur J Neurol. 2018 Dec;25(12):1439-1445.
Chataway J, Schuerer N, Alsanousi A, et al. Effect of **high-dose simvastatin** on brain atrophy and disability in secondary progressive multiple sclerosis (**MS-STAT**): a randomised, placebo-controlled, phase 2 trial. Lancet 2014; online March 19.
Chataway J, Martin K, Barrell K, et al. Effects of **ATX-MS-1467** immunotherapy over 16 weeks in relapsing multiple sclerosis. Neurology. 2018 Mar 13;90(11):e955-e962.

Chiaravalloti ND, Moore NB, Nikelshpur OM, DeLuca J. An RCT to treat **learning impairment** in multiple sclerosis: the MEMREHAB trial. Neurology 2013;81:2066–2072.
Chilcott J, McCabe C, Tappenden P, et al. Cost Effectiveness of Multiple Sclerosis Therapies Study Group. Modelling the cost effectiveness of interferon beta and glatiramer acetate in the management of multiple sclerosis. Commentary: evaluating disease modifying treatments in multiple sclerosis. BMJ. 2003 Mar 8;326(7388):522; discussion 522.
Chitnis T, Ness J, Krupp L, et al. Clinical features of **neuromyelitis optica in children**: US Network of Pediatric MS Centers report. Neurology. 2016 Jan 19;86(3):245-52.
Chitnis T, Arnold DL, Banwell B, et al; PARADIGMS Study Group. Trial of **Fingolimod versus Interferon Beta-1a in Pediatric Multiple Sclerosis**. N Engl J Med. 2018 Sep 13;379(11):1017-1027.
Ciccarelli O, Barkhof F, Bodini B, et al. **Pathogenesis of multiple sclerosis**: insights from **molecular and metabolic imaging**. Lancet Neurol. 2014 Aug;13(8):807-822.
Ciccone A, Beretta S, Brusaferri F, et al. **Corticosteroids** for the long-term treatment in multiple sclerosis. Cochrane Database Syst Rev. 2008 Jan 23;(1):CD006264. There is no enough evidence that long-term corticosteroid treatment delays progression of long term disability in patients with MS. Since one study at high risk of bias showed that the administration of pulsed high dose i. v. MP is associated with a significant reduction in the risk of long term disability progression in patients with RR MS, an adequately powered, a quality RCT is needed to investigate this finding.
Clerico M, Faggiano F, Palace J, Rice G, Tintorè M, Durelli L. Recombinant **interferon beta** or glatiramer acetate for delaying conversion of the **first demyelinating event to multiple sclerosis**. Cochrane Database Syst Rev. 2008 Apr 16;(2):CD005278. The efficacy of IFN beta treatment on preventing the conversion from CIS to CDMS was confirmed over two years of follow-up. Since patients had some clinical heterogeneity (length of follow-up, clinical findings of initial attack), it could be useful for the clinical practice to further analyse the efficacy of IFN beta treatment in different patient subgroups.
Clerico M, Schiavetti I, De Mercanti SF, et al. Treatment of Relapsing-Remitting Multiple Sclerosis **After 24 Doses of Natalizumab**: Evidence From an Italian Spontaneous, Prospective, and Observational Study (the **TY-STOP** Study). JAMA Neurol. 2014 Jun 30.
Clifford DB. Lessons from the clinic: A case of **natalizumab-associated PML**. Neurology. 2011 Feb 8;76(6):574.
Cohen JA, Imrey PB, Calabresi PA, et al.; **ACT** Investigators. Results of the Avonex Combination Trial (ACT) in relapsing-remitting MS. Neurology. 2009 Feb 10;72(6):535-41. This trial did not demonstrate benefit of adding low-dose oral methotrexate or every other month IV methylprednisolone to interferon beta-1a in relapsing-remitting multiple sclerosis.
Cohen, JA., Barkhof F, Comi G, et al., **TRANSFORMS** Study Group, Oral **Fingolimod** or Intramuscular **Interferon** for Relapsing Multiple Sclerosis. N Engl J Med 2010 0: NEJMoa0907839
Cohen JA, Chun J. Mechanisms of **Fingolimod's** Efficacy and Adverse Effects in Multiple Sclerosis. Annals of Neurology. Accepted manuscript online: 21 MAR 2011: 1-59.
Cohen JA, Krishnan AV, Goodman AD, et al. The Clinical Meaning of **Walking Speed** as Measured by the Timed 25-Foot Walk in Patients With Multiple Sclerosis. JAMA Neurol. 2014 Sep 1.
Cohen JA, Khatri B, Barkhof F, et al; **TRANSFORMS** (Trial Assessing injectable interferoN vS. FTY720 Oral in RRMS) Study Group. **Long-term (up to 4.5 years)** treatment with **fingolimod** in multiple sclerosis: results from the extension of the randomised TRANSFORMS study. J Neurol Neurosurg Psychiatry. 2015 Jun 25.
Cohen J, Belova A, Selmaj K, et al; Glatiramer Acetate Clinical Trial to Assess Equivalence With Copaxone (**GATE**) Study Group. **Equivalence of Generic Glatiramer** Acetate in Multiple Sclerosis: A Randomized Clinical Trial. JAMA Neurol. 2015 Oct 12:1-9.
Cohen JA, Arnold DL, Comi G, et al, for the **RADIANCE** Study Group. Safety and efficacy of the selective sphingosine 1- phosphate receptor modulator **ozanimod** in relapsing multiple sclerosis (**RADIANCE**): a randomised, placebo-controlled, phase 2 trial. Lancet Neurol 2016; online Feb 12.
Coles A. The fragile benefit of BENEFIT [editorial]. Lancet Neurol. 2007;6:753-4.
Coles AJ, Fox E, Vladic A, et al. **Alemtuzumab versus interferon beta-1a** in early relapsing-remitting multiple sclerosis: post-hoc and subset analyses of clinical efficacy outcomes. **CAMMS223**. Lancet Neurol. 2011 Mar 10.
Coles AJ, Fox E, Vladic A, et al. **Alemtuzumab more effective than interferon β-1a** at 5-year follow-up of **CAMMS223** Clinical Trial. Neurology. 2012 Apr 3;78(14):1069-78.
Coles AJ, Cohen JA, Fox EJ, et al. **Alemtuzumab CARE-MS II 5-year** follow-up: Efficacy and safety findings. Neurology. 2017 Sep 12;89(11):1117-1126
Comabella M. Risk of multiple sclerosis in **children with acute demyelination**. Lancet Neurol. 2011 Mar 31.
Comabella M, Caminero AB, Malhotra S, et al. **TNFRSF1A polymorphisms** rs1800693 and rs4149584 in patients with multiple sclerosis. Neurology 2013;80:2010–2016.
Comabella M, Montalban X. **Body fluid biomarkers** in multiple sclerosis. Lancet Neurol. 2014 Jan;13(1):113-26.
Comi G, Filippi M, Wolinsky JS. European/Canadian multicenter, double-blind, randomized, placebo-controlled study of the effects of glatiramer acetate on magnetic resonance imaging-measured disease activity and burden in patients with relapsing multiple sclerosis. European/Canadian Glatiramer Acetate Study Group. Ann Neurol 2001;49:290-7.
Comi G, Filippi M, Barkhof F, et al. Effect of **early interferon treatment** on conversion to definite multiple sclerosis: a randomised study. Lancet. 2001;357:1576−82.
Comi G, Kappos L, Selmaj KW, et al. Safety and efficacy of **ozanimod versus interferon beta-1a** in relapsing multiple sclerosis (SUNBEAM): a multicentre, randomised, minimum 12-month, phase 3 trial. Lancet Neurol. 2019 Sep 3.
Comi G, Martinelli V, Rodegher M, et al. for the PreCISe study group. Effect of glatiramer acetate on conversion to **clinically definite** multiple sclerosis in patients with clinically isolated syndrome (**PreCISe study**): a randomised, double-blind, placebo-controlled trial. Lancet. 2009 Oct 6. [Epub ahead of print]
Comi G, De Stefano N, Freedman M, et al. Comparison of **two dosing frequencies of subcutaneous interferon beta-1a** in patients with a first clinical demyelinating event suggestive of multiple sclerosis (**REFLEX**): a phase 3 randomised controlled trial. Lancet Neurol 2011; published online Dec 5. (Rebif 44ug sc three times a week or once a week x 2 years)
Comi G et al. Placebo-controlled trial of oral **laquinimod** for multiple sclerosis. (**ALLEGRO**) N Engl J Med 2012 Mar 15; 366:1000. (n=1106, 2yrs, ↑ALT 5 vs 2%)
Comi G, Radaelli M, Soelberg Sørensen P. **Evolving concepts in the treatment** of relapsing multiple sclerosis. Lancet. 2016 Nov 23. pii: S0140-6736(16)32388-1.
Confavreux C, Vukusic S, Moreau T, Adeleine P. **Relapses and progression of disability** in multiple sclerosis. N Engl J Med. 2000 Nov 16;343(20):1430-8.
Confavreux C, O'Connor P, Comi G, et al, for the the **TOWER** Trial Group. Oral **teriflunomide** for patients with relapsing multiple sclerosis (TOWER): a randomised, double-blind, placebo-controlled, phase 3 trial. Lancet Neurol 2014; online Jan 23.
Connick P, Kolappan M, Crawley C, et al. **Autologous mesenchymal stem cells** for the treatment of secondary progressive multiple sclerosis: an open-label phase 2a proof-of-concept study. Lancet Neurol 2012
Conway D, Cohen JA. **Combination therapy** in multiple sclerosis. Lancet Neurol. 2010 Mar;9(3):299-308.
Corboy JR, Weinshenker BG, Wingerchuk DM. Comment on **2018 American Academy of Neurology guidelines on disease-modifying therapies in MS**. Neurology. 2018 Jun 12;90(24):1106-1112.
Corey-Bloom J, Wolfson T, Gamst A, et al. Smoked cannabis for spasticity in multiple sclerosis: a randomized, placebo-controlled trial. CMAJ. 2012 May 14.
Correale J, Farez MF, Ysrraelit MC. Increase in multiple sclerosis activity **after assisted reproduction technology**. Ann Neurol. 2012 Oct 3.
Cortese I, Ohayon J, Fenton K, et al. Cutaneous adverse events in multiple sclerosis patients treated with **daclizumab**. Neurology. 2016 Mar 1;86(9):847-55.
Cortese M, Yuan C, Chitnis T, et al. No association between dietary **sodium intake** and the risk of multiple sclerosis. Neurology 2017;89:1322–1329.
Cortese M, Chitnis T, Ascherio A, Munger KL. Total **intake of different minerals and the risk of multiple sclerosis**. Neurology. 2019 Apr 30;92(18):e2127-e2135.

Cortese R, Magnollay L, Tur C, et al. Value of the **central vein sign at 3T** to differentiate MS from seropositive NMOSD. Neurology 2018;90:e1183–e1190.
Cossburn M, Pace AA, Jones J, et al. Autoimmune disease after **alemtuzumab** treatment for multiple sclerosis in a multicenter cohort. Neurology. 2011 Aug 9;77(6):573-9.
Cossburn MD, Harding K, Ingram G, et al. Clinical relevance of differential lymphocyte recovery after **alemtuzumab** therapy for multiple sclerosis. Neurology. 2013 Jan 1;80(1):55-61.
Costello F, Modi J, Lautner D, et al. Validity of the diagnostic criteria for **chronic cerebrospinal venous insufficiency** and association with multiple sclerosis. CMAJ. 2014 Jun 2.
Cotter J, Firth J, Enzinger C, Kontopantelis et al. **Social cognition** in multiple sclerosis: A systematic review and meta-analysis.Neurology. 2016 Oct 18;87(16):1727-1736.
Coyle PK. **Pediatric multiple sclerosis**: just like their elders? Arch Neurol. 2011 Apr;68(4):419-21.
Cree BAC, Hollenbach JA, Bove R, MS-EPIC Team, et al. **Silent progression in disease activity**-free relapsing multiple sclerosis. Ann Neurol. 2019 May;85(5):653-666.
Cree BA, Stuart WH, Tornatore CS, et al. Efficacy of Natalizumab Therapy in Patients of African Descent With Relapsing Multiple Sclerosis: Analysis of AFFIRM and SENTINEL Data. Arch Neurol. 2011 Apr;68(4):464-8.
Croteau D, Flowers C, Kulick CG, et al. Acute acalculous cholecystitis: a new safety risk for patients with MS treated with **alemtuzumab**. Neurology 2018;90:e1548–e1552
Culpepper WJ, Marrie RA, Langer-Gould A, et al; United States Multiple Sclerosis Prevalence Workgroup (MSPWG). Validation of an **algorithm for identifying MS cases** in administrative health claims datasets. Neurology. 2019 Mar 5;92(10):e1016-e1028.
Dalla Costa G, Martinelli V, Moiola L, et al. **Serum neurofilaments increase at PML onset in natalizumab-treated MS patients**. Ann Neurol. 2019 Feb 13.
Dalla Costa G, Martinelli V, Sangalli F, et al. **Prognostic value of serum neurofilaments in patients with clinically isolated syndromes**. Neurology 2019;92:e733–e741.
Dang X, Koralnik IJ. Gone over to the dark side: **Natalizumab-associated JC virus** infection of neurons in cerebellar gray matter. Ann Neurol. 2013 Aug 2.
De Angelis F, John NA, Brownlee WJ. **Disease-modifying therapies for multiple sclerosis**. BMJ. 2018 Nov 27;363:k4674.
de Flon P, Gunnarsson M, Laurell K, et al. Reduced inflammation in relapsing-remitting multiple sclerosis after therapy switch to **rituximab**. Neurology. 2016 Jul 12;87(2):141-7.
De Giglio L, De Luca F, Gurreri F, et al. Effect of **dalfampridine on information processing speed** impairment in multiple sclerosis. Neurology. 2019 Jul 22.
de Jong HJI, Kingwell E, Shirani A, et al. Evaluating the safety of **β-interferons in MS**: A series of nested case-control studies. Neurology. 2017 Jun 13;88(24):2310-2320.
De Meo E, Meani A, Moiola L, et al. **Dynamic gray matter volume changes** in pediatric multiple sclerosis: A 3.5 year MRI study. Neurology. 2019 Apr 9;92(15):e1709-e1723.
De Stefano N, Stromillo ML, Giorgio A, et al. Long-term assessment of **no evidence of disease activity** in relapsing-remitting MS. Neurology. 2015 Nov 10;85(19):1722-3.
Debs R, Maillart E, Fahed R, et al. Extensive brain demyelinating lesions under **natalizumab**: The role of anti-natalizumab antibodies. Neurology. 2015 Nov 3;85(18):1630-2.
Deisenhammer F. **Neutralizing Antibodies** to Interferon-beta and other Immunological Treatments for Multiple Sclerosis: Prevalence and Impact on Outcomes. CNS Drugs. 2009;23(5):379-96. doi: 10.2165/00023210-200923050-00003.
DeLorenze GN, et al. Epstein-Barr virus and multiple sclerosis: evidence of association from a prospective study with long-term follow-up. Arch Neurol. 2006 Jun;63(6):839-44.
Devonshire V, Havrdova E, Radu EW, et al. **Relapse and disability** outcomes in patients with multiple sclerosis treated with **fingolimod**: subgroup analyses of the double-blind, randomised, placebo-controlled **FREEDOMS** study. Lancet Neurol 2012
D'haeseleer Miguel, Cambron Melissa, Vanopdenbosch Ludo, et al. **Vascular aspects** of multiple sclerosis. The Lancet Neurology 1 July 2011 (Volume 10 Issue 7 Pages 657-666.
Dickens AM, Larkin JR, Griffin JL, et al. A **type 2 biomarker** separates relapsing-remitting from secondary progressive multiple sclerosis. Neurology 2014;83:1492–1499.
Dilokthornsakul P, Valuck RJ, Nair KV, et al. **Multiple sclerosis prevalence** in the United States commercially insured population. Neurology. 2016 Mar 15;86(11):1014-21.
Disanto G, Watson CT, Meier UC, et al. **Month of birth** and thymic output. JAMA Neurol. 2013 Apr 1;70(4):527-8.
Disanto G, Barro C, Benkert P, et al. **Serum neurofilament light**: A biomarker of neuronal damage in multiple sclerosis. Ann Neurol. 2017 May 16
Disanto G, Zecca C, MacLachlan S, et al. **Prodromal symptoms** of multiple sclerosis in primary care. Ann Neurol. 2018 May 8.
Dobson R, Giovannoni G, Ramagopalan S. The **month of birth effect** in multiple sclerosis: systematic review, meta-analysis and effect of latitude. J Neurol Neurosurg Psychiatry. 2012 Nov 14.
Dobson R, Rudick RA, Turner B, et al. Assessing treatment **response to interferon-β: Is there a role for MRI**? Neurology. 2014 Jan 21;82(3):248-54
Doepp F, Würfel JT, Pfueller CF, et al. **Venous drainage** in multiple sclerosis: A combined MRI and ultrasound study. Neurology. 2011 Nov 8;77(19):1745-51.
Dorans KS, Massa J, Chitnis T, et al. **Physical activity** and the incidence of multiple sclerosis. Neurology. 2016 Oct 25;87(17):1770-1776.
Dyment DA, Cader MZ, Chao MJ, et al. Exome sequencing identifies a novel multiple sclerosis susceptibility variant in the **TYK2 gene**. Neurology. 2012 Jul 31;79(5):406-11.
Edan G, Kappos L, Montalbán X, et al. **BENEFIT** Study Group. **Long-term** impact of **interferon beta-1b** in patients with **CIS**: 8-year follow-up of BENEFIT. J Neurol Neurosurg Psychiatry. 2014 Nov;85(11):1183-9.
Egeberg MD, Oh CY, Bainbridge JL. Clinical Overview of **Dalfampridine**: An Agent With a Novel Mechanism of Action to Help With Gait Disturbances. Clin Ther. 2012 Nov 1.
Ehde DM, Elzea JL, Verrall AM, et al. Efficacy of a **Telephone-Delivered Self-Management** Intervention for Persons With Multiple Sclerosis: A Randomized Controlled Trial With a One-Year Follow-Up. Arch Phys Med Rehabil. 2015 Nov;96(11):1945-1958.e2.
Eijlers AJ, Meijer KA, Wassenaar TM, et al. **Increased default-mode network centrality** in cognitively impaired multiple sclerosis patients. Neurology. 2017 Mar 7;88(10):952-960.
Eisele P, Griebe M, Szabo K, et al. Investigation of **leptomeningeal enhancement** in MS: a postcontrast FLAIR MRI study. Neurology 2015;84:770–775.
Elkins J, et al. Safety and efficacy of **natalizumab** in patients with acute ischaemic **stroke** (**ACTION**): a randomised, placebo-controlled, double-blind phase 2 trial. Lancet Neurol 2017; 16: 217–26.
EMA Jan/12 European and U.S. regulators are reviewing Novartis AG's (NOVN) **Gilenya** pill for multiple sclerosis after reports of **11 deaths** among patients who took the drug.
Ermis U, Weis J, Schulz JB. **PML** in a patient treated with **fumaric acid**. N Engl J Med 2013;368:1657-8.
Eshaghi A, Kievit RA, Prados F, et al. Applying causal models to explore the **mechanism of action of simvastatin** in progressive multiple sclerosis. Proc Natl Acad Sci U S A. 2019 May 9.
Eshaghi A, Wottschel V, Cortese R, et al. **Gray matter MRI** differentiates **neuromyelitis optica** from multiple sclerosis using random forest. Neurology. 2016 Dec 6;87(23):2463-2470
Evans E, Piccio L, Cross AH. Use of **Vitamins and Dietary Supplements** by Patients With Multiple Sclerosis: A Review. JAMA Neurol. 2018 Apr 23.
Fabis Pedrini MJ, Seewann A, et al. **Helicobacter pylori infection** as a **protective factor against multiple sclerosis risk** in females. J Neurol Neurosurg Psychiatry. 2015 Jan 19.
Farez MF, Correale J. Yellow Fever Vaccination and Increased Relapse Rate in Travelers With Multiple Sclerosis. Arch Neurol. 2011 Jun 13.
Farez MF, Correale J, Armstrong MJ, et al. Practice guideline update summary: **Vaccine-preventable infections and immunization in multiple sclerosis**: Report of the Guideline Development, Dissemination, and Implementation Subcommittee of the American Academy of Neurology. Neurology. 2019 Aug 28.
Farez MF, Fiol MP, Gaitán MI, et al. **Sodium intake** is associated with increased disease activity in multiple sclerosis. J Neurol Neurosurg Psychiatry. 2014 Aug 28.
Fassas A et al. Long-term results of **stem cell transplantation** for MS: A single-center experience. Neurology 2011 Mar 22; 76:1066.
Fazekas F, et al. Randomised placebo-controlled trial of monthly intravenous immunoglobulin therapy in relapsing-remitting multiple sclerosis. Austrian Immunoglobulin in Multiple Sclerosis Study

Group. Lancet. 1997 Mar 1;349(9052):589-93.
FDA Dec/11 has received a report of a patient with multiple sclerosis (MS) who **died** within 24 hours of taking the first dose of **Gilenya (fingolimod).** At this time, FDA cannot conclude whether the drug resulted in the patient's death.
FDA May/12 warned clinicians on Thursday that "**liberation therapy**," an experimental procedure that uses angioplasty balloons or stents to open narrowed veins in the chest and neck, has not been approved to treat chronic cerebrospinal venous insufficiency (**CCSVI**) and could be dangerous. Liberation therapy has been associated with one death due to a brain hemorrhage and one stroke, says the FDA. Other possible risks include blood clots, cranial nerve damage, and migrating stents.
FDA is alerting the public that a patient in Europe diagnosed with possible multiple sclerosis (MS) has developed a rare and serious brain infection after taking the drug Gilenya (fingolimod). This is the first case of progressive multifocal leukoencephalopathy (**PML**), reported following the administration of **Gilenya** to a patient who had not previously received Tysabri (natalizumab), an MS drug associated with a higher risk of PML.
FDA Nov/14 is warning that a patient with multiple sclerosis (MS) who was being treated with **Tecfidera (dimethyl fumarate)** developed a rare and serious brain infection called progressive multifocal leukoencephalopathy (**PML**), and later died. The patient who died was not taking any other drugs that affect the immune system or drugs that are thought to be associated with PML.
FDA Aug/15 is warning that a case of definite **progressive multifocal leukoencephalopathy (PML)** and a case of probable PML have been reported in patients taking **Gilenya (fingolimod)** for multiple sclerosis (MS).
FDA Nov/18: Gilenya (**fingolimod**): Drug Safety Communication - Severe Worsening of Multiple Sclerosis After Stopping the Medicine.
FDA Nov/18: Lemtrada (**alemtuzumab**): Drug Safety Communication -Warning That Rare but Serious Cases of **Stroke and Tears in the Lining of Arteries** in the Head and Neck Have Occurred in Patients with Multiple Sclerosis.
Feinstein A, Freeman J, Lo AC. Treatment of **progressive multiple sclerosis**: what works, what does not, and what is needed. Lancet Neurol. 2015 Feb;14(2):194-207.
Fernández Ó, Giovannoni G, Fox RJ, et al. Efficacy and Safety of Delayed-release **Dimethyl Fumarate** for Relapsing-remitting Multiple Sclerosis in Prior Interferon Users: An Integrated Analysis of **DEFINE** and **CONFIRM**. Clin Ther. 2017 Aug;39(8):1671-1679.
Ferraro D, Camera V, Vitetta F, et al. Acute coronary syndrome associated with alemtuzumab infusion in multiple sclerosis. Neurology. 2018 May 1;90(18):852-854.
Fiddes B, Wason J, Kemppinen A, et al. Confounding underlies the apparent '**month of birth**' effect in multiple sclerosis. Ann Neurol. 2013 Jun 6.
Filippi M, Wolinsky JS, Comi G; CORAL Study Group. Effects of oral glatiramer acetate on clinical and MRI-monitored disease activity in patients with relapsing multiple sclerosis: a multicentre, double-blind, randomised, placebo-controlled study. Lancet Neurol. 2006 Mar;5(3):213-20. Erratum in: Lancet Neurol. 2006 May;5(5):383.
Filippi M, Rocca MA, Camesasca F, et al. **Interferon {beta}-1b and glatiramer** acetate effects on permanent **black hole evolution**. Neurology. 2011 Apr 5;76(14):1222-8.
Filippi M, Rocca MA, Barkhof W et al. Association between **pathological and MRI findings** in multiple sclerosis. Lancet Neurol. 2012 Apr;11(4):349-360.
Filippi M, Rocca MA, Horsfield MA, et al. **Imaging Cortical Damage** and Dysfunction in Multiple Sclerosis. JAMA Neurol. 2013 Mar 4:1-9.
Filippini G, Del Giovane C, Vacchi L, D'Amico R, Di Pietrantonj C, Beecher D, Salanti G. **Immunomodulators and immunosuppressants for multiple sclerosis**: a **network meta-analysis**. Cochrane Database of Systematic Reviews 2013, Issue 6. Art. No.: CD008933. DOI: 10.1002/14651858.CD008933.pub2. Our review should provide some guidance to clinicians and patients. On the basis of high quality evidence, **natalizumab and IFNß-1a (Rebif)** are superior to all other treatments for preventing clinical relapses in RRMS in the short-term(24months) compared to placebo. Moderate quality evidence supports a protective effect of natalizumab and IFNß-1a (Rebif) against disability progression in RRMS in the short-termcompared to placebo. These treatments are associated with long-termserious adverse events and their benefit-risk balance might be unfavourable. IFNß-1b (Betaseron) and mitoxantrone probably decreased the odds of the participants with RRMS having relapses, compared with placebo (moderate quality of evidence). The benefit-risk balance with azathioprine is uncertain, however this agent might be effective in decreasing the odds of the participants with RRMS having relapses and disability progression over 24 to 36 months, compared with placebo. The lack of convincing efficacy data shows that IFNß-1a (Avonex), intravenous immunoglobulins, cyclophosphamide and long-term steroids have an unfavourable benefit-risk balance in RRMS. None of the included treatments are effective in decreasing disability progression in patients with progressive MS. It is important to consider that the clinical effects of all these treatments beyond two years are uncertain, a relevant point for a disease of 30 to 40 years duration. Direct head-to-head comparison(s) between natalizumab and IFNß-1a (Rebif) or between azathioprine and IFNß-1a (Rebif) should be top priority on the research agenda and follow-up of the trial cohorts should be mandatory.
Filippi M, Preziosa P, Copetti M, et al. **Gray matter damage** predicts the accumulation of **disability** 13 years later in MS. Neurology. 2013 Nov 12;81(20):1759-67.
Filippi M, Rocca MA, et al, on behalf of the MAGNIMS Study Group. **MRI criteria** for the diagnosis of multiple sclerosis: **MAGNIMS** consensus guidelines. Lancet Neurol 2016; online Jan 25.
Filippi M, Preziosa P, Meani A, et al. Prediction of a multiple sclerosis **diagnosis in patients with clinically isolated syndrome** using the **2016 MAGNIMS and 2010 McDonald criteria**: a retrospective study. Lancet Neurol. 2017 Dec 21.
Filippi M, et al. Prediction of multiple sclerosis diagnosis with **clinically isolated syndrome** using **2016 MAGNIMS & 2010 McDonald criteria**: retrospective study. Lancet Neurol 2017; online Dec 21.
Filli L, Zörner B, Kapitza S, et al. Monitoring long-term efficacy of **fampridine in gait-impaired** patients with multiple sclerosis. Neurology 2017;88:832–841.
Fine AJ, Sorbello A, Kortepeter C, et al. Progressive multifocal leukoencephalopathy after **natalizumab discontinuation**. Ann Neurol. 2013 Nov 16.
Fitzgerald KC, Munger KL, Köchert K, et al. Association of **Vitamin D Levels** With Multiple Sclerosis Activity & Progression in Patients Receiving Interferon Beta-1b. JAMA Neurol. 2015 Oct 12:1-8.
Fitzgerald KC, Munger KL, Hartung HP, et al. **Sodium intake** and multiple sclerosis activity and progression in BENEFIT. Ann Neurol. 2017 May 26.
Fitzgerald KC, Tyry T, Salter A, et al. **Diet quality** is associated with disability and symptom severity in multiple sclerosis. Neurology. 2017 Dec 6.
Forrestel AK, Modi BG, Longworth S, et al. Primary Cutaneous **Cryptococcus** in a Patient With Multiple Sclerosis Treated With **Fingolimod**. JAMA Neurol. 2016 Jan 11:1-2.
Fox RJ, Rae-Grant A. Chronic cerebrospinal venous insufficiency (**CCSVI**): Have we found the cause and cure of MS? Neurology. 2011 Jul 12;77(2):98-100.
Fox RJ, Miller DH, Phillips JT, et al. Placebo-controlled phase 3 study of oral **BG-12** or glatiramer in multiple sclerosis. N Engl J Med 2012;367:1087-97.
Fox RJ. **Complementary and alternative medicine** in multiple sclerosis. Neurology. 2014 Mar 25;82(12):e103-7.
Fox RJ, Cree BAC, de Sèze J, et al. MS disease activity in RESTORE: a randomized 24-week natalizumab treatment interruption study. Neurology 2014;82:1491–1498.
Fox RJ, Coffey CS, Conwit R, et al. Phase 2 Trial of **Ibudilast in Progressive Multiple Sclerosis**. N Engl J Med. 2018 Aug 30;379(9):846-855.
Fox RJ, Cosenza C, Cripps L, et al. A survey of **risk tolerance to multiple sclerosis therapies**. Neurology. 2019 Apr 2;92(14):e1634-e1642.
Fox RJ, Coffey CS, Conwit R, et al; NN102/**SPRINT-MS**. Phase 2 Trial of **Ibudilast in Progressive Multiple Sclerosis**. N Engl J Med. 2018 Aug 30;379(9):846-855.
Fragomeni MO, Bichuetti DB, Oliveira EML. **Pediatric-onset multiple sclerosis in Brazilian patients**: Clinical features, treatment response and comparison to pediatric neuromyelitis optica spectrum disorders. Mult Scler Relat Disord. 2018 Jul 20;25:138-142.
Fragoso YD, Finkelsztejn A, Kaimen-Maciel DR, et al. Long-Term Use of **Glatiramer Acetate by 11 Pregnant** Women with Multiple Sclerosis: A Retrospective, Multicentre Case Series. CNS Drugs. 2010 Aug 31. doi: 10.2165/11538960-000000000-00000. [Epub ahead of print]
Frederick MC, Bourdette D. **MS and bone marrow transplant**: Not for most patients. Neurology. 2017 May 30;88(22):e219-e220.
Freedman MS, Patry DG, Grand'Maison F, Myles ML, Paty DW, Selchen DH; Canadian MS Working Group. **Treatment optimization** in multiple sclerosis. Can J Neurol Sci. 2004 May;31(2):157-68.

Freedman MS, Bar-Or A, Oger J, et al. On behalf of the MAESTRO-01 Investigators. A phase III study evaluating the efficacy and safety of **MBP8298** in secondary progressive MS. Neurology. 2011 Oct 18;77(16):1551-1560. (not provide a clinical benefit)
Freedman MS, Wolinsky JS, Wamil B, et al; For the **Teriflunomide** Multiple Sclerosis Trial Group and the MRI Analysis Center. Teriflunomide added to interferon-β in relapsing multiple sclerosis: A randomized phase II trial. Neurology. 2012 Jun 5;78(23):1877-1885.
Freedman MS, Selchen D, Arnold DL, et al; Canadian Multiple Sclerosis Working Group. **Treatment optimization in MS: Canadian MS Working Group** updated recommendations. Can J Neurol Sci. 2013;40:307-323.
Frohman EM, Havrdova E, Lublin F, et al. Most patients with multiple sclerosis or a clinically isolated demyelinating syndrome should be treated at the time of diagnosis. Arch Neurol. 2006 Apr;63(4):614-9.
Frohman EM, Racke MK, Raine CS. **Multiple sclerosis**--the plaque and its pathogenesis. N Engl J Med. 2006 Mar 2;354(9):942-55.
Frohman EM, Monaco MC, Remington G, et al. **JC Virus in CD34+ and CD19+ Cells** in Patients With Multiple Sclerosis Treated With Natalizumab. JAMA Neurol. 2014 Mar 24
Gaetano L, Häring DA, Radue EW, et al. **Fingolimod** effect on gray matter, thalamus, and white matter in patients with multiple sclerosis. Neurology. 2018 Apr 10;90(15):e1324-e1332.
Gaitán MI, de Alwis MP, Sati P, et al. Multiple sclerosis shrinks intralesional, and enlarges extralesional, brain **parenchymal veins**. Neurology. 2013 Jan 8;80(2):145-51.
Galea I, Ward-Abel N, Heesen C. **Relapse** in multiple sclerosis. BMJ. 2015 Apr 14;350:h1765.
Gandhi S, Marr K, Mancini M, et al. **No association between variations in extracranial venous anatomy** and clinical outcomes in multiple sclerosis patients over 5 years. BMC Neurol. 2019 Jun 11;19(1):121.
Garrett B, Dmytriw AA, Maxner C. **Acute optic neuritis** in multiple sclerosis. CMAJ. 2016 Jun 14;188(9):E199.
Gasperi C, Salmen A, Antony G, et al. Association of **Intrathecal Immunoglobulin G Synthesis With Disability Worsening in Multiple Sclerosis**. JAMA Neurol. 2019 Apr 29.
Gass A, Rocca MA, Agosta F, et al; **MAGNIMS** Study Group. **MRI monitoring** of pathological changes in the spinal cord in patients with multiple sclerosis. Lancet Neurol. 2015 Apr;14(4):443-54.
Gelfand JM, Cree BA, McElroy J, et al. **Vitamin D** in African Americans with multiple sclerosis. Neurology. 2011 May 24;76(21):1824-30.
Geurts JJ, Calabrese M, Fisher E, Rudick RA. Measurement and clinical effect of **grey matter pathology** in multiple sclerosis. Lancet Neurol. 2012 Dec;11(12):1082-92.
Gheuens S, Smith DR, Wang X, Alsop DC, et al. Simultaneous **PML-IRIS after discontinuation of natalizumab** in a patient with MS. Neurology. 2012 May 1;78(18):1390-3.
Ghezzi A, Banwell B, Boyko A, et al. The management of multiple sclerosis in children: a European view. Mult Scler. 2010;16(10):1258-1267.
Gholipour T, Healy B, Baruch NF, et al. Demographic and clinical characteristics of **malignant** multiple sclerosis. Neurology. 2011 Jun 7;76(23):1996-2001.
Giampiero A. Chronic cerebrospinal venous insufficiency (**CCSVI**) and susceptibility to multiple sclerosis. Ann Neurol. 2011 Apr 12. doi: 10.1002/ana.22451.
Gilli F, Navone ND, Perga S, et al. **Loss of Braking Signals** During Inflammation: A Factor Affecting the Development and Disease Course of Multiple Sclerosis. Arch Neurol. 2011 Mar 14.
Giorgio A, Battaglini M, Rocca MA, et al. **Location of brain lesions** predicts conversion of clinically isolated syndromes to multiple sclerosis. Neurology 2013;80:234–241.
Giovannoni G, Comi G, Cook S, et al. the **CLARITY** Study Group, A Placebo-Controlled Trial of Oral **Cladribine** for Relapsing Multiple Sclerosis. N Engl J Med 2010 0: NEJMoa0902533.
Giovannoni G, Cook S, Rammohan K, et al; on behalf of the **CLARITY** study group. Sustained disease-activity-free status in patients with relapsing-remitting multiple sclerosis treated with **cladribine** tablets in the CLARITY study: a post-hoc and subgroup analysis. Lancet Neurol. 2011 Mar 10.
Giovannoni G, Cohen JA, Coles AJ, et al.**Alemtuzumab** improves preexisting disability in active relapsing-remitting MS patients. Neurology. 2016 Nov 8;87(19):1985-1992.
Gladstone DE, et al. High-dose cyclophosphamide (200mg/kg over 4 days) for moderate to severe refractory multiple sclerosis. Arch Neurol. 2006 Oct;63(10):1388-93. Epub 2006 Aug 14.
Gold R, Kappos L, Arnold DL, et al. Placebo-controlled phase 3 study of oral **BG-12** for relapsing multiple sclerosis. N Engl J Med 2012;367:1098-107.
Gold R, Giovannoni G, Selmaj K, et al; **SELECT** study investigators. **Daclizumab** high-yield process in relapsing-remitting multiple sclerosis (SELECT): a randomised, double-blind, placebo-controlled trial. Lancet. 2013 Jun 22;381(9884):2167-75.
Goodin DS, Reder AT, Ebers GC, et al. **Survival in MS**: A randomized cohort study **21 years** after the start of the pivotal **IFNβ-1b** trial. Neurology. 2012 Apr 24;78(17):1315-22.
Gold R, Arnold DL, Bar-Or A, et al. **Long-term effects** of delayed-release **dimethyl fumarate** in multiple sclerosis: Interim analysis of **ENDORSE**, a randomized extension study. Mult Scler. 2017 Feb;23(2):253-265.
Goldman MD, Motl RW, Scagnelli J, et al. Clinically meaningful performance benchmarks in MS: **Timed 25-Foot Walk and the real world**.Neurology. 2013 Nov 19;81(21):1856-63.
Goodman AD, Brown TR, Edwards KR, et al. A phase 3 trial of extended release oral **dalfampridine** in multiple sclerosis. Ann Neurol 2010; 68: 494–502.
Gorman MP, Healy BC, Polgar-Turcsanyi M, Chitnis T. Increased relapse rate in **pediatric-onset** compared with adult-onset multiple sclerosis. Arch Neurol. 2009 Jan;66(1):54-9.
Gorman MP, Tillema JM, Ciliax AM, Guttmann CR, Chitnis T. **Daclizumab** use in patients with pediatric multiple sclerosis. Arch Neurol. 2012 Jan;69(1):78-81.
Granqvist M, Boremalm M, Poorghobad Aet al. Comparative Effectiveness of **Rituximab** and Other Initial Treatment Choices for Multiple Sclerosis. JAMA Neurol. 2018 Jan 8.
Granqvist M, Burman J, Gunnarsson M, et al. Comparative effectiveness of **dimethyl fumarate as the initial and secondary treatment** for MS. Mult Scler. 2019 Aug 8:1352458519866600.
Graves JS, Chitnis T, Weinstock-Guttman B, et al. **Maternal and Perinatal Exposures** (**pesticide**) Are Associated With Risk for Pediatric-Onset Multiple Sclerosis. Pediatrics. 2017;139(4):e20162838
Gray OM, McDonnell GV, Forbes RB. A systematic review of oral **methotrexate** for multiple sclerosis. Mult Scler. 2006 Aug;12(4):507-10.
Green AJ, McQuaid S, Hauser SL, Allen IV, Lyness R. **Ocular pathology in multiple sclerosis**: retinal atrophy and infl ammation irrespective of disease duration. Brain 2010; 133: 1591–601.
Green AJ, Gelfand JM, et al. **Clemastine fumarate** as a remyelinating therapy for multiple sclerosis (ReBUILD): a randomised, controlled, double-blind, crossover trial. Lancet 2017; online Oct 10.
Greenfield AL, Hauser SL. **B Cell Therapy** for Multiple Sclerosis: Entering an Era. Ann Neurol. 2017 Dec 15.
Grover SA, Aubert-Broche B, Fetco D, et al. Lower **physical activity** is associated with higher disease burden in pediatric multiple sclerosis. Neurology. 2015 Aug 12.
Grover SA, Sawicki CP, Kinnett-Hopkins D, et al. **Physical Activity** and Its Correlates in Youth with Multiple Sclerosis. J Pediatr. 2016 Oct 4.
Gyang TV, Hamel J, Goodman AD, et al. **Fingolimod-associated PML** in a patient with prior immunosuppression. Neurology. 2016 May 10;86(19):1843-5.
Hacohen Y, Mankad K, Chong WK, et al. **Diagnostic algorithm for relapsing acquired demyelinating syndromes in children**. Neurology. 2017 Jul 18;89(3):269-278.
Hader WJ, Yee IM. **Incidence and prevalence** of multiple sclerosis in Saskatoon, Saskatchewan. Neurology. 2007 Sep 18;69(12):1224-9.
Haghikia A, Haghikia A, Hellwig K, et al. Regulated **microRNAs in the CSF** of patients with multiple sclerosis: a case-control study. Neurology 2012;79:2166–2170.
Haghikia A, Langer-Gould A, Rellensmann G, et al. **Natalizumab** Use During the **Third Trimester of Pregnancy**. JAMA Neurol. 2014 May 12.
Hapfelmeier A, Gasperi C, Donnachie E, Hemmer B. A large case-control study on **vaccination as risk factor for multiple sclerosis**. Neurology 2019;93:e908–e916.
Harding K, Williams O, Willis M, et al. Clinical Outcomes of **Escalation vs Early Intensive Disease-Modifying Therapy** in Patients With Multiple Sclerosis. JAMA Neurol. 2019 Feb 18.
Harding KE, Wardle M, Carruthers R, et al. **Socioeconomic status and disability progression** in multiple sclerosis: A multinational study. Neurology. 2019 Mar 26;92(13):e1497-e1506.

Hardy TA, Miller DH. **Baló's concentric sclerosis**. Lancet Neurol. 2014 Jul;13(7):740-746.
Harris EC, Palmer KT, Cox V, et al. **Mortality from multiple sclerosis in British military personnel**. Occup Med (Lond). 2017 Aug 1;67(6):448-452
Harrison DM, Cottom D, Rao JK et al. **In the Clinic: Multiple Sclerosis**. Ann Intern Med Apr 1, 2014. ITC4-2 1-16.
Harroud A, Morris JA, Forgetta V, et al. **Effect of age at puberty on risk** of multiple sclerosis: a mendelian randomization study. Neurology 2019;92:e1803–e1810.
Hartung HP, Freedman MS, et al. For the BENEFIT Study Group. **Interferon {beta}-1b-neutralizing antibodies 5 years** (**BENEFIT**) after clinically isolated syndrome. Neurology. 2011 Aug 17.
Hartung DM, Bourdette DN, Ahmed SM, et al. The **cost of multiple sclerosis drugs** in the US and the pharmaceutical industry: Too big to fail? Neurology. 2015 Apr 24.
Hasan SK, Buttari F, Ottone T, et al. Risk of **acute promyelocytic leukemia** in multiple sclerosis: Coding variants of DNA repair genes. Neurology. 2011 Mar 22;76(12):1059-65.
Haselkorn JK, Hughes C, Rae-Grant A, et al. Summary of comprehensive systematic review: **Rehabilitation** in multiple sclerosis: Report of the Guideline Development, Dissemination, and Implementation Subcommittee of the American Academy of Neurology. Neurology. 2015 Nov 24;85(21):1896-903.
Hatcher SE, Waubant E, et al. **Rebound syndrome** in patients with multiple sclerosis after cessation of **fingolimod treatment** [online May 2, 2016].JAMA Neurol. doi:10.1001 /jamaneurol.2016.0826.
Hauser SL, Bar-Or A, Comi G, et aql. **Ocrelizumab** versus Interferon Beta-1a in Relapsing Multiple Sclerosis. N Engl J Med. 2016 Dec 21.
Havla JB, Pellkofer HL, Meinl I, et al. Rebound of disease activity after **withdrawal of fingolimod** (FTY720) treatment. Arch Neurol. 2012 Feb;69(2):262-4.
Havrdova E, Arnold DL, Cohen JA, et al. **Alemtuzumab CARE-MS I 5-year** follow-up: Durable efficacy in the absence of continuous MS therapy. Neurology. 2017 Sep 12;89(11):1107-1116.
Hawker K, O'Connor P, Freedman MS, et al. OLYMPUS trial group. **Rituximab** in patients with primary progressive multiple sclerosis: Results of a randomized double-blind placebo-controlled multicenter trial. Ann Neurol. 2009 Oct;66(4):460-71.
Health Canada June/08 There have been rare reports of serious liver injury in patients receiving Tysabri, occurring as early as 6 days after first dose. Tysabri product label has been updated for liver injury, hypersensitivity reactions and herpes infections.
Health Canada Feb/12 is informing Canadians of an ongoing safety review of the multiple sclerosis (MS) drug **Gilenya** (the brand name for **fingolimod**). The review was initiated following reports of serious adverse events, including 11 deaths reported internationally. No deaths have been reported in Canada.
Health Canada Aug/12 GILENYA (**fingolimod**) - Stronger recommendations regarding first-dose **cardiovascular monitoring** and use in patients with pre-existing cardiovascular conditions.
Health Canada Feb/15: **TECFIDERA and the risk of PML** is being communicated to health professionals and to the public.
Health Canada Sep/15 is informing Canadians that the drug label (product monograph) for the multiple sclerosis drug **Gilenya** (**fingolimod**) has been updated with new safety information on the risk of **skin cancer**, as well as a rare brain infection known as **progressive multifocal leukoencephalopathy (PML).**
Health Canada Mar/18: **ZINBRYTA** (**daclizumab beta**) – Voluntary **Withdrawal** in Canada due to Risk of Encephalitis.
Hedström AK, Akerstedt T, Hillert J, et al. **Shift work** at young age is associated with increased risk for multiple sclerosis. Ann Neurol. 2011 Oct 17.
Hedström AK, et al. **High consumption of coffee is associated with decreased multiple sclerosis** risk; results from two independent studies. J Neurol Neurosurg Psychiatry. 2016 May;87(5):454-60.
Hedstrom AK, Hossjer O, Katsoulis M, et al. **Organic solvents and MS susceptibility**: interaction with MS risk HLA genes. Neurology 2018; 91:e455–e462.
Heesen C, Gold SM. Don't stress about it!: Is **stress management** a disease-modifying therapy for multiple sclerosis? Neurology. 2012 Jul 31;79(5):398-9.
Heine M, van de Port I, Rietberg MB, et al. **Exercise therapy** for fatigue in multiple sclerosis. Cochrane Database Syst Rev. 2015 Sep 11;9:CD009956. Exercise therapy can be prescribed in people with MS without harm. Exercise therapy, and particularly endurance, mixed, or `other` training, may reduce self reported fatigue. However, there are still some important methodological issues to overcome. Unfortunately, most trials did not explicitly include people who experienced fatigue, did not target the therapy on fatigue specifically, and did not use a validated measure of fatigue as the primary measurement of outcome.
Hellwig K, Schimrigk S, Fischer M, et al. Allergic and nonallergic delayed infusion reactions during **natalizumab** therapy. Arch Neurol. 2008 May;65(5):656-8. **Delayed infusion reactions** occurred in 4 of 40 relapse-remitting multiple sclerosis patients treated with natalizumab. Our cases illustrate that some of these infusion reactions may be treated effectively with steroids and reduction of the infusion rate. In cases of antibody-mediated reactions, treatment should be stopped immediately.
Hellwig K, Gold R, Marousi S, et al. **Immune reconstitution inflammatory syndrome** after withdrawal of **natalizumab**? Neurology. 2011 Apr 12;76(15):1362-3.
Hellwig K, Haghikia A, Gold R. **Pregnancy and natalizumab**: results of an observational study in 35 accidental pregnancies during natalizumab treatment. Mult Scler. 2011 Aug;17(8):958-63.
Hellwig K, Rockhoff M, Herbstritt S, et al. **Exclusive Breastfeeding** and the Effect on Postpartum Multiple Sclerosis Relapses. JAMA Neurol. 2015 Aug 31.
Hemmer B, Srivastava R. Hunting for **autoantibodies** in multiple sclerosis. Neurology. 2013 Sep 10;81(11):944-5.
Hemmer B, Kerschensteiner M, Korn T. Role of the **innate and adaptive immune responses** in the course of multiple sclerosis. Lancet Neurol. 2015 Apr;14(4):406-419.
Henault D, Galleguillos L, Moore C, et al. Basis for **fluctuations in lymphocyte counts in fingolimod**-treated patients with multiple sclerosis. Neurology. 2013 Nov 12;81(20):1768-72.
Hebert JR, Corboy JR, Vollmer T, et al. Efficacy of **Balance and Eye-Movement Exercises** for Persons With Multiple Sclerosis (**BEEMS**). Neurology 2018;90:e797–e807.
Hermann R, Litwin JS, Friberg LE, et al. Effects **of cladribine tablets on heart rate, atrio-ventricular conduction and cardiac repolarization** in patients with relapsing multiple sclerosis. Br J Clin Pharmacol. 2019 Mar 18.
Hernan MA, Alonso A, Hernandez-Diaz S. **Tetanus vaccination** and risk of multiple sclerosis: a systematic review. Neurology. 2006 Jul 25;67(2):212-5. Tetanus vaccination is associated with a lower risk of multiple sclerosis.
Hesse D, Frederiksen JL, Koch-Henriksen N, et al. **Methylprednisolone does not** restore biological response in multiple sclerosis patients with **neutralizing antibodies** against interferon-beta. Eur J Neurol. 2009 Jan;16(1):43-7. Monthly pulsed MP treatment in NAb positive patients has no beneficial effect on NAb status or IFN-beta bioactivity.
Ho P-R, Koendgen H, Campbell N, et al. Risk of **natalizumab-associated progressive multifocal leukoencephalopathy** in patients with multiple sclerosis:a retrospective analysis of data from four clinical studies. Lancet Neurol 2017; online Sept 29.
Hobart J, Blight AR, Goodman A, et al. **Timed 25-Foot Walk**: Direct evidence that improving 20% or greater is clinically meaningful in MS. Neurology. 2013 Apr 16;80(16):1509-17.
Hodel J, Darchis C, Outteryck O, et al. **Punctate pattern**: A promising imaging marker for the diagnosis of **natalizumab-associated PML**. Neurology. 2016 Mar 23.
Hohlfeld R, et al. The search for the target antigens of multiple sclerosis, part 1: **autoreactive CD4+ T lymphocytes** as pathogenic effectors and therapeutic targets. Lancet Neurol. 2015 Dec 23.
Hohlfeld R, et al. The search for the target antigens of multiple sclerosis, part 2: **CD8+ T cells, B cells, and antibodies** in the focus of reverse-translational research. Lancet Neurol. 2015 Dec 23.
Holmøy T, von der Lippe H, Leegaard TM. Listeria monocytogenes **infection associated with alemtuzumab** - - a case for better preventive strategies. BMC Neurol. 2017 Apr 4;17(1):65.
Hommes OR, et al. **Intravenous immunoglobulin** in secondary progressive multiple sclerosis: randomised placebo-controlled trial. Lancet. 2004 Sep 25-Oct 1;364(9440):1149-56.
Honce JM, Nair KV, Sillau S, et al. **Rituximab vs placebo induction prior to glatiramer acetate monotherapy** in multiple sclerosis. Neurology. 2019 Feb 12;92(7):e723-e732.
Horton L, Conger A, Conger D, et al. Effect of **4-aminopyridine** on **vision** in multiple sclerosis patients with optic neuropathy. Neurology. 2013 May 14;80(20):1862-6.

Houtchens MK, Edwards NC, Schneider G, et al. **Pregnancy rates** and outcomes in women **with and without MS** in the United States. Neurology 2018;91: e1559–e1569.
Houtchens MK, Edwards NC, Phillips AL. **Relapses and disease-modifying drug treatment in pregnancy** and live birth in US women with MS. Neurology. 2018 Oct 23;91(17):e1570-e1578.
Hu X, Cui Y, White J, et al. Title: Pharmacokinetics and Pharmacodynamics of **Peginterferon Beta-1a** in Patients with Relapsing-Remitting Multiple Sclerosis in the Randomised ADVANCE Study. Br J Clin Pharmacol. 2014 Sep 29.
Huang D. Disseminated **cryptococcosis** in a patient with multiple sclerosis treated with **fingolimod**. Neurology. 2015 Sep 15;85(11):1001-3.
Hughes J, Jokubaitis V, Lugaresi A, et al. Association of **Inflammation and Disability Accrual in Patients With Progressive-Onset Multiple Sclerosis**. JAMA Neurol. 2018 Aug 6.
Hulst HE, Steenwijk MD, Versteeg A, et al. **Cognitive impairment** in MS: Impact of white matter integrity, gray matter volume, and lesions. Neurology. 2013 Mar 12;80(11):1025-32.
Hunt D, Kavanagh D, Drummond I, et al. **Thrombotic microangiopathy** associated with **interferon beta**. N Engl J Med. 2014 Mar 27;370(13):1270-1.
Huppke B, Ellenberger D, Hummel H, et al. **Association of Obesity** With Multiple Sclerosis Risk and Response to First-line Disease Modifying Drugs in Children. JAMA Neurol. 2019 Jul 15.
Huppke P, Stark W, Zürcher C, Huppke B, Brück W, Gärtner J. **Natalizumab use in pediatric** multiple sclerosis. Arch Neurol. 2008 Dec;65(12):1655-8. Natalizumab treatment was effective and well tolerated in our pediatric patients with RRMS who did not respond to initial immunomodulatory treatments. Therefore, it is a promising second-line therapy for pediatric patients with RRMS.
Huynh JL, Casaccia P. **Epigenetic mechanisms** in multiple sclerosis: implications for pathogenesis and treatment. Lancet Neurol. 2013 Feb;12(2):195-206.
Iacobaeus E, Burkill S, Bahmanyar S, et al. The **national incidence of PML in Sweden**, 1988–2013. Neurology 2018;90:e498–e506.
Iaffaldano P, Simone M, Lucisano G, et al. **Prognostic indicators** in **pediatric clinically isolated syndrome**. Ann Neurol. 2017 Apr 25
Issa NP, Hentati A. **VZV encephalitis** that developed in an immunized patient during **fingolimod** therapy. Neurology. 2015 Jan 6;84(1):99-100.
Isobe N, Gourraud PA, Harbo HF, et al. **Genetic risk variants in African Americans** with multiple sclerosis. Neurology. 2013 Jul 16;81(3):219-227.
Iuppa CA, Diefenderfer LA. **Risperidone-Induced Pisa Syndrome** in MS: Resolution with Lurasidone and Recurrence with Chlorpromazine. Ann Pharmacother. 2013 Sep;47(9):1223-8.
Jacobs LD, Beck RW, Simon JH, et al. Intramuscular **interferon beta-1a** therapy initiated during a **first demyelinating** event in multiple sclerosis. N Engl J Med. 2000;343:898−904.
Jagannath VA, Filippini G, Di Pietrantonj C, et al. **Vitamin D for the management of multiple sclerosis**. Cochrane Database Syst Rev. 2018 Sep 24;9:CD008422. To date, very low-quality evidence suggests no benefit of vitamin D for patient-important outcomes among people with MS. Vitamin D appears to have no effect on recurrence of relapse, worsening of disability measured by the Expanded Disability Status Scale (EDSS), and MRI lesions. Effects on health-related quality of life and fatigue are unclear. Vitamin D3 at the doses and treatment durations used in the included trials appears to be safe, although available data are limited. Seven ongoing studies will likely provide further evidence that can be included in a future update of this review.
Jelinek GA, et al. **Latitude, sun exposure and vitamin D** supplementation: associations with quality of life and disease outcomes in a large international cohort of people with multiple sclerosis. BMC Neurol. 2015 Aug 5;15:132.
Johnson KP, Brooks BR, Cohen JA, Ford CC, Goldstein J, Lisak RP, et al. Copolymer 1 reduces relapse rate and improves disability in relapsing-remitting multiple sclerosis: results of a phase III multicenter, double-blind placebo-controlled trial. The Copolymer 1 Multiple Sclerosis Study Group. Neurology 1995;45:1268-76.
Johnson KP, Brooks BR, Cohen JA, et al.; Copolymer 1 Multiple Sclerosis Study Group. Copolymer 1 reduces relapse rate and improves disability in relapsing-remitting multiple sclerosis: results of a phase III multicenter, double-blind, placebo-controlled trial. 1995. Neurology. 2001 Dec;57(12 Suppl 5):S16-24.
Johnson KP, Brooks BR, Ford CC, Goodman AD, et al. Glatiramer acetate (Copaxone): comparison of continuous versus delayed therapy in a six-year organized multiple sclerosis trial. Mult Scler. 2003 Dec;9(6):585-91.
Jokubaitis VG, Li V, Kalincik T, et al. **Fingolimod after natalizumab** and the risk of short-term **relapse**. Neurology 2014;82:1204–1211.
Jokubaitis VG, Spelman T, Kalincik Tet, et al. **Predictors of long-term disability** accrual in relapse-onset multiple sclerosis. Ann Neurol. 2016 May 4.
Kalincik T, Horakova D, Spelman T, et al; on behalf of the MSBase Study Group. **Switch to natalizumab vs fingolimod** in active relapsing-remitting multiple sclerosis. Ann Neurol. 2014 Dec 27.
Kalincik T, Brown JWL, Robertson N. Treatment eff ectiveness of **alemtuzumab** compared with **natalizumab, fingolimod, and interferon beta** in relapsing-remitting multiple sclerosis: a cohort study. Lancet Neurol 2017, online Feb 10.
Kalincik T et al. Treatment effectiveness of **alemtuzumab compared with natalizumab**, fingolimod, and interferon beta in relapsing-remitting multiple sclerosis: A cohort study. Lancet Neurol 2017 Apr; 16:271.
Kantarci OH, Pirko I, Rodriguez M. **Novel immunomodulatory approaches** for the management of multiple sclerosis. Clin Pharmacol Ther. 2013 Jan;95(1):32-44
Kapoor Raju, Furby Julian, Hayton Thomas et al; **Lamotrigine for neuroprotection** in secondary progressive multiple sclerosis: a randomised, double-blind, placebo-controlled, parallel-group trial, The Lancet Neurology, Available online 8 June 2010. (not successful)
Kapoor R, Ho P-R, Campbell N, et al. Effect of **natalizumab** on disease progression in **secondary progressive multiple sclerosis** (**ASCEND**): a phase 3, randomised, double-blind, placebo-controlled trial with an open-label extension. Lancet Neurol 2018; online Mar 12.
Kappos L, et al. Long-term subcutaneous interferon beta-1a therapy in patients with relapsing-remitting MS. (PRISMS) study Neurology. 2006 Sep 26;67(6):944-53. Despite the limitations inherent in any long-term study (for example, potential differences between returning and nonreturning patients), these results indicate that patients with relapsing-remitting multiple sclerosis can experience sustained benefit over many years from early interferon beta-1a subcutaneous therapy three times weekly compared with patients whose treatment is delayed. This effect was more apparent in the patients receiving the higher dose.
Kappos L, et al.; FTY720 D2201 Study Group. Oral fingolimod (FTY720) for relapsing multiple sclerosis. N Engl J Med. 2006 Sep 14;355(11):1124-40.
Kappos L, et al. Treatment with interferon beta-1b delays conversion to clinically definite and McDonald MS in patients with clinically isolated syndromes. Neurology. 2006 Aug 16; [Epub ahead of print] Betaseron **BENEFIT**
Kappos L, Freedman MS, Polman CH, Edan G, Hartung HP, Miller DH, Montalban X, Barkhof F, Radu EW, Bauer L, Dahms S, Lanius V, Pohl C, Sandbrink R; **BENEFIT** Study Group. Effect of early versus delayed interferon beta-1b treatment on disability after a first clinical event suggestive of multiple sclerosis: a 3-year follow-up analysis of the BENEFIT study. Lancet. 2007 Aug 4;370(9585):389-97. Our data suggest that early initiation of treatment with interferon beta-1b prevents the development of confirmed disability, supporting its use after the first manifestation of relapsing-remitting MS.
Kappos L, Freedman MS, Polman CH, et al.; for the **BENEFIT** Study Group. Long-term effect of early treatment with interferon beta-1b after a first clinical event suggestive of multiple sclerosis: 5-year active treatment extension of the phase 3 BENEFIT trial. Lancet Neurol. 2009 Sep 10. Effects on the rate of conversion to CDMS and the favourable long-term safety and tolerability profile support early initiation of treatment with interferon beta-1b, although a delay in treatment by up to 2 years did not affect long-term disability outcomes.
Kappos, Ludwig, Radue, EW, O'Connor, P, et al. **FREEDOMS** Study Group, A Placebo-Controlled Trial of Oral **Fingolimod** in Relapsing Multiple Sclerosis. N Engl J Med 2010 0: NEJMoa0909494.
Kappos L, Li D, Calabresi PA, et al. **Ocrelizumab** in relapsing-remitting multiple sclerosis: a phase 2, randomised, placebo-controlled, multicentre trial. Lancet 2011; published online Nov 1. D

Kappos L, Hartung H-P, et al, for the **ATAMS** Study Group. **Atacicept** in multiple sclerosis (ATAMS): a randomised, placebo-controlled, double-blind, phase 2 trial. Lancet Neurol 2014; online Mar 6.
Kappos L, Mehling M, Arroyo R, et al. Randomized trial of **vaccination in fingolimod-treated patients** with multiple sclerosis. Neurology. 2015 Jan 30.
Kappos L, O'Connor P, Radue EW, et al. Long-term effects of **fingolimod** in multiple sclerosis: The randomized **FREEDOMS** extension trial. Neurology. 2015 Apr 14;84(15):1582-91.
Kappos L, Radue EW, Comi G, et al. **Switching from natalizumab to fingolimod**: a randomized, placebocontrolled study in RRMS. Neurology 2015;85:29–39.
Kappos L, Wiendl H, Selmaj K, et al. **Daclizumab HYP** versus Interferon Beta-1a in Relapsing Multiple Sclerosis. N Engl J Med. 2015 Oct 8;373(15):1418-28.
Kappos L, Li DKB, Stüve O, et al. Safety and efficacy of **siponimod** (BAF312) in patients with relapsing-remitting multiple sclerosis: dose-blinded, randomized extension of the phase 2 **BOLD** study [online July 5, 2016].JAMA Neurol. doi:10.1001/jamaneurol.2016.1451.
Kappos L, Edan G, Freedman MS, et al. The **11-year long-term follow-up** study from the randomized **BENEFIT** CIS trial. Neurology. 2016 Aug 10
Kappos L, Edan G, Freedman MS, et al. The 11-**year longterm** follow-up study from the randomized **BENEFIT CIS** trial. Neurology 2016;87:978–987.
Kappos L, et al. **Siponimod** versus placebo in secondary progressive multiple sclerosis (**EXPAND**): a double-blind, randomised, phase 3 study. Lancet. 2018 Mar 1;391(10127):1263-1273.
Karceski S. How **comorbid conditions affect the choice of treatment** in multiple sclerosis. Neurology. 2017 Nov 28;89(22):e265-e267.
Karlsson G, Francis G, Koren G, et al. Pregnancy outcomes in the clinical development program of **fingolimod** in multiple sclerosis. Neurology 2014;82:674–680.
Kelly VM, Nelson LM, Chakravarty EF. **Obstetric outcomes** (pregnancy) in women with multiple sclerosis and epilepsy. Neurology. 2009 Nov 18. [Epub ahead of print]
Khalil M, Langkammer C, Ropele S, et al. Determinants of **brain iron** in multiple sclerosis: a quantitative 3T MRI study. Neurology 2011;77:1691–1697.
Khalil M, Langkammer C, Pichler A, et al. Dynamics of **brain iron** levels in multiple sclerosis: a longitudinal 3T MRI study. Neurology 2015;84:2396–2402.
Khan O, Rieckmann P, Boyko A, et al; for the GALA Study Group. **Three times weekly glatiram**er acetate in relapsing-remitting multiple sclerosis. Ann Neurol. 2013 May 20.
Khoury SJ.; Healy BC.; Kivisakk P; et al. A Randomized Controlled Double-Masked Trial of **Albuterol** Add-on Therapy in Patients With Multiple Sclerosis. Arch Neurol. 2010;67(9):1055-1061.
Kieseier BC and Hartung HP. Current Disease Modifying Therapies in MS. Semin Neurol 2003; 23(2): 133-145.
Kieseier BC, Wiendl H. Transforming multiple sclerosis trials into practical reality. Lancet Neurol. 2011 May 13.
Kim H, Lee EJ, Kim SK, et al. **Efficacy and safety of alemtuzumab** in Korean multiple sclerosis patients. Mult Scler Relat Disord. 2019 May;30:247-251.
Kinkel RP, Kollman C, O'Connor P, et al. **IM interferon beta-1a** delays definite multiple sclerosis **5 years after a first demyelinating event**. Neurology 2006; 66: 678–84.
Kinkel RP, Dontchev M, Kollman C, et al; for the Controlled High-Risk Avonex Multiple Sclerosis Prevention Study in Ongoing Neurological Surveillance Investigators. Association Between Immediate Initiation of Intramuscular Interferon Beta-1a at the Time of a Clinically Isolated Syndrome and Long-term Outcomes: A **10-Year Follow-up** of the Controlled High-Risk **Avonex** Multiple Sclerosis Prevention Study in Ongoing Neurological Surveillance. (**CHAMPS**) Arch Neurol. 2012 Feb;69(2):183-190.
Kinney MO, McDonnell G, Wattjes MP, et al. Tumefactive multiple sclerosis lesions under **fingolimod** treatment. Neurology. 2013 Jul 23;81(4):403.
Kister I, Chamot E, Salter AR, et al. **Disability** in multiple sclerosis: A reference for patients and clinicians. Neurology. 2013 Mar 12;80(11):1018-24.
Kister I, Corboy JR. **Reducing costs** while enhancing quality of care in MS. Neurology. 2016 Sep 2
Kita M, Fox RJ, Gold R, et al. Effects of Delayed-Release **Dimethyl Fumarate** (DMF) on Health-Related Quality of Life in Patients With Relapsing-Remitting Multiple Sclerosis: An Integrated Analysis of the Phase 3 **DEFINE** and **CONFIRM** Studies. Clin Ther. 2014 Oct 11.
Kleiter I, Hellwig K, Berthele A, et al. for the Neuromyelitis Optica Study Group. Failure of **Natalizumab** to Prevent Relapses in Neuromyelitis Optica. Arch Neurol. 2012 Feb;69(2):239-245.
Kleiter I, Schröder M, Lürding R, et al. Early changes on electroencephalography in **natalizumab**-associated progressive multifocal leucoencephalopathy. Mult Scler. 2010 Jun;16(6):749-53.
Koch-Henriksen N, et al. Danish Multiple Sclerosis Group. A randomized study of two interferon-beta treatments in relapsing-remitting multiple sclerosis. Neurology. 2006 Apr 11;66(7):1056-60. Epub 2006 Mar 1. In this study, 250 microg interferon-beta-1b (Betaseron) administered every other day did not prove clinically superior to once-a-week 22 microg interferon-beta-1a.(Rebif)
Koch-Henriksen N, Thygesen LC, Stenager E, et al. I**ncidence of MS has increased markedly over six decades** in Denmark particularly with late onset and in women. Neurology. 2018 May 29;90(22):e1954-e1963.
Kolber Michael, Makus Ken, Allan G. Michael, et al. **Vascular intervention** for multiple sclerosis (CCSVI). Can Fam Physician June 2011 57: 676.
Kooi EJ, Strijbis EM, van der Valk P, Geurts JJ. Heterogeneity of **cortical lesions** in multiple sclerosis: Clinical and pathologic implications. Neurology. 2012 Sep 25;79(13):1369-76.
Kopke S, Kern S, Ziemssen T, et al. Evidence-based **patient information programme** in early multiple sclerosis: a randomised controlled trial. J Neurol Neurosurg Psychiatry. 2013 Oct 8.
Kopke S, Solari A, Rahn A, et al. **Information provision for people with multiple sclerosis**. Cochrane Database Syst Rev. 2018 Oct 14;10:CD008757. Information provision for people with MS seems to increase disease-related knowledge, with less clear results on decision making and quality of life. The included studies in this review reported no negative side effects of providing disease-related information to people with MS. Interpretation of study results remains challenging due to the marked heterogeneity of interventions and outcome measures.
Koralnik IJ. Finger pointing to **JC virus**: A tale of **two indexes**. Ann Neurol. 2014 Nov 7.
Kornek B, Aboul-Enein F, Rostasy K, et al. **Natalizumab** therapy for highly active **pediatric** multiple sclerosis. JAMA Neurol. 2013 Apr 1;70(4):469-75.
Kotzamani D, Panou T, Mastorodemos V, et al. Rising incidence of multiple sclerosis in **females associated with urbanization**. Neurology. 2012 May 29;78(22):1728-35.
Kousin-Ezewu O, Azzopardi L, Parker RA, et al. **Accelerated lymphocyte recovery after alemtuzumab** does not predict multiple sclerosis activity. Neurology 2014;82:2158–2164.
Kowalec K, McKay KA, Patten SB, et al; CIHR Team in Epidemiology and Impact of Comorbidity on Multiple Sclerosis (**ECoMS**). **Comorbidity** increases the risk of relapse in multiple sclerosis: A prospective study. Neurology. 2017 Dec 12;89(24):2455-2461.
Kremer S, Lamy J, Magnus A, et al. Evaluation of an **albumin-binding gadolinium contrast** agent in multiple sclerosis. Neurology 2013;81:206–210.
Krumbholz M, Pellkofer H, Gold R, Hoffmann LA, Hohlfeld R, Kumpfel T. **Delayed Allergic Reaction to Natalizumab** Associated With Early Formation of Neutralizing Antibodies. Arch Neurol. 2007 Sep;64(9):1331-1333. Clinicians and patients should be alert not only to immediate but also to significantly delayed substantial allergic reactions to natalizumab.
Krupp LB, Christodoulou C, Melville P, et al. Multicenter randomized clinical trial of **donepezil** for memory impairment in multiple sclerosis. Neurology. 2011 Apr 26;76(17):1500-7. (**not work**)
Krysko KM, Graves J, et al; US Network of Pediatric MS Centers. Use of newer disease-modifying therapies in **pediatric multiple sclerosis** in the US. Neurology. 2018 Nov 6;91(19):e1778-e1787.
Krysko KM, Henry RG, Cree BAC, et al. **Telomere length is associated with disability progression** in multiple sclerosis. Ann Neurol. 2019 Sep 4
Kuhle J, Kropshofer H, Haering DA, et al. **Blood neurofilament light chain** as a biomarker of MS disease activity and treatment response. Neurology 2019;92: e1007–e1015.
Kuhle J, Pohl C, Mehling M, et al. Lack of association between antimyelin antibodies and progression to multiple sclerosis. N Engl J Med. 2007 Jan 25;356(4):371-8. Presence of anti-MOG or anti-MBP or both was not significantly associated with conversion to CDMS in our CIS cohort. However, patients with anti-myelin oligodendrocyte glycoprotein (anti-MOG) and anti-myelin basic protein antibodies (anti-MBP) had higher lesion load & more disseminated lesions in cranial MRI as well as higher values for CSF leucocytes and intrathecal IgG production. Our data support a

Kuhle J, Gosert R, B¨uhler R, et al. Management and outcome of **CSF-JC virus PCR-negative PML** in a natalizumab-treated patient with MS. Neurology 2011; 77:2010 –2016.
Kuhle J, Disanto G, Lorscheider J, et al. **Fingolimod and CSF neurofilament light chain levels** in relapsing-remitting multiple sclerosis. Neurology 2015;84:1639–1643.
Kuhle J, Nourbakhsh B, Grant D, et al. **Serum neurofilament** is associated with progression of brain atrophy and disability in early MS. Neurology 2017;88:826–831.
La Mantia L, Di Pietrantonj C, Rovaris M, et al. **Interferons-beta versus glatiramer** acetate for relapsing-remitting multiple sclerosis. Cochrane Database Syst Rev. 2014 Jul 26;7:CD009333.
The effects of IFNs-beta and GA in the treatment of patients with RRMS, including clinical (e.g. patients with relapse, risk to progression) and MRI (Gd-enhancing lesions) activity measures, seem to be similar or to show only small differences. When MRI lesion load accrual is considered, the effect of the two treatments differs, in that IFNs-beta were found to limit the increase in lesion burden as compared with GA. Evidence was insufficient for a comparison of the effects of the two treatments on patient-reported outcomes, such as quality of life measures.
Landi D, De Rossi N, Zagaglia S, et al. No evidence of beneficial effects of **plasmapheresis in natalizumab associated PML**. Neurology 2017;88:1144–1152.
Langer-Gould A, Huang S, Van Den Eeden SK, et al. **Vitamin d**, pregnancy, breastfeeding, and postpartum multiple sclerosis relapses. Arch Neurol. 2011 Mar;68(3):310-3.
Langer-Gould A, Zhang JL, Chung J, Yeung Y, Waubant E, Yao J. Incidence of acquired **CNS demyelinating syndromes** in a multiethnic cohort of **children**. Neurology 2011;77:1143–1148.
Langer-Gould A, Brara SM, Beaber BE, et al. **Childhood obesity and risk of pediatric** multiple sclerosis and clinically isolated syndrome. Neurology. 2013 Feb 5;80(6):548-52.
Langer-Gould A, Brara SM, Beaber BE, Zhang JL. Incidence of multiple sclerosis in multiple **racial and ethnic groups**. Neurology. 2013 May 7;80(19):1734-9.
Langer-Gould A, Qian L, Tartof SY, et al. **Vaccines** and the Risk of Multiple Sclerosis and Other Central Nervous System Demyelinating Diseases. JAMA Neurol. 2014 Oct 20.
Langer-Gould A, Smith JB, Hellwig K, et al. **Breastfeeding, ovulatory years**, and risk of multiple sclerosis. Neurology. 2017 Jul 12.
Langer-Gould A, Wu J, Lucas R, et al. **Epstein-Barr virus, cytomegalovirus**, and multiple sclerosis susceptibility: A multiethnic study. Neurology. 2017 Sep 26;89(13):1330-1337.
Lanzillo R, Orefice G, Quarantelli M, et al. **Atorvastatin** Combined To Interferon to Verify the Efficacy (**ACTIVE**) in relapsing-remitting active multiple sclerosis patients: a longitudinal controlled trial of combination therapy. Mult Scler. 2010 Feb 11.
Laplaud DA, Casey R, Barbin L, et al. Comparative effectiveness of **teriflunomide vs dimethyl fumarate** in multiple sclerosis. Neurology. 2019 Aug 13;93(7):e635-e646.
Lapucci C, Saitta L, Bommarito G, et al. How much do **periventricular lesions** assist in distinguishing migraine with aura from CIS? Neurology. 2019 Apr 9;92(15):e1739-e1744.
Laroni A, Signori A, Maniscalco GT, et al; iMUST group. Assessing association of **comorbidities with treatment choice and persistence in MS**: A real-life multicenter study. Neurology. 2017 Nov 1.
Laupacis A, Lillie E, Dueck A, et al. Association between chronic cerebrospinal venous insufficiency (**CCSVI**) and multiple sclerosis: a meta-analysis. CMAJ. 2011 Oct 3.
Laursen JH, Søndergaard HB, Sørensen PS, et al. Association between age at onset of multiple sclerosis and **vitamin D** level-related factors. Neurology. 2016 Jan 5;86(1):88-93.
Le Page E, Veillard D, Laplaud DA, et al. **Oral versus intravenous high-dose methylprednisolone** for treatment of relapses in patients with multiple sclerosis (**COPOUSEP**): a randomised, controlled, double-blind, non-inferiority trial. Lancet. 2015 Jun 26
Leavitt VM, Sumowski JF, Chiaravalloti N, DeLuca J. **Warmer outdoor temperature** is associated with worse **cognitive** status in multiple sclerosis. Neurology 2012;78: 964 –968.
Leist TP, Comi G, Cree BAC, et al, on behalf of the oral **cladribine** for early MS (**ORACLE MS**) Study Group. Effect of oral cladribine on time to conversion to clinically definite multiple sclerosis in patients with a fi rst demyelinating event (ORACLE MS): a phase 3 randomised trial. Lancet Neurol 2014; online Feb 4.
Li DK, Paty DW. Magnetic resonance imaging results of the PRISMS trial: a randomized, double-blind, placebo-controlled study of interferon-beta1a in relapsing-remitting multiple sclerosis. Prevention of Relapses and Disability by Interferon-beta1a Subcutaneously in Multiple Sclerosis. Ann Neurol 1999;46:197-206.
Li Y, Munger KL, Batool-Anwar S, et al. Association of multiple sclerosis with **restless legs syndrome** and other sleep disorders in women. Neurology. 2012 May 8;78(19):1500-6.
Lieberman LA, Zeng W, Singh C, et al. **CD62L** is **not** a reliable biomarker for predicting **PML** risk in natalizumab-treated R-MS patients. Neurology. 2016 Jan 26;86(4):375-81.
Limmroth V, Barkhof F, et al. for the ATL1102 Study Group. **CD49d antisense drug ATL1102** reduces disease activity in patients with relapsing-remitting MS. Neurology 2014;83:1780–1788.
Linker RA, Chan A, Sommer M, et al. **Plasma exchange** therapy for steroid-refractory superimposed relapses in secondary progressive multiple sclerosis. J Neurol. 2007 Sep;254(9):1288-9.
Løken-Amsrud KI, Holmøy T, Bakke SJ, et al. **Vitamin D** and disease activity in multiple sclerosis before and during interferon-β treatment. Neurology. 2012 Jun 13.
Longbrake EE, Cross AH. Effect of Multiple Sclerosis Disease-Modifying Therapies on **B Cells and Humoral Immunity**. JAMA Neurol. 2015 Dec 28:1-7.
Loonstra FC, Verberk IMW, Wijburg MT, et al. Serum neurofilaments as candidate **biomarkers of natalizumab associated progressive multifocal leukoencephalopathy**. Ann Neurol. 2019 Jun 13.
Lovera JF, Kim E, Heriza E, et al. **Ginkgo biloba** does not improve cognitive function in MS: A randomized placebo-controlled trial. Neurology. 2012 Sep 18;79(12):1278-84.
Lu E, Wang BW, Guimond C, et al. Disease-modifying drugs for multiple sclerosis in **pregnancy**: A systematic review. Neurology. 2012 Sep 11;79(11):1130-5.
Lu E, Zhao Y, Zhu F, et al; On behalf of the British Columbia Multiple Sclerosis Clinic Neurologists. **Birth hospitalization** in mothers with multiple sclerosis and their newborns. Neurology. 2013 Jan 29;80(5):447-452.
Lublin FD, Cofield SS, Cutter GR, et al. Randomized study **combining interferon & glatiramer** acetate in multiple sclerosis. (**CombiRx**) Ann Neurol. 2013Feb 19. (not produce a significant benefit)
Lublin FD, Reingold SC, Cohen JA, et al. **Defining the clinical course of multiple sclerosis: The 2013 revisions**. Neurology. 2014 Jul 15;83(3):278-286.
Lublin F, Miller DH, et al. Oral **fingolimod** in **primary progressive multiple sclerosis** (**INFORMS**): a phase 3, randomised, double-blind, placebo-controlled trial. Lancet 2016; online Jan 27.
Lucas RM et al. Sun exposure and **vitamin D** are independent risk factors for CNS demyelination. *Neurology* 2011 Feb 8; 76:540.
Lucchinetti CF, Popescu BFG, Bunyan RF, et al. **Inflammatory cortical demyelination** in early multiple sclerosis. N Engl J Med 2011;365:2188-97.
Lunde HB, Assmus J, Kjell-Morten M, et al. **Survival and cause of death** in multiple sclerosis: a 60-year longitudinal population study. J Neurol Neurosurg Psychiatry. 2017 Apr 1.
Maarouf A, Audoin B, Pariollaud F, et al. Increased total **sodium concentration in gray matter** better explains cognition than atrophy in MS. Neurology. 2017 Jan 17;88(3):289-295.
Major EO, Yousry TA, Clifford DB. **Pathogenesis of progressive multifocal leukoencephalopathy and risks** associated with treatments for multiple sclerosis: a decade of lessons learned. Lancet Neurol 2018; 17: 467–80.
Makhani N, Gorman MP, Branson HM, et al. **Cyclophosphamide** therapy in pediatric multiple sclerosis. Neurology. 2009 May 13. Cyclophosphamide is an option for the treatment of children with aggressive multiple sclerosis refractory to first-line therapies. Recommendations regarding patient selection, treatment administration, and monitoring are discussed.
Makhani N, Ngan BY, Kamath BM, et al. **Glatiramer** acetate-induced acute **hepatotoxicity** in an adolescent with MS. Neurology. 2013 Aug 27;81(9):850-2.
Malik MT, Healy BC, Benson LA, et al. Factors associated with recovery from acute **optic neuritis** in patients with multiple sclerosis. Neurology. 2014 Jun 17;82(24):2173-9.
MacDonald SC, McElrath TF, Hernández-Díaz S. **Pregnancy Outcomes in Women with Multiple Sclerosis**. Am J Epidemiol. 2018 Aug 28.
Mancardi GL, Sormani MP, Gualandi F, et al. **Autologous hematopoietic stem cell transplantation** in multiple sclerosis: a phase II trial. Neurology 2015;84:981–988.
Maranzano J, Rudko DA, Nakamura K, et al. **MRI evidence** of acute inflammation in **leukocortical lesions** of patients with early multiple sclerosis. Neurology. 2017 Jul 19.
Marder E, Gupta P, Greenberg BM, et al. No Cerebral or Cervical Venous Insufficiency (**CCSVI**) in US Veterans With Multiple Sclerosis. Arch Neurol. 2011 Aug 8.
Marrie RA, Bernstein CN, Peschken CA, et al. **Intensive care** unit admission in multiple sclerosis: Increased incidence and increased mortality. Neurology. 2014 May 7.

Marrie RA, Elliott L, Marriott J, et al. Dramatically changing **rates and reasons for hospitalization** in multiple sclerosis. Neurology. 2014 Sep 2;83(10):929-37.
Marrie RA, Elliott L, Marriott J, Cossoy M, Tennakoon A, Yu N. **Comorbidity increases the risk of hospitalizations** in multiple sclerosis. Neurology 2015;84:350–358.
Marrie RA, Elliott L, Marriott J, et al. Effect of **comorbidity on mortality** in multiple sclerosis. Neurology. 2015 May 27.
Marrie RA, Garland A, Schaffer SA, et al. Traditional risk factors may not **explain increased incidence of myocardial infarction** in MS. Neurology. 2019 Apr 2;92(14):e1624-e1633.
Marrie RA, O'Mahony J, Maxwell C, etal; Canadian Pediatric Demyelinating Disease Network. Incidence and **prevalence of MS in children**: A population-based study in Ontario, Canada. Neurology. 2018 Oct 23;91(17):e1579-e1590.

Marrie RA, Patten SB, Tremlett H, et al. **Sex differences** in comorbidity at diagnosis of multiple sclerosis: a population-based study. Neurology 2016;86:1279–1286.
Marrie RA, Salter A, Tyry T, et al. High hypothetical interest in **physician-assisted death** in multiple sclerosis. Neurology. 2017 Apr 18;88(16):1528-1534.
Marriott JJ, Miyasaki JM, Gronseth G, O'Connor PW. Evidence Report: The efficacy and safety of **mitoxantrone** (Novantrone) in the treatment of multiple sclerosis: Report of the Therapeutics and Technology Assessment Subcommittee of the American Academy of Neurology (AAN) . Neurology. 2010 May 4;74(18):1463-70. http://www.neurology.org/cgi/reprint/74/18/1463
The accumulated Class III and IV evidence suggests an increased incidence of systolic dysfunction and therapy-related acute leukemia (TRAL) with mitoxantrone therapy. Systolic dysfunction occurs in approximately 12% of patients with MS treated with mitoxantrone, congestive heart failure occurs in approximately 0.4%, and leukemia occurs in approximately 0.8%. The number needed to harm is 8 for systolic dysfunction and 123 for TRAL.
Martinelli Boneschi F, Rovaris M, et al. Effects of glatiramer acetate on relapse rate and accumulated disability in multiple sclerosis: meta-analysis of three double-blind, randomized, placebo-controlled clinical trials. Mult Scler. 2003 Aug;9(4):349-55.
Martinelli V et al. The Italian Mitoxantrone Group. **Acute myeloid leukemia** in Italian patients with multiple sclerosis treated with **mitoxantrone**. Neurology. 2011 Nov 22;77(21):1887-1895.
Marcus JF, Shalev SM, Harris CA, et al. **Severe hypercalcemia following vitamin d supplementation** in a patient with multiple sclerosis: a note of caution. Arch Neurol. 2012 Jan;69(1):129-32.
Massacesi L, Parigi A, Barilaro A, et al. Efficacy of azathioprine on multiple sclerosis new brain lesions evaluated using magnetic resonance imaging. Arch Neurol. 2005 Dec;62(12):1843-7.
Massey TH, Smith R, Sadiq S, et al. **Rescue** of severe brain and cervical cord **IRIS by restarting natalizumab** in a pregnant MS patient. Neurology. 2017 Feb 14;88(7):711-713.
Mateen FJ. Multiple sclerosis in **resource-limited settings**: Research opportunities in an unequal world. Neurology. 2019 Jul 23;93(4):176-180.
Mattoscio M, Nicholas R, Sormani MP, et al. **Hematopoietic mobilization**: Potential biomarker of response to natalizumab in multiple sclerosis. Neurology. 2015 Apr 7;84(14):1473-82.
Mayo Clinic tools for healthier lives www.mayoclinic.com/health/multiple-sclerosis/ds00188
McCarthy CL, Tuohy O, Compston DA, et al. **Immune competence after alemtuzumab** treatment of multiple sclerosis. Neurology. 2013 Sep 3;81(10):872-6.
McKay KA, Hillert J, Manouchehrinia A. **Long-term disability progression** of pediatric-onset multiple sclerosis. Neurology. 2019 Jun 11;92(24):e2764-e2773
McKay KA, Manouchehrinia A, Berrigan L, et al. Long-term **cognitive outcomes** in patients with pediatric-onset vs adult-onset multiple sclerosis [online June 17, 2019]. JAMA Neurol. doi:10.1001/jamaneurol.2019.1546
McKay KA, Tremlett H, Fisk JD, et al. **Psychiatric comorbidity** is associated with **disability** progression in multiple sclerosis. Neurology. 2018 Apr 10;90(15):e1316-e1323.
McLoughlin JV, Lord SR, Barr CJ, et al. **Dorsiflexion assist orthosis** reduces the physiological cost and mitigates deterioration in strength and balance associated with walking in people with multiple sclerosis. Arch Phys Med Rehabil. 2015 Feb;96(2):226-232.e1.
McNamara PH, Redmond JM, Doherty CP, et al. **Varicella-zoster virus encephalitis** and vasculopathy in a patient treated with **fingolimod**. Neurology. 2013 Jul 16;81(3):306.
Meca-Lallana JE, Hernández-Clares R, et al. **Plasma exchange** for steroid-refractory relapses in multiple sclerosis: an observational, MRI pilot study. Clin Ther. 2013 Apr;35(4):474-85.
Medical Letter. **Dalfampridine** (Ampyra) for MS. Sept 20, 2010.
Mehta D, Miller C, Arnold DL, et al. Effect of **dimethyl fumarate on lymphocytes in RRMS**: Implications for clinical practice. Neurology. 2019 Apr 9;92(15):e1724-e1738.
Meijer KA, Eijlers AJC, Douw L, et al. **Increased connectivity of hub networks** and cognitive impairment in multiple sclerosis. Neurology. 2017 May 30;88(22):2107-2114.
Meinl E, Meister G. **MicroRNAs in the CSF**: Macro-advance in MS? Neurology. 2012 Nov 27;79(22):2162-3.
Menge T, Stüve O, Kieseier BC, Hartung HP. **Alemtuzumab**: the advantages and challenges of a novel therapy in MS. Neurology 2014;83:87–97.
Metz LM, Li DKB, Traboulsee AL, et al. Trial of **minocycline** in a **clinically isolated syndrome of multiple sclerosis**. N Engl J Med 2017;376:2122-33.
MHRA Dec/13 There have been 2 fatal cases of haemophagocytic syndrome in MS patients treated with **fingolimod**. Early diagnosis and treatment of haemophagocytic syndrome increases the chance of survival.
MHRA Mar/15 **Dimethyl fumarate (Tecfidera): fatal P**ML in an MS patient with severe, prolonged lymphopenia. Check full blood counts before prescribing dimethyl fumarate and then every 6 to 12 months. Stop treatment immediately if you suspect progressive multifocal leukoencephalopathy.
MHRA Apr/16 **Natalizumab (Tysabri▼): progressive multifocal leukoencephalopathy**—updated advice to support early detection. Perform a quantitative serum anti-JCV antibody test—including index value—to support risk stratification for progressive multifocal leukoencephalopathy.
https://www.gov.uk/drug-safety-update/natalizumab-tysabri-progressive-multifocal-leukoencephalopathy-updated-advice-to-support-early-detection
MHRA Apr/16 **Dimethyl fumarate (Tecfidera):** updated advice on risk of progressive multifocal leukoencephalopathy. Cases of progressive multifocal leukoencephalopathy have been reported in patients taking dimethyl fumarate for multiple sclerosis, who all had prolonged lymphopenia.
https://www.gov.uk/drug-safety-update/dimethyl-fumarate-tecfidera-updated-advice-on-risk-of-progressive-multifocal-leukoencephalopathy
MHRA Apr/16 **Fingolimod** (Gilenya▼): risks of **progressive multifocal leukoencephalopathy**, basal-cell carcinoma, and opportunistic infections. The immunomodulatory effects of fingolimod increase the risk of progressive multifocal leukoencephalopathy and opportunistic infections.
https://www.gov.uk/drug-safety-update/fingolimod-gilenya-risks-of-progressive-multifocal-leukoencephalopathy-basal-cell-carcinoma-and-opportunistic-infections
MHRA Dec/17: **Cladribine** (Litak, Leustat) for leukaemia: reports of progressive multifocal encephalopathy (PML); stop treatment if PML suspected
MHRA Dec/17: **Fingolimod** can cause persistent bradycardia, which can increase the risk of serious cardiac arrhythmias.
MHRA Dec/17: **Fingolimod** monitor patients closely for skin cancers.
MHRA Jan/18: **Daclizumab** (Zinbryta▼) & risk of severe liver injury: new restrictions to use and strengthened liver monitoring. The use of daclizumab (daclizumab beta) is now restricted to adults with relapsing multiple sclerosis who have had an inadequate response to at least 2 other disease-modifying therapies (DMTs) and for whom other DMTs are contraindicated or unsuitable.
MHRA Mar/18: **Daclizumab** (Zinbryta▼): suspension and recall for safety reasons; review patients as soon as possible and start alternative therapy.The European Medicines Agency (EMA) has recommended the immediate suspension of the marketing authorisation and recall of daclizumab (Zinbryta) in the EU following reports of serious inflammatory brain disorders, including

encephalitis and meningoencephalitis, in patients with multiple sclerosis
Micieli JA, Margolin E. A 30-year-old woman with vision loss and painful eye movements. (**Optic neuritis**) CMAJ. 2015 Jun 16;187(9):673-5.
Midaglia L, Gratacòs M, Caronna E, et al. **Myasthenia gravis following alemtuzumab therapy for multiple sclerosis**. Neurology. 2018 Sep 25;91(13):622-624.
Mikaeloff Y, et al **Hepatitis B vaccination** and the risk of childhood-onset multiple sclerosis. Arch Pediatr Adolesc Med. 2007 Dec;161(12):1176-82. Vaccination against HB does not seem to increase the risk of a first episode of MS in childhood.
Mikaeloff Y, Caridade G, Suissa S, Tardieu M. **Hepatitis B vaccine** and the risk of CNS inflammatory demyelination in childhood. Neurology. 2008 Oct 8. [Epub ahead of print] Hepatitis B vaccination does not generally increase the risk of CNS inflammatory demyelination in childhood. However, the Engerix B vaccine appears to increase this risk, particularly for confirmed multiple sclerosis, in the longer term. Our results require confirmation in future studies.
Mikol DD, Barkhof F, Chang P, et al. **REGARD** study group. Comparison of subcutaneous interferon beta-1a with glatiramer acetate in patients with relapsing multiple sclerosis (the REbif vs Glatiramer Acetate in Relapsing MS Disease [REGARD] study): a multicentre, randomised, parallel, open-label trial. Lancet Neurol. 2008 Oct;7(10):903-14.
Miller AE, Wolinsky JS, Kappos L, et al, for the **TOPIC** Study Group. Oral **teriflunomide** for patients with a fi rst clinical episode suggestive of multiple sclerosis (TOPIC): a randomised, double-blind, placebo-controlled, phase 3 trial. Lancet Neurol 2014; published online Sept 3.
Miller AE. **Teriflunomide**: A Once-Daily Oral Medication for the Treatment of Relapsing Forms of Multiple Sclerosis. Clin Ther. 2015 Sep 10.
Miller DH, Leary SM. **Primary-progressive** multiple sclerosis. Lancet Neurol. 2007 Oct;6(10):903-12.
Miller DH, Weber T, Grove R, et al. **Firategrast** for relapsing remitting multiple sclerosis: a phase 2, randomised, double-blind, placebo-controlled trial. Lancet Neurol 2012; publised online Jan 6.
Miller DH, Chard DT, Ciccarelli O. **Clinically isolated syndromes**. Lancet Neurol. 2012 Feb;11(2):157-69.
Miller DH, Fox RJ, Phillips JT, et al. **CONFIRM** study investigators. Effects of delayed-release **dimethyl fumarate** on **MRI** measures in the phase 3 CONFIRM study. Neurology. 2015 Mar 17;84(11):1145-52.
Minden SL, Feinstein A, Kalb RC, et al. Evidence-based guideline: Assessment and management of **psychiatric disorders** in individuals with MS: Report of the Guideline Development Subcommittee of the American Academy of Neurology (AAN) . Neurology. 2014 Jan 14;82(2):174-81
Miravalle A, Jensen R, et al. **Immune reconstitution inflammatory syndrome** in patients with multiple sclerosis following cessation of **natalizumab** therapy. Arch Neurol. 2011 Feb;68(2):186-91.
Moen SM, Celius EG, Sandvik L, et al. **Low bone mass** in newly diagnosed multiple sclerosis and clinically isolated syndrome. Neurology. 2011 Jul 12;77(2):151-7.
Mohr DC, Lovera J, Brown T, et al. A randomized trial of **stress management** for the prevention of new brain lesions in MS. Neurology. 2012 Jul 31;79(5):412-9.
Mokry LE, Ross S, Ahmad OS, et al. **Vitamin D** and Risk of Multiple Sclerosis: A Mendelian Randomization Study. PLoS Med. 2015 Aug 25;12(8):e1001866.
Mokry LE, Ross S, Timpson NJ, et al. **Obesity** and Multiple Sclerosis: A Mendelian Randomization Study. PLoS Med. 2016 Jun 28;13(6):e1002053.
Montalban X, Arnold DL, Weber MS, et al. **Placebo-Controlled Trial of an Oral BTK Inhibitor** in Multiple Sclerosis. N Engl J Med. 2019 May 10. evobrutinib
Montalban X, Hauser SL, Kappos L, et al. **Ocrelizumab** versus Placebo in Primary Progressive Multiple Sclerosis. N Engl J Med. 2016 Dec 21.
Montgomery S, Hiyoshi A, Burkill S, et al. **Concussion** in adolescence and risk of multiple sclerosis. Ann Neurol. 2017 Sep 4.
Morrow SA, Fraser JA, Day Cet al. Effect of Treating Acute **Optic Neuritis With Bioequivalent Oral vs Intravenous Corticosteroids**: A Randomized Clinical Trial.
Mowry E, Waubant E, McCulloch C et al. **Vitamin D status** predicts new brain MRI activity in multiple sclerosis Ann Neurol. 2012 Mar 19.
Mowry EM,Azevedo CJ,McCulloch CE,et al.**Body mass index,but not vitaminD status, is associated with brain volume change** in MS. Neurology 2018;91: e2256–e2264.
MS disease activity in **RESTORE**: A randomized 24-week **natalizumab** treatment interruption study. Neurology. 2015 Feb 24;84(8):862.
Mugglestone MA, Eunson P, Guideline Development Group. **Spasticity in children** and young people with non-progressive brain disorders: summary of NICE guidance. BMJ. 2012 Jul 26;345:e4845.
Mullen JT, Vartanian TK, Atkins MB. **Melanoma** complicating treatment with **natalizumab** for multiple sclerosis. N Engl J Med. 2008 Feb 7;358(6):647-8.
Multiple Sclerosis Society for Professionals www.mssociety.org.uk/for_professionals/index.html
Munger KL, et al. Serum 25-hydroxyvitamin D levels and risk of multiple sclerosis. JAMA. 2006 Dec 20;296(23):2832-8. The results of our study suggest that high circulating levels of vitamin D are associated with a lower risk of multiple sclerosis.
Munger KL, Fitzgerald KC, Freedman MS, et al. No association of multiple sclerosis activity and progression with **EBV** or tobacco use in **BENEFIT**. Neurology. 2015 Nov 10;85(19):1694-701.
Munger KL, et al. **Vitamin D** status during pregnancy & risk of multiple sclerosis in offspring of women in the Finnish Maternity Cohort [online Mar 7/16]. JAMA Neurol. doi:10.1001/jamaneurol.2015.4800.
Munger KL, Hongell K, Åivo J, et al. **25-Hydroxyvitamin D deficiency** and risk of MS among women in the Finnish Maternity Cohort. Neurology 2017;89:1578–1583.
Munger KL, Hongell K, Cortese M, et al. **Epstein-Barr virus** and multiple sclerosis risk in the Finnish Maternity Cohort. Ann Neurol. 2019 Jun 21
Munk Nielsen N, Corn G, et al. Multiple sclerosis among **first- and second-generation immigrants in Denmark**: a population-based cohort study. Brain. 2019 Jun 1;142(6):1587-1597.
Muraro PA, Pasquini M, Atkins HL, et al; Multiple Sclerosis–Autologous Hematopoietic Stem Cell Transplantation (**MS-AHSCT**) Long-term Outcomes Study Group. Long-term outcomes after **autologous hematopoietic stem cell transplantation** for multiple sclerosis [online Feb 20, 2017].JAMA Neurol. doi:10.1001/jamaneurol.2016 .5867
Murray TJ. Diagnosis and treatment of multiple sclerosis. BMJ. 2006 Mar 4;332(7540):525-7.
N'gbo N'gbo Ikazabo R, Mostosi C, et al. **Immune-Reconstitution Inflammatory Syndrome** in Multiple Sclerosis Patients Treated With **Natalizumab**: A Series of 4 Cases. Clin Ther. 2016 Feb 4.
Nair KP, Marsden J. The management of **spasticity** in adults. BMJ. 2014 Aug 5;349:g4737.
Naismith RT, Bourdette D. **Interruption of natalizumab** therapy for multiple sclerosis: What are the risks? Neurology. 2011 May 31;76(22):1854-5.
Namaka M, Pollitt-Smith M, Gupta A, et al. The clinical importance of neutralizing antibodies in relapsing-remitting multiple sclerosis. Curr Med Res Opin. 2006 Feb;22(2):223-39.The induction of NAbs in IFN-beta treated patients reduce clinical effect and accelerate disease progression.
Namaka M, et al . Corticosteroids and Multiple Sclerosis: To Treat or Not to Treat: CPJ 2005;138 (6):54-59.
Nash RA, Hutton GJ, Racke MK, et al. High-Dose Immunosuppressive Therapy and **Autologous Hematopoietic Cell Transplantation** for Relapsing-Remitting Multiple Sclerosis (HALT-MS): A 3-Year Interim Report. JAMA Neurol. 2014 Dec 29.
Nash RA, Hutton GJ, Racke MK, et al. **High-dose immunosuppressive therapy and autologous HCT** for relapsing-remitting MS. Neurology. 2017 Feb 28;88(9):842-852.
National Multiple Sclerosis Society. Disease Management Consensus Paper. (http://www.nationalmssociety.org/pdf/forpros/Exp_Consensus.pdf. Accessed April 2,2005.
Negahban H, Rezaie S, Goharpey S. **Massage therapy and exercise** therapy in patients with multiple sclerosis: a randomized controlled pilot study. Clin Rehabil. 2013 Jul 4.
Negrotto L, Farez MF, Correale J. Immunologic Effects of **Metformin and Pioglitazone** Treatment on Metabolic Syndrome and Multiple Sclerosis. JAMA Neurol. 2016 Mar 7.
Nerrant E, Salsac C, Charif M, et al. Lack of confirmation of **anti-inward rectifying potassium channel 4.1 antibodies** as reliable markers of multiple sclerosis. Mult Scler 2014; online April 22.

NICE: National Institute for Health and Clinical Excellence**. Natalizumab** for the treatment of adults with highly active relapsing-remitting multiple sclerosis. London (UK): National Institute for Health & Clinical Excellence (NICE); 2007 Aug. 21 p. (Technology appraisal guidance; no. 127). Natalizumab is recommended as an option for the treatment only of rapidly evolving severe relapsing–remitting multiple sclerosis (RES). RES is defined by two or more disabling relapses in 1 year, and one or more gadolinium-enhancing lesions on brain magnetic resonance imaging (MRI) or a significant increase in T2 lesion load compared with a previous MRI. People currently receiving natalizumab, but for whom treatment would not have been recommended according to the above section of this guidance, should have the option to continue therapy until they and their clinicians consider it appropriate to stop.

NICE: Cohen D. NICE rules out NHS prescription of fingolimod for multiple sclerosis. BMJ. 2011 Aug 10;343:d5117.

NICE: National Institute for Health and Care Excellence. **Teriflunomide** for treating relapsing-remitting multiple sclerosis. London (UK): National Institute for Health and Care Excellence 2014 Jan.

NICE: National Institute for Health and Care Excellence. **Alemtuzumab** for treating relapsing–remitting multiple sclerosis. London (UK): National Institute for Health and Care Excellence 2014 May.

NICE: National Institute for Health and Care Excellence. **Management of multiple sclerosis in primary and secondary care**. (Clinical Guideline 186.) 2014. www.nice.org.uk/Guidance/CG186.

NICE: National Institute for Health and Care Excellence. **Dimethyl fumarate** for treating relapsing-remitting multiple sclerosis. London (UK): NICE; 2014 Aug.

Nicolini LA, Canepa P, Caligiuri P, et al. **Fulminant Hepatitis** Associated With Echovirus 25 During **Treatment With Ocrelizumab** for Multiple Sclerosis. JAMA Neurol. 2019 Apr 8.

Nielsen NM, Munger KL, Koch-Henriksen N, et al. **Neonatal vitamin D** status and risk of multiple sclerosis: a population-based case-control study. Neurology 2017;88:44–51.

Nikfar Shekoufeh, Rahimi Roja, Abdollahi Mohammad, A meta-analysis of the efficacy and tolerability of **interferon-[beta]** in multiple sclerosis, overall and by drug and disease type, Clinical Therapeutics, Volume 32, Issue 11, October 2010, Pages 1871-1888, ISSN 0149-2918, DOI: 10.1016/j.clinthera.2010.10.006.

Nieuwkamp DJ, Murk JL, van Oosten BW, et al; PML in Dutch MS Patients Consortium. **PML** in a patient without severe lymphocytopenia receiving **dimethyl fumarate**. N Engl J Med. 2015 Apr 9;372(15):1474-6.

Nolan D, Castley A, Tschochner M et al. Contributions of **vitamin D** response elements and HLA promoters to multiple sclerosis risk. Neurology. 2012 Aug 7;79(6):538-46.

Nolan R, Gelfand JM, Green AJ. **Fingolimod** treatment in multiple sclerosis leads to **increased macular volume**. Neurology. 2013 Jan 8;80(2):139-44.

Nolan RC, Liu M, Akhand O, et al; IMSVISUAL Consortium. Optimal **Inter-Eye Difference Thresholds by OCT in MS**: An International Study. Ann Neurol. 2019 Mar 9.

Novakova L, Zetterberg H, Sundström P, et al. Monitoring disease activity in multiple sclerosis using **serum neurofilament light protein**. Neurology. 2017 Nov 28;89(22):2230-2237.

Novotna M, Paz Soldán MM, Abou Zeid N, et al. **Poor early relapse recovery** affects **onset of progressive disease** course in multiple sclerosis. Neurology. 2015 Aug 25;85(8):722-9.

Noyes K, Bajorska A, Chappel A, et al. Cost-effectiveness of **disease-modifying therapy** for multiple sclerosis: A population-based study. Neurology July 20, 2011 WNL.0b013e3182270402.

Oh J, Saidha S, Chen M, et al. **Spinal cord quantitative MRI** discriminates between disability levels in multiple sclerosis. Neurology. 2013 Feb 5;80(6):540-547.

Oh J, Calabresi PA. **Emerging injectable therapies** for multiple sclerosis. Lancet Neurol. 2013 Sep 30.

Oh J, Saidha S, Cortese I, et al. **Daclizumab-induced** adverse events in multiple organ systems in multiple sclerosis. Neurology. 2014 Mar 18;82(11):984-8.

Ohayon J, Oh U, Richert N, et al. CNS vasculitis in a patient with MS on **daclizumab** monotherapy. Neurology. 2013 Jan 29;80(5):453-7.

Okuda DT, Mowry EM, Beheshtian A, et al. Incidental MRI anomalies suggestive of multiple sclerosis. The **radiologically isolated syndrome**. Neurology. 2008 Dec 10. [Epub ahead of print] Individuals with MRI anomalies highly suggestive of demyelinating pathology, not better accounted for by another disease process, are very likely to experience subsequent radiologic or clinical events related to multiple sclerosis.

O'Connor P, Comi G, Montalban X, Antel J, et al. ; FTY720 D2201 Study Group. Oral **fingolimod** (FTY720) in multiple sclerosis: two-year results of a phase II extension study. Neurology. 2009 Jan 6;72(1):73-9. Once-daily oral treatment with FTY720, 1.25 or 5.0 mg, for up to 2 years, was well tolerated and was associated with low relapse rates and lesion activity.

O'Connor P, Filippi M, Arnason B, et al. for the **BEYOND** Study Group. 250 mug or 500 mug interferon beta-1b versus 20 mg glatiramer acetate in relapsing-remitting multiple sclerosis: a prospective, randomised, multicentre study. Lancet Neurol. 2009 Oct;8(10):889-897. Epub 2009 Sep 2.

O'Connor PW, Goodman A, Kappos L, et al. Disease activity return during **natalizumab treatment interruption** in patients with multiple sclerosis. Neurology. 2011 May 31;76(22):1858-65.

O'Connor Paul, Wolinsky Jerry S., Confavreux Christian. Randomized Trial of Oral **Teriflunomide** for Relapsing Multiple Sclerosis. (**TEMSO**) N Engl J Med 2011;365:1293-303.

O'Connor P, Goodman A, Kappos L, et al. Long-term safety and effectiveness of **natalizumab** redosing and treatment in the STRATA MS Study. Neurology. 2014 Jul 1;83(1):78-86.

O'Connor P, Comi G, Freedman MS, et al; Teriflunomide Multiple Sclerosis Oral (TEMSO) Trial Group and the MRI-AC in Houston, Texas; **Teriflunomide** Multiple Sclerosis Oral TEMSO Trial Group and the MRI-AC in Houston Texas. Long-term safety and efficacy of teriflunomide: Nine-year follow-up of the randomized **TEMSO** study. Neurology. 2016 Feb 10.

Oliveria SF, Rodriguez RL, Bowers D, et al. Safety and efficacy of **dual-lead thalamic deep brain stimulation** for patients with treatment-refractory multiple sclerosis tremor: a single-centre, randomised, single-blind, pilot trial. Lancet Neurol 2017; online June 19.

Ontaneda D, Thompson AJ, Fox RJ, Cohen JA. **Progressive multiple sclerosis**: prospects for disease therapy, repair, and restoration of function. Lancet. 2016 Nov 23.

Optic Neuritis Study Group. Multiple sclerosis risk after **optic neuritis**: final optic neuritis treatment trial follow-up. Arch Neurol 2008;65:727-732. {InfoPOEMS: After 15 years of follow up, 50% of patients with optic neuritis went on to develop multiple sclerosis (MS). Patients with 1 or more white matter lesions on magnetic resonance imaging (MRI) have the greatest risk of developing MS. (LOE = 1b-)}

Ortiz-Pérez S, Martínez-Lapiscina EH, Gabilondo I, et al. **Retinal periphlebitis** is associated with multiple sclerosis severity. Neurology. 2013 Sep 3;81(10):877-81.

Orton SM, Wald L, Confavreux C, et al. Association of **UV radiation** with multiple sclerosis prevalence and sex ratio in France. Neurology. 2011 Feb 1;76(5):425-31.

Ontaneda D, Fox RJ, Chataway J. Clinical trials in **progressive** multiple sclerosis: lessons learned and future perspectives. Lancet Neurol. 2015 Feb;14(2):208-223.

Otto C, Oltmann A, Stein A, et al. Intrathecal **EBV antibodies** (**Epstein-Barr virus**) are part of the polyspecific immune response in multiple sclerosis. Neurology. 2011 Apr 12;76(15):1316-21.

Pachner AR, Cadavid D, Wolansky L, Skurnick J. Effect of **anti-IFN{beta} antibodies on MRI lesions** of MS patients in the BECOME study. Neurology. 2009 Nov 3;73(18):1485-92. High levels of anti-interferon beta (IFNbeta) antibodies, which result in diminished bioactivity, are correlated with reduced therapeutic efficacy of IFNbeta.

Pachner AR, Warth JD, Pace A, Goelz S; INSIGHT investigators. Effect of **neutralizing antibodies** on biomarker responses to interferon beta: the INSIGHT study. Neurology. 2009 Nov

Pakpoor J, Goldacre R, Schmierer K, et al. **Testicular hypofunction** and multiple sclerosis risk: A record-linkage study. Ann Neurol. 2014 Aug 18.

Palace J, Duddy M, Bregenzer T, et al. Effectiveness and **cost-effectiveness** of **interferon beta and glatiramer** acetate in the UK Multiple Sclerosis Risk Sharing Scheme at 6 years: a clinical cohort study with natural history comparator. Lancet Neurol. 2015 Apr 1.

Palmer AM. New and **emerging immune-targeted drugs** for the treatment of multiple sclerosis. Br J Clin Pharmacol. 2013 Nov 20.

Pan F, Goh JW, Cutter G, et al. Long-Term **Cost-Effectiveness Model of Interferon Beta-1b** in the Early Treatment of Multiple Sclerosis in the United States. Clin Ther. 2012 Aug 17.

Pappolla A, Midaglia L, Boix Rodríguez CP, et al. **Simultaneous CMV and Listeria infection following alemtuzumab treatment** for multiple sclerosis. Neurology. 2019 Feb 5;92(6):296-298.

Pascual AM, Téllez N, Boscá I, Mallada J, et al. Revision of the risk of secondary **leukemia after mitoxantrone** in multiple sclerosis populations is required. Mult Scler. 2009 Oct 13.

Patsopoulos NA et al. **Genome-wide meta-analysis** identifies novel multiple sclerosis susceptibility loci. Ann Neurol. 2011 Dec;70(6):897-912.

Paty DW, Li DK. Interferon beta-1b is effective in relapsing-remitting multiple sclerosis. II. MRI analysis results of a multicenter, randomized, double-blind, placebo-controlled trial. UBC MS/MRI Study Group and the IFNB Multiple Sclerosis Study Group. Neurology 1993;43:662-7.
Paz Soldán MM, Novotna M, Abou Zeid N, et al. **Relapses and disability** accumulation in **progressive multiple sclerosis**. Neurology. 2015 Jan 6;84(1):81-8.
Pearson M, Dieberg G, Smart N. **Exercise** as a Therapy for Improvement of Walking Ability in Adults With Multiple Sclerosis: A Meta-Analysis. Arch Phys Med Rehabil. 2015 Jul;96(7):1339-1348.e7.
Pelletier Daniel, Hafler David A. **Fingolimod** for Multiple Sclerosis. N Engl J Med 2012; 366:339-347.
Perry M, Swain S, Kemmis-Betty S, et al; Guideline Development Group. **Multiple sclerosis**: summary of **NICE** guidance. BMJ. 2014 Oct 8;349:g5701.
Petersen ER, Oturai AB, Koch-Henriksen N, et al. **Smoking affects the interferon beta treatment** response in multiple sclerosis. Neurology. 2018 Feb 13;90(7):e593-e600.
Pfender N, Jelcic I, Linnebank M, et al. Reactivation of **herpesvirus under fingolimod**: A case of severe herpes simplex encephalitis. Neurology. 2015 Jun 9;84(23):2377-8.
Pfeuffer S, Beuker C, Ruck T, et al. **Acute cholecystitis** during treatment with **alemtuzumab** in 3 patients with RRMS.Neurology. 2016 Nov 29;87(22):2380-2381.
Pharmacist's Letter: Immunomodulators used in the Treatment of MS. Jan 2007.
Pharmacist's Letter. **Drugs Used to Treat Multiple Sclerosis Symptoms**. Mar, 2010.
Pignolet B, Schwab N, Schneider-Hohendorf T, et al. **CD62L test at 2 years of natalizumab predicts progressive multifocal leukoencephalopathy**. Neurology. 2016 Dec 6;87(23):2491-2494.
Pilz G, Harrer A, Wipfler P, et al. **Tumefactive MS lesions under fingolimod**: a case report and literature review. Neurology 2013;81:1654–1658.
Pittock SJ, Weinshenker BG, Noseworthy JH, Lucchinetti CF, Keegan M, Wingerchuk DM, Carter J, Shuster E, Rodriguez M. Not every patient with multiple sclerosis should be treated at time of diagnosis. Arch Neurol. 2006 Apr;63(4):611-4.
Plavina T, Subramanyam M, Bloomgren G, et al. **Anti-JCV antibody levels** in serum or plasma further define risk of **natalizumab**-associated PML. Ann Neurol. 2014 Oct 1.
Plavina T, Muralidharan KK, Kuesters G, et al. Reversibility of the effects of **natalizumab** on peripheral immune cell dynamics in MS patients. Neurology. 2017 Oct 10;89(15):1584-1593.
Polman CH, et al. Diagnostic criteria for multiple sclerosis: 2005 revisions to the "McDonald Criteria". Ann Neurol. 2005 Dec;58(6):840-6.
Polman CH et al. **Diagnostic criteria for multiple sclerosis: 2010 revisions to the "McDonald criteria**." *Ann Neurol* 2011 Jan 11; [e-pub ahead of print]. (http://dx.doi.org/10.1002/ana.22366)
Polman C, Reingold S, Banwell B, et al. Diagnostic Criteria for Multiple Sclerosis: 2010 Revisions to the "McDonald Criteria."Annals of Neurology.2011 Jan 11; 3-76.
Polman Chris H, Bertolotto Antonio, Deisenhammer Florian et al; Recommendations for clinical use of data on **neutralising antibodies** to **interferon-beta** therapy in multiple sclerosis, The Lancet Neurology, Volume 9, Issue 7, July 2010, Pages 740-750.
Polman CH, O'Connor PW, Havrdova E, et al. A randomized, placebo-controlled trial of **natalizumab** for relapsing multiple sclerosis. N Engl J Med. 2006 Mar 2;354(9):899-910
Pohl D, Waubant E, Banwell B, et al. Treatment of **pediatric** multiple sclerosis and variants. Neurology. 2007 Apr 17;68(16 Suppl 2):S54-65.
Ponsonby A-L, Lucas RM, van der Mei IA, et al. Offspring number, **pregnancy, and risk of a first clinical demyelinating event**: the **AusImmune** Study. Neurology 2012;78: 867– 874.
Portaccio E, Ghezzi A, Hakiki B, et al; For the MS Study Group of the Italian Neurological Society. **Breastfeeding** is not related to postpartum relapses in multiple sclerosis. Neurology. 2011 Jul 12;77(2):145-150.
Portaccio E, Annovazzi P, Ghezzi A, et al; MS Study Group of the Italian Neurological Society. **Pregnancy** decision-making in women with multiple sclerosis treated with **natalizumab**: I: **Fetal risks**. Neurology. 2018 Mar 6;90(10):e823-e831.
Portaccio E, Moiola L, Martinelli V, et al; MS Study Group of the Italian Neurological Society. **Pregnancy** decision-making in women with multiple sclerosis treated with **natalizumab**: II: **Maternal risks**. Neurology. 2018 Mar 6;90(10):e832-e839.
Pottgen J, Moss-Morris R, Wendebourg JM, et al. Randomised controlled trial of a **self-guided online fatigue intervention in multiple sclerosis**. J Neurol Neurosurg Psychiatry. 2018 Mar 16.
Poulin F, Rico P, Côté J, Bégin LR. Interferon beta-induced **panniculitis** mimicking acute appendicitis. Arch Dermatol. 2009 Aug;145(8):916-7.
3;73(18):1493-500. These data provide evidence that high titers of neutralizing antibodies abolish the in vivo response to interferon beta.
PRISMS Study Group and the University of British Columbia MS/MRI Analysis Group. PRISMS-4: long-term efficacy of interferon-beta-1a in relapsing MS [published correction appears in Neurology 2001;57:1146]. Neurology 2001;56:1628-36.
Prosperini L, Castelli L, De Luca F, et al. **Task-dependent deterioration of balance** underpinning cognitive-postural interference in MS. Neurology. 2016 Sep 13;87(11):1085-92.
Prosperini L, Lucchini M, Haggiag S, et al. **Fingolimod vs dimethyl fumarate** in multiple sclerosis: A real-world propensity score-matched study. Neurology. 2018 Jul 10;91(2):e153-e161.
Pucci E, Giuliani G, Solari A, Simi S, Minozzi S, Di Pietrantonj C, Galea I. **Natalizumab** for relapsing remitting multiple sclerosis. Cochrane Database of Systematic Reviews 2011, Issue 10. Art. No.: CD007621. DOI: 10.1002/14651858.CD007621.pub2. Although one trial did not contribute to efficacy results due to its duration, we found robust evidence in favour of a reduction in relapses and disability at 2 years in RRMS patients treated with NTZ. The drug was well tolerated. There are current significant safety concerns due to reporting of an increasing number of PML cases in patients treated with NTZ. This review was unable to provide an up-to-date systematic assessment of the risk due to the maximum 2 year-duration of the trials included. An independent systematic review of the safety profile of NTZ is warranted. NTZ should be used only by skilled neurologists in MS centres under surveillance programs.
Purchiaroni F, Salvetti M, Buscarinu MC, et al. **Eosinophilic gastroenteritis** in a woman with multiple sclerosis on **dimethyl fumarate**. Neurology. 2016 Aug 30;87(9):952-3.
Quintana FJ, Patel B, Yeste A, et al; Canadian Pediatric Demyelinating Disease Network. **Epitope spreading** as an early pathogenic event in pediatric multiple sclerosis. Neurology. 2014 Dec 9;83(24):2219-26.
Racke MK, Lovett-Racke AE, Karandikar NJ. The **mechanism** of action of **glatiramer** acetate treatment in multiple sclerosis. Neurology. 2010 Jan 5;74 Suppl 1:S25-30.
Radue EW, Barkhof F, Kappos L, et al. Correlation between **brain volume loss** and clinical and MRI outcomes in multiple sclerosis. Neurology. 2015 Feb 24; 84(8):784-93.
Rae-Grant A, Bennett A, Sanders AE, et al. **Quality improvement** in neurology: Multiple sclerosis quality measures: Executive summary. Neurology. 2015 Nov 24;85(21):1904-8.
Rae-Grant A, Day GS, Marrie RA, et al. **Practice guideline** recommendations summary: **Disease-modifying therapies for adults with multiple sclerosis**: Report of the Guideline Development, Dissemination, and Implementation Subcommittee of the American Academy of Neurology (**AAN**). Neurology. **2018** Apr 24;90(17):777-788.
Rae-Grant A, Day GS, Marrie RA, et al. **Comprehensive systematic review summary**: Disease-modifying therapies for adults with multiple sclerosis: Report of the Guideline Development, Dissemination, and Implementation Subcommittee of the American Academy of Neurology (**AAN**). Neurology. **2018** Apr 24;90(17):789-800.
Ramagopalan SV, Meier UC, Conacher M, et al. Role of the **HLA System** in the Association Between Multiple Sclerosis and **Infectious Mononucleosis**. Arch Neurol. 2011 Apr;68(4):469-72.
Ramagopalan SV, Handel AE, Giovannoni G, et al. Relationship of **UV exposure** to prevalence of multiple sclerosis in England. Neurology. 2011 Apr 19;76(16):1410-4. PubMed PMID: 21502600.
Ramanujam R, Hedström AK, Manouchehrinia A, et al. Effect of **Smoking Cessation** on Multiple Sclerosis Prognosis. JAMA. Neurol. 2015 Sep 8:1-7.
Ramo-Tello C et al. A randomized clinical trial of **oral versus intravenous methylprednisolone** for relapse of MS. Mult Scler 2014 May; 20:717
Rapaport B, Karceski S. Multiple sclerosis and stress (**patient page**). Neurology. 2012 Jul 31;79(5):e47-9.

Rauer S, Marks R, Urbach H, et al. Treatment of Progressive Multifocal **Leukoencephalopathy with Pembrolizumab**. N Engl J Med. 2019 Apr 25;380(17):1676-1677.
Rauer S, Stork L, Urbach H, et al. **Drug reaction** with eosinophilia and systemic symptoms **after daclizumab therapy**. Neurology. 2018 Jul 24;91(4):e359-e363.
Ravnborg M, Sørensen PS, Andersson M, et al. **Methylprednisolone** in combination with interferon beta-1a for relapsing-remitting multiple sclerosis (**MECOMBIN** study): a multicentre, double-blind, randomised, placebo-controlled, parallel-group trial. Lancet Neurol. 2010Jun 7. Interpretation Monthly pulses of methylprednisolone 500mg po od x 3 days per month for 3-4yrs in combination with interferon beta-1a do not seem to affect disability progression any more than interferon beta-1a treatment alone. More research is required to assess whether this treatment regimen might benefit particular pt subsets.
Reich DS, Lucchinetti CF, Calabresi PA. **Multiple Sclerosis**. N Engl J Med. 2018 Jan 11;378(2):169-180.
Renoux C, Vukusic S, et al. Adult Neurology Departments KIDMUS Study Group. Natural history of multiple sclerosis with childhood onset. N Engl J Med. 2007 Jun 21;356(25):2603-13. Patients with **childhood-onset** multiple sclerosis take longer to reach states of irreversible disability but do so at a younger age than patients with adult-onset multiple sclerosis.
Rice CM, Kemp K, Wilkins A, Scolding NJ. **Cell therapy** for multiple sclerosis: an evolving concept with implications for other neurodegenerative diseases. Lancet. 2013 Oct 5;382(9899):1204-1213.
Ricklin ME, Lorscheider J, Waschbisch A, et al. T-cell response against **varicella-zoster virus** in **fingolimod**-treated MS patients. Neurology. 2013 Jul 9;81(2):174-81.
Rigau V, Mania A, Béfort P, et al. Lethal multiple sclerosis **relapse after natalizumab withdrawal**. Neurology. 2012 Nov 27;79(22):2214-6.
Rigotti DJ, Inglese M, Kirov II, et al. Two-year serial whole-brain **N-acetyl-L-aspartate** in patients with relapsing-remitting multiple sclerosis. Neurology. 2012 May 1;78(18):1383-9.
Riise T, Mohr DC, Munger KL, Rich-Edwards JW, Kawachi I, Ascherio A. **Stress** and the risk of multiple sclerosis. Neurology. 2011 May 31;76(22):1866-71.
Ristori G, Romano S, Cannoni S, et al. Effects of **Bacille Calmette-Guérin** after the first demyelinating event in the CNS. Neurology 2014;82:41–48.
Rizzo Matthew. **Impaired Driving From Medical Conditions**: A 70-Year-Old Man Trying to Decide if He Should Continue Driving. JAMA. 2011;305(10):1018-1026.
Rocca MA, Absinta M, Amato MP, et al. **Posterior brain damage and cognitive impairment** in pediatric multiple sclerosis. Neurology 2014;82:1314–1321.
Rocca MA, Amato MP, De Stefano N, et. al. **Clinical and imaging assessment of cognitive dysfunction** in multiple sclerosis. Lancet Neurol. 2015 Feb 3. pii: S1474-4422(14)70250-9.
Rocca MA, Battaglini M, Benedict RH, et al. **Brain MRI atrophy** quantification in MS: From methods to clinical application. Neurology. 2017 Jan 24;88(4):403-413.
Rodger IW, Dilar D, Dwyer J, et al. Evidence against the Involvement of **Chronic Cerebrospinal Venous Abnormalities** in Multiple Sclerosis. A Case-Control Study. PLoS One. 2013 Aug 14;8(8):e72495.
Rodríguez Cruz PM, Matthews L, Boggild M, et al. Time- and Region-Specific **Season of Birth** Effects in Multiple Sclerosis in the United Kingdom. JAMA Neurol. 2016 Jun 27.
Rolf L, Muris AH, Damoiseaux J, et al. Paroxysmal **atrial fibrillation** after initiation of **fingolimod** for multiple sclerosis treatment. Neurology. 2014 Mar 18;82(11):1008-9.
Romme Christensen J, Ratzer R, Börnsen L, et al. **Natalizumab** in **progressive MS**: Results of an open-label, phase 2A, proof-of-concept trial. Neurology. 2014 Apr 29;82(17):1499-507.
Roostaei T, Sadaghiani S, Park MTM, et al. Channelopathy- related **SCN10A gene variants predict cerebellar dysfunction** in multiple sclerosis. Neurology 2016;86:410–417.
Rosenkranz T, Novas M, Terborg C. **PML** in a patient with lymphocytopenia treated with **dimethyl fumarate**. N Engl J Med. 2015 Apr 9;372(15):1476-8.
Rossi S, Studer V, Motta C, et al. **Neuroinflammation drives anxiety and depression** in relapsing-remitting multiple sclerosis. Neurology. 2017 Sep 26;89(13):1338-1347.
Rotstein DL, Healy BC, Malik MT, et al. Evaluation of **No Evidence of Disease Activity in a 7-Year** Longitudinal Multiple Sclerosis Cohort. JAMA Neurol. 2014 Dec 22.
Rotstein DL, Chen H, Wilton AS, et al. **Temporal trends** in multiple sclerosis prevalence and incidence in a large population. Neurology. 2018 Apr 17;90(16):e1435-e1441.
Ruck T, Pfeuffer S, Schulte-Mecklenbeck A, et al. **Vitiligo after alemtuzumab treatment**: Secondary autoimmunity is not all about B cells. Neurology. 2018 Dec 11;91(24):e2233-e2237.
Rudick RA, Lee JC, Cutter GR, et al. Disability Progression in a Clinical Trial of Relapsing-Remitting Multiple Sclerosis: Eight-Year Follow-up. Arch Neurol. 2010 Jul 12.
Ruet A, Deloire M, Charré-Morin J, et al. **Cognitive impairment** differs between primary progressive and relapsing-remitting MS. Neurology. 2013 Apr 16;80(16):1501-8.
Runia TF, Hop WCJ, de Rijke YB, Buljevac D, Hintzen RQ. **Lower serum vitamin D** levels are associated with a higher relapse risk in multiple sclerosis. Neurology 2012; 79:261–266.
Rush R, Kumbhare D. **Spasticity**. CMAJ. 2014 Nov 17.
Saarela M, Senthil K, Jones J, et al. **Hemophagocytic lymphohistiocytosis** in 2 patients with multiple sclerosis treated with **alemtuzumab**. Neurology. 2018 May 1;90(18):849-851.
Sadaka Y et al. 2010 **McDonald criteria for diagnosing pediatric** multiple sclerosis. Ann Neurol 2012 Mar 4.
Saguil A, Kane S, Farnell E. **Multiple Sclerosis: A Primary Care Perspective**. Am Fam Physician. 2014;90(9):644-652.
Saidha S, Sotirchos ES, Ibrahim MA, et al. **Microcystic macular oedema**, thickness of the inner nuclear layer of the retina, and disease characteristics in multiple sclerosis: a retrospective study. Lancet Neurol 2012: online Oct 3.
Saidha S, Sotirchos ES, Oh J, et al. Relationships Between **Retinal Axonal and Neuronal Measures** and Global Central Nervous System Pathology in Multiple Sclerosis. Arch Neurol. 2012 Oct 1:1-10.
Salzer J, Svenningsson R, Alping P, et al. **Rituximab** in multiple sclerosis: a retrospective observational study on safety and efficacy. Neurology 2016;87:2074–2081.
San-Juan-Rodriguez A, Good CB, Heyman RA, et al. **Trends in Prices, Market Share, and Spending** on Self-administered Disease-Modifying Therapies for Multiple Sclerosis in Medicare Part D. JAMA Neurol. 2019 Aug 26.
Saure C, Warnke C, Zohren F, et al. **Natalizumab** and Impedance of the Homing of CD34+ Hematopoietic Progenitors. Arch Neurol. 2011 Nov;68(11):1428-31.
Sawcer S, Franklin RJ, Ban M. Multiple sclerosis **genetics**. Lancet Neurol. 2014 May 19.
Scalfari A, Neuhaus A, Daumer M, Ebers GC, Muraro PA. **Age and disability accumulation** in multiple sclerosis. Neurology. 2011 Sep 27;77(13):1246-52.
Scalfari A, Neuhaus A, Daumer M, et al. **Early relapses, onset of progression, and late outcome** in multiple sclerosis. JAMA Neurol. 2013 Feb 1;70(2):214-22.
Scalfari A, Knappertz V, Cutter G, et al. **Mortality** in patients with multiple sclerosis. Neurology. 2013 Jul 9;81(2):184-192.
Scarpazza C, Prosperini L, De Rossi N, et al. To do or not to do? **Plasma exchange** and timing of steroid administration in **PML**. Ann Neurol. 2017 Oct 10.
Schippling S, Kempf C, Büchele F, et al. JCV granule cell neuronopathy and **GCN-IRIS** under **natalizumab** treatment. Ann Neurol. 2013 Jul 19.
Schoonheim MM, Popescu V, Rueda Lopes FC, et al. **Subcortical atrophy** and cognition: sex effects (men) in multiple sclerosis. Neurology 2012;79:1754 –1761.
Schoonheim MM, Hulst HE, Brandt RB, et al. **Thalamus structure** and function determine severity of **cognitive impairment** in multiple sclerosis. Neurology 2015;84:776–783.
Schoonheim MM, Ciccarelli O. The value of including **thalamic atrophy** as a clinical trial endpoint in multiple sclerosis. Neurology. 2018 Apr 10;90(15):677-678.
Schwab N, Schneider-Hohendorf T, Posevitz V, et al. **L-Selectin** is a possible biomarker for individual PML risk in natalizumab-treated MS patients. Neurology 2013;81:865–871.
Schwab N, Schneider-Hohendorf T, et al. **Natalizumab-associated PML**: challenges with incidence, resulting risk, and risk stratification. Neurology 2017;88:1197–1205.
Schweikert A, Kremer M, Ringel F, et al. Primary central nervous system **lymphoma** in a patient treated with **natalizumab**. Ann Neurol. 2009 Sep;66(3):403-6.
Seewann A, Kooi E-J, Roosendaal SD, et al. Postmortem verification of MS cortical lesion detection with **3D DIR**. Neurology 2012;78:302–308. (Double inversion recovery)
Sellebjerg F, Barnes D, Filippini G, et al. EFNS Task Force on Treatment of Multiple Sclerosis Relapses. EFNS guideline on treatment of multiple sclerosis relapses: report of an EFNS task force on

treatment of multiple sclerosis relapses. Eur J Neurol. 2005 Dec;12(12):939-46.
Selmaj K, Li DKB, et al. **Siponimod** for patients with relapsing-remitting multiple sclerosis (BOLD): an adaptive, dose-ranging, randomised, phase 2 study. Lancet Neurol 2013; online June 11.
Serra A, Skelly MM, Jacobs JB, et al. Improvement of internuclear ophthalmoparesis in multiple sclerosis with **dalfampridine**. Neurology. 2014 Jul 8;83(2):192-4.
Sharac J, McCrone P, Sabes-Figuera R. **Pharmacoeconomic** considerations in the treatment of multiple sclerosis. Drugs. 2010 Sep 10;70(13):1677-91. doi: 10.2165/11538000-000000000-00000.
Sheikh SI, Nestorov I, Russell H, et al. Tolerability and pharmacokinetics of delayed-release **dimethyl fumarate** administered with and without aspirin in healthy volunteers. Clin Ther. 2013 Oct;35(10):1582-1594.e9.
Shery T, et al. The effects of gabapentin and memantine in acquired and congenital nystagmus - A retrospective study. Br J Ophthalmol. 2006 Mar 23; [Epub ahead of print]
Shirani A et al. Association between use of **interferon beta and progression of disability** in patients with relapsing-remitting multiple sclerosis. JAMA 2012 Jul 18; 308:247.
Siddiqui AH, Zivadinov R, Benedict RHB, et al. Prospective randomized trial of **venous angioplasty in MS (PREMiSe).** Neurology 2014;83:441–449.
Sidhom Y, Maillart E, Tezenas du Montcel S, et al. **Fast multiple sclerosis progression in North Africans**: both genetics and environment matter. Neurology 2017;88:1218–1225.
Simon JH, Jacobs LD, Campion M, Wende K, Simonian N, Cookfair DL, et al. Magnetic resonance studies of intramuscular interferon beta-1a for relapsing multiple sclerosis. The Multiple Sclerosis Collaborative Research Group. Ann Neurol 1998;43:79-87.
Simone AM, Ferraro D, Vitetta F, et al. Severe **anemia** in a patient with multiple sclerosis treated with **natalizumab**. Neurology. 2014 Jul 22;83(4):374-5.
Simpson R, Simpson S, Ramparsad N, et al. Mindfulness-based **interventions for mental well-being** among people with multiple sclerosis: a systematic review and meta-analysis of randomised controlled trials. J Neurol Neurosurg Psychiatry. 2019 Jun 13.
Sinnecker T, Clarke MA, Meier D, et al. Evaluation of the **Central Vein Sign as a Diagnostic Imaging Biomarker** in Multiple Sclerosis. JAMA Neurol. 2019 Aug 19.
Soini E, Joutseno J, Sumelahti ML. **Cost-Utility of First-Line Disease-Modifying Treatments** for Relapsing-Remitting Multiple Sclerosis. Clin Ther. 2017 Feb 13.
Soilu-Hänninen M, Aivo J, Lindström BM, et al. A randomised, double blind, placebo controlled trial with **vitamin D3** as an add on treatment to interferon β-1b in patients with multiple sclerosis. J Neurol Neurosurg Psychiatry. 2012 May;83(5):565-71.
Solomon AJ, Klein EP, Bourdette D. "**Undiagnosing**" multiple sclerosis: The challenge of misdiagnosis in MS. Neurology. 2012 Jun 12;78(24):1986-91.
Solomon AJ, Naismith RT, Cross AH. **Misdiagnosis of multiple sclerosis**: impact of the 2017 McDonald criteria on clinical practice. Neurology 2019;92:26–33.
Sombekke MH, Wattjes MP, Balk LJ, et al. **Spinal cord lesions** in patients with clinically isolated syndrome: A powerful tool in diagnosis and prognosis. Neurology. 2013 Jan 1;80(1):69-75.
Steri M, Orrù V, Idda ML, et al. **Overexpression of the cytokine BAFF** and autoimmunity risk. N Engl J Med 2017;376:1615- 26.
Sumowski JF, Rocca MA, Leavitt VM, et al. **Brain reserve and cognitive reserve** protect against cognitive decline over 4.5 years in MS. Neurology. 2014 May 20;82(20):1776-83.
Sorensen PS, Deisenhammer F, Duda P, et al. EFNS Task Force on Anti-IFN-beta Antibodies in Multiple Sclerosis. Guidelines on use of anti-IFN-beta antibody measurements in multiple sclerosis: report of an EFNS Task Force on IFN-beta antibodies in multiple sclerosis. Eur J Neurol. 2005 Nov;12(11):817-27.
Sorensen PS, Mellgren SI, Svenningsson A, et al. NORdic trial of oral Methylprednisolone as add-on therapy to Interferon beta-1a for treatment of relapsing-remitting Multiple Sclerosis (**NORMIMS** study): a randomised, placebo-controlled trial. Lancet Neurol. 2009 Apr 29. [Epub ahead of print] Oral methylprednisolone given in pulses every 4 weeks as an add-on therapy to subcutaneous interferon beta-1a in patients with relapsing-remitting multiple sclerosis leads to a significant reduction in relapse rate. However, because of the small number of patients and the high dropout rate, these findings need to be corroborated in larger cohorts.
Sørensen PS, Koch-Henriksen N, Jensen PE. **Neutralizing antibodies** against interferon-{beta} do not predispose antibodies against natalizumab. Neurology. 2011 Feb 22;76(8):759-60.
Sorensen PS, Lycke J, Erälinna JP, et al; for the **SIMCOMBIN** study investigators. **Simvastatin** as add-on therapy to interferon beta-1a for relapsing-remitting multiple sclerosis (SIMCOMBIN study): a placebo-controlled randomised phase 4 trial. Lancet Neurol. 2011 Jul 8. (We found no beneficial effect of simvastatin)
Sorensen PS, Lisby S, Grove R, et al. Safety and efficacy of **ofatumumab** in relapsing-remitting multiple sclerosis: A phase 2 study. Neurology. 2014 Feb 18;82(7):573-81.
Sormani MP, Li DK, Bruzzi P, et al. **Combined MRI lesions and relapses** as a surrogate for disability in multiple sclerosis. Neurology 2011;77:1684 –1690.
Sormani MP, Bruzzi P. **MRI lesions** as a surrogate for relapses in multiple sclerosis: a meta-analysis of randomised trials. Lancet Neurol 2013; online June 3.
Sormani MP, Gasperini C, Romeo M, et al. Assessing response to **interferon-b** in a multicenter dataset of patients with MS. Neurology 2016;87:134–140.
Sormani MP, Muraro PA, Schiavetti I, et al. **Autologous hematopoietic stem cell transplantation** (aHSCT) in multiple sclerosis: a meta-analysis. Neurology 2017;88:2115–2122.
Sotirchos ES, Bhargava P, Eckstein C, et al. Safety and immunologic effects of **high- vs low-dose cholecalciferol** in multiple sclerosis. Neurology. 2016 Jan 26;86(4):382-90.
Spelman T, Gray O, Trojano M, et al. **Seasonal variation** of relapse rate in multiple sclerosis is **latitude-dependent**. Ann Neurol. 2014 Oct 4.
Srivastava R, Aslam M, Kalluri SR, et al. **Potassium channel KIR4.1** as an immune target in multiple sclerosis. N Engl J Med 2012;367:115-23.
Stampanoni Bassi M, Iezzi E, et al. **Obesity worsens central inflammation** and disability in multiple sclerosis. Mult Scler. 2019 Jun 4:1352458519853473.
Staples Judith, Ponsonby Anne-Louise, Lim Lynette. Low maternal exposure to **ultraviolet radiation** in pregnancy, month of birth, and risk of multiple sclerosis in offspring: longitudinal analysis. BMJ 2010;340:c1640, doi: 10.1136/bmj.c1640 (Published 29 April 2010)
Stein MS, Liu Y, Gray OM, et al. A randomized trial of high-dose **vitamin D2** in relapsing-remitting multiple sclerosis. Neurology 2011;77:1611–1618.
Stewart N, Simpson S Jr, van der Mei I, et al. **Interferon-β and serum 25-hydroxyvitamin D** interact to modulate relapse risk in MS. Neurology. 2012 Jun 13.
Street D, Halfpenny CA, Galea I. **CNS inflammation** other than multiple sclerosis: How likely is diagnosis? Neurology. 2014 Apr 1;82(13):1187-9.
Strupp M, Kalla R, Claassen J, et al. A randomized trial of **4-aminopyridine** in EA2 and related familial episodic ataxias. Neurology. 2011 Jul 19;77(3):269-75.
Stürner KH, et al. A standardised frankincense extract reduces disease activity in relapsing-remitting multiple sclerosis (the SABA phase IIa trial). J Neurol Neurosurg Psychiatry. 2017 Dec 16.
Stüve O, Cravens PD, Frohman EM, et al. Immunologic and clinical status **14 months after cessation of natalizumab** therapy. Neurology. 2008 Nov 5. [Epub ahead of print] This is the first long-term follow-up of patients who discontinued natalizumab. We did not observe a clinical, radiographic, or immunologic rebound phenomenon after discontinuation of natalizumab therapy.
Sumowski JF, Rocca MA, Leavitt VM, et al. **Brain reserve and cognitive reserve** in multiple sclerosis: What you've got and how you use it. Neurology. 2013 Jun 11;80(24):2186-93.
Sumowski JF, Rocca MA, Leavitt VM, et al. **Brain reserve** against physical disability progression over 5 years in multiple sclerosis. Neurology. 2016 May 24;86(21):2006-9.
Sumowski JF, McDonnell GV, Bourdette D. **Diet** in multiple sclerosis: Science takes a seat at the table. Neurology. 2017 Dec 6.
Sumowski JF, Benedict R, Enzinger C, et al. **Cognition in multiple sclerosis**: State of the field and priorities for the future. Neurology. 2018 Feb 6;90(6):278-288.
Sundqvist E, Sundström P, Lindén M, et al. Lack of replication of interaction between **EBNA1 IgG and smoking** in risk for multiple sclerosis. Neurology. 2012 Sep 25;79(13):1363-8.
Svenningsson A, Dring AM, Fogdell-Hahn A, et al. Fatal neuroinflammation in a case of multiple sclerosis with **anti-natalizumab antibodies**. Neurology. 2013 Mar 5;80(10):965-7.
Sweetser MT, Dawson KT, Bozic C. Manufacturer's **(dimethyl fumarate, fumaric acid)** response to case reports of **PML**. N Engl J Med. 2013 Apr 25;368(17):1659-61.

Tan CS, Koralnik IJ. **Progressive multifocal leukoencephalopathy** (PML) and other disorders caused by JC virus: clinical features and pathogenesis. Lancet Neurol. 2010 Apr;9(4):425-37.
Tan IL, McArthur JC, Clifford DB, Major EO, Nath A. Immune reconstitution inflammatory syndrome **(IRIS) in natalizumab-associated PML**. Neurology. 2011 Aug 10.
Tankou SK, Regev K, Healy BC, et al. A **probiotic modulates the microbiome and immunity in multiple sclerosis**. Ann Neurol. 2018 Apr 20.
Tao C, Simpson S Jr, et al; MSBase Study Group. **Higher latitude** is significantly associated with an earlier age of disease onset in multiple sclerosis. J Neurol Neurosurg Psychiatry. 2016 Nov 3.
Tavazzi E, Rovaris M, La Mantia L. **Drug therapy for multiple sclerosis**. CMAJ. 2014 Aug 5;186(11):833-840. Epub 2014 Apr 22. Review.
Thomas K, Schultheiss T, Ziemssen T. **Neuroborreliosis** during **natalizumab** treatment in multiple sclerosis. Neurology. 2013 Sep 10;81(11):1012-4.
Thompson Alan J, Toosy Ahmed T, Ciccarelli Olga, Pharmacological management of **symptoms in multiple sclerosis**: current approaches and future directions, The Lancet Neurology, Volume 9, Issue 12, December 2010, Pages 1182-1199, ISSN 1474-4422, DOI: 10.1016/S1474-4422(10)70249-0.
Thompson AJ, Banwell BL, Barkhof F, et al. **Diagnosis** of multiple sclerosis: **2017 revisions of the McDonald criteria**. Lancet Neurol 2017; published online Dec 21.
Thompson AJ, Baranzini SE, Geurts J, et al. **Multiple sclerosis- Seminar**. Lancet. 2018 Mar 22.
Thormann A, Sørensen PS, Koch-Henriksen N, et al. **Comorbidity in multiple sclerosis** is associated with diagnostic delays and increased **mortality**. Neurology. 2017 Oct 17;89(16):1668-1675.
Tian DC, Shi K, Zhu Z, et al. **Fingolimod** enhances the efficacy of delayed alteplase administration in acute ischemic stroke by promoting anterograde reperfusion and retrograde collateral flow. Ann Neurol. 2018 Oct 8.
Torkildsen O, Wergeland S, Bakke S, et al. **ω-3 Fatty Acid Treatment** in Multiple Sclerosis (**OFAMS** Study): A Randomized, Double-Blind, Placebo-Controlled Trial. Arch Neurol. 2012 Apr 16.
Torres-Moreno MC, Papaseit E, Torrens M, Farré M. Assessment of efficacy and tolerability of **medicinal cannabinoids in patients with multiple sclerosis**: a systematic review and meta-analysis. JAMA Netw Open. 2018;1(6):e183485.
Tortorella C, Direnzo V, D'Onghia M, Trojano M. **Brainstem PML lesion mimicking MS plaque in a natalizumab**-treated MS patient. Neurology. 2013 Oct 15;81(16):1470-1.
Tramacere I, Del Giovane C, Filippini G. Association of **Immunotherapies With Outcomes** in Relapsing-Remitting Multiple Sclerosis. JAMA. 2016 Jan 26;315(4):409-10.
Tremlett H, Zhu F, Ascherio A, et al. **Sun exposure** over the life course and associations with multiple sclerosis. Neurology. 2018 Apr 3;90(14):e1191-e1199.
Trampe AK, Hemmelmann C, Stroet A, et al. **Anti-JC virus antibodies** in a large German natalizumab-treated multiple sclerosis cohort. Neurology. 2012 May 29;78(22):1736-42.
Truini A, Prosperini L, Calistri V, et al. A **dual concurrent mechanism** explains trigeminal neuralgia in patients with multiple sclerosis. Neurology. 2016 May 31;86(22):2094-9.
Tsagkas C, Magon S, Gaetano L, et al. **Spinal cord volume loss**: a marker of disease progression in multiple sclerosis. Neurology 2018;91:e349–e358.
Tsivgoulis G, Mantatzis M, Bogiatzi C, et al. **Extracranial venous hemodynamics in multiple sclerosis**: A case-control study. Neurology. 2011 Sep 27;77(13):1241-5.
Tullman M, Chartier-Kastler E, Kohan A, et al. Low-dose **onabotulinumtoxinA improves urinary symptoms in noncatheterizing patients with MS**. Neurology. 2018 Aug 14;91(7):e657-e665.
Tuohy O, Costelloe L, Hill-Cawthorne G, et al. **Alemtuzumab** treatment of multiple sclerosis: long-term safety and efficacy. J Neurol Neurosurg Psychiatry. 2015 Feb;86(2):208-15.
Tur C, Montalban X, Tintoré M, et al. **Interferon Beta-1b** for the Treatment of Primary Progressive Multiple Sclerosis: Five-Year Clinical Trial Follow-up. Arch Neurol. 2011 Nov;68(11):1421-7.
Tur C, Ramagopalan S, Altmann DR, et al. **HLA-DRB1*15** influences the development of **brain tissue damage** in early PPMS. Neurology. 2014 Nov 4;83(19):1712-8.
Tzartos JS, Khan G, Vossenkamper A, et al. Association of innate immune activation with latent **Epstein-Barr virus** in active MS lesions. Neurology 2012;78:15–23.
Uccelli A, Ginocchio F, Mancardi GL, et al. Primary varicella zoster infection associated with **fingolimod** treatment. Neurology. 2011 Mar 15;76(11):1023-4.
UCSF MS-EPIC Team, Cree BAC, Hollenbach JA, Bove R, et al. Silent Progression in **Disease activity-Free Relapsing Multiple Sclerosis**. Ann Neurol. 2019 Mar 9.
Ueda P, Rafatnia F, Bäärnhielm M, et al. **Neonatal vitamin D** status and risk of multiple sclerosis. Ann Neurol. 2014 Jul 1.
van Amerongen G, et al. Effects on **Spasticity and Neuropathic Pain** of an Oral Formulation of **Δ9-Tetrahydrocannabinol** in Patients With Progressive Multiple Sclerosis. Clin Ther. 2017 Feb 9.
van der Kop ML, Pearce MS, Dahlgren L, et al. **Neonatal and delivery outcomes** in women with multiple sclerosis. Ann Neurol. 2011 Jun 27. doi: 10.1002/ana.22483.
van der Voort LF, Gilli F, Bertolotto A, Knol DL, Uitdehaag BM, Polman CH, Killestein J. Clinical Effect of Neutralizing Antibodies to Interferon Beta That Persist Long After Cessation of Therapy for Multiple Sclerosis. Arch Neurol. 2010 Feb 8.
van der Voort Laura F.; Gilli Francesca; Bertolotto Antonio; et al. Clinical Effect of **Neutralizing Antibodies to Interferon Beta** That Persist Long After Cessation of Therapy for Multiple Sclerosis. Arch Neurol. 2010;0(2010):2010.21.
van der Vuurst de Vries RM, et al. **Soluble CD27 levels** in cerebrospinal fluid as a prognostic biomarker in clinically isolated syndrome [online Jan 3, 2017]. JAMA Neurol. doi:10.1001/jamaneurol.2016.4997
van der Vuurst de Vries RM, Mescheriakova JY, Wong YYM, et al. **Application of the 2017 Revised McDonald Criteria for Multiple Sclerosis** to Patients With a Typical Clinically Isolated Syndrome. JAMA Neurol. 2018 Aug 6.
Van Der Walt A, Sung S, Spelman T, et al. A double-blind, randomized, controlled study of **botulinum toxin type A** in MS-related tremor. Neurology. 2012 Jul 3;79(1):92-9.
Van Haren K, Waubant E. Therapeutic advances in **pediatric multiple sclerosis**. J Pediatr. 2013 Sep;163(3):631-7.
van Oosten BW, Killestein J, Barkhof F, Polman CH, Wattjes MP. **PML** in a patient treated with **dimethyl fumarate** from a compounding pharmacy. N Engl J Med 2013;368:1658-9.
van Pelt ED, Mescheriakova JY, Makhani N, et al. **Risk genes** associated with **pediatric-onset MS** but not with monophasic acquired CNS demyelination. Neurology. 2013 Dec 3;81(23):1996-2001.
Vellinga MM, Castelijns JA, Barkhof F, et al. **Postwithdrawal rebound increase in T2 lesional activity in natalizumab**-treated MS patients. Neurology. 2007 Sep 13; [Epub ahead of print] n=21
Venci JV, Gandhi MA. **Dimethyl fumarate (Tecfidera)**: a new oral agent for multiple sclerosis. Ann Pharmacother. 2013 Dec;47(12):1697-702
Vennegoor A, Wattjes MP, van Munster ET, et al. Indolent course of **progressive multifocal leukoencephalopathy** (PML) during natalizumab treatment in MS. Neurology. 2011 Feb 8;76(6):574-6.
Verhey LH, Branson HM, Shro MM, et al. **MRI parameters** for prediction of multiple sclerosis **diagnosis in children** with acute CNS demyelination: a prospective national cohort study. Lancet Neurol 2011; published online Nov 7, 2011. DOI:10.1016/S1474-4422(11)70250-2.
Vilariño-Güell C, Zimprich A, Martinelli-Boneschi F, et al. **Exome sequencing** in multiple sclerosis families **identifies 12 candidate genes** and nominates biological pathways for the genesis of disease. PLoS Genet. 2019 Jun 6;15(6):e1008180.
Villar LM, García-Sánchez MI, Costa-Frossard L, et al. Immunological markers of optimal response to **natalizumab** in multiple sclerosis. Arch Neurol. 2012 Feb;69(2):191-7.
Villar LM, Costa-Frossard L, Masterman T, et al. lipid-specific IgM bands in csf associated with a reduced risk of developing pml during treatment with **natalizumab**. Ann Neurol. 2015 Jan 7.
Visaria J, Thomas N, Gu T, et al. Understanding the **Patient's Journey** in the **Diagnosis and Treatment of Multiple Sclerosis** in Clinical Practice. Clin Ther. 2018 May 23.
Viscidi RP, Khanna N, Tan CS, et al. **JC virus antibody** and viremia as predictors of progressive multifocal leukoencephalopathy in human immunodeficiency virus-1-infected individuals. Clin Infect Dis. 2011 Oct;53(7):711-5.
Voskuhl RR, Wang H, et al. **Estriol combined with glatiramer** acetate for women with relapsing-remitting multiple sclerosis: randomised, placebo-controlled, phase 2 trial. Lancet Neurol. 2015 Nov 24.

Voskuhl R. **Rebound Relapses After Ceasing Another Disease-Modifying Treatment** in Patients With Multiple Sclerosis: Are There Lessons to Be Learned? JAMA Neurol. 2016 May 2
Vukusic S, Rollot F, Casey R, et al. Progressive Multifocal Leukoencephalopathy Incidence and Risk Stratification Among **Natalizumab** Users in France. JAMA Neurol. 2019 Sep 3.
Waldman A, Ghezzi A, Bar-Or A, et al. **Multiple sclerosis in children**: an update on clinical diagnosis, therapeutic strategies, and research. Lancet Neurol. 2014 Sep;13(9):936-948.
Wallin MT, Culpepper WJ, Campbell JD, et al; US Multiple Sclerosis Prevalence Workgroup. the **prevalence of MS in the United States**: A population-based estimate using health claims data. Neurology. 2019 Mar 5;92(10):e1029-e1040.
Walter O, Treiner E, Bonneville F, et al. Treatment of Progressive Multifocal **Leukoencephalopathy with Nivolumab**. N Engl J Med. 2019 Apr 25;380(17):1674-1676.
Wang G, Marrie RA, Salter AR, et al. **Health insurance** affects the **use of disease-modifying therapy** in multiple sclerosis.Neurology. 2016 Jul 26;87(4):365-74.
Warnke C, Mausberg AK, Stettner M, et al. **Natalizumab affects the T-cell receptor** repertoire in patients with multiple sclerosis. Neurology 2013;81:1400–1408.
Warnke C, von Geldern G, Markwerth P, et al. The **CSF JCV antibody index** for diagnosis of **natalizumab**-associated **PML**. Ann Neurol. 2014 Apr 11.
Warnke C, Dehmel T, Ramanujam R, et al. Initial **lymphocyte count and low BMI** may affect **fingolimod-induced lymphopenia**. Neurology. 2014 Dec 2;83(23):2153-7.
Wattjes MP, Killestein J. **PML after natalizumab discontinuation**: Few and true? Ann Neurol. 2014 Jan 20
Waubant E, Banwell B, Wassmer E, et al; IPMSSG. **Clinical trials of disease-modifying agents in pediatric MS**: Opportunities, challenges, and recommendations from the IPMSSG. Neurology. 2019 May 28;92(22):e2538-e2549
Waubant E, Mowry EM, Krupp L, et al. For the US Pediatric MS Network. **Common viruses associated with lower pediatric** multiple sclerosis risk. Neurology. 2011 Jun 7;76(23):1989-1995.
Waubant E, Pelletier D, Mass M, et al. on the behalf of the **ITN STAyCIS** Study Group; ITN020AI Study Management Team. Randomized controlled trial of **atorvastatin** in clinically isolated syndrome: The STAyCIS study. Neurology. 2012 Apr 10;78(15):1171-1178.
Waubant E, Cross A. **MS and related disorders**: groundbreaking news. Lancet Neurol. 2014 Jan;13(1):11-3
Way SW, Popko B. Harnessing the integrated **stress response** for the treatment of multiple sclerosis. Lancet Neurol. 2016 Feb 9.
Weber-Schoendorfer C, Schaefer C. Multiple sclerosis, immunomodulators, and **pregnancy** outcome: a prospective observational study. Mult Scler. 2009 Sep;15(9):1037-42. Our findings suggest that neither GA nor IFN constitutes a major risk for prenatal developmental toxicity.
Wehrum T, Beume LA, Stitch O, et al. Activation of disease during therapy with **alemtuzumab** in 3 patients with multiple sclerosis. Neurology 2018;90:e601–e605.
West TW, Cree BA. **Natalizumab dosage suspension**: are we helping or hurting? Ann Neurol. 2010 Sep;68(3):395-9.
What place for {blacktriangledown}**cannabis extract** in MS? Drug Ther Bull. 2012 Dec;50(12):141-4.
Whiting P, et al. Accuracy of magnetic resonance imaging for the diagnosis of multiple sclerosis: systematic review. BMJ. 2006 Mar 24; [Epub ahead of print] (InfoPOEMs: Magnetic resonance imaging (MRI) is not particularly useful in either ruling in or ruling out multiple sclerosis (MS). Relying on it to make the diagnosis will result in overdiagnosis of patients, and using it to rule out MS will cause you to miss approximately half the patients who will eventually be given a clinical diagnosis. (LOE = 1a))
Wiggermann V, Hernández Torres E, Vavasour IM, et al. **Magnetic resonance frequency shifts** during acute MS lesion formation. Neurology 2013;81:211–218.
Wijburg MT, Kleerekooper I, Lissenberg-Witte BI, et al. Association of **progressive multifocal leukoencephalopathy lesion volume** with JC virus polymerase chain reaction results in cerebrospinal fluid of natalizumab-treated patients with multiple sclerosis [online Mar 12, 2018].JAMA Neurol. doi:10.1001/jamaneurol.2018.0094
Wijnands JMA, Kingwell E, Zhu F, et al. **Health-care use before a first demyelinating event** suggestive of a multiple sclerosis **prodrome**: a matched cohort study. Lancet Neurol 2017; 16: 445–51.
Wingerchuk DM, Weinshenker BG. **Disease modifying therapies for relapsing multiple sclerosis**. BMJ. 2016 Aug 22;354:i3518
Wolinsky JS, Montalban X, Hauser SL, et al. Evaluation of **no evidence of progression or active disease** (NEPAD) in patients with **primary progressive multiple sclerosis** in the **ORATORIO** trial. Ann Neurol. 2018 Aug 29
Wong YYM, Bruijstens AL, Barro C, et al. **Serum neurofilament light chain** in pediatric MS and other acquired demyelinating syndromes. Neurology. 2019 Sep 3;93(10):e968-e974.
Wynn D, Kaufman M, Montalban X, et al. for the **CHOICE** investigators. **Daclizumab** in active relapsing multiple sclerosis (CHOICE study): a phase 2, randomised, double-blind, placebo-controlled, add-on trial with interferon beta. Lancet Neurol. 2010 Feb 15.
Xia Z, Steele SU, Bakshi A, et al. Assessment of early evidence of multiple sclerosis in a prospective study of high-risk **family members** [online Jan 17, 2017]. JAMA Neurol. doi:10.1001/jamaneurol.2016.5056
Yadav V, Bever C Jr, Bowen J, et al. Summary of evidence-based guideline: **Complementary and alternative medicine** in multiple sclerosis: Report of the Guideline Development Subcommittee of the American Academy of Neurology. Neurology. 2014 Mar 25;82(12):1083-92.
Yadav V, Narayanaswami P. **Complementary and alternative medical therapies in multiple sclerosis**-the american academy of neurology guidelines: a commentary. Clin Ther. 2014 Dec 1;36(12):1972-8.
Yamaguchi Y, Torisu H, Kira R, et al. A nationwide survey of **pediatric acquired demyelinating syndromes in Japan**. Neurology. 2016 Nov 8;87(19):2006-2015.
Yea C, Tellier R, Chong P, et al; On behalf of the Canadian Pediatric Demyelinating Disease Network. **Epstein-Barr virus** in oral shedding of children with multiple sclerosis. Neurology. 2013 Sep 6.
Yeh EA, Waubant E, Krupp LB, et al.; for the National Network of Pediatric MS Centers of Excellence. Multiple Sclerosis Therapies in **Pediatric Patients With Refractory Multiple Sclerosis**. Arch Neurol. 2010 Dec 13.
Yeung J, Cauquil C, Saliou G, et al. **Varicella-zoster virus** acute myelitis in a patient with MS treated with **natalizumab**. Neurology. 2013 May 7;80(19):1812-3.
Zajicek J. Diagnosis and disease modifying treatments in multiple sclerosis. Postgrad Med J. 2005 Sep;81(959):556-61.
Zamboni P, Tesio L, Galimberti S, et al; Brave Dreams Research Group. Efficacy and safety of **extracranial vein angioplasty (CCSVI) in multiple sclerosis**: a randomized clinical trial. [online Nov 18, 2017].JAMA Neurol. doi:10.1001 /jamaneurol.2017.3825
Zastepa E, Fitz-Gerald L, Hallett M, et al. **Naive CD4 T-cell activation** identifies MS patients having rapid transition to progressive MS. Neurology. 2014 Feb 14.
Zhang J, Shi S, Zhang Y, et al. **Alemtuzumab versus interferon beta 1a** for relapsing-remitting multiple sclerosis. CochraneDatabase of Systematic Reviews 2017, Issue 11. Art.No.:CD010968. There is low- to moderate-quality evidence that annual intravenous cycles of alemtuzumab at a dose of 12 mg per day or 24 mg per day reduces the proportion of participants with relapses, disease progression, change of EDSS score and developing new T2 lesions on MRI over 24 to 36 months in comparison with subcutaneous IFN beta-1a 44 µg three times per week. Alemtuzumab appeared to be relatively well tolerated. The most frequently reported adverse events were infusion-associated reactions, infections and autoimmune events. The use of alemtuzumab requires careful monitoring so that potentially serious adverse effects can be treated early and effectively.
Zhang T, Tremlett H, Leung S, et al. **CIHR** Team in the Epidemiology and Impact of Comorbidity on Multiple Sclerosis. Examining the effects of **comorbidities** on disease-modifying therapy use in multiple sclerosis. Neurology. 2016 Apr 5;86(14):1287-95

Zhang T, Tremlett H, Zhu F, et al. Effects of **physical comorbidities on disability progression** in multiple sclerosis. Neurology. 2018 Jan 30;90(5):e419-e427.
Zheng C, He L, Liu L, Zhu J, Jin T. The efficacy of **vitamin D** in multiple sclerosis: A meta-analysis. Mult Scler Relat Disord. 2018 May 12;23:56-61.
Zhu Z, Fu Y, Tian D, et al. Combination of an Immune Modulator **Fingolimod with Alteplase** in Acute Ischemic Stroke: A Pilot Trial. Circulation. 2015 Jul 22.
Zimmermann HG, Knier B, Oberwahrenbrock T, et al. Association of Retinal Ganglion Cell Layer Thickness With Future Disease Activity in Patients With Clinically Isolated Syndrome. JAMA Neurol. 2018 Apr 23.
Zipp F, Gold R, Wiendl H. Identification of **Inflammatory Neuronal Injury** and Prevention of Neuronal Damage in Multiple Sclerosis: Hope for Novel Therapies? JAMA Neurol. 2013 Oct 21.
Zivadinov R, Weinstock-Guttman B, Hashmi K, et al. **Smoking** is associated with increased lesion volumes and brain atrophy in multiple sclerosis. Neurology. 2009 Aug 18;73(7):504-10.
Zivadinov R, Marr K, Cutter G, et al. Prevalence, sensitivity, and specificity of chronic cerebrospinal venous insufficiency (**CCSVI**) in MS. Neurology. 2011 Jul 12;77(2):138-44.
Zuluaga MI, Otero-Romero S, Rovira A, et al. **Menarche, pregnancies, and breastfeeding** do not modify long-term prognosis in multiple sclerosis. Neurology. 2019 Mar 26;92(13):e1507-e1516.
Zurawski J, et al. Use of **Magnetic Resonance Imaging** to Visualize Leptomeningeal Inflammation in Patients With Multiple Sclerosis: A Review. JAMA Neurol. 2017 Jan 1;74(1):100-109.

National Multiple Sclerosis Society. Disease Management Consensus Paper. (http://www.nationalmssociety.org/pdf/forpros/Exp_Consensus.pdf. Accessed April 2,2005.

[65] Cohen BA, Khan O, Jeffery DR, Bashir K, et al. Identifying and treating patients with suboptimal responses. Neurology. 2004 Dec 28;63(12 Suppl 6):S33-40.
[66] Cohen BA, Mikol DD. Mitoxantrone treatment of multiple sclerosis: safety considerations. Neurology. 2004 Dec 28;63(12 Suppl 6):S28-32.
[67] Cohen BA, Jeffery DR. Identification of suboptimal responders to immune modulating agents and the role of mitoxantrone in worsening multiple sclerosis. Neurology. 2004 Dec 28;63(12 Suppl 6):S1-2.
[68] Rizvi SA, Zwibel H, Fox EJ. Mitoxantrone for multiple sclerosis in clinical practice. Neurology. 2004 Dec 28;63(12 Suppl 6):S25-7.
[69] Hartung HP, Gonsette R, Konig N, et al.; Mitoxantrone in Multiple Sclerosis Study Group (**MIMS**). Mitoxantrone in progressive multiple sclerosis: a placebo-controlled, double-blind, randomised, multicentre trial. Lancet. 2002 Dec 21-28;360(9350):2018-25.
[70] van de Wyngaert FA, Beguin C, D'Hooghe MB, et al. A double-blind clinical trial of mitoxantrone versus methylprednisolone in relapsing, secondary progressive multiple sclerosis. Acta Neurol Belg. 2001 Dec;101(4):210-6.
[71] Millefiorini E, Gasperini C, Pozzilli C, et al. Randomized placebo-controlled trial of mitoxantrone in relapsing-remitting multiple sclerosis: 24-month clinical and MRI outcome. J Neurol. 1997 Mar;244(3):153-9.
[72] Edan G, Miller D, Clanet M, et al. Therapeutic effect of mitoxantrone combined with methylprednisolone in multiple sclerosis: a randomised multicentre study of active disease using MRI and clinical criteria. J Neurol Neurosurg Psychiatry. 1997 Feb;62(2):112-8.
[73] Bastianello S, Pozzilli C, D'Andrea F, et al. A controlled trial of mitoxantrone in multiple sclerosis: serial MRI evaluation at one year. Can J Neurol Sci. 1994 Aug;21(3):266-70.
[74] Goodin DS, Arnason BG, Coyle PK, et al.; Therapeutics and Technology Assessment Subcommittee of the American Academy of Neurology. The use of mitoxantrone (Novantrone) for the treatment of multiple sclerosis: report of the Therapeutics and Technology Assessment Subcommittee of the American Academy of Neurology. Neurology. 2003 Nov 25;61(10):1332-8.
[75] Scott LJ, Figgitt DP. Mitoxantrone: a review of its use in multiple sclerosis. CNS Drugs. 2004;18(6):379-96.
[76] Fox EJ. Management of worsening multiple sclerosis with mitoxantrone: a review. Clin Ther. 2006 Apr;28(4):461-74.
Le Page E, Leray E, Taurin G, et al. Mitoxantrone as induction treatment in aggressive relapsing remitting multiple sclerosis: treatment response factors in a 5 year follow-up observational study of 100 consecutive patients. J Neurol Neurosurg Psychiatry. 2008 Jan;79(1):52-6.
Le Page E, Leray E, Edan G. Longterm safety profile of mitoxantrone in a French cohort of 802 multiple sclerosis patients: a 5-year prospective study. Mult Scler 2011;17:867-75.
[77] Pozzilli C, Antonini G, Bagnato F, et al. Monthly corticosteroids decrease neutralizing antibodies to IFNbeta1 b: a randomized trial in multiple sclerosis. J Neurol. 2002 Jan;249(1):50-6.
[78] Rio J, Nos C, Marzo ME, Tintore M, Montalban X. Low-dose steroids reduce flu-like symptoms at the initiation of IFNbeta-1b in relapsing-remitting MS. Neurology. 1998 Jun;50(6):1910-2.
[79] Visser LH, Beekman R, Tijssen CC, et al. A randomized, double-blind, placebo-controlled pilot study of i.v. immune globulins in combination with i.v. methylprednisolone in the treatment of relapses in patients with MS. Mult Scler. 2004 Feb;10(1):89-91.
[80] Craig J, Young CA, Ennis M, et al. A randomised controlled trial comparing rehabilitation against standard therapy in multiple sclerosis patients receiving intravenous steroid treatment. J Neurol Neurosurg Psychiatry. 2003 Sep;74(9):1225-30.
[81] Beck RW, Trobe JD, Moke PS, et al. Optic Neuritis Study Group. High- and low-risk profiles for the development of multiple sclerosis within 10 years after optic neuritis: experience of the optic neuritis treatment trial. Arch Ophthalmol. 2003 Jul;121(7):944-9.
[82] van de Wyngaert FA, Beguin C, D'Hooghe MB, et al. A double-blind clinical trial of mitoxantrone versus methylprednisolone in relapsing, secondary progressive multiple sclerosis. Acta Neurol Belg. 2001 Dec;101(4):210-6.
[83] Edan G, Miller D, Clanet M, et al.. Therapeutic effect of mitoxantrone combined with methylprednisolone in multiple sclerosis: a randomised multicentre study of active disease using MRI and clinical criteria. J Neurol Neurosurg Psychiatry. 1997 Feb;62(2):112-8.
[84] Cazzato G, Mesiano T, Antonello R, et al. Double-blind, placebo-controlled, randomized, crossover trial of high-dose methylprednisolone in patients with chronic progressive form of multiple sclerosis. Eur Neurol. 1995;35(4):193-8.
[85] Beck RW, Cleary PA, Anderson MM Jr, et al. A randomized, controlled trial of corticosteroids in the treatment of acute optic neuritis. The Optic Neuritis Study Group. N Engl J Med. 1992 Feb 27;326(9):581-8.
[86] Filippini G, Brusaferri F, Sibley WA, et al. Corticosteroids or ACTH for acute exacerbations in multiple sclerosis. Cochrane Database Syst Rev. 2000;(4):CD001331.
Martinelli V, Rocca MA, Annovazzi P, et al. A short-term randomized MRI study of high-dose **oral** vs intravenous methylprednisolone in MS. Neurology. 2009 Dec 1;73(22):1842-8.
[87] Sharrack B, Hughes RA, Morris RW, et al. The effect of oral and intravenous methylprednisolone treatment on subsequent relapse rate in multiple sclerosis. J Neurol Sci. 2000 Feb 1;173(1):73-7.
[88] Sellebjerg F, Frederiksen JL, Nielsen PM, Olesen J. [Randomized controlled trial of high-dose peroral methylprednisolone in attacks of multiple sclerosis] Ugeskr Laeger. 1999 Nov 29;161(48):6625-9.
[89] Sellebjerg F, Frederiksen JL, Nielsen PM, Olesen J. Double-blind, randomized, placebo-controlled study of oral, high-dose methylprednisolone in attacks of MS. Neurology. 1998 Aug;51(2):529-34.
[90] Barnes D, Hughes RA, Morris RW, et al. Randomised trial of oral and intravenous methylprednisolone in acute relapses of multiple sclerosis. Lancet. 1997 Mar 29;349(9056):902-6.
[91] Filipini G, Brusaferri F, Sibley WA et al. Corticosteroids or ACTH for acute exacerbations in MS. Cochrane DataBase Syst Rev 2000;CD001331.
[92] Wenning GK, Wietholter H, Schnauder G et al. Recovery of the HTPA axis from suppression by short-term, high dose IV prednisolone therapy in patients with MS. Acta Neurol Scand 1994;89:270-273.
[93] Morrow SA, Stoian CA, Dmitrovic J, Chan SC, Metz LM. The bioavailability of IV methylprednisolone and oral prednisone in multiple sclerosis. Neurology. 2004 Sep 28;63(6):1079-80.

Approach to Migraine: Considerations

- ACUTE:
  - may consider metoclopramide or domperidone 1st; NSAID and/or triptan also recommended first line;
  - IV prochlorperazine + diphenhydramine more effective relief than IV hydromorphone (Sustained relief after 1 dose NNT=4 (2-9).
  - in very severe attacks, SC sumatriptan likely to be most effective & rapid; consider need for rapid onset vs recurrence, GI tolerance of po form, etc.
  - Link to Review Article in AFP Feb 2011: http://www.aafp.org/afp/2011/0201/p271.html
  - Published case reports of 7 successfully treated patients with beta blocker eye drops. (Oral beta blockers not effective for acute migraine.) Mo Med 2014 Jul-Aug;111(4):283-8.
- PROPHYLAXIS: 1st line: beta-blockers (propranolol, metoprolol), TCAs, valproic acid, topiramate.
- MENSTRUAL Related Migraine (MRM): - severity may be increased; duration of headache may be longer and may be harder to treat than regular migraine
  - may consider NSAID or triptan for short-term treatment, several days before and during menstruation [20].

Agents not effective or too many side effects:

- SSRIs, clonidine, methylsergide, oxcarbazepine, melatonin

Discontinued:

ERGOTS	**Methysergide SANSERT** PL (2mg tab ☎ ▼) -**D/C** by Co	**3rd line** - for prevention of severe recurrent migraine unresponsive to other agents (seldom used) **CI** •hypertension, cardiac, liver,kidney, lung & collagen dx; þ -porphyria concern. •thrombophlebitis & pregnancy	**Retroperitoneal, cardiac & pulmonary fibrosis** **⇨ do not use for >6 months duration without weaning & a 1-2 month drug holiday!** Nausea, muscle cramps, ↑weight, ↓hair, claudication, hallucinations	•Do NOT use within 24hr of **triptans** (risk of ↑ vasoconstriction/spasm) ↑ toxicity of ergots with: clarithromycin,erythromycin, propranolol & protease inhibitors	•Serotonin-2 receptor antagonist with carotid vasoconstrictor effect •Active metabolite •	*2-8mg/d* 2mg po BID cc 2mg po TID cc	**79** **113**

References: RxFiles – MIGRAINE AGENTS

[1] Diener Hc et al. Antimigraine drugs. J Neurol 1999;246:515-19.

[2] Evans RW and Lipton RB. Topics in migraine management. Neurol Clinics 2001:19(1):1-21.

[3] Smith MA and Ross MB. Oral 5HT1 receptor agonists for migraine: comparative considerations. Formulary 1999; 34:324-38.

[4] Gawel MJ, et al. A systematic review of the use of triptans in acute migraine. Can J neurol Sci 2001;28:30-41.

[5] Lewis D, Ashwal S, Hershey A, Hirtz D, Yonker M, Silberstein S. Practice Parameter: Pharmacological treatment of migraine headache in **children and adolescents**: Report of the American Academy of Neurology Quality Standards Subcommittee and the Practice Committee of the Child Neurology Society. **Neurology. 2004** Dec 28;63(12):2215-24.

[6] Diener HC et al. A practical guide to the management and prevention of migraine. Drugs 1998;56:811-24.

[7] Pryse-Phillips WE et al. Guidelines for the diagnosis and management of migraine in clinical practice. CAN Med Assoc J 1997;156(9): 1273-87.

[8] Ferrari MD et al. Oral triptans in acute migraine treatment: a meta analysis of 53 trials. The Lancet 2001;358: 1668-75.

[9] Limmroth V and Michel M. The prevention of migraine: a critical review with special emphasis on B-adrenoceptor blockers. Br J Cin Pharmacol 2001;52:237-43.

[10] Brandes J, Saper J, Diamond M, et al. Topiramate for Migraine Prevention: A Randomized Controlled Trial. JAMA 2004;291 965-973.

[11] Silberstein SD, Neto W, Schmitt J, Jacobs D; MIGR-001 Study Group. Topiramate in migraine prevention: results of a large controlled trial. Arch Neurol. 2004 Apr;61(4):490-5.

[12] Storey JR et al …Headache 2001;41:968-1000.

[13] Topiramate (Topamax) for prevention of migraine. Med Lett Drugs Ther. 2005 Jan 31;47(1201):9-10.
Silberstein S, Lipton R, Dodick D, et al. Topiramate treatment of chronic migraine: a randomized, placebo-controlled trial of quality of life and other efficacy measures. Headache. 2009 Sep;49(8):1153-62.
Linde M, Mulleners WM, Chronicle EP, et al. **Topiramate for the prophylaxis of episodic migraine** in adults. Cochrane Database Syst Rev. 2013 Jun 24;6:CD010610. Meta-analysis demonstrates that topiramate in a 100 mg/day dosage is effective in reducing headache frequency and reasonably well-tolerated in adult patients with episodic migraine. This provides good evidence to support its use in routine clinical management. More studies designed specifically to compare the efficacy or safety of topiramate versus other interventions with proven efficacy in the prophylaxis of migraine are needed.

[14] Diener HC, Tfelt-Hansen P, Dahlof C, Lainez MJ, Sandrini G, Wang SJ, Neto W, Vijapurkar U, Doyle A, Jacobs D; MIGR-003 Study Group. Topiramate in migraine prophylaxis—results from a placebo-controlled trial with propranolol as an active control. J Neurol. 2004 Aug;251(8):943-50.

[15] Diener HC, Rahlfs VW, Danesch U. The first placebo-controlled trial of a special butterbur root extract for the prevention of migraine: reanalysis of efficacy criteria. Eur Neurol. 2004;51(2):89-97. Epub 2004 Jan 28.
Holland S, Silberstein SD, Freitag F, et al. Evidence-based guideline update: **NSAIDs and other complementary treatments** for episodic migraine prevention in adults: Report of the Quality Standards Subcommittee of the American Academy of Neurology (AAN) and American Headache Society (AHS). Neurology. 2012 Apr 24;78(17):1346-53.

[16] Blumenfeld A. Botulinum toxin type A as an effective prophylactic treatment in primary headache disorders. Headache. 2003 Sep;43(8):853-60.
Chilson CN, Brown SJ. Role of botulinum toxin type a in the prophylactic treatment of migraine headaches. Ann Pharmacother. 2005 Dec;39(12):2081-5. Epub 2005 Nov 1.
Blumenfeld AM, Schim JD, Chippendale TJ. Botulinum toxin type a and divalproex sodium for prophylactic treatment of episodic or chronic migraine. Headache. 2008 Feb;48(2):210-

20. Epub 2007 Nov 28. Both BoNTA and DVPX significantly reduced disability associated with migraine; BoNTA had a favorable tolerability profile compared with DVPX.
Naumann M, So Y, Argoff CE, Childers MK, Dykstra DD, Gronseth GS, Jabbari B, Kaufmann HC, Schurch B, Silberstein SD, Simpson DM; Therapeutics and Technology Assessment Subcommittee of the American Academy of Neurology. Assessment: Botulinum neurotoxin in the treatment of autonomic disorders and pain (an evidence-based review): report of the Therapeutics and Technology Assessment Subcommittee of the American Academy of Neurology. Neurology. 2008 May 6;70(19):1707-14. Botulinum neurotoxin (BoNT) should be offered as a treatment option for the treatment of axillary hyperhidrosis and detrusor overactivity (Level A), should be considered for palmar hyperhidrosis, drooling, and detrusor sphincter dyssynergia after spinal cord injury (Level B), and may be considered for gustatory sweating and low back pain (Level C). BoNT is probably ineffective in episodic migraine and chronic tension-type headache (Level B). There is presently no consistent or strong evidence to permit drawing conclusions on the efficacy of BoNT in chronic daily headache (mainly transformed migraine) (Level U). While clinicians' practice may suggest stronger recommendations in some of these indications, evidence-based conclusions are limited by the availability of data.
Lipton RB, Varon SF, Grosberg B,et al. OnabotulinumtoxinA improves quality of life and reduces impact of chronic migraine. Neurology. 2011 Oct 11;77(15):1465-72.
Jackson JL, Kuriyama A, Hayashino Y. Botulinum toxin A for prophylactic treatment of migraine and tension headaches in adults: a meta-analysis. JAMA. 2012 Apr 25;307(16):1736-45.

[18] Linde K, Streng A, Jurgens S, et al. Acupuncture for patients with migraine: a randomized controlled trial. JAMA. 2005 May 4;293(17):2118-25. . (InfoPOEMs: Acupuncture and sham acupuncture are equally more effective than no treatment in patients with migraine headaches. These results defend the adage that doing something is better than doing nothing. (LOE = 1b)). & Coeytaux RR, Kaufman JS, Kaptchuk TJ, et al. A randomized, controlled trial of **acupuncture** for chronic daily headache. Headache. 2005 Oct;45(9):1113-23.
Linde K, Allais G, Brinkhaus B, Manheimer E, Vickers A, White AR. **Acupuncture** for migraine prophylaxis. Cochrane Database Syst Rev. 2009 Jan 21;(1):CD001218. In the previous version of this review, evidence in support of acupuncture for migraine prophylaxis was considered promising but insufficient. Now, with 12 additional trials, there is consistent evidence that acupuncture provides additional benefit to treatment of acute migraine attacks only or to routine care. There is no evidence for an effect of 'true' acupuncture over sham interventions, though this is difficult to interpret, as exact point location could be of limited importance. Available studies suggest that acupuncture is at least as effective as, or possibly more effective than, prophylactic drug treatment, and has fewer adverse effects. Acupuncture should be considered a treatment option for patients willing to undergo this treatment.
Jena S, Witt CM, Brinkhaus B, Wegscheider K, Willich SN. Acupuncture in patients with headache. Cephalalgia. 2008 Sep;28(9):969-79. Epub 2008 Jul 8. Acupuncture plus routine care in patients with headache was associated with marked clinical improvements compared with routine care alone.
Li Y, Zheng H, Witt CM, et al. **Acupuncture** for migraine prophylaxis: a randomized controlled trial. CMAJ. 2012 Jan 9.
Zhao L, Chen J, Li Y, et al. The long-term effect of **acupuncture** for migraine prophylaxis: a randomized clinical trial [online Feb 20, 2017].
JAMA Intern Med. doi:10.1001 /jamainternmed.2016.9378

[19] Chronicle E, Mulleners W. Anticonvulsant drugs for migraine prophylaxis. Cochrane Database Syst Rev. 2004;(3):CD003226.

[20] Mathew NT, Rapoport A, Saper J, et al. Efficacy of **gabapentin** in migraine prophylaxis. Headache. 2001 Feb;41(2):119-28.
Jafarian S, et al. Gabapentin for prevention of **hypobaric hypoxia-induced headache**: randomized double-blind clinical trial. J Neurol Neurosurg Psychiatry. 2008 Mar;79(3):321-3. Epub 2007 Oct 26.
Linde M, Mulleners WM, Chronicle EP, et al. **Gabapentin or pregabalin for the prophylaxis of episodic migraine in adults.** Cochrane Database Syst Rev. 2013 Jun 24;6:CD010609. doi: 10.1002/14651858.CD010609. The pooled evidence derived from trials of gabapentin suggests that it is not efficacious for the prophylaxis of episodic migraine in adults. Since adverse events were common among the gabapentin-treated patients, it is advocated that gabapentin should not be used in routine clinical practice. Gabapentin enacarbil is not efficacious for the prophylaxis of episodic migraine in adults. There is no published evidence from controlled trials of pregabalin for the prophylaxis of episodic migraine in adults.

[21] Pringsheim T, Davenport WJ, Dodick D. Acute treatment and prevention of menstrually related migraine headache: evidence-based review. Neurology. 2008 Apr 22;70(17):1555-63

Other sources:

1. Goadsby PJ, Lipton RB, Ferrari MD. Migraine – current understanding and treatment. N Engl J Med 2002: 346(4):257-270.
2. Adelman JA and Adelman RD. Current options for the prevention and treatment of migraine. Clinical Therapeutics 2001;23(6):772-788.
3. Silberstein SD, Goadsby PJ, Lipton RB. Management of migraine – an algorithmic approach. Neurololgy 2000; 55(Suppl 2): S46-52.
4. Morey SS. Practice guidelines…on migraine (a 5 part series…) Amer Family Physician 2000;61;1915ff 62: 2145-51, 2359-60, 2535-39.
5. Becker WJ. Evidence based migraine prophylactic drug therapy. Can J Neurol Sci 1999; 26(Suppl 3): S27-32.
6. Drug Information Handbook 8th edition.
7. Drugs in Pregnancy & Lactation 9th edition (Briggs G, Freeman R, Yaffe S). Lippincott Williams & Wilkins 2011, Philidelphia PA.
8. Handbook of Clinical Drug Data 9th edition (Anderson P, Knoben J, Troutman W). Appleton & Lange 1999, Stamford CT.
9. Pharmacotherapy Handbook 2nd edition (Wells B, Dipiro J, Schwinghammer T, Hamilton C). Appleton & Lange 2000, Stamford CT.
10. Therapeutic Choices 4rd edition (Gray J). Canadian Pharmacists Association 2003.
11. Snow V, Weiss K, Wall EM, Mottur-Pilson C; American Academy of Family Physicians; American College of Physicians-American Society of Internal Medicine. Pharmacologic management of acute attacks of migraine and prevention of migraine headache. Ann Intern Med. 2002 Nov 19;137(10):840-9.
12. Lipton RB, Baggish JS, Stewart WF, Codispoti JR, Fu M. Efficacy and safety of acetaminophen in the treatment of migraine: results of a randomized, double-blind, placebo-controlled, population-based study. Arch Intern Med. 2000 Dec 11-25;160(22):3486-92.
13. Lewis DW. Headaches in children and adolescents. Am Fam Physician. 2002 Feb 15;65(4):625-32.
14. Micromedex 2014
15. Treatment Guidelines **Medical Letter: Drugs for Migraine**. March 2008; 6(67):17-22. (Updated Feb 2011) (Updated Dec 2013) (**New & Updated Feb 2017**)
16. Schreiber CP, Hutchinson S, Webster CJ, Ames M, Richardson MS, Powers C. Prevalence of migraine in patients with a history of self-reported or physician-diagnosed "**sinus**" headache. Arch Intern Med. 2004 Sep 13;164(16):1769-72.
17. Colman I, Brown MD, Innes GD, et al. Parenteral **metoclopramide** for acute migraine: meta-analysis of randomised controlled trials. BMJ. 2004 Dec 11;329(7479):1369-73.
18. Lewis D, Ashwal S, Hershey A, Hirtz D, Yonker M, Silberstein S. Practice Parameter: Pharmacological treatment of migraine headache **in children and adolescents**: Report of the

American Academy of Neurology Quality Standards Subcommittee and the Practice Committee of the Child Neurology Society. **Neurology. 2004** Dec 28;63(12):2215-24.
19. Ferrari MD, Goadsby PJ, Roon KI, Lipton RB. Triptans (serotonin, 5-HT1B/1D agonists) in migraine: detailed results and methods of a meta-analysis of 53 trials. Cephalalgia. 2002 Oct;22(8):633-58. Erratum in: Cephalalgia. 2003 Feb;23(1):71. (**low doses effective**)
20. Hall GC, Brown MM, Mo J, MacRae KD. Triptans in migraine: the risks of stroke, cardiovascular disease, and death in practice. Neurology. 2004 Feb 24;62(4):563-8.
21. Mauskop A, Graff-Radford S. Special treatment situations: **alternative** headache **treatments**. In: Standards of care for headache diagnosis and treatment. Chicago (IL): National Headache Foundation; 2004. p. 115-22.
22. Colman I, Brown MD, Innes GD, et al. Parenteral **dihydroergotamine** for acute migraine headache: a systematic review of the literature. Ann Emerg Med 2005;45:393-401. (InfoPOEMs: Dihydroergotamine is not as effective as sumatriptan (Imitrex) when used by itself for the acute treatment of migraine. When used in combination with an anti-emetic it is at least as effective as analgesics. It should be used as a second-line treatment in patients who don't initially respond to the treatments that are more likely to work. (LOE = 1a-))
23. Schuurmans A, van Weel C. Pharmacologic treatment of migraine. **Comparison of guidelines**. Can Fam Physician. **2005** Jun;51:838-43.
24. Moja P, Cusi C, Sterzi R, Canepari C. Selective serotonin re-uptake inhibitors (**SSRIs**) for preventing migraine and tension-type headaches. Cochrane Database Syst Rev. 2005 Jul 20;(3):CD002919. CONCLUSIONS: Over 2 months of treatment, SSRIs are no more efficacious than placebo in patients with migraine. In patients with chronic TTH, SSRIs are less efficacious than tricyclic antidepressants. In comparison with SSRIs, the burden of adverse events in patients receiving tricyclics was greater. These results are based on short-term trials and may not generalise to longer-term treatment.
25. Maizels M. The patient with daily headaches. Am Fam Physician. 2004 Dec 15;70(12):2299-306.
26. Diener HC, Gendolla A, et al. Almotriptan in migraine patients who respond poorly to oral sumatriptan: a double-blind, randomized trial. Headache. 2005 Jul-Aug;45(7):874-82.
27. Damen L, Bruijn JK, Verhagen AP, et al. Symptomatic treatment of migraine in **children**: a systematic review of medication trials. Pediatrics. 2005 Aug;116(2):e295-302.
28. Combination Use of **Triptans and NSAIDs** for Migraine. Pharmacist's Letter. Dec 05.
29. Smith TR, Sunshine A, Stark SR, et al. **Sumatriptan and naproxen** sodium for the acute treatment of migraine. Headache. 2005 Sep;45(8):983-91.
30. Winner P, Pearlman EM, Linder SL, et al.; **Topiramate Pediatric** Migraine Study Investigators. Topiramate for migraine prevention in children: a randomized, double-blind, placebo-controlled trial. Headache. 2005 Nov-Dec;45(10):1304-12.
31. Bartolini M, Silvestrini M, Taffi R, et al. Efficacy of **topiramate and valproate** in chronic migraine. Clin Neuropharmacol. 2005 Nov-Dec;28(6):277-9.
32. Silberstein SD, Freitag FG, Rozen TD, et al. CAPSS-223 Investigators. Tramadol/acetaminophen for the treatment of acute migraine pain: findings of a randomized, placebo-controlled trial. Headache. 2005 Nov-Dec;45(10):1317-27.
33. Goadsby PJ. Recent advances in the diagnosis and management of migraine. BMJ. 2006 Jan 7;332(7532):25-9.
34. Tepper SJ, Cady R, Dodick D, et al. Oral sumatriptan for the acute treatment of **probable migraine**: first randomized, controlled study. Headache. 2006 Jan;46(1):115-24.
35. Rothner AD, Wasiewski W, Winner P, Lewis D, et al. Zolmitriptan oral tablet in migraine treatment: high **placebo** responses in **adolescents**. Headache. 2006 Jan;46(1):101-9.
36. Winner P, Rothner AD, et al. Sumatriptan nasal spray in **adolescent** migraineurs: a randomized, double-blind, placebo-controlled, acute study. Headache. 2006 Feb;46(2):212-22.
37. Wheeler SD. **Donepezil** treatment of topiramate-related cognitive dysfunction. Headache. 2006 Feb;46(2):332-5.
38. Modi S, Lowder DM. Medications for migraine **prophylaxis**. Am Fam Physician. 2006 Jan 1;73(1):72-8.
39. Dodick DW. Clinical practice. **Chronic daily headache**. N Engl J Med. 2006 Jan 12;354(2):158-65. Erratum in: N Engl J Med. 2006 Feb 23;354(8):884.
40. Wenzel RG, Schwarz K, Padiyara RS. **Topiramate** for migraine prevention. Pharmacotherapy. 2006 Mar;26(3):375-87.
41. Rigatelli G, Braggion G, Aggio S, Chinaglia M, Cardaioli P. Primary **patent foramen ovale** closure to relieve severe migraine. Ann Intern Med. 2006 Mar 21;144(6):458-60.
42. Diener HC, et al. Efficacy and tolerability of diclofenac potassium sachets in migraine: a randomized, double-blind, cross-over study in comparison with diclofenac potassium tablets and placebo. Cephalagia. 2006 May;26(5):537-47.
43. Brandes JL. The influence of **estrogen** on migraine: a systematic review. JAMA. 2006 Apr 19;295(15):1824-30. Epidemiological, pathophysiological, and clinical evidence link estrogen to migraine headaches. Triptans appear to provide acute relief and also may be useful for headache prevention.
44. Shaygannejad V, et al. Comparison of the effect of **topiramate & sodium valporate** in migraine prevention: a randomized blinded crossover study. Headache. 2006 Apr;46(4):642-8.
45. Goldstein J, et al. **Acetaminophen, aspirin, and caffeine** (Excedrin) in combination versus ibuprofen for acute migraine: results from a multicenter, double-blind, randomized, parallel-group, single-dose, placebo-controlled study. Headache. 2006 Mar;46(3):444-53.
46. Charles JA, et al. Prevention of migraine with **olmesartan** in patients with hypertension/prehypertension. Headache. 2006 Mar;46(3):503-7. Tronvik E, et al. Prophylactic treatment of migraine with an angiotensin II receptor blocker (**candesartan**): a randomized controlled trial. JAMA. 2003 Jan 1;289(1):65-9.
47. Zeeberg P, Olesen J, Jensen R. Probable **medication-overuse headache**: the effect of a 2-month drug-free period. Neurology. 2006 Jun 27;66(12):1894-8. Epub 2006 May 17.
48. Rizatriptan vs risatriptan plus trimebutine for the acute treatment of migraine: a double blind, randomized, cross-over, placebo-controlled study. Cephalgia 2006;26:871-4.
49. Kurth T, et al. Migraine and risk of **cardiovascular** disease in women. JAMA. 2006 Jul 19;296(3):283-91. Erratum in: JAMA. 2006 Jul 19;296(3):1 p following 291. In this large, prospective cohort of women, active migraine with aura was associated with increased risk of major CVD, myocardial infarction, ischemic stroke, and death due to ischemic CVD, as well as with coronary revascularization and angina. (InfoPOEMs: Women suffering from active migraines with aura are at an increased risk of ischemic vascular events, including coronary heart disease and stroke. In general, this correlates to 18 additional cardiovascular events for every 10,000 women per year. Women with active migraine without aura are not at an increased risk of ischemic vascular disease. (LOE = 2b-))
50. van Ettekoven H, Lucas C. Efficacy of **physiotherapy** including a craniocervical training programme for tension-type headache; an RCT. Cephalalgia. 2006 Aug;26(8):983-91.
51. Rapoport A, et al. Long-term migraine prevention with **topiramate**: open-label extension of pivotal trials. Headache. 2006 Jul-Aug;46(7):1151-60.

52. Ahonen K, et al. A randomized trial of rizatriptan in migraine attacks in children. Neurology. 2006 Aug 30; [Epub ahead of print]
53. Ahonen K, et al. **Nasal sumatriptan** is effective in treatment of migraine attacks in **children**: A randomized trial. Neurology. 2004 Mar 23;62(6):883-7.
54. Cittadini E, et al. Effectiveness of **Intranasal Zolmitriptan** in Acute **Cluster** Headache: Randomized, Placebo-Controlled, Double-blind Crossover Study. Arch Neurol. 2006 Sep 11.
55. Detsky ME, et al. Does this patient with headache have a **migraine** or **need neuroimaging**? JAMA. 2006 Sep 13;296(10):1274-83. The best predictors can be summarized by the mnemonic POUNDing (Pulsating, duration of 4-72 hOurs, Unilateral, Nausea, Disabling). The presence of 4 simple historical features can accurately diagnose migraine. Several individual clinical features were found to be associated with a significant intracranial abnormality, and patients with these features should undergo neuroimaging. (InfoPOEMs: Useful clinical criteria from the history and physical for distinguishing migraine from tension-type headache include: nausea, photophobia, phonophobia, and exacerbation by physical activity. Combined findings useful for distinguishing migraine can be summarized by the mnemonic: POUNDing (Pulsatile quality; duration of 4 to 72 hOurs; Unilateral location; Nausea or vomiting; Disabling intensity). Patients with 4 or more of these criteria are most likely to have migraine headaches. Criteria increasing the risk of intracranial pathology include: cluster-type headache; abnormal neurologic examination result; undefined headache; headache with aura; headache aggravated by exertion or valsalva-like maneuver; and headache with vomiting. No clinical features from the history and physical are useful for significantly reducing the likelihood of intracranial pathology. (LOE = 3a))
56. Honkaniemi J, et al. **Haloperidol** in the acute treatment of migraine: a randomized, double-blind, placebo-controlled study. Headache. 2006 May;46(5):781-7.
57. Evers S, et al. Treatment of childhood migraine attacks with **oral zolmitriptan** and **ibuprofen**. Neurology. 2006 Aug 8;67(3):497-9. Epub 2006 Jun 14.
58. Kanai A, Saito M, Hoka S. Subcutaneous **sumatriptan** for refractory **trigeminal neuralgia**. Headache. 2006 Apr;46(4):577-82; discussion 583-4.
59. Tozer BS, Boatwright EA, David PS, et al. Prevention of migraine in **women** throughout the life span. Mayo Clin Proc. 2006 Aug;81(8):1086-91; quiz 1092.
60. Mellick LB, McIlrath ST, Mellick GA. Treatment of headaches in the ED with lower cervical **intramuscular bupivacaine** injections: a 1-year retrospective review of 417 patients. Headache. 2006 Oct;46(9):1441-9.
61. Brighina F, Palermo A, Aloisio A, Francolini M, Giglia G, Fierro B. **Levetiracetam** in the Prophylaxis of Migraine With Aura: A 6-Month Open-label n=16 Study. Clin Neuropharmacol. 2006 November/December;29(6):338-342.
62. Becker WJ, Christie SN, Ledoux S, Binder C. **Topiramate prophylaxis** and response to triptan treatment for acute migraine. Headache. 2006 Oct;46(9):1424-30. Although topiramate prophylaxis did reduce migraine attack frequency, in this pilot study topiramate prophylactic migraine treatment did not increase the proportion of patients pain-free 2 hours after symptomatic triptan therapy.
63. Monastero R, Camarda C, Pipia C, Camarda R. **Prognosis** of migraine headaches in **adolescents**: A 10-year follow-up study. Neurology. 2006 Oct 24;67(8):1353-6.
64. Wammes-van der Heijden EA, et al. Risk of **ischemic complications** related to the intensity of triptan and **ergotamine** use. Neurology. 2006 Oct 10;67(7):1128-34. In general practice, triptan overuse does not increase the risk of ischemic complications. Overuse of ergotamine may increase the risk of these complications, especially in those simultaneously using cardiovascular drugs.
65. Membe S, McGahan L, Cimon K, et al. Tryptans for Acute Migraine. Technology Report 72. CADTH. March 2007. Accessed at: http://www.cadth.ca/media/pdf/I4001_tr_Triptans_e.pdf .
66. Brandes JL, Kudrow D, Stark SR, et al. Sumatriptan-naproxen for the acute treatment of migraine: A randomized trial. JAMA 2007;297:1443-1454. {InfoPOEMs Jun07: A single-tablet combination of sumatriptan (85 mg) plus naproxen sodium (500 mg) was better than either agent alone in the treatment of acute migraine. Outcomes measured included 2-hour headache relief and 24-hour sustained pain-free response. This fixed combination is currently under FDA review and will be marketed under the trade name Trexima. This study used a single pill combination, but separate pills taken concurrently are likely to be equally efficacious (and potentially less expensive as generics). (LOE = 1b-)}
67. EFNS Migraine 2007 Guidelines http://www.efns.org/files/guideline_37.pdf
68. Tfelt-Hansen P, Steiner TJ. **Over-the-Counter** Triptans for Migraine : What are the Implications? CNS Drugs. 2007;21(11):877-83. In 2006, the triptans sumatriptan 50mg and naratriptan 2.5mg were approved as over-the-counter (OTC) drugs in pharmacies in the UK and Germany, respectively. Both drugs have been used in a large number of patients with migraine and are considered to have good safety profiles.
69. Pascual J, Mateos V, Roig C, et al. Marketed oral **triptans** in the acute treatment of migraine: a **systematic review** on efficacy and tolerability. Headache. 2007 Sep;47(8):1152-68.
70. Diener HC, et al. **Cessation versus continuation** of 6-month migraine preventive therapy with topiramate (PROMPT): a randomised, double-blind, placebo-controlled trial. Lancet Neurol. 2007 Dec;6(12):1054-62. Epub 2007 Nov 7. Sustained benefit was reported after discontinuation of topiramate, although number of migraine days did increase. These findings suggest that patients should be treated for 6 months, with the option to continue to 12 months in some patients.
71. Loder E, Rizzoli P. **Tension-type headache**. BMJ. 2008 Jan 12;336(7635):88-92.
72. Dodick D, Freitag F. Evidence-based understanding of **medication-overuse headache**: clinical implications. Headache. 2006 Nov;46 Suppl 4:S202-11.
73. Silberstein S, Saper J, Berenson F, et al. **Oxcarbazepine** in migraine headache: a double-blind, randomized, placebo-controlled study. Neurology. 2008 Feb 12;70(7):548-55. Overall, oxcarbazepine was safe and well tolerated; however, oxcarbazepine did not show efficacy in the prophylactic treatment of migraine headaches.
74. Colman I, Friedman BW, Brown MD, et al. Parenteral **dexamethasone** for acute severe migraine headache: meta-analysis of randomised controlled trials for preventing recurrence. BMJ. 2008 Jun 9. [Epub ahead of print] When added to standard abortive therapy for migraine headache, single dose parenteral dexamethasone is associated with a 26% relative reduction in headache recurrence (number needed to treat=9) within 72 hours.
Donaldson D, et al. IV dexamethasone vs placebo as adjunctive therapy to reduce the recurrence rate of acute migraine headaches: a multicenter, double-blinded, placebo-controlled randomized clinical trial. Am J Emerg Med. 2008 Feb;26(2):124-30.
Kelly AM, Kerr D, Clooney M. Impact of oral dexamethasone versus placebo after ED treatment of migraine with phenothiazines on the rate of recurrent headache: a randomised controlled trial. Emerg Med J. 2008 Jan;25(1):26-9.
Rowe BH, Colman I, Edmonds ML, Blitz S, Walker A, Wiens S. Randomized controlled trial of intravenous dexamethasone to prevent relapse in acute migraine headache. Headache. 2008 Mar;48(3):333-40. Epub 2007 Nov 28.
Friedman BW, Greenwald P, Bania TC, et al. Randomized trial of IV dexamethasone for acute migraine in the emergency department. Neurology. 2007 Nov 27;69(22):2038-44. Epub 2007 Oct 17.
75. Kurth T, Schürks M, Logroscino G, Gaziano JM, Buring JE. Migraine, **vascular risk**, and cardiovascular events in women: prospective cohort study. BMJ. 2008 Aug 7;337:a636. doi: 10.1136/bmj.a636. The association between migraine with aura and cardiovascular disease varies by vascular risk status. Information on history of migraine and vascular risk status might help to identify women at increased risk for specific future cardiovascular disease events.

76. Friedman BW, Esses D, Solorzano C, et al. A randomized controlled trial of prochlorperazine versus metoclopramide for treatment of acute migraine. Ann Emerg Med. 2008 Oct;52(4):399-406. Epub 2007 Nov 19.
77. Friedman BW, Bender B, Davitt M, et al. A Randomized Trial of Diphenhydramine as Prophylaxis Against Metoclopramide-Induced Akathisia in Nauseated Emergency Department Patients. Ann Emerg Med. 2008 Sep 22. [Epub ahead of print]
78. Bigal M, Sheftell F, Tepper S, Tepper D, Ho TW, Rapoport A. A randomized double-blind study comparing **rizatriptan, dexamethasone**, and the combination of both in the acute treatment of **menstrually related migraine**. Headache. 2008 Oct;48(9):1286-93. Rizatriptan is an effective treatment for MRM. RI+DE is significantly more effective than RI alone, although is associated with higher rate of adverse events.The combination should be considered for subjects with high disability, incomplete relief, or recurrence of pain with triptan monotherapy.The use of DE alone in the treatment of MRM is not justified based on our data.
79. Linde K, Allais G, Brinkhaus B, Manheimer E, Vickers A, White AR. **Acupuncture** for migraine prophylaxis. Cochrane Database Syst Rev. 2009 Jan 21;(1):CD001218. In the previous version of this review, evidence in support of acupuncture for migraine prophylaxis was considered promising but insufficient. Now, with 12 additional trials, there is consistent evidence that acupuncture provides additional benefit to treatment of acute migraine attacks only or to routine care. There is no evidence for an effect of 'true' acupuncture over sham interventions, though this is difficult to interpret, as exact point location could be of limited importance. Available studies suggest that acupuncture is at least as effective as, or possibly more effective than, prophylactic drug treatment, and has fewer adverse effects. Acupuncture should be considered a treatment option for patients willing to undergo this treatment.
80. Linder SL, Mathew NT, Cady RK, Finlayson G, Ishkanian G, et al. Efficacy and tolerability of **almotriptan in adolescents**: a randomized, double-blind, placebo-controlled trial. Headache. 2008 Oct;48(9):1326-36. Epub 2008 May 14. Oral almotriptan was efficacious for relieving migraine headache pain in adolescents, with the 12.5-mg dose associated with the most favorable efficacy profile with respect to relieving headache pain and associated symptoms of migraine (photophobia and phonophobia). Almotriptan treatment was well tolerated in this adolescent population.
81. Lewis D, Winner P, Saper J, et al. Randomized, double-blind, placebo-controlled study to evaluate the efficacy and safety of **topiramate** for migraine prevention in **pediatric** subjects 12 to 17 years of age. Pediatrics. 2009 Mar;123(3):924-34.
82. Friedman BW, Kapoor A, Friedman MS, et al. The relative efficacy of meperidine for the treatment of acute migraine: a meta-analysis of randomized controlled trials. Ann Emerg Med. 2008 Dec;52(6):705-13. Epub 2008 Jul 16. Meperidine (pethidine, Demerol) is much less effective than dihydroergotamine in relieving migraine within 1 hour of treatment. Antiemetics are also more effective than meperidine. Ketorolac (Toradol) is equally effective as meperidine and has a similar gastrointestinal side effect profile. (LOE = 1a-)
83. Scher Ann I.; Gudmundsson Larus S.; Sigurdsson Sigurdur; et al. Migraine Headache in Middle Age and **Late-Life Brain Infarcts**. JAMA. 2009;301(24):2563-2570.
84. Guerrera M. et al. Therapeutic Uses of **Magnesium**. Am Fam Physician. 2009; 80(1):157-162.
85. Grande RB et al. Severity of Dependence Scale detects people with medication overuse: The **Akershus** study of chronic headache. J Neurol Neurosurg Psychiatry 2009 Jul; 80:784.
86. CADTH HTIS: Botulinum Toxin A for Headaches in Adults: A review of clinicial effectiveness and safety. http://www.cadth.ca/index.php/en/hta/programs/htis
Simpson DM, Hallett M, Ashman EJ, et al. Practice guideline update summary: Botulinum neurotoxin for the treatment of blepharospasm, cervical dystonia, adult spasticity, and **headache**: Report of the Guideline Development Subcommittee of the American Academy of Neurology (**AAN**). Neurology. 2016 May 10;86(19):1818-26.
87. Evers S, Afra J, Frese A, Goadsby PJ, Linde M, et al. **EFNS guideline** on the drug treatment of migraine--revised report of an EFNS task force. Eur J Neurol. 2009 Sep;16(9):968-81.
88. Hedlund C, Rapoport AM, Dodick DW, et al. **Zolmitriptan** nasal spray in the acute treatment of **cluster** headache: a meta-analysis of two studies. Headache. 2009Oct;49(9):1315-23.
89. Cunnington M, Ephross S, Churchill P. The Safety of Sumatriptan and Naratriptan in **Pregnancy**: What Have We Learned? Headache. 2009 Oct 5. [Epub ahead of print]
90. Schürks Markus, Rist Pamela M, et al. Migraine and **cardiovascular** disease: systematic review and meta-analysis. BMJ 2009;339:b3914, doi: 10.1136/bmj.b3914 (Published 27Oct09)
91. Etminan M, Takkouche B, et al. Risk of ischaemic **stroke** in people with migraine: systematic review and meta-analysis of observational studies. BMJ. 2005 Jan 8;330(7482):63.
92. Loder EW, Buse DC, Golub JR. Headache and combination estrogen-progestin oral contraceptives: integrating evidence, guidelines, and clinical practice. Headache. 2005 Mar;45(3):224-31.
93. FDA Dec/09 notified health care professionals and patients about the increased risk of neural tube defects and other major birth defects, such as craniofacial defects and cardiovascular **malformations**, in babies exposed to **valproate** sodium and related products (valproic acid and divalproex sodium) during pregnancy.
94. Cohen Anna S.; Burns Brian; Goadsby Peter J. **High-Flow Oxygen** for Treatment of **Cluster** Headache: A Randomized Trial. *JAMA*. 2009;302(22):2451-2457.
95. Silberstein S, Lipton R, Dodick D, et al. **Topiramate** treatment of chronic migraine: a randomized, placebo-controlled trial of quality of life and other efficacy measures. Headache. 2009 Sep;49(8):1153-62.
96. Vikelis M, Rapoport AM. Role of **antiepileptic drugs** as preventive agents for migraine. CNS Drugs. 2010 Jan 1;24(1):21-33. doi: 10.2165/11310970-000000000-00000.
97. Kostic MA, Gutierrez FJ, Rieg TS, et al. A Prospective,Randomized Trial of Intravenous **Prochlorperazine** Versus Subcutaneous Sumatriptan in Acute Migraine Therapy in the Emergency Department. Ann Emerg Med. 2009 Dec31.
98. Kelly AM, Walcynski T, Gunn B. The relative efficacy of **phenothiazines** for the treatment of acute migraine: a meta-analysis. Headache. 2009 Oct;49(9):1324-32. Epub 2009 Jun 2.
99. Gales Barry J, Bailey Emilee K, Reed Ashley N, et al. **Angiotensin**-Converting Enzyme Inhibitors and Angiotensin Receptor Blockers for the Prevention of Migraines. Ann Pharmacother. 2010 Feb;44(2):360-6. Epub 2010 Jan 19.
100. Calhoun AH, Ford S, Millen C, Finkel AG, Truong Y, Nie Y. The Prevalence of **Neck Pain** in Migraine. Headache. 2010 Jan 20.
101. Pringsheim T, Davenport WJ, Becker WJ. **Prophylaxis** of migraine headache. CMAJ. 2010 Feb 16.
102. Lipton RB, Dodick DW, Silberstein SD, et al. Single-pulse **transcranial magnetic stimulation** for acute treatment of migraine with aura: a randomised, double-blind, parallel-group, sham-controlled trial. Lancet Neurol. 2010 Apr;9(4):373-380. Epub 2010 Mar 4.
103. Goadsby PJ, Sprenger T. Current practice and future directions in the prevention and acute management of **migraine**. Lancet Neurol. 2010 Mar; 9 (3):285-298.
104. Evers S, Marziniak M. Clinical features, pathophysiology, and treatment of **medication-overuse** headache. Lancet Neurol. 2010 Apr;9(4):391-401.

105. Dodick DW, Freitag F, Banks J, et al. CAPSS-277 Investigator Group. **Topiramate versus amitriptyline** in migraine prevention: a 26-week, multicenter, randomized, double-blind, double-dummy, parallel-group noninferiority trial in adult migraineurs. Clin Ther. 2009 Mar;31(3):542-59.
106. Law S, Derry S, Moore RA. **Triptans for acute cluster** headache. Cochrane Database Syst Rev. 2010 Apr 14;4:CD008042. Zolmitriptan and sumatriptan are effective in the acute treatment of cluster headaches & may provide a useful treatment option, potentially offering convenience over oxygen therapy and a better safety and tolerability profile than ergotamine. Non-oral routes of administration are likely to provide better and more rapid responses.
107. Kirthi V, Derry S, Moore RA, McQuay HJ. **Aspirin with or without an antiemetic** for acute migraine headaches in adults. Cochrane Database Syst Rev. 2010 Apr 14;4:CD008041. Aspirin 1000 mg is an effective treatment for acute migraine headaches, similar to sumatriptan 50 mg or 100 mg. Addition of metoclopramide 10 mg improves relief of nausea and vomiting. Adverse events were mainly mild and transient, and were slightly more common with aspirin than placebo, but less common than with sumatriptan 100 mg.
108. Pringsheim T, Davenport WJ, Becker WJ. **Prophylaxis of migraine** headache. CMAJ. 2010 Apr 20;182(7):E269-76. Epub 2010 Feb 16.
109. Verhagen AP, Damen L, Berger MY, et al. **Lack of benefit for prophylactic drugs of tension-type headache in adults: a systematic review.** Fam Pract. 2010 Apr;27(2):151-65.
110. Edvinsson L, Linde M. New drugs in migraine treatment and prophylaxis: **telcagepant and topiramate**. Lancet. 2010 Apr 21. [Epub ahead of print]
111. Prior MJ, Codispoti JR, Fu M. A randomized, placebo-controlled trial of acetaminophen for treatment of migraine headache. Headache. 2010May;50(5):819-33.
Derry S, Moore RA, McQuay HJ. Paracetamol (**acetaminophen**) with or without an antiemetic for acute migraine headaches in adults. Cochrane Database Syst Rev. 2010 Nov 10;11:CD008040. Paracetamol 1000 mg alone is an effective treatment for acute migraine headaches, and the addition of 10 mg metoclopramide gives short-term efficacy equivalent to oral sumatriptan 100 mg. Adverse events with paracetamol did not differ from placebo; ``major`` adverse events were slightly more common with sumatriptan than with paracetamol plus metoclopramide.
Derry S, Moore RA. Paracetamol (**acetaminophen**) with or without an antiemetic for acute migraine headaches in adults. Cochrane Database Syst Rev. 2013 Apr 30;4:CD008040. Paracetamol 1000 mg alone is statistically superior to placebo in the treatment of acute migraine, but the NNT of 12 for pain-free response at two hours is inferior to at of other commonly used analgesics. Given the low cost and wide availability of paracetamol, it may be a useful first choice drug for acute migraine in those with contraindications to, or who cannot tolerate, non-steroidal anti-inflammatory drugs (NSAIDs) or aspirin. The addition of 10 mg metoclopramide gives short-term efficacy equivalent to oral sumatriptan 100 mg. Adverse events with paracetamol did not differ from placebo; serious and/or severe adverse events were slightly more common with sumatriptan than with paracetamol plus metoclopramide.
112. Friedman BW, Solorzano C, Esses D,et al. Treating Headache Recurrence After Emergency Department Discharge: A Randomized Controlled Trial of **Naproxen Versus Sumatriptan**. Ann Emerg Med. 2010 Mar 18.
113. Duong S, Bozzo P, Nordeng H, Einarson A. Safety of **triptans** for migraine headaches during **pregnancy and breastfeeding**. Can Fam Physician. 2010 Jun;56(6):537-9.
114. Loder, Elizabeth. **Triptan Therapy** in Migraine. N Engl J Med 2010 363: 63-70.
115. Borhani Haghighi A, Motazedian S, Rezaii R, et al. Cutaneous application of **menthol 10% solution** as an abortive treatment of migraine without aura: a randomised, double-blind, placebo-controlled, crossed-over study. Int J Clin Pract. 2010 Mar;64(4):451-6.
116. Trucco M, Meineri P, Ruiz L, Gionco M; Gruppo Neurologico Ospedaliero Interregionale per lo Studio delle Cefalee (Neurological Hospital Interregional Group for the Study of Headaches). **Medication overuse headache**: withdrawal and prophylactic therapeutic regimen. Headache. 2010 Jun;50(6):989-97.
117. Johnston MM, Rapoport AM. Triptans for the management of migraine. Drugs. 2010 Aug 20;70(12):1505-18. doi: 10.2165/11537990-000000000-00000.
118. Gudmundsson LS, Scher AI, Aspelund T, et al. **Migraine with aura** and **risk of cardiovascular** and all cause mortality in men and women: prospective cohort study. BMJ. 2010 Aug 24;341:c3966. doi: 10.1136/bmj.c3966.
119. Kurth T, Kase CS, Schürks M, et al. **Migraine and risk of haemorrhagic stroke** in women: prospective cohort study. BMJ. 2010 Aug 24;341:c3659. doi: 10.1136/bmj.c3659.
120. MacGregor EA. Prevention and treatment of **menstrual migraine**. Drugs. 2010 Oct 1;70(14):1799-818. doi: 10.2165/11538090-000000000-00000. Evidence of efficacy, with acceptable safety and tolerability, exists for sumatriptan 50 and 100mg, mefenamic acid 500mg, rizatriptan 10mg and combination sumatriptan/naproxen 85mg/500mg. There is grade B evidence of efficacy for short-term prophylaxis with transcutaneous estradiol 1.5mg, frovatriptan 2.5mg twice daily and naratriptan 1mg twice daily. Contraceptive strategies offer the opportunity for treating menstrual migraine in women who also require effective contraception.
121. Holroyd Kenneth A, Cottrell Constance K, O'Donnell Francis J, et al. Effect of preventive **(β blocker) treatment, behavioural migraine management, or their combination** on outcomes of optimised acute treatment in frequent migraine: randomised controlled trial. BMJ 341:doi:10.1136/bmj.c4871 (29 Sept 2010).
122. Francis GJ, Becker WJ, Pringsheim TM. Acute and preventive pharmacologic treatment of **cluster headache**. Neurology. 2010 Aug 3;75(5):463-73.
123. Rabbie R, Derry S, Moore RA, McQuay HJ. **Ibuprofen with or without an antiemetic for acute migraine headaches** in adults. Cochrane Database of Systematic Reviews 2010, Issue 10. Art. No.: CD008039. DOI: 10.1002/14651858.CD008039.pub2. Ibuprofen is an effective treatment for acutemigraine headaches, providing pain relief in about half of sufferers, but complete relief from pain and associated symptoms for only aminority.NNTs for all efficacy outcomes were better with 400mg than 200 mg in comparisons with placebo, and soluble formulations provided more rapid relief. Adverse events were mostly mild and transient, occurring at the same rate as with placebo.
124. Jackson JL, Shimeall W, Sessums L, et al. **Tricyclic antidepressants and headaches**: systematic review and meta-analysis. BMJ 341:doi:10.1136/bmj.c5222 (Published 20 Oct 10).
125. Robberstad L, Dyb G, Hagen K, et al.An **unfavorable lifestyle** and recurrent headaches among adolescents: the HUNT study. Neurology. 2010 Aug 24;75(8):712-7.
126. Spector JT, Kahn SR, Jones MR, et al. Migraine headache and **ischemic stroke risk**: an updated meta-analysis. Am J Med 2010;123:612–24.
127. Pringsheim T, Davenport WJ, Becker WJ. **Prophylaxis of migraine headache**. CMAJ. 2010 Apr 20;182(7):E269-76.
128. Raieli V, Compagno A, Brighina F, et al. Prevalence of **red ear syndrome in juvenile** primary headaches. Cephalalgia. 2010 Dec 1.
129. Medical Letter: Treatment Guidelines. **Drugs for Migraine.** Feb 2011. **Dec 2013**.
130. Gilmore B, Michael M. **Treatment of acute migraine headache**. Am Fam Physician. 2011 Feb 1;83(3):271-80.
131. Bigal ME, Serrano D, Buse D, et al. Acute migraine medications and evolution from episodic to chronic migraine: a **longitudinal population based Study** (**AMPP**). Headache 2008;48:1157–1168.
132. Manack A, Buse DC, Serrano D, et al. **Rates, predictors, and consequences of remission** from chronic migraine to episodic migraine. Neurology 2011; 76:711–718.

133. Fenstermacher N, Levin M, Ward T. Pharmacological **prevention of migraine**. BMJ. 2011 Feb 18;342:d583. doi: 10.1136/bmj.d583.
134. Sun-Edelstein C, Mauskop A. Alternative headache treatments: **nutraceuticals, behavioral and physical treatments**. Headache. 2011 Mar;51(3):469-83.
135. Bond DS, Vithiananthan S, Nash JM, et al. Improvement of migraine headaches in severely obese patients after **bariatric surgery**. Neurology. 2011 Mar 29;76(13):1135-8.
136. Russell MB, Ducros A. Sporadic & familial **hemiplegic** migraine: pathophysiological mechanisms, clinical characteristics, diagnosis, and management. Lancet Neurol. 2011 Mar 30.
137. Krymchantowski AV, Jevoux CC. **Topiramate vs Divalproex** Sodium in the Preventive Treatment of Migraine:A Prospective "Real-World" Study. Headache.2011Apr;51(4):554-8.
138. Hakim SM. **Warfarin** for refractory chronic cluster headache: a randomized pilot study. Headache 2011;51:713-25.
139. **ICSI**: Institute for Clinical Systems Improvement. Diagnosis and treatment of **headache**. Bloomington (MN): Institute for Clinical Systems Improvement (ICSI); 2011 Jan.
140. Mancia G, Agabiti-Rosei E, Ambrosioni E, et al. **Hypertension and migraine** comorbidity: Prevalence and risk of **cerebrovascular** events. Evidence from a large, multicenter, cross-sectional survey in Italy (MIRACLES study). J Hypertens 2011; 29:309-318.
141. Schafer AM, Rains JC, Penzien DB, et al. Direct costs of preventive headache treatments: comparison of **behavioral and pharmacologic** approaches. Headache. 2011 Jun;51(6):985-91. doi: 10.1111/j.1526-4610.2011.01905.x.
142. Health Canada July/11 is informing health professionals and consumers that the labelling information for the drug **metoclopramide** is being updated to include stronger warnings on the risk of a movement disorder known as "**tardive dyskinesia**."
143. McCandless RT, Arrington CB, Nielsen DC, Bale et al. **Patent foramen ovale in children** with migraine headaches. J Pediatr. 2011 Aug;159(2):243-247.e1.
144. Cady RK, Goldstein J, Nett R, et al. A Double-Blind Placebo-Controlled Pilot Study of Sublingual **Feverfew and Ginger** (LipiGesic(TM) M) in the Treatment of Migraine. Headache. 2011 Jul;51(7):1078-86.
145. Posadzki P, Ernst E. **Spinal manipulations for cervicogenic headaches**: a systematic review of randomized clinical trials.Headache. 2011 Jul;51(7):1132-9.
146. Basurto Ona X, Martínez García L, Solà I, Bonfill Cosp X. Drug therapy for treating **post-dural puncture headache**. Cochrane Database of Systematic Reviews 2011, Issue 8. Art. No.: CD007887.
147. Pluta Ryszard M., Lynm Cassio, Golub Robert M.. JAMA Patient Page: **Tension-Type Headache**. JAMA. 2011;306(4):450.doi:10.1001/jama.2011.886
148. Khatami R, Tartarotti S, Siccoli MM, et al. Long-term efficacy of **sodium oxybate** in 4 patients with chronic cluster headache. Neurology. 2011 Jul 5;77(1):67-70.
149. Leroux E, Valade D, Taifas I, et al. **Suboccipital steroid injections** for transitional treatment of patients with more than two cluster headache attacks per day: a randomised, double-blind,placebo-controlled trial. Lancet Neurol. 2011 Sep 6.
150. Marine L, Castro P, Enriquez A, et al. **Four-limb acute ischemia** induced by **ergotamine** in an AIDS patient treated with **protease inhibitors**. Circulation. 2011 Sep 20;124(12):1395-7.
151. Merikangas KR, Cui L, Richardson AK, et al. Magnitude, impact, and stability of **primary headache subtypes**: 30 year prospective Swiss cohort study. BMJ. 2011 Aug 25;343:d5076.
152. Varkey E, Cider A, Carlsson J, Linde M. **Exercise** as migraine prophylaxis: A randomized study using relaxation and topiramate as controls. Cephalalgia. 2011 Sep 2.
153. Dakka Y, Warra N, Albadareen RJ, et al. Headache rate and cost of care **following lumbar puncture** at a single tertiary care hospital. Neurology. 2011 Jul 5;77(1):71-4.
154. Lipton RB, Varon SF, Grosberg B,et al. **OnabotulinumtoxinA** improves quality of life and reduces impact of chronic migraine. Neurology. 2011 Oct 11;77(15):1465-72.
155. Nagy AJ, Gandhi S, Bhola R, Goadsby PJ. Intravenous **dihydroergotamine** for inpatient management of refractory primary headaches. Neurology. 2011 Nov 15;77(20):1827-32.
156. Lipton RB, Bigal ME, Diamond M, et al.; AMPP Advisory Group. **Migraine prevalence**, disease burden, and the need for preventive therapy. Neurology. 2007 Jan 30;68(5):343-9.
157. Li Y, Zheng H, Witt CM, et al. **Acupuncture** for migraine prophylaxis: a randomized controlled trial. CMAJ. 2012 Jan 9.
158. Kelley NE, Tepper DE. **Rescue therapy for acute migraine**, part 1: triptans, dihydroergotamine, and magnesium. Headache. 2012 Jan;52(1):114-28.
159. Goundry B, Bell L, Langtree M, Moorthy A. Diagnosis and management of **Raynaud's phenomenon**. BMJ. 2012 Feb 7;344:e289.
160. Pringsheim T, Davenport WJ, Mackie G, et al, for the **Canadian Headache Society Prophylactic Guidelines** Development Group. Canadian Headache Society guideline for migraine prophylaxis. Can J Neurol Sci 2012; 39(2 Suppl 2):S1-61.
161. Smelt AF, Blom JW, Dekker F, et al. A proactive approach to **migraine in primary care**: a pragmatic randomized controlled trial. CMAJ. 2012 Mar 6;184(4):E224-31.
162. Silberstein SD, Dodick DW, Lindblad AS, et al. Randomized, placebo-controlled trial of **propranolol added to topiramate** in chronic migraine. Neurology. 2012 Feb 29.
163. Kelley NE, Tepper DE. Rescue therapy for acute migraine, **part 1: triptans, dihydroergotamine**, **and magnesium**. Headache. 2012 Jan;52(1):114-28.
164. Kelley NE, Tepper DE. Rescue therapy for acute migraine, **part 2: neuroleptics,antihistamines**, **and others**. Headache. 2012 Feb;52(2):292-306.
165. Kelley NE, Tepper DE. Rescue therapy for acute migraine, **part 3: opioids, NSAIDs, steroids, and post-discharge medications**. Headache. 2012 Mar;52(3):467-82.
166. Nesbitt AD, Goadsby PJ. **Cluster headache**. BMJ. 2012 Apr 11;344:e2407.
167. Holland S, Silberstein SD, Freitag F, et al. Evidence-based guideline update: **NSAIDs and other complementary treatments** for episodic migraine prevention in adults: Report of the Quality Standards Subcommittee of the American Academy of Neurology (AAN) and American Headache Society (AHS). Neurology. 2012 Apr 24;78(17):1346-53.
168. Silberstein SD, Holland S, Freitag F, et al. Evidence-based guideline update: **Pharmacologic treatment for episodic migraine prevention in adults**: Report of the Quality Standards Subcommittee of the American Academy of Neurology (AAN) and American Headache Society (AHS). Neurology. 2012 Apr 24;78(17):1337-45.
169. Jackson JL, Kuriyama A, Hayashino Y. **Botulinum toxin A for prophylactic** treatment of migraine and tension headaches in adults: a meta-analysis. JAMA. 2012 Apr 25;307(16):1736-45.

170. Derosier FJ, Lewis D, Hershey AD, et al. Randomized Trial of **Sumatriptan and Naproxen** Sodium Combination in Adolescent Migraine. Pediatrics. 2012 May 14.
171. Tfelt-Hansen P, Olesen J. Taking the **negative view of current migraine treatments**: the unmet needs. CNS Drugs. 2012 May 1;26(5):375-82.
172. Bryans R, Descarreaux M, Duranleau M, et al. Evidence-based guidelines for **chiropractic treatment** of **adults** with headache. J Manipulative Physiol Ther 2011 Jun;34(5):274-89. http://files.chiropracticcanada.ca/Headache%20CPG%20final%20Jan2012_English.pdf
173. Canadian Agency for Drugs and Technologies in Health, 2012. **Triptans** for migraine headaches: a review of clinical evidence on **safety** [online]. Available: http://www.cadth.ca/media/pdf/htis/mar-2012/RC0333%20Triptans%20Final.pdf
174. Ozkurt B, Cinar O, Cevik E, et al. Efficacy of **high-flow oxygen** therapy in all types of headache: prospective, randomized, placebo-controlled trial. Am J Emerg Med. 2012 May 2.
175. Evers S, Jensen R, European Federation of Neurological Societies. Treatment of **medication overuse** headache--guideline of the EFNS headache panel. Eur J Neurol 2011 Sep;18(9):1115-21.
176. Rist PM, Kang JH, Buring JE et al. Migraine and **cognitive decline** among women: prospective cohort study. BMJ. 2012 Aug 8;345:e5027.
177. Kelley SA, Hartman AL, Kossoff EH. **Comorbidity** of migraine in **children** presenting with epilepsy to a tertiary care center. Neurology. 2012 Jul 31;79(5):468-73.
178. Magis D, Schoenen J. Advances and challenges in **neurostimulation** for headaches. Lancet Neurol. 2012 Aug;11(8):708-19.
179. Sanford M. **Frovatriptan**: a review of its use in the acute treatment of migraine. CNS Drugs. 2012 Sep 1;26(9):791-811.
180. Lateef TM, Cui L, Nelson KB, et al. Physical **Comorbidity** of Migraine and Other Headaches in US **Adolescents**. J Pediatr. 2012 Aug;161(2):308-313.e1.
181. **NICE**: Headaches: Diagnosis and management of headaches in young people and adults Sep 2012 http://guidance.nice.org.uk/CG150
182. Radtke A, von Brevern M, et al. **Vestibular migraine**: Long-term follow-up of clinical symptoms and vestibulo-cochlear findings. Neurology. 2012 Oct 9;79(15):1607-14.
183. Gelfand AA, Thomas KC, Goadsby PJ. Before the headache: **Infant colic** as an early life expression of migraine. Neurology. 2012 Sep 25;79(13):1392-6.
184. Arruda MA, Bigal ME. Migraine and migraine subtypes in **preadolescent children**: Association with **school performance**. Neurology. 2012 Oct 30;79(18):1881-8.
185. Palm-Meinders IH, Koppen H, Terwindt GM, et al. **Structural brain changes in migraine**. (**CAMERA-2**) JAMA. 2012;308(18):1889-1897.
186. Hansen JM, Lipton RB, Dodick DW, et al. Migraine headache is **present in the aura phase**: A prospective study. Neurology. 2012 Nov 13;79(20):2044-2049.
187. Kjaergaard M, Eggen AE, Mathiesen EB, Jorde R. Association Between Headache and **Serum 25-Hydroxyvitamin D**; the Tromsø Study: Tromsø 6. Headache. 2012 Sep 13.
188. Lateef T, Cui L, Heaton L, et al. Validation of a **migraine interview for children** and adolescents. Pediatrics. 2013Jan;131(1):e96-e102.
189. Mohammadianinejad SE, Abbasi V, Sajedi SA, et al. **Zonisamide versus topiramate** in migraine prophylaxis: a double-blind randomized clinical trial. Clin Neuropharmacol. 2011 Jul-Aug;34(4):174-7.
190. Hougaard A, Amin F, Hauge AW, Ashina M, Olesen J. Provocation of migraine with aura using **natural trigger factors**. Neurology 2013;80:428–431.
191. Taggart E, Doran S, Kokotillo A, et al. **Ketorolac** in the Treatment of Acute Migraine: A Systematic Review. Headache. 2013 Jan 8.
192. Schoenen J, Vandersmissen B, Jeangette S, et al. Migraine prevention with a supraorbital transcutaneous stimulator: A randomized controlled trial. Neurology. 2013 Feb 19;80(8):697-704.
193. Afridi SK, Giffin NJ, Kaube H, et al. A randomized controlled trial of **intranasal ketamine** in migraine with prolonged aura. Neurology. 2013 Feb 12;80(7):642-7.
194. Goadsby PJ, Silberstein SD. **Migraine triggers**: Harnessing the messages of clinical practice. Neurology. 2013 Jan 29;80(5):424-5.
195. Hougaard A, Amin F, Hauge AW, et al. Provocation of migraine with aura using **natural trigger factors**. Neurology. 2013 Jan 29;80(5):428-31.
196. Romanello S, Spiri D, Marcuzzi E, et al. Association between **childhood migraine and history of infantile colic**. JAMA. 2013;309(15):1607-1612.
197. El-Chammas K, Keyes J, Thompson N, et al. Pharmacologic **treatment of pediatric headaches**: a meta-analysis. JAMA Pediatr. 2013 Mar 1;167(3):250-8.
198. Kranick SM, Campen CJ, Kasner SE, et al. Headache as a **risk factor for neurovascular events** in pediatric brain tumor patients. Neurology 2013;80:1452–1456.
199. Amin FM, Asghar MS, Anders H, et al. Magnetic resonance **angiography** of intracranial and extracranial arteries in patients with spontaneous migraine without aura: a cross sectional study. Lancet Neurol 2013; online April 9.
200. FDA May/13 is advising health care professionals and women that the anti-seizure medication **valproate** sodium and related products, valproic acid and divalproex sodium, are contraindicated and should **not be taken by pregnant women for the prevention of migraine headaches**.
201. Hainer B, Matheson EM. Approach to **Acute Headache in Adults**. Am Fam Physician. 2013;87(10):682-687.
202. Spoendlin J, Voegel JJ, et al. Migraine, triptans, and the risk of developing **rosacea**: A population-based study within the United Kingdom. J Am Acad Dermatol. 2013 May 1.
203. Kirthi V, Derry S, Moore RA. **Aspirin with or without an antiemetic** for acute migraine headaches in adults. Cochrane Database Syst Rev. 2013 Apr 30;4:CD008041. doi: 10.1002/14651858.CD008041.pub3. We found no new studies since the last version of this review. Aspirin 1000 mg is an effective treatment for acute migraine headaches, similar to sumatriptan 50 mg or 100 mg. Addition of metoclopramide 10 mg improves relief of nausea and vomiting. Adverse events were mainly mild and transient, and were slightly more common with aspirin than placebo, but less common than with sumatriptan 100 mg.
204. Woodruff AE, Cieri NE, Abeles J, Seyse SJ. **Abdominal migraine** in adults: a review of pharmacotherapeutic options. Ann Pharmacother. 2013 Jun;47(6):e27.
205. Gudmundsson LS, Scher AI, Sigurdsson S, et al. Migraine, depression, and brain volume: The AGES-Reykjavik Study. Neurology. 2013 May 22.
206. Beithon J, Gallenberg M, Johnson K, Kildahl P, et al. **Diagnosis and treatment of headache**. Bloomington (MN): Institute for Clinical Systems Improvement (**ICSI**); 2013 Jan.
207. Derry S, Rabbie R, Moore RA. **Diclofenac with or without an antiemetic** for acute migraine headaches in adults. Cochrane Database Syst Rev. 2013 Apr 30;4:CD008783. doi: 10.1002/14651858.CD008783.pub3 Oral diclofenac potassium 50 mg is an effective treatment for acute migraine, providing relief from pain and associated symptoms, although only a minority of patients experience pain-free responses. Adverse events are mostly mild and transient and occur at the same rate as with placebo.
208. Kruit MC, Thijs RD, Ferrari MD, et al. **Syncope and orthostatic intolerance** increase risk of brain lesions in migraineurs and controls. Neurology. 2013 May 21;80(21):1958-1965.

209. Rabbie R, Derry S, Moore RA. **Ibuprofen with or without an antiemetic** for acute migraine headaches in adults. Cochrane Database Syst Rev. 2013 Apr 30;4:CD008039. doi: 10.1002/14651858.CD008039.pub3. We found no new studies since the last version of this review. Ibuprofen is an effective treatment for acute migraine headaches, providing pain relief in about half of sufferers, but complete relief from pain and associated symptoms for only a minority. NNTs for all efficacy outcomes were better with 400 mg than 200 mg in comparisons with placebo, and soluble formulations provided more rapid relief. Adverse events were mostly mild and transient, occurring at the same rate as with placebo.
210. Shamliyan TA, Kane RL, Taylor FR.. **Migraine in adults: Preventive** pharmacologic treatments. AHRQ Comparative Effectiveness Review. Rockville (MD): Agency for Healthcare Research and Quality (US); 2013 Apr. Report No.: 13-EHC068-EF. For chronic migraine, onabotulinumtoxin A reduced migraine attacks but increased the risk of adverse effects and treatment discontinuation due to adverse effects. For episodic migraine, approved drugs are effective but increase risk of adverse effects and treatment discontinuation due to adverse effects. Some off-label beta blockers and angiotensin inhibiting drugs are effective without bothersome harms and therefore offer the best benefits-to-harms ratio. We could not determine the long-term (i.e., trials of more than 3 months' duration), preventive benefits and adherence with drugs. Evidence on improving quality of life was inconsistent across individual drugs. Evidence for individualized treatment decisions is very limited. Future research should examine the role of patient characteristics on drug benefits and safety.
211. Shamliyan TA, Choi JY, Ramakrishnan R, et al. **Preventive Pharmacologic Treatments for Episodic** Migraine in Adults. J Gen Intern Med. 2013 Apr 17.
212. Weaver-Agostoni. **Cluster Headache**. Am Fam Physician. 2013;88(2):122-128.
213. Furman JM, Marcus DA, Balaban CD. **Vestibular migraine**: clinical aspects and pathophysiology. Lancet Neurol. 2013 Jul;12(7):706-15.
214. Lu SR, Fuh JL, Wang SJ, et al. Incidence and Risk Factors of **Chronic Daily Headache** in Young Adolescents: A School Cohort Study. Pediatrics. 2013 Jun 17.
215. Arevalo-Rodriguez I, Ciapponi A, et al. Posture and fluids for preventing **post-dural puncture headache**. Cochrane Database of Systematic Reviews 2013, Issue 7. Art. No.: CD009199. DOI:10.1002/14651858.CD009199.pub2. There is no evidence from RCTs that suggests that routine bed rest after dural puncture is beneficial for the prevention of PDPH onset. The role of fluid supplementation in the prevention of PDPH remains unclear.
216. Linde M, Mulleners WM, Chronicle EP, McCrory DC. **Antiepileptics other than gabapentin, pregabalin, topiramate, and valproate for the prophylaxis** of episodic migraine in adults. Cochrane Database Syst Rev. 2013 Jun 24;6:CD010608. Available evidence does not allow robust conclusions regarding the efficacy of antiepileptic drugs other than gabapentin,pregabalin, topiramate, and valproate in the prophylaxis of episodic migraine among adults. Acetazolamide, carisbamate, clonazepam, lamotrigine, oxcarbazepine, and vigabatrin were not more effective than placebo in reducing headache frequency. In one trial each, carbamazepine and levetiracetam were significantly superior to placebo in reducing headache frequency, and there was no significant difference in proportion of responders between zonisamide and active comparator.
217. DeVries A et al. CT scan utilization patterns in pediatric patients with recurrent headache. Pediatrics 2013 Jul; 132:e1.
218. Linde M, Mulleners WM, Chronicle EP, et al. **Topiramate for the prophylaxis of episodic migraine** in adults. Cochrane Database Syst Rev. 2013 Jun 24;6:CD010610. Meta-analysis demonstrates that topiramate in a 100 mg/day dosage is effective in reducing headache frequency and reasonably well-tolerated in adult patients with episodic migraine. This provides good evidence to support its use in routine clinical management. More studies designed specifically to compare the efficacy or safety of topiramate versus other interventions with proven efficacy in the prophylaxis of migraine are needed.
219. Stewart WF, Roy J, Lipton RB. **Migraine prevalence, socioeconomic status, and social causation**. Neurology. 2013 Sep 10;81(11):948-55.
220. Worthington I, Pringsheim T, Gawel1 MJ, et al; on behalf of the **Canadian** Headache Society **Acute Migraine Treatment Guideline** Development Group. Canadian Headache Society guideline. Acute drug therapy for migraine headache. Can J Neurol Sci 2013;40(5 Suppl 3):1-86.
221. Bashir A et al. Migraine and **structural changes in the brain**: A systematic review and meta-analysis.Neurology 2013 Aug 29; [e-pub ahead of print].
222. Sheridan DC, Meckler GD, Spiro DM, et al. **Diagnostic Testing and Treatment of Pediatric** Headache in the Emergency Department. J Pediatr. 2013 Aug 20.
223. Ramsden CE, Faurot KR, Zamora D, et al. Targeted alteration of **dietary n-3 and n-6 fatty acids** for the treatment of chronic headaches: A randomized trial. Pain. 2013 Jul 22.
224. Mar S, Kelly JE, Isbell S, et al. Prevalence of white matter lesions and stroke in children with migraine. Neurology. 2013 Sep 16.
225. Hamedani AG, Rose KM, Peterlin BL, et al. Migraine and **white matter hyperintensities**: The ARIC MRI study. Neurology. 2013 Oct 8;81(15):1308-1313.
226. Shamliyan TA, Choi JY, Ramakrishnan R, et al. **Preventive pharmacologic treatments for episodic** migraine in adults. J Gen Intern Med. 2013 Sep;28(9):1225-37.
227. Cernuda-Morollón E, Larrosa D, Ramón C, et al. Interictal increase of **CGRP levels** in peripheral blood as a biomarker for chronic migraine. Neurology 2013;81:1191–1196.
228. Bashir A, Lipton RB, Ashina S, Ashina M. Migraine and **structural changes** in the brain: A systematic review and meta-analysis. Neurology. 2013 Aug 28.
229. McGregor EA. **In the Clinic: Migraine**. Ann Intern Med. 2013 Nov 5;159(9):ITC5-1.
230. Asadollahi S, Heidari K, Vafaee R, et al. **Promethazine Plus Sumatriptan** in the Treatment of Migraine: A Randomized Clinical Trial. Headache. 2013 Nov 1.
231. Saper JR, Da Silva AN. **Medication overuse headache**: history, features, prevention and management strategies. CNS Drugs. 2013 Nov;27(11):867-77.
232. Law S, Derry S, Moore RA. **Sumatriptan plus naproxen** for acute migraine attacks in adults. Cochrane Database Syst Rev. 2013 Oct 21;10:CD008541. Combination treatment was effective in the acute treatment of migraine headaches. The effect was greater than for the same dose of either sumatriptan or naproxen alone, but additional benefits over sumatriptan alone are not large. More participants achieved good relief when medication was taken early in the attack, when pain was still mild. Adverse events were more common with the combination and sumatriptan alone than with placebo or naproxen alone.
233. Bethell C, Kemper KJ, Gombojav N, Koch TK. **Complementary and Conventional Medicine** Use Among Youth With Recurrent Headaches. Pediatrics. 2013 Oct 14.
234. Meissner K, Fässler M, Rücker G, et al. Differential Effectiveness of Placebo Treatments: A Systematic Review of **Migraine Prophylaxis**. JAMA Intern Med. 2013 Oct 14.
235. Loder E, Burch R, Rizzoli P. The 2012 **AHS/AAN guidelines for prevention of episodic migraine**: a summary and comparison with other recent clinical practice guidelines. Headache. 2012 Jun;52(6):930-45.
236. Saper JR, Da Silva AN. **Medication overuse headache**: history, features, prevention and management strategies. CNS Drugs. 2013 Nov;27(11):867-77.
237. Peterlin BL, Rosso AL, Williams MA, et al. Episodic migraine and **obesity** and the influence of age, race, and sex. Neurology. 2013 Oct 8;81(15):1314-21.
238. Thorlund K, Mills EJ, et al. **Comparative efficacy of triptans** for the abortive treatment of migraine: A multiple treatment comparison meta-analysis. Cephalalgia. 2013 Dec 19.
239. Gupta S, Oosthuizen R, Pulfrey S. Treatment of **acute migraine in the emergency department**. Can Fam Physician. 2014 Jan;60(1):47-9
240. Law S, Derry S, Moore RA. **Triptans for acute cluster** headache. Cochrane Database Syst Rev. 2013 Jul 17;7:CD008042. Based on limited data, subcutaneous sumatriptan 6 mg was superior to intranasal zolmitriptan 5 mg or 10 mg for rapid (15 minute)responses, which are important in this condition. Oral routes of administration are not appropriate.

241. Crock C, Orsini F, Lee KJ, et al. **Headache after lumbar puncture**: randomised crossover trial of 22-gauge versus 25-gauge needles. Arch Dis Child. 2013 Nov 14.
242. Powers SW, Kashikar-Zuck SM, Allen JR, et al. **Cognitive behavioural therapy plus amitriptyline** for chronic migraine in children and adolescents: a randomized clinical trial. JAMA. 2013 Dec 25;310(24):2622-30.
243. Hoffmann J, Goadsby PJ. **Emerging Targets** in Migraine. CNS Drugs. 2013 Dec 8.
244. Callaghan BC, Kerber KA, Pace RJ, et al. **Headaches and Neuroimaging**: High Utilization and Costs Despite Guidelines. JAMA Intern Med. 2014 Mar 17.
245. Friedman BW, Garber L, Yoon A, et al. Randomized trial of **IV valproate vs metoclopramide vs ketorolac** for acute migraine. Neurology. 2014 Mar 18;82(11):976-83.
246. Sherwood M, Goldman RD. Effectiveness of **riboflavin** in pediatric migraine prevention. Can Fam Physician. 2014 Mar;60(3):244-6.
247. Maizels M, Blumenfeld A, Burchette R. A combination of **riboflavin**, **magnesium**, and **feverfew** for migraine prophylaxis: a randomized trial. Headache. 2004 Oct;44(9):885-90.
248. Mattimoe D, Newton W. High-dose **riboflavin** for migraine prophylaxis. J Fam Pract. 1998 Jul;47(1):11.
249. Schwedt TJ. **Chronic migraine**. BMJ. 2014 Mar 24.
250. Pringsheim T, Becker WJ. **Triptans** for symptomatic treatment of **migraine** headache. BMJ. 2014 Apr 7;348:g2285.
251. Yancey JR, Sheridan R, Koren KG. **Chronic Daily Headache**-Diagnosis and Management. Am Fam Physician. 2014;89(8):642-648.
252. Srikiatkhachorn A, le Grand SM, Supornsilpchai W, Storer RJ. Pathophysiology of **medication overuse headache** -- an update. Headache. 2014;54:204-210.
253. Jürgens TP, Schulte LH, May A. **Migraine trait symptoms** in migraine with and without aura. Neurology. 2014 Apr 22;82(16):1416-24.
254. Lipton RB, Buse DC, Hall CB, et al. Reduction in perceived **stress as a migraine trigger**: Testing the "let-down headache" hypothesis. Neurology. 2014 Apr 22;82(16):1395-401.
255. Deaton TL, Mauro LS. **Topiramate** for migraine **prophylaxis** in **pediatric** patients. Ann Pharmacother. 2014 May;48(5):638-43.
256. Saguil A, Lax JW. **Acute migraine treatment in emergency** settings. Am Fam Physician. 2014 May 1;89(9):742-4.
257. Petersen AS, Barloese MC, Jensen RH. **Oxygen** treatment of **cluster** headache: A review. Cephalalgia. 2014 Apr 10.
258. Bird S,Derry S,Moore RA. **Zolmitriptan** for acute migraine attacks in adults. Cochrane Database of Systematic Reviews 2014, Issue 5. Art. No.: CD008616. DOI: 10.1002/14651858.CD008616.pub2. Zolmitriptan is effective as an abortive treatment for migraine attacks for some people, but is associated with increased adverse events compared to placebo. Zolmitriptan 2.5 mg and 5 mg benefited the same proportion of people as sumatriptan 50 mg, although not necessarily the same individuals, for headache relief at two hours.
259. Biedroł A, Kaciłski M, Skowronek-Bała B. **Stabbing headache** in an 8-year-old girl: primary or drug induced headache? Pediatrics. 2014 Apr;133(4).
260. Sacco S, Ornello R, Ripa P, et al. Migraine and **hemorrhagic stroke**: a meta-analysis. Stroke 2013;44:3032–8.
261. Derry CJ, Derry S, Moore RA. **Sumatriptan (all routes of administration) for acute migraine** attacks in adults - overview of Cochrane reviews. Cochrane Database of Systematic Reviews 2014, Issue 5. Art. No.: CD009108. DOI: 10.1002/14651858.CD009108.pub2. Sumatriptan is an effective abortive treatment for acute migraine attacks, but is associated with increased adverse events relative to placebo. The route of administration influences efficacy, particularly within the first hour after administration. Subcutaneous sumatriptan shows the greatest efficacy in terms of pain relief, but at the expense of relatively high levels of adverse events, and with a high financial cost compared with other routes. Information about the relative efficacy of the different routes of administration for different outcomes should help to inform decisions about the suitability of sumatriptan as a migraine treatment, as well as about the most appropriate way to administer the treatment for individual patients.
262. Monteith T, Gardener H, Rundek T, et al. Migraine, **white matter hyperintensities**, and subclinical brain infarction in a diverse community: the northern Manhattan study. Stroke. 2014 Jun;45(6):1830-2.
263. Stovner LJ, Linde M, Gravdahl GB, et al. A comparative study of **candesartan versus propranolol for migraine prophylaxis**: a randomised, triple-blind, placebo-controlled, double cross-over study. Cephalalgia. 2013;34:523-532.
264. Tronvik E, Stovner LJ, Helde G, et al. **Prophylactic** treatment of migraine with an **angiotensin II receptor blocker**: a randomized controlled trial. JAMA. 2003 Jan 1;289(1):65-9.
265. Weinman D, Nicastro O, Akala O, et al. Parenteral Treatment of **Episodic Tension-Type Headache**: A Systematic Review. Headache. 2014 Jan 16.
266. Dodick DW, Goadsby PJ, Spierings ELH, et al. Safety and effi cacy of **LY2951742, a monoclonal antibody to calcitonin gene-related peptide**, for the prevention of migraine: a phase 2, randomised, double-blind, placebo-controlled study Lancet Neurol 2014; online Aug 11.
267. Wells RE, Burch R, Paulsen RH, et al. **Meditation** for Migraines: A Pilot Randomized Controlled Trial. Headache. 2014 Jul 18.
268. Kristoffersen ES, Straand J, Vetvik KG, et al. **Brief intervention** for **medication-overuse** headache in primary care. The **BIMOH** study: a double-blind pragmatic cluster randomised parallel controlled trial. J Neurol Neurosurg Psychiatry. 2014 Aug 11.
269. Ephross SA, Sinclair SM. Final results from the **16-year sumatriptan, naratriptan, and treximet pregnancy registry**. Headache. 2014;54:1158-1172.
270. Migliazzo CV, Hagan JC 3rd. **Beta blocker eye drops** for treatment of acute migraine. Mo Med. 2014 Jul-Aug;111(4):283-8.
271. Ho TW, Connor KM, Zhang Y, et al. Randomized controlled trial of the CGRP receptor antagonist **telcagepant** for migraine prevention. Neurology. 2014 Sep 9;83(11):958-66.
272. Dodick DW, Goadsby PJ, Spierings EL, et al. Safety and efficacy of **LY2951742**, a monoclonal antibody to **calcitonin gene-related peptide**, for the prevention of migraine: a phase 2, randomised, double-blind, placebo-controlled study. Lancet Neurol 2014; 13: 885–92.
273. Rothrock J. Triptans, SSRIs/SNRIs and Serotonin Syndrome in Headache Toolbox. American Headache Society 2010. Accessed online at http://www.americanheadachesociety.org/assets/1/7/Triptans_June_2010.pdf
274. Faria V, Linnman C, Lebel A, et al. Harnessing the **placebo effect in pediatric migraine** clinic. J Pediatr. 2014 Oct;165(4):659-65.
275. Huang L, Bocek M, Jordan JK, et al. **Memantine** for the Prevention of Primary Headache Disorders. Ann Pharmacother. 2014 Nov;48(11):1507 1511.
276. Pdf Chakraborty S, Miller WD. Imaging in a 35-year-old woman with **progressive headache**. CMAJ. 2014 Dec 9;186(18):1391-3
277. Post J, Moriates C. When does an adult with headaches **need central nervous system imaging**? Cleve Clin J Med. 2014 Dec;81(12):719-20.

278. Winter AC, Rice MS, Fortner RT, et al. **Migraine and breast cancer** risk: a prospective cohort study and meta-analysis. J Natl Cancer Inst. 2014 Dec 12;107(1).
279. Mafi JN, Edwards ST, et al. Trends in the **Ambulatory Management of Headache**: Analysis of NAMCS and NHAMCS Data 1999-2010. J Gen Intern Med. 2015 Jan 8.
280. Peng KP, Chen YT, Fuh JL, Tang CH, Wang SJ. Increased **risk of Bell palsy** in patients with migraine: a nationwide cohort study. Neurology 2015;84:116–124.
281. Thomas MC, Musselman ME, Shewmaker J. **Droperidol** for the Treatment of Acute Migraine Headaches. Ann Pharmacother. 2015 Feb;49(2):233-240.
282. Tietjen GE, Buse DC, Fanning KM, et al. **Recalled maltreatment**, migraine, and tension-type headache: results of the AMPP Study. Neurology 2015;84:132–140.
283. Burch RC, Loder S, Loder E, Smitherman TA. The **prevalence and burden of migraine and severe headache in the United States**: updated statistics from government health surveillance studies. Headache. 2015 Jan;55(1):21-34.
284. Marmura MJ, Silberstein SD, Schwedt TJ. The **acute treatment of migraine in adults: the american headache society** (AHS) evidence assessment of migraine pharmacotherapies. Headache. 2015 Jan;55(1):3-20.
285. Bachur RG, Monuteaux MC, Neuman MI. A **Comparison of Acute Treatment Regimens** for Migraine in the **Emergency Department.** Pediatrics. 2015 Jan 26.
286. Moraska AF, Stenerson L, Butryn N, et al. Myofascial Trigger Point-focused Head and Neck **Massage for Recurrent Tension-type Headache**: A Randomized, Placebo-controlled Clinical Trial. Clin J Pain. 2015 Feb;31(2):159-68.
287. Dayan PS, Holmes JF, Hoyle J Jr, et al; for the Pediatric Emergency Care Applied Research Network (PECARN). **Headache in Traumatic Brain Injuries** From Blunt Head Trauma. Pediatrics. 2015 Feb 2.
288. Malem A, Farnworth D. **Headache, flashing lights, and blurred vision**. (hypertensive retinopathy)BMJ. 2015 Feb 2;350:h446.
289. Lipton RB, Fanning KM, Serrano D, et al. **Ineffective acute treatment of episodic migraine is associated with new-onset chronic migraine**. Neurology 2015;84:688–695.
290. Nesbitt AD, Marin JC, Tompkins E, et al. Initial use of a novel **noninvasive vagus nerve stimulator** for cluster headache treatment. Neurology. 2015 Mar 24;84(12):1249-53.
291. Banzi R, Cusi C, Randazzo C, et al. Selective serotonin reuptake inhibitors (**SSRIs**) and serotonin-norepinephrine reuptake inhibitors (**SNRIs**) for the **prevention of tension-type headache in adults**. Cochrane Database Syst Rev. 2015 May 1;5:CD011681. Since the last version of this review, the new included studies have not added high quality evidence to support the use of SSRIs or venlafaxine (a SNRI) as preventive drugs for tension-type headache. Over two months of treatment, SSRIs or venlafaxine are no more effective than placebo or amitriptyline in reducing headache frequency in patients with chronic tension-type headache. SSRIs seem to be less effective than tricyclic antidepressants in terms of intake of analgesic medications. Tricyclic antidepressants are associated with more adverse events; however, this did not cause a greater number of withdrawals. No reliable information is available at longer follow-up. Our conclusion is that the use of SSRIs and venlafaxine for the prevention of chronic tension-type headache is not supported by evidence.
292. Banzi R, Cusi C, Randazzo C, et al. Selective serotonin reuptake inhibitors (**SSRIs**) and serotonin-norepinephrine reuptake inhibitors (**SNRIs**) for the **prevention of migraine** in **adults**. Cochrane Database Syst Rev. 2015 Apr 1;4:CD002919. Since the last version of this review, the new included studies have not added high quality evidence to support the use of SSRIs or venlafaxine as preventive drugs for migraine. There is no evidence to consider SSRIs or venlafaxine as more effective than placebo or amitriptyline in reducing migraine frequency, intensity, and duration over two to three months of treatment. No reliable information is available at longer-term follow-up. Our conclusion is that the use of SSRIs and SNRIs for migraine prophylaxis is not supported by evidence.
293. Hansen JM, Goadsby PJ, Charles A. Reduced efficacy of **sumatriptan** in migraine with **aura vs without aura**. Neurology 2015;84:1880–1885.
294. Ducros A, Biousse V. Headache arising from idiopathic **changes in CSF pressure**. Lancet Neurol. 2015 Jun;14(6):655-668.
295. Eken C. Critical reappraisal of **intravenous metoclopramide** in migraine attack: a systematic review and meta-analysis. Am J Emerg Med. 2015 Mar;33(3):331-7. The existing data, albeit of poor quality, demonstrate that intravenous metoclopromide (Reglan) is effective in reducing pain and decreasing the need for rescue treatment in patients with acute migraine. (LOE = 1a-).
296. Goldman RD, Meckler GD. **Intranasal sumatriptan** for migraine in **children**. Can Fam Physician. 2015 May;61(5):435-7.
297. Malik R, Freilinger T, Winsvold BS, et al; International Headache Genetics Consortium, Dichgans M; METASTROKE Collaboration of the International Stroke Genetics Consortium. Shared **genetic basis for migraine and ischemic stroke**: A genome-wide analysis of common variants. Neurology. 2015 May 26;84(21):2132-45.
298. Ramsden CE, Faurot KR, Zamora D, et al. Targeted alterations in **dietary n-3 and n-6 fatty acids** improve life functioning and reduce psychological distress among patients with **chronic headache**: a secondary analysis of a randomized trial. Pain. 2015 Apr;156(4):587-96.
299. Thornby KA, Henneman A, Brown DA. Evidence-Based Strategies to Reduce **Intravenous Immunoglobulin-Induced Headaches**. Ann Pharmacother. 2015 Jun;49(6):715-726.
300. Becker WJ, Findlay T, Moga C, et al. **Guideline for primary care management of headache in adults. Can** Fam Physician. 2015 Aug;61(8):670-9. Review.
301. Derry S, Wiffen PJ, Moore RA, et al. **Ibuprofen for acute treatment of episodic tension-type headache** in adults. Cochrane Database Syst Rev. 2015 Jul 31;7:CD011474. Ibuprofen 400 mg provides an important benefit in terms of being pain free at 2 hours for a small number of people with frequent episodic tension-type headache who have an acute headache with moderate or severe initial pain. There is no information about the lesser benefit of no worse than mild pain at 2 hours.
302. Wider B, Pittler MH, Ernst E. **Feverfew for preventing migraine**. Cochrane Database Syst Rev. 2015 Apr 20;4:CD002286. Since the last version of this review, one larger rigorous study has been included, reporting a difference in effect between feverfew and placebo of 0.6 attacks per month. This adds some positive evidence to the mixed and inconclusive findings of the previous review. However, this constitutes low quality evidence, which needs to be confirmed in larger rigorous trials with stable feverfew extracts and clearly defined migraine populations before firm conclusions can be drawn. It appears from the data reviewed that feverfew is not associated with any major safety concerns.
303. Knowles S, Oh P, Gomes T; Ontario Drug Policy Research Network. **Triptans for Acute Migraine**: Drug Class Review to Help Inform Policy Decisions. Headache. 2015 Jul;55 Suppl 4:191-8.
304. Monteith TS, Gardener H, Rundek T, et al. **Migraine and risk of stroke** in older adults: Northern Manhattan Study. Neurology. 2015 Aug 25;85(8):715-21.
305. Diener HC, Charles A, Goadsby PJ, et al. **New therapeutic approaches** for the prevention and treatment of migraine. Lancet Neurol. 2015 Oct;14(10):1010-22.
306. Kurth T, Scher AI. **Suicide risk** is elevated in migraineurs who have comorbid fibromyalgia. Neurology. 2015 Aug 21.

307. Liu HY, Fuh JL, Lin YY, et al. **Suicide risk** in patients with migraine and comorbid fibromyalgia. Neurology. 2015 Aug 21.
308. Robbins MS, Farmakidis C, Dayal AK, et al. **Acute headache diagnosis in pregnant women**: A hospital-based study. Neurology. 2015 Aug 19.
309. Bigal ME, Dodick DW, Rapoport AM, et al. Safety, tolerability, and efficacy of **TEV-48125** for preventive treatment of high-frequency episodic migraine: a multicentre, randomised, double-blind, placebo-controlled, phase 2b study. Lancet Neurol 2015; online Sept 30.
310. Bigal ME, Edvinsson L, Rapoport AM, et al. Safety, tolerability, and efficacy of **TEV-48125** for preventive treatment of chronic migraine: a multicentre, randomised, double-blind, placebo-controlled, phase 2b study. Lancet Neurol 2015; online Sept 30.
311. Buettner C, Nir RR, Bertisch SM, et al. **Simvastatin and Vitamin D** for Migraine Prevention: A Randomized Controlled Trial. Ann Neurol. 2015 Sep 29.
312. Robbins MS, Farmakidis C, Dayal AK, et al. **Acute headache diagnosis in pregnant women**: A hospital-based study. Neurology. 2015 Sep 22;85(12):1024-30.
313. Li L, et al; Oxford Vascular Study. Age-specific association of migraine with **cryptogenic TIA and stroke**: Population-based study. Neurology. 2015 Oct 27;85(17):1444-51.
314. Peterlin BL, Mielke MM, Dickens AM, et al. Interictal, circulating **sphingolipids** in women with episodic migraine: A case-control study. Neurology. 2015 Oct 6;85(14):1214-23.
315. Rayhill ML, Sharon R, et al. **Registration status and outcome reporting of trials** published in core headache medicine journals. Neurology. 2015 Nov 17;85(20):1789-94.
316. Rodés-Cabau J, Horlick E, Ibrahim R, et al. Effect of **Clopidogrel and Aspirin vs Aspirin** Alone on Migraine Headaches After **Transcatheter Atrial Septal Defect Closure**: The CANOA Randomized Clinical Trial. JAMA. 2015 Nov 9:1-8.
317. Viana M, Sances G, Ghiotto N, et al. **Variability of the characteristics of a migraine attack** within patients. Cephalalgia. 2015 Oct 23.
318. Amin FM, Hougaard A, et al. Change in **brain network connectivity** during PACAP38-induced migraine attacks: A resting-state functional MRI study. Neurology. 2016 Jan 12;86(2):180-7.
319. Martin VT, Fanning KM, et al. **Asthma is a risk factor** for new onset chronic migraine: Results from American migraine prevalence and prevention study. Headache. 2015 Nov 19.
320. Mawet J, Eikermann-Haerter K, Park KY, et al. **Sensitivity to acute cerebral ischemic** injury in migraineurs: a retrospective case-control study. Neurology 2015;85:1945–1949.
321. Leone M, Proietti Cecchini A. Long-term use of **daily sumatriptan injections** in severe drug-resistant chronic **cluster headache**. Neurology. 2016 Jan 12;86(2):194-5.
322. Martin VT, Pavlovic J, Fanning KM, et al. **Perimenopause and Menopause** Are Associated With High Frequency Headache in Women With Migraine: Results of the American Migraine Prevalence and Prevention Study. Headache. 2016 Jan 21.
323. Montagni I, Guichard E, Carpenet C, et al. **Screen time exposure** and reporting of headaches in young adults: A cross-sectional study. Cephalalgia.2015 Dec 2.
324. Sun H, et al. Safety and efficacy of **AMG 334** for prevention of episodic migraine: a randomised, double-blind, placebo-controlled, phase 2 trial. Lancet Neurol 2016; online Feb 12.
325. Eller M, Gelfand AA, Riggins NY, et al. Exacerbation of headache during **dihydroergotamine for chronic migraine** does not alter outcome. Neurology. 2016 Mar 1;86(9):856-9.
326. Arevalo-Rodriguez I, Ciapponi A, Roque I Figuls M, et al. Posture and fluids for preventing **post-dural puncture headache**.Cochrane Database Syst Rev. 2016 Mar 7;3:CD009199. Since the previous version of this review, we found one new study for inclusion, but the conclusion remains unchanged. We considered the quality of the evidence for most of the outcomes assessed in this review to be low to moderate. As identified studies had shortcomings on aspects related to randomization and blinding of outcome assessment, we therefore downgraded the quality of the evidence. In general, there was no evidence suggesting that routine bed rest after dural puncture is beneficial for the prevention of PDPH onset. The role of fluid supplementation in the prevention of PDPH remains unclear.
327. Richer L, Billinghurst L, Linsdell MA, et al. Drugs for the **acute treatment of migraine in children and adolescents**. Cochrane Database of Systematic Reviews 2016, Issue 4. Art. No.: CD005220. Low quality evidence from two small trials shows that ibuprofen appears to improve pain freedom for the acute treatment of children with migraine. We have only limited information on adverse events associated with ibuprofen in the trials included in this review. Triptans as a class are also effective at providing pain freedom in children and adolescents but are associated with higher rates of minor adverse events. Sumatriptan plus naproxen sodium is also effective in treating adolescents with migraine.
328. Wells RE, Turner DP, Lee M, Bishop L, Strauss L. Managing **Migraine During Pregnancy** and Lactation. Curr Neurol Neurosci Rep. 2016 Apr;16(4):40.
329. Linde K, Allais G, Brinkhaus B, et al. **Acupuncture for the prevention of tension-type headache**. Cochrane Database Syst Rev. 2016 Apr 19;4:CD007587. The available results suggest that acupuncture is effective for treating frequent episodic or chronic tension-type headaches, but further trials - particularly comparing acupuncture with other treatment options - are needed.
330. Akram H, Miller S, Lagrata S, et al. **Ventral tegmental area deep brain stimulation** for refractory chronic cluster headache. Neurology. 2016 May 3;86(18):1676-82.
331. Koppen H, Palm-Meinders IH, Mess WH, et al. **Systemic right-to-left shunts**, ischemic brain lesions, and persistent migraine activity. Neurology. 2016 May 3;86(18):1668-75.
332. FDA June/16 is investigating the risk of serious burns and potential permanent scarring with the use of **Zecuity** (sumatriptan iontophoretic transdermal system) patch for migraine headaches. Since marketing of the Zecuity patch began in Sept 2015, a large number of patients have reported they experienced burns or scars on the skin where the patch was worn.
333. Kurth T, Winter AC, Eliassen AH, et al. **Migraine and risk of cardiovascular disease in women**: prospective cohort study. (NHS II). BMJ 2016;353:i2610.
334. Goncalves AL, Martini Ferreira A, Ribeiro RT, et al. Randomised clinical trial comparing **melatonin 3 mg, amitriptyline 25 mg and placebo for migraine prevention**. J Neurol Neurosurg Psychiatry. 2016 May 10.
335. Bigal ME, Dodick DW, et al. **TEV-48125** for the preventive treatment of chronic migraine: Efficacy at early time points. Neurology. 2016 Jul 5;87(1):41-48.
336. Giffin NJ, Lipton RB, Silberstein SD, et al. The migraine **postdrome**: An **electronic diary** study. Neurology. 2016 Jul 19;87(3):309-13
337. Linde K, Allais G, Brinkhaus B, et al. **Acupuncture for the prevention of episodic migraine**. Cochrane Database Syst Rev. 2016 Jun 28;6:CD001218. The available evidence suggests that adding acupuncture to symptomatic treatment of attacks reduces the frequency of headaches. Contrary to the previous findings, the updated evidence also suggests that there is an effect over sham, but this effect is small. The available trials also suggest that acupuncture may be at least similarly effective as treatment with prophylactic drugs. Acupuncture can be considered a treatment option for patients willing to undergo this treatment. As for other migraine treatments, long-term studies, more than one year in duration, are lacking.
338. Mattle HP, Evers S, et al. **Percutaneous closure of patent foramen ovale** in migraine with aura, a randomized controlled trial. Eur Heart J. 2016 Jul 7;37(26):2029-36.
339. Pavlović JM, Allshouse AA, , et al. **Sex hormones** in women with and without migraine: Evidence of migraine-specific hormone profiles. Neurology. 2016 Jul 5;87(1):49-56.

340. Silberstein SD, et al. Chronic migraine headache prevention with noninvasive **vagus nerve stimulation**: The **EVENT** study. Neurology. 2016 Aug 2;87(5):529-38
341. Stubberud A, Varkey E, McCrory DC, Pedersen SA, Linde M. **Biofeedback** as Prophylaxis for Pediatric Migraine: A Meta-analysis. Pediatrics. 2016 Aug;138(2)
342. Friedman BW. **Managing Migraine**. Ann Emerg Med. 2016 Aug 7. pii: S0196-0644(16)30301-8.
343. Le Gal J, Michel J-F, Rinaldi VE, et al. Association between **functional gastrointestinal disorders** and migraine in children and adolescents: a case-control study. Lancet Gastroenterol Hepatol 2016; online Aug 24.
344. Chou DE, Tso AR, Goadsby PJ. **Aprepitant** for the management of nausea with inpatient **IV dihydroergotamine**. Neurology. 2016 Sep 14.
345. Martin AT, Pinney SM, Xie C, et al. Headache Disorders May Be a Risk Factor for the **Development of New Onset Hypothyroidism**. Headache. 2016 Sep 27.
346. Veys L, Derry S, Moore RA. **Ketoprofen for episodic tension-type headache in adults**. Cochrane Database Syst Rev. 2016 Sep 22;9:CD012190. Ketoprofen 25 mg provided a small benefit compared with placebo in terms of being pain-free at two hours or having mild or no pain at two hours for people with frequent episodic TTH who have an acute headache of moderate or severe intensity. Its use was associated with more people experiencing adverse events. Ketoprofen 25 mg was not superior to paracetamol 1000 mg for any efficacy outcome.
347. Uthaikhup S, et al. Effectiveness of **physiotherapy for seniors with recurrent headaches** associated with neck pain & dysfunction: randomized controlled trial. Spine J. 2016 Aug 4.
348. Verslegers WR, et al. **Long-term use of daily sumatriptan injections in severe drug-resistant chronic cluster headache**. Neurology. 2016 Oct 4;87(14):1522-1523.
349. Louter MA, Wilbrink LA, Haan J, et al. **Cluster headache and depression**. Neurology. 2016 Nov 1;87(18):1899-1906.
350. Powers SW, Coffey CS, Chamberlin LA, et al; **CHAMP** Investigators.. Trial of **Amitriptyline, Topiramate, and Placebo** for Pediatric Migraine. N Engl J Med. 2016 Oct 27.
351. Louter MA, Pelzer N, de Boer I, et al. Prevalence of **lifetime depression** in a large hemiplegic migraine cohort. Neurology. 2016 Nov 29;87(22):2370-2374.
352. Sheridan DC, Meckler GD. **Inpatient Pediatric Migraine Treatment**: Does Choice of Abortive Therapy Affect Length of Stay? J Pediatr. 2016 Sep 12.
353. Vetvik KG, MacGregor EA. **Sex differences** in the epidemiology, clinical features, and pathophysiology of migraine. Lancet Neurol. 2016 Nov 8.
354. Androulakis XM, Kodumuri N, Giamberardino LD, et al. **Ischemic stroke subtypes** and migraine with visual aura in the ARIC study. Neurology. 2016 Dec 13;87(24):2527-2532
355. Avcu N, Doğan NÖ, Pekdemir M, et al. **Intranasal Lidocaine** in Acute Treatment of Migraine: A Randomized Controlled Trial. Ann Emerg Med. 2016 Nov 23
356. Davenport WJ, Pringsheim TM. A 32-year-old woman with **headache**. CMAJ. 2016 Dec 6;188(17-18):E533-E534.
357. Robbins NM, et al. Safety of **domperidone in treating nausea associated with dihydroergotamine** infusion and headache. Neurology. 2016 Dec 13;87(24):2522-2526.
358. Sposato LA, Peterlin BL. **Cardioembolism** as the unsuspected missing link between migraine and ischemic stroke. Neurology. 2016 Dec 13;87(24):2504-2505.
359. De Giuli V, Grassi M, Lodigiani C, et al. Association between **migraine and cervical artery dissection**: the Italian Project on Stroke in Young Adults [online Mar 6, 2017].JAMA Neurol. doi:10.1001/jamaneurol.2016.5704.
360. Krause SJ, Stillman MJ, Tepper DE, Zajac D. A Prospective Cohort Study of **Outpatient Interdisciplinary Rehabilitation** of Chronic Headache Patients. Headache. 2017 Mar;57(3):428-440.
361. Timm FP, Houle TT, et al. Migraine and **risk of perioperative ischemic stroke** and hospital readmission: hospital based registry study. BMJ. 2017 Jan 10;356:i6635.
362. Begasse de Dhaem O, Minen MT. **Emerging Subspecialties in Neurology**: Headache medicine. Neurology. 2017 Mar 28;88(13):e122-e125
363. Lund N, Barloese M, et al. **Chronobiology differs between men and women** with cluster headache, clinical phenotype does not. Neurology. 2017 Mar 14;88(11):1069-1076.
364. Zhao L, et al. The long-term effect of **acupuncture for migraine prophylaxis**: randomized clinical trial [Feb 20/17].JAMA Intern Med. doi:10.1001 /jamainternmed.2016.9378
365. Chee J, Lau TP. Severe **postpartum headache**. BMJ. 2017 Apr 27;357:j1856.
366. MacGregor EA. **Migraine (In the Clinic).** Ann Intern Med. 2017 Apr 4;166(7):ITC49-ITC64.
367. Tepper S, Ashina M, Reuter U, et al. Safety and efficacy of **erenumab** for preventive treatment of chronic migraine: a randomised, double-blind, placebo-controlled phase 2 trial. Lancet Neurol 2017; online April 28.
368. Gelaye B, Sacco S, Brown WJ, et al. **Body composition status** and the risk of migraine: A meta-analysis. Neurology. 2017 May 9;88(19):1795-1804.
369. Millstine D, Chen CY, Bauer B. **Complementary and integrative medicine in the management of headache**. BMJ. 2017 May 16;357:j1805.
370. Schulte LH, Allers A, May A. **Hypothalamus** as a **mediator of chronic migraine**: Evidence from high-resolution fMRI. Neurology. 2017 May 23;88(21):2011-2016.
371. Anderson D, Ahmed SN. **Ectopic tooth**: an unusual cause of headache. CMAJ. 2017 May 29;189(21):E749.
372. Müller KI, Alstadhaug KB, Bekkelund SI. A randomized trial of **telemedicine** efficacy and safety for nonacute headaches. Neurology. 2017 Jul 11;89(2):153-162
373. Probyn K, Bowers H, Caldwell F, et al. **Prognostic factors for chronic headache**: A systematic review. Neurology. 2017 Jun 14.
374. Sakulchit T, Meckler GD, Goldman RD. **Topiramate for pediatric migraine prevention**. Can Fam Physician. 2017 Jul;63(7):529-531
375. Tso AR, Patniyot IR, Gelfand AA, et al. Increased rate of **venous thrombosis** may be associated with inpatient **dihydroergotamine** treatment. Neurology. 2017 Jun 14.
376. Young N et al. Multicenter prevalence of **opioid medication use as abortive** therapy in the **emergency department** treatment of migraine headaches. Am J Emerg Med 2017 Jun 16.
377. Bear JJ, Gelfand AA, Goadsby PJ, et al. **Occipital headaches** and neuroimaging in children. Neurology. 2017 Aug 1;89(5):469-474.
378. Charles A. Migraine. N Engl J Med. 2017 Aug 10;377(6):553-561
379. Jackson JL, Mancuso JM, Nickoloff S, et al. **Tricyclic and Tetracyclic Antidepressants for the Prevention** of Frequent Episodic or Chronic Tension-Type Headache in Adults: A Systematic Review and Meta-Analysis. J Gen Intern Med. 2017 Jul 18.
380. Liu Y, Dong Z, et al. Migraine Prevention Using Different Frequencies of **Transcutaneous Occipital Nerve Stimulation**: A Randomized Controlled Trial. Journal of Pain.2017;18(8):1006-1015

381. Scher AI, Buse DC, et al. **Comorbid pain and migraine chronicity**: The Chronic Migraine Epidemiology and Outcomes Study. Neurology. 2017 Aug 1;89(5):461-468.
382. Finkel AG, Klaric JS, et al. Staying in service with **posttraumatic headache**: A retrospective cohort study of patient outcome. Neurology. 2017 Sep 12;89(11):1186-1194.
383. McClafferty H, Vohra S, Bailey M, et al. **Pediatric Integrative Medicine**. Pediatrics. 2017. 2017;140(3):e20171961
384.Tso AR, Marin J, Goadsby PJ. **Noninvasive Vagus Nerve Stimulation** for Treatment of Indomethacin-Sensitive Headaches. JAMA Neurol. 2017 Aug 28.
385. Ashina M, Dodick D, Goadsby PJ, et al. **Erenumab** (AMG 334) in episodic migraine: Interim analysis of an ongoing open-label study. Neurology. 2017 Aug 23
386. Scher AI, Rizzoli PB, Loder EW. **Medication overuse headache**: an entrenched idea in need of scrutiny. Neurology 2017;89:1296–1304.
387. Charleston Iv L, Burke JF. Do **racial/ethnic disparities exist** in recommended migraine treatments in US ambulatory care? Cephalalgia. 2017 Jan 1:333102417716933
388. Hong AS, Ross-Degnan D, Zhang F, Wharam JF. Clinician-Level Predictors for **Ordering Low-Value Imaging**. JAMA Intern Med. 2017 Sep 25.
389. Lantz M, Sieurin J, Sjölander A, et al. **Migraine and risk of stroke**: a national population-based twin study. Brain. 2017 Oct 1;140(10):2653-2662.
390. Perry JJ, Sivilotti MLA, et al. Validation of the **Ottawa Subarachnoid Hemorrhage Rule in patients with acute headache**. CMAJ. 2017 Nov 13;189(45):E1379-E1385
391. Akram H, Miller S, Lagrata S, et al. Optimal **deep brain stimulation** site and target connectivity for chronic **cluster headache**. Neurology. 2017 Nov 14;89(20):2083-2091.
392. Friedman BW, et al. Randomized study of IV **prochlorperazine plus diphenhydramine vs IV hydromorphone** for migraine. Neurology. 2017 Nov 14;89(20):2075-2082
393. Palm-Meinders IH, Arkink EB, Koppen H, et al. Volumetric brain changes in **migraineurs** from the general population. Neurology. 2017 Nov 14;89(20):2066-2074.
394. Goadsby PJ, Reuter U, Hallström Y, et al. A controlled trial of **erenumab** for episodic migraine. N Engl J Med 2017;377:2123-32.
395. Silberstein SD, Dodick DW, Bigal ME, et al. **Fremanezumab** for the preventive treatment of chronic migraine. N Engl J Med 2017;377:2113-22.
396. Kim J, Cho SJ, Kim WJ, et al. **Insufficient sleep is prevalent among migraineurs**: a population-based study. J Headache Pain. 2017 Dec;18(1):50.
397. Tobis JM, et al. **Percutaneous Closure of Patent Foramen Ovale in Patients With Migraine**: The **PREMIUM** Trial. J Am Coll Cardiol. 2017 Dec 5;70(22):2766-2774.
398. Charles A. The **pathophysiology of migraine**: implications for clinical management. Lancet Neurol. 2017 Dec 8.
399. Hoffmann J, May A. Diagnosis, pathophysiology, and management of **cluster headache**. Lancet Neurol. 2017 Nov 23.
400. Skljarevski V, et al. Effect of Different Doses of **Galcanezumab** vs Placebo for Episodic Migraine Prevention: A Randomized Clinical Trial. JAMA Neurol. 2017 Dec 18.
401. Stensland SØ, Zwart JA, et al. The **headache of terror**: A matched cohort study of adolescents from the Utøya and the HUNT Study. Neurology. 2017 Dec 13.
402. Tobis JM, et al. **Percutaneous Closure of Patent Foramen Ovale** in Patients With Migraine: The **PREMIUM** Trial. J Am Coll Cardiol. 2017 Dec 5;70(22):2766-2774.
403. Adelborg K, Szépligeti SK, Holland-Bill L. **Migraine and risk of cardiovascular diseases**: Danish population based matched cohort study. BMJ 2018;360:k96.
404. Jarvis S, Dassan P, Piercy CN. **Managing migraine in pregnancy**. BMJ. 2018 Jan 25;360:k80.
405. Angus-Leppan H, Saatci D, Sutcliffe A, et al. **Abdominal migraine**. BMJ. 2018 Feb 19;360:k179.
406. Lai JT, Liu TC. Proposal for a New Diagnosis for **Cochlear Migraine**. JAMA Otolaryngol Head Neck Surg. 2018 Jan 18.
407. Mayans L, Walling A. **Acute Migraine Headache**: Treatment Strategies. Am Fam Physician. 2018;97(4):243-251
408. Orlova Y, Rizzoli P, Loder E. Association of **Coprescription of Triptan Antimigraine Drugs and Selective Serotonin Reuptake Inhibitor or Selective Norepinephrine Reuptake** Inhibitor Antidepressants With **Serotonin Syndrome**. JAMANeurol. 2018 Feb 26.
409. Dodick DW. **Migraine**. Lancet. 2018 Mar 6.
410. Micieli A, Robblee J. **Medication-overuse headache**. CMAJ. 2018 Mar 12;190(10):E296.
411. Patterson-Gentile C, Szperka CL. The Changing Landscape of **Pediatric Migraine Therapy**: A Review. JAMA Neurol. 2018 Mar 12.
412. Boddhula SK, Boddhula S, Gunasekaran K, et al. An unusual cause of thunderclap headache after eating the hottest pepper in the world - "The Carolina Reaper". BMJ Case Rep. 2018 Apr 9;2018.
413. Güven B, Güven H, Çomoğlu SS. **Migraine and Yawning**. Headache. 2018 Feb;58(2):210-216.
414. Wu C, Guan D, Ren M, et al. Aminophylline for treatment of **postdural puncture headache**: A randomized clinical trial. Neurology. 2018 Apr 24;90(17):e1523-e1529.
415. Cossack M, Nabrinsky E, Turner H, et al. Timolol Eyedrops in the Treatment of Acute Migraine Attacks: A Randomized Crossover Study. JAMA Neurol. 2018 May 14.
416. Dodick DW, Silberstein SD, Bigal ME, et al. Effect of **fremanezumab** compared with placebo for **prevention of episodic migraine**: a randomized clinical trial [online May 15, 2018]. JAMA. doi:10.1001/jama.2018.4853
417. Filipovic B, de Ru JA, Hakim S, et al. Treatment of Frontal Secondary Headache Attributed to Supratrochlear and Supraorbital Nerve Entrapment With Oral Medication or **Botulinum Toxin Type A vs Endoscopic Decompression Surgery**. JAMA Facial Plast Surg. 2018 May 10.
418. Gormley P, Kurki MI, Hiekkala ME, et al. Common Variant Burden Contributes to the **Familial Aggregation of Migraine** in 1,589 Families. Neuron. 2018 Apr 27.
419. Loder EW, Burch RC. Who Should Try New **Antibody Treatments for Migraine**? JAMA Neurol. 2018 May 21.
420. Stauffer VL, Dodick DW, Zhang Q, et al. Evaluation of **Galcanezumab** for the Prevention of Episodic Migraine: The **EVOLVE-1** Randomized Clinical Trial. JAMA Neurol. 2018 May 29.
421. Herd CP, Tomlinson CL, Rick C, et al. **Botulinum toxins for the prevention of migraine** in adults. Cochrane Database of Systematic Reviews 2018, Issue 6. Art. No.: CD011616. In chronic migraine, botulinum toxin type A may reduce the number of migraine days per month by 2 days compared with placebo treatment. Non-serious adverse events were probably experienced by 60/100 participants in the treated group compared with 47/100 in the placebo group. For people with episodic migraine, we remain uncertain whether or not this treatment is effective because the quality of this limited evidence is very low.

422. Leite Pacheco R, de Oliveira Cruz Latorraca C, Adriano Leal Freitas da Costa A, et al. **Melatonin for preventing primary headache**: A systematic review. Int J Clin Pract. 2018 May 24:e13203. This review found that so far there are few clinical trials, with poor methodological quality about melatonin for primary headaches. The available evidence is not sufficient to support the use of melatonin in clinical practice for this population.
423. Schulte LH, Allers A, May A. Visual stimulation leads to activation of the **nociceptive trigeminal nucleus in chronic migraine**. Neurology. 2018 May 29;90(22):e1973-e1978.
424. Tassorelli C, Grazzi L, de Tommaso M, et al. Noninvasive **vagus nerve stimulation** as acute **therapy for migraine**: The randomized PRESTO study. Neurology. 2018 Jun 15.
425. Zorrilla-Vaca A, Mathur V, Wu CL, Grant MC. The Impact of **Spinal Needle Selection on Postdural Puncture Headache**: A Meta-Analysis and Metaregression of Randomized Studies. Reg Anesth Pain Med. 2018 Jul;43(5):502-508.
426. Pdf Hwang J-H, Tsai S-J, Liu T-C, Chen Y-C, Lai J-T. **Association of tinnitus and other cochlear disorders with a history of migraines** [online July 12, 2018]. JAMA Otolaryngol Head Neck Surg. doi:10.1001/jamaoto.2018.0939
427. Lipton RB, Goadsby PJ. Comment: Noninvasive **neurostimulation for migraine** should be part of the general neurologist's therapeutic armamentarium. Neurology. 2018 Jul 24;91(4):167.
428. van Oosterhout WPJ, Schoonman GG, van Zwet EW, et al. **Female sex hormones in men with migraine**. Neurology. 2018 Jun 27.
429. Vollesen ALH, Snoer A, Beske RP, et al. Effect of **infusion of calcitonin gene-related peptide on cluster headache attacks**: a randomized clinical trial [online July 9, 2018]. JAMA Neurol. doi:10.1001/jamaneurol.2018.1675
430. Mollan SP, Spitzer D, Nicholl DJ. **Raised intracranial pressure in those presenting with headache**. BMJ. 2018 Oct 4;363:k3252
431. Snoer A, Lund N, Beske R, et al. **Cluster headache beyond the pain phase**: A prospective study of 500 attacks. Neurology. 2018 Aug 28;91(9):e822-e831.
432. VanderPluym J, Dodick DW, Lipton RB, et al. **Fremanezumab for preventive treatment of migraine**: Functional status on headache-free days. Neurology. 2018 Sep 18;91(12):e1152-e1165.
433. GBD 2016 Headache Collaborators. Global, regional, and national **burden of migraine and tension-type headache**, 1990-2016: a systematic analysis for the Global Burden of Disease Study 2016. Lancet Neurol. 2018 Nov;17(11):954-976.
434. Kontorinis G, Tyagi A, Crowther JA. **Recurrent vertigo** associated with headaches. BMJ. 2018 Oct 31;363:k1807.
435. Reuter U, Goadsby PJ, Lanteri-Minet M, et al. **Efficacy and tolerability of erenumab** in patients with episodic migraine in whom two-to-four previous preventive treatments were unsuccessful: a randomised, double-blind, placebo-controlled, phase 3b study. (**LIBERTY**) Lancet 2018; published online Oct 22.
436. Kuca B, Silberstein SD, Wietecha L, et al. **Lasmiditan is an effective acute treatment for migraine**: A phase 3 randomized study. Neurology. 2018 Nov 16.
437. Reisman AM, Robbins BT, Chou DE, et al. Ticagrelor for Refractory Migraine/Patent Foramen Ovale (**TRACTOR**): An open-label pilot study. Neurology. 2018 Nov 27;91(22):1010-1017.
438. Sen S, Androulakis XM, Duda V, et al. Migraine with **visual aura a risk factor for incident atrial fibrillation**: A cohort study. Neurology. 2018 Nov 14.
439. Sommer RJ, Nazif T, Privitera L, Robbins BT. Retrospective review of **thienopyridine therapy in migraineurs with patent foramen ovale**. Neurology. 2018 Nov 27;91(22): 1002-1009.
440. Detke HC, Goadsby PJ, Wang S, et al. **Galcanezumab in chronic migraine**: The randomized, double-blind, placebo-controlled REGAIN study. Neurology. 2018 Nov 16.
441. Hamilton KT, Robbins MS. Migraine **Treatment in Pregnant Women** Presenting to Acute Care: A Retrospective Observational Study. Headache. 2018 Nov 7.
442. Sen S, Androulakis XM, Duda V, et al. Migraine with **visual aura is a risk factor for incident atrial fibrillation**: a cohort study. Neurology 2018;91:e2202–e2210.
443. Albrecht P, Jansen A, Lee JI, et al. High prevalence of **neutralizing antibodies after long-term botulinum neurotoxin therapy**. Neurology. 2019 Jan 1;92(1):e48-e54.
444. Fagherazzi G, El Fatouhi D, Fournier A, et al. Associations between **migraine and type 2 diabetes in women**: findings from the E3N cohort study [online Dec 17, 2018]. JAMA Neurol. doi:10.1001/jamaneurol.2018.3960
445. Ha H, Gonzalez A. **Migraine Headache Prophylaxis**. Am Fam Physician. 2019; 99(1):17-24.
446. American Headache Society. The American Headache Society Position Statement On **Integrating New Migraine Treatments** Into Clinical Practice. Headache. 2019 Jan;59(1):1-18.
447. Latev A, Friedman BW, Irizarry E, et al. A Randomized Trial of a Long-Acting **Depot Corticosteroid Versus Dexamethasone** to Prevent Headache Recurrence Among Patients With Acute Migraine Who Are Discharged From an Emergency Department. Ann Emerg Med. 2018 Nov 15.
448. Loder E, Renthal W. **Calcitonin Gene-Related Peptide Monoclonal Antibody Treatments** for Migraine. JAMA Intern Med. 2019 Jan 14.
449. Wang R, Liu R, Dong Z, et al. **Unnecessary neuroimaging** for patients with primary headaches. Headache. 2018;23.
450. Androulakis XM, Sen S, Kodumuri N, et al. Migraine **Age of Onset and Association With Ischemic Stroke** in Late Life: 20 Years Follow-Up in ARIC. Headache. 2019 Jan 21.
451. Kim SK, Hong SM, Park IS, Choi HG. Association Between Migraine and **Benign Paroxysmal Positional Vertigo Among Adults** in South Korea. JAMA Otolaryngol Head Neck Surg. 2019 Jan 24.
452. Pearson SM, Burish MJ, Shapiro RE, et al. Effectiveness of **Oxygen and Other Acute Treatments** for Cluster Headache: Results From the Cluster Headache Questionnaire, an International Survey. Headache. 2019 Feb;59(2):235-249.
453. Stilling JM, Monchi O, Amoozegar F, Debert CT. **Transcranial Magnetic and Direct Current Stimulation** (TMS/tDCS) for the Treatment of Headache: A Systematic Review. Headache. 2019 Jan 23

454. Vatzaki E, Straus S, Dogne JM, et al. Latest **clinical recommendations on valproate use** for migraine prophylaxis in women of childbearing age: overview from European Medicines Agency and European Headache Federation. J Headache Pain. 2018 Aug 14;19(1):68.
455. Domínguez C, López A, Ramos-Cabrer P, et al. **Iron deposition in periaqueductal gray matter** as a potential biomarker for chronic migraine. Neurology. 2019 Mar 5;92(10):e1076-e1085.
456. Ismail OM, Poole ZB, Bierly SL, et al. Association Between **Dry Eye Disease and Migraine Headaches** in a Large Population-Based Study. JAMA Ophthalmol. 2019 Mar 7.
458. Lapucci C, Saitta L, Bommarito G,et al. How much do **periventricular lesions assist in distinguishing migraine with aura from CIS**? Neurology. 2019 Apr 9;92(15):e1739-e1744.
459. Onderwater GLJ, Ligthart L, Bot M, et al. Large-scale **plasma metabolome analysis reveals alterations in HDL metabolism** in migraine. Neurology. 2019 Apr 16;92(16):e1899-e1911.
460. Deen M, Hougaard A, Hansen HD, et al. Association Between **Sumatriptan Treatment During a Migraine Attack and Central 5-HT1B Receptor Binding**. JAMA Neurol. 2019 May 28.
461. Onderwater GLJ, van Oosterhout WPJ, Schoonman GG, et al. Alcoholic beverages as trigger factor and the effect on **alcohol consumption behavior in patients with migraine**. Eur J Neurol. 2019 Apr;26(4):588-595.
462. Pijpers JA, Kies DA, Louter MA, et al. **Acute withdrawal and botulinum toxin A** in chronic migraine with medication overuse: a double-blind randomized controlled trial. Brain. 2019 May 1;142(5):1203-1214.
463. Lipton RB, Tepper SJ, Reuter U, et al. **Erenumab in chronic migraine**:Patient-reported outcomes in a randomized double-blind study. Neurology. 2019 May 7;92(19):e2250-e2260.
464. Nagata JM, Weiser SD, Gooding HC, et al. Association Between **Food Insecurity and Migraine** Among US Young Adults. JAMA Neurol. 2019 Jun 24.
465. Tepper SJ, Diener HC, Ashina M, et al. **Erenumab in chronic migraine with medication overuse**: Subgroup analysis of a randomized trial. Neurology. 2019 May 14;92(20):e2309-e2320.
466. Goadsby PJ, Dodick DW, Leone M, et al. Trial of **Galcanezumab in Prevention of Episodic Cluster Headache**. N Engl J Med. 2019 Jul 11;381(2):132-141.
467. Li V, McArdle H, Trip SA. **Vestibular migraine**. BMJ. 2019 Jul 3;366:l4213.
468. Lipton RB, Croop R, Stock EG, et al. **Rimegepant,** an Oral Calcitonin Gene-Related Peptide Receptor Antagonist, for Migraine. N Engl J Med. 2019 Jul 11;381(2):142-149.
469. Croop R, Goadsby PJ, Stock DA, et al. Efficacy, safety, and tolerability of **rimegepant orally disintegrating tablet** for the acute treatment of migraine: a randomised, phase 3, double-blind, placebo-controlled trial. Lancet. 2019 Jul 12.
470. Ford JH, Ayer DW, Zhang Q, et al. Two randomized **migraine studies of galcanezumab**: Effects on patient functioning and disability. Neurology. 2019 Jul 30;93(5):e508-e517.
471. Sharpe L, Dudeney J, Williams ACC, et al. **Psychological therapies** for the prevention of migraine in adults. Cochrane Database Syst Rev. 2019 Jul 2;7:CD012295. This review identified 21 studies of psychological interventions for the management of migraine. We did not find evidence that psychological interventions affected migraine frequency, a result based on four studies of primarily brief treatments. Those who received psychological interventions were twice as likely to be classified as responders in the short term, but this was based on very low-quality evidence and there was no evidence of an effect of psychological intervention compared to control at follow-up.
472. Steinberg A, Josefsson P, Alexanderson K, Sjöstrand C. **Cluster headache**: Prevalence, sickness absence, and disability pension in working ages in Sweden. Neurology. 2019 Jul 23;93(4):e404-e413.
473. Ferrari MD, Diener HC, Ning X, et al. **Fremanezumab versus placebo** for migraine prevention in patients with documented failure to up to four migraine preventive medication classes (FOCUS): a randomised, double-blind, placebo-controlled, phase 3b trial. Lancet. 2019 Aug 16.
474. Fiedler-Kelly JB, Cohen-Barak O, Morris DN, et al. Population pharmacokinetic modeling and simulation of **fremanezumab** in healthy subjects and patients with migraine. Br J Clin Pharmacol. 2019 Aug 16.
475. Oskoui M, Pringsheim T, Holler-Managan Y, et al. Practice guideline update summary: **Acute treatment of migraine in children and adolescents**: Report of the Guideline Development, Dissemination, and Implementation Subcommittee of the American Academy of Neurology and the American Headache Society. Neurology. 2019 Aug 14.
476. Oskoui M, Pringsheim T, Billinghurst L, et al. Practice guideline update summary: **Pharmacologic treatment for pediatric migraine prevention**: Report of the Guideline Development, Dissemination, and Implementation Subcommittee of the American Academy of Neurology and the American Headache Society. Neurology. 2019 Aug 14.
477. Tfelt-Hansen P, Messlinger K. Why is the **therapeutic effect of acute antimigraine drugs** delayed? A review of controlled trials and hypotheses about the delay of effect. Br J Clin Pharmacol. 2019 Aug 6.
478. Morton RE, St John PD, Tyas SL. **Migraine and the risk** of all-cause dementia, Alzheimer's disease, and vascular dementia: A prospective cohort study in community-dwelling older adults. Int J Geriatr Psychiatry. 2019 Sep 4.
479. Mostofsky E, Mittleman MA, Buettner C, et al. Prospective Cohort Study of **Caffeinated Beverage Intake as a Potential Trigger** of Headaches among Migraineurs. Am J Med. 2019 Aug 2.
480. Wei DY, Khalil M, Goadsby PJ. **Managing cluster headache**. Pract Neurol. 2019 Jul 5.
481. Lambru G, Rantell K, Levy A, Matharu MS. A prospective comparative study and analysis of **predictors of SUNA and SUNCT**. Neurology. 2019 Sep 17;93(12):e1127-e1137.
482. Moore AR, Wieczorek PM, Carvalho JCA. Association Between **Post-Dural Puncture Headache After Neuraxial Anesthesia** in Childbirth and Intracranial Subdural Hematoma. JAMA Neurol. 2019 Sep 16.
483. Ziegeler C, May A. **Facial presentations** of migraine, TACs, and other paroxysmal facial pain syndromes. Neurology. 2019 Sep 17;93(12):e1138-e1147.

References – RxFiles Migraine/Headache Overview

[1] Pringsheim T, Davenport W, Mackie G, Worthington I, Aube M, Christie SN, Gladstone J, Becker WJ. Canadian Headache Society Prophylactic Guidelines Development Group. Canadian Headache Society Guideline for Migraine Prophylaxis. *Canadian Journal of Neurological Sciences* 2012; 39(2) Suppl 2: S1-59.

[1b] Jelinski SE, Becker WJ, Christie SN et al. Clinical features and pharmacological treatment of migraine patients referred to headache specialists in Canada. *Cephalalgia* 2006; 26:578–588.

[2] Gilmore B, Magdalena M. Treatment of Acute Migraine Headache. *Am Fam Physician* 2011; 83(3):271-280.

[3] Worthington I, Pringsheim T, Gawal M, et al. Canadian Headache Society Acute Migraine Treatment Guideline Development Group. Can J Neurol Sci. 2013;40:Suppl. 3. S1-S80.

[4] Shamliyan TA, Kane RL, Taylor FR. Migraine in Adults: Preventive Pharmacologic Treatments. Comparative Effectiveness Review No. 103. (Prepared by the University of Minnesota Evidence-based Practice Center under Contract No. 290-2007-10064-I) AHRQ Publication No. 13-EHC068-EF. Rockville, MD: Agency for Healthcare Research and Quality; April 2013. www.effectivehealthcare.ahrq.gov/reports/final.cfm.

[5] Lipton RB, Scher AI, Kolodner K, et al. Migraine in the United States: epidemiology and patterns of health care use. Neurology. 2002 Mar 26;58(6):885-94. PMID 11914403

[6] Lipton RB, Bigal ME, Diamon M, et al. Migraine prevalence, disease burden, and the need for preventive therapy. Neurology. 2007 Jan 30;68(5):343-9. PMID 17261680

[7] Silberstein SD. Practice parameter: Evidence-based guidelines for migraine headache (an evidence-based review). Report of the Quality Standards Subcommittee of the American Academy of Neurology. *Neurology* 2000; 55(6):754-762.

[8] McCrory DC, Gray RN. Oral sumatriptan for acute migraine. *Cochrane Database Syst Rev* 2003;(3):CD002915.

[9] Ferrari MD, et al. Oral triptans (serotonin 5-HT1B/1D agonists) in acute migraine treatment: a meta-analysis of 53 trials. *Lancet* 2001; 358:1668-75.

[10] Migraine Patient Decision Aid: Is one triptan better than another? NPC 2009, http://www.npc.nhs.uk/therapeutics/pain/migraine/resources/pda_migraine.pdf accessed October 15, 2013

[11] Goadsby PJ, Goldberg J, Silberstein SD. Migraine in pregnancy. BMJ. 2008 Jun 28;336(7659):1502-4.

[12] Martin V, Behbehani MM. Toward a Rational Understanding of Migraine Trigger Factors. *Med Clin North Am* 2001; 85(4): 911-941.

[13] Kelman L. The triggers or precipitants of the acute migraine attack. *Cephalalgia* 2007 May; 27(5):394-402

[14] Clinch R. Evaluation of acute headaches in adults. Am Fam Physician 2001;63:685-92.

[15] Beithon J, Gallenberg M, Johnson K, Kildahl P, Krenik J, Liebow M, Linbo L, Myers C, Peterson S, Schmidt J, Swanson J. Institute for Clinical Systems Improvement. Diagnosis and Treatment of Headache. http://bit.ly/Headache0113. Updated January 2013.https://www.icsi.org/_asset/qwrznq/Headache.pdf.3, accessed October 25, 2013

[16] Hainer BL, Matheson EM. Approach to Acute Headache in Adults. Am Fam Physician. 2013;87(10):682-7

[17] Purdy RA. Neurological Disorders: Headache in Adults. e-Therapeutics. July 2011. Accessed: October 2012

[18] Headache Classification Subcommitee of the International Headache Society. The International Classification of Headache Disorders, 2nd ed. *Cephalgia* 2004; 24 (suppl 1). Available from: http://www.ihs-headache.org/upload/ct_clas/ihc_II_main_no_print.pdf Accessed on: 29 January 2013.

[19] Institute for Clinical Systems Improvement (ICSI). Diagnosis and treatment of headache. Bloomington (MN): Institute for Clinical Systems Improvement (ICSI); 2011 Jan. 84 p. [147 references]

[20] Saguil A, Lax J. Implementing AHRQ Effective Health Care Reviews. Helping Clinicians Make Better Treatment Choices. Acute Migraine Treatment in Emergency Settings. American Family Physician; 2014;89(9):742-4.

[1] Miyasaki JM, Martin W, Suchowersky O, Weiner WJ, Lang AE. Practice parameter: initiation of treatment for Parkinson's disease: an evidence-based review: report of the Quality Standards Subcommittee of the **American** Academy of Neurology. Neurology. **2002** Jan 8;58(1):11-7.
Postuma RB, Berg D, Stern M, et al. **MDS clinical diagnostic criteria for Parkinson's disease**. Mov Disord. 2015 Oct;30(12):1591-601.
Zesiewicz, T. A., Sullivan, K. L., Arnulf, I., et al. **AAN Practice Parameter**: Treatment of **nonmotor symptoms of Parkin**son disease: Report of the Quality Standards Subcommittee of the American Academy of Neurology. Neurology **2010** 74: 924-931.
Young GB, Findlay JM, Benstead TJ, et al; Canadian Neurological Sciences Federation team. **Canadian Guidelines on Parkinson's Disease**. Can J Neurol Sci. 2012 July;(39)4.
Grimes D, Fitzpatrick M, Gordon J. **Canadian guideline for Parkinson disease.** CMAJ **2019**;191:E989-1004.

[2] Therapeutic Choices 4rd Edition, 2003
[3] **Treatment Guidelines**: **Drugs for Parkinson's Disease**. **The Medical Letter**: June, 2004 (Vol 2, Issue 22) pp. 41-46. Updated Oct, 2007; Jan 2011; Nov 2013 & **Nov 2017.**
Chou KL. In the Clinic: **Parkinson Disease**. Ann Intern Med Nov 6, 2012. ITC5-2.
[4] Micromedex 2018
[5] Guttman M, Kish SJ, Furukawa Y. Current concepts in the **diagnosis and management** of **Parkinson's disease**. **CMAJ**. **2003** Feb 4;168(3):293-301.
[6] Rascol O, Goetz C, Koller W, Poewe W, Sampaio C. Treatment interventions for **Parkinson's** disease: an **evidence based** assessment. **Lancet**. **2002** May 4;359(9317):1589-98.
[7] Olanow CW, Watts RL, Koller WC. An **algorithm** (decision tree) for the management of Parkinson's disease (**2001**): treatment guidelines. Neurology. 2001 Jun;56(11 Suppl 5):S1-S88.
[8] Olanow CW, Agid Y, Mizuno Y, et al. **Levodopa** in the treatment of Parkinson's disease: current controversies. Mov Disord. 2004 Sep;19(9):997-1005.
Lewitt PA. Levodopa for the treatment of Parkinson's disease. N Engl J Med. 2008 Dec 4;359(23):2468-76.
[9] Nyholm D, Nilsson Remahl AI, et al. **Duodenal** levodopa infusion monotherapy vs oral polypharmacy in advanced Parkinson disease. Neurology. 2005 Jan 25;64(2):216-23.
Calandrella D, Romito LM, Elia AE, et al. Albanese A. **Causes of withdrawal of duodenal levodopa infusion** in advanced Parkinson disease. Neurology. 2015 Mar 25.
[10] Nahata MC, Morosco RS, Leguire LE. Development of two stable oral suspensions of levodopa-carbidopa for children with amblyopia. J Pediatr Ophthalmol Strabismus. 2000 Nov-Dec;37(6):333-7.
[11] The Hospital for Sick Children -SickKids: oral suspension levodopa-carbidopa formula last revised March 2002 http://www.sickkids.ca/pharmacy/custom/levodopa.asp
[12] **Stalevo** for Parkinson's disease. Med Lett Drugs Ther. 2004 May 10;46(1182):39-40.
[13] Ahlskog JE, Muenter MD. Frequency of **levodopa**-related dyskinesias and motor fluctuations as estimated from the cumulative literature. Mov Disord. 2001 May;16(3):448-58.
[14] Koller WC, Hutton JT, Tolosa E, et al. Immediate-release & **controlled**-**release** carbidopa/levodopa in PD: a 5-year randomized multicenter study. Carbidopa/Levodopa Study Group. Neurology. 1999 Sep 22;53(5):1012-9.
[15] Fahn S, Oakes D, Shoulson I, Kieburtz K, Rudolph A, Lang A, Olanow CW, et al. Parkinson Study Group. **Levodopa** and the progression of Parkinson's disease. N Engl J Med. 2004 Dec 9;351(24):2498-508.
[16] Inzelberg R, Schechtman E, Nisipeanu P. **Cabergoline**, **pramipexole** and **ropinirole** used as monotherapy in early Parkinson's disease: an evidence-based comparison. Drugs Aging. 2003;20(11):847-55.
[17] Albin RL, Frey KA. Initial agonist treatment of Parkinson disease: a critique. Neurology. 2003 Feb 11;60(3):390-4.
Stowe R, Ives Nj, Clarke C et al. **Dopamine agonist therapy in early Parkinson's disease. Cochrane** Database Syst Rev. 2008 Apr 16;(2):CD006564. This meta-analysis confirms that motor complications are reduced with dopamine agonists compared to levodopa, but also establishes that other important side-effects are increased and symptom control is poorer with agonists. Larger, long-term comparative trials assessing patient-rated quality of life are needed to assess more reliably the balance of benefits and risks of dopamine agonists compared to levodopa.
Antonini A, Tolosa E, Mizuno Y, Yamamoto M, Poewe WH. A reassessment of risks and benefits of dopamine agonists in Parkinson's disease. Lancet Neurol. 2009 Aug 24. [Epub ahead of print]
[18] Holloway RG, Shoulson I, Fahn S, et al. Parkinson Study Group. **Pramipexole vs levodopa** as initial treatment for Parkinson disease: a 4-year randomized controlled trial. Arch Neurol. 2004 Jul;61(7):1044-53.
[19] Navan P, Findley LJ, Jeffs JA, Pearce RK, et al. Randomized, double-blind, 3-month parallel study of the effects of **pramipexole**, **pergolide**, and placebo on Parkinsonian tremor. Mov Disord. 2003 Nov;18(11):1324-31.
[20] Parkinson Study Group. **Pramipexole vs levodopa** as initial treatment for Parkinson disease: A randomized controlled trial. Parkinson Study Group (CALM-PD). JAMA. 2000 Oct 18;284(15):1931-8.
[21] Guttman M. Double-blind comparison of **pramipexole & bromocriptine** treatment with placebo in advanced Parkinson's disease. International Pramipexole-Bromocriptine Study Group. Neurology. 1997 Oct;49(4):1060-5.
[22] Moller JC, Oertel WH, Koster J, Pezzoli G, Provinciali L. Long-term efficacy and safety of **pramipexole** in advanced Parkinson's disease: results from a European multicenter trial. Mov Disord. 2005 May;20(5):602-10.
[23] Holman AJ, Myers RR. A randomized, double-blind, placebo-controlled trial of **pramipexole**, a dopamine agonist, in patients with fibromyalgia receiving concomitant medications. Arthritis Rheum. 2005 Aug;52(8):2495-505.
[24] Whone AL, Watts RL, Stoessl AJ, et al.; **REAL-PET** Study Group. Slower progression of Parkinson's disease with **ropinirole versus levodopa**: The REAL-PET study. Ann Neurol. 2003 Jul;54(1):93-101.
[25] Korczyn AD, Brunt ER, Larsen JP, et al. A 3-year randomized trial of **ropinirole** and bromocriptine in early Parkinson's disease. The 053 Study Group. Neurology. 1999 Jul 22;53(2):364-70. Erratum in: Neurology 1999 Sep 22;53(5):1162.
[26] Rascol O, Brooks DJ, Korczyn AD, et al. A **five-year** study of the incidence of dyskinesia in patients with early Parkinson's disease who were treated with **ropinirole or levodopa**. 056 Study Group. N Engl J Med. 2000 May 18;342(20):1484-91.
[27] Cassano P, Lattanzi L, Fava M, Navari S, Battistini G, Abelli M, Cassano GB. **Ropinirole** in treatment-resistant depression: a 16-week pilot study. Can J Psychiatry. 2005 May;50(6):357-60.
[28] van Hilten JJ, Ramaker C, Van de Beek WJ, Finken MJ. Bromocriptine for **levodopa**-induced motor complications in Parkinson's disease. Cochrane Database Syst Rev. 2000;(2):CD001203.
[29] Ramaker C, Hilten JJ. **Bromocriptine/levodopa** combined versus levodopa alone for early Parkinson's disease. Cochrane Database Syst Rev. 2002;(2):CD003634.
[30] Lees AJ, Katzenschlager R, Head J, Ben-Shlomo Y. **Ten-year** follow-up of three different initial treatments in de-novo PD: a randomized trial (PDRGUK). Neurology. 2001 Nov 13;57(9):1687-94.
[31] Hely MA, Morris JG, Reid WG, Trafficante R. Sydney multicenter study of Parkinson's disease: Non-L-dopa-responsive problems dominate at **15 years**. Mov Disord. 2004 Nov 18
[32] Hely MA, Morris JG, Traficante R, et al. The sydney multicentre study of Parkinson's disease: progression and mortality at **10 years**. J Neurol Neurosurg Psychiatry. 1999 Sep;67(3):300-7.
[33] Bracco F, Battaglia A, Chouza C, et al. PKDS009 Study Group. The long-acting dopamine receptor agonist **cabergoline** in early Parkinson's disease: final results of a 5-year, double-blind, levodopa-controlled study. CNS Drugs. 2004;18(11):733-46.
[34] Rinne UK, Bracco F, Chouza C, et al. Early treatment of Parkinson's disease with **cabergoline** (**3-5yr trial)** delays the onset of motor complications. Results of a double-blind levodopa controlled trial. The PKDS009 Study Group. Drugs. 1998;55 Suppl 1:23-30.
[35] Pinero A, Marcos-Alberca P, Fortes J. **Cabergoline**-related severe restrictive mitral regurgitation. N Engl J Med. 2005 Nov 3;353(18):1976-7.
[36] Clarke CE, Guttman M. **Dopamine agonist** monotherapy in Parkinson's disease. Lancet. 2002 Nov 30;360(9347):1767-9.
Katzenschlager R, Head J, Schrag A, Ben-Shlomo Y, Evans A, Lees AJ; On behalf of the Parkinson's Disease Research Group of the United Kingdom. Fourteen-year final report of the randomized **PDRG-UK** trial comparing three initial treatments in PD. Neurology. 2008 Jun 25. [Epub ahead of print] Initial treatment with the dopamine agonist bromocriptine did not reduce mortality or motor disability and the initially reduced frequency in motor complications was not sustained. We found no evidence of a long-term benefit or clinically relevant disease-modifying effect with initial dopamine agonist treatment.
[37] Frucht S, Rogers JD, Greene PE, Gordon MF, Fahn S. **Falling asleep** at the wheel: motor vehicle mishaps in persons taking **pramipexole** and **ropinirole**. Neurology. 1999 Jun 10;52(9):1908-10.
[38] Hobson DE, Lang AE, Martin WR, et al. **Excessive daytime sleepiness** and sudden-onset **sleep** in Parkinson disease: a survey by the Canadian Movement Disorders Group. JAMA. 2002 Jan 23-30;287(4):455-63.
[39] Paus S, Brecht HM, Koster J, Seeger G, Klockgether T, Wullner U. **Sleep attacks**, daytime sleepiness, and dopamine agonists in Parkinson's disease. Mov Disord. 2003 Jun;18(6):659-67.
Tholfsen LK, Larsen JP, Schulz J, et al. Development of excessive daytime sleepiness in early Parkinson disease. Neurology. 2015 Jul 14;85(2):162-8.
[40] Driver-Dunckley E, Samanta J, Stacy M. Pathological **gambling** associated with dopamine agonist therapy in Parkinson's disease. Neurology. 2003 Aug 12;61(3):422-3.
Moore TJ, Glenmullen J, Mattison DR. Reports of pathological gambling, hypersexuality, and compulsive shopping associated with dopamine receptor agonist drugs [online October 20, 2014]. JAMA Intern Med. doi: 10.1001/jamainternmed.2014.5262.
Corvol JC, Artaud F, Cormier-DeQuaire F, et al. Longitudinal analysis of impulse control disorders in Parkinson disease. Neurology 2018;91:e189–e201.
[41] Dodd ML, Klos KJ, Bower JH, Geda YE, Josephs KA, Ahlskog JE. Pathological **Gambling** Caused by Drugs Used to Treat Parkinson Disease. Arch Neurol. 2005 Jul 11; [Epub ahead of print]
[42] April,2003 Health Canada warning **Permax** and **cardiac valvulopathy** http://www.hc-sc.gc.ca/hpfb-dgpsa/tpd-dpt/permax_dhpl_e.pdf
[43] Van Camp G, Flamez A, Cosyns B, et al. Treatment of Parkinson's disease with **pergolide** and relation to restrictive **valvular** heart disease. Lancet. 2004 Apr 10;363(9416):1179-83.
[44] Van Camp G, Flamez A, Cosyns B, Goldstein J, Perdaens C, Schoors D. Heart **valvular** disease in patients with Parkinson's disease treated with high-dose **pergolide**. Neurology. 2003 Sep 23;61(6):859-61.
[45] Pinero A, Marcos-Alberca P, Fortes J. **Cabergoline**-related severe restrictive mitral regurgitation. N Engl J Med. 2005 Nov 3;353(18):1976-7. (Concern because reports of drug being abused: may prolong orgasms in men) (Yamamoto M, Uesugi T, Nakayama T. Dopamine agonists and cardiac **valvulopathy** in Parkinson disease: a case-control study. Neurology. 2006 Oct 10;67(7):1225-9. The frequency of valvulopathy was significantly increased in the cabergoline group. Our results indicate that high cumulative dose and long-term treatment with cabergoline are risk factors for valvulopathy in patients with Parkinson disease. & Junghanns S, Fuhrmann JT, et al. **Valvular heart disease** in Parkinson's disease patients treated with dopamine agonists: A reader-blinded monocenter echocardiography study. Mov Disord. 2006 Nov 8; [Epub ahead of print] Our data suggest that ergot DAs are associated with higher prevalence of VHD compared to non-ergot DAs and controls. Standard echocardiography seems sufficient to detect VHD in PD patients treated with DAs.) (Schade R, Andersohn F, Suissa S, et al. Dopamine agonists and the risk of cardiac-valve regurgitation. N Engl J Med 2007; 356:29-38. (InfoPOEMs: The risk of cardiac valve damage is elevated in patients taking pergolide (Permax) or cabergoline (Dostinex), especially if the dose is higher than 3 mg per day and the drug is taken for more than 6 months. The absolute risk is modest: approximately 2.5 additional cases of valve damage for every 1000 patients who take one of the drugs for 1 year. (LOE = 3b))
Zanettini R, Antonini A, Gatto G, et al. Valvular heart disease and the use of dopamine agonists for Parkinson's disease. N Engl J Med 2007; 356:39-46. Roth BL. Drugs and valvular heart disease. N Engl J Med 2007; 356:6-9. According to a Perspective accompanying the two studies, the new findings support prior clinical and mechanistic evidence for a link between a histologically distinct fibrotic valvulopathy and treatment with drugs that block the serotonin receptor 5-hydroxytryptamine 2B (5-HT2B). Pergolide and cabergoline have that biochemical action in common, while the other studied dopamine antagonists don't have significant effects on **5-HT2B**.)
Colao A, Galderisi M, Di Sarno A, et al. Increased prevalence of tricuspid regurgitation in patients with prolactinomas chronically treated with cabergoline. J Clin Endocrinol Metab. 2008 Oct;93(10):3777-84. Epub 2008 Aug 5.
[46] Katzenschlager R, Sampaio C, Costa J, Lees A. **Anticholinergics** for symptomatic management of Parkinson's disease. Cochrane Database Syst Rev. 2003;(2):CD003735.
[47] Ancelin ML, et al. Non-degenerative mild **cognitive impairment** in elderly people and use of **anticholinergic** drugs: longitudinal cohort study. BMJ. 2006 Feb 25;332(7539):455-9. Epub 2006 Feb 1.
[48] Uitti RJ, Rajput AH, Ahlskog JE, Offord KP, Schroeder DR, Ho MM, et al. **Amantadine** treatment is an independent predictor of improved survival in Parkinson's disease. Neurology. 1996 Jun;46(6):1551-6.
[49] Inzelberg R, Bonuccelli U, Schechtman E, Miniowich A, Strugatsky R, CeravoloR, Logi C, Rossi C, Klein C, Rabey JM. Association between amantadine and the onset of dementia in Parkinson's disease. Mov Disord. 2006 May 16; [Epub ahead of print]
[50] Thomas A, Iacono D, Luciano AL, Armellino K, Di Iorio A, Onofrj M. Duration of **amantadine** benefit on dyskinesia of severe Parkinson's disease. J Neurol Neurosurg Psychiatry. 2004 Jan;75(1):141-3.
Ory-Magne F, Corvol JC, Azulay JP, et al. Withdrawing amantadine in dyskinetic patients with Parkinson disease: the AMANDYSK trial. Neurology 2014;82:300–307.
[51] Crosby NJ, Deane KH, Clarke CE. **Amantadine** for dyskinesia in Parkinson's disease. Cochrane Database Syst Rev. 2003;(2):CD003467.
Elahi B, Phielipp N, Chen R. **N-methyl-d-aspartate antagonists (amantadine)** in levodopa induced dyskinesia: a meta-analysis. Can J Neurol Sci. 2012 Jul;39(4):465-72.
Gottwald MD, Aminoff MJ. Emerging Therapies for **Dopaminergic-induced Dyskineasias** in Parkinson's Disease. Annals of Neurology. Accepted manuscript online: 16 MAR 2011; 1-17.
[52] Brooks DJ, Sagar H; UK-Irish Entacapone Study Group. **Entacapone** is beneficial in both fluctuating and non-fluctuating patients with Parkinson's disease: a randomised, placebo controlled, double blind, six month study. J Neurol Neurosurg Psychiatry. 2003 Aug;74(8):1071-9.
[53] Myllyla VV, Kultalahti ER, Haapaniemi H, Leinonen M; FILOMEN Study Group. Twelve-month safety of **entacapone** in patients with Parkinson's disease. Eur J Neurol. 2001 Jan;8(1):53-60.
[54] **Entacapone** improves motor fluctuations in levodopa-treated Parkinson's disease patients. Parkinson Study Group. Ann Neurol. 1997 Nov;42(5):747-55.
[55] Larsen JP, Worm-Petersen J, Siden A, Gordin A, et al.; NOMESAFE Study Group. The tolerability and efficacy of entacapone over **3 years** in patients with Parkinson's disease. Eur J Neurol. 2003 Mar;10(2):137-46.
[56] Poewe WH, Deuschl G, Gordin A, Kultalahti ER, Leinonen M; Celomen Study Group. Efficacy and safety of **entacapone** in Parkinson's disease patients with suboptimal levodopa response: a 6-month randomized placebo-controlled double-blind study in Germany and Austria (Celomen study).

Acta Neurol Scand. 2002 Apr;105(4):245-55.
[57] Deane K, Spieker S, Clarke C. **Catechol-O-methyltransferase** inhibitors for levodopa-induced complications in Parkinson's disease. Cochrane Database Syst Rev. 2004 Oct 18;(4):CD004554.
[58] Olanow CW, Kieburtz K, Stern M, et al.; US01 Study Team. Double-blind, placebo-controlled study of **entacapone** in **levodopa**-treated patients with stable Parkinson disease. Arch Neurol. 2004 Oct;61(10):1563-8.
[59] Mortality in **DATATOP**: a multicenter trial in early Parkinson's disease. Parkinson Study Group. Ann Neurol. 1998 Mar;43(3):318-25.
[60] Impact of **deprenyl** and **tocopherol** treatment on Parkinson's disease in DATATOP patients requiring levodopa. Parkinson Study Group. Ann Neurol. 1996 Jan;39(1):37-45.
[61] Impact of deprenyl and **tocopherol** treatment on Parkinson's disease in DATATOP subjects not requiring levodopa. Parkinson Study Group. Ann Neurol. 1996 Jan;39(1):29-36.
[62] Waters CH, Sethi KD, Hauser RA, et al.; Zydis **Selegiline** Study Group. Zydis selegiline reduces off time in Parkinson's disease patients with motor fluctuations: a 3-month, randomized, placebo-controlled study. Mov Disord. 2004 Apr;19(4):426-32.
[63] Olanow CW, Myllyla VV, Sotaniemi KA, et al. Effect of **selegiline** on mortality in patients with Parkinson's disease: a meta-analysis. Neurology. 1998 Sep;51(3):825-30.
[64] Mortality in **DATATOP**: a multicenter trial in early Parkinson's disease. Parkinson Study Group. Ann Neurol. 1998 Mar;43(3):318-25.
[65] Macleod A, Counsell C, Ives N, Stowe R. Monoamine oxidase B inhibitors for early Parkinson's disease. Cochrane Database Syst Rev. 2005 Jul 20;(3):CD004898.
[66] Ives NJ, Stowe RL, Marro J, et al. **Monoamine oxidase type** B inhibitors in early Parkinson's disease: meta-analysis of 17 randomised trials involving 3525 patients. BMJ. 2004 Sep 11;329(7466):593.
[67] Palhagen S, Heinonen E, Hagglund J, Kaugesaar T, Maki-Ikola O, Palm R; Swedish Parkinson Study Group. **Selegiline** slows the progression of the symptoms of Parkinson disease. Neurology. 2006 Apr 25;66(8):1200-6. Epub 2006 Mar 15.
[68] Van Gerpen JA. **Drug-induced** parkinsonism. Neurologist. 2002 Nov;8(6):363-70. (Cersosimo MG, Koller WC. The diagnosis of manganese-induced parkinsonism. Neurotoxicology. 2005 Nov 30; [Epub ahead of print])
Esper CD, Factor SA. Failure of recognition of drug-induced parkinsonism in the elderly. Mov Disord. 2007 Dec 7; [Epub ahead of print]
Hawthorne JM, Caley CF. Extrapyramidal Reactions Associated With Serotonergic Antidepressants. Ann Pharmacother. 2015 Oct;49(10):1136-52.
López-Sendón J, Mena M, & de Yébenes J, Drug-induced parkinsonism, Expert Opinion on Drug Safety, 2013;12:4, 487-496, DOI: 10.1517/14740338.2013.787065

[69] Witjas T, Kaphan E, Azulay JP, Blin O, Ceccaldi M, Pouget J, Poncet M, Cherif AA. **Nonmotor fluctuations** in Parkinson's disease: frequent and disabling. Neurology. 2002 Aug 13;59(3):408-13.
Zesiewicz, T. A., Sullivan, K. L., Arnulf, I., et al. AAN Practice Parameter: Treatment of nonmotor symptoms of Parkinson disease: Report of the Quality Standards Subcommittee of the American Academy of Neurology. Neurology 2010 74: 924-931.
Leentjens AF. The role of dopamine agonists in the treatment of depression in patients with Parkinson's disease: a systematic review. Drugs. 2011 Feb 12;71(3):273-86. doi: 10.2165/11585380-000000000-00000.
[70] Leroi I, Brandt J, Reich SG, Lyketsos CG, Grill S, Thompson R, Marsh L. Randomized placebo-controlled trial of **donepezil** in cognitive impairment in Parkinson's disease. Int J Geriatr Psychiatry. 2004 Jan;19(1):1-8.
Emre M, et al. **Rivastigmine** for dementia associated with Parkinson's disease. (Express) N Engl J Med. 2004 Dec 9;351(24):2509-18. (Wesnes KA, et al. Benefits of rivastigmine on attention in dementia associated with Parkinson disease. Neurology. 2005 Nov 22;65(10):1654-6.)
McKeith I, Del Ser T, Spano P, et al. Efficacy of **rivastigmine** in dementia with Lewy bodies: A randomised, double-blind, placebo-controlled international study. Lancet 2000;356:2031-2036.
Maidment I, Fox C, Boustani M. Cholinesterase inhibitors for Parkinson's disease dementia. Cochrane Database Syst Rev. 2006 Jan 25;(1):CD004747.
Almaraz AC, Driver-Dunckley ED, Woodruff BK, et al. Efficacy of **rivastigmine** for cognitive symptoms in Parkinson disease with **dementia**. Neurologist. 2009 Jul;15(4):234-7. Rivastigmine therapy for PDD is associated with significant tradeoffs in efficacy and adverse effects. Carefully monitored trials of rivastigmine may provide meaningful benefits for a minority of PDD patients.
Rolinski M, Fox C, Maidment I, McShane R. Cholinesterase inhibitors for dementia with Lewy bodies, Parkinson's disease dementia and cognitive impairment in Parkinson's disease. Cochrane Database Syst Rev. 2012 Mar 14;3:CD006504. doi: 10.1002/14651858.CD006504.pub2.
Pagano G, Rengo G, Pasqualetti G, et al. **Cholinesterase inhibitors** for Parkinson`s disease: a systematic review and meta-analysis. J Neurol Neurosurg Psychiatry. 2014 Sep 15.

[71] Adler CH, Caviness JN, Hentz JG, Lind M, Tiede J. Randomized trial of **modafinil** for treating subjective daytime sleepiness in patients with Parkinson's disease. Mov Disord. 2003 Mar;18(3):287-93. & Ondo WG, Fayle R, Atassi F, Jankovic J. **Modafinil** for daytime somnolence in Parkinson's disease: double blind, placebo controlled parallel trial. J Neurol Neurosurg Psychiatry. 2005 Dec;76(12):1636-9.
Zesiewicz, T. A., Sullivan, K. L., Arnulf, I., et al. AAN Practice Parameter: Treatment of nonmotor symptoms of Parkinson disease: Report of the Quality Standards Subcommittee of the American Academy of Neurology. Neurology 2010 74: 924-931.
[72] Ondo WG, Hunter C, Moore W. A double-blind placebo-controlled trial of **botulinum toxin B** for sialorrhea in Parkinson's disease. Neurology. 2004 Jan 13;62(1):37-40. (Wieler M, Camicioli R, Jones CA, Martin WR. **Botulinum** toxin injections do not improve **freezing of gait** in Parkinson disease.Neurology. 2005 Aug 23;65(4):626-8.)(Lagalla G, et al. Botulinum toxin type A for drooling in Parkinson's disease: A double-blind, randomized, placebo-controlled study. Mov Disord. 2006 Jan 26; [Epub ahead of print])
Mittal SO, Machado D, Richardson D, et al. **Botulinum Toxin i**n Parkinson Disease Tremor: A Randomized, Double-Blind, Placebo-Controlled Study With a Customized Injection Approach. Mayo Clin Proc. 2017 Sep;92(9):1359-1367.

[73] Dewey RB Jr, Hutton JT, LeWitt PA, Factor SA. A randomized, double-blind, placebo-controlled trial of subcutaneously injected **apomorphine** for parkinsonian off-state events. Arch Neurol. 2001 Sep;58(9):1385-92.
Stacy M. Apomorphine: North American clinical experience. Neurology. 2004 Mar 23;62(6 Suppl 4):S18-21.
Apomorphine for Advanced Parkinson's disease. Med Lett Drugs Ther. **2005** Jan 17;47(1200):7-8.
Haq IU, Lewitt PA, Fernandez HH. Apomorphine therapy in Parkinson's disease: a review. Expert Opin Pharmacother. 2007 Nov;8(16):2799-809.
[74] Morgante L, Epifanio A, Spina E, et al. **Quetiapine** and **clozapine** in parkinsonian patients with dopaminergic psychosis. Clin Neuropharmacol. 2004 Jul-Aug;27(4):153-6.
Morgante L, Epifanio A, Spina E, Zappia M, Di Rosa AE, et al. Quetiapine and clozapine in parkinsonian patients with dopaminergic psychosis. Clin Neuropharmacol. 2004 Jul-Aug;27(4):153-6.
Ondo WG, Tintner R, Dat Voung K, Lai D, Ringholz G. Double-blind, placebo-controlled, unforced titration parallel trial of quetiapine for dopaminergic-induced hallucinations in Parkinson's disease. Mov Disord. 2005 Mar 30.
[75] Pollak P, Tison F, Rascol O, et al. **Clozapine** in drug induced psychosis in Parkinson's disease: a randomised, placebo controlled study with open follow up. J Neurol Neurosurg Psychiatry. 2004 May;75(5):689-95.
Clozapine in drug-induced psychosis in Parkinson's disease. The French Clozapine Parkinson Study Group. Lancet. 1999 Jun 12;353(9169):2041-2.
Low-dose **clozapine** for the treatment of drug-induced psychosis in Parkinson's disease. The Parkinson Study Group. N Engl J Med. 1999 Mar 11;340(10):757-63.
[76] Crosby NJ, Deane KH, Clarke CE. **Beta-blocker** therapy for tremor in Parkinson's disease. Cochrane Database Syst Rev. 2003;(1):CD003361.
[77] Impact of deprenyl and tocopherol treatment on Parkinson's disease in DATATOP patients requiring levodopa. Parkinson Study Group. Ann Neurol. 1996 Jan;39(1):37-45. (Etminan M, Gill SS, Samii A. Intake of **vitamin E**, vitamin C, and carotenoids and the risk of Parkinson's disease: a meta-analysis. Lancet Neurol. 2005 Jun;4(6):362-5.) (Pham DQ, Plakogiannis R. Vitamin e supplementation in Alzheimer's disease, Parkinson's disease, tardive dyskinesia, and cataract: part 2. Ann Pharmacother. 2005 Dec;39(12):2065-71. Epub 2005 Nov 15.)
Parkinson Study Group QE3 Investigators. A Randomized Clinical Trial of High-Dosage Coenzyme **Q10** in Early Parkinson Disease: No Evidence of Benefit. JAMA Neurol. 2014 Mar 24.
[78] Walter BL, Vitek JL. **Surgical** treatment for Parkinson's disease. Lancet Neurol. 2004 Dec;3(12):719-28.
[79] Valerie C. Anderson; Kim J. Burchiel; Penelope Hogarth; et al. **Pallidal vs Subthalamic** Nucleus Deep Brain Stimulation in Parkinson Disease. Arch Neurol. 2005;62:554-560.
Williams A, Gill S, Varma T, et al. on behalf of the **PD SURG** Collaborative Group. Deep brain stimulation plus best medical therapy versus best medical therapy alone for advanced Parkinson's disease (PD SURG trial): a randomised, open-label trial. Lancet Neurol. 2010 Apr 28.
Follett, Kenneth A., Weaver, Frances M., Stern, Matthew, et al. the CSP 468 Study Group, **Pallidal versus Subthalamic** Deep-Brain Stimulation for Parkinson's Disease. N Engl J Med 2010 362: 2077-2091.
Brennan KA, Genever RW. Managing **Parkinson's disease during surgery**. BMJ. 2010 Nov 1;341:c5718. doi: 10.1136/bmj.c5718.
Bronstein JM, Tagliati M, Alterman RL, et al. **Deep brain stimulation** for Parkinson disease: an expert consensus and review of key issues. Arch Neurol. 2011 Feb;68(2):165.
Savica R, Matsumoto JY, Josephs KA, et al. **Deep brain stimulation** in benign tremulous parkinsonism. Arch Neurol. 2011 Aug;68(8):1033-6.
Castrioto A, Lozano AM, Poon YY, et al.Ten-Year Outcome of **Subthalamic Stimulation** in Parkinson Disease: A Blinded Evaluation. Arch Neurol. 2011 Aug 8.
Deuschl G, Schade-Brittinger C, Krack P, et al. A randomized trial of deep-brain stimulation for Parkinson's disease. New Engl J Med 2006; 355: 896–908.
Moro E, Lozano AM, Pollak P, et al. Long-term results of a multicenter study on subthalamic and pallidal stimulation in Parkinson's disease. Mov Disord 2010; 25: 578–86.
Okun MS, Gallo BV, Mandybur G, et al, for the SJM DBS Study Group. Subthalamic deep brain stimulation with a constant-current device in Parkinson's disease: an open-label randomised controlled trial. Lancet Neurol 2012; published online Jan 11.
Machado A, Fernandez HH, Deogaonkar M. **Deep brain stimulation**: What can patients expect from it? Cleveland Clinic Journal of Medicine 2012; 79(2):113-120;doi:10.3949/ccjm.78gr.11006. (generally appendicular symptoms such as limb tremor & rigidity more responsive)
Sharma A, Szeto K, Desilets AR. Efficacy and Safety of **Deep Brain Stimulation** as an Adjunct to Pharmacotherapy for the Treatment of Parkinson Disease (February). Ann Pharmacother. 2012 Jan 10.
Tarsy D. Treatment of Parkinson disease: a 64-year-old man with **motor complications** of advanced Parkinson disease. JAMA. 2012 Jun 6;307(21):2305-14.
Weaver FM, Follett KA, Stern M, et al; For the CSP 468 Study Group. Randomized trial of **deep brain stimulation** for Parkinson disease: Thirty-six-month outcomes. Neurology. 2012 Jul 3;79(1):55-65.
Okun MS. **Deep-brain stimulation** for Parkinson's disease. N Engl J Med. 2012 Oct 18;367(16):1529-38.
Schuepbach WMM et al. Neurostimulation for Parkinson's disease with early motor complications. (**EARLYSTIM**) N Engl J Med 2013 Feb 14; 368:610.
Desouza R, Moro E, Lang A, et al. Timing of deep brain stimulation in Parkinson's disease: A need for reappraisal? Ann Neurol. 2013 Mar 8.
Deuschl G, Agid Y. Subthalamic neurostimulation for Parkinson's disease with early fluctuations: balancing the risks and benefits. Lancet Neurol. 2013 Oct;12(10):1025-34.
Buhmann C, Maintz L, Hierling J, et al. Effect of subthalamic nucleus deep brain stimulation on driving in Parkinson disease. Neurology. 2014 Jan 7;82(1):32-40.
Palfi S, Gurruchaga JM, Ralph GS, et al. Long-term safety and tolerability of ProSavin, a lentiviral vector-based gene therapy for Parkinsons disease: a dose escalation, open-label, phase 1/2 trial. Lancet 2014; online Jan 10.
Chan AK, McGovern RA, Brown LT, et al. **Disparities in Access to Deep B rain Stimulation Surgery** for Parkinson Disease: Interaction Between African American Race and Medicaid Use. JAMA Neurol. 2014 Jan 6.
Willis AW, Schootman M, Kung N, et al.**Disparities in deep brain stimulation surgery among insured elders** with Parkinson disease. Neurology. 2014 Jan 14;82(2):163-71.
Castrioto A, Lhommée E, Moro E, et al. Mood and behavioural effects of **subthalamic stimulation** in Parkinson's disease. Lancet Neurol. 2014 Mar;13(3):287-305.
Welter ML, Schüpbach M, Czernecki V, et al. Optimal target localization for **subthalamic stimulation in patients** with Parkinson disease. Neurology. 2014 Apr 15;82(15):1352-61.
Floden D, Cooper SE, Griffith SD, et al. Predicting quality of life outcomes after **subthalamic nucleus deep brain stimulation**. Neurology. 2014 Oct 28;83(18):1627-33.
Jennings D, Siderowf A, Stern M, et al; PARS Investigators. **Imaging prodromal Parkinson** disease: The Parkinson Associated Risk Syndrome Study. Neurology. 2014 Nov 4;83(19):1739-46.
Robert GH, Le Jeune F, Lozachmeur C, et al. **Preoperative** factors of **apathy in subthalamic stimulated Parkinson** disease: A PET study. Neurology. 2014 Oct 28;83(18):1620-6.
DeLong MR, Huang KT, Gallis J, et al. Effect of Advancing Age on Outcomes of **Deep Brain Stimulation** for Parkinson Disease. JAMA Neurol. 2014 Aug 25.
Katz M, San Luciano M, Carlson K, et al. The **differential effects of DBS target** on motor subtypes in Parkinson's disease. Ann Neurol. 2015 Jan 27.
Jung YJ, Kim HJ, Jeon BS, Park H, LeeWW, Paek SH. An 8-year follow-up on the effect of **subthalamic nucleus deep brain stimulation** on pain in Parkinson disease [online March 23, 2015]. JAMA Neurol. doi:10.1001/jamaneurol.2015
Odekerken VJ, Boel JA, Geurtsen GJ, et al; NSTAPS Study Group. Neuropsychological outcome after **deep brain stimulation** for Parkinson disease. Neurology. 2015 Mar 31;84(13):1355-61.

Na YC, Chang WS, Jung HH, et al. Unilateral magnetic resonance-guided focused ultrasound pallidotomy for Parkinson disease. Neurology. 2015 Aug 11;85(6):549-51.
Timmermann L, Jain R, Chen L, et al. Multiple-source current steering in subthalamic nucleus deep brain stimulation for Parkinson's disease (the VANTAGE study): a non-randomised, prospective, multicentre, open-label study. Lancet Neurol. 2015 May 28.
Odekerken VJ, Boel JA, Schmand BA, et al. NSTAPS study group. GPi vs STN deep brain stimulation for Parkinson disease: Three-year follow-up. Neurology. 2016 Feb 23;86(8):755-761.
Mansouri A, Taslimi S, Badhiwala JH, et al. Deep brain stimulation for Parkinson's disease: meta-analysis of results of randomized trials at varying lengths of follow-up. J Neurosurg. 2017 Jun 30:1-15.
Bond AE, Shah BB, Huss DS, et al. Safety and Efficacy of Focused Ultrasound Thalamotomy for Patients With Medication-Refractory, Tremor-Dominant Parkinson Disease: A Randomized Clinical Trial. JAMA Neurol. 2017 Oct 30.
Brodsky MA, Anderson S, Murchison C, et al. Clinical outcomes of asleep vs awake deep brain stimulation for Parkinson disease. Neurology 2017;89:1944–1950.
Gratwicke J, Zrinzo L, Kahan J, et al. Bilateral deep brain stimulation of the nucleus basalis of Meynert for Parkinson disease dementia: a randomized clinical trial [online Dec 18, 2017].JAMA Neurol. doi:10.1001 /jamaneurol.2017.3762
Ramirez-Zamora A, Ostrem JL. Globus Pallidus Interna or Subthalamic Nucleus Deep Brain Stimulation for Parkinson Disease: A Review. JAMA Neurol. 2018 Jan 22.
Lhommee E, Wojtecki L, et al. Behavioural outcomes of subthalamic stimulation and medical therapy versus medical therapy alone for Parkinson's disease with early motor complications (EARLYSTIM trial): secondary analysis of an open-label randomised trial. Lancet Neurol 2018; 17: 223–31.
Arlotti M, Marceglia S, Foffani G, et al. Eight-hours adaptive deep brain stimulation inpatients with Parkinson disease. Neurology 2018;90:e971–e976.
Rughani A, Schwalb JM, Sidiropoulos C, et al. Congress of Neurological Surgeons Systematic Review and Evidence-Based Guideline on Subthalamic Nucleus and Globus Pallidus Internus Deep Brain Stimulation for the Treatment of Patients With Parkinson's Disease: Executive Summary. Neurosurgery. 2018 Jun 1;82(6):753-756.
Hacker ML, DeLong MR, Turchan M, et al. Effects of deep brain stimulation on rest tremor progression in early stage Parkinson disease. Neurology. 2018 Jul 31;91(5):e463-e471.
Artusi CA, Dwivedi AK, Romagnolo A, et al. Association of Subthalamic Deep Brain Stimulation With Motor, Functional, and Pharmacologic Outcomes in Patients With Monogenic Parkinson Disease: A Systematic Review and Meta-analysis. JAMA Netw Open. 2019 Feb 1;2(2):e187800.
Schuepbach WMM, Tonder L, Schnitzler A, et al. Quality of life predicts outcome of deep brain stimulation in early Parkinson disease. Neurology 2019;92:e1109–e1120.
[86] Backstrom D, Granasen G, Domellof ME, et al. **Early predictors of mortality in parkinsonism and Parkinson disease**: A population-based study. Neurology. 2018 Oct 31.
[87] Postuma RB, Gagnon JF, Bertrand JA, et al. Parkinson risk in **idiopathic REM sleep behavior disorder**: Preparing for neuroprotective trials. Neurology. 2015 Mar 17;84(11):1104-13.
88. Pierantozzi M, et al. **Helicobacter pylori eradication** and l-dopa absorption in patients with PD and motor fluctuations. Neurology. 2006 Jun 27;66(12):1824-9.

Additional articles:

Aasly JO, Shi M, Sossi V et al. Cerebrospinal fluid amyloid β and tau in **LRRK2 mutation carriers**. Neurology. 2012 Jan 3;78(1):55-61.
Abbott RD, Ross GW, Duda JE, et al. **Excessive daytime sleepiness** and topographic expansion of Lewy pathology. Neurology. 2019 Oct 8;93(15):e1425-e1432.
Abbott RD, Ross GW, Petrovitch H, et al. **Midlife milk consumption** and substantia nigra neuron density at death. Neurology 2016;86:512–519.
Adler CH, Dugger BN, Hinni ML, et al. **Submandibular gland needle biopsy** for the diagnosis of Parkinson disease. Neurology. 2014 Mar 11;82(10):858-64.
Adler CH, Beach TG, Hentz JG, et al. **Low clinical diagnostic accuracy of early vs advanced Parkinson** disease: clinicopathologic study. Neurology 2014;83:406–412.
Ahn J, Lee JY, Kim TW, et al. **Retinal thinning associates with nigral dopaminergic loss** in de novo Parkinson disease. Neurology. 2018 Sep 11;91(11):e1003-e1012.
Akhtar RS, Mano T. **High serum neurofilament light chain predicts a worse fate** in early parkinsonism. Neurology. 2019 Mar 26;92(13):595-596.
Alcalay RN, Caccappolo E, Mejia-Santana H, et al. **Cognitive performance of GBA mutation carriers** with early onset PD: the CORE-PD study. Neurology 2012;78:1434–1440.
Almaraz AC, Driver-Dunckley ED, Woodruff BK, et al. Efficacy of **rivastigmine** for cognitive symptoms in Parkinson disease with **dementia**. Neurologist. 2009 Jul;15(4):234-7. Rivastigmine therapy for PDD is associated with significant tradeoffs in efficacy and adverse effects. Carefully monitored trials of rivastigmine may provide meaningful benefits for a minority of PDD patients.
Alves G, Lange J, Blennow K, et al. **CSF Ab42 predicts** early-onset dementia in Parkinson disease. Neurology 2014;82:1784–1790.
Amara AW, Memon AA. Effects of **Exercise** on Non-Motor Symptoms in Parkinson's Disease. Clin Ther. 2017 Nov 30.
Amato N, Manconi M, Möller JC, et al. **Levodopa-induced dyskinesia** in Parkinson's disease: **sleep matters**.Ann Neurol. 2018 Oct 17.
Anang JB, Gagnon JF, Bertrand JA, et al. **Predictors of dementia** in Parkinson disease: A prospective cohort study. Neurology. 2014 Sep 30;83(14):1253-60.
Antonini A, Cilia R. **Behavioural adverse effects of dopaminergic** treatments in Parkinson's disease: incidence, neurobiological basis, management and prevention. Drug Saf. 2009;32(6):475-88. doi: 10.2165/00002018-200932060-00004.
Antonini A. The conundrum of **neuroprotection** in Parkinson's disease. Lancet Neurol. 2011 Apr 7.
Arbouw ME, Movig KL, Koopmann M, Poels PJ, Guchelaar HJ, Egberts TC, Neef C, et al. **Glycopyrrolate for sialorrhea** in Parkinson disease: a randomized, double-blind, crossover trial. Neurology. 2010 Apr 13;74(15):1203-7. Oral glycopyrrolate 1 mg 3 times daily is an effective and safe therapy for sialorrhea in Parkinson disease. Classification of evidence: This study provides Class I evidence that glycopyrrolate 1 mg 3 times daily is more effective than placebo in reducing sialorrhea in patients with Parkinson disease during a 4-week study.
Arlotti M, Marceglia S, Foffani G, et al. Eight-hours adaptive **deep brain stimulation** inpatients with Parkinson disease. Neurology 2018;90:e971–e976.
Armstrong MJ, Miyasaki JM. Evidence-based guideline: Pharmacologic treatment of **chorea** in Huntington disease: Report of the Guideline Development Subcommittee of the American Academy of Neurology. Neurology. 2012 Aug 7;79(6):597-603. (tetrabenazine, amantadine or riluzole)
Artusi CA, Dwivedi AK, Romagnolo A, et al. Association of **Subthalamic Deep Brain Stimulation** With Motor, Functional, and Pharmacologic Outcomes in Patients With Monogenic Parkinson Disease: A Systematic Review and Meta-analysis. JAMA Netw Open. 2019 Feb 1;2(2):e187800.
Astradsson A, Aziz T. Parkinson's disease: **fetal cell or stem cell derived treatments**. BMJ. 2016 Jan 7;352:h6340.
Athauda D, Maclagan K, Skene SS, et al. **Exenatide** once weekly versus placebo in Parkinson's disease: a randomised, double-blind, placebo-controlled trial. Lancet. 2017 Aug 3.
Baig F, Kelly MJ, Lawton MA, et al. **Impulse control disorders** in Parkinson disease and RBD: A longitudinal study of severity. Neurology. 2019 Aug 13;93(7):e675-e687.
Barber Thomas M., Kenkre Julia, Garnett Catherine, et al. **Recurrence of hyperprolactinaemia following discontinuation of dopamine agonist** therapy in patients with prolactinoma occurs commonly especially in **macroprolactinoma**. Article first published online: 9 NOV 2011.
Barichella M, Cereda E, Pinelli G, et al. Muscle-targeted **nutritional support for rehabilitation in patients with parkinsonian** syndrome. Neurology. 2019 Jul 30;93(5):e485-e496.
Barichella M, Pacchetti C, Bolliri C, et al. **Probiotics and prebiotic fiber** for **constipation** associated with Parkinson disease: An RCT. Neurology. 2016 Sep 20;87(12):1274-1280
Barker RA, Barrett J, Mason SL, Björklund A. **Fetal dopaminergic transplantation** trials and the future of neural grafting in Parkinson's disease. Lancet Neurol. 2013 Jan;12(1):84-91.
Barone P, et al. and the Depression/Parkinson Italian Study Group. **Pramipexole versus sertraline** in the treatment of **depression** in Parkinson's disease : A national multicenter parallel-group randomized study. J Neurol. 2006 Apr 20; [Epub ahead of print]
Barone P, Poewe W, Albrecht S et al. **Pramipexole** for the treatment of **depressive** symptoms in patients with Parkinson's disease: a randomised, double-blind, placebo-controlled trial. Lancet Neurol. 2010 May 7.
Barrett MJ, Blair JC, Sperling SA, Smolkin ME, Druzgal TJ. **Baseline symptoms and basal forebrain volume predict future psychosis** in early Parkinson disease. Neurology 2018;90:e1618–e1626
Beck CA et al. National randomized controlled trial of **virtual** house **calls** for Parkinson disease.Neurology 2017 Aug 16.
Beck CA, Beran DB, Biglan KM, et al.Parkinson Investigators. National randomized controlled trial of **virtual house** calls for Parkinson disease. Neurology. 2017 Sep 12;89(11):1152-1161.
Becker C, Jick SS, Meier CR. Use of antihypertensives and the risk of Parkinson disease. Neurology. 2008 Feb 6; [Epub ahead of print] Current long-term use of **calcium channel blockers** was associated with a significantly reduced risk of a Parkinson disease diagnosis, while the risk was not materially altered for users of angiotensin converting enzyme inhibitors or beta-blockers and, with less statistical precision, for users of angiotensin II antagonists.
Beecham GW, Dickson DW, Scott WK, et al. **PARK10** is a major **locus** for sporadic neuropathologically confirmed Parkinson disease. Neurology 2015;84:972–980.
Bega D, Krainc D. Long-term clinical outcomes after **fetal cell transplantation** in parkinson disease: implications for the future of cell therapy. JAMA. 2014 Feb 12;311(6):617-8
Bender A, et al. **Creatine** supplementation in Parkinson disease: a placebo-controlled randomized pilot trial. Neurology. 2006 Oct 10;67(7):1262-4. Cr improved patient mood and led to a smaller dose increase of dopaminergic therapy but had no effect over 2yrs on overall Unified Parkinson's Disease Rating Scale scores or dopamine transporter SPECT.
Benn M, Nordestgaard BG, Frikke-Schmidt R, et al. **Low LDL cholesterol, PCSK9 and HMGCR genetic variation**, and risk of Alzheimer's disease and Parkinson's disease: Mendelian randomisation study. BMJ. 2017 Apr 24;357:j1648.
Benninger DH, Berman BD, Houdayer E, et al. **Intermittent theta-burst transcranial magnetic stimulation** for treatment of Parkinson disease. Neurology. 2011 Feb 15;76(7):601-9.
Berardelli A, Wenning GK, Antonini A, et al. **EFNS/MDS-ES recommendations for the diagnosis of Parkinson's** disease. Eur J Neurol. 2013 Jan;20(1):16-34.
Berg D, Seppi K, Behnke S, et al. **Enlarged substantia nigra hyperechogenicity** and risk for Parkinson disease: a 37-month 3-center study of 1847 older persons. Arch Neurol. 2011 Jul;68(7):932-7.
Berg D, Lang AE, Postuma RB, et al. Changing the research criteria for the **diagnosis of Parkinson's disease**: obstacles and opportunities. *Lancet Neurol* 2013; online April 11.
Berg D, Postuma RB, Adler CH, et al. **MDS research criteria for prodromal Parkinson's disease**. Mov Disord. 2015 Oct;30(12):1600-11.
Bhatia KP, Bain P, et al; Tremor Task Force of the **International Parkinson and Movement Disorder Society**. Consensus Statement on the **classification of tremors**. from the task force on tremor of the International Parkinson and Movement Disorder Society. Mov Disord. 2018 Jan;33(1):75-87.

Binde CD, Tvete IF, Gåsemyr J, et al. A multiple treatment comparison meta-analysis of **monoamine oxidase type B inhibitors for Parkinson's disease**. Br J Clin Pharmacol. 2018 May 30.
Bjornestad A, Tysnes OB, Larsen JP, et al. **Loss of independence** in early Parkinson disease: A 5-year population-based incident cohort study. Neurology. 2016 Sep 2.
Bloem BR, Munneke M. Revolutionising management of chronic disease: the **ParkinsonNet approach**. BMJ. 2014 Mar 19
Boeve BF. The window of **"idiopathic" REM sleep behavior disorder** in the evolution of prototypical Parkinson's disease. Lancet Neurol 2013.
Bohnen NI, Frey KA, Studenski S, et al. **Gait speed** in Parkinson disease correlates with cholinergic degeneration. Neurology. 2013 Sep 27.
Bohnen NI, Kanel P, Zhou Z, et al**. Cholinergic system changes** of falls and freezing of gait in Parkinson disease. Ann Neurol. 2019 Feb 5.
Bonakdar RA, Guarneri E. **Coenzyme Q10**. Am Fam Physician. 2005 Sep 15;72(6):1065-70.
Bond AE, Shah BB, Huss DS, et al. Safety and Efficacy of **Focused Ultrasound Thalamotomy** for Patients With Medication-Refractory, Tremor-Dominant Parkinson Disease: A Randomized Clinical Trial. JAMA Neurol. 2017 Oct 30.
Bonnici André, Ruiner Carola-Ellen, St-Laurent Lyne, et al. An Interaction Between **Levodopa and Enteral Nutrition** Resulting in Neuroleptic Malignant–Like Syndrome and Prolonged ICU Stay. Ann Pharmacother .44:1504-1507.
Brandt-Christensen M, Kvist et al. Treatment with **antidepressants and lithium is associated** with increased risk of treatment with antiparkinson drugs: a pharmacoepidemiological study. J Neurol Neurosurg Psychiatry. 2006 Jun;77(6):781-3.
Brashear A, Cook JF, Hill DF, et al. **Psychiatric disorders** in rapid-onset dystonia-parkinsonism. Neurology. 2012 Sep 11;79(11):1168-73.
Brauer R, Bhaskaran K, Chaturvedi N, et al. **Glitazone** Treatment and Incidence of Parkinson's Disease among People with Diabetes: A Retrospective Cohort Study. PLoS Med. 2015 Jul 21;12(7):e1001854.
Breen DP, Vuono R, Nawarathna U, et al. **Sleep** and Circadian Rhythm Regulation in Early Parkinson Disease. JAMA Neurol.2014 Mar 31.
Brennan KA, Genever RW. Managing **Parkinson's disease during surgery**. BMJ. 2010 Nov 1;341:c5718. doi: 10.1136/bmj.c5718.
Brilliant MH, Vaziri K, Connor TB Jr, et al. Mining Retrospective Data for Virtual Prospective Drug Repurposing: **L-DOPA** and **Age-related Macular Degeneration**. Am J Med. 2015 Oct 30.
Brockmann K, Hilker R, Pilatus U, et al. **GBA-associated PD**: neurodegeneration, altered membrane metabolism, and lack of energy failure. Neurology 2012;79:213–220.
Brodsky MA, Anderson S, Murchison C, et al. Clinical outcomes of **asleep vs awake deep brain stimulation** for Parkinson disease. Neurology 2017;89:1944–1950.
Bronstein JM, Tagliati M, Alterman RL, et al. **Deep Brain Stimulation** for Parkinson Disease: An Expert Consensus and Review of Key Issues. Arch Neurol. 2010 Oct 11.
Brüggemann N, Spiegler J, Hellenbroich Y, et al. Beneficial Prenatal **Levodopa** Therapy in Autosomal Recessive **Guanosine Triphosphate Cyclohydrolase 1 Deficiency**. Arch Neurol. 2012 Apr 2.
Brys M, Fox MD, Agarwal S, Biagioni et al. **Multifocal repetitive TMS** for motor and mood symptoms of Parkinson disease: A randomized trial. Neurology. 2016 Nov 1;87(18):1907-1915
Buchman AS, Leurgans SE, Yu L, et al. **Incident parkinsonism** in older adults without Parkinson disease. Neurology. 2016 Sep 6;87(10):1036-44.
Buchman AS, Yu L, Wilson RS, et al. Progressive parkinsonism in older adults is related to the burden of **mixed brain pathologies**. Neurology. 2019 Apr 16;92(16):e1821-e1830.
Buhmann C, Maintz L, Hierling J, et al. Effect of **subthalamic nucleus deep brain stimulation** on driving in Parkinson disease. Neurology. 2014 Jan 7;82(1):32-40.
Burciu RG, Chung JW, Shukla P, et al. Functional **MRI of disease progression** in Parkinson disease and atypical parkinsonian syndromes. Neurology. 2016 Aug 16;87(7):709-17
Burke WJ, Bronstein JM, Fitzmaurice A. Aldehyde dehydrogenase variation enhances effect of **pesticides** associated with Parkinson disease. Neurology. 2014 Nov 11;83(20):1879-80.
Butcher NJ, Kiehl TR, Hazrati LN, et al. Association Between Early-Onset Parkinson Disease and **22q11.2 Deletion Syndrome**: Identification of a Novel Genetic Form of Parkinson Disease and Its Clinical Implications. JAMA Neurol. 2013 Sep 9.
Büchele F, Hackius M, Schreglmann SR, et al. **Sodium Oxybate for Excessive Daytime Sleepiness** and Sleep Disturbance in Parkinson Disease: A Randomized Clinical Trial. JAMA Neurol. 2017 Nov 6.
Cagnan H, Pedrosa D, Little S, et al. Stimulating at the right time: phase-specific **deep brain stimulation**. Brain. 2017 Jan;140(Pt 1):132-145
Calandrella D, Romito LM, Elia AE, et al. Albanese A. Causes of withdrawal of **duodenal levodopa infusion** in advanced Parkinson disease. Neurology. 2015 Mar 25.
Callaghan RC, Cunningham JK, Sajeev G, Kish SJ. Incidence of Parkinson's disease among hospital patients with **methamphetamine**-use disorders. Mov Disord. 2010 Aug 24.
Camacho-Soto A, Warden MN, Searles Nielsen S, et al. **Traumatic Brain Injury** in the Prodromal Period of Parkinson Disease: A Large Epidemiological Study Using Medicare Data. Ann Neurol. 2017 Oct 10.
Canning CG, Sherrington C, Lord SR, et al. **Exercise for falls prevention** in Parkinson disease: A randomized controlled trial. Neurology. 2015 Jan 20;84(3):304-12.
Carlesimo GA, Piras F, Assogna F, Pontieri FE, Caltagirone C, Spalletta G. **Hippocampal abnormalities and memory deficits** in Parkinson disease: A multimodal imaging study. Neurology. 2012 Jun 12;78(24):1939-45.
Castrioto A, Lozano AM, Poon YY, Lang AE, Fallis M, Moro E. **Ten-Year Outcome of Subthalamic Stimulation** in Parkinson Disease: A Blinded Evaluation. Arch Neurol. 2011 Aug 8.
Castrioto A, Lhommée E, Moro E, et al. Mood and behavioural effects of **subthalamic stimulation** in Parkinson's disease. Lancet Neurol. 2014 Mar;13(3):287-305.
Centi J, Freeman R, Gibbons CH, et al. Effects of **orthostatic hypotension on cognition** in Parkinson disease. Neurology 2017;88:17–24.
Cereda E, Barichella M, Cassani E, et al. Clinical features of **Parkinson disease when onset of diabetes came first**: A case-control study.Neurology. 2012 May 8;78(19):1507-11.
Chan AK, McGovern RA, Brown LT, et al. **Disparities in Access to Deep Brain Stimulation Surgery** for Parkinson Disease: Interaction Between African American Race and Medicaid Use. JAMA Neurol. 2014 Jan 6.
Chen H, Jacobs E, Schwarzschild MA, McCullough ML, Calle EE, Thun MJ, Ascherio A. **Nonsteroidal antiinflammatory** drug use and the risk for Parkinson's disease. Ann Neurol. 2005 Dec;58(6):963-7.
Chen H, Shrestha S, Huang X, et al. **Olfaction** and incident Parkinson disease in US white and black older adults. Neurology 2017;89:1441–1447.
Chen JJ, Swope DM. **Pharmacotherapy for Parkinson's disease**. Pharmacotherapy. 2007 Dec;27(12 Pt 2):161S-73S.
Cheng EM, Tonn S, Swain-Eng R, et al. American Academy of Neurology Parkinson Disease Measure Development Panel. Quality improvement in neurology: **AAN Parkinson disease quality measures**: report of the Quality Measurement and Reporting Subcommittee of the American Academy of Neurology. Neurology. 2010 Nov 30;75(22):2021-7.
Chou KL. In the Clinic: **Parkinson Disease**. Ann Intern Med Nov 6, 2012. ITC5-2.
Chu Y, Buchman AS, Olanow CW, et al. Do subjects with **minimal motor features have prodromal PD**? Ann Neurol. 2018 Feb 8.
Chung SJ, Bae YJ, Jun S,et al**. Dysautonomia is associated with structural and functional alterations** in Parkinson disease. Neurology. 2019 Mar 26;92(13):e1456-e1467.
Cilia R, Laguna J, Cassani E, et al. **Mucuna pruriens** in Parkinson disease: A double-blind, randomized, controlled, crossover study. Neurology. 2017 Aug 1;89(5):432-438.
Chung KA, Lobb BM, Nutt JG, Horak FB. Effects of a central cholinesterase inhibitor (donepezil) on reducing falls in Parkinson disease. Neurology. 2010 Sep 1.
Clarke CE. **Parkinson's disease**. BMJ. 2007 Sep 1;335(7617):441-5.
Clarke CE, Patel S, Ives N, et al. **Physiotherapy and occupational therapy** vs no therapy in mild to moderate Parkinson disease: a randomized clinical trial [online January 19, 2016].JAMA Neurol. doi:10.1001/jamaneurol.2015.4452.
Clarke CE, Patel S, Ives N, et al. Clinical effectiveness and cost-effectiveness of **physiotherapy and occupational therapy** versus no therapy in mild to moderate Parkinson`s disease: a large pragmatic randomised controlled trial (PD REHAB). Health Technol Assess. 2016 Aug;20(63):1-96.
Cochrane CJ, Ebmeier KP. **Diffusion tensor imaging** (MRI) in parkinsonian syndromes: A systematic review and meta-analysis. Neurology. 2013 Feb 26;80(9):857-64.
Connolly Barbara S., Lang Anthony E.. **Pharmacological Treatment of Parkinson Disease**-A Review. JAMA. 2014;311(16):1670-1683. doi:10.1001/jama.2014.3654.
Connor KI, Cheng EM, Barry F, et al. Randomized trial of **care management** to improve Parkinson disease care quality. Neurology 2019;92:e1831–e1842.
Contarino MF, Bour LJ, Verhagen R, et al. **Directional steering**: A novel approach to deep brain stimulation. Neurology. 2014 Sep 23;83(13):1163-9.
Corvol JC, Artaud F, Cormier-DeQuaire F, et al. Longitudinal analysis of **impulse control disorders in Parkinson disease**. Neurology 2018;91:e189–e201.
Crane PK, Gibbons LE, Dams-O'Connor K, et al. Association of **Traumatic Brain Injury** With Late-Life Neurodegenerative Conditions and Neuropathologic Findings. JAMA Neurol. 2016 Jul 11.
Crawford P, Zimmerman EE, **Tremor: Sorting Through the Differential Diagnosis**. Am Fam Physician. 2018;97(3):180-186.
Criswell SR, Perlmutter JS, Videen TO, et al. Reduced uptake of **[18F]FDOPA PET** in asymptomatic **welders** with occupational manganese exposure. Neurology. 2011 Apr 12;76(15):1296-301.
Crizzle AM, Classen S, Uc EY. Parkinson disease and **driving**: An evidence-based review. Neurology. 2012 Nov 13;79(20):2067-74.
Cummings J, Isaacson S, Mills R, et al. **Pimavanserin** for patients with Parkinson's disease psychosis-a randomised, placebo-controlled phase 3 trial. Lancet 2013; Nov 1.
Cumming K, Macleod AD, Myint PK, et al. **Early weight loss** in parkinsonism predicts poor outcomes: Evidence from an incident cohort study. Neurology. 2017 Nov 28;89(22):2254-2261.
Cury RG, Fraix V, Castrioto A, et al. **Thalamic deep brain stimulation** for tremor in Parkinson disease, essential tremor, and dystonia. Neurology. 2017 Sep 26;89(13):1416-1423.
Dahodwala N, Shah K, He Y, et al. **Sex disparities** in access to caregiving in Parkinson disease. Neurology. 2017 Dec 1.
Damier P, Al-Hashel J. Recommendations for the Treatment of Patients With Parkinson Disease **During Ramadan**. JAMA Neurol. 2016 Dec 27.
Darweesh SKL, Wolters FJ, Postuma RB, et al. Association between **poor cognitive functioning and risk of incident parkinsonism**: the Rotterdam Study [online September 25, 2017]. JAMA Neurol. doi:10.1001/jamaneurol.2017.2248
Dawson BK, Fereshtehnejad SM, Anang JBM, et al. Office-Based Screening for Dementia in Parkinson Disease: The **Montreal Parkinson Risk of Dementia Scale** in 4 Longitudinal Cohorts. JAMA Neurol. 2018 Mar 26.
de la Fuente-Fernández R. Role of **DaTSCAN** and clinical diagnosis in Parkinson disease. Neurology 2012;78:696–701.
de la Riva P, Smith K, Xie SX, et al. Course of **psychiatric symptoms and global cognition** in early Parkinson disease. Neurology. 2014 Sep 16;83(12):1096-103.
de Lau LM, Schipper CM, Hofman A, et al. Prognosis of Parkinson disease: risk of dementia and mortality: the Rotterdam Study. Arch Neurol. 2005 Aug;62(8):1265-9. (InfoPOEMs: Patients with Parkinson's disease, especially those with at least one apolipoprotein E (APOE) gene epsilon2 allele, are at increased risk of developing dementia. Furthermore, patients with Parkinson's disease have a higher mortality risk, especially those who have had the disease the longest. (LOE = 1b))
De Pablo-Fernandez E, Goldacre R, Pakpoor J, et al. Association between **diabetes and subsequent Parkinson disease**: A record-linkage cohort study. Neurology. 2018 Jun 13.
De Pablo-Fernández E, Lees AJ, Holton JL, Warner TT. Prognosis and Neuropathologic Correlation of **Clinical Subtypes of Parkinson Disease**. JAMA Neurol. 2019 Jan 14.
Dalvin LA, Damento GM, Yawn BP, et al. Parkinson Disease and **Melanoma**: Confirming and Reexamining an Association. Mayo Clin Proc. 2017 Jul;92(7):1070-1079
Dehay B, Bourdenx M, Gorry P, et al. **Targeting α-synuclein** for treatment of Parkinson's disease: mechanistic and therapeutic considerations. Lancet Neurol. 2015 Jun 3.
Del Din S, Elshehabi M, Galna B, et al. **Gait analysis** with wearables predicts conversion to Parkinson's disease. Ann Neurol. 2019 Jul 11.
Deleu D, et al. Effects of **caffeine** on levodopa pharmacokinetics and pharmacodynamics in Parkinson disease. Neurology. 2006 Sep 12;67(5):897-9. Caffeine administered before levodopa may improve its pharmacokinetics in some parkinsonian patients.
DeLong MR, Huang KT, Gallis J, et al. Effect of Advancing Age on Outcomes of **Deep Brain Stimulation** for Parkinson Disease. JAMA Neurol. 2014 Aug 25.
Dembek TA, Roediger J, Horn A, et al**. Probabilistic Sweetspots Predict Motor Outcome for DBS** in Parkinson's Disease. Ann Neurol. 2019 Aug 3.

DeMaagd, George and Ashok Philip. “Parkinson's Disease and Its Management: Part 3: Nondopaminergic and Nonpharmacological Treatment Options” P & T : a peer-reviewed journal for formulary management vol. 40,10 (2015): 668-79.

Derkinderen P, Rouaud T, Lebouvier T, et al. Parkinson disease: The **enteric nervous system** spills its guts. Neurology. 2011 Nov 8;77(19):1761-7.

Desouza R, Moro E, Lang A, et al. Timing of **deep brain stimulation** in Parkinson's disease: A need for reappraisal? Ann Neurol. 2013 Mar 8.

Deuel L, Collins AE, Maa EH, et al. **Dravet syndrome and parkinsonism**: A case report investigating the dopaminergic system. Neurology. 2019 Aug 23.

Deuschl G, et al.; German Parkinson Study Group,Neurostimulation Section. A randomized trial of **deep-brain stimulation** for Parkinson's disease. N Engl J Med. 2006 Aug 31;355(9):896-908. (InfoPOEMs: Deep-brain stimulation poses risks, but also offers mild to moderate improvement in motor function for patients with severe Parkinson's disease (PD) who are already using maximal medical therapy. (LOE = 1b-))

Deuschl G, Agid Y. **Subthalamic neurostimulation** for Parkinson's disease with early fluctuations: balancing the risks and benefits. Lancet Neurol. 2013 Oct;12(10):1025-34.

Devos D, Dujardin K, Poirot I, Moreau C, Cottencin O, Thomas P, Destée A, Bordet R, Defebvre L. Comparison of **desipramine and citalopram** treatments for depression in Parkinson's disease: a double-blind, randomized, placebo-controlled study. Mov Disord. 2008 Apr 30;23(6):850-7.

Devos D, Moreau C, Dujardin K, et al. New **Pharmacological Options for Treating Advanced** Parkinson's Disease. Clin Ther. 2013 Sep 5.

di Biase L, Brittain JS, Shah SA, et al. **Tremor stability index**: a new tool for differential diagnosis in tremor syndromes. Brain. 2017 Jul 1;140(7):1977-1986.

Dickerson LM, Young SE, Simpson WM, Nashelsky J. Treatment of early Parkinson's disease. Am Fam Physician. 2005 Aug 1;72(3):497-500.

Ding H, Dhima K, Lockhart KC, et al. Unrecognized **vitamin D3 deficiency** is common in Parkinson disease: Harvard Biomarker Study. Neurology. 2013 Sep 25.

Dirkx MF, Zach H, Bloem BR, Hallett M, Helmich RC. The nature of **postural tremor in Parkinson disease**. Neurology 2018;90:e1095–e1103.

Dobkin RD, Menza M, Allen LA, et al. **Cognitive-behavioral therapy for depression in Parkinson’s** disease: a random ized, controlled trial. Am J Psychiatry 2011; 168:1066–1074.

Dore DD, Trivedi AN, Mor V, Friedman JH, et al. **Atypical antipsychotic** use and risk of **fracture in persons** with Parkinsonism. Mov Disord. 2009 Jul 30. [Epub ahead of print] Use of an AA was associated with a higher rate of fracture in persons with parkinsonism.

Dorsey ER, Deuel LM, Beck CA, et al. **Group patient visits** for Parkinson disease: A randomized feasibility trial. Neurology. 2011 May 3;76(18):1542-7.

Dorsey ER, Bloem BR. The **Parkinson Pandemic**-A Call to Action. JAMA Neurol. 2017 Nov 13.

Driver Jane A, Logroscino Giancarlo, Lu Linda, et al. Use of non-steroidal anti-inflammatory drugs **(NSAIDs)** and risk of Parkinson’s disease: nested case-control study. BMJ 2011;342:doi:10.1136/bmj.d198 (20 Jan 2011) –no association found

Dubois B, Tolosa E, Katzenschlager R, et al. **Donepezil in Parkinson's disease dementia**: A randomized, double-blind efficacy and safety study. Mov Disord. 2012 Sep 1;27(10):1230-8.

Edwards JD, Hauser RA, O’Connor ML, et al. Randomized trial of **cognitive speed of processing training** in Parkinson disease. Neurology 2013;81:1284–1290.

Egeberg A, Hansen PR, Gislason GH, Thyssen JP. Exploring the association between **rosacea** and Parkinson disease: a Danish nationwide cohort study [online March 21, 2016].JAMA Neurol. doi:10.1001/jamaneurol.2016.0022.

Ekman U, Eriksson J, Forsgren L, et al. **Functional brain activity and presynaptic dopamine uptake** in patients with Parkinson's disease and mild cognitive impairment: a cross-sectional study. Lancet Neurol. 2012 Jun 26.

Elahi B, Phielipp N, Chen R. **N-methyl-d-aspartate antagonists (amantadine)** in levodopa induced dyskinesia: a meta-analysis. Can J Neurol Sci. 2012 Jul;39(4):465-72.

Elbers RG, Berendse HW, Kwakkel G. **Treatment of Fatigue** in Parkinson Disease. JAMA. 2016 Jun 7;315(21):2340-1.

Emre M, Tsolaki M, Bonuccelli Uet al; 11018 Study Investigators. **Memantine** for patients with **Parkinson's disease dementia** or dementia with **Lewy bodies**: a randomised, double-blind, placebo-controlled trial. Lancet Neurol. 2010 Oct;9(10):969-77.

Engeln M, Fasano S, Ahmed SH, et al. L-**dopa gains psychostimulant-like properties** after nigral dopaminergic loss. Ann Neurol. 2013 Mar 12.

Espay AJ, Dwivedi AK, Payne M, et al. **Methylphenidate for gait** impairment in Parkinson disease: A randomized clinical trial. Neurology. 2011 Apr 5;76(14):1256-62.

Espay AJ, Fasano A, van Nuenen BFL, Payne MM, Snijders AH, Bloem BR. “**On” state freezing** of gait in Parkinson disease: a paradoxical **levodopa-induced** complication. Neurology 2012;78:454 – 457

Espay AJ, Norris MM, Eliassen JC, et al. **Placebo effect of medication cost** in Parkinson disease: a randomized doubleblind study. Neurology 2015;84:794–802.

Espay AJ, Lang AE. Common **Myths in the Use of Levodopa** in Parkinson Disease: When Clinical Trials Misinform Clinical Practice. JAMA Neurol. 2017 May 1.

Espay AJ, Morgante F, Merola A, et al. **Levodopa-induced dyskinesia** in Parkinson disease:Current and **Evolving Concepts**. Ann Neurol. 2018 Oct 24.

Evatt ML, Delong MR, Khazai N, Rosen A, Triche S, Tangpricha V. Prevalence of **vitamin d insufficiency** in patients with Parkinson disease and Alzheimer disease. Arch Neurol. 2008 Oct;65(10):1348-52. This report of 25(OH)D concentrations in a predominantly white PD cohort demonstrates a significantly higher prevalence of **hypovitaminosis in PD** vs both healthy controls and patients with AD. These data support a possible role of vitamin D insufficiency in PD.

Evatt ML, Delong MR, Kumari M, et al; for the Parkinson Study Group **DATATOP** Investigators. High Prevalence of **Hypovitaminosis D** Status in Patients With Early Parkinson Disease. Arch Neurol. 2011 Mar;68(3):314-319.

Ewenczyk C, Mesmoudi S, Gallea C, et al. **Antisaccades** in Parkinson disease: A new marker of postural control? Neurology. 2017 Feb 28;88(9):853-861.

Factor SA, Bennett A, Hohler AD, et al. **Quality improvement in neurology**: Parkinson disease update quality measurement set: **Executive summary**. Neurology. 2016 Jun 14;86(24):2278-83.

Fang X, Han D, Cheng Q, et al. Association of levels of **physical activity with risk of Parkinson disease**: a systematic review and meta-analysis. JAMA Open Netw. 2018;1(5):e182421.

Fasano A, Daniele A, Albanese A. Treatment of motor and non-motor features of Parkinson's disease with **deep brain stimulation**. Lancet Neurol. 2012 May;11(5):429-42.

Fasano A, Visanji NP, Liu LW, et al. **Gastrointestinal dysfunction** in Parkinson's disease. Lancet Neurol. 2015 Jun;14(6):625-639.

Faust-Socher A, Kenett Y, Cohen O, et al. **Enhanced Creative Thinking under Dopaminergic Therapy** in Parkinson's Disease. Ann Neurol. 2014 May 10.

FDA Drug Safety Communication: Ongoing Safety Review of **Stalevo** (entacapone/carbidopa/levodopa) and possible development of **Prostate Cancer** in **STRIDE-PD** trial. Mar/10 http://www.fda.gov/Drugs/DrugSafety/PostmarketDrugSafetyInformationforPatientsandProviders/ucm206363.htm In that trial, 3.7% of pts taking Stalevo developed prostate cancer over a mean follow-up of 2.7 years, compared with 0.9% of patients taking carbidopa/levodopa (Sinemet) (odds ratio, 4.2). Previous trials of Stalevo and Comtan (entacapone) did not find an association with prostate cancer. FDA Drug Safety Communication Aug/10 : Patients taking **Stalevo** (carbidopa/levodopa plus entacapone) for Parkinson disease might be at greater risk for **cardiovascular events** than those taking Sinemet (carbidopa/levodopa), according to the FDA. The agency conducted a meta-analysis after the STRIDE-PD trial found a higher rate of myocardial infarction in patients using Stalevo. The meta-analysis of 15 clinical trials found an association between Stalevo and cardiovascular events (relative risk, 2.46), but the results were no longer significant after excluding the STRIDE-PD data. Then FDA statement Aug 2019: no increased risk of prostate cancer with the use of entacapone or Stalevo.

FDA Sep/12 notified healthcare profesionals about a possible increased risk of **heart failure with Mirapex (pramipexole)**. Results of recent studies suggest a potential risk of heart failure that needs further review of available data.

FDA Oct/15 safety review has found no **clear evidence of an increased risk of heart attacks, stroke, or other cardiovascular events associated with the use of entacapone** for the treatment of Parkinson’s disease. As a result, recommendations for using Comtan (entacapone) and Stalevo (a combination of entacapone, carbidopa, and levodopa) will remain the same in the drug labels.

FDA Sep/18: U.S. Food and Drug Administration (FDA) has completed a review of all postmarketing reports of deaths and serious adverse events (SAEs) reported with the use of Nuplazid (pimavanserin). Based on an analysis of all available data, FDA did not identify any new or unexpected safety findings with Nuplazid, or findings that are inconsistent with the established safety profile.

FDA Aug/19 review finds no increased risk of prostate cancer with Parkinson’s disease medicines, **Comtan (entacapone) and Stalevo (a combination of entacapone, carbidopa, and levodopa).**

Fedorova TD, Seidelin LB, Knudsen K, et al. **Decreased intestinal acetylcholinesterase** in early Parkinson disease: An (11)C-donepezil PET study. Neurology. 2017 Feb 21;88(8):775-781.

Fernandez HH. **Updates in the medical management** of Parkinson disease. Cleve Clin J Med. 2012 Jan;79(1):28-35.

Fereshtehnejad SM, Romenets SR, Anang JB, et al. **New Clinical Subtypes of Parkinson Disease** and Their Longitudinal Progression: A Prospective Cohort Comparison With Other Phenotypes. JAMA Neurol. 2015 Jun 15.

Ferreira JJ, Katzenschlager R, Bloem BR, et al. Summary of the recommendations of the **EFNS/MDS-ES review on therapeutic management of Parkinson's disease**. Eur J Neurol. 2013 Jan;20(1):5-15.

Ferreira JJ, Lees A, Rocha J-F, et al, Bi-Park 1 investigators. **Opicapone** as an adjunct to levodopa in patients with Parkinson’s disease and end-of-dose motor fluctuations: a randomised, double-blind, placebo-controlled and active-controlled parallel-group trial. Lancet Neurol 2015; online Dec 22.

Ferreira JJ, Lees AJ, Poewe W, et al. Effectiveness of **opicapone and switching from entacapone** in fluctuating Parkinson disease. Neurology. 2018 Apr 25.

Firbank MJ, Parikh J, Murphy N, et al. **Reduced occipital GABA in Parkinson disease with visual hallucinations**. Neurology. 2018 Aug 14;91(7):e675-e685.

Fitzmaurice AG, Rhodes SL, Cockburn M, et al. Aldehyde dehydrogenase variation enhances effect of **pesticides** associated with Parkinson disease. Neurology. 2014 Feb 4;82(5):419-26.

Floden D, Cooper SE, Griffith SD, et al. Predicting quality of life outcomes after **subthalamic nucleus deep brain stimulation**. Neurology. 2014 Oct 28;83(18):1627-33.

Flynn A, Allen NE, Dennis S, et al. Home-based **prescribed exercise improves balance-related activities** in people with Parkinson's disease and has benefits similar to centre-based exercise: a systematic review. J Physiother. 2019 Oct;65(4):189-199.

Follett, Kenneth A., Weaver, Frances M., Stern, Matthew, et al. the CSP 468 Study Group, Pallidal versus Subthalamic Deep-Brain **Stimulation** for Parkinson's Disease. N Engl J Med 2010 362: 2077-2091.

Ford GA, Bhakta BB, Cozens A, et al. Safety and efficacy of **co-careldopa as an add-on therapy** to occupational and physical therapy in patients after stroke (DARS): a randomised, double-blind, placebo-controlled trial. Lancet Neurol. 2019 Jun;18(6):530-538.

Fornarino S, Stagnaro M, Rinelli M, et al. Paroxysmal features responding to **flunarizine** in a child with rapid-onset dystonia-parkinsonism. Neurology. 2014 Jun 3;82(22):2037-8.

Forsaa EB, Larsen JP, Wentzel-Larsen T, et al. A 12-year population-based study of **psychosis in Parkinson disease**. Arch Neurol. 2010 Aug;67(8):996-1001.

Fox SH, Katzenschlager R, Lim S-Y, et al. The **Movement Disorder Society Evidence**-Based Medicine Review Update: treatments for the **motor symptoms** of Parkinson's disease. Mov Disord 2011;26:Suppl 3:S2-S41.

Fralick M, Sacks CA, Kesselheim AS. Assessment of Use of Combined **Dextromethorphan and Quinidine in Patients With Dementia or Parkinson Disease** After US Food and Drug Administration Approval for **Pseudobulbar Affect**. JAMA Intern Med. 2019 Jan 7.

Fraser KB, Moehle MS, Alcalay RN, West AB; LRRK2 Cohort Consortium. **Urinary LRRK2 phosphorylation** predicts parkinsonian phenotypes in G2019S LRRK2 carriers. Neurology 2016;86:994–999

Friedman JH, Chang V. **Crack cocaine use** due to dopamine agonist therapy in Parkinson disease. Neurology. 2013 Jun 11;80(24):2269-70.

Frithsen IL, Simpson WM Jr. Recognition and management of acute medication **poisoning**. Am Fam Physician. 2010 Feb 1;81(3):316-23.

Fullard ME, Thibault DP, Hill A, et al. Utilization of **rehabilitation therapy services** in Parkinson disease in the United States. Neurology. 2017 Sep 12;89(11):1162-1169.

Fujimaki M, Saiki S, Li Y, et al. Serum **caffeine** and metabolites are reliable biomarkers of early Parkinson disease. Neurology 2018;90:e404–e411.

Funayama M, Ohe K, Amo T, et. al. **HCHD2 mutations** in autosomal dominant late-onset Parkinson's disease: a genome-wide linkage and sequencing study. Lancet Neurol. 2015 Feb 3. pii: S1474-4422(14)70266-2.

Gagne JJ, Power MC. **Anti-inflammatory drugs** and risk of Parkinson disease: a meta-analysis. Neurology 2010;74:995–1002.

Gallo V, Vineis P, Cancellieri M, et al. Exploring causality of the association between **smoking and Parkinson's disease**. Int J Epidemiol. 2018 Nov 20.

Ganesan M, Sathyaprabha TN, Pal PK, et al. **Partial Body Weight-Supported Treadmill Training** in Patients With Parkinson Disease: Impact on Gait and Clinical Manifestation. Arch Phys Med Rehabil. 2015 Sep;96(9):1557-65.

Gan-Or Z, Bar-Shira A, Dahary D, et al. Association of Sequence Alterations in the **Putative Promoter of RAB7L1** With a Reduced Parkinson Disease Risk. Arch Neurol. 2012 Jan;69(1):105-10.

Gan-Or Z, Ozelius LJ, Bar-Shira A, et al. The p.**L302P mutation** in the lysosomal enzyme gene SMPD1 is a risk factor for Parkinson disease. Neurology 2013;80:1606–1610.

Gan-Or Z, Amshalom I, Kilarski LL, et al. Differential effects of **severe vs mild GBA mutations** on Parkinson disease. Neurology 2015;84:880–887.

Gao X, Chen H, Schwarzschild MA, et al. Use of **ibuprofen and risk of Parkinson disease**. Neurology. 2011 Mar 8;76(10):863-9.
Gao X, Simon K, Schwarzschild M et al. Prospective Study of **Statin Use** and Risk of Parkinson Disease Arch Neurol. 2012;69(3):380-384.
Gao X, Cassidy A, Schwarzschild MA, Rimm EB, Ascherio A. Habitual intake of **dietary flavonoids** and risk of Parkinson disease. Neurology 2012;78:1138 –1145.
Gao X, O'Reilly ÉJ, Schwarzschild MA, et al. Prospective study of **plasma urate** and risk of Parkinson disease in men and women. Neurology. 2016 Feb 9;86(6):520-6.
Gardner RC, Burke JF, Nettiksimmons J, et al. **Traumatic brain injury** in later life increases risk for Parkinson's disease. Ann Neurol. 2015 Feb 27.
Gardner RC, Byers AL, Barnes DE, et al. **Mild TBI and risk of Parkinson disease**: A Chronic Effects of Neurotrauma Consortium Study. Neurology. 2018 Apr 18.
Gardner RC, Byers AL, Barnes DE, et al. **Mild TBI** and risk of Parkinson disease: A Chronic Effects of Neurotrauma Consortium Study. Neurology. 2018 May 15;90(20):e1771-e1779.
Gazewood JD, Richards DR, Clebak K. **Parkinson Disease**: An Update. Am Fam Physician. 2013;87(4):267-273.
GBD 2016 Parkinson's Disease Collaborators. **Global, regional, and national burden** of Parkinson's disease, 1990-2016: a systematic analysis for the Global Burden of Disease Study 2016. Lancet Neurol. 2018 Nov;17(11):939-953.
Giacino JT et al. Placebo-controlled trial of **amantadine for severe traumatic brain injury**. N Engl J Med 2012 Mar 1; 366:819.
Gitchel GT, Wetzel PA, Baron MS. Pervasive **Ocular Tremor** in Patients With Parkinson Disease. Arch Neurol. 2012 Apr 9.
Gjerstad MD, Tysnes OB, Larsen JP. Increased risk of **leg motor restlessness but not RLS** in early Parkinson disease. Neurology 2011;77:1941–1946.
Godau J, Knauel K, Weber K et al. Serum **insulinlike growth factor 1** as possible marker for risk and early diagnosis of Parkinson disease. Arch Neurol. 2011 Jul;68(7):925-31.
Goetz CG, Poewe W, Rascol O, Sampaio C. **Evidence-based medical review** update: pharmacological and surgical treatments of Parkinson's disease: 2001 to 2004. Mov Disord. **2005** May;20(5):523-39.
Goetz CG, Pal G. **Initial management of Parkinson's disease**. BMJ. 2014 Dec 19;349:g6258.
Goldman SM, Marek K, Ottman R, et al. Concordance for Parkinson's **Disease in Twins**: a 20-Year Update. Ann Neurol. 2019 Feb 20.
Goldman SM, Quinlan PJ, Ross GW, et al. **Solvent exposures** and parkinson disease risk in twins. Ann Neurol. 2011 Nov 14.
Goodarzi Z, Mrklas KJ, Roberts DJ, et al. Detecting **depression** in Parkinson disease: A systematic review and meta-analysis.Neurology. 2016 Jun 29.
Gottwald MD, Aminoff MJ. Emerging Therapies for **Dopaminergic-induced Dyskineasias** in Parkinson's Disease. Annals of Neurology. Accepted manuscript online: 16 MAR 2011; 1-17.
Gratwicke J, Zrinzo L, Kahan J, et al. **Bilateral deep brain stimulation** of the nucleus basalis of Meynert for Parkinson disease dementia: a randomized clinical trial [online Dec 18, 2017].JAMA Neurol. doi:10.1001 /jamaneurol.2017.3762
Gross RE, Watts RL, et al. Spheramine Investigational Group. Intrastriatal transplantation of microcarrier-bound human **retinal pigment epithelial cells versus sham surgery** in patients with advanced Parkinson's disease: a double-blind, randomised, controlled trial. Lancet Neurol. 2011 May 10.
Grosset KA, et al. **Problematic gambling** on dopamine agonists: Not such a rarity. Mov Disord. 2006 Sep 29; [Epub ahead of print]
Grosset DG, Macphee GJ, Nairn M; Guideline Development Group. Diagnosis and pharmacological management of Parkinson's disease: summary of **SIGN** guidelines. BMJ. 2010 Jan 12;340:b5614. doi: 10.1136/bmj.b5614.
Grover S, Lill CM, Kasten M, et al. **Risky behaviors** and Parkinson disease: A mendelian randomization study. Neurology. 2019 Oct 8;93(15):e1412-e1424.
Gruntz K, Bloechliger M, Becker C, et al. Parkinson's disease and the **risk of epileptic seizures**. Ann Neurol. 2018 Jan 25.
Gustafsson H, Aasly J, Ståhle S, et al. **Low muscle strength** in late adolescence and Parkinson disease later in life. Neurology. 2015 May 5;84(18):1862-9.
Gustafsson H, Nordström A, Nordström P. **Depression and subsequent risk of Parkinson disease**: A nationwide cohort study. Neurology. 2015 Jun 16;84(24):2422-9.
Hacker ML, DeLong MR, Turchan M, et al. Effects of **deep brain stimulation on rest tremor progression in early stage Parkinson disease**. Neurology. 2018 Jul 31;91(5):e463-e471.
Hall S, Surova Y, Öhrfelt A, et al. **CSF biomarkers** and clinical progression of Parkinson disease. Neurology. 2015 Jan 6;84(1):57-63.
Hammond FM et al. Effectiveness of **amantadine** hydrochloride in the reduction of chronic **traumatic brain injury** irritability and aggression. J Head Trauma Rehabil 2013 Nov 20.
Hansson O, Janelidze S, Hall S, et al. **Blood-based NfL**: a biomarker for differential diagnosis of parkinsonian disorder. Neurology 2017;88:930–937.
Harvey AR, Baker LB, Reddihough DS, et al. **Trihexyphenidyl for dystonia in cerebral palsy.** Cochrane Database Syst Rev. 2018 May 15;5:CD012430. At present, there is insufficient evidence regarding the effectiveness of trihexyphenidyl for people with cerebral palsy for the outcomes of: change in dystonia, adverse effects, increased upper limb function and improved participation in activities of daily living. The study did not measure pain or quality of life. There is a need for larger randomised, controlled, multicentre trials that also examine the effect on pain and quality of life in order to determine the effectiveness of trihexyphenidyl for people with cerebral palsy.
Hassan A, Benarroch EE. **Heterogeneity of the midbrain** dopamine system: Implications for Parkinson disease. Neurology. 2015 Nov 17;85(20):1795-805.
Hauser RA. Long-term care of Parkinson's disease. Strategies for managing "**wearing off**" symptom re-emergence and dyskinesias. Geriatrics. 2006 Sep;61(9):14-20.
Hauser RA, Hsu A, Kell S, et al, for the IPX066 ADVANCE-PD investigators. **Extended-release carbidopa-levodopa (IPX066)** compared with immediate-release carbidopa-levodopa in patients with Parkinson's disease and motor fl uctuations: a phase 3 randomised, double-blind trial. Lancet Neurol 2013; online Feb 26.
Hauser RA, Olanow CW, Kieburtz KD, et al. **Tozadenant (SYN115)** in patients with Parkinson's disease who have motor fl uctuations on levodopa: a phase 2b, double-blind, randomised trial. Lancet Neurol 2014; online July 7.
Hauser RA, Stocchi F, Rascol O, et al. **Preladenant** as an Adjunctive Therapy With Levodopa in Parkinson Disease: Two Randomized Clinical Trials and Lessons Learned. JAMA Neurol. 2015 Dec;72(12):1491-500.
Hawthorne JM, Caley CF. Extrapyramidal Reactions Associated With Serotonergic Antidepressants. Ann Pharmacother. 2015 Oct;49(10):1136-52.
Health Canada Aug/07: Eli Lilly Canada advises Healthcare Professionals that they will **cease sale of Permax** August 30, 2007 due to risk of cardiac valvulopathy.
Health Canada Jul/16 is informing Canadians that two unauthorized health products were seized from Next Level Fitness in Richmond and in Surrey,BC. The products **TRT** (Testosterone Booster) and **Freak'n Test** (Testosterone Enhancer) were labelled to contain a prescription drug substance (L-dopa) that may pose serious health risks to Canadians.
Health Canada Jan/17 is advising Canadians that it has seized three unauthorized workout supplements from Reflex Supplements at #105–10712, 78 Ave., Grande Prairie, AB. "**Animal PM**" is labelled to **contain L-dopa** while "Blade" is labelled to contain yohimbine.
Health Canada Jul/17: Man XXX has undeclared **levodopa** by the Australia Therapeutic Goods Administration.
Hellwig S, Amtage F, Kreft A, et al**. [18F]FDG-PET** is superior to [123I]IBZM-SPECT for the differential diagnosis of parkinsonism. Neurology. 2012 Sep 25;79(13):1314-22.
Henderson EJ, Lord SR, Brodie MA, et al. **Rivastigmine for gait stability** in patients with Parkinson's disease (ReSPonD): a randomised, double-blind, placebo-controlled, phase 2 trial. Lancet Neurol 2016; online Jan 12.
Herz DM, Haagensen BN, Christensen MS, et al. The **acute brain response to levodopa heralds dyskinesias** in Parkinson disease. Ann Neurol. 2014 May 28.
Hilfiker-Kleiner D, Haghikia A, Berliner D, et al. **Bromocriptine** for the treatment of **peripartum cardiomyopathy**: a multicentre randomized study. Eur Heart J. 2017 Sep 14;38(35):2671-2679.
Hodgins David C, Stea Jonathan N, Grant Jon E. **Gambling disorders**. www.thelancet.com Published online May 19, 2011 DOI:10.1016/S0140-6736(10)62185-X
Holman AJ, Myers RR. A randomized, double-blind, placebo-controlled trial of **pramipexole**, a dopamine agonist, in patients with **fibromyalgia** receiving concomitant medications. Arthritis Rheum. 2005 Aug;52(8):2495-505.
Hong JY, Oh JS, Lee I, et al. **Presynaptic dopamine depletion** predicts **levodopa-induced dyskinesia** in de novo Parkinson disease. Neurology 2014;82:xx–xx.
Honma M, Masaoka Y, Kuroda T, et al. Impairment of cross-modality of **vision and olfaction** in Parkinson disease. Neurology. 2018 Mar 13;90(11):e977-e984.
Homayoun H. In the Clinic: Parkinson Disease. Ann Intern Med. 2018 Sep 4;169(5):ITC33-ITC48.
Hopfner F, Wod M, Höglinger GU, et al. Use of **β2-adrenoreceptor agonist and antagonist drugs and risk of Parkinson** disease. Neurology. 2019 Jul 9;93(2):e135-e142.
Hu Y, Yu SY, Zuo LJ, et al. Parkinson disease with **REM sleep behavior disorder**: Features, α-synuclein, and inflammation. Neurology. 2015 Mar 3;84(9):888-94.
Huang MH, Cheng CM, Huang KL, et al. **Bipolar disorder and risk** of Parkinson disease: a nationwide longitudinal study. Neurology 2019;92:e2735–e2742.
Hughes KC, Gao X, Kim IY, et al. Intake of **dairy foods** and risk of Parkinson disease. Neurology. 2017 Jul 4;89(1):46-52.
Hurwitz B. The art of medicine-**Parkinson's Disease: What's in the name**. Lancet. 2017; 389:2098-2099
Hutchinson M. At last, a **gene therapy** for Parkinson's disease? Lancet Neurol. 2011 Apr;10(4):290-1.
Iacono D, Geraci-Erck M, Rabin ML, et al. **Parkinson disease and incidental Lewy body disease**: Just a question of time? Neurology. 2015 Nov 10;85(19):1670-9.
International Parkinon Disease Genomics Consortium. Imputation of sequence variants for identification of **genetic risks for Parkinson's disease**: a meta-analysis of **genome-wide association studies**. Lancet. Online Feb. 2, 2011.
Ir anzo A, Tolosa E, Gelpi E, et al. Neurodegenerative disease status and post-mortem pathology in idiopathic **rapid-eye-movement sleep behaviour disorder**: an observational cohort study. Lancet Neurology 2013.
Irwin DJ, White MT, Toledo JB, et al. **Neuropathologic substrates** of Parkinson disease dementia. Ann Neurol. 2012 Jun 13.
Jacova C, Factor SA. **Phosphodiesterase 4:** Rethinking cognition in Parkinson disease. Neurology. 2017 Aug 8;89(6):530-531.
Jankovic J, Goodman I, Safirestein B, et al. Safety and tolerability of **multiple ascending doses of PRX002/RG7935**, an anti–α-synuclein **monoclonal antibody**, in patients with Parkinson disease: a randomized clinical trial [June 18, 2018]. JAMA Neurol. doi:10.1001/jamaneurol.2018.1487
Janelidze S, Lindqvist D, Francardo V, et al. Increased **CSF biomarkers of angiogenesis** in Parkinson disease. Neurology 2015;85:1834–1842.
Jankovic J, Watts RL, Martin W, Boroojerdi B. Transdermal **rotigotine**: double-blind, placebo-controlled trial in Parkinson disease. Arch Neurol. 2007 May;64(5):676-82.
Jennings D, Siderowf A, Stern M, et al; PARS Investigators. **Imaging prodromal Parkinson** disease: The Parkinson Associated Risk Syndrome Study. Neurology. 2014 Nov 4;83(19):1739-46.
Jiang H, He P, Adler CH, et al. **Bid signal pathway** components are identified in the temporal cortex with Parkinson disease. Neurology 2012;79:1767–1773.
Jost WH, Friedman A, Michel O, et al. **SIAXI**: Placebo-controlled, randomized, double-blind study of **incobotulinumtoxinA for sialorrhea**. Neurology. 2019 Apr 23;92(17):e1982-e1991.
Jung Kang U, Auinger P; On behalf of the Parkinson Study Group ELLDOPA Investigators, Mendis T. **Activity enhances dopaminergic long-duration response** in Parkinson disease. Neurology. 2012 Apr 10;78(15):1146-1149.
Jung YJ, Kim HJ, Jeon BS, Park H, LeeWW, Paek SH. An 8-year follow-up on the effect of **subthalamic nucleus deep brain stimulation** on pain in Parkinson disease [online March 23, 2015]. JAMA Neurol. doi:10.1001/jamaneurol.2015
Junghanns S, Fuhrmann JT, et al. **Valvular heart disease** in Parkinson's disease patients treated with dopamine agonists: A reader-blinded monocenter echocardiography study. Mov Disord. 2006 Nov 8; [Epub ahead of print] Our data suggest that ergot DAs are associated with higher prevalence of VHD compared to non-ergot DAs and controls. Standard echocardiography seems sufficient to detect VHD in PD patients treated with DAs.
Juttukonda MR, Franco G, Englot DJ, et al. **White matter differences between essential tremor and Parkinson disease**. Neurology. 2019 Jan 1;92(1):e30-e39.
Kaasinen V, Vahlberg T. **Striatal dopamine** in Parkinson's disease: A meta-analysis of imaging studies. Ann Neurol. 2017 Nov 22.

Kalia LV, Lang AE. **Parkinson's disease**. Lancet. 2015 Apr 17.

Kang JH, Irwin DJ, Chen-Plotkin AS, et al; and the Parkinson's Progression Markers Initiative. Association of **Cerebrospinal Fluid β-Amyloid 1-42, T-tau, P-tau181, and α-Synuclein Levels** With Clinical Features of Drug-Naive Patients With Early Parkinson Disease. JAMA Neurol. 2013 Aug 26.

Karlawish J, Cary M, Moelter ST, et al. Cognitive impairment and PD patients' capacity to **consent to research**. Neurology 2013;81:801–807.

Katz M, San Luciano M, Carlson K, et al. The **differential effects of DBS target** on motor subtypes in Parkinson's disease. Ann Neurol. 2015 Jan 27.

Katzenschlager R, Poewe W, Rascol O, et al**. Apomorphine subcutaneous infusion in patients with Parkinson's disease with persistent motor fluctuations** (TOLEDO): a multicentre, double-blind, randomised, placebo-controlled trial. Lancet Neurol. 2018 Sep;17(9):749-759.

Kenborg L, Rugbjerg K, Lee PC, et al. **Head injury** and risk for Parkinson disease: Results from a Danish case-control study. Neurology. 2015 Mar 17;84(11):1098-103.

Khan S, Gill SS, Mooney L, et al. Combined **pedunculopontine subthalamic stimulation (DBS)** in Parkinson disease. Neurology 2012;78:1090 –1095.

Kia DA, Noyce AJ, White J, et al. Mendelian randomization study shows **no causal relationship between circulating urate levels and Parkinson's disease**. Ann Neurol. 2018 Jul 16.

Killinger BA, Madaj Z, Sikora JW, et al. The **vermiform appendix** impacts the risk of developing Parkinson's disease. Sci Transl Med. 2018 Oct 31;10(465).

Kim IY, O'Reilly ÉJ, Hughes KC, et al. Integration of **risk factors** for Parkinson disease in 2 large longitudinal cohorts. Neurology. 2018 Apr 11.

Kim R, Lee J, Kim HJ, et al. **CSF β-amyloid(42) and risk of freezing of gait** in early Parkinson disease. Neurology. 2019 Jan 1;92(1):e40-e47.

Kipfer S, Stephan MA, Schüpbach WM, et al. **Resting tremor** in Parkinson disease: a negative predictor of levodopa-induced dyskinesia. Arch Neurol. 2011 Aug;68(8):1037-9.

Kirsch-Darrow L, et al. Dissociating **apathy and depression** in Parkinson disease. Neurology. 2006 Jul 11;67(1):33-8.

Klein C, Prokhorov T, et al. Long-term Follow-up (24 Months) of **Quetiapine** Treatment in Drug-induced Parkinson Disease Psychosis. Clin Neuropharmacol. 2006 Jul-Aug;29(4):215-9.

Klepitskaya O, Liu Y, Sharma S, et al. **Deep brain stimulation improves restless legs syndrome in patients with Parkinson disease**. Neurology. 2018 Sep 11;91(11):e1013-e1021.

Klibanski, Anne. **Prolactinomas**. N Engl J Med 2010 362: 1219-1226.

Khoo TK, Yarnall AJ, Duncan GW, et al. The spectrum of **nonmotor symptoms** in early Parkinson disease. Neurology. 2013 Jan 15;80(3):276-81.

Kobylecki CJ, Nordestgaard BG, Afzal S. **Plasma urate and risk of Parkinson's disease**: a Mendelian randomization study. Ann Neurol. 2018 Jul 16.

Koo BB, Chow CA, Shah DR, et al. **Demoralization** in Parkinson disease. Neurology. 2018 May 1;90(18):e1613-e1617.

Korczyn AD. **Vascular Parkinsonism--characteristics, pathogenesis and treatment**. Nat Rev Neurol. 2015 Jun;11(6):319-26.

Kostic VS, Agosta F, Pievani M et al. Pattern of **brain tissue loss** associated with **freezing of gait** in Parkinson disease. Neurology. 2012 Feb 7;78(6):409-16.

Kotagal V, Albin RL, Müller MLTM, et al. **Modifiable cardiovascular risk factors** and axial motor impairments in Parkinson disease. Neurology 2014;82:1514–1520.

Koychev I, Okai D. **Cognitive-behavioural therapy for non-motor symptoms** of Parkinson's disease: a clinical review. Evid Based Ment Health. 2017 Jan 10.

Knekt Paul; Kilkkinen Annamari; Rissanen Harri; et al. Serum **Vitamin D** and the Risk of Parkinson Disease Arch Neurol. 2010;67(7):808-811.

Krack P, Batir A, Van Blercom N, et al. Five-year follow-up of **bilateral stimulation of the subthalamic nucleus** in advanced Parkinson's disease. N Engl J Med 2003;349:1925-34.

Kubu CS, Cooper SE, Machado A, Frazier T, Vitek J, Ford PJ. Insights gleaned by measuring **patients' stated goals for DBS**: More than tremor. Neurology. 2017 Jan 10;88(2):124-130.

Kumlien E, Lundberg PO. **Seizure risk** associated with **neuroactive drugs**: data from the **WHO** adverse drug reactions database. Seizure. 2010 Mar;19(2):69-73.

Kummer BR, Diaz I, Wu X, et al. **Associations between cerebrovascular risk factors** and parkinson disease. Ann Neurol. 2019 Aug 29.

Kwok JYY, Kwan JCY, Auyeung M, et al. Effects of **Mindfulness Yoga vs Stretching and Resistance** Training Exercises on Anxiety and Depression for People With Parkinson Disease: A Randomized Clinical Trial. JAMA Neurol. 2019 Apr 8.

Lake MG, Krook LS, Cruz SV. **Pituitary adenomas**: an overview. Am Fam Physician. 2013 Sep 1;88(5):319-27.

Lanier JB, Mote MB, Clay EC. Evaluation and management of **orthostatic hypotension**. Am Fam Physician. 2011 Sep 1;84(5):527-36.

Latourelle JC, Beste MT, Hadzi TC, et al. Large-scale identification of **clinical and genetic predictors of motor progression** in patients with newly diagnosed Parkinson's disease: a longitudinal cohort study and validation. Lancet Neurol 2017; online Sept 25.

Lee DH, Oh JS, Ham JH, et al. Is **normosmic** Parkinson disease a unique clinical **phenotype**? Neurology 2015;85: 1270–1275.

Lee J, Kim Y, Kim YL. **Non-pharmacological therapies** for **sleep disturbances** in people with **Parkinson's d**isease: A systematic review. J Adv Nurs. 2018 Apr 27.

Lee PC, Bordelon Y, Bronstein J, Ritz B. **Traumatic brain injury, paraquat exposure**, and their relationship to Parkinson disease. Neurology. 2012 Nov 13;79(20):2061-6.

Lee PC, Ahmed I, Loroit MA, et al. **Smoking and Parkinson disease**: evidence for gene-by-smoking interactions. Neurology 2018;90:e583–e592.

Lee JY, Seo S, Lee JS, Kim HJ, Kim YK, Jeon BS. **Putaminal serotonergic innervation**: monitoring dyskinesia risk in Parkinson disease. Neurology 2015;85:853–860.

Lee Y-C et al. **Discontinuation of statin** therapy associates with Parkinson disease: A population-based study. Neurology 2013 Jul 24.

Leentjens AF. The role of **dopamine agonists in the treatment of depression** in patients with Parkinson's disease: a systematic review. Drugs. 2011 Feb 12;71(3):273-86. doi: 10.2165/11585380-000000000-00000.

Leentjens AF, Moonen AJ, Dujardin K, et al. **Modeling depression** in Parkinson disease:Disease-specific and nonspecific risk factors. Neurology. 2013 Sep 17;81(12):1036-1043.

Lees A. Alternatives to levodopa in the initial treatment of early Parkinson's disease. Drugs Aging. 2005;22(9):731-40.

Lees AJ, Hardy J, Revesz T. **Parkinson's disease**. Lancet. 2009 Jun 13;373(9680):2055-66.

Lees AJ, Ferreira J, Rascol O, et al. **Opicapone** as Adjunct to Levodopa Therapy in Patients With Parkinson Disease and Motor Fluctuations: A Randomized Clinical Trial. JAMA Neurol. 2016 Dec 27.

Leung IH, Walton CC, Hallock H, et al. **Cognitive training** in Parkinson disease: A systematic review and meta-analysis. Neurology. 2015 Oct 30.

Lewitt PA, Rezai AR, Leehey MA, et al. **AAV2-GAD gene therapy** for advanced Parkinson's disease: a double-blind, sham-surgery controlled, randomised trial. Lancet Neurol. 2011 Apr;10(4):309-19.

Lewitt PA, Hauser RA, Lu M, et al. Randomized clinical trial of **fipamezole** (90mg tid) for dyskinesia in Parkinson disease (FJORD study). Neurology. 2012 Jun 27.

LeWitt PA, Li J, Lu M, et al; Parkinson Study Group–**DATATOP** Investigators.. **Metabolomic biomarkers** as strong correlates of Parkinson disease progression. Neurology. 2017 Feb 28;88(9):862-869.

Lexicomp Online® , Lexi-interact® , Hudson, Ohio: Lexi-comp Inc; February 12, 2018

Lhommee E, Wojtecki L, et al. Behavioural outcomes of **subthalamic stimulation and medical therapy versus medical therapy alone** for Parkinson's disease with early motor complications (**EARLYSTIM** trial): secondary analysis of an open-label randomised trial. Lancet Neurol 2018; 17: 223–31.

Li F et al. **Tai chi** and postural stability in patients with Parkinson's disease. N Engl J Med 2012 Feb 9; 366:511.

Lin CH, Li CH, Yang KC, et al. Blood NfL: A **biomarker for disease severity and progression** in Parkinson disease. Neurology. 2019 Sep 10;93(11):e1104-e1111.

Lin KD, Yang CY, Lee MY, et al. **Statin** Therapy Prevents the Onset of Parkinson Disease in Patients with Diabetes. Ann Neurol. 2016 Jul 29

Lin WY, Lin MS, Weng YH, et al. Association of **Antiviral Therapy With Risk** of Parkinson Disease in Patients With Chronic Hepatitis C Virus Infection. JAMA Neurol. 2019 Jun 5.

Ling H, Kearney S, Yip HL, et al. Parkinson's disease **without nigral degeneration**: a pathological correlate of scans without evidence of dopaminergic deficit (SWEDD)? J Neurol Neurosurg Psychiatry. 2016 Jun;87(6):633-41.

Little S, Pogosyan A, Neal S, et al. **Adaptive deep brain stimulation** in advanced Parkinson disease. Ann Neurol. 2013 Jul 12.

Liu B, Fang F, Pedersen NL, et al. **Vagotomy** and Parkinson disease: A Swedish register-based matched-cohort study. Neurology. 2017 Apr 26.

Liu G, Locascio JJ, Corvol C, et al. Assessment of a **clinical-genetic score for the prediction of cognition** in Parkinson's disease: a longitudinal analysis of nine cohorts. Lancet Neurol 2017; online June 16.

Liu G, Sterling NW, Kong L, et al. **Statins** may facilitate Parkinson's disease: Insight gained from a large, national claims database. Mov Disord. 2017 Jun;32(6):913-917.

Liu R, Gao X, Lu Y, Chen H. Meta-analysis of the relationship between **Parkinson disease and melanoma**. Neurology. 2011 Jun 7;76(23):2002-9.

Liu R, Umbach DM, Peddada SD, et al. Potential sex differences in **nonmotor symptoms** in early drug-naive Parkinson disease. Neurology. 2015 May 26;84(21):2107-15.

Liu S-Y, Wile DJ, Fu J, et al. The effect of **LRRK2 mutations** on the cholinergic system in manifest and premanifest stages of Parkinson's disease: a cross-sectional PET study. Lancet Neurol 2018; online Feb 15.

Liu S, Hu C, Peters J, et al. Pharmacokinetics and Pharmacodynamics of **Ropinirole in Patients with Prolactinomas**. Br J Clin Pharmacol. 2018 Oct 25.

Loane C, Wu K, Bain P, et al. **Serotonergic loss in** motor circuitries correlates with severity of action-postural **tremor** in PD. Neurology. 2013 May 14;80(20):1850-5.

Löhle M, Mende J, Wolz M, et al. **Putaminal dopamine turnover** in de novo Parkinson disease predicts later motor complications. Neurology. 2016 Jan 19;86(3):231-40.

Maas RPPWM, Wassenberg T, Lin JP,et al**. l-Dopa in dystonia**: A modern perspective. Neurology. 2017 May 9;88(19):1865-1871

Mamikonyan E, Siderowf AD, Duda JE, Potenza MN, Horn S, Stern MB, Weintraub D. Long-term follow-up of **impulse control disorders** in Parkinson's disease. Mov Disord. 2007 Oct 25; [Epub ahead of print] For PD patients who develop an ICD in the context of DA treatment, discontinuing or significantly decreasing DA exposure, even when offset by an increase in levodopa treatment, is associated with remission of or significant reduction in ICD behaviors without worsening in motor symptoms.

Mantri S, Fullard M, Gray SL, et al. Patterns of **Dementia Treatment and Frank Prescribing Errors in Older Adults With Parkinson Disease.** JAMA Neurol. 2018 Oct 1.

Maraganore DM, et al.; Genetic Epidemiology of Parkinson's Disease (GEO-PD) Consortium. Collaborative analysis of **alpha-synuclein gene** promoter variability and Parkinson disease. JAMA. 2006 Aug 9;296(6):661-70.

Marín-Lahoz J, Sampedro F, Martinez-Horta S, et al. **Depression as a risk factor for impulse control disorders** in Parkinson's disease. Ann Neurol. 2019 Aug 15.

Marks Jr William J, Bartus Raymond T, Siffert Joao, et al. **Gene delivery of AAV2-neurturin** for Parkinson's disease: a double-blind, randomised, controlled trial, The Lancet Neurology, Volume 9, Issue 12, Dec 2010

Marques TM, van Rumund A, Oeckl P, et al. **Serum NFL discriminates** Parkinson disease from atypical parkinsonisms. Neurology. 2019 Mar 26;92(13):e1479-e1486.

Marras C, Gruneir A, Rochon P, et al. **Dihydropyridine calcium channel blockers** and the progression of parkinsonism. Ann Neurol. 2012 Mar;71(3):362-9.

Martínez-Fernández R, Rodríguez-Rojas R, del Álamo M, et al. **Focused ultrasound subthalamotomy** in patients with asymmetric Parkinson's disease: a pilot study. Lancet Neurol 2017; online Dec 1.

McDonnell MN, Rischbieth B, Schammer TT, et al. **Lee Silverman Voice Treatment (LSVT)-BIG** to improve motor function in people with Parkinson's disease: a systematic review and meta-analysis. Clin Rehabil. 2017 Oct 1:269215517734385.

Medical Letler. **Rotigotine** (Neupro) for Parkinson's Disease. Aug 27,2007.

Mehrholz J, Friis R, Kugler J, Twork S, Storch A, Pohl M. **Treadmill training** for patients with Parkinson's disease. Cochrane Database Syst Rev. 2010 Jan 20;(1):CD007830.

Menza M, Defronzo Dobkin R, Marin H, Mark MH, Gara M, Buyske S, Bienfait K, Dicke A. A controlled trial of antidepressants in patients with Parkinson disease and depression. Neurology. 2008 Dec 17. [Epub ahead of print] n=52. Though relatively modest in size, this is the largest placebo-controlled trial done to date in patients with Parkinson disease (PD) and depression. **Nortriptyline** was efficacious in the treatment of depression and paroxetine CR was not.

Mery VP, Gros P, Lafontaine AL, et al. **Reduced cognitive function** in patients with Parkinson disease and **obstructive sleep apnea**. Neurology. 2017 Mar 21;88(12):1120-1128.
Mestre TA, Shah P, Marras C, et al. Another face of **placebo: The lessebo** effect in Parkinson disease: Meta-analyses. Neurology. 2014 Apr 22;82(16):1402-9.
Metzer WS, Rodrigues FB. **Managing treatment fluctuations** in Parkinson disease: "On" again-, "off" again. Neurology. 2019 Mar 26;92(13):597-598.
Milber JM, Noorigian JV, Morley JF, et al. **Lewy pathology** is not the first sign of degeneration in vulnerable neurons in Parkinson disease. Neurology. 2012 Dec 11;79(24):2307-2314.
Miocinovic S, Somayajula S, Chitnis S, et al. History, applications, and mechanisms of **deep brain stimulation**. JAMA Neurol. 2013 Feb 1;70(2):163-71.
Mok KY, Sheerin U, Simon-Sanchez J, et al. **Deletions at 22q11.2** in idiopathic Parkinson's disease: a retrospective combined analysis of genome-wide association data. Lancet Neurol 2016; online March 23.
Mollenhauer Brit, Locascio Joseph J, Schulz-Schaeffer Walter, et al. **[alpha]-Synuclein and tau concentrations** in cerebrospinal fluid of patients presenting with parkinsonism: a cohort study, The Lancet Neurology, Volume 10, Issue 3, March 2011
Mollenhauer B, Zimmermann J, Sixel-Döring F, et al. Monitoring of **30 marker candidates** in early Parkinson disease as progression markers. Neurology 2016;87:168–177.
Mollenhauer B, Caspell-Garcia CJ, Coffey CS, et al; Parkinson's Progression Marker Initiative. **Longitudinal CSF biomarkers** in patients with early Parkinson disease and healthy controls. Neurology. 2017 Nov 7;89(19):1959-1969.
Monteiro L, Souza-Machado A, Valderramas S et al. The Effect of **Levodopa on Pulmonary Function** in Parkinson's Disease: A Systematic Review and Meta-Analysis. Clin Ther. 2012 Mar 30.
Moore TJ, Glenmullen J, Mattison DR. Reports of **pathological gambling, hypersexuality, and compulsive shopping associated with dopamine receptor agonist drugs** [online October 20, 2014]. JAMA Intern Med. doi: 10.1001/jamainternmed.2014.5262.
Moreno GM, Gandhi R, Lessig SL, et al. **Mortality** in patients with Parkinson disease psychosis receiving **pimavanserin and quetiapine**. Neurology. 2018 Oct 23;91(17):797-799.
Moreau C, Delval A, Defebvre L, et al; for the Parkgait-II study group. **Methylphenidate for gait hypokinesia and freezing** in patients with Parkinson's disease undergoing subthalamic stimulation: a multicentre, parallel, randomised, placebo-controlled trial. Lancet Neurol. 2012 May 31.
Morgante F, Fasano A, Ginevrino M, et al. **Impulsive-compulsive behaviors** in parkin-associated Parkinson disease. Neurology. 2016 Oct 4;87(14):1436-1441.
Morelli M, Arabia G, Novellino F, et al. **MRI measurements predict PSP** in unclassifiable parkinsonisms: A cohort study. Neurology. 2011 Sep 13;77(11):1042-7.
Moro E, Lozano AM, Pollak P, et al. Long-term results of a multicenter study on **subthalamic and pallidal stimulation** in Parkinson's disease. Mov Disord 2010; 25: 578–86.
Mortimer JA, Borenstein AR, Nelson LM. Associations of **welding and manganese** exposure with Parkinson disease: Review and meta-analysis. Neurology. 2012 Sep 11;79(11):1174-80.
Muller T, Mohr J. Recent Clinical Advances in Pharmacotherapy for Levodopa-induced dyskinesia. Drugs. 2019; Jul 23. doi: 10.1007/s40265-019-01170-5. [Epub ahead of print]
Murata M, Odawara T, Hasegawa K, et al. Adjunct **zonisamide** to levodopa **for DLB parkinsonism**: a randomized, double-blind phase 2 study. Neurology 2018;90: e664–e672.
Muzerengi S, Clarke CE. **Initial drug treatment** in Parkinson's disease. BMJ. 2015 Sep 18;351:h4669.
Na YC, Chang WS, Jung HH, et al. **Unilateral magnetic resonance-guided focused ultrasound pallidotomy** for Parkinson disease. Neurology. 2015 Aug 11;85(6):549-51.
Nalls MA, McLean CY, Rick J, for the Parkinsons Disease Biomarkers Program and Parkinsons Progression Marker Initiative investigators. Diagnosis of Parkinsons disease on the **basis of clinical and genetic classification**: population-based modelling study. Lancet Neurol 2015; online Aug 11.
Ni Z, Bahl N, Gunraj CA, Mazzella F, Chen R. Increased **motor cortical facilitation** and decreased inhibition in Parkinson disease. Neurology. 2013 May 7;80(19):1746-53.
NICE: National Institute for Health and Clinical Excellence - **Parkinson's disease**: diagnosis and management in primary and secondary care. June 2006. http://www.nice.org.uk/nicemedia/pdf/cg035niceguideline.pdf.
NICE: National Institute for Health and Care Excellence. **Parkinson's** disease in adults: diagnosis and management (NICE guideline NG71). 2017. www.nice.org.uk/guidance/ng71.
NICE: National Institute for Health and Care Excellence. **Parkinson's disease**: quality standard QS164. Feb 2018.https://www.nice.org.uk/guidance/QS164
Niccolini F, Wilson H, Pagano G, et al. Loss of **phosphodiesterase 4** in Parkinson disease: Relevance to **cognitive deficits**. Neurology. 2017 Aug 8;89(6):586-593
Nielsen HH, Qiu J, Friis S, Wermuth L, Ritz B. Treatment for **Helicobacter pylori** infection and risk of Parkinson's disease in Denmark. Eur J Neurol. 2012 Jun;19(6):864-9.
Nielsen SS, Franklin GM, Longstreth WT, et al**. Nicotine from edible Solanaceae** and risk of Parkinson disease. Ann Neurol. 2013 May 9.
NINDS NET-PD Investigators. A randomized, double-blind, futility clinical trial of **creatine and minocycline** in early Parkinson disease. Neurology. 2006 Mar 14;66(5):664-71. Epub 2006 Feb 15.
NINDS Exploratory Trials in Parkinson Disease (NET-PD) FS-ZONE Investigators. **Pioglitazone** in early Parkinson's disease: a phase 2, multicentre, double-blind, randomised trial. Lancet Neurol. 2015 Jun 23.
Nissinen H, Kuoppamäki M, Leinonen M, Schapira AH. **Early** versus delayed initiation of **entacapone** in levodopa-treated patients with Parkinson's disease: a long-term, retrospective analysis. Eur J Neurol. 2009 Jun 30. [Epub ahead of print] These data suggest that early rather than delayed addition of entacapone to levodopa/DDCI in PD patients with wearing-off provides a modest clinical benefit over levodopa/DDCI that is maintained for up to 5 years.
Nolano M, Provitera V, Manganelli F, et al. **Loss of cutaneous large and small fibers** in naive and **l-dopa-treated** PD patients. Neurology. 2017 Aug 22;89(8):776-784
Nonnekes J, Janssen S, Bloem BR. **Superficial brain stimulation** to overcome freezing of **gait** in Parkinson disease. Neurology. 2017 Mar 15.
Nonnekes J, Ružicka E, Nieuwboer A, et al. Compensation **Strategies for Gait Impairments** in Parkinson Disease: A Review. JAMA Neurol. 2019 Mar 25.
Nonnekes J, Snijders AH, Nutt JG, Deuschl G, Giladi G, Bloem BR. **Freezing of gait**: a practical approach to management. Lancet Neurol 2015; online May 25.
Noyce AJ, Bestwick JP, Silveira-Moriyama L, et al. Meta-analysis of early **nonmotor features and risk factors** for Parkinson disease. Ann Neurol. 2012 Jul 10.
Norcliffe-Kaufmann L, Martinez J, Axelrod F, Kaufmann H. **Hyperdopaminergic crises in familial dysautonomia**: A randomized trial of **carbidopa**. Neurology. 2013 Apr 23;80(17):1611-7.
Nutt JG, Wooten GF. Clinical practice. Diagnosis and initial management of Parkinson's disease. N Engl J Med. 2005 Sep 8;353(10):1021-7.
Obeso JA, Rodriguez-Oroz MC, Stamelou M, et al. The expanding universe of **disorders of the basal ganglia**. Lancet. 2014 Jun 18.
Odekerken VJJ, van Laar T, Staal MJ, et al. **Subthalamic nucleus (STN) versus globus pallidus (GPi) bilateral deep brain stimulation** for advanced Parkinson's disease (NSTAPS study): a randomised controlled trial . Lancet Neurol 2012; online Nov 16.
Odekerken VJ, Boel JA, Geurtsen GJ, et al; **NSTAPS** Study Group. Neuropsychological outcome after **deep brain stimulation** for Parkinson disease. Neurology. 2015 Mar 31;84(13):1355-61.
Odekerken VJ, Boel JA, Schmand BA, et al. NSTAPS study group. **GPi vs STN deep brain stimulation** for Parkinson disease: Three-year follow-up. Neurology. 2016 Feb 23;86(8):755-761.
Olde Dubbelink KT, Hillebrand A, Twisk JW, et al. **Predicting dementia** in Parkinson disease by combining **neurophysiologic and cognitive markers**. Neurology. 2014 Jan 21;82(3):263-70
Okai D, Askey-Jones S, Samuel M, et al. Trial of **CBT (cognitive behavioral therapy) for impulse control behaviors** affecting Parkinson patients and their caregivers. Neurology 2013;80:792–799.
Okun MS, et al. **Testosterone** therapy in men with Parkinson disease: results of the TEST-PD Study. Arch Neurol. 2006 May;63(5):729-35.
Okun MS, Gallo BV, Mandybur G, et al, for the **SJM DBS** Study Group. **Subthalamic deep brain stimulation** with a constant-current device in Parkinson's disease: an open-label randomised controlled trial. Lancet Neurol 2012
Okun MS. **Deep-brain stimulation** for Parkinson's disease. N Engl J Med. 2012 Oct 18;367(16):1529-38.
Okun MS. **Management of Parkinson Disease in 2017:** Personalized Approaches for Patient-Specific Needs. JAMA. 2017 Aug 21.
Olanow CW, Rascol O, Hauser R, et al. **ADAGIO Study** Investigators. A double-blind, delayed-start trial of **rasagiline** in Parkinson's disease. N Engl J Med. 2009 Sep 24;361(13):1268-78.
Olanow CW, Kieburtz K, Odin P, et al, for the LCIG Horizon Study Group. Continuous intrajejunal infusion of levodopa-carbidopa (AbbVie) intestinal gel for patients with advanced Parkinsons disease: a randomised, controlled, double-blind, double-dummy study. Lancet Neurol 2013; online Dec 20.
Olsen AL, Feany MB. **PARP Inhibitors** and Parkinson's Disease. N Engl J Med. 2019 Jan 31;380(5):492-494.
Ondo WG, Kenney C, Sullivan K, et al. Placebo-controlled trial of **lubiprostone** for constipation associated with Parkinson disease. Neurology. 2012 May 22;78(21):1650-4.
Ory-Magne F, Corvol JC, Azulay JP, et al. **Withdrawing amantadine** in dyskinetic patients with Parkinson disease: the AMANDYSK trial. Neurology 2014;82:300–307.
Oosterveld LP, Allen JC Jr, Ng EY, et al. Greater motor progression in patients with Parkinson disease who carry **LRRK2 risk variants**. Neurology. 2015 Aug 26.
Othman AA, Dutta S. Population Pharmacokinetics of Levodopa in Subjects with Advanced Parkinson's Disease: **Levodopa-Carbidopa Intestinal Gel Infusion versus Oral Tablets**. Br J Clin Pharmacol. 2014 Jan 17
Ozelius LJ, et al. **LRRK2** G2019S as a cause of Parkinson's disease in Ashkenazi Jews. N Engl J Med. 2006 Jan 26;354(4):424-5.
Paepegaey AC, Salenave S, Kamenicky P, et al. **Cabergoline Tapering** is Almost Always Successul in Patients with **Macroprolactinomas**. J Endocrine Society. March 2017:1(3);221-230.
Pagan F, Hebron M, Valadez EH, et al. **Nilotinib** effects in Parkinson's disease and dementia with Lewy bodies. J Parkinsons Dis. 2016 Jul 11.
Pagano G, Rengo G, Pasqualetti G, et al. **Cholinesterase inhibitors** for Parkinson`s disease: a systematic review and meta-analysis. J Neurol Neurosurg Psychiatry. 2014 Sep 15.
Pagano G, Polychronis S, Wilson H, et al. **Diabetes mellitus** and Parkinson disease. Neurology 2018;90:e1654–e1662.
Pagonabarraga J, Kulisevsky J, Strafella AP, et al. **Apathy** in Parkinson's disease: clinical features, neural substrates, diagnosis, and treatment. Lancet Neurol. 2015 May;14(5):518-531.
Pakpoor J, Noyce A, Goldacre R, et al. **Viral hepatitis (B & C)** and Parkinson disease: A national record-linkage study. Neurology. 2017 Mar 29.
Palfi S, Gurruchaga JM, Ralph GS, et al. Long-term safety and tolerability of **ProSavin, a lentiviral vector**-based **gene therapy** for Parkinsons disease: a dose escalation, open-label, phase 1/2 trial. Lancet 2014; online Jan 10.
Papay K, Xie SX, Stern M, et al. **Naltrexone** for impulse control disorders in Parkinson disease: A placebo-controlled study. Neurology. 2014 Aug 26;83(9):826-33.
Pappatà S, Santangelo G, Aarsland D, et al. Mild cognitive impairment in drug-naive patients with PD is associated with cerebral hypometabolism. Neurology. 2011 Oct 4;77(14):1357-62.
Parkkinen L, O'Sullivan SS, Kuoppamaki M, et al. Does **levodopa accelerate the pathologic process** in Parkinson disease brain? Neurology 2011;77;1420 –1426.
Parkinson Study Group **CALM** Cohort Investigators. Long-term Effect of Initiating Pramipexole vs Levodopa in Early Parkinson Disease. Arch Neurol. 2009 Mar 9. [Epub ahead of print] The policies of initial pramipexole and initial levodopa use followed by open-label levodopa use resulted in similar self-reported disability 6 years after randomization. Persistent differences favoring initial pramipexole were seen in the rates of dopaminergic motor complications, with less severe somnolence favoring initial levodopa.
Parkinson Study Group SURE-PD Investigators, Schwarzschild MA, Ascherio A, Beal MF, et al. **Inosine** to Increase Serum and Cerebrospinal Fluid Urate in Parkinson Disease: A Randomized Clinical Trial. JAMA Neurol. 2013 Dec 23.
Parkinson Study Group QE3 Investigators. A Randomized Clinical Trial of **High-Dosage Coenzyme Q10** in Early Parkinson Disease: No Evidence of Benefit. JAMA Neurol. 2014 Mar 24.
Paul KC, Schulz J, Bronstein JM, et al. Association of **Polygenic Risk Score** With Cognitive Decline and Motor Progression in Parkinson Disease. JAMA Neurol. 2018 Jan 16.
Payer DE, Guttman M, Kish SJ, et al. D3 dopamine receptor-preferring **[11C]PHNO PET imaging** in Parkinson patients with dyskinesia. Neurology. 2016 Jan 19;86(3):224-30.
PD-MED Collaborative Group. Long-term effectiveness of **dopamine agonists and monoamine oxidase B inhibitors compared with levodopa** as initial treatment for Parkinson's disease (PD MED): a large, open-label, pragmatic randomised trial. Lancet 2014; online June 11.
Pedersen KF, Larsen JP, Tysnes O-B, Alves G. Prognosis of **mild cognitive impairment** in early Parkinson disease: the Norwegian ParkWest Study [online March 25, 2013]. JAMA Neurol. doi:10.1001/jamaneurol.2013.2110.
Pedersen KF, Larsen JP, Tysnes OB, et al. **Natural course of mild cognitive impairment** in Parkinson disease: A 5-year population-based study. Neurology. 2017 Feb 21;88(8):767-774.
Peña J, Ibarretxe-Bilbao N, García-Gorostiaga I, Gomez-Beldarrain MA, et al. Improving **functional disability and cognition** in Parkinson disease: Randomized controlled trial. Neurology. 2014 Dec 2;83(23):2167-74.
Pereira JB, Svenningsson P, Weintraub D, et al. **Initial cognitive decline** is associated with cortical thinning in early Parkinson disease. Neurology. 2014 Jun 3;82(22):2017-25.

Peter I, Dubinsky M, Bressman S, et al. **Anti-tumor necrosis factor therapy** and incidence of Parkinson disease among patients with **inflammatory bowel disease**. JAMA Neurol 2018; online April 23, 2018.

Petrou M, Bohnen NI, Müller ML, et al. **Aβ-amyloid deposition** in patients with Parkinson disease at risk for development of dementia. Neurology. 2012 Sep 11;79(11):1161-7.

Petzinger GM, Fisher BE, McEwen S, et al. **Exercise-enhanced neuroplasticity** targeting motor and cognitive circuitry in Parkinson's disease. Lancet Neurol. 2013 Jul;12(7):716-26.

Pezzoli G, Cereda E. Exposure to **pesticides or solvents** and risk of Parkinson disease. Neurology. 2013 May 28;80(22):2035-41.

Pharmacist's Letter Oct 2006. Alternative or **Off-label** Routes of Drug Administration. (Vaginal administration of: bromocriptine; Sublingual Atropine eye drops or Atroven nasal spray to ↓ saliva & drooling))

Pharmacist's Letter Oct 2006. Azilect (**rasagiline** mesylate). (see also Medical Letter Dec 4/18,2006)

Pharmacist's Letter Feb 2007. Drug Induced **heart valve dysfunction**.

Pharmacists Letter. Neupro (**Rotigotine** transdermal system). June 2007.

Pichler I, Del Greco M F, Gögele M, et al; International Parkinson's Disease Genomics Consortium; et al. Serum **iron levels** and the risk of Parkinson disease: a mendelian randomization study. PLoS Med. 2013 Jun;10(6):e1001462.

Pigott K, Rick J, Xie SX, et al. Longitudinal study of **normal cognition** in Parkinson disease. Neurology 2015; 85:1276–1282.

Poewe WH, Rascol O, Quinn N, Tolosa E, Oertel WH, Martignoni E, Rupp M, Boroojerdi B; SP 515 Investigators. Efficacy of pramipexole and transdermal rotigotine in advanced Parkinson's disease: a double-blind, double-dummy, randomised controlled trial. Lancet Neurol. 2007 Jun;6(6):513-20. 204 patients were randomly assigned to receive **rotigotine** (up to 16mg per day), 201 to receive **pramipexole** (up to 4.5mg per day), and 101 to receive placebo for 6 months. In terms of change in absolute off time, rotigotine was non-inferior to pramipexole. Continuous delivery of rotigotine as transdermal patches could offer similar efficacy to oral pramipexole in patients with fluctuating Parkinson's disease over 6 months of treatment.

Poewe W. Treatments for Parkinson disease--**past achievements and current clinical needs**. Neurology. 2009 Feb 17;72(7 Suppl):S65-73.

Poewe W, Rascol O, Barone P, et al. For the Pramipexole ER Studies Group. **Extended-release pramipexole** in early Parkinson disease: A 33-week randomized controlled trial. Neurology. 2011 Aug 23;77(8):759-766.

Poewe W, Seppi K. **Insulin** signalling: new target for Parkinson's treatments? Lancet. 2017 Aug 3.

Poewe W, Seppi K, Fitzer-Attas CJ, et al; for the **Rasagiline-for-MSA** investigators. Efficacy of **rasagiline** in patients with the parkinsonian variant of multiple system atrophy: a randomised, placebo-controlled trial. Lancet Neurol. 2014 Dec 5.

Postuma RB, Lang AE, Munhoz RP et al. **Caffeine** for treatment of Parkinson disease: A randomized controlled trial. Neurology. 2012 Aug 14;79(7):651-8.

Postuma RB, Berg D, Stern M, et al. **MDS clinical diagnostic criteria for Parkinson's disease**. Mov Disord. 2015 Oct;30(12):1591-601.

Postuma RB;Anang J;Pelletier A;Joseph L;Moscovich. **Caffeine as symptomatic treatment** for Parkinson disease (**Cafe-PD**): A randomized trial. Neurology. 2017 Sep 27.

Postuma RB, Anang J, Pelletier A, et al. **Caffeine** as symptomatic treatment for Parkinson disease (Café-PD): A randomized trial. Neurology. 2017 Sep 27.

Prange S, Danaila T, Laurencin C, et al. **Age and time course of long-term motor and nonmotor complications** in Parkinson disease. Neurology. 2019 Jan 8;92(2):e148-e160.

Quiroga MJ, Carroll DW, Brown TM. **Ascorbate- and zinc-responsive** parkinsonism. Ann Pharmacother. 2014 Nov;48(11):1515-20.

Rabinak Christina A.; Nirenberg Melissa J.. **Dopamine Agonist Withdrawal Syndrome** in Parkinson Disease. Arch Neurol. 2010;67(1):58-63.

Raccagni C, Nonnekes J, Bloem BR, et al. **Gait and postural disorders** in parkinsonism: a clinical approach. J Neurol. 2019 May 22.

Racette BA, Searles Nielsen S, Criswell SR, et al. Dose-dependent progression of parkinsonism in **manganese-exposed welders**. Neurology. 2016 Dec 28.

Rae CL, Nombela C, Rodríguez PV, et al. **Atomoxetine** restores the response **inhibition network** in Parkinson's disease. Brain. 2016 Aug;139(Pt 8):2235-48.

Rajabally YA, Martey J. **Neuropathy** in Parkinson disease: prevalence and determinants. Neurology 2011;77:1947–1950. (Vitamin B12 deficiency association)

Rajput AH, Rajput ML, Ferguson LW, Rajput A. Baseline motor findings and Parkinson disease **prognostic subtypes**. Neurology. 2017 Jul 11;89(2):138-143.

Ramirez-Zamora A, Ostrem JL. **Globus Pallidus Interna or Subthalamic Nucleus Deep Brain Stimulation** for Parkinson Disease: A Review. JAMA Neurol. 2018 Jan 22.

Rascol O, Brooks DJ, Melamed E, et al. **Rasagiline** as an adjunct to levodopa in patients with Parkinson's disease and motor fl uctuations (**LARGO**, Lasting eff ect in Adjunct therapy with Rasagiline Given Once daily, study): a randomised, double-blind, parallel-group trial. Lancet 2005; 365: 947–54.

Rascol O, Fitzer-Attas CJ, Hauser R, et al. A double-blind,delayed-start trial of **rasagiline** in Parkinson's disease (the **ADAGIO** study): prespecified and post-hoc analyses of the need for additional therapies, changes in UPDRS scores, and non-motor outcomes. Lancet Neurol. 2011 Apr 7.

Rees K, Stowe R, Patel S, Ives N, Breen K, Clarke CE, Ben-Shlomo Y. **Helicobacter pylori** eradication for Parkinson's disease. Cochrane Database Syst Rev. 2011 Nov 9;(11):CD008453. There is currently a lack of evidence on the effects of screening and treating H pylori in patients with Parkinson'sdisease. There is limited evidence to suggest that H Pylori eradication improves the absorption of levodopa and improves motor symptoms.

Renoux C, Dell'Aniello S, Khairy P, et al. Ventricular **tachyarrhythmia** and sudden cardiac death with **domperidone** use in Parkinson's Disease. Br J Clin Pharmacol. 2016 Apr

Ricciardi L, Lambert C, De Micco R, et al. Can we predict development of **impulsive-compulsive behaviours** in Parkinson's disease? J Neurol Neurosurg Psychiatry. 2017 Oct 27.

Richard IH, McDermott MP, Kurlan R, et al. A randomized, double-blind, placebo-controlled trial of antidepressants (paroxetine, venlafaxine) in Parkinson disease. (**SAD-PD**) Neurology 2012;78:1229–1236.

Ritz B, Lee PC, Lassen CF, Arah OA. **Parkinson disease and smoking** revisited: ease of quitting is an early sign of the disease. Neurology 2014;83:1396–1402.

Rizek P, Kumar N, Jog MS. An **update on the diagnosis and treatment of Parkinson disease. CMAJ**. 2016 Nov 1;188(16):1157-1165.

Rizzo Matthew. **Impaired Driving From Medical Conditions**: A 70-Year-Old Man Trying to Decide if He Should Continue Driving. JAMA. 2011;305(10):1018-1026.Published online March 1, 2011. doi:10.1001/jama.2011.252

Rizzo G, Copetti M, Arcuti S, et al. **Accuracy of clinical diagnosis of Parkinson disease**: A systematic review and meta-analysis. Neurology. 2016 Feb 9;86(6):566-76.

Robert G, Le Jeune F, Lozachmeur C, et al. **Apathy** in patients with Parkinson disease without dementia or depression: A PET study. Neurology. 2012 Sep 11;79(11):1155-60.

Robert GH, Le Jeune F, Lozachmeur C, et al. **Preoperative** factors of **apathy in subthalamic stimulated Parkinson** disease: A PET study. Neurology. 2014 Oct 28;83(18):1620-6.

Robottom BJ, Weiner WJ, Factor SA. Movement disorders **emergencies part 1: (neuroleptic malignant syndrome, Parkinsonism hyperpyrexia & serotonin syndrome)** hypokinetic disorders. Arch Neurol. 2011 May;68(5):567-72.

Rocca WA, Bower JH, Maraganore DM, Ahlskog JE, Grossardt BR, et al.. Increased risk of parkinsonism in women who underwent **oophorectomy before menopause**. Neurology. 2007 Aug 29; [Epub ahead of print] Both unilateral and bilateral oophorectomy performed prior to menopause may be associated with an increased risk of parkinsonism and the effect may be age-dependent. However, our findings await independent replication.

Rochester L, Galna B, Lord S, et al. **Decrease in Aβ42** predicts dopa-resistant **gait progression** in early Parkinson disease. Neurology. 2017 Apr 18;88(16):1501-1511.

Rochon PA, Stukel TA, Sykora K, Gill S, Garfinkel S, et al. **Atypical antipsychotics and parkinsonism**. Arch Intern Med. 2005 Sep 12;165(16):1882-8. CONCLUSIONS: The risk of development of parkinsonism associated with the use of high-dose atypical antipsychotics was **similar** to that associated with the use of typical antipsychotics. Caution should be used when prescribing atypical antipsychotic therapy at high doses.

Rodriguez-Oroz MC. **Deep brain stimulation** for advanced Parkinson's disease. Lancet Neurol. 2010 Apr 28. [Epub ahead of print]

Rogers G, Davies D, Pink J, et al. Parkinson's disease: summary of **updated NICE guidance**. BMJ. 2017 Jul 27;358:j1951.

Rolinski M, Fox C, Maidment I, McShane R. **Cholinesterase inhibitors** for **dementia with Lewy bodies**, Parkinson's disease dementia and cognitive impairment in Parkinson's disease. Cochrane Database Syst Rev. 2012 Mar 14;3:CD006504.

Rongve A, Aarsland D. Management of Parkinson's disease **dementia** : practical considerations. Drugs Aging. 2006;23(10):807-22.

Roos E, Grotta A, Yang F, et al. **Body mass index, sitting time, and risk of Parkinson disease**. Neurology. 2018 Apr 17;90(16):e1413-e1417.

Ross OA, Soto-Ortolaza AI, Heckman MG, et al. on behalf of the Genetic Epidemiology Of Parkinson's Disease (GEO-PD) Consortium. Association of **LRRK2 exonic variants** with susceptibility to Parkinson's disease:a case-control study. Lancet Neurol. 2011 Oct;10(10):898-908.

Rosso AL, Bohnen NI, Launer LJ, Aizenstein HJ, Yaffe K, Rosano C. **Vascular and dopaminergic contributors** to mild parkinsonian signs in older adults. Neurology. 2017 Dec 15.

Roussakis AA, Politis M, Towey D, Piccini P. **Serotonin-to-dopamine transporter ratios** in Parkinson disease: Relevance for dyskinesias. Neurology. 2016 Mar 22

Rugbjerg K, Ritz B, Korbo L, Martinussen N, Olsen JH. Risk of Parkinson's disease after hospital **contact for head injury**: population based case-control study. BMJ. 2008 Dec 15;337:a2494. doi: 10.1136/bmj.a2494. The steeply increased frequency of hospital contacts for a head injury during the months preceding the date at which Parkinson's disease was first recorded is a consequence of the evolving movement disorder rather than its cause.

Rughani A, Schwalb JM, Sidiropoulos C, et al. Congress of Neurological Surgeons Systematic Review and Evidence-Based Guideline on **Subthalamic Nucleus and Globus Pallidus Internus Deep Brain Stimulation** for the Treatment of Patients With Parkinson's Disease: Executive Summary. Neurosurgery. 2018 Jun 1;82(6):753-756.

Rutten S, Vriend C, Smit JH, et al. **Bright light therapy** for depression in Parkinson disease: A randomized controlled trial. Neurology. 2019 Feb 15.

Safarpour D, Thibault DP, DeSanto CL, et al. **Nursing home and end-of-life care** in Parkinson disease. Neurology. 2015 Aug 4;85(5):413-9.

Safety signals for two novel drugs: Nuplazid and Entresto. Institute for Safe Medication Practices. Available at: ismp.org/sites/default/files/attachments/2018-01/2017Q1_0.pdf. Accessed January 7th, 2018.

Saiki S, Sasazawa Y, Fujimaki M, et al. A **metabolic profile of polyamines** in parkinson disease: A promising biomarker. Ann Neurol. 2019 Jun 2.

Salat D, Noyce AJ, Schrag A, et al. Challenges of modifying disease progression in **prediagnostic Parkinson's disease**. Lancet Neurol. 2016 Mar 15.

Samii A, Etminan M, Wiens MO, Jafari S. NSAID use and the risk of **Parkinson's disease**: systematic review and meta-analysis of observational studies. Drugs Aging. 2009;26(9):769-79.

Saunders-Pullman R, Mirelman A, Alcalay RN,et al; **LRRK2 Ashkenazi Jewish Consortium**. Progression in the LRRK2-Asssociated Parkinson Disease Population. JAMA Neurol. 2018 Jan 8.

Savica R, Matsumoto JY, Josephs KA, et al. **Deep brain stimulation** in benign tremulous parkinsonism. Arch Neurol. 2011 Aug;68(8):1033-6.

Savica R, Grossardt BR, Bower JH, et al. **Time Trends** in the Incidence of Parkinson Disease. JAMA Neurol. 2016 Jun 20.

Savica R, Grossardt BR, Bower JH, et al. **Survival and Causes of Death** Among People With Clinically Diagnosed Synucleinopathies With Parkinsonism: A Population-Based Study. JAMA Neurol. 2017 May 15.

Savica R, Grossardt BR, Rocca WA, Bower JH. **Parkinson disease with and without Dementia**: A prevalence study and future projections. Mov Disord. 2018 Jan 22.

Schapira AH, Barone P, Hauser RA, et al. For the Pramipexole ER Studies Group. **Extended-release pramipexole** in advanced Parkinson disease: A randomized controlled trial. Neurology. 2011 Aug 23;77(8):767-774.

Schapira AHV, McDermott MP, Barone P, et al. **Pramipexole** in patients with early Parkinson's disease (**PROUD**): a randomised delayed-start trial. Lancet Neurol 2013; online May 31

Schapira AH, Olanow CW, Greenamyre JT, et al. Slowing of **neurodegeneration** in Parkinson's disease and Huntington's disease: future therapeutic perspectives. Lancet. 2014 Jun 18.

Schapira AH, Fox SH, Hauser RA, et al. Assessment of Safety and Efficacy of **Safinamide** as a Levodopa Adjunct in Patients With Parkinson Disease and **Motor Fluctuations**: A Randomized Clinical Trial. JAMA Neurol. 2016 Dec 12.

Schapira AHV, Chaudhuri KR, Jenner P. **Non-motor features of Parkinson disease**.Nat Rev Neurosci. 2017 Jul;18(7):435-450.

Schenkman M, Moore CG, Kohrt WM, et al. Effect of **High-Intensity Treadmill Exercise** on Motor Symptoms in Patients With De Novo Parkinson Disease: A Phase 2 Randomized Clinical Trial. JAMA Neurol. 2017 Dec 11.

Scher AI, Ross GW, Sigurdsson S, et al. **Midlife migraine** and late-life parkinsonism: AGES-Reykjavik Study. Neurology. 2014 Sep 30;83(14):1246-52.

Schneider RB, Biglan KM. The **promise of telemedicine** for chronic neurological disorders: the example of Parkinson's disease. Lancet Neurol. 2017 May 26.

Schrag A, Horsfall L, Walters K, Noyce A, Petersen I. **Prediagnostic presentations** of Parkinson's disease in primary care: a case-control study. Lancet Neurol 2014; online Nov 27. http://dx.doi.org/10.1016/S1474-4422(14)70287-X.

Schrag A, Siddiqui UF, Anastasiou Z, et al. **Clinical variables and biomarkers** in prediction of **cognitive impairment** in patients with newly diagnosed Parkinson's disease: a cohort study. Lancet Neurol 2016; online Nov 17.

Schreiner SJ, Imbach LL, Werth E, et al. **Slow-wave sleep and motor progression** in Parkinson disease. Ann Neurol. 2019 Mar 18.

Schuepbach WMM et al. **Neurostimulation** for Parkinson's disease with early motor complications. (**EARLYSTIM**) N Engl J Med 2013 Feb 14; 368:610.

Schwarzschild MA, Macklin EA, Bakshi R, et al; SURE-PD Investigators. Sex differences by design and outcome in the **Safety of Urate Elevation** in PD (SURE-PD) trial. Neurology. 2019 Oct 1;93(14):e1328-e1338.

Searles Nielsen S, Warden MN, Camacho-Soto A, et al. A **predictive model** to identify Parkinson disease from administrative claims data. Neurology. 2017 Oct 3;89(14):1448-1456

Searles Nielsen S, Gross A, Camacho-Soto A, et al. **β2-adrenoreceptor medications** and risk of Parkinson disease. Ann Neurol. 2018 Sep 17.

Seidel K, Bouzrou M, Heidemann N, et al. **Involvement of the cerebellum** in Parkinson's disease and Dementia with Lewy bodies. Ann Neurol. 2017 Apr 25

Seppi K, Weintraub D, Coelho M, et al. The **Movement Disorder Society** Evidence-Based Medicine Review Update: Treatments for the **non-motor symptoms** of Parkinson's disease. Mov Disord. 2011 Oct;26 Suppl 3:S42-80. The treatments that are efficacious for the management of the different non-motor symptoms are as follows: pramipexole for the treatment of depressive symptoms, clozapine for the treatment of psychosis, rivastigmine for the treatment of dementia, and botulinum toxin A (BTX-A) and BTX-B as well as glycopyrrolate for the treatment of sialorrhea. The practical implications for these treatments, except for glycopyrrolate, are that they are clinically useful.

Shamir R, Klein C, Amar D, et al. Analysis of **blood-based gene expression** in idiopathic Parkinson disease. Neurology. 2017 Oct 17;89(16):1676-1683.

Shanahan J, Morris ME, Bhriain ON, et al. **Dance for People With Parkinson** Disease: What Is the Evidence Telling Us?. Arch Phys Med Rehabil. 2015 Jan;96(1):141-153.

Sharma JC, Ross IN, et al. Relationship between **weight, levodopa and dyskinesia**: the significance of levodopa dose per kilogram body weight. Eur J Neurol. 2008 May;15(5):493-6. Higher levodopa dose per kilogram body weight is an independently significant factor for developing dyskinesia.

Sharma A, Szeto K, Desilets AR. Efficacy and Safety of **Deep Brain Stimulation** as an Adjunct to Pharmacotherapy for the Treatment of Parkinson Disease (February). Ann Pharmacother. 2012 Jan 10.

Sharma M, Ioannidis JP, Aasly JO et al. Large-scale replication and heterogeneity in Parkinson disease **genetic loci**. Neurology. 2012 Aug 14;79(7):659-667.

Shen CC, Tsai SJ, Perng CL, et al. Risk of **Parkinson disease after depression**: A nationwide population-based study. Neurology. 2013 Oct 2.

Shin JH, Park KW, Heo KO, et al. **Urodynamic study for distinguishing multiple system atrophy** from Parkinson disease. Neurology. 2019 Sep 3;93(10):e946-e953.

Shulman LM, Katzel LI, Ivey FM, et al. Randomized clinical trial of **3 types of physical exercise** for patients with Parkinson disease (online November 5, 2012). Arch Neurol. doi:10.1001/jamaneurol.2013.646.

Shults CW, Oakes D, Kieburtz K, et al; Parkinson Study Group. Effects of coenzyme Q10 in early Parkinson disease: evidence of slowing of the functional decline. Arch Neurol. 2002 Oct;59(10):1541-50.

Siddiqui MA, Plosker GL. **Rasagiline**. Drugs Aging. 2005;22(1):83-91; discussion 93-4. (Goetz CG, et al.; Parkinson Study Group **TEMPO** and **PRESTO** Investigators. Safety of rasagiline in elderly patients with Parkinson disease. Neurology. 2006 May 9;66(9):1427-9.)(Rascol O, et al;**LARGO** study group. Rasagiline as an adjunct to levodopa in patients with parkinson's disease and motor fluctuations (LARGO, Lasting effect in Adjunct therapy with Rasagiline Given Once daily, study): a randomised, double-blind, parallel-group trial. Lancet. 2005 Mar 12-18;365(9463):947-4.)(Parkinson Study Group. A randomized placebo-controlled trial of rasagiline in levodopa-treated patients with Parkinson disease and motor fluctuations: the PRESTO study. Arch Neurol. 2005 Feb;62(2):241-8.) (see also Pharmacist's Letter July 2006: New Treatments: Azilect & Zelapar)

Simeonova M, de Vries F, Pouwels S, et al. Increased risk of all-cause mortality associated with **domperidone use in Parkinson's patients**: a population-based cohort study in the UK. Br J Clin Pharmacol. 2018 Jul 5.

Sixel-Do¨ring F, Trautmann E, Mollenhauer B, Trenkwalder C. Associated factors for **REM sleep behavior disorder** in Parkinson disease. Neurology 2011;77:1048 –1054

Smith KM, Eyal E, Weintraub D; for the **ADAGIO** Investigators. Combined **Rasagiline and Antidepressant** Use in Parkinson Disease in the ADAGIO Study: Effects on Nonmotor Symptoms and Tolerability. JAMA Neurol. 2014 Nov 24.

South AR, Somers SM, Jog MS. **Gum chewing improves** swallow frequency and latency in Parkinson patients: a preliminary study. Neurology. 2010 Apr 13;74(15):1198-202.

Sperling SA, Shah BB, Barrett MJ, et al. **Focused ultrasound thalamotomy in Parkinson disease**: Nonmotor outcomes and quality of life. Neurology. 2018 Oct 2;91(14):e1275-e1284.

Stepens A, Logina I, Liguts V, et al. A Parkinsonian syndrome in methcathinone users and the role of **manganese**. N Engl J Med. 2008 Mar 6;358(10):1009-17. Our observation of a distinctive extrapyramidal syndrome, changes in the MRI signal in the basal ganglia, and elevated blood manganese levels in methcathinone (ephedrone) users suggests that manganese in the methcathinone solution causes a persistent neurologic disorder.

Sterling NW, Wang M, et al. Stage-dependent **loss of cortical gyrification** as Parkinson disease "unfolds". Neurology. 2016 Mar 22

Stocchi F, Vacca L, Ruggieri S, Olanow CW. Intermittent vs **continuous** levodopa administration in patients with advanced Parkinson disease: a clinical and pharmacokinetic study. Arch Neurol. 2005 Jun;62(6):905-10.

Stocchi F, Rascol O, Kieburtz K, et al. Initiating **levodopa/carbidopa therapy with and without entacapone** in early Parkinson disease: the **STRIDE-PD** study. Ann Neurol. 2010 Jul;68(1):18-27.

Stocchi F, Abbruzzese G, Ceravolo R, et al; FORTE Study Group. Prevalence of **fatigue** in Parkinson disease and its clinical correlates. Neurology. 2014 Jul 15;83(3):215-20.

Stocchi F, Rascol O, Hauser RA,et al. Randomized trial of **preladenant**, given as **monotherapy**, in patients with early Parkinson disease. Neurology. 2017 Jun 6;88(23):2198-2206.

Stoessl AJ, Lehericy S, Strafella AP. **Imaging** insights into **basal ganglia** function, Parkinson's disease, and dystonia. Lancet. 2014 Jun 18.

Storch A, Jost WH, Vieregge P, et al. Randomized, Double-blind, Placebo-Controlled Trial on Symptomatic Effects of **Coenzyme Q10** 100mg tid in Parkinson Disease. Arch Neurol. 2007 May 14; [Epub ahead of print] N=131 3months. Nanoparticular CoQ(10) at a dosage of 300 mg/d is safe and well tolerated and leads to plasma levels similar to 1200 mg/d of standard formulations. Add-on CoQ(10) does not display symptomatic effects in midstage Parkinson disease.

Storch A, Schneider CB, Wolz M, et al. **Nonmotor fluctuations** in Parkinson disease: Severity and correlation with motor complications. Neurology. 2013 Feb 26;80(9):800-809.

Stowe R, Ives N, Clarke CE, Deane K; et al. Evaluation of the efficacy and safety of **adjuvant treatment to levodopa therapy** in Parkinson s disease patients with motor complications. Cochrane Database Syst Rev. 2010 Jul 7;7:CD007166. Compared to placebo, adjuvant therapy reduces off-time, levodopa dose, and improves UPDRS scores in PD patients who develop motor complications on levodopa therapy. However, this is at the expense of increased dyskinesia and numerous other side-effects. Indirect comparisons suggest that dopamine agonist therapy may be more effective than COMTI and MAOBI therapy, which have comparable efficacy. However, as indirect comparisons should be interpreted with caution, direct head-to-head randomised trials assessing the impact of these different drug classes on overall patient-rated quality of life are needed.

Sturkenboom IHWM, Graff MJL, Hendriks JCM, et al, for the **OTiP** study group. Effi cacy of **occupational therapy** for patients with Parkinson's disease: a randomised controlled trial. Lancet Neurol 2014; online April 9.

Svenningsson P, Westman E, Ballard C, Aarsland D. **Cognitive impairment** in patients with Parkinson's disease: diagnosis, biomarkers, and treatment. Lancet Neurol. 2012 Aug;11(8):697-707.

Tanner CM, Kamel F, Ross GW, et al. **Rotenone, Paraquat** and Parkinson's Disease. Environ Health Perspect. 2011 Jan 26.

Tanner CM. A second honeymoon for Parkinson's disease? N Engl J Med 2013 Feb 14; 368:675.

Tarsy D. Treatment of Parkinson disease: a 64-year-old man with **motor complications** of **advanced Parkinson disease**. JAMA. 2012 Jun 6;307(21):2305-14.

Tessitore A, Esposito F, Vitale C, et al. **Default-mode network** connectivity (via **MRI**) in cognitively unimpaired patients with Parkinson disease. Neurology. 2012 Dec 4;79(23):2226-2232.

Thenganatt MA, Jankovic J. **Parkinson Disease Subtypes**. JAMA Neurol. 2014 Feb 10

Tholfsen LK, Larsen JP, Schulz J, et al. Development of **excessive daytime sleepiness** in early Parkinson disease. Neurology. 2015 Jul 14;85(2):162-8.

Tholfsen LK, Larsen JP, Schulz J, et al. **Changes in insomnia subtypes** in early Parkinson disease. Neurology. 2017 Jan 24;88(4):352-358.

Thompson T, Poulter D, Miles C, et al. **Driving impairment and crash risk in Parkinson disease**: A systematic review and meta-analysis. Neurology. 2018 Sep 4;91(10):e906-e916.

Thomsen TR, Galpern WR, Asante A, Arenovich T, Fox SH. **Ipratropium bromide spray as treatment for sialorrhea** in Parkinson's disease. Mov Disord. 2007 Sep 17; [Epub ahead of print] Ipratropium bromide spray had no significant effect on weight of saliva produced. There was a mild effect of treatment on subjective measures of sialorrhea.

Tinazzi M, Fasano A, Geroin C, et al; Italian **Pisa Syndrome** Study Group. Pisa syndrome in Parkinson disease: An observational multicenter Italian study. Neurology. 2015 Nov 17;85(20):1769-79.

Timmermann L, Jain R, Chen L, et al. Multiple-source current steering in **subthalamic nucleus deep brain stimulation** for Parkinson's disease (the VANTAGE study): a non-randomised, prospective, multicentre, open-label study. Lancet Neurol. 2015 May 28.

Tolosa E, Wenning G, Poewe W. The **diagnosis** of Parkinson's disease. Lancet Neurol. 2006 Jan;5(1):75-86.

Tomlinson CL, Patel S, Meek C et al. **Physiotherapy intervention** in Parkinson's disease: systematic review and meta-analysis. BMJ. 2012 Aug 6;345:e5004.

Torti M, Alessandroni J, Bravi D, et al. CLINICAL AND PHARMACOKINETICS EQUIVALENCE OF MULTIPLE DOSES OF **LEVODOPA BENSERAZIDE GENERIC FORMULATION VERSUS THE ORIGINATOR (MADOPAR®).** Br J Clin Pharmacol. 2019 Aug 4.

Trenkwalder C, Kuoppamaki M, Vahteristo M, et al**. Increased dose of carbidopa with levodopa and entacapone** improves ``off`` time in a randomized trial. Neurology. 2019 Mar 1.

Tsai HH, Liou HH, Muo CH, et al. **Hepatitis C virus infection as a risk factor** for Parkinson disease: A nationwide cohort study. Neurology. 2015 Dec 23.

Tsai SC, Sheu SY, Chien LN, etal. High exposure compared with standard exposure to **metoclopramide associated with a higher risk of parkinsonism**: a nationwide population-based cohort study. Br J Clin Pharmacol. 2018 May 10.

Tsang EW, Hamani C, Moro E, et al. **Subthalamic deep brain stimulation** at individualized frequencies for Parkinson disease. Neurology. 2012 Jun 12;78(24):1930-8.

Turcano P, Mielke MM, Bower JH, et al. **Levodopa-induced dyskinesia in Parkinson disease**: A population-based cohort study. Neurology. 2018 Dec 11;91(24):e2238-e2243.

Uc EY, Rizzo M, et al. **Driving** with distraction in Parkinson disease. Neurology. 2006 Nov 28;67(10):1774-80.

Uc EY, Rizzo M, Johnson AM, et al. **Real-life driving** outcomes in Parkinson disease. Neurology. 2011 May 31;76(22):1894-902.

Uc EY, Doerschug KC, Magnotta V, et al. Phase I/II randomized trial of **aerobic exercise** in Parkinson disease in a community setting. Neurology. 2014 Jul 29;83(5):413-25.

Uc EY, Rizzo M, O'Shea AMJ, et al. Longitudinal decline of **driving safety** in Parkinson disease. Neurology. 2017 Nov 7;89(19):1951-1958.

van der Heeden JF, Marinus J, Martinez-Martin P, van Hilten JJ. Importance of **nondopaminergic features** in evaluating disease severity of Parkinson disease. Neurology 2014;82:412–418.

van der Heeden JF, Marinus J, Martinez-Martin P, et al. **Postural instability and gait** are associated with severity and prognosis of Parkinson disease. Neurology. 2016 Jun 14;86(24):2243-50.

van der Holst HM, van Uden IWM, Tuladhar AM, et al. **Cerebral small vessel disease** and incident parkinsonism: the RUN DMC study. Neurology 2015;85:1569–1577.

van der Marck MA, Munneke M, Mulleners W, et al; for the **IMPACT** study group. **Integrated multidisciplinary** care in Parkinson's disease: a non-randomised, controlled trial (IMPACT). Lancet Neurol. 2013 Aug 23.

Van Nimwegen M, Speelman AD, Overeem S, et al. Promotion of **physical activity and fitness** in sedentary patients with Parkinson's disease: randomised controlled trial. (**ParkFit**) BMJ 2013;346:f576.

Velseboer DC, Broeders M, Post B, et al; CARPA Study Group. Prognostic factors of **motor impairment, disability, and quality of life in newly diagnosed PD**. (**CARPA**) Neurology. 2013 Feb 12;80(7):627-33.

Velseboer DC, de Bie RMA, Wieske L, et al. Development and external **validation of a prognostic model in newly diagnosed Parkinson** disease. Neurology 2016;86: 986–993.

Verschuur CVM, Suwijn SR, Boel JA, et al. Randomized delayed- start trial of **levodopa in Parkinson's disease**. (LEAP) N Engl J Med 2019; 380: 315-24.

Videnovic A, Klerman EB, Wang W, et al. **Timed light therapy for sleep and daytime sleepiness** associated with Parkinson disease: a randomized clinical trial [online Feb 20, 2017].JAMA Neurol. doi:10.1001 /jamaneurol.2016.5192

Vilas D, Iranzo A, Tolosa E, et al. Assessment of **α-synuclein in submandibular glands** of patients with **idiopathic rapid-eye-movement sleep behaviour** disorder: a case-control study. Lancet Neurol 2016; online March 30.

Vlad SC, Miller DR, Kowall NW, Felson DT. **Protective effects of NSAIDs** on the development of Alzheimer disease. Neurology 2008;70:1672–1677.
Villumsen M, Aznar S, Pakkenberg B, et al. **Inflammatory bowel disease** increases the risk of Parkinson's disease: a Danish nationwide cohort study 1977-2014. Gut. 2018 May 21.
Volta M, Milnerwood AJ, et al. Insights from **late-onset familial parkinsonism** on the pathogenesis of idiopathic Parkinson's disease. Lancet Neurol. 2015 Oct;14(10):1054-64.
Voon V, Sohr M, Lang A, et al. **Impulse Control Disorders** in Parkinson Disease: A Multicenter Case-control study. Annals of Neurology. 2011 Jan 10; 1-33.
Voon V, Napier TC, Frank MJ, et al. **Impulse control disorders and levodopa-induced dyskinesias** in Parkinson's disease: an update. Lancet Neurol. 2017 Mar;16(3):238-250.
Vu TC, Nutt JG, Holford NH. **Progression of Motor and Non-Motor Features** of Parkinson's Disease and Their Response to Treatment. Br J Clin Pharmacol. 2012 Jan 29.
Wahner AD, Bronstein JM, Bordelon YM, Ritz B. **Nonsteroidal anti-inflammatory drugs** may protect against Parkinson disease. Neurology. 2007 Nov 6;69(19):1836-42. Our study contributes to the growing body of literature suggesting a protective role for nonsteroidal anti-inflammatory drugs (NSAIDs) in Parkinson disease (PD).
Weaver FM, Follett K, Stern M, Hur K, et al. 468 Study Group. **Bilateral deep brain stimulation** vs best medical therapy for patients with advanced Parkinson disease: a randomized controlled trial. JAMA. 2009 Jan 7;301(1):63-73. In this randomized controlled trial of patients with advanced PD, deep brain stimulation was more effective than best medical therapy in improving on time without troubling dyskinesias, motor function, and quality of life at 6 months, but was associated with an increased risk of serious adverse events.
Weaver FM, Follett KA, Stern M, et al; For the CSP 468 Study Group. Randomized trial of **deep brain stimulation** for Parkinson disease: Thirty-six-month outcomes. Neurology. 2012 Jul 3;79(1):55-65.
Weintraub D, et al. Association of dopamine agonist use with **impulse control** disorders in Parkinson disease. Arch Neurol. 2006 Jul;63(7):969-73.
Weintraub D, Hurtig HI. Presentation and management of **psychosis** in **Parkinson's disease and dementia with Lewy bodies**. Am J Psychiatry. 2007 Oct;164(10):1491-8.
Weintraub D, Koester J, Potenza MN, Siderowf AD, Stacy M, Voon V, Whetteckey J, Wunderlich GR, Lang AE. **Impulse control disorders** in Parkinson disease: a cross-sectional study of 3090 patients. Arch Neurol. 2010 May;67(5):589-95.
Weintraub D, Chen P, Ignacio RV, et al. Patterns and trends in **antipsychotic prescribing** for Parkinson disease psychosis. Arch Neurol. 2011 Jul;68(7):899-904.
Weintraub D, Papay K, Siderowf A; for the Parkinson's Progression Markers Initiative. **Screening for impulse control symptoms** in patients with de novo Parkinson disease: A case-control study. Neurology. 2013 Jan 8;80(2):176-180.
Weintraub D, Chiang C, Kim HM, et al. Association of **Antipsychotic Use With Mortality** Risk in Patients With Parkinson Disease. JAMA Neurol. 2016 Mar 21
Welk B, McArthur E, Morrow SA, et al. Association Between **Gadolinium Contrast Exposure** and the Risk of Parkinsonism. JAMA. 2016 Jul 5;316(1):96-98.
Welter ML, Schüpbach M, Czernecki V, et al. Optimal target localization for **subthalamic stimulation in patients** with Parkinson disease. Neurology. 2014 Apr 15;82(15):1352-61.
Wile DJ, Agarwal PA, Schulzer M, et al. Serotonin and dopamine transporter **PET changes** in the premotor phase of **LRRK2 parkinsonism**: cross-sectional studies. Lancet Neurol 2017; 16: 351–59.
Williams A, Gill S, Varma T, et al. on behalf of the **PD SURG** Collaborative Group. **Deep brain stimulation plus best medical** therapy versus best medical therapy alone for advanced Parkinson's disease (PD SURG trial): a randomised, open-label trial. Lancet Neurol. 2010 Apr 28.
Williams-Gray CH, et al. **Cognitive deficits and psychosis** in Parkinson's disease: a review of pathophysiology and therapeutic options. CNS Drugs. 2006;20(6):477-505.
Williams-Gray CH, Mason SL, Evans JR, et al. The CamPaIGN study of Parkinson`s disease: 10-year **outlook in an incident population**-based cohort. J Neurol Neurosurg Psychiatry. 2013 Jul 23.
Williams JR, Hirsch ES, Anderson K, et al. A comparison of **nine scales to detect depression in Parkinson disease**: Which scale to use? Neurology. 2012 Mar 27;78(13):998-1006. The GDS-30 may be the most efficient depression screening scale to use in PD because of its brevity, favorable psychometric properties, and lack of copyright protection. However, all scales studied, except for the UPDRS Depression, are valid screening tools when PD-specific cutoff scores are used.
Willis AW, Evanoff BA, Lian M, et al. Metal Emissions and Urban Incident Parkinson Disease: A Community Health Study of Medicare Beneficiaries by Using Geographic Information Systems. Am J Epidemiol. 2010 Oct 19. (Copper & manganese associated with risk)
Willis AW, Schootman M, Evanoff BA, Perlmutter JS, Racette BA. **Neurologist care in Parkinson disease**: a utilization, outcomes, and survival study. Neurology 2011;77:851– 857.
Willis AW, Schootman M, Kung N, Evanoff BA, Perlmutter JS, Racette BA. **Predictors of Survival** in Patients With Parkinson Disease. Arch Neurol. 2012 Jan 2. (**Dementia** increases mortality)
Willis AW, Schootman M, Tran R, et al. **Neurologist-associated** reduction in PD-related hospitalizations and health care expenditures. Neurology. 2012 Oct 23;79(17):1774-80.
Willis AW, Schootman M, Kung N, et al.**Disparities in deep brain stimulation surgery among insured elders** with Parkinson disease. Neurology. 2014 Jan 14;82(2):163-71
Wills AA, Pérez A, Wang J, et al; NINDS Exploratory Trials in Parkinson Disease (**NET-PD**) Investigators. Association Between **Change in Body Mass Index**, Unified Parkinson's Disease Rating Scale Scores, and Survival Among Persons With Parkinson Disease: Secondary Analysis of Longitudinal Data From NINDS Exploratory Trials in Parkinson Disease Long-term Study 1. JAMA Neurol. 2016 Jan 11:1-8.
Winer JR, Maass A, Pressman P, et al. Associations Between **Tau, β-Amyloid, and Cognition in Parkinson Disease**. JAMA Neurol. 2017 Dec 11.
Winser SJ, Tsang WW, Krishnamurthy K, Kannan P. Does **Tai Chi** improve balance and reduce **falls** incidence in neurological disorders? A systematic review and meta-analysis. Clin Rehabil. 2018 May 1:269215518773442.
Writing Group for the NINDS Exploratory Trials in Parkinson Disease (NET-PD) Investigators, Kieburtz K, Tilley BC, Elm JJ, et. al. Effect of **creatine monohydrate** on clinical progression in patients with Parkinson disease: a randomized clinical trial. JAMA. 2015 Feb 10; 313(6):584-93.
Wu SS, Frucht SJ. Treatment of Parkinson's disease : what's on the horizon? CNS Drugs. 2005;19(9):723-43.
Xiao B, Deng X, Ng EY, et al. Association of **LRRK2 Haplotype** With Age at Onset in Parkinson Disease. JAMA Neurol. 2017 Nov 13.
Yamamoto M, Uesugi T, Nakayama T. Dopamine agonists and cardiac **valvulopathy** in Parkinson disease: a case-control study. Neurology. 2006 Oct 10;67(7):1225-9. The frequency of valvulopathy was significantly increased in the cabergoline group. Our results indicate that high cumulative dose and long-term treatment with cabergoline are risk factors for valvulopathy in patients with Parkinson disease.
Yang Y, Teja S, Baig K. Bilateral **corneal edema associated with amantadine**. CMAJ. 2015 Oct 20;187(15):1155-8.
Yarnall AJ, Breen DP, Duncan GW, et al. On behalf of the ICICLE-PD Study Group. Characterizing mild **cognitive impairment** in incident Parkinson disease: The ICICLE-PD Study. Neurology. 2013 Dec 20.
Yoo HS, Chung SJ, Lee YH, et al. **Levodopa-induced dyskinesia** is closely linked to progression of frontal dysfunction in PD. Neurology. 2019 Mar 26;92(13):e1468-e1478.
Yoon EJ, Ismail Z, Hanganu A, et al. **Mild behavioral impairment is linked to worse cognition and brain atrophy** in Parkinson disease. Neurology. 2019 Jul 18.
Young GB, Findlay JM, Benstead TJ, et al; Canadian Neurological Sciences Federation team. **Canadian Guidelines on Parkinson's Disease**. Can J Neurol Sci. 2012 July;(39)4.
Ypinga JHL, de Vries NM, Boonen LHHM, et al. Effectiveness and costs of specialized **physiotherapy** given via ParkinsonNet: a retrospective analysis of medical claims data. Lancet Neurol 2017; online Dec 12.
Yu X, Du T, Song N, et al. Decreased **iron levels** in the temporal cortex in postmortem human brains with Parkinson disease. Neurology. 2013 Jan 29;80(5):492-5.
Zanetti R, Loria D, Rosso S. Melanoma, Parkinson's disease and levodopa: causal or spurious link? A review of the literature. Melanoma Res. 2006 Jun;16(3):201-6.
Zanetti R, Rosso S. Levodopa and the risk of **melanoma**. Lancet. 2007 Jan 27;369(9558):257-8.
Zesiewicz, T. A., Sullivan, K. L., Arnulf, I., et al. **AAN Practice Parameter**: Treatment of **nonmotor symptoms of Parkin**son disease: Report of the Quality Standards Subcommittee of the American Academy of Neurology. Neurology 2010 74: 924-931.
Zhan A, Mohan S, Tarolli C, et al. **Using Smartphones and Machine Learning** to Quantify Parkinson Disease Severity: The Mobile Parkinson Disease Score. JAMA Neurol. 2018 Mar 26.
Zhuo C, Xue R, Luo L, et al. Efficacy of **antidepressive medication for depression** in Parkinson disease: a network meta-analysis. Medicine (Baltimore). 2017 Jun;96(22):e6698.

Guidelines AAN:

Cheng EM, Tonn S, Swain-Eng R, et al.; For the American Academy of Neurology Parkinson Disease Measure Development Panel. **Quality improvement** in neurology: AAN Parkinson disease quality measures: Report of the Quality Measurement and Reporting Subcommittee of the American Academy of Neurology. Neurology. 2010 Nov 30;75(22):2021-2027. http://www.neurology.org/content/75/22/2021.full.pdf+html

Miyasaki JM, et al.; Quality Standards Subcommittee of the American Academy of Neurology. Practice Parameter: evaluation and treatment of **depression, psychosis, and dementia** in Parkinson disease (an evidence-based review): report of the Quality Standards Subcommittee of the American Academy of Neurology. Neurology. 2006 Apr 11;66(7):996-1002. http://www.neurology.org/cgi/reprint/66/7/996 Screening tools are available for depression and dementia in patients with PD, but more specific validated tools are needed. There are no widely used, validated tools for psychosis screening in Parkinson disease (PD). Clozapine successfully treats psychosis in PD. Cholinesterase inhibitors are effective treatments for dementia in PD, but improvement is modest and motor side effects may occur.

Pahwa R, et al.; Quality Standards Subcommittee of the American Academy of Neurology. Practice Parameter: treatment of Parkinson disease with **motor fluctuations and dyskinesia** (an evidence-based review): report of the Quality Standards Subcommittee of the American Academy of Neurology. Neurology. 2006 Apr 11;66(7):983-95. http://www.neurology.org/cgi/reprint/66/7/983 1. Entacapone and rasagiline should be offered to reduce off time (Level A). Pergolide, pramipexole, ropinirole, and tolcapone should be considered to reduce off time (Level B). Apomorphine, cabergoline, and selegiline may be considered to reduce off time (Level C). 2. The available evidence does not establish superiority of one medicine over another in reducing off time (Level B). Sustained release carbidopa/levodopa and bromocriptine may be disregarded to reduce off time (Level C). 3. Amantadine may be considered to reduce dyskinesia (Level C). 4. Deep brain stimulation of the STN may be considered to improve motor function and reduce off time, dyskinesia, and medication usage (Level C). There is insufficient evidence to support or refute the efficacy of DBS of the GPi or VIM nucleus of the thalamus in reducing off time, dyskinesia, or medication usage, or to improve motor function. 5. Preoperative response to levodopa predicts better outcome after DBS of the STN (Level B).

Suchowersky O, et al.; Quality Standards Subcommittee of the American Academy of Neurology. Practice Parameter: **neuroprotective strategies and alternative** therapies for Parkinson disease (an evidence-based review): report of the Quality Standards Subcommittee of the American Academy of Neurology. Neurology. 2006 Apr 11;66(7):976-82. http://www.neurology.org/cgi/reprint/66/7/976 1. Levodopa does not appear to accelerate disease progression. 2. No treatment has been shown to be neuroprotective. 3. There is no evidence that vitamin or food additives can improve motor function in PD. 4. Exercise may be helpful in improving motor function. 5. Speech therapy may be helpful in improving speech volume. 6. No manual therapy has been shown to be helpful in the treatment of motor symptoms, although studies in this area are limited. Further studies using a rigorous scientific method are needed to determine efficacy of alternative therapies.

Suchowersky O, et al. Quality Standards Subcommittee of the American Academy of Neurology. Practice Parameter: diagnosis and prognosis of **new onset Parkinson** disease (an evidence-based review): report of the Quality Standards Subcommittee of the American Academy of Neurology. Neurology. 2006 Apr 11;66(7):968-75. http://www.neurology.org/cgi/reprint/66/7/968 1. Early falls, poor response to levodopa, symmetry of motor manifestations, lack of tremor, and early autonomic dysfunction are probably useful in distinguishing other parkinsonian syndromes from Parkinson disease (PD). 2. Levodopa or apomorphine challenge and olfactory testing are probably useful in distinguishing PD from other parkinsonian syndromes. 3. Predictive factors for more rapid motor progression, nursing home placement, and shorter survival time include older age at onset of PD, associated comorbidities, presentation with rigidity and bradykinesia, and decreased dopamine responsiveness. Future research into methods for earlier and more accurate diagnosis of the disease and identification and clarification of predictive factors of rapid disease progression is warranted.

Guidelines Canadian:
Young GB, Findlay JM, Benstead TJ, et al; Canadian Neurological Sciences Federation team. **Canadian Guidelines on Parkinson's Disease**. Can J Neurol Sci. 2012 July;(39)4.
Grimes D, Fitzpatrick M, Gordon J. **Canadian guideline for Parkinson disease.** CMAJ **2019**;191:E989-1004.

Guidelines EFNS 2006:
Horstink M, Tolosa E, Bonuccelli U, Deuschl G, Friedman A, Kanovsky P, Larsen JP, Lees A, Oertel W, Poewe W, Rascol O, Sampaio C, European Federation of Neurological Societies, Movement Disorder Society-European Section. Review of the therapeutic management of Parkinson's disease. Report of a joint task force of the EFNS and the MDS-ES. Part II: late (complicated) Parkinson's disease. Eur J Neurol 2006 Nov;13(11):1186-202.

Horstink M, Tolosa E, Bonuccelli U, Deuschl G, Friedman A, Kanovsky P, Larsen JP, Lees A, Oertel W, Poewe W, Rascol O, Sampaio C, European Federation of Neurological Societies, Movement Disorder Society-European Section. Review of the therapeutic management of Parkinson's disease. Report of a joint task force of the European Federation of Neurological Societies and the Movement Disorder Society-European Section. Part I: early (uncomplicated) Parkinson's disease. Eur J Neurol 2006 Nov;13(11):1170-85.

Guidelines NICE 2006:
NICE: National Institute for Health and Clinical Excellence - **Parkinson's disease**: diagnosis and management in primary and secondary care. June 2006. http://www.nice.org.uk/nicemedia/pdf/cg035niceguideline.pdf.

Guidelines SIGN 2010:
SIGN-Scottish Intercollegiate Guidelines Network-Diagnosis and management of Parkinson's disease-SIGN-Jan 2010 http://www.sign.ac.uk/pdf/sign113.pdf

Antiepileptics- References:

Useful websites: www.epilepsy.org.uk , www.epilepsyfoundation.org , www.epilepsy.com , www.ibe-epilepsy.org , www.sign.ac.uk , www.nice.org.uk , & www.aana.com .

1. Browne TR, Holmes GL. Epilepsy. N Engl. J Med 2001;344:1145-51.
2. Holmes LB, Harvey EA. The Teratogenicity of Anticonvulsant Drugs. N Engl. J Med 2001;344:1132-38.
3. Medical Letter-Zonisamide for Epilepsy. Vol.42 (Issue 1089) Oct2,2000.
4. Medical Letter-Two new drugs Oxcarbazepine &Levetiracetam for Epilepsy. Vol.42 (Issue 1076) Apr 17,2000.
5. Sabers A, Gram L. Newer Anticonvulsants-Comparative Review of Drug Interactions & Adverse Effects. Drugs 2000 Jul; 60 (1):23-33.
6. Expert Consensus Guideline Series- Treatment of Epilepsy; Epilepsy & Behavior 2, A1-A50 2001.
7. Drugs for **Epilepsy**: **Treatment Guidelines** from the Medical Letter, May **2003, Updated June 2008, Feb 2012,** (**Updated July 2017**)
8. Drug Information Handbook 10th edition, 2002-2003
9. Drugs in Pregnancy & Lactation 11th edition, 2017 (see also http://www.aedpregnancyregistry.org/.)
10. Geriatric Dosage Handbook 7th Edition, 2002
11. Handbook of Clinical Drug Data 10th edition, 2002
12. Therapeutic Choices 4rd edition, 2003
13. Clinical Handbook of Psychotropic Drugs 13th edition (Bezchlibnyk-Butler,Jeffries) 2003
14. Pharmacotherapy Handbook 2nd edition (Wells,Dipiro et al.)
15. Therapeutic Choices 4th edition 2003
16. Micromedex 2018
17. Patsalos PN, Perucca E. Clinically important drug interactions in epilepsy: general features and interactions between antiepileptic drugs. Lancet Neurol. 2003 Jun;2(6):347-56.
18. Patsalos PN, Perucca E. Clinically important drug interactions in epilepsy: interactions between antiepileptic drugs and other drugs. Lancet Neurol. 2003 Aug;2(8):473-81.
19. Sirven JI, Waterhouse E. Management of status epilepticus. Am Fam Physician. 2003 Aug 1;68(3):469-76.
20. Chang BS, Lowenstein DH. Epilepsy. N Engl J Med. 2003 Sep 25;349(13):1257-66.
21. Blume WT. Diagnosis and management of epilepsy. CMAJ. 2003 Feb 18;168(4):441-8.
22. Suzette M. LaRoche, MD; Sandra L. Helmers, MD **The New Antiepileptic Drugs** -Scientific Review *JAMA.* 2004;291:605-614. (& Clinical Applications p. 615-620).
23. Tatum WO 4th, Liporace J, Benbadis SR, Kaplan PW. Updates on the treatment of epilepsy in women. Arch Intern Med. 2004 Jan 26;164(2):137-45.
24. French JA, Kanner AM, Bautista J, et al.; Therapeutics & Technology Assessment Subcommittee of the American Academy of Neurology; Quality Standards Subcommittee of the AAN; American Epilepsy Society. **Efficacy and tolerability of the new antiepileptic drugs I: treatment of new onset epilepsy**: report of the Therapeutics & Technology Assessment Subcommittee & Quality Standards Subcommittee of the American Academy of Neurology & the American Epilepsy Society. **Neurology. 2004** Apr 27;62(8):1252-60. http://www.neurology.org/cgi/reprint/62/8/1252.pdf
25. French JA, Kanner AM, Bautista J et al.; Therapeutics and Technology Assessment Subcommittee of the American Academy of Neurology; Quality Standards Subcommittee of the AAN; American Epilepsy Society. **Efficacy and tolerability of the new antiepileptic drugs II: treatment of refractory epilepsy**: report of the Therapeutics and Technology Assessment Subcommittee and Quality Standards Subcommittee of the American Academy of Neurology and the American Epilepsy Society. **Neurology. 2004** Apr 27;62(8):1261-73. http://www.neurology.org/cgi/reprint/62/8/1261.pdf
26. National Institute for Clinical Excellence. Newer drugs for epilepsy. London: **NICE London, March 2004** http://www.nice.org.uk/pdf/TA076fullguidance.pdf
    NICE: National Institute for Health and Clinical Excellence. The **epilepsies**: the diagnosis and management of the epilepsies in adults and children in primary and secondary care (update). (Clinical guideline 137.) Jan **2012**. http://guidance.nice.org.uk/CG137.
27. de Haan GJ, Edelbroek P, Segers J, et al. Gestation-induced changes in lamotrigine pharmacokinetics: a monotherapy study. Neurology. 2004 Aug 10;63(3):571-3.
28. Beghi E. Efficacy and tolerability of the new antiepileptic drugs: **comparison of two recent guidelines**. Lancet Neurol. 2004 Oct;3(10):618-21.
29. McCorry D, Chadwick D, Marson A. Current drug treatment of epilepsy in adults. Lancet Neurol. 2004 Dec;3(12):729-35.
30. Glauser, Tracy A., Cnaan, Avital, Shinnar, Shlomo, et al. the Childhood **Absence Epilepsy** Study Group, **Ethosuximide**, Valproic Acid, and Lamotrigine in Childhood Absence Epilepsy. N Engl J Med 2010 362: 790-799. Ethosuximide and valproic acid are more effective than lamotrigine in the treatment of childhood absence epilepsy. Ethosuximide is associated with fewer adverse attentional effects.
    Masur D, Shinnar S, Cnaan A, et al. Pretreatment cognitive deficits and medication impact (**valproic acid, ethosuximide, lamotrigine**) on attention in **childhood absence epilepsy**. Neurology 2013;81:1572–1580.
31. Doose DR, et al. Effect of topiramate or carbamazepine on the pharmacokinetics of an oral contraceptive containing norethindrone and ethinyl estradiol in healthy obese and nonobese female subjects. Epilepsia. 2003 Apr;44(4):540-9.
32. Leppik IE, Bergey GK, Ramsay RE, et al. Advances in antiepileptic drug treatments. A rational basis for selecting drugs for older patients with epilepsy. Geriatrics. 2004 Dec;59(12):14-8, 22-4.
33. P-Codrea Tigaran S, Sidenius P, Dam M. Lamotrigine-induced rash--worth a rechallenge. Acta Neurol Scand. 2005 Mar;111(3):191-4.
34. Camfield P, Camfield C. The frequency of intractable seizures after stopping AEDs in seizure-free children with epilepsy. Neurology. 2005 Mar 22;64(6):973-5.
35. Cunnington M, et al; International **Lamotrigine Pregnancy Registry** Scientific Advisory Committee. Lamotrigine and the risk of malformations in pregnancy. Neurology. 2005 Mar 22;64(6):955-60.
    CONCLUSIONS: The risk of all major birth defects after first-trimester exposure to lamotrigine monotherapy (2.9%) was similar to that in the general population and in other registries enrolling women exposed to antiepileptic monotherapy (3.3% to 4.5%). However, the sample size was too small to detect any but very large increases in specific birth defects.
36. Wyszynski DF, et al.; Antiepileptic Drug Pregnancy Registry. Increased rate of major malformations in offspring exposed to valproate during pregnancy. Neurology. 2005 Mar 22;64(6):961-5.
37. Mockenhaupt M, Messenheimer J, et al. Risk of Stevens-Johnson syndrome and toxic epidermal necrolysis in new users of antiepileptics. Neurology. 2005 Apr 12;64(7):1134-8.

(see also http://www.fda.gov/medwatch/SAFETY/2005/trileptal_hcp.pdf ; April/05 Health Canada warning http://www.hc-sc.gc.ca/hpfb-dgpsa/tpd-dpt/trileptal_hpc_e.html)

38. Marson A, Jacoby A, Johnson A, et al.; Medical Research Council **MESS** Study Group. **Immediate versus deferred** antiepileptic drug treatment for **early epilepsy and single** seizures: a randomised controlled trial. Lancet. 2005 Jun 28;365(9476):2007-13 & ACP Journal Club . (INTERPRETATION: Immediate antiepileptic drug treatment reduces the occurrence of seizures in the next 1-2 years, but does not affect long-term remission in individuals with single or infrequent seizures.) (Hirtz D, et al.; Quality Standards Subcommittee of the American Academy of Neurology; Practice Committee of the Child Neurology Society. Practice parameter: treatment of the child with a **first unprovoked** seizure: Report of the Quality Standards Subcommittee of the American Academy of Neurology & the Practice Committee of the Child Neurology Society. Neurology. 2003 Jan 28;60(2):166-75)(Pohlmann-Eden B, et al. The **first seizure** and its management in adults and children. BMJ. 2006 Feb 11;332(7537):339-42) Steering Committee on Quality Improvement and Management, Subcommittee on Febrile Seizures American Academy of Pediatrics. **Febrile seizures**: clinical practice guideline for the long-term management of the child with simple febrile seizures. Pediatrics. 2008 Jun;121(6):1281-6.
Perucca Emilio, Tomson Torbjorn, The pharmacological **treatment of epilepsy** in adults, The Lancet Neurology, Volume 10, Issue 5, May 2011, Pages 446-456, ISSN 1474-4422.
Krumholz A, Wiebe S, Gronseth GS, et al. Evidence-based guideline: **Management of an unprovoked first seizure in adults**: Report of the Guideline Development Subcommittee of the **American Academy of Neurology** (**AAN**) and the **American Epilepsy Society (AES)**. Neurology. 2015 Apr 21;84(16):1705-13.

39. Rowan AJ, Ramsay RE, Collins JF, et al.; VA Cooperative Study 428 Group. New onset **geriatric epilepsy**: a randomized study of **gabapentin, lamotrigine, and carbamazepine**. Neurology. 2005 Jun 14;64(11):1868-73. CONCLUSIONS: The main limiting factor in patient retention was adverse drug reactions. Patients taking lamotrigine (LTG) or gabapentin (GBP) did better than those taking carbamazepine. Seizure control was similar among groups. LTG and GBP should be considered as initial therapy for older patients with newly diagnosed seizures.
40. Johnson BA, et al. Use of oral topiramate to promote smoking abstinence among alcohol-dependent smokers in an RCT. Arch Intern Med. 2005 Jul 25;165(14):1600-5.
41. Artama M, Auvinen A, Raudaskoski T, et al. Antiepileptic drug use of women with epilepsy and congenital malformations in offspring. Neurology. 2005 Jun 14;64(11):1874-8. CONCLUSION: Excess risk was confined to patients using **valproate** during pregnancy. The risk for malformations was not elevated in offspring of mothers using carbamazepine, oxcarbazepine, or phenytoin (as monotherapy or polytherapy without valproate).
42. Eberhard-Gran M, Eskild A, Opjordsmoen S. Treating mood disorders during pregnancy: safety considerations. Drug Saf. 2005;28(8):695-706.
43. Spina E, Perugi G. Antiepileptic drugs: indications other than epilepsy. Epileptic Disord. 2004 Jun;6(2):57-75.
44. Nadkarni S, LaJoie J, Devinsky O. Current treatments of epilepsy. Neurology. 2005 Jun 28;64(12 Suppl 3):S2-11.
45. Geerts AT, Niermeijer JM, Peters AC, et al. Four-year outcome after early withdrawal of antiepileptic drugs in childhood epilepsy. Neurology. 2005 Jun 28;64(12):2136-8.
46. Mattson RH, Cramer JA, Collins JF. A comparison of valproate with carbamazepine for the treatment of complex partial seizures and secondarily generalized tonic-clonic seizures in adults. The Department of Veterans Affairs Epilepsy Cooperative Study No. 264 Group. N Engl J Med. 1992 Sep 10;327(11):765-71.
47. Smith DB, Mattson RH, Cramer JA, et al. Results of a nationwide Veterans Administration Cooperative Study comparing the efficacy and toxicity of carbamazepine, phenobarbital, phenytoin, and primidone. Epilepsia. 1987;28 Suppl 3:S50-8.
48. Wyszynski DF, Nambisan M, Surve T, et al.; Antiepileptic Drug Pregnancy Registry. Increased rate of major malformations in offspring exposed to valproate during pregnancy. Neurology. 2005 Mar 22;64(6):961-5.
49. Holmes LB, Wyszynski DF, Lieberman E. The AED (antiepileptic drug) **pregnancy registry**: a **6-year** experience. Arch Neurol. 2004 May;61(5):673-8.
50. Polycarpou A, Papanikolaou P, Ioannidis J, Contopoulos-Ioannidis D. Anticonvulsants for alcohol withdrawal. Cochrane Database Syst Rev. 2005 Jul 20;(3):CD005064.
51. Ratilal B, Costa J, Sampaio C. Anticonvulsants for preventing seizures in patients with chronic subdural haematoma. Cochrane Database Syst Rev. 2005 Jul 20;(3):CD004893.
52. Wiffen P, Collins S, McQuay H, Carroll D, Jadad A, Moore A. Anticonvulsant drugs for acute and chronic pain. Cochrane Database Syst Rev. 2005 Jul 20;(3):CD001133. CONCLUSIONS: Although anticonvulsants are used widely in chronic pain surprisingly few trials show analgesic effectiveness. Only one studied considered cancer pain. There is no evidence that anticonvulsants are effective for acute pain. In chronic pain syndromes other than trigeminal neuralgia, anticonvulsants should be withheld until other interventions have been tried. While gabapentin is increasingly being used for neuropathic pain the evidence would suggest that it is not superior to carbamazepine.
53. Pandya KJ, Morrow GR, Roscoe JA, et al. **Gabapentin** for hot flashes in 420 women with breast cancer: a randomised double-blind placebo-controlled trial. Lancet. 2005 Sep 3-9;366(9488):818-24. Gabapentin is effective in the control of hot flashes at a dose of 900 mg/day, but not at a dose of 300 mg/day. This drug should be considered for treatment of hot flashes in women with breast cancer. (InfoPOEMs: Women with a history of breast cancer may obtain some relief from hot flashes with 900 mg gabapentin daily. The 300 mg daily dose was not effective. (LOE = 1b-))
54. Williams LJ, Rasmussen SA, Flores A, et al. Decline in the prevalence of **spina bifida** and anencephaly by race/ethnicity: 1995-2002. Pediatrics. 2005 Sep;116(3):580-6.
55. **Pregabalin** for Neuropathic Pain & Epilepsy. The Medical Letter Sept 12,2005 p. 75-76.
56. Walker M. **Status epilepticus**: an evidence based guide. BMJ. 2005 Sep 24;331(7518):673-7.
57. Rickels K, Pollack MH, et al. Pregabalin for treatment of generalized anxiety disorder: a 4-week, multicenter, double-blind, placebo-controlled trial of pregabalin and alprazolam. Arch Gen Psychiatry. 2005 Sep;62(9):1022-30.
58. Kalviainen R, Eriksson K, Parviainen I. Refractory generalised convulsive status epilepticus : a guide to treatment. CNS Drugs. 2005;19(9):759-68.
59. Health Canada Sept/04 Lamictal warning with birth control pills http://www.hc-sc.gc.ca/dhp-mps/alt_formats/hpfb-dgpsa/pdf/medeff/lamictal_pa-ap_e.pdf
60. Prasad K, Al-Roomi K, Krishnan P, Sequeira R, Prasad K. Anticonvulsant therapy for **status epilepticus**. **Cochrane** Database Syst Rev. 2005 Oct 19;(4):CD003723. AUTHORS' CONCLUSIONS: **Lorazepam is better than diazepam or phenytoin** alone for cessation of seizures and carries a lower risk of continuation of status epilepticus requiring a different drug or general anaesthesia. Both lorazepam and diazepam are better than placebo for the same outcomes. In the treatment of premonitory seizures, diazepam 30 mg in an intrarectal gel is better than 20 mg for cessation of seizures without a statistically significant increase in adverse effects. Universally accepted definitions of premonitory, early, established and refractory status epilepticus are required.
Meierkord H, Boon P, Engelsen B, Gocke K, Shorvon S, Tinuper P, Holtkamp M, European Federation of Neurological Societies. **EFNS** guideline on the management of status

epilepticus in adults. Eur J Neurol 2010 Mar;17(3):348-55.

61. Perucca E. **Birth defects** after prenatal exposure to antiepileptic drugs. Lancet Neurol. 2005 Nov;4(11):781-6.
Tomson T, Battino D, Bonizzoni E, et al. Dose-dependent risk of **malformations** with antiepileptic drugs: an analysis of data from the **EURAP** epilepsy and pregnancy registry. *Lancet Neurol* 2011; published online June 6. DOI:10.1016/S1474-4422(11)70107-7.
Vajda FJ, O'Brien TJ, Graham JE, et al. Dose dependence of fetal malformations associated with valproate. Neurology. 2013 Sep 10;81(11):999-1003.
Tomson T, Battino D, Bonizzoni E, et al; EURAP Study Group. Dose-dependent teratogenicity of valproate in mono- and polytherapy: An observational study. Neurology. 2015 Sep 8;85(10):866-72.
62. Chen DK, So YT, Fisher RS; Therapeutics and Technology Assessment Subcommittee of the American Academy of Neurology. Use of **serum prolactin** in diagnosing epileptic seizures: report of the Therapeutics and Technology Assessment Subcommittee of the American Academy of Neurology. Neurology. 2005 Sep 13;65(5):668-75.
63. Berry JD, Petersen KL. A single dose of **gabapentin** reduces acute pain and allodynia in patients with **herpes zoster**. Neurology. 2005 Aug 9;65(3):444-7.
64. Steinhoff BJ, et al. The LAM-SAFE Study Group. The **LAM-SAFE** Study: Lamotrigine versus carbamazepine or valproic acid in newly diagnosed focal and generalised epilepsies in adolescents and adults. Seizure. 2005 Nov 5
CONCLUSIONS: This study indicates that the effectiveness of LTG in focal and generalised epilepsy syndromes as initial monotherapy in patients >/=12 years is in the range of standard first-line antiepileptic drugs.
65. Leppik IE; Epilepsy Foundation of America. Choosing an antiepileptic. Selecting drugs for **older patients** with epilepsy. Geriatrics. 2005 Nov;60(11):42-7. (Sirven JI, Ozuna J; Epilepsy Foundation of America. **Diagnosing epilepsy in older adults**: what does it mean for the primary care physician? Geriatrics. 2005 Oct;60(10):30-5).
66. Treatment Guidelines from The **Medical Letter**: **Drugs for Epilepsy. Nov 2005**.
67. Ficker DM, Privitera M, Krauss G, et al. Improved tolerability and efficacy in epilepsy patients with **extended-release carbamazepine**. Neurology. 2005 Aug 23;65(4):593-5.
68. Meador KJ, Loring DW, Vahle VJ, et al. **Cognitive** and behavioral effects of **lamotrigine** and topiramate in healthy volunteers. Neurology. 2005 Jun 28;64(12):2108-14.
69. Biton V, Bourgeois BF; YTC/YTCE Study Investigators. **Topiramate** in patients with **juvenile myoclonic** epilepsy. Arch Neurol. 2005 Nov;62(11):1705-8.
70. Crawford P. Best practice guidelines for the management of **women with epilepsy**. Epilepsia. 2005 Nov;46 Suppl 9:117-24.
71. Abou-Khalil B. Benefit-risk assessment of **levetiracetam** in the treatment of partial seizures. Drug Saf. 2005;28(10):871-90.
72. Tatum WO 4th, Liporace J, Benbadis SR, Kaplan PW. Updates on the treatment of **epilepsy in women**. Arch Intern Med. 2004 Jan 26;164(2):137-45.
73. Kaaja E, Kaaja R, Matila R, Hiilesmaa V. Enzyme-inducing antiepileptic drugs in **pregnancy and the risk of bleeding** in the neonate. Neurology. 2002 Feb 26;58(4):549-53.
74. Brodie MJ, Kwan P. Epilepsy in **elderly people**. BMJ. 2005 Dec 3;331(7528):1317-22.
75. Brodie MJ, Overstall PW, Giorgi L. Multicentre, double-blind, randomised comparison between **lamotrigine and carbamazepine** in **elderly** patients with newly diagnosed epilepsy. The UK Lamotrigine Elderly Study Group. Epilepsy Res. 1999 Oct;37(1):81-7.
76. Walker M, Cross H, Smith S, Yet al. **Nonconvulsive status epilepticus**: Epilepsy Research Foundation Workshop Reports. Epileptic Disord. 2005 Sep;7(3):253-96.
77. Biton V, Sackellares JC, et al. Double-blind, placebo-controlled study of **lamotrigine in primary generalized tonic-clonic seizures**. Neurology. 2005 Dec 13;65(11):1737-43.
78. Seizure control & treatment in pregnancy. Observations from the EURAP Epilepsy Pregnancy Registry. Neurology. 2005 Dec 28; CONCLUSIONS: The majority of patients with epilepsy maintain seizure control during pregnancy. The apparently higher risk of seizures among women treated with oxcarbazepine & the more frequent increases in drug load in the oxcarbazepine & lamotrigine cohorts prompts further studies on relationships with pharmacokinetic changes. Risks associated with status epilepticus appear to be lower than previously reported.
79. Brodie MJ, Perucca E, Ryvlin P, Ben-Menachem E, Meencke HJ; Levetiracetam Monotherapy Study Group. Comparison of levetiracetam and controlled-release carbamazepine in newly diagnosed epilepsy. Neurology 2007;68:402–408.
80. Mattson RH, Cramer JA, Collins JF, Smith DB, Delgado-Escueta AV, Browne TR, Williamson PD, Treiman DM, McNamara JO, McCutchen CB, et al. Comparison of carbamazepine, phenobarbital, phenytoin, and primidone in partial and secondarily generalized tonic-clonic seizures. N Engl J Med. 1985 Jul 18;313(3):145-51.
81. Perucca E. Clinically relevant drug interactions with antiepileptic drugs. Br J Clin Pharmacol. 2006 Mar;61(3):246-55.
82. Merideth CH. A single-center, double-blind, placebo-controlled evaluation of lamotrigine in the treatment of obesity in adults. J Clin Psychiatry. 2006 Feb;67(2):258-62.
83. Zupanc ML. Antiepileptic drugs and hormonal contraceptives in adolescent women with epilepsy. Neurology. 2006 Mar 28;66(6 Suppl 3):S37-45.
84. Pohlmann-Eden B, et al. The **first seizure** and its management in adults and children. BMJ. 2006 Feb 11;332(7537):339-42.
85. Gamble C, et al. A meta-analysis of individual patient responses to lamotrigine or carbamazepine monotherapy.Neurology. 2006 May 9;66(9):1310-7.
86. Meierkord H, et al. EFNS guideline on the management of status epilepticus. Eur J Neurol. 2006 May;13(5):445-50. The preferred treatment pathway for generalised convulsive status epilepticus (GCSE) is intravenous (i.v.) administration of 4 mg of lorazepam or 10 mg of diazepam directly followed by 15-18 mg/kg of phenytoin or equivalent fosphenytoin. If seizures continue for more than 10 min after first injection another 4 mg of lorazepam or 10 mg of diazepam is recommended. Refractory GCSE is treated by anaesthetic doses of midazolam, propofol or barbiturates; the anaesthetics are titrated against an electroencephalogram burst suppression pattern for at least 24 h. The initial therapy of non-convulsive SE depends on the type and the cause. In most cases of absence SE, a small i.v. dose of lorazepam or diazepam will terminate the attack. Complex partial SE is initially treated such as GCSE, however, when refractory further non-anaesthetising substances should be given instead of anaesthetics. In subtle SE i.v. anaesthesia is required.
87. Pressler RM, et al. Effect of lamotrigine on cognition in children with epilepsy. Neurology. 2006 May 23;66(10):1495-9.
88. Bekkelund SI, Lilleng H, Tonseth S. **Gabapentin** may cause reversible **visual field constriction**. BMJ. 2006 May 20;332(7551):1193.
89. Health Canada Aug/06 **Lamictal** warning with non-syndromic **oral clefts**. Emerging data from the North American Antiepileptic Drug (NAAED) Pregnancy Registry suggest an association between LAMICTAL and an increased risk of non-syndromic oral clefts over the reference population for the registry (ie. Active Malformations Surveillance Program at Brigham and Women's Hospital in Boston, USA)1. Recently published data from the Registry report three cases of isolated, non syndromic cleft palate and two cases of isolated, non syndromic cleft lip without cleft palate in infants from 564 first trimester lamotrigine monotherapy exposures giving a rate of 8.9 per 1,000, as compared to 0.37 per 1000 in the reference population for that registry. The prevalence of oral clefts noted in the NAAED registry is also higher than the background prevalence of non-syndromic oral clefts

reported in the literature, including studies from the United States, Australia and Europe. While different studies have differing results due to geographic and case ascertainment variations, the reported range is 0.50 to 2.16/1000 3-17. To assist with the assessment of risk, analysis of data from additional pregnancy registries, with approximately 2200 additional lamotrigine monotherapy first trimester exposures has been conducted, and 4 additional non-syndromic cases of oral cleft have been identified. http://www.hc-sc.gc.ca/dhp-mps/medeff/advisories-avis/prof/2006/lamictal_2_hpc-cps_e.html (see also Pharmacist's Letter Sept 2006.)

Dolk H, Jentink J, Loane M, Morris J, de Jong-van den Berg LT; EUROCAT Antiepileptic Drug Working Group. Does lamotrigine use in pregnancy increase orofacial cleft risk relative to other malformations? Neurology. 2008 Sep 2;71(10):714-22. Epub 2008 Jul 23. We find no evidence of a specific increased risk of isolated orofacial clefts relative to other malformations due to lamotrigine (LTG) monotherapy. Our study is not designed to assess whether there is a generalized increased risk of malformations with LTG exposure.

Madadi P, Ito S. **Perinatal exposure to maternal lamotrigine**: Clinical considerations for the mother and child. Can Fam Physician. 2010 Nov;56(11):1132-4.

Holmes LB, Baldwin EJ, Smith CR, Habecker E, Glassman L, Wong SL, Wyszynski DF. Increased frequency of isolated cleft palate in infants exposed to lamotrigine during pregnancy. Neurology. 2008 May 27;70(22 Pt 2):2152-8.

90. Trevathan E, et al. **Lamotrigine** adjunctive therapy among **children** & **adolescents** with primary generalized tonic-clonic seizures.Peds.2006 Aug;118(2):e371-8.Epub2006Jul 17.
91. Siddall PJ, et al. **Pregabalin** (150-600mg/d) in central neuropathic pain assoc. with **spinal cord** injury: a placebo-controlled trial.Neurology.2006Nov28;67(10):1792-800.12wk n=137
92. Hunt S, Craig J, Russell A, et al. **Levetiracetam** in **pregnancy**: preliminary experience from the UK Epilepsy and Pregnancy Register. Neurology. 2006 Nov 28;67(10):1876-9. Three of 117 exposed pregnancies had an MCM (2.7%; 95% CI 0.9% to 7.7%); all 3 were exposed to other AEDs.
93. Banu SH, et al. Side effects of **phenobarbital** and **carbamazepine** in childhood epilepsy: randomised controlled trial. BMJ. 2007 Jun 9;334(7605):1207. Epub 2006 Dec 4. n=108 12 months. There was no excess in behavioural side effects with phenobarbital in children with epilepsy in a country with limited resources.
94. Pugh MJ, Foreman PJ, et al. Prescribing Antiepileptics for the **Elderly** : Differences between Guideline Recommendations and Clinical Practice. Drugs Aging. 2006;23(11):861-75.
95. Nikolajsen L, et al. A Randomized Study of the Effects of **Gabapentin** on **Postamputation** Pain. Anesthesiology. 2006 Nov;105(5):1008-1015. Gabapentin administered in the first 30 postoperative days after amputation does not reduce the incidence or intensity of postamputation pain.
96. Christensen J, Sabers A, Sidenius P. **Oxcarbazepine** concentrations during **pregnancy**: a retrospective study in patients with epilepsy. Neurology. 2006 Oct 24;67(8):1497-9. The mean dose-corrected concentration of MHD was decreased during 9 pregnancies (analysis of variance, p = 0.0016), being 72% (SD = 13%) in the first trimester, 74% (SD = 17%) in the second trimester, 64% (SD = 6%) in the third trimester, and 108% (SD = 18%) after pregnancy vs the dose-corrected concentration before pregnancy.
97. Welch BJ, et al. Biochemical and **stone-risk** profiles with **topiramate** treatment. Am J Kidney Dis. 2006 Oct;48(4):555-63.
98. Tomson T, et al. **Valproate** effects on kinetics of **lamotrigine** in **pregnancy** and treatment with oral contraceptives. Neurology. 2006 Oct 10;67(7):1297-9. Valproate seems to reduce the induction of lamotrigine metabolism associated with pregnancy or use of contraceptives.
99. Pharmacist's Letter Oct 2006. Alternative or **Off-label** Routes of Drug Administration. (Rectal carbamazepine, clonazepam, diazepam, phenobarbital & valproic acid)
100. Vajda FJ, et al. **Foetal malformations** and seizure control: 52 months data of the **Australian** Pregnancy Registry. Eur J Neurol. 2006 Jun;13(6):645-54.
101. Vajda FJ, et al. Critical relationship between sodium **valproate** dose and human **teratogenicity**: results of the Australian register of anti-epileptic drugs in pregnancy. J Clin Neurosci. 2004 Nov;11(8):854-8.
102. Adab N, et al. Common antiepileptic drugs in **pregnancy** in women with epilepsy. Cochrane Database Syst Rev. 2004;(3):CD004848.
103. Breen DP, Davenport RJ. **Teratogenicity** of antiepileptic drugs. BMJ. 2006 Sep 23;333(7569):615-6.
104. Malaga I, Sanmarti FX. Two cases of painful **gynecomastia** and lower extremity pain in association with **pregabalin** therapy. Epilepsia. 2006 Sep;47(9):1576-9.
105. Harden CL, et al. **Hormone replacement therapy** in women with epilepsy: a randomized, double-blind, placebo-controlled study. Epilepsia. 2006 Sep;47(9):1447-51. CEE/MPA is associated with a dose-related increase in seizure frequency in postmenopausal women with epilepsy.
106. Adab N. Therapeutic Monitoring of Antiepileptic Drugs during **Pregnancy** and in the Postpartum Period : Is It Useful? CNS Drugs. 2006;20(10):791-800.
107. Varghese SP, et al. **Lamotrigine**-induced toxic **epidermal necrolysis** in three patients treated for bipolar disorder. Pharmacotherapy. 2006 May;26(5):699-704.
108. Donati F, et al. Oxcarbazepine Cognitive Study Group. Effects of **oxcarbazepine** on **cognitive** function in children and adolescents with partial seizures. Neurology. 2006 Aug 22;67(4):679-82.
109. Meador KJ, et al.; **NEAD** Study Group. In utero antiepileptic drug exposure: **fetal** death and **malformations**. Neurology. 2006 Aug 8;67(3):407-12. More adverse outcomes were observed in pregnancies with in utero valproate exposure vs the other antiepileptic drugs (AEDs). These results combined with several recent studies provide strong evidence that valproate poses the highest risk to the fetus. For women who fail other AEDs and require valproate, the dose should be limited if possible.
110. Nicolaidou P, et al. Effects of anticonvulsant therapy on **vitamin D** status in children: prospective monitoring study. J Child Neurol. 2006 Mar;21(3):205-9.
111. van der Lee MJ, et al. **Lopinavir/ritonavir** reduces lamotrigine plasma concentrations in healthy subjects. Clin Pharmacol Ther. 2006 Aug;80(2):159-68.
112. Bates DE, Herman RJ. Carbamazepine toxicity induced by **lopinavir/ritonavir** and **nelfinavir**. Ann Pharmacother. 2006 Jun;40(6):1190-5. Epub 2006 May 23.
113. Ho KY, Gan TJ, Habib AS. **Gabapentin** and **postoperative pain** - a systematic review of randomized controlled trials. Pain. 2006 Jul 15; [Epub ahead of print]
114. Misra UK, Kalita J, Patel R. Sodium **valproate vs phenytoin** in **status epilepticus**: a pilot study. Neurology. 2006 Jul 25;67(2):340-2.
115. EURAP Study Group. Seizure control and treatment in **pregnancy**: observations from the **EURAP** epilepsy pregnancy registry. Neurology. 2006 Feb 14;66(3):354-60. Epub 2005 Dec 28.
116. Morrow J, et al. Malformation risks of antiepileptic drugs in **pregnancy**: a prospective study from the **UK Epilepsy** and Pregnancy Register. J Neurol Neurosurg Psychiatry. 2006 Feb;77(2):193-8. Epub 2005 Sep 12. Only 4.2% of live births to women with epilepsy had an MCM. The MCM rate for polytherapy exposure was greater than for monotherapy

exposure. Polytherapy regimens containing valproate had significantly more MCMs than those not containing valproate.
For monotherapy exposures, carbamazepine was associated with the lowest risk of MCM.
117. Zupanc ML. Antiepileptic drugs and **hormonal contraceptives** in adolescent women with epilepsy. Neurology. 2006 Mar 28;66(6 Suppl 3):S37-45.
118. Blum D, et al. **Cognitive** effects of **lamotrigine** compared with **topiramate** in patients with epilepsy. Neurology. 2006 Aug 8;67(3):400-6.
119. Koren G, et al. Major **malformations** with valproic acid. Can Fam Physician. 2006 Apr;52:441-2, 444, 447. The risks appear to begin increasing at doses of 600 mg/d and to become more prominent at doses above 1000 mg/d.
120. Sadleir LG, Scheffer IE. **Febrile seizures**. BMJ. 2007 Feb 10;334(7588):307-11.
121. McIntyre J, et al. Safety and efficacy of buccal midazolam versus rectal diazepam for emergency treatment of seizures in children: a randomised controlled trial. Lancet. 2005 Jul 16-22;366(9481):205-10. Buccal midazolam was more effective than rectal diazepam for children presenting to hospital with acute seizures and was not associated with an increased incidence of respiratory depression.
122. Widdess-Walsh P, Kotagal P, Jeha L, Wu G, Burgess R. Multiple auras: clinical significance and pathophysiology. Neurology. 2007 Aug 21;69(8):755-61. Most patients who report **multiple aura** types have localized epilepsy in the nondominant hemisphere, and are **good surgical candidates.**
123. Lyseng-Williamson KA, Yang LP. Topiramate: a review of its use in the treatment of epilepsy. Drugs. 2007;67(15):2231-56.
124. Tomson T, Hiilesmaa V. **Epilepsy in pregnancy**. BMJ. 2007 Oct 13;335(7623):769-73.
125. Berkovic SF, Knowlton RC, Leroy RF, Schiemann J, Falter U; Levetiracetam N01057 Study Group. Placebo-controlled study of levetiracetam in idiopathic generalized epilepsy. Neurology. 2007 Oct 30;69(18):1751-60. Epub 2007 Jul 11. Adjunctive levetiracetam is an effective and well-tolerated antiepileptic drug for treating generalized tonic-clonic seizures in patients with idiopathic generalized epilepsies.
126. Johnson BA, Rosenthal N, Capece JA, et al, for the Topiramate for Alcoholism Advisory Board and the Topiramate for Alcoholism Study Group. Topiramate for alcohol dependence. A randomized controlled trial. JAMA 2007;298(14):1641-1651. {InfoPOEMs: Topiramate (Topamax) is somewhat more effective than placebo in helping adults with alcohol dependence reduce heavy drinking (number needed to treat [NNT] = 7) and achieve abstinence (NNT = 9). Unfortunately, less than one-third of the patients in the active treatment group significantly reduced their drinking compared with baseline amounts and less than one-fifth achieved continuous abstinence for 28 days or more. As a safety precaution, topiramate was discontinued after 14 weeks and no further follow up is reported. Thus, long-term efficacy remains unknown. (LOE = 1b)}
127. Marson AG, Al-Kharusi AM, Alwaidh M, et al; **SANAD** Study group. The SANAD study of effectiveness of valproate, lamotrigine, or topiramate for generalised and unclassifiable epilepsy: an unblinded randomised controlled trial. Lancet. 2007 Mar 24;369(9566):1016-26. Valproate is better tolerated than topiramate and more efficacious than lamotrigine, and should remain the drug of first choice for many patients with generalised and unclassified epilepsies. However, because of known potential adverse effects of valproate during pregnancy, the benefits for seizure control in women of childbearing years should be considered.
128. Marson AG, Al-Kharusi AM, Alwaidh M, et al. **SANAD** Study group. The SANAD study of effectiveness of carbamazepine, gabapentin, lamotrigine, oxcarbazepine, or topiramate for treatment of partial epilepsy: an unblended randomised controlled trial. Lancet. 2007 Mar 24;369(9566):1000-15. Lamotrigine is clinically better than carbamazepine, the standard drug treatment, for time to treatment failure outcomes and is therefore a cost-effective alternative for patients diagnosed with partial onset seizures.
129. Pennell PB, Peng L, Newport DJ, et al. **Lamotrigine in pregnancy**. Clearance, therapeutic drug monitoring, and seizure frequency. Neurology. 2007 Nov 28; [Epub ahead of print]
130. Krumholz A, Wiebe S, Gronseth G, et al. Quality Standards Subcommittee of the American Academy of Neurology; American Epilepsy Society. Practice Parameter: **evaluating** an apparent **unprovoked first seizure in adults** (an evidence-based review): report of the Quality Standards Subcommittee of the American Academy of Neurology and the American Epilepsy Society. Neurology. 2007 Nov 20;69(21):1996-2007. EEG should be considered as part of the routine neurodiagnostic evaluation of adults presenting with an apparent unprovoked first seizure (Level B). Brain imaging with CT or MRI should be considered as part of the routine neurodiagnostic evaluation of adults presenting with an apparent unprovoked first seizure (Level B). Laboratory tests, such as blood counts, blood glucose, and electrolyte panels (particularly sodium), lumbar puncture, and toxicology screening may be helpful as determined by the specific clinical circumstances based on the history, physical, and neurologic examination, but there are insufficient data to support or refute recommending any of these tests for the routine evaluation of adults presenting with an apparent first unprovoked seizure (Level U).
131. Battino D, Tomson T. Management of **Epilepsy during Pregnancy**. Drugs. 2007;67(18):2727-46.
132. Brodtkorb E, Reimers A. Seizure control and pharmacokinetics of antiepileptic drugs in pregnant women with epilepsy. Seizure. 2007 Dec 22; [Epub ahead of print]
133. Westin AA, Reimers A, Helde G, Nakken KO, Brodtkorb E. Serum concentration/dose ratio of **levetiracetam** before, during and after **pregnancy**. Seizure. 2008 Jan 2; [Epub ahead of print] Serum concentrations of LEV declined significantly in the third trimester of pregnancy and increased rapidly after delivery.
134. Noachtar S, Andermann E, Meyvisch P, Andermann F, Gough WB, Schiemann-Delgado J; N166 Levetiracetam Study Group. Levetiracetam for the treatment of idiopathic generalized epilepsy with myoclonic seizures. Neurology. 2008 Feb 19;70(8):607-16.
135. Obermann M, Yoon MS, Sensen K, Maschke M, Diener HC, Katsarava Z. Efficacy of **pregabalin** in the treatment of **trigeminal neuralgia**. Cephalalgia. 2008 Feb;28(2):174-81. Epub 2007 Nov 26.
136. Butt DA, Lock M, Lewis JE, Ross S, et al. Gabapentin for the treatment of menopausal hot flashes: a randomized controlled trial. Menopause. 2007 Oct 2; [Epub ahead of print]
137. Purcell TB, McPheeters RA, Feil M, Chavez R. Rapid oral loading of carbamazepine in the emergency department. Ann Emerg Med. 2007 Aug;50(2):121-6.
138. Pack AM, Morrell MJ, Randall A, et al. Bone health in young women with epilepsy after one year of antiepileptic drug monotherapy. Neurology. 2008 Apr 29;70(18):1586-93. In contrast, those treated with carbamazepine, lamotrigine, and valproate did not have detectable adverse effects on bone turnover or bone mineral density. These results raise **concerns about the long-term effects of phenytoin monotherapy on bone** in young women with epilepsy.
139. Neal EG, Chaffe H, Schwartz RH, et al. The **ketogenic diet** for the treatment of childhood epilepsy: a randomised controlled trial. Lancet Neurol. 2008 Jun;7(6):500-6. Epub 2008 May 2. The results from this trial of the ketogenic diet support its use in children with treatment-intractable epilepsy.
140. Alvestad S, Lydersen S, Brodtkorb E. Cross-reactivity pattern of rash from current aromatic antiepileptic drugs. Epilepsy Res. 2008 May 17. [Epub ahead of print] LTG appears to be involved in cross-reactions less often than CBZ, OXC and PHT.
141. Woods SW, Saksa JR, Baker CB, Cohen SJ, Tek C. Effects of levetiracetam (0.5-3g/d) on **tardive dyskinesia**: a randomized, double-blind, placebo-controlled study. J Clin

Psychiatry. 2008 Apr;69(4):546-54. (n=50 12+12 weeks) Levetiracetam appeared effective for TD in this study. The mechanisms of its therapeutic effect are unclear but may involve reducing neuronal hypersynchrony in basal ganglia.

142. LeLorier J, Duh MS, Paradis PE, Lefebvre P, Weiner J, Manjunath R, Sheehy O. Clinical consequences of generic substitution of lamotrigine for patients with epilepsy. Neurology. 2008 May 27;70(22 Pt 2):2179-86. A higher propensity to switch back to branded medications was observed among antiepileptic drug users compared to users of antihypertensives and antihyperlipidemics, similar to findings from Andermann et al. Switch to **generic lamotrigine** was significantly associated with increased physician visits and hospitalizations.
143. Johnson BA, Rosenthal N, et al.**Topiramate for Alcoholism** Advisory Board; Topiramate for Alcoholism Study Group. Improvement of physical health and quality of life of alcohol-dependent individuals with topiramate treatment: US multisite randomized controlled trial. Arch Intern Med. 2008 Jun 9;168(11):1188-99.
144. Hunt S, Russell A, Smithson WH, Parsons L, Robertson I, Waddell R, Irwin B, Morrison PJ, Morrow J, Craig J; UK Epilepsy and Pregnancy Register. **Topiramate** in pregnancy: preliminary experience from the UK Epilepsy and **Pregnancy Register**. Neurology. 2008 Jul 22;71(4):272-6. The number of outcomes of human pregnancies exposed to topiramate is low, but the major congenital malformation rate for topiramate polytherapy raises some concerns. Overall, the rate of oral clefts observed was 11 times the background rate. Although the present data provide new information, they should be interpreted with caution due to the sample size and wide confidence intervals.
FDA Mar/11 notified healthcare professionals and patients of an increased risk of development of cleft lip and/or cleft palate (oral clefts) in infants born to women treated with Topamax (topiramate) during pregnancy. Because of new human data that show an increased risk for oral clefts, topiramate is being placed in Pregnancy Category D.
145. Vestergaard M, Pedersen MG, Ostergaard JR, et al. Death in children with **febrile seizures**: a population-based cohort study. Lancet. 2008 Aug 9;372(9637):457-63. Long-term mortality is not increased in children with febrile seizures, but there seems to be a small excess mortality during the 2 years after complex febrile seizures. Parents should be reassured that death after febrile seizures is very rare, even in high-risk children.
146. French JA, Pedley TA. Clinical practice. **Initial management of epilepsy**. N Engl J Med. 2008 Jul 10;359(2):166-76.
147. Faught E, Duh MS, Weiner JR, Guérin A, Cunnington MC. **Nonadherence** to antiepileptic drugs and increased mortality. Findings from the RANSOM Study. Neurology. 2008 Jun 18. [Epub ahead of print] These findings suggest that nonadherence to antiepileptic drugs can have serious or fatal consequences for patients with epilepsy.
148. Bell GS, et al. Drowning in people with epilepsy: how great is the risk? Neurology. 2008 Aug 19;71(8):578-82. The risk of drowning in people with epilepsy is raised 15- to 19-fold compared with people in the general population. It is important that people with epilepsy and their carers be informed of these risks so that deaths can be prevented.
149. Michael B, Marson AG. **Clobazam** as an add-on in the management of refractory epilepsy. Cochrane Database Syst Rev. 2008 Apr 16;(2):CD004154.Clobazam as an add-on treatment may reduce seizure frequency and may be most effective in partial onset seizures. However, it is not clear who will best benefit and over what time-frame.
150. Boardman LA, Cooper AS, Blais LR, Raker CA. Topical gabapentin in the treatment of localized and generalized **vulvodynia**. Obstet Gynecol. 2008 Sep;112(3):579-85.
151. Hirsch LJ, Arif H, Nahm EA, Buchsbaum R, Resor SR Jr, Bazil CW. **Cross-sensitivity of skin rashes** with antiepileptic drug use. Neurology. 2008 Nov 4;71(19):1527-34. There was evidence of specific cross-sensitivity between CBZ and PHT, and between CBZ and PB. Cross-sensitivity rates between certain antiepileptic drugs (AEDs) are high, especially when involving carbamazepine and phenytoin. Specific cross-sensitivity rates provided here may be useful for AED selection and counseling in individual patients.
152. Cheuk DK, Wong V. Acupuncture for epilepsy. Cochrane Database Syst Rev. 2008 Oct 8;(4):CD005062. The current evidence does not support acupuncture as a treatment for epilepsy.
153. Bromley RL, Mawer G, Clayton-Smith J, Baker GA; Liverpool and Manchester Neurodevelopment Group. **Autism** spectrum disorders following in utero exposure to antiepileptic drugs. Neurology. 2008 Dec 2;71(23):1923-4.
154. Choi H, Sell RL, Lenert L, Muennig P, et al. Epilepsy **surgery** for pharmacoresistant temporal lobe epilepsy: a decision analysis. JAMA. 2008 Dec 3;300(21):2497-505.
155. Kimia AA, Capraro AJ, Hummel D,et al. Utility of **lumbar puncture** for first simple febrile seizure among children 6 to 18 months of age. Pediatrics. 2009 Jan;123(1):6-12. The risk of bacterial meningitis presenting as first simple febrile seizure at ages 6 to 18 months is very low. American Academy of Pediatrics recommendations should be reconsidered.
156. Levi N, Bastuji-Garin S, Mockenhaupt M, Roujeau JC, et al. Medications as risk factors of **stevens-johnson syndrome** and toxic epidermal necrolysis in children: a pooled analysis. Pediatrics. 2009 Feb;123(2):e297-304. Epub 2009 Jan 19. We confirmed 4 previously highly suspected drug risk factors for Stevens-Johnson syndrome/toxic epidermal necrolysis in children: antiinfective sulfonamides, phenobarbital, carbamazepine, and lamotrigine. Among more unexpected risk factors, we suspect that acetaminophen (paracetamol) use increases the risk of Stevens-Johnson syndrome or toxic epidermal necrolysis.
157. Medical Letter Mar 9/09. **Rufinamide**-Banzel for Epilepsy.
158. Schomer DL, Black PM. A 24-year-old woman with **intractable seizures**: review of surgery for epilepsy. JAMA. 2008 Dec 3;300(21):2527-38. Epub 2008 Nov 4. (Kwan P, Brodie MJ. Early identification of refractory epilepsy. N Engl J Med. 2000 Feb 3;342(5):314-9.)
159. Harden CL, et al. Therapeutics and Technology Assessment Subcommittee of the American Academy of Neurology. Reassessment: **neuroimaging** in the emergency patient presenting with seizure (an evidence-based review): report of the Therapeutics and Technology Assessment Subcommittee of the AAN. Neurology 2007 Oct 30;69(18):1772-80.
160. Christensen J, et al. Long-term risk of epilepsy **after traumatic brain injury** in children and young adults: a population-based cohort study. Lancet. 2009 Feb 20. [Epub ahead print]
161. Meador KJ, Baker GA, Browning N, et al. **Cognitive function** at 3 years of age after **fetal exposure** to antiepileptic drugs. N Engl J Med. 2009 Apr 16;360(16):1597-605.
162. Harden CL, Meador KJ, Pennell PB, et al. American Academy of Neurology (**AAN**); American Epilepsy Society. Management issues for women with epilepsy-**Focus on pregnancy** (an evidence-based review): II. **Teratogenesis and perinatal outcomes**: Report of the Quality Standards Subcommittee and Therapeutics and Technology Subcommittee of the

American Academy of Neurology and the American Epilepsy Society. Epilepsia. 2009 May;50(5):1237-46. (Valproate should be avoided during the first trimester of pregnancy. Among the other findings: Women with epilepsy who take antiepileptic drugs have twice the risk for delivering babies with Apgar scores under 7. Valproate is associated with increased risk for congenital malformations. Avoiding valproate, phenobarbital, and phenytoin during pregnancy may reduce the risk for poor cognitive outcomes (all are class D drugs), while carbamazepine (class C) "probably does not produce cognitive impairments." Monotherapy for epilepsy is preferable to polytherapy, if possible, to reduce poor cognitive outcomes. http://www.aan.com/globals/axon/assets/5476.pdf

163. Jacob K, Trainer PJ. **Topiramate** can induce **hypoadrenalism** in patients taking oral corticosteroid replacement. BMJ. 2009 Jan 8;338:a1788. doi: 10.1136/bmj.39588.561840.BD.
164. Christensen J, Pedersen MG, Pedersen CB, et al. Long-term risk of epilepsy **after traumatic brain injury** in children and young adults: a population-based cohort study. Lancet. 2009 Mar 28;373(9669):1105-10. Epub 2009 Feb 21.
165. Hamed SA, Abdella MM. The risk of asymptomatic **hyperammonemia** in children with idiopathic epilepsy treated with valproate: Relationship to blood **carnitine** status. Epilepsy Res. 2009 May 13. [Epub ahead of print]
166. Harden CL, Pennell PB, Koppel BS, et al. American Academy of Neurology (**AAN**); American Epilepsy Society. Management issues for women with epilepsy--focus on pregnancy (an evidence-based review): III. **Vitamin K, folic acid, blood levels, and breast-feeding**: Report of the Quality Standards Subcommittee and Therapeutics and Technology Assessment Subcommittee of the American Academy of Neurology and the American Epilepsy Society. Epilepsia. 2009 May;50(5):1247-55. PubMed PMID: 19507305.
Primidone and levetiracetam probably transfer into breast milk in clinically important amounts. Valproate, phenobarbital, phenytoin, and carbamazepine probably are not transferred into breast milk in clinically important amounts. Pregnancy probably causes an increase in the clearance and a decrease in the concentrations of lamotrigine, phenytoin, and, to a lesser extent carbamazepine, and possibly decreases the level of levetiracetam and the active oxcarbazepine metabolite, the monohydroxy derivative (MHD). Supplementing WWE with at least 0.4 mg of folic acid before pregnancy may be considered. Monitoring of lamotrigine, carbamazepine, and phenytoin levels during pregnancy should be considered, and monitoring of levetiracetam and oxcarbazepine (as MHD) levels may be considered.
167. Yoo L, Matalon D, Hoffman RS, et al. Treatment of **Pregabalin** Toxicity by Hemodialysis in a Patient With Kidney Failure. Am J Kidney Dis. 2009 Jun 2. [Epub ahead of print]
168. Mindikoglu AL, Magder LS, Regev A. Outcome of **liver transplantation** for drug-induced acute liver failure in the United States: analysis of the united network for organ sharing database. Liver Transpl. 2009 Jul;15(7):719-29. Being on life support, DIALF due to antiepileptics (at age less than 18), and elevated serum creatinine were independent pretransplant predictors of poor survival after LT for DIALF.
169. **Lacosamide** for epilepsy. Med Lett Drugs Ther. 2009 Jun 29;51(1315):50-2.
170. **Driving**: Determining Medical Fitness to Operate Motor Vehicles CMA Driver's Guide 7th Ed http://www.cma.ca/index.cfm/ci_id/18223/la_id/1.htm
Seizures: http://www.cma.ca/multimedia/CMA/Content_Images/Inside_cma/WhatWePublish/Drivers_Guide/Section10_e.pdf
171. McNally MA, Pyzik PL, et al. Empiric use of potassium citrate reduces **kidney-stone** incidence with the ketogenic diet. Pediatrics. 2009 Aug;124(2):e300-4. Epub 2009 Jul 13.
172. Scarmeas N, Honig LS, Choi H, et al. Seizures in **Alzheimer** disease: who, when, and how common? Arch Neurol. 2009 Aug;66(8):992-7.
173. Lossius MI, Taubøll E, Mowinckel P, Gjerstad L. Reversible effects of antiepileptic drugs on **thyroid hormones** in men & women with epilepsy: A prospective randomized double-blind withdrawal study. Epilepsy Behav. 2009 Jul 29. [Epub ahead of print]
174. Stöllberger C, Höftberger R, et al. **Lamotrigine**-trigged obstructive hypertrophic **cardiomyopathy**, epilepsy & metabolic myopathy. Int J Cardiol. 2009 Jul 4. [Epub ahead of print]
175. Motamedi M, Karvigh SA, Sahraian MA, Azimi AR, et al. **Lamotrigine** and **twin pregnancy**, incidental event or possible correlation? Seizure. 2009 Jul 6. [Epub ahead of print]
176. Moore RA, Straube S, Wiffen PJ, et al. **Pregabalin** for **acute and chronic pain** in adults. Cochrane Database Syst Rev. 2009 Jul 8;(3):CD007076. Pregabalin has proven efficacy in neuropathic pain conditions and fibromyalgia. A minority of patients will have substantial benefit with pregabalin, and more will have moderate benefit. Many will have no or trivial benefit, or will discontinue because of adverse events. Individualisation of treatment is needed to maximise pain relief and minimise adverse events. There is no evidence to support the use of pregabalin in acute pain scenarios.
177. Longo B, Forinash AB, Murphy JA. **Levetiracetam** Use in Pregnancy (October). Ann Pharmacother. 2009 Aug 18. [Epub ahead of print]
178. Daniels ZS, et al. **Obesity** is a common comorbidity for pediatric patients with untreated, newly diagnosed epilepsy.Neurology.2009 Sep1;73(9):658-64.Epub 2009May 27.
179. Veiby G, Daltveit AK, Engelsen BA, Gilhus NE. Pregnancy, delivery, and outcome for the child in maternal epilepsy. Epilepsia. 2009 Sep;50(9):2130-9. Epub 2009 Jun 1. Adverse pregnancy and birth outcome in women with epilepsy is mainly confined to AED-exposed pregnancies, although some risks are associated also with untreated epilepsy. The risk for congenital malformations was lower than previously reported. This could be due to a shift in AED selection, folic acid supplement, or possibly reflect the true risks in an unselected epilepsy population.
180. Fortinguerra, Filomena, Clavenna, Antonio, Bonati, Maurizio. Psychotropic Drug Use During **Breastfeedi**ng: A Review of the Evidence. Pediatrics 2009 124: e547-e556.
181. Striano P, Zara F, Minetti C, et al. **Chitosan** may decrease serum valproate and increase the risk of seizure reappearance. BMJ. 2009 Sep 24;339:b3751. doi: 10.1136/bmj.b3751.
182. Vajda FJ, et al. The **teratogenic** risk of antiepileptic drug polytherapy. Epilepsia. 2009 Oct 8. Coadministration with lamotrigine may lower the fetal risk of valproate therapy.
183. Brandt C, et al. Retention rate of **pregabalin** in drug-resistant epilepsy: 1-year follow-up, single-centre observation in 105 consecutive, adult patients. Seizure.2009 Nov;18(9):634-8.
184. Kelly VM, Nelson LM, Chakravarty EF. **Obstetric outcomes** (pregnancy) in women with multiple sclerosis and epilepsy. Neurology. 2009 Nov 18. [Epub ahead of print]
185. FDA Dec/09 notified health care professionals and patients about the increased risk of neural tube defects and other major birth defects, such as craniofacial defects and cardiovascular **malformations**, in babies exposed to **valproate** sodium and related products (valproic acid and divalproex sodium) during pregnancy.
186. Gibbons RD.; Hur Kwan; et al. Relationship Between Antiepileptic Drugs and **Suicide** Attempts in Patients With Bipolar Disorder. Arch Gen Psychiatry. 2009;66(12):1354-1360.
187. Robson WL. Clinical practice. Evaluation and management of **enuresis**. N Engl J Med. 2009 Apr 2;360(14):1429-36.
188. Kumlien E, Lundberg PO. **Seizure risk** associated with neuroactive drugs: Data from the WHO adverse drug reactions database. Seizure. 2009 Dec 23.
The 10 drugs most frequently associated with convulsive ADRs were maprotilene (14.42%), escitaloprame (9.78%), buproprione (9.49%), clozapine (9.0%), chlorprothiexene (8.89%), amoxapine (8.74%), donepezil (8.40%), rivastigmine (6.41%), quetiapine (5.90%) and trimipramine (5.69%).
189. Vikelis M, Rapoport AM. Role of **antiepileptic drugs** as preventive agents for migraine. CNS Drugs. 2010 Jan 1;24(1):21-33. doi: 10.2165/11310970-000000000-00000.
190. Kwan J, Wood E. Antiepileptic drugs for the primary and secondary prevention of seizures **after stroke**. Cochrane Database Syst Rev. 2010 Jan 20;(1):CD005398.
191. Powell G, Saunders M, Marson AG. Immediate-release vs controlled-release **carbamazepine** in the treatment of epilepsy. Cochrane Database Syst Rev. 2010 Jan 20;(1):CD007124.

192. Wiffen PJ, Collins S, McQuay HJ, Carroll D, Jadad A, Moore RA. Anticonvulsant drugs for **acute and chronic pain**. Cochrane Database Syst Rev. 2010 Jan 20;(1):CD001133.
193. Koch MW, Polman SK. **Oxcarbazepine versus carbamazepine** monotherapy for partial onset seizures. Cochrane Database Syst Rev. 2009 Oct 7;(4):CD006453.
194. RA, Gallagher JC. **Drug Fever**. Pharmacotherapy. 2010 Jan;30(1):57-69.
195. van Rooij LG, Toet MC, van Huffelen AC, et al. Effect of treatment of subclinical **neonatal seizures** detected with aEEG: randomized, controlled trial. Pediatrics. 2010 Feb;125(2):e358-66. Epub 2010 Jan 25.
196. Patel A, Pyzik PL, Turner Z, Rubenstein JE, Kossoff EH. Long-term outcomes of children treated with the **ketogenic diet** in the past. Epilepsia. 2010 Feb 1.
197. Bialer M, et al. Pharmacokinetic interactions of topiramate. Clin Pharmacokinet. 2004;43(12):763-80.
198. Mazurkiewicz-Bełdzińska M, Szmuda M, Matheisel A. Long-term efficacy of **valproate** versus lamotrigine in treatment of idiopathic generalized epilepsies in children and adolescents. Seizure. 2010 Feb 16.
199. Michoulas A, Farrell K. Medical Management of **Lennox-Gastaut Syndrome**. CNS Drugs. 2010 Feb 16.
200. Cumbo E, Ligori LD. **Levetiracetam**, lamotrigine, and phenobarbital in patients with epileptic seizures and Alzheimer's disease. Epilepsy Behav. 2010 Feb 24.
201. Salinsky M, Storzbach D, Munoz S. Cognitive effects of **pregabalin** in healthy volunteers: A double-blind, placebo-controlled trial. Neurology. 2010 Mar 2;74(9):755-61.
202. Simpson DM, Schifitto G, Clifford DB, et al. 1066 HIV Neuropathy Study Group.**Pregabalin** for painful HIV neuropathy: a randomized, double-blind, placebo-controlled trial. Neurology. 2010 Feb 2;74(5):413-20. In this study, patients with HIV-associated peripheral neuropathy taking pregabalin (Lyrica) had no more pain relief than patients taking placebo. (LOE = 2b)
203. Patorno E; Bohn RL.; Wahl PM.; Avorn Jerry; et al. Anticonvulsant Medications and the Risk of **Suicide**, **Attempted Suicide**, or Violent Death. JAMA. 2010;303(14):1401-1409.
204. Vedula SS, Bero L, Scherer RW, Dickersin K. Outcome reporting in **industry-sponsored trials of gabapentin** for off-label use. N Engl J Med. 2009 Nov 12;361(20):1963-71.
205. Harden CL, Hopp J, Ting TY, et al. Practice parameter update: management issues for women with epilepsy--focus on pregnancy (an evidence-based review): obstetrical **complications and change in seizure frequency**. Report of the Quality Standards Subcommittee [trunc]. Neurology 2009 Jul 14;73(2):126-32.
206. Ziegler D, Hidvégi T, Gurieva I, et al.; **Lacosamide** SP743 Study Group. Efficacy and safety of lacosamide in painful diabetic neuropathy. Diabetes Care. 2010 Apr;33(4):839-41.
207. Labiner DM et al. **Generic antiepileptic drugs** and associated medical resource utilization in the United States. *Neurology* 2010 Apr 14.
208. Jentink, Janneke, Loane, Maria A., Dolk, Helen, et al. the EUROCAT Antiepileptic Study Working Group, **Valproic** Acid Monotherapy in Pregnancy and Major **Congenital** Malformations. N Engl J Med 2010 362: 2185-2193. Six of the 14 were significantly associated with valproic acid use, compared with no exposure to antiepileptic drugs: spina bifida (odds ratio, 12.7), atrial septal defect (2.5), cleft palate (5.2), hypospadias (4.8), polydactyly (2.2), and craniosynostosis (6.8).
209. Straube S, Derry S, Moore RA, et al. Single dose oral **gabapentin** for established **acute postoperative pain** in adults. Cochrane Database Syst Rev. 2010 May 12;5:CD008183.
210. Minozzi S, Amato L, Vecchi S, Davoli M. Anticonvulsants for **alcohol withdrawal**. Cochrane Database Syst Rev. 2010 Mar 17;3:CD005064.
211. Arana A et al. **Suicide-related events** in patients treated with antiepileptic drugs. N Engl J Med 2010 Aug 5; 363:542.
212. Dressler A, Stöcklin B, Reithofer E, et al. Long-term outcome & tolerability of the **ketogenic diet** in drug-resistant childhood epilepsy-The Austrian experience. Seizure.2010Jun 30.
213. McMullan J, Sasson C, Pancioli A, et al. Midazolam versus diazepam for the treatment of status epilepticus in children and young adults: a meta-analysis. Acad Emerg Med. 2010 Jun;17(6):575-82. Non-IV midazolam, compared to non-IV or IV diazepam, is safe and effective in treating SE. Comparison to lorazepam, evaluation in adults, and prospective confirmation of safety and efficacy is needed.
214. Ramsay E, Faught E, Krumholz A, et al.; for the CAPSS-272 Study Group. Efficacy, tolerability, and safety of rapid initiation of **topiramate versus phenytoin** in patients with new-onset epilepsy: A randomized double-blind clinical trial. Epilepsia. 2010 Jul 14.
215. Kimia A et al. **Yield of lumbar puncture** among children who present with their first complex febrile seizure. Pediatrics 2010 Jul; 126:62.
216. Goldstein LH, Chalder T, Chigwedere C, et al. **Cognitive-behavioral therapy** for psychogenic nonepileptic seizures: a pilot RCT. Neurology. 2010 Jun 15;74(24):1986-94.
217. Andersohn F, Schade R, Willich SN, Garbe E. Use of antiepileptic drugs in epilepsy and the **risk of self-harm or suicidal behavior**. Neurology. 2010 Jul 27;75(4):335-40.
218. Labiner DM et al. **Generic antiepileptic drugs** and associated medical resource utilization in the United States. Neurology 2010 Apr 14. In this retrospective study of adults with seizure disorders in managed care settings, the use of generic anticonvulsants was associated with slightly more hospitalizations and usage of outpatient services. But keep in mind that retrospective studies have many limitations and randomized trials often negate their findings. (LOE = 2b)
219. Tengstrand M, Star K, van Puijenbroek EP, Hill R. **Alopecia** in association with **lamotrigine** use: an analysis of individual case safety reports in a global database. Drug Saf. 2010 Aug 1;33(8):653-8. doi: 10.2165/11536190-000000000-00000.
220. Holsti M et al. **Intranasal midazolam** vs **rectal diazepam** for the home treatment of acute seizures in pediatric patients with epilepsy. *Arch Pediatr Adolesc Med* 2010 Aug; 164:747.
221. Pontari Michel A.; Krieger John N.; Litwin Mark S.; et al.; for the Chronic Prostatitis Collaborative Research Network-2. **Pregabalin** for the Treatment of Men With Chronic Prostatitis/Chronic Pelvic Pain Syndrome: A Randomized Controlled Trial. Arch Intern Med. 2010;170(17):1586-1593. Pregabalin therapy for 6 weeks was not superior to placebo use in the rate of a 6-point decrease (improvement) in the NIH-CPSI total score in men with CP/CPPS.
222. Visser, Annemarie M., Jaddoe, Vincent W. V., Hofman, Albert, et al. **Fetal Growth** Retardation and Risk of **Febrile Seizures**. Pediatrics 2010 0: peds.2010-0518.
223. Sukumaran SC et al. **Polytherapy increases the risk of infertility** in women with epilepsy. *Neurology* 2010 Oct 12; 75:1351.
224. Madadi P, Ito S. **Perinatal exposure to maternal lamotrigine**: Clinical considerations for the mother and child. Can Fam Physician. 2010 Nov;56(11):1132-4.
225. Meador KJ, Baker GA, Browning N, et al.; For the NEAD Study Group. Effects of **breastfeeding in children** of women taking antiepileptic drugs. Neurology. 2010 Nov 24.
226. Lee SA, Lee HW, Heo K, et al. **Cognitive and behavioral effects of lamotrigine and carbamazepine** monotherapy in patients with newly diagnosed or untreated partial epilepsy.

Seizure. 2010 Nov 9.
227. Jentink Janneke, Dolk Helen, Loane Maria A, et al., for the EUROCAT Antiepileptic Study Working Group. Intrauterine exposure to **carbamazepine** and specific congenital **malformations**: systematic review and case-control study. BMJ 341:doi:10.1136/bmj.c6581 (Published 2 Dec 2010). (eg. **spina bifida**, though the risk is less than with valproic acid) Nulman I. **Carbamazepine in pregnancy**. BMJ. 2010 Dec 2;341:c6582. doi: 10.1136/bmj.c6582.
228. Kazmin, Aleksey, Wong, RC., Sermer, M, et al. **Antiepileptic drugs in pregnancy** and hemorrhagic disease of the newborn: An update. Can Fam Physician 2010 56: 1291-1292
229. Bonnett L J, Tudur-Smith C, Williamson P R, et al.. **Risk of recurrence after a first seizure and implications for driving**: further analysis of the Multicentre study of early Epilepsy and Single Seizures. BMJ 341:doi:10.1136/bmj.c6477 (Published 7 Dec 2010).
230. Sillanpää Matti, Shinnar Shlomo, **Long-Term Mortality** in Childhood-Onset Epilepsy. N Engl J Med 2010; 363:2522-2529.
231. Jette Nathalie; Lix Lisa M; Metge CJ; et al. Association of Antiepileptic Drugs With **Nontraumatic Fractures**: Population-Based Analysis. Arch Neurol. 2011;68(1):107-112.
232. Warlow C. **Driving** after a first seizure. BMJ. 2010 Dec 7;341:c6890. doi: 10.1136/bmj.c6890.
233. Subcommittee on Febrile Seizures, **Neurodiagnostic Evaluation of the Child With a Simple Febrile Seizure.** Pediatrics 2011 127: 389-394.
234. Gaily E, Kantola-Sorsa E, Hiilesmaa V, et al. **Normal intelligence** in children with prenatal exposure to **carbamazepine**. Neurology. 2004 Jan 13;62(1):28-32.
235. Linnebank M, Moskau S, Semmler A, et al Antiepileptic drugs interact with **folate and vitamin B12** serum levels. Ann Neurol. 2011 Jan 19. doi: 10.1002/ana.22229.
236. FDA Mar/11 notified healthcare professionals and patients of an increased risk of development of **cleft lip and/or cleft palate (oral clefts)** in infants born to women treated with Topamax (**topiramate**) during pregnancy. Because of new human data that show an increased risk for oral clefts, topiramate is being placed in Pregnancy Category D.
237. Rizzo Matthew. **Impaired Driving From Medical Conditions**: A 70-Year-Old Man Trying to Decide if He Should Continue Driving. JAMA. 2011;305(10):1018-1026.
238. Pesaturo KA, Spooner LM, Belliveau P. **Vigabatrin for infantile spasms**. Pharmacotherapy. 2011 Mar;31(3):298-311.
239. Kwon C, Liu M, Quan H, et al. **Motor vehicle accidents, suicides, and assaults** in epilepsy: A population-based study. Neurology. 2011 Mar 1;76(9):801-6.
240. Sethi NK, Labiner DM, Helmers SL. **Generic antiepileptic** drugs and associated medical resource utilization in the United States. Neurology. 2011 Feb 8;76(6):583-4.
241. McClelland S 3rd, Guo H, Okuyemi KS. Population-Based Analysis of Morbidity and **Mortality Following Surgery** for Intractable Temporal Lobe Epilepsy in the United States. Arch Neurol. 2011 Feb 14.
242. Drazkowski JF, Sirven JI. **Motor vehicle crashes, suicides, and assaults**: The dangers of epilepsy? Neurology. 2011 Mar 1;76(9):770-1.
243. Patel A, Wordell C, Szarlej D. **Alternatives to sodium amobarbital in the wada test**. Ann Pharmacother. 2011 Mar;45(3):395-401.
244. McCormack Mark, Alfirevic Ana, Bourgeois S, et al. **HLA-A*3101** and Carbamazepine-Induced Hypersensitivity Reactions in Europeans. N Engl J Med 2011; 364:1134-1143.
245. Chen Pei, Lin Juei-Jueng, et al. Taiwan SJS Consortium. Carbamazepine-Induced Toxic Effects and **HLA-B*1502** Screening in Taiwan. N Engl J Med 2011; 364:1126-1133.
246. Kossoff EH, Zupec-Kania BA, Amark PE, et al. Charlie Foundation, Practice Committee of the Child Neurology Society; Practice Committee of the Child Neurology Society; International **Ketogenic Diet** Study Group. Optimal clinical management of children receiving the ketogenic diet: recommendations of the International Ketogenic Diet Study Group. Epilepsia. 2009 Feb;50(2):304-17.
247. Abend NS, Gutierrez-Colina AM, Topjian AA, et al. **Nonconvulsive seizures** are common in **critically ill children**. Neurology. 2011 Mar 22;76(12):1071-7.
248. Mindikoglu AL, King D, Magder LS, et al. **Valproic Acid-associated acute liver failure in children**: case report and analysis of liver transplantation outcomes in the United States. J Pediatr. 2011 May;158(5):802-7.
249. Modi AC., Rausch JR., Glauser TA. Patterns of **Nonadherence** to Antiepileptic Drug Therapy in Children With Newly Diagnosed Epilepsy. JAMA. 2011;305(16):1669-1676.
250. Parmet Sharon, Lynm Cassio, Golub Robert M. JAMA **Patient Page Epilepsy**. JAMA. 2011;305(16):1722.doi:10.1001/jama.305.16.1722.
251. Brodie MJ, Perucca E, Ryvlin P, Ben-Menachem E, Meencke HJ, Levetiracetam Monotherapy Study Group. Comparison of **levetiracetam and controlled-release carbamazepine** in newly diagnosed epilepsy. Neurology. 2007 Feb 6;68(6):402-8.
252. Arya R, Gulati S, Kabra M, Sahu JK, Kalra V. **Folic acid** supplementation prevents phenytoin-induced gingival overgrowth in children. Neurology. 2011 Apr 12;76(15):1338-43.
253. Linnebank M, Moskau S, Semmler A, et al. **Antiepileptic drugs interact with folate** and vitamin B12 serum levels. Ann Neurol. 2011 Feb;69(2):352-9. doi: 10.1002/ana.22229.
254. Perucca Emilio, Tomson Torbjorn, The pharmacological **treatment of epilepsy** in adults, The Lancet Neurology, Volume 10, Issue 5, May 2011, Pages 446-456, ISSN 1474-4422.
255. Wightman Rachel S, Zell-Kanter Michele, Van Roo Jon, et al. **Zonisamide Toxicity** in a Patient with an Intentional Overdose. Articles Ahead of Print published on 1 April 2011.
256. Sun Y, Vestergaard M, Christensen J, Olsen J. **Breastfeeding** and risk of epilepsy in childhood: a birth cohort study. J Pediatr. 2011 Jun;158(6):924-9.
257. Josephson CB, Leach JP, Duncan R, et al. On behalf of the Scottish Audit of Intracranial Vascular Malformations (SAIVMs) steering committee and collaborators. Seizure risk from **cavernous or arteriovenous malformations**: Prospective population-based study. Neurology. 2011 May 3;76(18):1548-1554.
258. Mølgaard-Nielsen D, Hviid A. **Newer-generation antiepileptic drugs and the risk of major birth defects**. JAMA. 2011 May 18;305(19):1996-2002.
259. Cunnington MC, Weil JG, Messenheimer JA, et al. Final results from 18 years of the International **Lamotrigine Pregnancy Registry**. Neurology. 2011 May 24;76(21):1817-23.
260. French JA, Abou-Khalil BW, Leroy RF, et al.; On behalf of the RESTORE 1/Study 301 Investigators. Randomized, double-blind, placebo-controlled trial of **ezogabine (retigabine)** in partial epilepsy. Neurology. 2011 May 3;76(18):1555-1563.
261. Sendra JM, Junyent TT, Pellicer MJR. **Pregabalin-Induced Hepatotoxicity**. Ahead of Print 1 June 2011, DOI 10.1345/aph.1Q032. Ann Pharmacother ;45:e32.

262. See S, Hendriks E, Hsiung L. **Akathisia Induced by Gabapentin Withdrawal**. Ahead of Print on 1 June 2011, DOI 10.1345/aph.1Q057. Ann Pharmacother ;45:e31.
263. McClelland S 3rd, Guo H, Okuyemi KS. Population-based analysis of morbidity and mortality following **surgery for intractable temporal lobe epilepsy** in the United States. Arch Neurol. 2011 Jun;68(6):725-9.
264. Holmes LB, Mittendorf R, Shen A, Smith CR, Hernandez-Diaz S. Fetal Effects of Anticonvulsant **Polytherapies: Different Risks From Different Drug Combinations**. Arch Neurol. 2011 Jun 13. (Monotherapy risk: with lamotrigine 1.9% & carbamazepine 2.9%, but increased if combined with valproate).
265. Tomson T, Battino D, Bonizzoni E, et al. Dose-dependent risk of **malformations** with antiepileptic drugs: an analysis of data from the **EURAP** epilepsy and pregnancy registry. *Lancet Neurol* 2011; published online June 6. DOI:10.1016/S1474-4422(11)70107-7. (Data: on lamotrigine, carbamazepine, valproate & phenobarbital).
266. Engel J Jr, Wiebe S, French J, et al; Quality Standards Subcommittee of the American Academy of Neurology (AAN); American Epilepsy Society; American Association of Neurological Surgeons. Practice parameter: **temporal lobe and localized neocortical resections** for epilepsy: report of the Quality Standards Subcommittee of the American Academy of Neurology, in association with the American Epilepsy Society and the American Association of Neurological Surgeons. Neurology. 2003;60(4):538-547.
Mohammed HS, Kaufman CB, Limbrick DD, et al. Impact of epilepsy surgery on seizure control and quality of life: A **26-year follow-up study**. Epilepsia. 2012 Feb 7.
Engel J Jr, McDermott MP, Wiebe S, et al. Early **surgical therapy** for drugresistant **temporal lobe epilepsy**: a randomized trial. (ERSET) JAMA. 2012;307(9):922-930.
Hildreth CJ, Lynm C, Golub RM. JAMA **patient page. Epilepsy surgery**. JAMA. 2012 Mar 7;307(9):985.
Moosa ANV, Gupta A, Jehi L, et al. Longitudinal seizure outcome and prognostic predictors after **hemispherectomy** in 170 children. Neurology 2013;80:253–260.
Josephson CB, Dykeman J, et al. Systematic review and meta-analysis of **standard vs selective temporal lobe epilepsy surgery**. Neurology. 2013 Apr 30;80(18):1669-1676.
Edelvik A, Rydenhag B, Olsson I, et al. Long-term outcomes of epilepsy surgery in Sweden: A national prospective and longitudinal study. Neurology. 2013 Aug 21.
Morris GL 3rd, Gloss D, Buchhalter J, et al. Evidence-based guideline update: **Vagus nerve stimulation** for the treatment of epilepsy: Report of the Guideline Development Subcommittee of the American Academy of Neurology. Neurology. 2013 Aug 28.
Jette N, Reid AY, Wiebe S. **Surgical management of epilepsy**. CMAJ. 2014 Sep 16;186(13):997-1004.
Ryvlin P, Cross JH, Rheims S. **Epilepsy surgery in children and adults**. Lancet Neurol. 2014 Nov;13(11):1114-1126.
Hamid H, Blackmon K, Cong X, et al. Mood, anxiety, and incomplete seizure control affect quality of life after **epilepsy surgery**. Neurology. 2014 Mar 11;82(10):887-94.
Salanova V, Witt T, Worth R, et al; For the SANTE Study Group. Long-term efficacy and safety of **thalamic stimulation** for drug-resistant partial epilepsy. Neurology. 2015 Feb 6.
Edelvik A, Flink R, Malmgren K. Prospective and longitudinal **long-term employment outcomes** after resective epilepsy **surgery**. Neurology. 2015 Oct 27;85(17):1482-90.
Barba C, Rheims S, Minotti L, et al. **Temporal plus epilepsy** is a major determinant of temporal lobe surgery failures. Brain. 2015 Dec 22.
Duncan JS, Winston GP, Koepp MJ, et al. **Brain imaging** in the assessment for epilepsy **surgery**. Lancet Neurol. 2016 Feb 23.
Jones AL, Cascino GD. Evidence on Use of **Neuroimaging** for **Surgical** Treatment of **Temporal Lobe Epilepsy**: A Systematic Review. JAMA Neurol. 2016 Feb 29.
Sperling MR, Barshow S, Nei M, Asadi-Pooya AA. A reappraisal of **mortality after epilepsy surgery**. Neurology 2016;86:1938–1944.
Kim DW, Lee SK, Moon HJ, et al. **Surgical Treatment** of Nonlesional Neocortical Epilepsy: Long-term Longitudinal Study. JAMA Neurol. 2017 Jan 3.
Szaflarski JP, Gloss D, Binder JR, et al. Practice guideline summary: Use of **fMRI in the presurgical evaluation** of patients with epilepsy: Report of the Guideline Development, Dissemination, and Implementation Subcommittee of the American Academy of Neurology. Neurology. 2017 Jan 24;88(4):395-402.
Vakharia VN, Duncan JS, Witt JA, et al. **Getting the best outcomes from epilepsy surgery**. Ann Neurol. 2018 Mar 13.
Baud MO, Perneger T, R´ acz A, et al. European trends in epilepsy surgery. Neurology 2018;91:e96–e106.
Rathore C, Jeyaraj MK, Dash GK, et al. Outcome after **seizure recurrence on antiepileptic drug withdrawal** following temporal lobectomy. Neurology. 2018 Jul 17;91(3):e208-e216.
Kang JW, Eom S, Hong W, et al. Long-term Outcome of Resective **Epilepsy Surgery in Patients With Lennox-Gastaut Syndrome**. Pediatrics. 2018 Sep 7.
Galovic M, Baudracco I, Wright-Goff E, et al. Association of **Piriform Cortex Resection** With Surgical Outcomes in Patients With Temporal Lobe Epilepsy. JAMA Neurol. 2019 Mar 11.
Bjellvi J, Olsson I, Malmgren K, Wilbe Ramsay K. Epilepsy duration and seizure **outcome in epilepsy surgery**: A systematic review and meta-analysis. Neurology. 2019 Jul 9;93(2):e159-e166.

267. Kwan P, Arzimanoglou A, Berg AT, et al. Definition of **drug resistant epilepsy**: consensus proposal by the ad hoc Task Force of the ILAE Commission on Therapeutic Strategies. Epilepsia. 2010;51(6):1069-1077.
268. Robottom BJ, Factor SA, Weiner WJ. Movement disorders emergencies part 2: hyperkinetic disorders (chorea, tics, ballism, myoclonus, dystonia). Arch Neurol. 2011 Jun;68(6):719-24.
269. Krumholz SD, Egilman DS, Ross JS. Study of Neurontin: Titrate to Effect, Profile of Safety (STEPS) trial: a narrative account of a **gabapentin seeding trial**.Arch Intern Med. 2011;171(12):1100-1107.
270. FDA & CDN June-July/11 notified healthcare professionals: children born to mothers who take the anti-seizure medication **valproate** sodium or related products (valproic acid and divalproex sodium) during pregnancy have an increased risk of **lower cognitive test scores** than children exposed to other anti-seizure medications during pregnancy.
271. Shorvon Simon, Tomson Torbjorn. **Sudden unexpected death** (SUDEP) in epilepsy. www.thelancet.com Online July 6, 2011. (↑: GTC, Males, long-duration hx & on polytherapy)

272. Mu J, Liu L, Zhang Q, et al. Causes of **death among people with convulsive epilepsy** in rural West China: A prospective study. Neurology. 2011 Jul 12;77(2):132-7.
273. Cummings C, et al. **Neurodevelopment** of children exposed in utero to lamotrigine, sodium valproate and carbamazepine. Arch Dis Child. 2011 Jul;96(7):643-7.
274. Hesdorffer DC, Logroscino G, Benn EKT, et al. **Estimating risk for developing epilepsy**: a population-based study in Rochester, Minnesota. Neurology 2011;76:23–2.
275. Kwan P, Schachter SC, Brodie MJ. **Drug-resistant epilepsy**. N Engl J Med. 2011 Sep 8;365(10):919-26.
276. Kwan P, Brodie MJ, Kälviäinen R, Yurkewicz L, Weaver J, Knapp LE. Efficacy and safety of **pregabalin versus lamotrigine** in patients with newly diagnosed partial seizures: a phase 3, double-blind, randomised, parallelgroup trial. Lancet Neurol 2011; published online Sept 1. (n=660 with a 52 week efficacy assessment phase.)
277. Wiebe S, Blume WT, Girvin JP, Eliasziw M. A randomized, controlled trial of **surgery for temporal-lobe epilepsy**. N Engl J Med 2001;345:311-8.
278. Téllez-Zenteno JF, Dhar R, Wiebe S. **Long-term seizure outcomes following epilepsy surgery**: a systematic review and meta-analysis. Brain 2005;128:1188-98.
279. Samuels N, Finkelstein Y, Singer SR, Oberbaum M. **Herbal medicine and epilepsy**: proconvulsive effects and interactions with antiepileptic drugs. Epilepsia 2008;49:373-80.
280. Weller M, Gorlia T, Cairncross JG, et al. Prolonged survival with **valproic acid** use in the EORTC/NCIC temozolomide trial for **glioblastoma**. Neurology 2011;77:1156 –1164.
281. Morrell MJ, **RNS System** in Epilepsy Study Group. **Responsive cortical stimulation** for the treatment of medically intractable partial epilepsy. Neurology 2011;77:1295–1304.
282. Fisher R, Salanova V, Witt T, et al. **Electrical stimulation** of the anterior nucleus of thalamus for treatment of refractory epilepsy. Epilepsia 2010;51:899 –908.
283. George R, Salinsky M, Kuzniecky R, et al. **Vagus nerve stimulation** for treatment of partial seizures: 3: long-term follow-up on first 67 patients exiting a controlled study:First International Vagus Nerve Stimulation Study Group. Epilepsia 1994;35:637– 643.
284. Fleisher AS, Truran D, Mai JT, et al. For the Alzheimer's Disease Cooperative Study. Chronic **divalproex** sodium use and brain atrophy in **Alzheimer** disease. Neurology. 2011 Sep 27;77(13):1263-1271.
285. Spriet I, Willems L. No interaction between valproate and **meropenem** in a cirrhotic patient. Ann Pharmacother. 2011 Sep;45(9):1167-8.
286. Ngugi AK, Kariuki SM, Bottomley C, et al..**Incidence of epilepsy**: A systematic review and meta-analysis. Neurology. 2011 Sep 6;77(10):1005-12.
287. Singh RK, Zecavati N, Singh J, et al. Seizures in Acute **Childhood** Stroke. J Pediatr. 2011 Sep 10.
288. de Tisi J, Bell GS, et al. The **long-term** (up to 19yrs) outcome of adult **epilepsy surgery**, patterns of seizure remission, and relapse: a cohort study. Lancet 2011; 378: 1388–95.
289. Bonnett LJ, Tudur-Smith C, Williamson PR, et al. **Risk of recurrence** after a first seizure and implications for driving: further analysis of the Multicentre study of early Epilepsy and Single Seizures . BMJ 2010; 341: c6477.
290. Fitzgerald CL, Jacobson MP. **Generic substitution of levetiracetam** resulting in increased incidence of breakthrough seizures (May). Ann Pharmacother. 2011 Apr 26.
291. Ho JM, Juurlink DN. Considerations when prescribing **trimethoprim-sulfamethoxazole**. CMAJ. 2011 Oct 11. (phenytoin DIs)
292. Holmes LB, Mittendorf R, Shen A, et al. **Fetal effects of anticonvulsant polytherapies** (especially with valproate): different risks from different drug combinations. Arch Neurol. 2011 Oct;68(10):1275-81.
293. Naeije G, Lorent S, Vincent JL, Legros B. Continuous **epileptiform discharges** in patients treated with **cefepime** or meropenem. Arch Neurol. 2011 Oct;68(10):1303-7.
294. Bausell R, Svoronos A, Lennihan L, Hirsch LJ. **Recovery after severe refractory status epilepticus and 4 months** of coma. Neurology. 2011 Oct 11;77(15):1494-5.
295. Ng YT, Conry JA, Drummond R, Stolle J, Weinberg MA; On behalf of the OV-1012 Study Investigators. Randomized, phase III study results of **clobazam in Lennox-Gastaut syndrome**. Neurology. 2011 Oct 11;77(15):1473-1481.
296. See S, Hendriks E, Hsiung L. **Akathisia induced by gabapentin** withdrawal. Ann Pharmacother. 2011 Jun;45(6):e31.
297. Cummings C, Stewart M, Stevenson M, et al. **Neurodevelopment** of children exposed in utero to **lamotrigine, sodium valproate and carbamazepine**. Arch Dis Child. 2011 Jul;96(7):643-7.
298. Tzatha E, Karceski SC. **Responsive neurostimulation** for the treatment of seizures that do not respond to medication. Neurology. 2011 Sep 27;77(13):e79-81.
299. Chaluvadi S, Chiang S, Tran L, Goldsmith CE, Friedman DE. Clinical experience with **generic levetiracetam** in people with epilepsy. Epilepsia. 2011 Apr;52(4):810-5.
300. Crump C, Sundquist K, Winkleby MA, Sundquist J. **Preterm birth** and risk of epilepsy in Swedish adults. Neurology. 2011 Oct 4;77(14):1376-82.
301. Nadebaum C, Anderson VA, Vajda F, et al. **Language skills** of school-aged children prenatally exposed to antiepileptic drugs (**valproate**). Neurology 2011;76:719–26.
302. Beghi E, D'Alessandro R, Beretta S, et al. Incidence and predictors of **acute symptomatic seizures after stroke**. Neurology 2011;77:1785–1793.
303. De Herdt V, Dumont F, Hénon H, et al. **Early seizures in intracerebral hemorrhage**: incidence, associated factors, and outcome. Neurology 2011;77:1794 –1800.
304. Devinsky O. **Sudden, unexpected death in epilepsy**. (SUDEP) N Engl J Med. 2011 Nov 10;365(19):1801-11.
305. Neligan A, Bell GS, Sander JW. **Sudden death in epilepsy**. (SUDEP) BMJ. 2011 Nov 15;343:d7303.
306. Hesdorffer DC, et al. ILAE Commission on Epidemiology; Subcommission on Mortality. Combined analysis of risk factors for **SUDEP**. Epilepsia. 2011 Jun;52(6):1150-9.
307. British National Formulary. What's new in BNF 62? Available: https://www.cppe.ac.uk/programmes/l/bnf62-h-01. [Accessed October 30 2011].
308. Yamada M, Welty TE. **Generic substitution** of antiepileptic drugs: a systematic review of prospective and retrospective studies. Ann Pharmacother. 2011 Nov;45(11):1406-15.
309. Fernandez EM, Franck AJ. **Lacosamide** for the treatment of **refractory status epilepticus**. Ann Pharmacother. 2011 Nov;45(11):1445-9.
310. Finkelstein Y, Soon GS, Acuna P, et al. Recurrence and outcomes of **stevens-johnson syndrome** and toxic epidermal necrolysis in children. Pediatrics. 2011 Oct;128(4):723-8.
311. Ryvlin P, Cucherat M, Rheims S. Risk of **sudden unexpected death** in epilepsy in patients given adjunctive antiepileptic treatment for refractory seizures: a meta-analysis of

placebo-controlled randomised trials. Lancet Neurol 2011; 10: 961–68.
312. Claassen C. Epilepsy therapeutics update: highlights from a pediatric pharmacist perspective. Pharmacy Practice CE Lesson, November 2011.
313. Irving G et al. Efficacy and tolerability of gastric-retentive gabapentin for the treatment of postherpetic neuralgia: results of a double-blind, randomized, placebo-controlled clinical trial. Clin J Pain 2009; 25:185. (gabapentin daily not better than placebo)
314. Wallace MS et al. Gabapentin extended-release tablets for the treatment of patients with postherpetic neuralgia: a randomized, double-blind, placebo-controlled, multicentre study. Clin Drug Investig 2010; 30:765. (gabapentin not better than placebo)
315. Syed TU et al. Can **semiology predict psychogenic nonepileptic seizures**? A prospective study. Ann Neurol 2011 Mar 17
316. Birbeck GL, French JA, Perucca E, et al. Evidence-based guideline: **Antiepileptic drug selection for people with HIV/AIDS**: Report of the Quality Standards Subcommittee of the American Academy of Neurology (**AAN**) and the Ad Hoc Task Force of the Commission on Therapeutic Strategies of the International League Against Epilepsy.Neurology. 2012 Jan 10;78(2):139-45.
317. Hamid H et al. Long-term association between **seizure outcome and depression** after resective epilepsy surgery. Neurology. 2011 Nov 9; 77(22):1972-6.
318. Salinsky M, Spencer D, Boudreau E, et al. **Psychogenic nonepileptic seizures in US veterans**. Neurology 2011;77:945–950.
319. Poolos NP, Warner LN, Humphreys SZ et al. Comparative efficacy of **combination drug therapy in refractory epilepsy**. Neurology. 2012 Jan 3;78(1):62-8. (combination valproate & lamotrigine showed superior efficacy)
320. Asadi-Pooya AA, Nikseresht A, Yaghoubi E et al. **Physical injuries** in patients with epilepsy and their associated risk factors. Seizure. 2011 Nov 28.
321. García-Morales I, Delgado RT, Falip M et al. Early clinical experience with **lacosamide** as adjunctive therapy in patients with **refractory focal epilepsy and nocturnal seizures**. Seizure. 2011 Dec;20(10):801-4.
322. Caraballo R, Vaccarezza M, Cersósimo R et al. Long-term follow-up of the **ketogenic diet** for refractory epilepsy: multicenter Argentinean experience in 216 pediatric patients. Seizure. 2011 Oct;20(8):640-5.
323. Legros B, Boon P, Ceulemans B et al. Development of an **electronic decision tool** to support appropriate treatment choice in adult patients with epilepsy - Epi-Scope(®). Seizure. 2012 Jan;21(1):32-9.
324. Sharma S, Sankhyan N, Gulati S et al. Use of the **modified Atkins diet** in infantile spasms refractory to first-line treatment. Seizure. 2012 Jan;21(1):45-8.
325. Yang CY et al. **Severe cutaneous adverse reactions** to antiepileptic drugs in Asians. Neurology. 2011 Dec 6;77(23):2025-33. (CBZ, PHT, and LTG were the major causative AEDs for SCARs.)
326. **NICE**: National Institute for Health and Clinical Excellence. The **epilepsies**: the diagnosis and management of the epilepsies in adults and children in primary and secondary care (update). (Clinical guideline 137.) Jan **2012**. http://guidance.nice.org.uk/CG137.
Delgado V, Sawyer L, Neilson J et al. Diagnosis and management of the epilepsies in adults and children: summary of updated NICE guidance. BMJ 2012;344:e281 Jan26,2012.
327. Russ SA, Larson K, Halfon N. A **National Profile of Childhood** Epilepsy and Seizure Disorder. Pediatrics. 2012 Jan 23.
328. Graves, R, Oehler K, et al. **Febrile Seizures**: Risks, Evaluation, and prognosis. Am Fam Physician. 2012 Jan 15;85(2):149-153.
329. Mohammed HS, Kaufman CB, Limbrick DD, et al. Impact of **epilepsy surgery** on seizure control and quality of life: A 26-year follow-up study. Epilepsia. 2012 Feb 7.
330. Adelöw C, Andersson T, Ahlbom A et al. **Hospitalization for psychiatric disorders** before and after onset of unprovoked seizures/epilepsy. Neurology. 2012 Feb 7;78(6):396-401.
331. Faught E, Richman J, Martin R, et al. **Incidence and prevalence** of epilepsy among **older** US Medicare beneficiaries. Neurology 2012;78:448 – 453
332. Silbergleit R, et al. **Intramuscular (midazolam) versus intravenous (lorazepam)** therapy for prehospital **status epilepticus**. (Rampart) N Engl J Med 2012;366:591-600. Intramuscular (IM) midazolam is the preferred initial treatment for patients with status epilepticus in the prehospital setting. Primary care physicians may want to keep a vial of midazolam around the office in case that rare patient has a seizure that continues for more than 5 minutes. (LOE = 1b)
333. Treiman DM, Meyers PD, Walton NY, et al. A comparison of **four treatments** for generalized convulsive **status epilepticus**. N Engl J Med 1998;339:792-8.
334. Alldredge BK, Gelb AM, et al. A comparison of **lorazepam, diazepam, and placebo** for the treatment of out-ofhospital **status epilepticus**. N Engl J Med 2001;345:631-7.
335. Hearn L, Derry S, Moore RA. **Lacosamide** for neuropathic pain and fibromyalgia in adults. Cochrane Database Syst Rev. 2012 Feb 15;2:CD009318. Lacosamide has limited efficacy in the treatment of peripheral diabetic neuropathy. Higher doses did not give consistently better efficacy, but were associated with significantly more adverse event withdrawals.
336. Striano P, Weber YG, Toliat MR, et al. **GLUT1 mutations** are a rare cause of familial idiopathic generalized epilepsy. Neurology 2012;78:557–562.
337. Bonnett L, Tudur-Smith C, Smith D, et al. **Prognostic factors** for time to treatment failure and time to 12 months of remission for patients with focal epilepsy: post-hoc, subgroup analyses of data from the **SANAD** trial. Lancet Neurol 2012.
338. Engel J Jr, McDermott MP, Wiebe S, et al. Early **surgical therapy** for drugresistant **temporal lobe epilepsy**: a randomized trial. (ERSET) JAMA. 2012;307(9):922-930. n=38
339. Irizarry M, Jin S; He F et al. Incidence of New-Onset Seizures in Mild to Moderate **Alzheimer Disease** Arch Neurol. 2012;69(3):368-372.
340. Baca CB et al. **Psychiatric and medical comorbidity** and quality of life outcomes in **childhood-onset epilepsy**. Pediatrics. 2011 Dec;128(6):e1532-43.
341. Schober E, Otto KP, Dost A, et al; German/Austrian DPV Initiative and the BMBF Competence Network Diabetes. Association of Epilepsy and **Type 1 Diabetes Mellitus** in Children and Adolescents: Is There an Increased Risk for Diabetic Ketoacidosis? J Pediatr. 2011 Nov 3.

342. Simms KM, Kortepeter C, Avigan M. **Lamotrigine and aseptic meningitis**. Neurology 2012;78:921–927.
343. Kimia AA et al. Yield of emergent **neuroimaging among children presenting with a first complex febrile seizure**. Pediatr Emerg Care 2012 Apr; 28:316.
344. Talati R, Scholle JM, et al. Efficacy and Safety of **Innovator versus Generic Drugs** in Patients with Epilepsy: Systematic Review. Pharmacotherapy. 2012 Apr;32(4):314-22.
345. Hesdorffer D, Ishihara L, Mynepalli L, et al. **Epilepsy, suicidality, and psychiatric disorders**: A bidirectional association Ann Neurol. 2012 Mar 29.
346. Forcelli P, Janssen M, Vicini S et al. **Neonatal exposure** to antiepileptic drugs disrupts striatal synaptic development Ann Neurol. 2012 Mar 29.
347. Quek AML, Britton JW, McKeon A, et al. **Autoimmune epilepsy**: clinical characteristics and response to immunotherapy [published online March 26, 2012]. Arch Neurol. 2012.
348. Lackner P, Koppelstaetter F, Ploner P, et al. **Cerebral vasospasm** following temporal lobe epilepsy surgery. Neurology 2012;78:1215–1220.
349. Englot DJ, Ouyang D, Garcia PA, Barbaro NM, Chang EF. **Epilepsy surgery trends** in the United States, 1990– 2008. Neurology 2012;78:1200 –1206.
350. Yang S-Y, Kim DG, Chung H-T, Paek SH. **Radiosurgery for unruptured cerebral arteriovenous malformations**: long-term seizure outcome. Neurology 2012;78:1292–1298.
351. Westwood AJ, Vendrame M, Montouris G, Auerbach SH. Pearls & Oy-sters: Treatment of central sleep apnea with topiramate. Neurology. 2012 Apr 17;78(16):e97-9.
352. Neligan A, Bell GS, Giavasi C, et al. Long-term risk of developing **epilepsy after febrile seizures**: A prospective cohort study. Neurology. 2012 Apr 10;78(15):1166-70.
353. Meador KJ, Baker GA, et al; NEAD Study Group. Effects of **fetal antiepileptic drug exposure**: Outcomes at age 4.5 year. Neurology. 2012 Apr 17;78(16):1207-1214.
354. Kinikar SA, Delate T, Menaker-Wiener CM, et al. Clinical Outcomes Associated with **Brand-to-Generic Phenytoin** Interchange. Ann Pharmacother. 2012 May;46(5):650-8.
355. Ludvigsson JF, Zingone F, Tomson T, et al. Increased risk of epilepsy in biopsy-verified **celiac disease**: A population-based cohort study. Neurology. 2012 May 1;78(18):1401-7.
356. Krauss GL, Serratosa JM, et al. Randomized phase III study 306: Adjunctive **perampanel** for refractory partial-onset seizures. Neurology. 2012 May 1;78(18):1408-15.
357. Pavlova MK, Woo Lee J, Yilmaz F, et al. **Diurnal pattern** of seizures outside the hospital: Is there a time of circadian vulnerability? Neurology. 2012 May 8;78(19):1488-92.
358. Brodie MJ, Barry SJE, Bamagous GA, Norrie JD, Kwan P. **Patterns of treatment response in newly** diagnosed epilepsy. Neurology 2012;78:1548 –1554.
359. Larson AM, Ryther RC, Jennesson M, et al. Impact of pediatric epilepsy on **sleep patterns** and behaviors in children and parents. Epilepsia. 2012 May 17.
360. Hernández-Díaz S, Smith CR, Shen A, et al; For the North American AED Pregnancy Registry; North American AED(Antiepileptic Drug) Pregnancy Registry; Scientific Advisory Committee; North American AED Pregnancy Registry. Comparative safety of **antiepileptic drugs during pregnancy**. Neurology. 2012 May 22;78(21):1692-1699.
361. Sanchez Ferna´ndez I, Takeoka M, Tas E, et al. **Early thalamic lesions** in patients with sleep-potentiated epileptiform activity. Neurology 2012;78:1721–1727.
362. Baulac M, Brodie MJ, Patten A, Segieth J, Giorgi L. Efficacy and tolerability of **zonisamide versus controlled-release carbamazepine** for newly diagnosed partial epilepsy: a phase 3, randomised, double-blind, non-inferiority trial. Lancet Neurol 2012; online June 8.
363. Herzog AG, Fowler KM, Smithson SD, et al; For the Progesterone Trial Study Group. **Progesterone** vs placebo therapy for women with epilepsy: A randomized clinical trial. Neurology. 2012 Jun 12;78(24):1959-1966. (Class III: cyclic progesterone is ineffective)
364. Go CY, Mackay MT, Weiss SK, et al. Evidence-based guideline update: Medical treatment of **infantile spasms**: Report of the Guideline Development Subcommittee of the **American** Academy of Neurology and the Practice Committee of the Child Neurology Society. Neurology. 2012 Jun 12;78(24):1974-80.
Shumiloff NA, Lam WM, Manasco KB. Adrenocorticotropic Hormone for the Treatment of West Syndrome in Children (May). Ann Pharmacother. 2013 Apr 19.
365. **Ketogenic diets** in the treatment of epilepsy. Drug Ther Bull. 2012 Jun;50(6):66-8.
366. Mbuba CK, Ngugi AK, Fegan G, et al. Risk factors associated with the **epilepsy treatment gap** in Kilfi , Kenya: a cross-sectional study. *Lancet Neurol* 2012; online July 6.
367. Shiek Ahmad B, Hill KD, O'Brien TJ, et al. **Falls and fractures** in patients chronically treated with antiepileptic drugs. Neurology. 2012 Jun 13.
368. de Laat SA, Hillegers MH, Jansen FE, et al. **Hallucinations After Withdrawal of Valproic Acid**. Pediatrics. 2012 Jun 11.
369. Stern RS. Clinical practice. **Exanthematous drug eruptions**. N Engl J Med. 2012 Jun 28;366(26):2492-501. (penicillin, cephalosporins, sulfonamides, antiseizure meds etc)
370. Bergey GK. **Autoantibodies** in the Patient With Drug-Resistant Epilepsy: Are We Missing a Treatable Etiology? Arch Neurol. 2012 Mar 26.
371. Tomson T, Battino D. **Teratogenic effects** of antiepileptic drugs. Seizure. 2008 Mar;17(2):166-71.
372. Klein P, Herr D, Pearl PL, et al. Phase 2 Safety and Feasibility Study of Treatment With **Levetiracetam** for Prevention of Posttraumatic Epilepsy. Arch Neurol. 2012 Jul 9:1-6.
373. Ryan NM, Birring SS, Gibson PG. **Gabapentin for refractory chronic** cough: a randomised, double-blind, placebo-controlled trial. *Lancet* 2012; published online Aug 28.
374. Yuen TI, Morokoff AP, Bjorksten A, et al. **Glutamate** is associated with a higher risk of seizures in patients with gliomas. Neurology 2012;79:883– 889.
375. Menon R, Rathore C, Sarma SP, Radhakrishnan K. Feasibility of **antiepileptic drug withdrawal** following extratemporal resective epilepsy **surgery**. Neurology 2012;79:770–776.
376. Shinnar S, Bello JA, Chan S, et al. **MRI abnormalities** following **febrile status epilepticus** in children: The **FEBSTAT** Study. Neurology 2012;79:871– 877.
Shinnar S, Hesdorffer DC, Nordli DR Jr, et al. Phenomenology of prolonged febrile seizures: results of the **FEBSTAT** study. *Neurology* 2008;71:170.
377. Zhao L, Chen CN, Hajji N, et al. Histone deacetylation inhibition in **pulmonary hypertension**: therapeutic potential of **valproic** Acid and suberoylanilide hydroxamic Acid. Circulation. 2012 Jul 24;126(4):455-67.
378. Gandy M, Sharpe L, Perry KN, et al. Assessing the efficacy of 2 **screening measures for depression** in people with epilepsy. Neurology. 2012 Jul 24;79(4):371-5.
379. Johnson EK, Lightdale JR, Nelson CP. Risk Factors for **Urolithiasis** in Gastrostomy Tube Fed Children: A Case-Control Study. Pediatrics. 2013 Jun 10. (**topiramate** use…)

379. Perucca P, Gilliam FG. **Adverse effects** of antiepileptic drugs. Lancet Neurol. 2012 Sep;11(9):792-802.

Adverse Effect on:		Most; and Least Likely Agents
Brain	Cognition	Barbs, Benzos
	Coordination	Barbs, Benzos, CBZ Phenytoin; 2nd gen less so and least with Levetiracetam, Gabapentin
	Language	Topiramate
	Behavior, Personality	Barbs, Levetiracetam, Topiramate, Vigabatrin (+ psychiatric history increase risk)
Blood		CBZ, Phenytoin, Valproate
Bone		CBZ, Valproate
Liver, Pancreas		Valproate
Skin		CBZ, OxyCarb, Lamotrigine, Phenytoin (also related to Asian/genetics, age – Peds and Geriatrics, prior hx of skin rx, high initial dose or rapid dose esculation, immune system disorders, Herpes virus reactivation)
Weight (gain also associated with ↑ risk of CVD)		↑: Gabapentin, Pregabalin, Vigabatrin, Valproate, CBZ (moderate); ↓:Topiramate
Pregnancy		Barbs, Topiramate,Valproate; CBZ, Phenytoin, Lamotrigine
Female Hormones		Valproate (↑Polycystic Ovarian Syndrome and Hirsuitism in ♀);Levetiracetam least effect on OCs
Metabolic Enzyme **Induction** (**Increased** metabolic clearance of other substrates and reduced efficacy)		Barbs, CBZ, Phenytoin (reduce levels of antimicrobials, immunosuppressants, OCs, cardiovascular meds, psychotropics, antineoplastics, antiepileptics)
Metabolic Enzyme **Inhibition** (**Decreased** metabolic clearance of other substrates and increased/prolonged effects)		Valproate (TCAs, Barbs, Benzos, CBZ, lamotrigine, warfarin, zidovudine)

380. Boshuisen K, Arzimanoglou A, Cross JH, et al; for the TimeToStop study group. Timing of **antiepileptic drug withdrawal** and long-term seizure outcome after paediatric epilepsy surgery (**TimeToStop**): a retrospective observational study. Lancet Neurol. 2012 Sep;11(9):784-791.
381. Hanly JG, Urowitz MB, Su L et al. Seizure disorders in **systemic lupus erythematosus** results from an international, prospective, inception cohort study. Ann Rheum Dis. 2012 Sep;71(9):1502-9.
382. French JA, Krauss GL, Biton V et al. Adjunctive **perampanel** for refractory partial-onset seizures: Randomized phase III study 304. Neurology. 2012 Aug 7;79(6):589-96.
383. Josephson CB, Bhattacharya JJ, Counsell CE et al; On behalf of the Scottish Audit of Intracranial Vascular Malformations (SAIVMs) steering committee and collaborators. Seizure risk with **AVM treatment** or conservative management: Prospective, population-based study. Neurology. 2012 Aug 7;79(6):500-507.
384. Stapf C. Interventional **AVM therapy** against epileptic seizures: Treatment between Scylla and Charybdis? Neurology. 2012 Aug 7;79(6):492-3.
385. Gómez-Zorrilla S, Ferraz AV, Pedrós C et al. **Levetiracetam**-induced drug reaction with **eosinophilia** and systemic symptoms syndrome. Ann Pharmacother. 2012 Jul;46(7-8):e20.
386. Rugg-Gunn FJ, Sander JW. Management of **chronic epilepsy**. BMJ. 2012 Jul 17;345:e4576.
387. Wilden JA, and Cohen-Gadol AA. **Evaluation** of **First Nonfebrile** Seizures. Am Fam Physician. 2012;86(4):334-340.
388. Splinter MY. **Ezogabine** (Retigabine) and Its Role in the Treatment of Partial-Onset Seizures: A Review. Clin Ther. 2012 Aug 20.
389. Camfield P, Camfield C. **Unprovoked status epilepticus**: the prognosis for otherwise normal children with focal epilepsy. Pediatrics. 2012 Sep;130(3):e501-6.
390. Jette N, Quan H, Tellez-Zenteno JF, et al. Development of an **online tool** to determine appropriateness for an **epilepsy surgery** evaluation. Neurology 2012;79:1084 –1093.
391. Morita DA, Glauser TA, Modi AC. Development and validation of the **Pediatric Epilepsy Side Effects Questionnaire**. (PESQ) Neurology 2012;79:1252–1258.
392. Dong D, Sung C, et al. Cost-effectiveness of **HLA-B*1502 genotyping** in adult patients with newly diagnosed epilepsy in Singapore. Neurology. 2012 Sep 18;79(12):1259-67.
393. Hakami T, Todaro M, et al. Substitution Monotherapy With **Levetiracetam** vs **Older Antiepileptic Drugs**: A Randomized Comparative Trial. Arch Neurol. 2012 Sep 3:1-9.
394. Speechley KN, Ferro MA, Camfield CS, et al. **Quality of life in children** with new-onset epilepsy: A 2-year prospective cohort study. Neurology. 2012 Oct 9;79(15):1548-1555.
395. Lin JJ, Mula M, Hermann BP. Uncovering the **neurobehavioural comorbidities** of epilepsy over the lifespan. Lancet. 2012 Sep 29;380(9848):1180-92.

396. Leppik IE, Walczak TS, Birnbaum AK. Challenges of **epilepsy in elderly people**. Lancet. 2012 Sep 29;380(9848):1128-30.
397. Shafi MM, Westover MB, Cole AJ, et al. **Absence of early epileptiform abnormalities** predicts lack of seizures on continuous EEG. Neurology. 2012 Oct 23;79(17):1796-801.
398. Hocker SE, Britton JW, Mandrekar JN, et al. Predictors of **Outcome in Refractory Status Epilepticus**. Arch Neurol. 2012 Oct 8:1-6.
399. Manjunath R, Paradis PE, Parisé H, et al. Burden of **uncontrolled epilepsy** in patients requiring an emergency room visit or hospitalization. Neurology.2012 Oct 30;79(18):1908-16.
400. Hrabok M, Sherman EM, Bello-Espinosa L, Hader W. **Memory and Health**-related Quality of Life in Severe Pediatric Epilepsy. Pediatrics. 2013 Jan 14.
401. Moosa ANV, Gupta A, Jehi L, et al. Longitudinal seizure outcome and prognostic predictors after **hemispherectomy** in 170 children. Neurology 2013;80:253–260.
402. Wiebe S, Berg AT. Big epilepsy surgery for little people: What's the full story on **hemispherectomy**? Neurology. 2013 Jan 15;80(3):232-3.
403. Harden CL, Pennell PB. **Neuroendocrine** considerations in the treatment of men and women with epilepsy. Lancet Neurol. 2013 Jan;12(1):72-83.
404. Rosati A, L'erario M, Ilvento L, et al. Efficacy and safety of **ketamine** in refractory status epilepticus in children. Neurology. 2012 Dec 11;79(24):2355-8.
405. Kesselheim AS, Misono AS, Shrank WH, et al. Variations in **pill appearance** of antiepileptic drugs and the risk of **nonadherence**. Arch Intern Med 31 Dec 2012,
406. Joshi SM, Singh RK, Shellhaas RA. **Advanced Treatments** for Childhood Epilepsy: **Beyond Antiseizure Medications**. Arch Pediatr Adolesc Med. 2012 Nov 12:1-8.
407. Mawhinney E, Craig J, Morrow J, et al. **Levetiracetam in pregnancy**: Results from the UK and Ireland epilepsy and pregnancy registers. Neurology. 2013 Jan 22;80(4):400-405.
408. Meador KJ, Baker GA, Browning N, et al, for the **NEAD** Study Group. **Fetal antiepileptic drug exposure and cognitive outcomes at age 6** years (NEAD study): a prospective observational study. Lancet Neurol 2013; online Jan 23.
409. Kesselheim AS, Stedman MR, Bubrick EJ, et al. Seizure outcomes following the use of **generic versus brand**-name antiepileptic drugs: a systematic review and meta-analysis. Drugs. 2010 Mar 26;70(5):605-21.
410. Ngugi AK, Bottomley C, Kleinschmidt I, et al, for the SEEDS group. Prevalence of **active convulsive epilepsy in sub-Saharan Africa** and associated risk factors: cross-sectional and case-control studies. Lancet Neurol 2013; online Jan 31.
411. Beslow LA, Abend NS, Gindville MC, et al. **Pediatric intracerebral hemorrhage**: acute symptomatic seizures and epilepsy [online Feb 7, 2013]. JAMA Neurology. 2013.
412. Bodalia PN, Grosso AM, Sofat R, et al. **Comparative Efficacy and Tolerability of Antiepileptic** Drugs for **Refractory Focal Epilepsy** Systematic Review and Network Meta-Analysis reveals the need for long-term comparator trials. Br J Clin Pharmacol. 2013 Jan 28.
Zaccara G, Sisodiya SM, Giovannelli F, et al. Network Meta-Analysis and the Comparison of Efficacy and Tolerability of Antiepileptic Drugs for Treatment of **Refractory** Focal Epilepsy. Br J Clin Pharmacol. 2013 Jun 6.
413. Fiest KM, Dykeman J, Patten SB, et al. **Depression in epilepsy**: A systematic review and meta-analysis. Neurology. 2013 Feb 5;80(6):590-9.
414. DeGiorgio CM, Soss J, Cook IA, et al. Randomized controlled trial of **trigeminal nerve stimulation** (eTNS) for drug-resistant epilepsy. Neurology 2013;80:786–791.
415. Vedula SS, Li T, Dickersin K. Differences in reporting of analyses in **internal company documents versus published** trial reports: comparisons in industry-sponsored trials in **off-label uses of gabapentin**. PLoS Med. 2013 Jan;10(1):e1001378.
416. Fields MC, Labovitz DL, French JA. **Hospital-onset seizures**: an inpatient study. JAMA Neurol. 2013 Mar 1;70(3):360-4.
417. Glass HC, Kan J, Bonifacio SL, Ferriero DM. **Neonatal seizures**: treatment practices among term and preterm infants. Pediatr Neurol. 2012 Feb;46(2):111-5.
418. Baca CB, Vickrey BG, Vassar S, et al. **Time to pediatric epilepsy surgery** is related to disease severity and nonclinical factors. Neurology. 2013 Mar 26;80(13):1231-1239.
419. Christensen J, Grønborg TK, Sørensen MJ, et al. **Prenatal valproate exposure and risk of autism** spectrum disorders and childhood autism. JAMA. 2013; 309(16):1696-1703.
420. FDA Apr/13 The anti-seizure drug **ezogabine** (Potiga) can cause **discoloration of both the skin and the retina**. It's unknown whether these changes are permanent or whether the retinal discoloration can lead to vision impairment. The skin discoloration includes blue pigmentation, most often around the lips or in the nail beds, but at times more widespread on the face and legs. In addition, scleral and conjunctival discoloration has been reported.
421. Sabers A. Algorithm for **lamotrigine** dose adjustment before, during, and after **pregnancy**. Acta Neurol Scand. 2012 Jul;126(1):e1-4.
422. Moore JL, Aggarwal P. **Lamotrigine** use in **pregnancy**. Expert Opin Pharmacother. 2012 Jun;13(8):1213-6.
423. Berg AT, Zelko FA, Levy SR, et al. Age at onset of epilepsy, **pharmacoresistance**, and **cognitive outcomes**: A prospective cohort study. Neurology. 2012 Sep 25;79(13):1384-91.
424. Nordli DR Jr, Moshé SL, Shinnar S, et al; Acute EEG findings in children with **febrile status epilepticus**: **FEBSTAT** study. Neurology. 2012 Nov 27;79(22):2180-2186.
425. Jackson DC, Dabbs K, Walker NM, et al. The Neuropsychological and Academic Substrate of **New/Recent-Onset Epilepsies**. J Pediatr. 2012 Dec 5.
426. Martinez A, Finegersh A, Cannon DM, et al. The **5-HT1A receptor and 5-HT transporter** in temporal lobe epilepsy. Neurology 2013;80:1465–1471.
427. Karceski S. **Temporal lobe epilepsy surgery**: What is the best approach? Neurology. 2013 Apr 30;80(18):e192-4.
428. Shumiloff NA, Lam WM, Manasco KB. **Adrenocorticotropic Hormone** for the Treatment of **West Syndrome** in Children (May). Ann Pharmacother. 2013 Apr 19.
429. Josephson CB, Dykeman J, et al. Systematic review and meta-analysis of **standard vs selective temporal lobe epilepsy surgery**. Neurology. 2013 Apr 30;80(18):1669-1676.
430. Cook MJ, O'Brien TJ, Berkovic SF, et al. Prediction of seizure likelihood with a long-term, **implanted seizure advisory system** in patients with drug-resistant epilepsy: a first-in-man study. Lancet Neurol 2013; online May 2.
431. Fujii H, Goel A, Bernard N, et al. **Pregnancy outcomes following gabapentin** use: Results of a prospective comparative cohort study. Neurology. 2013 Apr 23;80(17):1565-1570.
432. Thompson DF, Brooks KG. **Gabapentin therapy of hiccups**. Ann Pharmacother. 2013 Jun;47(6):897-903.

433. Kaiboriboon K, Bakaki PM, Lhatoo SD, et al. Incidence and prevalence of treated epilepsy among poor health and **low-income Americans**. Neurology. 2013 May 21;80(21):1942-9.
434. Pardoe HR, Berg AT, Jackson GD. Sodium **valproate** use is associated with **reduced** parietal lobe thickness and **brain volume**. Neurology. 2013 May 14;80(20):1895-900.
435. Berg AT, Nickels K, Wirrell EC, et al. **Mortality** Risks in New-Onset Childhood Epilepsy. Pediatrics. 2013 Jun 10.
436. Feldmann M, Asselin M-C, Liu J, et al. **P-glycoprotein expression** and function in patients with temporal lobe epilepsy: a case-control study. Lancet Neurol 2013; online June 18.
437. Krueger DA, Wilfong AA, Holland-Bouley K, et al. **Everolimus** treatment of refractory epilepsy in **tuberous sclerosis complex**. Ann Neurol. 2013 Jun 24.
438. Wiffen PJ, Derry S, Lunn MP, et al. **Topiramate** for neuropathic pain and fibromyalgia in adults. Cochrane Database Syst Rev. 2013 Aug 30;8:CD008314. doi: 10.1002/14651858.CD008314.pub3. Topiramate is without evidence of efficacy in diabetic neuropathic pain, the only neuropathic condition in which it has been adequately tested.
439. Ryvlin P, Nashef L, Lhatoo SD, et al. Incidence and mechanisms of **cardiorespiratory arrests** in epilepsy monitoring units (MORTEMUS): a retrospective study. Lancet Neurol 2013; online Sept 4.
440. Veiby G, Daltveit AK, Schjølberg S, et al. Exposure to antiepileptic **drugs in utero and child development**-A prospective population-based study. Epilepsia. 2013 Jul 19.
441. Abend NS, Arndt DH, Carpenter JL, et al. Electrographic seizures in **pediatric ICU patients**: Cohort study of risk factors and mortality. Neurology. 2013 Jul 23;81(4):383-391.
442. Fazel S, Wolf A, Långström N, Newton CR, Lichtenstein P. **Premature mortality in epilepsy** and the role of psychiatric comorbidity: a total population study. Lancet 2013; online July 22.
443. Vossel KA, Beagle AJ, Rabinovici GD, et al. Seizures and Epileptiform Activity in the Early Stages of Alzheimer Disease. JAMA Neurol. 2013 Jul 8:1-9.
444. Gallagher R, Apostle N. Peripheral edema with pregabalin. CMAJ. 2013 Jul 9;185(10):E506.
445. Vajda FJ, O'Brien TJ, Graham JE, et al. Dose dependence of **fetal malformations associated with valproate**. Neurology. 2013 Sep 10;81(11):999-1003.
446. Hakami T, McIntosh A, Todaro M, et al**. MRI-identified pathology** in adults with new-onset seizures. Neurology. 2013 Sep 3;81(10):920-7.
447. Tradounsky G. Seizures in **palliative care**. Can Fam Physician. 2013 Sep;59(9):951-5.
448. Nyberg J, Aberg MA, Torén K, et al. **Cardiovascular fitness** and later risk of epilepsy: A Swedish population-based cohort study. Neurology. 2013 Sep 17;81(12):1051-7.
449. Veiby G, Engelsen BA, Gilhus NE. Early Child Development and Exposure to **Antiepileptic Drugs Prenatally and Through Breastfeeding**: A Prospective Cohort Study on Children of Women With Epilepsy. JAMA Neurol. 2013 Sep 23.
450. Lamberts RJ, Gaitatzis A, Sander JW, et al. **Postictal generalized EEG suppression**: An inconsistent finding in people with **multiple seizures**. Neurology. 2013 Aug 21.
451. Edelvik A, Rydenhag B, Olsson I, et al. **Long-term outcomes of epilepsy surgery** in Sweden: A national prospective and longitudinal study. Neurology. 2013 Aug 21.
452. Sugerman DT. JAMA **patient page. Seizures**. JAMA. 2013 Sep 18;310(11):1195.
453. Baca CB, Vickrey BG, Vassar SD, et al. **Injuries in Adolescents with Childhood-Onset Epilepsy** Compared with Sibling Controls. J Pediatr. 2013 Sep 18.
454. Masur D, Shinnar S, Cnaan A, et al. Pretreatment cognitive deficits and medication impact (**valproic acid, ethosuximide, lamotrigine**) on attention in **childhood absence epilepsy**. Neurology 2013;81:1572–1580.
455. Abend NS, Arndt DH, Carpenter JL, et al. **Electrographic seizures in pediatric ICU** patients: cohort study of risk factors and mortality. Neurology. 2013 Jul 23;81(4):383-91.
456. Mullen SA, Carvill GL, Bellows S, et al. Copy number **variants are frequent in genetic generalized epilepsy** with **intellectual disability**. Neurology. 2013 Sep 25.
457. Morris GL 3rd, Gloss D, Buchhalter J, et al. Evidence-based guideline update: **Vagus nerve stimulation** for the treatment of epilepsy: Report of the Guideline Development Subcommittee of the American Academy of Neurology (AAN). Neurology. 2013 Aug 28.
458. Hardies K, Weckhuysen S, Peeters E, et al. **Duplications of 17q12** can cause familial fever-related epilepsy syndromes. Neurology. 2013 Sep 18.
459. Dlugos D, Shinnar S, Cnaan A, et al. **Pretreatment EEG in childhood absence epilepsy**: associations with attention and treatment outcome. Neurology 2013;81:150–156.
460. FDA Nov/13 Potiga (**Ezogabine**) -approved changes to the drug label, underscoring risks of abnormalities to the retina in the eye, potential vision loss, and skin discoloration, all of which may become permanent. The revised label includes a new boxed warning, because of the risk of abnormalities to the retina. FDA advises that Potiga use be limited to patients who have not responded adequately to several alternative therapies to decrease the frequency of seizures, or epilepsy, and for whom the benefits of treatment outweigh the risks.
461. Uceyler N, Sommer C, Walitt B, et al. **Anticonvulsants for fibromyalgia**. Cochrane Database Syst Rev. 2013 Oct 16;10:CD010782. The anticonvulsant, pregabalin, demonstrated a small benefit over placebo in reducing pain and sleep problems. Pregabalin use was shown not to substantially reduce fatigue compared with placebo. Study dropout rates due to adverse events were higher with pregabalin use compared with placebo. Dizziness was a particularly frequent adverse event seen with pregabalin use.
462. FDA Dec/13 is warning the public that the anti-seizure drug Onfi **(clobazam) can cause rare but serious skin reactions** that can result in permanent harm and death.
463. Oltrogge KM, Peppard WJ, Saleh M, et al. **Phenytoin** removal by continuous venovenous **hemofiltration**. Ann Pharmacother. 2013 Sep;47(9):1218-22.
464. Dell'orto VG, Belotti EA, et al. Metabolic disturbances and **renal stone** promotion on treatment with **topiramate**: a systematic review. Br J Clin Pharmacol. 2013 Nov 13.
465. Esaian D, et al. **Ketamine** continuous infusion for refractory status epilepticus in a patient with anticonvulsant hypersensitivity syndrome. Ann Pharmacother. 2013 Vov;47(11):1569-76.
466. Wiffen PJ, Derry S, Moore RA. **Lamotrigine for chronic neuropathic pain and fibromyalgia** in adults. Cochrane Database Syst Rev. 2013 Dec 3;12:CD006044. Large, high-quality, long-duration studies reporting clinically useful levels of pain relief for individual participants provided no convincing evidence that lamotrigine is effective in treating neuropathic pain and fibromyalgia at doses of about 200 to 400 mg daily.

467. Shallcross R, Bromley RL, Cheyne CP, et al. On behalf of the Liverpool and Manchester Neurodevelopment Group and The UK Epilepsy and Pregnancy Register. In utero exposure to **levetiracetam vs valproate**: Development and language at 3 years of age. Neurology. 2014 Jan 8.
468. Senf P, Schmitz B, Holtkamp M, Janz D. Prognosis of **juvenile myoclonic epilepsy 45 years after onset**: Seizure outcome and predictors. Neurology. 2013 Dec 10;81(24):2128-33.
469. Holtkamp M, Kowski AB, Merkle H, et al. Long-term outcome in epilepsy with **grand mal on awakening - 40 years** of follow-up. Ann Neurol. 2014 Jan 7.
470. Arntz RM, Maaijwee NA, et al. **Epilepsy after TIA or stroke** in young patients impairs long-term functional outcome: FUTURE Study. Neurology. 2013 Nov 26;81(22):1907-13
471. Pugh MJ, Hesdorffer D, Wang CP, et al. Temporal trends in new exposure to antiepileptic drug monotherapy and **suicide-related behavior**. Neurology. 2013 Nov 26;81(22):1900-6
472. Battino D, Tomson T, Bonizzoni E, et al. **EURAP** Study Group. **Seizure control and treatment changes in pregnancy**: observations from the EURAP epilepsy pregnancy registry. Epilepsia. 2013 Sep;54(9):1621-7.
473. Fernandez A, Lantigua H, Lesch C, et al. High-dose **midazolam** infusion for refractory status epilepticus. Neurology. 2013 Dec 20.
474. Hernánde Pdf Cardamone M, Flanagan D, Mowat D, et al. Mammalian Target of **Rapamycin Inhibitors** for Intractable Epilepsy and Subependymal Giant Cell Astrocytomas in Tuberous Sclerosis Complex. J Pediatr. 2014 Feb 8.
475. Franceschetti S, Michelucci R, Canafoglia L, et al. **Progressive myoclonic epilepsies**: definitive and still undetermined causes. Neurology 2014;82:405–411.
476. French J, Kwan P, Fakhoury T, et al. **Pregabalin** monotherapy in patients with partial-onset seizures: A historical-controlled trial. Neurology. 2014 Feb 18;82(7):590-7.
477. Hamid H, Blackmon K, Cong X, et al. Mood, anxiety, and incomplete seizure control affect quality of life after **epilepsy surgery**. Neurology. 2014 Mar 11;82(10):887-94.
478. Jette N, Trevathan E. Saving lives by treating epilepsy in **developing countries**. Neurology. 2014 Feb 18;82(7):552-3.
479. Modi AC, Rausch JR, Glauser TA. Early **pediatric antiepileptic drug nonadherence** is related to lower long-term seizure freedom. Neurology. 2014 Jan 24.
480. Ong MS, Kohane IS, Cai T, et al. Population-Level Evidence for an **Autoimmune Etiology** of Epilepsy. JAMA Neurol. 2014 Mar 31.
481. Schmidt D, Schachter SC. **Drug treatment** of **epilepsy in adults**. BMJ. 2014 Feb 28;348:g254.
482. Seinfeld S, Shinnar S, Sun S, et al. **Emergency management of febrile status epilepticus**: Results of the **FEBSTAT** study. Epilepsia. 2014 Feb 6.
483. Sutter R, Marsch S, Fuhr P, Kaplan PW, Rüegg S. **Anesthetic drugs** in status epilepticus: risk or rescue? A 6-year cohort study. Neurology 2014;82:656–664.
484. Thakur KT, Probasco JC, Hocker SE, et al. **Ketogenic diet** for adults in super-refractory status epilepticus. Neurology. 2014 Jan 22.
485. Wagenman KL, Blake TP, Sanchez SM, et al. **Electrographic status epilepticus** and long-term outcome in critically ill children. Neurology. 2014 Feb 4;82(5):396-404.
486. Zakrzewska JM, Linskey ME. **Trigeminal neuralgia**. BMJ. 2014 Feb 17;348:g474.
487. Hernández-Díaz S, Mittendorf R, Smith CR, et al. North American Antiepileptic Drug Pregnancy Registry. Association between **topiramate** and **zonisamide** use during **pregnancy** and low birth weight. Obstet Gynecol. 2014 Jan;123(1):21-8.
488. Pdf Fisher RS, Acevedo C, Arzimanoglou A, et al. A practical clinical **definition of epilepsy**. Epilepsia. 2014 Apr 14.
489. Plecko B, Paul K, Mills P, et al. **Pyridoxine** responsiveness in novel mutations of the **PNPO gene**. Neurology. 2014 Apr 22;82(16):1425-33.
490. Prasad V, Kendrick D, Sayal K, et al. **Injury Among Children** and Young Adults With Epilepsy. Pediatrics. 2014 Apr 14.
491. Angus-Leppan H. **First seizures** in **adults**. BMJ. 2014 Apr 15
492. Kang H, et al. Long-term use of **valproic acid** in US veterans is associated with a reduced risk of smoking-related cases of head and neck **cancer**. Cancer. 2014 Mar24.
493. Glass HC, Wusthoff CJ, Shellhaas RA, et al. Risk factors for **EEG seizures** in **neonates** treated with **hypothermia**: a multicenter cohort study. Neurology 2014;82:1239–1244.
494. Kato M, Saitsu H, Murakami Y, et al. **PIGA mutations** cause early-onset epileptic encephalopathies and distinctive features. Neurology. 2014 Apr 4.
495. Moeller F, Groening K, Moehring J, et al. **EEG-fMRI** in myoclonic astatic epilepsy (Doose syndrome). Neurology 2014;82:1508–1513.
496. Sharma S, Jain P, Gulati S, et al. Use of the **Modified Atkins Diet** in **Lennox Gastaut Syndrome**. J Child Neurol. 2014 Mar 20.
497. Toledano M, Britton JW, McKeon A, et al. Utility of an **immunotherapy** trial in evaluating patients with presumed **autoimmune epilepsy**. Neurology 2014;82:xxx–xxx.
498. Chamberlain JM, Okada P, Holsti M, et al; Pediatric Emergency Care Applied Research Network (PECARN). **Lorazepam vs diazepam** for pediatric status epilepticus: a randomized clinical trial. JAMA. 2014 Apr 23-30;311(16):1652-60.
499. Camfield CS, Camfield PR. **Rolandic epilepsy** has little effect on adult life 30 years later: A population-based study. Neurology. 2014 Apr 1;82(13):1162-6.
500. Cheuk DK, Wong V. **Acupuncture for epilepsy**. Cochrane Database Syst Rev. 2014 May 7;5:CD005062. Available RCTs are small, heterogeneous and have high risk of bias. The current evidence does not support acupuncture for treating epilepsy.
501. Huff JS, Melnick ER, Tomaszewski CA, et al. American College of Emergency Physicians. Clinical policy: critical issues in the **evaluation and management** of adult patients presenting to the **emergency department** with seizures. Ann Emerg Med. 2014 Apr;63(4):437-447.e15.
502. Picard F, Makrythanasis P, Navarro V, et al. **DEPDC5 mutations** in families presenting as autosomal dominant nocturnal frontal lobe epilepsy. Neurology. 2014 May 9.
503. Margolis JM, Chu BC, et al. Effectiveness of **Antiepileptic Drug Combination Therapy for Partial-Onset Seizures** Based on Mechanisms of Action. JAMA Neurol. 2014 Jun 9.
504. Meador KJ, Baker GA, Browning N, et al; for the Neuro developmental Effects of Antiepileptic Drugs (NEAD) Study Group. **Breastfeeding in Children** of Women Taking Antiepileptic Drugs: **Cognitive Outcomes** at Age 6 Years. JAMA Pediatr. 2014 Jun 16.
505. Dulac O, Plecko B, Gataullina S, et al. Occasional seizures, epilepsy, and **inborn errors of metabolism**. Lancet Neurol. 2014 Jul;13(7):727-739.

506. Brown JW, Lawn ND, Lee J, et al. When is it safe to **return to driving** following first-ever seizure? J Neurol Neurosurg Psychiatry. 2014 Apr 25.
507. Reilly C, Atkinson P, Das KB, et al. **Neurobehavioral Comorbidities** in Children With Active Epilepsy: A Population-Based Study. Pediatrics. 2014 May 26.
508. Costa J, Fareleira F, Ascencao R, Borges M, Sampaio C, Vaz-Carneiro A. Clinical comparability of the new antiepileptic drugs in refractory partial epilepsy: a systematic review and meta-analysis. Epilepsia 2011;52:1280-91.
509. Ranganathan LN, Ramaratnam S. Rapid versus slow **withdrawal of antiepileptic drugs**. Cochrane Database Syst Rev. 2006 Apr 19;(2):CD005003. In view of methodological deficiencies and small sample size, in the solitary study identified, we cannot derive any reliable conclusions regarding the optimal rate of tapering of AEDs. Further studies are needed in adults as well as in children to investigate the rate ofwithdrawal of AEDs and to study the effects of variables such as seizure types, its aetiology, mental retardation, EEG abnormalities, presence of neurological deficits and other co-morbidities on the rate of tapering.
510. Cagnetti C, Lattanzi S, Foschi N, et al. Seizure course **during pregnancy in catamenial epilepsy**. Neurology. 2014 Jul 22;83(4):339-44.
511. Bonnett LJ, Tudur Smith C, Donegan S, et al. Treatment outcome **after failure of a first antiepileptic drug**. Neurology. 2014 Aug 5;83(6):552-60.
512. International League Against Epilepsy Consortium on Complex Epilepsies. Electronic address: epilepsy-austin@unimelb.edu.au. **Genetic determinants of common epilepsies**: a meta-analysis of genome-wide association studies. Lancet Neurol. 2014 Jul 30.
513. Ghosh S, Jehi LE. **New-onset epilepsy in the elderly**: Challenges for the internist. Cleve Clin J Med. 2014 Aug;81(8):490-498.
514. Herzog AG, Frye CA; Progesterone Trial Study Group. **Allopregnanolone levels** and seizure frequency in progesterone-treated women with epilepsy. Neurology. 2014 Jul 22;83(4):345
515. Simonato M, Brooks-Kayal AR, Engel J Jr, et al. The challenge and promise of epilepsy **therapy development in animal models**. Lancet Neurology 2014; online Augst 11.
516. Chung WH, Chang WC, Lee YS, et al; Taiwan Severe Cutaneous Adverse Reaction Consortium; Japan Pharmacogenomics Data Science Consortium. Genetic variants associated with **phenytoin-related severe cutaneous adverse reactions**. JAMA. 2014 Aug 6;312(5):525-34.
517. Ferro MA, Chin RF, Camfield CS, et al. **Convulsive status epilepticus** and health-related **quality of life in children** with epilepsy. Neurology. 2014 Aug 19;83(8):752-7.
518. Bech BH, Kjaersgaard MI, et al. Use of **antiepileptic drugs during pregnancy** and risk of spontaneous abortion and stillbirth: population based cohort study. BMJ. 2014 Aug 21.
519. Roberts JI, Hrazdil C, Wiebe S, et al. Feasibility of using an **online tool** to assess appropriateness for an **epilepsy surgery** evaluation. Neurology. 2014 Sep 2;83(10):913-9.
520. DeGiorgio CM, Miller PR, et al. **Fish oil (n-3 fatty acids)** in drug resistant epilepsy: a randomised placebo-controlled crossover study. J Neurol Neurosurg Psychiatry. 2014 Sep 8.
521. Stretton J, Winston G, Sidhu M, et al. **Neural correlates of working memory** in temporal lobe epilepsy: an fMRI study. Neuroimage 2012;60:1696–1703.
522. Ibrahim GM, Rutka JT, Snead OC 3rd. **Epilepsy surgery in childhood**: no longer the treatment of last resort. CMAJ. 2014 Sep 16;186(13):973-4.
523. Vadlamudi L, Milne RL, Lawrence K, et al. **Genetics of epilepsy**: The testimony of twins in the molecular era. Neurology. 2014 Sep 16;83(12):1042-8.
524. Jette N, Reid AY, Wiebe S. **Surgical management of epilepsy**. CMAJ. 2014 Sep 16;186(13):997-1004.
525. Ba-Diop A, Marin B, Druet-Cabanac M, et al. Epidemiology, causes, and treatment of **epilepsy in sub-Saharan Africa**. Lancet Neurol. 2014 Oct;13(10):1029-1044.
526. Bauer M, Karch R, Zeitlinger M, et al. In vivo **P-glycoprotein function** before and after **epilepsy surgery**. Neurology. 2014 Oct 7;83(15):1326-31.
527. Wandschneider B, Stretton J, Sidhu M, et al. **Levetiracetam reduces abnormal network activations** in temporal lobe epilepsy. Neurology. 2014 Oct 21;83(17):1508-12.
528. Frampton JE. **Pregabalin**: a review of its use in adults with **generalized anxiety disorder**. CNS Drugs. 2014 Sep;28(9):835-54.
529. Ryvlin P, Cross JH, Rheims S. **Epilepsy surgery in children and adults**. Lancet Neurol. 2014 Nov;13(11):1114-1126.
530. Dugan P, Carlson C, Bluvstein J, et al; EPGP Investigators. **Auras in generalized epilepsy**. Neurology. 2014 Oct 14;83(16):1444-9.
531. Bromley R,Weston J, Adab N, et al. . Treatment for **epilepsy in pregnancy**: neurodevelopmental outcomes in the child. Cochrane Database of Systematic Reviews 2014, Issue 10. Art. No.: CD010236. DOI: 10.1002/14651858.CD010236.pub2. The most important finding is the reduction in IQ in the VPA exposed group, which are sufficient to affect education and occupational outcomes in later life. However, for some women VPA is the most effective drug at controlling seizures. Informed treatment decisions require detailed counselling about these risks at treatment initiation and at pre-conceptual counselling. We have insufficient data about newer AEDs, some of which are commonly prescribed, and further research is required. Most women with epilepsy should continue their medication during pregnancy as uncontrolled seizures also carries a maternal risk.
532. Broomall E, Natale JE, Grimason M, et al. Pediatric super-**refractory status epilepticus treated with allopregnanolone**. Ann Neurol. 2014 Oct 31.
533. Nevalainen O, Ansakorpi H, Simola M, et al. **Epilepsy related clinical characteristics and mortality**: a systematic review and meta-analysis. Neurology 2014;83:1968–1977.
534. Singh RK, Joshi SM, Potter DM, et al. Cognitive outcomes in febrile infection-related epilepsy syndrome treated with the **ketogenic diet**. Pediatrics. 2014 Nov;134(5):e1431-5.
535. Ngugi AK, Bottomley C, Fegan G, et al. **Premature mortality** in active convulsive epilepsy in rural Kenya: causes and associated factors. Neurology. 2014 Feb 18;82(7):582-9.
536. Jovanović M, Sokić D, Grabnar I, et al. Effect of Long-term **Topiramate** Therapy on Serum Bicarbonate and Potassium Levels in Adult Epileptic Patients. Ann Pharmacother. 2014 May 8;48(8):992-997.
537. Markman JD, Frazer ME, Rast SA, et al. Double-blind, randomized, controlled, crossover trial of **pregabalin for neurogenic claudication**. Neurology. 2014 Dec 10.
538. Chen Z, Liew D, Kwan P. Effects of a **HLA-B*15:02 screening** policy on **antiepileptic drug use** and severe **skin reactions**. Neurology. 2014 Nov 25;83(22):2077-84.
539. Klein P, Tyrlikova I, Mathews GC. **Dietary** treatment in adults with **refractory epilepsy**: A review. Neurology. 2014 Nov 18;83(21):1978-1985.
540. Modi AC, Wu YP, Rausch JR, et al. **Antiepileptic drug nonadherence** predicts pediatric epilepsy seizure outcomes. Neurology. 2014 Nov 25;83(22):2085-90.

541. Shimabukuro K, Gibbon F, et al. **DRESS** associated with **perampanel** administration in a child with drug-resistant epilepsy. Neurology. 2014 Dec 2;83(23):2188.
542. Westall CA, Wright T, Cortese F, et al. **Vigabatrin retinal toxicity** in children with infantile spasms: An observational cohort study. Neurology. 2014 Dec 9;83(24):2262-8.
543. Baker GA, Bromley RL, Briggs M, et al. **IQ at 6 years after in utero exposure to antiepileptic drugs**: A controlled cohort study. Neurology. 2014 Dec 24.
544. Italiano D, Capuano A, Alibrandi A, et al. **Indications of newer and older antiepileptic drug use**: findings from a southern Italian general practice setting from 2005-2011. Br J Clin Pharmacol. 2014 Dec 31.
545. Roberts JI, Hrazdil C, Wiebe S, et al. **Neurologists' knowledge** of and attitudes toward **epilepsy surgery**: a national survey. Neurology 2015;84:159–166.
546. Bergey GK, Morrell MJ, Mizrahi EM, et al. Long-term treatment with **responsive brain stimulation** in adults with refractory partial seizures. Neurology. 2015 Jan 23.
547. Jehi L, Yardi R, Chagin K, et al. Development and validation of **nomograms to provide individualised predictions of seizure** outcomes after epilepsy surgery: a retrospective analysis. Lancet Neurol 2015; online Jan 29.
548. Jobst BC, Cascino GD. **Resective epilepsy surgery** for drug-resistant focal epilepsy: a review. JAMA. 2015 Jan 20;313(3):285-93.
549. Liebenthal JA, Wu S, Rose S, Ebersole JS, Tao JX. Association of **prone position with sudden unexpected death in epilepsy**. Neurology 2015;84:703–709.
550. Bergey GK, Morrell MJ, Mizrahi EM, et al. Long-term treatment with responsive **brain stimulation** in adults with refractory partial seizures. Neurology 2015;84:810–817.
551. Wasade VS, Elisevich K, Tahir R, et al. Long-term seizure and psychosocial outcomes after **resective surgery** for intractable epilepsy. Epilepsy Behav. 2015 Jan 19;43C:122-127.
552. Wen X, Meador KJ, Hartzema A. **Antiepileptic drug use by pregnant women** enrolled in Florida Medicaid. Neurology 2015;84:944–950.
553. Cardenas DD, Emir B, Parsons B. Examining the Time to Therapeutic Effect of **Pregabalin** in **Spinal Cord Injury** Patients With Neuropathic Pain. Clin Ther. 2015 Apr 4.
554. Lebow J, Chuy JA, Cedermark K, Cook K, Sim LA. The Development or **Exacerbation of Eating Disorder Symptoms** After **Topiramate** Initiation. Pediatrics. 2015 Apr 6.
555. Moshé SL, Perucca E, Ryvlin P, et al. Epilepsy: new advances. Lancet. 2014 Sep 23.
556. Pressler RM, Boylan GB, Marlow N, et al; Neonatal seizure treatment with Medication Off-patent (**NEMO**) consortium. **Bumetanide** for the treatment of seizures in newborn babies with hypoxic ischaemic encephalopathy (NEMO): an open-label, dose finding, and feasibility phase 1/2 trial. Lancet Neurol. 2015 Mar 9.
557. Salanova V, Witt T, Worth R, et al; For the SANTE Study Group. Long-term efficacy and safety of **thalamic stimulation** for drug-resistant partial epilepsy. Neurology. 2015 Feb 6.
558. Betjemann JP, Lowenstein DH. **Status epilepticus in adults**. Lancet Neurol. 2015 Apr 20.
559. Boshuisen K, van Schooneveld MM, Uiterwaal CS, et al; TimeToStopcognitive outcome study group. **IQ improves after antiepileptic drug withdrawal** following pediatric epilepsy surgery. Ann Neurol. 2015 Apr 21.
560. Krumholz A, Wiebe S, Gronseth GS, et al. Evidence-based guideline: **Management of an unprovoked first seizure in adults**: Report of the Guideline Development Subcommittee of the **American Academy of Neurology** (**AAN**) and the **American Epilepsy Society (AES)**. Neurology. 2015 Apr 21;84(16):1705-13.
561. Wibisono C, Rowe N, Beavis E, et al. **Ten-year single-center experience of the ketogenic diet**: factors influencing efficacy, tolerability, and compliance. J Pediatr. 2015 Apr;166(4):1030-1036.
562. Betjemann JP, Josephson SA, Lowenstein DH, et al. Trends in **Status Epilepticus-Related Hospitalizations and Mortality**: Redefined in US Practice Over Time. JAMA Neurol. 2015 Apr 27.
563. Fayed N, Davis AM, Streiner DL, et al. **Children's perspective of quality of life** in epilepsy. Neurology 2015;84:1830–1837.
564. Kariuki SM, Kakooza-Mwesige A, Wagner RG, et al; **SEEDS** Writing Group. Prevalence and factors associated with **convulsive status epilepticus** in Africans with epilepsy. Neurology. 2015 May 5;84(18):1838-45.
565. French JA, Gil-Nagel A, Malerba S, et al. Time to prerandomization monthly seizure count in **perampanel** trials: A novel epilepsy endpoint. Neurology 2015;84:2014–2020.
566. Gidal BE, Laurenza A, Hussein Z, et al. **Perampanel** efficacy and tolerability with enzyme-inducing AEDs in patients with epilepsy. Neurology. 2015 May 12;84(19):1972-80.
567. Sciegienka A, Argo T, Cantrell M, et al. Association between **topiramate** use and **serum bicarbonate** levels in a veteran population. Ann Pharmacother. 2015 Jun;49(6):670-3.
568. FDA Jun/15 Potiga (**ezogabine**): Drug Safety Communication - FDA Determines 2013 Labeling Adequate to Manage Risks of Retinal Abnormalities, Potential Vision Loss, and Skin Discoloration
569. Huttunen J, Kurki MI, von Und Zu Fraunberg M, et al. **Epilepsy after aneurysmal subarachnoid hemorrhage**: A population-based, long-term follow-up study. Neurology. 2015 Jun 2;84(22):2229-37.
570. Jung DE, Yu R, Yoon JR, et al. **Neuropsychological effects** of **levetiracetam and carbamazepine** in children with focal epilepsy. Neurology 2015;84:2312–2319.
571. Ryvlin P, Cucherat M, Rheims S. **Risk of sudden unexpected death** in epilepsy in patients given adjunctive antiepileptic treatment for refractory seizures: a meta-analysis of placebo-controlled randomised trials. Lancet Neurol. 2011 Nov;10(11):961-8.
572. Sánchez Fernández I, Abend NS, Agadi S, et al; Pediatric Status Epilepticus Research Group (**pSERG**). **Time from convulsive status epilepticus** onset to anticonvulsant administration in children. Neurology. 2015 Jun 9;84(23):2304-11.
573. Cook M, Baker N, Lanes S, et al. **Incidence of stroke and seizure in Alzheimer's disease dementia**. Age Ageing. 2015 May 24.
574. MacDonald SC, Bateman BT, McElrath TF, Hernández-Díaz S. Mortality and morbidity during delivery hospitalization among **pregnant women with epilepsy** in the United States [online July 6, 2015].JAMA Neurol. doi:10.1001 /jamaneurol.2015.1017.

575. Cirillo M, Venkatesan C, et al. Case Report: Intravenous and **Oral Pyridoxine** Trial for Diagnosis of Pyridoxine-Dependent Epilepsy. Pediatrics. 2015 Jul;136(1):e257-61.
576. Leung JG, Hall-Flavin D, Nelson S, et al. The Role of **Gabapentin in the Management of Alcohol Withdrawal and Dependence**. Ann Pharmacother. 2015 May 12.
577. Chen HY, Albertson TE, Olson KR. Treatment of **drug-induced seizures**. Br J Clin Pharmacol. 2015 Jul 14.
578. Dayan PS, Lillis K, Bennett J, et al. Prevalence of and Risk Factors for **Intracranial Abnormalities** in Unprovoked Seizures. Pediatrics. 2015 Jul 20.
579. Hixson JD, Barnes D, Parko K, et al. Patients optimizing **epilepsy management via an online community**: The POEM Study. Neurology. 2015 Jul 14;85(2):129-36.
580. Lamberts RJ, Blom MT, Wassenaar M, et al. **Sudden cardiac arrest** in people with epilepsy in the community: circumstances and risk factors. Neurology 2015;85: 212–218.
581. Kim SH, Korff CM, Kim AJ, et al. A practical, simple, and useful method of **categorizing interictal EEG features in children**. Neurology. 2015 Aug 4;85(5):471-8.
582. Ryan JL, McGrady ME, Guilfoyle SM, et al. **Health care charges for youth with newly diagnosed epilepsy**. Neurology. 2015 Aug 11;85(6):490-7.
583. Spatola M, Novy J, Du Pasquier R, et al. **Status epilepticus of inflammatory etiology**: A cohort study. Neurology. 2015 Aug 4;85(5):464-70.
584. Tomson T, Battino D, Bonizzoni E, et al. **Antiepileptic drugs and intrauterine death**: A prospective observational study from EURAP. Neurology. 2015 Jul 17.
585. Guo J, Guo J, Li J, et al. **Statin treatment reduces the risk of poststroke seizures**. Neurology 2015;85:701–707.
586. Jhagroo RA, Wertheim ML, et al. Alkali replacement raises urinary citrate excretion in patients with **topiramate-induced hypocitraturia**. Br J Clin Pharmacol. 2015 Aug 22.
587. Louie JM, Raphael KL, Barker B. **Levetiracetam** Use With Continuous **Renal Replacement Therapy**. Ann Pharmacother. 2015 Sep;49(9):1079-80.
588. Patel N, Ram D, Swiderska N, et al. **Febrile seizures**. BMJ. 2015 Aug 18;351:h4240.
589. Viale L, Allotey J, et al, **EBMCONNECT** Collaboration. **Epilepsy in pregnancy** and reproductive outcomes: a systematic review and meta-analysis. Lancet 2015; online Aug 26.
590. Caudle KE, Rettie AE, Whirl-Carrillo M, et al. Clinical pharmacogenetics implementation consortium guidelines for **CYP2C9 and HLA-B genotypes and phenytoin dosing**. Clin Pharmacol Ther. 2014 Nov;96(5):542-8.
591. French JA, Krauss GL, Wechsler RT, et al. **Perampanel** for tonic-clonic seizures in idiopathic generalized epilepsy: A randomized trial. Neurology. 2015 Aug 21.
592. Friedman D, Devinsky O. Cannabinoids in the Treatment of Epilepsy. N Engl J Med. 2015 Sep 10;373(11):1048-58.
593. Howell KB, McMahon JM, et al. **SCN2A encephalopathy**: A major cause of epilepsy of infancy with migrating focal seizures. Neurology. 2015 Sep 15;85(11):958-66.
594. Tomson T, Battino D, et al; EURAP Study Group. Dose-dependent **teratogenicity of valproate** in mono- and polytherapy: An observational study. Neurology. 2015 Sep 8;85(10):866-72.
595. Baca CB, Barkley GL. Can **big data help us close an epilepsy care gap**? Neurology. 2015 Aug 26.
596. Grinspan ZM, Shapiro JS, Abramson EL, et al. Predicting **frequent ED** use by people with epilepsy with health information exchange data. Neurology. 2015 Aug 26.
597. Tang V, Poon WS, Kwan P. **Mindfulness-based therapy** for drug-resistant epilepsy: An assessor-blinded randomized trial.Neurology. 2015 Sep 2.
598. Kawai AT, Martin D, Kulldorff M, et al. Febrile **Seizures After 2010-2011 Trivalent Inactivated Influenza Vaccine**. Pediatrics. 2015 Sep 14.
599. Meletti S, Slonkova J, Mareckova I, et al. **Claustrum damage** and refractory status epilepticus following febrile illness. Neurology. 2015 Oct 6;85(14):1224-32.
600. Shinnar S, Cnaan A, Hu F, et al; Childhood Absence Epilepsy Study Group. **Long-term outcomes of generalized tonic-clonic seizures in a childhood** absence epilepsy trial. Neurology. 2015 Sep 29;85(13):1108-14.
601. Sutter R, Rüegg S, Tschudin-Sutter S. **Seizures as adverse events of antibiotic drugs**: A systematic review. Neurology. 2015 Sep 23.
602. Busch RM, Love TE, Jehi LE, et al. Effect of **invasive EEG monitoring on cognitive outcome** after left temporal lobe epilepsy surgery. Neurology. 2015 Oct 27;85(17):1475-81.
603. Devinsky O, Asato M, Camfield P, et al. Delivery of epilepsy care to adults with **intellectual and developmental disabilities**. Neurology. 2015 Oct. 27;85(17):1512-21.
604. Edelvik A, Flink R, Malmgren K. Prospective and longitudinal **long-term employment outcomes** after resective epilepsy **surgery**. Neurology. 2015 Oct 27;85(17):1482-90.
605. Saavalainen T, Jutila L, et al. **Temporal anteroinferior encephalocele**: An underrecognized etiology of temporal lobe epilepsy? Neurology. 2015 Oct 27;85(17):1467-74.
606. Vertigan AE, Kapela SL, Ryan NM, et al. **Pregabalin** and speech pathology combination therapy for refractory **chronic cough**: A randomised controlled trial. Chest. 2015 Oct 8.
607. Alexandre V, Mercedes B, Valton L, et al. **Risk factors of postictal generalized EEG suppression** in generalized convulsive seizures. Neurology 2015;85:1598–1603. (Whatever the type of GCS, occurrence of PGES was prevented by early administration of **oxygen**.)
608. Brigo F, Igwe SC. Antiepileptic drugs for the treatment of **infants with severe myoclonic epilepsy**. Cochrane Database Syst Rev. 2015 Oct 19;10:CD010483. Data derived from two small RCTs indicate that STP is significantly better than placebo with regards to 50% or greater reduction in seizure frequency and seizure freedom. Adverse effects occurred more frequently with STP. Additional adequately powered studies with long-term follow-up should be conducted to unequivocally establish the long-term efficacy and tolerability of STP in the treatment of patients with SMEI.
609. Gaspard N, Foreman BP, Alvarez V, et al; Critical Care EG Monitoring Research Consortium (CCEMRC); Critical Care EEG Monitoring Research Consortium CCEMRC. **New-onset refractory status epilepticus**: Etiology, clinical features, and outcome. Neurology. 2015 Aug 21.
610. Olsen M, Thygesen SK, Østergaard JR, et al. Hospital-Diagnosed **Pertussis Infection** in Children and Long-term Risk of Epilepsy. JAMA. 2015 Nov 3;314(17):1844-1849.
611. Srinivasakumar P, Zempel J, et al. **Treating EEG Seizures in Hypoxic Ischemic Encephalopathy**: A Randomized Controlled Trial. Pediatrics. 2015 Nov;136(5):e1302-9.
612. Vollono C, Fuggetta F, Cioni B, et al. Teaching NeuroImages: **Obstructive sleep apnea triggered** by **vagus nerve stimulation**. Neurology. 2015 Nov 3;85(18):e140.
613. Wu YW, Sullivan J, McDaniel SS, et al. Incidence of **Dravet Syndrome** in a US Population. Pediatrics. 2015 Nov;136(5):e1310-5.

614. Asadi P, Monsef Kasmaei V, et al. Prevalence of **Tramadol Consumption** in **First Seizure** Patients; a One-Year Cross-sectional Study. Emerg (Tehran). 2015 Fall;3(4):159-61.
615. Arya R, Kothari H, Zhang Z, et al. Efficacy of **nonvenous medications** for **acute convulsive seizures**: A network meta-analysis. Neurology. 2015 Oct 28.
616. Kessing LV, et al. Use of **Lithium** and **Anticonvulsants** and the Rate of **Chronic Kidney Disease**: A Nationwide Population-Based Study. JAMA Psychiatry. 2015 Nov 4:1-10.
617. Lecker I, Wang DS, Whissell PD, et al. **Tranexamic acid**-associated seizures: Causes and treatment. Ann Neurol. 2015 Nov 18.
618. Navarro V, Dagron C, Elie C, et al; **SAMUKeppra** investigators. Prehospital treatment with **levetiracetam plus clonazepam** or placebo plus clonazepam in status epilepticus (SAMUKeppra): a randomised, double-blind, phase 3 trial. Lancet Neurol. 2015 Nov 25.
619. Bagnall RD, et al. Exome-based analysis of cardiac arrhythmia, respiratory control and epilepsy **genes** in **sudden unexpected death in epilepsy**. Ann Neurol. 2015 Dec 24.
620. Burneo JG, Shariff SZ, Liu K, et al. **Disparities in surgery** among patients with intractable epilepsy in a universal health system. Neurology. 2016 Jan 5;86(1):72-8.
621. Devinsky O, Marsh E, Friedman D, et al. **Cannabidiol** in patients with treatment-resistant epilepsy: an open-label interventional trial. Lancet Neurol. 2015 Dec 23.
622. Hesdorffer DC, Ishihara L, Webb DJ, et al. Occurrence and Recurrence of **Attempted Suicide** Among People With Epilepsy. JAMA Psychiatry. 2015 Dec 9:1-7.
623. Josephson CB, Sauro K, Wiebe S, et al. Medical vs invasive therapy in **AVM-related epilepsy**: Systematic review and meta-analysis. Neurology. 2016 Jan 5;86(1):64-71.
624. Knupp KG, Coryell J, et al; Pediatric Epilepsy Research Consortium. Response To Treatment In A Prospective National **Infantile Spasms** Cohort. Ann Neurol. 2015 Dec 24.
625. Sauro KM, Wiebe S, Dunkley C, et al. The current **state of epilepsy guidelines**: A systematic review. Epilepsia. 2015 Dec 10.
626. Lwin EM, Ellis D, Song Y, et al. Stability Studies of Extemporaneously Compounded **Clobazam Oral Suspension**. Ann Pharmacother. 2015 Nov 23.
627. Tomson T, Battino D, Perucca E. **Valproic acid after five decades of use in epilepsy**: time to reconsider the indications of a time-honoured drug. Lancet Neurol 2016; 15: 210–18.
628. Barba C, Rheims S, Minotti L, et al. **Temporal plus epilepsy** is a major determinant of temporal lobe surgery failures. Brain. 2015 Dec 22.
629. De Marchis GM, Pugin D, Meyers E, et al. Seizure burden in **subarachnoid hemorrhage** associated with functional and cognitive outcome. Neurology 2016;86:253–260.
630. Meador KJ, Loring DW. **Developmental effects of antiepileptic drugs** and the need for improved regulations. Neurology. 2016 Jan 19;86(3):297-306.
631. Pitkänen A, Roivainen R, Lukasiuk K. Development of **epilepsy after ischaemic stroke**. Lancet Neurol. 2015 Nov 13.
632. Raftopoulos R, Hickman SJ, Toosy AT, et al. **Phenytoin for neuroprotection** in patients with acute optic neuritis: a randomised, placebo-controlled, phase 2 trial. Lancet Neurol 2016; online Jan 25.
633. Krishnamurthy KB. **Epilepsy-In the Clinic**. Ann Intern Med. 2016 Feb 2;164(3):ITC17-ITC32.
634. Privitera M, Welty TE, et al. **Generic-to-generic lamotrigine switches** in people with epilepsy: the randomised controlled EQUIGEN trial. Lancet Neurol 2016; online Feb 11.
635. Afawi Z, Oliver KL, Kivity S, et al. **Multiplex families** with epilepsy: Success of clinical and molecular genetic characterization. Neurology. 2016 Feb 23;86(8):713-722.
636. Devinsky O, Spruill T, Thurman D, Friedman D. Recognizing and **preventing epilepsy-related mortality**: A call for action. Neurology. 2016 Feb 23;86(8):779-786.
637. Glauser T, Shinnar S, Gloss D, et al. Evidence-Based Guideline: **Treatment of Convulsive Status Epilepticus in Children and Adults**: Report of the Guideline Committee of the **American Epilepsy Society**. Epilepsy Curr. 2016 Jan-Feb;16(1):48-61.
638. Hong SJ, Bernhardt BC, Schrader DS, et al. **Whole-brain MRI phenotyping** in dysplasia-related frontal lobe epilepsy. Neurology. 2016 Feb 16;86(7):643-50.
639. Keezer MR, Bell GS, et al. Cause of **death and predictors of mortality** in a community-based cohort of people with epilepsy. Neurology 2016;86:704–712.
640. McTague A, Howell KB, Cross JH, et al. The genetic landscape of the **epileptic encephalopathies** of infancy and childhood. Lancet Neurol. 2015 Nov 16.
641. Mersfelder TL, Nichols WH. **Gabapentin**: Abuse, Dependence, and Withdrawal. Ann Pharmacother. 2015 Dec 31.
642. Sillanpää M, Gissler M, Schmidt D. Efforts in **Epilepsy Prevention in the Last 40 Years**: Lessons From a Large Nationwide Study. JAMA Neurol. 2016 Feb 15.
643. Xiao F, An D, Lei D, Li L, Real-time effects of centrotemporal spikes on cognition in **rolandic epilepsy**: An EEG-fMRI study. Neurology. 2016 Feb 9;86(6):544-51.
644. Duncan JS, Winston GP, Koepp MJ, et al. **Brain imaging** in the assessment for epilepsy **surgery**. Lancet Neurol. 2016 Feb 23.
645. Jones AL, Cascino GD. Evidence on Use of **Neuroimaging** for **Surgical** Treatment of **Temporal Lobe Epilepsy**: A Systematic Review. JAMA Neurol. 2016 Feb 29.
646. Ting TY, Jiang W, Lionberger R, et al. **Generic lamotrigine versus brand-name Lamictal bioequivalence** in patients with epilepsy: A field test of the FDA bioequivalence standard. Epilepsia. 2015;56:1415-1424.
647. Buckley MS, Reeves BA, et al. Correlation of **Free and Total Phenytoin Serum Concentrations** in Critically Ill Patients. Ann Pharmacother. 2016 Apr;50(4):276-81.
648. Kiang TK, Ensom MH. A Comprehensive Review on the Predictive Performance of the **Sheiner-Tozer and Derivative Equations for the Correction of Phenytoin** Concentrations. Ann Pharmacother. 2016 Apr;50(4):311-25.
649. Leong C, Mamdani MM, Gomes T, et al. **Antiepileptic use for epilepsy and nonepilepsy disorders**: A population-based study (1998-2013). Neurology. 2016 Feb 5.
650. Berg AT, Baca CB, Rychlik K, et al. **Determinants of Social Outcomes** in Adults With Childhood-onset Epilepsy. Pediatrics. 2016 Mar 16.
651. Chen Z, Liew D, Kwan P. Real-world cost-effectiveness of **pharmacogenetic screening** for epilepsy treatment. **(HLA-B*15:02)** Neurology 2016;86:1086–1094.
652. Lattanzi S, Cagnetti C, Foschi Net al. **Brivaracetam** add-on for refractory focal epilepsy: A systematic review and meta-analysis. Neurology. 2016 Apr 5
653. Pourzitaki C, Tsaousi G, Apostolidou E, et al. Efficacy and safety of **prophylactic levetiracetam** in supratentorial **brain tumour surgery**: a systematic review and meta-analysis. Br J Clin Pharmacol. 2016 Mar 5
654. Sperling MR, French J, Jacobson MP, et al; Study 045 and 046 Investigators. Conversion to **eslicarbazepine acetate monotherapy**: A pooled analysis of 2 phase III studies.

Neurology. 2016 Mar 22;86(12):1095-102.
655. Tu YF, Wang LW, Wang ST, et al. **Postnatal Steroids** and Febrile Seizure Susceptibility in Preterm Children. Pediatrics. 2016 Mar 24.
656. Zhang YX, Shen CH, Lai QL, et al. Effects of **antiepileptic drug on thyroid hormones** in patients with epilepsy: A meta-analysis. Seizure. 2016 Feb;35:72-9.
657. Burkholder DB, Britton JW, Rajasekaran V, et al. **Routine vs extended outpatient EEG** for the detection of interictal epileptiform discharges. Neurology. 2016 Mar 16.
658. French JA, Berg MJ. The place of **generic modified-release formulations for epilepsy**: Slow and steady. Neurology. 2016 Mar 25
659. Hildebrand MS, Myers CT, Carvill GL, Ret al. A targeted **resequencing gene panel** for **focal epilepsy**. Neurology. 2016 Mar 30
660. Johnson EL, Chang YT, Davit B, Gidal BE, Krauss GL. **Assessing bioequivalence of generic modified-release antiepileptic drugs**. Neurology 2016;86:1597–1604.
661. Marson A, Guerrini R. **Testing HLA-B*15:02: Is it worth it**? Neurology. 2016 Mar 22
662. Pdf Chui CS, Chan EW, Wong AY, et al. Association between **oral fluoroquinolones and seizures**: A self-controlled case series study. Neurology. 2016 May 3;86(18):1708-15.
663. Dolk H, Wang H, Loane M, et al. **Lamotrigine use in pregnancy** and risk of orofacial cleft and other congenital anomalies. Neurology. 2016 May 3;86(18):1716-25.
664. Hainque E, Vidailhet M, Cozic N, et al. A randomized, controlled, double-blind, crossover trial of **zonisamide in myoclonus-dystonia**. Neurology. 2016 May 3;86(18):1729-35.
665. Leone MA, Giussani G, Nolan SJ, et al. **Immediate antiepileptic drug treatment, versus placebo**, deferred, or no treatment for **first unprovoked seizure**. Cochrane Database Syst Rev. 2016 May 6;5:CD007144. Treatment of the first unprovoked seizure reduces the risk of a subsequent seizure but does not affect the proportion of patients in remission in the long-term. Antiepileptic drugs are associated with adverse events, and there is no evidence that they reduce mortality. In light of this review, the decision to start antiepileptic drug treatment following a first unprovoked seizure should be individualized and based on patient preference, clinical, legal, and socio-cultural factors.
666. Winterfeld U, Merlob P, Baud D, et al. **Pregnancy outcome following maternal exposure to pregabalin** may call for concern. Neurology. 2016 May 18.
667. Mintzer S, French JA, Perucca E, et al. Is a **separate monotherapy indication warranted for antiepileptic drugs**? Lancet Neurol. 2015 Dec;14(12):1229-40.
668. Pitkänen A, Löscher W, Vezzani A, et al. Advances in the development of **biomarkers for epilepsy**. Lancet Neurol 2016; 15: 843–56.
669. Sperling MR, Barshow S, Nei M, Asadi-Pooya AA. A reappraisal of **mortality after epilepsy surgery**. Neurology 2016;86:1938–1944.
670. Fox CK, Glass HC, Sidney S, et al. **Neonatal seizures** triple the risk of a remote seizure after perinatal ischemic stroke. Neurology. 2016 May 6.
671. Kinney MO, Morrow J. **Epilepsy in pregnancy**. BMJ. 2016 Jun 2;353:i2880.
672. Aaberg KM, Bakken IJ, Lossius MI, Lund et al. **Comorbidity and Childhood Epilepsy**: A Nationwide Registry Study.Pediatrics. 2016 Aug 1
673. Ben-Menachem E, Mameniškienė R, et al. Efficacy and safety of **brivaracetam** for partial-onset seizures in 3 pooled clinical studies. Neurology. 2016 Jul 19;87(3):314-23.
674. Bertelsen EN, Larsen JT, Petersen L, et al. Childhood Epilepsy, Febrile Seizures, and Subsequent **Risk of ADHD**. Pediatrics. 2016 Jul 13.
675. Chen Z, Liew D, Kwan P. Excess **mortality and hospitalized morbidity** in **newly treated epilepsy** patients. Neurology. 2016 Aug 16;87(7):718-25.
676. Chong L, Jamieson NJ, Gill D, Singh-et al. **Children's Experiences of Epilepsy**: A Systematic Review of Qualitative Studies. Pediatrics. 2016 Aug 10.
677. Gollwitzer S, Kostev K, Hagge M, et al. **Nonadherence** to antiepileptic drugs in Germany: A retrospective, population-based study. Neurology. 2016 Aug 2;87(5):466-72
678. Sundelin HE, Larsson H, Lichtenstein P, et al. **Autism** and epilepsy: A population-based nationwide cohort study. Neurology. 2016 Jul 12;87(2):192-7.
679. Zelcer M, Goldman RD. **Intranasal midazolam** for seizure cessation in the community setting. Can Fam Physician. 2016 Jul;62(7):559-61.
680. Bromley RL, Calderbank R, Cheyne CP, et al. **Cognition in school-age children exposed to levetiracetam, topiramate, or sodium valproate**. Neurology. 2016 Aug 31.
681. French JA, Lawson JA, Yapici Z, Ikeda et al. Adjunctive **everolimus** therapy for treatment-resistant focal-onset seizures associated with **tuberous sclerosis** (EXIST-3): a phase 3, randomised, double-blind, placebo-controlled study. Lancet. 2016 Sep 6.
682. Matsuda KM, Sharma D, Schonfeld AR et al. **Gabapentin** and **pregabalin** for the treatment of chronic **pruritus**. J Am Acad Dermatol. 2016 Sep;75(3):619-625.
683. Overwater IE, et al. **Sirolimus** for epilepsy in children with **tuberous sclerosis** complex: A randomized controlled trial. Neurology. 2016 Sep 6;87(10):1011-8.
684. French J, Glue P, Friedman D, et al. Adjunctive **pregabalin vs gabapentin for focal seizures**: Interpretation of comparative outcomes. Neurology. 2016 Sep 20;87(12):1242-1249.
685. Health Canada Sep/16 Zarontin (**ethosuximide**) - Defective Capsules Associated with Reduced Efficacy (Increased Frequency of Seizures) - Erfa Canada 2012 Inc. Erfa Canada 2012 Inc. and Health Canada have received reports of broken or leaking Zarontin soft gel capsules. Administration of defective Zarontin soft gel capsules can be associated with a lack of efficacy (increased frequency of seizures).
686. Hoda S, O'Brien J, Gamble J. **Intractable seizures** in a toddler after application of an over-the-counter local anesthetic cream (**lidocaine**). CMAJ. 2016 Oct 4;188(14):1030-1032.
687. Zelano J. **Poststroke epilepsy**: update and future directions. Ther Adv Neurol Disord. 2016 Sep;9(5):424-35.
688. Alvarez V, Lee JW, Westover MB, et al. **Therapeutic coma** for status epilepticus: differing practices in a prospective multicenter study. Neurology 2016;87:1650–1659.
689. Auerbach DS, McNitt S, Gross RA, et al. **Genetic biomarkers** for the risk of seizures in **long QT syndrome**. Neurology. 2016 Oct 18;87(16):1660-1668.
690. Health Canada Oct/16 . Summary safety review – **gabapentin** – assessing the potential risk of **serious breathing problems**. September 16, 2016. www.hc-sc.gc.ca/dhp-mps/medeff/reviews-examens/gabapentin-eng.php (accessed October 6, 2016).
691. Kesselheim AS, Bykov K, Gagne JJ, et al. **Switching generic antiepileptic** drug **manufacturer** not linked to seizures: A case-crossover study. Neurology. 2016 Sep 28.
692. Rayner G, Jackson GD, Wilson SJ. Mechanisms of **memory impairment** in epilepsy depend on age at disease onset. Neurology. 2016 Oct 18;87(16):1642-1649.
693. Tao JX, Davis AM. Management of an **Unprovoked First Seizure** in Adults. JAMA. 2016 Oct 18;316(15):1590-1591.

694. Zhang L, Li S, Li H, Zou X. **Levetiracetam vs. brivaracetam** for adults with refractory focal seizures: a meta-analysis and indirect comparison. Seizure. 2016;39:28-33.
695. Bromley RL, Calderbank R, et al. **Cognition** in school-age children exposed to **levetiracetam,topiramate, or sodium valproate**. Neurology. 2016 Nov 1;87(18):1943-1953.
696. Gidal BE, et al. Deconstructing **tolerance** with **clobazam**: Post hoc analyses from an open-label extension study. Neurology. 2016 Oct 25;87(17):1806-1812.
697. Hornik CP, et al. Electronic Health Records and Pharmacokinetic Modeling to Assess the Relationship between **Ampicillin Exposure** and Seizure Risk in Neonates. J Pediatr. 2016 Nov;178:125-129.e1
698. Siegel J, Tatum WO. **Hand postures** in primary and secondary generalized tonic-clonic seizures. Neurology. 2016 Oct 25;87(17):1802-1805.
699. Guo J, Kim R, Chen Y, et al. Mechanism of **impaired consciousness in absence seizures**: a crosssectional study. Lancet Neurol 2016; 15: 1336–45.
700. Reeves D, DiDominick S, Finn S, et al. **Methotrexate** Elimination When Coadministered With **Levetiracetam**. Ann Pharmacother. 2016 Dec;50(12):1016-1022.
701. Thodeson DM, Reiber DC, Dolce AM, et al. **Fosphenytoin-induced dyskinesias** in an infant with Sturge-Weber syndrome. Neurology. 2016 Apr 19;86(16):1561-2.
702. Weston J, Bromley R, Jackson CF, et al. **Monotherapy treatment of epilepsy in pregnancy**: congenital malformation outcomes in the child. Cochrane Database of Systematic Reviews 2016, Issue 11. Art. No.: CD010224. Exposure in the womb to certain AEDs carried an increased risk of malformation in the foetus and may be associated with specific patterns of malformation. Based on current evidence, LEV and LTG exposure carried the lowest risk of overall malformation; however, data pertaining to specific malformations are lacking. Physicians should discuss both the risks and treatment efficacy with the patient prior to commencing treatment.
703. Nolan SJ, Tudur Smith C, Weston J, et al. **Lamotrigine versus carbamazepine monotherapy for epilepsy**: an individual participant data review. Cochrane Database Syst Rev. 2016 Nov 14;11:CD001031. Lamotrigine was significantly less likely to be withdrawn than carbamazepine but the results for time to first seizure suggested that carbamazepine may be superior in terms of seizure control. A choice between these first-line treatments must be made with careful consideration. We recommend that future trials should be designed to the highest quality possible with consideration of masking, choice of population, classification of seizure type, duration of follow-up, choice of outcomes and analysis, and presentation of results.
704. O'Callaghan FJ, Edwards SW, Alber FD, et al. Safety and effectiveness of **hormonal treatment versus hormonal treatment with vigabatrin** for **infantile spasms (ICISS)**: a randomised, multicentre, open-label trial. Lancet Neurol. 2016 Nov 9.
705. Shellhaas R, Chang T, Wusthoff C, et al. **Treatment Duration After Acute Symptomatic Seizures in Neonates**: A Multicenter Cohort Study. J Pediatr. 2016 Nov 7.
706. Baulac M, Rosenow F, Toledo M, et al. Efficacy, safety, and tolerability of **lacosamide monotherapy versus controlled-release carbamazepine** in patients with newly diagnosed epilepsy: a phase 3, randomised, double-blind, non-inferiority trial. Lancet Neurol 2016; online Nov 23.
707. Busch RM, Floden DP, Prayson B, et al. Estimating risk of **word-finding problems in adults undergoing epilepsy surgery**. Neurology. 2016 Nov 29;87(22):2363-2369.
708. Henshall DC, Hamer HM, Pasterkamp RJ, et al. **MicroRNAs in epilepsy**: pathophysiology and clinical utility. Lancet Neurol. 2016 Dec;15(13):1368-1376.
709. Siefkes HM, Holsti M, et al. **Seizure Treatment in Children Transported to Tertiary Care**: Recommendation Adherence and Outcomes. Pediatrics.2016;138(6):e20161527
710. Devinsky O, Marsh E, Friedman D, et al. **Cannabidiol** in patients with treatment-resistant epilepsy: an open-label interventional trial. Lancet Neurol 2016; 15: 270–78.
711. Engel J Jr. What can we do for people with **drug-resistant epilepsy**? The 2016 Wartenberg Lecture. Neurology. 2016 Dec 6;87(23):2483-2489.
712. Krueger DA, Wilfong AA, Mays M, et al. Long-term treatment of epilepsy with **everolimus in tuberous sclerosis**. Neurology. 2016 Dec 6;87(23):2408-2415
713. Chen CB, Hsiao YH, Wu T, et al. Risk and association of **HLA with oxcarbazepine-induced cutaneous adverse reactions in Asians**. Neurology. 2017 Jan 3;88(1):78-86.
714. Gavvala JR, Schuele SU. **New-Onset Seizure in Adults and Adolescents**: A Review. JAMA. 2016 Dec 27;316(24):2657-2668
715. Gavvala JR, Schuele SU. JAMA **Patient Page**: Epilepsy. JAMA. 2016 Dec 27;316(24):2686
716. Glauser T et al. Evidence-based guideline: Treatment of **convulsive status epilepticus** in children and adults: Report of the Guideline Committee of the **American Epilepsy Society**. Epilepsy Curr 2016Jan/Feb; 16:48.
717. Legriel S, Lemiale V, Schenck M, et al. **Hypothermia for Neuroprotection** in Convulsive Status Epilepticus. N Engl J Med. 2016 Dec 22;375(25):2457-2467.
718. Licchetta L, Bisulli F, Vignatelli L, et al. **Sleep-related hypermotor epilepsy**: Long-term outcome in a large cohort. Neurology. 2017 Jan 3;88(1):70-77.
719. Naidech AM, Beaumont J, Jahromi B, et al. Evolving use of **seizure medications after intracerebral hemorrhage**: a multicenter study. Neurology 2017;88:52–56.
720. Rom AL, Wu CS, Olsen J, et al. **Parental rheumatoid arthritis** and childhood epilepsy: A nationwide cohort study. Neurology. 2016 Dec 13;87(24):2510-2516.
721. Cnaan A, Shinnar S, Arya R, et al. **Second monotherapy** in **childhood absence** epilepsy. Neurology. 2017 Jan 10;88(2):182-190.
722. **Epi4K** & Epilepsy Phenome/Genome project. **Ultra-rare genetic variation** in common epilepsies: a case-control sequencing study. Lancet Neurol 2017; 16: 135–43.
723. Kim DW, Lee SK, Moon HJ, et al. **Surgical Treatment** of Nonlesional Neocortical Epilepsy: Long-term Longitudinal Study. JAMA Neurol. 2017 Jan 3.
724. Messe SR, Sansing LH, Cucchiara BL, et al. **Prophylactic antiepileptic drug** use is associated with poor outcome **following ICH**. (**CHANT**) Neurocrit Care 2009;11:38–44.
725. Hemphill JC 3rd, Greenberg SM, Anderson CS, et al; American Heart Association Stroke Council.; Council on Cardiovascular and Stroke Nursing.; Council on Clinical Cardiology.. **Guidelines for the Management of Spontaneous Intracerebral Hemorrhage**: A Guideline for Healthcare Professionals From the **American** Heart Association/American Stroke Association. Stroke. 2015 Jul;46(7):2032-60.
726. Naidech AM, Garg RK, Liebling S, et al. **Anticonvulsant use** and outcomes after **intracerebral hemorrhage**. Stroke 2009;40:3810–3815. (phenytoin worse)
727. Sheth KN, Martini SR, et al. Prophylactic antiepileptic drug use and outcome in the ethnic/racial variations of intracerebral hemorrhage study. Stroke 2015;46:3532–3535. (**ERICH**)

728. Naidech AM, Beaumont J, Jahromi B, et al. Evolving use of **seizure medications after intracerebral hemorrhage**: a multicenter study. Neurology 2017;88:52–56.
729. Fiest KM, Sauro KM, Wiebe S, et al. **Prevalence and incidence of epilepsy**: A systematic review and meta-analysis of international studies. Neurology. 2017 Jan 17;88(3):296-303.
730. Lapham G, Gaillard WD, Sexter J, et al. Increasing Awareness of **Sudden Death** in Pediatric Epilepsy Together. Pediatrics. 2017 Jan 23.
731. Szaflarski JP, Gloss D, Binder JR, et al. Practice guideline summary: Use of **fMRI in the presurgical evaluation** of patients with epilepsy: Report of the Guideline Development, Dissemination, and Implementation Subcommittee of the American Academy of Neurology. Neurology. 2017 Jan 24;88(4):395-402.
740. Garnett WR. **Antiepileptic drug treatment**: Outcomes and adherence. Pharmacotherapy 2000;20:191S–199S.
741. Offringa, Martin, et al. "**Prophylactic drug** management for **febrile seizures in children**." *The Cochrane Library* (2017).
742. Canadian League Against Epilepsy. **Clobazam Shortage** 2016. Retrieved from https://medsask.usask.ca/documents/drug-shortages/Clobazam%20Shortage_2016_Final.pdf on April 30, 2017.
743. Aaberg KM, Gunnes N, Bakken IJ, et al. **Incidence and Prevalence of Childhood Epilepsy**: A Nationwide Cohort Study. Pediatrics. 2017;139(5):e20163908
744. Adams J, Alipio-Jocson V, Inoyama K, et al. **Methylphenidate**, cognition, and epilepsy: A double-blind, placebo-controlled, single-dose study. Neurology. 2017 Jan 31;88(5):470-476
745. Agulnik A, Kelly DP, Bruccoleri R, et al. Combination Clearance Therapy and **Barbiturate Coma for Severe Carbamazepine Overdose**. Pediatrics. 2017;139(5):e20161560
746. Al-Aqeel S, Gershuni O, Al-Sabhan J, et al. Strategies for **improving adherence** to antiepileptic drug treatment in people with epilepsy. Cochrane Database Syst Rev. 2017 Feb 3;2:CD008312. Behavioural interventions such as intensive reminders and the use of mixed interventions demonstrate some positive results; however, we need more reliable evidence on their efficacy, derived from carefully-designed randomised controlled trials before we can draw a firm conclusion. Since the last version of this review, none of the new relevant studies have provided additional information that would lead to significant changes in our conclusions. This current update includes 12 studies, of which six came from the latest searches.
747. Baca CB, Barry F, Vickrey BG, et al. **Social outcomes** of young adults with childhood-onset epilepsy: A case-sibling-control study. Epilepsia. 2017 Apr 4.
748. Bauerschmidt A, Martin A, Claassen J. Advancements in the **critical care management of status epilepticus**. Curr Opin Crit Care. 2017 Feb 14.
749. Berg M, Welty TE, Gidal BE, et al. **Bioequivalence between generic and branded lamotrigine** in people with epilepsy: the **EQUIGEN** randomized clinical trial [online June 26, 2017].JAMA Neurol. doi:10.1001/jamaneurol.2017.0497
750. Berg AT, Coryell J, Saneto RP, et al. Early-Life Epilepsies and the Emerging Role of **Genetic Testing**. JAMA Pediatr. 2017 Jul 31.
751. Berl MM, Goodkin HP, Kroner BL, et al. **Sudden Death in Epilepsy**: Knowledge among Pediatric Providers. J Pediatr. 2017 Jun 16.
752. Birnbaum AK, Leppik IE, Svensden K, et al. Prevalence of epilepsy/seizures as a comorbidity of neurologic disorders **in nursing homes**. Neurology. 2017 Feb 21;88(8):750-757.
753. Brigo F, Igwe SC. **Ethosuximide, sodium valproate or lamotrigine for absence seizures** in children and adolescents. Cochrane Database Syst Rev. 2017 Feb 14;2:CD003032. With regards to both efficacy and tolerability, ethosuximide represents the optimal initial empirical monotherapy for children and adolescents with absence seizures. However, if absence and generalised tonic-clonic seizures coexist, valproate should be preferred, as ethosuximide is probably inefficacious on tonic-clonic seizures.
754. Burton A. What about a **seizure-alert dog**? Lancet Neurol. 2017 Apr;16(4):265-266.
755. Busch RM, Floden DP, Ferguson L, et al. Neuropsychological outcome following **frontal lobectomy** for pharmacoresistant epilepsy in adults. Neurology. 2017 Feb 14;88(7):692-700.
756. Caciagli L, Bernasconi A, Wiebe S, et al. A meta-analysis on **progressive atrophy** in intractable temporal lobe epilepsy: Time is brain? Neurology. 2017 Aug 1;89(5):506-516.
757. Cervenka MC, Hocker S, Koenig M, et al. Phase I/II multicenter **ketogenic diet** study for adult superrefractory status epilepticus. Neurology. 2017 Mar 7;88(10):938-943
758. Choi H, Pack A, Elkind MS, et al. Predictors of incident **epilepsy in older adults**: The Cardiovascular Health Study. Neurology. 2017 Feb 28;88(9):870-877.
759. Cohen AL, Jones LK, Parisi JE, et al. Intractable Epilepsy and Progressive **Cognitive Decline** in a Young Man. JAMA Neurol. 2017 Jun 1;74(6):737-740.
760. Cooper TE, Wiffen PJ, Heathcote LC, et al. **Antiepileptic drugs for chronic non-cancer pain** in children and adolescents. Cochrane Database Syst Rev. 2017 Aug 5;8:CD012536. This review identified only two small studies, with insufficient data for analysis.As we could undertake no meta-analysis, we were unable to comment about efficacy or harm from the use of antiepileptic drugs to treat chronic non-cancer pain in children and adolescents. Similarly, we could not comment on our remaining secondary outcomes: Carer Global Impression of Change; requirement for rescue analgesia; sleep duration and quality; acceptability of treatment; physical functioning; and quality of life.We know from adult randomised controlled trials that some antiepileptics, such as gabapentin and pregabalin, can be effective in certain chronic pain conditions.We found no evidence to support or refute the use of antiepileptic drugs to treat chronic non-cancer pain in children and adolescents.
761. Devinsky O, Cross JH, Laux L, et al. Trial of **cannabidiol** for drug-resistant seizures in the **Dravet syndrome**. N Engl J Med 2017;376:2011-20.
762. Drugs for **Epilepsy**: **Treatment Guidelines** from the Medical Letter, May **2003, Updated June 2008, Feb 2012,** (**Updated July 2017**)
763. Gaston TE, Bebin EM, Cutter GR, et al; UAB CBD Program. **Interactions between cannabidiol and commonly used antiepileptic drugs**. Epilepsia. 2017 Aug 6.
764. Gooneratne IK, Wimalaratna M, Ranaweera AKP, et al. **Contraception advice for women with epilepsy**. BMJ. 2017 May 11;357:j2010.
765. Gupta A, Yek C, Hendler RS. **Phenytoin Toxicity**-Performance Improvement. JAMA. 2017 Jun 20;317(23):2445-2446
766. Harden C, Tomson T, Gloss D, et al. Practice guideline summary: **sudden unexpected death** in epilepsy incidence rates and risk factors: report of the Guideline Development, Dissemination, and Implementation Subcommittee of the American Academy of Neurology (**AAN**) and the American Epilepsy Society (AES). Neurology 2017;88:1674–1680.
767. He X, Doucet GE, Pustina D, et al. Presurgical **thalamic** "**hubness**" predicts surgical outcome in temporal lobe epilepsy. Neurology. 2017 Jun 13;88(24):2285-2293.

768. Herzog AG, Mandle HB, Cahill KE, et al. Predictors of **unintended pregnancy** in women with epilepsy. Neurology. 2017 Feb 21;88(8):728-733.
769. Huttunen J, Lindgren A, Kurki MI, et al. Epilepsy-associated long-term mortality **after aneurysmal subarachnoid hemorrhage**. Neurology. 2017 Jun 14.
770. Jackson GD, Pedersen M, Harvey AS. **How small can the epileptogenic region be**? A case in point. Neurology. 2017 May 23;88(21):2017-2019.
771. Josephson CB, Lowerison M, et al. **Association of Depression** and Treated Depression With Epilepsy and Seizure Outcomes: A Multicohort Analysis. JAMA Neurol. 2017 Feb 27.
772. Joutsa J, Rinne JO, Hermann B, et al. Association Between Childhood-Onset Epilepsy and **Amyloid Burden** 5 Decades Later. JAMA Neurol. 2017 Mar 27.
773. Kessler SK, Shinnar S, Cnaan A, et al. **Pretreatment seizure semiology** in childhood absence epilepsy. Neurology. 2017 Jul 19.
774. Korff CM, Dale RC. The **Immune System** in Pediatrics Seizures and Epilepsies. Pediatrics. 2017;140(3):e20163534
775. Lahti AM, Saloheimo P, Huhtakangas J, et al. **Poststroke epilepsy** in long-term survivors of primary **intracerebral hemorrhage**. Neurology. 2017 Jun 6;88(23):2169-2175.
776. Lamberink HJ, Otte WM, Geerts AT, et al. Individualised **prediction model of seizure recurrence and long-term outcomes** after withdrawal of antiepileptic drugs in seizure-free patients: a systematic review and individual participant data meta-analysis. Lancet Neurol. 2017 May 5.
777. Liu G, Slater N., Perkins A. **Epilepsy: Treatment Options**. Am Fam Physician. 2017;96(2):87-96.
778. Lyndon A, Audrey S, Wells C, et al. Risk to **heroin users** of polydrug use of pregabalin or gabapentin. Addiction. 2017 May 10.
779. Lloyd RO, O'Toole JM, Pavlidis E, et al. **Electrographic Seizures** during the Early Postnatal Period in Preterm Infants. J Pediatr. 2017 Mar 30.
780. Manford M. **Recent advances in epilepsy**. J Neurol. 2017 Jan 24.
781. Meador KJ, Lindhout D. Epilepsy and **unintended pregnancies**. Neurology. 2017 Feb 21;88(8):724-725
782. MHRA Apr/17 Babies born to mothers who take **valproate** medicines (Epilim▼, Depakote▼) during pregnancy have a 30–40% risk of **developmental disability** and a 10% risk of birth defects.
782. Myers KA, McMahon JM, et al. **Fatal Cerebral Edema** with Status Epilepticus in Children with **Dravet Syndrome**: Report of 5 Cases. Pediatrics. 2017;139(4):e20161933
783. Nevitt SJ, Sudell M, Weston J et al. **Antiepileptic drug monotherapy for epilepsy**: a network meta-analysis of individual participant data. Cochrane Database of Systematic Reviews 2017, Issue 6. Art. No.: CD011412. Overall, the high-quality evidence provided by this review supports current guidance (e.g. NICE) that carbamazepine and lamotrigine are suitable first-line treatments for individuals with partial onset seizures and also demonstrates that levetiracetam may be a suitable alternative. High-quality evidence from this review also supports the use of sodium valproate as the first-line treatment for individuals with generalised tonic-clonic seizures (with or without other generalised seizure types) and also demonstrates that lamotrigine and levetiracetam would be suitable alternatives to either of these first-line treatments, particularly for those of childbearing potential, for whom sodium valproate may not be an appropriate treatment option due to teratogenicity.
784. Offringa M, Newton R, Cozijnsen MA, et al. **Prophylactic drug management for febrile seizures in children**. Cochrane Database Syst Rev. 2017 Feb 22;2:CD003031. We found reduced recurrence rates for children with febrile seizures for intermittent diazepam and continuous phenobarbitone, with adverse effects in up to 30%. Apparent benefit for clobazam treatment in one trial needs to be replicated to be judged reliable. Given the benign nature of recurrent febrile seizures, and the high prevalence of adverse effects of these drugs, parents and families should be supported with adequate contact details of medical services and information on recurrence, first aid management and, most importantly, the benign nature of the phenomenon.
785. Patorno E, Bateman BT, Huybrechts KF, et al. **Pregabalin use early in pregnancy** and the risk of major congenital malformations. Neurology. 2017 May 23;88(21):2020-2025.
786. Picard RW, Migliorini M, Caborni C, et al. **Wrist sensor** reveals sympathetic hyperactivity and hypoventilation before probable **SUDEP**. Neurology. 2017 Aug 8;89(6):633-635
787. Razaz N, Tedroff K, Villamor E, et al. **Maternal Body Mass Index** in Early Pregnancy and Risk of Epilepsy in Offspring. JAMA Neurol. 2017 Apr 3.
788. Razaz N, Tomson T, Wikström AK, et al. Association Between **Pregnancy** and Perinatal Outcomes Among Women With Epilepsy. JAMA Neurol. 2017 Jul 3.
789. Rech MA, Barbas B, Chaney W, et al. When to Pick the Nose: Out-of-Hospital and Emergency Department **Intranasal Administration of Medications**. Ann Emerg Med. 2017 Mar 25. (midazolam)
790. Rosenthal ES, Claassen J, Wainwright MS, et al. **Brexanolone** as Adjunctive Therapy in Super-Refractory Status Epilepticus. Ann Neurol. 2017 Aug 5.
791. Scheffer IE, Berkovic S, Capovilla G, et al. **ILAE classification of the epilepsies**: Position paper of the ILAE Commission for Classification and Terminology. Epilepsia. 2017 Mar 8.
792. Semmlack S, Yeginsoy D, Spiegel R, et al. **Emergency response to out-of-hospital status epilepticus**: A 10-year observational cohort study. Neurology. 2017 Jul 25;89(4):376-384.
793. Shepshelovich D, Schechter A, Calvarysky B, et al. **Medication-induced SIADH**: distribution and characterization according to medication class. Br J Clin Pharmacol. 2017 Feb 7.
794. Shi YW, Min FL, Zhou D, et al. **HLA-A*24:02** as a common risk factor for antiepileptic drug-induced **cutaneous adverse reactions**. Neurology. 2017 Jun 6;88(23):2183-2191.
795. Shiner B, Westgate CL, Bernardy NC, et al. **Anticonvulsant Medication Use** in Veterans With **Posttraumatic Stress Disorder**. J Clin Psychiatry. 2017 May;78(5):e545-e552
796. Siddiqi OK, Elafros MA, Bositis CM, et al. **New-onset seizure in HIV-infected** adult Zambians: A search for causes and consequences. Neurology. 2017 Jan 31;88(5):477-482.
797. Steger M, Schneemann M, Fox M. Systemic review: the pathogenesis and pharmacological treatment of **hiccups**. Aliment Pharmacol Ther. 2015 Nov;42(9):1037-50.
798. Sveinsson O, Andersson T, Carlsson S, et al. The incidence of **SUDEP**: A nationwide population-based cohort study. Neurology. 2017 Jul 11;89(2):170-177.
799. Tang JY, Kiang TKL, Ensom MHH. Pharmacokinetic Interactions between **Valproic Acid and Lorazepam** (**PIVOtAL** Study): A Review of Site-Specific Practices. Can J Hosp Pharm. 2017 May-Jun;70(3):171-178.
800. Tobochnik S, Fahlstrom R, Shain C, et al. **Familial aggregation of focal seizure semiology** in the Epilepsy Phenome/Genome Project. Neurology. 2017 Jul 4;89(1):22-28.

801. Torolira D, Suchomelova L, Wasterlain CG, Niquet J. **Phenobarbital and Midazolam** Increase Neonatal Seizure-Associated Neuronal Injury. Ann Neurol. 2017 May 26.
802. Vossel KA, Tartaglia MC, Nygaard HB, et al. **Epileptic activity in Alzheimer's disease**: causes and clinical relevance. Lancet Neurol. 2017 Apr;16(4):311-322.
803. Wandschneider B, Burdett J, Townsend L, et al. Effect of **topiramate and zonisamide** on **fMRI cognitive networks**. Neurology. 2017 Mar 21;88(12):1165-1171.
804. Zaccara G, Giovannelli F, et al. **Do antiepileptic drugs increase the risk of infectious diseases**? A meta-analysis of placebo-controlled studies. Br J Clin Pharmacol. 2017 Mar 31.
805. Zack MM, Kobau R. National and State Estimates of the **Numbers of Adults and Children with Active Epilepsy** - **United States**, 2015. MMWR Morb Mortal Wkly Rep. 2017 Aug 11;66(31):821-825.
806. Berl MM, Goodkin HP, Kroner BL, et al. **Sudden Death in Epilepsy**: Knowledge among Pediatric Providers. J Pediatr. 2017 Jun 16.
807. Devinsky O, Friedman D, Cheng JY, et al. **Underestimation of sudden deaths** among patients with seizures and epilepsy. Neurology 2017; 89:886–892.
808. Shellhaas RA, Wusthoff CJ, Tsuchida TN, et al. **Profile of neonatal epilepsies**: characteristics of a prospective US cohort. Neurology 2017;89:893–899.
809. Bissell DM, Anderson KE, Bonkovsky HL. **Porphyria**. N Engl J Med. 2017 Aug 31;377(9):862-872.
810. Schuele SU. **Sudden unexpected death in epilepsy**: Taking another look. Neurology. 2017 Aug 29;89(9):e117-e119
811. Tolbert D, Reid S, Harris S, et al. **Vigabatrin Lacks Proarrhythmic** Potential: Results from a Thorough **QT/QTc** Study in Healthy Volunteers. Clin Ther. 2017 Aug;39(8):1639-1648.
812. Veroniki AA, Rios P, Cogo E, et al. Comparative safety of **antiepileptic drugs for neurological development in children exposed during pregnancy** and breast feeding: a systematic review and network meta-analysis. BMJ Open. 2017 Jul 20;7(7):e017248.
813. Giliberto JP, et al. Unilateral Laryngoscopic Findings Associated With Response to **Gabapentin in Patients With Chronic Cough**. JAMA Otolaryngol Head Neck Surg. 2017 Sep 14.
814. Wang JZ, Vyas MV, Saposnik G, et al. Incidence and management of **seizures after ischemic stroke**: Systematic review and meta-analysis. Neurology. 2017 Aug 23.
815. Zhang YH, Burgess R, Malone JP, et al. Genetic **epilepsy with febrile seizures** plus: refining the spectrum. Neurology 2017;89:1210–1219.
816. Bell GS, de Tisi J, et al. Factors affecting seizure **outcome after epilepsy surgery**: an observational series. J Neurol Neurosurg Psychiatry. 2017 Nov;88(11):933-940.
817. Cohen-Israel M, Berger I, Martonovich EY, et al. Short and Long Term Complications of **In Utero Exposure to Lamotrigine**. Br J Clin Pharmacol. 2017 Oct 18.
818. Nagan M, Caffarelli M, Donatelli S, Rosman NP. **Epilepsy or a seizure disorder? Parental knowledge** and misconceptions about terminology. J Pediatr 2017.
819. Reznik ME, Merkler AE, Mahta A, et al. Long-term **risk of seizures in adult survivors of sepsis**. Neurology. 2017 Oct 3;89(14):1476-1482
820. Struck AF, Ustun B, Rodriguez Ruiz A, et al. Association of an **electroencephalography-based risk score** with seizure probability in hospitalized patients [online Oct 9, 2017]. JAMA Neurol. doi:10.1001/jamaneurol.2017.2459
821. Blumcke I, Spreafico R, et al; EEBB Consortium. **Histopathological Findings** in Brain Tissue Obtained during Epilepsy Surgery. N Engl J Med. 2017 Oct 26;377(17):1648-1656.
822. Dwivedi R, Ramanujam B, Chandra PS, et al. **Surgery for Drug-Resistant Epilepsy in Children**. N Engl J Med. 2017 Oct 26;377(17):1639-1647.
823. Shinnar RC, Shinnar S, Cnaan A, et al; Childhood Absence Epilepsy Study Group. **Pretreatment behavior and subsequent medication effects** in childhood absence epilepsy. Neurology. 2017 Oct 17;89(16):1698-1706.
824. Allendorfer JB, Arida RM. Role of **Physical Activity and Exercise** in Alleviating Cognitive Impairment in People With Epilepsy. Clin Ther. 2017 Dec 20
825. Augustin K, et al. Mechanisms of action for the medium-chain triglyceride **ketogenic diet** in neurological and metabolic disorders. Lancet Neurol. 2018 Jan;17(1):84-93.
826. Beniczky S, Conradsen I, Henning O, Fabricius M, Wolf P. **Automated real-time detection** of tonic-clonic seizures using a wearable EMG device. Neurology 2018;90: e428–e434.
827. Benoist GE, van der Doelen MJ, Ter Heine R, et al. A clinically relevant decrease in **abiraterone exposure associated with carbamazepine** use in a patient with castration-resistant metastatic prostate cancer. Br J Clin Pharmacol. 2018 Jan 31.
828. Bjørk M, Riedel B, Spigset O, et al. Association of **Folic Acid Supplementation During Pregnancy With the Risk of Autistic Traits** in Children Exposed to Antiepileptic Drugs In Utero. JAMA Neurol. 2017 Dec 26
829. Bromley RL, Weston J, et al. **Maternal Use of Antiepileptic Agents During Pregnancy** and Major Congenital Malformations in Children. JAMA. 2017 Nov 7;318(17):1700-1701.
830. Burman J, Zelano J. **Epilepsy in multiple sclerosis**: A nationwide population-based register study. Neurology. 2017 Dec 12;89(24):2462-2468.
831. Chen Z, Brodie MJ, Liew D, et al. Treatment Outcomes in Patients with **Newly Diagnosed Epilepsy Treated With Established and New Antiepileptic Drugs**: A **30-Year Longitudinal Cohort** Study. JAMA Neurol. 2017 Dec 26
832. Elger CE, Hoppe C. **Diagnostic challenges in epilepsy**: seizure under-reporting and seizure detection. Lancet Neurol. 2018 Mar;17(3):279-288.
833. Elkjær LS, Bech BH, Sun Y, et al. Association between **prenatal valproate exposure and performance on standardized language and mathematics tests** in school-aged children [online Feb 19, 2018].JAMA Neurol. doi: 10.1001/jamaneurol.2017 .5035.
834. Gaínza-Lein M, Sánchez Fernández I, Jackson M, et al; Pediatric Status Epilepticus Research Group. Association of **time to treatment** with short-term outcomes for **pediatric patients with refractory convulsive status epilepticus** [published online January 22, 2018].JAMA Neurol. doi:10.1001 /jamaneurol.2017.4382
835. Grinspan ZM, Shellhaas RA, Coryell J, et al. Comparative Effectiveness of **Levetiracetam vs Phenobarbital for Infantile Epilepsy**. JAMA Pediatr. 2018 Feb 12.
836. Gruntz K, Bloechliger M, Becker C, et al. **Parkinson's disease and the risk of epileptic seizures**. Ann Neurol. 2018 Jan 25.
837. Håberg SE, Aaberg KM, Surén P, et al. **Epilepsy in Children After Pandemic Influenza Vaccination**. Pediatrics. 2018 Feb 15.
838. Hamid SHM, Whittam D, Saviour M, et al. **Seizures and Encephalitis** in Myelin Oligodendrocyte Glycoprotein IgG Disease vs Aquaporin 4 IgG Disease. JAMA Neurol. 2017 Nov 13.

839. Hauser WA. **Questioning the Effectiveness of Newer Antiseizure Medications**. JAMA Neurol. 2017 Dec 26
840. Hernandez-Diaz S, Huybrechts KF, Desai RJ, et al. **Topiramate use early in pregnancy** and the risk of oral clefts: A pregnancy cohort study. Neurology. 2018 Jan 23;90(4):e342-e351.
841. Johansen ME. **Gabapentinoid Use in the United States** 2002 Through 2015. JAMA Intern Med. 2018 Jan 2.
842. Keni RR, Jose M, Sarma PS, et al. **Teratogenicity of antiepileptic dual therapy**: Dose-dependent, drug-specific, or both? Neurology. 2018 Feb 27;90(9):e790-e796.
843. Loddenkemper T. **Conscious control of breathing: A key to SUDEP prevention**? Ann Neurol. 2018 Feb 8.
844. Mahler B, Carlsson S, Andersson T, et al. **Risk for injuries and accidents in epilepsy**: A prospective population-based cohort study. Neurology. 2018 Feb 27;90(9):e779-e789.
845. McCormack M, Gui H, et al. **Genetic variation in CFH predicts phenytoin induced maculopapular exanthema** in European-descent patients. Neurology 2018; 90:e332–e341.
846. McTague A, Martland T, Appleton R. **Drug management for acute tonic-clonic convulsions including convulsive status epilepticus in children**. Cochrane Database of Systematic Reviews 2018, Issue 1. Art. No.: CD001905. We have not identified any new high-quality evidence on the efficacy or safety of an anticonvulsant in stopping an acute tonic-clonic convulsion that would inform clinical practice. There appears to be a very low risk of adverse events, specifically respiratory depression. Intravenous lorazepam and diazepam appear to be associated with similar rates of seizure cessation and respiratory depression. Although intravenous lorazepam and intravenous diazepam lead to more rapid seizure cessation, the time taken to obtain intravenous access may undermine this effect. In the absence of intravenous access, buccal midazolam or rectal diazepam are therefore acceptable first-line anticonvulsants for the treatment of an acute tonic-clonic convulsion that has lasted at least five minutes. There is no evidence provided by this review to support the use of intranasal midazolam or lorazepam as alternatives to buccal midazolam or rectal diazepam.
847. MHRA Nov/17: **Gabapentin has been associated with a rare risk of severe respiratory depression** even without concomitant opioid medicines. Patients with compromised respiratory function, respiratory or neurological disease, renal impairment, concomitant use of central nervous system (CNS) depressants, and elderly people might be at higher risk of experiencing severe respiratory depression. Dose adjustments might be necessary in these patients.
848. Meador KJ, Shin C. Pitfalls in developing **precision medicine for genetic epilepsy**. Neurology. 2017 Dec 1
849. Meador KJ. **Periconceptional Folate Supplementation and the Risk of Autism** Following Antiepileptic Drug Exposure. JAMA Neurol. 2017 Dec 26.
850. Mullen SA, Carney PW, Roten A, et al. **Precision therapy for epilepsy due to KCNT1 mutations**: A randomized trial of oral quinidine. Neurology. 2017 Dec 1.
851. Nagan M, Caffarelli M, Donatelli S, et al. **Epilepsy or a Seizure Disorder**? Parental Knowledge and Misconceptions About Terminology. J Pediatr. 2017 Dec;191:197-203.e5.
852. Nevitt SJ, Sudell M, Weston J, et al. **Antiepileptic drug monotherapy for epilepsy**: a network meta-analysis of individual participant data. Cochrane Database Syst Rev. 2017 Dec 15;12:CD011412.
853. Persson M, Razaz N, et al. Five and 10 minute Apgar scores and risks of **cerebral palsy and epilepsy**: population based cohort study in Sweden. BMJ. 2018 Feb 7;360:k207.
854. Picard RW, Migliorini M, Caborni C, et al. **Wrist sensor** reveals sympathetic hyperactivity and hypoventilation before **probable SUDEP**. Neurology 2017;89: 633–635.
855. Slovin S, et al. Seizure Rates in **Enzalutamide-Treated** Men With Metastatic Castration-Resistant Prostate Cancer and **Risk of Seizure**: The **UPWARD** Study. JAMA Oncol. 2017 Dec 7.
856. Thiele EA, Marsh ED, French JA, et al. **Cannabidiol** in patients with seizures associated **with Lennox-Gastaut syndrome** (**GWPCARE4**): a randomised, double-blind, placebo-controlled phase 3 trial. Lancet 2018; published online Jan 24.
857. Wang TR, Bailey RC, Goodkin HP, Mahaney KB. Tends in **intracranial monitoring for pediatric medically intractable epilepsy**: 2000–2012. Neurology 2018;90: e771–e778.
858. Bailey JN, de Nijs L, Bai D, et al. Variant Intestinal-Cell Kinase in **Juvenile Myoclonic Epilepsy**. N Engl J Med. 2018 Mar 15;378(11):1018-1028.
859. Wiggs KK, Chang Z, Quinn PD, et al. **Attention-deficit/hyperactivity disorder medication** and seizures. Neurology. 2018 Feb 23.
860. Haut SR, Lipton RB, Cornes S, et al. **Behavioral interventions** as a treatment for epilepsy: A multicenter randomized controlled trial. Neurology. 2018 Mar 13;90(11):e963-e970.
861. Spencer DD, Gerrard JL, Zaveri HP. The roles of **surgery and technology** in understanding focal epilepsy and its comorbidities. Lancet Neurol 2018; 17: 373–82.
862. Stockings E, et al. Evidence for **cannabis and cannabinoids** for epilepsy: a systematic review of controlled and observational evidence. J Neurol Neurosurg Psychiatry. 2018 Mar 6.
863. Health Canada Apr/18 is advising Canadians that AA Pharma Inc. is voluntarily recalling two lots of **Primidone tablets because they contain high levels of lead**.
864. Mushiroda T, Takahashi Y, Onuma T, et al. Association of **HLA-A*31:01 screening** with the incidence of **carbamazepine-induced cutaneous adverse reactions** in a Japanese population [online Apr 2, 2018].JAMA Neurol. doi: 10.1001/jamaneurol.2018.0278
865. Sundelin HEK, Chang Z, Larsson H, et al. **Epilepsy, antiepileptic drugs, and serious transport accidents**: a nationwide cohort study. Neurology 2018;90:e1111–e1118.
866. Devinsky O, Patel AD, Thiele EA, et al. Randomized, dose-ranging safety trial of **cannabidiol in Dravet syndrome**. Neurology. 2018 Apr 3;90(14):e1204-e1211.
867. Groton HC, Webb RT, Carr MJ, et al. Risk of **unnatural mortality in people with epilepsy** [online April 9, 2018].JAMA Neurol. doi:10.1001/jamaneurol.2018 .0333
868. Taipale H, Gomm W, et al. Use of **Antiepileptic Drugs and Dementia Risk**-an Analysis of Finnish Health Register and German Health Insurance Data. J Am Geriatr Soc. 2018 Mar 22.
869. Angus-Leppan H, Liu RSN. Weighing the **risks of valproate in women who could become pregnant**. BMJ. 2018 Apr 18;361:k1596.
870. Haberg SE, Aaberg KM, Suren P, et al. **Epilepsy in Children After Pandemic Influenza Vaccination**. Pediatrics. 2018 Feb 15.
871. Joshi S, Rajasekaran K, Hawk KM, et al. **Status epilepticus**: Role for etiology in determining **response to benzodiazepines**. Ann Neurol. 2018 Mar 24.
872. Tomson T, Battino D, Bonizzoni E, et al. Comparative risk of **major congenital malformations with eight different antiepileptic drugs**: a prospective cohort study of the **EURAP registry**. Lancet Neurol 2018; online April 18.
873. Vakharia VN, Duncan JS, Witt JA, et al. **Getting the best outcomes from epilepsy surgery**. Ann Neurol. 2018 Mar 13.

874. Wieck A, Jones S. **Dangers of valproate in pregnancy**. BMJ. 2018 Apr 18;361:k1609.
875. Chin A. **Copper Deficiency** Anemia and Neutropenia Due to **Ketogenic Diet**. Pediatrics. 2018 Apr 25.
876. FDA Apr/18: is warning that the medicine Lamictal (**lamotrigine**) for seizures and bipolar disorder can cause a rare but very serious reaction that excessively activates the body's infection-fighting immune system. The immune system reaction, called **hemophagocytic lymphohistiocytosis (HLH),** causes an uncontrolled response by the immune system. HLH typically presents as a persistent fever, usually greater than 101°F, and it can lead to severe problems with blood cells and organs throughout the body such as the liver, kidneys, and lungs.
878. MHRA Apr/18: **Valproate** medicines (Epilim▼, Depakote▼): **contraindicated in women and girls of childbearing potential** unless conditions of Pregnancy Prevention Programme are met.
879. Pennell PB, French JA, Harden CL, et al. **Fertility and Birth Outcomes in Women** With Epilepsy Seeking Pregnancy. JAMA Neurol. 2018 Apr 30.
880. Sánchez Fernández I, Gaínza-Lein M, Abend NS, et al. Factors associated with **treatment delays in pediatric refractory convulsive status epilepticus**. Neurology. 2018 Apr 11.
881. Aaberg KM, Bakken IJ, Lossius MI, et al. **Short-term Seizure Outcomes in Childhood Epilepsy**. Pediatrics. 2018 May 22.
882. Devinsky O, Patel AD, Cross JH, et al. Effect of **Cannabidiol** on Drop Seizures in the **Lennox-Gastaut Syndrome**. N Engl J Med. 2018 May 17;378(20):1888-1897.
883. Ridsdale L, et al. **Self-Management education for adults** with poorly controlled epILEpsy [**SMILE** (UK)]: a randomised controlled trial. Health Technol Assess 2018;22(21).
884. Thangaratinam S, Marlin N, Newton S, et al. **AntiEpileptic drug Monitoring in PREgnancy** (**EMPiRE**): a double-blind randomised trial on effectiveness and acceptability of monitoring strategies. Health Technol Assess. 2018 May;22(23):1-152.
885. Alkawadri R, Burgess RC, Kakisaka Y, et al. Assessment of the Utility of **Ictal Magnetoencephalography in the Localization of the Epileptic Seizure** Onset Zone. JAMA Neurol. 2018 Jun 11.
886. Birch DG, Bernstein PS, Iannacone A, et al. Effect of **Oral Valproic Acid vs Placebo for Vision Loss** in Patients With Autosomal Dominant Retinitis Pigmentosa: A Randomized Phase 2 Multicenter Placebo-Controlled Clinical Trial. JAMA Ophthalmol. 2018 Jun 7.
887. Noble AJ, Reilly J, Temple J, et al. **Cognitive-behavioural therapy** does not meaningfully reduce depression in most people with epilepsy: a systematic review of clinically reliable improvement. J Neurol Neurosurg Psychiatry. 2018 May 7.
888. Parvizi J, Gururangan K, Razavi B, et al. **Detecting silent seizures** by their sound. Epilepsia. 2018 Apr;59(4):877-884.
889. Qato DM, Ozenberger K, Olfson M. Prevalence of **Prescription Medications With Depression as a Potential Adverse Effect Among Adults** in the United States. JAMA. 2018 Jun 12;319(22):2289-2298. (eg. Gabapentin, cyclobenzaprine)
890. Sveinsson O, Andersson T, Carlsson S, et al. Circumstances of **SUDEP**: A nationwide population-based case series. Epilepsia. 2018 May;59(5):1074-1082.
891. Courchia B, Kurtom W, Pensirikul A, et al. **Topiramate** for Seizures in Preterm Infants and the **Development of Necrotizing Enterocolitis**. Pediatrics. 2018 Jun 14.
892. Crawford MJ, Sanatinia R, Barrett B, et al; LABILE study team. The Clinical Effectiveness and Cost-Effectiveness of **Lamotrigine in Borderline Personality Disorder**: A Randomized Placebo-Controlled Trial. Am J Psychiatry. 2018 Apr 6
893. Farrokh S, Tahsili-Fahadan P, Ritzl EK, et al. Antiepileptic drugs in **critically ill patients**. Crit Care. 2018 Jun 7;22(1):153.
894. Lacey AS, Pickrell WO, Thomas RH, et al. **Educational attainment** of children born to mothers with epilepsy. J Neurol Neurosurg Psychiatry. 2018 Jul;89(7):736-740.
895. Lin HW, Ho YF, Lin FJ. **Statin use associated with lower risk of epilepsy** after intracranial haemorrhage: A population-based cohort study. Br J Clin Pharmacol. 2018 May 1.
896. Murata M, Odawara T, Hasegawa K, et al. Adjunct **zonisamide to levodopa for DLB parkinsonism**: a randomized, double-blind phase 2 study. Neurology 2018;90: e664–e672.
897. Devinsky O, Kim A, Friedman D, et al. Incidence of **cardiac fibrosis in SUDEP** and control cases. Neurology. 2018 Jul 3;91(1):e55-e61.
898. Domjanović IK, Lovrić M, Trkulja V, et al. Interaction between **ABCG2 421C>A polymorphism and valproate** in their effects on steady-state disposition of lamotrigine in adults with epilepsy. Br J Clin Pharmacol. 2018 May 23.
899. Enke O, New HA, New CH, et al. **Anticonvulsants in the treatment of low back pain** and lumbar radicular pain: a systematic review and meta-analysis. CMAJ. 2018 Jul 3;190(26):E786-E793.
900. Kanner AM, Ashman E, Gloss D, et al. Practice guideline update summary: **Efficacy and tolerability of the new antiepileptic drugs** I: Treatment of **new-onset epilepsy**: Report of the Guideline Development, Dissemination, & Implementation Subcommittee of the American Academy of Neurology (**AAN**) & the American Epilepsy Society. Neurology. 2018 Jun 13. Kanner AM, Ashman E, Gloss D, et al. Practice guideline update summary: Efficacy and tolerability of the **new antiepileptic drugs** II: **Treatment-resistant epilepsy**: Report of the Guideline Development, Dissemination, and Implementation Subcommittee of the American Academy of Neurology (**AAN**) and the American Epilepsy Society. Neurology. 2018 Jul 10;91(2):82-90.
901. Marchi` o M, Roli L, Giordano C, et al. High plasma levels of **ghrelin and des-acyl ghrelin in responders to antiepileptic** drugs. Neurology 2018;91:e62–e66.
902. Vu LC, Piccenna L, Kwan P, et al. **New-onset epilepsy in the elderly**. Br J Clin Pharmacol. 2018 Jun 1.
903. Baud MO, Perneger T, R´ acz A, et al. European trends in epilepsy surgery. Neurology 2018;91:e96–e106.
904. Keller AE, Whitney R, Li SA, et al. Incidence of sudden unexpected death in epilepsy in children is similar to adults. Neurology 2018;91: e107–e111.

905. Johnson EL, Krauss GL, Lee AK, et al. Association Between **Midlife Risk Factors and Late-Onset Epilepsy**: Results From the Atherosclerosis Risk in Communities Study. JAMA Neurol. 2018 Jul 23.
906. Nevitt SJ, Tudur Smith C, Weston J, et al. **Lamotrigine versus carbamazepine monotherapy for epilepsy: an individual participant data review.** Cochrane Database Syst Rev. 2018 Jun 28;6:CD001031. Moderate quality evidence indicates that treatment failure for any reason related to treatment or due to adverse events occurs significantly earlier on carbamazepine than lamotrigine, but the results for time to first seizure suggested that carbamazepine may be superior in terms of seizure control. The choice between these first-line treatments must be made with careful consideration.
907. Rathore C, Jeyaraj MK, Dash GK, et al. **Outcome after seizure recurrence** on antiepileptic drug withdrawal following temporal lobectomy. Neurology. 2018 Jul 17;91(3):e208-e216.
908. Tamilia E, Park EH, Percivati S, et al. **Surgical resection of ripple onset predicts outcome in pediatric epilepsy**. Ann Neurol. 2018 Jul 18.
909. Abu-Baker A, Parker A, Ramalingam S, et al. **Valproic acid is protective in cellular and worm models of oculopharyngeal muscular dystrophy**. Neurology. 2018 Aug 7;91(6):e551-e561.
910. Husain AM, Lee JW, Kolls BJ, et al. Randomized trial of **lacosamide vs fosphenytoin for nonconvulsive seizures**. Ann Neurol. 2018 May 7.
911. Coryell J, Gaillard WD, Shellhaas RA, et al. **Neuroimaging of Early Life Epilepsy**. Pediatrics. 2018 Aug 8.
912. Panchaud A, Cohen JM, Patorno E, et al. **Anticonvulsants and the risk of perinatal bleeding complications**: A pregnancy cohort study. Neurology. 2018 Aug 7;91(6):e533-e542.
913. Zhang JH, Han X, Zhao HW, et al. Personalized prediction model for **seizure-free epilepsy with levetiracetam therapy**: A retrospective data analysis using Support Vector Machine. Br J Clin Pharmacol. 2018 Jul 24.
914. Gorton HC, Webb RT, Carr MJ, DelPozo-Banos M, John A, Ashcroft DM. Risk of **unnatural mortality in people with epilepsy** [online April 9, 2018]. JAMA Neurol.
915. Jacobs J, Wu JY, Perucca P, et al. **Removing high-frequency oscillations**: A prospective multicenter study on seizure outcome. Neurology. 2018 Sep 11;91(11):e1040-e1052.
916. Kang JW, Eom S, Hong W, et al. Long-term Outcome of Resective **Epilepsy Surgery in Patients With Lennox-Gastaut Syndrome**. Pediatrics. 2018 Sep 7.
917. Lawson JA, Scheffer IE. Therapeutic Use of **medicinal cannabis in difficult to manage epilepsy**. Br J Clin Pharmacol. 2018 Aug 7.
918. MHRA Sep/18: **Valproate medicines** must not be used in women of childbearing potential unless the Pregnancy Prevention Programme is in place.
920. Neal A, Carne R, Odell M, et al. Characteristics of **motor vehicle crashes associated with seizure**: Car crash semiology. Neurology. 2018 Sep 18;91(12):e1102-e1111.
921. Gomes T, Greaves S, van den Brink W, et al. **Pregabalin and the Risk for Opioid-Related Death**: A Nested Case-Control Study. Ann Intern Med. 2018 Aug 21.
922. Husebye ESN, Gilhus NE, Riedel B, et al. **Verbal abilities in children of mothers with epilepsy**: Association to maternal folate status. Neurology. 2018 Aug 28;91(9):e811-e821.
923. Karanam A, Pennell PB, et al. **Lamotrigine clearance increases by 5 weeks gestational age**: Relationship to estradiol concentrations and gestational age. Ann Neurol. 2018 Aug 31.
924. Lang JD, Kostev K, Dogan Onugoren M, et al. **Switching the manufacturer of anti-epileptic drugs is associated with higher risk of seizures**. Ann Neurol. 2018 Oct 8.
925. Lawson JA, Scheffer IE. Therapeutic use of **medicinal cannabis** in difficult to manage epilepsy. Br J Clin Pharmacol. 2018 Aug 7.
926. Murata S, Okasora K, Tanabe T, et al. **Acetaminophen and Febrile Seizure Recurrences During the Same Fever Episode**. Pediatrics. 2018 Oct 8.
927. Uski J, Lamusuo S, Teperi S, et al. **Mortality after traumatic brain injury** and the effect of **posttraumatic epilepsy**. Neurology. 2018 Aug 28;91(9):e878-e883.
928. van der Linden H Jr, Carvalho MD, van der Linden V, et al. Epilepsy Profile in Infants with **Congenital Zika Virus Infection**. N Engl J Med. 2018 Aug 30;379(9):891-892.
929. Voinescu PE, Park S, Chen LQ, et al. **Antiepileptic drug clearances during pregnancy** and clinical implications for women with epilepsy. Neurology. 2018 Sep 25;91(13):e1228-e1236.
930. Bao EL, Chao LY, Ni P, et al. **Antiepileptic drug treatment after an unprovoked first seizure**: a decision analysis. Neurology 2018;91:e1429–e1439.
931. Herzog AG, Mandle HB, MacEachern DB. Association of **Unintended Pregnancy With Spontaneous Fetal Loss** in Women With Epilepsy: Findings of the Epilepsy Birth Control Registry. JAMA Neurol. 2018 Oct 15.
932. Karceski S. **Pregnancy, anti-seizure medications, and seizures**. Neurology. 2018 Sep 25;91(13):e1271-e1274.
933. van der Lende M, Hesdorffer DC, Sander JW, Thijs RD. **Nocturnal supervision and SUDEP risk** at different epilepsy care settings, 2018. Neurology 2018;91:e1508–e1518.
934. Christensen J, Vestergaard C, Hammer Bech B. **Maternal death** in women with epilepsy: Smaller scope studies. Neurology. 2018 Oct 30;91(18):e1716-e1720.
935. Sarycheva T, Lavikainen P, Taipale H, et al. **Antiepileptic Drug Use and the Risk of Stroke** Among Community-Dwelling People **With Alzheimer Disease**: A Matched Cohort Study. J Am Heart Assoc. 2018 Sep 18;7(18):e009742.
936. SoRelle JA, Thodeson DM, Arnold S, et al. Clinical Utility of **Reinterpreting Previously Reported Genomic Epilepsy Test Results** for Pediatric Patients. JAMA Pediatr. 2018 Nov 5:e182302.
937. Tolete P, Knupp K, Karlovich M, et al. **Lorcaserin therapy** for severe epilepsy of childhood onset: A case series. Neurology. 2018 Oct 30;91(18):837-839.
938. Arends J, Thijs RD, Gutter T,et al; and the Dutch Tele-Epilepsy Consortium. **Multimodal nocturnal seizure detection** in a residential care setting: A long-term prospective trial. Neurology. 2018 Nov 20;91(21):e2010-e2019.
939. Baud MO, Rao VR. **Gauging seizure risk**. Neurology. 2018 Nov 20;91(21):967-973.
940. Jun JS, Lee ST, Kim R, et al. **Tocilizumab treatment** for new-onset refractory status epilepticus. Ann Neurol. 2018 Nov 8.
941. van Diessen E, Lamberink HJ, Otte WM, et al. A **Prediction Model to Determine Childhood Epilepsy** After 1 or More Paroxysmal Events. Pediatrics. 2018 Nov 2.

942. Yang YT, Szaflarski JP. The US Food and Drug Administration's Authorization of the **First Cannabis-Derived Pharmaceutical**: Are We Out of the Haze? JAMA Neurol. 2018 Nov 19.
943. Arends J, Thijs RD, Gutter T,et al; and the Dutch Tele-Epilepsy Consortium. Multimodal **nocturnal seizure detection** in a residential care setting: A long-term prospective trial. Neurology. 2018 Nov 20;91(21):e2010-e2019.
944. Baud MO, Rao VR. **Gauging seizure risk**. Neurology. 2018 Nov 20;91(21):967-973.

945. Federico CA, Wang T, Doussau A, et al. Assessment of **Pregabalin Postapproval Trials** and the Suggestion of Efficacy for New Indications: A Systematic Review. JAMA Intern Med. 2018 Nov 26.
946. Hughes DM, Bonnett LJ, Czanner G, et al. Identification of patients **who will not achieve seizure remission within 5 years on AEDs**. Neurology 2018;91:e2035–e2044.
947. Jun JS, Lee ST, Kim R, Chu K, Lee SK. **Tocilizumab treatment** for new-onset refractory status epilepticus. Ann Neurol. 2018 Nov 8.
948. Van Diessen E, Lamberink HJ, Otte WM, et al. A Prediction Model to Determine **Childhood Epilepsy After 1 or More Paroxysmal Events**. Pediatrics. 2018 Nov 2.
949. Yang YT, Szaflarski JP. The US Food and Drug Administration's **Authorization of the First Cannabis-Derived Pharmaceutical**: Are We Out of the Haze? JAMA Neurol. 2018 Nov 19.
950. Andrews JP, Gummadavelli A, Farooque P, et al. Association of **Seizure Spread With Surgical Failure** in Epilepsy. JAMA Neurol. 2018 Dec 3.
951. Dreier JW, Pedersen CB, Cotsapas C, Christensen J. **Childhood seizures and risk of psychiatric disorders** in adolescence and early adulthood: a Danish nationwide cohort study. Lancet Child Adolesc Health. 2018 Dec 6.
952. Hamberger MJ, MacAllister WS, Seidel WT, et al. **Noninvasive identification of seizure lateralization** in children: name that thing. Neurology 2019;92: e1–e8.
953. Nishiyama M, Takami Y, Ishida Y, eta l. **Lipid and thyroid hormone levels in children with epilepsy** treated with **levetiracetam or carbamazepine**: A prospective observational study. Epilepsy Behav. 2018 Nov 27;90:15-19.
954. Supasitthumrong T, Bolea-Alamanac BM, Asmer S, et al. **Gabapentin and pregabalin to treat aggressivity in dementia**: sa systematic review and illustrative case reports. Br J Clin Pharmacol. 2018 Dec 21.
955. Chelmowski MK, Morris GL 3rd. **Cyclical Sweating Caused by Temporal Lobe Seizures**. Ann Intern Med. 2019 Jan 15.
956. Christensen J, Pedersen LH, Sun Y, et al. Association of **prenatal exposure to valproate and other antiepileptic drugs** with risk for attention-deficit/hyperactivity disorder in offspring. JAMA Network Open 2019;2(1):e186606.
957. Lennox R, Mangin D. **Gabapentin misuse**. CMAJ. 2019 Jan 14;191(2):E47.
958. Blank LJ, Crispo JAG, Thibault DP, Davis KA, Litt B, Willis AW. **Readmission after seizure** discharge in a nationally representative sample. Neurology 2019;92:e429–e442.
959. Josephson CB, Engbers JDT, Jette N, et al. Prediction Tools for Psychiatric **Adverse Effects After Levetiracetam** Prescription. JAMA Neurol. 2019 Jan 28
960. Kellinghaus C, Rossetti AO, Trinka E, et al. Factors predicting **cessation of status epilepticus** in clinical practice - data from a prospective observational registry (SENSE). Ann Neurol. 2019 Jan 20.
961. Lavikainen P, Taipale H, Tanskanen A, et al. Antiepileptic Drugs and Accumulation of Hospital Days Among **Persons With Alzheimer's Disease**. J Am Med Dir Assoc. 2019 Jan 7.
962. Rheims S, Alvarez BM, Alexandre V, et al; REPO2MSE study group**. Hypoxemia** following generalized convulsive seizures: Risk factors and effect of oxygen therapy. Neurology. 2019 Jan 15;92(3):e183-e193.
963. Sánchez Fernández I, Loddenkemper T, Gaínza-Lein M, et al. **Diagnostic yield of genetic tests** in epilepsy: A meta-analysis and cost-effectiveness study. Neurology. 2019Jan4.
964. Thijs RD, Surges R, O'Brien TJ, Sander JW. **Epilepsy in adults**. Lancet. 2019 Jan 24.
965. Vilella L, Lacuey N, Hampson JP, et al. **Postconvulsive central apnea** as a biomarker for sudden unexpected death in epilepsy (SUDEP). Neurology 2019;92:e171–e182.
966. Yang J, Ma P, Bullman J, Nicholls A, Chen C. Adjustment of the area under the concentration curve by terminal rate constant for bioequivalence assessment in a parallel-group **study of lamotrigine**. Br J Clin Pharmacol. 2018 Dec 3.
967. Derry S, Bell RF, Straube S, et al. **Pregabalin for neuropathic pain in adults**. Cochrane Database Syst Rev. 2019 Jan 23;1:CD007076. Evidence shows efficacy of pregabalin in postherpetic neuralgia, painful diabetic neuralgia, and mixed or unclassified post-traumatic neuropathic pain, and absence of efficacy in HIV neuropathy; evidence of efficacy in central neuropathic pain is inadequate. Some people will derive substantial benefit with pregabalin; more will have moderate benefit, but many will have no benefit or will discontinue treatment.
968. Driot D, Jouanjus E, Oustric S, et al. **Patterns of gabapentin and pregabalin use and misuse**: results of a population-based cohort study in France. Br J Clin Pharmacol. 2019 Feb 8.
969. Duez L, Tankisi H, Hansen PO, et al. **Electromagnetic source imaging in presurgical workup of patients with epilepsy**: A prospective study. Neurology. 2019 Feb 5;92(6):e576-e586.
970. Rayner G, Tailby C, Jackson G, Wilson S. Looking beyond lesions for **causes of neuropsychological impairment in epilepsy**. Neurology. 2019 Feb 12;92(7):e680-e689.
971. Brigo F, Lattanzi S, Igwe SC, et al. **Zonisamide add-on therapy** for focal epilepsy. Cochrane Database Syst Rev. 2018 Oct 18;10:CD001416. When used as an add-on treatment in people with focal epilepsy uncontrolled by one or more concomitant antiepileptic drugs, moderate-quality evidence found that zonisamide was more successful than placebo at reducing the frequency of seizures by at least 50%. We were unable to identify minimum effective and maximum tolerated doses. The included trials evaluated a maximum stable-dose phase of 18 weeks, so results cannot be used to confirm longer periods of efficacy in seizure control. The results cannot be extrapolated to monotherapy or to people with other seizure types or epilepsy syndromes.
972. Galovic M, Baudracco I, Wright-Goff E, et al. Association of **Piriform Cortex Resection** With Surgical Outcomes in Patients With Temporal Lobe Epilepsy. JAMA Neurol. 2019 Mar 11.

973. Johnson EL, Krauss GL, Lee AK, et al. Association between **white matter hyperintensities, cortical volumes, and late-onset epilepsy**. Neurology. 2019 Feb 26;92(9):e988-e995.
974. Wolking S, May P, Mei D, et al. Clinical spectrum of **STX1B-related epileptic disorders**. Neurology. 2019 Mar 12;92(11):e1238-e1249.
975. Goodman CW, Brett AS. A Clinical Overview of **Off-label Use of Gabapentinoid** Drugs. JAMA Intern Med. 2019 Mar 25.
976. González Otárula KA, Mikhaeil-Demo Y, Bachman EM, et al. **Automated seizure detection accuracy** for ambulatory EEG recordings. Neurology. 2019 Apr 2;92(14):e1540-e1546.
977. Kim H, Faught E, Thurman DJ, et al. **Antiepileptic Drug Treatment Patterns** in Women of Childbearing Age With Epilepsy. JAMA Neurol. 2019 Apr 1.
978. Nijs J, Polli A, Willaert W, et al. **Central sensitisation**: another label or useful diagnosis? Drug Ther Bull. 2019 Apr;57(4):60-63.
979. Smith DK, Sadler KP, Benedum M. **Febrile Seizures**: Risks, Evaluation, and Prognosis. Am Fam Physician. 2019 Apr 1;99(7):445-450.
980. Balciuniene J, DeChene ET, Akgumus G, et al. Use of a **Dynamic Genetic Testing Approach** for Childhood-Onset Epilepsy. JAMA Netw Open. 2019 Apr 5;2(4):e192129.
981. Deng L, Gidding H, Macartney K, et al. **Postvaccination** Febrile Seizure Severity and Outcome. Pediatrics. 2019 Apr 19.
982. Kokkinos V, Sisterson ND, Wozny TA, Richardson RM. Association of **Closed-Loop Brain Stimulation** Neurophysiological Features With Seizure Control Among Patients With Focal Epilepsy. JAMA Neurol. 2019 Apr 15.
983. Sutter R, Semmlack S, Opic P, et al. Untangling **operational failures of** the Status Epilepticus Severity Score (**STESS**). Neurology. 2019 Apr 23;92(17):e1948-e1956.
984. Crandall LG, Lee JH, Stainman R, et al. Potential Role of Febrile Seizures and Other Risk Factors Associated With Sudden Deaths in Children. JAMA Netw Open. 2019 Apr 5;2(4):e192739.
985. Ellis CA, Churilov L, Epstein MP, et al. Epilepsy in Families: Age at onset is a familial trait, independent of syndrome. Ann Neurol. 2019 May 2.
986. Reyes A, Kaestner E, Bahrami N, et al. Cognitive phenotypes in temporal lobe epilepsy are associated with distinct patterns of white matter network abnormalities. Neurology. 2019 Apr 23;92(17):e1957-e1968.
987. Chang SM, Messersmith H, Ahluwalia M, et al. **Anticonvulsant prophylaxis and steroid use in adults with metastatic brain tumors**: summary of SNO and ASCO endorsement of the Congress of Neurological Surgeons guidelines. Neuro Oncol. 2019 Mar 18;21(4):424-427.
988. Dalziel SR, Borland ML, Furyk J, et al. **Levetiracetam versus phenytoin for second-line treatment** of convulsive status epilepticus in children (ConSEPT): an open-label, multicentre, randomised controlled trial. Lancet. 2019 Apr 17.
989. Gingras MA, Lieu A, Papillon-Ferland L, et al. Retrospective Cohort Study of the Prevalence of **Off-label Gabapentinoid Prescriptions in Hospitalized Medical Patients**. J Hosp Med. 2019 May 12;14:E1-E4
990. Neligan A, Noyce AJ, Gosavi TD, et al. **Change in mortality of generalized convulsive status epilepticus in high-income countries** over time: a systematic review and meta-analysis [online May 28, 2019]. JAMA Neurol. doi:10.1001/jamaneurol.2019.1268
991. Wimpelmann J, Høvik H, Riedel B, Slørdal L. The **interaction between rifampicin and lamotrigine**: A case report. Br J Clin Pharmacol. 2019 May 29.
992. Cuello Oderiz C, von Ellenrieder N, Dubeau F, et al. Association of **Cortical Stimulation-Induced Seizure With Surgical Outcome** in Patients With Focal Drug-Resistant Epilepsy. JAMA Neurol. 2019 Jun 10.
993. Fern´andez IS, Ga´õnza-Lein M, Lamb N, Loddenkemper T. **Meta-analysis and costeffectiveness of second-line antiepileptic drugs** for status epilepticus. Neurology 2019; 92:e2339–e2348.
994. Herzog AG, Mandle HB, MacEachern DB. Prevalence of **highly effective contraception use by women with epilepsy**. Neurology. 2019 Jun 11;92(24):e2815-e2821.
995. Kim T, Kulick CG, Kortepeter CM, Brinker A, Waldron P. **Hemophagocytic lymphohistiocytosis associated with the use of lamotrigine.** Neurology 2019;92:e2401–e2405.
996. Molero Y, Larsson H, D'Onofrio BM, et al. **Associations between gabapentinoids** and suicidal behaviour, unintentional overdoses, injuries, road traffic incidents, and violent crime: population based cohort study in Sweden. BMJ. 2019 Jun 12;365:l2147.
997. Blotiere PO, Raguideau F, Weill A, et al. Risks of 23 specific **malformations associated with prenatal exposure to 10 antiepileptic drugs**. Neurology. 2019 Jun 12.
998. Huber-Mollema Y, Oort FJ, Lindhout D, Rodenburg R. **Behavioral problems in children** of mothers with epilepsy **prenatally exposed** to valproate, carbamazepine, lamotrigine, or levetiracetam monotherapy. Epilepsia. 2019 Jun;60(6):1069-1082.
999. Luedke MW, Blalock DV, Goldstein KM, et al. **Self-management** of Epilepsy. A systematic review. Ann Intern Med. 2019. [Epub ahead of print]. doi:10.7326/M19-0458.
1000. Nevitt SJ, Sudell M, Tudur Smith C, et al. **Topiramate versus carbamazepine monotherapy** for epilepsy: an individual participant data review. Cochrane Database Syst Rev. 2019 Jun 24;6:CD012065. For individuals with focal onset seizures, there is moderate-certainty evidence that carbamazepine is less likely to be withdrawn and high-certainty evidence that 12-month remission will be achieved earlier than with topiramate. We did not find any differences between the drugs in terms of the other outcomes measured in the review and for individuals with generalised tonic-clonic seizures or unclassified epilepsy; however, we encourage caution in the interpretation of results including small numbers of participants with these seizure types.
1001. Somogyi AA, Barratt DT, Phillips EJ, et al. High and variable population **prevalence of HLA-B*56:02** in Indigenous Australians and relation to phenytoin-associated **DRESS**. Br J Clin Pharmacol. 2019 Jun 17.
1002. Ter Heine R, Kane SP, Huitema ADR, et al. **Non-linear protein binding of phenytoin** in clinical practice - development and validation of a mechanistic prediction model. Br J Clin Pharmacol. 2019 Jul 3.
1003. Groeneveld GJ, Martin JH. **Parasitic pharmacology**: A plausible mechanism of action for cannabidiol. Br J Clin Pharmacol. 2019 Jul 10.

1004. Rhee TG, Ross JS. Association Between **Industry Payments to Physicians and Gabapentinoid Prescribing**. JAMA Intern Med. 2019 Jul 8.
1005. Sathe AG, Tillman H, Coles LD, et al. **Underdosing of Benzodiazepines** in Patients with Status Epilepticus Enrolled in Established Status Epilepticus Treatment Trial. Acad Emerg Med. 2019 Jun 4.
1006. Blotière PO, Raguideau F, Weill A, Elefant E, et al. Risks of **23 specific malformations** associated with prenatal exposure to 10 antiepileptic drugs. Neurology. 2019 Jul 9;93(2):e167-e180.
1007. Gilliam FG, Black K, Carter J, et al. A Trial of **Sertraline or Cognitive Behavior Therapy** for Depression in Epilepsy. Ann Neurol. 2019 Jul 29.
1008. Overwater IE, Rietman AB, Mous SE, et al. A randomized controlled trial with **everolimus for IQ and autism** in tuberous sclerosis complex. Neurology. 2019 Jul 9;93(2):e200-e209.
1009. Panebianco M, Bresnahan R, Hemming K, et al. **Pregabalin add-on for drug-resistant focal epilepsy**. Cochrane Database Syst Rev. 2019 Jul 9;7:CD005612. Pregabalin, when used as an add-on drug for treatment-resistant focal epilepsy, is significantly more effective than placebo at producing a 50% or greater seizure reduction and seizure freedom. Results demonstrated efficacy for doses from 150 mg/day to 600 mg/day, with increasing effectiveness at 600 mg doses, however issues with tolerability were noted at higher doses. The trials included in this review were of short duration, and longer-term trials are needed to inform clinical decision making.
1010. Verducci C, Hussain F, Donner E, et al. **SUDEP** in the North American SUDEP Registry: The full spectrum of epilepsies. Neurology. 2019 Jul 16;93(3):e227-e236.
1011. Warren AEL, Harvey AS, Vogrin SJ, et al. The epileptic network of **Lennox-Gastaut syndrome**: Cortically driven and reproducible across age. Neurology. 2019 Jul 16;93(3): e215-e226.
1012. Kearney H, Byrne S, Cavalleri GL, Delanty N. Tackling Epilepsy With **High-definition Precision Medicine**: A Review. JAMA Neurol. 2019 Aug 5.
1013. Lowerison MW, Josephson CB, Jetté N, et al. Association of **Levels of Specialized Care With Risk of Premature Mortality** in Patients With Epilepsy. JAMA Neurol. 2019 Aug 5
1014. Tomson T, Battino D, Bonizzoni E, et al. **Declining malformation rates with changed antiepileptic drug prescribing**: an observational study. Neurology 2019;93:e831–e840.
1015. EURAP Study Group. Seizure control and treatment in **pregnancy**: observations from the EURAP epilepsy pregnancy registry. Neurology. 2006 Feb 14;66(3):354-60.
1016. Navarro VJ, Senior JR. Drug-related hepatotoxicity. N Engl J Med. 2006 Feb 16;354(7):731-9. (Bohan TP, et al. Effect of L-carnitine treatment for valproate-induced hepatotoxicity. Neurology. 2001 May 22;56(10):1405-9.)
1017. Farkas V, Steinborn B, Flamini JR, et al. Efficacy and tolerability of adjunctive **lacosamide in pediatric patients with focal seizures**. Neurology. 2019 Sep 17;93(12):e1212-e1226.
1018. Ferando I, Soss JR, Elder C, et al. **Hand posture as localizing sign** in adult focal epileptic seizures. Ann Neurol. 2019 Sep 9.
1019. Pang TD, Nearing BD, Krishnamurthy KB, et al. **Cardiac electrical instability** in newly diagnosed/chronic epilepsy tracked by Holter and ECG patch. Neurology. 2019 Sep 3;93(10):450-458.
1020. Wang Z, Larivière S, Xu Q, et al. Community-informed **connectomics of the thalamocortical system in generalized epilepsy**. Neurology. 2019 Sep 10;93(11):e1112-e1122.

Further investigations for Special Circumstances

Bleeding Disorders- ↑ suspicion when initial onset of menses is heavy & regular bleeding patterns or presents with suggestive sx: postpartum hemorrhage; surgery-related bleeding, & bleeding associated with dental procedures; or frequent bruising, epistaxis, and bleeding gums. Further investigations: platelet count, PTT, INR, von Willebrand factor,& ristocetin factor

Peri-menopausal- consider endometrial sampling first line due to ↑ risk of endometrial hyperplasia/carcinoma in patients >45yrs or <45 WITH hx of unopposed estrogen exposure, failed medical management, or persistent AUB.

Uterine Fibroids (leiomyomas) & AUB Treatment[32,33,34,35]

Uterine fibroids are commonly found in women in the middle to later reproductive years & are associated with symptoms such as heavy bleeding, menstrual pain, pressure in the lower abdomen, infertiliy, & recurrent miscarriages. Uterine fibroids are thought to be estrogen and progesterone dependent because they shrink after menopause. Traditionally treatment has been the surgical route (myomectomy or hysterectomy), but drug treatments are becoming more relevant:

Agents currently used for Uterine Fibroids

1. GnRH agonists: ↓ uterine fibroid size (by ≤50%) & ↓ uterine fibroid-related symptoms, but treatment restricted to 3-6 months due to hypoestrogenic AE & fibroids return to pretreatment size once agents are stopped
2. LNG-IUS MIRENA: ↓ menstrual blood loss related to uterine fibroids & ↑ hemoglobin in women with anemia, but is not beneficial for uterine regression
3. Ulipristal FIBRISTAL: selective progesterone receptor modulator; ↓ uterine fibroid volume (≤31% vs placebo ↑ 3%); controls bleeding & faster onset of amenorrhea (noninferior & more sustained effect than leuprolide acetate); no serious side effects
4. Elagolix ORILISSA: GnRH antagonist; ↓ menstrual blood loss (reduction in baseline bleeding by ≥50% = 31% vs. 94%); ↓ uterine fibroid volume (mean percentage change since baseline 4.6% vs. -39.6%). Potential for add-back therapy to ↓ adverse events[36]

Agents in the Clinical Trial Pipeline for the indication of Uterine Fibroid Associated Abnormal Uterine Bleeding:

- Mifepristone MIFEPREX: competitively binds & antagonizes progesterone receptors; inconsistent evidence on effect of uterine size reduction (0 to 50%); ↑ endometrial hyperplasia with no atypia (unsure of clinical implications)
- Asoprisnil: selective progesterone receptor modulator with high receptor & tissue specificity; 25mg/day ↓ volume by ≤36%; ↓ bloating, pelvic pain, & uterine artery blood flow; minimal hypoestrogenic effects
- Telapristone PROELLEX: selective progesterone modulator; doses of 12.5, 25, & 50mg ↓ fibroid size by 10.6, 32.6, & 40.3% respectively (leuprolide acetate 32.6% & placebo 10.6% ↓)
- Aromatase inhibitors (letrozole, anastrozole, fadrozole): antiestrogen; ↓ size of fibroid & symptoms (menstrual volume, duration of menstruation, & dysmenorrhea); no serious side effects reported

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[1] Singh S, Best C, Dunn S, Leyland N, Wolfman WL, et al.; Clinical Practice – Gynaecology Committee; Society of Obstetricians and Gynaecologists of Canada. Abnormal uterine bleeding in pre-menopausal women. J Obstet Gynaecol Can. 2013 May;35(5):473-9.

[2] Davidson BR, Dipiero CM, Govoni KD, Littleton SS, Neal JL. Abnormal uterine bleeding during the reproductive years. J Midwifery Womens Health. 2012 May-Jun;57(3):248-54.

[3] Sweet MG, Schmidt-Dalton TA, Weiss PM, Madsen KP. Evaluation and management of abnormal uterine bleeding in premenopausal women. Am Fam Physician. 2012 Jan 1;85(1):35-43.

[4] Bordman R, Telner D, Jackson B, Little D, Gamache N. An Approach to the diagnosis and management of benign uterine conditions in primary care. Second. 2010. Centre for Effective Practice and Ontario College of Family Physicians. Accessed October 4, 2013 from: http://machealth.ca/programs/buc/m/resources/26.aspx.

[5] Ely JW, Kennedy CM, Clark EC, Bowdler NC. Abnormal uterine bleeding: a management algorithm. J Am Board Fam Med. 2006 Nov-Dec;19(6):590-602.

[6] American College of Obstetricians and Gynecologists. ACOG committee opinion no. 557: Management of acute abnormal uterine bleeding in nonpregnant reproductive-aged women. Obstet Gynecol. 2013 Apr;121(4):891-6.

[7] Morrell MJ, Hayes FJ, Sluss PM, et al. Hyperandrogenism, ovulatory dysfunction, and polycystic ovary syndrome with valproate versus lamotrigine. *Ann Neurol*. 2008;64(2):200–211.

[8] Madhusoodanan S, Parida S, Jimenez C. Hyperprolactinemia associated with psychotropics—a review. *Hum Psychopharmacol*. 2010;25(4):281–297.

[9] O'Malley P. Selective serotonin reuptake inhibitors and abnormal bleeding. Implications for the clinical nurse specialist. Clin Nurse Spec. 2004 Mar-Apr;18(2):65-7.

[10] Committee on Practice Bulletins—Gynecology. Practice bulletin no. 136: management of abnormal uterine bleeding associated with ovulatory dysfunction. Obstet Gynecol. 2013 Jul;122(1):176-85.

[11] Matteson KA, Abed H, Wheeler TL 2nd, Sung VW, Rahn DD, Schaffer JI, Balk EM;Society of Gynecologic Surgeons Systematic Review Group. A systematic review comparing hysterectomy with less-invasive treatments for abnormal uterine bleeding. J Minim Invasive Gynecol. 2012 Jan-Feb;19(1):13-28.

[12] Marret H, Fauconnier A, Chabbert-Buffet N, Cravello L, Golfier F, Gondry J, Agostini A,et al.; CNGOF Collège National des Gynécologues et Obstétriciens Français. Clinical practice guidelines on menorrhagia: management of abnormal uterine bleeding before menopause. Eur J Obstet Gynecol Reprod Biol. 2010 Oct;152(2):133-7.

[13] Learman LA, Summitt RJ, Varner RE, et al. Hysterectomy versus expanded medical treatment for abnormal uterine bleeding: clinical outcomes in the medicine or surgery trial. *Obstet Gynecol*. 2004;103(5):824-833.

[14] Showstack J, Lin F, Learman LA, et al. Randomized trial of medical treatment versus hysterectomy for abnormal uterine bleeding: resource use in theMedicine or Surgery (Ms) trial. *Am J Obstet Gynecol*. 2006;194(2):332-338.

[15] Jensen B, Regier L, Downey S, Karlson P, Taylor J. RxFiles Over the Counter Products Summary Chart. RxFiles, Drug Comparison Charts, 9th edition. 2012. Accessed online at: http://www.rxfiles.ca/rxfiles/uploads/documents/members/CHT-OTCs.pdf

[16] Munro MG, Critchley HO, Broder MS, Fraser IS; FIGO Working Group on Menstrual Disorders. FIGO classification system (PALM-COEIN) for causes of abnormal uterine bleeding in nongravid women of reproductive age. Int J Gynaecol Obstet. 2011 Apr;113(1):3-13.
Munro MG, Critchley HOD, Fraser IS; **FIGO Menstrual Disorders** Committee. The **two FIGO systems** for normal and abnormal uterine bleeding symptoms and classification of causes of abnormal uterine bleeding in the reproductive years: 2018 revisions. Int J Gynaecol Obstet. 2018 Sep 10.

[17] Telner DE, Jakubovicz D. Approach to diagnosis and management of abnormal uterine bleeding. Can Fam Physician. 2007 Jan;53(1):58-64.

[18] Shawki O, Wahba A, Magon N. Abnormal uterine bleeding in midlife: The role of levonorgestrel intrauterine system. J Midlife Health. 2013 Jan;4(1):36-9.

[19] Duckitt K. Medical management of perimenopausal menorrhagia: an evidence-based approach. Menopause Int. 2007 Mar;13(1):14-8.

[20] Beasley A. Contraception for specific populations. Semin Reprod Med. 2010 Mar;28(2):147-55.

[21] World Health Organization, Department of Reproductive Health. Medical elgibility criteria for contraceptive use, fourth edition. 2010.

[22] Hardman SM, Gebbie AE. Hormonal contraceptive regimens in the perimenopause. Maturitas. 2009 Jul 20;63(3):204-12.

[23] Lidegaard Ø. Hormonal contraception and venous thromboembolic risk in midlife women. Maturitas. 2013 Jan;74(1):1-2.
[24] Kaunitz, A., Inki, P. The Levonorgestrel-Releasing Intrauterine System in Heavy Menstrual Bleeding. Drugs. 2012;72 (2):193-215.
[25] ACOG Practice Bulletin No. 110: noncontraceptive uses of hormonal contraceptives. Obstet Gynecol. 2010 Jan;115(1):206-18.
[26] Inki P, Hurskainen R, Palo P, Ekholm E, Grenman S, Kivelä A, Kujansuu E, Teperi J, Yliskoski M, Paavonen J. Comparison of ovarian cyst formation in women using the levonorgestrel-releasing intrauterine system vs. hysterectomy. Ultrasound Obstet Gynecol. 2002 Oct;20(4):381-5.
[27] Regier L, Downey S. RxFiles Hormonal Contraception Summary Chart. RxFiles, Drug Comparison Charts, 9th edition. 2012. Accessed online at: http://www.rxfiles.ca/rxfiles/uploads/documents/members/CHT-OCs-Color.pdf
[28] Espey E. Levonorgestrel intrauterine system--first-line therapy for heavy menstrual bleeding. N Engl J Med. 2013 Jan 10;368(2):184-5.
[29] Palmara V, Sturlese E, Villari D, Giacobbe V, Retto A, Santoro G. Levonorgestrel-releasing intrauterine device in the treatment of abnormal uterinebleeding: a 6- and 12-month morphological and clinical follow-up. Aust N Z J Obstet Gynaecol. 2013 Aug;53(4):381-5.
[30] Robinson JA, Burke AE. Obesity and hormonal contraceptive efficacy. Womens Health (Lond Engl). 2013 Sep;9(5):453-66.
[31] Madden T, Proehl S, Allsworth JE, Secura GM, Peipert JF. Naproxen or estradiol for bleeding and spotting with the levonorgestrel intrauterine system: a randomized controlled trial. Am J Obstet Gynecol. 2012 Feb;206(2):129.e1-8
[32] Tristan M, Orozco LJ, Steed A, Ramírez-Morera A, Stone P. Mifepristone for uterine fibroids. Cochrane Database Syst Rev. 2012
[33] Therapeutic Research Center. New Drug: Fibristal (Ulipristal). Pharmacist's Letter.2013.
[34] Sangkomkamhang US, Lumbiganon P, Laopaiboon M, Mol BW. Progestogens orprogestogen-releasing intrauterine systems for uterine fibroids. Cochrane Database Syst Rev. 2013.
[35] Islam MS, Protic O, Giannubilo SR, Toti P, Tranquilli AL, Petraglia F, Castellucci M, Ciarmela P. Uterine leiomyoma: available medical treatments and new possible therapeutic options. J Clin Endocrinol Metab. 2013 Mar;98(3):921-34.
[36] Carr BR, Stewart EA, Archer DF, Al-Hendy A, Bradley L, et al. **Elagolix Alone or With Add-Back Therapy in Women With Heavy Menstrual Bleeding and Uterine Leiomyomas: A Randomized Controlled Trial**. Obstet Gynecol. 2018 Nov;132(5):1252-1264

Additional References:

ACOG: American College of Obstetricians and Gynecologists.Committee Opinion No. 580. **Von Willebrand Disease** in women. Obstet Gynecol 2013 Dec; 122:1368.
ACOG: American College of Obstetricians and Gynecologists. ACOG Committee Opinion No. 734: The role of **transvaginal ultrasonography in evaluating the endometrium of women** with postmenopausal bleeding. Obstet Gynecol 2018 May; 131:e124.
ACOG Committee Opinion No. 760: **Dysmenorrhea and Endometriosis** in the Adolescent. Obstet Gynecol. 2018 Dec;132(6):e249-e258.
Agarwal N, Gupta M, Kriplani A, Bhatla N, Singh N. Comparison of **combined hormonal vaginal ring with ultralow-dose combined oral contraceptive pills** in the management of heavy menstrual bleeding: A pilot study. J Obstet Gynaecol. 2015 Jul 23:1-5.
Akkan S, Corbacioglu SK, Aytar H, et al. Evaluating **Effectiveness of Nasal Compression With Tranexamic Acid** Compared With Simple Nasal Compression and Merocel Packing: A Randomized Controlled Trial. Ann Emerg Med. 2019 May 9.
Ammerman SR, Nelson AL. A new progestogen-only medical therapy for outpatient management of acute, abnormal uterine bleeding: a pilot study. Am J Obstet Gynecol. 2013 Jun;208(6):499.e1-5.
Beyda R, Johari D. **Tranexamic acid** for upper gastrointestinal bleeding. Acad Emerg Med. 2019 Jul 22.
Bofill Rodriguez M, Lethaby A, Low C, Cameron IT. **Cyclical progestogens for heavy menstrual bleeding**. Cochrane Database of Systematic Reviews 2019, Issue 8. Art. No.: CD001016. DOI: 10.1002/14651858.CD001016.pub3
Boonyawat K, O'Brien SH, Bates SM. **How we treat heavy menstrual bleeding associated with anticoagulants**. Blood. 2017 Nov 1.
Bs D, Nanda SK. The role of sevista in the management of dysfunctional uterine bleeding. J Clin Diagn Res. 2013 Jan;7(1):132-4.
Burnett M, Lemyre M. **SOGC: No. 345-Primary Dysmenorrhea Consensus Guideline**. J Obstet Gynaecol Can. 2017 Jul;39(7):585-595.
Carr BR, Stewart EA, Archer DF, et al. **Elagolix Alone** or With **Add-Back Therapy** in Women With **Heavy Menstrual Bleeding and Uterine Leiomyomas**: A Randomized Controlled Trial. Obstet Gynecol. 2018 Oct 5.
Chandraharan E, Krishna A. **Diagnosis and management of postpartum haemorrhage**. BMJ. 2017 Sep 27;358:j3875
Chornenki NLJ, Um KJ, Mendoza PA, et al. Risk of **venous and arterial thrombosis in non-surgical patients receiving systemic tranexamic acid**: A systematic review and meta-analysis. Thromb Res. 2019 Jul;179:81-86.
Clark TJ, Middleton LJ, Cooper NA, et al. A randomised controlled trial of **Outpatient versus inpatient Polyp Treatment (OPT)** for abnormal uterine bleeding. Health Technol Assess. 2015 Jul;19(61):1-194.
Clarke MA, Long BJ, Del Mar Morillo A, et al. **Association of Endometrial Cancer Risk** With Postmenopausal Bleeding in Women: A Systematic Review and Meta-analysis. JAMA Intern Med. 2018 Sep 1;178(9):1210-1222.
Committee on Practice Bulletins—Gynecology. Practice bulletin no. 128: diagnosis of abnormal uterine bleeding in reproductive-aged women. Obstet Gynecol. 2012 Jul;120(1):197-206.
Coomarasamy A, Devall AJ, Cheed V, et al. A Randomized Trial of **Progesterone in Women with Bleeding in Early Pregnancy**. (PRISM) N Engl J Med. 2019 May 9;380(19):1815-1824.
Cooper NA, Barton PM, Breijer M, et al. **Cost-effectiveness of diagnostic strategies** for the management of abnormal uterine bleeding (heavy menstrual bleeding and post-menopausal bleeding): a decision analysis. Health Technol Assess. 2014 Apr;18(24):1-202.
Cooper NAM, Clark TJ, Middleton L, Diwakar L, Smith P, Denny E, et al. Outpatient versus inpatient **uterine polyp treatment** for abnormal uterine bleeding: randomised controlled non-inferiority study. BMJ 2015;350:h1398.
De La Cruz MSD, Buchanan EM. **Uterine Fibroids**: Diagnosis and Treatment. Am Fam Physician. 2017;95(2):100-107.
Deligeoroglou E, Karountzos V, Creatsas G. Abnormal uterine bleeding and dysfunctional uterine bleeding in pediatric and adolescent gynecology. Gynecol Endocrinol. 2013 Jan;29(1):74-8.
Engelberg D, Pankratieva E, Liauchonak I. Diagnostic value of **hysteroscopy in abnormal uterine bleeding**. Can Fam Physician. 2018 Jun;64(6):442-444.
European Medicines Agency. 2018. **Esmya: new measures to minimise risk of rare but serious live injury [**online]. Available: https://www.gov.uk/drug-safety-update/esmya-ulipristal-acetate-and-risk-of-serious-liver-injury-new-restrictions-to-use-and-requirements-for-liver-function-monitoring-before-during-and-after-treatmetn [Accessed 18 January 2019]
Farquhar C. **Oral contraceptive pill for heavy menstrual bleeding**. Cochrane Database Syst Rev. 2009.
Farrow LS, Smith TO, Ashcroft GP, et al. A systematic review of **Tranexamic acid** in hip fracture surgery. Br J Clin Pharmacol. 2016 Aug 4.
Gayet-Ageron A et al. Effect of treatment delay on the effectiveness and safety of **antifibrinolytics in acute severe haemorrhage**: A meta-analysis of individual patient-level data from 40 138 bleeding patients. Lancet 2017 Nov 7.
Hartmann KE, Velez Edwards DR, Savitz DA, et al. Prospective Cohort Study of **Uterine Fibroids and Miscarriage Risk**. Am J Epidemiol. 2017 Nov 15;186(10):1140-1148.
Health Canada Mar/18 is advising Canadians that it will be conducting a safety review of **Fibristal (ulipristal acetate),** a medication used to treat uterine fibroids in women. Health Canada's review is a result of Canadian and European reports of serious adverse events affecting the liver.
Health Canada's Jan/19, review of the available information concluded that there may be a link between Fibristal use and risk of serious liver injury. Health Canada reviewed the risk of liver injury with the use of Fibristal after becoming aware of four international reports of liver injury leading to liver transplants.
Hoellen F, Griesinger G, Bohlmann MK. Therapeutic drugs in the **treatment of symptomatic uterine fibroids**. Expert Opin Pharmacother. 2013 Oct;14(15):2079-85.
Johnston LR, Rodriguez CJ, Elster EA, Bradley MJ. Evaluation of **Military Use of Tranexamic Acid and Associated Thromboembolic Events**. JAMA Surg. 2017 Oct 25.
Kaunitz AM. Abnormal Uterine Bleeding **in Reproductive-Age Women.** JAMA. 2019 May 9
Ker K, Prieto-Merino D, Roberts I. Systematic review, meta-analysis and meta-regression of the effect of **tranexamic acid** on surgical blood loss. Br J Surg 2013;100:1271–9.
Ker K, Shakur H, Roberts I. Does **tranexamic acid** prevent postpartum haemorrhage? A systematic review of randomised controlled trials. BJOG. 2016 Oct;123(11):1745-52.
Lecker I, Wang DS, Whissell PD, et al. **Tranexamic acid-associated seizures**: Causes and treatment. Ann Neurol. 2015 Nov 18.
Lethaby a, Cooke I, Rees MC. Progesterone or progestogen-releasing intrauterine systems for heavy menstrual bleeding. Cochrane Database Syst Rev. 2010.
Lethaby A, Duckitt K, Farquhar C. Non-steroidal anti-inflammatory drugs forheavy menstrual bleeding. Cochrane Database Syst Rev. 2013.

Lethaby A, Farquhar C, Cooke I. Antifibrinolytics for heavy menstrual bleeding. Cochrane Database Syst Rev. 2010.

Lethaby A, Hussain M, Rishworth JR, et al. **Progesterone or progestogen-releasing intrauterine systems for heavy menstrual bleeding**. Cochrane Database Syst Rev. 2015 Apr 30;4:CD002126. The levonorgestrel-releasing intrauterine device (LNG IUS) is more effective than oral medication as a treatment for heavy menstrual bleeding (HMB). It is associated with a greater reduction in HMB, improved quality of life and appears to be more acceptable long term but is associated with more minor adverse effects than oral therapy.When compared to endometrial ablation, it is not clear whether the LNG IUS offers any benefits with regard to reduced HMB and satisfaction rates and quality of life measures were similar. Some minor adverse effects were more common with the LNG IUS but it appeared to be more cost effective than endometrial ablation techniques.The LNG IUS was less effective than hysterectomy in reducing HMB. Both treatments improved quality of life but the LNG IUS appeared more cost effective than hysterectomy for up to 10 years after treatment.

Lethaby A;Puscasiu L;Vollenhoven B. **Preoperative medical therapy before surgery for uterine fibroids**. Cochrane Database Syst Rev. 2017 Nov 15;11:CD000547. A rationale for the use of preoperative medical therapy before surgery for fibroids is to make surgery easier. There is clear evidence that preoperative GnRHa reduces uterine and fibroid volume, and increases preoperative haemoglobin levels, although GnRHa increases the incidence of hot flushes. During hysterectomy, blood loss, operation time and complication rates were also reduced. Evidence suggests that ulipristal acetate may offer similar advantages (reduced fibroid volume and fibroid-related bleeding and increased haemoglobin levels) although replication of these studies is advised before firm conclusions can be made.

Lethaby A, Wise MR, Weterings MA, et al. **Combined hormonal contraceptives** for heavy menstrual bleeding. Cochrane Database Syst Rev. 2019 Feb 11;2:CD000154. Moderate-quality evidence suggests that the combined oral contraceptive pill over six months reduces HMB in women with unacceptable HMB from 12% to 77% (compared to 3% in women taking placebo). When compared with other medical options for HMB, COCP was less effective than the LNG IUS. Limited evidence suggested that COCP and CVR had similar effects. There was insufficient evidence to determine comparative efficacy of combined hormonal contraceptives with NSAIDs, or long course progestogens.

Liu JH, Soper D, Lukes A, et al. **Ulipristal Acetate for Treatment of Uterine Leiomyomas**: A Randomized Controlled Trial. Obstet Gynecol. 2018 Oct 5.

Lukes AS, Soper D, Harrington A, et al. **Health-Related Quality of Life With Ulipristal Acetate** for Treatment of **Uterine Leiomyomas**: A Randomized Controlled Trial. Obstet Gynecol. 2019 May;133(5):869-878.

Lumsden MA, Hamoodi I, Gupta J, Hickey M. **Fibroids**: diagnosis and management. BMJ. 2015 Oct 13;351:h4887.

Manno D, Ker K, Roberts I. How effective is **tranexamic acid** for acute gastrointestinal bleeding? BMJ. 2014 Feb 17;348:g1421.

Martinelli I, Lensing AW, Middeldorp S, et al. **Recurrent venous thromboembolism and abnormal uterine bleeding with anticoagulant and hormone therapy use**. Blood. 2015 Dec 22.

Matteson KA, Rahn DD, Wheeler TL 2nd, Casiano E, Siddiqui NY, Harvie HS, Mamik MM, Balk EM, Sung VW; Society of Gynecologic Surgeons Systematic Review Group. Nonsurgical management of heavy menstrual bleeding: a systematic review. Obstet Gynecol. 2013 Mar;121(3):632-43.

McGuire C, Nurmsoo S, Samargandi OA, Bezuhly M. Role of Tranexamic Acid in Reducing Intraoperative Blood Loss and Postoperative Edema and Ecchymosis in Primary Elective Rhinoplasty: A Systematic Review and Meta-analysis. JAMA Facial Plast Surg. 2019 Jan 3.

McNamara M, Batur P, DeSapri KT**. In the Clinic: Perimenopause**. Ann Intern Med. 2015 Feb 3;162(3):ITC1.

MHRA Feb/18 **Esmya**: no new treatment courses prescribed until further notice. Temporary safety measures have been introduced whilst the EMA review is ongoing following a further case of **serious liver injury** requiring liver transplant.

Middleton LJ, Champaneria R, Daniels JP, Bhattacharya S, Cooper KG, Hilken NH, et al. Hysterectomy, endometrial destruction, and levonorgestrel releasing intrauterine system (Mirena) for heavy menstrual bleeding: systematic review and meta-analysis of data from individual patients. BMJ. 2010 Aug 16;341:c3929.

Munro MG, Critchley HOD, Fraser IS; **FIGO Menstrual Disorders** Committee. The **two FIGO systems** for normal and abnormal uterine bleeding symptoms and classification of causes of abnormal uterine bleeding in the reproductive years: 2018 revisions. Int J Gynaecol Obstet. 2018 Sep 10.

Myles PS, Smith JA, Forbes A, et al. **Tranexamic Acid** in Patients Undergoing Coronary-Artery Surgery. N Engl J Med. 2016 Oct 23.

NICE: National Guideline Alliance. **Endometriosis: diagnosis and management**. London (UK): National Institute for Health and Care Excellence (NICE); 2017 Sep 6.

Pattanittum P, Kunyanone N, Brown J, et al. **Dietary supplements for dysmenorrhoea**. Cochrane Database Syst Rev. 2016 Mar 22;3:CD002124. There is no high quality evidence to support the effectiveness of any dietary supplement for dysmenorrhoea, and evidence of safety is lacking. However for several supplements there was some low quality evidence of effectiveness and more research is justified.

Peragallo Urrutia R, Coeytaux RR, McBroom AJ, Gierisch JM, Havrilesky LJ, Moorman PG, Lowery WJ, Dinan M, Hasselblad V, Sanders GD, Myers ER. Risk of Acute Thromboembolic Events With Oral Contraceptive Use: A Systematic Review and Meta-analysis. Obstet Gynecol. 2013 Aug;122(2, PART 1):380-389.

Pinkerton JV. Pharmacological therapy for abnormal uterine bleeding. Menopause. 2011 Apr;18(4):453-61.

Ray S, Ray A. **Non-surgical interventions for treating heavy menstrual bleeding (menorrhagia) in women with bleeding disorders**. Cochrane Database Syst Rev. 2016 Nov 10;11:CD010338. Evidence from randomised controlled studies on the effect of desmopressin when compared to placebo in reducing menstrual blood loss is very limited and inconclusive. Two studies, each with a very limited number of participants, have shown uncertain effects in menstrual blood loss and adverse effects. A non-randomised comparison in one of the studies points to the value of combining desmopressin and tranexamic acid, which needs to be tested in a formal randomised controlled study comparison.When tranexamic acid was compared to desmopressin, a single study showed a reduction in menstrual blood loss with tranexamic acid use compared to desmopressin.There is a need to evaluate non-surgical methods for treating of menorrhagia in women with bleeding disorders through randomised controlled studies. Such methods would be more acceptable than surgery for women wishing to retain their fertility. Given that women may need to use these treatments throughout their entire reproductive life, long-term side-effects should be evaluated.

Roberts TE, Tsourapas A, Middleton LJ, Champaneria R, Daniels JP, Cooper KG, et al. Hysterectomy, endometrial ablation, and levonorgestrel releasing intrauterine system (Mirena) for treatment of heavy menstrual bleeding: cost effectiveness analysis. BMJ. 2011 Apr 26;342:d2202.

Rott H. Thrombotic risks of oral contraceptives. Curr Opin Obstet Gynecol.2012 Aug;24(4):235-40.

Sentilhes L, Winer N, Azria E, et al. **Tranexamic Acid** for the Prevention of Blood Loss after Vaginal Delivery. N Engl J Med. 2018 Aug 23;379(8):731-742.

Shakur H, Beaumont D, Pavord S, et al. **Antifibrinolytic drugs for treating primary postpartum haemorrhage**. Cochrane Database Syst Rev. 2018 Feb 20;2:CD012964. TXA when administered intravenously reduces mortality due to bleeding in women with primary PPH, irrespective of mode of birth, and without increasing the risk of thromboembolic events. Taken together with the reliable evidence of the effect of TXA in trauma patients, the evidence suggests that TXA is effective if given as early as possible.Facilities for IV administration may not be available in non-hospital settings therefore, alternative routes to IV administration need to be investigated.

Sholzberg M, Teitel J, Hicks LK. A 24-year-old woman with **heavy menstrual bleeding**. CMAJ. 2017 Jun 5;189(22):E779-E780.

Simon JA. Future developments in the medical treatment of abnormal uterine bleeding: what can we expect? Menopause. 2011 Apr;18(4):462-6.

Simon JA, Catherino W, Segars JH, et al. **Ulipristal Acetate for Treatment of Symptomatic Uterine Leiomyomas**: A Randomized Controlled Trial. Obstet Gynecol. 2018 Mar;131(3):431-439.

SOGC: Society of Obstetricians and Gynaecologists of Canada. **Menstrual suppression in special circumstances**. http://sogc.org/wp-content/uploads/2014/10/JOGC-Oct2014-CPG-313_Eng_Online-Complete.pdf accessed Nov/14.

SOGC: Burnett M, Lemyre M. **SOGC**: Society of Obstetricians and Gynaecologists of Canada. SOGC clinical practice guideline No. 345-**Primary Dysmenorrhea Consensus Guideline**. J Obstet Gynaecol Can. 2017 Jul;39(7):585-595.

Sprigg N, Flaherty K, Appleton JP, et al; TICH-2 Investigators. **Tranexamic acid for hyperacute primary IntraCerebral Haemorrhage** (TICH-2): an international randomised, placebo-controlled, phase 3 superiority trial. Lancet. 2018 May 26;391(10135):2107-2115.

Sprigg N, Flaherty K, Appleton JP, et al. **Tranexamic acid** to improve functional status in adults with spontaneous **intracerebral haemorrhage**: the TICH-2 RCT. Health Technol Assess. 2019 Jul;23(35):1-48.

Stewart EA. Clinical practice. **Uterine fibroids**. N Engl J Med. 2015 Apr 23;372(17):1646-55.

Suh-Burgmann E, Hung YY, Mura J. Abnormal vaginal bleeding after epidural steroid injection: a paired observation cohort study. Am J Obstet Gynecol. 2013 Sep;209(3):206.e1-6.

Taylor HS, Giudice LC, Lessey BA, et al. Treatment of **endometriosis-associated pain** with **elagolix**, an oral GnRH antagonist. N Engl J Med 2017;377:28-40.

Topsoee MF, Bergholt T, Ravn P, et al. Anti-hemorrhagic effect of prophylactic **tranexamic acid** in benign hysterectomy-a double-blinded randomized placebo-controlled trial. Am J Obstet Gynecol. 2016 Jul;215(1):72.e1-8.

Tsai MC, Goldstein SR. Office diagnosis and management of abnormal uterine bleeding. Clin Obstet Gynecol. 2012 Sep;55(3):635-50.

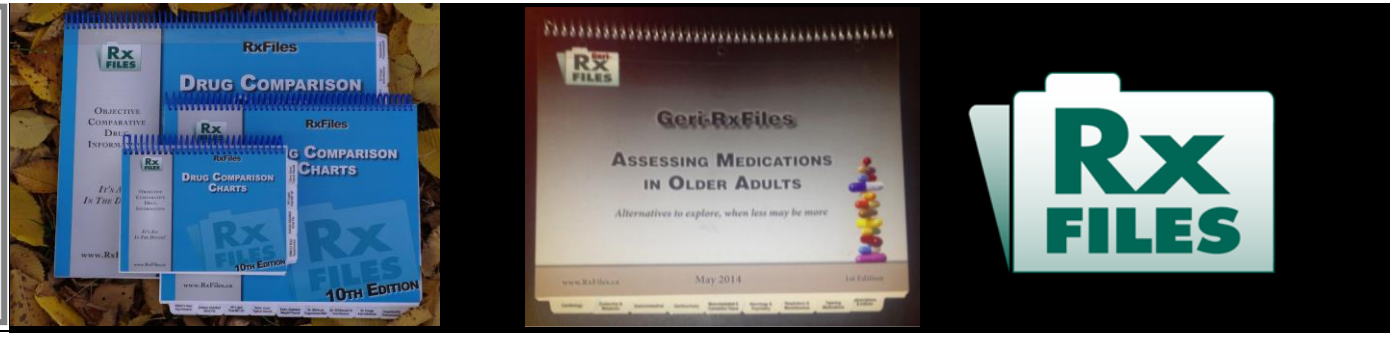
Vilos GA, Allaire C, Laberge PY, et al; Uterine Leiomyomas Working Group, Society of Obstetricians and Gynaecologists of Canada. (**SOGC**) The **management of uterine leiomyomas**. J Obstet Gynaecol Can 2015;37(2):157-78. http://sogc.org/wp-content/uploads/2015/02/gui318CPG1502ErevB1.pdf (accessed June 9, 2015).

Wand O, Guber E, Guber A, et al. **Inhaled Tranexamic Acid** for **Hemoptysis Treatment**: A Randomized Controlled Trial. Chest. 2018 Dec;154(6):1379-1384

Wheeler TL 2nd, Murphy M, Rogers RG, Gala R, Washington B, Bradley L, Uhlig K; Society of Gynecologic Surgeons Systematic Review Group. Clinical practice guideline for abnormal uterine bleeding: hysterectomy versus alternative therapy. J Minim Invasive Gynecol. 2012 Jan-Feb;19(1):81-8.

Wilkinson JP, Kadir RA. Management of abnormal uterine bleeding in adolescents. J Pediatr Adolesc Gynecol. 2010 Dec;23(6 Suppl):S22-30.

WOMAN Trial Collaborators.. Effect of **early tranexamic acid** administration on **mortality, hysterectomy, and other morbidities** in women with **post-partum haemorrhage** (**WOMAN**): an international, randomised, double-blind, placebo-controlled trial. Lancet. 2017 Apr 26.
Wouk N, Helton M. **Abnormal Uterine Bleeding in Premenopausal Women**. Am Fam Physician. 2019 Apr 1;99(7):435-443.
Xie J, Zhang S, Chen G, et al. Optimal route for administering **tranexamic acid in primary unilateral total hip arthroplasty**: results from a multicenter cohort study. Br J Clin Pharmacol. 2019 Jun 24.
Zahed R, Mousavi et al. Topical **Tranexamic Acid** Compared With Anterior Nasal Packing for Treatment of Epistaxis in Patients Taking Antiplatelet Drugs: Randomized Controlled Trial. Acad Emerg Med. 2017 Nov 10.
Zigler RE, Madden T, Ashby C, et al. **Ulipristal Acetate for Unscheduled Bleeding in Etonogestrel Implant** Users: A Randomized Controlled Trial. Obstet Gynecol. 2018 Oct;132(4):888-894.



RxFiles – Abnormal Uterine Bleeding – Tx Chart

Developed by Kellie Towriss, BSP (Pharmacy Resident, Saskatoon Health Region (2013; last revised, June 2015)

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References: 1. Biological activity and therapeutic management. OC Chart. Organon Canada Ltd. 1997. 2. Dickey R. Managing Oral Contraceptive Patients, 9th edition. Essential Medical Information Systems, Durant, OK. 1998. 3. Product monographs. 4. www.RxFiles.ca-Jan00.

References (page 125):

1. Society of Obstetricians and Gynaecologists of Canada (**SOGC**). The Canadian Consensus Conference on Contraception. J Obstet Gynaecol Can. **2004** Mar;26(3):219-96.
SOGC: Society of Obstetricians and Gynaecologists of Canada. **Canadian contraception consensus** (**Part 1 of 4**). J Obstet Gynaecol Can 2015;37(10):S1–28. http://sogc.org/wp-content/uploads/2015/11/gui329Pt1CPG1510.pdf (accessed December 8, 2015).
SOGC: Society of Obstetricians and Gynaecologists of Canada. **Canadian contraception consensus** (**Part 2 of 4**). J Obstet Gynaecol Can 2015;37(11):S1–39. http://sogc.org/wp-content/uploads/2015/11/gui329Pt2CPG1511E.pdf (accessed December 8, 2015).
2. Sherif K. Benefits and risks of oral contraceptives. Am J Obstet Gynecol. 1999; 180: S343-8.
3. Venous thromboembolic disease and combined oral contraceptives: results of international multicentre case-control study. World Health Organization Collaborative Study of Cardiovascular Disease and Steroid Hormone Contraception. Lancet. 1995; 346: 1575-82
4. Effect of different progestagens in low estrogen oral contraceptives on venous thromboembolic disease. World Health Organization Collaborative Study of Cardiovascular Disease and Steroid Hormone Contraception. Lancet. 1995; 346: 1582-8.
5. Kemmeren JM, Algra A, Grobbee DE. Third generation oral contraceptives and risk of venous thrombosis: meta-analysis. BMJ. 2001 Jul 21;323(7305):131-4.
6. Acute myocardial infarction and combined oral contraceptives: results of international multicentre case-control study. World Health Organization Collaborative Study of Cardiovascular Disease and Steroid Hormone Contraception. Lancet. 1997; 349: 1202-9
7. Schlesselman J. Net effect of oral contraceptive use in risk or cancer in women in United States. Obstet Gynecol. 1995; 85: 793-801.
8. Hatcher R et al. Contraceptive Technology, 16th edition. New York, Irvington, 1994.
9. Dickey R. Managing Oral Contraceptive Patients, 9th edition. Essential Medical Information Systems, Durant, OK. 1998.
10. Petitti, Diana B. Combo Estrogen-Progestin Oral Contraceptives. NEJM 2003;349:1443-1450.
11. Treatment Guidelines: **Choice of Contraceptives**. Medical Letter: Dec 2010; p. 89-96. **Oct 2018.**
12. Society of Obstetricians & Gynaecologists of Canada www.sexualityandu.ca ; http://www.sogc.org
13. Iversen L, Fielding S, Lidegaard Ø, Mørch LS, Skovlund CW, Hannaford PC. **Association between contemporary hormonal contraception and ovarian cancer in women of reproductive age in Denmark: prospective, nationwide cohort study.** BMJ. 2018 Sep 26;362:k3609. doi: 10.1136/bmj.k3609.
14. Choice of contraceptives. Med Lett Drugs Ther. 2018 Oct 8;60(1557):161-168.
15. Simmons KB, Haddad LB, Nanda K, Curtis KM. Drug interactions between non-rifamycin antibiotics and hormonal contraception: a systematic review. Am J Obstet Gynecol. 2018 Jan;218(1):88-97.

Contraceptive, Combination Hormonal Products Additional references:

AAP: Committee on Adolescence. **Emergency contraception**. Pediatrics. 2012 Dec;130(6):1174-82.
Abou-Setta AM, et al. **Levonorgestrel**-releasing intrauterine device (LNG-IUD) for symptomatic **endometriosis** following surgery. Cochrane Database Syst Rev. 2006 Oct 18;(4):CD005072.
ACOG Frequently Asked Questions #114, **Emergency Contraception**. http://www.acog.org/~/media/For%20Patients/faq114.pdf?dmc=1&ts=20121127T1830130312. Accessed 1/6/13
ACOG Committee Opinion. Access to **Emergency Contraception**. Number 542, November 2012. www.acog.org/Resources_And_Publications/Committee_Opinions/Committee_on_Health_Care_for_Underserved_Women/Access_to_Emergency_Contraception. Accessed January 10, 2013.
ACOG- Practice bulletin no. 121: **Long-acting reversible contraception**: Implants and intrauterine devices. Obstet Gynecol 2011 Jul; 118:184.
ACOG: Committee opinion no. 539: **adolescents and long-acting reversible contraception**: implants and intrauterine devices. Obstet Gynecol. 2012 Oct;120(4):983-8.
ACOG: Committee Opinion No 544: **Over-the-Counter Access to Oral Contraceptives**. Obstet Gynecol. 2012 Dec;120(6):1527-31.
ACOG: American College of Obstetricians & Gynecologists Committee on Gynecologic Practice. ACOG Committee Opinion No. 602: **Depot medroxyprogesterone acetate and bone effects**. Obstet Gynecol. 2014June 2014.
ACOG: Committee opinion no. 615: **access to contraception**. Obstet Gynecol. 2015 Jan;125(1):250-5.
ACOG Practice Bulletin No. 152: **Emergency Contraception**. Obstet Gynecol. 2015 Sep;126(3):e1-e11.
ACOG: Committee Opinion No. 642: **Increasing Access to Contraceptive Implants and Intrauterine Devices** to Reduce Unintended Pregnancy. Obstet Gynecol. 2015 Oct;126(4):e44-8.
ACOG: Committee Opinion No. 670: **Immediate Postpartum Long-Acting Reversible Contraception**. Obstet Gynecol. 2016 Aug;128(2):e32-7.
ACOG: Committee Opinion No. 710: **Counseling Adolescents About Contraception**. Obstet Gynecol. 2017 Aug;130(2):e74-e80.
ACOG: Committee on Practice Bulletins-Gynecology, Long-Acting Reversible Contraception Work Group. Practice Bulletin No. 186: **Long-Acting Reversible Contraception: Implants and Intrauterine Devices**. Obstet Gynecol. 2017 Nov;130(5):e251-e269.
ACOG: Committee Opinion No. 788: **Over-the-Counter Access to Hormonal Contraception**. Obstet Gynecol. 2019 Oct;134(4):e96-e105.
Adab P, Jiang CQ, Rankin E, et al. **Breastfeeding practice, oral contraceptive use and risk of rheumatoid arthritis** among Chinese women: the Guangzhou Biobank Cohort Study. Rheumatology(Oxford). 2014 Jan 6.
Agostino H, Di Meglio G. **Low-dose** oral contraceptives in adolescents: how low can you go? J Pediatr Adolesc Gynecol. 2010 Aug;23(4):195-201.
Ahmed S, Li Q, Liu L, Tsui AO. **Maternal deaths averted** by contraceptive use: an analysis of 172 countries. Lancet. 2012 Jul 9.
Akers AY, Steinway C, Sonalkar S, et al. **Reducing Pain During Intrauterine Device Insertion**: A Randomized Controlled Trial in Adolescents and Young Women. Obstet Gynecol. 2017 Sep 5.
Akers AY et al. **Reducing pain during intrauterine device insertion**: A randomized controlled trial in adolescents and young women. (lidocaine)Obstet Gynecol 2017 Sep 05; 130:795.
Ali M et al. Extended use **up to 5 years** of the **etonogestrel**-releasing subdermal contraceptive implant: Comparison to levonorgestrel-releasing subdermal implant. Hum Reprod 2016 Sep 26.
Albrecht K, Callhoff J, Buttgereit F, et al. The association between the use of **oral contraceptives and patient-reported outcomes in an early arthritis cohort**. Arthritis Care Res (Hoboken). 2015 Aug 14.
Albaladejo A. **Contraceptive shortages mean Venezuela's** people face a sexual health emergency. BMJ. 2018 Mar 23;360:k1197.
Al Khalifah RA et al. **Metformin or oral contraceptives for adolescents with polycystic ovarian syndrome**: A meta-analysis. Pediatrics 2016 May; 137:e20154089.
Al Khalifah RA, Florez ID, Dennis B, et al. Metformin or Oral Contraceptives for Adolescents With **Polycystic Ovarian Syndrome**: A Meta-analysis. Pediatrics. 2016 May;137(5).
Alkema L, Kantorova V, Menozzi C, Biddlecom A. National, regional, and **global rates and trends in contraceptive prevalence** and unmet need for family planning between 1990 and 2015: a systematic and comprehensive analysis. Lancet 2013; online March 12.
Allen RH, Cwiak CA, Kaunitz AM. Contraception in **women over 40 years of age**. CMAJ. 2013 Apr 16;185(7):565-73.
Almstedt Shoepe H, Snow CM. Oral contraceptive use in young women is associated with lower bone mineral density than that of controls. Osteoporos Int. 2005 May 19; [Epub ahead of print]
Alpañés M, et al. **Combined oral contraceptives plus spironolactone** compared with **metformin in women with polycystic ovary syndrome**: one-year randomized clinical trial. Eur J Endocrinol. 2017 Nov;177(5):399-408.
American College of Obstetricians and Gynecologists (ACOG). Emergency contraception. Washington (DC): American College of Obstetricians and Gynecologists (ACOG); 2005 Dec. 10 p. (ACOG practice bulletin; no. 69).
American College of Obstetricians and Gynecologists (ACOG). **Emergency contraception**. Washington (DC): American College of Obstetricians and Gynecologists (ACOG); 2010 May. (ACOG practice bulletin; no. 112).
American College of Obstetricians and Gynecologists (ACOG). **Noncontraceptive uses of hormonal contraceptives**. Washington (DC): American College of Obstetricians and Gynecologists (ACOG); 2010 Jan. 13 p. (ACOG practice bulletin; no. 110).
American College of Obstetricians and Gynecologists (ACOG): Practice Bulletin #121 "Long-Acting Reversible Contraception: **Implants and Intrauterine Devices**" in the July 2011 issue of Obstetrics & Gynecology.

Amy JJ, Tripathi V. Contraception for women: an evidence based overview. BMJ. 2009 Aug 7;339:b2895. doi: 10.1136/bmj.b2895.
Anderl C, Li G, Chen FS. Oral contraceptive use in adolescence predicts lasting **vulnerability to depression in adulthood**. J Child Psychol Psychiatry. 2019 Aug 28.
Andersen L, Friis S, Hallas J, et al. **Hormonal contraceptive use and risk of glioma** among younger women a nationwide case-control study. Br J Clin Pharmacol. 2014 Oct 26.
Anderson FD, Hait H. A multicenter, randomized study of an extended cycle oral contraceptive. Contraception. 2003 Aug;68(2):89-96. Erratum in: Contraception. 2004 Feb;69(2):175.
Anderson DC, Sullivan DM. **Plan B and the german catholic bishops**. Ann Pharmacother. 2013 Jul;47(7-8):1079-80.
Aptekman M, Rashid M, Wright V, Dunn S. **Unmet contraceptive needs among refugees**. Can Fam Physician. 2014 Dec;60(12):e613-9.
Austin Harland, Lally Cathy, et al. Hormonal contraception, **sickle cell** trait, and risk for venous thromboembolism among **African American** women. American Journal of Obstetrics & Gynecology - June 2009 (Vol. 200, Issue 6, Pages 620.e1-620.e3, DOI: 10.1016/j.ajog.2009.01.038)
Baillargeon JP, McClish DK, et al. Association between the current use of low-dose oral contraceptives and **cardiovascular arterial disease**: a meta-analysis. J Clin Endocrinol Metab. 2005 Jul;90(7):3863-70.Epub 2005Apr 6.
Barrionuevo P, Nabhan M, Altayar O, et al. **Treatment Options for Hirsutism**: A Systematic Review and Network Meta-Analysis. J Clin Endocrinol Metab. 2018 Apr 1;103(4):1258-1264.
de Bastos M, Stegeman BH, Rosendaal F, et al. Combined oral contraceptives: **venous thrombosis**. Cochrane Database Syst Rev 2014;3:CD010813. All combined oral contraceptives investigated in this analysis were associated with an increased risk of venous thrombosis. The effect size depended both on the progestogen used and the dose of ethinylestradiol. Risk of venous thrombosis for combined oral contraceptives with 30-35 µg ethinylestradiol and gestodene, desogestrel, cyproterone acetate and drospirenone were similar, and about 50-80% higher than with levonorgestrel. The combined oral contraceptive with the lowest possible dose of ethinylestradiol and good compliance should be prescribed-that is, 30 µg ethinylestradiol with levonorgestrel.
Bateson D, McNamee K, Briggs P. **Newer non-oral hormonal contraception**. BMJ. 2013 Feb 14;346:f341.
Batra P, Rafie S, Zhang Z, et al. An Evaluation of the Implementation of **Pharmacist-Prescribed Hormonal Contraceptives in California**. Obstet Gynecol. 2018 Apr 6.
Batur P. **Emergency contraception**: Separating fact from fiction. Cleve Clin J Med. 2012 Nov;79(11):771-6.
Beaber EF, Buist DS, Barlow WE, et al. Recent Oral Contraceptive Use by Formulation and **Breast Cancer Risk** among Women 20 to 49 Years of Age. Cancer Res. 2014 Aug 1;74(15):4078-89.
Beasley A et al. Randomized clinical trial of **self versus clinical administration of subcutaneous depot medroxyprogesterone** acetate. Contraception 2014 May; 89:352.
Becker NV, Polsky D. Women Saw Large **Decrease In Out-Of-Pocket Spending For Contraceptives** After ACA Mandate Removed Cost Sharing. Health Aff (Millwood). 2015 Jul 1;34(7):1204-11.
Behre HM, Zitzmann M, Anderson RA, et al. Efficacy and Safety of an **Injectable Combination Hormonal Contraceptive for Men**. J Clin Endocrinol Metab. 2016 Oct 27:jc20162141.
Beksinska ME, Smit JA, et al. Prospective study of weight change in new adolescent users of **DMPA**, NET-EN, COCs, nonusers and discontinuers of hormonal contraception. Contraception. 2010 Jan;81(1):30-4.
Bellizzi S, Sobel HL, Obara H, Temmerman M. **Underuse of modern methods of contraception**: underlying causes and consequent undesired pregnancies in 35 low- and middle-income countries. Hum Reprod. 2015 Feb 3.
Bellows BK et al. **Cost-effectiveness of emergency contraception** options over 1 year. Am J Obstet Gynecol 2018 May; 218:508.e1.
Bender NM, Segall-Gutierrez P, Najera SO, et al. Effects of **progestin-only** long-acting contraception on metabolic markers in **obese** women. Contraception. 2013 Jan 2.
Bermas BL. Oral contraceptives in systemic **lupus** erythematosus -- a tough pill to swallow? N Engl J Med. 2005 Dec 15;353(24):2602-4.
Bernier MO, Mikaeloff Y, Hudson M, Suissa S. Combined oral contraceptive use and the risk of systemic **lupus** erythematosus. Arthritis Rheum. 2009 Apr 15;61(4):476-81.
Bialer M, et al. Pharmacokinetic interactions of topiramate. Clin Pharmacokinet. 2004;43(12):763-80.
Birth Control: What You Should Know. Am Fam Physician. 2015 May 1;91(9)
Bissell DM, Anderson KE, Bonkovsky HL. **Porphyria**. N Engl J Med. 2017 Aug 31;377(9):862-872.
Black A, Francoeur D, Rowe T, Collins J, Miller D, Brown T, David M, Dunn S, Fisher WA, Fleming N, Fortin CA, Guilbert E, Hanvey L, Lalonde A, Miller R, Morris M, O'Grady T, Pymar H, Smith T, Henneberg E; Society of Obstetricians and Gynaecologists of Canada. **SOGC** clinical practice guidelines: Canadian contraception consensus. J Obstet Gynaecol Can. 2004 Mar;26(3):219-96.
Black A, Guilbert E; Costescu D, et al; Contraception Consensus Working Group, Society of Obstetricians and Gynaecologists of Canada. (**SOGC**) **Canadian contraception consensus (Part 3 of 4)**: Chapter 7 – **Intrauterine contraception**. J Obstet Gynaecol Can 2016;38:182-222. www.jogc.com/article/S1701-2163(15)00024-9/pdf (accessed April 6, 2016).
Black A, Guilbert E, Costescu D, et al. **SOGC clinical practice guideline. No. 329. Canadian contraception consensus. Part 4 of 4.** Chapter 9: Combined hormonal contraception. J Obstet Gynaecol Can 2017;39:229-68.e5
Blumenthal PD, Edelman A. Hormonal contraception. Obstet Gynecol. 2008 Sep;112(3):670-84.
Bonnema RA., McNamara MC., Spencer AL.,**Contraception Choices in Women with Underlying Medical Conditions**. Am Fam Physician. 2010 Sep 15;82(6):621-628.
Bonny AE et al. A pilot study of **depot medroxyprogesterone acetate pharmacokinetics** and **weight gain** in adolescent females. Contraception 2014 May; 89:357.
Bosworth MC, Olusola PL, Low SB. An update on **emergency contraception**. Am Fam Physician. 2014 Apr 1;89(7):545-50.
Boulet SL, D'Angelo DV, Morrow B, et al. **Contraceptive Use Among Nonpregnant and Postpartum Women** at Risk for Unintended Pregnancy, and Female High School Students, in the Context of Zika Preparedness - United States,2011-2013 and 2015. MMWR Morb Mortal Wkly Rep. 2016 Aug 5;65(30):780-7
Brinkman SA, Johnson SE, Codde JP, et al. Efficacy of **Infant Simulator Programmes** to Prevent Teenage Pregnancy: a School-Based Cluster Randomised Controlled Trial in Western Australia. Lancet. 2016 Aug 24.
British National Formulary 2005
Brown J, Farquhar C. An **overview of treatments for endometriosis**. JAMA. 2015 Jan 20;313(3):296-7.
Brunson MR, Klein DA, Olsen CH, et al. **Postpartum contraception**: initiation and effectiveness in a large universal healthcare system. Am J Obstet Gynecol. 2017 Jul;217(1):55.e1-55.e9.
Burke HM et al. Observational study of the acceptability of **Sayana Press** among **intramuscular DMPA** users in Uganda and Senegal. Contraception 2014 May; 89:361.
Burke HM et al. Provider acceptability of **Sayana Press**: Results from community health workers and clinic-based providers in Uganda and Senegal. Contraception 2014 May; 89:368.
Byrne EB, Anahtar MN, Doherty KE, et al. Association between **injectable progestin-only contraceptives and HIV acquisition** and HIV target cell frequency in the female genital tract in South African women: a prospective cohort study. Lancet Infect Dis 2015; online Dec 23.
Caddy S, Yudin MH, Hakim J, Money DM, Infectious Disease Committee. **SOGC**-Best practices to **minimize risk of infection with intrauterine device insertion**. J Obstet Gynaecol Can. 2014 Mar;36(3):266-74.
Calhoun A. Combined hormonal contraceptives: Is it time to reassess their role in **migraine**? Headache 2011. Published online ahead of print January 6, 2012.
Camacho EM, Lunt M, Farragher TM, et al. The relationship between oral contraceptive use and functional outcome in women with recent **onset inflammatory polyarthritis**: Results from the Norfolk Arthritis Register (NOAR). Arthritis Rheum. 2011 Apr 22. doi: 10.1002/art.30416.
Cameron ST, Glasier A, Chen ZE, Johnstone A, Dunlop C, Heller R. Effect of **contraception provided at termination of pregnancy** and incidence of subsequent termination of pregnancy. BJOG. 2012 Aug;119(9):1074-80.
Canning D, Schultz TP. The **economic consequences** of reproductive health and **family planning**. Lancet. 2012 Jul 9.
Carmo LSMP, Braga GC, Ferriani RA, et al. Timing of **Etonogestrel-Releasing Implants and Growth of Breastfed Infants**: A Randomized Controlled Trial. Obstet Gynecol. 2017 Jun 6.
Caso V, Falorni A, Bushnell CD, et al. **Pregnancy, Hormonal Treatments for Infertility, Contraception, and Menopause** in Women After Ischemic Stroke: A Consensus Document. Stroke. 2017 Feb;48(2):501-506.
Castellsagué X, Díaz M, et al. **Intrauterine device use**, cervical infection with human papillomavirus, and risk of **cervical cancer**: a pooled analysis of 26 epidemiological studies. Lancet Oncol 2011; online Sept 13.
CDA Diane 35 response http://www.dermatology.ca/english/public-patients/Diane35-Fact-Sheet_e.pdf
Centers for Disease Control and Prevention (CDC). Division of Reproductive Health, National Center for Chronic Disease Prevention and Health Promotion. U.S. selected practice recommendations for contraceptive use, 2013: adapted from the World Health Organization Selected Practice Recommendations for Contraceptive Use, 2nd edition. *MMWR Recomm Rep* 2013;62(RR05):1-60.
CDC: Centers for Disease Control and Prevention (CDC). U.S. medical eligibility criteria for contraceptive use, 2010: adapted from the World Health Organization medical eligibility criteria for contraceptive use, 4th edition. MMWR Recomm Rep 2010 Jun 18;59(RR-4):1-86. **CDC** has released **medical eligibility criteria for contraceptive use to help U.S. healthcare providers** counsel patients about their contraceptive choices. The criteria, published in MMWR, are modified from the World Health Organization's 2009 guidance. The CDC offers modified recommendations about contraception for U.S. women who have venous thromboembolism, valvular heart disease, ovarian cancer, and uterine fibroids, as well as women who are postpartum and breast-feeding. It also gives additional guidance on contraception for women with rheumatoid arthritis, previous

bariatric surgery, peripartum cardiomyopathy, endometrial hyperplasia, inflammatory bowel disease, and organ transplantation. http://www.cdc.gov/mmwr/pdf/rr/rr59e0528.pdf
CDC: Update to **CDC's U.S. Medical Eligibility Criteria** for Contraceptive Use, 2010: Revised Recommendations for the Use of Contraceptive Methods During the Postpartum Period. http://www.cdc.gov/mmwr/pdf/wk/mm6026.pdf
CDC: Centers for Disease Control and Prevention. **Sexual experience and contraceptive use among female teens** — United States, 1995, 2002, and 2006–2010. MMWR Morb Mortal Wkly Rep 2012 May 4; 61:297.
Champaloux SW, Tepper NK, Curtis KM, et al. **Contraceptive Use Among Women With Medical Conditions** in a Nationwide Privately Insured Population. Obstet Gynecol. 2015 Dec;126(6):1151-9.
Chang T, Davis MM, Kusunoki Y, et al. **Sexual Behavior and Contraceptive Use** among 18- to 19-Year-Old Adolescent Women by Weight Status: A Longitudinal Analysis. J Pediatr. 2015 Jun 25.
Chang T, Davis MM, Kusunoki Y, et al. **Sexual Behavior and Contraceptive** Use among 18- to 19-Year-Old Adolescent Women by Weight Status: A Longitudinal Analysis. J Pediatr. 2015 Sep;167(3):586-92.
Charlton BM, Rich-Edwards JW, Colditz GA, et al. **Oral contraceptive use and mortality after 36 years** of follow-up in the Nurses' Health Study: prospective cohort study. BMJ. 2014 Oct 31;349:g6356.
Charlton BM, Mølgaard-Nielsen D, Svanström H, et al. Maternal use of **oral contraceptives and risk of birth defects** in Denmark: prospective, nationwide cohort study. BMJ. 2016 Jan 6;352:h6712.
Chee M, Zhang JX, Ngooi S, et al. **Generic Substitution Rates** of Oral Contraceptives and Associated Out-of-Pocket Cost Savings Between January 2010 and December 2014. JAMA Intern Med. 2018 Jan 16.
Chen MJ, Hou MY, Hsia JK, et al. **Long-Acting Reversible Contraception Initiation With a 2- to 3-Week Compared With a 6-Week Postpartum Visit**. Obstet Gynecol. 2017 Sep 5
Cheng L, et al. Interventions for emergency contraception. Cochrane Database Syst Rev. 2008 Apr 16;(2):CD001324. Mifepristone middle dose (25-50 mg) was superior to other hormonal regimens. Mifepristone low dose (<25 mg) could be more effective than levonorgestrel 0.75 mg (two doses) but this was not conclusive. Levonorgestrel proved more effective than the Yuzpe regimen. The copper IUD was another effective emergency contraceptive that can provide ongoing contraception.
Cheng L, Che Y, Gulmezoglu AM. Interventions for **emergency contraception**. Cochrane Database Syst Rev. 2012 Aug 15;8:CD001324. Intermediate-dose mifepristone (25-50 mg) was superior to LNG and Yuzpe regimens. Mifepristone low dose (< 25 mg) may be more effective than LNG (0.75 mg two doses), but this was not conclusive. UPA may be more effective than LNG. LNG proved to be more effective than the Yuzpe regimen. The copper IUD was the most effective EC method and was the only EC method to provide ongoing contraception if left in situ.
Ciccariello C. **Defunding Planned Parenthood**-The Stakes for America's Women. JAMA Intern Med. 2017 Feb 3
Clark MK, et al. **Bone mineral density** loss and recovery during 48 months in first-time users of depot **medroxyprogesterone** acetate. Fertil Steril. 2006 Nov;86(5):1466-74. Epub 2006 Sep 25.
Cleland K, Raymond E, Trussell J, Cheng L, Zhu H. **Ectopic pregnancy and emergency contraceptive pills**: a systematic review. Obstet Gynecol. 2010 Jun;115(6):1263-6.
Cleland K, Zhu H, Goldstuck N, Cheng L, Trussell J. The efficacy of **intrauterine devices for emergency contraception**: a systematic review of 35 years of experience. Human Reproduction doi:10.1093/humrep/des140.
Clinical Effectiveness Unit. **Drug interactions** with hormonal contraception. London (UK): Faculty of Sexual and Reproductive Healthcare; 2012 Jan.
Collaborative Group on Epidemiological Studies of **Ovarian Cancer**, Beral V, Doll R, Hermon C, Peto R, Reeves G. Ovarian cancer and oral contraceptives: collaborative reanalysis of data from 45 epidemiological studies including 23,257 women with ovarian cancer and 87,303 controls. Lancet. 2008 Jan 26;371(9609):303-14. Use of oral contraceptives confers long-term protection against ovarian cancer. These findings suggest that oral contraceptives have already prevented some 200,000 ovarian cancers and 100,000 deaths from the disease, and that over the next few decades the number of cancers prevented will rise to at least 30,000 per year.
Collaborative Group on Epidemiological Studies on Endometrial Cancer. **Endometrial cancer and oral contraceptives**: an individual participant meta-analysis of 27 276 women with endometrial cancer from 36 epidemiological studies. Lancet Oncol 2015; online Aug 5.
Compassionate Contraceptive Assistance Program SGOC: http://www.sogc.org/projects/ccap_e.asp
Cortessis VK, Barrett M, Brown Wade N, et al. **Intrauterine Device Use and Cervical Cancer Risk**: A Systematic Review and Meta-analysis. Obstet Gynecol. 2017 Nov 3.
Creinin MD, et al. **Progesterone receptor modulator** for emergency contraception: a randomized controlled trial. Obstet Gynecol. 2006 Nov;108(5):1089-97.
Creinin MD, Meyn LA, Borgatta L, et al. Multicenter comparison of the contraceptive ring and patch: a randomized controlled trial. Obstet Gynecol. 2008 Feb;111(2 Pt 1):267-77. The majority of women who are using oral contraceptives (OCs) and try the vaginal ring continue with the ring rather than go back to OCs. Most women who try patches go back to OCs. It is uncertain whether the nonmasked nature of the trial, which was funded by the manufacturer of the vaginal ring, introduced bias into the study. (LOE = 1b-)
Curtis KM, Jatlaoui TC, Tepper NK, et al. **U.S. Selected Practice Recommendations for Contraceptive Use**, 2016. MMWR Recomm Rep. 2016 Jul 29;65(4):1-66.
Curtis KM, Peipert JF. **Long-Acting Reversible Contraception**. N Engl J Med. 2017 Feb 2;376(5):461-468.
D'Cruz DP. Systemic **lupus** erythematosus. BMJ. 2006 Apr 15;332(7546):890-4.
Daniels K, Jones J, Abma J. Use of **emergency contraception** among women aged 15-44: United States, 2006-2010. NCHS Data Brief. 2013 Feb;(112):1-8.
Daniels K, Daugherty J, Jones J, et al. Current **Contraceptive Use and Variation** by Selected Characteristics Among Women Aged 15-44: United States, 2011-2013. Natl Health Stat Report. 2015 Nov;(86):1-15.
Darroch JE, Singh S. **Trends in contraceptive need and use in developing countries in 2003, 2008, and 2012**: an analysis of national surveys. Lancet. 2013 May 18;381(9879):1756-62.
Davis AR, Westhoff C, O'Connell K, Gallagher N. Oral contraceptives for dysmenorrhea in adolescent girls. Obstet Gynecol 2005; 106:97-104. (InfoPOEMs: This trial substantiates previous observational data that low-dose oral contraceptives (OCs) are effective treatment for dysmenorrhea in adolescents. Although just one formulation was used in this study, the results are likely generalizable to all combination oral contraceptives. (LOE = 1b))
de Ziegler D, Gayet V, Aubriot FX, et al. Use of oral contraceptives in women with **endometriosis** before assisted reproduction treatment improves outcomes. Fertil Steril. 2010 Jul 21.
DeFroda SF, Bokshan SL, Worobey S, et al. Oral contraceptives provide **protection against anterior cruciate ligament tears**: a national database study of 165,748 female patients. Phys Sportsmed. 2019 Mar 26:1-5.
Diedrich JT, Klein DA, Peipert JF. **Long-acting reversible contraception in adolescents**: a systematic review and meta-analysis. Am J Obstet Gynecol. 2017 Apr;216(4):364.e1-364.e12.
Di Meglio G, Crowther C, Simms J; Canadian Paediatric Society, Adolescent Health Committee. Position statement. **Contraceptive care for Canadian youth**. https://www.cps.ca/en/documents/position/contraceptive-care (accessed June 4, 2018).
Dinger JC, Cronin M, Möhner S, Schellschmidt I, et al. Oral contraceptive effectiveness according to **body mass** index, weight, age, and other factors. Am J Obstet Gynecol. 2009 Sep;201(3):263.e1-9. Epub 2009 May 30.
Dinger JC, Heinemann LA, Kühl-Habich D. The safety of a **drospirenone**-containing oral contraceptive: final results from the **European Active Surveillance Study** on oral contraceptives based on 142,475 women-years of observation. Contraception. 2007 May;75(5):344-54.
Dinger J, Assmann A, Möhner S, Minh TD. Risk of **venous thromboembolism** and the use of **dienogest- and drospirenone-containing** oral contraceptives: results from a German case-control study. J Fam Plann Reprod Health Care. 2010 Jul;36(3):123-9.
Dinger J, Minh TD, Buttmann N, Bardenheuer K. **Effectiveness of oral contraceptive** pills in a large U.S. cohort comparing progestogen and regimen. Obstet Gynecol. 2011 Jan;117(1):33-40. There are fewer unintended pregnancies with the use of an oral contraceptive (OC) regimen with a progestogen of long half-life, such as drospirenone or norethisterone, when taken for a cycle of 24 days plus 4 days as compared with the standard 21 days plus 7 days (LOE = 2b)
Dinger J, Möhner S, Heinemann K. Cardiovascular risk associated with the use of an **etonogestrel-containing vaginal ring**. Obstet Gynecol. 2013 Oct;122(4):800-8.
Doose DR, et al. Effect of topiramate or carbamazepine on the pharmacokinetics of an oral contraceptive containing norethindrone and ethinyl estradiol in healthy obese and nonobese female subjects. Epilepsia. 2003 Apr;44(4):540-9.
Dude A, Neustadt A, Martins S, et al. Use of **withdrawal and unintended pregnancy** among females 15-24 years of age. Obstet Gynecol. 2013 Sep
Dunn Nick. Oral contraceptives and **venous thromboembolism**. BMJ 2009;339:b3164, doi: 10.1136/bmj.b3164 (Published 13 August 2009)
Dunn S, Brooks M**. Mifepristone- Five Thing to Know** about. CMAJ. 2018 Jun 4;190(22):E688.
ECHO **HIV incidence** among women using intramuscular depot medroxyprogesterone acetate, a copper intrauterine device, or a levonorgestrel implant for contraception: a randomised, multicentre, open-label trial. Lancet. 2019 Jun 13.
Edelman AB, et al. Continuous oral contraceptives: are bleeding patterns dependent on the hormones given? Obstet Gynecol. 2006 Mar;107(3):657-65. CONCLUSION: The addition of 10 mug of ethinyl E2 to a 20 mug ethinyl E2 pill containing levonorgestrel or norethindrone acetate did not improve bleeding patterns. During continuous dosing, the use of oral contraceptives containing 1,000 mug norethindrone acetate resulted in more days of amenorrhea and fewer days of spotting than preparations containing 100 mug levonorgestrel.
Edelman AB, et al. Continuous or extended cycle vs. cyclic use of combined oral contraceptives for contraception. Cochrane Database Syst Rev. 2005 Jul 20;(3):CD004695.
Edelman AB, Carlson NE, Cherala G, et al. Impact of **obesity** on oral contraceptive pharmacokinetics and hypothalamic-pituitary-ovarian activity. Contraception. 2009 Aug;80(2):119-27. Epub 2009 Jun 4.
Eggebroten JL, Sanders JN, Turok DK. **Immediate postpartum intrauterine device and implant program** outcomes: a prospective analysis. Am J Obstet Gynecol. 2017 Jul;217(1):51.e1-51.e7.

Eliscu AH, Burstein GR. Updates in Contraceptive **Counseling for Adolescents**. J Pediatr. 2016 Jun 10.
Espey E, et al. Effect of progestin compared with combined oral contraceptive pills on **lactation**: a randomized controlled trial. *Obstet Gynecol*. January 2012;119(1):5–13.
Etminan, Mahyar, Delaney, Joseph A.C., Bressler, Brian, et al. Oral contraceptives and the risk of **gallbladder disease**: a comparative safety study. CMAJ 2011 0: cmaj.110161. (small significant increase)
Farquhar C, Rombauts L, Kremer JA, et al. **Oral contraceptive pill, progestogen or oestrogen pretreatment for ovarian stimulation protocols** for women undergoing **assisted reproductive techniques**. Cochrane Database Syst Rev. 2017 May 25;5:CD006109. Among women undergoing ovarian stimulation in antagonist protocols, COCP pretreatment was associated with a lower rate of live birth or ongoing pregnancy than no pretreatment. There was insufficient evidence to determine whether rates of live birth or ongoing pregnancy were influenced by pretreatment with progestogens or oestrogens, or by COCP pretreatment using other stimulation protocols. Findings on adverse events were inconclusive, except that progesterone pretreatment may reduce the risk of ovarian cysts in agonist cycles, and COCP in antagonist cycles may reduce the risk of pregnancy loss compared with no pretreatment in agonist cycles.
FDA Oct/11 released the final report of an FDA-funded study looking into the risk for venous thromboembolism (VTE) in women taking oral contraceptives containing drospirenone. As previously reported by Medscape Medical News, on September 26 the FDA said preliminary findings from the study indicate that women who use **drospirenone-containing birth control pills have an approximately 1.5-fold increase** in the risk of developing blood clots relative to women using other types of hormonal contraceptives.
FDA Drug Safety Communication Sept/11: Safety review update on the possible increased risk of blood clots with birth control pills containing drospirenone. http://www.fda.gov/Drugs/DrugSafety/ucm273021.htm (Accessed November 29th, 2011).
FDA Apr/12 has completed its review of recent observational (epidemiologic) studies regarding the risk of blood clots in women taking drospirenone-containing birth control pills.Based on this review, FDA has concluded that **drospirenone**-containing birth control pills may be associated with a higher risk for blood clots than other progestin-containing pills. . Report that some epidemiologic studies reported as high as a three-fold increase in the risk of blood clots for drospirenone-containing products when compared to products containing levonorgestrel or some other progestins, whereas other epidemiological studies found no additional risk of blood clots with drospirenone-containing products.
FDA Nov/16 **Essure** labeling now includes the addition of a boxed warning and a Patient Decision Checklist, both intended to support patient counseling and understanding of benefits and risks associated with Essure, as well as what to expect during and after the Essure procedure. The boxed warning includes safety statements to clearly communicate significant side effects or adverse outcomes associated with this device and information about the potential need for removal.
FDA May/18: Allergan recently identified, through a physician report, that four placebo capsules were placed out of order in a sample pack of **TAYTULLA** and the first four days of therapy had four non-hormonal placebo capsules instead of active capsules.
Fine P et al. **Ulipristal acetate** taken 48-120 hours after intercourse for emergency contraception. Obstet Gynecol 2010; 115:257.
Finer LB, Philbin JM. **Sexual Initiation, Contraceptive Use, and Pregnancy Among Young Adolescents**. Pediatrics. 2013 Apr 1.
Finer LB, Zolna MR. **Declines in Unintended Pregnancy** in the United States, 2008-2011. N Engl J Med. 2016 Mar 3;374(9):843-5
Fisher WA, Black A. Contraception in Canada: a **review** of method choices, characteristics, adherence and approaches to counselling. CMAJ 2007;176:953-61.
Foster DG, Hulett D, Bradsberry M, Darney P, Policar M. Number of oral contraceptive pill **packages dispensed** and subsequent unintended pregnancies. Obstet Gynecol. 2011 Mar;117(3):566-72.
Francis JKR, Gold MA. **Long-Acting Reversible Contraception for Adolescents**: A Review. JAMA Pediatr. 2017 May 30.
FSRH : Clinical Effectiveness Unit. **Contraception for women aged over 40 years**. London (UK): Faculty of Sexual and Reproductive Healthcare (FSRH); 2017 Aug.
FSRH Guideline (April 2019) **Overweight, Obesity and Contraception**. BMJ Sex Reprod Health. 2019 Apr;45(Suppl 2):1-69.
Gaffield ME, Culwell KR, Lee CR. The use of hormonal contraception among women taking **anticonvulsant therapy**. Contraception. 2011 Jan;83(1):16-29. Epub 2010 Sep 15.
Gallo MF, et al. Combination contraceptives: effects on weight. *The Cochrane Database of Systematic Reviews* 2006, Issue 1.
CONCLUSIONS: Available evidence was insufficient to determine the effect of combination contraceptives on weight, but no large effect was evident.
Gallo MF, Grimes DA, Schulz KF. **Cervical cap versus diaphragm** for contraception. Cochrane Database Syst Rev. 2002;(4):CD003551.
Gallo MF, Lopez LM, Grimes DA, et al. **Combination contraceptives: effects on weight**. Cochrane Database Syst Rev. 2011 Sep 7;9:CD003987. Available evidence was insufficient to determine the effect of combination contraceptives on weight, but no large effect was evident.
Gallo MF, Lopez LM, Grimes DA, et al. **Combination contraceptives: effects on weight**. Cochrane Database Syst Rev. **2014** Jan 29;1:CD003987. Available evidence was insufficient to determine the effect of combination contraceptives on weight, but no large effect was evident.
Gallo MF, Legardy-Williams J, Hylton-Kong T, et al. Association of **Progestin** Contraceptive Implant and **Weight Gain**. (Sino-implant levonorgestrel) Obstet Gynecol. 2016 Mar;127(3):573-6.
Gemzell-Danielsson K. Mechanism of action of **emergency contraception**. Contraception. 2010 Nov;82(5):404-9.
Gemzell-Danielsson K, Cho S, Inki P, et al. Use of contraceptive methods and contraceptive recommendations among health care providers actively involved in contraceptive counseling - results of an international survey in 10 countries. Contraception. 2012 Dec;86(6):631-8.
Gentile GP, et al. Hormone levels before and after **tubal sterilization**. Contraception. 2006 May;73(5):507-11. Epub 2006 Feb 23. There were no significant hormonal changes in sterilized women over a period of 2 yrs when compared with their baseline levels or when compared with unsterilized age-matched controls.
Glasier AF, Cameron ST, Fine PM, et al. **Ulipristal** acetate versus levonorgestrel for emergency contraception: a randomised non-inferiority trial and meta-analysis. Lancet. 2010 Jan 28. 375:555.
Glasier A, Cameron ST, et al. Can we identify women at **risk of pregnancy** despite using emergency contraception? Data from randomized trials of **ulipristal acetate and levonorgestrel**. Contraception. 2011 Oct;84(4):363-7.
Giuseppina Di Meglio, Colleen Crowther, Joanne Simms; Canadian Paediatric Society, Adolescent Health Committee. Position Statement: **Contraceptive care for Canadian youth**. CPS. 2018 May 31.
Goldthwaite LM, Cahill EP, Voedisch AJ, Blumenthal PD. **Postpartum intrauterine devices**: clinical and programmatic review. Am J Obstet Gynecol. 2018 Jul 19.
Gomes MP, Deitcher SR. Risk of venous thromboembolic disease associated with hormonal contraceptives and hormone replacement therapy: a clinical review. Arch Intern Med. 2004 Oct 11;164(18):1965-76.
Gomez AM. Availability of **Pharmacist-Prescribed Contraception in California**, 2017. JAMA. 2017 Dec 12;318(22):2253-2254.
Gooneratne IK, Wimalaratna M, Ranaweera AKP, et al. **Contraception advice for women with epilepsy**. BMJ. 2017 May 11;357:j2010.
Goshtasebi A, Subotic Brajic T, Scholes D, et al. **Adolescent use of combined hormonal contraception** and peak **bone mineral density a**ccrual: A meta-analysis of international prospective controlled studies. Clin Endocrinol (Oxf). 2019 Jan 7.
Goundry B, Bell L, Langtree M, Moorthy A. Diagnosis and management of Raynaud's phenomenon. BMJ. 2012 Feb 7;344:e289.
Goyal V et al. **Postabortion contraceptive use and continuation when long-acting reversible contraception is free**. Obstet Gynecol 2017 Apr; 129:655.
Greene Foster D, Hulett D, Bradsberry M, et al. Number of oral contraceptive pill **packages dispensed** and subsequent unintended pregnancies. Obstet Gynecol 2011;117:566-72.
Greene MF, Drazen JM. A New Label for **Mifepristone**. N Engl J Med. 2016 Jun 9;374(23):2281-2.
Grimes DA, Jones LB, Lopez LM, Schulz KF. Oral contraceptives for functional **ovarian cysts**. Cochrane Database Syst Rev. 2006 Oct 18;(4):CD006134. Although widely used for treating functional ovarian cysts, combined oral contraceptives appear to be of no benefit. Watchful waiting over several cycles is appropriate. Should cysts persist, surgical management is often indicated.
Grimes DA, Jones LB, Lopez LM, et al. Oral contraceptives for functional **ovarian cysts**. Cochrane Database Syst Rev. 2009 Apr 15;(2):CD006134. Although widely used for treating functional ovarian cysts, combined oral contraceptives appear to be of no benefit. Watchful waiting for two or three cycles is appropriate. Should cysts persist, surgical management is often indicated.
Gronich N, Lavi I, Rennert G. Higher risk of venous **thrombosis** associated with **drospirenone**-containing oral contraceptives: population-based cohort study. CMAJ 2011Nov 7.
Grossman D. Moving Oral **Contraceptives Over-the-Counter** as a Strategy to Reduce Unintended Pregnancy. Ann Intern Med. 2013 Mar 26.
Guiahi M et al. Short-term treatment of bothersome **bleeding for etonogestrel implant users using a 14-day oral contraceptive pill regimen**: A randomized controlled trial. Obstet Gynecol 2015 Sep; 126:508.
Guilbert E, Black A, Dunn S, Senikas V, Berube J, et al. **Missed hormonal contraceptives**: new recommendations. (SOGC) J Obstet Gynaecol Can 2008 Nov;30(11):1050-62, 1063-77.
http://www.sogc.org/jogc/abstracts/200811_SOGCClinicalPracticeGuidelines_1.pdf

Guilbert E, Boroditsky R, Black A, Kives S, Leboeuf M, Mirosh M, Senikas V, Wagner MS, Weir E, York-Lowry J, Reid R, Trussell J; Society of Obstetricians and Gynaecologists of Canada. Canadian Consensus Guideline on Continuous and Extended Hormonal Contraception, 2007. J Obstet Gynaecol Can. 2007 Jul;29(7 Suppl 2):S1-32.
Gurtcheff SE, Turok DK, et al. **Lactogenesis after early postpartum use of the contraceptive implant (Implanon)**: a randomized controlled trial. Obstet Gynecol. 2011 May;117(5):1114-21. (1-3 day postpartum vs 4 wks)
Hannaford PC, Selvaraj S, Elliott AM, et al. Cancer risk among users of oral contraceptives: cohort data from the Royal College of General Practitioner?s oral contraception study. BMJ 2007;335(7621):651-659. {InfoPOEMs Jan07: Oral contraceptive (OC) use does not increase a woman's overall risk of cancer and may slightly decrease it. However, the risk for particular cancers may be increased or decreased, depending on the duration of use & the length of time since last use. (LOE = 1b)}
Hannaford Philip C, Iversen Lisa, Macfarlane Tatiana V, et al. **Mortality** among contraceptive pill users: cohort evidence from Royal College of General Practitioners' Oral Contraception Study. BMJ 2010
Hapgood JP, Kaushic C, Hel Z. **Hormonal Contraception and HIV-1 Acquisition**: Biological Mechanisms. Endocr Rev. 2018 Jan 4.
Harel Z et al. Recovery of **bone mineral density** in adolescents following the use of depot **medroxyprogesterone** acetate contraceptive injections. Contraception 2010 Apr; 81:281.
Hargreave M, Mørch LS, Andersen KK, et al. Maternal use of hormonal contraception and **risk of childhood leukaemia**: a nationwide, population-based cohort study. Lancet Oncol. 2018 Oct;19(10):1307-1314.
Harmon QE, Umbach DM, Baird DD. Use of **Estrogen-Containing Contraception** Is Associated With Increased Concentrations of 25-Hydroxy **Vitamin D**. J Clin Endocrinol Metab. 2016 Aug 4.
Harper CC, Rocca CH, Thompson KM, et al. **Reductions in pregnancy rates in the USA with long-acting reversible contraception**: a cluster randomized trial. Lancet 2015; online June 17.
Havrilesky LJ, Gierisch JM, Moorman PG, et al. Oral Contraceptive Use for the Primary Prevention of **Ovarian Cancer**. AHRQ Comparative Effectiveness Review. Rockville (MD): Agency for Healthcare Research and Quality (US); 2013 June. Report No.:13-E002-EF There is insufficient evidence to recommend for or against the use of OCs solely for the primary prevention of ovarian cancer.
Havrilesky LJ, Moorman PG, Lowery WJ, et al. Oral contraceptive pills as primary **prevention for ovarian cancer**: a systematic review and meta-analysis. Obstet Gynecol. 2013 Jul;122(1):139-47.
Health Canda June/10 **MIRENA** (Levonorgestrel-Releasing Intrauterine System) - Potential Risk of Uterine Perforation - Bayer Inc. Bayer Inc., in collaboration with Health Canada, would like to remind you of important safety information regarding reports of uterine perforation in women treated with MIRENA.
Health Canada Dec/11 has completed a safety review of drospirenone-containing oral contraceptives (marketed under the brand names Yasmin and Yaz) with respect to the risk of blood clots (venous thromboembolism, or VTE). The review determined that **drospirenone-containing birth** control pills may be associated with a risk of blood clots that is **1.5 to 3 times higher than other birth control pills**.
Health Canada May/13: **Diane-35** supports current labelling and use. The review of the safety of the anti-acne medication Diane-35 has found that the drug's benefits continue to outweigh the risks, when used as authorized.
Health Canada Sep/13 **Freya-28**, an oral contraceptive (birth control product), is being voluntarily recalled from the Canadian market by Mylan Pharmaceuticals after a pharmacy reported that a placebo pill was found in place of an active pill in one package.
Health Canada Sep/13 **Esme-28** (DIN 02388146), an oral contraceptive (birth control product), is being voluntarily recalled from the Canadian market by Mylan Pharmaceuticals.
Health Canada Mar/14 has asked companies to add new warnings to product packages advising that Emergency contraceptive pills, also known as the "morning after" pill,are less effective in **women weighing 165 to 176 pounds (75-80 kg),** and are **not effective** in women over 176 pounds (**80 kg**).
Health Canada May/16 **ESSURE** (permanent birth control system) – Risk of Serious Complications - Bayer Inc. These include changes in menstrual bleeding, unintended pregnancy, chronic pain, perforation and migration of device, allergy and sensitivity or immune-type reactions. Some complications may be considered serious.
Health Canada Nov/17 **MIFEGYMISO (mifepristone and misoprostol tablets) - Updates** to Product Monograph and Risk Management Plan. http://healthycanadians.gc.ca/recall-alert-rappel-avis/hc-sc/2017/65030a-eng.php
Health Canada Dec/17 is advising consumers and health care professionals that complaints have been received for packages of **Alesse 21 (21 active pills) and Alesse 28** (21 active pills, 7 that contain no hormones). The blister packages for both contained an active (pink) pill that was roughly half the proper size.
Health Canada Dec/17 and Pfizer Canada Inc. have received reports for packages of **ALESSE 21 and ALESSE 28** where the blister packages contained a single active (pink) tablet that was **broken**. This could reduce the dose of hormones and potentially result in an unintended pregnancy due to insufficient action of the contraceptive hormones levonorgestrel and ethinyl estradiol.
Health Canada Feb/18: **Alysena 28** birth control pill: One lot recalled due to chipped pills, which may reduce effectiveness in preventing pregnancy. Health Canada is informing Canadians that all lots of both Alysena 21 and Alysena 28 may have **chipped pills**.
Health Canada Jun/18: Pfizer Canada Inc. has notified Health Canada that it has received complaints of **broken or chipped pills involving Demulen 30**, a prescription birth control pill.
Health Canada Apr/19 is informing Canadians that the prescribing and patient information for **Mifegymiso** has been updated to reflect that an ultrasound is no longer required before the drug is prescribed.
Heinemann K, Reed S, Moehner S, et al. Risk of **uterine perforation with levonorgestrel-releasing and copper intrauterine devices** in the European Active Surveillance Study on Intrauterine Devices. Contraception. 2015 Apr;91(4):274-9.
Heit JA, Kobbervig CE, James AH, et al. Trends in the incidence of venous **thromboembolism during pregnancy** or postpartum: a 30-year population-based study. Ann Intern Med. 2005 Nov 15;143(10):697-706.
Heliövaara-Peippo S, Hurskainen R, Teperi J, et al. Quality of life and costs of **levonorgestrel-releasing intrauterine system or hysterectomy** in the treatment of **menorrhagia**: a 10-year randomized controlled trial. Am J Obstet Gynecol. 2013 Dec;209(6):535.e1-535.e14.
Henney JE, Gayle HD. Time to Reevaluate U.S. **Mifepristone Restrictions**. N Engl J Med. 2019 Jun 26.
Herndon EJ, Zieman M. New contraceptive options. Am Fam Physician. 2004 Feb 15;69(4):853-60. Review. Erratum in: Am Fam Physician. 2004 Apr 15;69(8):1863.
Herzog AG, Mandle HB, MacEachern DB. Prevalence of highly **effective contraception use by women with epilepsy**. Neurology. 2019 Jun 11;92(24):e2815-e2821.
HHS Aug 2011.: Affordable Care Act Ensures Women Receive **Preventive Services at No Additional Cost** (including **contraception**). http://www.hhs.gov/news/press/2011pres/08/20110801b.html
Hickey M, Ballard K, Farquhar C. **Endometriosis**. BMJ. 2014 Mar 19;348
Hicks CW, Rome ES. **Menstrual manipulation**: options for suppressing the cycle. Cleve Clin J Med. 2010 Jul;77(7):445-53.
Hofmeister S, Bodden S. **Premenstrual Syndrome and Premenstrual Dysphoric Disorder**. Am Fam Physician. 2016 Aug 1;94(3):236-40
Hornberger LL and AAP Committee on Adelescene. Diagnosis of **Pregnancy** and Providing Options **Counseling** for the **Adolescent Patient**. Pediatrics. 2017;140(3):e20172273
Horga M, Gerdts C, Potts M. The remarkable story of **Romanian women's struggle to manage their fertility**. J Fam Plan Reprod Health Care 2013;39:2-4.
Hou MY, Hurwitz S, Kavanagh E, et al. Using daily **text-message reminders** to improve adherence with oral contraceptives: a randomized controlled trial. Obstet Gynecol. 2010 Sep;116(3):633-40.
Hsiang D, Dunn S. **Emergency contraception**. CMAJ. 2016 Dec 6;188(17-18):E536.
Huber J, Walch K. Treating **acne** with oral contraceptives: use of lower doses. Contraception. 2006 Jan;73(1):23-9. Epub 2005 Sep 26.
Huq FY et al. Menstrual problems and contraception in women of reproductive age **receiving oral anticoagulation**. Contraception2011 Aug; 84:128.
Iliadou A, Milsom I, Pedersen NL, et al. Risk of **urinary incontinence** symptoms in oral contraceptive users: a national cohort study from the Swedish Twin Register. Fertil Steril. 2009 Aug;92(2):428-33. Epub 2008 Aug 15.
International Collaboration of Epidemiological Studies of **Cervical Cancer**, Appleby P, Beral V, Berrington de González A, et al. Cervical cancer and hormonal contraceptives: collaborative reanalysis of individual data for 16,573 women with cervical cancer and 35,509 women without cervical cancer from 24 epidemiological studies. Lancet. 2007 Nov 10;370(9599):1609-21. The relative risk of cervical cancer is increased in current users of oral contraceptives and declines after use ceases. 10 years' use of oral contraceptives from around age 20 to 30 years is estimated to increase the cumulative incidence of invasive cervical cancer by age 50 from 7.3 to 8.3 per 1000 in less developed countries and from 3.8 to 4.5 per 1000 in more developed countries.
International Federation of Gynecology and Obstetrics (FIGO) and International Consortium for Emergency Contraception (ICEC). Emergency Contraception Statement, March 2011. http://www.emergencycontraception.org/publications/PDFs/policy/MOA_ENG_2011.pdf . Accessed January 10, 2013.
Iversen L, Fielding S, Lidegaard Ø, et al. Association between contemporary **hormonal contraception and ovarian cancer** in women of reproductive age in Denmark: prospective, nationwide cohort study. BMJ. 2018 Sep 26;362:k3609.
Iversen L, Sivasubramaniam S, et al. **Lifetime cancer risk and combined oral contraceptives**: the Royal College of General Practitioners' Oral Contraception Study. Am J Obstet Gynecol. 2017 Jun;216(6):580.e1-580.e9.
James AH, et al. Incidence & risk factors for stroke in pregnancy and the puerperium. Obstet Gynecol. 2005 Sep;106(3):509-16. (InfoPOEMs: Hospitalization with a diagnosis of stroke in pregnancy or puerperium occurs in 34 per 100,000 deliveries in the United States. It occurs in more that 50 per 100,000 in African American women and women older than 35 years. The most common comorbid conditions associated with increased risk are migraine headache and hypertension (including gestational hypertension). (LOE = 2c))
Jarolimova J, Kabakyenga J, Bennett K, et al. **Contraceptive use following unintended pregnancy** among Ugandan women living with HIV. PLoS One. 2018 Oct 25;13(10):e0206325.

Jatlaoui TC, Whiteman MK, Jeng G, et al. **Intrauterine Device Expulsion** After Postpartum Placement: A Systematic Review and Meta-analysis. Obstet Gynecol. 2018 Oct;132(4):895-905.
Jensen, Jeffrey T. Effective **Treatment of Heavy Menstrual Bleeding** With Estradiol Valerate and Dienogest (**Natazia**): A Randomized Controlled Trial. *Obstet Gynecol.* 2011;117:773-774, 777-787.
Jick SS, Kaye JA, Russmann S, Jick H. Risk of nonfatal venous thromboembolism with oral contraceptives containing norgestimate or desogestrel compared with oral contraceptives containing levonorgestrel. Contraception. 2006 Jun;73(6):566-70. Epub 2006 Mar 29. The incidence rates of VTE were 30.6 (95% CI, 25.5-36.5), **53.5** (95% CI, 42.9-66.0) and 27.1 (95% CI, 21.1-34.3) per 100,000 woman-years for users of norgestimate-, **desogestrel**- and levonorgestrel-containing OCs, respectively.
Jick SS, Hernandez RK. Risk of non-fatal **venous thromboembolism** in women using oral contraceptives containing **drospirenone** compared with women using oral contraceptives containing **levonorgestrel**: case-control study using United States claims data. BMJ 2011;342:d2151.
Jin J. JAMA **patient page. Oral contraceptives**. JAMA. 2014 Jan 15;311(3):321.
Johnson-Agbakwu C, Brown L, Yuan J, et al. Effects of **Flibanserin** on the Pharmacokinetics of a **Combined Ethinylestradiol/Levonorgestrel** Oral Contraceptive in Healthy Premenopausal Women: A Randomized Crossover Study. Clin Ther. 2017 Nov 30.
Jones, Claire, Chan, Crystal, Farine, Dan. **Sex in pregnancy**. CMAJ 2011 0: cmaj.091580.
Judge-Golden CP, Smith KJ, Mor MK, Borrero S. **Financial Implications of 12-Month Dispensing** of Oral Contraceptive Pills in the Veterans Affairs Health Care System. JAMA Intern Med. 2019 Jul 8
Kahlenborn C, Modugno F, Potter DM, Severs WB. Oral contraceptive use as a risk factor for premenopausal **breast cancer**: a meta-analysis. Mayo Clin Proc. 2006 Oct;81(10):1290-302. Use of OCs is associated with an increased risk of premenopausal breast cancer, especially with use before first full term pregnancy in parous women.
Kakaire O, Byamugisha JK, Tumwesigye NM, et al. **Intrauterine Contraception Among Women Living With Human Immunodeficiency Virus**: A Randomized Controlled Trial. Obstet Gynecol. 2015 Nov;126(5):928-34.
Kamel H et al. Risk of a **thrombotic event after the 6-week postpartum** period. N Engl J Med 2014 Feb 13.
Katzman DK, Taddeo D; **Canadian Paediatric Society**, Adolescent Health Committee. **Emergency contraception**. Paediatr Child Health 2010;15(6):363-372. http://www.cps.ca/english/statements/am/ah10-02.htm
Kaunitz AM. Clinical practice. **Hormonal contraception in women of older reproductive age**. N Engl J Med. 2008 Mar 20;358(12):1262-70.
Kaunitz AM, Portman D, Westhoff CL, et al. **Low-dose levonorgestrel and ethinyl estradiol patch and pill**: a randomized controlled trial. Obstet Gynecol. 2014 Feb;123(2 Pt 1):295-303.
Kavanaugh ML et al. Changes in use of **long-acting reversible contraceptive** methods among U.S. women, 2009–2012. Obstet Gynecol 2015 Oct 5.
Kazerooni R, Blake A, Thai J. Predictors of **Pregnancy** in Female Veterans Receiving a **Hormonal Contraceptive Pill, Patch, or Ring**. Ann Pharmacother. 2015 Dec;49(12):1284-90.
Keenan Jeffrey A. **Ulipristal Acetate**: Contraceptive or Contragestive? Articles Ahead of Print published on 1 June 2011, DOI 10.1345/aph.1Q248. Ann Pharmacother ;45:813-815.
Khalili H, Neovius M, Ekbom A, et al. **Oral Contraceptive Use and Risk of Ulcerative Colitis Progression: A Nationwide Study.**Am J Gastroenterol. 2016 Oct 11.
Kharbanda EO, Stuck L, Molitor B, Nordin JD. **Missed opportunities for pregnancy prevention** among insured adolescents. JAMA Pediatr. 2014 Dec 1;168(12):e142809.
Kilgore KP, Lee MS, Leavitt JA, et al. A Population-Based, Case-Control Evaluation of the Association between **Hormonal Contraceptives and Idiopathic Intracranial Hypertension**. Am J Ophthalmol. 2018 Sep 21.

Klein DA, Arnold JJ, Reese ES. **Provision of Contraception**-Key Recommendations from the **CDC**, Am Fam Physician. 2015;91(9):625-633.
Klok FA, Schreiber K, Stach K, et al. **Oral contraception and menstrual bleeding during treatment of venous thromboembolism**: Expert opinion versus current practice: Combined results of a systematic review, expert panel opinion and an international survey. Thromb Res. 2017 May;153:101-107
Koo EB, Petersen TD, Kimball AB. Meta-analysis comparing efficacy of **antibiotics versus oral contraceptives in acne vulgaris**. J Am Acad Dermatol. 2014 May 28.
Kortsmit K, Williams L, Pazol K, et al. Condom use with **long-acting reversible contraception vs non–long-acting reversible contraception hormonal methods** among postpartum adolescents [online May 20, 2019]. JAMA Pediatr.doi:10.1001/jamapediatrics.2019.1136
Koulouri O, Conway GS. Management of **hirsutism**. BMJ. 2009 Mar 27;338:b847. doi: 10.1136/bmj.b847.
Kourtis AP, Mirza A, AAP Committee on Pediatric AIDS. **Contraception for HIV-Infected Adolescents**. Pediatrics.2016;138(3):e20161892
Kroll R, et al. The efficacy and safety of a low-dose, **91-day, extended-regimen** oral contraceptive with continuous ethinyl estradiol. Contraception. 2010 Jan;81(1):41-8.
Kromm J, Jeerakathil T. **Cyproterone acetate-ethinyl estradiol** use in a 23-year-old woman with **stroke**. CMAJ. 2014 Jun 10;186(9):690-3.
Kumar MM. **Long-Acting Reversible Contraceptives for Adolescents**: More Complex Than "First-Line". JAMA Pediatr. 2017 Nov 20.
Langlade C, Gouverneur A, Bosco-Lévy P, et al. **Adverse events reported for** levonorgestrel-releasing IUD **Mirena**® in France and impact of media coverage. Br J Clin Pharmacol. 2019 Jun 19.
Larivee N, Suissa S, Khosrow-Khavar F, et al. **Drospirenone**-containing oral contraceptive pills and the **risk of venous thromboembolism**: a systematic review of observational studies. BJOG. 2017 Mar 9.
Lawrence HC. Unfettered **Access to Reliable Contraception**: Pharmacist Prescription Derails a Definitive Solution. Ann Intern Med. 2016 Mar 1.
Lazorwitz A, Aquilante CL, Oreschak K, et el. Influence of **Genetic Variants on Steady-State Etonogestrel Concentrations** Among Contraceptive Implant Users. Obstet Gynecol. 2019 Mar 11.
Legro RS, Pauli JG, Kunselman AR, et al. Effects of **Continuous versus Cyclic** Oral Contraception: A Randomized Controlled Trial. J Clin Endocrinol Metab. 2007 Dec 4; [Epub ahead of print] Continuous oral contraception does not result in a reduction of bleeding days over a 168d period of observation, but provides greater suppression of the ovary and endometrium. These effects are associated with improved patient symptomatology.
Lesnewski R, Prine L, Ginzburg R. **Preventing Gaps when Switching** Contraceptives. Am Fam Physician. 2011 Mar 1;83(5):567-570.
Lethaby A, Wise MR, Weterings MA, et al. **Combined hormonal contraceptives for heavy menstrual bleeding**. Cochrane Database Syst Rev. 2019 Feb 11;2:CD000154. Moderate-quality evidence suggests that the combined oral contraceptive pill over six months reduces HMB in women with unacceptable HMB from 12% to 77% (compared to 3% in women taking placebo). When compared with other medical options for HMB, COCP was less effective than the LNG IUS. Limited evidence suggested that COCP and CVR had similar effects. There was insufficient evidence to determine comparative efficacy of combined hormonal contraceptives with NSAIDs, or long course progestogens.
Levi EE, Stuart GS, Zerden ML, et al. **Intrauterine Device Placement During Cesarean Delivery** and Continued Use 6 Months Postpartum: A Randomized Controlled Trial. Obstet Gynecol. 2015 Jul;126(1):5-11.
Levy DP et al. **Ulipristal** acetate for **emergency contraception**: Postmarketing experience after use by more than 1 million women. Contraception 2014 May; 89:431.
Leyland N, Casper R, Laberge P, Singh SS, Allen L, Arendas K. **Endometriosis**: diagnosis and management. J Obstet Gynaecol Can 2010 Jul;32(7 Suppl 2):S1-32.
Liao PV, Dollin J. Half a century of the **oral contraceptive pill: Historical review** and view to the future. Can Fam Physician. 2012 Dec;58(12):e757-60.
Lidegaard Øjvind, Løkkegaard Ellen, Svendsen Anne Louise, et al. Hormonal contraception and risk of **venous thromboembolism**: Denmark national follow-up study. BMJ 2009;339:b2890, doi: 10.1136/bmj.b2890
Lidegaard Ø, Nielsen LH, Skovlund CW, et al. Risk of **venous thromboembolism** from use of oral contraceptives containing different progestogens and oestrogen doses: Danish cohort study, 2001-9. BMJ 2011;343:d6423.
Lidegaard O, Nielsen LH, Skovlund CW, et al. **Venous thrombosis** in users of **non-oral hormonal contraception**: follow-up study, Denmark 2001-10. BMJ. 2012 May 10;344:e2990. doi: 10.1136/bmj.e2990.
Lidegaard Ø, Løkkegaard E, Jensen A, Skovlund CW, Keiding N. **Thrombotic stroke and myocardial infarction** with hormonal contraception. N Engl J Med 2012;366:2257-66.
Linden JA. Clinical practice. Care of the adult patient **after sexual assault**. N Engl J Med. 2011 Sep 1;365(9):834-41.
Loder EW, et al. **Headache** as a side effect of combination estrogen-progestin oral contraceptives: a systematic review. Am J Obstet Gynecol. 2005 Sep;193(3 Pt 1):636-49. (InfoPOEMs: There is not a clearly documented causal relationship between headaches and oral contraceptives (OCs). Headaches that patients attribute to initiation of OCs tend to improve over time. There is no evidence to support change of formulation to manage headache. Manipulation of estrogen withdrawal has not been sufficiently studied. (LOE = 1a-))
Loder EW, Buse DC, Golub JR. **Headache** and combination estrogen-progestin oral contraceptives: integrating evidence, guidelines, and clinical practice. Headache. 2005 Mar;45(3):224-31.
Lopez LM, Newmann SJ, Grimes DA, Nanda K, Schulz KF. **Immediate start** of hormonal contraceptives for contraception. *Cochrane Database Syst Rev.* 2008;(2):CD006260.
Lopez LM, et al. **Skin patch and vaginal ring versus combined oral contraceptives** for contraception. Cochrane Database Syst Rev. 2008 Jan 23;(1):CD003552. Effectiveness rates were similar for the methods compared. The patch group had better compliance than the COC group. Compared to COC users, patch users had more side effects. Ring users generally had fewer adverse events than COC users but more vaginal irritation and discharge. The patch could lead to more discontinuation while the vaginal ring showed little difference. High losses to follow up can affect the validity of the results.
Lopez LM, Grimes DA, Chen-Mok M, et al. Hormonal contraceptives for **contraception in overweight or obese women**. Cochrane Database Syst Rev. 2010 Jul 7;7:CD008452. Body weight addresses overall body size, while BMI generally

reflects the amount of fat. Only one of three studies using BMI found a higher pregnancy risk for overweight women. The efficacy of implants and injectable contraceptives may be unaffected by body mass. The field could use trials of contraceptive methods with groups stratified by BMI. The current evidence on effectiveness by BMI is limited. However, the contraceptive methods examined here are still among the most effective when the recommended regimen is followed.

Lopez LM, Edelman A, Chen-Mok M, Trussell J, Helmerhorst FM. **Progestin-only contraceptives: effects on weight**. Cochrane Database Syst Rev. 2011 Apr 13;4:CD008815. We found little evidence of weight gain when using POCs. Mean gain was less than 2 kg for most studies up to 12 months, and usually similar for the comparison group using another contraceptive.

Lopez LM, Hiller JE, Grimes DA, et al. **Education** for contraceptive use by women after childbirth. Cochrane Database Syst Rev. 2012 Aug 15;8:CD001863. The overall quality of evidence was moderate. Half of these postpartum interventions led to fewer repeat pregnancies or births or more contraceptive use.

Lopez L, et al. Oral contraceptives containing **drospirenone for premenstrual syndrome**. Cochrane Database Syst Rev. 2008 Jan 23;(1):CD006586. Drospirenone plus EE 20 mug may help treat premenstrual symptoms in women with PMDD.

Lopez LM, Grimes DA, Gallo MF, Schulz KF. Skin patch and **vaginal ring versus combined oral contraceptives** for contraception. Cochrane Database Syst Rev. 2010 Mar 17;3:CD003552. Effectiveness was similar for the methods compared. The patch could lead to more discontinuation while the vaginal ring showed little difference. The patch group had better compliance than the COC group but more side effects. Ring users generally had fewer adverse events than COC users but more vaginal irritation and discharge.

Lopez LM, Edelman A, Chen-Mok M, et al. **Progestin-only contraceptives: effects on weight**. Cochrane Database Syst Rev. 2011 Apr 13;4:CD008815. We found little evidence of weight gain when using POCs. Mean gain was less than 2 kg for most studies up to 12 months, and usually similar for the comparison group using another contraceptive. Appropriate counseling about typical weight gain may help reduce discontinuation of contraceptives due to perceptions of weight gain.

Lopez LM, Newmann SJ, Grimes DA, et al. **Immediate start of hormonal contraceptives** for contraception. Cochrane Database Syst Rev. 2012 Dec 12;12:CD006260. doi: 10.1002/14651858.CD006260.pub3. We found limited evidence that immediate start of hormonal contraception reduces unintended pregnancies or increases method continuation. However, the pregnancy rate was lower with immediate start of DMPA versus another method.

Lopez LM, Stockton LL, ChenM, SteinerMJ, GalloMF. **Behavioral interventions for improving dual-method contraceptive use**. Cochrane Database of Systematic Reviews 2014, Issue 3. Art. No.: CD010915. DOI: 10.1002/14651858.CD010915.pub2. We found few behavioral interventions for improving dual-method contraceptive use and little evidence of effectiveness. Amultifaceted program showed some effect but only had self-reported outcomes. Two trials were more applicable to clinical settings and had objective outcomesmeasures, but neither showed any effect.The included studies had adequate information on intervention fidelity and sufficient follow-up periods for change to occur.

Lopez LM, Grimes DA, Schulz KF, et al. Steroidal contraceptives: effect on **bone fractures** in women. Cochrane Database Syst Rev. 2014 Jun 24;6:CD006033. Whether steroidal contraceptives influence fracture risk cannot be determined from existing information. The evidence quality was considered moderate overall, largely due to the trials of DMPA, implants, and the patch versus ring. The COC evidence varied in quality but was low overall. Many trials had small numbers of participants and some had large losses. Health care providers and women should consider the costs and benefits of these effective contraceptives. For example, injectable contraceptives and implants provide effective, long-term birth control yet do not involve a daily regimen. Progestin-only contraceptives are considered appropriate for women who should avoid estrogen due to medical conditions.

Lopez LM, Grey TW, Stuebe AM, et al. **Combined hormonal versus nonhormonal versus progestin-only contraception in lactation**. Cochrane Database Syst Rev. 2015;(3):CD003988. Results were not consistent across the 11 trials. The evidence was limited for any particular hormonal method. The quality of evidence was moderate overall and low for three of four placebo-controlled trials of COCs or POPs. The sensitivity analysis included six trials with moderate quality evidence and sufficient outcome data. Five trials indicated no significant difference between groups in breastfeeding duration (etonogestrel implant insertion times, COC versus POP, and LNG-IUS). For breast milk volume or composition, a COC study showed a negative effect, while an implant trial showed no significant difference. Of four trials that assessed infant growth, three indicated no significant difference between groups. One showed greater weight gain in the etonogestrel implant group versus no method but less versus DMPA.

Lopez LM, Grey TW, Chen M, et al. **Theory-based interventions for contraception.** Cochrane Database Syst Rev. 2016 Nov 23;11:CD007249. The overall quality of evidence was moderate. Trials based on social cognitive theory focused on adolescents and provided multiple sessions. Those using motivational interviewing had a wider age range but specific populations. Sites with low resources need effective interventions adapted for their settings and their typical clients. Reports could be clearer about how the theory was used to design and implement the intervention.

Loulergue P, Coriat R, Mir O. **Recurrent Transaminitis** Induced by Oral Contraceptives **During HIV Infection**. Ann Pharmacother. 2015 Feb;49(2):258-9.

Lumsden MA, Gebbie A, Holland C. Managing **unscheduled bleeding** in non-pregnant premenopausal women. BMJ. 2013 Jun 4;346:f3251.

Maïmoun L, Renard E, Lefebvre P, et al. Oral contraceptives partially **protect from bone loss** in young women with anorexia nervosa. Fertil Steril. 2019 May;111(5):1020-1029.e2.

Maino A, Siegerink B, Algra A, et al. **Recurrence and Mortality in Young Women With Myocardial Infarction or Ischemic Stroke**: Long-term Follow-up of the Risk of Arterial Thrombosis in Relation to Oral **Contraceptives** (**RATIO**) Study. JAMA Intern Med. 2015 Nov 23:1-3.

Maloney JM, Dietze P Jr, Watson D, et al. Treatment of **Acne** Using a 3-Milligram Drospirenone/20-Microgram Ethinyl Estradiol Oral Contraceptive Administered in a 24/4 Regimen: A Randomized Controlled Trial. Obstet Gynecol. 2008 Oct;112(4):773-781.

Malvezzi M, Carioli G, Rodriguez T, et al. Global trends and predictions in **ovarian cancer mortality**. Ann Oncol. 2016 Sep 5

Mantha S, Karp R, Raghavan V et al. Assessing the risk of venous **thromboembolic events in women taking progestin-only** contraception: a meta-analysis. BMJ. 2012 Aug 7;345:e4944.

Marchbanks PA, Curtis KM, Mandel MG, Oral contraceptive formulation and **risk of breast cancer**. Contraception. 2012;85:342-350.

Margel David, Fleshner Neil E. Oral contraceptive use is associated with **prostate cancer**: an ecological study. BMJ Open 2011;1:e000311 doi:10.1136/bmjopen-2011-000311.

Marions L et al. Effect of **emergency contraception** with levonorgestrel or mifepristone on ovarian function. Contraception2004 May; 69:373-7.

Martinelli I, Lensing AW, Middeldorp S, et al. Recurrent venous **thromboembolism and abnormal uterine bleeding with anticoagulant and hormone therapy use**. Blood. 2016 Mar 17;127(11):1417-25.

McCarthy FP, O'Brien U, Kenny LC. The management of **teenage pregnancy**. BMJ. 2014 Oct 15;349:g5887.

McCartney CR, Marshall JC. CLINICAL PRACTICE. **Polycystic Ovary Syndrome**. N Engl J Med. 2016 Jul 7;375(1):54-64.

McNicholas C, Zhao Q, Secura G, et al. Contraceptive failures in **overweight and obese** combined hormonal contraceptive users. Obstet Gynecol. 2013 Mar;121(3):585-92.

McNicholas C, Maddipati R, et al. Use of the **etonogestrel implant and levonorgestrel intrauterine device beyond** the u.s. Food and drug administration-approved **duration**. Obstet Gynecol. 2015 Mar;125(3):599-604.

McNicholas C et al. **Prolonged use of the etonogestrel implant and levonorgestrel intrauterine device** — two years beyond FDA-approved duration. Am J Obstet Gynecol 2017 Jan 29. This large study adds to a growing body of evidence demonstrating the effectiveness of the etonogestrel implant for 5 years and the 52-mg LNG-IUD for up to 7 years. Women of any age can use the implant for up to 5 years (NEJM JW Womens Health Nov 2016 and Hum Reprod 2016; 31:2491). Among the 3 available doses of the LNG-IUD, extended use should only be considered for the 52-mg dose. Younger LNG-IUD users have slightly higher risk for pregnancy; accordingly, to balance risk and benefit for my patients who would like to consider extended use of the 52-mg LNG-IUD, I offer those who are younger than 35 up to 6 years of use, and those who are 35 or older up to 7 years of use. For women who prefer to exchange their 52-mg LNG-IUD with a new device at 5 years, I accede to their preference.

Medical Letter. Three new oral contraceptives. (Yaz, Seasonique, Loestrin 24 Fe) Sept 25, 2006.

Medical Letter. A New Progestin Implant (Implanon) Oct 9,2006.

Medical Letter. **Plan B** OTC. Sept 11, 2006.

Medical Letter. Combination Oral Contraceptives and the Risk of **Venous Thromboembolism**. Mar 22, 2010.

Medical Letter- Treatment Guidelines: **Choice of Contraceptives**. Dec 2007; p. 101-108. (Updated Dec 2010), Updated Oct 2018.

Menke MN, King WC, White GE, et al. Conception rates and contraceptive use after **bariatric surgery among women with infertility**: Evidence from a prospective multicenter cohort study. Surg Obes Relat Dis. 2019 Jan 11.

MHRA June/16 **Nexplanon** (**etonogestrel**) contraceptive implants: reports of device in vasculature and lung.

Michels KA, Pfeiffer RM, Brinton LA, et al. Modification of the Associations Between Duration of **Oral Contraceptive Use and Ovarian, Endometrial, Breast, and Colorectal Cancers**. JAMA Oncol. 2018 Jan 18.

Michels KA, Brinton LA, Pfeiffer RM, et al. **Oral Contraceptive Use and Risks of Cancer** in the NIH-AARP Diet and Health Study. Am J Epidemiol. 2018 Jan 31.

Mifeprex REMS Study Group., Raymond EG, Blanchard K, Blumenthal PD, et al. **Sixteen Years of Overregulation**: Time to Unburden Mifeprex. N Engl J Med. 2017 Feb 23;376(8):790-794

Miller PE, Brown L, Khandheria P, Resar JR. **Ischemic Stroke Occurring During Intercourse** in Young Women on Oral Contraceptives. Am J Cardiol. 2014 May 17.

Miller TA, Allen RH, Kaunitz AM, Cwiak CA. **Contraception for midlife** women: a review. Menopause. 2018 Jul;25(7):817-827.

Miner PD, Canobbio MM, Pearson DD, et al. Contraceptive Practices of Women **with Complex Congenital Heart Disease**. Am J Cardio. 2017.

Mody SK, Farala JP, Jimenez B, et al. **Paracervical Block for Intrauterine Device Placement** Among Nulliparous Women: A Randomized Controlled Trial. Obstet Gynecol. 2018 Sep;132(3):575-582.

Monge ME, Dwivedi P, Zhou M, et al. A tiered analytical approach for investigating **poor quality emergency contraceptives**. PLoS One. 2014 Apr 18;9(4):e95353.

Moniz MH, Davis MM, Chang T. **Attitudes About Mandated Coverage** of Birth Control Medication and Other Health Benefits in a US National Sample. JAMA. 2014 Apr 22.

Moorman PG, Havrilesky LJ, Gierisch JM, et al. Oral Contraceptives and **Risk of Ovarian Cancer** and **Breast Cancer** Among High-Risk Women: A Systematic Review and Meta-Analysis. J Clin Oncol. 2013 Oct 21.

Morch Lina Steinrud; Lokkegaard Ellen; Andreasen Anne Helms; et al. Hormone Therapy and **Ovarian Cancer**. JAMA. 2009;302(3):298-305.

Mørch LS, Skovlund CW, Hannaford PC, et al. **Contemporary hormonal contraception and the risk of breast cancer**. N Engl J Med 2017;377:2228-39.

Munro MG, et al. Oral **medroxyprogesterone** acetate and combination oral contraceptives for **acute uterine bleeding**: a randomized controlled trial. Obstet Gynecol. 2006 Oct;108(4):924-9. This randomized trial is limited by sample size but suggests that both regimens may be effective and reasonably well tolerated.

Murray Horwitz ME, Ross-Degnan D, Pace LE. Contraceptive Initiation Among Women in the United States: **Timing, Methods Used, and Pregnancy Outcomes**. Pediatrics. 2019 Jan 15.

Neuhaus CP, Nagler AR, Orlow SJ. **Teens, Acne, and Oral Contraceptive Pills**: The Need for Greater Clarity on When Teens Can Consent. JAMA Dermatol. 2017 Jan 11.

NICE: National Institute for Health and Care Excellence, 2014. **Contraceptive services with a focus on young people up to the age of 25** (PH51) [online]. Available: http://guidance.nice.org.uk/PH51 [Accessed 21May14].

Noé G, Croxatto HB, Salvatierra AM, et al. Contraceptive efficacy of emergency contraception with **levonorgestrel** given before or after ovulation. Contraception. 2011 Nov;84(5):486-92. The efficacy of LNG-EC has been overestimated in studies using presumptive menstrual cycle data. Our results confirm previous similar studies and demonstrate that LNG-EC does not prevent embryo implantation and therefore cannot be labeled as abortifacient. …when used after ovulation has occurred, the number of observed and expected pregnancies is not statistically different, indicating that no reproductive process subsequent to ovulation is interfered with by LNG-EC….In conclusion, LNG-EC is highly effective for preventing unintended pregnancy when it is used before ovulation, but when used after ovulation, it is completely unable to prevent pregnancy because it has no effect on subsequent reproductive processes, including implantation of the embryo.

Norman WV, Soon JA. **Requiring physicians to dispense mifepristone**: an unnecessary limit on safety and access to medical abortion. CMAJ. 2016 Dec 6;188(17-18):E429-E430.

Novikova N, Weisberg E, Stanczyk FZ, Croxatto HB, Fraser IS. Effectiveness of **levonorgestrel emergency contraception** given before or after ovulation—a pilot study. Contraception 2007; 75:112–118.

O'Brien SH, Koch T, Vesely SK, et al. Hormonal Contraception and **Risk of Thromboembolism** in Women With Diabetes. Diabetes Care. 2016 Nov 29.

Odmark IS, Bixo M, Englund D, Risberg B, Jonsson B, Olsson SE. Endometrial safety and bleeding pattern during a five-year treatment with long-cycle hormone therapy. Menopause. 2005 Nov-Dec;12(6):699-707. Epub 2005 Nov 8. (InfoPOEMs: In this small study, continuous estrogen therapy combined with 14 days of progestin every 3 months (long-cycle therapy) did not result in endometrial hyperplasia or cancer. (LOE = 1b))

Oedingen C, Scholz S, Razum O Systematic review and meta-analysis of the association of **combined oral contraceptives on the risk of venous thromboembolism**: The role of the progestogen type and estrogen dose. Thromb Res. 2018 May;165:68-78.

Orbo A, Vereide A, Arnes M, et al. **Levonorgestrel-impregnated intrauterine device** as treatment for **endometrial hyperplasia**: a national multicentre randomised trial. BJOG. 2013 Nov 28.

Orbo A, Arnes M, Vereide AB, et al. Relapse risk of **endometrial hyperplasia after treatment with the levonorgestrel-impregnated intrauterine system or oral progestogens**. BJOG. 2015 Dec 2.

Orellana C, Saevarsdottir S, Klareskog L, et al. **Oral contraceptives, breastfeeding** and the **risk of developing rheumatoid arthritis**: results from the Swedish EIRA study. Ann Rheum Dis. 2017 Aug 17.

Oringanje C, Meremikwu MM, Eko H, et al. **Interventions for preventing unintended pregnancies among adolescents**. Cochrane Database Syst Rev. 2016;(2):CD005215. A combination of educational and contraceptive-promoting interventions appears to reduce unintended pregnancy among adolescents. Evidence for programme effects on biological measures is limited. The variability in study populations, interventions and outcomes of included trials, and the paucity of studies directly comparing different interventions preclude a definitive conclusion regarding which type of intervention is most effective.

Osayande AS, Mehulic S. Diagnosis and initial management of **dysmenorrhea**. Am Fam Physician. 2014 Mar 1;89(5):341-6.

Ott MA, Sucato GS; COMMITTEE ON ADOLESCENCE; COMMITTEE ON ADOLESCENCE. **Contraception for adolescents.** Pediatrics. 2014 Oct;134(4):e1257-81.

Pace LE, Dusetzina SB, Murray Horwitz ME, et al. Utilization of **Long-Acting Reversible Contraceptives** in the United States After vs Before the 2016 US Presidential Election. JAMA Intern Med. 2019 Feb 4.

Panzer C, et al. Impact of oral contraceptives on sex hormone-binding globulin & androgen levels: a retrospective study in women with sexual dysfunction. J Sex Med. 2006 Jan;3(1):104-13.

Parkin L, Sharples K, Hernandez RK, Jick SS. Risk of **venous thromboembolism** in users of oral contraceptives containing **drospirenone or levonorgestrel**: nested case-control study based on UK General Practice Research Database. BMJ 2011;342:d2139.

Patel P, Leeder JS, Piquette-Miller M, et al. **Aprepitant and Fosaprepitant Drug Interactions**: A Systematic Review. Br J Clin Pharmacol. 2017 May 4.

Peipert JF, Madden T, Allsworth JE, et al. Preventing Unintended Pregnancies by Providing **No-Cost Contraception**. Obstet Gynecol. 2012 Oct 3.

Peragallo Urrutia R, Coeytaux RR, et al. Risk of **acute thromboembolic events** with oral contraceptive use: a systematic review and meta-analysis. Obstet Gynecol. 2013 Aug;122(2 Pt 1):380-9.

Petri M, Kim MY, Kalunian KC, Grossman J, et al. Combined Oral Contraceptives in Women with Systemic **Lupus** Erythematosus. N Engl J Med. 2005 Dec 15;353(24):2550-2558. (InfoPOEMs: This study found that oral contraceptives are safe and do not increase the risk of flares in women with systemic lupus erythematosus (SLE). Another study in the same issue of the journal found no difference in clinical outcomes for women randomized to an oral contraceptive, progestin-only pill, or intrauterine device (N Engl J Med 2005;353:2539-49). (LOE = 1b))

Pharmacist's Letter: **Emergency Contraception: FAQS.** Nov 2016.

Pharmacist's Letter: **Hormonal Contraception** July 2006

Pharmacist's Letter. Single dose regimen (1.5mg) for **Plan B**. June 2007.

Pilz S, Obeid R, Schwetz V, et al. Title: Hormonal Contraceptive Use is Associated with Higher Total but Unaltered Free **25-Hydroxyvitamin D Serum Concentrations**. J Clin Endocrinol Metab. 2018 Apr 16.

Polis CB, Grimes DA, Schaffer K, Blanchard K, Glasier A, Harper C. **Advance provision of emergency contraception** for pregnancy prevention. Cochrane Database of Systematic Reviews 2007, Issue 2. Art. No.: CD005497.

Polis CB, Curtis KM. Use of hormonal **contraceptives and HIV acquisition** in women: a systematic review of the epidemiological evidence. Lancet Infect Dis. 2013 Jul 18.

Polis CB, Curtis KM, Hannaford PC, et al. **Update on hormonal contraceptive methods and risk of HIV acquisition** in women: a systematic review of epidemiological evidence, 2016. AIDS. 2016 Aug 5.

Politi MC, Sonfield A, Madden T. Addressing Challenges to Implementation of the **Contraceptive Coverage Guarantee of the Affordable Care Act**. JAMA. 2016 Feb 16;315(7):653-4.

Polonsky M. **Cancer and contraception**: Release date May 2012 SFP Guideline #20121. Contraception. 2012 Jun 7.

Prabakar I, Webb A. **Emergency contraception**. BMJ. 2012 Mar 19;344:e1492

Practice Committee of the American Society for Reproductive Medicine. **Combined hormonal contraception and the risk of venous thromboembolism**: a guideline. Fertil Steril. 2017 Jan;107(1):43-51.

Prescott HM. "An Uncommonly **Silly Law**"--Contraception and Disparities in the United States. N Engl J Med. 2016 Feb 25;374(8):706-8.

Prey Bd, Talavlikar R, Mangat R, et al. Induced **abortion and contraception use: Among immigrant** and Canadian-born women in Calgary, Alta. Can Fam Physician. 2014 Sep;60(9):e455-63.

Prine L, Shah M. **Long-Acting Reversible Contraception**: Difficult Insertions and Removals. Am Fam Physician. 2018 Sep 1;98(5):304-309. PubMed PMID: 30216029.

Quint EH, O'Brien RF; Committee on Adolescence; North American Society for Pediatric and Adolescent Gynecology. **Menstrual Management for Adolescents With Disabilities**. Pediatrics. 2016 Jul;138(1).

Raymond EG, Halpern V, Lopez LM. **Pericoital oral contraception with levonorgestrel**: a systematic review. Obstet Gynecol. 2011 Mar;117(3):673-81.

Raymond EG, Cleland K. **Emergency Contraception**. N Engl J Med. 2015 Apr 2;372(14):1342-1348.

Raymond EG, Weaver MA, Tan YL, et al. Effect of Immediate Compared With Delayed Insertion of **Etonogestrel Implants** on **Medical Abortion** Efficacy and Repeat Pregnancy: A Randomized Controlled Trial. Obstet Gynecol. 2016 Feb;127(2):306-12.

Raymond EG, et al. Effects of **Depot Medroxyprogesterone** Acetate Injection Timing **on Medical Abortion** Efficacy and Repeat Pregnancy: A Randomized Controlled Trial. Obstet Gynecol. 2016 Oct;128(4):739-45

Reed B, Harlow S, Legocki L, et al. Oral contraceptive use and **risk of vulvodynia**: a population-based longitudinal study. BJOG. 2013 Aug 13.

Richards C. **Protecting and Expanding Access to Birth Control**. N Engl J Med. 2016 Mar 3;374(9):801-3.

Roach RE, Helmerhorst FM, Lijfering WM, et al. **Combined oral contraceptives: the risk of myocardial infarction and ischemic stroke**. Cochrane Database Syst Rev 2015;8: CD011054. This network meta-analysis showed that the risk of myocardial infarction or ischemic stroke was only increased in women using COCs containing ≥ 50 µg of estrogen. Regarding myocardial infarction or ischemic stroke, prescribing COCs with < 50 µg of estrogen seems safe. When combined with the results of studies on the risk of venous thrombosis in COC users, it seems that the COC pill containing levonorgestrel and 30 µg of estrogen is the safest oral form of hormonal contraception.

Rodriguez MI, Chang R, Thiel de Bocanegra H. The impact of **postpartum contraception** on reducing preterm birth: findings from California. Am J Obstet Gynecol 2015;213:703.e1–6.

Rose SB, Lawton BA. Impact of **long-acting reversible contraception on return for repeat abortion**. Am J Obstet Gynecol. 2012 Jan;206(1):37.e1-6. (esp. IUD)

Rosenfield RL. **Hirsutism**. N Engl J Med. 2005 Dec 15;353(24):2578-88.

Rott H. **Thrombotic risks** of oral contraceptives. Curr Opin Obstet Gynecol. 2012 Jun 8.

Russell VM, et al. The association between **discontinuing hormonal contraceptives** and wives' marital satisfaction depends on **husbands' facial attractiveness**. Proc Natl Acad Sci U S A. 2014 Dec 2;111(48):17081-6.

Salem J, Dureau P, Bachelot A, et al. **Association of Oral Contraceptives With Drug-Induced QT Interval Prolongation** in Healthy Nonmenopausal Women. *JAMA Cardiol*. 2018 Aug 1.

Sanchez-Guerrero J, Uribe AG, Jimenez-Santana L, et al. A Trial of Contraceptive Methods in Women with Systemic **Lupus** Erythematosus. N Engl J Med. 2005 Dec 15;353(24):2539-2549.

Sanders AP, Sanders BH. **Retained intrauterine devices in pregnancy**. CMAJ. 2018 Apr 9;190(14):E440.

Schrager S, Falleroni J, Edgoose J. Evaluation and Treatment of **Endometriosis**. Am Fam Physician. 2013;87(2):107-113.

Schürks Markus, Rist Pamela M, et al. **Migraine** and cardiovascular disease: systematic review and meta-analysis. BMJ 2009;339:b3914, doi: 10.1136/bmj.b3914 (Published 27Oct09)

Secura GM, Adams T, Buckel CM, et al. Change in **sexual behavior with provision of no-cost contraception**. Obstet Gynecol. 2014 Apr;123(4):771-6.

Secura GM, Madden T, McNicholas C, et al. Provision of **no-cost, long-acting contraception and teenage pregnancy**. N Engl J Med. 2014 Oct 2;371(14):1316-23.

Sedgh G, Singh S, Hussain R. **Intended and unintended pregnancies worldwide** in 2012 and recent trends. Stud Fam Plann. 2014 Sep;45(3):301-14.

Sedlak T, Bairey Merz CN, Shufelt C, et al. Contraception in patients with **heart failure**. Circulation. 2012 Sep 11;126(11):1396-400.

Seeger JD, Loughlin J, Eng PM, Clifford CR, Cutone J, Walker AM. Risk of thromboembolism in women taking ethinylestradiol/drospirenone and other oral contraceptives. Obstet Gynecol. 2007 Sep;110(3):587-93.
Ethinylestradiol/drospirenone initiators and initiators of other oral contraceptives are **similarly** likely to experience **thromboembolism**.

sexualityandU.ca website (supported by SOGC) http://sexualityandu.ca/professionals/index.aspx

Shaarawy M, et al. Effects of the long-term use of depot medroxyprogesterone acetate as hormonal contraceptive on bone mineral density and biochemical markers of bone remodeling. Contraception. 2006 Oct;74(4):297-302.

Shafran DM, Wu C. Treatment of venous **thromboembolism in a 22-year-old woman taking an oral contraceptive pill**. CMAJ. 2017 Nov 27;189(47):E1459-E1460.

Shapiro S. Combined hormonal contraceptives and the **risk of venous and arterial thromboembolism** and cardiovascular death: misuse of automated databases. J Fam Plann Reprod Health Care. 2013 Apr;39(2):89-96.

Shen J, Che Y, Showell E, et al. Interventions for **emergency contraception**. Cochrane Database Syst Rev. 2017 Aug 2;8:CD001324.

Shen J, Che Y, Showell E, et al. Interventions for **emergency contraception**. Cochrane Database Syst Rev. 2019 Jan 20;1:CD001324. Levonorgestrel and mid-dose mifepristone (25 mg to 50 mg) were more effective than Yuzpe regimen. Both mid-dose (25 mg to 50 mg) and low-dose mifepristone(less than 25 mg) were probably more effective than levonorgestrel (1.5 mg). Mifepristone low dose (less than 25 mg) was less effective than mid-dose mifepristone. UPA may be more effective than levonorgestrel.Levonorgestrel users had fewer side effects than Yuzpe users, and appeared to be more likely to have a menstrual return before the expected date. UPA users were probably more likely to have a menstrual return after the expected date. Menstrual delay was probably the main adverse effect of mifepristone and seemed to be dose-related. Cu-IUD may be associated with higher risks of abdominal pain than ECPs.

Shrader SP, Hall LN, Ragucci KR, Rafie S. Updates in hormonal **emergency contraception**. Pharmacotherapy. 2011 Sep;31(9):887-95.

Shufelt CL, Bairey Merz CN. Contraceptive hormone use and **cardiovascular disease**. *J Am Coll Cardiol* 2009; 53:221-231

Sidneya S, Cheethamb TC, Connell FA, et al. Recent combined hormonal contraceptives (CHCs) and the risk of **thromboembolism** and other cardiovascular events in new users. Contraception 2013; 87:93-100.

Sieving RE, McRee AL, McMorris BJ, et al. Prime Time: Sexual Health Outcomes at 24 Months for a **Clinic-Linked Intervention** to Prevent Pregnancy Risk Behaviors. JAMA Pediatr. 2013 Feb 25:1-8.

Simmons KB, Haddad LB, Nanda K, et al. **Drug interactions between non-rifamycin antibiotics and hormonal contraception**: a systematic review. Am J Obstet Gynecol. 2018 Jan;218(1):88-97.e14.

Skovlund CW, Mørch LS, Kessing LV, Lidegaard Ø. **Association of hormonal contraception with depression**. JAMA Psychiatry. 2016;73(11):1154-1162

Skovlund CW, Mørch LS, Kessing LV, et al. Association of **Hormonal Contraception With Suicide Attempts** and Suicides. Am J Psychiatry. 2017 Nov 17:appiajp201717060616.

Smith C, Gold J, Ngo TD, Sumpter C, Free C. **Mobile phone-based interventions** for improving contraception use. Cochrane Database of Systematic Reviews 2015, Issue 6. Art. No.: CD011159. DOI: 10.1002/14651858.CD011159.pub2. Our review provides limited evidence that interventions delivered by mobile phone can improve contraception use. Whilst evidence suggests that a series of interactive voice messages and counsellor support can improve post-abortion contraception, and that a mixture of uni-directional and interactive daily educational text messages can improve OC adherence, the cost-effectiveness and long-term effects of these interventions remain unknown. Further high-quality trials are required to robustly establish the effects of interventions delivered by mobile phone to improve contraception use.

Smoley BA, Robinson CM. **Natural Family Planning**. Am Fam Physician. 2012 Nov 15;86(10):924-928.

Smulders B, van Oirschot SM, Farquhar C, et al. Oral contraceptive pill, progestogen or estrogen pre-treatment for **ovarian stimulation protocols** for women undergoing assisted reproductive techniques. Cochrane Database Syst Rev. 2010 Jan 20;(1):CD006109.

Snow Sara E, Melillo Stephanie N, Jarvis Courtney I. **Ulipristal Acetate** for Emergency Contraception. Articles Ahead of Print published on 1 June 2011, DOI 10.1345/aph.1P704. Ann Pharmacother ;45:780-786.

SOGC: Nov 2008 Missed Contraceptives: http://www.sogc.org/jogc/abstracts/200811_SOGCClinicalPracticeGuidelines_1.pdf

SOGC: Society of Obstetricians and Gynaecologists of Canada. **Emergency contraception**. SOGC clinical practice guideline. J Obstet Gynaecol Can 2012;34:870-8. www.sogc.org/guidelines/documents/gui280CPG1209E.pdf

SOGC: Society of Obstetricians and Gynaecologists of Canada. **Diane-35** and risk of venous thromboembolism (**VTE**). Position statement. February 19, 2013. www.sogc.org/media/documents/medDiane35VTE130219.pdf

SOGC: Society of Obstetricians and Gynaecologists of Canada. **Menstrual suppression in special circumstances**. http://sogc.org/wp-content/uploads/2014/10/JOGC-Oct2014-CPG-313_Eng_Online-Complete.pdf

SOGC: Society of Obstetricians and Gynaecologists of Canada. **Canadian contraception consensus** (**Part 1 of 4**). J Obstet Gynaecol Can 2015;37(10):S1–28.
http://sogc.org/wp-content/uploads/2015/11/gui329Pt1CPG1510.pdf (accessed December 8, 2015).

SOGC: Society of Obstetricians and Gynaecologists of Canada. **Canadian contraception consensus** (**Part 2 of 4**). J Obstet Gynaecol Can 2015;37(11):S1–39.
http://sogc.org/wp-content/uploads/2015/11/gui329Pt2CPG1511E.pdf (accessed December 8, 2015).

Song IH, Borland J, Chen S, et al. **Dolutegravir** Has No Effect on the Pharmacokinetics of Oral Contraceptives With Norgestimate and Ethinyl Estradiol. Ann Pharmacother. 2015 Jul;49(7):784-9.

Speroff, Leon, and Daniel R. Mishell Jr. "The postpartum visit: it's time for a change in order to optimally initiate contraception." Contraception 78 (2008): 90-98

Srivastava A, Patel N. **Autosomal dominant polycystic kidney disease**. Am Fam Physician. 2014 Sep 1;90(5):303-7.

Steenland MW, Pace LE, Sinaiko AD, et al. Association Between South Carolina Medicaid's Change in Payment for Immediate Postpartum **Long-Acting Reversible Contraception and Birth Intervals**. JAMA. 2019 Jun 3.

Stegeman BH, de Bastos M, Rosendaal FR, et al. Different combined oral contraceptives and the **risk of venous thrombosis**: systematic review and network meta-analysis. BMJ. 2013 Sep 12;347:f5298.

Steiner RJ et al. **Long-acting reversible contraception and condom use** among female US high school students: Implications for sexually transmitted infection prevention. JAMA Pediatr 2016 Mar 14.

Stern LF, Simons HR, Kohn JE, et al. **Differences in Contraceptive Use** Between Family Planning Providers and the U.S. Population: Results of a Nationwide Survey. Contraception. 2015 Feb 19.

Stevenson AJ, Flores-Vazquez IM, Allgeyer RL, et al. Effect of **Removal of Planned Parenthood** from the Texas Women's Health Program. N Engl J Med. 2016 Feb 2.

Stewart FH, Kaunitz AM, Laguardia KD, et al. Extended use of transdermal norelgestromin/ethinyl estradiol: a randomized trial. Obstet Gynecol. 2005 Jun;105(6):1389-96.

Sufrin CB et al. **Neisseria gonorrhea and Chlamydia trachomatis screening at intrauterine device insertion** and pelvic inflammatory disease. Obstet Gynecol 2012 Dec; 120:1314.

Sun F, Sebastiani P, Schupf N, et al. **Extended maternal age** at birth of last child and women's longevity in the Long Life Family Study. Menopause. 2014 Jun 23.

Swartz RH, Ladhani NNN, Foley N, et al; Heart and Stroke Foundation Canadian Stroke Best Practice Committees. Canad**ian stroke best practice consensus statement: secondary stroke prevention during pregnancy**. Int J Stroke 2017 (accessed December 12, 2017).

Sweet MG, Schmidt-Dalton TA, Weiss PM, Madsen KP. Evaluation and management of **abnormal uterine bleeding** in premenopausal women. Am Fam Physician. 2012 Jan 1;85(1):35-43.

Templeton A, Grimes DA. A **Request for Abortion**. N Engl J Med 2011; 365:2198-2204.

Thirumalai A, Ceponis J, Amory JK, et al. Effects of 28 Days of **Oral Dimethandrolone Undecanoate in Healthy Men**: A Prototype Male Pill. J Clin Endocrinol Metab. 2019 Feb 1;104(2):423-432.

Thonneau P, et al. Risk factors for **IUD failure**: results of a large multicentre case-control study. Hum Reprod. 2006 Oct;21(10):2612-6. Epub 2006 Jun 14. Only a history of previous IUD expulsion was found to be a risk factor for failure, indicating that these women should have regular medical and echographical follow-up. Comparing the efficacy rate of various types of IUDs, we found a clear advantage for levonorgestrel-releasing devices.

Tozer BS, Boatwright EA, David PS, et al. Prevention of **migraine** in women throughout the life span. Mayo Clin Proc. 2006 Aug;81(8):1086-91; quiz 1092.

Trenor, Cameron C., III, Chung, Richard J., Michelson, Alan D., et al. Hormonal Contraception and **Thrombotic Risk**: A Multidisciplinary Approach. Pediatrics 2011 127: 347-357.

Trezza C, Ford SL, et al. Lack of Effect of Oral **Cabotegravir** on the Pharmacokinetics of a **Levonorgestrel/Ethinyl Estradiol**-Containing Oral Contraceptive in Healthy Adult Females. Br J Clin Pharmacol. 2017 Jan 14.
Troskie C, Soon JA, et al. **Regulatory approval time** for hormonal contraception in Canada, the United States and the United Kingdom, 2000-2015: a retrospective data analysis. CMAJ Open. 2016 Nov 3;4(4):E654-E660.
Trussell J et al. New **estimates of the effectiveness of the Yuzpe regimen** of emergency contraception. Contraception 1998; 57:363.
Turok DK, Leeman L, Sanders JN, et al. **Immediate postpartum levonorgestrel intrauterine device insertion and breast-feeding** outcomes: a noninferiority randomized controlled trial. Am J Obstet Gynecol. 2017 Aug 23.
Tworoger SS, Fairfield KM, Colditz GA, Rosner BA, Hankinson SE. Association of oral contraceptive use, other contraceptive methods, and infertility with **ovarian cancer** risk. Am J Epidemiol. 2007 Oct 15;166(8):894-901. Epub 2007 Jul 26. Results suggest that the beneficial effect of oral contraceptives on ovarian cancer risk attenuates after 20 years since last use. Furthermore, tubal ligation, intrauterine device use, and infertility were associated with ovarian cancer risk.
Urrutia RP, Polis CB. **Fertility awareness** based methods for pregnancy prevention. BMJ. 2019 Jul 11;366:l4245.
van Hylckama Vlieg A, Helmerhorst F M, Vandenbroucke J P, et al. The venous **thrombotic risk** of oral contraceptives, effects of oestrogen dose and progestogen type: results of the MEGA case-control study. BMJ 2009;339:b2921, doi: 10.1136/bmj.b2921 (Published 13 August 2009)
Van Vliet HA, Grimes DA, Lopez LM, et al. **Triphasic versus monophasic** oral contraceptives for contraception. Cochrane Database Syst Rev. 2011 Nov 9;11:CD003553. The available evidence is insufficient to determine whether triphasic OCs differ from monophasic OCs in effectiveness, bleeding patterns or discontinuation rates. Therefore, we recommend monophasic pills as a first choice for women starting OC use. Large, high-quality RCTs that compare triphasic and monophasic OCs with identical progestogens are needed to determine whether triphasic pills differ from monophasic OCs.
Vinogradova Y, Coupland C, et al. Use of combined oral contraceptives and **risk of venous thromboembolism**: nested case-control studies using the QResearch and CPRD databases. BMJ. 2015 May 26;350:h2135.
Wahlsten LR, Eckardt H, Lyngbæk S, et al. **Symptomatic venous thromboembolism** following fractures distal to the knee: a nationwide Danish cohort study. J Bone Joint Surg Am. 2015 Mar 18;97(6):470-7. (risk with oral contraceptives & NSAIDs)
Watson S, Härmark L. **Desogestrel and panic attacks** - a new suspected adverse drug reaction reported by patients and health care professionals on spontaneous reports. Br J Clin Pharmacol. 2018 May 24.
Weill A, et al. **Low dose oestrogen combined oral contraception and risk of pulmonary embolism, stroke, and myocardial infarction** in five million French women: cohort study. BMJ 2016;353:i2002.
Westhoff C, et al. Initiation of Oral Contraceptives Using a **Quick Start** Compared With a Conventional Start: A Randomized Controlled Trial. Obstet Gynecol. 2007 Jun;109(6):1270-1276. Protocols that require a woman to wait until the next menses to start hormonal contraceptives are an obstacle to contraceptive initiation. Directly observed, immediate initiation of the pill improves short-term continuation. (InfoPOEMs: The immediate start of oral contraceptives (OCs) in young women improves initiation, but not continuation of use, and does not decrease pregnancy rates. (LOE = 1b))
Westhoff CL, Torgal AH, Mayeda ER, et al. Pharmacokinetics of a combined oral contraceptive in **obese** and normal-weight women. Contraception. 2010 Jun;81(6):474-80.
Westhoff CL et al. **Body weight** does not impact pregnancy rates during use of a low-dose extended-regimen 91-day oral contraceptive. Contraception 2012 Mar; 85:235. (LoSEASONIQUE)
Wiebe E, Kaczorowski J, Mackay J. **Mood and sexual side effects** of hormonal contraception: Physicians' and residents' knowledge, attitudes, and practices. Can Fam Physician. 2012 Nov;58(11):e677-83.
Wiebe E. Contraceptive **practices and attitudes among immigrant and nonimmigrant** women in Canada. Can Fam Physician. 2013 Oct;59(10):e451-5.
Wiegratz I, Kuhl H. **Long-cycle treatment** with oral contraceptives. Drugs. 2004;64(21):2447-62.
Wiegratz I, et al. Fertility after discontinuation of treatment with an oral contraceptive containing 30 microg of ethinyl estradiol and 2 mg of dienogest. Fertil Steril. 2006 Jun;85(6):1812-9. The present prospective study revealed only a slight delay in regaining fertility during the first three cycles after cessation of EE/DNG. Thereafter, the cumulative rate of conception did not differ from that observed in fertile women who attempted to become pregnant without prior contraception.
Wiesinger H, Berse M, et al. Pharmacokinetic interaction between the **CYP3A4 inhibitor ketoconazole and the hormone drospirenone** in combination with **ethinylestradiol or estradiol**. Br J Clin Pharmacol. 2015 Aug 14.
Wilkinson TA, Clark P, Rafie S, et al. **Access** to **Emergency Contraception** After Removal of Age Restrictions. Pediatrics. 2017;140(1):e20164262
Wilkinson TA, Fahey N, Shields C, et al. **Pharmacy communication** to adolescents and their physicians regarding access to **emergency contraception**. Pediatrics. 2012 Apr;129(4):624-9.
Williams T, Mortada R, Porter S. Diagnosis and Treatment of **Polycystic Ovary Syndrome**. Am Fam Physician. 2016 Jul 15;94(2):106-13.
Winner B, Peipert JF, Zhao Q, et al. **Effectiveness of long-acting reversible contraception**. N Engl J Med. 2012 May 24;366(21):1998-2007.
Wong CL, Farquhar C, Roberts H, et al. Oral contraceptive pill as treatment for **primary dysmenorrhoea**. Cochrane Database Syst Rev. 2009 Apr 15;(2):CD002120. There is limited evidence for pain improvement with the use of the OCP (both low and medium dose oestrogen) in women with dysmenorrhoea. There is no evidence of a difference between different OCP preparations.
Woodhams EJ, Gilliam M, **In the Clinic: Contraception**. Ann Intern Med Oct 2, 2012. ITC4-2. (choices for post-partum and breastfeeding)
Woodhams EJ, Gilliam M**. Contraception**. Ann Intern Med. 2019 Feb 5;170(3):ITC18-ITC32.
Worly BL, Gur TL, Schaffir J. The relationship between **progestin hormonal contraception and depression**: a systematic review. Contraception. 2018 Feb 20.
Wu C, Grandi S, Filion K, Abenhaim H, Joseph L, Eisenberg M. **Drospirenone**-containing oral contraceptive pills and the risk of venous and arterial **thrombosis**: a systematic review. BJOG. 2013 Mar 26.
Xu H et al. Contraceptive failure rates of **etonogestrel subdermal implants in overweight** and obese women. Obstet Gynecol 2012 Jul; 120:21.
Xu H, Eisenberg DL, Madden T, Secura GM, Peipert JF. **Medical contraindications** in women seeking combined hormonal contraception. Am J Obstet Gynecol. 2014 Mar;210(3):210.e1-5.
Yang YT, Kozhimannil KB, Snowden JM. **Pharmacist-Prescribed Birth Control in Oregon and Other States**. JAMA. 2016 Mar 28.
Zapata LB, Pazol K, Dehlendorf C, et al. **Contraceptive Counseling** in Clinical Settings: An Updated Systematic Review. Am J Prev Med. 2018 Nov;55(5):677-690.
Zethraeus N, Dreber A, Ranehill E, et al. A **first-choice combined oral contraceptive influences general well-being in healthy women**: a double-blind, randomized, placebo-controlled trial. Fertil Steril. 2017 Apr 19.
Zhang L et al. **Pregnancy outcome after levonorgestrel**-only emergency contraception failure: A prospective cohort study. Hum Reprod 2009 Mar 31; [e-pub ahead of print].
Zuurbier SM, Arnold M, Middeldorp S, et al. Risk of **cerebral venous thrombosis** in **obese** women [online March 14, 2016].JAMA Neurol. doi:10.1001/jamaneurol.2016.0001. 10.

Link to CDC – Medical Eligibility for Contraceptive Use – detailed chart:
https://www.cdc.gov/reproductivehealth/contraception/pdf/summary-chart-us-medical-eligibility-criteria_508tagged.pdf

References: Hormonal Birth Control Options – www.RxFiles.ca

[1] Black A, Francoeur D, Rowe T, et al. Canadian contraception consensus. J Obstet Gynaecol Can. 2004 Feb;26(2):143-56, 158-74.
SOGC: Society of Obstetricians and Gynaecologists of Canada. **Canadian contraception consensus** (**Part 1 of 4**). J Obstet Gynaecol Can 2015;37(10):S1–28. http://sogc.org/wp-content/uploads/2015/11/gui329Pt1CPG1510.pdf (accessed December 8, 2015).
SOGC: Society of Obstetricians and Gynaecologists of Canada. **Canadian contraception consensus** (**Part 2 of 4**). J Obstet Gynaecol Can 2015;37(11):S1–39. http://sogc.org/wp-content/uploads/2015/11/gui329Pt2CPG1511E.pdf (accessed December 8, 2015).
[2] Herndon EJ, Zieman M. New contraceptive options. Am Fam Physician. 2004 Feb 15;69(4):853-60. Review. Erratum in: Am Fam Physician. 2004 Apr 15;69(8):1863.
[3] Choice of contraceptives. Treat Guidel Med Lett. 2004 Aug;2(24):55-62.
[4] Micromedex 2017
[5] Johnson BA. Insertion and removal of intrauterine devices. Am Fam Physician. 2005 Jan 1;71(1):95-102.
Middleton L. J., Champaneria R., Daniels J. P., et al. on behalf of the International Heavy Menstrual Bleeding Individual Patient Data Meta-analysis Collaborative Group. Hysterectomy, endometrial destruction, and levonorgestrel releasing intrauterine system (Mirena) for heavy menstrual bleeding: systematic review and meta-analysis of data from individual patients. BMJ 2010;341:c3929, doi: 10.1136/bmj.c3929 (Published 16 August 2010)
Gupta J, Kai J, Middleton L, Pattison H, Gray R, Daniels J; ECLIPSE Trial Collaborative Group. Levonorgestrel intrauterine system versus medical therapy for menorrhagia. N Engl J Med. 2013 Jan 10;368(2):128-37.
[6] Choice of contraceptives. Med Lett Drugs Ther. 2018 Oct 8;60(1557):161-168.

Additional sources:
AAP: Committee on Adolescence. **Emergency contraception**. Pediatrics. 2012 Dec;130(6):1174-82.
Abou-Setta AM, et al. **Levonorgestrel**-releasing intrauterine device (LNG-IUD) for symptomatic **endometriosis** following surgery. Cochrane Database Syst Rev. 2006 Oct 18;(4):CD005072.
ACOG Frequently Asked Questions #114, **Emergency Contraception**. http://www.acog.org/~/media/For%20Patients/faq114.pdf?dmc=1&ts=20121127T1830130312. Accessed 1/6/13
ACOG Committee Opinion. Access to **Emergency Contraception**. Number 542, November 2012. www.acog.org/Resources_And_Publications/Committee_Opinions/Committee_on_Health_Care_for_Underserved_Women/
ACOG: Practice Bulletin #121 "Long-Acting Reversible Contraception: **Implants and Intrauterine Devices**" is published in the July 2011 issue of Obstetrics & Gynecology.
ACOG- Practice bulletin no. 121: **Long-acting reversible contraception**: Implants and intrauterine devices. Obstet Gynecol 2011 Jul; 118:184.
ACOG: Committee opinion no. 539: **adolescents and long-acting reversible contraception**: implants and intrauterine devices. Obstet Gynecol. 2012 Oct;120(4):983-8.
ACOG: Committee Opinion No 544: **Over-the-Counter Access to Oral Contraceptives**. Obstet Gynecol. 2012 Dec;120(6):1527-31.
ACOG: American College of Obstetricians & Gynecologists Committee on Gynecologic Practice. ACOG Committee Opinion No. 602: **Depot medroxyprogesterone acetate and bone effects**. Obstet Gynecol. 2014June 2014.
ACOG Practice Bulletin No. 152: **Emergency Contraception**. Obstet Gynecol. 2015 Sep;126(3):e1-e11.
ACOG: Committee Opinion No. 642: **Increasing Access to Contraceptive Implants and Intrauterine Devices** to Reduce Unintended Pregnancy. Obstet Gynecol. 2015 Oct;126(4):e44-8.
ACOG: Committee Opinion No. 670: **Immediate Postpartum Long-Acting Reversible Contraception**. Obstet Gynecol. 2016 Aug;128(2):e32-7.
ACOG: Committee Opinion No. 710: **Counseling Adolescents About Contraception**. Obstet Gynecol. 2017 Aug;130(2):e74-e80.
ACOG: Committee on Practice Bulletins-Gynecology, Long-Acting Reversible Contraception Work Group. Practice Bulletin No. 186: **Long-Acting Reversible Contraception: Implants and Intrauterine Devices**. Obstet Gynecol. 2017 Nov;130(5):e251-e269.
Adab P, Jiang CQ, Rankin E, et al. **Breastfeeding practice, oral contraceptive use and risk of rheumatoid arthritis** among Chinese women: the Guangzhou Biobank Cohort Study. Rheumatology(Oxford). 2014 Jan 6.
Agostino H, Di Meglio G. **Low-dose** oral contraceptives in adolescents: how low can you go? J Pediatr Adolesc Gynecol. 2010 Aug;23(4):195-201.
Albrecht K, Callhoff J, Buttgereit F, et al. The association between the use of **oral contraceptives and patient-reported outcomes in an early arthritis cohort**. Arthritis Care Res (Hoboken). 2015 Aug 14.
Ahmed S, Li Q, Liu L, Tsui AO. **Maternal deaths averted** by contraceptive use: an analysis of 172 countries. Lancet. 2012 Jul 9.
Akers AY, Steinway C, Sonalkar S, et al. **Reducing Pain During Intrauterine Device Insertion**: A Randomized Controlled Trial in Adolescents and Young Women. Obstet Gynecol. 2017 Sep 5.
Akers AY et al. **Reducing pain during intrauterine device insertion**: A randomized controlled trial in adolescents and young women. (lidocaine) Obstet Gynecol 2017 Sep 05; 130:795.
Al Khalifah RA et al. **Metformin or oral contraceptives for adolescents with polycystic ovarian syndrome**: A meta-analysis. Pediatrics 2016 May; 137:e20154089.
Al Khalifah RA, Florez ID, et al. Metformin or Oral Contraceptives for Adolescents With **Polycystic Ovarian Syndrome**: A Meta-analysis. Pediatrics. 2016 May;137(5).
Albaladejo A. **Contraceptive shortages mean Venezuela's** people face a sexual health emergency. BMJ. 2018 Mar 23;360:k1197.
Ali M et al. Extended use **up to 5 years** of the **etonogestrel**-releasing subdermal contraceptive implant: Comparison to levonorgestrel-releasing subdermal implant. Hum Reprod 2016 Sep 26.
Alkema L, Kantorova V, Menozzi C, Biddlecom A. National, regional, and **global rates and trends in contraceptive prevalen**ce and unmet need for family planning between 1990 and 2015: a systematic and comprehensive analysis. Lancet 2013; online March 12.
Allen RH, Cwiak CA, Kaunitz AM. Contraception in **women over 40 years of age**. CMAJ. 2013 Apr 16;185(7):565-73.
Alpañés M, et al. **Combined oral contraceptives plus spironolactone** compared with **metformin in women with polycystic ovary syndrome**: one-year randomized clinical trial. Eur J Endocrinol. 2017 Nov;177(5):399-408.
American College of Obstetricians and Gynecologists (ACOG). **Noncontraceptive uses of hormonal contraceptives**. Washington (DC): American College of Obstetricians and Gynecologists (ACOG); 2010 Jan. 13 p. (ACOG practice bulletin; no. 110).
Amin O, Howlett DC. An unusual cause of right iliac fossa pain. BMJ. 2018 Nov 14;363:k4153 **((IUD migration)**
Amy JJ, Tripathi V. Contraception for women: an **evidence** based overview. BMJ. 2009 Aug 7;339:b2895. doi: 10.1136/bmj.b2895.
Andersen L, Friis S, Hallas J, et al. **Hormonal contraceptive use and risk of glioma** among younger women a nationwide case-control study. Br J Clin Pharmacol. 2014 Oct 26.
Aptekman M, Rashid M, Wright V, Dunn S. **Unmet contraceptive needs among refugees**. Can Fam Physician. 2014 Dec;60(12):e613-9.
Bakhru A, Stanwood N. Performance of contraceptive patch compared with **oral contraceptive** pill in a high-risk population. Obstet Gynecol. 2006 Aug;108(2):378-86.

Batra P, Rafie S, Zhang Z, et al. An Evaluation of the Implementation of **Pharmacist-Prescribed Hormonal Contraceptives in California**. Obstet Gynecol. 2018 Apr 6.
Bateson D, McNamee K, Briggs P. **Newer non-oral hormonal contraception**. BMJ. 2013 Feb 14;346:f341.
Batur P. **Emergency contraception**: Separating fact from fiction. Cleve Clin J Med. 2012 Nov;79(11):771-6.
Beaber EF, Buist DS, Barlow WE, et al. Recent Oral Contraceptive Use by Formulation and **Breast Cancer Risk** among Women 20 to 49 Years of Age. Cancer Res. 2014 Aug 1;74(15):4078-89.
Beasley A et al. Randomized clinical trial of **self versus clinical administration of subcutaneous depot medroxyprogesterone** acetate. Contraception 2014 May; 89:352.
Becker NV, Polsky D. Women Saw Large **Decrease In Out-Of-Pocket Spending For Contraceptives** After ACA Mandate Removed Cost Sharing. Health Aff (Millwood). 2015 Jul 1;34(7):1204-11.
Bednarek PH et al. **Immediate versus delayed IUD insertion** after uterine aspiration. N Engl J Med 2011 Jun 9; 364:2208.
Beksinska ME, Smit JA, Kleinschmidt I, et al. Prospective study of weight change in new adolescent users of **DMPA**, NET-EN, COCs, nonusers and discontinuers of hormonal contraception. Contraception. 2010 Jan;81(1):30-4.
Bellizzi S, Sobel HL, Obara H, Temmerman M. **Underuse of modern methods of contraception**: underlying causes and consequent undesired pregnancies in 35 low- and middle-income countries. Hum Reprod. 2015 Feb 3.
Bender NM, Segall-Gutierrez P, Najera SO, et al. Effects of **progestin-only** long-acting contraception on metabolic markers in **obese** women. Contraception. 2013 Jan 2.
Berenson A, et al. Complications and Continuation of Intrauterine Device Use Among Commercially Insured Teenagers Obstetrics & Gynecology: 2013 May; 121: 5: 951-958.
Berenson AB, Rahman M. Changes in weight, total fat, percent body fat, and central-to-peripheral fat ratio associated with injectable and oral contraceptive use. Am J Obstet Gynecol. 2009 Mar;200(3):329.e1-8. n=703 3yrs. Bodyweight and fat significantly increase with the use of DMPA. After discontinuation of DMPA, some decrease in bodyweight and fat occurs when NH is used.
Birth Control: What You Should Know. Am Fam Physician. 2015 May 1;91(9)
Bissell DM, Anderson KE, Bonkovsky HL. **Porphyria**. N Engl J Med. 2017 Aug 31;377(9):862-872.
Black A, Guilbert E; Costescu D, et al; Contraception Consensus Working Group, Society of Obstetricians and Gynaecologists of Canada. (**SOGC**) **Canadian contraception consensus (Part 3 of 4)**: Chapter 7 – **Intrauterine contraception**. J Obstet Gynaecol Can 2016;38:182-222. www.jogc.com/article/S1701-2163(15)00024-9/pdf (accessed April 6, 2016).
Black A, Guilbert E, Costescu D, et al. **SOGC clinical practice guideline. No. 329. Canadian contraception consensus. Part 4 of 4.** Chapter 9: Combined hormonal contraception. J Obstet Gynaecol Can 2017;39:229-68.e5
Blumenthal PD, Edelman A. Hormonal contraception. Obstet Gynecol. 2008 Sep;112(3):670-84.
Behre HM, Zitzmann M, Anderson RA, et al. Efficacy and Safety of an **Injectable Combination Hormonal Contraceptive for Men**. J Clin Endocrinol Metab. 2016 Oct 27:jc20162141.
Bonnema RA., McNamara MC., Spencer AL., **Contraception Choices in Women with Underlying Medical Conditions**. Am Fam Physician. 2010 Sep 15;82(6):621-628.
Bonny AE, et al. Weight gain in obese and nonobese adolescent girls initiating depot medroxyprogesterone, oral contraceptive pills, or no hormonal contraceptive method. Arch Pediatr Adolesc Med. 2006 Jan;160(1):40-5.
Bonny AE et al. A pilot study of **depot medroxyprogesterone** acetate **pharmacokinetics** and **weight gain** in adolescent females. Contraception 2014 May; 89:357.
Boulet SL, D'Angelo DV, Morrow B, et al. **Contraceptive Use Among Nonpregnant and Postpartum Women** at Risk for Unintended Pregnancy, and Female High School Students, in the Context of Zika Preparedness - United States,2011-2013 and 2015. MMWR Morb Mortal Wkly Rep. 2016 Aug 5;65(30):780-7
Brinkman SA, Johnson SE, Codde JP, et al. Efficacy of **Infant Simulator Programmes** to Prevent Teenage Pregnancy: a School-Based Cluster Randomised Controlled Trial in Western Australia. Lancet. 2016 Aug 24.
Brown J, Farquhar C. An **overview of treatments for endometriosis**. JAMA. 2015 Jan 20;313(3):296-7.
Brunson MR, et al. **Postpartum contraception**: initiation and effectiveness in a large universal healthcare system. Am J Obstet Gynecol. 2017 Jul;217(1):55.e1-55.e9.
Burke HM et al. Observational study of the acceptability of **Sayana Press** among **intramuscular DMPA** users in Uganda and Senegal. Contraception 2014 May; 89:361.
Burke HM et al. Provider acceptability of **Sayana Press**: Results from community health workers and clinic-based providers in Uganda and Senegal. Contraception 2014 May; 89:368.
Byrne EH, Anahtar MN, Cohen KE, et al. Association between **injectable progestin-only contraceptives and HIV acquisition** and HIV target cell frequency in the female genital tract in South African women: a prospective cohort study. Lancet Infect Dis. 2015 Dec 23.
Caddy S, Yudin MH, Hakim J, Money DM, Infectious Disease Committee. **SOGC**-Best practices to **minimize risk of infection with intrauterine device insertion**. J Obstet Gynaecol Can. 2014 Mar;36(3):266-74.
Calhoun A. Combined hormonal contraceptives: Is it time to reassess their role in **migraine**? Headache 2011. Published online ahead of print January 6, 2012.
Camacho EM, Lunt M, Farragher TM, et al. The relationship between oral contraceptive use and functional outcome in women with recent **onset inflammatory polyarthritis**: Results from the Norfolk Arthritis Register (NOAR). Arthritis Rheum. 2011 Apr 22. doi: 10.1002/art.30416.
Cameron ST, Glasier A, Chen ZE, et al. Effect of **contraception provided at termination of pregnancy** and incidence of subsequent termination of pregnancy. BJOG. 2012 Aug;119(9):1074-80.
Campbell SJ, Cropsey KL, Matthews CA. Intrauterine device use in a high-risk population: experience from an urban university clinic. Am J Obstet Gynecol. 2007 Aug;197(2):193.e1-6; discussion 193.e6-7. IUD/IUS use appears to be safe, acceptable, and feasible in high-risk patients. The IUS (Mirena) had lower rates of complications and greater acceptability than the IUD.
Canning D, Schultz TP. The **economic consequences** of reproductive health and **family planning**. Lancet. 2012 Jul 9.
Carmo LSMP, Braga GC, et al. Timing of **Etonogestrel-Releasing Implants and Growth of Breastfed Infants**: A Randomized Controlled Trial. Obstet Gynecol. 2017 Jun 6.
Caso V, Falorni A, Bushnell CD, et al. **Pregnancy, Hormonal Treatments for Infertility, Contraception, and Menopause** in Women After Ischemic Stroke: A Consensus Document. Stroke. 2017 Feb;48(2):501-506.
Castellsagué X, Díaz M, et al. **Intrauterine device use**, cervical infection with human papillomavirus, and risk of **cervical cancer**: a pooled analysis of 26 epidemiological studies. Lancet Oncol 2011; online Sept 13.
CDC: Centers for Disease Control and Prevention (CDC). **U.S. medical eligibility criteria** for contraceptive use, 2010: adapted from the World Health Organization medical eligibility criteria for contraceptive use, 4th edition. MMWR Recomm Rep 2010 Jun 18;59(RR-4):1-86. **CDC** has released **medical eligibility criteria for contraceptive use to help U.S. healthcare providers** counsel patients about their contraceptive choices. The criteria, published in MMWR, are modified from the World Health Organization's 2009 guidance. The CDC offers modified recommendations about contraception for U.S. women who have venous thromboembolism, valvular heart disease, ovarian cancer, and uterine fibroids, as well as women who are postpartum and breast-feeding. It also gives additional guidance on contraception for women with rheumatoid arthritis, previous bariatric surgery, peripartum cardiomyopathy, endometrial hyperplasia, inflammatory bowel disease, and organ transplantation. http://www.cdc.gov/mmwr/pdf/rr/rr59e0528.pdf
CDC: 2011 **Update** to **CDC's U.S. Medical Eligibility Criteria** for Contraceptive Use, 2010: Revised Recommendations for the Use of Contraceptive Methods During the Postpartum Period. http://www.cdc.gov/mmwr/pdf/wk/mm6026.pdf
CDC **Update to CDC's U.S. Medical Eligibility Criteria** for Contraceptive Use, 2010: Revised Recommendations for the Use of Hormonal Contraception Among Women at High Risk for HIV Infection or Infected with HIV. Weekly. June 22, 2012 / 61(24);449-452. http://www.cdc.gov/mmwr/preview/mmwrhtml/mm6124a4.htm?s_cid=mm6124a4_x
CDC: Centers for Disease Control and Prevention. **Sexual experience and contraceptive use among female teens** — United States, 1995, 2002, and 2006–2010. MMWR Morb Mortal Wkly Rep 2012 May 4; 61:297.
Centers for Disease Control and Prevention (CDC). Division of Reproductive Health, National Center for Chronic Disease Prevention and Health Promotion. U.S. selected practice recommendations for contraceptive use, 2013: adapted from the World Health Organization Selected Practice Recommendations for Contraceptive Use, 2nd edition. *MMWR Recomm Rep* 2013;62(RR05):1-60.

Champaloux SW, Tepper NK, Curtis KM, et al. **Contraceptive Use Among Women With Medical Conditions** in a Nationwide Privately Insured Population. Obstet Gynecol. 2015 Dec;126(6):1151-9.
Chang T, Davis MM, Kusunoki Y, et al. **Sexual Behavior and Contraceptive Use** among 18- to 19-Year-Old Adolescent Women by Weight Status: A Longitudinal Analysis. J Pediatr. 2015 Jun 25.
Chang T, Davis MM, Kusunoki Y, et al. **Sexual Behavior and Contraceptive** Use among 18- to 19-Year-Old Adolescent Women by Weight Status: A Longitudinal Analysis. J Pediatr. 2015 Sep;167(3):586-92.
Charlton BM, Rich-Edwards JW, Colditz GA, et al. **Oral contraceptive use and mortality after 36 years** of follow-up in the Nurses' Health Study: prospective cohort study. BMJ. 2014 Oct 31;349:g6356.
Charlton BM, Mølgaard-Nielsen D, Svanström H, et al. Maternal use of **oral contraceptives and risk of birth defects** in Denmark: prospective, nationwide cohort study. BMJ. 2016 Jan 6;352:h6712.
Chee M, Zhang JX, Ngooi S, et al. **Generic Substitution Rates** of Oral Contraceptives and Associated Out-of-Pocket Cost Savings Between January 2010 and December 2014. JAMA Intern Med. 2018 Jan 16.
Chen MJ, Hou MY, et al. **Long-Acting Reversible Contraception Initiation With a 2- to 3-Week Compared With a 6-Week Postpartum Visit**. Obstet Gynecol. 2017 Sep 5
Cheng L, Che Y, Gulmezoglu AM. Interventions for **emergency contraception**. Cochrane Database Syst Rev. 2012 Aug 15;8:CD001324. Intermediate-dose mifepristone (25-50 mg) was superior to LNG and Yuzpe regimens. Mifepristone low dose (< 25 mg) may be more effective than LNG (0.75 mg two doses), but this was not conclusive. UPA may be more effective than LNG. LNG proved to be more effective than the Yuzpe regimen. The copper IUD was the most effective EC method and was the only EC method to provide ongoing contraception if left in situ.
Ciccariello C. **Defunding Planned Parenthood**-The Stakes for America's Women. JAMA Intern Med. 2017 Feb 3
Clark MK, et al. Bone mineral density loss and recovery during 48 months in first-time users of depot medroxyprogesterone acetate. Fertil Steril. 2006 Nov;86(5):1466-74. Epub 2006 Sep 25. Depot MPA-related BMD loss is substantial but occurs mostly during the first 2 years of DMPA use. Therefore, longer use may not substantially increase the risk of osteoporosis. The prolonged recovery time suggests the need to consider timing of use in relation to menopause or other factors that may impede bone remodeling.
Cleland K, Zhu H, Goldstuck N, et al. The efficacy of **intrauterine devices for emergency contraception**: a systematic review of 35 years of experience. Human Reproduction doi:10.1093/humrep/des140.
Clinical Effectiveness Unit. **Drug interactions** with hormonal contraception. London (UK): Faculty of Sexual and Reproductive Healthcare; 2012 Jan.
Cole JA, Norman H, Doherty M, Walker AM. Venous thromboembolism, myocardial infarction, and stroke among **transdermal** contraceptive system users. Obstet Gynecol. 2007 Feb;109(2 Pt 1):339-46. There was a more than **two-fold increase** in the risk of venous thromboembolism associated with the transdermal contraceptive system.
Collaborative Group on Epidemiological Studies of **Ovarian Cancer**, Beral V, Doll R, Hermon C, Peto R, Reeves G. Ovarian cancer and oral contraceptives: collaborative reanalysis of data from 45 epidemiological studies including 23,257 women with ovarian cancer and 87,303 controls. Lancet. 2008 Jan 26;371(9609):303-14. Use of oral contraceptives confers long-term protection against ovarian cancer. These findings suggest that oral contraceptives have already prevented some 200,000 ovarian cancers and 100,000 deaths from the disease, and that over the next few decades the number of cancers prevented will rise to at least 30,000 per year.
Collaborative Group on Epidemiological Studies on Endometrial Cancer. **Endometrial cancer and oral contraceptives**: an individual participant meta-analysis of 27 276 women with endometrial cancer from 36 epidemiological studies. Lancet Oncol 2015; online Aug 5.
Cortessis VK, Barrett M, Brown Wade N, et al. **Intrauterine Device Use and Cervical Cancer Risk**: A Systematic Review and Meta-analysis. Obstet Gynecol. 2017 Nov 3.
Creinin MD, Meyn LA, Borgatta L, et al. Multicenter comparison of the contraceptive ring and patch: a randomized controlled trial. Obstet Gynecol. 2008 Feb;111(2 Pt 1):267-77. The majority of women who are using oral contraceptives (OCs) and try the **vaginal ring** continue with the ring rather than go back to OCs. Most women who try patches go back **to OCs**. It is uncertain whether the nonmasked nature of the trial, which was funded by the manufacturer of the vaginal ring, introduced bias into the study. (LOE = 1b-)
Culwell KR, Curtis KM. Use of contraceptive methods by women with **current venous thrombosis** on anticoagulant therapy: a systematic review. Contraception. 2009 Oct;80(4):337-45. Epub 2009 Jun 10. Levonorgestrel-IUD may be an effective treatment for menorrhagia secondary to anticoagulation or bleeding disorders & may be safer alternative to invasive treatment (hysterectomy).
Curtis KM, Martins SL. **Progestogen-only** contraception and bone mineral density: a systematic review. Contraception. 2006 May;73(5):470-87. Epub 2006 Feb 20.
Curtis KM, Ravi A, Gaffield ML. **Progestogen-only** contraceptive use in obese women. Contraception. 2009 Oct;80(4):346-54. Epub 2009 Jun 10. Adolescent DMPA users who are obese may gain more weight than normal weight users. This observation was not seen in adult DMPA users or adolescent Norplant users.
Curtis KM, Jatlaoui TC, Tepper NK, et al. **U.S. Selected Practice Recommendations for Contraceptive Use**, 2016. MMWR Recomm Rep. 2016 Jul 29;65(4):1-66.
Curtis KM, Peipert JF. **Long-Acting Reversible Contraception**. N Engl J Med. 2017 Feb 2;376(5):461-468.
Daniels K, Daugherty J, Jones J, et al. Current **Contraceptive Use and Variation** by Selected Characteristics Among Women Aged 15-44: United States, 2011-2013. Natl Health Stat Report. 2015 Nov;(86):1-15.
Darroch JE, Singh S. **Trends in contraceptive need and use in developing countries in 2003, 2008, and 2012**: an analysis of national surveys. Lancet. 2013 May 18;381(9879):1756-62.
Diedrich JT, et al. **Long-acting reversible contraception in adolescents**: a systematic review and meta-analysis. Am J Obstet Gynecol. 2017 Apr;216(4):364.e1-364.e12.
Dinger JC, et al. Oral contraceptive effectiveness according to **body mass index**, weight, age, and other factors. Am J Obstet Gynecol. 2009 Sep;201(3):263.e1-9.
Dinger JC, Heinemann LA, Kühl-Habich D. The safety of a **drospirenone**-containing oral contraceptive: final results from the **European Active Surveillance Study** on oral contraceptives based on 142,475 women-years of observation. Contraception. 2007 May;75(5):344-54.
Dinger J, Minh TD, Buttmann N, Bardenheuer K. **Effectiveness of oral contraceptive** pills in a large U.S. cohort comparing progestogen and regimen. Obstet Gynecol. 2011 Jan;117(1):33-40. There are fewer unintended pregnancies with the use of an oral contraceptive (OC) regimen with a progestogen of long half-life, such as drospirenone or norethisterone, when taken for a cycle of 24 days plus 4 days as compared with the standard 21 days plus 7 days (LOE = 2b)
Dogterom P, van den Heuvel MW, Thomsen T. Absence of pharmacokinetic interactions of the combined contraceptive vaginal ring **NuvaRing** with oral amoxicillin or doxycycline in two randomised trials. Clin Pharmacokinet. 2005;44(4):429-38.
Dude A, Neustadt A, Martins S, et al. Use of **withdrawal and unintended pregnancy** among females 15-24 years of age. Obstet Gynecol. 2013 Sep
Dunn Nick. Oral contraceptives and **venous thromboembolism**. BMJ 2009;339:b3164, doi: 10.1136/bmj.b3164 (Published 13 August 2009)
Dunn S, Brooks M. Mifepristone- Five Thing to Know about. CMAJ. 2018 Jun 4;190(22):E688.
ECHO **HIV incidence** among women using intramuscular depot medroxyprogesterone acetate, a copper intrauterine device, or a levonorgestrel implant for contraception: a randomised, multicentre, open-label trial. Lancet. 2019 Jun 13.
Edelman A, et al. Continuous or extended cycle vs. cyclic use of combined oral contraceptives for contraception. Cochrane Database Syst Rev. 2005 Jul 20;3:CD004695.
Edelman A, et al. Continuous versus cyclic use of combined oral contraceptives for contraception: systematic Cochrane review of randomized controlled trials. Hum Reprod. 2006 Mar;21(3):573-8.
Eggebroten JL,et al. **Immediate postpartum intrauterine device and implant program** outcomes: a prospective analysis. Am J Obstet Gynecol. 2017 Jul;217(1):51.e1-51.e7.
Eliscu AH, Burstein GR. Updates in Contraceptive **Counseling for Adolescents**. J Pediatr. 2016 Jun 10.
Espey E, et al. Effect of progestin compared with combined oral contraceptive pills on **lactation**: a randomized controlled trial. *Obstet Gynecol*. January 2012;119(1):5–13.
Etminan, Mahyar, Delaney, Joseph A.C., Bressler, Brian, et al. Oral contraceptives and the risk of **gallbladder disease**: a comparative safety study. CMAJ 2011 0: cmaj.110161.
Evra patch FDA warning Nov/05 http://www.fda.gov/bbs/topics/news/2005/NEW01262.html (& An Update on Ortho Evra & the Risk of Thromboembolism Pharmacist's Letter Dec 2005).
Health Canada Mar/06 http://www.hc-sc.gc.ca/ahc-asc/media/advisories-avis/2006/2006_14_e.html
Health Canada Nov/06 http://www.hc-sc.gc.ca/dhp-mps/medeff/advisories-avis/prof/2006/evra_hpc-cps_e.html
Health Canada Jan/08 Canadian Adverse Reaction Newsletter Evra: http://www.hc-sc.gc.ca/dhp-mps/medeff/bulletin/carn-bcei_v18n1_e.html

FDA BCDSP VTE & PE Evra Risk Jan/08 http://www.fda.gov/bbs/topics/NEWS/2008/NEW01781.html

Farquhar C, Rombauts L, Kremer JA, et al. **Oral contraceptive pill, progestogen or oestrogen pretreatment for ovarian stimulation protocols** for women undergoing **assisted reproductive techniques**. Cochrane Database Syst Rev. 2017 May 25;5:CD006109. Among women undergoing ovarian stimulation in antagonist protocols, COCP pretreatment was associated with a lower rate of live birth or ongoing pregnancy than no pretreatment. There was insufficient evidence to determine whether rates of live birth or ongoing pregnancy were influenced by pretreatment with progestogens or oestrogens, or by COCP pretreatment using other stimulation protocols. Findings on adverse events were inconclusive, except that progesterone pretreatment may reduce the risk of ovarian cysts in agonist cycles, and COCP in antagonist cycles may reduce the risk of pregnancy loss compared with no pretreatment in agonist cycles.

FDA Apr/12 has completed its review of recent observational (epidemiologic) studies regarding the risk of blood clots in women taking drospirenone-containing birth control pills.Based on this review, FDA has concluded that **drospirenone**-containing birth control pills may be associated with a higher risk for blood clots than other progestin-containing pills. . Report that some epidemiologic studies reported as high as a three-fold increase in the risk of blood clots for drospirenone-containing products when compared to products containing levonorgestrel or some other progestins, whereas other epidemiological studies found no additional risk of blood clots with drospirenone-containing products.

FDA Nov/16 **Essure** labeling now includes the addition of a boxed warning and a Patient Decision Checklist, both intended to support patient counseling and understanding of benefits and risks associated with Essure, as well as what to expect during and after the Essure procedure. The boxed warning includes safety statements to clearly communicate significant side effects or adverse outcomes associated with this device and information about the potential need for removal.

FDA May/18: Allergan recently identified, through a physician report, that four placebo capsules were placed out of order in a sample pack **of TAYTULLA** and the first four days of therapy had four non-hormonal placebo capsules instead of active capsules.

Finer LB, Philbin JM. **Sexual Initiation, Contraceptive Use, and Pregnancy Among Young Adolescents**. Pediatrics. 2013 Apr 1.

Finer LB, Zolna MR. **Declines in Unintended Pregnancy** in the United States, 2008-2011. N Engl J Med. 2016 Mar 3;374(9):843-52.

Fisher WA, Black A. Contraception in Canada: a **review** of method choices, characteristics, adherence and approaches to counselling. **CMAJ 2007**;176:953-61.

Foster DG, Hulett D, et al. Number of oral contraceptive pill **packages dispensed** and subsequent unintended pregnancies. Obstet Gynecol. 2011 Mar;117(3):566-72.

Foster DG et al. Interest in and experience with **IUD self-removal**. Contraception 2014 Jul; 90:54.

Francis JKR, Gold MA. **Long-Acting Reversible Contraception for Adolescents**: A Review. JAMA Pediatr. 2017 May 30.

FSRH : Clinical Effectiveness Unit. **Contraception for women aged over 40 years**. London (UK): Faculty of Sexual and Reproductive Healthcare (FSRH); 2017 Aug.

Gaffield ME, Culwell KR, Lee CR. The use of hormonal contraception among women taking **anticonvulsant therapy**. Contraception. 2011 Jan;83(1):16-29. Epub 2010 Sep 15.

Gai L, Zhang J, Zhang H, et al. The effect of depot **medroxyprogesterone acetate (DMPA) on bone mineral density** (BMD) and evaluating changes in BMD after discontinuation of DMPA in Chinese women of reproductive age. Contraception. 2011 Mar;83(3):218-22.

Gallo MF, Grimes DA, Lopez LM, Schulz KF. Non-latex versus latex male **condoms** for contraception. Cochrane Database Syst Rev. 2006 Jan 25;(1):CD003550. Although the nonlatex condoms were associated with higher rates of clinical breakage than their latex comparison condoms, the new condoms still provide an acceptable alternative for those with allergies, sensitivities, or preferences that might prevent the consistent use of latex condoms. The contraceptive efficacy of the nonlatex condoms requires more research.

Gallo M, et al. Combination injectable contraceptives for contraception. Cochrane Database Syst Rev. 2005 Jul 20;3:CD004568.

Gallo MF, Grimes DA, Schulz KF. **Cervical cap versus diaphragm** for contraception. Cochrane Database Syst Rev. 2002;(4):CD003551.

Gallo MF, Lopez LM, Grimes DA, et al. **Combination contraceptives: effects on weight**. Cochrane Database Syst Rev. 2011 Sep 7;9:CD003987. Available evidence was insufficient to determine the effect of combination contraceptives on weight, but no large effect was evident.

Gallo MF, Lopez LM, Grimes DA, et al. **Combination contraceptives: effects on weight.** Cochrane Database Syst Rev. **2014** Jan 29;1:CD003987. Available evidence was insufficient to determine the effect of combination contraceptives on weight, but no large effect was evident.

Gallo MF, Legardy-Williams J, Hylton-Kong T, et al. Association of **Progestin** Contraceptive Implant and **Weight Gain**. (Sino-implant levonorgestrel) Obstet Gynecol. 2016 Mar;127(3):573-6.

Gemzell-Danielsson K. Mechanism of action of **emergency contraception**. Contraception. 2010 Nov;82(5):404-9.

Gemzell-Danielsson K, Cho S, Inki P, et al. Use of contraceptive methods and contraceptive recommendations among health care providers actively involved in contraceptive counseling - results of an international survey in 10 countries. Contraception. 2012 Dec;86(6):631-8.

Giles SL, Lester F. Should women with HIV, or at high risk of contracting **HIV, use progestogen-containing contraception**? BMJ. 2013 Nov 14;347:f6695.

Gomes MP, Deitcher SR. Risk of **venous thromboembolic disease** associated with hormonal contraceptives and hormone replacement therapy: a clinical review. Arch Intern Med. 2004 Oct 11;164(18):1965-76. http://archinte.ama-assn.org/cgi/reprint/164/18/1965.pdf

Guilbert ER et al. The use of **depot-medroxyprogesterone acetate** in contraception and its potential impact on skeletal health. *Contraception* 2009 Mar; 79:167.

Health Canada Mirena & uterine perforation warning 2006. http://www.hc-sc.gc.ca/dhp-mps/medeff/bulletin/carn-bcei_v16n1_e.html#2

Gomez AM. Availability of **Pharmacist-Prescribed Contraception in California**, 2017. JAMA. 2017 Dec 12;318(22):2253-2254.

Gooneratne IK, Wimalaratna M, Ranaweera AKP, et al. **Contraception advice for women with epilepsy**. BMJ. 2017 May 11;357:j2010.

Goyal V et al. **Postabortion contraceptive use and continuation when long-acting reversible contraception is free**. Obstet Gynecol 2017 Apr; 129:655.

Greene FD, Hulett D, Bradsberry M, et al. Number of oral contraceptive pill **packages dispensed** and subsequent unintended pregnancies. Obstet Gynecol 2011;117:566-72.

Greene MF, Drazen JM. A New Label for **Mifepristone**. N Engl J Med. 2016 Jun 9;374(23):2281-2.

Grimes DA, Lopez LM, O'Brien PA, Raymond EG. Progestin-only pills for contraception. Cochrane Database Syst Rev. 2010 Jan 20;(1):CD007541.

Grimes DA, Lopez LM, Schulz KF, et al. **Immediate post-partum insertion of intrauterine devices**. Cochrane Database Syst Rev. 2010 May 12;5:CD003036.

Gronich N, Lavi I, Rennert G. Higher risk of venous **thrombosis** associated with **drospirenone**-containing oral contraceptives: population-based cohort study. CMAJ 2011Nov 7.

Grossman D. Moving Oral **Contraceptives Over-the-Counter** as a Strategy to Reduce Unintended Pregnancy. Ann Intern Med. 2013 Mar 26.

Guiahi M et al. Short-term treatment of bothersome **bleeding for etonogestrel implant users using a 14-day oral contraceptive pill regimen**: A randomized controlled trial. Obstet Gynecol 2015 Sep; 126:508.

Guilbert E, Boroditsky R, Black A, Kives S, Leboeuf M, Mirosh M, Senikas V, Wagner MS, Weir E, et al. Society of Obstetricians and Gynaecologists of Canada. Canadian Consensus Guideline on **Continuous and Extended Hormonal Contraception**, 2007. J Obstet Gynaecol Can. 2007 Jul;29(7 Suppl 2):S1-32.

Gupta J, Kai J, Middleton L, Pattison H, Gray R, Daniels J; **ECLIPSE** Trial Collaborative Group. Levonorgestrel intrauterine (Mirena) system versus medical therapy for menorrhagia. N Engl J Med. 2013 Jan 10;368(2):128-37.

Gurtcheff SE, Turok DK, et al. **Lactogenesis** after early postpartum use of the **contraceptive implant (Implanon)**: a randomized controlled trial. Obstet Gynecol. 2011 May;117(5):1114-21. {Lactation delay, failure, and continuation were not increased among women who received the etonogestrel contraceptive implant within the first 3 days postpartum versus the standard practice of insertion at 4 weeks. Women who intended to use this form of contraception were more likely to actually receive it when the insertion was done during their postpartum hospital stay. (LOE = 1b)}

Hannaford Philip C, Iversen Lisa, Macfarlane Tatiana V, et al. **Mortality** among contraceptive pill users: cohort evidence from Royal College of General Practitioners' Oral Contraception Study. BMJ 2010

Hapgood JP, Kaushic C, Hel Z. **Hormonal Contraception and HIV-1 Acquisition**: Biological Mechanisms. Endocr Rev. 2018 Jan 4.

Hardeman J, Weiss BD. **Intrauterine devices**: An update. Am Fam Physician. 2014;89(6):445-450.

Harel Z et al. Recovery bone mineral density in adolescents following the use of depot **medroxyprogesterone** acetate contraceptive injections. Contraception 2010Apr; 81:281.

Hargreave M, Mørch LS, Andersen KK, et al. Maternal use of hormonal contraception and risk of childhood leukaemia: a nationwide, population-based cohort study. Lancet Oncol. 2018 Oct;19(10):1307-1314.

Harmon QE, Umbach DM, Baird DD. Use of **Estrogen-Containing Contraception** Is Associated With Increased Concentrations of 25-Hydroxy **Vitamin D**. J Clin Endocrinol Metab. 2016 Aug 4.

Harper CC, Rocca CH, Thompson KM, et al. **Reductions in pregnancy rates in the USA with long-acting reversible contraception**: a cluster randomized trial. Lancet 2015; online June 17.

Havrilesky LJ, Gierisch JM, Moorman PG, et al. Oral Contraceptive Use for the Primary Prevention of **Ovarian Cancer**. AHRQ Comparative Effectiveness Review. Rockville (MD): Agency for Healthcare Research and Quality (US); 2013 June. Report No.:13-E002-EF There is insufficient evidence to recommend for or against the use of OCs solely for the primary prevention of ovarian cancer.

Havrilesky LJ, Moorman PG, Lowery WJ, et al. Oral contraceptive pills as primary **prevention for ovarian cancer**: a systematic review and meta-analysis. Obstet Gynecol. 2013 Jul;122(1):139-47.

Health Canda June/10 **MIRENA** (Levonorgestrel-Releasing Intrauterine System) - Potential Risk of Uterine Perforation - Bayer Inc. Bayer Inc., in collaboration with Health Canada, would like to remind you of important safety information regarding reports of uterine perforation in women treated with MIRENA.

Health Canada Dec/11 has completed a safety review of drospirenone-containing oral contraceptives (marketed under the brand names Yasmin and Yaz) with respect to the risk of blood clots (venous thromboembolism, or VTE). The review determined that **drospirenone-containing birth** control pills may be associated with a risk of blood clots that is **1.5 to 3 times higher than other birth control pills**.

Health Canada Sep/13 **Freya-28**, an oral contraceptive (birth control product), is being voluntarily recalled from the Canadian market by Mylan Pharmaceuticals after a pharmacy reported that a placebo pill was found in place of an active pill in one package.

Health Canada Sep/13 **Esme-28** (DIN 02388146), an oral contraceptive (birth control product), is being voluntarily recalled from the Canadian market by Mylan Pharmaceuticals.

Health Canada May/16 **ESSURE** (permanent birth control system) – Risk of Serious Complications - Bayer Inc. These include changes in menstrual bleeding, unintended pregnancy, chronic pain, perforation and migration of device, allergy and sensitivity or immune-type reactions. Some complications may be considered serious.

Health Canada Nov/17 **MIFEGYMISO (mifepristone and misoprostol tablets) - Updates** to Product Monograph and Risk Management Plan. http://healthycanadians.gc.ca/recall-alert-rappel-avis/hc-sc/2017/65030a-eng.php

Health Canada Dec/17 is advising consumers and health care professionals that complaints have been received for packages of **Alesse 21 (21 active pills) and Alesse 28** (21 active pills, 7 that contain no hormones). The blister packages for both contained an active (pink) pill that was roughly half the proper size.

Health Canada Dec/17 and Pfizer Canada Inc. have received reports for packages of **ALESSE 21 and ALESSE 28** where the blister packages contained a single active (pink) tablet that was **broken**. This could reduce the dose of hormones and potentially result in an unintended pregnancy due to insufficient action of the contraceptive hormones levonorgestrel and ethinyl estradiol.

Health Canada Feb/18: **Alysena 28** birth control pill: One lot recalled due to chipped pills, which may reduce effectiveness in preventing pregnancy. Health Canada is informing Canadians that all lots of both Alysena 21 and Alysena 28 may have **chipped pills**.

Health Canada Jun/18: Pfizer Canada Inc. has notified Health Canada that it has received complaints of **broken or chipped pills involving Demulen 30**, a prescription birth control pill.

Health Canada Apr/19 is informing Canadians that the prescribing and patient information for Mifegymiso has been updated to reflect that an ultrasound is no longer required before the drug is prescribed.

Heinemann K, Reed S, Moehner S, et al. Risk of **uterine perforation with levonorgestrel-releasing and copper intrauterine devices** in the European Active Surveillance study on Intrauterine Devices. Contraception. 2015 Apr;91(4):274-9.

Heliövaara-Peippo S, Hurskainen R, Teperi J, et al. Quality of life and costs of **levonorgestrel-releasing intrauterine system or hysterectomy** in the treatment of **menorrhagia**: a 10-year randomized controlled trial. Am J Obstet Gynecol. 2013 Dec;209(6):535.e1-535.e14.

Herzog AG, Mandle HB, MacEachern DB. Prevalence of **highly effective contraception use by women with epilepsy**. Neurology. 2019 Jun 11;92(24):e2815-e2821.

HHS Aug 2011.: Affordable Care Act Ensures Women Receive **Preventive Services at No Additional Cost** (incl. **contraception**). http://www.hhs.gov/news/press/2011pres/08/20110801b.html

Hickey M, Ballard K, Farquhar C. **Endometriosis**. BMJ. 2014 Mar 19;348

Hicks CW, Rome ES. **Menstrual manipulation**: options for suppressing the cycle. Cleve Clin J Med. 2010 Jul;77(7):445-53.

Hidalgo MM, Hidalgo-Regina C, Bahamondes MV, et al. Serum levonorgestrel levels & endometrial thickness during extended use of the **levonorgestrel-releasing intrauterine** system. Contraception. 2009 Jul;80(1):84-9. Epub 2009 Feb 27. During extended use of the LNG-IUS, serum LNG levels were nearly half those found in the first 2 months of use (Wilcoxon signed rank test); serum E(2) levels were normal. Despite the very thin endometrium, menstrual bleeding was reinstated in many cases. At the end of its 5-year life span, there is a window for changing the LNG-IUS, and physicians and users should not be concerned about delaying replacement of the device for a short time beyond the approved life span; however, maintaining the same device long after its approved life span cannot be recommended.

Hofmeister S, Bodden S. **Premenstrual Syndrome and Premenstrual Dysphoric Disorder**. Am Fam Physician. 2016 Aug 1;94(3):236-40

Hofmeyr GJ, Singata M, Lawrie TA. **Copper containing intra-uterine devices versus depot progestogens** for contraception. Cochrane Database Syst Rev. 2010 Jun 16;6:CD007043. In the populations studied, the IUD was more effective than hormonal contraception with respect to pregnancy prevention.

Horga M, Gerdts C, Potts M. The remarkable story of **Romanian women's struggle to manage their fertility**. J Fam Plan Reprod Health Care 2013;39:2-4.

Hornberger LL & AAP Committee on Adelescene. **Diagnosis of Pregnancy & Providing Options Counseling for the Adolescent Patient**. Pediatrics. 2017;140(3):e20172273

Hsiang D, Dunn S. **Emergency contraception**. CMAJ. 2016 Dec 6;188(17-18):E536.

Huq FY et al. Menstrual problems and contraception in women of reproductive age **receiving oral anticoagulation**. Contraception2011 Aug; 84:128.

International Federation of Gynecology and Obstetrics (FIGO) and International Consortium for Emergency Contraception (ICEC). Emergency Contraception Statement, March 2011. http://www.emergencycontraception.org/publications/PDFs/policy/MOA_ENG_2011.pdf . Accessed January 10, 2013.

Iversen L, Fielding S, Lidegaard Ø, et al. Association between **contemporary hormonal contraception and ovarian cancer** in women of reproductive age in Denmark: prospective, nationwide cohort study. BMJ. 2018 Sep 26;362:k3609.

Iversen L, Sivasubramaniam S, et al. **Lifetime cancer risk and combined oral contraceptives**: the Royal College of General Practitioners' Oral Contraception Study. Am J Obstet Gynecol. 2017 Jun;216(6):580.e1-580.e9.

Jarolimova J, Kabakyenga J, Bennett K, et al. Contraceptive use following **unintended pregnancy among Ugandan women** living with HIV. PLoS One. 2018 Oct 25; 13(10):e0206325.

Jatlaoui TC, Whiteman MK, Jeng G, et al. **Intrauterine Device Expulsion** After Postpartum Placement: A Systematic Review and Meta-analysis. Obstet Gynecol. 2018 Oct;132(4):895-905.

Jick SS, Hagberg KW, Hernandez RK, Kaye JA. Postmarketing study of **ORTHO EVRA** and levonorgestrel oral contraceptives containing hormonal contraceptives with 30 mcg of ethinyl estradiol in relation to nonfatal venous **thromboembolism**. Contraception. 2010 Jan;81(1):16-21.

Jick SS, Hernandez RK. Risk of non-fatal venous **thromboembolism** in women using oral contraceptives containing **drospirenone** compared with women using oral contraceptives containing **levonorgestrel**: case-control study using United States claims data. BMJ 2011;342:d2151.

Jin J. JAMA **patient page. Oral contraceptives**. JAMA. 2014 Jan 15;311(3):321.

Johnson-Agbakwu C, Brown L, Yuan J, et al. Effects of **Flibanserin** on the Pharmacokinetics of a **Combined Ethinylestradiol/Levonorgestrel** Oral Contraceptive in Healthy Premenopausal Women: A Randomized Crossover Study. Clin Ther. 2017 Nov 30.

Jones, Claire, Chan, Crystal, Farine, Dan. **Sex in pregnancy**. CMAJ 2011 0: cmaj.091580.

Judge-Golden CP, Smith KJ, Mor MK, Borrero S. Financial Implications of **12-Month Dispensing of Oral Contraceptive Pills** in the Veterans Affairs Health Care System. JAMA Intern Med. 2019 Jul 8

Kakaire O, Byamugisha JK, et al. **Intrauterine Contraception Among Women Living With Human Immunodeficiency Virus**: Randomized Controlled Trial. Obstet Gynecol. 2015 Nov;126(5):928-34.

Kaunitz AM. Clinical practice. **Hormonal contraception in women of older reproductive age**. N Engl J Med. 2008 Mar 20;358(12):1262-70.

Kaunitz, Andrew M. "Postpartum and postabortal contraception." Up to Date. 15 Aug. 2008. 27 Feb. 2009 <http://www.utdol.com/home/index.html>.

Kaunitz AM, Meredith S, et al. **Levonorgestrel-releasing intrauterine system** and endometrial ablation in heavy menstrual bleeding: a systematic review and meta-analysis. Obstet Gynecol. 2009 May;113(5):1104-16. Based on the meta-analysis of six randomized clinical trials, the efficacy of the levonorgestrel intrauterine system in the management of heavy menstrual bleeding appears to have similar therapeutic effects to that of endometrial ablation up to 2 years after treatment. {InfoPOEMs Jun09: The levonorgestrel-releasing intrauterine system (LNG-IUS) is as effective as endometrial ablation for the treatment of heavy menses. Its advantages include lower cost, less invasiveness, and retained fertility. (LOE = 1b)}

Kaunitz AM, Darney PD, Ross D, Wolter KD, Speroff L. **Subcutaneous DMPA** vs.intramuscular DMPA: a 2-year randomized study of contraceptive efficacy and bone mineral density. Contraception. 2009 Jul;80(1):7-17. Epub 2009 Mar 27. DMPA-SC is an effective and well-tolerated contraceptive option, providing comparable efficacy and BMD safety to DMPA-IM.

Kaunitz AM, Bissonnette F, Monteiro I, et al. **Levonorgestrel**-Releasing Intrauterine System or Medroxyprogesterone for Heavy Menstrual Bleeding: A Randomized Controlled Trial. Obstet Gynecol. 2010 Sep;116(3):625-632.

Kaunitz AM, Inki P. The **levonorgestrel-releasing intrauterine system** in heavy menstrual bleeding: a benefit-risk review. Drugs. 2012 Jan 22;72(2):193-215.

Kavanaugh ML et al. Characteristics of women in the United States who use **long-acting reversible contraceptive** methods. Obstet Gynecol 2011 Jun; 117:1349.

Kavanaugh ML et al. Changes in use of **long-acting reversible contraceptive** methods among U.S. women, 2009–2012. Obstet Gynecol 2015 Oct 5.

Kazerooni R, Blake A, Thai J. Predictors of **Pregnancy** in Female Veterans Receiving a **Hormonal Contraceptive Pill, Patch, or Ring**. Ann Pharmacother. 2015 Dec;49(12):1284-90.

Khalili H, Neovius M, Ekbom A, et al. **Oral Contraceptive Use and Risk of Ulcerative Colitis Progression: A Nationwide Study.**Am J Gastroenterol. 2016 Oct 11.

Klein DA, Arnold JJ, Reese ES. **Provision of Contraception**-Key Recommendations from the **CDC**, Am Fam Physician. 2015;91(9):625-633.

Klok FA, Schreiber K, Stach K, et al. **Oral contraception and menstrual bleeding during treatment of venous thromboembolism**: Expert opinion versus current practice: Combined results of a systematic review, expert panel opinion and an international survey. Thromb Res. 2017 May;153:101-107

Kourtis AP, Mirza A, AAP Committee on Pediatric AIDS. **Contraception for HIV-Infected Adolescents**. Pediatrics.2016;138(3):e20161892

Kroll R, et al. The efficacy and safety of a low-dose, **91-day, extended-regimen** oral contraceptive with continuous ethinyl estradiol. Contraception. 2010 Jan;81(1):41-8.

Kromm J, Jeerakathil T. **Cyproterone acetate-ethinyl estradiol** use in a 23-year-old woman with **stroke**. CMAJ. 2014 Jun 10;186(9):690-3.

Kulier R, et al. Copper containing, framed intra-uterine devices for contraception. Cochrane Database Syst Rev. 2006 Jul 19;3:CD005347.

Kumar MM. **Long-Acting Reversible Contraceptives for Adolescents**: More Complex Than "First-Line". JAMA Pediatr. 2017 Nov 20.

Langlade C, Gouverneur A, Bosco-Lévy P, et al. **Adverse events reported** for levonorgestrel-releasing IUD **Mirena**® in France and impact of media coverage. Br J Clin Pharmacol. 2019 Jun 19.

Larivee N, Suissa S, Khosrow-Khavar F, et al. **Drospirenone**-containing oral contraceptive pills and the **risk of venous thromboembolism**: a systematic review of observational studies. BJOG. 2017 Mar 9.

Lawrence HC. Unfettered **Access to Reliable Contraception**: Pharmacist Prescription Derails a Definitive Solution. Ann Intern Med. 2016 Mar 1.

Lazorwitz A, Aquilante CL, Oreschak K, et el. **Influence of Genetic Variants on Steady-State Etonogestrel Concentrations** Among Contraceptive Implant Users. Obstet Gynecol. 2019 Mar 11.

Le YC, Rahman M, Berenson AB. Early weight gain predicting later **weight gain** among depot **medroxyprogesterone** acetate users. Obstet Gynecol. 2009 Aug;114(2 Pt 1):279-84. Most DMPA users who gain excessive weight experience more than a 5% weight increase within 6 months.

Legro RS, Pauli JG, Kunselman AR, et al. Effects of **Continuous versus Cyclic** Oral Contraception: A Randomized Controlled Trial. J Clin Endocrinol Metab. 2007 Dec 4; [Epub ahead of print] Continuous oral contraception does not result in a reduction of bleeding days over a 168d period of observation, but provides greater suppression of the ovary and endometrium. These effects are associated with improved patient symptomatology.

Lesnewski R, Prine L, Ginzburg R. **Preventing Gaps when Switching** Contraceptives. Am Fam Physician. 2011 Mar 1;83(5):567-570.

Lethaby A, Penninx J, Hickey M, et al. Endometrial resection and ablation techniques for **heavy menstrual bleeding**.Cochrane Database Syst Rev. 2013 Aug 30;8:CD001501.

Levi EE, Stuart GS, Zerden ML, et al. **Intrauterine Device Placement During Cesarean Delivery** and Continued Use 6 Months Postpartum: A Randomized Controlled Trial. Obstet Gynecol. 2015 Jul;126(1):5-11.

Lewis C et al. **Intrauterine contraception**: Impact of provider **training** on participant knowledge and provision. Contraception 2013 Aug; 88:226.

Leyland N, Casper R, Laberge P, Singh SS, Allen L, Arendas K. **Endometriosis**: diagnosis and management. J Obstet Gynaecol Can 2010 Jul;32(7 Suppl 2):S1-32.

Liao PV, Dollin J. Half a century of the **oral contraceptive pill: Historical review** and view to the future. Can Fam Physician. 2012 Dec;58(12):e757-60.

Lidegaard Øjvind, Løkkegaard Ellen, Svendsen Anne Louise, et al. Hormonal contraception and risk of venous **thromboembolism**: Denmark national follow-up study. BMJ 2009;339:b2890, doi: 10.1136/bmj.b2890 (Published 13 August 2009)

Lidegaard Ø, Nielsen LH, Skovlund CW, Skjeldestad FE, Løkkegaard E. Risk of venous thromboembolism from use of oral contraceptives containing different progestogens and oestrogen doses: Danish cohort study, 2001-9. BMJ 2011;343:d6423.

Lidegaard O, Nielsen LH, et al. **Venous thrombosis** in users of **non-oral hormonal contraception**: follow-up study, Denmark 2001-10. BMJ. 2012 May 10;344:e2990.

Lidegaard Ø, Løkkegaard E, Jensen A, Skovlund CW, et al. **Thrombotic stroke and myocardial infarction** with hormonal contraception. N Engl J Med 2012;366:2257-66.

Lopez LM, et al. Skin patch and vaginal ring versus combined oral contraceptives for contraception. Cochrane Database Syst Rev. 2008 Jan 23;(1):CD003552. Effectiveness rates were similar for the methods compared. The patch group had better compliance than the COC group. Compared to COC users, patch users had more side effects. Ring users generally had fewer adverse events than COC users but more vaginal irritation and discharge. The patch could lead to more discontinuation while the vaginal ring showed little difference. High losses to follow up can affect the validity of the results.

Lopez LM, Grimes DA, Gallo MF, Schulz KF. Skin patch and **vaginal ring versus combined oral contraceptives** for contraception. Cochrane Database Syst Rev. 2010 Mar 17;3:CD003552. Effectiveness was similar for the methods compared. The patch could lead to more discontinuation while the vaginal ring showed little difference. The patch group had better compliance than the COC group but more side effects. Ring users generally had fewer adverse events than COC users but more vaginal irritation and discharge.

Lopez LM, Newmann SJ, Grimes DA, Nanda K, Schulz KF. Immediate start of hormonal contraceptives for contraception. *Cochrane Database Syst Rev.* 2008;(2):CD006260.

Lopez LM, Grimes DA, Chen-Mok M, et al. Hormonal contraceptives for **contraception in overweight or obese women**. Cochrane Database Syst Rev. 2010 Jul 7;7:CD008452. Body weight addresses overall body size, while BMI generally reflects the amount of fat. Only one of three studies using BMI found a higher pregnancy risk for overweight women. The efficacy of implants and injectable contraceptives may be unaffected by body mass. The field could use trials of contraceptive methods with groups stratified by BMI. The current evidence on effectiveness by BMI is limited. However, the contraceptive methods examined here are still among the most effective when the recommended regimen is followed.

Lopez LM, Edelman A, Chen-Mok M, et al. **Progestin-only contraceptives: effects on weight**. Cochrane Database Syst Rev. 2011 Apr 13;4:CD008815. We found little evidence of weight gain when using POCs. Mean gain was less than 2 kg for most studies up to 12 months, and usually similar for the comparison group using another contraceptive. Appropriate counseling about typical weight gain may help reduce discontinuation of contraceptives due to perceptions of weight gain.

Lopez LM, Newmann SJ, Grimes DA, et al. **Immediate start of hormonal contraceptives** for contraception. Cochrane Database Syst Rev. 2012 Dec 12;12:CD006260. doi: 10.1002/14651858.CD006260.pub3. We found limited evidence that immediate start of hormonal contraception reduces unintended pregnancies or increases method continuation. However, the pregnancy rate was lower with immediate start of DMPA versus another method.

Lopez LM, Hiller JE, Grimes DA, et al. **Education** for contraceptive use by women after childbirth. Cochrane Database Syst Rev. 2012 Aug 15;8:CD001863. The overall quality of evidence was moderate. Half of these postpartum interventions led to fewer repeat pregnancies or births or more contraceptive use.

Lopez LM, Stockton LL, ChenM, SteinerMJ, GalloMF. **Behavioral interventions for improving dual-method contraceptive** use. Cochrane Database of Systematic Reviews 2014, Issue 3. Art. No.: CD010915. DOI: 10.1002/14651858.CD010915.pub2. We found few behavioral interventions for improving dual-method contraceptive use and little evidence of effectiveness. Amultifaceted program showed some effect but only had self-reported outcomes. Two trials were more applicable to clinical settings and had objective outcomesmeasures, but neither showed any effect.The included studies had adequate information on intervention fidelity and sufficient follow-up periods for change to occur.

Lopez LM, Grimes DA, Schulz KF, et al. Steroidal contraceptives: effect on **bone fractures** in women. Cochrane Database Syst Rev. 2014 Jun 24;6:CD006033. Whether steroidal contraceptives influence fracture risk cannot be determined from existing information. The evidence quality was considered moderate overall, largely due to the trials of DMPA, implants, and the patch versus ring. The COC evidence varied in quality but was low overall. Many trials had small numbers of participants and some had large losses. Health care providers and women should consider the costs and benefits of these effective contraceptives. For example, injectable contraceptives and implants provide effective, long-term birth control yet do not involve a daily regimen. Progestin-only contraceptives are considered appropriate for women who should avoid estrogen due to medical conditions.

Lopez LM, Grey TW, Stuebe AM, et al. **Combined hormonal versus nonhormonal versus progestin-only contraception in lactation**. Cochrane Database Syst Rev. 2015;(3):CD003988. Results were not consistent across the 11 trials. The evidence was limited for any particular hormonal method. The quality of evidence was moderate overall and low for three of four placebo-

controlled trials of COCs or POPs. The sensitivity analysis included six trials with moderate quality evidence and sufficient outcome data. Five trials indicated no significant difference between groups in breastfeeding duration (etonogestrel implant insertion times, COC versus POP, and LNG-IUS). For breast milk volume or composition, a COC study showed a negative effect, while an implant trial showed no significant difference. Of four trials that assessed infant growth, three indicated no significant difference between groups. One showed greater weight gain in the etonogestrel implant group versus no method but less versus DMPA.

Lopez LM, Grey TW, Chen M, et al. **Theory-based interventions for contraception.** Cochrane Database Syst Rev. 2016 Nov 23;11:CD007249. The overall quality of evidence was moderate. Trials based on social cognitive theory focused on adolescents and provided multiple sessions. Those using motivational interviewing had a wider age range but specific populations. Sites with low resources need effective interventions adapted for their settings and their typical clients. Reports could be clearer about how the theory was used to design and implement the intervention.

Loprinzi CL, et al. Phase III comparison of depomedroxyprogesterone acetate to venlafaxine for managing hot flashes: North Central Cancer Treatment Group Trial N99C7. J Clin Oncol. 2006 Mar 20;24(9):1409-14. Epub 2006 Feb 27.

Loulergue P, Coriat R, Mir O. **Recurrent Transaminitis** Induced by Oral Contraceptives **During HIV Infection**. Ann Pharmacother. 2015 Feb;49(2):258-9.

Lumsden MA, Gebbie A, Holland C. Managing **unscheduled bleeding** in non-pregnant premenopausal women. BMJ. 2013 Jun 4;346:f3251.

Madden T, Proehl S, Allsworth JE, et al. **Naproxen** or estradiol for bleeding and **spotting with the levonorgestrel intrauterine system**: a randomized controlled trial. Am J Obstet Gynecol. 2012 Feb;206(2):129.e1-8.

Maïmoun L, Renard E, Lefebvre P, et al. Oral contraceptives **partially protect from bone loss** in young women with anorexia nervosa. Fertil Steril. 2019 May;111(5):1020-1029.e2.

Maino A, Siegerink B, Algra A, et al. **Recurrence and Mortality in Young Women With Myocardial Infarction or Ischemic Stroke**: Long-term Follow-up of the Risk of Arterial Thrombosis in Relation to Oral **Contraceptives** (**RATIO**) Study. JAMA Intern Med. 2015 Nov 23:1-3.

Malvezzi M, Carioli G, Rodriguez T, et al. Global trends and predictions in **ovarian cancer mortality**. Ann Oncol. 2016 Sep 5

Mantha S, Karp R, Raghavan V et al. Assessing the risk of **venous thromboembolic events in women taking progestin-only** contraception: a meta-analysis. BMJ. 2012 Aug 7;345:e4944.

Marchbanks PA, Curtis KM, Mandel MG, Oral contraceptive formulation and **risk of breast cancer**. Contraception. 2012;85:342-350.

Marions L et al. Effect of **emergency contraception** with levonorgestrel or mifepristone on ovarian function. Contraception2004 May; 69:373-7.

Marjoribanks J, Lethaby A, Farquhar C. Surgery versus medical therapy for heavy menstrual bleeding. Cochrane Database Syst Rev. 2006 Apr 19;(2):CD003855. Surgery, especially hysterectomy, reduces menstrual bleeding at one year more than medical treatments but LNG-IUS appears equally effective in improving quality of life. The evidence for longer term comparisons is weak and inconsistent. Oral medication suits a minority of women long term.

Margel David, Fleshner Neil E. Oral contraceptive use is associated with **prostate cancer**: an ecological study. BMJ Open 2011;1:e000311 doi:10.1136/bmjopen-2011-000311.

Martinelli I, et al. Recurrent venous **thromboembolism and abnormal uterine bleeding with anticoagulant and hormone therapy use**. Blood. 2016 Mar 17;127(11):1417-25.

McCarthy FP, O'Brien U, Kenny LC. The management of **teenage pregnancy**. BMJ. 2014 Oct 15;349:g5887.

McNicholas C, Zhao Q, Secura G, et al. Contraceptive failures in **overweight and obese** combined hormonal contraceptive users. Obstet Gynecol. 2013 Mar;121(3):585-92.

McNicholas C, Maddipati R, et al. Use of the **etonogestrel implant and levonorgestrel intrauterine device beyond** the u.s. Food and drug administration-approved **duration**. Obstet Gynecol. 2015 Mar;125(3):599-604.

McNicholas C et al. **Prolonged use of the etonogestrel implant and levonorgestrel intrauterine device** — two years beyond FDA-approved duration. Am J Obstet Gynecol 2017 Jan 29. This large study adds to a growing body of evidence demonstrating the effectiveness of the etonogestrel implant for 5 years and the 52-mg LNG-IUD for up to 7 years. Women of any age can use the implant for up to 5 years (NEJM JW Womens Health Nov 2016 and Hum Reprod 2016; 31:2491). Among the 3 available doses of the LNG-IUD, extended use should only be considered for the 52-mg dose. Younger LNG-IUD users have slightly higher risk for pregnancy; accordingly, to balance risk and benefit for my patients who would like to consider extended use of the 52-mg LNG-IUD, I offer those who are younger than 35 up to 6 years of use, and those who are 35 or older up to 7 years of use. For women who prefer to exchange their 52-mg LNG-IUD with a new device at 5 years, I accede to their preference.

Medical Letter. Three new oral contraceptives. (Yaz, Seasonique, Loestrin 24 Fe) Sept 25,2006.

Medical Letter. Combination Oral Contraceptives and the Risk of **Venous Thromboembolism**. Mar 22, 2010.

Medical Letter- Treatment Guidelines: **Choice of Contraceptives**. Dec 2007; p. 101-108. Updated Dec 2010. **(Updated Oct 2018).**

Meier C, Brauchli YB, Jick SS, Kraenzlin ME, Meier CR. Use of Depot **Medroxyprogesterone Acetate and Fracture Risk**. J Clin Endocrinol Metab. 2010 Aug 4.

Meng X, Li S, Duan W, et al. Secular Trend of **Age at Menarche in Chinese Adolescents** Born From 1973 to 2004. Pediatrics.2017;140(2):e20170085

Menke MN, King WC, White GE, et al. Conception rates and **contraceptive use after bariatric surgery among women with infertility**: Evidence from a prospective multicenter cohort study. Surg Obes Relat Dis. 2019 Jan 11.

MHRA June/16 **Nexplanon** (**etonogestrel**) contraceptive implants: reports of device in vasculature and lung.

Michels KA, Pfeiffer RM, Brinton LA, et al. Modification of the Associations Between Duration of **Oral Contraceptive Use and Ovarian, Endometrial, Breast, and Colorectal Cancers**. JAMA Oncol. 2018 Jan 18.

Michels KA, Brinton LA, Pfeiffer RM, et al. **Oral Contraceptive Use and Risks of Cancer** in the NIH-AARP Diet and Health Study. Am J Epidemiol. 2018 Jan 31.

Mifeprex REMS Study Group., Raymond EG, Blanchard K, et al. **Sixteen Years of Overregulation**: Time to Unburden Mifeprex. N Engl J Med. 2017 Feb 23;376(8):790-794

Miller L, et al. Extended Regimens of the Contraceptive Vaginal Ring: A Randomized Trial. Obstet Gynecol. 2005 Sep;106(3):473-482.

Miller PE, Brown L, Khandheria P, Resar JR. **Ischemic Stroke Occurring During Intercourse** in Young Women on Oral Contraceptives. Am J Cardiol. 2014 May 17.

Miller TA, Allen RH, Kaunitz AM, Cwiak CA. **Contraception for midlife** women: a review. Menopause. 2018 Jul;25(7):817-827.

Miner PD, Canobbio MM, Pearson DD, et al. Contraceptive Practices of Women **with Complex Congenital Heart Disease**. Am J Cardio. 2017.

Mody SK, Farala JP, Jimenez B, et al. **Paracervical Block for Intrauterine Device Placement** Among Nulliparous Women: A Randomized Controlled Trial. Obstet Gynecol. 2018 Sep;132(3):575-582.

Monge ME, Dwivedi P, Zhou M, et al. A tiered analytical approach for investigating **poor quality emergency contraceptives**. PLoS One. 2014 Apr 18;9(4):e95353.

Moniz MH, Davis MM, Chang T. **Attitudes About Mandated Coverage** of Birth Control Medication and Other Health Benefits in a US National Sample. JAMA. 2014 Apr 22.

Mørch LS, Skovlund CW, Hannaford PC, et al. **Contemporary hormonal contraception and the risk of breast cancer**. N Engl J Med 2017;377:2228-39.

Murray Horwitz ME, Ross-Degnan D, Pace LE. Contraceptive Initiation Among Women in the United States: **Timing, Methods Used, and Pregnancy Outcomes**. Pediatrics. 2019 Jan 15.

Nelson A, Apter D, Hauck B, et al. **Two low-dose levonorgestrel intrauterine contraceptive** systems: a randomized controlled trial. Obstet Gynecol. 2013 Dec;122(6):1205-13

Neuhaus CP, Nagler AR, Orlow SJ. **Teens, Acne, and Oral Contraceptive Pills**: The Need for Greater Clarity on When Teens Can Consent. JAMA Dermatol. 2017 Jan 11.

Newman, Adam. Inadvertent use of a **levonorgestrel-releasing intrauterine device as postcoital** contraception. Can Fam Physician 2010 56: 1301-1302

Noé G, Croxatto HB, Salvatierra AM, et al. Contraceptive efficacy of emergency contraception with **levonorgestrel** given before or after ovulation. Contraception. 2011 Nov;84(5):486-92. The efficacy of LNG-EC has been overestimated in studies using presumptive menstrual cycle data. Our results confirm previous similar studies and demonstrate that LNG-EC does not prevent embryo implantation and therefore cannot be labeled as abortifacient.

> …when used after ovulation has occurred, the number of observed and expected pregnancies is not statistically different, indicating that no reproductive process subsequent to ovulation is interfered with by LNG-EC….In conclusion, LNG-EC is highly effective for preventing unintended pregnancy when it is used before ovulation, but when used after ovulation, it is completely unable to prevent pregnancy because it has no effect on subsequent reproductive processes, including implantation of the embryo.

Norman WV, Soon JA. **Requiring physicians to dispense mifepristone**: an unnecessary limit on safety and access to medical abortion. CMAJ. 2016 Dec 6;188(17-18):E429-E430.

Novikova N, Weisberg E, Stanczyk FZ, Croxatto HB, Fraser IS. Effectiveness of **levonorgestrel emergency contraception** given before or after ovulation—a pilot study. Contraception 2007; 75:112–118.

O'Brien SH, Koch T, Vesely SK, et al. Hormonal Contraception and **Risk of Thromboembolism** in Women With Diabetes. Diabetes Care. 2016 Nov 29.

Odmark IS, Bixo M, Englund D, Risberg B, Jonsson B, Olsson SE. Endometrial safety and bleeding pattern during a five-year treatment with long-cycle hormone therapy. Menopause. 2005 Nov-Dec;12(6):699-707. Epub 2005 Nov 8. (InfoPOEMs: In this small study, continuous estrogen therapy combined with 14 days of progestin every 3 months (long-cycle therapy) did not result in endometrial hyperplasia or cancer. (LOE = 1b))
Orbo A, Vereide A, Arnes M, et al. **Levonorgestrel-impregnated intrauterine device** as treatment for **endometrial hyperplasia**: a national multicentre randomised trial. BJOG. 2013 Nov 28.
Orbo A, Arnes M, Vereide AB, et al. Relapse risk of **endometrial hyperplasia** after treatment with the **levonorgestrel-impregnated intrauterine system or oral progestogens**. BJOG. 2015 Dec 2.
Oringanje C, Meremikwu MM, Eko H, et al. **Interventions for preventing unintended pregnancies among adolescents**. Cochrane Database Syst Rev. 2016;(2):CD005215. A combination of educational and contraceptive-promoting interventions appears to reduce unintended pregnancy among adolescents. Evidence for programme effects on biological measures is limited. The variability in study populations, interventions and outcomes of included trials, and the paucity of studies directly comparing different interventions preclude a definitive conclusion regarding which type of intervention is most effective.
Orellana C, Saevarsdottir S, Klareskog L, et al. **Oral contraceptives, breastfeeding** and the **risk of developing rheumatoid arthritis**: results from the Swedish EIRA study. Ann Rheum Dis. 2017 Aug 17.
Osayande AS, Mehulic S. Diagnosis and initial management of **dysmenorrhea**. Am Fam Physician. 2014 Mar 1;89(5):341-6.
Ott MA, Sucato GS; COMMITTEE ON ADOLESCENCE; COMMITTEE ON ADOLESCENCE. **Contraception for adolescents.** Pediatrics. 2014 Oct;134(4):e1257-81.
Parkin L, Sharples K, Hernandez RK, Jick SS. Risk of **venous thromboembolism** in users of oral contraceptives containing **drospirenone or levonorgestrel**: nested case-control study based on UK General Practice Research Database. BMJ 2011;342:d2139.
Patel P, Leeder JS, Piquette-Miller M, et al. **Aprepitant and Fosaprepitant Drug Interactions**: A Systematic Review. Br J Clin Pharmacol. 2017 May 4.
Peipert JF, Madden T, Allsworth JE, et al. Preventing Unintended Pregnancies by Providing **No-Cost Contraception**. Obstet Gynecol. 2012 Oct 3.
Peragallo Urrutia R, Coeytaux RR, et al. Risk of **acute thromboembolic events** with oral contraceptive use: a systematic review and meta-analysis. Obstet Gynecol. 2013 Aug;122(2 Pt 1):380-9.
Pijuan-Domènech A, Baró-Mariné F, Rojas-Torrijos M, et al. Usefulness of **progesterone-only** components for contraception in patients with **congenital heart disease**. Am J Cardiol. 2013 Aug 15;112(4):590-3.
Polonsky M. **Cancer and contraception**: Release date May 2012 SFP Guideline #20121. Contraception. 2012 Jun 7.
Prabakar I, Webb A. **Emergency contraception**. BMJ. 2012 Mar 19;344:e1492
Pederson HB, Curtis KM. Long-Acting Methods of Contraception. N Engl J Med 2005;353:2169-75.
Pharmacist's Letter: **Hormonal Contraception** July 2006
Pharmacists Letter. Canadian Consensus Guideline on **Continuous and Extended Hormonal Contraception**, 2007. Aug 2007.
Pijuan-Domènech A, Baró-Mariné F, Usefulness of **Progesterone-Only** Components for Contraception in Patients With **Congenital Heart Disease**. Am J Cardiol. 2013 May 22.
Polis CB, Curtis KM. Use of **hormonal contraceptives and HIV** acquisition in women: a systematic review of the epidemiological evidence. Lancet Infect Dis. 2013 Jul 18.
Polis CB, Curtis KM, Hannaford PC, et al. **Update on hormonal contraceptive methods and risk of HIV acquisition** in women: a systematic review of epidemiological evidence, 2016. AIDS. 2016 Aug 5.
Politi MC, et al. Addressing Challenges to Implementation of the **Contraceptive Coverage Guarantee of the Affordable Care Act**. JAMA. 2016 Feb 16;315(7):653-4.
Practice Committee of the American Society for Reproductive Medicine. **Combined hormonal contraception and the risk of venous thromboembolism**: a guideline. Fertil Steril. 2017 Jan;107(1):43-51.
Prescott HM. "An Uncommonly **Silly Law**"--Contraception and Disparities in the United States. N Engl J Med. 2016 Feb 25;374(8):706-8.
Prey Bd, Talavlikar R, Mangat R, et al. Induced **abortion and contraception use: Among immigrant** and Canadian-born women in Calgary, Alta. Can Fam Physician. 2014 Sep;60(9):e455-63.
Quint EH, O'Brien RF; Committee on Adolescence; North American Society for Pediatric and Adolescent Gynecology. **Menstrual Management for Adolescents With Disabilities.** Pediatrics. 2016 Jul;138(1).
Rahman M, Berenson AB. Predictors of higher **bone mineral density loss** and use of depot **medroxyprogesterone** acetate. Obstet Gynecol. 2010 Jan;115(1):35-40. The risk of higher BMD loss associated with DMPA use may be reduced by quitting smoking and increasing calcium intake. Having had a child is also protective.
Ralph LJ, McCoy SI, Shiu K, Padian NS. **Hormonal contraceptive use and women's risk of HIV acquisition**: a meta-analysis of observational studies. Lancet Infect Dis 2015; online Jan 9.
Raymond EG, Cleland K. **Emergency Contraception**. N Engl J Med. 2015 Apr 2;372(14):1342-1348.
Raymond EG, Weaver MA, Tan YL, et al. Effect of Immediate Compared With Delayed Insertion of **Etonogestrel Implants** on **Medical Abortion** Efficacy and Repeat Pregnancy: A Randomized Controlled Trial. Obstet Gynecol. 2016 Feb;127(2):306-12.
Raymond EG, Weaver MA, Louie KS, et al. Effects of **Depot Medroxyprogesterone** Acetate Injection Timing **on Medical Abortion** Efficacy and Repeat Pregnancy: A Randomized Controlled Trial. Obstet Gynecol. 2016 Oct;128(4):739-45
Richards C. **Protecting and Expanding Access to Birth Control**. N Engl J Med. 2016 Mar 3;374(9):801-3.
Roach RE, Helmerhorst FM, Lijfering WM, et al. **Combined oral contraceptives: the risk of myocardial infarction and ischemic stroke**. Cochrane Database Syst Rev 2015;8: CD011054. This network meta-analysis showed that the risk of myocardial infarction or ischemic stroke was only increased in women using COCs containing ≥ 50 µg of estrogen. Regarding myocardial infarction or ischemic stroke, prescribing COCs with < 50 µg of estrogen seems safe. When combined with the results of studies on the risk of venous thrombosis in COC users, it seems that the COC pill containing levonorgestrel and 30 µg of estrogen is the safest oral form of hormonal contraception.
Roberts T E, Tsourapas A, Middleton L J, et al. **Hysterectomy**, endometrial ablation, & levonorgestrel releasing intrauterine system (**Mirena**) for treatment of **heavy menstrual bleeding**: cost effectiveness analysis. BMJ 2011;342:doi:10.1136/bmj.d2202
Rodriguez MI, Chang R, Thiel de Bocanegra H. The impact of **postpartum contraception** on reducing preterm birth: findings from California. A m J Obstet Gynecol 2015;213:703.e1–6.
Rosenberg L, Zhang Y, Constant D et al. Bone status after cessation of use of injectable **progestin** contraceptives. Contraception. 2007 Dec;76(6):425-31. Epub 2007 Nov 9. The data suggest that **bone loss during IPC use is reversible** and that this loss of bone is completely recovered several years after cessation of use. sexualityandU.ca website (supported by **SOGC**) http://sexualityandu.ca/professionals/index.aspx
Rott H. **Thrombotic risks** of oral contraceptives. Curr Opin Obstet Gynecol. 2012 Jun 8.
Sanders AP, Sanders BH. **Retained intrauterine devices in pregnancy**. CMAJ. 2018 Apr 9;190(14):E440.
Schrager S, Falleroni J, Edgoose J. Evaluation and Treatment of **Endometriosis**. Am Fam Physician. 2013;87(2):107-113.
Swartz RH, Ladhani NNN, Foley N, et al; Heart and Stroke Foundation Canadian Stroke Best Practice Committees. Canad**ian stroke best practice consensus statement: secondary stroke prevention during pregnancy**. Int J Stroke 2017 (accessed December 12, 2017).
Secura GM, Adams T, Buckel CM, et al. Change in **sexual behavior with provision of no-cost contraception**. Obstet Gynecol. 2014 Apr;123(4):771-6.
Secura GM, Madden T, McNicholas C, et al. Provision of **no-cost, long-acting contraception and teenage pregnancy**. N Engl J Med. 2014 Oct 2;371(14):1316-23.
Sedgh G, Singh S, Hussain R. **Intended and unintended pregnancies worldwide** in 2012 and recent trends. Stud Fam Plann. 2014 Sep;45(3):301-14.
Sedlak T, Bairey Merz CN, Shufelt C, et al. Contraception in patients with **heart failure**. Circulation. 2012 Sep 11;126(11):1396-400.
Shabaan MM, Zakherah MS, El-Nashar SA, Sayed GH. **Levonorgestrel-releasing intrauterine system** compared to low dose combined oral contraceptive pills for idiopathic **menorrhagia**: a randomized clinical trial. Contraception. 2011 Jan;83(1):48-54.
Shaamash AH, et al. A comparative study of the levonorgestrel-releasing intrauterine system Mirena(R) versus the Copper T380Aintrauterine device during lactation: breast-feeding performance, infant growth and infant development. Contraception. 2005 Nov;72(5):346-51. Epub 2005 Jul 6.
Shaarawy M, et al. Effects of the long-term use of depot medroxyprogesterone acetate as hormonal contraceptive on bone mineral density and biochemical markers of bone remodeling. Contraception. 2006 Oct;74(4):297-302. Epub 2006 Jun 16.
Shafran DM, Wu C. Treatment of venous **thromboembolism in a 22-year-old woman taking an oral contraceptive pill**. CMAJ. 2017 Nov 27;189(47):E1459-E1460.

Shapiro S. Combined hormonal contraceptives and the **risk of venous and arterial thromboembolism** and cardiovascular death: misuse of automated databases. J Fam Plann Reprod Health Care. 2013 Apr;39(2):89-96.

Shen J, Che Y, Showell E, et al. **Interventions for emergency contraception**. Cochrane Database Syst Rev. 2017 Aug 2;8:CD001324.

Shen J, Che Y, Showell E, et al. Interventions for emergency contraception. Cochrane Database Syst Rev. 2019 Jan 20;1:CD001324. Levonorgestrel and mid-dose mifepristone (25 mg to 50 mg) were more effective than Yuzpe regimen. Both mid-dose (25 mg to 50 mg) and low-dose mifepristone(less than 25 mg) were probably more effective than levonorgestrel (1.5 mg). Mifepristone low dose (less than 25 mg) was less effective than mid-dose mifepristone. UPA may be more effective than levonorgestrel.Levonorgestrel users had fewer side effects than Yuzpe users, and appeared to be more likely to have a menstrual return before the expected date. UPA users were probably more likely to have a menstrual return after the expected date. Menstrual delay was probably the main adverse effect of mifepristone and seemed to be dose-related. Cu-IUD may be associated with higher risks of abdominal pain than ECPs.

Sidneya S, Cheethamb TC, Connell FA, et al. Recent **combined hormonal contraceptives** (CHCs) and the risk of **thromboembolism** and other cardiovascular events in new users. Contraception 2013; 87:93-100.

Sieving RE, McRee AL, McMorris BJ, et al. Prime Time: Sexual Health Outcomes at 24 Months for a **Clinic-Linked Intervention** to Prevent Pregnancy Risk Behaviors. JAMA Pediatr. 2013 Feb 25:1-8.

Simmons KB, Haddad LB, Nanda K, et al. **Drug interactions between non-rifamycin antibiotics and hormonal contraception**: a systematic review. Am J Obstet Gynecol. 2018 Jan;218(1):88-97.e14.

Skovlund CW, Mørch LS, Kessing LV, Lidegaard Ø. **Association of hormonal contraception with depression**. JAMA Psychiatry. 2016;73(11):1154-1162

Skovlund CW, et al. Association of **Hormonal Contraception With Suicide Attempts** and Suicides. Am J Psychiatry. 2017 Nov 17:appiajp201717060616.

Smoley BA, Robinson CM. **Natural Family Planning**. Am Fam Physician. 2012 Nov 15;86(10):924-928.

Speroff, Leon, and Daniel R. Mishell Jr. "The postpartum visit: it's time for a change in order to optimally initiate contraception." Contraception 78 (2008): 90-98

Shufelt CL, Bairey Merz CN. Contraceptive hormone use and **cardiovascular disease**. J Am Coll Cardiol 2009; 53:221-231.

Smith C, Gold J, Ngo TD, Sumpter C, Free C. **Mobile phone-based interventions** for improving contraception use. Cochrane Database of Systematic Reviews 2015, Issue 6. Art. No.: CD011159. DOI: 10.1002/14651858.CD011159.pub2. Our review provides limited evidence that interventions delivered by mobile phone can improve contraception use. Whilst evidence suggests that a series of interactive voice messages and counsellor support can improve post-abortion contraception, and that a mixture of uni-directional and interactive daily educational text messages can improve OC adherence, the cost-effectiveness and long-term effects of these interventions remain unknown. Further high-quality trials are required to robustly establish the effects of interventions delivered by mobile phone to improve contraception use.

SOGC: Nov 2008 **Missed Contraceptives**: http://www.sogc.org/jogc/abstracts/200811_SOGCClinicalPracticeGuidelines_1.pdf

SOGC: Society of Obstetricians and Gynaecologists of Canada. **Emergency contraception**. SOGC clinical practice guideline. J Obstet Gynaecol Can 2012;34:870-8. www.sogc.org/guidelines/documents/gui280CPG1209E.pdf

SOGC: Society of Obstetricians and Gynaecologists of Canada. **Diane-35** and risk of venous thromboembolism (**VTE**). Position statement. February 19, 2013. www.sogc.org/media/documents/medDiane35VTE130219.pdf

SOGC: Society of Obstetricians and Gynaecologists of Canada. **Menstrual suppression in special circumstances**. http://sogc.org/wp-content/uploads/2014/10/JOGC-Oct2014-CPG-313_Eng_Online-Complete.pdf

SOGC: Society of Obstetricians and Gynaecologists of Canada. **Canadian contraception consensus** (**Part 1 of 4**). J Obstet Gynaecol Can 2015;37(10):S1–28. http://sogc.org/wp-content/uploads/2015/11/gui329Pt1CPG1510.pdf (accessed December 8, 2015).

SOGC: Society of Obstetricians and Gynaecologists of Canada. **Canadian contraception consensus** (**Part 2 of 4**). J Obstet Gynaecol Can 2015;37(11):S1–39. http://sogc.org/wp-content/uploads/2015/11/gui329Pt2CPG1511E.pdf (accessed December 8, 2015).

Soini T, Hurskainen R, Grénman S, et al. **Cancer Risk in Women Using the Levonorgestrel**-Releasing Intrauterine System in Finland. Obstet Gynecol. 2014 Jul 7

Song IH, Borland J, Chen S, et al. **Dolutegravir** Has No Effect on the Pharmacokinetics of Oral Contraceptives With Norgestimate and Ethinyl Estradiol. Ann Pharmacother. 2015 Jul;49(7):784-9.

Srivastava A, Patel N. **Autosomal dominant polycystic kidney disease**. Am Fam Physician. 2014 Sep 1;90(5):303-7.

Steenland MW, Pace LE, Sinaiko AD, Cohen JL. Association Between South Carolina Medicaid's Change in Payment for Immediate **Postpartum Long-Acting Reversible Contraception and Birth Intervals**. JAMA. 2019 Jun 3.

Stegeman BH, de Bastos M, Rosendaal FR, et al. Different combined oral contraceptives and the **risk of venous thrombosis**: systematic review and network meta-analysis. BMJ. 2013 Sep 12;347:f5298.

Steiner MJ, Kwok C, Stanback J, et al. Injectable contraception: what should the longest interval be for reinjections? Contraception. 2008 Jun;77(6):410-4. Epub 2008 Apr 10. Extending the current WHO **grace period for DMPA reinjection from 2 to 4 weeks** does not increase pregnancy risk and could increase contraceptive continuation.

Steiner RJ et al. **Long-acting reversible contraception and condom use** among female US high school students: Implications for sexually transmitted infection prevention. JAMA Pediatr 2016 Mar 14.

Stern LF, Simons HR, Kohn JE, et al. **Differences in Contraceptive Use** Between Family Planning Providers and the U.S. Population: Results of a Nationwide Survey. Contraception. 2015 Feb 19.

Stevenson AJ, Flores-Vazquez IM, Allgeyer RL, et al. Effect of **Removal of Planned Parenthood** from the Texas Women's Health Program. N Engl J Med. 2016 Feb 2.

Stewart FH, Kaunitz AM, Laguardia KD, et al. Extended use of transdermal norelgestromin/ethinyl estradiol: a randomized trial. Obstet Gynecol. 2005 Jun;105(6):1389-96.

Sulak PJ, Kuehl TJ, Coffee A, Willis S. Prospective analysis of occurrence and management of breakthrough bleeding during an **extended oral contraceptive** regimen. Am J Obstet Gynecol. 2006 Apr 27; [Epub ahead of print]

Sulak PJ, et al. Frequency and management of breakthrough bleeding with **continuous use of the transvaginal** contraceptive **ring**: a randomized controlled trial. Obstet Gynecol. 2008 Sep;112(3):563-71.

Sufrin CB et al. **Neisseria gonorrhea and Chlamydia trachomatis screening at intrauterine device insertion** and pelvic inflammatory disease. Obstet Gynecol 2012 Dec; 120:1314.

Sun F, Sebastiani P, Schupf N, et al. **Extended maternal age** at birth of last child and women's longevity in the Long Life Family Study. Menopause. 2014 Jun 23.

Sweet MG, Schmidt-Dalton TA, Weiss PM, Madsen KP. Evaluation and management of **abnormal uterine bleeding** in premenopausal women. Am Fam Physician. 2012 Jan 1;85(1):35-43.

Templeton A, Grimes DA. A **Request for Abortion**. N Engl J Med 2011; 365:2198-2204.

Thirumalai A, Ceponis J, Amory JK, et al. Effects of 28 Days of **Oral Dimethandrolone Undecanoate in Healthy Men**: A Prototype Male Pill. J Clin Endocrinol Metab. 2019 Feb 1;104(2):423-432.

Thonneau P, et al. Risk factors for **IUD failure**: results of a large multicentre case-control study. Hum Reprod. 2006 Oct;21(10):2612-6. Epub 2006 Jun 14. Only a history of previous IUD expulsion was found to be a risk factor for failure, indicating that these women should have regular medical and echographical follow-up. Comparing the efficacy rate of various types of IUDs, we found a clear advantage for levonorgestrel-releasing devices.

Trenor, Cameron C, Chung, Richard J., Michelson, Alan D., et al. Hormonal Contraception and **Thrombotic Risk**: A Multidisciplinary Approach. Pediatrics 2011 127: 347-357.

Trezza C, Ford SL, et al. Lack of Effect of Oral **Cabotegravir** on the Pharmacokinetics of a **Levonorgestrel/Ethinyl Estradiol**-Containing Oral Contraceptive in Healthy Adult Females. Br J Clin Pharmacol. 2017 Jan 14.

Troskie C, Soon JA, et al. **Regulatory approval time** for hormonal contraception in Canada, the United States and the United Kingdom, 2000-2015: a retrospective data analysis. CMAJ Open. 2016 Nov 3;4(4):E654-E660.

Trussell J. Contraceptive failure in the United States. Contraception. 2004 Aug;70(2):89-96.

Tsai R, Schaffir J. Effect of depot **medroxyprogesterone** acetate on **postpartum depression**. Contraception. 2010 Aug;82(2):174-7. Epub 2010 Apr 13. Administration of DMPA in the immediate postpartum period does not appear to predispose women to PPD.

Turok DK, Leeman L, Sanders JN, et al. **Immediate postpartum levonorgestrel intrauterine device insertion and breast-feeding** outcomes: a noninferiority

randomized controlled trial. Am J Obstet Gynecol. 2017 Aug 23.
Urrutia RP, Polis CB. **Fertility awareness** based methods for pregnancy prevention. BMJ. 2019 Jul 11;366:l4245.
Van Houdenhoven K, et al. Uterine perforation in women using a levonorgestrel-releasing intrauterine system. Contraception. 2006 Mar;73(3):257-60. Epub 2005 Oct 21.
van Hylckama Vlieg A, Helmerhorst F M, Vandenbroucke J P, et al. Venous **thrombotic risk** of oral contraceptives, effects of oestrogen dose and progestogen type: results of the MEGA case-control study. BMJ 2009;339:b2921, doi: 10.1136/bmj.b2921 (Published 13 August 2009)
Van Vliet HA, Grimes DA, Lopez LM, et al. **Triphasic versus monophasic** oral contraceptives for contraception. Cochrane Database Syst Rev. 2011 Nov 9;11:CD003553.
The available evidence is insufficient to determine whether triphasic OCs differ from monophasic OCs in effectiveness, bleeding patterns or discontinuation rates. Therefore, we recommend monophasic pills as a first choice for women starting OC use. Large, high-quality RCTs that compare triphasic and monophasic OCs with identical progestogens are needed to determine whether triphasic pills differ from monophasic OCs.
Vieira CS, Bahamondes MV, de Souza RM, et al. Effect of antiretroviral therapy including **lopinavir/ritonavir or efavirenz on etonogestrel**-releasing implant pharmacokinetics in HIV-positive women. J Acquir Immune Defic Syndr. 2014 Aug 1;66(4):378-85.
Vinogradova Y, Coupland C, et al. Use of combined oral contraceptives and **risk of venous thromboembolism**: nested case-control studies using the QResearch and CPRD databases. BMJ. 2015 May 26;350:h2135.
Wahlsten LR, Eckardt H, Lyngbæk S, et al. **Symptomatic venous thromboembolism** following fractures distal to the knee: a nationwide Danish cohort study. J Bone Joint Surg Am. 2015 Mar 18;97(6):470-7. (risk with oral contraceptives & NSAIDs)
Watson S, Härmark L. **Desogestrel and panic attacks** - a new suspected adverse drug reaction reported by patients and health care professionals on spontaneous reports. Br J Clin Pharmacol. 2018 May 24.
Weill A, et al. **Low dose oestrogen combined oral contraception and risk of pulmonary embolism, stroke, and myocardial infarction** in five million French women: cohort study. BMJ 2016;353:i2002.
Westhoff CL, Torgal AH, Mayeda ER, et al. Pharmacokinetics of a combined oral contraceptive in **obese** and normal-weight women. Contraception. 2010 Jun;81(6):474-80.
Westhoff CL et al. **Body weight** does not impact pregnancy rates during use of a low-dose extended-regimen 91-day oral contraceptive. Contraception 2012 Mar; 85:235. (LoSEASONIQUE)
Wiebe E, Kaczorowski J, Mackay J. **Mood and sexual side effects** of hormonal contraception: Physicians' and residents' knowledge, attitudes, and practices. Can Fam Physician. 2012 Nov;58(11):e677-83.
Wiegratz I, Kuhl H. Long-cycle treatment with oral contraceptives. Drugs. 2004;64(21):2447-62.
Wiesinger H, Berse M, et al. Pharmacokinetic interaction between the **CYP3A4 inhibitor ketoconazole and the hormone drospirenone** in combination with **ethinylestradiol or estradiol**. Br J Clin Pharmacol. 2015 Aug 14.
Wilailak S, Vipupinyo C, Suraseranivong V, et al. **Depot medroxyprogesterone** acetate and epithelial **ovarian cancer**: a multicentre case-control study. BJOG. 2012 May;119(6):672-7.
Wilkinson TA, Clark P, Rafie S, et al. **Access to Emergency Contraception After Removal of Age Restrictions**. Pediatrics. 2017;140(1):e20164262
Winner B, Peipert JF, Zhao Q, et al. **Effectiveness of long-acting reversible contraception**. N Engl J Med. 2012 May 24;366(21):1998-2007.
Woodhams EJ, Gilliam M, **In the Clinic: Contraception**. Ann Intern Med Oct 2, 2012. ITC4-2.
Worly BL, Gur TL, Schaffir J. The relationship between **progestin hormonal contraception and depression**: a systematic review. Contraception. 2018 Feb 20.
Wu C, Grandi S, Filion K, Abenhaim H, Joseph L, Eisenberg M. Drospirenone-containing oral contraceptive pills and the risk of venous and arterial thrombosis: a systematic review. BJOG. 2013 Mar 26.
Xu H et al. Contraceptive failure rates of **etonogestrel subdermal implants in overweight** and obese women. Obstet Gynecol 2012 Jul; 120:21.
Yang YT, Kozhimannil KB, Snowden JM. **Pharmacist-Prescribed Birth Control in Oregon and Other States**. JAMA. 2016 Mar 28.
Zapata LB, Pazol K, Dehlendorf C, et al. **Contraceptive Counseling** in Clinical Settings: An Updated Systematic Review. Am J Prev Med. 2018 Nov;55(5):677-690.
Zethraeus N, Dreber A, Ranehill E, et al. A **first-choice combined oral contraceptive influences general well-being in healthy women**: a double-blind, randomized, placebo-controlled trial. Fertil Steril. 2017 Apr 19.
Zuurbier SM, Arnold M, Middeldorp S, et al. Risk of **cerebral venous thrombosis** in **obese** women [online Mar 14/16].JAMA Neurol. doi:10.1001/jamaneurol.2016.0001. 10.

Original Reviewers of Herbal Options for Postmenopausal Symptoms in Women:
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Online Extras 💻

Pearls for post-menopausal hormone therapy (HT):

- ♀ without hx of hysterectomy who are on estrogen should use a progestogen to protect against endometrial hyperplasia & carcinoma
- If last menstrual period < 1yr prior, a sequential combined regimen recommended (e.g. continuous estrogen with 12-14 days progestogen/month)
- If last menstrual period > 1yr prior, ♀ who wish to avoid monthly withdrawal bleed, may start continuous combined regimen
- If breakthrough bleeding occurs following switch to continuous combined & does not settle within 3-6months, consider switch back to sequential for 1 or more years
- If bleeding is heavy or erratic on sequential regimen, consider ↑ dose of progestagen (e.g. double)
- Persistent bleeding beyond 6 months warrants referral/investigation
- 90% of ♀ persisting with regimens will eventually be bleed free
- If AEs 2° to progestagen (mood swings, PMS like effects, androgenic effects), may ↓ dose by ½ &/or ↓ duration to 7 -10 days
- HT prescribed before age 60 has a favorable benefit/risk profile
- If using HT after age 60 lower doses (lowest effective dose) especially prudent due to gradually increasing risk
- Venlafaxine (75mg/day) was equal to low dose estrogen (estradiol 0.5mg/day) for treatment of vasomotor symptoms in a RCT. Joffe H et al., 2014.

Original derivations of herbal products: black cohosh = rhizome/root; chasteberry = fruit; dong quai = root; evening primorse oil = seed; red clover = flower top; wild yam = rhizome/root; valerian = root

References: *The Rx Files* Postmenopausal & Herbal Pharmacotherapy

[1] Kronenberg F, Fugh-Berman A. Complementary and alternative medicine for menopausal symptoms: a review of randomized, controlled trials. Ann Intern Med. 2002 Nov 19;137(10):805-13. (Nedrow A, et al **Complementary and alternative** therapies for the management of menopause-related symptoms: a systematic evidence review. Arch Intern Med. 2006 Jul 24;166(14):1453-65. (InfoPOEMs: There is no evidence of benefit of acupuncture, magnet therapy, stress reduction, exercise, progressive muscle relaxation, or traditional Chinese herbal therapy on menopausal symptoms. Black cohosh, which has been associated with liver toxicity, and soy supplements may decrease hot flashes in some patients, and osteopathic manipulation was effective in one study. (LOE = 1a-)))

[2] Utiger RD. The need for more vitamin D. N Eng J Med 1998;338:828-9.
Hanley DA, Cranney A, Jones G, et al. **Vitamin D in adult** health & disease: a review and **guideline statement from Osteoporosis Canada**–summary.CMAJ 2010 0: cmaj.091062.
Vitamin D supplementation: Recommendations for Canadian mothers and infants. Paediatr Child Health 2007;12(7):583-9. Reference No. FNIM07-01.
http://www.cps.ca/english/statements/ii/fnim07-01.htm
IOM (Institute of Medicine): Dietary Reference Intakes for **Calcium and Vitamin D** Nov,2010. http://www.iom.edu/~/media/Files/Report%20Files/2010/Dietary-Reference-Intakes-for-Calcium-and-Vitamin-D/Vitamin%20D%20and%20Calcium%202010%20Report%20Brief.pdf
Rosen Clifford J. **Vitamin D Insufficiency**. N Engl J Med 2011; 364:248-254.
Bosomworth, N.J. Mitigating epidemic vitamin D deficiency: The agony of evidence. Can Fam Physician 2011 57: 16-20.
Bischoff-Ferrari HA, Willett WC, Oray EJ, et al. A pooled analysis of **vitamin D dose** requirements for fracture prevention. N Engl J Med 2012;367:40-9. {highest actual-intake quartile (792 to 2000 IU daily), there was a 30% reduction in hip fracture incidence}

[3] Boucher M, Murphy G, Goyle D, et al. Bisphosphonates and teriparatide of r the prevention of osteoporotic fractures in postmenopausal women [Technology overview no 22]. Ottawa: Canadian Agency for Drugs and Technologies in Health; 2006.
http://www.cadth.ca/index.php/en/hta/reports-publications/search/publication/660

[4] Bygdeman M, Swahn ML. Replens versus dienoestrol cream in the symptomatic treatment of vaginal atrophy in postmenopausal women. Maturitas 1996;23:259-63.

[55] Krebs EE, Ensrud KE, MacDonald R, Wilt TJ. Phytoestrogens for treatment of menopausal symptoms: a systematic review. Obstet Gynecol. 2004 Oct;104(4):824-36. Review.

[56] Lethaby A, Marjoribanks J, Kronenberg F, Roberts H, Eden J, Brown J. Phytoestrogens for menopausal vasomotor symptoms. Cochrane Database Syst Rev. 2013 Dec 10;12:CD001395. doi: 10.1002/14651858.CD001395.pub4. Review.

[5] Newton KM, Reed SD, LaCroix AZ, Grothaus LC, Ehrlich K, Guiltinan J. Treatment of vasomotor symptoms of menopause with black cohosh, multibotanicals, soy, hormone therapy, or placebo. Ann Intern Med 2006;145:869-879.
{InfoPOEMS-Feb07: Neither soy, black cohosh, or a naturopathic multibotanical was effective in decreasing the duration or severity of vasomotor symptoms. These results are similar to other research findings. (LOE = 1b) }

[6] Geller SE, Shulman LP, van Breemen RB, et al. Safety and efficacy of black cohosh and red clover for the management of vasomotor symptoms: a randomized controlled trial. Menopause. 2009 Jul 15. [Epub ahead of print] Compared with placebo, black cohosh and red clover did not reduce the number of vasomotor symptoms. Safety monitoring indicated that chemically and biologically standardized extracts of black cohosh and red clover were safe during daily administration for 12 months.

[7] Pepping J. Black cohosh: Cimicifuga racemosa. Am.J Health Syst.Pharm. 1999;56:1400-02.

[8] Leach MJ, Moore V. **Black cohosh** (Cimicifuga spp.) for menopausal symptoms. Cochrane Database of Systematic Reviews 2012, Issue 9. Art. No.: CD007244. DOI: 10.1002/14651858.CD007244.pub2. There is currently insufficient evidence to support the use of black cohosh for menopausal symptoms.

[9] Jacobson JS, Troxel AB, Evans J et al. Randomized trial of black cohosh for the treatment of hot flashes among women with a history of breast cancer. J Clin Oncol 2001;19:2739-45. (Pockaj BA, et al. Phase III double-blind, randomized, placebo-controlled crossover trial of black cohosh in the management of hot flashes: NCCTG Trial N01CC1. J Clin Oncol. 2006 Jun 20;24(18):2836-41.)

[10] Liske E, Hanggi W, et al. Physiological investigation of a unique extract of black cohosh (Cimicifugae racemosae rhizoma): a 6-month clinical study demonstrates no systemic estrogenic effect. J Womens Health Gend Based.Med 2002;11:163-74.

[11] The Canadian consensus conference on menopause and osteoporosis. J Obstet Gynaecol Can 2001;23:1-90.

[12] Therapeutic Research Faculty. Natural Database Monographs. Natural Database . 2002. Ref Type: Electronic Citation.

[13] Shuster J. Black cohosh root? Chasteberry tree? Seizures! Hospital Pharmacy 1996;31:1553-4.

[14] Amato P, Christophe S, Mellon P. Estrogenic activity of herbs commonly used as remedies fo menopausal symptoms. Menopause 2002;9:145-50.

[15] Facts and comparisons. The review of natural products (formerly the Lawrence Review of natural products). In: DerMarderosian A, editor. St. Louis MO, 2002.

[16] Morelli V, Naquin C. Alternative therapies for traditional disease states: menopause. Am.Fam.Physician 2002;66:129-34.
Jurgens T, Whelan AM. Advising patients on the use of natural health products to treat premenstrual syndrome. Can Pharm J 2009;142:228-233.

[17] Hirata JD, Swiersz LM, Zell B, Small R, Ettinger B. Does dong quai have estrogenic effects in postmenopausal women? A double-blind, placebo-controlled trial. Fertil.Steril. 1997;68:981-6.

[18] Scott GN, Elmer GW. Update on natural product--drug interactions. Am.J Health Syst.Pharm 2002;59:339-47.

[19] Chandler F. Herbs: everyday reference for health professionals. Ottawa, Canadian Pharmacists Association & Canadian Medical Association. 2000.

[20] Page RL, Lawrence JD. Potentiation of warfarin by dong quai. Pharmacotherapy 1999;19:870-876.

[21] Fugh-Berman A. Herb-drug interactions. Lancet 2000;355:134-8.

[22] Chenoy R, Hussain S, Tayob Y, O'Brien PMS, Moss MY, Morse PF. Effect of oral gamolenic acid from evening primrose oil on menopausal flushing. BMJ 1994;308:501-3.

[23] Clifton-Bligh PB, Baber RJ, Fulcher GR, Nery ML, Moreton T. The effect of isoflavones extracted from red clover (Rimostil) on lipid and bone metabolism. Menopause. 2001;8:259-65.

[24] Albertazzi P, Pansini F, Bonaccorsi G, Zanotti L, Forini E, De Aloysio D. The effect of dietary soy supplementation on hot flushes. Obstet.Gynecol 1998;91:6-11.

[25] Quella SK, Loprinzi CL, Barton DL et al. Evaluation of soy phytoestrogens for the treatment of hot flashes in breast cancer survivors: A North Central Cancer Treatment Group Trial. J Clin Oncol 2000;18:1068-74.
Levis S, Strickman-Stein N, Ganjei-Azar P, et al. Soy isoflavones in the prevention of menopausal bone loss and menopausal symptoms: a randomized, double-blind trial. Arch Intern Med. 2011;171 (15):1363-1369. Soy isoflavone supplementation had no effect

on bone mineral density over the 2 years of this study, but increased the percentage of women reporting hot flashes. (LOE = 1b-)
Lethaby A, Marjoribanks J, Kronenberg F, et al. Phytoestrogens for menopausal vasomotor symptoms. Cochrane Database Syst Rev. 2013 Dec 10;12:CD001395. No conclusive evidence shows that phytoestrogen supplements effectively reduce the frequency or severity of hot flushes and night sweats in perimenopausal or postmenopausal women, although benefits derived from concentrates of genistein should be further investigated.
Franco OH, Chowdhury R, Troup J, et al. Use of **Plant-Based** Therapies and **Menopausal Symptoms**: A Systematic Review and Meta-analysis. JAMA. 2016 Jun 21;315(23):2554-63.

[26] Kreijkamp-Kaspers S, Kok L, Grobbee DE, et al. Effect of soy protein containing isoflavones on cognitive function, bone mineral density, and plasma lipids in postmenopausal women: a randomized controlled trial. **JAMA. 2004** Jul 7;292(1):65-74.
[27] Alexandersen P, Toussaint A, Christiansen C, et al. Ipriflavone in the treatment of postmenopausal osteoporosis: a randomized controlled trial. JAMA. 2001 Mar 21;285(11):1482-8.
[28] Anderson JW, Johnstone BM, Cook-Newell ME. Meta-analysis of the effects of soy protein intake on serum lipids. N Engl J Med 1995;333:276-82.
[29] Potter SM, Baum JA, Teng H, Stillman RJ, Shay NF, Erdman JW, Jr. Soy protein and isoflavones: their effects on blood lipids and bone density in postmenopausal women. Am.J Clin Nutr. 1998;68:1375S-1379S.
Wong WW, Lewis RD, Steinberg FM, et al. **Soy** isoflavone supplementation and bone mineral density in menopausal women: a 2-y multicenter clinical trial. Am J Clin Nutr. 2009 Sep 16. Daily supplementation with 120 mg soy hypocotyl isoflavones reduces whole-body bone loss but does not slow bone loss at common fracture sites in healthy postmenopausal women.
[30] Duncan AM, Underhill KE, Xu X, Lavalleur J, Phipps WR, Kurzer MS. Modest hormonal effects of soy isoflavones in postmenopausal women. J Clin frinol.Metab 1999;84:3479-84.
[31] Balk J, Whiteside D, Naus, G et al. A pilot study of the effects of phytoestrogen supplementation on postmenopausal endometrium. J Soc Gynecol Invest 2002;9:238-42.
Steinberg FM, Murray MJ, Lewis RD, et al.Clinical outcomes of a 2-y soy isoflavone supplementation in menopausal women. Am J Clin Nutr. 2010 Dec 22.
Kang, Xinmei, Zhang, Qingyuan, Wang, Shuhuai, et al. Effect of soy isoflavones on breast cancer recurrence and death for patients receiving adjuvant endocrine therapy. CMAJ 2010 182: 1857-1862.
Ollberding NJ, Lim U, Wilkens LR, et al. Legume, soy, tofu, and isoflavone intake and endometrial cancer risk in postmenopausal women in the multiethnic cohort study. J Natl Cancer Inst. 2012 Jan 4;104(1):67-76.
[32] O'Hara M, Kiefer D, Farrell K, Kemper K. A review of 12 commonly used medicinal herbs. Arch.Fam.Med 1998;7:523-36.
[33] Klepser TB, Klepser ME. Unsafe and potentially safe herbal therapies. Am.J Health Syst.Pharm 1999;56:125-38.
[34] Garges HP, Varia I, Doraiswamy PM. Cardiac complications and delirium associated with valerian root withdrawal. JAMA 1998;280:1566-7.
[35] Bedard M. Dong quai for women. Canadian Pharmaceutical Journal 2002;135:20-1.
[36] Solomon PR, Adams F, Silver A, Zimmer J, DeVeaux R. Ginkgo for memory enhancement: a randomized controlled trial. JAMA 2002;288:835-40.
[37] Micromedex 2016
[38] Wassertheil-Smoller S, Hendrix SL, Limacher M, Heiss G, et al.; **WHI** Investigators. Effect of estrogen plus progestin on stroke in postmenopausal women: the Women's Health Initiative: a randomized trial. JAMA. 2003 May 28;289(20):2673-84.
[39] Rapp SR, Espeland MA, et al.; **WHIMS**. Effect of estrogen plus progestin on global cognitive function in postmenopausal women: the Women's Health Initiative Memory Study: a randomized controlled trial. JAMA. 2003 May 28;289(20):2663-72.
Resnick SM, Espeland MA, Jaramillo SA, Hirsch C, Stefanick ML, Murray AM, Ockene J, Davatzikos C. Postmenopausal hormone therapy and regional brain volumes: the WHIMS-MRI Study. Neurology. 2009 Jan 13;72(2):135-42. Conjugated equine estrogens with or without MPA are associated with greater brain atrophy among women aged 65 years and older; however, the adverse effects are most evident in women experiencing cognitive deficits before initiating hormone therapy.
Coker LH, Hogan PE, Bryan NR, et al. Postmenopausal hormone therapy and subclinical cerebrovascular disease: the WHIMS-MRI Study. Neurology. 2009 Jan 13;72(2):125-34. Conjugated equine estrogen-based hormone therapy was not associated with a significant increase in ischemic brain lesion volume relative to placebo. This finding was consistent within each trial and in pooled analyses across trials.
[40] Shumaker SA, Legault C, et al.; **WHIMS**. Estrogen plus progestin & the incidence of dementia & mild cognitive impairment in postmenopausal women: Women's Health Initiative Memory Study: a randomized controlled trial. JAMA. 2003 May 28;289(20):2651-62. Estrogen plus progestin therapy increased the risk for probable dementia in postmenopausal women aged 65 years or older. In addition, estrogen plus progestin therapy did not prevent mild cognitive impairment in these women. (Shumaker SA, et al.; Women's Health Initiative Memory Study. Conjugated equine estrogens and incidence of probable dementia and mild cognitive impairment in postmenopausal women: Women's Health Initiative Memory Study. JAMA. 2004 Jun 23;291(24):2947-58. Estrogen therapy alone did not reduce dementia or MCI incidence and increased the risk for both end points combined.) (Maki PM, Gast MJ, Vieweg AJ, Burriss SW, Yaffe K. Hormone therapy in menopausal women with cognitive complaints: a randomized , double-blind trial. Neurology. 2007 Sep 25;69(13):1322-30. n=180. Cognitive Complaints in Early Menopause Trial (COGENT-stopped beause of WHI). There were no differences between groups on any cognitive or QoL measures, except for an increase in sexual interest and thoughts with HT. With the power to detect an effect size of >or=0.45, this study suggests potential modest negative effects on verbal memory that are consistent with previous hormone therapy trials in older women.) Petitti DB, Crooks VC, Chiu V, Buckwalter JG, Chui HC. Incidence of dementia in long-term hormone users. Am J Epidemiol. 2008 Mar 15;167(6):692-700. Epub 2008 Jan 23. After adjustment for age, education, and medical history, hazard ratios for incident dementia were 1.34 (95% confidence interval: 0.95, 1.89) in estrogen/progestin users and 1.23 (95% confidence interval: 0.94, 1.59) in estrogen users. These findings do not provide support for an effect of estrogen or estrogen/progestin use in preventing **dementia**.
[41] Khan MA, Hlatky MA, Liu MW, Lin F, ET AL. **HERS** Investigators. Effect of postmenopausal hormone therapy on coronary heart disease events after percutaneous transluminal coronary angioplasty. Am J Cardiol. 2003 Apr 15;91(8):989-91, A7.
[42] Hays J, Ockene JK, Brunner RL, Kotchen JM, et al.; **WHI** Investigators. Effects of estrogen plus progestin on health-related quality of life. N Engl J Med. 2003 May 8;348(19):1839-54. Epub 2003 Mar 17
[43] Grady D, Yaffe K, Kristof M, Lin F, Richards C, Barrett-Connor E. Effect of postmenopausal hormone therapy on cognitive function: the Heart and Estrogen/progestin Replacement Study. Am J Med. 2002 Nov;113(7):543-8.
[44] Byington RP, Furberg CD, et al.; Heart and Estrogen/Progestin Replacement Study Research Group. Effect of estrogen plus progestin on progression of carotid atherosclerosis in postmenopausal women with heart disease: **HERS B-mode substudy**. Arterioscler Thromb Vasc Biol. 2002 Oct 1;22(10):1692-7.
[45] Hulley S, Furberg C, Barrett-Connor E, Cauley J, et al.; HERS Research Group. Noncardiovascular disease outcomes during 6.8 years of hormone therapy: Heart and Estrogen/progestin Replacement Study follow-up (**HERS II**). JAMA. 2002 Jul 3;288(1):58-66.
[46] Hlatky MA, Boothroyd D, Vittinghoff E, Sharp P, Whooley MA; Heart and Estrogen/Progestin Replacement Study (**HERS**) Research Group. Quality-of-life and depressive symptoms in postmenopausal women after receiving hormone therapy: results from the Heart and Estrogen/Progestin Replacement Study (HERS) trial. JAMA. 2002 Feb 6;287(5):591-7.
47[47] Simon JA, Hunninghake DB, et al. Effect of estrogen plus progestin on risk for biliary tract surgery in postmenopausal women with coronary artery disease. The Heart and Estrogen/progestin Replacement Study. Ann Intern Med. 2001 Oct 2;135(7):493-501.
[48] Cauley JA, Black DM, Barrett-Connor E, Harris F, et al. Effects of hormone replacement therapy on clinical fractures and height loss: The Heart and Estrogen/Progestin Replacement Study (**HERS**). Am J Med. 2001 Apr 15;110(6):442-50.
[49] Chelebowski R, Hendrix S, Langer R, Stefanick M, et al. Influence of Estrogen Plus Progestin on Breast Cancer and Mammography in Healthy Postmenopausal Women. The Women's Health Initiative (**WHI**) Randomized Trial. JAMA 2003;289:3243-53. (Stefanick ML, et al. WHI Investigators. Effects of conjugated equine estrogens on breast cancer and mammography screening in postmenopausal women with hysterectomy. JAMA. 2006 Apr 12;295(14):1647-57. (InfoPOEMs: Estrogen therapy alone does not increase the risk of breast cancer in postmenopausal women with prior hysterectomy. Women receiving estrogen are more likely to require further testing as a result of questionably abnormal mammogram results, potentially leading to heightened anxiety and a reduced quality of life. The decision to use estrogen in postmenopausal women after hysterectomy should be individualized on the basis of overall potential risks and benefits. Women most likely to benefit from estrogen therapy include those with disabling hot flashes and an increased risk of osteoporotic fractures. Treatment should be limited whenever possible to the first 5 years (or less) after menopause. (LOE = 1b)))
[50] Treatment Guidelines: **Drugs for Prevention & Treatment of Postmenopausal Osteoporosis**. **The Medical Letter**: November, **2002**; (3) pp. 13-18, & **October 2005, & REVISED Oct 2008**..
[51] Hersh AL, Stefanick ML, Stafford RS. National use of postmenopausal hormone therapy: annual trends and response to recent evidence. JAMA. 2004 Jan 7;291(1):47-53.
[52] Holmberg L., Anderson H., for the HABITS steering and data monitoring committees; **HABITS** (hormonal replacement therapy after breast cancer--is it safe?), a randomised comparison: trial stopped; Published online February 3, 2004.
[53] Johnston SL, Farrell SA, Bouchard C, et al.; SOGC Joint Committee-Clinical Practice Gynaecology and Urogynaecology. The detection and management of vaginal atrophy. J Obstet Gynaecol Can. 2004 May;26(5):503-15.
SOGC 2014: Society of Obstetricians and Gynaecologists of Canada. **Managing menopause**. J Obstet Gynaecol Can 2014;36(9 eSuppl A):S1–S80. http://sogc.org/wp-content/uploads/2014/09/gui311CPG1409Eabstract1.pdf (accessed October 1, 2014).
[54] Ockene JK, Barad DH, Cochrane BB, Larson JC, et al. Symptom experience after discontinuing use of estrogen plus progestin. JAMA. 2005 Jul 13;294(2):183-93. (Haimov-Kochman R, et al. **Gradual discontinuation** of hormone therapy does not prevent the reappearance of climacteric symptoms: a randomized prospective study. Menopause. 2006 May 25; [Epub ahead of print]
[55] Women's Health Initiative (**WHI**). Effects of Conjugated Equine **Estrogen** in Postmenopausal Women with Hysterectomy. Principal results from the Womens Health Initiative Randomized Controlled Trial. JAMA 2004;291:1701-1712.(Brunner RL, Gass M, Aragaki A, et al. Effects of Conjugated Equine Estrogen on Health-Related **Quality of Life** in Postmenopausal Women With Hysterectomy: Results From the Women's Health Initiative Randomized Clinical Trial. Arch Intern Med. 2005 Sep 26;165(17):1976-86).(Hsia J, et al. Conjugated Equine Estrogens and Coronary Heart Disease: The Women's Health Initiative. Arch Intern Med. 2006 Feb 13;166(3):357-65. CONCLUSIONS: Conjugated equine estrogens provided no overall protection against myocardial infarction or coronary death in generally healthy postmenopausal women during a 7-year period of use. There was a suggestion of lower coronary heart disease risk with CEE among women 50 to 59 years of age at baseline.)
Anderson GL, Chlebowski RT, Aragaki AK, et al. Conjugated equine oestrogen and breast cancer incidence and mortality in postmenopausal women with hysterectomy: extended follow-up of the Women's Health Initiative randomised placebo-controlled trial. *Lancet Oncol* 2012; online March 7.
[56] Women's Health Initiative (**WHI**). Risks and benefits of estrogen plus progestin in healthy postmenopausal women. Principal results from the Womens Health Initiative Randomized Controlled Trial. JAMA 2002;288:321-33.
Manson JE, Hsia J, Johnson KC, Rossouw JE, et al; Women's Health Initiative Investigators (**WHI**). Estrogen plus progestin and the risk of coronary heart disease. N Engl J Med. 2003 Aug 7;349(6):523-34.
Wathen CN, Feig DS, Feightner JW, et al. Hormone replacement therapy for the primary prevention of chronic diseases: recommendation statement from the Canadian Task Force on Preventive Health Care. CMAJ. 2004 May 11;170(10):1535-1537.
Dominic J. Cirillo, BS; Robert B. Wallace, MD, MSc; Rebecca J. Rodabough, MS; Philip Greenland, MD; Andrea Z. LaCroix, PhD; Marian C. Limacher, MD; Joseph C. Larson, MS. Effect of Estrogen Therapy on Gallbladder Disease. JAMA. 2005;293:330-339.
Hendrix SL, Cochrane BB, Nygaard IE, Handa VL, Barnabei VM, Iglesia C, Aragaki A, Naughton MJ, Wallace RB, McNeeley SG. Effects of estrogen with and without progestin on urinary incontinence. JAMA. 2005 Feb 23;293(8):935-48.
Espeland MA, Rapp SR, Shumaker SA, et al.; Women's Health Initiative Memory Study. Conjugated equine estrogens and global cognitive function in postmenopausal women: Women's Health Initiative Memory Study. JAMA. 2004 Jun 23;291(24):2959-68.
(Rossouw JE, Prentice RL, Manson JE, et al. Postmenopausal hormone therapy and risk of cardiovascular disease by age and years since menopause. JAMA 2007; 297:1465-1477. Women who initiated hormone therapy closer to menopause tended to have reduced CHD risk compared with the increase in CHD risk among women more distant from menopause, but this trend test did not meet our criterion for statistical significance. A similar nonsignificant trend was observed for total mortality but the risk of stroke was elevated regardless of years since menopause.)
57. Mitchell CM, Reed SD, Diem S, et al. Efficacy of **vaginal estradiol or vaginal moisturizer vs placebo for treating postmenopausal vulvovaginal symptoms**: a randomized clinical trial [online Mar 19, 2018].JAMA Intern Med. doi:10.1001/jamainternmed.2018.0116

Health Initiative and the ensuing drop in the use of hormone-replacement therapy among postmenopausal women in the United States.

Beral V, Million Women Study Collaborators. Ovarian cancer and hormone replacement therapy in the Million Women Study. Lancet 2007; DOI:10.1016/S0140-6736(07)60534-0.

Beral V; Million Women Study Collaborators; Bull D, Green J, Reeves G. Ovarian cancer and hormone replacement therapy in the **Million Women Study**. Lancet. 2007 May 19;369(9574):1703-10. Women who use HRT are at an increased risk of both incident and fatal ovarian cancer. Since 1991, use of HRT has resulted in some 1300 additional ovarian cancers and 1000 additional deaths from the malignancy in the UK.

Manson JE, Allison MA, Rossouw JE, Carr JJ, Langer RD, Hsia J, Kuller LH, Cochrane BB, Hunt JR, Ludlam SE, Pettinger MB, Gass M, Margolis KL, Nathan L, Ockene JK, Prentice RL, Robbins J, Stefanick ML; WHI and WHI-CACS Investigators. Estrogen therapy and **coronary-artery calcification**. N Engl J Med. 2007 Jun 21;356(25):2591-602. n=1064 Among women 50 to 59 years old at enrollment, the calcified-plaque burden in the coronary arteries after trial completion was lower in women assigned to estrogen only than in those assigned to placebo.

Vickers MR, MacLennan AH, Lawton B, et al. Main morbidities recorded in the Women's International Study of Long Duration Oestrogen After Menopause (**WISDOM**): a randomized controlled trial of hormone replacement therapy in postmenopausal women. BMJ 2007; DOI:10.1136/bmj.39266.425069 Hormone replacement therapy increases cardiovascular and thromboembolic risk when started many years after the menopause. The results are consistent with the findings of the women's health initiative study and secondary prevention studies. Research is needed to assess the long term risks and benefits of starting hormone replacement therapy near the menopause, when the effect may be different.

Kerlikowske K, Miglioretti DL, Buist DS, Walker R, Carney PA. **Declines in Invasive Breast Cancer** and Use of Postmenopausal Hormone Therapy in a Screening Mammography Population. J Natl Cancer Inst. 2007 Aug 14; [Epub ahead of print] Our finding of a statistically significant decline in the rate of ER-positive invasive breast cancer in a screening mammography population after the start of a concomitant substantial decline in postmenopausal hormone therapy use suggests that a decline in screening mammography rates is unlikely to account for the recent decline in US breast cancer incidence.

Li CI, Malone KE, Porter PL, et al. Relationship between Menopausal Hormone Therapy and Risk of Ductal, Lobular, and Ductal-Lobular Breast Carcinomas. Cancer Epidemiol Biomarkers Prev. 2008 Jan;17(1):43-50. Current CHT users for **>/=3 years have a substantially increased risk of lobular carcinomas**. Although lobular carcinomas are less common than ductal carcinomas (approximately 16% versus 70% of all invasive breast cancers in the United States), this duration is shorter than the 5 years of use widely cited to be needed to confer an increased risk of breast cancer overall.

Chlebowski RT, Anderson G, Pettinger M, et al. for the Women's Health Initiative Investigators. Estrogen Plus Progestin and **Breast Cancer Detection by Means of Mammography and Breast Biopsy**. Arch Intern Med. 2008 Feb 25;168(4):370-377. Use of conjugated equine estrogens plus medroxyprogesterone acetate for approximately 5 years resulted in more than 1 in 10 and 1 in 25 women having otherwise avoidable mammogram abnormalities and breast biopsies, respectively, and compromised the diagnostic performance of both. This adverse effect on breast cancer detection should be incorporated into risk-benefit discussions with women considering even short-term combined hormone therapy.

Heiss G, Wallace R, Anderson GL, et al. WHI Investigators. Health risks and benefits **3 years after stopping** randomized treatment with estrogen and progestin. JAMA. 2008 Mar 5;299(9):1036-45. The increased cardiovascular risks in the women assigned to CEE plus MPA during the intervention period were not observed after the intervention. A greater risk of fatal & nonfatal malignancies occurred after intervention in the CEE plus MPA group & the global risk index was 12% higher in women randomly assigned to receive CEE plus MPA compared with placebo.

Rohan TE, Negassa A, Chlebowski RT, et al.Conjugated Equine Estrogen and Risk of **Benign Proliferative Breast Disease**: WHI - A Randomized Controlled Trial. J Natl Cancer Inst. 2008 Apr 8; [Epub ahead of print] Use of 0.625 mg/d of CEE was associated with a statistically significant increased risk of benign proliferative breast disease.

Bray PF, Larson JC, Lacroix AZ, et al. Women's Health Initiative Investigators. Usefulness of baseline lipids and C-reactive protein in women receiving menopausal hormone therapy as predictors of treatment-related coronary events. Am J Cardiol. 2008 Jun 1;101(11):1599-1605. Epub 2008 Apr 2. In conclusion, postmenopausal women with **undesirable lipid levels** had excess coronary heart disease risk when using CEE with or without MPA. However, women with favorable lipid levels, especially LDL/HDL cholesterol ratio <2.5, did not have increased risk of coronary heart disease with CEE with or without MPA irrespective of hs-CRP.

Resnick SM, Espeland MA, Jaramillo SA, Hirsch C, Stefanick ML, Murray AM Ockene J, Davatzikos C. Postmenopausal hormone therapy and regional **brain volumes**: the WHIMS-MRI Study. Neurology. 2009 Jan 13;72(2):135-42. Conjugated equine estrogens with or without MPA are associated with greater brain atrophy among women aged 65 years and older; however, the adverse effects are most evident in women experiencing cognitive deficits before initiating hormone therapy.

Coker LH, Hogan PE, Bryan NR, et al. Postmenopausal hormone therapy and **subclinical cerebrovascular disease**: the WHIMS-MRI Study. Neurology. 2009 Jan 13;72(2):125-34. Conjugated equine estrogen-based hormone therapy was not associated with a significant increase in ischemic brain lesion volume relative to placebo. This finding was consistent within each trial and in pooled analyses across trials.

Chlebowski RT, Kuller LH, Prentice RL, Stefanick ML, et al. WHI Investigators. **Breast cancer** after use of estrogen plus progestin in postmenopausal women. N Engl J Med. 2009 Feb 5;360(6):573-87. The increased risk of breast cancer associated with the use of estrogen plus progestin declined markedly soon after discontinuation of combined hormone therapy and was unrelated to changes in frequency of mammography.

Shetty KD, Vogt WB, Bhattacharya J. Hormone replacement therapy and cardiovascular health in the United States. Med Care. 2009 May;47(5):600-6. Decreased HRT use was not associated with reduced acute stroke rate but was associated with a decreased **acute myocardial infarction** rate among women. Our results suggest that observational data can provide correct inferences on clinical outcomes in the overall population if a suitable natural experiment is identified.

Prentice RL, Manson JE, Langer RD, et al. Benefits and risks of postmenopausal hormone therapy when it is initiated **soon after menopause**. (WHI) Am J Epidemiol. 2009 Jul 1;170(1):12-23. Epub 2009 May 25. These analyses provide little support for the hypothesis of favorable effects among women who initiate postmenopausal estrogen use soon after menopause, either for coronary heart disease or for health benefits versus risk indices considered.

Chlebowski RT, Schwartz AG, Wakelee H, et al. for the Women's Health Initiative Investigators. Oestrogen plus progestin and lung cancer in postmenopausal women (Women's Health Initiative trial): a post-hoc analysis of a randomised controlled trial. Lancet. 2009 Sep 18.

Espeland MA, Tindle HA, Bushnell CA, et al. for the Women's Health Initiative Memory Study. Brain Volumes, Cognitive Impairment, and Conjugated Equine Estrogens. J Gerontol A Biol Sci Med Sci. 2009 Sep 3.

Crandall Carolyn J.; Aragaki Aaron K.; Chlebowski Rowan T.; et al. New-Onset **Breast Tenderness** After Initiation of Estrogen Plus Progestin Therapy and Breast Cancer Risk. Arch Intern Med. 2009;169(18):1684-1691.

Toh Sengwee, Hernández-Díaz Sonia, Logan Roger, Et al. **Coronary Heart Disease** in Postmenopausal Recipients of Estrogen Plus Progestin Therapy: Does the Increased Risk Ever Disappear?: A Randomized Trial. Ann Intern Med February 16, 2010.

Manson JE, Allison MA, Carr JJ, et al. for the Women's Health Initiative and Women's Health Initiative-**Coronary Artery Calcium** Study Investigators. Calcium/vitamin D supplementation and coronary artery calcification in the Women's Health Initiative. Menopause. 2010 Jun 14.

Harman S. Mitchell. Therapeutics: Women's Health Initiative (WHI) randomised ontrolled trial: Combined estrogen plus progestin may reduce coronary heart disease risk after 5 years of use in postmenopausal women starting treatment within 10 years of menopause, Evid Based Med 2010;15:69-70 doi:10.1136/ebm1079

Chlebowski RT., Anderson GL., Manson JE., et al. **Lung Cancer** Among Postmenopausal Women Treated With Estrogen Alone in the Women's Health Initiative (WHI) Randomized Trial. Journal of the National Cancer Institute Advance Access published Aug 13, 2010.

Chlebowski Rowan T.; Anderson Garnet L.; Gass Margery; et al. for the WHI Investigators Estrogen Plus Progestin and **Breast Cancer Incidence and Mortality** in Postmenopausal Women. JAMA. 2010;304(15):1684-1692.

LaCroix AZ, Chlebowski RT, Manson JE, et al; WHI Investigators. Health outcomes **after stopping conjugated equine estrogens** among postmenopausal women with prior hysterectomy: a randomized controlled trial. JAMA. 2011;305(13): 1305-1314.

De P, Neutel CI, Olivotto I, Morrison H. **Breast cancer incidence and hormone replacement therapy in Canada**. J Natl Cancer Inst. 2010 Oct 6;102(19):1489-95.

Anderson GL, Chlebowski RT, Aragaki AK, et al. Conjugated equine **oestrogen and breast cancer** incidence and mortality in postmenopausal women with hysterectomy: extended follow-up of the Women's Health Initiative randomised placebo-controlled trial. *Lancet Oncol* 2012; online March 7.

Henderson VW, Lobo RA. Hormone therapy and the risk of stroke: perspectives 10 years after the Women's Health Initiative trials. Climacteric. 2012 Jun;15(3):229-34.

Wild RA, Wu C, Curb JD, Martin LW, Phillips L, Stefanick M, Trevisan M, Manson JE. Coronary heart disease events in the Women's Health Initiative hormone trials: effect modification by **metabolic syndrome**. A nested case-control study within the Women's Health Initiative randomized clinical trials. Menopause. 2012 Oct 25.

Chlebowski RT, Manson JE, Anderson GL, et al. Estrogen Plus Progestin and **Breast Cancer** Incidence and Mortality in the Women's Health Initiative Observational Study. J Natl Cancer Inst. 2013 Mar 29.

Espeland MA, Shumaker SA, Leng I, et al. Long-term effects on cognitive function of postmenopausal hormone therapy prescribed to women aged 50 to 55 years (WHIMSY) [online June 24, 2013]. JAMA Intern Med. doi:10.1001/jamainternmed.2013.6827.

Manson JE, Chlebowski RT, Stefanick ML, et al. Menopausal hormone therapy and health outcomes during the intervention and extended poststopping phases of theWomen's Health Initiative (WHI) randomized trials. JAMA. doi:10.1001/jama.2013.278040.

Coker LH, Espeland MA, Hogan PE, et al; for the WHIMS-MRI Study Group. Change in **brain and lesion volumes after CEE therapies**: the **WHIMS-MRI** studies. Neurology 2014;82:427–434.

Espeland MA, Brinton RD, Manson JE, et al; **WHIMS-MRI2** Study Group. **Postmenopausal hormone therapy, type 2 diabetes** mellitus, and **brain volumes**. Neurology. 2015 Sep 29;85(13):1131-8.

Chlebowski RT, Anderson GL, Sarto GE, et al. Continuous Combined **Estrogen Plus Progestin and Endometrial Cancer**: The **Women's Health Initiative** Randomized Trial. J Natl Cancer Inst. 2015 Dec 14;108(3).

Hyland A, Piazza K, Hovey KM, et al. Associations between lifetime **tobacco exposure with infertility and age at natural menopause**: the **Women's Health Initiative** Observational Study. Tob Control. 2015 Dec 14.

Gong Z, Aragaki AK, Chlebowski RT, et al. Diabetes, metformin and incidence of and death from **invasive cancer in postmenopausal women**: Results from the women's health initiative (**WHI**). Int J Cancer. 2016 Apr 15;138(8):1915-27.

Chlebowski RT, Rohan TE, Manson JE, et al. **Breast Cancer After Use of Estrogen Plus Progestin and Estrogen Alone**: Analyses of Data From 2 Women's Health Initiative(**WHI**) Randomized Clinical Trials. JAMA Oncol. 2015 Jun

Crandall CJ, Hovey KM, Andrews C, et al. Comparison of **clinical outcomes** among users of **oral and transdermal estrogen** therapy in the Women's Health Initiative (**WHI**) Observational Study. Menopause. 2017 Jul 10.

Crandall CJ, Hovey KM, Andrews CA, et al. **Breast cancer, endometrial cancer, and cardiovascular events in** participants who used **vaginal estrogen** in the **Women's Health Initiative (WHI)** Observational Study. Menopause. 2017 Aug 14.

Manson JE, Aragaki AK, Rossouw JE, et al. **Menopausal hormone therapy and long-term all-cause and cause-specific mortality**: the **Women's Health Initiative (WHI)** randomized trials.JAMA. doi:10.1001/jama.2017.11217

Chlebowski RT, Aragaki AK, Anderson GL, et al. **Low-Fat Dietary Pattern and Breast Cancer Mortality** in the Women's Health Initiative (WHI) Randomized Controlled Trial. J Clin Oncol. 2017 Sep 1;35(25):2919-2926.

[57] Wan YL, Holland C. The efficacy of levonorgestrel intrauterine systems for endometrial protection: a systematic review. Climacteric. 2011 Dec;14(6):622-32.

[58] Gruber DM, Sator MO, Kirchengast S. Effect of percutaneous androgen replacement therapy on body composition and body weight in postmentopausal women. Maturitas 1998;29:253-9.11

59 Rahimikian F, Rahimi R, Golzareh P, et al. Effect of **Foeniculum vulgare Mill. (fennel)** on menopausal symptoms in postmenopausal women: a randomized, triple-blind, placebo-controlled trial. Menopause. 2017 May 15.

Additional references:

AACE- Goodman NF, Cobin RH, Ginzburg SB, Katz IA, Woode DE. American Association of Clinical Endocrinologists medical guidelines for clinical practice for the diagnosis and treatment of **menopause**. Endocr Pract 2011 Nov-Dec;17(Suppl 6):1-25. https://www.aace.com/files/menopause.pdf

AACE-Cobin RH, et al; AACE Reproductive Endocrinology Scientific Committee. **American** Association of Clinical Endocrinologists (**AACE**), American College of Endocrinology (**ACE**) **Postion statement on menopause-2017 update**. Endocr Pract. 2017 Jul;23(7):869-880.

ACOG Committee Opinion No. 565: **Hormone therapy and heart disease**. Obstet Gynecol. 2013 Jun;121(6):1407-10.

ACOG Committee on Gynecological Practice. ACOG: **Postmenopausal estrogen therapy: Route of administration** and risk of venous thromboembolism. Obstet Gynecol 2013 Apr; 121:887.

ACOG Practice bulletin no. 141: management of **menopausal symptoms**. Obstet Gynecol. 2014 Jan;123(1):202-16

ACOG: Committee Opinion No. 659: The Use of **Vaginal Estrogen** in Women With a History of **Estrogen-Dependent Breast Cancer**. Obstet Gynecol. 2016 Mar;127(3):e93-e96.

ACOG: Committee Opinion No. 698: **Hormone Therapy in Primary Ovarian Insufficiency**. Obstet Gynecol. 2017 May;129(5):e134-e141.

Agarwal A, Deepinder F, Cocuzza M, Short RA, Evenson DP. Effect of vaginal **lubricants on sperm motility** and chromatin integrity: a prospective comparative study. Fertil Steril. 2008 Feb;89(2):375-9. Epub 2007 May 16.

Agha-Hosseini M, Kashani L, Aleyaseen A, et al. Crocus sativus L. (**saffron**) in the treatment of premenstrual syndrome: a double-blind, randomised and placebo-controlled trial. BJOG. 2008 Mar;115(4):515-9. Saffron was an effective treatment for premenstrual syndrome (PMS) in this well-designed but small and short-term study. Consider recommending saffron, if cost is not an obstacle. Larger and longer studies are needed to confirm this result. (LOE = 1b)

Akhila V, Pratapkumar. A comparison of **transdermal and oral HRT** for menopausal symptom control. Int J Fertil Womens Med. 2006 Mar-Apr;51(2):64-9.

Alhola P, Polo-Kantola P, Erkkola R, Portin R. **Estrogen** therapy and **cognition**: **a 6-year** single-blind follow-up study in postmenopausal women. Neurology. 2006 Aug 22;67(4):706-9.

Apostolakis S, Sullivan RM, Olshansky B, et al. **Hormone replacement therapy** and adverse outcomes in women with **atrial fibrillation**: an analysis from the atrial fibrillation follow-up investigation of rhythm management trial. Stroke. 2014 Oct;45(10):3076-9.

Appiah D, Winters SJ, Muldoon SB, et al. **Androgens, Bilateral Oophorectomy, and Cardiovascular Disease** Mortality in Postmenopausal Women With and Without Diabetes: The Study of Osteoporotic Fractures. Diabetes Care. 2015 Oct 12.

Aromatase Inhibitors and Vaginal Estrogen, Pharmacist's Letter May 2006

Asllanaj E, Bano A, Glisic M, et al. **Age at natural menopause and life expectancy with and without type 2 diabetes**. Menopause. 2018 Oct 8.

Atema V, van Leeuwen M, Oldenburg HS, et al. An **Internet-based cognitive behavioral therapy** for treatment-induced menopausal symptoms in breast cancer survivors: results of a pilot study. Menopause. 2017 Feb 13.

Avis NE, Crawford SL, Greendale G, et al; **Study of Women's Health Across the Nation (SWAN)**. **Duration of menopausal vasomotor symptoms** over the menopause transition [online February 16, 2015]. JAMA Intern Med. doi:10.1001/jamainternmed.2014.8063.

Avis NE, Coeytaux RR, Levine B, et al. Trajectories of response to **acupuncture** for menopausal vasomotor symptoms: the Acupuncture in Menopause study. Menopause. 2016 Sep 26.

Avis NE, Colvin A, Karlamangla AS, et al. Change in **sexual functioning** over the menopausal transition: results from the Study of Women's Health Across the Nation. Menopause. 2016 Oct 31.

Avis NE, Levine BJ, Danhauer S, Coeytaux RR. A pooled analysis of three studies of **nonpharmacological interventions for menopausal hot flashes.** Menopause. 2018 Oct 22.

Bachmann GA, Schaefers M, Uddin A, Utian WH. Lowest Effective Transdermal 17{beta}-Estradiol Dose for Relief of Hot Flushes in Postmenopausal Women: A Randomized Controlled Trial. Obstet Gynecol. 2007 Oct;110(4):771-779. **Micro-dose E2 (0.014 mg/d) was clinically and statistically significantly more effective** than placebo in reducing the number of moderate and severe hot flushes, with a 41% responder rate, supporting the concept of the lowest effective dose. Many women complaining of menopausal hot flushes will get relief from ultra-low-dose hormone therapy patches, so it makes sense to start low in the effort to minimize dosing. (LOE = 1b)

Baill IC, Castiglioni A. **Health Maintenance in Postmenopausal Women**. Am Fam Physician. 2017;95(9):561-570.

Barakat RR, et al.; Gynecologic Oncology Group Study. Randomized double-blind trial of **estrogen replacement therapy** versus placebo in **stage I or II endometrial cancer**: a Gynecologic Oncology Group Study. J Clin Oncol. 2006 Feb 1;24(4):587-92.

Basson R. Clinical practice. **Sexual desire** and arousal disorders in women. N Engl J Med. 2006 Apr 6;354(14):1497-506.

Benetti-Pinto CL, Menezes C, Yela DA, Cardoso TM. **Sleep quality and fatigue** in women with premature ovarian insufficiency receiving hormone therapy: a comparative study. Menopause. 2019 Jul 8.

Beral V, Reeves G, Bull D, Green J; for the **Million Women Study Collaborators**. **Breast Cancer Risk** in Relation to the Interval Between Menopause and Starting Hormone Therapy. J Natl Cancer Inst. 2011 Jan 28.

Bergendal A, Kieler H, Sundström A, et al. **Risk of venous thromboembolism** associated with local and systemic use of hormone therapy in peri- and postmenopausal women and in relation to **type** and **route** of administration. Menopause. 2016 Mar 18.

Berglind IA et al. **Hormone therapy and risk of cardiovascular outcomes and mortality** in women treated with **statins**. Menopause 2015 Apr; 22:369.

Beresford SA, et al. Low-fat dietary pattern and risk of colorectal cancer: the Women's Health Initiative Randomized Controlled Dietary Modification Trial.JAMA. 2006 Feb 8;295(6):643-54.

Berry DA, et al.; Cancer Intervention and Surveillance Modeling Network (CISNET) Collaborators Effect of **screening and adjuvant** therapy on mortality from **breast cancer**. N Engl J Med. 2005 Oct 27;353(17):1784-92. (InfoPOEMs: Almost half of the reduction in breast cancer mortality over the past decade can be attributed to the increased use of screening mammography; the remainder appears to be due to improvements in therapy. (LOE = 1b))

Bhupathiraju SN, Grodstein F, Stampfer MJ, et al. **Vaginal estrogen use and chronic disease risk** in the Nurses' Health Study. Menopause. 2018 Dec 17.

Birnbaum W, Marshall L, Werner R, et al. **Oestrogen versus androgen in hormone-replacement therapy for complete androgen insensitivity syndrome**: a multicentre, randomised, double-dummy, double-blind crossover trial. Lancet Diabetes Endocrinol. 2018 Jul 31.

Boardman HMP, Hartley L, Eisinga A, et al. **Hormone therapy for preventing cardiovascular disease in post-menopausal women**. Cochrane Database of Systematic Reviews 2015, Issue 3 . Art. No.: CD002229. DOI: 10.1002/14651858.CD002229.pub4. Our review findings provide strong evidence that treatment with hormone therapy in post-menopausal women overall, for either primary or secondary prevention of cardiovascular disease events has little if any benefit and causes an increase in the risk of stroke and venous thromboembolic events.

Boneva RS, Lin JM, Unger ER. Early menopause and other gynecologic risk indicators for **chronic fatigue syndrome** in women. Menopause. 2015 Feb 2.

Boskey ER, Taghinia AH, Ganor O. Association of **Surgical Risk With Exogenous Hormone Use** in Transgender Patients: A Systematic Review. JAMA Surg. 2018 Dec 5.

Bove R, Secor E, Chibnik LB, et al. **Age at surgical menopause** influences **cognitive decline** and Alzheimer pathology in older women. Neurology 2014;82:222–229.

Brandes JL. The influence of estrogen on **migraine**: a systematic review. JAMA. 2006 Apr 19;295(15):1824-30.

Briggs GE, Freeman RK, Yaffe SJ, editors. Drugs in Pregnancy and Lactation. 9th ed. Williams and Wilkins; Philadelphia, PA: 2011

Brown CS, Bachmann GA, Wan J, Foster DC; Gabapentin (GABA) Study Group. **Gabapentin for the Treatment of Vulvodynia**: A Randomized Controlled Trial. Obstet Gynecol. 2018 Jun;131(6):1000-1007.

Budhathoki S, Iwasaki M, Sawada N, et al; JPHC Study Group. **Soy food and isoflavone intake and endometrial cancer** risk: the Japan Public Health Center-based prospective study. BJOG. 2014 Jun 18.

Buist D. S., MAnderson, ,et al. Short-Term **Hormone Therapy Suspension and Mammography** Recall: A Randomized Trial. Ann Intern Med 2009; 752-765.

Butts SF, Sammel MD, et al. **Cigarettes, genetic background,** and **menopausal timing**: the presence of single nucleotide polymorphisms in cytochrome P450 genes is associated with increased risk of natural menopause in European-American smokers. Menopause. 2014 Jan 20.

Buyon JP, Petri MA, Kim MY, et al. The effect of **combined estrogen and progesterone** hormone replacement therapy on disease activity in systemic **lupus** erythematosus: a randomized trial. Ann Intern Med. 2005 Jun 21;142(12 Pt 1):953-62.

Canonico M, Oger E, Plu-Bureau G, et al; Estrogen and Thromboembolism Risk (**ESTHER**) Study Group. Hormone therapy and venous thromboembolism among postmenopausal women: impact of the route of estrogen administration and progestogens: the ESTHER study.Circulation. 2007 Feb 20;115(7):840-5. **Oral but not transdermal estrogen** is associated with an increased **VTE risk**. In addition, our data suggest that norpregnane derivatives may be thrombogenic, whereas micronized progesterone and pregnane derivatives appear safe with respect to thrombotic risk. If confirmed, these findings could benefit women in the management of their menopausal symptoms with respect to the VTE risk associated with oral estrogen and use of progestogens.

Canonico M, Plu-Bureau G, Lowe GD, Scarabin PY. Hormone replacement therapy and **risk of venous thromboembolism** in postmenopausal women: systematic review and meta-analysis. BMJ. 2008 May 20. [Epub ahead of print] Oral oestrogen increases the risk of venous thromboembolism, especially during the first year of treatment. **Transdermal oestrogen may be safer** with respect to thrombotic risk.

Canonico M and Scarabin P-Y.**Oral versus transdermal estrogens and venous thromboembolism** in postmenopausal women: What is new since 2003? Menopause 2016 Jun; 23:587.

Canonico M, Carcaillon L, Plu-Bureau G, et al. **Postmenopausal Hormone Therapy and Risk of Stroke**: Impact of the Route of Estrogen Administration and Type of Progestogen. Stroke. 2016 Jul;47(7):1734-41.

Carcaillon L, Brailly-Tabard S, Ancelin ML, et al. High plasma estradiol interacts with diabetes on **risk of dementia** in older postmenopausal women. Neurology. 2014 Feb 11;82(6):504-11

Caro-Bruce E, Flaxman G. **Vulvar pruritus** in a postmenopausal woman. CMAJ. 2014 Jun 10;186(9):688-9.

Carrasquilla GD, Frumento P, Berglund A, et al. **Postmenopausal hormone therapy and risk of stroke**: A pooled analysis of data from population-based cohort studies. PLoS Med. 2017 Nov 17;14(11):e1002445.

Carris N, Kutner S, Reilly-Rogers S. New Pharmacological Therapies for Vasomotor Symptom Management: Focus on **Bazedoxifene/Conjugated Estrogens and Paroxetine Mesylate**. Ann Pharmacother. 2014 Oct;48(10):1343-1349.

Carroll DG, Kelley KW. Use of **antidepressants for management of hot flashes**. Pharmacotherapy. 2009 Nov;29(11):1357-74.

Casini ML, et al. Psychological assessment of the effects of treatment with **phytoestrogens** on postmenopausal women: a randomized, double-blind, crossover, placebo-controlled study. Fertil Steril. 2006 Apr;85(4):972-8. (InfoPOEMs: Isoflavone treatment enhanced **mood** in healthy postmenopausal women, but did not improve scores on cognitive measures. The overall risks and benefits of long-term treatment remain uncertain. (LOE = 1b))

Caso V, Falorni A, Bushnell CD, et al. **Pregnancy, Hormonal Treatments for Infertility, Contraception, and Menopause** in Women **After Ischemic Stroke**: A Consensus Document. Stroke. 2017 Feb;48(2):501-506.

Cathcart-Rake EJ, Ruddy KJ, Gupta R, et al. **Amenorrhea after lung cancer treatment**. Menopause. 2018 Aug 27.

Chan W, Drummond A, Kelly M. **Deep vein thrombosis in a transgender woman**. (estradiol, estrogen) CMAJ. 2017 Apr 3;189(13):E502-E504.

Cheong JL. Retinal vein thrombosis associated with a herbal **phytoestrogen** preparation (black cohosh, dong quai, red clover & wold Mexican yam) in a susceptible patient. Postgrad Med J. 2005 Apr;81(954):266-7.

Cherry N, McNamee R, Heagerty A, et al. Long-term safety of **unopposed estrogen** used by women surviving **myocardial infarction**: 14-year follow-up of the **ESPRIT** randomised controlled trial. BJOG. 2014 Feb 18.

Chlebowski RT., Anderson GL., Manson JE., et al. **Lung Cancer** Among Postmenopausal Women Treated With Estrogen Alone in the Women's Health Initiative (WHI) Randomized Trial. Journal of the National Cancer Institute Advance Access published Aug 13, 2010.

Chlebowski RT, Anderson GL, Sarto GE, et al. Continuous Combined **Estrogen Plus Progestin and Endometrial Cancer**: The **Women's Health Initiative** Randomized Trial. J Natl Cancer Inst. 2015 Dec 14;108(3).

Chlebowski RT, Mortimer JE, Crandall CJ, et al. Persistent **vasomotor symptoms and breast cancer** in the Women's Health Initiative. Menopause. 2018 Dec 28.

Chlebowski RT, Rohan TE, Manson JE, et al. **Breast Cancer After Use of Estrogen Plus Progestin and Estrogen Alone**: Analyses of Data From 2 Women's Health Initiative Randomized Clinical Trials. JAMA Oncol. 2015 Jun

Chotirmall SH, Smith SG, Gunaratnam C, et al. Effect of **Estrogen on Pseudomonas Mucoidy and Exacerbations in Cystic Fibrosis**. N Engl J Med. 2012 May 20.

Chiu HY, Pan CH, Shyu YK, Han BC, Tsai PS. Effects of **acupuncture on menopause**-related symptoms and quality of life in women in natural menopause: a meta-analysis of randomized controlled trials. Menopause. 2015 Feb;22(2):234-44.

Cintron D, Lahr BD, Bailey KR, et al. Effects of **oral versus transdermal menopausal hormone treatments** on self-reported **sleep** domains and their association with vasomotor symptoms in recently menopausal women enrolled in the Kronos Early Estrogen Prevention Study (**KEEPS**). Menopause. 2017 Aug 21.

Cobin RH, Goodman NF; AACE Reproductive Endocrinology Scientific Committee. **American** Association of Clinical Endocrinologists (**AACE**), American College of Endocrinology (**ACE**) **Postion statement on menopause-2017 update**. Endocr Pract. 2017 Jul;23(7):869-880.

Cody JD, Richardson K, Moehrer B, et al. Oestrogen therapy for **urinary incontinence** in post-menopausal women. Cochrane Database Syst Rev. 2009 Oct 7;(4):CD001405.

Cody JD, Jacobs ML, Richardson K, et al. **Oestrogen therapy for urinary incontinence** in post-menopausal women. Cochrane Database Syst Rev. 2012 Oct 17;10:CD001405. doi: 10.1002/14651858.CD001405.pub3. Urinary incontinence may be improved with the use of local oestrogen treatment. However, there was little evidence from the trials on the period after oestrogen treatment had finished and no information about the long-term effects of this therapy was given. Conversely, systemic hormone replacement therapy using conjugated equine oestrogen may worsen incontinence.

Col NF, Fairfield KM, Ewan-Whyte C, Miller H. **In the clinic. Menopause**. Ann Intern Med. 2009 Apr 7;150(7):ITC4-1-15; quiz ITC4-16,.

Collaborative Group on Hormonal Factors in Breast Cancer. Menarche, menopause, and breast cancer risk: individual participant meta-analysis, including 118,964 women with breast cancer from 117 epidemiological studies. Lancet Oncol. 2012 Oct 16.

Collaborative Group on Hormonal Factors in Breast Cancer. **Type and timing of menopausal hormone therapy and breast cancer risk**: individual participant meta-analysis of the worldwide epidemiological evidence. Lancet. 2019 Aug 29.

Collaborative Group On Epidemiological Studies Of . **Menopausal hormone use and ovarian cancer risk**: individual participant meta-analysis of 52 epidemiological studies. Lancet. 2015 Feb 12.

Crandall C, Yildiz V, Wactawski-Wenda J, Johnson K, Chen Z, Going S, et al. **Postmenopausal weight change and incidence of fracture**: post hoc findings from the Womens Health Initiative (WHI) Observational Study and Clinical Trials. BMJ 2015;350:h25.

Crandall CJ, Hovey KM, Andrews C, et al. Comparison of clinical outcomes among users of **oral and transdermal** estrogen therapy in the Women's Health Initiative Observational Study. Menopause. 2017 Jul 10.

Cranney A, et al.; Clinical Guidelines Committee of Osteoporosis Canada. **Parathyroid hormone** for the treatment of osteoporosis: a systematic review. CMAJ. 2006 Jul 4;175(1):52-9.

Cramer H, Rabsilber S, Lauche R, et al. **Yoga** and meditation for menopausal symptoms in breast cancer survivors-A randomized controlled trial. Cancer. 2015 Mar 4.

Crawford SL, Crandall CJ, Derby CA, et al. Menopausal hormone therapy **trends before versus after 2002**: impact of the Women's Health Initiative Study Results. Menopause. 2018 Dec 21.

Cummings SR, Ettinger B, Delmas PD, et al. **LIFT** Trial Investigators. The effects of **tibolone** in older postmenopausal women. N Engl J Med. 2008 Aug 14;359(7):697-708. Tibolone reduced the risk of fracture and breast cancer and possibly colon cancer but increased the risk of stroke in older women with osteoporosis. For every 1000 women treated for 1 year with tibolone, there will be approximately 9 fewer vertebral fractures, 7 fewer nonvertebral fractures, 2 fewer breast cancers, 1 fewer colon cancer, 2 more strokes, and 1 additional endometrial cancer. Although the authors recommend that tibolone not be used in women older than 70 years or in those who have risk factors for stroke, it is hard to see a compelling advantage of this drug for any group of women since bisphosphonates provide a safer way to prevent fracture.

Cunha EP, Azevedo LH, Pompei LM, et al. Effect of **abrupt discontinuation versus gradual dose reduction** of postmenopausal hormone therapy on hot flushes. Climacteric. 2010 Feb 12.

Curb JD, et al. **Venous thrombosis and conjugated equine estrogen** in women without a uterus. Arch Intern Med. 2006 Apr 10;166(7):772-80. During a mean of 7.1 years, VT occurred in 111 women randomly assigned to receive estrogen (3.0 per 1000 person-years) and 86 randomly assigned to receive placebo (2.2 per 1000 person-years; hazard ratio, 1.32; 95% confidence interval, 0.99-1.75). Deep venous thrombosis was reported in 85 women randomly assigned to receive estrogen (2.3 per 1000 person-years) and 59 randomly assigned to receive placebo (1.5 per 1000 person-years; hazard ratio, 1.47; 95% confidence interval, 1.06-2.06).An early increased VT risk is associated with use of estrogen, especially within the first 2 years, but this risk increase is less than that for estrogen plus progestin.

Curhan SG, Eliassen AH, Eavey RD, et al. Menopause and **postmenopausal hormone therapy** and risk of **hearing loss**. Menopause. 2017 May 8.

Daley A, Stokes-Lampard H, Thomas A, MacArthur C. **Exercise for vasomotor menopausal symptoms**. Cochrane Database of Systematic Reviews 2014, Issue 11. Art. No.: CD006108. DOI: 10.1002/14651858.CD006108.pub4. Evidence was insufficient to show whether exercise is an effective treatment for vasomotor menopausal symptoms. One small study suggested thatHT is more effective than exercise. Evidence was insufficient to show the relative effectiveness of exercise when compared with HT or yoga.

Daley A, Thomas A, Roalfe A, et al. The effectiveness of **exercise as treatment for vasomotor menopausal symptoms**: randomised controlled trial. BJOG. 2014 Dec 17.

David PS, Kling JM, Vegunta S, et al. Vasomotor symptoms in women over 60: results from the Data Registry on **Experiences of Aging, Menopause, and Sexuality (DREAMS)**. Menopause. 2018 May 7.

Daly B, Olopade OI, Hou N, et al. Evaluation of the Quality of **Adjuvant Endocrine Therapy Delivery for Breast Cancer** Care in the United States. JAMA Oncol. 2017 Feb 2.

de Blok CJM, Wiepjes CM, Nota NM, et al. **Breast cancer risk in transgender people** receiving hormone treatment: nationwide cohort study in the Netherlands. BMJ. 2019 May 14;365:l1652.

de Kat AC, van der Schouw YT, Eijkemans MJC, et al. Can **menopause prediction be improved with multiple AMH measurements**? Results from the prospective Doetinchem Cohort Study. J Clin Endocrinol Metab. 2019 Apr 22.

Dekosky ST, Williamson JD, Fitzpatrick AL, et al.; for the Ginkgo Evaluation of Memory (GEM) Study Investigators. Ginkgo biloba for Prevention of Dementia: A Randomized Controlled Trial. JAMA. 2008 Nov 19;300(19):2253-2262. (n=3,069 6.1yrs) In this study, G biloba at 120 mg twice a day was not effective in reducing either the overall incidence rate of dementia or AD incidence in elderly individuals with normal cognition or those with MCI.

den Heijer M, Bakker A, Gooren L. **Long term hormonal treatment for transgender people**. BMJ. 2017 Nov 30;359:j5027.

Dickson G. Gynescomastia. Am Fam Physician. 2012 Apr 1;85(7):716-722.

Dodd JM, Flenady V, Cincotta R, Crowther CA. Prenatal administration of progesterone for preventing preterm birth. Cochrane Database Syst Rev. 2006 Jan 25;(1):CD004947.

Donneyong MM, Bykov K, Bosco-Levy P, et al. Risk of mortality with concomitant use of **tamoxifen and selective serotonin reuptake inhibitors**: multi-database cohort study. BMJ. 2016 Sep 30;354:i5014.

Dunneram Y, Greenwood DC, Burley VJ, et al. **Dietary intake and age at natural menopause**: results from the UK Women's Cohort Study. J Epidemiol Community Health. 2018 Apr 30.

Edey KA, Rundle S, Hickey M. **Hormone replacement therapy for women previously treated for endometrial cancer**. Cochrane Database Syst Rev. 2018 May 15;5:CD008830. Currently, there is insufficient high-quality evidence to inform women considering HRT after treatment for endometrial cancer. The available evidence (both the single RCT and non-randomised evidence) does not suggest significant harm, if HRT is used after surgical treatment for early-stage endometrial cancer.

Ee C, Xue C, Chondros P, et al. **Acupuncture** for Menopausal Hot Flashes: A Randomized Trial. Ann Intern Med. 2016 Jan 19.

Ee C, French SD, Xue CC, et al. **Acupuncture** for menopausal hot flashes: clinical evidence update and its relevance to decision making. Menopause. 2017 Mar 27.

Eeles RA, Morden JP, Gore M, et al. **Adjuvant Hormone Therapy** May Improve Survival in Epithelial **Ovarian Cancer**: Results of the AHT Randomized Trial. J Clin Oncol. 2015 Sep 28.

Eliassen A. Heather; Hankinson Susan E.; Rosner Bernard; et al. **Physical Activity and Risk of Breast Cancer** Among Postmenopausal Women. Arch Intern Med. 2010;170(19):1758-1764.

Elavsky S, Gonzales JU, Proctor DN, et al. Effects of **physical activity on vasomotor symptoms**: examination using objective and subjective measures. Menopause. 2012 Jun 25.

Elkins GR, Fisher WI, Johnson AK, Carpenter JS, Keith TZ. Clinical **hypnosis** in the treatment of postmenopausal hot flashes: a randomized controlled trial. Menopause. 2012 Oct 22

Ensrud KE, Joffe H, Guthrie KA, et al. Effect of **escitalopram on insomnia** symptoms and subjective sleep quality in healthy perimenopausal and postmenopausal women with hot flashes: a randomized controlled trial. Menopause. 2012 Mar 19.

Epperson CN, Shanmugan S, Kim DR, et al. New onset executive function difficulties at menopause: a possible role for **lisdexamfetamine**. Psychopharmacology (Berl). 2015 Jun 11.

Espeland MA, Shumaker SA, Leng I, et al. Long-term effects on cognitive function of postmenopausal hormone therapy prescribed to women aged 50 to 55 years (WHIMSY) [online June 24, 2013]. JAMA Intern Med. doi:10.1001/jamainternmed.2013.6827.

Espeland MA, Brinton RD, Manson JE, et al; **WHIMS-MRI2** Study Group. **Postmenopausal hormone therapy, type 2 diabetes** mellitus, and **brain volumes**. Neurology. 2015 Sep 29;85(13):1131-8.

Fagerholm R, Faltinova M, Aaltonen K, et al. **Family history** influences the **tumor characteristics and prognosis of breast cancers** developing during postmenopausal hormone therapy. Fam Cancer. 2018 Jul;17(3):321-331.

Farquhar CM, et al., the Cochrane HT Study Group. **Long term hormone therapy** for perimenopausal and postmenopausal women. Cochrane Database Syst Rev. 2005 Jul 20;3:CD004143.

Faubion SS, Sood R, Thielen JM, et al. **Caffeine** and menopausal symptoms: what is the association? Menopause. 2014 Jul 21.

FDA Concern over Bio-Identicals Jan/08: **Bio-Identicals: Sorting Myths from Facts** http://www.fda.gov/consumer/updates/bioidenticals010908.html.

Freedman RR, Kruger ML, Tancer ME. **Escitalopram** treatment of menopausal hot flashes. Menopause. 2011 Apr 30. (not effective)

Freeman Ellen W., Guthrie Katherine A., Caan Bette, et al. Efficacy of **Escitalopram for Hot Flashes** in Healthy Menopausal Women: A Randomized Controlled Trial. JAMA. 2011;305(3):267-274.doi:10.1001/jama.2010.2016.

Freeman EW et al. **Duration of menopausal hot flushes** and associated risk factors. Obstet Gynecol 2011 May; 117:1095.

Freeman EW, Sammel MD, Sanders RJ. **Risk of long-term hot flashes** after natural menopause: evidence from the Penn Ovarian Aging Study cohort. Menopause. 2014 Jan 27.

Freeman EW, Sammel MD, Gross SA, Pien GW. **Poor sleep in relation to natural menopause**: a population-based 14-year follow-up of midlife women. Menopause. 2014 Dec 29.

Furness S, Roberts H, Marjoribanks J, et al. Hormone therapy in postmenopausal women and risk of **endometrial hyperplasia**. Cochrane Database Syst Rev. 2012 Aug 15;8:CD000402. Hormone therapy for postmenopausal women with an intact uterus should comprise both estrogen and progestogen to reduce the risk of endometrial hyperplasia.

Ford O, Lethaby A, et al. **Progesterone** for Premenstrual Syndrome. Cochrane Database Syst Rev. 2006 Oct 18;(4):CD003415. We could not say that progesterone helped women with PMS, nor that it was ineffective. Neither trial distinguished a subgroup of women who benefited.

Fournier A, Fritel X, Panjo H, et al. **Health characteristics of women** beginning postmenopausal hormone therapy: have they changed since the publication of the Women's Health Initiative? Menopause. 2014 Jul;21(7):687-93.

Franco OH, Chowdhury R, Troup J, et al. Use of **Plant-Based** Therapies and **Menopausal Symptoms**: A Systematic Review and Meta-analysis. JAMA. 2016 Jun 21;315(23):2554-63.

Galvan T, Camuso J, Sullivan K, et al. Association of **estradiol with sleep apnea** in **depressed** perimenopausal and postmenopausal women: a preliminary study. Menopause. 2016 Sep 19.

Garcia MK, Graham-Getty L, Haddad R, et al. Systematic review of **acupuncture to control hot flashes** in cancer patients. Cancer. 2015 Nov 15;121(22):3948-58.

Garcia MK, Graham-Getty L, Haddad R, et al. Systematic review of **acupuncture** to control hot flashes in cancer patients. Cancer. 2015 Nov 15;121(22):3948-58.

Gartlehner G, Patel SV, Feltner C, et al. **Hormone therapy for the primary prevention of chronic conditi**ons in postmenopausal women: evidence report and systematic review for the US Preventive Services Task Force **USPSTF** [Dec 12, 2017].JAMA. doi:10.1001/jama.2017 .16952

Gartoulla P, Davis SR, Worsley R, et al. Use of **complementary and alternative medicines** for menopausal symptoms in Australian women aged 40-65 years. Med J Aust. 2015 Aug 3;203(3):146.

Gartoulla P, Worsley R, Bell RJ, Davis SR. Moderate to severe **vasomotor and sexual symptoms remain problematic for women aged 60 to 65 years**. Menopause. 2015;22:694-701.

Gass ML, Maki PM, Shifren JL, et al. **NAMS** supports judicious use of **systemic hormone therapy for women aged 65 years and older**. Menopause. 2015 Jul;22(7):685-6.

Gass M, Larson J, Cochrane B, et al. **Sexual activity and vaginal symptoms** in the postintervention phase of the Women's Health Initiative Hormone Therapy Trials. Menopause. 2017 Nov 13.

Gast GCM, Pop VJM, Samsioe GN, et al. **Vasomotor menopausal symptoms** are associated with **increased risk of coronary heart disease**. Menopause 2011; 18:146-151.

Gaudard AM, Silva de Souza S, Puga ME, et al. **Bioidentical hormones for women with vasomotor symptoms**. Cochrane Database Syst Rev. 2016 Aug 1;8:CD010407. There was low to moderate quality evidence that BHT in various forms and doses is more effective than placebo for treating moderate to severe menopausal hot flushes. There was low to moderate quality evidence of higher rates of adverse effects such as headache, vaginal bleeding, breast tenderness and skin reactions in the BHT group. There was some evidence to suggest that higher doses of BHT are associated with greater effectiveness but also with higher risk of adverse effects. Although all the included studies used unopposed estrogen, it is recommended best practice to use progestogen therapy in women with a uterus taking estrogen in order to avoid endometrial hyperplasia, regardless of the source of the estrogen. No data are yet available about the safety of BHT with regard to long-term outcomes such as heart attack, stroke and breast cancer.There was no good evidence of a difference in effectiveness between BHT and CEE, and findings with regard to adverse effects were inconsistent. The quality of the evidence was too low to reach any firm conclusions.The main limitations in the quality of the evidence were study risk of bias (mainly due to poor reporting of methods), imprecision and lack of data suitable for analysis.

Genazzani AR et al. Effect of 1-year, low-dose **DHEA** therapy (10mg daily) on climacteric symptoms and female sexuality. Climacteric. 2011 Dec;14(6):661-8.

mg genistein plus calcium, vitamin D(3), and a healthy diet was associated with favorable effects on both glycemic control and some cardiovascular risk markers in a cohort of osteopenic, postmenopausal women. D'Anna R, Cannata ML, Atteritano M, et al. Effects of the phytoestrogen genistein on hot flushes, endometrium, and vaginal epithelium in postmenopausal women: a 1-year randomized, double-blind, placebo-controlled study. Menopause. 2007 Jul-Aug;14(4):648-55. The phytoestrogen genistein has been shown to be effective on vasomotor symptoms without an adverse effect on endometrium. Marini H, Minutoli L, Polito F, et al. Effects of the phytoestrogen genistein on bone metabolism in osteopenic postmenopausal women: a randomized trial. Ann Intern Med. 2007 Jun 19;146(12):839-47. Summary for patients in: Ann Intern Med. 2007 Jun 19;146(12):I34. Twenty-four months of tx with genistein has positive effects on BMD in osteopenic postmenopausal women.

Georgakis MK, Thomopoulos TP, Diamantaras AA, et al. Association of **Age at Menopause and Duration of Reproductive Period With Depression After Menopause**: A Systematic Review and Meta-analysis. JAMA Psychiatry. 2016 Jan 6:1-12.

Getahun D, Nash R, Flanders WD, et al. **Cross-sex Hormones and Acute Cardiovascular Events in Transgender Persons**: A Cohort Study. Ann Intern Med. 2018 Jul 10.

Geukes M et al. The impact of **menopausal symptoms on work** ability. Menopause 2012 Mar; 19:278.

Gibson CJ, Li Y, Bertenthal D, et al. Menopause **symptoms and chronic pain in a national sample of midlife women veterans**. Menopause. 2019 Mar 4.

Gleason CE, Dowling NM, Wharton W, et al. Effects of **Hormone Therapy on Cognition and Mood** in Recently Postmenopausal Women: Findings from the Randomized, Controlled **KEEPS**-Cognitive and Affective Study. PLoS Med. 2015 Jun 2;12(6):e1001833.

Goldman RD. Child Health Update: **Estrogen cream for labial adhesion in girls**. Can Fam Physician. 2013 Jan;59(1):37-8.

Gomes MP, Deitcher SR. Risk of venous thromboembolic disease associated with hormonal contraceptives and hormone replacement therapy: a clinical review. Arch Intern Med. 2004 Oct 11;164(18):1965-76.

Goodwin JW, Green SJ, et al Phase III randomized placebo-controlled trial of two doses of **megestrol** acetate as treatment for menopausal symptoms in women with breast cancer: Southwest Oncology Group Study 9626. J Clin Oncol. 2008 Apr 1;26(10):1650-6. MA significantly reduced vasomotor symptoms with durable benefit over 6 months. MA 20 mg/d is the preferred dose. There was no significant impact on other menopausal symptoms.

Gordon JL, et al. Efficacy of **transdermal estradiol and micronized progesterone** in the prevention of **depressive symptoms** in the menopause transition: a randomized clinical trial [online Jan 10, 2018].JAMA Psychiatry. doi:10.1001/jamapsychiatry.2017.3998.

Gordon PR, et al. **Sertraline** to treat hot flashes: a randomized controlled, double-blind, crossover trial in a general population. Menopause. 2006 Jul-Aug;13(4):568-75.

Goundry B, Bell L, Langtree M, Moorthy A. Diagnosis and management of **Raynaud's phenomenon**. BMJ. 2012 Feb 7;344:e289.

Grady D. Clinical practice. **Management of menopausal symptoms**. N Engl J Med. 2006 Nov 30;355(22):2338-47.

Grady D, Cohen B, Tice J, et al. **Ineffectiveness of sertraline** for treatment of menopausal hot flushes: a randomized controlled trial. N=99 6weeks. Obstet Gynecol. 2007 Apr;109(4):823-30. Treatment with sertraline did not improve hot flush frequency or severity in generally healthy perimenopausal and postmenopausal women, but was associated with bothersome side effects. (InfoPOEMs: Sertraline is no better than placebo for the treatment of menopausal hot flushes. (LOE = 1b))

Grant MD, Marbella A, Wang AT, et al. **Menopausal Symptoms**: Comparative Effectiveness of Therapies **AHRQ Comparative Effectiveness** Reviews. Rockville (MD): Agency for Healthcare Research and Quality (US); 2015 Mar. Report No.: 147(15)-EHC005-EF. Women experiencing symptoms of menopause can consider a number of potential treatments of varying efficacy. From a large body of evidence, there is considerable certainty that estrogens are the most effective treatment for relieving vasomotor symptoms and are accompanied by the greatest improvement in quality-of-life measures. For other common symptoms-psychological, urogenital, and sleep disturbance-although estrogens are effective, some nonhormonal agents compare favorably. Estrogens are accompanied by potential long-term harms that require consideration. There is limited evidence on the potential consequences of long-term use of nonhormonal agents when those agents are used to treat menopausal symptoms.

Gray KE, Katon JG, LeBlanc ES, et al. **Vasomotor symptom characteristics**: are they risk factors for **incident diabetes**? Menopause. 2017 Dec 4.

Green SM, Donegan E, Frey BN, et al. **Cognitive behavior therapy for menopausal symptoms** (CBT-Meno): a randomized controlled trial. Menopause. 2019 May 15.

Greendale GA, Ishii S, Huang MH, et al. Predicting the **Timeline to the Final Menstrual Period**: The Study of Women's Health Across the Nation. J Clin Endocrinol Metab. 2013 Mar 26.

Grindler NM, Allsworth JE, Macones GA, et al. **Persistent organic pollutants and early menopause** in u.s. Women. PLoS One. 2015 Jan 28;10(1):e0116057.

Grodstein F, Manson JE, et al. Postmenopausal hormone therapy and stroke: role of time since menopause and age at initiation of hormone therapy. Arch Intern Med. 2008 Apr 28;168(8):861-6. (Nurses' Health Study) Hormone therapy is associated with an increased **risk of stroke**, and this increased risk does not appear to be related to the timing of the initiation of HT. In younger women, with lower stroke risk, the attributable risk of stroke owing to hormone use is modest and might be minimized by lower doses and shorter treatment duration.

Guimaraes P, et al. **Progestin** negatively affects hearing in aged women. Proc Natl Acad Sci U S A. 2006 Sep 19;103(38):14246-9. Epub 2006 Sep 7.

Gupta A. **Hormone Therapy-Related Hot Flashes and Their Management**. JAMA Oncol. 2017 Dec 28.

Gurka MJ, Vishnu A, Santen RJ, et al. Progression of **Metabolic Syndrome** Severity During the Menopausal Transition. J Am Heart Assoc. 2016 Aug 3;5(8)

Guthrie KA, LaCroix AZ, Ensrud KE, et al. Pooled Analysis of Six Pharmacologic and **Nonpharmacologic Interventions for Vasomotor Symptoms**. Obstet Gynecol. 2015 Aug;126(2):413-22.

Guthrie KA et al. Effects of **pharmacologic and nonpharmacologic interventions on insomnia symptoms and subjective sleep quality in women with hot flashes**: A pooled analysis of individual participant data from 4 MsFLASH trials. Sleep 2017 Nov 20;

Haimov-Kochman R, et al. Gradual discontinuation of hormone therapy does not prevent the reappearance of climacteric symptoms: a randomized prospective study. Menopause. 2006 May 25; [Epub ahead of print]

Haimov-Kochman R, Hochner-Celnikier D. Hot flashes revisited: pharmacological and herbal options for hot flashes management. What does the evidence tell us? Acta Obstet Gynecol Scand. 2005 Oct;84(10):972-9. CONCLUSIONS: A critical review of the literature shows that progesterone may have an independent effect on relieving hot flashes. New nonhormonal agents such as selective serotonin-uptake-inhibitor anti-depressants and a new anti-convulsant gabapentin yielded promising results on small well-conducted studies. Isoflavone's effect on hot flashes is variable and inconsistent, and only modest and delayed improvement of symptoms could be expected by BC and vitamin E. There are insufficient data on the other herbal alternative therapies at this time. Well-designed large studies are needed to further explore new modalities of treatment.

Hall E, Frey BN, Soares CN. **Non-hormonal treatment strategies for vasomotor symptoms**: a critical review. Drugs. 2011 Feb 12;71(3):287-304. doi: 10.2165/11585360-000000000-00000.

Hall PS et al. **Reproductive factors** and incidence of **heart failure** hospitalization in the Women's Health Initiative. J Am Coll Cardiol 2017 May 15.

Harman SM, Black DM, Naftolin F, et al. **Arterial Imaging** Outcomes and Cardiovascular Risk Factors in **Recently Menopausal Women**: A Randomized Trial. Ann Intern Med. 2014 Jul 29.

Hautamäki H, Haapalahti P, Savolainen-Peltonen H, et al. **Premenstrual symptoms in fertile age** are associated with impaired quality of life, but not hot flashes, in recently postmenopausal women. Menopause. 2014 May 12.

Hayes Laura P, Carroll Dana G, Kelley Kristi W. Use of **Gabapentin for the Management of Natural or Surgical Menopausal** Hot Flashes. Articles Ahead of Print published 22 February 2011, DOI 10.1345/aph.1P366.

He J, Gu D, Wu X, Chen J, Duan X, Chen J, Whelton PK. Effect of **soybean** protein on blood pressure: a randomized, controlled trial. Ann Intern Med. 2005 Jul 5;143(1):1-9. Summary for patients in: Ann Intern Med. 2005 Jul 5;143(1):I11.

Health Canada Dec/05 Notice to Discontinue **Climacteron** http://www.hc-sc.gc.ca/dhp-mps/alt_formats/hpfb-dgpsa/pdf/medeff/climacteron_hpc-cps_e.pdf

Health Canada Aug/06 & Jan/10 is advising consumers about a possible link between health products containing herbal medicine **black cohosh** and liver damage. A number of international case reports of liver damage suspected to be associated with the use of black cohosh, including three case reports in Canada and one published case of death in the United States. http://www.hc-sc.gc.ca/ahc-asc/media/advisories-avis/2006/2006_72_e.html , http://www.hc-sc.gc.ca/dhp-mps/medeff/bulletin/carn-bcei_v20n1-eng.php#_Black_cohosh_products

Health Canada Jan/08 is warning Canadians not to use the unauthorized product **RGC-RMC Rheumax Capsule** (batch number REM1-SI93016N). This batch of RGC-RMC Rheumax Capsule has been found to contain **progesterone**, a steroid hormone that can have adverse effects on the brain, breast and skin and should only be taken if prescribed by a health professional.

Health Canada Dec/13 General Nutrition Centres Company (GNC), in consultation with Health Canada, is voluntarily recalling its natural health product "**Women's Phytoestrogen Formula**" – used for the relief of menopausal symptoms – due to possible contamination with chloramphenicol.

Health Canada May/14 has requested that Christmas Natural Foods Ltd. stop selling and recall its unauthorized health product, **Heartland Natural Wild Yam Moisturizing Cream**, after testing conducted by the Department identified a undisclosed prescription drug ingredient, progesterone.

Health Canada Oct/16 FASLODEX (**fulvestrant**) can interfere with antibody based **estradiol measurement** by immunoassay due to structural similarity of fulvestrant and estradiol. This can result in falsely elevated estradiol levels.

Henderson VW, St John JA, Hodis HN, et al; For the **WISH** Research Group. Long-term **soy isoflavone supplementation** and cognition in women: A randomized, controlled trial. Neurology. 2012 Jun5;78(23):1841-1848.

Henderson VW, St John JA, Hodis HN, et al. **Cognitive effects** of **estradiol** after menopause: A randomized trial of the timing hypothesis. Neurology. 2016 Jul 15

Herber-Gast GC, Mishra GD. Early severe **vasomotor** menopausal symptoms are **associated with diabetes**. Menopause. 2014 Jan 6.

Hickey M, Elliott J, Davison SL. Hormone replacement therapy. BMJ. 2012 Feb 16;344:e763.

Hickey M, Szabo RA, Hunter MS. **Non-hormonal treatments for menopausal symptoms**. BMJ. 2017 Nov 23;359:j5101.

Hill DA, Hill SR. Counseling patients about **hormone therapy and alternatives for menopausal symptoms**. Am Fam Physician. 2010 Oct 1;82(7):801-7.

Hill DA, Crider M, Hill SR. **Hormone Therapy and Other Treatments for Symptoms of Menopause**. Am Fam Physician. 2016;94(11):884-889.

Hodis HN and Mack WJ.**Hormone therapy and risk of all-cause mortality in women treated with statins**. Menopause 2015 Apr; 22:363.

Hodis HN, Mack WJ, Henderson VW, et al. Vascular effects of **early versus late postmenopausal treatment** with estradiol. (**ELITE**) N Engl J Med 2016; 374:1221-31.

Holmberg L, Iversen OE, Rudenstam CM, et al. On behalf of the **HABITS** Study Group. **Increased Risk of Recurrence After Hormone Replacement Therapy in Breast Cancer Survivors**. J Natl Cancer Inst. 2008 Mar 25; [Epub ahead of print]. After extended follow-up, there was a clinically and statistically significant increased risk of a new breast cancer event in survivors who took HT.

Howard BV, et al. Low-fat dietary pattern and risk of cardiovascular disease: the Women's Health Initiative Randomized Controlled Dietary Modification Trial. JAMA. 2006 Feb 8;295(6):655-66.

Howard BV, et al. Low-fat dietary pattern and weight change over 7 years: the Women's Health Initiative Dietary Modification Trial. JAMA. 2006 Jan 4;295(1):39-49.

Huang Alison J.; Subak Leslee L.; Wing Rena et al; for the Program to Reduce Incontinence by Diet and Exercise Investigators An **Intensive Behavioral Weight Loss** Intervention and Hot Flushes in Women. Arch Intern Med. 2010;170(13):1161-1167.

Huang AJ, Grady D, Jacoby VL, Blackwell TL, Bauer DC, Sawaya GF. **Persistent hot flushes** in older postmenopausal women. Arch Intern Med. 2008 Apr 28;168(8):840-6. For a substantial minority of women, hot flushes are a persistent source of discomfort into the late postmenopausal years. Identification of risk factors for hot flushes may help guide evaluation and treatment in this population.

Huang AJ, Phillips S, Schembri M, et al. **Device-guided slow-paced respiration** for menopausal hot flushes: a randomized controlled trial. Obstet Gynecol. 2015 May;125(5):1130-8.

Huang H, Guo J, Chen Q, et al. The **Synergistic effects of vitamin D and estradiol deficiency** on metabolic syndrome in Chinese postmenopausal women. Menopause. 2019 Jun 10.

Hyland A, Piazza K, Hovey KM, et al. Associations between lifetime **tobacco exposure with infertility and age at natural menopause**: the **Women's Health Initiative** Observational Study. Tob Control. 2015 Dec 14.

Imtiaz B, Tuppurainen M, Rikkonen T, et al. **Postmenopausal hormone therapy and Alzheimer disease**: A prospective cohort study. Neurology. 2017 Feb 15.

Ismail SI, Bain C, Hagen S. Oestrogens for treatment or prevention of **pelvic organ prolapse** in postmenopausal women. Cochrane Database Syst Rev. 2010 Sep 8;9:CD007063. There was limited evidence from randomised controlled trials regarding the use of oestrogens for the prevention and management of pelvic organ prolapse. The use of local oestrogen in conjunction with pelvic floor muscle training before surgery may reduce the incidence of post-operative cystitis within four weeks after surgery.

Jacobson BC, Moy B, Colditz GA, Fuchs CS. Postmenopausal hormone use and symptoms of gastroesophageal reflux. Arch Intern Med. 2008 Sep 8;168(16):1798-804. Postmenopausal use of estrogens, selective estrogen receptor modulators, or OTC hormone preparations is associated with a greater likelihood of symptoms of **GERD**.

Jamilian M, Asemi Z. The Effects of **Soy Isoflavones** on Metabolic Status of Patients With Polycystic Ovary Syndrome. J Clin Endocrinol Metab. 2016 Aug 4:jc20161762.

Javed AA, Mayhew AJ, Shea AK, Raina P. Association Between **Hormone Therapy and Muscle Mass** in Postmenopausal Women: A Systematic Review and Meta-analysis. JAMA Netw Open. 2019 Aug 2;2(8):e1910154

Jin J. **Vaginal and Urinary Symptoms of Menopause**. JAMA. 2014 Apr 4; 317(13):1388.

Jin J. **Hormone Therapy for Primary Prevention of Chronic Conditions** in Postmenopausal Women. JAMA. 2017 Dec 12;318(22):2265.

Jing Z, Yang X, Ismail KM, Chen X, Wu T. Chinese herbal medicine for premenstrual syndrome. Cochrane Database Syst Rev. 2009 Jan 21;(1):CD006414. It is rare in PMS management that efficacy claims are substantiated by clinical trials. One of the identified trials was well designed and reported on the effectiveness of **Jingqianping** in the treatment of premenstrual syndrome Qiao 2002. However, currently there is insufficient evidence to support the use of chinese herbal medicine for PMS and further, well controlled, trials are needed before any final conclusions could be drawn.

Joffe H, Guthrie KA, LaCroix AZ, et al. **Low-Dose Estradiol** and the Serotonin-Norepinephrine Reuptake Inhibitor **Venlafaxine** for Vasomotor Symptoms: A Randomized Clinical Trial. JAMA Intern Med. 2014 May 26.

Jones ME, Schoemaker MJ, Wright L, et al. **Menopausal hormone therapy and breast cancer**: what is the true size of the increased risk? Br J Cancer. 2016 Aug 23;115(5):607-15.

Jung JH, Bang CH, Song GG, et al. **Knee osteoarthritis and menopausal hormone therapy** in postmenopausal women: a nationwide cross-sectional study. Menopause. 2018 Dec 21

Jurgens T, Whelan AM. Advising patients on the use of **natural health products to treat premenstrual** syndrome. Can Pharm J 2009;142:228-233.

Kannan P, Claydon LS. Some **physiotherapy** treatments may relieve **menstrual pain in women with primary dysmenorrhea**: a systematic review. J Physiother. 2014 Mar;60(1):13-21.

Kantarci K, Lowe VJ, Lesnick TG, et al. Early **Postmenopausal Transdermal 17β-Estradiol** Therapy and Amyloid-β Deposition. J Alzheimers Dis. 2016 May 7.

Kantarci K, Tosakulwong N, Lesnick TG, et al. Effects of **hormone therapy on brain structure**: A randomized controlled trial. (**KEEPS**) Neurology. 2016 Aug 30;87(9):887-96.

Kantarci K, Tosakulwong N, Lesnick TG, et al. **Brain structure and cognition** 3 years after the end of an early menopausal hormone therapy trial. Neurology. 2018 Apr 17;90(16):e1404-e1412.

Kaunitz AM, Manson JE. **Management of menopausal symptoms**. Obstet Gynecol. 2015;126:859-876.

Kaya C, Dincer Cengiz S, Cengiz B, Akgun G. The long-term effects of low-dose 17beta-**estradiol** and dydrogesterone hormone replacement therapy on 24-h ambulatory **blood pressure** in hypertensive postmenopausal women: a 1-year randomized, prospective study. Climacteric. 2006 Dec;9(6):437-45.

Keaney JF Jr, Solomon CG. **Postmenopausal Hormone Therapy and Atherosclerosis--Time Is of the Essence**. N Engl J Med. 2016 Mar 31;374(13):1279-80

Kerlikowske K, Cook AJ, Buist DS, et al. **Breast Cancer Risk by Breast Density**, Menopause, and Postmenopausal Hormone Therapy Use. J Clin Oncol. 2010 Jul 19.

Kioumourtzoglou MA, Coull BA, O'Reilly ÉJ, et al. Association of **Exposure to Diethylstilbestrol During Pregnancy** With Multigenerational Neurodevelopmental Deficits. JAMA Pediatr. 2018 May 21.

Klein DA, Paradise SL, Goodwin ET, **Caring for Transgender and Gender-Diverse Persons: What Clinicians Should Know**. Am Fam Physician. 2018; 98(11): 645-653.

Kling JM, Manson JE, Naughton MJ, et al. Association of **sleep disturbance** and **sexual function** in postmenopausal women. Menopause. 2017 Jan 30.

Korhonen K, Auvinen A, Lyytinen H, et al. A nationwide cohort study on the incidence of **meningioma** in women using postmenopausal hormone therapy in Finland. Am J Epidemiol. 2012 Feb 15;175(4):309-14.

Kornstein SG, Jiang Q, Reddy S, Musgnung JJ, Guico-Pabia CJ. Short-term efficacy and safety of **desvenlafaxine** in a randomized, placebo-controlled study of perimenopausal and postmenopausal women with major depressive disorder. J Clin Psychiatry. 2010 Aug;71(8):1088-96.

Korownyk C, Allan GM, McCormack J. **Bioidentical hormone micronized progesterone**. Can Fam Physician. 2012 Jul;58(7):755.

Kotsopoulos J, Gronwald J, Karlan BY, et al. **Hormone Replacement Therapy** After **Oophorectomy and Breast Cancer Risk** Among BRCA1 Mutation Carriers. JAMA Oncol. 2018 Apr 19.

Kroenke CH, Caan BJ, Stefanick ML, et al. Effects of a **dietary intervention and weight change** on vasomotor symptoms in the Women's Health Initiative. Menopause. 2012 Jul 9.

Kuh D, Cooper R, Moore A, et al. Age at menopause and lifetime **cognition**: Findings from a British birth cohort study. Neurology. 2018 Apr 11.

Labrie F, Archer DF, Koltun W, et al; members of the VVA Prasterone Research Group. Efficacy of **intravaginal dehydroepiandrosterone (DHEA)** on moderate to severe **dyspareunia** and vaginal dryness, symptoms of vulvovaginal atrophy, and of the genitourinary syndrome of menopause. Menopause. 2015 Dec 28.

Lacey JV Jr, et al. Menopausal hormone therapy and **ovarian cancer risk** in the National Institutes of Health-AARP Diet and Health Study Cohort. J Natl Cancer Inst. 2006 Oct 4;98(19):1397-405. Long durations of use of unopposed estrogen and of estrogen plus progestin, especially sequential regimens, are associated with increased ovarian cancer risk.

Lambiase MJ, Thurston RC. **Physical activity and sleep** among midlife women with vasomotor symptoms. Menopause. 2013 Sep;20(9):946-52.

Lammerink EA, de Bock GH, Schröder CP, Mourits MJ. The management of **menopausal** symptoms in **breast cancer survivors**: A case-based approach. Maturitas. 2012 Aug 7.

Langer RD. The **evidence base for HRT**: what can we believe? Climacteric. 2017 Apr;20(2):91-96

Laughlin-Tommaso SK, Khan Z, Weaver AL, et al. **Cardiovascular and metabolic morbidity after hysterectomy with ovarian conservation**: a cohort study. Menopause. 2017 Dec 28.

Leach MJ, Moore V. **Black cohosh** (Cimicifuga spp.) for menopausal symptoms. Cochrane Database of Systematic Reviews 2012, Issue 9. Art. No.: CD007244. DOI: 10.1002/14651858.CD007244.pub2. There is currently insufficient evidence to support the use of black cohosh for menopausal symptoms.

LeBlanc ES, Hedlin H, Qin F, et al. **Calcium and vitamin D supplementation** do not influence menopause-related symptoms: Results of the Women's Health Initiative Trial. Maturitas. 2015 May 22.

Lee AW, Ness RB, Roman LD, et al. Association Between Menopausal **Estrogen-Only Therapy and Ovarian Carcinoma Risk**. Obstet Gynecol. 2016 May;127(5):828-36.

Lee S, Kolonel L, Wilkens L, Wan P, Henderson B, Pike M. Postmenopausal hormone therapy and **breast cancer** risk: The multiethnic cohort. Int J Cancer. 2005 Sep 16; [Epub ahead of print]

Lemaitre RN, Weiss NS, Smith NL, Psaty BM, Lumley T, Larson EB, Heckbert SR. **Esterified estrogen and conjugated equine estrogen** and the risk of incident myocardial infarction and stroke. Arch Intern Med. 2006 Feb 27;166(4):399-404.

Lenart BA, Lorich DG, Lane JM. **Atypical fractures of the femoral diaphysis** in postmenopausal women taking alendronate.N Engl J Med. 2008 Mar 20;358(12):1304-6.

Lesi G, Razzini G, Musti MA, et al. **Acupuncture** As an Integrative Approach for the Treatment of **Hot Flashes** in Women With Breast Cancer: A Prospective Multicenter Randomized Controlled Trial (AcCliMaT). J Clin Oncol. 2016 Mar 28.

Lethaby A, Suckling J, Barlow D, et al. Hormone replacement therapy in postmenopausal women: **endometrial hyperplasia and irregular bleeding**. Cochrane Database Syst Rev. 2004;(3):CD000402.

Lethaby A, Hogervorst E, Richards M, Yesufu A, Yaffe K. Hormone replacement therapy for **cognitive function** in postmenopausal women. Cochrane Database Syst Rev. 2008 Jan 23;(1):CD003122. There is good evidence that both ERT and HRT do not prevent cognitive decline in older postmenopausal women when given as short term or longer term (up to five years) therapy. It is not known whether either specific types of ERT or HRT have specific effects in subgroups of women, although there was evidence that combined hormone therapy in similarly aged women was associated with a decrement in a number of verbal memory tests and a small improvement in a test of figural memory.

Lethaby AE, Brown J, Marjoribanks J, Kronenberg F, Roberts H, Eden J. **Phytoestrogens** for vasomotor menopausal symptoms. Cochrane Database Syst Rev. 2007 Oct 17;(4):CD001395.

Lethaby A, Marjoribanks J, Kronenberg F, et al. **Phytoestrogens** for menopausal vasomotor symptoms. Cochrane Database Syst Rev. 2013 Dec 10;12:CD001395. No conclusive evidence shows that phytoestrogen supplements effectively reduce the frequency or severity of hot flushes and night sweats in perimenopausal or postmenopausal women, although benefits derived from concentrates of genistein should be further investigated.

Lethaby A, Ayeleke RO, Roberts H. **Local oestrogen for vaginal atrophy** in **postmenopausal** women. Cochrane Database of Systematic Reviews 2016, Issue 8. Art. No.: CD001500. There was no evidence of a difference in efficacy between the various intravaginal oestrogenic preparations when compared with Each other. However, there was low-quality evidence that intra-vaginal oestrogenic preparations improve the symptoms of vaginal atrophy in postmenopausal women when compared to placebo. There was low-quality evidence that oestrogen cream may be associated with an increase in endometrial thickness compared to oestrogen ring; this may have been due to the higher doses of cream used. However there was no evidence of a difference in the overall body of evidence in adverse events between the various oestrogenic preparations compared with each other or with placebo.

Levis S, Strickman-Stein N, Ganjei-Azar P, et al. **Soy isoflavones** in the prevention of menopausal bone loss and menopausal symptoms: a randomized, double-blind trial. (SPARE) Arch Intern Med. 2011;171 (15):1363-1369. (200mg for 2yrs did not prevent bone loss or menopausal symptoms)

Li L, Lv Y, Xu L, et al. Quantitative Efficacy of **Soy Isoflavones on Menopausal Hot Flashes**. Br J Clin Pharmacol. 2014 Oct 15.

Libby V, Lee M, Liu JH. **Transgender health**: Hormonal management at 50 years and beyond. Maturitas. 2019 Aug;126:34-37.

Lindblad BE, Håkansson N, Philipson B, Wolk A. Hormone Replacement Therapy in Relation to Risk of **Cataract** Extraction A Prospective Study of Women. Ophthalmology. 2010 Mar;117(3):424-430. Epub 2010 Jan 4.

Lindh-Åstrand L et al. A randomized controlled study of **taper-down or abrupt discontinuation** of hormone therapy in women treated for vasomotor symptoms. Menopause 2010 Jan/Feb; 17:72.

Liu Z, Ai Y, Wang W, et al. **Acupuncture for symptoms in menopause transition: a randomized controlled trial.** Am J Obstet Gynecol. 2018 Oct;219(4):373.e1-373.e10.

Loibl S, Schwedler K, von Minckwitz G, Strohmeier R, Mehta K, Kaufmann M. **Venlafaxine** 37.5mg bid is superior to clonidine 0.075 mg twice a day (n=64, 4 weeks) as treatment of hot flashes in breast cancer patients--a double-blind, randomized study. Ann Oncol. 2007 Apr;18(4):689-93. Epub 2007 Jan 17. Venlafaxine is significantly more effective in reducing the frequency of hot flashes in breast cancer patients than clonidine.

Loprinzi CL, Sloan J, Stearns V, et al. Newer antidepressants and gabapentin for hot flashes: an individual patient pooled analysis. J Clin Oncol. 2009 Jun 10;27(17):2831-7. Epub 2009 Mar 30. Some newer antidepressants and gabapentin, within 4 weeks of therapy initiation, decrease hot flashes more than placebo.

Lorenz TK, McGregor BA, Vitzthum VJ. Presence of **young children at home** may moderate development of **hot flashes** during the menopausal transition. Menopause. 2014 Sep 15.

Low Dog T. Menopause: a review of **botanical** dietary supplements. Am J Med. 2005 Dec 19;118(12 Suppl 2):98-108.

Liu B, Beral V, Balkwill A, Green J, Sweetland S, Reeves G; for the Million Women Study Collaborators. **Gallbladder disease and use of transdermal** versus oral hormone replacement therapy in postmenopausal women: prospective cohort study. BMJ. 2008 Jul 10;337:a386. doi: 10.1136/bmj.a386. Gallbladder disease is common in postmenopausal women and use of hormone replacement therapy increases the risk. Use of transdermal therapy rather than oral therapy over a five year period could **avoid one cholecystectomy in every 140 users**.

Liu B. Is **transdermal menopausal** hormone therapy a safer option than oral therapy? CMAJ. 2013 Apr 16;185(7):549-50.

Løkkegaard E, Andreasen AH, Jacobsen RK, Nielsen LH, Agger C, Lidegaard O. Hormone therapy and risk of myocardial infarction: a national register study. Eur Heart J. 2008 Sep 30. [Epub ahead of print] In a National cohort study, we found that HT **regimen and route** of application could modify the influence of HT on the risk of MI.

Lokkegaard E, Nielsen LH, Keiding N. **Risk of Stroke** with Various Types of Menopausal Hormone Therapies-A National Cohort Study. Stroke.2017;48:2266-2269

Lund KS, Siersma V, Brodersen J, Waldorff FB. Efficacy of a standardised **acupuncture approach for women with bothersome menopausal symptoms**: a pragmatic randomised study in primary care (the ACOM study). BMJ Open. 2019 Feb 19;9(1):e023637.

Lyytinen H, Pukkala E, Ylikorkala O. **Breast cancer** risk in postmenopausal women using **estrogen-only** therapy. Obstet Gynecol. 2006 Dec;108(6):1354-60. Estradiol for 5 years or more, either orally or transdermally, means 2-3 extra cases of breast cancer per 1,000 women who are followed for 10 years. Oral estradiol use for less than 5 years, oral estriol, or vaginal estrogens were not associated with a risk of breast cancer.

Maalouf Naim M.; Sato Alicia H.; Welch Brian J.; et al. Postmenopausal Hormone Use and the Risk of **Nephrolithiasis**: Results From the Women's Health Initiative Hormone Therapy Trials. Arch Intern Med. 2010;170(18):1678-1685.

Mackenzie R, et al. **Progesterone** for the prevention of **preterm birth** among women at increased risk: a systematic review and meta-analysis of randomized controlled trials. Am J Obstet Gynecol. 2006 May;194(5):1234-42. Epub 2006 Apr 21. InfoPOEMS – July 28, 2006: Bottom Line: Second-trimester progestational agents significantly reduce the risk of birth before 37 weeks' gestation for women at increased risk of preterm birth. Reduction in perinatal mortality or serious morbidity has not yet been established. (LOE = 1a-)

Madalinska JB, et al. The impact of hormone replacement therapy on menopausal symptoms in younger high-risk women **after prophylactic salpingo-oophorectomy**. J Clin Oncol. 2006 Aug 1;24(22):3576-82.

Maki PM, Rubin LH, Fornelli D, et al. Effects of botanicals and combined hormone therapy on cognition in postmenopausal women. Menopause. 2009 Jul 8. [Epub ahead of print] PubMed PMID: 19590458. Results indicate that a **red clover** (phytoestrogen) supplement or **black cohosh** has no effects on cognitive function. CEE/MPA reduces objective hot flashes but worsens some aspects of verbal memory.

Management of symptomatic **vulvovaginal atrophy**: 2013 position statement of The North American Menopause Society. Menopause. 2013 Sep;20(9):888-902.

Mann E, Smith MJ, Hellier J, et al. **Cognitive behavioural treatment** for women who have menopausal symptoms after breast cancer treatment (**MENOS 1**): a randomised controlled trial. Lancet Oncol 2012

Manson JE, Aragaki AK, Bassuk SS, et al. **Menopausal Estrogen-Alone Therapy** and Health Outcomes in Women With and Without Bilateral Oophorectomy: A Randomized Trial. Ann Intern Med. 2019 Sep 10.

Manson JE, Chlebowski RT, Stefanick ML, et al. Menopausal hormone therapy and health outcomes during the intervention and **extended poststopping phases of theWomen's Health Initiative**(WHI) randomized trials. JAMA. doi:10.1001/jama.2013.278040.

Manson JE, Kaunitz AM. **Menopause Management**--Getting Clinical Care Back on Track. N Engl J Med. 2016 Mar 3;374(9):803-6.

Mansoor H, Elgendy IY, Segal R, et al. **Duration of Reproductive Years and the Risk of Cardiovascular and Cerebrovascular Events** in Older Women: Insights from the National Health and Nutrition Examination Survey. J Womens Health (Larchmt). 2017 May 19.

Marjoribanks J, Brown J, O`Brien PM, et al. **Selective serotonin reuptake inhibitors for premenstrual syndrome**. Cochrane Database Syst Rev. 2013 Jun 7;6:CD001396. doi: 10.1002/14651858.CD001396.pub3.
SSRIs are effective in reducing the symptoms of PMS, whether taken in the luteal phase only or continuously. Adverse effects are relatively frequent, the most common being nausea and asthenia. Adverse effects are dose-dependent.

Marjoribanks J, Farquhar C, Roberts H, et al. **Long-term hormone therapy for perimenopausal and postmenopausal women**. Cochrane Database of Systematic Reviews 2017, Issue 1. Art. No.: CD004143. Women with intolerable menopausal symptoms may wish to weigh the benefits of symptom relief against the small absolute risk of harm arising from short-term use of low-dose HT, provided they do not have specific contraindications. HT may be unsuitable for some women, including those at increased risk of cardiovascular disease, increased risk of thromboembolic disease (such as those with obesity or a history of venous thrombosis) or increased risk of some types of cancer (such as breast cancer, in women with a uterus). The risk of endometrial cancer among women with a uterus taking oestrogen-only HT is well documented. HT is not indicated for primary or secondary prevention of cardiovascular disease or dementia, nor for prevention of deterioration of cognitive function in postmenopausal women. Although HT is considered effective for the prevention of postmenopausal osteoporosis, it is generally recommended as an option only for women at significant risk for whom non-oestrogen therapies are unsuitable. Data are insufficient for assessment of the risk of long-term HT use in perimenopausal women and in postmenopausal women younger than 50 years of age.

Marjoribanks J, Farquhar C, Roberts H, et al. **Long term hormone therapy for perimenopausal and postmenopausal women.**Cochrane Database Syst Rev. 2012 Jul 11;7:CD004143. HT is not indicated for primary or secondary prevention of cardiovascular disease or dementia, nor for preventing deterioration of cognitive function in postmenopausal women. Although HT is considered effective for the prevention of postmenopausal osteoporosis, it is generally recommended as an option only for women at significant risk, for whom non-oestrogen therapies are unsuitable. There are insufficient data to assess the risk of long term HT use in perimenopausal women or postmenopausal women younger than 50 years of age.

Marsh WK, Bromberger JT, Crawford SL, et al. **Lifelong estradiol exposure and risk of depressive symptoms** during the transition to menopause and postmenopause. Menopause. 2017 Jul 17.

Martin VT, Pavlovic J, Fanning KM, et al. Perimenopause and Menopause Are Associated With **High Frequency Headache** in Women With Migraine: Results of the American Migraine Prevalence and Prevention Study. Headache. 2016 Jan 21.

Matthews KA, Gibson CJ, El Khoudary SR, Thurston RC. Changes in **Cardiovascular Risk Factors by Hysterectomy Status with and without Oophorectomy**: Study of Women's Health across the Nation. J Am Coll Cardiol. 2013 May 15.

McClung MR. Osteopenia: to treat or not to treat? Ann Intern Med. 2005 May 3;142(9):796-7.

McGarry K, Geary M, Gopinath V. Beyond Estrogen: **Treatment Options for Hot Flashes**. Clin Ther. 2018 Sep 12.

McNamara M, Batur P, DeSapri KT. **In the Clinic: Perimenopause**. Ann Intern Med. 2015 Feb 3;162(3):ITC1.

McTiernan A, Martin CF, Peck JD, ET AL.; WHI Mammogram Density Study Investigators. Estrogen-plus-progestin use and mammographic density in postmenopausal women: women's health initiative randomized trial. J Natl Cancer Inst. 2005 Sep 21;97(18):1366-76.
CONCLUSIONS: Use of up to 2 years of estrogen plus progestin was associated with increases in mammographic density.

Medical Letter. Low dose **Transdermal Estrogens**. Aug 27,2007.

Medical Letter. Bioidentical Hormones. May 31, 2010.

Medical Letter. **Drugs for Menopausal Symptoms**. May 28, 2012.

Melisko ME, Goldman ME, Hwang J, et al. **Vaginal Testosterone Cream vs Estradiol Vaginal Ring for Vaginal Dryness** or **Decreased Libido in Women Receiving Aromatase Inhibitors** for Early-Stage **Breast Cancer**: A Randomized Clinical Trial. JAMA Oncol. 2016 Nov 10.

MHRA Dec/11 In response to an urgent notice issued by the MHRA, **Bee Health Ltd has agreed to stop marketing FSC Black Cohosh 1000 mg** due to concerns about the high dosage of black cohosh in the product. The MHRA advises consumers not to take the FSC Black Cohosh product as it equates to 50 times the dose approved for traditional herbal medicinal products used to relieve menopausal symptoms. It is not known what the risks or effects on the body could be associated with such a high level of Black Cohosh.

Mikkola TS, Tuomikoski P, Lyytinen H, et al. **Increased cardiovascular mortality risk in women discontinuing postmenopausal hormone therapy**. J Clin Endocrinol Metab. 2015 Sep 28:jc20151864.

Mikkola TS, Savolainen-Peltonen H, Tuomikoski P, et al. Reduced risk of **breast cancer mortality** in women using postmenopausal hormone therapy: a Finnish nationwide comparative study. Menopause. 2016 Jul 25.

Miller VM, Hodis HN, Lahr BD, et al. Changes in **carotid artery intima-media thickness 3 years after cessation of menopausal hormone therapy**: follow-up from the Kronos Early Estrogen Prevention Study. Menopause. 2018 Jul 16.

Mishra GD, Kuh D. **Health symptoms during midlife** in relation to menopausal transition: British prospective cohort study. BMJ 2012;344:e402.

Mishra GD, Pandeya N, Dobson AJ, et al. **Early menarche, nulliparity and the risk for premature and early natural menopause**. Hum Reprod.2017 Jan 24.

Mohammed K, Abu Dabrh AM, Benkhadra K, et al. **Oral vs transdermal estrogen therapy** and vascular events: a systematic review and meta-analysis. J Clin Endocrinol Metab. 2015;100:4012-4020.

Molano JR. **Hormone therapy and brain structure** in postmenopausal women. Neurology. 2016 Aug 30;87(9):e100-2

Mollard E, Pedro S, Chakravarty E, et al. The impact of **menopause on functional status in women with rheumatoid arthritis**. Rheumatology (Oxford). 2018 Jan 29.

Moore HC, Unger JM, Phillips KA, et al; the POEMS/S0230 Investigators. **Goserelin for Ovarian Protection** during Breast-Cancer Adjuvant Chemotherapy. N Engl J Med. 2015 Mar 5;372(10):923-932

Morch Lina Steinrud; Lokkegaard Ellen; Andreasen Anne Helms; et al. Hormone Therapy and **Ovarian Cancer**. JAMA. 2009;302(3):298-305.

Motivala A, Pitt B. **Drospirenone** for oral contraception and hormone replacement therapy : are its cardiovascular risks and benefits the same as other progestogens? Drugs. 2007;67(5):647-55. Our review of the literature suggests that because of its anti-mineralocorticoid effects, drospirenone in conjunction with estrogen may prevent the development of cardiovascular disease in both pre- and post-menopausal women.

Moyer AM, de Andrade M, Faubion SS, et al. **SLCO1B1 genetic variation and hormone therapy** in menopausal women. Menopause. 2018 May 7.

Muka T, Oliver-Williams C, Kunutsor S, et al. Association of **age at onset of menopause and time since onset of menopause with cardiovascular outcomes**, intermediate vascular traits, and all-cause mortality: a systematic review and meta-analysis [online Sept 14, 2016]. JAMA Cardiol. doi:10.1001/jamacardio.2016.2415.

Muka T, Asllanaj E, Avazverdi N, et al. **Age at natural menopause and risk of type 2 diabetes**: a prospective cohort study. Diabetologia. 2017 Jul 18

Mytton J, Evison F, Chilton PJ, et al. **Removal of all ovarian tissue versus conserving ovarian tissue at time of hysterectomy** in premenopausal patients with benign disease: study using routine data and data linkage. BMJ. 2017 Feb 6;356:j372.

NAMS: North American Menopause Society. The **North American Menopause Society Statement on Continuing Use of Systemic Hormone Therapy After Age 65**. Menopause. 2015 Jul;22(7):693.

NAMS: The **2017 hormone therapy position statement of The North American Menopause Society**. Menopause. 2017 Jun 22.

National Institutes of Health. National Institutes of Health State-of-the-Science Conference statement: **management of menopause-related** symptoms. Ann Intern Med. 2005 Jun 21;142(12 Pt 1):1003-13. Epub 2005 May 27.

Nedrow A, Miller J, Walker M, Nygren P, Huffman LH, Nelson HD. **Complementary and alternative** therapies for the management of menopause-related symptoms: a systematic evidence review. Arch Intern Med. 2006 Jul 24;166(14):1453-65.

Nelson HD, et al. **Nonhormonal therapies for menopausal hot flashes: systematic review** and meta-analysis. JAMA. 2006 May 3;295(17):2057-71. The SSRIs or SNRIs, clonidine, and gabapentin trials provide evidence for efficacy; however, effects are less than for estrogen, few trials have been published and most have methodological deficiencies, generalizability is limited, and adverse effects and cost may restrict use for many women. These therapies may be most useful for highly symptomatic women who cannot take estrogen but are not optimal choices for most women. (InfoPOEMs: Evidence supports the nonhormonal treatment of menopausal hot flashes with paroxetine (Paxil), clonidine (Catapres), gabapentin (Neurontin), and soy isoflavone extract. The overall effect size of all nonhormonal treatments is less than that of estrogen. Treatment should be individualized according to symptom severity and risk profiles. (LOE = 1a-)) (Reddy SY, et al. Gabapentin, Estrogen, and Placebo for Treating Hot Flushes: A Randomized Controlled Trial. Obstet Gynecol. 2006 Jul;108(1):41-48. Despite the small scale of this study, (12 week n=60) gabapentin appears to be as effective as estrogen in the treatment of postmenopausal hot flushes. (InfoPOEMs: In this small study, high-dose gabapentin (Neurontin) was as effective as the usual dose of conjugated equine estrogens (Premarin) for the treatment of menopausal vasomotor symptoms. Larger studies are needed to confirm this result. (LOE = 1b))) (Loprinzi CL, et al. Phase III comparison of depomedroxyprogesterone acetate to venlafaxine for managing hot flashes: North Central Cancer Treatment Group Trial N99C7. J Clin Oncol. 2006 Mar 20;24(9):1409-14. Epub 2006 Feb 27.)(Butt DA, Lock M, Lewis JE, Ross S, Moineddin R. Gabapentin for the treatment of menopausal hot flashes: a randomized controlled trial. Menopause. 2007 Oct 2; [Epub ahead of print]) Loprinzi CL, Sloan J, Stearns V, et al. Newer antidepressants and gabapentin for hot flashes: an individual patient pooled analysis. J Clin Oncol. 2009 Jun 10;27(17):2831-7. Epub 2009 Mar 30. Some newer antidepressants and gabapentin, within 4 weeks of therapy initiation, decrease hot flashes more than placebo.

Nelson HD. **Menopause**. Lancet. 2008 Mar 1;371(9614):760-70.

Nelson HD, Walker M, Zakher B, Mitchell J. **Menopausal Hormone Therapy for the Primary Prevention of Chronic Conditions**: A Systematic Review to Update the U.S. Preventive Services Task Force Recommendations (**USPSTF**). Ann Intern Med. 2012 May 28.

Newman-Casey PA, Talwar N, Nan B, et al. The Potential Association Between Postmenopausal Hormone Use and **Primary Open-Angle Glaucoma**. JAMA Ophthalmol. 2014 Jan 30.

Newton KM, Reed SD, Guthrie KA, et al. Efficacy of **yoga for vasomotor** symptoms: a randomized controlled trial. Menopause. 2013 Sep 16

NICE: National Institute for Health and Care Excellence. **Menopause: diagnosis and management of menopause. (NICE guideline 23.)** 2015. www.nice.org.uk/guidance/ng23.

Njor SH, Hallas J, Schwartz W, Lynge E, Pedersen AT. Type of hormone therapy and risk of **misclassification at mammography** screening. Menopause. 2010 Aug 19.

North American Menopause Society. Recommendations for **estrogen and progestogen use** in peri-and postmenopausal women: October 2004 position statement of The North American Menopause Society. Menopause. 2004 Nov-Dec;11(6 Pt 1):589-600. **North American Menopause Society Management of osteoporosis** in postmenopausal women: 2006 position statement of The North American Menopause Society. Menopause. 2006 May-Jun;13(3):340-67; quiz 368-9. (Utian WH, Archer DF, Bachmann GA, et al. Estrogen and progestogen use in postmenopausal women: July 2008 position statement of The North American Menopause Society. (**NAMS**) Menopause. **2008** Jul-Aug;15(4 Pt 1):584-602. http://www.menopause.org/PSHT08.pdf Recent data support the initiation of HT around the time of menopause to treat menopause-related symptoms; to treat or reduce the risk of certain disorders, such as osteoporosis or fractures in select postmenopausal women; or both. The benefit-risk ratio for menopausal HT is favorable close to menopause but decreases with aging and with time since menopause in previously untreated women.)

North American Menopause Society. **NAMS**: Management of **osteoporosis in postmenopausal women**: **2010** position statement of The North American Menopause Society. Menopause. **2010** Jan-Feb;17(1):25-54.

North American Menopause Society (**NAMS**). The **2012** hormone therapy position statement of the North American Menopause Society. Menopause 2012 Mar;19(3):257-71.

North American Menopause Society. The role of **local vaginal estrogen for treatment of vaginal atrophy** in postmenopausal women: **2007 position statement** of The North American Menopause Society. Menopause. 2007 May-Jun;14(3):370-1. The choice of therapy should be guided by clinical experience and patient preference. Progestogen is generally not indicated when low-dose estrogen is administered locally for vaginal atrophy. Data are insufficient to recommend annual endometrial surveillance in asymptomatic women using vaginal ET. Vaginal ET should be continued for women as long as distressful symptoms remain. For women treated for non-hormone-dependent cancer, management of vaginal atrophy is similar to that for women without a cancer history. For women with a history of hormone-dependent cancer, management recommendations are dependent upon each woman's preference in consultation with her oncologist.

North American Menopause Society. **NAMS**: **Estrogen and progestogen use** in postmenopausal women: 2010 position statement of The North American Menopause Society. Menopause. **2010** Feb 12. [Epub ahead of print] Recent data support the initiation of HT around the time of menopause to treat menopause-related symptoms; to treat or reduce the risk of certain disorders, such as osteoporosis or fractures in select postmenopausal women; or both. The benefit-risk ratio for menopausal HT is favorable for women who initiate HT close to menopause but decreases in older women and with time since menopause in previously untreated women. http://www.menopause.org/PSht10.pdf

North American Menopause Society. **NAMS**: **Nonhormonal management of menopause-associated vasomotor symptoms**: 2015 position statement of The North American Menopause Society. Menopause. 2015 Nov;22(11):1155-74.

North American Menopause Society. **NAMS**: The North American Menopause Society Statement on **Continuing Use of Systemic Hormone Therapy After Age 65**. Menopause. 2015 Jul;22(7):693.

Nota NM, Wiepjes CM, de Blok CJM, et al. The Occurrence of **Acute Cardiovascular Events in Transgender Individuals** Receiving Hormone Therapy: Results from a Large Cohort Study. Circulation. 2019 Feb 18.

Oates J. The Effect of **Yoga on Menstrual Disorders**: A Systematic Review. Altern Complement Med. 2017 Feb 16

Oliveira Filho RV, Antunes NJ, Ilha JO, et al. Pharmacokinetics and pharmacodynamics of **3 dosages of oestriol after continuous vaginal ring administration for 21 days in healthy, postmenopausal women**. Br J Clin Pharmacol. 2018 Nov 27.

Orleans RJ, Li L, Kim MJ, et al. FDA approval of **paroxetine for menopausal hot flushes**. N Engl J Med. 2014 May 8;370(19):1777-9.

Oskarsson V, Orsini N, Sadr-Azodi O, et al. Postmenopausal hormone replacement therapy and **risk of acute pancreatitis**: a prospective cohort study. CMAJ. 2014 Jan 27

Osmers R, Friede M, et al. Efficacy and safety of isopropanolic **black cohosh** extract for climacteric symptoms. Obstet Gynecol 2005; 105:1074-83. (InfoPOEMs: This study reports that isopropanolic black cohosh extract (Remifemin) at a dose of 20 mg twice daily is statistically more effective than placebo for the treatment of menopausal vasomotor symptoms. These results will probably be used to promote its use. However, the authors did not supply sufficient data to determine the extent of benefit or the number needed to treat. This evidence is insufficient to determine whether black cohosh has a clinically relevant effect in treating menopausal symptoms. (LOE = 1b-)) CONCLUSION: This isopropanolic extract of black cohosh root stock is effective in relieving climacteric symptoms, especially in early climacteric women.

Ouyang P, et al.; for the Estrogen And Graft Atherosclerosis Research (**EAGAR**) investigators. Randomized trial of hormone therapy in women after coronary bypass surgery Evidence of differential effect of hormone therapy on angiographic progression of disease in saphenous vein grafts and native coronary arteries. Atherosclerosis. 2006 Jan 23; [Epub ahead of print]

Palmert Mark R, Dunkel Leo. **Delayed Puberty**. N Engl J Med 2012; 366:443-453.

Panay N, Hamoda H, Arya R, Savvas M; on behalf of The British Menopause Society and Women's Health Concern. The **2013 British Menopause Society & Women's Health Concern recommendations on hormone replacement therapy**. Menopause Int. 2013 May 24.

Pandya KJ, Morrow GR, Roscoe JA, et al. **Gabapentin** for hot flashes in 420 women with breast cancer: a randomised double-blind placebo-controlled trial. Lancet. 2005 Sep 3-9;366(9488):818-24. Gabapentin is effective in the control of hot flashes at a dose of 900 mg/day, but not at a dose of 300 mg/day. This drug should be considered for treatment of hot flashes in women with breast cancer. (InfoPOEMs: Women with a history of breast cancer may obtain some relief from hot flashes with 900 mg gabapentin daily. The 300 mg daily dose was not effective. (LOE = 1b-))

Papadakis G, Hans D, Gonzalez-Rodriguez E, et al. The Benefit of Menopausal Hormone Therapy on **Bone Density and Microarchitecture Persists After its Withdrawal**. J Clin Endocrinol Metab. 2016 Nov 17:jc20162695.

Papadakis GE, Hans D, Rodriguez EG, et al. **Menopausal hormone therapy** is associated with reduced total and visceral **adiposity**, the OsteoLaus cohort. J Clin Endocrinol Metab. 2018 Mar 27.

Parker WH, Feskanich D, Broder MS, et al. Long-Term **Mortality Associated With Oophorectomy Compared With Ovarian Conservation** in the Nurses' Health Study. Obstet Gynecol. 2013 Apr;121(4):709-716.

Pattimakiel L, Thacker HL. Bioidentical hormone therapy: Clarifying the misconceptions. Cleve Clin J Med. 2011 Dec;78(12):829-36.

Peng W, Adams J, Sibbritt DW, et al. Critical review of **complementary and alternative medicine** use in menopause: focus on prevalence, motivation, decision-making, and communication. Menopause. 2013 Oct 7

Pharmacist's Letter. **Angeliq** (Estradiol & Drospirenone) Dec 2008.

Phillips TJ, Symons J, Menon S; HT Study Group. Does hormone therapy improve age-related skin changes in postmenopausal women? A randomized, double-blind, double-dummy, placebo-controlled multicenter study assessing the effects of norethindrone acetate and ethinyl estradiol in the improvement of mild to moderate age-related skin changes in postmenopausal women. J Am Acad Dermatol. 2008 Jul 12. [Epub ahead of print] Low-dose hormone therapy for 48 weeks in postmenopausal women did not significantly alter mild to moderate age-related facial skin changes. This study found **no benefit** for hormone replacement therapy (HRT) with progesterone and estrogen in reducing age-related adverse **skin changes** (ie, wrinkling and crows' feet) in postmenopausal women. (LOE = 1b-)

Pinkerton JV. What are the **concerns about custom-compounded "bioidentical" hormone** therapy? Menopause. 2014 Dec;21(12):1298-300.

Pinkerton JV.Money talks: Untreated **hot flashes cost women, the workplace, and society**. Menopause 2015 Mar; 22:254.

Pinkerton JV et al. **Compounded bioidentical hormone therapy**: Identifying use trends and knowledge gaps among US women. Menopause 2015 Sep; 22:926.

Pinkerton JV, Constantine GD. **Compounded non-FDA-approved menopausal hormone therapy** prescriptions have increased: results of a pharmacy survey. Menopause 2016;23:XXX-XXX.

Pockaj B ; Gallagher J ; Loprinzi C et al. Phase III double-blind, randomized, placebo-controlled crossover trial of black cohosh in the management of hot flashes: J Clin Oncol. 2006; 24:2836-41. CONCLUSION: This trial failed to provide any evidence that black cohosh reduced hot flashes more than Pl.

Politano CA, Costa-Paiva L, Aguiar LB, et al. **Fractional CO2 laser versus promestriene and lubricant** in genitourinary syndrome of menopause: a randomized clinical trial. Menopause. 2019 Aug;26(8):833-840.

Politi MC, et al. Revisiting the **duration of vasomotor symptoms** of menopause: a meta-analysis. J Gen Intern Med. 2008 Sep;23(9):1507-13. Epub 2008 Jun 3. Our findings suggest a median symptom duration of about 4 years among symptomatic women. A longer symptom duration may affect treatment decisions and clinical guidelines. Further prospective, longitudinal studies of menopausal symptoms should be conducted to confirm these results.

Poornima IG, Mackey RH, et al; W**HI and WHI-CAC Study** Investigators. **Coronary Artery Calcification(CAC)** and Post-Trial Cardiovascular Events and Mortality Within the Women's Health Initiative (WHI) **Estrogen-Alone** Trial. J Am Heart Assoc. 2017 Oct27;6(11).

Portman DJ, Bachmann GA, Simon JA; and the **Ospemifene** Study Group. Ospemifene, a novel selective estrogen receptor modulator for treating dyspareunia associated with postmenopausal vulvar and vaginal atrophy. Menopause. 2013 Jan 28.

Posadzki P, Lee MS, Moon TW, Choi TY, Park TY, Ernst E. Prevalence of **complementary and alternative medicine** (CAM) use by menopausal women: a systematic review of surveys. Maturitas. 2013;75:34-43.

Power L, Lefas G, Lambert P, et al. **Hormone Use After Nonserous Epithelial Ovarian Cancer:** Overall and Disease-Free Survival**.** Obstet Gynecol. 2016 May;127(5):837-47.

Prague JK, Roberts RE, Comninos AN, et al. **Neurokinin 3 receptor antagonism** as a novel treatment for menopausal hot flushes: a phase 2, randomised, double-blind, placebo-controlled trial. Lancet 2017; online April 3.

Prieto-Alhambra D, Javaid MK, Judge A, et al; COASt Study Group. **Hormone replacement therapy and mid-term implant survival following knee or hip arthroplasty** for osteoarthritis: a population-based cohort study. Ann Rheum Dis. 2015 Mar;74(3):557-63.

Racine A, Bijon A, Fournier A, et al. **Menopausal hormone therapy and risk of cholecystectomy**: a prospective study based on the French E3N cohort. CMAJ. 2013 Mar 18.

Rada G, Capurro D, Pantoja T, et al. **Non-hormonal interventions for hot flushes in women with a history of breast cancer**. Cochrane Database of Systematic Reviews 2010, Issue 9. Art. No.: CD004923. DOI: 10.1002/14651858.CD004923.pub2. Clonidine, SSRIs and SNRIs, gabapentin and relaxation therapy showed a mild to moderate effect on reducing hot flushes in women with a history of breast cancer.

Rahman I, Akesson A, Wolk A. Relationship between **age at natural menopause and risk of heart failure**. Menopause. 2014 May 12.

Reddy SY, Warner H, Guttuso T, et al. Gabapentin, estrogen, and placebo for treating hot flashes: a randomized controlled trial. Obstet Gynecol 2006;108:41-48. InfoPoems: In this small study, high-dose gabapentin (Neurontin) was as effective as the usual dose of conjugated equine estrogens (Premarin) for the treatment of menopausal vasomotor symptoms. Larger studies are needed to confirm this result. (LOE = 1b)

Reed SD, Newton KM, Garcia RL, et al. Complex **hyperplasia** with and without atypia: clinical outcomes and implications of **progestin therapy**. Obstet Gynecol. 2010 Aug;116(2 Pt 1):365-73.

Reed SD, Newton KM, LaCroix AZ, et al. Vaginal, endometrial, and reproductive hormone findings: randomized, placebo-controlled trial of **black cohosh**, multibotanical herbs, and dietary soy for vasomotor symptoms: the Herbal Alternatives for Menopause (**HALT**) Study. Menopause. 2008 Jan-Feb;15(1):51-8.

Reed SD, Mitchell CM, Joffe H, Cohen L, Shifren JL, Newton KM, Freeman EW, Larson JC, Manson JE, LaCroix AZ, Guthrie KA. **Sexual function** in women on **estradiol or venlafaxine** for **hot flushes**: a randomized controlled trial. Obstet Gynecol. 2014 Aug;124(2 Pt 1):233-41.

Reed SD, Guthrie KA, Newton KM, et al. **Menopausal** quality of life: RCT of **yoga, exercise, and omega-3 supplements**. Am J Obstet Gynecol 2014;210:244.e1–11.

Renoux Christel, Dell'Aniello Sophie, Garbe Edeltraut, et al. **Transdermal and oral hormone replacement therapy** and the risk of stroke: a nested case-control study. BMJ 2010;340:c2519, doi: 10.1136/bmj.c2519 (Published 3 June 2010)

Reynolds K, et al. A meta-analysis of the effect of **soy protein** supplementation on serum lipids. Am J Cardiol. 2006 Sep 1;98(5):633-40. Epub 2006 Jul 12.

Reynolds EE, Bates C, Richardson M, et al. **Should This Patient Receive Hormone Therapy for Her Menopausal Symptoms**?: Grand Rounds Discussion From Beth Israel Deaconess Medical Center. Ann Intern Med. 2018 Feb 6;168(3):203-209.

Roberts H. **Managing the menopause**. BMJ. 2007 Apr 7;334(7596):736-41.

Robinson WR, Nichols HB, Tse CK, et al. Associations of **Premenopausal Hysterectomy and Oophorectomy With Breast Cancer** Among Black and White Women: The Carolina Breast Cancer Study, 1993-2001. Am J Epidemiol. 2016 Sep 1;184(5):388-99

Rocca WA, Bower JH, Maraganore DM, et al. Increased risk of **cognitive impairment** or dementia in women who underwent **oophorectomy before menopause**. Neurology 2007;69:1074–1083.

Rogines-Velo MP et al. Effect of **medroxyprogesterone on depressive symptoms** in depressed and nondepressed perimenopausal and postmenopausal women after discontinuation of transdermal estradiol therapy. Menopause2012 Apr; 19:471.

Romieu I, Fabre A, Fournier A, Kauffmann F, Varraso R, Mesrine S, Leynaert B, Clavel-Chapelon F. Postmenopausal hormone therapy and **asthma onset** in the E3N cohort. Thorax. 2010 Feb 8.

Rooney JPK, Visser AE, D'Ovidio F, et al. A case-control study of **hormonal exposures as etiologic factors for ALS** in women: Euro-MOTOR. Neurology. 2017 Aug 23

Rosenberg L, Palmer JR, Wise LA, Adams-Campbell LL. A prospective study of female **hormone use** and breast cancer among **black women**. Arch Intern Med. 2006 Apr 10;166(7):760-5.

Roth JA, Etzioni R, Waters TM, et al. **Economic Return From the Women's Health Initiative Estrogen Plus Progestin Clinical Trial (WHI)**: A Modeling Study. Ann Intern Med. 2014 May 6;160(9):594-602.

Royal College of Obstetricians and Gynaecologists (**RCOG**). **Venous thromboembolism and hormone replacement therapy**. London (UK): Royal College of Obstetricians and Gynaecologists (RCOG); 2011 May

Ruiz MP, Huang Y, Hou JY, et al. All-cause mortality in young women with **endometrial cancer receiving progesterone therapy**. Am J Obstet Gynecol. 2017 Dec;217(6):669.e1-669.e13.

Ryan J, Scali J, Carrière I, et al. Impact of a **premature menopause on cognitive function** in later life. BJOG. 2014 May 7.

Saccomani S, Lui-Filho JF, Juliato CR, et al. Does **obesity increase the risk of hot flashes** among midlife women? A population-based study. Menopause. 2017 May 29.

Sacks FM, Lichtenstein A, Van Horn L, Harris W, Kris-Etherton P, Winston M. **Soy** Protein, Isoflavones, and Cardiovascular Health. An **American Heart Association** Science Advisory for Professionals From the Nutrition Committee. Circulation. 2006 Jan 17; [Epub ahead of print]

Saensak S, Vutyavanich T, Somboonporn W, Srisurapanont M. **Relaxation** for perimenopausal and postmenopausal symptoms. Cochrane Database Syst Rev. 2014 Jul 20;7:CD008582. Evidence is insufficient to show the effectiveness of relaxation techniques as treatment for menopausal vasomotor symptoms, or to determine whether this treatment is more effective than no treatment, placebo, acupuncture, superficial needle insertion or paced respiration.

Salpeter SR, et al. Brief report: **Coronary heart disease** events associated with hormone therapy in **younger and older** women. A meta-analysis. J Gen Intern Med. 2006 Apr;21(4):363-6. Hormone therapy reduces the risk of CHD events in younger postmenopausal women. In older women, HT increases, then decreases risk over time.(Alexandersen P, et al. The long-term impact of 2-3 years of hormone replacement therapy on cardiovascular mortality and atherosclerosis in healthy women. Climacteric. 2006 Apr;9(2):108-18.)

Samsioe G, et al. Estalis 50/140 Study Group. **Endometrial safety**, overall safety and tolerability of transdermal continuous combined hormone replacement therapy over 96 weeks: a randomized open-label study. Climacteric. 2006 Oct;9(5):368-79. Continuous combined transdermal HRT with E2/NETA shows no evidence of an increased endometrial hyperplasia or endometrial cancer risk over a 96-week period.

Sanchez-Spitman A et al. **Tamoxifen pharmacogenetics and metabolism**: Results from the prospective CYPTAM study. J Clin Oncol 2019 Mar 10:37(8):636-646.

Sanghvi MM, Aung N, Cooper JA, et al. The impact of **menopausal hormone therapy (MHT) on cardiac structure and function**: Insights from the UK Biobank imaging enhancement study. PLoS One. 2018 Mar 8;13(3):e0194015.

Santen RJ, Allred DC, Ardoin SP, et al. **Postmenopausal Hormone Therapy**: An **Endocrine Society** Scientific Statement. J Clin Endocrinol Metab. **2010** Jun 21. http://www.endo-society.org/journals/ScientificStatements/upload/jc-2009-2509v2.pdf

Santen RJ, Kagan R, Altomare CJ, et al. Current and Evolving Approaches to Individualizing **Estrogen Receptor-Based Therapy** Approaches for Menopausal Women. J Clin Endocrinol Metab. 2014 Jan 1

Santen RJ, Stuenkel CA, Davis SR, et al. **Managing menopausal symptoms** and associated clinical issues in **breast cancer survivors**. J Clin Endocrinol Metab. 2017 Aug 2.

Santoro N, Braunstein GD, Butts CL, et al **Compounded Bioidentical Hormones** in Endocrinology Practice: An **Endocrine Society Scientific Statement**. J Clin Endocrinol Metab. 2016 Apr;101(4):1318-43.

Santoro N, Johnson J. **Diagnosing the Onset** of Menopause. JAMA. 2019 Jul 22.

Sarrel PM, Njike VY, Vinante V, Katz DL. The **mortality toll of estrogen avoidance**: an analysis of excess deaths among hysterectomized women aged 50 to 59 years. Am J Public Health 2013.

Sarrel P et al. Incremental direct and indirect **costs of untreated vasomotor symptoms**. Menopause 2015 Mar; 22:260.

Sarri G, Pedder H, Dias S, et al. **Vasomotor symptoms resulting from natural menopause**: a systematic review and network meta-analysis of treatment effects from the National Institute of Health and Care Excellence guideline on menopause. BJOG. 2017 Mar 9

Savolainen-Peltonen H, Hautamäki H, Tuomikoski P, Ylikorkala O, Mikkola TS. Health-related quality of life in women **with or without hot flashes**: a randomized placebo-controlled trial with **hormone therapy**. Menopause. 2013 Nov 11.

Savolainen-Peltonen H, Rahkola-Soisalo P, Hoti F, et al . Use of postmenopausal hormone therapy and **risk for Alzheimer's disease in Finland**: nationwide case-control study. BMJ 2018;364:l665.

Savolainen-Peltonen H, Rahkola-Soisalo P, Hoti F, et al. Use of **postmenopausal hormone therapy and risk of Alzheimer's disease in Finland**: nationwide case-control study. BMJ. 2019 Mar 6;364:l665

Savonitto S, Colombo D, Franco N, et al. **Age at menopause** and extent of coronary artery disease among post-menopausal women with **acute coronary syndromes**. Am J Med. 2016 Jun 16.

Schabath MB, Hernandez LM, Wu X, Pillow PC, Spitz MR. Dietary **phytoestrogens** and lung cancer risk. JAMA. 2005 Sep 28;294(12):1493-504.

Scheffers CS, Armstrong S, Cantineau AE, et al. **Dehydroepiandrosterone** for women in the **peri- or postmenopausal phase**.Cochrane Database Syst Rev. 2015 Jan 22;1:CD011066.
There is no evidence that DHEA improves quality of life but there is some evidence that it is associated with androgenic side effects. There is uncertainty whether DHEA decreases menopausal symptoms, but DHEA may slightly improve sexual function compared with placebo.

Schierbeck LL, Rejnmark L, Tofteng CL, et al. Effect of **hormone replacement therapy on cardiovascular events** in recently postmenopausal women: randomised trial. (**DOPS**) BMJ. 2012 Oct 9;345:e6409.

Schwartz AG, Ray RM, Cote ML, et al. Hormone Use, Reproductive History and **Risk of Lung Cancer**: The Women's Health Initiative Studies. J Thorac Oncol. 2015 Apr 3.

Schwartz AG, Ray RM, Cote ML, et al. Hormone Use, Reproductive History, and Risk of **Lung Cancer**: The Women's Health Initiative Studies. J Thorac Oncol. 2015 Jul;10(7):1004-13.

Sestak I, et al. Influence of hormone replacement therapy on **tamoxifen-induced vasomotor** symptoms. J Clin Oncol. 2006 Aug 20;24(24):3991-6.

Setty P, Redekal L, Warren MP. **Vaginal estrogen** use and effects on quality of life and **urogenital** morbidity in postmenopausal women after publication of the Women's Health Initiative in New York City. Menopause. 2015 Aug 8.

Shah NR, Jones JB, Aperi J, Shemtov R, Karne A, Borenstein J. **Selective Serotonin Reuptake Inhibitors** for Premenstrual Syndrome and Premenstrual Dysphoric Disorder: A Meta-Analysis. Obstet Gynecol. 2008 May;111(5):1175-1182. Selective serotonin reuptake inhibitors were found to be effective in treating premenstrual symptoms, with continuous dosing regimens favored for effectiveness.

Shams T, Firwana B, Habib F, et al. **SSRIs for Hot Flashes**: A Systematic Review and Meta-Analysis of Randomized Trials. J Gen Intern Med. 2013 Jul 26.

Shapley M, Blagojevic M, Jordan K, Croft P. The **spontaneous resolution of heavy menstrual** bleeding in the perimenopausal years. BJOG. 2012 Feb 8.

Shao H, Breitner JCS, Whitmer RA, et al. **Hormone therapy and Alzheimer** disease dementia: new findings from the **Cache County Study**. Neurology 2012;79:1846 –1852.

Shu XO, Zheng Y, Cai H, Gu K, Chen Z, Zheng W, Lu W. **Soy food intake and breast cancer** survival. JAMA. 2009 Dec 9;302(22):2437-43.

Simon J, Nachtigall L, Gut R, Lang E, Archer DF, Utian W. Effective treatment of vaginal atrophy with an ultra-low-dose estradiol vaginal tablet. Obstet Gynecol. 2008 Nov;112(5):1053-60. After 12 weeks of treatment, an ultra-low-dose **10-microgram E2 vaginal tablet (Vagifem),** compared with placebo, demonstrated significant improvement for the primary endpoints: vaginal cytology and pH and most bothersome urogenital symptoms score. In this study a 10-mcg estradiol vaginal tablet used twice weekly was better than placebo for the reduction of bothersome postmenopausal vaginal symptoms. The tablet currently on the market (Vagifem, by the same manufacturer) is 25 mcg. Perhaps once weekly use of the available tablet would be equivalent to twice weekly use of the lower dose, but that would require another study that the manufacturer is unlikely to fund. (LOE = 2b)

Simon JA, Lin VH, Radovich C, Bachmann GA; The **Ospemifene** Study Group. One-year long-term safety extension study of ospemifene for the treatment of vulvar and vaginal atrophy in postmenopausal women with a uterus. Menopause. 2012 Nov 8.

Simon JA, Laliberté F, Duh MS, et al. **Venous thromboembolism** and cardiovascular disease complications in menopausal women using **transdermal versus oral estrogen** therapy. Menopause. 2016 Feb 26.

SOGC 2009 Menopause and Osteoporosis Update 2009-SOGC Jan 2009. http://www.sogc.org/media/pdf/advisories/Meno-Osteo-Update_JOGC-Jan_09.pdf

SOGC 2014: Society of Obstetricians and Gynaecologists of Canada. **Managing menopause**. J Obstet Gynaecol Can 2014;36(9 eSuppl A):S1–S80. http://sogc.org/wp-content/uploads/2014/09/gui311CPG1409Eabstract1.pdf (accessed October 1, 2014).

Star Trial (Study of Tamoxifen and Raloxifene) for Breast Cancer Prevention Medical Letter May 8, 2006 & Pharmacist's Letter May 2006. InfoPOEMs: Tamoxifen (Nolvadex, Tamofen) and raloxifene (Evista) are similarly effective for reducing the risk of invasive breast cancer in postmenopausal women. Although women taking tamoxifen are at an increased risk of thromboembolic events and cataracts, they report improved sexual function compared with women taking raloxifene. All-cause mortality and overall quality-of-life were similar in both treatment groups. (LOE = 1b-).

Stefanick ML, et al. WHI Investigators. Effects of conjugated equine estrogens on breast cancer and mammography screening in postmenopausal women with hysterectomy. JAMA. 2006 Apr 12;295(14):1647-57. (InfoPOEMs: Estrogen therapy alone does not increase the risk of breast cancer in postmenopausal women with prior hysterectomy. Women receiving estrogen are more likely to require further testing as a result of questionably abnormal mammogram results, potentially leading to heightened anxiety and a reduced quality of life. The decision to use estrogen in postmenopausal women after hysterectomy should be individualized on the basis of overall potential risks and benefits. Women most likely to benefit from estrogen therapy include those with disabling hot flashes and an increased risk of osteoporotic fractures. Treatment should be limited whenever possible to the first 5 years (or less) after menopause. (LOE = 1b))

Shah NR, Borenstein J, Dubois RW. Postmenopausal hormone therapy and **breast cancer**: a systematic review and meta-analysis. Menopause. 2005 Nov-Dec;12(6):668-78. (InfoPOEMs: This meta-analysis of 13 large observational studies found that combined estrogen and progestin hormone therapy (CHT) for postmenopausal women is more likely than estrogen-only hormone therapy (ET) to be associated with breast cancer. This result is concondant with clinical trial data from the Women's Health Initiative (WHI). There is still uncertainty about whether ET increases the risk of breast cancer, based on the heterogeneity found in this meta-analysis and the discordance of these results with those from the WHI. (LOE = 2a))

Shifren JL, Crandall CJ, Manson JE. **Menopausal Hormone Therapy**. JAMA. 2019 May 30.

Shifren JL, Zincavage R, Cho EL, et al. Women's experience of **vulvovaginal symptoms** associated with menopause. Menopause. 2018 Dec 10.

Shike M, Doane AS, Russo L, et al. The effects of **soy supplementation** on gene expression in **breast cancer**: a randomized placebo-controlled study. J Natl Cancer Inst. 2014 Sep 4;106(9).

Smith NL, Blondon M, Wiggins KL, et al. Lower Risk of Cardiovascular Events in Postmenopausal Women Taking Oral Estradiol Compared With Oral Conjugated Equine Estrogens. JAMA Intern Med. 2013 Sep 30.

Snitz Beth E.; O'Meara Ellen S.; Carlson Michelle C.; et al. for the **Ginkgo** Evaluation of Memory (**GEM**) Study Investigators. Ginkgo biloba for Preventing Cognitive Decline in Older Adults: A Randomized Trial. JAMA. 2009;302(24):2663-2670. Compared with placebo, the use of G biloba, 120 mg twice daily, did not result in less cognitive decline in older adults with normal cognition or with mild cognitive impairment.

Somunkiran A, Erel CT, Demirci F, Senturk ML. The effect of **tibolone** versus 17beta-estradiol on climacteric symptoms in women with surgical menopause: A randomized, cross-over study. Maturitas. 2006 Jul 8; [Epub ahead of print]

Spack NP. Management of **transgenderism**. JAMA. 2013 Feb 6;309(5):478-84.

Stearns V, Slack R, Greep N, et al. **Paroxetine** is an effective treatment **for hot flashes**: results from a prospective randomized clinical trial. J Clin Oncol. 2005 Oct 1;23(28):6919-30.

Steinauer JE, Waetjen LE, Vittinghoff E, Subak LL, Hulley SB, Grady D, Lin F, Brown JS. Postmenopausal hormone therapy: does it cause incontinence? Obstet Gynecol. 2005 Nov;106(5 Pt 1):940-5.

Srivastava A, Patel N. **Autosomal dominant polycystic kidney disease**. Am Fam Physician. 2014 Sep 1;90(5):303-7.

Stiles VH, Metcalf BS, Knapp KM, et al. A small amount of precisely measured high-intensity **habitual physical activity predicts bone health** in pre- and post-menopausal women in UK Biobank. Inter J Epidemiol. 2017,1-10.

Stuenkel CA, Davis SR, Gompel A, et al. **Treatment of Symptoms of the Menopause**: An Endocrine Society Clinical Practice Guideline. J Clin Endocrinol Metab. 2015 Nov;100(11):3975-4011.

Stuenkel CA, Manson JE. **Compounded Bioidentical Hormone Therapy**: Does the Regulatory Double Standard Harm Women? JAMA Intern Med. 2017 Oct 9.

Suckling J, Lethaby A, Kennedy R. **Local oestrogen for vaginal atrophy** in postmenopausal women. Cochrane Database Syst Rev. 2003;(4):CD001500. (see also Pharmacist's Letter May 2006)

Suckling J, Lethaby A, Kennedy R. **Local oestrogen for vaginal atrophy** in postmenopausal women. Cochrane Database Syst Rev. 2006 Oct 18;(4):CD001500.

Suckling JA, Kennedy R, Lethaby A, Roberts H. **Local oestrogen for vaginal atrophy** in postmenopausal women. Cochrane Database of Systematic Reviews 2006, Issue 4. Art. No.: CD001500. Creams, pessaries, tablets and the oestradiol vaginal ring appeared to be equally effective for the symptoms of vaginal atrophy. One trial found significant side effects following cream (conjugated equine oestrogen) administration when compared to tablets causing uterine bleeding, breast pain and perineal pain. Another trial found significant endometrial overstimulation following use of the cream (conjugated equine oestrogen) when compared to the ring. As a treatment choice women appeared to favour the oestradiol-releasing vaginal ring for ease of use, comfort of product and overall satisfaction.

Sullivan SD, Lehman A, Nathan NK, et al. **Age of menopause and fracture risk** in postmenopausal women randomized to calcium + vitamin D, hormone therapy, or the combination: results from the Women's Health Initiative Clinical Trials. Menopause. 2017 Apr;24(4):371-378.

Svejme O, Ahlborg H, et al. **Early menopause** and risk of osteoporosis, fracture and mortality: a 34-year prospective observational study in 390 women. BJOG. 2012 Apr 25.

Szegda KL, Whitcomb BW, Purdue-Smithe AC, et al. **Adult adiposity and risk of early menopause**. Hum Reprod. 2017 Oct 25:1-10

Taylor HS, Tal A, Pal L, et al. Effects of **Oral vs Transdermal Estrogen Therapy on Sexual Function** in Early Postmenopause: Ancillary Study of the Kronos Early Estrogen Prevention Study (**KEEPS**). JAMA Intern Med. 2017 Aug 28

Tamimi RM, Hankinson SE, Chen WY, Rosner B, Colditz GA. Combined **estrogen and testosterone** use and risk of breast cancer in postmenopausal women. Arch Intern Med. 2006 Jul 24;166(14):1483-9.

Terry MB, Daly MB, Phillips KA, et al. Risk-Reducing **Oophorectomy and Breast Cancer Risk Across the Spectrum** of Familial Risk. J Natl Cancer Inst. 2018 Nov 28.

Thurston RC, Ewing LJ, Low CA, et al. **Behavioral weight loss** for the management of menopausal hot flashes: a pilot study. Menopause. 2014 Jun 23.

Thurston RC, Johnson BD, Shufelt CL, et al. **Menopausal symptoms and cardiovascular disease mortality** in the Women's Ischemia Syndrome Evaluation (**WISE**). Menopause. 2017 Feb;24(2):126-132.

Thurston RC, Chang Y, Barinas-Mitchell E, et al. Physiologically assessed **hot flashes and endothelial function** among midlife women. Menopause. 2017 Apr 10.

Triebner K, Johannessen A, Puggini L, et al. **Menopause as a predictor of new-onset asthma**: A longitudinal Northern European population study. J Allergy Clin Immunol. 2016 Jan;137(1):50-57.e6.

Triebner K, Matulonga B, Johannessen A, et al. **Menopause** Is Associated with **Accelerated Lung Function Decline**. Am J Respir Crit Care Med. 2017 Apr 15;195(8):1058-1065.

Trock BJ, Meta-analysis of **soy intake and breast cancer risk**. J Natl Cancer Inst. 2006 Apr 5;98(7):459-71. Soy intake may be associated with a small reduction in breast cancer risk. However, this result should be interpreted with caution due to potential exposure misclassification, confounding, and lack of a dose response. Given these caveats and results of some experimental studies that suggest adverse effects from soy constituents, recommendations for high-dose isoflavone supplementation to prevent breast cancer or prevent its recurrence are premature. (InfoPOEMs: If the existing research results are true, high soy intake is associated with a small protective effect against breast cancer. However, the published studies have enough flaws to make me question this effect. (LOE = 3a-))

Uebelhack R, et al. **Black cohosh and St. John's wort** for climacteric complaints: a randomized trial. (n=301 16weeks) Obstet Gynecol. 2006 Feb;107(2 Pt 1):247-55.

Umar S, Rabinovitch M, Eghbali M. Estrogen Paradox in **Pulmonary Hypertension**: Current Controversies and Future Perspectives. Am J Respir Crit Care Med. 2012 May 3.

Unfer V, Casini ML, Costabile L, Mignosa M, Gerli S, Di Renzo GC. **Endometrial effects** of long-term treatment with **phytoestrogens**: a randomized, double-blind, placebo-controlled study. Fertil Steril. 2004 Jul;82(1):145-8, quiz 265.

USPSTF: U.S. Preventive Services Task Force. Hormone therapy for the **prevention of chronic conditions** in postmenopausal women: recommendations from the U.S. Preventive Services Task Force. Ann Intern Med. 2005 May 17;142(10):855-60.
(InfoPOEMS: Estrogen/progestin therapy should not routinely be used to prevent chronic disease in postmenopausal women. The Task Force making this recommendation did not address short-term (1-2 years) treatment of symptoms of menopause. The risks with chronic therapy are minimal, but so are the benefits to chronic disease prevention. (LOE = 1a))

USPSTF-US Preventive Services Task Force . Menopausal hormone therapy for the **primary prevention of chronic conditions**: US Preventive Services Task Force Recommendation Statement. Ann Intern Med **2012**. The USPSTF recommends against the use of combined estrogen and progestin for the prevention of chronic conditions in postmenopausal women. (Grade D recommendation) The USPSTF recommends against the use of estrogen for the prevention of chronic conditions in postmenopausal women who have had a hysterectomy. (Grade D recommendation).

USPSTF: US Preventive Services Task Force. **Hormone therapy for the primary prevention of chronic conditions in postmenopausal women**: US Preventive Services Task Force recommendation statement [Dec 12, 2017].JAMA. doi:10.1001/jama.2017.18261

Vaidya D, Becker DM, Bittner V, et al. **Ageing, menopause, and ischaemic heart disease** mortality in England, Wales, and the United States: modeling study of national mortality data. BMJ 2011; 343: DOI:10.1136/bmj.d5179

Vellas B, Coley N, Ousset P-J, et al, for the GuidAge Study Group. Long-term use of standardised **ginkgo biloba extract** for the prevention of Alzheimer's disease (**GuidAge**): a randomised placebo-controlled trial. Lancet Neurol 2012; online Sept 6

Venetkoski M, Savolainen-Peltonen H, Rahkola-Soisalo P, et al. Increased **cardiac and stroke death risk in the first year after discontinuation of postmenopausal hormone therapy**. Menopause. 2017 Nov 13.
Verkaik S, Kamperman AM, van Westrhenen R, Schulte PFJ. The treatment of **premenstrual syndrome with preparations of Vitex agnus castus**: a systematic review and meta-analysis. Am J Obstet Gynecol. 2017 Aug;217(2):150-166.
Vinogradova Y, Coupland C, Hippisley-Cox J. Use of hormone replacement therapy and **risk of venous thromboembolism**: nested case-control studies using the QResearch and CPRD databases. BMJ. 2019 Jan 9;364:k4810.
Vitolins MZ, Griffin L, Tomlinson WV, et al. Randomized Trial to Assess the Impact of **Venlafaxine and Soy Protein** on Hot Flashes and Quality of Life in Men With Prostate Cancer. J Clin Oncol. 2013 Sep 30. (neither effective)
Visvanathan K, et al. American society of clinical oncology clinical practice guideline update on pharmacologic interventions including **tamoxifen, raloxifene, and aromatase inhibition for breast cancer risk reduction**. J Clin Oncol. 2009 Jul 1;27(19):3235-58. Epub 2009 May 26.
Vogel VG, Costantino JP, Wickerham DL, et al. (NSABP). Effect of **tamoxifen vs raloxifene** on the risk of developing invasive breast cancer and other disease outcomes. The NSABP study of tamoxifen and raloxifene (STAR) P-2 trial. JAMA 2006;295:2727-2741 (InfoPOEMs: Tamoxifen (Nolvadex, Tamofen) and raloxifene (Evista) are similarly effective for reducing the risk of invasive breast cancer in postmenopausal women. Although women taking tamoxifen are at an increased risk of thromboembolic events and cataracts, they report improved sexual function compared with women taking raloxifene. All-cause mortality and overall quality-of-life were similar in both treatment groups. (LOE = 1b-))
Waetjen LE, Brown JS, Vittinghoff E, et al. The Effect of Ultralow-Dose Transdermal Estradiol on **Urinary Incontinence** in Postmenopausal Women. Obstet Gynecol. 2005 Nov;106(5):946-952.
Wei D, Chen Y, Wu C, et al. Effect and safety of **paroxetine for vasomotor symptoms**: systematic review and meta-analysis. BJOG. 2016 Apr 7.
Welton AJ, Vickers MR, Kim J, et al. for the **WISDOM** team. Health related quality of life after combined hormone replacement therapy: randomised controlled trial. BMJ. 2008 Aug 21;337:a1190. doi: 10.1136/bmj.a1190. Combined HRT started many years after the menopause can improve health related quality of life.
Whelan AM, Jurgens TM, Trinacty M. **Bioidentical Progesterone Cream** for Menopause-Related Vasomotor Symptoms: Is it Effective? Ann Pharmacother. 2013 Jan;47(1):112-6.

Woods GN, Huang MH, Cawthon PM, et al. Patterns of **menopausal hormone therapy use and hyperkyphosis** in older women. Menopause. 2018 Feb 16.
Yaffe K, Vittinghoff E, Ensrud KE, Johnson KC, Diem S, Hanes V, Grady D. Effects of ultra-low-dose transdermal estradiol on **cognition** and health-related quality of life. Arch Neurol. 2006 Jul;63(7):945-50.
Yang L, Hu X, Zhang H, et al. Association of bone mineral density with a first-degree family history of diabetes in normoglycemic postmenopausal women. Menopause. 2019 Aug 19.
Ycaza Herrera A, Hodis HN, Mack WJ, et al. **Estradiol** Therapy After Menopause **Mitigates Effects of Stress on Cortisol and Working Memory**. J Clin Endocrinol Metab. 2017 Nov 2.
Yoon BK, Chin J, Kim JW, et al. **Menopausal hormone therapy and mild cognitive impairmen**t: a randomized, placebo-controlled trial. Menopause. 2018 May 29.
Yonkers KA, Kornstein SG, Gueorguieva R, et al. Symptom-Onset Dosing of **Sertraline for the Treatment of Premenstrual Dysphoric Disorder**: A Randomized Clinical Trial. JAMA Psychiatry. 2015 Sep 9:1-8.
Zhang FF, Haslam DE, Terry MB, Knight et al. **Dietary isoflavone intake and all-cause mortality in breast cancer survivors**: The Breast Cancer Family Registry. Cancer. 2017 Mar 6.
Zhang L, Li Y, Wang C, et al. Early menarche is associated with an **increased risk of type 2 diabetes** in rural Chinese women and is partially mediated by BMI: the Henan Rural Cohort Study. Menopause. 2019 Jul 29.
Zhao D, Guallar E, Ouyang P, et al. **Endogenous sex hormones and incident cardiovascular disease** in post-menopausal women. J Am Coll Cardiol 2018;71:2555–66.
Zhu D, Chung HF, Pandeya N, et al. **Body mass index and age at natural menopause**: an international pooled analysis of 11 prospective studies. Eur J Epidemiol. 2018 Feb 19.
Zhu L, Jiang X, Sun Y, Shu W. Effect of **hormone therapy on the risk of bone fractures**: a systematic review and meta-analysis of randomized controlled trials. Menopause. 2015 Oct 27.
Zhu X, Proctor M, Bensoussan A, Wu E, Smith CA. **Chinese herbal medicine** for primary dysmenorrhoea. Cochrane Database Syst Rev. 2008 Apr 16;(2):CD005288. The review found promising evidence supporting the use of Chinese herbal medicine for primary dysmenorrhoea; however, results are limited by the poor methodological quality of the included trials.
Zhu X, Liew Y, Liu ZL. **Chinese herbal medicine** for menopausal symptoms. Cochrane Database Syst Rev. 2016 Mar 15;3:CD009023.
We found insufficient evidence that Chinese herbal medicines were any more or less effective than placebo or HT for the relief of vasomotor symptoms. Effects on safety were inconclusive. The quality of the evidence ranged from very low to moderate; there is a need for well-designed randomised controlled studies.
Zsido RG, Heinrich M, Slavich GM, et al. Association of **Estradiol and Visceral Fat With Structural Brain Networks** and Memory Performance in Adults. JAMA Netw Open. 2019 Jun 5;2(6):e196126.

Osteoporosis:
AAOS- Guideline on the Treatment of Symptomatic Osteoporotic Spinal Compression Fractures- **Vertebroplasty** 2010 Recommendations http://www.aaos.org/Research/guidelines/SCFsummary.pdf
Abrahamsen B. **Bisphosphonate adverse effects**, lessons from large databases. Curr Opin Rheumatol. 2010 Jul;22(4):404-9.
Abrahamsen B. **Adverse effects of bisphosphonates**. Calcif Tissue Int. 2010. Jun;86(6):421-35. Epub 2010 Apr 21.
Alibhai SM, Duong-Hua M, et al. Impact of **androgen deprivation therapy** on cardiovascular disease and diabetes. J Clin Oncol. 2009 Jul 20;27(21):3452-8. Epub 2009 Jun 8.
Aloia JF, Talwar SA, Pollack S, Yeh J. A randomized controlled trial of **vitamin D3** supplementation in African American women. Arch Intern Med. 2005 Jul 25;165(14):1618-23.
Alonso-Coello P, García-Franco AL, Guyatt G, Moynihan R. Drugs for **pre-osteoporosis: prevention or disease mongering**? BMJ. 2008 Jan 19;336(7636):126-9.
Amin S, et al. **Estradiol, testosterone**, and the risk for hip fractures in **elderly men** from the Framingham Study. Am J Med. 2006 May;119(5):426-33.
Armingeat T, et al. **Intravenous pamidronate** for **pain relief** in recent osteoporotic vertebral compression fracture: a randomized double-blind controlled study. Osteoporos Int. 2006 Aug 8; [Epub ahead of print]
Avenell A, Gillespie WJ, Gillespie LD, et al. Vitamin D and vitamin D analogues for preventing fractures associated with involutional and post-menopausal osteoporosis. Cochrane Database Syst Rev. 2005 Jul 20;(3):CD000227& ACP Journal Club . AUTHORS' CONCLUSIONS:
Frail older people confined to institutions may sustain fewer hip and other non-vertebral fractures if given vitamin D with calcium supplements. Effectiveness of vitamin D alone in fracture prevention is unclear. There is no evidence of advantage of analogues of vitamin D compared with vitamin D. Calcitriol may be associated with an increased incidence of adverse effects. Dose, frequency, and route of administration of vitamin D in older people require further investigation.
Barrett-Connor E, Grady D, et al.; **MORE** Investigators (Multiple Outcomes of Raloxifene Evaluation). Raloxifene and **cardiovascular** events in osteoporotic postmenopausal women: four-year results from the MORE randomized trial. JAMA. 2002 Feb 20;287(7):847-57.
Bashutski JD, Eber RM, Kinney JS, et al. **Teriparatide and Osseous Regeneration** in the Oral Cavity. N Engl J Med. 2010 Oct 16. (n=40, 6 weeks, 1yr follow up)
Bauer DC, Black D, Ensrud K, Thompson D, Hochberg M, Nevitt M, et al. Upper gastrointestinal tract safety profile of **alendronate**: the Fracture Intervention Trial. Arch Intern Med 2000;160:517-25.
Baxter NN, Habermann EB, Tepper JE, Durham SB, eta l. Risk of pelvic fractures in older women following **pelvic irradiation**. JAMA. 2005 Nov 23;294(20):2587-93. (InfoPOEMs: Pelvic irradiation significantly increases the risk of pelvic fractures in older women. Treatment for anal cancer is associated with the highest risk of pelvic fracture. (LOE = 2b-))
Bean GR, Kimler BF, Seewaldt VL. Long-term **raloxifene** in a woman at high risk for **breast cancer**. N Engl J Med. 2006 Oct 12;355(15):1620-2.
Bell Katy J L, Hayen Andrew, Macaskill Petra, et al. Value of routine **monitoring of bone mineral density** after starting bisphosphonate treatment: secondary analysis of trial data**.** BMJ 2009;338:b2266, doi: 10.1136/bmj.b2266 (Published 23 June 2009)
Berger C, Langsetmo L, Joseph L, Hanley DA, et al. Canadian Multicentre Osteoporosis Study Research Group. Change in bone mineral density as a function of age in women and men and association with the use of antiresorptive agents. CMAJ. 2008 Jun 17;178(13):1660-8. (CaMos)
The period of accelerated loss of bone mineral density in the hip bones occurring among women and men older than 65 may be an important contributor to the increased incidence of hip fracture among patients in that age group. The extent of bone loss that we observed in both sexes indicates that, in the absence of additional risk factors or therapy, repeat testing of bone mineral density to diagnose osteoporosis could be delayed to **every 5 years**.
Berry SD, Samelson EJ, Hannan MT, et al. **Second hip fracture** in older men and women: the framingham study. Arch Intern Med. 2007 Oct 8;167(18):1971-6. Following a first hip fracture, 2.5% of subjects experienced a second hip fracture within 1 year, and 8.2% of subjects (9.7% of women) experienced a second hip fracture within 5 years. One-year mortality following an initial hip fracture was 15.9% compared with 1-year mortality following a second hip fracture of 24.1%. Among survivors of an initial hip fracture, the incidence of a second hip fracture is substantial. Older age and functional status may be important predictors of a second hip fracture.
Berry S, Waldron T, Winquist E, Lukka H. The use of **bisphosphonates** in men with hormone-refractory **prostate cancer**: a systematic review of randomized trials. Can J Urol. 2006 Aug;13(4):3180-8.
Bertone-Johnson ER et al. Vitamin D supplementation and **depression** in the **Women's Health Initiative** Calcium and Vitamin D Trial. Am J Epidemiol 2012 Jul 1; 176:1.
Bhasin S, et al. **Testosterone therapy** in adult men with androgen deficiency syndromes: an endocrine society clinical practice guideline. J Clin Endocrinol Metab. 2006 Jun;91(6):1995-2010. Epub 2006 May 23. Erratum in: J Clin Endocrinol Metab. 2006 Jul;91(7):2688.
Bilezikian JP. **Osteonecrosis of the jaw**--do bisphosphonates pose a risk? N Engl J Med. 2006 Nov 30;355(22):2278-81.
Bingham CO 3rd, et al. Risedronate decreases biochemical markers of cartilage degradation but does not decrease symptoms or slow radiographic progression in patients with **medial compartment osteoarthritis** of the knee: Results of the two-year multinational knee osteoarthritis structural arthritis study. Arthritis Rheum. 2006 Oct 30;54(11):3494-3507 [Epub ahead of print]
Bischoff-Ferrari HA, Willett WC, Wong JB, et al. Fracture prevention with vitamin D supplementation: a meta-analysis of randomized controlled trials. JAMA. 2005 May 11;293(18):2257-64 & ACP Journal Club . (Oral vitamin D supplementation between 700 to 800 IU/d appears to reduce the risk of hip and any nonvertebral fractures in ambulatory or institutionalized elderly persons. An oral vitamin D dose of 400 IU/d is not sufficient for fracture prevention.)(InfoPOEMs: Supplementation with calcium 1000 mg and vitamin D3 800 IU daily decreases the likelihood that older people will experience a first hip fracture or other nonvertebral fracture. The dose of calcium is lower than the 1500 mg daily that is recommended and usually used; the vitamin D dose is higher than the dose usually used in comparison studies with other drugs. These results conflict with 2 large studies in patients at high risk or with a previous osteoporotic fracture for whom these doses did not decrease the rate of fracture (BMJ 2005; 330:1003-06 and Lancet 2005; 365:1621-28). (LOE = 1a))
Bischoff-Ferrari HA, et al. Effect of cholecalciferol plus calcium on falling in ambulatory older men and women: a 3-year randomized controlled trial. Arch Intern Med. 2006 Feb 27;166(4):424-30. (InfoPOEMs: Treating older women with vitamin D and calcium decreases their likelihood of experiencing a fall, although the change in fall rate does not occur quickly. The effect is more pronounced in inactive women. (LOE = 1b))
Bischoff-Ferrari HA, Willett WC, Oray EJ, et al. A pooled analysis of **vitamin D dose** requirements for fracture prevention. N Engl J Med 2012;367:40-9. {highest actual-intake quartile (792 to 2000 IU daily), there was a 30% reduction in hip fracture incidence}
Bisphosphonate-associated **jaw osteonecrosis.** Pharmacist's Letter August 2006. (Bilezikian JP. Osteonecrosis of the jaw--do bisphosphonates pose a risk? N Engl J Med. 2006 Nov 30;355(22):2278-81. Woo SB, Hellstein JW, Kalmar JR. Bisphosphonates and osteonecrosis of the jaw. Ann Intern Med. 2006 Nov 21;145(10):792. (50 cases in those receiving po bisphosphonates for osteoporosis))
Bjelakovic G, Gluud LL, Nikolova D, et al. **Vitamin D supplementation for prevention of mortality** in adults. Cochrane Database of Systematic Reviews 2011, Issue 7. Art. No.: CD007470. DOI: 10.1002/14651858.CD007470.pub2. Vitamin D in the form of vitamin D3 seems to decrease mortality in predominantly elderly women who are mainly in institutions and dependent care. Vitamin D2, alfacalcidol, and calcitriol had no statistically significant effect on mortality. Vitamin D3 combined with calcium significantly increased nephrolithiasis. Both alfacalcidol and calcitriol significantly increased hypercalcaemia.
Black DM, Cummings SR, Karpf DB, et al. Randomised trial of effect of **alendronate** on risk of fracture in women with **existing vertebral fractures**. Fracture Intervention Trial Research Group (**FIT**). Lancet 1996;348:1535-41.
Black DM, Bilezikian JP, Ensrud KE, et al. PaTH Study Investigators. One year of alendronate after one year of **parathyroid** hormone (1-84) for osteoporosis. N Engl J Med. 2005 Aug 11;353(6):555-65.
Black DM, Greenspan SL, Ensrud KE, et al.; PaTH Study Investigators. The effects of **parathyroid hormone and alendronate** alone or in combination in postmenopausal osteoporosis. N Engl J Med. 2003 Sep 25;349(13):1207-15. Epub 2003 Sep 20.
Black DM, Thompson DE, Bauer DC, et al. Fracture risk reduction with alendronate in women with osteoporosis: the Fracture Intervention Trial. **FIT** Research Group [published correction appears in J Clin Endocrinol Metab 2001;86:938]. J Clin Endocrinol Metab 2000;85:4118-24.

Black DM, Delmas PD, Eastell R, et al. **HORIZON** Pivotal Fracture Trial. **Once-yearly zoledronic** acid for treatment of postmenopausal osteoporosis. N Engl J Med. 2007 May 3;356(18):1809-22. Treatment with zoledronic acid reduced the risk of morphometric vertebral fracture by 70% during a 3-year period, as compared with placebo (3.3% in the zoledronic-acid group vs. 10.9% in the placebo group; relative risk, 0.30; 95% confidence interval [CI], 0.24 to 0.38) and reduced the risk of hip fracture by 41% (1.4% in the zoledronic-acid group vs. 2.5% in the placebo group; hazard ratio, 0.59; 95% CI, 0.42 to 0.83). Nonvertebral fractures, clinical fractures, and clinical vertebral fractures were reduced by 25%, 33%, and 77%, respectively (P<0.001 for all comparisons). Zoledronic acid was also associated with a significant improvement in bone mineral density and bone metabolism markers. Adverse events, including change in renal function, were similar in the two study groups. However, serious atrial fibrillation occurred more frequently in the zoledronic acid group 1.3 vs 0.5% (in 50 vs. 20 patients, P<0.001). A once-yearly infusion of zoledronic acid during a 3-year period significantly reduced the risk of vertebral, hip, and other fractures.

Black, Dennis M., Kelly, Michael P., Genant, Harry K., et al. the Fracture Intervention Trial (FIT,FLEX) and HORIZON Pivotal Fracture Trial Steering Committees, Bisphosphonates and Fractures of the **Subtrochanteric or Diaphyseal Femur**. N Engl J Med 2010 0: NEJMoa1001086.

Bliuc D, Nguyen ND, Milch VE, Nguyen TV, Eisman JA, Center JR. **Mortality risk** associated with low-trauma osteoporotic fracture and subsequent fracture in men and women. JAMA. 2009 Feb 4;301(5):513-21. In a sample of older women and men, all low-trauma fractures were associated with increased mortality risk for 5 to 10 years. Subsequent fracture was associated with increased mortality risk for an additional 5 years.

Bolland MJ, Barber PA, Doughty RN, et al.. Vascular events in healthy older women receiving calcium supplementation: randomised controlled trial. BMJ. 2008 Jan 15; [Epub ahead of print] Calcium supplementation in healthy postmenopausal women is associated with upward trends in cardiovascular event rates.

Bolland Mark J, Avenell Alison, Baron John A, et al, Effect of **calcium** supplements on risk of **myocardial infarction** and cardiovascular events: meta-analysis. BMJ 2010;341:c3691.

Boonen S, et al. Effect of osteoporosis treatments on risk of **non-vertebral fractures**: review and meta-analysis of intention-to-treat studies. Osteoporos Int. 2005 Oct;16(10):1291-8. Epub 2005 Jun 29.

Boonen S, Sellmeyer DE, Lippuner K, Orlov-Morozov A, Abrams K, Mesenbrink P,Eriksen EF, Miller PD. **Renal safety of annual zoledronic** acid infusions in osteoporotic postmenopausal women. Kidney Int. 2008 May 28. [Epub ahead of print] We found that transient changes in renal function can occur following an annual zoledronic acid infusion but, in the long term, renal function was not different from control patients.

Bonnick S, et al. Comparison of **weekly** treatment of postmenopausal osteoporosis with **alendronate versus risedronate** over two years. J Clin Endocrinol Metab. 2006 Jul;91(7):2631-7. Epub 2006 Apr 24.

Bordeleau L, Pritchard KI, Loprinzi CL, et al. Multicenter, Randomized, Cross-Over Clinical Trial of **Venlafaxine Versus Gabapentin** {venlafaxine (37.5 mg daily for 7 days followed by 75 mg daily for 21 days) versus gabapentin (300 mg once per day for 3 days, then 300 mg twice per day for 3 days, then 300 mg three times per day for 22 days)} for the Management of Hot Flashes in Breast Cancer Survivors. J Clin Oncol. 2010 Nov 8.

Bosland MC, Kato I, Zeleniuch-Jacquotte A, et al. Effect of **soy protein isolate supplementation on biochemical recurrence of prostate cancer** after radical prostatectomy: a randomized trial. JAMA. 2013 Jul 10;310(2):170-8.

Brown JP, et al. **Canadian consensus conference on osteoporosis, 2006 update**. J Obstet Gynaecol Can. 2006 Feb;28(2 Suppl 1):S95-S112. http://sogc.org/guidelines/documents/JOGC-suppl-1eng-osteoporosis.pdf

Brown JP, Josse RG; Scientific Advisory Council of the Osteoporosis Society of Canada. **2002 clinical practice guidelines for the diagnosis and management of osteoporosis in Canada**. CMAJ. 2002 Nov 12;167(10 Suppl):S1-34. Review. Erratum in: CMAJ. 2003 Feb 18;168(4):400. CMAJ. 2003 Mar 18;168(6):676.. CMAJ. 2003 Mar 4;168(5):544. http://www.cmaj.ca/cgi/content/full/167/10_suppl/s1

Brown JP, Kendler DL, McClung MR, Emkey RD, Adachi JD, Bolognese MA, et al. The efficacy and tolerability of risedronate once a week for the treatment of postmenopausal osteoporosis. Calcif Tissue Int 2002;71:103-11.

Buchbinder, Rachelle, Osborne, Richard H., Ebeling, Peter R., et al.. A Randomized Trial of **Vertebroplasty** for Painful Osteoporotic Vertebral Fractures. N Engl J Med 2009 361: 557-568.

Cadarette SM, Katz JN, Brookhart MA, Stürmer T, Stedman MR, Solomon DH. **Relative effectiveness of osteoporosis drugs** for preventing nonvertebral fracture. Ann Intern Med. 2008 May 6;148(9):637-46. Differences in fracture risk between risedronate or raloxifene and alendronate were small. Nasal calcitonin recipients may have a higher risk for nonvertebral fractures compared with alendronate recipients.

Calle EE, Feigelson HS, Hildebrand JS, Teras LR, Thun MJ, Rodriguez C. Postmenopausal hormone use and **breast cancer** associations differ by hormone regimen and histologic subtype. Cancer. 2009 Jan 20. [Epub ahead of print] Use of E + P is more detrimental to the breast than E-only use, in terms of both ductal and lobular cancer. The findings from the current study suggest a window of 2 to 3 years for the risks of E + P both to become apparent after initial use and to attenuate after cessation.

Canalis E, Giustina A, Bilezikian JP. Mechanisms of **anabolic therapies** for osteoporosis. N Engl J Med. 2007 Aug 30;357(9):905-16.

Casele H, et al. **Bone density** changes in women who receive **thromboprophylaxis** in pregnancy. Am J Obstet Gynecol. 2006 Oct;195(4):1109-13. In this study, the incidence of clinically significant bone loss (> or = 10%) in the femur in women who received thromboprophylaxis in pregnancy is approximately 2% 2.5% and appears to be similar, regardless of whether the patient receives low molecular weight heparin therapy or unfractionated heparin therapy.

Cauley JA, Robbins J, Chen Z, Cummings SR, Jackson RD, LaCroix AZ, et al. Effects of **estrogen plus progestin** on risk of fracture and bone mineral density: the Women's Health Initiative (**WHI**) randomized trial. JAMA 2003;290:1729-38.

Cauley JA, Hochberg MC, Lui LY, Palermo L, Ensrud KE, Hillier TA, Nevitt MC,

Cauley JA, Lacroix AZ, Wu L, Horwitz M, et al. Serum 25-hydroxyvitamin D concentrations and risk for **hip fractures**. Ann Intern Med. 2008 Aug 19;149(4):242-50. Low serum 25(OH) vitamin D concentrations are associated with a higher risk for hip fracture.

Center JR, Bliuc D, Nguyen TV, Eisman JA. **Risk of subsequent fracture after low-trauma fracture** in men and women. JAMA. 2007 Jan 24;297(4):387-94. After an initial low-trauma fracture, absolute risk of subsequent fracture was similar for men and women. This increased risk occurred for virtually all clinical fractures and persisted for up to 10 years.

Che M, Ettinger B, Nguyen MT, Pressman AR, Johnston J. High-dose **corticosteroid** exposure and osteoporosis intervention in adults. Ann Allergy Asthma Immunol. 2006 Oct;97(4):497-501.

Chesnut CH 3d, Silverman S, Andriano K, Genant H, et al. A randomized trial of nasal spray salmon **calcitonin** in postmenopausal women with established osteoporosis: the Prevent Recurrence of Osteoporotic Fractures Study. **PROOF** Study Group. Am J Med 2000;109:267-76. CONCLUSION: Salmon calcitonin nasal spray at a dose of 200 IU daily significantly reduces the risk of new vertebral fractures in postmenopausal women with osteoporosis The reductions in vertebral fractures in the 100-IU (RR = 0.85, 95% CI: 0.60- to 1.21) and the **400-IU** (RR = 0.84, 95% CI: 0.59- to 1.18) groups were not significantly different from placebo. .

Cheung AM, Tile L, Lee Y, et al. **Vitamin K Supplementation** in Postmenopausal Women with Osteopenia (ECKO Trial): A Randomized Controlled Trial. PLoS Med. 2008 Oct 14;5(10):e196. [Epub ahead of print] Daily 5 mg of vitamin K1 supplementation for 2 to 4 y does not protect against age-related decline in BMD, but may protect against fractures and cancers in postmenopausal women with osteopenia. More studies are needed to further examine the effect of vitamin K on fractures and cancers.

Cockayne S, Adamson J, Lanham-New S, Shearer MJ, Gilbody S, Torgerson DJ. **Vitamin K and the Prevention of Fractures:** Systematic Review and Meta-analysis of Randomized Controlled Trials. Arch Intern Med. 2006 Jun 26;166(12):1256-61.

Cohen S, Levy RM, Keller M, Boling E, Emkey RD, Greenwald M, et al. **Risedronate** therapy prevents corticosteroid-induced bone loss: a twelve-month, multicenter, randomized, double-blind, placebo-controlled, parallel-group study. Arthritis Rheum 1999;42:2309-18.

Cosman F, Nieves J, Zion M, Woelfert L, Luckey M, Lindsay R. **Daily and cyclic parathyroid** hormone in women receiving alendronate. N Engl J Med. 2005 Aug 11;353(6):566-75.

Cosman F, Wermers RA, Recknor C, Mauck KF, Xie L, Glass EV, Krege JH. Effects of **Teriparatide** in Postmenopausal Women with Osteoporosis on **Prior Alendronate or Raloxifene**: Differences between Stopping and Continuing the Antiresorptive Agent.J Clin Endocrinol Metab. 2009 Jul 7. [Epub ahead of print] In women with osteoporosis treated with antiresorptives, greater bone turnover increases were achieved by switching to teriparatide, while greater BMD increases were achieved by adding teriparatide.

Cranney A, Adachi JD. Benefit-risk assessment of raloxifene in postmenopausal osteoporosis. Drug Saf. 2005;28(8):721-30.

Cranney A, et al. Clinical Guidelines Committee of **Osteoporosis Canada**. **Parathyroid hormone** for the treatment of osteoporosis: a systematic review. CMAJ. 2006 Jul 4;175(1):52-9. (InfoPOEMs: There is consistent evidence that human parathyroid hormone (hPTH) reduces the risk of recurrent fracture in very high-risk women with osteoporosis and a history of fracture. An accompanying guideline reports that the number needed to treat (NNT) with hPTH 34 (teriparatide [Forteo]) for 21 months to prevent one vertebral fracture is 11 and the NNT for 21 months to prevent one nonvertebral fracture is 34. This compares with NNTs of 9 and 34, respectively, for 36 months of alendronate. Given the much lower cost and greater convenience of alendronate and other bisphosphonates, teriparatide should be reserved for a very select group of very osteoporotic patients. (LOE = 1a))

Cummings SR, Black DM, Thompson DE, Applegate WB, Barrett-Connor E, Musliner TA, et al. Effect of **alendronate** on risk of fracture in women with **low bone density** but without vertebral fractures: results from the Fracture Intervention Trial (**FIT**). JAMA 1998;280:2077-82. CONCLUSIONS: In women with low BMD but without vertebral fractures, 4 years of alendronate safely increased BMD and decreased the risk of first vertebral deformity. Alendronate significantly reduced the risk of clinical fractures among women with osteoporosis but not among women with higher BMD. Alendronate increased BMD at all sites studied (P<.001) and reduced clinical fractures from 312 in the placebo group to 272 in the intervention group, but **not significantly** so (14% reduction; relative hazard [RH], 0.86; 95% confidence interval [CI], 0.73-1.01).

Cummings SR. **A 55-year-old woman with osteopenia**. JAMA. 2006 Dec 6;296(21):2601-10. (Khosla S, Melton LJ 3rd. Clinical practice. **Osteopenia**. N Engl J Med. 2007 May 31;356(22):2293-300.)

Cummings SR, Schwartz AV, Black DM. **Alendronate and atrial fibrillation**. N Engl J Med. 2007 May 3;356(18):1895-6. Serious atrial fibrillation: 1.5% alendronate vs 1% placebo during an average of 4 years of the FIT trial.

Cummings SR et al. **Lasofoxifene** in postmenopausal women with osteoporosis. N Engl J Med 2010 Feb 25; 362:686.

Cummings SR. **Long-term risk of incident vertebral fractures**. JAMA. 2007 Dec 19;298(23):2761-7. Low BMD and prevalent vertebral fractures are independently related to new vertebral fractures over 15 years of follow-up. Women with a prevalent vertebral fracture have a substantially increased absolute risk of an incident fracture, especially if they have osteoporosis diagnosed by BMD.

Cummings, Steven R., Martin, Javier San, McClung, Michael R., et al., the **FREEDOM** Trial, **Denosumab** for Prevention of Fractures in Postmenopausal Women with Osteoporosis. N Engl J Med 2009 0: NEJMoa0809493

Davis SR, Castelo-Branco C, Chedraui P, et al; as the Writing Group of the International Menopause Society for World Menopause Day 2012. Understanding **weight gain at menopause**. Climacteric. 2012 Oct;15(5):419-29.

De Groen PC, Lubbe DF, Hirsch LJ, Daifotis A, Stephenson W, Freedholm D, et al. Esophagitis associated with the use of **alendronate**. N Engl J Med 1996;335:1016-21.

de Nijs RN, et al. STOP Investigators. **Alendronate or alfacalcidol** in **glucocorticoid-induced** osteoporosis. N Engl J Med. 2006 Aug 17;355(7):675-84.

Delmas PD, et al. **Intravenous ibandronate** injections in postmenopausal women with osteoporosis: One-year results from the dosing intravenous administration study. Arthritis Rheum. 2006 Jun;54(6):1838-46. As assessed by BMD, intravenous injections of ibandronate (2 mg every 2 months or 3 mg every 3 months) are at least as effective as the regimen of 2.5 mg orally daily, which has proven antifracture efficacy, and are well tolerated.

Dormuth CR, Carney G, Carleton B, et al. **Thiazolidinediones** and fractures in men and women. *Arch Intern Med*. 2009; 169:1395-1402.

Downey TW, et al. **Adherence and persistence** associated with the pharmacologic treatment of osteoporosis in a managed care setting. South Med J. 2006 Jun;99(6):570-5. (InfoPOEMs: Approximately half the women initially prescribed a bisphosphonate -- daily or weekly treatment -- will not be taking it after 3months, and only 1 in 5 will be taking it after a year. Since this short duration is unlikely to provide them with meaningful benefit, the money spent on bone mineral density testing and the rest of the diagnostic work-up and follow-up, along with the cost of the initial drug therapy, is essentially wasted on 4 of 5 women diagnosed with osteoporosis. (LOE = 1b))

Ebeling PR. Clinical practice. **Osteoporosis in men**. N Engl J Med. 2008 Apr 3;358(14):1474-82.

Eneroth M, Olsson UB, Thorngren KG. **Nutritional Supplementation** Decreases Hip Fracture-related Complications. Clin Orthop Relat Res. 2006 Oct;451:212-7.

Ensrud K, et al Effect of **raloxifene** on **cardiovascular adverse events** in postmenopausal women with osteoporosis. Am J Cardiol. 2006 Feb 15;97(4):520-7. Epub 2006 Jan 4. Conclusion, we found no evidence of a beneficial or harmful effect of raloxifene on the incidence of cardiovascular events overall, or coronary or cerebrovascular events, in postmenopausal osteoporotic women at relatively low risk of cardiovascular events.

Ensrud KE, Ewing SK, Taylor BC, et al.; for the Study of Osteoporotic Fractures Research Group. Comparison of 2 Frailty Indexes for Prediction of Falls, Disability, Fractures, and Death in Older Women. Arch Intern Med. 2008 Feb 25;168(4):382-389. The simple **SOF index** (components of weight loss, inability to rise from a chair 5 times without using arms, and reduced energy level) predicts risk of falls, disability, fracture, and death as well as the more complex CHS index and may provide a useful definition of frailty to identify older women at risk of adverse health outcomes in clinical practice.

Etminan M, et al. Use of Oral Bisphosphonates and the Risk of Aseptic **Osteonecrosis**: A Nested Case-Control Study. J Rheumatol. 2008 Jan 15; [Epub ahead of print] In this cohort of elderly cardiovascular patients, an association was observed between oral bisphosphonate use and aseptic osteonecrosis.

Ettinger B, et al. Reduction of vertebral fracture risk in postmenopausal women with **osteoporosis** treated with **raloxifene**: a 3-yr randomized clinical trial. Multiple Outcomes of Raloxifene Evaluation (**MORE**) Investigators [correction JAMA 1999;282:2124]. JAMA 1999;282:637-45. CONCLUSIONS: In postmenopausal women with osteoporosis, raloxifene increases bone mineral density in the spine and femoral neck and reduces risk of vertebral fracture.

Ettinger B, Pressman A, Schein J, Chan J, Silver P, Connolly N. **Alendronate** use among 812 women: prevalence of gastrointestinal complaints, noncompliance with patient instructions, and discontinuation. J Managed Care Pharm 1998;4:488-92.

Favus Murray J., **Bisphosphonates for Osteoporosis**. N Engl J Med 2010; 363:2027-2035.

FDA July/11 notified healthcare professionals and patients about its ongoing review of data from published studies to evaluate whether use of **oral bisphosphonate** drugs is associated with an increased risk of cancer of the esophagus. FDA has not concluded that taking an oral bisphosphonate drug increases the risk of **esophageal cancer**. There are insufficient data to recommend endoscopic screening of asymptomatic patients.

Finkelstein JS, Hayes A, Hunzelman JL, Wyland JJ, Lee H, Neer RM. The effects of **parathyroid hormone, alendronate, or both** in men with osteoporosis. N Engl J Med. 2003 Sep 25;349(13):1216-26. Epub 2003 Sep 20.

Fogelman I, Ribot C, Smith R, et al. **Risedronate** reverses bone loss in postmenopausal women with **low bone mass**: results from a multinational, double-blind, placebo-controlled trial. **BMD-MN** Study Group. J Clin Endocrinol Metab. 2000 May;85(5):1895-900.

Formoso G, Perrone E, Maltoni S, et al. Short and long term effects of **tibolone** in postmenopausal women. Cochrane Database Syst Rev. 2012 Feb 15;2:CD008536. Tibolone, used at the daily dose of 2.5 mg, may be less effective than combined HT in alleviating menopausal symptoms although it reduced the incidence of vaginal bleeding. There was evidence that treatment with combined HT was more effective in managing menopausal symptoms than was tibolone. Available data on the long term safety of tibolone is concerning given the increase in the risk of breast cancer in women who had already suffered from breast cancer in the past and in a separate trial the increase in the risk of stroke in women whose mean age was over 60 years.

Freeman EW, Rickels K, Sammel MD, Lin H, Sondheimer SJ. Time to relapse after short- or long-term treatment of severe premenstrual syndrome with **sertraline**. Arch Gen Psychiatry. 2009 May;66(5):537-44.

Gafni RI, et al. **Tenofovir** disoproxil fumarate and an optimized background regimen of antiretroviral agents as salvage therapy: impact on bone mineral density in HIV-infected children. Pediatrics. 2006 Sep;118(3):e711-8. Epub 2006 Aug 21.

Gallagher JC, Levine JP. **Preventing osteoporosis** in symptomatic postmenopausal women. Menopause. 2010 Aug 5.

Ganti AK, Sahmoun AE, Panwalkar AW, Tendulkar KK, Potti A. Hormone replacement therapy is associated with decreased survival in women with **lung cancer.** J Clin Oncol. 2006 Jan 1;24(1):59-63. Epub 2005 Nov 28.

Gaudio A, Morabito N. Pharmacological management of severe postmenopausal osteoporosis. Drugs Aging. 2005;22(5):405-17.

Gillespie WJ, Gillespie LD, Parker MJ. **Hip protectors for preventing hip fractures** in older people. Cochrane Database Syst Rev. 2010 Oct 6;10:CD001255. The effectiveness of the provision of hip protectors in reducing the incidence of hip fracture in older people is still not clearly established, although they may reduce the rate of hip fractures if made available to frail older people in nursing care.

Gnant M, Mlineritsch B, Schippinger W, et al. ABCSG-12 Trial Investigators, Marth C. Endocrine therapy plus **zoledronic acid in premenopausal breast cancer**. N Engl J Med. 2009 Feb 12;360(7):679-91. The addition of zoledronic acid to adjuvant endocrine therapy improves disease-free survival in premenopausal patients with estrogen-responsive early breast cancer.

Grant AM, Avenell A, Campbell MK, et al.; Oral vitamin D3 and calcium for secondary prevention of low-trauma fractures in elderly people (Randomised Evaluation of **Calcium Or vitamin D**, **RECORD**): a randomised placebo-controlled trial. Lancet. 2005 May;365(9471):1621-8 & ACP Journal Club. (InfoPOEMs: The combination of calcium 1000 mg and vitamin D3 800 IU was ineffective in preventing fractures in 2 studies enrolling a total of more than 8500 participants, almost all of whom were female and at least 70 years old and either had a previous osteoporotic fracture or were at high risk. The dose of calcium is lower than the 1500 mg commonly recommended and used. These results conflict with a meta-analysis that found that the combination therapy reduced fracture rate, including hip fracture, in older patients who have not had a previous hip or nonvertebral fracture (JAMA 2005; 293:2257-64). (LOE = 1b))

Greenblatt D. Treatment of postmenopausal osteoporosis. Pharmacotherapy. 2005 Apr;25(4):574-84.

Greenspan SL, Resnick NM, Parker RA. Combination therapy with **hormone replacement and alendronate** for prevention of bone loss in elderly women: a randomized controlled trial. JAMA. 2003 May 21;289(19):2525-33.

Greenspan SL, Emkey RD, Bone HG, et al. Significant differential effects of **alendronate, estrogen, or combination** therapy on the rate of bone loss after discontinuation of treatment of postmenopausal osteoporosis. A randomized, double-blind, placebo-controlled trial. Ann Intern Med. 2002 Dec 3;137(11):875-83. Summary for patients in: Ann Intern Med. 2002 Dec 3;137(11):I31.

Grey A, Bolland MJ, Wattie D, Horne A, Gamble G, Reid IR. The antiresorptive effects of a single dose of zoledronate persist for two years: a randomized, placebo-controlled trial in osteopenic postmenopausal women. J Clin Endocrinol Metab. 2009 Feb;94(2):538-44. n=50. Antiresorptive effects of a single 5-mg dose of **zoledronate** are sustained for at least 2 yr. The magnitudes of the effects on markers of bone turnover and bone mineral density are comparable at 12 and 24 months. Administration of zoledronate at intervals of up to 2 yr may be associated with antifracture efficacy; clinical trials to investigate this possibility are justified.

Grossman JM, Gordon R, Ranganath VK, et al. **American College of Rheumatology (ACR) 2010** recommendations for the prevention and treatment of **glucocorticoid-induced osteoporosis**. Arthritis Care Res (Hoboken). 2010 Jul 26.

Hanley DA, Cranney A, Jones G, et al. **Vitamin D in adult** health & disease: a review and **guideline statement from Osteoporosis Canada**–summary.CMAJ 2010 0: cmaj.091062.

Harris ST, Watts NB, Genant HK, et al. Effects of **risedronate** treatment on vertebral and nonvertebral fractures in women with postmenopausal **osteoporosis**: a randomized controlled trial. Vertebral Efficacy with Risedronate Therapy (**VERT**) Study Group. JAMA 1999;282:1344-52. Treatment with 5 mg/d of risedronate, compared with placebo, decreased the cumulative incidence of new vertebral fractures by 41 % (95% confidence interval [CI], 18%-58%) over 3 years (11.3 % vs 16.3%; P= .003). A fracture reduction of 65% (95% CI, 38%-81 %) was observed after the first year (2.4% vs 6.4%; P<.001). The cumulative incidence of nonvertebral fractures over 3 years was reduced by 39% (95% CI, 6%-61 %) (5.2 % vs 8.4%; P = .02). Bone mineral density increased significantly compared with placebo at the lumbar spine (5.4% vs 1.1 %), femoral neck (1.6% vs -1.2%), femoral trochanter (3.3% vs -0.7%), and midshaft of the radius (0.2% vs -1.4%). Bone formed during risedronate treatment was histologically normal. The overall safety profile of risedronate, including gastrointestinal safety, was similar to that of placebo. CONCLUSIONS: These data suggest that risedronate therapy is effective and well tolerated in the treatment of women with established postmenopausal osteoporosis who had at least 1 **vertebral fracture at baseline**.

Health Canada May 2006: The **RUTH** study demonstrated an **increase in mortality due to stroke** for Evista compared to placebo. The incidence of stroke mortality was 1.5 per 1,000 women per year for placebo versus 2.2 per 1,000 women per year for Evista (p=0.0499). The incidence of stroke, myocardial infarction, hospitalized acute coronary syndrome, cardiovascular mortality, or overall mortality (all causes combined) was comparable for Evista and placebo. http://www.hc-sc.gc.ca/dhp-mps/medeff/advisories-avis/prof/2006/evista_hpc-cps_e.html Barrett-Connor E, et al.; Raloxifene Use for The Heart (**RUTH**) Trial Investigators. Effects of raloxifene on cardiovascular events and breast cancer in postmenopausal women. N=10,101 5.6yrs N Engl J Med. 2006 Jul 13;355(2):125-37. (InfoPOEMs: For every 1000 women who take raloxifene for 5 years, we can expect 4 to 5 additional strokes, 6 additional episodes of venous thromboembolism (VTE), 6 fewer invasive breast cancers, and 6 to 7 fewer clinical vertebral fractures. The cost for this mixed bag of benefits and harms would be approximately $1000 per woman per year, for a total cost of $5,000,000 at current drug prices. (LOE = 1b))

Health Canada May/12: Cases of severe, sometimes **fatal, symptomatic hypocalcemia associated with XGEVA (denosumab)** treatment have been reported in cancer patients with bone metastases

Heaney RP, Zizic TM, Fogelman I, Olszynski WP, et al. **Risedronate** reduces the risk of **first vertebral fracture in osteoporotic women**. Osteoporos Int. 2002;13(6):501-5.

Heckbert SR, Li G, Cummings SR, Smith NL, Psaty BM. Use of alendronate and risk of incident **atrial fibrillation** in women. Arch Intern Med. 2008 Apr 28;168(8):826-31. Ever use of alendronate was associated with an increased risk of incident AF in clinical practice.

Hippisley-Cox Julia, Coupland Carol, Predicting risk of osteoporotic fracture in men and women in England and Wales: prospective derivation and validation of **QFractureScores.** BMJ 2009;339:b4229, doi: 10.1136/bmj.b4229 (Published 19 November 2009)

Hippisley-Cox J, Coupland C. Derivation and validation of **updated QFracture algorithm** to predict risk of osteoporotic fracture in primary care in the United Kingdom: prospective open cohort study. BMJ. 2012 May 22;344:e3427.

Hodis HN, Mack WJ, Azen SP, ET AL. Women's Estrogen-Progestin Lipid-Lowering Hormone Atherosclerosis Regression Trial Research Group (**WELL-HART**). Hormone therapy and the progression of coronary-artery atherosclerosis in postmenopausal women. N Engl J Med. 2003 Aug 7;349(6):535-45.

Hoes JN, et al. EULAR evidence-based management of systemic **glucocorticoid therapy** in rheumatic diseases. Ann Rheum Dis. 2007 Dec;66(12):1560-7. Epub 2007 Jul 27. **Algorithm** provided

Holder KK, Kerley SS. Alendronate for fracture prevention in postmenopause. Am Fam Physician. 2008 Sep 1;78(5):579-81. For vertebral fractures, a 45 percent relative risk reduction was found (relative risk [RR] = 0.55; 95% confidence interval [CI], 0.45 to 0.67). This was significant for primary prevention, with a 45 percent relative risk reduction (RR = 0.55; 95% CI, 0.38 to 0.80) and 2 percent absolute risk reduction; and for secondary prevention, with 45 percent relative risk reduction (RR = 0.55; 95% CI, 0.43 to 0.69) and 6 percent absolute risk reduction. For nonvertebral fractures, a 16 percent relative risk reduction was found (RR = 0.84; 95% CI, 0.74 to 0.94). This was significant for secondary prevention, with a 23 percent relative risk reduction (RR = 0.77; 95% CI, 0.64 to 0.92) and a 2 percent absolute risk reduction, but not for primary prevention (RR = 0.89; 95% CI, 0.76 to 1.04). There was a 40 percent relative risk reduction in hip fractures (RR = 0.60; 95% CI, 0.40 to 0.92), but only secondary prevention was significant, with a 53 percent relative risk reduction (RR = 0.47; 95% CI, 0.26 to 0.85) and a 1 percent absolute risk reduction. At 10 mg of alendronate per day, clinically important and statistically significant reductions in vertebral, nonvertebral, hip, and wrist fractures were observed for secondary prevention. The authors found no statistically significant results for primary prevention, with the exception of vertebral fractures, for which the reduction was clinically important.

Hou N, Hong S, Wang W, et al. **Hormone Replacement Therapy and Breast Cancer**: Heterogeneous Risks by Race, Weight, and Breast Density. J Natl Cancer Inst. 2013 Sep 3.

Howe TE, Shea B, Dawson LJ, et al. **Exercise for preventing and treating osteoporosis** in postmenopausal women. *Cochrane Database of Systematic Reviews* 2011, Issue 7. Art. No.: CD000333. DOI: 10.1002/14651858.CD000333.pub2. Our results suggest a relatively small statistically significant, but possibly important, effect of exercise on bone density compared with control groups. Exercise has the potential to be a safe and effective way to avert bone loss in postmenopausal women.

Ing-Lorenzini K, Desmeules J, Plachta O, Suva D, Dayer P, Peter R. **Low-energy femoral fractures** associated with the long-term use of bisphosphonates: a case series from a Swiss university hospital. Drug Saf. 2009;32(9):775-85. doi: 10.2165/00002018-200932090-00002.

Ioannidis G, Papaioannou A, Hopman WM, et al. Relation between **fractures and mortality**: results from the Canadian Multicentre Osteoporosis Study. CMAJ. 2009 Aug 4. [Epub ahead of print]

Irani J, Salomon L, Oba R, Bouchard P, Mottet N. Efficacy of venlafaxine, **medroxyprogesterone** acetate, and cyproterone acetate for the treatment of vasomotor hot flushes in men taking gonadotropin-releasing hormone analogues for prostate cancer: a double-blind, randomised trial. Lancet Oncol. 2009 Dec 4.

Jaakkola S, Lyytinen H, Pukkala E, Ylikorkala O. **Endometrial cancer** in postmenopausal women using estradiol-progestin therapy. Obstet Gynecol. 2009 Dec;114(6):1197-204. Use of a continuous rather than a sequential estradiol-progestin regimen decreases the risk of endometrial cancer, whereas the route of administration or type of progestin does not differ in terms of endometrial cancer risk.

Jackson RD, LaCroix AZ, Gass M, et al.; Women's Health Initiative Investigators. Calcium plus vitamin D supplementation and the risk of fractures. N Engl J Med. 2006 Feb 16;354(7):669-83. Among healthy postmenopausal women, calcium with vitamin D supplementation resulted in a small but significant improvement in hip bone density, did not significantly reduce hip fracture, and increased the risk of kidney stones. (InfoPOEMs: The ability of a small dose of calcium and vitamin D to prevent fractures in healthy community-dwelling women is modest at best. This study used a relatively low dose of vitamin D (less than the 700 IU to 800 IU found most beneficial in previous studies), and the patients were generally at low risk of fracture. Perhaps that explains the discordance of these findings with the bulk of the literature on this topic. (LOE = 1b))

Jacoby Vanessa L.; Grady Deborah; Wactawski-Wende Jean; et al. **Oophorectomy vs Ovarian Conservation With Hysterectomy**: Cardiovascular Disease, Hip Fracture, and Cancer in the Women's Health Initiative Observational Study. Arch Intern Med. 2011;171(8):760-768.

Järvinen TL, Sievänen H, Khan KM, Heinonen A, Kannus P. Shifting the focus in fracture prevention **from osteoporosis to falls**. BMJ. 2008 Jan 19;336(7636):124-6.

Jones GL, Ledger W, Mitchell C. Suspected **premature menopause**. BMJ. 2008 Apr 12;336(7648):833.

Kakaria PJ, Nashel DJ, Nylen ES. Debilitating muscle cramps after **teriparatide** therapy. Ann Intern Med. 2005 Feb 15;142(4):310.

Kallmes, David F., Comstock, Bryan A., Heagerty, Patrick J., et al. A Randomized Trial of **Vertebroplasty** for Osteoporotic Spinal Fractures. N Engl J Med 2009 361: 569-579.

Karim R, Dell RM, Greene DF, et al. Hip fracture in postmenopausal women **after cessation of hormone therapy**: results from a prospective study in a large health management organization. Menopause. 2011 Nov;18(11):1172-7.

Kelly R, Taggart H. Incidence of gastrointestinal side effects due to **alendronate** is high in clinical practice. BMJ 1997;315:1235.

Kahn SE, et al. **Rosiglitazone-associated fractures** in type 2 diabetes: an Analysis from A Diabetes Outcome Progression Trial (ADOPT). Diabetes Care. 2008 May;31(5):845-51. Epub 2008 Jan 25. Further investigation into the risk factors and underlying pathophysiology for the increased fracture rate in women taking rosiglitazone is required to relate them to preclinical data and better understand the clinical implications of and possible interventions for these findings.

Kemmler Wolfgang; von Stengel Simon; Engelke Klaus; et al. **Exercise** Effects on Bone Mineral Density, Falls, Coronary Risk Factors, and Health Care Costs in Older Women: The Randomized Controlled Senior Fitness and Prevention (**SEFIP**) Study. Arch Intern Med. 2010;170(2):179-185.

Khalili H, Higuchi LM, Ananthakrishnan AN, et al. Hormone Therapy **Increases Risk of Ulcerative Colitis** but not Crohn's Disease. Gastroenterology. 2012 Jul 27.

Khan AA, Sándor GK, Dore E, et al. Canadian Association of Oral and Maxillofacial Surgeons. **Canadian consensus practice guidelines for bisphosphonate associated osteonecrosis of the jaw**. J Rheumatol. 2008 Jul;35(7):1391-7. Epub 2008 Jun 1. Erratum in: J Rheumatol. 2008 Aug;35(8):1688. J Rheumatol. 2008 Oct;35(10):2084.

Khosla S. Update in **male osteoporosis**. J Clin Endocrinol Metab. 2010 Jan;95(1):3-10.

Khosla S, Burr D, Cauley J, Dempster DW,et al.; **American** Society for Bone and Mineral Research. **Bisphosphonate-associated osteonecrosis** of the jaw: report of a task force of the American Society for Bone and Mineral Research. J Bone Miner Res. 2007 Oct;22(10):1479-91.

Korownyk, Christina, Allan, G. Michael, Kolber, Michael R. **Bone mineral density testing**: Too much of a good thing? Can Fam Physician 2010 56: 1299.

Korpelainen Raija; Keinanen-Kiukaanniemi Sirkka; Nieminen Pentti; et al. Long-term Outcomes of **Exercise**: Follow-up of a Randomized Trial in Older Women With Osteopenia. Arch Intern Med. 2010;170(17):1548-1556.

Koskela-Niska V, Lyytinen H, Riska A, Pukkala E, Ylikorkala O. **Ovarian cancer** risk in postmenopausal women using estradiol-progestin therapy - a nationwide study. Climacteric. 2012 May 28.

Lacy MQ, et al. Mayo clinic consensus statement for the use of **bisphosphonates in multiple myeloma**. Mayo Clin Proc. 2006 Aug;81(8):1047-53.

Langsetmo L, Nguyen TV, Nguyen D, et al. Independent external validation of **nomograms for predicting risk of low-trauma fracture and hip fracture** CMAJ 2010 0: cmaj.100458.

Lenart BA, Lorich DG, Lane JM. **Atypical fractures** of the femoral diaphysis in postmenopausal women taking **alendronate**. N Engl J Med. 2008 Mar 20;358(12):1304-6.

Leslie WD, Berger C, Langsetmo L, et al. Construction and validation of a simplified fracture risk assessment tool for Canadian women and men: results from the CaMos and Manitoba BMD cohorts. Osteoporos Int. (**CAROC** 2010) In press.
h ttp://osteoporosis.bluerush.ca/www/pdf/caroc_oct_2010.pdf

Leslie WD., Morin S, Lix LM. A Before-and-After Study of **Fracture Risk Reporting** and Osteoporosis treatment Initiation. *Ann Intern Med* November 2, 2010 153:580-586.

Levis S, Strickman-Stein N, Ganjei-Azar P, et al. Soy isoflavones in the prevention of menopausal bone loss and menopausal symptoms: a randomized, double-blind trial. Arch Intern Med. 2011;171 (15):1363-1369. Soy isoflavone supplementation had no effect on bone mineral density over the 2 years of this study, but increased the percentage of women reporting hot flashes. (LOE = 1b-)

Li Kuanrong, Kaaks R, Linseisen J, et al. Associations of **dietary calcium intake and calcium supplementation** with **myocardial infarction** and stroke risk and overall cardiovascular mortality in the Heidelberg cohort of the European Prospective Investigation into Cancer and Nutrition study (EPIC-Heidelberg). Heart 2012. (In press)

Liberman UA, Weiss SR, Broll J, Minne HW, Quan H, Bell NH, et al. Effect of oral **alendronate** on bone mineral density and the incidence of fractures in postmenopausal osteoporosis. The **Alendronate Phase III** Osteoporosis Treatment Study Group. N Engl J Med 1995;333:1437-43.

Liberman UA. **Long-term safety of bisphosphonate** therapy for osteoporosis : a review of the evidence. Drugs Aging. 2006;23(4):289-98.

Lim LS, Fink HA, Kuskowski MA, Taylor BC, Schousboe JT, Ensrud KE; for the Osteoporotic Fractures in Men (MrOS) Study Group. Loop Diuretic Use and Increased Rates of Hip Bone Loss in Older Men: The Osteoporotic Fractures in Men Study. Arch Intern Med. 2008 Apr 14;168(7):735-740. We conclude that loop diuretic use in older men is associated with increased rates of hip bone loss. These results suggest that the potential for bone loss should be considered when **loop diuretics** are prescribed to older patients in clinical practice.

Lim LS, Hoeksema LJ, Sherin K; **ACPM** Prevention Practice Committee. **Screening** for osteoporosis in the adult U.S. population: ACPM position statement on preventive practice. Am J Prev Med. 2009 Apr;36(4):366-75.

Lippman ME, et al. Effect of **raloxifene** on the incidence of **invasive breast cancer** in postmenopausal women with osteoporosis categorized by breast cancer risk. (From MORE & CORE trials)Clin Cancer Res. 2006 Sep 1;12(17):5242-7.

Liu RH, Albrecht J, Werth VP. Cross-sectional study of bisphosphonate use in dermatology patients receiving **long-term oral corticosteroid** therapy. Arch Dermatol. 2006 Jan;142(1):37-41.

Liu H, Michaud K, et al. The **Cost-effectiveness** of Therapy With **Teriparatide** and Alendronate in Women With Severe Osteoporosis. Arch Intern Med. 2006 Jun 12;166(11):1209-17.

Liu H, Paige NM, Goldzweig CL, Wong E, et al. **Screening for osteoporosis in men**: a systematic review for an American College of Physicians guideline. Ann Intern Med. 2008 May 6;148(9):685-701. Review. Summary for patients in: Ann Intern Med. 2008 May 6;148(9):I35. Key risk factors for low BMD-mediated fracture include increased age, low body weight, weight loss, physical inactivity, prolonged corticosteroid use, previous osteoporotic fracture, and androgen deprivation therapy. Non-DXA tests either are too insensitive or have insufficient data to reach conclusions.

Long CY, Liu CM, Hsu SC, Wu CH, Wang CL, Tsai EM. A randomized comparative study of the effects of oral and **topical** estrogen therapy on the vaginal vascularization and sexual function in hysterectomized postmenopausal women. Menopause. 2006 Sep-Oct;13(5):737-43.

Lopez LM, Edelman A, Chen-Mok M, Trussell J, Helmerhorst FM. **Progestin-only contraceptives: effects on weight**. Cochrane Database Syst Rev. 2011 Apr 13;4:CD008815. We found little evidence of weight gain when using POCs.
Mean gain was less than 2 kg for most studies up to 12 months, and usually similar for the comparison group using another contraceptive.

Luckey M, Kagan R, Greenspan S, Bone H, Kiel RD, Simon J, Sackarowitz J, Palmisano J, Chen E, Petruschke RA, de Papp AE. Once-weekly **alendronate 70 mg and raloxifene 60 mg** daily in the treatment of postmenopausal osteoporosis. Menopause. 2004 Jul-Aug;11(4):405-15.

Lyles KW, Colon-Emeric CS, Magaziner JS, Adachi JD, Pieper CF, Mautalen C,et al. the **HORIZON** Recurrent Fracture Trial. **Zoledronic** Acid and Clinical Fractures and Mortality after Hip Fracture. N Engl J Med. 2007 Sep 17. An annual infusion of zoledronic acid within 90 days after repair of a low-trauma hip fracture was associated with a **reduction in the rate of new clinical fractures and improved survival**.

Mackey DC, Lui LY, Cawthon PM, et al. Study of Osteoporotic Fractures (SOF) and Osteoporotic Fractures in Men Study (MrOS) Research Groups. **High-trauma fractures** and low bone mineral density in older women and men. JAMA. 2007 Nov 28;298(20):2381-8. Similar to low-trauma nonspine fractures, high-trauma nonspine fractures are associated with low BMD and increased risk of subsequent fracture in older adults. High-trauma nonspine fractures should be included as outcomes in osteoporosis trials and observational studies.

Maclean C, Newberry S, et al. **Systematic Review**: Comparative Effectiveness of Treatments to **Prevent Fractures** in Men & Women with Low Bone Density or Osteoporosis. Ann Intern Med. 2007 Dec 17; [Epub ahead of print] Although good evidence suggests that many agents are effective in preventing osteoporotic fractures, data are insufficient to determine the relative efficacy or safety of these agents.

Magliano DJ, Rogers SL, Abramson MJ, Tonkin AM. Hormone therapy and **cardiovascular disease**: a systematic review and meta-analysis. BJOG. 2006 Jan;113(1):5-14.

Main C, Knight B, Moxham T, et al. **Hormone therapy for preventing cardiovascular disease** in post-menopausal women. Cochrane Database Syst Rev 2013;(4):CD002229.

Martino S, Cauley JA, Barrett-Connor E, et al. Continuing outcomes relevant to Evista (**CORE**): **breast cancer incidence** in postmenopausal osteoporotic women in a randomized trial of raloxifene. J Natl Cancer Inst 2004; 96:1751-61.

Martino S, Disch D, Dowsett SA, Keech CA, Mershon JL. Safety assessment of **raloxifene over eight years** in a clinical trial setting. Curr Med Res Opin. 2005 Sep;21(9):1441-52.

Mauck KF, Cuddihy MT, Atkinson EJ, Melton LJ 3rd. Use of clinical prediction rules in detecting osteoporosis in a population-based sample of postmenopausal women. Arch Intern Med 2005;165:530-36. (InfoPOEMs: Clinical prediction rules for low bone mineral density have limited usefulness in postmenopausal women. They may be most useful in selecting women to screen who are between 60 and 65 years old. Universal screening is already advocated for women 65 and older. For women younger than 60 the usefulness is limited by a combination of poor specificity of the rules and poor correlation of bone density with fracture risk. However, a low prediction rule score might assure a few women that they don't need to be tested. (LOE = 1b))

Mazziotti G, Canalis E, Giustina A. **Drug-induced osteoporosis**: mechanisms and clinical implications. Am J Med. 2010 Oct;123(10):877-84.

McClung MR, Geusens P, Miller PD, et al. Effect of **risedronate** on the risk of hip fracture in elderly women. Hip Intervention Program Study Group (**HIP**). N Engl J Med 2001;344:333-40. CONCLUSIONS: Risedronate significantly reduces the risk of hip fracture among elderly women with confirmed **osteoporosis** but not among elderly women selected primarily on the basis of risk factors other than low bone mineral density. RESULTS: Overall, the incidence of hip fracture among all the women assigned to risedronate was 2.8%, as compared with 3.9 % among those assigned to placebo (relative risk, 0.7; 95 percent confidence interval, 0.6 to 0.9; P=0.02). In the group of women with osteoporosis (those 70 to 79 years old), the incidence of hip fracture among those assigned to risedronate was 1.9 percent, as compared with 3.2 percent among those assigned to placebo (relative risk, 0.6; 95 percent confidence interval, 0.4 to 0.9; P=0.009). In the group of women selected primarily on the basis of nonskeletal risk factors (those at least 80 years of age), the incidence of hip fracture was 4.2 percent among those assigned to risedronate and 5.1 percent among those assigned to placebo (P=0.35).

McClung MR, San Martin J, Miller PD, et al. Opposite bone remodeling effects of **teriparatide** and **alendronate** in increasing bone mass. Arch Intern Med. 2005 Aug 8-22;165(15):1762-8.

McClung MR, Lewiecki EM, Cohen SB, et al. AMG 162 Bone Loss Study Group. **Denosumab** in postmenopausal women with low bone mineral density. N Engl J Med. 2006 Feb 23;354(8):821-31.

McKague M, Jorgenson D, Buxton KA. **Ocular side effects of bisphosphonates**: A case report and literature review. Can Fam Physician. 2010 Oct;56(10):1015-7.

Medical Letter Aug 14/28,2006. **Intravenous Ibandronate** (Boniva)

Medical Letter - Treatment Guidelines. **Drugs for Postmenopausal Osteoporosis**. **Oct 2008**.

Menopause: The Journal of The North American Menopause Society Vol. 17, No. 2, pp. 242/255 DOI: 10.1097/gme.0b013e3181d0f6b9. {tapering estrogen when stopping results in similar side effects to just stopping without taper.}

Meier C, Kraenzlin ME, Bodmer M, Jick SS, Jick H, Meier CR. Use of **thiazolidinediones and fracture risk**. Arch Intern Med. 2008 Apr 28;168(8):820-5. This analysis provides further evidence of a possible association between long-term use of thiazolidinediones and fractures, particularly of the hip and wrist, in patients with diabetes mellitus.

MHRA Oct/12 The UK Medicines and Healthcare products Regulatory Agency (MHRA) has issued a reminder about a potential adverse effect of **liver problems** when using **Black Cohosh** to relieve symptoms of the menopause. The MHRA has issued a press release reminding people about the risk of liver problems with Black Cohosh, following a serious case of liver failure resulting in a liver transplant suspected to have been caused by a herbal product containing Black Cohosh. The investigation of this case and of the product involved is ongoing. To date, the MHRA has received **53 reports** of adverse reactions suspected to be associated with the use of Black Cohosh products through the Yellow Card Scheme.

Michaelsson K, Bergstrom R, Mallmin H, Holmberg L, Wolk A, Ljunghall S. Screening for osteopenia and osteoporosis: selection by body composition. Osteoporos Int 1996;6:120-6.

Michalska D, et al. The effect of **raloxifene after discontinuation** of long-term **alendronate** treatment of postmenopausal osteoporosis. J Clin Endocrinol Metab. 2006 Mar;91(3):870-7. Epub 2005 Dec 13.

Mok Chi Chiu, Ying King Yee, To Chi Hung, et al. **Raloxifene for prevention of glucocorticoid-induced bone loss**: a 12-month randomised double-blinded placebo-controlled trial. Ann Rheum Dis 2011;70:778-784 Published Online First: 27 December 2010.

National Osteoporosis Foundation. Physician's guide to prevention and treatment of osteoporosis. Accessed June 21, 2004, at: http://www.nof.org/professionals/clinical/clinical.htm.

Nelson HD, Helfand M, Woolf SH, Allan JD. Screening for postmenopausal osteoporosis: a review of the evidence for the **U.S. Preventive Services Task Force**. Ann Intern Med 2002;137:529-41.

Neer RM, Arnaud CD, Zanchetta JR, et al. Effect of **parathyroid hormone** (1-34) on fractures and bone mineral density in postmenopausal women with osteoporosis. N Engl J Med 2001;344:1434-41.RESULTS: New vertebral fractures occurred in 14 percent of the women in the placebo group and in 5 percent and 4 percent, respectively, of the women in the 20-microg and 40-microg parathyroid hormone groups; the respective relative risks of fracture in the 20-microg and 40-microg groups, as compared with the placebo group, were 0.35 and 0.31 (95 percent confidence intervals, 0.22 to 0.55 and 0.19 to 0.50). New nonvertebral fragility fractures occurred in 6 percent of the women in the placebo group and in 3 percent of those in each parathyroid hormone group (relative risk, 0.47 and 0.46, respectively [95 percent confidence intervals, 0.25 to 0.88 and 0.25 to 0.861). As compared with placebo, the 20-microg and 40-microg doses of parathyroid hormone increased bone mineral density by 9 and 13 more percentage points in the lumbar spine and by 3 and 6 more percentage points in the femoral neck; the 40-microg dose decreased bone mineral density at the shaft of the radius by 2 more percentage points. Both doses increased total-body bone mineral by 2 to 4 more percentage points than did placebo. Parathyroid hormone had only minor side effects (occasional nausea and headache). CONCLUSIONS: Treatment of postmenopausal osteoporosis with parathyroid hormone (1-34) decreases the risk of vertebral and nonvertebral fractures; increases vertebral, femoral, and total-body bone mineral density; and is well tolerated. The 40-microg dose increased bone mineral density more than the 20-microg dose but had similar effects on the risk of fracture and was more likely to have side effects.

Nevitt MC, Chen P, Dore RK, Reginster JY, Kiel DP, Zanchetta JR, Glass EV, Krege JH. Reduced risk of back pain following **teriparatide** treatment: a meta-analysis. Osteoporos Int. 2005 Sep 2; [Epub ahead of print]

Nice Oct 2008: Primary Prevention http://guidance.nice.org.uk/TA160 & Secondary Prevention of Osteoporosis http://guidance.nice.org.uk/TA161 **Guidelines**

North American Menopause Society. **NAMS**: Management of **osteoporosis in postmenopausal women**: **2010** position statement of The North American Menopause Society. Menopause. **2010** Jan-Feb;17(1):25-54.

North American Menopause Society. **Management of osteoporosis in postmenopausal women: 2006** position statement of The North American Menopause Society. Menopause. 2006 May-Jun;13(3):340-67; quiz 368-9.

Obermayer-Pietsch BM, Marin F, McCloskey EV, et al.; for the EUROFORS Investigators. Effects of **Two Years of Daily Teriparatide** Treatment on Bone Mineral Density in Postmenopausal Women with Severe Osteoporosis with and without Prior Antiresorptive Treatment. J Bone Miner Res. 2008 May 27. Nausea (13.3%) and arthralgia (11.7%) were the most commonly reported adverse events. Asymptomatic hypercalcemia was reported in 5.0% of patients. Teriparatide treatment for 24 months is associated with a significant increase in BMD in patients with and without previous AR use. Prior AR treatment modestly blunted the BMD response to teriparatide. Safety was consistent with current prescribing label information.

O'donnell S, Cranney A, Wells G, Adachi J, Reginster J. Strontium ranelate for preventing and treating postmenopausal osteoporosis. Cochrane Database Syst Rev. 2006 Jul 19;3:CD005326.

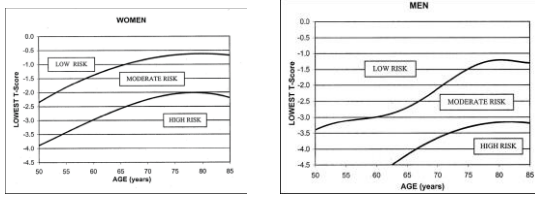
Orwoll E, Alendronate for the treatment of **osteoporosis in men**. N Engl J Med. 2000 Aug 31;343(9):604-10.

Orwoll E, et al. Osteoporotic Fractures in **Men** Study Group. Endogenous **testosterone** levels, physical performance, and fall risk in older men. Arch Intern Med. 2006 Oct 23;166(19):2124-31. Falls were common among older men. Fall risk was higher in men with lower bioavailable testosterone levels. The effect of testosterone level was independent of poorer physical performance, suggesting that the effect of testosterone on fall risk may be mediated by other androgen actions.

Quandt SA, Thompson DE, et al. Fracture Intervention Trial Research Group. Effect of alendronate on vertebral fracture risk in women with bone mineral density T scores of-1.6 to -2.5 at the femoral neck: the Fracture Intervention Trial. (**FIT**). Mayo Clin Proc. 2005 Mar;80(3):343-9.

Qaseem A, Snow V, Shekelle P, Hopkins R Jr, et al. Clinical Efficacy Assessment Subcommittee of the American College of Physicians. **Screening for osteoporosis in men**: a clinical practice guideline from the American College of Physicians. Ann Intern Med. 2008

May 6;148(9):680-4. Summary for patients in: Ann Intern Med. 2008 May 6;148(9):I35.
Pack AM, Morrell MJ, et al. Bone health in young women with epilepsy after one year of antiepileptic drug monotherapy. Neurology. 2008 Apr 29;70(18):1586-93. In contrast, those treated with carbamazepine, lamotrigine, and valproate did not have detectable adverse effects on bone turnover or bone mineral density. These results raise **concerns about the long-term effects of phenytoin monotherapy on bone** in young women with epilepsy.
Palmieri C, Macgregor T, Girgis S, Vigushin D. Serum 25 **hydroxyvitamin D** levels in early and advanced **breast cancer**. J Clin Pathol. 2006 Oct 17; [Epub ahead of print]
Pham AN, Datta SK, Weber TJ, et al. **Cost-Effectiveness of Oral Bisphosphonates** for Osteoporosis at Different Ages and Levels of **Life Expectancy**. J Am Geriatr Soc. 2011 Aug 30. doi: 10.1111/j.1532-5415.2011.03571.x.
Papaioannou, Alexandra, Morin, Suzanne, Cheung, Angela M., et al. **2010 clinical practice guidelines for the diagnosis and management of osteoporosis in Canada**: summary CMAJ 2010 0: cmaj.100771.
Parker M, Johansen A. **Hip fracture**. BMJ. 2006 Jul 1;333(7557):27-30.
Pharmacists Letter. **New Developments with Bisphosphonate** Therapy. June 2007.
Planas J, Trilla E, Raventós C, et al. Alendronate decreases the fracture risk in patients with prostate cancer on **androgen-deprivation therapy** and with severe osteopenia or osteoporosis. BJU Int. 2009 Jun 22. [Epub ahead of print]
Porthouse J, Cockayne S, King C, et al. Randomised controlled trial of **calcium** and supplementation with **cholecalciferol (vitamin D3)** for prevention of fractures in primary care. BMJ. 2005 Apr 30;330(7498):1003 & ACP Journal Club.
Prieto-Alhambra D, Javaid MK, Judge A, et al. Hormone replacement therapy and mid-term **implant survival following knee or hip arthroplasty** for osteoarthritis: a population-based cohort study. Ann Rheum Dis. 2014 Jan 22
Prince RL, Austin N, Devine A, Dick IM, Bruce D, Zhu K. Effects of ergocalciferol added to calcium on the risk of falls in elderly high-risk women. Arch Intern Med. 2008 Jan 14;168(1):103-8. Patients with a history of falling and vitamin D insufficiency living in sunny climates benefit from ergocalciferol supplementation in addition to calcium, which is associated with a 19% reduction in the relative risk of falling, mostly in winter.
Prince RL, et al. Effects of **calcium** supplementation on clinical fracture and bone structure: results of a 5-year, double-blind, placebo-controlled trial in elderly women. Supplementation with calcium carbonate tablets supplying 1200 mg/d is ineffective as a public health intervention in preventing clinical fractures in the ambulatory elderly population owing to poor long-term compliance, but it is effective in those patients who are compliant. Arch Intern Med. 2006 Apr 24;166(8):869-75. (InfoPOEMs: In women older than 70 years, calcium supplementation does not decrease fracture risk. In women who took at least 80% of their dosage, however, fractures were significantly decreased. There were not enough hip fractures in the study groups to determine whether calcium had any effect on hip fracture. (LOE = 1b-))
Prithwish De, C. Ineke Neutel, Ivo Olivotto, et al. **Breast Cancer Incidence and Hormone Replacement Therapy in Canada**. JNCI J Natl Cancer Inst first published online September 23, 2010 doi:10.1093/jnci/djq345.
Prior JC, Elliott TG, Norman E, et al. **Progesterone therapy**, endothelial function and cardiovascular risk factors: A 3-month randomized, placebo-controlled trial in healthy early postmenopausal women. *PLoS ONE* 2014; 9:e84698.
Qaseem A, Snow V, Shekelle P, Hopkins R Jr, Forciea MA, Owens DK; Clinical Efficacy Assessment Subcommittee of the American College of Physicians. **Pharmacologic treatment** of low bone density or osteoporosis to prevent fractures: a clinical practice guideline from the American College of Physicians. Ann Intern Med. 2008 Sep 16;149(6):404-15.
QFractureScore http://www.qfracture.org/
Rad M, et al. Comparative effects of a contraceptive **vaginal ring** delivering a nonandrogenic progestin & **continuous ethinyl estradiol** & a **combined oral contraceptive** containing levonorgestrel on **hemostasis** variables. Am J Obstet Gynecol. 2006 Jul;195(1):72-7.
Rahmani, Poupak, Morin, Suzanne. **Prevention of osteoporosis**-related fractures among postmenopausal women and older men. CMAJ 2009 0: cmaj.080709
Raisz LG. Clinical practice. **Screening for osteoporosis**. N Engl J Med. 2005 Jul 14;353(2):164-71.
Recommendations for the prevention and treatment of glucocorticoid-induced osteoporosis: 2001 update. American College of Rheumatology Ad Hoc Committee on **Glucocorticoid-Induced Osteoporosis**. Arthritis Rheum 2001;44:1496-503.
Reginster JY, Felsenberg D, Boonen S, et al. Effects of long-term **strontium** ranelate treatment on the risk of nonvertebral and vertebral fractures in postmenopausal osteoporosis: Results of a five-year, randomized, placebo-controlled trial. Arthritis Rheum. 2008 May 31;58(6):1687-1695. [Epub ahead of print] Our findings indicate that treatment of postmenopausal osteoporosis with strontium ranelate results in a sustained reduction in the incidence of osteoporotic nonvertebral fractures, including hip fractures, and vertebral fractures over 5 years.
Reginster J, Minne HW, Sorensen OH, Hooper M, et al. Randomized trial of the effects of **risedronate** on vertebral fractures in women with established postmenopausal osteoporosis. Vertebral Efficacy with Risedronate Therapy (**VERT**) Study Group. Osteoporos Int 2000;11:83-91.
Reid IR, Brown JP, Burckhardt P, et al. Intravenous **zoledronic** acid in postmenopausal women with **low bone mineral density**. N Engl J Med. 2002 Feb 28;346(9):653-61.
Reid DM, Hughes RA, Laan RF, et al. Efficacy and safety of daily **risedronate** in the treatment of corticosteroid-induced osteoporosis in men and women: a randomized trial. European Corticosteroid-Induced Osteoporosis Treatment Study. J Bone Miner Res 2000;15:1006-13.
Reid IR, Miller P, Lyles K, et al. Comparison of a single infusion of **zoledronic** acid with risedronate for Paget's disease. N Engl J Med. 2005 Sep 1;353(9):898-908.
Reid IR, Mason B, et al. Randomized controlled trial of **calcium** in healthy older women. Am J Med. 2006 Sep;119(9):777-85.
Reid DM, et al.; HORIZON investigators. **Zoledronic acid and risedronate** in the prevention and treatment of **glucocorticoid-induced** osteoporosis (HORIZON): a multicentre, double-blind, double-dummy, randomised controlled trial. Lancet. 2009 Apr 11;373(9671):1253-63.
Ringe JD, Faber H, Fahramand P, Schacht E. **Alfacalcidol** versus plain vitamin D in the treatment of **glucocorticoid/inflammation-induced osteoporosis**. J Rheumatol Suppl. 2005 Sep;76:33-40.
Rizzoli R, Greenspan SL, Bone G 3d, Schnitzer TJ, Watts NB, Adami S, et al. Two-year results of **once-weekly** administration of **alendronate** 70 mg for the treatment of postmenopausal osteoporosis. J Bone Miner Res 2002;17:1988-96.
Robbins J, Aragaki AK, Kooperberg C, et al. Factors associated with 5-year risk of hip fracture in postmenopausal women. JAMA. 2007 Nov 28;298(20):2389-98. This **algorithm, based on 11 clinical factors**, may be useful to predict the 5-year risk of hip fracture among postmenopausal women of various ethnic backgrounds.
Robbins JA, Aragaki A, Crandall CJ, et al. Women's Health Initiative (WHI) clinical trials: interaction of **calcium and vitamin D** with hormone therapy. Menopause. 2013 Jun 24.
Rosen CJ. Clinical practice. Postmenopausal osteoporosis. N Engl J Med. **2005** Aug 11;353(6):595-603.
Rosen CJ, et al. **Fosamax** Actonel Comparison Trial Investigators. Treatment with once-weekly alendronate 70 mg vs once-weekly risedronate 35 mg in women with postmenopausal osteoporosis: a randomized double-blind study.J Bone Miner Res.2005 Jan;20(1):141-51.
Ruggiero SL, Fantasia J, Carlson E. Bisphosphonate-related **osteonecrosis** of the jaw: background and guidelines for diagnosis, staging and management. Oral Surg Oral Med Oral Pathol Oral Radiol Endod. 2006 Oct;102(4):433-41. Epub 2006 Jul 31.
Ruggiero SL, Dodson TB, Assael LA, Landesberg R, Marx RE, Mehrotra B; American Association of Oral and Maxillofacial Surgeons. American Association of Oral and Maxillofacial Surgeons position paper on **bisphosphonate-related osteonecrosis of the jaws**--2009 update. J Oral Maxillofac Surg. 2009 May;67(5 Suppl):2-12.
Saag KG, Emkey R, Schnitzer TJ, Brown JP, Hawkins F, Goemaere S, et al. **Alendronate** for the prevention and treatment of glucocorticoid-induced osteoporosis. Glucocorticoid-Induced Osteoporosis Intervention Study Group. N Engl J Med 1998;339:292-9.
Saag KG, Shane E, Boonen S, Marín F, et al. **Teriparatide** or Alendronate in **Glucocorticoid-Induced Osteoporosis**. N Engl J Med. 2007 Nov 15;357(20):2028-2039. Among patients with osteoporosis who were at high risk for fracture, bone mineral density increased more in patients receiving teriparatide than in those receiving alendronate.
Saag KG, Zanchetta JR, Devogelaer JP, et al. Effects of **teriparatide versus alendronate** for treating **glucocorticoid**-induced osteoporosis: Thirty-six-month results of a randomized, double-blind, controlled trial. Arthritis Rheum. 2009 Oct 29;60(11):3346-3355.
Sainz M., et al. **Strontium ranelate may cause alopecia** BMJ 2009;338:b1494, doi: 10.1136/bmj.b1494
Salpeter SR, Cheng J, Thabane L, et al. Bayesian meta-analysis of **hormone therapy** and **mortality** in **younger** postmenopausal women. Am J Med. 2009 Nov;122(11):1016-1022.e1.
Sanders Kerrie M.; Stuart Amanda L.; Williamson Elizabeth J.; et al. **Annual High-Dose Oral Vitamin D (500,000IU x1/yr for 3-5yrs**: increased falls & fractures) and Falls and Fractures in Older Women: A Randomized Controlled Trial. JAMA. 2010;303(18):1815-1822.
Sato Y, Iwamoto J, Kanoko T, Satoh K. **Risedronate** sodium therapy for prevention of hip fracture in men 65 years or older after stroke. Arch Intern Med. 2005 Aug 8-22;165(15):1743-8.
Sato Y, Kanoko T, Satoh K, Iwamoto J. The prevention of hip fracture with **risedronate** and ergocalciferol plus calcium supplementation in elderly women with Alzheimer disease: a randomized controlled trial. Arch Intern Med. 2005 Aug 8-22;165(15):1737-42.
Schierbeck LL, Rejnmark L, Tofteng CL, et al. Effect of hormone replacement therapy on **cardiovascular events in recently postmenopausal women**: randomised trial. BMJ. 2012 Oct 9;345:e6409.
Schousboe JT, Nyman JA, Kane RL, Ensrud KE. **Cost-effectiveness** of alendronate therapy for **osteopenic** postmenopausal women. Ann Intern Med. 2005 May 3;142(9):734-41.
Schousboe JT, Ensrud KE, Nyman JA, Melton LJ 3rd, Kane RL. **Universal bone densitometry screening** combined with alendronate therapy for those diagnosed with osteoporosis is highly cost-effective for elderly women. J Am Geriatr Soc. 2005 Oct;53(10):1697-704.
Schwartz AV, et al. **Thiazolidinedione** use and **bone loss** in older diabetic adults. J Clin Endocrinol Metab. 2006 Sep;91(9):3349-54. Epub 2006 Apr 11.
Sedghizadeh PP, Stanley K, Caligiuri M, Hofkes S, et al. Oral bisphosphonate use and the prevalence of **osteonecrosis of the jaw**: An institutional inquiry. J Am Dent Assoc. 2009 Jan;140(1):61-6. These patients represented one in 23 of the patients receiving alendronate, or approximately **4 percent of the population**. The findings from this study indicated that even short-term oral use of alendronate led to ONJ in a subset of patients after certain dental procedures were performed.
Seeman E, Delmas PD. **Bone quality**--the material and structural basis of bone strength and fragility. N Engl J Med. 2006 May 25;354(21):2250-61.
Shane E, Burr D, Ebeling PR, Abrahamsen B, et al. **Atypical subtrochanteric and diaphyseal femoral fractures**: Report of a task force of the American Society for Bone and Mineral Research. J Bone Miner Res. (ASBMR) 2010 Sep 14.
Sharpe KH, McClements P, Clark DI, et al. Reduced risk of oestrogen receptor positive **breast cancer** among peri- and post-menopausal women in **Scotland following a striking decrease** in use of hormone replacement therapy. Eur J Cancer. 2010 Jan 30.
Shimon I, Eshed V, Doolman R, Sela BA, Karasik A, Vered I. Alendronate for osteoporosis in men with androgen-repleted hypogonadism. Osteoporos Int. 2005 Dec;16(12):1591-6. Epub 2005 Mar 15.
Siffledeen JS, Fedorak RN, Siminoski K, et al. Randomized trial of etidronate plus calcium and vitamin D for treatment of low bone mineral density in **Crohn's disease**. Clin Gastroenterol Hepatol. 2005 Feb;3(2):122-32. Low bone mineral density is frequently associated with Crohn's disease. Supplementation with daily calcium and vitamin D is associated with increases in bone mineral density. The addition of oral etidronate does not further enhance bone mineral density.
Siminoski K, Leslie WD, Frame H, Hodsman A, Josse RG, Khan A, Lentle BC,Lévesque J, Lyons DJ, Tarulli G, Brown JP; Canadian Association of Radiologists. **Recommendations for bone mineral density reporting in Canada**. Can Assoc Radiol J. 2005 Jun;56(3):178-88.



Zones of fracture risk for women & men. (See also **WHO 10yr Probability of Fracture Algorithm called FRAX** http://www.shef.ac.uk/FRAX/index.htm)

Siris ES, Miller PD, Barrett-Connor E, Faulkner KG, Wehren LE, Abbott TA, et al. Identification and fracture outcomes of undiagnosed low bone mineral density in postmenopausal women: results from the National Osteoporosis Risk Assessment. JAMA 2001;286:2815-22.
Siris ES, Harris ST, Eastell R, et al.; Continuing Outcomes Relevant to Evista (**CORE**) Investigators. Skeletal effects of raloxifene after 8 years: results from the continuing outcomes relevant to Evista (CORE) study. J Bone Miner Res. 2005 Sep;20(9):1514-24. Epub 2005 May 16.

An **annual i.m. injection of 300 000 IU vitamin D(2)** is not effective in preventing non-vertebral fractures among elderly men and women resident in the general population.
Smith, Matthew R., Egerdie, Blair, Toriz, Narciso Hernandez, et al., the Denosumab **HALT** Prostate Cancer Study Group, **Denosumab** in Men Receiving Androgen-Deprivation Therapy for Prostate Cancer. N Engl J Med 2009 0: NEJMoa0809003
SOGC 2006 Menopause Consensus Report. A Journalist's Menopause Handbook: A companion guide to the Society of Obstetricians and Gynaecologists of Canada Menopause Consensus Report. http://www.sogc.org/media/pdf/advisories/Menopause-journalists-guide_e.pdf (2006 Menopause Consensus Report. Pharmacist's Letter Mar 2006)
SOGC 2009 Menopause and Osteoporosis Update 2009-SOGC Jan 2009. http://www.sogc.org/media/pdf/advisories/Meno-Osteo-Update_JOGC-Jan_09.pdf
Solomon DH, Avorn J, Katz JN, Finkelstein JS, Arnold M, Polinski JM, Brookhart MA. **Compliance** with osteoporosis medications. Arch Intern Med. 2005 Nov 14;165(20):2414-9.
Sørensen HT, et al. Use of bisphosphonates among women & risk of **atrial fibrillation & flutter**: population based case-control study. BMJ. 2008Mar 11; [Epub ahead of print] No evidence was found that use of bisphosphonates increases the risk of atrial fibrillation & flutter.
Sprague BL, Trentham-Dietz A, Cronin KA. A sustained **decline in postmenopausal hormone use**: results from the National Health and Nutrition Examination Survey, 1999-2010. Obstet Gynecol. 2012 Sep;120(3):595-603.
Stoch SA, Saag KG, Greenwald M, et al. Once-weekly oral alendronate 70 mg in patients with **glucocorticoid-induced** bone loss: a 12-month randomized, placebo-controlled clinical trial. J Rheumatol. 2009 Aug;36(8):1705-14.
Suckling JA, Kennedy R, Lethaby A, Roberts H. **Local oestrogen for vaginal atrophy** in postmenopausal women. Cochrane Database of Systematic Reviews 2006, Issue 4. Art. No.: CD001500. DOI: 10.1002/14651858.CD001500.pub2. Creams, pessaries, tablets and the oestradiol vaginal ring appeared to be equally effective for the symptoms of vaginal atrophy. One trial found significant side effects following cream (conjugated equine oestrogen) administration when compared to tablets causing uterine bleeding, breast pain and perineal pain. Another trial found significant endometrial overstimulation following use of the cream (conjugated equine oestrogen) when compared to the ring. As a treatment choice women appeared to favour the oestradiol-releasing vaginal ring for ease of use, comfort of product and overall satisfaction.
Sweet MG, Sweet JM, Jeremiah MP, Galazka SS. **Diagnosis and treatment of osteoporosis**. Am Fam Physician. 2009 Feb 1;79(3):193-200.
Sweetland S, Beral V, Balkwill A, et al. The **Million Women Study Collaborators**. Venous thromboembolism risk in relation to use of different types of postmenopausal hormone therapy in a large prospective study. J Thromb Haemost. 2012 Sep 10.
Szmuilowicz ED, Manson JE, Rossouw JE et al. **Vasomotor symptoms and cardiovascular events** in postmenopausal women. Menopause 2011; DOI: 10.1097/gme.0b013e3182014849.
Taggart H, Bolognese MA, Lindsay R, Ettinger MP, Mulder H, Josse RG, et al. Upper gastrointestinal tract safety of risedronate: a pooled analysis of 9 clinical trials [published correction appears in Mayo Clin Proc 2002;77:601]. Mayo Clin Proc 2002;77:262-70.
The role of **calcium** in peri- and postmenopausal women: 2006 position statement of The North American Menopause Society. Menopause. 2006 Nov-Dec;13(6):862-77.
Tuomikoski P et al. **Coronary heart disease mortality and hormone therapy before and after the Women's Health Initiative (WHI) .** Obstet Gynecol 2014 Nov; 124:947.
USPSTF: U.S. Preventive Services Task Force. **Screening for osteoporosis** in postmenopausal women: recommendations and rationale. Ann Intern Med 2002;137:526-8.
USPSTF: Menopausal Hormone Therapy to **Prevent Chronic Conditions**: U.S. Preventive Services Task Force Recommendation Statement. Ann Intern Med. 2012 Oct 23.
Uitterlinden AG, et al.; APOSS Investigators; EPOS Investigators; EPOLOS Investigators; FAMOS Investigators; LASA Investigators; Rotterdam Study Investigators; GENOMOS Study. The association between common **vitamin D receptor gene** variations and osteoporosis: a participant-level meta-analysis. Ann Intern Med. 2006 Aug 15;145(4):255-64.
Van den Wyngaert T, Huizing MT, Vermorken JB. Bisphosphonates and **osteonecrosis** of the jaw: cause and effect or a post hoc fallacy? Ann Oncol. 2006 Aug;17(8):1197-204.
Van Leer P. The Risk of **Cardiovascular Disease, Fracture, Dementia, and Cancer After Long-Term Hormone Therapy in Perimenopausal and Postmenopausal Women**. Am Fam Physician. 2018 Jul 15;98(2):117-118.
Van Poznak CH, Temin S, Yee GC, et al. American Society of Clinical Oncology (**ASCO**) Executive Summary of the Clinical Practice Guideline Update on the Role of **Bone-Modifying Agents in Metastatic Breast Cancer**. J Clin Oncol. 2011 Feb 22.
Villar J, Abdel-Aleem Het al.; World Health Organization Calcium Supplementation for the Prevention of Preeclampsia Trial Group. World Health Organization randomized trial of calcium supplementation among low calcium intake pregnant women. Am J Obstet Gynecol. 2006 Mar;194(3):639-49. CONCLUSION: A 1.5-g calcium/day supplement did not prevent preeclampsia but did reduce its severity, maternal morbidity, and neonatal mortality, albeit these were secondary outcomes.
Vis M, Bultink IE, Dijkmans BA, Lems WF. The effect of **intravenous pamidronate** versus oral alendronate on bone mineral density in patients with osteoporosis. Osteoporos Int. 2005 May 10; [Epub ahead of print]
Vogel VG, et al. Effects of Tamoxifen vs Raloxifene on the Risk of Developing Invasive Breast Cancer and Other Disease Outcomes: The NSABP Study of Tamoxifen and Raloxifene (**STAR**) P-2 Trial. JAMA. 2006 Jun 5; Raloxifene is as effective as tamoxifen in reducing the risk of invasive breast cancer and has a lower risk of thromboembolic events and cataracts but a nonstatistically significant higher risk of noninvasive breast cancer. The risk of other cancers, fractures, ischemic heart disease, and stroke is similar for both drugs. (Land SR, et al. Patient-Reported Symptoms and **Quality of Life** During Treatment With Tamoxifen or Raloxifene for Breast Cancer Prevention: The NSABP Study of Tamoxifen and Raloxifene (STAR) P-2 Trial. JAMA. 2006 Jun 5; [Epub ahead of print] No significant differences existed between the tamoxifen and raloxifene groups in patient-reported outcomes for physical health, mental health, and depression, although the tamoxifen group reported better sexual function. Although mean symptom severity was low among these postmenopausal women, those in the tamoxifen group reported more gynecological problems, vasomotor symptoms, leg cramps, and bladder control problems, whereas women in the raloxifene group reported more musculoskeletal problems, dyspareunia, and weight gain.)
Wallach S, Cohen S, Reid DM, Hughes RA, Hosking DJ, Laan RF, et al. Effects of **risedronate** treatment on bone density and vertebral fracture in patients on corticosteroid therapy. Calcif Tissue Int 2000;67:277-85.
Wactawski-Wende J, et al.; Women's Health Initiative Investigators. Calcium plus vitamin D supplementation and the risk of colorectal cancer. N Engl J Med. 2006 Feb 16;354(7):684-96. Erratum in: N Engl J Med. 2006 Mar 9;354(10):1102. (InfoPOEMs: A modest dose of calcium and vitamin D does not alter the risk of colorectal cancer in healthy, normal-risk women. (LOE = 1b))
Walter C, Al-Nawas B, du Bois A, Buch L, Harter P, Grötz KA. Incidence of bisphosphonate-associated **osteonecrosis of the jaws in breast cancer** patients. Cancer. 2009 Jan 20. [Epub ahead of print] With a prevalence of 5.3%, BP-ONJ in breast cancer patients has become a relevant disease that should be discussed with patients for whom bisphosphonates have been recommended. Appropriate dental care before bisphosphonate therapy commences has been advised to reduce the occurrence of BP-ONJ.
Walter C, Al-Nawas B, Grötz KA, Thomas C, Thüroff JW, Zinser V, Gamm H, Beck J, Wagner W. Prevalence and Risk Factors of Bisphosphonate-Associated **Osteonecrosis of the Jaw in Prostate Cancer** Patients with Advanced Disease Treated with Zoledronate. Eur Urol. 2008 Jun 26. [Epub ahead of print] Eight of 43 patients developed BP-ONJ (18.6%). The reason for this relatively high incidence compared to other studies might be the prospective study design and thorough dental examination. In studies with such small numbers as have been published to date, nondetection or nonreported cases of BP-ONJ have an influence on the outcome. The incidence of BP-ONJ in patients with pCA might be an underestimated problem.
Ward E, Gold EB, Johnson WO, et al. Patterns of **Cardiometabolic Health as Midlife Women Transition to Menopause**: A Prospective Multi-Ethnic Study. J Clin Endocrinol Metab. 2018 Oct 25.
Warensjö Eva, Byberg Liisa, Melhus Håkan, et al. **Dietary calcium intake** and risk of fracture and osteoporosis: prospective longitudinal cohort study. BMJ 2011;342:doi:10.1136/bmj.d1473 (Published 24 May 2011)
Weinstein RS, Roberson PK, Manolagas SC. **Giant osteoclast** formation and long-term oral bisphosphonate therapy. N Engl J Med. 2009 Jan 1;360(1):53-62. Long-term alendronate treatment is associated with an increase in the number of osteoclasts, which include distinctive giant, hypernucleated, detached osteoclasts that are undergoing protracted apoptosis.
Wells G, Cranney A, Peterson J, Boucher M, et al. **Alendronate** for the primary & secondary prevention of osteoporotic fractures in postmenopausal women. **Cochrane** Database Syst Rev. **2008** Jan 23;(1):CD001155. At 10 mg per day, both clinically important and statistically significant reductions in vertebral, non-vertebral, hip and wrist fractures were observed for secondary prevention ('gold' level evidence, www.cochranemsk.org). We found no statistically significant results for primary prevention, with the exception of vertebral fractures, for which the reduction was clinically important ('gold' level evidence).
Wells G, Cranney A, Peterson J, Boucher M, Shea B, Robinson V, Coyle D, Tugwell P. **Etidronate** for the primary and secondary prevention of osteoporotic fractures in postmenopausal women. **Cochrane** Database Syst Rev. **2008** Jan 23;(1):CD003376. Etidronate, at 400 mg per day, demonstrated a statistically significant and clinically important benefit in the secondary prevention of vertebral fractures. No statistically significant reductions in vertebral fractures were observed when it was used for primary prevention. In addition, no statistically significant reductions in non-vertebral, hip, or wrist fractures were found, regardless of whether etidronate was used for primary or secondary prevention. The level of evidence for all outcomes is Silver (www.cochranemsk.org.).
Wells G, Cranney A, Peterson J, Boucher M, Shea B, Robinson V, Coyle D, Tugwell P. **Risedronate** for the primary and secondary prevention of osteoporotic fractures in postmenopausal women. **Cochrane** Database Syst Rev. **2008** Jan 23;(1):CD004523. At 5 mg/day a statistically significant and clinically important benefit in the secondary prevention of vertebral, non-vertebral and hip fractures was observed, but not for wrist. The level of evidence for secondary prevention is Gold (www.cochranemsk.org) for vertebral and non-vertebral and Silver for hip and wrist. There were no statistically significant reductions in the primary prevention of vertebral and non-vertebral fractures. The level of evidence is Silver.
Winzenberg T, Shaw K, Fryer J, Jones G. Effects of **calcium** supplementation on bone density in healthy children: meta-analysis of randomised controlled trials. BMJ. 2006 Sep 15; [Epub ahead of print]
Wong R, Wiffen PJ. **Bisphosphonates** for the relief of pain secondary to **bone metastases**. Cochrane Database Syst Rev. 2002;(2):CD002068.
Wysowski DK, Chang JT. **Alendronate and risedronate: reports of severe bone, joint, and muscle pain**. Arch Intern Med. 2005 Feb 14;165(3):346-7.
Wysowski DK. Reports of **esophageal cancer** with oral bisphosphonate use. N Engl J Med. 2009 Jan 1;360(1):89-90.
Zandi PP et al. Hormone replacement therapy and incidence of **Alzheimer disease** in older women: The Cache County Study.JAMA 2002 Nov 6; 288:2123-9.
Zeydan B, Tosakulwong N, Schwarz CG, et al. Association of **Bilateral Salpingo-Oophorectomy Before Menopause Onset With Medial Temporal Lobe Neurodegeneration**. JAMA Neurol. 2018 Oct 15.
Zhao M, Whitcomb BW, Purdue-Smithe AC, et al. **Physical activity is not related to risk of early menopause** in a large prospective study. Hum Reprod. 2018 Aug 21.
Zhu L, Jiang X, Sun Y, Shu W. Effect of **hormone therapy on the risk of bone fractures**: a systematic review and meta-analysis of randomized controlled trials. Menopause. 2015 Oct 27.
Zizic TM. Pharmacologic prevention of osteoporotic fractures. Am Fam Physician. 2004 Oct 1;70(7):1293-300.
Zuo SW, Wu H, Shen W. **Vaginal estrogen and mammogram results**: case series and review of literature on treatment of **GSM in breast cancer survivors**. Menopause. 2018 Mar 12.

Bioidentical Hormone:

Progesterone cream no more effective than placebo for relief of menopausal symptoms" was the conclusion in a double-blind placebo-controlled study to evaluate the effect of progesterone cream on postmenopausal women (Menopause International, Volume 15, Issue 2, June 2009, Pages 63-69
Medical Letter. Bioidentical Hormones. May 31, 2010.
Menopause: The Journal of The North American Menopause Society Vol. 17, No. 2, pp. 242/255.
FDA press release: http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/2008/ucm116832.htm
Pattimakiel L, Thacker HL. Bioidentical hormone therapy: Clarifying the misconceptions. Cleve Clin J Med. 2011 Dec;78(12):829-36.

Links:

NAMS: Position Statements: http://www.menopause.org/aboutmeno/consensus.aspx
The North American Menopause Society www.menopause.org
National Library of Medicine, MedlinePlus www.nlm.nih.gov/medlineplus/menopause.html

Fetal Morbidity or mortality

- Defining the type of HTN is important for non-BP management & follow-up screening during pregnancy & postpartum. However, blood pressure targets are similar and antihypertensive therapy is the same regardless of type.

- Supplements for the prevention of preeclampsia:
  - Fish oils: supplements (e.g. evening primrose) have not been shown to ↓ risk of preeclampsia.
  - P Watch mercury levels in dietary fish (see Extras). Evening primrose may delay rupture of membranes, augment oxytocin, etc.
  - Vitamin E & C: does not ↓ risk of preeclampsia; may ↓ placental abruption (NNT=333) & ↑ risk of
  - P GestHTN and premature rupture of membranes (NNH=19).

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Postpartum Depression:

- Edinburgh Postnatal Depression Scale: http://www2.aap.org/sections/scan/practicingsafety/Toolkit_Resources/Module2/EPDS.pdf
- more evidence in postpartum population compared to PHQ-9
- was developed for use at the 6-8 week postnatal visit; 10 questions; self-administered based on how the mother has felt during the *previous week*.
- Interpretation of Scale: ≥10 (range 9-13) possible depression; maximum score 30

TSH Trimester Specific Targets for Hypothyroidism

The 2011 American Thyroid Association (ATA) Guideline recommends a first trimester TSH target of <2.5mIU/L, and second & third trimester TSH targets of <3mIU/L.[12] These goals are often attainable with an increase in the levothyroxine dose, especially when the targets are met in early pregnancy. However, in clinical practice, there may be the rare occasion when it is difficult to reach the second & third trimester TSH target of <3mIU/L. This may occur when the levothyroxine dose required to achieve a TSH <3mIU/L results in symptoms of hyperthyroidism (e.g. maternal palpitations, failure to gain weight in either mother and/or fetus, or the development of maternal mood disorders). It may also result when pregnant patients are non-compliant with their levothyroxine as they are hesitant to take medications or increase their doses during pregnancy. In these rare situations, if a second and third trimester TSH <3mIU/L cannot be tolerated or attained, a TSH of <3.5mIU/L may be reasonable.

In 2012, the ATA & American Association of Clinical Endocrinologists released guidelines suggestion the following TSH targets: first trimester ≤ 2.5mIU/L, second trimester ≤ 3mIU/L & third trimester ≤ 3.5mIU/L.[12]

References: Peri-Pregnancy Drug Treatment Considerations

General References:

Briggs G et al. Drugs in Pregnancy and Lactation, 9th edition. 2011.

LactMed. http://toxnet.nlm.nih.gov/

Other References:

[1] Health Canada. **Prenatal Nutrition Guidelines** for Health Professionals. 2009. http://www.hc-sc.gc.ca/fn-an/alt_formats/hpfb-dgpsa/pdf/pubs/guide-prenatal-eng.pdf (Accessed December 5th, 2011).

Who should take vitamin supplements? Med Lett Drugs Ther. 2011 Dec 12;53(1379-1380):101-3.

Wilson RD et al; Genetics Committee of the Society of Obstetricians and Gynaecologists of Canada and The Motherisk Program. **Pre-conceptional vitamin/folic acid supplementation** 2007: the use of folic acid in combination with a multivitamin supplement for the prevention of neural tube defects and other congenital anomalies. J Obstet Gynaecol Can. 2007 Dec;29(12):1003-26.

American Academy of Pediatrics. Policy Statement - SECTION ON BREASTFEEDING. Breastfeeding and the use of human milk. Pediatrics. 2012 Mar;129(3):e827-41.

Fernandes TF et al. Effect on Infant Illness of Maternal Supplementation With 400 000 IU Vs 200 000 IU of Vitamin A. Pediatrics. 2012 Mar 12.

[2] Health Canada. Food & Nutrition: High Dose **Folic Acid Supplementation** – Questions and Answers for Health Professionals. 2010.

Talaulikar VS, Arulkumaran S. **Folic acid** in obstetric practice: a review. Obstet Gynecol Surv. 2011 Apr;66(4):240-7.

Kennedy D, Koren G. Motherisk Update: Identifying women who might benefit from higher doses of folic acid in pregnancy. CFP 2012; 58:394-7.

[3] Canadian Pediatric Society. **Vitamin D Supplementation**: Recommendations for Canadian mothers and infants. 2007, Reaffirmed 2010. http://www.cps.ca/english/statements/ii/fnim07-01.htm#RECOMMENDATIONS (Accessed December 5th, 2011).

Institute of Medicine. Dietary Reference Intakes for Calcium and Vitamin D, 2011.

RxFiles Q&A Summary: Vitamin D – Therapeutic Overview and Evaluation of Evidence for Current Claims, 2010.

De-Regil LM et al. Vitamin D supplementation for women during pregnancy. Cochrane Database Syst Rev. 2012 Feb 15;2:CD008873.
Whitehouse AJ et al. Maternal Serum Vitamin D Levels During Pregnancy and Offspring Neurocognitive Development. Pediatrics. 2012 Feb 13.
Vanstone MB et al. Hypercalcemia in Children Receiving Pharmacologic Doses of Vitamin D. Pediatrics.2012 Mar 12.

[4] Anemia Review Panel. Anemia Guidelines for Family Medicine. 2nd ed. Toronto: MUMS Guideline Clearinghouse; 2008.

[5] **Diabetes Guidelines:**

Canadian Diabetes Association. Clinical Practice Guidelines: **Diabetes and Pregnancy**. 2013. http://guidelines.diabetes.ca/executivesummary/ch36 Accessed April 9, 2013.
Canadian Diabetes Association. Clinical Practice Guidelines for the Prevention and Management of Diabetes in Canada: **Diabetes and Pregnancy**. 2008. Pages S168-180.
American Diabetes Association. Standards of Medical Care in Diabetes 2012. Diabetes Care 2012;35:S11-S63.
American Diabetes Association. (ADA 2016): Standards of Medical Care in Diabetes-2016: Summary of Revisions. Diabetes Care. (American Diabetes Association) 2016 Jan;39 Suppl 1:S4-5.
ADA 2018: American Diabetes Association. 13. Management of Diabetes in **Pregnancy**: Standards of Medical Care in Diabetes-2018. Diabetes Care. 2018 Jan;41(Suppl 1):S137-S143.

NICE 2008 Guidelines: Diabetes in pregnancy management of diabetes and its complications from preconception to the postnatal period. http://www.nice.org.uk/nicemedia/live/11946/41320/41320.pdf (Accessed January 30, 2012)

[6] Other Diabetes References:

Pollex E et al. Safety of **insulin glargine** use in pregnancy: a systematic review and meta-analysis. Ann Pharmacother. 2011 Jan;45(1):9-16.
Louie JC et al. A randomized controlled trial investigating the effects of a **low-glycemic index diet** on pregnancy outcomes in gestational diabetes mellitus. Diabetes Care. 2011 Nov;34(11):2341-6.
Bell R et al. Peri-conception hyperglycaemia & nephropathy are associated with risk of congenital anomaly in women with pre-existing diabetes: a population-based cohort study. Diabetologia. 2012 Feb 8.
Murphy HR et al. Effectiveness of a regional prepregnancy care program in women with type 1 and type 2 diabetes: benefits beyond glycemic control. Diabetes Care. 2010 Dec;33(12):2514-20.
Simmons D et al. Gestational diabetes mellitus: NICE for the U.S.? A comparison of the American Diabetes Association and the American College of Obstetricians and Gynecologists guidelines with the U.K. National Institute for Health and Clinical Excellence guidelines. Diabetes Care. 2010 Jan;33(1):34-7. Epub 2009 Oct 16.
Lapolla A, Dalfrà MG, Fedele D. Pregnancy complicated by diabetes: what is the best level of HbA1c for conception? Acta Diabetol. 2010 Sep;47(3):187-92. Epub 2010 May 26.
Guerin A et al. Use of maternal GHb concentration to estimate the risk of congenital anomalies in the offspring of women with prepregnancy diabetes. Diabetes Care. 2007 Jul;30(7):1920-5.
Hartling L, Dryden DM, Guthrie A et al. Benefits and Harms of Treating Gestational Diabetes Mellitus: A Systematic Review and Meta-analysis for the U.S. Preventive Services Task Force and the National Institutes of Health Office of Medical Applications of Research. Ann Intern Med. 2013 Jul 16;159(2):123-9.
Donovan L, Hartling L, Muise M, Guthrie et all. Screening tests for gestational diabetes: a systematic review for the U.S. Preventive Services Task Force. Ann Intern Med. 2013 Jul 16;159(2):115-22.

[7] **Metformin & Glyburide Use During Pregnancy:**

Rowan JA et al. MiG Trial Investigators. Metformin versus insulin for the treatment of gestational diabetes. N Engl J Med.2008 May 8;358(19):2003-15.
Rowan JA et al. Metformin in gestational diabetes: the offspring follow-up (MiG TOFU): body composition at 2 years of age. Diabetes Care. 2011 Oct;34(10):2279-84.
Dhulkotia JS et al. Oral hypoglycemic agents vs insulin in management of gestational diabetes: a systematic review and metaanalysis. Am J Obstet Gynecol. 2010 Nov;203(5):457.e1-9.
Moore LE et al. Metformin compared with glyburide in gestational diabetes: a randomized controlled trial. Obstet Gynecol. 2010 Jan;115(1):55-9.
Briggs G et al. Drugs in Pregnancy and Lactation, 9th edition. 2011.
Ijäs H, Vääräsmäki M, Morin-Papunen L et al. Metformin should be considered in the treatment of gestational diabetes: a prospective randomised study. BJOG. 2011 Jun;118(7):880-5.

[8] Davenport MH et al. A walking intervention improves capillary glucose control in women with gestational diabetes mellitus: a pilot study. Appl Physiol Nutr Metab. 2008 Jun;33(3):511-7.
Stafne SN et al. Regular exercise during pregnancy to prevent gestational diabetes: a randomized controlled trial. Obstet Gynecol. 2012 Jan;119(1):29-36.

[9] **Hypertension Guidelines:**

Magee LA et al. Hypertension Guideline Committee; Strategic Training Initiative in Research in the Reproductive Health Sciences (STIRRHS) Scholars. Diagnosis, evaluation, and management of the **hypertensive disorders of pregnancy**. J Obstet Gynaecol Can. 2008 Mar;30(3 Suppl):S1-48.
Magee LA, Pels A, Helewa M, Rey E, von Dadelszen P; Hypertension Guideline Committee, Magee LA, Audibert F, Bujold E, Côté AM, Douglas MJ, Eastabrook G, Firoz T, Gibson P, Gruslin A, Hutcheon J, Koren G, Lange I, Leduc L, Logan AG, MacDonell KL, Moutquin JM, Sebbag I. Diagnosis, evaluation, and management of the hypertensive disorders of pregnancy: executive summary. J Obstet Gynaecol Can. 2014 May;36(5):416-38. PubMed PMID: 24927294.
Royal College of Obstetricians and Gynecologists. **Hypertension in pregnancy**: the management of hypertensive disorders during pregnancy. **2011 NICE Guidelines.**

Other Hypertension References:

Raheem IA et al. Oral nifedipine versus intravenous labetalol for acute blood pressure control in hypertensive emergencies of pregnancy: a randomised trial. BJOG. 2012 Jan;119(1):78-85.
Fraser A et al. Associations of Pregnancy Complications with Calculated CVD Risk & Cardiovascular Risk Factors in Middle Age: The Avon Longitudinal Study of Parents and Children. Circulation. 2012 Feb 17.
Shennan AH et al. Are most maternal deaths from pre-eclampsia avoidable? Lancet. 2011 Dec 14.
Bukowski R et al. Delivery of a small for gestational age infant and greater maternal risk of ischemic heart disease. PLoS ONE. March 2012.
Mannisto T, Mendola P, Vaarasmaki M, Jarvelin M-R, Hartikainen A-L, Pouta A, Suvanto E. Elevated blood pressure in pregnancy and subsequent chronic disease risk. Circulation. 2013;127:681–690.
Bramham K, Nelson-Piercy C, Brown MJ, Chappell LC. **Postpartum management of hypertension**. BMJ. 2013 Feb 25;346:f894.

[10] Conde-Agudelo A et al. Supplementation with **vitamins C and E during pregnancy for the prevention of preeclampsia** and other adverse maternal and perinatal outcomes: a systematic review and metaanalysis. Am J Obstet Gynecol. 2011 Jun;204(6):503.e1-12.
Roberts JM et al. National Institute of Child Health and Human Development Maternal-Fetal Medicine Units Network. **Vitamins C and E** to prevent complications of pregnancy-associated hypertension. NEJM. 2010 Apr 8;362(14):1282-91.
[11] Li DK et al. Maternal exposure to **angiotensin converting enzyme inhibitors** in the first trimester and risk of malformations in offspring: a retrospective cohort study. BMJ. 2011 Oct 18;343.
Vasilakis-Scaramozza C, Aschengrau A, Cabral HJ, Jick SS. Antihypertensive drugs and the risk of congenital anomalies. Pharmacotherapy. 2013 May;33(5):476-82.

[12] **Thyroid Guidelines:** Stagnaro-Green A et al. American Thyroid Association Taskforce on Thyroid Disease During Pregnancy and Postpartum. **Guidelines of the American Thyroid Association** for the diagnosis and management of thyroid disease during pregnancy and postpartum. Thyroid. 2011 Oct;21(10):1081-125.
Garber JR, Cobin RH, Gharib H et al. **Clinical Practice Guidelines for Hypothyroidism** in Adults: Co-sponsored by American Association of Clinical Endocrinologists and the American Thyroid Association. Endocr Pract. 2012 Sep 11:1-207.
[13] **Other Thyroid References:**
Chen CH et al. Risk of adverse perinatal outcomes with antithyroid treatment during pregnancy: a nationwide population-based study. BJOG. 2011 Oct;118(11):1365-73.
Lazarus JH et al. Antenatal thyroid screening and childhood cognitive function. N Engl J Med.2012 Feb 9;366(6):493-501.
Brent GA. The debate over thyroid-function screening in pregnancy. N Engl J Med. 2012 Feb 9;366(6):562-3.
Cooper DS, Biondi B. Subclinical thyroid disease. Lancet. 2012 Jan 20.
Stagnaro-Green A. Screening pregnant women for overt thyroid disease. JAMA. 2015 Feb 10; 313(6):565-6.
Sullivan KM. Iodine supplementation for pregnancy and lactation: United States and Canada: recommendations of the American Thyroid Association. Thyroid. 2007 May;17(5):483-4.
Reid SM, Middleton P, Cossich MC, et al. Interventions for clinical and subclinical hypothyroidism pre-pregnancy and during pregnancy. Cochrane Database Syst Rev. 2013 May 31;5:CD007752. doi:
Medici M, Timmermans S, Visser W, et al. Maternal thyroid hormone parameters during early pregnancy and birth weight: the Generation R Study. J Clin Endocrinol Metab. 2013 Jan;98(1):59-66.

Infectious Disease References:
[14] Anti-infective Review Panel. Anti-infective guidelines for community-acquired infections. Toronto: MUMS Guideline Clearinghouse; 2012.
[15] Capital Health Regional Pharmacy Services. Bugs & Drugs. Edmonton; 2006.
[16] Canadian Guidelines on Sexually Transmitted Infections, 2008 Edition. Ottawa, ON: Public Health Agency of Canada.
[17] CDC 2010 STI Clinical Guidelines. http://www.cdc.gov/std/treatment/2010/STD-Treatment-2010-RR5912.pdf (Accessed January 2012).
[18] American College of Obstetricians & Gynaecologists. Committee Opinion #485. Prevention of Early-Onset Group B Streptococcal Disease in Newborns. April 2011.
Society of Obstetricians & Gynaecologists. Clinical Practice Guidelines: The prevention of early-onset neonatal Group B Streptococcal Disease. September 2004.
[19] Public Health Service Task Force Recommendations for Use of Antiretroviral Drugs in Pregnant HIV-Infected Women for Maternal Health and Interventions to Reduce Perinatal HIV Transmission in the United States. September 14, 2011. 1-207. Avalaible at http://aidsinfo.nih.gov/contentfiles/PerinatalGL.pdf. Accessed February 15, 2012.
Saskatchewan Prevention Institute. HIV/AIDS & Pregnancy: A guide to care. 2011.
[20] Yudin M et al. SOGC Clinical Practice Guidelines: 2008 Screening and management of **bacterial vaginosis** in pregnancy.
Society of Obstetricians & Gynaecologists. Clinical Practice Guidelines: Management of Group B Steptococcal Bacteriuria in Pregnancy. May 2012.
Steer JA, Lamagni T, Healy B et al. Guidelines for prevention and control of group A streptococcal infection in acute healthcare and maternity settings in the UK. J Infect. 2012 Jan;64(1):1-18.
Cantoni L, Ronfani L, Da Riol R et al. Physical Examination Instead of Laboratory Tests for Most Infants Born to Mothers Colonized with Group B Streptococcus: Support for the Centers for Disease Control and Prevention's 2010 Recommendations. J Pediatr. 2013 Mar 8.

[21] **Genital Herpes Simplex:**
Money D, Steben M; Society of Obstetricians and Gynaecologists of Canada. SOGC clinical practice guidelines: Guidelines for the management of herpes simplex virus in pregnancy. Number 208, June 2008. Int J Gynaecol Obstet. 2009 Feb;104(2):167-71.
Hollier LM, Wendel GD. Third trimester antiviral prophylaxis for preventing maternal genital herpes simplex virus (HSV) recurrences and neonatal infection. Cochrane Database Syst Rev. 2008 Jan 23;(1):CD004946.
Su C, McKay B. Treatment of HSV Infection in late pregnancy. Am Fam Physician. 2012 Feb 15;85(4):390-393.
Kang SH et al. Safety of antiviral medication for the treatment of herpes during pregnancy. Can Fam Physician. 2011 Apr;57(4):427-8.
[22] **Urinary Tract Infections/Asymptomatic Bacteriuria:**
Widmer M et al. Duration of treatment of asymptomatic bacteriuria during pregnancy. Cochrane Database of Systematic Reviews 2011, Issue 12. Art. No.: CD000491.
Guinto VT et al. Different antibiotic regimens for treating asymptomatic bacteriuria in pregnancy. Cochrane Database of Systematic Reviews 2010, Issue 9. Art. No.: CD007855.
Lee M et al. Motherisk Update: Urinary tract infections in pregnancy. Can Fam Physician June 2008 54: 853-854

[23] **Other Infectious Disease References:**
Medical Letter. Vaccines and Pregnancy. Medical Letter 2011; 53(1378):94-96.
CADTH. Rapid Response Report: Treatment of Yeast Infections in Breastfeeding Mothers and Babies – Clinical Evidence and Guidelines. November 2011.
Dauby N et al. Uninfected but not unaffected: chronic maternal infections during pregnancy, fetal immunity, and susceptibility to postnatal infections. Lancet Infect Dis. 2012 Feb 23.

Narducci A, Einarson A, Bozzo P. Human papillomavirus vaccine and pregnancy. Canadian Family Physician 2012;58:268-9.
McCartney M. Streptococcus B in pregnancy: to screen or not to screen? BMJ. 2012 Apr 18;344:e2803.
[24] Bozzo P et al. Motherisk Update: Safety of skin care products during pregnancy. Canadian Family Physician 2011;57:665-667.
[25] Namazy JA, Schatz M. **Asthma and pregnancy**. J Allergy Clin Immunol. 2011 Dec;128(6):1384-1385.

Depression References:

[26] Yonkers KA et al. The management of depression during pregnancy: a report from the American Psychiatric Association and the American College of Obstetricians and Gynecologists. Gen Hosp Psychiatry. 2009 Sep-Oct;31(5):403-13.
Cohen LS et al. Relapse of major depression during pregnancy in women who maintain or discontinue antidepressant treatment. JAMA. 2006 Feb 1;295(5):499-507.
Canadian Pediatric Society Position Statement. Selective serotonin reuptake inhibitors in pregnancy and infant outcomes. Pedatric Child Health 2011; 16(9):562.
American Psychiatric Association. 2010 Practice Guideline for the Treatment of Patients with Major Depressive Disorder, 3rd edition. http://psychiatryonline.org/data/Books/prac/PG_Depression3rdEd.pdf Accessed February 21st, 2012.
Bonari L et al. Risks of untreated depression during pregnancy. Can Fam Physician. 2004 Jan;50:37-9.
National Institute for Health and Clinical Excellence. NICE Clinical Guideline 45 – Antenatal and postnatal mental health: Clinical management and service guidance. February 2007. http://www.nice.org.uk/nicemedia/live/11004/30433/30433.pdf Accessed February 21st, 2012.
Ryan D, Milis L, Misri N. Depression during pregnancy. Can Fam Physician. 2005 Aug;51:1087-93.
Stewart DE. Clinical practice. Depression during pregnancy. N Engl J Med. 2011 Oct 27;365(17):1605-11.
Davalos DB, Yadon CA, Tregellas HC. Untreated prenatal maternal depression and the potential risks to offspring: a review. Arch Womens Ment Health. 2012 Feb;15(1):1-14.
Rubinchik SM, Kablinger AS, Gardner JS. Medications for panic disorder and generalized anxiety disorder during pregnancy. Prim Care Companion J Clin Psychiatry. 2005;7(3):100-5.
Galbally M, Snellen M, Lewis AJ. A review of the use of psychotropic medication in pregnancy. Curr Opin Obstet Gynecol. 2011 Dec;23(6):408-14.
Einarson A. Motherisk Update: Paroxetine use in pregnancy and increased risk of heart defects. Canadian Family Physician 2010;56:767-8.
Occhiogrosso M, Omran SS, Altemus M. Persistent pulmonary hypertension of the newborn and selective serotonin reuptake inhibitors: lessons from clinical and translational studies. Am J Psychiatry. 2012 Feb 1;169(2):134-40.
Patil AS et al. Antidepressants in pregnancy: a review of commonly prescribed medications. Obstet Gynecol Surv. 2011 Dec;66(12):777-87.
Kalra S, Einarson A, Koren G. Taking antidepressants during late pregnancy. Canadian Family Physician 2005; 51: 1077-8.
Fortinguerra F et al. Psychotropic drug use during breastfeeding: a review of the evidence. Pediatrics 2009;124(4):547-556.
Flynn HA et al. Comparative performance of the Edinburgh Postnatal Depression Scale and the Patient Health Questionnaire-9 in pregnant and postpartum women seeking psychiatric services. Psychiatry Res. 2011 May 15;187(1-2):130-4.
Shah N. Mood disorder in the perinatal period. BMJ. 2012 Mar 1;344:e1209.
Viguera AC et al. Episodes of mood disorders in 2,252 pregnancies and postpartum periods. Am J Psychiatry. 2011 Nov;168(11):1179-85.
Howell EA, et al. Reducing postpartum depressive symptoms among black and latina mothers: a randomized controlled trial. Obstet Gynecol. 2012 May;119(5):942-9.
Koren G, Nordeng H. Antidepressant use during pregnancy: the **benefit-risk ratio**. Am J Obstet Gynecol. 2012 Feb 21.
Mann R, Adamson J, Gilbody SM. Diagnostic accuracy of case-finding questions to **identify perinatal depression**. CMAJ. 2012 Apr 2.
Jimenez-Solem E, Andersen JT, Petersen M, et al. SSRI Use During Pregnancy and Risk of **Stillbirth and Neonatal Mortality**. Am J Psychiatry. 2013 Jan 30.
[27] Natural Medicines Comprehensive Database. Natural Medicines Used During Pregnancy & Lactation. http://naturaldatabase.therapeuticresearch.com.ezproxy.shirp.ca/ce/CECourse.aspx?cs=&pm=5&s=nd&pc=11-102&searchid=31811148#keywordanchor (Accessed December 29th, 2011)
Health Canada. Women's Health Information: Pregnancy – Herbal Remedies. http://www.sogc.org/health/pregnancy-herbal_e.asp (Accessed December 29th, 2011)
Mozurkewich EL, Klemens C. Omega-3 fatty acids and pregnancy: current implications for practice. Curr Opin Obstet Gynecol. 2012 Mar;24(2):72-7.
Imhoff-Kunsch B et al. Prenatal docosahexaenoic Acid supplementation and infant morbidity: randomized controlled trial. Pediatrics. 2011 Sep;128(3):e505-12.
[28] Society of Obstetricians and Gynaecologists of Canada. 2002 Clinical Practice Guidelines: The management of **nausea and vomiting** of pregnancy. J Obstet Gynaecol Can 2002;24(10):817-23.
Maitre S, Neher J, Safranek S. Ginger for the treatment of **nausea and vomiting** in pregnancy. American Family Physician 2011;84(10).
[29]Rebordosa C et al. Use of acetaminophen during pregnancy and risk of adverse pregnancy outcomes. Int J Epidemiol. 2009 Jun;38(3):706-14.
Babb M, Koren G, Einarson A. Treating pain during pregnancy. Can Fam Physician. 2010 Jan;56(1):25, 27.
[30] Cupp M. Analgesics in Pregnancy and Lactation. Pharmacists Letter. February 2012.
O'Mara. New pregnancy warnings: opioids, topiramate, and antipsychotics. Pharmacist's Letter. April 2011.
Nakhai-Pour HR et al. Use of nonaspirin nonsteroidal anti-inflammatory drugs during pregnancy and the risk of spontaneous abortion. CMAJ. 2011 Oct 18;183(15):1713-20.
Palacioz K. NSAIDs and Miscarriage. Pharmacist's Letter. October 2003.
Edwards DV, Aldridge T, Baird D et al. Periconceptional OTC NSAID exposure and risk for spontaneous abortion. ObsGyn 2012; 120(1):113-122.
[31] Nappi RE, Albani F, Sances G, Terreno E, Brambilla E, Polatti F. **Headaches** during pregnancy. Curr Pain Headache Rep. 2011 Aug;15(4):289-94.
Gilmore B, Michael M. Treatment of acute **migraine headache**. Am Fam Physician. 2011 Feb 1;83(3):271-80.
[32]Wiener S. Diagnosis and management of Candida of the nipple and breast. JMidwifery Womens Health. 2006 Mar-Apr;51(2):125-8.

[33] Davies GA et al. Society of Obstetricians and Gynecologists of Canada, SOGC Clinical Practice Obstetrics Committee. **Joint SOGC/CSEP clinical practice guideline: exercise in pregnancy and the postpartum period**. Can J Appl Physiol. 2003 Jun;28(3):330-41.
Szymanski LM, Satin AJ. Exercise during pregnancy: fetal responses to current public health guidelines. Obstet Gynecol. 2012 Mar;119(3):603-10.
Wise et al. A prospective cohort study of physical activity and time to pregnancy. Fertility and Sterility. 2012.
Hui A et al. Lifestyle intervention on diet and exercise reduced excessive gestational weight gain in pregnant women under a randomized controlled trial. BJOG 2012(1);119:70-77.
[34] Health Canada. Mercury in Fish: Question and Answers, January 2011. http://www.hc-sc.gc.ca/fn-an/securit/chem-chim/environ/mercur/merc_fish_qa-poisson_qr-eng.php (Accessed February 9, 2012).
Health Canada. Eating well with Canada's Food Guide – First Nations, Inuit and Metis, March 2010. http://www.hc-sc.gc.ca/fn-an/pubs/fnim-pnim/index-eng.php#a_7 (Accessed February 9, 2012).
[35] Davies GA et al. Society of Obstetricians and Gynaecologists of Canada. **Obesity in pregnancy**. J Obstet Gynaecol Can. 2010 Feb;32(2):165-73.
Arendas K, Qiu Q, Gruslin A. **Obesity** in pregnancy: pre-conceptional to postpartum consequences. J Obstet Gynaecol Can. 2008 Jun;30(6):477-88.
Baker JL et al. Breastfeeding reduces postpartum weight retention. Am J Clin Nutr. 2008 Dec;88(6):1543-51.
[36] Health Canada. Canadian Gestational Weight Gain Recommendations. http://www.hc-sc.gc.ca/fn-an/nutrition/prenatal/qa-gest-gros-qr-eng.php (Accessed December 1st, 2011)
[37] Society of Obstetricians and Gynaecologists of Canada. 2010 Alcohol use and pregnancy: consensus clinical guidelines. Journal of Obstetrics and Gynaecology Canada 2010; 32(8):supplement 3.
Nice FJ, Luo AC. Medications and breast-feeding: Current concepts. J Am Pharm Assoc (2003). 2012 Jan 1;52(1):86-94.
Dynamed. Medication and drug exposure during pregnancy. Accessed February 22, 2012.
Patra J et al. Dose-response relationship between alcohol consumption before and during pregnancy and the risks of low birthweight, preterm birth and small for gestational age (SGA)-a systematic review and meta-analyses. BJOG. 2011 Nov;118(12):1411-21.
Sayal K, Draper ES, Fraser R, et al. Light drinking in pregnancy and mid-childhood mental health and learning outcomes. Arch Dis Child 2013;98:107–11.
[38] Health Canada. Health Canada Reminds Canadians to Manage Caffeine Consumption, March 2010. http://www.hc-sc.gc.ca/ahc-asc/media/advisories-avis/_2010/2010_40-eng.php (Accessed December 5th, 2011).
Santos IS, Matijasevich A, Domingues MR. Maternal Caffeine Consumption and Infant Nighttime Waking: Prospective Cohort Study. Pediatrics. 2012 Apr 2.
[39] Koren G. Pharmacokinetics in pregnancy; clinical significance. J Popul Ther Clin Pharmacol. 2011;18(3):e523-7.
CADTH. Rapid Response Update: Second hand smoke and pregnancy women – clinical evidence. February 7th, 2012.
Nice FJ, Luo AC. Medications and breast-feeding: Current concepts. J Am Pharm Assoc (2003). 2012 Jan 1;52(1):86-94.
Filion KB et al. The effect of smoking cessation counselling in pregnant women: a meta-analysis of randomised controlled trials. BJOG. 2011 Nov;118(12):1422-8.
CADTH Rapid Response: Smoking cessation interventions for pregnancy women and mothers of infants – a review of the clinical effectiveness, safety & guidelines. March 2012.
CAN-ADAPTT: Practice-informed and evidence-based smoking cessation guideline [Internet]. Toronto: Canadian Action Network for the Advancement, Dissemination and Adoption of Practice-informed Tobacco (CAN-ADAPTT); 2011. http://www.can-adaptt.net/English/Guideline/Introduction.aspx. Accessed March 12, 2012.
Coleman T et al. A randomized trial of nicotine-replacement therapy patches in pregnancy. NEJM 2012; 366(9):808-18.
Oncken C. Commentary - Nicotine replacement for smoking cessation during pregnancy. NEJM 2012; 366(9):846-7.
Milidou I et al. Nicotine replacement therapy during pregnancy and infantile colic in the offspring. Pediatrics 2012;652-8.
Baardman ME et al. Combined adverse effects of maternal smoking and high body mass index on heart development in offspring: evidence for interaction? Heart. 2012 Mar;98(6):474-9.
Mackay DF et al. Impact of Scotland's Smoke-Free Legislation on Pregnancy Complications: Retrospective Cohort Study. PLoS Med. 2012 Mar;9(3):e1001175.
Chamberlain C, O`Mara-Eves A, Oliver S, et al. Psychosocial interventions for supporting women to stop smoking in pregnancy. Cochrane Database Syst Rev. 2013 Oct 23;10:CD001055.
[40]Black A et al. Society of Obstetricians and Gynaecologists of Canada. SOGC clinical practice guidelines: **Canadian contraception consensus**. J Obstet Gynaecol Can. 2004 Mar;26(3):219-96.
Black A et al. Society of Obstetricians and Gynaecologists of Canada. **Canadian contraception consensus**. J Obstet Gynaecol Can. 2004 Apr;26(4):347-87, 389-436.
Centers for Disease Control and Prevention (CDC). Update to CDC's U.S. Medical Eligibility Criteria for Contraceptive Use, 2010: revised recommendations for the use of contraceptive methods during the postpartum period. MMWR Morb Mortal Wkly Rep. 2011 Jul 8;60(26):878-83.
Truitt ST et al. Combined hormonal versus nonhormonal versus progestin-only contraception in lactation. Cochrane Database of Systematic Reviews 2003, Issue 2. Art. No.: CD003988.
[41]Academy Of Breastfeeding Medicine Protocol Committee. ABM Clinical Protocol #9: Use of galactogogues in initiating or augmenting the rate of maternal milk secretion (First Revision January 2011). Breastfeed Med. 2011 Feb;6(1):41-9.
Mannion C, Mansell D. Breastfeeding self-efficacy and the use of prescription medication: a pilot study. Obstet Gynecol Int. 2012;2012:562704. Epub 2011 Dec 15.
Natural Medicines Comprehensive Database. Blessed thistle, caraway, fennel, fenugreek, and Goat's rue Monographs. http://naturaldatabase.therapeuticresearch.com.cyber.usask.ca/home.aspx?cs=&s=ND. (Accessed February 9, 2012).
Health Canada Advisory: Domperidone Maleate Association with Serious Abnormal Heart Rhythms and Sudden Death (Cardiac Arrest) - For Health Professionals. http://www.hc-sc.gc.ca/dhp-mps/medeff/advisories-avis/prof/_2012/domperidone_hpc-cps-eng.php. Accessed March 14th, 2012.
Oladapo OT, Fawole B. Treatments for suppression of lactation. Cochrane Database of Systematic Reviews 2009, Issue 1. Art. No.: CD005937. DOI: 10.1002/14651858.CD005937.pub2.
[42] Vause TD et al. Society of Obstetricians and Gynecologists of Canada. Ovulation induction in **polycystic ovary syndrome**. J Obstet Gynaecol Can. 2010 May;32(5):495-502.
Wilson JF. In the clinic. The polycystic ovary syndrome. Ann Intern Med. 2011 Feb 1;154(3):ITC2-2-ITC2-15; quiz ITC2-16. Review.
Fauser BC et al. Consensus on women's health aspects of polycystic ovary syndrome (PCOS): the Amsterdam ESHRE/ASRM-Sponsored 3rd PCOS Consensus Workshop Group. Fertil Steril. 2012 Jan;97(1):28-38.e25.

Additional References:

AAP Committee on Nutrition , AAP Section on Breastfeeding, AAP Committee on Feuts and Newborn. **Donor Human Milk** for the High-Risk Infant: Preparation, Safety, and Usage Options in the United States. Pediatrics. 2017;139(1):e20163440

Abalos E, Duley L, Steyn DW. **Antihypertensive drug therapy** for mild to moderate hypertension during pregnancy. Cochrane Database Syst Rev. 2014 Feb 6;2:CD002252.

Abalos E, Duley L, Steyn DW, et al. **Antihypertensive drug therapy for mild to moderate hypertension during pregnancy**. Cochrane Database Syst Rev. 2018 Oct 1;10:CD002252. Antihypertensive drug therapy for mild to moderate hypertension during pregnancy reduces the risk of severe hypertension. The effect on other clinically important outcomes remains unclear. If antihypertensive drugs are used, beta blockers and calcium channel blockers appear to be more effective than the alternatives for preventing severe hypertension. High-quality large sample-sized randomised controlled trials are required in order to provide reliable estimates of the benefits and adverse effects of antihypertensive treatment for mild to moderate hypertension for both mother and baby, as well as costs to the health services, women and their families.

Abel KM, Heuvelman HP, et al. **Severe bereavement stress during the prenatal** and childhood periods and risk of psychosis in later life: population based cohort study. BMJ. 2014 Jan 21;348:f7679

Abdul Sultan A, Tata LJ, West J, et al. Risk factors for first venous **thromboembolism** around pregnancy: a population based cohort study from the United Kingdom. Blood. 2013 Apr 2.

Abdul Sultan A, West J, Tata LJ, et al. Risk of **first venous thromboembolism in pregnant** women in hospital: population based cohort study from England. BMJ. 2013 Nov 7;347:f6099.

Abernethy C, McCall KE, Cooper G, et al. Determining the pattern and prevalence of **alcohol consumption** in pregnancy by measuring biomarkers in meconium. Arch Dis Child Fetal Neonatal Ed. 2017 Jul 4.

Abrams EM, Sicherer SH. **Maternal peanut consumption and risk of peanut allergy** in childhood. CMAJ. 2018 Jul 9;190(27):E814-E815.

Abrams SA; Committee on Nutrition. Calcium and vitamin d requirements of enterally fed preterm infants. Pediatrics. 2013 May;131(5):e1676-83.

Abu-Raya B, Edwards KM. Optimizing the Timing of **Vaccine Administration** During Pregnancy. JAMA. 2019 Feb 25.

Academy of Breastfeeding Medicine. ABM Clinical Protocol #15: **Analgesia and Anesthesia for the Breastfeeding Mother,** Revised 2012. Breastfeed Med 2012 Dec;7:547-53.

Academy of Breastfeeding Medicine. Recommendations for **preprocedural fasting for the breastfed infant: "NPO" Guidelines**. Breastfeed Med 2012 Jun;7(3):197-202.

Achebe MM, Gafter-Gvili A. How I treat anemia in **pregnancy: iron, cobalamin and folate**. Blood. 2016 Dec 29.

ACOG: Committee opinion no. 597: **labor induction or augmentation and autism**. Obstet Gynecol. 2014 May;123(5):1140-2.

ACOG Practice bulletin no. 150: **early pregnancy loss**. Obstet Gynecol. 2015 May;125(5):1258-67.

ACOG Committee Opinion No. 638: First-Trimester Risk Assessment for **Early-Onset Preeclampsia**. Obstet Gynecol. 2015 Sep;126(3):e25-7.

ACOG: Committee Opinion No. 650: **Physical Activity** and Exercise During Pregnancy and the Postpartum Period. Obstet Gynecol. 2015 Dec;126(6):e135-42.

ACOG: Practice Bulletin No 156: **Obesity in Pregnancy**. Obstet Gynecol. 2015 Dec;126(6):e112-26.

ACOG Committee on Obstetric Practice. Committee Opinion No. 623: **Emergent therapy for acute-onset, severe hypertension during pregnancy** and the postpartum period. Obstet Gynecol. 2015 Feb;125(2):521-5.

ACOG: Committee Opinion No. 660: **Family Building Through Gestational Surrogacy**. Obstet Gynecol. 2016 Mar;127(3):e97-e103.

ACOG: Committee Opinion No. 659: The Use of **Vaginal Estrogen** in Women With a History of **Estrogen-Dependent Breast Cancer**. Obstet Gynecol. 2016 Mar;127(3):e93-e96.

ACOG: Committee Opinion No. 658: Optimizing Support for **Breastfeeding** as Part of Obstetric Practice. Obstet Gynecol. 2016 Feb;127(2):e86-92.

ACOG: Committee Opinion No. 664: **Refusal of Medically Recommended Treatment** During Pregnancy. Obstet Gynecol. 2016 Jun;127(6):e175-82.

ACOG: Committee Opinion No. 669: **Planned Home Birth**. Obstet Gynecol. 2016 Aug;128(2):e26-31.

ACOG: Committee Opinion No. 670: **Immediate Postpartum Long-Acting Reversible Contraception**. Obstet Gynecol. 2016 Aug;128(2):e32-7.

ACOG:Committee Opinion No.677: **Antenatal Corticosteroid Therapy** for Fetal Maturation. Obstet Gynecol. 2016 Oct;128(4):e187-94.

ACOG: Committee Opinion No. 679: **Immersion in Water During Labor and Delivery**. Obstet Gynecol. 2016 Nov;128(5):e231-e236

ACOG Committee Opinion No. 684: **Delayed Umbilical Cord Clamping** After Birth. Obstet Gynecol. 2017 Jan;129(1):e5-e10.

ACOG Committee on Obstetric Practice.. ACOG Committee Opinion No. 474: **nonobstetric surgery during pregnancy**. Obstet Gynecol. 2011 Feb;117(2 Pt1):420-1.

ACOG: Committee Opinion No. 687: Approaches to **Limit Intervention During Labor and Birth**. Obstet Gynecol. 2017 Feb;129(2):e20-e28.

ACOG: Committee Opinion No. 690: **Carrier Screening** in the **Age of Genomic Medicine**. Obstet Gynecol. 2017 Mar;129(3):e35-e40

ACOG: Committee Opinion No. 691: **Carrier Screening for Genetic Conditions**. Obstet Gynecol. 2017 Mar;129(3):e41-e55.

ACOG: Committee Opinion No. 711: **Opioid Use and Opioid Use Disorder** in Pregnancy. Obstet Gynecol. 2017 Aug;130(2):e81-e94.

ACOG Committee Opinion No. 733: **Employment Considerations During Pregnancy and the Postpartum Period**. Obstet Gynecol. 2018 Apr;131(4):e115-e123.

ACOG: **Postpartum Pain Management**. Obstet Gynecol. 2018 May 17.

ACOG: Committee Opinion No. 732: **Influenza Vaccination During Pregnancy**. Obstet Gynecol. 2018 Apr;131(4):e109-e114.

ACOG: Committee Opinion No. 741: **Maternal Immunization**. Obstet Gynecol. 2018 Jun;131(6):e214-e217.

ACOG Committee Opinion No. 743: Low-Dose Aspirin Use During Pregnancy. Obstet Gynecol. 2018 Jul;132(1):e44-e52.

ACOG Committee Opinion No. 746: Air Travel During Pregnancy. Obstet Gynecol. 2018 Aug;132(2):e64-e66.

ACOG Committee Opinion No. 762: Prepregnancy Counseling. Obstet Gynecol. 2019 Jan;133(1):e78-e89.

ACOG: Practice Bulletin No. 200: Early Pregnancy Loss. Obstet Gynecol. 2018 Aug 28.

ACOG Committee Opinion No. 762: Prepregnancy Counseling. Obstet Gynecol. 2019 Jan;133(1):e78-e89.

ACOG Practice Bulletin No. 212: **Pregnancy and Heart Disease**. Obstet Gynecol. 2019 May;133(5):e320-e356.

ACOG Committee Opinion No. 767 Summary: **Emergent Therapy for Acute-Onset, Severe Hypertension** During Pregnancy and the Postpartum Period. Obstet Gynecol.2019 Feb;133(2):409-412.

ACOG Practice Bulletin No. 203: **Chronic Hypertension** in Pregnancy. Obstet Gynecol. 2019 Jan;133(1):e26-e50.

ACOG: Committee Opinion No. 711: **Opioid Use and Opioid Use Disorder** in Pregnancy. Obstet Gynecol. 2017 Aug;130(2):e81-e94.

Acosta CD, Harrison DA, Rowan K, Lucas DN, Kurinczuk JJ, Knight M. **Maternal morbidity and mortality** from severe **sepsis**: a national cohort study. BMJ Open. 2016 Aug 23;6(8):e012323

ADA 2017: **American Diabetes Association**.. 13. **Management of Diabetes in Pregnancy**. Diabetes Care. 2017 Jan;40(Suppl 1):S114-S119.

Adam S, Ammori B, Soran H, et al. Pregnancy after bariatric surgery: screening for gestational diabetes. BMJ. 2017 Feb 3;356:j533.

Adane AA, Mishra GD, Tooth LR. **Diabetes in Pregnancy and Childhood Cognitive Development**: A Systematic Review. Pediatrics. 2016 May;137(5).

Adashi EY. Brief Commentary: **Marijuana Use** During Gestation and Lactation-Harmful Until Proved Safe. Ann Intern Med. 2019 Jan 8.
Adiong JP, Kim E, Koren G, et al. Consuming **non-alcoholic beer and other beverages** during pregnancy and breastfeeding. Can Fam Physician. 2014 Aug;60(8):724-5.
Admon LK, Bart G, Kozhimannil KB, et al. **Amphetamine- and Opioid-Affected Births**: Incidence, Outcomes, and Costs, United States, 2004-2015. Am J Public Health. 2018 Nov 29:e1-e7.
Ahun MN, Geoffroy MC, Herba CM, et al. **Timing and Chronicity of Maternal Depression** Symptoms and Children's Verbal Abilities. J Pediatr. 2017 Sep 6.
Aiken ARA, et al. Self reported outcomes and adverse events after **medical abortion through online telemedicine**: population based study in Republic of Ireland & Northern Ireland. BMJ. 2017 May 16;357:j2011.
Alabdulrazzaq F, Koren G. **Topical corticosteroid** use during pregnancy. Can Fam Physician. 2012 Jun;58(6):643-4.
Alabdulrazzaq F, Koren G. Fetal safety of **calcium channel blockers**. Can Fam Physician. 2012 Jul;58(7):746-7.
Albright CM, Ali TN, Lopes V et al. The **Sepsis in Obstetrics Score**: a model to identify risk of morbidity from sepsis in pregnancy. Am J Obstet Gynecol. 2014 Jul;211(1):39.e1-8.
Alexopoulos AS, Blair R, Peters AL. Management of **Preexisting Diabetes in Pregnancy**: A Review. JAMA. 2019 May 14;321(18):1811-1819.
Alfirevic Z, Keeney E, Dowswell T, et al. **Methods to induce labour**: a systematic review, network meta-analysis and cost-effectiveness analysis. BJOG. 2016 Mar 22.
Allen VM, Yudin MH. Management of **group B streptococcal** bacteriuria in pregnancy. J Obstet Gynaecol Can 2012 May;34(5):482-6.
Alqudah A, McKinley MC, McNally R, et al. **Risk of pre-eclampsia in women taking metformin**: a systematic review and meta-analysis. Diabet Med. 2018 Feb;35(2):160-172.
Alroughani R, Alowayesh MS, Ahmed SF, et al. Relapse occurrence in women with **multiple sclerosis during pregnancy** in the new treatment era. Neurology. 2018 Mar 6;90(10):e840-e846.
Amant F et al. Long-term cognitive and cardiac outcomes after **prenatal exposure to chemotherapy** in children aged 18 months or older: an observational study. Lancet Oncol. 2012 Mar;13(3):256-64.
Amant F, Vandenbroucke T, et al; International Network on Cancer, Infertility, and Pregnancy (INCIP). Pediatric Outcome after **Maternal Cancer Diagnosed during Pregnancy**. N Engl J Med. 2015 Sep 28.
Ambasta A, Malebranche M. **Opioid use disorder** in pregnancy. CMAJ. 2019 Sep 23;191(38):E1057.
Academy of Family Physicians. Clinical practice guideline: planning for **labor and vaginal birth after cesarean**. Leawood (KS): American Academy of Family Physicians; 2014 May.
American College of Obstetricians and Gynecologists (**ACOG**). **Chronic hypertension in pregnancy**. Washington (DC): American College of Obstetricians and Gynecologists (ACOG); 2012 Feb. 12.
American College of Obstetricians and Gynecologists. **ACOG** Committee opinion no. 549: **obesity in pregnancy**. Obstet Gynecol. 2013 Jan;121(1):213-7.
American College of Obstetricians and Gynecologists. **ACOG** Committee opinion no 611: method for **estimating due date**. Obstet Gynecol. 2014 Oct;124(4):863-6.
Ananth CV, Goldenberg RL, Friedman AM, et al. Association of **Temporal Changes in Gestational Age With Perinatal Mortality** in the United States, 2007-2015. JAMA Pediatr. 2018 May 14.
Ananth CV, Keyes KM, Wapner RJ. **Pre-eclampsia rates in the United States**, 1980-2010: age-period-cohort analysis. BMJ. 2013 Nov 7;347:f6564.
Andersen JT, Andersen NL, Horwitz H, et al. Exposure to **Selective Serotonin Reuptake Inhibitors in Early Pregnancy and the Risk of Miscarriage**. Obstet Gynecol. 2014 Sep 5.
Andersen SL, Knøsgaard L, Olsen J, et al. **Maternal thyroid function**, use of antithyroid drugs in early pregnancy and birth defects. J Clin Endocrinol Metab. 2019 Aug 13.
Andersen SL, Olsen J, Laurberg P. **Antithyroid Drug Side Effects** in the Population and in Pregnancy. J Clin Endocrinol Metab. 2016 Jan 27
Anderson C, Engel SM, Mersereau JE, et al. Birth Outcomes Among Adolescent and **Young Adult Cancer Survivors**. JAMA Oncol. 2017 Mar 23.
Andrikopoulou M, Purisch SE, Handal-Orefice R, et al. **Low-dose aspirin** is associated with reduced spontaneous **preterm birth** in nulliparous women. Am J Obstet Gynecol. 2018 Oct;219(4):399.e1-399.e6.
Angulo-Barroso RM, Li M, Santos DC, et al. **Iron Supplementation** in Pregnancy or Infancy and Motor Development: A Randomized Controlled Trial. Pediatrics. 2016 Mar 2.
Angus-Leppan H, Liu RSN. **Weighing the risks of valproate in women who could become pregnant.** BMJ. 2018 Apr 18;361:k1596.
Ankcorn M, Evans C, Green ST. **Acute painless hepatitis** in pregnancy-a cause for concern? BMJ. 2014 Dec 30;349:g7686.
Apostolakis-Kyrus K, Valentine C, Defranco E. Factors Associated with **Breastfeeding Initiation in Adolescent Mothers**. J Pediatr. 2013 Jul 26.
Arany ZP, Walker CM, Wang L. Case records of the Massachusetts General Hospital. Case 22-2014. A 40-year-old woman with **postpartum dyspnea and hypoxemia**. N Engl J Med. 2014 Jul 17;371(3):261-9.
Arany Z, Elkayam U. **Peripartum Cardiomyopathy**. Circulation. 2016 Apr 5;133(14):1397-409.
Arnold MJ, Dhaliwal S. Complementary and Integrative **Treatments for Pain Management in Labor**. Am Fam Physician. 2019 Feb 1;99(3):154-156.
Asztalos EV, Hannah ME, Hutton EK, et al. Twin Birth Study: 2-year **neurodevelopmental** follow-up of the randomized trial of **planned cesarean or planned vaginal delivery** for twin pregnancy. Am J Obstet Gynecol. 2016 Mar;214(3):371.
Attenello FJ, Wen T, Cen SY, et al. Incidence of “never events” among **weekend admissions versus weekday admissions** to US hospitals: national analysis. BMJ 2015;350:h1460.
Auger N, Park AL, Zoungrana H, et al. Rates of **stillbirth by gestational age** and cause in Inuit and First Nations populations in Quebec. CMAJ. 2013 Apr 2;185(6):E256-62.
Auger N, Fraser WD, Healy-Profitós J, et al. Association Between **Preeclampsia and Congenital Heart Defects**. JAMA. 2015 Oct 20;314(15):1588-98.
Auger N et al. **Preeclampsia** and long-term risk of **maternal retinal disorders**. Obstet Gynecol 2016 Dec2.
August P, Malha L. **Post Partum Hypertension**: "It Ain't Over 'til It's Over". Circulation. 2015 Sep 28.
Aune D, Saugstad OD, Henriksen T, et al. **Maternal body mass index and the risk of fetal death, stillbirth, and infant death**: a systematic review and meta-analysis. JAMA. 2014 Apr 16;311(15):1536-46.
Aune D, Schlesinger S, Henriksen T, et al. **Physical activity and the risk of preterm birth**: a systematic review and meta-analysis of epidemiological studies. BJOG. 2017 Apr 4.
Awwad J, Usta I, Ghazeeri G, et al. A randomised controlled double-blind clinical trial of **17-hydroxyprogesterone caproate for the prevention of preterm birth** in twin gestation (PROGESTWIN): evidence for reduced neonatal morbidity. BJOG. 2014 Aug 27.
Baaqeel H, Baaqeel R. Timing of administration of **prophylactic antibiotics for caesarean section**: a systematic review and meta-analysis. BJOG. 2013 May;120(6):661-9.
Bacq Y, Sentilhes L, Reyes HB, et al. Efficacy of **ursodeoxycholic acid** in treating intrahepatic cholestasis of pregnancy: a meta-analysis. Gastroenterology 2012;143:1492–501.
Bailey RL, Pac SG, Fulgoni VL 3rd, et al. Estimation of **Total Usual Dietary Intakes** of Pregnant Women in the United States. JAMA Netw Open. 2019 Jun 5;2(6):e195967.
Bain E, Pierides KL, Clifton VL, et al. Interventions for **managing asthma in pregnancy**. Cochrane Database of Systematic Reviews 2014, Issue 10. Art. No.: CD010660. DOI: 10.1002/14651858.CD010660.pub2.
Based on eight included trials, of moderate quality overall, no firm conclusions about optimal interventions for managing asthma in pregnancy can be made. Five trials assessing pharmacological interventions did not provide clear evidence of benefits or harms to support or refute current practice. While inhaled magnesium sulphate for acute asthma was shown to reduce exacerbations, this was in one small trial of unclear quality, and thus this finding should be interpreted with caution. Three trials assessing non-pharmacological interventions provided some support for the use of such strategies, however were not powered to detect differences in importantmaternal and infant outcomes. While a FENO-based algorithm reduced exacerbations, the effects on perinatal outcomes were less certain, and thus widespread implementation is not yet appropriate. Similarly, though positive effects on asthma control were shown with PMR and pharmacist-led management, the evidence to date is insufficient to draw definitive conclusions. In view of the limited evidence base, further randomised trials are required to determine the most effective and safe interventions for asthma in pregnancy. Future trials must be sufficiently powered, and well-designed, to allow differences in important outcomes for mothers and babies to be detected. The impact on health services

requires evaluation. Any further trials assessing pharmacological interventions should assess novel agents or those used in current practice. Encouragingly, at least five trials have been identified as planned or underway.
Baker T, Datta P, Rewers-Felkins K, Thompson H, Kallem RR, Hale TW. Transfer of **inhaled cannabis into human breast milk**. Obstet Gynecol. 2018;131:783-788.
Bakian AV, VanDerslice JA. **Pesticides and autism**. BMJ. 2019 Mar 20;364:l1149.
Bakkebø T, Widnes SF, et al. **Physicians' Perception of Teratogenic Risk** and Confidence in Prescribing Drugs in Pregnancy-Influence of Norwegian **Drug Information Centers**. Clin Ther. 2016 Mar 10.
Balaraman S, Schafer JJ, Tseng AM, et al. Plasma **miRNA Profiles** in Pregnant Women PredictInfant Outcomes following **Prenatal Alcohol Exposure**. PLoS One. 2016 Nov 9;11(11):e0165081
Balci A, Sollie-Szarynska KM, van der Bijl AG, et al. Prospective validation and assessment of **cardiovascular and offspring risk** models for pregnant women with **congenital heart disease**. Heart. 2014 Jul 17.
Balinskaite V, et al. Risk of Adverse Pregnancy Outcomes Following **Nonobstetric Surgery** During Pregnancy: Estimates From a Retrospective Cohort Study of 6.5 Million Pregnancies. Ann Surg. 2016 Sep 14.
Ball SJ, Pereira G, Jacoby P, de Klerk N, Stanley FJ. Re-evaluation of the link between **interpregnancy interval and adverse birth outcomes**: retrospective cohort study matching two intervals per mother. BMJ 2014;349:g4333.
Balsells M, García-Patterson A, Solà I, Roqué M, Gich I, Corcoy R. **Glibenclamide (glyburide), metformin, and insulin for the treatment of gestational diabetes**: a systematic review and meta-analysis. BMJ 2015;350:h102.
Ban L, Tata LJ, Fiaschi L, et al. Limited Risks of Major Congenital Anomalies in Children of Mothers With IBD and Effects of Medications. Gastroenterology. 2014 Jan;146(1):76-84.
Bandoli G, Palmsten K, et al. A Review of Systemic **Corticosteroid Use in Pregnancy** and the Risk of Select Pregnancy and Birth Outcomes. Rheum Dis Clin North Am. 2017 Aug;43(3):489-502.
Bao W, Bowers K, Tobias DK, et al. **Prepregnancy low-carbohydrate dietary pattern and risk of gestational diabetes** mellitus: a prospective cohort study. Am J Clin Nutr. 2014 Apr 9;99(6):1378-1384.
Bao W, Tobias DK, Olsen SF, Zhang C. **Pre-pregnancy fried food** consumption and the risk of gestational diabetes mellitus: a prospective cohort study. Diabetologia. 2014 Oct 11.
Bao W, Tobias DK, Hu FB, et al. Pre-pregnancy **potato consumption** and risk of gestational diabetes mellitus: prospective cohort study. BMJ. 2016 Jan 12;352:h6898.
Barakat R, Pelaez M, Cordero Y, et al. **Exercise during pregnancy** protects against **hypertension and macrosomia**: randomized clinical trial. Am J Obstet Gynecol. 2016 May;214(5):649.e1-8.
Barash JH, Buchanan EM, Hillson C. Diagnosis and management of **ectopic pregnancy**. Am Fam Physician. 2014 Jul 1;90(1):34-40.
Barbui C, Ostuzzi G. Beneficial and harmful consequences of prepartum and postpartum antidepressant exposure. Evid Based Ment Health. 2014 Aug;17(3):69-71.
Bardos J, Hercz D, Friedenthal J, et al. A national survey on public perceptions of **miscarriage**. Obstet Gynecol. 2015 Jun;125(6):1313-20.
Bar-Gil Shitrit A, Ben Ya'acov A, Livovsky DM, et al**. Exposure to Vedolizumab in IBD Pregnant Women** Appears of Low Risk for Mother and Neonate: A First Prospective Comparison Study. Am J Gastroenterol. 2019 Mar 5.
Barker M, Dombrowski SU, Colbourn T. et al. Intervention strategies to improve **nutrition and health behaviours before conception**. Lancet. 2018 Apr 16.
Barlow J, Smailagic N, Huband N, Roloff V, Bennett C. **Group-based parent training** programmes for improving parental psychosocial health. Cochrane Database of Systematic Reviews 2014, Issue 5. Art. No.: CD002020. DOI: 10.1002/14651858.CD002020.pub4. The findings of this review support the use of parenting programmes to improve the short-term psychosocial wellbeing of parents. Further input may be required to ensure that these results are maintained. More research is needed that explicitly addresses the benefits for fathers, and that examines the comparative effectiveness of different types of programme along with the mechanisms by which such programmes bring about improvements in parental psychosocial functioning.
Barrett JFR et al. A randomized trial of **planned cesarean or vaginal delivery for twin pregnancy**. N Engl J Med 2013 Oct 3; 369:1295.
Bartick MC, Stuebe AM, Schwarz EB, et al. Cost Analysis of Maternal Disease Associated With Suboptimal **Breastfeeding**. Obstet Gynecol. 2013 Jun 5.
Barton SE, Najita JS, Ginsburg ES, et al. **Infertility, infertility treatment, and achievement of pregnancy** in female survivors of childhood cancer: a report from the Childhood Cancer Survivor Study cohort. Lancet Oncol 2013; online July 13.
Bartsch E, Medcalf KE, Park AL, Ray JG; High Risk of Pre-eclampsia Identification Group. **Clinical risk factors for pre-eclampsia** determined in early pregnancy: systematic review and meta-analysis of large cohort studies. BMJ. 2016 Apr 19;353:i1753.
Bartsch E, Medcalf KE, Park AL, Ray JG. High Risk of Pre-eclampsia Identification Group. Clinical **risk factors for pre-eclampsia** determined in early pregnancy: systematic review and meta-analysis of large cohort studies. BMJ2016;353:i1753.
Bateman BT, Huybrechts KF, Fischer MA, et al. **Chronic Hypertension in Pregnancy and the Risk of Congenital Malformations**: A Cohort Study. Am J Obstet Gynecol. 2014 Sep 26.
Bateman BT, Hernandez-Diaz S, Fischer MA, Seely EW, Ecker JL, Franklin JM, et al. **Statins** and congenital malformations: cohort study. BMJ 2015;350:h1035.
Bateman BT, Patorno E, Desai RJ, et al. Late **Pregnancy Beta-β Blocker Exposure** and Risks of Neonatal Hypoglycemia and Bradycardia. Pediatrics. 2016 Sep;138(3).
Basatemur E, Gardiner J, Williams C, et al. **Maternal Prepregnancy BMI and Child Cognition**: A Longitudinal Cohort Study. Pediatrics. 2013 Jan;131(1):56-63.
Bateman BT, Hernandez-Diaz S, Huybrechts KF, et al. Patterns of Outpatient Antihypertensive Medication Use During Pregnancy in a Medicaid Population. Hypertension. 2012 Sep 10.
Bateman BT, Hernandez-Diaz S, Rathmell JP, et al. Patterns of Opioid Utilization in Pregnancy in a Large Cohort of Commercial Insurance Beneficiaries in the United States. Anesthesiology. 2014 Feb 12.
Bateman BT, Patorno E, Desai RJ, et al. **Angiotensin-Converting Enzyme Inhibitors** and the Risk of Congenital Malformations. Obstet Gynecol. 2017 Jan;129(1):174-184.
Bateman BT, Ho E, et al. The risk of congenital malformations associated with **exposure to β-blockers** early in pregnancy: a meta-analysis. *Hypertension*. 2013;62:375-381.
Bateman BT, Cole NM, Maeda A, et al. **Patterns of Opioid Prescription and Use After Cesarean Delivery**. Obstet Gynecol. 2017 Jun 6.
Bateman BT, Heide-Jørgensen U, Einarsdottir K, et al.**Beta-blocker use in pregnancy** and the risk for **congenital malformations**. An international cohort study. Ann Intern Med. 2018. [Epub ahead of print].
Bates JE, Almast J, Augustine EF. Neonatal dentate nucleus **T2 hyperintensity after in utero metronidazole** exposure. Neurology. 2015 Sep 15;85(11):1006.
Bath SC, Steer CD, Golding J, Emmett PM, Rayman MP. Eff ect of inadequate **iodine status in UK pregnant women** on cognitive outcomes in their children: results from the Avon Longitudinal Study of Parents and Children (ALSPAC). Lancet 2013; online May 22.
Baud O et al. Association between early low-dose **hydrocortisone therapy in extremely preterm neonates and neurodevelopmental outcomes** at 2 years of age. JAMA 2017 Apr 4; 317:1329.
Bauer ME, et al. **Maternal sepsis** mortality and morbidity during hospitalization for delivery: temporal trends and independent associations for severe sepsis. Anesth Analg. 2013 Oct;117(4):944-50.
Beau AB, Montastruc JL, Lacroix I, et al. **Atropinic burden** of drugs during pregnancy and psychological development of children: a cohort study in the EFEMERIS database. Br J Clin Pharmacol. 2016 Apr 16.
Been JV, Lugtenberg MJ, Smets E, et al. **Preterm birth and childhood wheezing** disorders: a systematic review and meta-analysis. PLoS Med. 2014 Jan 28;11(1):e1001596.
Behnia F, Peltier M, et al. High **bisphenol** A(BPA) concentration in the maternal, but not fetal, compartment increases the risk of spontaneous preterm delivery. J Matern Fetal Neonatal Med. 2016 Feb 24:1-7.

Behnke M, Smith VC; Committee on Substance Abuse, Committee on Fetus and Newborn. **Prenatal Substance Abuse**: Short- and Long-term Effects on the Exposed Fetus. Pediatrics. 2013 Feb 25.
Belfort MB, Rifas-Shiman SL, Kleinman KP, et al. **Infant Feeding and Childhood Cognition** at Ages 3 and 7 Years: Effects of **Breastfeeding** Duration and Exclusivity. JAMA Pediatr. 2013 Jul 29.
Belfort MA, Saade GR, Thom E, et al; Eunice Kennedy Shriver National Institute of Child Health and Human Development Maternal–Fetal Medicine Units Network. A Randomized Trial of **Intrapartum Fetal ECG** ST-Segment Analysis. N Engl J Med. 2015 Aug 13;373(7):632-41.
Belfort MB, Anderson PJ, et al. **Breast Milk Feeding**, Brain Development, and Neurocognitive Outcomes: A 7-Year Longitudinal Study in Infants Born at Less Than 30 Weeks' Gestation. J Pediatr. 2016 Jul 26.
Bénard-Laribière A, Pambrun E, Sutter-Dallay AL, et al. Patterns of **antidepressant use during pregnancy**: a nationwide population-based cohort study. Br J Clin Pharmacol. 2018 Apr 17.
Bérard A, Sheehy O, Zhao J-P, et al. Associations between **low- and high-dose oral fluconazole and pregnancy outcomes**: 3 nested case-control studies. CMAJ 2019;191:E179-87.
Berard A, Zhao JP, Sheehy O. **Sertraline** use during pregnancy and the risk of major malformations. Am J Obstet Gynecol. 2015 Jun;212(6):795.e1-795.e12.
Bérard A, Sheehy O, Zhao JP, et al. Use of **macrolides during pregnancy** and the risk of birth defects: a population-based study. Pharmacoepidemiol Drug Saf. 2015 Oct 29.
Bérard A, Iessa N, Chaabane S. et al. The risk of major cardiac malformations associated with **paroxetine** use during the **first trimester** of **pregnancy**: A systematic review and meta-analysis. Br J Clin Pharmacol. 2015 Nov 27.
Bérard A, Zhao JP, Sheehy O. Success of **smoking cessation** interventions during pregnancy. Am J Obstet Gynecol. 2016 Jul 8.
Bérard A, Sheehy O, Zhao JP, et al. **SSRI and SNRI use during pregnancy** and the risk of persistent pulmonary hypertension of the newborn. Br J Clin Pharmacol. 2016 Nov 22.
Bérard A, Zhao JP, Sheehy O. **Antidepressant use during pregnancy** and the risk of major congenital malformations in a cohort of depressed pregnant women: an updated analysis of the Quebec Pregnancy Cohort. BMJ Open. 2017 Jan 12;7(1):e013372.
Bédard A, Northstone K, Henderson AJ, et al. **Maternal intake of sugar** during pregnancy and childhood respiratory and atopic outcomes. Eur Respir J. 2017 Jul 5;50(1)
Bérard A, Zhao JP, Shui I, et al. **Leflunomide** use during pregnancy and the risk of adverse pregnancy outcomes. Ann Rheum Dis. 2018 Apr;77(4):500-509.
Bergink V et al. **Prevention of postpartum psychosis and mania** in women at high risk. Am J Psychiatry 2012 Mar 8.
Bergman H, Melamed N, Koren G. **Pruritus in pregnancy**: Treatment of dermatoses unique to pregnancy. Can Fam Physician. 2013 Dec;59(12):1290-4
Bernard JY, De Agostini M, et al; EDEN Mother-Child Cohort Study Group. **Breastfeeding Duration and Cognitive** Development at 2 and 3 Years of Age in the EDEN Mother-Child Cohort. J Pediatr. 2013 Jan 10.
Bernstein PS et al. National Partnership for Maternal Safety: Consensus bundle on severe **hypertension during pregnancy** and the postpartum period. Obstet Gynecol 2017 Aug; 130:347.
Bettiol A, Lombardi N, Marconi E, et al. The use of **complementary and alternative medicines during breastfeeding**: results from the Herbal supplements in Breastfeeding InvesTigation (HaBIT) study. Br J Clin Pharmacol. 2018 May 16.
Bhutta ZA, Das JK, Rizvi A, et al; The Lancet Nutrition Interventions Review Group, and the Maternal and Child Nutrition Study Group. Evidence-based interventions for improvement of maternal and child **nutrition**: what can be done and at what cost? Lancet. 2013 Jun 5.
Bhutta ZA, Black RE. **Global maternal, newborn, and child health**--so near and yet so far. N Engl J Med. 2013 Dec 5;369(23):2226-35
Bianchi DW, Chudova D, Sehnert AJ, et al. **Noninvasive Prenatal Testing** and Incidental Detection of Occult Maternal Malignancies. JAMA. 2015 Jul 14;314(2):162-169.
Bibian C, Quilez RM, Gil J et al. Clinical Relevance Of The (S)-**Citalopram-Omeprazole** Interaction In Geriatric Patients. Br J Clin Pharmacol. 2013 Aug 7.
Biggs MA, Upadhyay UD, et al. Women's Mental Health and Well-being 5 Years After Receiving or Being **Denied an Abortion**: A Prospective, Longitudinal Cohort Study. JAMA Psychiatry. 2016 Dec 14.
Bilder DA, Bakian AV, Viskochil J, et al. **Maternal prenatal weight gain** and **autism** spectrum disorders. Pediatrics. 2013 Nov;132(5):e1276-83.
Billionnet C, Mitanchez D, Weill A, et al. **Gestational diabetes** and adverse perinatal outcomes from 716,152 births in France in 2012. Diabetologia. 2017 Feb 15.
Birthplace in England Collaborative Group. Perinatal and maternal outcomes by planned place of birth for healthy women with low risk pregnancies: the Birthplace in England national prospective cohort study. BMJ. 2011 Nov 23;343:d7400. doi: 10.1136/bmj.d7400.
Bisgaard H, Stokholm J, Chawes BL, et al. **Fish oil–derived fatty acids** in pregnancy and wheeze and asthma in offspring. N Engl J Med 2016;375:2530-9.
Bjørk M, Riedel B, et al. Association of **Folic Acid Supplementation During Pregnancy With the Risk of Autistic Traits** in Children **Exposed to Antiepileptic Drugs** In Utero. JAMA Neurol. 2017 Dec 26
Black M, Bhattacharya S, Philip S, et al. **Planned Cesarean Delivery** at Term and Adverse Outcomes in Childhood Health. JAMA. 2015 Dec 1;314(21):2271-2279.
Bliddal M, Pottegård A, et al. **Degenerative musculoskeletal conditions** in women according to pre-pregnancy BMI, pregnancy-related weight changes and parity. Arthritis Rheumatol. 2015 Dec 29.
Bø K, Artal R, Barakat R,et al. **Exercise and pregnancy in recreational and elite athletes**: 2016 evidence summary from the IOC expert group meeting, Lausanne. Part 2-the effect of exercise on the fetus, labour and birth. Br J Sports Med. 2016 Oct 12.
Bodén R, Lundgren M, Brandt L, et al. **Antipsychotics During Pregnancy**: Relation to Fetal and Maternal Metabolic Effects Antipsychotics During Pregnancy. Arch Gen Psychiatry. 2012 Jul 1;69(7):715-21.
Bodén R, Lundgren M, Brandt L, Reutfors J, Andersen M, Kieler H. Risks of adverse pregnancy and birth outcomes in women treated or not treated with **mood stabilisers** for bipolar disorder: population based cohort study. BMJ 2012;345:e7085.
Bodurtha J, Strauss JF 3rd. Genomics and perinatal care. N Engl J Med. 2012 Jan 5;366(1):64-73. Review.
Boelig RC, Barton SJ, Saccone G, et al. **Interventions for treating hyperemesis gravidarum**. Cochrane Database of Systematic Reviews 2016, Issue 5. Art. No.: CD010607. DOI: 10.1002/14651858.CD010607.pub2. On the basis of this review, there is little high-quality and consistent evidence supporting any one intervention, which should be taken into account when making management decisions. There was also very limited reporting on the economic impact of hyperemesis gravidarum and the impact that interventions may have.
Bohren MA, Hofmeyr GJ, Sakala C, et al. **Continuous support for women during childbirth**. Cochrane Database of Systematic Reviews 2017, Issue 7. Art. No.: CD003766. Continuous support during labour may improve outcomes for women and infants, including increased spontaneous vaginal birth, shorter duration of labour, and decreased caesarean birth, instrumental vaginal birth, use of any analgesia, use of regional analgesia, low five-minute Apgar score and negative feelings about childbirth experiences.
Boivin A, Luo ZC, Audibert F, et al. Pregnancy complications among women **born preterm**. CMAJ. 2012 Sep 24.
Bond DM, Gordon A, Hyett J, de Vries B, Carberry AE, Morris J. Planned **early delivery versus expectant management** of the term suspected compromised baby for improving outcomes. Cochrane Database of Systematic Reviews 2015, Issue 11. Art. No.: CD009433. DOI: 10.1002/14651858.CD009433.pub2. A policy for planned early delivery versus expectant management for a suspected compromised fetus at term does not demonstrate any differences in major outcomes of perinatal mortality, significant neonatal or maternal morbidity or neurodevelopmental disability. In women randomised to planned

early delivery, the gestational age at birth was on average 10 days earlier, women were less likely to have a baby beyond 40 weeks' gestation, they were more likely to be induced and infants were more likely to be admitted to intermediate care nursery. There was also a significant difference in the proportion of babies with a birthweight centile < 2.3rd, however this did not translate into a reduction in morbidity. The review is informed by only one large trial and two smaller trials assessing fetuses with IUGR or oligohydramnios and therefore cannot be generalised to all term pregnancies with suspected fetal compromise. There are other indications for suspecting compromise in a fetus at or near term such as maternal perception of DFM, and ultrasound and/or CTG abnormalities. Future randomised trials need to assess effectiveness of timing of delivery for these indications.

Bond DM, Middleton P, Levett KM, et al. **Planned early birth versus expectant management for women with preterm prelabour** rupture of membranes prior to 37 weeks` gestation for improving pregnancy outcome. Cochrane Database Syst Rev. 2017 Mar 3;3:CD004735. With the addition of five randomised controlled trials (2927 women) to this updated review, we found no clinically important difference in the incidence of neonatal sepsis between women who birth immediately and those managed expectantly in PPROM prior to 37 weeks' gestation. Early planned birth was associated with an increase in the incidence of neonatal RDS, need for ventilation, neonatal mortality, endometritis, admission to neonatal intensive care, and the likelihood of birth by caesarean section, but a decreased incidence of chorioamnionitis.

Bonham CA, Patterson KC, Strek ME. **Asthma Outcomes** and Management During Pregnancy. Chest. 2017 Aug 31.

Bornehag CG, Reichenberg A, Hallerback MU, et al. **Prenatal exposure to acetaminophen and children's language development** at 30 months. Eur Psychiatry. 2017 Nov 10.

Botto LD, Krikov S, Carmichael SL, et al; National Birth Defects Prevention Study. **Lower rate of selected congenital heart defects with better maternal diet quality**: a population-based study. Arch Dis Child Fetal Neonatal Ed. 2015 Aug 24.

Boukhris T, Sheehy O, Mottron L, et al. **Antidepressant Use** During Pregnancy and the Risk of **Autism Spectrum Disorder** in Children. JAMA Pediatr. 2015 Dec 14:1-8.

Boulvain M, Senat M-V, Perrotin F, et al, for the Groupe de Recherche en Obstetrique et Gynecologie (GROG). **Induction of labour versus expectant management for large-for-date fetuses**: a randomised controlled trial. Lancet 2015; online April 9.

Boyle EM et al. Effects of gestational age at birth on health outcomes at 3 and 5 years of age: population based cohort study. BMJ. 2012 Mar 1;344:e896.

Bozzo P, Koren G, Ito S. Health Canada advisory on **domperidone**: Should I avoid prescribing domperidone to women to increase milk production? Can Fam Physician. 2012 Sep;58(9):952-3.

Bramante CT, Spiller P, Landa M. **Fish Consumption During Pregnancy**: An Opportunity, Not a Risk. JAMA Pediatr. 2018 Jul 23.

Bramham K, Nelson-Piercy C, Brown MJ, Chappell LC. **Postpartum management of hypertension**. BMJ. 2013 Feb 25;346:f894.

Bramham K, Parnell B, Nelson-Piercy C, et al. **Chronic hypertension** and pregnancy outcomes: systematic review and meta-analysis. BMJ 2014;348:g2301.

Brandlistuen RE et al. Behavioural effects of **fetal antidepressant exposure** in a Norwegian cohort of discordant siblings. Int J Epidemiol 2015 Apr 14.

Brännström M, Johannesson L, Bokström H, et al. **Livebirth after uterus transplantation**. Lancet. 2014 Oct 6.

Bredin SS, Foulds HJ, Burr JF, Charlesworth SA. Risk assessment for **physical activity and exercise clearance: In pregnant** women without contraindications. Can Fam Physician. 2013 May;59(5):515-7.

Brickner ME. Cardiovascular management in **pregnancy: congenital heart disease**. Circulation. 2014 Jul 15;130(3):273-82.

Briller J, Koch AR, Geller SE. **Maternal Cardiovascular Mortality** in Illinois, 2002-2011. Obstet Gynecol. 2017 Apr 4.

Brinkman SA, Johnson SE, et al. Efficacy of **infant simulator programmes to prevent teenage pregnancy**: a school-based cluster randomised controlled trial in Western Australia. Lancet 2016; online Aug 25

Broekhuijsen K, van Baaren G, van Pampus M, et al. **Immediate delivery versus expectant monitoring for hypertensive** disorders of pregnancy between 34 and 37 weeks of gestation (**HYPITAT-II**): a multicentre, open label randomised controlled trial. Lancet 2015; online March 25.

Brogly SB, Saia KA, Walley AY, et al. **Prenatal Buprenorphine Versus Methadone** Exposure and Neonatal Outcomes: Systematic Review and Meta-Analysis. Am J Epidemiol. 2014 Aug 22.

Bromley R,Weston J, Adab N, et al. . Treatment for **epilepsy in pregnancy**: neurodevelopmental outcomes in the child. Cochrane Database of Systematic Reviews 2014, Issue 10. Art. No.: CD010236. DOI: 10.1002/14651858.CD010236.pub2. The most important finding is the **reduction in IQ in the VPA exposed group**, which are sufficient to affect education and occupational outcomes in later life. However, for some women VPA is the most effective drug at controlling seizures. Informed treatment decisions require detailed counselling about these risks at treatment initiation and at pre-conceptual counselling. We have insufficient data about newer AEDs, some of which are commonly prescribed, and further research is required. Most women with epilepsy should continue their medication during pregnancy as uncontrolled seizures also carries a maternal risk.

Bromley RL, Weston J, Marson AG. **Maternal Use of Antiepileptic Agents** During Pregnancy and Major Congenital Malformations in Children. JAMA. 2017 Nov 7;318(17):1700-1701.

Broskey NT, Wang P, et al. **Early Pregnancy Weight Gain** Exerts the Strongest Effect on Birth Weight, Posing a Critical Time to Prevent Childhood Obesity. Obesity (Silver Spring). 2017 Sep;25(9):1569-1576.

Brouwer J, Laven JS, Hazes JM, et al. **Miscarriages in female rheumatoid arthritis patients** - associations with serology, disease activity and anti-rheumatic treatment. Arthritis Rheumatol. 2015 Apr 30.

Brown AS, et al. Association of **selective serotonin reuptake inhibitor** exposure during pregnancy with **speech, scholastic, and motor disorders** in offspring [online Oct 12, 2016]. JAMA Psychiatry. doi:10.1001/jamapsychiatry.2016.2594

Brown HK, Ray JG, Liu N, et al. **Rapid repeat pregnancy** among women with intellectual and developmental disabilities: a population-based cohort study. CMAJ. 2018 Aug 13;190(32):E949-E956.

Brown J;Grzeskowiak L;Williamson K;et al. **Insulin for the treatment of women with gestational diabetes**. Cochrane Database Syst Rev. 2017 Nov 5;11:CD012037. The main comparison in this review is insulin versus oral anti-diabetic pharmacological therapies. Insulin and oral anti-diabetic pharmacological therapies have similar effects on key health outcomes. The quality of the evidence ranged from very low to moderate, with downgrading decisions due to imprecision, risk of bias and inconsistency. For the other comparisons of this review (insulin compared with non-pharmacological interventions, different insulin analogies or different insulin regimens), there is insufficient volume of high-quality evidence to determine differences for key health outcomes. Long-term maternal and neonatal outcomes were poorly reported for all comparisons. The evidence suggests that there are minimal harms associated with the effects of treatment with either insulin or oral anti-diabetic pharmacological therapies. The choice to use one or the other may be down to physician or maternal preference, availability or severity of GDM. Further research is needed to explore optimal insulin regimens. Further research could aim to report data for standardised GDM outcomes.

Bruinsma FJ, Quinn MA. The risk of preterm birth following treatment for precancerous changes in the cervix: a systematic review and meta-analysis. BJOG. 2011 Aug;118(9):1031-41.

Buck Louis GM, Sapra KJ, Schisterman EF, et al. **Lifestyle and pregnancy loss** in a contemporary cohort of women recruited before conception: The LIFE Study. Fertil Steril. 2016 Mar 22.

Bukowski R et al. Delivery of a small for gestational age infant and greater maternal risk of ischemic heart disease. PLoS ONE2012 Mar; 7:e33047.

Bunyavanich S, Rifas-Shiman SL, Platts-Mills TA, et al. Prenatal, perinatal, and childhood **vitamin D** exposure and their association with childhood allergic rhinitis and allergic sensitization. J Allergy Clin Immunol. 2016 Feb 10. pii: S0091-6749(16)00035-X.

Butler DC, Heller MM, Murase JE. Safety of **dermatologic medications** in pregnancy and lactation: Part II. Lactation. J Am Acad Dermatol. 2014 Mar;70(3):417.e1-10; quiz 427.

Buyon JP, Kim MY, Guerra MM, Laskin CA, Petri M, Lockshin MD, et al. Predictors of pregnancy outcomes in patients with **lupus**. A cohort study. Ann Intern Med. 2015;163:•••-•••. doi:10.7326/M14-2235

Cagnetti C, Lattanzi S, Foschi N, et al. **Seizure course** during pregnancy in catamenial epilepsy. Neurology. 2014 Jul 22;83(4):339-44.

Callaghan WM et al. Severe **maternal morbidity** among delivery and postpartum hospitalizations in the United States. Obstet Gynecol 2012 Nov; 120:1029.

Camacho E et al. Multiple adverse pregnancy outcomes before symptom onset are associated with a worse disease outcome in women with recent-onset inflammatory polyarthritis. Ann Rheum Dis. 2012 Apr;71(4):528-33.

Camelo CastilloW, Boggess K, Stürmer T, et al. Association of adverse pregnancy outcomes with **glyburide vs insulin** in women with gestational diabetes [online March 30, 2015]. JAMA Pediatr. doi:10.1001/jamapediatrics.2015.74.

Canadian HIV Pregnancy Planning Guideline Development Team Core Working Group. **Canadian HIV pregnancy planning guidelines**. J Obstet Gynaecol Can 2012;34:575–90. www.sogc.org/guidelines/documents/gui278CPG1206E.pdf

Cardonick E. Treatment of maternal cancer and fetal development. Lancet Oncol.2012 Mar;13(3):218-20. Epub 2012 Feb 10.

Carlsen SM, Martinussen MP, Vanky E. Metformin's Effect on **First-Year Weight Gain (on offspring)**: A Follow-up Study. Pediatrics. 2012 Oct 15.

Croles FN, Nasserinejad K, Duvekot JJ, et al. Pregnancy, **thrombophilia, and the risk of a first venous thrombosis**: systematic review and bayesian meta-analysis. BMJ. 2017 Oct 26;359:j4452.

Carruthers J, Holmes A, Majeed A. A suspected **viral rash in pregnancy**. BMJ.2017 Mar 3;356:j512.

Carson MP, Chen KK. **Hypertension** in a woman planning pregnancy. CMAJ. 2014 Feb 4;186(2):129-30

Carwile JL, Mahalingaiah S, Winter MR, et al. **Prenatal drinking-water exposure to tetrachloroethylene** and ischemic placental disease: a retrospective cohort study. Environ Health. 2014 Sep 30;13:72.

Casey BM, Duryea EL, Abbassi-Ghanavati M, et al. **Glyburide** in Women With Mild **Gestational Diabetes**: A Randomized Controlled Trial. Obstet Gynecol. 2015 Aug;126(2):303-9.

Castanon A, Landy R, Brocklehurst P, et al; PaCT Study Group. Risk of **preterm delivery** with increasing **depth of excision for cervical intraepithelial neoplasia** in England: nested case-control study. BMJ. 2014 Nov 5;349:g6223.

Catalano PM, McIntyre HD, Cruickshank JK, et al. **HAPO** Study Cooperative Research Group. The **hyperglycemia and adverse pregnancy outcome study**: associations of GDM and obesity with pregnancy outcomes. Diabetes Care. 2012 Apr;35(4):780-6.

Catalano PM, Shankar K. **Obesity and pregnancy**: mechanisms of short term and long term adverse consequences for mother and child. BMJ. 2017 Feb 8;356:j1

Cauldwell M, Dos Santos F, Steer PJ, et al. **Pregnancy in women with congenital heart disease**. BMJ. 2018 Mar 9;360:k478.

Cavadino A, Prieto-Merino D, Morris JK. Identifying signals of **potentially harmful medications in pregnancy**: use of the double false discovery rate method to adjust for multiple testing. Br J Clin Pharmacol. 2018 Oct 23.

Celermajer DS. Manipulating nature: might there be a cardiovascular price to pay for the miracle of **assisted conception**? Circulation. 2012 Apr 17;125(15):1832-4.

Chaillet N, Dumont A, Abrahamowicz M, et al; QUARISMA Trial Research Group. A Cluster-Randomized Trial to **Reduce Cesarean Delivery** Rates in Quebec. N Engl J Med. 2015 Apr 30;372(18):1710-1721

Chan F, Koren G. **Is periconceptional opioid use safe**? Can Fam Physician. 2015 May;61(5):431-3.

Chan J, Natekar A, Koren G. **Hot yoga** and pregnancy: Fitness and hyperthermia. Can Fam Physician. 2014 Jan;60(1):41-2

Chan J, Natekar A, Einarson A, et al. Risks of **untreated depression** in pregnancy. Can Fam Physician. 2014 Mar;60(3):242-3.

Chan WS, Spencer FA, Lee AY, et al. Safety of withholding anticoagulation in pregnant women with suspected **deep vein thrombosis following negative serial compression ultrasound** and iliac vein imaging. CMAJ. 2013 Mar 5;185(4):E194-200.

Chandranipapongse W, Koren G. **Preconception counseling for preventable risks**. Can Fam Physician. 2013 Jul;59(7):737-9.

Chang E. **Preterm birth and the role of neuroprotection**. BMJ. 2015 Jan 20;350:g6661.

Chang S, Zeng L, Brouwer ID, et al. Effect of **Iron Deficiency Anemia in Pregnancy** on Child **Mental Development** in Rural China. Pediatrics. 2013 Feb 11.

Chang S, Zeng L, Brouwer ID, Kok FJ, Yan H. Effect of **iron deficiency anemia in pregnancy** on child mental development in rural China. Pediatr 2013;131:e755-63.

Chang T, Choi H, Richardson CR, et al. Implications of **teen birth** for overweight and obesity in adulthood. Am J Obstet Gynecol. 2013 Apr 12.

Chang Z, Spong C, Jesus AA, et al. **Anakinra** use **during pregnancy** in patients with cryopyrin-associated periodic syndromes (CAPS). Arthritis Rheumatol. 2014 Sep 15.

Chappell LC, Bell JL, Smith A, et al. **Ursodeoxycholic acid versus placebo** in women with intrahepatic cholestasis of pregnancy (PITCHES): a randomised controlled trial. Lancet. 2019 Aug 1.

Chappell LC, Duckworth S, Seed PT, et al. Diagnostic accuracy of placental growth factor in women with suspected preeclampsia: A prospective multicenter study. Circulation 2013.

Chappell LC, Seed PT, Myers J, et al. Exploration and confirmation of **factors associated with uncomplicated pregnancy** in nulliparous women: prospective cohort study. BMJ 2013;347:f6398.
This study implies that individually targeted lifestyle interventions (normalising maternal weight, increasing prepregnancy fruit intake, reducing blood pressure, stopping misuse of drugs) may increase the likelihood of normal pregnancy outcomes.

Charles R, Swales C, Bonnett T, et al. **Hypertensive disorder** of pregnancy. BMJ. 2017 Feb 2;356:j285

Charlton BM, Mølgaard-Nielsen D, Svanström H, et al. Maternal use of **oral contraceptives and risk of birth defects** in Denmark: prospective, nationwide cohort study. BMJ. 2016 Jan 6;352:h6712.

Chatur S, Islam S, Moore LE, et al. **Incidence of Syncope** During Pregnancy: Temporal Trends and Outcomes. J Am Heart Assoc. 2019 May 21;8(10):e011608.

Chaudhry SA, Gad N, Koren G. **Toxoplasmosis and pregnancy**. Can Fam Physician. 2014 Apr;60(4):334-6.

Chaudhry SA, Koren G. **Hepatitis A** infection during pregnancy. Can Fam Physician. 2015 Nov;61(11):963-4.

Chee J, Lau TP. Severe **postpartum headache**. BMJ. 2017 Apr 27;357:j1856.

Chemtob CM, Gudiño OG, Laraque D. **Maternal Posttraumatic Stress Disorder** and Depression in Pediatric Primary Care: Association With Child Maltreatment and Frequency of Child Exposure to Traumatic

Events. JAMA Pediatr. 2013 Sep 2.
Chen LW, Fitzgerald R, Murrin CM, et al;Lifeways Cross Generation Cohort Study. Associations of **maternal caffeine intake with birth outcomes**: results from the Lifeways Cross Generation Cohort Study. Am J Clin Nutr. 2018 Oct 19.
Cheong-See F, Schuit E, Arroyo-Manzano D, et al. Prospective risk of **stillbirth and neonatal complications in twin pregnancies**: systematic review and meta-analysis. BMJ. 2016 Sep 6;354:i4353.
Chisolm MS, Payne JL. Management of **psychotropic drugs during pregnancy**. BMJ. 2016 Jan 20;532:h5918.
Choi JS, Koren G, Nulman I. Pregnancy and **isotretinoin therapy**. CMAJ. 2013 Mar 19;185(5):411-3.
Chou HH, Chiou MJ, Liang FW, et al. Association of **maternal chronic disease with risk of congenital heart disease in offspring**. CMAJ. 2016 Dec 6;188(17-18):E438-E446.
Chow CK, Koren G. **Sedating drugs and breastfeeding**. Can Fam Physician. 2015 Mar;61(3):241-3.
Chow EJ, et al. **Pregnancy after chemotherapy** in male and female survivors of childhood cancer treated between 1970 and 1999: a report from the Childhood Cancer Survivor Study cohort. Lancet Oncol. 2016 Mar 22.
Christensen J, Pedersen LH, Sun Y, et al. Association of prenatal **exposure to valproate and other antiepileptic drugs** with risk for attention-deficit/hyperactivity disorder in offspring. JAMA Network Open 2019;2(1):e186606.
Christensen J, Vestergaard C, Hammer Bech B. **Maternal death in women with epilepsy**: Smaller scope studies. Neurology. 2018 Oct 30;91(18):e1716-e1720.
Christensen J, Pedersen LH, Sun Y, et al. **Association of prenatal exposure to valproate and other antiepileptic drugs with risk for attention-deficit/hyperactivity disorder in offspring**. JAMA Network Open 2019;2(1):e186606.
Ciardulli A, Saccone G, Anastasio H, et al. **Less-Restrictive Food Intake During Labor** in Low-Risk Singleton Pregnancies: A Systematic Review and Meta-analysis. Obstet Gynecol. 2017 Mar;129(3):473-480.
Cirillo PM, et al. **Pregnancy Complications and Cardiovascular Disease Death**: 50-Year Follow-Up of the Child Health and Development Studies Pregnancy Cohort. Circulation. 2015 Sep 29;132(13):1234-42.
Clark CT, Klein AM, Perel JM et al. **Lamotrigine dosing for pregnant patients** with bipolar disorder. Am J Psychiatry. 2013 Nov 1;170(11):1240-7.
Clark KM, Li M, et al. Breastfeeding, **Mixed, or Formula Feeding** at 9 Months of Age and the Prevalence of **Iron Deficiency** and Iron Deficiency Anemia in Two Cohorts of Infants in China. J Pediatr. 2016 Nov 8.
Cleary KL, Siddiq Z, Ananth CV, et al. Use of **Antihypertensive Medications During Delivery Hospitalizations Complicated by Preeclampsia**. Obstet Gynecol. 2018 Feb 5.
Clowse ME, Förger F, et al. Minimal to no transfer of **certolizumab pegol into breast milk:** results from **CRADLE**, a prospective, postmarketing, multicentre, pharmacokinetic study. Ann Rheum Dis. 2017 Nov;76(11):1890-1896.
Cnattingius S, Villamor E. **Weight change** between **successive pregnancies** and risks of **stillbirth and infant mortality**: a nationwide cohort study. Lancet 2015; online Dec 2.
Cohen-Israel M, Berger I, Martonovich EY, et al. Short and Long Term Complications of **In Utero Exposure to Lamotrigine**. Br J Clin Pharmacol. 2017 Oct 18.
Cohen E, Horváth-Puhó E, Ray JG, et al. **Cardiovascular Disease Among Women Who Gave Birth to an Infant With a Major Congenital Anomaly**. JAMA Netw Open. 2018;1(5):e182320.
Cohen E, Horváth-Puhó E, et al. Association Between the **Birth of an Infant With Major Congenital Anomalies** and Subsequent **Risk of Mortality in Their Mothers**. JAMA. 2016 Dec 20;316(23):2515-2524.
Cohen LS, Viguera AC, McInerney KA, et al. **Reproductive Safety of Second-Generation Antipsychotics**: Current Data From the Massachusetts General Hospital National Pregnancy Registry for Atypical Antipsychotics. Am J Psychiatry. 2015 Oct 6:appiajp201515040506.
Cohen LS, Góez-Mogollón L, Sosinsky AZ, et al. **Risk of Major Malformations in Infants Following First-Trimester Exposure to Quetiapine**. Am J Psychiatry. 2018 Aug 16:appiajp201818010098.
Collins CT et al. **Docosahexaenoic acid and bronchopulmonary dysplasia** in preterm infants. N Engl J Med 2017 Mar 30; 376:1245.
Collins S, RamsayM, Slack MPE, et al. Risk of invasive **Haemophilus influenzae infection during pregnancy** and association with adverse fetal outcomes. JAMA. doi:10.1001/jama.2014.1878.
Committee on Fetus and Newborn. **Planned Home Birth**. Pediatrics. 2013 Apr 29.
Committee on Infectious Diseases; Committee on Nutrition. Consumption of **Raw or Unpasteurized Milk** and Milk Products by Pregnant Women and Children. Pediatrics. 2013 Dec 16
Committee Opinion No. 637: **Marijuana** Use During Pregnancy and Lactation. Obstet Gynecol. 2015 Jul;126(1):234-8.
Connelly KJ, Boston BA, Pearce EN, et al. Congenital hypothyroidism caused by excess **prenatal maternal iodine ingestion**. J Pediatr. 2012 Oct;161(4):760-2.
Coomarasamy A et al. A randomized trial of **progesterone** in women with recurrent **miscarriages**. (Promise) N Engl J Med 2015 Nov 26; 373:2141.
Coomarasamy A, Williams H, Truchanowicz E, et al. A Randomized Trial of **Progesterone** in Women with **Recurrent Miscarriages**. (**Promise**) N Engl J Med. 2015 Nov 26;373(22):2141-8.
Coomarasamy A, Williams H, Truchanowicz E, et al. **PROMISE**: **first-trimester progesterone therapy** in women with a history of unexplained **recurrent miscarriages** - a randomised, double-blind, placebo-controlled, international multicentre trial and economic evaluation. Health Technol Assess. 2016 May;20(41):1-92.
Cook J, Jarvis S, Knight M, Dhanjal M. **Multiple repeat caesarean section** in the UK: incidence and consequences to mother and child. A national, prospective, cohort study. BJOG. 2012 Oct 24.
Cook JL, Green CR, Lilley CM, et al. **Fetal alcohol spectrum disorder**: a guideline for diagnosis across the lifespan. CMAJ 2015 Dec. 14 [Epub ahead of print].
Cooper S, Taggar J, Lewis S, Marlow N, Dickinson A, Whitemore R, Coleman T; for the **Smoking, Nicotine and Pregnancy (SNAP)** Trial Team. Effect of nicotine patches in pregnancy on infant and maternal outcomes at 2 years: follow-up from the randomised, double-blind, placebo-controlled SNAP trial. Lancet Respir Med. 2014 Aug 8.
Cooper WO, Cheetham TC, Li DK, et al. Brief report: risk of adverse fetal outcomes associated with **immunosuppressive medications** for chronic immune-mediated diseases in pregnancy. Arthritis Rheumatol. 2014 Feb;66(2):444-50.
Cooper S, Lewis S, Thornton JG, et al. The **SNAP** trial: a randomised placebo-controlled trial of **nicotine replacement therapy in pregnancy** - clinical effectiveness and safety until 2 years after delivery, with economic evaluation. Health Technol Assess. 2014 Aug;18(54):1-128.
Cooper C, Harvey NC, Bishop NJ, et al, and the MAVIDOS Study Group. **Maternal gestational vitamin D** supplementation and off spring bone health (MAVIDOS): a multicentre, double-blind, randomised placebo-controlled trial. Lancet Diabetes Endocrinol 2016; online March 1.
Copp AJ, Stanier P, Greene ND. **Neural tube defects**: recent advances, unsolved questions, and controversies. Lancet Neurol. 2013 Jun 18.
Corsi DJ, Walsh L, Weiss D, et al. Association between **self-reported prenatal cannabis use and maternal, perinatal, and neonatal outcomes** [June 18, 2019]. JAMA. doi:10.1001/jama.2019.8734.
Cossette B, Forget A, Beauchesne MF, et al. Impact of **maternal use of asthma-controller therapy** on perinatal outcomes. Thorax. 2013 Apr 13. doi: 10.1136/thoraxjnl-2012-203122.
Costello JM, Pasquali SK, Jacobs JP, et al.. Gestational age at birth and outcomes after **neonatal cardiac surgery**: an analysis of the Society of Thoracic Surgeons Congenital Heart Surgery Database.

Circulation. 2014;129:2511–2517.
Coughlin CG, Blackwell KA, Bartley C, Hay M, Yonkers KA, Bloch MH. Obstetric and neonatal outcomes after **antipsychotic medication exposure** in pregnancy. Obstet Gynecol. 2015 May;125(5):1224-35.
Council on Environmental Health. **Iodine Deficiency**, Pollutant Chemicals, and the Thyroid: New Information on an Old Problem. Pediatrics. 2014 May 26.
Cnattingius S, Villamor E, Johansson S, et al. **Maternal obesity** and risk of preterm delivery. JAMA. 2013 Jun 12;309(22):2362-70.
Cnattingius S, Villamor E. **Weight change between successive pregnancies** and risks of stillbirth and infant mortality: a nationwide cohort study. Lancet. 2015 Dec 2.
Craciunas L, Tsampras N, Coomarasamy A, et al. **Intrauterine administration of human chorionic gonadotropin (hCG) for subfertile women** undergoing assisted reproduction. Cochrane Database Syst Rev. 2016 May 20;5:CD011537. The pregnancy outcome for cleavage-stage ETs using an IC-hCG dose of 500 IU or greater is promising. However, given the small size and the variable quality of the trials and the fact that the positive finding was from a subgroup analysis, the current evidence for IC-hCG treatment does not support its use in assisted reproduction cycles. A definitive large clinical trial with live birth as the primary outcome is recommended. There was no evidence that miscarriage was influenced by intrauterine hCG administration, irrespective of embryo stage at transfer or dose of IC-hCG. There were too few events to allow any conclusions to be drawn with regard to other complications.
Cragan JD, Young BA, Correa A. **Renin-Angiotensin System Blocker Fetopathy**. J Pediatr. 2015 Aug 5.
Creanga AA, Berg CJ, Syverson C, et al. **Pregnancy-related mortality** in the United States, 2006-2010. Obstet Gynecol. 2015 Jan;125(1):5-12.
Cressman AM, Pupco A, Kim E, et al. **Smoking cessation** therapy during pregnancy. Can Fam Physician. 2012 May;58(5):525-7.
Crider KS, Cordero AM, Qi YP, Mulinare J, Dowling NF, Berry RJ. **Prenatal folic acid and risk of asthma in children**: a systematic review and meta-analysis. Am J Clin Nutr. 2013 Sep 4.
Crider KS, Devine O, Hao L, et al. Population **red blood cell folate** concentrations for prevention of neural tube defects: bayesian model. BMJ. 2014 Jul 29;349:g4554
Cristofalo EA, Schanler RJ, Blanco CL, et al. Randomized Trial of Exclusive **Human Milk versus Preterm Formula** Diets in Extremely Premature Infants. J Pediatr. 2013 Aug 20.
Crochet JR, Bastian LA, Chireau MV. Does this woman have an **ectopic pregnancy**?: the rational clinical examination systematic review. JAMA. 2013 Apr 24;309(16):1722-9.
Crowther CA, McKinlay CJ, Middleton P, et al. Repeat doses of **prenatal corticosteroids** for women at risk of **preterm birth** for improving neonatal health outcomes. Cochrane Database Syst Rev. 2015 Jul 5;7:CD003935. The short-term benefits for babies of less respiratory distress and fewer serious health problems in the first few weeks after birth support the use of repeat dose(s) of prenatal corticosteroids for women still at risk of preterm birth seven days or more after an initial course. These benefits were associated with a small reduction in size at birth. The current available evidence reassuringly shows no significant harm in early childhood, although no benefit.Further research is needed on the long-term benefits and risks for the woman and baby. Individual patient data meta-analysis may clarify how to maximise benefit and minimise harm.
Crume TL, Juhl AL, Brooks-Russell A, et al. **Cannabis Use During the Perinatal Period** in a State With Legalized Recreational and Medical Marijuana: The Association Between **Maternal Characteristics, Breastfeeding Patterns, and Neonatal Outcomes**. J Pediatr. 2018 Jun;197:90-96.
Cruz MO et al. What is the optimal time for delivery in women with **gestational hypertension**? Am J Obstet Gynecol 2012 Sep; 207:214.e1.
Curran EA, Dalman C, Kearney PM, et al. Association Between **Obstetric Mode of Delivery and Autism Spectrum Disorder**: A Population-Based Sibling Design Study. JAMA Psychiatry. 2015 Jun 24.
D`Anna R, et al. **Myo-inositol Supplementation** for Prevention of Gestational Diabetes in Obese Pregnant Women: A Randomized Controlled Trial. Obstet Gynecol. 2015 Aug;126(2):310-5.
D'Souza R, Kingdom J. **Preeclampsia**. CMAJ. 2016 Nov 1;188(16):1178.
D'Souza R, Ostro J, Shah PS, et al. **Anticoagulation** for **pregnant** women with **mechanical heart valves**: a systematic review and meta-analysis. European Heart J. 2017;38:1509-1516.
Daly N, Carroll C, Flynn I, et al. Evaluation of point-of-care **maternal glucose measurements** for the diagnosis of gestational diabetes mellitus. BJOG. 2016 Aug 17.
Daly N, Farren M, McKeating A, et al. A Medically Supervised **Pregnancy Exercise Intervention** in Obese Women: A Randomized Controlled Trial. Obstet Gynecol. 2017 Nov;130(5):1001-1010.
Damkier P, Christensen LS, Broe A. Patterns and predictors for **prescription of psychotropics and mood-stabilizing antiepileptics during pregnancy** in Denmark 2000-2016. Br J Clin Pharmacol. 2018 Aug 5.
Daniel S, Doron M, Fishman B, et al. The safety of **amoxicillin and clavulanic acid use** during the first trimester of pregnancy. Br J Clin Pharmacol. 2019 Sep 5.
Daniel S, Koren G, Lunenfeld E, et al. Fetal exposure to **nonsteroidal anti-inflammatory drugs** and spontaneous abortions. CMAJ. 2014 Mar 18;186(5)
Daniel S, Matok I, et al. Major malformations following exposure to **nonsteroidal antiinflammatory drugs** (NSAIDs) during the first trimester of pregnancy. J Rheumatol. 2012 Nov;39(11):2163-9.
Daraki V, Roumeliotaki T, Chalkiadaki G, et al. **Low maternal vitamin D** status in pregnancy increases the risk of **childhood obesity**. Pediatr Obes. 2018 Jan 28.
Darling AL, Rayman MP, Steer CD, et al. Association between **maternal vitamin D** status in pregnancy and neurodevelopmental outcomes in childhood: results from the Avon Longitudinal Study of Parents and Children (**ALSPAC**). Br J Nutr. 2017 Jul 12:1-11
Darmasseelane K, Hyde MJ, Santhakumaran S, et al. **Mode of delivery and offspring body mass index**, overweight and obesity in adult life: a systematic review and meta-analysis. PLoS One. 2014 Feb 26;9(2).
Davis EF, Lazdam M, Lewandowski AJ, et al. **Cardiovascular Risk Factors in Children and Young Adults Born to Preeclamptic Pregnancies**: A Systematic Review. Pediatrics. 2012 May 21.
Davies MJ, Moore VM, Willson KJ, et al. **Reproductive Technologies** and the Risk of Birth Defects. N Engl J Med. 2012 May 5.
Daw JR et al. Prescription drug use in pregnancy: a retrospective, population-based study in British Columbia, Canada (2001-2006). Clin Ther. 2012 Jan;34(1):239-249.e2. Epub 2011 Dec 14.
Dean CR, Shemar M, Ostrowski GAU, Painter RC. Management of severe pregnancy **sickness and hyperemesis gravidarum**. BMJ. 2018 Nov 30;363:k5000.
De Groot L, Abalovich M, Alexander EK, et al. 2012 Management of **thyroid dysfunction during pregnancy and postpartum**: an Endocrine Society clinical practice guideline. J Clin Endocrinol Metab 97:2543–2565.
de Haas M, Thurik FF et al. Sensitivity of **fetal RHD screening** for safe guidance of targeted anti-D immunoglobulin prophylaxis: prospective cohort study of a nationwide programme in the Netherlands. BMJ. 2016 Nov 7;355:i5789.
de Jonge A, Mesman JA, Manniën J, et al. Severe adverse maternal outcomes among low risk women with planned **home versus hospital births** in the Netherlands: nationwide cohort study. BMJ. 2013 Jun 13;346:f3263.
de Jong PG, Kaandorp S, Di Nisio M, et al. **Aspirin and/or heparin** for women with unexplained **recurrent miscarriage** with or without inherited **thrombophilia**. Cochrane Database Syst Rev. 2014 Jul 4;7:CD004734. There is a limited number of studies on the efficacy and safety of aspirin and heparin in women with a history of at least two unexplained miscarriages with or without inherited thrombophilia. Of the nine reviewed studies quality varied, different treatments were studied and of the studies at low risk of bias only one was placebo-controlled. No beneficial effect of anticoagulants

in studies at low risk of bias was found. Therefore, this review does not support the use of anticoagulants in women with unexplained recurrent miscarriage. The effect of anticoagulants in women with unexplained recurrent miscarriage and inherited thrombophilia needs to be assessed in further randomised controlled trials; at present there is no evidence of a beneficial effect.

de Steenwinkel FD, Hokken-Koelega AC, Hazes JM, et al. Does medication or disease activity during pregnancy in patients with rheumatoid arthritis (RA), **Influence bone density** of their 7-year-old offspring? Arthritis Rheum. 2013 Nov 18.

de Steenwinkel FD, Hokken-Koelega AC, de Ridder MA, et al. Rheumatoid arthritis during **pregnancy and postnatal catch-up growth** in the offspring. Arthritis Rheumatol. 2014 Feb 27.

De Leo S, Pearce EN. **Autoimmune thyroid disease** during pregnancy. Lancet Diabetes Endocrinol. 2017 Dec 12.

Delgado Nunes V, Gholitabar M, Sims JM, Bewley S; Guideline Development Group. **Intrapartum care of healthy women and their babies**: summary of updated **NICE** guidance. BMJ. 2014 Dec 3;349:g6886.

Denison F, Norwood P, Bhattacharya S, et al. Association between maternal **body mass index during pregnancy**, short-term morbidity, and increased health service costs: a population-based study. BJOG. 2013 Sep 18.

Dennis CL, Dowswell T. **Psychosocial and psychological interventions for preventing postpartum depression**. Cochrane Database Syst Rev. 2013 Feb 28;2:CD001134. doi: 10.1002/14651858.CD001134.pub3. Overall, psychosocial and psychological interventions significantly reduce the number of women who develop postpartum depression. Promising interventions include the provision of intensive, professionally-based postpartum home visits, telephone-based peer support, and interpersonal psychotherapy.

Dennis CL, Jackson K, Watson J. Interventions for treating **painful nipples among breastfeeding** women. Cochrane Database Syst Rev. 2014 Dec 15;12:CD007366.

Deputy NP, Sharma AJ, Kim SY, et al. Prevalence and Characteristics Associated With **Gestational Weight Gain Adequacy**. Obstet Gynecol. 2015 Mar 5.

Desai RJ, Huybrechts KF, Hernandez-Diaz S et al. Exposure to prescription **opioid analgesics** in utero and risk of neonatal abstinence syndrome: population based cohort study. BMJ. 2015 May 14;350

Desai RJ, Huybrechts KF, Bateman BT, et al. Patterns and secular trends in use of **immunomodulatory agents during pregnancy** in women with **rheumatologic conditions**. Arthritis Rheumatol. 2015 Nov 25.

Desai RJ, et al. Risk of **serious infections associated with use of immunosuppressive agents** in pregnant women with autoimmune inflammatory conditions: cohort study. BMJ. 2017 Mar 6;356:j895.

Deshauer S, Wyne A. **Subclinical hypothyroidism** in pregnancy. CMAJ. 2017 Jul 17;189(28):E941

Deshpande NA, James NT, Kucirka LM et al. Pregnancy outcomes of liver transplant recipients: A systematic review and meta-analysis. Liver Transpl. 2012 Jun;18(6):621-9.

Devine RE, McCleary N, Sheikh A, et al. **Acid-suppressive medications during pregnancy** and risk of asthma and allergy in children: A systematic review and meta-analysis. J Allergy Clin Immunol. 2016 Dec 20.

Dhalwani NN, Szatkowski L, Coleman T, et al. **Nicotine Replacement Therapy** in Pregnancy and Major Congenital Anomalies in Offspring. Pediatrics. 2015 Apr 6.

Dhana K, Haines J, Liu G, et al. Association between **maternal adherence to healthy lifestyle practices and risk of obesity in offspring**: results from two prospective cohort studies of mother-child pairs in the United States. BMJ. 2018 Jul 4;362:k2486.

Diaz SD, Smith LM, Lagasse LL, et al. Effects of Prenatal **Methamphetamine** Exposure on Behavioral and Cognitive Findings at 7.5 Years of Age. J Pediatr. 2014 Mar 12.

Dickson B, Mansfield C, Guiahi M, et al. Recommendations From Cannabis Dispensaries About **First-Trimester Cannabis Use**. Obstet Gynecol. 2018 May 7.

Dodd JM, Turnbull D, McPhee AJ, et al. **Antenatal lifestyle** advice for women who are **overweight or obese**: **LIMIT** randomised trial. BMJ. 2014 Feb 10;348:g1285.

Domar AD, et al. The risks of **selective serotonin reuptake inhibitor** use in infertile women: a review of the impact on fertility, pregnancy, neonatal health and beyond. Hum Reprod. 2012 Oct 31.

Dombrowski JG, Souza RM, Lima FA, et al. Association of **Malaria Infection During Pregnancy With Head Circumference of Newborns** in the Brazilian Amazon. JAMA Netw Open. 2019 May 3;2(5):e193300.

Domenjoz I, Kayser B, Boulvain M. Effect of **physical activity** during pregnancy on **mode of delivery**. Am J Obstet Gynecol. 2014 Oct;211(4):401.e1-11.

Donauer S, Chen A, Xu Y, et al. Prenatal Exposure to **Polybrominated Diphenyl Ethers and Polyfluoroalkyl Chemicals** and Infant Neurobehavior. J Pediatr. 2014 Dec 16.

Donovan L, Hartling L, Muise M, et al. **Screening tests for gestational diabetes**: a systematic review for the u.s. Preventive services task force. (**USPSTF**) Ann Intern Med. 2013 Jul 16;159(2):115-22.

Dooley R, Dooley J, Antone I, et al. **Narcotic tapering** in pregnancy using long-acting morphine: an 18-month prospective cohort study in northwestern Ontario. Can Fam Physician. 2015 Feb;61(2):e88-95.

Dooley J, Gerber-Finn L, et al. **Buprenorphine-naloxone use in pregnancy** for treatment of opioid dependence: Retrospective cohort study of 30 patients. Canadian Family Physician. 2016;62(4):e194-e200.

Doubilet PM et al. Diagnostic criteria for **nonviable pregnancy** early in the first trimester. N Engl J Med 2013 Oct 10; 369:1443.

Dowlati Y et al. Selective **dietary supplementation** in early postpartum is associated with high resilience against depressed mood. Proc Natl Acad Sci U S A 2017 Mar 28; 114:3509.

Dreier JW, Andersen AM, Berg-Beckhoff G. Systematic Review and Meta-analyses: **Fever in Pregnancy** and Health Impacts in the Offspring. Pediatrics. 2014 Feb 24.

Dresang LT, Yonke N. Management of **Spontaneous Vaginal Delivery**. Am Fam Physician. 2015 Aug 1;92(3):202-8.

Dreyer K, van Rijswijk J, Mijatovic V, et al. **Oil-Based or Water-Based Contrast for Hysterosalpingography** in **Infertile Women**. N Engl J Med. 2017 May 18.

Duan L, Ng A, Chen W, et al. **β-Blocker Exposure** in Pregnancy and Risk of Fetal Cardiac Anomalies. JAMA Intern Med. 2017 Apr 17.

Dude A, Neustadt A, Martins S, et al. Use of **withdrawal and unintended pregnancy** among females 15-24 years of age. Obstet Gynecol. 2013 Sep

Duerden EG, Guo T, Dodbiba L, et al. **Midazolam** dose correlates with abnormal hippocampal growth and neurodevelopmental outcome in **preterm infants**. Ann Neurol. 2016 Jan 11.

Duijts L, Jaddoe VW, van der Valk RJ et al. Fetal exposure to maternal and paternal smoking and the risks of wheezing in preschool children: the Generation R Study. Chest. 2012 Apr;141(4):876-85.

Duley L, Meher S, Jones L. Drugs for treatment of **very high blood pressure** during pregnancy. Cochrane Database Syst Rev. 2013 Jul 31;7:CD001449. doi: 10.1002/14651858.CD001449.pub3. Until better evidence is available the choice of antihypertensive should depend on the clinician`s experience and familiarity with a particular drug; on what is known about adverse effects; and on women`s preferences. Exceptions are nimodipine, magnesium sulphate (although this is indicated for women who require an anticonvulsant for prevention or treatment of eclampsia), diazoxide and ketanserin, which are probably best avoided.

Dunn S, Brooks M. **Mifepristone- Five Thing to Know** about. CMAJ. 2018 Jun 4;190(22):E688.

Easterling T, Mundle S, Bracken H, et al. **Oral antihypertensive regimens (nifedipine retard, labetalol, and methyldopa**) for management of severe hypertension in pregnancy: an open-label, randomised controlled trial. Lancet. 2019 Aug 1.

Edlow JA, Caplan LR, O'Brien K, Tibbles CD. Diagnosis of **acute neurological emergencies** in pregnant and post-partum women. Lancet Neurol. 2013 Feb;12(2):175-85.

Edwards AC, Ohlsson H, Svikis DS, et al. **Protective Effects of Pregnancy on Risk of Alcohol Use Disorder**. Am J Psychiatry. 2018 Nov 29:appiajp201818050632.

Ehrlich SF, Hedderson MM, Xu F, Ferrara A. **Diagnostic thresholds for pregnancy hyperglycemia**, maternal weight status and the risk of childhood obesity in a diverse Northern California cohort using health care delivery system data. PLoS One. 2019 May 10;14(5):e0216897.

Einarson A. **Antidepressant use during** pregnancy: Navigating the sea of information. Can Fam Physician. 2013 Sep;59(9):941-4.
Eisele TP, Larsen DA, , et al. **Malaria prevention** in pregnancy, birthweight, and neonatal mortality: a meta-analysis of 32 national cross-sectional datasets in Africa. Lancet Infect Dis 2012; Sept 18.
Ejaz R, Leibson T, Koren G. **Selective serotonin reuptake inhibitor discontinuation during pregnancy**: at what risk? Can Fam Physician. 2014 Dec;60(12):1105-6.
Eke AC, Saccone G, Berghella V. **Selective serotonin reuptake inhibitor (SSRI) use during pregnancy and risk of preterm birth**: a systematic review and meta-analysis. BJOG. 2016 Nov;123(12):1900-1907.
El Marroun H, Jaddoe VW, Hudziak JJ, et al. Maternal Use of **Selective Serotonin Reuptake Inhibitors**, Fetal Growth, and Risk of Adverse Birth Outcomes. Arch Gen Psychiatry. 2012 Mar 5.
Elchert J, Beaudrot M, DeFranco E. **Gestational weight gain in adolescent** compared with adult pregnancies: an age specific body mass index approach. J Pediatr July 2015.
Elkayam U, Jalnapurkar S, Barakkat MN, et al. **Pregnancy-associated acute myocardial infarction**: a review of contemporary experience in 150 cases between 2006 and 2011. Circulation. 2014 Apr 22;129(16):1695-702.
Emond A, Ingram J, Johnson D, et al. Randomised controlled trial of early **frenotomy in breastfed infants** with mild-moderate tongue-tie**.** Arch Dis Child Fetal Neonatal Ed. 2013 Nov 18.
Endres LK, Straub H, McKinney C, et al. Community Child Health Network of the Eunice Kennedy Shriver National Institute of Child Health and Human Development. **Postpartum weight retention** risk factors and relationship to obesity at 1 year. Obstet Gynecol. 2015 Jan;125(1):144-52.
Engeland A, Bjørge T, Daltveit AK, et al. Effects of **preconceptional paternal drug exposure** on birth outcomes: cohort study of 340,000 pregnancies using Norwegian population-based databases. Br J Clin Pharmacol. 2012 Aug 17.
Englund-Ogge L, Brantsæter AL, Sengpiel V, Haugen M, Birgisdottir BE, Myhre R, et al. **Maternal dietary patterns** and preterm delivery: results for large prospective cohort study. BMJ 2014;348:g1446.
Eskild A. Mothers who give birth to offspring with **low birth weight may have increased risk for cardiovascular death**. BMJ Evid Based Med. 2019 Feb;24(1):39-40.
Etheredge AJ, Premji Z, Gunaratna NS, et al. **Iron Supplementation** in Iron-Replete and Nonanemic Pregnant Women in Tanzania: A Randomized Clinical Trial. JAMA Pediatr. 2015 Aug 17.
Factor-Litvak P, Insel B, Calafat AM, et al. Persistent Associations between Maternal Prenatal Exposure to **Phthalates** on Child IQ at Age 7 Years. PLoS One. 2014 Dec 10;9(12):e114003.
Farahi N, Zolotor A. Recommendations for **Preconception Counseling** and Care. Am Fam Physician. 2013;88(8):499-506.
Farren J, Jalmbrant M, Ameye L, et al. **Post-traumatic stress**, **anxiety and depression following miscarriage or ectopic pregnancy**: a prospective cohort study. BMJ Open. 2016 Nov 2;6(11):e011864.
Fawole B, Hofmeyr GJ. **Maternal oxygen administration for fetal distress**. Cochrane Database Syst Rev. 2012 Dec 12;12:CD000136. doi: 10.1002/14651858.CD000136.pub2.
Feghali MN, Scifres CM. **Novel therapies for diabetes mellitus in pregnancy**. BMJ. 2018 Jul 16;362:k2034.
Feig DS, Shah BR, Lipscombe LL, Wu CF, Ray JG, et al. (2013) **Preeclampsia** as a risk factor for diabetes: a population-based cohort study. PLoS Med 10: e1001425. 10.1371/journal.pmed.1001425
Feig DS, Donovan LE, Corcoy R, et al. **Continuous glucose monitoring** in women with **type 1 diabetes in pregnancy** (**CONCEPTT**): a multicentre international randomised controlled trial. Lancet 2017. doi:S0140-6736(17)32400-5.
Felder JN, Baer RJ, Rand L, et al. **Sleep Disorder** Diagnosis During **Pregnancy** and Risk of **Preterm Birth**. Obstet Gynecol. 2017 Aug 4.
Feldkamp ML, Carey JC, Byrne JLB, Krikov S, Botto LD. **Etiology and clinical presentation of birth defects**: population based study. BMJ. 2017 May 30;357:j2249.
Feldman R et al. **Maternal-preterm skin-to-skin contact** enhances child physiologic organization and cognitive control across the first 10 years of life. Biol Psychiatry 2013 Oct 3.
Ferguson KK, McElrath TF, Meeker JD. **Environmental phthalate exposure** and preterm birth [online November 18, 2013]. *JAMA Pediatr*. doi:10.1001/jamapediatrics.2013.3699.
Fernández-Barrés S, Vrijheid M, Manzano-Salgado CB, et al; Infancia y Medio Ambiente (INMA) Project. The Association of **Mediterranean Diet during Pregnancy with Longitudinal Body Mass** Index Trajectories and Cardiometabolic Risk in Early Childhood. J Pediatr. 2018 Nov 12.
Finer LB, Zolna MR. **Declines in Unintended Pregnancy** in the United States, 2008-2011. N Engl J Med. 2016 Mar 3;374(9):843-52.
Fishel S, Baker D, Elson J, et al. Precision Medicine in **Assisted Conception**: A Multicenter Observational Treatment Cohort Study of the Annexin A5 M2 Haplotype as a Biomarker for Antithrombotic Treatment to Improve Pregnancy Outcome. EBioMedicine. 2016 Jul 15.
Fleming TP, Watkins AJ, Velazquez MA, et al. Origins of **lifetime health around the time of conception**: causes and consequences. Lancet. 2018 Apr 16.
Flenady V, Wojcieszek AM, Papatsonis DN, et al. **Calcium channel blockers for inhibiting preterm birth**. Cochrane Database Syst Rev 2014;6:CD002255. Calcium channel blockers (mainly nifedipine) for women in preterm labour have benefits over placebo or no treatment in terms of postponement of birth thus, theoretically, allowing time for administration of antenatal corticosteroids and transfer to higher level care. Calcium channel blockers were shown to have benefits over betamimetics with respect to prolongation of pregnancy, serious neonatal morbidity, and maternal adverse effects. Calcium channel blockers may also have some benefits over ORAs and magnesium sulphate, although ORAs results in fewer maternal adverse effects. However, it must be noted that no difference was shown in perinatal mortality, and data on longer-term outcomes were limited. Further, the lack of blinding of the intervention diminishes the strength of this body of evidence. Further well-designed tocolytic trials are required to determine short- and longer-term infant benefit of CCBs over placebo or no treatment and other tocolytics, particularly ORAs. Another important focus for future trials is identifying optimal dosage regimens of different types of CCBs (high versus low, particularly addressing speed of onset of uterine quiescence) and formulation (capsules versus tablets). All future trials on tocolytics for women in preterm labour should employ blinding of the intervention and outcome assessment, include measurement of longer-term effects into early childhood, and also costs.
Flynn JT, Ng DK, Chan GJ, et al; Chronic Kidney Disease in Children Study. The Effect of **Abnormal Birth History on Ambulatory Blood Pressure** and Disease Progression in Children with Chronic Kidney Disease. J Pediatr. 2014 Mar 31.
Forinash AB, Yancey AM, Barnes KN, Myles TD. The Use of **Galactogogues in the Breastfeeding** Mother (October). Ann Pharmacother. 2012 Sep 25.
Forno E, Young OM, Kumar R, et al. **Maternal Obesity** in Pregnancy, Gestational Weight Gain, and Risk of Childhood **Asthma**. Pediatrics. 2014 Aug;134(2):e535-e546.
Forthun I, Wilcox AJ, Strandberg-Larsen K, et al. **Maternal Prepregnancy BMI** and Risk of **Cerebral Palsy** in Offspring.Pediatrics. 2016 Sep 8.
Frazier AL, Camargo CA Jr, Malspeis S, et al. Prospective Study of **Peripregnancy Consumption of Peanuts or Tree Nuts** by Mothers and the Risk of Peanut or Tree Nut Allergy in Their Offspring. JAMA Pediatr. 2013 Dec 23
Frederiksen BN, Rivera MI, Ahrens KA, et al. Clinic-Based Programs to **Prevent Repeat Teen Pregnancy**: A Systematic Review. Am J Prev Med. 2018 Nov;55(5):736-746.
Fujii H, Goel A, Bernard N, et al. Pregnancy outcomes following gabapentin use: Results of a prospective comparative cohort study. Neurology. 2013 Apr 23;80(17):1565-1570.
Furu K, Kieler H, et al. **Selective serotonin reuptake inhibitors and venlafaxine** in early pregnancy and risk of birth defects: population based cohort study and sibling design. BMJ 2015;350h1798.
Furukawa TA. Adverse effects of **antidepressants during pregnancy**. Evid Based Ment Health. 2014 Nov;17(4):103-4.

Gade EJ, Thomsen S, Lindenberg S, et al. **Asthma affects time to pregnancy and fertility**: a register-based twin study. Eur Respir J. 2013 Nov 14.
Gagliardi L, Rusconi F, Bellù R, et al; the Italian Neonatal Network. Association of **Maternal Hypertension** and Chorioamnionitis With Preterm Outcomes. Pediatrics. 2014 Jun 9.
Gandhi S, Ganame J, Whitlock R, et al. Double Trouble: A Case of **Valvular Disease in Pregnancy**. Circulation. 2016 May 31;133(22):2206-11.
Gao SY, Wu QJ, Zhang TN, et al. **Fluoxetine and congenital malformations**: a systematic review and meta-analysis of cohort studies. Br J Clin Pharmacol. 2017 May 17
Garcia-Larsen V, et al. **Diet during pregnancy** and infancy and risk of allergic or autoimmune disease: A systematic review and meta-analysis. PLoS Med. 2018 Feb 28;15(2):e1002507.
Gardosi J, Madurasinghe V, Williams M, Malik A, Francis A. **Maternal and fetal risk factors for stillbirth**: population based study. BMJ 2013;346:f108.
Garne E, Vinkel Hansen A, Morris J, et al. Risk of **congenital anomalies after exposure to asthma medication** in the first trimester of pregnancy - a cohort linkage study. BJOG. 2016 May 12.
Gelfand AA, Thomas KC, Goadsby PJ. Before the **headache: Infant colic** as an early life expression of migraine. Neurology. 2012 Sep 25;79(13):1392-6. (maternal migraine)
Gennari-Moser C, Escher G, Kramer S, et al. **Normotensive Blood Pressure in Pregnancy**: The Role of Salt and Aldosterone. Hypertension. 2013 Dec 2
Georgalas I, Petrou P, Koutsandrea C. Safety of **intravitreal anti-VEGFs** during pregnancy is unclear. BMJ. 2012 Jul 9;345:e4526.
Getahun D, Rhoads GG, Demissie K, et al. In utero exposure to ischemic-hypoxic conditions and **attention-deficit/hyperactivity disorder**. Pediatrics. 2013 Jan;131(1):e53-61.
Ghossein-Doha C, Peeters L, van Heijster S, et al. **Hypertension after preeclampsia** is preceded by changes in cardiac structure and function. Hypertension 2013.
Gibreel A, Maheshwari A, Bhattacharya S. **Clomiphene citrate in combination with gonadotropins** for controlled ovarian stimulation in women undergoing in vitro fertilization. Cochrane Database Syst Rev. 2012 Nov 14;11:CD008528. doi: 10.1002/14651858.CD008528.pub2.
Gibson KS, Waters TP, Bailit JL. Maternal and neonatal outcomes in **electively induced low-risk term pregnancies**. Am J Obstet Gynecol. 2014 Sep;211(3):249.e1-249.e16.
Gidaya NB, Lee BK, Burstyn I, et al. In utero Exposure to **β-2-Adrenergic Receptor Agonist Drugs and Risk for Autism** Spectrum Disorders. Pediatrics. 2016 Jan 6.
Gillman MW, Rifas-Shiman SL, Fernandez-Barres S, et al. **Beverage Intake** During Pregnancy and Childhood Adiposity. Pediatrics. 2017;140(2):e20170031
Given JE, Loane M, Luteijn JM, et al. EUROmediCAT signal detection: an evaluation of selected **congenital anomaly-medication associations**. Br J Clin Pharmacol. 2016 Mar 29.
Givertz MM. Cardiology patient page: peripartum cardiomyopathy. Circulation. 2013 May 21;127(20):e622-6.
Gladstone RA, Pudwell J, Nerenberg KA, et al. **Cardiovascular Risk Assessment** and Follow-Up of Women After Hypertensive Disorders of Pregnancy: A Prospective Cohort Study. J Obstet Gynaecol Can. 2019 Jan 14.
Godfrey LM, Erramouspe J, Cleveland KW. **Teratogenic Risk of Statins** in Pregnancy (October). Ann Pharmacother. 2012 Oct 2.
Goel A, Maski MR, Bajracharya S, et al. Epidemiology and Mechanisms of **De Novo and Persistent Hypertension in the Postpartum Period**. Circulation. 2015 Sep 28.
Goldberg O, Koren G, Landau D, et al. Exposure to **nitrofurantoin during the first trimester** of pregnancy and the risk for major malformations. J Clin Pharmacol. 2013 Sep;53(9):991-5.
Goldie MH, Brightling CE. **Asthma in pregnancy**. The Obstetrician & Gynaecologist 2013;15:241–5.
Goldstein RF, Abell SK, Ranasinha S, et al. Association of **gestational weight gain with maternal and infant outcomes**: a systematic review and meta-analysis.JAMA. doi:10.1001/jama.2017.3635
Goler N, Conway A, Young-Wolff KC. Data Are Needed on the **Potential Adverse Effects of Marijuana Use in Pregnancy**. Ann Intern Med. 2018 Aug 21.
Goodwin RD, Cheslack-Postava K, Nelson DB, et al. **Smoking** during pregnancy in the United States, 2005-2014: The role of **depression**. Drug Alcohol Depend. 2017 Jul 18;179:159-166.
Gordon A, Raynes-Greenow C, Bond D, et al. **Sleep Position**, Fetal Growth Restriction, and Late-**Pregnancy Stillbirth**: The Sydney Stillbirth Study. Obstet Gynecol. 2015 Jan 7.
Gotestam Skorpen C, Hoeltzenbein M, Tincani A, et al. The EULAR points to consider for use of **antirheumatic drugs before pregnancy**, and during pregnancy and **lactation**. Ann Rheum Dis. 2016 Feb 17. pii: annrheumdis-2015-208840.
Gould JF et al. Seven-year follow-up of children born to women in a randomized trial of **prenatal DHA supplementation**. JAMA 2017 Mar 21; 317:1173.
Goya M, Pratcorona L, Merced C, et al. **Cervical pessary** in pregnant women with a short cervix (PECEP): an open-label randomised controlled trial. Lancet. 2012 Apr 2.
Goya M, de la Calle M, Pratcorona L, et al. **Cervical pessary** to **prevent preterm birth** in women with twin gestation and sonographic short cervix: a multicenter randomized controlled trial (PECEP-Twins). Am J Obstet Gynecol. 2016 Feb;214(2):145-52.
Goyal M et al. Frequency of **pregnancy testing among adolescent emergency department visits**. Acad Emerg Med 2013 Aug; 20:816.
Goyal MK et al. Underuse of **pregnancy testing for women prescribed teratogenic medications** in the emergency department. Acad Emerg Med 2015 Jan 29.
Graner S, et al. **Neuraminidase inhibitors** during pregnancy and risk of adverse neonatal outcomes and congenital malformations: population based European register study. BMJ. 2017 Feb 28;356:j629.
Granfors M, Akerud H, Skogö J, et al. **Targeted thyroid testing** during pregnancy in clinical practice. Obstet Gynecol. 2014 Jul;124(1):10-5.
Grant CC, Stewart AW, Scragg R, et al. **Vitamin D During Pregnancy** and Infancy and Infant Serum 25-Hydroxyvitamin D Concentration. Pediatrics. 2013 Dec 16
Gravett CA, Gravett MG, Martin ET, et al. **Serious and life-threatening pregnancy-related infections**: opportunities to reduce the global burden. PLoS Med. 2012 Oct;9(10):e1001324.
Green R, Lanphear B, Hornung R, et al. Association Between **Maternal Fluoride Exposure** During Pregnancy and IQ Scores in Offspring in Canada. JAMA Pediatr. 2019 Aug 19.
Greer IA. CLINICAL PRACTICE. Pregnancy Complicated by **Venous Thrombosis**. N Engl J Med. 2015 Aug 6;373(6):540-7.
Gregory DS, Wu V, Tuladhar P. The Pregnant Patient: **Managing Common Acute Medical Problems**. Am Fam Physician. 2018;98(9):595-602.
Grieger JA, Grzeskowiak LE, Bianco-Miotto T, et al. **Pre-pregnancy fast food and fruit intake is associated with time to pregnancy**. Hum Reprod. 2018 May 4.
Dodd JM, Louise J, Deussen AR, et al. Effect of **metformin in addition to dietary and lifestyle advice for pregnant women who are overweight or obese**: the GRoW randomised, double-blind, placebo-controlled trial. Lancet Diabetes Endocrinol. 2018 Dec 4.
Grieger JA, Bianco-Miotto T, Grzeskowiak LE, et al. **Metabolic syndrome in pregnancy and risk for adverse pregnancy outcomes**: A prospective cohort of nulliparous women. PLoS Med. 2018 Dec 4;15(12):e1002710.
Griffiths PD, Bradburn M, Campbell MJ, et al. Use of **MRI** in the diagnosis of **fetal brain abnormalities** in utero (**MERIDIAN**): a multicentre, prospective cohort study. Lancet. 2016 Dec 14.
Grigoriadis S, Graves L, Peer M, et al. **Benzodiazepine Use** During Pregnancy Alone or in Combination With an Antidepressant and Congenital Malformations: Systematic Review and Meta-Analysis. J Clin Psychiatry. 2019 Jul 9;80(4).
Grigoriadis S, VonderPorten EH, Mamisashvili L, et al. **Antidepressant exposure** during pregnancy and congenital malformations: is there an association? A systematic review and meta-analysis of the best

evidence. J Clin Psychiatry 2013;74:e293–308.
Grigoriadis S, VonderPorten EH, Mamisashvili L, et al. The effect of **prenatal antidepressant exposure** on neonatal adaptation: a systematic review and meta-analysis. J Clin Psychiatry 2013;74:e309–20.
Grigoriadis S, Vonderporten EH, Mamisashvili L, et al. Prenatal exposure to **antidepressants and persistent pulmonary hypertension** of the newborn: systematic review and meta-analysis. BMJ. 2014 Jan 14
Grigoriadis S, Wilton AS, Kurdyak PA, et al. **Perinatal suicide** in Ontario, Canada: a 15-year population-based study. CMAJ. 2017 Aug 28;189(34):E1085-E1092
Grimshaw KE, Maskell J, Oliver EM, et al. **Diet and food allergy development during infancy**: Birth cohort study findings using prospective food diary data. J Allergy Clin Immunol. 2013 Jul 23.
Grivell RM, Yelland LN, Deussen A, et al. **Antenatal dietary and lifestyle advice** for women who are overweight or obese and the effect on fetal growth and adiposity: the LIMIT randomised trial. BJOG. 2016 Jan;123(2):233-43.
Grobman WA, Rice MM, Reddy UM, et al. **Labor Induction versus Expectant Management in Low-Risk Nulliparous Women**. N Engl J Med. 2018 Aug 9;379(6):513-523.
Grossman D, White K, Hopkins K, et al. Change in **Distance to Nearest Facility and Abortion** in Texas, 2012 to 2014. JAMA. 2017 Jan 24;317(4):437-439.
Grove K, Lewis AJ, Galbally M. Prenatal **Antidepressant Exposure and Child Motor Development**: A Meta-analysis. Pediatrics. 2018 Jun 21.
Grzeskowiak LE, Pedersen LH, Morrison JL. **Antidepressant Use** and Gestational Hypertension: Does Evidence Support Causality? Br J Clin Pharmacol. 2012 Sep 20.
Grzeskowiak LE, et al. **Prenatal antidepressant exposure** and **child behavioural outcomes** at 7 years of age: a study within the Danish National Birth Cohort. BJOG. 2016 Nov;123(12):1919-1928.
Grzeskowiak LE, Leggett C, Costi L, et al. Impact of **Serotonin Reuptake Inhibitor Use on Breast Milk Supply** in Mothers of Preterm Infants: A Retrospective Cohort Study. Br J Clin Pharmacol. 2018 Mar 9.
Gunderson EP, Hedderson MM, Chiang V, et al. **Lactation intensity** and postpartum maternal **glucose** tolerance and insulin resistance in women with recent GDM: the SWIFT cohort. Diabetes Care 2012;35:50–6.
Gunderson EP et al. **Lactation duration and midlife atherosclerosis**. Obstet Gynecol 2015 Aug; 126:381. –
Gunderson EP, Hurston SR, Ning X, et al. Study of Women, Infant Feeding and Type 2 Diabetes After GDM Pregnancy Investigators. **Lactation and Progression to Type 2 Diabetes** Mellitus After Gestational Diabetes Mellitus: A Prospective Cohort Study. Ann Intern Med. 2015 Nov 24:889-898.
Gunderson EP, Lewis CE, Lin Y, et al. **Lactation Duration and Progression to Diabetes** in Women Across the Childbearing Years: The 30-Year CARDIA Study. JAMA Intern Med.2018 Jan 16.
Gutierrez-Galve L, Stein A, Hanington L, et al. **Paternal Depression in the Postnatal Period** and Child Development: Mediators and Moderators. Pediatrics. 2015 Jan 5.
Gutierrez-Galve L, Stein A, Hanington L, et al. Association of **Maternal and Paternal Depression in the Postnatal Period** With **Offspring Depression** at Age 18 Years. JAMA Psychiatry. 2018 Dec 26.
Gyamfi-Bannerman C, Thom EA, Blackwell SC, et al; NICHD Maternal–Fetal Medicine Units Network. **Antenatal Betamethasone** for Women at Risk for Late **Preterm Delivery**. N Engl J Med. 2016 Feb 4.
Gyhagen M, Bullarbo M, Nielsen T, Milsom I. A comparison of the long-term consequences of **vaginal delivery versus caesarean** section on the prevalence, severity and bothersomeness of **urinary incontinence** subtypes: a national cohort study in primiparous women. BJOG. 2013 Nov;120(12):1548-55.
Gyhagen M, Bullarbo M, Nielsen T, et al. Prevalence and risk factors for **pelvic organ prolapse** 20 years after childbirth: a national cohort study in singleton primiparae after vaginal or caesarean delivery. BJOG 2013;120:152–60.
H Al Wattar B, Dodds J, Placzek A, et al; ESTEEM study group. **Mediterranean-style diet** in pregnant women with metabolic risk factors (ESTEEM): A pragmatic multicentre randomised trial. PLoS Med. 2019 Jul 23;16(7):e1002857.
Ha S, Sundaram R, Buck Louis GM, et al. **Ambient air pollution and the risk of pregnancy loss**: a prospective cohort study. Fertil Steril. 2017 Nov 14.
Haas DM, Caldwell DM, Kirkpatrick P, McIntosh JJ, Welton NJ. **Tocolytic therapy** for preterm delivery: systematic review and network meta-analysis. BMJ. 2012 Oct 9;345:e6226.
Haas DM, Morgan S, Contreras K. **Vaginal preparation with antiseptic solution before cesarean section** for preventing postoperative infections. Cochrane Database Syst Rev. 2014 Dec 21;12:CD007892. Vaginal preparation with povidone-iodine solution immediately before cesarean delivery reduces the risk of postoperative endometritis. This benefit is particularly realized for women undergoing cesarean delivery, who are already in labor or who have ruptured membranes. As a simple, generally inexpensive intervention, providers should consider implementing preoperative vaginal cleansing with povidone-iodine before performing cesarean deliveries.
Håberg SE, Trogstad L, Gunnes N, et al. Risk of **fetal death after pandemic influenza virus infection or vaccination**. N Engl J Med. 2013 Jan 24;368(4):333-40.
Hagan JF, Balachova T, Bertrand J, et al. Neurobehavioral disorder associated with prenatal **alcohol** exposure. Pediatrics. 2016;138(4):e20151553
Haghikia A, Langer-Gould A, Rellensmann G, et al. **Natalizumab** Use During the Third Trimester of Pregnancy. JAMA Neurol. 2014 May 12.
Hagnäs MP, Cederberg H, Jokelainen J, et al. Association of **maternal smoking** during pregnancy with aerobic fitness of offspring in young adulthood: a prospective cohort study. BJOG. 2015 Dec 9.
Hahn SA, Lavonas EJ, et al. American College of Emergency Physicians. Clinical policy: critical issues in the initial **evaluation and management of patients presenting to the emergency department** in early pregnancy. Ann Emerg Med 2012 Sep;60(3):381-90.e28.
Haider BA, Olofin I, Wang M, Spiegelman D, Ezzati M, Fawzi WW. Anaemia, **prenatal iron use**, and risk of adverse pregnancy outcomes: systematic review and meta-analysis. BMJ2013;346:f3443.
Haider BA, Bhutta ZA. **Multiple-micronutrient supplementation** for women during pregnancy. Cochrane Database Syst Rev. 2017 Apr 13;4:CD004905. Our findings support the effect of MMN supplements with **iron and folic acid** in improving some birth outcomes. Overall, pregnant women who received MMN supplementation had fewer low birthweight babies and small-for-gestational-age babies. The findings, consistently observed in several systematic evaluations of evidence, provide a basis to guide the replacement of iron and folic acid with MMN supplements containing iron and folic acid for pregnant women in low and middle-income countries where MMN deficiencies are common among women of reproductive age. Efforts could focus on the integration of this intervention in maternal nutrition and antenatal care programs in low and middle-income countries.
Hall J, Cho HD, Guo Y, et al **Association of Rates of Smoking During Pregnancy With Corporate Tobacco Sales Policies**. JAMA Pediatr. 2019 Jan 14.
Hallamaa L, Cheung YB, Maleta K, et al. **Child Health Outcomes After Presumptive Infection Treatment in Pregnant Women**: A Randomized Trial. Pediatrics. 2018 Feb 22.
Hamilton KT, Robbins MS. **Migraine Treatment** in Pregnant Women Presenting to Acute Care: A Retrospective Observational Study. Headache. 2018 Nov 7.
Handal M, Skurtveit S, Furu K, et al. **Motor development in children prenatally exposed to selective serotonin reuptake inhibitors**: a large population-based pregnancy cohort study. BJOG. 2015 Sep 15.
Hansen C, Desai S, Bredfeldt C, et al. A Large, Population-Based Study of 2009 **Pandemic Influenza** A Virus Subtype H1N1 Infection Diagnosis During Pregnancy and Outcomes for Mothers and Neonates. J Infect Dis. 2012 Oct;206(8):1260-8.
Hämeen-Anttila K, Jyrkkä J, Enlund H, et al. **Medicines information** needs during pregnancy: a multinational comparison. BMJ Open. 2013 Apr 26;3(4).

Hammers AL, Sanchez-Ramos L, Kaunitz AM. Antenatal exposure to **indomethacin increases the risk of severe intraventricular hemorrhage, necrotizing enterocolitis, and periventricular leukomalacia**: a systematic review with metaanalysis. Am J Obstet Gynecol. 2015 Apr;212(4):505.e1-13.

Hanley GE, Smolina K, Mintzes B, et al. **Postpartum Hemorrhage** and Use of **Serotonin Reuptake Inhibitor Antidepressants** in Pregnancy. Obstet Gynecol. 2016 Mar;127(3):553-61.

Hannigan LJ, Eilertsen EM, Gjerde LC, et al. **Maternal prenatal depressive symptoms and risk for early-life psychopathology in offspring**: genetic analyses in the Norwegian Mother and Child Birth Cohort Study. Lancet Psychiatry. 2018 Oct;5(10):808-815.

Harel Z, McArthur E, Hladunewich M, et al. **Serum Creatinine Levels Before, During, and After Pregnancy**. JAMA. 2019 Jan 15;321(2):205-207

Harrington RA, Lee LC, Crum RM, et al. **Prenatal SSRI Use and Offspring With Autism** Spectrum Disorder or Developmental Delay. Pediatrics. 2014 Apr 14.

Harris SJ, Janssen PA, Saxell L, et al. Effect of a **collaborative interdisciplinary** maternity care program on perinatal outcomes. CMAJ. 2012 Sep 10.

Harrison D, Reszel J, Bueno M, et al. **Breastfeeding for procedural pain in infants beyond the neonatal period**. Cochrane Database Syst Rev. 2016 Oct 28;10:CD011248. We conclude, based on the 10 studies included in this review, that breastfeeding may help reduce pain during vaccination for infants beyond the neonatal period. Breastfeeding consistently reduced behavioural responses of cry duration and composite pain scores during and following vaccinations. However, there was no evidence that breastfeeding had an effect on physiological responses. No studies included in this review involved populations of hospitalised infants undergoing other skin-breaking procedures. Although it may be possible to extrapolate the review results to this population, further studies of efficacy, feasibility, and acceptability in this population are warranted.

Harrod CS, Chasan-Taber L, Reynolds RM, et al. **Physical Activity** in Pregnancy and Neonatal Body Composition: The Healthy Start Study. Obstet Gynecol. 2014 Jul 7.

Harrod CS, Reynolds RM, Chasan-Taber L, et al. Quantity and timing of **maternal prenatal smoking on neonatal body composition**: the healthy start study. J Pediatr. 2014 Oct;165(4):707 12.

Haug EB, Horn J, Markovitz AR, et al. Association of Conventional Cardiovascular Risk Factors With **Cardiovascular Disease After Hypertensive Disorders** of Pregnancy: Analysis of the Nord-Trøndelag Health Study. JAMA Cardiol. 2019 Jun 12.

Hayes RM et al. **Maternal antidepressant use** and adverse outcomes: A cohort study of 228,876 pregnancies. Am J Obstet Gynecol 2012 Jul; 207:49.e1.

Hayward RM, Foster E, Tseng ZH. Maternal and Fetal Outcomes of Admission for Delivery in Women With **Congenital Heart Disease**. JAMA Cardiol. 2017 Apr 12.

Health Canada July/12 "**Fu Fang Zaoren Jiaonang**": A Potentially Dangerous Product for Pregnant Women. "Fu Fang Zaoren Jiaonang," an unauthorized natural health product promoted for anxiety and/or insomnia, has been removed from sale after testing by Health Canada confirmed the presence of the ingredient L-tetrahydropalmatine that could cause damage to vital organs such as the liver, most notably in pregnant women.

Healy CM, Rench MA, Swaim LS, et al. Association Between **Third-Trimester Tdap Immunization and Neonatal Pertussis Antibody Concentration**. JAMA. 2018 Oct 9;320(14):1464-1470.

Hellwig K, Haghikia A, Gold R. Pregnancy and **natalizumab**: results of an observational study in 35 accidental pregnancies during natalizumab treatment. Mult Scler. 2011 Aug;17(8):958-63.

Hellwig K, Rockhoff M, Herbstritt S, et al. Exclusive **Breastfeeding** and the Effect on **Postpartum Multiple Sclerosis Relapses**. JAMA Neurol. 2015 Aug 31.

Henderson JT, Whitlock EP, O'Connor E, et al. **Low-Dose Aspirin** for Prevention of Morbidity and Mortality From **Preeclampsia**: A Systematic Evidence Review for the U.S. Preventive Services Task Force. (USPSTF) Ann Intern Med. 2014 Apr 8.

Hendriks E, MacNaughton H, MacKenzie MC. **First Trimester Bleeding**: Evaluation and Management. Am Fam Physician. 2019 Feb 1;99(3):166-174.

Henriksson P, Westerlund E, Wallén H, et al. Incidence of **pulmonary and venous thromboembolism in pregnancies after in vitro fertilisation**: cross sectional study. BMJ. 2013 Jan 15;346:e8632.

Henriksen L, Wu CS, Secher NJ, et. al. **Medical Augmentation of Labor** and the Risk of ADHD in Offspring: A Population-Based Study. Pediatrics. 2015 Feb 9. pii: peds.2014-1542.

Henry D, Dormuth C, Winquist B, et al. Occurrence of pregnancy and pregnancy outcomes **during isotretinoin therapy**. CMAJ. 2016 Apr 25

Herba CM, Tremblay RE, Boivin M, et al. **Maternal Depressive** Symptoms and Children's Emotional Problems: Can **Early Child Care** Help Children of Depressed Mothers? JAMA Psychiatry. 2013 Jun 19:1-9.

Herd P et al. The implications of **unintended pregnancies for mental health** in later life. Am J Public Health 2016 Mar; 106:421.

Hernández-Díaz S, Smith CR, Shen A, et al; For the North American AED Pregnancy Registry; North American AED(Antiepileptic Drug) Pregnancy Registry; Scientific Advisory Committee; North American AED Pregnancy Registry. Comparative safety of **antiepileptic drugs during pregnancy**. Neurology. 2012 May 22;78(21):1692-1699.

Hernández-Díaz S, Mittendorf R, Smith CR, et al. North American Antiepileptic Drug Pregnancy Registry. Association between **topiramate and zonisamide use during pregnancy** and low birth weight. Obstet Gynecol. 2014 Jan;123(1):21-8.

Hernández-Díaz S, McElrath TF, Pennell PB, et al. Fetal Growth and Premature Delivery in Pregnant Women on **Anti-epileptic Drugs**. Ann Neurol. 2017 Aug 30.

Hernandez-Diaz S, Huybrechts KF, Desai RJ, et al. **Topiramate** use early in pregnancy and the risk of oral clefts: A pregnancy cohort study. Neurology. 2017 Dec 27

Hernandez-Diaz S, Huybrechts KF, Desai RJ, et al. **Topiramate use early in pregnancy** and the risk of **oral clefts**: A pregnancy cohort study. Neurology. 2018 Jan 23;90(4):e342-e351.

Herrell HE. **Nausea and Vomiting of Pregnancy**. Am Fam Physician. 2014;89(12):965-970.

Herzog AG, Mandle HB, Cahill KE, et al. Predictors of **unintended pregnancy in women with epilepsy**. Neurology. 2017 Feb 21;88(8):728-733.

Herzog AG, Mandle HB, et al. Association of **Unintended Pregnancy With Spontaneous Fetal Loss in Women With Epilepsy**: Findings of the Epilepsy Birth Control Registry. JAMA Neurol. 2018 Oct 15.

Hillier TA, Pedula KL, Vesco KK, et al. Impact of **Maternal Glucose and Gestational Weight Gain on Child Obesity** over the First Decade of Life in Normal Birth Weight Infants. Matern Child Health J. 2016May 6.

Hillman SC, Stokes-Lampard H, Kilby MD. **Intrahepatic cholestasis** of pregnancy. BMJ. 2016 Apr 21;353:i1236

Himes SK, Tassiopoulos K, Yogev R, et al; Pediatric HIV/AIDS Cohort Study (PHACS). **Antiretroviral Drugs in Meconium**: Detection for Different Gestational Periods of Exposure. J Pediatr. 2015 May 19.

Hinkle S, Laughon S, Catov J, Olsen J, Bech B. **First trimester coffee and tea** intake and risk of gestational diabetes mellitus: a study within a national birth cohort. BJOG. 2015 Feb;122(3):420-8.

Hinkle SN, Buck Louis GM, Rawal S,et al. A longitudinal study of **depression** and **gestational diabetes** in pregnancy and the postpartum period. Diabetologia. 2016 Sep 19.

Hinkle SN, Mumford SL, Grantz KL, et al. Association of **nausea and vomiting during pregnancy with pregnancy loss**: a secondary analysis of a randomized clinical trial [online Sept 26, 2016]. JAMA Intern Med. doi: 10.1001/jamainternmed.2016.5641

Hiscock H, Cook F, Bayer J, et al. Preventing **early infant sleep and crying problems** and postnatal depression: a randomized trial. Pediatrics. 2014 Feb;133(2):e346-54.

Hochner H, Friedlander Y, Calderon-Margalit R et al. Associations of maternal prepregnancy body mass index and gestational weight gain with adult offspring cardiometabolic risk factors: the Jerusalem Perinatal Family Follow-up Study. Circulation. 2012 Mar 20;125(11):1381-9.

Hodgkinson JA, Tucker KL, Crawford C, et al. Is self **monitoring of blood pressure** in pregnancy safe and effective? BMJ. 2014 Nov 18;349:g6616.

Hodnett ED, Downe S, Walsh D. **Alternative versus conventional institutional settings for birth**. Cochrane Database of Systematic Reviews 2012, Issue 8. Art. No.: CD000012. DOI: 10.1002/14651858.CD000012.pub4. Hospital birth centres are associated with lower rates of medical interventions during labour and birth and higher levels of satisfaction, without increasing risk to mothers or babies.

Hodyl NA, Stark MJ, Scheil W, et al. Perinatal outcomes following **maternal asthma** and cigarette smoking during pregnancy. Eur Respir J. 2013 Jul 30.

Hofmeyr GJ, Betrán AP, Singata-Madliki M, et al. Prepregnancy and early pregnancy **calcium supplementation among women at high risk of pre-eclampsia**: a multicentre, double-blind, randomised, placebo-controlled trial. Lancet. 2019 Jan 26;393(10169):330-339.

Hofmeyr GJ, Lawrie TA, Atallah ÁN, Duley L, Torloni MR. **Calcium supplementation during pregnancy** for preventing hypertensive disorders and related problems. Cochrane Database of Systematic Reviews 2014, Issue 6. Art. No.: CD001059. DOI: 10.1002/14651858.CD001059.pub4. Calcium supplementation (_ 1 g/day) is associated with a significant reduction in the risk of pre-eclampsia, particularly for women with low calcium diets. The treatment effectmay be overestimated due to small-study effects or publication bias. It also reduces preterm birth and the occurrence of the composite outcome 'maternal death or serious morbidity'. We considered these benefits to outweigh the increased risk of HELLP syndrome, which was small in absolute numbers. The World Health Organization recommends calcium 1.5 g to 2 g daily for pregnant women with low dietary calcium intake. The limited evidence on low-dose calcium supplementation suggests a reduction in pre-eclampsia, but needs to be confirmed by larger, high-quality trials. Pending such results, in settings of low dietary calcium where high-dose supplementation is not feasible, the option of lower-dose supplements (500 to 600 mg/day) might be considered in preference to no supplementation.

Hofmeyr GJ, Belizán JM, von Dadelszen P; **Calcium** and **Pre-eclampsia** (CAP) Study Group. Low-dose calcium supplementation for preventing pre-eclampsia: a systematic review and commentary. BJOG. 2014 Jul;121(8):951-7.

Hohwü L, Li J, Olsen J, et al. **Severe maternal stress** exposure due to bereavement before, during and after pregnancy and risk of overweight and **obesity** in young adult men: a Danish National Cohort Study. PLoS One. 2014 May 14;9(5):e97490.

Hollams EM, de Klerk NH, Holt PG, Sly PD. Persistent Effects of **Maternal Smoking during Pregnancy on Lung Function and Asthma in Adolescents**. Am J Respir Crit Care Med. 2013 Nov 19.

Homer CS, Ryan C, Leap N, et al. Group versus conventional antenatal care for women. Cochrane Database Syst Rev. 2012 Nov 14;11:CD007622. doi: 10.1002/14651858.CD007622.pub2.

Honigberg MC, Givertz MM. **Peripartum cardiomyopathy**. BMJ. 2019 Jan 30;364:k5287.

Hornig M et al. **Prenatal fever and autism risk**. Mol Psychiatry 2017 Jun 13.

Houtchens MK, Edwards NC, Schneider G, et al. **Pregnancy rates and outcomes in women with and without MS** in the United States. Neurology 2018;91: e1559–e1569.

Houtchens MK, Edwards NC, Phillips AL. **Relapses and disease-modifying drug treatment in pregnancy and live birth in US women with MS**. Neurology. 2018 Oct 23;91(17):e1570-e1578.

Howard LM, Megnin-Viggars O, Symington I, Pilling S; Guideline Development Group. **Antenatal and postnatal mental health**: summary of updated NICE guidance. BMJ. 2014 Dec 18;349:g7394.

Howley MM, Carter TC, Browne ML, et al; National Birth Defects Prevention Study. **Fluconazole** use and birth defects in the National Birth Defects Prevention Study. Am J Obstet Gynecol. 2015 Nov 27.

Huang W, Molitch M. Evaluation and Management of **Galactorrhea**. Am Fam Physician. 2012;85(11):1073-1080.

Hughes RC, Moore MP, Gullam JE, et al. An Early Pregnancy **HbA1c ≥5.9%** (41 mmol/mol) Is Optimal for Detecting Diabetes and Identifies Women at Increased Risk of Adverse Pregnancy Outcomes. Diabetes Care. 2014 Nov;37(11):2953-9.

Humphriss R, Hall A, May M, et al. **Prenatal alcohol exposure** and childhood balance ability: findings from a UK birth cohort study. BMJ Open. 2013 Jun 20;3(6).

Hussen HI, Persson M, et al. **Maternal overweight and obesity** are associated with increased risk of type 1 **diabetes** in offspring of parents without diabetes regardless of ethnicity. Diabetologia. 2015 May 6.

Hutchinson EA, De Luca CR, Doyle LW, et al. **School-age Outcomes of Extremely Preterm** or Extremely Low Birth Weight Children. Pediatrics. 2013 Mar 18.

Hutton EK, Hannah ME, Ross S, et al. Maternal outcomes at 3 months **after planned caesarean section versus planned vaginal birth** for twin pregnancies in the Twin Birth Study: a randomised controlled trial. BJOG. 2015 Aug 20.

Huybrechts KF, Palmsten K, Avorn J, et al. **Antidepressant use in pregnancy** and the risk of cardiac defects. N Engl J Med. 2014 Jun 19;370(25):2397-407.

Huybrechts KF, Bateman BT, Palmsten K, et al. **Antidepressant use late in pregnancy** and risk of persistent pulmonary hypertension of the newborn. JAMA. 2015 Jun 2;313(21):2142-51.

Huybrechts KF, Bateman BT, Desai RJ, et al. Risk of **neonatal drug withdrawal** after intrauterine co-exposure to **opioids** and **psychotropic** medications: cohort study. BMJ. 2017 Aug 2;358:j3326.

Huybrechts KF, Hernández-Díaz S, Patorno E, et al. **Antipsychotic Use** in Pregnancy and the Risk for Congenital Malformations. JAMA Psychiatry. 2016 Aug 17.

Huybrechts KF, Hernández-Díaz S, Straub L, et al. Association of **maternal first trimester ondansetron use with cardiac malformations** and **oral clefts** in offspring [online Dec 18, 2018.] JAMA. doi:10.1001/jama.2018.18307

Hviid A et al. Use of **selective serotonin reuptake inhibitors during pregnancy and risk of autism**. N Engl J Med 2013 Dec 19; 369:2406.

Hvolgaard Mikkelsen S, et al. **Maternal Caffeine Consumption during Pregnancy** and **Behavioral Disorders** in 11-Year-Old Offspring: A Danish National Birth Cohort Study. J Pediatr. 2017 Oct;189:120-127.e1.

Hynes KL, Otahal P, Hay I, Burgess JR. Mild **Iodine Deficiency** During Pregnancy Is Associated With Reduced Educational Outcomes in the Offspring: 9-Year Follow-up of the Gestational Iodine Cohort. J Clin Endocrinol Metab. 2013 May;98(5):1954-62.

Iams JD, Lynch CD. Stillbirth and lessons for pregnancy care. JAMA. 2011 Dec 14;306(22):2506-7.

Iams JD. Clinical practice. Prevention of **preterm parturition**. N Engl J Med. 2014 Jan 16

Illi S, Weber J, Zutavern A, et al. **Perinatal** influences on the development of **asthma and atopy in childhood**. Ann Allergy Asthma Immunol. 2014 Feb;112(2):132-139.e1.

Indraratna PL, Virk S, Gurram D, et al. Use of colchicine in pregnancy: a systematic review and meta-analysis. Rheumatology (Oxford). 2017 Sep 23.

Jarvis S, Dassan P, Piercy CN. **Managing migraine in pregnancy**. BMJ. 2018 Jan 25;360:k80.

Leong C, Raymond C, Château D, et al. **Psychotropic Drug Use** before, during, and after Pregnancy: A Population-Based Study in a Canadian Cohort (2001-2013). Can J Psychiatry. 2017 Aug;62(8):543-550.

International Weight Management in Pregnancy (i-WIP) Collaborative Group. Effect of diet and physical activity based interventions in pregnancy on gestational **weight gain** and pregnancy outcomes: meta-analysis of individual participant data from randomised trials. BMJ. 2017 Jul 19;358:j3119

Ishibashi K, Aiba T, Kamiya C, et al. **Arrhythmia risk and β-blocker therapy** in pregnant women with long QT syndrome. Heart. 2017 Mar 14.

Iumer I, Hadar E, Hadden DR, et al. **Diabetes and pregnancy**: an endocrine society clinical practice guideline. J Clin Endocrinol Metab. 2013 Nov;98(11):4227-49.

Jaafar SH, Lee KS, Ho JJ. Separate care for new mother and infant versus rooming-in for increasing the duration of **breastfeeding**.Cochrane Database of Systematic Reviews 2012, Issue 9. We found little evidence to support or refute the practice of mother-infant separation versus rooming-in. Therefore, we see no reason to practise it. We recommend a well designed RCT to investigate full mother-infant rooming-in versus partial rooming-in or separate care on all of the primary and secondary outcomes suggested.

Jackson RA et al. My **obstetrician got me fired**: How work notes can harm pregnant patients and what to do about it. Obstet Gynecol 2015 Aug; 126:250.

Jaddoe VW, de Jonge L, Hofman A, Franco OH, et al. **First trimester fetal growth restriction and cardiovascular risk** factors in school age children: population based cohort study. BMJ 2014;348:g14.

Jain V, Chari R, Maslovitz S, et al. **SOGC**: Guidelines for the Management of a **Pregnant Trauma Patient**. J Obstet Gynaecol Can. 2015 Jun;37(6):553-74.

Jais X, Olsson KM, Barbera JA, et al. Pregnancy outcomes in **pulmonary arterial hypertension** in the modern management era. Eur Respir J. 2012 Oct;40(4):881-5.

Janecka M,Kodesh A,Levine SZ,etal.Association of **autism spectrum disorder with prenatal exposure to medication** affecting neurotransmitter systems [online Oct 31, 2018]. JAMA Psychiatry. doi:10.1001/jamapsychiatry.2018.2728

Jang H, Bae JB, Dardiotis E, et al. Differential effects of **completed and incomplete pregnancies on the risk of Alzheimer disease**. Neurology. 2018 Aug 14;91(7):e643-e651.

Jarde A, Morais M, et al. **Neonatal Outcomes** in Women With Untreated Antenatal **Depression** Compared With Women Without Depression: A Systematic Review and Meta-analysis. JAMA Psyc. 2016 Jun 8.

Jarman M, Yuan Y, Pakseresht M, et al. Patterns and trajectories of **gestational weight gain**: a prospective cohort study. CMAJ Open. 2016 Jun 23;4(2):E338-45

Jasani B, Simmer K, Patole SK, et al. **Long chain polyunsaturated fatty acid supplementation** in infants born at term. Cochrane Database Syst Rev. 2017 Mar 10;3:CD000376. Most of the included RCTs reported no beneficial effects or harms of LCPUFA supplementation on neurodevelopmental outcomes of formula-fed full-term infants and no consistent beneficial effects on visual acuity. Routine supplementation of full-term infant milk formula with LCPUFA cannot be recommended at this time.

Jebeile H, Mijatovic J, Louie JC, et al. A systematic review and meta-analysis of **energy intake and weight gain** in pregnancy. Am J Obstet Gynecol 2016;214(4):465–83.

Jeejeebhoy FM, Zelop CM, et al; American Heart Association Emergency Cardiovascular Care Committee, Council on Cardiopulmonary, Critical Care, Perioperative and Resuscitation, Council on Cardiovascular Diseases in the Young, and Council on Clinical Cardiology. **Cardiac Arrest in Pregnancy**: Scientific Statement From the American Heart Association. Circulation. 2015 Nov 3;132(18):1747-73.

Jensen ET, van der Burg JW, O'Shea TM, et al. The Relationship of **Maternal Prepregnancy Body Mass Index** and Pregnancy Weight Gain to Neurocognitive Function at Age 10 Years among Children Born Extremely Preterm. J Pediatr. 2017 Mar 21.

Jensen HM, Gron R, Lidegaard O, et al. **Maternal depression, antidepressant use in pregnancy and Apgar scores in infants**. Br J Psychiatry. 2013 May;202(5):347-51.

Jimenez-Solem E, Andersen JT, Petersen M, et al. SSRI Use During Pregnancy and Risk of **Stillbirth and Neonatal Mortality**. Am J Psychiatry. 2013 Jan 30.

Jin J. **Babies With Low Birth Weight**. JAMA. 2015 Jan 27;313(4):432.

Jin J. Treatments for **Nausea and Vomiting** During Pregnancy. JAMA. 2016 Oct 4;316(13):1420.

Jo H, Schieve LA, Sharma AJ, et al. **Maternal prepregnancy body mass index** and child psychosocial development at 6 years of age. Pediatrics. 2015 May;135(5)

Johal T, Lees CC, Everett TR, et al. The **nitric oxide pathway** and possible therapeutic options in **pre-eclampsia**. Br J Clin Pharmacol. 2013 Dec 9

Johansen SL, Robakis TK, Williams KE, Rasgon NL. **Management of perinatal depression** with non-drug interventions. BMJ. 2019 Feb 25;364:l322.

Johansson K et al. **Outcomes of pregnancy after bariatric surgery**. N Engl J Med 2015 Feb 26; 372:814.

Johansson S, Villamor E, Altman M, et al. **Maternal overweight and obesity in early pregnancy and risk of infant mortality**: a population based cohort study in Sweden. BMJ 2014;349:g6572.

Johnson KC, Laprairie JL, Brennan PA, et al. **Prenatal Antipsychotic Exposure and Neuromotor Performance** During Infancy. Arch Gen Psychiatry. 2012 Apr 2.

Johnson EL, Burke AE, Wang A, et al. **Unintended pregnancy, prenatal care, newborn outcomes, and breastfeeding in women with epilepsy**. Neurology. 2018 Sep 11;91(11):e1031-e1039.

Jones HE, Deppen K, Hudak ML, et al. Clinical care for **opioid-using** pregnant and postpartum women: the role of obstetric providers. Am J Obstet Gynecol. 2014 Apr;210(4):302-10.

Jones I, Shakespeare J. **Postnatal depression**. BMJ. 2014 Aug 14;349:g4500.

Jones I, Chandra PS, Dazzan P, et al. **Bipolar disorder, affective psychosis, and schizophrenia** in pregnancy and the post-partum period. Lancet. 2014 Nov 15;384(9956):1789-99.

Jones LV, Ray A, Moy FM, et al. **Techniques of monitoring blood glucose** during pregnancy for women with pre-existing diabetes. Cochrane Database Syst Rev. 2019 May 23;5:CD009613. Two new studies (406 women) have been incorporated to one of the comparisons for this update. Although the evidence suggests that CGM in comparison to intermittent glucose monitoring may reduce hypertensive disorders of pregnancy, this did not translate into a clear reduction for pre-eclampsia, and so this result should be viewed with caution. No differences were observed for other primary outcomes for this comparison.

Jones M, Lewis S, Parrott S, et al. **Re-starting smoking** in the postpartum period after receiving a smoking cessation intervention: a systematic review. Addiction. 2016 Mar 16.

Jonsdottir OH et al. Timing of the **introduction of complementary foods** in infancy: A randomized controlled trial. Pediatrics 2012 Dec; 130:1038.

Jordan S, Morris JK, Davies GI, et al. **Selective Serotonin Reuptake Inhibitor (SSRI) Antidepressants in Pregnancy and Congenital Anomalies**: Analysis of Linked Databases in Wales, Norway and Funen, Denmark. PLoS One. 2016 Dec 1;11(12):e0165122.

Jordan SJ et al. **Breastfeeding and endometrial cancer risk:** An analysis from the Epidemiology of Endometrial Cancer Consortium. Obstet Gynecol 2017 Jun; 129:1059.

Josephson CD, Caliendo AM, Easley KA, et al. Blood Transfusion and **Breast Milk Transmission of Cytomegalovirus** in Very Low-Birth-Weight Infants : A Prospective Cohort Study. JAMA Pediatr. 2014 Sep 22.

Judy AE, McCain CL, Lawton ES, et al. **Systolic Hypertension, Preeclampsia-Related Mortality, and Stroke** in California. Obstet Gynecol. 2019 Jun;133(6):1151-1159.

Julvez J, Méndez M, Fernandez-Barres S, et al. Maternal Consumption of **Seafood in Pregnancy** and Child Neuropsychological Development: A Longitudinal Study Based on a Population With High Consumption Levels. Am J Epidemiol. 2016 Jan 5.

Jumah NA, Graves L, Kahan M. The management of **opioid dependence during pregnancy** in rural and remote settings. CMAJ. 2015 Jan 6;187(1):E41-E46.

Jumah NA, Edwards C, Balfour-Boehm J, et al. Observational study of the safety of **buprenorphine+naloxone in pregnancy** in a rural and remote population. BMJ Open. 2016 Oct 31;6(10):e011774.

Jurkovic D, Overton C, Bender-Atik R. Diagnosis and management of **first trimester miscarriage**. BMJ. 2013 Jun 19;346:f3676.

Kales SN, Thompson AM. A young woman concerned about **mercury**. CMAJ. 2016 Feb 2;188(2):133-4.
Kallioinen M, Eadon H, Murphy MS et al. Developmental follow-up of children and young people born **preterm**: summary of NICE guidance. BMJ. 2017 Aug 10;358:j3514
Kamel H et al. Risk of a **thrombotic event after the 6-week postpartum** period. N Engl J Med 2014 Feb 13.
Kamel H, Roman MJ, Pitcher A, et al. Pregnancy and the Risk of **Aortic Dissection or Rupture**: A Cohort-Crossover Analysis. Circulation. 2016 Aug 16;134(7):527-33.
Kaplan YC, Koren G, Bozzo P. **Fluconazole** exposure during pregnancy. Can Fam Physician. 2015 Aug;61(8):685-6
Kaplan YC, Ozsarfati J, Nickel C, et al. Reproductive Outcomes Following **Hydroxychloroquine** Use for Autoimmune Diseases: A Systematic Review and Meta-analysis. Br J Clin Pharmacol. 2015 Dec 23.
Kaplan YC, Koren G, Ito S, et al. **Fluconazole** use during breastfeeding. Can Fam Physician. 2015 Oct;61(10):875-6.
Karanam A, Pennell PB, French JA, et al. **Lamotrigine clearance increases by 5 weeks gestational age**: Relationship to estradiol concentrations and gestational age. Ann Neurol. 2018 Aug 31.
Karceski S. **Pregnancy, anti-seizure medications, and seizures**. Neurology. 2018 Sep 25;91(13):e1271-e1274.
Karlsson G, Francis G, Koren G, et al. Pregnancy outcomes in the clinical development program of **fingolimod** in multiple sclerosis. Neurology 2014;82:674–680.
Kassebaum NJ, et al. Global, regional, and national levels and causes of **maternal mortality** during 1990-2013: a systematic analysis for the Global Burden of Disease Study 2013. Lancet. 2014 May 2.
Kazemier BM, Koningstein FN, Schneeberger C, et al. Maternal and neonatal consequences of treated and untreated **asymptomatic bacteriuria in pregnancy**: a prospective cohort study with an embedded randomized controlled trial. Lancet Infect Dis 2015; online Aug 6.
Kazerooni R, Blake A, Thai J. Predictors of Pregnancy in Female Veterans Receiving a **Hormonal Contraceptive Pill, Patch, or Ring**. Ann Pharmacother. 2015 Dec;49(12):1284-90.
Keim SA, Hogan JS, McNamara KA, et al. **Microbial Contamination** of **Human Milk** Purchased Via the Internet. Pediatrics. 2013 Oct 21.
Kelly D, O'Dowd T, Reulbach U. Use of **folic acid supplements** and risk of cleft lip and palate in infants: a population-based cohort study. Br J Gen Pract 2012; doi:10.3399/ bjgp12X652328.
Kelly L, Guilfoyle J, Dooley J, et al. Incidence of **narcotic abuse during pregnancy** in northwestern Ontario: Three-year prospective cohort study. Can Fam Physician. 2014 Oct;60(10):e493-8.
Kelly Y, Iacovou M, Quigley M, et al. **Light drinking versus abstinence** in pregnancy - behavioural and cognitive outcomes in 7-year-old children: a longitudinal cohort study. BJOG. 2013 Apr 17.
Keenan K, Hipwell AE, Bortner J, et al. Association between **fatty acid supplementation and prenatal stress** in African Americans: a randomized controlled trial. Obstet Gynecol. 2014 Dec;124(6):1080-7.
Keni RR, Jose M, Sarma PS, et al. **Teratogenicity of antiepileptic dual therapy**: Dose-dependent, drug-specific, or both? Neurology. 2018 Feb 27;90(9):e790-e796.
Kfouri J, D'Souza R. **Antenatal corticosteroids**. CMAJ. 2017 Feb 27;189(8):E319.
Khalifeh H, Hunt IM, Appleby L, et al. **Suicide in perinatal and non-perinatal women** in contact with psychiatric services: 15 year findings from a UK national inquiry. Lancet Psychiatry 2016;3(3):233–42.
Khan F, Vaillancourt C, Bourjeily G. **Diagnosis and management of deep vein thrombosis** in pregnancy. BMJ. 2017 May 31;357:j2344.
KhandwalaYS, BakerVL, ShawGM, StevensonD, LuY, EsienbergML. Association of **paternal age and perinatal outcomes** between 2007 and 2016 in the United States: population based cohort study. BMJ 2018;k4372.
Kharbanda EO, Vazquez-Benitez G, Lipkind HS, et al. Evaluation of the Association of **Maternal Pertussis Vaccination** With Obstetric Events and Birth Outcomes. JAMA. 2014 Nov 12;312(18):1897-1904.
Kharbanda EO, Vazquez-Benitez G, Lipkind HS, et al. Risk of **Spontaneous Abortion After Inadvertent Human Papillomavirus Vaccination in Pregnancy**. Obstet Gynecol. 2018 Jul;132(1):35-44.
Khashan AS, Evans M, Kublickas M, et al. **Preeclampsia and risk of end stage kidney disease**: A Swedish nationwide cohort study. PLoS Med. 2019 Jul 30;16(7):e1002875.
Khoshnood B, Loane M, de Walle H, et al. Long term trends in the prevalence of **neural tube defects (folic acid**) in Europe: population based study. BMJ 2015;351:h5949.
Kiefte-de Jong JC, Jaddoe VW, Uitterlinden AG, et al. Levels of **antibodies against tissue transglutaminase** during pregnancy are associated with reduced fetal weight and birth weight. Gastroenterology. 2013 Apr;144(4):726-735.e2.
Kieler H, Artama M, Engeland A, et al. Selective serotonin reuptake inhibitors during pregnancy and risk of persistent pulmonary hypertension in the newborn: population based cohort study from five Nordic countries. BMJ 2012;344:d8012.
Kim C, Barnard S, Neilson JP, et al. **Medical treatments for incomplete miscarriage**. Cochrane Database Syst Rev. 2017 Jan 31;1:CD007223. The available evidence suggests that medical treatment, with misoprostol, and expectant care are both acceptable alternatives to routine surgical evacuation given the availability of health service resources to support all three approaches. Further studies, including long-term follow-up, are clearly needed to confirm these findings. There is an urgent need for studies on women who miscarry at more than 13 weeks' gestation.
Kim SC, Hernandez-Diaz S. Editorial: safety of **immunosuppressive drugs** in pregnant women with systemic inflammatory diseases. Arthritis Rheumatol. 2014 Feb;66(2):246-9.
Kim SY, Sharma AJ, et al. Association of **Maternal Body Mass Index**, Excessive Weight Gain, and Gestational Diabetes Mellitus With Large-for-Gestational-Age Births. Obstet Gynecol. 2014 Apr;123(4):737-44.
Kingston D, Heaman M, Fell D, Chalmers B; on behalf of the Maternity Experiences Study Group of the Canadian Perinatal Surveillance System, Public Health Agency of Canada. Comparison of **Adolescent, Young Adult, and Adult Women's Maternity Experiences** and Practices. Pediatrics. 2012 Apr 23.
Kinney MO, Morrow J. **Epilepsy in pregnancy**. BMJ. 2016 Jun 2;353:i2880.
Kirby N, Kilsby A, Walker R. **Assessing low mood** during pregnancy. BMJ. 2019 Jul 29;366:l4584.
Kivistö J, Lehto SM, Halonen K, et al. Maternal Use of **Selective Serotonin Reuptake Inhibitors** and **Lengthening of the Umbilical Cord**: Indirect Evidence of Increased Foetal Activity-A Retrospective Cohort Study. PLoS One. 2016 Apr 29;11(4).
Kjær MM, Lauenborg J, Breum BM, Nilas L. The **risk of adverse pregnancy outcome after bariatric surgery**: a nationwide register-based matched cohort study. Am J Obstet Gynecol. 2013 Jun;208(6):464.e1-5.
Klebanoff MA, Keim SA. Maternal **Caffeine** Intake During Pregnancy and Child Cognition and Behavior at 4 and 7 Years of Age. Am J Epidemiol. 2015 Nov 18.
Knight H, Gurol-Urganci I, van der Meulen J, et al. **Vaginal birth after caesarean section**: a cohort study investigating factors associated with its uptake and success. BJOG. 2013 Nov 20.
Koren G. Is **ondansetron** safe for use during pregnancy? Can Fam Physician. 2012 Oct;58(10):1092-3.
Koren G. **Treating morning sickness PRN**? Can Fam Physician. 2013 Feb;59(2):150-1.
Koren G, Carey N, Gagnon R, Maxwell C, Nulman I, Senikas V. **Cancer chemotherapy** and pregnancy. J Obstet Gynaecol Can. 2013 Mar;35(3):263-78.
Koren G, Madjunkova S, Maltepe C. **Bias against the null hypothesis: Scaring pregnant women** about drugs in pregnancy. Can Fam Physician. 2014 May;60(5):441-2.
Koren G. **Polyunsaturated fatty acids** and fetal brain development. Can Fam Physician. 2015 Jan;61(1):41-2.
Kourtis AP, Read JS, Jamieson DJ. **Pregnancy and Infection**. N Engl J Med. 2014 Jun 5;370(23):2211-2218.

Koutrolou-Sotiropoulou P, Parikh PB, Miller C, et al. Impact of **Heart Disease on Maternal and Fetal Outcomes in Pregnant Women**. Am J Cardiol. 2015 Aug 1;116(3):474-80
Koyanagi A, Zhang J, Dagvadorj A, et al. **Macrosomia** in 23 developing countries: an analysis of a multicountry, facility-based, cross-sectional survey. Lancet. 2013 Jan 3.
Kramer CK, Campbell S, Retnakaran R. **Gestational diabetes** and the risk of cardiovascular disease in women: a systematic review and meta-analysis. Diabetologia. 2019 Mar 7.
Krans EE and Patrick SW.**Opioid use** disorder in pregnancy: Health policy and practice in the midst of an epidemic. Obstet Gynecol 2016 Jul; 128:4.
Kronenfeld N, Ziv Baran T, Berlin M, et al. **Chronic use of psychotropic medications in breastfeeding** women: Is it safe? PLoS One. 2018 May 21;13(5):e0197196.
Kubo A, Ferrara A, Windham GC, et al. **Maternal hyperglycemia** during pregnancy predicts **adiposity of the offspring**. Diabetes Care. 2014 Nov;37(11):2996-3002.
Kulkarni AD et al. **Fertility treatments and multiple births** in the United States. N Engl J Med 2013 Dec 5; 369:2218.
Kulkarni J. **Perimenopausal depression** - an under-recognised entity. Aust Prescr. 2018 Dec;41(6):183-185.
Kulkarni J, Worsley R, Gilbert H, et al. A prospective cohort study of **antipsychotic medications in pregnancy**: the first 147 pregnancies and 100 one year old babies. PLoS One. 2014 May 2;9(5):e94788.
Kuppermann M, Pena S, Bishop JT, et al. Effect of enhanced information, values clarification, and removal of financial barriers on use of **prenatal genetic testing**: a randomized clinical trial. JAMA. 2014.
Kvigne VL, Randall B, Simanton EG, et al. **Blood Alcohol Levels** for American Indian Mothers and Newborns. Pediatrics. 2012 Sep 10.
Kwan ML, Miglioretti DL, Marlow EC, et al. **Trends in Medical Imaging** During Pregnancy in the United States and Ontario, Canada, 1996 to 2016. JAMA Netw Open. 2019 Jul 3;2(7):e197249.
Kyrgiou M, Mitra A, Arbyn M, et al. **Fertility and early pregnancy** outcomes after treatment for **cervical intraepithelial neoplasia**: systematic review and meta analysis. BMJ. 2014 Oct 28;349:g6192.
Lahti-Pulkkinen M, Bhattacharya S, Wild SH, et al. Consequences of being **overweight or obese during pregnancy on diabetes in the offspring**: a record linkage study in Aberdeen, Scotland. Diabetologia. 2019 Jun 19.
Lakhi N, Govind A. Unplanned pregnancy in a woman with **Crohn** disease. Can Fam Physician. 2012 May;58(5):531-2.
Lam J, Kelly L, Ciszkowski C et al. Central nervous system depression of neonates breastfed by mothers receiving oxycodone for postpartum analgesia. J Pediatr. 2012 Jan;160(1):33-7.e2.
Lamain-de Ruiter M, et al. External validation of prognostic models to **predict risk of gestational diabetes** mellitus in one Dutch cohort: prospective multicentre cohort study. BMJ. 2016 Aug 30;354:i4338.
Lamont K, Scott NW, Jones GT, Bhattacharya S. **Risk of recurrent stillbirth**: systematic review and meta-analysis. BMJ. 2015 Jun 24;350:h3080.
Langan RC, Goodbred AJ. Identification and **Management of Peripartum Depression**. Am Fam Physician. 2016;93(10):852-858.
Langlois E, Cusson-Dufour C, Moumneh T, et al. Could the **YEARS algorithm be used to exclude pulmonary embolism** during pregnancy? Data from the CT-PE-pregnancy study. J Thromb Haemost. 2019 May 20.
Larson JJ, Graham DL, Singer LT, et al. **Cognitive and Behavioral Impact on Children Exposed to Opioids** During Pregnancy. Pediatrics. 2019 Aug;144(2).
Lassi ZS, Salam RA, Haider BA, et al. **Folic acid supplementation** during pregnancy for maternal health and pregnancy outcomes. Cochrane Database Syst Rev. 2013 Mar 28;(3):CD006896
Lawlor DA, Wills AK, Fraser A, et al. Association of maternal **vitamin D status during pregnancy** with bone-mineral content in off spring: a prospective cohort study. Lancet 2013; online March 19.
Lavecchia M, Chari R, Campbell S, et al. **Ondansetron in pregnancy and the risk of congenital malformations**: a systematic review. J Obstet Gynaecol Can 2018;40:910-8.
Lebrun-Vignes B, Le Cleach L, Giraudeau B, Chosidow O. Safety of **topical corticosteroid** use during pregnancy. Arch Dermatol. 2012 Apr;148(4):525-7.
Lecarpentier E, Morel O, Fournier T, Elefant E, Chavatte-Palmer P, Tsatsaris V. **Statins and Pregnancy**: Between Supposed Risks and Theoretical Benefits. Drugs. 2012 Apr 5.
Leeman L, Dresang LT, Fontaine P. **Hypertensive Disorders of Pregnancy**. Am Fam Physician. 2016;93(2):121-127.
LeFevre ML. **Low-Dose Aspirin Use for the Prevention of Morbidity and Mortality From Preeclampsia**: U.S. Preventive Services Task Force Recommendation Statement (USPSTF) . Ann Intern Med. 2014 Sep9.
Legro RS, Dodson WC, et al. Randomized Controlled Trial of **Preconception Interventions in Infertile Women With Polycystic Ovary Syndrome**. J Clin Endocrinol Metab. 2015 Sep 24:jc20152778.
Lei Q, Zhou X, Zhou YH, et al. **Prehypertension During Normotensive Pregnancy** and Postpartum Clustering of Cardiometabolic Risk Factors: A Prospective Cohort Study. Hypertension. 2016 Jun 27.
Lensen SF, Manders M, Nastri CO, et al. **Endometrial injury for pregnancy following sexual intercourse or intrauterine insemination**. Cochrane Database Syst Rev. 2016 Jun 14;6:CD011424. It is uncertain whether endometrial injury improves the probability of pregnancy and live birth/ongoing pregnancy in women undergoing IUI or attempting to conceive via sexual intercourse. The pooled results should be interpreted with caution as we graded the quality of the evidence as either low or very low. The main reasons we downgraded the quality of the evidence were most included studies were at a high risk of bias and had an overall low level of precision.
Leung AM, Pearce EN, Braverman LE, et al. **AAP recommendations on iodine** nutrition during pregnancy and lactation. Pediatrics. 2014 Oct;134(4):e1282
Leverrier-Penna S, Mitchell RT, Becker E, et al. **Ibuprofen** is **deleterious** for the development of **first trimester human fetal ovary** ex vivo. Hum Reprod. 2018 Feb 2.
Levie D, Korevaar TIM, Bath SC, et al. **Thyroid Function in Early Pregnancy, Child IQ, and Autistic Traits**: a Meta-analysis of Individual-participant Data. J Clin Endocrinol Metab. 2018 May 10.
Levine SZ, et al. Association of Maternal Use of **Folic Acid and Multivitamin Supplements in the Periods Before and During Pregnancy With the Risk of Autism** Spectrum Disorder in Offspring. JAMA Psychiatry. 2018 Jan 3.
Li DK, Ferber JR, Odouli R, Quesenberry C. Use of **nonsteroidal antiinflammatory drugs** during pregnancy and the risk of miscarriage. Am J Obstet Gynecol. 2018 Sep;219(3):275.e1-275.e8.
Li J, Robinson M, Malacova E, et al. **Maternal Life Stress Events** in Pregnancy Link to Children's School Achievement at Age 10 Years. J Pediatr. 2012 Oct 17.
Li N, Li Z, Ye R, et al. Impact of **Periconceptional Folic Acid Supplementation** on Low Birth Weight and Small-for-Gestational-Age Infants in China: A Large Prospective Cohort Study. J Pediatr. 2017 May 22.
Li Y, Ley SH, Tobias DK, Chiuve SE, et al. Birth weight and later life adherence to **unhealthy lifestyles** in predicting type 2 diabetes: prospective cohort study. BMJ. 2015 Jul 21;351:h3672.
Li Z, Ye R, Zhang L, Li H, Liu J, Ren A. **Folic Acid Supplementation** During Early Pregnancy and the Risk of Gestational Hypertension and Preeclampsia. Hypertension. 2013 Feb 11.
Liew Z, Ritz B, Rebordosa C, Lee PC, Olsen J. **Acetaminophen** use during pregnancy, behavioural problems, and hyperkinetic disorders [online February 24, 2014]. JAMA Pediatr. doi:10.1001/jamapediatrics.2013.4914.
Lim Angelina, Stewart Kay, König Kai, et al. Systematic Review of the Safety of Regular Preventive Asthma Medications During Pregnancy. Ann Pharmacother July/August 2011 45:931-945.
Lima FV, Yang J, Xu J, et al. National Trends and In-Hospital Outcomes in Pregnant Women **with Heart Disease** in the USA. Am J Cardio. 2017.
Lind JN, Interrante JD, Ailes ED, et al. **Maternal Use of Opioids During Pregnancy and Congenital Malformations**: A Systematic Review. Peds. 2017;139(6):e20164131
Lindblad AJ, Koppula S. **Ginger for nausea and vomiting** of pregnancy. Can Fam Physician. 2016 Feb;62(2):145.
Linder K, Schleger F, Kiefer-Schmidt I, et al. **Gestational Diabetes** Impairs Human **Fetal Postprandial Brain Activity**. J Clin Endocrinol Metab. 2015 Oct 14:jc20152692.

Lisonkova S, Muraca GM, Potts J, et al. Association between **prepregnancy body mass index and severe maternal morbidity**.JAMA. doi:10.1001/jama.2017.16191
Liu C, Cnattingius S, Bergström M, Östberg V, Hjern A. **Prenatal parental depression and preterm birth**: a national cohort study. BJOG. 2016 Jan 19.
Liu JM, Mei Z, Ye R, et al. **Micronutrient Supplementation** and Pregnancy Outcomes: Double-Blind Randomized Controlled Trial in China. JAMA Intern Med. 2013 Jan 7:1-7.
Liu S, Joseph KS, Lisonkova S et al; Canadian **Perinatal Surveillance System** (Public Health Agency of Canada). Association between maternal chronic conditions and congenital heart defects: a population-based cohort study. Circulation. 2013 Aug 6;128(6):583-9.
Liu S, Rouleau J, León JA, et al; Canadian Perinatal Surveillance System. Impact of **pre-pregnancy diabetes mellitus on congenital anomalies, Canada**, 2002-2012. Health Promotion and Chronic Disease Prevention in Canada: Research, Policy and Practice 2015;35(5). http://www.phac-aspc.gc.ca/publicat/hpcdp-pspmc/35-5/index-eng.php (accessed July 21, 2015).
Liu X, Olsen J, Pedersen LH, et al. **Antidepressant Use** During Pregnancy and Asthma in the Offspring. Pediatrics. 2015 Mar 9.
Liu X, Agerbo E, Li J, et al. **Depression and Anxiety in the Postpartum Period and Risk of Bipolar Disorder**: A Danish Nationwide Register-Based Cohort Study. J Clin Psychiatry. 2017 May;78(5):e469-e476.
Liu X, Agerbo E, Schlünssen V, et al. **Maternal asthma** severity and control during pregnancy and risk of offspring asthma. J Allergy Clin Immunol. 2017 Jun 27.
Liu X, Agerbo E, Ingstrup KG, et al. **Antidepressant use during pregnancy and psychiatric disorders in offspring**: Danish nationwide register based cohort study. BMJ 2017;358:j3668.
Liu Y, Colditz GA, Rosner B, et al. **Alcohol Intake** Between Menarche and First Pregnancy: A Prospective Study of Breast Cancer Risk. J Natl Cancer Inst. 2013 Aug 28.
Loibl S, Han S, von Minckwitz G, et al. Treatment of **breast cancer during pregnancy**: an observational study. Lancet Oncol 2012; published online Aug 16.
Loomans EM, Hofland L, van der Stelt O, et al. **Caffeine Intake** During Pregnancy and Risk of Problem Behavior in 5- to 6-Year-Old Children. Pediatrics. 2012 Jul 9.
Louis JM, Mogos MF, Salemi JL, et al. **Obstructive sleep apnea** and severe maternal-infant morbidity/mortality in the United States, 1998-2009. Sleep. 2014 May 1;37(5):843-9.
Løvvik TS, Carlsen SM, Salvesen Ø, et al. Use of **metformin to treat pregnant women with polycystic ovary syndrome** (PregMet2): a randomised, double-blind, placebo-controlled trial. Lancet Diabetes Endocrinol 2019; published online Feb 18.
Lowe WL Jr, Scholtens DM, Lowe LP, et al; HAPO Follow-up Study Cooperative Research Group. Association of **Gestational Diabetes With Maternal Disorders of Glucose Metabolism and Childhood** Adiposity. JAMA. 2018 Sep 11;320(10):1005-1016.
Lowe WL Jr, Lowe LP, Kuang A, et al; HAPO Follow-up Study Cooperative Research Group. **Maternal glucose levels during pregnancy and childhood adiposity in the Hyperglycemia and Adverse Pregnancy** Outcome Follow-up Study. Diabetologia. 2019 Jan 15.
Lu E, Wang BW, Guimond C, et al. **Disease-modifying drugs for multiple sclerosis** in pregnancy: A systematic review. Neurology. 2012 Sep 11;79(11):1130-5.
Ludwig DS, Rouse HL, Currie J. **Pregnancy weight gain and childhood body weight**: a within-family comparison. PLoS Med. 2013 Oct;10(10):e1001521.
Ludvigsson JF, Neovius M, Söderling J, et al. Periconception **glycaemic control in women with type 1 diabetes and risk of major birth defects**: population based cohort study in Sweden. BMJ. 2018 Jul 5;362:k2638.
Lugo-Candelas C, Cha J, et al. Associations Between **Brain Structure and Connectivity in Infants and Exposure to Selective Serotonin Reuptake Inhibitors During Pregnancy**. JAMA Pediatr. 2018 Apr 9.
Luke B, Brown MB, Wantman E, et al. Cumulative birth rates with linked **assisted reproductive technology** cycles. N Engl J Med. 2012 Jun 28;366(26):2483-91.
Lund M, Pasternak B, Davidsen RB, et al. Use of macrolides in mother and child and risk of infantile hypertrophic pyloric stenosis: nationwide cohort study. BMJ. 2014 Mar 11.
Lupattelli A, Chambers CD, Bandoli G, et al. Association of Maternal Use of **Benzodiazepines and Z-Hypnotics During Pregnancy** With Motor and Communication Skills and Attention-Deficit/Hyperactivity Disorder kSymptoms in Preschoolers. JAMA Netw Open. 2019 Apr 5;2(4):e191435.
Lutsiv O, Giglia L, Pullenayegum E et al. A Population-Based Cohort Study of **Breastfeeding According to Gestational Age** at Term Delivery. J Pediatr. 2013 Aug 3.
Luu TM, Katz SL, Leeson P, et al. **Preterm birth**: risk factor for early-onset chronic diseases. CMAJ. 2016 Jul 12;188(10):736-46.
Luyckx VA, Bertram JF, Brenner BM et al. Effect of fetal and child health on kidney development and long-term risk of hypertension and kidney disease. Lancet. 2013 May 30.
Lv C, Chen C, Chen Q, et al. **Multiple pregnancies and the risk of diabetes mellitus** in postmenopausal women. Menopause. 2019 May 6.
Lytvyn L, Siemieniuk RA, Dilmitis S, et al. Values and preferences of women living with **HIV who are pregnant, postpartum or considering pregnancy** on choice of antiretroviral therapy during pregnancy. BMJ Open. 2017 Sep 11;7(9):e019023.
Lytzen R, Vejlstrup N, Bjerre J, et al. Live-born **major congenital heart disease** in Denmark: incidence, detection rate, and **termination of pregnancy rate** from 1996 to 2013 [online July 18, 2018]. JAMA Cardiol.doi:10.1001/jamacardio.2018.2009
MacDonald SC, Bateman BT, McElrath TF, Hernández-Díaz S. Mortality and morbidity during delivery hospitalization among **pregnant women with epilepsy** in the United States [online July 6, 2015]. JAMA Neurol. doi:10.1001 /jamaneurol.2015.1017.
Macdonald-Wallis C, Lawlor DA, Fraser A, et al. **Blood pressure change** in normotensive, gestational hypertensive, preeclamptic, and essential hypertensive pregnancies. Hypertension. 2012 Jun;59(6):1241-8.
Macdonald-Wallis C, Silverwood RJ, de Stavola BL, et al. **Antenatal blood pressure** for prediction of pre-eclampsia, preterm birth, and small for gestational age babies: development and validation in two general population cohorts. BMJ. 2015 Nov 17;351:h5948.
MacDonald SC, McElrath TF, Hernández-Díaz S. **Pregnancy Outcomes in Women with Multiple Sclerosis**. Am J Epidemiol. 2018 Aug 28.
MacDorman MF, Declercq E, Cabral H, et al. Recent Increases in the **U.S.Maternal Mortality Rate**: Disentangling Trends From Measurement Issues. Obstet Gynecol. 2016 Aug 5.
Mackay E, Dalman C, Karlsson H, Gardner RM. Association of **gestational weight gain** and maternal body mass index in early pregnancy with risk for nonaffective **psychosis** in offspring [online Feb 22, 2017].JAMA Psychiatry. doi:10.1001/jamapsychiatry.2016.4257
Mackin ST, Nelson SM, Kerssens JJ, et al. **Diabetes and pregnancy**: national trends over a 15 year period. Diabetologia. 2018 Jan 11.
MacMahon E. Investigating the pregnant woman exposed to a child with a rash. BMJ. 2012 Mar 26;344:e1790. (chickenpox)
Maeda A, Bateman BT, Clancy CR, Creanga AA, Leffert LR. **Opioid Abuse and Dependence** during Pregnancy: Temporal Trends and Obstetrical Outcomes. Anesthesiology. 2014 Dec;121(6):1158-65.
Magee LA, Pels A, Helewa M, et al; **Canadian Hypertensive Disorders of Pregnancy (HDP)** Working Group. Diagnosis, evaluation, and management of the **hypertensive disorders of pregnancy**.http://download.journals.elsevierhealth.com/pdfs/journals/2210-7789/PIIS221077891400004X.pdf(accessed June 25, 2014).
Magee LA, von Dadelszen P, Rey E, et al. **Less-tight versus tight control of hypertension in pregnancy**. N Engl J Med 2015; 372:407-17.

Magee LA, Pels A, Helewa M, Rey E, von Dadelszen P; **Canadian Hypertensive Disorders of Pregnancy (HDP)** Working Group; Canadian Hypertensive Disorders of Pregnancy HDP Working Group. The **hypertensive disorders of pregnancy** (29.3). Best Pract Res Clin Obstet Gynaecol. 2015 Jul;29(5):643-57.

Magnus MC, Miliku K, Bauer A, et al. **Vitamin D and risk of pregnancy related hypertensive disorders**: mendelian randomisation study. BMJ. 2018 Jun 20;361:k2167.

Magnus MC, Wilcox AJ, Morken NH, et al. Role of **maternal age and pregnancy history in risk of miscarriage**: prospective register based study. BMJ. 2019 Mar 20;364:l869.

Mahadevan U et al. Drug safety and risk of **adverse outcomes for pregnant patients with inflammatory bowel diseases**. Gastroenterology 2016 Oct 18.

Mahadevan U, Robinson C, Bernasko N, et al**. Inflammatory Bowel Disease** in Pregnancy Clinical Care Pathway: A Report From the American Gastroenterological Association (AGA) IBD Parenthood Project Working Group. Inflamm Bowel Dis. 2019 Mar 1.

Maher GM, O'Keeffe GW, Kearney PM, et al. Association of **Hypertensive Disorders of Pregnancy With Risk of Neurodevelopmental Disorders** in Offspring: A Systematic Review and Meta-analysis. JAMA Psychiatry. 2018 Jun 6.

Main EK et al. National Partnership for Maternal Safety: **Consensus bundle on obstetric hemorrhage**. Obstet Gynecol 2015 Jul; 126:155.

Makrides M, Best K, Yelland L, et al. A Randomized **Trial of Prenatal n-3 Fatty Acid Supplementation** and Preterm Delivery. N Engl J Med. 2019 Sep 12;381(11):1035-1045.

Makrides M, Crosby DD, Bain E, et al. **Magnesium supplementation** in pregnancy. Cochrane Database Syst Rev. 2014 Apr 3;4:CD000937. There is not enough high-quality evidence to show that dietary magnesium supplementation during pregnancy is beneficial.

Makrides M, Gould JF, Gawlik NR, et al. Four-Year Follow-up of Children Born to Women in a Randomized Trial of **Prenatal DHA Supplementation**. JAMA. 2014 May 7;311(17):1802-4.

Malinowski AK, Shehata N, D'Souza R, et al. **Prophylactic transfusion for pregnant women** with sickle cell disease: a systematic review and meta-analysis. Blood. 2015 Aug 24.

Malm H, et al. Pregnancy Complications Following **Prenatal Exposure to SSRIs or Maternal Psychiatric Disorders**: Results From Population-Based National Register Data. Am J Psychiatry. 2015 Aug 4

Mamluk L, Edwards HB, Savović J, et al. Low **alcohol consumption** and pregnancy and childhood outcomes: time to change guidelines indicating apparently 'safe' levels of alcohol during pregnancy? A systematic review and meta-analyses. BMJ Open. 2017 Aug 3;7(7):e015410

Man KKC, Chan EW, Ip P, et al. **Prenatal antidepressant use and risk of attention-deficit/hyperactivity disorder** in offspring: population based cohort study. BMJ 2017;357:j2350.

Männistö T, Mendola P, Vääräsmäki M, et al. **Elevated blood pressure** in pregnancy and subsequent chronic disease risk. Circulation 2013; 127:681-690.

Maraka S, O'Keeffe DT, Montori VM. **Subclinical Hypothyroidism** During Pregnancy-Should You Expect This When You Are Expecting?: A Teachable Moment. JAMA Intern Med. 2015 May 4.

Marc I, Toureche N, Ernst E, et al. **Mind-body interventions during pregnancy** for preventing or treating women's anxiety. Cochrane Database of Systematic Reviews 2011, Issue 7. Art. No.: CD007559. DOI: 10.1002/14651858.CD007559.pub2. Mind-body interventions might benefit women's anxiety during pregnancy. Based on individual studies, there is some but no strong evidence for the effectiveness of mind-body interventions for the management of anxiety during pregnancy. The main limitations of the studies were the lack of blinding and insufficient details on the methods used for randomization.

Marcus AP, Marcus DM, Ayis S, et al. Spontaneous pregnancies following **discontinuation of IVF/ICSI treatment**: an internet-based survey. Hum Fertil (Camb). 2016 Jun;19(2):134-41.

Mardy AH, Ananth CV, Grobman WA, et al. A **prediction model of vaginal birth** after cesarean in the preterm period. Am J Obstet Gynecol. 2016 Jun 1.

Margulis AV, Andrews EB. The **Safety of Medications in Pregnant Women**: An Opportunity to Use Database Studies. Pediatrics. 2017;140(1):e20164194.

Martin RM, Patel R, Kramer MS, et al. Effects of promoting longer-term and exclusive **breastfeeding on adiposity** and insulin-like growth factor-I at age 11.5 years: a randomized trial. JAMA. 2013 Mar 13;309(10):1005-13.

Martinez de Tejada B, Karolinski A, et al. **Prevention of preterm delivery with vaginal progesterone** in women with preterm labour (4P): randomised double-blind placebo-controlled trial. BJOG. 2014 Sep 11.

Maslova E, Granström C, Hansen S, et al. **Peanut and tree nut consumption** during pregnancy and allergic disease in children-should mothers decrease their intake? Longitudinal evidence from the Danish National Birth Cohort. J Allergy Clin Immunol. 2012 Sep;130(3):724-32.

Mather M, Wiles K, O'Brien P. Should women **abstain from alcohol throughout pregnancy**? BMJ. 2015 Oct 6;351:h5232.

Matlow JN, Pupco A, Bozzo P, Koren G. **Tdap vaccination** during pregnancy to reduce pertussis infection in young infants. Can Fam Physician. 2013 May;59(5):497-8.

Matro R et al. Exposure concentrations of **infants breastfed by women receiving biologic therapies for inflammatory bowel diseases** and effects of breastfeeding on infections and development. Gastroenterology 2018 May 29.

Matzon JL, Lutsky KF, Ricci EK, Beredjiklian PK. Considerations in the **Radiologic Evaluation of the Pregnant Orthopaedic Patient**. J Am Acad Orthop Surg. 2015 Aug;23(8):485-91.

Mawhinney E, Craig J, Morrow J, et al. **Levetiracetam in pregnancy**: Results from the UK and Ireland epilepsy and pregnancy registers. Neurology. 2013 Jan 22;80(4):400-405.

McCarthy, Fergus, O'Keeffe et al. Association Between **Maternal Alcohol Consumption** in Early Pregnancy and Pregnancy Outcomes. Obstetrics&Gynecology. September 2013.

McCarthy FP, O'Brien U, Kenny LC. The management of **teenage pregnancy**. BMJ. 2014 Oct 15;349:g5887.

Morales E, Garcia-Esteban R, Asensio de la Cruz O, et al. Intrauterine and early postnatal exposure to **outdoor air pollution and lung function** at preschool age. Thorax. 2014 Oct 20.

McDonagh MS, Matthews A, et al. **Depression Drug Treatment Outcomes in Pregnancy and the Postpartum Period**: A Systematic Review and Meta-analysis. Obstet Gynecol. 2014 Sep;124(3):526-34.

McDonald E, Gartland D, Small R, Brown S. **Dyspareunia and childbirth**: a prospective cohort study. BJOG. 2015 Jan 21.

McEvoy CT, Schilling D, Clay N, et al. **Vitamin C supplementation** for pregnant smoking women and pulmonary function in their newborn infants: a randomized clinical trial. JAMA. doi:10.1001/jama.2014.5217.

McParlin C, O'Donnell A, Robson SC, et al. Treatments for **Hyperemesis Gravidarum and Nausea and Vomiting** in Pregnancy: A Systematic Review. JAMA. 2016 Oct 4;316(13):1392-1401

McQuire C, Paranjothy S, Hurt L, et al. Objective Measures of **Prenatal Alcohol Exposure**: A Systematic Review. Pediatrics. 2016 Sep;138(3).

Meador KJ, Baker GA, Browning N, et al; For the NEAD Study Group. Effects of **fetal antiepileptic drug exposure**: Outcomes at age 4.5 years. Neurology. 2012 Apr 17;78(16):1207-1214.

Meador KJ, Baker GA, et al, **NEAD** Study Group. **Fetal antiepileptic drug exposure** and **cognitive outcomes at age 6 years** (NEAD study): a prospective observational study. Lancet Neurol 2013; online Jan 23.

Meador KJ, Lindhout D. **Epilepsy and unintended pregnancies**. Neurology. 2017 Feb 21;88(8):724-725

Meador KJ. Periconceptional **Folate Supplementation and the Risk of Autism** Following Antiepileptic Drug Exposure. JAMA Neurol. 2017 Dec 26.

Meher S, et al. **Antiplatelet therapy before or after 16 weeks` gestation** for **preventing preeclampsia**: an individual participant data meta-analysis. Am J Obstet Gynecol. 2017 Feb;216(2):121-128.e2.

Mehta B, Luo Y, Xu J, et al. Trends in Maternal and Fetal Outcomes Among Pregnant Women **With Systemic Lupus** Erythematosus in the United States: A Cross-sectional Analysis. Ann Intern Med. 2019 Jul 9.

Mehta N, Chen K, Powrie RO. **Prescribing for the pregnant patient**. Cleve Clin J Med. 2014 Jun;81(6):367-372.
Mehrabadi A, Liu S, Bartholomew S, et al; Canadian Perinatal Surveillance System (Public Health Agency of Canada). **Hypertensive disorders of pregnancy** and the recent increase in obstetric acute renal failure in Canada: population based retrospective cohort study. BMJ. 2014 Jul 30
Melchiorre K, Sharma R, Thilaganathan B. **Cardiovascular implications in preeclampsia**: an overview. Circulation. 2014 Aug 19;130(8):703-14.
Mendez-Figueroa H, Schuster M, Maggio L, et al. **Gestational Diabetes Mellitus and Frequency of Blood Glucose Monitoring**: A Randomized Controlled Trial. Obstet Gynecol. 2017 Jul;130(1):163-170.
Mendola P, Wallace M, Hwang BS, et al. **Preterm birth and air pollution**: Critical windows of exposure for women with asthma. J Allergy Clin Immunol. 2016 Feb 23.
Metz TD, Rovner P, Hoffman MC, Allshouse et al.**Maternal Deaths From Suicide and Overdose** in Colorado, 2004-2012. Obstet Gynecol.2016 Nov 3.
Mhyre JM, Tsen LC, Einav S, et al. **Cardiac Arrest** during Hospitalization for Delivery in the United States, 1998-2011. Anesthesiology. 2014 Apr;120(4):810-8.
Middleton P, Gomersall JC, Gould JF et al, **Omega-3 fatty acid** addition during pregnancy. *Cochrane Database Syst Rev*2018*;(*11*):*CD003402.
Mikkelsen EM, Riis AH, Wise LA, et al. **Alcohol consumption and fecundability**: prospective Danish cohort study. BMJ 2016;354:i4262.
Millard LA, Lawlor DA, Fraser A, Howe LD. **Physical activity during pregnancy and offspring cardiovascular risk** factors: findings from a prospective cohort study. BMJ Open. 2013 Sep 25;3(9):e003574.
Miller BJ, Murray L, Beckmann MM, et al. **Dietary supplements for preventing postnatal depression**. Cochrane Database Syst Rev. 2013 Oct 24;10:CD009104. There is insufficient evidence to conclude that selenium, DHA or EPA prevent postnatal depression. There is currently no evidence to recommend any other dietary supplement for prevention of postnatal depression.
Miller EC, Gatollari HJ, Too G, et al. Risk Factors for Pregnancy-Associated **Stroke in Women With Preeclampsia**. Stroke. 2017 May 25.
Miller EC, Boehme AK, Chung NT, et al. **Aspirin reduces long-term stroke risk in women with prior hypertensive disorders of pregnancy**. Neurology 2019;92:e305–e316.
Mireku MO,Davidson LL, Boivin MJ, et al. Prenatal Iron Deficiency. **Neonatal Ferritin and Infant Cognitive Function**. Pediatrics.2016;138(6):e20161319
Mishanina E, Rogozinska E, Thatthi T, et al. Use of **labour induction and risk of cesarean delivery**: a systematic review and meta-analysis. CMAJ. 2014 Apr 28.
Mitchell AA, Gilboa SM, Werler MM, et al. National Birth Defects Prevention Study. **Medication use during pregnancy**, with particular focus on prescription drugs: 1976-2008. Am J Obstet Gynecol. 2011 Jul;205(1):51.e1-8.
Modesto T, Tiemeier H, et al. **Maternal Mild Thyroid Hormone Insufficiency** in Early Pregnancy and Attention deficit/ Hyperactivity Disorder Symptoms in Children. JAMA Pediatr. 2015 Sep 1;169(9):838-845.
Mol BW, Roberts CT, Thangaratinam S, et al. Pre-eclampsia. Lancet. 2015 Sep 2.
Mol F, van Mello NM, Strandell A, et al. **Salpingotomy versus salpingectomy** in women with **tubal pregnancy** (ESEP study): an open-label, multicentre, randomised controlled trial. Lancet 2014; online Feb 3.
Moleti M, Trimarchi F, Tortorella G, et al. F. Effects of **Maternal Iodine Nutrition** and Thyroid Status on Cognitive Development in Offspring: A Pilot Study. Thyroid. 2015 Nov 20.
Mølgaard-Nielsen D, Svanström H, Melbye M, et al. Association Between Use of Oral **Fluconazole** During Pregnancy and Risk of Spontaneous Abortion and Stillbirth. JAMA. 2016 Jan 5;315(1):58-67.
Molina G, Weiser TG, Lipsitz SR, et al. Relationship between **cesarean delivery rate and maternal and neonatal mortality**.JAMA. doi:10.1001 /jama.2015.15553.
Molvi SN, Mir S, Rana VS, Jabeen F, Malik AR. Role of **antihypertensive therapy in mild to moderate pregnancy-induced hypertension**: a prospective randomized study comparing **labetalol with alpha methyldopa**. Arch Gynecol Obstet. 2012 Jun;285(6):1553-62.
Molyneaux E, Poston L, Ashurst-Williams S, et al. **Obesity and Mental Disorders** During Pregnancy and Postpartum: A Systematic Review and Meta-analysis. Obstet Gynecol. 2014 Apr;123(4):857-67.
Molyneaux E, Trevillion K, Howard LM. **Antidepressant treatment for postnatal depression**. JAMA. 2015 May 19;313(19):1965-6.
Molyneaux E, Telesia LA, Henshaw C, et al. **Antidepressants for preventing postnatal depression**. Cochrane Database Syst Rev. 2018 Apr 18;4:CD004363. Due to the limitations of the current evidence base, such as the low statistical power of the included studies, it is not possible to draw any clear conclusions about the effectiveness of antidepressants for the prevention of postnatal depression. It is striking that no new eligible trials have been completed in the period of over a decade since the last published version of this review. Larger trials are needed which include comparisons of antidepressant drugs with other prophylactic treatments (e.g. psychological interventions), and examine adverse effects for the fetus or infant. Future reviews in this area may benefit from broadening their focus to examine the effectiveness of antidepressants for the prevention of perinatal (i.e. antenatal or postnatal) depression, which could include studies comparing antidepressant discontinuation with continuation for the prevention of relapse of depression during pregnancy and the postnatal period.
Money D, Allen VM, Infectious Disease Committee. The **prevention of early-onset neonatal group B streptococcal disease**. J Obstet Gynaecol Can. 2013 Oct;35(10):939-51.
Money D, Tulloch K, Boucoiran I, Caddy S; Infectious Diseases Committee, Yudin MH, Allen V, Bouchard C, et al. Guidelines for the **care of pregnant women living with HIV** and interventions to reduce perinatal transmission: executive summary. J Obstet Gynaecol Can. 2014 Aug;36(8):721-51.
Moore A, Doull M, Grad R, et al. Recommendations on **screening for asymptomatic bacteriuria in pregnancy.** CMAJ. 2018 Jul 9;190(27):E823-E830.
Moore HB, Juarez-Colunga E, Bronsert M et al. Effect of Pregnancy on Adverse Outcomes **After General Surgery**. JAMA Surg. 2015 May 13.
Moore JL, Aggarwal P. **Lamotrigine** use in pregnancy. Expert Opin Pharmacother. 2012 Jun;13(8):1213-6.
Morales-Suarez-Varela MM, Bille C, Christensen K, Olsen J. **Smoking habits, nicotine use**, and congenital malformations. Obstet Gynecol. 2006 Jan;107(1):51-7.
Morales E, Guxens M, Llop S, et al; on behalf of the INMA Project. Circulating **25-Hydroxyvitamin D3** in Pregnancy and Infant Neuropsychological Development. Pediatrics. 2012 Sep 17.
Morgan S, Koren G, Bozzo P. Is **caffeine consumption** safe during pregnancy? Can Fam Physician. 2013 Apr;59(4):361-2.
Morris RK, Riley RD, Doug M, et al. Diagnostic accuracy of spot urinary protein and albumin to creatinine ratios for detection of significant proteinuria or adverse pregnancy outcome in patients with suspected pre-eclampsia: systematic review and meta-analysis. BMJ. 2012 Jul 9;345:e4342.
Moss DA, Snyder MJ, Lu L. **Options for women with unintended pregnancy**. Am Fam Physician. 2015 Apr 15;91(8):544-9.
Mourtakos SP, Tambalis KD, et al. **Maternal lifestyle characteristics during pregnancy**, and the risk of obesity in the offspring: a study of 5,125 children. BMC Pregnancy Childbirth. 2015 Mar 21;15:66.
Mousa HA, Blum J, Abou El Senoun G, et al. Treatment for **primary postpartum haemorrhage**. Cochrane Database Syst Rev. 2014 Feb 13;2:CD003249.
Muanda FT, Sheehy O, Bérard A. **Use of antibiotics** during pregnancy and risk of spontaneous abortion. CMAJ. 2017 May 1;189(17):E625-E633
Muanda FT, Sheehy O, Bérard A. **Use of antibiotics** during pregnancy and the risk of major congenital malformations: A population based cohort study. Br J Clin Pharmacol. 2017 Jul 19.
Muanda FT, Sheehy O, Bérard A. Use of **trimethoprim-sulfamethoxazole** during pregnancy and risk of **spontaneous abortion**: a nested case control study. Br J Clin Pharmacol. 2018 Feb 8.
Muktabhant B, Lawrie TA, Lumbiganon P, et al. **Diet or exercise, or both, for preventing excessive weight gain** in pregnancy. Cochrane Database Syst Rev. 2015 Jun 11;6:CD007145. High-quality evidence indicates that diet or exercise, or both, during pregnancy can reduce the risk of excessive GWG. Other benefits may include a lower risk of caesarean delivery, macrosomia, and neonatal respiratory morbidity, particularly for high-risk women receiving combined diet and exercise interventions. Maternal hypertension may also be reduced. Exercise appears to be an important part of controlling weight gain in pregnancy and more research is needed to establish safe guidelines. Most included studies were carried out in developed countries and it is not clear whether these results are widely applicable to lower income settings.

Mumford SL, Garbose RA, Kim K, et al. Association of **preconception serum 25-hydroxyvitamin D concentrations with livebirth and pregnancy loss**: a prospective cohort study. Lancet Diabetes Endocrinol. 2018 May 30.

Mundle S, et al. **Foley catheterisation versus** oral **misoprostol** for **induction** of **labour** in hypertensive women in India (**INFORM**): multicentre, open-label, randomised controlled. Lancet 2017; online June 28.

Munger KL, Åivo J, Hongell K, et al. **Vitamin D status** during pregnancy and risk of **multiple sclerosis** in offspring of women in the Finnish Maternity Cohort [online March 7, 2016]. JAMA Neurol..

Munk-Olsen T, Laursen TM, Meltzer-Brody S et al. **Psychiatric disorders with postpartum onset**: possible early manifestations of bipolar affective disorders. Arch Gen Psychiatry. 2012 Apr;69(4):428-34.

Munk-Olsen T, Liu X, Viktorin A, et al. Maternal and **infant outcomes associated with lithium use** in pregnancy: an international collaborative meta-analysis of six cohort studies. Lancet Psychiatry. 2018 Jun 18.

Murase JE, Heller MM, Butler DC. Safety of **dermatologic medications in pregnancy and lactation**. *J Am Acad Dermatol* 2014;70:401-14 (part I) and 417-26 (part II).

Murase JE, Heller MM, Butler DC. Safety of **dermatologic medications** in **pregnancy and lactation**: Part I. Pregnancy. J Am Acad Dermatol. 2014 Mar;70(3):401.e1-14; quiz 415.

Murji A, Crosier R, Rasuli P. **Non-obstetric diagnostic imaging** in pregnancy. CMAJ. 2015 Nov 17;187(17):1309.

Murphy KE, Willan AR, Hannah ME, et al. Effect of **Antenatal Corticosteroids** on Fetal Growth and Gestational Age at Birth. Obstet Gynecol. 2012 May;119(5):917-923.

Murphy NJ, Quinlan JD. **Trauma in pregnancy**: assessment, management, and prevention. Am Fam Physician. 2014 Nov 15;90(10):717-22.

Mwaniki MK, Atieno M, Lawn JE, et al. **Long-term neurodevelopmental outcomes after intrauterine and neonatal insults**: a systematic review. Lancet 2012;379:445–52.

Myers ER, Aubuchon-Endsley N, Bastian LA, et al. Efficacy and Safety of **Screening for Postpartum Depression**. **AHRQ** Comparative Effectiveness Review. Rockville (MD): Agency for Healthcare Research and Quality (US); 2013 Apr. Report No.:13-EHC064-E.

Myles N, Newall H, Ward H, Large M. Systematic meta-analysis of individual **selective serotonin reuptake inhibitor** medications and congenital malformations. Aust N Z J Psychiatry. 2013 Nov;47(11):1002-12.

Nachum Z, Zafran N, et al. **Glyburide Versus Metformin and Their Combination for the Treatment of Gestational Diabetes** Mellitus: A Randomized Controlled Study. Diabetes Care. 2017 Mar;40(3):332-337.

Nadeem S, Hashmat S, Defreitas MJ, et al. **Renin Angiotensin System Blocker Fetopathy**: A Midwest Pediatric Nephrology Consortium Report. J Pediatr. 2015 Oct;167(4):881-5.

Namouz-Haddad S, Nulman I. Safety of treatment of **obsessive compulsive disorder** in pregnancy and puerperium. Can Fam Physician. 2014 Feb;60(2):133-6.

Nascimento SL, Pudwell J, Surita FG, et al. The effect of **physical exercise strategies on weight loss** in postpartum women: a systematic review and meta-analysis. Int J Obes (Lond). 2013 Sep 19.

Nascimento LB, et al. Symptomatic **dengue infection during pregnancy** and livebirth outcomes in Brazil, 2007–13: a retrospective observational cohort study. Lancet Infect Dis 2017; online May 18.

Nathan HL,Duhig K, Hezelgrave NL, et al. **Blood pressure measurement** in pregnancy. The Obstetrician and Gynaecologist. 2015.

Nelson S, Haig C, McConnachie A, etal . **Maternal thyroid function** and child educational attainment: prospective cohort study. BMJ 2018;360:k452. 10.1136/bmj.k452.

Nembhard WN, et al. Maternal and infant genetic variants, maternal periconceptional use of **selective serotonin reuptake inhibitors**, and risk of congenital heart defects in offspring: population based study. BMJ. 2017 Mar 6;356:j832.

Neuman G, Colantonio D, Delaney S, et al. Bupropion and Escitalopram During Lactation. Ann Pharmacother. 2014 Apr 14;48(7):928-931.

Nevers W, Pupco A, Koren G, et al. Safety of **tacrolimus in pregnancy**. Can Fam Physician. 2014 Oct;60(10):905-6.

Newman L, Kamb M, Hawkes S, Gomez G, Say L, Seuc A, et al. Global estimates of **syphilis in pregnancy** and associated adverse outcomes: analysis of multinational antenatal surveillance data. PLoS Med2013;10(2):e1001396.

Newport DJ, Calamaras MR, DeVane CL, et al. **Atypical antipsychotic** administration during late pregnancy: **placental passage** and obstetrical outcomes. Am J Psychiatry. 2007 Aug;164(8):1214-20.

Newsome K, Alverson CJ, Williams J, et al. **Outcomes of infants born to women with influenza A(H1N1)pdm09**. Birth Defects Res. 2019 Jan 15;111(2):88-95.

Nezvalová-Henriksen K, Spigset O, et al. Effects of **ibuprofen, diclofenac, naproxen and piroxicam** on the course of pregnancy and pregnancy outcome: a prospective cohort study. BJOG 2013;120:948–59.

NICE: National Institute for Health and Care Excellence. **Intrapartum care**: care of healthy women and their babies during childbirth. (Clinical Guideline 109.) 2014. www.nice.org.uk/guidance/cg190.

NICE: National Institute for Health and Care Excellence. **Antenatal and postnatal mental health**: Clinical management and service guidance (update). (Clinical Guideline 192.) 2014. http://guidance.nice.org.uk/CG192.

NICE: National Institute for Health and Care Excellence. **Preterm labour**. (New guideline 25.) 2015. http://www.nice.org.uk/guidance/ng25.

NICE: National Institute for Health and Care Excellence. **Preterm labour and birth. NICE** guideline No 25. 2015.

Nicolaides KH, Syngelaki A, Poon LC, et al. A Randomized Trial of a **Cervical Pessary** to **Prevent Preterm Singleton Birth**. N Engl J Med. 2016 Mar 17;374(11):1044-52.

Nielsen BW, Scott RC. Brain abnormalities in fetuses: **in-utero MRI versus ultrasound**. Lancet. 2016 Dec 14.

Norby U, Forsberg L, Wide K, et al. Neonatal Morbidity **After Maternal Use of Antidepressant Drugs** During Pregnancy. Pediatrics.2016:138(5):e20160181

Nordqvist M, Jacobsson B, Brantsæter AL, et al. Timing of **probiotic milk consumption** during pregnancy and effects on the incidence of preeclampsia and preterm delivery: a prospective observational cohort study in Norway. BMJ Open. 2018 Jan 23;8(1):e018021.

Nørgård BM, et al. Reassuring results on **birth outcomes** in children fathered by men treated with **azathioprine/6-mercaptopurine** within 3 months before conception: nationwide cohort study. Gut. 2016 Jul 25.

Noten AM, Loomans EM, Vrijkotte TG, et al. **Maternal hypothyroxinaemia** in early pregnancy and school performance in 5-year-old offspring. Eur J Endocrinol. 2015 Aug 25.

Nour MM, Nakashima I, Coutinho E, et al. Pregnancy outcomes in **aquaporin-4-positive neuromyelitis optica spectrum disorder**. Neurology. 2016 Jan 5;86(1):79-87.

Novikova N, Hofmeyr GJ, Cluver C. **Tranexamic acid for preventing postpartum haemorrhage**. Cochrane Database Syst Rev. 2015 Jun 16;6:CD007872. TA (in addition to uterotonic medications) decreases postpartum blood loss and prevents PPH and blood transfusions following vaginal birth and CS in women at low risk of PPH based on studies of mixed quality. There is insufficient evidence to draw conclusions about serious side effects, but there is an increase in the incidence of minor side effects with the use of TA. Effects of TA on thromboembolic events and mortality as well as its use in high-risk women should be investigated further.

Oboho I, Reed C, Gargiullo P, et al. The benefit of early **influenza antiviral treatment of pregnant women** hospitalized with laboratory-confirmed influenza. J Infect Dis. 2016 Feb 3.

Ohlsson A, Shah VS, Stade BC. **Vaginal chlorhexidine** during labour to prevent early-onset **neonatal group B streptococcal infection**. Cochrane Database Syst Rev. 2014 Dec 14;12:CD003520. The quality of the four included trials varied as did the risk of bias and the quality of the evidence using GRADE was very low. Vaginal chlorhexidine was not associated with reductions in any of the primary outcomes of early-onset GBS disease (sepsis and/or meningitis) or GBS pneumonia. Vaginal chlorhexidine may reduce GBS colonization of neonates. The intervention was associated with an increased risk of maternal mild adverse effects. The review currently does not support the use of vaginal disinfection with chlorhexidine in labour for preventing early-onset disease. Results should be interpreted with caution as the methodological quality of the studies was poor. As early-onset GBS disease is a rare condition trials with very large sample sizes are needed to assess the effectiveness of vaginal chlorhexidine to reduce its occurrence. In the era of intrapartum antibiotic prophylaxis, such trials may be difficult to justify especially in developed countries.

Nicklas JM, Zera CA, England LJ, et al. A **web-based lifestyle intervention** for women with recent **gestational diabetes** mellitus: a randomized controlled trial. Obstet Gynecol. 2014 Sep;124(3):563-70.

Nielsen-Saines K, Komarow L, Cu-Uvin S et al. Infant Outcomes After Maternal Antiretroviral Exposure in Resource-Limited Settings. Pediatrics. 2012 Jun;129(6):e1525-e1532.

Nielsen OH, Loftus EV, Jess T. Safety of **TNF-α inhibitors during IBD pregnancy**: a systematic review. BMC Med 2013;11:174.

Noel N, Wechsler B, Nizard J, et al. **Behcet's disease** and pregnancy. Arthritis Rheum. 2013 Jun 18.

Nordeng H, Lupattelli A, Romoren M, et al. Neonatal outcomes after gestational **exposure to nitrofurantoin**. Obstet Gynecol. 2013 Feb;121(2 Pt 1):306-13.

Nordin JD, Kharbanda EO, Benitez GV, Nichol et al. Maternal safety of **trivalent inactivated influenza** vaccine in pregnant women. Obstet Gynecol. 2013 Mar;121(3):519-25.

Nunes MC, Cutland CL, Madhi SA. **Influenza Vaccination during Pregnancy** and **Protection against Pertussis**. N Engl J Med. 2018 Mar 29;378(13):1257-1258.

O'Connor DL, Gibbins S, Kiss A, et al. Effect of **Supplemental Donor Human Milk Compared With Preterm Formula on Neurodevelopment** of Very Low-Birth-Weight Infants at 18 Months: A Randomized Clinical Trial. JAMA. 2016 Nov 8;316(18):1897-1905

O'Leary CM, Taylor C, Zubrick SR, Kurinczuk JJ, Bower C. **Prenatal alcohol exposure** and educational achievement in children aged 8-9 years. Pediatrics. 2013 Aug;132(2):e468-75.

O'Neill SM, Agerbo E, Kenny LC, et al. **Cesarean Section** and Rate of Subsequent Stillbirth, Miscarriage, and Ectopic Pregnancy: A Danish Register-Based Cohort Study. PLoS Med. 2014 Jul 1;11(7):e1001670.

Oakeshott P, Chappell LC. Management of a new pregnancy in a woman with **chronic hypertension**. BMJ. 2016 Jun 6;353:i1497.

Oberg AS, Hernandéz-Diaź S, Frisell T, et al. Genetic contribution to **postpartum haemorrhage** in Swedish population: cohort study of 466 686 births. BMJ. 2014 Aug 13;349:g4984.

Ohlsson A, Shah VS. Intrapartum antibiotics for known maternal **Group B streptococcal** colonization. Cochrane Database Syst Rev. 2012 Nov 10;1:CD007467. DOI: 10.1002/14651858.CD007467.pub3. Intrapartum antibiotic prophylaxis appeared to reduce EOGBSD, but this result may well be a result of bias as we found a high risk of bias for one or more key domains in the study methodology and execution. There is lack of evidence from well designed and conducted trials to recommend IAP to reduce neonatal EOGBSD. Ideally the effectiveness of IAP to reduce neonatal GBS infections should be studied in adequately sized double-blind controlled trials. The opportunity to conduct such trials has likely been lost, as practice guidelines (albeit without good evidence) have been introduced in many jurisdictions.

Ohlsson A, Shah VS, Stade BC. **Vaginal chlorhexidine** during labour to prevent early-onset **neonatal group B streptococcal infection**. Cochrane Database Syst Rev. 2014 Dec 14;12:CD003520. The quality of the four included trials varied as did the risk of bias and the quality of the evidence using GRADE was very low. Vaginal chlorhexidine was not associated with reductions in any of the primary outcomes of early-onset GBS disease (sepsis and/or meningitis) or GBS pneumonia. Vaginal chlorhexidine may reduce GBS colonization of neonates. The intervention was associated with an increased risk of maternal mild adverse effects. The review currently does not support the use of vaginal disinfection with chlorhexidine in labour for preventing early-onset disease. Results should be interpreted with caution as the methodological quality of the studies was poor. As early-onset GBS disease is a rare condition trials with very large sample sizes are needed to assess the effectiveness of vaginal chlorhexidine to reduce its occurrence. In the era of intrapartum antibiotic prophylaxis, such trials may be difficult to justify especially in developed countries.

Okesene-Gafa KAM, Li M, McKinlay CJD, et al. Effect of **antenatal dietary interventions in maternal obesity on pregnancy weight-gain and birthweight:** Healthy Mums and Babies (HUMBA) randomized trial. Am J Obstet Gynecol. 2019 Aug;221(2):152.e1-152.e13.

Oliveira LG, Capp SM, You WB, et al. **Ondansetron compared with doxylamine and pyridoxine** for treatment of nausea in pregnancy: a randomized controlled trial. Obstet Gynecol. 2014 Oct;124(4):735-42.

Oppermann M, Padberg S, et al. **Angiotensin-II-receptor-1-antagonist fetopathy** - Risk assessment, critical time period, and vena cava thrombosis as a possible new feature. Br J Clin Pharmacol. 2012 Jul 23.

Orbach H, Matok I, Gorodischer R, et al. **Hypertension and antihypertensive drugs in pregnancy** and perinatal outcomes. Am J Obstet Gynecol. 2012 Nov 15.

Ordean A, Kahan M, Graves L, et al. Integrated care for **pregnant women on methadone** maintenance treatment: Canadian primary care cohort study. Can Fam Physician. 2013 Oct;59(10):e462-9.

Orellana C, Wedrén S, Källberg H, et al. **Parity and the risk of developing rheumatoid arthritis**: results from the Swedish Epidemiological Investigation of Rheumatoid Arthritis study. Ann Rheum Dis. 2014 Apr 1;73(4):752-5.

Oswald C, Higgins CC, Assimakopoulos D. Optimizing **pain relief during pregnancy** using manual therapy. Can Fam Physician. 2013 Aug;59(8):841-2.

Øyen N, Diaz LJ, Leirgul E, et al. **Prepregnancy diabetes and offspring risk of congenital heart disease**: a nationwide cohort study. Circulation. 2016;133:2243–2253.

Özkan M, Çakal B, Karakoyun S, et al. **Thrombolytic therapy** for the treatment of prosthetic heart valve thrombosis in pregnancy with low-dose, slow infusion of tissue-type plasminogen activator. Circulation. 2013 Jul 30;128(5):532-40.

Pace R, Brazeau AS, Meltzer S, et al. Conjoint Associations of **Gestational Diabetes and Hypertension With Diabetes, Hypertension, and Cardiovascular Disease** in Parents: A Retrospective Cohort Study. Am J Epidemiol. 2017 Nov 15;186(10):1115-1124.

Palacio M, et al. **Vaginal progesterone** as maintenance treatment after an episode of **preterm labour** (**PROMISE**) study: a multicentre, double-blind, randomised, placebo-controlled trial. BJOG. 2016 Mar 30.

Palinski W. Effect of **maternal cardiovascular conditions and risk factors on offspring cardiovascular disease**. Circulation. 2014 May 20;129(20):2066-77.

Palmsten K, Hernández-Díaz, Huybrechts KF, et al. Use of **antidepressants near delivery and risk of postpartum hemorrhage**: cohort study of low income women in the United States. BMJ 2013;347:f4877.

Palmsten K, Hernández-Díaz S, et al. The **Most Commonly Dispensed Prescription Medications Among Pregnant Women** Enrolled in the U.S. Medicaid Program. Obstet Gynecol. 2015 Sep;126(3):465-73.

Panagiotou OA, Befano BL, et al; on behalf of the Costa Rica HPV Vaccine Trial (CVT) Group. Effect of bivalent **human papillomavirus (HPV) vaccination** on pregnancy outcomes: long term observational follow-up in the Costa Rica HPV Vaccine Trial. BMJ 2015;351:h4358..

Panchaud A, Rousson V, Vial T, et al. **Pregnancy outcomes in women on metformin for diabetes or other indications** among those seeking teratology information services. Br J Clin Pharmacol. 2017 Dec 7.

Panchaud A, Cohen JM, Patorno E, et al. **Anticonvulsants and the risk of perinatal bleeding complications**: A pregnancy cohort study. Neurology. 2018 Aug 7;91(6):e533-e542.

Papadopoulou E, et al. Maternal **caffeine intake** during pregnancy and childhood growth and overweight: results from a large Norwegian prospective observational cohort study. BMJ Open. 2018 Apr 23;8(3):e018895.

Parent B, Martopullo I, Weiss NS, et al. **Bariatric surgery** in women of childbearing age, timing between an operation and birth, and associated perinatal complications [online October 19, 20].

Parikh NI, Norberg M, et al. Association of Pregnancy Complications and Characteristics With Future Risk of **Elevated Blood Pressure**: The Västerbotten Intervention Program. Hypertension. 2017 Jan 30.

Park S, Choi NK. **Breastfeeding and Maternal Hypertension**. Am J Hypertens. 2018 Jan 25.

Park Y, Hernandez-Diaz S, Bateman BT, et al. Continuation of **Atypical Antipsychotic Medication During Early Pregnancy and the Risk of Gestational Diabetes**. Am J Psychiatry. 2018 Jun 1;175(6):564-574.

Parker M, Rifas-Shiman SL, Oken E, et al. Second Trimester Estimated Fetal Weight and **Fetal Weight Gain** Predict Childhood Obesity. J Pediatr. 2012 Jun 7.
Parr CL, Magnus MC, et al. **Vitamin A and D intake in pregnancy, infant supplementation, and asthma development**: the Norwegian Mother and Child Cohort. Am J Clin Nutr. 2018 May 1;107(5):789-798.
Partanen E, Kujala T, Tervaniemi M, Huotilainen M. **Prenatal music exposure** induces long-term neural effects. PLoS One. 2013 Oct 30;8(10):e78946.
Pasternak B, Svanström H, et al. Vaccination against **pandemic A/H1N1 2009 influenza in pregnancy** and risk of fetal death: cohort study in Denmark. BMJ 2012;344:e2794.
Pasternak B, Svanstro¨m H, Mølgaard-Nielsen D, et al. Risk of adverse fetal outcomes following administration of a pandemic influenza A**(H1N1) vaccine** during pregnancy. JAMA. 2012;308(2):165-174.
Pasternak B et al. **Ondansetron in pregnancy** and risk of adverse fetal outcomes. N Engl J Med 2013 Feb 28; 368:814.
Pasternak B, Wintzell V, Furu K, et al. **Oral Fluconazole in Pregnancy** and Risk of Stillbirth and Neonatal Death. JAMA. 2018 Jun 12;319(22):2333-2335.
Patel JP, Green B, Patel RK, et al. Population pharmacokinetics of **enoxaparin** during the antenatal period. Circulation. 2013 Sep 24;128(13):1462-9.
Patorno E, Bateman BT, Huybrechts KF, et al. **Pregabalin use early in pregnancy** and the risk of major congenital malformations. Neurology. 2017 May 23;88(21):2020-2025.
Patorno E, Huybrechts KF, Bateman BT, et al. **Lithium Use** in Pregnancy and the Risk of Cardiac Malformations. N Engl J Med. 2017 Jun 8;376(23):2245-2254.
Patton GC, Romaniuk H, Spry E, et al. Prediction of **perinatal depression** from adolescence and before conception (VIHCS): 20-year prospective cohort study. Lancet 2015; online June 11.
Patrick SW, Davis MM, Lehman CU, et al. Increasing incidence and geographic distribution of **neonatal abstinence syndrome**: United States 2009 to 2012. J Perinatol. 2015 Apr 30.
Patrick SW, Schiff DM; Committee on Substance Use and Prevention. A Public Health Response to **Opioid Use in Pregnancy**. Pediatrics. 2017 Feb 20.
Paul IM, Downs DS, Schaefer EW, et al. **Postpartum Anxiety** and Maternal-Infant Health Outcomes. Pediatrics. 2013 Mar 4.
Pearson RM et al. **Maternal depression** during pregnancy and the postnatal period: Risks and possible mechanisms for offspring depression at age 18 years. JAMA Psychiatry 2013 Oct 9.
Pearson RM, Carnegie RE, Cree C, et al. Prevalence of **Prenatal Depression Symptoms Among 2 Generations of Pregnant Mothers**The Avon Longitudinal Study of Parents and Children. *JAMA Network Open.*2018;1(3):e180725.
Pena-Rosas JP, De-Regil LM, Dowswell T, et al. **Intermittent oral iron supplementation** during pregnancy**.** Cochrane Database Syst Rev. 2012 Jul 11;7:CD009997. The present systematic review is the most comprehensive summary of the evidence assessing the benefits and harms of intermittent iron supplementation regimens in pregnant women on haematological and pregnancy outcomes. The findings suggest that intermittent iron+folic acid regimens produce similar maternal and infant outcomes at birth as daily supplementation but are associated with fewer side effects. Women receiving daily supplements had increased risk of developing high levels of Hb in mid and late pregnancy but were less likely to present mild anaemia near term.
Peña-Rosas JP, De-Regil LM, Dowswell T, Viteri FE. **Daily oral iron supplementation** during pregnancy. Cochrane Database of Systematic Reviews 2012, Issue 12. Art. No.: CD004736. DOI: 10.1002/14651858.CD004736.pub4. Prenatal supplementation with daily iron are effective to reduce the risk of low birthweight, and to prevent maternal anaemia and iron deficiency in pregnancy. Associated maternal side effects and particularly high Hb concentrations during pregnancy at currently used doses suggest the need to update recommendations on doses and regimens for routine iron supplementation.
Pense J, Neher JO, Kelsberg G, et al. **Micronutrient Supplementation** During Pregnancy. Am Fam Physician. 2015 Aug 1;92(3):222-3.
Pedersen M, Bernard C, Giorgis-Allemand L, et al. **Ambient air pollution and low birthweight**: a European cohort study (ESCAPE). Lancet Resp Med. 2013 Nov 1(9) 695-704
Persaud N, Chin J, Walker M. Should **doxylamine-pyridoxine** be used for nausea and vomiting of **pregnancy**? J Obstet Gynaecol Can. 2014 Apr;36(4):343-8.
Persson M, Cnattingius S, et al. Risk of **major congenital malformations in relation to maternal overweight and obesity severity**: cohort study of 1.2 million singletons. BMJ. 2017 Jun 14;357:j2563
Persson M, Razaz N, Edstedt Bonamy AK, et al. **Maternal Overweight and Obesity and Risk of Congenital Heart Defects**. J Am Coll Cardiol. 2019 Jan 8;73(1):44-53.
Petersen I, Evans SJ, et al. **Selective serotonin reuptake inhibitors and congenital heart anomalies**: comparative cohort studies of women treated before and during pregnancy and their children. J Clin Psychiatry. 2016 Jan;77(1):e36-42.
Petersen I, Peltola T, Kaski S, et al. **Depression, depressive symptoms** and treatments in women who have recently given birth: UK cohort study. BMJ Open. 2018 Oct 8(10):e022152
Peters SAE, Yang L, Guo Y, et al. **Breastfeeding and the Risk of Maternal Cardiovascular Disease**: A Prospective Study of 300 000 Chinese Women. J Am Heart Assoc. 2017 Jun 21;6(6).
Petersen TG, Liew Z, Andersen AN, et al. Use of paracetamol (**acetaminophen**), **ibuprofen or aspirin** in **pregnancy** and **risk of cerebral palsy** in the child. Int J Epidemiol. 2018 Feb 1;47(1):121-130.
Peterson C, Grosse SC, Oster ME, et al. Cost-effectiveness of **routine screening for critical congenital heart disease** in US newborns. Pediatrics 2013.
Petrangelo A, Czuzoj-Shulman N, Balayla J, Abenhaim HA. **Cannabis Abuse or Dependence During Pregnancy**: A Population-Based Cohort Study on 12 Million Births. J Obstet Gynaecol Can. 2019 May;41(5):623-630.
Phelan S, Hagobian T, Brannen A, et al. Effect of an **internet-based program on weight loss for low-income postpartum women**: a randomized clinical trial.JAMA. doi:10.1001/jama.2017.7119
Phipps MG, Raker CA, Ware CF, et al. Randomized controlled trial to **prevent postpartum depression in adolescent mothers**. Am J Obstet Gynecol. 2013 Mar;208(3):192.e1-6.
Piccinini-Vallis H. Clinician self-efficacy in **initiating discussions about gestational weight gain**. Can Fam Physician. 2017 Jul;63(7):e341-e349.
Piccoli GB, Cabiddu G, Attini R, et al. Risk of Adverse Pregnancy Outcomes in Women with **CKD**. J Am Soc Nephrol. 2015 Mar 12.
Polis RL, Gussman D, Kuo YH. **Yoga** in Pregnancy: An Examination of Maternal and Fetal Responses to 26 Yoga Postures. Obstet Gynecol. 2015 Dec;126(6):1237-41.
Pomar L, Vouga M, Lambert V, et al. Maternal-fetal transmission and adverse perinatal outcomes in pregnant women infected with **Zika virus**: prospective cohort study in French Guiana. BMJ. 2018 Oct 31;363:k4431.
Poon S, Pupco A, Koren G, et al. Safety of the newer class of **opioid antagonists** in pregnancy. Can Fam Physician. 2014 Jul;60(7):631-2.
Pope E, Koren G, Bozzo P. **Sugar substitutes** during pregnancy. Can Fam Physician. 2014 Nov;60(11):1003-5.
Porto AM, Coutinho IC, Correia JB, Amorim MM. Effectiveness of antenatal corticosteroids in reducing respiratory disorders in late preterm infants:randomised clinical trial. BMJ. 2011 Apr 12;342:d1696.
Powles K, Gandhi S. **Postpartum hypertension**. CMAJ. 2017 Jul 10;189(27):E913.
Preisler J, Kopeika J, Ismail L, et al. Defining **safe criteria to diagnose miscarriage**: a prospective observational multicentre study. BMJ 2015;351:h4579
Priest JR, Yang W, Reaven G, et al. **Maternal Midpregnancy Glucose Levels** and Risk of Congenital Heart Disease in Offspring. JAMA Pediatr. 2015 Oct 12:1-5.
Pryor J, Patrick SW, Sundermann AC, et al. Pregnancy Intention and **Maternal Alcohol Consumption**. Obstet Gynecol. 2017 Mar 6.
Putnam-Hornstein E, Prindle JJ, Leventhal JM. **Prenatal Substance Exposure** and Reporting of Child Maltreatment by Race and Ethnicity. Pediatrics. 2016 Sep;138(3)
Putnam KT, Wilcox M, et al. Clinical **phenotypes of perinatal depression** and time of symptom onset: analysis of data from an International Consortium. Lancet Psychiatry. 2017 May 2
Quinlan JD, Murphy NJ. **Cesarean Delivery**: Counseling Issues and Complication Management. Am Fam Physician. 2015;91(3):178-184.
Radeva-Petrova D, Kayentao K, Ter Kuile FO, et al. Drugs for **preventing malaria in pregnant women** in endemic areas: any drug regimen versus placebo or no treatment. Cochrane Database Syst Rev. 2014

Oct 10;10:CD000169. Routine chemoprevention to prevent malaria and its consequences has been extensively tested in RCTs, with clinically important benefits on anaemia and parasitaemia in the mother, and on birthweight in infants.
Rafael TJ, Berghella V, Alfirevic Z. **Cervical stitch** (cerclage) for preventing preterm birth in multiple pregnancy. Cochrane Database of Systematic Reviews 2014, Issue 9. Art. No.: CD009166. DOI: 10.1002/14651858.CD009166.pub2. This review is based on limited data from five small studies of average to above average quality. For multiple gestations, there is no evidence that cerclage is an effective intervention for preventing preterm births and reducing perinatal deaths or neonatal morbidity.
Rai D, Lee BK, Dalman C, et al. **Parental depression, maternal antidepressant use during pregnancy, and risk of autism** spectrum disorders: population based case-control study. BMJ. 2013 Apr 19;346:f2059.
Ranthe MF, Andersen EA, Wohlfarht J, et al. **Pregnancy loss and later risk of atherosclerotic disease**. Circulation 2013; DOI:10.1161/circulationaha.112.000285.
Rao R, Gaw SL, Han CS, et al. **Zika Risk** and Pregnancy in Clinical Practice: Ongoing Experience as the Outbreak Evolves. Obstet Gynecol. 2017 May 5.
Rasmussen SA, Barfield W, Honein MA. **Protecting Mothers and Babies** – A Delicate Balancing Act. N Engl J Med. 2018 Jul 24.
Rawal S, Hinkle SN, Bao W, et al. A longitudinal study of **iron status during pregnancy** and the risk of gestational diabetes: findings from a prospective, multiracial cohort. Diabetologia. 2016 Nov 10.
Rawal S, Tsai MY, Hinkle SN, et al. A Longitudinal Study of **Thyroid Markers across Pregnancy and the Risk of Gestational Diabetes**. J Clin Endocrinol Metab. 2018 Jun 7.
Rawlinson WD, Boppana SB, et al. Congenital **cytomegalovirus** infection in pregnancy and the neonate: consensus recommendations for prevention, diagnosis, and therapy. Lancet Infect Dis. 2017 Mar 10.
Ray JG, Huang T, Meschino WS, et al. Prenatal **biochemical screening and long term risk of maternal cardiovascular disease**: population based cohort study. BMJ. 2018 Jul 11;362:k2739.
Ray JG, Vermeulen MJ, Bharatha A, et al. Association Between **MRI Exposure** During Pregnancy and Fetal and Childhood Outcomes. JAMA. 2016 Sep 6;316(9):952-61
Raymond EG, Weaver MA, Tan YL, et al. Effect of Immediate Compared With Delayed Insertion of **Etonogestrel Implants** on **Medical Abortion** Efficacy and Repeat Pregnancy: A Randomized Controlled Trial. Obstet Gynecol. 2016 Feb;127(2):306-12.
Ravi K, Sweetser S. **Persistent nausea and vomiting in pregnancy**. Gastroenterology. 2014 Jan;146(1):33-323
Razaz N, Tedroff K, Villamor E, et al. **Maternal Body Mass Index** in Early Pregnancy and Risk of Epilepsy in Offspring. JAMA Neurol. 2017 Apr 3.
Razaz N, Avitan T, Ting J, et al. **Perinatal outcomes** in multifetal pregnancy **following fetal reduction**. CMAJ. 2017 May 8;189(18):E652-E658
Razaz N, Tomson T, Wikström AK, et al. Association Between Pregnancy and Perinatal Outcomes Among Women **With Epilepsy**. JAMA Neurol. 2017 Jul 3.
Redelmeier DA, May SC, Thiruchelvam D, Barrett JF. **Pregnancy and the risk of a traffic crash**. CMAJ. 2014 May 12.
Redelmeier DA, May SC, Thiruchelvam D, et al. Pregnancy and the risk of a **traffic crash**. CMAJ. 2014 Jul 8;186(10):742-50.
Reefhuis J, Devine O, Friedman JM, et al; National Birth Defects Prevention Study. Specific **SSRIs and birth defects**: bayesian analysis to interpret new data in the context of previous reports. BMJ. 2015 Jul 8;351:h3190.
Reese JA, Peck JD, Deschamps DR, et al. **Platelet Counts during Pregnancy**. N Engl J Med. 2018 Jul 5;379(1):32-43.
Regan AK, Moore HC, et al. **Seasonal Trivalent Influenza Vaccination** During Pregnancy and the Incidence of Stillbirth: Population-Based Retrospective Cohort Study. Clin Infect Dis. 2016 Mar 30.
Regitz-Zagrosek V, Roos-Hesselink JW, Bauersachs J, et al. 2018 ESC Guidelines for the **management of cardiovascular diseases during pregnancy**. Eur Heart J. 2018 Sep 7;39(34):3165-3241.
Remaeus K, Johansson K, Askling J, et al. **Juvenile onset arthritis and pregnancy** outcome: a population-based cohort study. Ann Rheum Dis. 2017 Nov;76(11):1809-1814.
Renault KM, Nørgaard K, Nilas L, et al. The Treatment of **Obese Pregnant Women (TOP)** study: a randomized controlled trial of the effect of physical activity intervention assessed by pedometer with or without dietary intervention in obese pregnant women. Am J Obstet Gynecol. 2014 Feb;210(2):134.e1-9.
Ren S, Haynes E, Hall E, et al.Periconception Exposure to **Air Pollution** and Risk of Congenital Malformations. J Pediatr. 2017 Dec 8.
Retnakaran R, Wen SW, Tan H, et al. Association of **Timing of Weight Gain in Pregnancy** With Infant Birth Weight. JAMA Pediatr. 2017 Dec 26.
Retnakaran R, Ye C, Hanley AJG, et al. Effect of **maternal weight**, adipokines, glucose intolerance and lipids on infant birth weight among women without gestational diabetes mellitus. CMAJ 2012; May 21 [
Retnakaran R, Shah BR. Fetal Sex and the Natural History of **Maternal Risk of Diabetes During** and After Pregnancy. J Clin Endocrinol Metab. 2015 May 20
Retnakaran R, Wen SW, et al. **Maternal Blood Pressure** Before Pregnancy and Sex of the Baby: A Prospective Preconception Cohort Study. Am J Hypertens. 2017 Jan 5.
Reutrakul S, Zaidi N, Wroblewski K, et al. Interactions Between **Pregnancy, Obstructive Sleep Apnea, and Gestational Diabetes Mellitus**. J Clin Endocrinol Metab. 2013 Aug 21.
Reynolds RM, Allan KM, Raja EA, et al. **Maternal obesity and premature mortality from cardiovascular event in adult offspring**: follow-up of 1 323 275 person-years. BMJ 2013;347:f4539.
Phupong V, Hanprasertpong T. **Interventions for heartburn in pregnancy**. Cochrane Database Syst Rev. 2015 Sep 19;9:CD011379. There are no large-scale RCTs to assess heartburn relief in pregnancy. This review of nine small studies (which involved data from only four small studies) indicates that there are limited data suggesting that heartburn in pregnancy could be completely relieved by pharmaceutical treatment. Three outcomes were assessed and assigned a quality rating using the GRADE methods. Evidence from two trials for the outcome of complete relief of heartburn was assessed as of moderate quality. Evidence for the outcomes of partial heartburn relief and side effects was graded to be of very low quality.
Ribeiro RMP, de Lima Moreira F, Dantas Moisés EC, et al. **Lopinavir/Ritonavir** treatment **increases the placental transfer of bupivacaine** enantiomers **in HIV-infected pregnant** women. Br J Clin Pharmacol. 2018 Jun 29.
Rich DQ, Liu K, Zhang J, et al. Differences in **Birth Weight** Associated with the 2008 Beijing Olympic **Air Pollution** Reduction: Results from a Natural Experiment. Environ Health Perspect. 2015 Apr 28.
Rich-Edwards JW. The predictive pregnancy: what complicated pregnancies tell us about mother's future cardiovascular risk. Circulation. 2012 Mar 20;125(11):1336-8.
Richmond RC, Timpson NJ, Felix JF, et al. Using **Genetic Variation** to Explore the Causal Effect of **Maternal Pregnancy Adiposity** on Future Offspring Adiposity: A Mendelian Randomisation Study. PLoS Med. 2017 Jan 24;14(1):e1002221
Robakis T, Williams K. **Atypical Antipsychotics** during pregnancy. Current Psychiatry 2013 July; 12(7).
Robbins MS, Farmakidis C, Dayal AK, et al. **Acute headache diagnosis** in pregnant women: A hospital-based study. Neurology. 2015 Sep 22;85(12):1024-30.
RobertsD,Brown J,MedleyN,Dalziel SR.**Antenatal corticosteroids for accelerating fetal lung maturation** forwomen at risk of pretermbirth.CochraneDatabase of SystematicReviews 2017, Issue 3. Art.No.:CD004454. Evidence from this update supports the continued use of a single course of antenatal corticosteroids to accelerate fetal lung maturation in women at risk of preterm birth. A single course of antenatal corticosteroids could be considered routine for preterm delivery. It is important to note that most of the evidence comes from high income countries and hospital settings; therefore, the results may not be applicable to low-resource settings with high rates of infections.
Roberge S, Bujold E, et al. Meta-analysis on **the effect of aspirin use for prevention of preeclampsia on placental abruption and antepartum hemorrhage**. Am J Obstet Gynecol. 2018 May;218(5):483-489.

Rodger MA, Hague WM, Kingdom J, et al. **Antepartum dalteparin** versus **no antepartum dalteparin** for the prevention of pregnancy complications in pregnant women with thrombophilia (TIPPS): a multinational open-label randomized trial. Lancet 2014; online July 25. http://dx.doi.org/10.1016/S0140-6736(14)60793-5.

Rogozinska E, Kara-Newton L, Zamora JR, et al. On-site test to **detect syphilis in pregnancy**: a systematic review of test accuracy studies. BJOG. 2016 Dec 28.

Rogne T, Tielemans MJ, Chong MF, et al. Associations of **Maternal Vitamin B12 Concentration in Pregnancy** With the Risks of Preterm Birth and Low Birth Weight: A Systematic Review and Meta-Analysis of Individual Participant Data. Am J Epidemiol. 2017 Jan 20.

Rolnik DL, Wright D, Poon LC, et al. **Aspirin versus Placebo** in Pregnancies at High Risk for **Preterm Preeclampsia**. N Engl J Med. 2017 Jun 28.

Rom AL, Wu CS, Olsen J, et al. Fetal growth and preterm birth in children exposed to maternal or paternal **rheumatoid arthritis**: a nationwide cohort study. Arthritis Rheumatol. 2014 Dec;66(12):3265-73.

Romøren M, Lindbaek M, Nordeng H. Pregnancy outcome after **gestational exposure to erythromycin**-a population-based register study from Norway. Br J Clin Pharmacol. 2012 Mar 30.

Roos-Hesselink JW, Ruys TPE, Stein JI, et al. Outcome of pregnancy in patients with structural or **ischaemic heart disease**: Results of a registry of the European Society of Cardiology. Eur Heart J 2012

Roos C, et al; APOSTEL-II Study. Effect of maintenance **tocolysis with nifedipine** in threatened preterm labor on perinatal outcomes: a randomized controlled trial. JAMA. 2013 Jan 2;309(1):41-7.

Rose O, Blanco E, Martinez SM, et al. **Developmental Scores at 1 Year With Increasing Gestational Age**, 37-41 Weeks. Pediatrics. 2013 Apr 15.

Rotem R, Fishman B, Daniel S, et al. Risk of **major congenital malformations following first-trimester exposure to vaginal azoles** used for treating vulvovaginal candidiasis: a population-based retrospective cohort study. BJOG. 2018 May 22.

Roth DE, Perumal N, Al Mahmud A, et al. Maternal **Vitamin D3 Supplementation** during the Third Trimester of Pregnancy: Effects on Infant Growth in a Longitudinal Follow-Up Study in Bangladesh. J Pediatr. 2013 Dec;163(6):1605-1611.e3.

Roth DE, Leung M, Mesfin E, et al. **Vitamin D supplementation during pregnancy**: state of the evidence from a systematic review of randomised trials. BMJ. 2017 Nov 29;359:j5237.

Roth DE, Morris SK, Zlotkin S, et al. **Vitamin D Supplementation in Pregnancy and Lactation and Infant Growth**. N Engl J Med. 2018 Aug 9;379(6):535-546.

Rough K, Seage GR 3rd, Williams PL, et al. Birth Outcomes for **Pregnant Women with HIV Using Tenofovir-Emtricitabine**. N Engl J Med. 2018 Apr 26;378(17):1593-1603.

Roussos-Ross K, Reisfield G, Elliot I, et al. **Opioid** use in pregnant women and the increase in neonatal abstinence syndrome: what is the cost? J Addict Med. 2015 May-Jun;9(3):222-5.

Rouzi AA, Alsibiani S, Mansouri N, et al. Randomized clinical trial between hourly titrated oral **misoprostol and vaginal dinoprostone** for induction of labor. Am J Obstet Gynecol. 2014 Jan;210(1):56.e1-6.

Rowan JA, Rush EC, Plank LD, et al. **Metformin in gestational diabetes**: the offspring follow-up (**MiG TOFU**): body composition and metabolic outcomes at 7-9 years of age. BMJ Open Diabetes Res Care. 2018 Apr 13;6(1):e000456.

Royal College of Obstretricians and Gynaecologists. The prevention of early-onset neonatal group B streptococcal disease. Green-top Guideline No. 36, 2nd edition. July 2012.

Royal College of Obstetricians and Gynaecologists (RCOG). Management of **beta thalassaemia** in pregnancy. London (UK): Royal College of Obstetricians and Gynaecologists (RCOG); 2014 Mar.

Rubinstein F, Micone P, Bonotti A, et al. "EVA" Study Research Group (Estudio "Embarazo y Vacuna Antigripal"). **Influenza A/H1N1 MF59 adjuvanted vaccine** in pregnant women and adverse perinatal outcomes: multicentre study. BMJ. 2013 Feb 4;346:f393.

Rundell K, Panchal B. **Preterm Labor: Prevention and Management**.Am Fam Physician. 2017;95(6):366-372.

Rungsiprakarn P, Laopaiboon M, Sangkomkamhang US, et al. Interventions for treating **constipation in pregnancy**. Cochrane Database Syst Rev. 2015 Sep 4;9:CD011448. There is insufficient evidence to comprehensively assess the effectiveness and safety of interventions (pharmacological and non-pharmacological) for treating constipation in pregnancy, due to limited data (few studies with small sample size and no meta-analyses). Compared with bulk-forming laxatives, stimulant laxatives appear to be more effective in improvement of constipation (moderate quality evidence), but are accompanied by an increase in diarrhoea (moderate quality evidence) and abdominal discomfort (low quality evidence) and no difference in women's satisfaction (moderate quality evidence). Additionally, fibre supplementation may increase frequency of stools compared with no intervention (moderate quality evidence), although these results were of moderate risk of bias.There were no data for a comparison of other types of interventions, such as osmotic laxatives, stool softeners, lubricant laxatives and enemas and suppositories.More RCTs evaluating interventions for treating constipation in pregnancy are needed. These should cover different settings and evaluate the effectiveness of various interventions (including fibre, osmotic, and stimulant laxatives) on improvement in constipation, pain on defecation, frequency of stools and consistency of stools.

Russo LM, Nobles C, Ertel KA, Chasan-Taber L, Whitcomb BW. **Physical Activity Interventions** in Pregnancy and Risk of **Gestational Diabetes** Mellitus: A Systematic Review and Meta-analysis. Obstet Gynecol. 2015 Mar;125(3):576-82.

Sabers A. Algorithm for **lamotrigine** dose adjustment before, during, and after pregnancy. Acta Neurol Scand. 2012 Jul;126(1):e1-4.

Saccone G, Berghella V. **Omega-3 supplementation** to prevent **recurrent preterm birth**: a systematic review and metaanalysis of randomized controlled trials. Am J Obstet Gynecol. 2015 Aug;213(2):135-40.

Saccone G, Berghella V. **Antenatal corticosteroids** for maturity of term or near term fetuses: systematic review and meta-analysis of randomized controlled trials. BMJ. 2016 Oct 12;355:i5044.

Saccone G, Schoen C, Franasiak JM, et al. **Supplementation with progestogens** in the first trimester of pregnancy to prevent miscarriage in women with unexplained recurrent miscarriage: a systematic review and meta-analysis of randomized, controlled trials. Fertil Steril. 2017 Feb;107(2):430-438.e3.

Sachs HC and the American Academy of Pediatrics Committee on Drugs. The **transfer of drugs and therapeutics into human breast milk**: an update on selected topics. Pediatrics 2013;132:e796–e809.

Sagedal LR, Overby NC, Bere E, et al. **Lifestyle intervention to limit gestational weight gain**: the Norwegian Fit for Delivery randomised controlled trial. BJOG. 2016 Jan 14.

Saito S, Minakami H, Nakai A, et al. Outcomes of **infants exposed to oseltamivir or zanamivir in utero** during pandemic (H1N1) 2009. Am J Obstet Gynecol. 2013 Apr 9.

Salim R, et al. Adjusting **enoxaparin dosage** according to anti-FXa levels and pregnancy outcome in thrombophilic women. A randomised controlled trial. Thromb Haemost. 2016 Jul 21;116(4).

Sanabria-Martínez G, García-Hermoso A, Poyatos-León R, et al. Effectiveness of **physical activity interventions on preventing gestational diabetes** mellitus and excessive maternal weight gain: a meta-analysis. BJOG. 2015 Jun 3.

Sandin S, Nygren KG, Iliadou A, et al. **Autism** and mental retardation among offspring born after **in vitro fertilization**. JAMA. 2013 Jul 3;310(1):75-84.

Sanghavi M, Rutherford JD. **Cardiovascular** physiology of **pregnancy**. Circulation. 2014 Sep 16;130(12):1003-8.

Sanghavi M, Parikh NI. Harnessing the Power of Pregnancy and Pregnancy-Related Events to **Predict Cardiovascular** Disease in Women. Circulation. 2017 Feb 7;135(6):590-592.

Sarri G, Davies M, Gholitabar M, Norman JE; Guideline Development Group. **Preterm labour**: summary of **NICE** guidance. BMJ. 2015 Nov 23;351:h6283.

Saso A, Kampmann B. **Vaccination against respiratory syncytial virus in pregnancy**: a suitable tool to combat global infant morbidity and mortality? Lancet Infect Dis. 2016 Jun 14.

Sathyanarayana S, Butts S, Wang C, et al. Early **Prenatal Phthalate Exposure**, Sex Steroid Hormones, and Newborn Birth Outcomes. J Clin Endocrinol Metab. 2017 Mar 9.
Sayal K, Draper ES, Fraser R, et al. **Light drinking** in pregnancy and mid-childhood mental health and learning outcomes. Arch Dis Child 2013;98:107–11.
Schaufelberger M. **Cardiomyopathy and pregnancy**. Heart. 2019 Jul 15. pii:heartjnl-2018-313476.
Scherrer U, Rimoldi SF, Rexhaj E, et al. Systemic and pulmonary vascular dysfunction in children conceived by **assisted reproductive technologies**. Circulation. 2012 Apr 17;125(15):1890-6.
Schleussner E, Kamin G, Seliger G, et al; ETHIG II group. **Low-molecular-weight heparin** for women with **unexplained recurrent pregnancy loss**: a multicenter trial with a minimization randomization scheme. Ann Intern Med. 2015 May 5;162(9):601-9.
Schliep KC, Mitchell EM, Mumford SL, et al. Trying to Conceive **After an Early Pregnancy Loss**: An Assessment on **How Long Couples Should Wait**. Obstet Gynecol. 2016 Feb;127(2):204-12.
Schmiegelow MD, Andersson C, Køber L, et al. **Prepregnancy obesity** and associations with **stroke and myocardial infarction** in women in the years after childbirth: a nationwide cohort study. Circulation. 2014 Jan 21;129(3):330-7.
Schmidt RJ, Iosif AM, Guerrero Angel E, Ozonoff S. Association of **Maternal Prenatal Vitamin Use With Risk for Autism Spectrum Disorder** Recurrence in Young Siblings. JAMA Psychiatry. 2019 Feb 27.
Schmitz T, Fuchs F, Closset E, et al. Outpatient **cervical ripening by nitric oxide donors** for prolonged pregnancy: a randomized controlled trial. Obstet Gynecol. 2014 Dec;124(6):1089-97.
Schoeps A, van Ewijk R, Kynast-Wolf G, et al.**Ramadan Exposure In Utero and Child Mortality in Burkina Faso**: Analysis of a Population-Based Cohort Including 41,025 Children. Am J Epidemiol. 2018 Oct 1;187(10):2085-2092.
Schreiber CA et al. **Mifepristone pretreatment** for the medical management of **early pregnancy loss**. N Engl J Med 2018 Jun 7; 378:2161.
Schreiber K, Hunt BJ. **Managing antiphospholipid syndrome** in pregnancy. Thromb Res. 2019 Sep;181 Suppl 1:S41-S46.
Schuit E, Stock S, Rode L, et al. Effectiveness of **progestogens to improve perinatal outcome in twin pregnancies**: an individual participant data meta- analysis. BJOG. 2014 Aug 22.
Schummers L, Hutcheon JA, Hacker MR, et al. Absolute Risks of **Obstetric Outcomes Risks by Maternal Age at First Birth**: A Population-based Cohort. Epidemiology. 2018 May;29(3):379-387.
Schummers L, Hutcheon JA, Hernandez-Diaz S, et al. Association of **short interpregnancy interval with pregnancy outcomes** according to maternal age [online Oct 29, 2018]. JAMA Intern Med. doi:10.1001/jamainternmed.2018.4696
Scifres CM, Feghali M, et al. **Large-for-Gestational-Age** Ultrasound Diagnosis and **Risk for Cesarean Delivery** in Women With Gestational Diabetes Mellitus. Obstet Gynecol. 2015 Nov;126(5):978-86.
Sedgh G, Singh S, Hussain R. **Intended and unintended pregnancies worldwide** in 2012 and recent trends. Stud Fam Plann. 2014 Sep;45(3):301-14.
Seely EW, Ecker J. **Chronic hypertension** in pregnancy. Circulation. 2014 Mar 18;129(11):1254-61.
Sengpiel V, Elind E, Bacelis J, et al. **Maternal caffeine intake** during pregnancy is associated with birth weight but not with gestational length: results from a large prospective observational cohort study. BMC Med. 2013 Feb 19;11(1):42.
Servey J, Chang J. **Over-the-Counter Medications in Pregnancy**. Am Fam Physician. 2014;90(8):548-555.
Seshadri S, Oakeshott P, Nelson-Piercy C, Chappell LC. **Prepregnancy** care. BMJ. 2012 May 31;344:e3467.
Shakib JH, Korgenski K, Presson AP, et al. **Influenza** in Infants Born to Women **Vaccinated During Pregnancy**. Pediatrics. 2016 Jun;137(6).
Shallcross R, Bromley RL, Cheyne CP, et al. On behalf of the Liverpool and Manchester Neurodevelopment Group and The UK Epilepsy and Pregnancy Register. In utero exposure to **levetiracetam vs valproate**: Development and language at 3 years of age. Neurology. 2014 Jan 8.
Shand AW, Algert CS, March L, et al. **Second pregnancy outcomes for women with systemic lupus erythematosus**. Ann Rheum Dis. 2013 Apr;72(4):547-51.
Sharma C, Soni A, Gupta A, et al. **Hydralazine vs nifedipine for acute hypertensive emergency in pregnancy**: a randomized controlled trial. Am J Obstet Gynecol. 2017 Dec;217(6):687.e1-687.e6.
Sharp A, CornforthC, JacksonR, etal . **Maternal sildenafil for severe growth restriction (STRIDER):** a multicentre randomised placebo-controlled double-blind trial. Lancet Child Adolesc Health 2018;2:93-102. 10.1016/S2352-4642(17)30173-6.
Shaw JG, Asch SM, Kimerling R, et al. **Posttraumatic stress disorder** and risk of spontaneous preterm birth. Obstet Gynecol. 2014 Dec;124(6):1111-9.
Sheehy O, Zhao JP, Bérard A. Association Between **Incident Exposure to Benzodiazepines in Early Pregnancy and Risk of Spontaneous Abortion**. JAMA Psychiatry. 2019 May 15.
Sheen JJ, Wright JD, Goffman D, et al. **Maternal Age and Risk for Adverse Outcomes**. Am J Obstet Gynecol. 2018 Aug 25.
Shen ZQ, Gao SY, Li SX, et al. **Sertraline** use in the first trimester and risk of congenital anomalies: a systemic review and meta-analysis of cohort studies. Br J Clin Pharmacol. 2016 Oct 22.
Sheridan E, Wright J, Small N, et al. Risk factors for **congenital anomaly in a multiethnic** birth cohort: an analysis of the Born in Bradford study. Lancet. 2013 Jul 3.
Shi H, Enriquez A, Rapadas M, et al. **NAD Deficiency**, **Congenital** Malformations, and **Niacin** Supplementation. N Engl J Med. 2017 Aug 10;377(6):544-552
Shrim A, Koren G, Yudin MH, Farine D. Management of **varicella infection (chickenpox) in pregnancy**. J Obstet Gynaecol Can 2012 Mar;34(3):287-92.
Siberry GK, Williams PL, Mendez H, et al. for Pediatric HIVAIDS Cohort Study (PHACS). Safety of **tenofovir** use during pregnancy: early growth outcomes in HIV-exposed uninfected infants. AIDS. 2012 Feb 29.
Siemieniuk RA, Foroutan F, Mirza R, et al. Antiretroviral therapy for pregnant women living with **HIV or hepatitis B**: a systematic review and meta-analysis. BMJ Open. 2017 Sep 11;7(9):e019022
Siemieniuk RAC, Lytvyn L, Mah Ming J, et al. Antiretroviral therapy in pregnant women living with **HIV**: a clinical practice guideline. BMJ. 2017 Sep 11;358:j3961.
SIGN: Scottish Intercollegiate Guidelines Network, 2012. Management of **perinatal mood disorders**: a national clinical guideline [online]. Available: http://www.sign.ac.uk/guidelines/fulltext/127/index.html
Silversides CK et al. Pregnancy outcomes in **women with heart disease**: The CARPREG II study. J Am Coll Cardiol 2018 May 29; 71:2419.
Simons FE, Schatz M. **Anaphylaxis** during pregnancy. J Allergy Clin Immunol. 2012 Sep;130(3):597-606.
Singh N, McLean K. **Intravascular contrast media** for imaging in breastfeeding women. CMAJ. 2012 Oct 2;184(14):E775.
Sinha A, Sazawal S, Pradhan A, Ramji S,OpiyoN. **Chlorhexidine skin or cord care** for prevention of mortality and infections in neonates. Cochrane Database of Systematic Reviews 2015, Issue 3. Art.No.: CD007835. DOI: 10.1002/14651858.CD007835.pub2. There is some uncertainty as to the effect of chlorhexidine applied to the umbilical cords of newborns in hospital settings on neonatal mortality. The quality of evidence for the effects on infection are moderate for cord application and low for application to skin. There is high-quality evidence that chlorhexidine skin or cord care in the community setting results in a 50% reduction in the incidence of omphalitis and a 12% reduction in neonatal mortality. Maternal vaginal chlorhexidine compared to usual care probably leads to no difference in neonatal mortality in hospital settings. Maternal vaginal chlorhexidine compared to usual care results in no difference in the risk of infections in hospital settings. The uncertainty over the effect of maternal vaginal chlorhexidine on mortality outcomes reflects small sample sizes and low event rates in the community settings.

Siu AL. Screening for **Iron Deficiency Anemia** and Iron Supplementation in Pregnant Women to Improve Maternal Health and Birth Outcomes: U.S. Preventive Services Task Force Recommendation Statement. Ann Intern Med. 2015 Sep 8.

Sjaarda LA, Radin RG, Silver RM et al. **Preconception low-dose aspirin** restores diminished pregnancy and live birth rates in women with low grade inflammation: a secondary analysis of a randomized trial. J Clin Endocrinol. Metab. 2017. Online.

Skeith L, Carrier M, Kaaja R, et al. A meta-analysis of **low-molecular-weight heparin to prevent pregnancy loss** in women with inherited thrombophilia. Blood. 2016 Mar 31;127(13):1650-5.

Skjaerven R, Wilcox AJ, Klungsøyr K, et al. **Cardiovascular mortality after pre-eclampsia** in one child mothers: prospective, population based cohort study. BMJ. 2012 Nov 27;345:e7677.

Slaughter SR, Hearns-Stokes R, van der Vlugt T, et al. **FDA approval of doxylamine-pyridoxine** therapy for use in pregnancy. N Engl J Med. 2014 Mar 20;370(12):1081-3.

Smilowitz NR, Gupta N, Guo Y, et al. **Acute Myocardial Infarction During Pregnancy** and the Puerperium in the United States. Mayo Clin Proc. 2018 Jul 15.

Smith LA, Burns E, Cuthbert A. **Parenteral opioids for maternal pain management** in labour. Cochrane Database of Systematic Reviews 2018, Issue 6. Art. No.: CD007396. Though most evidence is of low- or very-low quality, for healthy women with an uncomplicated pregnancy who are giving birth at 37 to 42 weeks, parenteral opioids appear to provide some relief from pain in labour but are associated with drowsiness, nausea, and vomiting in the woman. Effects on the newborn are unclear. Maternal satisfaction with opioid analgesia was largely unreported.

Smith RB, Fecht D, Gulliver J, et al. Impact of **London's road traffic air and noise pollution** on birth weight: retrospective population based cohort study. 2017;395:j5299. doi:10.1136/bmj.j5299

Smoley BA, Robinson CM. **Natural Family Planning**. Am Fam Physician. 2012 Nov 15;86(10):924-928.

Smy L, Chan AC, Bozzo P, et al. Is it safe to use **inhaled corticosteroids in pregnancy**? Can Fam Physician. 2014 Sep;60(9):809-12.

Sng BL, LeongWL, Zeng Y, Siddiqui FJ, AssamPN, LimY, Chan ESY, Sia AT. **Early versus late initiation of epidural analgesia for labour**. Cochrane Database of Systematic Reviews 2014, Issue 10. Art. No.: CD007238. DOI: 10.1002/14651858.CD007238.pub2. There is predominantly high-quality evidence that early or late initiation of epidural analgesia for labour have similar effects on all measured outcomes. However, various forms of alternative pain relief were given to women who were allocated to delayed epidurals to cover that period of delay, so that is it hard to assess the outcomes clearly. We conclude that for first time mothers in labour who request epidurals for pain relief, it would appear that the time to initiate epidural analgesia is dependent upon women's requests.

Snowden JM, Tilden EL, Snyder J, et al. **Planned out-of-hospital birth and birth outcomes**. N Engl J Med 2015; 373: 2642-53.

SOGC: Society of Obstetricians and Gynaecologists of Canada, Okun N, Sierra S. **SOGC**-**Pregnancy outcomes after assisted human reproduction**. J Obstet Gynaecol Can. 2014 Jan;36(1):64-83.

SOGC: Society of Obstetricians and Gynaecologists of Canada. **SOGC**: **Diagnosis, evaluation, and management of the hypertensive disorders of pregnancy**: executive summary. J Obstet Gynaecol Can 2014;36:416-38. http://sogc.org/wp-content/uploads/2014/05/gui307CPG1405E1.pdf?1668a1(accessed June 25, 2014).

SOGC: Society of Obstetricians and Gynaecologists of Canada, **SOGC**: Wilson RD; Genetics Committee, Society of Obstetricians and Gynaecologists of Canada. **Pre-conception folic acid and multivitamin** supplementation for the primary and secondary prevention of neural tube defects and other folic acid-sensitive congenital anomalies. J Obstet Gynaecol Can 2015;37(6):534-49. http://sogc.org/wp-content/uploads/2015/06/gui324CPG1505E.pdf (accessed June 15, 2015).

SOGC: Society of Obstetricians and Gynaecologists of Canada, **SOGC**: Jain V, Chari R, et al. Guidelines for the Management of a **Pregnant Trauma Patient**. J Obstet Gynaecol Can. 2015 Jun;37(6):553-74.

SOGC: Ordean A, Wong S, Graves L. No. 349-**Substance Use in Pregnancy**. J Obstet Gynaecol Can. 2017 Oct;39(10):922-937.e2.

SOGC: Castillo E, Poliquin V. No. 357-**Immunization in Pregnancy**. J Obstet Gynaecol Can. 2018 Apr;40(4):478-489.

Sovio U, White IR, Dacey A, et al. **Screening for fetal growth restriction with universal third trimester ultrasonography** in nulliparous women in the Pregnancy Outcome Prediction (POP) study: a prospective cohort study. Lancet 2015; online Sept 8.

Spaan JJ, Brown MA. Can we **protect the kidneys after hypertensive** pregnancy? CMAJ. 2013 Feb 19;185(3):199-200.

Sridhar SB, Darbinian J, Ehrlich SF, et al. **Maternal gestational weight gain** and offspring risk for childhood overweight or obesity. Am J Obstet Gynecol. 2014 Apr 12.

Sridharan K, Sequeira RP. Drugs for treating **severe hypertension in pregnancy**:A network meta-analysis and trial sequential analysis of randomized clinical trials. Br J Clin Pharmacol. 2018 Jul 4.

Staff AC, Redman CW, et al; Global Pregnancy Collaboration (CoLab)*. Pregnancy and Long-Term Maternal **Cardiovascular Health**: Progress Through Harmonization of Research Cohorts and Biobanks. Hypertension. 2016 Feb;67(2):251-60.

Stagnaro-Green A, Sullivan S, Pearce EN. **Iodine supplementation** during pregnancy and lactation. JAMA. 2012 Dec 19;308(23):2463-4.

Stagnaro-Green A. **Screening pregnant women for overt thyroid disease**. JAMA. 2015 Feb 10; 313(6):565-6.

Stephenson J, Heslehurst N, Hall J, et al. Before the beginning: **nutrition and lifestyle in the preconception period** and its importance for future health. Lancet. 2018 Apr 16.

Stephansson O, Johansson K, Söderling J, et al. **Delivery outcomes in term births after bariatric surgery**: Population-based matched cohort study. PLoS Med. 2018 Sep 26;15(9):e1002656.

Steinhoff MC, Omer SB, Roy E, Arifeen et al. Neonatal outcomes after influenza immunization during pregnancy: a randomized controlled trial. CMAJ. 2012 Apr 3;184(6):645-53.

Steinhoff MC, MacDonald N, Pfeifer D, et al. **Influenza vaccine in pregnancy**: policy and research strategies. Lancet. 2014 May 10;383(9929):1611-3.

Stensballe LG, Simonsen J, Jensen SM, et al. Use of **Antibiotics during Pregnancy** Increases the Risk of **Asthma** in Early Childhood. J Pediatr. 2012 Nov 6.

Stephansson O, Kieler H, Haglund B, et al. **Selective serotonin reuptake inhibitors during pregnancy** and risk of stillbirth and infant mortality. JAMA. 2013 Jan 2;309(1):48-54.

Stephens S, Ford E, Paudyal P, et al. Effectiveness of **Psychological Interventions for Postnatal Depression** in Primary Care: A Meta-Analysis. Ann Fam Med. 2016 Sep;14(5):463-72.

Stergiakouli E, Thapar A, Davey Smith G. Association of **Acetaminophen** Use During Pregnancy With Behavioral Problems in Childhood: Evidence Against Confounding. JAMA Pediatr. 2016 Aug 15.

Stern SJ, Matok I, Kapur B, Koren G. Dosage Requirements for **Periconceptional Folic Acid** Supplementation: Accounting for BMI and Lean Body Weight. J Obstet Gynaecol Can. 2012 Apr;34(4):374-8.

Stevens W, Shih T, Incerti D, et al. Short-term **costs of preeclampsia** to the United States healthcare system. Am J Obstet Gynecol 2017, in press.

Stillbirth Collaborative Research Network Writing Group. Association between stillbirth and risk factors known at pregnancy confirmation. JAMA. 2011 Dec 14;306(22):2469-79.

Stillbirth Collaborative Research Network Writing Group. Causes of death among stillbirths. JAMA. 2011 Dec 14;306(22):2459-68.

Showell MG, Brown J, Clarke J, Hart RJ. **Antioxidants for female subfertility**. Cochrane Database Syst Rev. 2013 Aug 5;8:CD007807. The quality of the evidence in the 'antioxidant versus placebo/no treatment' and in the 'antioxidant versus antioxidant' comparisons was assessed to be 'very low'. Antioxidants were not associated with an increased live birth rate or clinical pregnancy rate. There was some evidence of an association of pentoxifylline with an increased clinical pregnancy rate; however, there were only three trials included in this comparison. Future trials may change this result. Variation in the types of antioxidants given meant that we could not assess whether one antioxidant was better than another. There did not appear to be any association of antioxidants with adverse effects for women, but data for these outcomes were limited.

Stancil SL, Miller M, Briggs H, et al. **Contraceptive provision to adolescent females prescribed teratogenic medications**. Pediatrics. 2016;137(1):e20151454

Steinberg ZL, Dominguez-Islas CP, Otto CM, et al. **Maternal and fetal outcomes of anticoagulation** in pregnant women with mechanical heart valves. J Am Coll Cardio 2017;69: 2681–91.
Stewart DE, Vigod S. **Postpartum Depression**. N Engl J Med. 2016 Dec;375(22):2177-2186.
Stewart ZA, Wilinska ME, Hartnell S, et al. **Closed-Loop Insulin Delivery** during Pregnancy in Women with Type 1 Diabetes. N Engl J Med. 2016 Aug 18;375(7):644-54
Stotland NE, Sutton P, Trowbridge J, et al. Counseling patients on **preventing prenatal environmental exposures** - a mixed-methods study of obstetricians. PLoS One. 2014 Jun 25;9(6):e98771
Stout MJ, Conner SN, Colditz GA, et al. The Utility of **12-Hour Urine Collection for the Diagnosis of Preeclampsia**: A Systematic Review and Meta-analysis. Obstet Gynecol. 2015 Oct;126(4):731-6.
Strand KM, Heimstad R, Iversen AC, et al. Mediators of the association between **pre-eclampsia and cerebral palsy**: population based cohort study. BMJ. 2013 Jul 9;347:f4089.
Stratakis N, Roumeliotaki T, Oken E, et al. **Fish Intake** in Pregnancy and Child Growth: A Pooled Analysis of 15 European and US Birth Cohorts. JAMA Pediatr. 2016 Feb 15.
Stratakis N, et al. **Fish and seafood consumption during pregnancy and the risk of asthma and allergic rhinitis** in childhood: a pooled analysis of 18 European and US birth cohorts. Int J Epidemiol. 2017 Oct 1;46(5):1465-1477.
Stremler R, Hodnett E, Kenton L, et al. Effect of **behavioural-educational intervention on sleep** for primiparous women and their infants in early postpartum: multisite randomised controlled trial. BMJ. 2013 Mar 20;346:f1164.
Stritzke AI, Seow CH. **Inflammatory bowel disease** in pregnancy. CMAJ. 2017 May 8;189(18):E669.
Stuart A and Källen K. **Risk of abdominal surgery** in pregnancy among women who have **undergone bariatric surgery**. Obstet Gynecol 2017 Apr 4.
Stuart JJ, Tanz LJ, Missmer SA, et al. **Hypertensive disorders of pregnancy and maternal cardiovascular disease risk factor development**. An observational cohort study. Ann Intern Med. 2018. [Epub ahead of print]. doi:10 .7326/M17-2740
Sucksdorff M, Lehtonen L, Chudal R, et al. **Preterm Birth and Poor Fetal Growth as Risk Factors of Attention-Deficit/Hyperactivity Disorder**. Pediatrics. 2015 Aug 24.
Sukumaran L, McCarthy NL, Kharbanda EO, et al. Association of **Tdap Vaccination** With Acute Events and Adverse Birth Outcomes Among Pregnant Women With Prior Tetanus-Containing Immunizations. JAMA. 2015 Oct 20;314(15):1581-7.
Sun F, Sebastiani P, Schupf N, et al. **Extended maternal age** at birth of last child and women's longevity in the Long Life Family Study. Menopause. 2014 Jun 23.
Suematsu Y, Obi Y, Shimomura A, et al. Risk of **Postoperative Venous Thromboembolism** Among Pregnant Women. Am J Cardiol. 2017 Aug 1;120(3):479-483.
Sullivan PM, Dervan LA, Reiger S, et al. Risk of **Congenital Heart Defects** in the Offspring of **Smoking Mothers**: A Population-Based Study. J Pediatr. 2015 Jan 9.
Sullivan SA. **Hypothyroidism in Pregnancy**. Clin Obstet Gynecol. 2019 Jun;62(2):308-319.
Sultan AA, West J, Grainge MJ, et al. Development and validation of **risk prediction model for venous thromboembolism in postpartum** women: multinational cohort study. BMJ. 2016 Dec 5;355:i6253.
Suren P, Roth C, Bresnahan M, et al. Association between maternal use of **folic acid** supplements and risk of **autism spectrum** disorders in children. JAMA. 2013;309(6):570-577.
Surkan PJ, Ettinger AK, Ahmed S, et al. Impact of **Maternal Depressive** Symptoms on Growth of Preschool- and School-Aged Children. Pediatrics. 2012 Sep 10.
Sutcliffe AG, Barnes J, Belsky J, et al. The health and development of children born to **older mothers** in the United Kingdom: observational study using longitudinal cohort data. BMJ. 2012 Aug 21;345:e5116.
Swamy GK and Heine RP.**Vaccinations for pregnant women**. Obstet Gynecol 2015 Jan; 125:212.
Swan SH, Sathyanarayana S, Barrett ES, et al. The **TIDES** Study Team. **First trimester phthalate exposure** and anogenital distance in newborns. Hum Reprod. 2015 Feb 18.
Swartz RH, Ladhani NNN, Foley N, et al; Heart and Stroke Foundation Canadian Stroke Best Practice Committees. Canadian stroke best practice consensus statement: **secondary stroke prevention during pregnancy**. Int J Stroke 2017 (accessed December 12, 2017).
Syngelaki A, Nicolaides KH, Balani J, et al. **Metformin** versus Placebo in **Obese Pregnant** Women without Diabetes Mellitus. N Engl J Med. 2016 Feb 4;374(5):434-43.
Tabet M, Flick LH, Tuuli MG, et al. **Prepregnancy body mass index** in a first uncomplicated pregnancy and outcomes of a second pregnancy. Am J Obstet Gynecol. 2015 Jun 20.
Tam WH, Ma RC, Ozaki R, et al. In Utero Exposure to **Maternal Hyperglycemia Increases Childhood Cardiometabolic Risk** in Offspring. Diabetes Care. 2017 Mar 9.
Tan M, Kim E, Koren G, Bozzo P. **Botulinum toxin type A** in pregnancy. Can Fam Physician. 2013 Nov;59(11):1183-4.
Tangren JS, Powe CE, Ankers E, et al. Pregnancy Outcomes **after** C**linical Recovery from AKI**. J Am Soc Nephrol. 2016 Dec 22.
Tappin D, Bauld L, Purves D, et al; Cessation in Pregnancy Incentives Trial (**CPIT**) Team. **Financial incentives** for **smoking cessation in pregnancy**: randomised controlled trial. BMJ. 2015 Jan 27;350:h134.
Taylor, Tricia. Treatment of **nausea and vomiting** in pregnancy. Australian Prescriber. AN INDEPENDENT REVIEW (2014): 42.
Taylor PN, Minassian C, Rehman A, et al. **TSH Levels and Risk of Miscarriage** in Women on Long-Term Levothyroxine: A Community-Based Study. J Clin Endocrinol Metab. 2014 Jul 24
Tegethoff M, Olsen J, Schaffner E, Meinlschmidt G. **Asthma During Pregnancy** and Clinical Outcomes in Offspring: A National Cohort Study. Pediatrics. 2013 Aug 5.
Tellez A, Rueda S, Conic RZ, et al. Risk factors and outcomes of **cutaneous melanoma** in women less than 50 years of age. (pregnancy) J Am Acad Dermatol. 2016 Jan 11.
Telner D, Barrett R, Shirodkar A, et al. **Preconception Health Care Tool**: One-stop shop for preconception care. Can Fam Physician. 2017 Nov;63(11):867-868.
Tertti K, Ekblad U, Koskinen P, et al. **Metformin Vs Insulin in Gestational Diabetes**. A Randomized Study Characterizing Metformin Patients Needing Additional Insulin. Diabetes Obes Metab. 2012 Sep 28.
Thangaratinam S, Rogozińska E, Jolly K, et al. Effects of **interventions in pregnancy on maternal weight** and obstetric outcomes: meta-analysis of randomised evidence. BMJ 2012;344:e2088.
The International Weight Management in Pregnancy (**i-WIP)** Collaborative Group. Effect of **diet and physical activity based interventions in pregnancy on gestational weight gain** and pregnancy outcomes: meta-analysis of individual participant data from randomised trials. BMJ 2017;358:j3119
Theilen LH et al. All-cause and cause-specific mortality after **hypertensive disease of pregnancy**. Obstet Gynecol 2016 Aug; 128:238.
Thompson MG, Kwong JC, Regan AK, et al; PREVENT Workgroup . **Influenza Vaccine Effectiveness in Preventing Influenza-associated Hospitalizations During Pregnancy**: A Multi-country Retrospective Test Negative Design Study, 2010-2016. Clin Infect Dis. 2018 Oct 11.
Timm NL. **Maternal Use of Oxycodone** Resulting in Opioid Intoxication in Her Breastfed Neonate. J Pediatr. 2012 Oct 10.
Tita ATN, Szychowski JM, Boggess K, et al. Adjunctive **azithromycin prophylaxis for cesarean delivery**. N Engl J Med 2016;375:1231-41.
Tkachenko E, Singer S, Sharma P, et al. US Food and Drug Administration Reports of Pregnancy and Pregnancy-Related **Adverse Events Associated With Isotretinoin**. JAMA Dermatol. 2019 Jul 17.
Tobias DK, Hu FB, Chavarro J, et al. **Healthful Dietary Patterns** and Type 2 Diabetes Mellitus Risk Among Women With a History of Gestational Diabetes Mellitus. Arch Intern Med. 2012 Sep 17:1-7.
Tobias DK, Stuart JJ, Li S, et al. Association of **history of gestational diabetes with long-term cardiovascular disease** risk in a large prospective cohort of US women [online Oct 16, 2017].

JAMA Intern Med. doi:10.1001/jamainternmed.2017.2790
Tolia VN, Patrick SW, Bennett MM, et al. Increasing Incidence of the **Neonatal Abstinence Syndrome** in U.S. Neonatal ICUs. N Engl J Med. 2015 Apr 26.
Tomson T, Battino D, Bonizzoni E, et al. **Antiepileptic drugs and intrauterine death**: A prospective observational study from EURAP. Neurology. 2015 Jul 17.
Tomson T, Battino D, Bonizzoni E, et al. Declining **malformation rates with changed antiepileptic drug prescribing**: an observational study. Neurology 2019;93:e831–e840.
Tomson T, Battino D, Perucca E. **Valproic acid** after five decades of use in epilepsy: time to reconsider the indications of a time-honoured drug. Lancet Neurol 2016; 15: 210–18.
Tomson T, et al. Comparative risk of **major congenital malformations with eight different antiepileptic drugs**: a prospective cohort study of the **EURAP registry**. Lancet Neurol 2018; online April 18.
Trapani A Jr, Gonçalves LF, et al. Perinatal and Hemodynamic Evaluation of **Sildenafil Citrate for Preeclampsia** Treatment: A Randomized Controlled Trial. Obstet Gynecol. 2016 Aug;128(2):253-9.
Travers CP, Clark RH, Spitzer AR, et al. Exposure to any **antenatal corticosteroids** and outcomes in preterm infants by gestational age: prospective cohort study. BMJ 2017;356:i1039.
Trivedi S, Williams C, Torrone E, Kidd S. National Trends and Reported Risk Factors Among **Pregnant Women With Syphilis** in the United States, 2012-2016. Obstet Gynecol. 2019 Jan;133(1):27-32.
Trottier M, Erebara A, Bozzo P. Treating **constipation** during pregnancy. Can Fam Physician. 2012 Aug;58(8):836-8.
Truong MB, Ngo E, Ariansen H, et al. **Community pharmacist counseling** in early pregnancy-Results from the SafeStart feasibility study. PLoS One. 2019 Jul 19;14(7):e0219424.
Tsao NW, et al. **Risk of preterm delivery and small-for-gestational-age births in women with autoimmune disease using biologics before or during pregnancy**: a population-based cohort study. Ann Rheum Dis. 2018 Mar 1.
Tuovinen S, Räikkönen K, Kajantie E, et al. **Hypertensive disorders** in pregnancy and **cognitive decline** in the offspring up to old age. Neurology. 2012 Oct 9;79(15):1578-1582.
Turner SD, Gomes T, Camacho X, et al. **Neonatal opioid withdrawal** and antenatal **opioid prescribing**. CMAJ Open. 2015 Jan 13;3(1):E55-61.
Tyrrell J, Richmond RC, Palmer TM, et al; Early Growth Genetics (EGG) Consortium. Genetic Evidence for Causal Relationships Between **Maternal Obesity-Related Traits and Birth Weight**. JAMA. 2016 Mar 15;315(11):1129-1140.
Udell JA, Lu H, Redelmeier DA. Long-term **cardiovascular risk in women prescribed fertility** therapy. J Am Coll Cardiol. 2013 Oct 29;62(18):1704-12.
Umaretiya PJ, Oberhelman SS, Cozine EW et al. **Maternal Preferences for Vitamin D Supplementation** in Breastfed Infants. Annals of Family Medicine. 2017; 15(1):68-70.
Underwood L, Waldie KE, et al. **Paternal Depression** Symptoms During Pregnancy and After Childbirth Among Participants in the Growing Up in New Zealand Study. JAMA Psychiatry. 2017 Feb 15.
Urquia ML, Berger H, Ray JG; for the Canadian Curves Consortium. Risk of adverse outcomes among infants of **immigrant women** according to **birth-weight curves** tailored to maternal world region of origin. CMAJ. 2014 Nov 10.
USPSTF:. **Folic acid supplementation** for the prevention of neural tube defects: US Preventive Services Task Force Recommendation Statement.JAMA. doi:10.1001 /jama.2016.19438
USPSTF: Curry SJ, Krist AH, Owens DK, et al. Interventions to Prevent Perinatal Depression: US Preventive Services Task Force Recommendation Statement. JAMA. 2019 Feb 12;321(6):580-587.
USPSTF: O'Connor E, Senger CA, Henninger ML, et al. Interventions to Prevent Perinatal Depression: Evidence Report and Systematic Review for the US Preventive Services Task Force. JAMA. 2019 Feb 12;321(6):588-601.
Ussher M, Lewis S, Aveyard P, et al. **Physical activity for smoking cessation** in pregnancy: randomised controlled trial. BMJ. 2015 May 14;350
Valensise H, Lo Presti D, Gagliardi G, et al. **Persistent maternal cardiac dysfunction after preeclampsia** identifies patients at risk for recurrent preeclampsia. *Hypertension* 2016.
Valente AM, Economy KE. **Preeclampsia**. Circulation. 2013 Oct 22;128(17):e344-5.
Valera-Gran D, García de la Hera M, Navarrete-Muñoz EM, et al; Infancia y Medio Ambiente (INMA) Project. **Folic Acid supplements** during pregnancy and child psychomotor development after the first year of life. JAMA Pediatr. 2014 Nov 3;168(11):e142611.
Valgeirsdottir H, Vanky E, Sundström-Poromaa I, et al. **Prenatal exposures and birth indices**, and subsequent risk of p**olycystic ovary syndrome**: a national registry-based cohort study. BJOG. 2018 Jun 12.
Van Boekholt AA, Hartong EG, Huntjens-Fleuren H, et al. **Quetiapine** concentrations during exclusive **breastfeeding** and maternal quetiapine use. Ann Pharmacother. 2015 Jun;49(6):743-4.
van der Pol LM, Tromeur C, Bistervels IM, et al. Pregnancy-Adapted **YEARS Algorithm for Diagnosis of Suspected Pulmonary Embolism**. N Engl J Med. 2019 Mar 21;380(12):1139-1149.
van der Waerden J, Galéra C, Larroque B, et al; EDEN Mother–Child Cohort Study Group. **Maternal Depression Trajectories and Children's Behavior** at Age 5 Years. J Pediatr. 2015 Apr 9.
van Gelder MMHJ, Rog A, Bredie SJH, et al. **Social media monitoring on the perceived safety of medication use** during pregnancy: a case study from The Netherlands. Br J Clin Pharmacol. 2019 Aug 4.
van Hagen IM, Roos-Hesselink JW, Ruys TPE, et al. **Pregnancy in women with a mechanical heart valve**: Data of the European Society of Cardiology Registry Of Pregnancy And Cardiac disease (ROPAC). Circulation. 2015;132:132–142.
van Hagen IM, Thorne SA, Taha N, et al; on behalf of the **ROPAC** Investigators and **EORP** Team. **Pregnancy outcomes in women with rheumatic mitral valve disease**: results from the Registry of Pregnancy and Cardiac Disease. Circulation. 2018;137:806–816.
Van Leer P. **Vitamin E in** Pregnancy. Am Fam Physician. 2017 Apr 1;95(7):Online.
van Leeuwen M, Louwerse MD, Opmeer BC et al. Glucose challenge test for detecting gestational diabetes mellitus: a systematic review. BJOG. 2012 Mar;119(4):393-401.
van Mens TE, Scheres LJJ, de Jong PG, et al. **Imaging for the exclusion of pulmonary embolism in pregnancy**. Cochrane Database of Systematic Reviews 2017, Issue 1. Art. No.: CD011053. Both CTPA and lung scintigraphy seem appropriate for exclusion of pulmonary embolism during pregnancy. However, the quality of the evidence mandates cautious adoption of this conclusion. Important limitations included poor reference standards, necessary assumptions in the analysis regarding inconclusive test results and the inherent inability of included studies to identify false positives. It is unclear which test has the highest accuracy. There is a need for direct comparisons between diagnostic methods, including MR, in prospective randomized diagnostic studies.
van Rossem L, Wijga AH, Gehring U, et al. **Maternal Gestational and Postdelivery Weight Gain** and Child Weight. Pediatrics. 2015 Oct 19.
Varner MW, Silver RM, Rowland Hogue CJ, et al; Eunice Kennedy Shriver National Institute of Child Health and Human Development Stillbirth Collaborative Research Network. Association between **stillbirth and illicit drug use and smoking** during pregnancy. Obstet Gynecol. 2014 Jan;123(1):113-25.
Vasileiou V, Kyratzoglou E, Paschou SA, et al. The impact of **environmental temperature on the diagnosis of gestational diabetes** mellitus. Eur J Endocrinol. 2018 Jan 23.
Vatzaki E, Straus S, Dogne JM, et al. Latest clinical recommendations on **valproate use for migraine prophylaxis in women of childbearing age**: overview from European Medicines Agency and European Headache Federation. J Headache Pain. 2018 Aug 14;19(1):68.
Vaughan Jones S, Ambros-Rudolph C, Nelson-Piercy C. **Skin disease** in pregnancy. BMJ. 2014 Jun 3;348:g3489.

Veiby G, Engelsen BA, Gilhus NE. Early Child Development and Exposure to **Antiepileptic Drugs Prenatally and Through Breastfeeding**: A Prospective Cohort Study on Children of Women With Epilepsy. JAMA Neurol. 2013 Sep 23.
Veiga-Lopez A, Kannan K, Liao C, et al. Gender-Specific Effects on Gestational Length and Birth Weight by Early Pregnancy **BPA Exposure**. J Clin Endocrinol Metab. 2015 Sep 25:jc20151724.
Venkatesh KK, Zlotnick C, Triche EW, et al. Accuracy of Brief Screening Tools for **Identifying Postpartum Depression** Among Adolescent Mothers. Pediatrics. 2013 Dec 16
Verburg PE, Tucker G, Scheil W, et al. **Sexual Dimorphism** in Adverse Pregnancy Outcomes - A Retrospective Australian Population Study 1981-2011. PLoS One. 2016 Jul 11;11(7)
Verhaegen J, Gallos ID, et al. Accuracy of single **progesterone test** to predict early pregnancy outcome in women with pain or bleeding: meta-analysis of cohort studies. BMJ. 2012 Sep 27;345:e6077.
Vesco KK, Leo MC, Karanja N, et al. One-year postpartum outcomes following a **weight management intervention** in pregnant women with obesity. Obesity (Silver Spring). 2016 Oct;24(10):2042-9.
Viale L, Allotey J, Cheong-See F, et al, for EBMCONNECT Collaboration. **Epilepsy in pregnancy and reproductive outcomes**: a systematic review and meta-analysis. Lancet 2015; online Aug 26
Vigod SN, Kurdyak PA, Dennis CL, et al. Maternal and newborn outcomes among women with schizophrenia: a retrospective population-based cohort study. BJOG. 2014 Apr;121(5):566-74.
Vigod SN, Tarasoff LA, Bryja B, et al. Relation between place of **residence and postpartum depression**. CMAJ. 2013 Aug 6.
Vigod SN, Wilson CA, Howard LM. **Depression in pregnancy**. BMJ. 2016 Mar 24;352:i1547.
Vijayaraghavan R, Verma S, Gupta N, Saw J. Pregnancy-related spontaneous **coronary artery dissection**. Circulation. 2014 Nov 18;130(21):1915-20.
Viktorin A, Uher R, Kolevzon A, et al. Association of **Antidepressant Medication Use During Pregnancy With Intellectual Disability in Offspring**. JAMA Psychiatry. 2017 Jul 12
Viktorin A, Levine SZ, Altemus M, et al. **Paternal use of antidepressants and offspring outcomes** in Sweden: nationwide prospective cohort study. BMJ. 2018 Jun 8;361:k2233.
Villamor E, Tedroff K, Peterson M, et al. Association Between **Maternal Body Mass Index** in Early Pregnancy and Incidence of **Cerebral Palsy**. JAMA. 2017 Mar 7;317(9):925-936.
Villar J, Papageorghiou AT, Pang R, et al; for the International Fetal and Newborn Growth Consortium for the 21st Century (INTERGROWTH-21(st)). The likeness of fetal growth and newborn size across non-isolated populations in the INTERGROWTH-21(st) Project: the **Fetal Growth Longitudinal Study** and Newborn Cross-Sectional Study. Lancet Diabetes Endocrinol. 2014 Jul 4
Vinding RK, Stokholm J, Sevelsted A, et al. Effect of **fish oil supplementation in pregnancy on bone, lean, and fat mass at six years**: randomised clinical trial. BMJ. 2018 Sep 4;362:k3312.
Vinet E et al. A population-based assessment of live births in women with systemic lupus erythematosus. Ann Rheum Dis. 2012 Apr;71(4):557-9. Epub 2011 Nov 14.
Vinet É, Pineau CA, Scott S, et al. Increased **congenital heart defects** in children born to **women with systemic lupus erythematosus**: results from the offspring of systemic lupus erythematosus mothers registry study. Circulation. 2015 Jan 13;131(2):149-56.
Vinter CA, Jensen DM, Ovesen P, Beck-Nielsen H, Jørgensen JS. The **LiP (Lifestyle in Pregnancy)** study: a randomized controlled trial of lifestyle intervention in 360 obese pregnant women. Diabetes Care 2011;34:2502–7.
Viteri OA, England JA, Alrais MA, et al. Association of **Nonsteroidal Antiinflammatory Drugs** and Postpartum Hypertension in Women With Preeclampsia With Severe Features. Obstet Gynecol. 2017 Sep 5.
Vogel JP, West HM, Dowswell T. Titrated oral **misoprostol for augmenting labour** to improve maternal and neonatal outcomes. Cochrane Database Syst Rev. 2013 Sep 23;9:CD010648. Important uncertainties still exist on the safety and acceptability of titrated oral misoprostol compared with intravenous oxytocin regimens in women with dystocia following spontaneous onset of labour. Although in facilities where electronic oxytocin infusion is not available, low-dose titrated misoprostol may offer a better alternative to an uncontrolled oxytocin infusion to avoid hyperstimulation.
Vogel JP, Nardin JM, Dowswell T, West HM, Oladapo OT. **Combination of tocolytic agents** for inhibiting preterm labour. Cochrane Database Syst Rev. 2014 Jul 11;7:CD006169. doi: 10.1002/14651858.CD006169.pub2.
Voinescu PE, Park S, Chen LQ, et al. **Antiepileptic drug clearances during pregnancy** and clinical implications for women with epilepsy. Neurology. 2018 Sep 25;91(13):e1228-e1236.
Volkow ND, Han B, Compton WM, Blanco C. **Marijuana Use** During Stages of Pregnancy in the United States. Ann Intern Med. 2017 Apr 18.
Volkow ND, Han B, Compton WM, McCance-Katz EF. **Self-reported medical and nonmedical cannabis use** among pregnant women in the United States [June 18, 2019]. JAMA. doi:10.1001/jama.2019.7982
Vrijkotte TGM, Hrudey EJ, Tickler TB. Early **maternal thyroid** function during gestation is associated with fetal growth, particularly in male newborns. J Clin Endocrinol. Metab. 2017. Online
Vutyavanich T, Wongtra-ngan S, Ruangsri R-a. **Pyridoxine** for nausea and vomiting of pregnancy: a randomized, double-blind, placebo-controlled trial. Am J Obstet Gynecol 1995;173:881-4
Walker I, Chappell LC, Williamson C. **Abnormal liver function** tests in pregnancy. BMJ. 2013 Oct 25;347:f6055.
Walker KF, Bugg GJ, Macpherson M, et al. Randomized trial of **labor induction** in women 35 years of age or older. (35/39) N Engl J Med 2016;374:813-22.
Walker KF, Dritsaki M, Bugg G, et al. **Labour induction near term** for women aged 35 or over: an economic evaluation. BJOG. 2017 Jan 11.
Walker KF, Kibuka M, Thornton JG, Jones NW. **Maternal position** in the second stage of labour for women **with epidural anaesthesia**. Cochrane Database Syst Rev. 2018 Nov 9;11:CD008070.
Wallenius M, Lie E, Daltveit AK, et al. **No excess risks in offspring** with paternal preconception exposure to **disease modifying anti-rheumatic drugs**. Arthritis Rheumatol. 2014 Nov 24.
Walsh JM, McGowan CA, Mahony R, et al. **Low glycaemic index diet** in pregnancy to prevent macrosomia (ROLO study): randomised control trial. BMJ. 2012 Aug 30;345:e5605.
Walsh LK, Donelle J, Dodds L, et al. Health outcomes of young children born to **mothers who received 2009 pandemic H1N1 influenza vaccination** during pregnancy: retrospective cohort study. BMJ. 2019 Jul 10;366:l4151.
Wang C, Wei Y, Zhang X, et al. A randomized clinical trial of **exercise during pregnancy to prevent gestational diabetes mellitus** and improve pregnancy outcome in overweight and obese pregnant women. Am J Obstet Gynecol. 2017 Apr;216(4):340-351.
Wang H, Wender-Ozegowska E, Garne E, et al. **Insulin analogues use in pregnancy** among women with pregestational diabetes mellitus and risk of congenital anomaly: a retrospective population-based cohort study. BMJ Open. 2018 Feb 24;8(2):e014972.
Wang IK, Muo CH, Chang YC, et al. Association between **hypertensive disorders during pregnancy and end-stage renal disease**: a population-based study. CMAJ. 2013 Jan 21.
Wang G, Divall S, Radovick S, et al. **Preterm birth and random plasma insulin levels** at birth and in early childhood. JAMA. 2014 Feb 12;311(6):587-96.
Wang H, Mueller NT, Li J, et al. Association of **Maternal Plasma Folate** and Cardiometabolic Risk Factors in Pregnancy with Elevated Blood Pressure of Offspring in Childhood. Am J Hypertens. 2017 Mar 6.
Wang M, Fontaine P. Common questions about **late-term and postterm pregnancy**. Am Fam Physician. 2014 Aug 1;90(3):160-5.
Wang Y, Liu G, Canfield MA, et al. **Racial/Ethnic differences in survival** of United States children with birth defects: a population-based study. J Pediatr. 2015 Apr;166(4):819-826.e2.
Webb S, Sherburn M, Ismail KM. Managing **perineal trauma** after childbirth. BMJ. 2014 Nov 25;349:g6829.
Weber KA, Mayo JA, et al. Occurrence of Selected **Structural Birth Defects Among Women With Preeclampsia and Other Hypertensive Disorders**. Am J Epidemiol. 2018 Apr 1;187(4):668-676.

Weber-Schoendorfer C, Chambers C, Wacker E, et al. Pregnancy outcome after rheumatologic methotrexate (MTX) treatment prior to or during early pregnancy: A prospective multicenter cohort study. Arthritis Rheumatol. 2014 Jan 27
Weber-Schoendorfer C, Hoeltzenbein M, Wacker E, et al. No evidence for an increased risk of adverse pregnancy outcome after paternal low-dose methotrexate: an observational cohort study. Rheumatology (Oxford). 2013 Dec 24
Weber-Schoendorfer C, Oppermann M, Wacker E, et al. Pregnancy outcome after **TNF-α inhibitor therapy** during the first trimester: a prospective multicentre cohort study. Br J Clin Pharmacol. 2015 Mar 25.
Webster K, Fishburn S, Maresh M, et al. **Diagnosis and management of hypertension** in pregnancy: summary of updated NICE guidance. BMJ. 2019 Sep 9;366:l5119.
Webster LM, et al. Impact of **Antihypertensive Treatment on Maternal and Perinatal Outcomes in Pregnancy** Complicated by Chronic Hypertension: A Systematic Review and Meta-Analysis. J Am Heart Assoc. 2017 May 17;6(5).
Webster LM, et al. **Labetalol Versus Nifedipine** as Antihypertensive Treatment for Chronic Hypertension in Pregnancy: A Randomized Controlled Trial. Hypertension. 2017 Nov;70(5):915-922.
Weissgerber TL, Turner ST, Mosley TH Jr, et al. **Hypertension in Pregnancy** and Future **Cardiovascular Event Risk in Siblings**. J Am Soc Nephrol. 2015 Aug 27.
Wells RE, Turner DP, Lee M, Bishop L, Strauss L. Managing **Migraine** During Pregnancy and Lactation. Curr Neurol Neurosci Rep. 2016 Apr;16(4):40.
Wenger NK. Recognizing **Pregnancy-Associated Cardiovascular Risk Factors**. Am J Cardiol. 2013 Oct 6.
Wen SW, White RR, Rybak N, et al; FACT Collaborating Group. **Effect of high dose folic acid supplementation in pregnancy on pre-eclampsia (FACT**): double blind, phase III, randomised controlled, international, multicentre trial. BMJ. 2018 Sep 12;362:k3478.
Wen X, Meador KJ, Hartzema A. **Antiepileptic drug use** by pregnant women enrolled in Florida Medicaid. Neurology 2015;84:944–950.
Werner EF, Hauspurg AK, Rouse DJ. A Cost-Benefit Analysis of **Low-Dose Aspirin** Prophylaxis for the Prevention of **Preeclampsia** in the United States. Obstet Gynecol. 2015 Dec;126(6):1242-50.
West HW, Juonala M, Gall SL, et al. **Exposure to Parental Smoking** in Childhood is Associated with Increased Risk of Carotid Atherosclerotic Plaque in Adulthood: The Cardiovascular Risk in Young Finns Study. Circulation. 2015 Mar 23.
West KP Jr, Shamim AA, Mehra S, et al. Effect of maternal **multiple micronutrient vs iron-folic acid supplementation** on infant mortality and adverse birth outcomes in rural Bangladesh: the JiVitA-3 randomized trial. JAMA. 2014 Dec 24-31;312(24):2649-58.
Westhoff G, Cotter AM, Tolosa JE. **Prophylactic oxytocin for the third stage of labour to prevent postpartum haemorrhage.**Cochrane Database Syst Rev. 2013 Oct 30;10:CD001808.
Which drugs are best for treating severe hypertension in pregnancy? Drug Ther Bull. 2019 Apr;57(4):53.
White SL, Pasupathy D, Sattar N, et al; **UPBEAT** Consortium. **Metabolic profiling of gestational diabetes** in obese women during pregnancy. Diabetologia. 2017 Aug 1.
WHO. WHO recommendations on **antenatal care** for a positive pregnancy experience. Online. 2016.
Wickham ME, Senthilselvan A, Wild TC, et al. **Maternal depressive symptoms** during childhood and risky adolescent health behaviors. Pediatrics. 2015 Jan;135(1):59-67.
Wiebe HW, Boulé NG, Chari R, et al. The Effect of **Supervised Prenatal Exercise** on Fetal Growth: A Meta-analysis. Obstet Gynecol. 2015 May;125(5):1185-94.
Wieck A, Jones S. **Dangers of valproate in pregnancy**. BMJ. 2018 Apr 18;361:k1609.
Wiegersma AM, Dalman C, Lee BK, et al. Association of **Prenatal Maternal Anemia With Neurodevelopmental Disorders**. JAMA Psychiatry. 2019 Sep 18:1-12.
Wikström AK, Gunnarsdottir J, Nelander M, et al. **Prehypertension** in Pregnancy and Risks of Small for Gestational Age Infant and Stillbirth. Hypertension. 2016 Feb 1.
Wiles JR, Isemann B, Ward LP, et al. Current Management of **Neonatal Abstinence Syndrome** Secondary to Intrauterine Opioid Exposure. J Pediatr. 2014 Jun 16.
Wiles JR, Isemann B, Mizuno T, et al. Pharmacokinetics of Oral **Methadone in the Treatment of Neonatal Abstinence Syndrome**: A Pilot Study. J Pediatr. 2015 Sep 10.
Wiles KS, Jarvis S, Nelson-Piercy C. Are we **overtreating subclinical hypothyroidism in pregnancy**? BMJ. 2015 Oct 12;351:h4726.
Williams CL, Bunch KJ, Stiller CA, et al. **Cancer risk** among children born after **assisted conception**. N Engl J Med. 2013 Nov 7;369(19):1819-27.
Williams D, Craft N. **Pre-eclampsia**. BMJ. 2012 Jul 19;345:e4437.
Williams Fl, Ogston S, Hume R, et al. **Supplemental Iodide** for Preterm Infants and Developmental Outcomes at 2 years: an RCT. Pediatrics. 2017;139(5):e20163703
Williams JF, Smith VC; Committee on Substance Abuse. **Fetal Alcohol Spectrum Disorders**. Pediatrics. 2015 Oct 19.
Windrim C, McGeer AJ, Murphy KE. **Exposure to rabies** during pregnancy. CMAJ. 2018 Oct 29;190(43):E1281-E1283.
Wisner KL, Sit DK, McShea MC, et al. Onset Timing, Thoughts of Self-harm, and Diagnoses in Postpartum Women With Screen-Positive **Depression** Findings. JAMA Psychiatry. 2013 Mar 13:1-9.
Wisner KL, Bogen DL, Sit D, McShea M, et al. Does **Fetal Exposure to SSRIs or Maternal Depression** Impact Infant Growth? Am J Psychiatry. 2013 Mar 20.
Wollenhaupt M, Chandrasekaran A, Tomianovic D. The safety of **oseltamivir in pregnancy**: an updated review of post-marketing data. Pharmacoepidemiol Drug Saf. 2014;23:1035-1042.
Woolner A, et al. The effect of method and **gestational age at termination of pregnancy** on future obstetric and perinatal outcomes: a register-based cohort study in Aberdeen, Scotland. BJOG. 2013 Oct 22.
Wortham JM, Hansen NI, et al; Eunice Kennedy Shriver NICHD Neonatal Research Network. **Chorioamnionitis** and Culture-Confirmed, Early-Onset **Neonatal Infections**. Pediatrics. 2016 Jan;137(1):1-11.
Wright D, Rolnik DL, Syngelaki A, et al. **Aspirin for Evidence-Based Preeclampsia Prevention** trial: effect of aspirin on length of stay in the neonatal intensive care unit. Am J Obstet Gynecol. 2018 Jun;218(6):612.e1-612.e6.
Wu P, Haththotuwa R, Kwok CS, et al. **Preeclampsia and Future Cardiovascular Health**: A Systematic Review and Meta-Analysis. Circ Cardiovasc Qual Outcomes. 2017 Feb;10(2).
Wu Q, Huang H, et al. **Telbivudine** prevents vertical transmission of **hepatitis B virus** from women with high viral loads: a prospective long-term study. Clin Gastroenterol Hepatol. 2015 Jun;13(6):1170-6.
Wyld ML, Clayton PA, Kennedy SE, et al. **Pregnancy outcomes for kidney transplant recipients** with transplantation as a child. JAMA Pediatr. 2015 Feb 2;169(2):e143626.
Yamamoto J, Donovan LE. **Managing thyroid disease** in women planning pregnancy. CMAJ. 2017 Jul 17;189(28):E940
Yang A, Ciolino JD, Pinheiro E, et al. **Neonatal Discontinuation Syndrome** in **Serotonergic Antidepressant-Exposed Neonates**. J Clin Psychiatry. 2017 May;78(5):605-611.
Yang F, Liang H, Chen J, et al. **Prenatal Paternal Selective Serotonin Reuptake Inhibitors** Use and Risk of ADHD in Offspring. Pediatrics. 2017 Dec 11.
Yang J, Baer RJ, Berghella V, et al. Recurrence of **Preterm Birth** and Early Term Birth. Obstet Gynecol. 2016 Jul 7.
Yarrington CD, Valente AM, Economy KE. **Cardiovascular Management in Pregnancy**: Antithrombotic Agents and Antiplatelet Agents. Circulation. 2015 Oct 6;132(14):1354-64.
Yawn BP et al. TRIPPD: A practice-based network effectiveness study of **postpartum depression** screening and management. Ann Fam Med 2012 Jul/Aug; 10:320.

Yawn BP, Bertram S, Kurland M, et al. Repeated **depression screening during the first postpartum year**. Ann Fam Med. 2015 May;13(3):228-34.
Yazdy M, Mitchell A, Tinker S et al. **Periconceptional Use of Opioids** and the Risk of Neural Tube Defects. Obstetrics&Gynecology. September 2013.
Yee LM et al. Using a **patient navigator to improve postpartum care** in an urban women's health clinic.Obstet Gynecol 2017 May; 129:925.
Yefet E, Schwartz N, Chazan B, Salim R, Romano S, Nachum Z. The safety of **quinolones and fluoroquinolones in pregnancy**: a meta-analysis. BJOG. 2018 Jan 10.
Yim CH. Update on the Management of **Thyroid Disease** during Pregnancy. Endocrinol Metab (Seoul). 2016 Aug 16.
Yonemoto N, Dowswell T, Nagai S, et al. Schedules for **home visits in the early postpartum period**. Cochrane Database Syst Rev. 2013 Jul 23;7:CD009326. Overall, findings were inconsistent. Postnatal home visits may promote infant health and maternal satisfaction. However, the frequency, timing, duration and intensity of such postnatal care visits should be based upon local needs.
Yonkers KA, Smith MV, Forray A, et al. Pregnant Women With Posttraumatic Stress Disorder and Risk of Preterm Birth. JAMA Psychiatry. 2014 Jun 11.
Yonkers KA, Gilstad-Hayden K, Forray A, Lipkind HS. Association of **Panic Disorder, Generalized Anxiety Disorder, and Benzodiazepine Treatment During Pregnancy** With Risk of Adverse Birth Outcomes. JAMA Psychiatry. 2017 Sep 13.
Young CB, Liu S, Muraca GM, et al**. Mode of delivery after a previous cesarean birth, and associated maternal and neonatal morbidity**. CMAJ. 2018 May 7;190(18):E556-E564.
Young L, Embleton ND, McCormick FM, et al. **Multinutrient fortification of human breast milk** for preterm infants following hospital discharge. Cochrane Database Syst Rev. 2013 Feb 28;2:CD004866. doi: 10.1002/14651858.CD004866.pub4. The limited available data do not provide convincing evidence that feeding preterm infants with multinutrient fortified breast milk compared with unfortified breast milk following hospital discharge affects important outcomes including growth rates during infancy.
Young-Wolff KC, Sarovar V, Tucker LY, et al. Association of **Nausea and Vomiting in Pregnancy With Prenatal Marijuana Use**. JAMA Intern Med. 2018 Aug 20.
Young-Wolff KC, Sarovar V, Tucker L-Y, et al. Self-reported daily, weekly, and monthly **marijuana use among women** before and during pregnancy. JAMA Netw Open. 2019;2(7):e196471. doi:10.1001/jamanetworkopen.2019.6471
Youngstrom M, Tita A, Grant J, et al. Perinatal Outcomes in Women With a **History of Chronic Hypertension but Normal Blood Pressures Before 20 Weeks of Gestation**. Obstet Gynecol. 2018 Apr 6.
Yuan C, Gaskins AJ, Blaine AI, et al. Association Between **Cesarean Birth** and **Risk of Obesity** in Offspring in Childhood, Adolescence, and Early Adulthood. JAMA Pediatr. 2016 Sep 6:e162385
Yusuf KK, Salihu HM, Wilson R, et al. Comparing **Folic Acid Dosage Strengths to Prevent Reduction in Fetal Size** Among Pregnant Women Who Smoked Cigarettes: A Randomized Clinical Trial. JAMA Pediatr. 2019 Mar 18.
Zaba B, Calvert C, Marston M, et al. Effect of **HIV infection on pregnancy-related mortality** in sub-Saharan Africa: secondary analyses of pooled community-based data from the network for Analysing Longitudinal Population-based HIV/AIDS data on Africa (ALPHA). Lancet. 2013 May 18;381(9879):1763-71.
Zakrzewski L, Sur D. **Immunizations in pregnancy**. Am Fam Physician. 2013 Jun 15;87(12):828-30.
Zash R, Jacobson DL, Diseko M, et al. Comparative Safety of **Antiretroviral** Treatment Regimens in **Pregnancy**. JAMA Pediatr. 2017 Aug 7:e172222.
Zash R, Makhema J, Shapiro RL. **Neural-Tube Defects with Dolutegravir Treatment** from the Time of Conception. N Engl J Med. 2018 Jul 24.
Zeisler H, Llurba E, Chantraine F, et al. Predictive value of the **sFlt-1:PlGF ratio** in women with suspected **preeclampsia**. N Engl J Med 2016;374:13-22.
Zerbo O, Yoshida C, Gunderson EP, et al. **Interpregnancy Interval and Risk of Autism** Spectrum Disorders. Pediatrics. 2015 Sep 14.
Zhang C, Tobias D, Chavarro J, Bao W, Wang D, Ley SH, et al. **Adherence to healthy lifestyle and risk of gestational** diabetes mellitus: prospective cohort study. BMJ 2014;349:g5450.
Zhang C, et al. Association of **Maternal Obesity With Longitudinal Ultrasonographic Measures of Fetal Growth**: Findings From the NICHD Fetal Growth Studies-Singletons. JAMA Pediatr. 2017 Nov 13.
Zhang Y, Gong Y, Xue H, et al. **Vitamin D and gestational diabetes** mellitus: a systematic review based on data free of Hawthorne effect. BJOG. 2017 Dec 15.
Zhu Z, Cheng Y, Zeng L, et al. Association of **Antenatal Micronutrient Supplementation With Adolescent Intellectual Development in Rural Western China**: 14-Year Follow-up From a Randomized Clinical Trial. JAMA Pediatr. 2018 Jul 9.
Zhu B, Ge X, et al. **Folic Acid Supplement** Intake in Early Pregnancy Increases **Risk of Gestational Diabetes** Mellitus: Evidence From a Prospective Cohort Study. Diabetes Care. 2016 Mar;39(3):e36-7.
Zhu JL, Olsen J, Sørensen HT, et al. **Prenatal Maternal Bereavement** and Congenital Heart Defects in Offspring: A Registry-Based Study. Pediatrics. 2013 Mar 25.
Zhu Y, Olsen SF, et al. **Maternal consumption of artificially sweetened beverages** during pregnancy, and offspring growth through 7 years of age: a prospective cohort study. Int J Epidemiol. 2017 Jun 6.
Zhu, Yeyi, et al. **Maternal dietary intakes of refined grains** during pregnancy and growth through the first 7 years of life among children born to women with gestational diabetes. American Journal of Clinical Nutrition. doi:10.3945/ajcn.116.136291

References (Pg 1 of 2; see more references online):

1. Natural Medicines Comprehensive Database 2005 & 2. Turner RB, Bauer R, Woelkart K, Hulsey TC, Gangemi JD. An evaluation of **Echinacea** angustifolia in experimental rhinovirus infections. N Engl J Med. 2005 Jul 28;353(4):341-8.
3. Taylor JA, Weber W, Standish L, Quinn H, Goesling J, McGann M, Calabrese C. Efficacy and safety of **echinacea** in treating upper respiratory tract infections in children: a randomized controlled trial (but ↑ rash). JAMA. 2003 Dec 3;290(21):2824-30.
4. Predy GN, Goel V, Lovlin R, Donner A, Stitt L, Basu TK. Efficacy of an extract of North American **ginseng** containing poly-furanosyl-pyranosyl-saccharides for preventing upper respiratory tract infections: a randomized controlled trial. CMAJ. 2005 Oct 25;173(9):1043-8. n=279 5. Turner RB. Studies of "natural" remedies for the common cold: pitfalls and pratfalls. CMAJ. 2005 Oct 25;173(9):1051-2. 6. NCCAM. Glucosamine/Chondroitin Arthritis Intervention Trial (GAIT). Available at http://nccam.nih.gov/research/results/gait. Accessed July 10, 2012. National Institutes of Health (NIH) **Glucosamine/Chondroitin** Arthritis Intervention Trial (**GAIT**) (The 1,538-patient GAIT trial compared the effectiveness and safety of these supplements taken alone and in combination in patients with painful knee osteoarthritis (WOMAC Pain 125-400 mm) treated at 16 academic medical centers in the U.S. The response rate for all patients was 60.1% in a placebo group, 64% in a glucosamine **hydrocholoride** arm (500 mg TID); 65.4% in a chondroitin alone arm (400 mg TID); & 66.6% in a glucosamine-plus-chondroitin arm (500 mg/400mg TID) (p=0.09), according to a study results reported at the American College of Rheumatology, San Diego Nov/05) http://nccam.nih.gov/news/19972000/121100/qa.htm
Other (Gait) Clegg, D, Reda, D. Harris, C et al. Glucosamine, Chondroitin Sulfate, and the Two in Combination for Painful Knee Osteoarthris. N Engl J Med 2006; 354:795-808
Sawitzke AD, Shi H, Finco MF, et al. Clinical efficacy and safety of glucosamine, chondroitin sulphate, their combination, celecoxib or placebo taken to treat osteoarthritis of the knee: 2-year results from GAIT. Annals of the Rheumatic Diseases. 2010; 69(8):1459–1464.
Sawitzke AD, Shi H, Finco MF, Dunlop DD et al.The effect of glucosamine and/or chondroitin sulfate on the progression of knee osteoarthritis: a report from the glucosamine/chondroitin arthritis intervention trial. Arthritis Rheum. 2008 Oct;58(10):3183-91.
7. **Lakota** web site: http://www.lakotaherbs.com/english/2_rheumatoid.php 8. Cold-fX (Standardized Oligo/polysaccharide Extract of **Panax quinquefolium**) Pharmacist Letter. Jan 2005 & Dec 2005. & 9. ColdfX website http://www.cvtechnologies.com/coldfx/default.aspx 10. Yuan CS, Wei G, Dey L, et al. Brief communication: American **ginseng** reduces **warfarin's** effect in healthy patients: a randomized, controlled Trial. Ann Intern Med. 2004 Jul 6;141(1):23-7. 11. Richy F, Bruyere O, Ethgen O, Cucherat M, Henrotin Y, Reginster JY. Structural and symptomatic efficacy of **glucosamine and chondroitin** in knee osteoarthritis: a comprehensive meta-analysis. Arch Intern Med. 2003 Jul 14;163(13):1514-22. 12. Herrero-Beaumont G et al. Effects of **glucosamine sulfate** on a 6-month control of knee osteoarthritis symptoms vs placebo & acetaminophen: Results from the Glucose Unum in Die Efficacy (**GUIDE**) Trial. ACR Meeting Nov 2005.
Also: (Martel-Pelletier Osteoarth Cart 2010, Hochberg Osteoarth Cart 2010, Vangsness Arthroscopy 2009, Gabay Arthr Rheum 2011. Jerosch Int J Rheum 2011), but we also still see reports of very little value (Sawitzke Ann Rheum Dis 2010, Altman Drugs Aging 2010. Wandel BMJ 2010, Berenbaum Osteoarth Cart 2011, Miller Rheum Dis Clin North Am 2011).
13 .Scroggie DA, et al. The effect of **glucosamine-chondroitin** supplementation on glycosylated hemoglobin levels in patients with type 2 diabetes mellitus: a placebo-controlled, double-blinded, randomized clinical trial. Arch Intern Med. 2003 Jul 14;163(13):1587-90.
14. Ryan MA, Christian RS, Wohlrabe J. **Handwashing** and respiratory illness among young adults in military training. Am J Prev Med. 2001 Aug;21(2):79-83.
15. Satomura K, et al.; Great Cold Investigators-I. Prevention of upper respiratory tract infections by **gargling** a randomized trial. Am J Prev Med. 2005 Nov;29(4):302-7. (InfoPOEMs: Gargling with water effectively reduces the risk of developing an upper respiratory tract infection (URTI). Nine individuals will need to gargle with water for 1 minute 3 times daily for 60 days to prevent 1 additional person from developing a URTI. Gargling with povidone-iodine was no more effective than usual care. (LOE = 1b-))
16. **Influenza vaccine** 2005-2006. Med Lett Drugs Ther. 2005 Oct 24;47(1220):85-7 **&** Jefferson T, Rivetti D, Rivetti A, et al. Efficacy and effectiveness of **influenza vaccines** in elderly people: a systematic review. Lancet. 2005 Oct 1;366(9492):1165-74. Epub 2005 Sep 22.
17. Arroll B. Non-antibiotic treatments for upper-respiratory tract infections (common cold). Respir Med. 2005 Dec;99(12):1477-84. CONCLUSION: Most non-antibiotic treatments for the common cold are **probably not effective**. The most promising are dextromethorphan, bisolvon and guaifenesin for cough, antihistamine-decongestant combinations for a wide range of symptoms, nasal decongestants (at least for the first dose) and possibly zinc lozenges.
18. Towheed TE, et al. Glucosamine therapy for treating osteoarthritis. Cochrane Database Syst Rev. Apr 18, 2005 & 19. Glucosamine & chondroitin: recent osteoarthritis research. Pharmacist's Letter Jan 2006.
19. Diagnosis & Management of Cough: Executive Summary. ACCP Evidence-Based Clinical Practice Guidelines. Chest 2006; 129:1S-23S. http://www.chestnet.org/downloads/journal/exec_sum.pdf
20. Clegg et al . National Institutes of Health (NIH) Glucosamine/Chondroitin Arthritis Intervention Trial (**GAIT**) Clegg DO, et al. Glucosamine, chondroitin sulfate, and the two in combination for painful knee osteoarthritis. N Engl J Med. 2006 Feb 23;354(8):795-808. CONCLUSIONS: Glucosamine and chondroitin sulfate alone or in combination did not reduce pain effectively in the overall group of patients with osteoarthritis of the knee. Exploratory analyses suggest that the combination of glucosamine and chondroitin sulfate may be effective in the subgroup of patients with moderate-to-severe knee pain. (The 1,538-pts GAIT trial compared the effectiveness & safety of these supplements taken alone and in combination in patients with painful knee osteoarthritis (WOMAC Pain 125-400 mm) treated at 16 academic medical centers in the U.S. The response rate for all patients was 60.1% in a placebo group, 64% in a glucosamine hydrocholoride arm (500 mg TID); 65.4% in a chondroitin alone arm (400 mg TID); & 66.6% in a glucosamine-plus-chondroitin arm (500 mg/400mg TID) (p=0.09), according to a study results reported at the American College of Rheumatology meeting in San Diego Nov/05).
http://nccam.nih.gov/news/19972000/121100/qa.htm (InfoPOEMs: Glucosamine HCl and chondroitin provides modest if any symptomatic benefit for patients with mild osteoarthritis of the knee. This study was well designed and avoided many of the design flaws of earlier studies. However, it had a high dropout rate (20%) and used a different glucosamine salt than most previous studies. In addition, post-hoc analysis suggests a large benefit in patients with moderate to severe pain. There were also consistent trends toward benefit for many secondary outcomes. (LOE = 1b))
21. McElhaney JE, Gravenstein S, Cole SK, Davidson E, O'neill D, Petitjean S, Rumble B, Shan JJ. A placebo-controlled trial of a proprietary extract of North American ginseng (CVT-E002) to prevent acute respiratory illness in institutionalized older adults. J Am Geriatr Soc. 2004 Jan;52(1):13-9. Erratum in: J Am Geriatr Soc. 2004 May;52(5):following 856. n=198
22. Pharmacist's Letter. Supplements for Prevention and Treatment of **Colds and Influenza**. Nov 2009.
23. Sawitzke AD, Shi H, Finco MF, et al.. Clinical efficacy and safety of **glucosamine, chondroitin sulphate, their combination, celecoxib or placebo** taken to treat osteoarthritis of the knee: 2-year results from **GAIT**. Ann Rheum Dis. 2010 Jun 4.
24. Kwoh CK, Roemer FW, Hannon MJ, et al. The **Joints on Glucosamine (JOG)** Study: The effect of oral glucosamine on joint structure, a randomized trial. Arthritis Rheumatol. 2014 Mar 11.

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Useful Herbal Websites

www.fda.gov/food/dietarysupplements/default.htm
www.quackwatch.com
www.ncahf.org
www.herbmed.org
www.consumerlab.com
www.naturaldatabase.com
www.mskcc.org/aboutherbs
www.hc-sc.gc.ca/dhp-mps/prodnatur/index-eng.php
www.herbs.orgmedlineplus.gov/druginfo/herb_All.html
Linus Pauling Institute lpi.oregonstate.edu;
National Center for Complementary and Integrative Health (NIH) nccih.nih.gov
Mayo Clinic www.mayoclinic.org/drugs-supplements

Herbals with Frequent Allergic Reactions American Journal of Medicine, Feb 1998

Agnus, Castus, Angelica, Aniseed, Apricot, Arnica, Artichoke, Asafoetida, Boneset, Cassia, Celery, Cinnamon, Cowslip, Dandelion, Elecampane, Euphobia, Feverfew, Fucus, Gravel Root, Gauicum, Holy Thistle, Hops, Hydrangea, Juniper, Lady's Slipper, Meadowsweet, Motherwort, Parsley, Pilewort, Plantain, Pulsatilla, Rosemary, Royal Jelly, Tansy, Wild Carrot & Yarrow.

HERBAL DRUG INTERACTION CHART

References:
1. Hansten and Horn's Drug Interactions Analysis and Management 2015.
2. AHFS Drug Information 2017.
3. American Family Physcian Mar 1/1999.
4. CPS - Product Monographs, 2017.
5. J Clin Pharmacol 1997;37:344-350.
6. Arthritis Rheum 1995;38:614-617.
7. BMJ 1994;308:1162.
8. The Lancet 2000;355:134-138.
9. NEJM 1998 339:847.
10. Pharmacy Practice June 1999 & June 2000
11. Natural Medicines Comprehensive Database 2016.
12. Review of Natural Products 2010.
13. Draves AH, Walker SE. Parthenolide content of Canadian commercial **feverfew** preparations (Label claims are misleading in most cases). CPJ Dec 2003/Jan 2004, Vol. 136, No. 10, p23-30.
14. Newmaster SG, Grguric M, Shanmughanandhan D, Ramalingam S, Ragupathy S. **DNA barcoding detects contamination and substitution** in North American herbal products. BMC Med. 2013;11:222.
15. Navarro VJ, Barnhart H, Bonkovsky HL, et al. **Liver injury from herbals and dietary supplements** in the U.S. Drug-Induced Liver Injury Network. Hepatology. 2014 Jul 12.
16. Navarro V, Khan I, Björnsson E, et al. **Liver Injury from Herbal and Dietary Supplements**. Hepatology. 2016 Sep 27.
17. Cohen PA, Maller G, DeSouza R, et al. Presence of **banned drugs in dietary supplements following FDA recalls**. JAMA. 2014 Oct 22 29;312(16):1691-3.
18. Geller AI, Shehab N, Weidle NJ, et al. **Emergency Department Visits for Adverse Events Related** to Dietary Supplements. N Engl J Med. 2015 Oct 15;373(16):1531-40.
19. Barry AR. **Patients' perceptions** and use of natural health products. Can Pharm J (Ott). 2018 Jun 4;151(4):254-262.

Additonal references:
Adams D, Dagenais S, Clifford T, et al. **Complementary and Alternative Medicine** Use by **Pediatric Specialty Outpatients**. Pediatrics. 2013 Jan 14.
Adams D, Whidden A, Honkanen M, et al. **Complementary and alternative** medicine: a survey of its use in **pediatric cardiology**. CMAJ Open. 2014 Oct 1;2(4):E217-24.
Adawi R, Walsh L. Bradycardia & edema in a patient receiving herbal therapy for fertility. Ann Intern Med. 2005 Nov 15;143(10):763. Although the specific ingredient responsible for the bradycardia and edema was not identified, a literature search identified some possibilities. There is a known association between **Aconitum napellus** and various arrhythmias, including severe bradycardia and left bundle-branch block pattern (1). **Licorice** contains glycyrrhizic acid, which inhibits renal 11[beta]-hydroxysteroid dehydrogenase and causes a state of mineralocorticoid excess by impeding inactivation of cortisol.
Agha-Hosseini M, Kashani L, et al. **Crocus sativus L. (saffron)** in the treatment of **premenstrual syndrome**: a double-blind, randomised and placebo-controlled trial. BJOG. 2008 Mar;115(4):515-9. Saffron was an effective treatment for PMS in this well-designed but small & short-term study. Consider recommending saffron, if cost is not an obstacle. Larger & longer studies are needed to confirm this result. (LOE = 1b)
Akturk HK, Chindris AM, Hines JM, Set al. Over-the-Counter "**Adrenal Support" Supplements Contain Thyroid and Steroid-Based Adrenal Hormones**. Mayo Clin Proc. 2018 Mar;93(3):284-290.
Alfalfa: Patients may ask about a widely reported recall of Caldwell Fresh Foods alfalfa sprouts. The company has recalled all of its raw sprouts (marketed under the brands Caldwell Fresh Foods, California Exotics, and Nature's Choice) because they may be contaminated with a strain of **salmonella**. Since March, at least 22 cases of salmonella infections in 10 states have been linked to the sprouts, according to the FDA. California has 11 confirmed cases; the 9 other affected states are Arizona, Colorado, Idaho, Illinois, Missouri, New Mexico, Nevada, Oregon, & Wisconsin. Six people have been hospitalized; no deaths have been reported. FDA news release (Free) Manufacturer press release (Free)
Ali WM, Al Habib KF, Al-Motarreh A, et al. Acute coronary syndrome use and **khat herbal amphetamine use (Catha edulis**). An observational report.Circulation 2011
Amsterdam JD, Li Y, Soeller I, et al. A randomized, double-blind, placebo-controlled trial of oral Matricaria recutita (**chamomile**) extract therapy for generalized anxiety disorder. J Clin Psychopharmacol. 2009 Aug;29(4):378-82. n=61 over 8 weeks. This is the first controlled clinical trial of chamomile extract for GAD. The results suggest that chamomile may have modest anxiolytic

activity in patients with mild to moderate GAD
Ang-Lee MK, Moss J, Yuan CS. **Herbal medicines and perioperative care**. JAMA 2001;286:208-16.
Anheyer D, Frawley J, Koch AK, et al. **Herbal Medicines for Gastrointestinal Disorders** in Children and Adolescents: A Systematic Review. Pediatrics. 2017;139(6):e20170062
Anwar M, Law R, Schier J. Notes from the Field: **Kratom (Mitragyna speciosa)** Exposures Reported to Poison Centers - United States, 2010-2015. MMWR Morb Mortal Wkly Rep. 2016 Jul 29;65(29):748-9
Arnold J, Ouwehand WH, Smith GA, Cohen H. A young woman with petechiae.Lancet. 1998 Aug 22;352(9128):618. (**tahini** (pulped sesame seeds))
Asher GN. Corbett AH, Hawke RL. **Common Herbal Dietary Supplement– Drug Interactions**. Am Fam Physician. 2017;96(2):101-107.
Australian Therapeutic Goods May/15: **Maxman Cialis** tablets contains undeclared sildenafil.
Australian Therapeutic Goods May/15: **Top Gun for Men** tablets contain undeclared tadalafil; **Power 1 tablets, Dr. Ming's Chinese capsule & Maxman Domina Tu Pareja** tablets contains undeclared sildenafil.
Australain Therapeutic Good Administration July/15 **Enhanced Vegetal Vigra capsules, Gold Viagra capsules, Majestic Lovezone tablets, Niu Mo Wang 'Bull Monster' tablets, North West Wolf capsules, Strong Horses capsules, Strong-SX capsules & USA Gold Ant** capsules contains sildenafil. **Gold Viagra** tablets (packaged as "**Kangaroo Sexually Invigorating Essence**") contains undeclared sildenafiland tadalafil.
Australain Therapeutic Good Administration:**OMG Slim** capsules contains Undeclaredsibutramine and orlistat.
Australian Therapeutic Goos Administration Oct/15 : **ActiveSlim slimming capsules** contains undeclared sibutramine.
Aviner S, Berkovitch M, Dalkian H, et al. Use of a homeopathic preparation (**Gali-col Baby**) for "infantile colic" and an apparent life-threatening event. Pediatrics. 2010 Feb;125(2):e318-23.
Awortwe C, Makiwane M, Reuter H, et al. **Critical evaluation of causality assessment of herb-drug interactions** in patients. Br J Clin Pharmacol. 2018 Apr;84(4):679-693.
Azuno Y, Yaga K, Sasayama T, Kimoto K. Thrombocytopenia induced by **Jui**, a traditional Chinese herbal medicine. Lancet. 1999 Jul 24;354(9175):304-5.
Bamford JTM, Ray S, Musekiwa A, et al. **Oral evening primrose oil and borage oil for eczema**. Cochrane Database of Systematic Reviews 2013, Issue 4. Art. No.: CD004416. DOI: 10.1002/14651858.CD004416.pub2. Oral borage oil and evening primrose oil lack effect on eczema; improvement was similar to respective placebos used in trials. Oral BO and EPO are not effective treatments for eczema. In these studies, along with the placebos, EPO and BO have the same, fairly common, mild, transient adverse effects, which are Mainly gastrointestinal.
Bandolier. **Avocado/soybean** unsaponifiables for OA. April 2004;122-23. Web site: http://www.jr2.ox.ac.uk/bandolier/band122/b122-3.html. The limited data to date support the safety and possible efficacy of ASU for osteoarthritis of the knee. More and longer studies are needed before we can recommend this to our patients without hesitation. (LOE = 1b-)
Barbosa-Cesnik C, Brown MB, Buxton M, et al. **Cranberry juice** fails to prevent recurrent urinary tract infection: results from a randomized placebo-controlled trial. Clin Infect Dis. 2011 Jan;52(1):23-30.
Barnes J. **Pharmacovigilance of herbal medicines** : a UK perspective. *Drug Saf*. 2003. 26(12): 829–51.
Barrett Bruce, Brown Roger, Rakel Dave, et al. **Echinacea** for Treating the Common Cold: A Randomized Trial. Ann Intern Med December 21, 2010 153:769-777.
Barry MJ, Meleth S, Lee JY, et al. Complementary and Alternative Medicine for Urological Symptoms (**CAMUS**) Study Group. Effect of increasing doses of **saw palmetto extract** on lower urinary tract symptoms: a randomized trial. JAMA. 2011 Sep 28;306(12):1344-51.
Bayles Bryan, Usatine Richard. **Evening primrose oil** . Am Fam Physician. 2009;80(12):1405–1408.
Benjamin J, Muir T, Briggs K, Pentland B. A case of cerebral haemorrhage-can **Ginkgo** biloba be implicated? Postgrad Med J. 2001 Feb;77(904):112-3.
Bent S, et al. Saw **palmetto** 160mg bid x1 yr for benign prostatic hyperplasia. N Engl J Med. 2006 Feb 9;354(6):557-66. n=255 (InfoPOEMs: The authors of this rigorously designed trial found that saw palmetto produces no improvement in symptoms for men with moderate to severe benign prostatic hyperplasia (BPH), a finding that differs from the bulk of the previous literature. (LOE = 1b))
Bettiol A, Lombardi N, Marconi E, et al. The use of **complementary and alternative medicines during breastfeeding**: results from the Herbal supplements in Breastfeeding InvesTigation (HaBIT) study. Br J Clin Pharmacol. 2018 May 16.
Bhandari N. Is **ayurveda** the key to universal healthcare in India? BMJ. 2015 May 28;350:h2879.
Biggee BA, et al. Effects of oral **glucosamine** sulphate on serum **glucose** & insulin during an oral glucose tolerance test of subjects with osteoarthritis. Ann Rheum Dis. 2006 Jul3; [Epub ahead of print] The results suggest that glucosamine ingestion may affect glucose levels and consequent glucose uptake in individuals who have untreated diabetes or glucose intolerance.
Birks J, Grimley EV, Van Dongen M. **Ginkgo bilo**ba for cognitive impairment and dementia. Cochrane Database Syst Rev. 2002;(4):CD003120. CONCLUSIONS: Ginkgo biloba appears to be safe in use with no excess side effects compared with placebo. Many of the early trials used unsatisfactory methods, were small, and we cannot exclude publication bias. Overall there is promising evidence of improvement in cognition and function associated with Ginkgo. However, the three more modern trials show inconsistent results. Our view is that there is need for a large trial using modern methodology and permitting an intention-to-treat analysis to provide robust estimates of the size and mechanism of any treatment effects.
Birdee GS, Phillips RS, Davis RB, Gardiner P. Factors associated with **pediatric use of complementary and alternative medicine**. Pediatrics. 2010 Feb;125(2):249-56. Epub 2010 Jan 25.
Birks J, Grimley Evans J. **Ginkgo biloba** for cognitive impairment and dementia. Cochrane Database Syst Rev. **2009** Jan 21;(1):CD003120. Ginkgo biloba appears to be safe in use with no excess side effects compared with placebo. Many of the early trials used unsatisfactory methods, were small, and publication bias cannot be excluded. The evidence that Ginkgo biloba has predictable and clinically significant benefit for people with dementia or cognitive impairment is inconsistent and unreliable.
Bishop, Felicity L., Prescott, Philip, Chan, Yean Koon, et al. Prevalence of Complementary Medicine Use in **Pediatric Cancer**: A Systematic Review. Pediatrics 2010 125: 768-776.
Black C, Clar C, Henderson R, et al. The clinical effectiveness of **glucosamine and chondroitin** supplements in slowing or arresting progression of osteoarthritis of the knee: a systematic review and economic evaluation. Health Technol Assess. **2009** Nov;13(52):1-148.
Blendon RJ, Benson JM, Botta MD, et al. **Users' views of dietary supplements**. JAMA Intern Med. 2013 Jan 14;173(1):74-6.
Bonakdar RA, Guarneri E. Coenzyme Q10. Am Fam Physician. 2005 Sep 15;72(6):1065-70.
Bonkovsky HL. Hepatotoxicity associated with supplements containing Chinese **green tea** (Camellia sinensis). Ann Intern Med. 2006 Jan 3;144(1):68-71. (Gloro R, Hourmand-Ollivier I, et al. Fulminant hepatitis during self-medication with hydroalcoholic extract of green tea. Eur J Gastroenterol Hepatol. 2005 Oct;17(10):1135-7.)
Bookstaver DA, Burkhalter NA, et al. Effect of **Coenzyme Q10 Supplementation (60mg po bid)** on Statin-Induced Myalgias. Am J Cardiol. 2012 May 17. n=76 no more effective than placebo
Borrelli F, Capasso R, Aviello G, Pittler MH, Izzo AA. Effectiveness and safety of **ginger** in the treatment of pregnancy-induced nausea and vomiting. Obstet Gynecol. 2005 Apr;105(4):849-56.
Boyd A, Bleakley C, Hurley DA, et al. Herbal medicinal products or preparations **for neuropathic pain**. Cochrane Database Syst Rev. 2019 Apr 2;4:CD010528.
Brenyo A, Aktas MK. Review of **Complementary and Alternative Medical Treatment of Arrhythmias**. Am J Cardiol. 2014 Mar 1;113(5):897-903.
Broussard CS, Louik C, Honein MA, Mitchell AA; National Birth Defects Prevention Study. Herbal use before and during **pregnancy**. Am J Obstet Gynecol. 2009 Dec 23. [Epub ahead of print]
Bruyere O, et al. **Glucosamine** sulfate reduces osteoarthritis progression in postmenopausal women with knee osteoarthritis: evidence from two 3-year studies. Menopause. 2004 Mar-Apr;11(2):138-43.
Buettner C, Yeh GY, Phillips RS, Mittleman MA, Kaptchuk TJ. Systematic review of the effects of **ginseng** on cardiovascular risk factors. Ann Pharmacother. 2006 Jan;40(1):83-95. Epub 2005 Dec 6.
Bruyere O, Pavelka K, Rovati LC, et al. Total joint replacement after **glucosamine** sulphate treatment in knee osteoarthritis: results of a mean 8-year observation of patients from two previous 3-year, randomised, placebo-controlled trials. Osteoarthritis Cartilage 2008; 16: 254–60.
CameronM, Chrubasik S. **Topical herbal therapies for treating osteoarthritis**. Cochrane Database of Systematic Reviews 2013, Issue 5. Art. No.: CD010538. DOI: 10.1002/14651858.CD010538. Although the mechanism of action of the topical medicinal plant products provides a rationale basis for their use in the treatment of osteoarthritis, the quality and quantity of current research studies of effectiveness are insufficient. Arnica gel probably improves symptoms as effectively as a gel containing non-steroidal anti-inflammatory drug, but with no better (and possibly worse) adverse event profile. Comfrey extract gel probably improves pain, and Capsicum extract gel probably will not improve pain or function at the doses examined in this review.
Cameron M, Chrubasik S. **Oral herbal therapies for treating osteoarthritis**. Cochrane Database Syst Rev. 2014 May 22;5:CD002947. Evidence for the proprietary ASU product Piasclidine® in the treatment of osteoarthritis symptoms seems moderate to high for short term use, but studies over a longer term and against an apparently active control are less convincing. Several other medicinal plant products, including extracts of Boswellia serrata, show trends of benefits that warrant further investigation in light of the fact that the risk of adverse events appear low.There is no evidence that Piasclidine® significantly improves joint structure, and limited evidence that it prevents joint space narrowing. Structural changes were not tested for with any other herbal intervention.Further investigations are required to determine optimum daily doses producing clinical benefits without adverse events.
Carney RM.; et al. **Omega-3 Augmentation of Sertraline** in Treatment of Depression in Patients With Coronary Heart Disease: A Randomized Controlled Trial. JAMA. 2009;302(15):1651-1657.
CDC: **Lead Poisoning** in Pregnant Women Who Used Ayurvedic Medications from India — New York City, 2011–2012. Weekly.August 24, 2012 / 61(33);641-646.
CDC: Nov/14 A premature infant in Connecticut died in October from gastrointestinal mucormycosis after receiving a dietary supplement contaminated with *Rhizopus oryzae*, the CDC reported last week. The infant, born at 29 weeks' gestation, received

ABC Dophilus Powder for 4 days, beginning on day one of life. The supplement is purported to contain probiotics and is marketed for infants and children.
Chaiyakunapruk N, Kitikannakorn N, Nathisuwan S, et al. The efficacy of **ginger** for the prevention of postoperative nausea and vomiting: a meta-analysis. Am J Obstet Gynecol. 2006 Jan;194(1):95-9.
Chalasani N, Vuppalanchi R, al; Drug-Induced Liver Injury Network Acute liver injury due to **flavocoxid (Limbrel),** a medical food for osteoarthritis. A case series. Ann Intern Med. 2012;156:857-60.
Chatterjee N, Domoto-Reilly K, Fecci PE, et al. **Licorice-associated reversible cerebral vasoconstriction** with PRES (**encephalopathy**). Neurology. 2010 Nov 23;75(21):1939-41.
Cheong JL. Retinal vein thrombosis associated with a herbal **phytoestrogen** preparation (black cohosh, dong quai, red clover & wold Mexican yam) in a susceptible patient. Postgrad Med J. 2005 Apr;81(954):266-7.
Chen XY, Wu TX, Liu GJ, et al. **Chinese medicinal herbs for influenza**. Cochrane Database Syst Rev. 2007 Oct 17;(4):CD004559. The present evidence is too weak to support or reject the use of Chinese medicinal herbs for preventing and treating influenza.
Chen CH, Dickman KG, Moriya M, et al. **Aristolochic acid-associated urothelial cancer** in Taiwan. Proc Natl Acad Sci U S A. 2012 Apr 9.
Chen HY, Lin YH, Wu JC, Chen et al. Characteristics of Pediatric **Traditional Chinese Medicine** Users in Taiwan: A Nationwide Cohort Study. Pediatrics. 2012 May 14. The use of TCM was correlated with both patient and parental factors, among which children's age and parental TCM use were the most prominent.
Chen F, Du M, Blumberg JB, et al. **Association Among Dietary Supplement Use, Nutrient Intake, and Mortality Among U.S. Adults**: A Cohort Study. Ann Intern Med. 2019 Apr 9.
Cheng CW, Wu TX, Shang HC, et al; CONSORT-CHM Formulas 2017 Group. CONSORT Extension for **Chinese Herbal Medicine Formulas 2017**: recommendations, explanation, and elaboration. Ann Intern Med. [Epub ahead of print]. doi: 10.7326/M16-2977
Ching CK, Chen SPL, Lee HHC, et al. **Adulteration of proprietary Chinese medicines** and health products with undeclared drugs: experience of a tertiary toxicology laboratory in Hong Kong. Br J Clin Pharmacol. 2017 Oct 1. (esp. sibutramine)
Chow T, Browne V, et al. **Ginkgo biloba** & acetazolamide prophylaxis for acute mountain sickness: a randomized, placebo-controlled trial. Arch Intern Med. 2005 Feb 14;165(3):296-301.
Chuchalin AG, Berman B, Lehmacher W. Treatment of acute bronchitis in adults with a pelargonium sidoides preparation (EPS 7630): a randomized, double-blind, placebo-controlled trial. Explore 2005;1:437-45. (InfoPOEMs: The pelargonium sidoides extract (Umckaloabo in Germany) produced a significantly greater reduction in symptoms of acute bronchitis than placebo, & more patients were satisfied with treatment. As with all herbal products, results may be different with pelargonium products other than this extract. (LOE = 1b))
Clegg et al . National Institutes of Health (NIH) Glucosamine/Chondroitin Arthritis Intervention Trial (**GAIT**) Clegg DO, et al. Glucosamine, chondroitin sulfate, and the two in combination for painful knee osteoarthritis. N Engl J Med. 2006 Feb 23;354(8):795-808. CONCLUSIONS: Glucosamine and chondroitin sulfate alone or in combination did not reduce pain effectively in the overall group of patients with osteoarthritis of the knee. Exploratory analyses suggest that the combination of glucosamine and chondroitin sulfate may be effective in the subgroup of patients with moderate-to-severe knee pain. (The 1,538-pts GAIT trial compared the effectiveness & safety of these supplements taken alone and in combination in patients with painful knee osteoarthritis (WOMAC Pain 125-400 mm) treated at 16 academic medical centers in the U.S. The response rate for all patients was 60.1% in a placebo group, 64% in a glucosamine hydrocholoride arm (500 mg TID); 65.4% in a chondroitin alone arm (400 mg TID); & 66.6% in a glucosamine-plus-chondroitin arm (500 mg/400mg TID) (p=0.09), according to a study results reported at the American College of Rheumatology meeting in San Diego Nov/05). http://nccam.nih.gov/news/19972000/121100/qa.htm (InfoPOEMs: Glucosamine HCl and chondroitin provides modest if any symptomatic benefit for patients with mild osteoarthritis of the knee. This study was well designed and avoided many of the design flaws of earlier studies. However, it had a high dropout rate (20%) and used a different glucosamine salt than most previous studies. In addition, post-hoc analysis suggests a large benefit in patients with moderate to severe pain. There were also consistent trends toward benefit for many secondary outcomes. (LOE = 1b)) Sawitzke AD, Shi H, Finco MF, Dunlop DD, Bingham CO 3rd, Harris CL, Singer NG, Bradley JD, Silver D, Jackson CG, Lane NE, Oddis CV, Wolfe F, Lisse J, Furst DE,Reda DJ, Moskowitz RW, Williams HJ, Clegg DO. The effect of glucosamine and/or chondroitin sulfate on the progression of knee osteoarthritis: A report from the glucosamine/chondroitin arthritis intervention trial. (GAIT) Arthritis Rheum. 2008 Sep 29;58(10):3183-3191. [Epub ahead of print] At 2 years, no treatment achieved a predefined threshold of clinically important difference in JSW loss as compared with placebo. However, knees with K/L grade 2 radiographic OA appeared to have the greatest potential for modification by these treatments.
Coghlan ML, Haile J, Houston J, et al. **Deep Sequencing of Plant and Animal DNA** Contained within Traditional Chinese Medicines Reveals Legality Issues and Health Safety Concerns. PLoS Genet. 2012 Apr;8(4):e1002657.
Cohen PA. American roulette--**contaminated dietary supplements**. N Engl J Med. 2009 Oct 15;361(16):1523-5. Epub 2009 Oct 7.
Cohen PA. **DMAA** as a dietary supplement ingredient. Arch Intern Med. 2012 Jul 9;172(13):1038-9.
Cohen PA. Hazards of hindsight--**monitoring the safety of nutritional supplements**. N Engl J Med. 2014 Apr 3;370(14):1277-80.
Cohen PA, Bloszies C, Yee C, et al. An **amphetamine isomer** whose efficacy and safety in humans has never been studied, **β-methylphenylethylamine (BMPEA),** is found in multiple dietary supplements. Drug Test Anal. 2015 Apr 7.
Cohen PA, Zeijlon R, Nardin R, et al. Hemorrhagic Stroke Probably Caused by Exercise Combined With a **Sports Supplement** Containing **β-Methylphenyl-ethylamine (BMPEA):** A Case Report. Ann Intern Med. 2015 Jun16;162(12):879-80.
Cohen PA, Wen A, Gerona R. Prohibited **stimulants in dietary supplements** after enforcement action by the US Food and Drug Administration [online Oct 22, 2018]. JAMA Intern Med. doi:10.1001/jamainternmed.2018.4846 FDA Oct/18: Fat Burners Zone is voluntarily recalling 1 lot of Zero Xtreme, capsules to the consumer level. FDA analysis has found Zero Xtreme to be tainted with sibutramine.
Cohen PA, Avula B, Venhuis B, et al. Pharmaceutical doses of the banned stimulant **oxilofrine (methylsynephrine)** found in dietary supplements sold in the USA. Drug Test Anal. 2016 Apr 7
Connor KM, Payne V, Davidson JR. **Kava** in generalized anxiety disorder: three placebo-controlled trials. Int Clin Psychopharmacol. 2006 Sep;21(5):249-53. No evidence of hepatotoxicity was found with kava, and all of the treatments were well tolerated. Findings from these three controlled trials do not support the use of kava in DSM-IV generalized anxiety disorder.
Cook R, Thomas V, Martin R; NIHR Dissemination Centre. Can treating **vitamin D deficiency reduce exacerbations of chronic obstructive pulmonary disease**? BMJ. 2019 Mar 18;364:l1025.
Coralic Z, Lenhoff T, Kanzaria HK, et al. A 120-Hour Case of Priapism from an Over-the-Counter Herbal Supplement (**African Black Ant: sildenafil**). Ann Pharmacother. 2013 Feb;47(2):289-90.
Cox MC, et al. Influence of **garlic** (Allium sativum) on the pharmacokinetics of docetaxel. Clin Cancer Res. 2006 Aug 1;12(15):4636-40. This study indicates that garlic does not significantly affect the disposition of docetaxel. However, it cannot be excluded that garlic decreases the clearance of docetaxel in patients carrying a CYP3A5*1A allele.
Cui T, Kovell RC, Brooks DC, et al. A Urologist's Guide to **Ingredients Found in Top-Selling Nutraceuticals for Men's Sexual Health**. J Sex Med. 2015 Nov;12(11):2105-17.
Cummings C; **Canadian Paediatric Society**, Community Paediatrics Committee. **Melatonin** for the management of sleep disorders in **children and adolescents**. Paediatr Child Health 2012;17:331-3. http://www.cps.ca/english/statements/CP/Melatonin.htm
Cvijovic K, Boon H, Barnes J et at. A **tool for rapid idenfification** of potential herbal medicine –drug interactions. Can Pharm J 2009;142:224-227. (September-October 2009) http://www.cpjournal.ca/archive/1913-701X/142/5/pdf/i1913-701X-142-5-e1.pdf
Cvijovic K, Boon H, Jaeger W, Vohra S; for the SONAR group. Polypharmacy, multiple **natural health products and hepatotoxicity**. CMAJ. 2011 Oct 4;183(14):E1085-E1089.
Dahmer S, Schiller RM. **Glucosamine**. Am Fam Physician. 2008 Aug 15;78(4):471-6.
Dahmer S, Scott E. Health effects of **hawthorn**. Am Fam Physician. 2010 Feb 15;81(4):465-8.
Davis SA, Feldman SR, Taylor SL. Use of St. **John's Wort in Potentially Dangerous Combinations**. J Altern Complement Med. 2014 Jun 23.
DeKlotz CMC, Roby KD, Friedlander SF. **Dietary Supplements**, **Isotretinoin**, and **Liver Toxicity** in Adolescents: A Retrospective Case Series. Pediatrics. 2017 Sep 1.
Dekosky ST, Williamson JD, Fitzpatrick AL, et al.; for the Ginkgo Evaluation of Memory (**GEM**) Study Investigators. **Ginkgo** biloba for Prevention of Dementia: A Randomized Controlled Trial. JAMA. 2008 Nov 19;300(19):2253-2262. (n=3,069 6.1yrs) In this study, G biloba at 120 mg twice a day was not effective in reducing either the overall incidence rate of dementia or AD incidence in elderly individuals with normal cognition or those with MCI.
Denham Bryan E. Dietary Supplements—**Regulatory Issues (DSHEA)** and Implications for Public Health. JAMA. 2011;Published online July 5, 2011. doi:10.1001/jama.2011.982
De Silva V, El-Metwally A, Ernst E, et al. Evidence for the efficacy of complementary and alternative medicines in the management of **osteoarthritis**: a systematic review. Rheumatology (Oxford). 2011 May;50(5):911-20. The available data for most complementary and alternative medicine (CAM) in treating patients with degenerative joint disease is limited. Topical **capsaicin** and S-adenosyl methionine (**SAMe**) appear to be effective in treating pain, but even these data are limited and potentially subject to bias in favor of publishing positive results. (LOE = 1a-)
De Smet PA. **Herbal remedies**. N Engl J Med. 2002 Dec 19;347(25):2046-56.
Deng H, Xu J. **Wendan decoction** (Traditional Chinese medicine) for schizophrenia. Cochrane Database Syst Rev. 2017 Jun 28;6:CD012217. Limited evidence suggests that WDD may have some positive short-term antipsychotic global effects compared to placebo or no treatment. However when WDD was compared with other antipsychotics there was no effect on global or mental state, but WDD was associated with fewer adverse effects. When WDD was combined with an antipsychotic, positive effects were found for global and mental state and the combination caused fewer adverse effects.
Devarbhavi H, Choudhury AK, Sharma MK, et al. **Drug-Induced Acute-on-Chronic Liver Failure in Asian Patients**. Am J Gastroenterol. 2019 Apr 22.
Dhesi Pavittarpaul; Ng Rita; Shehata Michael M.; Shah Prediman K.. Ventricular Tachycardia After Ingestion of **Ayurveda Herbal** Antidiarrheal Medication Containing **Aconitum**. Arch Intern Med. 2010;170(3):303-305.
Dhiman RK, Chawla YK. Herbal medicines for liver diseases. Dig Dis Sci. 2005 Oct;50(10):1807-12. (InfoPOEMs: There is insufficient evidence to recommend most commonly used herbal medicines for the treatment of liver disease. Of the 4 products evaluated in this review -- Phyllanthus, Silybum marianum (milk thistle), **glycyrrhizin** (licorice root extract), and Liv 52 (a mixture of herbs) -- available evidence supports only the use of the **licorice root extract** in the treatment of subacute liver failure and the prevention of hepatocellular carcinoma in patients with chronic hepatitis C. (LOE = 2a))
DMAA: July 25/12- Manufacturers of some sports supplements are falsely claiming a compound known as DMAA is a natural substance derived from geraniums, researchers say. Instead, research shows that DMAA is synthetic, consisting of four compounds called stereoisomers. DMAA (1,3-dimethylamylamine) is a stimulant found in some nutritional and sport supplements.

Dodge HH, Zitzelberger T, Oken BS, et al. A randomized placebo-controlled trial of ginkgo biloba for the prevention of cognitive decline. Neurology. 2008 Feb 27; [Epub ahead of print] n=118 42 month In unadjusted analyses, **ginkgo biloba** extract (GBE) neither altered the risk of progression from normal to Clinical Dementia Rating (CDR) = 0.5, nor protected against a decline in memory function. Secondary analysis taking into account medication adherence showed a protective effect of GBE on the progression to CDR = 0.5 and memory decline.

Draves AH, Walker SE. Analysis of the hypericin and pseudohypericin content of commercially available **St John's Wort** preparations. Can J Clin Pharmacol. 2003 Fall;10(3):114-8.

Drieling RL.; Gardner CD.; Ma Jun; et al. No Beneficial Effects of **Pine Bark Extract** 200mg daily on Cardiovascular Disease Risk Factors. Arch Intern Med. 2010;170(17):1541-1547. n=130, 12 wk.

Effect of **Gamma-Linolenic Acid** on the Transcriptional activity of the Her- 2/neu (erbB-2) oncogene. Journal of the National Cancer Institute, Vol. 97, No. 21, November 2, 2005, p. 1611-1615.

El Refaeey A, Selem A, Badawy A. Combined **coenzyme Q10** and clomiphene citrate for ovulation induction in clomiphene- citrate-resistant polycystic ovary syndrome. Reprod Biomed Online. 2014 Jul;29(1):119-24.

Elderberry extract has long been used as a folk remedy for cold and influenza symptoms. A recent randomized trial provides evidence for its efficacy (level 2 [mid-level] evidence). During the spring 2009 influenza season in China, 64 patients with ≥ 3 influenza-like symptoms (fever, headache, myalgias, coughing, nasal mucus discharge, nasal congestion) were randomized within 24 hours of symptom onset to elderberry extract lozenge (175 mg) vs. placebo orally 4 times daily for 2 days. After 48 hours, the rate of complete symptom relief was higher in the elderberry group (28% vs. 0%, no p value reported), with at least some symptom relief (only 0-2 mild symptoms remaining) reported in 88% vs. 16% for placebo (no p value reported). Elderberry extract was associated with significantly improved symptom severity scores for headache, nasal congestion, muscle aches, and fever at 24 hours ($p < 0.001$) and for all symptoms at 48 hours ($p < 0.001$). The elderberry group had higher symptom scores at baseline, however, suggesting that the groups may have been at different stages in their overall illness course despite randomization within 24 hours (Online J Pharmacol Pharmacokin 2009;5:32).

Eldridge WB, Foster C, Wyble L. Neonatal Abstinence Syndrome Due to **Maternal Kratom Use**. Pediatrics. 2018 Nov 7.

Ernst E. **Cardiovascular adverse effects of herbal medicines**: a systematic review of the recent literature. Can J Cardiol. 2003;19:818-27.

Fava M, Alpert J, et al. A Double-blind, Randomized Trial of **St John's Wort**, Fluoxetine, and Placebo in Major Depressive Disorder. J Clin Psychopharmacol. 2005 Oct;25(5):441-447.

FDA May 2007 FDA chemical analysis revealed that **Energy Max** contains thione analog of sildenafil, a substance with a structure similar to sildenafil, the active ingredient in Viagra, an FDA-approved drug for ED.Substances like this are called analogs because they have a structure similar to another drug and may cause similar side effects and drug interactions. **True Man** contains a thione analog of sildenafil or piperadino vardenafil, an analog of vardenafil, the active ingredient in Levitra, another FDA-approved prescription drug for ED. Neither the thione analog of sildenafil nor piperadino vardenafil are components of approved drug products.

FDA Feb/08 Palo Alto Labs and FDA notified consumers and healthcare professionals of a voluntary nationwide recall of two dietary supplements, **Aspire36** and **Aspire Lite**. The products were recalled because they were found to contain Aildenafil in trace amounts and Dimethyl sildenafil thione, an analog of Sildenafil, a drug used to treat erectile dysfunction.

FDA Mar/08 The U.S. Food and Drug Administration is advising consumers not to purchase or use "**Blue Steel**" or "**Hero**" products, marketed nationally as dietary supplements, because these products contain undeclared ingredients similar to sildenafil.

FDA April/08 **Herbal Science International**, Inc. and FDA informed consumers and healthcare professionals of a nationwide recall of twelve dietary supplements that contain ephedra, aristolochic acid or human placenta because they may present a serious health hazard to consumers. FDA has long regarded dietary supplements containing ephedra, a botanical that contains ephedrine alkaloids, as a potential health hazards because the alkaloid raises blood pressure and otherwise stress the circulatory system.

FDA May/08 is requesting that the manufacturer of **Xiadafil** — an "all natural" dietary supplement sold to treat erectile dysfunction — recall all its stock from natural food stores & discontinue marketing it on the Web since it contains an analog of sildenafil.

FDA May/08 notified consumers and healthcare professionals that supplement products sold under the brand name of **Viril-ity Power** (VIP) Tablets is being recalled because one lot was found to contain a potentially harmful undeclared ingredient, hydroxyhomosildenafil, an analog of sildenafil.

FDA May/08 The US Food and Drug Administration advised consumers not to use the products **Total Body Formula** in Tropical Orange and Peach Nectar flavours, and **Total Body Mega Formula** in Orange/Tangerine flavour, because they contain high doses of selenium and chromium.

FDA July/08 Jack Distribution, LLC issued a voluntary nationwide recall of selected lots of **Rize 2 The Occasion Capsules** and **Rose 4 Her Capsules**, marketed as dietary supplements. The products were recalled because certain lots contained thiomethisosildenafil, an undeclared analog of sildenafil, a FDA-approved drug used for Erectile Dysfunction.

FDA July/08 not to buy or use **Viapro** 375mg Capsules because one lot of the product was found to contain a potentially harmful undeclared ingredient, thio-methisosildenafil, an analog of sildenafil.

FDA Nov/08 Balanced Health Products, Inc. announced a recall of **STARCAPS** due to the presence of an undeclared drug ingredient, Bumetanide. Bumetanide is a diuretic indicated for the treatment of edema associated with congestive heart failure, hepatic and renal disease including nephrotic syndrome.

FDA Nov/08 Fashion Sanctuary announced a recall of **Zhen De Shou Fat Loss** Capsules because FDA analysis found the product to contain undeclared sibutramine, an FDA approved drug used as an appetite suppressant for weight loss.

FDA Dec/08 alerted consumers not to purchase or consume more than **25 different products** marketed for weight loss because they contain undeclared, active pharmaceutical ingredients that may put consumers' health at risk. The undeclared active pharmaceutical ingredients in some of these products include sibutramine (a controlled substance), rimonabant (a drug not approved for marketing in the USA), phenytoin (an anti-seizure medication), and phenolphthalein (a solution used in chemical experiments and a suspected cancer causing agent). The weight loss products, some of which are marked as "dietary supplements," are promoted and sold on various web sites and in some retail stores. FDA advises consumers who use the products to stop taking them and consult their healthcare professional immediately as the health risks posed by these products can be serious (for example, high blood pressure, seizures, tachycardia, palpitations, heart attack or stroke). FDA also encourages consumers to seek guidance from healthcare professional before purchasing weight loss products. See the FDA News Release for a listing of the names of the 25 referenced products. Read the MedWatch 2008 safety summary, including links to the News Release and Questions and Answers, at: http://www.fda.gov/medwatch/safety/2008/safety08.htm#Weight

FDA Jan/09 notified consumers not to take **Venom HYPERDRIVE 3.0**, a product sold as a dietary supplement but containing sibutramine.

FDA Apr/09: **ABC Beauty Supply** & FDA notified consumers and healthcare professionals of a recall of 34 dietary supplement products. FDA lab analyses identified undeclared **sibutramine**, an FDA- approved drug, used as an appetite suppressant for weight loss. http://www.fda.gov/oc/po/firmrecalls/universalabc04_09.html

FDA Apr/09 Nature & Health Co. and FDA notified healthcare professionals of a recall of a supplement product, **Libimax**. FDA analysis found the product contains tadalafil

FDA May/09 warned consumers to immediately stop using **Hydroxycut** products by Iovate Health Sciences, Inc. Hydroxycut products are associated with a number of serious **liver injuries**. Hydroxycut products are dietary supplements that are marketed for weight-loss, as fat burners, as energy-enhancers, as low carb diet aids, and for water loss under the **Iovate and MuscleTech brand** names. FDA has received 23 reports of serious health problems ranging from jaundice and elevated liver enzymes, an indicator of potential liver injury, to liver damage requiring liver transplant. One death due to liver failure has been reported to FDA. Other health problems reported include seizures; cardiovascular disorders; and rhabdomyolysis, a type of muscle damage that can lead to other serious health problems such as kidney failure.

FDA May/18: laboratory analysis confirmed that Best Candy contains nortadalafil.

FDA June/09 notified consumers and healthcare professionals to discontinue use of three **Zicam Nasal Gel/Nasal Swab** products sold over-the-counter as cold remedies because they are associated with the loss of sense of smell that may be long-lasting or permanent.

FDA July/09 and Haloteco notified healthcare professionals and consumers of a nationwide voluntary recall of Libipower Plus. Lab analysis of **Libipower Plus** samples were found to contain undeclared Tadalalafil.

FDA July/09 notified healthcare professionals that four weight loss dietary supplements sold and marketed by the firm (**Slimbionic, One Weight Loss Pill, SlimDemand Capsules, Botanical Weight Loss**) contain sibutramine.

FDA Aug/09 not to use body-building products marketed as containing steroids or steroid-like substances. The affected products are TREN-Xtreme, MASS Xtreme, ESTRO Xtreme, AH-89-Xtreme, HMG Xtreme, MMA-3 Xtreme, VNS-9 Xtreme, and TT-40-Xtreme..

FDA Nov/09 notified consumers that **Stiff Nights**, a product sold as a dietary supplement, contains sulfoaildenafil, a chemical similar to sildenafil (Viagra).

FDA Nov/09 & GMP Herbal Products notified consumers and healthcare professionals of a recall of **Pai You Guo**, a weight loss dietary supplement, due to the presence sibutramine & phenolphthalein.

FDA Nov/09 & RockHard Laboratories notified consumers that **RockHard Weekend**, a product sold as a dietary supplement, contains sulfoaildenafil, an analogue of sildenafil.

FDA Nov/09 & IDS Sports notified consumers that five of the IDS's dietary supplement products (**Bromodrol, Dual Action Grow Tabs, Grow Tabs, Mass Tabs, and Ripped Tabs TR**) contain the following undeclared substances, which FDA considers to be steroids: "Madol," "Turinabol," "Superdrol," &/or "Androstenedione."

FDA Dec/09 for **S-DROL**: a voluntary recall by the manufacturer of one lot (lot# 810481, expiry date 01/2012) of S-DROL after FDA testing found it to contain undeclared desoxymethyltestosterone.

FDA Dec/09 warned consumers to stop using bodybuilding products manufactured by American Cellular Labs after they were found to contain unauthorized synthetic steroids in **TREN-Xtreme, MASS Xtreme, ESTRO Xtreme, AH-89-Xtreme, HMG Xtreme, MMA-3 Xtreme, VNS-9 Xtreme, TT-40-Xtreme.**

FDA Dec/09 warned that **Atlas Operations, Inc**. notified consumers of a nationwide recall of the company's dietary supplements for sexual enhancement. These products are sold as dietary supplements throughout the USA. FDA lab analyses found that the products tested from certain batches contain Sulfoaildenafil.

FDA Dec/09 The Texas Department of State Health Services and FDA notified healthcare professionals and consumers, especially pregnant or breastfeeding women, to avoid consuming a product called "**Nzu**", taken as a traditional remedy for morning sickness,because of the potential health risks from high levels of lead and arsenic, noted on laboratory analysis by Texas DSHS. Nzu, which is sold at African specialty stores is also called Calabash clay, Calabar stone, Mabele, Argile and La Craie. It generally resembles balls of clay or mud and is usually sold in small plastic bags with a handwritten label identifying it as "Nzu" or "Salted Nzu."

FDA Jan/10 & **MuscleMaster(dot)com**, Inc. notified consumers and healthcare professionals of the voluntary nationwide recall of all lots and expiration dates of the seventeen dietary supplements listed in the firm press release, sold between June 1, 2009 and November 17, 2009. FDA informed MuscleMaster(dot)com that it believes that the recalled products contain ingredients that are **steroids**.

FDA Jan/10 notified consumers and healthcare professionals about a counterfeit and potentially harmful version of **Alli 60 mg capsules** (120 count refill kit). The **counterfeit** version contained the controlled substance sibutramine and did not contain orlistat, the active ingredient.

FDA Mar/10 & Natural Wellness notified consumers that **MasXtreme**, a product sold as a dietary supplement contains aildenafil close in structure to sildenafil and is expected to possess a similar pharmacological and adverse event profile as well as the drug phentolamine which is an alpha-adrenergic blocker.

FDA Apr/10 & Kanec USA notified healthcare professionals of a nationwide recall of **Stud Capsule For Men** [Lot #060607-01/060108-01, Exp 6-2013], after being informed by FDA that laboratory analysis of a sample found the product to be adulterated with sildenafil, an FDA approved drug.

FDA May/10 notified healthcare professionals, their patients, and consumers not to consume **Vita Breath**, a dietary supplement manufactured by American Herbal Lab and marketed at health fairs and on the Internet, because the product may contain hazardous levels of lead.

FDA June/10 **Magic Power Coffee**: Product marketed as a dietary supplement for sexual enhancement contains the drug ingredient hydroxythiohomosildenafil.

FDA July/10 analysis of **Que She** found that it contains: fenfluramine – a stimulant drug withdrawn from the U.S. market in 1997 after studies demonstrated that it caused serious heart valve damage, propranolol – a prescription beta blocker drug that can pose a risk to people with bronchial asthma and certain heart conditions, sibutramine – a controlled substance and prescription weight loss drug, sibutramine was the subject of a recent study whose preliminary findings showed an association between sibutramine use and increased risk of heart attack and stroke in patients who have a history of heart disease, & ephedrine – a stimulant drug that is legally marketed over-the-counter for temporary relief of asthma but can pose a risk to people with certain cardiovascular conditions.

FDA Aug/10 lab analysis of **Solo Slim** was found to contain the undeclared drug ingredient Didesmethyl Sibutramine.

FDA Aug/10 lab analysis of **Revivexxx Extra Strength** was found to contain undeclared tadalafil.

FDA Aug/10 notified Novacare LLC that certain products appear to contain sulfoaildenafil: **Stiff Nights, Aziffa, Size Matters, Erex, Mojo, Hard Drive, Eyeful, Red Magic, Straight Up, Zotrex, Monster Excyte, WOW, Xaitrex, Verect, Prolatis, Xytamax, Maxyte, Libidinal, OMG, OMG45, and Zilex (with Golden Spear) summers**.

FDA July/10 lab analysis of **Slim-30** Herb Supplement distributed by the company was found to contain undeclared N-Desmethyl Sibutramine and traces of Sibutramine.

FDA July/10 & Good Health, Inc. is conducting a voluntary recall after FDA lab analyses found that the product tested from certain batches of **Vialipro** contain Sulfoaildenafil.

FDA July/10 lab analysis of this herb supplement, **Joyful Slim** Herb Supplement, was found to contain the undeclared drug, desmethyl sibutramine.

FDA July/10 warned consumers not to consume or use **Miracle Mineral Solution**, an oral liquid solution also known as "Miracle Mineral Supplement" or "**MMS**." The product, when used as directed, produces an industrial bleach.

FDA July/10 notified consumers that lab analysis of lots of ejaculoid **XXTREME** and **stimuloid II** found that the products, sold as dietary supplements, contain sulfoaildenafil FDA Aug/10 had Lab analysis of **Mr. Magic** to contain hydroxythiohomosildenafil and sulfoaildenafil.

FDA Aug/10 analyzed **TimeOut** and determined that it contains hydroxythiohomosildenafil.

FDA Sep/10: Products marketed as dietary supplements contain **aromatase inhibitors**, commonly known as "ATD." Adverse events associated with the use of aromatase inhibitors could include the following: decreased rate of bone maturation and growth, decreased sperm production, infertility, aggressive behavior, adrenal insufficiency, kidney failure, and liver dysfunction. Advanced Muscle Science (Arom-X, Arom-X UTT, Arom-XL, 4-AD, and Decavol), ArimaDex, Clomed, Off Cycle II Hardcore, iForce – Reversitol.

FDA Oct/10 advised consumers to avoid "**chelation**" products that are marketed over-the-counter (OTC) to prevent or treat diseases. There are serious safety issues associated with chelation products. Depending on the condition, when relying on unproven OTC chelation products to treat serious conditions, patients may delay seeking effective medical care. Even when used under medical supervision, these products can cause serious harm, including dehydration, kidney failure, and death.

FDA Nov/10 ISSUE: Lab analysis has found **Duro Extend** Capsules for Men to contain Sulfoaidenafil, an analogue of Sildenafil.

FDA Dec/10 warned consumers not to use **Man Up Now** capsules, marketed as a dietary supplement for sexual enhancement, because FDA analysis determined that the product contains sulfoaildenafil.

FDA Dec/10 notified the public that testing determined that **RockHard Weekend** Lot Numbers 100159 and 100260 sold as blister packs, 3ct bottles and 8ct bottles &

Pandora Lot Numbers 100378 sold as blister packs & **Passion Coffee** contain an analogue of sildenafil.

FDA Dec/10 has received multiple reports of adverse events associated with the use of **Fruta Planta**, including several cardiac events and one death. FDA laboratory analysis confirmed that Fruta Planta contains sibutramine.

FDA Jan/11 laboratory analysis confirmed that **Celerite Slimming Capsules** contain sibutramine

FDA Mar/11 lab analysis of **Svelte 30** orange & gray capsules determined that the product contains Sibutramine.

FDA Mar/11 notified Biotab Nutraceuticals, Inc. that two lots of counterfeit product purporting to be **Extenze** contain undeclared drug ingredients. Specifically, lot 0709241 contains tadalafil and sildenafil, and lot 0509075 contains tadalafil and sibutramine.

FDA Mar/11 laboratory analysis confirmed that **Black Ant** contains sildenafil.

FDA Mar/11 **:** USA Far Ocean Group, Inc. issues voluntary nationwide recall of **U-Prosta**, a product marketed as a dietary supplement that contains undeclared terazosin.

FDA Mar/11 ISSUE: Tested samples of **Soladek** contained levels of vitamin A and vitamin D that were many times the recommended daily allowances for these vitamins.

FDA Mar/11 laboratory analyses of **Celerite Slimming Tea**: Recall - were found to contain undeclared Sibutramine.

FDA Mar/11 ISSUE: FDA lab analysis of **X-Hero** found the product contains sulfosildenafil, the analogue of the active ingredient of an FDA-approved drug. In addition, FDA analysis of **Male Enhancer** sample found the product contains tadalafil.

FDA Apr/11 Lab analyses of **Best Enhancer** found that the product contain Sulfoaildenafil.

FDA Apr/11 "**U-Prosta Natural support for prostate health**" is being voluntarily recalled in Canada by Sunnylife International Inc. after the U.S. Food and Drug Administration (FDA) found the product contains undeclared terazosin.

FDA May/11 **Regenerect**: Recall - Undeclared Drug Ingredient of lab confirmed the presence of Sulfoaildenafil.

FDA May/11 laboratory analysis confirmed that "**Slim Xtreme Herbal Slimming Capsule**" contains sibutramine.

FDA June/11 lab analyses found Via **Xtreme Ultimate Sexual Enhancer Dietary** Supplement for Men to contain sulfoaildenafil methanesulfonate.

FDA June/11 Nature Relief and FDA notified the public of a recall of **Nature Relief Instant Wart and Mole Remover**. FDA has advised that the active ingredient, calcium oxide, can cause severe burns of the skin, particularly to areas of thin or sensitive skin, such as the face, area around the eyes, and genitalia.

FDA July/11 is advising consumers not to purchase or use "**Slim Forte Slimming Capsules**," "**Slim Forte Slimming Coffee**," and "**Botanical Slimming Soft Gel & Slim Forte Double Power Slimming Capsules.** FDA laboratory analysis confirmed that these products contain sibutramine.

FDA Oct/11 notified the manufacturer that lab analyses found that the product; **Uprizing 2.0** , sold as a testosterone booster, contains superdrol, a synthetic steroid, making it an unapproved new drug.

FDA Nov/11 lab analysis for Lot 10090571 found **Virility Max** to contain sulfoaildenafil.

FDA Dec/11 Eclectic Institute is voluntarily recalling specific lots of its freeze-dried capsules containing **Gotu Kola** (Centella asiatica) and **Bladderwrack** (Fucus vesiculosus) capsules because of potential Salmonella contamination.

FDA Feb/12 Healthy People Co. notified the public of a recall of the company's dietary supplements sold under the brand names Healthy People Co. FDA lab analysis confirmed the presence of Sibutramine and Tadalafil, making these products unapproved new drugs. (Mince Belle Dietary Supplement, PERFECT Men Dietary Supplement , EVERLAX Dietary Supplement, EVER Slim Dietary Supplement, Herbal Drink Acai-man Mangosteen Dietary Supplement, EVER SLIM Shake Mix Dietary Supplement)

FDA Feb/12 Regeneca, Inc. notifed the public of a nationwide recall of **RegenArouse**, Lot Number 130100. FDA lab analysis confirmed the presence of Tadalafil.

FDA Feb/12 is advising consumers not to purchase or use "**Hard Ten Days**," & "**Man King**" a product for sexual enhancement sold on various websites. FDA laboratory analysis confirmed that "Hard Ten Days" contains sildenafil

FDA Feb/12 is advising consumers not to purchase or use "**Japan Weight Loss Blue**," a product for weight loss sold on various websites, laboratory analysis confirmed that "Japan Weight Loss Blue" contains sibutramine, analogs of sibutramine, and ephedrine alkaloids.

FDA Mar/12 notified healthcare professionals and warned consumers not to use skin creams, beauty and antiseptic soaps, or lotions that might contain **mercury**. The products are marketed as **skin lighteners and anti-aging** treatments that remove age spots, freckles, blemishes and wrinkles. Adolescents also may use these products as acne treatments.

FDA Apr/12 laboratory analysis confirmed that "**Japan Rapid Weight Loss Diet Pills Yellow**" contains sibutramine and phenolphthalein.

FDA Apr/12 laboratory analysis confirmed that "**France T253**" contains sildenafil.

FDA Apr/12 is advising consumers not to purchase or use "**X-Rock**," a product for sexual enhancement manufactured by CRM Laboratories and sold on various websites, including www.xrockme.com. FDA laboratory analysis confirmed that "X-Rock" contains sildenafil and hydroxythiohomosildenafil.

FDA Apr/12 laboratory analysis confirmed that "**Instant Hard Rod**" contains aminotadalafil. FDA laboratory analysis confirmed that "**ZenMaxx**" contains aminotadalafil. FDA laboratory analysis confirmed that "**RigiRx Plus**" contains aminotadalafil.

FDA May/12 is advising consumers not to purchase or use "**VMaxx Rx**," a product for sexual enhancement sold on various websites, including www.vmaxxrx.com. FDA laboratory analysis confirmed that "VMaxx Rx" contains the undeclared ingredient sulfoaildenafil. FDA is also advising consumers not to purchase or use "**Boost — Ultra Sexual Enhancement Formula**." This product is promoted and sold on various websites, including www.boostultra.biz. FDA laboratory analysis confirmed that "Boost—Ultra Sexual Enhancement Formula" contains sildenafil. FDA is also advising consumers not to purchase or use "**Firminite**," a product for sexual enhancement sold on various websites, including **www.firminite.com.** FDA laboratory analysis confirmed that "Firminite" contains tadalafil.

FDA May/12 West Coast Nutritionals, Ltd. is conducting a recall of all lots of their dietary supplements **Firminite, Extra Strength Instant Hot Rod, and Libidron** to the consumer level. An FDA lab analysis of Firminite was found to contain undeclared Tadalafil.

FDA May/12 is advising consumers not to purchase or use "**EreXite**," a product for sexual enhancement sold on various websites, including www.amazon.com. FDA laboratory analysis confirmed that "EreXite" contains tadalafil.

FDA June/12 cautioned late last week against using **Reumofan Plus**, a dietary supplement marketed as a "natural" pain reliever for arthritis, osteoporosis, and other conditions. The drug, which is made in Mexico but available online, contains unlabeled and potentially harmful pharmaceutical ingredients: diclofenac, methocarbamol & sometimes dexamethasone. (Dec/12 FDA: Reumofan Plus is being relabeled and sold under the name "**WOW**.")

FDA June/12 Botanical Laboratories Inc. and FDA notified consumers and healthcare professionals of a recall of **Wellesse Digestive 3 in 1 Health liquid dietary supplement**. A supplier of one of the ingredients indicated the ingredient has the potential to be contaminated with Salmonella.

FDA Aug/12 CRM Laboratories is conducting a consumer/user level recall of all X-ROCK 3 Day Pill For Men and Z-ROCK products sold between October, 2011 and April, 2012. Finished product of

X-ROCK 3 Day Pill for Men and Z-ROCK was tested and found to contain an analogue of an ingredient in an FDA-approved drug. Analytical tests conducted by the FDA concluded that the products contained sildenafil and hydroxythiohomosildenafil.

FDA Aug/12 is issuing an updated alert that **Reumofan Plus and Reumofan Plus Premium** contain undeclared active ingredients found in prescription drugs that should be used only under the supervision of a health care professional. It contains Diclofenac Sodium and Methocarbamol.

FDA Sep/12 Brand New Energy and FDA notified the public of a recall of all lot codes of **EphBurn 25**. One lot of EphBurn 25 sampled by the FDA was found to contain ephedrine alkaloids, making it an unapproved drug.

FDA Sep/12: Body Basics Inc. announced that it is conducting a voluntary nationwide recall of **ACTRA-Sx 500 Dietary Supplement Capsules**, Lot 008-A, Expiration December 2013. The Company, through independent lab analysis, has confirmed the presence of Sildenafil Citrate.

FDA Sep/12 is warning consumers not to use **Intestinomicina**, a drug product manufactured in El Salvador, because it contains the prescription drug ingredient, Chloramphenicol.

FDA Sep/12 Evol Nutrition Associates, Inc./Red Dawn ("Evol Nutrition") notified the public of a nationwide recall of all lots of two dietary supplement products distributed by the company under the names **Mojo Nights and Mojo Nights for Her** to the consumer level. Testing by the FDA revealed the presence of undeclared tadalafil and sildenafil in Mojo Nights (Evol Nutrition is also recalling Mojo Nights for Her).

FDA Oct/12 is advising consumers not to purchase or use "**Ultimate Formula Bee Pollen Capsules (Ultimate Formula**)," or "**Zi Xiu Tang Bee Pollen Capsules**," also referred to as "**Zi Xiu Tang Beauty, Face & Figure Capsule**," a product promoted and sold for weight loss because they contain sibutramine.

FDA Dec/12: **Libigrow, Libigrow XXXtreme, Blue Diamond, Blue Diamond Platinum, Mojo Nights, Mojo Nights Supreme, And Casanova**: Recall - Undeclared Ingredients Sulfoaildenafil and Thioaildenafil.

FDA Dec/12 is advising consumers not to purchase or use "**SLIMDIA Revolution**," a product promoted and sold for weight loss on various websites, including www.pinkfatty.com, and in some retail stores since it contains Sibutramine.

FDA Jan/13 is advising consumers not to purchase or use "**MAXILOSS** Weight Advanced," a product promoted and sold for weight loss on various websites, includingwww.dreamlifeweightloss.com, and in some retail stores since it contains sibutramine.

FDA Jan/13 Freedom Trading is conducting a voluntary consumer recall of a product sold as a dietary supplement under the brand name of **Super Power**. This product was sold between August 2012 and January 2013 nationwide & the products contained trace amounts of sildenafil.

FDA Feb/13 Olaax Corp announced a nationwide recall of the company's dietary supplement sold under the brand name **Maxiloss Weight Advanced Softgels** to the user level, because FDA testing found the Maxiloss Weight Advanced product to contain Sibutramine.

FDA Mar/13 Green Planet, Inc. notified the public of a recall of its dietary supplement product **Night Bullet**. Analytical tests conducted by the FDA found that the product contains trace amounts of Sulfohydroxyhomosildenafil and Aminotadalafil, which are analogues of sildenafil.

FDA Apr/13 laboratory analysis confirmed that "**Ninja Mojo"& "Love Rider**" contains tadalafil. FDA also confirmed that "**AFFIRM XL**" contains the undeclared ingredient sulfoaildenafil.

FDA Apr/13 Consumer Concepts, Inc. notified the public of a consumer/user level recall of all **ROCK-It MAN** Male Enhancement Capsules sold between October, 2012 and April, 2013. Analytical tests conducted by the FDA concluded that the product contained hydroxythiohomosildenafil.

FDA Apr/13 **Affirm XL**, Inc. is conducting a voluntary recall to the consumer level after FDA lab analysis testing found the product to contain an analogue of sildenafil.

FDA Apr/13 says it wants to make sure that supplements containing the **stimulant dimethylamylamine (DMAA)** are not distributed or sold in the U.S. The agency's action comes after reports of illness and death associated with DMAA-containing supplements. It has warned companies that use of DMAA in dietary supplements is illegal. One company, USPLabs, has defended its use. The company makes "**Jack3d**," which contains DMAA and is described as a "pre-exercise CNS-carnosine-ATP augmentor." It's sold on the Web.

FDA Apr/13 laboratory analysis confirmed that "**Sex Plus**" contains undeclared sildenafil, tadalafil, sulfosildenafil and dimethylacetildenafil. FDA laboratory analysis confirmed that "**Zoom-Zooma-Zoom**" contains sildenafil, the active ingredient in the FDA-approved prescription drug Viagra.

FDA May/13 American Lifestyle is announcing that it is conducting a voluntary recall of all lots of **Vicerex** UPC 893490820087 and **Black Ant** UPC 4026666142546. Laboratory analysis conducted by the FDA has determined the Vicerex product contains undeclared tadalafil and the Black Ant product contains undeclared sildenafil.

FDA May/13 is advising consumers not to purchase or use "**Bullet Proof**," a product promoted and sold for sexual enhancement on various websites and in some retail stores. FDA laboratory analysis confirmed that "Bullet Proof" contains tadalafil. Plus Chang Kwung announced today that it is conducting a voluntary nationwide recall of the company's dietary supplements sold under the brand name **Lightning Rod** (500 mg per capsule packaged in 3-count, UPC 6 89076 20257 2 and 12-count bottles, UPC 6 89076 20297 8), because FDA testing found the Lightning Rod Capsules to contain an analogue of Sildenafil.

FDA May/13: BeaMonstar Products notified the public that it is recalling its **SexVoltz, Velextra, and Amerect** capsules. Laboratory analysis conducted by the FDA on SexVoltz and Velextra has determined these products contain undeclared tadalafil.

FDA Jun/13 FDA laboratory analysis confirmed that "**Bethel 30**", & "**XIYOUJI QINGZHI CAPSULE**" & **JaDera** contains sibutramine. .

FDA Jun/13 laboratory analysis confirmed that "**Reload**" , "**Cave Diver**" , "**Super Cheetah**", "**Nights to Remember**" , & "**X Zen Platinum**", contains sildenafil.

FDA Jun/13 A sample of **Extreme Body Slim, Fat Zero, Fruit & Plant Slimming, & Paiyouji Plus** all contains silbutramine.

FDA Jun/13 A sample of **Royal Dragon Herbal Tonic Balls** contains vardenafil.

FDA Jun/13 Beta Labs has recalled certain lots of **Oxyphen, Phentalene, Phen FX, and Red Vipers** because they contain 1,3 dimethylamylamine (DMAA), the FDA announced over the weekend. The products are used as pre-workout stimulants and for weight loss, but the agency has previously warned that DMAA can be dangerous: it can elevate blood pressure and lead to cardiovascular complications. One distributor, GNC, faces FDA seizure of over 3000 cases of two other DMAA-containing products, **Jack3d and OxyElitePro**. Although the manufacturer of those supplements has ceased production, GNC continues to sell its remaining stocks, according to the *New York Times*.

FDA July/13 **Clalis, Exten 1300 & MaxTreme Zen** contains sildenafil, while **MVP Mega** contains talalafil.

FDA July/13 **Meizi Revolution, Strawberry Balance** contains silbutramine. **Silver Sword** & **Clalis** contains sildenafil.

FDA Aug/13 Volcano Company is recalling all lots of **Volcano Male Enhancement Liquid and Volcano Male Enhancement Capsules** to the consumer level. FDA test results revealed the Volcano Male Enhancement Liquid has been found to contain undeclared Desmethyl Carbodenafil, Dimethylsildenafil, and Dapoxetine.

FDA Aug/13 Purity First Health Products is recalling two lots of **Healthy Life Chemistry B-50** (100 capsules), one lot of **Healthy Life Chemistry Multi-Mineral** (200 capsules) and all lot numbers for **Healthy Life Chemistry Vitamin C** (200 capsules). The B-50 capsules were found on testing by FDA to contain Methasterone (a schedule III controlled substance) and Dimethazine. Testing of the Multi-Mineral and Vitamin C capsules appear to indicate the presence of Dimethyltestosterone.

FDA Aug/13 Herbal Give Care LLC issued a voluntarily recall of all lots of **Esbelin silouttete** and **Esbelin siloutte Herbal Blend with L-Carnitine** (30 Capsules), to the consumer level. The products have been found to contain undeclared Sibutramine, N-Desmethylsibutramine, and N-di-Desmethylsibutramine.

FDA Aug/13 Bethel Nutritional Consulting, Inc., New York, NY, is voluntarily recalling **Quick Thin and Bethel Advance** to the consumer level. These products have been found to contain Sibutramine and Phenolphthalein, and may pose a threat to consumers.

FDA Aug/13 Health and Beyond LLC is voluntarily recalling quantity lots of product **Tranquility**. The products have been found to contain a trace of Doxepin which is a pharmaceutical for sleep and Chlorpormazine for psychotic disorders.

FDA Aug/13 CTV Best Group announced that it is conducting a voluntary nationwide recall of all lots of a dietary supplement products distributed by the company under the names **BEST SLIM 40 Pills** to the consumer level. Testing by FDA revealed the presence of Sibutramine in Best Slim.

FDA Aig/13 Herbal Give Care LLC is voluntarily recalling all lots of **Esbelder man (30 capsules), Esbelder fem (30 capsules) and Esbelder siloutte** (30 capsules) to the consumer level. The products have been found to contain undeclared Sibutramine, N-Desmethylsibutramine, and N-di-Desmethylsibutramine.

FDA Aug/13: Jack Rabbit Inc. announced that it is conducting a voluntary nationwide recall of one lot of the company's dietary supplement product sold under the name **Jack Rabbit**. FDA lab analysis of the product was found to contain Sildenafil and Tadalafil.

FDA Aug/13 laboratory analysis confirmed that **Ortiga** contains the prescription drug ingredient, diclofenac.

FDA Aug/13 Hardmenstore.com is voluntarily recalling 1000 lots of **72HP, Evil Root and Pro Power Max** at the consumer level. According to representatives of the FDA, 72HP, Evil Root and Pro Power Max have reportedly been found to contain amounts of the PDE-5 Inhibitor, sildenafil.

FDA Sep/13 Ge Pharma, LLC is recalling **Creafuse Powder Grape** Lot# GE4568 and Creafuse Powder Fruit Punch Lot #GE4570, because they contain 1,3 dimethylamylamine (DMAA). DMAA is commonly used as a stimulant, pre-workout, and weight loss ingredient in dietary supplement products.

FDA Sep/13 laboratory analysis confirmed that **Shou Fu Ti Tun Guo Xiang Xing Jian Fei Jiao Nang** contains sibutramine.

FDA Sep/13 is advising consumers not to purchase or use **XZone Premium**, a product promoted and sold for sexual enhancement. FDA laboratory analysis confirmed that XZone Premium contains sildenafil, tadalafil, and dapoxetine.
FDA Sep/13 is advising consumers not to purchase or use **Wood-E**, a product promoted and sold for sexual enhancement. FDA laboratory analysis confirmed that Wood-E contains sildenafil.
FDA Sep/13 is advising consumers not to purchase or use **Xzen 1200, Xzen Gold or Xzen XPress**, products promoted and sold for sexual enhancement. FDA laboratory analysis confirmed that it contains either sildenafil & tadalafil.
FDA Sep/13 Haute Health, LLC is voluntarily recalling all lots of **Virilis Pro, PHUK and Prolifta** at the retail and consumer level. Virilis Pro, PHUK and Prolifta have been found to contain amounts of the PDE-5 Inhibitor sildenafil.
FDA Oct/13 along with the Centers for Disease Control and Prevention (CDC) and the Hawaii Department of Health (DOH), are investigating a growing number of reports of acute non-viral hepatitis in Hawaii. The Hawaii DOH has reported that 24 of these cases share a common link to a dietary supplement product labeled as **OxyElite Pro**.

FDA Oct/13: B@B Trade, Inc., Florida is voluntarily recalling all lots of **Slim Fortune, Lidiy, and Slim Expert** to the consumer level. The FDA laboratory analysis of these dietary supplements found to contain undeclared Sibutramine,
FDA Oct/13 is advising consumers not to purchase or use **Perfect Body Solutions or Burn 7.** FDA laboratory analyses confirmed that Perfect Body Solutions and Burn 7 contain sibutramine.
FDA Oct/13 is advising consumers not to purchase or use **Dr. Mao Slimming Capsules**. FDA laboratory analysis confirmed that Dr. Mao Slimming Capsules contain sibutramine.
FDA Oct/13 is advising consumers not to purchase or use **Bella Vi Insane Amp'd or Bella Vi Amp'd Up & Be Inspired.** FDA laboratory analyses confirmed that Bella Vi Insane Amp'd and Bella Vi Amp'd Up contain sibutramine.
FDA Nov/13: Fossil Fuel Products, LLC, is recalling lots QL110714A102 and QL110408B046 of "**RezzRX**." Laboratory analysis conducted by the FDA determined the RezzRX lot QL110714A102 contains undeclared hydroxylthiohomosildenafil and aminotadalafil and RezzRX lot QL110408B046 contains undeclared hydroxylthiohomosildenafil.
FDA Nov/13: Jobbers Wholesale is recalling Lot No. KWAKPMC030505175957019 of **Rhino 5 Plus**, Lot No. JBP-L-1270-70 of **Maxtremezen** and Lot No. KWAKPMC03050517 of **Extenzone**. FDA analysis found these products to contain undeclared desmethylcarbondenafil and dapoxetine, making these products unapproved new drugs.
FDA Nov/13 Vitality Research Labs is recalling lots K58Q and F50Q of **VitaliKOR Fast Acting**. FDA laboratory analysis on VitaliKOR has determined that this product contains undeclared Vardenafil and Tadalafil.
FDA Nov/13: Tendex is voluntarily recalling Lot# F51Q of P-Boost and Lot # F51Q of NatuRECT to the consumer level. FDA laboratory analysis on Lot# F51Q of **P-Boost**, which the firm also labels as **NatuRECT**, has determined that this product contains undeclared tadalafil.
FDA Nov/13 **SlimExtra Herbal** capsules contain silbutramine.
FDA Nov/13 **Alpha Male** contains sildenafil & other analogs.
FDA Dec/13 IQ Formulations, of Sunrise, Florida is initiating a recall of all lots of its 45-capsule bottles of **Hydravax** due to potential inclusion of an unlisted ingredient. The FDA has advised IQ Formulations that an analysis of a sample from one lot of Hydravax (Lot # 2458, Exp # 07/16) revealed the presence of an undeclared ingredient – a diuretic.
FDA Dec/13 is advising consumers to immediately stop using a product called **Mass Destruction**, marketed as a dietary supplement for muscle growth. The product is labeled to contain at least one synthetic anabolic steroid and has been linked to at least one reported serious illness.
FDA Dec/13 laboratory analysis found the **Burn 7 Capsules** to contain undeclared Sibutramine.
FDA Jan/14 Midwest Wholesale is voluntarily recalling the following products Boost**: Ultra, XZone Gold, Sexy Monkey, Triple MiracleZen Platinum, Magic for Men, "New" Extenze, and New XZen Platinum**. FDA analysis found these products to contain undeclared Sildenafil and/or Tadalafil.
FDA Jan/14 is advising consumers not to purchase or use **Magic Slim or Dream Body Slimming Capsule**, products promoted and sold for weight loss and sold on various websites and in some stores, since FDA lab analysis confirmed they contains sibutramine.
FDA Jan/14: **JINQIANGBUDOR Red Dragon** & **Tiger King** contains sildenafil; **Bali Mojo** & **Vimax** contains tadalafil; SexRx Contains both sildenafil and tadalafil.
FDA Jan/14 **Citrus Fit Gold**, **Hot Detox** & **Thinogenics** contains sibutramine. **Tonic Life BP** contains phenolphthalein.
FDA Mar/14 is advising consumers not to purchase or use **Vitaccino Coffee**, a product promoted and sold for weight loss. FDA laboratory analysis confirmed that Vitaccino Coffee contains sibutramine.
FDA Mar/14 Terra-Medica, Inc. is voluntarily recalling 56 lots of **Pleo-FORT, Pleo-QUENT, Pleo-NOT, Pleo-STOLO, Pleo-NOTA-QUENT, and Pleo-EX homeopathic** drug products in liquid, tablet, capsule, ointment, and suppository forms to the consumer level. FDA has determined that these products have the potential to contain penicillin or derivatives of penicillin.
FDA Mar/14: New Life Nutritional Center is recalling all lots of "**Super Fat Burner capsules, Maxi Gold capsules and Esmeralda softgels**" to the user level after FDA analysis revealed the products contain undeclared active pharmaceutical ingredients: sibutramine, phenolphthalein or a combination of both sibutramine and phenolphthalein.
FDA Mar/14: **Bella Vi Insane Bee Pollen Capsules, Bella Vi BTrim Ultimate Boost, Bella Vi BTrim Max, Bella Vi Extreme Accelerator, Bella Vi Insane Amp'd, and Bella Vi Amp'd U**, contain silbutramine with or without phenolphthalein.
FDA Mar/14: Nova Products, Inc. issued a voluntary recall of the following products: **African Black Ant (Lot# 2006-000926), Black Ant (Lot# 2006-3627878), XZen Gold (Lot# 130310GL), ZXen Platinum (Lot# 130520PL), XZen 1200 (Lot# 13051012), XZone Gold (Lot# 131110GL), and XZone 1200 (Lot# 13071012)** at the retail level. FDA laboratory analysis on these products has determined that they contain undeclared amounts of sildenafil and tadalafil.

FDA Apr/14: FDA analysis on **New You** contains silbutramine.
FDA Apr/14 has tested multiple **Zi Xiu Tang Bee Pollen** products from various distributors in the United States (US). All products that have been tested, including those that claim to be "genuine" and "anti-counterfeit," have been found to contain one or both of the undeclared drug ingredients sibutramine and Phenolphthalein.
FDA Apr/14 laboratory analysis confirmed that **Infinity** & **Lite Fit** USA contains sibutramine.
FDA apr/14 is advising consumers not to purchase or use **S.W.A.G,** a product promoted and sold for sexual enhancement. FDA laboratory analysis confirmed that S.W.A.G contains sildenafil.
FDA Apr/14: Nature's Universe notified the public it is recalling all lots of **Thinogenics** product sold prior to February 6, 2014 to the user level after FDA analysis revealed that the affected product contained undeclared sibutramine.
FDA Apr/14: Nano Well-being Health Inc. issued a voluntary recall of **Super Arthgold**, 500 mg capsules to the consumer level. FDA laboratory analysis has found the product to contain chlorzoxazone, diclofenac and indomethacin.
FDA May/14 laboratory analysis confirmed that **Slim Trim U** & **Natural Body Solution** contains sibutramine.
FDA May/14: Eugene Oregon, Inc. is voluntarily conducting this recall because FDA analysis of **African Black Ant, Black Ant, and Mojo Risen** distributed to a third party revealed that the distributed products contained undeclared amounts of the active pharmaceutical ingredients sildenafil and tadalafil.
FDA May/14 is advising consumers not to purchase or use **Asset Bee Pollen**, a product promoted and sold for weight loss because it contains sibutramine.
FDA May/14 is advising consumers not to purchase or use **Asset Bold**, a product promoted and sold for weight loss. FDA laboratory analysis confirmed that Asset Bold contains sibutramine.
FDA May/14 is advising consumers not to purchase or use **MV5 Days**, a product promoted and sold for sexual enhancement. FDA laboratory analysis confirmed that MV5 Days contains sildenafil.
FDA Jun/14: advising consumers not to purchase or use **Eyeful** contains hydroxythiohomosildenafil; **Liu Bian Li** contains sildenafil; **Dick's Hard Up** contains tadalafil; **3 Hard Knights** contains sildenafil and thiosildenafil; **Full Throttle On Demand** contains propoxyphenyl sildenafil; GoldReallas contains sildenafil and thiosildenafil.
FDA June/14 laboratory analysis confirmed that **Zhen Gong Fu** contains sildenafil.
FDA Jun/14 laboratory analysis confirmed that **La Jiao Shou Shen** contains sibutramine
FDA Jun/14 laboratory analysis confirmed that **Gold Vigra & Miraculous Evil Root** contains sildenafil. FDA laboratory analysis confirmed that **Sport Burner & Toxin Discharged** Tea contains fluoxetine. FDA laboratory analysis confirmed that **Sliming Diet** contains sibutramine.
FDA July/14 laboratory analysis confirmed that **Mix Fruit Slimming, Lingzhi Cleansed Slim Tea, 24 Ince, Lipo 8 Burn Slim, Sliming (sic) Diet By Pretty, & Trim-Fast Slimming Softgel** contains sibutramine.
FDA July/14: **Lian Zhan Qi Tian capsules & Weekend Warrior** contains thiosildenafil.
FDA July/14: **Vitaccino Coffee, Collagen Slim, & Sulami** contains sibutramine.
FDA July/14: **Fruta Bio, Jianfeijindan Activity Girl, & LTD Japanese Chinese Formula** pill for weight reduction contains sibutramine and/or phenolphthalein.
FDA Aug/14 Regeneca Worldwide a division of VivaCeuticals, Inc., is conducting a voluntary nationwide recall of its **RegenESlim** appetite control dietary supplement, lot # EX0616R15814 and lot #11414RE5516, because FDA analysis confirmed the presence of DMAA.
FDA Aug/14 is advising consumers not to purchase or use **Arize**, a product promoted and sold for sexual enhancement. FDA laboratory analysis confirmed that Arize contains sulfoaildenafil; and Herbal Vigor Quick Fix contains tadalafil.
FDA Sep/14 laboratory analysis confirmed that **Best Line Suplemento Alimenticio Capsules** contains sibutramine.

FDA Sep/14 laboratory analysis confirmed that **LX1** contains undeclared DMAA, also known as 1,3-dimethylamylamine, methylhexanamine or geranium extract.
FDA Sep/14 laboratory analysis confirmed that **Mezo** contains benzylsibutramine, a substance structurally similar to sibutramine.
FDA Sep/14 laboratory analysis confirmed that **Japan Hokkaido Slimming Weight Loss Pills** contain sibutramine, benzocaine, phenolphthalein and diclofenac.
FDA Sep/14 warns parents and caregivers not to use "**Bo Ying compound**" manufactured by Eu Yan Sang (Hong Kong) Ltd. due to the potential lead poisoning risk associated with the product.
FDA Oct/14 laboratory analysis confirmed that **Sit and Slim II** contains sibutramine.
FDA Nov/14 is advising consumers not to purchase or use **V26 Slimming Coffee**. FDA laboratory analysis confirmed that V26 Slimming Coffee contains sibutramine.
FDA Oct/14 laboratory analysis found that "**Ginseng Kianpi Pil**" contains dexamethasone, a corticosteroid commonly used to treat inflammatory conditions, and cyproheptadine.
FDA Nov/14 is advising consumers not to purchase or use **Mayhem**, a product labeled as a dietary supplement that is promoted to increase appetite and muscle growth, because it contains an undeclared dexamethasone and cyproheptadine.
FDA Nov/14 Solgar, Inc. is voluntarily recalling **ABC Dophilus Powder**. Testing conducted by the Centers for Disease Control revealed the presence of Rhizopus oryzae in 1.75 oz (50 g) containers of Solgar ABC Dophilus Powder, which may cause Mucormycosis.
FDA Nov/14: REFA Enterprises is voluntarily recalling one lot each of: **Forever Beautiful Bee Pollen** (UPC # 6333090804632), **Forever Beautiful Infinity** (UPC # 633090804649). The products have been found to contain undeclared Sibutramine or a combination of both Sibutramine and Phenolphthalein through FDA laboratory analyses.
FDA Nov/14 is advising consumers not to purchase or use **Bee Slim, Bee Thin & Super Extreme Accelerator**. FDA laboratory analysis confirmed that they contain sibutramine.
FDA Nov/14 is advising consumers not to purchase or use **Black Storm**. FDA laboratory analysis confirmed that Black Storm contains sildenafil.
FDA Nov/14 laboratory analysis confirmed that **Slim-Vie** containssibutramine.
FDA Dec/14 Bethel Nutritional Consulting, Inc. is recalling one lot of **SLIM-K Capsules** to the consumer level. The firm was informed by the US Food and Drug Administration (FDA) that a sample of SLIM-K collected and tested by the FDA was found to contain sibutramine, desmethylsibutramine, and phenolphthalein.
FDA Dec/14 Bethel Nutritional Consulting, Inc. is recalling one lot of **B-Lipo Capsules** to the consumer level. The firm was informed by the US Food and Drug Administration (FDA) that a sample of B-Lipo Capsules collected and tested by the FDA was found to contain lorcaserin.
FDA Dec/14 Bethel Nutritional Consulting, Inc. is recalling one lot of **SLIM-K Capsules** to the consumer level. The firm was informed by the US Food and Drug Administration (FDA) that a sample of SLIM-K collected and tested by the FDA was found to contain sibutramine, desmethylsibutramine, and phenolphthalein.
FDA Dec/14 Bethel Nutritional Consulting, Inc. is recalling one lot of **B-Lipo Capsules** to the consumer level. The firm was informed by the US Food and Drug Administration (FDA) that a sample of B-Lipo Capsules collected and tested by the FDA was found to contain lorcaserin.
FDA Dec/14 is warning health professionals of the risks associated with the regarding use of dietary supplements containing live bacteria or yeast in immunocompromised persons. A premature infant administered a dietary supplement, ABC Dophilus Powder (**Solgar**), as part of in-hospital course of treatment, developed gastrointestinal mucormycosis caused by the mold Rhizopus oryzae and died. Rhizopus oryzae mold was found to be present as a contaminant in an unopened container of the ABC Dophilus Powder, which is formulated to contain three species of live bacteria.
FDAJan/15 is alerting consumers and health care professionals that **counterfeit versions of Cialis 20 mg tablets** were found in the mail on its way to a U.S. consumer.
FDAJan/15 laboratory analysis confirmed that **Happy Passengers** contains sildenafil.
FDA Feb/15 laboratory analysis confirmed that **Black King Kong, Germany Niubian, Tibet Babao, 72HP, Night Man, & Libigrow XXX Treme** contains sildenafil.
FDA Feb/15 laboratory analysis confirmed that **Botanical Slimming (Red), & Oxy ELITE Pro Super Thermogenic** (Lot# 216732, Exp. 04/17) contains fluoxetine.
FDA Feb/15 laboratory analysis confirmed that **Lean Body Extreme** contains sibutramine, desmethyl sibutramine, phenolphthalein, and sildenafil.
FDA Feb/15 laboratory analysis confirmed that **Nine Slim, & Seven Slim** contains phenolphthalein.
FDA Mar/15 laboratory analysis confirmed that **Santi Scalper, Vigra, Vigour 300, Sex Men, Super Hard, Plant Vigra, MME MAXMAN, Hard Wang & FX3000** contains sildenafil.
FDA Mar/15 laboratory analysis confirmed that **Elimulating Weight & Toxin Keeping Beauty** contains sibutramine
FDA Mar/15 laboratory analysis confirmed that **Bigger Longer More Time More Sperms (sic), Black Ant King, African Superman & Black Mamba Premium c**ontains sildenafil.
FDA Mar/15 laboratory analysis confirmed that **Black Mamba Hyperrush & L-Carnitine Sob Strengthening Version Slimming Miracle Capsule** contains sibutramine.
FDA Apri/15 A dietary supplement marketed to body builders and purported to contain **anabolic steroids** is linked to serious liver injury, the FDA warned on Monday. The agency has so far received three reports of adverse events associated with **Tri-Methyl Xtreme**, which is sold on the internet and in some retail stores and gyms.
FDA May/15 laboratory analysis confirmed that **Asihuri Plus Fortecontains** dexamethasone, a corticosteroid, and phenylbutazone.
FDA May/15 laboratory analysis confirmed that **Ginseng She Lian Wan** contains dexamethasone, a corticosteroid, and chlorpheniramine.
FDA May/15 laboratory analysis confirmed that **Jianbu Huqian Wan** contains dexamethasone, a corticosteroid, chlorpheniramine, and furosemide.
FDA May/15 laboratory analysis confirmed that **Saurean Fong Sep Lin** contains dexamethasone, a corticosteroid, and cyproheptadine.
FDA May/15 laboratory analysis confirmed that **Black Panther** contains sildenafil.
FDA May/15 laboratory analysis confirmed that **Viagra 007c**ontains sildenafil.
FDA May/15 laboratory analysis confirmed that **King of Romance** contains sildenafil.
FDA May/15 laboratory analysis confirmed that **Li Da Dai Dai Hua Slimming Capsule** contains sibutramine.
FDA May/15 laboratory analysis confirmed that **Slim Forte Slimming** Capsule contains sibutramine.
FDA Apr/15 laboratory analysis confirmed that **Superior** contains sibutramine.
FDA Apr/15 laboratory analysis confirmed that **Fatloss Slimming Beauty** contains sildenafil.
FDA Apr/15 laboratory analysis confirmed that **Extreme Diamond 3000** contains desmethyl carbodenafil and dapoxetine.
FDA May/15 **Samurai-X, Happy Passengers, & AMPD Gold Bee Pollen** contains undeclared sildenafil.
FDA May/15 **Yanhee Slim & iNSANE Bee Pollen** contains undeclared lorcaserin; **EDGE Amplified Weight Release** contains undeclared phenolphthalein and fluoxetine; **iNDiGO & BtRim Max** contains undeclared phenolphthalein.
FDA May/15: **Black King Kong, Tibet Babao, Vigour 300, Hard Wang**, **FX3000, Sex Men, Vigra, Plant Vigra, Santi Scalper, Baolong, Rhino Blitz Gold 3000, Vim-25, Black Mamba Premium, Bigger Longer More Time More Sperms (sic), Herb Viagra, & La Pepa Negra** contains undeclared sildenafil.
FDA May/15: **Male Silkworm Moth Nourishing Oral Liquid** contains undeclared vardenafil.
FDA May/15: **Nine Slim & Seven Slim** contains undeclared phenolphthalein.
FDA May/15: **Oxy ELITE Pro Super Thermogenic** contains undeclared fluoxetine.
FDA May/15: **Elimulating Weight & Toxin Keeping Beauty & L-Carnitine Sob Strengthening Version Slimming Miracle Capsule** contains undeclared sibutramine.
FDA May/15: **Lean Body Extreme** contains undeclared sibutramine, desmethyl sibutramine, phenolphthalein & sildenafil.
FDA May/15: **Diablos Eca Fire Caps** contains undeclared sildenafil, phenolphthalein, sibutramine & deisobutylbenzylsibutramine.
FDA July 15: **Extreme Diamond 3000** contains Undeclared desmethyl carbodenafil and dapoxetine.
FDA July 15: **Black Mamba Hyperrush & Ultra ZX** contains Undeclared sibutramine and phenolphthalein.
FDA July 15:**Botanical Slimming (Red) & Xcel** contains Undeclared fluoxetine.
FDA July 15:**Green Algae Combination** by Crane Beauty contains Undeclared lorcaserin.
FDA July 15:**Natural Max Slimming** contains Undeclared sildenafil, fluoxetine, and sibutramine.
FDA July 15: **Ultimate Boost & Xcel Advanced** contains Undeclared phenolphthalein.
FDA Aug/15 R Thomas Marketing, through its websites www.herbviagra.com and www.herbsviagra.com, sold the supplements under the names **Black Ant, Herb Viagra, Real Skill and Stree Overlord**. All four items contain undeclared sildenafil.
FDA Oct/15 **Kaboom Action Strips** 12 Pack contains undeclared sulfoaildenafil.
FDA Oct/15 **Lida DaiDaiHua** contains undeclared sibutramine & phenolphthalein.
FDA Sep/15: Consumers who have used any of the **Baidyanath brand Ayurvedic dietary supplements** listed in theConsumer Advice Notice should stop using them and consult their health care provider. Testing by the New York Department of Health and the U.S. Food and Drug Administration (FDA) has found that these products contain high levels of lead and/or mercury,

FDA Sep/15: **Miracle Diet 30** has been found to contain undeclared phenolphthalein,
FDA Sep/15: **Miracle Rock 48** has been found to contain undeclared thiosildenafil.
FDA Oct/15 laboratory analysis confirmed that **Wild Sexx Capsules** contains sildenafil and tadalafil.
FDA Oct/15 laboratory analysis confirmed that **Ultra SX Capsules, Super Dragon 6000 Capsules, Sex-Love Secret Code Capsules, Paradise Suplemento Natural Ultra Plus Capsules, APEXXX, & S.W.A.G.G.E.R Extreme Capsules** contains sildenafil.
FDA Oct/15 laboratory analysis confirmed that **Fuel Up High Octane, & Fuel Up Plus** contains hydroxythiohomosildenafil.
FDA Oct/15 laboratory analysis confirmed that **Xtreme Fat Burner Capsules** contains phenolphthalein.
FDA Oct/15 laboratory analysis confirmed that **Tip-Top Shape, Lishou Slimming Coffee, & Basha Nut 100% Fruit Soft Gel Capsules** contains sibutramine.
FDA Nov/15 laboratory analysis confirmed that **Perfect Slim Fast Track Slim & Slyn** Both contains fluoxetine.
FDA Nov/15 laboratory analysis confirmed that **Super Herbs** contains sibutramine and desmethylsiburamine.
FDA Nov/15 laboratory analysis confirmed that **Zero Fat & SPCARET Princess Diet** contains sibutramine.
FDA Nov/15 laboratory analysis confirmed that **Rhino X, Effective Viagra, Sex Drive Capsules, XForMan Plus & Australia Kangaroo Essence** contains sildenafil.
FDA Dec/15 Lucy's Weight Loss System is voluntarily recalling all lots of **Pink Bikini White powder Capsules**, 30 white (750MG per capsule) to the consumer level. Pink Bikini has been found positive for diclofenac.
FDA Dec/15 Lipo Escultura Corp. of Brooklyn, NY (dba JAT Productos Naturales Corp., and JAT Natural Products Corp.) are voluntarily recalling all **Lipo Escultura** within expiry to the consumer level since contains sibutramine and diclofenac.
FDA Dec/15 has warned five dietary supplement makers nationwide for their use of the substance Picamilon as an ingredient in their products. **Picamilon** is not a dietary ingredient, the FDA says, and therefore declaring it as such in product labeling causes the companies' products to be misbranded.
FDA Dec/15 laboratory analysis confirmed that **Rhino Big Horn 3000** contains desmethyl carbodenafil and sildenafil.
FDA Dec/15 laboratory analysis confirmed that **OrgaZen 3000, OrgaZen 3500, & Rhino 7 Blue 9000** contains tadalafil.
FDA Dec/15 laboratory analysis confirmed that **Triple Power Zen Gold 2000, Triple Power Zen Plus 2000, Xtra Zone 2200, Xtra Zone 2400, Xtra Zone 2600, & Diamond 3500** contains sildenafil and tadalafil.
FDA Dec/15 laboratory analysis confirmed that **Triple MiracleZen Extreme 1750 mg, MiracleZen Gold 1750 mg & Triple MiracleZen Plus 1500 mg** contains sildenafil, tadalafil and dapoxetine.
FDA Dec/15 laboratory analysis confirmed that **Eros Power Zone 1900** contains desmethyl carbodenafil and dapoxetine.
FDA Dec/15 laboratory analysis confirmed that **X Again Platinum** contains sildenafil, tadalafil and dapoxetine.
FDA Dec/15 laboratory analysis confirmed that **Evolve Bee Pollen, Jenesis, Prime Bee Pollen & Oasis Bee Pollen** contains sibutramine.
FDA Dec/15: laboratory analysis confirmed that **La'Trim Plus** contains sibutramine.
FDA Dec/15: Nuway Distributors llc is voluntarily recalling all lots of **Apexxx** tablets to the consumer level. FDA analysis found Apexxx to contain amounts of the PDE-5 Inhibitor, sildenafil.
FDA's Dec/15 analysis found the **Smart Lipo** products to contain undeclared sibutramine, desmethylsibutramine, and phenolphthalein.
FDA Dec/15 laboratory analysis confirmed that **Thirty Plus** contains sibutramine.
FDA Dec/15 laboratory analysis confirmed that **Power Tiger-X** contains sulfoaildenafil.
FDA Dec/15 BeeXtreme LLC is recalling all lots of **La' Trim Plus, Jenesis and Oasis products** from the market. Recent Analysis by the Food and Drug Administration has found undeclared Sibutramine and Phenolphthalein.
FDA: Jan/16 U.S. Marshals have seized nearly a half a million dollars' worth of dietary supplements containing **kratom (Mitragyna speciosa),** a plant-based substance that people use recreationally or to self-treat opioid addiction. The supplement (marketed as RelaKzpro) could pose a risk to public health, the FDA says, because it has narcotic-like effects and can potentially be abused. Kratom, which grows in Southeast Asia, affects the brain the same way opiates do. Risks associated with consuming the substance include nervousness, respiratory depression, and vomiting. Additionally, withdrawal can cause aggression, hostility, muscle and bone aches, and jerky limb movements. Importation of kratom was banned by the FDA in 2014. The agency says there is "inadequate information" that supplements with kratom don't present a risk for illness or injury, and it warns people not to use the substance. FDA news release (Free)
FDA Jan/16: Shakti Group USA LLC is recalling 50 gm and 100 gm sizes of L.G Compounded **Asafoetida Powder**, both coded with Lot Number: 2323 because it has the potential to be contaminated with Salmonella, an organism which can cause serious and sometimes fatal infections in young children, frail or elderly people, and others with weakened immune systems.
FDA Jan/16: R Thomas Marketing LLC is voluntarily recalling all lots of the following products to the consumer level: **Black Ant, Herb Viagra, Real Skill, Stree Overlord, Weekend Prince, & African Black Ant**. These products were tested by the FDA and found to contain sildenafil.
FDA Jan/16 is warning consumers not to use **Licorice Coughing Liquid**, a cough syrup product sold over-the-counter, because it contains unidentified morphine.
FDA Jan/16 laboratory analysis confirmed that **Wonder-Erect Male Gum & Wonder-Erect Male Pills** contains vardenafil.
FDA Jan/16 is warning consumers not to purchase or use a skin whitening cream called "Crema Piel De Seda," due to the risk of mercury poisoning.
FDA Jan/16 is warning consumers not to use "**Bentonite Me Baby**" by Alikay Naturals because of a potential lead poisoning risk.
FDA Jan/16 analysis of **Pink Bikini** (white capsules, blue capsules and gold capsules) and Shorts on the Beach (blue capsules and gold capsules) found these products to be tainted with Sibutramine, Phenolphthalein, and/or Diclofenac.
FDA Jan/16 is warning consumers not to purchase or use a skin whitening cream called "**Crema Piel De Seda**," due to the risk of mercury poisoning.
FDA laboratory analysis confirmed that Ginseng Power-X contains sildenafil and sulfoaildenafil.
FDA Feb/16 laboratory analysis confirmed that **Ninja-X** contains sildenafil and thiosildenafil.
FDA lFeb/16 aboratory analysis confirmed that **Golden Night** contains sildenafil and hydroxythiohomosildenafil.
FDA laboratory analysis confirmed that **Boss Number #Six** contains tadalafil.
FDA Feb/16 laboratory analysis confirmed that **Mamba is Hero** contains sildenafil, desmethyl carbodenafil, and dapoxetine
FDA Feb/16 laboratory analysis confirmed that **Zhong Hua Niu Bian, Weekend Prince, Bull & Bull's Genital** contains sildenafil.
FDA Mar/16 laboratory analysis confirmed that **Sextra** contains sildenafil.
FDA Mar/16 laboratory analysis confirmed that **ENVY BP** contains sibutramine.
FDA Mar/16 laboratory analysis confirmed that **Propell Platinum** contains sibutramine.
FDA Apr/16 Invisiblu International LLC is voluntarily recalling one lot of **Continuum Labs LGD-Xtreme**, 3 mg to the retail and consumer level. The product has been found to contain LGD-4033 Ligandrol, an investigational drug not approved for use. The risks of using this product are unknown.
FDA Apr/16 Super Herbs is voluntarily recalling all bottles of **SUPER HERBS**, light green and dark green capsules to the consumer level after FDA laboratory testing found SUPER HERBS to contain sibutramine, desmethylsibutramine, and/or phenolphthalein.
FDA Apr/16 laboratory analysis confirmed that **3rd Degree & Black Gold X** contains sibutramine.
FDA Apr/16 laboratory analysis confirmed that **Black Label X** contains sildenafil.
FDA May/16 laboratory analysis confirmed that **Step 2** contains sibutramine.
FDA May/16: SOS Telecom, Inc. is voluntarily recalling all lots of the following products (**Tiger-X, Ninja-X, Ginseng Power-X, & Super Samurai-X**) to the consumer level because these products were tested by the FDA and found to contain sildenafil.
FDA June/16: Pharmavite LLC is recalling specific lots of **Nature Made** products due to possible Salmonella or Staphylococcus aureus contamination.
FDA June/16: The **Body Shot Bar** is voluntarily recalling all lots distributed March 1- May 6 2016 of Step 2 60 gold capsule (350MG per) capsules to the consumer level. Step 2 has been found positive for Sibutramine after FDA sampling and testing.
FDA July/16 laboratory analysis confirmed that **Xcelerated Weight Loss Charged Up, Xcelerated Weight Loss Turbo Charge** contains sibutramine.
FDA July/16 laboratory analysis confirmed that **Xcelerated Weight Loss Ultra Max** contains phenolphthalein and sildenafil.
FDA July 16 laboratory analysis confirmed **Super Shangai, Shangai Ultra X & Power Spring (XXX) Oral Liquid** contains sildenafil.
FDA July 16 laboratory analysis confirmed that **Slim Fit X, & Mang Luk Power Slim Detox** contains sibutramine and desmethylsibutramine.
FDA July 16 laboratory analysis confirmed that **Mang Luk Power Slim, Maxx Easy** contains sibutramine.
FDA July/16: Dream Body Weight Loss is voluntarily recalling all lots of **Dream Body Extreme Gold 800mg 30 gold capsules, Dream Body 450mg 30 white capsules, and Dream Body Advanced 400mg 30 purple capsules to the consumer level. The Dream Body Extreme 800mg Gold, Dream Body 450mg and Dream Body Advanced 400mg** have been found to contain sibutramine.
FDA July/16: FDA laboratory analysis confirmed that **Dream Body Advanced + Acai Weight Loss & Cleanse** contains sibutramine, fluoxetine and sildenafil.
FDA July/16: FDA laboratory analysis confirmed that **Dream Body Extreme Gold** contains sibutramine, fluoxetine and sildenafil.
FDA July/16: FDA laboratory analysis confirmed that **Dream Body Original Formula, SBF Bee Pollen & Extra Slim Plus Acai Berry Weight Loss Formula** contains sibutramine.

FDA Jul/16 laboratory analysis confirmed that **Ziyinzhuangyang** contains sildenafil.
FDA Jul/16 laboratory analysis confirmed that **Zi Xiu Tang Beauty Face & Figure Capsule** contains phenolphthalein and fluoxetine.
FDA Jul/16 Laboratory analysis confirmed that **Weili (一炮到天亮or Yi Pao Dao Tian Liang)** contains sildenafil.
FDA Jul/16 laboratory analysis confirmed that **Ultimate Lean** contains sibutramine and desmethylsibutramine.
FDA Aug/16 laboratory analysis confirmed that **One More Knight 1750** contains tadalfil and dapoxetine.
FDA Aug/16 laboratory analysis confirmed that **Master Zone 1500** contains sildenafil and tadalfil.
FDA Aug/16 laboratory analysis confirmed that **Love4Long** contains sildenafil.
FDA Aug/16 laboratory analysis confirmed that **Natural Eruption** contains sibutramine.
FDA Aug/16 Ton Shen Health of Chicago, IL, is recalling its "**DHZC-2**" Tablets because they have the potential to be contaminated with elevated levels of lead.
FDA Aug/16 laboratory analysis confirmed that **De Guo Hei Bei (德国黑倍), Boss-Rhino Gold X-tra Strength, & Anaconda Strong Formula** contains sildenafil.
FDA Aug/16 laboratory analysis confirmed that **Citrus' Fit** contains sibutramine and desmethylsibutramine.
FDA Aug/16 laboratory analysis confirmed that **Adelgazantes R-II** contains sibutramine.
FDA Aug/16 is investigating **DHZC-2** tablets by Ton Shen Health/Life Rising for lead and other hazardous material and is also investigating to see if other Life Rising products from this company may be similarly affected.
FDA Aug/16 laboratory analysis confirmed that **Kopi Jantan Tradisional Natural Herbs Coffee** contains desmethyl carbodenafil.
FDA Oct/16 laboratory analysis confirmed **that Zi Su Body Fat Health II** contains sibutramine and phenolphthalein.
FDA Nov/16: Ton Shen Health of Chicago, IL, is recalling its Life Rising brand "**Side Head Regulator TT**" Tablets because they have tested positive for elevated levels of lead for children under the age of 18.
FDA Nov/16: Love My Tru Body is voluntarily recalling all of **Skinny Bee Diet 500 mg** to the consumer level after FDA laboratory testing found Skinny Bee Diet to contain sibutramine, desmethylsibutramine, and/phenolphthalein.
FDA Nov/16 laboratory analysis confirmed that ABX Weight Loss contains sibutramine.
FDA Nov/16 Nutra Manufacturing, Inc. announced a nationwide, voluntary recall of one lot of **GNC Women's Ultra Mega Time Release dietary supplement** product sold in 180 count containers UPC 048107158910, lot number 3044FQ2024, with an expiration date of June 2018 due to the fact the product may contain an undeclared major food allergen, milk.
FDA Nov/16: Raritan Pharmaceuticals is a contract manufacturer of these products for **Homeolab USA that supplies the belladonna blends to Raritan Pharmaceuticals**. These products were distributed Nationwide: 1) Product: **CVS Homeopathic Infants' Teething Tablet** 135 tablets, UPC: 050428424162, Lots: 41116 and 43436; 2) Product: **Kids Relief Homeopathic Ear Relief Oral Liquid** 0.85 fl. oz., UPC: 778159090639, Lot: 35254 3) Product: **CVS Homeopathic Kids' Ear Relief Liquid** 0.85 fl. oz., UPC: 050428441633, Lot: 33149.
FDA Nov/16: NutriVitaShop, also doing business as Naturecom Inc. Lake Forest, CA is requesting the nationwide recall of its **DMAA net weight 500g** because there may be presence of DMAA. Lot numbers include #20141102, 20150715, 20151022, 20160226, 20160701, 20161017 and 20150323. DMAA net weight 500g is packaged in approximately 8" x 11" silver and clear mylar ziplock bags that contain 500g of DMAA. DMAA is also known as 1,3-dimethylamylamine, methylhexanamine, or geranium extract.
FDA Dec/16 Ultimate Body–Tox is voluntarily recalling all lots of **Ultimate Body Tox PRO** capsules to the consumer level. FDA analyses of this product found it to contain undeclared sibutramine.
FDA Dec/16 laboratory analysis confirmed that **Triple Green Capsules, Rhino 9 Premium 3500, Rhino 8 Platinum 8000, Rhino 7K 9000 Male Performance Booster, Duramaxxx, Rhino 5 1500, Lang Yi Hao, Bl4ck 4K capsules, Big Penis Male Sexual Stimulant, Power Male Sexual Stimulant, 90° Jiushidu capsules, Black Mamba 2 Premium, Black 3K Plus Male Sexual Enhancement Capsules & African Viagra** contains sildenafil.
FDA Dec/16 laboratory analysis confirmed that **Queen Slimming Soft Gel** contains sibutramine.
FDA Jan/17: **ABX Weight Loss, Ultimate Body Tox** has undeclared sibutramine.
FDA Jan/17: **Accelerator Boost** has undeclared phenolphthalein.
FDA Jan/17: **Results & Zi Su Body Fat Health II** has undeclared sibutramine and phenolphthalein.
FDA Jan/17: **Skinny Bee Diet** has undeclared desmethylsibutramine, sibutramine, and phenolphthalein.
FDA Jan/17: **Supreme Slim 5.7** has undeclared phenolphthalein and sildenafil.
FDA Jan/17: **Ready Man!** Has undeclared sildenafil.
FDA Jan/17: **Side Head Regulator TT Tablet** has high levels of lead.
FDA Jan/17 is warning consumers not to purchase or use **PNC-27**, a product promoted and sold through http://PNC27.com, as a treatment or cure for cancer. An FDA laboratory discovered the bacteria Variovorax paradoxus in a PNC-27 solution sample for inhalation.
FDA Jan/17 announced that its laboratory analysis found inconsistent amounts of **belladonna, a toxic substance, in certain homeopathic teething tablets**, sometimes far exceeding the amount claimed on the label.
FDA Feb/17 laboratory analysis confirmed that **Goldreallas XXX, Goldreallas Original, Ginseng for Reinforcing Kidney, Old Chinese, & Shenjingpian** contains sildenafil.
FDA Feb/17 laboratory analysis confirmed that **Lean Extreme Max, Slimming Plus Advanced, Platinum Weight Solution – Fat Loss Metabolizer & X-treme Beauty Slim** contains sibutramine.
FDA Feb/17 Kingsway Trading Inc. is recalling its 1.06 oz (30g) bottles of "**Well Balance Xanthium & Siler Combo (Bi Yan Pian)"** Batch No. 130401 & Batch No. 150201 because they contain the presence of undeclared Ephedra Herba (ma huang), an FDA banned item.
FDA Mar/17 laboratory analysis confirmed that **Arouse-Plus** contains tadalafil.
FDA Mar/17 laboratory analysis confirmed that **Bazook Bullet** contains aminotadalafil.
FDA Mar/17 **A&H Focal Inc**. is voluntarily recalling all lots marketed as dietary supplements for male sexual enhancement from January 2014 to present. These products have been historically tested by the FDA and found to contain PDE-5 Inhibitors (i.e.sildenafil, tadalafil, vardenafil, etc.).
FDA Mar/17: Regeneca Worldwide, a division of VivaCeuticals, Inc. is conducting a nationwide recall of its entire line of herbal and dietary supplement products pursuant to a Consent Decree entered by the federal court for the Central District of California. This recall applies to all products manufactured and sold between June 1, 2011 and February 8, 2017. These products include, but are not limited to **RegeneSlim, RegenErect, RegeneArouse**, **RegeneBlend, RegeneBoost, RegeneBlast, and RegeneFit**.
FDA Mar/17 analyzed samples of La Bri's Body Health Atomic and found it to contain the undeclared ingredient sibutramine.
FDA Apr/17 Organic Herbal Supply Supplement Products: Recall - undeclared Drug Ingredients: **Including Uproar, Cummor, Zrect, LabidaMAX, Monkey Business, Xrect, Rectalis, Tornado, Zdaily, BigNHard, Enhancerol Natural Male Enhancement capsules**- found the products to contain Tadalafil.
FDA May/17 laboratory analysis confirmed that **Big N Hard** contains tadalafil.
FDA May/17 laboratory analysis confirmed that **Cummor & Monkey Business** contains N-desmethyl tadalafil.
FDA May/17 laboratory analysis confirmed that **Xrect** contains tadalafil and descarbonsildenafil.
FDA May/17 laboratory analysis confirmed that **Tornado** contains nortadalafil.
FDA May/17 laboratory analysis confirmed that **Z Daily** contains homosildenafil.
FDA May/17 Genetic Edge Compounds recalled all lot codes of **GEC Laxoplex dietary supplement** capsules distributed between February 2, 2015- May 2, 2017 to the retail level and consumer level. FDA analysis found GEC Laxoplex to be tainted with anabolic steroids and steroid like substances
FDA May/17: Dynamic Technical Formulations LLC. is voluntarily recalling all lots of **Tri-Ton**. This product was sold in 90 count bottles as a dietary supplement and includes all lot number and expiration dates of the product. FDA lab analysis of Tri-Ton was found to contain andarine and ostarine which are selective androgen receptor modulators (SARMs) that are considered unapproved drugs and anabolic steroid-like substances.
FDA May/17: MusclMasster, LLC is recalling all bottles of **Al-Er-G Capsules**. During a recent FDA inspection, it was discovered that this product contained Ephedra Herb, an FDA banned ingredient.

FDA May/17 Caverflo.com is voluntarily recalling all lots of **Caverflo Natural Herbal Coffee**, 25 grams to the consumer level. FDA laboratory analysis confirmed the presence of Sildenafil and Tadalafil.
FDA Jun/17: FDA posted warning letters to Flex Fitness/Big Dan's Fitness, AndroPharm, and Hardcore Formulations for illegally marketed products labeled to contain steroid and steroid-like substances and promoted to increase muscle mass and strength.
FDA Jun/17 laboratory analysis confirmed that **XXX Zone Platinum & Triple Premium Zen Gold 1300mg** contains sildenafil, tadalafil and dapoxetine.
FDA Jun/17 laboratory analysis confirmed that **Triple X 2000** contains tadalafil and dapoxetine.
FDA Jun/17 laboratory analysis confirmed that **Macho Man 3000, Monster X 1350, Royal Master, & Love Zen 3000** contains tadalafil.
FDA Jun/17 laboratory analysis confirmed that **Own the Knight 1750** contains tadalafil and dapoxetine.
FDA Jun/17 laboratory analysis confirmed that **Xzone Gold, Super Panther 7K & Triple Miracle Zen Plus 1200mg** contains sildenafil and tadalafil.
FDA Jun/17 laboratory analysis confirmed that **Man of Steel 2 & Man of Steel** contains sildenafil.
FDA Jul/17: Hardcore Formulations is voluntarily recalling all lots and expiration dates of **Ultra-Sten and D-Zine capsules** to the consumer level. These products are labeled to contain methylstenbolone (Ultra-Sten) and dymethazine (D-Zine), which are considered to be derivatives of anabolic steroids.
FDA Jul/17: Andropharm is voluntarily recalling all lots of **Sten Z and M1 Alpha capsules** to the consumer level because these products contain derivatives of anabolic steroids rendering them unapproved drugs for which safety and efficacy have not been established and therefore subject to recall.
FDA Jul/17 laboratory analysis confirmed that **Kingdom Honey for Her, Kingdom Honey for Him, & Royal Honey VIP** contains tadalafil.
FDA Jul/17 laboratory analysis confirmed that **Rhino 7 Platinum 5000** contains sildenafil.
FDA Jul/17: **EZ Weight Loss TX** is voluntarily recalling all lots of **La Bri's Body Health Atomic and Xplode capsules** to the consumer level since it was tainted with sibutramine.
FDA Jul/17:**Bestherbs Coffee LLC** is voluntarily recalling all lots of **New of Kopi Jantan Tradisional Natural Herbs Coffee**, 13 grams to the consumer level. FDA laboratory analysis confirmed the presence of desmethyl carbodenafil.
FDA Aug/17: warning parents and caregivers not to use "**Balguti Kesaria (or Kesaria Balguti) Ayurvedic Medicine**" due to the risk of lead poisoning.
FDA Aug/17: Man of Steel is voluntarily recalling 175 lots of **Man of Steel 1 and Man of Steel 2**, 4000mg at the retail level. The products have been found to contained undeclared Sildenafil.
FDA Aug/17: warning consumers not to drink **Longjack Coffee**, in addition to other instant coffee products that have been recalled recently – **Kopi Jantan Tradisional Natural Herbs Coffee, CaverFlo Coffee, and AMPT Coffee**. These products are made in Malaysia, and promoted and sold online for sexual enhancement. These products are labeled to contain instant coffee, non-dairy creamer, and other ingredients. However, FDA laboratory analysis confirmed: **CaverFlo Coffee and AMPT Coffee** contain undeclared sildenafil and tadalafil; **Longjack Coffee and Kopi Jantan Tradisional Natural Herbs Coffee** contain undeclared desmethyl carbodenafil, an analogue of sildenafil; and All of these products contain undeclared milk.
FDA Aug/17: Centurion Labs is voluntarily recalling 1 lot of **Ninjacof** (Lot# 200N1601) and 1 lot of **Ninjacof A** (Lot# 201NA1601) manufactured by Vilvet and distributed by Centurion Labs to the retail level due to potential contamination with Burkholderia cepacia.
FDA Aug/17 laboratory analysis confirmed that **Physic Candy – Curve & Physic Candy-Define** contains sibutramine.
FDA Sep/17: **Rhino 7, Papa Zen, Fifty Shades, and Grande X Dietary Supplements** by Gadget Island: Recall - Undeclared Drug Ingredients.The products have been found to contain undeclared Active Pharmaceutical Ingredients sildenafil, desmethyl carbodenafil and tadalafil.
FDA Sep/17: Natures Supplement, Inc. is voluntarily recalling 260 bottles of **Vegetable Vigra**, 200 mg capsules to the consumer level. FDA analysis found this product to be tainted with Sidenafil.
FDA Oct/17 laboratory analysis confirmed that **A1 Slim** contains sibutramine and phenolphthalein.
FDA Oct/17 laboratory analysis confirmed that **Tiger 5000** contains sildenafil and tadalafil.
FDA Oct/17 is reminding people to keep the **black licorice** in check. Eating 2 oz. a day for 2 weeks or more could lead to a cardiac arrhythmia in adults aged 40 and older. Glycyrrhizin, which comes from licorice root, can lead to a drop in potassium levels, the agency says. This, in turn, can result in arrhythmia, hypertension, edema, lethargy, and congestive heart failure.
FDA Oct/17 laboratory analysis confirmed that **Linsen Double Caulis Plus** (靈仙双藤素) contains dexamethasone.
FDA Nov/17 laboratory analysis confirmed that **Hard Times for Men** contains sildenafil.
FDA Nov/17 said it is aware of 36 deaths involving products made with **kratom** and hundreds of calls to poison control centers, which increased tenfold between 2010 and 2015. The FDA banned its importation in 2014, but in the years since, the agency has seized large amounts of kratom-containing dietary supplements.
FDA Nov/17 is investigating serious adverse events involving **Limbrel (flavocoxid),** a product in capsule form currently being marketed as a medical food to manage the metabolic processes associated with osteoarthritis. While a range of adverse events have been reported, two serious and potentially life-threatening medical conditions are among them: drug-induced liver injury and hypersensitivity pneumonitis.
FDA Dec/17 laboratory analysis confirmed that **Chao Jimengnan** contains sildenafil.
FDA Dec/17: Nutra Labs Inc. is voluntarily recalling lots sold by their firm of the male enhancement supplements **Bull 1800 mg Capsules** with the production date of 05/08/2016, and **Chao Jimengnan** 150 mg Tablets with Lot # 20151018 to the consumer level. FDA analysis found the products to be tainted with sildenafil, 0.026mg/capsule for Bull, and 70.46mg/tablet for Chao Jimengnan respectively.
FDA Dec/17: Marmex Corp is voluntarily recalling all lots of **Blue Pearl All Natural Male Enhancement Supplement**, 500mg to the consumer level. FDA analysis has found the products to contain sildenafil.
FDA Jan/18: **Flawless Beauty**, LLC is voluntarily recalling all lots of nineteen different products sold individually or as part of multi-unit kits alleged by the U.S. Food and Drug Administration ("FDA") to be misbranded or unapproved new drugs pursuant to the Federal Food, Drug, and Cosmetic Act. The FDA believes that these drugs present serious public health risks. All products were sold and distributed over the Internet to U.S. and foreign customers. All glutathione products were sold in multi-vial whitening kits, either alone or in combination with ampules of vitamin C and sterile water. Vials or ampules of vitamin C or sterile water purchased separately or as part of these whitening kits are also recalled.
FDA Jan/18: Arthri-D is recalling its Dietary Supplement "**Arthri-D 120ct**" Lot#1701-092 because it may be contaminated with Salmonella.
FDA Jan/18: Break Ventures/California Basics is recalling its Dietary Supplement "**Zero for Him 150ct**" Lot# 1710-638 because it may be contaminated with Salmonella.
FDA Mar/18: Bella All Natural is voluntarily recalling its **Diet Capsules labeled as Bella**, Lot Number MFD:10.15.2017 EXP: 10.14.2019, to the consumer level. This recall has been initiated due to presence of sibutramine.
FDA Mar/18:PDX Aromatics of Portland, Oregon DBA Kraken Kratom, Phytoextractum, and Soul Speciosa, has initiated a recall of certain **kratom-containing powder products** because it has the potential to be contaminated with Salmonella.
FDA Mar/18: Tamarack is voluntarily recalling Eclipse **Kratom-containing** powder products because it has the potential to be contaminated with Salmonella.
FDA Apr/18: issued a mandatory recall order for all food products containing powdered **kratom** manufactured, processed, packed, or held by Triangle Pharmanaturals LLC, after several were found to contain salmonella.
FDA Mar/18: laboratory analysis confirmed that **Black Lion Pill** contains sildenafil.
FDA Mar/18: laboratory analysis confirmed that **Red Zone Xtreme 3000 & Rhino 69 Extreme 50000** contains tadalafil.
FDA Apr/18: Club 13 is recalling **Maeng Da Red kratom powder**, since these products have the potential to be contaminated with Salmonella.
FDA Apr/18: Overland Park, KS, Epic Products, LLC is voluntarily recalling all lots of **Euphoric capsules**, packaged in 1 count blister cards, 3 count bottles, and 12 count bottles to the consumer level. FDA analysis found samples of Euphoric to be tainted with undeclared sildenafil and tadalafil,
FDA Apr/18: AMA Wholesale Inc. (Distributor/Re-seller), is voluntarily recalling **Rhino 69 Extreme 50000** capsules to the consumer level. FDA analysis found the product to be tainted with undeclared tadalafil.
FDA Apr/18: Viable Solutions of Nampa, ID has initiated a recall of certain **Kratom-containing powder products**, because it has the potential to be contaminated with Salmonella.
FDA Apr/18: NGB Corp. of West Jordan, Utah is voluntarily recalling **NxtGen Botanicals Maeng Da Kratom** labeled bottles of encapsulated product because it has the potential to be contaminated with Salmonella
FDA May/18: MBI Distributing, Inc. is voluntarily recalling all lots of homeopathic Teething Drops, Nausea Drops, Intestinal Colic Drops, Stomach Calm, Expectorant Cough Syrup, Silver-Zinc Throat Spray, and Argentum Elixir, within expiry, to the consumer level. The drug products have been found to be manufactured with a lack of adequate controls.
FDA May/18: 7K and Poseidon 4500 by Shoreside Enterprises: Voluntary Recall - Due to Presence of Undeclared Sildenafil and Tadalafil.
FDA May/18: Herb-X Solutions X-Jow Pain Gel is used as an external analgesic and the United Exchange Acne Shave Moisturizer and Acne Shave Shave Cream with Acne. FDA Jun/18: Homeopathic Teething Drops, Nausea Drops, Intestinal Colic Drops, Stomach Calm, Expectorant Cough Syrup, Silver-Zinc Throat Spray, and Argentum Elixir by
FDA Jun/18: **Kratom (mitragyna speciosa**) Powder Products by Gaia Ethnobotanical: Recall - Due to **Potential Salmonella Contamination**
FDA Jul/18: **Blissful Remedies**., is voluntarily **recalling only Lot No.: 112710** with expiration 03/2019 found embedded on the top of package of **kratom (*mitragyn a speciosa*) powder products**, it manufactured, processed, packed, and/or held, between "March 1, 2018" to "April 30, 2018" to the consumer level. The products have been found by the U.S. Food and Drug Administration ("FDA") via sample testing to have **salmonella contamination**.
FDA July/18: laboratory analysis confirmed that **Maximum Powerful contains sildenafil**.
FDA Jul/18: laboratory analysis confirmed that **Grakcu Capsule, C.U. Plus, Dale Mas contains sildenafil and tadalafil**.

FDA Jul/18: laboratory analysis confirmed that **Asunsa contains sibutramine, N-desmethylsibutramine, benzylsibutramine, phenolphthalein and diclofenac**.
FDA July/18: laboratory analysis confirmed that **Lyn DTOX FS3 contains sibutramine and N-desmethylsibutramine**.
FDA Aug/18: is **advising consumers not to purchase or use Nuvitra**, a product promoted for weight loss. This product was identified during an examination of international mail shipments. FDA laboratory analysis confirmed that Nuvitra contains **sibutramine and fluoxetine.**
FDA Aug/18: **laboratory analysis confirmed that XXXPlosion Ultra, Ding Ji Wei Ge, 5K & Panther Power Platinum 11000 contains sildenafil**.
FDA Sep/18: laboratory analysis confirmed that **Extenze Nutritional Supplement, Extenze Plus, PremierZen Gold 4000 contains sildenafil**.
FDA Sep/18: laboratory analysis confirmed that **Slimming Capsule contains sibutramine and phenolphthalein**.
FDA Sep/18: laboratory analysis confirmed that **BodySlim Herbal & Easy 2 Slim contains sibutramine**.
FDA Oct/18: laboratory analysis confirmed that **ProSolution, V-Max, USA for Women, Strong Horses & FX75000 contains sildenafil**.
FDA Oct/18: laboratory analysis confirmed that **Green Lean Body Capsule * Baschi Quick Slimming Capsule contains sibutramine and N-desmethylsibutramine**.
FDA Oct/18: laboratory analysis confirmed that **Shengan Natural Model, Like Slim Coffee & In Shape contains sibutramine**.
FDA Nov/18: Several samples of the **botanical kratom have tested positive for nickel and lead at levels not safe for humans**, according to recent analyses done by the FDA. Some people use kratom, which contains opioids, to self-treat opioid addiction and other conditions. The tests of 26 kratom products were conducted as part of the agency's investigation into a salmonella outbreak associated with kratom. The levels of nickel and lead detected aren't likely to induce heavy metal poisoning from a single use, the FDA said, but they could with chronic use.
FDA Dec/18: **laboratory analysis confirmed that MOB Candy & Willy Go Wild contains sildenafil and tadalafil**.
FDA Jan/19: laboratory analysis confirmed that **The Silver Bullet** contains sildenafil and tadalafil.
FDA Jan/19: laboratory analysis confirmed that **Slimina** contains sibutramine.
FDA Jan/19: laboratory analysis confirmed that **GoLean Detox & Slimmer Extreme Thermogenic Formula** contains sibutramine and phenolphthalein.
FDA Jan/19: laboratory analysis confirmed that **Ultra Fit, 1 Day Diet** contains sibutramine and N-desmethylsibutramine.
FDA Jan/19: laboratory analysis confirmed that **Red Stallion Extra Strong** contains tadalafil.
FDA Jan/19: laboratory analysis confirmed that **Natural V=GRA, Yong Gang, Silver Bullet 10x & Black King Kong** contains sildenafil and tadalafil.
FDA Jan/19: laboratory analysis confirmed that **Golden Ant, Instinct Best Sexual Enjoyment & Nectar Del Amor** contains sildenafil.
FDA Jan/19: laboratory analysis confirmed that **Slim Bio Capsules** contain sibutramine, N-desmethylsibutramine, sildenafil, tadalafil, benproperine and diphenhydramine.
FDA Feb/19: **GoLean Detox Capsules** by GoLean Detox USA: Recall - Due to Presence of Undeclared Sibutramine and Phenolphthalein.
FDA Mar/19**:** Select **Kratom Products** by Sunstone Organics: Recall - Due to Potential Contamination by Salmonella.
FDA Apr/19: **Aphrodisiac Capsules** by SD Import: Recall - Due to Presence of Undeclared Sildenafil.
FDA Apr/19: **BLUEFUSION Capsules** by Ata Int.: Recall - Due to Presence of Undeclared Sildenafil, Tadalafil, Desmethyl Carbodenafil, Dithiodesmethyl Carbodenafil, Scutellarin and Daidzein
FDA May/19: The **Beast Capsules by STIFF BOY**: Recall - Due to Presence of Undeclared Sildenafil
FDA May/19: laboratory analysis confirmed that **Man Fuel Shooter (Tropical Fruit Flavor) contains tadalafil and desmethyl carbodenafil**.
FDA May/19: laboratory analysis confirmed that **Man Fuel Xtreme Edition contains sildenafil, dithiodesmethyl carbodenafil and desmethyl carbodenafil**.
FDA Jun/19: laboratory analysis confirmed that **Peru Maca & Germany Black Gorilla** contains sildenafil.
FDA Jun/19: laboratory analysis confirmed that **Adelgasin Plus, Lishou Fuling Jiaonang & Absolute Nine Slim** contains sibutramine and N-desmethyl sibutramine.
FDA Jun/19: laboratory analysis confirmed that **Super Slimming Herb & Detoxi Slim** contains sibutramine.
Fish Oil Testing: Independent test for contaminants Nutrasource Diagnostics at the University of Guelp www.nutrasource.ca/ifos_new
Fisher P, Ernst E. Should doctors recommend **homeopathy**? BMJ. 2015 Jul 14;351:h3735.

Fleshner N, Harvey M, et al. Evidence for contamination of herbal **erectile dysfunction** products with phosphodiesterase type 5 inhibitors. J Urology 2005; 174:636-41.(InfoPOEMs: At least some natural products marketed for the treatment of erectile dysfunction are adulterated with phosphodiesterase type 5 inhibitors. Many of these products claim to be free of adverse effects but in truth may be potentially fatal to patients concomitantly using nitrates. (LOE = 4)) Two of 7 products (Super-X and Stamina-RX) contained significant amounts of **sildenafil** (Viagra, 30 mg) and tadalafil (Cialis, 20 mg), respectively.
Fox RJ. Complementary and alternative medicine in **multiple sclerosis**. Neurology. 2014 Mar 25;82(12):e103-7.
Fransen M, Agaliotis M, Nairn L, et al. **Glucosamine and chondroitin** for knee osteoarthritis: a double-blind randomised placebo-controlled clinical trial evaluating single and combination regimens. Ann Rheum Dis. 2014 Jan 6.
Freeman MP, Mischoulon D, Tedeschini E, et al. **Complementary and alternative medicine for major depressive** disorder: a meta-analysis of patient characteristics, placebo-response rates, and treatment outcomes relative to standard antidepressants. J Clin Psychiatry. 2010 Jun;71(6):682-8. Participants in CAM trials were more likely to be female and to have a lower placebo-response rate compared to those in standard antidepressant trials for MDD. Trials of standard antidepressants and CAM therapies were composed of patients with similar depression severity.
Fried MW, Navarro VJ, Afdhal N, et al; Silymarin in NASH and C Hepatitis (SyNCH) Study Group. Effect of **silymarin (milk thistle)** on liver disease in patients with chronic hepatitis C unsuccessfully treated with interferon therapy: a randomized controlled trial. JAMA. 2012 Jul 18;308(3):274-82.
Gabay C, Medinger-Sadowski C, Gascon D, et al. Symptomatic effect of **chondroitin sulfate 4&6** in hand osteoarthritis the finger osteoarthritis chondroitin treatment study (FACTS). Arthritis Rheum. 2011 Sep 6.
Gagnier JJ, van Tulder MW, Berman B, Bombardier C. Herbal medicine for low back pain: a Cochrane review. Spine. 2007 Jan 1;32(1):82-92. **Harpagophytum procumbens, Salix alba, and Capsicum** frutescens seem to reduce pain more than placebo. Additional trials testing these herbal medicines against standard treatments will clarify their equivalence in terms of efficacy. The quality of reporting in these trials was generally poor; thus, trialists should refer to the CONSORT statement in reporting clinical trials of herbal medicines. (InfoPOEMs: If these authors have included all the relevant studies, it appears that there is modest evidence that herbal remedies (oral Harpagophytum procumbens [devil's claw] and Salix alba [white willow bark], as well as topical Capsicum frutescens [cayenne]) alleviate acute episodes of chronic nonspecific low back pain in adults. In general, the reporting of the trials included in this systematic review was poor. Finally, this body of literature is prone to bias in favor of publishing positive results. (LOE = 1a-)) See also Cochrane Database Syst Rev. 2006 Apr 19;(2):CD004504.
Gagnier JJ, Oltean H, van Tulder MW, et al. **Herbal Medicine for Low Back Pain**: A Cochrane Review. Spine (Phila Pa 1976). 2016 Jan;41(2):116-33. The body of evidence of the effectiveness of herbal products in the treatment of low back pain is limited to a handful of small studies. Topical capsicum (cayenne), which has been studied most frequently, appears to be more effective than placebo in relieving pain. (LOE = 1a-)
Gardiner P, Phillips R et al. Herbal and Dietary Supplement- **Drug Interactions in Patients with Chronic Illnesses**. Am Fam Physician. 2008;77 (1):73-78.
Gardiner P, et al. Factors associated with dietary **supplement use** among prescription medication users. Arch Intern Med. 2006 Oct 9;166(18):1968-74. One in 4 prescription medication users took an NVDS in the prior 12 months, yet the majority did not share this with a conventional medical professional.
Gardner CD, Lawson LD, Block E, et al. Effect of raw garlic versus commercial **garlic** supplements on plasma lipid concentrations in adults with moderate hypercholesterolemia. Arch Int Med 2007; 167:346-353. None of the forms of garlic used in this study, including raw garlic, when given at an approximate dose of a 4-g clove per day, 6 d/wk for 6 months, had statistically or clinically significant effects on LDL-C or other plasma lipid concentrations in adults with moderate hypercholesterolemia.
Garg AX, Devereaux PJ, Hill A, et al;Curcumin AAA AKI Investigators. Oral **curcumin in elective abdominal aortic aneurysm repair**: a multicentre randomized controlled trial. CMAJ. 2018 Oct 29;190(43):E1273-E1280.
Gastpar M, et al. Comparative Efficacy and Safety of a Once-Daily Dosage of **Hypericum** Extract STW3-VI and Citalopram in Patients with Moderate Depression: A Double-Blind, Randomised, Multicentre, Placebo-Controlled Study.Pharmacopsychiatry. 2006 Mar;39(2):66-75.
Geller SE, Shulman LP, van Breemen RB, et al. Safety and efficacy of **black cohosh** and red clover for the management of vasomotor symptoms: a randomized controlled trial. Menopause 2009;16:1156–66.
Genazzani AR et al. Effect of 1-year, low-dose **DHEA** therapy (10mg daily) on climacteric symptoms and female sexuality. Climacteric. 2011 Dec;14(6):661-8.

Geng J, Dong J, Ni H, et al. Ginseng for cognition. Cochrane Database of Systematic Reviews 2010, Issue 12. Art. No.: CD007769. DOI: 10.1002/14651858.CD007769.pub2. Currently, there is a lack of convincing evidence to show a cognitive enhancing effect of Panax ginseng in healthy participants and no high quality evidence about its efficacy in patients with dementia. Randomized, double-blind, placebo-controlled, parallel group trials with large sample sizes are needed to further investigate the effect of ginseng on cognition in different populations, including dementia patients.

Genistein: Atteritano M, Marini H, Minutoli L, et al. Effects of the phytoestrogen genistein on some predictors of cardiovascular risk in osteopenic, postmenopausal women: a two-year randomized, double-blind, placebo-controlled study. J Clin Endocrinol Metab. 2007 Aug;92(8):3068-75. Epub 2007 May 22. These results suggest that 54mg genistein plus calcium, vitamin D(3), and a healthy diet was associated with favorable effects on both glycemic control and some cardiovascular risk markers in a cohort of osteopenic, postmenopausal women. D'Anna R, Cannata ML, Atteritano M, et al. Effects of the phytoestrogen genistein on hot flushes, endometrium, and vaginal epithelium in postmenopausal women: a 1-year randomized, double-blind, placebo-controlled study. Menopause. 2007 Jul-Aug;14(4):648-55. The phytoestrogen genistein has been shown to be effective on vasomotor symptoms without an adverse effect on endometrium. Marini H, Minutoli L, Polito F, et al. Effects of the phytoestrogen genistein on bone metabolism in osteopenic postmenopausal women: a randomized trial. Ann Intern Med. 2007 Jun 19;146(12):839-47. Summary for patients in: Ann Intern Med. 2007 Jun 19;146(12):I34. Twenty-four months of tx with genistein has positive effects on BMD in osteopenic postmenopausal women.

Gershman K, Timm K, Frank M, et al. Deaths in Colorado Attributed to **Kratom**. N Engl J Med. 2019 Jan 3;380(1):97-98.

Gertsch JH, Basnyat B, et al. Randomised, double blind, placebo controlled comparison of **ginkgo biloba** and acetazolamide for prevention of acute mountain sickness among Himalayan trekkers: the prevention of high altitude illness trial (PHAIT). BMJ. 2004 Apr 3;328(7443):797. Epub 2004 Mar 11.

Goey AK, Meijerman I, Rosing H, et al. The effect of **Echinacea purpurea on the pharmacokinetics of docetaxel**. Br J Clin Pharmacol. 2013 May 23.

Gökmen MR, Lord GM. **Aristolochic** acid nephropathy. BMJ. 2012 Jun 15;344:e4000.

Gökmen MR, Cosyns JP, Arlt VM, et al. The epidemiology,diagnosis, and management of **aristolochic Acid nephropathy**: a narrative review. Ann Intern Med. 2013 Mar 19;158(6):469-77.

Goldbach-Mansky R., et al. Comparison of **Tripterygium wilfordii** Hook F Versus Sulfasalazine in the Treatment of Rheumatoid Arthritis: A Randomized Trial. Ann Intern Med 2009; 229-240.

Goldberg DS, Forde KA, Carbonari DM, et al. Population-representative Incidence of **Drug-induced Acute Liver Failure** Based on an Analysis of an Integrated Healthcare System. Gastroenterology. 2015 Feb 27. pii: S0016-5085(15)00299-1. (**acetaminophen, herbal, antimicrobial** etc.)

Gommans YMM, Runhaar J, Jacobs ML, Bierma-Zeinstra SMA. The Effect of Prolonged **Glucosamine** Usage on HbA1c Levels and New-Onset Diabetes Mellitus in Overweight and Obese Middle-Aged Women. Am J Med. 2017 Jun;130(6):731-737.e6.

Gordon RY.; Cooperman T; Obermeyer W; et al. Marked Variability of Monacolin Levels in Commercial **Red Yeast Rice** Products: Buyer Beware! Arch Intern Med. 2010;170(19):1722-1727.

Grant SJ, Bensoussan A, Chang D, Kiat H, Klupp NL, Liu JP, Li X. Chinese herbal medicines for people with **impaired glucose tolerance or impaired fasting blood glucose**. Cochrane Database Syst Rev. 2009 Oct 7;(4):CD006690. The positive evidence in favour of Chinese herbal medicines for the treatment of IGT or IFG is constrained by the following factors: lack of trials that tested the same herbal medicine, lack of details on co-interventions, unclear methods of randomisation, poor reporting and other risks of bias.

Greco A et al. Acute hepatitis caused by a **natural lipid-lowering** product: when "alternative" medicine is no "alternative" at all. J Hepatology 2009; 50:1273.

Gregory P. Availability of **DMAA Supplements** (Jack3d, OxyELITE Pro,…) Despite US Food and Drug Administration Action. Arch Intern Med. 2012 Dec 3:1-2.

Grim CCA, Meynaar IA, Hammer S, et al. **Severe Hyponatremia After Drinking Horsetail Juice**. Ann Intern Med. 2018 May 29.

Grossman E, et al. **Melatonin** reduces night blood pressure in patients with nocturnal hypertension. Am J Med. 2006 Oct;119(10):898-902. n=38 4weeks

Guo R, Canter PH, Ernst E. A systematic review of randomised clinical trials of individualised herbal medicine in any indication. Postgrad Med J. 2007 Oct;83(984):633-7. There is a sparsity of evidence regarding the effectiveness of individualised herbal medicine & **no convincing evidence to support the use of individualised herbal medicine in any indication**.

Gunton JE, Cheung NW, et al. **Chromium** Supplementation Does Not Improve Glucose Tolerance, Insulin Sensitivity, or Lipid Profile: A randomized, placebo-controlled, double-blind trial of supplementation in subjects with impaired glucose tolerance. Diabetes Care. 2005 Mar;28(3):712-3.

Hadley S, Petry JJ. **Valerian**. Am Fam Physician. 2003 Apr 15;67(8):1755-8.

Haebich G, Katugampola R. **Phytophotodermatitis** triggered by **parsnips**. BMJ. 2017 Jun 15;357:j2383.

Hao, Jiang, Cheng, et al. **Traditional Chinese Medicine for Cardiovascular Disease**-Evidence and Potential Mechanisms. JACC. June 20, 2017;69(24):2952-66.

Harel Z, Harel S, Wald R, Mamdani M, Bell CM. The Frequency and Characteristics of **Dietary Supplement Recalls in the United States**. JAMA Intern Med. 2013 Apr 15:1-3.

Health Canada is warning consumers: Jan/06 African herbal products **M2 Formula** & **Energy 2000** pose potential health risks http://www.hc-sc.gc.ca/ahc-asc/media/advisories-avis/2006/2006_01_e.html

Health Canada is warning Aril/06 consumers not to not to use advises consumers not to use unauthorized products containing **anabolic steroids** (Five products containing illegal anabolic steroids, as they can potentially cause serious health issues such as liver disorders and heart problems. The five products are: Anabolic Xtreme Superdrol, Methyl-1-P, Ergomax LMG, Prostanozoland, and FiniGenX Magnum Liquid.)

Health Canada is warning consumers not to not to use **Kaizen Ephedrine HCL tablets for weight loss Dec/05** http://www.hc-sc.gc.ca/ahc-asc/media/advisories-avis/2005/2005_138_e.html

Health Canada is warning consumers not to ingest the herb **chaparral** in the form of loose leaves, teas, capsules or bulk herbal products because of the risk of liver and kidney problems. Dec/05 http://www.hc-sc.gc.ca/ahc-asc/media/advisories-avis/2005/2005_135_e.html

Health Canada is warning consumers not to use certain **Ayurvedic medicinal** products because they contain high levels of heavy metals such as lead, mercury and/or arsenic. July/05 http://www.hc-sc.gc.ca/english/protection/warnings/2005/2005_80.html

Health Canada Jan/06 Natural health product **Libidfit** may pose health risks (promoted for sexual enhancement and erectile dysfunction, but contains an undeclared amount of a pharmaceutical ingredient similar to sildenafil) http://www.hc-sc.gc.ca/ahc-asc/media/advisories-avis/2006/2006_02_e.html

Health Canada is warning consumers Feb/06: Not to use the Chinese medicinal product White Peony Scar-repairing pills, manufactured in Hong Kong by White Peony Pharmaceuticals Limited, due to high levels of lead. http://www.hc-sc.gc.ca/ahc-asc/media/advisories-avis/2006/2006_05_e.html

Health Canada is warning consumers Feb/06 not to use 13 Chinese herbal products manufactured by the Hong Kong Chi Chun Tang Herbal Factory due to bacterial contamination that could lead to serious health risks. http://www.hc-sc.gc.ca/ahc-asc/media/advisories-avis/2006/2006_08_e.html

Health Canada advises consumers April/06 not to use Super Fat Burning and LiDa Daidaihua Slimming Capsules for weight loss because they have been found to contain sibutramine http://www.hc-sc.gc.ca/ahc-asc/media/advisories-avis/2006/2006_15_e.html

Health Canada is advising consumers Apr/06 not to use unapproved products containing **yohimbine or yohimbe bark**, including Strauss Energy SIX capsules. Yohimbine is a prescription substance that can pose serious health risks for people with underlying risk factors. http://www.hc-sc.gc.ca/ahc-asc/media/advisories-avis/2006/2006_16_e.html

Health Canada is advising consumers Apr/06 not to use unapproved Miracle Bion products as it could be contaminated with bacteria such as *E. coli*. http://www.hc-sc.gc.ca/ahc-asc/media/advisories-avis/2006/2006_23_e.html

Health Canada May/06 is warning consumers not to use the product **Nasutra** because it has been found to contain the sildenafil (chemical name for Viagra) that could lead to serious health risks, especially for patients with existing medical conditions such as heart problems, those who may be taking heart medications, or those who may be at risk for strokes.

Health Canada May/06 is advising consumers not to use Ocean Plasma **Isotonic Living Water and Ocean Plasma Hypertonic Living Water** because they are unapproved products that contain unacceptable amounts of aerobic bacteria.

Health Canada June/06 is advising consumers not to use four unapproved **Ayurvedic medicinal products** from India because they contain high levels of lead and/or mercury. http://www.hc-sc.gc.ca/ahc-asc/media/advisories-avis/2006/2006_46_e.html

Health Canada July/06 is advising Fat Rapid Loss Capsules (Xin Yan Zi Pai Mei Zi Jiao Nang) because may contain sibutramine http://www.hc-sc.gc.ca/ahc-asc/media/advisories-avis/2006/2006_55_e.html

Health Canada July/06 is advising consumers not to use 4 foreign health products due to concerns about possible side-effects: **Zhuifeng Tougu Wan** & **Fufang LuHui Jiaonang**, two traditional Chinese medicines that contain toxic levels of mercury; **Safi**, a herbal product manufactured in India and Pakistan that contains toxic levels of arsenic; and **Baike Wan**, a herbal product from Malaysia that contains the prescription drugs piroxicam and frusemide, and the over-the- counter drug chlorpheniramine.

Health Canada Aug/06 is advising consumers not to use **Salt Spring Herbals Sleep Well Dietary Supplement** because a sample has been found to contain **estazolam.**

Health Canada Warns Consumers August 04, 2006 Not To Use **Neophase** Formula For Men Due To Potential Health Risks which has been found to contain an undeclared ingredient similar to the active pharmaceutical ingredient found in Viagra. http://www.hc-sc.gc.ca/ahc-asc/media/advisories-avis/2006/2006_67_e.html

Health Canada Aug/06 is reminding consumers not to use Miracle II Miracle Neutralizer or any other products exported or sold by Tedco, Inc. of Louisiana because they could contain harmful bacteria. http://www.hc-sc.gc.ca/ahc-asc/media/advisories-avis/2006/2006_68_e.html

Health Canada Aug/06 is advising consumers about a possible link between health products containing the herbal medicine **black cohosh and liver damage**. There have been a number of international case reports of liver damage suspected to be associated with the use of black cohosh, including three case reports in Canada and one published case of death in the United States. http://www.hc-sc.gc.ca/ahc-asc/media/advisories-avis/2006/2006_72_e.html

Health Canada Aug/06 is advising consumers not to use four foreign health products due to concerns about possible side-effects: **Reduce Weight**, a proprietary Chinese Medicine marketed as a weight-loss product. Contains the prescription drug sibutramine (the generic name for Meridia) **Yixinjiaonang**, a proprietary Chinese medicine marketed as a sexual enhancement & erectile dysfunction product, contains the prescription drug tadalafil (the generic name for Cialis) **Meng Rong**, a proprietary Chinese medicine marketed as a sexual enhancement and erectile dysfunction product, contains the prescription drug sildenafil (the generic name for Viagra) **VG**, a proprietary Chinese medicine marketed as a sexual enhancement and erectile dysfunction product, contains the prescription drug sildenafil (the generic name for Viagra) http://www.hc-sc.gc.ca/ahc-asc/media/advisories-avis/fpa-ape/index_e.html

Health Canada Aug/06 is advising consumers not to use **Salt Spring Herbals Sleep Well** Dietary Supplement because a sample analyzed by Health Canada has been found to contain the undeclared drug Estazolam. http://www.hc-sc.gc.ca/ahc-asc/media/advisories-avis/2006/2006_82_e.html

Health Canada Aug/06 is advising consumers not to use two foreign health products due to concerns about possible side-effects: **Chao Nongsu Qingzhi Jiaonang** (OPC Care) is promoted as a weight-loss product. The product is adulterated with sibutramine and mazindol, two prescription medications used to suppress appetite. **Conting Qianweisu Slimming Herbs** Capsule is marketed as a weight-loss product. The product is adulterated with sibutramine, a prescription medication used to suppress appetite. http://www.hc-sc.gc.ca/ahc-asc/media/advisories-avis/fpa-ape/2006/2006_84_e.html http://www.hc-sc.gc.ca/ahc-asc/media/advisories-avis/fpa-ape/2006/2006_83_e.html

Health Canada Sept/06 advises against use of the **Ayurvedic medicinal product Jambrulin** due to lead content http://www.hc-sc.gc.ca/ahc-asc/media/advisories-avis/2006/2006_89_e.html

Health Canada Sept/06 is warning consumers not to use the natural health product **Libidus** because it contains an undeclared pharmaceutical ingredient, a modified form of vardenafil.

Health Canada Oct/06 is advising consumers not to use the unauthorized natural health products **Emperor's Tea Pill (Tian Huang Bu Xin Wan)** and **Hepatico Extract (Shu Gan Wan)** because certain lots of these products contain high levels of lead and mercury. http://www.hc-sc.gc.ca/ahc-asc/media/advisories-avis/2006/2006_98_e.html

Heath Canada Nov/ 06 is warning Canadians not to use the unauthorized product **Embrun de mer** promoted for the treatment of skin irritation in newborns and adults because it contains unacceptable amounts of harmful bacteria.

Health Canada Dec/06 is advising consumers not to use a product called **Eden Herbal Formulations Sleep Ease Dietary Supplement**, because it was found to contain an undeclared drug estazolam http://www.hc-sc.gc.ca/ahc-asc/media/advisories-avis/2006/2006_127_e.html

Health Canada Dec/06 is advising consumers not to use two foreign health products due to concerns about possible side-effects: **Slim & Detox Peptide**, which are weight-loss products. Containing the prescription drug sibutramine (the generic name for Meridia) http://www.hc-sc.gc.ca/ahc-asc/media/advisories-avis/fpa-ape/index_e.html

Health Canada Jan/07 is advising consumers not to use **Kang Da** and **four unlabelled products** are marketed as herbal sexual enhancements and treatments for erectile dysfunction. The products are adulterated with a prescription medication used in the treatment of sexual dysfunction. **Qing Zhi** and one unlabelled product are marketed as herbal weight-loss products. The products are adulterated with sibutramine, a prescription medication used to suppress appetite.

Health Canada Feb/07 is advising consumers not to use a product called **Sleepees**, because it was found to contain an undeclared drug **estazolam**, which can be habit-forming when used for as little as a few months. http://www.hc-sc.gc.ca/ahc-asc/media/advisories-avis/2007/2007_16_e.html

Health Canada Feb/07 is updating Canadians about adverse reaction reports it has received concerning the use of **EMPowerplus**, a vitamin mineral supplement, for serious medical conditions. Health Canada has received nine case reports of serious adverse reactions associated with the use of EMPowerplus. Most of the adverse reactions relate to worsening of psychiatric symptoms in those patients with serious underlying mental health problems, such as bipolar disorder and depression.

Health Canada Feb/07 is advising consumers not to use the following product listed in the table below due to concerns about possible side-effects. More info **Power 58; Platinum Power 58; Ehanix; Jolex; Onyo; Deguozonghengtianxia** because they contained acetildenafil. Acetildenafil is an analogue of sildenafil, a prescription medication indicated for treatment of erectile dysfunction.

Health Canada Mar/07 is Health Canada is advising consumers not to use **MIAOZI Slimming Capsules** because they have been found to contain sibutramine, a prescription medication that should only be taken under medical supervision.

Health Canada Mar/07 is warning consumers not to use the unauthorized natural health product **XOX For Men**, because it contains an undeclared pharmaceutical ingredient, tadalafil, an ingredient found in the prescription drug Cialis. The use of XOX For Men could pose serious health risks, especially for patients with existing medical conditions such as heart problems, those taking heart medication, or those at risk of stroke.

Health Canada Mar/07 is warning consumers not to use the unauthorized product **Vigorect** Oral Gel Shooter, because it contains an undeclared drug substance tadalafil.

Health Canada Apr/07 is warning consumers about **Bitter orange** & cardiovascular reactions in the Canadian Adverse Reactions April 2007 Newsletter.

Health Canada Apr/07 is warning consumers from The Hong Kong Department of Health found **Lanmei Keili Ji to be adulterated with gliclazide**, a hypoglycaemic agent (lowers blood sugar). The Hong Kong Department of Health found **Lexscl Fat Rapid Loss capsules to be adulterated with sibutramine** and thyroid hormones. The United States Food and Drug Administration found **V.MAX and Rhino Max (Rhino V Max) to contain undeclared amounts of aminotadalafil**, an analogue of tadalafil, used to treat erectile dysfunction.

Health Canada April/07is advising consumers not to use a product called **Eden Herbal Formulations Serenity Pills II** because it contains the undeclared drug **estazolam**.

Health Canada April/07is advising consumers not to use a product **FibreChoice plus Multivitamins** is marketed as a fibre supplement. The product is contaminated with **fish gelatin**, a known allergen that could cause life-threatening reactions in some sensitive individuals.

Health Canada May/07 is warning consumers **Urat Madu** capsules are marketed for the treatment of erectile dysfunction. The product is adulterated with **sildenafil**, a prescription drug that has been associated with serious side effects including sudden vision loss, penile tissue damage and urinary tract infection.

Health Canada May/07 is advising consumers not to use **Xiaokeshuping Jiangtangning Jiaonang** capsules in Hong Kong to contain the undeclared pharmaceutical drugs phenformin, rosiglitazone, and glibenclamide, which may be used in diabetes to lower blood sugar.

Health Canada May/07 is advising consumers that **HS Joy of Love** product is marketed as a dietary supplement and was found to contain piperadino **vardenafil**.

Health Canada May/07 is advising consumers not to use 6 foreign health products due to concerns about possible side-effects: **Power 58 Extra, Platinum Power 58 Extra, Enhanix New Extra Men's Formula, Valentino, King Power Oral Solution, and Stretch Up** Capsules are marketed as treatments for erectile dysfunction. The products contain analogues of sildenafil and vardenafil, which are prescription drugs used for the treatment of erectile dysfunction.

Health Canada June/07 is advising consumers not to use **Optimum Health Care SleePlus TCM** or **BYL SleePlus**, because the products contain the undeclared drug **clonazepam.**

Health Canada June/07 is warning consumers not to use the product **Encore Tabs for Men**, because it contains an undeclared pharmaceutical ingredient similar to the approved drug tadalafil.

Health Canada July/07 is warning Canadians not to use the dietary supplement **MdMt**, or any other supplements containing the synthetic steroids methyl-1-testosterone or methyldienolone that are obtained without a prescription, due to potentially serious health risks including reduced fertility and liver disorders.

Health Canada July/07 is warning consumers not to use **Zencore** Tabs, a product advertised as a dietary supplement for sexual enhancement, because it contains an undeclared pharmaceutical ingredient similar to the approved drug tadalafil.

Health Canada July/07 & the US Food and Drug Administration (FDA) found ***Liviro3*** to contain tadalafil, a prescription drug that should only be taken under the guidance of a health professional.

Health Canada July/07 is advising consumers not to use the sleep supplement product **Optimum Health Care Sleep Easy**, because it contains the undeclared drug clonazepam.

Health Canada July/07 is advising consumers not to use 8 foreign health products due to concerns about possible side-effects: **Jie Jie Pills** and **Chuan Xiong Cha Tiao Wan** are proprietary Chinese medicines that have been found to contain aristolochic acid, a natural toxin known to cause kidney failure and cancer in humans. Medsafe, the New Zealand health

regulatory authority, advised the public not to use the products **Darling Capsules**, **Dali Capsules**, **Spanish Fly Capsules**, and an unnamed product, because they were found to contain sildenafil. Medsafe also advised the public not to use the product **Dai Dai Hua Jiao Nang** because it was found to contain sibutramine. The Hong Kong Department of Health [HKDH] found batch #WA00030 of the product K**ui Hua Chut Lee San Bird's Nest & Pearl** to exceed the acceptable limit for microbiological contaminants set out by the HKDH. Further investigation revealed that this product also exceeded the limit for bacterial contamination in Natural Health Products in Canada.

Health Canada Aug/07 Consumers who use **Excite for women or Ultimates for men** may be at risk of serious side effects similar to those associated with sildenafil.

Health Canada Aug/07 is advising Canadians of a recall in the United States of one lot of **Metaboslim Apple Cider Vinegar**, which is marketed as a dietary supplement, because it has been found to contain **sibutramine**, a prescription medication that should only be taken under medical supervision.

Health Canada Sept/07 is advising consumers not to use 13 foreign health products due to concerns about possible side-effects: **Jacaranda**, **Queenmer Fat Loss**, **Li Da Dai Dai Hua Jiao Nang, J-minus** and **Jelimel Slimming Capsules**. These products are promoted for weight loss and have been found to be adulterated with the prescription drug sibutramine. Sibutramine is used for treating obesity and should only be taken under the supervision of a health professional. **Junyu Jiaonanyihao** has been found to contain the undeclared prescription drugs sibutramine and dexamethasone, as well as phenolphthalein, which is currently prohibited in Canada. **Satis 60 Hours Ever Lasting Formula** is used for the treatment of erectile dysfunction/sexual enhancement. It was found to contain piperidenafil an analogue of vardenafil, a drug that should only be used under the supervision of a health professional. **Qiangli Zhuanggutongbiling** has reportedly been used for joint pain and stiffness. It was found to contain the undeclared prescription drugs prednisolone acetate, cortisone acetate, piroxicam, and diclofenac. **Heng Tong Jiangtangning Jiaonang** was found to contain the prohibited drug phenformin, and the prescription drug glibenclamide (glyburide) which should only be taken under the supervision of a health professional. **Endopile Capsules** is used for the treatment of hemorrhoids and piles, and related symptoms and was found to contain potentially toxic levels of lead and mercury. **BuXie PaiDu XiaoDou Su** is used as an acne treatment and was found to contain the prescription drug rifampicin (rifampin). **True Man** and **Energy Max** are used as sexual enhancement/ erectile dysfunction products and were found to contain an analogue of sildenafil or vardenafil which are prescription medications.

Health Canada Sept/07 is advising consumers not to use 5 foreign health products due to concerns about possible side-effects: **Top Gun for Men Herbal Extracts** has been found to contain a substance similar to tadalafil. **Oyster Plus** has been found to contain tadalafil. **Deguozhanjiang** contains sildenafil and tadalafil, prescription drugs used for the treatment of erectile dysfunction. **Chongcaoliubian Jiaonang** and **Santi Scalper Penis Erection** Capsule contain sildenafil.

Health Canada Sept/07: **Khun-Phra** is a health product promoted for pain relief that has been found to contain the undeclared drugs dexamethasone, prednisolone, phenylbutazone, diazepam, cyproheptadine and mebhydrolin.. **Asam Urat Flu Tulang, PJ Dewandaru** is a health product promoted to treat joint pain, rheumatism and arthritis. It has been found to contain the undeclared drugs dexamethasone, diclofenac and acetaminophen.

Health Canada Oct/07 Foreign Product Alerts: ***Zhen Feng Da Brand Xi Tong Wan*** is promoted as a pain reliever. Lot #060908 has been found to contain undeclared indomethacin, a prescription anti-inflammatory drug that should only be taken under the guidance of a health professional. ***Wellring Brand Yin Qiao Jie Du*** is a health product promoted to treat cold and flu symptoms. Lot#51005 has been found to contain undeclared acetaminophen. ***Gu Ci Dan*** and ***Xu Log Bou*** are promoted as pain relievers and have been found to contain undeclared indomethacin. Indomethacin is a prescription anti-inflammatory drug that should only be taken under the guidance of a health professional.

Health Canada Oct/07 is advising, especially pregnant & breastfeeding women, not to use **Calabash chalk** because of the potential health risk due to high levels of lead.

Health Canada Oct/07: Foreign Product Alerts: **Red Yeast Rice, Red Yeast Rice/Policosonal Complex and Cholestrix, and Xie Gan Wan**. Red Yeast Rice, Red Yeast Rice/Policosonal Complex and Cholestrix are promoted as dietary supplements for the treatment of high cholesterol. These products may contain **lovastatin**, a prescription medication for the treatment of high cholesterol that should only be taken under the guidance of a health professional.
Xie Gan Wan is a Proprietary Chinese Medicine with unknown indication for use. Xie Gan Wan, was found to contain **Aristolochia** plant species.

Health Canada Oct/07: **Royal Medic No.1 Chinese Caterpillar Fungus** is a proprietary Chinese medicine promoted as a general health tonic, but Health Canada advises Canadians not to use this product due to microbial contamination. **Steripaste Medicated Paste Bandages** may not be sterile therefore there is a possibility the bandage may cause a wound infection.

Health Canada Nov/07 is advising consumers not to use **Axcil** and **Desirin**, are promoted as natural sexual enhancement/ erectile dysfunction products. Consumers are warned not to use Axcil and Desirin because both products were found to contain the prescription drug **sildenafil**.

Health Canada Dec/07 is advising Canadians not to use unauthorized products manufactured by **Wild Vineyard** because of the potential health risk to consumers. Wild Vineyard is not authorized to manufacture, package, label or import natural health products in Canada.

Health Canada Jan/08 is advising consumers not to use 2 foreign health products due to concerns about possible side-effects: **Baby's Bliss Gripe Water** (apple flavour), code 26952V, a natural health product given to infants to ease stomach discomfort and gas, was found to contain the parasite cryptosporidium. Cryptosporidium may cause severe, chronic or even fatal effects, especially in infants. **Zhong Ti Xiao Er Jian Pi San** is a natural health product. Batch number JPS0704 has been recalled due to microbial contamination.

Health Canada Jan/08 is warning Canadians not to use the unauthorized product **Yeniujyn** because the product contains heavy metal contaminants and may pose a serious health risk. Yeniujyn is advertised as a natural health product, for adults and children, to be used "to cure involuntary passage of urine diseases." The product was found to contain high levels of **lead and arsenic**.

Health Canada Jan/08 is warning Canadians not to use the unauthorized product 1- ZhenZhu HouFengSan Penji; Vyling Cornu Saigae Tataricae Cooling Tea; Natorny Kwek's Herb 106; Chinese Herbal Heritage Herbal Slimming Tea; Vyling Urticaria Itch-Killer A; Vyling Water- Melon Pearls Powder; Phoenix Brand Tea For Sore Throat And Fever; Qing Yin Bai Hua Tea; and Yinqiao Flu & Fever Tea. **Nine specific batches** of Chinese medicines and teas manufactured in Singapore that have been recalled due to microbial (bacterial) and/or yeast and mould **contamination**.
Physio Care Lida Dai Dai Hua Jiao Nang Slimming Capsules (batch number 28012007 / expiration date: Jan 2009). This product is promoted for weight loss and has been found to contain a derivative of the prescription drug **sibutramine**.
RGC-RMC Rheumax Capsule (batch number REM1-SI93016N). This batch of RGC-RMC Rheumax Capsule has been found to contain **progesterone**, a steroid hormone that can have adverse effects on the brain, breast and skin and should only be taken if prescribed by a health professional.

Health Canada Feb/08 warning Canadians not to use Foreign Products: 1) **Jingzhi Kesou Tanchuan; Guanxin Suhe capsules**; **Qing Re An Cang Wan**; & **Guan Xin Su He** 2) **Xiao Qin Long Capsules** 3) **Xiao Qin Long Wan**; **Chuan Xiong Cha Tiao Wan Tablets**; **Bai Tou Weng Wan**
4) **Wannianqing Pai Danggui Niantong Tang** (batch number 050401) These products have been found to contain aristolochic acid, a toxin associated with serious and potentially fatal health effects.

Health Canada Feb/08 warning Canadians not to **use VPX 'No Shotgun' and BSN 'Cell Mass' Body Building Powders** These products have been found to contain coumarin.

Health Canada Feb/08 warning Canadians not to use 1) Ding Lu Brand Guipi Wan (batch number 060401); Ding Lu Brand Bushen Yijing Wan (batch number 060401); Ding Lu Brand Shiquan Dabu Wan (batch number 060401); **Ding Lu Brand Xiangsha Liujun Wan** (batch number 060401); Ding Lu Brand Xiaoyao Wan (batch number 060401); Medco Brand Vitality Essence Extract Of Deer Fetus (batch number 61007); Plasmin (batch number 20060102) 2) **Yogaraja Gulgulu**

Pills (batch number GK039) and Pilsol Capsule 3) **Conforer Global Yang Tonic-2** (batch number 060117) 4) **Liang Gel San Concentrated Powder** (batch number G3238913) and **Qing Xin Lian Zi Yin Concentrated** Powder (batch number G3239274) These products were found to contain excessive amounts of heavy metals.

Health Canada Mar/08 is warning consumers not to use **Libidus**, an unauthorized product promoted on the web site of the manufacturer for the treatment of erectile dysfunction. The product may pose serious health risks, as it was found to contain the undeclared prescription drug sildenafil.

Health Canada April/08 is warning consumers not to use Foreign Product Alert: **Tetrasil, Genisil, Aviralex, OXi-MED, Beta-mannan Micronutrient, Qina** and **SlicPlus**. They are marketed for the prevention or treatment of a variety of sexually transmitted diseases.

Health Canada April//08 is advising consumers not to use 2 foreign products, **Aspire 36** & **Aspire Lite**, because they were found to contain undeclared sildenafil analogues.

Health Canada April/08 is warning consumers not to use **Vigoureux**, an unauthorized product promoted for the treatment of erectile dysfunction. The product may pose serious health risks, as it was found to contain the prescription drug sildenafil

Health Canada April/08 is advising consumers not to use 2 foreign health products due to concerns about possible side-effects: **Tian Li** was found to contain tadalafil and hydroxyhomosildenafil, and should only be taken under the guidance of a healthcare professional. **Xian Zhi Wei II** was found to contain sibutramine and phenolphthalein, which are not meant for self-care and may cause serious side effects.

Health Canada April/08 is advising consumers not to use The Hong Kong Department of Health advised the public not to use the product **Tian Sheng Yi Bao** because it was found to contain two pharmaceutical products, glibenclamide and phenformin

Health Canada April/08 is advising consumers about The Health Sciences Authority (HSA) of Singapore recalled **Qili Brand Tongbianling Jiaonang, Sincere Brand ChuanXinLian Jiaonang, Xiangyao Brand Xiangyao Weian Jiaonang, Biflora Brand Fufang Danshen Pian (film-coated), Biflora Brand 306 Xiaoyan Jiedu capsules, and Xiang Sha Liu Jun Wan** as they were found to contain high levels of arsenic and/or mercury that exceeded the permissible limits outlined by the HSA standards of safety and quality.

Health Canada May/08 is advising consumers not to use **vpxl No1** Dietary Supplement for Men was found to contain tadalafil

Health Canada May/08 is reminding consumers who choose to use unapproved Ayurvedic medicinal products that some of these products may contain high levels of heavy metals. Consumption of excessive amounts of heavy metals, such as lead, mercury, and arsenic, pose serious health risks.

Health Canada May/08 is warning consumers not to use **Trophic Kelp & Glutamic Acid HCl** due to the health risk posed by exposure to high levels of iodine.

Health Canada May/08 is warning consumers not to use **Desire**, an unauthorized product promoted to enhance male sexual performance as this product may pose serious health risks in certain patients. Lot 0070263 of the product was found to contain the prescription drug phentolamine.

Health Canada June/08 is advising that **Desire** contains Phentolamine, which should only be used under the supervision of a health care professional.

Health Canada June/08 **6-OXO**, which contains the compound 4-androstene-3,6,17-trione, is an unauthorized natural health product in Canada. **1-AD** contains 1-androstenediol, an anabolic steroid that is regulated as a controlled substance in Canada

Health Canada July/08 Foreign Product Alerts: **Super Shangai,Strong Testis, Shangai Ultra, Shangai Ultra X, Lady Shangai, Shangai Regular (also known as Shangai Chaojimengnan), Actra-Sx, An unknown product containing the plant Lycium barbarum L., Adam Free, NaturalUp, Erextra, Yilishen, Blue Steel, Hero, & Naturalë Super Plus.** These products have been found to contain sildenafil or an unapproved substance similar to sildenafil.

Health Canada July/08 is advising consumers not to use 4 foreign health products due to concerns about possible side-effects: Wodibo. **Wodibo** is promoted as an all-natural Chinese potency-enhancing product for the treatment of erectile dysfunction. The Danish Medicines Agency has warned against the use of Wodibo because it was found to contain sildenafil and tadalafil, prescription drugs authorized for treatment of erectile dysfunction. Both of these medications should only be used under the supervision of a health care professional. **Viril-Ity-Power** (VIP) Tabs. The U.S. Food and Drug Administration has warned consumers not to use Viril-Ity-Power (VIP) Tabs because it was found to contain an undeclared ingredient similar to the prescription drug sildenafil. The product has been recalled by the manufacturer in the U.S. **Therma Power** (red and blue varieties) and **Grenade Fat Burner**. The U.K. Medicines and Healthcare products Regulatory Agency (MHRA) warned consumers not to use the ephedrine-containing products Therma Power (red variety) and Grenade Fat Burner after the products were associated with serious adverse reactions. The MHRA also warned consumers to not use the ephedrine-free Therma Power (blue variety) because it contains synephrine and caffeine, a combination that has been associated with cardiovascular adverse reactions.

Health Canada Aug/08 is advising consumers not to use 9 foreign health products due to concerns about possible side-effects: **Dan Bai Shou Shen Su** was found to contain undeclared thyroid hormones and sibutramine. **Karntien and Karntien Easy to Slim** were adulterated with sibutramine and a compound that is similar in structure to sibutramine (N-desmethylsibutramine). **Armstrong Natural Herbal Supplement, Enhanix New Extra Men's Formula, Power 58 Extra, and Platinum Power 58 Extra** were adulterated with tadalafil or unapproved substances with structures similar to tadalafil and vardenafil. **More Slim** was found to contain the undeclared pharmaceutical ingredient sibutramine. **Soloslim** was found to contain an undeclared substance similar in structure to the prescription drug sibutramine. It also contains the prescription drug L-carnitine, as well as synephrine, which is not authorized for sale in weight loss products in Canada.

Health Canada Aug/08 is advising consumers not to use 8 foreign health products due to concerns about possible side-effects: The Hong Kong Department of Health warned against the use of Natural (Xin Yi Dai) and Lasmi because Natural (Xin Yi Dai) was found to contain sibutramine and phenolphthalein, and Lasmi was found to contain sibutramine and spironolactone. The Hong Kong Department of Health warned against the use of AA Qu Feng Shu Jin Wan because it was found to contain the undeclared pharmaceutical ingredient dexamethasone. Apisate contained fenfluramine and Energy ll contained sibutramine. Obat Asam Urat and Asam Urat both contained dexamethasone, phenylbutazone and piroxicam. The Hong Kong Department of Health warned against the use of Slim 3in1 (Xiao Nan zhi Bao) because it was found to contain the undeclared pharmaceutical ingredients sibutramine and phenolphthalein.

Health Canada Sept/08 is advising consumers not to use any unauthorized health products sold under the brand names **Life Choice, Healthy Choice, Doctor's Choice and Your Choice** as well as other products without a brand name. All of these unauthorized health products have the same identifying image on their label.

Health Canada Sep/08 is advising consumers not to use 3 foreign health products due to concerns about possible side-effects: The Hong Kong Department of Health warned consumers not to buy or use **Lover Liquid Nutriment Herbal Supplement and Onyo** because they were found to contain undeclared pharmaceutical ingredients. **Lover Liquid Nutriment Herbal Supplement** was found to contain sildenafil while Onyo was found to contain sildenafil, as well as unapproved substances with structures similar to sildenafil and vardenafil. The U.S. Food and Drug Administration warned consumers not to use the product **Rose 4 Her** because it was found to contain an undeclared ingredient similar to the prescription drug sildenafil.

Health Canada Sep/08 is advising consumers not to use 6 foreign health products due to concerns about possible side-effects: The Hong Kong Department of Health warned consumers not to buy or use **Dr. Life** or **Chong Cao Ju Wang** because they were found to contain undeclared pharmaceutical ingredients. Dr. Life contains an unauthorised substance similar in structure to tadalafil while Chong Cao Ju Wang contains sildenafil. The Hong Kong Department of Health warned against the use of **Hanguo shoushen yihao** (meiti xing) because it was found to contain the undeclared pharmaceutical ingredient sibutramine. The U.S. Food and Drug Administration alerted consumers to a voluntary recall of 32-ounce plastic bottles of **Liquimax Complete Nutrition Multivitamin Formula** (UPC codes 7497052290, 7497023607 or 7497023696) because the product may contain undeclared fish (not shellfish), tree nuts (almonds, pecans, and/or walnuts), and wheat. People with sensitivities to fish, tree nuts and/or wheat may risk serious or life-threatening allergic reactions if they consume these products. The Hong Kong Department of Health warned against the use of **ARMA - Sin Gang San** and **New ARMA - Sin Gang San** because they were found to contain the undeclared pharmaceutical ingredients sibutramine and fenfluramine.

Health Canada Oct/08 is advising consumers not to use 2 foreign health products due to concerns about possible side-effects: Swissmedic warned consumers not to buy or use the product **Powertabs** because it contains an unauthorised substance similar in structure to sildenafil. The Hong Kong Department of Health warned consumers not to buy or use **Sweet Energizer Vitality** Candy because it was found to contain an unauthorised substance similar in structure to tadalafil.

Health Canada Nov/08 is advising consumers not to use 5 foreign health products due to concerns about possible side-effects: The Hong Kong Department of Health warned consumers not to buy or use **Lu Quan** because it contains undeclared glibenclamide and sildenafil. The Hong Kong Department of Health warned consumers not to buy or use **Fat Killer, Carbohydrate Cut and Sugar-Carbohydrate Cut** because they contain sibutramine and an unauthorised substance similar in structure to sibutramine, and **Zhuang Yao Gu Shen** Capsule because it contains sildenafil.

Health Canada Nov/08 is advising consumers not to use 13 foreign health products due to concerns about possible side-effects: The U.S. FDA warned consumers not to buy or use **Viapro** because it contains an unauthorised substance similar in structure to sildenafil. Sildenafil is a prescription drug used in the treatment of erectile dysfunction and should only be used under the supervision of a health care practitioner.
The U.S. Food and Drug Administration informed consumers of a voluntary manufacturer recall of these 12 products because they contain human **placenta, aristolochic acid and/or ephedra**, and may pose serious health risks. All 12 products are manufactured by **Jen-On Herbal Science** International Inc. (also known as **Herbal Science International Inc**.). Consumers who had purchased these products were advised to discontinue their use immediately and return them to the place of purchase for a full refund.

Health Canada Nov/08 is warning consumers not to use **Firm Dose** and **Granite Rooster**, two products promoted to enhance male sexual performance, as these products may pose serious health risks. Firm Dose was found to contain similar to sildenafil, while Granite Rooster was found to contain similar to tadalafil.

Health Canada Nov/08 is advising consumers not to use the unauthorized product, Kwan Loong Medicated Oil, as it contains chloroform. Foreign Product Alerts: Seng Jong Tzu Tong Tan,Tou Tong San (Headache Formula),Du Huo Ji Sheng ,Tang (Du Huo Joint Relief), Wu Yao Shun Qi San, Qing Bi Tang (Nasal Cleanser), Zhong Fong Huo Luo Wan (Stroke Revito Formula), Xiao Qing Long Tang (Little Green Dragon), Ding Chuan Tang (Breathe Smooth), Xiao Xu Ming Tang, Feng Shi Zhi Tong Wan (Joint Relief),,Guo Min Bi Yan Wan, Fang Feng Tong Sheng San.

Health Canada Jan 2009 is advising consumers not to use 4 foreign products: **Zhuang Tjar Gere** because it contains the undeclared prescription drugs sildenafil & tadalafil, **Zhixhue** Capsules manufactured by Vital Pharmaceutical Holdings Ltd. due to concerns of serious side- effects including liver dysfunction, **Tonik Warisan Banjar** because it contains undeclared dexamethasone & **Healthily Slim** because it contains sibutramine.

Health Canada Mar/09 Foreign Product Alerts: **68 Weight Loss Products**; Best-life Fat Burning Capsules; Bevidan;Huiji Yin Chiao Chieh Tu Pien; Relacore -plus Lami, Linglongquxian, Menergy M-Essence, Nyal Day & Night Cold & Flu Fighter (AUST L 146264), Nyal Cold & Flu Fighter (AUST L 146263), 999 Radix Notoginseng, Batch no. 0807021, Slim Pure, Carbohydrate, Kalomee, K Carbohydrate, K Tighten Slim, & K Slimming Pills.
http://www.hc-sc.gc.ca/ahc-asc/media/advisories-avis/_fpa-ape_2009/index-eng.php

Health Canada June/09 Foreign Product Alerts: **Fangocur Mineral Drink** (undeclared arsenic); **Jia Yi Jian** (undeclared sibutramine & tadalafil);**Fortodol**, which is also sold under the names (undeclared nimesulide with liver concern) of Donsbach Miradin, Lepicol Miradin, Leppin Miradin, & Miradin; **Shan Dian Qiang Xiao Shou** (undeclared sibutramine & phenolphthalein); **Zencore Plus** (undeclared benzamidenafil) & **Zhong Guo Shen Fang** (undeclared med like sildenafil).

Health Canada June/09 is warning consumers not to use the unauthorized product **Slim Magic Herbal**, which is promoted as a weight-loss product, as it was found to contain an undeclared pharmaceutical ingredient similar to the prescription drug sibutramine.

Health Canada is warning consumers not to use the unauthorized product **Nutural Slim**, which is promoted as a weight-loss product, as it was found to contain the undeclared pharmaceutical ingredient sibutramine and also an undeclared pharmaceutical ingredient similar to sibutramine.

Health Canada June/09 warns of foreign Product Alerts: **Herbal Xenicol** because it contains undeclared cetilistat. **BioEmagrecim**, which the FDA had previously warned contained sibutramine, was also found to contain fluoxetine, furosemide and fenproporex. Products: **Slimbionic, Xsvelten, 999 Fitness Essence, 24" ince, Light Some, Paiyouji, Pearl White Slimming, & Reducing Weight Easily** contain undeclared pharmaceutical ingredients (sibutramine and/or phenolphthalein) and/or excessive levels of lead, and may cause serious health effects..

Health Canada July/09 is warning consumers not to use the unauthorized health product labelled as **Specific-Formula Arthro-Ace** as it was found to contain undeclared dexamethasone and may cause serious health effects.

Health Canada July/09 is warning that the Singapore Health Sciences Authority (HSA) warned consumers to not buy or use **Air Ikan Haruan** after it was found to contain undeclared dexamethasone. The Hong Kong Department of Health warned consumers not to buy or use the product **Neovidan** after it was found to contain undeclared prednisolone and mefenamic acid. Plus the Singapore Health Sciences Authority (HSA) warned consumers to not buy or use **XP Tongkat Ali Supreme** after it was found to contain undeclared tadalafil.

Health Canada Aug/09 is advising via Singapore Health Sciences Authority (HSA) warned that **Delima Raja Urat** contains undeclared dexamethasone, chlorpheniramine, pheniramine and sibutramine, while **Cao Gen Bai Lin Wan** contains undeclared dexamethasone and chlorpheniramine.

Health Canada Oct/09: **Bao Ling**- The Singapore Health Sciences Authority advised consumers not to buy or use since contained undeclared betamethasone, hydrochlorothiazide & chlorpheniramine. **Dynasty Worldwide Jinglida So Young Formula**- The Singapore Health Sciences Authority (HSA) warned consumers to not buy or use since contained undeclared aminotadalafil. **STEAM** lot#80214, 90260 -The U.S. FDA informed consumers of a voluntary manufacturer recall of two lots of STEAM after FDA testing found these lots to contain undeclared sulfoaildenafil (lot# 80214) & undeclared tadalafil (lot# 90260). **Syntrax Fyre (contained Yohimbine)**, **Texiao Fengshi Gutong Ling (contained indomethacin)**, **Kam Yuen Brand Wan Ying Yang Gan Wan (contained sildenafil)** - The Hong Kong Department of Health warned consumers not to buy or use these three products after they were found

to contain undeclared pharmaceutical substances.

Health Canada Nov/09 is advising Canadians not to consume Chaotic Beverages sold under the brand names Mind Strike, Fearocity, Elixir of Tenacity and Power Pulse because they are unauthorized products marketed to a vulnerable population (children) with ingredients that may pose a health risk. **Mind Strike:** Contains an unknown amount of caffeine despite advertising that it is not an energy drink and contains several herbs which are not included in Health Canada's list of botanicals with a history of safe use in children. **Fearocity:** Contains an unknown amount of caffeine, several herbs not included in Health Canada's list of botanicals with a history of safe use in children, taurine at an unacceptable level for children, and niacin at a level three times higher than that recommended for children aged 1 to 13 years. **Elixir of Tenacity:** Contains green tea extract, which is not included in Health Canada's list of botanicals with a history of safe use in children, and vitamin A at a level unacceptable for children aged 1 to 8 years. **Power Pulse:** Contains chromium picolinate at levels of possible concern in a product taken by children.

Health Canada Nov/09 is warning consumers not to use Herblex "**Once More**"since it was found to contain sildenafil.

Health Canada Dec/09 is advising Canadians not to use certain Acai Berry products after a large number of shipments of adulterated products were stopped at the border. The product names include: **Anti-Aging Acai Berry, Guarana Blast, Brazillian Pure, Anti-aging Vital Rez V, Weight Loss VitalAcai, Dietary Supplement Acai Power Blast and Muscle Mass**. These products advertised for anti-aging and weight loss were found to contain undeclared sildenafil.

Health Canada Dec/09 is warning consumers not to use "**RevolutionDS Weight Loss**", an unauthorized health product promoted for weight loss, because it contains benzylpiperazine (BZP), and may pose serious health risks.

Health Canada Dec/09 is advising consumers not to use the following foreign health products: 1. **Power-Plus P**: The Singapore Health Sciences Authority issued a recall notice for Power-Plus P (expiry date 03/03/2011) after it was found to contain undeclared tadalafil. 2. **Show Party**: The Hong Kong Department of Health warned consumers not to buy or consume Show Party [shou-shen pai] after it was found to contain undeclared sibutramine and phenolphthalein. 3. **Zeng Da Yan Shi Wan**: The Hong Kong Department of Health warned consumers not to buy or use after it was found to contain undeclared sildenafil.

Health Canada Jan/10 informs that Finish Food Safety Authority: **Full Contact Max Potency** contains thio-sildenafil and thio-homosildenafil; Singapore Health Sciences Authority: **M-Action** contains desmethylacetildenafil and acetilacid. U.S. FDA: **RockHard Weekend** contains sulfoaildenafil; & **Pai You Guo** contains sibutramine and phenolphthalein. Hong Kong Department of Health: **Ku Xiu Ba Xiang Jian Fei Wan** contains sibutramine and an unauthorized substance similar to sibutramine; **Super Slim (Yani)** contains sibutramine and phenolphthalein; **SHoufsy** contains sibutramine & **MIGAC (sic) FAT BURMING (sic) FACTOR** contains sibutramine.

Health Canada Jan/10 is advising consumers not to use the unauthorized product "**Stiff Nights**" after the U.S Food and Drug Administration (FDA) found that this product contains an undeclared substance similar to the prescription drug sildenafil.

Health Canada Jan/10 is warning consumers not to use the unauthorized product "**The Slimming Coffee**," which was previously sold as "**Lose Weight Coffee**," because it was found to contain sibutramine.

Health Canada Jan/10 is advising consumers not to use any unauthorized health products sold under the brand names **Natural Choice Vitamin B-17**, **Natural Choice Kava Kava** and **Natural Choice Lithium Orotate**. The unauthorized Natural Choice Vitamin B-17, according to what is listed on the product label, contains amygdalin which is a compound derived from bitter apricot kernels that has the potential to release cyanide when ingested by humans. The unauthorized Natural Choice Kava Kava, according to what is listed on the product label, contains kava lactones & agencies have received reports associating the use of kava with serious liver dysfunction.

Health Canada Jan/10 is advising Canadians that natural health products containing the ingredient **glucomannan** in tablet, capsule or powder form, which are currently on the Canadian market, have a potential for harm if taken without at least 8 ounces of water or other fluid.

Health Canada Feb/10 is advising consumers that the unauthorized product "**Complete 7-Day Cleanse**" is being recalled because it contains a number of active ingredients with a combined effect that may pose serious health risks. "Complete 7-Day Cleanse" is a multi-ingredient natural health product promoted for "cleansing" or removing toxins from the body. According to package labelling, the product contains over 30 active ingredients, some having a diuretic (water pill) or laxative (stimulant, and bulk-forming) effect.

Health Canada Feb/10: **2H & 2D**- Hong Kong Department of Health (HKDH) warned consumers not to buy or use 2H & 2Dafter it was found to contain undeclared tadalafil. Products distributed by **Atlas Operations Inc**. The FDA informed consumers of a voluntary recall by Atlas Operations Inc. of certain lots of some products that were found to contain undeclared sulfoaildenafil, which is an unauthorized substance similar to sildenafil. Products distributed by **Bodybuilding.com** The FDA informed consumers of a voluntary recall of 65 bodybuilding products as these products may contain the following anabolic steroids: "Superdrol," "Madol," "Tren," "Androstenedione," and/or "Turinabol." **STRO Emperor** Capsules The Irish Medicines Board warned consumers not to buy or use STRO Emperor Capsules after it was found to contain undeclared tadalafil. **Tian Yang Xu Huo Oral Ulcer** Capsule Singapore Health Sciences Authority issued a recall notice for one batch (batch number 0812003, expiry date 11.2011) of Tian Yang Xu Huo Oral Ulcer Capsuleafter it was found to contain undeclared aristolochic acid.

Health Canada Mar/10 is warning Canadians that an unapproved health product, **POWER-MAX** that contains sildenafil.

Health Canada Mar/10 is warning Canadians that an unauthorized health product, "**Herbal Diet Natural**" has been found on the Canadian market and contains an undeclared pharmaceutical ingredient similar to the prescription drug sibutramine.

Health Canada is warning Canadians that an unauthorized health product, "**West Pharm Therma Lean Fat Burner Energizer**" was found on the Canadian market. West Pharm Therma Lean Fat Burner Energizer contains Ephedrine and caffeine, which combined together, may cause serious and possibly fatal adverse effects.

Health Canada Apr/10 is warning Canadians that an unauthorized health product, "**Slim-30**" distributed in Ontario and Quebec by Duxx Enterprises Inc., contains an undeclared pharmaceutical ingredient similar to the prescription drug, sibutramine.

Health Canada May/10 consumers not to use the following foreign health products due to concerns about possible adverse reactions: 1. **Ba Bao Xiao Ke Dan** The Hong Kong Department of Health warned consumers not to buy or use Ba Bao Xiao Ke Dan after it was found to contain undeclared glibenclamide. 2. **Bao Shu Tang Wu Zi Yan Zong Wan** The Hong Kong Department of Health warned consumers not to buy or use Bao Shu Tang Wu Zi Yan Zong Wan after it was found to contain excessive levels of lead, a heavy metal. 3. **Lin Yan Yin Chiao** The Singapore Health Sciences Authority issued a recall notice for one batch (batch# JI0324, expiry date 03/2011) of Lin Yan Yin Chiao after it was found to contain undeclared chlorpheniramine and paracetamol (acetaminophen). 4. **Man Power** The Hong Kong Department of Health warned consumers not to buy or use Man Power product after it was found to contain undeclared tadalafil. 5. 17 products sold through **MuscleMaster.com** (see Foreign Product Alert for a complete product list) The FDA informed consumers of a voluntary recall of the 17 bodybuilding products as they may contain the following anabolic steroids: "Superdrol," "Madol," "Tren," "Androstenedione," and/or "Turinabol." 6. **Seven Slim 7 Seshou** (Qingchun Shaonüxing, Jieshixing, Guifurenxing, Songchixing), Shoushen Jiaoguan-Tinei Yundong Wan

(Jian Xiabanshen, Jian Quanshen Feipang) The Hong Kong Department of Health warned consumers not to buy or use the six products listed above after they were found to contain undeclared sibutramine and phenolphthalein.

Health Canada May/10 is advising consumers not to use 1. **Botanical Slimming 100% Natural Soft Gel, also sold as Meizitang** The Australian Therapeutic Goods Administration warned consumers not to buy or use this product after it was found to contain undeclared sibutramine. 2. **Marsha Slim Plus** The Hong Kong Department of Health warned consumers not to buy or use Marsha Slim Plus after it was found to contain undeclared sibutramine, an unauthorized substance similar to sibutramine and phenolphthalein. 3. **S&S Super Slender** The Hong Kong Department of Health warned consumers not to buy or use S&S Super Slender after two samples were found to contain agent similar to sibutramine. One of the tested samples also contained undeclared sibutramine and phenolphthalein.

Health Canada June/10 is warning Canadians that the unauthorized health products "**Vigofit**" and "**Once More**," which are promoted to enhance male sexual performance, have been seized by Health Canada inspectors from retail stores in Abbotsford and Surrey, British Columbia. These two products contain sildenafil.

Health Canada June/10 is advising consumers not to use the following foreign health products due to concerns about possible adverse reactions: 1. **COMECOO, ZHONGCAOYAO-JIANKANGJIANFEI** The Hong Kong Department of Health warned consumers not to buy or consume these two products after they were found to contain undeclared phenolphthalein, sibutramine and two unauthorized substances similar to sibutramine. 2. **Qingzhi Santian Shou** The Hong Kong Department of Health warned consumers not to buy or consume Qingzhi Santian Shou after it was found to contain undeclared sibutramine and an unauthorized substance similar to sibutramine. 3. **Vita Breath** The U.S. FDA warned consumers not to buy or consume Vita Breath because it may contain hazardous levels of lead, which is a heavy metal.

Health Canada July/10 is advising consumers not to use the following foreign health product(s) due to concerns about possible adverse reactions: 1. **Stud Capsule For Men** The U.S. FDA informed consumers of a voluntary recall of one lot (Lot #060607-01/060108-01 Exp 6-2013) after it was found to contain undeclared Sildenafil. 2. **Po Chai Pills** (capsule form) The Hong Kong Department of Health warned consumers not to buy or use this product after it was found to contain undeclared sibutramine and phenolphthalein. Sibutramine is a prescription drug and should only be used under the supervision of a health care practitioner while phenolphthalein is no longer authorized for sale in Canada because it may cause cancer. Po Chai Pills (capsule form) has been recalled by the manufacturer. 3. **LiPO-8 Cap and Glucomi 600 Cap** The Hong Kong Department of Health warned consumers not to buy or use these products because they contain undeclared sibutramine.

Health Canada July/10 is advising Canadians about "**UP Ultimate Performance for Men**", an unauthorized health product containing undeclared sildenafil.

Health Canada July/10 is advising consumers not to use the following foreign health products due to concerns about possible adverse reactions: **1 Body Beautiful** The Hong Kong Department of Health warned consumers not to buy or consume *1 Body Beautiful* after it was found to contain undeclared phenolphthalein and sibutramine. 2. **USA Yaku Cell Slimming Capsules, Dong Gua Pai You Su, Qing Gua Pai You Su, and Mu Gua Pai You Su** The Hong Kong Department of Health warned consumers not to buy or consume these four products after they were found to contain undeclared phenolphthalein, sibutramine and an unauthorized substance similar to sibutramine. 3. **Atlas Operations Inc. expands its U.S. recall of over 30 sexual enhancement supplements** The U.S. FDA informed consumers of an expanded recall of certain lots of products after some were found to contain undeclared sulfoaildenafil. The products are being voluntarily recalled nationwide in the U.S. by the company Atlas Operations Inc. 4. **Stallion, SZM Formula for Men, Tomcat Ali and Volcanic** New Zealand's Medsafe warned consumers not to buy or use these four products after they were found to contain undeclared tadalafil. 5. **Vitalex for men and Vitalex for women** The U.S. FDA informed consumers that the *Vitalex*products were found to contain acetildenafil, which is an unauthorized substance similar to sildenafil and may pose similar health risks.

Health Canada Aug/10 says **Fulda Unitang Herbs Sleep Plus**, an unauthorized product promoted as an herbal sleep aid, has been found to contain high levels of estazolam.

Health Canada July/10 Unauthorized Health Products Sold by **Marigold Natural Pharmacy Ltd**. May Pose Health Risks. These products (http://www.hc-sc.gc.ca/ahc-asc/media/advisories-avis/_2010/2010_126bk-eng.php) were made available to Canadians via the company's pharmacy in Courtenay, British Columbia and via their website (http://www.marigoldnaturalpharmacy.com).

Health Canada July/10 is advising consumers not to use the following foreign health product(s): **Huo Luo Jing Dan** The Singapore Health Sciences Authority warned consumers not to buy or consume Huo Luo Jing Dan after it was found to contain undeclared indomethacin, dexamethasone and prednisolone.
Kam Chik San The Hong Kong Department of Health (HKDH) cautioned against the use of **Kam Chik San** after samples were found to contain mercury at a level much higher than permitted by the HKDH. **Magic Power Coffee** The U.S. FDA warned consumers not to buy or use Magic Power Coffee after it was found to contain undeclared hydroxythiohomosildenafil, which is an unauthorized substance similar to sildenafil.
Que She The U.S. FDA warned consumers not to buy or use Que She after it was found to contain undeclared fenfluramine, propranolol, sibutramine and ephedrine. **Sheng Yuan Fang** The Hong Kong Department of Health (HKDH) warned consumers not to buy or use Sheng Yuan Fang after it was found to contain undeclared phenolphthalein and sibutramine.

Health Canada July/10 is informing Canadians that **Marché Euromix**, a retail store in Pierrefonds (Montréal), was found to be selling a health product that was not authorized for sale by Health Canada and that closely resembled in appearance an authorized drug, Viagra.

Health Canada Aug/10: "**SeXXX DRIVE**", promoted as a herbal supplement to enhance male sexual performance, & Health Canada found hydroxyhomosildenafil.

Health Canada Aug/10 has seized the unauthorized sexual enhancement supplements "**Male Enhancement ExtenZe**" and "**Women ExtenZe**" imported and sold by the Happy Paradise Adult Store in Burnaby, British Columbia. The labels of each of these unauthorized products list the prescription ingredient pregnenolone and the controlled drug, DHEA (dehydroepiandrosterone). The labels of the unauthorized "Male Enhancement ExtenZe Nutritional Supplements" list the ingredient yohimbe extract (bark).

Health Canada Sep/10 **E.O.D. Erection on Demand**" being promoted as a herbal to enhance male sexual performance, the product was tested by Health Canada and found to contain tadalafil.

Health Canada Sep/10: "**Arth-Forth**", an unauthorized product promoted as an herbal supplement and distributed by Ka Wing Hong Ltd., was tested by Health Canada and found to contain a steroid prescription drug, dexamethasone.

Health Canada Sep/10 is advising consumers not to use : 1. **Golden aryuru, Baisheng wei ge, Zhonghua niubian, Ten ka dai 1 bou, Kuai gan bei zeng chao yue zi wo (Happy felling doubly increase [sic]), Ling tou lang, SkyFruit, Chu bi ho ken, Jinbolang, Suika Koso, Lov, I ka ou (2009 nen sin hoso) and/or I ka ou (saisinsui shutsu hoso)** The Japanese Ministry of Health, Labour and Welfare warned consumers not to buy or use the 12 products listed above because they were found to contain undeclared sildenafil and/or other unauthorized substances similar to sildenafil that may pose similar health risks (norhongdenafil, acetil acid, and tioqinapiperifil). 2. **Joyful Slim Herb** Supplement The U.S. FDA informed consumers of a recall of one lot (#101408) of Joyful Slim Herb Supplement after FDA tests found it to contain undeclared desmethyl sibutramine. The lot is

being voluntarily recalled nationwide in the U.S. by the company J & H Besta Corp. 3. **Vialipro** The U.S. FDA informed consumers of a recall of certain lots of Vialipro after FDA tests found product samples to contain undeclared sulfoaildenafil, which is an unauthorized substance similar to sildenafil and may pose similar health risks.

Health Canada Sep/10 **Exemption number**: This will help with the backlog of applications for a licence. Exemptions will be given to natural products that have passed an initial assessment of safety, quality, and efficacy. These products will be given an exemption number (EN)...instead of a Natural Product Number (NPN) or Drug Identification Number-Homeopathic Medicine (DIN-HM)...until they are fully reviewed by Health Canada.

Health Canada Nov/10 **Amana Care Seven Slim Herbal Capsules**: The Israel Ministry of Health informed consumers that it found the product Amana Care Seven Slim Herbal Capsules to contain undeclared sibutramine and residue of sildenafil. Arrow Brand Medicated Oil & Embrocation: The U.S. FDA warned consumers not to buy or use **Arrow Brand Medicated Oil & Embrocation** because it contains ingredients that are potentially poisonous, particularly in children. **Beijing 101 Hair Consultants: Hair Growth Formula D-2653-Band Hair Growth Tonic E-0583-D**: The Singapore Health Sciences Authority advised consumers to stop using one batch of these products (Beijing 101 Hair Consultants Hair Growth Formula D-2653-B batch# 20091201, and Hair Growth Tonic E-0583-D batch# 20091201) after testing of these batches revealed the presence of undeclared minoxidil. **101 Zhangguang: Gold 101 Super Effective Hair Growth Agentand Fabao 101D Doctor Zhao's Chinese Traditional Herbal Hair Care Formula**: The Hong Kong Department of Health warned consumers not to buy or use these two products after they were found to contain undeclared minoxidil.

Health Canada Nov/10 is advising consumers not to use the following foreign health products due to concerns about possible adverse reactions: **1. Goya–Bitter Melon - Miyura Fit'x Capsules** contained undeclared phenolphthalein and sibutramine **2. MasXtreme** contains undeclared aminotadalafil while the other (#911035) contains undeclared aildenafil and phentolamine **3. Mr. Magic Male Enhancer from Don Wands** contained hydroxythiohomosildenafil and sulfoaildenafil **4. So Hard for Men - Pulse8 for Women - The Rock – Tonic 66** contained the undeclared pharmaceutical substances tadalafil, sildenafil, and/or hydroxyhomosildenafil **5. Solo Slim Extra Strength - Revivexxx Extra Strength** contained undeclared didesmethyl sibutramine **6. TimeOut** contained undeclared hydroxythiohomosildenafil.

Health Canada Nov/10 "**Fat Burner No. 1**" (labelled in Chinese characters translated as "**Qian Mei Yin Zi**", an unauthorized Chinese herbal weight loss medicine, is being voluntarily recalled by Ying Tai TCM Supplying Ltd. after Health Canada lab tests revealed the product contains two pharmaceutical ingredients: a chemical similar to sibutramine (N,N- didesmethylsibutramine), and sildenafil.

Health Canada Dec/10 "**Durazest**" and "**Once More**": Certain lots of two male sex enhancement products recalled as they may pose serious health risks. Certain lots (listed below) of two health products promoted for male sexual enhancement, "Durazest for Men" and "Once More," have been voluntarily recalled by Natural Performance Products Ltd. Health Canada laboratory tests identified the presence of a chemical similar to tadalafil (nortadalafil) in one lot of each product.

Health Canada Dec/10 is informing Canadians that NorthRegentRx has begun to voluntarily recall its product, **ResurreXX** from the Canadian market. NorthRegentRx is requesting that wholesalers, distributors and retailers stop sale of this product since contained an undeclared substance "hydroxyhomosildenafil".

Health Canada Dec/10 has been advised "**Flat Stomach Concept Extra**" is being voluntarily recalled by Les Produits Naturels Leblanc Inc due to missing label statements related to duration of use, risks and contraindications. Information missing from the label of Flat Stomach, a product contained within the Flat Stomach Concept Extra kit, may result in potential chronic use of aloe, which can lead to bowel dependence, and electrolyte imbalance.

Health Canada Dec/10 is advising consumers not to use the following foreign health products due to concerns about possible adverse reactions: 1. **Slimming Beauty Bitter Orange Slimming Capsule** (Slimming Beauty) The U.S. Food and Drug Administration warned consumers not to buy or use Slimming Beauty after FDA lab tests revealed that this product contains undeclared sibutramine. 2. **Shaguar, Signature Signergy, VIGRX (green capsule), VIGRX (white capsule), VigRx, VigRX Plus** New Zealand's MedSafe warned consumers to not buy or use these products after they were found to contain undeclared sildenafil, hydroxyhomosildenafil, thiosildenafil, and/or tadalafil. 3. **ArimaDex**, **Clomed** The U.S. Food and Drug Administration informed consumers that ArimaDex and Clomed are being recalled in the U.S. because they may contain an aromatase inhibitor. ArimaDex and Clomed are being voluntarily recalled by G.E.T. and KiloSports Inc., respectively.

Health Canada Dec/10 Three Probiotic Natural Health Products May Pose Serious Health Risks to Canadians with Milk or Soy Allergies. Consumers with milk or soy allergies are advised that three probiotic natural health products are being voluntarily recalled from the market because they are labelled as not containing dairy(milk) and/or soy but may contain trace amounts of milk or soy protein from ingredients used in the production process. **Saccharomyces Boulardii** (NPN 80013551) Advanced Orthomolecular Research Inc. (AOR); **Herbasaurs Bifidophilus for Kids** (NPN 80015508) & **Acidophilus Bifidobacterium** (NPN 80015336) by Nature's Sunshine Products of Canada Ltd & **Cultures de Yogourt 2 Milliards** (NPN 80013273 Bio-Dis Inc.

Health Canada Jan/11 The product **Synerate**, manufactured for Strive and distributed by Upper 49th, is being voluntarily recalled from the Canadian market because of the risk of serious, potentially fatal adverse effects from the combination of the ingredients in the product. Synerate, a product used for weight loss or body building, contains caffeine and synephrine, which is similar to ephedrine.

Health Canada Jan/11 **Nutrex Research Lipo 6X** is being voluntarily recalled from the Canadian market because of the risk of serious, potentially fatal adverse effects from the combination of the ingredients in the product. It contains caffeine and synephrine, which is similar to ephedrine.

Health Canada Feb/11 is advising consumers not to use the following foreign health products promoted for sexual enhancement due to the presence of unauthorized substances (PDE5 derivatives eg. sildenafil): **1. Aziffa, Erex, Eyeful, Hard Drive, Libidinal, Maxyte, Mojo, Monster Excyte, OMG, OMG45, Prolatis, Red Magic, Size Matters, Stiff Nights, Straight Up, Verect, WOW, Xaitrex, Xytamax, Zilex (with Golden Spear), Zotrex 2. Prolatis' Duro Extend Capsules For Men 3. Tiger King 4. Vigor-25, Man Up Now**

Health Canada Feb/11 is advising consumers not to use the following foreign health products due to concerns about possible adverse reactions: **1. Fruta Planta, Reduce Weight Fruta Planta** The U.S. FDA warned consumers not to buy or use Fruta Planta and Reduce Weight Fruta Planta after FDA lab tests revealed that this product contains undeclared sibutramine. **2. RockHard Weekend (lots 100159 and 100260 sold as blister packs, 3-count bottles and 8-count bottles)** The U.S. FDA informed consumers of a nationwide voluntary recall of certain lots (see above) of RockHard Weekend and Pandora after lab tests confirmed the products contain an unauthorized substance similar to sildenafil that may pose similar heath risks. **3. Slimming Factor** The Australian TGA warned consumers not to buy or use Slimming Factor after TGA lab tests confirmed the presence of the undeclared substances sibutramine, fenfluramine and phenolphthalein. According to the TGA release, the product is sold over the Internet.

Health Canada Mar/11 is advising consumers not to use the following foreign health products due to concerns about possible adverse reactions: **1. Celerite Slimming Capsules:** The U.S. FDA informed consumers of a company recall of Celerite™ Slimming Capsules after it was found to contain undeclared sibutramine. **2. Herbal Flos Lonicerae (Herbal Xenicol) Natural Weight Loss Formula:** The product was found to contain undeclared sibutramine at more than twice the dose that was normally prescribed before sibutramine was removed from the UK market in 2010. **3. Magicream:** The Irish Medicines Board warned consumers not to buy or use Magicream after it was found to contain undeclared clobetasol propionate and ketoconazole. **4. Nite Rider Maximum Sexual Enhancer for Men - STUD Capsule for Men:** The U.S. FDA informed consumers of a company recall of these products after they were found to contain undeclared sildenafil.

Health Canada April/11 Consumers with milk or soy allergies are advised that four probiotic natural health products {**Saccharomyces Boulardii (NPN 80013551), Herbasaurs Bifidophilus for Kids (NPN 80015508), Acidophilus Bifidobacterium (NPN 80015336), Cultures de Yogourt 2 Milliards (NPN 80013273)**} are being voluntarily recalled from the market because they are labelled as not containing dairy (milk) and/or soy but may contain trace amounts of milk or soy protein from ingredients used in the production process.

Health Canada Apr/11 has identified the presence of microbial contamination in "**Mary Ginseng House 100% Pure High Calibre Pow Sum Ontario Ginseng**", that may pose a health risk to immune-compromised individuals.

Health Canada May/11 "**Omega Alpha Kidney Flush**" Being Recalled from the Canadian Market: May Cause Serious Adverse Reactions in Pregnant Women and Kidney Disease Patients.

Health Canada May/11 is advising consumers not to use the following foreign health products due to concerns about possible adverse reactions: **1. Dr. Health Series CM Factor** The Hong Kong Department of Health warned consumers not to buy or use this product after it was found to contain an unauthorized substance similar to sibutramine that may pose similar health risks. **2. Gold Seagull Long Zhi Wan, Venergy** The Hong Kong Department of Health advised consumers not to buy or use these products after Gold Seagull Long Zhi Wan was found to

contain undeclared glibenclamide, while Venergy was found to contain undeclared sildenafil. **3. JianBu HuQian Wan** The HSA warned consumers not to buy or use JianBu HuQian Wan after it was found to contain undeclared dexamethasone and chlorpheniramine. **4. Rock Hard Extreme, Passion Coffee** The U.S. FDA advised consumers not to buy or use these products after they were found to contain undeclared sulfoaildenafil, which is an unauthorized substance similar to sildenafil and may pose similar health risks.

Health Canada July/11 "**Man Up Now**" Removed From Sale at Delta and Surrey Stores: May Pose Serious Health Risks to Canadians, was removed from sale at "O! Behave" retail stores in Delta and Surrey, B.C. after Health Canada's testing identified undeclared sildenafil.

Health Canada July/11 is advising Canadians that we have updated our list of unauthorized health products. These products were also removed from sale at Male and Female Harmony retail stores in Richmond and Burnaby, B.C., along with the Happy Paradise Adult Store in Burnaby. {**Sildenafil: in BAOLONG Switzerland Rolex 168 Prolong Time, BAOLONG Yilishen, Black Gold, Herbal Viagra, "Jin Chong Chao - Golden Cordyceps", Lubiangaowansu, MAGNA-RX, MAXMAN II capsules, Shenrong dabuwan, Traditional Chinese Medicine Viagra, V100, VIGER, VigRX for Men, VINIX capsules, Wolf, "XiongBaTian", Zang Gong Mi Lian Nan Bao} & Zeng Bei Jiu Zhan-Tadalafil.**

Health Canada July/11 is advising consumers not to use the following foreign health products due to concerns about possible adverse reactions: **1. Beline Capsules** The U.K. Medicine and Healthcare products Regulatory Agency (MHRA) advised consumers not to use *Beline Capsules* after it was found to contain undeclared chlorpheniramine, an over-the-counter antihistamine drug. **2. Black Ant** The U.S. Food and Drug Administration warned consumers to immediately stop using *Black Ant* after it was found to contain undeclared sildenafil at an amount three times the starting dosage for the approved prescription drug product. **3. [Hua Tuo Brand] Youzhi Baoying Dan, [Lee Sze] Texiao Houtong Wan and Prolonged Man Power Essence** The Hong Kong Department of Health (HKDH) warned consumers to not use these products after they were found to contain excessive levels of mercury, lead, or arsenic, which are heavy metals. **4. Natural Vigra VIAGRA Tablets and Satibo Capsules** The Australian Therapeutic Goods Administration (TGA) advised consumers to stop using *Natural Vigra VIAGRA Tablets* after it was found to contain undeclared sildenafil, and *Satibo Capsules* after it was found to contain undeclared tadalafil and hydroxyhomosildenafil. **5. Slim Xtreme Herbal Slimming Capsules** The U.S. Food and Drug Administration informed consumers of a voluntary recall after *Slim Xtreme Herbal Slimming Capsules* was found to contain undeclared sibutramine. **6. X-Hero and Male Enhancer** The U.S. Food and Drug Administration informed consumers of a voluntary recall after *X-Hero* was found to contain undeclared sulfosildenafil while *Male Enhancer* was found to contain undeclared tadalafil.

Health Canada July/11 is advising Canadians that we have updated our list of unauthorized health products to include a new product, **Tibet Babao**, which was found to contain undeclared sildenafil, a prescription erectile dysfunction drug. This product and several others have been removed from sale at the **Happy Paradise Adult Store in Burnaby, B.C**.

Health Canada Aug/11 is advising consumers not to use the following foreign health products due to concerns about possible adverse reactions: **1. Celerite Slimming Tea** The U.S. FDA informed consumers of a company recall of Celerite Slimming Tea after it was found to contain undeclared sibutramine. **2. Pink Lady for Women Capsules, St Nirvana Herbal Slimming Capsules** The Australian TGA warned consumers not to use these products after Pink Lady for Women Capsules was found to contain undeclared tadalafil while St Nirvana Herbal Slimming Capsules was found to contain undeclared sibutramine and phenolphthalein. According to the TGA advisories, these products are sold over the Internet. **3. Fifteen products promoted for weight loss** The Hong Kong Department of Health (HKDH) warned consumers not to buy or use these 15 products after they were found to contain at least one of the following undeclared substances: phenolphthalein, sibutramine, and/or an unauthorized substance similar to sibutramine.

Health Canada Sep/11 **Bi Yan Pian** Recalled Due to Excessive Amount of Mercury. Wing Quon Enterprises Ltd has initiated a stop sale and is voluntarily recalling a natural health product, Bi Yan Pian (NPN# 80023876) from the Canadian market after the product was found to contain an excessive amount of mercury.

Health Canada Oct/11 is advising Canadians not to use these foreign health products as they may pose a health risk. **Slim Forte Slimming Capsules**, **Slim Forte Double Power Slimming Capsules**, **Slim Forte Slimming Coffee** and **Meizitang Botanical Slimming Soft Gel**-The U.S. Food and Drug Administration warned that these weight loss products contain an unauthorized drug (sibutramine). **OxyELITE Pro capsules and Pure Fat Three Days Reduce Weight capsules**- The Australian Therapeutic Goods Administration warned that these weight loss products contain an unauthorized drug (sibutramine), or a prescription drug (yohimbine). **SXL Sexcellence sachets**- The Australian Therapeutic Goods Administration warned that this sexual enhancement product contains an unauthorized drug (sulfosildenafil). [W.S] **Gan Mao Ling and Chaisentomg Baby's Kam Chik San Powder** - The Hong Kong Department of Health warned that these Chinese health products contain excessive levels of heavy metals (lead or arsenic). **Huo Li Bao and Ren Sem Tu Chon Chin Kuo Pill** - The Singapore Health Sciences Authority warned that these Chinese pain-relief products contain prescription and/or over-the-counter drugs (furosemide, piroxicam, chlorpheniramine, and/or dexamethasone).

Health Canada Nov/11 is advising Canadians not to use these foreign health products as they may pose a health risk. **1. Zhui Feng Bao Wei San** The Singapore Health Sciences Authority warned that this health product contains excessive levels of microbial contamination. **2. Metabolic Advantage** The Singapore Health Sciences Authority warned that this weight-loss product contains prescription drugs (thyroid hormones). **3. Majun Dua Istimewa, Raja Maajun-Jerat Dan Seret Angin, and Horkut Chooi Foong Hor Lok Tan** The Singapore Health Sciences Authority warned that these traditional medicines contain undeclared prescription and over-the-counter drugs (dexamethasone, indomethacin, chlorpheniramine, dextromethorphan and acetaminophen). **4. Tian Ma Tu Chung Seven Leave Ginseng, Vall-Boon Tongkat Al, and Pao Ni Kang** The Singapore Health Sciences Authority warned that these traditional herbal products contain prescription and over-the-counter drugs (dexamethasone, ketoconazole, repaglinide, pheniramine, and chlorpheniramine). **5. Slimming Kapsul** The Hong Kong Department of Health warned that this weight-loss product contains an unauthorized drug (sibutramine) and a prescription drug (spironolactone). **6. Pancre-Plus** The Hong Kong Department of Health warned that this counterfeit Chinese medicine contains an unauthorized drug (phenformin) and a prescription drug (glyburide). **7. Maxidus capsules, Chao Jimengnan SuperPowerful Man tablets, Fu Yuan Chun capsules, and Qing Tian Zhu tablets** The Australian Therapeutic Goods Administration warned that these sexual enhancement products contain prescription drugs (sildenafil, tadalafil) and/or unauthorized drugs (sulfohydroxyhomosildenafil, sulfosildenafil).

Health Canada Nov/11: An unauthorized health product, "**Stiff One Hard 169**" is being voluntarily recalled from the Canadian market after Health Canada's testing identified an undeclared prescription medication in the product (thiodimethylsildenafil, an undeclared substance similar to the prescription medication sildenafil).

Health Canada Dec/11 is advising "**Yanshiwang**", "**Jin Kong Fu**" and "**Chong Cao She Bian Zhuang Yang Dan**". These products were removed from sale at Male and Female Harmony retail stores in Richmond and Burnaby, B.C., along with the Happy Paradise Adult Store in Burnaby. These contained sildenafil.

Health Canada Jan/12 advises: 1)**17 weight loss products (see Alert for a complete list)** A-Slim 100% Natural Slimming Capsule, Acai Berry Soft Gel ABC, Advanced Slim 5 > DaiDaiHuaJiaoNang, Dream Body Slimming Capsule, Fruit Plant Lossing Fat Capsule, Health Slimming Coffee, Ja Dera 100% Natural Weight Loss Supplement, Leisure 18 Slimming Coffee, Lishou, Magic Slim Tea, Magic Slim Weight Reduction Capsule, P57 Hoodia, Pai You Guo Slim Tea, PhentraBurn Slimming Capsules, Slender Slim 11 Tengda. The U.S. Food and Drug Administration warned that these weight loss products contain unauthorized drugs (sibutramine, phenolphthalein). **2. Uprizing 2.0** The U.S. Food and Drug Administration warned that this body building product contains a controlled prescription drug (superdrol). **3. Get Stiff, Maxi Mize** New Zealand's Medsafe warned that these sexual enhancement products contain prescription drugs (tadalafil, vardenafil, yohimbine) and/or unauthorized drugs (hydroxyhomosildenafil, hydroxythiohomosildenafil). **4. Ying Da Wang tablets** The Australian Therapeutic Goods Administration warned that this sexual enhancement product contains a prescription drug (sildenafil). **5. Slimina weightloss capsules, S-shape slim capsules** The Australian Therapeutic Goods Administration warned that these weight loss products contain prescription drugs (propranolol, nifedipine) and/or unauthorized drugs (sibutramine, fenfluramine, phenolphthalein). **6. Athri-Eze, Sear Heang Tienchi Tu Chung Wan, Wiku Jahe Kencur (Akur Mujarab), Cap Wijaya Kusuma (An Ki It)** The Singapore Health Sciences Authority warned that these Traditional Chinese or Traditional Malay Jamu products contain prescription and/or over-the-counter drugs (dexamethasone, prednisolone, furosemide, allopurinol, acetaminophen, chlorpheniramine), and/or an unauthorized drug (phenylbutazone). **7. Cardiotium, Paidusu, SlimEasy Herbs Capsule, Tianran Zuanshi Xianweisu** The Hong Kong Department of Health warned that these health products contain prescription drugs (losartan, atorvastatin, thyroxine) and/or unauthorized drugs (sibutramine, phenolphthalein). Consult a health care practitioner immediately if you have taken "Cardiotium" while pregnant. The use of losartan during pregnancy can cause injury and even death to the fetus. **8. [LuShenPai] Specific Hou Ton Qing, [AA] Pe Min Kan Wan** The Hong Kong Department of Health warned that these traditional Chinese health products contain excessive levels of heavy metals (arsenic or mercury).

Health Canada Feb/12 is advising Canadians that using "MMS", also known as **Miracle Mineral Solution or Miracle Mineral Supplement** may cause serious health problems. The product information lists sodium chlorite as an ingredient and is promoted as a substance that can cleanse toxins from the human body.

Health Canada Feb/12 seized a variety of **Stiff4Ever** and **PurePillz** products from The Love Shop retail outlets located in Ontario. These products are unauthorized drugs and are considered potentially dangerous to the health and safety of Canadians. Health Canada tested the Stiff4Ever products, advertised as male sexual stimulants, and identified sildenafil. The labels of the PurePillz products (see below) state that they contain BZP and TFMPP. Benzylpiperazine (BZP) is a synthetic substance with stimulant-like effects, while 3-trifluoromethylphenylpiperazine

(TFMPP) is a synthetic substance with hallucinogen-like effects.

Health Canada Mar/12 **Power-X**" has been removed from a Canadian retail location after Health Canada's testing identified undeclared thiodimethylsildenafil which is similar to the prescription medication sildenafil.

Health Canada May/12: Unauthorized health products, **"X-Rock", "Kaboom" and "One For Her"** have been removed from sale from various retail outlets in British Columbia and Saskatchewan. Health Canada's testing identified undeclared prescription drugs sildenafil and tadalafil, and an undeclared substance, hydroxythiohomosildenafil, which is similar to sildenafil.

Health Canada May/12 **1. CanSui; Lexscl Fat Rapid Loss Capsule; The Extreme-thin Fat Burning Bomb; Xiu Zhi Su L-Carnitine Slimming Capsule** The Hong Kong Department of Health warned that these weight loss products contain unauthorized drugs (sibutramine, phenolphthalein). **2. Jin Yu Tang Tai Han Kang Pai Pu Ling Jiao Nang; TangBaoKouFuYiDaoSuJiaoNang; Tangren 365 Kangxunpai sangge huoyisu jiaonang; Tong Ren Xiu Fu Kou Fu Yi Dao Su** The Hong Kong Department of Health warned these products, promoted to control high blood sugar, contain a combination of prescription drugs (metformin, glibenclamide [also known as glyburide], rosiglitazone, glimepiride, hydrochlorothiazide) and unauthorized drugs (phenolphthalein, phenformin). **3. [Chung Lien Kulin Brand] Anshen Bunai Pian** The Hong Kong Department of Health warned that this traditional Chinese health product, used for insomnia, contains excessive levels of the heavy metal mercury. **4. Lipro Diet Pills; Xiyouji Qingzhi weight loss capsules** The Australian Therapeutic Goods Administration warned that these weight loss products contain an unauthorized drug (sibutramine). **5. AdvanceMen capsules; Miraculous Evil Root tablets** The Australian Therapeutic Goods Administration warned that these sexual enhancement products contain either a prescription drug (sildenafil) or an unauthorized drug (sulfoaildenafil).

Health Canada June/12 **1. African Black Ant; France T253; Hard Ten Days; Man King; Stree Overlord** : The U.S. Food and Drug Administration warned that these sexual enhancement products contain prescription drugs (sildenafil. One product also contains tadalafil). **2. RegenArouse; RegenErect:** The U.S. Food and Drug Administration informed of a recall because these sexual enhancement products contain a prescription drug (tadalafil). **3. Mince Belle; Everlax; Ever Slim; Ever Slim Shake Mix (Strawberry); Ever Slim Shake Mix (Chocolate); Acai-Man Mangosteen Herbal Drink; Perfect Men:** The U.S. Food and Drug Administration informed of a recall because these weight loss and sexual enhancement products contain prescription drugs (sibutramine or tadalafil). **4. Japan Weight Loss Blue, Japan Rapid Weight Loss Diet Pills Green; Japan Rapid Weight Loss Diet Pills Yellow:** The U.S. Food and Drug Administration warned that these weight loss products contain prescription drugs (sibutramine, ephedrine alkaloids) and unauthorized drugs (phenolphthalein, and substances similar to sibutramine). **5. Koff & Kold; Kold Sore:** The U.S. Food and Drug Administration informed of a recall because these cough and cold products were found to be non-sterile. **6. Ling Zhi She Xiang Tong Mai Dan:** The Hong Kong Department of Health warned this health product contains a prescription drug (dexamethasone). **7. Q & N Omega Tree:** The Singapore Health Sciences Authority informed of a recall after this product was found to contain controlled drug substances (cannabinol and tetrahydrocannabinol (THC)).

Health Canada June/12 **Natural Vigor Maximum** (Exemption Number: 138273) has been removed from sale from various retail outlets in Ontario after testing by Health Canada identified a hidden ingredient (dimethylhomosildenafil).

Health Canada Jun/12 testing has identified that the weight loss product "**ZXT Gold**" bee pollen capsules contain hidden pharmaceutical ingredients (sibutramine and phenolphthlalein).

Health Canada July/12 **Lightning Rod**, an unauthorized sexual enhancement product, has been removed from sale from various retail outlets in Ontario, British Columbia and Saskatchewan after testing by Health Canada identified a hidden ingredient (hydroxythiohomosildenafil).

Health Canada July/12 "**Fu Fang Zaoren Jiaonang**": A Potentially Dangerous Product for Pregnant Women. "Fu Fang Zaoren Jiaonang," an unauthorized natural health product promoted for anxiety and/or insomnia, has been removed from sale after testing by Health Canada confirmed the presence of the ingredient L-tetrahydropalmatine that could cause damage to vital organs such as the liver, most notably in pregnant women.

Health Canada July/12 **Vine Essence** has been recalled after testing by Health Canada identified a quantity of lead that exceeds Departmental acceptable limits and low levels of undeclared acetaminophen.

Health Canada Aug/12 These products are not authorized for sale in Canada and have not been found on the Canadian market, but they may have been brought into the country by travellers or purchased over the Internet. **1. Boost – Ultra Sexual Enhancement Formula; EreXite; Mojo Nights:** The U.S. Food and Drug Administration advised consumers not to buy or use these products after they were found to contain one or more of the following undeclared drug ingredients: tadalafil, sildenafil, and unauthorized substances similar to sildenafil that may pose similar health risks. **2. Firminite; Extra Strength Instant Hot Rod; Libidron:** The U.S. Food and Drug Administration informed consumers of a company recall after these products were found to contain undeclared tadalafil. **3. [Hu Qiu] Niu Huang Xiao Yan Wan:** The Hong Kong Department of Health warned consumers to not use this product after it was found to contain an excessive level of mercury. **4. Instant Hard Rod; RigiRx Plus; ZenMaxx**: The U.S. Food and Drug Administration advised consumers not to buy or use these products after they were found to contain undeclared aminotadalafil, which is similar to tadalafil and may pose similar health risks. **5. VMaxx Rx:** The U.S. Food and Drug Administration informed consumers of a company recall of certain lots of *VMaxx Rx* after the product was found to contain undeclared sulfoaildenafil.

Health Canada Aug/12: **Burnaby, B.C. Store (U-Box) Selling Potentially Dangerous Weight Loss Products.** Further to our previous communications, Health Canada is advising Canadians that four products promoted for weight loss have been seized from "U-Box," a store in Burnaby, B.C. Health Canada testing has identified they contain hidden drug ingredients (sibutramine and phenolphthalein) that may pose serious health risks. Caffeine was also found in some of the products and was not listed on the product label.

Health Canada Sep/12: **Zhuifeng Tougu Wan**", an unauthorized natural health product, is being voluntarily recalled after testing identified levels of mercury that are far beyond the allowable limit set by Health Canada.

Health Canada Oct/12 The natural health product "**Pollen Allergy**" (NPN 80035736), now sold as "**Tongqiao Biyan Pian**," is being recalled from the Canadian market after testing conducted by Health Canada identified levels of arsenic that exceed Departmental allowable limits.

Health Canada Dec/12 Three unauthorized health products -- "**Man Up Now", "Black Ant", "Triple Power Zen Gold 1200mg**"-- are being recalled by DVDXPRO after testing by Health Canada identified undeclared ingredients-sildenafil and/or tadalafil.

Health Canada Dec/12 is advising Canadians that three unauthorized products "**Goya Bittermelon", "S-organic Cocoa+L-carnitine", or "KaBaNa L-Carnitine 360 Slimming Coffee**", promoted for weight loss have been seized from "Cube Inc.", a box-store in Richmond, B.C. These products contain hidden drug ingredients (sibutramine and phenolphthalein) that may pose serious health risks. Caffeine was also found in two products and was not listed on the product label.

Health Canada Dec/12 is advising Four unauthorized natural health products have been removed from sale as they may pose serious risks to the health of Canadians. The "**ExtenZe**" products are promoted as sexual enhancement products and contain ingredients that legally require they be sold with a prescription in Canada. ExtenZe Max Strength Gelcaps, ExtenZe Original Tablets, ExtenZe Natural Female Tablets, and ExtenZe Big Cherry Flavour Liquid: Three of these unauthorized products list the prescription ingredient pregnenolone and the controlled drug DHEA (dehydroepiandrosterone) & three of these unauthorized products contain the prescription medication yohimbine (either as yohimbine HCl or as yohimbe extract).

Health Canada Jan/13: 1) **Muscletech Hydroxystim capsules**- The Australian Therapeutic Goods Administration (TGA) warned consumers not to purchase or use this product after it was found to contain 1,3-dimethylamylamine (DMAA), a drug that is not approved for sale in Canada. **2. [W.S.] Tian Ma Toutong Wan; Shi Hu Ye Guang Wan (Ye Guang Wan); Nai Chang Ming Yan Pills (Ming Yan Pills); [Fung Shing Pai] Tian-Ma Wan; Bak Foong Pills (11 products) .** The Hong Kong Department of Health has warned consumers not to purchase or use certain batches of these products after they were found to contain excessive levels of lead or mercury.

Health Canada Feb/13: Two unauthorized health products "**18 Again" and "Stiff 4 Hours**" were tested by Health Canada and were found to contain hidden ingredients (sildenafil or tadalafil) that may pose serious risks to the health of Canadians.

Health Canada Mar/13: An unauthorized natural health product, "**Libigrow**" was tested by Health Canada and found to contain hidden ingredients (sildenafil and tadalafil) that may pose serious risks to the health of Canadians. "Libigrow" was being sold at two retail locations in the province of Québec: Boutique Sexie folie Inc. (Sainte-Catherine) and at Boutique Érotique 5ième avenue Inc. (Valleyfield).

Health Canada Apr/13 **1. Diet Garcinia Forte; Shan Dian Shou; Aulura Energy Dietary Supplement** The Hong Kong Department of Health has advised consumers not to use these products after they were found to contain sibutramine and phenolphthalein, drug ingredients that were not declared on their product label. Shan Dian Shou also contains the undeclared prescription drug sildenafil. **2. Snake Powder Capsule for Rheumatism; Jia Rong Zhuang Gu Tong Bi Jiaonang; Long Ren Tang Fu She Gu Rang Jiao Nang** The Hong Kong Department of Health advised consumers not to use these products after they were found to contain multiple prescription and non-prescription drugs that were not declared on their product label.

(prednisone, indomethacin, diclofenac, hydrochlorothiazide, cimetidine, prednisone, theophylline, dexamethasone etc). **3. Tinea Schwartz's; Tiao Jing Bu Xue Pills; Yeung Ng Tong Tin Hee Pills** The Hong Kong Department of Health advised consumers not to use these products after they were found to contain prescription drugs that were not declared on their product label (prednisone, indomethacin, diclofenac). **4. Quan Xie Jin Gu Tong; Xinhuang Pian; Jin Gu Feng Shi Kang Jiao Nang** The Hong Kong Department of Health advised consumers not to use these products after they were found to contain multiple prescription and non-prescription drugs that were not declared on their product label. (prednisone, piroxicam, diclofenac, indomethacin, naproxen).

Health Canada May/13 Two unauthorized health products — **"Stiff Nights" and "Stiff 4 Hours"** — were tested by Health Canada and were found to contain hidden ingredients (sildenafil and/or tadalafil) that may pose serious risks to the health of Canadians. The products were being sold at Saints N Sinners Ltd, 1715 Centre Street N.W., Calgary, Alberta.

Health Canada June/13 is advising Canadians not to use these foreign health products as they may pose a health risk. **1. Flutulang, Kapsul Gaut (Asam Urat), and True ProLife Vegrow** The Health Science Authority of Singapore advised consumers not to use these products after they were found to contain phenylbutazone, chlorpheniramine, dexamethasone, and a chemical compound similar to the prescription drug sildenafil.
2. Jinmaoshiwang tablets, Naturally Kouxan Best Slim capsules, and Majestic Slimming capsules The Australian Therapeutic Goods Administration advised consumers not to use these products after they were found to contain sildenafil, sibutramine and phenolphthalein. **3. WOW, Super Power and SLIMDIA Revolution** The U.S. Food and Drugs Administration (FDA) warned consumers not to use these products after they were found to contain diclofenac sodium, methocarbamol, dexamethasone, sildenafil and sibutramine. **4. Libigrow XXXtreme, Blue Diamond, Blue Diamond Platinum, Mojo Nights Supreme, and Casanova** The U.S. Food and Drugs Administration warned consumers not to use these products after they were found to contain sildenafil, sulfoaildenafil and thioaildenafil.

Health Canada Aug/13 is advising Canadians not to use these foreign health products as they may pose a health risk. **1. Brazilian Slimming Coffee, Leisure 18 Slimming Coffee, 7 Days Slimming Coffee, Brazilian 7 Days Slimming Coffee, Beauty Secret Slimming Coffee, Body Beauty 5 Days Slimming Coffee, Leisure 18 Slimming Mango Juice, Leisure 18 Slimming Orange Juice, Authentic Leisure 18 Slimming Orange Juice, Super Slim Orange Juice, Coffee Fashion Slimming** The Hong Kong Department of Health has advised consumers not to use these products after they were found to contain the undeclared drug ingredients sibutramine and/or phenolphthalein. http://healthycanadians.gc.ca/recall-alert-rappel-avis/hc-sc/2013/34859a-eng.php **2. Steelman Capsules 2** The Hong Kong Department of Health has advised consumers not to use this product after it was found to contain undeclared aminotadalafil. http://healthycanadians.gc.ca/recall-alert-rappel-avis/hc-sc/2013/34861a-eng.php **3. CO Feng Shi Gu Tong Ning Jiao Nang** The Hong Kong Department of Health has advised consumers not to use this product after it was found to contain undeclared prednisone, diclofenac, ibuprofen, hydrochlorothiazide, metoclopramide and trimethoprim. http://healthycanadians.gc.ca/recall-alert-rappel-avis/hc-sc/2013/34861a-eng.php **4. Fu Fang Feng Shi Gu Kang Ling Jiao Nang** The Hong Kong Department of Health has advised consumers not to use this product after it was found to contain undeclared prednisone, diclofenac, ibuprofen, indomethacin, piroxicam and metoclopramide. http://healthycanadians.gc.ca/recall-alert-rappel-avis/hc-sc/2013/34861a-eng.php **5. Best Slim capsules, Meizi Evolution Botanical Slimming soft gel capsules** The Australian Therapeutic Goods Administration warned consumers not to use these products after they were found to contain the undeclared drug sibutramine. http://healthycanadians.gc.ca/recall-alert-rappel-avis/hc-sc/2013/34869a-eng.php **6. Libigirl capsules** The Australian Therapeutic Goods Administration warned consumers not to use this product after it was found to contain the undeclared prescription drugs sildenafil and tadalafil. http://healthycanadians.gc.ca/recall-alert-rappel-avis/hc-sc/2013/34869a-eng.php **7. Albuterex Xtreme Formula** The Australian Therapeutic Goods Administration has warned consumers not to use this product after it was found to contain undeclared theophylline, yohimbine and high amounts of undeclared caffeine. http://healthycanadians.gc.ca/recall-alert-rappel-avis/hc-sc/2013/34863a-eng.php **8. Albutarex Xtreme and Albutarex Femme Formula** The Australian Therapeutic Goods Administration has warned consumers not to use these products after they were found to contain undeclared theophylline and high amounts of undeclared caffeine. http://healthycanadians.gc.ca/recall-alert-rappel-avis/hc-sc/2013/34863a-eng.php

Health Canada Aug/13 **Prema G** (Granules packaged in tea packets, NPN: 80035944) was tested by Canada Border Services Agency and found to contain a hidden ingredient (hydroxyhomosildenafil thione).

Health Canada Oct/13 is warning consumers not to use unauthorized **Compound Danshen Dripping Pills** after it was associated with a Canadian case of methemoglobinemia, a rare but serious condition which may result in coma or death.

Health Canada Oct/13 Natural health product (**Spectrazyme**) recalled due to potential contamination with the antibiotic chloramphenicol. Metagenics Canada, in consultation with Health Canada, is voluntarily recalling its natural health product "Spectrazyme" – a digestive aid – due to a possible contamination with chloramphenicol, an antibiotic that may pose serious health risks to consumers.

Health Canada Oct/13 Natural health product (**Flora Essentials**) recalled due to potential contamination with the antibiotic chloramphenicol.

Health Canada Oct/13 Natural health products (**Kamizym-U and Kamizym+)** recalled due to potential contamination with the antibiotic chloramphenicol.

Health Canada Oct/13 wishes to inform Canadians that seized natural health products being sold by Lion King Health Enterprises Group Ltd., 1328-8368 Capstan Way, Richmond, BC. were tested and found to contain hidden ingredients and unauthorized substances similar to the prescription drug, sildenafil. (**North America Dami Ana 600mg, South America Maca 600mg, Ashwagandha 600mg, Optimusman 350mg, Superman 350mg, Innerget Instant Erection (NPN#80041194), Innerget Prolonged Performance (NPN#80041194), Innerget Everlasting Strength (NPN#80041194), Megaton 2080**.)

Health Canada Nov/13 is advising Canadians not to use these foreign health products as they may pose a health risk. These products have been found by regulators in other countries to contain drug ingredients or soy milk allergens that are not declared on the product labels, or a high level of microbial contamination. Prescription drugs should only be taken under the supervision of a healthcare professional. These products are not authorized for sale in Canada and have not been found on the Canadian market, but they may have been brought into the country by travellers or purchased over the Internet:

1. **Protein Extract and artiph**en http://healthycanadians.gc.ca/recall-alert-rappel-avis/hc-sc/2013/36237a-eng.php ;
2. **Aisiyuan V26 Slimming Granules, AcaiBerry Living-XS, and 4C Cosmoslim** , http://healthycanadians.gc.ca/recall-alert-rappel-avis/hc-sc/2013/36269a-eng.php ;
3. **MAXILOSS Weight Advanced** http://healthycanadians.gc.ca/recall-alert- rappel-avis/hc-sc/2013/36197a-eng.php;
4. **14 sexual enhancement products** http://healthycanadians.gc.ca/recall-alert-rappel-avis/hc-sc/2013/36233a-eng.php ;
5. **Ginseng Baji Gu Ci Wan, Tu Chong Ginseng Wan Le Seang and X-Tract Nature** http://healthycanadians.gc.ca/recall-alert-rappel-avis/hc-sc/2013/36359a-eng.php ;
6. **Ziyinzhuangyang tablets, Maxman III, and Mojo Risen** http://healthycanadians.gc.ca/recall-alert-rappel-avis/hc-sc/2013/36519a-eng.php ;
7. **Kyuwei** http://healthycanadians.gc.ca/recall-alert-rappel-avis/hc-sc/2013/36515a-eng.php ;
8. **ESV Extra Strong Version, MSV Strong Version, RL Rapid Loss, My Slimmer Me (MSM) soft gel capsules, Natural Miaotiaoyishen capsules, and Paiyouji Natural Slimming Capsules** http://healthycanadians.gc.ca/recall-alert-rappel-avis/hc-sc/2013/36521a-eng.php.

Health Canada Dec/13 has updated the list of natural health products seized from **Lion King Health Enterprises Group** Ltd., 1328 - 8638 Capstan Way, Richmond, B.C. that have been tested and found to contain hidden ingredients and unauthorized substances similar to the prescription drug tadalafil.

Health Canada Dec/13 General Nutrition Centres Company (GNC), in consultation with Health Canada, is voluntarily recalling its natural health product "**Women's Phytoestrogen Formula**" – used for the relief of menopausal symptoms – due to possible contamination with chloramphenicol.

Health Canada Dec/13 testing of an unauthorized natural health product, **MaxHIMize**, found it to contain bacteria (Enterococcus durans and Bacillus spp) and undeclared caffeine that could present a risk to health. MaxHIMize is being promoted as a dietary supplement and for erectile dysfunction.

Health Canada Feb/14: 1. **Hairegenerator** The Hong Kong Department of Health warned consumers not to use this product after samples of the product were found to exceed the permissible limit for mercury. The level of mercury exceeds Health Canada's acceptable limits as well. 2. **Li Long Mei Guo Mo Bang, and Ginseng Tu chong Wan Lin Heong** The Singapore Health Sciences Authority warned consumers not to use this product after it was found to contain sildenafil, a drug ingredient that was not declared on the product label. 3. **Lightning 10.0+, LV Shou Reduces Fat, and STB Summit of the Thin Body S Woman Degreasing Burning Pill** The Hong Kong Department of Health warned consumers not to use this product after it was found to contain sibutramine, phenolphthalein, and indomethacin.

Health Canada Mar/14 is advising Canadians not to use these foreign health products as they may pose a health risk. 1. Xiang Gang Tian Long Sheng Wu Ke Ji Di Qi Dai Chi Jiu Zhan Shen http://www.healthycanadians.gc.ca/recall-alert-rappel-avis/hc-sc/2014/38599a-eng.php was found to contain **sildenafil**. 2. Various Sexual Enhancement Products http://www.healthycanadians.gc.ca/recall-alert-rappel-avis/hc-sc/2014/38577a-eng.php was found to have **sildenafil** and **tadalafil.** 3. Majestic Slim Perfect and Yixiu L-Carnitine Slimming Capsules http://www.healthycanadians.gc.ca/recall-alert-rappel-avis/hc-sc/2014/38609a-eng.php was found to contain **sildenafil** and **phenolphthalein.**

Health Canada Mar/14: **Zyrexin**, tested by Health Canada at the border was found to contain a hidden prescription drug ingredient **(Yohimbine)** .

Health Canada Apr/14 has seized the unauthorized drug, "**L-Showm Weight Loss Pills**", being sold at the U-Box store, located at 2809-4500 Kingsway, Burnaby, BC. Health Canada testing found that it contained an undisclosed ingredient, phenolphthalein.

Health Canada Apr/14: Four unauthorized drugs being sold at two SVN FUEL stores - one in Burnaby and one in Coquitlam, B.C. - were seized by Health Canada as they contain ingredients that are potentially dangerous to the health of consumers. The products, and the unapproved ingredients they contain, include **Jack3d** (DMAA (1, 3-dimethylamylamine), **Red Rockets** (ephedrine and caffeine), **West Pharm Therma Lean** (ephedrine and caffeine), and **OxyElite Pro** (1, 3-dimethylamylamine HCl and Yohimbe Bark extract). They were being promoted for weight management.

Health Canada Apr/14: 1) **San Xiao Ping Tang Jin Qi Jiao Nang**: The Hong Kong Department of Health warned consumers not to use this product after it was found to contain phenformin, pioglitazoneand glibenclamide**. 2) Volcano Male Enhancement** liquid & caps: The U.S. Food and Drug Administration warned consumers not to use these products after they were found to contain desmethyl carbodenafil, dimethylsildenafil and dapoxetine**. 3) Dr. Larry's Tranquility**: The U.S. Food and Drug Administration warned consumers not to use this product after it was found to contain undeclared doxepin and chlorpromazine.

Health Canada Apr/14: Nano Well-being Health Inc. issued a voluntary recall of **Super Arthgold**, 500 mg capsules to the consumer level. FDA laboratory analysis has found the product to contain chlorzoxazone, diclofenac and indomethacin, making it an

unapproved new drug.

Health Canada May/14 **Blue Stinger** contains sulfoaildenafil**; 72 HP, Evil root and Pro Power Max** contains sildenafil**; Esbelin siloutte te, Esbelin Siloutte Herbal blend with L-Carnitine, Esbelder man**, **Esbelder fem, Esbelder siloutte** contains Sibutramine, N-Desmethylsibutramine, and N-di-Desmethylsibutramine; **Instant Slim** contains sibutramine and phenolphthalein; **Jack Rabbit** contains sildenafil and tadalafil**; Live Clinical 90 caps** contains milk, **Ortiga** contains diclofenac.

Health Canada May/14 One lot of **Lite Fit USA** (Lot Number 13165, Exp. 05/17) is being voluntarily recalled in the U.S. after analysis by the U.S. Food and Drug Administration revealed the lot contains the undeclared prescription drug sibutramine.

Health Canada May/14 has requested that Christmas Natural Foods Ltd. stop selling and recall its unauthorized health product, **Heartland Natural Wild Yam Moisturizing Cream**, after testing conducted by the Department identified a undisclosed prescription drug ingredient, progesterone.

Health Canada May/14: 1. **VitaliKOR**: FDA found vardenafil and tadalafil**;** 2. **Slim Fortune, Lidiy & Slim Expert** FDA found sibutramine**;** 3. **Vigor Tea sachets:** Australian Therapeutic Goods Administration found sulfoaildenafil**;** 4. **Prolifta capsules, PHUK and Virilis Pro:** FDA found **sildenafil;** 5. **Dr. Mao Slimming capsules, Perfect Body Solutions, Burn 7**: FDA found sibutramine; **Bella Vi Insane Amp'd Up, Be Inspired, Goodliness Fat Reducing capsules, Jimpness Beauty Fat Loss capsules**: FDA found sibutramine and phenolphthalein; 6. **Nature Most Laboratories Vanilla Almond, and Strawberry Banana Whey Power products**: FDA found undeclared milk, soy and almond allergens**;** 7. **Wood-E, Xzen Gold, Xzen XPress, XZen 1200, and XZone Premium**: FDA found Wood-E contains sildenafil, Xzen Gold and Xzen XPress contain sildenafil and tadalafil, & XZen 1200 contains tadalafil.

Health Canada June/14: **Bali Mojo & Vimax** contains tadalafil., **LOVher capsule**s contains tadalafil, sildenafil and diclofenac. **Erec-Bull,** contains yohimbine. **Best Whips & JINQIANGBUDOR Red Dragon** contains sildenafil. **Super Hard t**ablets contains sildenafil. **CONTROL All Natural Sexual Enhancement** contains sulfoaildenafil and dimethylsildenafil. **Phen Tabz contains dimethylamylamine (DMAA). Asset Extreme, Asset Extreme Plus, Meizitang Citrus, Slimming Diet Berry Plus, Citrus Fit Gold, Hot Detox, Thinogenics** contains sibutramine. **Tonic Life BP & Slimfast capsules** contains phenolphthalein . **Dr**. **Ming's Chinese Capsule**, **Magic Slim and Apple's Quic**k **Impact Weight Loss** contains sibutramine and phenolphthalein. **Pro ArthMax** contains diclofenac, ibuprofen, naproxen, indomethacin, chlorzoxazone. **Adipotrim XT** contains fluoxetine. **StemAlive** contains milk.

Health Canada July/14: **Wing Cheong Tong] Bak Feng Pill, [Yee On Tong] Bak Feng Pill, and Beijing Bak Feng Pill**: The Hong Kong Department of Health warned consumers not to use these products after they were found to contain excessive levels of lead. **Bella Vi Insane Bee Pollen Capsules, Bella Vi BTrim Ultimate Boost, Bella Vi BTrim Max, Bella Vi Extreme Accelerator**: The United States Food and Drug Administration (FDA) warned consumers not to use these products after they were found to contain undeclared sibutramine and/or phenolphthalein. **Super Fat Burner capsules, Maxi Gold capsules, and Esmeralda softgels**: The United States Food and Drug Administration (FDA) warned consumers not to use these products after they were found to contain undeclared sibutramine and phenolphthalein. **MME Naturally Maxman capsules, Blue Fantasy capsules, African Superman tablets, and MosKa** – energy for adults: The Australian Therapeutic Goods Administration (TGA) warned consumers not to use these products after they were found to containsildenafil. **Powerful leg-slimming capsules, Pink grain herbal slimming capsules, and Night fat-burning capsules**: The Australian Therapeutic Goods Administration (TGA) warned consumers not to use these products after they were found to contain undeclared phenolphthalein and diclofenac. The product, Night fat-burning slimming capsules, was also found to contain undeclaredtheophylline. **Zi Xiu Tang Pollen capsule and Zi Xiu Tang Beauty Face and Figure capsule**: The Australian Therapeutic Goods Administration (TGA) warned consumers not to use these products after they were found to contain undeclared sibutramine, phenolphthalein, diclofenac, and ibuprofen. The product, Zi Xiu Tang Beauty Face and Figure capsule, was also found to contain undeclared glibenclamide, and indomethacin.

Health Canada Aug/14 is informing healthcare professionals about a suspected drug interaction between **efavirenz (Sustiva) and ginkgo biloba**. The report is based on a 2012 published case report involving a Canadian patient with HIV infection.(1)

Heath Canada Aug/14: The United States Food and Drug Administration (FDA) warned consumers not to use the products **MV5 Days and S.W.A.G**., and the Australian Therapeutic Goods Administration (TGA) warned consumers not to use the product **Zhansheng Weige Cahoyue Xilishi tablets**, after they were found to contain sildenafil. The Australian Therapeutic Goods Administration (TGA) warned consumers not to use the product **Sanovera Starter capsules**, the Hong Kong Department of Health warned consumers not to use the product **Yanhee Slim** and the United States Food and Drug Administration (FDA) warned consumers not to use the products **Infinity, Asset Bee Pollen, Asset Bold, Slim Trim U, and Natural Body Solution** after they were found to contain undeclared sibutramine. The Medicines and Healthcare Products Regulatory Agency (United Kingdom) warned consumers not to use the product **Shwasa Sanjeevani** and the Singapore Health Sciences Authority warned consumers not to use the product **Golden Dragon Linzi Dong Mai Dan** after they were found to contain dexamethasone. The Singapore Health Sciences Authority warned consumers not to use **Herbal Health Jointcare** after it was found to contain betamethasone-17-valerate, furosemide, piroxicam, chlorpheniramine and famotidine. The Australian Therapeutic Goods Administration (TGA) warned consumers not to use **Robust tablets** after it was found to contain aminotadalafil. The Australian Therapeutic Goods Administration (FDA) warned consumers not to use **3x Slimming Powder Capsules** after it was found to contain undeclared sibutramine and phenolphthalein. The Singapore Health Sciences Authority warned consumers not to use **Herbal Health RU Special Cream, Herbal Health YI Special Cream, Herbal Health JI Special Cream, and Herbal Health XIANG Special Cream** after they were found to contain chlorpheniramine, clotrimazole, miconazole and terbinafine. The Singapore Health Sciences Authority warned consumers not to use **Herbal Health V+** after it was found to contain sildenafil and tadalafil. The Singapore Health Sciences Authority warned consumers not to use **Herbal Health Backplus** 500mg after it was found to contain tadalafil.

Health Canada Sep/14: **La Jiao Shou Shen, B-Perfect, Diet Master, Super Slim, Slim Max**: The United States Food and Drug Administration (FDA) warned consumers not to use these products after they were found to contain undeclared sibutramine and phenolphthalein. **Sport Burner** :The United States Food and Drug Administration (FDA) warned consumers not to use the product Sport Burner after it was found to contain undeclared fluoxetine. Health Canada Sep/14: **Gold Vigra, Liu Bian Li, GoldReallas, Black Ant Strong, My Man His Enhancer 12 Pack, Top Man 3 and Vigour 800**: The United States Food and Drug Administration (FDA) warned consumers not to use the products **Gold Vigra, Liu Bian Li and GoldReallas**, and the Australian Therapeutic Goods Administration (TGA) warned consumers not to use the products **Black Ant Strong, My Man His Enhancer 12 Pack, Top Man 3 and Vigour 800**, after they were found to contain sildenafil.

Dick's Hard Up, P-Boost, and NatuRECT: United States Food and Drug Administration (FDA) warned consumers not to use these products after they were found to contain tadalafil. **3 Hard Knights**: The United States Food and Drug Administration (FDA) warned consumers not to use this product after it was found to contain sildenafil andthiosildenafil. **Germany Niubian**: The Australian Therapeutic Goods Administration (TGA) warned consumers not to use the product after it was found to contain sildenafil and zopiclone. **Alpha Male**: The United States Food and Drug Administration (FDA) warned consumers not to use this product after it was found to contain sildenafil,aminotadalafil, sulfosildenafil, sulfoaildenafil, hydroxythiohomosildenafil, and dimethylsildenafil. **REDDES (or REDDIES)** and **The Rock**: The Australian Therapeutic Goods Administration (TGA) warned consumers not to use these products after they were found to containsulfosildenafil and hydroxyhomothiosildenafil. **Full Throttle On Demand**: The United States Food and Drug Administration warned consumers not to use this product after it was found to contain propoxyphenyl sildenafil. **RezzRX**: The United States Food and Drug Administration warned consumers not to use this product after it was found to containhydroxythiohomosildenafil and/or aminotadalafil. **Play Hard for Men**: The Australian Therapeutic Goods Administration (TGA) warned consumers not to use this product after it was found to contain yohimbine andhydroxyhomothiosildenafil. **Rhino 5 Plus, Maxtremezen, and Extenzone**: The United States Food and Drug Administration warned consumers not to use these products after they were found to contain desmethylcarbondenafil and dapoxetine. Health Canada Sep/14: **JIN LONG Snakes Bones Rheumatic Capsules**- The Singapore Health Sciences Authority warned consumers not to use this product after it was found to contain betamethasone, piroxicam,oxethazaine, paracetamol (also known as acetaminophen) and furosemide.

Health Canada Oct/14 is warning Canadians of the serious risks to health associated with use of the unauthorized drug product **Miracle Mineral Solution (MMS),** which was sold as a treatment for serious diseases such as cancer through the website www.buymms.biz. MMS contains sodium chlorite, which is a chemical used mainly as a textile bleaching agent and disinfectant and may pose serious risks to health if ingested. An alternate format of MMS, labelled as CDS, is also available for sale on the website and would pose a similar risk.

Health Canada Nov/14: An unauthorized health product, **Gra-MaxX Gold**, was seized by Health Canada as it contains an undeclared drug: N-Ethyl Tadalafil.

Health Canada Nov/14: A vendor in Atlantic Canada (www.health-recovery-info.com) is selling **Miracle Mineral Solution (MMS),** an unauthorized drug product (containing sodium chlorite) which Health Canada has previously warned may pose serious risks to health if ingested.

Health Canada Dec/14 is following up with Rapha Biotech Inc. **RAPHA Vitamin B1** (NPN: 80036493) -- undeclared ingredients: sibutramine, desmethyl sibutramine. **Gra-MaxX Gold** (yellow label) -- undeclared ingredient: N-ethyl tadalafil. **Rapha Diet** (700 mg, 270 Capsules) -- undeclared ingredient: caffeine. **Rapha Diet** (630 mg, 270 Capsules) -- undeclared ingredients: amphetamine, methamphetamine.

Health Canada Dec/14: "**Herberex**" (NPN 80041180) is being recalled nationwide after Health Canada testing confirmed it contains an undeclared drug: tadalafil.

Health Canada Dec/14: **Hydro-Lean** was seized from two Calgary stores because the label indicates it contains a combination of ingredients that can cause serious health risks (ephedrine and caffeine).

Health Canada Dec/14: "**Jetfuel Superburn**" is being recalled after Health Canada tests confirmed it contains two undeclared amphetamine-like drug substances that pose serious health risks (beta-methylphenethylamine and phenylpropylmethylamine).

Health Canada Dec/14: The United States Food and Drug Administration (FDA) warned consumers not to use the products **Lingzhi Cleansed Slim Tea, Trim-Fast Slimming Softgel, Sliming Diet By Pretty White, Lipo 8 Burn Slim, and Best Line Suplemento Alimenticio Capsules**. Tthe Hong Kong Department of Health warned consumers not to use the products **Slim Perfect Arm and Slim Perfect Legs** and the Australian Therapeutics Goods Administration (TGA) warned consumers not to use the product **Slyn Both Green capsules** after they were found to contain undeclaredsibutramine. The United States Food and Drug Administration (FDA) also warned consumers not to use the product **Mezo** after it was found to contain benzylsibutramine. **Mix Fruit Slimming**: The United States Food and Drug Administration (FDA) warned consumers not to use this product after it was found to contain undeclaredsibutramine and phenolphthalein.

Health Canada Dec/14: The Australian Therapeutic Goods Administration (TGA) warned consumers not to use the products **Zhansheng Weige Chaoyue Xilishi, Chong Cao Zhag Bian Bao, Night Man, and MMC Sex Men capsules** and the United Stated Food and Drug Administration (FDA) warned consumers not to use the product **O.M.G.** after they were found to contain sildenafil. **Arize**: The United Stated Food and Drug Administration (FDA) warned consumers not to use the product Arize after it was found

to containsulfoaildenafil. **Herbal Vigor Quick Fix**: The United Stated Food and Drug Administration (FDA) warned consumers not to use the product **Herbal Vigor Quick Fix** after it was found to contain tadalafil.

Health Canada Dec/14: **LX1**: The United States Food and Drug Administration (FDA) warned consumers not to use this product after it was found to contain undeclared1,3-dimethylamylamine (DMAA).

Health Canada Dec/14: **Joint-Soft**: The Singapore Health Sciences Authority warned consumers not to use the product **JOINT-SOFT** after it was found to contain piroxicam anddexamethasone. The Singapore Health Sciences Authority warned consumers not to use the product **KEBIGUTAIJIAONANG** after it was found to containpiroxicam, hydrochlorothiazide, and prednisone. The Singapore Health Sciences Authority warned consumers not to use the product **Pil Raja Urat Asli** after it was found to contain piroxicam and indomethacin.

Health Canada Dec/14: **Bo Ying compound**: The United States Food and Drug Administration (FDA) warned consumers not to use this product after it was found to contain high levels of lead.

Health Canada Dec/14: "**Forta for Men**" (NPN 80045132) is being recalled after Health Canada testing confirmed it contains an undeclared drug: homosildenafil.

Health Canada Dec/14: Samson's Supplements stores in Calgary that pose a risk to health. **Nutrex Research Lipo6 Black, Nutrex Research Lipo6 Black Hers, Nutrex Research Lipo6 Unlimited, Nutrex Research Lipo6 Black Ultra Concentrate, West Pharm Yohimbe** Extract (bottle of 50 and 100 capsules), **West Pharm Yohimbe Extract** (bottle of 50 and 100 capsules), **NutraKey Yohimbine** HCl contains Yohimbine. **West Pharm Xtra Lean, West Pharm ThermaLean, West Pharm ThermoMAXXX** (bottle of 80 and 160 capsules), **Twinlab Ripped Fuel** contains Ephedrine and Caffeine. None of the products are approved for sale. The products are promoted for body building purposes, including for weight loss and increased energy, or for sexual enhancement.

Health Canada Jan/15: **Star Majestic Slimming**- Undeclared sibutramine & phenolphthalein via Australian Therapeutic Goods Administration. **Sit and Slim II**-Undeclared sibutramine & phenolphthalein via FDA.
Ginseng Kianpi Pil- Undeclared dexamethasone & chlorpheniramine via FDA. **Mayhem**- Undeclared dexamethasone & cyproheptadine via FDA.
Du Zhong Jin Gu Wan- Undeclared dexamethasone, chlorpheniramine & diclofenac via Singapore Health Sciences Authority.

Health Canada Jan/15 is reminding Canadians about the risks of purchasing unlicensed **home-use diagnostic** test kits following recent compliance and enforcement actions undertaken by the Department.

Health Canada Feb/15: Two unauthorized health products that may pose serious health risks were removed from sale by Health Canada. These products, "**MRM DHEA**" (labelled to contain DHEA) and "**Altimate Fat Burner Maximum Burn**" (labelled to contain DHEA, Yohimbe, caffeine and ephedrine) were being sold by Nature's Source, Unit #7, 2943 Major Mackenzie Drive, Vaughan, Ontario.

Health Canada Mar/15 advises- FDA Mar/15 **ABC Dophilus Powder**: undeclared fungus(Rhizopus oryzae). **Feng Shi Ling**: undeclared diclofenac & indomethacin. FDA Mar/15 **Bee Slim** & **Bee Thin** has undeclaried silbutramine.
FDA Mar/15 **Black Storm**: undeclared sildenafil. Australian Therapeutic Goods Administration **Max Hard**: undeclared sildenafil & aminotadalafil. **Rock Hard**: undeclared tadalafil. Singapore Health Sciences Authority Mar/15:
SPARTA X: undeclared hydroxyhomosildenafil & hydroxythiohomosildenafil. Singapore Health Sciences Authority Mar/15: **MAGIC PENIS** undeclared sildenafil. Singapore Health Sciences Authority Mar/15
MR ZACK POWERBRO: undeclared propoxyphenyl hydroxyhomosildenafil, propoxyphenyl aildenafil, propoxyphenyl thiohydroxyhomosildenafil & propoxyphenyl thioaildenafil. Singapore Health Sciences Authority Mar/15
Nutri Drops Grapefruit Diet: Undeclared sibutramine undeclared benzyl sibutramine & phenolphthalein.

Health Canada Mar/15 advisory regarding "**Altimate Fat Burner Maximum Burn**" being sold by Nature's Source in Vaughan, Ont., the Department received a complaint about the product also being sold at Nature's Source, 2391 Trafalgar Rd., Unit #6 in Oakville, Ont. Altimate Fat Burner Maximum Burn is an unauthorized health product labelled to contain DHEA, yohimbe, caffeine and ephedrine.

Health Canada Apr/15 testing has found that two unauthorized health products, "**Enhance**" and "**Natural-Power**," contain undeclared sildenafil.

Health Canada Apr/15: St. Francis Herb Farm "**Bulklax V**" and "**All Seasons Detox Kit**" recalled due to high levels of lead and/or arsenic.

Health Canada Apr/15 has suspended the licences of two natural health products containing the ingredient male fern (**Dryopteris filix-max**), "**Paranil**" and "**W.-W**. Safety information has raised potential concerns regarding effects of the specific ingredient at higher doses. Using the affected products may pose a serious health risk.

Health Canada Mar/15 is reminding Canadians that consuming a product sold as "**Miracle Mineral Solution**" (MMS) may pose serious health risks, following a Health Canada seizure of an MMS product from a vendor in Burin, Newfoundland on March 25, 2015.

Health Canada Apr/15 has suspended the licence of Filix Mas, a homeopathic product, because it contains the ingredient male fern (**Dryopteris filix-max**).

Health Canada May/15 **NaturaLyte Sodium Bicarbonate Liquid Concentrate** - Possible Bacterial Contamination - Fresenius Medical Care Canada, Inc.

Health Canada May/15 Recall of "**Galenic Health Ginger in Bentonite**" due to unacceptable levels of lead for children and adolescents.

Health Canada May/15 is warning consumers that an unauthorized drug, "**Stiff Rock**" promoted for male sexual performance enhancement was seized from Boutique Érotique 5ième avenue (also known as Boutique Érotique Liberté), 507 Gande-Île, Valleyfield, QC after Health Canada testing confirmed that the product contained drug ingredients: sildenafil; aminotadalafil; and hydroxythiohomosildenafil.

Health Canada Jun/15 is warning consumers that **Body Bentonite Unique Healing Powder** by Donna Pessin was found to contain high levels of metals

Health Canada Jun/15 requests quarantine of drugs linked to **Zhejiang Hisun Pharma** due to data integrity concerns.

Health Canada Jun/15: Three unauthorized health products that may pose serious risks to the health of Canadians were seized by Health Canada. The products, "**Sport X Ephedrine**", "**DHEA 25**" and "**Promatrix DHEA 25**" were being sold by S&H Health Foods, 2150 Burnhamthorpe Rd. W., Mississauga.

Health Canada Jul/15 is advising Canadians that it has received a serious domestic adverse reaction report of abnormal heart rhythms associated with the ingestion of "**Remogen**" (containing **ibogaine**), an unauthorized natural health product in Canada that may pose serious health risks. Canadians who have used this product and have concerns about their health should speak with their healthcare practitioner.

Health Canada Jul/15: Recall of Additional Lots of **NaturaLyte Sodium Bicarbonate** Liquid Concentrate due to Potential Bacterial Contamination.

Health Canada aug/15 is advising consumers that it is introducing label changes for certain homeopathic products that fall under the Natural Health Product Regulations (NHPR). More particularly, Health Canada is requesting the addition of statements on **homeopathic nosode products to make it clear that they are not vaccines or alternatives to vaccines** to improve the safe use of these products.

Health Canada Aug/15-Australian Therapeutic Goods Administration has **Golden Root Complex Capsules & Bushen Famous Men Capsules & Laopiaoke Capsules** with undeclared sildenafil.

Health Canada Aug/15-FDA has **Akttive Capsules & Zero Xtreme Capsules** with undeclared silbutramine.

Health Canada Nov/15:**Dragon Power**, an unauthorized product sold at The Herb Depot, 407-409 Dundas Street West, Toronto, Ontario, was found to contain an undeclared sildenafil.

Health Canada Nov/15: Various **Ayurvedic medicinal products** were found to contain high levels of heavy metals which may pose serious health risks. These products are not authorized for sale in Canada and have not been found on the Canadian market, but they may have been brought into the country by travellers or purchased over the Internet. (**Brahmi Vati Buddhivardhak; Bruhat Vata Chintamani Rasa; Chandraprabha Vati; Punarnavadi Mandoor; Yogaraja Guggulu**)

Health Canada Dec/15 informed Canadians that an unauthorized health product, **Natrol DHEA** 25 mg, was being sold on amazon.ca for hormonal management. This product may pose a serious risk to the health of Canadians.

Health Canada Dec/15: **Mega Power** contains tadalafil .

Health Canada Dec/15: **Biseptol 480** contains sulfamethoxazole & trimethoprim.

Health Canada Dec/15: **Naproxen E**mo contains naproxen.

Health Canada Dec/15: **Oxycort** contains oxytetracycline & hydrocortisone.

Health Canada Dec/15: **Herba Pini Syrop** contains codeine.

Health Canada Feb/16: "**Forta for Men**", is being recalled after testing confirmed one lot contains an undeclared drug: tadalafil.

Healh Canada Feb/16 is advising Canadians who purchased **Novodalin B17**, an unauthorized natural health product claiming to treat cancer to stop using the product and contact their doctor for appropriate follow-up. No health products containing B17 or amygdalin have been authorized by Health Canada to treat cancer or any other condition. Novodalin B17 being sold online by cdnf.com also poses serious risks to health as it is labelled to contain apricot kernel extract. Apricot kernels may contain amygdalin, a compound derived from bitter apricot kernels that has the potential to release cyanide when ingested by humans

Health Canada Feb/16 is advising Canadians that a number of potentially dangerous unauthorized health products labelled as **B17/amygdalin/bitter apricot kernel** were available for sale in Canada.

Health Canada Mar/16: **Forta for Men Daily, Forta Xpload and Durazest For Men Volume**- may contain an undeclared drug: sildenafil.

Health Canada Mar/16 says S **Lion Juice Orange 10 gm** by Singapore Health Science Authority undeclared propoxyphenyl thioaidenafil.

Health Canada Mar/16 says **S Lion Juice 20 gm** by Singapore Health Science Authority undeclared thiodimethylsildenafil.

Health Canada Mar/16 says **S Lion Juice 10 gm** by Singapore Health Science Authority undeclared thiodimethylsildenafil and tadalafil.

Health Canada Mar/16 says **S Lion Juice 1** by Singapore Health Science Authority undeclared aminotadalafil and thiodimethylsildenafil

Health Canada Mar/16 says **Rhino 7 3000 & Rhino 7 Platinum 3000 Capsules** by FDA contains undeclared desmethyl carbondenafil and dapoxetine.

Health Canada Mar/16 says **Power Khan** by FDA contains undeclared sildenafil and thiosildenafil.

Health Canada Mar/16 says Australian Therapeutic Goods Administration: **Hongkong Tianli Biological 'Power' tablets, Longue Jambe Frères (Brother Long Legs) tablets** contains undeclared sildenafil.

Health Canada Mar/16 says Asia Black**, Black Widow 25, Burn Fat Now, Extreme Stack, Fataway Ultimate Stack, MaxOut Body, Metabolic Accelerator, Methyldrene Original 25 Dietary Supplements, ThermoFX, Thermogenic Fat Burner & Thin and Slim Naturally** by FDA contains undeclared salicylic acid.

Health Canada Mar/16 says **BASCHI Quick Slimming capsules** by Australian Therapeutic Goods Administration contains undeclared sibutramine.

Health Canada Mar/16 says **Basha Nut 100% Fruit Soft Gel Capsules**, **Ultimate Herbal Slimcap, Lishou Slimming Coffee, Meizi Super Power Fruits Herbal Slimming Formula, NATUREAL & Tip-Top Shape** by FDA contains undeclared sibutramine.
Health Canada Mar/16 says **Miracle Diet 30 & Xtreme Fat Burner Capsules** by FDA contains undeclared phenolphthalein.
Health Canada Mar/16 says **New Queen Slimming soft gel capsules** by Australian Therapeutic Goods Administration contains undeclared sibutramine.
Health Canada Mar/16 says **Perfect Slim Fast Track Slim & Slyn Both** by FDA contains undeclared fluoxetine
Health Canada Mar/16 says **Pink Bikini and Shorts on the Beach Blue Edition & Pink Bikini and Shorts on the Beach Blue Gold Edition** by FDA contains undeclared sibutramine and phenolphthalein.
Health Canada Mar/16 says **Super Herbs** by FDA contains undeclared sibutramine and desmethylsibutramine
Health Canada Mar/16 says **Baidyanath brand Agnitundi Bati, Baidyanath brand Arogyavardhini Bati, Baidyanath brand Brahmi Bati, Baidyanath brand Chitrakadi Bati, Baidyanath brand Gaisantak Bati, Baidyanath brand Marichyadi Bati, Baidyanath brand Rajahpravartini Bati, Baidyanath brand Saptamrit Lauh, Baidyanath brand Sarivadi Bati, Baidyanath brand Shankh Bati,** by FDA contains undeclared elevated levels of lead and mercury.
Health Canada seized six unauthorized products being promoted as dietary supplements from Herc's Nutrition, 175 Fletchers Creek Blvd., Brampton, Ontario.
(**RapidFire, Black Magic, China White & Lipo-Cuts** contains Yohimbine and ephedra. **Hydroxycut Hardcore Next Gen & Psychotic** contains Yohimbine.
Health Canada Mar/16: **Ejaculoid & Animal Test & Dust V2**: Yohimbine.
Health Canada Mar/16: **RSE7EN**: Desmethyl carbodenafil & dapoxetine, **Extreme Diamond 2000**: Desmethyl carbodenafil, **Master Zone 1500 & MV7 days 3500 or 2000**: Sildenafil & tadalafil, **Black Magic & Rock Hard Weekend**: Sildenafil, **Black Panther**: Sildenafil & desmethyl carbodenafil & dapoxetine, **Mamba is Hero**: Sildenafil & dimethyl carbodenafil & dapoxetine, **Black Mamba premium**: Desmethyl carbodenafil & dapoxetine,
Health Canada Apr/16: Australian Therapeutic Goods Administration says **100% healthy food for men tablets, & V-MAX Herbal Tablets** contains undeclared sildenafil.
Health Canada Apr/16: is advising Canadians that an unauthorized drug, **URX Bombshell**, labelled to contain prescription drug substances (yohimbine and rauwolfia), was being sold on Kijiji and at DiscountSupplementsCo.com
Health Canada Apr/16 seized seventeen unauthorized health products from the retailer, **Matrioshka Russian Delicatessen**, in Calgary, Alberta. Two unauthorized products were labelled with prescription drug ingredients (captopril and sulfanilamide).
Health Canada May/16 is warning Canadians not to purchase or use '**LifeGive'** health products to treat diseases such as cancer and dementia.
Health Canada May/16 seized an unauthorized product being promoted as a dietary supplement, **Animal Test**, from Supplement King, 1250 Brant Street, Unit 9a, Burlington, Ontario. This product contains yohimbine, a prescription drug ingredient.
Health Canada June/16: Australian Therapeutic Goods Administration-**Excellence Losing Weight capsules** contains undeclared silbutramine & Natural Model capsules contains undeclared sibutramine and phenolphthalein.
.Health Canada June/16: Singapore Health Sciences Authority-**Meizitang Botanical Slimming 100% Natural Soft Gel** contains undeclared diclofenac.
Health Canada June/16: FDA says **Boss Number #Six** contains undeclared tadalafil; **Bull & Bull's Genital** contains undeclared sildenafil; **Ginseng Power-X** contains undeclared sildenafil and sulfoaildenafil; **Golden Night** contains undeclared sildenafil and hydroxythiohomosildenafil; **Neophase Natural Sex Enhancer** contains undeclared hydroxyacetildenafil; **Weekend Prince** contains undeclared sildenafil; & **Wonder-Erect Male Gum** contains undeclared vardenafil.
Health Canada June/16: Australian Therapeutic Goods Administration- **Half Quite tablets** contains undeclared sildenafil; contains undeclared sildenafil and oxytetracycline; **Maxagra capsules** contains undeclared sildenafil and oxytetracycline; **Ninja-X** contains undeclared sildenafil and thiosildenafil; **Sextra capsules** contains Undeclared sildenafil and yohimbine & **Zhong Hua Niu Bian** tablets contains undeclared chloramphenicol and sildenafil.
Health Canada June/16: Australian Therapeutic Goods Administration-**Amazon Tonic III** contains undeclared oleandrin.
Health Canada June/16: FDA says **Bentonite Me Baby** contains elevated levels of lead, Crema Piel de Seda contains elevated levels of mercury, & Licorice Coughing Liquid contains undeclared morphine.
Health Canada June/16 is reminding Canadians about the serious risks posed by the unauthorized product "**Animal Test**,"after identifying additional retailers and a distributor selling the product which contained yohimbine.
Health Canada July/16: FDA says **Best Bentonite Clay** contains elevated levels of lead.
Health Canada July/16: FDA says **Sextra, & Zlimxter Capsules** contains undeclared sildenafil.
Health Canada July/16: FDA says **Dynamizm Capsules, ENVY BP, Propell Platinum, Xerophagy Capsules, & Sextra** contains undeclared sibutramine.
Health Canada July/16: FDA says **Salute Capsules** undeclared sildenafil, thiosildenafil, and sulfoaildenafil.
Health Canada July/16: FDA says **Eradicate Capsules** undeclared sibutramine and desmethylsibutramine.
Health Canada July/16: Australian Therapeutic Goods Administration says **Leisure Slimming capsules** contains undeclared sibutramine and phenolphthalein.
Health Canada July/16: Australian Therapeutic Goods Administration says **U Slimming and U Plus Slimming capsules** undeclared sibutramine, phenolphthalein, diclofenac, and lignocaine.
Health Canada July/16: Australian Therapeutic Goods Administration says **MMC Zang Ba Bao tablets, Super Bull 6000 Herbal capsules, & U.S. Black Gold tablets** undeclared sildenafil.
Health Canada July/16: **Wonderblue & B-Hard on Demand** has undeclared sildenafil as well as thiodimethylsildenafil and/or thiomethisosildenafil.
Health Canada Aug/16 is advising consumers not to use the weight loss product **AlgoSlim**, distributed via mail order by E Sélection. The package does not contain unauthorized AlgoSlim and instead contains an authorized product, Slite-T, from a lot that expired in June 2012.
Health Canada Jul/16 is informing Canadians that two unauthorized health products were seized from Next Level Fitness in Richmond and in Surrey,BC. The products **TRT (Testosterone Booster) and Freak'n Test (Testosterone Enhancer)** were labelled to contain a prescription drug substance (L-dopa) that may pose serious health risks to Canadians.
Health Canada July/16 **DR's Secret Bio Herbs Coffee** undeclared tadalafil
Health Canada July/16 **Exhilarate** undeclared sibutramine, desmethylsibutramine, phenolphthalein.
Health Canada July/16 **Ultimate Nutrition Amino Gold Capsules 1000mg, Ultimate Nutrition Amino Gold Tablets (1000mg) & Ultimate Nutrition Amino Gold Tablets (1500mg)** undeclared milk.
Health Canada Aug/16: Australian Therapeutic Goods Administration-King-**Wolf Tablets** undeclared sildenafil.
Health Canada Aug/16: Australian Therapeutic Goods Administration- **MAGNA-RX Capsules** undeclared sildenafil & acetaminophen.
Health Canada Aug/16: FDA-**My Steel Woody** undeclared sildenafil.
Health Canada Aug/16: Australian Therapeutic Goods Administration- **Black Storm tablets** undeclared sildenafil and vardenafil.
Health Canada Aug/16: FDA- **Dream Body Advanced + Acai Weight Loss & Cleanse, & Dream Body Extreme Gold** undeclared sibutramine, fluoxetine, and sildenafil.
Health Canada Aug/16: FDA- **Dream Body 450mg, Dream Body Original Formula, Dream Body Advanced 400mg, Extra Slim Plus Acai Berry Weight Loss Formula, Lose Weight Coffee & SBF Bee Pollen** undeclared silbutramine.
Health Canada Aug/16: Hong Kong Department of Health- **Lose Weight Coffee** undeclared silbutramine.
Health Canada Aug/16: Hong Kong Department of Health-TANGKE **TEGONGYIHAOJIAONANG** undeclared phenformin and glibenclamide.
Health Canada Aug/16: Hong Kong Department of Health-**4L Slimness and 4L Slimburn Plus** undeclared diclofenac.
Health Canada Sep/16 seized an unauthorized product called "**Black Orange**" from Keebo Sports Supplements at 2101 Quance St., Regina, Saskatchewan. The product is sold as a pre-workout stimulant and is labelled to contain ingredients that can pose serious health risks (yohimbine HCl, a prescription drug, and the combination of ephedrine and caffeine).
Health Canada Sep/16 is advising Canadians that Healthy Body Services Inc. has initiated a voluntary recall of two lots (G4016A and G4016) of Allmax-brand "**Rapidcuts Shredded**" capsules (NPN 80041658) because the product contains a prescription drug (yohimbine hydrochloride) not listed on the label.
Health Canada Sep/16 seized five unauthorized products promoted as workout or weight loss supplements from Keebo Sports Supplements at 1504 St. Mary's Road, Winnipeg, Manitoba. The products are labelled to contain various prescription and other drug substances that may pose serious risks to the health of Canadians. **Yohimbine** by Prime Nutrition contains Yohimbine HCl. **Diesel Fuel Stim** By Tokkyo Nutrition contains Rauwolfia Vomitoria Extract (std. min 90% alpha yohimbinw [sic]) (rootbark). **Amp-Stim** by Logan Carter contains Rauwolfia Vomitoria Extract (std. min 90% alpha yohimbine) (rootbark). **HydroxyElite** by Hi-Tech Pharmaceuticals, Inc. contains 1,3 Dimethyamylamine HCl. **Andro Quad** by Primeval Labs contains Epiandrosterone 4-androsterone.
Health Canada Sep/16 is informing Canadians that Healthy Body Services Inc. is expanding its voluntary recall of Allmax-brand "**Rapidcuts Shredded**" capsules (NPN 80041658). All lots are now being recalled as a precaution after certain lots were found to contain an undeclared prescription drug (yohimbine hydrochloride).
Health Canada Oct/16: **Anaconda Strong Formula, Boss-Rhino Gold X-tra Strength, De Guo Hei Bei (德国黑鹏), Libigirl, Power Spring (XXX) Oral Liquid, Shangai Ultra X, Super Shangai, The Golden Root, Weili (一炮到天亮or Yi Pao Dao Tian Liang) , Ziyinzhuangyang**, -Undeclared sildenafil by United States Food and Drug Administration.
Health Canada Oct/16: **Ant Power tablets, Man King capsules**, -Undeclared sildenafil by Australian Therapeutic Goods Administration.
Health Canada Oct/16: **Golden Ant tablets**-Undeclared sildenafil and chloramphenicol byAustralian Therapeutic Goods Administration.
Health Canada Oct/16: **Xcelerated Weight Loss Ultra Max**- Undeclared phenolphthalein and sildenafil by United States Food and Drug Administration.
Health Canada Oct/16: **Adelganzantes R-II, Mang Luk Power Slim, Xcelerated Weight Loss Charged Up, & Xcelerated Weight Loss Turbo Charge**--Undeclared sibutramine by United States Food and Drug Administration.
Health Canada Oct/16: **B-finn**- Undeclared orlistat and 2-(diphenylmethyl)pyrrolidine (desoxy-D2PM)by Hong Kong Department of Health.
Health Canada Oct/16: **Citrus' Fit, Mang Luk Power Slim Detox, Slim Fit X, & Ultimate Lean** -Undeclared sibutramine and desmethylsibutramine by United States Food and Drug Administration.

Health Canada Oct/16: **Double S**- Undeclared sibutramine by Hong Kong Department of Health.
Health Canada Oct/16: **Maxx Easy**-Undeclared sibutramine and lorcaserin, and orlistat by United States Food and Drug Administration.
Health Canada Oct/16: **Mi Show Slimming capsules**- Undeclared sibutramine by Australian Therapeutic Goods Administration.
Health Canada Oct/16: **Xcelerated Weight Loss Ultra Max**- Undeclared phenolphthalein and sildenafil by United States Food and Drug Administration.
Health Canada Oct/16: **Zi Xiu Tang Beauty Face and Figure Capsule**- Undeclared phenolphthalein and fluoxetine by United States Food and Drug Administration.
Health Canada Oct/16 has requested that **SurThrival** voluntarily recall all lots of its colostrum products because they contain undeclared milk allergens, which may pose serious health risks to people who are allergic or hypersensitive to cow's milk.
Health Canada Oct/16 is informing Canadians that the product **Nature's Power Solutions Acidophilus Blend** contains undeclared milk allergens.
Health Canada Nov/16: **One More Knight 1750** has undeclared tadalafil and dapoxetine by the United States Food and Drug Administration.
Health Canada Nov/16: **Love4Long** has undeclared sildenafil by the United States Food and Drug Administration.
Health Canada Nov/16: **Kopi Jantan Tradisional Natural Herbs Coffee** has undeclared desmethyl carbodenafil by the United States Food and Drug Administration.
Health Canada Nov/16: **Natural Eruption** has undeclared sibutramine by the United States Food and Drug Administration.
Health Canada Nov/16: **DHZC-2 Tablet** has elevated levels of lead by the United States Food and Drug Administration.
Health Canada Nov/16: **Snake Powder Capsules** has undeclared dexamethasone, chloramphenicol, chlorpheniramine, ibuprofen, and tetracycline by the Singapore Health Sciences Authority.
Health Canada Nov/16: **JC Gold** has undeclared dexamethasone, dexchlorpheniramine, and frusemide (furosemide) by the Singapore Health Sciences Authority.
Health Canada Nov/16: **Tu Cho Pan Chi Pain** has undeclared dexamethasone, chlorpheniramine, and frusemide (furosemide) by the Singapore Health Sciences Authority.
Heallth Canada Nov/16: "**Phytovie Acore Vrai Calamus" herbal tea**, an unauthorized natural health product, is being recalled after Health Canada testing found it to contain excessive levels of beta-asarone.
Health Canada Dec/16 reports: Australian Therapeutic Goods Administration: **Bee Sexy Slimming capsules** undeclared sibutramine; Australian Therapeutic Goods Administration: **Biolo World Slimming capsules**-undeclared sibutramine and phenolphthalein; Hong Kong Department of Health: **ele Slim Shot**-undeclared orlistat; Singapore Health Sciences Authority: **LifeSparks 100% Natural PAIN RELIEF SUPPLEMENT**- undeclared chlorpheniramine, dexamethasone, diclofenac, paracetamol (acetaminophen), piroxicam, sulphamethoxazole; Singapore Health Sciences Authority: **LONGRED Oyster-x**-undeclared sildenafil; FDA: **Stiff Bull Herbal Coffee**-undeclared desmethyl carbodenafil; & Australian Therapeutic Goods Administration: **Wolfish Shark Viagra** tablets-undeclared sildenafil.
Health Canada Dec/16 is advising Canadians that the unauthorized product "**Control-Max**" may pose serious health risks as it is labelled to contain a prescription drug (yohimbine).
Health Canada Dec/16 is advising Canadians that three unauthorized products, "**Lithium Plus, Serotonin Support, and Brain Support**," may pose serious health risks because they may contain the prescription drug Lithium Orotate.
Health Canada Jan/17 is advising Canadians that it has seized the unauthorized health product "**Blow**", by Limitless Pharma, from Atomik Nutrition at 450 Boulevard de Mortagne, Boucherville, QC. "Blow" is promoted as a pre-workout supplement and is labelled to contain the unauthorized drug 1,3 Dimethylamylamine (DMAA), which may pose serious health risks such as high blood pressure and stroke.
Health Canada Jan/17 is advising Canadians that it has seized unauthorized health products being sold at 24 Hour Adult Mart on Yonge St., Toronto, ON. Three of the seized products are "**poppers**" labelled to contain alkyl nitrites.
Health Canada Jan/17 is advising Canadians that it has seized three unauthorized workout supplements from Reflex Supplements at #105–10712, 78 Ave., Grande Prairie, AB. "**Animal PM**" is labelled to contain L-dopa while "**Blade**" is labelled to contain yohimbine.
Health Canada Feb/17 is advising Canadians that a safety review has found a risk of serious skin burns with the use of certain over-the-counter (OTC) topical pain relievers containing **menthol**.
Health Canada Feb/17 is advising Canadians that it has seized unauthorized health products promoted as workout, weight loss and dietary supplements from **Atomik Nutrition** at 102-90 Boul. Saint-Jean-Baptiste, Châteauguay, QC (see table below). The products are labelled to contain various drugs, including prescription and controlled drugs, **Dymethazine**: Osmo Pharma-17ß–hydroxy–2α,17–dimethyl–5α–androstan–3–one azine; **DHEA**: Osmo Pharma- Dehydroepiandrosterone (DHEA); **Amped**:Osmo Pharma-Corynanthe Extract (Pausinystalia Yohimbe Bark); **Exo-13 Exothermic Fatburner**: Prime Nutrition-1,3-Dimethylamylamine, Caffeine Anhydrous, Yohimbine HCl, Bitter Orange Extract 30%; **Insane Cutz**: Insane Labz-Rauwolfia Vomitoria Extract (std. min. 90% alpha Yohimbine); **Yohimbine HCl**:Primaforce-Yohimbine HCl; & **Dust Extreme**: Blackstone Labs- 1,3 DMAA (Dimethylamylamine), Caffeine Anhydrous.
Health Canada Mar/17: 90° **Jiushidu Capsules, African Viagra, Big Penis Male Sexual Stimulant, Black Mamba 2 Premium, Black 3K Plus Male Sexual Enhancement Capsules, Bl4ck 4K Capsules, Duramaxxx, Power Male Sexual Stimulant, Rhino 5 1500 Capsules, Rhino 7K 9000 Male Performance Booster, Rhino 8 Platinum 8000, Rhino 9 Premium 3500 & Triple Green Capsules** contains undeclared sildenafil.
Health Canada Mar/17: **Megajex Natural Male Sex Enhancer Dietary Supplement** contains undeclared sildenafil & tadalafil.
Health Canada Mar/17: **Queen Slimming Soft Gel** contains undeclared sibutramine
Health Canada Mar/17: **VIP Bio Mangosteen Complex** contains undeclared sibutramine & phenolphthalein.
Health Canada Mar/17 is advising Canadians that the unauthorized health product "**PureCare Herbal Cream**" may pose serious health risks. The product is promoted as a natural treatment for eczema and psoriasis in children and babies. Health Canada testing confirmed the presence of a prescription steroid (clobetasol propionate) and another ingredient (phenoxylethanol) not declared on the product label.
Health Canada Mar/17: **Chao Jimengnan Super Powerful Man Tablets & Zhen Gongfu capsules** has undeclared sildenafil by the Australian Therapeutic Goods Administration.
Health Canada Mar/17: **GoldReallas Original & GoldReallas XXX** has undeclared sildenafil & thiosildenafil by the FDA.
Health Canada Mar/17: **Impeous Man capsules** has undeclared sildenafil & phenolphthalein by the Australian Therapeutic Goods Administration.
Health Canada Mar/17: **Old Chinese & Shenjingpian** has undeclared sildenafil by the FDA.
Health Canada Mar/17: **XtraHRD** has undeclared N-desmethyl tadalafil by the FDA.
Health Canada Mar/17: **CA NI Slim BELLANCE** has undeclared orlistat by the Hong Kong Department of Health.
Health Canada Mar/17: **Lean Extreme Max & X-treme Beauty Slim** has undeclared sibutramine by the FDA.
Health Canada Mar/17: **Platinum Max Strength Blue Pill Version, Slimming Plus Advanced & Platinum Weight Loss Solution** has undeclared sibutramine & phenolphthalein by the FDA.
Health Canada Mar/17 is advising Canadians that it has seized multiple unauthorized health products from three retailers in Ontario (see table below). The products are promoted for sexual enhancement and were found to contain, or are labelled to contain, prescription drugs that may pose serious risks to the health of Canadians. Hespeler Road Adult SuperStore (261 Hespeler Road, Cambridge ON): **LipsTenZen, Super Panther 7K & Thunder Bull 7K** contains Yohimbe. **One More Knight** contains tadalafil and dapoxetine. **MV7 Days 2000** contains sildenafil and tadalafil. Naughty Shop (330 Wellington Rd. S, London ON): **LipsTenZen, Super Panther 7K & Triple Green** contains Yohimbe. VXI Multimedia (800 Petrolia Road, Unit 18, Toronto, ON): **Opti-Sildenafil** 100 mg contains sildenafil, **Opti-Tadalafil** 20 mg contains tadalafil.
Health Canada Apr/17 is advising Canadians that it has seized the unauthorized injectable health product "**Botulax**" and unauthorized medical sutures "**The Lift II**" from SPMU-MTS Studio, at 8788 McKim Way, Unit 1200, in Richmond, BC. Both products may pose serious risks to the health of Canadians.
Health Canada Apr/17 is advising Canadians that the unauthorized health product "**Rhino Blitz Gold**" may pose serious health risks, after testing confirmed it contains an undeclared prescription drug (sildenafil).
Health Canada Apr/17 is warning Canadians about unauthorized health products, including unauthorized prescription drugs, sold **online at sarms.ca.**
Health Canada Apr/17 laboratory tests have confirmed that two additional unauthorized products seized from **24 Hour Adult Mart in Toronto** contain undeclared tadalafil.
Health Canada May/17 is advising Canadians that it has seized the unauthorized health product "**Dust Extreme**" by Blackstone Labs, from Minotaure Nutrition, in Terrebonne, QC. "Dust Extreme" is promoted as a pre-workout supplement and is labelled to contain the unauthorized drug 1,3 Dimethylamylamine (DMAA).
Health Canada May/17 is advising Canadians that it has identified two unauthorized health products, "**Super Panther 7K**" and "**Triple Green**," sold at Rixxx Adult Store at 2839 Saint Joseph Boulevard in Ottawa, ON. The products are promoted for sexual enhancement and are labelled to contain yohimbe.
Health Canada May/17: **Africa Black Ant capsules & Australia Kangaroo Essence** by Australia Therapeutic Goods Administration has undeclared sildenafil.

Health Canada May/17: **Arouse-Plus & Bazook Bullet** by FDA has undeclared tadalafil.
Health Canada May/17: **Anyang Herbal Blue** by Singapore Health Sciences Authority has undeclared sibutramine.
Health Canada May/17: **Anyang Herbal Red** by Singapore Health Sciences Authority has undeclared diclofenac, phenolphthalein, and sibutramine.
Health Canada May/17: **Change Me Herbal Slimming Capsules & Ultimate & Herbal Slim Weight Loss capsules** by Australia Therapeutic Goods Administration has undeclared sibutramine.
Health Canada May/17: **Placebo tablets** by Australia Therapeutic Goods Administration has undeclared clenbuterol.
Health Canada May/17 is advising Canadians that the unauthorized health products "**Black Mamba 2 Premium**" and "**ExtenZe**" are labelled to contain drugs that may pose serious health risks (DHEA, pregnenolone, and yohimbe/yohimbine).
Health Canada May/17 is advising Canadians that **Garnoff Botanicals** is voluntarily recalling unauthorized "High By Nature" kratom products (Mitragyna speciosa) because they may pose serious health risks when swallowed or inhaled.
Health Canada May/17 is advising Canadians that multiple unauthorized health products seized from **two retailers in Scarbofrough, ON**, may pose serious risks to health. Products seized include "poppers" and products promoted for sexual enhancement.
Adult Store 2365 Eglinton Ave E Scarborough ON had Rochfort 10mL-Isobutyl nitrite; Finegra-100-Sildenafil; Super Panther 7K-Yohimbe; Premium X Pulse 2000-Yohimbe; Premium Pro Power 3500-Yohimbe bark extract; Hard Rock 3800-Yohimbe bark extract; XXL Ant 3000-Yohimbe bark extract; Black Mamba 2 Premium-Yohimbe; Mamba is Hero-Yohimbe, sildenafil, desmethyl carbodenafil and dapoxetine; Master Zone 1500- Sildenafil and tadalafil. Homerama Adult Video 2524 Eglinton Ave E Scarborough had ONWet XXX-Yohimbe; 7K-Yohimbe; Super Panther 7K-Yohimbe; Passion Classic- Yohimbe; Titanium 4000-Sildenafil and tadalafil. Adult Store 2365 Eglinton Ave E Scarborough ON had Zhen Gongfu-previous testing of product with similar packaging, identified as containing undeclared sildenafil; Stiff Rock- previous testing of product with similar packaging, identified as containing undeclared sildenafil; One For Her- previous testing of product with similar packaging, identified as containing undeclared tadalafil; Rush 10mL, Super Rush 10mL & Blue Boy 10mL-previously seized products with similar packaging were labelled to contain alkyl nitrites. Homerama Adult Video 2524 Eglinton Ave E Scarborough ON had Rush 10mL, Super Rush 10ml, Jungle Juice Gold Label 10mL, Jungle Juice Gold Label 30mL, Jungle Juice Platinum 10mL, & Jungle Juice Platinum 30mL previously seized products with similar packaging were labelled to contain alkyl nitrites.
Health Canada May/17 is advising Canadians that multiple unauthorized products labelled to contain **L-tryptophan or lithium orotate** were being sold on amazon.ca, and may pose serious health risks.
Health Canada Jun/17 is advising Canadians that RGR Canada Inc. is voluntarily recalling unauthorized "**Matrix Red Vein Thai**," "**Matrix White Vein Thai**" and "**Medicine Man Lone Wolf**" **kratom** capsules.
Health Canada June/17: **VENERGY Capsule** 100mg has undeclared sildenafil by the Hong Kong Department of Health.
Health Canada June/17: **Nangen Zengzhangsu** undeclared sildenafil by Australia Therapeutic Goods Administration.
Health Canada June/17: **Lose Weight capsules** has undeclared sibutramine and diclofenac by Australia Therapeutic Goods Administration.
Health Canada June/17: **Slim-Vie Slimming Capsules** has undeclared sibutramine, sildenafil, and phenolphthalein by Australia Therapeutic Goods Administration.
Health Canada June/17: **PHQ 1001 Khasiat Penawar Herba Qaseh Serata Herb** has undeclared dexamethasone, piroxicam, griseofulvin and paracetamol by Singapore Health Sciences Authority.
Health Canada June/17: **TONIK TUAN HAJI 1921** has undeclared dexamethasone by Hong Kong Department of Health.
Health Canada Jun/17 is advising Canadians that the unauthorized sexual enhancement product "**Super Panther 7K,"** labeled to contain a drug (yohimbe).
Health Canada Jun/17 is advising Canadians that it has seized unauthorized "**Jupiter**" and "**Kratom Zone**" kratom products from two retail stores in Edmonton, AB. Kratom may pose serious health risks when swallowed or inhaled.
Health Canada Jun/17 is advising Canadians that the unauthorized sexual enhancement product "**Rhino 69 Extreme 10K**" may pose serious health risks because its label says that it contains a prescription drug (yohimbe extract (bark)).
Health Canada Jul/17 is advising Canadians that it has seized several unauthorized **kratom products from Culture Rising** at 1248 Main St E, Milton, ON.
Health Canada Jul/17 is advising Canadians that the unauthorized sexual enhancement product "**Black Mamba Premium**" may pose serious health risks because its label says it contains a drug called yohimbe.
Health Canada July/17 is advising Canadians that the unauthorized natural health product promoted as a workout supplement "**Fluffy Unicorn**" may pose serious health risks.
Health Canada laboratory testing found that the product contains undeclared synephrine, and higher levels of caffeine than declared on the label.
Health Canada Jul/17: **Man XXX** has undeclared levodopa by the Australia Therapeutic Goods Administration.
Health Canada Jul/17: **Big N Hard** has undeclared tadalafil by the United States Food and Drug Administration.
Health Canada Jul/17: **Black Gorilla, Maxman IV, Maxman Premium, Maxman V, MMC Maxman XI, New Advanced Technological, V9 Male Sexual Stimulant, Real Skill Male Sexual Stimulant, & Rize N Shine** has undeclared sildenafil by the Australia Therapeutic Goods Administration.
Health Canada Jul/17: **Cummor & Monkey Business** has undeclared N-desmethyl tadalafil by the United States Food and Drug Administration.
Health Canada Jul/17: **Dragon Max, Oh Baby!, & XXXL Penis Enlarging Ointment** has undeclared tadalafil by the Australia Therapeutic Goods Administration.
Health Canada Jul/17: **Tornado** has undeclared nortadalafil by the United States Food and Drug Administration.
Health Canada Jul/17: **Xrect** has undeclared tadalafil and descarbonsildenafil by the United States Food and Drug Administration.
Health Canada Jul/17: **Z Daily** has undeclared homosildenafil by the United States Food and Drug Administration.
Health Canada aug/17 is advising Canadians that "**Selekta Pregnenolone**," an unauthorized prescription product sold online at www.antyler.com, may pose serious health risks.
Health Canada Nov/17: review concluded that there may be a link between the use of **green tea extract** and a risk of rare and unpredictable liver injury.
Health Canada Mar/18 is advising Canadians that **Sisu Inc. has voluntarily recalled numerous natural health products because the glass bottles** that the products are packaged in may contain glass fragments.
Health Canada Mar/18 is advising Canadians that "**Beyond Yourself Multi Athlete**" multivitamin and unauthorized "Multi-Vitamines" sold in bulk were seized from several Shop Santé stores in Quebec because they may pose serious health risks.
Health Canada Mar/18: is advising Canadians that two versions of the sexual enhancement product "**Leopard Miracle of Honey**" may pose serious health risks. Both versions are labelled as being approved by Health Canada, with NPN 80073650.
Health Canada's testing found that both versions of the product contain the undeclared prescription drug sildenafil.
Health Canada Apr/18: is advising Canadians that one lot of "**Organic Traditions Shatavari Powder**" is being voluntarily recalled by Advantage Health Matters Inc. Company testing found Salmonella bacteria contamination.
Health Canada Apr/18: One lot of Traditional Medicinals "**Throat Coat Lemon Echinacea**" herbal tea recalled because of potential contamination with Salmonella
Health Canada May/18 has seized four unauthorized drugs from Gigi's Market, 23 Montreal Road, Ottawa, ON. The products (Ampicillin, Kamox, Medampi and Medomox) are labelled to contain antibiotic drugs (ampicillin or amoxicillin) that can only be dispensed by a healthcare professional to a patient with a valid prescription.
Health Canada May/18 is advising Canadians that it has seized an unauthorized "Botox" product and other unauthorized health products from Arshia Hair Salon and Spa (6062A Yonge Street) in Toronto, ON, because they may pose serious health risks
Health Canada Aug/18: testing **of Jian Pai Natural Skin Care Cream, also called ''Yikangshuang," found that it contains two antifungal drugs (fluconazole and miconazole**) that are not listed on the product label.
Health Canada Sep/18: Canadians should not buy or use health products that contain 2,4-dinitrophenol, more commonly known as **DNP**, because it is toxic and can cause death. Products containing DNP are primarily marketed towards bodybuilders and are promoted online as a "fat burner" or "shredder" and for weight loss.
Health Canada Nov/18 is advising Canadians that **two versions of "Vita-X Revitalizing Capsules" by Lanlay Healthmetic Inc**., promoted for "long lasting vital energy for men," **may pose serious health risks & may contain sildenafil.**
Health Canada Jan/19: inspectors have seized products, ingredients and equipment from A1 Herbal Ayurvedic Clinic Ltd. in Surrey, British Columbia (31-8430, 128 Street), and from an affiliated clinic in Brampton, Ontario (11-351 Parkhurst Square). The seizures came after the British Columbia Centre for Disease Control informed Health Canada of **a case of heavy metal toxicity** involving a patient who was using products from the Surrey clinic. Laboratory testing identified lead and mercury in the products.
Health Canada Jan/19: **Quizz capsules** contain undeclared lead & mercury.

Heck AM, DeWitt BA, Lukes AL. Potential interactions between alternative therapies and warfarin. Am J Health Syst Pharm. 2000 Jul 1;57(13):1221-7; quiz 1228-30. Review.
Hemby SE, McIntosh S, Leon F, et al. Abuse liability and therapeutic potential of the **Mitragyna speciosa (kratom) alkaloids mitragynine and 7-hydroxymitragynine**. Addict Biol. 2018 Jun 27.
Henley DV, Lipson N, Korach KS, Bloch CA. Prepubertal gynecomastia linked to lavender and tea tree oils. N Engl J Med. 2007 Feb 1;356(5):479-85.
Herbal medicines for osteoarthritis. DTB 2012;50:8-12 doi:10.1136/dtb.2011.02.0081.
Herrero-Beaumont G et al. Effects of glucosamine sulfate on a 6-month control of knee osteoarthritis symptoms vs placebo & acetaminophen: Results from the Glucose Unum in Die Efficacy (**GUIDE**) Trial. ACR Meeting Nov 2005.
Herrero-Beaumont G, Ivorra JA, Del Carmen Trabado M, et al. Glucosamine sulfate in the treatment of knee osteoarthritis symptoms: A randomized, double-blind, placebo-controlled study using acetaminophen as a side comparator. Arthritis Rheum. 2007 Jan 30;56(2):555-567 [Epub ahead of print] (n=318 over 6 months)
Herriman M, Fletcher L, Tchaconas A, et al. **Dietary Supplements and Young Teens**: Misinformation and Access Provided by Retailers. Pediatrics. 2017 Jan 2. (**creatine, testosterone**)
Toovey OT, Edmond IR, Makris N. Acute severe hyponatraemia secondary to polydipsia and associated herbal remedy use. BMJ Case Rep. 2016 Sep 28;2016. (? Valerian root)
Hoban CL, Byard RW, Musgrave IF. A comparison of patterns of **spontaneous adverse drug reaction reporting with St. John's Wort and fluoxetine** during the period 2000-2013. Clin Exp Pharmacol Physiol. 2015 Jul;42(7):747-51.

Hochberg MC, Martel-Pelletier J, Monfort J, et al. on behalf of the **MOVES** Investigation Group. Combined **chondroitin sulfate and glucosamine** for painful knee osteoarthritis: a multicentre, randomised, double-blind, non-inferiority trial versus celecoxib. Ann Rheum Dis. 2015 Jan 14.

Hochberg MC, Martel-Pelletier J, Monfort J, et al; **MOVES** Investigation Group. **Combined chondroitin sulfate and glucosamine** for painful knee osteoarthritis: a multicentre, randomised, double-blind, non-inferiority trial versus celecoxib. Ann Rheum Dis. 2016 Jan;75(1):37-44. For patients with painful knee osteoarthritis, a high-dose combination of glucosamine hydrochloride 1500 mg and chondroitin 1200 mg was as effective in lessening pain and stiffness and improving function as **celecoxib** (Celebrex) 200 mg. Other studies have not found benefit. It's time for someone (not me) to really analyze all the studies of chondroitin/glucosamine to determine who is most likely to benefit. (LOE = 1b)

Holbrook AM, Pereira JA, Labiris R, McDonald H, et al. Systematic overview of **warfarin and its drug and food interactions**. Arch Intern Med. 2005 May 23;165(10):1095-106.

Hrastinger A, Dietz B, Bauer R, Sagraves R, Mahady G. Is there clinical evidence supporting the use of botanical dietary supplements in **children**?J Pediatr. 2005 Mar;146(3):311-7.

Hu Z, Yang X, Ho PC, Chan SY, Heng PW, Chan E, Duan W, Koh HL, Zhou S. **Herb-drug interactions: a literature review**. Drugs. **2005**;65(9):1239-82.

Huppertz A, Werntz L, Meid AD, et al. Rivaroxaban and macitentan can be co-administered without dose adjustment but the **combination of rivaroxaban and St. John´s Wort should be avoided**. Br J Clin Pharmacol. 2018 Sep 7.

Hypericum Depression Trial Study Group. Effect of Hypericum perforatum (**St John's wort**) in major depressive disorder: a randomized controlled trial. **JAMA. 2002** Apr 10;287(14):1807-14.

IBISWorld. **Vitamin & Supplement Manufacturing in the US**: Market Research Report.http://www.ibisworld.com/industry/default.aspx?indid=490 Accessed October 12, 2016.

Idan Amanda, Griffiths Kaye A., Harwood D. Tim, et al. Long-Term Effects of **Dihydrotestosterone** Treatment on Prostate Growth in Healthy, Middle-Aged Men Without Prostate Disease: A Randomized, Placebo-Controlled Trial. Ann Intern Med November 16, 2010 153:621-632.

Interactions with herbal products: what do we know? Drug Ther Bull. 2014 Feb;52(2):18-21.

Jagdis A, Sussman G. Anaphylaxis from **bee pollen** supplement. CMAJ 2012.

Jakkula M, Boucher TA, Beyendorff U, et al. A randomized trial of **Chinese herbal medicines** for the treatment of symptomatic hepatitis C. Arch Intern Med. 2004 Jun 28;164(12):1341-6.

Jou J, Johnson PJ. **Nondisclosure of Complementary and Alternative Medicine Use** to Primary Care Physicians: Findings From the 2012 National Health Interview Survey. JAMA Intern Med. 2016 Apr 1

Kahan A, Uebelhart D, De Vathaire F, Delmas PD, et al. Long-term effects of **chondroitins 4 and 6 sulfate** on knee osteoarthritis: The study on osteoarthritis progression prevention, a two-year, randomized, double-blind, placebo-controlled trial. Arthritis Rheum. 2009 Jan 29;60(2):524-533. [Epub ahead of print] We performed an international, randomized, double-blind, placebo-controlled trial in which 622 patients with knee OA were randomly assigned to receive either 800 mg CS (n = 309 patients) or placebo (n = 313 patients) once daily for 2 years. The long-term combined structure-modifying and symptom-modifying effects of CS suggest that it could be a disease-modifying agent in patients with knee OA.

Kantor ED, Rehm CD, Du M, White E, Giovannucci EL. **Trends in dietary supplement use among US adults from 1999-2012**. JAMA. doi:10.1001/jama.2016.14403

Karsch-Völk M, Barrett B, Kiefer D, et al. **Echinacea for preventing and treating the common cold**. Cochrane Database of Systematic Reviews 2014, Issue 2. Art. No.: CD000530. DOI:10.1002/14651858.CD000530.pub3. Echinacea products have not here been shown to provide benefits for treating colds, although, it is possible there is a weak benefit from some Echinacea products: the results of individual prophylaxis trials consistently show positive (if non-significant) trends, although potential effects are of questionable clinical relevance.

Karsch-Völk M, Barrett B, Linde K. **Echinacea** for preventing and treating the common cold. JAMA. 2015 Feb 10; 313(6):618-9.

Kassab S, Cummings M, Berkovitz S, van Haselen R, Fisher P. Homeopathic medicines for adverse effects of cancer treatments. Cochrane Database Syst Rev. 2009 Apr 15;(2):CD004845. This review found preliminary data in support of the efficacy of **topical calendula** for prophylaxis of acute dermatitis during radiotherapy & **Traumeel S mouthwash** in the treatment of chemotherapy-induced stomatitis. These trials need replicating. There is no convincing evidence for the efficacy of homeopathic medicines for other adverse effects of cancer treatments.

Katri Räikkönen et al. **Maternal licorice consumption during pregnancy and pubertal, cognitive and psychiatric outcomes in children**. *American Journal of Epidemiology*, 2017.

Kellermann AJ, C Kloft. Is there a risk of bleeding associated with standardized **ginkgo biloba** extract therapy? A systematic review and meta-analysis. Pharmacotherapy 2011 May;31(5):490–502.

Kemper KJ, Vohra S, Walls R; Task Force on Complementary and Alternative Medicine; Provisional Section on Complementary, Holistic, and Integrative Medicine. American Academy of Pediatrics. The use of **complementary and alternative medicine in pediatrics**. Pediatrics. 2008 Dec;122(6):1374-86.

Kenny AM, Boxer RS, Kleppinger A, et al. **Dehydroepiandrosterone (DHEA)** combined with exercise improves muscle strength and physical function in frail older women. J Am Geriatr Soc. 2010 Sep;58(9):1707-14.

Kim MG, Kim Y, Jeon JY, et al. Effect of fermented **Red ginseng** on cytochrome **P450** and **P-glycoprotein activity** in healthy subjects, as evaluated using the cocktail approach. Br J Clin Pharmacol. 2016 Aug 6

Kleefstra N, et al. **Chromium** tx has no effect in patients with poorly controlled, insulin-treated type 2 diabetes in an obese Western population: a randomized, double-blind, placebo-controlled trial. Diabetes Care. 2006 Mar;29(3):521-5.

Kligler B, Teets R, Quick M. **Complementary/Integrative Therapies That Work**: A Review of the Evidence. Am Fam Physician. 2016;94(5):369-374.

Kobak KA, Taylor LV, Warner G, Futterer R. **St. John's Wort** Versus Placebo in Social Phobia: Results From a Placebo-Controlled Pilot Study. J Clin Psychopharmacol. 2005 Feb;25(1):51-8.

Kobak KA, Taylor LV, et al. **St John's wort** versus placebo in obsessive-compulsive disorder: results from a double-blind study. Int Clin Psychopharmacol. 2005;20(6):299-304.

Kokubo Y, Iso H, Saito I, et al. The impact of **green tea and coffee** consumption on the reduced risk of stroke incidence in Japanese population: The Japan public health center-based study cohort. Stroke 2013 .

Konstantatos A, Shiv Kumar M, Burrell A, et al. An unusual presentation of chronic **cyanide toxicity** from self-prescribed **apricot kernel extract**. BMJ Case Rep. 2017 Sep 11;2017.

Krisanaprakornkit T, Krisanaprakornkit W, Piyavhatkul N, et al. **Meditation therapy** for anxiety disorders. Cochrane Database Syst Rev 2007; 3:CD004998.

Kronenberg F, Fugh-Berman A. Complementary and alternative medicine for **menopausal symptoms**: a review of randomized, controlled trials. Ann Intern Med. 2002 Nov 19;137(10):805-13.

Kuriyama S, et al. **Green tea** consumption and mortality due to cardiovascular disease, cancer, and all causes in Japan: the Ohsaki study. JAMA. 2006 Sep 13;296(10):1255-65. Green tea consumption is associated with reduced mortality due to all causes and due to cardiovascular disease but not with reduced mortality due to cancer. (InfoPOEMs: Green tea consumption is associated with reduced cardiovascular and all-cause mortality, but not cancer mortality. Women appear to benefit more than men: Men's mortality was significantly reduced only in those consuming more than 5 cups per day. Furthermore, there appears to be no benefit of green tea consumption in smokers. (LOE = 2b-))

Kwoh CK, Roemer FW, Hannon MJ, et al. The **Joints on Glucosamine (JOG)** Study: The effect of oral glucosamine on joint structure, a randomized trial. Arthritis Rheumatol. 2014 Mar 11.

Laing C, et al. **Chinese herbal** (**Longdan Xierganwan**) uropathy and nephropathy. Lancet. 2006 Jul 22;368(9532):338.

Larsson SC, Wolk A. **Tea Consumption and Ovarian Cancer** Risk in a Population-Based Cohort. Arch Intern Med. 2005 Dec 12;165(22):2683-2686.

Laube R, Liu K. An unwanted complement: Rare case of **potential liver injury induced by an interaction between ginseng and atorvastatin**. Br J Clin Pharmacol. 2019 Apr 13.

Lauche R, Graf N, Cramer H, et al. Efficacy of **Cabbage Leaf Wraps** in the Treatment of Symptomatic Osteoarthritis of the Knee: A Randomized Controlled Trial. Clin J Pain. 2016 Nov;32(11):961-971.

Layne K, Ferro A. **Traditional Chinese Medicines in the management of cardiovascular diseases**: a comprehensive systematic review. Br J Clin Pharmacol. 2016 May 14.

Leach MJ, Moore V. **Black cohosh** (Cimicifuga spp.) for menopausal symptoms. Cochrane Database of Systematic Reviews 2012, Issue 9. Art. No.: CD007244. DOI: 10.1002/14651858.CD007244.pub2. There is currently insufficient evidence to support the use of black cohosh for menopausal symptoms.

Lee IT, Chan YC, Lin CW, Lee WJ, Sheu WH. Effect of **cranberry extracts** on lipid profiles in subjects with Type 2 diabetes. Diabet Med. 2008 Dec;25(12):1473-7. Cranberry supplements are effective in reducing atherosclerotic cholesterol profiles, including LDL cholesterol and total cholesterol levels, as well as total : HDL cholesterol ratio, and have a neutral effect on glycaemic control in Type 2 diabetic subjects taking oral glucose-lowering agents.

Lee RT, Barbo A, Lopez G, et al. National Survey of **US Oncologists' Knowledge, Attitudes, and Practice Patterns Regarding Herb and Supplement Use by Patients With Cancer**. J Clin Oncol. 2014 Dec 20;32(36):4095-101.

León H, Shibata MC, Sivakumaran S, Dorgan M, Chatterley T, Tsuyuki RT. Effect of **fish oil** on arrhythmias and mortality: systematic review. BMJ. 2008 Dec 23;337

Levy I, Attias S, Ben-Arye E, et al. Adverse Events associated with **Interactions with Dietary and Herbal Supplements among Inpatients**. Br J Clin Pharmacol. 2016 Oct 19.

Leyer GJ, Li S, Mubasher ME, Reifer C, et al. **Probiotic** effects on cold and influenza-like symptom incidence and duration in children. Pediatrics. 2009 Aug;124(2):e172-9. Epub 2009 Jul 27.

Li H, Guo F, Luo YC, Zhu JP, Wang JL. Efficacy of **tripterygium glycosides** tablet in treating ankylosing spondylitis: a systematic review and meta-analysis of randomized controlled trials. Clin Rheumatol. 2015 Aug 9.

Li S, Zhang X, Fang Q, et al. **Ginkgo biloba extract** improved cognitive and neurological functions of acute ischaemic stroke: a randomised controlled trial. Stroke Vasc Neurol. 2017 Dec 18;2(4):189-197.

Li X, Zhang J, Huang J, et al. A multicenter randomized double-blind parallel-group placebo-controlled study of the effects of **qili qiangxin** capsules in patients with chronic heart failure. J Am Coll Cardiol 2013.

Lian F, Li G, Chen X, et al. **Chinese Herbal Medicine Tianqi** Reduces Progression From Impaired Glucose Tolerance to Diabetes: A Double-Blind, Randomized, Placebo-Controlled, Multicenter Trial. J Clin Endocrinol Metab. 2014 Jan 16

Liatsos GD, Moulakakis A, Ketikoglou I, Klonari S. Possible **green tea-induced thrombotic thrombocytopenic purpura**. Am J Health Syst Pharm. 2010 Apr 1;67(7):531-4.
Lidder S, Webb AJ. Vascular effects of **dietary nitrate** (as found in green leafy vegetables & beetroot) via the Nitrate-Nitrite-Nitric Oxide pathway. Br J Clin Pharmacol. 2012 Aug 13.
Lim WS, Gammack JK, Van Niekerk J, Dangour AD. **Omega 3 fatty acid** for the prevention of dementia. Cochrane Database Syst Rev. 2006 Jan 25;(1):CD005379.
Lim Alissa, Cranswick Noel, South Michael. Adverse events associated with the use of complementary and **alternative medicine in children**. Arch Dis Child archdischild183152 Online First: 22 December 2010 doi:10.1136/adc.2010.183152. (Including 4 deaths when failure to use conventional medicine in favor of CAM therapies.)
Liu J, Manheimer E, Yang M. Herbal medicines for treating **HIV infection** and AIDS. Cochrane Database Syst Rev. 2005 Jul 20;(3):CD003937.
Liu ZL, Liu ZJ, Liu JP, Yang M, Kwong J. Herbal medicines for **viral myocarditis**. Cochrane Database Syst Rev. 2010 Jul 7;7:CD003711. Some herbal medicines may lead to improvement of symptoms, ventricular premature beat, electrocardiogram, level of myocardial enzymes, and cardiac function in viral myocarditis.
Liu ZL, Liu JP, Zhang AL, et al. **Chinese herbal medicines for hypercholesterolemia**. Cochrane Database Syst Rev. 2011 Jul 6;7:CD008305. Some herbal medicines may have cholesterol-lowering effects. Our findings have to be interpreted with caution due to high or unclear risk of bias of the included trials. {22 RCTs, n=2130, range of 1-6 months with mean duration 2.3 +/- 1.3 months, high or unclear risk of ibias, no outcome data (too short & too small), no SAEs; **Xuezhikang** most commonly used; possible TC lowering (-0.90mmol/L vs inositol nicotinate)}.
Linde K, Mulrow CD, Berner M, **St John's** wort for depression. Cochrane Database Syst Rev. 2005 Apr 18;(2):CD000448. CONCLUSIONS: Current evidence (37 trials) regarding hypericum extracts is inconsistent and confusing. In patients who meet criteria for major depression, several recent placebo-controlled trials suggest that the tested hypericum extracts have minimal beneficial effects while other trials suggest that hypericum and standard antidepressants have similar beneficial effects. As the preparations available on the market might vary considerably in their pharmaceutical quality, the results of this review apply only to the products tested in the included studies.
Linde K, Berner MM, Kriston L. **St John`s wort** for major depression. Cochrane Database Syst Rev. 2008 Oct 8;(4):CD000448. The available evidence suggests that the hypericum extracts tested in the included trials a) are superior to placebo in patients with major depression; b) are similarly effective as standard antidepressants; c) and have fewer side effects than standard antidepressants. The association of country of origin and precision with effects sizes complicates the interpretation.
Linde K, Alscher A, Friedrichs C, et al. **Belief in and use of complementary therapies** among family physicians, **internists and orthopaedists in Germany** - cross-sectional survey. Fam Pract. 2014 Nov 7.
Liperoti R, Vetrano DL, Bernabei R, et al. **Herbal Medications in Cardiovascular Medicine**. J Am Coll Cardiol. 2017 Mar 7;69(9):1188-1199.
Liu Y, Liu JP, Xia Y. **Chinese herbal medicines for treating osteoporosis**. Cochrane Database Syst Rev. 2014 Mar 6;3:CD005467. Current findings suggest that the beneficial effect of Chinese herbal medicines in improving BMD is still uncertain and more rigorous studies are warranted.
Lokhorst B, Rolfes L, Jessurun NT. Interaction of OTC drug **noscapine and acenocoumarol and phenprocoumon**. Br J Clin Pharmacol. 2019 May;85(5):1041-1043.
Lovera JF, Kim E, Heriza E, et al. **Ginkgo biloba** does not improve cognitive function in MS: A randomized placebo-controlled trial. Neurology. 2012 Sep 18;79(12):1278-84.
Lv QW, Zhang W, Shi Q, et al. Comparison of **Tripterygium wilfordii Hook F** with **methotrexate** in the treatment of active rheumatoid arthritis (TRIFRA): a randomised, controlled clinical trial. Ann Rheum Dis. 2014 Apr 14.
Ma H, Li X, Sun D, et al. Association of **habitual glucosamine use with risk of cardiovascular disease: prospective study in UK Biobank**. BMJ. 2019 May 14;365:l1628.
Macdonald R, Tacklind JW, Rutks I, Wilt TJ. **Serenoa repens** (Saw palmetto) monotherapy for benign prostatic hyperplasia (BPH): an updated Cochrane systematic review. BJU Int. 2012 May 2. Serenoa repens Adverse events were generally mild and comparable to placebo. Therapy does not improve LUTS or Q(max) compared with placebo in men with BPH, even at double and triple the usual dose.
MacFarquhar Jennifer K.; Broussard Danielle L.; Melstrom Paul; et al. Acute **Selenium** Toxicity Associated With a Dietary Supplement. Arch Intern Med. 2010;170(3):256-261.
Mackay L, Abrahams R. Novel case of maternal and **neonatal kratom dependence and withdrawal**. Can Fam Physician. 2018 Feb;64(2):121-122.
Medina-Caliz I, Garcia-Cortes M, Gonzalez-Jimenez A, et al. **Herbal and Dietary Supplement-induced Liver Injuries** in the Spanish DILI Registry. Clin Gastroenterol Hepatol. 2018 Jan 4. (esp. anabolic androgenic steroids)
Madisch A, et al. Treatment of irritable bowel syndrome with herbal preparations: results of a double-blind, randomized, placebo-controlled, multi-centre trial. Aliment Pharmacol Ther. 2004;19:271-9.
Marcocci C, Kahaly GJ, Krassas GE., et al. for the European Group on Graves' Orbitopathy. **Selenium and the Course of Mild Graves' Orbitopathy**. N Engl J Med 2011; 364:1920-1931.
Marples, Brian November 1, 2007 -- Patients with prostate cancer should be warned against using over-the-counter prostate-related health supplements because these items could make normal prostate cells more sensitive than usual to the effects of radiation, researchers reported here at the 49th annual meeting of the American Society for Therapeutic Radiology and Oncology (ASTRO). Researchers at William Beaumont Hospitals, Royal Oak, Michigan, United States, led by Brian Marples, PhD, Biology Radiologist, Department of Radiation Oncology, William Beaumont Hospitals, Royal Oak, Michigan, United States, tested three prostate-specific dietary supplements: Trinovin (red clover, biochanin A, formononetin, daidzein, genistein [phytoestrogen]), Provelex (lycopene, soy, saw palmetto, quercetin [phytoestrogen], selenium) and **ProstateRx (saw palmetto).** Their findings indicated that ProstateRx and other similar health store items were problematic in patients undergoing radiotherapy.
Martel-Pelletier J, Roubille C, Abram F, et al. First-line analysis of the effects of treatment on progression of **structural changes in knee osteoarthritis** over 24 months: data from the osteoarthritis initiative progression cohort. (**glucosamine & chondroitin sulfate**) Ann Rheum Dis. 2015 Mar;74(3):547-56.
Martin DJ, Partridge BJ, Shields W. Hepatotoxicity Associated With the **Dietary Supplement N.O.-XPLODE**. Ann Intern Med. 2013 Oct 1;159(7):503-504.
Mathie RT, Frye J, Fisher P. **Homeopathic Oscillococcinum** for preventing and treating influenza and influenza-like illness. Cochrane Database Syst Rev2012;12:CD001957. There is insufficient good evidence to enable robust conclusions to be made about Oscillococcinum(®) in the prevention or treatment of influenza and influenza-like illness.
Mazza M, Capuano A, Bria P, Mazza S. **Ginkgo biloba and donepezil**: a comparison in the treatment of Alzheimer's dementia in a randomized placebo-controlled double-blind study. Eur J Neurol. 2006 Sep;13(9):981-5.
Mazzanti G, Moro PA, Raschi E, et al. **Adverse reactions** to **dietary supplements containing red yeast rice**: assessment of cases from the Italian surveillance system. Br J Clin Pharmacol. 2017 Jan 17.
MBI Distributing: Recall - Due to a Lack of Adequate Controls Shield are used as topical acne medications- may be contaminated with bacteria.
McCartney M. How the **UK drug regulator (MHRA) became the herbalists' marketeer**. BMJ. 2014 May 9;348:g3194.
McDonnell WM, Bhattacharya R, Halldorson JB. Fulminant Hepatic Failure After Use of the Herbal Weight-Loss Supplement **Exilis**. Ann Intern Med. 2009 Nov 3;151(9):673-674.
McGarry A, McDermott M, Kieburtz K, et al. A randomized, double-blind, placebo-controlled trial of **coenzyme Q10 in Huntington disease**. Neurology. 2017 Jan 10;88(2):152-159.
Medical Letter. Dehydroepiandrosterone (**DHEA**). Vol 47 (Issue 1208) May 9, 2005 p.37-38.
Medicines and Healthcare products Regulatory Agency (MHRA) Dec/07 said: **Xiao Qin Long Wan**, a cold and flu medicine; pain reliever **Chuan Xiong Cha Tiao Wan**; **Bai Tou Weng Wan**, sold for stomach problems, and **Xie Gan Wan**, used to treat stress may contain Aristolochicia, which in unlicensed medicines was banned in UK in 1999
Melchart D, Linde K, Fischer P, **Echinacea** for preventing and treating the **common cold**. Cochrane Database Syst Rev. 2000;(2):CD000530. CONCLUSIONS: The majority of the available studies report positive results. However there is not enough evidence to recommend a specific Echinacea product, or Echinacea preparations for the treatment or prevention of common colds.
MHRA Aug 2011 issues warning over traditional Chinese medicines containing **Lei Gong Teng** (**tripterygium wilfordii**)
MHRA Dec/11Health Sciences Authority in Singapore has issued a press release warning the public of four adulterated health products. **ATHRI-Eze** - is marketed as a traditional Chinese medicine and packaged in a bottle of 20 white capsules. **SEAR HEANG TIENCHI TU CHUNG WAN** - claims to treat rheumatic pain and backache and is sold in a bottle of 40 black pills with a red label. **CAP WIJAYA KUSUMA (AN KI IT)** and **WIKU JAHE KENCUR (AKUR MUJARAB)** - are promoted as Malay Jamu (postnatal) medicines, which are packed in foil sachets of brown powder and are labelled to treat rheumatoid and arthritic conditions.These four products have been found to contain undeclared pharmaceutical medicines. Ingredients found include: dexamethasone, furosemide, paracetamol, chlorpheniramine (also known as chlorphenamine), phenylbutazone, allopurinol & prednisolone.
MHRA Dec/11 In response to an urgent notice issued by MHRA, Bee Health Ltd has agreed to stop marketing FSC Black Cohosh 1000 mg due to concerns about the high dosage of black cohosh in the product. The MHRA advises consumers not to take the FSC Black Cohosh product as it equates to 50 times the dose approved for traditional herbal medicinal products used to relieve menopausal symptoms. It is not known what the risks or effects on the body could be associated with such a high level of Black Cohosh.
MHRA Jan/12 Consumers are advised not to take unlicensed **Butterbur (Petasites hybridus)** herbal remedies. Butterbur contains pyrrolizidine alkaloids (PAs) which studies have shown can result in serious liver damage and organ failure. PAs have also been shown to lead to cancer in animals. Butterbur is most commonly used to treat migraine and hayfever. Butterbur products have been associated with cases of liver toxicity; 40 cases have been reported in the literature. Of these cases, nine were of acute hepatitis and two of

the nine cases resulted in liver failure requiring transplantation. The cases of liver toxicity appear to have occurred with extracts of Butterbur where the PAs had been removed and only small amounts remained. There is some evidence that other constituents found in Butterbur such as the sesquiterpene constituents for example petasin may be implicated in the liver toxicity.

MHRA Feb/12 Herbal sliming products found to contain potentially dangerous undeclared pharmaceuticals: **Expelling Grease Slimming Abdomen, V12 Fruit Slimming, 100% Natural Weight Loss Coffee, Leisure 18 Slimming Orange Juice, Fashion Slimming Milk Shake, Langli, Ya Buk & Fruit and vegetables lose weight**. MHRA has received advice from the Danish Medicines Agency that these unlicensed products have been tested and found to contain the Prescription Only Medicine Sibutramine.

MHRA Feb/12 has received advice from AGES PharmMed in Austria and the Danish Medicines Agency, warning that these unlicensed products have been tested and found to contain Tadalafil and/or Sildenafil: **AH Free/Reflexit, Stree Overlord, Man King, VigRX, Maxman, Maxman III, Viriya, & Imbiza for Men.**

MHRA Feb/12 Following a safety alert issued in October 2010 about slimming products containing Paiyouji the Agency has received a further complaint about a product called '**Paiyouji Plus - Fast Acting Slimming Tea**'. This product has been tested by the Agency and, as in the case of other Paiyouji products, found to contain sibutramine.

MHRA Mar/12 Traditional Chinese Medicine (TCM) **Anshen Bunao Pian** (Chung Lien Kulin Brand) has been found by the Department of Health in Hong Kong to contain 55 times the level of mercury permitted in China. Acute mercury poisoning can damage the neurological system and kidneys. The product is manufactured in mainland China and imported by Fung Wah (HK) Company.

MHRA July/12 Department of Health in Hong Kong have issued a warning asking members of the public not to buy or consume an oral product called '**Ling Zhi She Xiang Tong Mai Dan'**, as it may contain an undeclared pharmaceutical, dexamethasone.

MHRA Aug/12 **Echinacea should not be given to children under 12 years**: Oral herbal products containing echinacea should not be given to children under 12 years, the Medicines and Healthcare products Regulatory Agency (MHRA) has warned. http://www.mhra.gov.uk/NewsCentre/Pressreleases/CON180627 [Accessed 24 October 2012].

MHRA: Austrian Sep/12 authorities have issued a warning for **Ramlostan Forte** manufactured by SC Parapharm, Romania. Ramlostan comes in white and blue packaging, with a picture of a ram at the top. Inside, there are ten blue capsules. The Austrian authority (AGES) has issued a warning for this product after finding it to contain Tadalafil.

MHRA Oct/12 The UK Medicines and Healthcare products Regulatory Agency (MHRA) has issued a reminder about a potential adverse effect of liver problems when using **Black Cohosh** to relieve symptoms of the menopause. The MHRA has issued a press release reminding people about the risk of liver problems with Black Cohosh, following a serious case of liver failure resulting in a liver transplant suspected to have been caused by a herbal product containing Black Cohosh. The investigation of this case and of the product involved is ongoing. To date, the MHRA has received 53 reports of adverse reactions suspected to be associated with the use of Black Cohosh.

MHRA, Viridian Nutrition has agreed to recall stocks of **Black Cohosh** Root Capsules, as some batches of the product have been found to contain an undeclared plant species in addition to the declared plant species. The product is labelled as containing Black Cohosh, which is the common name of Cimicifuga racemosa, as specified in the European, British and American Pharmacopoeia. However tests carried out on the product have shown that the product also contains other Cimicifuga species, probably Cimicifuga foetida.

MHRA Nov/12 has received advice from the Danish Medicines Agency that this unlicensed product, **Ultra Slim** has been tested and found to contain the Prescription Only Medicine Sibutramine.

MHRA Nov/12 has received advice from the Ministry of Health, Jerusalem warning that this unlicensed product, **Shark Essence** has been tested and found to contain Tadalafil and Sildenafil.

MHRA Dec/12 Medicines and Healthcare products Regulatory Agency, 2012. Liver failure case highlights need to use **Black Cohosh** remedies carefully [online].

Available: http://www.mhra.gov.uk/NewsCentre/Pressreleases/CON199545

MHRA Feb/13 is advising consumers not to use the products specified below due to sibutramine content. Product names**: Fashion Slimming Coffee, L-Carnitine + P57, L-CarnitinL 360 Slimming Coffee, Brazil Potent Slimming Coffee sachets, Coffee 26 Original sachets, Coffee Nature Fashion Slimming sachets, Slender Capsule, Slim-1.**

MHRA Feb/13 Hong Kong Department of Health issues warnings about **Traditional Chinese Medicines (TCM) found to contain heavy** metals. Product names: [W.S.] Tian Ma Toutong Wan; Shi Hu Ye Guang Wan (Ye Guang Wan); Nai Chang Ming Yan Pills (Ming Yan Pills); [Fung Shing Pai] Tian-Ma Wan; Bak Foong Pills (11 products - see below for details).

MHRA Aug/13 has recently been made aware of several unlicensed herbal products which have been found to contain **heavy metals**: **Bak Foong Pills, Hairegenerator, Niu-Huang Chieh-tu-pien, Divya Kaishore Guggul, Chandraprabha Vati.**

MHRA May/14: Advising consumers not to use Ayurvedic Herbal Medicine **Shwasa Sanjeevani** as it has been found to contain dexamethasone. Hong Kong Department of Health found that samples of **Hairegenerator** exceeded the permissible limit for mercury. Singapore Health Sciences Department **Li Long Mei Guo Mo Bang** because it contains sildenafil & **Ginseng Tu chong Wan Lin Heong** contains dexamethasone.

MHRA Feb/16 Class 2 medicines recall: **Asda, St John's Wort, HRI Good Mood and Superdrug St John's Wort tablets** THR 02231/0002 because of product contamination.

MHRA Mar/18: **Yiganerjing Cream** are urged to discontinue use immediately as it contains an undisclosed steroid and two antifungal ingredients.

Michel BA, Stucki G, Frey D, et al. **Chondroitins** 4 and 6 sulfate in osteoarthritis of the knee: a randomized, controlled trial. Arthritis Rheum 2005; 52:779-86.
(InfoPOEMs: After 2 years of treatment, chondroitin sulfate had no effect on comfort in patients with severe degenerative arthritis of the knee. Compared with placebo, however, it appears that chondroitin may have a small protective effect on the joint. The clinical relevance of this effect not known. (LOE = 1b))

Mills E, Singh R, Ross C, Ernst E. Sale of **kava** extract in some health food stores. CMAJ. 2003 Nov 25;169(11):1158-9. (January 2002, Health Canada issued an advisory, followed by a ban in August 2002, on the sale of herbal kava. One month after the advisory, 22 (67%) of 33 health food stores approached were selling kava. Two months after the ban, 17 (57%) of 30 stores continued to sell kava. These findings demonstrate that health food stores may need to be better informed about the sale of restricted natural health products.

Misaka S, Yatabe J, Müller F, et al. **Green tea** ingestion greatly reduces plasma concentrations of **nadolol** in healthy subjects. *Clin Pharmacol Ther* 2014.

Miyasaka LS, Atallah AN, Soares BG. **Valerian** for anxiety disorders. Cochrane Database Syst Rev 2006; 4:CD004515. This paper and [17**]

Miyasaka LS, Atallah AN, Soares BG. **Passiflora** for anxiety disorder. Cochrane Database Syst Rev 2007; 1:CD004518.

Mischoulon D. Update and critique of **natural remedies as antidepressant treatments**. Psychiatr Clin North Am 2007; 30:51-68.

Murphy RK, Ketzler L, Rice RD, et al. Oral **Glucosamine Supplements as a Possible Ocular Hypertensive Agent**. JAMA Ophthalmol. 2013 May 23:1-3.

Nahas R, Moher M. **Complementary and alternative medicine** for the treatment of type 2 diabetes. Can Fam Physician. 2009 Jun;55(6):591-6. Chromium, and possibly gymnema, appears to improve glycemic control. Fibre, green tea, and fenugreek have other benefits but there is little evidence that they substantially improve glycemic control. Further research on bitter melon and cinnamon is warranted. There is no complementary and alternative medicine research addressing microvascular or macrovascular clinical outcomes.

Nahas Richard, Sheikh Osmaan. **Complementary and alternative medicine** for the treatment of **major depressive disorder** Can Fam Physician June 2011 57: 659-663. (**St John's wort & exercise**)

Nahin RL, Pecha M, Welmerink DB, et al. Ginkgo Evaluation of Memory Study Investigators. Concomitant use of **prescription drugs and dietary supplements** in ambulatory elderly people. J Am Geriatr Soc. 2009 Jul;57(7):1197-205.

Nahin RL, Boineau R, Khalsa PS, et al. Evidence-Based Evaluation of **Complementary Health Approaches for Pain Management** in the United States. Mayo Clin Proc. 2016 Sep;91(9):1292-306

Nair KS, et al. **DHEA** in elderly **women** and **DHEA or testosterone** in elderly men. N Engl J Med. 2006 Oct 19;355(16):1647-59. (see also Pharmacist's Letter: Anti-aging Effects of DHEA. Dec/06)
(n= 2yr 87 males, 57 women) Men who received testosterone had a slight increase in fat-free mass, and men in both treatment groups had an increase in BMD at the femoral neck. Women who received DHEA had an increase in BMD at the ultradistal radius. Neither DHEA nor low-dose testosterone replacement in elderly people has physiologically relevant beneficial effects on body composition, physical performance, insulin sensitivity, or quality of life. (InfoPOEMs: There is no evidence that supplementation with dehydroepiandrosterone (DHEA) or testosterone has any meaningful clinical benefit for older patients with low serum levels of those hormones. (LOE = 1b))

Neale C, Camfield D, et al. Cognitive effects of two nutraceuticals **Ginseng and Bacopa** benchmarked against modafinil: a review and comparison of effect sizes. Br J Clin Pharmacol. 2012 Oct 9.

Necyk C, Tsuyuki RT, Boon H, et al. **Pharmacy study of natural health product adverse reactions (SONAR):** a cross-sectional study using active surveillance in community pharmacies to detect adverse events associated with natural health products and assess causality. BMJ Open. 2014 Mar 28;4(3):e003431.

Nelson KM, Dahlin JL, Bisson J, et al. The Essential Medicinal Chemistry of **Curcumin**. (**turmeric**)J Med Chem. 2017 Jan 11.

Newton KM, Reed SD, LaCroix AZ, et al. Treatment of vasomotor symptoms ofmenopausewith **black cohosh**, multibotanicals, soy, hormone therapy, or placebo: a randomized trial. Ann Intern Med 2006;145:869–79.

Nicolai SP, Kruidenier LM, Bendermacher BL, et al. **Ginkgo biloba for intermittent claudication**. Cochrane Database Syst Rev. 2013 Jun 6;6:CD006888. doi: 10.1002/14651858.CD006888.pub3.

Overall, there is no evidence that Ginkgo biloba has a clinically significant benefit for patients with peripheral arterial disease.
Nieminen TH, Hagelberg NM, Saari TI, Neuvonen M, Laine K, Neuvonen PJ, Olkkola KT. **St John's wort greatly reduces the concentrations of oral oxycodone**. Eur J Pain. 2010 Jan 25.
Nightingale G, et al. A pharmacist-led medication assessment used to determine a more precise estimation of the **prevalence of complementary and alternative medication (CAM) use among ambulatory senior** adults with cancer. J Geriatr Oncol. 2015 Aug 12.
Ngo MQ, Nguyen NN, Shah SA. Oral **aloe vera** for treatment of diabetes mellitus and dyslipidemia. Am J Health Syst Pharm. 2010 Nov 1;67(21):1804, 1806, 1808.
Oct/13 The workout supplement marketed as "**Craze**" contains a potentially dangerous designer drug — a methamphetamine analog — according to an article in Drug Testing and Analysis. The analog, N,alpha-diethyl-phenylethylamine (N,alpha-DEPEA), was found in three different samples of the product obtained from separate sources and analyzed by two labs. The product's label claims it contains phenylethylamines derived from dendrobium, but the authors say the component identified as N,alpha-DEPEA has never been identified in dendrobium. They say the amounts of N,alpha-DEPEA found "strongly suggest" that it's not a minor contaminant, adding that if their findings are confirmed, the FDA should "remove all N,alpha-DEPEA-containing supplements from the marketplace." The Boston Globe reports that another supplement, "**Detonate**," also contained N,alpha-DEPEA upon analysis.
Ogbogu U, Necyk C. **Community Pharmacists' Views and Practices Regarding Natural Health Products Sold in Community Pharmacies**. PLoS One. 2016 Sep 23;11(9):e0163450.
Olsen EO, O'Donnell J, Mattson CL, et al. Notes from the Field: Unintentional **Drug Overdose Deaths with Kratom** Detected - 27 States, July 2016-December 2017. MMWR Morb Mortal Wkly Rep. 2019 Apr 12;68(14):326-327
Oltean H, Robbins C, van Tulder MW, et al. **Herbal medicine for low-back pain**. Cochrane Database Syst Rev. 2014 Dec 23;12:CD004504. C. frutescens (Cayenne) reduces pain more than placebo. Although H. procumbens, S. alba, S. officinale L., S. chilensis, and lavender essential oil also seem to reduce pain more than placebo, evidence for these substances was of moderate quality at best. Additional well-designed large trials are needed to test these herbal medicines against standard treatments. In general, the completeness of reporting in these trials was poor. Trialists should refer to the CONSORT statement extension for reporting trials of herbal medicine interventions.
Onder G, Liperoti R. JAMA **Patient Page**. **Herbal Medications**. JAMA. 2016 Mar 8;315(10):1068.
Ondrizek RR, Chan PJ, Patton WC, King A. Inhibition of human **sperm** motility by specific herbs used in alternative medicine (eg. St. John's Wort). J Assist Reprod Genet. 1999 Feb;16(2):87-91.
Ooi CP, Yassin Z, Hamid TA. **Momordica charantia** for type 2 diabetes mellitus. Cochrane Database Syst Rev. 2010 Feb 17;2:CD007845.
Or F, Kim Y, Simms J, Austin SB. Taking Stock of Dietary Supplements' **Harmful Effects on Children, Adolescents, and Young Adults**. J Adolesc Health. 2019 Jun 3.
Papakostas GI, Mischoulon D, Shyu I, Alpert JE, Fava M. S-adenosyl methionine (SAMe) augmentation of serotonin reuptake inhibitors for antidepressant nonresponders with major depressive disorder: double-blind, randomized clinical trial. Am J Psychiatry. 2010 Aug;167(8):942-8. These preliminary results suggest that **SAMe can be an effective**, well-tolerated, and safe adjunctive treatment strategy for SRI nonresponders with major depressive disorder and warrant replication.
Parasrampuria J, Schwartz K, Petesch R. Quality control of **dehydroepiandrosterone** dietary supplement products. JAMA. 1998 Nov 11;280(18):1565.
Patrick K, Stanbrook MB. Take **turmeric** with a grain of salt. CMAJ. 2018 Oct 29;190(43):E1270.
Pelegrin S, Galtier F, Chalançon A, et al. Effects of **Nigella sativa seeds (black cumin) on insulin secretion** and lipid profile: a pilot study in healthy volunteers. Br J Clin Pharmacol. 2019 Mar 15.
Peng CC, Glassman PA, Trilli LE, et al. Incidence and severity of **potential drug-dietary supplement interactions** in primary care patients: an exploratory study of 2 outpatient practices. Arch Intern Med. 2004 Mar 22;164(6):630-6.
Perri D, Dugoua JJ, Mills E, Koren G. Safety & efficacy of echinacea (E. angustafolia, purpurea & pallida) during pregnancy & lactation. Can J Clin Pharmacol.2006 Fall;13(3):e262-7.Epub 2006Nov3.
Perry, Rachel, Hunt, Katherine, Ernst, Edzard. Nutritional Supplements and Other Complementary Medicines for **Infantile Colic**: A Systematic Review. Pediatrics 2011 127: 720-733
Pharmacist's Letter: Health Benefits of Drinking **Green Tea.** Nov 2006.
Pharmacist's Letter. Is **Chondroitin** effective for Osteoarthritis. June 2007. (Best evidence is with glucosamine sulfate called DONA by Rotta Pharmaceuticals)
Pharmacist's Letter. **New Health Canada Rules Allow More Health Claims for Natural Products**. April 2008.
Pharmacist's Letter. **Hawthorn for Heart Failure**. April 2008.
Pharmacist's Letter. **Flaxseed**: Is It As Beneficial As Fish Oil? July 2009.
Pharmacist's Letter. **Supplements for Prevention and Treatment of Colds and Influenza**. Nov 2009.
Pittler MH, Ernst E. **Horse chestnut** seed extract for chronic venous insufficiency. Cochrane Database Syst Rev. 2006 Jan 25;(1):CD003230. The evidence presented implies that HCSE is an efficacious & safe short-term treatment for CVI. However, several caveats exist and more rigorous RCTs are required to confirm the efficacy of this treatment option.
Pittler MH, Ernst E. **Kava** extract for treating anxiety. Cochrane Database Syst Rev. 2003;(1):CD003383. CONCLUSIONS: Compared with placebo, kava extract appears to be an effective symptomatic treatment option for anxiety. The data available from the reviewed studies suggest that kava is relatively safe for short-term treatment (1 to 24 weeks), although more information is required. Further rigorous investigations, particularly into the long-term safety profile of kava are warranted.
Pittler MH, Ernst E. **Feverfew** for preventing migraine. Cochrane Database Syst Rev. 2004;(1):CD002286. CONCLUSIONS: There is insufficient evidence from randomised, double-blind trials to suggest an effect of feverfew over & above placebo for preventing migraine. It appears from the data reviewed that feverfew presents no major safety problems.
Pittler MH, Guo R, Ernst E. **Hawthorn extract** for treating chronic heart failure. Cochrane Database Syst Rev 2008; DOI: 10.1002/14651858.CD005312.pub2. (Not included in the review was the survival and Prognosis: Investigation of Crataegus Extract WS1442 in CHF (**SPICE**) trial, which was ongoing as Pittler et al were screening relevant trials. As reported by heartwire when the study was later presented at the American College of Cardiology 2007 Scientific Sessions, adding the herbal to ACE inhibitors, beta blockers, and other components of contemporary therapy failed to alter a composite primary end point that included sudden cardiac death, death due to progressive heart failure, fatal or nonfatal MI, and HF hospitalization at 24 months. The trial did support hawthorn extract's good safety record, however.)
Podolsky SH, Kesselheim AS. **Regulating Homeopathic Products** - A Century of Dilute Interest. N Engl J Med. 2016 Jan 21;374(3):201-3.
Portnoi G, Chng LA, et al. Prospective comparative study of the safety & effectiveness of **ginger for the treatment of nausea and vomiting in pregnancy**. Am J Obstet Gynecol. 2003 Nov;189(5):1374-7.
Posadzki P, Watson L, Ernst E. **Herb-drug interactions**: an overview of systematic reviews. Br J Clin Pharmacol. 2012 Jun 1.
Post S, Spiller HA, Chounthirath T, Smith GA. **Kratom exposures** reported to United States poison control centers: 2011-2017. Clin Toxicol (Phila). 2019 Feb 20:1-8
Pottie K, Premji K, Cheskey SL. **Critical elevation of international normalized ratio** in an elderly woman using a **natural health product**. Can Fam Physician. 2017 Jul;63(7):536-537.
Prasad K, Sharma V, Lackore K, et al. Use of **Complementary Therapies** in Cardiovascular Disease. Am J Cardiol. 2012 Nov 24.
Predy GN, Goel V, Lovlin R, et al. Efficacy of an extract of North American **ginseng (Cold-fx)** containing poly-furanosyl-pyranosyl-saccharides for preventing upper respiratory tract infections: a randomized controlled trial. CMAJ. 2005 Oct 25;173(9):1043-8. INTERPRETATION: Ingestion of a poly-furanosyl-pyranosyl-saccharide-rich extract of the roots of North American ginseng in a moderate dose **400mg (2 capsules) over 4 months** reduced the mean number of colds per person (0.99 vs 0.71), the proportion of subjects who experienced 2 or more colds (24.8 vs 10%), the severity of symptoms and the number of days cold symptoms were reported (from 11.1 days to only 8.7 days). The number of people with 1 cold was 64.4 vs 56.1% with Cold-fX in **healthy** 18-65yrs old (mean 43yrs), n=323 with a history of at least 2 colds in the previous year. Limitations: not virologically proven influenza or more typical common cold illnesses studied will be important in the future, only most severe illnesses were evaluated, mechanism of action & true active constituents are not known.
Qato DM, Alexander GC, et al. Use of **prescription & over-the-counter medications and dietary supplements** among older adults in the United States. JAMA. 2008 Dec 24;300(24):2867-78.
Qato DM, Alexander GC, Guadamuz JS, et al. Prevalence of **Dietary Supplement Use in US Children and Adolescents**, 2003-2014. JAMA Pediatr. 2018 Jun 18.
Qato DM, Wilder J, Schumm LP, et al. **Changes in Prescription and Over-the-Counter Medication and Dietary Supplement Use Among Older Adults in the United States**, 2005 vs 2011. JAMA Intern Med. 2016 Apr 1
Qiu GX, Weng XS, Zhang K, et al. [A multi-central, randomized, controlled clinical trial of **glucosamine** hydrochloride/sulfate in the treatment of knee osteoarthritis.] Zhonghua Yi Xue Za Zhi. 2005 Nov;85(43):3067-70.
Quinn JF.; Raman R,Thomas RG.; et al. **Docosahexaenoic Acid (DHA) Supplementation** and Cognitive Decline in Alzheimer Disease: A Randomized Trial. *JAMA*. 2010;304(17):1903-1911.
Rahimikian F, Rahimi R, Golzareh P, et al. Effect of **Foeniculum vulgare Mill. (fennel)** on menopausal symptoms in postmenopausal women: a randomized, triple-blind, placebo-controlled trial. Menopause. 2017 May 15.
Rambaldi A, Jacobs BP, Iaquinto G. **Milk thistle** for alcoholic and/or hepatitis B or C virus liver diseases. Cochrane Database Syst Rev. 2005 Apr 18;(2):CD003620. CONCLUSIONS: Our results question the beneficial effects of milk thistle for patients with alcoholic and/or hepatitis B or C virus liver diseases and highlight the lack of high-quality evidence to support this intervention. Adequately conducted and reported randomised clinical trials on milk thistle versus placebo are needed.
Ramos-Esquivel A, Víquez-Jaikel Á, Fernández C. Potential Drug-Drug and Herb-Drug **Interactions in Patients With Cancer**: A Prospective Study of Medication Surveillance. J Oncol Pract. 2017 Jul;13(7):e613-e622
Rao N, Spiller HA, Hodges NL, et al. An **Increase in Dietary Supplement Exposures Reported to US Poison Control Centers**. J Med Toxicol. 2017 Jul 24.
Ravindran AV, Lam RW, Filteau MJ, et al. Canadian Network for Mood and Anxiety Treatments (**CANMAT**) clinical guidelines for the management of major depressive disorder in adults. V.

Complementary and alternative medicine treatments. J Affect Disord. 2009 Aug 8. [Epub ahead of print]

Red yeast: Most clinical studies have used a specific brand product (Cholestin). However, most other red yeast brands contain similar amount of red yeast, 600 mg. For hypercholesterolemia, a typical dose of red yeast is 1200 mg two times daily with food (2624). A total daily dose of 2400 mg red yeast contains approximately 9.6 mg total statins, of which 7.2 mg is lovastatin (2624). For dyslipidemia related to HIV infection, 1200 mg twice daily has been used (9475). www.naturaldatabase.com

Reeds Dominic N., Patterson Bruce W., Okunade Adewole, et al. **Ginseng and Ginsenoside** Re Do Not Improve β-Cell Function or Insulin Sensitivity in Overweight and Obese Subjects With Impaired Glucose Tolerance or Diabetes. Diabetes Care May 2011 34:1071-1076; published ahead of print March 16, 2011, doi:10.2337/dc10-2299

Regina A, Majlesi N. Notes from the Field. **Thyrotoxicosis After Consumption of Dietary Supplements** Purchased Through the Internet — Staten Island, New York, 2015. MMWR Morb Mortal Wkly Rep 2016;65:353–354.

Reginster JY, Deroisy R, Rovati LC, et al. Long-term eff ects of **glucosamine** sulphate on osteoarthritis progression: a randomised, placebo-controlled clinical trial. Lancet 2001; 357: 251–56.

Reginster JY, Dudler J, et al. Pharmaceutical-grade **Chondroitin sulfate is as effective as celecoxib** and superior to placebo in symptomatic **knee osteoarthritis**: the ChONdroitin versus CElecoxib versus Placebo Trial (**CONCEPT**). Ann Rheum Dis. 2017 May 22.

Reichenbach S, et al. **Meta-analysis: chondroitin** for osteoarthritis of the knee or hip. Ann Intern Med. 2007 Apr 17;146(8):580-90. Large-scale, methodologically sound trials indicate that the symptomatic benefit of chondroitin is minimal or nonexistent.

Reinhart KM, Coleman CI, Teevan C, et al. Effects of **garlic on blood pressure** in patients with and without systolic hypertension: a meta-analysis. Ann Pharmacother. 2008 Dec;42(12):1766-71. Epub 2008 Nov 18. This meta-analysis suggests that garlic is associated with blood pressure reductions in patients with an elevated SBP although not in those without elevated SBP.

Revol B, Gautier-Veyret E, Arrivé C, et al. Pharmacokinetic herb-drug interaction between **ginger and crizotinib**. Br J Clin Pharmacol. 2019 Jan 30.

Richy F, et al. Structural and symptomatic efficacy of **glucosamine and chondroitin** in knee osteoarthritis: a comprehensive meta-analysis. Arch Intern Med. 2003 Jul 14;163(13):1514-22.

Ringdahl E, Pandit S. Treatment of **Knee Osteoarthritis**. Am Fam Physician. 2011;83(11):1287-1292.

Rockwell S, Liu Y, Higgins SA. Alteration of the effects of cancer therapy agents on breast cancer cells bythe herbal medicine **black cohosh**.Breast Cancer Res Treat. 2005 Apr;90(3):233-9.

Roman-Blas JA, et al. **Chondroitin sulfate plus glucosamine** sulfate shows no superiority over placebo in a randomized, double-blind, placebo-controlled clinical trial in patients with knee osteoarthritis. (**CS/GS Combined Therapy**) Arthr Rheum. 2016 Jul 31

Roman-Blas JA, Castañeda S, Sánchez-Pernaute O, et al. Combined Treatment With **Chondroitin Sulfate and Glucosamine Sulfate** Shows No Superiority Over Placebo for Reduction of Joint Pain and Functional Impairment in Patients With Knee Osteoarthritis: A Six-Month Multicenter, Randomized, Double-Blind, Placebo-Controlled Clinical Trial. Arthritis Rheumatol. 2017 Jan;69(1):77-85.

Roselle H et al. Symptomatic hepatitis associated with the use of herbal **red yeast rice**. Ann Intern Med 2008; 149:516.

Rosenblatt M, Mindel J. Spontaneous hyphema associated with ingestion of **Ginkgo** biloba extract. N Engl J Med. 1997 Apr 10;336(15):1108.

Rowin J, Lewis SL. Spontaneous bilateral subdural hematomas associated with chronic **Ginkgo** biloba ingestion. Neurology. 1996 Jun;46(6):1775-6.

Rozendaal RM, et al. Effect of **glucosamine sulfate on hip osteoarthritis**: a randomized trial. Ann Intern Med. 2008 Feb 19;148(4):268-77. Glucosamine sulfate was no better than placebo in reducing symptoms and progression of hip osteoarthritis.

Runhaar J, van Middelkoop M, Reijman M, et al. Prevention of Knee Osteoarthritis in Overweight Females: The First Preventive Randomized Controlled Trial in Osteoarthritis (**glucosamine**) . Am J Med. 2015 Mar 26. pii: S0002-9343(15)00244-2.

Runhaar J, Rozendaal RM, et al. Subgroup analyses of the effectiveness of oral **glucosamine** for knee and hip osteoarthritis: a systematic review and individual patient data meta-analysis from the OA trial bank. Ann Rheum Dis. 2017 Nov;76(11):1862-1869.

Saeed SA, et al. **Herbal and Dietary Supplements** for Treatment of **Anxiety** Disorders. American Family Physician 2007;76:549-56. Kava potential for mild to moderate anxiety. Inositol modest effects with panic or OCD disorder. Not encourage St. John's wort, valerian, Sympathyl or passionflower.

Saito YA, Rey E, Almazar-Elder AE, et al. A randomized, double-blind, placebo-controlled trial of **St John's wort** for treating irritable bowel syndrome. Am J Gastroenterol. 2010 Jan;105(1):170-7. Epub 2009 Oct 6. SJW was a less effective treatment for IBS than placebo.

Samuels N, Finkelstein Y, Singer SR, Oberbaum M. **Herbal medicine and epilepsy**: proconvulsive effects and interactions with antiepileptic drugs. Epilepsia 2008;49:373-80.

Sanford NN, Sher DJ, Ahn C, et al. Prevalence and Nondisclosure of Complementary and **Alternative Medicine Use in Patients With Cancer** and Cancer Survivors in the United States. JAMA Oncol. 2019 Apr 11.

Saper RB, Kales SN, Paquin J, Burns MJ, Eisenberg DM, Davis RB, Phillips RS. Heavy metal content of **ayurvedic** herbal medicine products. JAMA. 2004 Dec 15;292(23):2868-73.

Saper RB, Phillips RS, Sehgal A, et al. Lead, mercury, and arsenic in US- and Indian-manufactured Ayurvedic medicines sold via the Internet. JAMA. 2008 Aug 27;300(8):915-23. Erratum in: JAMA. 2008 Oct 8;300(14):1652. **One-fifth** of both US-manufactured and Indian-manufactured Ayurvedic medicines purchased via the Internet contain **detectable lead, mercury, or arsenic**.

Sarris J, Byrne GJ. A systematic review of **insomnia and complementary medicine**. Sleep Med Rev. 2011 Apr;15(2):99-106.

Sarris J. **Nutrients and herbal supplements** for mental health. Australian Prescriber. 2014 Jun;37:90-3

Sawitzke AD, Shi H, Finco MF, Dunlop DD, et al.. Clinical efficacy and safety of **glucosamine, chondroitin sulphate, their combination, celecoxib or placebo** taken to treat osteoarthritis of the knee: 2-year results from **GAIT**. Ann Rheum Dis. 2010 Jun 4.

Schabath MB, Hernandez LM, Wu X, Pillow PC, Spitz MR. Dietary **phytoestrogens** and lung cancer risk. JAMA. 2005 Sep 28;294(12):1493-504.

Scheffers CS, Armstrong S, Cantineau AE, et al. **Dehydroepiandrosterone for women in the peri- or postmenopausal phase**.Cochrane Database Syst Rev. 2015 Jan 22;1:CD011066. There is no evidence that DHEA improves quality of life but there is some evidence that it is associated with androgenic side effects. There is uncertainty whether DHEA decreases menopausal symptoms, but DHEA may slightly improve sexual function compared with placebo.

Schoonees A, Visser J, Musekiwa A, Volmink J. **Pycnogenol**® for the treatment of chronic disorders. Cochrane Database of Systematic Reviews 2012, Issue 2. Art. No.: CD008294. DOI: 10.1002/14651858.CD008294.pub3. Oxidative stress has been implicated in the development of a number of conditions including cancer, arthritic disorders and cardiovascular disease. Pycnogenol®, a herbal dietary supplement derived from French maritime pine bark extract, is standardised to contain 70% procyanidin which is a powerful antioxidant. Pycnogenol® is marketed as a supplement for preventing or treating a wide range of chronic conditions.Current evidence is insufficient to support Pycnogenol® use for the treatment of any chronic disorder. Well-designed, adequately powered trials are needed to establish the value of this treatment.

Scroggie DA, Albright A. The effect of **glucosamine-chondroitin** supplementation on glycosylated hemoglobin levels in patients with type 2 diabetes mellitus: a placebo-controlled, double-blinded, randomized clinical trial. Arch Intern Med. 2003 Jul 14;163(13):1587-90.

Seeff LB, Bonkovsky HL, Navarro VJ, Wang G. **Herbal Products and the Liver:** A Review of Adverse Effects and Mechanisms. Gastroenterology. 2015 Mar;148(3):517-532.e3.

Segal R, Pilote L. **Warfarin interaction with Matricaria chamomilla**. CMAJ. 2006 Apr 25;174(9):1281-2.

Sengupta G et al. Comparison of **Murraya koenigii- and Tribulus terrestris-Based** Oral Formulation Versus Tamsulosin in the Treatment of Benign Prostatic Hyperplasia in Men Aged >50 Years: A Double-Blind, Double-Dummy, Randomized Controlled Trial. Clin Ther. 2011 Dec; 33(12):1943-52.

Shah SA, Sander S, White CM, et al. Evaluation of echinacea for the prevention and treatment of the common cold: a meta-analysis. Lancet Infect Dis. 2007 Jul;7(7):473-80. Erratum in: Lancet Infect Dis. 2007 Sep;7(9):580. Published evidence **supports echinacea's** benefit in decreasing the incidence and duration of the common cold.

Shang A, Huwiler-Müntener K, et al. Are the clinical effects of **homoeopathy** placebo effects? Comparative study of placebo-controlled trials of homoeopathy and allopathy. The Lancet - Vol. 366, Issue 9487, 27 August 2005, Pages 726-732. (InfoPOEMs: High-quality studies demonstrate that homeopathy are no more effective than placebo. (LOE = 1a-))

Shelton RC, Keller MB, et al. Effectiveness of **St John's wort** in major depression: a randomized controlled trial. **JAMA. 2001** Apr 18;285(15):1978-86.

Singapore Health Sciences Authority July/15: **Skinny 22**" contains Undeclared phenolphthalein.

Singh JA, Noorbaloochi S, MacDonald R, Maxwell LJ. **Chondroitin for osteoarthritis**. Cochrane Database Syst Rev. 2015 Jan 28;1:CD005614. A review of randomized trials of mostly low quality reveals that chondroitin (alone or in combination with glucosamine) was better than placebo in improving pain in participants with osteoarthritis in short-term studies. The benefit was small to moderate with an 8 point greater improvement in pain (range 0 to 100) and a 2 point greater improvement in Lequesne's index (range 0 to 24), both seeming clinically meaningful. These differences persisted in some sensitivity analyses and not others. Chondroitin had a lower risk of serious adverse events compared with control. More high-quality studies are needed to explore the role of chondroitin in the treatment of osteoarthritis. The combination of some efficacy and low risk associated with chondroitin may explain its popularity among patients as an over-the-counter supplement.

Skalli S, Zaid A, Soulaymani R. **Drug interactions with herbal medicines**. *Ther Drug Monit*. 2007. 29(6): 679–86.

Smith C, Crowther C, Willson K, Hotham N, McMillian V. A randomized controlled trial of **ginger** to treat nausea and vomiting in pregnancy. Obstet Gynecol. 2004 Apr;103(4):639-45.

Snitz Beth E.; O'Meara Ellen S.; Carlson Michelle C.; et al. for the **Ginkgo** Evaluation of Memory (**GEM**) Study Investigators. Ginkgo biloba for Preventing Cognitive Decline in Older Adults: A Randomized Trial. JAMA. 2009;302(24):2663-2670. Compared with placebo, the use of G biloba, 120 mg twice daily, did not result in less cognitive decline in older adults with normal cognition or with mild cognitive impairment.

Squadrito F, Marini H, Bitto A, et al. **Genistein** in the metabolic syndrome: results of a randomized clinical trial. J Clin Endocrinol Metab. 2013 Aug;98(8):3366-74.

Siegel AB, Stebbing J. **Milk thistle**: early seeds of potential. Lancet Oncol. 2013 Sep;14(10):929-30.

Spilchuk V, Thompson A. **Chronic arsenic poisoning** from traditional Chinese medicine. CMAJ. 2019 Apr 15;191(15):E424.

Stage TB, Pedersen RS, Damkier P, et al. Intake of **St. John's wort improves the glucose tolerance in healthy subjects that ingest metformin** compared to metformin alone. Br J Clin Pharmacol. 2014 Sep 16.

Stanbrook M. **Natural health products should be sold separately from drugs**. CMAJ. 2017 Jun 26;189(25):E848

Storch A, Jost WH, Vieregge P, et al. Randomized, Double-blind, Placebo-Controlled Trial on Symptomatic Effects of **Coenzyme Q10** 100mg tid in Parkinson Disease. Arch Neurol. 2007 May 14; [Epub ahead of print] N=131 3months. Nanoparticular CoQ(10) at a dosage of 300 mg/d is safe and well tolerated and leads to plasma levels similar to 1200 mg/d of standard formulations. Add-on CoQ(10) does not display symptomatic effects in midstage Parkinson disease.

Stranges S, Marshall JR, Natarajan R, et al. Effects of Long-Term Selenium Supplementation on the Incidence of Type 2 Diabetes: A Randomized Trial. Ann Intern Med. 2007 Jul 9; [Epub ahead of print] Selenium supplementation does not seem to prevent type 2 diabetes, and it may increase risk for the disease.

Strewler A, Conroy R, Kao H. Approach to **Overuse of Herbal and Dietary Supplements**: A Teachable Moment. JAMA Intern Med. 2014 May 26.

Striano P, Zara F, Minetti C, Striano S. **Chitosan** may decrease serum valproate and increase the risk of seizure reappearance. BMJ. 2009 Sep 24;339:b3751. doi: 10.1136/bmj.b3751.

Sun YE, Wang W, Qin J. **Anti-hyperlipidemia of garlic by reducing the level of total cholesterol and low-density lipoprotein**: A meta-analysis. Medicine (Baltimore). 2018 May;97(18):e0255.

Suzuki E, Yorifuji T, Takao S, et al. **Green tea** consumption and mortality among Japanese elderly people: the prospective Shizuoka elderly cohort. Ann Epidemiol. 2009 Oct;19(10):732-9.

Szegedi A, Kohnen R, Dienel A, Kieser M. Acute treatment of moderate to severe depression with hypericum extract WS 5570 (**St John's wort**): randomised controlled double blind non-inferiority trial versus paroxetine. **BMJ. 2005** Feb 11; [Epub ahead of print] (InfoPOEMs: In patients with moderate to severe depression, St John's wort was at least as effective as paroxetine after 6 weeks of therapy. It was also better tolerated than paroxetine. More than half the patients receiving St John's wort required 600 mg 3 times a day of a product with less of the purported active ingredients than is commonly used in other studies. Patients in clinical practice may experience a benefit at a dose of 300 mg 3 times daily using commercial products that contain more of the active ingredients. (LOE = 1b))

Tachjian A, Maria V, Jahangir A. Use of **herbal products** and potential interactions in patients with **cardiovascular diseases**. J Am Coll Cardiol. 2010 Feb 9;55(6):515-25.

Tacklind J, Macdonald R, Rutks I, et al. **Serenoa repens** (Saw palmetto) for benign prostatic hyperplasia. Cochrane Database Syst Rev. 2012 Dec 12;12:CD001423. doi: 10.1002/14651858.CD001423.pub3. Serenoa repens, at double and triple doses, did not improve urinary flow measures or prostate size in men with lower urinary tract symptoms consistent with BPH.

Taibi DM, Landis CA, Petry H, Vitiello MV. A systematic review of **valerian as a sleep aid**: safe but not effective. Sleep Med Rev. 2007 Jun;11(3):209-30.

Takwale A, Tan E, Agarwal S, et al. Efficacy and tolerability of **borage oil** in adults and children with atopic eczema: randomised, double blind, placebo controlled, parallel group trial BMJ 2003;327:1385, doi:10.1136/bmj.327.7428.1385

Taylor MA, Reilly D, Llewellyn-Jones RH, McSharry C, Aitchison TC. Randomised controlled trials of **homoeopathy versus placebo** in perennial allergic rhinitis with overview of four trial series. BMJ 2000;321:471-6.

Taylor James A.,et al. Efficacy and Safety of **Echinacea** in Treating Upper Respiratory Tract Infections in Children. A Randomized Controlled Trial. JAMA. 2003;290:2824-2830. CONCLUSIONS: Echinacea purpurea, as dosed in this study, was not effective in treating URI symptoms in patients 2 to 11 years old, and its use was associated with an increased risk of rash.

Teschke Rolf; Schulze Johannes. Risk of **Kava Hepatotoxicity** and the FDA Consumer Advisory. *JAMA.* 2010;304(19):2174-2175.

Teschke R, Sarris J, Schweitzer I. Kava hepatotoxicity in traditional and modern use: the presumed Pacific kava paradox hypothesis revisited. Br J Clin Pharmacol. 2012 Feb;73(2):170-4.

Teschke R, Frenzel C, Glass X, et al. **Herbal hepatotoxicity**: A critical review. Br J Clin Pharmacol. 2012 Jul 26.

…accidental reexposure and/or thorough causality assessment methods have provided clear evidence for hepatotoxic properties of some herbal products, in addition to GC (4,5). Among these are Ayurvedic herbs (38), Chaparral (12), Chinese herbal mixture (10,13,68), Germander (9,15), few Herbalife products (21,22), Ho Shou Wu (69), Jin Bu Huan (11,70), Kava (71), Ma Huang (72), Mistletoe (7), Senna (8), and Syo Saiko To (14). As opposed to these herbs and herbal products, causality could not be established for herbs such as black cohosh (BC) (36,39,57) and Pelargonium sidoides (PS) (64-67), using the CIOMS scale (33,35).

Timmer A, Gunther J, Motschall E, et al. **Pelargonium sidoides** extract for treating acute respiratory tract infections. Cochrane Database Syst Rev. 2013 Oct 22;10:CD006323. P. sidoides may be effective in alleviating symptoms of acute rhinosinusitis and the common cold in adults, but doubt exists. It may be effective in relieving symptoms in acute bronchitis in adults and children, and sinusitis in adults. The overall quality of the evidence was considered low for main outcomes in acute bronchitis in children and adults, and very low for acute sinusitis and the common cold. Reliable data on treatment for other ARIs were not identified.

Towheed TE, Maxwell L, Anastassiades TP, et al. **Glucosamine** therapy for treating osteoarthritis. Cochrane Database Syst Rev. 2005 Apr 18;(2):CD002946. CONCLUSIONS: This update includes 20 studies with 2570 patients. Pooled results from studies using a non-Rotta preparation or adequate allocation concealment failed to show benefit in pain and WOMAC function while those studies evaluating the Rotta preparation show that glucosamine was superior to placebo in the treatment of pain and functional impairment resulting from symptomatic OA. WOMAC outcomes of pain, stiffness and function did not show a superiority of glucosamine over placebo for both Rotta and non-Rotta preparations of glucosamine. Glucosamine was as safe as placebo.

Trebaticka J, et al. Treatment of ADHD with French maritime **pine bark extract, Pycnogenol**((R)). Eur Child Adolesc Psychiatry. 2006 May 13; [Epub ahead of print] (n=61 4weeks)

Trinh K, Cui X, Wang YJ. Chinese herbal medicine for chronic neck pain due to cervical degenerative disc disease. Spine (Phila Pa 1976). 2010 Nov 15;35(24):2121-7. There is low quality evidence that an oral herbal medication, **Compound Qishe** Tablet, reduced pain more than placebo or **Jingfukang** and a topical herbal medicine, **Compound Extractum Nucis Vomicae**, reduced pain more than Diclofenac Diethylamine Emulgel.

Tsai HH, Lin HW, Simon Pickard A, Tsai HY, Mahady GB. Evaluation of documented drug **interactions and contraindications associated with herbs and dietary supplements**: a systematic literature review. Int J Clin Pract. 2012 Nov;66(11):1056-1078.

Tsai KK, Wang CH. Acute epiglottitis following traditional **Chinese gua sha therapy**. CMAJ. 2014 May 13;186(8):E298.

Tsitsikas DA, Emery M, Pomfret S, et al. Anaemia and unexplained abdominal pain: looking for a lead. BMJ. 2012 May 2;344:e2996. (**lead from ayuverdic remedies**)

Tucker J, Fischer T, Upjohn L, et al. **Unapproved Pharmaceutical Ingredients Included in Dietary Supplements** Associated With US Food and Drug Administration Warnings. *JAMA Netw Open.*2018;1(6):e183337.

Turner RB, Bauer R, Woelkart K et al. An Evaluation of **Echinacea angustifolia** in Experimental Rhinovirus Infections NEJM 2005;353:341-348. CONCLUSIONS: The results of this study indicate that extracts of E. angustifolia root, either alone or in combination, do not have clinically significant effects on infection with a rhinovirus or on the clinical illness that results from it.

Uebelhack R, et al. **Black cohosh and St. John's wort** for climacteric complaints: a randomized trial. (n=301 16weeks) Obstet Gynecol. 2006 Feb;107(2 Pt 1):247-55.

Vadillo-Ortega F, Perichart-Perera O, Espino S, Avila-Vergara MA, Ibarra I, Ahued R, et al. Effect of supplementation during pregnancy with **L-arginine** and antioxidant vitamins in medical food on pre-eclampsia in high risk population: randomised controlled trial. BMJ 2011;342:d2901.

van Gurp G, Meterissian GB, Haiek LN, McCusker J, Bellavance F. **St John's wort** or sertraline? Randomized controlled trial in primary care. Can Fam Physician. 2002 May;48:905-12.

Van Wagoner RM, Eichner A, Bhasin S, et al. Chemical composition and labeling of substances marketed as **selective androgen receptor modulators** and sold via the internet. JAMA. doi:10.1001/jama.2017.17069 (**SARMs: eg. Ostarine, LGD-4033, Andarine, ibutamoren, GW501516, SR9009**)

Vanherweghem JL, et al. Rapidly progressive **interstitial renal fibrosis** in young women: association with **slimming regimen** including **Chinese herbs**. Lancet. 1993 Feb 13;341(8842):387-91.

Vellas B, Coley N, Ousset P-J, et al, for the GuidAge Study Group. Long-term use of standardised **ginkgo biloba extract** for the prevention of Alzheimer's disease (**GuidAge**): a randomised placebo-controlled trial. Lancet Neurol 2012; online Sept 6

Verkaik S, Kamperman AM, van Westrhenen R, Schulte PFJ. The treatment of premenstrual syndrome with preparations of **Vitex agnus castus**: a systematic review and meta-analysis. Am J Obstet Gynecol. 2017 Aug;217(2):150-166.

Viswanathan L, Vigersky RA. The effect of herbal medications on **thyroid hormone economy and estrogen-sensitive hepatic proteins** in a patient with prostate cancer. Arch Intern Med. 2012 Jan 9;172(1):58-60. (PC-SPES etc.)

Vogel JH, Bolling SF, et al. American College of Cardiology Foundation Task Force on Clinical Expert Consensus Documents (Writing Committee to Develop an Expert Consensus Document on Complementary and Integrative Medicine). Integrating **complementary medicine into cardiovascular medicine**. A report of the American College of Cardiology Foundation Task Force on Clinical Expert Consensus. J Am Coll Cardiol. 2005 Jul 5;46(1):184-221.

Vo KT, Tabas JA, Smollin CG. Alternating **Ventricular Complexes** After Overdose From an Herbal Medication. JAMA Intern Med. 2017 Jun 5 (**Aconite alkaloids**)

von Arnim U, Peitz U, Vinson B, Gundermann KJ, Malfertheiner P. **STW 5**, a phytopharmacon for patients with functional dyspepsia: results of a multicenter, placebo-controlled double-blind study.

Am J Gastroenterol. 2007 Jun;102(6):1268-75. This placebo-controlled study with an 8-wk treatment period documents the efficacy of STW 5 in FD.
Wandel S, Jüni P, Tendal B, Effects of **glucosamine, chondroitin**, or placebo in patients with osteoarthritis of hip or knee: network meta-analysis. BMJ 341:doi:10.1136/bmj.c4675 (Pub 16 Sept 2010)
Wang C, Cao B, Liu QQ, et al. **Oseltamivir Compared With the Chinese Traditional Therapy Maxingshigan-Yinqiaosan** in the Treatment of H1N1 Influenza: A Randomized Trial. Ann Intern Med. 2011 Aug 16;155(4):217-225.
Wargo KA, Allman E, Ibrahim F. A possible case of **saw palmetto-induced pancreatitis**. South Med J. 2010 Jul;103(7):683-5.
White B. **Ginger**: an overview. Am Fam Physician. 2007 Jun 1;75(11):1689-91.
Wildi LM, Raynauld JP, Martel-Pelletier J, et al. Chondroitin sulphate reduces both cartilage volume loss and bone marrow lesions in knee osteoarthritis patients starting as early as 6 months after initiation of therapy: a randomised, double-blind, placebo-controlled pilot study using MRI. Ann Rheum Dis. 2011 Mar 1. (n=69)
Wilkens Philip; Scheel Inger B.; Grundnes Oliver; et al. Effect of **Glucosamine** on Pain-Related Disability in Patients With Chronic Low **Back Pain** and Degenerative Lumbar Osteoarthritis: A Randomized Controlled Trial. JAMA. 2010;304(1):45-52.
Williamson E. **Drug interactions between herbal and prescription medicines**. *Drug Saf*. 2003. 26(15): 1075–92.
Wooltorton E. Herbal **kava**: reports of liver toxicity. CMAJ. 2002 Mar 19;166(6):777.
Wyman M, Lenoard M, Morledge T. **Coenzyme Q10**: A therapy for hypertension and statin-induced myalgia? Cleveland Clinic Journal of Medicine 2010; 77(7):435-442
Yadav V, Bever C Jr, Bowen J, et al. Summary of evidence-based guideline: **Complementary and alternative medicine in multiple sclerosis**: Report of the Guideline Development Subcommittee of the American Academy of Neurology. Neurology. 2014 Mar 25;82(12):1083-92.
Yale SH., Liu K., **Echinacea** purpurea therapy for the treatment of the common cold. Arch Intern Med. 2004;164:1237-41.
Yang YC, Lu FH, Wu JS, Wu CH, Chang CJ. The protective effect of habitual **tea** consumption on hypertension. Arch Intern Med. 2004 Jul 26;164(14):1534-40.
Yang X, Zeng X, Wu T. **Chuanxiong** preparations for preventing stroke. Cochrane Database Syst Rev. 2010 Jan 20;(1):CD006765.
Yang S, Eaton CB, McAlindon TE, et al. Effects of **glucosamine and chondroitin** on treating knee osteoarthritis: An analysis with marginal structural models. Arthritis Rheumatol. 2014 Nov 4.
Ye P, Lu ZL, Du BM, et al; for the CCSPS Investigators. Effect of **xuezhikang** on cardiovascular events and mortality in elderly patients with a history of myocardial infarction: a subgroup analysis of elderly subjects from the china coronary secondary prevention study. J Am Geriatr Soc. 2007 Jul;55(7):1015-22. n=1445
Young JM, Florkowski CM, Molyneux SL, et al. Effect of coenzyme Q(10) 200mg/d supplementation on simvastatin-induced myalgia. Am J Cardiol. 2007 Nov 1;100(9):1400-3. Epub 2007 Aug 16. n=44 12weeks In conclusion, **coenzyme Q(10) supplementation did not improve statin tolerance or myalgia**, although further studies are warranted.
Yuan CS, Wei G, Dey L, et al. Brief communication: **American ginseng** reduces warfarin's effect in healthy patients: a randomized, controlled Trial. Ann Intern Med. 2004 Jul 6;141(1):23-7.
White B. **Ginger**: an overview. Am Fam Physician. 2007 Jun 1;75(11):1689-91.
Wildi LM, Raynauld JP, Martel-Pelletier J, et al. **Chondroitin sulphate** reduces both cartilage volume loss and bone marrow lesions in knee osteoarthritis patients starting as early as 6 months after initiation of therapy: a randomised, double-blind, placebo-controlled pilot study using MRI. Ann Rheum Dis. 2011 Mar 1.
Wu T, Chen X, Duan X, Juan N, Liu G, Qiao J, Wang Q, Wei J, Zhen J, Zhou L. **Chinese medicinal herbs** for acute bronchitis. Cochrane Database Syst Rev. 2005 Jul 20;(3):CD004560.
Wu T, et al. **Tongxinluo** (**Tong xin luo or Tong-xin-luo**) capsule for unstable angina pectoris. Cochrane Database Syst Rev. 2006 Oct 18;(4):CD004474. Due to the methodological limitations of the studies, the evidence is insufficient to make any conclusive recommendations about the use of this treatment for patients presenting with unstable angina. Large high quality randomised controlled trials are warranted.
Wen MC, et al. Efficacy and tolerability of anti-asthma herbal medicine intervention in adult patients with moderate-severe allergic asthma. J Allergy Clin Immunol. 2005 Sep;116(3):517-24. CONCLUSION: Anti-asthma herbal medicine intervention appears to be a safe and effective alternative medicine for treating asthma. In contrast with prednisone, **ASHMI** had no adverse effect on adrenal function and had a beneficial effect on T(H)1 and T(H)2 balance.
Zell-Kanter M, Quigley MA, Leikin JB. Reduction in **ephedra** poisonings after FDA ban. N Engl J Med. 2015 May 28;372(22):2172-4.
Zeng X, Liu M, Yang Y, Li Y, Asplund K, Zeng X. **Ginkgo biloba** for acute ischaemic stroke. Cochrane Database Syst Rev. 2005 Oct 19;(4):CD003691.
Zhang HW, Lin ZX, Tung YS, Kwan TH, Mok CK, Leung C, Chan LS. **Cordyceps sinensis (a traditional Chinese medicine)** for treating chronic kidney disease. Cochrane Database of Systematic Reviews 2014, Issue 12. Art. No.: CD008353. DOI: 10.1002/14651858.CD008353.pub2. We found that Cordyceps preparation, as an adjuvant therapy to conventional medicine, showed potential promise to decrease serum creatinine, increase creatine clearance, reduce proteinuria and alleviate CKD-associated complications, such as increased haemoglobin and serum albumin. However, definitive conclusions could not be made because of the low quality of evidence.
Zhao M, Zheng R, Jiang J, et al. **Topical lipophilic epigallocatechin-3-gallate** on **herpes labialis**: a phase II clinical trial of AverTeaX formula. Oral Surg Oral Med Oral Pathol Oral Radiol. 2015 Dec;120(6):717-24. It is therefore incumbent on the oral health professional to continue to evaluate emerging evidence and to carefully and cautiously recommend nutraceuticals to their patients. At a minimum, based on this new study, it appears that AverTeaX and green tea antioxidants have the potential to provide effective topical treatment for recurrent herpes labialis.
Zheng GH, Liu JP, Chu JF, et al. **Xiongshao** for restenosis after percutaneous coronary intervention in patients with coronary heart disease. Cochrane Database Syst Rev. 2013 May 31;5:CD009581. doi: 10.1002/14651858.CD009581.pub2. The summary estimates indicate a protective effect of Xiongshao on restenosis and suggest that Xiongshao capsule may be used to prevent restenosis after a PCI procedure in CHD patients. However, this evidence is derived from small randomised trials, all conducted in China, and two of the included trials showed important methodological limitations that undermine the validity of the findings.
Zhu X, ProctorM, Bensoussan A,Wu E, Smith CA. **Chinese herbalmedicine for primary dysmenorrhoea**. CochraneDatabase of Systematic Reviews 2008, Issue 2. Art. No.: CD005288. DOI: 10.1002/14651858.CD005288.pub3. The review found promising evidence supporting the use of Chinese herbal medicine for primary dysmenorrhoea; however, results are limited by the poor methodological quality of the included trials.
Zhu X, Liew Y, Liu ZL. **Chinese herbal medicine for menopausal symptoms**. Cochrane Database Syst Rev. 2016 Mar 15;3:CD009023. We found insufficient evidence that Chinese herbal medicines were any more or less effective than placebo or HT for the relief of vasomotor symptoms. Effects on safety were inconclusive. The quality of the evidence ranged from very low to moderate; there is a need for well-designed randomised controlled studies.
Zick SM, Gillespie B, Aaronson KD. The effect of Crataegus oxycantha special extract WS 1442 (**hawthorn**) on clinical progression in patients with mild to moderate symptoms of **heart failure**. Eur J Heart Fail. 2008 Jun;10(6):587-93. Epub 2008 May 19. CSE does not reduce heart failure progression in patients who have HF. CSE appears to increase the early risk of HF progression.

Case Reports

Ang-Lee MK, Moss J, Yuan CS. **Herbal medicines and perioperative care**. JAMA 2001;286:208-16.
Bardia A, Nisly NL, Zimmerman MB, et al. Use of herbs among adults based on evidence-based indications: findings from the National Health Interview Survey. Mayo Clin Proc 2007;82:561-6
Barnes PM, Powell-Griner E, McFann K, Nahin RL. Complementary and alternative medicine use among adults: United States, 2002. Adv Data 2004;(343):1-19.
Bebbington A, Kulkarni R, Roberts P. Ginkgo biloba: Persistent bleeding after total hip arthroplasty caused by herbal self-medication. J Arthroplasty 2005;20:125-6.
Benjamin J, Muir T, Briggs K, Pentland B. A case of cerebral haemorrhage-can Ginkgo biloba be implicated? Postgrad Med J 2001;77:112-3.
Bent S, Goldberg H, Padula A, Avins AL. Spontaneous bleeding associated with Ginkgo biloba. A case report and systematic review of the literature. J Gen Intern Med 2005;20;657-61.
Chalasani N, Vuppalanchi R, al; Drug-Induced Liver Injury Network Acute liver injury due to **flavocoxid (Limbrel),** a medical food for osteoarthritis. A case series. Ann Intern Med. 2012;156:857-60.
Chatterjee N, Domoto-Reilly K, Fecci PE, et al. **Licorice-associated reversible cerebral vasoconstriction** with PRES (encephalopathy). Neurology. 2010 Nov 23;75(21):1939-41.
Cheema P, El-Mefty O, Jazieh AR. Intraoperative haemorrhage associated with the use of extract of Saw Palmetto herb: a case report and review of literature. J Intern Med 2001;250:167-9.
Dhesi Pavittarpaul; Ng Rita; Shehata MM.; et al. Ventricular Tachycardia After Ingestion of **Ayurveda Herbal** Antidiarrheal Medication Containing Aconitum. Arch Intern Med. 2010;170(3):303-305.
Destro MW, Speranzini MB, Cavalheiro Filho C, et al. Bilateral haematoma after rhytidoplasty and blepharoplasty following chronic use of Ginkgo biloba. Br J Plast Surg 2005;58:100-1.
Doyle H, Kargin M. Herbal stimulant containing ephedrine has also caused psychosis. BMJ 1996;313:756.
Eisenberg DM, Davis RB, Ettner SL, et al. Trends in alternative medicine use in the United States, 1990-1997. Results of a follow-up national survey. JAMA 1998;280:1569-75.
Fessenden JM, Wittenborn W, Clarke L. Gingko biloba: a case report of herbal medicine and bleeding postoperatively from a laparoscopic cholecystectomy. Am Surg 2001;67:33-5.

Firenzuoli F, Gori L, Galapai C. Adverse reaction to an adrenergic herbal extract (Citrus aurantium). Phytomedicine 2005;12:247-8.
Fong KC, Kinnear PE. Retrobulbar haemorrhage associated with chronic Ginkgo biloba ingestion. Postgrad Med J 2003;79:531-2.
Gange CA, Madias C, Felix-Getzik EM, et al. Variant angina associated with bitter orange in a dietary supplement. Mayo Clin Proc 2006;81:545-8.
Greco A et al. Acute hepatitis caused by a **natural lipid-lowering** product: when "alternative" medicine is no "alternative" at all. J Hepatology 2009; 50:1273.
Haller CA, Benowitz NL. Adverse cardiovascular and central nervous system events associated with dietary supplements containing ephedra alkaloids. N Engl J Med 2000;343:1833-8.
Hauser D, Gayowski T, Singh N. Bleeding complications precipitated by unrecognized Gingko biloba use after liver transplantation. Transpl Int 2002;15:377-9.
Irefin S, Sprung J. A possible cause of cardiovascular collapse during anesthesia: long-term use of St. John's Wort. J Clin Anesth 2000;12:498-9.
Jacobs KM, Hirsch KA. Psychiatric complications of Ma-huang. Psychosomatics 2000;41:58-62.
Jordan S, Murty M, Pilon K. Products containing bitter orange or synephrine: suspected cardiovascular adverse reactions. Canadian Adverse Reaction Newsletter 2004;14:3-4.
Kennedy J. Herb and supplement use in the US adult population. Clin Ther 2005;27:1847-58.
Keogh AM, Baron DW. Sympathomimetic abuse and coronary artery spasm. Br Med J 1985;291:940.
Liatsos GD, Moulakakis A, Ketikoglou I, Klonari S. Possible **green tea-induced thrombotic thrombocytopenic purpura**. Am J Health Syst Pharm. 2010 Apr 1;67(7):531-4.
MacFarquhar Jennifer K.; Broussard Danielle L.; Melstrom Paul; et al. Acute **Selenium** Toxicity Associated With a Dietary Supplement. Arch Intern Med. 2010;170(3):256-261.
McDonnell WM, Bhattacharya R, Halldorson JB. Fulminant Hepatic Failure After Use of the Herbal Weight-Loss Supplement Exilis. Ann Intern Med. 2009 Nov 3;151(9):673-674.
Meisel C, Johne A, Roots I. Fatal intracerebral mass bleeding associated with Ginkgo biloba and ibuprofen. Atherosclerosis 2003;167:367.
Miller LG, Freeman B. Possible subdural hematoma associated with Ginkgo biloba. J Herb Pharmacotherapy 2002;2:57-63.
Morgenstern LB, Viscoli CM, Kernan WN, et al. Use of Ephedra-containing products and risk for hemorrhagic stroke. Neurology 2003;60:132-5.
Nasir JM, Durning SJ, Ferguson M, et al. Exercise-induced syncope associated with QT prolongation and ephedra-free Xenadrine. Mayo Clin Proc 2004;79:1059-62.
Nykamp DL, Fackih MN, Compton AL. Possible association of acute lateral-wall myocardial infarction and bitter orange supplement. Ann Pharmacother 2004;38:812-6.
Penzak SR, Jann MW, Cold JA, et al. Seville (sour) orange juice: synephrine content and cardiovascular effects in normotensive adults. J Clin Pharmacol 2001;41:1059-63.
Pottie K, Premji K, Cheskey SL. **Critical elevation of international normalized ratio** in an elderly woman using a **natural health product**. Can Fam Physician. 2017 Jul;63(7):536-537.
Roselle H et al. Symptomatic hepatitis associated with the use of herbal red yeast rice. Ann Intern Med 2008; 149:516.
Rosenblatt M, Mindel T. Spontaneous hyphema associated with ingestion of Gingko biloba extract. N Engl J Med 1997;336:1108.
Rowin J, Lewis SL. Spontaneous bilateral subdural hemotomas with chronic Gingko biloba ingestion. Neurology 1996;46:1775-6.
Toovey OT, Edmond IR, Makris N. Acute severe hyponatraemia secondary to polydipsia and associated herbal remedy use. BMJ Case Rep. 2016 Sep 28;2016. (? Valerian root)
Vale S. Subarachnoid haemorrhage associated with Ginkgo biloba. Lancet 1998;352:36.
Verhelst X, Burvenich P, Van Sassenbroeck D, et al. Acute hepatitis after treatment for hair loss with oral **green tea** extracts (Camellia Sinensis). Acta Gastroenterol Belg. 2009 Apr-Jun;72(2):262-4.
Vo KT, Tabas JA, Smollin CG. Alternating **Ventricular Complexes** After Overdose From an Herbal Medication. JAMA Intern Med. 2017 Jun 5 (**Aconite alkaloids**)
Walton R, Manos GH. Psychosis related to ephedra-containing herbal supplement use. South Med J 2003;96:718-20.
Wang CC, Kennedy J, Wu CH. **Alternative Therapies as a Substitute for Costly Prescription Medications**: Results from the 2011 National Health Interview Survey. Clin Ther. 2015 Mar 4.
Wang ZS, Liu XK, Li J. Woman With Yellow Palms and Soles. JAMA. 2017 Apr 18;317(15):1574-1575. (**Carotenemia: in Nature Made Beta Carotene**)
Wargo KA, Allman E, Ibrahim F. A possible case of **saw palmetto-induced pancreatitis**. South Med J. 2010 Jul;103(7):683-5.
Wu D, Huang Y, Gu Y, et al. Efficacies of different preparations of **glucosamine** for the treatment of osteoarthritis: a meta-analysis of randomised, double-blind, placebo-controlled trials. Int J Clin Pract. 2013 Jun;67(6):585-94.
Wyman M, Lenoard M, Morledge T. **Coenzyme Q10**: A therapy for hypertension and statin-induced myalgia? Cleveland Clinic Journal of Medicine 2010; 77(7):435-442; doi:10.3949/ccjm.77a.09078
Xiong X, Wang P, Li X, Zhang Y. The effect of **Chinese herbal medicine Jian Ling Decoction** for the treatment of essential hypertension: a systematic review. BMJ Open. 2015 Feb 4; 5(2):e006502.
Yeh GY, Davis RB, Phillips RS. Use of complementary therapies in patients with cardiovascular disease. Am J Cardiol 2006;98:673-80.
Yeu E, Grostern R. Saw palmetto and intraoperative floppy-iris syndrome. J Cataract Refract Surg. 2007 May;33(5):927-8.
Zhang, Yuanting, Fein, Elizabeth B., Fein, Sara B. Feeding of **Dietary Botanical Supplements and Teas to Infants** in the United States. Pediatrics 2011 0: peds.2010-2294

Top Herbal Products (Jan 2008): http://www.medscape.com/viewprogram/8494_pnt

Health Canada: Natural Health Products Directorate[Jan/04]: 1-888-774-5555; 86 monographs;>3000NPN's
http://www.hc-sc.gc.ca/ahc-asc/branch-dirgen/hpfb-dgpsa/nhpd-dpsn/index_e.html

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RxFiles Over-The-Counter (OTC) Chart- References [Sept 2019 update]

1. Gunn VL, Taha SH, Liebelt EL, Serwint JR. Toxicity of over-the-counter cough and cold medications. Pediatrics. 2001 Sep;108(3):E52 (Hatton RC, Winterstein AG, McKelvey RP, Shuster J, Hendeles L. Efficacy and safety of oral phenylephrine: systematic review and meta-analysis. Ann Pharmacother. 2007 Mar;41(3):381-90. Epub 2007 Jan 30. There is insufficient evidence that oral phenylephrine is effective for nonprescription use as a decongestant. The Food and Drug Administration should require additional studies to show the safety and efficacy of phenylephrine.)
   Vernacchio L, Kelly JP, Kaufman DW, Mitchell AA. Cough and cold medication use by US children, 1999-2006: results from the slone survey. Pediatrics. 2008 Aug;122(2):e323-9. Approximately 1 in 10 US children uses a cough and cold medication in a given week. The especially high prevalence of use among children of young age is noteworthy, given concerns about potential adverse effects and the lack of data on the efficacy of cough and cold medications in this age group. Rimsza ME, Newberry S. Unexpected infant deaths associated with use of cough and cold medications. Pediatrics. 2008 Aug;122(2):e318-22. Review of these infants' deaths raises concern about the role of the over-the-counter cough and cold medications in these deaths. These findings support the recommendation that such medications not be given to infants.
   Vernacchio L, Kelly JP, Kaufman DW, Mitchell AA. Pseudoephedrine use among US children, 1999-2006: results from the Slone survey. Pediatrics. 2008 Dec;122(6):1299-304. Pseudoephedrine exposure, mostly in the form of multiple-ingredient products, is common among US children, especially children who are younger than 2 years, who are at the highest risk for toxicity and for whom safe dosing recommendations are lacking. Concerning patterns of use include taking >1 pseudoephedrine-containing product concurrently and using pseudoephedrine for extended periods. Pediatric pseudoephedrine use seems to be declining since the institution of the 2005 Combat Methamphetamine Epidemic Act.
   Dart RC, Paul IM, et al. Pediatric fatalities associated with over the counter (nonprescription) cough and cold medications. Ann Emerg Med. 2009 Apr;53(4):411-7. Epub 2008 Dec 19.
   Lokker Nicole, Sanders Lee, Perrin Eliana M. et al. Parental Misinterpretations of Over-the-Counter Pediatric Cough and Cold Medication Labels. Pediatrics 2009 123: 1464-1471.
   Shefrin AE, Goldman RD. Use of over-the-counter cough and cold medications in children. Can Fam Physician. 2009 Nov;55(11):1081-3.
   Kuehn Bridget M. Medical News & Perspectives: Withdrawal of Infant Cold Medicines Decreases ED Visits by Half, CDC Finds. *JAMA*. 2010;304(24):2686.doi:10.1001/jama.2010.1831
   Goldman RD; Canadian Paediatric Society, Drug Therapy and Hazardous Substances Committee. Treating cough and cold: guidance for caregivers of children and youth. Paediatr Child Health 2011;16:5646. www.cps.ca/English/statements/DT/TreatingCough.htm.
   Hampton LM, Nguyen DB, Edwards JR, et al. Cough and Cold Medication Adverse Events After Market Withdrawal and Labeling Revision. Pediatrics. 2013 Nov 11.
   van Driel ML, Scheire S, Deckx L, et al. What treatments are effective for common cold in adults and children? BMJ. 2018 Oct 10;363:k3786.
2. De Sutter AI, van Driel ML, Kumar AA, Lesslar O, Skrt A. Oral antihistamine-decongestant-analgesic combinations for the common cold. Cochrane Database Syst Rev. 2012 Feb 15;(2):CD004976.
3. Thirion, DJG. Viral Rhinitis, Influenza, Rhinosinusitis and Pharyngitis. In: Compendium of Therapeutics for Minor Ailments. Ottawa, ON: Canadian Pharmacists Association. [Updated May 2016; Accessed June 2019].
4. Deckx L, De Sutter AI, Guo L, Mir NA, van Driel ML. Nasal decongestants in monotherapy for the common cold. Cochrane Database Syst Rev. 2016 Oct 17;10:CD009612.
5. De Sutter AI, Saraswat A, van Driel ML. Antihistamines for the common cold. Cochrane Database Syst Rev. 2015 Nov 29;(11):CD009345.
6. Vaidyanathan S, Williamson P, Clearie K, et al. Fluticasone Reverses Oxymetazoline Induced Tachyphylaxis of Response and Rebound Congestion. Am J Respir Crit Care Med. 2010 Mar 4.
   Baroody FM, Brown D, Gavanescu L, et al. Oxymetazoline adds to the effectiveness of fluticasone furoate in the treatment of perennial allergic rhinitis. J Allergy Clin Immunol. 2011 Apr;127(4):927-34.
7. Smith SM, Schroeder K, Fahey T. Over-the-counter medications for acute cough in children and adults in ambulatory settings. Cochrane Database of Systematic Reviews 1999, Issue 1. Art. No.: CD001831. DOI: 10.1002/14651858.CD001831.pub3. {Acute cough is a common and troublesome symptom in people who suffer from acute upper respiratory tract infection (URTI). Many people self-prescribe over-the-counter (OTC) cough preparations and health practitioners often recommend their use for the initial treatment of cough. The results of this review suggest that there is no good evidence for or against the effectiveness of OTC medications in acute cough. The results of this review have to be interpreted with caution because the number of studies in each category of cough preparations was small. Many studies were of low quality and very different from each other, making evaluation of overall efficacy difficult. http://www.cochrane.org/reviews/en/ab001831.html }Allan G. Michael, Korownyk Christina, Kolber Michael. Do cough suppressants or honey help pediatric cough? Can Fam Physician April 2011 57: 435
   Singh M, Singh M. Heated, humidified air for the common cold. Cochrane Database Syst Rev. 2011 May 11;5:CD001728.
   Boulet LP, Côté G. Cough: etiology, evaluation and treatments. Update 2012. http://www.respiratoryguidelines.ca/sites/all/files/cough_toolkit.pdf (accessed January 9, 2012).
   Oduwole O, Meremikwu MM, Oyo-Ita A, et al. Honey for acute cough in children. Cochrane Database Syst Rev. 2012 Mar 14;3:CD007094. Honey may be better than `no treatment` and diphenhydramine in the symptomatic relief of cough but not better than dextromethorphan
   Bettiol S, Wang K, Thompson MJ, et al. Symptomatic treatment of the cough in whooping cough. Cochrane Database Syst Rev. 2012 May 16;5:CD003257. There is insufficient evidence to draw conclusions about the effectiveness of interventions for the cough in whooping cough.
   Ryan NM, Birring SS, Gibson PG. Gabapentin for refractory chronic cough: a randomised, double-blind, placebo-controlled trial. Lancet 2012; published online Aug 28.
   Morice AH, Menon MS, Mulrennan SA, et al. Opiate therapy in chronic cough. Am J Respir Crit Care Med 2007; 175: 312–15.
   Cohen HA, Rozen J, Kristal H, et al. Effect of Honey on Nocturnal Cough and Sleep Quality: A Double-blind, Randomized, Placebo-Controlled Study. Pediatrics. 2012 Aug 6.
   Chang AB, Robertson CF, Paul van Asperen P, et al. A Cough Algorithm for Chronic Cough in Children: A Multicenter, Randomized Controlled Study. Pediatrics. 2013 Apr 22.
   McCallum GB, Bailey EJ, Morris PS, et al. Clinical pathways for chronic cough in children. Cochrane Database Syst Rev. 2014 Sep 22;9:CD006595. Current evidence suggests that using a clinical algorithm for the management of children with chronic cough in hospital outpatient settings is more effective than providing wait-list care. Futher high-quality randomised controlled trials are needed to perform ongoing evaluation of cough management pathways in general practitioner and other primary care settings.
   Irwin RS, French CT, Lewis SZ, et al; CHEST Expert Cough Panel; CHEST Expert Cough Panel. Overview of the Management of Cough: CHEST Guideline and Expert Panel Report. Chest. 2014 Oct 1;146(4):885-9.
   Paul IM, Beiler JS, Vallati JR, et al. Placebo Effect in the Treatment of Acute Cough in Infants and Toddlers: A Randomized Clinical Trial. JAMA Pediatr. 2014 Oct 27.
   Oduwole O, Meremikwu MM, Oyo-Ita A, et al. Honey for acute cough in children. Cochrane Database Syst Rev. 2014 Dec 23;12:CD007094. Honey may be better than `no treatment`, diphenhydramine and placebo for the symptomatic relief of cough, but it is not better than dextromethorphan. None of the included studies assessed the effect of honey on `cough duration` because intervention and follow-up were for one night only. There is no strong evidence for or against the use of honey.
   Goldman RD. Honey for treatment of cough in children. Can Fam Physician. 2014 Dec;60(12):1107-8, 1110.
   Cash H, Trosman S, Abelson T, et al. Chronic Cough in Children. JAMA Otolaryngol Head Neck Surg. 2015 Mar 19.
   Smith SM, Schroeder K, Fahey T. Over-the-counter (OTC) medications for acute cough in children and adults in community settings. Cochrane Database Syst Rev 2014;11:CD001831. The results of this review have to be interpreted with caution because the number of studies in each category of cough preparations was small. Availability, dosing and duration of use of over-the-counter cough medicines vary significantly in different countries. Many studies were poorly reported making assessment of risk of bias difficult and studies were also very different from each other, making evaluation of overall efficacy difficult. There is no good evidence for or against the effectiveness of OTC medicines in acute cough. This should be taken into account when considering prescribing antihistamines and centrally active antitussive agents in children; drugs that are known to have the potential to cause serious harm.

Gibson P, Wang G, McGarvey L, et al. Treatment of Unexplained Chronic Cough: CHEST Guideline and Expert Panel Report. Chest. 2015 Oct 1.
Vertigan AE, Kapela SL, Ryan NM, et al. Pregabalin and speech pathology combination therapy for refractory chronic cough: A randomised controlled trial. Chest. 2015 Oct 8.
Vertigan AE, Murad MH, Pringsheim T, Feinstein A, Chang AB, Newcombe PA, Rubin BK, McGarvey LP, Weir K, Altman KW, Weinberger M, Irwin RS, CHEST Expert Cough Panel. Somatic cough syndrome (previously referred to as psychogenic cough) and tic cough (previously referred to as habit cough) in adults and children:
CHEST guideline and Expert Panel report. Chest. 2015 Jul;148(1):24-31.
Gibson PG, Vertigan AE. Management of chronic refractory cough. BMJ. 2015 Dec 14;351:h5590.
Vertigan AE, Kapela SL, Ryan NM, et al. Pregabalin and Speech Pathology Combination Therapy for Refractory Chronic Cough: A Randomized Controlled Trial. Chest. 2016 Mar;149(3):639-48.
Smith JA, Woodcock A. Chronic Cough. N Engl J Med. 2016 Oct 20;375(16):1544-1551
Chang AB, Oppenheimer JJ, Weinberger MM, et al. CHEST Expert Cough Panel.. Use of management pathways or algorithms in children with chronic cough: CHEST Guideline and Expert Panel Report. Chest. 2017 Jan 16.
Green JL et al. Safety profile of cough and cold medication use in pediatrics. Pediatrics 2017 Jun; 139:e20163070.
Malesker MA, Callahan-Lyon P, Ireland B, Irwin RS; CHEST Expert Cough Panel. Pharmacological and Non-Pharmacological Treatment for Acute Cough Associated with the Common Cold. CHEST Expert Panel Report. Chest. 2017 Aug 21.
Rosen MJ, Ireland B, Narasimhan M, French C, Irwin RS; CHEST Expert Cough Panel. Cough in Ambulatory Immunocompromised Adults: CHEST Expert Panel Report. Chest. 2017 Aug 19.
Giliberto JP, Dibildox D, Merati A. Unilateral Laryngoscopic Findings Associated With Response to Gabapentin in Patients With Chronic Cough. JAMA Otolaryngol Head Neck Surg. 2017 Sep 14.
Irwin RS, French CL, Chang AB, Altman KW; CHEST Expert Cough Panel Group. Classification of Cough as a Symptom in Adults and Management Algorithms: CHEST Guideline and Expert Panel Report. Chest. 2017 Oct 25.
Michaudet C, Malaty J. Chronic Cough: Evaluation and Management. Am Fam Physician. 2017;96(9):575-580.
Malesker MA, Callahan-Lyon P, Ireland B, Irwin RS; CHEST Expert Cough Panel. Pharmacologic and Nonpharmacologic Treatment for Acute Cough Associated With the Common Cold: CHEST Expert Panel Report. Chest. 2017 Nov;152(5):1021-1037.
Chua K-P, Shrime MG, Conti RM. Effect of FDA Investigation on Opioid Prescribing to Children After Tonsillectomy/Adenoidectomy. Pediatrics. 2017;140(6):e20171765
Oduwole O, Udoh EE, Oyo-Ita A, et al. Honey for acute cough in children. Cochrane Database Syst Rev. 2018 Apr 10;4:CD007094. Honey probably relieves cough symptoms to a greater extent than no treatment, diphenhydramine, and placebo, but may make little or no difference compared to dextromethorphan. Honey probably reduces cough duration better than placebo and salbutamol. There was no strong evidence for or against using honey. Most of the children received treatment for one night, which is a limitation to the results of this review. There was no difference in occurrence of adverse events between the honey and control arms.Drugs for Cough. Medical Letter. Dec 2018.
van Driel ML, Scheire S, Deckx L, et al. What treatments are effective for common cold in adults and children? BMJ. 2018 Oct 10;363:k3786.
Health Canada Feb/19: is advising that Canadian children and adolescents (under 18 years of age) should not use cough and cold products containing codeine, hydrocodone and normethadone, as a precautionary measure.
Chang AB, Oppenheimer JJ, Kahrilas PJ, et al; CHEST Expert Cough Panel. Chronic cough and gastroesophageal reflux in children - CHEST Guideline and Expert Panel Report. Chest. 2019 Apr 16.

8. Thirion, DJG. Acute Cough. In: Compendium of Therapeutics for Minor Ailments. Ottawa, ON: Canadian Pharmacists Association. [Updated June 2019; Accessed June 2019].
9. Malesker MA, Callahan-Lyon P, Ireland B, Irwin RS; CHEST Expert Cough Panel. Pharmacologic and Nonpharmacologic Treatment for Acute Cough Associated With the Common Cold: CHEST Expert Panel Report. Chest. 2017 Nov;152(5):1021-1037.
10. Treatment of cough in adults. Pharmacy Letter. 2018 January 1.
11. Becker LA, Hom J, Villasis-Keever M, van der Wouden JC. Beta2-agonists for acute cough or a clinical diagnosis of acute bronchitis. Cochrane Database Syst Rev. 2015 Sep 3;(9):CD001726.
12. Treatment Guidelines: Drugs for Allergic Disorders. The Medical Letter: May, 2017; pg. 71-81.
13. Sur DK, Plesa ML. Treatment of Allergic Rhinitis. Am Fam Physician. 2015 Dec 1;92(11):985-92.
Plaut M, Alleric Rhinitis. N Engl J Med 2005;353:193-44. (Medical Letter. Treatment Guidelines. Drugs for Allergic Disorders. Feb 2010, revised May 2013.)
Sussman G, Sussman D, Sussman A. Intermittent allergic rhinitis. CMAJ. 2010 Jun 15;182(9):935-7.
Sur DK, Scandale S. Treatment of allergic rhinitis. Am Fam Physician. 2010 Jun 15;81(12):1440-6.
So M, Bozzo P, Inoue M, Einarson A. Safety of antihistamines during pregnancy and lactation. Can Fam Physician. 2010 May;56(5):427-9.
Radulovic S, Calderon MA, Wilson D, Durham S. Sublingual immunotherapy for allergic rhinitis. Cochrane Database of Systematic Reviews 2010, Issue 12. Art. No.: CD002893. DOI: 10.1002/14651858.CD002893.pub2. This updated review reinforces the conclusion of the original 2003 Cochrane Review that sublingual immunotherapy is effective for allergic rhinitis and has been proven to be a safe route of administration.
Schaefer P. Urticaria: evaluation and treatment. Am Fam Physician. 2011 May 1;83(9):1078-84.
Griffin G, Flynn CA. Antihistamines and/or decongestants for otitis media with effusion (OME) in children. Cochrane Database Syst Rev. 2011 Sep 7;9:CD003423. The pooled data demonstrate no benefit and some harm from the use of antihistamines or decongestants alone or in combination in the management of OME, therefore we recommend against their use.
Schaefer P. Acute and Chronic Urticaria: Evaluation and Treatment. Am Fam Physician. 2017;95(11):717-724.
Barniol C, Dehours E, Mallet J, et al. Levocetirizine and Prednisone Are Not Superior to Levocetirizine Alone for the Treatment of Acute Urticaria: A Randomized Double-Blind Clinical Trial. Ann Emerg Med. 2017 May 2.
Medical Letter. Treatment Guidelines. OTC Drugs for Seasonal Allergies. Apr 2019.
Kulthanan K, Hunnangkul S, Tuchinda P, et al. Treatments of cold urticaria: A systematic review. J Allergy Clin Immunol. 2019 Apr;143(4):1311-1331.
14. Kendrick, J. Allergic Rhinitis. In: Compendium of Therapeutics for Minor Ailments. Ottawa, ON: Canadian Pharmacists Association. [Updated August 2018; Accessed June 2019].
15. Seidman MD, Gurgel RK, Lin SY, et al. Clinical practice guideline: allergic rhinitis executive summary. Otolaryngol Head Neck Surg. 2015 Feb;152(2):197-206.
16. Friesen, AM. Conjunctivitis. In: Compendium of Therapeutics for Minor Ailments. Ottawa, ON: Canadian Pharmacists Association. [Updated April 2019; Accessed June 2019].
17. Sánchez-Hernández MC, Montero J, Rondon C, et al.; SEAIC 2010 Rhinoconjunctivitis Committee; Spanish Group Ocular Surface-GESOC. Consensus document on allergic conjunctivitis (DECA). J Investig Allergol Clin Immunol. 2015;25(2):94-106.
18. Sharma M, Bennett C, Cohen SN, et al. **H1-antihistamines for chronic spontaneous urticaria**. Cochrane Database Syst Rev. 2014 Nov 14;11:CD006137. Although the results of our review indicate that at standard doses of treatment, several antihistamines are effective when compared with placebo, all results were gathered from a few studies or, in some cases, from single-study estimates. The quality of the evidence was affected by the small number of studies in each comparison and the small sample size for many of the outcomes, prompting us to downgrade the quality of evidence for imprecision (unless stated for each comparison, the quality of the evidence was low).No single H1-antihistamine stands out as most effective. Cetirizine at 10 mg once daily in the short term and in the intermediate term was found to be effective in completely suppressing urticaria. Evidence is limited for desloratadine given at 5 mg once daily in the intermediate term and at 20 mg in the short term. Levocetirizine at 5 mg in the intermediate but not short term

was effective for complete suppression. Levocetirizine 20 mg was effective in the short term, but 10 mg was not. No difference in rates of withdrawal due to adverse events was noted between active and placebo groups. Evidence forimprovement in quality of life was insufficient.

19. Moayyedi P, Lacy BE, Andrews CN, Enns RA, Howden CW, Vakil N. ACG and CAG Clinical Guideline: Management of Dyspepsia. Am J Gastroenterol. 2017 Jul;112(7):988-1013.
20. Veldhuyzen van Zanten SJ, Bradette M, et al; Canadian Dyspepsia Working Group. Evidence-based recommendations for short- and long-term management of uninvestigated dyspepsia in primary care: an update of the Canadian Dyspepsia Working Group (CanDys) clinical management tool. Can J Gastroenterol. 2005 May;19(5):285-303. Review. PubMed PMID: 15915244.
21. Kahrilas, PK. (2019). Medical Management of gastroesophageal reflux disease in adults. *UpToDate*. Retrieved June, 2019, from https://www.uptodate.com/contents/medical-management-of-gastroesophageal-reflux-disease-in-adults?search=medical%20management%20of%20gastroesophageal%20ref&source=search_result&selectedTitle=5~150&usage_type=default&display_rank=5
22. American College of Gastroenterology Chronic Constipation Task Force. An evidence-based approach to the management of chronic constipation in North America. Am J Gastroenterol 2005; 100:S1-S4. (InfoPOEMs: Diagnostic testing is not needed for most patients with chronicconstipation. The evidence is strongest for the efficacy of psyllium, polyethylene glycol, lactulose, and tegaserod. Research is not available to support the routine use of stimulant laxatives, lubricants, stool softeners, calcium polycarbophil, bran, or any herbal products. (LOE = 1a)) & Hsieh C. Treatment of constipation in older adults. Am Fam Physician. 2005 Dec 1;72(11):2277-84.

Radaelli F, Meucci G, Imperiali G, Spinzi G, Strocchi E, Terruzzi V, Minoli G. High-Dose Senna Compared with Conventional PEG-ES Lavage as Bowel Preparation for Elective Colonoscopy: A Prospective, Randomized, Investigator-Blinded Trial. Am J Gastroenterol. 2005 Dec;100(12):2674-80. (Rendeli C, et al. Polyethylene glycol 4000 vs. lactulose for the treatment of neurogenic constipation in myelomeningocele children: a randomized-controlled clinical trial.Aliment Pharmacol Ther. 2006 Apr 15;23(8):1259-65.) (Freedman SB, Adler M, Seshadri R, Powell EC. Oral ondansetron for gastroenteritis in a pediatric emergency department. N Engl J Med. 2006 Apr 20;354(16):1698-705.) (Gastrointestinal Drug Use in Pregnancy. Pharmacist's Letter Dec/06) Di Palma JA, Cleveland MV, McGowan J, et al. A randomized, multicenter comparison of polyethylene glycol laxative and tegaserod in treatment of patients with chronic constipation. Am J Gastro. 2007 Sep;102(9):1964-71. Epub 2007 Jun 15. (n=237 4 weeks) While PEG laxative and tegaserod are safe for their intended use in chronic constipation, PEG had superior efficacy, caused fewer headaches, and produced greater improvement of constipation symptoms.

Thomson MA, Jenkins HR, Bisset WM, Heuschkel R, Kalra DS, Green MR, Wilson DC, Geraint M. Polyethylene glycol 3350 (6.9 g sachet)plus electrolytes for chronic constipation in children: a double blind, placebo controlled, crossover study. Arch Dis Child. 2007 Nov;92(11):996-1000. Epub 2007 Jul 11. PEG+E is significantly more effective than placebo, and appears to be safe and well tolerated in the treatment of chronic constipation in children.

Candy D, Belsey J. Macrogol (polyethylene glycol) laxatives in children with functional constipation and faecal impaction: a systematic review. Arch Dis Child. 2009 Feb;94(2):156-60. Epub 2008 Nov 19. In this systematic review that only included published studies, polyethylene glycol (PEG) was effective in treating functional constipation in children. PEG was clearly better than placebo and slightly more effective than lactulose, but no better than milk of magnesia. (LOE = 1a-)

McCallum IJ, Ong S, Mercer-Jones M. Chronic constipation in adults. BMJ. 2009 Mar 20;338:b831. doi: 10.1136/bmj.b831.

Chung S, Cheng A, Goldman RD. Polyethylene glycol 3350 without electrolytes for treatment of childhood constipation. Can Fam Physician. 2009 May;55(5):481-2.

Bekkali, Noor-L-Houda, van den Berg, Maartje-Maria, Dijkgraaf, Marcel G.W., et al. Rectal Fecal Impaction Treatment in Childhood Constipation: Enemas Versus High Doses Oral PEG. Pediatrics 2009 124: e1108-e1115.

Coleman J, Spurling G. Constipation in people with learning disability. BMJ. 2010 Jan 26;340:c222. doi: 10.1136/bmj.c222.

Matro R, Shnitser A, Spodik M, et al. Efficacy of Morning-Only Compared With Split-Dose Polyethylene Glycol Electrolyte Solution for Afternoon Colonoscopy: A Randomized Controlled Single-Blind Study. Am J Gastroenterol. 2010 Apr 20

Bardisa-Ezcurra Lauren, Ullman Roz, Gordon Jenny, on behalf of the Guideline Development Group. Diagnosis and management of idiopathic childhood constipation: summary of NICE guidance. BMJ 2010;340:c2585, doi: 10.1136/bmj.c2585.

Lee-Robichaud H, Thomas K, Morgan J, et al. Lactulose versus Polyethylene Glycol for Chronic Constipation. Cochrane Database Syst Rev. 2010 Jul 7;7:CD007570. Polyethylene Glycol should be used in preference to Lactulose in the treatment of Chronic Constipation.

Roerig JL, Steffen KJ, Mitchell JE, Zunker C. Laxative abuse: epidemiology, diagnosis and management. Drugs. 2010 Aug 20;70(12):1487-503. doi: 10.2165/11898640-000000000-00000.

Ford AC, Suares NC. Effect of laxatives and pharmacological therapies in chronic idiopathic constipation: systematic review and meta-analysis. Gut. 2011 Feb;60(2):209-18.

Attaluri A, Donahoe R, Valestin J, Brown K, Rao SS. Randomised clinical trial: dried plums (prunes) vs. psyllium for constipation. Aliment Pharmacol Ther. 2011 Apr;33(7):822-8. doi: 10.1111/j.1365-2036.2011.04594.x.

Varughese S, Kumar AR, George A, et al. Morning-only one-gallon polyethylene glycol improves bowel cleansing for afternoon colonoscopies: a randomized endoscopist-blinded prospective study. Am J Gastroenterol. 2010 Nov;105(11):2368-74.

Tabbers Merit M., Chmielewska Ania, Roseboom Maaike G., et al. Fermented Milk Containing Bifidobacterium lactis DN-173 010 in Childhood Constipation: A Randomized, Double-Blind, Controlled Trial. Pediatrics 2011; 127:6 e1392-e1399; May 23, 2011.

Kamm MA, Mueller-Lissner S, Wald A, Richter E, Swallow R, Gessner U. Oral bisacodyl is effective and well-tolerated in patients with chronic constipation. Clin Gastroenterol Hepatol. 2011 Jul;9(7):577-83.

Tabbers Merit M., Boluyt Nicole, Berger Marjolein Y.,et al. Nonpharmacologic Treatments for Childhood Constipation: Systematic Review. Pediatrics 2011; peds.2011-0179; published ahead of print September 26, 2011, doi:10.1542/peds.2011-0179

Aune D et al. Dietary fibre, whole grains, and risk of colorectal cancer: Systematic review and dose-response meta-analysis of prospective studies. BMJ 2011 Nov 10; 343:d6617.

Rowan-Legg A; Canadian Paediatric Society, Community Paediatrics Committee. Managing functional constipation in children. Paediatr Child Health 2011;16(10):661-5.

www.cps.ca/english/statements/CP/Constipation.htm (accessed December 14, 2011).

Gallegos-Orozco JF, Foxx-Orenstein AE, Sterler SM, et al. Chronic constipation in the elderly. Am J Gastroenterol. 2012 Jan;107(1):18-25.

Ori Y, Rozen-Zvi B, Chagnac A, et al. Fatalities and Severe Metabolic Disorders Associated With the Use of Sodium Phosphate Enemas: A Single Center's Experience. Arch Intern Med. 2012 Feb 13;172(3):263-5.

Agrawal A et al. Secondary prophylaxis of hepatic encephalopathy in cirrhosis: An open-label, randomized controlled trial of lactulose, probiotics, and no therapy. Am J Gastroenterol 2012 Jul; 107:1043.

Gordon M, Naidoo K, Akobeng AK, et al. Osmotic and stimulant laxatives for the management of childhood constipation. Cochrane Database Syst Rev. 2012 Jul 11;7:CD009118.

Ford AC, Talley NJ. Laxatives for chronic constipation in adults. BMJ. 2012 Oct 1;345:e6168.

Auth MK, Vora R, Farrelly P, Baillie C. Childhood constipation. BMJ. 2012 Nov 13;345:e7309.

Bharucha AE, Pemberton JH, Locke GR 3rd. American gastroenterological association (AGA) technical review on constipation. Gastroenterology. 2013 Jan;144(1):218-38.

American Gastroenterological Association (AGA) , Bharucha AE, Dorn SD, Lembo A, Pressman A. American gastroenterological association medical position statement on constipation. Gastroenterology. 2013 Jan;144(1):211-7.

Gandell D, Straus SE, Bundookwala M, et al. Treatment of constipation in older people. CMAJ. 2013 May 14;185(8):663-70.

Kew ST, Chakravarthi S. Images in clinical medicine: Melanosis coli. N Engl J Med. 2013 Jun 13;368(24):2303.

FDA Jan/14 is warning that the over-the-counter constipation drug sodium phosphate (marketed as Fleet, and generics) has been tied to heart and kidney damage and even death when patients exceed the recommended dose. The agency has identified over 50 serious adverse events related to dehydration and electrolyte disturbances (sodium, calcium, and phosphate) with both the oral and rectal formulations. Most cases occurred in older adults and children younger than 5 years.

23. Bowles-Jordan, J. Constipation. In: Compendium of Therapeutics for Minor Ailments. Ottawa, ON: Canadian Pharmacists Association. [Updated September 2018; Accessed June 2019].
24. Chaun,H. Constipation in Adults. In: Compendium of Therapeutic Choices. Ottawa, ON: Canadian Pharmacists Association. [Updated April 2018; Accessed June 2019].
25. Wald,A. (2019). Management of chronic constipation in adults. *UpToDate*. Retrieved June, 2019, from https://www.uptodate.com/contents/management-of-chronic-constipation-in-adults?search=constipaion&source=search_result&selectedTitle=1~150&usage_type=default&display_rank=1
26. Lee-Robichaud H, Thomas K, Morgan J, Nelson RL. Lactulose versus Polyethylene Glycol for Chronic Constipation. Cochrane Database Syst Rev. 2010 Jul 7;(7):CD007570
27. Kao,D. Diarrhea. In: Compendium of Therapeutic Choices. Ottawa, ON: Canadian Pharmacists Association. [Updated April 2018; Accessed June 2019].
28. Forrester, A. Diarrhea. In: Compendium of Therapeutics for Minor Ailments. Ottawa, ON: Canadian Pharmacists Association. [Updated September 2018; Accessed June 2019].
29. LaRocque, R. (2019). Approach to the adult with acute diarrhea in resource-rich settings. *UpToDate*. Retrieved June, 2019, from https://www.uptodate.com/contents/management-of-chronic-constipation-in-adults?search=constipaion&source=search_result&selectedTitle=1~150&usage_type=default&display_rank=1
30. Riddle MS, DuPont HL, Connor BA. ACG Clinical Guideline: Diagnosis, Treatment, and Prevention of Acute Diarrheal Infections in Adults. Am J Gastroenterol. 2016 May;111(5):602-22.
31. Zaid MR, Hasan M, Khan AA. Attapulgite in the treatment of acute diarrhoea: a double-blind placebo-controlled study. J Diarrhoeal Dis Res. 1995 Mar;13(1):44-6.
32. DuPont HL, Ericsson CD, DuPont MW, et al. A randomized, open-label comparison of nonprescription loperamide and attapulgite in the symptomatic treatment of acute diarrhea. Am J Med. 1990 Jun 20;88(6A):20S-23S.
33. Guo Q, Goldenberg JZ, Humphrey C, et al. Probiotics for the prevention of pediatric antibiotic-associated diarrhea. Cochrane Database Syst Rev. 2019 Apr 30;4:CD004827.
34. Blaabjerg S, Artzi DM, Aabenhus R. Probiotics for the Prevention of Antibiotic-Associated Diarrhea in Outpatients-A Systematic Review and Meta-Analysis. Antibiotics (Basel). 2017 Oct 12;6(4).
35. Schnadower D, Tarr PI, Casper TC, et al. Lactobacillus rhamnosus GG versus Placebo for Acute Gastroenteritis in Children. N Engl J Med. 2018 Nov 22;379(21):2002-2014.
36. Beleznay, K. Acne. In: Compendium of Therapeutic Choices. Ottawa, ON: Canadian Pharmacists Association. [Updated June 2019; Accessed June 2019].
37. Sihota, A. Acne. In: Compendium of Therapeutics for Minor Ailments. Ottawa, ON: Canadian Pharmacists Association. [Updated September 2018; Accessed June 2019].
38. Graber,E. (2019). Treatment of acne vulgaris. *UpToDate*. Retrieved June, 2019, from https://www.uptodate.com/contents/treatment-of-acne-vulgaris?search=acne&source=search_result&selectedTitle=1~150&usage_type=default&display_rank=1
39. Asai Y, Baibergenova A, Dutil M, et al. Management of acne: Canadian clinical practice guideline. CMAJ. 2016 Feb 2;188(2):118-126.
40. Zaenglein AL, Pathy AL, Schlosser BJ, et al. Guidelines of care for the management of acne vulgaris. J Am Acad Dermatol. 2016 May;74(5):945-73.e33.
41. Hauk L. Acne Vulgaris: Treatment Guidelines from the AAD. Am Fam Physician. 2017 Jun 1;95(11):740-741.
42. Drugs for acne. Med Lett Drugs Ther. 2016 Feb 1;58(1487):13-5. Review. Erratum in: Med Lett Drugs Ther. 2016 Feb 15;58(1488):24.
43. Miller, PF. Fungal Skin Infections. In: Compendium of Therapeutics for Minor Ailments. Ottawa, ON: Canadian Pharmacists Association. [Updated January 2018; Accessed June 2019].
44. Goldstein, A. (2019). Dermatophyte (tinea) infections. *UpToDate*. Retrieved June, 2019, from https://www.uptodate.com/contents/dermatophyte-tinea-infections?search=dermatophyte%20infections&source=search_result&selectedTitle=1~143&usage_type=default&display_rank=1
45. Crawford F, Hollis S. Topical treatments for fungal infections of the skin and nails of the foot. Cochrane Database Syst Rev. 2007 Jul 18;(3):CD001434. Review. PubMed PMID: 17636672.
46. Pappas PG, Kauffman CA, Andes DR, et al. Clinical Practice Guideline for the Management of Candidiasis: 2016 Update by the Infectious Diseases Society of America. Clin Infect Dis. 2016 Feb 15;62(4):e1-50.
47. Sobel,J. (2019). Candida vulvovaginitis:Treatment. *UpToDate*. Retrieved June, 2019, from https://www.uptodate.com/contents/candida-vulvovaginitis-treatment?search=Candida%20vulvocaginitis&source=search_result&selectedTitle=1~150&usage_type=default&display_rank=1
48. Weinstein, M. Atopic Dermatitis. In: Compendium of Therapeutic Choices. Ottawa, ON: Canadian Pharmacists Association. [Updated March 2018; Accessed June 2019].
49. Wong ITY, Tsuyuki RT, Cresswell-Melville A, Doiron P, Drucker AM. Guidelines for the management of atopic dermatitis (eczema) for pharmacists. Can Pharm J (Ott). 2017 May 30;150(5):285-297.
50. Sihota, A. Atopic, Contact, and Stasis Dermatitis. In: Compendium of Therapeutics for Minor Ailments. Ottawa, ON: Canadian Pharmacists Association. [Updated September 2018; Accessed June 2019].
51. Brod,B. (2019). Management of allergic contact dermatitis. *UpToDate*. Retrieved June, 2019, from https://www.uptodate.com/contents/management-of-allergic-contact-dermatitis?search=management%20of%20allergic%20contact%20dermatitis&source=search_result&selectedTitle=1~116&usage_type=default&display_rank=1
52. Goldner R., Fransway A. (2019). Irritant contact dermatitis in adults. *UpToDate*. Retrieved June, 2019, from https://www.uptodate.com/contents/irritant-contact-dermatitis-in-adults?search=irritant%20contact%20dermatitis%20in%20adults&source=search_result&selectedTitle=1~49&usage_type=default&display_rank=1
53. Nakhla, N., Butt, K. Diaper Dermatitis. In: Compendium of Therapeutics for Minor Ailments. Ottawa, ON: Canadian Pharmacists Association. [Updated September 2018; Accessed June 2019].
54. Williams HC. Established corticosteroid creams should be applied only once daily in patients with atopic eczema. BMJ. 2007 Jun 16;334(7606):1272
55. Matterne U, Böhmer MM, Weisshaar E, Jupiter A, Carter B, Apfelbacher CJ. Oral H1 antihistamines as 'add-on' therapy to topical treatment for eczema. Cochrane Database Syst Rev. 2019 Jan 22;1:CD012167.
56. Maarouf M, Shi VY. Bleach for Atopic Dermatitis. Dermatitis. 2018 May/Jun;29(3):120-126.
57. Mallin, A. Plantar Warts. In: Compendium of Therapeutics for Minor Ailments. Ottawa, ON: Canadian Pharmacists Association. [Updated September 2018; Accessed June 2019].
58. Mulhem E, Pinelis S. Treatment of nongenital cutaneous warts. Am Fam Physician. 2011 Aug 1;84(3):288-93. Review. PubMed PMID: 21842775.
59. Pharmacists' Letter Canada. Tell Patients to be Persistent When Treating Warts
60. Kwok CS, Gibbs S, Bennett C, Holland R, Abbott R. Topical treatments for cutaneous warts. Cochrane Database Syst Rev. 2012 Sep 12;(9):CD001781.
61. Sterling JC, Gibbs S, Haque Hussain SS, Mohd Mustapa MF, Handfield-Jones SE. British Association of Dermatologists' guidelines for the management of cutaneous warts 2014. Br J Dermatol. 2014 Oct;171(4):696-712.
62. Cummings C, Finlay JC, MacDonald NE. Head lice infestations: A clinical update. Paediatr Child Health. 2018 Feb;23(1):e18-e24.
63. Miller,P. Parasitic Skin Infections: Lice and Scabies. In: Compendium of Therapeutics for Minor Ailments. Ottawa, ON: Canadian Pharmacists Association. [Updated November 2018; Accessed June 2019].
64. Goldstein, A., Goldstein, B. (2019). Pediculosis Capitis *UpToDate*. Retrieved June, 2019, from https://www.uptodate.com/contents/pediculosis-capitis?search=pediculosis%20capitis&source=search_result&selectedTitle=1~20&usage_type=default&display_rank=1
65. Meltzer EO, Ratner PH, McGraw T. Phenylephrine hydrochloride modified-release tablets for nasal congestion: a randomized, placebo-controlled trial in allergic rhinitis patients. Ann Allergy Asthma Immunol. 2016 Jan;116(1):66-71.

Others:

- Bachert C. A review of the efficacy of desloratadine, fexofenadine, and levocetirizine in the treatment of nasal congestion in patients with allergic rhinitis. Clin Ther. 2009 May;31(5):921-44.

- Melvin TA, Patel AA. Pharmacotherapy for allergic rhinitis. Otolaryngol Clin North Am. 2011 Jun;44(3):727-39, x.
- Castillo M, Scott NW, Mustafa MZ, Mustafa MS, Azuara-Blanco A. Topical antihistamines and mast cell stabilisers for treating seasonal and perennial allergic conjunctivitis. Cochrane Database Syst Rev. 2015 Jun 1;(6):CD009566.
- Wise SK, Lin SY, Toskala E, et al. International Consensus Statement on Allergy and Rhinology: Allergic Rhinitis. Int Forum Allergy Rhinol. 2018 Feb;8(2):108-352.
- Dykewicz MS, Wallace DV, Baroody F, et al. Treatment of seasonal allergic rhinitis: An evidence-based focused 2017 guideline update. Ann
- Allergy Asthma Immunol. 2017 Dec;119(6):489-511.e41. [long article reviewing studies; INAH+INCS may be a benefit]
- Feld L, Cifu AS. Management of Dyspepsia. JAMA. 2018 May 1;319(17):1816-1817
- Pittayanon R, Yuan Y, Bollegala NP, et al. Prokinetics for functional dyspepsia. Cochrane Database Syst Rev. 2018 Oct 18;10:CD009431.
- Pinto-Sanchez MI, Yuan Y, Hassan A, Bercik P, Moayyedi P. Proton pump inhibitors for functional dyspepsia. Cochrane Database Syst Rev. 2017 Nov 21;11:CD011194.
- Shin JM, Sachs G. Pharmacology of proton pump inhibitors. Curr Gastroenterol Rep. 2008 Dec;10(6):528-34.
- Paquette IM, Varma M, Ternent C, et al. The American Society of Colon and Rectal Surgeons' Clinical Practice Guideline for the Evaluation and Management of Constipation. Dis Colon Rectum. 2016 Jun;59(6):479-92.
- Wald A. Is chronic use of stimulant laxatives harmful to the colon? J Clin Gastroenterol. 2003 May-Jun;36(5):386-9. Review. PubMed PMID: 12702977.
- Educate Patients not to rely on probiotics for acute diarrhea and vomiting – Pharmacist Letter- 19
- Newlove-Delgado T, Abbott RA, Martin AE. Probiotics for Children With Recurrent Abdominal Pain. JAMA Pediatr. 2019 Feb 1;173(2):183
- Margarido Lda C. Oral treatments for fungal infections of the skin of the foot. Sao Paulo Med J. 2014;132(2):127. PubMed PMID: 24714996.
- van Schalkwyk J, Yudin MH; INFECTIOUS DISEASE COMMITTEE. Vulvovaginitis: screening for and management of trichomoniasis, vulvovaginal candidiasis, and bacterial vaginosis. J Obstet Gynaecol Can. 2015 Mar;37(3):266-274.
- AAAAI contact dermatis overview (just a website, but this was the only thing that mentioned astringent, calamine etc.)
- Usatine RP, Riojas M. Diagnosis and management of contact dermatitis. Am Fam Physician. 2010 Aug 1;82(3):249-55. Review. PubMed PMID: 20672788.

Original References:

1. RxTx
Patient Self-Care, first edition. CPhA; Ottawa, Canada: 2002
2. Compendium of Nonprescription Products. CPhA; Ottawa, Canada: 2002-3.
3. Therapeutic Choices, Fifth edition. CPhA: Ottawa, Canada: 2007.
4. Drug Information Handbook, 18th edition. APhA; Hudson, Ohio; 2009.
5. **Treatment Guidelines**: Drugs for Allergic Disorders. The **Medical Letter**: May, **2017**; pg. 71-81.
6. Reid RL, et al. SOGC (Society of Obstetricians & Gynaecologists of Canada)-Menopause & **Osteoporosis Update 2009**. JOGC. **2009**. http://www.sogc.org/guidelines/documents/Menopause_JOGC-Jan_09.pdf;
7. **Canadian Osteoporosis** Guide Papaioannou CMAJ **2010 7**. Drugs in Pregnancy & Lactation, 9th ed. Briggs GE; 2008.
8. Black RA, Hill DA. Over-the-counter medications in **pregnancy**. Am Fam Physician. 2003 Jun 15;67(12):2517-24.
9. Demoly P, Piette V, Daures JP. Treatment of allergic rhinitis during **pregnancy**. Drugs. 2003;63(17):1813-20.
10. Blaiss MS; US FDA; ACAAI-ACOG(American College of Allergy, Asthma, & Immunology and American College of Obstetricians & Gynecologists.). Management of rhinitis and asthma in **pregnancy**. Ann Allergy Asthma Immunol. 2003 Jun;90(6 Suppl 3):16-22.
11. Richter JE. Gastroesophageal reflux disease during **pregnancy**. Gastroenterol Clin North Am. 2003 Mar;32(1):235-61.
12. Schroeder K, Fahey T. Systematic review of randomised controlled trials of over the counter **cough** medicines for acute cough in adults. BMJ. 2002 Feb 9;324(7333):329-31. (Smith J, Owen E, Earis J, Woodcock A. Effect of codeine on objective measurement of cough in chronic obstructive pulmonary disease. J Allergy Clin Immunol. 2006 Apr;117(4):831-5. Epub 2006 Feb 7.)
13. Morice AH, Kastelik JA. Cough. 1: Chronic **cough** in adults. Thorax. 2003 Oct;58(10):901-7.
Irwin RS, et al. American College of Chest Physicians (ACCP). Diagnosis and management of **cough executive summary: ACCP** evidence-based clinical practice guidelines. Chest. 2006 Jan;129(1 Suppl):1S-23S.
http://www.chestjournal.org/cgi/content/full/129/1_suppl/1S
Pharmacist's Letter Oct/006. Pharmacologic Treatment of Cough: Evidence-based guidelines.
Yoder KE, et al. Child assessment of dextromethorphan, diphenhydramine, and placebo for nocturnal cough due to upper respiratory infection. Clin Pediatr (Phila). 2006 Sep;45(7):633-40.
Morice AH, Fontana GA, Belvisi MG, et al. European Respiratory Society (ERS). ERS guidelines on the assessment of cough. Eur Respir J. 2007 Jun;29(6):1256-76.
Morice AH, McGarvey L, Pavord I; British Thoracic Society Cough Guideline Group. Recommendations for the management of cough in adults. Thorax. 2006 Sep;61 Suppl 1:i1-24.
Woodhead M, Blasi F, Ewig S, et al. European Respiratory Society; European Society of Clinical Microbiology and Infectious Diseases. Guidelines for the management of adult lower respiratory tract infections. Eur Respir J. 2005 Dec;26(6):1138-80.
Tan T, Little P, Stokes T; Guideline Development Group. Antibiotic prescribing for self limiting respiratory tract infections in primary care: summary of NICE guidance. BMJ. 2008 Jul 23;337:a437. doi: 10.1136/bmj.a437.
14. Smucny JJ, Flynn CA, Becker LA, Glazier RH. Are beta2-agonists effective treatment for acute bronchitis or acute cough in patients without underlying pulmonary disease? A systematic review. J Fam Pract. 2001 Nov;50(11):945-51.
15. Smucny J, Flynn C, Becker L, Glazier R. Beta2-agonists for acute bronchitis. Cochrane Database Syst Rev. 2004;(1):CD001726. (Tomerak A, Vyas H, Lakenpaul M, et al. Inhaled beta2-agonists for treating non-specific chronic cough in children. Cochrane Database Syst Rev. **2005** Jul 20;(3):CD005373.) Smucny J, Becker L, Glazier R. Beta2-agonists for acute bronchitis. Cochrane Database Syst Rev. 2006 Oct 18;(4):CD001726.
16. Van Cauwenberge P, Bachert C, Passalacqua G, Bousquet J et al. Consensus statement on the treatment of allergic rhinitis. European Academy of Allergology and Clinical Immunology. Allergy. 2000 Feb;55(2):116-34.
17. Bousquet J, Van Cauwenberge P, Khaltaev N; Aria Workshop Group; World Health Organization. Allergic rhinitis and its impact on asthma (**ARIA**). J Allergy Clin Immunol. **2001** Nov;108(5 Suppl):S147-334. http://www.whiar.com
18. Lee EE, Maibach HI. Treatment of urticaria. An evidence-based evaluation of antihistamines. Am J Clin Dermatol. 2001;2(1):27-32.
19. Casale TB, Blaiss MS, et al. Antihistamine Impairment Roundtable. First do no harm: managing antihistamine impairment in patients with allergic rhinitis. J Allergy Clin Immunol. 2003 May;111(5):S835-42.
20. Berger WE. Overview of allergic rhinitis. Ann Allergy Asthma Immunol. 2003 Jun;90(6 Suppl 3):7-12.
21. Bender BG, Berning S, Dudden R, Milgrom H, Tran ZV. Sedation and performance impairment of diphenhydramine and second-generation antihistamines: a meta-analysis. J Allergy Clin Immunol. 2003:111:770-776.
Medscape CME Sept 23,2003 by Dr. Bender & Milgrom availablet at http://www.medscape.com/viewprogram/2673_pnt accessed Nov14,2003.
22. Murdoch D, Goa K, Keam S. Desloratadine: An Update of its Efficacy in the Management of Allergic Disorders. Drugs. 2003;63(19):2051-2077.
23. Simons FE, J Semus M, Goritz SS, Simons KJ. H1-antihistaminic activity of cetirizine and fexofenadine in allergic children. Pediatr Allergy Immunol. 2003 Jun;14(3):207-11.
24. Stevenson J, et al. ETAC Study Gp. Long-term evaluation of the impact of the h1-receptor antagonist **cetirizine** on behavioral, cognitive & psychomotor development of very young children **1-2yr** with **atopic dermatitis**. Pediatr Res. 2002 Aug;52(2):251-7.
25 Schenkel E, Corren J, Murray JJ. Efficacy of once-daily desloratadine/pseudoephedrine for relief of nasal congestion. Allergy Asthma Proc. 2002 Sep-Oct;23(5):325-30. (Raphael GD, Angello JT, Wu MM, Druce HM. Efficacy of **diphenhydramine** vs desloratadine & placebo in patients with moderate-to-severe seasonal allergic rhinitis. Ann Allergy Asthma Immunol. 2006 Apr;96(4):606-14.)
26. Horak F, Stubner P, Zieglmayer R, et al. Controlled comparison of the efficacy and safety of cetirizine 10 mg o.d. and fexofenadine 120 mg o.d. in reducing symptoms of seasonal allergic rhinitis. Int Arch Allergy Immunol. 2001 May;125(1):73-9.
27. Van Adelsberg J, Philip G, Pedinoff AJ, Meltzer EO, et al.. For the Montelukast Fall Rhinitis Study Group. Montelukast improves symptoms of seasonal allergic rhinitis over a 4-week treatment period. Allergy. 2003 Dec;58(12):1268-76.
28. Montelukast (singulair) for allergic rhinitis. Med Lett Drugs Ther. 2003 Mar 17;45(1152):21-2.
29. Nathan RA. Pharmacotherapy for allergic rhinitis: a critical review of leukotriene receptor antagonists compared with other treatments. Ann Allergy Asthma Immunol. 2003 Feb;90(2):182-90.
30. Salib RJ, Howarth PH. Safety and tolerability profiles of intranasal antihistamines and intranasal corticosteroids in the treatment of allergic rhinitis. Drug Saf. 2003;26(12):863-93.
31. Yanez A, Rodrigo GJ. Intranasal corticosteroids versus topical H1 receptor antagonists for the treatment of allergic rhinitis: a systematic review with meta-analysis. Ann Allergy Asthma Immunol. 2002 Nov;89(5):479-84.
32. Trangsrud AJ, Whitaker AL, Small RE. Intranasal corticosteroids for allergic rhinitis. Pharmacotherapy. 2002 Nov;22(11):1458-67.
33. Nielsen LP, Mygind N, Dahl R. Intranasal corticosteroids for allergic rhinitis: superior relief? Drugs. 2001;61(11):1563-79.
34. Weiner JM, Abramson MJ, Puy RM. Intranasal corticosteroids versus oral H1 receptor antagonists in allergic rhinitis: systematic review of randomised controlled trials. BMJ. 1998 Dec 12;317(7173):1624-9.
Nasser M, Fedorowicz Z, Aljufairi H, et al. **Antihistamines used in addition to topical nasal steroids** for intermittent and persistent allergic rhinitis in children. Cochrane Database Syst Rev. 2010 Jul 7;7:CD006989. In view of the lack of evidence for the benefit or lack of benefit of antihistamine add-on therapy with topical nasal steroids for children with intermittent or persistent allergic rhinitis, it is important that clinicians are mindful of the adverse effects of antihistamines and the additional costs that may be incurred.
35. Moayyedi P, Soo S, Deeks J, Forman D, Harris A, Innes M, Delaney B. Systematic review: Antacids, H2-receptor antagonists, prokinetics, bismuth and sucralfate therapy for non-ulcer **dyspepsia**. Aliment Pharmacol Ther. 2003 May 15;17(10):1215-27.

36. Delaney BC, Moayyedi P, Forman D. Initial management strategies for **dyspepsia**. Cochrane Database Syst Rev. 2003;(2):CD001961.
37. Lembo A, Camilleri M. Chronic **constipation**. N Engl J Med. 2003 Oct 2;349(14):1360-8.
38. Webster GF. **Acne** vulgaris. BMJ. 2002 Aug 31;325(7362):475-9.
39. Leyden JJ. A review of the use of combination therapies for the treatment of **acne** vulgaris. J Am Acad Dermatol. 2003 Sep;49(3 Suppl):S200-10.
40. Berson DS, Chalker DK, Harper JC, Leyden JJ, Shalita AR, Webster GF. Current concepts in the treatment of **acne**: report from a clinical roundtable. Cutis. 2003 Jul;72(1 Suppl):5-13.
41. Watson MC, Grimshaw JM, Bond CM, Mollison J, Ludbrook A. Oral versus intra-vaginal imidazole and triazole **anti-fungal** agents for the treatment of uncomplicated vulvovaginal candidiasis (thrush): a systematic review. BJOG. 2002 Jan;109(1):85-95.
42. Hart R, Bell-Syer SE, Crawford F, Torgerson DJ, Young P, Russell I. Systematic review of topical treatments for **fungal** infections of the skin and nails of the feet. BMJ. 1999 Jul 10;319(7202):79-82.
43. Gupta AK, Chow M, Daniel CR, Aly R. Treatments of **tinea pedis**. Dermatol Clin. 2003 Jul;21(3):431-62.
44. Gupta AK, Chaudhry M, Elewski B. **Tinea corporis**, tinea **cruris**, tinea **nigra**, and **piedra**. Dermatol Clin. 2003 Jul;21(3):395-400
45. Leung DY, Bieber T. **Atopic dermatitis**. Lancet. 2003 Jan 11;361(9352):151-60.
46. Correale CE, Walker C, Murphy L, Craig TJ. **Atopic dermatitis**: a review of diagnosis and treatment. Am Fam Physician. 1999 Sep 15;60(4):1191-8, 1209-10.
47. Gibbs S, Harvey I, Sterling J, Stark R. Local treatments for cutaneous **warts**: systematic review. BMJ. 2002 Aug 31;325(7362):461.
48. Stulberg DL, Hutchinson AG. Molluscum contagiosum and **warts**. Am Fam Physician. 2003 Mar 15;67(6):1233-40.
49. Bedinghaus JM, Niedfeldt MW. Over-the-counter **foot** remedies. Am Fam Physician. 2001 Sep 1;64(5):791-6.
Gibbs S, Harvey I. T opical treatments for cutaneous **warts**. Cochrane Database Syst Rev. 2006;(3): CD001781.
Bruggink, Sjoerd C., Gussekloo, Jacobijn, Berger, Marjolein Y., et al. **Cryotherapy** with liquid nitrogen versus topical salicylic acid application for cutaneous warts in primary care: a randomized controlled trial CMAJ 2010 0: cmaj.092194.
Kwok CS, Holland R, Gibbs S. Efficacy of topical treatments for cutaneous warts: a meta-analysis and pooled analysis of randomized controlled trials. Br J Dermatol 2011; online 11 January.
Cockayne S, Hewitt C, Hicks K, Jayakody S, Kang'ombe AR, Stamuli E, et al. **Cryotherapy versus salicylic acid** for the treatment of plantar warts (verrucae): a randomised controlled trial. BMJ 2011;342:d3271.
Mulhem E, Pinelis S. Treatment of **nongenital cutaneous warts**. Am Fam Physician. 2011 Aug 1;84(3):288-93.
Cockayne S, Curran M, Denby G, et al. EVerT: **cryotherapy versus salicylic acid** for the treatment of verrucae - a randomised controlled trial. Health Technol Assess. 2011 Sep;15(32):1-170.
Kwok CS, Gibbs S, Bennett C, et al. **Topical treatments for cutaneous warts**. Cochrane Database Syst Rev. 2012 Sep 12;9:CD001781.
Bruggink SC, Eekhof JA, Egberts PF, van Blijswijk SC, Assendelft WJ, Gussekloo J. **Natural course of cutaneous warts** among primary schoolchildren: a prospective cohort study. Ann Fam Med. 2013 Sep-Oct;11(5):437-41.
Craw L, Wingert A, Lara-Corrales I. Are **salicylic formulations, liquid nitrogen or duct tape** more effective than placebo for the treatment of warts in paediatric patients who present to ambulatory clinics? Paediatr Child Health. 2014 Mar;19(3):126-7.
Lynch MD, Cliffe J, Morris-Jones R. Management of **cutaneous viral warts**. BMJ. 2014 May 27;348:g3339

50. Nash B. Treating **head lice**. BMJ. 2003 Jun 7;326(7401):1256-7.(Leung AK, Fong JH, Pinto-Rojas A. Pediculosis capitis. J Pediatr Health Care. 2005 Nov-Dec;19(6):369-73.)
51. Frankowski BL, Weiner LB; Committee on School Health the Committee on Infectious Diseases. American Academy of Pediatrics. **Head lice**. Pediatrics. 2002 Sep;110(3):638-43.
Frankowski, B., & Bocchini, J. (**2010**). **Head Lice** *PEDIATRICS*, *126* (2), 392-403 DOI: 10.1542/peds.2010-1308
52. Villar J, Merialdi M, et al. Nutritional interventions during pregnancy for the prevention or treatment of maternal morbidity and preterm delivery: an overview of randomized controlled trials. J Nutr. 2003 May;133(5 Suppl 2):1606S-1625S.(Fawzi WW, Msamanga GI, et al. Vitamins and perinatal outcomes among HIV-negative women in Tanzania. N Engl J Med. 2007 Apr 5;356(14):1423-31. Multivitamin supplementation reduced the incidence of low birth weight and small-for-gestational-age births but had no significant effects on prematurity or fetal death. Multivitamins should be considered for all pregnant women in developing countries.)
Shah PS, Ohlsson A. Effects of **prenatal multimicronutrient supplementation** on pregnancy outcomes: a meta-analysis. CMAJ. 2009 Jun 9;180(12):E99-E108. Prenatal multimicronutrient supplementation was associated with a significantly reduced risk of low birth weight & with improved birth weight when compared with iron-folic acid supplementation. There was no significant effect of multimicronutrient supplementation on the risk of preterm birth or small-for-gestational-age infants.
Catov JM, Bodnar LM, Olsen J, Olsen S, Nohr EA. **Periconceptional multivitamin** use and risk of preterm or small-for-gestational-age births in the Danish National Birth Cohort. Am J Clin Nutr. 2011 Sep;94(3):906-12.
Persson LÅ, Arifeen S, Ekstro¨m E-C, et al. **MINIMat** Study Team. Effects of **prenatal micronutrient and early food supplementation** on maternal hemoglobin, birth weight, and infant mortality among children in Bangladesh: the MINIMat randomized trial. JAMA. 2012;307(19):2050- 2059.
53. Morris CD, Carson S. Routine **vitamin** supplementation to prevent cardiovascular disease: a summary of the evidence for the U.S. Preventive Services Task Force. Ann Intern Med. 2003 Jul 1;139(1):56-70.
54. Vivekananthan DP, Penn MS, Sapp SK, Hsu A, Topol EJ. Use of antioxidant **vitamins** for the prevention of cardiovascular disease: meta-analysis of randomised trials. Lancet. 2003 Jun 14;361(9374):2017-23.
55. http://www.hc-sc.gc.ca/hpfb-dgpsa/tpd-dpt/adrv13n1_e.pdf
56. Cass E. et al. Hazards of **phenylephrine** topical medication in persons taking propranolol CMAJ 1979 120: 1261-1262.
57. Veldhuyzen van Zanten SJ, Flook N, et al. An evidence-based approach to the management of uninvestigated **dyspepsia** in the era of Helicobacter pylori. Canadian Dyspepsia Working Group. CMAJ. 2000 Jun 13;162(12 Suppl):S3-23.
58. Drossman DA, Camilleri M, Mayer EA, Whitehead WE. AGA technical review on **irritable bowel syndrome**. Gastroenterology. 2002 Dec;123(6):2108-31.
59. Spanier JA, Howden CW, Jones MP. A systematic review of alternative therapies in the **irritable bowel syndrome**. Arch Intern Med. 2003 Feb 10;163(3):265-74.
60. Jones J, Boorman J, Cann P, Forbes A, Gomborone J, et al. British Society of Gastroenterology guidelines for the management of the **irritable bowel syndrome**. Gut. 2000 Nov;47 Suppl 2:ii1-19.
61. Paterson WG, Thompson WG, Vanner SJ, et al. Recommendations for the management of **irritable bowel syndrome** in family practice. IBS Consensus Conference Participants. CMAJ. 1999 Jul 27;161(2):154-60.
62. Rucker D, Allan JA, Fick GH, Hanley DA. **Vitamin D** insufficiency in a population of healthy western Canadians. CMAJ. 2002 Jun 11;166(12):1517-24.
63. Scavone JM, et al. Pharmacokinetics and pharmacodynamics of diphenhydramine 25 mg in young and elderly volunteers. J Clin Pharmacol. 1998 Jul;38(7):603-9. (Merenstein D, et al. The Trial of Infant Response to **Diphenhydramine**: The TIRED Study--A Randomized, Controlled, Patient-Oriented Trial. Arch Pediatr Adolesc Med. 2006 Jul;160(7):707-712.)
64. Kernan WN, Viscoli CM, Brass LM, Broderick JP, Brott T, Feldmann E, Morgenstern LB, Wilterdink JL, Horwitz RI. Phenylpropanolamine and the risk of hemorrhagic stroke. N Engl J Med. 2000 Dec 21;343(25):1826-32.
65. Jones MP, Talley NJ, Nuyts G, Dubois D. Lack of objective evidence of efficacy of laxatives in chronic constipation. Dig Dis Sci. 2002 Oct;47(10):2222-30.
66. Focht DR 3rd, Spicer C, Fairchok MP. The efficacy of duct tape vs cryotherapy in the treatment of verruca vulgaris (the common wart). Arch Pediatr Adolesc Med. 2002 Oct;156(10):971-4. (de Haen M, et al. Efficacy of duct tape vs placebo in the treatment of verruca vulgaris (warts) in primary school children. Arch Pediatr Adolesc Med. 2006 Nov;160(11):1121-5.) (Wenner R, Askari SK, Cham PM, Kedrowski DA, Liu A, Warshaw EM. Duct tape for the treatment of common warts in adults: a double-blind randomized controlled trial. Arch Dermatol. 2007 Mar;143(3):309-13. (n=90) Patients were instructed to wear the pads for 7 consecutive days and leave the pad off on the seventh evening. This process was repeated for 2 months or until the wart resolved, whichever occurred first. Of patients with complete resolution, 6 (75%) in the treatment group and 3 (33%) in the control group had recurrence of the target wart by the sixth month. CONCLUSION: We found no statistically significant difference between duct tape and moleskin for the treatment of warts in an adult population. (InfoPOEMs: Occlusion with transparent duct tape is no more or less effective than occlusion with moleskin. The low success rate overall argues against any effect for occlusion. One interesting suggestion is that since hypnosis has been shown to be an effective treatment, perhaps that is the mechanism by which duct tape occlusion works, and perhaps adults are less suggestible than children. While this may not be the final word on this topic, it is discouraging news for the good folks at the American Duct Tape Council.))
Bavinck JNB, Eekhof JAH, Bruggink SC. Treatments for common and plantar warts. BMJ 2011;342:d3119.
Goldman RD. Duct tape for warts in children: Should nature take its course? Can Fam Physician. 2019 May;65(5):337-338.
67. Sano M, Ernesto C, Thomas RG, Klauber MR, et al. A controlled trial of selegiline, alpha-tocopherol, or both as treatment for Alzheimer's disease. The Alzheimer's Disease Cooperative Study. N Engl J Med. 1997 Apr 24;336(17):1216-22.
68. Tabet N, Birks J, Grimley Evans J. Vitamin E for Alzheimer's disease. Cochrane Database Syst Rev. 2000;(4):CD002854.
69. Brown BG, Zhao XQ, Chait A, Fisher LD, et al. Simvastatin and niacin, antioxidant vitamins, or the combination for the prevention of coronary disease. N Engl J Med. 2001 Nov 29;345(22):1583-92.
70. Patient information & other useful links to the American Podiatric Medical Association http://www.apma.org/topics/Warts.htm
71. Watson MC, Grimshaw JM, Bond CM, Mollison J, Ludbrook A Oral versus intra-vaginal imidazole and triazole anti-fungal treatment of uncomplicated vulvovaginal candidiasis (thrush). (Cochrane Review). In: The Cochrane Library, Issue 4, 2003.
72. De Sutter AIM, Lemiengre M, Campbell H, Mackinnon HF Antihistamines for the common cold (Cochrane Review). In: The Cochrane Library, Issue 4, 2003. Chichester, UK: John Wiley & Sons, Ltd. -WITHDRAWN
73. Taverner D, Bickford L, Draper M Nasal decongestants for the common cold (Cochrane Review). In: The Cochrane Library, Issue 4, 2003. Chichester, UK: John Wiley & Sons, Ltd. (Infant Deaths Associated with Cough and Cold Medications --- Two States, 2005 http://www.cdc.gov/mmwr/preview/mmwrhtml/mm5601a1.htm)- WITHDRAWN
Pharmacist's Letter- Efficacy of oral phenylephrine. Feb,2008
Vaidyanathan S, Williamson P, Clearie K, et al. **Fluticasone Reverses Oxymetazoline** Induced Tachyphylaxis of Response and Rebound Congestion. Am J Respir Crit Care Med. 2010 Mar 4.
Umoren R, Odey F, Meremikwu MM. **Steam inhalation or humidified oxygen** for acute bronchiolitis in children up to three years of age. Cochrane Database Syst Rev. 2011 Jan 19;1:CD006435. Steam inhalation (or cool mist therapy) is commonly used to treat acute bronchiolitis in resource-constrained settings. One study was eligible for inclusion and found that nebulised salbutamol was an effective intervention for young children with bronchiolitis but mist in a tent did not lead to a significant decrease in RDS score. Since only one study was analysed it would be misleading to conclude that mist therapy is ineffective in children with bronchiolitis. We conclude that there is insufficient evidence to inform practice regarding using steam inhalation or mist therapy for acute bronchiolitis in kids up to three year old.
Fashner J, Ericson K, Werner S. Treatment of the Common Cold in Children and Adults. Am Fam Physician. 2012;86(2):153-159.
Meltzer EO et al. Oral phenylephrine HCl for nasal congestion in seasonal allergic rhinitis: A randomized, open-label, placebo-controlled study. J Allergy Clin Immunol Pract 2015 Sep/Oct; 3:702.
Stavert B, McGuinness MB, Harper CA, Guymer RH, Finger RP. Cardiovascular Adverse Effects of Phenylephrine Eyedrops: A Systematic Review and Meta-analysis. JAMA Ophthalmol. 2015 Jun;133(6):647-52.

Meltzer EO, Ratner PH, McGraw T. Phenylephrine hydrochloride modified-release tablets for nasal congestion: a randomized, placebo-controlled trial in allergic rhinitis patients. Ann Allergy Asthma Immunol. 2016 Jan;116(1):66-71.

74. Schroeder K, Fahey T Over-the-counter medications for acute cough in children and adults in ambulatory settings (Cochrane Review). In: The Cochrane Library, Issue 4, 2003. Chichester, UK: John Wiley & Sons, Ltd.
Cals JW, Francis NA. Acute cough in adults. BMJ. 2010 Feb 12;340:c574. doi:10.1136/bmj.c574.
75. Marshall I Zinc for the common cold (Cochrane Review). In: The Cochrane Library, Issue 4, 2003. Chichester, UK: John Wiley & Sons, Ltd.
Prasad AS, Beck FW, Bao B, Snell D, Fitzgerald JT. Duration and severity of symptoms and levels of plasma interleukin-1 receptor antagonist, soluble tumor necrosis factor receptor, and adhesion molecules in patients with common cold treated with zinc acetate. J Infect Dis. 2008 Mar 15;197(6):795-802. Administration of zinc lozenges was associated with reduced duration and severity of cold symptoms. We related the improvement in cold symptoms to the antioxidant and anti-inflammatory properties of zinc.
Singh M, Das RR. **Zinc for the common cold**. Cochrane Database of Systematic Reviews 2011, Issue 2. Art. No.: CD001364. DOI: 10.1002/14651858.CD001364.pub3. Zinc administered within 24 hours of onset of symptoms reduces the duration and severity of the common cold in healthy people. When supplemented for at least five months, it reduces cold incidence, school absenteeism and prescription of antibiotics in children. There is potential for zinc lozenges to produce side effects. In view of this and the differences in study populations, dosages, formulations and duration of treatment, it is difficult to make firm recommendations about the dose, formulation and duration that should be used.
Science M, Johnstone J, Roth DE, et al. Zinc for the treatment of the common cold: a systematic review and meta-analysis of randomized controlled trials. CMAJ. 2012 May 7.
Hemilä H, Petrus EJ, Fitzgerald JT, et al. Zinc acetate lozenges for treating the common cold: an individual patient data meta-analysis. Br J Clin Pharmacol. 2016 Jul 5.

76. Gunn VL, Taha SH, Liebelt EL, Serwint JR. Toxicity of over-the-counter cough and cold medications. Pediatrics. 2001 Sep;108(3):E52 (Hatton RC, Winterstein AG, McKelvey RP, Shuster J,
Hendeles L. Efficacy and safety of oral phenylephrine: systematic review and meta-analysis. Ann Pharmacother. 2007 Mar;41(3):381-90. Epub 2007 Jan 30. There is insufficient evidence that oral phenylephrine is effective for nonprescription use as a decongestant. The Food and Drug Administration should require additional studies to show the safety and efficacy of phenylephrine.) Vernacchio L, Kelly JP, Kaufman DW, Mitchell AA. Cough and cold medication use by US children, 1999-2006: results from the slone survey. Pediatrics. 2008 Aug;122(2):e323-9. Approximately 1 in 10 US children uses a cough and cold medication in a given week. The especially high prevalence of use among children of young age is noteworthy, given concerns about potential adverse effects and the lack of data on the efficacy of cough and cold medications in this age group. Rimsza ME, Newberry S. Unexpected infant deaths associated with use of cough and cold medications. Pediatrics. 2008 Aug;122(2):e318-22. Review of these infants' deaths raises concern about the role of the over-the-counter cough and cold medications in these deaths. These findings support the recommendation that such medications not be given to infants.
Vernacchio L, Kelly JP, Kaufman DW, Mitchell AA. Pseudoephedrine use among US children, 1999-2006: results from the Slone survey. Pediatrics. 2008 Dec;122(6):1299-304. Pseudoephedrine exposure, mostly in the form of multiple-ingredient products, is common among US children, especially children who are younger than 2 years, who are at the highest risk for toxicity and for whom safe dosing recommendations are lacking. Concerning patterns of use include taking >1 pseudoephedrine-containing product concurrently and using pseudoephedrine for extended periods. Pediatric pseudoephedrine use seems to be declining since the institution of the 2005 Combat Methamphetamine Epidemic Act.
Dart RC, Paul IM, et al. Pediatric fatalities associated with over the counter (nonprescription) cough and cold medications. Ann Emerg Med. 2009 Apr;53(4):411-7. Epub 2008 Dec 19.
Lokker Nicole, Sanders Lee, Perrin Eliana M. et al. Parental Misinterpretations of Over-the-Counter Pediatric Cough and Cold Medication Labels. Pediatrics 2009 123: 1464-1471.
Shefrin AE, Goldman RD. Use of over-the-counter cough and cold medications in children. Can Fam Physician. 2009 Nov;55(11):1081-3.
Kuehn Bridget M. Medical News & Perspectives: Withdrawal of Infant Cold Medicines Decreases ED Visits by Half, CDC Finds. *JAMA*. 2010;304(24):2686.doi:10.1001/jama.2010.1831
Goldman RD; Canadian Paediatric Society, Drug Therapy and Hazardous Substances Committee. Treating cough and cold: guidance for caregivers of children and youth. Paediatr Child Health 2011;16:564-6. www.cps.ca/English/statements/DT/TreatingCough.htm (accessed December 12, 2011).
Hampton LM, Nguyen DB, Edwards JR, et al. Cough and Cold Medication Adverse Events After Market Withdrawal and Labeling Revision. Pediatrics. 2013 Nov 11.
van Driel ML, Scheire S, Deckx L, et al. **What treatments are effective for common cold** in adults and children? BMJ. 2018 Oct 10;363:k3786.

77. Use of codeine- and dextromethorphan-containing cough remedies in children. American Academy of Pediatrics. Committee on Drugs. Pediatrics. 1997 Jun;99(6):918-20.
78. Albanes D, Heinonen OP, Taylor PR, et al. Alpha-Tocopherol and beta-carotene supplements and lung cancer incidence in the alpha-tocopherol, beta-carotene cancer prevention study (ATBC): effects of base-line characteristics and study compliance (**ATBC** trial). J Natl Cancer Inst. 1996 Nov 6; 88: 1560-70.
Omenn GS, Goodman GE, Thornquist MD, et al. Effects of a combination of beta carotene and vitamin A on lung cancer and cardiovascular disease. (**CARET**) N Engl J Med. 1996 May 2;334(18):1150-5.
79. Zandi PP, Anthony JC, Khachaturian AS, Stone SV, Gustafson D, Tschanz JT, Norton MC, Welsh-Bohmer KA, Breitner JC. Reduced risk of Alzheimer disease in users of antioxidant vitamin supplements: the cache county study. Arch Neurol. 2004 Jan; 61(1): 82-8.
Chan JM, Oh WK, Xie W, Regan MM, Stampfer MJ, King IB, Abe M, Kantoff PW. Plasma Selenium, Manganese Superoxide Dismutase, and Intermediate- or High-Risk Prostate Cancer. J Clin Oncol. 2009 Jun 15. [Epub ahead of print]
Kryscio RJ, Abner EL, Caban-Holt A, et al. Association of antioxidant supplement use and dementia in the Prevention of **Alzheimer's Disease by Vitamin E and Selenium** trial (**PREADViSE**) [online Mar 20, 2017].JAMA Neurol. doi:10.1001/jamaneurol.2016.5778 (no benefit)

80. Michaelsson K, Lithell H, et al. Serum retinol levels and the risk of fracture. N Engl J Med. 2003 Jan 23; 348(4): 287-94. (Rothman KJ, Moore LL, Singer MR, Nguyen US, et al. Teratogenicity of high vitamin A intake. N Engl J Med. 1995 Nov 23;333(21):1369-73.)
81 Fairfield KM, Fletcher RH. Vitamins for chronic disease prevention in adults: scientific review. JAMA. 2002 Jun 19; 287(23): 3116-26. Review. Erratum in: JAMA 2002 Oct 9;288(14):1720.
82. Wagstaff AJ, Frampton JE, Croom KF. Tegaserod: a review of its use in the management of irritable bowel syndrome with constipation in women. Drugs. 2003;63(11):1101-20.
83. European Nicotinamide Diabetes Intervention Trial Group, European Nicotinamide Diabetes Intervention Trial (ENDIT): a randomised controlled trial of intervention before the onset of type 1 diabetes. Lancet 2004; 363: 925-31.
84. Al-Gurairi FT, Al-Waiz M, Sharquie KE. Oral zinc sulphate in the treatment of recalcitrant viral warts: randomized placebo-controlled clinical trial. Br J Dermatol. 2002 Mar;146(3):423-31.
85. Hendry, J . Ocular Disorders Associated with Increased Risk of Mortality, But Zinc Therapy Appears to Reduce Mortality Arch Ophthalmol 2004;122:716-726.
Evans JR, Lawrenson JG. Antioxidant vitamin and mineral supplements for slowing the progression of age-related macular degeneration. Cochrane Database Syst Rev. 2012 Nov 14;11:CD000254. doi: 10.1002/14651858.CD000254.pub3. People with AMD may experience delay in progression of the disease with antioxidant vitamin and mineral supplementation.
86. Holmes R., et al. Evaluation of the Patient with Chronic Cough. Am Fam Physician. 2004 May 1;69(9):2159-66.
Bailey E, Morris P, Kruske S, Chang A. **Clinical pathways** for chronic cough in **children**. Cochrane Database Syst Rev. 2008 Apr 16;(2):CD006595. Without further available evidence, recommendations for the use of clinical pathways for the treatment of chronic cough in children cannot be made. Until further evidence is available, the decision for further investigation and treatment for the child presenting with chronic cough should be made on an individual basis (i.e. dependent on symptoms and signs) with consideration for existing data from other Cochrane reviews on specific treatments for cough. Trials are required to provide evidence on the effectiveness of clinical pathways for the treatment of chronic cough in children.
Chang A, Peake J, McElrea M. **Anti-histamines** for prolonged non-specific cough in **children**. Cochrane Database Syst Rev. 2008 Apr 16;(2):CD005604. This review has significant limitations. However, our finding of uncertain efficacy of anti-histamines for chronic cough are similar to that for acute cough in children. In contrast to recommendations in adults with chronic cough, anti-histamines cannot be recommended as empirical therapy for children with chronic cough. If anti-histamines were to be trialled in these children, current data suggest a clinical response (time to response) occurs within two weeks of therapy. However the use of anti-histamines in children with non-specific cough has to be balanced against the well known risk of adverse events especially in very young children.
Barraclough K. Chronic cough in adults. BMJ. 2009 Apr 24;338:b1218. doi: 10.1136/bmj.b1218.
Chang CC, Cheng AC, Chang AB. Over-the-counter (OTC) medications to reduce cough as an adjunct to antibiotics for acute pneumonia in children and adults. Cochrane Database Syst Rev. 2014 Mar 10;3:CD006088. There is insufficient evidence to decide whether OTC medications for cough associated with acute pneumonia are beneficial. Mucolytics may be beneficial but there is insufficient evidence to recommend them as an adjunctive treatment for acute pneumonia. This leaves only theoretical recommendations that OTC medications containing codeine and antihistamines should not be used in young children.

87. Feldman S., et al. Diagnosis and Treatment of Acne. Am Fam Physician. 2004 May 1;69(9):2123-30.
88. Haider A, Shaw JC. Treatment of acne vulgaris. JAMA. 2004 Aug 11;292(6):726-35.
89. James, W.D., Acne. N Engl J Med 2005;352:1463-72. (Ozolins M, Eady EA, et al. Randomised controlled multiple treatment comparison to provide a cost-effectiveness rationale for the selection of antimicrobial therapy in acne. Health Technol Assess. 2005 Jan;9(1):iii-212.)
90. Eidelman RS, Hollar D, Hebert PR, Lamas GA, Hennekens CH. Randomized trials of vitamin E in the treatment and prevention of cardiovascular disease. Arch Intern Med. 2004 Jul 26;164(14):1552-6.
91. Fawzi WW, Msamanga GI, Spiegelman D, et al. A randomized trial of multivitamin supplements and HIV disease progression and mortality. N Engl J Med. 2004 Jul 1;351(1):23-32. (McGrath N, Bellinger D, Robins J, Msamanga GI, Tronick E, Fawzi WW. Effect of maternal multivitamin supplementation on the mental and psychomotor development of children who are born to HIV-1-infected mothers in Tanzania. Pediatrics. 2006 Feb;117(2):e216-25.)
Chang CC, Cheng AC, Chang AB. Over-the-counter (OTC) medications to reduce cough as an adjunct to antibiotics for acute pneumonia in children and adults. Cochrane Database Syst Rev. 2007 Oct 17;(4):CD006088. There is insufficient evidence to decide whether OTC medications for cough associated with acute pneumonia are beneficial. Mucolytics may be, but there is insufficient evidence to recommend them as an adjunctive treatment of acute pneumonia. This leaves only theoretical recommendations that OTC medications containing codeine and antihistamines should not be used in young children.

92. Paul IM, Yoder KE, Crowell KR, Shaffer ML, McMillan HS, Carlson LC, Dilworth DA, Berlin CM Jr. Effect of dextromethorphan, diphenhydramine, and placebo on nocturnal cough and sleep quality for coughing children and their parents. Pediatrics. 2004 Jul;114(1):e85-90.
93. Sobel JD., Wiesenfeld HC., et al. Maintenance Fluconazole Therapy for Recurrent Vulvovaginal Candidiasis. N Engl J Med. 2004 Aug 26;351(9):876-83.
94. Pirotta M. et al. Effect of lactobacillus in preventing post-antibiotic vulvovaginal candidiasis: a randomised controlled trial. BMJ. 2004 Aug 27 online p 1-5.
95. Feskanich D, Singh V, Willett WC, Colditz GA. Vitamin A intake and hip fractures among postmenopausal women. JAMA. 2002 Jan 2;287(1):47-54.
96. Goodman GE, Thornquist MD, Balmes J, Cullen MR, Meyskens FL Jr, Omenn GS, Valanis B, Williams JH Jr. The Beta-Carotene and Retinol Efficacy Trial: incidence of lung cancer and cardiovascular disease mortality during 6-year follow-up after stopping beta-carotene and retinol supplements (CARET). J Natl Cancer Inst. 2004 Dec 1;96(23):1743-50.
Benn CS, Diness BR, Roth A, Nante E, Fisker AB, Lisse IM, Yazdanbakhsh M, Whittle H, Rodrigues A, Aaby P. Effect of 50 000 IU vitamin A given with BCG vaccine on mortality in infants in Guinea-Bissau: randomised placebo controlled trial. BMJ. 2008 Jun 16. [Epub ahead of print] Vitamin A supplementation given with BCG vaccine at birth had no significant benefit in this African setting. Although little doubt exists that vitamin A supplementation reduces mortality in older children, a global recommendation of supplementation for all newborn infants may not contribute to better survival.
Gogia S, Sachdev HS. Neonatal vitamin A supplementation for prevention of mortality and morbidity in infancy: systematic review of randomised controlled trials. BMJ. 2009 Mar 27;338:b919. doi: 10.1136/bmj.b919.
Benn CS, Fisker AB, Napirna BM, et al.. Vitamin A supplementation and BCG vaccination at birth in low birthweight neonates: two by two factorial randomized controlled trial. BMJ. 2010 Mar 9.
Fernandes TF, Figueiroa JN, Grande de Arruda IK, Diniz AD. Effect on Infant Illness of Maternal Supplementation With **400 000 IU Vs 200 000 IU of Vitamin A**. Pediatrics. 2012 Mar 12.
Mactier H, McCulloch DL, Hamilton R, et al. **Vitamin A** Supplementation Improves Retinal Function in Infants at Risk of Retinopathy of Prematurity. J Pediatr. 2012 Jan 25.
Tolia VN, Murthy K, McKinley PS, et al. The Effect of the National Shortage of **Vitamin A** on Death or Chronic Lung Disease in Extremely Low-Birth-Weight Infants. JAMA Pediatr. 2014 Sep 15.
*Edmond KM, Newton S, Shannon C, et al. Eff ect of early **neonatal vitamin A** supplementation on mortality during infancy in Ghana (Neovita): a randomised, double-blind, placebo-controlled trial. Lancet 2014; online Dec 11.*
*Masanja H, Smith ER, Muhihi A, et al, for the Neovita Tanzania Study Group. Eff ect of neonatal **vitamin A supplementation on mortality** in infants in Tanzania: a randomised, double-blind, placebo-controlled trial. Lancet 2014; online Dec 11.*
*Mazumder S, Taneja S, Bhatia K, et al, for the Neovita India Study Group. Efficacy of early **neonatal supplementation with vitamin A** to reduce mortality in infancy in Haryana, India: a randomised, double-blind, placebo-controlled trial. Lancet 2014; online Dec 11.*
Beste LA, Moseley RH, Saint S, Cornia PB. Clinical Problem-Solving. Too Much of a Good Thing. (**Hypervitaminosis A**) N Engl J Med. 2016 Mar 3;374(9):873-8.
Imdad A, Ahmed Z, Bhutta ZA. **Vitamin A supplementation for the prevention of morbidity and mortality in infants one to six months of age**. Cochrane Database of Systematic Reviews 2016, Issue 9. Art. No.: CD007480. There is no convincing evidence that vitamin A supplementation for infants one to six months of age results in a reduction in infant mortality or morbidity in low- and middle-income countries. There is an increased risk of bulging fontanelle with vitamin A supplementation in this age group; however, there were no reported subsequent complications because of this adverse effect.
Haider BA, Sharma R, Bhutta ZA. Neonatal vitamin A supplementation for the prevention of mortality and morbidity in term neonates in low and middle income countries. Cochrane Database of Systematic Reviews 2017, Issue 2. Art. No.: CD006980.Given the high burden of death among children younger than five years of age in low and middle income countries, and the fact that mortality in infancy is a major contributory cause, it is critical to obtain sound scientific evidence of the effect of vitamin A supplementation during the neonatal period on infant mortality and morbidity. Evidence provided in this review does not indicate a potential beneficial effect of vitamin A supplementation among neonates at birth in reducing mortality during the first six months or 12 months of life. Given this finding and the absence of a clear indication of the biological mechanism through which vitamin A could affect mortality, along with substantial conflicting findings from individual studies conducted in settings with potentially varying levels of maternal vitamin A deficiency and infant mortality, absence of follow-up studies assessing any long-term impact of a bulging fontanelle after supplementation and the finding of a potentially harmful effect among female infants, additional research is warranted before a decision can be reached regarding policy recommendations for this intervention.
Deep Garg B, Bansal A, Kabra NS. Role of **vitamin A supplementation in prevention of Bronchopulmonary dysplasia** in extremely low birth weight neonates: A systematic review of randomized trials. J Matern Fetal Neonatal Med. 2018 Feb 15:1-201.

97. Miller ER 3rd, Pastor-Barriuso R, Dalal D, Riemersma RA, Appel LJ, Guallar E. Meta-Analysis: High-Dosage Vitamin E Supplementation May Increase All-Cause Mortality. Ann Intern Med. 2004 Nov 10.
98. Bjelakovic G, Nikolova D, Simonetti RG, Gluud C. Antioxidant supplements for prevention of gastrointestinal cancers: a systematic review and meta-analysis. Lancet. 2004 Oct 2;364(9441):1219-28. (Bjelakovic G, et al. Meta-analysis: antioxidant supplements for primary and secondary prevention of colorectal adenoma. Aliment Pharmacol Ther. 2006 Jul 15;24(2):281-91. (InfoPOEMs: Antioxidant supplementation for up to 6 years does not decrease the risk of colorectal adenomatous polyps and thus, by extension, does not reduce the risk of colorectal cancer. Vitamin E may increase the risk of colorectal adenoma. (LOE = 1a-)). (Wright ME, et al. Higher baseline serum concentrations of vitamin E are associated with lower total and cause-specific mortality in the Alpha-Tocopherol, Beta-Carotene Cancer Prevention Study. (ATBC Study) Am J Clin Nutr. 2006 Nov;84(5):1200-7.) [Bjelakovic G, Nikolova D, Gluud LL, Simonetti RG, Gluud C. Mortality in Randomized Trials of Antioxidant Supplements for Primary and Secondary Prevention: Systematic Review and Meta-analysis. JAMA. 2007 Feb 28;297(8):842-57. Treatment with beta carotene, vitamin A, and vitamin E may increase mortality. The potential roles of vitamin C and selenium on mortality need further study. (InfoPOEMs: Current evidence suggests that regular supplementation with the antioxidants beta carotene, vitamin A, and vitamin E increases mortality risk in adults. This report found no evidence of benefit or harm from supplementation with vitamin C and selenium. (LOE = 1a-))]
Slatore CG, Littman AJ, Au DH, Satia JA, White E. Long-term use of supplemental multivitamins, vitamin C, vitamin E, and folate does not reduce the risk of lung cancer. Am J Respir Crit Care Med. 2008 Mar 1;177(5):524-30. Epub 2007 Nov 7. Supplemental multivitamins, vitamin C, vitamin E, and folate were not associated with a decreased risk of lung cancer. Supplemental vitamin E was associated with a small increased risk. Patients should be counseled against using these supplements to prevent lung cancer.
Bjelakovic G, Nikolova D, Gluud LL, Simonetti RG, Gluud C. Antioxidant supplements for prevention of mortality in healthy participants and patients with various diseases. Cochrane Database Syst Rev. 2008 Apr 16;(2):CD007176. We found no evidence to support antioxidant supplements for primary or secondary prevention. **Vitamin A, beta-carotene, and vitamin E may increase mortality**. Future randomised trials could evaluate the potential effects of vitamin C and selenium for primary and secondary prevention.
Schürks Markus, Glynn Robert J, Rist Pamela M, et al. Effects of **vitamin E on stroke subtypes**: meta-analysis of randomised controlled trials. BMJ 341:doi:10.1136/bmj.c5702 (Published 4 November 2010).
Klein EA, Thompson IM Jr, Tangen CM, et al. Vitamin E and the risk of prostate cancer: the Selenium and Vitamin E Cancer Prevention Trial (**SELECT**). JAMA. 2011 Oct 12;306(14):1549-56.
99. Simons FE. Advances in H1-**antihistamines**. N Engl J Med. 2004 Nov 18;351(21):2203-17.(Berger WE, et al. Efficacy of desloratadine, 5 mg, compared with fexofenadine, 180 mg, in patients with symptomatic seasonal allergic rhinitis. Allergy Asthma Proc. 2006 May-Jun;27(3):214-23. & Merenstein D, et al. The trial of infant response to diphenhydramine: the TIRED study--a randomized, controlled, patient-oriented trial. Arch Pediatr Adolesc Med. 2006 Jul;160(7):707-12. (InfoPOEMs: Diphenhydramine was no more effective (and was technically less effective) than placebo in reducing parental attention in infants with frequent nocturnal awakenings. (LOE = 2b)) & Raphael GD, et al. Efficacy of diphenhydramine 50mg tid vs desloratadine 5mg od and placebo in patients with moderate-to-severe seasonal allergic rhinitis. Ann Allergy Asthma Immunol. 2006 Apr;96(4):606-14. Diphenhydramine, 50 mg, given for 1 week provided statistically significant and clinically superior improvements in symptoms compared with 5 mg of desloratadine in patients with moderate-to-severe SAR. Somnolence occurred more frequently with diphenhydramine (22.1%) compared with desloratadine (4.5%) and placebo (3.4%).)
So M, Bozzo P, Inoue M, Einarson A. Safety of **antihistamines during pregnancy** and lactation. Can Fam Physician. 2010 May;56(5):427-9.
100. The Medical Letter, Treatment Guidelines, **Antifungal Drugs**. Dec, 2009 . **Aug 2012.**
Nurbhai M, Grimshaw J, Watson M, Bond C, Mollison J, Ludbrook A. Oral versus intra-vaginal imidazole and triazole anti-fungal treatment of uncomplicated vulvovaginal candidiasis (thrush). Cochrane Database Syst Rev. 2007 Oct 17;(4):CD002845. No statistically significant differences were observed in clinical cure rates of anti-fungals administered by the oral and intra-vaginal routes for the treatment of uncomplicated vaginal candidiasis.
101. Muller-Lissner SA, Kamm MA, Scarpignato C, Wald A. Myths and misconceptions about chronic constipation. Am J Gastroenterol. 2005 Jan;100(1):232-42.
102. Lonn E, Bosch J, Yusuf S, Sheridan P, Pogue J, Arnold JM, Ross C, Arnold A, Sleight P, Probstfield J, Dagenais GR; HOPE and HOPE-TOO Trial Investigators. Effects of long-term vitamin E supplementation on cardiovascular events and cancer: a randomized controlled trial. JAMA. 2005 Mar 16;293(11):1338-47. The HOPE and **HOPE-TOO** Trial Investigators*. Effects of Long-term **Vitamin E** Supplementation on Cardiovascular Events and Cancer
A Randomized Controlled Trial. JAMA. 2005;293:1338-1347. (InfoPOEMs: Vitamin E supplementation does not reduce the risk of cancer or major cardiovascular events in patients at high risk for vascular disease, but may increase the risk of heart failure. (LOE = 1b)) (Lonn E, Yusuf S, Arnold MJ, et al.; Heart Outcomes Prevention Evaluation **(HOPE) 2** Investigators. **Homocysteine** lowering with folic acid and B vitamins in vascular disease. N Engl J Med. 2006 Apr 13;354(15):1567-77. Epub 2006 Mar 12. (InfoPOEMs: Supplementation with folic acid and B vitamins is ineffective for adults 55 years and older with known cardiovascular disease (CVD) or diabetes. A second report in the same issue found that similar supplementation in patients with a recent acute myocardial infarction was not helpful and may actually increase the risk of a bad cardiovascular outcome (relative risk = 1.22; 95% CI, 1.0 - 1.5). (LOE = 1b))))
103. El-Kadiki A, Sutton AJ. Role of multivitamins and mineral supplements in preventing infections in elderly people: systematic review and meta-analysis of randomised controlled trials.
BMJ. 2005 Mar 31; [Epub ahead of print] (Hercberg S, et al. The SU.VI.MAX Study: a randomized, placebo-controlled trial of the health effects of antioxidant vitamins and minerals. Arch Intern Med. 2004 Nov 22;164(21):2335-42.)
Neuhouser ML, Wassertheil-Smoller S, Thomson C, Aragaki A, Anderson GL, Manson JE, Patterson RE, Rohan TE, van Horn L, Shikany JM, Thomas A, Lacroix A, Prentice RL. Multivitamin Use and Risk of Cancer and Cardiovascular Disease in the Women's Health Initiative Cohorts (WHI). Arch Intern Med. 2009 Feb 9;169(3):294-304. After a median follow-up of 8.0 and 7.9 years in the clinical trial and observational study cohorts, respectively, the Women's Health Initiative study provided convincing evidence that multivitamin use has little or no influence on the risk of common cancers, CVD, or total mortality in postmenopausal women.
Christen WG, Glynn RJ, Chew EY, Albert CM, Manson JE. Folic acid, pyridoxine, and cyanocobalamin combination treatment and age-related macular degeneration in women: the Women's Antioxidant and Folic Acid Cardiovascular Study. Arch Intern Med. 2009 Feb 23;169(4):335-41. These randomized trial data from a large cohort of women at high risk of cardiovascular disease indicate that daily supplementation with folic acid, pyridoxine, and cyanocobalamin may reduce the risk of **AMD**.
Larsson SC, Orsini N, Wolk A. **Vitamin B6** and Risk of Colorectal Cancer: A Meta-analysis of Prospective Studies. JAMA. 2010 Mar 17;303(11):1077-83.
Kirkwood BR, Hurt L, Amenga-Etego S et al; for the ObaapaVitA Trial Team. Effect of **vitamin A** supplementation in women of reproductive age on maternal survival in Ghana (ObaapaVitA): a cluster-randomised, placebo-controlled trial. Lancet. 2010 Apr 30.
Checkley, William, West, Keith P., Jr., Wise, Robert A., et al. Maternal **Vitamin A** Supplementation and **Lung Function** in Offspring. N Engl J Med 2010 362: 1784-1794.

House AA.; Eliasziw Misha; Cattran Daniel C.; et al. Effect of **B-Vitamin** Therapy on Progression of Diabetic Nephropathy: A Randomized Controlled Trial. JAMA. 2010;303(16):1603-1609.

*Study of the Effectiveness of Additional Reductions in Cholesterol and Homocysteine (**SEARCH**) Collaborative Group. Effects of **Homocysteine-Lowering** With Folic Acid Plus Vitamin B12 vs Placebo on Mortality and Major Morbidity in Myocardial Infarction Survivors: A Randomized Trial. JAMA. 2010;303(24):2486-2494.*

*McCance DR, Holmes VA, Maresh MJ, et al.; for the Diabetes and **Pre-eclampsia** Intervention Trial (**DAPIT**) Study Group. Vitamins C and E for prevention of pre-eclampsia in women with type 1 diabetes (DAPIT): a randomised placebo-controlled trial. Lancet. 2010 Jun 25.*

*Roberts JM, Myatt L, et al. Eunice Kennedy Shriver National Institute of Child Health & Human Development Maternal-Fetal Medicine Units Network, Vitamins C & E to Prevent Complications of **Pregnancy-Associated Hypertension**. N Engl J Med 2010 362: 1282-91.*

*van den Broek N, Dou L, Othman M, et al. **Vitamin A supplementation during pregnancy** for maternal and newborn outcomes. Cochrane Database Syst Rev. 2010 Nov 10;11:CD008666. The pooled results of two large trials in Nepal and Ghana (with almost 95,000 women) do not currently suggest a role for antenatal vitamin A supplementation to reduce maternal or perinatal mortality. However the populations studied were probably different with regard to baseline vitamin A status and there were problems with follow-up of women. There is good evidence that antenatal vitamin A supplementation reduces maternal anaemia for women who live in areas where vitamin A deficiency is common or who are HIV-positive. In addition the available evidence suggests a reduction in maternal infection, but these data are not of a high quality.*

*Imdad A, Herzer K, Mayo-Wilson E, Yakoob MY, Bhutta ZA. **Vitamin A supplementation** for preventing morbidity and mortality in children from 6 months to 5 years of age. Cochrane Database of Systematic Reviews 2010, Issue 12. Art. No.: CD008524. DOI: 10.1002/14651858.CD008524.pub2. VAS is effective in reducing all-cause mortality by about 24% compared to no treatment. In our opinion, given the evidence that VAS causes considerable reduction in child mortality, further placebo-controlled trials of VAS in children between 6 months and 5 years of age are not required.*

*Christian Parul, Murray-Kolb Laura E., Khatry Subarna K., et al. **Prenatal Micronutrient Supplementation (iron/folic)** and Intellectual and Motor Function in Early School-aged Children in Nepal. JAMA. 2010;304(24):2716-723.doi:10.1001/jama.2010.1861.*

*Mayo-Wilson E, Imdad A, Herzer K, Yakoob MY, Bhutta ZA. **Vitamin A supplements** for preventing mortality, illness, and blindness in children aged under 5: systematic review and meta-analysis. BMJ 2011;343:d5094.*

Mursu J, Robien K, Harnack LJ, Park K, Jacobs DR Jr. Dietary supplements and mortality in older women: the Iowa Women's Health Study. Arch Intern Med. 2011;171(18):1625-1633.

Medical Letter. **Who should take vitamin supplements**. Dec 12/26, 2011.

Shankar P, Boylan M, Sriram K. Micronutrient deficiencies after bariatric surgery. Nutrition. 2010 Nov-Dec;26(11-12):1031-7.

Schmitz J, West KP Jr, Khatry SK, LeClerq SC, Karna SL, Katz J, et al. **Vitamin A** supplementation in preschool children and risk of **hearing loss** as adolescents and young adults in rural Nepal: randomised trial cohort follow-up study. BMJ 2012;344:d7962.

Andreeva VA, Touvier M, Kesse-Guyot E, et al. B Vitamin and/or ω-3 Fatty Acid Supplementation and Cancer: Ancillary Findings From the Supplementation With Folate, Vitamins B6 and B12, and/or Omega-3 Fatty Acids (**SU.FOL.OM3**) Randomized Trial. Arch Intern Med. 2012 Apr 9;172(7):540-7.

Song Y, Manson JE, Lee IM, et al. Effect of Combined Folic Acid, Vitamin B6, and Vitamin B12 on Colorectal Adenoma. J Natl Cancer Inst. 2012 Oct 12.

Isanaka S, Mugusi F, Hawkins C, et al. Effect of high-dose vs standard-dose multivitamin supplementation at the initiation of HAART on **HIV** disease progression and mortality in Tanzania: a randomized controlled trial. JAMA. 2012 Oct 17;308(15):1535-44.

Sesso HD, Christen WG, Bubes V, et al. **Multivitamins in the prevention of cardiovascular disease** in men: the Physicians' Health Study II (**PHS-II**) randomized controlled trial. JAMA. 2012;308(17):1751-1760. (no benefit)

Gaziano MJ, Sesson HD, Christen WG, et al. **Multivitamins in the prevention of cancer** in men: the Physicians' Health Study II (**PHS-II**) randomized controlled trial [published online October 17, 2012]. JAMA. doi:10.1001/jama.2012.14641. (some benefit)

Awasthi S, Peto R, Read S, et al, and the **DEVTA** (Deworming and Enhanced Vitamin A) team**. Vitamin A** supplementation every 6 months with retinol in 1 million pre-school children in north India: DEVTA, a cluster-randomised trial. Lancet 2013; online March 14.

Hemila H, Louhiala P. **Vitamin C for preventing and treating pneumonia**. Cochrane Database Syst Rev. 2013 Aug 8;8:CD005532. The prophylactic use of vitamin C to prevent pneumonia should be further investigated in populations who have a high incidence of pneumonia, especially if dietary vitamin C intake is low. Similarly, the therapeutic effects of vitamin C should be studied, especially in patients with low plasma vitamin C levels. The current evidence is too weak to advocate prophylactic use of vitamin C to prevent pneumonia in the general population.

Fortmann SP, Burda BU, Senger CA et al. Vitamin and Mineral Supplements in the Primary Prevention of **Cardiovascular Disease and Cancer**: An Updated Systematic Evidence Review for the U.S. Preventive Services Task Force. Ann Intern Med. 2013 Nov 12.

Christen WG, Glynn RJ, Manson JE, et al. A **Multivitamin Supplement and Cataract** and Age-Related Macular Degeneration in a Randomized Trial of Male Physicians. Ophthalmology. 2013 Nov 20.

Ji Y, Tan S, Xu Y, Chandra A, et al. **Vitamin B supplementation, homocysteine levels, and the risk of cerebrovascular disease**: a meta-analysis. Neurology. 2013 Oct 8;81(15):1298-307.

Grodstein F, O'Brien J, Kang JH, Dushkes R, Cook NR, Okereke O, et al. Long-term **multivitamin supplementation and cognitive** function in men. A randomized trial. Ann Intern Med. 2013;159:806-14.

Lamas GA, Boineau R, Goertz C, Mark DB, Rosenberg Y, Stylianou M, et al; **TACT** (Trial to Assess Chelation Therapy) Investigators. Oral high-dose multivitamins and minerals **after myocardial infarction**. A randomized trial. Ann Intern Med. 2013;159:797-804.

United States Preventive Services Task Force. **Vitamin, mineral, and multivitamin supplements for the primary prevention of cardiovascular disease and cancer**: **USPSTF** statement. *Ann Intern Med* 2014.

Day GS, Del Campo CM. Wernicke encephalopathy: a medical emergency. (**thiamine** deficiency) CMAJ. 2014 May 13;186(8):E295.

*van der Zwaluw NL, Dhonukshe-Rutten RA, van Wijngaarden JP, et al. Results of 2-year **vitamin B treatment** on **cognitive performance**: Secondary data from an RCT. Neurology. 2014 Dec 2;83(23):2158-66.*

*West KP Jr, Shamim AA, Mehra S, et al. Effect of **maternal multiple micronutrient vs iron-folic acid supplementation** on **infant mortality** and adverse birth outcomes in rural Bangladesh: the JiVitA-3 randomized trial. JAMA. 2014 Dec 24-31;312(24):2649-58.*

*Cereda E, Klersy C, Serioli M, et al; OligoElement Sore Trial Study Group. A nutritional formula enriched with **arginine, zinc, and antioxidants for the healing of pressure ulcers**: a randomized trial. Ann Intern Med. 2015 Feb 3;162(3):167-74.*

Rautiainen S, Gaziano JM, et al. Effect of baseline nutritional status on **long-term multivitamin use and cardiovascular disease risk**: a secondary analysis of the **Physicians' Health Study II** randomized clinical trial [online Apr 5, 2017]. JAMA Cardiol. doi:10.1001/jamacardio.2017 .0176

Wolf HT, Hegaard HK, Huusom LD, Pinborg AB. **Multivitamin use and adverse birth outcomes in high-income countries**: a systematic review and meta-analysis. Am J Obstet Gynecol. 2017 Oct;217(4):404.e1-404.e30.

Manson JE, Bassuk SS. **Vitamin and Mineral Supplements: What Clinicians Need to Know**. JAMA. 2018 Feb 5.

Kim J, Choi J, Kwon SY, et al. Association of **multivitamin and mineral supplementation and risk of cardiovascular disease**: a systematic review and meta-analysis. Circ Cardiovasc Qual Outcomes. 2018;11:e004224.

Bennett SE, Schmitt WP, Stanford FC, et al. Case 22-2018: A 64-Year-Old Man with Progressive Leg Weakness, Recurrent Falls, and Anemia. N Engl J Med. 2018 Jul 19;379(3):282-289. (Vitamin deficiency)

Loyal J, Taylor JA, Phillipi CA, et al. Factors **Associated With Refusal of Intramuscular Vitamin K in Normal Newborns**. Pediatrics. 2018 Jul 20.

Vaezipour N, Leibundgut K. **Nonalimental Scurvy With Relapse Symptoms After Stopping Oral Vitamin C Supplementation**. Pediatrics. 2018 Aug;142(2).

Rutjes AW, Denton DA, Di Nisio M, et al. Vitamin and mineral supplementation **for maintaining cognitive function in cognitively healthy people** in mid and late life. Cochrane Database Syst Rev. 2018 Dec 17;12:CD011906. We did not find evidence that any vitamin or mineral supplementation strategy for cognitively healthy adults in mid or late life has a meaningful effect on cognitive decline or dementia, although the evidence does not permit definitive conclusions. There were very few data on supplementation starting in midlife (< 60 years); studies designed to assess cognitive outcomes tended to be too short to assess maintenance of cognitive function; longer studies often had other primary outcomes and used cognitive measures which may have lacked sensitivity. The only positive signals of effect came from studies of long-term supplementation with antioxidant vitamins.

Schmidt RJ, Iosif AM, Guerrero Angel E, Ozonoff S. Association of **Maternal Prenatal Vitamin Use With Risk for Autism** Spectrum Disorder Recurrence in Young Siblings. JAMA Psychiatry. 2019 Feb 27.

Chen F, Du M, Blumberg JB, et al. Association Among Dietary Supplement Use, Nutrient Intake, and Mortality Among U.S. Adults: A Cohort Study. Ann Intern Med. 2019 Apr 9.

Masnadi Shirazi K, Nikniaz Z, Masnadi Shirazi A, Rohani M. **Vitamin A supplementation decreases disease activity** index in patients with ulcerative colitis: A randomized controlled clinical trial. Complement Ther Med. 2018 Dec;41:215-219.

Meyer HE, Willett WC, Fung TT, et al. Association of High Intakes of **Vitamins B6 and B12 From Food and Supplements With Risk of Hip Fracture** Among Postmenopausal Women in the Nurses' Health Study. JAMA Netw Open. 2019 May 3;2(5):e193591.

Pdf Bailey RL, Pac SG, Fulgoni VL 3rd, et al. Estimation of Total Usual Dietary Intakes of Pregnant Women in the United States. JAMA Netw Open. 2019 Jun 5;2(6):e195967.

Pdf Centeno Tablante E, Pachón H, Guetterman HM, Finkelstein JL. Fortification of wheat and maize flour with folic acid for population health outcomes. Cochrane Database Syst Rev. 2019 Jul 1;7:CD012150. Fortification of wheat flour with folic acid may reduce the risk of neural tube defects; however, this outcome was only reported in one non-RCT. Fortification of wheat or maize flour with folic acid (i.e. alone or with other micronutrients) may increase erythrocyte and serum/plasma folate concentrations. Evidence is limited for the effects of folic acid-fortified wheat or maize flour on haemoglobin levels or anaemia. The effects of folic acid fortification of wheat or maize flour on other primary outcomes assessed in this review is not known.

Pdf Trevisan C, Piovesan F, Lucato P, et al. Parathormone, vitamin D and the risk of atrial fibrillation in older adults: A prospective study. Nutr Metab Cardiovasc Dis. 2019 May 29.

Pdf Wang G, Liu X, Bartell TR, et al. Vitamin D Trajectories From Birth to Early Childhood and Elevated Systolic Blood Pressure During Childhood and Adolescence. Hypertension. 2019 Jul 1:HYPERTENSIONAHA11913120.

Pdf Bailey RL, Pac SG, Fulgoni VL 3rd, et al. Estimation of Total Usual Dietary Intakes of Pregnant Women in the United States. JAMA Netw Open. 2019 Jun 5;2(6):e195967.

104. Andres E, Loukili NH, Noel E, et al. Vitamin B(12) (cobalamin) deficiency in elderly patients. CMAJ. 2004 Aug 3;171(3):251-259. (Butler CC, et al. Oral vitamin B12 versus intramuscular vitamin B12 for vitamin B12 deficiency: a systematic review of randomized controlled trials. Fam Pract. 2006 Jun;23(3):279-85. Epub 2006 Apr 3. The evidence derived from these limited studies suggests that 2000 microg doses of oral vitamin B(12) daily and 1000 microg doses initially daily and thereafter weekly and then monthly may be as effective as intramuscular administration in obtaining short-term haematological and neurological responses in vitamin B(12)-deficient patients. (InfoPOEMs: Based on 2 small studies, both oral and intramuscular (IM) vitamin B12 replacement increase serum B12 levels and improve neurological outcomes. Oral vitamin B12 replacement should be considered for patients with documented deficiency. It is available over the counter in 1000 mcg and 2000 mcg doses in the United States. (LOE = 2a)))
Castelli M. Cristina, Friedman Kristen, Sherry James, et al. Comparing the Efficacy and Tolerability of a New Daily Oral Vitamin B12 Formulation and Intermittent Intramuscular Vitamin B12 in Normalizing Low Cobalamin Levels: A Randomized, Open-Label, Parallel-Group Study, Clinical Therapeutics, Volume 33, Issue 3, March 2011, Pages 358-371.e2

Malouf R, Areosa Sastre A. **Vitamin B12** for cognition. Cochrane Database of Systematic Reviews 2003, Issue 3. Art. No.: CD004394. DOI: 10.1002/14651858.CD004394.

Roumeliotis N, Dix D, Lipson A. Vitamin B12 deficiency in infants secondary to maternal causes. CMAJ. 2012 Oct 2;184(14):1593-8.

Stabler SP. Clinical practice. Vitamin B12 deficiency. N Engl J Med. 2013 Jan 10;368(2):149-60.

Kolber MR, Houle SK. **Oral vitamin B12**: a cost-effective alternative. Can Fam Physician. 2014 Feb;60(2):111-2.

Hooshmand B, Mangialasche F, Kalpouzos G, et al. Association of **Vitamin B12, Folate, and Sulfur Amino** Acids With Brain Magnetic Resonance Imaging Measures in Older Adults: A Longitudinal Population-Based Study. JAMA Psychiatry. 2016 Jun 1;73(6):606-13.

Matthews DE, Beatty SJ, Grever GM, et al. Comparison of 2 Population Health Management Approaches to Increase **Vitamin B12** Monitoring in Patients Taking **Metformin**. Ann Pharmacother. 2016 Oct;50(10):840-6.

Tavares J, Eugénio G, Calretas S, et al. A link between asthenia, pallor, and jaundice (**Vitamin B12**). BMJ. 2016 Jun 7;353:i2937.

Rogne T, Tielemans MJ, Chong MF, et al. Associations of **Maternal Vitamin B12 Concentration in Pregnancy** With the Risks of Preterm Birth and Low Birth Weight: A Systematic Review and Meta-Analysis of Individual Participant Data. Am J Epidemiol. 2017 Jan 20.

Langan, RC, Goodgred AJ, **Vitamin B12 Deficiency**: Recognition and Management. Am Fam Physician. 2017;96(6):384-389.

DeFilippis EM, Petersen A, Yialamas MA. Progressive Weakness and Memory Impairment in a Middle-aged Man. JAMA. 2018 Jul 10;320(2):197-198. (Vitamin B12 defficiency)

Schijns W, Homan J, van der Meer L, et al. Efficacy of oral compared with intramuscular vitamin B-12 supplementation after Roux-en-Y gastric bypass: a randomized controlled trial. Am J Clin Nutr. 2018 Jul 1;108(1):6-12.

DeFilippis EM, Petersen A, Yialamas MA. Progressive Weakness and Memory Impairment in a Middle-aged Man. JAMA. 2018 Jul 10;320(2):197-198. (Vitamin B12 defficiency)

Wang H, Li L, Qin LL, et al. **Ora**l vitamin B(12**) versus intramuscular** vitamin B(12) for vitamin B(12) deficiency. Cochrane Database Syst Rev. 2018 Mar 15;3:CD004655. Low quality evidence shows oral and IM vitamin B12 having similar effects in terms of normalising serum vitamin B12

Hogan C, Little BP, Carlson JCT, et al. Case 5-2019: A 48-Year-Old Woman with **Delusional Thinking and Paresthesia of the Right Hand**. N Engl J Med. 2019 Feb 14;380(7):665-674.

Williamson J, Huda S, Damodaran D. **Nitrous oxide myelopathy** with functional vitamin B (12) deficiency. BMJ Case Rep. 2019 Feb 13;12(2).

Meyer HE, Willett WC, Fung TT, et al. Association of High Intakes of Vitamins B6 and **B12 From Food and Supplements With Risk of Hip Fracture** Among Postmenopausal Women in the Nurses' Health Study. JAMA Netw Open. 2019 May 3;2(5):e193591.

Sukumar N, Saravanan P. Investigating **vitamin B12 deficiency**. BMJ. 2019 May 10;365:l1865.

Francis A, Crossley R, Brady S. **Subacute progressive sensorimotor symptoms**. BMJ. 2019 Jun 11;365:l1923.

Zwart SR, Laurie SS, Chen JJ, et al. Association of **Genetics and B Vitamin Status** With the Magnitude of Optic Disc Edema During 30-Day Strict Head-Down Tilt Bed Rest. JAMA Ophthalmol. 2019 Aug 15.

105. Ronald C. Petersen, Ph.D., M.D., Ronald G. Thomas, Ph.D., Michael Grundman, M.D., M.P.H., et al., for the Alzheimer's Disease Cooperative Study Group Vitamin E and Donepezil for the Treatment of Mild Cognitive Impairment Published at www.nejm.org April 13, 2005
106. Viera AJ, Hoag S, Shaughnessy J. Management of irritable bowel syndrome. Am Fam Physician. 2002 Nov 15;66(10):1867-74. (Sharara AI, et al. A randomized double-blind placebo-controlled trial of rifaximin in patients with abdominal bloating and flatulence. Am J Gastroenterol. 2006 Feb;101(2):326-33. (InfoPOEMs: A 10-day course of rifaximin (Xifaxan) reduced symptoms of bloating and flatulence in patients with and without irritable bowel syndrome (IBS). Another study found a reduction in abdominal symptoms in patients with diverticulitis who were treated for 7 days each month for 1 year, suggesting that cyclic administration may be an option. Although larger, longer-term studies are needed before we widely adopt this approach for all our patients with IBS, it could be considered now for patients with especially troublesome symptoms. (LOE = 1b))) (Robinson A, et al. A randomised controlled trial of **self-help interventions** in patients with a primary care diagnosis of irritable bowel syndrome. Gut. 2006 May;55(5):643-8. Epub 2005 Aug 12.)
107. Villamor E, Saathoff E, Bosch RJ, Hertzmark E, Baylin A, Manji K, Msamanga G, Hunter DJ, Fawzi WW. Vitamin supplementation of HIV-infected women improves postnatal child growth. Am J Clin Nutr. 2005 Apr;81(4):880-8.
108. Kris-Etherton PM, Lichtenstein AH, Howard BV, et al. Nutrition Committee of the American Heart Association Council on Nutrition, Physical Activity, and Metabolism. Antioxidant vitamin supplements and cardiovascular disease. Circulation. 2004 Aug 3;110(5):637-41.
109. Porthouse J, Cockayne S, King C, et al. Randomised controlled trial of **calcium** and supplementation with **cholecalciferol (vitamin D3)** for prevention of fractures in primary care. BMJ. 2005 Apr 30;330(7498):1003.
110. Grant AM, Avenell A, et al.; Oral **vitamin D3 and calcium** for secondary prevention of low-trauma fractures in elderly people (Randomised Evaluation of **Calcium Or vitamin D**, **RECORD**): a randomised placebo-controlled trial. Lancet. 2005 May;365(9471):1621-8.
111. Bischoff-Ferrari HA, Willett WC, Wong JB, et al. Fracture prevention with **vitamin D** supplementation: a meta-analysis of randomized controlled trials. JAMA. 2005 May 11;293(18):2257-64. (Oral vitamin D supplementation between 700 to 800 IU/d appears to reduce the risk of hip and any nonvertebral fractures in ambulatory or institutionalized elderly persons. An oral vitamin D dose of 400 IU/d is not sufficient for fracture prevention.)(Wactawski-Wende J, Kotchen JM, Anderson GL, et al.; Women's Health Initiative Investigators. Calcium plus vitamin D supplementation and the risk of colorectal cancer. N Engl J Med. 2006 Feb 16;354(7):684-96.)(Jackson RD, LaCroix AZ, Gass M, et al.; Women's Health Initiative Investigators. Calcium plus vitamin D supplementation and the risk of fractures. N Engl J Med. 2006 Feb 16;354(7):669-83. Among healthy postmenopausal women, calcium with vitamin D supplementation resulted in a small but significant improvement in hip bone density, did not significantly reduce hip fracture, and increased the risk of kidney stones.) (Villar J, Abdel-Aleem Het al.; World Health Organization Calcium Supplementation for the Prevention of Preeclampsia Trial Group. World Health Organization randomized trial of calcium supplementation among low calcium intake pregnant women. Am J Obstet Gynecol. 2006 Mar;194(3):639 -49. CONCLUSION: A 1.5-g calcium/day supplement did not prevent preeclampsia but did reduce its severity, maternal morbidity, and neonatal mortality, albeit these were secondary outcomes) & (Bischoff-Ferrari HA, et al. Effect of cholecalciferol plus calcium on falling in ambulatory older men and women: a 3-year randomized controlled trial. Arch Intern Med. 2006 Feb 27;166(4):424-30.) Wactawski-Wende J, et al.; Women's Health Initiative Investigators. Calcium plus vitamin D supplementation and the risk of colorectal cancer. N Engl J Med. 2006 Feb 16;354(7):684-96. Erratum in: N Engl J Med. 2006 Mar 9;354(10):1102. (InfoPOEMs: A modest dose of calcium and vitamin D does not alter the risk of colorectal cancer in healthy, normal-risk women. (LOE = 1b)) (Prince RL, et al. Effects of **calcium** supplementation on clinical fracture and bone structure: results of a 5-year, double-blind, placebo-controlled trial in elderly women. Supplementation with calcium carbonate tablets supplying 1200 mg/d is ineffective as a public health intervention in preventing clinical fractures in the ambulatory elderly population owing to poor long-term compliance, but it is effective in those patients who are compliant. Arch Intern Med. 2006 Apr 24;166(8):869-75.)(Greer FR, Krebs NF; American Academy of **Pediatrics** Committee on Nutrition. Optimizing bone health and calcium intakes of infants, children, and adolescents. Pediatrics. 2006 Feb;117(2):578-85.) (Brown SJ. The Role of Vitamin D in Multiple Sclerosis (June). Ann Pharmacother. 2006 May 9; [Epub ahead of print]) (Medical Letter: Calcium & Vitamin D supplements July 31,2006) (Palmieri C, Macgregor T, Girgis S, Vigushin D. Serum 25 hydroxyvitamin D levels in early and advanced breast cancer. J Clin Pathol. 2006 Oct 17; [Epub ahead of print]) Winzenberg T, Shaw K, Fryer J, Jones G. Effects of calcium supplementation on bone density in healthy children: meta-analysis of randomised controlled trials. BMJ. 2006 Sep 15; [Epub ahead of print] The small effect of calcium supplementation on bone mineral density in the upper limb is unlikely to reduce the risk of fracture, either in childhood or later life, to a degree of major public health importance. & Chan GM, et al. Effects of dietary calcium intervention on adolescent mothers and newborns: A randomized controlled trial. Obstet Gynecol. 2006 Sep;108(3 Pt 1):565-71. (Holick MF. **Vitamin D deficiency**. N Engl J Med. 2007 Jul 19;357(3):266-81.)
Autier P, Gandini S. Vitamin D Supplementation and **Total Mortality**: A Meta-analysis of Randomized Controlled Trials. Arch Intern Med. 2007 Sep 10;167(16):1730-7. Intake of ordinary doses of vitamin D supplements seems to be associated with decreases in total mortality rates. The relationship between baseline vitamin D status, dose of vitamin D supplements, and total mortality rates remains to be investigated. Population-based, placebo-controlled randomized trials with total mortality as the main end point should be organized for confirming these findings. (Tang BM, Eslick GD, Nowson C, Smith C, Bensoussan A. Use of calcium or calcium in combination with vitamin D supplementation to prevent fractures and bone loss in people aged 50 years and older: a meta-analysis. Lancet. 2007 Aug 25;370(9588):657-66. Evidence supports the use of calcium, or calcium in combination with vitamin D supplementation, in the preventive treatment of osteoporosis in people aged 50 years or older. For best therapeutic effect, we recommend minimum doses of 1200 mg of calcium, and 800 IU of vitamin D (for combined calcium plus vitamin D supplementation).) Freedman DM, Looker AC, Chang SC, Graubard BI. Prospective study of serum vitamin D and cancer mortality in the United States. J Natl Cancer Inst. 2007 Nov 7;99(21):1594-602. Epub 2007 Oct 30.
Lappe JM, Travers-Gustafson D, Davies KM, Recker RR, Heaney RP. Vitamin D and calcium supplementation reduces cancer risk: results of a randomized trial. Am J Clin Nutr. 2007 Jun;85(6):1586-91.
Barger-Lux MJ, Heaney RP. Effects of above average summer sun exposure on serum 25-hydroxyvitamin D and calcium absorption. J Clin Endocrinol Metab. 2002 Nov;87(11):4952-6.
Prince RL, Austin N, Devine A, Dick IM, Bruce D, Zhu K. Effects of ergocalciferol added to calcium on the risk of falls in elderly high-risk women. Arch Intern Med. 2008 Jan 14;168(1):103-8. Patients with a history of falling and vitamin D insufficiency living in sunny climates benefit from ergocalciferol supplementation in addition to calcium, which is associated with a 19% reduction in the relative risk of falling, mostly in winter.
Levine RJ, Hauth JC, Curet LB, et al. Trial of **calcium to prevent preeclampsia**. N Engl J Med 1997;337:69-76.
Zipitis CS, Akobeng AK. Vitamin D Supplementation in Early Childhood and Risk of Type 1 Diabetes: a Systematic Review and Meta-analysis. Arch Dis Child. 2008 Mar 13; [Epub ahead of print] Vitamin D supplementation in early childhood may offer protection against the development of type 1 **diabetes**.
Hoogendijk WJ, Lips P, Dik MG, Deeg DJ, Beekman AT, Penninx BW. **Depression** is associated with decreased 25-hydroxyvitamin D and increased parathyroid hormone levels in older adults. Arch Gen Psychiatry. 2008 May;65(5):508-12. The results of this large population-based study show an association of depression status and severity with decreased serum 25(OH)D levels and increased serum PTH levels in older individuals.
Ahn J, Peters U, Albanes D, et al. For the Prostate, Lung, Colorectal, and Ovarian Cancer Screening Trial Project Team. Serum Vitamin D Concentration and Prostate Cancer Risk: A Nested Case-Control Study. J Natl Cancer Inst. 2008 May 27. [Epub ahead of print] The findings of this large prospective study do not support the hypothesis that vitamin D is associated with decreased risk of **prostate cancer**; indeed, higher circulating 25(OH)D concentrations may be associated with increased risk of aggressive disease.
Bischoff-Ferrari HA, Rees JR, Grau MV, Barry E, Gui J, Baron JA. Effect of calcium supplementation on fracture risk: a double-blind randomized controlled trial. Am J Clin Nutr. 2008 Jun;87(6):1945-51. A total of 930 participants (72% men; mean age: 61 y) were randomly assigned to receive 4 yr of treatment with 3 g CaCO(3) (1200 mg elemental Ca) daily or placebo and were followed for a mean of 10.8 yr. Calcium supplementation reduced the risk of all fractures and of minimal trauma fractures among healthy individuals. The benefit appeared to dissipate after treatment was stopped.
Sievenpiper JL, McIntyre EA, Verrill M, Quinton R, Pearce SH. **Unrecognised severe vitamin D deficiency**. BMJ. 2008 Jun 14;336(7657):1371-4.
Giovannucci E, Liu Y, Hollis BW, Rimm EB. 25-hydroxyvitamin D and risk of **myocardial infarction** in men: a prospective study. Arch Intern Med. 2008 Jun 9;168(11):1174-80. Low levels of 25(OH)D are associated with higher risk of myocardial infarction in a graded manner, even after controlling for factors known to be associated with coronary artery disease.
Dobnig H, Pilz S, Scharnagl H, Renner W, Seelhorst U, Wellnitz B, Kinkeldei J, Boehm BO, Weihrauch G, Maerz W. Independent association of low serum 25-hydroxyvitamin d and 1,25-dihydroxyvitamin d levels with all-cause and cardiovascular **mortality**. Arch Intern Med. 2008 Jun 23;168(12):1340-9. Low 25-hydroxyvitamin D and 1,25-dihydroxyvitamin D levels are independently associated with all-cause and cardiovascular mortality. A causal relationship has yet to be proved by intervention trials using vitamin D.
Melamed ML, Michos ED, et al. 25-hydroxyvitamin d levels and the risk of mortality in the general population. Arch Intern Med. 2008 Aug 11;168(15):1629-37. The lowest quartile of 25(OH)D level (<17.8 ng/mL) is independently associated with **all-cause mortality** in the

general population.

Cauley JA, Lacroix AZ, Wu L, Horwitz M, et al. Serum 25-hydroxyvitamin D concentrations and risk for **hip fractures**. Ann Intern Med. 2008 Aug 19;149(4):242-50. Low serum 25(OH) vitamin D concentrations are associated with a higher risk for hip fracture.

Chlebowski RT, Johnson KC, Kooperberg C, et al. for the Women's Health Initiative Investigators. (WHI) Calcium Plus Vitamin D Supplementation and the Risk of Breast Cancer. J Natl Cancer Inst. 2008 Nov 11. [Epub ahead of print] Calcium and vitamin D supplementation did **not reduce invasive breast cancer** incidence in postmenopausal women. In addition, 25-hydroxyvitamin D levels were not associated with subsequent breast cancer risk. These findings do not support a relationship between total vitamin D intake and 25-hydroxyvitamin D levels with breast cancer risk.

Bacon CJ, Gamble GD, Horne AM, Scott MA, Reid IR. High-dose oral vitamin D(3) supplementation in the elderly. Osteoporos Int. 2008 Dec 20. [Epub ahead of print] Sixty-three elderly participants were randomized to three regimens of vitamin D supplementation: a 500,000-IU loading dose; the **loading dose plus** 50,000 IU/month; or **50,000 IU/month**. Large loading doses of vitamin D(3) rapidly and safely normalize 25OHD levels in the frail elderly. Monthly dosing is similarly effective and safe, but takes 3-5 months for plateau 25OHD levels to be reached.

Holick MF, Biancuzzo RM, Chen TC, Klein EK, Young A, Bibuld D, Reitz R, Salameh W, Ameri A, Tannenbaum AD. Vitamin D2 is as effective as vitamin D3 in maintaining circulating concentrations of 25-hydroxyvitamin D. J Clin Endocrinol Metab. 2008 Mar;93(3):677-81. Epub 2007 Dec 18. A 1000 IU dose of **vitamin D2 daily was as effective as 1000 IU vitamin D3** in maintaining serum 25-hydroxyvitamin D levels and did not negatively influence serum 25-hydroxyvitamin D3 levels. Therefore, vitamin D2 is equally as effective as vitamin D3 in maintaining 25-hydroxyvitamin D status.

Wagner CL, Greer FR; American Academy of Pediatrics Section on Breastfeeding; American Academy of Pediatrics Committee on Nutrition. Prevention of rickets and vitamin D deficiency in infants, children, and adolescents. Pediatrics. 2008 Nov;122(5):1142-52. Erratum in: Pediatrics. 2009 Jan;123(1):197.

Bischoff-Ferrari HA, Willett WC, Wong JB, et al. Prevention of nonvertebral fractures with oral vitamin D and dose dependency: a meta-analysis of randomized controlled trials. Arch Intern Med. 2009 Mar 23;169(6):551-61. Nonvertebral fracture prevention with vitamin D is dose dependent, and a higher dose should reduce fractures by at least 20% for individuals aged 65 years or older. Vitamin D at dosages **greater than 400 IU per day** is effective in decreasing nonvertebral fractures, including hip fractures.

Kumar J, Muntner P, Kaskel FJ, Hailpern SM, Melamed ML. Prevalence and Associations of 25-Hydroxyvitamin D Deficiency in US Children: NHANES 2001-2004. Pediatrics. 2009 Aug 3. [Epub ahead of print] 25(OH)D deficiency is common in the general US pediatric population and is associated with adverse cardiovascular risks.

Bordelon P, Ghetu MV, Langan RC. Recognition and management of vitamin D deficiency. Am Fam Physician. 2009 Oct 15;80(8):841-6.

Bischoff-Ferrari H A, Dawson-Hughes B, Staehelin H B, et al. Fall prevention with supplemental and active forms of vitamin D: a meta-analysis of randomised controlled trials. BMJ 2009;339:b3692, doi: 10.1136/bmj.b3692 (Published 1 October 2009)

Ginde AA, Liu MC, Camargo CA Jr. Demographic differences and trends of vitamin D insufficiency in the US population, 1988-2004. Arch Intern Med. 2009 Mar 23;169(6):626-32.

Chung M, Balk EM, Brendel M, et al. Vitamin D and calcium: a systematic review of health outcomes. Evid Rep Technol Assess (Summ). 2009 Jul;183: 1-342.

Palmer SC, McGregor DO, Macaskill P, et al. Meta-analysis: vitamin D compounds in chronic kidney disease. Ann Intern Med. 2007;147(12):840–853.

Pearce Simon HS, Cheetham Tim D. Diagnosis and management of vitamin D deficiency. BMJ 2010;340:b5664, doi: 10.1136/bmj.b5664 (Published 11 January 2010)

Wang, Lu, Manson, JoAnn E. Song, Yiqing et al. Systematic Review: Vitamin D and Calcium Supplementation in Prevention of Cardiovascular Events. *Ann Intern Med* March 2, 2010 152:315-323; doi:10.1059/0003-4819-152-5-201003020-00010.

Anastassios G. Pittas, Mei Chung, Thomas Trikalinos, Et al. Systematic Review: Vitamin D and Cardiometabolic Outcomes. *Ann Intern Med* March 2, 2010 152:307-314; doi:10.1059/0003-4819-152-5-201003020-00009.

Vitamin D supplementation: Recommendations for Canadian mothers and infants. Paediatr Child Health 2007;12(7):583-9. Reference No. FNIM07-01. http://www.cps.ca/english/statements/ii/fnim07-01.htm

Hofmeyr GJ, Lawrie TA, Atallah AN, et al. **Calcium supplementation during pregnancy** for preventing hypertensive disorders and related problems. Cochrane Database Syst Rev. 2010 Aug 4;8:CD001059.

Straube S, Derry S, Moore RA, et al. Vitamin D for the treatment of chronic painful conditions in adults. Cochrane Database Syst Rev. 2010 Jan 20;(1):CD007771.

Casey CF, Slawson DC, Neal LR. VItamin D Supplementation in Infants, Children, and Adolescents. Am Fam Physician. 2010 Mar 15;81(6):745-8.

*Bischoff-Ferrari Heike A.; Dawson-Hughes Bess; Platz Andreas; et al. Effect of **High-Dosage Cholecalciferol** (2000 vs 800 IU/day) and Extended Physiotherapy on Complications After Hip Fracture: A Randomized Controlled Trial. Arch Intern Med. 2010;170(9):813-820.*

*Smith H, Anderson F, Raphael H, Maslin P, Crozier S, Cooper C. Effect of annual intramuscular vitamin D on fracture risk in elderly men and women--a population-based, randomized, double-blind, placebo-controlled trial. Rheumatology (Oxford). 2007 Dec;46(12):1852-7. Epub 2007 Nov 12. An **annual i.m. injection of 300 000 IU** vitamin D(2) is not effective in preventing non-vertebral fractures among elderly men and women resident in the general population.*

*Sanders Kerrie M.; Stuart Amanda L.; Williamson Elizabeth J.; et al. Annual **High-Dose Oral Vitamin D** (500,000IU x1/yr for 3-5yrs: increased falls & fractures) and Falls and Fractures in Older Women: A Randomized Controlled Trial. JAMA. 2010;303(18):1815-1822.*

*Terushkin V et al. Estimated equivalency of **vitamin D production from natural sun exposure** versus oral vitamin D supplementation across seasons at two US latitudes. J Am Acad Dermatol 2010 Jun; 62:929.e1.*

Perrine, Cria G., Sharma, Andrea J., Jefferds, Maria Elena D., et al. Adherence to Vitamin D Recommendations Among US Infants. Pediatrics 2010 125: 627-632.

*Llewellyn David J.; Lang Iain A.; Langa Kenneth M.; et al. Vitamin D and Risk of **Cognitive Decline** in Elderly Persons Arch Intern Med. 2010;170(13):1135-1141. Conclusion: Low levels of vitamin D were associated with substantial cognitive decline in the elderly population studied over a 6-year period, which raises important new possibilities for treatment and prevention.*

*Knekt Paul; Kilkkinen Annamari; Rissanen Harri; et al. Serum Vitamin D and the Risk of **Parkinson Disease** Arch Neurol. 2010;67(7):808-811.*

*Hanley DA, Cranney A, Jones G, et al. **Vitamin D in adult** health & disease: a review and **guideline statement from Osteoporosis Canada**–summary.CMAJ 2010 0: cmaj.091062.*

Ascherio A, Munger KL, Simon KC. Vitamin D and **multiple sclerosis**. Lancet Neurol. 2010 Jun;9(6):599-612.

Bolland Mark J, Avenell Alison, Baron John A, et al, Effect of **calcium** supplements on risk of **myocardial infarction** and cardiovascular events: meta-analysis. BMJ 2010;341:c3691.

Kalyani RR, Stein B, Valiyil R, et al. Vitamin D treatment for the prevention of **falls** in older adults: systematic review and meta-analysis. J Am Geriatr Soc. 2010 Jul;58(7):1299-310. Epub 2010 Jun 23. Vitamin D treatment effectively reduces the risk of falls in older adults.

Lappe JM, Travers-Gustafson D, Davies KM, Recker RR, Heaney RP. Vitamin D and calcium supplementation reduces **cancer risk**: results of a randomized trial. Am J Clin Nutr. 2007 Jun;85(6):1586-91

Vatanparast H, Dolega-Cieszkowski JH, Whiting SJ. Many adult Canadians are not meeting current **calcium recommendations from food and supplement** intake. Appl Physiol Nutr Metab. 2009 Apr;34(2):191-6.

Winzenberg TM, Powell S, Shaw KA, Jones G. **Vitamin D** supplementation for improving bone mineral density in **children**. Cochrane Database of Systematic Reviews 2010, Issue 10. Art. No.: CD006944. DOI: 10.1002/14651858.CD006944.pub2. These results do not support vitamin D supplementation to improve bone density in healthy children with normal vitamin Dlevels, but suggest that supplementation of deficient children may be clinically useful.

Papaioannou, Alexandra, Morin, Suzanne, Cheung, Angela M., et al. **2010 clinical practice guidelines for the diagnosis and management of osteoporosis in Canada**: summary CMAJ 2010 0: cmaj.100771.

IOM (Institute of Medicine): Dietary Reference Intakes for **Calcium and Vitamin D** Nov,2010.
http://www.iom.edu/~/media/Files/Report%20Files/2010/Dietary-Reference-Intakes-for-Calcium-and-Vitamin-D/Vitamin%20D%20and%20Calcium%202010%20Report%20Brief.pdf

Michael YL, Whitlock EP, Lin JS, Fu R, O'Connor EA, Gold R. Primary care-relevant interventions to prevent falling in older adults: a systematic evidence review for the u.s. Preventive services task force (**USPSTF**). Ann Intern Med. 2010 Dec 21;153(12):815-25.

Zhu K, Austin N, Devine A, et al. A randomized controlled trial of the effects of vitamin D on **muscle strength** and mobility in older women with vitamin D insufficiency. J Am Geriatr Soc. 2010 Nov;58(11):2063-8. doi: 10.1111/j.1532-5415.2010.03142.x.

Rosen Clifford J. **Vitamin D Insufficiency**. N Engl J Med 2011; 364:248-254.

Bosomworth, N.J. Mitigating epidemic vitamin D deficiency: The agony of evidence. Can Fam Physician 2011 57: 16-20.

Panel on Prevention of Falls in Older Persons, **American Geriatrics Society (AGS)** and British Geriatrics Society. Summary of Updated American Geriatrics Society/British Geriatrics Society Clinical Practice Guideline for **Prevention of Falls in Older Persons**. Article first published online: 13 JAN 2011 DOI: 10.1111/j.1532-5415.2010.03234.x http://onlinelibrary.wiley.com/doi/10.1111/j.1532-5415.2010.03234.x/pdf

Winzenberg Tania, Powell Sandi, Shaw Kelly Anne, et al. Effects of vitamin D supplementation on bone density in healthy **children**: systematic review and meta-analysis. BMJ 2011;342:doi:10.1136/bmj.c7254 (Published 25 January 2011).

Langer-Gould A, Huang S, Van Den Eeden SK, et al. Vitamin d, pregnancy, breastfeeding, and postpartum **multiple sclerosis** relapses. Arch Neurol. 2011 Mar;68(3):310-3.

*Bolland MJ, Grey A, Avenell A, et al. **Calcium supplements with or without vitamin D** and risk of cardiovascular events: reanalysis of the Women's Health Initiative limited access dataset and meta-analysis. BMJ 2011; DOI: doi:10.1136/bmj.d2040.*

Beauchet O, Annweiler C, Verghese J, et al. Biology of gait control: vitamin D involvement. Neurology 2011;76:1617–1622.

*Warensjö Eva, Byberg Liisa, Melhus Håkan, et al. **Dietary calcium intake** and risk of fracture and osteoporosis: prospective longitudinal cohort study. BMJ 2011;342:doi:10.1136/bmj.d1473 (Published 24 May 2011)*

Kumar Geeta Trilok, Sachdev Harshpal Singh, Chellani Harish, et al. Effect of weekly vitamin D supplements on mortality, morbidity, and growth of low birthweight term infants in India up to age 6 months: randomised controlled trial. BMJ 2011;342:doi:10.1136/bmj.d2975

*Holick Michael F., Binkley Neil C., Bischoff-Ferrari Heike A., et al. Evaluation, Treatment, and Prevention of Vitamin D Deficiency: an **Endocrine Society** Clinical Practice Guideline JCEM 2011 jc.2011-0385.*

Gelfand JM, Cree BA, McElroy J, et al. **Vitamin D** in African Americans with multiple sclerosis. Neurology. 2011 May 24;76(21):1824-30.

BC Guideline: Medical Services Commission. **Vitamin D testing protocol**. British Columbia Medical Services Commission; 2010 Oct 1. http://www.bcguidelines.ca/pdf/vitamind.pdf

Bjelakovic G, Gluud LL, Nikolova D, et al. **Vitamin D supplementation for prevention of mortality** in adults. Cochrane Database of Systematic Reviews 2011, Issue 7. Art. No.: CD007470. DOI: 10.1002/14651858.CD007470.pub2. Vitamin D in the form of vitamin D3 seems to decrease mortality in predominantly elderly women who are mainly in institutions and dependent care. Vitamin D2, alfacalcidol, and calcitriol had no statistically significant effect on mortality. Vitamin D3 combined with calcium significantly increased nephrolithiasis. Both alfacalcidol and calcitriol significantly increased hypercalcaemia.

Sanders KM, Stuart AL, Williamson EJ, Jacka FN, Dodd S, Nicholson G, Berk M. Annual high-dose vitamin D3 and **mental well-being**: randomised controlled trial. Br J Psychiatry. 2011 May;198(5):357-64. (no benefit in older women)

Tang JY, Fu T, Leblanc E, et al. Calcium plus vitamin D supplementation and the risk of **nonmelanoma and melanoma skin cancer**: post hoc analyses of the women`s health initiative randomized controlled trial. J Clin Oncol. 2011 Aug 1;29(22):3078-84.

Skversky AL, Kumar J, Abramowitz MK, et al. Association of **Glucocorticoid Use and Low 25-Hydroxyvitamin D Levels**: Results from the National Health and Nutrition Examination Survey (NHANES): 2001-2006. J Clin Endocrinol Metab. 2011 Sep 28.

Jacobsen RB, Hronek BW, Schmidt GA, Schilling ML. **Hypervitaminosis D Associated with a Vitamin D Dispensing Error** (October). Ann Pharmacother. 2011 Sep 13.

*Buppasiri P, Lumbiganon P, Thinkhamrop J, et al. Calcium supplementation (other than for preventing or treating hypertension) for improving pregnancy and infant outcomes. Cochrane Database of Systematic Reviews 2011, Issue 10. Art. No.: CD007079. DOI: 10.1002/14651858.CD007079.pub2. Calcium supplementation is associated with a significant protective benefit in the prevention of **pre-eclampsia**, and should be used for this indication according to a previous review. This review indicates that there are no additional benefits for calcium supplementation in prevention of preterm birth or low infant birth weight.*

*Stein MS, Liu Y, Gray OM, et al. A randomized trial of high-dose vitamin D2 in relapsing-remitting **multiple sclerosis**. Neurology 2011;77:1611–1618.*

Avenell A, MacLennan GS, Jenkinson DJ, et al. Long-term follow-up for mortality and cancer in a randomized placebo-controlled trial of vitamin D3 and/or calcium (**RECORD** trial). J Clin Endocrinol Metab 2011; DOI:10.1210jc.2011-1309.

Chung M, Lee J, Terasawa T, et al. **Vitamin D With or Without Calcium** Supplementation for Prevention of Cancer and **Fractures**: An Updated Meta-analysis for the U.S. Preventive Services Task Force (USPSTF). Ann Intern Med. 2011 Dec 20;155(12):827-38.

Pérez-López FR, Brincat M, Erel CT, et al. **EMAS** position statement: Vitamin D and postmenopausal health. Maturitas. 2011 Nov 17.

McGreevy C, Williams D. New insights about vitamin D and **cardiovascular disease**: a narrative review. Ann Intern Med. 2011 Dec 20;155(12):820-6.

Marcus JF, Shalev SM, Harris CA, et al. **Severe hypercalcemia following vitamin d supplementation** in a patient with multiple sclerosis: a note of caution. Arch Neurol. 2012 Jan;69(1):129-32.

Murad MH, Elamin KB, Abu Elnour NO, et al. Clinical review: The effect of **vitamin D on falls**: a systematic review and meta-analysis. J Clin Endocrinol Metab. 2011 Oct;96(10):2997-3006.

Thadhani R; Appelbaum E; Pritchett Y, et al. **Vitamin D** therapy (paricalcitol) and cardiac structure and function in patients with **chronic kidney disease**: The **PRIMO** randomized controlled trial. JAMA 2012; 307:674-684.

Muir SW, Montero-Odasso M. Effect of vitamin D supplementation on **muscle strength, gait and balance** in older adults: a systematic review and meta-analysis. J Am Geriatr Soc. 2011 Dec;59(12):2291-300.

De-Regil LM, Palacios C, Ansary A, et al. Vitamin D supplementation for women during **pregnancy**. Cochrane Database Syst Rev. 2012 Feb 15;2:CD008873.

Kunisaki KM, Niewoehner DE, Connett JE; COPD Clinical Research Network. Vitamin D levels and risk of acute exacerbations of **chronic obstructive pulmonary disease**: a prospective cohort study. Am J Respir Crit Care Med 2012;185:286–290.

Lehouck A, Mathieu C, Carremans C, Baeke F, Verhaegen J, Van Eldere J, et al. High doses of vitamin D to reduce exacerbations in **chronic obstructive pulmonary disease**. A randomized trial. Ann Intern Med. 2012;156:105-14

Manaseki-Holland S, Maroof Z, Bruce J, et al. Effect on the incidence of **pneumonia** of vitamin D supplementation by quarterly bolus dose to infants in Kabul: a randomised controlled superiority trial. Lancet. 2012 Apr 14;379(9824):1419-27.

de Boer IH, Levin G, Robinson-Cohen C, et al. Serum 25-hydroxyvitamin d concentration and risk for major clinical disease events in a community-based population of older adults: a cohort study. Ann Intern Med. 2012 May 1;156(9):627-34.

Barake M, Daher RT, Salti I, Cortas et al. **25-hydroxyvitamin D assay variations** and impact on clinical decision making. J Clin Endocrinol Metab. 2012 Mar;97(3):835-43.

Li Kuanrong, Kaaks R, Linseisen J, et al. Associations of **dietary calcium intake and calcium supplementation** with **myocardial infarction** and stroke risk and overall cardiovascular mortality in the Heidelberg cohort of the European Prospective Investigation into Cancer and Nutrition study (EPIC-Heidelberg). Heart 2012. (In press)

Rejnmark L, Avenell A, Masud T, et al. **Vitamin D with Calcium Reduces Mortality**: Patient Level Pooled Analysis of 70,528 Patients from Eight Major Vitamin D Trials. J Clin Endocrinol Metab. 2012 May 17.

Bischoff-Ferrari HA, Willett WC, Oray EJ, et al. A pooled analysis of **vitamin D dose** requirements for fracture prevention. N Engl J Med 2012;367:40-9. {highest actual-intake quartile (792 to 2000 IU daily), there was a 30% reduction in hip fracture incidence}

Ali SN, Tan T, Meeran K, Wynne K. A man with anxiety, confusion, and red eyes. (induced by **calcium supplements**) BMJ. 2012 Jul 5;345:e4443.

Bailey RL, Fulgoni VL 3rd, Keast DR, Lentino CV, Dwyer JT. Do Dietary Supplements Improve Micronutrient Sufficiency in Children and Adolescents? J Pediatr. 2012 Jun 18. (low in calcium & Vit D intake)

Bertone-Johnson ER et al. Vitamin D supplementation and **depression** in the **Women's Health Initiative** Calcium and Vitamin D Trial. Am J Epidemiol 2012 Jul 1; 176:1.

Kjærgaard M, Waterloo K, Wang CE, et al. Effect of vitamin D supplement on depression scores in people with low levels of serum 25-hydroxyvitamin D: nested case-control study and randomised clinical trial. Br J Psychiatry. 2012 Jul 12.

Wu AC, Tantisira K, Li L, et al; for the Childhood Asthma Management Program Research Group. Effect of Vitamin D and **Inhaled Corticosteroid Treatment** on Lung Function in Children. Am J Respir Crit Care Med. 2012 Sep 15;186(6):508-513.

Morales E, Guxens M, Llop S, et al; on behalf of the INMA Project. Circulating 25-Hydroxyvitamin D3 in Pregnancy and **Infant Neuropsychological** Development. Pediatrics. 2012 Sep 17.

Balion C, Griffith LE, Strifler L, et al. Vitamin D, cognition, and dementia: A systematic review and meta-analysis. Neurology. 2012 Sep 25;79(13):1397-405.

Halicioglu O, Sutcuoglu S, Koc F, et al. Vitamin D Status of Exclusively Breastfed 4-Month-Old Infants Supplemented During Different Seasons. Pediatrics. 2012 Sep 24.

Murdoch DR, Slow S, Chambers ST, et al. Effect of vitamin D3 supplementation on upper respiratory tract infections in healthy adults: the VIDARIS randomized controlled trial. JAMA. 2012;308(13):1333-1339.

Schreuder F, Bernsen RM, van der Wouden JC. Vitamin d supplementation for nonspecific **musculoskeletal pain** in non-Western immigrants: a randomized controlled trial. Ann Fam Med. 2012 Nov;10(6):547-55.

McAlindon T, LaValley M, Schneider E, et al. Effect of vitamin D supplementation on **progression of knee pain and cartilage volume loss** in patients with symptomatic osteoarthritis: a randomized controlled trial. JAMA. 2013 Jan 9;309(2):155-62.

Turer CB, Lin H, Flores G. Prevalence of **Vitamin D Deficiency Among Overweight and Obese** US Children. Pediatrics. 2013 Jan;131(1):e152-61.

Noordam R, de Craen AJ, Pedram P, et al. Levels of 25-hydroxyvitamin D in familial **longevity**: the Leiden Longevity Study. CMAJ. 2012 Nov 5.

Xiao Q, Murphy RA, Houston DK, Harris TB, Chow WH, Park Y. Dietary and supplemental **calcium intake and cardiovascular disease mortality**. (NIH-AARP) JAMA Intern Med 2013.

Rossom RC, Espeland MA, Manson JE, et al. Calcium and vitamin D supplementation and **cognitive impairment** in the women's health initiative (WHI). J Am Geriatr Soc. 2012 Dec;60(12):2197-205.

Anglin RE, Samaan Z, Walter SD, McDonald SD. Vitamin D deficiency and **depression** in adults: systematic review and meta-analysis. Br J Psychiatry. 2013 Feb;202:100-7.

Vimaleswaran KS, Berry DJ, Lu C, et al; Genetic Investigation of Anthropometric Traits (GIANT) consortium, Streeten EA, Theodoratou E, et al. Causal Relationship between Obesity and Vitamin D Status: Bi-Directional Mendelian Randomization Analysis of Multiple Cohorts. PLoS Med. 2013 Feb;10(2):e1001383.

Goswami R, Vatsa M, Sreenivas V, et al. **Skeletal muscle strength** in young Asian Indian females after vitamin D and calcium supplementation: a double-blind randomized controlled clinical trial. J Clin Endocrinol Metab. 2012 Dec;97(12):4709-16.

Michaëlsson K, Melhus H, Warensjö Lemming E, et al. Long term **calcium intake and rates of all cause and cardiovascular mortality**: community based prospective longitudinal cohort study. BMJ. 2013 Feb 12;346:f228.

Lawlor DA, Wills AK, Fraser A, et al. Association of maternal **vitamin D status during pregnancy** with bone-mineral content in off spring: a prospective cohort study. Lancet 2013; online March 19.

Aghajafari F, Nagulesapillai T, Ronksley PE, Tough SC, O'Beirne M, Rabi DM. Association between maternal serum 25-hydroxyvitamin D level and **pregnancy and neonatal outcomes**: systematic review and meta-analysis of observational studies. BMJ 2013;346:f1169.

Aucoin M, Weaver R, Thomas R, et al. Vitamin D status of **refugees arriving in Canada**: Findings from the Calgary Refugee Health Program. Can Fam Physician. 2013 Apr;59(4):e188-94.

Abrams SA; the Committee on Nutrition. Calcium and Vitamin D Requirements of Enterally Fed **Preterm Infants**. Pediatrics. 2013 Apr 29.

Gallo S, Comeau K, Vanstone C, et al. Effect of different dosages of oral vitamin D supplementation on vitamin D status in healthy, **breastfed infants**: a randomized trial. JAMA. 2013;309(17):1785-1792.

Langsetmo L, Berger C, Kreiger N, et al; the CaMos Group. **Calcium and Vitamin D Intake and Mortality**: Results from the Canadian Multicentre Osteoporosis Study (CaMos). J Clin Endocrinol Metab. 2013 May 24.

Robinson-Cohen C, Hoofnagle AN, Ix JH, et al.Racial differences in the association of serum 25-hydroxyvitamin D concentration with coronary heart disease events. JAMA. 2013;310(2):179-188.

Kasahara AK, Singh RJ, Noymer A. Vitamin D (25OHD) Serum **Seasonality** in the United States. PLoS One. 2013 Jun 21;8(6):e65785.

Dore RK. Should healthy people take **calcium and vitamin D to prevent fractures**? What the US Preventive Services Task Force and others say. Cleve Clin J Med. 2013 Jun;80(6):341-4.

Witham MD, Price RJG, Struthers AD, et al. Cholecalciferol treatment to reduce **blood pressure** in older patients with isolated systolic hypertension. The **VitDISH** randomized controlled trial. JAMA Intern Med 2013.

Sohl E, van Schoor NM, de Jongh RT, et al. Vitamin D Status Is Associated With **Functional Limitations and Functional Decline** in Older Individuals. J Clin Endocrinol Metab. 2013 Jul 17

Aluisio AR, Maroof Z, Chandramohan D, et al. Vitamin D3 Supplementation and Childhood **Diarrhea**: A Randomized Controlled Trial. Pediatrics. 2013 Sep 9.

Chlebowski RT, Pettinger M, Johnson KC, et al. Calcium Plus Vitamin D Supplementation and **Joint Symptoms** in Postmenopausal Women in the Women's Health Initiative Randomized Trial. J Acad Nutr Diet. 2013 Aug 14.

Caruso TJ, Fuzaylov G. Images in clinical medicine. Severe vitamin D deficiency--**rickets**. N Engl J Med. 2013 Aug 29;369(9):e11.

Reid IR, Bolland MJ, Grey A. Effects of **vitamin D supplements** on bone mineral density: a systematic review and meta-analysis. Lancet 2013; online Oct 11.

Powe CE, Evans MK, Wenger J, et al. **Vitamin D-binding protein** and vitamin D status of black Americans and white Americans. N Engl J Med 2013;369:1991-2000.

Feskanich D, Bischoff-Ferrari HA, Frazier L, WillettWC. **Milk consumption** during teenage years and risk of hip fractures in older adults [online November 18, 2013]. JAMA Pediatr. doi:10.1001/jamapediatrics.2013.3821.

Soilu-Hänninen M, Aivo J, Lindström BM, et al. A randomised, double blind, placebo controlled trial with vitamin D3 as an add on treatment to interferon β-1b in patients with **multiple sclerosis.** J Neurol Neurosurg Psychiatry. 2012 May;83(5):565-71.

Lavie CJ, Dinicolantonio JJ, Milani RV, O'Keefe JH. **Vitamin d** and cardiovascular (**atorvastatin myalgias**) health. Circulation. 2013 Nov 26;128(22):2404-6.

Kara C, Gunindi F, Ustyol A, Aydin M. **Vitamin d intoxication due to an erroneously manufactured** dietary supplement in seven children. Pediatrics. 2014 Jan;133(1):e240-4.

Elder CJ, Bishop NJ. **Rickets**. Lancet. 2014 Jan 9

Wingate KE, Jacobson K, Issenman R, et al. **25-Hydroxyvitamin D** Concentrations in Children with Crohn's Disease Supplemented with Either **2000 or 400 IU Daily** for 6 Months: A Randomized Controlled Study. J Pediatr. 2014 Jan 11

Bjelakovic G, Gluud LL, Nikolova D, et al. Vitamin D supplementation for prevention of **mortality in adults**. **Cochrane** Database Syst Rev. **2014** Jan 10;1:CD007470. Vitamin D3 seemed to decrease mortality in elderly people living independently or in institutional care. Vitamin D2, alfacalcidol and calcitriol had no statistically significant beneficial effects on mortality. Vitamin D3 combined with calcium increased nephrolithiasis. Both alfacalcidol and calcitriol increased hypercalcaemia. Because of risks of attrition bias originating from substantial dropout of participants and of outcome reporting bias due to a number of trials not reporting on mortality, as well as a number of other weaknesses in our evidence, further placebo-controlled randomised trials seem warranted.

American Geriatrics Society Workgroup on Vitamin D Supplementation for Older Adults. Recommendations Abstracted from the American Geriatrics Society Consensus Statement on Vitamin D for Prevention of Falls and Their Consequences. J Am Geriatr Soc. 2013 Dec 18.

Wepner F, Scheuer R, Schuetz-Wieser B, et al. Effects of vitamin D on patients with **fibromyalgia** syndrome: A randomized placebo-controlled trial. Pain. 2014 Feb;155(2):261-8

Schnatz PF, Jiang X, Vila-Wright S,et al. **Calcium/vitamin D** supplementation, serum 25-hydroxyvitamin D concentrations, and cholesterol profiles in the Women's Health Initiative calcium/vitamin D randomized trial. Menopause. 2014 Mar 3.

Oberhelman SS, Meekins ME, Fischer PR, et al. Maternal vitamin D supplementation to improve the vitamin D status of breast-fed infants: a randomized controlled trial. Mayo Clin Proc. 2013 Dec;88(12):1378-87.

Autier P, Boniol M, Pizot C, et al. **Vitamin D status and ill health**: a systematic review. Lancet Diabetes Endocrinol. 2014 Jan;2(1):76-89.

Chowdhury R, Kunutsor, S, Vitezova A, Oliver-Williams C, Kiefte-de Jong J, Khan H, et al. **Vitamin D and risk of cause specific death**: systematic review and meta-analysis of prospective observational and randomised intervention studies. BMJ 2014;348:g1903.

Theodoratou E, Tzoulaki I, Lina Z, Ioannidis JP. **Vitamin D and multiple health outcomes**: umbrella review of systematic reviews and meta-analyses of observational studies and randomised trials. BMJ 2014;348:g2035.

Lindqvist PG. On the possible link between vitamin d deficiency and **cardiovascular disease**: should we d-lighten our lives? Circulation. 2014 Apr 1;129(13)

Lindblad AJ, Garrison S, McCormack J. **Testing vitamin D levels**. Can Fam Physician. 2014 Apr;60(4):351.

Avenell A, Mak JC, O`Connell D. **Vitamin D and vitamin D analogues for preventing fractures** in post-menopausal women and older men. Cochrane Database Syst Rev. 2014 Apr 14;4:CD000227. Vitamin D alone is unlikely to prevent fractures in the doses and formulations tested so far in older people. Supplements of vitamin D and calcium may prevent hip or any type of fracture. There was a small but significant increase in gastrointestinal symptoms and renal disease associated with vitamin D and calcium. This review found that there was no increased risk of death from taking calcium and vitamin D.

Bolland MJ, Grey A, Gamble GD, et al. The effect of **vitamin D supplementation on skeletal, vascular, or cancer outcomes**: a trial sequential meta-analysis. Lancet Diabetes Endocrinol. 2014 Apr;2(4):307-20.

Bjelakovic G, Gluud LL, Nikolova D, Whitfield K, Krstic G, Wetterslev J, Gluud C. Vitamin D supplementation for **prevention of cancer** in adults. Cochrane Database of Systematic Reviews 2014, Issue 6. Art. No.: CD007469. DOI: 10.1002/14651858.CD007469.pub2. There is currently no firm evidence that vitamin D supplementation decreases or increases cancer occurrence in predominantly elderly community-dwelling women. Vitamin D supplementation decreased cancer mortality and vitamin D supplementation decreased all-cause mortality, but these estimates are at risk of type I errors due to the fact that too few participants were examined, and to risks of attrition bias originating from substantial dropout of participants. Combined vitamin D and calcium supplements increased nephrolithiasis, whereas it remains unclear from the included trials whether vitamin D , calcium, or both were responsible for this effect.

Castro M, King TS, Kunselman SJ, et al; for the National Heart, Lung, and Blood Institute's AsthmaNet. Effect of Vitamin D3 on **Asthma Treatment** Failures in Adults With Symptomatic Asthma and Lower Vitamin D Levels: The **VIDA** Randomized Clinical Trial. JAMA. 2014 May 18.
Gallagher JC, Smith LM, Yalamanchili V. Incidence of hypercalciuria and hypercalcemia during vitamin D and calcium supplementation in older women. Menopause. 2014 Jun 16.
Goodall EC, Granados AC, Luinstra K, et al. Vitamin D3 and **gargling for the prevention of upper respiratory tract infections**: a randomized controlled trial. BMC Infect Dis. 2014 May 19;14(1):273.
Schöttker B, Jorde R, Peasey A, et al; Consortium on Health and Ageing: Network of Cohorts in Europe and the United States **(CHANCES). Vitamin D and mortality**: meta-analysis of individual participant data from a large consortium of cohort studies from Europe and the United States. BMJ. 2014 Jun 17;348:g3656.
Welles CC, Whooley MA, Karumanchi SA, et al. Vitamin d deficiency and **cardiovascular events in patients with coronary heart disease**: data from the heart and soul study. Am J Epidemiol. 2014 Jun 1;179(11):1279-87.
Vimaleswaran KS, Cavadino A, Berry DJ, et al. Association of vitamin D status with **arterial blood pressure and hypertension risk**: A Mendelian randomisation study. *Lancet Diabetes Endocrinol* 2014.
Hofmeyr GJ, Lawrie TA, Atallah ÁN, Duley L, Torloni MR. **Calcium supplementation during pregnancy for preventing hypertensive disorders and related problems**. Cochrane Database of Systematic Reviews 2014, Issue 6. Art. No.: CD001059. DOI: 10.1002/14651858.CD001059.pub4.
Calcium supplementation (_ 1 g/day) is associated with a significant reduction in the risk of pre-eclampsia, particularly for women with low calcium diets. The treatment effectmay be overestimated due to small-study effects or publication bias. It also reduces preterm birth and the occurrence of the composite outcome 'maternal death or serious morbidity'. We considered these benefits to outweigh the increased risk of HELLP syndrome, which was small in absolute numbers. The World Health Organization recommends calcium 1.5 g to 2 g daily for pregnant women with low dietary calcium ntake. The limited evidence on low-dose calcium supplementation suggests a reduction in pre-eclampsia, but needs to be confirmed by larger, high-quality trials. Pending such results, in settings of low dietary calcium where high-dose supplementation is not feasible, the option of lower-dose supplements (500 to 600 mg/day) might be considered in preference to no supplementation.
Littlejohns TJ, Henley WE, Lang IA, et al. Vitamin D and the **risk of dementia and Alzheimer disease**. Neurology. 2014 Sep 2;83(10):920-8.
Ye Z, Sharp SJ, Burgess S, et al; InterAct Consortium, Langenberg C, Wareham NJ, Forouhi NG. Association between **circulating 25-hydroxyvitamin D and incident type 2 diabetes**: a mendelian randomization study. Lancet Diabetes Endocrinol. 2014 Sep 30.
Amrein K, Schnedl C, Holl A, et al. Effect of High-Dose **Vitamin D3** on Hospital Length of Stay in **Critically Ill** Patients With Vitamin D Deficiency: The **VITdAL-ICU** Randomized Clinical Trial. JAMA. 2014 Oct 15;312(15):1520 1530.
Camargo CA Jr, Ganmaa D, Sidbury R, et al. Randomized trial of vitamin D supplementation for winter-related **atopic dermatitis** in children. J Allergy Clin Immunol. 2014 Oct;134(4):831 835.e1.
Lee GJ, Birken CS, Parkin PC, et al; for the TARGet Kids! Collaboration. Consumption of **non-cow's milk beverages and serum vitamin D levels** in early childhood. CMAJ. 2014 Oct 20.
Newberry SJ, Chung M, Shekelle PG, et al. **Vitamin D and Calcium: A** Systematic Review of Health Outcomes (Update). Evidence Report/Technology Assessment No. 217. AHRQ Comparative Effectiveness Review. Rockville (MD): Agency for Healthcare Research and Quality (US); 2014 Sept. Report No.: 14-E004-EF.
Borzutzky A, Grob F, Camargo CA Jr, et al. **Vitamin d deficiency** rickets in an adolescent with severe **atopic dermatitis**. Pediatrics. 2014 Feb;133(2):e451-4.
Singh P, Trivedi N. **Tanning beds** and hypervitaminosis d: a case report. Ann Intern Med. 2014 Jun 3;160(11):810-1.
*Afzal S, Brøndum-Jacobsen P, Bojesen SE, Nordestgaard BG. **Genetically low vitamin D** concentrations and increased **mortality**: mendelian randomization analysis in three large cohorts. BMJ. 2014 Nov 18;349:g6330.*
*LeBlanc ES, Zakher B, Daeges M, et al. **Screening for Vitamin D Deficiency**: A Systematic Review for the U.S. Preventive Services Task Force. **(USPSTF)** Ann Intern Med. 2014 Nov 25.*
*LeFevre ML. **Screening for Vitamin D Deficiency** in Adults: U.S. Preventive Services Task Force Recommendation Statement. **(USPSTF)** Ann Intern Med. 2014 Nov 25.*
*McNally JD, Iliriani K, Pojsupap S, et al. Rapid **Normalization of Vitamin D Levels**: A Meta Analysis. Pediatrics. 2015 Jan;135(1):e152-e166.*
*Toffanello ED, Coin A, Perissinotto E, et al. **Vitamin D deficiency predicts cognitive decline** in older men and women: The Pro.V.A. Study. Neurology. 2014 Dec 9;83(24):2292-8.*
*Turner AN, Carr Reese P, Fields KS, et al. A blinded, randomized controlled trial of high-dose **vitamin D** supplementation to reduce recurrence of **bacterial vaginosis**. Am J Obstet Gynecol. 2014 Nov;211(5):479.e1-479.e13.*
Arora P, Song Y, Dusek J, et al. **Vitamin D** Therapy in Individuals With Prehypertension or Hypertension: The **DAYLIGHT** Trial. Circulation. 2015 Jan 20;131(3):254-62.
Bodnar LM, Platt RW, Simhan HN. **Early-Pregnancy** Vitamin D Deficiency and Risk of Preterm Birth Subtypes. Obstet Gynecol. 2015 Jan 7.
Meyer HE, Holvik K, Lips P. Should vitamin D supplements be recommended to **prevent chronic diseases**? BMJ. 2015 Jan 29;350:h321.
Dudenkov DV, Yawn BP, Oberhelman SS, et al. **Changing Incidence of Serum 25-Hydroxyvitamin D Values Above 50 ng/mL**: A 10-Year Population-Based Study. Mayo Clin Proc. 2015 May;90(5):577-86.
Martineau AR, Hanifa Y, Witt KD, et al. Double-blind randomised controlled trial of **vitamin D3 supplementation for the prevention of acute respiratory infection** in older adults and their carers (ViDiFlu). Thorax. 2015 Jun 10.
Straube S, Derry S, Straube C, et al. **Vitamin D for the treatment of chronic painful conditions** in adults. Cochrane Database Syst Rev. 2015 May 6;5:CD007771. The evidence addressing the use of vitamin D for chronic pain now contains more than twice as many studies and participants than were included in the original version of this review. Based on this evidence, a large beneficial effect of vitamin D across different chronic painful conditions is unlikely. Whether vitamin D can have beneficial effects in specific chronic painful conditions needs further investigation.
Birken CS, Lobovic G, Anderson LN, et al. Association between **vitamin D and circulating lipids** in early **childhood**.*PLoS One* 2015.
Hansen KE, Johnson RE, Chambers KR, et al. Treatment of **Vitamin D Insufficiency in Postmenopausal Women**: A Randomized Clinical Trial. JAMA Intern Med. 2015 Aug 3.
Javed A, Kullo IJ, Babu Balagopal P, et al. Effect of **vitamin D(3) treatment on endothelial function in obese adolescents**. Pediatr Obes. 2015 Aug 14.
Mokry LE, Ross S, Ahmad OS, et al. **Vitamin D and Risk of Multiple Sclerosis**: A Mendelian Randomization Study. PLoS Med. 2015 Aug 25;12(8):e1001866.
Houston DK, Tooze JA, et al. Delivery of a Vitamin D Intervention in **Homebound Older Adults Using a Meals-on-Wheels Program**: A Pilot Study. J Am Geriatr Soc. 2015 Aug 16.
Jelinek GA, Marck CH, Weiland TJ, et al. Latitude, sun exposure and vitamin D supplementation: associations with quality of life and disease outcomes in a large international cohort of people with **multiple sclerosis**. BMC Neurol. 2015 Aug 5;15:132.
Munasinghe LL, Willows N, Yuan Y, et al. **Dietary reference intakes for vitamin D** based on the revised 2010 dietary guidelines are not being met by children in Alberta, Canada. Nutr Res 2015; online August 14, 2015.
Miller JW, Harvey DJ, Beckett LA, et al. Vitamin D Status and Rates of **Cognitive Decline** in a Multiethnic Cohort of Older Adults. JAMA Neurol. 2015 Sep 14.
Hollis BW, Wagner CL, Howard CR, et al. **Maternal versus infant vitamin D supplementation during lactation**: a randomized controlled trial. Pediatrics. 2015;136(4):625–634
Bolland ML, Leung W, Tai V, et al. **Calcium intake and risk of fracture**: systematic review. BMJ 2015;351:h4580.
Tai V, Leung W, Grey A. Reid IR, Bolland MJ. **Calcium intake and bone mineral density**: systematic review and meta-analysis. BMJ 2015;351:h4183.
Baron JA, Barry EL, Mott LA, et al. A Trial of **Calcium and Vitamin D** for the Prevention of **Colorectal Adenomas**. N Engl J Med. 2015 Oct 15;373(16):1519-30.
Fitzgerald KC, Munger KL, Köchert K, et al. Association of **Vitamin D** Levels With **Multiple Sclerosis** Activity and Progression in Patients Receiving Interferon Beta-1b. JAMA Neurol. 2015 Oct 12:1-8.
Denlinger LC, King TS, Cardet JC, et al; National Heart Lung and Blood Institute AsthmaNet Investigators. **Vitamin D Supplementation and the Risk of Colds** in Patients with Asthma. Am J Respir Crit Care Med. 2015 Nov 5.
Bischoff-Ferrari HA, Dawson-Hughes B, Orave JE, et al. **Monthly high-dose vitamin D** treatment for the prevention of **functional decline** [online Jan 4, 2016].JAMA Intern Med. doi:10.1001/jamainternmed.2015.7148.
Laursen JH, Søndergaard HB, Sørensen PS, et al. Association between age at onset of **multiple sclerosis** and vitamin D level-related factors. Neurology. 2016 Jan 5;86(1):88-93.
Sethuraman G, Marwaha RK, Challa A, et al. Vitamin D: A New Promising Therapy for **Congenital Ichthyosis**. Pediatrics. 2016 Jan;137(1):1-5.
Tazzyman S, Richards N, Trueman AR, et al. Vitamin D associates with improved quality of life in participants with **irritable bowel syndrome**: outcomes from a pilot trial. BMJ Open Gastroenterol. 2015 Dec 21;2(1):e000052.
Chawes BL, Bønnelykke K, Stokholm J, et al. Effect of vitamin D3 supplementation during pregnancy on risk of persistent **wheeze** in the offspring.JAMA. doi:10.1001/jama.2015.18318
Litonjua AA, Carey VJ, Laranjo N, et al. Effect of prenatal supplementation with vitamin D on **asthma or recurrent wheezing** in offspring by age 3 years: the VDAART randomized clinical trial. JAMA. doi:10.1001/jama.2015.18589.
Bunyavanich S, Rifas-Shiman SL, Platts-Mills TA, et al. Prenatal, perinatal, and childhood vitamin D exposure and their association with **childhood allergic rhinitis and allergic sensitization**. J Allergy Clin Immunol. 2016 Feb 10. pii: S0091-6749(16)00035-X.
Cooper C, Harvey NC, Bishop NJ, et al, and the MAVIDOS Study Group. **Maternal gestational vitamin D supplementation and off spring** bone health (**MAVIDOS**): a multicentre, double-blind, randomised placebo-controlled trial. Lancet Diabetes Endocrinol 2016; online March 1.
Lima GL, Paupitz J, et al. Vitamin D Supplementation in Adolescents and Young Adults With **Juvenile Systemic Lupus Erythematosus** for Improvement in Disease Activity and Fatigue Scores: A Randomized, Double-Blind, Placebo-Controlled Trial. Arthritis Care Res 2016 Jan;68(1):91-8.
Denlinger LC, King TS, Cardet JC, et al; NHLBI AsthmaNet Investigators. Vitamin D Supplementation and the **Risk of Colds in Patients with Asthma**. Am J Respir Crit Care Med. 2016 Mar 15;193(6):634-41.
Jin X, Jones G, Cicuttini F, et al. Effect of Vitamin D Supplementation on **Tibial Cartilage Volume and Knee Pain** Among Patients With Symptomatic Knee Osteoarthritis: A Randomized Clinical Trial. JAMA. 2016 Mar 8;315(10):1005-13.
Nielson CM, Jones KS, Chun RF, et al; Osteoporotic Fractures in Men (MrOS) Research Group. **Role of Assay Type in Determining Free 25-Hydroxyvitamin D** Levels in Diverse Populations. N Engl J Med. 2016 Mar 23.
Witte KK, Byrom R, Gierula J, et al. Effects of vitamin D on **cardiac function** in patients with chronic HF: The **VINDICATE** Study.*J Am Coll Cardiol* 2016.
Mason C, Tapsoba JD, Duggan C, et al. Effects of **Vitamin D** Supplementation on Lean Mass, Muscle Strength, and Bone Mineral Density During Weight Loss: A Double-Blind Randomized Controlled Trial. J Am Geriatr Soc. 2016 Apr 5.
Kabbani TA et al. Association of **vitamin D** level with clinical status in **inflammatory bowel disease**: A 5-year longitudinal study. Am J Gastroenterol 2016 May; 111:712.
Tebben PJ, Singh RJ, Kumar R. **Vitamin D**-mediated hypercalcemia-Mechanism, diagnosis and treatment. Endocr Rev. 2016 Sep 2:er20161070.
Kern J, Kern S, Blennow K, et al. **Calcium supplementation** and risk of **dementia** in women with cerebrovascular disease. Neurology. 2016 Aug 17.
Boyd C, Moodambail A. Severe **hypercalcaemia** in a child secondary to use of **alternative therapies**. BMJ Case Rep. 2016 Oct 6;2016.
Chung M, Tang AM, Fu Z, et al. **Calcium Intake and Cardiovascular Disease Risk**: An Updated Systematic Review and Meta-analysis. Ann Intern Med. 2016 Oct 25.
Kopecky SL, Bauer DC, Gulati M, et al. Lack of **Evidence Linking Calcium With or Without Vitamin D Supplementation to Cardiovascular Disease** in Generally Healthy Adults: A Clinical Guideline From the National Osteoporosis Foundation and the American Society for Preventive Cardiology. Ann Intern Med. 2016 Oct 25.
Moon RJ, Harvey NC, Cooper C, et al. Determinants of the **Maternal 25-Hydroxyvitamin D Response to Vitamin D** Supplementation During **Pregnancy**. J Clin Endocrinol Metab. 2016 Oct 27:jc20162869.
Moreira-Lucas TS, et al. Effect of **vitamin D supplementation on oral glucose tolerance** in individuals with low vitamin D status and increased risk for developing type 2 diabetes (EVIDENCE): a double-blind, randomized, placebo-controlled clinical trial. Diabetes Obes Metab. 2016 Sep 26.
Spector TD, Levy L. **Should healthy people take a vitamin D supplement in winter months**? BMJ. 2016 Nov 23;355:i6183
Ginde AA, Blatchford P, Breese K, et al. **High-Dose Monthly Vitamin D for Prevention of Acute Respiratory Infection** in Older Long-Term Care Residents: A Randomized Clinical Trial. J Am Geriatr Soc. 2016 Nov 16.
Libman H, Malabanan AO, Strewler GJ, et al. **Should We Screen for Vitamin D Deficiency**?: Grand Rounds Discussion From Beth Israel Deaconess Medical Center. Ann Intern Med. 2016 Dec 6;165(11):800-807.
Manson JE, Brannon PM, Rosen CJ, et al. Vitamin D Deficiency - **Is There Really a Pandemic**? N Engl J Med. 2016 Nov 10;375(19):1817-1820.
Mokry LE, Ross S, Morris JA, et al. Genetically decreased vitamin D and **risk of Alzheimer disease**. Neurology. 2016 Dec 13;87(24):2567-2574
Barry EL, Peacock JL, Rees JR, et al. Vitamin D Receptor Genotype, **Vitamin D3 Supplementation**, and **Risk of Colorectal Adenomas**: A Randomized Clinical Trial. JAMA Oncol. 2016 Dec 15.

Umaretiya PJ, Oberhelman SS, Cozine EW et al. **Maternal Preferences** for **Vitamin D Supplementation in Breastfed Infants**. Annals of Family Medicine. 2017; 15(1):68-70.
Basatemur E, Horsfall L, Marston L, et al. **Trends in the Diagnosis of Vitamin D Deficiency**. Pediatrics. 2017 Feb 3.
Laurent MR, Gielen E, Pauwels S, et al. **Hypervitaminosis D Associated With Tanning Bed** Use: A Case Report. Ann Intern Med. 2017 Jan 17;166(2):155-156.
Martineau AR, Jolliffe DA, Hooper RL, et al. **Vitamin D supplementation to prevent acute respiratory tract infections**: systematic review and meta-analysis of individual participant data. BMJ 2017;356:i6583.
Scragg R, Stewart AW, Waayer D, et al. Effect of monthly **high-dose (100,000 IU) vitamin D supplementation on cardiovascular disease** in the the Vitamin D Assessment Study **(ViDA)** : a randomized clinical trial [online Apr 5, 2017].JAMA Cardiol. doi: 10.1001/jamacardio.2017.0175
Chin K, Zhao D, Tibuakuu M, et al. Physical Activity, Vitamin D, and Incident **Atherosclerotic Cardiovascular Disease** in Whites and Blacks: The **ARIC** Study. J Clin Endocrinol Metab. 2017 Apr 1;102(4):1227-1236.
Gianfrancesco MA, Stridh P, Rhead B, et al. Evidence for a causal relationship between low vitamin D, **high BMI, and pediatric-onset MS**. Neurology. 2017 Apr 25;88(17):1623-1629.
Hall SC, Agrawal DK. Vitamin D and **Bronchial Asthma**: An Overview of Data From the Past 5 Years. Clin Ther. 2017 Apr 24.
Kim M. Pfotenhauer, Jay H. Shubrook. Vitamin D Deficiency, Its **Role in Health and Disease**, and Current Supplementation Recommendations. *The Journal of the American Osteopathic Association*, 2017.
Pfotenhauer KM, Shubrook JH. Vitamin D Deficiency, Its Role in **Health and Disease**, and Current Supplementation Recommendations. J Am Osteopath Assoc. 2017 May 1;117(5):301-305.
Lappe J, Watson P, Travers-Gustafson D, et al. Effect of vitamin D and calcium supplementation on **cancer incidence** in older women.JAMA. doi:10.1001/jama.2017.2115
Manousaki D, Paternoster L, Standl M, et al. **Vitamin D levels** and susceptibility to asthma, elevated immunoglobulin E levels, and atopic dermatitis: A Mendelian randomization study. PLoS Med. 2017 May 9;14(5):e1002294.
de Abajo FJ, Rodríguez-Martín S, Rodríguez-Miguel A, et al. Risk of Ischemic Stroke Associated With **Calcium Supplements With or Without Vitamin D:** A Nested Case-Control Study. J Am Heart Assoc. 2017 May 18;6(5).
de Oliveira DL, Hirotsu C, Tufik S, et al. The interfaces between **vitamin D, sleep and pain**. J Endocrinol. 2017 May 23.
Zittermann A, Ernst JB, Prokop S, et al. Effect of **vitamin D on all-cause mortality in heart failure** (**EVITA**): a 3-year randomized clinical trial with 4000 IU vitamin D daily. Eur Heart J. 2017 May 12.
Aglipay M, Birken CS, Parkin PC, et al. Effect of **High-Dose vs Standard-Dose Wintertime Vitamin D Supplementation on Viral Upper Respiratory Tract Infections** in Young Healthy Children. JAMA. 2017 Jul 18;318(3):245-254.
Alansari K, Davidson BL, Yousef KI, et al. **Rapid vs Maintenance Vitamin D Supplementation in Deficient Asthmatic** Children to Prevent Exacerbations. Chest. 2017 Jun 23.
Darling AL, Rayman MP, Steer CD, et al. Association between **maternal vitamin D status in pregnancy and neurodevelopmental outcomes in childhood**: results from the Avon Longitudinal Study of Parents and Children (ALSPAC). Br J Nutr. 2017 Jul 12:1-11
Sowah D, Fan X, Dennett L, et al. **Vitamin D levels and deficiency with different occupations**: a systematic review. BMC Public Health. 2017 Jun 22;17(1):519.
Tripkovic L, et al. Daily supplementation with **15 µg vitamin D(2) compared with vitamin D(3) to increase wintertime 25-hydroxyvitamin D status** in healthy South Asian and white European women: a 12-wk randomized, placebo-controlled food-fortification trial. Am J Clin Nutr. 2017 Jul 5.
Collins M, Young M. Benign **Neonatal Shudders, Shivers, Jitteriness, or Tremors** : Early **Signs of Vitamin D Deficiency**. Peds. 2017 ;140(2) :e20160719
Anderson-Berry A, Thoene M, Wagner J, et al. Randomized trial of two doses of **vitamin D3 in preterm infants** <32 weeks: Dose impact on achieving desired serum 25(OH)D3 in a NICU population. PLoSOne. 2017 Oct 10;12(10):e0185950.
Gruson D, Pouleur AC, Makris K, et al. Systematic **vitamin D** supplementation and monitoring: improving outcomes in **heart failure**? Eur J Heart Fail. 2017 May;19(5):686-687.
Joliffe DA, Greenberg L, Hooper RL, et al. **Vitamin D** supplementation to **prevent asthma exacerbations**: a systematic review and meta-analysis of individual participant data. Lancet Respir Med 2017; online Oct 3.
Dimitrakopoulou VI, Tsilidis KK, Haycock PC, et al. Circulating **vitamin D** concentration and risk of **seven cancers**: Mendelian randomisation study. BMJ 2017;359:j4761.
Kerley CP, Power C, Gallagher L, et al. Lack of effect of vitamin D(3) supplementation in **autism**: a 20-week, placebo-controlled RCT. Arch Dis Child. 2017 Nov;102(11):1030-1036.
Saha S, Goswami R, Ramakrishnan L, et al. Vitamin D and calcium supplementation, **skeletal muscle strength and serum testosterone** in young healthy adult males: Randomized Control Trial. Clin Endocrinol (Oxf). 2017 Nov 2.
Chu J, Gallos I, Tobias A, et al. **Vitamin D and assisted reproductive treatment** outcome: a systematic review and meta-analysis. Hum Reprod. 2017 Nov 15:1-16
Roth DE, Leung M, Mesfin E, et al. **Vitamin D supplementation during pregnancy**: state of the evidence from a systematic review of randomised trials. BMJ. 2017 Nov 29;359:j5237.
Wu DM, Wen X, Han XR, et al. Relationship Between Neonatal **Vitamin D at Birth and Risk of Autism Spectrum Disorders**: the NBSIB Study. J Bone Miner Res. 2017 Nov 27.
Cano A, Chedraui P, Goulis DG, et al.**Calcium** in the **prevention of postmenopausal osteoporosis**: **EMAS** clinical guide. Maturitas. 2018 Jan;107:7-12.
Goodwill AM, Szoeke C. A Systematic Review and Meta-Analysis of The Effect of Low **Vitamin D on Cognition**. J Am Geriatr Soc. 2017 Oct;65(10):2161-2168.
Raed A, Bhagatwala J, Zhu H, et al. Dose responses of **vitamin D3 supplementation on arterial stiffness** in overweight African Americans with vitamin D deficiency: A placebo controlled randomized trial. PLoS One. 2017 Dec 7;12(12):e0188424.
Zhao JG, Zeng XT, Wang J, et al. Association Between **Calcium or Vitamin D Supplementation and Fracture Incidence** in **Community-Dwelling Older Adults**: A Systematic Review and Meta-analysis. JAMA. 2017 Dec 26;318(24):2466-2482.
Nowak A, Boesch L, Andres E, et al. Effect of **vitamin D3 on self-perceived fatigue**: A double-blind randomized placebo-controlled trial. Medicine (Baltimore). 2016 Dec;95(52):e5353.
Degerud E, Nygård O, de Vogel S, et al. Plasma 25-hydroxyvitamin D and mortality in patients with suspected **stable angina pectoris**. J Clin Endocrinol Metab. 2018 Jan 9.
Mulrennan S, Knuiman M, Walsh JP, et al. Vitamin D and **respiratory health** in the Busselton Healthy Ageing Study. Respirology. 2018 Jan 24.
Williams CE, Williams EA, Corfe BM. Vitamin D status in **irritable bowel syndrome** and the impact of supplementation on symptoms: what do we know and what do we need to know? Eur J Clin Nutr. 2018 Jan 25.
Budhathoki S, et al; Japan Public Health Center-based Prospective Study Group. **Plasma 25-hydroxyvitamin D concentration** and subsequent **risk of total and site specific cancers** in Japanese population: large case-cohort study within Japan Public Health Center-based Prospective Study cohort. BMJ. 2018 Mar 7;360:k671.
Daraki V, Roumeliotaki T, Chalkiadaki G, et al. Low maternal **vitamin D** status in pregnancy increases the risk of **childhood obesity**. Pediatr Obes. 2018 Jan 28.
LeFevre ML, LeFevre NM. **Vitamin D screening and supplementation in community-dwelling adults**: common questions and answers. Am Fam Physician. 2018; 97(4): 254-260.
Taylor PN, Davies JS. A review of the growing risk of **vitamin D toxicity from inappropriate practice**. Br J Clin Pharmacol. 2018 Mar 2.
Zhang Y, Gong Y, Xue H, et al. **Vitamin D and gestational diabetes mellitus**: a systematic review based on data free of Hawthorne effect. BJOG. 2017 Dec 15.
Crockett SD, Barry EL, Mott LA, et al. **Calcium and vitamin D supplementation and increased risk of serrated polyps**: results from a randomised clinical trial. Gut. 2018 Mar 1.
Jin J. Vitamin D and Calcium Supplements for Preventing Fractures. JAMA. 2018 Apr 17;319(15):1630.
Park SK, Garland CF, Gorham ED, et al. Plasma 25-hydroxyvitamin D concentration and risk of type 2 diabetes and pre-diabetes: 12-year cohort study. PLoS One. 2018 Apr 19;13(4):e0193070.
de Koning EJ, Elstgeest LEM, Comijs HC, et al. **Vitamin D Status and Depressive Symptoms in Older Adults**: A Role for Physical Functioning? Am J Geriatr Psychiatry. 2018 Mar 12.
Evans E, Piccio L, Cross AH. Use of **Vitamins and Dietary Supplements by Patients With Multiple Sclerosis**: A Review. JAMA Neurol. 2018 Apr 23.
Parr CL, Magnus MC, Karlstad Ø, et al. **Vitamin A and D intake in pregnancy, infant supplementation, and asthma development**: the Norwegian Mother and Child Cohort. Am J Clin Nutr. 2018 May 1;107(5):789-798.
Pilz S, Obeid R, Schwetz V, et al. Title: **Hormonal Contraceptive** Use is Associated with Higher Total but Unaltered **Free 25-Hydroxyvitamin D Serum Concentrations**. J Clin Endocrinol Metab. 2018 Apr 16.
Saleem J, Zakar R, Zakar MZ, et al. **High-dose vitamin D3 in the treatment of severe acute malnutrition**: a multicenter double-blind randomized controlled trial. Am J Clin Nutr. 2018 May 1;107(5):725-733.
Bi WG, Nuyt AM, Weiler H, Leduc L, Santamaria C, Wei SQ. Association between **vitamin D supplementation during pregnancy and offspring growth, morbidity, and mortality**: a systematic review and meta-analysis [online May 29, 2018]. JAMA Pediatr. doi:10.1001/jamapediatrics.2018.0302
Dudenkov DV, Mara KC, Petterson TM, et al. Serum **25-Hydroxyvitamin D** Values and Risk of All- cause and **Cause-Specific Mortality**: A Population-Based Cohort Study. Mayo Clin Proc. 2018 May 2.
Hibbs AM, Ross K, Kerns LA, et al. Effect of **vitamin D supplementation on recurrent wheezing** in black infants who were born preterm: **the D-Wheeze** randomized clinical trial. JAMA. doi:10.1001/jama.2018.5729
Mumford SL, Garbose RA, Kim K, et al. Association of **preconception serum 25-hydroxyvitamin D concentrations with livebirth and pregnancy loss**: a prospective cohort study. Lancet Diabetes Endocrinol. 2018 May 30.
Rosendahl J, Valkama S, Holmlund-Siula E, et al. Effect of higher vs standard dosage of **vitamin D3 supplementation on bone strength and infection in healthy infants**: a randomized clinical trial [online May 29, 2018]. JAMA Pediatr. doi:10.1001/jamapediatrics.2018.0602
Magnus MC, Miliku K, Bauer A, et al. **Vitamin D** and risk of **pregnancy related hypertensive disorders**: mendelian randomisation study. BMJ. 2018 Jun 20;361:k2167.
McCullough ML, Zoltick ES, Weinstein SJ, et al. Circulating **Vitamin D and Colorectal Cancer** Risk: An International Pooling Project of 17 Cohorts. J Natl Cancer Inst. 2018 Jun 14.
Soininen S, Eloranta AM, Viitasalo A, et al. **Serum 25-hydroxyvitamin D**, Plasma Lipids, and Associated Gene Variants in Prepubertal Children. J Clin Endocrinol Metab. 2018 May 9.
Zadro JR, Shirley D, Ferreira M, Carvalho Silva AP, et al. Is **Vitamin D Supplementation** Effective for **Low Back Pain**? A Systematic Review and Meta-Analysis. Pain Physician. 2018 Mar;21(2):121-145.
Das RR, Singh M, Naik SS. Vitamin D as an adjunct to antibiotics for the treatment of acute childhood pneumonia. Cochrane Database of Systematic Reviews 2018, Issue 7. Art. No.: CD011597. We are uncertain as to whether vitamin D has an important effect on outcomes because the results were imprecise. No major adverse events were reported. We assessed the quality of the evidence as very low to low. Several trials are ongoing and may provide additional information.
Jennings A, Cashman KD, Gillings R, et al. A Mediterranean-like dietary pattern with vitamin D3 (10 µg/d) supplements reduced the rate of bone loss in older Europeans with osteoporosis at baseline: results of a 1-y randomized controlled trial. Am J Clin Nutr. 2018 Jul 11.
Scragg R, Khaw KT, Toop L, et al. **Monthly High-Dose Vitamin D Supplementation and Cancer Risk**: A Post Hoc Analysis of the Vitamin D Assessment Randomized Clinical Trial **(ViDA)**. JAMA Oncol. 2018 Jul 19:e182178.
Machado MRM, de Sousa Almeida-Filho B, De Luca Vespoli H, et al**. Low pretreatment serum concentration of vitamin D at breast cancer diagnosis in postmenopausal women**. Menopause. 2018 Sep 17.
Roth DE, Morris SK, Zlotkin S, et al. **Vitamin D Supplementation in Pregnancy and Lactation and Infant Growth.** N Engl J Med. 2018 Aug 9;379(6):535-546.
Bolland MJ, Grey A, Avenell A. Effects of **vitamin D supplementation on musculoskeletal health**: a systematic review, meta-analyses, and trial-sequential analyses. Lancet Diabetes Endocrinol 2018; online Oct 9.
Jagannath VA, Filippini G, Di Pietrantonj C, et al. **Vitamin D for the management of multiple sclerosis.** Cochrane Database Syst Rev. 2018 Sep 24;9:CD008422. To date, very low-quality evidence suggests no benefit of vitamin D for patient-important outcomes among people with MS. Vitamin D appears to have no effect on recurrence of relapse, worsening of disability measured by the Expanded Disability Status Scale (EDSS), and MRI lesions. Effects on health-related quality of life and fatigue are unclear. Vitamin D3 at the doses and treatment durations used in the included trials appears to be safe, although available data are limited. Seven ongoing studies will likely provide further evidence that can be included in a future update of this review.
Bi WG, Nuyt AM, Weiler H, Leduc L, Santamaria C, Wei SQ. Association between vitamin D supplementation during **pregnancy and offspring growth, morbidity, and mortality**: a systematic review and meta-analysis [online May 29, 2018]. JAMA Pediatr. doi:10.1001/jamapediatrics.2018.0302
Mason C, Tapsoba JD, Duggan C, et al. Effects of Vitamin D3 Supplementation on **Lean Mass, Muscle Strength, and Bone Mineral Density During Weight Loss**: A Double-Blind Randomized Controlled Trial. J Am Geriatr Soc. 2016 Apr;64(4):769-78.
Hu J, Jia J, Zhang Y, et al. Effects of vitamin D(3) supplementation on **cognition and blood lipids**: a 12-month randomised, double-blind, placebo-controlled trial. J Neurol Neurosurg Psychiatry. 2018 Oct 2.
Owusu JE, Islam S, Katumuluwa SS, et al. **Cognition** and Vitamin D in Older African-American Women- Physical performance and **Osteoporosis prevention** with vitamin D in older African Americans Trial and Dementia. J Am Geriatr Soc. 2018 Oct 25.
Manson JE, Cook NR, Lee I-M, et al. **Vitamin D supplements and prevention of cancer and cardiovascular disease**. (**VITAL**) N Engl J Med. DOI: 10.1056/NEJMoa1809944.
Marawan A, Kurbanova N, Qayyum R. Association between serum **vitamin D levels and cardiorespiratory fitness** in the adult population of the USA. Eur J Prev Cardiol. 2018 Oct 30:2047487318807279
Dai Q, Zhu X, Manson JE, Song Y, et al**. Magnesium status and supplementation influence vitamin D** status and metabolism: results from a randomized trial. Am J Clin Nutr. 2018 Dec 1;108(6):1249-1258.
Zhang Y, Darssan D, Pascoe EM, et al. **Vitamin D** status and mortality risk among **patients on dialysis**: a systematic review and meta-analysis of observational studies. Nephrol Dial Transplant. 2018 Oct 1;33(10):1742-1751.

Hofmeyr GJ, Betrán AP, Singata-Madliki M, et al. Prepregnancy and early pregnancy **calcium supplementation among women at high risk of pre-eclampsia**: a multicentre, double-blind, randomised, placebo-controlled trial. Lancet. 2019 Jan 26;393(10169):330-339.
Jolliffe DA, Ganmaa D, Wejse C, et al. Adjunctive vitamin **D in tuberculosis treatment**: meta-analysis of individual participant data. Eur Respir J. 2019 Feb 6.
Jolliffe DA, Greenberg L, Hooper RL, et al. Vitamin D **to prevent exacerbations of COPD**: systematic review and meta-analysis of individual participant data from randomised controlled trials. Thorax. 2019 Jan 10.
Sengler C, Zink J, Klotsche J, et al. Vitamin D deficiency is **associated with higher disease activity and the risk for uveitis** in juvenile idiopathic arthritis - data from a German inception cohort. Arthritis Res Ther. 2018 Dec 13;20(1):276.
Valladares T, Cardoso MR, Aldrighi JM. Higher serum levels of vitamin D are **associated with lower blood glucose levels**. Menopause. 2019 Jan 18.
Martineau AR, Jolliffe DA, Greenberg L, et al. Vitamin D supplementation to **prevent acute respiratory infections**: individual participant data meta-analysis. Health Technol Assess. 2019 Jan;23(2):1-44.
Moon RJ, Curtis EM, Cooper C, et al. Vitamin D supplementation: **are multivitamins sufficient**? Arch Dis Child. 2019 Feb 25.
Anjum I, Jaffery SS, Fayyaz M, Samoo Z, Anjum S. The Role of Vitamin D in **Brain Health**: A Mini Literature Review. Cureus. 2018 Jul 10;10(7):e2960.
Bose S, Diette GB, Woo H, et al. Vitamin D status **modifies the response to indoor particulate** matter in obese urban children with asthma. J Allergy Clin Immunol Pract. 2019 Feb 11.
Bowman K, Jones L, Pilling LC, et al. Vitamin D levels and **risk of delirium**: A mendelian randomization study in the UK Biobank. Neurology. 2019 Mar 19;92(12):e1387-e1394.
Brustad N, Eliasen AU, Stokholm J, et al. High-Dose Vitamin D **Supplementation During Pregnancy and Asthma in Offspring** at the Age of 6 Years. JAMA. 2019 Mar 12;321(10):1003-1005.
Cook R, Thomas V, Martin R; NIHR Dissemination Centre. Can treating vitamin D deficiency **reduce exacerbations of chronic obstructive pulmonary disease**? BMJ. 2019 Mar 18;364:l1025.
Henderson CM, Fink SL, Bassyouni H, et al. **Vitamin D-Binding Protein Deficiency** and Homozygous Deletion of the GC Gene. N Engl J Med. 2019 Mar 21;380(12):1150-1157.
Larsson SC, Flicker L. Vitamin D: A novel **protective factor for delirium**? Neurology. 2019 Mar 19;92(12):553-554.
Cook R, Thomas V, Martin R; NIHR Dissemination Centre. Can treating **vitamin D deficiency reduce exacerbations of chronic obstructive pulmonary disease**? BMJ. 2019 Mar 18;364:l1025.
Ng K, Nimeiri HS, McCleary NJ, et al. Effect of High-Dose vs Standard-Dose **Vitamin D3 Supplementation** on Progression-Free Survival Among Patients With Advanced or Metastatic **Colorectal Cancer**: The SUNSHINE Randomized Clinical Trial. JAMA. 2019 Apr 9;321(14):1370-1379.
Urashima M, Ohdaira H, Akutsu T, et al. Effect of **Vitamin D Supplementation** on Relapse-Free Survival Among Patients With **Digestive Tract Cancers**: The **AMATERASU** Randomized Clinical Trial. JAMA. 2019 Apr 9;321(14):1361-1369.
Barbarawi M, Kheiri B, Zayed Y, et al. Vitamin D supplementation and **cardiovascular disease risks** in more than 83 000 individuals: meta-analysis of 21 randomized clinical trials [online June 19, 2019]. JAMA Cardiol. doi:10.1001/jamacardio.2019.1870
Huang H, Guo J, Chen Q, et al. The Synergistic effects of **vitamin D and estradiol deficiency** on metabolic syndrome in Chinese postmenopausal women. Menopause. 2019 Jun 10.
Pittas AG, Dawson-Hughes B, Sheehan P, et al. Vitamin D supplementation and **prevention of type 2 diabetes**. (D2d trial) N Engl J Med. DOI: 10.1056/NEJMoa1900906.
Alkhatatbeh M, Abdul-Razzak KK. **Neuropathic pain** is not associated with serum vitamin D but **is associated with female gender in patients with type 2 diabetes mellitus**. BMJ Open Diabetes Res Care. 2019 Jun 12;7(1):e000690.
Trevisan C, Piovesan F, Lucato P, et al. Parathormone, vitamin D and the **risk of atrial fibrillation** in older adults: A prospective study. Nutr Metab Cardiovasc Dis. 2019 May 29.
Wang G, Liu X, Bartell TR, et al. Vitamin D **Trajectories From Birth to Early Childhood and Elevated Systolic Blood Pressure** During Childhood and Adolescence. Hypertension. 2019 Jul 1:HYPERTENSIONAHA11913120.
Aguiar M, Andronis L, Pallan M, et al. The economic case for prevention of population vitamin D deficiency: a modelling study using data from England and Wales. Eur J Clin Nutr. 2019 Aug 20.
Bristow SM, Horne AM, Gamble GD, et al. Dietary Calcium Intake and Bone Loss Over 6 Years in Osteopenic Postmenopausal Women. J Clin Endocrinol Metab. 2019 Aug 1;104(8):3576-3584.
Burt LA, Billington EO, Rose MS, et al. Effect of High-Dose Vitamin D Supplementation on Volumetric Bone Density and Bone Strength: A Randomized Clinical Trial. JAMA. 2019 Aug 27;322(8):736-745.
Harrison SR, Li D, Jeffery LE, et al. Vitamin D, Autoimmune Disease and Rheumatoid Arthritis. Calcif Tissue Int. 2019 Jul 8.
Nørrisgaard PE, Haubek D, Kühnisch J, et al. Association of High-Dose Vitamin D Supplementation During Pregnancy With the Risk of Enamel Defects in Offspring: A 6-Year Follow-up of a Randomized Clinical Trial. JAMA Pediatr. 2019 Aug 5.
Zhang Y, Fang F, Tang J, et al. Association between vitamin D supplementation and mortality: systematic review and meta-analysis. BMJ. 2019 Aug 12;366:l4673.

112. *Stainer R, Matthews S, Arshad SH, et al. Efficacy and acceptability of a new topical skin lotion of sodium cromoglicate (Altoderm) in **atopic dermatitis** in children aged 2 to 12 years: A double-blind, randomized, placebo-controlled trial. Br J Dermatol 2005; 152:334-41. (InfoPOEMs:* Topical cromolyn lotion provides a statistically significant, but not clinically significant, benefit for children with atopic eczema. (LOE = 1b) *)*

113. *White KC. Anemia is a poor predictor of **iron** deficiency among toddlers in the United States: For heme the bell tolls. Pediatrics 2005; 115:315-20.* (InfoPOEMs: These study results present a quandary: We cannot feel assured that a young child doesn't have anemia if they show a normal hemoglobin level, and we can't be sure that he or she has anemia if the hemoglobin level is low. Screening for iron deficiency in toddlers by checking serum hemoglobin misses most children with a deficiency, and most of the children with anemia do not have an iron deficiency. As the author of this study suggests, it might make more sense to continue low-dose supplementation of iron in all children rather than use a policy of screen and treat. (LOE = 1c)) (Rimon E, et al. Are we giving too much iron? Low-dose iron therapy is effective in octogenarians. Am J Med. 2005 Oct;118(10):1142-7. CONCLUSIONS: Low-dose iron treatment is effective in elderly patients with iron-deficiency anemia. It can replace the commonly used higher doses and can significantly reduce adverse effects.) Iron deficiency anemia USPSTF 2006 http://www.ahrq.gov/clinic/uspstf06/ironsc/ironrs.htm (Drueke TB, et al. Normalization of Hemoglobin Level in Patients with Chronic Kidney Disease and Anemia. N Engl J Med. 2006 Nov 16;355(20):2071-2084. In patients with chronic kidney disease, early complete correction of anemia does not reduce the risk of cardiovascular events. & Singh AK, et al. Correction of Anemia with Epoetin Alfa in Chronic Kidney Disease. N Engl J Med. 2006 Nov 16;355(20):2085-2098. The use of a target hemoglobin level of 13.5 g per deciliter (as compared with 11.3 g per deciliter) was associated with increased risk and no incremental improvement in the quality of life. If epoetin alfa (Epogen) is used in patients with chronic kidney disease, the target hemoglobin should be 11.3 g/dL rather than 13.5 g/dL. A higher hemoglobin target was more likely to lead to death or adverse cardiac events (number needed to treat to harm [NNTH] = 25 for 16 months). (InfoPoems LOE =1b)) (Ceriani Cernadas JM, et al. The effect of timing of cord clamping on neonatal venous hematocrit values and clinical outcome at term: a randomized, controlled trial. Pediatrics. 2006 Apr;117(4):e779-86. Epub 2006 Mar 27. & van Rheenen PF, Brabin BJ. A practical approach to timing cord clamping in resource poor settings. BMJ. 2006 Nov 4;333(7575):954-8. & Lozoff B, Jimenez E, Smith JB. Double burden of iron deficiency in infancy & low socioeconomic status: longitudinal analysis of cognitive test scores to age 19yrs. Arch Pediatr Adolesc Med. 2006 Nov;160(11):1108-13.)
Mursu J, Robien K, Harnack LJ, Park K, Jacobs DR Jr. Dietary supplements and mortality in older women: the Iowa Women's Health Study. Arch Intern Med. 2011;171(18):1625-1633.
Baker, Robert D., Greer, Frank R., THE COMMITTEE ON NUTRITION, Clinical Report--Diagnosis and Prevention of **Iron Deficiency and Iron-Deficiency Anemia** in Infants and Young Children (0-3 Years of Age). (AAP) Pediatrics 2010 0: peds.2010-2576.
Lozoff B et al. Iron-fortified vs low-**iron infant formula: Developmental outcome at 10 years**. Arch Pediatr Adolesc Med2011 Nov 7; [e-pub ahead of print],
Pena-Rosas JP, De-Regil LM, et al. **Intermittent oral iron supplementation during pregnancy.** Cochrane Database Syst Rev. 2012 Jul 11;7:CD009997. The present systematic review is the most comprehensive summary of the evidence assessing the benefits and harms of intermittent iron supplementation regimens in pregnant women on haematological and pregnancy outcomes. The findings suggest that intermittent iron+folic acid regimens produce similar maternal and infant outcomes at birth as daily supplementation but are associated with fewer side effects. Women receiving daily supplements had increased risk of developing high levels of Hb in mid and late pregnancy but were less likely to present mild anaemia near term.
Peña-Rosas JP, De-Regil LM, Dowswell T,Viteri FE. **Daily oral iron supplementation during pregnancy**. Cochrane Database of Systematic Reviews 2012, Issue 12. Art. No.: CD004736.DOI: 10.1002/14651858.CD004736.pub4. Prenatal supplementation with daily iron are effective to reduce the risk of low birthweight, and to prevent maternal anaemia and iron deficiency in pregnancy. Associated maternal side effects and particularly high Hb concentrations during pregnancy at currently used doses suggest the need to update recommendations on doses and regimens for routine iron supplementation.
Maguire JL, Salehi L, Birken CS, et al. Association Between Total Duration of Breastfeeding and Iron Deficiency. Pediatrics. 2013 Apr 15.

114. *Spandorfer PR, Alessandrini EA, Joffe MD, Localio R, Shaw KN. Oral versus intravenous **rehydration** of moderately dehydrated children: A randomized, controlled trial. Pediatrics 2005; 115:295-301. (InfoPOEMs:* In the emergency setting, oral rehydration therapy is as effective as intravenous rehydration in children with moderate dehydration. Administered every 5 minutes by parents, oral rehydration resulted in fewer hospitalizations. Most children (92%) who were placed in the oral rehydration group were able to drink the prescribed amount. (LOE = 1b)) (Hartling L, Bellemare et al. Oral versus intravenous rehydration for treating dehydration due to gastroenteritis in children. Cochrane Database Syst Rev. 2006 Jul 19;3:CD004390.) (Pharmacist's Letter April 2007. Oral rehydration therapy.)
Freedman SB, Cho D, Boutis K, et al. Assessing the **palatability** of oral rehydration solutions in school-aged children: a randomized crossover trial. Arch Pediatr Adolesc Med. 2010 Aug;164(8):696-702. Sucralose-sweetened oral rehydration solutions (**Pedialyte and Pediatric Electrolyte**) were significantly more palatable than was a comparable rice-based solution (Enfalyte).
Rouhani, Shada, Meloney, Laura, Ahn, Roy, et al. **Alternative Rehydration Methods: A Systematic Literature Review and Lessons for Resource-Limited Care.** Pediatrics 2011 0: peds.2010-0952.
Freedman SB, Willan AR, Boutis K, et al. Effect of **Dilute Apple Juice** and Preferred Fluids vs Electrolyte Maintenance Solution on Treatment Failure Among Children With Mild Gastroenteritis: A Randomized Clinical Trial. JAMA. 2016 Apr 30.
Gregorio GV, Gonzales MLM, Dans LF, Martinez EG. **Polymer-based oral rehydration solution for treating acute watery diarrhoea**. Cochrane Database of Systematic Reviews 2016, Issue 12. Art. No.: CD006519. Polymer-based ORS shows advantages compared to glucose-based ORS (at ≥ 310 mOsm/L). Comparisons favoured polymer-based ORS over ORS ≤ 270 but analysis was underpowered.

115. *Sato Y, Honda Y, Iwamoto J, Kanoko T, Satoh K. Effect of **folate** and **mecobalamin** on hip fractures in patients with stroke. A randomized controlled trial. JAMA 2005; 293:1082-88.* (InfoPOEMs: Combined supplementation with oral high dose folate and mecobalamin reduces the risk of hip fractures in elderly patients with stroke and elevated homocysteine levels. The baseline fracture rate in this population is higher than generally reported and all study subjects had low baseline serum levels of folate and vitamin B12. Since the adverse risk of treatment is minimal, it makes sense to consider supplementation at this time in similar patients. (LOE = 1b)) (Devalia V. Diagnosing vitamin B-12 deficiency on the basis of serum B-12 assay. BMJ. 2006 Aug 19;333(7564):385-6.) (Headstrom PD, Rulyak SJ, Lee SD. Prevalence of and risk factors for vitamin B(12) deficiency in patients with Crohn's disease. Inflamm Bowel Dis. 2007 Sep 20; [Epub ahead of print] Vitamin B(12) abnormalities are common in patients with CD and patients with a prior ileal or ileocolonic resection are at particular risk.)
Eussen SJ, de Groot LC, Clarke R, Schneede J, Ueland PM, Hoefnagels WH, et al. Oral cyanocobalamin supplementation in older people with vitamin B12 deficiency: a dose-finding trial. Arch Intern Med 2005;165(10):1167-72.
Butler CC, Vidal-Alaball J, Cannings-John R, McCaddon A, Hood K, Papaioannou A, et al. Oral vitamin B12 versus intramuscular vitamin B12 for vitamin B12 deficiency: a systematic review of randomized controlled trials. Fam Pract 2006;23(3):279-85.
Volkov I, Rudoy I, Freud T, Sardal G, Naimer S, Peleg R, Press Y. Effectiveness of vitamin B12 in treating recurrent aphthous stomatitis: a randomized, double-blind, placebo-controlled trial. J Am Board Fam Med. 2009 Jan-Feb;22(1):9-16. Compared with placebo, sublingual vitamin B12 significantly reduced the average duration of recurrent aphthous stomatitis, the number of aphthous ulcers, and the subjective level of pain. Treatment was only effective after 5 months, so shorter treatment courses may not be effective. (LOE = 1b-)
Langan RC, Zawistoski KJ. Update on **Vitamin B12 Deficiency**. Am Fam Physician. 2011 Jun 15;83(12):1425-1430.
McMahon JA, Green TJ, Skeaff CM, Knight RG, Mann JI, Williams SM. A controlled trial of homocysteine lowering and cognitive performance. N Engl J Med. 2006;354(26):2764-2772.
Roumeliotis N, Dix D, Lipson A. Vitamin B12 deficiency in infants secondary to maternal causes. CMAJ. 2012 Jun 18.

Hunt A, Harrington D, Robinson S. Vitamin B12 deficiency. BMJ. 2014 Sep 4;349:g5226.
Lewerin C, Nilsson-Ehle H, Jacobsson S, et al. Low **holotranscobalamin and cobalamins** predict incident **fractures** in elderly men: the MrOS Sweden. Osteoporos Int. 2014 Jan;25(1):131-40
Pfisterer KJ, Sharratt MT, Heckman GG, et al. **Vitamin B(12) status** in older adults living in Ontario long-term care homes: prevalence and incidence of deficiency with supplementation as a protective factor. Appl Physiol Nutr Metab. 2016 Jan 19:1-4.
McMahon B, Kamath S. Pancytopenia in a Patient With Hypothyroidism. (**Vitamin B12: pernicious anemia**) JAMA. 2016 Apr 19;315(15):1648-9.
Ray JG, Wyatt PR, Thompson MD, et al. **Vitamin B12 and the risk of neural tube defects** in a folic-acid-fortified population. Epidemiology. 2007 May;18(3):362-6.
DeFilippis EM, Petersen A, Yialamas MA. Progressive Weakness and Memory Impairment in a Middle-aged Man. JAMA. 2018 Jul 10;320(2):197-198. (Vitamin B12 defficiency)

116. Williams HC. Clinical practice. **Atopic dermatitis**. N Engl J Med. 2005 Jun 2;352(22):2314-24.
(dos Santos RV, Magerl M, Mlynek A, Lima HC. Suppression of histamine- and allergen-induced skin reactions: comparison of first- and second-generation antihistamines. Ann Allergy Asthma Immunol. 2009 Jun;102(6):495-9. These results indicate that hydroxyzine is more effective than nsAHs when given as recommended in suppressing histamine-induced or allergic skin reactions. Our results suggest that higher doses of nsAHs than those currently recommended are required for the treatment of skin responses to obtain antihistaminic and antiallergic effects that are equivalent to those of fgAHs.)
Barniol C, Dehours E, Mallet J, et al. **Levocetirizine** and Prednisone Are Not Superior to Levocetirizine Alone for the Treatment of **Acute Urticaria**: A Randomized Double-Blind Clinical Trial. Ann Emerg Med. 2017 May 2.
Wong ITY, Tsuyuki RT, Cresswell-Melville A, et al. Guidelines for the management of atopic dermatitis (eczema) for pharmacists. Can Pharm J (Ott). 2017 May 30;150(5):285-297.
Chopra R, Vakharia PP, Sacotte R, et al. Efficacy of bleach baths in reducing severity of atopic dermatitis: A systematic review and meta-analysis. Ann Allergy Asthma Immunol. 2017 Nov;119(5):435-440.
Nowak D, Yeung J. Diagnosis and treatment of pruritus. Can Fam Physician. 2017 Dec;63(12):918-924.
Santer M, Ridd MJ, Francis NA, et al. **Emollient bath additives** for the treatment of childhood eczema (**BATHE**): multicentre pragmatic parallel group randomised controlled trial of clinical and cost effectiveness. BMJ. 2018 May 3;361:k1332.

117. FDA Warns Against Abuse of **Dextromethorphan** May/05 http://origin.www.fda.gov/bbs/topics/ANSWERS/2005/ANS01360.html (Detromethorphan abuse, Pharmacist's Letter Feb 2007.)
Misuse of Over-the-Counter Cough and Cold Medications among Persons Aged 12 to 25, Jan, 2008 http://oas.samhsa.gov/2k8/cough/cough.htm
Antoniou T, Juurlink DN. **Dextromethorphan abuse**. CMAJ. 2014 Nov 4;186(16):E631.
Eggleston W, Clark KH, Marraffa JM. **Loperamide Abuse** Associated With Cardiac Dysrhythmia and Death. Ann Emerg Med. 2016 Apr 26.
Antoniou T, Juurlink DN. Loperamide abuse. CMAJ. 2017 Jun 12;189(23):E803.
Stefek B, Wolfe LT, Cohen M. Brugada Syndrome Associated With Adolescent **Loperamide Abuse**. Pediatrics. 2018 Sep 25. pii: e20181423.

118. Eussen SJ, de Groot LC, Clarke R, Schneede J, Ueland PM, Hoefnagels WH, van Staveren WA. Oral **cyanocobalamin** supplementation in older people with vitamin B12 deficiency: a dose-finding trial. Arch Intern Med. 2005 May 23;165(10):1167-72.
119. Leung DY, Nicklas RA, Li JT, Bernstein IL, et al. Disease management of **atopic dermatitis**: an updated practice parameter. Joint Task Force on Practice Parameters. Ann Allergy Asthma Immunol. 2004 Sep;93(3 Suppl 2):S1-21.
120. *Kamm MA, Muller-Lissner S, Talley NJ, et al. Tegaserod for the treatment of chronic constipation: a randomized, double-blind, placebo-controlled multinational study. Am J Gastroenterol 2005;100:362-72.* (InfoPOEMs: Tegaserod is a safe and effective treatment for chronic
constipation. Although some benefit was seen at a dose of 2 mg twice daily, a better treatment effect was seen at 6 mg twice daily, and the higher dose was similarly tolerated. However, tegaserod is much more expensive than alternatives like colchicine. Since pts receiving 6 mg tegaserod had a mean of 0.6 additional complete spontaneous bowel movements per week than those taking placebo, the cost for each one was more than $60. (LOE = 1b))
121. Drugs for **acne**, rosacea and psoriasis. Treat Guidel Med Lett. 2005 Jul;3(35):49-56.
122. I-Min Lee, MBBS, ScD; Nancy R. Cook, ScD; et al. **Vitamin E** in the Primary Prevention of Cardiovascular Disease and Cancer: The **Women's Health Study**: A Randomized Controlled Trial. JAMA. 2005;294:56-65.
Conclusions The data from this large trial indicated that **600 IU of natural-source vitamin E** taken every other day provided no overall benefit for major cardiovascular events or cancer, did not affect total mortality, and decreased cardiovascular mortality in healthy women. These data do **not support** recommending vitamin E supplementation for cardiovascular disease or cancer prevention among healthy women. (InfoPOEMs: Vitamin E does not reduce the risk of cardiovascular disease, cancer, or total mortality among healthy women 45 years or older. (LOE = 1b))
Zhang SM, Cook NR, Albert CM, Gaziano JM, Buring JE, Manson JE. Effect of combined folic acid, vitamin B6, and vitamin B12 on cancer risk in women: a randomized trial. (WAFACS) JAMA. 2008 Nov 5;300(17):2012-21. Combined folic acid, vitamin B(6), and vitamin B(12) treatment had no significant effect on overall risk of total invasive cancer or breast cancer among women during the folic acid fortification era.
123. *Ramkumar D, Rao SS. Efficacy and safety of traditional medical remedies for chronic* **constipation***: a systematic review. Am J Gastroenterol 2005; 100:936-71.* (InfoPOEMs: The best evidence supports polyethylene glycol, tegaserod, psyllium, and lactulose for adults with chronic constipation. Tegaserod is much more expensive than the other 3 drugs and its long-term safety data are not available. Evidence is lacking for many commonly used preparations, but the absence of evidence is not evidence of ineffectiveness. (LOE = 1a-)) (Rubin G, Dale A. Chronic constipation in children. BMJ. 2006 Nov 18;333(7577):1051-5. & Muller-Lissner S, et al. Safety, Tolerability, and Efficacy of Tegaserod over 13 Months in Patients with Chronic Constipation. Am J Gastroenterol. 2006 Nov;101(11):2558-69. Tegaserod has a favorable safety profile and is well tolerated during continuous long-term treatment in patients with CC. & Altomare DF, et al. Red hot chili pepper and hemorrhoids: the explosion of a myth: results of a prospective, randomized, placebo-controlled, crossover trial. Dis Colon Rectum. 2006 Jul;49(7):1018-23. (InfoPOEMs: This study found no evidence to support the popular contention that spicy foods, including red hot chili peppers, exacerbates hemorrhoid symptoms. Clinicians need not warn patients with hemorrhoids to avoid spicy foods. (LOE = 1b)) & Loening-Baucke V, Pashankar DS. A randomized, prospective, comparison study of polyethylene glycol 3350 without electrolytes and milk of magnesia for children with constipation and fecal incontinence. Pediatrics. 2006 Aug;118(2):528-35.)
124. Hill N, Moor G, Cameron MM, Butlin A, et al. Single blind, randomised, comparative study of the **Bug Buster** kit and over the counter pediculicide treatments against head **lice** in the United Kingdom. BMJ. 2005 Aug 13;331(7513):384-7. Epub 2005 Aug 5. (InfoPOEMs: Approximately half of children using a special lice comb (Bug Buster) every 3 days for 9 days will be lice-free at a 2-week follow-up. This rate was higher than that of either of 2 commonly used pediculocides, although they were only used once instead of the frequently recommended twice. Combing is not technically difficult as long as conditioner has been used on the hair, though the squirm factor in the child and the squeamish factor in the parent who combs out live lice makes it less desirable. (LOE = 1b-)) (Thomas DR, et al. Surveillance of insecticide resistance in head lice using biochemical and molecular methods. Arch Dis Child. 2006 Jun 14; [Epub ahead of print]) (Resultz: New OTC Head Lice Treatment. Pharmacist's Letter Sept 2006)
Canadian Paediatric Society. Head lice infestations: a clinical update. http://cps.ca/English/statements/ID/id08-06.pdf
Jahnke C, et al. Accuracy of Diagnosis of Pediculosis Capitis: Visual Inspection vs Wet Combing. Arch Dermatol. 2009 Mar;145(3):309-13. **Wet combing** is a very accurate method to diagnose active head lice infestation. Visual inspection is the method of choice, if one aims to determine the frequency of carriers of eggs or nits.
Stough D, Shellabarger S, Quiring J, et al. Efficacy and Safety of **Spinosad** and Permethrin Creme Rinses for Pediculosis Capitis (Head Lice). Pediatrics. 2009 Aug 24.
Chosidow, Olivier, Giraudeau, Bruno, Cottrell, Jeremy, et al. **Oral Ivermectin** versus Malathion Lotion for Difficult-to-Treat Head Lice. N Engl J Med 2010 362: 896-905.
Cole SW, Lundquist LM. Spinosad for treatment of head lice infestation. Ann Pharmacother. 2011 Jul;45(7-8):954-9.
Smith CH, Goldman RD. An incurable itch: **Head lice**. Can Fam Physician. 2012 Aug;58(8):839-41.
Gunning, K, Pippitt K, Kiraly B, Sayler M. Pediculosis and Scabies: a treatment Update. Am Fam Phys 2012 86;6:535-41. Non RX Treatment: Wet combing cure rates can be inmproved from 50% to about 75% by increasing the duration to Q2-3 days x 24 days (vs 2 wks); Cetaphil Gentle Skin Cleanser has been used as a dry on suffication tx with eradication rate similar to first line agents but not well studied (Pearlman DL in Pediatrics 2004; 114(3):e275-279.
Pariser DM, Meinking TL, Bell M, Ryan WG. Topical 0.5% **ivermectin** lotion for treatment of head lice. N Engl J Med 2012; 367:1687-93.
Burgess IF, Brunton ER, Burgess NA. Single application of 4% dimeticone liquid gel versus two applications of 1% permethrin creme rinse for treatment of head louse infestation: a randomised controlled trial. BMC Dermatol. 2013 Apr 1;13:5.
Deeks LS, Naunton M, Currie MJ, et al. Topical **ivermectin** 0.5% lotion for treatment of head lice. Ann Pharmacother. 2013 Sep;47(9):1161-7.
Early, J., Macnaughton, H. Ivermectin Lotion (Sklice) for Head Lice. American Family Physician. 2014.
Devore CD, Schutze GE; Council on School Health and Committee on Infectious Diseases. **Head Lice**. Pediatrics. 2015 Apr 27.
Micali G, Lacarrubba F. Images in Clinical Medicine. Phthiriasis Palpebrarum (**crab lice**) in a Child. N Engl J Med. 2015 Dec 31;373(27):e35.
Koch E, Clark JM, Cohen Bet al. **Management of Head Louse** Infestations in the United States-A Literature Review. Pediatr Dermatol. 2016 Sep;33(5):466-72.
Cummings C, Finlay JC, MacDonald NE; **Canadian Paediatric Society**, Community Paediatrics Committee. Head lice infestations: a clinical update. Posted online September 22, 2016.www.cps.ca/en/documents/position/head-lice (accessed October 6, 2016).
Cummings C, Finlay JC, MacDonald NE. **Head lice infestations**: A clinical update. Paediatr Child Health. 2018 Feb;23(1):e18-e24.
Gunning K, Kiraly B, Pippitt K. **Lice and Scabies**: Treatment Update. Am Fam Physician. 2019;99(10):635-642.

125. Salerno SM, Jackson JL, Berbano EP. Effect of oral **pseudoephedrine** on blood pressure and heart rate: a meta-analysis. Arch Intern Med. 2005 Aug 8-22;165(15):1686-94. (InfoPOEMs: Overall, immediate-release pseudoephedrine produces a small increase in systolic blood pressure (1.5 mmHg) but has no effect on diastolic blood pressure. Sustained-release products do not affect blood pressure. Both types of products increase heart rate to a small degree. Unlike its cousin phenylpropanolamine, pseudoephedrine rarely causes large increases in blood pressure, although its effect on blood pressure is dose-related and a marked effect could occur with overdose. (LOE = 1a))
126. Avenell A, Campbell MK, Cook JA, et al. Effect of **multivitamin** and multimineral supplements on morbidity from infections in older people (MAVIS trial): pragmatic, randomised, double blind, placebo controlled trial. BMJ. 2005 Aug 6;331(7512):324-9.
127. Brooks WA, et al. Effect of weekly zinc supplements on incidence of pneumonia and diarrhoea in children younger than 2 years in an urban, low-income population in Bangladesh: randomised controlled trial. The Lancet Early Online Publication, 23 August 2005
Roy SK, Hossain MJ, Khatun W, et al. Zinc supplementation in children with cholera in Bangladesh: randomized controlled trial. BMJ. 2008 Jan 8; [Epub ahead of print]
Lassi ZS, Haider BA, Bhutta ZA. **Zinc** supplementation for the prevention of **pneumonia** in children aged 2 months to 59 months. Cochrane Database Syst Rev. 2010 Dec 8;12:CD005978.
Lassi ZS, Moin A, Bhutta ZA. Zinc supplementation for the prevention of pneumonia in children aged 2 months to 59 months. Cochrane Database Syst Rev. 2016 Dec 4;12:CD005978.
Patro Bernadeta, Szymanski Henryk, Szajewska Hania, Oral Zinc for the Treatment of Acute Gastroenteritis in Polish Children: A Randomized, Double-Blind, Placebo-Controlled Trial, The Journal of Pediatrics, Volume 157, Issue 6, December 2010

Basnet S, Shrestha PS, Sharma A, et al. A Randomized Controlled Trial of **Zinc** as Adjuvant Therapy for Severe Pneumonia in Young Children. Pediatrics. 2012 Mar 5.
Bhatnagar S, Wadhwa N, Aneja S, et al. **Zinc** as adjunct treatment in infants aged between 7 and 120 days with probable serious bacterial infection: a randomised, double-blind, placebo-controlled trial. Lancet 2012. online May 31.
Lazzerini M, Ronfani L. Oral zinc for treating **diarrhoea** in children. Cochrane Database Syst Rev. 2012 Jun 13;6:CD005436. In areas where the prevalence of zinc deficiency or the prevalence of moderate malnutrition is high, zinc may be of benefit in children aged six months or more.The current evidence does not support the use of zinc supplementation in children below six months of age.
Malik A, Taneja DK, Devasenapathy N, Rajeshwari K. Short-Course Prophylactic **Zinc** Supplementation for Diarrhea Morbidity in Infants of 6 to 11 Months. Pediatrics. 2013 Jun 3.
Mayo-Wilson E, Junior JA, Imdad A, Dean S, Chan XHS, Chan ES, Jaswal A, Bhutta ZA. **Zinc supplementation** for preventing mortality, morbidity, and growth failure in children aged 6 months to 12 years of age. Cochrane Database of Systematic Reviews 2014, Issue 5. Art. No.: CD009384. DOI: 10.1002/14651858.CD009384.pub2. In our opinion, the benefits of preventive zinc supplementation outweigh the harms in areas where the risk of zinc deficiency is relatively high. Further research should determine optimal intervention characteristics such as supplement dose.

129. **Vitamin** Supplements. The Medical Letter. July 18,2005. (see also Pharmacist's Letter July 2006 " Multivitamins/Minerals & Chronic Disease Prevention") (Huang HY, et al. The Efficacy and Safety of Multivitamin and Mineral Supplement Use To Prevent Cancer and Chronic Disease in Adults: A Systematic Review for a National Institutes of Health State-of-the-Science Conference. Ann Intern Med. 2006 Jul 31; [Epub ahead of print])
Leung AM, Pearce EN, Braverman LE. **Iodine** content of prenatal multivitamins in the United States. N Engl J Med. 2009 Feb 26;360(9):939-40.
Kawai K, Spiegelman D, Shankar AH, Fawzi WW. Maternal multiple micronutrient supplementation and pregnancy outcomes in developing countries: meta-analysis and meta-regression. Bull World Health Organ. 2011 Jun 1;89(6):402-411B.
Imhoff-Kunsch B, Stein AD, Martorell R, et al. Prenatal **Docosahexaenoic Acid Supplementation** and Infant Morbidity: Randomized Controlled Trial. Pediatrics. 2011 Aug 1.
Andreeva VA, et al. **B Vitamin and/or ω-3 Fatty Acid** Supplementation and Cancer: Ancillary Findings From the Supplementation With Folate, Vitamins B6 and B12, and/or Omega-3 Fatty Acids (**SU.FOL.OM3**) Randomized Trial. Arch Intern Med. 2012 Feb 13.
Jenkins DJA, Spence JD, Giovannucci EL, et al. Supplemental **Vitamins and Minerals for CVD Prevention** and Treatment. J Am Coll Cardiol. 2018 Jun 5;71(22):2570-2584.

130. Douglas RM, Hemila H, D'Souza R, Chalker EB, Treacy B. **Vitamin C** for preventing and treating the common cold. Cochrane Database Syst Rev. 2004 Oct 18;(4):CD000980.
Douglas RM, Hemilä H, Chalker E, Treacy B. Vitamin C for preventing and treating the common cold. Cochrane Database Syst Rev. 2007 Jul 18;(3):CD000980. (Possible benefit to reduce risk of colds if severe physical exercise or cold environment eg. marathon runners, Skiers)
Smith A, Di Primio G, Humphrey-Murto S. **Scurvy** in the developed world. CMAJ. 2011 Aug 9
Thomas LD, Elinder CG, Tiselius HG, et al. **Ascorbic Acid Supplements and Kidney Stone** Incidence Among Men: A Prospective Study. JAMA Intern Med. 2013 Feb 4:1-2.
Hemilä H, Chalker E. **Vitamin C for preventing and treating the common cold**. Cochrane Database Syst Rev. 2012 Nov 29;1:CD000980. DOI: 10.1002/14651858.CD000980.pub4. The failure of vitamin C supplementation to reduce the incidence of colds in the general population indicates that routine vitamin C supplementation is not justified, yet vitamin C may be useful for people exposed to brief periods of severe physical exercise. Regular supplementation trials have shown that vitamin C reduces the duration of colds, but this was not replicated in the few therapeutic trials that have been carried out. Nevertheless, given the consistent effect of vitamin C on the duration and severity of colds in the regular supplementation studies, and the low cost and safety, it may be worthwhile for common cold patients to test on an individual basis whether therapeutic vitamin C is beneficial for them.
McEvoy CT, Schilling D, Clay N, et al. **Vitamin C supplementation** for pregnant smoking women and pulmonary function in their newborn infants: a randomized clinical trial. JAMA. doi:10.1001/jama.2014.5217.
Hafez D, Saint S, Griauzde Jet al. Clinical Problem-Solving. A Deficient Diagnosis. (**Vitamin C: scurvy**) N Engl J Med. 2016 Apr 7
Mitchell LV, Wilson MR, Holmes S. A historic disease still prevalent today (**Vitamin C deficiency-scurvy**). BMJ. 2017 Mar 16;356:j1013.
Vaezipour N, Leibundgut K. Nonalimental Scurvy With Relapse Symptoms After Stopping Oral Vitamin C Supplementation. Pediatrics. 2018 Aug;142(2).
Nair, A., Chattopadhyay, I., Williams, R., et al. Lethargy, rash and bruising. BMJ 2018;363:k4676 (**Vitamin C deficiency - scurvy**)

131. Robertson J, Iemolo F, Stabler SP, Allen RH, Spence JD. **Vitamin B12**, homocysteine and carotid plaque in the era of folic acid fortification of enriched cereal grain products. CMAJ. 2005 Jun 7;172(12):1569-73.
132. Vidal-Alaball J, Butler C, Cannings-John R, et al. Oral vitamin B12 versus intramuscular vitamin B12 for vitamin B12 deficiency. Cochrane Database Syst Rev. 2005 Jul 20;(3):CD004655. CONCLUSIONS: The evidence derived from these limited studies suggests that 2000 mcg doses of oral vitamin B12 daily and 1000 mcg doses initially daily and thereafter weekly and then monthly may be as effective as intramuscular administration in obtaining short term haematological and neurological responses in vitamin B12 deficient patients.
133. Medical Letter, **Drugs for Head lice**. Vol 47 (Issue 1215/1216) Aug 15/29,2005. p.68-70.
134. Farvid MS, Jalali M, Siassi F, Hosseini M. Comparison of the Effects of **Vitamins and/or Mineral Supplementation** on Glomerular and Tubular Dysfunction in Type 2 Diabetes. Diabetes Care. 2005 Oct;28(10):2458-64.
135. Margolis DJ, Bowe WP, Hoffstad O, Berlin JA. Antibiotic treatment of **acne** may be associated with upper respiratory tract infections. Arch Dermatol. 2005 Sep;141(9):1132-6.
136. Bonakdar RA, Guarneri E. **Coenzyme Q10**. Am Fam Physician. 2005 Sep 15;72(6):1065-70.
137. *American College of Gastroenterology Chronic Constipation Task Force. An evidence-based approach to the management of chronic **constipation** in North America. Am J Gastroenterol 2005; 100:S1-S4.* (InfoPOEMs: Diagnostic testing is not needed for most patients with chronic constipation. The evidence is strongest for the efficacy of psyllium, polyethylene glycol, lactulose, and tegaserod. Research is not available to support the routine use of stimulant laxatives, lubricants, stool softeners, calcium polycarbophil, bran, or any herbal products. (LOE = 1a)) & Hsieh C. Treatment of constipation in older adults. Am Fam Physician. 2005 Dec 1;72(11):2277-84. Radaelli F, Meucci G, Imperiali G, Spinzi G, Strocchi E, Terruzzi V, Minoli G. High-Dose **Senna Compared with Conventional PEG-ES** Lavage as Bowel Preparation for Elective Colonoscopy: A Prospective, Randomized, Investigator-Blinded Trial. Am J Gastroenterol. 2005 Dec;100(12):2674-80. (Rendeli C, et al. **Polyethylene glycol 4000** vs. lactulose for the treatment of neurogenic constipation in myelomeningocele children: a randomized-controlled clinical trial.Aliment Pharmacol Ther. 2006 Apr 15;23(8):1259-65.) (Freedman SB, Adler M, Seshadri R, Powell EC. Oral **ondansetron** for gastroenteritis in a pediatric emergency department. N Engl J Med. 2006 Apr 20;354(16):1698-705.) (**Gastrointestinal Drug Use in Pregnancy**. Pharmacist's Letter Dec/06) Di Palma JA, Cleveland MV, McGowan J, et al. A randomized, multicenter comparison of polyethylene glycol laxative and tegaserod in treatment of patients with chronic constipation. Am J Gastro. 2007 Sep;102(9):1964-71. Epub 2007 Jun 15. (n=237 4 weeks) While PEG laxative and tegaserod are safe for their intended use in chronic constipation, **PEG had superior efficacy, caused fewer headaches**, and produced greater improvement of constipation symptoms.
Thomson MA, Jenkins HR, Bisset WM, Heuschkel R, Kalra DS, Green MR, Wilson DC, Geraint M. Polyethylene glycol 3350 (6.9 g sachet)plus electrolytes for chronic constipation in children: a double blind, placebo controlled, crossover study. Arch Dis Child. 2007 Nov;92(11):996-1000. Epub 2007 Jul 11. PEG+E is significantly more effective than placebo, and appears to be safe and well tolerated in the treatment of chronic constipation in children.
Candy D, Belsey J. Macrogol (polyethylene glycol) laxatives in children with functional constipation and faecal impaction: a systematic review. Arch Dis Child. 2009 Feb;94(2):156-60. Epub 2008 Nov 19. In this systematic review that only included published studies, polyethylene glycol (PEG) was effective in treating functional constipation in children. PEG was clearly better than placebo and slightly more effective than lactulose, but no better than milk of magnesia. (LOE = 1a-)
McCallum IJ, Ong S, Mercer-Jones M. **Chronic constipation** in adults. BMJ. 2009 Mar 20;338:b831. doi: 10.1136/bmj.b831.
Chung S, Cheng A, Goldman RD. **Polyethylene glycol 3350** without electrolytes for treatment of **childhood** constipation. Can Fam Physician. 2009 May;55(5):481-2.
Bekkali, Noor-L-Houda, van den Berg, Maartje-Maria, Dijkgraaf, Marcel G.W., et al. Rectal Fecal Impaction Treatment in Childhood Constipation: **Enemas Versus High Doses Oral PEG**. Pediatrics 2009 124: e1108-e1115.
Coleman J, Spurling G. Constipation in people with **learning disability**. BMJ. 2010 Jan 26;340:c222. doi: 10.1136/bmj.c222.
Matro R, Shnitser A, Spodik M, et al. Efficacy of **Morning-Only** Compared With Split-Dose **Polyethylene Glycol** Electrolyte Solution for Afternoon Colonoscopy: A Randomized Controlled Single-Blind Study. Am J Gastroenterol. 2010 Apr 20
Bardisa-Ezcurra Lauren, Ullman Roz, Gordon Jenny, on behalf of the Guideline Development Group. Diagnosis and management of idiopathic childhood constipation: summary of **NICE guidance**. BMJ 2010;340:c2585, doi: 10.1136/bmj.c2585.
Lee-Robichaud H, Thomas K, Morgan J, et al. **Lactulose versus Polyethylene Glycol** for Chronic Constipation. Cochrane Database Syst Rev. 2010 Jul 7;7:CD007570. Polyethylene Glycol should be used in preference to Lactulose in the treatment of Chronic Constipation.
Roerig JL, Steffen KJ, Mitchell JE, Zunker C. **Laxative abuse**: epidemiology, diagnosis and management. Drugs. 2010 Aug 20;70(12):1487-503. doi: 10.2165/11898640-000000000-00000.
Ford AC, Suares NC. Effect of laxatives and pharmacological therapies in **chronic idiopathic constipation**: systematic review and meta-analysis. Gut. 2011 Feb;60(2):209-18.
Attaluri A, Donahoe R, Valestin J, Brown K, Rao SS. Randomised clinical trial: **dried plums (prunes)** vs. psyllium for constipation. Aliment Pharmacol Ther. 2011 Apr;33(7):822-8. doi: 10.1111/j.1365-2036.2011.04594.x.
Varughese S, Kumar AR, George A, et al. Morning-only one-gallon **polyethylene glycol** improves bowel cleansing for afternoon colonoscopies: a randomized endoscopist-blinded prospective study. Am J Gastroenterol. 2010 Nov;105(11):2368-74.
Tabbers Merit M., Chmielewska Ania, Roseboom Maaike G., et al. Fermented Milk Containing **Bifidobacterium lactis DN-173 010** in Childhood Constipation: A Randomized, Double-Blind, Controlled Trial. Pediatrics 2011; 127:6 e1392-e1399; May 23, 2011.
Kamm MA, Mueller-Lissner S, Wald A, Richter E, Swallow R, Gessner U. Oral **bisacodyl** is effective and well-tolerated in patients with chronic constipation. Clin Gastroenterol Hepatol. 2011 Jul;9(7):577-83.
Tabbers Merit M., Boluyt Nicole, Berger Marjolein Y.,et al. **Nonpharmacologic Treatments for Childhood Constipation**: Systematic Review. Pediatrics 2011; peds.2011-0179; published ahead of print September 26, 2011, doi:10.1542/peds.2011-0179
Aune D et al. **Dietary fibre, whole grains, and risk of colorectal cancer**: Systematic review and dose-response meta-analysis of prospective studies. BMJ 2011 Nov 10; 343:d6617.
Rowan-Legg A; Canadian Paediatric Society, Community Paediatrics Committee. Managing functional constipation in children. Paediatr Child Health 2011;16(10):661-5. www.cps.ca/english/statements/CP/Constipation.htm (accessed December 14, 2011).
Gallegos-Orozco JF, Foxx-Orenstein AE, Sterler SM, et al. **Chronic constipation** in the elderly. Am J Gastroenterol. 2012 Jan;107(1):18-25.
Ori Y, Rozen-Zvi B, Chagnac A, et al. **Fatalities** and Severe Metabolic Disorders Associated With the Use of **Sodium Phosphate Enemas**: A Single Center's Experience. Arch Intern Med. 2012 Feb 13;172(3):263-5.
Agrawal A et al. Secondary prophylaxis of **hepatic encephalopathy** in cirrhosis: An open-label, randomized controlled trial of **lactulose**, **probiotics**, and no therapy. Am J Gastroenterol 2012 Jul; 107:1043.
Gordon M, Naidoo K, Akobeng AK, et al. Osmotic and stimulant laxatives for the management of childhood constipation. Cochrane Database Syst Rev. 2012 Jul 11;7:CD009118.
Ford AC, Talley NJ. Laxatives for chronic constipation in adults. BMJ. 2012 Oct 1;345:e6168.
Auth MK, Vora R, Farrelly P, Baillie C. **Childhood constipation**. BMJ. 2012 Nov 13;345:e7309.
Bharucha AE, Pemberton JH, Locke GR 3rd. **American gastroenterological association (AGA)** technical review on **constipation**. Gastroenterology. 2013 Jan;144(1):218-38.
American Gastroenterological Association (AGA) , Bharucha AE, Dorn SD, Lembo A, Pressman A. American gastroenterological association medical position statement on **constipation**. Gastroenterology. 2013 Jan;144(1):211-7.
Gandell D, Straus SE, Bundookwala M, et al. Treatment of **constipation in older people**. CMAJ. 2013 May 14;185(8):663-70.
Kew ST, Chakravarthi S. Images in clinical medicine: **Melanosis coli**. N Engl J Med. 2013 Jun 13;368(24):2303.

FDA Jan/14 is warning that the over-the-counter constipation drug sodium phosphate (marketed as Fleet, and generics) has been tied to heart and kidney damage and even death when patients exceed the recommended dose. The agency has identified over 50 serious adverse events related to dehydration and electrolyte disturbances (sodium, calcium, and phosphate) with both the oral and rectal formulations. Most cases occurred in older adults and children younger than 5 years.

138. Bonaa KH for the NORVIT Study Group. **NORVIT**: Randomised trial of homocysteine-lowering with B vitamins for secondary prevention of cardiovascular disease after acute myocardial infarction. European Society of Cardiology, Sept 3-7, 2005, Abstract 1334.
140. Vahedi H, Merat S, et al. The effect of **fluoxetine** in patients with pain and constipation-predominant **irritable bowel syndrome**: a double-blind randomized-controlled study. Aliment Pharmacol Ther. 2005 Sep 1;22(5):381-5.
141. Gilbert C, Mazzotta P, Loebstein R, Koren G. Fetal safety of drugs used in the treatment of allergic rhinitis: a critical review. Drug Saf. 2005;28(8):707-19.
142. Plaut M, Alleric Rhinitis. N Engl J Med 2005;353:193-44. (Medical Letter. Treatment Guidelines. Drugs for **Allergic Disorders**. Feb 2010, revised **May 2013.**)
Sussman G, Sussman D, Sussman A. Intermittent **allergic rhinitis**. CMAJ. 2010 Jun 15;182(9):935-7.
Sur DK, Plesa ML. Treatment of Allergic Rhinitis. Am Fam Physician. 2015 Dec 1;92(11):985-92.
So M, Bozzo P, Inoue M, Einarson A. Safety of **antihistamines during pregnancy** and lactation. Can Fam Physician. 2010 May;56(5):427-9.
Radulovic S, Calderon MA, Wilson D, Durham S. **Sublingual immunotherapy** for allergic rhinitis. *Cochrane Database of Systematic Reviews* 2010, Issue 12. Art. No.: CD002893. DOI: 10.1002/14651858.CD002893.pub2. This updated review reinforces the conclusion of the original 2003 Cochrane Review that sublingual immunotherapy is effective for allergic rhinitis and has been proven to be a safe route of administration.
Schaefer P. **Urticaria**: evaluation and treatment. Am Fam Physician. 2011 May 1;83(9):1078-84.
Griffin G, Flynn CA. **Antihistamines and/or decongestants for otitis media with effusion (OME)** in children. Cochrane Database Syst Rev. 2011 Sep 7;9:CD003423. The pooled data demonstrate no benefit and some harm from the use of antihistamines or decongestants alone or in combination in the management of OME, therefore we recommend against their use.
Schaefer P. **Acute and Chronic Urticaria**: Evaluation and Treatment. Am Fam Physician. 2017;95(11):717-724.
Barniol C, Dehours E, Mallet J, et al. **Levocetirizine** and Prednisone Are Not Superior to Levocetirizine Alone for the Treatment of **Acute Urticaria**: A Randomized Double-Blind Clinical Trial. Ann Emerg Med. 2017 May 2.
Medical Letter. Treatment Guidelines. OTC Drugs for **Seasonal Allergies**. Apr 2019.
Kulthanan K, Hunnangkul S, Tuchinda P, et al. Treatments of cold **urticaria**: A systematic review. J Allergy Clin Immunol. 2019 Apr;143(4):1311-1331.

143. Ullrich C, Wu A, et al. Screening healthy infants for iron deficiency using reticulocyte hemoglobin content. JAMA. 2005 Aug 24;294(8):924-30. (InfoPOEMs: A low reticulocyte hemoglobin content (RHC) has a higher sensitivity for the accurate detection of early iron deficiency in infants than a standard hemoglobin measurement. Randomized trials comparing infants undergoing screening with either technique or no screening at all are now necessary to assess the long-term value of screening. (LOE = 2b))
144. Thavendiranathan P, et al. Do blood tests cause anemia in hospitalized patients? The effect of diagnostic phlebotomy on hemoglobin and hematocrit levels. J Gen Intern Med. 2005 Jun;20(6):520-4. (InfoPOEMs: The typical patient admitted for a 6-day admission will have 75 mL of blood drawn and this will drop his or her hemoglobin by 0.79 g/dL (7.9 g/L) and hematocrit by 2.1 percentage points. As a result, 1 in 6 patients will become anemic as a result of blood draws. (LOE = 2b))
145. Kim HS, Park DH, Kim JW, Jee MG, Baik SK, Kwon SO, Lee DK. Effectiveness of **walking exercise** as a bowel preparation for colonoscopy: a randomized controlled trial. Am J Gastroenterol. 2005 Sep;100(9):1964-9.
146. Welch HG, Woloshin S, Schwartz LM. Skin biopsy rates & incidence of **melanoma**: population based ecological study. BMJ. 2005 Sep 3;331(7515):481. Epub 2005 Aug 4. (InfoPOEMs: This study provides preliminary evidence that the incidence of melanoma is increasing not because of factors such as skin burns and ozone layer holes, but simply because more dermatologists are biopsying more lesions. In a 5-year period the incidence of melanoma increased 2.4-fold, whereas the biopsy rate over this same period increased a similar 2.5 times. (LOE = 2c))
147. Benn CS, et al. Randomised study of effect of different doses of vitamin A on childhood morbidity and mortality. BMJ. 2005 Nov 23; [Epub ahead of print] CONCLUSIONS: Half the dose of vitamin A currently recommended by WHO may provide equally good or better protection against mortality but not against morbidity.
150. Ringe JD, Faber H, Fahramand P, Schacht E. **Alfacalcidol** versus plain vitamin D in the treatment of **glucocorticoid/inflammation-induced osteoporosis**. J Rheumatol Suppl. 2005 Sep;76:33-40.
151. Arroll B. Non-antibiotic treatments for upper-respiratory tract infections (common cold). Respir Med. 2005 Dec;99(12):1477-84. CONCLUSION: Most non-antibiotic treatments for the common cold are probably not effective. The most promising are dextromethorphan, bisolvon and guiaphenesin for cough, antihistamine-decongestant combinations for a wide range of symptoms, nasal decongestants (at least for the first dose) and possibly zinc lozenges.
152. Larson AM, et al, and the Acute Liver Failure Study Group. Acetaminophen-Induced Acute Liver Failure: Results of a US Muticenter, Prospective Study. Hepatology; Dec 2005. (of 662 consecutive acute liver failure pts over 6yrs: 42% from acetaminophen liver injury; 48% were unintentional overdoses; only 65% of pts survived) (Navarro VJ, Senior JR. Drug-related hepatotoxicity. N Engl J Med. 2006 Feb 16;354(7):731-9.) (Kuffner EK, Temple AR, Cooper KM, Baggish JS, Parenti DL. Retrospective analysis of transient elevations in alanine aminotransferase during long-term treatment with acetaminophen in osteoarthritis clinical trials. Curr Med Res Opin. 2006 Nov;22(11):2137-48.)
153. Bobat R, Coovadia H, Stephen C, Naidoo KL, McKerrow N, Black RE, Moss WJ. Safety and efficacy of **zinc** supplementation for children with HIV-1 infection in South Africa: a randomised double-blind placebo-controlled trial. Lancet. 2005 Nov 26;366(9500):1862-7.
154. Health Canada warning Dec/05 Oral fleet (a concern in renal impairment or if electrolyte imbalances & if not adequate hydration): http://www.hc-sc.gc.ca/dhp-mps/alt_formats/hpfb-dgpsa/pdf/medeff/phosphate_solutions_2_hpc-cps_e.pdf & Pharmacist's Letter June 2006. July/09 Health Canada: Oral sodium phosphate products are no longer authorized for purgative use - Pharmascience Inc. and Odan Laboratories Ltd.
155. Poole KE, Loveridge N, Barker PJ, et al. Reduced **Vitamin D** in Acute Stroke. Stroke. 2005 Dec 1; [Epub ahead of print]
156. Park Y, Hunter DJ, Spiegelman D, et al. Dietary **fiber** intake and risk of colorectal cancer: a pooled analysis of prospective cohort studies. JAMA. 2005 Dec 14;294(22):2849-57. (InfoPOEMs: A diet high in fiber is not independently associated with a reduced risk of colorectal cancer. Patients consuming food and nutrients high in fiber are more likely to engage in other behaviors associated with a lower cancer risk. (LOE = 2a))
157. Scharman EJ, et al. **Diphenhydramine & dimenhydrinate poisoning**: an evidence-based consensus guideline for out-of-hospital management. Washington (DC): American Association of Poison Control Centers; Aug 2005. http://www.aapcc.org/FinalizedPMGdlns/diphenhydramine%20guideline%20for%20AAPCC%20_2_.pdf
158. Manoguerra AS, et al. **Iron ingestion**: an evidence-based consensus guideline for out-of-hospital management. Clin Toxicol (Phila) 2005;43(6):553-70 http://www.aapcc.org/FinalizedPMGdlns/iron%20guideline%20for%20AAPCC%202005-5-3.pdf
159. Berger WE. The safety and efficacy of **desloratadine** for the management of allergic disease. Drug Saf. 2005;28(12):1101-18.
160. Ryder KM, Shorr RI, Bush AJ, Kritchevsky SB, Harris T, Stone K, Cauley J, Tylavsky FA. **Magnesium** intake from food and supplements is associated with **bone mineral density** in healthy older white subjects. J Am Geriatr Soc. 2005 Nov;53(11):1875-80.
161. van Leeuwen R, Boekhoorn S, Vingerling JR, Witteman JC, Klaver CC, Hofman A, de Jong PT. Dietary intake of **antioxidants and risk of age-related macular degeneration**. JAMA. 2005 Dec 28;294(24):3101-7. (InfoPOEMs: A high dietary intake of beta carotene, vitamins C and E, and zinc reduces the risk of age-related macular degeneration (AMD). (LOE = 2b-)) (Rumbold AR, Crowther CA, Haslam RR, Dekker GA, Robinson JS; ACTS Study Group. Vitamins C and E and the risks of **preeclampsia and perinatal** complications. N Engl J Med. 2006 Apr 7;354(17):1796-806.) Cook NR, Albert CM, Gaziano JM, Zaharris E, MacFadyen J, Danielson E, Buring JE, Manson JE. A randomized factorial trial of vitamins C and E and beta carotene in the secondary prevention of cardiovascular events in women: results from the **Women's Antioxidant Cardiovascular Study**. Arch Intern Med. 2007 Aug 13-27;167(15):1610-8. There were no overall effects of ascorbic acid, vitamin E, or beta carotene on cardiovascular events among women at high risk for CVD.
Grodstein F, Kang JH, Glynn RJ, Cook NR, Gaziano JM. A randomized trial of **beta carotene** supplementation and **cognitive** function in men: the Physicians' Health Study II. Arch Intern Med. 2007 Nov 12;167(20):2184-90. We did not find an impact of short-term beta carotene supplementation on cognitive performance, but long-term supplementation may provide cognitive benefits.
Chong EW, Wong TY, Kreis AJ, Simpson JA, Guymer RH. Dietary antioxidants and primary prevention of age-related macular degeneration: systematic review and meta-analysis. BMJ 2007;335(7623):755-763. Neither high dietary nor supplemental intake of antioxidants reduced the risk of new-onset age-related macular degeneration (AMD). (LOE = 1a) There is insufficient evidence to support the role of dietary antioxidants, including the use of dietary antioxidant supplements, for the primary prevention of early AMD.)
Ellis JM, Tan HK, Gilbert RE, et al. Supplementation with antioxidants and folinic acid for children with Down's syndrome: randomised controlled trial. BMJ. 2008 Feb 22; [Epub ahead of print] This study provides no evidence to support the use of antioxidant or folinic acid supplements in children with Down's syndrome.
Christen WG, Glynn RJ, Chew EY, et al. Vitamin E and age-related cataract in a randomized trial of women. Ophthalmology. 2008 May;115(5):822-829.e1. Epub 2007 Dec 11. These data from a large trial of apparently healthy female health professionals with 9.7 years of treatment and follow-up indicate that 600 IU natural-source vitamin E taken every other day provides no benefit for age-related cataract or subtypes.
Bjelakovic G, Nikolova D, Gluud LL, Simonetti RG, Gluud C. Antioxidant supplements for prevention of mortality in healthy participants and patients with various diseases. Cochrane Database Syst Rev. 2008 Apr 16;(2):CD007176. We found no evidence to support antioxidant supplements for primary or secondary prevention. **Vitamin A, beta-carotene, and vitamin E may increase mortality**. Future randomised trials could evaluate the potential effects of vitamin C and selenium for primary and secondary prevention.
Sesso HD, Buring JE, Christen WG, et al. Vitamins E and C in the Prevention of Cardiovascular Disease in Men: The **Physicians' Health Study II** Randomized Controlled Trial. JAMA. 2008 Nov 9. [Epub ahead of print] In this large, long-term trial of male physicians, neither vitamin E nor vitamin C supplementation reduced the risk of major cardiovascular events. These data provide no support for the use of these supplements for the prevention of cardiovascular disease in middle-aged and older men.
Lippman SM, Klein EA, Goodman PJ, Lucia MS, et al. Effect of Selenium and Vitamin E on Risk of Prostate Cancer and Other Cancers: The Selenium and Vitamin E Cancer Prevention Trial (**SELECT**). JAMA. 2008 Dec 9. [Epub ahead of print] Selenium 200ug or vitamin E 400IU , alone or in combination at the doses and formulations used, did not prevent prostate cancer in this population of relatively healthy men.
Gaziano JM, Glynn RJ, Christen WG, Kurth T, et al. Vitamins E and C in the Prevention of Prostate and Total Cancer in Men: The **Physicians' Health Study II** Randomized Controlled Trial. JAMA. 2008 Dec 9. [Epub ahead of print] In this large, long-term trial of male physicians, neither vitamin E nor C supplementation reduced the risk of prostate or total cancer. These data provide no support for the use of these supplements for the prevention of cancer in middle-aged and older men.
Smedts HP, de Vries JH, Rakhshandehroo M, et al. High maternal **vitamin E** intake by diet or supplements is associated with congenital heart defects in the offspring. BJOG. 2009 Feb;116(3):416-23. High maternal vitamin E intake is associated with congenital heart defects with a dose-response gradient. Although causality has not been demonstrated, the association is biologically plausible and may be sufficient to discourage women of child-bearing age from taking vitamin E supplements. (LOE = 3b)
Ristow M et al. Antioxidants prevent health-promoting effects of physical exercise in humans. Proc Natl Acad Sci U S A 2009 May 26; 106:8665. (http://dx.doi.org/10.1073/pnas.0903485106)
Chan JM, Oh WK, Xie W, Regan MM, Stampfer MJ, King IB, Abe M, Kantoff PW. Plasma **Selenium**, Manganese Superoxide Dismutase, and Intermediate- or High-Risk Prostate Cancer. J Clin Oncol. 2009 Jun 15. [Epub ahead of print]
Sanyal, Arun J., Chalasani, Naga, Kowdley, Kris V., et al. the NASH CRN, Pioglitazone, **Vitamin E**, or Placebo for **Nonalcoholic Steatohepatitis**. N Engl J Med 2010 0: NEJMoa0907929.
Mattias Johansson; Caroline Relton; Per Magne Ueland et al; Serum B Vitamin Levels and Risk of Lung Cancer JAMA. 2010;303(23):2377-2385. Conclusion Serum levels of **vitamin B6 and methionine** were inversely associated with risk of lung cancer.
Schürks Markus, Glynn Robert J, Rist Pamela M, et al. Effects of **vitamin E on stroke** subtypes: meta-analysis of randomised controlled trials. BMJ 341:doi:10.1136/bmj.c5702 (Published 4 November 2010).

Christen WG, Glynn RJ, Chew EY, Buring JE. **Vitamin E** and age-related macular degeneration in a randomized trial of women. Ophthalmology. 2010 Jun;117(6):1163-8.
Morris Martha Clare, Tangney Christine C. A Potential **Design Flaw of Randomized Trials of Vitamin Supplements**. JAMA. 2011;305(13):1348-1349.doi:10.1001/jama.2011.383
West KP Jr, et al. Effects of **vitamin A or beta carotene** supplementation on pregnancy-related mortality and infant mortality in rural Bangladesh: a cluster randomized trial. JAMA. 2011 May 18;305(19):1986-95. (not reduce all-cause maternal, fetal or infant mortality)
Klein EA, Thompson IM Jr, Tangen CM, et al. Vitamin E and the risk of prostate cancer: the Selenium and **Vitamin E Cancer** Prevention Trial (**SELECT**). JAMA. 2011 Oct 12;306(14):1549-56.
Darlow BA, Graham PJ. **Vitamin A** supplementation to prevent mortality and short- and long-term **morbidity in very low birthweight infants**. Cochrane Database Syst Rev. 2011 Oct 5;(10):CD000501.
Bjelakovic G, Nikolova D, Gluud LL, Simonetti RG, Gluud C. **Antioxidant supplements** for prevention of mortality in healthy participants and patients with various diseases. Cochrane Database of Systematic Reviews 2012, Issue 3. Art. No.: CD007176. DOI: 10.1002/14651858.CD007176.pub2. We found no evidence to support antioxidant supplements for primary or secondary prevention. **Beta-carotene and vitamin E seem to increase mortality, and so may higher doses of vitamin A.**
Siriwardena AK, Mason JM, Sheen AJ, et al. Antioxidant Therapy Does Not Reduce Pain in Patients With Chronic Pancreatitis: The ANTICIPATE Study. Gastroenterology. 2012 Sep;143(3):655-663.e1.
Hankey GJ. Vitamin Supplementation and **Stroke** Prevention. Stroke. 2012 Aug 7.
Evans JR, Lawrenson JG. Antioxidant vitamin and mineral supplements for slowing the progression of age-related macular degeneration. Cochrane Database Syst Rev. 2012 Nov 14;11:CD000254. doi: 10.1002/14651858.CD000254.pub3. People with AMD may experience delay in progression of the disease with antioxidant vitamin and mineral supplementation.
Myung SK, Ju W, Cho B, et al; for the Korean Meta-Analysis (KORMA) Study Group. Efficacy of **vitamin and antioxidant** supplements in prevention of **cardiovascular disease**: systematic review and meta-analysis of randomised controlled trials. BMJ. 2013 Jan 18;346:f10.
Bjelakovic G, Nikolova D, Gluud C. **Antioxidant supplements to prevent mortality**. JAMA. 2013 Sep 18;310(11):1178-9.
Fortmann SP, Burda BU, Senger CA et al. Vitamin and Mineral Supplements in the Primary Prevention of **Cardiovascular Disease and Cancer**: An Updated Systematic Evidence Review for the U.S. Preventive Services Task Force. Ann Intern Med. 2013 Nov 12.
Christen WG, Glynn RJ, Gaziano JM, et al. Age-Related Cataract in Men in the Selenium and Vitamin E Cancer Prevention Trial Eye Endpoints Study: A Randomized Clinical Trial. JAMA Ophthalmol. 2014 Sep 18.
Wu J, Cho E, Willett WC, et al. Intakes of Lutein, Zeaxanthin, and Other Carotenoids and Age-Related Macular Degeneration During 2 Decades of Prospective Follow-up. JAMA Ophthalmol. 2015 Oct 8:1-10.
Vitoria I, López B, Gómez J, et al. Improper Use of a Plant-Based **Vitamin C**-Deficient Beverage (almond) Causes Scurvy in an Infant. Pediatrics. 2016 Jan 18.
Hafez D, Saint S, Griauzde Jet al. Clinical Problem-Solving. A Deficient Diagnosis. (**Vitamin C: scurvy**) N Engl J Med. 2016 Apr 7
Sano M, Aisen PS, Andrews HF, et al; International Down Syndrome and Alzheimer's Disease Consortium. **Vitamin E** in aging persons with **Down syndrome**: A randomized, placebo-controlled clinical trial. Neurology. 2016 May 31;86(22):2071-6.
Lance P, Alberts DS, Thompson PA, et al. Colorectal Adenomas in Participants of the SELECT Randomized Trial of Selenium and Vitamin E for Prostate Cancer Prevention. Cancer Prev Res (Phila). 2016 Oct 24.
Al-Khudairy L, Flowers N, Wheelhouse R, et al. **Vitamin C supplementation for the primary prevention of cardiovascular disease**. Cochrane Database of Systematic Reviews 2017, Issue 3. Art. No.: CD011114. Currently, there is no evidence to suggest that vitamin C supplementation reduces the risk of CVD in healthy participants and those at increased risk of CVD, but current evidence is limited to one trial of middle-aged and older male physicians from the USA. There is limited low- and very low-quality evidence currently on the effect of vitamin C supplementation and risk of CVD risk factors.
Van Leer P. **Vitamin E** in Pregnancy. Am Fam Physician. 2017 Apr 1;95(7):Online.
Farina N, Llewellyn D, Isaac MGEKN, et al. **Vitamin E for Alzheimer`s dementia** and mild cognitive impairment. Cochrane Database Syst Rev. 2017 Apr 18;4:CD002854. We found no evidence that the alpha-tocopherol form of vitamin E given to people with MCI prevents progression to dementia, or that it improves cognitive function in people with MCI or dementia due to AD. However, there is moderate quality evidence from a single study that it may slow functional decline in AD. Vitamin E was not associated with an increased risk of serious adverse events or mortality in the trials in this review. These conclusions have changed since the previous update, however they are still based on small numbers of trials and participants and further research is quite likely to affect the results.
Kryscio RJ, Abner EL, Caban-Holt A, et al. Association of antioxidant supplement use and dementia in the Prevention of **Alzheimer's Disease by Vitamin E and Selenium** trial (**PREADViSE**) [online Mar 20, 2017].JAMA Neurol. doi:10.1001/jamaneurol.2016.5778
Lee AY, Butt T, Chew E, et al. Cost-effectiveness of **age-related macular degeneration study supplements** in the UK: combined trial and real-world outcomes data. Br J Ophthalmol. 2017 Aug 23
Evans JR, Lawrenson JG. **Antioxidant vitamin and mineral supplements for slowing the progression of age-related macular degeneration**. Cochrane Database Syst Rev. 2017 Jul 31;7:CD000254. People with AMD may experience some delay in progression of the disease with multivitamin antioxidant vitamin and mineral supplementation. This finding was largely drawn from one large trial, conducted in a relatively well-nourished American population. We do not know the generalisability of these findings to other populations. Although generally regarded as safe, vitamin supplements may have harmful effects. A systematic review of the evidence on harms of vitamin supplements is needed. Supplements containing lutein and zeaxanthin are heavily marketed for people with age-related macular degeneration but our review shows they may have little or no effect on the progression of AMD.

162. Chen SC, et al. Nonsurgical management of partial adhesive small-bowel obstruction with oral therapy: a randomized controlled trial. CMAJ. 2005 Nov 8;173(10):1165-9. (InfoPOEMs: The combination of magnesium oxide, Lactobacillus acidophilus, and simethicone appears to reduce length of stay and the need for surgery in patients with partial small bowel obstruction, although this study was limited by a failure to completely blind patients and their caregivers. (LOE = 1b))
163. Saary J, et al. A systematic review of contact dermatitis treatment and prevention. J Am Acad Dermatol. 2005 Nov;53(5):845. (InfoPOEMs: Barrier creams, high-lipid content moisturizing creams, fabric softeners, and cotton glove liners are effective for preventing irritative contact dermatitis. Rhus dermatitis can be reduced or prevented with quaternium 18 bentonite (organoclay) lotion and a topical skin protectant. The chelator diethylenetriamine pentaacetic acid is effective in preventing nickel, chrome, and copper dermatitis. Steroid preparations are effective in the treatment of both irritative and contact dermatitis. (LOE = 1a-))
Usatine RP, Riojas M. Diagnosis and management of **contact dermatitis**. Am Fam Physician. 2010 Aug 1;82(3):249-55.
164. Alonso-Coello P, Mills E, Heels-Ansdell D, Lopez-Yarto M, Zhou Q, Johanson JF, Guyatt G. **Fiber** for the treatment of **hemorrhoids** complications: a systematic review and meta-analysis. Am J Gastroenterol. 2006 Jan;101(1):181-8.
165. Tubelius P, Stan V, Zachrisson A. Increasing work-place healthiness with the probiotic **Lactobacillus** reuteri: a randomised, double-blind placebo-controlled study. Environ Health. 2005 Nov 7;4:25. (InfoPOEMs: This study provides preliminary, limited evidence for a beneficial effect of Lactobacillus reuteri in reducing sick leave among healthy adults. The sponsorship (and authorship) by the manufacturer and the lack of intention-to-treat analysis means that we should watch for confirmatory studies before broadly recommending this to our patients. (LOE = 2b)) & see Pharmacist's Letter Probiotics July 2006.
(Szajewska H, Ruszczynski M, et al. Probiotics in the prevention of antibiotic-associated diarrhea in children: a meta-analysis of randomized controlled trials. J Pediatr. 2006 Sep;149(3):367-372. Probiotics reduce the risk of AAD in children. For every 7 patients that would develop diarrhea while being treated with antibiotics, one fewer will develop AAD if also receiving probiotics. (InfoPOEMs: Probiotics appear to prevent antibiotic-associated diarrhea in children. However, the limited number of trials included in this study, their overall limited quality, and the potential for publication bias suggest that the data are too limited for certainty. (LOE = 1a-))
(Medical Letter. **Probiotics**. Aug 13,2007.) Clarification: Saccharomyces cerevisiae (including S boulardii)
Kale-Pradhan PB, Jassal HK, Wilhelm SM. Role of Lactobacillus in the prevention of antibiotic-associated diarrhea: a meta-analysis. Pharmacotherapy. 2010 Feb;30(2):119-26. The probiotic Lactobacillus is effective in preventing antibiotic-associated diarrhea (AAD) in adults, though perhaps not in children. (LOE = 1a-)
Hojsak I, Abdovic S, Szajewska H, Milosevic M, Krznaric Z, Kolacek S. Lactobacillus GG in the Prevention of Nosocomial Gastrointestinal and Respiratory Tract Infections. Pediatrics. 2010 Apr 19. [Epub ahead of print]
Deshpande G, Rao S, Patole S, et al. Updated meta-analysis of probiotics for preventing necrotizing enterocolitis in preterm neonates. Pediatrics. 2010 May;125(5):921-30. Epub 2010 Apr 19
Allen SJ, Martinez EG, Gregorio GV, Dans LF. **Probiotics for treating acute infectious diarrhoea**. Cochrane Database of Systematic Reviews 2010, Issue 11. Art. No.: CD003048. DOI: 10.1002/14651858.CD003048.pub3. Used alongside rehydration therapy, probiotics appear to be safe and have clear beneficial effects in shortening the duration and reducing stool frequency in acute infectious diarrhoea. However, more research is needed to guide the use of particular probiotic regimens in specific patient groups.
Bernaola Aponte G, Bada Mancilla CA, Carreazo Pariasca NY, Rojas Galarza RA. Probiotics for treating persistent diarrhoea in children. Cochrane Database of Systematic Reviews 2010, Issue 11. Art. No.: CD007401. DOI: 10.1002/14651858.CD007401.pub2. There is limited evidence suggesting probiotics may be effective in treating persistent diarrhoea in children.
Coccorullo P, Strisciuglio C, Martinelli M, et al. **Lactobacillus reuteri (DSM 17938)** in infants with functional chronic constipation: a double-blind, randomized, placebo-controlled study. J Pediatr. 2010 Oct;157(4):598-602.
Thomas, Dan W., Greer, Frank R., Committee on Nutrition; Section on Gastroenterology, Hepatology, and Nutrition, Clinical Report--**Probiotics and Prebiotics in Pediatrics.** Pediatrics 2010 0: peds.2010-2548.
Riquelme AJ, Calvo MA, Guzmán AM, et al. Saccharomyces cerevisiae fungemia after Saccharomyces boulardii treatment in **immunocompromised patients**. J Clin Gastroenterol. 2003 Jan;36(1):41-3.
Elias, Jackie, Bozzo, Pina, Einarson, Adrienne. Are **probiotics safe for use during pregnancy and lactation**? Can Fam Physician 2011 57: 299-301.
Hao Q, Lu Z, Dong BR, Huang CQ, Wu T. **Probiotics for preventing acute upper respiratory tract infections**. Cochrane Database of Systematic Reviews 2011, Issue 9. Art. No.: CD006895. DOI: 10.1002/14651858.CD006895.pub2. Probiotics were better than placebo in reducing the number of participants experiencing episodes of acute URTIs, the rate ratio of episodes of acute URTI and reducing antibiotic use. This indicates that probiotics may be more beneficial than placebo for preventing acute URTIs.
Pozzoni P, Riva A, Bellatorre AG, et al. **Saccharomyces boulardii** for the Prevention of **Antibiotic-Associated Diarrhea** in Adult Hospitalized Patients: A Single-Center, Randomized, Double-Blind, Placebo-Controlled Trial. Am J Gastroenterol. 2012 Apr 3. In elderly hospitalized patients, S. boulardii was not effective in preventing the development of AAD.
Agustina R, Kok FJ, van de Rest O, et al. Randomized trial of probiotics and calcium on diarrhea and respiratory tract infections in Indonesian children. Pediatrics. 2012 May;129(5):e1155-64. RC milk, alone or with L casei, did not reduce diarrhea or ARTIs in indonesian children. L reuteri may prevent diarrhea, especially in children with lower nutritional status.
Hempel S, Newberry SJ, Maher AR, et al. Probiotics for the prevention and treatment of **antibiotic-associated diarrhea**: a systematic review and meta-analysis. JAMA. 2012 May 9;307(18):1959-69.
Videlock EJ, Cremonini F. Meta-analysis: probiotics in **antibiotic-associated diarrhoea**. Aliment Pharmacol Ther. 2012 Jun;35(12):1355-69.
Johnston BC, Ma SS, Goldenberg JZ, et al. **Probiotics for the prevention of Clostridium difficile**–associated diarrhea: a systematic review and meta-analysis. Ann Intern Med 2012.
Canadian Paediatric Society. Position statement. Using probiotics in the paediatric population.www.cps.ca/en/documents/position/probiotics-in-the-paediatric-population (accessed January 7, 2013).
Goldenberg JZ, Ma SSY, Saxton JD, et al. **Probiotics for the prevention of Clostridium difficile**-associated diarrhea in adults and children. Cochrane Database of Systematic Reviews 2013, Issue 5. Based on this systematic review andmeta-analysis of 23 randomized controlled trials including 4213 patients,moderate quality evidence suggests that probiotics are both safe and effective for preventing Clostridium difficile-associated diarrhea.
Gutierrez-Castrellon P, Lopez-Velazquez G, Diaz-Garcia L, et al. **Diarrhea in Preschool Children** and **Lactobacillus reuteri**: A Randomized Controlled Trial. Pediatrics. 2014 Mar 17
Feizizadeh S, Salehi-Abargouei A, Akbari V. Efficacy and Safety of **Saccharomyces boulardii** for Acute Diarrhea. Pediatrics. 2014 Jun 23.
AlFaleh K, Anabrees J. **Probiotics for prevention of necrotizing enterocolitis in preterm infants**. Cochrane Database of Systematic Reviews 2014, Issue 4. Art. No.: CD005496. DOI: 10.1002/14651858.CD005496.pub4. Enteral supplementation of probiotics prevents severe NEC and all cause mortality in preterm infants. Our updated review of available evidence strongly supports a change in practice. Head to head comparative studies are required to assess the most effective preparations, timing, and length of therapy to be utilized.

166. Bonaa KH, Njolstad I, Ueland PM, et al. Homocysteine Lowering and Cardiovascular Events after Acute Myocardial Infarction. N Engl J Med. 2006 Mar 12; [Epub ahead of print] & Homocysteine Lowering with Folic Acid and B Vitamins in Vascular Disease. N Engl J Med. 2006 Mar 12; [Epub ahead of print]. (Folate Status in Women of Childbearing Age, by Race/Ethnicity --- United States, 1999--2000, 2001--2002, and 2003—2004 http://www.cdc.gov/mmwr/preview/mmwrhtml/mm5551a2.htm) (Durga J, van Boxtel MPJ, Schouten EG, et al. Effect of 3-year **folic acid** supplementation on **cognitive function** in older adults in the FACIT trial: a randomised, double blind, controlled trial. Lancet 2007; 369:208-216. Folic acid supplementation for 3 years significantly improved domains of cognitive function that tend to decline with age. (De Wals P, Tairou F, Van Allen MI, et al. **Reduction in neural-tube defects after folic acid** fortification in Canada. N Engl J Med. 2007 Jul 12;357(2):135-42. Food fortification with folic acid was associated with a significant reduction in the rate of neural-tube defects in Canada. The decrease was greatest in areas in which the baseline rate was high.)
Wald NJ, Law MR, Morris JK, Wald DS. Quantifying the effect of folic acid. Lancet. 2001 Dec 15;358(9298):2069-73.
Jenkins KJ, Correa A, et al. American Heart Association Council on Cardiovascular Disease in the Young. Noninherited risk factors and **congenital cardiovascular defects**: current knowledge: a scientific statement from the American Heart Association Council on Cardiovascular Disease in the Young: endorsed by the American Academy of Pediatrics. Circulation. 2007 Jun 12;115(23):2995-3014. Epub 2007 May 22.
Wilson RD, Johnson JA, et al. Pre-conceptional vitamin/folic acid supplementation 2007: the use of **folic acid in combination with a multivitamin** supplement for the prevention of neural tube defects and other congenital anomalies. J Obstet Gynaecol Can 2007;29:1003-26.
Wilson RD, Johnson JA, Wyatt P, Allen V, Gagnon A, Langlois S, Blight C, Audibert F, Désilets V, Brock JA, Koren G, Goh YI, Nguyen P, Kapur B; Genetics Committee of the **Society of Obstetricians and Gynaecologists of Canada and The Motherrisk** Program. Pre-conceptional vitamin/folic acid supplementation 2007: the use of **folic acid** in combination with a multivitamin supplement for the prevention of neural tube defects and other congenital anomalies. J Obstet Gynaecol Can. 2007 Dec;29(12):1003-26.
Malouf R, Grimley Evans J. Folic acid with or without vitamin B12 for the prevention and treatment of healthy elderly and demented people. Cochrane Database Syst Rev. 2008 Oct 8;(4):CD004514. The small number of studies which have been done provide no consistent evidence either way that folic acid, with or without vitamin B12, has a beneficial effect on cognitive function of unselected healthy or cognitively impaired older people. In a preliminary study, folic acid was associated with improvement in the response of people with Alzheimer`s disease to cholinesterase inhibitors. In another, long-term use appeared to improve the cognitive function of healthy older people with high homocysteine levels. More studies are needed on this important issue.
Ionescu-Ittu R, Marelli AJ, Mackie AS, Pilote L. Prevalence of severe congenital heart disease **after folic acid fortification** of grain products: time trend analysis in Quebec, Canada. BMJ 2009;338:b1673
U.S. Preventive Services Task Force. Folic acid for the prevention of neural tube defects: U.S. Preventive Services Task Force recommendation statement. Ann Intern Med 2009 May 5;150(9):626-31. The USPSTF recommends that all women planning or capable of pregnancy take a daily supplement containing 0.4 to 0.8 mg (400 to 800 micrograms) of folic acid.
Wolff T, Witkop CT, Miller T, Syed SB; U.S. Preventive Services Task Force. Folic acid supplementation for the prevention of neural tube defects: an update of the evidence for the U.S. Preventive Services Task Force. Ann Intern Med. 2009 May 5;150(9):632-9.
Ebbing Marta; Bonaa Kaare Harald; Nygard Ottar; et al. **Cancer** Incidence and Mortality After Treatment With Folic Acid and Vitamin B12 (Norvit & Wenbit). JAMA. 2009;302(19):2119-2126.
Clarke R. Halsey J, Lewington S, et al. Effects of lowering homocystein levels with B vitamins (folic acid) on cardiovascular disease, cancer, and cause-specific mortality. Meta-analysis of 8 randomized trials involving 37 485 individuals. Arch Intern Med 2010; 170:1622-1631.
Colapinto, Cynthia K., O'Connor, Deborah L., Tremblay, Mark S.**Folate status of the population in the Canadian** Health Measures Survey. CMAJ 2010 0: cmaj.100568
Nilsson Torbjörn K., Yngve Agneta, Böttiger Anna K., et al. High Folate Intake Is Related to Better **Academic Achievement** in Swedish Adolescents. Pediatrics 2011; peds.2010-1481; published ahead of print July 11, 2011, doi:10.1542/peds.2010-1481
Koren G. **Folic acid and colorectal cancer**: unwarranted fears. Can Fam Physician. 2011 Aug;57(8):889-90.
Roth C, Magnus P, Schjølberg S, et al. **Folic** acid supplements in pregnancy and **severe language delay** in children. JAMA. 2011 Oct 12;306(14):1566-73.
Sadighi Z, Butler IJ, Koenig MK. Adult-Onset **Cerebral Folate Deficiency**. Arch Neurol. 2012 Feb 27.
Kennedy D, Koren G. Identifying women who might benefit from **higher doses of folic acid in pregnancy**. Can Fam Physician. 2012 Apr;58(4):394-7.
Linabery AM, Johnson KJ, Ross JA. **Childhood Cancer** Incidence Trends in Association With US **Folic** Acid Fortification (1986-2008). Pediatrics. 2012 May 21.
Vollset SE, Clarke R, Lewington S, et al, B-Vitamin Treatment Trialists' Collaboration. Eff ects of **folic acid** supplementation on overall and site-specifi c **cancer** incidence during the randomised trials: meta-analyses of data on 50 000 individuals. Lancet 2013; online Jan 25.
Suren P, Roth C, Bresnahan M, et al. Association between maternal use of folic acid supplements and risk of **autism spectrum disorders** in children. JAMA. 2013;309(6):570-577.
Roffman JL, Lamberti JS, Achtyes E, et al. Randomized Multicenter Investigation of **Folate Plus Vitamin B12** Supplementation in **Schizophrenia**. JAMA Psychiatry. 2013 Mar 6:1-9. (may help negative symptoms)
Figueiredo JC, Grau MV, Haile RW, et al. **Folic acid and risk of prostate cancer**: results from a randomized clinical trial. J Natl Cancer Inst. 2009 Mar 18;101(6):432-5.
Crider KS, Devine O, Hao L, et al. Population **red blood cell folate** concentrations for prevention of neural tube defects: bayesian model. BMJ. 2014 Jul 29;349:g4554
Theisen-Toupal J, Horowitz G, Breu A. Low yield of outpatient serum **folate testing**: eleven years of experience. JAMA Intern Med. 2014 Oct 1;174(10):1696-7.
Valera-Gran D, García de la Hera M, Navarrete-Muñoz EM, et al; Infancia y Medio Ambiente (INMA) Project. **Folic Acid** supplements during pregnancy and child psychomotor development after the first year of life. JAMA Pediatr. 2014 Nov 3;168(11):e142611.
Khoshnood B, Loane M, de Walle H, et al. Long term trends in the prevalence of **neural tube defects** (folic acide) in Europe: population based study. BMJ 2015;351:h5949.
Xu X, Qin X, Li Y, et al. Efficacy of **Folic Acid** Therapy on the Progression of Chronic Kidney Disease: The Renal Substudy of the China Stroke Primary Prevention Trial. JAMA Intern Med. 2016 Aug 22.
Lassi ZS, Salam RA, Haider BA, et al. **Folic acid supplementation** during **pregnancy** for maternal health and pregnancy outcomes. Cochrane Database Syst Rev. 2013 Mar 28;(3):CD006896
Liu S, Joseph KS, Luo W, et al. Effect of **Folic Acid** Food Fortification in Canada on Congenital Heart Disease Subtypes. Circulation. 2016 Aug 30;134(9):647-55.
USPSTF: US Preventive Services Task Force. **Folic acid supplementation** for the prevention of neural tube defects: US Preventive Services Task Force Recommendation Statement.JAMA. doi:10.1001 /jama.2016.19438
Zhao M, Wu G, Li Y, et al. Meta-analysis of **folic acid** efficacy trials in stroke prevention: Insight into effect modifiers. Neurology. 2017 May 9;88(19):1830-1838.
Li N, Li Z, Ye R, et al. Impact of **Periconceptional Folic Acid Supplementation** on Low Birth Weight and Small-for-Gestational-Age Infants in China: A Large Prospective Cohort Study. J Pediatr. 2017 May 22.
Zhu B, Ge X, Huang K, et al. **Folic Acid Supplement Intake in Early Pregnancy Increases Risk of Gestational Diabetes Mellitus**: Evidence From a Prospective Cohort Study. Diabetes Care. 2016 Mar;39(3):e36-7.
Levine SZ, Kodesh A, Viktorin A, et al. Association of Maternal Use of **Folic Acid and Multivitamin Supplements in the Periods Before and During Pregnancy With the Risk of Autism** Spectrum Disorder in Offspring. JAMA Psychiatry. 2018 Jan 3.
Mills JL, Molloy AM, Reynolds EH. Do the benefits of **folic acid fortification outweigh the risk of masking vitamin B(12) deficiency**? BMJ. 2018 Mar 1;360:k724.
Eryilmaz H, Dowling KF, Huntington FC, et al. Association of **Prenatal Exposure to Population-Wide Folic Acid Fortification** With Altered Cerebral Cortex Maturation in Youths. JAMA Psychiatry. 2018 Jul 3.
Wen SW, White RR, Rybak N, et al; FACT Collaborating Group. Effect of **high dose folic acid supplementation in pregnancy on pre-eclampsia (FACT)**: double blind, phase III, randomised controlled, international, multicentre trial. BMJ. 2018 Sep 12;362:k3478.
Yusuf KK, Salihu HM, Wilson R, et al. Comparing Folic Acid Dosage Strengths to **Prevent Reduction in Fetal Size Among Pregnant Women Who Smoked Cigarettes**: A Randomized Clinical Trial. JAMA Pediatr. 2019 Mar 18.
Centeno Tablante E, Pachón H, Guetterman HM, Finkelstein JL. Fortification of wheat and maize flour with folic acid for population health outcomes. Cochrane Database Syst Rev. 2019 Jul 1;7:CD012150. Fortification of wheat flour with folic acid may reduce the risk of neural tube defects; however, this outcome was only reported in one non-RCT. Fortification of wheat or maize flour with folic acid (i.e. alone or with other micronutrients) may increase erythrocyte and serum/plasma folate concentrations. Evidence is limited for the effects of folic acid-fortified wheat or maize flour on haemoglobin levels or anaemia. The effects of folic acid fortification of wheat or maize flour on other primary outcomes assessed in this review is not known.

167. Mucha SM, deTineo M, Naclerio RM, Baroody FM. Comparison of **montelukast and pseudoephedrine** in the treatment of allergic rhinitis. Arch Otolaryngol Head Neck Surg. 2006 Feb;132(2):164-72.
168. Dodd SR, et al. In a systematic review, infrared ear thermometry for fever diagnosis in children finds poor sensitivity. J Clin Epidemiol. 2006 Apr;59(4):354-7. Epub 2006 Feb 20. (InfoPOEMs: Ear thermometry will only detect approximately two thirds of febrile children. Although it is fast and easy, the use of ear thermometry should be limited to those situations in which it doesn't matter if fever is present. (LOE = 1a-))
169. Poston L, et al. Vitamins in Pre-eclampsia (VIP) Trial Consortium. **Vitamin C and vitamin E** in pregnant women at risk for pre-eclampsia (VIP trial): randomised placebo-controlled trial. Lancet. 2006 Apr 8;367(9517):1145-54. (InfoPOEMs: Supplementation with vitamins C and E during pregnancy does not reduce the risk of preeclampsia but does increase the risk of low birth weight. (LOE = 1b))
170. DHA Supplementation during Pregnancy & Lactation. Pharmacist's Letter Aug,2006.
171. Pharmacist's Letter. **Vitamin D and Calcium**: Not just for Bones anymore . July 2007.
172. InfoPOEM Feb08: Honey for cough. {A single dose of honey is effective at decreasing cough severity and sleep disruption in children with cough due to uncomplicated upper respiratory infections. Please remember that honey should never be given to infants because of the risk of botulism. (LOE = 2b)}
173. Paul IM, Beiler J, McMonagle A, Shaffer ML, Duda L, Berlin CM Jr. Effect of **honey**, dextromethorphan, and no treatment on nocturnal cough and sleep quality for coughing children and their parents. Arch Pediatr Adolesc Med. 2007 Dec;161(12):1140-6.
174. Smith SM, Schroeder K, Fahey T. Over-the-counter medications for acute cough in children and adults in ambulatory settings. Cochrane Database of Systematic Reviews 1999, Issue 1. Art. No.: CD001831. DOI: 10.1002/14651858.CD001831.pub3. {Acute cough is a common and troublesome symptom in people who suffer from acute upper respiratory tract infection (URTI). Many people self-prescribe over-the-counter (OTC) cough preparations and health practitioners often recommend their use for the initial treatment of cough. The results of this review suggest that there is no good evidence for or against the effectiveness of OTC medications in acute cough. The results of this review have to be interpreted with caution because the number of studies in each category of cough preparations was small. Many studies were of low quality and very different from each other, making evaluation of overall efficacy difficult. http://www.cochrane.org/reviews/en/ab001831.html }
Allan G. Michael, Korownyk Christina, Kolber Michael. Do cough suppressants or honey help pediatric cough? Can Fam Physician April 2011 57: 435.
Singh M, Singh M. **Heated, humidified air for the common cold**. Cochrane Database Syst Rev. 2011 May 11;5:CD001728.
Boulet LP, Côté G. **Cough**: etiology, evaluation and treatments. Update 2012. http://www.respiratoryguidelines.ca/sites/all/files/cough_toolkit.pdf (accessed January 9, 2012).
Oduwole O, Meremikwu MM, Oyo-Ita A, et al. **Honey for acute cough** in children. Cochrane Database Syst Rev. 2012 Mar 14;3:CD007094. Honey may be better than `no treatment` and diphenhydramine in the symptomatic relief of cough but not better than dextromethorphan
Bettiol S, Wang K, Thompson MJ, et al. Symptomatic treatment of the cough in **whooping cough**. Cochrane Database Syst Rev. 2012 May 16;5:CD003257. There is insufficient evidence to draw conclusions about the effectiveness of interventions for the cough in whooping cough.
Ryan NM, Birring SS, Gibson PG. Gabapentin for refractory chronic cough: a randomised, double-blind, placebo-controlled trial. Lancet 2012; published online Aug 28.

Morice AH, Menon MS, Mulrennan SA, et al. Opiate therapy in chronic cough. Am J Respir Crit Care Med 2007; 175: 312–15.
Cohen HA, Rozen J, Kristal H, et al. Effect of Honey on Nocturnal Cough and Sleep Quality: A Double-blind, Randomized, Placebo-Controlled Study. Pediatrics. 2012 Aug 6.
Chang AB, Robertson CF, Paul van Asperen P, et al. A Cough Algorithm for Chronic Cough in Children: A Multicenter, Randomized Controlled Study. Pediatrics. 2013 Apr 22.
McCallum GB, Bailey EJ, Morris PS, et al. **Clinical pathways for chronic cough in children**. Cochrane Database Syst Rev. 2014 Sep 22;9:CD006595. Current evidence suggests that using a clinical algorithm for the management of children with chronic cough in hospital outpatient settings is more effective than providing wait-list care. Futher high-quality randomised controlled trials are needed to perform ongoing evaluation of cough management pathways in general practitioner and other primary care settings.
Irwin RS, French CT, Lewis SZ, et al; CHEST Expert Cough Panel; CHEST Expert Cough Panel. Overview of the **Management of Cough: CHEST Guideline** and Expert Panel Report. Chest. 2014 Oct 1;146(4):885-9.
Paul IM, Beiler JS, Vallati JR, et al. **Placebo Effect** in the Treatment of **Acute Cough** in Infants and Toddlers: A Randomized Clinical Trial. JAMA Pediatr. 2014 Oct 27.
Oduwole O, Meremikwu MM, Oyo-Ita A, et al. **Honey for acute cough in children.** Cochrane Database Syst Rev. 2014 Dec 23;12:CD007094. Honey may be better than `no treatment`, diphenhydramine and placebo for the symptomatic relief of cough, but it is not better than dextromethorphan. None of the included studies assessed the effect of honey on `cough duration` because intervention and follow-up were for one night only. There is no strong evidence for or against the use of honey.
Goldman RD. **Honey for treatment of cough** in children. Can Fam Physician. 2014 Dec;60(12):1107-8, 1110.
Cash H, Trosman S, Abelson T, et al. **Chronic Cough in Children**. JAMA Otolaryngol Head Neck Surg. 2015 Mar 19.
Smith SM, Schroeder K, Fahey T. **Over-the-counter (OTC) medications for acute cough** in children and adults in community settings. Cochrane Database Syst Rev 2014;11:CD001831. The results of this review have to be interpreted with caution because the number of studies in each category of cough preparations was small. Availability, dosing and duration of use of over-the-counter cough medicines vary significantly in different countries. Many studies were poorly reported making assessment of risk of bias difficult and studies were also very different from each other, making evaluation of overall efficacy difficult. There is no good evidence for or against the effectiveness of OTC medicines in acute cough. This should be taken into account when considering prescribing antihistamines and centrally active antitussive agents in children; drugs that are known to have the potential to cause serious harm.
Gibson P, Wang G, McGarvey L, et al. Treatment of **Unexplained Chronic Cough: CHEST Guideline** and Expert Panel Report. Chest. 2015 Oct 1.
Vertigan AE, Kapela SL, Ryan NM, et al. **Pregabalin** and speech pathology combination therapy for refractory **chronic cough**: A randomised controlled trial. Chest. 2015 Oct 8.
Vertigan AE, Murad MH, Pringsheim T, Feinstein A, Chang AB, Newcombe PA, Rubin BK, McGarvey LP, Weir K, Altman KW, Weinberger M, Irwin RS, CHEST Expert Cough Panel. Somatic cough syndrome (previously referred to as psychogenic cough) and tic cough (previously referred to as habit cough) in adults and children: CHEST guideline and Expert Panel report. Chest. 2015 Jul;148(1):24-31.
Gibson PG, Vertigan AE. Management of chronic refractory cough. BMJ. 2015 Dec 14;351:h5590.
Vertigan AE, Kapela SL, Ryan NM, et al. Pregabalin and Speech Pathology Combination Therapy for Refractory Chronic Cough: A Randomized Controlled Trial. Chest. 2016 Mar;149(3):639-48.
Smith JA, Woodcock A. Chronic Cough. N Engl J Med. 2016 Oct 20;375(16):1544-1551
Chang AB, Oppenheimer JJ, Weinberger MM, et al. CHEST Expert Cough Panel.. Use of management pathways or algorithms in children with chronic cough: CHEST Guideline and Expert Panel Report. Chest. 2017 Jan 16.
Green JL et al. Safety profile of cough and cold medication use in pediatrics. Pediatrics 2017 Jun; 139:e20163070.
Malesker MA, Callahan-Lyon P, Ireland B, Irwin RS; CHEST Expert Cough Panel. Pharmacological and Non-Pharmacological Treatment for Acute Cough Associated with the Common Cold. CHEST Expert Panel Report. Chest. 2017 Aug 21.
Rosen MJ, Ireland B, Narasimhan M, French C, Irwin RS; CHEST Expert Cough Panel. Cough in Ambulatory Immunocompromised Adults: CHEST Expert Panel Report. Chest. 2017 Aug 19.
Giliberto JP, Dibildox D, Merati A. Unilateral Laryngoscopic Findings Associated With Response to Gabapentin in Patients With Chronic Cough. JAMA Otolaryngol Head Neck Surg. 2017 Sep 14.
Irwin RS, French CL, Chang AB, Altman KW; CHEST Expert Cough Panel Group. Classification of Cough as a Symptom in Adults and Management Algorithms: CHEST Guideline and Expert Panel Report. Chest. 2017 Oct 25.
Michaudet C, Malaty J. Chronic Cough: Evaluation and Management. Am Fam Physician. 2017;96(9):575-580.
Malesker MA, Callahan-Lyon P, Ireland B, Irwin RS; CHEST Expert Cough Panel. Pharmacologic and Nonpharmacologic Treatment for Acute Cough Associated With the Common Cold: CHEST Expert Panel Report. Chest. 2017 Nov;152(5):1021-1037.
Chua K-P, Shrime MG, Conti RM. Effect of FDA Investigation on Opioid Prescribing to Children After Tonsillectomy/Adenoidectomy. Pediatrics. 2017;140(6):e20171765
Oduwole O, Udoh EE, Oyo-Ita A, et al. Honey for acute cough in children. Cochrane Database Syst Rev. 2018 Apr 10;4:CD007094. Honey probably relieves cough symptoms to a greater extent than no treatment, diphenhydramine, and placebo, but may make little or no difference compared to dextromethorphan. Honey probably reduces cough duration better than placebo and salbutamol. There was no strong evidence for or against using honey. Most of the children received treatment for one night, which is a limitation to the results of this review. There was no difference in occurrence of adverse events between the honey and control arms.
Drugs for Cough. Medical Letter. Dec 2018.
van Driel ML, Scheire S, Deckx L, et al. What treatments are effective for common cold in adults and children? BMJ. 2018 Oct 10;363:k3786.
Health Canada Feb/19: is advising that Canadian children and adolescents (under 18 years of age) should not use cough and cold products containing codeine, hydrocodone and normethadone, as a precautionary measure.
Chang AB, Oppenheimer JJ, Kahrilas PJ, et al; CHEST Expert Cough Panel**. Chronic cough and gastroesophageal reflux** in children - CHEST Guideline and Expert Panel Report. Chest. 2019 Apr 16.
DeGeorge KC, Ring DJ, Dalrymple SN. Treatment of the Common Cold. Am Fam Physician. 2019 Sep 1;100(5):281-289.
Horton DB, Gerhard T, Strom BL. Trends in Cough and Cold Medicine Recommendations for Children in the United States, 2002-2015. JAMA Pediatr. 2019 Jul 29

175. Pynnonen MA, Mukerji SS, Kim HM, Adams ME, Terrell JE. Nasal saline for chronic sinonasal symptoms: a randomized controlled trial. Arch Otolaryngol Head Neck Surg. 2007 Nov;133(11):1115-20. Nasal irrigation (nasal washing) using a stream of normal saline, is more effective in decreasing general nasal or sinus symptoms than saline spray. The saline can be made at home, purchased as a kit, or adminstered using a neti pot. Direct your patients to an online source of video (eg, www.youtube.com) to see how it is administered. (LOE = 1b)
Yoder JS, Straif-Bourgeois S, Roy SL, et al. Primary Amebic Meningoencephalitis Deaths Associated With Sinus Irrigation Using Contaminated Tap Water. Clin Infect Dis. 2012 Aug 22.
176. Aisen PS, Schneider LS, Sano M, et al. Alzheimer Disease Cooperative Study (ADCS). High-dose **B vitamin supplementation** and cognitive decline in Alzheimer disease: a randomized controlled trial. JAMA. 2008 Oct 15;300(15):1774-83. This regimen of high-dose B vitamin supplements does not slow cognitive decline in individuals with mild to moderate AD.
177. Health Canada Releases Decision on the Labelling of Cough and Cold Products for Children Dec 2008. http://www.hc-sc.gc.ca/ahc-asc/media/advisories-avis/_2008/2008_184-eng.php
Ostroff C, Lee CE, McMeekin J. Unapproved prescription cough, cold, and allergy drug products: recent **US Food and Drug Administration** regulatory action on unapproved cough, cold, and allergy medications. Chest. 2011;140 (2): 295-300.
Health Canada Apr/16 reminds parents not to give cough and cold medication to children under 6 years old.
178. Shaikh U, Byrd RS, Auinger P. **Vitamin and mineral supplement use by children** and adolescents in the 1999-2004 National Health and Nutrition Examination Survey: relationship with nutrition, food security, physical activity, and health care access. Arch Pediatr Adolesc Med. 2009 Feb;163(2):150-7. A large number of US children and adolescents use vitamin and mineral supplements, which for most may not be medically indicated. Such supplements contribute significantly to total dietary intakes of vitamins and minerals, and studies of nutrition should include their assessment. Since vitamin and mineral supplement users report greater health care access, health care providers may be in a position to provide screening and counseling regarding dietary adequacy and indications for supplement use.
179. Rabago D, Zgierska A. **Saline nasal irrigation** for upper respiratory conditions. Am Fam Physician. 2009 Nov 15;80(10):1117-9.
180. Eekhof JA, Neven AK, Gransjean SP, Assendelft WJ. **Minor dermatologic ailments**: how good is the **evidence** for common treatments? J Fam Pract. 2009 Sep;58(9):E2.
181. Baldwin S, Odio MR , Haines SL, et al. Skin benefits from continuous topical administration of a zinc oxide/petrolatum formulation by a novel disposable **diaper**. J Eur Acad Dermatol Venereol. 2001;15(suppl 1):S5-S11.
182. Shanler SD, Ondo AL. Successful treatment of the erythema and flushing of rosacea using a topically applied selective alpha1-adrenergic receptor agonist, **oxymetazoline**. Arch Dermatol. 2007 Nov;143(11):1369-71.
183. Vaidyanathan S, Williamson P, Clearie K, et al. Fluticasone Reverses Oxymetazoline Induced Tachyphylaxis of Response and Rebound Congestion. Am J Respir Crit Care Med. 2010 Mar 4.
Baroody FM, Brown D, Gavanescu L, et al. Oxymetazoline adds to the effectiveness of fluticasone furoate in the treatment of perennial allergic rhinitis. J Allergy Clin Immunol. 2011 Apr;127(4):927-34.
184. May/10 Novartis Consumer Health Canada Inc., in consultation with Health Canada, would like to bring to your attention important safety information concerning the differences between our product Maalox Multi Action liquid and other Maalox liquid products. Maalox Multi Action contains bismuth subsalicylate, which is chemically related to acetylsalicylic acid (ASA) and can lead to similar adverse effects, such as bleeding. Other Maalox liquid products are mineral based, contain different ingredients, and are indicated for different symptoms. However, due to the similarity in the name, label and package between **Maalox Multi Action** and other Maalox liquid products, they have the potential to be confused and result in medication incidents.
185. Paul, Ian M., Beiler, Jessica S., King, Tonya S., Cet al. **Vapor Rub**, Petrolatum, and No Treatment for Children With Nocturnal Cough and Cold Symptoms. Pediatrics 2010 0: peds.2010-1601.
Little P, Stuart B, Mullee M, et al. Effectiveness of steam inhalation and nasal irrigation for chronic or recurrent sinus symptoms in primary care: a pragmatic randomized controlled trial. CMAJ. 2016 Jul 18.
186. FDA Mar/11 ISSUE: Tested samples of **Soladek** contained levels of vitamin A and vitamin D that were many times the recommended daily allowances for these vitamins.
187. Anti-infective Review Panel. **Anti-infective Guidelines for Community-acquired Infections**. Canadian - New-**2012**. Toronto: MUMS Guideline Clearinghouse. http://www.mumshealth.com/
188. CDC Dec/11 Two people in Louisiana have died this year from primary amebic meningoencephalitis after using tap water to irrigate their sinuses with neti pots, prompting the state's health department to remind consumers to use only distilled, sterile, or boiled water in **neti pots**. To avoid infections caused by ***Naegleria fowleri***, the CDC also recommends thoroughly rinsing neti pots after each use and letting the devices air dry completely.
189. Reamy BV, Bunt CW, Fletcher S. A diagnostic approach to **pruritus**. Am Fam Physician. 2011 Jul 15;84(2):195-202.
190. Chalasani N et al. The diagnosis and management of **non-alcoholic fatty liver disease (NAFLD)**: Practice guideline by the American Association for the Study of Liver Diseases, American College of Gastroenterology, and the American Gastroenterological Association. Hepatology 2012 Jun; 55:2005. (Vitamin E: at a dose of 800 IU/day improves liver histology in nondiabetic adults with biopsy-proven NASH and therefore can be recommended in this specific NAFLD population. (Note: some evidence exists that high-dose vitamin E intake increases risks for all-cause mortality and prostate cancer.)
191. FDA Oct/12 is warning healthcare professionals & the public that accidental ingestion by children of **over-the-counter eye drops** used to relieve redness and nasal decongestant sprays can result in serious and life-threatening adverse events. The eye drops and nasal sprays that have been involved in the cases of accidental ingestion contain the active ingredients **tetrahydrozoline, oxymetazoline, or naphazoline**.
192. Yosipovitch G, Bernhard JD. Clinical practice. **Chronic pruritus**. N Engl J Med.2013 Apr 25;368(17):1625-34.

193. Mazer-Amirshahi M, Reid N, van den Anker J, Litovitz T. Effect of **Cough and Cold Medication Restriction and Label Changes on Pediatric Ingestions** Reported to United States **Poison Centers**. J Pediatr. 2013 Jun 12.
194. Goldman RD. **Bismuth salicylate for diarrhea** in children. Can Fam Physician. 2013 Aug;59(8):843-4.
195. Health Canada is releasing an updated Labelling Standard for **acetylsalicylic acid (ASA) products for use in adults and children aged 12 years and older**.
196. Oner T, Guven B, Tavli V, et al. **Postural Orthostatic Tachycardia Syndrome** (POTS) and **Vitamin B12** Deficiency in Adolescents. Pediatrics. 2013 Dec 23
197. Atkinson HC, Stanescu I, Anderson BJ. **Increased phenylephrine plasma levels with administration of acetaminophen**. N Engl J Med. 2014 Mar 20;370(12):1171-2.
198. Farina E.K., Austin K.G. & Lieberman H.R. (2014). **Concomitant Dietary Supplement** and Prescription Medication Use Is Prevalent among US Adults with Doctor-Informed Medical Conditions, Journal of the Academy of Nutrition and Dietetics, DOI: 10.1016/j.jand.2014.01.016
199. Murase JE, Heller MM, Butler DC. Safety of dermatologic medications in pregnancy and lactation. J Am Acad Dermatol 2014;70:401-14 (part I) and 417-26 (part II).
200. Sharma M, Bennett C, Cohen SN, et al. **H1-antihistamines for chronic spontaneous urticaria**. Cochrane Database Syst Rev. 2014 Nov 14;11:CD006137. Although the results of our review indicate that at standard doses of treatment, several antihistamines are effective when compared with placebo, all results were gathered from a few studies or, in some cases, from single-study estimates. The quality of the evidence was affected by the small number of studies in each comparison and the small sample size for many of the outcomes, prompting us to downgrade the quality of evidence for imprecision (unless stated for each comparison, the quality of the evidence was low).No single H1-antihistamine stands out as most effective. Cetirizine at 10 mg once daily in the short term and in the intermediate term was found to be effective in completely suppressing urticaria. Evidence is limited for desloratadine given at 5 mg once daily in the intermediate term and at 20 mg in the short term. Levocetirizine at 5 mg in the intermediate but not short term was effective for complete suppression. Levocetirizine 20 mg was effective in the short term, but 10 mg was not. No difference in rates of withdrawal due to adverse events was noted between active and placebo groups. Evidence for improvement in quality of life was insufficient.
201. Almeida OP et al. **B vitamins** to enhance treatment response to antidepressants in middle-aged and older adults: Results from the **B-VITAGE** randomised, double-blind, placebo-controlled trial. Br J Psychiatry 2014 Sep 25.
202. Kakigi CL, Singh K, Wang SY, et al. Self-reported **Calcium Supplementation and Age-Related Macular Degeneration**. JAMA Ophthalmol. 2015 Jul 1;133(7):746-54.
203. Chen AC, Martin AJ, Choy B, et al. A Phase 3 Randomized Trial of Nicotinamide for Skin-Cancer Chemoprevention. N Engl J Med. 2015 Oct 22;373(17):1618-26.
204. Nordt SP, Vivero LE, Cantrell FL. Not Just a Drop in the Bucket-Inversion of **Oxymetazoline** Nasal Decongestant Container Increases Potential for Severe Pediatric **Poisoning**. J Pediatr. 2016 Jan;168:240-1.
205. Pucker AD, Ng SM, Nichols JJ. Over the counter (OTC) **artificial tear drops for dry eye syndrome.** Cochrane Database Syst Rev. 2016 Feb 23;2:CD009729. OTC artificial tears may be safe and effective means for treating dry eye syndrome; the literature indicates that the majority of OTC artificial tears may have similar efficacies. This conclusion could be greatly skewed by the inconsistencies in study designs and inconsistencies in reporting trial results. Additional research is therefore needed before we can draw robust conclusions about the effectiveness of individual OTC artificial tear formulations.
206. Hooshmand B, Mangialasche F, Kalpouzos G, et al. Association of **Vitamin B12, Folate, and Sulfur Amino** Acids With Brain Magnetic Resonance Imaging Measures in Older Adults: A Longitudinal Population-Based Study. JAMA Psychiatry. 2016 Jun 1;73(6):606-13.
207. Matthews DE, Beatty SJ, Grever GM, et al. Comparison of 2 Population Health Management Approaches to Increase **Vitamin B12** Monitoring in Patients Taking **Metformin**. Ann Pharmacother. 2016 Oct;50(10):840-6.
208. Tavares J, Eugénio G, Calretas S, et al. A link between asthenia, pallor, and jaundice (**Vitamin B12**). BMJ. 2016 Jun 7;353:i2937.
209. Vogrig A, Zanoni T, Moretto G. Nystagmus and Lower Extremity Hyperalgesia After Colectomy. (Wernicke encephalopathy: **Thiamine**) JAMA. 2016 Oct 11;316(14):1488-1489.
210. Amstrong-Javors A, Pratt J, Kharasch S. **Wernicke Encephalopathy (thiamine)** in **Adolescents after Bariatric Surgery**: Case Report and Review. Pediatrics. 2016;138(6):e20161039.
211. Witt M, Kvist N, Jørgensen MH, et al.; Netherlands Study group of Biliary Atresia Registry (NeSBAR).. **Prophylactic Dosing of Vitamin K to Prevent Bleeding**. Pediatrics. 2016 May;137(5).
212. Whiting SJ, Langlois KA, Vatanparast H, Greene-Finestone LS. The vitamin D status of Canadians relative to the 2011 Dietary Reference Intakes: An examination in children and adults with and without supplement use. Am J ClinNutr 2011 Jul;94(1): 128-35
213. Evans JR;Lawrenson JG. **Antioxidant vitamin and mineral supplements** for slowing the progression of **age-related macular degeneration**. Cochrane Database Syst Rev. 2017 Jul 31;7:CD000254.
214. Finsterer J. Low risk of ischaemic stroke in **hyperhomocysteinaemia**. Lancet Neurol. 2017;16:682-683.
215. Shi H, Enriquez A, Rapadas M, et al. NAD Deficiency, Congenital Malformations, and **Niacin Supplementation**. N Engl J Med. 2017 Aug 10;377(6):544-552
216. Spence JD, Yi Q, Hankey GJ. **B vitamins in stroke prevention**: time to reconsider. Lancet Neurol.2017;16:750-760.
217. Brasky TM, White E, Chen CL. Long-Term, Supplemental, One-Carbon Metabolism-Related **Vitamin B** Use in Relation to **Lung Cancer** Risk in the Vitamins and Lifestyle (**VITAL**) Cohort. J Clin Oncol. 2017 Aug 22:JCO2017727735
218. DeVilbiss EA, Magnusson C, Gardner RM, et al. **Antenatal nutritional supplementation** and **autism spectrum** disorders in the Stockholm youth cohort: population based cohort study. BMJ. 2017 Oct 4;359:j4273.
219. Jacobson D, Mireskandari K, Cohen E. An 11-Year-Old Boy With **Vision Loss**. JAMA Pediatr. 2017 Oct 2. (**Vitamin A deficiency**)
220. FDA Nov/17 is alerting the public, health care providers, lab personnel, and lab test developers that **biotin** can significantly interfere with certain lab tests and cause incorrect test results which may go undetected. Biotin in blood or other samples taken from patients who are ingesting high levels of biotin in dietary supplements can cause clinically significant incorrect lab test results. The FDA has seen an increase in the number of reported adverse events, including one death, related to biotin interference with lab tests. Biotin in patient samples can cause falsely high or falsely low results, depending on the test. Incorrect test results may lead to inappropriate patient management or misdiagnosis. For example, a falsely low result for **troponin**, a clinically important biomarker to aid in the diagnosis of heart attacks, may lead to a missed diagnosis and potentially serious clinical implications. The FDA has received a report that one patient taking high levels of biotin died following falsely low troponin test results when a troponin test known to have biotin interference was used. The FDA is aware of people taking high levels of biotin that would interfere with lab tests. Many dietary supplements promoted for hair, skin, and nail benefits contain biotin levels up to 650 times the recommended daily intake of biotin. Physicians may also be recommending high levels of biotin for patients with certain conditions such as multiple sclerosis (MS). Biotin levels higher than the recommended daily allowance may cause interference with lab tests.
221. Health Canada Jan/18 is advising Canadians that one bottle of children's "**Flintstones Plus Iron**" multivitamins (NPN 02247995) was returned to a pharmacy containing unidentified capsules instead of the proper chewable tablets, which are multi-coloured tablets shaped like Flintstones characters.
222. Marra MV, Bailey RL. Position of the Academy of Nutrition and Dietetics: **Micronutrient Supplementation**. J Acad Nutr Diet. 2018 Nov;118(11):2162-2173.
223.Hartman S, Brown E, Loomis E, Russell HA. **Gastroenteritis in Children**. Am Fam Physician. 2019 Feb 1;99(3):159-165.
224. Christakos S, Li S, De La Cruz J, Bikle DD. New developments in our understanding of **vitamin metabolism, action and treatment**. Metabolism. 2019 Sep;98:112-120.
225. Harrison R, Warburton V, Lux A, Atan D. **Blindness Caused by a Junk Food Diet**. Ann Intern Med. 2019 Sep 3.
226. Nastro A, Rosenwasser N, Daniels SP, et al. **Scurvy Due to Selective Diet** in a Seemingly Healthy 4-Year-Old Boy. Pediatrics. 2019 Aug 14.
227. Punzalan C, Budnitz DS, Chirtel SJ, et al. **Swallowing Problems and Dietary Supplements**: Data From U.S. Food and Drug Administration Adverse Event Reports, 2006-2015. Ann Intern Med. 2019 Aug 20.

References: ADHD Treatment Chart

[1] Virani A. Attention-Deficity Hyperactivity Disorder. Therapeutic Choices 5th Edition 2007.

[2] Micromedex 2018

[3] Lexi-comp 2018

[4] Canadian Attention Deficit Hyperactivity Disorder Resource Alliance (**CADDRA**). *Canadian ADHD Practice Guidelines 2007-2008*. Toronto (ON): CADDRA; 2007.
Available at: http://www.caddra.ca/english/2007-08_guidelines_pdfs/2007-08_Caddra_Guidelines.pdf (accessed April 22, 2008).
Feldman M, Bélanger S; Canadian Paediatric Society, Community Paediatrics Committee, Psychosocial Paediatrics Committee. Extended-release medications for children and adolescents with attention-deficit hyperactivity disorder. Paediatr Child Health 2009;14(9):593-597. http://www.cps.ca/english/statements/CP/CP09-04.pdf
Canadian ADHD Resource Alliance. CADDRA Canadian ADHD practice guidelines third edition (2011). (accessed January 28, 2011). http://www.caddra.ca/cms4/pdfs/caddraGuidelines2011.pdf
Canadian ADHD Resource Alliance (**CADDRA**). Canadian ADHD practice guidelines, **4th ed**, Toronto ON: CADDRA; **2018**.

[5] Pliszka SR *et al*. AACAP Official Action. Practice Parameter for the Assessment and Treatment of Children and Adolescents With Attention-Deficit/Hyperactivity Disorder. *J Am Acad Child Adolesc Psychiatry* 2007;46:894-921.
American Academy of Pediatrics (AAP): Subcommittee on Attention-Deficit/Hyperactivity Disorder, Steering Committee on Quality Improvement and Management. ADHD: Clinical Practice Guideline for the Diagnosis, Evaluation, and Treatment of Attention-Deficit/Hyperactivity Disorder in Children and Adolescents. Pediatrics. 2011 Oct 16. **Updated Oct 2019**.

[6] Virani A. Advances in ADHD Treatment: an overview for pharmacists. Canadian Pharmacists Association Advancement 2005 Learning Series.

[7] Compendium of Pharmaceuticals and Specialties 2008. Available at: http://www.e-cps.ca

[8] The Medical Letter. Drugs for the Treatment of ADHD. Treatment Guidelines from the Medical Letter. Nov 2006. Vol. 4 (Issue 51). **Updated Mar 2015**.

9 Compendium of Pharmaceuticals and Specialties 2010. Available at: http://www.e-cps.ca

10 Rappley M. Attention deficit-hyperactivity disorder. NEJM 2005; 352:165-173.

[11] Daviss W B et al. Clonidine for Attention-Deficit/Hyperactivity Disorder II. ECG Changes and Adverse Events Analysis. *J Am Acad Chid Adolesc Psychiatry* 2008;47:189-198.

[12] Banaschewski T, Roessner V, Dittman RW, Santosh PJ, Rothenberger A. Non-stimulant medication in the treatment of ADHD. *Eur Child Adolesc Psychiatry* 2004;13(Suppl 1):102–116.

[13] Einarson TR, Iskedjian M. Novel antipsychotics for patients with attention-deficit hyperactivity disorder: A systematic review. 17. 2001. Ottawa, Canadian Coordinating Office for Health Technology Assessment (CCOHTA).
Available at: http://cadth.ca/media/pdf/114_antipsychotic_adhd_tr_e.pdf, (accessed on May 7, 2008).

[14] Food and Drug Administration. Modafinil Serious Skin Reactions http://www.fda.gov/cder/dsn/2007_fall/postmarketing.htm#modafinil, (accessed on May 9, 2008).

[15] American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders, 4 th ed, Text Revision. Arlington, VA: American Psychiatric Press, Inc.; 2000.

[16] American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders, 4 th ed, Text Revision. Arlington, VA: American Psychiatric Press, Inc.; 2000.

[17] Hallowell EM, Ratey JJ. *Driven to Distraction*

[18] American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders, 4 th ed, Text Revision. Arlington, VA: American Psychiatric Press, Inc.; 2000.

[19] Hallowell EM, Ratey JJ. *Driven to Distraction*

[20] American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders, 4 th ed, Text Revision. Arlington, VA: American Psychiatric Press, Inc.; 2000. (**DSM-5** revisions 2013)

[21] Conners CK, March JS, Frances A, Wells KC, Ross R. The Expert Consensus Guideline Series: Treatment of Attention-Deficit/Hyperactivity Disorder. *J Attention Disord*. 2001;4(suppl 1):7-128.

[22] Safren SA. Cognitive-behavioural approaches to ADHD Treatment in adulthood. *J Clin Psychiatry* 2006;67(suppl 8):46-50.
Richardson M, Moore DA, Gwernan-Jones R, et al. Non-pharmacological interventions for attention-deficit/hyperactivity disorder (ADHD) delivered in school settings: systematic reviews of quantitative and qualitative research. Health Technol Assess. 2015 Jun;19(45):1-470. Findings suggest some beneficial effects of non-pharmacological interventions for ADHD used in school settings, but substantial heterogeneity in effect sizes was seen across studies. The qualitative reviews demonstrate the importance of the context in which interventions are used.

[23] **MTA** Cooperative Group. A 14-month randomized clinical trial of treatment strategies for attention-deficit/hyperactivity disorder. *Arch Gen Psychiatry* 1999;56:1073-1086. (n=579; 14months)

[24] **MTA** Cooperative Group. A 14-month randomized clinical trial of treatment strategies for attention-deficit/hyperactivity disorder. *Arch Gen Psychiatry* 1999;56:1073-1086.

[25] Abikoff H, Hechtman L, Klein RG, et al. Symptomatic improvement in children with ADHD treated with long-term methylphenidate and multimodal psychosocial treatment. *J Am Acad Child Adolesc Psychiatry* 2004;43:802-811.

[26] Jadad AR, Boyle M, Cunningham C, Kim M, Schachar R. Treatment of attention-deficit/hyperactivity disorder. Evid Rep Technol Assess (Summ). 1999 Nov: 1-341. Available at: http://www.ahcpr.gov (accessed May 1, 2008).

[27] Swanson JM, Kraemer HC, Hinshaw SP, Arnold LE et al. Clinical relevance of the primary findings of the **MTA**: success rates based on severity of ADHD and ODD symptoms at the end of treatment. *J Am Acad Child Adolesc Psychiatry*. 2001;40:168-79.
Molina BS, Hinshaw SP, Swanson JM, et al. MTA Cooperative Group. The **MTA** at 8 years: prospective follow-up of children treated for combined-type ADHD in a multisite study. J Am Acad Child Adolesc Psychiatry. 2009 May;48(5):484-500.

[28] Chan E. The role of complementary and alternative medicine in attention-defcit hyperactivity disorder. *J Dev Behav Pediatr* 2002;23(1 Suppl):S37-45.
Weber W, Vander Stoep A, McCarty RL, et al. Hypericum perforatum (St John's wort) for attention-deficit/hyperactivity disorder in children and adolescents: a randomized controlled trial. JAMA. 2008 Jun 11;299(22):2633-41. In this study, use of H. perforatum for treatment of ADHD over the course of 8 weeks did not improve symptoms.
Cala S, Crismon ML, Baumgartner J. A survey of herbal use in children with attention-deficit-hyperactivity disorder or depression. Pharmacotherapy. 2003 Feb;23(2):222-30. Herbal medicines were given most frequently for a behavioral condition, with ginkgo biloba, echinacea, and St. John's wort most prevalent.
Millichap JG, Yee MM. The **Diet Factor** in Attention-Deficit/Hyperactivity Disorder. Pediatrics. 2012 Jan 9. (**additive-free, oligoantigenic/elimination diets, iron/zinc/omega-3 supplements**)

[29] Villalaba L. Follow up review of AERS search identifying cases of sudden death occurring with drugs used for the treatment of attention deficit hyperactivity disorder ADHD.
Available at: http://www.fda.gov/ohrms/dockets/ac/06/briefing/2006-4210b_07_01_safetyreview.pdf (accessed May 2, 2008).
Gould, Madelyn S., Walsh, B. Timothy, et al. Sudden Death and Use of Stimulant Medications in Youths. Am J Psychiatry 2009 0: appi.ajp.2009.09040472.
Schelleman H, Bilker WB, Kimmel SE, et al. Methylphenidate and risk of serious cardiovascular events in adults. Am J Psychiatry 2012; 169:178–18. (a 1.8 fold increase in sudden death or ventricular arrhythmia, but no dose response)

[30] Villalaba L. Follow up review of AERS search identifying cases of sudden death occurring with drugs used for the treatment of attention deficit hyperactivity disorder ADHD.
Available at: http://www.fda.gov/ohrms/dockets/ac/06/briefing/2006-4210b_07_01_safetyreview.pdf (accessed May 2, 2008).
Schelleman Hedi, Bilker Warren B., Strom Brian L., et al. **Cardiovascular Events** and Death in Children Exposed and Unexposed to ADHD Agents. Pediatrics 2011; peds.2010-3371.
Cooper WO, Habel LA, Sox CM, et al. ADHD drugs and **serious cardiovascular events in children and young adults**. N Engl J Med. 2011 Nov 17;365(20):1896-904.
Habel LA, Cooper WO, Sox CM, et al. ADHD medications and risk of **serious cardiovascular events** in young and middle-aged adults. [published online December 12, 2011.] JAMA. doi:10.1001/JAMA.2011.1830.

[31] a) Health Canada. Attention Deficit Hyperactivity Disorder (ADHD) Drugs: Updated and Standardized Labelling Regarding Very Rare Cardiac-Related Adverse Events. May 2006.
Available at: http://www.hc-sc.gc.ca/dhp-mps/medeff/advisories-avis/prof/2006/adhd-tdah_medic_hpc-cps_e.html (accessed May 2, 2008).
b) Hecthman L, Greenfield B. Long-term use of stimulants in children with attention deficit hyperactivity disorder. *Pediatr Drugs* 2003; 5:787-794.

c) Gould, Madelyn S., Walsh, B. Timothy, et al. **Sudden Death** and Use of Stimulant Medications in Youths. Am J Psychiatry 2009 0: appi.ajp.2009.09040472.
d) Winterstein, Almut Gertrud, Gerhard, Tobias, Shuster, Jonathan, Saidi, Arwa. **Cardiac Safety** of Methylphenidate Versus Amphetamine Salts in the Treatment of ADHD Pediatrics 2009 124: e75-e80.
e) Schelleman Hedi, Bilker Warren B., Strom Brian L., et al. **Cardiovascular Events** and Death in Children Exposed and Unexposed to ADHD Agents. Pediatrics 2011; peds.2010-3371.
f) Shin JY, Roughead EE, Park BJ, et al. **Cardiovascular safety of methylphenidate** among children and young people with attention-deficit/hyperactivity disorder (ADHD): nationwide self controlled case series study. BMJ. 2016 May 31;353:i2550.

[32] Vetter VL *et al*. Cardiovascular Monitoring of Children and Adolescents with heart Disease Receiving Stimulant Drugs. A Scientific Statement from the American Heart Association Council on Cardiovascular disease in the Young Congenital Cardiac Defects Committee and the Council on Cardiovascular Nursing. *Circulation*. Published online April 21, 2008. DOI: 10.1161/CIRCULATIONAHA.107.189473.
(Perrin JM, Friedman RA, Knilans TK; Black Box Working Group; Section on Cardiology and Cardiac Surgery. Cardiovascular monitoring and stimulant drugs for attention-deficit/hyperactivity disorder. Pediatrics. 2008 Aug;122(2):451-3.)
October 27, 2009 -- Electrocardiograms (ECG) are not recommended as a routine step prior to starting medications employed to control attention deficit/hyperactivity disorder (ADHD), according to a joint statement issued by the Canadian Cardiovascular Society (CCS), the Canadian Pediatric Society (CPS), and the Canadian Academy of Child and Adolescent Psychiatry (CACAP).
Warren AE, Hamilton RM, Bélanger SA, et al. Cardiac risk assessment before the use of stimulant medications in children and youth: A joint position statement by the Canadian Paediatric Society, the Canadian Cardiovascular Society, and the Canadian Academy of Child and Adolescent Psychiatry. Can J Cardiol. 2009 Nov;25(11):625-30.
Bélanger SA, Warren AE, Hamilton RM, et al. Cardiac risk assessment before the use of stimulant medications in children and youth. A joint position statement by the Canadian Paediatric Society, the Canadian Cardiovascular Society, and the Canadian Academy of Child and Adolescent Psychiatry. Paediatr Child Health 2009;14(9):579-585. http://www.cps.ca/English/statements/PP/CPS09-02.pdf
Thomas PE et al. Impact of the American Heart Association scientific statement on screening electrocardiograms and stimulant medications. Arch Pediatr Adolesc Med 2011 Feb; 165:166.
Vitiello B, Elliott GR, Swanson JM, et al. Blood Pressure and **Heart Rate** Over 10 Years in the Multimodal Treatment Study of Children With ADHD (**MTA**) . Am J Psychiatry. 2011 Sep 2.
Leslie LK, Rodday AM, Saunders TS et al. **Cardiac Screening** Prior to Stimulant Treatment of ADHD: A Survey of US-Based Pediatricians. Pediatrics. 2012 Jan 16.

[33] Polzer J, Bangs ME, Zhang S, Dellva MA, Tauscher-Visniewski S, Acharya N, et al. Meta-Analysis of Aggression or Hostility Events in Randomized, Controlled Clinical Trials of Atomoxetine for ADHD. *Biol Psychiatry* 2007;61:713–719.

[34] Poulton A. Growth on stimulant medication; clarifying the confusion: a review. *Arch Dis Child.* 2005;90;801-806.
Swanson J, Greenhill L, Wigal T, et al. Stimulant-related reductions of growth rates in the **PATS**. J Am Acad Child Adolesc Psychiatry. 2006 Nov;45(11):1304-13. For 95 children who remained on medication, annual growth rates were 20.3% less than expected for height (5.41 cm/yr-6.79 cm/yr=-1.38 cm/yr) and 55.2% for weight (1.07 kg/yr-2.39 kg/yr=-1.32 kg/yr).
Faraone SV, Biederman J, Morley CP, Spencer TJ. Effect of Stimulants on Height and Weight: A Review of the Literature. J Am Acad Child Adolesc Psychiatry. 2008 Jun 20. [Epub ahead of print] Treatment with stimulants in childhood modestly reduced expected height and weight. Although these effects attenuate over time and some data suggest that ultimate adult growth parameters are not affected, more work is needed to clarify the effects of continuous treatment from childhood to adulthood. Although physicians should monitor height, deficits in height and weight do not appear to be a clinical concern for most children treated with stimulants.
Schwartz BS, Bailey-Davis L, Bandeen-Roche K, et al. Attention Deficit Disorder, Stimulant Use, and Childhood Body Mass Index Trajectory. Pediatrics. 2014 Mar 17.

[35] **MTA** Cooperative Group. National Institute of Mental Health multimodal treatment study of ADHD follow-up: changes in effectiveness and growth after the end of treatment. *Pediatrics* 2004;113:762-769.

[36] **MTA** Cooperative Group. Effects of stimulant medication on **growth rates across 3 years** in the MTA follow-up. *J Am Acad Child Adolesc Psychiatry 2007*;46:1015-1027.
Harstad EB, Weaver AL, Katusic SK, et al. **ADHD, Stimulant Treatment**, and **Growth**: A Longitudinal Study. Pediatrics. 2014 Sep 1.

[37] Wilens TE, Lenard MD, Adler A, Adams J, Sgambati S, Rotrosen J, Sawtelle R, Utzinger L, Fusillo S. Misuse and diversion of stimulants prescribed for ADHD: a systematic review of the literature. *J Am Acad Child Adolesc Psychiatry* 2008;47:21-31.

[38] Wilens TE, Faraone SV, Biederman J, Gunawardene S. Does stimulant therapy of attention-deficit/hyperactivity disorder beget later substance abuse? A meta-analytic review of the literature. *Pediatrics* 2003;111:179-185.

[39] Biederman J, Monuteaux MC, Spencer T, Wilens TE, MacPherson HA, Faraone SV. Stimulant therapy and risk for subsequent substance use disorders in male adults with ADHD: a naturalistic controlled 10-year follow-up study. *Am J Psychiatry* 2008;165, 597–603.
Biederman, Joseph, Monuteaux, Michael C., et al. Do **Stimulants Protect Against Psychiatric Disorders** in Youth With ADHD? A 10-Year Follow-up Study Pediatrics 2009 124: 71-78

[40] Mannuzza S, Klein RG, Truong NL, Moulton JL III, Roizen ER, Howell KH, Castellanos FX. Age of methylphenidate treatment initiation in children with ADHD and later substance abuse: prospective follow-up into adulthood. *Am J Psychiatry* 2008;165: 604–609.
Wilens TE, Adamson J, Monuteaux MC, et al. Effect of prior stimulant treatment for attention-deficit/hyperactivity disorder on subsequent risk for cigarette smoking and alcohol and drug use disorders in adolescents. Arch Pediatr Adolesc Med. 2008 Oct;162(10):916-21. Stimulant therapy does not increase but rather reduces the risk for cigarette smoking and SUDs in adolescents with ADHD.
Setlik J, Bond GR, Ho M. Adolescent Prescription ADHD Medication Abuse Is Rising Along With Prescriptions for These Medications. Pediatrics. 2009 Aug 24.
Quinn PD, Chang Z, Hur K, et al. ADHD Medication and Substance-Related Problems. Am J Psychiatry. 2017 Jun 29:appiajp201716060686.

[41] Dopheide JA, Theesen KA, Malkin M. Chapter 61: Childhood Disorders. In: DiPirio JT, Talbert RL, Hayes PE et al, eds. Pathophysiologic Approach. 6th Edition, McGraw-Hill Co., Inc., NY, 2005.
45 Humphreys C, Garcia-Bournissen F, Ito S, Koren G. Exposure to attention deficit hyperactivity disorder medications during pregnancy. Canadian Family Physician 2011; 53:1153-55.
46. Thomas R, Sanders S, Doust J, Beller E, Glasziou P. Prevalence of Attention Deficit/Hyperactivity Disorder: A Systematic Review and Meta-analysis. Pediatrics 2015; 135(4).
47. Dynamed 2019.

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Additional ADHD Treatment References:

AACAP-Practice parameter on the use of **psychotropic medication in children and adolescents**. J Am Acad Child Adolesc Psychiatry. 2009 Sep;48(9):961-73.
Abbas R, Childress AC, Nagraj P, et al. **Relative Bioavailability of Methylphenidate Extended-release Chewable Tablets** Chewed Versus Swallowed Whole. Clin Ther. 2018 Apr 24.
Adams J, Alipio-Jocson V, Inoyama K, et al. **Methylphenidate, cognition, and epilepsy**: A double-blind, placebo-controlled, single-dose study. Neurology. 2017 Jan 31;88(5):470-476
Admon LK, Bart G, Kozhimannil KB, et al. **Amphetamine- and Opioid-Affected Births**: Incidence, Outcomes, and Costs, United States, 2004-2015. Am J Public Health. 2018 Nov 29:e1-e7.
Agnew-Blais JC, Polanczyk GV, Danese A, et al. Evaluation of the **Persistence, Remission, and Emergence of Attention-Deficit/Hyperactivity Disorder in Young Adulthood**. JAMA Psychiatry. 2016 May 18. doi: 10.1001/jamapsychiatry.2016.0465.
Aguirre Castaneda RL, Kumar S, Voigt RG, et al. **Childhood Attention-Deficit/Hyperactivity Disorder, Sex, and Obesity**: A Longitudinal Population-Based Study. Mayo Clin Proc. 2016 Feb 3.
Ahuja A, Martin J, Langley K, et al. **Intellectual Disability** in Children with Attention Deficit Hyperactivity Disorder. J Pediatr. 2013 Apr 19.
Aman MG, Bukstein OG, et al. What does **risperidone** add to parent training and stimulant for severe aggression in child **attention-deficit/hyperactivity** disorder? J Am Acad Child Adolesc Psychiatry. 2014 Jan;53(1):47-60.e1.
American Academy of Pediatrics (AAP): Subcommittee on Attention-Deficit/Hyperactivity Disorder, Steering Committee on Quality Improvement and Management. ADHD: Clinical Practice Guideline for the Diagnosis, Evaluation, and Treatment of Attention-Deficit/Hyperactivity Disorder in Children and Adolescents. Pediatrics. 2011 Oct 16. **Updated Oct 2019**.
American Psychiatric Association Brochures: http://www.healthyminds.org/Functional-Library/brochures.aspx
Amiri S, Farhang S, Ghoreishizadeh MA, Malek A, Mohammadzadeh S. Double-blind controlled trial of **venlafaxine** for treatment of adults with attention deficit/hyperactivity disorder. Hum Psychopharmacol. 2012 Jan;27(1):76-81.
Anagnostou E, Zwaigenbaum L, Szatmari P, et al. **Autism spectrum disorder**: advances in evidence-based practice. CMAJ. 2014 Jan 13
Ask H, Gustavson K, Ystrom E, et al. Association of **Gestational Age at Birth** With Symptoms **of Attention-Deficit/Hyperactivity Disorder in Children**. JAMA Pediatr. 2018 Jun 25.

Barbaresi WJ, Colligan RC, Weaver AL, et al. **Mortality (suicide), ADHD, and Psychosocial Adversity** in Adults With Childhood ADHD: A Prospective Study. Pediatrics. 2013 Mar 4.

Barbaresi WJ. Improving Care for Children With ADHD: The Information is Just a **Rating Scale Away**. Pediastrics. 2016 Feb 29.

Barnett R. **Attention deficit hyperactivity disorder**. Lancet. 2016 Feb 20;387(10020):737.

Bateman B, et al. The effects of a double blind, placebo controlled, **artificial food colourings and benzoate preservative** challenge on hyperactivity in a general population sample of preschool children. Arch Dis Child. 2004 Jun;89(6):506-11.

Battleday R, Brem AK. **Modafinil** for cognitive **neuroenhancement** in healthy non-sleep-deprived subjects: a systematic review. Eur Neuropsychopharmacol2015,.

Bélanger SA, Andrews D, Gray C, et al; Canadian Paediatric Society, Mental Health and Developmental Disabilities Committee. ADHD in children and youth: Part 1—**Etiology, diagnosis, and comorbidity**. Paediatr Child Health 2018;23:447-53. https://www.cps.ca/en/documents/position/adhd-etiology-diagnosis-and-comorbidity (accessed November 14, 2018).

Bennett, Amanda E., Power, Thomas J., Eiraldi, Ricardo B., et al. Identifying Learning Problems in Children Evaluated for ADHD: The Academic Performance Questionnaire (**APQ**). Pediatrics 2009 124: e633-e639.

Bertelsen EN, Larsen JT, Petersen L, et al. Childhood **Epilepsy**, Febrile Seizures, and Subsequent Risk of ADHD. Pediatrics. 2016 Jul 13.

Bezchlibnyk-Butler KZ. **Clinical Handbook of Psychotropic Drugs, 22nd Ed**. 22nd Editors: Procyshyn RM, Bezchlibnyk-Butler KZ, Jeffries JJ. Hogrefe Publishing, Massachusetts, 2017.

Biederman, Joseph, Monuteaux, Michael C., et al. Do Stimulants **Protect Against Psychiatric Disorders** in Youth With ADHD? A 10-Year Follow-up Study Pediatrics 2009 124: 71-78

Biederman J, DiSalvo M, Fried R, et al. Quantifying the **Protective Effects of Stimulants** on Functional Outcomes in Attention-Deficit/Hyperactivity Disorder: A Focus on Number Needed to Treat Statistic and Sex Effects. J Adolesc Health. 2019 Jul 3.

Biederman J, Spencer TJ, Monuteaux MC, et al. A naturalistic 10-year prospective study of **height and weight** in children with attention-deficit hyperactivity disorder grown up: sex and treatment effects. J Pediatr. 2010 Oct;157(4):635-40, 640.e1.

Biederman J, Melmed RD, Patel A, et al. A randomized, double-blind, placebo-controlled study of **Guanfacine** extended release in children and adolescents with attention-deficit/hyperactivity disorder. Pediatrics. 2008 Jan;121(1):e73-e84.

Bloch MH, Panza KE, Landeros-Weisenberger A, Leckman JF. Meta-analysis: treatment of attention-deficit/hyperactivity disorder in children with **comorbid tic disorders**. J Am Acad Child Adolesc Psychiatry. 2009 Sep;48(9):884-93.

Blumer JL, Findling RL, Shih WJ, et al. Controlled clinical trial of **zolpidem** failed to decrease latency for the treatment of insomnia associated with attention-deficit/ hyperactivity disorder in children 6 to 17 years of age. Pediatrics. 2009 May;123(5):e770-6.

Bolea-Alamanac BM, Green A, Verma G, et al. **Methylphenidate use in pregnancy and lactation**, a systematic review of evidence. Br J Clin Pharmacol. 2013 Apr 18.

Bouchard MF, Bellinger DC, Wright RO, Weisskopf MG. Attention-Deficit/Hyperactivity Disorder and Urinary Metabolites of Organophosphate **Pesticides**. Pediatrics. 2010 May 17.

Bouziane C, Filatova OG, Schrantee A, et al. **White Matter by Diffusion MRI Following Methylphenidate** Treatment: A Randomized Control Trial in Males with Attention-Deficit/Hyperactivity Disorder. Radiology. 2019 Aug 13:182528.

Brinkman WB, Sherman SN, Zmitrovich AR, et al. **Parental angst** making and revisiting decisions about treatment of attention-deficit/hyperactivity disorder. Pediatrics. 2009 Aug;124(2):580-9. Epub 2009 Jul 27.

Brinkman WB, Epstein JN, Auinger P, et al. Association of attention-deficit/hyperactivity disorder and **conduct disorder with early tobacco and alcohol use**. Drug Alcohol Depend. 2014 Dec 2.

Brinkman WB, Sucharew H, Majcher JH, et al. Predictors of **Medication Continuity in Children With ADHD**. Pediatrics. 2018 Jun;141(6).

Brook JS, Brook DW, Zhang C, et al. Adolescent ADHD and adult **physical and mental health, work performance, and financial stress**. Pediatrics. 2013 Jan;131(1):5-13.

Brosco JP, Bona A. **Changes in Academic Demands** and Attention-Deficit/Hyperactivity Disorder in Young Children. JAMA Pediatr. 2016 Feb 22.

Brownley KA, Berkman ND, Peat CM, et al. **Binge-eating disorder** in adults: a systematic review and meta-analysis. Ann Intern Med. 2016. [Epub ahead of print]. doi: 10 .7326/M15-2455. (Cognitive behavioral therapy, lisdexamfetamine, SGAs, topiramate)

Bowers S. **Why are we failing young patients with ADHD**? BMJ. 2014 Oct 13;349:g6082.

Candy B Jones L Williams R Tookman A King M. **Psychostimulants for depression**. Cochrane Database Syst Rev. 2008 Apr 16;(2):CD006722. There is some evidence that in the short-term, PS reduce symptoms of depression. Whilst this reduction is statistically significant, the clinical significance is less clear.

Carroll AE, Bauer NS, Dugan TM, et al. Use of a **Computerized Decision Aid for ADHD Diagnosis**: A Randomized Controlled Trial. Pediatrics. 2013 Aug 19.

Castells X, Ramos-Quiroga JA, Bosch R, et al. **Amphetamines for Attention Deficit Hyperactivity Disorder (ADHD) in adults**. Cochrane Database of Systematic Reviews 2011, Issue 6. Art. No.: CD007813. DOI: 10.1002/14651858.CD007813.pub2. Amphetamines improved short-term ADHD symptom severity. MAS also increased retention in treatment. Amphetamines were associated with higher attrition due to adverse events. The short study length and the restrictive inclusion criteria limit the external validity of these findings.

Caye A, Rocha TB, Anselmi L, et al. Attention-Deficit/Hyperactivity Disorder Trajectories From **Childhood to Young Adulthood**: Evidence From a **Birth Cohort** Supporting a Late-onset Syndrome. JAMA Psychiatry. 2016 May 18.

CDC June/10 About one fifth of US high school students reported ever having used **prescription drugs not prescribed** to them, such as OxyContin, Percocet, Vicodin, Adderall, Ritalin, and Xanax. The CDC reports the first assessment of such use within the National Youth Risk Behavior Survey. In addition, prescription drug abuse was more common among white than Hispanic or black students. The agency highlighted these findings from the 2009 survey in the context of an ongoing national trend toward higher rates of nonsuicide-related overdoses and deaths associated with prescription drug abuse. 2009 National Youth Risk Behavior Survey (Free PDF)CDC news release (Free) 2007 *MMWR* article on unintentional poisoning deaths (Free)

Chan E, Fogler JM, Hammerness PG. **Treatment of Attention-Deficit/Hyperactivity Disorder** in **Adolescents**: A Systematic Review. JAMA. 2016 May 10;315(18):1997-2008.

Chang LY, Wang MY, Tsai PS. **Diagnostic Accuracy of Rating Scales** for Attention-Deficit/Hyperactivity Disorder: A Meta-analysis. Pediatrics. 2016 Feb 29.

Chang Z, Lichtenstein P, D'Onofrio BM, et al. Serious **Transport Accidents** in Adults With Attention-Deficit/Hyperactivity Disorder and the Effect of Medication: A Population-Based Study. JAMA Psychiatry. 2014 Jan 29

Chang Z, Quinn PD, Hur K, et al. Association between medication use for attention-deficit/ hyperactivity disorder and **risk of motor vehicle crashes** [online May 10, 2017].JAMA Psychiatry. doi:10.1001/jamapsychiatry.2017.0659

Charach A, Carson P, Fox S, et al. **Interventions for Preschool Children** at High Risk for ADHD: A Comparative Effectiveness Review. Pediatrics. 2013 Apr 1. (PBT: parent behaviour training)

Chen LY, Crum RM, Strain EC, et al. Prescriptions, nonmedical use, and **emergency department visits involving prescription stimulants**. J Clin Psychiatry. 2016 Feb 16.

Chen MH, Lan WH, Bai YM, et al. Influence of **Relative Age** on Diagnosis and Treatment of Attention-Deficit Hyperactivity Disorder in Taiwanese Children. J Pediatr. 2016 Mar 2.

Chen Q, Sjölander A, Runeson B, et al. Drug treatment for attention-deficit/hyperactivity disorder and **suicidal behaviour**: register based study. BMJ. 2014 Jun 18;348:g3769.

Chen VC, Chan HL, Wu SI, et al. Attention-Deficit/Hyperactivity Disorder and **Mortality Risk in Taiwan**. JAMA Netw Open. 2019 Aug 2;2(8):e198714.

Cheng C, La Grenade L, Diak IL, et al. **Chemical Leukoderma** Associated with **Methylphenidate Transdermal System**: Data From the US Food and Drug Administration Adverse Event Reporting System. J Pediatr. 2016 Oct 10.

Ching C, Eslick GD, Poulton AS. Evaluation of **methylphenidate safety and maximum-dose titration rationale** in attention-deficit/hyperactivity disorder: a meta-analysis [online May 28, 2019].JAMA Pediatr. doi:10.1001/jamapediatrics.2019.0905

Chorozoglou M, Smith E, Koerting J, et al. **Preschool hyperactivity is associated with long-term economic burden**: evidence from a longitudinal health economic analysis of costs incurred across childhood, adolescence and young adulthood. J Child Psychol Psychiatry 2015;56:966–75.

Christakis DA. **Rethinking Attention-Deficit/Hyperactivity Disorder**. JAMA Pediatr. 2016 Jan 4:1-2.

Chudal R, Joelsson P, Gyllenberg D, et al. **Parental age and the risk** of attention-deficit/hyperactivity disorder: a nationwide, population-based cohort study. J Am Acad Child Adolesc Psychiatry. 2015 Jun;54(6):487-94.e1.

Citrome L. **Lisdexamfetamine** for **binge eating disorder** in adults: a systematic review of the efficacy and safety profile for this newly approved indication - what is the number needed to treat, number needed to harm and likelihood to be helped or harmed?. Int J Clin Pract. 2015 Mar 6.

Clark B, Bélanger SA; Canadian Paediatric Society, Mental Health and Developmental Disabilities Committee. ADHD in children and youth: Part 3—**Assessment and treatment with comorbid ASD, ID, or prematurity**. Paediatr Child Health 2018;23:485-90. https://www.cps.ca/en/documents/position/adhd-comorbid-asd-id-or-prematurity (accessed November 14, 2018).

Coffey SF. Banducci AN, Vinci C. Common Questions About **Cognitive Behavior Therapy** for Psychiatric Disorders. Am Fam Physician. 2015;92(9):807-812.

Coker TR, Elliott MN, Toomey SL, et al. **Racial and Ethnic Disparities** in ADHD Diagnosis and Treatment. Pediatrics. 2016 Aug 23.

Collins KP, Cleary SD. **Racial and ethnic disparities in parent-reported diagnosis of ADHD**: National Survey of Children's Health (2003, 2007, and 2011). J Clin Psychiatry. 2015 Dec 8.

Conklin, Heather M., Lawford, Joanne, et al. Side Effects of Methylphenidate in Childhood **Cancer Survivors**: A Randomized Placebo-Controlled Trial Pediatrics 2009 124: 226-233.

Conklin HM., Reddick WE., Ashford J, et al. Long-Term Efficacy of Methylphenidate in Enhancing Attention Regulation, Social Skills, and Academic Abilities of **Childhood Cancer Survivors**. *JCO* JCO.2010.28.4026; published online on September 13, 2010.;

Connor DF, Findling RL, Kollins SH, et al. Effects of **Guanfacine** extended release on oppositional symptoms in children aged 6-12 years with attention-deficit hyperactivity disorder and oppositional symptoms: a randomized, double-blind, placebo-controlled trial. CNS Drugs. 2010 Sep 1;24(9):755-68.

Conrad P, Bergey MR. The impending **globalization of ADHD**: Notes on the **expansion** and growth of a **medicalized disorder**. Soc Sci Med. 2014 Dec;122:31-43.

Cooper WO, Habel LA, Sox CM, et al. **ADHD drugs and serious cardiovascular events** in children and young adults. N Engl J Med2011; DOI:10.1056/NEJMoa1110212.

Cortese S. **Psychosis** during Attention Deficit-Hyperactivity Disorder Treatment with Stimulants. N Engl J Med. 2019 Mar 21;380(12):1178-1180

Cortese S, Coghill D. **Twenty years of research** on attention-deficit/hyperactivity disorder (ADHD): looking back, looking forward. Evid Based Ment Health. 2018 Nov; 21(4):173-176.

Cortese S, Ramos Olazagasti MA, Klein RG, et al. **Obesity in Men** With Childhood ADHD: A 33-Year Controlled, Prospective, Follow-up Study. Pediatrics. 2013 May 20.

Cortese S, Moreira-Maia CR, St Fleur D, et al. Association Between **ADHD and Obesity**: A Systematic Review and Meta-Analysis. Am J Psychiatry. 2016 Jan;173(1):34-43.

Cortese S, Sun S, Zhang J, et al. Association between **attention deficit hyperactivity disorder and asthma**: a systematic review and meta-analysis and a Swedish population-based study. Lancet Psychiatry 2018; published online July 24.

Cortese S, Adamo N, Del Giovane C, et al. Comparative **efficacy and tolerability of medications for attention-deficit hyperactivity disorder in children, adolescents, and adults**: a systematic review and network meta-analysis. Lancet Psychiatry 2018; published online Aug 7.

Cross-Disorder Group of the Psychiatrics Genomics Consortium. Identification of **risk loci with shared effects on five major psychiatric disorders**: a genome-wide analysis. Lancet 2013; online Feb 28.

Cummings JR, Ji X, Allen L, et al. **Racial and Ethnic Differences in ADHD** Treatment Quality Among Medicaid-Enrolled Youth. Peds. 2017;139(6):e20162444.

Curry A, Yerys B, Metzger K, et al. Traffic crashes, violations, and suspensions among **young drivers with ADHD**. Pediatrics. 2019;143(6):e20182305

Curry AE, Metzger KB, Pfeiffer MR, et al. **Motor Vehicle Crash Risk** Among Adolescents and Young Adults With Attention-Deficit/Hyperactivity Disorder. JAMA Pediatr. 2017 Jun 12.

Dalsgaard S, Kvist AP, Leckman JF, et al. **Cardiovascular Safety of Stimulants** in Children with Attention-Deficit/Hyperactivity Disorder: A Nationwide Prospective Cohort Study. J Child Adolesc Psychopharmacol. 2014 Jun 23.

Dalsgaard S, Ostergaard SD, Leckman JF, et al. **Mortality in children, adolescents, and adults** with attention deficit hyperactivity disorder: a nationwide cohort study. Lancet 2015; online Feb 26

Dalsgaard S, Leckman JF, Mortensen PB, et al. Effect of **drugs on the risk of injuries in children** with attention deficit hyperactivity disorder: a prospective cohort study. Lancet Psychiatry. 2015 Aug;2(8):702-9.

Danielson ML, Visser SN, Chronis-Tuscano A, DuPaul GJ. A National Description of **Treatment among United States Children and Adolescents with Attention-Deficit/Hyperactivity Disorder**. J Pediatr. 2017 Nov 10.

Davidson MA. ADHD in **adults**: a review of the literature. J Atten Disord. 2008 May;11(6):628-41. Epub 2007 Dec 19.

De Crescenzo F, Cortese S, Adamo N, et al. **Pharmacological and non-pharmacological treatment of adults with ADHD**: a meta-review. Evid Based Ment Health. 2016 Dec 19.

de Kieviet JF, van Elburg RM, Lafeber HN, Oosterlaan J. Attention Problems of **Very Preterm Children** Compared with Age-Matched Term Controls at School-Age. J Pediatr. 2012 Jun 14.

Denchev P, Kaltman J, Schoenbaum M, et a. Modeled economic evaluation of alternative strategies to **reduce sudden cardiac** death among children treated for attention deficit/hyperactivity disorder. Circulation 2010; DOI:10.1161/CIRCULATIONAHA.109.901256.

Dunne EM, Hearn LE, Rose JJ, Latimer WW. ADHD as a risk factor for **early onset and heightened adult problem severity of illicit substance** use: an accelerated gateway model. Addict Behav. 2014 Dec;39(12):1755-8.

Efron D, Sciberras E, Anderson V, et al. **Functional status in children with ADHD at age 6-8:** a controlled community study. Pediatrics. 2014 Oct;134(4):e992-e1000.

Eiland LS, Bell EA, Erramouspe J. **Priapism** Associated With the Use of **Stimulant Medications** and **Atomoxetine** for Attention-Deficit/Hyperactivity Disorder in Children. Ann Pharmacother. 2014 Oct;48(10):1350-1355.

Epstein JN, Langberg JM, Lichtenstein PK, et al. Use of an **Internet Portal** to Improve Community-Based Pediatric ADHD Care: A Cluster Randomized Trial. Pediatrics. 2011 Oct 17.

Epstein JN, Kelleher KJ, Baum Ret al. Impact of a **Web-Portal Intervention** on Community ADHD Care and Outcomes. Pediatrics. 2016 Aug;138(2)

Epstein T, Patsopoulos NA, Weiser M. **Immediate-release methylphenidate** for attention deficit hyperactivity disorder (ADHD) in adults. Cochrane Database Syst Rev. 2014 Sep 18;9:CD005041. Data from randomized controlled trials suggest that immediate-release methylphenidate is efficacious for treating adults with ADHD with symptoms of hyperactivity, impulsivity, and inattentiveness, and for improving their overall clinical condition. Trial data suggest that adverse effects from immediate-release methylphenidate for adults with ADHD are not of serious clinical significance, although this conclusion may be limited, certainly in the case of weight loss, by the short duration of published studies.

Epstein JN, Kelleher KJ, Baum R, et al. **Variability in ADHD Care in Community**-Based Pediatrics. Pediatrics. 2014 Nov 3.

Espay AJ, Dwivedi AK, Payne M, et al. **Methylphenidate** for gait impairment in **Parkinson disease**: A randomized clinical trial. Neurology. 2011 Apr 5;76(14):1256-62. (lack of benefit)

Faraone SV, Glatt SJ. A comparison of the efficacy of medications for adult attention-deficit/hyperactivity disorder using meta-analysis of **effect sizes**. J Clin Psychiatry. 2009 Dec 29.

Faraone SV, McBurnett K, Sallee FR, et al. **Guanfacine** Extended Release: A Novel Treatment for Attention-Deficit/Hyperactivity Disorder in Children and Adolescents. Clin Ther. 2013 Oct 16.

Faraone SV. Attention deficit hyperactivity disorder and **premature death**. Lancet. 2015 Feb 24.

FDA is warning consumers and health care professionals about a **counterfeit version of Teva Pharmaceutical Industries' Adderall 30 milligram tablets** that is being purchased on the Internet. FDA's preliminary laboratory tests revealed that the counterfeit version of Teva's Adderall 30 mg tablets contained the wrong active ingredients. Adderall contains four active ingredients – dextroamphetamine saccharate, amphetamine aspartate, dextroamphetamine sulfate, and amphetamine sulfate. Instead of these active ingredients, the counterfeit product contained tramadol and acetaminophen, which are ingredients in medicines used to treat acute pain.

FDA Dec/13 is warning that **methylphenidate products**, one type of stimulant drug used to treat attention deficit hyperactivity disorder (ADHD), may in rare instances cause prolonged and sometimes painful erections known as **priapism**.

Feldman HM, Reiff MI. Clinical practice. **Attention deficit-hyperactivity disorder in children and adolescents**. N Engl J Med. 2014 Feb 27;370(9):838-46.

Feldman ME, Charach A, Bélanger SA; Canadian Paediatric Society, Mental Health and Developmental Disabilities Committee. **ADHD in children and youth: Part 2—Treatment**. Paediatr Child Health 2018;23:462-72. https://www.cps.ca/en/documents/position/adhd-2-treatment (accessed November 14, 2018).

Felt BT, Biermann B, Christner J et al. **Diagnosis and Management of ADHD in Children**. Am Fam Physician. 2014;90(7):456-464.

Feuer AJ, Thai A, Demmer RT, et al. Association of **Stimulant Medication Use With Bone Mass** in Children and Adolescents With Attention-Deficit/Hyperactivity Disorder. JAMA Pediatr. 2016 Oct 3:e162804.

Fiks AG, Mayne S, Debartolo E, et al. **Parental Preferences** and Goals Regarding ADHD Treatment. Pediatrics. 2013 Sep 2.

Fiks AG, Ross ME, Mayne SL, et al. **Preschool ADHD diagnosis and stimulant use before and after the 2011 AAP Practice Guideline**. Pediatrics. 2016;138(6):e20162025

Findling RL, Bukstein OG, et al. A randomized, double-blind, placebo-controlled, parallel-group study of **methylphenidate transdermal system** in pediatric patients with attention-deficit/hyperactivity disorder. J Clin Psychiatry. 2008 Jan;69(1):149-59.

Fitzgerald C, Dalsgaard S, Nordentoft M, et al. **Suicidal behaviour** among persons with attention-deficit hyperactivity disorder. Br J Psychiatry. 2019 Jun 7:1-6.

Fleming M, Fitton CA, Steiner MFC, et al. **Educational and Health Outcomes** of Children Treated for Attention-Deficit/Hyperactivity Disorder. JAMA Pediatr. 2017 May 1:e170691.

Franz AP, Bolat GU, Bolat H, et al. Attention-deficit/hyperactivity disorder and **very preterm/very low birth weight**: a meta-analysis. Pediatrics. 2018;141(1):e20171645

Fritz KM, O'Connor PJ. **Acute Exercise** Improves Mood and Motivation in Young Men with ADHD Symptoms. Med Sci Sports Exerc. 2016 Jun;48(6):1153-60.

Froehlich TE, Brinkman WB. **Multimodal Treatment of the School-aged Child** With Attention-Deficit/Hyperactivity Disorder. JAMA Pediatr. 2017 Dec 11.

Froehlich TE. ADHD Medication Adherence in College Students-A Call to Action for Clinicians and Researchers: Commentary on "**Transition to College and Adherence to Prescribed Attention Deficit Hyperactivity Disorder Medication**". J Dev Behav Pediatr. 2018 Jan;39(1):77-78.

Gadow KD, Arnold LE, Molina BS, et al. **Risperidone added** to parent training and stimulant medication: effects on attention-deficit/hyperactivity disorder, oppositional defiant disorder, conduct disorder, and peer aggression. J Am Acad Child Adolesc Psychiatry. 2014 Sep;53(9):948-959.e1.

Gellad WF, Stein BD, Ruder T, et al. **Geographic Variation in Receipt of Psychotherapy** in Children Receiving Attention-Deficit/Hyperactivity Disorder Medications. JAMA Pediatr. 2014 Sep 22.

Getahun D, Rhoads GG, Demissie K, et al. **In utero exposure to ischemic-hypoxic conditions** and attention-deficit/hyperactivity disorder. Pediatrics. 2013 Jan;131(1):e53-61.

Getahun D, Jacobsen SJ, Fassett MJ, et al. **Recent Trends** in Childhood Attention-Deficit/Hyperactivity Disorder. JAMA Pediatr. 2013 Jan 21:1-7.

Gillies D, Sinn JKh, Lad SS, et al. **Polyunsaturated fatty acids (PUFA)** for attention deficit hyperactivity disorder (ADHD) in children and adolescents. Cochrane Database Syst Rev. 2012 Jul 11;7:CD007986. Overall, there is little evidence that PUFA supplementation provides any benefit for the symptoms of ADHD in children and adolescents.

Ginsberg Y, Lindefors N. **Methylphenidate treatment of adult male prison inmates** with attention-deficit hyperactivity disorder: randomised double-blind placebo-controlled trial with open-label extension. Br J Psychiatry [Internet]. 2012 Jan [cited 2017 Jun 8];200(1):68-73.

Gloss D, Varma JK, Pringsheim T, et al. Practice advisory: The utility of **EEG theta/beta power ratio** in ADHD diagnosis: Report of the Guideline Development, Dissemination, and Implementation Subcommittee of the American Academy of Neurology.Neurology. 2016 Oct 19.

Goldman RD. ADHD stimulants and their effect on **height** in children. Can Fam Physician. 2010 Feb;56(2):145-6.

Goldstein LB, Lennihan L, Rabadi MJ, et al. Effect of **Dextroamphetamine on Poststroke** Motor Recovery: A Randomized Clinical Trial. JAMA Neurol. 2018 Aug 27.

Goode AP, Coeytaux RR, Maslow GR, et al. **Nonpharmacologic Treatments for Attention-Deficit/Hyperactivity Disorder**: A Systematic Review. Pediatrics. 2018 Jun;141(6).

Goodman DM, Livingston EH. JAMA **patient page. Attention-deficit/hyperactivity disorder**. JAMA. 2013 May 1;309(17):1843.

Gordon-Lipkin E, Marvin AR, Law JK, et al**. Anxiety and Mood Disorder in Children With Autism Spectrum Disorder and ADHD**. Pediatrics. 2018 Apr;141(4).

Gorman DA, Abi-Jaoude E. Managing attention-deficit/hyperactivity disorder. CMAJ. 2013 Jun 24.

Graf WD, Nagel SK, Epstein LG, et al. **Pediatric neuroenhancement**: Ethical, legal, social, and neurodevelopmental implications. Neurology. 2013 Mar 13.

Greenhill LL, Posner K, Vaughan BS, Kratochvil CJ. Attention deficit hyperactivity disorder in **preschool** children. Child Adolesc Psychiatr Clin N Am. 2008 Apr;17(2):347-66, ix.

Gustavson K, Ystrom E, Stoltenberg C, et al. **Smoking in pregnancy** and child ADHD. Pediatrics. 2017;139(2):e20162509

Hammerness P, Joshi G, Doyle R et al. Do Stimulants **Reduce** the Risk for Cigarette **Smoking** in Youth with Attention-Deficit Hyperactivity Disorder? A Prospective, Long-Term, Open-Label Study of Extended-Release Methylphenidate. J Pediatr. 2012 Aug 7.

Harris MN, Voigt RG, Barbaresi WJ, et al. ADHD and **learning disabilities** in former late preterm infants: a population-based birth cohort. Pediatrics. 2013 Sep;132(3):e630-6.

Harstad E, Levy S; COMMITTEE ON SUBSTANCE ABUSE. **Attention-Deficit/Hyperactivity Disorder and Substance Abuse**. Pediatrics. 2014 Jun 30.

Harstad EB, Weaver AL, Katusic SK, et al. **ADHD, Stimulant Treatment**, and **Growth**: A Longitudinal Study. Pediatrics. 2014 Sep 1.

Hauck TS, Lau C, Wing LL, et al. **ADHD Treatment in Primary Care**. Can J Psychiatry 2017 Jan 1:706743716689055.

Health Canada Oct/11, is notifying healthcare professionals, patients and their caregivers of important safety information from clinical studies regarding the risk of **increased blood pressure** and **increased heart rate** with the use of STRATTERA **(atomoxetine)**.

Health Canada Mar/15 **ADHD drugs may increase risk of suicidal thoughts** and behaviours in some people; benefits still outweigh risks. Stronger, clearer warnings on the risk of suicidal thoughts and behaviours are being incorporated into the prescribing information for drugs used in the management of Attention Deficit Hyperactivity Disorder (ADHD).

Health Canada Apr/15: **Methylphenidate** Products – Risk of Priapism - Janssen Inc. - Novartis Pharmaceuticals - Purdue Pharma Inc. Prolonged and painful erections (**priapism**) have been very rarely reported in patients, including children, taking methylphenidate products. The prescribing information for these products has been updated to include this information.

Health Canada June/19: When used during pregnancy, **ALERTEC (modafinil)** has been associated with cases of major fetal congenital malformations, including congenital cardiac anomalies.

Henriksen L, Wu CS, Secher NJ, et. al. **Medical Augmentation of Labor** and the Risk of ADHD in Offspring: A Population-Based Study. Pediatrics. 2015 Feb 9. pii: peds.2014-1542.

Hines JL, King TS, Curry WJ. The **adult ADHD self-report scale for screening** for adult attention deficit-hyperactivity disorder (ADHD). J Am Board Fam Med. 2012 Nov;25(6):847-53. In this study, the 6-question screening tool was 92% sensitive and 69% specific in detecting adults with attention deficit-hyperactivity disorder (ADHD) in the primary care setting. The authors note that the reported population prevalence is 4.4%, which correlates with an expected positive predictive value of 12% (88% false positive rate) and a negative predictive value of 99%. Since approximately 7 of 8 of the positive results will be falsely positive, it remains important to obtain evidence from randomized trials that evaluate whether implementing this screening tool is cost-effective and leads to a clinically significant changes in treatment or outcomes. (LOE = 2b-)

Hoang U, James AC, Liyanage H, et al. **Determinants of inter-practice variation** in ADHD diagnosis and stimulant prescribing: cross-sectional database study of a national surveillance network. BMJ Evid Based Med. 2019 Aug;24(4):155-161.

Hodgkin D, Horgan CM, Quinn AE, et al. Management of **newer medications** for attention-deficit/hyperactivity disorder in commercial health plans. Clin Ther. 2014 Dec 1;36(12):2034-46.

Hoogman M, Bralten J, Hibar DP, et al. **Subcortical brain volume differences** in participants with attention deficit hyperactivity disorder in children and adults: a cross- sectional mega-analysis. Lancet Psychiatry 2017; online Feb 15.

Hoover RM, Hayes VA, Erramouspe J. Association Between **Prenatal Acetaminophen Exposure** and Future Risk of Attention Deficit/Hyperactivity Disorder in Children. Ann Pharmacother. 2015 Dec;49(12):1357-61.

Hosang GM, Lichtenstein P, Ronald A, et al. Association of Genetic and Environmental Risks for Attention-Deficit/Hyperactivity Disorder **With Hypomanic Symptoms in Youths**. JAMA Psychiatry. 2019 Aug 14.

Huang L, Wang Y, Zhang Let al. **Maternal Smoking** and Attention-Deficit/Hyperactivity Disorder **in Offspring**: A Meta-analysis. Pediatrics. 2017 Dec 29.

Huang KL, Wei HT, Hsu JW, et al. Risk of **suicide attempts** in adolescents and young adults with attention-deficit hyperactivity disorder: a nationwide longitudinal study. Br J Psychiatry. 2018 Apr;212(4):234-238.

Hudak ML, Tan RC et al. **Neonatal Drug Withdrawal**. Pediatrics. 2012 Jan 30.

Hudson JI, McElroy SL, Ferreira-Cornwell MC, et al. Efficacy of **Lisdexamfetamine in Adults With Moderate to Severe Binge-Eating Disorder**: A Randomized Clinical Trial. JAMA Psychiatry. 2017 Jul 12.

Huhn M, TardyM, Spineli LM, et al. Efficacy of **pharmacotherapy and psychotherapy** for adult psychiatric disorders: a systematic overview of meta-analyses [online April 30, 2014]. JAMA Psychiatry. doi:10.1001/jamapsychiatry.2014.112.

Humphreys KL, Eng T, Lee SS. **Stimulant Medication and Substance Use Outcomes**: A Meta-analysis. JAMA Psychiatry. 2013 Jul 1;70(7):740-9.

Huybrechts K, Broms G, Christensen L, et al. Association between **methylphenidate and amphtetamine use in pregnancy and risk of congenital malformations**. JAMA Psychiatry2017;(December). doi:10.1001/jamapsychiatry.2017.3644.

ICSI: Institute for Clinical Systems Improvement. Diagnosis and management of attention deficit hyperactivity disorder in primary care for school-age children and adolescents. Bloomington (MN): Institute for Clinical Systems Improvement (ICSI); 2010 Mar.

ICSI: Dobie C, Donald WB, Hanson M, Heim C, Huxsahl J, Karasov R, Kippes C, Neumann A, Spinner P, Staples T, Steiner L, Institute for Clinical Systems Improvement (ICSI). Diagnosis and management of attention deficit hyperactivity disorder in primary care for school-age children and adolescents. Bloomington (MN): Institute for Clinical Systems Improvement (ICSI); 2012 Mar.

Jasinski DR, Krishnan S. Abuse liability and safety of oral **lisdexamfetamine dimesylate in individuals with a history of stimulant abuse**. J Psychopharmacol. 2009 Jun;23(4):419-27.

Jimenez ME, Guevara JP. A 7-year-old boy experiencing **difficulty at school**. CMAJ. 2013 Sep 3.

Jo H, Schieve LA, Sharma AJ, et al. **Maternal Prepregnancy Body Mass Index** and Child Psychosocial Development at 6 Years of Age. Pediatrics. 2015 Apr 27

Ju-Young S, Roughead L, Park B-J, Pratt N. **Cardiovascular safety of methylphenidate** among children and young people with attention-deficit/hyperactivity disorder (ADHD): nationwide self controlled case series study. BMJ 2016;353:i2550.

Kaland ME, Klein-Schwartz. Comparison of **lisdexamfetamine and dextroamphetamine exposures reported to U.S. poison centers**. J Clin Toxicol. 2015; 53(5): 477-485.

Kale N. **Urine Drug Tests**: Ordering and Interpretation. Am Fam Physician. 2019;99(1):33-39.

Karceski S. **Diagnosis** of attention-deficit/hyperactivity disorder. Neurology. 2016 Nov 29;87(22):e272-e274

Keenan HT, Hall GC, Marshall SW. Early **head injury** and attention deficit hyperactivity disorder: retrospective cohort study. BMJ. 2008 Nov 6;337:a1984. doi: 10.1136/bmj.a1984. Medically attended head injury before 2 years of age does not seem to be causal in the development of attention deficit hyperactivity disorder. Medically attended injury before 2 years of age may be a marker for subsequent diagnosis of attention deficit hyperactivity disorder.

Kelly AS, Rudser KD, Dengel DR, et al. **Cardiac Autonomic Dysfunction** and **Arterial Stiffness** among Children and Adolescents with Attention Deficit Hyperactivity Disorder Treated with **Stimulants**. J Pediatr. 2014 Jul 8.

Kemper AR, et al. **Attention deficit hyperactivity disorder**: diagnosis & treatment in children & adolescents. Comparative Effectiveness Review No. 203. AHRQ Publication No. 18-EHC005-EF. Rockville, MD: Agency for Healthcare Research & Quality; Jan/18.

Khalife N, Kantomaa M, Glover V, et al. Childhood attention-deficit/hyperactivity disorder symptoms are **risk factors for obesity and physical inactivity** in adolescence. J Am Acad Child Adolesc Psychiatry. 2014 Apr;53(4):425-36.

King S, Griffin S, Hodges Z, Weatherly H, et al. A **systematic review** and economic model of the effectiveness and cost-effectiveness of methylphenidate, dexamfetamine and atomoxetine for the treatment of attention deficit hyperactivity disorder in children and adolescents. Health Technol Assess. 2006 Jul;10(23):iii-iv, xiii-146.

King SA, Casavant MJ, Spiller HA, et al. **Pediatric ADHD Medication** Exposures Reported to US **Poison Control Centers**. Pediatrics. 2018 May 21.

Klein RG, Mannuzza S, Olazagasti MA, et al. **Clinical and Functional Outcome** of Childhood Attention-Deficit/Hyperactivity Disorder **33 Years Later**. Arch Gen Psychiatry. 2012 Oct 15:1-9.

Kollins SH, Jain R, Brams M, et al. **Clonidine Extended-Release** Tablets as Add-on Therapy to Psychostimulants in Children and Adolescents With ADHD. Pediatrics. 2011 May 9.

Königs M, Heij HA, van der Sluijs JA, et al. **Pediatric Traumatic Brain Injury** and Attention Deficit. Pediatrics. 2015 Aug 3.

Kooij SJ, Bejerot S, Blackwell A, et al. **European consensus** statement on diagnosis and treatment of **adult ADHD**: The European Network Adult ADHD. BMC Psychiatry. 2010 Sep 3;10:67. ADHD often presents as an impairing lifelong condition in adults, yet it is currently underdiagnosed and treated in many European countries, leading to ineffective treatment and higher costs of illness. Expertise in diagnostic assessment and treatment of ADHD in adults must increase in psychiatry. Instruments for screening and diagnosis of ADHD in adults are available and appropriate treatments exist, although more research is needed in this age group.

Kotte A, Joshi G, Fried R, et al. **Autistic traits** in children with and without ADHD. Pediatrics. 2013 Sep;132(3):e612-22.

Kratochvil, Christopher J., Vaughan, Brigette S., Stoner, Julie A., et al. A Double-Blind, Placebo-Controlled Study of **Atomoxetine in Young Children** With ADHD. Pediatrics 2011 127: e862-e868. (age 5-6yr n=101 over 8weeks)

Krisanaprakornkit T, Ngamjarus C, Witoonchart C, Piyavhatkul N. **Meditation therapies** for attention-deficit/hyperactivity disorder (ADHD). Cochrane Database of Systematic Reviews 2010, Issue 6. Art. No.: CD006507. As a result of the limited number of included studies, the small sample sizes and the high risk of bias, we are unable to draw any conclusions regarding the effectiveness of meditation therapy for ADHD.

Kurlan R. Clinical practice. **Tourette's Syndrome**. N Engl J Med. 2010 Dec 9;363(24):2332-8.

Larson K, Russ SA, Kahn RS, Halfon N. Patterns of **Comorbidity, Functioning, and Service Use for US Children With ADHD**, 2007. Pediatrics. 2011 Mar;127(3):462-70.

Larsson H, Rydén E, Boman M, et al. **Risk of bipolar disorder and schizophrenia** in relatives of people with attention-deficit hyperactivity disorder. Br J Psychiatry. 2013 Aug;203:103-106.

Lavigne JV, Dulcan MK, LeBailly SA, Binns HJ, Cummins TK, Jha P. **Computer-assisted management** of attention-deficit/hyperactivity disorder. Pediatrics. 2011 Jul;128(1):e46-53.

Law EC, Sideridis GD, Prock LA, et al. Attention-Deficit/Hyperactivity Disorder in Young Children: **Predictors of Diagnostic Stability**. Pediatrics. 2014 Mar 17.

Layton TJ, Barnett ML, Hicks TR, Jena AB. **Attention Deficit-Hyperactivity Disorder and Month of School Enrollment**. N Engl J Med. 2018 Nov 29;379(22):2122-2130.

LeBlond E, Smith-Paine J, Riemersma JJ, et al. **Influence of Methylphenidate** on Long-Term Neuropsychological and Everyday Executive Functioning After Traumatic Brain Injury in Children with Secondary Attention Problems. J Int Neuropsychol Soc. 2019 Aug;25(7):740-749.

Leslie LK, Rodday AM, Saunders TS et al. **Cardiac Screening** Prior to Stimulant Treatment of ADHD: A Survey of US-Based Pediatricians. Pediatrics. 2012 Jan 16.

Lichtenstein P et al. Medication for attention deficit–hyperactivity disorder and **criminality**. N Engl J Med 2012 Nov 22; 367:2006.

Liew Z, Ritz B, Rebordosa C, Lee PC, Olsen J. **Acetaminophen** use during pregnancy, behavioural problems, and hyperkinetic disorders [online February 24, 2014]. *JAMA Pediatr*. doi:10.1001/jamapediatrics.2013.4914.

Linden S, Bussing R, Kubilis P, et al. Risk of **Suicidal Events With Atomoxetine** Compared to Stimulant Treatment: A Cohort Study. Pediatrics. 2016 May;137(5).

Lindstrom, Karolina, Lindblad, Frank, Hjern, Anders. **Preterm Birth** and Attention-Deficit/Hyperactivity Disorder in Schoolchildren. Pediatrics 2011 127: 858-865

Ljung T, Chen Q, Lichtenstein P, et al. Common Etiological Factors of Attention-Deficit/Hyperactivity Disorder and **Suicidal Behavior**: A Population-Based Study in Sweden. JAMA Psychiatry. 2014 Jun 25.

Lopez PL, Torrente FM, Ciapponi A,et al. **Cognitive behavioural interventions** for attention deficit hyperactivity disorder (ADHD) in adults. Cochrane Database of Systematic Reviews 2018, Issue 3. Art. No.: CD010840. There is low-quality evidence that cognitive-behavioural-based treatments may be beneficial for treating adults with ADHD in the short term. Reductions in core symptoms of ADHD were fairly consistent across the different comparisons: in CBT plus pharmacotherapy versus pharmacotherapy alone and in CBT versus waiting list. There is low-quality evidence that CBT may also improve common secondary disturbances in adults with ADHD, such as depression and anxiety.

Lovegrove MC, Mathew J, Hampp C, et al. Emergency Hospitalizations for Unsupervised **Prescription Medication Ingestions by Young Children**. Pediatrics. 2014 Sep 15. (buprenorphine & clonidine concerning)

Lupattelli A, Chambers CD, Bandoli G, et al. Association of **Maternal Use of Benzodiazepines and Z-Hypnotics During Pregnancy** With Motor and Communication Skills and Attention-Deficit/Hyperactivity Disorder kSymptoms in Preschoolers. JAMA Netw Open. 2019 Apr 5;2(4):e191435.

MacKenzie LE, Abidi S, Fisher HL, et al. **Stimulant Medication and Psychotic Symptoms** in **Offspring of Parents** With Mental Illness. Pediatrics. 2016 Jan;137(1):1-10.

Maher GM, O'Keeffe GW, Kearney PM, et al. Association of **Hypertensive Disorders of Pregnancy With Risk of Neurodevelopmental Disorders** in Offspring: A Systematic Review and Meta-analysis. JAMA Psychiatry. 2018 Jun 6.

Man KK, Chan EW, Coghill D, et al. **Methylphenidate and the Risk of Trauma**. Pediatrics. 2014 Dec 15.

Man KKC, Coghill D, Chan EW, et al. Association of **Risk** of **Suicide** Attempts With **Methylphenidate** Treatment. JAMA Psychiatry. 2017 Jul 26.

Marchese M, Koren G, Bozzo P. Is it safe to **breastfeed while taking methylphenidate**? Can Fam Physician. 2015 Sep;61(9):765-6.

Martinsson L, Hårdemark H, Eksborg S. Amphetamines for improving **recovery after stroke**. Cochrane Database Syst Rev 2007; 1: CD002090.

May DE, Kratochvil CJ. Attention-deficit hyperactivity disorder: recent **advances in paediatric pharmacotherapy**. Drugs. 2010;70(1):15-40.

Mazurek MO, Engelhardt CR. **Video game use** in boys with autism spectrum disorder, ADHD, or typical development. Pediatrics. 2013 Aug;132(2):260-6.

McCann D, Barrett A, Cooper A, et al. Food additives and hyperactive behaviour in 3-year-old and 8/9-year-old children in the community: a randomised, double-blinded, placebo-controlled trial. Lancet. 2007 Nov 3;370(9598):1560-7. Erratum in: Lancet. 2007 Nov 3;370(9598):1542.

McCarthy H, Skokauskas N, Mulligan A, et al. Attention Network **Hypoconnectivity** With Default and Affective Network Hyperconnectivity in Adults Diagnosed With Attention- Deficit/Hyperactivity Disorder in Childhood. JAMA Psychiatry. 2013 Oct 16.

McClure I. Has **Ritalin replaced the rod**?. BMJ. 2012;345:e8532

McElroy SL, Hudson JI, Mitchell JE, et al. Efficacy and Safety of **Lisdexamfetamine for Treatment of Adults With Moderate to Severe Binge-Eating Disorder**: A Randomized Clinical Trial. JAMA Psychiatry. 2015 Jan 14.

McKeown C, Hisle-Gorman E, Eide M, et al. Association of **Constipation and Fecal Incontinence** With Attention-Deficit/Hyperactivity Disorder. Pediatrics. 2013 Oct 21.

McLennan JD. Understanding attention deficit hyperactivity **disorder as a continuum**. Can Fam Physician. 2016 Dec;62(12):979-982

McMartin SE, Kingsbury M, Dykxhoorn J, et al. Time trends in symptoms of **mental illness in children and adolescents** in Canada. CMAJ. 2014 Nov 3

Medical Letter: **Treatment Guidelines – Drugs for Treatment of ADHD**. May 2011. **Updated Mar 2015**.

Millichap JG, Yee MM. The **Diet Factor** in Attention-Deficit/Hyperactivity Disorder. Pediatrics. 2012 Jan 9.

Miller M, Musser ED, Young GS, et al. **Sibling recurrence risk and cross-aggregation of attention-deficit/hyperactivity disorder and autism spectrum disorder** [online Dec 10, 2018]. JAMA Pediatr.

Minton O, Richardson A, Sharpe M, Hotopf M, Stone P. Drug therapy for the management of **cancer-related fatigue**. Cochrane Database Syst Rev. 2010 Jul 7;7:CD006704. There is increasing evidence that psychostimulant trials provide evidence for improvement in CRF at a clinically meaningful level. There is still a requirement for a large scale RCT of methylphenidate to confirm the preliminary results from this review. There is new safety data which indicates that the haemopoietic growth factors are associated with increased adverse outcomes. These drugs can no longer be recommended in the treatment of CRF. Readers of the first review should re-read the document in full.

Miodovnik A, Harstad E, Sideridis G, Huntington N. Timing of the Diagnosis of **Attention-Deficit/Hyperactivity Disorder and Autism** Spectrum Disorder. Pediatrics. 2015 Sep 14.

Molina BS, Flory K, Hinshaw SP, et al. **Delinquent behavior** and **emerging substance use** in the **MTA** at 36 months: prevalence, course, and treatment effects. J Am Acad Child Adolesc Psychiatry. 2007 Aug;46(8):1028-40.

Molina BS, Hinshaw SP, Swanson JM, et al. **MTA** Cooperative Group. The MTA at 8 years: prospective follow-up of children treated for combined-type ADHD in a multisite study. J Am Acad Child Adolesc Psychiatry. 2009 May;48(5):484-500.

Moran LV, Ongur D, Hsu J, et al. **Psychosis with Methylphenidate or Amphetamine** in Patients with ADHD. N Engl J Med. 2019 Mar 21;380(12):1128-1138

Morgan PL, Staff J, Hillemeier MM, et al. **Racial and Ethnic Disparities** in ADHD Diagnosis From Kindergarten to Eighth Grade. Pediatrics. 2013 Jun 24.

Morrow RL, Garland J, Wright JM et al. Influence of relative **age on diagnosis and treatment** of attention-deficit/hyperactivity disorder in children. CMAJ. 2012 Mar 5. (effect in age 6-12)

Mosholder AD, Gelperin K, Hammad TA, et al. **Hallucinations** and other psychotic symptoms associated with the use of attention-deficit/hyperactivity disorder drugs in children. Pediatrics. 2009 Feb;123(2):611-6.

Murphy TK, Lewin AB, Storch EA, Stock S, American Academy of Child and Adolescent Psychiatry (**AACAP**) Committee on Quality Issues (CQI). Practice parameter for the assessment and treatment of **children and adolescents with tic disorders**. J Am Acad Child Adolesc Psychiatry. 2013 Dec;52(12):1341-59.

Narad M, Garner AA, Brassell AA, et al. Impact of **Distraction on the Driving Performance** of Adolescents With and Without Attention-Deficit/Hyperactivity Disorder. JAMA Pediatr. 2013 Aug 12.

Narad ME, Kennelly M, Zhang N, et al. **Secondary Attention-Deficit/Hyperactivity Disorder** in Children and Adolescents 5 to 10 Years **After Traumatic Brain Injury**. JAMA Pediatr. 2018 Mar 19.

National Initiative for Children's Healthcare Quality **Tool Kit** http://www.nichq.org/adhd.html

Newcorn JH, et al. **Atomoxetine** and **osmotically released methylphenidate** for the treatment of attention deficit hyperactivity disorder: acute comparison and differential response. Am J Psychiatry. 2008 Jun;165(6):721-30. Epub 2008 Feb 15. Response was significantly greater with osmotically released methylphenidate than with atomoxetine. One-third of patients who received methylphenidate followed by atomoxetine responded better to one or the other, suggesting that there may be **preferential responders**.

Newcorn JH et al. **Extended-release guanfacine** hydrochloride in 6–17-year olds with ADHD: A randomised-withdrawal maintenance of efficacy study. J Child Psychol Psychiatry 2016 Feb 12.

NICE Sept/08 Attention deficit hyperactivity disorder: Diagnosis and management of ADHD in children, young people and adults http://www.nice.org.uk/guidance/index.jsp?action=byID&o=12061 Kendall T, Taylor E, Perez A, Taylor C; Guideline Development Group. Diagnosis and management of attention-deficit/hyperactivity disorder in children, young people, and adults: summary of NICE guidance. BMJ. 2008 Sep 24;337:a1239. doi: 10.1136/bmj.a1239.

NICE: National Institute for Health and Care Excellence (**NICE**). Attention deficit hyperactivity disorder: **diagnosis and management**. London (UK): National Institute for Health and Care Excellence (NICE); 2016 Feb. 41 p. (Clinical guideline; no. 72).

NICE: National Institute for Health and Care Excellence. Attention deficit hyperactivity disorder**: diagnosis and management** (NG87). 2018. nice. org.uk/ guidance/ ng87 (Accessed 28 Aug 2018).

Nikolas MA, Elmore AL, Franzen L, et al. **Risky bicycling behavior** among youth with and without attention-deficit hyperactivity disorder. J Child Psychol Psychiatry. 2015 Nov 27.

Nigg JT, Lewis K, Edinger T, et al. Meta-analysis of attention-deficit/hyperactivity disorder or attention- deficit/hyperactivity disorder symptoms, **restriction diet, and synthetic food color additives**. J Am Acad Child Adolesc Psychiatry. 2012 Jan;51(1):86-97.e8.

Nigg JT. Toward an Emerging Paradigm for **Understanding Attention-Deficit/Hyperactivity Disorder** and Other Neurodevelopmental, Mental, and Behavioral Disorders: **Environmental Risks and Epigenetic Associations**. JAMA Pediatr. 2018 May 21.

Nomura Y, Marks DJ, Grossman B, et al. Exposure to gestational **diabetes mellitus and low socioeconomic status**: effects on neurocognitive development and risk of attention-deficit/hyperactivity disorder in offspring [Jan 2,12]. Arch Pediatr Adolesc Med.

Nörby U, Winbladh B, Källén K. **Perinatal Outcomes After Treatment With ADHD Medication During Pregnancy**. Pediatrics. 2017 Nov 10.

Norman LJ, Carlisi C, Lukito S, et al. **Structural and Functional Brain Abnormalities** in Attention-Deficit/Hyperactivity Disorder and Obsessive-Compulsive Disorder: A Comparative Meta-analysis. JAMA Psychiatry. 2016 Jun 8.

Nuijten M, Blanken P, van de Wetering B, et al. Sustained-release **dexamfetamine** in the treatment of chronic **cocaine-dependent** patients on heroin-assisted treatment: a randomised, double-blind, placebo-controlled trial. Lancet. 2016 Mar 22.

Nuwwareh, S, Cimon, K, Ford, K and Weiss, M. Pharmacological and Nonpharmacological Therapies for **Adults with Attention-Deficit/Hyperactivity Disorder**: Systematic Review and Meta-analysis of Clinical Evidence [Internet] Ottawa:

Canadian Agency for Drugs and Technologies in Health (CADTH); 2011 (Rapid Response Report: Systematic Review). [cited 2011-09-21]. Available from:http://www.cadth.ca/media/pdf/htis/sept-2011/RE0026_ADHD_in%20adults_e.pdf
Ormhøj SS, Pottegård A, Gasse C, et al. Use of **attention-deficit/hyperactivity disorder medication among older adults in Denmark**. Br J Clin Pharmacol. 2018 Mar 1.
Otasowie J, Castells X, Ehimare UP, et al. **Tricyclic antidepressants** for attention deficit hyperactivity disorder (ADHD) in children and adolescents. Cochrane Database Syst Rev. 2014 Sep 19;9:CD006997.
Most evidence on TCAs relates to desipramine. Findings suggest that, in the short term, desipramine improves the core symptoms of ADHD, but its effect on the cardiovascular system remains an important clinical concern. Thus, evidence supporting the clinical use of desipramine for the treatment of children with ADHD is low.
Padala PR;Padala KP; et al. **Methylphenidate for Apathy in Community-Dwelling Older Veterans With Mild Alzheimer`s Disease**: A Double-Blind, Randomized, Placebo-Controlled Trial**.** Am J Psychiatry. 2017 Sep 15:appiajp201717030316.
Palamar JJ, Le A. Discordant reporting of **nonmedical amphetamine use among Adderall-using high school seniors** in the US. Drug Alcohol Depend. 2017 Oct 20;181:208-212
Pappadopulos E et al. **Medication adherence in the MTA**: **Saliva methylphenidate samples** versus parent report and mediating effect of concomitant behavioral treatment. J Am Acad Child Adolesc Psychiatry 2009 May; 48:501.
Park P, Caballero J, Omidian H. Use of **serotonin norepinephrine reuptake inhibitors** in the treatment of attention-deficit hyperactivity disorder in pediatrics. Ann Pharmacother. 2014 Jan;48(1):86-92
Park-Wyllie L, et al. Differences in Adverse Event Reporting Rates of **Therapeutic Failure Between Two Once-Daily Extended-Release Methylphenidate Medications in Canada**: Analysis of Spontaneous Adverse Event Reporting Databases. Clin Ther. 2017 Oct 5.
Pasker-de Jong PC, Zielhuis GA, van Gelder MM, et al. Antihypertensive treatment during pregnancy and functional development at primary school age in a historical cohort study. BJOG. 2010 May 12. Conclusions In this hypothesis-generating study, **labetalol exposure** in utero seemed to increase the risk of ADHD among children of primary school age, whereas prenatal methyldopa exposure might influence sleep.
Pauly V, Frauger E, Lepelley M, et al. Patterns and profiles of **Methylphenidate use in both children and adults**. Br J Clin Pharmacol. 2018 Mar 7.
Pelsser LM, Frankena K, Toorman J, et al. Effects of a **restricted elimination diet** on the behaviour of children with attention-deficit hyperactivity disorder (**INCA study**): a randomised controlled trial. Lancet. 2011 Feb 5;377(9764):494-503.
Pérez de Los Cobos J, Siñol N, Pérez V, Trujols J. Pharmacological and clinical dilemmas of **prescribing in co-morbid adult** attention-deficit/hyperactivity disorder and addiction. Br J Clin Pharmacol. 2012 Dec 7.
Perera FP, Chang HW, Tang D, et al. Early-life exposure to **polycyclic aromatic hydrocarbons** and ADHD behavior problems. PLoS One. 2014 Nov 5;9(11):e111670.
Pham T et al**. Household diversion** of prescription stimulants: Medication **misuse by parents** of children with attention-deficit/hyperactivity disorder. J Child Adolesc Psychopharmacol 2017 Jul 7.
Pharmacist's Letter. **Managing ADHD Stimulant Side Effects**. Mar 2013.
Philipsen A, Jans T, Graf E, et al; Comparison of **Methylphenidate and Psychotherapy** in Adult ADHD Study (**COMPAS**) Consortium. Effects of Group Psychotherapy, Individual Counseling, Methylphenidate, and Placebo in the Treatment of Adult Attention-Deficit/Hyperactivity Disorder: A Randomized Clinical Trial. JAMA Psychiatry. 2015 Nov 4:1-13.
Pontifex MB, Saliba BJ, Raine LB, et al. **Exercise Improves** Behavioral, Neurocognitive, and Scholastic Performance in Children with Attention-Deficit/Hyperactivity Disorder. J Pediatr. 2012 Oct 17.
Post RE, Kurlansik SL. Diagnosis and Management of Attention-Deficit/Hyperactivity Disorder in **Adults**. Am Fam Physician. 2012 May 1;85(9):890-896.
Pringsheim T, Steeves T. Pharmacological treatment for Attention Deficit Hyperactivity Disorder (ADHD) in children with **comorbid tic disorders**. Cochrane Database Syst Rev. 2011;4:CD007990. Methylphenidate, clonidine, guanfacine, desipramine and atomoxetine appear to reduce ADHD symptoms in children with tics. Although stimulants have not been shown to worsen tics in most people with tic disorders, they may nonetheless exacerbate tics in individual cases. In these instances, treatment with alpha agonists or atomoxetine may be an alternative. Although there is evidence that desipramine is effective for both tics and ADHD in children, safety concerns will likely continue to limit its use in this population.
Proal E, Reiss PT, Klein RG, et al.. **Brain Gray Matter Deficits** at 33-Year Follow-up in Adults With Attention-Deficit/Hyperactivity Disorder Established in Childhood. Arch Gen Psychiatry. 2011 Nov;68(11):1122-34.
Punja S, Shamseer L, Hartling L, et al. **Amphetamines for attention deficit hyperactivity disorder (ADHD) in children and adolescents**. Cochrane Database Syst Rev. 2016;2:CD009996. Most of the included studies were at high risk of bias and the overall quality of the evidence ranged from low to very low on most outcomes. Although amphetamines seem efficacious at reducing the core symptoms of ADHD in the short term, they were associated with a number of adverse events. This review found no evidence that supports any one amphetamine derivative over another, and does not reveal any differences between long-acting and short-acting amphetamine preparations. Future trials should be longer in duration (i.e. more than 12 months), include more psychosocial outcomes (e.g. quality of life and parent stress), and be transparently reported.
Quinn PD, Chang Z, Hur K, et al. ADHD Medication and **Substance-Related Problems**. Am J Psychiatry. 2017 Jun 29:appiajp201716060686.
Ra CK, Cho J, Stone MD, et al. Association of **digital media use with subsequent symptoms of attention-deficit/hyperactivity disorder** among adolescents [July 17, 2018]. JAMA. doi:10.1001/jama.2018.8931
Rabaeys H, Bijleveld HA, Devroey D. Influence of **Methylphenidate on the Frequency of Stuttering**: A Randomized Controlled Trial. Ann Pharmacother. 2015 Oct;49(10):1096-104.
Rader R, McCauley L, Callen EC. Current strategies in the **diagnosis and treatment** of childhood attention-deficit/hyperactivity disorder. Am Fam Physician. 2009 Apr 15;79(8):657-65.
Renoux C, Shin JY, Dell'Aniello S, et al. **Prescribing Trends** of Attention-Deficit Hyperactivity Disorder (**ADHD**) Medications in **UK Primary Care**, 1995-2015. Br J Clin Pharmacol. 2016 May 4.
Richardson M, Moore DA, Gwernan-Jones R, et al. **Non-pharmacological interventions for attention-deficit/hyperactivity disorder (ADHD**) delivered in school settings: systematic reviews of quantitative and qualitative research. Health Technol Assess. 2015 Jun;19(45):1-470. Findings suggest some beneficial effects of non-pharmacological interventions for ADHD used in school settings, but substantial heterogeneity in effect sizes was seen across studies. The qualitative reviews demonstrate the importance of the context in which interventions are used.
Ríos-Hernández A, Alda JA, Farran-Codina A, et al.The **Mediterranean Diet** and ADHD in Children and Adolescents. Pediatrics. 2017 Feb;139(2)
Roessner V, Plessen KJ, Rothenberger A, et al; **ESSTS Guidelines** Group. European clinical guidelines for **Tourette syndrome and other tic disorders**. Part II: pharmacological treatment. Eur Child Adolesc Psychiatry 2011;20:173-96.
Safren SA, Sprich S, Mimiaga MJ, et al. **Cognitive behavioral therapy vs relaxation** with educational support for medication-treated adults with ADHD and persistent symptoms: a randomized controlled trial. JAMA. 2010 Aug 25;304(8):875-80.
Sagiv SK, Thurston SW, Bellinger DC, et al. Prenatal exposure to **mercury and fish consumption** during pregnancy and attention deficit/hyperactivity disorder–related behavior in children (online October 8, 2012). Arch Pediatr Adolesc Med. 2012.
Sangal RB, Blumer JL, Lankford DA, et al. **Eszopiclone for insomnia** associated with attention-deficit/hyperactivity disorder. Pediatrics. 2014 Oct;134(4):e1095-103.
Santosh P. Stimulant medication to treat attention-deficit/hyperactivity disorder. BMJ. 2017 Jul 14;358:j2945.
Sayal K et al. **Relative age within the school year and diagnosis** of attention-deficit hyperactivity disorder: A nationwide population-based study. Lancet Psychiatry 2017 Nov; 4:868.
Scahill L, McCracken JT, King BH, et al. Extended-Release **Guanfacine** for Hyperactivity in Children With Autism Spectrum Disorder. Am J Psychiatry. 2015 Aug 28:appiajp201515010055.
Scammell TE. **Narcolepsy**. N Engl J Med. 2015 Dec 31;373(27):2654-62.
Schachter HM, Pham B, King J, Langford S, Moher D. How efficacious and safe is short-acting methylphenidate for the treatment of attention-deficit disorder in children and adolescents? A **meta-analysis**. CMAJ. 2001 Nov 27;165(11):1475-88.
Scheffler RM, Brown TT, Fulton BD, et al. Positive association between attention-deficit/ hyperactivity disorder medication use and **academic achievement** during elementary school. Pediatrics. 2009 May;123(5):1273-9.
Schelleman Hedi, Bilker Warren B., Strom Brian L., et al. **Cardiovascular Events** and Death in Children Exposed and Unexposed to ADHD Agents. Pediatrics 2011; peds.2010-3371.
Schoenberger SD, Agarwal A. Images in clinical medicine. **Talc retinopathy. (methylphenidate IV abuse)** N Engl J Med. 2013 Feb 28;368(9):852.
Schoenfelder EN, Faraone SV, Kollins SH. Stimulant Treatment of **ADHD and Cigarette Smoking**: A Meta-Analysis. Pediatrics. 2014 May 12.
Schwartz BS, Bailey-Davis L, Bandeen-Roche K, et al. Attention Deficit Disorder, Stimulant Use, and **Childhood Body Mass Index Trajectory**. Pediatrics. 2014 Mar 17.
Sciberras E, Mueller KL, Efron D, et al. **Language Problems** in Children With ADHD: A Community-Based Study. Pediatrics. 2014 Apr 21.
Sciberras E, Lycett K, Efron D, et al. **Anxiety in Children** With Attention-Deficit/Hyperactivity Disorder. Pediatrics. 2014 Apr 21.
Setlik J, Bond GR, Ho M. Adolescent Prescription ADHD Medication **Abuse** Is Rising Along With Prescriptions for These Medications. Pediatrics. 2009 Aug 24.
Sharma A, Couture J. A review of the pathophysiology, etiology, and **treatment of attention-deficit hyperactivity disorder** (ADHD). Ann Pharmacother. 2014 Feb;48(2):209-25.
Shaw P, Sharp WS, Morrison M, et al. Psychostimulant treatment and the **developing cortex** in attention deficit hyperactivity disorder. Am J Psychiatry. 2009 Jan;166(1):58-63. Epub 2008 Sep 15. These findings show no evidence that psychostimulants were associated with slowing of overall growth of the cortical mantle.
Shin JY, Roughead EE, Park BJ, et al. **Cardiovascular safety of methylphenidate** among children and young people with attention-deficit/hyperactivity disorder (ADHD): nationwide self controlled case series study. BMJ. 2016 May 31;353:i2550.
Shram MJ, Quinn AM, Chen N, et al. Differences in the In Vitro and In Vivo Pharmacokinetic Profiles of **Once-Daily Modified-Release Methylphenidate Formulations in Canada**: Examination of Current Bioequivalence Criteria. Clin Ther. 2012 Apr 16.
Shyu YC, Lee SY, Yuan SS, et al. **Seasonal Patterns of Medications** for Treating Attention-Deficit/Hyperactivity Disorder: Comparison of **Methylphenidate** and **Atomoxetine**. Clin Ther. 2016 Feb 10.
Sibley MH et al. **Late-onset ADHD** reconsidered with comprehensive repeated assessments between ages 10 and 25. Am J Psychiatry 2017 Oct 20;
Sikes C, Stark JG, et al. Pharmacokinetics of a New **Amphetamine Extended-Release Oral Liquid Suspension** Under Fasted and Fed Conditions in Healthy Adults: A Randomized, Open-Label, Single-Dose, 3-Treatment Study. Clin Ther. 2017 Nov 22.
Silva D, Colvin L, Hagemann E, et al. **Environmental Risk Factors** by Gender Associated With Attention-Deficit/Hyperactivity Disorder. Pediatrics. 2013 Dec 2
Simonneau G, Humbert M. **Amphetamine Derivatives and the Risk of Pulmonary Arterial Hypertension**: A New Chapter of the Story. Am J Respir Crit Care Med. 2017 Oct 18.
Solanto MV, Marks DJ, Wasserstein J, Mitchell K, Abikoff H, Alvir JM, Kofman MD. Efficacy of **Meta-Cognitive Therapy** for Adult ADHD. Am J Psychiatry. 2010 Mar 15.

Sonuga-Barke EJ, et al. **Nonpharmacological Interventions** for ADHD: Systematic Review and Meta-Analyses of Randomized Controlled Trials of Dietary and Psychological Treatments. Am J Psychiatry. 2013 Jan 30. (free fatty acids, artificial food color…)

Sourander A, Sucksdorff M, Chudal R, et al. **Prenatal Cotinine Levels** and ADHD Among Offspring. Pediatrics. 2019 Mar;143(3).

Southammakosane C, Schmitz K. Pediatric **Psychopharmacology for Treatment of ADHD, Depression, and Anxiety**. Pediatrics. 2015 Aug;136(2):351-9.

Soyer J, Jean-Louis J, Ospina LH, et al. **Visual disorders with psychostimulants**: a paediatric case report. Paediatr Child Health 2019;24:148-50.

Spencer AE et al. Examining the association between **posttraumatic stress disorder** and attention-deficit/hyperactivity disorder: A systematic review and meta-analysis. J Clin Psychiatry 2015 May 18.

Spencer AE, Faraone SV, Bogucki OE, et al. Examining the association between **posttraumatic stress disorder** and attention-deficit/hyperactivity disorder: a systematic review and meta-analysis. J Clin Psychiatry. 2015 May 12.

Stage C, Jürgens G, Guski LS, et al. The impact of **CES1 genotypes** on the pharmacokinetics of **methylphenidate** in healthy Danish subjects. Br J Clin Pharmacol. 2017 Jan 14.

Stavrinos D, Biasini FJ, Fine PR, Hodgens JB, Khatri S, Mrug S, Schwebel DC. Mediating factors associated with **pedestrian injury** in children with attention-deficit/hyperactivity disorder. Pediatrics. 2011 Aug;128(2):296-302.

Steiner NJ, Frenette EC, Rene KM, et al. **In-School Neurofeedback** Training for ADHD: Sustained Improvements From a Randomized Control Trial. Pediatrics. 2014 Mar;133(3):483-92.

Storebo OJ, Elmose Andersen M, Skoog M, et al. **Social skills training** for attention deficit hyperactivity disorder (ADHD) in children aged 5 to 18 years. Cochrane Database Syst Rev. 2019 Jun 21;6:CD008223. The review suggests that there is little evidence to support or refute social skills training for children and adolescents with ADHD. We may need more trials that are at low risk of bias and a sufficient number of participants to determine the efficacy of social skills training versus no training for ADHD. The evidence base regarding adolescents is especially weak.

Storebo OJ, Skoog M, Damm D, et al. **Social skills training** for Attention Deficit Hyperactivity Disorder (ADHD) in children aged 5 to 18 years. Cochrane Database Syst Rev. 2011 Dec 7;12:CD008223. The review suggests that there is little evidence to support or refute social skills training for adolescents with ADHD.

Storebø OJ, Krogh HB, Ramstad E, et al. **Methylphenidate** for attention-deficit/hyperactivity disorder in **children** and **adolescents**: Cochrane systematic review with meta-analyses and trial sequential analyses of randomised clinical trials. BMJ 2015;351:h5203.

Storebo OJ, Ramstad E, Krogh HB, et al. **Methylphenidate for children and adolescents** with attention deficit hyperactivity disorder (ADHD). Cochrane Database Syst Rev. 2015 Nov 25;11:CD009885.
The results of meta-analyses suggest that methylphenidate may improve teacher-reported ADHD symptoms, teacher-reported general behaviour, and parent-reported quality of life among children and adolescents diagnosed with ADHD. However, the low quality of the underpinning evidence means that we cannot be certain of the magnitude of the effects. Within the short follow-up periods typical of the included trials, there is some evidence that methylphenidate is associated with increased risk of non-serious adverse events, such as sleep problems and decreased appetite, but no evidence that it increases risk of serious adverse events.Better designed trials are needed to assess the benefits of methylphenidate. Given the frequency of non-serious adverse events associated with methylphenidate, the particular difficulties for blinding of participants and outcome assessors point to the advantage of large, 'nocebo tablet' controlled trials. These use a placebo-like substance that causes adverse events in the control arm that are comparable to those associated with methylphenidate. However, for ethical reasons, such trials should first be conducted with adults, who can give their informed consent.Future trials should publish depersonalised individual participant data and report all outcomes, including adverse events. This will enable researchers conducting systematic reviews to assess differences between intervention effects according to age, sex, comorbidity, type of ADHD and dose. Finally, the findings highlight the urgent need for large RCTs of non-pharmacological treatments.

Storebø OJ, Simonsen E, Gluud C. **Methylphenidate** for attention-deficit/hyperactivity disorder in **children and adolescents**.JAMA. doi:10.1001/jama.2016.3611.

Storebø OJ, Pedersen N, Ramstad E, et al. **Methylphenidate** for attention deficit hyperactivity disorder (ADHD) in children and adolescents - assessment of adverseevents in non-randomised studies. Cochrane Database Syst Rev. 2018 May 9;5:CD012069.

Sturman N, Deckx L, van Driel ML **Methylphenidate for children and adolescents with autism spectrum disorder.** Cochrane Database Syst Rev. 2017 Nov 21;11:CD011144. We found that short-term use of methylphenidate might improve symptoms of hyperactivity and possibly inattention in children with ASD who are tolerant of the medication, although the low quality of evidence means that we cannot be certain of the true magnitude of any effect. There was no evidence that methylphenidate has a negative impact on the core symptoms of ASD, or that it improves social interaction, stereotypical behaviours, or overall ASD. The evidence for adverse events is of very low quality because trials were short and excluded children intolerant of methylphenidate in the test-dose phase. Future RCTs should consider extending the duration of treatment and follow-up. The minimum clinically important difference also needs to be confirmed in children with ASD using outcome scales validated for this population.

Sucksdorff M, Lehtonen L, Chudal R, et al. **Preterm Birth and Poor Fetal Growth as Risk Factors** of Attention-Deficit/Hyperactivity Disorder. Pediatrics. 2015 Aug 24.

Sun S, Kuja-Halkola R, Faraone SV, et al. Association of **Psychiatric Comorbidity With the Risk of Premature Death** Among Children and Adults With Attention-Deficit/Hyperactivity Disorder. JAMA Psychiatry. 2019 Aug 7.

Szobot CM, Bukstein O. Attention deficit hyperactivity disorder and **substance use disorders**. Child Adolesc Psychiatr Clin N Am. 2008 Apr;17(2):309-23, viii.

Taranto-Montemurro L, Messineo L, Sands SA, et al. The Combination of **Atomoxetine and Oxybutynin Greatly Reduces Obstructive Sleep Apnea Severity**. A Randomized, Placebo-controlled, Double-Blind Crossover Trial. Am J Respir Crit Care Med 2019 May 15;199(10):1267-1276.

Taylor E. Attention deficit hyperactivity disorder: **overdiagnosed or diagnoses missed**? Arch Dis Child. 2017;102:376-379

Thakur GA, Sengupta SM, Grizenko N, et al. Family-based association study of **ADHD and genes increasing the risk for smoking** behaviours. Arch Dis Child. 2012 Oct 29.

Thapar A, Cooper M. **Attention deficit hyperactivity disorder**. Lancet. 2015 Sep 16.

Thomas R, Mitchell GK, Batstra L. Attention-deficit/hyperactivity disorder: are we **helping or harming**? BMJ. 2013 Nov 5;347:f6172

Thomas R, Sanders S, Doust J, et al. **Prevalence** of Attention-Deficit/Hyperactivity Disorder: A Systematic Review and Meta-analysis. Pediatrics. 2015 Mar 2. pii: peds.2014-3482.

Thomson A, Maltezos S, Paliokosta E, et al. **Risperidone** for attention-deficit hyperactivity disorder in people with **intellectual disabilities**. Cochrane Database Syst Rev. 2009 Apr 15;(2):CD007011. There is no evidence from RCTs that risperidone is effective for the treatment of ADHD in people with ID. Prescribing in this population can only be based on open-label studies or extrapolation from research in people with autism and disruptive behaviour disorders; however these studies have not investigated people with ID separately so there are reservations regarding the applicability of these findings.

Toce MS, Farias M, Bruccoleri R, et al. A Case Report of Reversible **Takotsubo Cardiomyopathy** after **Amphetamine/Dextroamphetamine** Ingestion in a 15-Year-Old Adolescent Girl. J Pediatr. 2016 Dec 13.

Trenque T, Claustre G, Herlem E, et al. **Methylphenidate and stuttering**. Br J Clin Pharmacol. 2019 Aug 16.

Tricco AC, Soobiah C, Berliner S, et al. Efficacy and safety of **cognitive enhancers** for patients with mild cognitive impairment: a systematic review and meta-analysis. CMAJ. 2013 Sep 16.

Tung I et al. **Patterns of comorbidity among girls** with ADHD: A meta-analysis. Pediatrics 2016 Oct;138:e20160430.

Ustun B, Adler LA, Rudin C, et al. The **World Health Organization (WHO) Adult Attention-Deficit/Hyperactivity Disorder Self-Report Screening Scale for** DSM-5. JAMA Psychiatry. 2017 Apr 5.

Vidal R, Castells J, Richarte V, et al. **Group therapy** for adolescents with attention-deficit/hyperactivity disorder: a randomized controlled trial. J Am Acad Child Adolesc Psychiatry 2015;54:275–82.

Viktorin A, Ryden E, Thase ME, et al. The Risk of **Treatment-Emergent Mania With Methylphenidate** in Bipolar Disorder. Am J Psychiatry. 2016 Oct 3:appiajp201616040467.

Visser SN, Bitsko RH, Danielson ML, et al. Treatment of Attention Deficit/Hyperactivity Disorder among **Children with Special Health Care Needs**. J Pediatr. 2015 Apr 1.

Vitiello B, Elliott GR, Swanson JM, et al. Blood Pressure and **Heart Rate** Over 10 Years in the Multimodal Treatment Study of Children With ADHD. Am J Psychiatry. 2011 Sep 2.

Volkow ND, Swanson JM. Clinical practice: **Adult** attention deficit-hyperactivity disorder (ADHD). N Engl J Med. 2013 Nov 14;369(20):1935-44.

Wang GS, Le Lait MC, Heard K. **Unintentional pediatric exposures** to central alpha-2 agonists (**clonidine**, guanfacine, tizanidine) reported to the national poison data system. J Pediatr. 2014 Jan;164(1):149-52.

Wei YJ, Zhu Y, Liu W, et al. **Prevalence of and Factors Associated With Long-term Concurrent Use of Stimulants and Opioids Among Adults With Attention-Deficit/Hyperactivity Disorder**. JAMA Netw Open. 2018;1(4):e181152.

Weintraub D, Mavandadi S, Mamikonyan E, et al. **Atomoxetine** for depression and other neuropsychiatric symptoms in Parkinson disease. Neurology. 2010 Aug 3;75(5):448-55.

Westover AN, Nakonezny PA. **Aortic dissection** in young adults who abuse amphetamines. Am Heart J 2010; 160:315-321.

Wiggs KK, Chang Z, Quinn PD, et al. **Attention-deficit/hyperactivity disorder medication and seizures**. Neurology. 2018 Feb 23.

Wilens T, Zulauf C, Martelon M, Morrison NR, Simon A, Carrellas NW, Yule A, Anselmo R. **Nonmedical Stimulant Use** in College Students: Association With Attention-Deficit/Hyperactivity Disorder and Other Disorders. J Clin Psychiatry. 2016 Jul;77(7):940-7.

Williams NM, Zaharieva I, Martin A, et al. **Rare chromosomal deletions and duplications** in attention-deficit hyperactivity disorder: a genome-wide analysis. Lancet. 2010 Oct 23;376(9750):1401-8.

Winhusen TM, Somoza EC, Brigham GS, et al. Impact of attention-deficit/hyperactivity disorder (ADHD) treatment on **smoking cessation** intervention in ADHD smokers: a randomized, double-blind, placebo-controlled trial. J Clin Psychiatry. 2010 May 18.

Winkelman TNA, Admon LK, Jennings L, et al. Evaluation of **Amphetamine-Related Hospitalizations and Associated Clinical Outcomes and Costs** in the United States. JAMA Netw Open. 2018;1(6):e183758.

Winterstein, Almut Gertrud, Gerhard, Tobias, Shuster, Jonathan, Saidi, Arwa. **Cardiac Safety** of Methylphenidate Versus Amphetamine Salts in the Treatment of ADHD Pediatrics 2009 124: e75-e80.

Winterstein AG, Gerhard T, Kubilis P, et al. **Cardiovascular safety** of central nervous system stimulants in children and adolescents: population based cohort study. BMJ. 2012 Jul 18;345:e4627.

Wolfe SM. Selling amphetamine emblazoned athletic shirts v **overselling amphetamines**: a tale of two entrepreneurs. BMJ. 2013 Oct 17;347:f6215.

Xu G, Strathearn L, Liu B, et al. **Twenty-Year Trends in Diagnosed Attention-Deficit/Hyperactivity Disorder Among US Children and Adolescents**, 1997-2016. JAMA Netw Open. 2018;1(4):e181471.

Xu, Xiaohui, Cook, Robert L., Ilacqua, Vito A., et al. Racial Differences in the Effects of Postnatal Environmental **Tobacco Smoke** on Neurodevelopment. Pediatrics 2010 0: peds.2009-3589

Yan L, Wang S, Yuan Y, Zhang J. **Effects of neurofeedback versus methylphenidate** for the treatment of ADHD: systematic review and meta-analysis of head-to-head trials. Evid Based Ment Health. 2019 Aug;22(3):111-117.

Yoshimasu K, Barbaresi WJ, Colligan RC, et al. **Written-Language Disorder** Among Children With and Without ADHD in a Population-Based Birth Cohort. Pediatrics. 2011 Aug 22.

Ystrom E, Gustavson K, Knnudsen PG, et al. **Prenatal exposure to acetaminophen** and risk of ADHD. Pediatrics.140(5):20163840

Zhang J, Díaz-Román A, Cortese S. **Meditation-based therapies for attention-deficit/hyperactivity disorder in children, adolescents and adults**: a systematic review and meta-analysis. Evid Based Ment Health. 2018 Aug;21(3):87-94
Zhang T, Sidorchuk A, Sevilla-Cermeño L, et al. Association of **Cesarean Delivery With Risk of Neurodevelopmental and Psychiatric Disorders** in the Offspring: A Systematic Review and Meta-analysis. JAMA Netw Open. 2019 Aug 2;2(8):e1910236.
Zoëga H, Rothman KJ, Huybrechts KF, et al. A Population-Based Study of Stimulant Drug Treatment of ADHD and **Academic Progress in Children**. Pediatrics. 2012 Jun 25.
Zoëga H, Valdimarsdóttir UA, Hernández-Díaz S. **Age, Academic Performance, and Stimulant Prescribing** for ADHD: A Nationwide Cohort Study. Pediatrics. 2012 Nov 19.
Zuvekas, Samuel H., Vitiello, Benedetto. **Stimulant Medication Use in Children**: A 12-Year Perspective. Am J Psychiatry 2011 0: appi.ajp.2011.11030387.

☎ = Exception Drug Status in SK ✘ = Non-formulary in SK ✆ =prior approval by NIHB ⊗=not covered NIHB ▼= covered NIHB **ADV**: advantage **AE**: adverse events; **CI**: contraindications

ANXIETY DISORDER MEDICATION Comparison Chart

[1] Therapeutic Choices 5th Edition, 2007

[2] Ontario Guidelines for the Management of Anxiety Disorders in Primary Care Fall 2000 1st Edition

[3] Micromedex 2018

[4] Treatment Guidelines: Drugs for Psychiatric Disorders. The Medical Letter: July, 2003; p. 69-76. (**Medical Letter** "Treatment Guidelines- Drugs for Psychiatric Disorders Vol 4 (Issue 46) **June 2006**.)
Treatment Guidelines: Drugs for **Anxiety Disorders**. The Medical Letter: Aug 2019.

[5] Modell JG, Katholi CR, Modell JD, et. al. Comparative sexual side effects of bupropion fluoxetine, paroxetine, and sertraline. Clin Pharmacol Ther 1997;61(4):476-87.

[6] Gonzalez M, Llorca G, Izquierdo JA, et.al. J Sex Marital Ther 1997;23(3):176-94.

[7] Which SSRI? Med Lett Drugs Ther. 2003 Nov 24;45(1170):93-95.

[8] Glassman AH, O'Connor CM, Califf RM, et al.; Sertraline Antidepressant Heart Attack Randomized Trial (SADHEART) Group. Sertraline treatment of major depression in patients with acute MI or unstable angina. JAMA. 2002 Aug 14;288(6):701-9.

[9] Fricchione G. Clinical practice. Generalized anxiety disorder. N Engl J Med. 2004 Aug 12;351(7):675-82.

[10] Jenike MA. Clinical practice. Obsessive-compulsive disorder. N Engl J Med. 2004 Jan 15;350(3):259-65.

[11] Stein DJ. Obsessive-compulsive disorder. Lancet. 2002 Aug 3;360(9330):397-405.

[12] Grinage BD. Diagnosis and management of post-traumatic stress disorder. Am Fam Physician. 2003 Dec 15; 68(12): 2401-8.

[13] Asnis GM, Kohn SR, Henderson M, Brown NL. SSRIs versus Non-SSRIs in Post-traumatic Stress Disorder : An Update with Recommendations. Drugs. 2004;64(4):383-404.

Additional articles:

AACAP-Practice parameter for assessment & treatment of children & adolescents with **obsessive-compulsive disorder**. J Am Acad Child Adolesc Psych 2012 Jan;51(1):98-113.

Abramowitz JS, Taylor S, McKay D. **Obsessive-compulsive disorder**. Lancet. 2009 Aug 8;374(9688):491-9.

Ahmadi N, Hajsadeghi F, Mirshkarlo HB, et al. **Post-traumatic stress disorder**, **coronary atherosclerosis, and mortality**. Am J Cardiol. 2011 Jul 1;108(1):29-33.

Akiki TJ, Abdallah CG. Are There Effective **Psychopharmacologic Treatments for PTSD**? J Clin Psychiatry. 2018 Dec 18;80(3).

Alderman CP, McCarthy LC, Condon JT, Marwood AC, Fuller JR. **Topiramate** in combat-related posttraumatic stress disorder. Ann Pharmacother. 2009 Apr;43(4):635-41. Epub 2009 Mar 31.

Alraies C, Keller E, Shaheen K et al. A 40-year-old woman with **excoriated skin lesions**. *Cleveland Clinic Journal of Medicine* 2011; 78(3):161-163; doi:10.3949/ccjm.78a.10042

American Psychiatric Association Brochures: http://www.healthyminds.org/Functional-Library/brochures.aspx

Amos T, Stein DJ, Ipser JC. Pharmacological interventions for **preventing post-traumatic stress disorder (PTSD).** Cochrane Database Syst Rev. 2014 Jul 8;7:CD006239. There is moderate quality evidence for the efficacy of hydrocortisone for the prevention of PTSD development in adults. We found no evidence to support the efficacy of propranolol, escitalopram, temazepam and gabapentin in preventing PTSD onset. The findings, however, are based on a few small studies with multiple limitations. Further research is necessary in order to determine the efficacy of pharmacotherapy in preventing PTSD and to identify potential moderators of treatment effect.

Amsterdam JD, Li Y, Soeller I, et al. A randomized, double-blind, placebo-controlled trial of oral Matricaria recutita (**chamomile**) extract therapy for generalized anxiety disorder. J Clin Psychopharmacol. 2009 Aug;29(4):378-82. n=61 over 8 weeks. This is the first controlled clinical trial of chamomile extract for GAD. The results suggest that chamomile may have modest anxiolytic activity in patients with mild to moderate GAD

Andersen BL, Derubeis RJ, Berman BS, et al. Screening, Assessment, and Care of **Anxiety and Depressive Symptoms in Adults With Cancer:** An American Society of Clinical Oncology Guideline Adaptation. J Clin Oncol. 2014 Apr 14.

Andersson E et al. **Internet-based cognitive behaviour therapy** for **obsessive–compulsive disorder**: A randomized controlled trial.Psychol Med 2012 Feb 21.

Andersson E, Hedman E, Enander J, et al**. d-Cycloserine** vs Placebo as Adjunct to Cognitive Behavioral Therapy for **Obsessive-Compulsive Disorder** and Interaction With Antidepressants: A Randomized Clinical Trial. JAMA Psychiatry. 2015 May 13.

Anthierens, Sibyl, Pasteels, Inge, Habraken, Hilde, et al. Barriers to nonpharmacologic treatments for **stress, anxiety, and insomnia**: Family physicians' attitudes toward benzodiazepine prescribing. Can Fam Physician 2010 56: e398-406.

Andrus MR, Gilbert E. Treatment of Civilian and Combat-Related Posttraumatic Stress Disorder with **Topiramate**. Ahead of Print 1Nov2010, DOI 10.1345/aph.1P163. Ann Pharmacother ;44:1810-1816.

APA: Stein MB, Goin MK, Pollack MH, Roy-Byrne P, Sareen J, Simon NM, et al. Treatment of patients with **panic disorder**. In: *APA practice guidelines* [database online]. Second Edition. Arlington(VA): American Psychiatric Association (**APA**) ; 2008. http://www.psychiatryonline.com/pracGuide/loadGuidelinePdf.aspx?file=PanicDisorder_2e_PracticeGuideline

APA: 2008 Practice Guideline for the Treatment of Patients With Panic Disorder http://www.psychiatryonline.com/pracGuide/loadGuidelinePdf.aspx?file=PanicDisorder_2e_PracticeGuideline

APA: Koran LM, Hanna GL, Hollander E, Nestadt G, Simpson HB; **American Psychiatric Association**. Practice guideline for the treatment of patients with **obsessive-compulsive** disorder. Am J Psychiatry. 2007 Jul;164(7 Suppl):5-53. http://www.psych.org/psych_pract/treatg/pg/OCDPracticeGuidelineFinal05-04-07.pdf

APA: American Guideline Development Panel for the Treatment of PTSD in Adults. Clinical practice guideline for the treatment of posttraumatic stress disorder (PTSD) in adults. Washington (DC): American Psychological Association; **2017** Feb 24.

Arane K, Behboudi A, Goldman RD. **Virtual reality for pain and anxiety management in children**. Can Fam Physician. 2017 Dec;63(12):932-934.

Archer J, Bower P, Gilbody S, et al. **Collaborative care** for depression and anxiety problems. Cochrane Database of Systematic Reviews 2012, Issue 10. Art. No.: CD006525. DOI: 10.1002/14651858.CD006525.pub2. Collaborative care is associated with significant improvement in depression and anxiety outcomes compared with usual care, and represents a useful addition to clinical pathways for adult patients with depression and anxiety

Arendt K, Thastum M, Hougaard E. Efficacy of a Danish version of the **Cool Kids program**: a randomized wait-list controlled trial. Acta Psychiatr Scand 2015.

Arroyo KJ, Ramos-Torres G, Mezones-Holguin E, et al. Association between **waist-to-height ratio and anxiety** in middle-aged women: a secondary analysis of a cross-sectional multicenter Latin American study. Menopause. 2018 Mar 5.

Aurora RN, Zak RS, Auerbach SH, et al. Standards of Practice Committee, American Academy of Sleep Medicine. Best practice guide for the treatment of **nightmare disorder in adults**. J Clin Sleep Med 2010 Aug 15;6(4):389-401. (prazosin, ? clonidine etc)

Bains M, Shortall C, Manzuangani T, et al. Identifying **post-traumatic stress disorder in forced migrants**. BMJ. 2018 May 10;361:k1608.

Baldwin DS, Huusom AK, Maehlum E. **Escitalopram** (5-20mg od) and **paroxetine** (20mg od) in the treatment of **generalised anxiety disorder**: Randomised, placebo-controlled, double-blind study. Br J Psychiatry. 2006 Sep;189:264-272. 12 weeks

Baldwin David, Woods Robert, Lawson Richard, et al. Efficacy of drug treatments for generalised anxiety disorder: systematic review and meta-analysis. BMJ 342:doi:10.1136/bmj.d1199 (Published 11 March 2011).

Barlow DH, Farchione TJ, Bullis JR, et al. The Unified Protocol for **Transdiagnostic** Treatment of Emotional Disorders Compared With **Diagnosis-Specific** Protocols for **Anxiety Disorders**: A Randomized Clinical Trial. JAMA Psychiatry. 2017 Aug 2

Barzilay R, Patrick A, Calkins ME, et al. **Obsessive-Compulsive Symptomatology** in Community Youth: Typical Development or a Red Flag for Psychopathology? J Am Acad Child Adolesc Psychiatry. 2019 Feb;58(2):277-286.e4.

Bass JK et al. Controlled trial of **psychotherapy for Congolese survivors of sexual violence**. N Engl J Med 2013 Jun 6; 368:2182.

Batelaan NM, Bosman RC, Muntingh A, et al. **Risk of relapse after antidepressant discontinuation in anxiety disorders, obsessive-compulsive disorder, and post-traumatic stress disorder**: systematic review and meta-analysis of relapse prevention trials. BMJ. 2017 Sep 13;358:j3927.

Bedi G. **3,4-Methylenedioxymethamphetamine** as a Psychiatric Treatment. JAMA Psychiatry. 2018 Mar 21.

Berger W et al. Pharmacologic alternatives to antidepressants in **posttraumatic stress disorder**: systematic review. Prog Neuropsychopharmacol Biol Psyc. 2009Mar17;33(2):169-80.

Berlin HA, Koran LM, Jenike MA, et al. Double-blind, placebo-controlled trial of **topiramate** augmentation in treatment-resistant obsessive-compulsive disorder. J Clin Psychiatry. 2010 Aug 10.

Bezchlibnyk-Butler KZ. **Clinical Handbook of Psychotropic Drugs, 22nd Ed**. 22nd Editors: Procyshyn RM, Bezchlibnyk-Butler KZ, Jeffries JJ. Hogrefe Publishing, Massachusetts, 2017.

Bighelli I, Castellazzi M, Cipriani A, et al. **Antidepressants versus placebo for panic disorder in adults**. Cochrane Database Syst Rev. 2018 Apr 5;4:CD010676. The identified studies comprehensively address the objectives of the present review.Based on these results, antidepressants may be more effective than placebo in treating panic disorder. Efficacy can be quantified as a NNTB of 7, implying that seven people need to be treated with antidepressants in order for one to benefit. Antidepressants may also have benefit in comparison with placebo in terms of number of dropouts, but a less favourable profile in terms of dropout due to adverse effects. However, the tolerability profile varied between different classes of antidepressants.The choice of whether antidepressants should be prescribed in clinical practice cannot be made on the basis of this review.

Bisson JI. **Post-traumatic stress disorder**. BMJ. 2007 Apr 14;334(7597):789-793.

Bisson JI, Roberts NP, Andrew M, Cooper R, Lewis C. **Psychological therapies for chronic post-traumatic stress disorder (PTSD)** in adults. Cochrane Database of Systematic Reviews 2013, Issue 12. Art. No.: CD003388. DOI: 10.1002/14651858.CD003388.pub4. The evidence for each of the comparisons made in this review was assessed as very low quality. This evidence showed that individual TFCBT and EMDR did better than waitlist/usual care in reducing clinician-assessed PTSD symptoms. There was evidence that individual TFCBT, EMDR and non-TFCBT are equally effective immediately post-treatment in the treatment of PTSD. There was some evidence that TFCBT and EMDR are superior to non-TFCBT between one to four months following treatment, and also that individual TFCBT, EMDR and non-TFCBT are more effective than other therapies. There was evidence of greater drop-out in active treatment groups. Although a substantial number of studies were included in the review, the conclusions are compromised by methodological issues evident in some. Sample sizes were small, and it is apparent that many of the studies were underpowered. There were limited follow-up data, which compromises conclusions regarding the long-term effects of psychological treatment.

Bisson JI, Cosgrove S, Lewis C, Robert NP. **Post-traumatic stress disorder**. BMJ. 2015 Nov 26;351:h6161.

Blanco C, Heimberg RG, Schneier FR, et al. A placebo-controlled trial of **phenelzine**, cognitive behavioral group therapy, and their combination for social anxiety disorder. Arch Gen Psychiatry. 2010 Mar;67(3):286-95.

Boelen PA, Smid GE. **Disturbed grief**: prolonged grief disorder and persistent complex bereavement disorder. BMJ. 2017 May 18;357:j2016

Bormann JE, Thorp SR, Smith E, et al. Individual **Treatment of Posttraumatic Stress Disorder Using Mantram Repetition**: A Randomized clinical Trial. Am J Psychiatry. 2018 Jun 20:appiajp201817060611.

Bradt J, Dileo C, ShimM. **Music** interventions for preoperative anxiety. Cochrane Database of Systematic Reviews 2013, Issue 6. Art. No.: CD006908. DOI: 10.1002/14651858.CD006908.pub2.

Bradwejn J, et al. **Venlafaxine** extended-release capsules in panic disorder: flexible-dose, double-blind, placebo-controlled study. Br J Psychiatry. 2005 Oct;187:352-9.

Brander G, et al. Association of **perinatal risk factors** with **obsessive-compulsive disorder**: population-based birth cohort, sibling control study [online Oct 5/16]. JAMA Psych.

Breilmann J, Girlanda F, Guaiana G, et al. **Benzodiazepines versus placebo for panic disorder in adults**. Cochrane Database Syst Rev. 2019 Mar 28;3:CD010677. Low-quality evidence shows a possible superiority of benzodiazepine over placebo in the short-term treatment of panic disorders. The validity of the included studies is questionable due to possible unmasking of allocated treatments, high dropout rates, and probable publication bias.

Brenes GA, Danhauer SC, Lyles MF, et al. **Telephone-Delivered Cognitive Behavioral Therapy** and **Telephone-Delivered Nondirective Supportive Therapy** for Rural Older Adults With Generalized Anxiety Disorder: A Randomized Clinical Trial. JAMA Psychiatry. 2015 Aug 5

Brennan BP, Jacoby RJ, Widge AS. A Case of Severe Intractable Contamination-Based Obsessive-Compulsive Disorder. JAMA Psychiatry. 2018 Aug 15.

Bruce SE, et al. Are **benzodiazepines** still the medication of choice for patients with panic disorder with or without agoraphobia? Am J Psychiatry. 2003 Aug;160(8):1432-8.

Bryant RA, Mastrodomenico J, Felmingham KL, et al. Treatment of acute stress disorder: a randomized controlled trial. Arch Gen Psychiatry. 2008 Jun;65(6):659-67. Exposure-based therapy leads to greater reduction in subsequent PTSD symptoms in patients with ASD when compared with cognitive restructuring. **Exposure** should be used in early intervention for people who are at high risk for developing PTSD.

Byers AL, Covinsky KE, Neylan TC, et al. Chronicity of **Posttraumatic Stress Disorder** and Risk of Disability in Older Persons. JAMA Psychiatry. 2014 Mar 19.

Canadian Anxiety Guideline July 2006 (Panic, PTSD, GAD, SAD, OCD & specific phobias) (see also Pharmacist's Letter: Management of Anxiety Disorders Nov 2006) http://www.cpa-apc.org/Publications/CJP/supplements/july2006/anxiety_guidelines_2006.pdf

Carmi L, Tendler A, Bystritsky A, et al. Efficacy and Safety of **Deep Transcranial Magnetic Stimulation** for Obsessive-Compulsive Disorder: A Prospective Multicenter Randomized Double-Blind Placebo-Controlled Trial. Am J Psychiatry. 2019 May 21:appiajp201918101180.

Chan CMH, Ng CG, Taib NA, et al. Course and predictors of **post-traumatic stress disorder** in a cohort of psychologically distressed patients with cancer: A 4-year follow-up study. Cancer. 2017 Nov 20.

Chan EW, Taylor DM, Knott JC, et al. Intravenous **droperidol or olanzapine** as an **adjunct to midazolam** for the acutely agitated patient: a multicenter, randomized, double-blind, placebo-controlled clinical trial. Ann Emerg Med. 2013 Jan;61(1):72-81.

Chemtob CM, Gudiño OG, Laraque D. **Maternal Posttraumatic Stress Disorder** and Depression in Pediatric Primary Care: Association With Child Maltreatment and Frequency of Child Exposure to Traumatic Events. JAMA Pediatr. 2013 Sep 2.

Chen JA, Ptaszek LM, Celano CM, Beach SR. Case 9-2019: A **62-Year-Old Man with Atrial Fibrillation, Depression**, and Worsening Anxiety. N Engl J Med. 2019 Mar 21;380(12):1167-1174.

Chen X, Broeyer F, de Kam M, et al. **Pharmacodynamic response profiles** of anxiolytic and sedative drugs. Br J Clin Pharmacol. 2016 Dec 6.

Chester SJ, Tyack Z, De Young A, et al. Efficacy of **hypnosis on pain, wound-healing, anxiety, and stress in children with acute burn injuries**: a randomized controlled trial. Pain. 2018 Sep;159(9):1790-1801.

Chugani DC, Chugani HT, Wiznitzer M, et al. Efficacy of Low-Dose **Buspirone** for Restricted and Repetitive Behavior in Young Children with **Autism** Spectrum Disorder: A Randomized Trial. J Pediatr. 2015 Dec 23.

Chugani DC, Chugani HT, Wiznitzer M, et al; Autism Center of Excellence Network. Efficacy of Low-Dose **Buspirone** for Restricted and Repetitive Behavior in Young Children with **Autism** Spectrum Disorder: A Randomized Trial. J Pediatr. 2016 Mar;170:45-53.e4.

Coffey SF. Banducci AN, Vinci C. Common Questions About **Cognitive Behavior Therapy** for Psychiatric Disorders. Am Fam Physician. 2015;92(9):807-812.

Cohen GH, Tamrakar S, Lowe S, et al. Comparison of **Simulated Treatment and Cost-effectiveness of a Stepped Care Case-Finding Intervention vs Usual Care** for **Posttraumatic Stress Disorder** After a Natural Disaster. JAMA Psychiatry. 2017 Oct 4.

Comer JS, Mojtabai R, Olfson M: **National trends in the antipsychotic treatment** of psychiatric outpatients with anxiety disorders. Am J Psychiatry 2011; 168:1057–1065.

Connolly SD, Bernstein GA, Work Group on Quality Issues. Practice parameter for the assessment and treatment of **children and adolescents with anxiety disorders**. J Am Acad Child Adolesc Psychiatry 2007 Feb;46(2):267-83.

Cordova MJ, Riba MB, Spiegel D. **Post-traumatic stress disorder and cancer**. Lancet Psychiatry. 2017 Jan 18.

Craske MG, Stein MB. **Anxiety**. Lancet. 2016 Jun 24. pii: S0140-6736(16)30381-6.

Crawford A. A 28-year-old military veteran with **nightmares and insomnia**. (PTSD) CMAJ. 2014 Mar 18;186(5):360-2.

Creswell C, Violato M, Fairbanks H, et al. Clinical outcomes and cost-effectiveness of **brief guided parent-delivered cognitive behavioural therapy** and solution-focused brief therapy for treatment of childhood **anxiety** disorders: a randomised controlled trial. Lancet Psychiatry. 2017 May 17.

Crum-Cianflone NF, Bagnell ME, Schaller E, et al. Impact of **combat deployment** and posttraumatic stress disorder on newly reported coronary heart disease among US active duty and reserve forces. Circulation. 2014;129:1813–1820.

Dannon PN, et al. **Three year naturalistic** outcome study of **panic** disorder patients treated with **paroxetine**. BMC Psychiatry. 2004 Jun 11;4:16.

Davidson J, et al. Treatment of **Posttraumatic Stress Disorder With Venlafaxine** Extended Release: A 6-Month Randomized Controlled Trial. Arch Gen Psychiatry. 2006 Oct;63(10):1158-1165. n=329

Davis LL, Kyriakides TC, Suris AM, et al. Effect of Evidence-Based **Supported Employment vs Transitional Work** on Achieving Steady Work Among Veterans With **Posttraumatic Stress Disorder**: A Randomized Clinical Trial.JAMA Psychiatry. 2018 Feb 28.

De Roos C et al. Comparison of **eye movement desensitization and reprocessing therapy, cognitive behavioral writing therapy**, and wait-list in **pediatric posttraumatic stress disorder** following single-incident trauma: A multicenter randomized clinical trial. J Child Psychol Psychiatry 2017 Jun 28.

DeMartini J, Patel G, Fancher TL. **Generalized Anxiety Disorder**. Ann Intern Med. 2019 Apr 2;170(7):ITC49-ITC64.
DeMartinis N, Rynn M, Rickels K, Mandos L. **Prior benzodiazepine use & buspirone** response in the treatment of generalized anxiety disorder. J Clin Psychiatry. 2000;61:91-94.
Deng LX, Khan AM, Drajpuch D, et al. Prevalence and correlates of **post-traumatic stress disorder** in adults with **congenital heart disease**. *Am J Cardiol* 2015.
Denys D, Mantione M, Figee M, et al. **Deep brain stimulation** of the nucleus accumbens for treatment-refractory obsessive-compulsive disorder. Arch Gen Psychiatry. 2010 Oct;67(10):1061-8.
Depping AM, Komossa K, Kissling W, Leucht S. **Second-generation antipsychotics for anxiety** disorders. Cochrane Database Syst Rev. 2010;(12):CD008120.
Dhillon S, Scott LJ, Plosker GL. **Escitalopram**: a review of its use in the management of anxiety disorders. CNS Drugs. 2006;20(9):763-90. Nevertheless, available clinical data indicate that escitalopram is an effective first-line treatment option for the management of GAD, SAD, panic disorder and OCD.
Donoghue AC, Roback MG, Cullen KR. Remission From Behavioral Dysregulation in a Child With PTSD After Receiving Procedural **Ketamine**. Pediatrics. 2015 Aug 10.
Donovan AL, Petersen TJ, Nadal-Vicens MF, Kamenker-Orlov YS. Case 1-2019: A 34-Year-Old Veteran with **Multiple Somatic Symptoms**. N Engl J Med. 2019 Jan 10;380(2):178-185.
Duffy M, Gillespie K, Clark DM. Post-traumatic stress disorder in the context of terrorism and other civil conflict in Northern Ireland: randomised controlled trial. BMJ. 2007 Jun 2;334(7604):1147. Epub 2007 May 11. Cognitive therapy is an effective treatment for post-traumatic stress disorder related to terrorism and other civil conflict.
Edmondson D, Richardson S, Falzon L, et al. Posttraumatic Stress Disorder Prevalence and Risk of Recurrence in **Acute Coronary Syndrome Patients**: A Meta-analytic Review. PLoS One. 2012;7(6):e38915.
Edmondson D, Richardson S, et al. Prevalence of **PTSD in Survivors of Stroke and Transient Ischemic Attack**: A Meta-Analytic Review. PLoS One. 2013 Jun 19;8(6):e66435.
Edmondson D, von Känel R. **Post-traumatic stress disorder and cardiovascular disease**. Lancet Psychiatry. 2017 Jan 18.
Eftekhari A, Ruzek JI, Crowley JJ, et al. Effectiveness of National Implementation of **Prolonged Exposure Therapy** in Veterans Affairs Care. JAMA Psychiatry. 2013 Jul 17.
Ehlers A, Hackmann A, Grey N, et al. A randomized controlled trial of **7-day intensive and standard weekly cognitive therapy for PTSD** and emotion-focused supportive therapy. Am J Psychiatry. 2014 Mar 1;171(3):294-304.
Emdin CA, Odutayo A, Wong CX, et al. Meta-Analysis of **Anxiety as a Risk Factor for Cardiovascular Disease**. Am J Cardiol. 2016 Aug 15;118(4):511-9
Engel CC, Jaycox LH, Freed MC, et al. Centrally assisted **collaborative telecare** for posttraumatic stress disorder and depression among military personnel attending primary care: a randomized clinical trial [published online June 13, 2016].JAMA Intern Med. doi:10.1001/jamainternmed.2016.2402.
Ertl V, Pfeiffer A, Schauer E, Elbert T, Neuner F. **Community-implemented trauma therapy** for former **child soldiers** in Northern Uganda: a randomized controlled trial. JAMA. 2011;306(5):503-512.
Farren J, Jalmbrant M, Ameye L, et al. Post-traumatic stress, anxiety and depression **following miscarriage or ectopic pregnancy**: a prospective cohort study. BMJ Open. 2016 Nov 2;6(11):e011864.
Fava M, Rush AJ, Alpert JE, et al. Difference in treatment outcome in outpatients with anxious versus nonanxious depression: a STAR*D report. Am J Psychiatry. 2008 Mar;165(3):342-51. Epub 2008 Jan 2. Adults with the combination of both anxiety and depression are significantly more difficult to successfully treat than patients with depression alone. (LOE = 1b-)
FDA Aug/11 Antidepressant **citalopram** (*Celexa*, Forest Laboratories) should not be used in doses higher than 40 mg per day because of concerns that it can cause potentially fatal changes in heart rhythm (eg. ↑ QT)
FDA Aug/18: cleared the Brains Way deep transcranial magnetic stimulation (TMS) device for the treatment of obsessive-compulsive disorder.
Feder A, Parides MK, Murrough JW, et al. Efficacy of Intravenous **Ketamine** for Treatment of Chronic Posttraumatic Stress Disorder: A Randomized Clinical Trial. JAMA Psychiatry. 2014 Apr 16.
Fenske JN, Schwenk TL. **Obsessive compulsive disorder**: diagnosis and management. Am Fam Physician. 2009 Aug 1;80(3):239-45.
Fenske JN, Petersen K. **Obsessive-Compulsive Disorder**: Diagnosis and Management. Am Fam Physician. 2015;92(10):896-903.
Freeman D, Dunn G, Startup H, et al. Effects of **cognitive behaviour** therapy for **worry on persecutory delusions** in patients with **psychosis** (**WIT**): a parallel, single-blind, randomized controlled trial with a mediation analysis. Lancet Psychiatry 2015;2:305–13.
Foa EB, McLean CP, Capaldi S, Rosenfield D. **Prolonged exposure vs supportive counseling** for sexual abuse-related PTSD in adolescent girls: a randomized clinical trial. JAMA. 2013 Dec 25;310(24):2650-7.
Foa EB, McLean CP, Zang Y, et al. Effect of **prolonged exposure therapy** delivered over 2 weeks vs 8 weeks vs present-centered therapy on **PTSD** symptom severity in military personnel: a randomized clinical trial.JAMA. doi:10.1001/jama.2017.21242
Forneris CA, Gartlehner G, Brownley KA, et al. Interventions to prevent **post-traumatic stress disorder**: a systematic review. Am J Prev Med. 2013 Jun;44(6):635-50
Fortinguerra, Filomena, Clavenna, Antonio, Bonati, Maurizio. Psychotropic Drug Use During **Breastfeeding**: A Review of the Evidence. Pediatrics 2009 124: e547-e556.
Fortney JC, Pyne JM, Kimbrell TA, et al. **Telemedicine-Based** Collaborative Care for **Posttraumatic** Stress Disorder: A Randomized Clinical Trial. JAMA Psychiatry. 2014Nov19.
Frampton JE. **Pregabalin**: a review of its use in adults with generalized anxiety disorder. CNS Drugs. 2014 Sep;28(9):835-54.
Franklin ME, Sapyta J, Freeman JB, et al. **Cognitive behavior therapy augmentation of pharmacotherapy** in pediatric obsessive-compulsive disorder: the Pediatric OCD Treatment Study II (**POTS II**) randomized controlled trial. JAMA. 2011 Sep 21;306(11):1224-32.
Frick A, Åhs F, Engman J, et al. Serotonin Synthesis and Reuptake in **Social Anxiety Disorder**: A **Positron Emission Tomography Study**. JAMA Psychiatry. 2015 Jun 17.

Fudim M, Cerbin LP, Devaraj S, et al. **Post-Traumatic Stress Disorder and Heart Failure** in Men Within the Veteran Affairs Health System. Am J Cardiol. 2018 Apr 11.

Galante J, Dufour G, Vainre M, et al. A **mindfulness-based intervention to increase resilience to stress in university students** (the **Mindfulness Student Study**): a pragmatic randomised controlled trial. Lancet Public Health 2017; online Dec 18.

Gale C, Davidson O. **Generalised anxiety disorder**. BMJ. 2007 Mar 17;334(7593):579-81.

Gao K, Muzina D, Gajwani P, Calabrese JR. Efficacy of **typical and atypical antipsychotics** for primary and comorbid **anxiety** symptoms or disorders: a review. J Clin Psychiatry. 2006 Sep;67(9):1327-40. Except for trifluoperazine, there is no large, well-designed study of antipsychotics in the treatment of primary or comorbid anxiety symptoms or disorders. The efficacy of these agents in various anxiety conditions needs to be further investigated with large, well-designed comparison studies.

Gartlehner G, Forneris CA, Brownley KA, et al. Interventions for the **prevention of posttraumatic stress disorder (PTSD)** in adults after exposure to psychological trauma. AHRQ Comparative Effectiveness Reviews. Rockville (MD): Agency for Healthcare Research and Quality (US); 2013 Apr. Report No.: 13-EHC062-EF. Evidence supporting the effectiveness of most interventions used to prevent PTSD is lacking. If available in a given setting, brief trauma-focused CBT might be the preferable choice for reducing PTSD symptom severity in persons with acute stress disorder and collaborative care might be preferred for trauma patients requiring surgical hospitalization; by contrast, debriefing appears to be an ineffective intervention to reduce symptoms and prevent PTSD.

Gibson CJ, Huang AJ, McCaw B, Subak LL, Thom DH, Van Den Eeden SK. Associations of **intimate partner violence, sexual assault, and posttraumatic stress disorder with menopause symptoms** among midlife and older women [online Nov 19, 2018]. JAMA Intern Med.

Gillies D, Taylor F, Gray C, O'Brien L, D'Abrew N. **Psychological therapies** for the treatment of **post-traumatic stress disorder** in children and adolescents. Cochrane Database of Systematic Reviews 2012, Issue 12. Art. No.: CD006726. DOI: 10.1002/14651858.CD006726.pub2. There is evidence for the effectiveness of psychological therapies, particularly CBT, for treating PTSD in children and adolescents for up to a month following treatment.

Gimson A, Schlosser M, Huntley JD, et al. Support for **midlife anxiety diagnosis as an independent risk factor for dementia**: a systematic review. BMJ Open. 2018 Apr 30;8(4):e019399.

Ginsburg GS, Becker EM, Keeton CP, et al. **Naturalistic Follow-up of Youths** Treated for Pediatric Anxiety Disorders. JAMA Psychiatry. 2014 Jan 29

Ginsburg GS et al. Preventing onset of anxiety disorders in **offspring of anxious parents**: randomized controlled trial of a family-based intervention. Am J Psychiatry 2015 Sep 25.

Ginsburg GS, Drake KL, Tein JY, et al. Preventing Onset of Anxiety Disorders in **Offspring of Anxious Parents**: A Randomized Controlled Trial of a Family-Based Intervention. Am J Psychiatry. 2015 Sep 25:appiajp201514091178.

Goddard AW, et al. Early coadministration of clonazepam with sertraline for panic disorder. Arch Gen Psychiatry. 2001 Jul;58(7):681-6.

Goldstein E, McDonnell C, Atchley R, et al. The Impact of **Psychological Interventions** on Posttraumatic Stress Disorder and Pain Symptoms: A Systematic Review and Meta-Analysis. Clin J Pain. 2019 Aug;35(8):703-712.

Gorman DA, Abi-Jaoude E. **Obsessive-compulsive disorder**. CMAJ. 2014 Aug 5;186(11):E435.

Goyal M, Singh S, Sibinga EM, et al. **Meditation Programs** for Psychological Stress and Well-being: A Systematic Review and Meta-analysis. JAMA Intern Med. 2014 Jan 6.

Grant JE, Odlaug BL, Kim SW. **N-acetylcysteine**, a glutamate modulator, in the treatment of **trichotillomania**: a double-blind, placebo-controlled study. Arch Gen Psychiatry. 2009 Jul;66(7):756-63.

Grant JE. **Obsessive–Compulsive Disorder**. N Engl J Med 2014;371:646-53.

Gratzer D, Khalid-Khan F. **Internet-delivered cognitive behavioural therapy** in the treatment of psychiatric illness. CMAJ. 2016 Mar 1;188(4):263-72.

Hanna GL, Hollander E, Nestadt G, Blair Simpson H. Treatment of patients with obsessive-compulsive disorder. In: *APA practice guidelines* [database online]. Arlington(VA): American Psychiatric Association (APA) 2007. Available: http://www.psychiatryonline.com/pracGuide/loadGuidelinePdf.aspx?file=OCDPracticeGuidelineFinal05-04-07

Hamani C, Pilitsis J, Rughani AI, Rosenow JM, et al. **Deep brain stimulation for obsessive-compulsive disorder**: systematic review and evidence-based guideline sponsored by the American Society for Stereotactic and Functional Neurosurgery and the Congress of Neurological Surgeons (CNS) and endorsed by the CNS and American Association of Neurological Surgeons. Neurosurgery. 2014 Oct;75(4):327-33.

Hansen MV, Halladin NL, Rosenberg J, Gögenur I, Møller AM. **Melatonin** for pre-and postoperative anxiety in adults. Cochrane Database Syst Rev. 2015 Apr 9;4:CD009861. When compared to placebo, melatonin given as premedication (tablets or sublingually) can reduce preoperative anxiety in adults (measured 50 to 100 minutes after administration). Melatonin may be equally as effective as standard treatment with midazolam in reducing preoperative anxiety in adults (measured 50 to 100 minutes after administration). The effect of melatonin on postoperative anxiety (measured 90 minutes and 6 hours after surgery) in adults is mixed but suggests an overall attenuation of the effect compared to preoperatively.

Hawkins EJ, Malte CA, Imel ZE, et al. Prevalence and trends of benzodiazepine use among Veterans Affairs patients with **posttraumatic stress disorder**, 2003-2010. Drug Alcohol Depend. 2012 Feb 2.

Hawkins NA, Soman A, Buchanan et al. Use of Medications for **Treating Anxiety and Depression in Cancer Survivors** in the United States. J Clin Oncol. 2017 Jan;35(1):78-85.

Hedman E, Andersson G, Andersson E, et al. **Internet-based cognitive-behavioural therapy** for severe health anxiety: randomised controlled trial. Br J Psychiatry. 2011 Mar;198:230-6.

Hedman E, Axelsson E, Gorling A, et al. **Internet-delivered exposure-based cognitive-behavioural therapy** and behavioural stress management for severe health anxiety: randomised controlled trial. Br J Psychiatry. 2014 Aug 7.

Hedman E, Andersson E, Ljótsson B, et al. Cost effectiveness of **internet-based cognitive behaviour therapy** and behavioural stress management for severe health anxiety. BMJ Open. 2016 Apr 25.

Hedman E, Axelsson E, Andersson E, et al. **Exposure-based cognitive-behavioural therapy** via the internet and as bibliotherapy for somatic symptom disorder and illness anxiety disorder: randomised controlled trial. Br J Psychiatry. 2016 Aug 4.

Hedman-Lagerlöf E, Tyrer P, Hague J, Tyrer H. **Health anxiety**. BMJ. 2019 Mar 12;364:l774.

Help for Anxiety and Panic Disorders. Am Fam Physician. 2015 May 1;91(9)

Hetrick SE, Purcell R, Garner B, et al. Combined **pharmacotherapy and psychological therapies** for post traumatic stress disorder (PTSD). Cochrane Database Syst Rev. 2010 Jul 7;7:CD007316. There is not enough evidence available to support or refute the effectiveness of combined psychological therapy and pharmacotherapy compared to either of these interventions alone.

Herr NR, Williams JW Jr, Benjamin S, et al. Does this patient have generalized anxiety or panic disorder? The rational clinical examination systematic review. JAMA. 2014 Jul 2;312(1):78-84.

Herring MP, O'Connor PJ, Dishman RK. The Effect of **Exercise** Training on Anxiety Symptoms Among Patients: A Systematic Review. Arch Intern Med. 2010;170(4):321-331.

Heyman I, Mataix-Cols D, Fineberg NA. **Obsessive-compulsive disorder**. BMJ. 2006 Aug 26;333(7565):424-9.

Hirschtritt ME, Bloch MH, Mathews CA. **Obsessive-Compulsive Disorder**: Advances in Diagnosis and Treatment. JAMA. 2017 Apr 4;317(13):1358-1367.

Hoffman V, Middleton JC, Feltner C, et al. **Psychological and pharmacological treatments for adults with posttraumatic stress disorder: a systematic review update. Comparative Effectiveness Review No. 207.** AHRQ Publication No. 18-EHC011-EF. PCORI Publication No. 2018-SR-01.

Hoge EA, Ivkovic A, Fricchione GL. **Generalized anxiety disorder**: diagnosis and treatment. BMJ. 2012 Nov 27;345:e7500.

Hodgins S, De Brito SA, Chhabra P, et al. Anxiety disorders among offenders with **antisocial** personality disorders: a distinct subtype? Can J Psychiatry. 2010 Dec;55(12):784-91.

Hodgins David C, Stea Jonathan N, Grant Jon E. **Gambling disorders**. www.thelancet.com Published online May 19, 2011 DOI:10.1016/S0140-6736(10)62185-X

Holbrook TL et al. **Morphine** use after combat injury in Iraq and **post-traumatic stress disorder**. *N Engl J Med* 2010 Jan 14; 362:110.

Hoskins M, Pearce J, Bethell A, et al. Pharmacotherapy for **post-traumatic stress disorder**: systematic review and meta-analysis. Br J Psychiatry. 2015 Feb;206(2):93-100.

Huhn M, TardyM, Spineli LM, et al. Efficacy of **pharmacotherapy and psychotherapy** for adult psychiatric disorders: a systematic overview of meta-analyses [online April 30, 2014]. JAMA Psychiatry. doi:10.1001/jamapsychiatry.2014.112.

Imai H, Tajika A, Chen P, et al. **Psychological therapies versus pharmacological interventions** for **panic disorder** with or without agoraphobia in adults. Cochrane Database Syst Rev 2016;10:CD011170. The evidence in this review was often imprecise. The superiority of either therapy over the other is uncertain due to the low and very low quality of the evidence with regard to short-term efficacy and treatment acceptability, and no data were available regarding adverse effects.

Ipser JC, et al. Pharmacotherapy **augmentation** strategies in treatment-resistant **anxiety** disorders. Cochrane Database Syst Rev. 2006 Oct 18;(4):CD005473.

Jackson JC, Pandharipande PP, Girard TD, et al. Bringing to light the Risk Factors And Incidence of Neuropsychological dysfunction in ICU survivors (BRAIN-ICU) study investigators. **Depression, post-traumatic stress disorder, and functional disability in survivors of critical illness in the BRAIN-ICU** study: a longitudinal cohort study. Lancet Respir Med. 2014 May;2(5):369-79.

Jolstedt M, Wahlund T, Lenhard F, et al. Efficacy and cost-effectiveness of **therapist-guided internet cognitive behavioural therapy** for paediatric anxiety disorders: a single-centre, single-blind, randomised controlled trial. Lancet Child Adolesc Health. 2018 Nov;2(11):792-801.

Jonas DE, Cusack K, Forneris CA, et al. **Psychological and pharmacological treatments for adults with posttraumatic stress disorder (PTSD). AHRQ** Comparative Effectiveness Reviews. Rockville (MD): Agency for Healthcare Research and Quality (US); 2013 Apr. Report No.: 13-EHC011-EF.

Jukić MM, Haslemo T, Molden E, et al. Impact of **CYP2C19** Genotype on **Escitalopram** Exposure and Therapeutic Failure: A Retrospective Study Based on 2,087 Patients. Am J Psychiatry. 2018 Jan 12:appiajp201717050550.

Kavan MG. Elsasser GN et al. **Generalized Anxiety Disorder**: Practical Assessment and Management. *Am Fam Physician.* 2009;79(9):785-791.

Komossa K, Depping AM, Meyer M, et al. **Second-generation antipsychotics for obsessive compulsive disorder**. Cochrane Database Syst Rev. 2010 Dec 8;12:CD008141.

Kampman M, et al. A randomized, double-blind, placebo-controlled study of the effects of adjunctive paroxetine in panic disorder patients unsuccessfully treated with cognitive-behavioral therapy alone. J Clin Psychiatry. 2002 Sep;63(9):772-7.

Katon WJ. Clinical practice. **Panic disorder**. N Engl J Med. 2006 Jun 1;354(22):2360-7.

Katzman MA, Bleau P, Blier P, et al; Canadian Anxiety Guidelines Initiative Group on behalf of the Anxiety Disorders Association of Canada/Association Canadienne des troubles anxieux and McGill University. **Canadian clinical practice guidelines for the management of anxiety, posttraumatic stress and obsessive-compulsive disorders**. BMC Psychiatry 2014;14(suppl 1):S1-83. www.biomedcentral.com/content/pdf/1471-244X-14-S1-S1.pdf (accessed July 17, 2014).

Kimerling R, Ouimette P, Prins A, et al. Brief report: Utility of a short **screening** scale for DSM-IV **PTSD** in primary care. J Gen Intern Med. 2006 Jan;21(1):65-7.

Kinrys G, Wygant LE, Pardo TB, Melo M. Levetiracetam for treatment-refractory posttraumatic stress disorder. J Clin Psychiatry. 2006 Feb;67(2):211-4.

Kiphuth IC, Utz KS, Noble AJ, et al. Increased Prevalence of **Posttraumatic Stress Disorder** in Patients **After Transient Ischemic Attack. Stroke**. 2014 Oct 2.

Klainin-Yobas P, Oo WN, Suzanne Yew PY, et al. Effects of **relaxation interventions on depression and anxiety among older adults**: a systematic review. Aging Ment Health. 2015 Jan 9:1-13.

Kobak KA, Taylor LV, et al. **St John's wort** versus placebo in obsessive-compulsive disorder: results from a double-blind study. Int Clin Psychopharmacol. 2005;20(6):299-304.

Komossa K, Depping AM, Meyer M, et al. **Second-generation antipsychotics** for obsessive compulsive disorder. Cochrane Database Syst Rev. 2010 Dec 8;12:CD008141. The available data of the effects of olanzapine in OCD are too limited to draw any conclusions. There is some evidence that adding quetiapine or risperidone to antidepressants increases efficacy, but this must be weighed against less tolerability and limited data.

Koran LM, Hanna GL, Hollander E, Nestadt G, Simpson HB; **American Psychiatric Association**. Practice guideline for the treatment of patients with **obsessive-compulsive** disorder. Am J Psychiatry. 2007 Jul;164(7 Suppl):5-53. http://www.psych.org/psych_pract/treatg/pg/OCDPracticeGuidelineFinal05-04-07.pdf

Kramer DN, Hertli MB, Landolt MA. Evaluation of an Early **Risk Screener for PTSD** in Preschool Children After Accidental Injury. Pediatrics. 2013 Sep 23.

Kronish IM, Lin JJ, Cohen BE, et al. **Posttraumatic Stress Disorder and Medication Nonadherence** in Patients With Uncontrolled Hypertension. JAMA Intern Med. 2013 Dec 2.

Krystal JH et al. Adjunctive **risperidone** treatment for antidepressant-resistant symptoms of chronic military service–related PTSD: randomized trial. JAMA 2011 Aug 3. (ineffective)

Kuhn E et al. A randomized controlled trial of a **smartphone app for posttraumatic stress** disorder symptoms. J Consult Clin Psychol 2017 Mar; 85:267.

Kumar KK, Appelboom G, Lamsam L, et al. Comparative effectiveness of **neuroablation and deep brain stimulation for treatment-resistant obsessive-compulsive disorder**: a meta-analytic study. J Neurol Neurosurg Psychiatry. 2019 Jan 24.

Kurlan R. Clinical practice. **Tourette's Syndrome**. N Engl J Med. 2010 Dec 9;363(24):2332-8.

Kuwert P, Pietrzak RH, Glaesmer H. **Trauma and posttraumatic stress** disorder in older adults. CMAJ. 2013 May 14;185(8):685.

Lazarov A, et al. Gaze-Contingent **Music Reward Therapy for Social Anxiety Disorder**: A Randomized Controlled Trial. Am J Psychiatry. 2017 Jan 20:appiajp201616080894.

Leichsenring F, Leweke F. **Social Anxiety Disorder**. N Engl J Med. 2017 Jun 8;376(23):2255-2264

Lenze EJ, Rollman BL, Shear MK, et al. **Escitalopram** for **older** adults with generalized anxiety disorder: a randomized controlled trial. JAMA. 2009 Jan 21;301(3):295-303. Older adults $^{n=177}$ with GAD randomized to escitalopram 10-20mg od had a higher cumulative response rate for improvement vs placebo over 12 weeks; however, response rates were not significantly different using an intention-to-treat analysis. Further study is required to assess efficacy and safety over longer treatment durations.

Leucht S, Hierl S, Kissling W, Dold M, Davis JM. Putting the **efficacy of psychiatric and general medicine medication** into perspective: review of meta-analyses. Br J Psychiatry 2012;200:97-106.

Lewis C, Pearce J, et al. Efficacy, cost-effectiveness and acceptability of **self-help** interventions for anxiety disorders: systematic review. Br J Psychiatry. 2012 Jan;200(1):15-21.

Locke AB, Kirst N, Shultz CG. Diagnosis and Management of **Generalized Anxiety Disorder and Panic Disorder in Adults**. Am Fam Physician. 2015;91(9):617-624.

Lohr JB, Palmer BW, et al. Is **Post-Traumatic Stress Disorder Associated with Premature Senescence**? A Review of the Literature. Am J Geriatr Psychiatry. 2015 May 4.

Lopes AC, Greenberg BD, Canteras MM, et al. **Gamma Ventral Capsulotomy** for Obsessive-Compulsive Disorder: A Randomized Clinical Trial. JAMA Psychiatry. 2014 Jul 23.

Lovell K, Bower P, Gellatly J, et al. Clinical effectiveness, cost-effectiveness and acceptability of low-intensity interventions in the management of obsessive-compulsive disorder: the **Obsessive-Compulsive** Treatment Efficacy randomised controlled Trial (**OCTET**). Health Technol Assess. 2017 Jun;21(37):1-132.

Lovell K, Bower P, Gellatly J, et al. Low-intensity cognitive-behaviour therapy interventions for **obsessive-compulsive disorder** compared to waiting list for therapist-led **cognitive behaviour therapy**: 3-arm randomised controlled trial of clinical effectiveness. PLoS Med. 2017 Jun 27;14(6):e1002337.

Mallet L, Polosan M, Jaafari N, et al. STOC Study Group. **Subthalamic nucleus stimulation** in severe obsessive-compulsive disorder. N Engl J Med. 2008 Nov 13;359(20):2121-34. These preliminary findings suggest that stimulation of the subthalamic nucleus may reduce the symptoms of severe forms of OCD but is associated with a substantial risk of serious adverse events.

Mac Donald CL et al. Detection of **blast-related traumatic brain injury** in U.S. military personnel. *N Engl J Med* 2011 Jun 2; 364:2091.

Machado A, Fernandez HH, Deogaonkar M. Deep brain stimulation: What can patients expect from it? (OCD) Cleveland Clinic Journal of Medicine 2012; 79(2):113-120.

Machado MO, Stergiopoulos V, Maes M, et al. Depression and Anxiety in **Adults With Hidradenitis Suppurativa**: A Systematic Review and Meta-analysis. JAMA Dermatol.2019 Jun 5

Magruder K, Serpi T, Kimerling R et al. Prevalence of **Posttraumatic Stress Disorder in Vietnam-Era Women** Veterans: The Health of Vietnam-Era Women's Study (HealthVIEWS). JAMA Psychiatry. 2015 Oct 7:1-8.

Maher AR et al. Efficacy and comparative effectiveness of **atypical antipsychotic medications for off-label uses in adults**. JAMA 2011 Sep 28; 306:1359.
[For generalized anxiety disorder, a pooled analysis of 3 trials showed that quetiapine was associated with a 26% greater likelihood of a favorable response (defined as at least 50%improvement on the Hamilton Anxiety Scale) compared with placebo. For obsessivecompulsive disorder, risperidone was associated with a 3.9-fold greater likelihood of a favorable response (defined as a 25% improvement on the Yale-Brown Obsessive Compulsive Scale) compared with placebo.]

Management of adults with **PTSD** part I: **background, diagnosis and psychological therapies**. Drug Ther Bull. 2014 Mar;52(3):33-6.

Management of adults with **PTSD** part II: **drugs and other interventions**. Drug Ther Bull. 2014 Apr;52(4):44-8.

Markowitz JC, Petkova E, Neria Y, et al. Is Exposure Necessary? A Randomized Clinical Trial of **Interpersonal Psychotherapy for PTSD**. Am J Psychiatry. 2015 Feb 13.

Marmar CR, Schlenger W, Henn-Haase C, et al. Course of Posttraumatic Stress Disorder **40 Years After the Vietnam War**: Findings From the National Vietnam Veterans Longitudinal Study. JAMA Psychiatry. 2015 Jul 22.

Mataix-Cols D, Boman M, et al. Population-Based, **Multigenerational Family Clustering Study of Obsessive-Compulsive Disorder**. JAMA Psychiatry. 2013 May 22:1-9.

Mavandadi S, Benson A, DiFilippo S, et al. A **Telephone-Based Program** to Provide Symptom Monitoring Alone vs Symptom Monitoring Plus Care Management for Late-Life Depression and Anxiety: A Randomized Clinical Trial. JAMA Psychiatry. 2015 Nov 11:1211-1218.

Mayo-Wilson E, Dias S, Mavranezouli I, et al. **Psychological and pharmacological interventions for social anxiety disorder** in adults: a systematic review and network meta-analysis. Lancet Psychiatry 2014;1:368–76.

McFall Miles, Saxon Andrew J., Malte Carol A., et al. for the CSP 519 Study Team. Integrating **Tobacco Cessation** Into Mental Health Care for Posttraumatic Stress Disorder: A Randomized Controlled Trial. JAMA. 2010;304(22):2485-2493.doi:10.1001/jama.2010.1769.

McFarlane AC. Is **screening for the psychological effects of war** useful? Lancet. 2017 Feb 16.

Macmanus D, Dean K, et al. **Violent offending by UK military** personnel deployed to Iraq and Afghanistan: a data linkage cohort study. Lancet. 2013 Mar 16;381(9870):907-17.

Marc I, Toureche N, Ernst E, et al. **Mind-body interventions during pregnancy** for preventing or treating women's anxiety. Cochrane Database of Systematic Reviews 2011, Issue 7. Art. No.: CD007559. DOI: 10.1002/14651858.CD007559.pub2. Mind-body interventions might benefit women's anxiety during pregnancy. Based on individual studies, there is some but no strong evidence for the effectiveness of mind-body interventions for the management of anxiety during pregnancy. The main limitations of the studies were the lack of blinding and insufficient details on the methods used for randomization.

Mason SM, Flint AJ, Roberts AL, et al. **Posttraumatic** Stress Disorder Symptoms and **Food Addiction** in Women by Timing and Type of Trauma Exposure. JAMA Psychiatry. 2014 Sep 17.

Mataix-Cols D. Clinical practice. **Hoarding** disorder. N Engl J Med. 2014 May 22;370(21):2023-30.
Mataix-Cols D, Fernández de la Cruz L, Monzani B, et al. **D-Cycloserine** Augmentation of Exposure-Based Cognitive Behavior Therapy for Anxiety, Obsessive-Compulsive, and Posttraumatic Stress Disorders: A Systematic Review and Meta-analysis. JAMA Psychiatry. 2017 Jan 25.
Mawanda F, et al. **PTSD**, **Psychotropic Medication Use**, and the Risk of **Dementia** Among US Veterans: A Retrospective Cohort Study. J Am Geriatr Soc. 2017 Feb 8.
Mayo-Wilson E, Montgomery P. **Media-delivered cognitive behavioural therapy and behavioural therapy** (selfhelp) for anxiety disorders in adults. *Cochrane Database of Systematic Reviews* 2013, Issue 9. Art. No.: CD005330. DOI:10.1002/14651858.CD005330.pub4. Self-help may be useful for people who are not able or are not willing to use other services for people with anxiety disorders; for people who can access it, face-to-face cognitive behavioural therapy is probably clinically superior. Economic analyses were beyond the scope of this review. Important heterogeneity was noted across trials.
McCall WV, Pillai A, Case D, McCloud L, et al. A Pilot, Randomized Clinical Trial of **Bedtime Doses of Prazosin Versus Placebo** in Suicidal Posttraumatic Stress Disorder Patients With Nightmares. J Clin Psychopharmacol. 2018 Dec;38(6):618-621.
Meier SM, Petersen L, Pedersen MG, et al. **Obsessive-Compulsive Disorder** as a **Risk Factor for Schizophrenia**: A Nationwide Study. JAMA Psychiatry. 2014 Sep 3.
Meier SM, Mattheisen M, Mors O, et al. **Mortality** Among Persons With **Obsessive-Compulsive Disorder** in Denmark. JAMA Psychiatry. 2016 Jan 27.
Merz J, Schwarzer G, Gerger H. Comparative Efficacy and Acceptability of **Pharmacological, Psychotherapeutic, and Combination Treatments** in Adults With Posttraumatic Stress Disorder: A Network Meta-analysis. JAMA Psychiatry. 2019 Jun 12.
Mills KL et al. Integrated **exposure-based therapy** for co-occurring **posttraumatic stress disorder** and substance dependence: A randomized controlled trial. JAMA 2012 Aug 15; 308:690.
Minassian A, Maihofer AX, Baker DG, et al; Marine Resiliency Study Team. Association of Predeployment **Heart Rate Variability** With Risk of Postdeployment Posttraumatic Stress Disorder in Active-Duty Marines. JAMA Psychiatry. 2015 Sep 9:1-8.
Mitchell AJ, Ferguson DW, Gill J, et al. **Depression and anxiety in long-term cancer survivors** compared with spouses and health controls: a systematic review and meta-analysis. Lancet Oncol 2013; online June 5.
Mitte K. A meta-analysis of the efficacy of psycho- and pharmacotherapy in **panic** disorder with and without agoraphobia. J Affect Disord. 2005 Sep;88(1):27-45.
Miyasaka LS, Atallah AN, Soares BG. **Valerian** for anxiety disorders. Cochrane Database Syst Rev. 2006 Oct 18;(4):CD004515.
Monson CM et al. Effect of **cognitive-behavioral couple therapy for PTSD**: A randomized controlled trial. JAMA 2012 Aug 15; 308:700.
Montgomery SA, et al. Efficacy and safety of **pregabalin** in the treatment of generalized anxietydisorder: a 6-week, multicenter, randomized, double-blind, placebo-controlled comparison of pregabalin and venlafaxine. J Clin Psychiatry. 2006 May;67(5):771-82.
Moreno-Peral P, Conejo-Cerón S, Rubio-Valera M, et al. Effectiveness of **psychological and/or educational interventions in the prevention of anxiety**: a systematic review, meta-analysis, and meta-regression [published online September 6, 2017]. .JAMA Psych. doi:10.1001/jamapsychiatry .2017.2509
Morgenthaler TI, Auerbach S, Casey KR, et al. Position Paper for the **Treatment of Nightmare Disorder in Adults**: An American Academy of Sleep Medicine Position Paper. J Clin Sleep Med. 2018 Jun 15;14(6):1041-1055.
Morina N, al. **Psychological interventions for post-traumatic stress** disorder and depression in young survivors of mass violence in low- and middle-income countries: meta-analysis. Br J Psychiatry. 2017 Feb 2.
Morina N, Malek M, Nickerson A, Bryant RA. **Psychological interventions for post-traumatic stress disorder** and depression in young survivors of mass violence in low- and middle-income countries: meta-analysis. Br J Psychiatry. 2017 Apr;210(4):247-254.
Moss J, Roberts MB, Shea L, et al. **Healthcare provider compassion is associated with lower PTSD symptoms** among patients with life-threatening medical emergencies: a prospective cohort study. Intensive Care Med. 2019 Mar 25
Murphy TK, et al. Clinical Factors Associated with Pediatric Autoimmune Neuropsychiatric Disorders Associated with **Streptococcal Infections**.(PANDAS) J Pediatr.2011Aug 24.
Namouz-Haddad S, Nulman I. Safety of treatment of **obsessive compulsive disorder in pregnancy** and puerperium. Can Fam Physician. 2014 Feb;60(2):133-6.
Nemeroff CB. Use of atypical antipsychotics in refractory depression and anxiety. J Clin Psychiatry. 2005;66 Suppl 8:13-21.
NICE Nov 2005 :Obsessive Compulsive Disorder: Core interventions in the treatment of **OCD** and body dysmorphic disorder http://www.nice.org.uk/page.aspx?o=cg031
NICE Mar 2005 Anxiety: Management of **post-traumatic stress disorder** in adults in primary, secondary and community care http://www.nice.org.uk/page.aspx?o=CG026
NICE Dec 2004 Anxiety: Management of anxiety (**panic disorder**, with or without agoraphobia, and generalised anxiety disorder) in adults in primary, secondary and community Care http://www.nice.org.uk/page.aspx?o=cg022fullguideline
NICE: National Institute for Health and Clinical Excellence. **Generalised anxiety disorder** and panic disorder (with or without agoraphobia) in adults: management in primary, secondary and community care. 2011. (Clinical guideline 113.) http://guidance.nice.org.uk/CG113 .
NICE: Pilling Stephen, Whittington Craig, Taylor Clare, et al. on behalf of the Guideline Development Group. Guidelines: Identification and care pathways for common mental health disorders: summary of NICE guidance. BMJ 2011;342:doi:10.1136/bmj.d2868 (Published 24 May 2011)
NICE: National Institute for Health and Clinical Excellence. Common mental health disorders: identification and **pathways to care**. (Clinical guideline CG123. 2011. http://guidance.nice.org.uk/CG123 .
NICE: National Institute for Health and Care Excellence. **Social anxiety disorder**: recognition, assessment and treatment of social anxiety disorder. (Clinical guideline 159.) 2013. http://guidance.nice.org.uk/CG159 .
Nidich S, Mills PJ, Rainforth M, et al. **Non-trauma-focused meditation versus exposure therapy** in veterans with post-traumatic stress disorder: a randomised controlled trial.

Lancet Psychiatry. 2018 Dec;5(12):975-986.
Niles BL, Mori DL, Polizzi CP, et al. Feasibility, qualitative findings and satisfaction of a brief **Tai Chi** mind-body programme for veterans with post-traumatic stress symptoms. BMJ Open. 2016 Nov 29;6(11):e012464.
Norman SB, Trim R, Haller M, et al. **Efficacy of Integrated Exposure Therapy vs Integrated Coping Skills Therapy for Comorbid Posttraumatic Stress Disorder and Alcohol Use** Disorder: A Randomized Clinical Trial. JAMA Psychiatry. 2019 Apr 24.
Ollendick TH, Öst LG, Farrell LJ. Innovations in the **psychosocial treatment of youth with anxiety disorders**: implications for a stepped care approach. Evid Based Ment Health. 2018 Aug;21(3):112-115.
Olthuis JV, Watt MC, Bailey K, Hayden JA, Stewart SH. **Therapist-supported Internet cognitive behavioural therapy** for anxiety disorders in adults. Cochrane Database of Systematic Reviews 2015, Issue 3. Art. No.: CD011565. DOI: 10.1002/14651858.CD011565. Therapist-supported ICBT appears to be an efficacious treatment for anxiety in adults. The evidence comparing therapist-supported ICBT to waiting list, attention, information, or online discussion group only control was low to moderate quality, the evidence comparing therapist-supported ICBT to unguided ICBT was low to very low quality, and comparisons of therapist-supported ICBT to face-to-face CBT was low to moderate quality.
O'Neil ME, Nugent SM, Morasco BJ, et al. Benefits and harms of plant-based **cannabis** for **posttraumatic stress disorder**. A systematic review. Ann Intern Med. 2017. [Epub ahead of print]. doi:10.7326/M17-0477
Orgeta V, Qazi A, Spector A, et al. **Psychological treatments** for depression and anxiety in dementia and mild cognitive impairment: systematic review and meta-analysis. Br J Psychiatry. 2015 Oct;207(4):293-8.
Orlovska S, et al. Association of **Streptococcal Throat Infection** With **Mental Disorders**: Testing Key Aspects of the **PANDAS** Hypothesis in a Nationwide Study. JAMA Psychiatry. 2017 May 24.
Ostacher MJ, Cifu AS. Management of **Posttraumatic Stress Disorder**. JAMA. 2018 Dec 17.
Parker AM, Sricharoenchai T, Raparla S, et al. **Posttraumatic** Stress Disorder in **Critical Illness Survivors**: A Metaanalysis. Crit Care Med. 2015 Feb 4.
Parmet Sharon, Lynm Cassio, Golub Robert M. JAMA **Patient Page Obsessive-Compulsive Disorder**. *JAMA*. 2011;305(18):1926.doi:10.1001/jama.305.18.1926
Patel G, Fancher TL. **In the Clinic: General Anxiety Disorder**. Ann Intern Med Dec 3, 2013 ITC6 1-12.
Patel MB, Jackson JC, et al. Incidence and Risk Factors for **ICU-related Posttraumatic Stress Disorder** In Veterans and Civilians. Am J Respir Crit Care Med. 2016 Jan 6.
Paul IM, Downs DS, Schaefer EW, et al. **Postpartum Anxiety** and Maternal-Infant Health Outcomes. Pediatrics. 2013 Mar 4.
Pavlova B, Perlis RH, et al. **Lifetime prevalence of anxiety disorders in people with bipolar disorder**: a systematic review and meta-analysis. Lancet Psychiatry. 2015 Aug;2(8):710-7.
Pérez-Vigil A, Fernández de la Cruz L, Brander G, et al. Association of **Obsessive-Compulsive Disorder With Objective Indicators of Educational Attainment**: A Nationwide Register-Based Sibling Control Study. JAMA Psychiatry. 2017 Nov 15.
Peskin M, et al. The relationship between **posttraumatic & depressive symptoms** during **virtual reality exposure therapy** with a cognitive enhancer. J Anxiety Disord. 2018 Mar 10.
Phipps S, Klosky JL, Long A, et al. **Posttraumatic Stress** and Psychological Growth in **Children With Cancer**: Has the Traumatic Impact of Cancer Been Overestimated? J Clin Oncol. 2014 Jan 21.
Pilling S, Mayo-Wilson E, Mavranezouli I, et al. Guideline Development Group. Recognition, assessment and treatment of **social anxiety disorder: summary of NICE** guidance. BMJ. 2013 May 22;346:f2541.
Pittler MH, Ernst E. **Kava extract for treating anxiety**. Cochrane Database Syst Rev. 2003;(1):CD003383. Compared with placebo, kava extract appears to be an effective symptomatic treatment option for anxiety. The data available from the reviewed studies suggest that kava is relatively safe for short-term treatment (1 to 24 weeks), although more information is required. Further rigorous investigations, particularly into the long-term safety profile of kava are warranted.
Pollack MH, et al. A double-blind study of the efficacy of **venlafaxine** extended-release, **paroxetine**, and placebo in the treatment of panic disorder. Depress Anxiety. 2006 Aug 7.
Pollack MH et al. A double-blind randomized controlled trial of **augmentation and switch strategies** for refractory **social anxiety disorder**. Am J Psychiatry 2014 Jan 1; 171:44.
Polosan M, Chabardes S, Bougerol T, et al. Long-term improvement in **obsessions and compulsions** with **subthalamic stimulation**. Neurology. 2016 Oct 25;87(17):1843-1844.
Polusny MA, Erbes CR, et al. **Mindfulness**-Based Stress Reduction for Posttraumatic Stress Disorder Among Veterans: A Randomized Clinical Trial. JAMA. 2015 Aug 4;314(5):456-65.
Pompoli A, Furukawa TA, Imai H, Tajika A, Efthimiou O, Salanti G. **Psychological therapies** for panic disorder **with or without agoraphobia** in adults: a network meta-analysis. Cochrane Database of Systematic Reviews 2016, Issue 4. Art. No.: CD011004. There is no high-quality, unequivocal evidence to support one psychological therapy over the others for the treatment of panic disorder with or without agoraphobia in adults. However, the results show that CBT - the most extensively studied among the included psychological therapies - was often superior to other therapies, although the effect size was small and the level of precision was often insufficient or clinically irrelevant.
Power MC, Kioumourtzoglou M-A, Hart JE, et al. The relation between past exposure to fine particulate **air pollution** and prevalent **anxiety**: observational cohort study. BMJ 2015;350:h1111
Preti A, Vrublevska J, Veroniki AA, et al. Prevalence and treatment of **panic disorder in bipolar disorder**: systematic review and meta-analysis. Evid Based Ment Health. 2018 May;21(2):53-60.
Primary Care **PTSD Screen (PC-PTSD)** 2012 http://www.ptsd.va.gov/PTSD/professional/pages/assessments/assessment-pdf/pc-ptsd-screen.pdf
Qureshi KL, Upthegrove R, Toman E, et al. **Post-traumatic stress disorder in UK civilians with traumatic brain injury**: an observational study of TBI clinic attendees to estimate PTSD prevalence and its relationship with radiological markers of brain injury severity. BMJ Open. 2019 Feb 19;9(2):e021675.

Raskind MA, Peskind ER, Hoff DJ, et al. A parallel group placebo controlled study of **prazosin** for trauma nightmares and sleep disturbance in combat veterans with post-traumatic stress disorder. Biol Psychiatry 2007;61:928-34.
Raskind MA, Peterson K, Williams T, et al. A Trial of **Prazosin for Combat Trauma PTSD** With Nightmares in Active-Duty Soldiers Returned From Iraq and Afghanistan. Am J Psychiatry. 2013 Jul 12.
Raskind MA, Peskind ER, Chow B, et al. Trial of **prazosin for post-traumatic stress disorder** in military veterans. N Engl J Med 2018;378:507-17.
Rauch SAM, Kim HM, Powell C, et al. **Efficacy of prolonged exposure, sertraline hydrochloride**, and their combination among combat veterans with posttraumatic stress disorder: a randomized clinical trial [Dec 5, 2018]. JAMA Psychiatry. doi:10.1001/jamapsychiatry.2018.3412
Reed RV, Fazel M, Goldring L. **Post-traumatic stress disorder**. BMJ. 2012 Jun 25;344:e3790.
Remes O, et al. **Sex differences** in the association between area **deprivation and generalised anxiety disorder**: British population study. BMJ Open. 2017 May 4;7(5):e013590.
Resick PA, Wachen JS, Dondanville KA, et al; **STRONG STAR** Consortium. Effect of **group vs individual cognitive processing** therapy in active-duty military seeking treatment for posttraumatic stress disorder: a randomized clinical trial [online Nov 23, 2016].JAMA Psychiatry.
Rickels K, Etemad B, Khalid-Khan S, et al. Time to relapse after 6 and **12 months' treatment** of generalized anxiety disorder with venlafaxine extended release. Arch Gen Psychiatry. 2010 Dec;67(12):1274-81.
Rickels K, Pollack MH, Feltner DE, et al. **Pregabalin** for Treatment of Generalized Anxiety Disorder: A 4-Week, Multicenter, Double-blind, Placebo-Controlled Trial of Pregabalin and Alprazolam. Arch Gen Psychiatry. 2005 Sep;62(9):1022-1030.
Robb AS, Cueva JE, Sporn J, et al. **Sertraline treatment of children and adolescents** with posttraumatic stress disorder: a double-blind, placebo-controlled trial. J Child Adolesc Psychopharmacol. 2010 Dec;20(6):463-71. Sertraline was a generally safe treatment in children and adolescents with PTSD, but did not demonstrate efficacy when compared to placebo during 10 weeks of treatment.
Roberts AL, Agnew-Blais JC, Spiegelman D, et al. **Posttraumatic Stress Disorder and Incidence of Type 2 Diabetes** Mellitus in a Sample of Women: A 22-Year Longitudinal Study. JAMA Psychiatry. 2015 Jan 7.
Roberts NP, Kitchiner NJ, Kenardy J, Bisson JI. Systematic review and meta-analysis of multiple-session early interventions following traumatic events. Am J Psychiatry. 2009 Mar;166(3):293-301. Epub 2009 Feb 2. Identification of a traumatic stress event within 3 months and treatment using trauma-focused **cognitive behavioral therapy** is beneficial for patients who meet DSM-IV criteria for the diagnosis of posttraumatic stress disorder (PTSD). It is uncertain whether individuals would benefit if they are symptomatic but do not meet diagnostic criteria for PTSD. (LOE = 1a-)
Roberts NP, Kitchiner NJ, Kenardy J, et al. **Multiple session early psychological interventions** for the prevention of post-traumatic stress disorder. Cochrane Database Syst Rev. 2019 Aug 8;8:CD006869.
Roest AM, de Jonge P, Williams CD, et al. **Reporting Bias** in Clinical Trials Investigating the Efficacy of **Second-Generation Antidepressants** in the Treatment of Anxiety Disorders: A Report of 2 Meta-analyses. JAMA Psychiatry. 2015 Mar 25.
Rollman BL, et al. **Telephone-Delivered Stepped Collaborative Care** for Treating Anxiety in Primary Care: A Randomized Controlled Trial. J Gen Intern Med. 2016 Oct 6.
Rona RJ, et al. **Post-deployment screening for mental disorders** & tailored advice about help-seeking in the UK military: cluster randomized controlled trial. Lancet. 2017 Feb 16.
Ross DA, et al. An **Integrated Neuroscience Perspective** on Formulation and Treatment Planning for **Posttraumatic Stress Disorder**: An Educational Review. JAMA Psychiatry. 2017 Apr 1;74(4):407-415.
Ross DA, Travis MJ, Arbuckle MR. **Posttraumatic Stress Disorder** in a Young Adult Military Veteran. JAMA Psychiatry. 2017 Apr 1;74(4):417-418.
Roy-Byrne PP, et al. A randomized effectiveness trial of **cognitive-behavioral therapy & medication** for primary care panic disorder. Arch Gen Psych. 2005 Mar;62(3):290-8.
Roy-Byrne PP, Craske MG, Stein MB. **Panic** disorder. Lancet. 2006 Sep 16;368(9540):1023-32.
Roy-Byrne P; Craske MG.; Sullivan G et al; Delivery of Evidence-Based Treatment for Multiple **Anxiety Disorders** in Primary Care: A Randomized Controlled Trial JAMA. 2010;303(19):1921-1928.
Rothbaum BO, Price M, Jovanovic T, et al. A Randomized, Double-Blind Evaluation of **d-Cycloserine or Alprazolam** Combined With Virtual Reality Exposure Therapy for **Posttraumatic** Stress Disorder in Iraq and Afghanistan War Veterans. Am J Psychiatry. 2014 Jun 1;171(6):640-8.
Saeed SA, et al. **Herbal and Dietary Supplements** for Treatment of Anxiety Disorders. American Family Physician 2007;76:549-56. Kava potential for mild to moderate anxiety. Inositol modest effects with panic or OCD disorder. Not encourage St. John's wort, valerian, Sympathyl or passionflower.
Saeed SA, Antonacci DJ, Bloch RM. **Exercise, yoga, and meditation** for depressive and anxiety disorders. Am Fam Physician. 2010 Apr 15;81(8):981-6.
Saeed SA, Cuningham K, Bloch R. **Depression and Anxiety Disorders**: Benefits of Exercise, Yoga, and Meditation. Am Fam Physician. 2019;99(10):620-627.
Sahraian A, Bigdeli M, Ghanizadeh A, Akhondzadeh S. **Topiramate as an adjuvant treatment** for obsessive compulsive symptoms in patients with bipolar disorder: a randomized double blind placebo controlled clinical trial. J Affect Disord. 2014 Sep;166:201-5.
Sareen J, et al. **Disability and poor quality of life** associated with comorbid **anxiety** disorders and physical conditions. Arch Intern Med. 2006 Oct 23;166(19):2109-16. After adjusting for sociodemographic factors and other common mental disorders, the presence of an anxiety disorder was significantly associated with thyroid disease, respiratory disease, gastrointestinal disease, arthritis, migraine headaches, and allergic conditions (adjusted odds ratios between 1.39 and 2.12; P<.05).
Scherrer JF, Salas J, Lustman PJ, et al. The Role of **Obesity** in the Association Between Posttraumatic Stress Disorder and Incident Diabetes. JAMA Psychiatry. 2018 Aug 8.
Scherrer JF, Salas J, Norman SB, et al. Association Between Clinically Meaningful Posttraumatic Stress Disorder Improvement and **Risk of Type 2 Diabetes**. JAMA Psychiatry. 2019 Aug 21.

Schneier FR. Clinical practice. Social anxiety disorder. N Engl J Med. 2006 Sep 7;355(10):1029-36.
Schneier FR, Neria Y, Pavlicova M, et al. **Combined Prolonged Exposure Therapy and Paroxetine for PTSD** Related to the World Trade Center Attack: A Randomized Controlled Trial. Am J Psychiatry. 2011 Sep 9.
Schnurr PP, et al. **Cognitive behavioral therapy for posttraumatic stress disorder** in women: a randomized controlled trial. JAMA. 2007 Feb 28;297(8):820-30.
Schuch FB, Stubbs B, Meyer J, et al. **Physical activity protects from incident anxiety**: A meta-analysis of prospective cohort studies. Depress Anxiety. 2019 Jun 17.
Schwartz C, Barican JL, Yung D, et al. Six decades of preventing and treating **childhood anxiety disorders**: a systematic review and meta-analysis to inform policy and practice. Evid Based Ment Health. 2019 Aug;22(3):103-110.
Schwartz TL, Siddiqui UA, Raza S, et al. **Acamprosate** Calcium as Augmentation Therapy for Anxiety Disorders (December). Ann Pharmacother. 2010 Nov 9.
Seng J, Low L, Sperlich M, et al. Post-traumatic stress disorder, **child abuse history, birthweight & gestational age**: a prospective cohort study. BJOG.2011Oct;118(11):1329-39.
Shalev AY et al. **Prevention of posttraumatic stress disorder** by early treatment: the Jerusalem Trauma Outreach and Prevention study. Arch Gen Psychiatry 2011 Oct 3
Shalev A, Liberzon I, Marmar C. **Post-Traumatic Stress Disorder**. N Engl J Med. 2017 Jun 22;376(25):2459-2469.
Shankman SA, Gorka SM, Katz AC, et al. **Side Effects to Antidepressant Treatment in Patients With Depression and Comorbid Panic** Disorder. J Clin Psychiatry. 2017 Jan 3.
Shaw JG, Asch SM, Kimerling R, et al. Posttraumatic stress disorder and risk of **spontaneous preterm birth**. Obstet Gynecol. 2014 Dec;124(6):1111-9.
Shekelle PG, Cook IA, Miake-Lye IM, et al. Benefits and harms of **cranial electrical stimulation** for chronic painful conditions, depression, anxiety, and insomnia. A systematic review. Ann Intern Med. 2018. [Epub ahead of print]. doi:10.7326 /M17-1970
Shiner B, Westgate CL, Bernardy NC, et al. **Anticonvulsant Medication Use in Veterans With Posttraumatic Stress Disorder**. J Clin Psychiatry. 2017 May;78(5):e545-e552
Simeon D, Stein DJ, Gross S, et al. A double-blind trial of **fluoxetine** in pathologic skin picking (**dermatotillomania**) . J Clin Psychiatry 1997; 58:341–347.
Sin J, Spain D, Furuta M, et al. **Psychological interventions for post-traumatic stress disorder (PTSD)** in people with severe mental illness. Cochrane Database Syst Rev. 2017 Jan 24;1:CD011464. Very few trials have investigated TFPIs for individuals with SMI and PTSD. Results from trials of TF-CBT are limited and inconclusive regarding its effectiveness on PTSD, or on psychotic symptoms or other symptoms of psychological distress. Only one trial evaluated EMDR and provided limited preliminary evidence favouring EMDR compared to waiting list. Comparing TF-CBT head-to-head with EMDR and brief psychoeducation respectively, showed no clear effect for either therapy. Both TF-CBT and EMDR do not appear to cause more (or less) adverse effects, compared to waiting list or usual care; these findings however, are mostly based on low to very low-quality evidence. Further larger scale trials are now needed to provide high-quality evidence to confirm or refute these preliminary findings, and to establish which intervention modalities and techniques are associated with improved outcomes, especially in the long term.
Skapinakis P et al. **Pharmacological and psychotherapeutic interventions** for management of **obsessive-compulsive** disorder in adults: A systematic review and network meta-analysis. Lancet Psychiatry 2016Jun 15; [e-pub].
Slee A, Nazareth I, Bondaronek P, et al. **Pharmacological treatments for generalised anxiety disorder**: a systematic review and network meta-analysis. Lancet. 2019 Jan 31.
Sloan DM, Marx BP, Lee DJ, et al. A **Brief Exposure-Based Treatment vs Cognitive Processing Therapy for Posttraumatic Stress Disorder**: A Randomized Noninferiority Clinical Trial. JAMA Psychiatry. 2018 Jan 17.
Smith TC, Ryan MA, Wingard DL, et al. Millennium Cohort Study Team. New onset and persistent symptoms of **post-traumatic stress disorder** self reported after deployment & combat exposures: prospective population based **US military** cohort study. BMJ. 2008 Feb 16;336(7640):366-71. Epub 2008 Jan 15. After adjustment for baseline characteristics, these prospective data indicate a threefold increase in new onset self reported post-traumatic stress disorder symptoms or diagnosis among deployed military personnel who reported combat exposures.
Smoller JW, Pollack MH, Wassertheil-Smoller S, Jackson RD, Oberman A, Wong ND, Sheps D. Panic Attacks and Risk of Incident **Cardiovascular Events** Among Postmenopausal Women in the Women's Health Initiative Observational Study. Arch Gen Psychiatry. 2007 Oct;64(10):1153-60. Panic attacks are relatively common among postmenopausal women and appear to be an independent risk factor for cardiovascular morbidity and mortality in older women.
Song H, Fang F, Tomasson G, et al. Association of **Stress-Related Disorders With Subsequent Autoimmune Disease**. JAMA. 2018 Jun 19;319(23):2388-2400.
Soomro G, Altman D, Rajagopal S, Oakley-Browne M. Selective serotonin re-uptake inhibitors (**SSRIs**) versus placebo for obsessive compulsive disorder (OCD). **Cochrane** Database Syst Rev. 2008 Jan 23;(1):CD001765. SSRIs are more effective than placebo for OCD, at least in the short-term, although there are differences between the adverse effects of individual SSRI drugs.
Sousa MB, et al. A randomized clinical trial of **cognitive-behavioral group** therapy **and sertraline** in the treatment of **OCD**. J Clin Psychiatry. 2006 Jul;67(7):1133-9.
Spencer AE, Faraone SV, Bogucki OE, et al. Examining the association between **posttraumatic stress disorder and attention-deficit/hyperactivity disorder**: a systematic review and meta-analysis. J Clin Psychiatry. 2015 May 12.
Spitzer RL, Kroenke K, Williams JB, Lowe B. A brief **measure** for assessing **generalized anxiety disorder**: the GAD-7. Arch Intern Med. 2006 May 22;166(10):1092-7.
Spoont M. JAMA **Patient page**. **Posttraumatic Stress Disorder (PTSD)**. JAMA. 2015 Aug 4;314(5):532
Spoont MR, Williams JW Jr, Kehle-Forbes S, et al. Does This Patient Have **Posttraumatic Stress Disorder**?: Rational Clinical Examination Systematic Review. JAMA. 2015 Aug 4;314(5):501-10.
Steenkamp MM, Litz BT, Hoge CW, et al. **Psychotherapy for Military-Related PTSD**: A Review of Randomized Clinical Trials. JAMA. 2015 Aug 4;314(5):489-500.
Stein D, et al. Pharmacotherapy for post traumatic stress disorder (**PTSD**). *The **Cochrane** Database of Systematic Reviews* 2006, Issue 1.
Stein MB, Goin MK, Pollack MH, Roy-Byrne P, Sareen J, Simon NM, et al. Treatment of patients with **panic disorder**. In: *APA practice guidelines* [database online]. Second Edition. Arlington(VA): American Psychiatric Association (**APA**) ; 2008. http://www.psychiatryonline.com/pracGuide/loadGuidelinePdf.aspx?file=PanicDisorder_2e_PracticeGuideline
Stein MB, Jain S, Giacino JT, et al. Risk of Posttraumatic Stress Disorder and Major Depression in **Civilian Patients After Mild Traumatic Brain Injury**: A TRACK-TBI Study. JAMA Psychiatry. 2019 Jan 30.

Stein MB, Ravindran LN, Simon NM, et al. **Levetiracetam** in generalized social anxiety disorder: a double-blind, randomized controlled trial. J Clin Psychiatry. 2009 Dec 15.
Stein MB, Kline NA, Matloff JC. Adjunctive **olanzapine** for SSRI-resistant combat-related PTSD: a double-blind, placebo-controlled study. Am J Psychiatry 2002;159:1777–9.
Stein MB, Sareen J. Generalized Anxiety Disorder. N Engl J Med. 2015 Nov 19;373(21):2059-2068.
Stein MB, Chen CY, Ursano RJ, et al. **Genome-wide Association Studies** of Posttraumatic Stress Disorder in 2 Cohorts of US Army Soldiers. JAMA Psychiatry. 2016 May 11.
Stein MB, Craske MG. **Treating Anxiety in 2017**: Optimizing Care to Improve Outcomes. JAMA. 2017 Jul 5.
Storch EA, Wilhelm S, Sprich S, et al. Efficacy of **augmentation of cognitive behavior therapy with weight-adjusted D-cycloserine** vs placebo in pediatric obsessive-compulsive disorder: a randomized clinical trial [online June 29, 2016].JAMA Psychiatry.
Strawn JR, Keeshin BR, et al. Psychopharmacologic treatment of **posttraumatic stress disorder in children** and adolescents: a review. J Clin Psychiatry. 2010 Apr 20.
Su K, Tseng P, Lin P, et al. Association of Use of **Omega-3 Polyunsaturated Fatty Acids With Changes in Severity of Anxiety** Symptoms: A Systematic Review and Meta-analysis. JAMA Netw Open. 2018;1(5):e182327.
Sumner JA, Kubzansky LD, Elkind MS, et al. **Trauma Exposure** and **Posttraumatic Stress Disorder** Symptoms Predict Onset of **Cardiovascular Events** in Women. Circulation. 2015 Jun 29.
Swedo SE, et al. The pediatric autoimmune neuropsychiatric disorders associated with **streptococcal** infection (**PANDAS**) subgroup: separating fact from fiction. Pediatrics. 2004 Apr;113(4):907-11.
Sloan DM, et al. A **Brief Exposure-Based Treatment vs Cognitive Processing Therapy** for **Posttraumatic Stress Disorder**: A Randomized Noninferiority Clinical Trial. JAMA Psychiatry. 2018 Jan 17.
Seitz DP, Adunuri N, Gill SS, et al. **Antidepressants for agitation and psychosis** in dementia. Cochrane Database Syst Rev. 2011 Feb 16;2:CD008191. Currently there are relatively few studies of antidepressants for the treatment of agitation and psychosis in dementia. The SSRIs sertraline and citalopram were associated with a reduction in symptoms of agitation when compared to placebo in two studies. Both SSRIs and trazodone appear to be tolerated reasonably well when compared to placebo, typical antipsychotics and atypical antipsychotics.
Shelby GD, Shirkey KC, Sherman AL, et al. **Functional Abdominal Pain** in Childhood and Long-term Vulnerability to Anxiety Disorders. Pediatrics. 2013 Aug 12.
Sher L, Braquehais MD, Casas M. **Posttraumatic stress disorder, depression, and suicide in veterans**. Cleveland Clinic Journal of Medicine 2012; 79(2):92-97.
Simon NM. **Treating complicated grief**. JAMA. 2013 Jul 24;310(4):416-23.
Simpson HB, Foa EB, Liebowitz MR, et al. **Cognitive-Behavioral Therapy vs Risperidone** for Augmenting Serotonin Reuptake Inhibitors in Obsessive-Compulsive Disorder: A Randomized Clinical Trial. JAMA Psychiatry. 2013 Sep 11.
Skapinakis P, Caldwell D, Hollingworth W, et al. A systematic review of the clinical effectiveness and cost-effectiveness of **pharmacological and psychological interventions** for the management of **obsessive-compulsive** disorder in **children/adolescents and adults**. Health Technol Assess. 2016;20:1-392.
Spencer AE et al. Examining the association between **posttraumatic stress disorder and attention-deficit/hyperactivity disorder**: A systematic review and meta-analysis. J Clin Psychiatry 2015 May 18.
Stanley MA et al. **Cognitive behavior therapy** for generalized anxiety disorder among older adults in primary care: A randomized clinical trial. JAMA 2009 Apr 8; 301:1460.
Stevens LM, Burke AE, Glass RM. JAMA **patient page. Posttraumatic stress disorder**. JAMA. 2007 Aug 1;298(5):588.
Taylor CB. **Panic disorder**. BMJ. 2006 Apr 22;332(7547):951-5.
Thirlwall K, Cooper PJ, Karalus J, et al. Treatment of child anxiety disorders via **guided parent-delivered cognitive-behavioural therapy**: randomised controlled trial. Br J Psychiatry. 2013 Aug 22.
Thompson RR, Holman EA, Silver RC. Media Coverage, Forecasted Posttraumatic Stress Symptoms, and Psychological **Responses Before and After an Approaching Hurricane**. JAMA Netw Open. 2019;2(1):e186228.
Tol WA, Barbui C, van Ommeren M. **Management of acute stress, PTSD, and bereavement: WHO** recommendations. JAMA. 2013 Aug 7;310(5):477-8.
Torpy JM, Burke AE, Golub RM. JAMA **patient page. Generalized Anxiety Disorder**. JAMA. 2011 Feb 2;305(5):522.
Torpy Janet M., Burke Alison E., Golub Robert M. JAMA Patient Page : **Panic Disorder**. JAMA. 2011;305(12):1256.doi:10.1001/jama.305.12.1256
Tran K, Moulton K, Santesso N, et al. **Cognitive processing therapy for post-traumatic stress disorder**: A systematic review and meta-analysis. CADTH; 2016 Mar. (CADTH health technology assessment; no. 141).
Treatment of **posttraumatic stress disorder**: an **assessment of the evidence**. Washington (DC): National Academies Home; 2008.
Twomey C, O'Reilly G, Byrne M. Effectiveness of **cognitive behavioural therapy** for **anxiety and depression** in primary care: a meta-analysis. Fam Pract. 2015 Feb;32(1):3-15.
Tyrer P, Baldwin D. **Generalised anxiety disorder**. Lancet. 2006 Dec 16;368(9553):2156-66.
Tyrer P, Cooper S, Salkovskis P, et al. Clinical and cost-eff ectiveness of **cognitive behaviour therapy** for health **anxiety** in medical patients: a multicentre randomised controlled trial. Lancet 2013; online Oct 18.
Tyrer P, Salkovskis P, Tyrer H, et al. **Cognitive-behaviour therapy** for health anxiety in medical patients (**CHAMP**): a randomised controlled trial with outcomes to 5 years. Health Technol Assess. 2017 Sep;21(50):1-58.
Ursano RJ, Bell C, et al. Practice guideline for the treatment of patients with acute stress disorder and **posttraumatic stress disorder**. Am J Psychiatry.2004;161(11 Suppl):i-31.
VA/DoD: Management of Post-Traumatic Stress Working Group. VA/DoD clinical practice guideline for management of post-traumatic stress. Washington (DC): Veterans Health Administration, Department of Defense; 2010.
VA/DoD: Management of Posttraumatic Stress Disorder Work Group. **VA/DoD clinical practice guideline for the management of posttraumatic stress disorder** and acute stress

disorder. Version 3.0. Washington (DC): Department of Veterans Affairs, Department of Defense; 2017 Jun.
Vaccarino V, Goldberg J, Rooks C, et al. **Posttraumatic stress disorder and incidence of coronary heart disease**: A twin study. J Am Coll Cardiol 2013.
Van Ameringen M, Mancini C, et al. A randomized, double-blind, placebo-controlled trial of **olanzapine** in the treatment of **trichotillomania**. J Clin Psychiatry. 2010 Apr 20.
van den Berg DP, de Bont PA, van der Vleugel BM, et al. **Prolonged Exposure vs Eye Movement Desensitization and Reprocessing vs Waiting List** for Posttraumatic Stress Disorder in Patients With a Psychotic Disorder: A Randomized Clinical Trial. JAMA Psychiatry. 2015 Jan 21.
Veale D, Roberts A. **Obsessive-compulsive disorder**. BMJ. 2014 Apr 7;348:g2183.
Vogel L. Growing consensus on link between **strep and obsessive-compulsive disorder**. CMAJ. 2018 Jan 22;190(3):E86-E87.
Walkup JT, Albano AM, et al. **Cognitive Behavioral Therapy, Sertraline, or a Combination** in Childhood Anxiety. (**CAMS**) N Engl J Med. 2008 Oct 30. [Epub ahead of print]
Wang Z, Whiteside SPH, Sim L, et al. Comparative effectiveness and safety of **cognitive behavioral therapy and pharmacotherapy for childhood anxiety disorders**: a systematic review and meta-analysis [online August 31, 2017].JAMA Pediatr. doi:10.1001/jamapediatrics .2017.3036
Warner CH, Warner CM, Appenzeller GN et al. **Identifying and Managing Posttraumatic Stress Disorder**. Am Fam Physician. 2013 Dec 15;88(12):827-834.
Warner CH, Warner CM, Appenzeller GN, Hoge CW. **Identifying and managing posttraumatic stress disorder**. Am Fam Physician. 2013 Dec 15;88(12):827-34.
Watkins LL, et al. Association of anxiety and depression with **all-cause mortality in individuals with coronary heart disease**. J Am Heart Assoc. 2013 Mar 19;2(2):e000068.
Watson S, Härmark L. **Desogestrel and panic attacks - a new suspected adverse drug reaction** reported by patients and health care professionals on spontaneous reports. Br J Clin Pharmacol. 2018 May 24.
Watterson RA, Williams JV, Lavorato DH, et al. Descriptive Epidemiology of **Generalized Anxiety Disorder in Canada**. Can J Psychiatry. 2016 Apr 15.
Weersing VR, Brent DA, et al. **Brief Behavioral Therapy for Pediatric Anxiety and Depression** in Primary Care: A Randomized Clinical Trial. JAMA Psychiatry. 2017 Apr 19.
Weich S, Pearce HL, Croft P, et al. Effect of **anxiolytic and hypnotic drug** prescriptions on mortality hazards: retrospective cohort study. BMJ. 2014 Mar 19;348:g1996.
Wensel TM, Powe KW, Cates ME. **Pregabalin** for the treatment of generalized anxiety disorder. Ann Pharmacother. 2012 Mar;46(3):424-9.
Wetherell JL, Petkus AJ, White KS, et al. Antidepressant medication augmented with **cognitive-behavioral therapy** for generalized anxiety disorder in older adults. Am J Psychiatry. 2013 Jul 1;170(7):782-9.
White CM. 3,4-Methylenedioxymethamphetamine's (**MDMA's**) Impact on **Posttraumatic** Stress Disorder. Ann Pharmacother. 2014 Apr 16;48(7):908-915.
Xue Y, Taub PR, Iqbal N et al. **Cardiac Biomarkers, Mortality**, and Post-Traumatic Stress Disorder in Military Veterans. Am J Cardiol. 2012 Feb 2.
Yonkers KA, Smith MV, Forray A, et al. **Pregnant Women** With **Posttraumatic** Stress Disorder and Risk of Preterm Birth. JAMA Psychiatry. 2014 Jun 11.
Yonkers KA, Gilstad-Hayden K, Forray A, Lipkind HS. Association of **Panic Disorder, Generalized Anxiety Disorder, and Benzodiazepine Treatment During Pregnancy** With Risk of Adverse Birth Outcomes. JAMA Psychiatry. 2017 Sep 13.
Yurgil KA, Barkauskas DA, Vasterling JJ, et al; for the Marine Resiliency Study Team. Association Between **Traumatic Brain Injury and Risk of Posttraumatic Stress Disorder** in Active-Duty Marines. JAMA Psychiatry. 2013 Dec 11
Zhou X, Zhang Y, Furukawa TA, et al. Different Types and **Acceptability of Psychotherapies for Acute Anxiety Disorders in Children and Adolescents**: A Network Meta-analysis. JAMA Psychiatry. 2018 Oct 31.
Zoellner LA, Roy-Byrne PP, Mavissakalian M, et al. Doubly Randomized Preference Trial of **Prolonged Exposure Versus Sertraline for Treatment of PTSD**. Am J Psychiatry. 2018 Oct 19:appiajp201817090995.

Metabolism of Benzodiazepines:

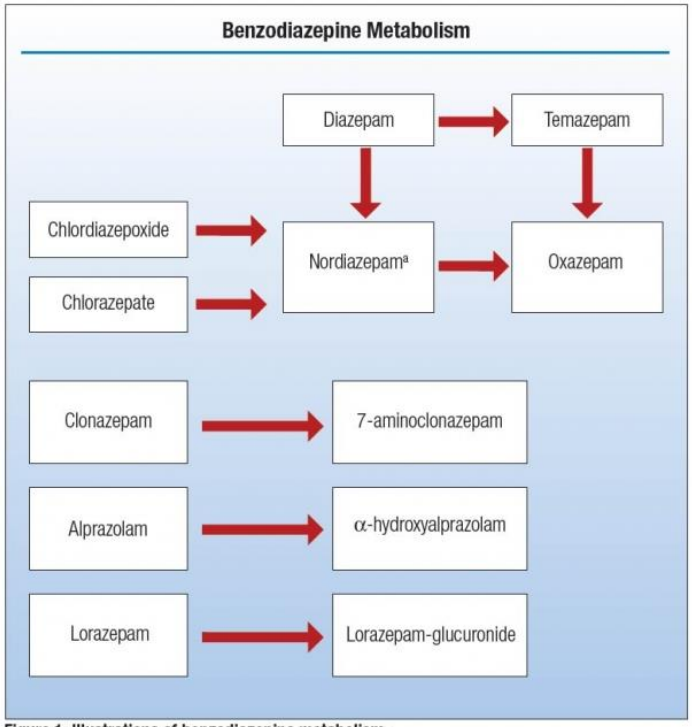

Figure 1: Illustrations of benzodiazepine metabolism.
Arrows indicate metabolic pathways
[a]Nordiazepam is also a metabolite of halazepam, medazepam, prazepam, and tetrazepam

BENZODIAZEPINE (BZ) COMPARISON CHART

[1] Micromedex 2018; Briggs GG, Freeman RK, Yaffe SJ. Drugs in Pregnancy and Lactation 11th Ed. Williams & Wilkins, Media, Pennsilvania, 2017.
[2] Nelson J, Chouinard G. Guidelines for the clinical use of benzodiazepines: pharmacokinetics, dependency, rebound and withdrawal. Canadian Society for Clinical Pharmacology. Can J Clin Pharmacol. 1999 Summer;6(2):69-83.
[3] Rickels K, DeMartinis N, Rynn M, Mandos L. Pharmacologic strategies for discontinuing benzodiazepine treatment. J Clin Psychopharmacol. 1999 Dec;19(6 Suppl 2):12S-16S.
[4] Teboul E, Chouinard G. A guide to benzodiazepine selection. Part II: Clinical aspects. Can J Psychiatry. 1991 Feb;36(1):62-73.
[5] Teboul E, Chouinard G. A guide to benzodiazepine selection. Part I: Pharmacological aspects. Can J Psychiatry. 1990 Nov;35(8):700-10.
[6] Baillargeon L, Landreville P, Verreault R, et al. Discontinuation of benzodiazepines among older insomniac adults treated with cognitive-behavioural therapy combined with gradual tapering: a randomized trial. CMAJ. 2003 Nov 11;169(10):1015-1020. (Benzodiazepines: How they work & how to withdraw "aka The **Ashton Manual**" protocol http://www.benzo.org.uk/manual/index.htm)
[7] Holbrook AM, Crowther R, Lotter A, Cheng C, King D. Meta-analysis of benzodiazepine use in the treatment of insomnia. CMAJ. 2000 Jan 25;162(2):225-33.
[8] Wagner AK, Zhang F, Soumerai SB, et al. Benzodiazepine use and hip fractures in the elderly: who is at greatest risk? Arch Intern Med. 2004 Jul 26;164(14):1567-72.
Saarelainen L, Tolppanen AM, Koponen M, et al. Risk of Hip Fracture in Benzodiazepine Users With and Without Alzheimer Disease. J Am Med Dir Assoc. 2016 Nov 12.

Additional references:

Agarwal SD, Landon BE. **Patterns in Outpatient Benzodiazepine Prescribing** in the United States. JAMA Netw Open. 2019 Jan 4;2(1):e187399.

Ait-Daoud N, Hamby AS, Sharma S, Blevins D. A Review of **Alprazolam Use, Misuse, and Withdrawal**. J Addict Med. 2018 Jan/Feb;12(1):4-10.

Alessi-Severini S, Bolton JM, Enns MW, et al. **Use of benzodiazepines** and related drugs in **Manitoba**: a population-based study. CMAJ Open. 2014 Oct 1;2(4):E208-16.

Amato L, Minozzi S, Vecchi S, Davoli M. Benzodiazepines for **alcohol withdrawal**. Cochrane Database Syst Rev. 2010 Mar 17;3:CD005063. Benzodiazepines showed a protective benefit against alcohol withdrawal symptoms, in particular seizures, when compared to placebo and a potentially protective benefit for many outcomes when compared with other drugs. Nevertheless, no definite conclusions about the effectiveness and safety of benzodiazepines was possible, because of the heterogeneity of the trials both in interventions and the assessment of outcomes.

American College of Obstetricians and Gynecologists (**ACOG**). Use of psychiatric medications during **pregnancy and lactation**. Washington (DC): American College of Obstetricians and Gynecologists (ACOG); 2008 Apr. 20 p. (ACOG practice bulletin; no. 92). [245 references]

An H, Godwin J. **Flumazenil in benzodiazepine overdose**. CMAJ. 2016 Dec 6;188(17-18):E537.

Anthierens, Sibyl, Pasteels, Inge, Habraken, Hilde, et al. Barriers to nonpharmacologic treatments for **stress, anxiety, and insomnia**: Family physicians' attitudes toward benzodiazepine prescribing. Can Fam Physician 2010 56: e398-406.

Arens AM, van Wijk XM, Vo KT, et al. Adverse Effects From **Counterfeit Alprazolam** Tablets. JAMA Intern Med. 2016 Aug 8

Aurora RN, Zak RS, Maganti RK, et al. Standards of Practice Committee, American Academy of Sleep Medicine. Best practice guide for the treatment of **REM sleep behavior** disorder (RBD). J Clin Sleep Med 2010 Feb 15;6(1):85-95.

Baandrup L, Ebdrup BH, Rasmussen JO, et al. **Pharmacological interventions for benzodiazepine discontinuation in chronic benzodiazepine users**. Cochrane Database Syst Rev. 2018 Mar 15;3:CD011481. Given the low or very low quality of the evidence for the reported outcomes, and the small number of trials identified with a limited number of participants for each comparison, it is not possible to draw firm conclusions regarding pharmacological interventions to facilitate benzodiazepine discontinuation in chronic benzodiazepine users.

Bachhuber MA, Hennessy S, et al. Increasing Benzodiazepine **Prescriptions and Overdose Mortality** in the United States, 1996-2013. Am J Public Health. 2016 Feb 18:e1-e3.

Barnett ML, Hicks TR, Jena AB. **Prescription Patterns of Family Members** After Discontinued Opioid or Benzodiazepine Therapy of Users. JAMA Intern Med. 2019 Jul 1.

Bell CM, Fischer HD, Gill SS, Zagorski B, Sykora K, Wodchis WP, Herrmann N, Bronskill SE, Lee PE, Anderson GM, Rochon PA. Initiation of benzodiazepines in the **elderly** after hospitalization. J Gen Intern Med. 2007 Jul;22(7):1024-9. Epub 2007 Apr 24. New benzodiazepine prescription after hospitalization occurs frequently in older adults and may result in chronic use. A systemic effort to address this risky practice should be considered.

Benzodiazepine Tapering Schedules & Information: http://www.benzo.org.uk/manual/index.htm

Bergman H, Bhoopathi PS, Soares-Weiser K. **Benzodiazepines for antipsychotic-induced tardive dyskinesia**. Cochrane Database Syst Rev. 2018 Jan 20;1:CD000205. There is only evidence of very low quality from a few small and poorly reported trials on the effect of benzodiazepines as an adjunctive treatment for antipsychotic-induced TD. These inconclusive results mean routine clinical use is not indicated and these treatments remain experimental.

Bezchlibnyk-Butler Clinical Handbook of Psychotropic Drugs, 17th Ed. 2007.

Bezchlibnyk-Butler KZ. **Clinical Handbook of Psychotropic Drugs, 22nd Ed**. 22nd Editors: Procyshyn RM, Bezchlibnyk-Butler KZ, Jeffries JJ. Hogrefe Publishing, Massachusetts, 2017.

Bhidayasiri R, Fahn S, Weiner WJ, et al. Evidence-based guideline: Treatment of **tardive syndromes**: Report of the Guideline Development Subcommittee of the American Academy of Neurology (AAN). Neurology. 2013 Jul 30;81(5):463-469. (clonazepam probably improves tardive dyskinesias-level B)

Billioti de Gage S, Bégaud B, Bazin F, Verdoux H, et al. Benzodiazepine use and **risk of dementia**: prospective population based study. BMJ. 2012 Sep 27;345:e6231.

Billioti de Gage S, Moride Y, Ducruet T, Kurth T, Verdoux H, Tournier M, et al. **Benzodiazepine use and risk of Alzheimer's** disease: case-control study. BMJ 2014;349:g5205.

Braun P, Greenberg D, Dasberg H, Lerer B: Core symptoms of posttraumatic stress disorder unimproved by alprazolam treatment. J Clin Psychiatry 1990, 51:236-238.

Breilmann J, Girlanda F, Guaiana G, et al. Benzodiazepines versus placebo for **panic disorder in adults**. Cochrane Database Syst Rev. 2019 Mar 28;3:CD010677. Low-quality evidence shows a possible superiority of benzodiazepine over placebo in the short-term treatment of panic disorders. The validity of the included studies is questionable due to possible unmasking of allocated treatments, high dropout rates, and probable publication bias.

Brett J, Murnion B. **Management of benzodiazepine misuse and dependence**. Australian Prescriber. Vol 38, Number 5, Oct 2015.

Brett J, Maust DT, Bouck Z, et al. **Benzodiazepine Use in Older Adults** in the United States, Ontario, and Australia from 2010 to 2016. J Am Geriatr Soc. 2018 Feb 12.

Bronskill SE, Campitelli MA, Iaboni A, et al. **Low-Dose Trazodone, Benzodiazepines, and Fall-Related Injuries in Nursing Homes**: A Matched-Cohort Study. J Am Geriatr Soc. 2018 Oct;66(10):1963-1971.

Bruining H, Passtoors L, et al. **Paradoxical Benzodiazepine Response**: A Rationale for Bumetanide in Neurodevelopmental Disorders? Pediatrics. 2015 Aug;136(2):e539-43.

Bushnell GA, Stürmer T, Gaynes BN, et al. Simultaneous **Antidepressant and Benzodiazepine New Use and Subsequent Long-term Benzodiazepine Use in Adults With Depression**, United States, 2001-2014. JAMA Psychiatry. 2017 Jun 7.

Cadogan CA, Ryan C, et al. **Benzodiazepine and Z-drug prescribing in Ireland**: analysis of national prescribing trends from 2005-2015. Br J Clin Pharmacol. 2018 Feb 28.

Calderon-Margalit R, Qiu C, Ornoy A, et al. Risk of preterm delivery and other adverse perinatal outcomes in relation to maternal use of psychotropic medications during pregnancy. Am J Obstet Gynecol. 2009 Dec;201(6):579.e1-8. Epub 2009 Aug 18. Maternal use of benzodiazepine during pregnancy was associated with an increased risk of preterm delivery (adjusted odds ratio, 6.79; 95% confidence interval, 4.01-11.5) and with increased risks of low birthweight, low Apgar score, neonatal intensive care unit admissions, and respiratory distress syndrome. Selective serotonin receptor inhibitors were associated with preterm deliveries only among women who started treatment after the first trimester. Benzodiazepine was associated highly with preterm delivery and other adverse perinatal outcomes.

Carico R, Zhao X, Thorpe CT, et al. Receipt of **Overlapping Opioid and Benzodiazepine Prescriptions Among Veterans** Dually Enrolled in Medicare Part D and the Department of Veterans Affairs: A Cross-sectional Study. Ann Intern Med. 2018 Oct 9.

Carrier JD, Roberge P, Courteau J, et al. **Predicting chronic benzodiazepine use in adults with depressive disorder**: Retrospective cohort study using administrative data in Quebec. Can Fam Physician. 2016 Aug;62(8):e473-83

Cassidy EM et al. **Symptom-triggered benzodiazepine therapy** for **alcohol withdrawal syndrome** in the emergency department:

A comparison with the standard fixed dose benzodiazepine regimen. Emerg Med J 2012 Oct; 29:802.

CDC June/10 About one fifth of US high school students reported ever having used prescription drugs not prescribed to them, such as OxyContin, Percocet, Vicodin, Adderall, Ritalin, and Xanax. The CDC reports the first assessment of such use within the National Youth Risk Behavior Survey. In addition, prescription drug abuse was more common among white than Hispanic or black students. The agency highlighted these findings from the 2009 survey in the context of an ongoing national trend toward higher rates of nonsuicide-related overdoses and deaths associated with prescription drug abuse. 2009 National Youth Risk Behavior Survey (Free PDF) CDC news release (Free) 2007 *MMWR* article on unintentional poisoning deaths (Free)

Chang CM, Wu EC, Chen CY, et al. Psychotropic Drugs and Risk of **Motor Vehicle Accidents**: a Population-based Case-Control Study. Br J Clin Pharmacol. 2012 Sep 12.

Chen Lori, Farrell Barbara, Ward Natalie, et al. **Discontinuing benzodiazepine therapy**: An interdisciplinary approach at a geriatric day hospital. Canadian Pharmacists Journal: November 2010, Vol. 143, No. 6, pp. 286-295.e1.

Chen TY, Winkelman JW, Mao WC, et al. The use of **benzodiazepine receptor agonists** and the risk of **pneumonia hospitalization**: a nationwide population-based, nested case control study. Chest. 2017 Aug 4.

Clegg A, Young JB. Which medications to avoid in people at **risk of delirium**: a systematic review. Age Ageing. 2011 Jan;40(1):23-9. (opiates and benzos)

Crabtree A, Rose C, Chong M, Smolina K. Effects of the **new prescribing standards in British Columbia** on consumption of opioids and benzodiazepines and z drugs. Can Fam Physician. 2019 May;65(5):e231-e237.

Crockford D, White WD, Campbell B. **Gabapentin** use in benzodiazepine dependence and detoxification. Can J Psychiatry. 2001 Apr;46(3):287.

Cunningham CM, Hanley GE, Morgan S. Patterns in the **use of benzodiazepines in British Columbia**: Examining the impact of increasing research and guideline cautions against long-term use. Health Policy. 2010 Apr 20.

Darker CD, Sweeney BP, Barry JM, Farrell MF, Donnelly-Swift E. **Psychosocial interventions for benzodiazepine harmful use, abuse or dependence**. Cochrane Database of Systematic Reviews 2015, Issue 5. Art. No.: CD009652. DOI: 10.1002/14651858.CD009652.pub2. CBT plus taper is effective in the short term (three month time period) in reducing BZD use. However, this is not sustained at six months and subsequently. Currently there is insufficient evidence to support the use of MI to reduce BZD use. There is emerging evidence to suggest that a tailored GP letter versus a generic GP letter, a standardised interview versus TAU, and relaxation versus TAU could be effective for BZD reduction. There is currently insufficient evidence for other approaches to reduce BZD use.

Denis C, Fatseas M, Lavie E, Auriacombe M. Pharmacological interventions for benzodiazepine mono-dependence management in outpatient settings. Cochrane Database Syst Rev. 2006 Jul 19;3:CD005194. The results of this systematic review point to the potential value of carbamazepine as an effective intervention for benzodiazepine gradual taper discontinuation. Carbamazepine has shown rather modest benefit in reducing withdrawal severity, although it did significantly improve drug-free outcome. Larger controlled studies are needed to confirm these benefits, to assess adverse effects and to identify when its clinical use might be most indicated. Other suggested treatment approaches to benzodiazepine discontinuation management should be explored (antidepressants, benzodiazepine receptors modulator).

de Lusignan S, Buxton N, Kent A. **New patient asking for a benzodiazepine** prescription. BMJ. 2008 Aug 28;337:a658. doi: 10.1136/bmj.a658.

Deprescribing Guideline and Algorithms (Benzodiazepine receptor agonits, Proton pump inhibitors, Antipsychotics, Antihyperglycemic) http://deprescribing.org/resources/deprescribing-guidelines-algorithms/

Duerden EG, Guo T, et al. Midazolam dose correlates with **abnormal hippocampal growth and neurodevelopmental outcome in preterm infants**. Ann Neurol. 2016 Jan 11.

Ekström MP, Bornefalk-Hermansson A, et al. Safety of **benzodiazepines and opioids** in very severe respiratory disease: national prospective study. BMJ. 2014 Jan 30;348.

Ensrud KE, et al.; Study of Osteoporotic Fractures Research Group. CNS-active medications and **risk for falls** in older women. J Am Geriatr Soc. 2002 Oct;50(10):1629-37.

FDA July/15 is warning about a **counterfeit version of the anxiety drug diazepam** (e.g., Valium) being sold online. About 700 patients in Africa have taken haloperidol pills that were mislabeled as diazepam, according to the World Health Organization. The counterfeit tablets: are light yellow; bear the letters AGOG on one side; are scored across the center on the other side. Some patients who took them experienced face, neck, and tongue dystonia.

FDA Aug/16 review has found that the growing **combined use of opioid medicines with benzodiazepines** or other drugs that depress the central nervous system (CNS) has resulted in serious side effects, including slowed or **difficult breathing and deaths**.

FDA Sep/17 is advising that the opioid addiction medications **buprenorphine and methadone** should not be withheld from patients taking **benzodiazepines** or other drugs that depress the central nervous system (CNS). The combined use of these drugs increases the risk of serious side effects; however, the harm caused by untreated opioid addiction usually outweighs these risks.

Fortinguerra, Filomena, Clavenna, Antonio, Bonati, Maurizio. Psychotropic Drug Use During **Breastfeeding**: A Review of the Evidence. Pediatrics 2009 124: e547-e556.

Franken LG, Masman AD, et al. **Hypoalbuminemia and decreased midazolam clearance** in terminally ill adult patients, an inflammatory effect? Br J Clin Pharmacol. 2017 Feb 8.

Friedman BW, Irizarry E, Solorzano C, et al. **Diazepam Is No Better Than Placebo When Added to Naproxen for Acute Low Back Pain**. Ann Emerg Med. 2017 Jan 19.

Garrido MM, Prigerson HG, et al. **Benzodiazepine and Sedative-hypnotic Use** Among Older Seriously Ill **Veterans**: **Choosing Wisely**? Clin Ther. 2014 Nov 1;36(11):1547-54.

Gehrie EA, Keiser A, Haglock-Adler CJ, et al. **Detecting Pharmaceuticals in the Red Blood Cell Inventory** of a Hospital Blood Bank. J Pediatr. 2017 Jun 29.

Gerlach LB, Maust DT, Leong SH, et al. **Factors Associated With Long-term Benzodiazepine Use Among Older Adults**. JAMA Intern Med. 2018 Sep 10.

Gillies D, Sampson S, Beck A, et al. **Benzodiazepines for psychosis-induced aggression or agitation**. Cochrane Database Syst Rev. 2013 Sep 18;9:CD003079. The evidence from trials for the use of benzodiazepines alone is not good. There were relatively little good data and most trials are too small to highlight differences in either positive or negative effects. Adding a benzodiazepine to other drugs does not seem to confer clear advantage and has potential for adding unnecessary adverse effects. Sole use of older antipsychotics unaccompanied by anticholinergic drugs seems difficult to justify.

Gorevski E, Bian B, Kelton CM, et al. **Utilization, Spending, and Price Trends** for Benzodiazepines in the US Medicaid Program: 1991-2009. Ann Pharmacother. 2012 Apr;46(4):503-12.

Gould RL, Coulson MC, Patel N, Highton-Williamson E, Howard RJ. **Interventions for reducing benzodiazepine use in older people**: metaanalysis of randomised controlled trials. Br J Psychiatry. 2014;204:98-107.

Gray SL, et al. Benzodiazepine use and **physical disability** in community-dwelling older adults. J Am Geriatr Soc. 2006 Feb;54(2):224-30.

Gray SL, Dublin S, Yu O, et al. Benzodiazepine use and **risk of incident dementia** or cognitive decline: prospective population based study. BMJ. 2016 Feb 2;352:i90.

Grigoriadis S, Graves L, Peer M, et al. Benzodiazepine **Use During Pregnancy** Alone or in Combination With an Antidepressant and Congenital Malformations: Systematic Review and Meta-Analysis. J Clin Psychiatry. 2019 Jul 9;80(4).
Gulland A. Sixty seconds on . . . **Xanax**. BMJ. 2018 Feb 12;360:k659.
Hawkins EJ, Malte CA, Imel ZE, et al. Prevalence and trends of **benzodiazepine use among Veterans Affairs** patients with posttraumatic stress disorder, 2003-2010. Drug Alcohol Depend. 2012 Feb 2.
Hayhoe B, Lee-Davey J. Tackling benzodiazepine misuse. BMJ. 2018 Jul 27;362:k3208.
Health Canada Aug/06 is advising consumers not to use **Salt Spring Herbals Sleep Well Dietary Supplement** because a sample has been found to contain **estazolam.**
Health Canada Dec/06 is advising consumers not to use a product called **Eden Herbal Formulations Sleep Ease Dietary Supplement**, because it was found to contain an undeclared drug estazolam http://www.hc-sc.gc.ca/ahc-asc/media/advisories-avis/2006/2006_127_e.html
Health Canada Feb/07 Health Canada is advising consumers not to use a product called **Sleepees**, because it was found to contain an undeclared drug **estazolam**, which can be habit-forming when used for as little as a few months. http://www.hc-sc.gc.ca/ahc-asc/media/advisories-avis/2007/2007_16_e.html
Health Canada April/07is advising consumers not to use a product called **Eden Herbal Formulations Serenity Pills II** because it contains the undeclared drug **estazolam**.
Health Canada June/07 is advising consumers not to use **Optimum Health Care SleePlus TCM** or **BYL SleePlus**, because the products contain the undeclared drug **clonazepam.**
Health Canada Aug/10 says **Fulda Unitang Herbs Sleep Plus**, an unauthorized product promoted as an herbal sleep aid, has been found to contain high levels of estazolam.
Health Canada Jan/18 is advising Canadians and healthcare professionals that new safety warnings will be added to the product safety information of the following sedative and anesthetic drugs when they are used in early childhood and during pregnancy: Diprivan (propofol), Ketalar (ketamine), Sevorane (sevoflurane), Suprane (desflurane), Forane/Isoflurane USP (isoflurane), **Ativan (lorazepam), midazolam**, phenobarbital and thiopental. The safety review for benzodiazepines (Ativan [lorazepam] and midazolam) and barbiturates (phenobarbital and thiopental) concluded that there is limited evidence linking the use of these drugs by pregnant women and young children to adverse effects on the development of children's brains. However, it is important to note that many of these sedatives may often be used in combination with other intravenous and inhaled anesthetics, which were found to have a risk of adverse effects related to the functioning of the brain.
Hemmelgarn B, et al. Benzodiazepine use and the risk of **motor vehicle crash** in the elderly. JAMA. 1997 Jul 2;278(1):27-31. CONCLUSIONS: Brief or extended periods of exposure to long-half-life benzodiazepines are associated with an increased risk of motor vehicle crash involvement in the elderly population. There is no such elevated risk for short-half-life benzodiazepines.
Hernandez I, He M, Brooks MM, et al. Exposure-Response Association Between **Concurrent Opioid and Benzodiazepine Use and Risk of Opioid-Related Overdose** in Medicare Part D Beneficiaries. JAMA Network Open. 2018;1(2):e180919.
Herrmann N, Gauthier S. **Diagnosis and treatment of dementia**: 6. Management of severe Alzheimer disease. CMAJ 2008;179(12):1279-87.
Hockenhull J, Amioka E, Black JC, et al. **Nonmedical use of alprazolam in the UK**: Results from a nationally representative survey. Br J Clin Pharmacol. 2019 Jun 4.
Hogan DB, Maxwell CJ, Fung TS, Ebly EM; Canadian Study of Health and Aging. Prevalence and potential consequences of benzodiazepine use in senior citizens: results from the Canadian Study of Health and Aging. Can J Clin Pharmacol. 2003 Summer;10(2):72-7.
Hood SD, Norman A, Hince DA, et al. "**Benzodiazepine dependence** and its treatment with low dose **flumazenil**." Br J Clin Pharmacol. 2012 Nov 5.
Hudak ML, Tan RC et al. **Neonatal Drug Withdrawal**. Pediatrics. 2012 Jan 30.
Huhn M, TardyM, Spineli LM, et al. Efficacy of **pharmacotherapy and psychotherapy** for adult psychiatric disorders: a systematic overview of meta-analyses [online April 30, 2014]. JAMA Psychiatry. doi:10.1001/jamapsychiatry.2014.112.
Hwang CS, Kang EM, Kornegay CJ, et al. Trends in the **concomitant prescribing of opioids and benzodiazepines**, 2002-2014. Am J Prev Med. 2016;51:151-160.
Jeffery MM, Hooten WM, Jena AB, et al. Rates of **Physician Coprescribing of Opioids and Benzodiazepines** After the Release of the Centers for Disease Control and Prevention Guidelines in 2016. JAMA Netw Open. 2019 Aug 2;2(8):e198325.
Johnson B, Streltzer J. **Risks associated with long-term benzodiazepine use**. Am Fam Physician. 2013 Aug 15;88(4):224-6.
Kale N. **Urine Drug Tests**: Ordering and Interpretation. Am Fam Physician. 2019;99(1):33-39.
Karttunen N, Taipale H, Hamina A. Concomitant use of benzodiazepines and opioids in **community-dwelling older people** with or without Alzheimer's disease – A nationwide register-based study in Finland. Int J Geriatr Psychiatry. 2018 Oct 29.
Kavan MG, Elsasser GN, Barone EJ. The Physician's Role in Managing **Acute Stress Disorder**. Am Fam Physician. 2012;86(7):643-649.
Katzman MA, Bleau P, Blier P, et al; Canadian Anxiety Guidelines Initiative Group on behalf of the Anxiety Disorders Association of Canada/Association Canadienne des troubles anxieux and McGill University. **Canadian clinical practice guidelines for the management of anxiety, posttraumatic stress and obsessive-compulsive disorders**. BMC Psychiatry 2014;14(suppl 1):S1-83.www.biomedcentral.com/content/pdf/1471-244X-14-S1-S1.pdf (accessed July 17, 2014).
Kelly LE, Poon S, Madadi P, Koren G. **Neonatal Benzodiazepines Exposure during Breastfeeding**. J Pediatr. 2012 Apr 13.
Klein LR, Driver BE, Miner JR, et al. Intramuscular **Midazolam, Olanzapine, Ziprasidone, or Haloperidol** for Treating Acute Agitation in the Emergency Department. Ann Emerg Med. 2018 Oct;72(4):374-385
Kok L, Slooter AJ, Hillegers MH, et al. **Benzodiazepine Use and Neuropsychiatric Outcomes in the ICU**: A Systematic Review. Crit Care Med. 2018 Jul 5.
Lader M. Benzodiazepine **Harm: How Can It Be Reduced**? Br J Clin Pharmacol. 2012 Aug 10.
Lakeview Health: link to benzo effects poster: http://www.lakeviewhealth.com/benzodiazepine-what-are-benzos-effects-usage-infographic.php
Lawlor DA, Patel R, Ebrahim S. Association between **falls** in elderly women and chronic diseases and drug use: cross sectional study. BMJ. 2003 Sep 27;327(7417):712-7.
Lin BM, et al. Association Between **Benzodiazepine Receptor Agonists and Snoring** Among Women in the Nurses' Health Study. JAMA Oto Head Neck Surg. 2016 Nov 17.
Lonardo NW, Mone MC, Nirula R, et al. **Propofol is associated with favorable outcomes compared with benzodiazepines** in ventilated intensive care unit patients.

Am J Respir Crit Care Med. 2014 Jun 1;189(11):1383-94.

Lonergan E, Luxenberg J, Areosa Sastre A, Wyller TB. Benzodiazepines for delirium. Cochrane Database Syst Rev. 2009 Jan 21;(1):CD006379. No adequately controlled trials could be found to support the use of benzodiazepines in the treatment of non-alcohol withdrawal related delirium among hospitalised patients, and at this time benzodiazepines cannot be recommended for the control of this condition. Because of the scarcity of trials with randomization of patients, placebo control, and adequate concealment of allocation of subjects, it is clear that further research is required to determine the role of benzodiazepines in the treatment of non-alcohol withdrawal related delirium.

Lovegrove MC, Mathew J, Hampp C, et al. **Emergency Hospitalizations for Unsupervised Prescription Medication Ingestions by Young Children.** Pediatrics. 2014 Sep 15. (buprenorphine & clonidine concerning)

Lugoboni F, Quaglio G. Exploring the dark side of the moon: the treatment of **benzodiazepine tolerance**. Br J Clin Pharmacol. 2013 Apr 25.

Lupattelli A, Chambers CD, Bandoli G, et al. **Association of Maternal Use of Benzodiazepines and Z-Hypnotics** During Pregnancy With Motor and Communication Skills and Attention-Deficit/Hyperactivity Disorder Symptoms in Preschoolers. JAMA Netw Open. 2019 Apr 5;2(4):e191435.

Manthey L, van Loenen-Frösch F, Giltay EJ, et al. High-dose **benzodiazepines prolong reaction times** in chronic users who have major depressive and/or anxiety disorders. Br J Clin Pharmacol. 2013 Aug 20.

Marra EM, et al. Benzodiazepine Prescribing in **Older Adults in U.S. Ambulatory Clinics and Emergency Departments** (2001-10). J Am Geriatr Soc. 2015 Sep 29.

Martin P, Tannenbaum C. A realist evaluation of patients' decisions to **deprescribe in the EMPOWER** trial. BMJ Open. 2017 May 4;7(4):e015959

Mayo-Smith MF, Beecher LH, Fischer TL, et al. Working Group on the Management of Alcohol Withdrawal Delirium, Practice Guidelines Committee, American Society of Addiction Medicine. Management of alcohol withdrawal delirium. An evidence-based practice guideline. Arch Intern Med. 2004 Jul 12;164(13):1405-12.

McCord J, Jneid H, et al**.** Management of **Cocaine-Associated Chest Pain** and Myocardial Infarction. A Scientific Statement From the American Heart Association Acute Cardiac Care Committee of the Council on Clinical Cardiology. Circulation online Mar 17,2008.

McIntosh B, Clark M, Spry C. *Benzodiazepines in Older Adults: A Review of Clinical Effectiveness, Cost-Effectiveness, and Guidelines* [Internet]. Ottawa: Canadian Agency for Drugs and Technologies in Health; 2011 (Rapid Response Report: Peer-Reviewed Summary with Critical Appraisal). [cited 2011-01-06]. Available from: http://www.cadth.ca/index.php/en/hta/reports-publications/search/publication/2773.

Moncada LV. Management of **falls in older persons**: a prescription for prevention. Am Fam Physician. 2011 Dec 1;84(11):1267-76.

Morin CM, et al. Randomized clinical trial of supervised tapering and cognitive behavior therapy to facilitate benzodiazepine discontinuation in older adults with chronic insomnia. Am J Psychiatry. 2004 Feb;161(2):332-42.

Mugunthan K, McGuire T, Glasziou P.. **Minimal interventions** to decrease long-term use of benzodiazepines in primary care: a systematic review and meta-analysis. Br J Gen Pract. 2011 Sept; 61.

Née M, Avalos M, Luxcey A, et al. Prescription medicine use by pedestrians and the risk of **injurious road traffic** crashes: A case-crossover study. PLoS Med. 2017 Jul 18;14(7):e1002347

Nejad SH, Schaefer PW, Bajwa EK, Smith FA. Case records of the Massachusetts General Hospital. Case 39-2012. A 55-year-old man with **alcoholism**, recurrent seizures, and agitation. N Engl J Med. 2012 Dec 20;367(25):2428-34.

Ntais C, Pakos E, Kyzas P, Ioannidis J. Benzodiazepines for alcohol withdrawal. **Cochrane Database Syst Rev. 2005** Jul 20;(3):CD005063.

Obiora E, Hubbard R, Sanders RD, Myles PR. The impact of benzodiazepines on occurrence of **pneumonia** and mortality from pneumonia: a nested case-control and survival analysis in a population-based cohort. Thorax. 2012 Dec 5.

Ogawa Y, Takeshima N, Hayasaka Y, et al. Antidepressants plus benzodiazepines **for adults with major depression**. Cochrane Database Syst Rev. 2019 Jun 3;6:CD001026. Combined antidepressant plus benzodiazepine therapy was more effective than antidepressants alone in improving depression severity, response in depression and remission in depression in the early phase. However, these effects were not maintained in the acute or the continuous phase. Combined therapy resulted in fewer dropouts due to adverse events than antidepressants alone, but combined therapy was associated with a greater proportion of participants reporting at least one adverse effect.The moderate quality evidence of benefits of adding a benzodiazepine to an antidepressant in the early phase must be balanced judiciously against possible harms and consideration given to other alternative treatment strategies when antidepressant monotherapy may be considered inadequate.

Ogbonna CI, Lembke A. **Tapering Patients Off of Benzodiazepines**. Am FamPhysician. 2017 Nov 1;96(9):606-610.

Olfson M, King M, Schoenbaum M. **Benzodiazepine use in the United States** [published online December 17, 2014]. JAMA Psychiatry. doi:10.1001/jamapsychiatry.2014.1763.

Orriols L, Luxcey A, Contrand B, et al. **Road traffic crash risk** associated with **benzodiazepine and z-hypnotic** use after implementation of a colour-graded pictogram: a responsibility study. Br J Clin Pharmacol. 2016 Aug 21.

Park TW, Saitz R, Ganoczy D, et al. **Benzodiazepine prescribing patterns and deaths from drug overdose** among US veterans receiving opioid analgesics: case-cohort study. BMJ. 2015 Jun 10;350:h2698.

Parker AJ, Marshall EJ, Ball DM. Diagnosis and management of **alcohol use disorders**. BMJ. 2008 Mar 1;336(7642):496-501.

Patel T, Slonim K, Lee L. Use of potentially **inappropriate medications among ambulatory home-dwelling elderly patients with dementia**: A review of the literature. Can Pharm J (Ott). 2017 May 1;150(3):169-183.

Patorno E, Glynn RJ, Levin R, et al. **Benzodiazepines** and risk of **all cause mortality** in adults: cohort study. BMJ. 2017 Jul 6;358:j2941.

Paulson SK, Wood-Horrall RN, Hoover R, et al. The Pharmacokinetics of the CYP3A Substrate **Midazolam After Steady-State Dosing of Delafloxacin**. Clin Ther. 2017 May 8.

Penninkilampi R, Eslick GD. A Systematic Review and Meta-Analysis of the **Risk of Dementia Associated with Benzodiazepine Use**, After Controlling for Protopathic Bias. CNS Drugs. 2018 Jun 20.

Pottegård A, Friis S, et al. Use of benzodiazepines or benzodiazepine related drugs and the **risk of cancer**: a population-based case-control study. Br J Clin Pharmacol. 2012 Oct 9.

Pottie K, Thompson W, Davies S, et al. **Deprescribing benzodiazepine receptor agonists**: Evidence-based clinical practice guideline. Can Fam Physician. 2018 May;64(5):339-351.

Purcell C, Davis A, Moolman N, Taylor SM (2019) **Reduction of benzodiazepine use in patients prescribed medical cannabis**, Cannabis and Cannabinoid Research 0:0, 1–5, DOI:

10.1089/ can.2018.0020.
Rapoport MJ, Lanctôt KL, Streiner DL, et al. Benzodiazepine use and **driving**: a meta-analysis. J Clin Psychiatry. 2009 Apr 21;70(5):663-73.
Richardson K, Mattishent K, Loke YK, et al. History of **Benzodiazepine Prescriptions and Risk of Dementia**: Possible Bias Due to Prevalent Users and Covariate Measurement Timing in a Nested Case-Control Study. Am J Epidemiol. 2019 Mar 27
Rickels K, et al. **Imipramine** and buspirone in treatment of patients with generalized anxiety disorder who are discontinuing long-term benzodiazepine therapy. Am J Psychiatry. 2000 Dec;157(12):1973-9.
Saarelainen L, Tolppanen AM, Koponen M, et al. **Risk of Hip Fracture in Benzodiazepine Users** With and Without Alzheimer Disease. J Am Med Dir Assoc. 2016 Nov 12.
Saarelainen L, et al. **Risk of death** associated with new **benzodiazepine** use among persons **with Alzheimer disease**: A matched cohort study. Int J Geriatr Psychiatry. 2017 Nov 15.
Sachdeva A, Chandra M, Deshpande SN. A Comparative Study of Fixed Tapering Dose Regimen versus Symptom-triggered Regimen of **Lorazepam for Alcohol Detoxification**. Alcohol Alcohol. 2014 Jan 8. "Symptom-triggered lorazepam treatment for alcohol withdrawal resulted in administration of lower total doses of medication for a shorter duration of treatment and was as safe as the fixed tapering dose."
Sathe AG, Tillman H, Coles LD, et al. **Underdosing of Benzodiazepines** in Patients with Status Epilepticus Enrolled in Established Status Epilepticus Treatment Trial. Acad Emerg Med. 2019 Jun 4.
Schuckit MA. Recognition and management of **withdrawal delirium (delirium tremens).** N Engl J Med. 2014 Nov 27;371(22):2109-13.
Sheehy O, Zhao JP, Bérard A. Association Between Incident **Exposure to Benzodiazepines in Early Pregnancy and Risk of Spontaneous Abortion**. JAMA Psychiatry. 2019 May 15.
Sigurdsson MI, Helgadottir S, Long TE, et al. Association Between Preoperative Opioid and Benzodiazepine **Prescription Patterns and Mortality After Noncardiac Surgery**. JAMA Surg. 2019 Jun 19:e191652.
Soyka M. **Treatment of Benzodiazepine Dependence**. N Engl J Med. 2017 Mar 23;376(12):1147-1157.
Stock CJ, Carpenter L, Ying J, Greene T. **Gabapentin versus chlordiazepoxide** for outpatient alcohol detoxification treatment. Ann Pharmacother. 2013 Jul;47(7-8):961-9.
Substance Abuse and Mental Health Services Administration **SAMHSA**, Center for Behavioral Health Quality and Statistics. (Nov 3, 2011). The DAWN Report: **Drug-Related Emergency Department Visits Attributed to Intentional Poisoning**. Rockville, MD. http://oas.samhsa.gov/2k11/DAWN040/WEB_DAWN_040.htm
Sun EC, Dixit A, Humphreys K, et al. Association between **concurrent use of prescription opioids and benzodiazepines and overdose**: retrospective analysis. BMJ 2017;356:j760.
Tapiainen V, Taipale H, Tanskanen A, et al. The risk of **Alzheimer's disease associated with benzodiazepines and related drugs**: a nested case-control study. Acta Psychiatr Scand. 2018 May 31.
Taipale H, Tolppanen AM, Koponen M, et al. Risk of **pneumonia associated with incident benzodiazepine use** among community-dwelling adults with Alzheimer disease. CMAJ. 2017 Apr 10;189(14):E519-E529
Tamblyn R, Abrahamowicz M, du Berger R, McLeod P, Bartlett G. A 5-year prospective assessment of the risk associated with individual benzodiazepines and doses in new elderly users. J Am Geriatr Soc. 2005 Feb;53(2):233-41. CONCLUSION: The risk of injury varied by benzodiazepine, independent of half-life, as did the risk associated with increasing dosage for individual products. Higher doses of oxazepam, flurazepam, and chlordiazepoxide are associated with the greatest risk of injury in the elderly.
Tannenbaum C, Paquette A, Hilmer S, et al. A systematic review of **amnestic and non-amnestic mild cognitive impairment** induced by anticholinergic, antihistamine, GABAergic and opioid drugs. Drugs Aging. 2012 Aug 1;29(8):639-58.
Tannenbaum C, Martin P, Tamblyn R, et al. **Reduction of Inappropriate Benzodiazepine** Prescriptions Among Older Adults Through Direct Patient Education: The **EMPOWER** Cluster Randomized Trial. JAMA Intern Med. 2014 Apr 14.
Thygesen LC, Pottegård A, et al. External adjustment of unmeasured confounders in a case-control study of **benzodiazepine use and cancer risk**. Br J Clin Pharmacol. 2017 Jun 9.
Tiihonen J, Suokas JT, et al. Polypharmacy with antipsychotics, antidepressants, or benzodiazepines and **mortality in schizophrenia**. Arch Gen Psychiatry. 2012 May;69(5):476-83.
Tiihonen J, Mittendorfer-Rutz E, Torniainen M et al. **Mortality and cumulative exposure to antipsychotics, antidepressants, and benzodiazepines** in patients with schizophrenia: an observational follow-up study. Am J Psychiatry 2016;173:600–6.
Treatment Guidelines from the Medical Letter. Pharmaceutical Drug Overdose. Sept 2006. (Benzodiazepines: flumazenil treatment)
U.S. Substance Abuse and Mental Health Services Administration, news release, June 9, 2011http://www.samhsa.gov/newsroom/advisories/1106082530.aspx Admissions for treatment of **benzodiazepine abuse nearly tripled in the United States between 1998 and 2008**, while overall admissions for substance abuse rose only 11 percent, according to a government study released Thursday. Benzodiazepines -- a class of drugs prescribed to treat anxiety, insomnia and seizure disorders -- include Valium, Halcion, Xanax, Ativan and Librium. Abuse of benzodiazepines, which were introduced in the 1950s to replace barbiturates, can lead to addiction, injury and death.The Substance Abuse and Mental Health Services Administration (SAMHSA) study found that admissions for treatment of benzodiazepine abuse among patients 12 and older rose from 22,400 in 1998 to 60,200 a decade later. Benzodiazepine-related admissions accounted for 3.2 percent of all substance abuse admissions in 2008, compared with 1.3 percent in 1998.
van der Hooft CS, Schoofs MW,et al. Inappropriate benzodiazepine use in older adults and the risk of fracture. Br J Clin Pharmacol. 2008 Aug;66(2):276-82. Epub 2008 May 6. These findings suggest that inappropriate benzodiazepine use according to the Beers criteria is not associated with increased risk of fracture. Daily dose and longer duration of use (>14 days) is associated with higher risk of fracture, irrespective of the type of benzodiazepine prescribed.
Vicens C, Bejarano F, Sempere E, et al. Comparative efficacy of **two interventions to discontinue long-term benzodiazepine use**: cluster randomised controlled trial in primary care. Br J Psychiatry. 2014 Feb 13.
Vinkers DJ, Gussekloo J, van der Mast RC, et al. Benzodiazepine use and risk of mortality in individuals aged 85 years or older. JAMA. 2003 Dec 10;290(22):2942-3.
Voshaar RC, Couvée JE, van Balkom AJ, Mulder PG, Zitman FG. Strategies for **discontinuing long-term** benzodiazepine use: meta-analysis. Br J Psychiatry. 2006 Sep;189:213-20.
Vozoris NT, Fischer HD, Wang X, et al. Benzodiazepine drug use and **adverse respiratory outcomes among older adults with COPD**. Eur Respir J 2014;online April 17, 2014.
Wagner AK, et al. Benzodiazepine use and **hip fractures** in the elderly: who is at greatest risk? Arch Intern Med. 2004 Jul 26;164(14):1567-72.

Wang PS, Bohn RL, Glynn RJ, Mogun H, Avorn J. Hazardous benzodiazepine regimens in the elderly: effects of half-life, dosage, and duration on risk of hip fracture. Am J Psychiatry. 2001 Jun;158(6):892-8. Even at modest doses, including some low doses currently advocated in prescribing guidelines for older patients, treatment with benzodiazepines appears to increase the risk of hip fracture. Patients appear to be particularly vulnerable immediately after initiating therapy and after more than 1 month of continuous use. Benzodiazepines with shorter half-lives appear to be no safer than longer half-life agents.

Warner M, Trinidad JP, Bastian BA, et al. **Drugs Most Frequently Involved in Drug Overdose Deaths**: United States, 2010-2014. Natl Vital Stat Rep. 2016 Dec;65(10):1-15.

Weinberg JA, Magnotti LJ, Fischer PE, et al. Comparison of intravenous ethanol versus diazepam for alcohol withdrawal prophylaxis in the trauma ICU: results of a randomized trial. J Trauma. 2008 Jan;64(1):99-104. Concerning the prophylaxis of AWS, intravenous ethanol offers no advantage over diazepam with respect to efficacy or adverse sedative effects. The purported benefit of intravenous ethanol as a prophylactic agent against AWS was not evident.

Willems IA, Gorgels WJ, Oude Voshaar RC, Mulder J, Lucassen PL. **Tolerance to benzodiazepines** among long-term users in primary care. Fam Pract. 2013 Mar 20.

Wong A, Benedict NJ, Armahizer MJ, et al. Evaluation of **adjunctive ketamine to benzodiazepines for management of alcohol withdrawal syndrome**. Ann Pharmacother. 2015 Jan;49(1):14-9.

Woolcott John C.; Richardson Kathryn J.; et al. Meta-analysis of the Impact of 9 Medication Classes on **Falls** in Elderly Persons. Arch Intern Med. 2009;169(21):1952-1960.

Yonkers KA, Gilstad-Hayden K, Forray A, Lipkind HS. Association of **Panic Disorder, Generalized Anxiety Disorder, and Benzodiazepine Treatment During Pregnancy** With Risk of Adverse Birth Outcomes. JAMA Psychiatry. 2017 Sep 13.

Zaman H, Sampson SJ, Beck ALS, et al. **Benzodiazepines for psychosis-induced aggression or agitation**. Cochrane Database of Systematic Reviews 2017, Issue 12. Art. No.: CD003079. The evidence from RCTs for the use of benzodiazepines alone is not good. There were relatively few good data. Most trials were too small to highlight differences in either positive or negative effects. Adding a benzodiazepine to other drugs does not seem to confer clear advantage and has potential for adding unnecessary adverse effects. Sole use of older antipsychotics unaccompanied by anticholinergic drugs seems difficult to justify. Much more high-quality research is still needed in this area.

Procyshyn RM, Bezchlibnyk-Butler KZ, Jeffries JJ. Clinical Handbook of Psychotropic Drugs, 22nd Ed. Hogrefe Publishing, Massachusetts, 2017.

[9] 9Vinkers CH, Olivier B. Mechanisms Underlying Tolerance after Long-Term Benzodiazepine Use: A Future for Subtype-Selective GABA(A) Receptor Modulators? Adv Pharmacol Sci. 2012;2012:416864. doi: 10.1155/2012/416864. Epub 2012 Mar 29.
PubMed PMID: 22536226; PubMed Central PMCID: PMC3321276.

💻 Bipolar Disorder: Online Extras

Previously Used Agents:

Gabapentin dose CrCl<60 **NEURONTIN**g (100,300,400 cap) (600ᶜ,800ᶜmg tab) ▼ Max of 4000mg/day	**Common**: somnolence, dizzy, ataxia, nystagmus, N/V, blurred vision,tremor,slurred speech,rash, behavioral changes in kids&↓WBC.**WEIGHT GAIN=+**(appears dose related), **euphoria**; ?akathisia on withdrawal	N/A **little effect as mood stabilizer**	√seizures; Option:Neuropathic pain &**Anxiolytic in severe PD& social phobia**,↓dose if ↓ renal fx, 3-25umol/l (? Significance/avail.)	Antacids ↓ by 20% absorption NO other sig. interactionsWith doses >600mg less is absorbed since mechanism is saturated	100mg hs (↑**100**-400mg/day increments) 3600mg/day	100mg po BID 300mg po BID **400mg po BID** 300mg po TID	19 32 **36** 42
Topiramate **TOPAMAX**g (25,50ˣ,100,200mg tab; 15, 25mg sprinkle cap) PL Hypospadias in male infants. Cleft lip/palate.	**Common**: nausea, dizzy, tremor, ataxia, somnolence, **cognitive dysfx**, headache, paresthesias, sedation, fatigue, diarrhea, metabolic acidosis, **nephrolithiasis & glaucoma** acute angle,stop tx! **WEIGHT GAIN= loss possible** (seems dose & duration dependent &> in ♀)	CNS AE synergize with agents such as divalproex	Weight loss~**4kg** ?dose related May minimize weight gain induced by other psychotropics √seizures; 80% Renal elimination √migraine prophylaxis + dva→↓ platelet&↑**encephalopathy** **Renal stones**1.5% thus try to ↑**fluid intake**	↓**Topiramate level** by: **CBZ**& phenytoin (40%), valproate(15%) ↑ **toxicity**of topiramate with: Ketogenic diet; Aceta-,dor-&metho-zolamide (topiramate has carbonic anhydrase inhib. properties) **Topiramate** >200mg/d↓**effectiveness** : **OCs** **oral contraceptives**	25mg hs ↑ only by **25-50mg/week** increments **250-400**mg/day	25mg po BID 50mg po BID **100mg po BID** 200mg po BID 400mg po hs Caution: ↓ **sweating** especially in children	62 114 **108** 154 154

Bipolar Disorder References:

1. Yatham LN, Kusumakar V, Parikh SV, Haslam DR, Matte R, Sharma V, Kennedy S. Bipolar depression: treatment options. Can J Psychiatry. 1997 Aug;42 Suppl 2:87S-91S.
2. Expert Consensus Guideline Series- Bipolar Disorder, Apr 00, Postgraduate Medicine
3. Practice guideline: Bipolar disorder treatment (revision). Am J Psychiatry. 2002 Apr;159(4 Suppl):1-50. www.psych.org/psych_pract/treatg/pg/Practice%20Guidelines8904/BipolarDisorder_2e.pdf
4. Belmaker RH. Bipolar disorder. N Engl J Med. 2004 Jul 29;351(5):476-86.
5. NICE UK guidelines 2014 www.nice.org.uk/guidance/cg185
6. CANMAT bipolar guidelines: www.canmat.org/guides.php
   2005 guidelines - Yatham LN, Kennedy SH, O'Donovan C, et al. Canadian Network for Mood and Anxiety Treatments. Canadian Network for Mood and Anxiety Treatments (CANMAT) guidelines for the management of patients with bipolar disorder: consensus and controversies. Bipolar Disord. 2005;7 Suppl 3:5-69. Review.
   2009 update - Yatham LN, Kennedy SH, Schaffer A, et al. Bipolar Disord. 2009 May;11(3):225-55.
   2013 update - Yatham LN, Kennedy SH, Parikh SV, et al. Bipolar Disord. 2013 Feb;15(1):1-44.
   Yatham LN, Kennedy SH, Parikh SV, et al. Canadian Network for Mood and Anxiety Treatments **(CANMAT) and International Society for Bipolar Disorders (ISBD) 2018 guidelines** for the management of patients with bipolar disorder. Bipolar Disord **2018**;20:97-170.
7. Bowden CL, Brugger AM, Swann AC, et al. Efficacy of divalproex vs lithium and placebo in the treatment of mania. The Depakote Mania Study Group. JAMA. 1994 Mar 23-30;271(12):918-24.
8. Ketter TA. Monotherapy versus combined treatment with second-generation antipsychotics in bipolar disorder. J Clin Psychiatry 2008; 69 Suppl 5:9.
9. Community survey of bipolar disorder in Canada: lifetime prevalence and illness characteristics. Can J Psychiatry. 2006 Jan;51(1):9-16.
10. Tohen, Mauricio, Bowden, Charles L., et al. Olanzapine plus carbamazepine v. **carbamazepine** alone in treating manic episodes. The British Journal of Psychiatry 2008 192: 135-143.
11. Yatham LN, Grossman F, Augustyns I, Vieta E, Ravindran A. Mood stabilisers plus risperidone or placebo in the treatment of acute mania. International, double-blind, randomised controlled trial. Br J Psychiatry. 2003 Feb;182:141-7.
12. Sachs GS, Vanderburg DG, Karayal ON, Kolluri S, Bachinsky M, Cavus I. Adjunctive oral ziprasidone in patients with acute mania treated with lithium or divalproex, part 1: results of a randomized, double-blind, placebo-controlled trial. J Clin Psychiatry. 2012 Nov;73(11):1412-9.
13. Tohen M, Vieta E, Calabrese J, Ketter TA, Sachs G, Bowden C, Mitchell PB, Centorrino F, Risser R, Baker RW, Evans AR, Beymer K, Dube S, Tollefson GD, Breier A. Efficacy of olanzapine and olanzapine-fluoxetine combination in the treatment of bipolar I depression. Arch Gen Psychiatry. 2003 Nov;60(11):1079-88.
14. Shulman KI, Almeida OP, Herrmann N, et al. **Delphi survey of maintenance lithium treatment in older adults with** bipolar disorder: An ISBD task force report. Bipolar Disord. 2018 Oct 30.

AAN-Practice Parameter Update: Management issues for women with epilepsy – focus on **pregnancy**(Valproate should be avoided during the first trimester of pregnancy. Among the other findings:Women with epilepsy who take antiepileptic drugs have twice the risk for delivering babies with Apgar scores under 7. Valproate is associated with increased risk for congenital malformations. Avoiding valproate, phenobarbital, and phenytoin during pregnancy may reduce the risk for poor cognitive outcomes (all are class D drugs), while carbamazepine (class C) "probably does not produce cognitive impairments." Monotherapy for epilepsy is preferable to polytherapy, if possible, to reduce poor cognitive outcomes.http://www.aan.com/globals/axon/assets/5476.pdf

Aggarwal SP, Zinman L, Simpson E et al; Northeast and Canadian Amyotrophic Lateral Sclerosis consortia. Safety and efficacy of **lithium** in combination with riluzole for treatment of **amyotrophic lateral sclerosis**: a randomised, double-blind, placebo-controlled trial. Lancet Neurol. 2010 May;9(5):481-8. Epub 2010 Apr 1.

Agnew-Blais J, Danese A. **Childhood maltreatment** and unfavourable clinical outcomes in bipolar disorder: a systematic review and meta-analysis. LancetPsychiatry. 2016 Feb 9.

AmericanCollege of Obstetricians and Gynecologists (**ACOG**). Use of psychiatric medications during **pregnancy and lactation**. Washington (DC): AmericanCollege of Obstetricians and Gynecologists (ACOG); 2008 Apr. 20 p. (ACOG practice bulletin; no. 92). [245 references]

American Psychiatric Association Brochures:http://www.healthyminds.org/Functional-Library/brochures.aspx

Amsterdam JD and Shults J. Efficacy and safety of long-term **fluoxetine versus lithium monotherapy of bipolar II disorder**: A randomized, double-blind, placebo-substitution study. Am J Psychiatry. 2010 Jul;167(7):792-800.

Amsterdam JD, Lorenzo-Luaces L, Soeller I, et al. Safety and effectiveness of **continuation antidepressant versus mood stabilizer monotherapy** for relapse-prevention of **bipolar II depression**: a randomized, double-blind, parallel-group, prospective study. J Affect Disord 2015;185:31–7.

Anderson IM, Haddad PM, Scott J. **Bipolar disorder**. BMJ. 2012 Dec 27;345:e8508.

Angstman K, Rasmussen NH. **Personality disorders**: review and clinical application in daily practice. Am Fam Physician. 2011 Dec 1;84(11):1253-60.

Arnulf I, Rico TJ, Mignot E. Diagnosis, disease course, and management of patients with **Kleine-Levin syndrome**. Lancet Neurol. 2012 Oct;11(10):918-28. (lithium)

Artama M, Auvinen A, Raudaskoski T, et al. Antiepileptic drug use of women with epilepsy and congenital malformations in offspring. Neurology. 2005 Jun 14;64(11):1874-8. CONCLUSION: Excess risk was confined to patients using **valproate** during pregnancy. The risk for malformations was not elevated in offspring of mothers using carbamazepine, oxcarbazepine, or phenytoin (as monotherapy or polytherapy without valproate).

Asenapine for bipolar I disorder? Drug Ther Bull. 2012 Jun;50(6):69-72.

Baker GA, Bromley RL, Briggs M, et al. **IQ at 6 years after in utero exposure to antiepileptic drugs**: A controlled cohort study. Neurology. 2014 Dec 24.

BALANCE investigators and collaborators. **Lithium plus valproate** combination therapy versus monotherapy for relapse prevention in bipolar I disorder (BALANCE): a randomized open-label trial. Lancet 2009; online Dec 23. Pdf

Bartoli F, Crocamo C, Clerici M, et al. **Allopurinol** as add-on **treatment for mania** symptoms in bipolar disorder: systematic review and meta-analysis of randomised controlled trials. Br J Psychiatry. 2016 Nov 17.

Bates DE, Herman RJ. **Carbamazepine** toxicity induced by **lopinavir/ritonavir** and nelfinavir. Ann Pharmacother. 2006 Jun;40(6):1190-5. Epub 2006 May 23.

Bauer M, Ritter P, Grunze H, Pfennig A. Treatment options for **acute depression in bipolar disorder**. Bipolar Disord. 2012 May;14 Suppl 2:37-50.

Bekkelund SI, Lilleng H, Tonseth S. **Gabapentin** may cause reversible **visual field constriction**. BMJ. 2006 May 20;332(7551):1193.

Bendz H, Schön S, Attman PO, Aurell M. **Renal failure** occurs in chronic **lithium**treatment but is uncommon. Kidney Int. 2009 Nov 25. [Epub ahead of print]

Berk M, Dodd S. Efficacy of **atypical antipsychotics** in bipolar disorder. **Drugs. 2005**;65(2):257-69.

Berk M, Daglas R, Dandash O, et al. **Lithium** in the maintenance phase following a first episode of mania: randomised controlled trial. Br J Psychiatry. 2017 Jun;210(6):413-421.

Bergink V et al. Prevention of **postpartum psychosis and mania** in women at high risk. Am J Psychiatry 2012 Mar 8.

Beynon S, Soares-Weiser K, et al. **Psychosocial interventions** for the prevention of relapse in bipolar disorder: systematic review of controlled trials. Br J Psychiatry. 2008 Jan;192(1):5-11.
Cognitive behavioral therapy and group **psychoeducation** reduce the risk of relapse in patients with stable bipolar disorder. (LOE = 1a)

Bezchlibnyk-Butler Clinical Handbook of Psychotropic Drugs, 17th Ed. 2007.

Bezchlibnyk-Butler KZ. **Clinical Handbook of Psychotropic Drugs, 22nd Ed**. 22nd Editors: Procyshyn RM, Bezchlibnyk-Butler KZ, Jeffries JJ. Hogrefe Publishing, Massachusetts, 2017.

Bialer M, et al. Pharmacokinetic interactions of topiramate. ClinPharmacokinet. 2004;43(12):763-80.

Bliss SA, Warnock JK. Psychiatric medications: **Adverse cutaneous drug reactions**. ClinDermatol. 2013 Jan;31(1):101-9.

Bodén R, Lundgren M, Brandt L, Reutfors J, et al. Risks of adverse **pregnancy and birth outcomes** in women treated or not treated with mood stabilisers for bipolar disorder: population based cohort study. BMJ 2012;345:e7085.

Bond DJ, Noronha MM, Kauer-Sant'anna M, Lam RW, Yatham LN. Antidepressant-Associated Mood Elevations in Bipolar II Disorder Compared With Bipolar I Disorder and Major Depressive Disorder: A Systematic Review and Meta-Analysis. J Clin Psychiatry. 2008 Jul 15:e1-e13. [Epub ahead of print] The risk of antidepressant-associated mood elevations in bipolar II disorder is intermediate between that in bipolar I disorder and MDD.

Bowden CL, et al. Impact of **lamotrigine** and **lithium** on **weight** in obese and nonobese patients with bipolar I disorder. Am J Psychiatry. 2006 Jul;163(7):1199-201. (InfoPOEMs: Obese patients with bipolar disorder may be more likely to maintain weight or lose weight while taking long-term lamotrigine (Lamictal) than while taking lithium. No significant differences in weight occurred among nonobese patients treated with either medication. Because of concerns about cost and about the quality of these 2 trials, it makes sense to begin treatment with lithium and consider changing to lamotrigine only if individuals begin to gain weight. (LOE = 2b))

Bowden CL, et al. A randomized, double-blind, placebo-controlled study of quetiapine or lithium as monotherapy for mania in bipolar disorder. J Clin Psychiatry. 2005 Jan;66(1):111-21.

Bowden CL, Calabrese JR, McElroy SL, et al. A randomized, placebo-controlled 12-month trial of divalproex and lithium in treatment of outpatients with bipolar I disorder. Divalproex Maintenance Study Group. Arch Gen Psychiatry. 2000 May;57(5):481-9.

Bowden CL, et al.; Lamictal 606 Study Group. A placebo-controlled 18-month trial of lamotrigine and lithium maintenance treatment in recently manic or hypomanic patients with bipolar I disorder. Arch Gen Psychiatry. 2003 Apr;60(4):392-400.

Brooks JO 3rd, Goldberg JF, Ketter TA, et al. Safety and tolerability associated with **second-generation antipsychotic** polytherapy in bipolar disorder: findings from the systematic Treatment enhancement program for bipolar disorder. J Clin Psychiatry. 2010 Sep 7. [Epub ahead of print]

Brown EB, et al. A 7-week, randomized, double-blind trial of **olanzapine/fluoxetine combination versus lamotrigine** in the treatment of bipolar I depression. J Clin Psychiatry. 2006 Jul;67(7):1025-33.

Calabrese JR, Huffman RF, White RL, et al. **Lamotrigine** in the acute treatment of bipolar depression: results of five double-blind, placebo-controlled clinical trials. Bipolar Disord.2008 Mar;10(2):323-33. Lamotrigine monotherapy did not demonstrate efficacy in the acute treatment of bipolar depression in four out of five placebo-controlled clinical studies. Lamotrigine was well tolerated in the acute treatment of bipolar depression.

Calabrese JR, Bowden CL, Sachs GS, et al. A double-blind placebo-controlled study of **lamotrigine monotherapy in outpatients with bipolar I depression**. Lamictal 602 Study Group. J Clin Psychiatry. 1999 Feb;60(2):79-88.

Calabrese JR, et al. A randomized, double-blind, placebo-controlled trial of quetiapine in the treatment of bipolar I or II depression. Am J Psychiatry. 2005 Jul;162(7):1351-60.(InfoPOEMs: In this short-term study, quetiapine was more effective than placebo in treating patients with a bipolar I or II disorder experiencing a major depressive episode. Because of the risk of extrapyramidal side effects, however, other treatment agents should be considered first. (LOE = 1b))

Calabrese JR, et al. A placebo-controlled 18-month trial of lamotrigine and lithium maintenancetreatment in recently depressed patients with bipolar I disorder.J Clin Psychiatry. 2003 Sep;64(9):1013-24.

Calabrese JR, et al. A 20-month, double-blind, maintenance trial of **lithium versus divalproex** in rapid-cycling bipolar disorder. Am J Psychiatry. 2005 Nov;162(11):2152-61.

Calkin CV, Ruzickova M, Uher R, et al. **Insulin resistance** and outcome in bipolar disorder. Br J Psychiatry. 2015 Jan;206(1):52-7.

Canetta SE, Bao Y, Co MD, et al. Serological Documentation of **Maternal Influenza Exposure** and Bipolar Disorder in Adult Offspring. Am J Psychiatry. 2014 Jan 31.

Chapel S, Chiu YY, Hsu J, et al. **Lurasidone** Dose Response in Bipolar Depression: A Population Dose-Response Analysis. ClinTher. 2015 Dec 22.

Chatterton ML, Stockings E, Berk M, et al. **Psychosocial therapies** for the adjunctive treatment of bipolar disorder in adults: network meta-analysis. Br J Psychiatry. 2017 Feb 16.

ChenPei, Lin Juei-Jueng, et al. Taiwan SJS Consortium.Carbamazepine-Induced Toxic Effects and **HLA-B*1502** Screening in Taiwan. N Engl J Med 2011; 364:1126-1133.

Chen CH, Lee CS, Lee MT, et al; the Taiwan Bipolar Consortium. **Variant GADL1 and Response to Lithium Therapy** in Bipolar I Disorder. N Engl J Med. 2013 Dec 25

Chen PH, Tsai SY, Pan CH, et al. **Mood stabilisers and risk of stroke** in bipolar disorder**.** Br J Psychiatry. 2018 Oct 8:1-6.

Chiesa A, Chierzi F, De Ronchi D, Serretti A. **Quetiapine for bipolar depression**: a systematic review and meta-analysis. IntClinPsychopharmacol. 2011 Nov 19.

Chiu, John F., Chokka, Pratap R. **Prevalence of Bipolar Disorder symptoms in Primary Care** (ProBiD-PC): A Canadian study. Can Fam Physician 2011 57: e58-67.

Christensen J, Grønborg TK, Sørensen MJ, et al. **Prenatal valproate exposure and risk of autism** spectrum disorders and childhood autism. JAMA. 2013; 309(16):1696-1703.

Cipriani A, Pretty H, Hawton K, Geddes JR. **Lithium** in the prevention of **suicidal** behavior and all-cause mortality in patients with mood disorders: a systematic review of randomized trials. Am J Psychiatry. 2005 Oct;162(10):1805-19. CONCLUSIONS: Lithium is effective in the prevention of suicide, deliberate self-harm, and death from all causes in patients with mood disorders.

Cipriani A, Rendell JM, Geddes J. **Olanzapine** in long-term treatment for bipolar disorder. Cochrane Database Syst Rev. 2009 Jan 21;(1):CD004367. Though based on a limited amount of information, there is evidence that olanzapine may prevent further mood episodes in patients who have responded to olanzapine during an index manic or mixed episode and who have not previously had a satisfactory response to lithium or valproate.

However, notwithstanding these positive results, the current evidence is stronger for lithium as first line maintenance treatment of bipolar disorder.
Cipriani A, Barbui C, et al. Comparative efficacy and acceptability of **anti-manic drugs in acute mania**: a multiple-treatments meta-analysis. Lancet 2011; published online Aug 17. Overall, antipsychotic drugs were significantly more effective than mood stabilisers. Risperidone, olanzapine, and haloperidol should be considered as among the best of the available options for the treatment of manic episodes.
But see editorial: Berk M, Malhi GS. Should antipsychotics take pole position in mania treatment?Lancet. 2011 Aug 16.
Cipriani A, Hawton K, Stockton S, Geddes JR. **Lithium in the prevention of suicide** in mood disorders: updated systematic review and meta-analysis. BMJ. 2013Jun 27;346:f3646.
Clinical Handbook of Psychotropic Drugs 13th Edition 2003, Bezchlibnyk-Butler,Jeffries
Clos S, Rauchhaus P, et al. **Long-term effect of lithium** maintenance therapy on **estimated glomerular filtration** rate in patients with affective disorders: a population-based cohort study. Lancet Psychiatry 2015;2:1075–83.
Craddock N, Sklar P. **Genetics** of bipolar disorder. Lancet. 2013 May 11;381(9878):1654-62.
Crawford MJ, MacLaren T, Reilly JG. Are mood stabilisers helpful in treatment of **borderline personality disorder**? BMJ. 2014 Sep 16;349:g5378.
Crawford MJ, Sanatinia R, Barrett B, et al; LABILE study team. The **Clinical Effectiveness and Cost-Effectiveness of Lamotrigine** in Borderline Personality Disorder: A Randomized Placebo-Controlled Trial. Am J Psychiatry. 2018 Apr 6
Cross-Disorder Group of the Psychiatrics Genomics Consortium. Identification of **risk loci with shared effects on five major psychiatric disorders**: a genome-wide analysis. Lancet 2013; online Feb 28.
Crump C, Sundquist K, Winkleby MA, Sundquist J. **Mental disorders and vulnerability** to **homicidal death**: Swedish nationwide cohort study. BMJ 2013;346:f557.
Crump C, Sundquist K, Winkleby MA, Sundquist J. **Comorbidities and Mortality** in Bipolar Disorder: A Swedish National Cohort Study. JAMA Psychiatry. 2013 Jul 17.
Cunnington M, et al; International Lamotrigine Pregnancy Registry Scientific Advisory Committee. Lamotrigine and the risk of malformations in pregnancy. Neurology. 2005 Mar 22;64(6):955-60.
Cutler AJ, Datto C, Nordenhem A, et al. **Extended-Release Quetiapine** as Monotherapy for the Treatment of Adults With Acute Mania: A Randomized, Double-Blind, 3-Week Trial. Clin Ther. 2011 Nov 3.
Damkier P, Christensen LS, Broe A. Patterns and predictors for prescription of **psychotropics and mood-stabilizing antiepileptics during pregnancy** in Denmark 2000-2016. Br J Clin Pharmacol. 2018 Aug 5.
de Haan GJ, Edelbroek P, Segers J, et al. Gestation-induced changes in lamotrigine pharmacokinetics: a monotherapy study. Neurology. 2004 Aug 10;63(3):571-3.
Duffy A, Goodday S, Keown-Stoneman C, et al. The **Emergent Course of Bipolar Disorder**: Observations Over Two Decades From the Canadian High-Risk Offspring Cohort. Am J Psychiatry. 2018 Dec 11:appiajp201818040461.
Duffy A, Horrocks J, Doucette S, Keown-Stoneman C, McCloskey S, Grof P. The developmental **trajectory of bipolar** disorder. Br J Psychiatry. 2013 Nov 21.
Dolk H, Jentink J, Loane M, et al; EUROCAT Antiepileptic Drug Working Group. Does **lamotrigine** use in pregnancy increase orofacial cleft risk relative to other malformations? Neurology. 2008 Sep 2;71(10):714-22.
We find no evidence of a specific increased risk of isolated orofacial clefts relative to other malformations due to lamotrigine (LTG) monotherapy. Our study is not designed to assess whether there is a generalized increased risk of malformations with LTG exposure.
Doose DR, et al. Effect of topiramate or carbamazepine on the pharmacokinetics of an oral contraceptive containing norethindrone and ethinyl estradiol in healthy obese and nonobese female subjects. Epilepsia. 2003 Apr;44(4):540-9.
Drug Information Handbook 10th Edition 2002-2003.
Drugs in Pregnancy & Lactation 9th Edition 2011.
Durgam S, Earley W, Lipschitz A, et al. An 8-Week Randomized, Double-Blind, Placebo-Controlled Evaluation of the Safety and Efficacy of **Cariprazine in Patients With Bipolar I Depression**. Am J Psychiatry. 2015 Nov 6
Earley W, Durgam S, Lu K, et al. Clinically relevant response and remission outcomes in **cariprazine**-treated patients with bipolar I disorder. J Affect Disord. 2017 Sep 25;226:239-244.
Earley W, Victoria Burgess M, Rekeda L, et al. **Cariprazine** Treatment of Bipolar Depression: A Randomized Double-Blind Placebo-Controlled Phase 3 Study. Am J Psychiatry. 2019 Mar 8:appiajp201818070824.
Eberhard-Gran M, Eskild A, Opjordsmoen S. Treating mood disorders during pregnancy: safety considerations. Drug Saf. 2005;28(8):695-706.
Eberhard-Gran M, Eskild A, Opjordsmoen S. Use of Psychotropic Medications in Treating Mood Disorders during Lactation:PracticalRecommendations.CNS Drugs.2006;20(3):187-98.
El-Mallakh RS, Vöhringer PA, et al. **Antidepressants worsen rapid-cycling course in bipolar depression: a STEP-BD** randomized clinical trial. J Affect Disord2015;184:318–21.
Fardet L et al. Suicidal behavior and severe **neuropsychiatric disorders following glucocorticoid** therapy in primary care. Am J Psychiatry 2012 May 1; 169:491.
Fazel S, Zetterqvist J, Larsson H, et al. Antipsychotics, mood stabilisers, and **risk of violent crime**. Lancet. 2014 May 7.
FDA Dec/09 notified health care professionals and patients about the increased risk of neural tube defects and other major birth defects, such as craniofacial defects and cardiovascular **malformations**, in babies exposed to **valproate** sodium and related products (valproic acid and divalproex sodium) during pregnancy.
FDA June/11 notified healthcare professionals that children born to mothers who take the anti-seizure medication **valproate** sodium or related products (valproic acid and divalproex sodium) during pregnancy have an increased risk of **lower cognitive test scores** than children exposed to other anti-seizure medications during pregnancy.
Findling RL, et al. Double-blind 18-month trial of lithium vs divalproex maintenance treatment in pediatric bipolar disorder.J Am Acad Child Adolesc Psychiatry.2005May;44(5):409-17.
Findling RL, Robb A, McNamara NK, et al. **Lithium** in the **Acute Treatment of Bipolar I Disorder**: A Double-Blind, Placebo-Controlled Study. Pediatrics. 2015 Oct 12.
Fleisher AS, Truran D, Mai JT, et al. For the Alzheimer's Disease Cooperative Study. Chronic **divalproex** sodium use and brain atrophy in **Alzheimer** disease. Neurology. 2011 Sep 27;77(13):1263-1271.
Forsmark CE, Swaroop Vege S, et al. **Acute Pancreatitis**. N Engl J Med. 2016 Nov 17;375(20):1972-1981 (azathioprine, 6-mercaptopurine, didanosine, valproic acid,angiotensin-converting–enzyme inhibitors, and mesalamine)
Fortinguerra, Filomena, Clavenna, Antonio, Bonati, Maurizio. Psychotropic Drug Use During **Breastfeeding**: A Review of the Evidence. Pediatrics 2009 124: e547-e556.
Frye Mark A., **Bipolar Disorder — A Focus on Depression**. N Engl J Med 2011; 364:51-59.
Gao K, Goto T, Yuan C, et al. A Pilot Study of the Effectiveness of **Lithium Versus Quetiapine** Immediate Release Monotherapy in Patients With Bipolar Spectrum Disorders. J Clin Psychopharmacol. 2018 Oct;38(5):422-434.
Gardner DM, Baldessarini RJ, Waraich P. Modern antipsychotic drugs: a **critical overview**. **CMAJ**. **2005** Jun 21;172(13):1703-11.
Geddes JR, Calabrese JR, et al. **Lamotrigine** for treatment of bipolar depression: independent meta-analysis and meta-regression of individual patient data from five randomised trials. Br J Psychiatry. 2009 Jan;194(1):4-9.
There is consistent evidence that lamotrigine has a beneficial effect on depressive symptoms in the depressed phase of bipolar disorder. The overall pool effect was modest, although the advantage over placebo was larger in more severely depressed participants.
Geddes JR, Miklowitz DJ. **Treatment of bipolar disorder**. Lancet. 2013 May 11;381(9878):1672-82.
Gelenberg AJ, Kane JM, KellerMB, et al. Comparison of standard and **low serum levels of lithium** for maintenance treatment of bipolar disorder. N Engl J Med. 1989 Nov 30;321(22):1489-93.
Recent findings about the limited nephrotoxicity of lithium, along with our observations, suggest that physicians should attempt to maintain serum lithium levels between 0.8 and 1.0 mmol per liter in most patients with bipolar disorder and that they should attempt to enhance patients' understanding of and compliance with this regimen.
Geller B, et al. A Randomized Controlled Trial of **Risperidone, Lithium, or Divalproex** Sodium for Initial Treatment of Bipolar I Disorder, Manic or Mixed Phase, in **Children & Adolescents**. Arch Gen Psychiatry. 2012 Jan 2.
Geriatric Dosage Handbook 7th Edition 2002
Gerrett D, Lamont T, Paton C, et al. Prescribing and **monitoring lithium therapy**: summary of a safety report from the National Patient Safety Agency. BMJ. 2010 Nov 19;341:c6258.
Gibbons RD.; Hur Kwan; et al. Relationship Between Antiepileptic Drugs and **Suicide** Attempts in Patients With Bipolar Disorder. Arch Gen Psychiatry. 2009;66(12):1354-1360.
Gilron I, Bailey JM, Tu D, Holden RR, et al. Morphine, gabapentin, or their combination for neuropathic pain. N Engl J Med. 2005 Mar 31;352(13):1324-34.
Gijsman HJ, Geddes JR, Rendell JM, et al. **Antidepressants** for bipolar depression: a **systematic review** of randomized, controlled trials. Am J Psychiatry. 2004 Sep;161(9):1537-47.
Goes FS, Pirooznia M, Parla JS, et al. **Exome Sequencing of Familial Bipolar Disorder**. JAMA Psychiatry.2016 Jun 1;73(6):590-7.
Goldberg JF, Burdick KE, Endick CJ. Preliminary randomized, double-blind, placebo-controlled trial of **pramipexole** added to mood stabilizers for treatment-resistant bipolar depression. Am J Psychiatry. 2004 Mar;161(3):564-6.

Goldsmith D, Wagstaff A, Ibbotson T, Perry C. Lamotrigine: A Review of its Use in Bipolar Disorder. Drugs. 2003;63(19):2029-2050.
Goldstein TR, Ha W, Axelson DA, et al. Predictors of Prospectively Examined **Suicide Attempts** Among Youth With Bipolar DisorderPredictors of Suicide Attempts. Arch Gen Psychiatry. 2012 Jul 2:1-10.
Goldstein BI, Carnethon MR, Matthews KA, et al. **Major Depressive Disorder and Bipolar Disorder Predispose Youth to Accelerated Atherosclerosis** and Early Cardiovascular Disease: A Scientific Statement From the American Heart Association (AHA). Circulation. 2015 Aug 10.
Goodwin GM, et al. A pooled analysis of 2 placebo-controlled 18-month trials of lamotrigine andlithium maintenance in bipolar I disorder.J Clin Psychiatry. 2004 Mar;65(3):432-41.
Goodwin FK, Fireman B, Simon GE, et al. **Suicide risk** in bipolar disorder during treatment with lithium and divalproex. JAMA. 2003 Sep 17;290(11):1467-73.
Goodwin GM, Consensus Group of the British Association for Psychopharmacology. Evidence-based guidelines for treating **bipolar disorder**: revised second editionrecommendations from the **British Association for Psychopharmacology**. J Psychopharmacol [Internet]. June 2009 [cited 2011 Feb 18]; 23(4):346-388. http://www.bap.org.uk/pdfs/Bipolar_guidelines.pdf
Goodwin GM, et al. Evidence-based **guidelines for treating bipolar disorder**: Revised third edition recommendations from the **British Association for Psychopharmacology**. J Psychopharmacol. **2016** Jun;30(6):495-553.
Gordon CE, Vantzelfde S, Francis JM. **Acetazolamide in Lithium-Induced Nephrogenic** Diabetes Insipidus. N Engl J Med. 2016 Nov 17;375(20):2008-2009.
Grande I, Berk M, Birmaher B, Vieta E. **Bipolar disorder**. Lancet. 2015 Sep 17.
Grunze H, Vieta E, Goodwin GM, et al. The **World Federation of Societies of Biological Psychiatry (WFSBP)** Guidelines for the Biological Treatment of Bipolar Disorders: **Update 2010 on the treatment of acute bipolar depression**. World J Biol Psychiatry 2010;11:81-109.
GulackBC, PuriNV, Kim WJ. **Stutter Exacerbated by Lithium** in a PediatricPatient with Bipolar Disorder (October). Ann Pharmacother. 2011 Sep 13.
Haas M, Delbello MP, et al. **Risperidone** for the treatment of acute mania in children andadolescents with bipolar disorder: a randomized, double-blind, placebo-controlled study. Bipolar Disord. 2009 Nov;11(7):687-700.
Hafeman DM, Merranko J, Goldstein TR, et al. Assessment of a **person-level risk calculator to predict new-onset bipolar spectrum disorder in youth at familial risk** [online July 5, 2017]. JAMA Psychiatry. doi:10.1001/jamapsychiatry.2017 .1763
Hage B, Britton B, Daniels D, et al. **Low cardiac vagal tone index** by heart rate variability differentiates bipolar from major depression. World J Biol Psychiatry. 2017 Oct 5:1-9.
Handbook of Clinical Drug Data 10th Edition 2002
Hartong EG, et al.; LitCar Group. Prophylactic efficacy of lithium versus carbamazepine in treatment-naïve bipolar patients.J Clin Psychiatry. 2003 Feb;64(2):144-51.
Hayes JF, Pitman A, Marston L, et al. **Self-harm, Unintentional Injury, and Suicide** in Bipolar Disorder During Maintenance Mood Stabilizer Treatment: A UK Population-Based Electronic Health Records Study. JAMA Psychiatry. 2016 Jun 1;73(6):630-7.
Hayes JF, et al. **Adverse Renal, Endocrine, Hepatic, and Metabolic Events** during **Maintenance Mood Stabilizer Treatment** for Bipolar Disorder: A Population-Based Cohort Study. PLoS Med. 2016 Aug 2;13(8):e1002058.
Health Canada Sept/04 Lamictal warning with birth control pills http://www.hc-sc.gc.ca/dhp-mps/alt_formats/hpfb-dgpsa/pdf/medeff/lamictal_pa-ap_e.pdf
Health Canada Aug/06 Lamictal warning with non-syndromic oral clefts.Emerging data from the North American Antiepileptic Drug (NAAED) Pregnancy Registry suggest an association between LAMICTAL® (lamotrigine) and an increased risk of non-syndromic oral clefts over the reference population for the registry (ie. Active Malformations Surveillance Program at Brigham and Women's Hospital in Boston, USA)1. Recently published data from the Registry report three cases of isolated, non syndromic cleft palate and two cases of isolated, non syndromic cleft lip without cleft palate in infants from 564 first trimester lamotrigine monotherapy exposures giving a rate of 8.9 per 1,000, as compared to 0.37 per 1000 in the reference population for that registry. The prevalence of oral clefts noted in the NAAED registry is also higher than the background prevalence of non-syndromic oral clefts reported in the literature, including studies from the United States, Australia and Europe. While different studies have differing results due to geographic and case ascertainment variations, the reported range is 0.50 to 2.16/1000 3-17. To assist with the assessment of risk, analysis of data from additional pregnancy registries, with approximately 2200 additional lamotrigine monotherapy first trimester exposures has been conducted, and 4 additional non-syndromic cases of oral cleft have been identified. http://www.hc-sc.gc.ca/dhp-mps/medeff/advisories-avis/prof/2006/lamictal_2_hpc-cps_e.html
Health Canada Jan/10 is advising consumers not to use any unauthorized health products sold under **Natural Choice Lithium Orotate**.
Health Canada Feb/14 is informing health professionals and patients of new safety information and treatment recommendations regarding the drug **lithium** and the risks of high blood calcium (hypercalcemia) sometimes associated with a hormone disorder known as hyperparathyroidism.
Health Canada Dec/16 is advising Canadians that three unauthorized products, "**Lithium Plus, Serotonin Support, and Brain Support**," may pose serious health risks because they may contain Lithium Orotate.
Health Canada May/17 is advising Canadians that multiple unauthorized products labelled to contain L-tryptophan or **lithium orotate** were being sold on amazon.ca, and may pose serious health risks.
Hemager N, Plessen KJ, Thorup A, et al. Assessment of **Neurocognitive Functions** in 7-Year-Old Children at **Familial High Risk for Schizophrenia or Bipolar Disorder:** The Danish High Risk and Resilience Study VIA 7. JAMA Psychiatry. 2018 Jun 20.
Hirschfeld RM, et al. Rapid antimanic effect of risperidone monotherapy: a 3-week multicenter, double-blind, placebo-controlled trial. Am J Psychiatry. 2004 Jun;161(6):1057-65.
Hoang U, Stewart R, Goldacre MJ. **Mortality after hospital discharge** for people with schizophrenia or bipolar disorder: retrospective study of linked English hospital episode statistics, 1999-2006. BMJ 2011;343:d5422.
Holtzheimer PE, Kelley ME, Gross RE et al. **Subcallosal Cingulate Deep Brain Stimulation** for Treatment-Resistant Unipolar and Bipolar Depression. Arch Gen Psychiatry.2012Jan2.
Hou L, Heilbronner U, et al. **Genetic variants** associated with response to **lithium** treatment in bipolar disorder: a genome-wide association study. Lancet 2016; online Jan 21.
Huang MH, Cheng CM, Huang KL, et al. Bipolar disorder and **risk of Parkinson disease**: a nationwide longitudinal study. Neurology 2019;92:e2735–e2742.
Huang RY, Hsieh KP, Huang WW, et al. Use of **lithium and cancer risk** in patients with bipolar disorder: population-based cohort study. Br J Psychiatry. 2016 Jul 7.
Hughes T, Cardno A, et al. **Unrecognised bipolar** disorder among UK primary care patients **prescribed antidepressants**: observational study. Br J Gen Pract. 2016 Feb;66(643):e71-7.
Huhn M, TardyM, Spineli LM, et al. Efficacy of **pharmacotherapy and psychotherapy** for adult psychiatric disorders: a systematic overview of meta-analyses [online April 30, 2014]. JAMA Psychiatry.
International Consortium on Lithium Genetics (ConLi+Gen), Amare AT, Schubert KO, Hou L, et al. Association of **Polygenic Score** for Schizophrenia and **HLA Antigen and Inflammation Genes** With **Response to Lithium** in Bipolar Affective Disorder: A Genome-Wide Association Study. JAMA Psychiatry. 2017 Nov 9.
Irwin KE, Freudenreich O, Peppercorn J, et al. Case Records of the Massachusetts General Hospital. Case 30-2016. A **63-Year-Old Woman with Bipolar Disorder**, Cancer, and Worsening Depression. (aromatase inhibitor, **lurasidone**) N Engl J Med. 2016 Sep 29;375(13):1270-81.
Jakes AD, Bhandari S. Investigating **polyuria**. BMJ. 2013 Dec 2;347:f6772
Jefferson JW. A clinician's guide to **monitoringkidney function in lithium**-treated patients. J Clin Psychiatry. 2010 Sep;71(9):1153-7.
Jentink, Janneke, Loane, Maria A., Dolk, Helen, et al. the EUROCAT Antiepileptic Study Working Group, **Valproic** Acid Monotherapy in Pregnancy and Major **Congenital** Malformations. N Engl J Med 2010 362: 2185-2193.
Jentink Janneke, Dolk Helen, Loane Maria A, et al., for the EUROCAT Antiepileptic Study Working Group. Intrauterine exposure to **carbamazepine** and specific congenital **malformations**: systematic review and case-control study. BMJ 341:doi:10.1136/bmj.c6581 (Published 2 Dec 2010). (eg. **spina bifida**, but less than valproate)
Jones I, Chandra PS, Dazzan P, et al.Bipolardisorder, affective psychosis, and schizophrenia in **pregnancy and the post-partum**period. Lancet. 2014 Nov15;384(9956):1789-99.
Jauhar S, Nour MM, Veronese M, et al. A test of the **transdiagnostic dopamine hypothesis** of psychosis using positron emission tomographic imaging in bipolar affective disorder and schizophrenia [online Oct 11, 2017]. JAMA Psychiatry. doi:10.1001/jamapsychiatry.2017.2943
Kang H, et al. Long-term use of **valproic acid** in US veterans is associated with a **reduced risk of smoking-related** cases of **head and neck cancer**. Cancer. 2014 Mar24.
Kazmin, Aleksey, Wong, Renee C., Sermer, M, et al.**Antiepileptic drugs in pregnancy** and hemorrhagic disease of the newborn: An update. Can Fam Physician 2010 56: 1291-1292
KempDE, Gao K, Fein EB, Chan PK, Conroy C, Obral S, Ganocy SJ, Calabrese JR. **Lamotrigine as add-on** treatment to **lithium and divalproex**: lessons learned from a double-blind, placebo-controlled trial in rapid-cycling bipolar disorder. BipolarDisord. 2012 Nov;14(7):780-9.

Kendall T, Morriss R, Mayo-Wilson E, et al; Guideline Development Group. Assessment and **management of bipolar disorder**: summary of updated **NICE** guidance. BMJ. 2014 Sep 25;349:g5673.
Kessing LV, Sondergard L, Kvist K, Andersen PK. Suicide risk in patients treated with lithium. Arch Gen Psychiatry. 2005 Aug;62(8):860-6.
Kessing LV, Hellmund G, Geddes JR, et al. Valproate vs. **lithium** in the treatment of bipolar disorder in clinical practice: observational nationwide register-based cohort study. Br J Psychiatry. 2011 May 18.
Kessing LV et al. Starting **lithium prophylaxis early v. late** in bipolar disorder. Br J Psychiatry 2014 Jul 10.
Kessing LV, Gerds TA, Feldt-Rasmussen B, et al. Use of **Lithium** and **Anticonvulsants** and the Rate of **Chronic Kidney Disease**: A Nationwide Population-Based Study. JAMA Psychiatry. 2015 Nov 4:1-10.
Kolar D. Current status of **electroconvulsive therapy** for mood disorders: a clinical review. Evid Based Ment Health. 2017 Jan 4.
Kowatch RA, Fristad M, Birmaher B, et al.; Child Psychiatric Workgroup on Bipolar Disorder. Treatment **guidelines for children and adolescents** with bipolar disorder. J Am Acad Child Adolesc Psychiatry. 2005 Mar;44(3):213-35.
Kripalani M, Shawcross J, Reilly J, Main J. **Lithium** and chronic kidney disease. BMJ. 2009 Jul 3;339:b2452. doi: 10.1136/bmj.b2452.
Lähteenvuo M, et al. **Real-World Effectiveness of Pharmacologic Treatments for the Prevention of Rehospitalization** in a Finnish Nationwide Cohort of Patients With Bipolar Disorder. JAMA Psychiatry. 2018 Feb 28.
Leverich GS, et al. Risk of **switch** in mood polarity to hypomania or mania in patients with bipolar depression during acute and continuation trials of **venlafaxine, sertraline, and bupropion** as adjuncts to mood stabilizers. Am J Psychiatry. 2006 Feb;163(2):232-9.
Li C-T et al. Association between **antidepressant resistance in unipolar depression** and subsequent bipolar disorder: Cohort study. Br J Psychiatry 2012 Jan; 200:45.
Li Z, Zhang C, Fan J, et al. **Brain-derived neurotrophic factor levels** and bipolar disorder in patients in their first depressive episode: 3-year prospective longitudinal study. Br J Psychiatry. 2014 Apr 24.
Lichtenstein P, Yip BH, Bjork C, et al. **Common genetic determinants of schizophrenia and bipolar disorder in Swedish families: a population-based study.** Lancet. 2009 Jan 17;373(9659):234-239.
Similar to molecular genetic studies, we showed evidence that schizophrenia and bipolar disorder partly share a common genetic cause. These results challenge the current nosological dichotomy between schizophrenia and
bipolar disorder, and are consistent with a reappraisal of these disorders as distinct diagnostic entities.
Liu X, Agerbo E, Li J, et al. **Depression and Anxiety in the Postpartum Period** and Risk of Bipolar Disorder: A Danish Nationwide Register-Based Cohort Study. J Clin Psychiatry. 2017 May;78(5):e469-e476.
Locklear JC, Alemayehu B, Brody RS, et al. Treatment Patterns, HealthCare Resource Utilization and Costs in Patients with Bipolar Disorder, Newly Treated with Extended Release or Immediate Release **Quetiapine** Fumarate using US Healthcare Administrative Claims Data. ClinTher. 2013 Nov 22.
Loebel A, Cucchiaro J, Silva R, et al. **Lurasidone** monotherapy in the treatment of bipolar I depression: a randomized, double-blind, placebo-controlled study. Am J Psychiatry. 2014 Feb 1;171(2):160-8.
Lyall LM, Penades N, Smith DJ. Changes in **prescribing for bipolar disorder between 2009 and 2016**: national-level data linkage study in Scotland. Br J Psychiatry. 2019 Feb 28:1-7.
Madadi P, Ito S. **Perinatal exposure tomaternal lamotrigine**: Clinical considerations for the mother and child. Can Fam Physician. 2010 Nov;56(11):1132-4.
MaherAR et al. Efficacy and comparative effectiveness of **atypical antipsychotic medications for off-label uses in adults**. JAMA 2011 Sep 28; 306:1359.
Malhi GS, McAulay C, Das P, Fritz K. **Maintaining mood stability in bipolar disorder**: a clinical perspective on pharmacotherapy. Evid Based Ment Health. 2015 Feb;18(1):1-6.
Martin A, Young C, Leckman JF, et al. Age effects on antidepressant-induced manic conversion. Arch PediatrAdolesc Med. 2004 Aug;158(8):773-80.
Mayer G. **Lithiumtreatment of Kleine-Levin syndrome**: An advance for a disorder of hypersomnolence. Neurology. 2015 Nov 10;85(19):1642-3.
McIntyre RS, Cohen M, et al. **Asenapine** versus olanzapine in acute mania: a double-blind extension study. Bipolar Disord. 2009Oct 14.
McClellan J, Kowatch R, et al, Work Group on Quality Issues. Practice parameter for the assessment and treatment of **children and adolescents with bipolar disorder**. J Am Acad Child Adolesc Psychiatry 2007 Jan;46(1):107-25.
McCormack Mark, Alfirevic Ana, Bourgeois S, et al.**HLA-A*3101** and Carbamazepine-Induced Hypersensitivity Reactions in Europeans. N Engl J Med 2011; 364:1134-1143.
McGirr A, Vöhringer PA, Ghaemi SN, et al. Safety and efficacy of **adjunctive second-generation antidepressant therapy with a mood stabiliser or an atypical antipsychotic in acute bipolar depression**: a systematic review and meta-analysis of randomised placebo-controlled trials. Lancet Psychiatry 2016; online Oct 26.
McIntyre RS, Subramaniapillai M, Lee Y, et al. Efficacy of **Adjunctive Infliximab vs Placebo** in the Treatment of Adults With Bipolar I/II Depression: A Randomized Clinical Trial. JAMA Psychiatry. 2019 May 8.
McKnight RF, Adida M, Budge K, Stockton S, Goodwin GM, Geddes JR. **Lithium toxicity profile**: a systematic review and meta-analysis. Lancet 2012.
MDQ Mood Disorder **Questionaire**http://www.dbsalliance.org/pdfs/MDQ.pdf
Meador KJ, Baker GA, Browning N, et al. **Cognitive function** at 3 years of age after **fetal exposure** to antiepileptic drugs. N Engl J Med. 2009 Apr 16;360(16):1597-605.
Meador KJ, Baker GA, Browning N, et al, the **NEAD** Study Group. **Fetal antiepileptic drug exposure and cognitive outcomes at age 6 years** (NEAD study): a prospective observational study. Lancet Neurol 2013; online Jan 23.
Medical Letter "Treatment Guidelines- Drugs for Psychiatric Disorders Vol 4 (Issue 46) June 2006.**June 2013.**
Medical Letter. Treatment Guidelines. Drugs for Depression and Bipolar Disorder. May 2010.
Mehrpooya M, Yasrebifar F, Haghighi M, et al. Evaluating the Effect of **Coenzyme Q10 Augmentation** on Treatment of Bipolar Depression: A Double-Blind Controlled Clinical Trial. J Clin Psychopharmacol. 2018 Oct;38(5):460-466
Merideth CH. A single-center, double-blind, placebo-controlled evaluation of lamotrigine in the treatment of obesity in adults. J Clin Psychiatry. 2006 Feb;67(2):258-62.
Merikangas KR, He JP, Rapoport J, et al. **Medication Use in US Youth**With Mental Disorders. JAMA Pediatr. 2013 Feb 1;167(2):141-8.
Merikangas KR, Swendsen J, Hickie IB, et al. Real-time Mobile Monitoring of the Dynamic Associations Among **Motor Activity, Energy, Mood, and Sleep** in Adults With Bipolar Disorder. JAMA Psychiatry. 2018 Dec 12.
Methaneethorn J. Population **Pharmacokinetics** of **Valproic Acid in Patients with Mania**: Implication for Individualized Dosing Regimens. Clin Ther. 2017 May 5.
Micromedex 2016
Miller S, Trisha S, Jim M, et al. **Mixed depression** in bipolar disorder: prevalence rate and clinical correlates during naturalistic follow-up in the stanley bipolar network. Am J Psychiat 2016;173:1015–23.
Mindikoglu AL, King D, Magder LS, et al. **Valproic Acid-associated acute liver failure in children**: case report and analysis of liver transplantation outcomes in the United States. J Pediatr. 2011 May;158(5):802-7.
Miura T, Noma H, Furukawa TA, et al. **Comparative efficacy and tolerability of pharmacological treatments** in the maintenance treatment of bipolar disorder: a systematic review and network meta-analysis. Lancet Psychiatry 2014;1:351–9.
Mølgaard-Nielsen D, Hviid A. **Newer-generation antiepileptic drugs and the risk of major birth defects**. JAMA. 2011 May 18;305(19):1996-2002.
Morriss R, Lobban F, Riste L, et al. Clinical effectiveness and acceptability of structured group **psychoeducation versus optimised unstructured peer support** for patients with remitted bipolar disorder (**PARADES**): a pragmatic, multicentre, observer-blind, randomised controlled superiority trial. Lancet Psychiatry 2016;3:1029–38.
Munk-Olsen T, Liu X, Viktorin A, et al. Maternal and infant outcomes associated with **lithium use in pregnancy**: an international collaborative meta-analysis of six cohort studies. Lancet Psychiatry. 2018 Jun 18.
Muzina DJ, Gao K, Kemp DE, et al. Acute efficacy of **divalproex** sodium versus placebo in mood stabilizer-naive bipolar i or ii depression: a double-blind, randomized, placebo-controlled trial. J Clin Psychiatry. 2010 Aug 24.
Navarro VJ, Senior JR. Drug-related **hepatotoxicity**. N Engl J Med. 2006 Feb 16;354(7):731-9. (Bohan TP, et al. Effect of L-carnitine treatment for valproate-induced hepatotoxicity. Neurology. 2001 May 22;56(10):1405-9.)
Nichols TA, Drayton SJ, Borckardt J, et al. **Lithium dosing equations**: are they accurate? Ann Pharmacother. 2014 May;48(5):596-600.
Nierenberg AA, et al. Treatment-resistant bipolar depression: a STEP-BD equipoise randomized effectiveness trial of antidepressant augmentation with **lamotrigine**, inositol, or risperidone. Am J Psychiatry. 2006 Feb;163(2):210-6.
Nierenberg AA, Friedman ES, Bowden CL, et al. Lithium treatment moderate-dose use study (**LiTMUS**) for bipolar disorder: a randomized comparative effectiveness trial of optimized personalized treatment with and without lithium. Am J Psychiatry. 2013 Jan 1;170(1):102-10.
Newport DJ, et al. **Lithium** Placental Passage and Obstetrical Outcome: Implications for Clinical Management During Late **Pregnancy**. Am J Psychiatry. 2005 Nov;162(11):2162-2170.
(CONCLUSIONS: Lithium completely equilibrates across the placenta; Withholding lithium therapy for 24-48 hours before delivery resulted in a 0.28 meq/liter reduction in maternal lithium concentration.)

Newport DJ, Stowe ZN, Viguera AC, et al. **Lamotrigine** in bipolar disorder: efficacy during **pregnancy**.Bipolar Disord. 2008 May;10(3):432-6.
NICE: National Collaborating Centre for Mental Health. **Bipolar disorder**: the management of bipolar disorder in adults, children and adolescents, in primary and secondary care London: National Institute for Health and Clinical Excellence; **2006** Jul [cited 2011 Feb 18]. (NICE clinical guideline 38).http://www.nice.org.uk/nicemedia/pdf/CG38niceguideline.pdf
NICE: National Institute for Health and Care Excellence (NICE). **Aripiprazole** for treating moderate to severe manic episodes in adolescents with bipolar I disorder. London (UK): (NICE); 2013 Jul.
NICE: National Institute for Health and Clinical Excellence. Bipolar disorder (update): the **management of bipolar disorder in adults, children and adolescents** in primary and secondary care. (Clinical Guideline 185.) **2014**. http://guidance.nice.org.uk/CG185.
Nicolaidou P, et al. Effects of **anticonvulsant** therapy on **vitamin D** status in children: prospective monitoring study. J Child Neurol. 2006 Mar;21(3):205-9.
Oquendo, Maria A., Galfalvy, Hanga C., Currier, Dianne, et al. Treatment of Suicide Attempters With Bipolar Disorder: A Randomized Clinical Trial Comparing **Lithium and Valproate** in the Prevention of Suicidal Behavior. Am J Psychiatry 2011 0: appi.ajp.2011.11010163.
Pacchiarotti I, Bond DJ, Baldessarini RJ, et al. The **International Society for Bipolar Disorders** (**ISBD**) Task Force Report on **Antidepressant Use in Bipolar Disorders**. Am J Psychiatry. 2013 Nov 1;170(11):1249-62.
Parboosing R, Bao Y, Shen L, et al. **Gestational Influenza** and Bipolar Disorder in Adult Offspring. JAMA Psychiatry. 2013 May 8:1-8.
Parker WF, Gorges RJ, Gao YN, et al. Association Between **Groundwater Lithium and the Diagnosis of Bipolar Disorder and Dementia** in the United States. JAMA Psychiatry. 2018 May 23.
Patel R, Reiss P, Shetty H, et al. **Do antidepressants increase the risk of mania and bipolar disorder in people with depression**? A retrospective electronic case register cohort study. BMJ Open. 2015 Dec 14;5(12):e008341.
Patorno E, Huybrechts KF, Bateman BT, et al. **Lithium Use in Pregnancy** and the Risk of Cardiac Malformations. N Engl J Med. 2017 Jun 8;376(23):2245-2254.
Patsalos PN, Perucca E. Clinically important drug interactions in epilepsy: general features and interactions between antiepileptic drugs. Lancet Neurol. 2003 Jun;2(6):347-56.
Patsalos PN, Perucca E. Clinically important drug interactions in epilepsy: interactions between antiepileptic drugs and other drugs. Lancet Neurol. 2003 Aug;2(8):473-81.
Pavlova B, Perlis RH, et al. **Lifetime prevalence of anxiety disorders** in people with bipolar disorder: a systematic review and meta-analysis. Lancet Psychiatry. 2015 Aug;2(8):710-7.
Pawar AS, Kattah AG. **Lithium-Induced Nephropathy**. N Engl J Med. 2018 Mar 15;378(11):1042.
Perlis RH, Sachs GS, Lafer B, et al. Effect of **abrupt change from standard to low serum levels of lithium**: a reanalysis of double-blind lithium maintenance data. Am J Psychiatry. 2002 Jul;159(7):1155-9.
Perucca E. **Birth defects** after prenatal exposure to antiepileptic drugs. Lancet Neurol. 2005 Nov;4(11):781-6.
Pharmacotherapy Handbook 2nd Edition (Wells,Dipiro et al.)
Phillips ML, Kupfer DJ. Bipolar disorder diagnosis: **challenges and future directions**. Lancet. 2013 May 11;381(9878):1663-71.
Post RM. Preventing the Malignant Transformation of Bipolar Disorder. JAMA. 2018 Mar 27;319(12):1197-1198.
Practice guideline for the treatment of patients with bipolar disorder (revision). Am J Psychiatry. **2002** Apr;159(4 Suppl):1-50.
Preti A, Vrublevska J, Veroniki AA, et al. **Prevalence and treatment of panic disorder in bipolar disorder**: systematic review and meta-analysis. Evid Based Ment Health. 2018 May;21(2):53-60.
Price A, Marzani-Nissen G. **Bipolar Disorders**: A Review. Am Fam Physician. 2012 Mar 1;85(5):483-493.
Rendell JM, Gijsman HJ, Keck P, Goodwin GM, Geddes JR. Olanzapine alone or in combination for acute mania. Cochrane Database Syst Rev. 2003;(3):CD004040.
Sachs G, et al. Quetiapine with lithium or divalproex for the treatment of bipolar mania: a randomized, double-blind, placebo-controlled study. Bipolar Disord. 2004 Jun;6(3):213-23.
Sachs GS, Nierenberg AA, Calabrese JR, et al. (**STEP-BD** trial) Effectiveness of **Adjunctive Antidepressant** Treatment for Bipolar Depression. N Engl J Med. 2007 Mar 28;
The use of adjunctive, standard antidepressant medication, as compared with the use of mood stabilizers, was not associated with increased efficacy or with increased risk of treatment-emergent affective switch. Longer-term studies are needed to fully assess the benefits & risks of antidepressant therapy for bipolar disorder.
Sala R, Goldstein BI, Wang S, et al. Increased Prospective Health Service Use for **Depression among Adults with Childhood Onset Bipolar Disorder**. J Pediatr. 2013 Jul 26.
Sampaio-Junior B, Tortella G, Borrione L, et al. Efficacy and Safety of **Transcranial Direct Current Stimulation as an Add-on Treatment for Bipolar Depression**: A Randomized Clinical Trial. JAMA Psychiatry. 2017 Dec 27.
Sanford M, Keating GM. **Quetiapine**: a review of its use in the management of bipolar depression. CNS Drugs. 2012 May 1;26(5):435-60.
Savitz JB, Teague TK, et al. Treatment of bipolar depression with **minocycline and/or aspirin**: an adaptive, 2×2 double-blind, randomized, placebo-controlled, phase IIA clinical trial. Transl Psychiatry. 2018 Jan 24;8(1):27.
Scarfi F, Arunachalam M. **Lithium acne**. CMAJ. 2013 Nov 9;185(17):1525.
Schoeyen HK, Kessler U, et al. **Treatment-Resistant Bipolar Depression**: A Randomized Controlled Trial of **Electroconvulsive Therapy Versus Algorithm-Based Pharmacological Treatment**. Am J Psychiatry. 2014 Sep 15.
Schroeder SA. A 51-year-old woman with bipolar disorder who wants to **quit smoking**.JAMA. 2009 Feb 4;301(5):522-31. Epub 2009 Jan 6.
Scherk H, Pajonk FG, Leucht S. Second-generation **antipsychotic** agents in the treatment of **acute mania**. A systematic review and meta-analysis of randomized controlled trials. Arch Gen Psychiatry 2007;64:442-455.
(InfoPOEMs: Antipsychotic agents plus mood stabilizers are superior to either group of medications alone in the treatment of acute mania. This review found no evidence of a superiority of second-generation antipsychotics over first-generation antipsychotics. (LOE = 1a))
Scott J, Murray G, Henry C, et al. **Activation in Bipolar Disorders**: A Systematic Review. JAMA Psychiatry. 2017 Feb 1;74(2):189-196.
Selten JP, Lundberg M, Rai D, Magnusson C. Risks for **Nonaffective Psychotic Disorder and Bipolar Disorder in Young People With Autism** Spectrum Disorder: A Population-Based Study. JAMA Psychiatry. 2015 Mar 25.
Shain BN; Committee on Adolescence. Collaborative **role** of the **pediatrician** in the diagnosis and management of bipolar disorder in adolescents. Pediatrics. 2012 Dec;130(6):e1725-42.
Shine B, McKnight RF, et al.**Long-term effects of lithium on renal, thyroid, and parathyroid function**: a retrospective analysis of laboratory data. Lancet 2015; online May 21.
Shorvon Simon, Tomson Torbjorn. **Sudden unexpected death**(SUDEP) in epilepsy. www.thelancet.com Online July 6, 2011. (↑: GTC, Males, long-duration hx& on polytherapy)
Sidor MM., MacQueen GM., **Antidepressants for the Acute** Treatment of Bipolar Depression: A Systematic Review & Meta-Analysis. J Clin Psychiatrydoi:10.4088/JCP.09r05385gre .
Sit DK, McGowan J, Wiltrout C, et al. **Adjunctive Bright Light Therapy** for Bipolar Depression: A Randomized Double-Blind Placebo-Controlled Trial. Am J Psychiatry. 2017 Oct 3:appiajp201716101200.
Smith EG, et al. **Mortality associated with lithium & valproate** treatment of US Veterans Health Administration patients with mental disorders. Br J Psychiatry. 2015 Jul;207(1):55-63.
Soczynska JK, et al. A pilot, open-label, 8-week study evaluating the efficacy, safety and tolerability of **adjunctive minocycline for the treatment of bipolar I/II depression**. Bipolar Disord. 2017 May;19(3):198-213.
Spencer JP, Gonzalez LS 3rd, Barnhart DJ. Medications in the breast-feeding mother. Am Fam Physician. 2001 Jul 1;64(1):119-26.
Spina E, et al. Effect of Adjunctive **Lamotrigine** Treatment on the Plasma Concentrations of **Clozapine**, **Risperidone** and **Olanzapine** in Patients With Schizophrenia or Bipolar Disorder. Ther Drug Monit. 2006 Oct;28(5):599-602.
These findings indicate that lamotrigine, at the dosages recommended for use as a mood stabilizer, does not affect the plasma levels of clozapine, risperidone, and their active metabolites. The modest elevation in plasma olanzapine concentration, possibly due to inhibition of UGT1A4-mediated olanzapine glucuronidation, is unlikely to be of clinical significance.
Sproule BA, Hardy BG, Shulman KI. Differential **pharmacokinetics of lithium in elderly patients**. Drugs Aging. 2000 Mar;16(3):165-77.
Srivastava S, Ketter TA. Clinical relevance of treatments for **acute bipolar disorder**: balancing therapeutic and adverse effects. ClinTher. 2011 Dec;33(12):B40-8.
Starzer MSK, Nordentoft M, Hjorthøj C. Rates and Predictors of **Conversion to Schizophrenia or Bipolar Disorder Following Substance-Induced Psychosis**. Am J Psychiatry. 2017 Nov 28:appiajp201717020223.
Steinan MK, Scott J, Lagerberg TV, et al. **Sleep problems in bipolar disorders**: more than just insomnia. Acta Psychiatr Scand 2016;133:368–77.
Stern RS. Clinical practice. **Exanthematous drug eruptions**. N Engl J Med. 2012 Jun 28;366(26):2492-501. (penicillin, cephalosporins, sulfonamides, antiseizure meds etc)
Stoffers J, Vollm BA, Rucker G, et al. Pharmacological interventions for **borderline personality disorder**. Cochrane Database Syst Rev. 2010 Jun 16;6:CD005653.
Suppes T, et al.Clinical outcome in a randomized 1-year trial of **clozapine** versus treatment asusual for patients with treatment-resistant illness and a history of mania.Am J Psychiatry. 1999 Aug;156(8):1164-9.
Swann AC, Lafer B, Perugi G, et al. **Bipolar mixed states**: anInternational Society for Bipolar Disorders (ISBD) task force report of symptom structure, course of illness, and diagnosis. Am J Psychiatry. 2013 Jan 1;170(1):31-42.

Swartz HA, Thase ME. Pharmacotherapy for the treatment of **acute bipolar ii depression**: current evidence. J Clin Psychiatry. 2010 Aug 10.
Szegedi A;Durgam S;Mackle M;et al. Randomized, Double-Blind, Placebo-Controlled Trial of **Asenapine Maintenance Therapy in Adults With an Acute Manic or Mixed Episode Associated With Bipolar I Disorder**. Am J Psychiatry. 2017 Sep 26:appiajp201716040419.
Talati A, Bao Y, Kaufman J, Shen L, Schaefer CA, Brown AS: **Maternal smoking during pregnancy and bipolar disorder** in offspring. Am J Psychiatry 2013; 170:1178–1185
Thase ME, Macfadden W, Weisler RH, Chang W, Paulsson B, Khan A, Calabrese JR; for the **BOLDER II** Study Group. Efficacy of **Quetiapine** Monotherapy in Bipolar I and II **Depression**: A Double-blind, Placebo-controlled Study (The BOLDER II Study). J ClinPsychopharmacol. 2006 Dec;26(6):600-609. The incidence of treatment-emergent mania or hypomania was lower with quetiapine treatment than placebo. This study demonstrates that quetiapine monotherapy is an effective and well-tolerated treatment for depressive episodes in bipolar disorder, confirming the results observed from a previous study (BipOLarDEpRession [BOLDER] I).
Therapeutic Choices 5th edition 2007.
Tiihonen J, Tanskanen A, Hoti F, et al. **Pharmacological treatments and risk of readmission to hospital for unipolar depression** in Finland: a nationwide cohort study. Lancet Psychiatry 2017; online June 1.
Tohen M, Goldberg JF, et al. A 12-week, double-blind comparison of **olanzapine vs haloperidol** in the treatment of acute mania. Arch Gen Psychiatry. 2003 Dec;60(12):1218-26.
Tohen M, et al. Relapse prevention in bipolar I disorder: 18-month comparison of **olanzapine**plus mood stabiliser v. mood stabiliser alone.Br J Psychiatry. 2004 Apr;184:337-45.
Tohen M, Greil W et al. **Olanzapine vs lithium** in the maintenance treatment of bipolar disorder: a 12-month double-blind RCT trial. Am J Psychiatry. 2005 Jul;162(7):1281-90.
Tohen M, et al. Randomized, placebo-controlled trial of **olanzapine** as maintenance therapy inpatients with bipolar I disorder responding to acute treatment with olanzapine. Am J Psychiatry. 2006 Feb;163(2):247-56.
Tohen M, McDonnell DP, Case M, et al. Randomised, double-blind, placebo-controlled study of **olanzapine in patients with bipolar I depression**. Br J Psychiatry. 2012 Aug 23.
Tomson T, et al. **Valproate** effects on **kinetics of lamotrigine** in pregnancy and treatment with oral contraceptives. Neurology. 2006 Oct 10;67(7):1297-9.
Valproate seems to reduce the induction of lamotrigine metabolism associated with pregnancy or use of contraceptives.
Tomson T, Battino D. **Teratogenic effects** of antiepileptic drugs. Seizure. 2008 Mar;17(2):166-71.
Torpy JM, Lynm C, Glass RM. JAMA **patient page. Bipolar disorder**. JAMA. 2009Feb 4;301(5):564.
Treatment Guidelines: Drugs for Psychiatric Disorders. **The Medical Letter**: July, **2003**; p. 69-76. (**Medical Letter "Treatment Guidelines- Drugs for Psychiatric Disorders** Vol 4 (Issue 46) **June 2006**.)
Medical Letter. Treatment Guidelines. Drugs for Depression and Bipolar Disorder. May 2010.
Truman CJ, Goldberg JF, Ghaemi SN, et al. Self-reported **history of manic/hypomanic switch associated with antidepressant use**: data from the Systematic Treatment Enhancement Program for Bipolar Disorder (STEP-BD). J Clin Psychiatry. 2007 Oct;68(10):1472-9.
Tsai AC, Rosenlicht NZ, Jureidini JN, et al. **Aripiprazole** in the maintenance treatment of bipolar disorder: a **critical** review of the evidence and its dissemination into the scientific literature. PLoS Med 2011;8:e1000434.
UKMND-LiCALS Study Group. **Lithium** in patients with **amyotrophic lateral sclerosis** (LiCALS): a phase 3 multicentre, randomised, double-blind, placebo-controlled trial. Lancet Neurol 2013; online Feb 27.
Vajda FJ, O'Brien TJ, Graham JE, et al. **Dose dependence of fetal malformations** associated with **valproate**. Neurology. 2013 Sep 10;81(11):999-1003.
van der Lee MJ, et al. **Lopinavir/ritonavir** reduces **lamotrigine** plasma concentrations in healthy subjects. Clin Pharmacol Ther. 2006 Aug;80(2):159-68.
van der Loos ML, Mulder PG, Hartong EG, et al.Efficacy and safety of **lamotrigine** as add-on treatment to lithium in bipolar depression: a multicenter, double-blind, placebo-controlled trial. J Clin Psychiatry. 2008 Dec 30.
Van Lieshout RJ, MacQueen GM. Efficacy and acceptability of **mood stabilisers** in the treatment of **acute bipolardepression**: systematic review. Br J Psychiatry. 2010Apr;196:266-73.
Mood stabilizers have an effect in some people with acute bipolar depression, decreasing depression symptoms by at least 50% in at least 1 additional patient of every 10 patients (**NNT=10**)who are given treatment instead of placebo. The mood stabilizers in the studies were the anticonvulsants carbamazepine (Tegretol), valproic acid (Depakote), and lamotrigine (Lamictal), and the atypical antipsychotics olanzapine (Zyprexa) and quetiapine (Serroquel). (LOE = 1a)
Varghese SP, et al. **Lamotrigine**-induced toxic **epidermal necrolysis** in three patients treated for bipolar disorder. Pharmacotherapy. 2006 May;26(5):699-704.
Veiby G, Engelsen BA, et al. Early Child Development and Exposure to **Antiepileptic Drugs Prenatally and Through Breastfeeding**: A Prospective Cohort Study on Children of Women With Epilepsy. JAMA Neurol. 2013 Sep 23.
Viguera AC, Newport DJ, Ritchie J, et al. **Lithium in breast milk** and nursing infants: clinical implications. Am J Psychiatry. 2007 Feb;164(2):342-5. Serum lithium levels in nursing infants were low and well tolerated.
No significant adverse clinical or behavioral effects in the infants were noted. These findings encourage reassessment of recommendations against lithium during breast-feeding and underscore the importance of close clinical monitoring of nursing infants.
Viktorin A, Ryden E, Thase ME, et al. The Risk of Treatment-Emergent **Mania With Methylphenidate** in Bipolar Disorder. Am J Psychiatry. 2016 Oct 3:appiajp201616040467.
Vishnu VY, Kesav P, Goyal MK, et al. Teaching NeuroImages: **Reversible paradoxical lithium neurotoxicity**. Neurology. 2013 Oct 1;81(14):e110.
Viktorin A, Lichtenstein P, et al. The risk of **switch to mania in patients with bipolar disorder during treatment with an antidepressant alone and in combination with a mood stabilizer**. Am J Psychiatry 2014; 171:1067–1073
Walshaw PD, Gyulai L,et al. Adjunctive thyroid hormone treatment in **rapid cycling bipolar disorder**: A double-blind placebo-controlled trial of **levothyroxine (L-T(4)) and triiodothyronine (T(3)).** Bipolar Disord. 2018 Jun
Ward RK, Zamorski MA. Benefits and risks of psychiatric medications during **pregnancy**. Am Fam Physician. 2002 Aug 15;66(4):629-36.
Weisler RH, NolenWA, Neijber A, Hellqvist A, Paulsson B; for the Trial 144 Study Investigators. Continuation of **quetiapine versus switching to placebo or lithium** for maintenance treatment of bipolar I disorder (trial 144: a randomized controlled study). J Clin Psychiatry. 2011 Oct 18.
Wilding J, Van Gaal L, Rissanen A, Vercruysse F, Fitchet M; OBES-002 Study Group. A randomized double-blind placebo-controlled study of the long-term efficacy and safety of **topiramate** in the treatment of **obese** subjects. Int J Obes Relat Metab Disord. 2004 Nov;28(11):1399-410.
Wyszynski DF, et al.; Antiepileptic Drug Pregnancy Registry. Increased rate of major **malformations** in offspring exposed to **valproate** during pregnancy. Neurology. 2005 Mar 22;64(6):961-5.
Yatham LN, Calabrese JR, Kusumakar V. **Bipolar depression**: criteria for treatment selection, definition of refractoriness, and treatment options. Bipolar Disord. 2003 Apr;5(2):85-97.
Yatham LN et al. Canadian Network for Mood & Anxiety Treatments (**CANMAT**) **guidelines** for the management of patients with bipolar disorder: update 2006. Bipolar Disorders **2006**:8: 1-19
Yatham LN, Kennedy SH, Parikh SV, et al. Canadian Network for Mood and Anxiety Treatments (**CANMAT**) and International Society for Bipolar Disorders (ISBD) collaborative update of CANMAT guidelines for the management of patients with bipolar disorder: **update 2013**. Bipolar Disord. 2012 Dec 12.
Yatham LN, et al. Optimal duration of **risperidone or olanzapine** adjunctive therapy to mood stabilizer following **remission of a manic episode**: **CANMAT** randomized double-blind trial. Mol Psychiatry. 2016 Aug;21(8):1050-6.
Yatham LN, Mackala S, et al. **Lurasidone** versus treatment as usual for cognitive impairment in **euthymic patients with bipolar I disorder**: a randomised, open-label, pilot study. Lancet Psychiatry 2017; published online Feb 6
Yatham LN, Kennedy SH, Parikh SV, et al. Canadian Network for Mood and Anxiety Treatments **(CANMAT) and International Society for Bipolar Disorders (ISBD) 2018 guidelines** for the management of patients with bipolar disorder. Bipolar Disord **2018**;20:97-170.
Young LT, Joffe RT, Robb JC, et al. Double-blind comparison of **addition of a second mood stabilizer versus an antidepressant** to an initial mood stabilizer for treatment of patients with bipolar depression. Am J Psychiatry. 2000 Jan;157(1):124-6.
Zarate CA Jr et al. Replication of **ketamine's** antidepressant efficacy in bipolar depression: A randomized controlled add-on trial. Biol Psychiatry 2012 Jun 1; 71:939.

RxFiles Related Documents:

Bipolar Disorder & Mood Stabilizer/Adjuvant Agent Comparison Chart http://www.rxfiles.ca/rxfiles/uploads/documents/members/Cht-psyc-moodstabalizers.pdf
Antipsychotic Comparison Chart http://www.rxfiles.ca/rxfiles/uploads/documents/members/Cht-Psyc-Neuroleptics.pdf
Antidepressant Comparison Chart http://www.rxfiles.ca/rxfiles/uploads/documents/members/cht-Psyc-Antidepressant.pdf
Peri-Pregnancy Chart http://www.rxfiles.ca/rxfiles/uploads/documents/members/CHT-Peri-Pregnancy-DrugTx.pdf
Q&A Are Antidepressants Safe during Pregnancy & Breastfeeding http://www.rxfiles.ca/rxfiles/uploads/documents/Antidepressants-PregnancyandBreastfeeding-QandA.pdf
Q&A Management of Bipolar Disorder during Pregnancy & Postpartum http://www.rxfiles.ca/rxfiles/uploads/documents/Bipolar-Pregnancy-QandA-Part-1-Text.pdf

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References for RxFiles Management of Bipolar Disorders during Pregnancy & Postpartum

1. J Yatham LN, Kennedy SH, Parikh SV et al. Canadian Network for Mood and Anxiety Treatments (CANMAT) and International Society for Bipolar Disorders (ISBD) collaborative update of **CANMAT guidelines** for the management of patients with bipolar disorder: update 2013. Bipolar Disord. 2013 Feb;15(1):1-44.
2. Yatham LN, Kennedy SH, Schaffer A et al. Canadian Network for Mood and Anxiety Treatments (CANMAT) and International Society for Bipolar Disorders (ISBD) collaborative update of **CANMAT guidelines** for the management of patients with bipolar disorder: update 2009. Bipolar Disord. 2009 May;11(3):225-55.
3. Yonkers KA, Vigod S, Ross LE. Diagnosis, pathophysiology, and management of mood disorders in pregnant and postpartum women. Obstet Gynecol. 2011 Apr;117(4):961-77.
4. **ACOG** Committee on Practice Bulletins--Obstetrics. ACOG Practice Bulletin: Clinical management guidelines for obstetrician-gynecologists number 92, April 2008 (replaces practice bulletin number 87, November 2007). Use of psychiatric medications during pregnancy and lactation. Obstet Gynecol. 2008 Apr;111(4):1001-20.
5. National Collaborating Centre for Mental Health (UK). Antenatal and Postnatal Mental Health: The **NICE Guideline** on Clinical Management and Service Guidance. Leicester (UK): British Psychological Society; 2007. http://www.nice.org.uk/nicemedia/live/11004/30433/30433.pdf. Accessed January 2013.
6. Viguera AC, Tondo L, Koukopoulos AE et al. Episodes of mood disorders in 2,252 pregnancies and postpartum periods. Am J Psychiatry. 2011 Nov;168(11):1179-85. doi: 10.1176/appi.ajp.2011.11010148. Epub 2011 Jul 28.
7. Sharma V, Penava D. Screening for bipolar disorder during pregnancy and the postpartum period. J Obstet Gynaecol Can. 2010 Mar;32(3):278-81.
8. Sharma V, Burt VK, Ritchie HL. Bipolar II postpartum depression: Detection, diagnosis, and treatment. Am J Psychiatry. 2009 Nov;166(11):1217-21.
9. Wood W. Lithium in pregnancy & lactation – safer than we thought? Mental Health Clinician 2012. College of Psychiatric & Neurologic Pharmacists. http://cpnp.org/resource/mhc/2012/06/lithium-pregnancy-lactation-safer-we-thought. Accessed January 2013.
10. Galbally M, Snellen M, Walker S, Permezel M. Management of antipsychotic and mood stabilizer medication in pregnancy: recommendations for antenatal care. Aust N Z J Psychiatry. 2010 Feb;44(2):99-108.
11. Yonkers KA, Wisner KL, Stowe Z, Leibenluft E, Cohen L, Miller L, Manber R, Viguera A, Suppes T, Altshuler L. Management of bipolar disorder during pregnancy and the postpartum period. Am J Psychiatry. 2004 Apr;161(4):608-20.
12. Anderson IM, Haddad PM, Scott J. Bipolar disorder. BMJ. 2012 Dec 27;345:e8508.
13. Briggs G et al. Drugs in Pregnancy and Lactation, 10th edition. 2015.
14. Adab N, Tudur SC, Vinten J et al. Common antiepileptic drugs in pregnancy in women with epilepsy. Cochrane Database Syst Rev. 2004;(3):CD004848.
15. Galbally M, Roberts M, Buist A; Perinatal Psychotropic Review Group. Mood stabilizers in pregnancy: a systematic review. Aust N Z J Psychiatry. 2010 Nov;44(11):967-77.
16. Tomson T, Battino D. Teratogenic effects of antiepileptic drugs. Lancet Neurol. 2012 Sep;11(9):803-13. doi: 10.1016/S1474-4422(12)70103-5. Epub 2012 Jul 16. Review.
17. Mølgaard-Nielsen D, Hviid A. Newer-generation antiepileptic drugs and the risk of major birth defects. JAMA. 2011 May 18;305(19):1996-2002.
18. Cummings C, Stewart M, Stevenson M, et al. Neurodevelopment of children exposed in utero to lamotrigine, sodium valproate and carbamazepine. Arch Dis Child (2011). doi:10.1136/2 of 5 adc.2009.176990.
19. Holmes LB, Mittendorf R, Shen A et al. Fetal effects of anticonvulsant polytherapies: different risks from different drug combinations. Arch Neurol. 2011 Oct;68(10):1275-81.
20. Moore JL, Aggarwal P. Lamotrigine use in pregnancy. Expert Opin Pharmacother. 2012 Jun;13(8):1213-6.

21. Tomson T, Battino D, Bonizzoni E et al; EURAP study group. Dose-dependent risk of malformations with antiepileptic drugs: an analysis of data from the EURAP epilepsy and pregnancy registry. Lancet Neurol. 2011 Jul;10(7):609-17.
22. Meador K, Baker G, Browning N et al. Fetal antiepileptic drug exposure & cognitive outcomes at age 6 years (NEAD study). Lancet. 2013. Epub http://dx.doi.org/10.1016/S1474-4422(12)70323-X.
23. Jentink J, Loane MA, Dolk H et al; EUROCAT Antiepileptic Study Working Group. Valproic acid monotherapy in pregnancy and major congenital malformations. N Engl J Med. 2010 Jun 10;362(23):2185-93.
24. Jentink J, Dolk H, Loane MA et al; EUROCAT Antiepileptic Study Working Group. Intrauterine exposure to carbamazepine and specific congenital malformations: systematic review and case-control study. BMJ. 2010 Dec 2;341:c6581.
25. Vajda FJ, Dodd S, Horgan D. Lamotrigine in epilepsy, pregnancy and psychiatry - a drug for all seasons? J Clin Neuro. 2013 Jan;20(1):13-6. Wakil L, Epperson CN, Gonzalez J et al. Neonatal outcomes with the use of lamotrigine for bipolar disorder in pregnancy and breastfeeding: a case series and review of the literature. Psychopharmacol Bull. 2009;42(3):91-8.
26. Sabers A. Algorithm for lamotrigine dose adjustment before, during, and after pregnancy. Acta Neurol Scand. 2012 Jul;126(1):e1-4.
27. Matok I, Pupco A, Koren G. Drug exposure in pregnancy and heart defects. J Cardiovasc Pharmacol. 2011 Jul;58(1):20-4.
28. Viguera AC, Newport DJ, Ritchie J et al. Lithium in breast milk and nursing infants: clinical implications. Am J Psychiatry. 2007 Feb;164(2):342-5.
29. Horton S, Tuerk A, Cook D et al. Maximum recommended dosage of lithium for pregnant women based on a PBPK model for lithium absorption. Adv Bioinformatics. 2012;2012:352729. doi: 10.1155/2012/352729. Epub 2012 May 30.
30. Harden CL, Pennell PB, Koppel BS et al; American Academy of Neurology; American Epilepsy Society. Practice parameter update:management issues for women with epilepsy--focus on pregnancy (an evidence-based review): vitamin K, folic acid, blood levels, and breastfeeding: report of the Quality Standards Subcommittee and Therapeutics and Technology Assessment Subcommittee of the American Academy of Neurology and American Epilepsy Society. Neurology. 2009 Jul 14;73(2):142-9.
31. Bergink V, Bouvy PF, Vervoort JS et al. Prevention of postpartum psychosis and mania in women at high risk. Am J Psychiatry. 2012 Jun;169(6):609-15.
32. Sharma V, Burt VK, Ritchie HL. Assessment and treatment of bipolar II postpartum depression: a review. J Affect Disord. 2010 Sep;125(1-3):18-26.
33. Sharma V, Xie B. Screening for postpartum bipolar disorder: validation of the mood disorder questionnaire. J Affect Disord. 2011 Jun;131(1-3):408-11.
34. Sharma V, Khan M, Corpse C, Sharma P. Missed bipolarity and psychiatric comorbidity in women with postpartum depression. Bipolar Disord. 2008 Sep;10(6):742-7.
35. Stanton C, Lawn JE, Rahman H, Wilczynska-Ketende K, Hill K. Stillbirth rates: delivering estimates in 190 countries. Lancet. 2006 May 6;367(9521):1487-94.
36. Tong S, Kaur A, Walker SP, Bryant V, Onwude JL, Permezel M. Miscarriage risk for asymptomatic women after a normal first-trimester prenatal visit. Obstet Gynecol. 2008 Mar;111(3):710-4.
37. Tomson T, Battino D, Bonizzoni E et al. Antiepileptic drugs and intrauterine death: A prospective observational study from EURAP. Neurology. 2015 Aug 18;85(7):580-8.
38. Bech BH, Kjaersgaard MI, Pedersen HS et al. Use of antiepileptic drugs during pregnancy and risk of spontaneous abortion and stillbirth: population based cohort study. BMJ. 2014 Aug 21;349:g5159.
39. Holmes LB, Baldwin EJ, Smith CR et al. Increased frequency of isolated cleft palate in infants exposed to lamotrigine during pregnancy. Neurology. 2008 May 27;70(22 Pt 2):2152-8.
40. Dolk H, Wang H, Loane M et al. Lamotrigine use in pregnancy and risk of orofacial cleft and other congenital anomalies. Neurology. 2016 May 3;86(18):1716-25.
41. National Collaborating Centre for Mental Health (UK). Antenatal and Postnatal Mental Health: The **NICE Guideline** on Clinical Management and Service Guidance. Leicester (UK): British Psychological Society; 2014. https://www.nice.org.uk/guidance/cg192/resources/antenatal-and-postnatal-mental-health-clinical-management-and-service-guidance-35109869806789. Accessed June 2016.
42. Chisolm MS, Payne JL. Management of psychotropic drugs during pregnancy. BMJ. 2016 Jan 20;532:h5918.
43. Vigod SN, Gomes T, Wilton AS, Taylor VH, Ray JG. Antipsychotic drug use in pregnancy: high dimensional, propensity matched, population based cohort study. BMJ. 2015 May 13;350:h2298.
44. Cohen LS, Viguera AC, McInerney KA et al. Reproductive Safety of Second-Generation Antipsychotics: Current Data From the Massachusetts General Hospital National Pregnancy Registry for Atypical Antipsychotics. Am J Psychiatry. 2016 Mar 1;173(3):263-70.
45. Peng M, Gao K, Ding Y et al. Effects of prenatal exposure to atypical antipsychotics on postnatal development and growth of infants: a case-controlled, prospective study. Psychopharmacology (Berl). 2013 Aug;228(4):577-84.
46. Viale L, Allotey J, Cheong-See F et al. Epilepsy in pregnancy and reproductive outcomes: a systematic review and meta-analysis. Lancet. 2015 Nov 7;386(10006):1845-52.

Additional References:

Christensen J, Grønborg TK, Sørensen MJ, et al. Prenatal valproate exposure and risk of autism spectrum disorders and childhood autism. JAMA. 2013; 309(16):1696-1703.

Clark CT, Klein AM, Perel JM et al. **Lamotrigine dosing for pregnant patients** with bipolar disorder. Am J Psychiatry. 2013 Nov 1;170(11):1240-7.

Duffy A, Goodday S, Keown-Stoneman C, et al. The **Emergent Course of Bipolar Disorder**: Observations Over Two Decades From the Canadian **High-Risk Offspring** Cohort. Am J Psychiatry. 2018 Dec 11:appiajp201818040461.

Hernández-Díaz S, Mittendorf R, Smith CR, et al. North American Antiepileptic Drug Pregnancy Registry. Association between **topiramate and zonisamide** use during pregnancy and low birth weight. Obstet Gynecol. 2014 Jan;123(1):21-8.

Jones I, Chandra PS, Dazzan P, et al. **Bipolar disorder, affective psychosis, and schizophrenia** in pregnancy and the post-partum period. Lancet. 2014 Nov 15;384(9956):1789-99.

Liu X, Agerbo E, Li J, et al. **Depression and Anxiety in the Postpartum Period** and Risk of Bipolar Disorder: A Danish Nationwide Register-Based Cohort Study. J Clin Psychiatry. 2017 May;78(5):e469-e476.

Munk-Olsen T, Liu X, Viktorin A, et al. Maternal and infant outcomes associated with **lithium use in pregnancy**: an international collaborative meta-analysis of six cohort studies. Lancet Psychiatry. 2018 Jun 18.

Patorno E, Huybrechts KF, Bateman BT, et al. **Lithium Use in Pregnancy** and the Risk of Cardiac Malformations. N Engl J Med. 2017 Jun 8;376(23):2245-2254.

Rai D, Lee BK, Dalman C, et al. Parental depression, maternal antidepressant use during pregnancy, and risk of autism spectrum disorders: population based case-control study. BMJ. 2013 Apr 19;346:f2059.

Virani A et al. Clinical Handbook of Psychotropic Drugs, 19th edition. 2012. Hogrefe Publishing.

Parboosing R, Bao Y, Shen L, Schaefer CA, Brown AS. Gestational influenza and bipolar disorder in adult offspring. JAMA Psychiatry. 2013 Jul 1;70(7):677-85.

2008 (Annuls Int Med, Nov 2008) - Highlights

- Since all of the drugs are about equally effective, consider adverse-effect profiles, costs, and patient preferences when choosing among them.
- Assess the patient's status regularly, beginning within 2 weeks after starting therapy.
- Modify treatment if there's no response within 2 months.
- Successful treatments of first episodes of major depression should continue for about 6 months; patients with a history of two or more episodes should undergo treatment for much longer periods.

Qaseem A, Snow V, Denberg TD, et al; Clinical Efficacy Assessment Subcommittee of American College of Physicians. (**ACP**) Using second-generation antidepressants to treat depressive disorders: a clinical practice guideline from the American College of Physicians. Ann Intern Med. 2008 Nov 18;149(10):725-33.

Additional **Antidepressant Chart** references:

AACAP-Practice parameter on the use of **psychotropic medication in children and adolescents**. J Am Acad Child Adolesc Psychiatry. 2009 Sep;48(9):961-73.

AACAP-Practice parameter for assessment & treatment of **children & adolescents with obsessive-compulsive disorder**. J Am Acad Child Adolesc Psych 2012 Jan;51(1):98-113.

Aalbers S;Fusar-Poli L;Freeman RE;Spreen M;Ket JC; **Music therapy for depression.** Cochrane Database Syst Rev. 2017 Nov 16;11:CD004517. Findings of the present meta-analysis indicate that music therapy provides short-term beneficial effects for people with depression. Music therapy added to treatment as usual (TAU) seems to improve depressive symptoms compared with TAU alone. Additionally, music therapy plus TAU is not associated with more or fewer adverse events than TAU alone. Music therapy also shows efficacy in decreasing anxiety levels and improving functioning of depressed individuals.

Aaronson ST, Sears P, Ruvuna F, et al. A 5-Year Observational Study of Patients With **Treatment-Resistant Depression Treated With Vagus Nerve Stimulation** or Treatment as Usual: Comparison of Response, Remission, and Suicidality. Am J Psychiatry. 2017 Mar 31:appiajp201716010034

Aarts N, Akoudad S, Noordam R, et al. Inhibition of **serotonin reuptake** by antidepressants and **cerebral microbleeds** in the general population. Stroke. 2014 Jul;45(7):1951-7.

Adams SM, Miller KE et al. Pharmacologic **Management of Adult Depression**. American Family Physician 2008; 77 (6): 785-792,795-796.

Adams HP Jr, Robinson RG. Improving Recovery **After Stroke**: A Role for Antidepressant Medications? Stroke. 2012 Aug 2.

Adamson BC, Ensari I, Motl RW. Effect of **Exercise on Depressive Symptoms** in Adults With Neurologic Disorders: A Systematic Review and Meta-Analysis. Arch Phys Med Rehabil. 2015 Jul;96(7):1329-38.

Adlington K. Pop a million happy pills? Antidepressants, nuance, and the media. BMJ. 2018 Mar 9;360:k1069.

Adli M, Hegerl U. Do we underestimate the benefits of antidepressants? Lancet. 2014 Apr 19;383(9926):1361-2.

Aga VM. When and How to Treat **Agitation in Alzheimer's Disease Dementia** With Citalopram and Escitalopram. Am J Geriatr Psychiatry. 2019 May 10.

Agabio R, Trogu E, Pani PP. Antidepressants for the treatment of people with co-occurring depression and alcohol dependence. Cochrane Database of Systematic Reviews 2018, Issue 4. Art. No.: CD008581. We found low-quality evidence supporting the clinical use of antidepressants in the treatment of people with co-occurring depression and alcohol dependence. Antidepressants had positive effects on certain relevant outcomes related to depression and alcohol use but not on other relevant outcomes. Moreover, most of these positive effects were no longer significant when studies with high risk of bias were excluded. Results were limited by the large number of studies showing high or unclear risk of bias and the low number of studies comparing one antidepressant to another or antidepressants to other medication. In people with co-occurring depression and alcohol dependence, the risk of developing adverse effects appeared to be minimal, especially for the newer classes of antidepressants (such as selective serotonin reuptake inhibitors). According to these results, in people with co-occurring depression and alcohol dependence, antidepressants may be useful for the treatment of depression, alcohol dependence, or both, although the clinical relevance may be modest.

Agrawal A, Nelson EC, Bucholz KK, et al. **Major depressive disorder**, **suicidal** thoughts and behaviours, and **cannabis** involvement in discordant twins: a retrospective cohort study. Lancet Psychiatry. 2017 Jul 24.

Agger JL, Schröder A, Gormsen LK, Jensen JS, Jensen TS, Fink PK. **Imipramine** versus placebo for **multiple functional somatic syndromes** (**STreSS-3**): a double-blind, randomised study. Lancet Psychiatry. 2017 Apr 10.

Ahun MN, Geoffroy MC, Herba CM, et al. **Timing and Chronicity of Maternal Depression Symptoms and Children's Verbal Abilities**. J Pediatr. 2017 Sep 6.

Alcántara C, Muntner P, Edmondson D, et al. Perfect storm: concurrent **stress and depressive** symptoms increase risk of **myocardial infarction** or death. Circ Cardiovasc Qual Outcomes. 2015 Mar;8(2):146-54.

Alexopoulos GS. **Depression in the elderly**. Lancet. 2005 Jun 4-10;365(9475):1961-70.

Allan GM, Virani AS, Ivers N. **Second-generation antidepressants**. Can Fam Physician. 2011 Oct;57(10):1143.

Almeida OP, Waterreus A, Hankey GJ. Preventing depression after stroke: Results from a randomized (**sertaline NS**) placebo-controlled trial. J Clin Psychiatry. 2006 Jul;67(7):1104-9.

Almeida OP et al. **B vitamins** to enhance treatment response to antidepressants in middle-aged and older adults: Results from the **B-VITAGE** randomised, double-blind, placebo-controlled trial. Br J Psychiatry 2014 Sep 25.

Almuwaqqat Z, Jokhadar M, Norby FL, et al. Association of **Antidepressant Medication Type With the Incidence of Cardiovascular Disease** in the ARIC Study. J Am Heart Assoc. 2019 Jun 4;8(11):e012503.

Alwan S, Reefhuis J, Botto LD, Rasmussen SA, Correa A, Friedman JM; National Birth Defects Prevention Study. Maternal use of **bupropion** and risk for **congenital heart defects**. Am J Obstet Gynecol. 2010 Apr 22.

American Psychiatric Association Brochures: http://www.healthyminds.org/Functional-Library/brochures.aspx

Amick HR, Gartlehner G, Gaynes BN, et al. **Comparative benefits and harms of second generation antidepressants and cognitive behavioral therapies** in initial treatment of major depressive disorder: systematic review and meta-analysis. BMJ 2015;351:h6019.

Anagnostou E, Zwaigenbaum L, Szatmari P, et al. **Autism spectrum disorder**: advances in evidence-based practice. CMAJ. 2014 Jan 13

Andersen BL, Derubeis RJ, Berman BS, et al. Screening, Assessment, and Care of **Anxiety and Depressive Symptoms in Adults With Cancer**: An American Society of Clinical Oncology Guideline Adaptation. J Clin Oncol. 2014 Apr 14.

Anderson C, Kirkpatrick S, Ridge D, et al. **Starting antidepressant use**: a qualitative synthesis of UK and Australian data. BMJ Open. 2015 Dec 30;5(12):e008636.

Angermann CE, Gelbrich G, Störk S, et al; **MOOD-HF** Study Investigators and Committee Members. Effect of **Escitalopram** on All-Cause Mortality and Hospitalization in Patients With **Heart Failure** and Depression: The MOOD-HF Randomized Clinical trial. JAMA. 2016 Jun 28;315(24):2683-2693.

Anglin R, Yuan Y, Moayyedi P, et al. Risk of Upper **Gastrointestinal Bleeding With Selective Serotonin Reuptake Inhibitors** With or Without Concurrent NonSteroidal Anti-Inflammatory Use: A Systematic Review and Meta-Analysis. Am J Gastroenterol. 2014 Jun;109(6):811-9.

Angstman K, Rasmussen NH. **Personality disorders**: review and clinical application in daily practice. Am Fam Physician. 2011 Dec 1;84(11):1253-60.

Appelhof BC, et al. Triiodothyronine (T3) addition to paroxetine in the treatment of major depressive disorder. J Clin Endocrinol Metab. 2004 Dec;89(12):6271-6.

Appleton KM, Sallis HM, Perry R, et al. **Omega-3 fatty acids** for depression in adults. Cochrane Database of Systematic Reviews 2015, Issue 11. Art. No.: CD004692. DOI: 10.1002/14651858.CD004692.pub4. At present, we do not have sufficient high quality evidence to determine the effects of n-3PUFAs as a treatment for MDD. Our primary analyses suggest a small-to-modest, non-clinically beneficial effect of n-3PUFAs on depressive symptomology compared to placebo; however the estimate is imprecise, and we judged the quality of the evidence on which this result is based to be low/very low. Sensitivity analyses, funnel plot inspection and comparison of our results with those of large well-conducted trials also suggest that this effect estimate is likely to be biased towards a positive finding for n-3PUFAs, and that the true effect is likely to be smaller. Our data, however, also suggest similar rates of adverse events and numbers failing to complete trials in n-3PUFA and placebo groups, but again our estimates are very imprecise. The one study that directly compares n-3PUFAs and antidepressants in our review finds comparable benefit. More evidence, and more complete evidence, are required, particularly regarding both the potential positive and negative effects of n-3PUFAs for MDD.

Archer J, Bower P, Gilbody S, et al. **Collaborative care** for depression and anxiety problems. Cochrane Database of Systematic Reviews 2012, Issue 10. Art. No.: CD006525. DOI: 10.1002/14651858.CD006525.pub2. Collaborative care is associated with significant improvement in depression and anxiety outcomes compared with usual care, and represents a useful addition to clinical pathways for adult patients with depression and anxiety

Armour M, Ee CC, Hao J, et al. **Acupuncture and acupressure** for premenstrual syndrome. Cochrane Database Syst Rev. 2018 Aug 14;8:CD005290.

Arora N, Knowles S, Gomes T, et al. **Interprovincial Variation in Antipsychotic and Antidepressant Prescriptions Dispensed** in the **Canadian Pediatric Population**. Can J Psychiatry. 2016 May 12.

Arroll B, Goodyear-Smith F, Crengle S, et al. Validation of **PHQ-2 and PHQ-9 to screen** for major depression in the primary care population. Ann Fam Med. 2010 Jul-Aug;8(4):348-53.

Attia E. **Eating disorders**. Ann Intern Med. 2012 Apr 3;156(7):ITC41.

Auerbach AD, Vittinghoff E, Maselli J, et al. **Perioperative Use of Selective Serotonin Reuptake Inhibitors** and Risks for Adverse Outcomes of Surgery. JAMA Intern Med. 2013 Apr 29:1-7.

Ayis SA, Rudd AG, Ayerbe L, Wolfe CDA. **Sex differences in trajectories of depression symptoms** and associations with 10-year mortality in patients with stroke: the South London Stroke Register. Eur J Neurol. 2019Jan7

Aziz MT, Good BL, Lowe DK. Serotonin-norepinephrine reuptake inhibitors for the management of **chemotherapy-induced peripheral neuropathy**. Ann Pharmacother. 2014 May;48(5):626-32

Bahar MA, Kamp J, Borgsteede SD, et al. The impact **of CYP2D6 mediated drug-drug interaction**: a systematic review on a combination of **metoprolol and paroxetine/fluoxetine**. Br J Clin Pharmacol. 2018 Sep 24.

Bali V, Johnson ML, Chen H, et al. Comparative **Cognitive Profile of Second-Generation Antidepressants in Elderly Nursing Home Residents** With Depression. Ann Pharmacother. 2015 Nov 25.

Ball S, Classi P, Dennehy EB. What happens next?: a claims database study of **second-line pharmacotherapy** in patients with major depressive disorder (MDD) who initiate selective serotonin reuptake inhibitor (SSRI) treatment. Ann Gen Psychiatry. 2014 Mar 19;13(1):8.

Ballard C, Corbett A. Management of **neuropsychiatric symptoms** in people with **dementia**. CNS Drugs. 2010 Sep 1;24(9):729-39. doi:10.2165/11319240-000000000-00000.

Bambauer KZ, et al. **Physician alerts** to increase antidepressant adherence: fax or fiction? Arch Intern Med. 2006 Mar 13;166(5):498-504.

Barak Y, Plopski I, et al. **Escitalopram versus risperidone** for the treatment of behavioral and psychotic symptoms associated with Alzheimer's disease: randomized double-blind pilot study. Int Psychogeriatr. 2011 Apr 15:1-5.

Barber JP, Barrett MS, Gallop R, et al. **Short-term dynamic psychotherapy versus pharmacotherapy** for major depressive disorder: a randomized, placebo-controlled trial. J Clin Psychiatry. 2012 Jan;73(1):66-73.

Barbui C, Cipriani A, Patel V, Ayuso-Mateos JL, van Ommeren M. Efficacy of **antidepressants and benzodiazepines in minor depression**: systematic review and meta-analysis. Br J Psychiatry. 2011 Jan;198:11-6.

Barbui C, Hotopf M, Freemantle N, et al. Selective serotonin reuptake inhibitors versus tricyclic and heterocyclic antidepressants: comparison of drug adherence. Cochrane Database Syst Rev. 2000;(4):CD002791.

Barbui C, Ostuzzi G. Beneficial and harmful consequences of **prepartum and postpartum antidepressant exposure**. Evid Based Ment Health. 2014 Aug;17(3):69-71.

Barker MM, Beresford B, Bland M, Fraser LK. Prevalence and Incidence of Anxiety and Depression Among **Children, Adolescents, and Young Adults With Life-Limiting Conditions**: A Systematic Review and Meta-analysis. JAMA Pediatr. 2019 Jul 8.

Barnes TR, Paton C. Do **antidepressants improve negative symptoms in schizophrenia**? BMJ. 2011 Jun 10;342:d3371. doi: 10.1136/bmj.d3371.

Barnes DE, Yaffe K, Byers AL, et al. Midlife vs Late-Life Depressive Symptoms and **Risk of Dementia**: Differential Effects for Alzheimer Disease and Vascular Dementia. Arch Gen Psychiatry. 2012 May;69(5):493-8.

Bartels C, Wagner M, Wolfsgruber S, et al. Impact of **SSRI Therapy on Risk of Conversion From Mild Cognitive Impairment to Alzheimer's Dementia** in Individuals With Previous Depression. Am J Psychiatry. 2017 Nov 28:appiajp201717040404.

Batelaan NM, Bosman RC, Muntingh A, et al. **Risk of relapse after antidepressant discontinuation** in **anxiety disorders, obsessive-compulsive disorder, and post-traumatic stress disorder**: systematic review and meta-analysis of relapse prevention trials. BMJ. 2017 Sep 13;358:j3927.

Baumeister H, Hutter N, Bengel J. Psychological and pharmacological interventions for **depression in patients with diabetes** mellitus: an abridged Cochrane review. Diabet Med. 2014 Jul;31(7):773-86. Psychological and pharmacological interventions positively affect depression outcomes in patients with diabetes at the end of treatment. Furthermore, short-term glycaemic control improved moderately in pharmacological trials. Most outcomes have not been investigated sufficiently. Moreover, there is a lack of follow-up data for pharmacological trials limiting the evidence on the sustainability of treatment effects.

Beardslee WR, Brent DA, Weersing VR, et al. **Prevention of Depression** in At-Risk Adolescents: Longer-term Effects. JAMA Psychiatry. 2013 Sep 4. (Cognitive-behavioral prevention-CBP useful)

Beck CA, Williams JV, Wang JL, et al. **Psychotropic medication use in Canada**. Can J Psychiatry. 2005 Sep;50(10):605-13. RESULTS: Overall psychotropic drug utilization was 7.2%. Utilization was higher for women and with increasing age. With any lifetime CIDI-diagnosed disorder assessed in the CCHS 1.2, utilization was 19.3%, whereas without such disorders, it was 4.1%. Selective serotonin reuptake inhibitors (SSRIs) were the most commonly used antidepressants for those with a past-year major depressive episode (17.8%), followed by venlafaxine (7.4%). Among people aged 15 to 19 years, antidepressant use was 1.8% overall and 11.7% among those with past-year depression; SSRIs made up the majority of use. Sedative-hypnotics were used by 3.1% overall, increasing with age to 11.1% over 75 years.

Bedson E, Bell D, Carr D, et al. **Folate Augmentation** of Treatment - Evaluation for Depression (FolATED): randomised trial and economic evaluation. Health Technol Assess. 2014 Jul;18(48):1-160.

Bellón JÁ, Conejo-Cerón S, Moreno-Peral P, et al. **Intervention to Prevent Major Depression in Primary Care**: A Cluster Randomized Trial. Ann Intern Med. 2016 Mar 29.

Beltman MW, Voshaar RC, Speckens AE. **Cognitive-behavioural therapy** for depression in people with a somatic disease: meta-analysis of randomised controlled trials. Br J Psychiatry. 2010 Jul;197(1):11-9.

Belvederi Murri M, Amore M, Menchetti M, et al. **Physical exercise** for late-life major depression. Br J Psychiatry. 2015 Jul 23. pii: bjp.bp.114.150516.

Bénard-Laribière A, Pambrun E, Sutter-Dallay AL, et al. Patterns of **antidepressant use during pregnancy**: a nationwide population-based cohort study. Br J Clin Pharmacol. 2018 Apr 17.

Berard A, Zhao JP, Sheehy O. **Sertraline use during pregnancy** and the risk of major malformations. Am J Obstet Gynecol. 2015 Jun;212(6):795.e1-795.e12.

Bérard A, Iessa N, Chaabane S. et al. The risk of major cardiac malformations associated with **paroxetine use during the first trimester of pregnancy**: A systematic review and meta-analysis. Br J Clin Pharmacol. 2015 Nov 27.

Bergfeld IO, Mantione M, Hoogendoorn MLC, et al. **Deep brain stimulation** of the ventral anterior limb of the internal capsule for treatment-resistant depression: a randomized clinical trial [online April 6, 2016]. JAMA Psychiatry. doi:10.1001 /jamapsychiatry.2016.0152.

Bergh S, Selbæk G, Engedal K. **Discontinuation of antidepressants** in people with **dementia** and neuropsychiatric symptoms (**DESEP** study): double blind, randomised, parallel group, placebo controlled trial. BMJ. 2012 Mar 9;344:e1566.

Bezchlibnyk-Butler Clinical Handbook of Psychotropic Drugs, 17th Ed. 2007.

Bezchlibnyk-Butler KZ. Clinical Handbook of Psychotropic Drugs, **22nd Ed**. 22nd Editors: Procyshyn RM, Bezchlibnyk-Butler KZ, Jeffries JJ. Hogrefe Publishing, Massachusetts, 2017.

Biesheuvel-Leliefeld KEM, et al. Effectiveness of **Supported Self-Help** in Recurrent Depression: A Randomized Controlled Trial in Primary Care. Psychother Psychosom. 2017 Jun 24;86(4):220-230.

Bighelli I, Castellazzi M, Cipriani A, et al. **Antidepressants versus placebo for panic disorder in adults**. Cochrane Database Syst Rev. 2018 Apr 5;4:CD010676. The identified studies comprehensively address the objectives of the present review.Based on these results, antidepressants may be more effective than placebo in treating panic disorder. Efficacy can be quantified as a NNTB of 7, implying that seven people need to be treated with antidepressants in order for one to benefit. Antidepressants may also have benefit in comparison with placebo in terms of number of dropouts, but a less favourable profile in terms of dropout due to adverse effects. However, the tolerability profile varied between different classes of antidepressants.The choice of whether antidepressants should be prescribed in clinical practice cannot be made on the basis of this review.

Biggs WS, Demuth RH, **Premenstrual Syndrome and Premenstrual Dysphoric Disorder**. Am Fam Physician. 2011 Oct 15;84(8):918-924.

Biskin RS, Paris J. Management of **borderline personality disorder**. CMAJ. 2012 Oct 1.

Bixby AL, VandenBerg A, Bostwick JR. Clinical management of **bleeding risk with antidepressants**. Ann Pharmacother 2019;53:186-94.

Blier P, Ward HE, Tremblay P, et al. **Combination of antidepressant medications** from treatment initiation for major depressive disorder: a double-blind randomized study. Am J Psychiatry. 2010 Mar;167(3):281-8.

Bliss SA, Warnock JK. Psychiatric medications: **Adverse cutaneous drug reactions**. Clin Dermatol. 2013 Jan;31(1):101-9.

Blumberger DM, Vila-Rodriguez F, Thorpe KE, et al. Effectiveness of theta burst versus high-frequency repetitive **transcranial magnetic stimulation** in patients with depression (**THREE-D**): a randomised non-inferiority trial. Lancet. 2018 Apr 28;391(10131):1683-1692.

Blumenthal JA, Babyak MA, O'Connor C, et al. Effects of **exercise training** on depressive symptoms in patients with chronic heart failure: the HF-ACTION randomized trial. JAMA. 2012 Aug 1;308(5):465-74.

Blumenthal SR, Castro VM, Clements CC, et al. An Electronic Health Records Study of **Long-Term Weight Gain** Following Antidepressant Use. JAMA Psychiatry. 2014 Jun 4.

Boal AH, Smith DJ, McCallum L, et al. Monotherapy with Major Antihypertensive Drug Classes and Risk of **Hopsital Admissions for Mood Disorders**. Hypertension.2016 :68 :00-00.

Bockting CLH, Klein NS, Elgersma HJ, et al. Effectiveness of **preventive cognitive therapy while tapering antidepressants versus maintenance** antidepressant treatment versus their combination in prevention of depressive relapse or recurrence (**DRD** study): a three-group, multicentre, randomised controlled trial. Lancet Psychiatry. 2018 Apr 3.

Boelen PA, Smid GE. **Disturbed grief**: prolonged grief disorder and persistent complex bereavement disorder. BMJ. 2017 May 18;357:j2016

Boers E, Afzali MH, Newton N, Conrod P. Association of **Screen Time** and Depression in Adolescence. JAMA Pediatr. 2019 Jul 15.
Bombardier Charles H.; Fann Jesse R.;. Temkin Nancy R et al; Rates of Major Depressive Disorder and Clinical Outcomes Following **Traumatic Brain Injury** JAMA. 2010;303(19):1938-1945.
Boinpally R, Gad N, Gupta S, et al. Influence of CYP3A4 Induction/Inhibition on the Pharmacokinetics of **Vilazodone** in Healthy Subjects. Clin Ther. 2014 Sep 15.
Boland EM, Rao H, Dinges DF, et al. Meta-Analysis of the **Antidepressant Effects of Acute Sleep Deprivation**. J Clin Psychiatry. 2017 Sep 19.
Bonde JP, Utzon-Frank N, Bertelsen M, et al. Risk of depressive disorder following **disasters and military deployment**: systematic review with meta-analysis. Br J Psychiatry. 2016 Feb 18.
Bosanquet K, et al. **CollAborative care** for Screen-Positive ElderRs with major depression (**CASPER** plus): a multicentred randomised controlled trial of clinical effectiveness and cost-effectiveness. Health Technol Assess. 2017 Nov;21(67):1-252.
Bot M, Brouwer IA, Roca M, et al; **MooDFOOD** Prevention Trial Investigators. Effect of **multinutrient supplementation and food-related behavioral activation therapy** on prevention of major depressive disorder among overweight or obese adults with subsyndromal depressive symptoms: the MooDFOOD randomized clinical trial [Mar 5, 2019]. JAMA. doi:10.1001/jama.2019.0556
Boukhris T, Sheehy O, Mottron L, et al. **Antidepressant Use During Pregnancy** and the **Risk of Autism** Spectrum Disorder in Children. JAMA Pediatr. 2015 Dec 14:1-8.
Boulenger JP, et al. A comparative study of the efficacy of long-term treatment with **escitalopram** and **paroxetine** in severely depressed patients. Curr Med Res Opin. 2006 Jul;22(7):1331-41.
Bourgeois J, Elseviers MM, Van Bortel L, Petrovic M, et al. The Use of **Antidepressants in Belgian Nursing Homes** : Focus on Indications and Dosages in the PHEBE Study. Drugs Aging. 2012 Sep;29(9):759-69.
Bower P, Kontopantelis E, Sutton A, et al. Influence of initial **severity of depression on effectiveness of low intensity interventions**: meta-analysis of individual patient data. BMJ. 2013 Feb 26;346:f540.
Bowes L, Joinson C, Wolke D, et al. **Peer victimisation** during adolescence and its impact on depression in early adulthood: a prospective cohort study in the United Kingdom. BMJ 2015;350:h2469.
Bowes L, Carnegie R, Pearson R, et al. Risk of depression and self-harm in teenagers identifying with **goth subculture**: a longitudinal cohort study. Lancet Psychiatry. 2015 Aug 20.
Brandlistuen RE et al. Behavioural effects of **fetal antidepressant exposure** in a Norwegian cohort of discordant siblings. Int J Epidemiol 2015 Apr 14.
Brännstrom J, Lövheim H, Gustafson Y, Nordström P. Association between antidepressant **drug use and hip fracture in older people** before and after treatment initiation [online Jan 2, 2019]. JAMA Psychiatry. doi:10.1001/jamapsychiatry.2018.3679
Braun UK, Pham C, Kunik ME. Recognizing and managing **depression at end of life**. Geriatrics. 2008 Jun;63(6):25-7.
Breen G, Webb BT, Butler AW, et al. A Genome-Wide Significant Linkage for Severe Depression on **Chromosome 3**: The Depression Network Study. Am J Psychiatry. 2011 May 15.
Brent DA, et al. Effect of a **Cognitive-Behavioral Prevention Program** on Depression 6 Years After Implementation Among At-Risk Adolescents: A Randomized Clinical Trial. JAMA Psychiatry. 2015 Sep 30:1-9.
Bridle C, Spanjers K, Patel S, et al. Effect of **exercise** on depression severity in older people: systematic review and meta-analysis of randomised controlled trials. Br J Psychiatry. 2012 Sep;201(3):180-5.
Bronskill SE, Campitelli MA, Iaboni A, et al. **Low-Dose Trazodone, Benzodiazepines, and Fall-Related Injuries in Nursing Homes**: A Matched-Cohort Study. J Am Geriatr Soc. 2018 Oct;66(10):1963-1971.
Brown AS, Gyllenberg D, Malm H, et al. Association of **selective serotonin reuptake inhibitor exposure during pregnancy** with **speech, scholastic, and motor disorders** in offspring [online Oct 12, 2016]. JAMA Psychiatry. doi:10.1001/jamapsychiatry.2016.2594
Brown GK, Ten Have T, Henriques GR, Xie SX, Hollander JE, Beck AT. **Cognitive therapy** for the prevention of suicide attempts: a randomized controlled trial. JAMA. 2005 Aug 3;294(5):563-70.
Brown HK, Ray JG, Wilton AS, et al. Association between **serotonergic antidepressant use during pregnancy and autism spectrum disorder** in children.JAMA. doi:10.1001 /jama.2017.3415
Brown J, O' Brien PM, Marjoribanks J, Wyatt K. **Selective serotonin reuptake inhibitors for premenstrual syndrome**. Cochrane Database Syst Rev. 2009 Apr 15;(2):CD001396.
Bruce ML, Ten Have TR, Reynolds CF 3rd, et al. **Reducing suicidal ideation and depressive symptoms in depressed older** primary care patients: a randomized controlled trial. JAMA. 2004 Mar 3;291(9):1081-91.
Bruce ML, Raue PJ, Reilly CF, et al. Clinical effectiveness of **integrating depression care management** into Medicare Home Health: the Depression **CAREPATH** Randomized Trial [online November 10, 2014]. JAMA Intern Med. doi:10.1001/jamainternmed.2014.5835.
Bruce ML, Lohman MC, Greenberg RL, et al. **Integrating Depression Care Management into Medicare Home Health** Reduces Risk of 30- and 60-Day Hospitalization: The Depression Care for Patients at Home Cluster-Randomized Trial. J Am Geriatr Soc. 2016 Oct 14.
Brunoni AR, Valiengo L, et al. The **Sertraline** (50mg/d) **vs Electrical Current** Therapy (tDCS) for Treating Depression Clinical Study: Results From a Factorial, Randomized, Controlled Trial. JAMA Psychiatry.2013 Feb 6:1-9.
Brunoni AR, Moffa AH, Fregni F, et al. **Transcranial direct current stimulation** for acute major depressive episodes: meta-analysis of individual patient data. Br J Psychiatry. 2016 Apr 7.
Brunoni AR, Chaimani A, et al. Repetitive **Transcranial Magnetic Stimulation** for the Acute Treatment of Major Depressive Episodes: A Systematic Review With Network Meta-analysis. JAMA Psychiatry. 2016 Dec 28.
Brunoni AR, Moffa AH, Sampaio-Junior B, et al. Trial of **electrical direct-current therapy versus escitalopram** for depression. (**ELECT-TDCS**) N Engl J Med 2017;376:2523-33.
Brunzell JD. Clinical practice. **Hypertriglyceridemia**. N Engl J Med. 2007 Sep 6;357(10):1009-17.
Brus O, Nordanskog P, Båve U, et al. Subjective **Memory Immediately Following Electroconvulsive Therapy**. J ECT. 2017 Jun;33(2):96-103
Buckley NA, Dawson AH, Isbister GK. **Serotonin syndrome**. BMJ. 2014 Feb 19;348:g1626.
Buntrock C et al. Effect of a **Web-based guided self**-help intervention for prevention of major depression in adults with subthreshold depression: A randomized clinical trial. JAMA 2016 May 3; 315:1854-63.
Burcu M, Zito JM, Safer DJ, et al. Association of **Antidepressant Medications With Incident Type 2 Diabetes** Among Medicaid-Insured Youths. JAMA Pediatr. 2017 Oct 16.
Burnett M, Lemyre M. SOGC: No. 345-Primary **Dysmenorrhea** Consensus Guideline. J Obstet Gynaecol Can. 2017 Jul;39(7):585-595.
Burns RB, Smetana GW, Brady R. Should This Patient Receive an Antidepressant?: Grand Rounds Discussion From Beth Israel Deaconess Medical Center. Ann Intern Med. 2017 Aug 1;167(3):192-199
Bushnell GA, et al. Simultaneous **Antidepressant and Benzodiazepine New Use and Subsequent Long-term Benzodiazepine Use in Adults With Depression**, United States, 2001-2014. JAMA Psychiatry. 2017 Jun 7.
Byatt N, Levin LL, Ziedonis D, et al. **Enhancing Participation in Depression Care** in Outpatient **Perinatal** Care Settings: A Systematic Review. Obstet Gynecol. 2015 Nov;126(5):1048-58.
Bykov K, Schneeweiss S, Donneyong MM, et al. Impact of an **Interaction Between Clopidogrel and Selective Serotonin Reuptake Inhibitors**.Am J Cardio (2016)
Caddy C, Amit BH, McCloud TL, et al. **Ketamine** and other **glutamate receptor modulators** for depression in adults. Cochrane Database Syst Rev. 2015 Sep 23;9:CD011612. We found limited evidence for ketamine's efficacy over placebo at time points up to one week in terms of the primary outcome, response rate. The effects were less certain at two weeks post-treatment. No significant results were found for the remaining ten glutamate receptor modulators, except for sarcosine being more effective than citalopram at four weeks. In terms of adverse events, the only significant differences in favour of placebo over ketamine were in regards to confusion and emotional blunting. Despite the promising nature of these preliminary results, our confidence in the evidence was limited by risk of bias and the small number of participants. Many trials did not provide information on all the prespecified outcomes and we found no data, or very limited data, on very important issues like suicidality, cognition, quality of life, costs to healthcare services and dropouts due to lack of efficacy.All included studies administered ketamine intravenously, which can pose practical problems in clinical practice. Very few trials were included in the meta-analyses for each comparison; the majority of comparisons contained only one study. Further RCTs (with adequate blinding) are needed to explore different modes of administration of ketamine with longer follow-up, which test the comparative efficacy of ketamine and the efficacy of repeated administrations.
Calarge CA, Mills JA, Janz KF, et al. **Composition in Adolescents During Treatment with Selective Serotonin Reuptake Inhibitors**. Peds. 2017;140(1):e20163943
Campbell AP, Phillips KM, Hoehle LP, et al. Depression symptoms and **lost productivity in chronic rhinosinusitis**. Ann Allergy Asthma Immunol. 2017 Mar;118(3):286-289.
Canadian Anxiety Guideline July 2006 (Panic, PTSD, GAD, SAD, OCD & specific phobias) http://www.cpa-apc.org/Publications/CJP/supplements/july2006/anxiety_guidelines_2006.pdf
Canadian Coalition for Seniors' Mental Health (**CCSMH**) National **Guidelines for Mental Health** 2006: http://www.ccsmh.ca/en/default.cfm http://www.ccsmh.ca/pdf/final%20supplement.pdf
Candy B Jones L Williams R Tookman A King M. Psychostimulants for depression. Cochrane Database Syst Rev. 2008 Apr 16;(2):CD006722. There is some evidence that in the short-term, PS reduce symptoms of depression. Whilst this reduction is statistically significant, the clinical significance is less clear.
Caparros-Gonzalez RA, et al. **Hair cortisol levels**, psychological stress and psychopathological symptoms as predictors of **postpartum depression**. PLoS One. 2017 Aug 28;12(8):e0182817.

Carhart-Harris RL, Bolstridge M, Rucker J, et al. **Psilocybin** with psychological support for treatment-resistant depression: an open-label feasibility study. Lancet Psychiatry. 2016 May 16

Carhart-Harris RL et al. **Psilocybin** for treatment-resistant depression: fMRI-measured brain mechanisms. Sci Rep 2017 Oct 13; 7:13187.

Carney RM.; et al. **Omega-3 Augmentation** of Sertraline in Treatment of Depression in Patients With Coronary Heart Disease: A Randomized Controlled Trial. JAMA. 2009;302(15):1651-1657.

Carrasco M, Volkmar FR, Bloch MH. Pharmacologic Treatment of Repetitive Behaviors in Autism Spectrum Disorders: Evidence of **Publication Bias**. Pediatrics. 2012 Apr 23. (serotonin receptor inhibitors –SRIs)

Carrier JD, Roberge P, Courteau J, et al. Predicting **chronic benzodiazepine use** in adults with depressive disorder: Retrospective cohort study using administrative data in Quebec. Can Fam Physician. 2016 Aug;62(8):e473-83

Castro-Alves LJ, Oliveira de Medeiros AC, Neves SP, et al. **Perioperative Duloxetine** to Improve Postoperative Recovery After Abdominal Hysterectomy: A Prospective, Randomized, Double-Blinded, Placebo-Controlled Study. Anesth Analg. 2016 Jan;122(1):98-104.

Chang CM, Wu EC, Chen CY, et al. Psychotropic Drugs and Risk of **Motor Vehicle Accidents**: a Population-based Case-Control Study. Br J Clin Pharmacol. 2012 Sep 12.

Chang SS, Stuckler D, Yip P, Gunnell D. Impact of 2008 global **economic crisis on suicide**: time trend study in 54 countries. BMJ. 2013 Sep 17;347:f5239.

Chang WP, Lin Y, Huang HL, et al. **Scoliosis** and the Subsequent Risk of Depression: A Nationwide Population-based Cohort Study in Taiwan. Spine (Phila Pa 1976). 2016 Feb;41(3):253-8.

Charles H. Bombardier; Jesse R. Fann; Nancy R. Temkin et al; Rates of Major Depressive Disorder and Clinical Outcomes Following **Traumatic Brain Injury** JAMA. 2010;303(19):1938-1945.

Chalder M, Wiles NJ, Campbell J, et al. **Facilitated physical activity** as a treatment for depressed adults: randomised controlled trial. (**TREAD**) BMJ. 2012 Jun6;344:e2758.

Chan J, Natekar A, Einarson A, et al. Risks of **untreated depression in pregnancy**. Can Fam Physician. 2014 Mar;60(3):242-3.

Chaudron, Linda H., Szilagyi, Peter G., Tang, Wan, et al. Accuracy of Depression **Screening Tools** for Identifying **Postpartum Depression** Among Urban Mothers. Pediatrics 2010 125: e609-e617.

Chen HY, Lin CL, Lai SW, Kao CH. Association of **Selective Serotonin Reuptake Inhibitor Use** and Acute Angle-Closure **Glaucoma**. J Clin Psychiatry. 2016 Jun;77(6):e692-6.

Cheng ER, Downs SM, Carroll AE. Prevalence of **Depression Among Fathers** at the Pediatric Well-Child Care Visit. JAMA Pediatr. 2018 Jul 23.

Chekroud AM, Gueorguieva R, Krumholz HM, et al. Reevaluating the **Efficacy and Predictability of Antidepressant Treatments**: A Symptom Clustering Approach. JAMA Psychiatry. 2017 Feb 22.

Chekroud SR, Gueorguieva R, Zheutlin AB, et al. Association between **physical exercise and mental health** in 1·2 million individuals in the USA between 2011 and 2015: a cross-sectional study. Lancet Psychiatry. 2018 Aug 8.

Chen HM, Yang YH, Chen KJ, et al. Antidepressants reduced risk of **mortality in patients with diabetes mellitus**: a population-based cohort study in Taiwan. J Clin Endocrinol Metab. 2019 Jul 2.

Cheung AH, Zuckerbrot RA, Jensen PS, et al. Guidelines for **Adolescent Depression in Primary Care** (**GLAD-PC**): **Part II**. **Treatment and Ongoing Management**. Pediatrics. 2018 Feb 26.

Chiu HL, Chan PT, Chu H, et al. Effectiveness of **Light Therapy** in Cognitively Impaired Persons: A Metaanalysis of Randomized Controlled Trials. J Am Geriatr Soc. 2017 Oct;65(10):2227-2234.

Chocron S, Vandel P, Durst C, et al. Antidepressant Therapy in Patients Undergoing **Coronary Artery Bypass Grafting: The MOTIV-CABG** Trial. Ann Thorac Surg. 2013 May;95(5):1609-18.

Choi KW, Chen C-Y, Stein MB, et al; Major Depressive Disorder Working Group of the Psychiatric Genomics Consortium. Assessment of bidirectional relationships between **physical activity and depression among adults**: a 2-sample mendelian randomization study [online Jan 23, 2019]. JAMA Psychiatry. doi:10.1001/jamapsychiatry.2018.4175

Choi-Kwon S, Han SW, Kwon SU, et al. **Fluoxetine Treatment in Poststroke** Depression, Emotional Incontinence, and Anger Proneness. A Double-Blind, Placebo-Controlled Study. Stroke. 2005 Nov 23; [Epub ahead of print]

Choi-Kwon S, Han K, Choi S, et al. **Poststroke depression** and emotional incontinence: Factors related to acute and subacute stages. Neurology. 2012 Apr 10;78(15):1130-7.

Chollet F et al. **Fluoxetine for motor recovery after acute ischaemic stroke** (**FLAME**): A randomised placebo-controlled trial. Lancet Neurol 2011 Feb; 10:123.

Chun-Fai-Chan B, Koren G, Fayez I, et al. Pregnancy outcome of women exposed to bupropion during pregnancy: A prospective comparative study. Am J Obstet Gynecol 2005; 192:932-36. (InfoPOEMs: Bupropion is not associated with increased rates of major malformations. It may be associated with an increase in spontaneous abortions. (LOE = 1b))

Christensen H, Batterham PJ, et al. Effectiveness of an **online insomnia program (SHUTi)** for prevention of depressive episodes (the GoodNight Study): a randomised controlled trial. Lancet Psychiatry. 2016 Jan 27.

Cipriani A, Brambilla P, Furukawa T, et al.Fluoxetine versus other types of pharmacotherapy for depression. Cochrane Database Syst Rev. 2005 Oct 19;4:CD004185. AUTHORS' CONCLUSIONS: There are statistically significant differences in terms of efficacy and tolerability between fluoxetine and certain ADs, but the clinical meaning of these differences is uncertain, and no definitive implications for clinical practice can be drawn. From a clinical point of view the analysis of antidepressants' safety profile (adverse effect and suicide risk) remains of crucial importance and more reliable data about these outcomes are needed. Waiting for more robust evidence, treatment decisions should be based on considerations of clinical history, drug toxicity, patient acceptability, and cost. We need for large, pragmatic trials, enrolling heterogeneous populations of patients with depression to generate clinically relevant information on the benefits and harms of competitive pharmacological options. A meta-analysis of individual patient data from the randomised trials is clearly necessary.

Cipriani A, Furukawa TA, Salanti G, Geddes JR, et al. Comparative efficacy and acceptability of 12 new-generation antidepressants: a **multiple-treatments meta-analysis**. Lancet. 2009 Jan 28. [Epub ahead of print] Clinically important differences exist between commonly prescribed antidepressants for both efficacy and acceptability in favour of escitalopram and sertraline. Sertraline might be the best choice when starting treatment for moderate to severe major depression in adults because it has the most favourable balance between benefits, acceptability, and acquisition cost.

Cipriani A, La Ferla T, Furukawa TA, et al. **Sertraline** versus other antidepressive agents for depression. Cochrane Database Syst Rev. 2009 Apr 15;(2):CD006117. This systematic review and meta-analysis highlighted a trend in favour of sertraline over other antidepressive agents both in terms of efficacy and acceptability, using 95% confidence intervals and a conservative approach, with a random effects analysis. However, the included studies did not report on all the outcomes that were pre-specified in the protocol of this review. Outcomes of clear relevance to patients and clinicians were not reported in any of the included studies.

Cipriani A, Purgato M, Furukawa TA, et al. **Citalopram versus other anti-depressive agents for depression.** Cochrane Database Syst Rev. 2012 Jul 11;7:CD006534. Some statistically significant differences between citalopram and other antidepressants for the acute phase treatment of major depression were found in terms of efficacy, tolerability and acceptability. Citalopram was more efficacious than paroxetine and reboxetine and more acceptable than tricyclics, reboxetine and venlafaxine, however, it seemed to be less efficacious than escitalopram.

Cipriani A, Zhou X, Del Giovane C, et al. **Comparative efficacy and tolerability of antidepressants for major depressive disorder in children and adolescents**: a network meta-analysis. Lancet 2016; online June 8

Cipriani A, et al. **Comparative efficacy and acceptability of 21 antidepressant drugs** for the **acute treatment** of **adults** with **major depressive disorder**: a systematic review and network meta-analysis. Lancet. 2018 Feb 20.

Clarke G, DeBar LL, Pearson JA, et al. **Cognitive Behavioral Therapy** in Primary Care for **Youth** Declining Antidepressants: A Randomized Trial. Pediatrics. 2016 May;137(5).

Clark M, Jansen K, and Cloy A. Treatment of **Childhood and Adolescent Depression**. Am Fam Physician. 2012;85(5):442-448.

Coelho HF, Boddy K, Ernst E. **Massage therapy** for the treatment of depression: a systematic review. Int J Clin Pract. 2008 Feb;62(2):325-33. Epub 2007 Dec 11. This review found no robust evidence supporting a recommendation for deep (Swedish) massage therapy as a sole or additive modality for treating unipolar depression. (LOE = 1a-)

Coffey SF. Banducci AN, Vinci C. Common Questions About **Cognitive Behavior Therapy** for Psychiatric Disorders. Am Fam Physician. 2015;92(9):807-812.

Cohen LS, et al. Relapse of major depression during **pregnancy** in women who maintain or discontinue antidepressant treatment. JAMA. 2006 Feb 1;295(5):499-507. CONCLUSIONS: Pregnancy is not "protective" with respect to risk of relapse of major depression. Women with histories of depression who are euthymic in the context of ongoing antidepressant therapy should be aware of the association of depressive relapse during pregnancy with antidepressant discontinuation.{InfoPOEMs Mar 2006: Nearly 50% of women currently receiving antidepressant medication will experience a relapse of major depression during pregnancy. The risk is highest for those discontinuing their medication (68% relapse rate). It is likely that this study sample consists of patients with a higher severity of illness than those found in a routine community practice, so the findings may not generalize to other settings. (LOE = 1b). Women maintaining their medication during pregnancy relapsed significantly less often than those who discontinued medication (26% vs 68%; number needed to treat (NNT)= 2; 95% CI, 1.8 - 4).}

Colfax GN, Santos GM, Das M, et al. **Mirtazapine to reduce methamphetamine use**: a randomized controlled trial. Arch Gen Psychiatry. 2011 Nov;68(11):1168-75.

Colman I, Naicker K, Zeng Y, et al. Predictors of long-term **prognosis of depression**. CMAJ 2011;183:1969-76.

Colucci VJ, Berry BD. **Heart failure** worsening and exacerbation after venlafaxine and duloxetine therapy. Ann Pharmacother. 2008 Jun;42(6):882-7. Epub 2008 Apr 29.

Conejo-Cerón S, et al. Effectiveness of **Psychological and Educational Interventions to Prevent Depression in Primary Care**: A Systematic Review and Meta-Analysis. Ann Fam Med. 2017 May;15(3):262-271.

Connolly KR, Thase ME. If at first you don't succeed: a review of the evidence for **antidepressant augmentation , combination and switching strategies**. Drugs 2011;71(1):43-64.

Conway CR, George MS, Sackeim HA. Toward an Evidence-Based, **Operational Definition of Treatment-Resistant Depression**: When Enough Is Enough. JAMA Psychiatry. 2016 Oct 26.

Coogan PF, Palmer JR, Strom BL, Rosenberg L. Use of selective serotonin reuptake inhibitors and the risk of **breast cancer**. Am J Epidemiol. 2005 Nov 1;162(9):835-8. Epub 2005 Sep 21.

Cook R, Thomas V, Martin R. **Does fluoxetine improve recovery after stroke**? BMJ. 2019 Mar 25;364:l1029.

Cooney GM, Dwan K, Greig CA, et al. **Exercise for depression**. Cochrane Database of Systematic Reviews 2013, Issue 9. Art. No.: CD004366. DOI: 10.1002/14651858.CD004366.pub6.
Exercise is moderately more effective than a control intervention for reducing symptoms of depression, but analysis of methodologically robust trials only shows a smaller effect in favour of exercise.

Cooney G, Dwan K, Mead G. **Exercise** for depression. JAMA. 2014 Jun 18;311(23):2432-3.

Cooper C, Katona C, Lyketsos K, et al. A Systematic Review of Treatments for **Refractory Depression in Older People**. Am J Psychiatry. 2011 Mar 31.

Cooper WO, Callahan ST, Shintani A, et al. Antidepressants and **suicide attempts in children**. Pediatrics. 2014 Feb;133(2):204-10.

Corathers SD, Kichler J, Jones NH, et al. Improving **depression screening for adolescents with type 1 diabetes**. Pediatrics. 2013 Nov;132(5):e1395-402.

Coupland C, Dhiman P, Morriss R, et al. Antidepressant use and risk of **adverse outcomes in older people**: population based cohort study. BMJ. 2011 Aug 2;343:d4551. doi: 10.1136/bmj.d4551.

Coupland CA, Dhiman P, Barton G, et al. A study of the **safety and harms of antidepressant drugs for older people**: a cohort study using a large primary care database. Health Technol Assess. 2011 Aug;15(28):1-202, iii-iv.

Coupland C, Hill T, Morriss R, et al. **Antidepressant use and risk of suicide and attempted suicide/self-harm in people aged 20 to 64**: cohort study using a primary care database. BMJ 2015;350:h517.

Coupland C, Hill T, Morriss R, et al. **Antidepressant use and risk of cardiovascular outcomes** in people aged 20 to 64: cohort study using primary care database. BMJ. 2016 Mar 22;352:i1350.

Courlet P, Guidi M, Glatard A,et al. **Escitalopram population pharmacokinetics in people living with HIV and in the psychiatric population**: drug-drug interactions and probability of target attainment. Br J Clin Pharmacol. 2019 May 29.

Crawford MJ, Thana L, Methuen C, et al. Impact of **screening for risk of suicide**: randomised controlled trial. Br J Psychiatry. 2011 May;198(5):379-84.

Crawford MJ, Thana L, Farquharson L, et al. Patient experience of **negative effects of psychological treatment**: results of a national survey†. Br J Psychiatry. 2016 Mar;208(3):260-5.

Croen LA et al. Antidepressant use during **pregnancy and childhood autism spectrum disorders**. Arch Gen Psychiatry 2011 Jul 4

Cronholm PF, Fogarty CT, Ambuel B, Harrison SL. **Intimate partner violence**. Am Fam Physician. 2011 May 15;83(10):1165-72.

Cross-Disorder Group of the Psychiatrics Genomics Consortium. Identification of risk **loci with shared effects on five major psychiatric disorders**: a genome-wide analysis. Lancet 2013; online Feb 28.

Crump C, Sundquist K, Winkleby MA, Sundquist J. **Mental disorders and vulnerability** to **homicidal death**: Swedish nationwide cohort study. BMJ 2013;346:f557.

Cuijpers P, Noma H, Karyotaki E, et al. Effectiveness and Acceptability of **Cognitive Behavior Therapy Delivery Formats** in Adults With Depression: A Network Meta-analysis. JAMA Psychiatry. 2019 Apr 17.

Cuijpers P, van Straten A, Smit F, Mihalopoulos C, Beekman A. Preventing the onset of depressive disorders: a meta-analytic review of psychological interventions. Am J Psychiatry. 2008 Oct;165(10):1272-80. Epub 2008 Sep 2.
Prevention of new cases of depressive disorders does seem to be possible. Prevention may become an important way, in addition to treatment, to reduce the enormous public health burden of depression in the coming years.

Cuijpers P, Hollon SD, van Straten A, et al. Does **cognitive behaviour therapy** have an enduring effect that is superior to keeping patients on continuation pharmacotherapy? A meta-analysis. BMJ Open. 2013 Apr 26;3(4).

Cuijpers P et al. **Interpersonal psychotherapy** for mental health problems: A comprehensive meta-analysis. Am J Psychiatry 2016 Apr 1.

da Silva J, Gonçalves-Pereira M, Xavier M, Mukaetova-Ladinska EB. **Affective disorders (depression) and risk of developing dementia**: systematic review. Br J Psychiatry. 2013 Mar;202:177-86.

Daly EJ, Singh JB, et al. Efficacy and Safety of **Intranasal Esketamine** Adjunctive to Oral Antidepressant Therapy in Treatment-Resistant Depression: A Randomized Clinical Trial. JAMA Psychiatry. 2017 Dec 27

Daly EJ, Trivedi MH, Janik A, et al. Efficacy of **Esketamine Nasal Spray Plus Oral Antidepressant Treatment for Relapse Prevention** in Patients With Treatment-Resistant Depression: A Randomized Clinical Trial. JAMA Psychiatry. 2019 Jun 5.

Danielsson B, Collin J, et al. **Antidepressants** and **antipsychotics** classified with **Torsades de Pointes** arrhythmia risk and mortality in older adults – a Swedish nationwide study. Br J Clin Pharmacol. 2015 Nov 17.

Davey CG, Chanen AM, Hetrick SE, et al. The addition of **fluoxetin**e to cognitive behavioural therapy for youth depression (YoDA-C): a randomised, double-blind, placebo-controlled, multicentre clinical trial. Lancet Psychiatry. 2019 Jul 29.

Davidson J, et al. Treatment of **Posttraumatic Stress Disorder With Venlafaxine** Extended Release: A 6-Month Randomized Controlled Trial. Arch Gen Psychiatry. 2006 Oct;63(10):1158-1165. n=329

Davidson KW, Rieckmann N, Clemow L, et al. Enhanced **depression care for patients with acute coronary syndrome** and persistent depressive symptoms: coronary psychosocial evaluation studies randomized controlled trial. Arch Intern Med. 2010 Apr 12;170(7):600-8.

Davidson KW, Bigger JT, et al. Centralized, stepped, patient preference-based treatment for patients with post-**acute coronary syndrome depression**: **CODIACS** Vanguard randomized controlled trial. JAMA Intern Med 2013.

Davis RN, Davis MM, Freed GL, Clark SJ. **Fathers' Depression** Related to Positive and Negative Parenting Behaviors With 1-Year-Old Children. Pediatrics. 2011 Mar 14.

de Graaf LE, Gerhards SA, Arntz A, et al. Clinical effectiveness of online computerised **cognitive-behavioural therapy** without support for depression in primary care: randomised trial. Br J Psychiatry. 2009 Jul;195(1):73-80.

de Groot M, Kollen BJ. Course of **bereavement** over 8-10 years in first degree relatives and spouses of people who **committed suicide**: longitudinal community based cohort study. BMJ. 2013 Oct 2;347:f5519.

De Vera MA, Bérard A. Antidepressant Use During **Pregnancy and the Risk of Pregnancy Induced Hypertension**. Br J Clin Pharmacol. 2012 Mar 21.

Dennis CL, et al. **Psychosocial and psychological interventions** for treating postpartum depression. Cochrane Database Syst Rev. 2007 Oct 17;(4):CD006116. Although the methodological quality of the majority of trials was, in general, not strong, the meta-analysis results suggest that psychosocial and psychological interventions are an effective treatment option for women suffering from postpartum depression.

Dennis M, Kadri A, Coffey J. Depression in **older people in the general hospital: a systematic review of screening** instruments. Age Ageing. 2012 Mar;41(2):148-54.

Depression scales The PHQ-9 is the 9 item depression scale of the Patient Health Questionnaire. The PHQ-9 is a powerful tool for assisting primary care clinicians in diagnosing depression as well as selecting and monitoring treatment. http://www.depression-primarycare.org/clinicians/toolkits/materials/forms/phq9/ **PHQ-2 Patient Health Questionnaire 2** about depressed mood and anhedonia: http://www.aafp.org/afp/20040915/1101.html

Deshauer D, Moher D, Fergusson D, et al. Selective serotonin reuptake inhibitors for unipolar depression: a systematic review of classic **long-term randomized controlled trials**. CMAJ. 2008 May 6;178(10):1293-301. There is a lack of classic randomized controlled trials of serotonin reuptake inhibitors lasting more than 1 year for the treatment of depression. The results of our systematic review support current recommendations for 6-8 months of antidepressant treatment following initial recovery but provide no guidance for longer treatment.

Desmarais JE, Looper KJ. Interactions between **tamoxifen and antidepressants via cytochrome P450 2D6**. J Clin Psychiatry. 2009 Dec;70(12):1688-97.

Dhillon S, Scott LJ, Plosker GL. **Escitalopram**: a review of its use in the management of anxiety disorders. CNS Drugs. 2006;20(9):763-90. Nevertheless, available clinical data indicate that escitalopram is an effective first-line treatment option for the management of GAD, SAD, panic disorder and OCD.

Diamond PR, Farmery AD, Atkinson S, et al. **Ketamine** infusions for treatment resistant depression: a series of 28 patients treated weekly or twice weekly in an ECT clinic. J Psychopharmacol. 2014 Apr 3.

Dias A, Azariah F, Anderson SJ, et al. Effect of a **lay counselor intervention** on prevention of major **depression in older adults living in low- and middle-income countries**: a randomized clinical trial [online Nov 7, 2018]. JAMA Psychiatry.

Diazgranados N, Ibrahim L, Brutsche NE, et al. A randomized add-on trial of an N-methyl-D-aspartate antagonist (**ketamine**) in treatment-resistant bipolar depression. Arch Gen Psychiatry. 2010 Aug;67(8):793-802.

Dickerson JF, Lynch FL, Leo MC, et al. **Cost-effectiveness of Cognitive Behavioral Therapy** for Depressed Youth Declining Antidepressants. Pediatrics. 2018 Jan 19.

Diem SJ et al. Rates of **bone loss among women initiating antidepressant** medication use in midlife. J Clin Endocrinol Metab 2013 Sep 3; [e-pub ahead of print].

Diez-Quevedo C, Masnou H, Planas R, et al. Prophylactic treatment with **escitalopram of pegylated interferon** alfa-2a-induced depression in hepatitis c: a 12-week, randomized, double-blind, placebo-controlled trial. J Clin Psychiatry. 2010 Oct 5.

Dinh KT, Reznor G, Muralidhar V, et al. Association of **Androgen Deprivation** Therapy With Depression in Localized Prostate Cancer. J Clin Oncol. 2016 Apr 11

Dobkin RD, Menza M, Allen LA, et al. **Cognitive-behavioral therapy for depression in Parkinson's** disease: a random ized, controlled trial. Am J Psychiatry 2011; 168:1066–1074.

Domar AD, Moragianni VA, Ryley DA, et al. The risks of **selective serotonin reuptake inhibitor use in infertile women**: a review of the impact on fertility, pregnancy, neonatal health and beyond. Hum Reprod. 2012 Oct 31.
Doshi P. Putting **GlaxoSmithKline to the test over paroxetine**. BMJ. 2013 Nov 12;347:f6754.
Douros A, Dell'Aniello S, Dehghan G, et al. Degree of serotonin reuptake inhibition of **antidepressants and ischemic risk**: A cohort study. Neurology. 2019 Sep 3;93(10):e1010-e1020.
Dowlati Y, Herrmann N, Swardfager WL, Reim EK, Lanctôt KL. Efficacy and tolerability of antidepressants for treatment of depression in **coronary artery disease**: a meta-analysis. Can J Psychiatry. 2010 Feb;55(2):91-9.
Dowlati Y et al. Selective **dietary supplementation in early postpartum** is associated with high resilience against depressed mood. Proc Natl Acad Sci U S A 2017 Mar 28; 114:3509.
Downar J, Blumberger DM, Daskalakis ZJ. **Repetitive transcranial magnetic stimulation**: an emerging treatment for medication-resistant depression. CMAJ. 2016 Nov 1;188(16):1175-1177
Donneyong MM, Bykov K, Bosco-Levy P, et al. Risk of **mortality** with concomitant use of **tamoxifen and selective serotonin reuptake inhibitors**: multi-database cohort study. BMJ. 2016 Sep 30;354:i5014.
Dowrick C, Frances A. **Medicalising unhappiness**: new classification of depression risks more patients being put on drug treatment from which they will not benefit. BMJ. 2013 Dec 9;347:f7140
Driessen E et al. The efficacy of **cognitive-behavioral therapy and psychodynamic therapy** in the outpatient treatment of major depression: A randomized clinical trial. Am J Psychiatry 2013 Sep 1; 170:1041.
Drudi LM, Ades M, et al. Association of depression with mortality in older adults **undergoing transcatheter or surgical aortic valve replacement** [online Jan 17, 2018].JAMA Cardiol. doi:10.1001/jamacardio.2017 .5064
Drug and Therapeutics Bulletin. Management of **seasonal affective disorder.** BMJ. 2010 May 21;340:c2135. doi: 10.1136/bmj.c2135.
Drummond N, McCleary L, Freiheit E, et al. **Antidepressant and antipsychotic** prescribing in primary care for **people with dementia**. Can Fam Physician. 2018 Nov;64(11):e488-e497.
Dudas R, Malouf R, McCleery J, et al. **Antidepressants for treating depression in dementia**. Cochrane Database Syst Rev. 2018 Aug 31;8:CD003944. The available evidence is of variable quality and does not provide strong support for the efficacy of antidepressants for treating depression in dementia, especially beyond 12 weeks. On the only measure of efficacy for which we had high-quality evidence (depression rating scale scores), antidepressants showed little or no effect. The evidence on remission rates favoured antidepressants but was of moderate quality, so future research may find a different result. There was insufficient evidence to draw conclusions about individual antidepressant drugs or about subtypes of dementia or depression. There is some evidence that antidepressant treatment may cause adverse events.
Duan-Porter W, Goldstein KM, McDuffie JR, et al. Reporting of **Sex Effects** by Systematic Reviews on Interventions for Depression, Diabetes, and Chronic Pain. Ann Intern Med. 2016 Aug 2;165(3):184-93
Duckworth K, Gilbody S. Should **Google offer an online screening test for depression**? BMJ. 2017 Sep 13;358:j4144
Dunlop BW et al. **Functional connectivity of the subcallosal cingulate cortex** and differential outcomes to treatment with **cognitive-behavioral therapy or antidepressant medication** for major depressive disorder. Am J Psychiatry 2017 Mar 24.
Dunlop BW et al. Effects of **patient preferences** on outcomes in the **Predictors of Remission** in Depression to Individual and Combined Treatments (**PReDICT**) Study. Am J Psychiatry 2017 Mar 24.
Dunlop BW, LoParo D, Kinkead B, et al. Benefits of Sequentially **Adding Cognitive-Behavioral Therapy or Antidepressant Medication for Adults With Nonremitting Depression**. Am J Psychiatry. 2019 Feb 15:appiajp201818091075.
Durand JP, Deplanque G, Montheil V, et al. Efficacy of **venlafaxine for the prevention and relief of oxaliplatin-induced acute neurotoxicity**: results of EFFOX, a randomized, double-blind, placebo-controlled phase III trial. Ann Oncol. 2011 Mar 22.
Earnshaw VA, Elliot MN, Reisner SL, et al. **Peer Victimization**, depressive symptoms, and **substance use**: A longitudinal analysis. Pediatrics. 2017;139(6):e20163426
Eating Disorder Treatment. Pharmacist's Letter. Aug 2006.
Earls, Marian F., THE COMMITTEE ON PSYCHOSOCIAL ASPECTS OF CHILD AND FAMILY HEALTH, Clinical Report--Incorporating Recognition and Management of **Perinatal and Postpartum Depression** Into Pediatric Practice. Pediatrics 2010 0: peds.2010-2348.
Earls MF, Yogman MW, Mattson G, et al; Committee on psychosocial aspects of child and family health. Incorporating **Recognition and Management of Perinatal Depression** Into Pediatric Practice. Pediatrics. 2018 Dec 17.
Eberhard-Gran M, Eskild A, Opjordsmoen S. Use of Psychotropic Medications in Treating Mood Disorders during **Lactation** : Practical Recommendations. CNS Drugs. 2006;20(3):187-98.

Elderly

[Baldwin RC, Anderson D, Black S, et al; Faculty of Old Age Psychiatry Working Group, Royal College of Psychiatrists. Guideline for the management of late-life depression in primary care. Int J Geriatr Psychiatry. 2003 Sep;18(9):829-38.
Charney et al. Depression and Bipolar Support Alliance. Depression and Bipolar Support Alliance consensus statement on the unmet needs in diagnosis and treatment of mood disorders in late life. Arch Gen Psychiatry. 2003 Jul;60(7):664-72.
Cooper C, Katona C, Lyketsos K, et al. A Systematic Review of Treatments for Refractory Depression in Older People. Am J Psychiatry. 2011 Mar 31.
Coupland C, Dhiman P, Morriss R, et al. Antidepressant use and risk of **adverse outcomes in older people**: population based cohort study. BMJ. 2011 Aug 2;343:d4551. doi: 10.1136/bmj.d4551.
Coupland CA, Dhiman P, Barton G, et al. A study of the **safety and harms of antidepressant drugs for older people**: a cohort study using a large primary care database. Health Technol Assess. 2011 Aug;15(28):1-202, iii-iv.
Cuijpers P, van Straten A, Smit F. Psychological treatment of late-life depression: a meta-analysis of randomized controlled trials. Int J Geriatr Psychiatry. 2006 Dec;21(12):1139-49.
Dombrovski AY, Mulsant BH. The evidence for electroconvulsive therapy (ECT) in the treatment of severe late-life depression. ECT: the preferred treatment for severe depression in late life. Int Psychogeriatr. 2007 Feb;19(1):10-4, 27-35; discussion 24-6.
Frank C. Pharmacologic treatment of **depression in the elderly**. Can Fam Physician. 2014 Feb;60(2):121-6.
Keller MB, McCullough JP, Klein DN, et al. A comparison of nefazodone, the cognitive behavioral-analysis system of psychotherapy, and their combination for the treatment of chronic depression. N Engl J Med. 2000 May 18;342(20):1462-70.
Kiosses DN, Ravdin LD, Gross JJ, et al. **Problem Adaptation Therapy** for Older Adults With Major Depression and Cognitive Impairment: A Randomized Clinical Trial. JAMA Psychiatry. 2014 Nov 5.
Lavretsky H et al. **Citalopram, methylphenidate, or their combination in geriatric depression**: A randomized, double-blind, placebo-controlled trial. Am J Psychiatry 2015 Feb 13.
Lenze EJ, Mulsant BH, Blumberger D, et al. Efficacy, safety, and tolerability of **augmentation pharmacotherapy** with **aripiprazole** for treatment-resistant depression in late life: a randomised, double-blind, placebo-controlled trial. Lancet 2015; online Sept 28.
MacQueen GM, Frey BN, Ismail Z, et al. Canadian Network for Mood and Anxiety Treatments (CANMAT) 2016 clinical guidelines for the management of adults with major depressive disorder: Section 6. youth, women, and the **elderly**. Can J Psychiatry. 2016;61(9):588-603.
Mojtabai R. **Diagnosing depression in older adults in primary care**. N Engl J Med. 2014 Mar 27;370(13):1180-2.
Mottram P, Wilson K, Strobl J. Antidepressants for depressed elderly. Cochrane Database Syst Rev. 2006 Jan 25;(1):CD003491. Our findings suggest that SSRIs and TCAs are of the same efficacy. However, we have found some evidence suggesting that TCA related antidepressants and classical TCAs may have different side effect profiles and are associated with differing withdrawal rates when compared with SSRIs.
Mukai Y, Tampi RR. Treatment of depression in the elderly: A review of the recent literature on the efficacy of single- versus dual-action antidepressants. Clin Ther. 2009 May;31(5):945-61. The available data, although limited, suggest that the dual-action agents (TCAs and SNRIs) do not appear to confer any additional benefits in efficacy over single-action agents (SSRIs) in the treatment of depression in the elderly.
Pinquart M, Duberstein PR, Lyness JM. Treatments for later-life depressive conditions: a meta-analytic comparison of pharmacotherapy and psychotherapy. Am J Psychiatry. 2006 Sep;163(9):1493-501. Given that psychotherapy and pharmacotherapy did not show strong differences in effect sizes, treatment choice should be based on other criteria, such as contraindications, treatment access, or patient preferences.
Reynolds CF 3rd, Frank E, Perel JM, et al. Nortriptyline and interpersonal psychotherapy as maintenance therapies for recurrent major depression: a randomized controlled trial in patients older than 59 years. JAMA. 1999 Jan 6;281(1):39-45.
Reynolds CF 3rd, et al. **Maintenance treatment** of major depression in **old age**. N Engl J Med. 2006 Mar 16;354(11):1130-8. CONCLUSIONS: Patients elderly 70 years of age or older with major depression who had a response to initial treatment with paroxetine and psychotherapy were less likely to have recurrent depression if they received two years of maintenance therapy with paroxetine. Monthly maintenance psychotherapy did not prevent recurrent depression. (InfoPOEMs: Prolonged treatment with paroxetine (Paxil) reduces the risk of recurrence of major depression in elderly patients. (LOE = 1b))
Rodda J, Walker Z, Carter J. Depression in **older adults**. BMJ. 2011 Sep 28;343:d5219. doi: 10.1136/bmj.d5219.
Sheline YI, Disabato BM, Hranilovich J, et al. Treatment course with antidepressant therapy in **late-life depression**. Am J Psychiatry. 2012 Nov 1;169(11):1185-93
Sjösten N, Kivelä SL. The effects of physical exercise on depressive symptoms among the aged: a systematic review. Int J Geriatr Psychiatry. 2006 May;21(5):410-8.
Sobieraj DM, Martinez BK, Hernandez AV, et al. Adverse Effects of Pharmacologic Treatments of Major Depression in Older Adults. J Am Geriatr Soc. 2019 May 29.
Steiner AJ, et al. Quality of Life, Functioning, and Depressive Symptom Severity in **Older Adults With Major Depressive Disorder Treated With Citalopram** in the **STAR*D** Study. J Clin Psychiatry. 2017 Jul;78(7):897-903.
Taylor WD. Clinical practice. **Depression in the elderly**. N Engl J Med. 2014 Sep 25;371(13):1228-36.

Thorlund K, Druyts E, Wu P, et al. Comparative efficacy and safety of **selective serotonin reuptake inhibitors and serotonin-norepinephrine reuptake inhibitors in older adults**: a network meta-analysis. J Am Geriatr Soc 2015;63:1002–9. (sertraline, paroxetine, duloxetine options)

Unützer J. Clinical practice. **Late-life depression**. N Engl J Med. 2007 Nov 29;357(22):2269-76.

Unützer J, Park M. Older adults with severe, treatment-resistant depression. JAMA. 2012 Sep 5;308(9):909-18.

Wilkinson P, Izmeth Z. **Continuation and maintenance treatments for depression in older people**. Cochrane Database Syst Rev. 2012 Nov 14;11:CD006727. doi: 10.1002/14651858.CD006727.pub2. The long-term benefits of continuing antidepressant medication in the prevention of recurrence of depression in older people are not clear and no firm treatment recommendations can be made on the basis of this review.

Wilkinson P, Izmeth Z. **Continuation and maintenance treatments for depression in older people**. Cochrane Database Syst Rev. 2016 Sep 9;9:CD006727. This updated Cochrane review supports the findings of the original 2012 review. The long-term benefits and harm of continuing antidepressant medication in the prevention of recurrence of depression in older people are not clear and no firm treatment recommendations can be made on the basis of this review. Continuing antidepressant medication for 12 months appears to be helpful with no increased harms; however, this was based on only three small studies, relatively few participants, use of a range of antidepressant classes, and clinically heterogeneous populations. Comparisons at other time points did not reach statistical significance.Data on psychological therapies and combined treatments were too limited to draw any conclusions on benefits and harms.The quality of the evidence used in reaching these conclusions was low and the review does not, therefore, offer clear guidance to clinicians and patients on best practice and matching interventions to particular patient characteristics.Of note, we identified no new studies that evaluated pharmacological or psychological interventions in the continuation and maintenance treatment of depression in older people. We are aware of studies conducted since the previous review that included both older people and adults under the age of 65 years, but these fall outside of the remit of this review. We believe that there remains a need for studies solely recruiting older people, particularly the `older old` with comorbid medical problems. However, these studies are likely to be challenging to conduct and may not, so far, have been prioritised by funders.

Wilson K, Mottram P. A comparison of side effects of selective serotonin reuptake inhibitors and tricyclic antidepressants in older depressed patients: a meta-analysis. Int J Geriatr Psychiatry. 2004 Aug;19(8):754-62.]

Ein N, Armstrong B, Vickers K The effect of a **very low calorie diet on subjective depressive symptoms and anxiety**: meta-analysis and systematic review. Int J Obes (Lond). 2018 Nov 23.

Eke AC, Saccone G, Berghella V. **Selective serotonin reuptake inhibitor (SSRI) use during pregnancy** and **risk of preterm birth**: a systematic review and meta-analysis. BJOG. 2016 Nov;123(12):1900-1907.

Ellard DR, Thorogood M, Underwood M, et al. **Whole home exercise** intervention for depression in older care home residents (the OPERA study): a process evaluation. BMC Med. 2014 Jan 3;12(1):1

Emslie GJ, Ventura D, Korotzer A, Tourkodimitris S. **Escitalopram in the Treatment of Adolescent Depression**: A Randomized Placebo-Controlled Multisite Trial. J Am Acad Child Adolesc Psychiatry. 2009 May 20. [Epub ahead of print]. In this study, escitalopram was effective and well tolerated in the treatment of depressed adolescents.

Emslie GJ, Mayes T, Porta G, et al. Treatment of **Resistant Depression in Adolescents** (**TORDIA**): Week 24 Outcomes. Am J Psychiatry. 2010 May 17.

Ensrud KE, et al. for Study of Osteoporotic Fractures Research Gp. Use of **selective serotonin reuptake inhibitors** and **sleep** disturbances in community-dwelling older women. J Am Geriatr Soc 2006 Oct;54(10):1508-15.

Erkkilä J, Punkanen M, Fachner J, et al. Individual **music therapy** for depression: randomised controlled trial. Br J Psychiatry. 2011 Aug;199(2):132-9.

Ernstsen L, Rangul V, Nauman J, et al. Protective Effect of Regular **Physical Activity** on Depression After Myocardial Infarction: The HUNT Study. Am J Med. 2016 Jan;129(1):82-88.e1.

Etminan M, Mikelberg FS, Brophy JM. Selective **Serotonin Reuptake Inhibitors** and the Risk of **Cataracts** A Nested Case-Control Study. Ophthalmology. 2010 Mar 6.

Everitt H, Baldwin DS, Stuart B, et al. Antidepressants for insomnia in adults. Cochrane Database Syst Rev. 2018 May 14;5:CD010753. We identified relatively few, mostly small studies with short-term follow-up and design limitations. The effects of SSRIs compared with placebo are uncertain with too few studies to draw clear conclusions. There may be a small improvement in sleep quality with short-term use of low-dose doxepin and trazodone compared with placebo. The tolerability and safety of antidepressants for insomnia is uncertain due to limited reporting of adverse events. There was no evidence for amitriptyline (despite common use in clinical practice) or for long-term antidepressant use for insomnia. High-quality trials of antidepressants for insomnia are needed.

Everson-Rose SA, Roetker NS, Lutsey PL, et al. Chronic Stress, Depressive Symptoms, Anger, Hostility, and Risk of Stroke and Transient Ischemic Attack in the Multi-Ethnic Study of Atherosclerosis. Stroke. 2014 Jul 10.

Eyding D, Lelgemann M, Grouven U, et al. Reboxetine for acute treatment of major depression: systematic review and meta-analysis of published and unpublished placebo and selective serotonin reuptake inhibitor controlled trials. BMJ. 2010 Oct 12;341:c4737. doi: 10.1136/bmj.c4737.

Fancher TL, Kravitz RL. **In the clinic. Depression**. Ann Intern Med. 2010 May 4;152(9):ITC51-15; quiz ITC5-16.

Fancourt D, Perkins R Effect of **singing interventions** on symptoms of postnatal depression: three-arm randomised controlled trial. Br J Psychiatry. 2018 Feb;212(2):119-121.

Fang F et al. **Suicide and cardiovascular death after a cancer diagnosis**. N Engl J Med 2012 Apr 5; 366:1310.

Fann JR, Bombardier CH, Richards JS, et al; for the **PRISMS** Investigators. **Venlafaxine** Extended-Release for Depression Following **Spinal Cord Injury**: A Randomized Clinical Trial. JAMA Psychiatry. 2015 Jan 21.

Farah WH, Alsawas M, Mainou M, et al. **Non-pharmacological treatment of depression**: a systematic review and evidence map. Evid Based Med. 2016 Dec;21(6):214-221.

Fardet L et al. Suicidal behavior and severe **neuropsychiatric disorders following glucocorticoid** therapy in primary care. Am J Psychiatry 2012 May 1; 169:491.

Fava M, et al. Efficacy and safety of **sildenafil** in men with **serotonergic antidepressant-associated erectile dysfunction**: results from a randomized, double-blind, placebo-controlled trial.J Clin Psychiatry.2006Feb;67(2):240-6.

Fava M, Rush AJ, Wisniewski SR, et al. A Comparison of Mirtazapine and Nortriptyline Following Two Consecutive Failed Medication Treatments for Depressed Outpatients: A **STAR*D** Report. Am J Psychiatry. 2006 Jul;163(7):1161-72. Following lack of remission or an inability to tolerate an initial trial of citalopram for up to 12 weeks (first step) and a second trial with either monotherapy involving another antidepressant or augmentation of citalopram with bupropion or buspirone (second step), adult outpatients (N=235) with nonpsychotic major depressive disorder were randomly assigned to 14 weeks of treatment with mirtazapine (up to 60 mg/day) (N=114) or nortriptyline (up to 200 mg/day) (N=121). For mirtazapine, remission rates were 12.3% and 8.0% per the Hamilton and QIDS-SR(16) scores, respectively. For nortriptyline, remission rates were 19.8% and 12.4%, respectively

Faye E, Corcos O, Lancelin F, et al. Antidepressant agents in **short bowel syndrome**. Clin Ther. 2014 Dec 1;36(12):2029-2033.e3.

Fazel S, Wolf A, Chang Z, et al. **Depression and violence**: a Swedish population study. Lancet Psychiatry. 2015 Mar

FDA: Oct/06 Letter regarding venlafaxine overdose concern http://www.fda.gov/medwatch/safety/2006/effexor_DHCPletter.pdf

FDA: Aug/11 Antidepressant citalopram (Celexa, Forest Laboratories) should not be used in doses higher than 40 mg per day because of concerns that it can cause potentially fatal changes in heart rhythm.

FDA: Dec/11 Selective Serotonin Reuptake Inhibitor Antidepressants: Use During Pregnancy & Potential Risk of Persistent Pulmonary Hypertension of the Newborn http://www.fda.gov/Safety/MedWatch/SafetyInformation/SafetyAlertsforHumanMedicalProducts/ucm283696.htm

FDA Aug/13 Health and Beyond LLC is voluntarily recalling quantity lots of product **Tranquility**. The products have been found to contain a trace of Doxepin which is a pharmaceutical for sleep and Chlorpormazine for psychotic disorders.

FDA Jun/14 laboratory analysis confirmed that **Sport Burner & Toxin Discharged Tea** contains fluoxetine.

FDA Feb/15 laboratory analysis confirmed that **Botanical Slimming (Red), & Oxy ELITE Pro Super Thermogenic** (Lot# 216732, Exp. 04/17) contains fluoxetine.

FDA July 15:**Botanical Slimming (Red) & Xcel** contains Undeclared fluoxetine.

FDA July 15:**Natural Max Slimming** contains Undeclared sildenafil, fluoxetine, andsibutramine.

FDA Jul/15 is warning health care professionals and patients that reports of confusion between the antidepressant **Brintellix** and anti-blood clotting medication **Brilinta** have resulted in the wrong medication being prescribed.

FDA Nov/15 laboratory analysis confirmed that **Perfect Slim Fast Track Slim & Slyn Both** contains fluoxetine.

FDA May/16 has approved a brand name change for the antidepressant Brintellix (**vortioxetine**) to decrease the risk of prescribing and dispensing errors resulting from name confusion with the blood-thinning medicine Brilinta (ticagrelor). The new brand name of the drug will be **Trintellix**.

Fenger-Grøn M, Vestergaard M, Pedersen HS, Frost L, et al. Depression, antidepressants, and **the risk of non-valvular atrial fibrillation**: A nationwide Danish matched cohort study. Eur J Prev Cardiol. 2018 Nov 19:2047487318811184.

Ferenchick EK, Ramanuj P, Pincus HA**. Depression in primary care**: part 1-screening and diagnosis. BMJ. 2019 Apr 8;365:l794.
Ferrari AJ, Charlson FJ, Norman RE, et al. **Burden of depressive disorders by country, sex, age, and year**: findings from the **global** burden of disease study 2010. PLoS Med. 2013 Nov;10(11):e1001547.
Fink M, Taylor MA. **Electroconvulsive therapy**: evidence and challenges. JAMA. 2007 Jul 18;298(3):330-2.
Fisher HL, Moffitt TE, Houts RM, et al. **Bullying victimisation** and risk of **self harm** in early adolescence: longitudinal cohort study. BMJ. 2012 Apr 26;344:e2683.
Flint AJ, Meyers BS, Rothschild AJ, et al. Effect of Continuing **Olanzapine vs Placebo on Relapse** Among Patients With Psychotic Depression in Remission: The STOP-PD II Randomized Clinical Trial. JAMA. 2019 Aug 20;322(7):622-631.
FOCUS Trial Collaboration. Effects of **fluoxetine on functional outcomes after acute stroke (FOCUS**): a pragmatic, double-blind, randomised, controlled trial. Lancet 2018; online Dec 5.
Foong AL, Grindrod KA, Patel T, et al. **Demystifying serotonin syndrome (or serotonin toxicity**). Can Fam Physician. 2018 Oct;64(10):720-727.
Foong AL, Patel T, Kellar J, Grindrod KA. The **scoop on serotonin syndrome**. Can Pharm J (Ott). 2018 May 30;151(4):233-239.
Ford AC, Quigley EM, Lacy BE, et al. Effect of **antidepressants and psychological therapies, including hypnotherapy, in irritable bowel syndrome**: systematic review and meta-analysis. Am J Gastroenterol. 2014 Sep;109(9):1350-65; quiz 1366.
Ford AC, Lacy BE, Harris LA, et al. **Effect of Antidepressants and Psychological Therapies in Irritable Bowel Syndrome: An Updated Systematic Review and Meta-analysis.** Am J Gastroenterol. 2018 Sep 3.
Forman-Hoffman V, McClure E, McKeeman J, et al. **Screening for major depressive disorder in children and adolescents**: a systematic review for the U.S. Preventive Services Task Force (**USPSTF**). Ann Intern Med. 2016.
Fournier Jay C.; DeRubeis Robert J.; Hollon Steven D.; et al. **Antidepressant Drug Effects and Depression Severity**: A Patient-Level Meta-analysis. JAMA. 2010;303(1):47-53.
Frank C. Pharmacologic treatment of **depression in the elderly**. Can Fam Physician. 2014 Feb;60(2):121-6.
Frank CR, Xiang X, Stagg BC, et al. Longitudinal Associations of **Self-reported Vision Impairment** With Symptoms of Anxiety and Depression Among Older Adults in the United States. JAMA Ophthalmol. 2019 May 16.
Freedland KE, Carney RM, Rich MW, Steinmeyer BC, Rubin EH. **Cognitive behavior therapy** for depression and self-care in heart failure patients: a randomized clinical trial [online September 28]. JAMA Intern Med. doi:10.1001 /jamainternmed.2015.5220.
Freeman MP, Mischoulon D, Tedeschini E, et al. **Complementary and alternative medicine for major depressive** disorder: a meta-analysis of patient characteristics, placebo-response rates, and treatment outcomes relative to standard antidepressants. J Clin Psychiatry. 2010 Jun;71(6):682-8. Participants in CAM trials were more likely to be female and to have a lower placebo-response rate compared to those in standard antidepressant trials for MDD. Trials of standard antidepressants and CAM therapies were composed of patients with similar depression severity.
Freeman Ellen W., Guthrie Katherine A., Caan Bette, et al. Efficacy of **Escitalopram for Hot Flashes** in Healthy Menopausal Women: A Randomized Controlled Trial. JAMA. 2011;305(3):267-274.doi:10.1001/jama.2010.2016.
Freeman EW, Sammel MD, Boorman DW, Zhang R. Longitudinal Pattern of **Depressive Symptoms Around Natural Menopause**. JAMA Psychiatry. 2013 Nov 13.
Friedman RA. **Antidepressants' black-box warning**--10 years later. N Engl J Med. 2014 Oct 30;371(18):1666-8.
Frolkis AD, Vallerand IA, Shaheen AA, et al. **Depression increases the risk of inflammatory bowel disease**, which may be **mitigated by the use of antidepressants in the treatment of depression**. Gut. 2018 Oct 18.
Furey ML, Drevets WC. Antidepressant efficacy of the antimuscarinic drug **scopolamine**: a randomized, placebo-controlled clinical trial. Arch Gen Psychiatry. 2006 Oct;63(10):1121-9.
Furu K, Kieler H, Haglund B, et al. **Selective serotonin reuptake inhibitors and venlafaxine in early pregnancy** and risk of birth defects: population based cohort study and sibling design. BMJ. 2015 Apr 17;350:h1798.
Furukawa TA. Adverse effects of **antidepressants during pregnancy**. Evid Based Ment Health. 2014 Nov;17(4):103-4.
Furukawa TA, Cipriani A, et al. **Placebo response rates in antidepressant trials**: a systematic review of published and unpublished double-blind randomised controlled studies. Lancet Psychiatry. 2016 Nov;3(11):1059-1066.
Furukawa TA, Cipriani A, Cowen PJ, et al. Optimal dose of selective serotonin reuptake inhibitors, **venlafaxine, and mirtazapine** in major depression: a systematic review and dose-response meta-analysis. Lancet Psychiatry. 2019 Jul;6(7):601-609.
Furukawa TA, Weitz ES, Tanaka S, et al. Initial severity of depression and efficacy of **cognitive-behavioural therapy**: individual-participant data meta-analysis of pill-placebo-controlled trials. Br J Psychiatry. 2017 Jan 19.
Furukawa TA, Cipriani A, Leucht S, et al. **Is placebo response in antidepressant trials rising or not**? A reanalysis of datasets to conclude this long-lasting controversy. Evid Based Ment Health. 2018 Feb;21(1):1-3.
Furukawa TA. Choosing the optimum strategy for rTMS. Evid Based Ment Health. 2018 May;21(2):77-78.
Gabriel M, Sharma V. **Antidepressant discontinuation syndrome**. CMAJ. 2017 May 29;189(21):E747.
Gafoor R, Booth HP, Gulliford MC. Antidepressant utilisation and incidence of **weight gain** during 10 years' follow-up: population based cohort study. BMJ 2018;361:k1951.
Gallo JJ, Morales KH, Bogner HR, et al. Long term effect of depression **care management on mortality in older adults**: follow-up of cluster randomized clinical trial in primary care. BMJ. 2013 Jun 5;346:f2570.
Gamble J, Creedy D, Moyle W, Webster J, McAllister M, Dickson P. Effectiveness of a counseling intervention after traumatic childbirth: A randomized trial. Birth 2005; 32:11-19. (InfoPOEMs: Women with trauma symptoms who receive face-to-face counseling during their hospital stay and phone counseling at 4 to 6 weeks postpartum are less likely to have persistent trauma symptoms or postpartum depression at 3 months. (LOE = 1b-))
Gamble JJ, Bi H, Bowen R, et al. **Ketamine-based anesthesia improves electroconvulsive therapy outcomes**: a randomized-controlled study. Can J Anaesth. 2018 Jun;65(6):636-646.
Gamble JM, Chibrikov E, Midodzi WK, et al. Examining the **risk of depression or self-harm associated with incretin-based therapies used to manage hyperglycaemia in patients with type 2 diabetes**: a cohort study using the UK Clinical Practice Research Datalink. BMJ Open. 2018 Oct 8;8(10):e023830.
Gandhi S, Shariff SZ, Al-Jaishi A, et al. **Second-Generation Antidepressants** and **Hyponatremia** Risk: A Population-Based Cohort Study of Older Adults. Am J Kidney Dis. 2016 Oct 20. pii: S0272-6386(16)30480-2.
Gao J, Lin M, Zhao J, et al. Different interventions for **post-ischaemic stroke depression** in different time periods: A single-blind randomized controlled trial with stratification by time after stroke. Clin Rehabil. 2016 Jan 27.
Gao SY, Wu QJ, Zhang TN, et al. **Fluoxetine and congenital malformations**: a systematic review and meta-analysis of cohort studies. Br J Clin Pharmacol. 2017 May 17
Garber J et al. Prevention of **depression in at-risk adolescents**: A randomized controlled trial. *JAMA* 2009 Jun 3; 301:2215. The **CB prevention program** had a significant prevention effect through the 9-month follow-up period based on both clinical diagnoses and self-reported depressive symptoms, but this effect was not evident for adolescents with a currently depressed parent.
Garcia ME, Ochoa-Frongia L, Moise N, et al. **Collaborative Care** for Depression among Patients with **Limited English Proficiency**: a Systematic Review. J Gen Intern Med. 2017 Dec 18.
Garland J, Virani A, Kutcher S. **CACAP 2008** position paper on using **SSRIs in children and adolescents** [Internet]. Ottawa: Canadian Academy of Child and Adolescent Psychiatry; 2008
Gartlehner G, Gaynes BN, Hansen RA, et al. Comparative **benefits and harms of second-generation antidepressants**: background paper for the American College of Physicians. Ann Intern Med. 2008 Nov 18;149(10):734-50.
Gartlehner G, Thaler K, Hansen RA, Gaynes BN. The general and comparative efficacy and safety of **duloxetine** in major depressive disorder: a systematic review and meta-analysis. Drug Saf. 2009;32(12):1159-73. doi: 10.2165/11318930-000000000-00000.
Gartlehner G, Hansen RA, Morgan LC, et al. Comparative Benefits and Harms of **Second-Generation Antidepressants** for Treating Major Depressive Disorder: An Updated Meta-analysis. Ann Intern Med. 2011 Dec 6;155(11):772-85. Current evidence does not warrant recommending a particular second-generation antidepressant on the basis of differences in efficacy. Differences in onset of action and adverse events may be considered when choosing a medication.
Gartlehner G, Nussbaumer B, Gaynes BN, et al. **Second-generation antidepressants for preventing seasonal affective disorder** in adults. Cochrane Database of Systematic Reviews 2015, Issue 11. Art. No.: CD011268. DOI: 10.1002/14651858.CD011268.pub2. Available evidence indicates that bupropion XL is an effective intervention for prevention of recurrence of SAD. Nevertheless, even in a high-risk population, four of five patients will not benefit from preventive treatment with bupropion XL and will be at risk for harm. Clinicians need to discuss with patients advantages and disadvantages of preventive SGA treatment and might want to consider offering other potentially efficacious interventions, which might confer lower risk of adverse events. Given the lack of comparative evidence, the decision for or against initiating preventive treatment of SAD and the treatment selected should be strongly based on patient preferences.
Gartlehner G, Gaynes BN, et al. **Comparative benefits & harms of antidepressants, psychological, complementary, & exercise treatments for major depression**: systematic review and meta-analysis. Ann Intern Med. 2016.
Gazewood JD, Slayton P, Degeorge K. **Vilazodone** (Viibryd) for the treatment of depression. Am Fam Physician. 2013 Aug 15;88(4):263-4.

Gebara MA, Shea ML, Lipsey KL, et al. Depression, Antidepressants, and **Bone Health** in Older Adults: A Systematic Review.J Am Geriatr Soc. 2014 Jul 15.
Gellis ZD, Kang-Yi C. Meta-analysis of the effect of **cardiac rehabilitation interventions on depression** outcomes in adults 64 years of age and older. Am J Cardiol. 2012 Nov 1;110(9):1219-24.
Georgakis MK, Thomopoulos TP, Diamantaras AA, et al. Association of **Age at Menopause and Duration of Reproductive Period With Depression After Menopause**: A Systematic Review and Meta-analysis. JAMA Psychiatry. 2016 Jan 6:1-12.
George MS, Lisanby SH, Avery D, et al. Daily left prefrontal **transcranial magnetic stimulation** (TMS) therapy for major depressive disorder: a sham-controlled randomized trial. Arch Gen Psychiatry. 2010 May;67(5):507-16.
Gerstein HC, Marcovina S, Akpunonu BE, et al. Association of **Depression With Accelerated Cognitive Decline** Among Patients With Type 2 **Diabetes in the ACCORD-MIND** Trial. JAMA Psychiatry. 2013 Aug 14.
Geschwind N, Peeters F, Huibers M, et al. Efficacy of **mindfulness-based cognitive therapy** in relation to prior history of depression: randomised controlled trial. Br J Psychiatry. 2012 Oct;201(4):320-5.
Gibbons RD, Brown CH, Hur K, et al. **Suicidal** Thoughts & Behavior With Antidepressant Treatment: Reanalysis of the Randomized Placebo-Controlled Studies of **Fluoxetine and Venlafaxine**. Arch Gen Psychiatry. 2012 Feb 6
Gibbons RD, Hur K, Brown CH, et al. **Benefits From Antidepressants**: Synthesis of 6-Week Patient-Level Outcomes From Double-blind Placebo-Controlled Randomized Trials of Fluoxetine and Venlafaxine. Arch Gen Psychiatry. 2012 Mar 5.
Gijsman HJ, Geddes JR, Rendell JM, et al. Antidepressants for bipolar depression: a systematic review of randomized, controlled trials. Am J Psychiatry. 2004 Sep;161(9):1537-47.
Gilbody S, Bower P, Fletcher J, Richards D, Sutton AJ. Collaborative Care for Depression: A Cumulative Meta-analysis and Review of **Longer-term Outcomes**. Arch Intern Med. 2006 Nov 27;166(21):2314-21.
Gilbody S, House A, Sheldon T, Gilbody S. **Screening** and case finding instruments for depression. Cochrane Database Syst Rev. 2005 Oct 19;(4):CD002792. AUTHORS' CONCLUSIONS: There is substantial evidence that routinely administered case finding/screening questionnaires for depression have minimal impact on the detection, management or outcome of depression by clinicians. Practice guidelines and recommendations to adopt this strategy, in isolation, in order to improve the quality of healthcare should be resisted. The longer term benefits and costs of routine screening/case finding for depression have not been evaluated. A two stage procedure for screening/case finding may be effective, but this needs to be evaluated in a large scale cluster randomised trial, with a prospective economic evaluation.
Gilbody S, Littlewood E, Hewitt C, et al, on behalf of the **REEACT** Team. **Computerised cognitive behaviour therapy** (**cCBT**) as treatment for depression in primary care (REEACT trial): large scale pragmatic randomised controlled trial. BMJ 2015;351:h5627.
Gilbody S, Lewis H, Adamson J, et al. Effect of **collaborative care** vs usual care on depressive symptoms in older adults with subthreshold depression: the CASPER randomized clinical trial. JAMA. doi:10.1001/jama.2017.0130
Gilliam FG, Black K, Carter J, et al. A Trial of **Sertraline or Cognitive Behavior Therapy** for Depression in Epilepsy. Ann Neurol. 2019 Jul 29.
Gilman SE, Sucha E, Kingsbury M, et al. **Depression and mortality** in a longitudinal study: 1952-2011. CMAJ. 2017 Oct 23;189(42):E1304-E1310.
Gitlin LN, Harris LF, McCoy MC, et al. A **home-based intervention** to reduce depressive symptoms and improve quality of life in older african americans: a randomized trial. Ann Intern Med. 2013 Aug 20;159(4):243-52.
Gladstone TRG, Terrizzi DA, Paulson A, et al. Effect of Internet-Based **Cognitive Behavioral Humanistic and Interpersonal Training vs Internet-Based General Health Education** on Adolescent Depression in Primary Care- A Randomized Clinical Trial. JAMA Netw Open. 2018;1(7):e184278.
Gobbi G, Atkin T, Zytynski T, et al. **Association of Cannabis Use** in Adolescence and Risk of Depression, Anxiety, and Suicidality in Young Adulthood: A Systematic Review and Meta-analysis. JAMA Psychiatry. 2019 Feb 13.
Golden RN, Gaynes BN, Ekstrom RD, et al. The efficacy of **light therapy** in the treatment of mood disorders: a review and meta-analysis of the evidence. Am J Psychiatry. 2005 Apr;162(4):656-62. (InfoPOEMs: The available published research literature provides very weak evidence that light therapy is effective for seasonal affective disorder (SAD) or nonseasonal depression. There seems to be a large acute effect of light therapy on symptoms of SAD in the first week of treatment but this effect disappears quickly thereafter. Light therapy has a moderate effect on patients with nonseasonal depression when studied for only 7 days. Light therapy does not produce an additional effect when combined with pharmacologic therapy. Light boxes are expensive and may not provide the results desired by patients with SAD. (LOE = 1a-))
Goldstein BI, Carnethon MR, Matthews KA, et al. Major **Depressive Disorder and Bipolar Disorder Predispose Youth to Accelerated Atherosclerosis** and Early Cardiovascular Disease: A Scientific Statement From the American Heart Association. Circulation. 2015 Aug 10.
Goldstein-Piekarski AN, Korgaonkar MS, Green E, et al. **Human amygdala engagement** moderated by early life stress exposure is a biobehavioral target for **predicting recovery on antidepressants**.PNAS :2016 Oct 10.
Goldstein JN, Dudzinski DM, Erickson TB, et al. Case 12-2018: A 30-Year-Old Woman with **Cardiac Arrest**. N Engl J Med. 2018 Apr 19;378(16):1538-1549. (**doxepin overdose**)
Golub JS, Brewster KK, Brickman AM, et al. Association of **Audiometric Age-Related Hearing Loss With Depressive Symptoms Among Hispanic Individuals**. JAMA Otolaryngol Head Neck Surg. 2018 Dec 6.
Gómez-Donoso C, Sánchez-Villegas A, Martínez-González MA, et al. **Ultra-processed food consumption and the incidence of depression** in a Mediterranean cohort: the SUN Project. Eur J Nutr. 2019 May 4.
Goodarzi Z, Mrklas KJ, Roberts DJ, et al. Detecting depression in **Parkinson** disease: A systematic review and meta-analysis.Neurology. 2016 Jun 29.
Goodman WK. **Electroconvulsive therapy (ECT)** in the spotlight. N Engl J Med. 2011 May 12;364(19):1785-7.
Goodyer I, Dubicka B, Wilkinson P, et al. Selective serotonin reuptake inhibitors (SSRIs) and routine specialist care with and without cognitive behaviour therapy in **adolescents** with major depression: randomised controlled trial. BMJ. 2007 Jul 21;335(7611):142. (ADAPT). For adolescents with moderate to severe major depression there is no evidence that the combination of CBT plus an SSRI in the presence of routine clinical care contributes to an improved outcome by 28 weeks compared with the provision of routine clinical care plus an SSRI alone.
Goodyer IM, Reynolds S, Barrett B, et al. **Cognitive behavioural therapy and short-term psychoanalytical psychotherapy** versus a brief psychosocial intervention in adolescents with unipolar major depressive disorder (IMPACT): a multicentre, pragmatic, observer-blind, randomised controlled superiority trial. Lancet Psychiatry 2016; online Nov 30.
Goodyer IM, Reynolds S, Barrett B, et al. **Cognitive-behavioural therapy** and short-term **psychoanalytic psychotherapy** versus brief psychosocial intervention in adolescents with unipolar major **depression** (IMPACT): a multicentre, pragmatic, observer-blind, randomized controlled trial. Health Technol Assess. 2017 Mar;21(12):1-94.
Gordon BR, McDowell CP, Hallgren M, et al. Association of **Efficacy of Resistance Exercise Training With Depressive Symptoms**: Meta-analysis and Meta-regression Analysis of Randomized Clinical Trials. JAMA Psychiatry. 2018 May 9.
Gordon CS, Waller JW, Cook RM, et al. Effect of **pulmonary rehabilitation** on symptoms of anxiety and depression in chronic obstructive pulmonary disease: a systematic review and meta-analysis. Chest. 2019 Apr 26.
Gordon JL, Rubinow DR, Eisenlohr-Moul TA, et al. Efficacy of **transdermal estradiol and micronized progesterone** in the prevention of depressive symptoms **in the menopause transition**: a randomized clinical trial [online Jan 10, 2018].JAMA Psychiatry. doi:10.1001/jamapsychiatry.2017.3998.
Gordon PR, et al. **Sertraline** to treat **hot flashes**: a randomized controlled, double-blind, crossover trial in a general population. Menopause. 2006 Jul-Aug;13(4):568-75.
Gram L. Fluoxetine. *N Engl J Med* 1994;331:1354-61. (**low dose ~5mg effective**)
Gratzer D, Khalid-Khan F. **Internet-delivered cognitive behavioural therapy** in the treatment of psychiatric illness. CMAJ. 2016 Mar 1;188(4):263-72.
Gregory A, Mallikarjun P, Upthegrove R. **Treatment of depression in schizophrenia**: systematic review and meta-analysis. Br J Psychiatry. 2017 Oct;211(4):198-204.
Green JM, Wood AJ, Kerfoot MJ, Trainor G, Roberts C, Rothwell J, et al. Group therapy for **adolescents with repeated self harm**: randomised controlled trial (ASSIST) with economic evaluation. BMJ 2011;342:d682.
Grigoriadis S, VonderPorten EH, Mamisashvili L, et al. **Antidepressant exposure** during pregnancy and congenital malformations: is there an association? A systematic review and meta-analysis of the best evidence. J Clin Psychiatry 2013;74:e293–308.
Grigoriadis S, VonderPorten EH, Mamisashvili L, et al. The effect of **prenatal antidepressant exposure** on neonatal adaptation: a systematic review and meta-analysis. J Clin Psychiatry 2013;74:e309–20.
Grigoriadis S, Vonderporten EH, Mamisashvili L, et al. Prenatal exposure to antidepressants and persistent pulmonary hypertension of the newborn: systematic review and meta-analysis. BMJ. 2014 Jan 14
Grove K, Lewis AJ, Galbally M. Prenatal **Antidepressant Exposure and Child Motor Development**: A Meta-analysis. Pediatrics. 2018 Jun 21.
Grzeskowiak LE, Morrison JL, Henriksen TB, et al. **Prenatal antidepressant exposure and child behavioural outcomes** at 7 years of age: a study within the Danish National Birth Cohort. BJOG. 2016 Nov;123(12):1919-1928.

Grzeskowiak LE, Leggett C, Costi L, et al. Impact of **Serotonin Reuptake Inhibitor Use on Breast Milk Supply** in Mothers of Preterm Infants: A Retrospective Cohort Study. Br J Clin Pharmacol. 2018 Mar 9.

Guaiana G, Barbui C, Hotopf M. **Amitriptyline for depression**. Cochrane Database Syst Rev. 2007 Jul 18;(3):CD004186. This present systematic review indicates that amitriptyline is at least as efficacious as other tricyclics or newer compounds. However, the burden of side-effects in patients receiving it was greater. In comparison with selective serotonin reuptake inhibitors amitriptyline was less well tolerated, and although counterbalanced by a higher proportion of responders, the difference was not statistically significant.

Guaiana G, Gupta S, Chiodo D, et al. **Agomelatine** versus other antidepressive agents for major depression. Cochrane Database of Systematic Reviews 2013, Issue 12. Art. No.: CD008851. DOI: 10.1002/14651858.CD008851.pub2. Agomelatine did not seem to provide a significant advantage in efficacy over other antidepressive agents for the acute-phase treatment of major depression. Agomelatine was better tolerated than paroxetine and venlafaxine in terms of overall side effects, and fewer participants treated with agomelatine dropped out of the trials due to side effects compared to sertraline and venlafaxine, but data were limited because the number of included studies was small.

Gueorguieva R, et al. **Trajectories of relapse in randomised, placebo-controlled trials of treatment discontinuation** in major depressive disorder: individual patient-level data meta-analysis. Lancet Psyc 2017; online Feb 8.

Guidi J, Tomba E, Fava GA. The Sequential Integration of **Pharmacotherapy and Psychotherapy** in the Treatment of Major Depressive Disorder: A Meta-Analysis of the Sequential Model and a Critical Review of the Literature. Am J Psychiatry. 2015 Oct 20:appiajp201515040476.

Guille C, Frank E, Zhao Z, et al. **Work-family conflict and the sex difference** in depression among training physicians.JAMA Intern Med. 2017. doi:10.1001/jamainternmed.2017.5138

Gunderson JG, Morey LC, Stout RL, et al. Major depressive disorder and **borderline personality disorder** revisited: longitudinal interactions. J Clin Psychiatry 2004;65:1049-56.

Gunderson John G., **Borderline Personality Disorder**. N Engl J Med 2011; 364:2037-2042.

Gunduz-Bruce H, Silber C, Kaul I, et al. **Trial of SAGE-217** in Patients with Major Depressive Disorder. N Engl J Med. 2019 Sep 5;381(10):903-911.

Guo N et al. Prevalence of **depression among women of reproductive age** in the United States. Obstet Gynecol 2018 Apr; 131:671.

Gustafsson H, Nordström A, Nordström P. **Depression and subsequent risk of Parkinson disease**: A nationwide cohort study. Neurology. 2015 Jun 16;84(24):2422-9.

Guterman EL, Allen IE, Josephson SA, et al. Association Between **Caregiver Depression and Emergency Department Use** Among Patients With Dementia. JAMA Neurol. 2019 Jul 8.

Gutierrez-Galve L, Stein A, Hanington L, et al. Association of **Maternal and Paternal Depression** in the Postnatal Period With Offspring Depression at Age 18 Years. JAMA Psychiatry. 2018 Dec 26.

Gutierrez-Galve L, Stein A, Hanington L, et al. **Paternal Depression** in the Postnatal Period and Child Development: Mediators and Moderators. Pediatrics. 2015 Jan 5.

Hackam DG, Mrkobrada M. Selective serotonin reuptake inhibitors and **brain hemorrhage**: A meta-analysis. Neurology. 2012 Oct 17.

Hackett ML, Anderson CS, House A, et al. Interventions for treating **depression after stroke**. Cochrane Database Syst Rev. 2008 Oct 8;(4):CD003437.

Hackett ML, Anderson CS, House A, Halteh C. Interventions for **preventing depression after stroke**. Cochrane Database of Systematic Reviews 2008, Issue 3. Ar t. No.: CD003689. A small but significant effect of psychotherapy on improving mood and preventing depression was identified. More evidence is required before recommendations can be made about th e routine use of such treatments after stroke.

Hadas I, Sun Y, Lioumis P, et al. Association of **Repetitive Transcranial Magnetic Stimulation Treatment With Subgenual Cingulate Hyperactivity** in Patients With Major Depressive Disorder: A Secondary Analysis of a Randomized Clinical Trial. JAMA Netw Open. 2019 Jun 5;2(6):e195578.

Hage B, Britton B, Daniels D, et al. **Low cardiac vagal tone index** by heart rate variability differentiates bipolar from major depression. World J Biol Psychiatry. 2017 Oct 5:1-9.

Hall-Flavin DK et al. Using a **pharmacogenomic algorithm** to guide the treatment of depression. Transl Psychiatry 2012 Oct 16; 2:e172.

Hallgren M, Helgadóttir B, Herring MP, et al. **Exercise and internet-based cognitive-behavioural therapy** for depression: multicentre randomised controlled trial with 12-month follow-up. Br J Psychiatry. 2016 Sep 8.

Halpern R, Nadkarni A, Kalsekar I, et al. Medical costs and hospitalizations among patients with depression treated with **adjunctive atypical** antipsychotic therapy: an analysis of health insurance claims data. Ann Pharmacother. 2013 Jul;47(7-8):933-45.

Hamad GG, Helsel JC, Perel JM, et al. The effect of **gastric bypass on the pharmacokinetics of serotonin reuptake inhibitors**. Am J Psychiatry. 2012 Mar;169(3):256-63.

Hamer M, David Batty G, Seldenrijk A, Kivimaki M. **Antidepressant** medication use and future **risk of cardiovascular disease**: the Scottish Health Survey. Eur Heart J. 2010 Nov 30.

Handal M, Skurtveit S, Furu K, et al. **Motor development in children prenatally exposed** to selective serotonin reuptake inhibitors: a large population-based pregnancy cohort study. BJOG. 2015 Sep 15.

Hanley GE, Smolina K, Mintzes B, et al. **Postpartum Hemorrhage** and Use of **Serotonin Reuptake Inhibitor Antidepressants** in **Pregnancy**. Obstet Gynecol. 2016 Mar;127(3):553-61.

Hannigan LJ, Eilertsen EM, Gjerde LC, et al. **Maternal prenatal depressive symptoms and risk for early-life psychopathology in offspring**: genetic analyses in the Norwegian Mother and Child Birth Cohort Study. Lancet Psychiatry. 2018 Oct;5(10):808-815.

Hansen RA, Gartlehner G, Lohr KN, et al. Efficacy and safety of second-generation antidepressants in the treatment of major depressive disorder. Ann Intern Med. 2005 Sep 20;143(6):415-26. CONCLUSIONS: Overall, second-generation antidepressants probably do not differ substantially for treatment of major depressive disorder. Choosing the agent that is most appropriate for a given patient is difficult. (InfoPOEMs: When it comes to the new, nontricyclic antidepressants, the medical literature does not give us any clear guidance as to which one is more effective, of faster onset, safer, or better tolerated. Sexual side effects are lower with bupropion and nausea seems to occur more often with venlafaxine. Other research has shown these new drugs to be no more effective or better tolerated than tricyclic antidepressants. For now, start your patient on your favorite antidepressant, with the realization that most patients will need to switch to another drug at least once. (LOE = 1a))

Hansen RA, Khodneva Y, Glasser SP, Qian J, Redmond N, Safford MM. Antidepressant Medication Use and Its Association With **Cardiovascular Disease** and All-Cause Mortality in the Reasons for Geographic and Racial Differences in Stroke (**REGARDS**) Study. Ann Pharmacother. 2016 Apr;50(4):253-61.

Haque R, Shi J, Schottinger JE, et al. **Tamoxifen and Antidepressant Drug Interaction** in a Cohort of 16 887 **Breast Cancer** Survivors. J Natl Cancer Inst. 2015 Dec 1;108(3).

Harmer CJ, Duman RS, Cowen PJ. **How do antidepressants work**? New perspectives for refining future treatment approaches. Lancet Psychiatry. 2017 Jan 30.

Harrington RA, Lee LC, Crum RM, et al. **Prenatal SSRI** Use and Offspring With **Autism** Spectrum Disorder or Developmental Delay. Pediatrics. 2014 Apr 14.

Harvey SB, Øverland S, Hatch SL, et al. **Exercise and the Prevention of Depression**: Results of the **HUNT** Cohort Study. Am J Psychiatry. 2017 Oct 3:appiajp201716111223.

Haslemo T, Eliasson E, Jukić MM, et al. **Significantly lower CYP2D6 metabolism measured as the O/N-desmethylvenlafaxine** metabolic ratio in carriers of **CYP2D6*41 versus CYP2D6*9 or CYP2D6*10** - A study on therapeutic drug monitoring data from 1,003 genotyped Scandinavian patients. Br J Clin Pharmacol. 2018 Oct 12.

Hatcher S, Arroll B. **Newer antidepressants** for the treatment of depression in adults. BMJ 2012; 344 doi: 10.1136/bmj.d8300 (19 January 2012).

Häuser W, Wolfe F, Tölle T, Uçeyler N, Sommer C. The role of **antidepressants in the management of fibromyalgia** syndrome: a systematic review and meta-analysis. CNS Drugs. 2012 Apr 1;26(4):297-307.

HäuserW, Urrútia G, Tort S, ÜçeylerN,Walitt B. Serotonin and noradrenaline reuptake inhibitors **(SNRIs) for fibromyalgia** syndrome. Cochrane Database of Systematic Reviews 2013, Issue 1. Art. No.: CD010292. DOI: 10.1002/14651858.CD010292. The SNRIs duloxetine and milnacipran provided a small incremental benefit over placebo in reducing pain.The superiority of duloxetine and milnacipran over placebo in reducing fatigue and limitations of QOL was not substantial. Duloxetine and milnacipran were not superior to placebo in reducing sleep problems. The dropout rates due to adverse events were higher for duloxetine and milnacipran than for placebo. The most frequently reported symptoms leading to stopping medication were nausea, dry mouth, constipation, headache, somnolence/dizziness and insomnia. Rare complications of both drugs may include suicidality, liver damage, abnormal bleeding, elevated blood pressure and urinary hesitation.

Hawkins NA, Soman A, Buchanan Lunsford N, et al. Use of **Medications for Treating Anxiety and Depression in Cancer Survivors** in the United States. J Clin Oncol. 2017 Jan;35(1):78-85.

Hawthorne JM, Caley CF. **Extrapyramidal Reactions** Associated With Serotonergic Antidepressants. Ann Pharmacother. 2015 Oct;49(10):1136-52.

Hawton K, Bergen H, Simkin S, Cooper J, Waters K, Gunnell D, et al. **Toxicity of antidepressants**: rates of suicide relative to prescribing and non-fatal overdose. Br J Psychiatry 2010;196:354-8.

Hayes RM et al. **Maternal antidepressant use** and adverse outcomes: A cohort study of 228,876 pregnancies. Am J Obstet Gynecol 2012 Jul; 207:49.e1.

Hazell P, O'Connell D, Heathcote D, Henry D. **Tricyclic drugs for depression in children and adolescents**. Cochrane Database Syst Rev. 2002;(2):CD002317. Data suggest tricyclic antidepressants are not useful in treating depression in pre pubertal children. There is marginal evidence to support the use of tricyclic antidepressants in the treatment of depression in adolescents, although the magnitude of effect is likely to be moderate at best.

Health Canada Oct/08 Venlafaxine overdose warning http://www.hc-sc.gc.ca/dhp-mps/medeff/advisories-avis/prof/_2008/venlaflaxine_hpc-cps-eng.php

Health Canada Feb/11 **Methylene blue injectable** in combination with serotonin reuptake inhibitors - Association with serotonin toxicity Cases of serotonin toxicity have been reported and published in association with the use

of methylene blue injectable in patients exposed to drugs with serotonin reuptake inhibition properties.
Health Canada Jan/12: Lundbeck Canada, in collaboration with Health Canada, would like to inform you that the antidepressant **Celexa® (citalopram** hydrobromide; also marketed as generics), should no longer be used at doses greater than **40 mg per day** due to study results indicating a dose-dependent potential for QT prolongation.
Health Canada May/12 is informing Canadians of a labelling update for the prescription drug **Cipralex** (the brand name of the drug **escitalopram**) regarding a dose-related risk of abnormal heart rhythms. Cipralex is used to treat depression and belongs to a family of drugs known as Selective Serotonin Reuptake Inhibitors (SSRIs). 10 mg per day is the maximum recommended dose for patients who: are 65 years of age or older, or have liver problems, or are taking the heartburn drugs omeprazole or cimetidine which can increase the blood level of Cipralex. 20 mg per day is still the maximum recommended dose for most other patients.
Health Canada Mar/14: REMERON / **REMERON RD (mirtazapine**) – Abnormal Heart Rhythm - Merck Canada Inc. Cases of abnormal heart rhythm (eg. **QT** prolongation) have been reported with the antidepressant REMERON / REMERON RD (mirtazapine) mainly with drug overdose or when taking other drugs known to cause heart rhythm problems. The product information has been updated.
Health Canada June/14: **Adipotrim XT** contains fluoxetine.
Health Canada Sep/14: **Sport Burner** :The United States Food and Drug Administration (FDA) warned consumers not to use the product Sport Burner after it was found to contain undeclared fluoxetine.
Health Canada Mar/16 says **Perfect Slim Fast Track Slim & Slyn Both** by FDA contains undeclared fluoxetine
Health Canada Apr/19: **BENLYSTA (belimumab**) - Increased Risk of Serious Depression, Suicidal Ideation or Behaviour, or Self-Injury.
Heath L, Gray SL, Boudreau DM, et al. **Cumulative Antidepressant Use and Risk of Dementia** in a Prospective Cohort Study. J Am Geriatr Soc. 2018 Sep 17.
Healy D. **Serotonin and depression**. BMJ. 2015 Apr 21; 350:h1771
Hearn JH, Cotter I, Finlay KA. Efficacy of Internet-Delivered Mindfulness for **Improving Depression in Caregivers of People With Spinal Cord Injuries and Chronic Neuropathic Pain**: A Randomized Controlled Feasibility Trial. Arch Phys Med Rehabil. 2019 Jan;100(1):17-25.
Hedayati S. Susan; Minhajuddin Abu T.; Afshar Masoud et al.Association Between Major Depressive Episodes in Patients With **Chronic Kidney Disease** and Initiation of Dialysis, Hospitalization, or Death JAMA. 2010;303(19):1946-1953.
Hedayati SS, et al. Effect of **sertraline** on depressive symptoms in patients with **chronic kidney disease** without dialysis dependence: the **CAST** randomized clinical trial. JAMA. doi:10.1001/jama.2017.17131
Helfer B, Samara MT, Huhn M, et al. Efficacy and safety of **antidepressants added to antipsychotics for schizophrenia**: a systematic review and meta-analysis. Am J Psychiatry. 2016;173:876-886.
Hegel M, Arndt S. Escitalopram and problem-solving therapy for prevention of **poststroke depression**: a randomized controlled trial. JAMA. 2008 May 28;299(20):2391-400. In this study of nondepressed patients with recent stroke, the use of escitalopram or problem-solving therapy resulted in a significantly lower incidence of depression over 12 months of treatment compared with placebo, but problem-solving therapy did not achieve significant results over placebo using the intention-to-treat conservative method of analysis.
Hendron D et al. **Tricyclic antidepressant overdose** in a toddler treated with **intravenous lipid emulsion**. Pediatrics. 2011 Dec;128(6):e1628-32.
Henssler J, et al. Trajectories of Acute Antidepressant Efficacy: **How Long to Wait for Response**? Systematic Review & Meta-Analysis of Long-Term, Placebo-Controlled Acute Treatment Trials. J Clin Psychiatry. 2018 Apr 3;79(3).
Herba CM, Tremblay RE, Boivin M, et al. **Maternal Depressive** Symptoms and Children's Emotional Problems: Can **Early Child Care** Help Children of Depressed Mothers? JAMA Psychiatry. 2013 Jun 19:1-9.
Herring MP, Puetz TW, O'Connor PJ, Dishman RK. Effect of **Exercise Training** on Depressive Symptoms Among Patients With a Chronic Illness: A Systematic Review and Meta-analysis of Randomized Controlled Trials. Arch Intern Med. 2012 Jan 23;172(2):101-11.
Hess C, Wang T, McCoy L, et al. **Unplanned Inpatient and Observation Rehospitalization after Acute Myocardial Infarction**: Insights from the **TRANSLATE-ACS** Study. Circulation. 2016;133:XX-XXX.
Hetland A, Carr DB. **Medications and impaired driving**. Ann Pharmacother. 2014 Apr;48(4):494-506.
Hetland AJ, Carr DB, Wallendorf MJ, et al. **Potentially Driver-Impairing(PDI) Medication Use** in Medically Impaired Adults Referred for Driving Evaluation. Ann Pharmacother. 2014 Apr;48(4):476-82.
Hetrick SE, Cox GR, Witt KG, et al. **Cognitive behavioural therapy** (**CBT**), third-wave CBT and interpersonal therapy (IPT) based interventions for preventing depression in children and adolescents. Cochrane Database Syst Rev. 2016 Aug 9;8:CD003380.
Hickie Ian B, Rogers Naomi L. Novel **melatonin-based therapies**: (agomelatine) potential advances in the treatment of major depression. www.thelancet.com Published May 18, 2011 DOI:10.1016/S0140-6736(11)60095-0.
Hicks JK, Bishop JR, Sangkuhl K, et al, Clinical Pharmacogenetics Implementation Consortium. Clinical Pharmacogenetics Implementation Consortium (CPIC) guideline for **CYP2D6** and **CYP2C19** genotypes and dosing of selective serotonin reuptake inhibitors. Clin Pharmacol Ther. 2015 Aug;98(2):127-34.
Hicks JK, et al. Clinical Pharmacogenetics Implementation Consortium guideline (CPIC) for **CYP2D6** and **CYP2C19** genotypes & dosing of **tricyclic antidepressants**: 2016 update. Clin Pharmacol Ther. 2017 Jul;102(1):37-44.
Hieronymus F, Lisinski A, Nilsson S, Eriksson E. Influence of **baseline severity on the effects of SSRIs in depression**: an item-based, patient-level post-hoc analysis. Lancet Psychiatry. 2019 Jul 11.
Hinkle SN, Buck Louis GM, Rawal S,et al. A longitudinal study of **depression and gestational diabetes in pregnancy** and the postpartum period. Diabetologia. 2016 Sep 19.
Hirschtritt ME, Kroenke K. **Screening for Depression**. JAMA. 2017 Aug 22;318(8):745-746.
Hoban CL, Byard RW, et al. A comparison of patterns of spontaneous **adverse drug reaction reporting with St. John's Wort and fluoxetine** during the period 2000-2013. Clin Exp Pharmacol Physiol. 2015 Jul;42(7):747-51.
Hockenberry JM, Joski P, Yarbrough C, Druss BG. **Trends in Treatment and Spending** for Patients Receiving Outpatient Treatment of Depression in the United States, 1998-2015. JAMA Psychiatry. 2019 Apr 24.
Hodgins David C, Stea Jonathan N, Grant Jon E. **Gambling disorders**. www.thelancet.com Published online May 19, 2011 DOI:10.1016/S0140-6736(10)62185-X
Hofmeister S, Bodden S. **Premenstrual Syndrome and Premenstrual Dysphoric Disorder**. Am Fam Physician. 2016 Aug 1;94(3):236-40.
Hollander E et al. A Double-Blind Placebo-Controlled Trial of **Fluoxetine for Repetitive Behaviors and Global Severity in Adult Autism** Spectrum Disorders. Am J Psychiatry. 2011 Dec 2.
Hollinghurst S, Carroll FE, Abel A, et al. Cost-effectiveness of **cognitive-behavioural therapy** as an adjunct to pharmacotherapy for treatment-resistant depression in primary care: economic evaluation of the CoBalT Trial. Br J Psychiatry. 2014 Jan;204(1):69-76.
Hollon SD, DeRubeis RJ, Fawcett J, et al. Effect of **Cognitive Therapy With Antidepressant Medications vs Antidepressants Alone** on the Rate of Recovery in Major Depressive Disorder: A Randomized Clinical Trial. JAMA Psychiatry. 2014 Aug 20.
Holmberg PJ, Arteaga G, Schiltz BM, et al. **Sertraline-Induced Rhabdomyolysis**, Trismus, and Cardiac Arrest in a Child. Pediatrics. 2018 Sep 7.
Honkola J, Hookana E, Malinen S, et al. Psychotropic medications (antipsychotics & antidepressants) and the **risk of sudden cardiac death** during an acute coronary event. Eur Heart J. 2012 Mar;33(6):745-51.
Hopkins K, Crosland P, Elliott N, Bewley S; Clinical Guidelines Update Committee B. Diagnosis and management of **depression in children and young people**: summary of updated **NICE** guidance. BMJ. 2015 Mar 4;350:h824.
Horowitz MA, Taylor D. **Tapering of SSRI treatment** to mitigate withdrawal symptoms. Lancet Psychiatry. 2019 Mar 5.
Howell EA, Balbierz A, Wang J, et al. Reducing **postpartum depressive symptoms** among black and latina mothers: a randomized controlled trial. Obstet Gynecol. 2012 May;119(5):942-9.
Hu LY, Liu CJ, Lu T, et al. **Delayed onset urticaria** in depressive patients with **bupropion** prescription: a nationwide population-based study. PLoS One. 2013 Nov 14;8(11)
Hubbard R, Lewis S, et al. **Bupropion** and the risk of sudden death: a self-controlled case-series analysis using The Health Improvement Network. Thorax. 2005 Oct;60(10):848-50. Epub 2005 Jul 29.
Hubsher G, Haider M, Okun MS. **Amantadine**: The journey from **fighting flu to treating Parkinson** disease. Neurology. 2012 Apr 3;78(14):1096-9.
Huckvale K, Torous J, Larsen ME. Assessment of the **Data Sharing and Privacy Practices of Smartphone Apps** for Depression and Smoking Cessation. JAMA Netw Open. 2019 Apr 5;2(4):e192542.
Huffman JC, Mastromauro CA, Beach SR, et al. Collaborative Care for **Depression and Anxiety Disorders in Patients With Recent Cardiac Events**: The Management of Sadness and Anxiety in Cardiology (MOSAIC)

Randomized Clinical Trial. JAMA Intern Med. 2014 Apr 14.
Hughes S, Cohen D, Jaggi R. Differences in **reporting serious adverse events** in industry sponsored clinical trial registries and journal articles on antidepressant and antipsychotic drugs: a cross-sectional study. BMJ Open. 2014 Jul 9;4(7):e005535.
Hughes T, Cardno A, West R, et al. **Unrecognised bipolar** disorder among UK primary care patients **prescribed antidepressants**: an observational study. Br J Gen Pract. 2016 Feb;66(643):e71-7.
Huhn M, TardyM, Spineli LM, et al. Efficacy of **pharmacotherapy and psychotherapy** for adult psychiatric disorders: a systematic overview of meta-analyses [online April 30, 2014]. JAMA Psychiatry. doi:10.1001/jamapsychiatry.2014.112.
Huijbers MJ, Spinhoven P, Spijker J, et al. **Discontinuation of antidepressant medication after mindfulness-based cognitive therapy** for recurrent depression: randomised controlled non-inferiority trial. Br J Psychiatry. 2016 Feb 18. pii: bjp.bp.115.168971.
Huijbers MJ, Wentink C, Speckens AEM. **Preventive cognitive therapy** could be a viable and effective addition to antidepressant medication in preventing relapse or recurrence in major depressive disorder. Evid Based Ment Health. 2019 Feb;22(1):e7.
Hunkeler EM, et al. Long term outcomes from the **IMPACT** randomised trial for depressed elderly patients in primary care. BMJ. 2006 Feb 4;332(7536):259-63. Epub 2006 Jan 20.
Huo YL, Qiao JM, Gao S. Association between **antidepressant medication use and epithelial ovarian cancer risk**: a systematic review and meta-analysis of observational studies. Br J Clin Pharmacol. 2018 Jan 2.
Hussain H, Dubicka B, Wilkinson P. Recent developments in the **treatment of major depressive disorder in children and adolescents**. Evid Based Ment Health. 2018 Aug;21(3):101-106.
Hurwitz R, Blackmore R, Hazell P, Williams K, Woolfenden S. **Tricyclic antidepressants for autism spectrum** disorders (ASD) in children and adolescents. Cochrane Database Syst Rev. 2012 Mar 14;3:CD008372. Clinicians considering the use of TCAs need to be aware of the limited and conflicting evidence of effect and the side effect profile when discussing this treatment option with people who have ASD and their carers.
Husseini N, Goldstein LB, Peterson ED,et al.**Depression and Antidepressant Use After Stroke** and Transient Ischemic Attack. Stroke. 2012 Mar 29.
Huybrechts KF, Palmsten K, Avorn J, et al. **Antidepressant use in pregnancy** and the risk of cardiac defects. N Engl J Med. 2014 Jun 19;370(25):2397-407.
Huybrechts KF, Bateman BT, Palmsten K, et al. **Antidepressant use late in pregnancy** and risk of persistent pulmonary hypertension of the newborn. JAMA. 2015 Jun 2;313(21):2142-51.
Hviid A et al. Use of **selective serotonin reuptake inhibitors during pregnancy and risk of autism**. N Engl J Med 2013 Dec 19; 369:2406.
ICSI Institute for Clinical Systems Improvement. **Major depression in adults in primary care**. Bloomington (MN): Institute for Clinical Systems Improvement (ICSI); 2010 May.
Ilgen MA, Kleinberg F, Ignacio RV, Bohnert et al. **Noncancer Pain Conditions and Risk of Suicide**. JAMA Psychiatry. 2013 May 22:1-6.
Incze MA. **I'm Worried About Depression**-What Should I Know? JAMA Intern Med. 2019 Sep 3.
Ingenhoven T, Lafay P, Rinne T, et al. Effectiveness of pharmacotherapy for **severe personality disorders**: meta-analyses of randomized controlled trials. J Clin Psychiatry 2010; 71:14-25.
Ionson E, Limbachia J, Rej S, et al. Effects of **Sahaj Samadhi meditation on heart rate variability and depressive symptoms in patients with late-life depression**. Br J Psychiatry. 2018 Nov 28:1-7.
Ismail Z, Elbayoumi H, Fischer CE, et al. Prevalence of **Depression in Patients With Mild Cognitive Impairment**: A Systematic Review and Meta-analysis. JAMA Psychiatry.2016 Nov 23.
Iwagami M, Tomlinson LA, Mansfield KE, et al.**Gastrointestinal bleeding risk of selective serotonin reuptake inhibitors** by level of kidney function: a population-based cohort study. Br J Clin Pharmacol. 2018 Jun 4.
Jacka FN, O'Neil A, Opie R,et al. A randomised controlled trial of **dietary improvement for adults** with major depression (the **'SMILES'** trial). BMC Med. 2017 Jan 30;15(1):23.
Jackson JL, Mancuso JM, Nickoloff S, et al. **Tricyclic** and **Tetracyclic** Antidepressants for the Prevention of Frequent Episodic or Chronic **Tension**-Type **Headache** in Adults: A Systematic Review and Meta-Analysis. J Gen Intern Med. 2017 Jul 18.
Jahoda A, Hastings R, et al. Comparison of **behavioural activation with guided self-help** for treatment of depression in **adults with intellectual disabilities**: a randomized controlled trial. Lancet Psychiatry 2017; online Nov 16.
Jakobsen JC, et al. **Selective serotonin reuptake inhibitors versus placebo** in patients with major depressive disorder- systematic review with meta-analysis and Trial Sequential Analysis. BMC Psychiatry. 2017 Feb 8;17(1):58.
Jakubovski E et al. Systematic review and meta-analysis: **Dose-response relationship of selective serotonin reuptake inhibitors** in major depressive disorder. Am J Psychiatry 2015 Nov 10. Focusing on efficacy and tolerability, investigators calculated number needed to treat (NNT) and number needed to harm (NNH). They used published dose ranges to convert SSRI doses to imipramine equivalents, with 100 mg of imipramine equivalent to: Sertraline, 120 mg.Fluvoxamine, 100 mg.Paroxetine, 20 mg.Fluoxetine, 20 mg.Citalopram, 33.3 mg.Escitalopram, 16.7 mg.
Janssen CW, Lowry CA, Mehl MR, et al. **Whole-Body Hyperthermia** for the Treatment of Major Depressive Disorder: A Randomized Clinical Trial. JAMA Psychiatry. 2016 May 12.
Jarde A, Morais M, et al. **Neonatal Outcomes** in Women With Untreated Antenatal **Depression** Compared With Women Without Depression: A Systematic Review and Meta-analysis. JAMA Psychiatry. 2016 Jun 8.
Jarrett RB, Minhajuddin A, Gershenfeld H, et al. **Preventing Depressive Relapse and Recurrence** in Higher-Risk Cognitive Therapy Responders: A Randomized Trial of Continuation Phase **Cognitive Therapy, Fluoxetine**, or Matched Pill Placebo. JAMA Psychiatry. 2013 Sep 4.
Jensen HM, Gron R, Lidegaard O, et al. **Maternal depression, antidepressant use in pregnancy and Apgar scores in infants.** Br J Psychiatry. 2013 May;202(5):347-51.
Jessurun N, van Puijenbroek EP, et al. **Inhibition** of CYP2D6 with low dose (5 mg) **paroxetine** in patients with high 10-**hydroxynortriptyline** serum levels - a review of routine practice. Br J Clin Pharmacol. 2017 Jan 29.
Jha MK, Rush AJ, Trivedi MH. When **Discontinuing SSRI Antidepressants Is a Challenge**: Management Tips. Am J Psychiatry. 2018 Dec 1;175(12):1176-1184.
Jiang W, Velazquez EJ, Kuchibhatla M, et al. Effect of **escitalopram on mental stress-induced myocardial ischemia**: results of the **REMIT** trial. JAMA. 2013 May 22;309(20):2139-49.
Jiang HY, Chen HZ, Hu XJ, et al. Use of Selective Serotonin Reuptake Inhibitors and **Risk of Upper Gastrointestinal Bleeding**: A Systematic Review and Meta-analysis. Clin Gastroenterol Hepatol. 2014 Jun 30.
Jimenez-Solem E, Andersen JT, Petersen M, et al. **SSRI Use During Pregnancy and Risk of Stillbirth and Neonatal Mortality**. Am J Psychiatry. 2013 Jan 30.
Jin J. JAMA Patient Page. **Screening for Depression**. JAMA. 2016 Jan 26;315(4):428.
Joffres M, Jaramillo A, Dickinson J, et al; **Canadian Task Force on Preventive Health Care (CTFPHC). Recommendations on screening** for depression in adults. CMAJ. 2013 May 13.
Johansen SL, Robakis TK, Williams KE, Rasgon NL. Management of **perinatal depression with non-drug interventions**. BMJ. 2019 Feb 25;364:l322.
Johnson EM, et al. **Cardiovascular changes** associated with **venlafaxine** in the treatment of late-life depression. Am J Geriatr Psychiatry. 2006 Sep;14(9):796-802.
Jones HE, Joshi A, et al. The effect of treatment with selective **serotonin** reuptake inhibitors in comparison to placebo in the **progression of dementia**: a systematic review and meta-analysis. Age Ageing. 2016 Jul;45(4):448-56.
Jones I, Shakespeare J. **Postnatal depression**. BMJ. 2014 Aug 14;349:g4500.
Jorge RE, Robinson RG, Arndt S, Starkstein S. Mortality and **poststroke depression**: a placebo-controlled trial of antidepressants. Am J Psychiatry. 2003 Oct;160(10):1823-9.
Jorge RE, Acion L, Moser D, et al. Escitalopram and enhancement of cognitive recovery **following stroke**. Arch Gen Psychiatry. 2010 Feb;67(2):187-96.
Jorge RE, Acion L, Burin DI, Robinson RG. **Sertraline** for Preventing Mood Disorders Following **Traumatic Brain Injury**: A Randomized Clinical Trial. JAMA Psychiatry. 2016 Oct 1;73(10):1041-1047.
Jørgensen TS, Wium-Andersen IK, et al. **Incidence of Depression After Stroke**,and Associated Risk Factors and Mortality Outcomes, in a Large Cohort of Danish Patients. JAMA Psychiatry. 2016 Sep 7.
Jørgensen TSH, et al. Incidence of **depression after stroke**, and associated risk factors and mortality outcomes, in a large cohort of Danish patients [online Sept 7, 16]. JAMA Psychiatry. doi:10.1001/jamapsychiatry.2016 .1932.
Josephson CB, Lowerison M, Vallerand I, et al. Association of Depression and Treated Depression With **Epilepsy and Seizure Outcomes**: A Multicohort Analysis. JAMA Neurol. 2017 Feb 27.
Joyce NR, Schuler MS, Hadland SE, et al. Variation in the 12-Month Treatment **Trajectories of Children and Adolescents After a Diagnosis of Depression**. JAMA Pediatr. 2018 Jan 1;172(1):49-56.
Judd LL et al. A new empirical **definition of major depressive episode recovery** and its positive impact on future course of illness. J Clin Psychiatry 2016 Aug; 77:1065.
Jukić MM, Haslemo T, E, et al. Impact of **CYP2C19 Genotype on Escitalopram** Exposure and Therapeutic Failure: A Retrospective Study Based on 2,087 Patients. Am J Psychiatry. 2018 Jan 12:appiajp201717050550.
Kaicker J, Bostwick J. **Co-ingestion of tricyclic antidepressants with selective norepinephrine reuptake inhibitors**: Overdose in the emergency department. Can Fam Physician. 2016 Jun;62(6):485-9.
Kaminsky BM, Bostwick JR, Guthrie SK. **Alternate Routes of Administration of Antidepressant** (buccal, sublingual, transdermal, rectal) and Antipsychotic Medications. Ann Pharmacother. 2015 Jul;49(7):808-17.

Kaneriya SH, Robbins-Welty GA, Smagula SF, et al. Predictors and Moderators of Remission With **Aripiprazole Augmentation** in Treatment-Resistant Late-Life Depression: An Analysis of the IRL-GRey Randomized Clinical Trial. JAMA Psychiatry. 2016 Apr 1

Kanes S, Colquhoun H, Gunduz-Bruce H, et al. **Brexanolone** (SAGE-547 injection) in post-partum depression: a randomised controlled trial. Lancet 2017; published online June 12.

Kang Seung-Gul, Yoon Byung-Mun, Park Young-Min. **Mirtazapine-Induced Hepatocellular-Type Liver Injury** Articles Ahead of Print published on 1 June 2011, DOI 10.1345/aph.1Q078. Ann Pharmacother ;45:825-826.

Kantor ED, Rehm CD, Haas JS, Chan AT, Giovannucci EL. **Trends in Prescription Drug Use** Among Adults in the United States From 1999-2012. JAMA. 2015 Nov 3;314(17):1818-31. (antidepressant use)

Kapil RP, et al. Effects of **Paroxetine, a CYP2D6 Inhibitor**, on Pharmacokinetic Properties of **Hydrocodone** After Coadministration With a Single-Entity, Once-Daily, Extended-Release Hydrocodone Tablet. Clin Ther. 2015 Sep 6.

Kaplan YC, Keskin-Arslan E, Acar S, et al. **Maternal SSRI** discontinuation, use, psychiatric disorder and the risk of **autism** in **children**: A meta-analysis of cohort studies. Br J Clin Pharmacol. 2017 Jul 21.

Karyotaki E, Riper H, et al. Efficacy of **Self-guided Internet-Based Cognitive Behavioral Therapy** in the Treatment of Depressive Symptoms: A Meta-analysis of Individual Participant Data. JAMA Psychiatry. 2017 Feb 22.

Katila H, Mezhebovsky I, Mulroy A, et al. Randomized, Double-Blind Study of the Efficacy and Tolerability of **Extended Release Quetiapine** Fumarate (Quetiapine XR) Monotherapy in Elderly Patients With Major Depressive Disorder. Am J Geriatr Psychiatry. 2012 Jun 7.

Kato T, Furukawa TA, Mantani A, et al. Optimising **first- and second-line treatment strategies for untreated major depressive disorder** - the **SUN☺D study:** a pragmatic, multi-centre, assessor-blinded randomised controlled trial. BMC Med. 2018 Jul 11;16(1):103.

Katon WJ, Lin EH, Von Korff M, et al. **Collaborative care for patients with depression** and chronic illnesses. N Engl J Med. 2010 Dec 30;363(27):2611-20.

Katz LY, Au W, Singal D, et al. **Suicide and suicide attempts in children and adolescents** in the child welfare system. CMAJ. 2011 Oct 17.

Kaufman KR, Podolsky D, Greenman D, Madraswala R. **Antidepressant-selective gynecomastia**. Ann Pharmacother. 2013 Jan;47(1):e6.

Kaup AR, Byers AL, Falvey C, et al. **Trajectories of Depressive Symptoms** in Older Adults and Risk of **Dementia**. JAMA Psychiatry. 2016 Mar 16.

Kavan MG, Elsasser GN, Barone EJ. The Physician's Role in Managing **Acute Stress Disorder**. Am Fam Physician. 2012;86(7):643-649.

Keks N, Hope J, Keogh S. **Switching and stopping antidepressants**. Aust Prescr. 2016 Jun;39(3):76-83.

Keller MB, Trivedi MH, Thase ME, et al. The Prevention of Recurrent Episodes of Depression with Venlafaxine for Two Years (**PREVENT**) Study: Outcomes from the **2-year** and combined maintenance phases. J Clin Psyc. 2007 Aug;68(8):1246-56. In this study, an additional 12 months of maintenance therapy with venlafaxine ER was effective in preventing recurrence of depression in pts who had been responders to venlafaxine ER after acute (10 weeks), continuation (6 months), and initial maintenance (12 months) therapy.

Kelleher I, Corcoran P, Keeley H, et al. **Psychotic Symptoms and Population Risk for Suicide Attempt**: A Prospective Cohort Study. JAMA Psychiatry. 2013 Jul 17.

Keller MB, Ryan ND, Strober M, et al. Efficacy of **paroxetine** in the treatment of adolescent major depression: a randomized, controlled trial. J Am Acad Child Adolesc Psychiatry. 2001 Jul;40(7):762-72.

Kellner CH, Greenberg RM, Murrough JW, et al. **ECT** in Treatment-Resistant Depression. Am J Psychiatry. 2012 Dec 1;169(12):1238-44.

Kelly CM, Juurlink DN, Gomes T, et al. **Selective serotonin reuptake inhibitors** (eg. Paroxetine) and breast cancer mortality in women receiving **tamoxifen**: a population based cohort study BMJ 2010;340:c693.

Kendall KM, Rees E, Bracher-Smith M, et al. Association of **Rare Copy Number Variants With Risk of Depression**. JAMA Psychiatry. 2019 Apr 17.

Kendel Friederike; Gelbrich Gotz; Wirtz Markus; et al. Predictive Relationship Between Depression and Physical Functioning After **Coronary Surgery**. Arch Intern Med. 2010;170(19):1717-1721.

Kennard BD, Emslie GJ, Mayes TL, et al. Sequential treatment with **fluoxetine and relapse--prevention CBT to improve outcomes in pediatric depression**. Am J Psychiatry. 2014 Oct;171(10):1083-90.

Kennedy SH, Andersen HF, Lam RW. Efficacy of **escitalopram** in the treatment of major depressive disorder compared with conventional selective serotonin reuptake inhibitors and **venlafaxine** XR: a meta-analysis. J Psychiatry Neurosci. 2006 Mar;31(2):122-31. Erratum in: J Psychiatry Neurosci. 2006 Jul;31(4):228.

Kennedy SH, et al. Sexual function during **bupropion** or paroxetine treatment of major depressive disorder. Can J Psychiatry. 2006 Mar;51(4):234-42.

Kennedy GJ, Marcus P. Use of antidepressants in **older patients** with co-morbid medical conditions: guidance from studies of depression in somatic illness. Drugs Aging. 2005;22(4):273-87.

Keshavarz H, Fitzpatrick-Lewis D, Streiner D, et al. **Screening for depression**: a systematic review and meta-analysis. Canadian Medical Association Open Access Journal. 1.4: E159-E167. 2014.

Kessler RC, Heeringa SG, Stein MB, et al; **Army STARRS** Collaborators. Thirty-day prevalence of **DSM-IV mental disorders** among nondeployed soldiers in the US Army: results from the Army Study to Assess Risk and Resilience in Servicemembers (Army STARRS) [online March 3, 2014]. JAMA Psychiatry. doi:10.1001/jamapsychiatry.2014.28.

Kessler RC, Warner CH, Ivany C, et al. for the **Army STARRS** Collaborators. **Predicting Suicides** After Psychiatric Hospitalization in US Army Soldiers: The Army Study to Assess Risk and Resilience in Servicemembers (Army STARRS). JAMA Psychiatry. 2014 Nov 12.

Kessler DS, MacNeill SJ, Tallon D, et al. **Mirtazapine added to SSRIs or SNRIs for treatment resistant depression in primary care**: phase III randomised placebo controlled trial (MIR). BMJ. 2018 Oct 31;363:k4218.

Khalifeh H, Hunt IM, Appleby L, et al. **Suicide in perinatal and non-perinatal women** in contact with psychiatric services: 15 year findings from a UK national inquiry. Lancet Psychiatry 2016;3(3):233–42.

Khambaty T, et al. Association Between Depressive Disorders and **Incident Acute Myocardial** Infarction in Human Immunodeficiency Virus-Infected Adults: Veterans Aging Cohort Study. JAMA Cardiol. 2016 Aug 24.

Khoza S, Barner JC, Bohman TM, Rascati K, Lawson K, Wilson JP. Use of antidepressant agents and the **risk of type 2 diabetes**. Eur J Clin Pharmacol. 2011 Nov 26.

Kim H, et al. **Monoamine transporter gene polymorphisms** and antidepressant response in Koreans with late-life depression. JAMA. 2006 Oct 4;296(13):1609-18.

Kim J, Farchione T, Potter A, et al. **Esketamine for Treatment-Resistant Depression** - First FDA-Approved Antidepressant in a New Class. N Engl J Med. 2019 May 22.

Kim JS, Lee EJ, Chang DI, et al; **EMOTION** investigators.. Efficacy of early administration of **escitalopram** on depressive and emotional symptoms and neurological dysfunction **after stroke**: a multicentre, double-blind, randomised, placebo-controlled study. Lancet Psychiatry. 2017 Jan;4(1):33-41.

Kim JM, Stewart R, Lee YS, et al. Effect of **Escitalopram vs Placebo Treatment for Depression on Long-term Cardiac Outcomes** in Patients With Acute Coronary Syndrome: A Randomized Clinical Trial. JAMA. 2018 Jul 24;320(4):350-358.

Kim JS, Zhang Y, Chang Y, et al. **Subclinical hypothyroidism** and incident depression in young and middle age adults. J Clin Endocrinol Metab. 2018 Feb 2.

Kim J-Y, Ko I, Kim MS, Yu MS, Cho B-J, Kim D-K. Association of **chronic rhinosinusitis with increased risk of depression and anxiety** in a nationwide insurance population [online Feb 7,2019]. JAMA Otolaryngol Head Neck Surg. doi:10.1001/jamaoto.2018.4103

King Bryan H; Hollander Eric; et al.; for the **STAART** Psychopharmacology Network Lack of Efficacy of Citalopram in Children With Autism Spectrum Disorders and High Levels of Repetitive Behavior: **Citalopram** Ineffective in Children With Autism Arch Gen Psychiatry. 2009;66(6):583-590.

King BH. Association Between Maternal Use of **SSRI Medications and Autism** in Their Children. JAMA. 2017 Apr 18;317(15):1568-1569

Kiosses DN, Ravdin LD, Gross JJ, et al. **Problem Adaptation Therapy** for Older Adults With Major Depression and Cognitive Impairment: A Randomized Clinical Trial. JAMA Psychiatry. 2014 Nov 5.

Kirsch I, Deacon BJ, Huedo-Medina TB, et al. Initial severity and **antidepressant benefits**: a meta-analysis of date submitted to the Food and Drug Administration. PLoS Med 2008;5:e45. (Limited or placebo like benefit)

Kisely S, Smith M, Lawrence D, Maaten S. **Mortality** in individuals who have had psychiatric treatment: Population-based study in Nova Scotia. Br J Psychiatry. 2005 Dec;187:552-558.

Kivistö J, et al. **Maternal Use of Selective Serotonin Reuptake Inhibitors** and **Lengthening of the Umbilical Cord**: Indirect Evidence of Increased Foetal Activity-A Retrospective Cohort Study. PLoS One. 2016 Apr 29;11(4).

Klainin-Yobas P, Oo WN, Suzanne Yew PY, et al. Effects of **relaxation interventions on depression and anxiety** among older adults: a systematic review. Aging Ment Health. 2015 Jan 9:1-13.

Kleinstäuber M, Witthöft M, Steffanowski A, van Marwijk H, Hiller W, Lambert MJ. **Pharmacological interventions for somatoform disorders** in adults. Cochrane Database of Systematic Reviews 2014, Issue 11. Art. No.: CD010628. DOI:10.1002/14651858.CD010628.pub2. The current review found very low-quality evidence for NGAs and low-quality evidence for NPs being effective in treating somatoform symptoms in adults when compared with placebo. There was some evidence that different classes of antidepressants did not differ in efficacy; however, this was limited and of low to very low quality. These results had serious shortcomings such as the high risk of bias, strong heterogeneity in the data, and small sample sizes. Furthermore, the significant effects of antidepressant treatment have to be balanced against the

relatively high rates of adverse effects. Adverse effects produced by medication can have amplifying effects on symptomperceptions, particularly in people focusing on somatic symptomswithoutmedical causes.We can only drawconclusions about short-term efficacy of the pharmacological interventions because no trial included follow-up assessments. For each of the comparisons where there were available data on acceptability rates (NGAs versus placebo, NPs versus placebo, TCAs versus other medication, and antidepressants versus a combination of an antidepressant and an antipsychotic), no clear differences between the intervention and comparator were found. Future high-quality research should be carried out to determine the effectiveness of medications other than antidepressants, to compare antidepressants more thoroughly, and to follow-up participants over longer periods (the longest follow up was just 12 weeks). Another idea for future research would be to include other outcomes such as functional impairment or dysfunctional behaviours and cognitions as well as the classical outcomes such as symptom severity, depression, or anxiety.

Koesters M, Guaiana G, Cipriani A, et al. **Agomelatine** efficacy and acceptability revisited: systematic review and meta-analysis of published and unpublished randomised trials. Br J Psychiatry. 2013 Sep;203:179-87.

Koesters M, Ostuzzi G, Guaiana G, et al. **Vortioxetine** for depression in adults. Cochrane Database Syst Rev. 2017 Jul 5;7:CD011520. : The place of vortioxetine in the treatment of acute depression is unclear. Our analyses showed vortioxetine may be more effective than placebo in terms of response, remission and depressive symptoms, but the clinical relevance of these effects is uncertain. Furthermore, the quality of evidence to support these findings was generally low. In comparison to SNRIs, we found no advantage for vortioxetine. Vortioxetine was less effective than duloxetine, but fewer people reported adverse effects when treated with vortioxetine compared to duloxetine.

Köhler O, Benros ME, Nordentoft M, et al. Effect of **Anti-inflammatory Treatment on Depression**, Depressive Symptoms, and Adverse Effects: A Systematic Review and Meta-analysis of Randomized Clinical Trials. JAMA Psychiatry. 2014 Oct 15.

Kohler O, Gasse C, Petersen L, et al. The effect of **concomitant treatment with SSRIs and statins**: a population-based study. Am J Psychiatry 2016;173:807–15.

Kok RM, Aartsen M, Nolen WA, et al. The Course of Adverse Effects of Nortriptyline and Venlafaxine in **Elderly** Patients with Major Depression. J Am Geriatr Soc. 2009;57:3112-7. (both equally well tolerated)

Kok RM, Reynolds CF 3rd. **Management of Depression in Older Adults**: A Review. JAMA. 2017 May 23;317(20):2114-2122.

Kolar D. Current status of **electroconvulsive therapy for mood disorders**: a clinical review. Evid Based Ment Health. 2017 Jan 4.

Komossa K, Depping AM, Gaudchau A, et al. **Second-generation antipsychotics for major depressive** disorder and dysthymia. Cochrane Database Syst Rev. 2010 Dec 8;12:CD008121

Korczak DJ, Madigan S, Colasanto M. Children's **Physical Activity** and Depression: A Meta-analysis. Pediatrics.2017;139(4):e20162266

Koren G, Nordeng H. **Antidepressant use during pregnancy**: the benefit-risk ratio. Am J Obstet Gynecol. 2012 Feb 21.

Korgaonkar MS, Rekshan W, Gordon E, et al. **Magnetic Resonance Imaging** Measures of Brain Structure to Predict Antidepressant Treatment Outcome in Major Depressive Disorder. EBioMedicine. 2014 Dec 3;2(1):37-45

Kovich H, Dejong A. Common Questions About the Pharmacologic **Management of Depression in Adults**. Am Fam Phy8ician.2015 Jul15;92(2):94-100.

Kraglund KL, Mortensen JK, Damsbo AG, et al. **Neuroregeneration and Vascular Protection by Citalopram in Acute Ischemic Stroke (TALOS)**. Stroke. 2018 Nov;49(11):2568-2576.

Kraus MR, et al. Therapy of interferon-induced depression in chronic **hepatitis C** with citalopram: a randomised, double-blind, placebo-controlled study. Gut. 2008 Apr;57(4):531-6. Epub 2007 Dec 13. The findings demonstrate clearly that citalopram treatment is highly effective in HCV patients on interferon therapy, when initiated after the onset of clinically relevant depressive symptoms. This suggests that a general SSRI prophylaxis is not necessary in these patients.

Kravitz RL, Franks P, Feldman MD, et al. **Patient engagement programs** for recognition and initial treatment of depression in primary care: a randomized trial. JAMA. 2013 Nov 6;310(17):1818-28.

Kroenke Kurt; Bair Matthew J.; Damush Teresa M.; et al. Optimized Antidepressant Therapy and Pain Self-management in Primary Care Patients With Depression and **Musculoskeletal Pain**: A Randomized Controlled Trial. JAMA. 2009;301(20):2099-2110. Optimized antidepressant therapy followed by a pain selfmanagement program resulted in substantial improvement in depression as well as moderate reductions in pain severity and disability.

Kruithof Maartje K, Bruins Nynke A, van Roon Eric N. Coma After **Overdose with Duloxetine**. Articles Ahead of Print published on 1 January 2011, DOI 10.1345/aph.1P432. Ann Pharmacother ;45:e5.

Kulkarni J. **Perimenopausal depression** - an under-recognised entity. Aust Prescr. 2018 Dec;41(6):183-185.

Kunutsor SK, Seidu S, Khunti K. **Depression, antidepressant use, and risk of venous thromboembolism**: systematic review and meta-analysis of published observational evidence. Ann Med. 2018 Jul 12:1-17.

Kupfer DJ, Frank E, Phillips ML. Major depressive disorder: new clinical, neurobiological, and treatment perspectives. Lancet. 2011 Dec 19.

Kurlansik SL, Ibay AD. **Seasonal Affective Disorder**. Am Fam Physician. 2012;86(11):1037-1041.

Kurlansik SL. Maffei MS. **Somatic Symptom Disorder**. Am Fam Physician. 2015;93(1):49-54.

Kuyken W, Hayes R, Barrett B, et al. Effectiveness and cost-effectiveness of **mindfulness-based cognitive therapy** compared with maintenance antidepressant treatment in the prevention of depressive relapse or recurrence (**PREVENT**): a randomised controlled trial. Lancet. 2015 Apr 20.

Kuyken W, Hayes R, Barrett B, et al. The effectiveness and cost-effectiveness of **mindfulness-based cognitive therapy** compared with maintenance antidepressant treatment in the prevention of depressive relapse/recurrence: results of a randomised controlled trial (the **PREVENT** study). Health Technol Assess. 2015 Sep;19(73):1-124.

Kuyken W, et al. Efficacy of **Mindfulness-Based Cognitive Therapy** in **Prevention of Depressive Relapse**: An Individual Patient Data Meta-analysis From Randomized Trials. JAMA Psychiatry. 2016 Jun 1;73(6):565-74.

Lam RW, et al. The Can-SAD study: a randomized controlled trial of the effectiveness of **light therapy** and fluoxetine in patients with winter seasonal affective disorder. Am J Psychiatry. 2006 May;163(5):805-12. (InfoPOEMs: Light therapy and fluoxetine (Prozac) are equally effective treatment options for patients with seasonal affective disorder (SAD). Patient preference and an individual assessment of risks and benefits should guide treatment selection. (LOE = 1b))

Lam RW, Parikh SV, Ramasubbu R, et al. Effects of combined **pharmacotherapy and psychotherapy** for improving work functioning in major depressive disorder. Br J Psychiatry. 2013 Nov;203(5):358-65.

Lam RW, Levitt AJ, et al. Efficacy of **Bright Light Treatment, Fluoxetine**, and the **Combination** in Patients With **Nonseasonal Major Depressive Disorder**: A Randomized Clinical Trial. JAMA Psychiatry. 2015 Nov 18:1-9.

Lancto KL, Lindsay MP, Smith EE, et al; Management of **Mood, Cognition and Fatigue Following Stroke** Best Practice Writing Group, the Heart & Stroke Canadian Stroke Best Practices and Quality Advisory Committee; in collaboration with the Canadian Stroke Consortium. Canadian Stroke Best Practice Recommendations: mood, cognition and fatigue following stroke, 6th edition update 2019. https://journals.sagepub.com/doi/pdf/10.1177/1747493019847334

Langan RC, Goodbred AJ. Identification and **Management of Peripartum Depression**. Am Fam Physician. 2016;93(10):852-858.

Lasalvia A, Zoppei S, Van Bortel T, et al, ASPEN/INDIGO Study Group. Global pattern of experienced and anticipated **discrimination** reported by people with major depressive disorder: a cross-sectional survey. Lancet 2012.

Lasserre AM, Glaus J, Vandeleur CL, et al. **Depression With Atypical Features and Increase in Obesity**, Body Mass Index, Waist Circumference, and Fat Mass: A Prospective, Population-Based Study. JAMA Psychiatry. 2014 Jun 4.

Lavretsky H et al. **Citalopram, methylphenidate, or their combination in geriatric depression**: A randomized, double-blind, placebo-controlled trial. Am J Psychiatry 2015 Feb 13.

Le Noury J, Nardo JM, Healy D, et al. **Restoring Study 329**: efficacy and harms of **paroxetine and imipramine in treatment of major depression in Adolescence**. BMJ. 2015 Sep 16;351:h4320.

LeBlanc A, Herrin J, Williams MD, et al. **Shared decision making for antidepressants** in primary care: a cluster randomized trial [online September 28, 2015].JAMA Intern Med. doi:10.1001 /jamainternmed.2015.5214.

Leenstra JL, Miller RC, Qin R, et al. **Doxepin Rinse** Versus Placebo in the Treatment of **Acute Oral Mucositis** Pain in Patients Receiving Head and Neck Radiotherapy With or Without Chemotherapy: A Phase III, Randomized, Double-Blind Trial (NCCTG-N09C6 [Alliance]). J Clin Oncol. 2014 May 20;32(15):1571-7.

Lenze EJ, Rollman BL, Shear MK, et al. **Escitalopram for older adults** with **generalized anxiety** disorder: a randomized controlled trial. JAMA. 2009 Jan 21;301(3):295-303. Older adults $^{n=177}$ with GAD randomized to escitalopram 10-20mg od had a higher cumulative response rate for improvement vs placebo over 12 weeks; however, response rates were not significantly different using an intention-to-treat analysis. Further study is required to assess efficacy and safety over longer treatment durations.

Lenze EJ, Mulsant BH, Blumberger D, et al. Efficacy, safety, and tolerability of **augmentation pharmacotherapy** with **aripiprazole** for treatment-resistant depression in late life: a randomised, double-blind, placebo-controlled trial. Lancet 2015; online Sept 28.

Leon AC, Solomon DA, Li C, et al. Antidepressants and **risks of suicide and suicide attempts**: a 27-year observational study. J Clin Psychiatry. 2011;72:580-586.

Leong C, Raymond C, Château D, et al. **Psychotropic Drug Use before, during, and after Pregnancy**: A Population-Based Study in a Canadian Cohort (2001-2013). Can J Psychiatry. 2017 Aug;62(8):543-550.

Leontjevas R, Gerritsen DL, Smalbrugge M, et al. A structural **multidisciplinary approach to depression** management in nursing-home residents: a multicentre, stepped-wedge cluster-randomised trial. Lancet 2013; online May.

Leucht S, Hierl S, Kissling W et al. Putting the efficacy of **psychiatric and general medicine medication into perspective**: review of meta-analyses. Br J Psychiatry. 2012 Feb;200:97-106.

Leverich GS, et al. Risk of switch in mood polarity to hypomania or mania in patients with bipolar depression during acute and continuation trials of venlafaxine, sertraline, and **bupropion** as adjuncts to mood stabilizers. Am J Psychiatry. 2006 Feb;163(2):232-9.

Levis B, Benedetti A, Thombs BD, et al Accuracy of **Patient Health Questionnaire-9 (PHQ-9) for screening** to detect major depression: individual participant data meta-analysis. BMJ. 2019 Apr 9;365:l1476.

Levkovitz Y, Tedeschini E, Papakostas GI. Efficacy of antidepressants for **dysthymia**: a meta-analysis of placebo-controlled randomized trials. J Clin Psychiatry. 2011 Apr;72(4):509-14.

Lewandowski RE, Acri MC, Hoagwood KE, et al. Evidence for the Management of **Adolescent Depression**. Pediatrics. 2013 Sep 16.

Lewis G, Mulligan J, Wiles N, et al. **Polymorphism of the 5-HT transporter** and response to antidepressants: randomised controlled trial. Br J Psychiatry. 2011 Jun;198:464-71.

Lewis G, Neary M, Polek E, et al. The association between **paternal and adolescent depressive symptoms**: evidence from two population-based cohorts.Lancet Psychiatry. 2017 Nov 13

Lewis H, Adamson J, Atherton K, et al. CollAborative care and active surveillance for **Screen-Positive EldeRs with subthreshold depression** (**CASPER**): a multicentred randomized controlled trial of clinical effectiveness and cost-effectiveness. Health Technol Assess. 2017 Feb;21(8):1-196.

Li C-T et al. Association between **antidepressant resistance in unipolar depression** and subsequent **bipolar disorder**: Cohort study. Br J Psychiatry 2012 Jan; 200:45.

Li CM, Zhang X, Hoffman HJ, et al. **Hearing Impairment** Associated With Depression in US Adults, National Health and Nutrition Examination Survey 2005-2010. JAMA Otolaryngol Head Neck Surg. 2014 Mar 6.

Li F, Liu X, Zhang D. **Fish consumption** and risk of depression: a meta-analysis. J Epidemiol Community Health. 2015 Sep 10.

Libby AM, Orton HD, Valuck RJ. Persisting decline in depression treatment **after FDA warnings**. Arch Gen Psychiatry. 2009 Jun;66(6):633-9.

Lichtman JH, Bigger JT Jr, Blumenthal JA, et al. **Depression and Coronary Heart Disease**. Recommendations for Screening, Referral, and Treatment. A Science Advisory From the American Heart Association Prevention Committee of the Council on Cardiovascular Nursing, Council on Clinical Cardiology, Council on Epidemiology and Prevention, and Interdisciplinary Council on Quality of Care and Outcomes Research. Circulation. 2008 Sep 29. [Epub ahead of print] **Patient Health Questionnaire** for Screening: http://www.phqscreeners.com/

Lichtman JH, Froelicher ES, Blumenthal JA, et al; on behalf of the American Heart Association Statistics Committee of the Council on Epidemiology and Prevention and the Council on Cardiovascular and Stroke Nursing. Depression as a Risk Factor for Poor Prognosis Among Patients With **Acute Coronary Syndrome**: Systematic Review and Recommendations: A Scientific Statement From the American Heart Association. Circulation. 2014 Feb 24

Lieb K, Völlm B, Rücker G, Timmer A, Stoffers JM. Pharmacotherapy for **borderline personality disorder**: Cochrane systematic review of randomised trials. Br J Psychiatry 2010;196:4-12.

Linde K, Berner MM, Kriston L. **St John`s wort** for major depression. Cochrane Database Syst Rev. 2008 Oct 8;(4):CD000448. The available evidence suggests that the hypericum extracts tested in the included trials a) are superior to placebo in patients with major depression; b) are similarly effective as standard antidepressants; c) and have fewer side effects than standard antidepressants. The association of country of origin and precision with effects sizes complicates the interpretation.

Linde K, Sigterman K, Kriston L, et al. Effectiveness of **Psychological Treatments for Depressive** Disorders in **Primary Care:** Systematic Review and Meta-Analysis. Ann Fam Med. 2015 Jan;13(1):56-68.

Linde K, Kriston L, Rücker G, et al. Efficacy and Acceptability of **Pharmacological Treatments** for Depressive Disorders in **Primary Care**: Systematic Review & Network Meta-Analysis. Ann Fam Med. 2015 Jan;13(1):69-79.

Lindsey WT. **Vilazodone** for the treatment of depression. Ann Pharmacother. 2011 Jul;45(7-8):946-53.

Linehan MM, et al. Two-Yr Randomized Controlled Trial & Follow-up of **Dialectical Behavior Therapy** vs Therapy by Experts for Suicidal Behaviors & Borderline Personality Disorder. Arch Gen Psyc. 2006 Jul;63(7):757-66.

Lipsman N, Sankar T, Downar J, et al. **Neuromodulation for treatment-refractory major depressive** disorder. CMAJ. 2014 Jan 7

Lisanby SH. **Electroconvulsive therapy** for depression. N Engl J Med. 2007 Nov 8;357(19):1939-45.

Little A., **Treatment-Resistant Depression**. Am Fam Physician. 2009;80(1):167-172.

Littman J, Halil R. Potential effects of **rational prescribing** on national health care spending: More than half a billion dollars in annual savings (escitalopram, esomeprazole, perindoril). Can Fam Physician. 2016 Mar;62(3):235-44.

Liu C, Cnattingius S, Bergström M, Östberg V, Hjern A. **Prenatal parental depression and preterm birth**: a national cohort study. BJOG. 2016 Jan 19.

Liu X, Olsen J, Pedersen LH, et al. **Antidepressant Use During Pregnancy and Asthma** in the Offspring. Pediatrics. 2015 Mar 9.

Liu X, Agerbo E, Ingstrup KG, et al. **Antidepressant use during pregnancy and psychiatric disorders** in offspring: Danish nationwide register based cohort study. BMJ 2017;358:j3668.

Liu XI, Schuette P, Burckart GJ, et al. A Comparison of Pediatric and Adult **Safety Studies for Antipsychotic and Antidepressant Drugs** Submitted to the United States Food and Drug Administration. J Pediatr. 2019 May;208:236-242.e3.

Löbner M, Pabst A, Stein J, et al. Computerized **cognitive behavior therapy for patients with mild to moderately severe depression** in primary care: A pragmatic cluster randomized controlled trial (@ktiv). J Affect Disord. 2018 Jun 5;238:317-326.

Locher C, Koechlin H, Zion SR, et al. Efficacy and safety of **selective serotonin reuptake inhibitors, serotonin-norepinephrine reuptake inhibitors**, and placebo **in common psychiatric disorders among children and adolescents**: a systematic review and meta-analysis [online August 30, 2017]. JAMA Psychiatry. doi:10.1001/jamapsychiatry.2017.2432

Lorenz T, Rullo J, Faubion S. **Antidepressant-Induced Female Sexual Dysfunction**. Mayo Clin Proc. 2016 Sep;91(9):1280-6.

Louter MA, Wilbrink LA, Haan J, et al. **Cluster headache and depression**. Neurology. 2016 Nov 1;87(18):1899-1906.

Louter MA, Pelzer N, de Boer I, et al. Prevalence of **lifetime depression in a large hemiplegic migraine cohort**. Neurology. 2016 Nov 29;87(22):2370-2374.

Lugo-Candelas C, Cha J, Hong S, et al. Associations Between **Brain Structure and Connectivity in Infants and Exposure to Selective Serotonin Reuptake Inhibitors During Pregnancy**. JAMA Pediatr. 2018 Apr 9.

MacQueen G, et al. Systematic Review of Clinical Practice Guidelines for **Failed Antidepressant Treatment Response** in Major Depressive Disorder, Dysthymia, & Subthreshold Depression in Adults. Can J Psychiatry. 2016 Aug 23.

Lu CY, Zhang F, Lakoma MD, et al. Changes in **antidepressant use by young people and suicidal behavior after FDA warnings** and media coverage: quasi-experimental study. BMJ. 2014 Jun 18;348:g3596.

Luby JL, Barch DM, Whalen D, et al. A Randomized Controlled Trial of **Parent-Child Psychotherapy Targeting Emotion Development** for Early Childhood Depression. Am J Psychiatry. 2018 Jun 20:appiajp201818030321.

Lucas M, Mirzaei F, Pan A, et al. **Coffee, caffeine**, and risk of depression among women. Arch Intern Med. 2011 Sep 26;171(17):1571-8.

Ludermir AB, Lewis G, Valongueiro SA, et al. **Violence against women** by their intimate partner during pregnancy and postnatal depression: a prospective cohort study. Lancet. 2010 Sep 11;376(9744):903-10.

Luk JW, Gilman SE, Haynie DL, et al. **Sexual Orientation and Depressive Symptoms** in Adolescents. Pediatrics. 2018 Apr 16.

Lurie I, Yang YX, Haynes K, et al. **Antibiotic exposure** and the risk for depression, anxiety, or psychosis: a nested case-control study. J Clin Psychiatry. 2015 Nov;76(11):1522-8.

Lustman PJ, et al. Sertraline for Prevention of Depression Recurrence in **Diabetes** Mellitus: A Randomized, Double-blind, Placebo-Controlled Trial. Arch Gen Psychiatry. 2006 May;63(5):521-9.

Lyoo IK, Yoon S, Kim TS, et al. A randomized, double-blind placebo-controlled trial of oral **creatine monohydrate** augmentation for enhanced response to a selective serotonin reuptake inhibitor in women with major depressive disorder. Am J Psychiatry. 2012 Sep 1;169(9):937-45.

Ma J, et al. Association between antidepressant use and prescribing of **gastric acid suppressants**. Can J Psychiatry. 2006 Mar;51(3):178-84.

Ma J, Rosas LG, Lv N, et al. Effect of integrated **behavioral weight loss treatment and problem-solving therapy** on body mass index and depressive symptoms among patients with obesity and depression: the RAINBOW randomized clinical trial [Mar 5, 2019]. JAMA. doi:10.1001/jama.2019.0557

Machado MO, Stergiopoulos V, Maes M, et al. Depression and Anxiety in **Adults With Hidradenitis Suppurativa**: A Systematic Review and Meta-analysis. JAMA Dermatol. 2019 Jun 5.

Machmutow K, Meister R, Jansen A, et al. **Comparative effectiveness of continuation and maintenance treatments for persistent depressive** disorder in adults. Cochrane Database Syst Rev. 2019 May 20;5:CD012855.

MacKenzie LE, Uher R, Pavlova B. **Cognitive performance in first-degree relatives** of individuals with vs without major depressive disorder: a meta-analysis [online Dec 26, 2018]. JAMA Psychiatry. doi:10.1001/jamapsychiatry.2018.3672

MacMillan HL et al. Canadian Task Force on Preventive Health Care. Screening for depression in primary care: recommendation statement from the Canadian Task Force on Preventive Health Care.CMAJ.2005Jan 4;172(1):33-5.

Macpherson H, Richmond S, Bland M, et al. **Acupuncture** and Counselling for Depression in Primary Care: A Randomised Controlled Trial. PLoS Med. 2013 Sep;10(9):e1001518.
MacQueen GM, Frey BN, Ismail Z, et al; **CANMAT** Depression Work Group. Canadian Network for Mood and Anxiety Treatments (CANMAT) **2016 clinical guidelines for the management of adults with major depressive** disorder: section 6. Special populations: **youth, women, and the elderly**. Can J Psychiatry 2016;August 2 [Epub ahead of print].
Magni LR, Purgato M, Gastaldon C, Papola D, Furukawa TA, Cipriani A, Barbui C. **Fluoxetine versus other types of pharmacotherapy** for depression. Cochrane Database of Systematic Reviews 2013, Issue 7. Art. No.: CD004185. DOI:10.1002/14651858.CD004185.pub3. The present study detected differences in terms of efficacy and tolerability between fluoxetine and certain ADs, but the clinical meaning of these differences is uncertain.Moreover, the assessment of quality with the risk of bias tool showed that the great majority of included studies failed to report details onmethodological procedures.
Magovern MK, DeGeorge KC. **Vortioxetine** (Brintellix) for the Treatment of Depression. Am Fam Physician. 2015 Mar 1;91(5):325-326.
Mahdanian AA, Rej S, Bacon SL, et al. **Serotonergic antidepressants and perioperative bleeding risk**: a systematic review. Expert Opin Drug Saf. 2014 Jun;13(6):695-704.
Mahmoud RA, Pandina GJ, Turkoz I, et al. **Risperidone** for treatment-refractory major depressive disorder: a randomized trial. Ann Intern Med. 2007 Nov 6;147(9):593-602. n=274 6wks. Risperidone (up to 2mg/d) augmentation produced a statistically significant mean reduction in depression symptoms, substantially increased remission and response, and improved other patient- and clinician-rated measures.
Malhi GS, Mann JJ. **Depression- Seminar**. Lancet. 2018 Nov 2.
Maljuric NM, Noordam R, Aarts N, et al. Use of **selective serotonin reuptake inhibitors** and the heart-rate corrected **QT interval** in a real-life setting: the population-based Rotterdam Study. Br J Clin Pharmacol. 2015 May 13.
Malins S, Kai J, Atha C, et al. **Cognitive behaviour therapy** for long-term frequent attenders in primary care: a feasibility case series and treatment development study. Br J Gen Pract2016;66:e729-36.
Malm H, Sourander A, et al. **Pregnancy Complications Following Prenatal Exposure to SSRIs** or Maternal Psychiatric Disorders: Results From Population-Based National Register Data. Am J Psychiatry. 2015 Aug 4
Maki PM, Kornstein SG, Joffe H, et al. Guidelines for the Evaluation and Treatment of **Perimenopausal Depression**: Summary and Recommendations. J Womens Health (Larchmt). 2018 Sep 5.
Makrides Maria; Gibson Robert A.;. McPhee Andrew J; et al.; and the DOMInO Investigative Team Effect of **DHA Supplementation** During Pregnancy on Maternal Depression and Neurodevelopment of Young Children: A Randomized Controlled Trial *JAMA*. 2010;304(15):1675-1683.
Mann JJ, Apter A, Bertolote J, et al. **Suicide prevention strategies**: a systematic review. JAMA. 2005 Oct 26;294(16):2064-74. CONCLUSIONS: Physician education in depression recognition and treatment and restricting access to lethal methods reduce suicide rates. Other interventions need more evidence of efficacy. Ascertaining which components of suicide prevention programs are effective in reducing rates of suicide and suicide attempt is essential in order to optimize use of limited resources.
Mann JJ. The **medical management of depression**. N Engl J Med. 2005 Oct 27;353(17):1819-34.
Manea L, Gilbody S, McMillan D. **Optimal cut-off score** for diagnosing depression with the Patient Health Questionnaire (**PHQ-9**): a meta-analysis. CMAJ 2012;184:E191-6.
Man KKC, Chan EW, Ip P, et al. **Prenatal antidepressant use and risk of attention-deficit/hyperactivity disorder** in offspring: population based cohort study. BMJ 2017;357:j2350.
Mann R, Adamson J, Gilbody SM. Diagnostic accuracy of case-finding questions to **identify perinatal depression**. CMAJ. 2012 Apr 2.
Marcum ZA, Perera S, Thorpe JM, et al. **Antidepressant Use and Recurrent Falls** in Community-Dwelling Older Adults: Findings From the Health ABC Study. Ann Pharmacother. 2016 Jul;50(7):525-33.
Marcy TR, Britton ML. Antidepressant-induced **sweating**.Ann Pharmacother. 2005 Apr;39(4):748-52. Epub 2005 Feb 22.
Marjoribanks J, Brown J, O`Brien PM, et al. **Selective serotonin reuptake inhibitors for premenstrual syndrome**. Cochrane Database Syst Rev. 2013 Jun 7;6:CD001396. doi: 10.1002/14651858.CD001396.pub3. SSRIs are effective in reducing the symptoms of PMS, whether taken in the luteal phase only or continuously. Adverse effects are relatively frequent, the most common being nausea and asthenia. Adverse effects are dose-dependent.
Mariappan P, Ballantyne Z, N'dow J, Alhasso A. Serotonin and noradrenaline reuptake inhibitors (SNRI) for stress urinary incontinence in adults. Cochrane Database Syst Rev. 2005 Jul 20;(3):CD004742.
Mata DA, Ramos MA, Bansal N, et al. Prevalence of **Depression and Depressive** Symptoms Among Resident Physicians: A Systematic Review and Meta-analysis. JAMA. 2015 Dec 8;314(22):2373-83.
Matcham F, Norton S, Steer S, Hotopf M. Usefulness of the **SF-36 Health Survey** in screening for depressive and anxiety disorders in **rheumatoid arthritis**. BMC Musculoskelet Disord. 2016 May 23;17(1):224.
Martin LA, Neighbors HW, Griffith DM. The Experience of **Symptoms of Depression in Men vs Women**: Analysis of the National Comorbidity Survey Replication. JAMA Psychiatry. 2013 Aug 28.
Martinez Carlos, Assimes TL, Mines D, et al. Use of **venlafaxine** compared with other antidepressants and the risk of **sudden cardiac death or near death**: a nested case-control study. BMJ 2010;340:c249. (5 Feb 2010)
Maslej MM, Bolker BM, et al. The **Mortality and Myocardial Effects of Antidepressants** Are Moderated by Preexisting Cardiovascular Disease: A Meta-Analysis. Psychother Psychosom. 2017 Sep 14;86(5):268-282.
Mathew SJ, Shah A, Lapidus K, et al. **Ketamine** for treatment-resistant unipolar depression: current evidence. CNS Drugs. 2012 Mar 1;26(3):189-204.
Maund E, Stuart B, Moore M, et al. Managing **Antidepressant Discontinuation**: A Systematic Review. Ann Fam Med. 2019 Jan;17(1):52-60.
Maund E, Tendal B, Hórbjartsson A, et al. **Coding of adverse events of suicidality in clinical study reports of duloxetine** for the treatment of major depressive disorder: qualitative study. BMJ 2014;348:g3555.
Maund E, Tendal B, et al. **Benefits and harms in clinical trials of duloxetine** for treatment of major depressive disorder: comparison of clinical study reports, trial registries, and publications. BMJ. 2014 Jun 4;348:g3510.
Maurer, D et al. **Screening for Depression**. Am Fam Physician. 2012 Jan 15;85(2):139-144.
Maurer DM, Raymond TJ, Davis BN. **Depression: Screening and Diagnosis**. Am Fam Physician. 2018;98(8):508-515.
Mavandadi S, Benson A, DiFilippo S, et al. A **Telephone-Based** Program to Provide Symptom Monitoring Alone vs Symptom Monitoring Plus Care Management for **Late-Life Depression** and Anxiety: A Randomized Clinical Trial. JAMA Psychiatry. 2015 Nov 11:1211-1218.
May HT, Horne BD, Knight S, et al. The association of **depression** at any time to the risk of death following **coronary artery disease diagnosis**. European Heart J. 2017;0:1-7
McCarron RM, Vanderlip ER, Rado J. **Depression- In the Clinic**. Ann Intern Med. 2016 Oct 4;165(7):ITC49-ITC64.
McCormack J, Korownyk C. **Effectiveness of antidepressants**. BMJ. 2018 Mar 9;360:k1073.
McCurdy AP, Boulé NG, Sivak A, Davenport MH. Effects of **Exercise** on Mild-to-Moderate Depressive Symptoms in the **Postpartum Period**: A Meta-analysis. Obstet Gynecol. 2017 Jun;129(6):1087-1097.
McDonagh M, Matthews A, Phillipi C, et al. **Antidepressant Treatment** of Depression During **Pregnancy and the Postpartum** Period. Evidence Report/Technology Assessment No. 216. Evid Rep Technol Assess (Full Rep). 2014 July;(216):1-308.
McDonagh MS, Matthews A, Phillipi C, et al. **Depression Drug Treatment Outcomes in Pregnancy and the Postpartum Period**: A Systematic Review and Meta-analysis. Obstet Gynecol. 2014 Sep;124(3):526-34.
McGirr A, Vöhringer PA, Ghaemi SN, et al. Safety and efficacy of **adjunctive second-generation antidepressant therapy with a mood stabiliser or an atypical antipsychotic in acute bipolar depression**: a systematic review and meta-analysis of randomised placebo-controlled trials. Lancet Psychiatry 2016; online Oct 26.
McGirr A, Berlim MT, Bond DJ, et al. **Adjunctive ketamine in electroconvulsive therapy**: updated systematic review and meta-analysis. Br J Psychiatry. 2017 Apr 6.
McGrath PJ, et al. **Predictors of relapse** in a prospective study of fluoxetine treatment of major depression. Am J Psychiatry. 2006 Sep;163(9):1542-8.
McGrath PJ, et al. Tranylcypromine Versus Venlafaxine Plus Mirtazapine Following Three Failed Antidepressant Medication Trials for Depression: A **STAR*D** Report. Am J Psychiatry. 2006 Sep;163(9):1531-41. Remission rates were modest for both the tranylcypromine group and the extended-release venlafaxine plus mirtazapine group, and the rates were not statistically different between groups. The lower side effect burden, lack of dietary restrictions, and ease of use of venlafaxine and mirtazapine suggest that this combination may be preferred over tranylcypromine for patients with highly treatment-resistant depression who have not benefited adequately from several prior treatments.
McIntyre A, et al. **Quetiapine** fumarate extended-release for the treatment of major depression with comorbid fibromyalgia syndrome: A double-blind, randomized, placebo-controlled study. Arthritis Rheum. 2013 Oct 21.
McLeod Melanie. An update on the pharmacotherapy of depression. Continuing Education Lesson. November 2011.
Mead GE, Morley W, Campbell P, Greig CA, McMurdo M, Lawlor DA. **Exercise for depression**. Cochrane Database Syst Rev. 2008 Oct 8;(4):CD004366.
Mead GE, Hsieh CF, Lee R, et al. Selective serotonin reuptake inhibitors **(SSRIs) for stroke recovery**. Cochrane Database Syst Rev. 2012 Nov 14;11:CD009286. SSRIs appeared to improve dependence, disability, neurological impairment, anxiety and depression after stroke, but there was heterogeneity between trials and methodological limitations in a substantial proportion of the trials

Mead GE, Hsieh CF, Hackett M. Selective serotonin reuptake inhibitors for **stroke recovery**. JAMA. 2013 Sep 11;310(10):1066-7.
Medical Letter, **Duloxetine** for Diabetic Neuropathic pain. Vol 47 (Issue 1215/1216) Aug 15/29,2005. p.67-68.
Medical Letter. "Treatment Guidelines- Drugs for Psychiatric Disorders Vol 4 (Issue 46) June 2006.
Medical Letter. Treatment Guidelines. Drugs for Depression and Bipolar Disorder. May 2010.
Medical Letter, **L-Methylfolate** for Depression or Schizoprenia. April 2010.
Meekums B, Karkou V, Nelson EA. **Dance movement** therapy for depression. Cochrane Database of Systematic Reviews 2015, Issue 2. Art. No.: CD009895. DOI: 10.1002/14651858.CD009895.pub2. The low-quality evidence from three small trials with 147 participants does not allow any firm conclusions to be drawn regarding the effectiveness of DMT for depression. Larger trials of high methodological quality are needed to assess DMT for depression, with economic analyses and acceptability measures and for all age groups.
Mehrotra R, Cukor D, Unruh M, et al. Comparative efficacy of therapies for treatment of depression for **patients undergoing maintenance hemodialysis**: a randomized clinical trial. Ann Intern Med. 2019. [Epub ahead of print]. doi:10 .7326/M18-2229.
Melhem NM, Porta G, Oquendo MA, et al. Severity and Variability of Depression Symptoms **Predicting Suicide Attempt in High-Risk Individuals**. JAMA Psychiatry. 2019 Feb 27.
Meltzer-Brody S, Colquhoun H, Riesenberg R, et al. **Brexanolone injection in post-partum depression**: two multicentre, double-blind, randomised, placebo-controlled, phase 3 trials. Lancet. 2018 Aug 31.
Mendle J, Ryan R, McKone K. Long-term associations of **age at menarche with depression symptoms and antisocial behaviors in adulthood**. Pediatrics. 2017;141(1):e20171703
Merikangas KR, He JP, Rapoport J, et al. **Medication Use in US Youth** With Mental Disorders. JAMA Pediatr. 2013 Feb 1;167(2):141-8.
Merry SN, Hetrick SE, Cox GR, et al. **Psychological and educational interventions for preventing depression** in children and adolescents. Cochrane Database of Systematic Reviews 2011, Issue 12. Art. No.: CD003380. DOI: 10.1002/14651858.CD003380.pub3. There is some evidence from this review that targeted and universal depression prevention programmes may prevent the onset of depressive disorders compared with no intervention.
Merry SN, Stasiak K, Shepherd M, et al. The effectiveness of **SPARX**, a computerised **self help intervention for adolescents** seeking help for depression: randomised controlled non-inferiority trial. BMJ. 2012 Apr 18
Messacar K, Sillau S, Hopkins SE, et al. Safety, tolerability, and efficacy of **fluoxetine as an antiviral for acute flaccid myelitis**. Neurology. 2019 Apr 30;92(18):e2118-e2126.
Mezzacappa A, Lasica PA, Gianfagna F, et al. Risk for **Autism Spectrum Disorders According to Period of Prenatal Antidepressant Exposure**: A Systematic Review and Meta-analysis. JAMA Pediatr. 2017 Apr 17.
MHRA UK **Reboxetine**: benefit-risk balance reviewed. Sept 2011. http://www.mhra.gov.uk/Safetyinformation/DrugSafetyUpdate/CON128957
MHRA Dec/11 **Citalopram and escitalopram** are associated with dose-dependent **QT interval** prolongation and should not be used in those with: congenital long QT syndrome; known pre-existing QT interval prolongation; or in combination with other medicines that prolong the QT interval. ECG measurements should be considered for patients with cardiac disease, and electrolyte disturbances should be corrected before starting treatment. For citalopram, new restrictions on the maximum daily doses now apply: 40 mg for adults; 20 mg for patients older than 65 years; and 20 mg for those with hepatic impairment. For escitalopram, the maximum daily dose for patients older than 65 years is now reduced to 10 mg/day; other doses remain unchanged.
MHRA Apr/19 : Clinical trials, including interim findings from a randomised trial, show an increased risk of depression, suicidal ideation or behaviour, or self-injury in patients with **systemic lupus erythematosus receiving belimumab**.
Miller L et al. **Religiosity** (spirituality) and major depression in adults at high risk: A ten-year prospective study. Am J Psychiatry 2011 Aug 24
Miller BJ, Murray L, Beckmann MM, et al. **Dietary supplements for preventing postnatal depression**. Cochrane Database Syst Rev. 2013 Oct 24;10:CD009104.
There is insufficient evidence to conclude that selenium, DHA or EPA prevent postnatal depression. There is currently no evidence to recommend any other dietary supplement for prevention of postnatal depression.
Miller M, Swanson SA, Azrael D, Pate V, Stürmer T. **Antidepressant Dose, Age, and the Risk of Deliberate Self-harm**. JAMA Intern Med. 2014 Apr 28.
Mines D, Hill D, Yu H, Novelli L. Prevalence of risk factors for **suicide in patients prescribed venlafaxine, fluoxetine, and citalopram**. Pharmacoepidemiol Drug Saf. 2005 Jun;14(6):367-72.
Mirza SS, Wolters FJ, Swanson SA, et al. **10-year trajectories of depressive symptoms and risk of dementia**: a population-based study. Lancet Psychiatry. 2016 Jul;3(7):628-35.
Mitchell AJ, Vaze A, Rao S. Clinical **diagnosis of depression in primary care**: a meta-analysis. Lancet. 2009 Jul 27. [Epub ahead of print]
Mitchell PH, Veith RC, Becker KJ, et al. Brief **psychosocial-behavioral intervention** with antidepressant reduces poststroke depression significantly more than usual care with antidepressant: living well with stroke: randomized, controlled trial. Stroke. 2009 Sep;40(9):3073-8.
Mitchell Alex J, Chan Melissa, Bhatti Henna, et al. Prevalence of **depression, anxiety, and adjustment disorder in oncological**, haematological, and palliative-care settings: a meta-analysis of 94 interview-based studies, The Lancet Oncology, Volume 12, Issue 2, Feb 2011, Pages 160-174, ISSN 1470-2045, DOI: 10.1016/S1470-2045(11)70002-X.
Mitchell AJ, Ferguson DW, Gill J, et al. **Depression and anxiety in long-term cancer survivors** compared with spouses and health controls: a systematic review and meta-analysis. Lancet Oncol 2013; online June 5.
Mohamed S, Johnson GR, Chen P, et al; **VAST-D** Investigators. Effect of antidepressant **switching (bupropion) vs augmentation (aripiprazole)** on remission among patients with major depressive disorder unresponsive to antidepressant treatment: the VAST-D randomized clinical trial. JAMA. doi:10.1001/jama.2017.8036
Mohammadinejad P, Arya P, Esfandbod M, et al. **Celecoxib Versus Diclofenac in Mild to Moderate Depression** Management Among Breast Cancer Patients: A Double-Blind, Placebo-Controlled, Randomized Trial. Ann Pharmacother. 2015 Sep;49(9):953-61.
Mohr DC, Ho J, Duffecy J, et al. Effect of **Telephone-Administered vs Face-to-face Cognitive Behavioral Therapy** on Adherence to Therapy and Depression Outcomes Among Primary Care Patients: A Randomized Trial Telephone vs In-Person Therapy for Depression. JAMA. 2012 Jun6;307(21):2278-85.
Moja P, Cusi C, Sterzi R, Canepari C. Selective serotonin re-uptake inhibitors (SSRIs) for preventing migraine and tension-type headaches. Cochrane Database Syst Rev. 2005 Jul 20;(3):CD002919. CONCLUSIONS: Over 2 months of treatment, SSRIs are no more efficacious than placebo in patients with migraine. In patients with chronic TTH, SSRIs are less efficacious than tricyclic antidepressants. In comparison with SSRIs, the burden of adverse events in patients receiving tricyclics was greater. These results are based on short-term trials and may not generalise to longer-term treatment.
Mojtabai R, Olfson M. Proportion of **antidepressants prescribed without a psychiatric diagnosis is growing**. Health Aff (Millwood). 2011 Aug;30(8):1434-42.
Mojtabai R. **Diagnosing depression in older adults in primary care**. N Engl J Med. 2014 Mar 27;370(13):1180-2.
Mojtabai R, Olfson M, Han B. National Trends in the **Prevalence and Treatment of Depression in Adolescents and Young Adults**. Pediatrics.2016;138(6):e20161878
Molyneaux E, Trevillion K, Howard LM. **Antidepressant treatment for postnatal depression**. JAMA. 2015 May 19;313(19):1965-6.
Molyneaux E, Telesia LA, Henshaw C, et al. Antidepressants for preventing postnatal depression. Cochrane Database Syst Rev. 2018 Apr 18;4:CD004363. Due to the limitations of the current evidence base, such as the low statistical power of the included studies, it is not possible to draw any clear conclusions about the effectiveness of antidepressants for the prevention of postnatal depression. It is striking that no new eligible trials have been completed in the period of over a decade since the last published version of this review. Larger trials are needed which include comparisons of antidepressant drugs with other prophylactic treatments (e.g. psychological interventions), and examine adverse effects for the fetus or infant. Future reviews in this area may benefit from broadening their focus to examine the effectiveness of antidepressants for the prevention of perinatal (i.e. antenatal or postnatal) depression, which could include studies comparing antidepressant discontinuation with continuation for the prevention of relapse of depression during pregnancy and the postnatal period.
Moncada LV. Management of **falls in older persons**: a prescription for prevention. Am Fam Physician. 2011 Dec 1;84(11):1267-76.
Montgomery SA, Baldwin DS, Blier P, et al. Which antidepressants have demonstrated superior efficacy? A review of the evidence. Int Clin Psychopharmacol. 2007 Nov;22(6):323-329. Only escitalopram was found to have definite superiority in the treatment of severe depression; probable superiority was identified for venlafaxine and possible superiority for milnacipran and clomipramine.
Moore M, Yuen HM, Dunn N, et al. Explaining the **rise in antidepressant prescribing**: a descriptive study using the general practice research database. BMJ. 2009 Oct 15;339:b3999. doi: 10.1136/bmj.b3999. (more long term users)
Moore RA, Derry S, Aldington D, et al. **Amitriptyline for neuropathic pain and fibromyalgia** in adults. Cochrane Database Syst Rev. 2012 Dec 12;12:CD008242. doi: 10.1002/14651858.CD008242.pub2. Amitriptyline has been a first-line treatment for neuropathic pain for many years. The fact that there is no supportive unbiased evidence for a beneficial effect is disappointing, but has to be balanced against decades of successful treatment in many patients with neuropathic pain or fibromyalgia.

Moore RA, Derry S, Aldington D, et al. **Amitriptyline for neuropathic pain** in adults. Cochrane Database Syst Rev. 2015 Jul 6;7:CD008242. Amitriptyline has been a first-line treatment for neuropathic pain for many years. The fact that there is no supportive unbiased evidence for a beneficial effect is disappointing, but has to be balanced against decades of successful treatment in many people with neuropathic pain. There is no good evidence of a lack of effect; rather our concern should be of overestimation of treatment effect. Amitriptyline should continue to be used as part of the treatment of neuropathic pain, but only a minority of people will achieve satisfactory pain relief. Limited information suggests that failure with one antidepressant does not mean failure with all.

Moran P, Coff ey C, Romaniuk H, et al. The natural history of **self-harm from adolescence to young adulthood**: a population-based cohort study. Lancet 2011; published online Nov 17. DOI:10.1016/S0140-6736(11)61141-0.

Morres ID, Hatzigeorgiadis A, Stathi A, et al. **Aerobic exercise for adult patients with major depressive disorder** in mental health services: A systematic review and meta-analysis. Depress Anxiety. 2019 Jan;36(1):39-53.

Mortensen JK, Larsson H, Johnsen SP, et al. Impact of **Prestroke Selective Serotonin Reuptake Inhibitor Treatment** on Stroke Severity and Mortality. Stroke. 2014 Jun 3.

Morthorst B, Krogh J, Erlangsen A, et al. Effect of **assertive outreach** after suicide attempt in the AID (assertive intervention for deliberate self harm) trial: randomised controlled trial. BMJ. 2012 Aug 22;345:e4972.

Mrug S, Orihuela C, Mrug M, Sanders PW. **Sodium and potassium excretion** predict increased depression in urban adolescents. Physiol Rep. 2019 Aug;7(16):e14213.

Mulvahill JS, Nicol GE, Dixon D, et al. Effect of **Metabolic Syndrome** on Late-Life Depression: Associations with Disease Severity and Treatment Resistance. J Am Geriatr Soc.2017 Dec;65(12):2651-2658.

Munson JC, Bynum JPW, Bell J-E, et al. Patterns of prescription drug use before and after **fragility fracture** [online August 22, 2016].JAMA Intern Med. doi:10.1001/jamainternmed.2016.4814

Murdoch D, Keam SJ. **Escitalopram**: a review of its use in the management of major depressive disorder. Drugs. 2005;65(16):2379-404.

Murrough JW, Iosifescu DV, Chang LC, et al. Antidepressant Efficacy of **Ketamine** in Treatment-Resistant Major Depression: A Two-Site Randomized Controlled Trial. Am J Psychiatry. 2013 Oct 1;170(10):1134-1142.

Musliner KL, Mortensen PB, McGrath JJ, et al; Bipolar Disorder Working Group of the Psychiatric Genomics Consortium. Association of **Polygenic Liabilities** for Major Depression, Bipolar Disorder, and Schizophrenia With Risk for Depression in the Danish Population. JAMA Psychiatry. 2019 Jan 30.

Musliner KL, Munk-Olsen T, Laursen TM, et al. Heterogeneity in **10-Year Course Trajectories of Moderate to Severe Major Depressive** Disorder: A Danish National Register-Based Study. JAMA Psychiatry. 2016 Apr 1

Musters C, McDonald E, Jones I. **Management of postnatal depression**. BMJ. 2008 Aug 8;337:a736. doi: 10.1136/bmj.a736.

Mutz J, Vipulananthan V, Carter B, et al. Comparative efficacy and acceptability of **non-surgical brain stimulation** for the acute treatment of major depressive episodes in adults: systematic review and network meta-analysis. BMJ. 2019 Mar 27;364:l1079.

Myers ER, Aubuchon-Endsley N, Bastian LA, et al. Efficacy and Safety of **Screening for Postpartum Depression**. AHRQ Comparative Effectiveness Review. Rockville (MD): Agency for Healthcare Research and Quality (US); 2013 Apr. Report No.:13-EHC064-E.

Myles N, Newall H, Ward H, Large M. Systematic meta-analysis of individual **selective serotonin reuptake inhibitor** medications and **congenital malformations**. Aust N Z J Psychiatry. 2013 Nov;47(11):1002-12.

Nahas Z, Marangell LB, Husain MM, et al. Two-Year Outcome of Vagus Nerve Stimulation (VNS) for Treatment of Major Depressive Episodes. J Clin Psychiatry. 2005 Sep;66(9):1097-1104.

Nahas Richard, Sheikh Osmaan. **Complementary and alternative medicine** for the treatment of major depressive disorder Can Fam Physician June 2011 57: 659-663. (**St John's wort & exercise**)

Nakagawa A, Mitsuda D, Sado M, et al. Effectiveness of Supplementary **Cognitive-Behavioral Therapy** for Pharmacotherapy-Resistant Depression: A Randomized Controlled Trial. J Clin Psychiatry. 2017 Feb 28.

Nakamura S, Kato K, Yoshida A, et al. Prognostic Value of **Depression**, Anxiety, and Anger in Hospitalized **Cardiovascular** Disease Patients for Predicting Adverse Cardiac Outcomes. Am J Cardiol. 2013 Feb 20.

Naparstek J, Wing RR, Xu X, Leahey TM. **Internet-delivered obesity treatment** improves symptoms of and risk for depression. Obesity (Silver Spring). 2017 Apr;25(4):671-675.

Navarro V, Gastó C, Torres X, et al. Continuation/maintenance treatment with nortriptyline (n=17) versus combined **nortriptyline and ECT** (n=16)in late-life psychotic depression: a two-year randomized study. Am J Geriatr Psychiatry. 2008 Jun;16(6):498-505. This study supports the judicious use of combined continuation/maintenance ECT and antidepressant treatment in elderly patients with psychotic unipolar depression who are ECT remitters.

Nelson JC, et al. **Mirtazapine** orally disintegrating tablets in depressed nursing home residents **85 years of age and older**. Int J Geriatr Psychiatry. 2006 Sep;21(9):898-901.

Nelson JC, Papakostas GI. Atypical **antipsychotic augmentation** in major depressive disorder: a meta-analysis of placebo-controlled randomized trials. Am J Psychiatry. 2009 Sep;166(9):980-91. Epub 2009 Aug 17.

Nelson JC, Devanand DP. A Systematic Review and Meta-Analysis of Placebo-Controlled Antidepressant Studies in People with **Depression and Dementia** J Am Geriatr Soc. 2011 Apr;59(4):577-85.

Nelson JC, Delucchi KL, Schneider LS. **Moderators of outcome in late-life depression**: a patient-level meta-analysis. Am J Psychiatry. 2013 Jun 1;170(6):651-9.

Nembhard WN, et al. Maternal and infant genetic variants, **maternal periconceptional use of selective serotonin reuptake inhibitors**, and risk of congenital heart defects in offspring: population based study. BMJ. 2017 Mar 6;356:j832.

Nemoda Z et al. **Maternal depression** is associated with DNA methylation changes in cord blood T lymphocytes and adult hippocampi. Transl Psychiatr 2015 Apr 7; 5:e545.

Netsi E, Pearson RM, Murray L, et al. Association of **persistent and severe postnatal depression** with child outcomes [online Jan 31, 2018].JAMA Psychiatry. doi:10.1001/jamapsychiatry.2017.4363

Neufeld SAS, Dunn VJ, Jones PB, et al. **Reduction in adolescent depression following contact with mental health services**: a longitudinal cohort study in the UK. Lancet Psychiatry 2017; online Jan 10.

Neuman G, Colantonio D, Delaney S, et al. **Bupropion and Escitalopram During Lactation**. Ann Pharmacother. 2014 Apr 14;48(7):928-931.

Newport DJ, Carpenter LL, McDonald WM, et al. **Ketamine** and **Other NMDA Antagonists**: Early Clinical Trials and Possible Mechanisms in Depression. Am J Psychiatry. 2015 Oct 1;172(10):950-66.

NICE: CG90 Depression in **adults**: quick reference guide Oct/2009 http://www.nice.org.uk/nicemedia/pdf/CG%2090%20QRG%20LR%20FINAL.pdf **Updated 2016**: https://www.nice.org.uk/guidance/cg90

NICE: CG91 National Collaborating Centre for Mental Health. Depression in adults with a chronic physical health problem. Treatment and management. London (UK): National Institute for Health and Clinical Excellence (NICE); 2009 Oct. 54 p. (Clinical guideline; no. 91). http://guidance.nice.org.uk/CG91

NICE: Jan **2011**: **Generalised anxiety disorder** (GAD) and panic disorder (PD) (with or without agoraphobia) in adults. http://guidance.nice.org.uk/CG113/QuickRefGuide/pdf/English ; http://guidance.nice.org.uk/CG113

NICE: Pilling Stephen, Whittington Craig, Taylor Clare, et al. on behalf of the Guideline Development Group. Guidelines: Identification and **care pathways for common mental health disorders**: summary of NICE guidance. BMJ 2011;342:doi:10.1136/bmj.d2868 (Published 24 May 2011)

NICE: National Institute for Health and Clinical Excellence. Common mental health disorders: identification and **pathways to care**. (Clinical guideline CG123. 2011. http://guidance.nice.org.uk/CG123 .

NICE: National Institute for Health and Clinical Excellence. **Self-harm**: longer-term management. (Clinical guideline CG133.) 2011. http://guidance.nice.org.uk/CG133.

NICE: National Institute for Health and Care Excellence. **Social anxiety disorder**: recognition, assessment and treatment of social anxiety disorder. (Clinical guideline 159.) 2013. http://guidance.nice.org.uk/CG159 .

NICE: National Institute for Health and Care Excellence. **Depression in children and young people**: Identification and management in primary, community and secondary care. (Clinical guideline 28.) 2015. www.nice.org.uk/guidance/cg28.

NICE: National Collaborating Centre for Mental Health. **Depression in children and young people**: identification and management in primary, community and secondary care. 2015 Mar.

Nierenberg AA, Fava M, Trivedi MH, et al. A comparison of **lithium and T(3)** augmentation following two failed medication treatments for depression: a **STAR*D** report. Am J Psychiatry. 2006 Sep;163(9):1519-30; quiz 1665. Remission rates with lithium (up to 900mg/d) and T(3) augmentation (up to 50ug/d) for participants who experienced unsatisfactory results with two prior medication treatments were modest and did not differ significantly. The lower side effect burden and ease of use of T(3) augmentation suggest that it has slight advantages over lithium augmentation for depressed patients who have experienced several failed medication trials.

Nieuwenhuijsen K, Faber B, Verbeek JH, et al. Interventions to **improve return to work** in depressed people. Cochrane Database Syst Rev. 2014 Dec 3;12:CD006237. We found moderate quality evidence that adding a work-directed intervention to a clinical intervention reduced the number of days on sick leave compared to a clinical intervention alone. We also found moderate quality evidence that enhancing primary or occupational care with cognitive behavioural therapy reduced sick leave compared to the usual care. A structured telephone outreach and care management program that included medication reduced sickness absence compared to usual care. However, enhancing primary care with a quality improvement program did not have a considerable effect on sickness absence. There was no evidence of a difference in effect on sickness absence of one antidepressant medication compared to another. More studies are needed on work-directed interventions. Clinical intervention studies should also include work outcomes to increase our knowledge on reducing sickness absence in depressed workers.

Nieuwsma JA, et al. Diagnostic accuracy of **screening tests and treatment for post–acute coronary syndrome depression**. A systematic review. Ann Intern Med. 2017. [Epub ahead of print]. doi:10 .7326/M17-1811

Nikoloski Z, Zhang A, Hopkin G, Mossialos E. Self-**reported Symptoms of Depression Among Chinese Rural-to-Urban Migrants** and Left-Behind Family Members. JAMA Netw Open. 2019 May 3;2(5):e193355.

Nillni YI, Wesselink AK, Gradus JL, et al. Depression, anxiety, and psychotropic medication use and **fecundability**. Am J Obstet Gynecol. 2016 Apr 27.

Noble AJ, Reilly J, Temple J, et al. **Cognitive-behavioural therapy does not meaningfully reduce depression** in most people **with epilepsy**: a systematic review of clinically reliable improvement. J Neurol Neurosurg Psychiatry. 2018 May 7.
Nock MK, Green JG, Hwang I, et al. Prevalence, Correlates, and Treatment of **Lifetime Suicidal Behavior Among Adolescents**: Results From the National Comorbidity Survey Replication Adolescent Supplement. JAMA Psychiatry. 2013 Jan 9:1-11.
Nock MK, Stein MB, Herringa SG, et al; **Army STARRS** Collaborators. Prevalence and correlates of **suicidal** behavior among soldiers: results from the Army Study to Assess Risk and Resilience in Servicemembers (Army STARRS) [online March 3, 2014]. JAMA Psychiatry. doi:10.1001/jamapsychiatry.2014.30.
Norby U, Forsberg L, Wide K, et al. **Neonatal Morbidity After Maternal** Use of **Antidepressant Drugs During Pregnancy**. Pediatrics.2016:138(5):e20160181
Norris D , Clark M. **Evaluation and Treatment of the Suicidal** Patient Am Fam Physician. 2012 Mar 15;85(6):602-605.
Nunns D, Murphy R. Assessment and management of **vulval pain**. BMJ. 2012 Mar 28;344:e1723.
Nussbaumer B, Kaminski-Hartenthaler A, Forneris CA, et al. **Light therapy for preventing seasonal affective disorder**. Cochrane Database of Systematic Reviews 2015, Issue 11. Art. No.: CD011269. DOI: 10.1002/14651858.CD011269.pub2. Evidence on light therapy as preventive treatment for patients with a history of SAD is limited. Methodological limitations and the small sample size of the only available study have precluded review author conclusions on effects of light therapy for SAD. Given that comparative evidence for light therapy versus other preventive options is limited, the decision for or against initiating preventive treatment of SAD and the treatment selected should be strongly based on patient preferences.
O'Brien Shaughn, Rapkin Andrea, Dennerstein Lorraine, et al. Diagnosis and management of **premenstrual disorders**. BMJ 2011;342:doi:10.1136/bmj.d2994 (Published 3 June 2011)
O'Brien EC, Greiner MA, Sims M, et al. **Depressive symptoms and risk of cardiovascular events** in African Americans: Findings from the Jackson Heart Study. *Circ Cardiovasc Qual Outcomes*. 2015; 8:552-559.
O'Connor BC, Lewandowski RE, Rodriguez S, et al. Usual Care for **Adolescent Depression** From Symptom Identification Through Treatment Initiation. JAMA Pediatr. 2016 Feb 1.
O`Connor EA, Whitlock EP, Beil TL, et al. **Screening for depression** in **adult patients** in primary care settings: a systematic evidence review. Ann Intern Med. 2009 Dec 1;151(11):793-803.
O'Connor E, Gaynes BN, Burda BU, et al. **Screening for and Treatment of Suicide** Risk Relevant to Primary Care: A Systematic Review for the U.S. Preventive Services Task Force. Ann Intern Med. 2013 Apr 23.
O'Connor E, Rossom RC, Henninger M, et al. Primary Care **Screening for and Treatment of Depression in Pregnant and Postpartum Women**: Evidence Report and Systematic Review for the US Preventive Services Task Force (**USPSTF**). JAMA. 2016 Jan 26;315(4):388-406.
O'Connor E, Senger CA, Henninger M, et al. **Interventions to Prevent Perinatal Depression**: A Systematic Evidence Review for the U.S. Preventive Services Task Force [Internet]. Rockville (MD): Agency for Healthcare C Research and Quality (US); 2019 Feb. Available from http://www.ncbi.nlm.nih.gov/books/NBK537819/
O'moore KA, Newby JM, et al. **Internet Cognitive-Behavioral Therapy** for Depression in Older Adults With Knee Osteoarthritis: A Randomized Controlled Trial. Arthritis Care Res (Hoboken). 2018 Jan;70(1):61-70.
Obayashi K, Saeki K, Kurumatani N. **Bedroom Light Exposure** at Night and the Incidence of Depressive Symptoms: A Longitudinal Study of the **HEIJO-KYO** Cohort.Am J Epidemiol. 2018 Mar 1;187(3):427-434.
Ogawa Y, Takeshima N, Hayasaka Y, et al. Antidepressants plus benzodiazepines for adults with major depression **.** Cochrane Database Syst Rev. 2019 Jun 3;6:CD001026. Combined antidepressant plus benzodiazepine therapy was more effective than antidepressants alone in improving depression severity, response in depression and remission in depression in the early phase. However, these effects were not maintained in the acute or the continuous phase. Combined therapy resulted in fewer dropouts due to adverse events than antidepressants alone, but combined therapy was associated with a greater proportion of participants reporting at least one adverse effect.The moderate quality evidence of benefits of adding a benzodiazepine to an antidepressant in the early phase must be balanced judiciously against possible harms and consideration given to other alternative treatment strategies when antidepressant monotherapy may be considered inadequate.
Oh SW, Kim J, Myung SK, et al. **Antidepressant Use and Risk of Coronary Heart** Disease: Meta-Analysis of Observational Studies. Br J Clin Pharmacol. 2014 Mar 20.
Ohayon MM, Mahowald MW, Dauvilliers Y, et al. Prevalence and comorbidity of **nocturnal wandering** in the US adult general population. Neurology.2012 May 15;78(20):1583-9. (association with SSRIs)
Olchanski N, McInnis Myers M, Halseth M, et al. The **Economic Burden** of **Treatment-Resistant Depression**. Clin Ther. 2013 Mar 12.
Oldham JM, Gabbard GO, Goin MK, et al. Practice guideline for the treatment of patients with **borderline personality disorder**. Am J Psychiatry 2001;158:Suppl:1-52.
Olfson M, Shaffer D, Marcus SC, Greenberg T. Relationship between antidepressant medication treatment and **suicide** in adolescents. Arch Gen Psychiatry. 2003 Oct;60(10):978-82.
Olfson M, Marcus SC, Tedeschi M, Wan GJ. **Continuity of antidepressant treatment** for adults with depression in the United States. Am J Psychiatry. 2006 Jan;163(1):101-8.
Olfson M, Blanco C, Marcus SC. **Treatment of Adult Depression in the United States**. JAMA Intern Med. 2016 Aug 29.
Omori IM, Watanabe N, Nakagawa A, et al. **Fluvoxamine** versus other anti-depressive agents for depression. Cochrane Database Syst Rev. 2010 Mar 17;3:CD006114.
Opel N, Redlich R, Dohm K, et al. Mediation of the influence of **childhood maltreatment** on depression relapse by cortical structure: a 2-year longitudinal observational study. Lancet Psychiatry. 2019 Apr;6(4):318-326.
O'reardon JP, et al. A randomized, placebo-controlled trial of sertraline in the treatment of **night eating syndrome**. Am J Psychiatry. 2006 May;163(5):893-8.
Ornstein KA, Aldridge MD, Garrido MM, et al. Association Between **Hospice Use and Depressive Symptoms** in Surviving Spouses. JAMA Intern Med. 2015 May 26.
Orriols L, Wilchesky M, Lagarde E, Suissa S. Prescription of antidepressants and the **risk of road traffic crash** in the elderly: a case-crossover study. Br J Clin Pharmacol. 2013 Nov;76(5):810-5.
Orgeta V, Qazi A, Spector A, et al. **Psychological treatments** for depression and anxiety in dementia and mild cognitive impairment: systematic review and meta-analysis. Br J Psychiatry. 2015 Oct;207(4):293-8.
Orgeta V, Brede J, Livingston G. **Behavioural activation** for depression in older people: systematic review and meta-analysis. Br J Psychiatry. 2017 Nov;211(5):274-279.
Ostuzzi G, Matcham F, Dauchy S, et al. **Antidepressants for the treatment of depression in people with cancer**. Cochrane Database Syst Rev. 2015 Jun 1;6:CD011006. Despite the impact of depression on people with cancer, available studies were very few and of low quality. This review found very low quality evidence for the effects of these drugs compared with placebo. On the basis of these results clear implications for practice cannot be made. The use of antidepressants in people with cancer should be considered on an individual basis and, considering the lack of head-to-head data, the choice of which agent should be prescribed may be based on the data on antidepressant efficacy in the general population of individuals with major depression, also taking into account that data on medically ill patients suggest a positive safety profile for the SSRIs. Large, simple, randomised, pragmatic trials comparing commonly used antidepressants versus placebo in people with cancer with depressive symptoms, with or without a formal diagnosis of a depressive disorder, are urgently needed to better inform clinical practice.
Ostuzzi G, Matcham F, Dauchy S, et al. Antidepressants for the treatment of depression in people with cancer. Cochrane Database Syst Rev. 2018 Apr 23;4:CD011006. Despite the impact of depression on people with cancer, the available studies were very few and of low quality. This review found very low certainty evidence for the effects of these drugs compared with placebo. On the basis of these results, clear implications for practice cannot be deduced. The use of antidepressants in people with cancer should be considered on an individual basis and, considering the lack of head-to-head data, the choice of which agent to prescribe may be based on the data on antidepressant efficacy in the general population of individuals with major depression, also taking into account that data on medically ill patients suggest a positive safety profile for the SSRIs. To better inform clinical practice, there is an urgent need for large, simple, randomised, pragmatic trials comparing commonly used antidepressants versus placebo in people with cancer who have depressive symptoms, with or without a formal diagnosis of a depressive disorder.
Overberg A, Morton S, Wagner E, Froberg B. Toxicity of **Bupropion Overdose Compared With Selective Serotonin Reuptake Inhibitors**. Pediatrics. 2019 Jul 5.
Morriss R, Kapur N, Byng R. Assessing risk of **suicide or self harm** in adults. BMJ. 2013 Jul 25;347:f4572.
Owenby RK, Brown LT, Brown JN. Use of **Risperidone** as Augmentation Treatment for Major Depressive Disorder (January). Ann Pharmacother. 2010 Dec 28.
Owens C, Owen G, Belam J, Lloyd K, Rapport F, Donovan J, et al. Recognising and responding to **suicidal crisis** within the **family and social network**: qualitative study. BMJ 2011;343;d5801.
Paine NJ, Bacon SL, Pelletier R, et al. Do Women With Anxiety or Depression Have **Higher Rates of Myocardial Ischemia** During Exercise Testing Than Men? Circ Cardiovasc Qual Outcomes. 2016 Jan;9(1):S53-61.
Palmer EC, Binns LN, Carey H. **Levomilnacipran**: A New Serotonin-Norepinephrine Reuptake Inhibitor for the Treatment of Major Depressive Disorder. Ann Pharmacother. 2014 May 8;48(8):1030-1039.
Palmsten K, Hernández-Díaz, Huybrechts KF, et al. Use of **antidepressants near delivery and risk of postpartum hemorrhage**: cohort study of low income women in the United States. BMJ 2013;347:f4877.
Pan An; Lucas Michel; Sun Qi; et al. **Bidirectional Association Between Depression and Type 2 Diabetes Mellitus** in Women. Arch Intern Med. 2010;170(21):1884-1891.
Pan A, Okereke OI, Sun Q, et al. Depression and **Incident Stroke** in Women. Stroke. 2011 Aug 11.
Pan A, Sun Q, Okereke OI, Rexrode KM, Hu FB. **Depression and risk of stroke** morbidity and mortality: a meta-analysis and systematic review. JAMA. 2011 Sep 21;306(11):1241-9.
Pan LA et al. Neurometabolic disorders: Potentially treatable abnormalities in patients with **treatment-refractory depression** and suicidal behavior. Am J Psychiatry 2016 Aug 13.

Pandya M, Pozuelo L, Malone D. **Electroconvulsive therapy** (ECT): what the internist needs to know. Cleve Clin J Med. 2007 Sep;74(9):679-85.
Papakostas GI, Thase ME, Fava M, Nelson JC, Shelton RC. Are antidepressant drugs that combine **serotonergic and noradrenergic mechanisms** of action more effective than the selective serotonin reuptake inhibitors in treating major depressive disorder? A meta-analysis of studies of newer agents. Biol Psychiatry. 2007 Dec 1;62(11):1217-27. Epub 2007 Jun 22.
Papakostas GI. Managing partial response or nonresponse: **switching, augmentation, and combination** strategies for major depressive disorder. J Clin Psychiatry. 2009;70 Suppl 6:16-25.
Papakostas GI, Mischoulon D, Shyu I, Alpert JE, Fava M. S-adenosyl methionine (SAMe) augmentation of serotonin reuptake inhibitors for antidepressant nonresponders with major depressive disorder: double-blind, randomized clinical trial. Am J Psychiatry. 2010 Aug;167(8):942-8. These preliminary results suggest that **SAMe can be an effective**, well-tolerated, and safe adjunctive treatment strategy for SRI nonresponders with major depressive disorder and warrant replication.
Papakostas GI et al. **Ziprasidone augmentation of escitalopram** for major depressive disorder: Efficacy results from a randomized, double-blind, placebo-controlled study. Am J Psychiatry 2015 Jun 18.
Parashar S, et al. Time course of depression and outcome of **myocardial infarction**. Arch Intern Med. 2006 Oct 9;166(18):2035-43.
Park LT, Zarate CA Jr. **Depression in the Primary Care Setting**. N Engl J Med. 2019 Feb 7;380(6):559-568.
Park SH, Han KS, Kang CB. Effects of **exercise** programs on depressive symptoms, quality of life and self-esteem in older people: A systematic review of randomized controlled trials. Appl Nurs Res. 2014 Jan 30.
Parkin L, Balkwill A, Sweetland S, et al. **Antidepressants, Depression, and Venous Thromboembolism Risk**: Large Prospective Study of UK Women. J Am Heart Assoc. 2017 May 17;6(5).
Parkman HP, Van Natta ML, Abell TL, et al. Effect of **nortriptyline** on symptoms of **idiopathic gastroparesis**: the NORIG randomized clinical trial. JAMA. 2013 Dec 25;310(24):2640-9.
Parmet S, Glass TJ, Glass RM. JAMA **patient page. Obsessive-compulsive disorder**. JAMA. 2004 Oct 27;292(16):2040.
Patatanian E, Toedter Williams N. Drug-Induced **Yawning**--A Review (October). Ann Pharmacother. 2011 Sep 20.
Patel G, Fancher TL, **In the Clinic: General Anxiety Disorder**. Ann Intern Med Dec 3, 2013 ITC6 1-12.
Patel R, Reiss P, Shetty H, et al. Do **antidepressants increase the risk of mania and bipolar disorder** in people with depression? A retrospective electronic case register cohort study. BMJ Open. 2015 Dec 14;5(12):e008341.
Patel V, Weobong B, et al. The Healthy Activity Program (**HAP**), a **lay counsellor-delivered brief psychological treatment** for severe depression, in primary care in India: a randomised controlled trial. Lancet. 2016 Dec 14.
Patton GC, Romaniuk H, Spry E, et al. Prediction of **perinatal depression** from adolescence and before conception (VIHCS): 20-year prospective cohort study. Lancet 2015; online June 11.
Paulden Mike, Palmer Stephen, Hewitt Catherine, et al. **Screening for postnatal** depression in primary care: cost effectiveness analysis. BMJ 2009;339:b5203, doi: 10.1136/bmj.b5203 (Published 22 Dec 2009)
Pearson RM et al. **Maternal depression during pregnancy** and the postnatal period: Risks and possible mechanisms for offspring depression at age 18 years. JAMA Psychiatry 2013 Oct 9.
Pearson RM, Carnegie RE, Cree C, et al. Prevalence of **Prenatal Depression** Symptoms Among 2 Generations of Pregnant MothersThe Avon Longitudinal Study of Parents and Children. JAMA Network Open.2018;1(3):e180725.
Peciña M, Bohnert AS, Sikora M, et al. Association Between **Placebo-Activated** Neural Systems and Antidepressant Responses: Neurochemistry of Placebo Effects in Major Depression. JAMA Psychiatry. 2015 Sep 30:1-8.
Pedersen LH, Henriksen TB, Olsen J. **Fetal Exposure to Antidepressants** and Normal Milestone Development at 6 and 19 Months of Age. Pediatrics. 2010 Feb 22.
Pedersen MG, Mortensen PB, Norgaard-Pedersen B, Postolache TT. **Toxoplasma gondii Infection** and Self-directed Violence in MothersToxoplasma Gondii and Self-directed Violence. Arch Gen Psychiatry. 2012 Jul 2:1-8.
Péquignot R, Dufouil C, Prugger C, et al. High Level of Depressive Symptoms at Repeated Study Visits and **Risk of Coronary Heart Disease and Stroke** over 10 Years in Older Adults: The Three-City Study. J Am Geriatr Soc. 2016 Jan;64(1):118-25.
Pettinati HM, Oslin DW, Kampman KM, et al. A Double-Blind, Placebo-Controlled Trial Combining **Sertraline and Naltrexone** for Treating Co-Occurring **Depression and Alcohol** Dependence. Am J Psychiatry. 2010 Mar 15.
Pergadia ML, Glowinski AL, Wray NR, et al. A **3p26-3p25 Genetic Linkage** Finding for DSM-IV Major Depression in Heavy Smoking Families. Am J Psychiatry. 2011 May 15.
Perkins S, et al. Self-help and Guided **Self-help** for **Eating Disorders**. Cochrane Database Syst Rev. 2006 Jul 19;3:CD004191.
Perrin JS, Merz S, Bennett DM, et al. **Electroconvulsive therapy** reduces frontal cortical connectivity in severe depressive disorder. Proc Natl Acad Sci U S A. 2012 Mar 19.
Petersen I, Evans SJ, Gilbert R, et al. **Selective serotonin reuptake inhibitors and congenital heart anomalies**: comparative cohort studies of women treated before and during pregnancy and their children. J Clin Psychiatry. 2016 Jan;77(1):e36-42.
Petersen I, Peltola T, Kaski S, et al. Depression, **depressive symptoms** and treatments **in women who have recently given birth**: UK cohort study. BMJ Open. 2018 Oct 8(10):e022152
Pharmacist's Letter May 2006: Pharmacotherapy of **Treatment-Resistant Depression**
Phillips ML. A Promising Future Role for Neuroimaging in Tracking and Predicting Relapse in Major Depressive Disorder. JAMA Psychiatry. 2018 Mar 28.
Phipps MG, Raker CA, Ware CF, et al. Randomized controlled trial to **prevent postpartum depression in adolescent mothers**.Am J Obstet Gynecol. 2013 Mar;208(3):192.e1-6.
Phillips JL, Norris S, Talbot J, et al. **Single, Repeated, and Maintenance Ketamine Infusions for Treatment-Resistant Depression**: A Randomized Controlled Trial. Am J Psychiatry. 2019 May 1;176(5):401-409.
PHQ-9 Patient Health Questionnaire: **Depression Screen** http://www.viha.ca/NR/rdonlyres/BCA23E92-223A-4A86-A07C-D45B37B5815E/8564/PHQ9PatientHealthQuestionnaireforDepression.pdf
Pinto Pereira SM, Geoffroy MC, Power C. Depressive Symptoms and **Physical Activity** During 3 Decades in Adult Life: Bidirectional Associations in a Prospective Cohort Study. JAMA Psychiatry. 2014 Oct 15.
Pinto-Sanchez MI, Hall GB, et al. **Probiotic Bifidobacterium longum NCC3001 Reduces Depression Scores** and Alters Brain Activity: a Pilot Study in Patients With Irritable Bowel Syndrome. Gastroenterology. 2017 May 5.
Pitman A, Suleman S, Hyde N, et al. Depression and anxiety in patients with cancer. BMJ. 2018 Apr 25;361:k1415.
Pitman A, Suleman S, Hyde N, et al. Exploring low mood in a person with cancer. BMJ. 2018 Apr 25;361:k1488.
Pizzagalli DA, Berretta S, Wooten D, et al. Assessment of **Striatal Dopamine Transporter Binding** in Individuals With Major Depressive Disorder: In Vivo Positron Emission Tomography and Postmortem Evidence. JAMA Psychiatry. 2019 May 1.
Pizzagalli DA, Webb CA, et al. **Pretreatment Rostral Anterior Cingulate Cortex Theta Activity** in Relation to Symptom Improvement in Depression: A Randomized Clinical Trial. JAMA Psychiatry. 2018 Apr 11.
Pizzi C, Rutjes AW, Costa GM, Fontana F, Mezzetti A, Manzoli L. Meta-Analysis of Selective Serotonin Reuptake Inhibitors in Patients With Depression and **Coronary Heart Disease**. Am J Cardiol. 2011 Jan 20.
Pols AD, Adriaanse MC, van Tulder MW, et al. Two-year effectiveness of a **stepped-care depression prevention** intervention and predictors of incident depression in primary care **patients with diabetes type 2** and/or **coronary heart disease** and subthreshold depression: data from the Step-Dep cluster randomised controlled trial. BMJ Open. 2018 Oct 28; 8(10):e020412.
Popova V, Daly EJ, Trivedi M, et al. Efficacy and Safety of Flexibly Dosed **Esketamine Nasal Spray Combined With a Newly Initiated Oral Antidepressant in Treatment-Resistant Depression**: A Randomized Double-Blind Active-Controlled Study. Am J Psychiatry. 2019 May 21:appiajp201919020172.
Portella MJ, de Diego-Adeliño J, Ballesteros J, et al. Can we really accelerate and enhance the selective serotonin reuptake inhibitor antidepressant effect? a randomized clinical trial and a meta-analysis of **pindolol** in nonresistant depression. J Clin Psychiatry. 2010 Oct 19
Posner K et al. The **columbia-suicide severity rating scale**: initial validity and internal consistency findings from three multisite studies with adolescents and adults. Am J Psychiatry. 2011 Dec 1;168(12):1266-77.
Povitz M, Bolo CE, Heitman SJ, et al. Effect of **treatment of obstructive sleep apnea on depressive symptoms**: systematic review and meta-analysis. PLoS Med. 2014 Nov 25;11(11):e1001762.
Prasad SM, Eggener SE, Lipsitz SR, et al. Effect of Depression on Diagnosis, Treatment, and Mortality of Men With Clinically Localized **Prostate Cancer**. J Clin Oncol. 2014 Jul 7.
Pratt LA, Brody DJ, Gu Q. **Antidepressant use in persons aged 12 and over**: United States, 2005–2008. NCHS data brief, no 76. Hyattsville, MD: National Center for Health Statistics. 2011. http://www.cdc.gov/nchs/data/databriefs/db76.pdf
Pringsheim T, Gardner D, Patten SB. Adjunctive treatment with **quetiapine** for major depressive disorder: are the benefits of treatment worth the risks? BMJ. 2015 Mar 4;350:h569.
Pringsheim T, Kelly M, Barbui C. **Stopping antidepressants following depression**. BMJ. 2016 Feb 18;352:i220.

Pritchett RV, Daley AJ, Jolly K. Does **aerobic exercise reduce postpartum depressive symptoms**? a systematic review and meta-analysis. Br J Gen Pract. 2017 Oct;67(663):e684-e691.

Purgato M, Papola D, Gastaldon C, et al. **Paroxetine versus other anti-depressive** agents for depression. *Cochrane Database of Systematic Reviews* 2014, Issue 4. Art. No.: CD006531. DOI: 10.1002/14651858.CD006531.pub2. Some possibly clinically meaningful differences between paroxetine and other ADs exist, but no definitive conclusions can be drawn from these findings. In terms of response, there was a moderate quality of evidence that citalopram was better than paroxetine in the acute phase (six to 12 weeks), although only one study contributed data. In terms of early response to treatment (one to four weeks) there was moderate quality of evidence that mirtazapine was better than paroxetine and that paroxetine was better than reboxetine. However there was no clear evidence that paroxetine was better or worse compared with other antidepressants at increasing response to treatment at any time point.

Putnam KT, Wilcox M, Robertson-Blackmore E, et al. Clinical **phenotypes of perinatal depression** and time of symptom onset: analysis of data from an International Consortium. Lancet Psychiatry. 2017 May 2

Qaseem A, Snow V, Denberg TD, et al; Clinical Efficacy Assessment Subcommittee of American College of Physicians. Using **second-generation antidepressants** to treat depressive disorders: a clinical practice guideline from the American College of Physicians (**ACP**). Ann Intern Med. 2008 Nov 18;149(10):725-33.

Qaseem A, Barry MJ, Kansagara D; Clinical Guidelines Committee of the American College of Physicians. **Nonpharmacologic versus pharmacologic treatment of adult** patients with major depressive disorder: a clinical practice guideline from the American College of Physicians (**ACP**). Ann Intern Med. 2016. [Epub ahead of print] doi:10 .7326/M15-2570

Qato DM, Ozenberger K, Olfson M. Prevalence of **Prescription Medications With Depression as a Potential Adverse Effect** Among Adults in the United States. JAMA. 2018 Jun 12;319(22):2289-2298. (eg. Gabapentin, cyclobenzaprine)

Qin P, Hawton K, Mortensen PB, et al. Combined effects of **physical illness and comorbid psychiatric disorder on risk of suicide** in a national population study. Br J Psychiatry. 2014 Feb 27.

Qin B, Zhang Y, Zhou X, et al. Selective Serotonin Reuptake Inhibitors Versus Tricyclic Antidepressants in **Young Patients**: A Meta-analysis of Efficacy and Acceptability. Clin Ther. 2014 Jul 2.

Quinn GR, Singer DE, Chang Y, et al. Effect of **selective serotonin reuptake inhibitors on bleeding risk** in patients with atrial fibrillation taking warfarin. Am J Cardiol. 2014 Aug 15;114(4):583-6.

Quintana DS, Steen NE, Andreassen OA. The Promise of **Intranasal Esketamine** as a Novel and Effective Antidepressant. JAMA Psychiatry. 2017 Dec 27.

Rabiee A, Nikayin S, Hashem MD, et al. Depressive Symptoms **After Critical Illness**: A Systematic Review and Meta-Analysis. Crit Care Med. 2016 Sep;44(9):1744-53

Radesky JS, Zuckerman B, Silverstein M, et al. **Inconsolable Infant Crying** and Maternal Postpartum Depressive Symptoms. Pediatrics. 2013 May 6.

Rahimi-Ardabili B, et al. **Finasteride-induced depression** : A prospective study. BMC Clin Pharmacol. 2006 Oct 7;6(1):7 [Epub ahead of print]

Rai D, Lee B, Dalman C, et al. **Antidepressants during pregnancy and autism in offspring**: population based cohort study. BMJ 2017;358:j2811.

Ramanuj P, Ferenchick EK, Pincus HA. **Depression in primary care**: part 2-management. BMJ. 2019 Apr 8;365:l835.

Ramos É, St-André M, Bérard A. Association between antidepressant use during pregnancy and infants born **small for gestational age (Venlafaxine).** Can J Psychiatry. 2010 Oct;55(10):643-52.

Rasmussen MH, et al. **Risk, treatment duration, and recurrence risk of postpartum affective disorder** in women with no prior psychiatric history: A population-based cohort study. PLoS Med. 2017 Sep 26;14(9):e1002392

Ravi S, Khalili H, Abbasian L, et al. Effect of **Omega-3 Fatty Acids** on Depressive Symptoms in HIV-Positive Individuals: A Randomized, Placebo-Controlled Clinical Trial. Ann Pharmacother. 2016 Oct;50(10):797-807

Rayner L, Price A, Evans A, Valsraj K, Higginson IJ, Hotopf M. **Antidepressants for depression in physically ill** people. Cochrane Database Syst Rev. 2010 Mar 17;3:CD007503.

Rector TS et al. Outcomes of **citalopram dosage risk mitigation in a veteran population**. Am J Psychiatry 2016 May 10.

Read J, Cunliffe S, Jauhar S, McLoughlin DM. **Should we stop using electroconvulsive therapy**? BMJ. 2019 Jan 9;364:k5233.

Reed SD, Guthrie KA, Joffe H, et al. **Sexual function in nondepressed women using escitalopram** for vasomotor symptoms: a randomized controlled trial. Obstet Gynecol. 2012 Mar;119(3):527-38.

Reefhuis J, Devine O, Friedman JM, et al; National Birth Defects Prevention Study. Specific **SSRIs and birth defects**: bayesian analysis to interpret new data in the context of previous reports. BMJ. 2015 Jul 8;351:h3190.

Reefhuis J, Devine O, Friedman JM, et al. Specific **SSRIs and birth defects**: Bayesian analysis to interpret new data in the context of previous reports. BMJ. 2015 Jul 8;351:h3190.

Reid Steven, Barbui Corrado. **Long term treatment of depression** with selective serotonin reuptake inhibitors and newer antidepressants. BMJ 2010;340:c1468, doi: 10.1136/bmj.c1468 (26 March 2010)

Reinhardt JP, Horowitz A, Cimarolli VR, Eimicke JP, Teresi JA. Addressing **Depression in a Long-term Care Setting**: A Phase II Pilot of Problem-solving Treatment. Clin Ther. 2014 Nov 1;36(11):1531-7.

Renoux C, Vahey S, Dell'Aniello S, Boivin J-F. Association of selective **serotonin reuptake inhibitors with the risk for spontaneous intracranial hemorrhage** [online Dec 5, 2016]. JAMA Neurol. doi:10.1001/jamaneurol.2016.4529

Reynolds CF 3rd, Butters MA, Lopez O, et al. Maintenance treatment of depression in old age: a randomized, double-blind, placebo-controlled evaluation of the efficacy and safety of **donepezil** combined with antidepressant pharmacotherapy. Arch Gen Psychiatry. 2011 Jan;68(1):51-60. (no clear benefit)

Reynolds CF 3rd, et al. **Maintenance treatment** of major depression in **old age**. N Engl J Med. 2006 Mar 16;354(11):1130-8. CONCLUSIONS: Patients elderly 70 years of age or older with major depression who had a response to initial treatment with paroxetine and psychotherapy were less likely to have recurrent depression if they received two years of maintenance therapy with paroxetine. Monthly maintenance psychotherapy did not prevent recurrent depression. (InfoPOEMs: Prolonged treatment with paroxetine (Paxil) reduces the risk of recurrence of major depression in elderly patients. (LOE = 1b))

Rhein J, Morawski BM, Hullsiek KH, et al. Efficacy of **adjunctive sertraline for the treatment of HIV-associated cryptococcal meningitis**: an open-label dose-ranging study. Lancet Infect Dis 2016; 16: 809–18.

Rice F, Sellers R, Hammerton G, et al. Antecedents of new-onset major depressive disorder in **children and adolescents at high familial risk** [online Dec 7, 2016].JAMA Psychiatry. doi:10.1001/jamapsychiatry.2016.3140

Richard IH, McDermott MP, Kurlan R, et al. A randomized, double-blind, placebo-controlled trial of antidepressants (**paroxetine, venlafaxine**) in **Parkinson** disease. (**SAD-PD**) Neurology 2012;78:1229–1236.

Richard E, Reitz C, Honig LH, et al. Late-Life Depression, Mild **Cognitive Impairment**, and **Dementia**. Arch Neurol. 2012 Dec 31:1-7.

Richards BL, Whittle SL, Buchbinder R. **Antidepressants** for **pain management** in **rheumatoid arthritis**. Cochrane Database Syst Rev. 2011 Nov 9;11:CD008920. There is currently insufficient evidence to support the routine prescription of antidepressants as analgesics in patients with RA as no reliable conclusions about their efficacy can be drawn from eight placebo RCTs.

Richards DA, Hill JJ, Gask L, et al. Clinical effectiveness of **collaborative care for depression in UK** primary care (CADET): cluster randomised controlled trial. BMJ. 2013 Aug 19;347:f4913.

Richards DA, Bower P, Chew-Graham C, et al. **Clinical effectiveness and cost-effectiveness** of collaborative care for depression in UK primary care (CADET): a cluster randomised controlled trial. Health Technol Assess. 2016 Feb;20(14):1-192.

Richards DA, et al. Cost and Outcome of **Behavioural Activation versus Cognitive Behavioural Therapy** for Depression (**COBRA**): a randomised, controlled, open-label, non-inferiority trial. Lancet 2016; online July 22.

Richards DA, et al. Cost & Outcome of BehaviouRal Activation (**COBRA**): randomised controlled trial of **behavioural activation versus cognitive-behavioural therapy** for depression. Health Technol Assess. 2017 Aug;21(46):1-366.

Richards JB, Papaioannou A, Adachi JD, et al. Effect of selective serotonin reuptake inhibitors on the **risk of fracture**. Arch Intern Med. 2007 Jan 22;167(2):188-94. Daily SSRI use in adults 50 years and older remained associated with a 2-fold increased risk of clinical fragility fracture after adjustment for potential covariates. Depression and fragility fractures are common in this age group, and the elevated risk attributed to daily SSRI use may have important public health consequences.

Richardson, Laura P., Rockhill, Carol, Russo, Joan E., et al. Evaluation of the **PHQ-2** as a Brief Screen for Detecting Major Depression Among **Adolescents**. Pediatrics 2010 125: e1097-e1103.

Richardson LP, McCauley E, Grossman DC, et al. Evaluation of the Patient Health Questionnaire-9 **(PHQ-9)** Item for Detecting Major Depression Among **Adolescents**. Pediatrics. 2010 Nov 1.

Richardson LP, Ludman E, McCauley E, et al. **Collaborative care for adolescents** with depression in primary care: a randomized clinical trial. JAMA. 2014 Aug 27;312(8):809-16.

Rickels K, Etemad B, Khalid-Khan S, et al. Time to relapse after 6 and **12 months' treatment** of **generalized anxiety disorder with venlafaxine** extended release. Arch Gen Psychiatry. 2010 Dec;67(12):1274-81.

Rimer J, Dwan K, Lawlor DA, et al. **Exercise for depression**. Cochrane Database Syst Rev. 2012 Jul 11;7:CD004366. Exercise seems to improve depressive symptoms in people with a diagnosis of depression when compared with no treatment or control intervention, however since analyses of methodologically robust trials show a much smaller effect in favour of exercise, some caution is required in interpreting these results.

Robinson RG, Jorge RE, Moser DJ, et al.; Vardenafil Study Site Investigators. Efficacy and tolerability of **vardenafil** in men with mild depression and erectile dysfunction: the depression-related improvement with vardenafil for

erectile response study. Am J Psychiatry. 2006 Jan;163(1):79-87.
Rodda J, Walker Z, Carter J. Depression in **older adults**. BMJ. 2011 Sep 28;343:d5219. doi: 10.1136/bmj.d5219.
Roest AM, de Jonge P, Williams CD, et al. **Reporting Bias** in Clinical Trials Investigating the Efficacy of **Second-Generation Antidepressants** in the Treatment of **Anxiety** Disorders: A Report of 2 Meta-analyses. JAMA Psychiatry. 2015 Mar 25.
Rogers MA, Greene MT, Young VB, et al. Depression, antidepressant medications, and risk of **Clostridium difficile infection**. BMC Med. 2013 May 7;11(1):121.
Rohan KJ, Mahon JN, Evans M, et al. Randomized Trial of **Cognitive-Behavioral Therapy Versus Light Therapy for Seasonal Affective Disorder**: Acute Outcomes. Am J Psychiatry. 2015 Apr 10.
Rohan KJ, Meyerhoff J, Ho SY, et al. Outcomes One and Two Winters Following **Cognitive-Behavioral Therapy or Light Therapy** for Seasonal Affective Disorder. Am J Psychiatry. 2015 Nov 5
Romera I et al. Early **switch strategy** in patients with major depressive disorder: A double-blind, randomized study. J Clin Psychopharmacol 2012 Aug; 32:479.
Roos E, Mariosa D, Ingre C, et al. Depression in **amyotrophic lateral sclerosis**. Neurology. 2016 Jun 14;86(24):2271-7.
Rosenberg PB, Drye LT, Martin BK, et al. DIADS-2 Research Group. **Sertraline** for the treatment of **depression in Alzheimer disease**. Am J Geriatr Psychiatry. 2010 Feb;18(2):136-45. CONCLUSIONS: Sertraline not effective.
Rosenthal LJ, Goldner WS, O'Reardon JP. **T3 Augmentation** in Major Depressive Disorder: Safety Considerations. Am J Psychiatry 168:10, October 2011.
Ross EL, Zivin K, Maixner DF. **Cost-effectiveness of Electroconvulsive Therapy** vs Pharmacotherapy/Psychotherapy for Treatment-Resistant Depression in the United States. JAMA Psychiatry. 2018 May 9.
Rotenstein LS, Ramos MA, Torre M, et al. Prevalence of depression, **depressive symptoms, and suicidal ideation among medical students**: a systematic review and meta-analysis.JAMA. doi:10.1001/jama.2016.17324
Rubio-Valera Maria, Serrano-Blanco Antoni, Magdalena-Belío Jesús, et al. Effectiveness of **Pharmacist Care in the Improvement of Adherence** to Antidepressants: A Systematic Review and Meta-Analysis. Articles Ahead of Print published on 1 January 2011, DOI 10.1345/aph.1P429. Ann Pharmacother ;45:39-48.
Rush AJ, et al. **STAR*D** Study. **Bupropion-SR, sertraline, or venlafaxine-XR after failure of SSRIs** (citalopram) for depression. n=727 N Engl J Med. 2006 Mar 23;354(12):1231-42. CONCLUSIONS: After unsuccessful treatment with an SSRI, approximately **one in four patients** had a **remission** of symptoms after switching to another antidepressant. Any one of the medications in the study provided a reasonable second-step choice for patients with depression. (InfoPOEMs: Bupropion SR (~283mg/d), sertraline(~136mg/d) & venlafaxine XR (~194mg/d) are equally effective at inducing remission or response in patients with persistent symptoms of depression despite initial treatment with citalopram (Celexa ~41mg/d). Most patients will not go into remission, though, and this study lacked a placebo control group. (LOE = 1b))
Rush AJ, Trivedi MH, Wisniewski SR, et al. Acute and Longer-Term Outcomes in Depressed Outpatients Requiring One or Several Treatment Steps: A **STAR*D** Report. Am J Psychiatry. 2006 Nov;163(11):1905-17. The QIDS-SR(16) remission rates were 36.8%, 30.6%, 13.7%, and 13.0% for the first, second, third, and fourth acute treatment steps, respectively. The overall cumulative remission rate was 67%.
Rush AJ, Wisniewski SR, Warden D, Luther JF, Davis LL, Fava M, Nierenberg AA,
Rush AJ, Warden D, Wisniewski SR, Fava M, Trivedi MH, Gaynes BN, Nierenberg AA. **STAR*D**: Revising Conventional Wisdom. CNS Drugs. 2009;23(8):627-47.
Rush AJ, Trivedi MH, Stewart JW, et al. **Combining Medications** to Enhance Depression Outcomes (CO-MED): Acute & Long-Term Outcomes of a Single-Blind Randomized Study. Am J Psychiatry. 2011 May 2. (Mono tx good)
Rushton WF, Charlton NP. **Dexmedetomidine** in the treatment of serotonin syndrome. Ann Pharmacother. 2014 Dec;48(12):1651-4.
Ryan D, Milis L, Misri N. Depression during **pregnancy**. Can Fam Physician. 2005 Aug;51:1087-93.
Robson WL. Clinical practice. Evaluation and management of **enuresis**. N Engl J Med. 2009 Apr 2;360(14):1429-36.
Rose Natalie; Koperski Sabrina; Golomb Beatrice A. Mood Food: **Chocolate** and Depressive Symptoms in a Cross-sectional Analysis. *Arch Intern Med*. 2010;170(8):699-703.
Runeson Bo, Tidemalm Dag, Dahlin Marie, et al. **Method of attempted suicide** as predictor of subsequent successful suicide: national long term cohort study. BMJ 2010;341:c3222, doi: 10.1136/bmj.c3222.
Saarto T, et al. Antidepressants for **neuropathic pain**. **Cochrane** Database Syst Rev. 2007 Oct 17;(4):CD005454.
Sackeim HA, Haskett RF, Mulsant BH, et al. Continuation pharmacotherapy in the prevention of relapse following **electroconvulsive therapy**: a randomized controlled trial. JAMA. 2001 Mar 14;285(10):1299-307.
Sackeim HA, Dillingham EM, et al. Effect of **concomitant pharmacotherapy on electroconvulsive** therapy outcomes: short-term efficacy and adverse effects. Arch Gen Psychiatry. 2009 Jul;66(7):729-37. The efficacy of ECT is substantially increased by the addition of an antidepressant medication, but such medications may differ in whether they reduce or increase cognitive adverse effects. High-dose, right-sided, unilateral ECT is at least equivalent to moderate-dosage bilateral ECT in efficacy, but retains advantages with respect to cognitive adverse effects.
Saczynski, J.S., Beiser, A., Seshadri, S., et al. **Depressive symptoms** and risk of dementia: The Framingham Heart Study. Neurology 2010 75: 35-41.
Saeed SA, Cuningham K, Bloch R. **Depression and Anxiety Disorders: Benefits of Exercise, Yoga, and Meditation**. Am Fam Physician. 2019;99(10):620-627.
Sanacora G, Frye MA, McDonald W, et al; American Psychiatric Association (**APA**) Council of Research Task Force on Novel Biomarkers and Treatments. A consensus statement on the use of **ketamine** in the treatment of mood disorders [online Mar 1, 2017].JAMA Psychiatry. doi:10.1001/jamapsychiatry.2017.0080
Sanchez-Spitman A et al. **Tamoxifen pharmacogenetics and metabolism**: Results from the prospective CYPTAM study. J Clin Oncol 2019 Mar 10; 37(8):636-646.
Sarris J, Murphy J, Mischoulon D, et al. **Adjunctive Nutraceuticals** for Depression: A Systematic Review and Meta-Analyses. Am J Psychiatry. 2016 Apr 26
Saveanu R, Etkin A, Duchemin AM, et al. The international Study to Predict Optimized Treatment in Depression (**iSPOT-D**): outcomes from the acute phase of antidepressant treatment. J Psychiatr Res. 2015;61:1-12.
Sayuk GS, Gott BM, Nix BD, Lustman PJ. **Improvement in sexual functioning** in patients with type 2 diabetes and depression treated with **bupropion**. Diabetes Care. 2011 Feb;34(2):332-4.
Schaakxs R et al. Associations between **age and the course of major depressive disorder**: A 2-year longitudinal cohort study. Lancet Psychiatry 2018 Jun 7.
Scheitz JF, Turc G, Kujala L, et al. **Intracerebral Hemorrhage and Outcome After Thrombolysis in Stroke Patients Using Selective Serotonin-Reuptake Inhibitors**. Stroke. 2017 Dec;48(12):3239-3244.
Scherrer JF, Salas J, Lustman PJ, et. al, **Change in opioid dose and change in depression** in a longitudinal primary care patient cohort. Pain. 2015 Feb;156(2):348-55.
Schneeweiss S, Patrick AR, Solomon DH, et al. Comparative Safety of Antidepressant Agents for **Children and Adolescents** Regarding **Suicidal Acts**. Pediatrics. 2010 Apr 12.
Schneier FR, Neria Y, Pavlicova M, et al. **Combined Prolonged Exposure Therapy and Paroxetine** for **PTSD** Related to the World Trade Center Attack: A Randomized Controlled Trial. Am J Psychiatry. 2011 Sep 9.
Schoenbaum M, Kessler RC, Gilman SE, et al; **Army STARRS** Collaborators. Predictors of **suicide** and accident death in the Army Study to Assess Risk and Resilience in Servicemembers (Army STARRS) [online March 3, 2014]. JAMAPsychiatry. doi:10.1001/jamapsychiatry.2013.4417.
Schramm E, Kriston L, Zobel I, et al. Effect of **Disorder-Specific vs Nonspecific Psychotherapy for Chronic Depression**: A Randomized Clinical Trial. JAMA Psychiatry. 2017 Feb 1.
Schultz JL, Killoran A, Nopoulos PC, et al. Evaluating **depression and suicidality in tetrabenazine users** with Huntington disease. Neurology. 2018 Jul 17;91(3):e202-e207.
Scoralick FM, Louzada LL, Quintas JL, et al. **Mirtazapine** does **not improve sleep** disorders in **Alzheimer's** disease: results from a double-blind, placebo-controlled pilot study. Psychogeriatrics. 2016 Jan 27.
Sebaaly JC, Cox S, Hughes CM, et al. Use of **fluoxetine in anorexia nervosa** before and after weight restoration. Ann Pharmacother. 2013 Sep;47(9):1201-5.
Seccareccia D, Gebara N. **Pruritus in palliative care**: Getting up to scratch. Canadian Family Physician, 2011 Sep;57(9):1010-3. (consider use of **paroxetine, mirtazapine**)
Second generation Antidepressants: **Drug Class Review Sept 2006** Oregon Health & Science University http://www.ohsu.edu/drugeffectiveness/reports/documents/SG%20Antidepressants%20Final%20Report%20u3.pdf
Seifert CF, Wiltrout TR. Calcaneal **Bone Mineral Density** in Young Adults Prescribed Selective Serotonin Reuptake Inhibitors. Clin Ther. 2013 Aug 16.
Seitz DP, Adunuri N, Gill SS, et al. **Antidepressants for agitation and psychosis** in dementia. Cochrane Database Syst Rev. 2011 Feb 16;2:CD008191. Currently there are relatively few studies of antidepressants for the treatment of agitation and psychosis in dementia. The SSRIs sertraline and citalopram were associated with a reduction in symptoms of agitation when compared to placebo in two studies. Both SSRIs and trazodone appear to be tolerated reasonably well when compared to placebo, typical antipsychotics and atypical antipsychotics.
Serfaty MA, et al. Clinical effectiveness of individual **cognitive behavioral therapy** for depressed **older** people in primary care: a randomized controlled trial. Arch Gen Psychiatry. 2009 Dec;66(12):1332-40.
Serfaty M, King M, Nazareth I, et al. Manualised cognitive-behavioural therapy in **treating depression in advanced cancer**: the CanTalk RCT. Health Technol Assess. 2019 May;23(19):1-106.
Serretti A, Chiesa A. **Treatment-emergent sexual dysfunction** related to antidepressants: a meta-analysis**.** J Clin Psychopharmacol. 2009 Jun;29(3):259-66.

Shah NR, Jones JB, Aperi J, Shemtov R, Karne A, Borenstein J. Selective Serotonin Reuptake Inhibitors for **Premenstrual Syndrome** and Premenstrual Dysphoric Disorder: A Meta-Analysis. Obstet Gynecol. 2008 May;111(5):1175-1182. Selective serotonin reuptake inhibitors were found to be effective in treating premenstrual symptoms, with continuous dosing regimens favored for effectiveness.

Shah AJ et al. Depression and history of attempted suicide as risk factors for **heart disease mortality** in young individuals. Arch Gen Psychiatry 2011 Nov; 68:1135.

Shah AJ, Ghasemzadeh N, Zaragoza-Macias E, et al. **Sex and age differences** in the association of depression with obstructive coronary **artery disease** and adverse cardiovascular events. J Am Heart Assoc. 2014 Jun 18;3(3).

Shaheen AA, Kaplan GG, Almishri W, et al. The impact of **depression and antidepressant usage on primary biliary cholangitis** clinical outcomes. PLoS One. 2018 Apr 4;13(4):e0194839.

Shams T, Firwana B, Habib F, et al. **SSRIs for Hot Flashes**: A Systematic Review and Meta-Analysis of Randomized Trials. J Gen Intern Med. 2013 Jul 26.

Shankman SA, Gorka SM, Katz AC, et al. **Side Effects** to **Antidepressant Treatment** in Patients With **Depression and Comorbid Panic Disorder**. J Clin Psychiatry. 2017 Jan 3.

Sharma T, Guski LS, Freund N, Gøtzsche PC. **Suicidality and aggression during antidepressant treatment**: systematic review and meta-analyses based on clinical study reports. BMJ 2016;352:i65.

Sharp RP, Welch EB. **Takotsubo cardiomyopathy** as a complication of **electroconvulsive therapy**. Ann Pharmacother. 2011 Dec;45(12):1559-65.

Sharpe M, Walker J, Hansen CH, et al; for the **SMaRT** (Symptom Management Research Trials) Oncology-2 Team. **Integrated collaborative care** for comorbid major **depression in patients with cancer** (SMaRT Oncology-2): a multicentre randomised controlled effectiveness trial. Lancet. 2014 Aug 27.

Shear MK, Reynolds CF 3rd, Simon NM, et al. **Optimizing Treatment of Complicated Grief**: A Randomized Clinical Trial. JAMA Psychiatry. 2016 Jun 8.

Sheline YI, Disabato BM, Hranilovich J, et al. Treatment course with antidepressant therapy in **late-life depression**. Am J Psychiatry. 2012 Nov 1;169(11):1185-93

Shelton RC, Osuntokun O, Heinloth AN, Corya SA. Therapeutic options for **treatment-resistant depression**. CNS Drugs. 2010 Feb 1;24(2):131-61. doi: 10.2165/11530280-000000000-00000.

Shen CC, Tsai SJ, Perng CL, et al. Risk of **Parkinson disease after depression**: A nationwide population-based study. Neurology. 2013 Oct 2.

Shen H, Magnusson C, Rai D, et al. Associations of **parental depression with child school performance** at age 16 years in Sweden [online February 3, 2016].JAMA Psychiatry. doi:10.1001/jamapsychiatry.2015.2917.

Shen ZQ, Gao SY, Li SX, et al. **Sertraline** use in the **first trimester and risk of congenital anomalies**: a systemic review and meta-analysis of cohort studies. Br J Clin Pharmacol. 2016 Oct 22.

Shepshelovich D, Schechter A, Calvarysky B, et al. **Medication-induced SIADH**: distribution and characterization according to medication class. Br J Clin Pharmacol. 2017 Feb 7.

Sher L, Braquehais MD, Casas M. **Posttraumatic stress disorder, depression, and suicide in veterans**. Cleveland Clinic Journal of Medicine 2012; 79(2):92-97.

Sheu YH, Lanteigne A, Stürmer T, et al. **SSRI use and risk of fractures** among perimenopausal women without mental disorders. Inj Prev. 2015 Jun 25.

Shilyansky C, Williams LM, Gyurak A, et al. Effect of **antidepressant treatment on cognitive impairments** associated with depression: a randomised longitudinal study. Lancet Psychiatry. 2016 May;3(5):425-35.

Shin J, Park M, Lee SH, et al. Risk of **intracranial haemorrhage in antidepressant users with concurrent use of non-steroidal anti-inflammatory drugs**: nationwide propensity score matched study. BMJ 2015;351:h3517.

Shinohara K, Tanaka S, Imai H, et al. Development and validation of a prediction model for the **probability of responding to placebo in antidepressant trials**: a pooled analysis of individual patient data. Evid Based Ment Health. 2019 Feb;22(1):10-16.

Shirayama T, et al. Usefulness of paroxetine in depressed men with paroxysmal **atrial fibrillation**. Am J Cardiol. 2006 Jun 15;97(12):1749-51. Epub 2006 Apr 21.

Short B, Fong J, Galvez V, et al. Side-effects associated with **ketamine** use in **depression**: a systematic review. Lancet Psychiatry. 2017 Jul 27

Siafis S, Papazisis G. Detecting a potential **safety signal of antidepressants and type 2 diabetes**: a pharmacovigilance-pharmacodynamic study. Br J Clin Pharmacol. 2018 Jun 28.

Siegmann EM, Müller HHO, Luecke C, et al. Association of **Depression and Anxiety Disorders With Autoimmune Thyroiditis**: A Systematic Review and Meta-analysis. JAMA Psychiatry. 2018 May 2.

Silverstein M, Cabral H, Hegel M, et al. Problem-solving education to **prevent depression among low-income mothers**: a path mediation analysis in a randomized clinical trial.JAMA Netw Open. 2018;1(2):e180334.

Silverstein M, Diaz-Linhart Y, Cabral H, et al. Efficacy of a **maternal depression prevention strategy in Head Start**: a randomized clinical trial [online June 14, 2017].JAMA Psychiatry. doi:10.1001/jamapsychiatry.2017.1001

Sim SS, Sun JT. **Ocular Flutter in the Serotonin Syndrome (venlafaxine)**. N Engl J Med. 2016 Nov 3;375(18):e38.

Sinyor M, Schaffer A, Nishikawa Y, et al. The association between **suicide deaths and** putatively harmful and protective factors **in media reports**. CMAJ. 2018 Jul 30;190(30):E900-E907.

Sirey JA, Banerjee S, Marino P, et al. **Adherence to Depression Treatment in Primary Care**: A Randomized Clinical Trial. JAMA Psychiatry. 2017 Sep 27.

Siu AL; U.S. Preventive Services Task Force. **Screening for depression in children and adolescents**: U.S. Preventive Services Task Force (**USPSTF**) recommendation statement. Ann Intern Med. 2016. [Epub ahead of print]

Shulman KI, Fischer HD, Herrmann N, et al. Current prescription patterns and safety profile of **irreversible monoamine oxidase inhibitors**: a population-based cohort study of older adults. J Clin Psychiatry. 2009 Oct 20.

Simon GE et al. **Antidepressants are not overprescribed for mild depression**. J Clin Psychiatry 2015 Nov 11.

Sinclair LI, Christmas DM, Hood SD, et al. **Antidepressant-induced jitteriness/anxiety syndrome**: systematic review. Br J Psychiatry. 2009 Jun;194(6):483-90.

Singh SP, Singh V, Kar N, Chan K. Efficacy of antidepressants in treating the **negative symptoms of chronic schizophrenia**: meta-analysis. Br J Psychiatry. 2010 Sep;197(3):174-9.

Sirey JA, Banerjee S, Marino P, et al. **Adherence to Depression Treatment in Primary Care**: A Randomized Clinical Trial. JAMA Psychiatry. 2017 Sep 27.

Siu AL; US Preventive Services Task Force (**USPSTF**). **Screening for depression in adults**: US Preventive Services Task Force recommendation statement [online January 26]

Shekelle PG, et al. Benefits and harms of **cranial electrical stimulation** for chronic painful conditions, depression, anxiety, and insomnia- systematic review. Ann Intern Med. 2018. [Epub ahead of print]. doi:10.7326 /M17-1970

Skinner R, McFaull S. **Suicide among children and adolescents in Canada**: trends and sex differences, 1980-2008. CMAJ. 2012 Apr 2.

Skovlund CW, Mørch LS, Kessing LV, et al. **Association** of **Hormonal Contraception With Depression**. JAMA Psychiatry. 2016 Sep 28.

Smith GE, Rasmussen KG, Cullum CM, et al. for the CORE Investigators. A randomized controlled trial comparing the memory effects of continuation **electroconvulsive therapy**(ECT) versus continuation pharmacotherapy: results from the consortium for research in ECT (CORE) study. J Clin Psychiatry. 2010 Feb;71(2):185-193.

Smith KJ, Peterson MD, O'Connell NE, et al. Risk of Depression and Anxiety in **Adults With Cerebral Palsy**. JAMA Neurol. 2018 Dec 28.

Smolderen KG, Spertus JA, Gosch K, et al. Depression treatment and health status outcomes in young patients with **acute myocardial infarction**: insights from the **VIRGO** study (Variation in Recovery: Role of Gender on Outcomes of Young AMI Patients). Circulation. 2017;135:1762–1764.

Smolderen KG, Buchanan DM, Gosch K, et al. Depression treatment and 1-year mortality following **acute myocardial infarction**: insights from the **TRIUMPH** registry (Translational ResearchInvestigating Underlying Disparities in Acute Myocardial Infarction Patients' Health Status). Circulation. 2017;135:1681–1689.

Smoller Jordan W.; Allison Matthew; Cochrane Barbara B.; J. et al. Antidepressant Use and Risk of Incident **Cardiovascular Morbidity and Mortality** Among Postmenopausal Women in the Women's Health Initiative Study. Arch Intern Med. 2009;169(22):2128-2139.

Sobieraj DM, Baker WL, Martinez BK, et al. **Adverse Effects of Pharmacologic Treatments** of Major Depression in Older Adults AHRQ Comparative Effectiveness Reviews. 2019 Mar.

Sobieraj DM, Martinez BK, Hernandez AV, et al. **Adverse Effects of Pharmacologic Treatments of Major Depression in Older Adults**. J Am Geriatr Soc. 2019 May 29.

Sockalingam S, Abbey SE. Managing depression **during hepatitis C** treatment. Can J Psychiatry. 2009 Sep;54(9):614-25.

Songprakun W, McCann TV. Evaluation of a **bibliotherapy manual** for reducing psychological distress in people with depression: a randomized controlled trial. J Adv Nurs. 2012 Mar 1.

Soomro GM. **Deliberate self-harm** (and attempted suicide). Clin Evid (Online). 2008;2008.

Soomro G, Altman D, Rajagopal S, Oakley-Browne M. Selective serotonin re-uptake inhibitors (**SSRIs**) versus placebo for obsessive compulsive disorder (OCD). **Cochrane** Database Syst Rev. 2008 Jan 23;(1):CD001765. SSRIs are more effective than placebo for OCD, at least in the short-term, although there are differences between the adverse effects of individual SSRI drugs.

Šóš P. Is there a future for other **glutamate receptor modulators** in the pharmacotherapy of mood disorders? Evid Based Ment Health. 2016 Aug;19(3):95-6.

Southammakosane C, Schmitz K. **Pediatric Psychopharmacology for Treatment of ADHD, Depression, and Anxiety**. Pediatrics. 2015 Aug;136(2):351-9.
Spielmans GI, Berman MI, et al. **Adjunctive atypical antipsychotic treatment** for major depressive disorder: a meta-analysis of depression, quality of life, and safety outcomes. PLoS Med. 2013 Mar;10(3):e1001403.
Ssegonja R, Nystrand C, Feldman I, et al. Indicated **preventive interventions for depression in children and adolescents**: A meta-analysis and meta-regression. Prev Med. 2018 Oct 2;118:7-15.
Stadlmann S, Portmann S, Tschopp S, Terracciano LM. **Venlafaxine-induced Cholestatic Hepatitis**: Case Report and Review of Literature. Am J Surg Pathol. 2012 Nov;36(11):1724-8.
Stall N, Godwin J, Juurlink D. **Bupropion abuse and overdose**. CMAJ. 2014 Sep 16;186(13):1015.
Stallard P, Sayal K, Phillips R, et al. Classroom based **cognitive behavioural therapy in reducing symptoms of depression in high risk adolescents:** pragmatic cluster randomised controlled trial. BMJ. 2012 Oct 5;345:e6058.
Stallard P, Phillips R, Montgomery A, et al. A cluster randomised controlled trial to determine the clinical effectiveness and cost-effectiveness of classroom-based **cognitive-behavioural therapy (CBT)** in reducing symptoms of depression in high-risk adolescents. Health Technol Assess. 2013 Oct;17(47):1-110.
Steinberg JR, Laursen TM, Adler NE, et al Examining the **association of antidepressant prescriptions with first abortion and first childbirth** [online May 30, 2018].JAMA Psychiatry. doi:10.1001/jamapsychiatry.2018.0849.
Steiner AJ, et al. Quality of Life, Functioning, and Depressive Symptom Severity in **Older Adults With Major Depressive Disorder Treated With Citalopram** in the **STAR*D** Study. J Clin Psychiatry. 2017 Jul;78(7):897-903.
Steiner M, Hirschberg AL, Bergeron R, et al. **Luteal phase** dosing with paroxetine controlled release (CR) in the treatment of premenstrual dysphoric disorder. Am J Obstet Gynecol. 2005 Aug;193(2):352-60.
Stearns V, Slack R, Greep N, et al. **Paroxetine** is an effective treatment **for hot flashes**: results from a prospective randomized clinical trial. J Clin Oncol. 2005 Oct 1;23(28):6919-30.
Stenman M, Holzmann MJ, Sartipy U. Relation of Major Depression to Survival After Coronary Artery Bypass Grafting. Am J Cardiol. 2014 Jun 18.
Stephens S, Ford E, Paudyal P, et al. Effectiveness of **Psychological Interventions** for **Postnatal Depression** in Primary Care: A Meta-Analysis. Ann Fam Med. 2016 Sep;14(5):463-72.
Sterke CS, Ziere G, van Beeck EF et al. Dose-response relationship between **Selective Serotonin Reuptake Inhibitors and Injurious Falls**: A study in Nursing Home Residents with Dementia. Br J Clin Pharmacol. 2012 Jan 18.
Stevens LM, Burke AE, Glass RM. JAMA **patient page. Posttraumatic stress disorder**. JAMA. 2007 Aug 1;298(5):588.
Stewart DE. Clinical practice. **Depression during Pregnancy**. N Engl J Med. 2011 Oct 27;365(17):1605-11.
Stewart DE, Vigod S. **Postpartum Depression**. N Engl J Med. 2016 Dec;375(22):2177-2186.
Stone MB. The **FDA warning on antidepressants and suicidality**--why the controversy? N Engl J Med. 2014 Oct 30;371(18):1668-71.
Strawbridge R, Carter B, Marwood L, et al. **Augmentation therapies for treatment-resistant depression**: systematic review and meta-analysis. Br J Psychiatry. 2018 Nov 20:1-10.
Streeter CC, Gerbarg PL, et al. Treatment of Major Depressive Disorder with **Iyengar Yoga and Coherent Breathing**: A Randomized Controlled Dosing Study. J Altern Complement Med. 2017 Mar;23(3):201-207.
Stubbs B, Vancampfort D, Hallgren M, et al. **EPA guidance on physical activity as a treatment for severe mental illness**: a meta-review of the evidence and Position Statement from the European Psychiatric Association (EPA), supported by the International Organization of Physical Therapists in Mental Health (IOPTMH). Eur Psychiatry. 2018 Oct;54:124-144.
Sujan AC, Rickert ME, Öberg AS, et al. Associations of **maternal antidepressant use during the first trimester of pregnancy** with preterm birth, small for gestational age, **autism** spectrum disorder, and attention-deficit/hyperactivity disorder in offspring.JAMA. doi:10.1001/jama.2017.3413
Sun J, Ma H, Yu C, et al. Association of major **depressive episodes with stroke risk** in a prospective study of 0.5 million Chinese adults. Stroke 2016;47:2203–8.
Suppes T, Silva R, et al. **Lurasidone** for the Treatment of Major Depressive Disorder With Mixed Features: A Randomized, Double-Blind, Placebo-Controlled Study. Am J Psychiatry. 2015 Nov 10:appiajp201515060770.
Suppli NP, Johansen C, Christensen J, et al. Increased Risk for **Depression After Breast Cancer**: A Nationwide Population-Based Cohort Study of Associated Factors in Denmark, 1998-2011. J Clin Oncol. 2014 Oct 27.
Surkan PJ, Ettinger AK, Ahmed S, et al. Impact of **Maternal Depressive** Symptoms on Growth of Preschool- and School-Aged Children. Pediatrics. 2012 Sep 10.
Swanson SA, Colman I. Association between **exposure to suicide and suicidality outcomes in youth**. CMAJ 2013;185:870-7.
Sylvester C, Menke M, Gopalan P. Selective **Serotonin Reuptake Inhibitors and Fertility:** Considerations for Couples Trying to Conceive. Harv Rev Psychiatry. 2019 Jan 22.
Tack J, et al. A controlled crossover study of the selective serotonin reuptake inhibitor **citalopram** in **irritable bowel syndrome**. Gut. 2006 Aug;55(8):1095-103. Epub 2006 Jan 9. (InfoPOEMs: Citalopram in a dose of 20 mg daily for 3 weeks (perhaps increasing to 40 mg at that time) modestly improves symptoms in patients with irritable bowel syndrome (IBS). Paroxetine showed a similar benefit in a previous study, so this is likely a class effect of serotonin specific reuptake inhibitors (SSRIs). (LOE = 1b))
TADS Team. The Treatment for Adolescents With Depression Study (TADS): Long-term Effectiveness and Safety Outcomes. Arch Gen Psychiatry. 2007 Oct;64(10):1132-1143. In adolescents with moderate to severe depression, treatment with fluoxetine alone or in combination with **CBT** accelerates the response. Adding CBT to medication enhances the safety of medication. Taking benefits and harms into account, combined treatment appears superior to either monotherapy as a treatment for major depression in adolescents.
Tamblyn R, Bates DW, Buckeridge DL, et al. Multinational comparison of new **antidepressant use in older adults**: a cohort study. BMJ Open. 2019 May 14;9(5):e027663.
Tan E, Smith CH, Goldman RD. **Antidepressants (eg. SSRIs)** for **functional gastrointestinal disorders in children**. Can Fam Physician. 2013 Mar;59(3):263-4.
Tanday S. **Duloxetine lessens joint pain in early-stage breast cancer**. Lancet Oncol. 2016 Dec 15.
Tarleton EK, Littenberg B, MacLean CD, et al. Role of **magnesium supplementation** in the treatment of depression: A randomized clinical trial. PLoS One. 2017 Jun 27;12(6):e0180067.
Taylor MJ, Freemantle N, Geddes JR, Bhagwagar Z. **Early Onset** of Selective **Serotonin Reuptake Inhibitor** Antidepressant Action: Systematic Review and Meta-analysis. Arch Gen Psychiatry. 2006 Nov;63(11):1217-23. Treatment with SSRIs is associated with symptomatic improvement in depression by the end of the first week of use, and the improvement continues at a decreasing rate for at least 6 weeks. (InfoPOEMs: Treatment of unipolar depression in adults with selective serotonin reuptake inhibitors (SSRIs) significantly improves symptoms in as quickly as 1 week. (LOE = 1a-))
Taylor D, Sparshatt A, Varma S, Olofinjana O. Antidepressant efficacy of **agomelatine**: meta-analysis of published and unpublished studies. BMJ 2014;348:g1888.
Taylor WD. Clinical practice. **Depression in the elderly**. N Engl J Med. 2014 Sep 25;371(13):1228-36.
Teichert M, Visser LE, Uitterlinden AG, et al. **Selective serotonin re-uptake inhibiting antidepressants** and the risk of overanticoagulation during acenocoumarol maintenance treatment. Br J Clin Pharmacol. 2011 Nov;72(5):798-805.
Tenback DE, et al. Evidence that **early extrapyramidal symptoms** predict later **tardive dyskinesia**: a prospective analysis of 10,000 patients in the European Schizophrenia Outpatient Health Outcomes (SOHO) study. Am J Psychiatry. 2006 Aug;163(8):1438-40.
Teo AR, Choi H, Andrea SB, et al. Does **Mode of Contact with Different Types of Social Relationships** Predict Depression in Older Adults? Evidence from a Nationally Representative Survey. J Am Geriatr Soc. 2015 Oct 6.
Tew JD Jr, et al. Impact of **Prior Treatment Exposure on Response** to Antidepressant Treatment in Late Life. Am J Geriatr Psychiatry. 2006 Nov;14(11):957-965.
Thakore NJ, Pioro EP. **Depression in ALS** in a large self-reporting cohort. Neurology. 2016 Mar 15;86(11):1031-8.
Thapar Anita, Collishaw Stephan, Potter Robert, et al. **Managing and preventing depression in adolescents**. BMJ 2010;340:c209, doi: 10.1136/bmj.c209 (Published 22 January 2010)
Thapar A, Collishaw S, Pine DS, Thapar AK. **Depression in adolescence**. Lancet. 2012 Feb 1.
Thase ME, et al. A Double-blind Comparison Between **Bupropion** XL and **Venlafaxine** XR: **Sexual Functioning**, Antidepressant Efficacy, and Tolerability. J Clin Psychopharmacol. 2006 Oct;26(5):482-488. In conclusion, in this patient population (ie, relatively young, sexually active outpatients), bupropion XL was at least as effective as venlafaxine XR and had a significantly more favorable sexual side effect profile. N=348 12 week
Thase ME, Rush AJ. When at first you don't succeed: sequential strategies for antidepressant nonresponders. J Clin Psychiatry. 1997;58 Suppl 13:23-9.
Thase ME, Friedman ES, Biggs MM, et al. **Cognitive Therapy Versus Medication** in Augmentation and Switch Strategies as Second-Step Treatments: A **STAR*D** Report. Am J Psychiatry. 2007 May;164(5):739-752. After an unsatisfactory response to citalopram, patients who consented to random assignment to either cognitive therapy or alternative pharmacologic strategies had generally comparable outcomes. Pharmacologic augmentation was more rapidly effective than cognitive therapy augmentation of citalopram, whereas switching to cognitive therapy was better tolerated than switching to a different antidepressant.
Thase ME, Larsen KG, Kennedy SH. Assessing the **`true` effect of active antidepressant therapy** v. placebo in major depressive disorder: use of a mixture model. Br J Psychiatry. 2011 Dec;199(6):501-7.

Thase ME. Using **adjunctive treatments** when first-line antidepressants fail. J Clin Psychiatry. 2012 Jan;73(1):e01.

Thase ME, Wright JH, Eells TD, et al. Improving the Efficiency of **Psychotherapy for Depression: Computer-Assisted Versus Standard CBT**. Am J Psychiatry. 2017 Oct 3:appiajp201717010089.

Then C-K et al. **Risk analysis** of use of different classes of **antidepressants on subsequent dementia**: A nationwide cohort study in Taiwan. PLoS One 2017 Apr 6; 12:e0175187.

Theunissen EL, Street D, et al. A randomized trial on the acute and steady-state effects of a new antidepressant, **vortioxetine** (Lu AA21004), on actual driving and cognition. Clin Pharmacol Ther. 2013 Jun;93(6):493-501.

Thoma NC, McKay D, Gerber AJ et al. A quality-based review of randomized controlled trials of **cognitive-behavioral therapy** for depression: an assessment and metaregression. Am J Psychiatry. 2012 Jan;169(1):22-30.

Thombs BD, de Jonge P, Coyne JC, Whooley MA, et al. Depression screening and patient outcomes in cardiovascular care: a systematic review. JAMA. 2008 Nov 12;300(18):2161-71. Depression treatment with medication or cognitive behavioral therapy in patients with cardiovascular disease is associated with modest improvement in depressive symptoms but no improvement in cardiac outcomes. No clinical trials have assessed whether screening for depression improves depressive symptoms or cardiac outcomes in patients with cardiovascular disease.

Thombs BD, Arthurs E, El-Baalbaki G, et al. Risk of bias from inclusion of patients who already have diagnosis of or are undergoing treatment for depression in diagnostic accuracy studies of **screening tools for depression**: systematic review. BMJ. 2011 Aug 18;343:d4825.

Thombs BD, Coyne JC, Cuijpers P, et al. Rethinking recommendations for **screening for depression in primary care**. CMAJ. 2012 Mar 6;184(4):413-8.

Thombs BD, Ziegelstein RC. Does **depression screening** improve depression outcomes in primary care? BMJ. 2014 Feb 4;348:g1253.

Thombs BD, Kwakkenbos L, Levis AW, et al. Addressing **overestimation of the prevalence of depression based on self-report screening questionnaires**. CMAJ. 2018 Jan 15;190(2):E44-E49.

Thorlund K, Druyts E, Wu P, et al. Comparative efficacy and safety of **selective serotonin reuptake inhibitors and serotonin-norepinephrine reuptake inhibitors in older adults**: a network meta-analysis. J Am Geriatr Soc 2015;63:1002–9. (sertraline, paroxetine, duloxetine options)

Thornicroft G, Chatterji S, Evans-Lacko S, et al. **Undertreatment** of people with major **depressive disorder in 21 countries**. Br J Psychiatry. 2016 Dec 1.

Tiihonen J, Tanskanen A, Hoti F, et al. Pharmacological treatments and **risk of readmission to hospital for unipolar depression** in Finland: a nationwide cohort study. Lancet Psychiatry 2017; online June 1.

Timonen M, Liukkonen T. **Management of depression in adults**. BMJ. 2008 Feb 23;336(7641):435-9.

Torpy JM, Burke AE, Golub RM. JAMA **patient page. Generalized Anxiety Disorder**. JAMA. 2011 Feb 2;305(5):522.

Torvinen-Kiiskinen S, Tolppanen AM, Koponen M, et al. **Antidepressant use and risk of hip fractures** among community-dwelling persons with and without Alzheimer's disease. Int J Geriatr Psychiatry. 2017 Jan 5

Toseeb U, Brage S, Corder K, et al. **Exercise and Depressive Symptoms** in **Adolescents**: A Longitudinal Cohort Study. JAMA Pediatr. 2014 Oct 13.

Tosh G, Clifton AV, Xia J, et al. **General physical health advice** for people with serious mental illness. Cochrane Database Syst Rev. 2014 Mar 28;3:CD008567.

Trangle M, Gursky J, Haight R, Hardwig J, Hinnenkamp T, Kessler D, Mack N, Myszkowski M. **Adult depression in primary care**. Bloomington (MN): Institute for Clinical Systems Improvement (**ICSI**); 2016 Mar.

Trangle M, Gursky J, Haight R, et al. **Adult depression in primary care**. Bloomington (MN): Institute for Clinical Systems Improvement (**ICSI**); 2016 Mar.

Treatment Guidelines from the Medical Letter. Pharmaceutical **Drug Overdose**. Sept 2006. (**TCAs**: sodium bicarbonate treatment)

Trivedi MH. **STAR*D** Selecting among **second-step antidepressant** medication monotherapies: predictive value of clinical, demographic, or first-step treatment features. Arch Gen Psychiatry. 2008 Aug;65(8):870-80. Clinical, demographic, and treatment history were of little value in recommending 1 medication vs another as a second-step treatment for major depressive disorder. Participants most likely to remit in the second step had less Axis I psychiatric disorder comorbidity, less social disadvantage, and at least a response to citalopram in the first step.

Trivedi MH, Rush AJ, Wisniewski SR, et al. Evaluation of Outcomes With Citalopram for Depression Using Measurement-Based Care in **STAR*D**: Implications for Clinical Practice. Am J Psychiatry. 2006 Jan;163(1):28-40. The mean exit citalopram dose was 41.8 mg/day. Remission rates were 28% (HAM-D) and 33% (QIDS-SR). The response rate was 47% (QIDS-SR) n=2,876.

Trivedi MH, et al. **STAR*D** Study Team. Medication **augmentation** after the **failure of SSRIs** for depression. n=565 N Engl J Med. 2006 Mar 23;354(12):1243-52. CONCLUSIONS: Augmentation of citalopram (40-60mg/d) with either sustained-release bupropion (~267mg/d) or buspirone (~41mg/d) appears to be useful in actual clinical settings. **Augmentation with sustained-release bupropion** does have certain advantages, including a greater reduction in the number and severity of symptoms and fewer side effects and adverse events. (InfoPOEMs: Buspirone and bupropion SR added to citalopram (Celexa) are similarly effective for patients with depression who do not initially respond to citalopram alone. Bupropion SR is somewhat better tolerated. The study was limited by the lack of a placebo control group. (LOE = 1b))

Trouvin AP, Perrot S, Lloret-Linares C. Efficacy of **Venlafaxine in Neuropathic Pain**: A Narrative Review of Optimized Treatment. Clin Ther. 2017 May 26.

Tsoi KKF, Chan JYC, Hirai HW, Wong SYS. Comparison of diagnostic performance of **two-question screen** and 15 depression screening instruments for older adults: systematic review and meta-analysis. Br J Psychiatry 2017. The two questions asked for symptoms in the past month are: (a) 'Have you been troubled by feeling down, depressed or hopeless?' and (b) 'Have you experienced little interest or pleasure in doing things?'

Tuccori M, Testi A, et al.Safety concerns associated with the use of serotonin reuptake inhibitors and other serotonergic/noradrenergic antidepressants during **pregnancy**: a review. Clin Ther. 2009 Jun;31(Pt 1):1426-53.

Turner EH, Matthews AM, Linardatos E, Tell RA, Rosenthal R. **Selective publication** of antidepressant trials and its influence on apparent efficacy. N Engl J Med. 2008 Jan 17;358(3):252-60.

Twomey C, O'Reilly G, Byrne M. Effectiveness of **cognitive behavioural therapy for anxiety and depression** in primary care: a meta-analysis. Fam Pract. 2015 Feb;32(1):3-15.

Uher R, Tansey KE, Dew T, et al. An **Inflammatory Biomarker** as a Differential Predictor of Outcome of Depression Treatment With **Escitalopram and Nortriptyline**. Am J Psychiatry. 2014 Jul 14.

Underwood M, Lamb SE, Eldridge S, et al. **Exercise for depression in elderly** residents of care homes: a cluster-randomised controlled trial. Lancet 2013; online May 2.

Underwood L, Waldie KE, Peterson E, et al. **Paternal Depression Symptoms During Pregnancy** and After Childbirth Among Participants in the Growing Up in New Zealand Study. JAMA Psychiatry. 2017 Feb 15.

Unützer J, Park M. **Older adults with severe**, treatment-resistant depression. JAMA. 2012 Sep 5;308(9):909-18.

Urquhart DM, Wluka AE, van Tulder M, et al. **Efficacy of Low-Dose Amitriptyline for Chronic Low Back Pain**: A Randomized Clinical Trial. JAMA Intern Med. 2018 Oct 1.

USPSTF: US Preventive Services Task Force. **Screening and treatment** for major depressive disorder in **children and adolescents**: recommendation statement. Pediatrics 2009 Apr;123(4):1223-8. Screen adolescents (12-18 years of age) for major depressive disorder when systems are in place to ensure accurate diagnosis, psychotherapy (cognitive-behavioral or interpersonal), and follow-up (B recommendation). Evidence is insufficient to warrant a recommendation to screen children (7-11 years of age) for major depressive disorder (I statement).

USPSTF: U.S. Preventive Services Task Force. **Screening** for **Depression in Adults**: U.S. Preventive Services Task Force Recommendation Statement . Ann Intern Med December 1, 2009 151:784-792. The U.S. Preventive Services Task Force (USPSTF) recommends screening adults for depression when staff-assisted depression care supports are in place to assure accurate diagnosis, effective treatment, and follow-up (grade B recommendation). It recommends against routinely screening adults for depression when staff-assisted depression care supports are not in place. There may be considerations that support screening for depression in an individual patient (grade C recommendation).

Urquhart D, et al. Antidepressants for non-specific **low back pain**. Cochrane Database Syst Rev. 2008 Jan 23;(1):CD001703. There is no clear evidence that antidepressants are more effective than placebo in the management of patients with chronic low-back pain.

Vahedi H, Merat S, et al. The effect of **fluoxetine** in patients with pain and constipation-predominant **irritable bowel syndrome**: a double-blind randomized-controlled study. Aliment Pharmacol Ther. 2005 Sep 1;22(5):381-5.

Valiengo LC, Goulart AC, et al. **Transcranial direct current stimulation** for the treatment of post-stroke depression: results from randomised, sham-controlled, double-blinded trial. J Neurol Neurosurg Psychiatry. 2016 Nov 4.

Vallerand IA, Lewinson RT, Parsons LM, et al. Assessment of a **Bidirectional Association Between Major Depressive Disorder and Alopecia Areata**. JAMA Dermatol. 2019 Jan 16.

van den Driest JJ, Bierma-Zeinstra SMA, Bindels PJE, Schiphof D. **Amitriptyline for musculoskeletal complaints**: a systematic review. Fam Pract. 2017 Apr 1;34(2):138-146.

van der Aa HP, van Rens GH, Comijs HC, et al. **Stepped care for depression and anxiety** in **visually impaired older adults**: multicentre randomised controlled trial. BMJ. 2015 Nov 23;351:h6127.

van der Hoeven N, Visser I, Schene A, et al. Severe hypertension related to **caffeinated coffee and tranylcypromine**: a case report. Ann Intern Med. 2014 May 6;160(9):657-8.

van der Meer RM, Willemsen MC, Smit F, et al. **Smoking cessation interventions** for smokers with current or past depression. Cochrane Database Syst Rev. 2013 Aug 21;8:CD006102. Evidence suggests that adding a psychosocial mood management component to a standard smoking cessation intervention increases long-term cessation rates in smokers with both current and past depression when compared with the standard intervention alone.

van der Waerden J, Galéra C, Larroque B, et al; EDEN Mother–Child Cohort Study Group. **Maternal Depression Trajectories and Children's Behavior** at Age 5 Years. J Pediatr. 2015 Apr 9.
van der Zee-van den Berg AI, Boere-Boonekamp MM, Groothuis-Oudshoorn CGM, Et al. Post-Up Study: **Postpartum Depression Screening** in Well-Child Care and Maternal Outcomes. Pediatrics. 2017 Sep 7.
van Gorp F, Whyte IM, Isbister GK. Clinical and ECG effects of **escitalopram overdose**. Ann Emerg Med. 2009 Sep;54(3):404-8.
van Gorp F, Duffull S, Hackett LP, et al. Population pharmacokinetics and pharmacodynamics of **escitolapram in overdose** and the effect of activated charcoal. Br J Clin Pharmacol 2012; 73: 402–10.
van Haelst IMM et al. Antidepressive treatment with **monoamine oxidase inhibitors** tranylcypromine, moclobemide & the occurance of intraoperative hemodynamic events: restrospective observational cohort study. *J Clin Psych* 2012Jul 10.
van Uden IW, van der Holst HM, van Leijsen EM, et al. Late-onset depressive symptoms **increase the risk of dementia** in small vessel disease. Neurology. 2016 Sep 13;87(11):1102-9.
Varigonda AL, et al. Systematic review and meta-analysis: **early treatment responses of selective serotonin reuptake inhibitors** in pediatric major depressive disorder. J Am Acad Child Adolesc Psychiatry 2015;54:557–64.
Veale D, Bewley A. **Body dysmorphic disorder**. BMJ. 2015 Jun 18;350:h2278.
Venkatesh KK, Zlotnick C, Triche EW, et al. Accuracy of Brief Screening **Tools for Identifying Postpartum Depression** Among Adolescent Mothers. Pediatrics. 2013 Dec 16
Victor M, Castro VM, Clements CC, Murphy SN, et al. **QT interval** and antidepressant (**citalopram, escitalopram, amitriptyline**) use: A cross sectional study of electronic health records. BMJ 2013.
Vieta E, Earley WR, Burgess MV, et al. **Long-term safety and tolerability of cariprazine as adjunctive therapy in major depressive disorder**. Int Clin Psychopharmacol. 2018 Dec 5.
Vignatelli L, D'Alessandro R, Candelise L. Antidepressant drugs for narcolepsy. Cochrane Database Syst Rev. 2005 Jul 20;(3):CD003724.
Vigod SN, Tarasoff LA, Bryja B, et al. Relation between place of **residence and postpartum depression**. CMAJ. 2013 Aug 6.
Vigod SN, Wilson CA, Howard LM. **Depression in pregnancy**. BMJ. 2016 Mar 24;352:i1547.
Viguera AC et al. Episodes of Mood Disorders in 2,252 **Pregnancies and Postpartum Periods**. Am J Psychiatry. 2011 Jul 28.
Viktorin A, Levine SZ, Altemus M, et al. **Paternal use of antidepressants and offspring outcomes** in Sweden: nationwide prospective cohort study. BMJ. 2018 Jun 8;361:k2233.
Viktorin A, Uher R, Kolevzon A, et al. Association of **Antidepressant Medication Use During Pregnancy With Intellectual Disability in Offspring**. JAMA Psychiatry. 2017 Jul 12
Vitolins MZ, Griffin L, et al. Randomized Trial to Assess the Impact of **Venlafaxine and Soy Protein** on Hot Flashes and Quality of Life in Men With Prostate Cancer. J Clin Oncol. 2013 Sep 30. (neither effective)
Voican CS, Corruble E, Naveau S, et al. **Antidepressant-Induced Liver Injury**: A Review for Clinicians. Am J Psychiatry. 2013 Dec 20
Vozoris NT, Wang X, Austin PC, et al. **Serotonergic antidepressant use and morbidity and mortality among older adults with COPD**. Eur Respir J. 2018 Jun 25.
Wagena EJ, Knipschild PG, Huibers MJ, et al. Efficacy of bupropion & nortriptyline for smoking cessation among people at risk for or with chronic obstructive pulmonary disease. Arch Intern Med. 2005 Oct 24;165(19):2286-92. CONCLUSIONS: Bupropion SR treatment is an efficacious aid to smoking cessation in patients with COPD. Nortriptyline treatment seems to be a useful alternative.
Wagner KD, Jonas J, Findling RL, Ventura D, et al. A double-blind, randomized, placebo-controlled trial of **escitalopram** in the treatment of **pediatric** depression. J Am Acad Child Adolesc Psychiatry. 2006 Mar;45(3):280-8.
Walfisch Asnat, Sermer Corey, Matok Ilan, et al. **Screening for depressive symptoms (EPDS scale). Motherisk.** Can Fam Physician July 2011 57: 777-778
Walitt B, Urrútia G, Nishishinya MB, Cantrell SE, Häuser W. **Selective serotonin reuptake inhibitors for fibromyalgia syndrome**. Cochrane Database Syst Rev. 2015;(6):CD011735. There is no unbiased evidence that SSRIs are superior to placebo in treating the key symptoms of fibromyalgia, namely pain, fatigue and sleep problems. SSRIs might be considered for treating depression in people with fibromyalgia. The black box warning for increased suicidal tendency in young adults aged 18 to 24, with major depressive disorder, who have taken SSRIs, should be considered when appropriate.
Walker J, Holm Hansen C, Martin P, et al. Prevalence, associations, and adequacy of treatment of **major depression** in **patients with cancer**: a cross-sectional analysis of routinely collected clinical data. Lancet Psychiatry 2014; published online Aug 28.
Walker J, Hansen CH, Martin P, et al; SMaRT (Symptom Management Research Trials) Oncology-3 Team. **Integrated collaborative care** for major depression comorbid with a poor prognosis cancer (**SMaRT Oncology-3**): a multicentre randomised controlled trial in patients with lung cancer. Lancet Oncol. 2014 Sep;15(10):1168-76.
Walsh BT, et al. Fluoxetine after weight restoration in anorexia nervosa: a randomized controlled trial. JAMA. 2006 Jun 14;295(22):2605-12. This study **failed** to demonstrate any benefit from fluoxetine in the treatment of patients with anorexia nervosa following weight restoration.
Walsh M, Knilans TK, Anderson JB, Czosek RJ. Successful treatment of **pallid breath-holding spells with fluoxetine**. Pediatrics. 2012 Sep;130(3):e685-9.
Walther A, Breidenstein J, Miller R. Association **of testosterone treatment with alleviation of depressive symptoms in men**: a systematic review and meta-analysis [online Nov 14, 2018]. JAMA Psychiatry.
Wang M, Szepietowska B, Polonsky B, et al. Risk of **Cardiac Events Associated With Antidepressant Therapy in Patients With Long QT Syndrome**. Am J Cardiol. 2018 Jan 15;121(2):182-187.
Wang Q, Hay M, Clarke D, Menahem S. The Prevalence and Predictors of **Anxiety and Depression** in Adolescents with **Heart Disease**. J Pediatr. 2012 May 26.
Wang YP, Chen YT, Tsai CF, et al. Short-term use of **serotonin reuptake inhibitors** and risk of upper **gastrointestinal bleeding**. Am J Psychiatry. 2014 Jan 1;171(1):54-61
Watanabe N, Omori IM, Nakagawa A, et al. **Mirtazapine** versus other antidepressive agents for depression. Cochrane Database Syst Rev. 2011 Dec 7;12:CD006528. Some statistically significant and possibly clinically meaningful differences between mirtazapine and other antidepressive agents were found for the acute-phase treatment of major depression. Mirtazapine is likely to have a faster onset of action than SSRIs during the acute-phase treatment. Dropouts occur similarly in participants treated with mirtazapine and those treated with other antidepressants, although the adverse event profile of mirtazapine is unique.
Warner CH, Bobo W, Warner C, Reid S, Rachal J. **Antidepressant discontinuation syndrome**. Am Fam Physician. 2006 Aug 1;74(3):449-56.
Watkins LL, Koch GG, Sherwood A, et al. Association of anxiety and depression with **all-cause mortality in individuals with coronary heart** disease. J Am Heart Assoc. 2013 Mar 19;2(2):e000068.
Watt JA, Gomes T, Bronskill SE, et al. Comparative risk of harm associated with **trazodone or atypical antipsychotic use in older adults with dementia**: a retrospective cohort study. CMAJ. 2018 Nov 26;190(47): E1376-E1383.
Weeke P, Jensen A, Folke F, et al. Antidepressant Use and **Risk of Out-of-Hospital Cardiac Arrest**: A Nationwide Case-Time-Control Study. Clin Pharmacol Ther. 2012 May 16.
Weersing VR, Brent DA, Rozenman MS, et al. **Brief Behavioral Therapy for Pediatric Anxiety and Depression** in Primary Care: A Randomized Clinical Trial. JAMA Psychiatry. 2017 Apr 19.
Wei D, Chen Y, Wu C, et al. Effect and safety of **paroxetine for vasomotor symptoms**: systematic review and meta-analysis. BJOG. 2016 Apr 7.
Wei F, Crain AL, Whitebird RR, et al. Effects of **paroxetine and sertraline on low-density lipoprotein cholesterol**: an observational cohort study. CNS Drugs. 2009 Oct;23(10):857-65.
Weiner RD. **Retrograde amnesia with electroconvulsive therapy (ECT):** characteristics and implications. Arch Gen Psychiatry. 2000 Jun;57(6):591-2.
Weintraub D, Rosenberg PB, Drye LT, et al. **DIADS-2** Research Group. Sertraline for the treatment of depression in Alzheimer disease: week-24 outcomes. Am J Geriatr Psychiatry. 2010 Apr;18(4):332-40.
Weiss A et al. Royal Australian and New Zealand College of Psychiatrists professional practice **guidelines for the administration of electroconvulsive therapy**. *Aust N Z J Psychiatry* 2019 Apr 10.
Weissman MM, et al; STAR*D-Child Team. Remissions in **maternal depression** and child psychopathology: a **STAR*D**-child report. JAMA. 2006 Mar 22;295(12):1389-98.
Weissman MM, Wickramaratne P, Nomura Y, Warner V, Pilowsky D, Verdeli H. **Offspring of depressed parents: 20 years later**. Am J Psychiatry. 2006 Jun;163(6):1001-8.
Weissman MM et al. Treatment of **maternal depression in a medication** clinical trial and its effect on children. Am J Psychiatry 2015 Jan 23.
Weissman MM, Berry OO, Warner V, Gameroff et al. A 30-Year Study of **3 Generations** at High Risk and Low Risk for Depression. JAMA Psychiatry. 2016 Aug 10.
Weitz ES, et al. Baseline Depression Severity as Moderator of Depression Outcomes Between **Cognitive Behavioral Therapy vs Pharmacotherapy**: An Individual Patient Data Meta-analysis. JAMA Psychiatry. 2015 Sep 23.
Weitzman M, Rosenthal DG, Liu YH. **Paternal depressive symptoms** and child behavioral or emotional problems in the United States. Pediatrics. 2011 Dec;128(6):1126-34.
Welk B, McArthur E, Ordon M, et al. Association of **Suicidality and Depression With 5alpha-Reductase Inhibitors** (eg. **finasteride**). JAMA Intern Med. 2017 Mar 20.
Wells KA, Losin WG. In vitro stability, potency, and dissolution of **duloxetine enteric-coated pellets after exposure to applesauce, apple juice, and chocolate pudding**. Clin Ther. 2008 Jul;30(7):1300-8.

Welsch P, Bernardy K, Derry S, et al. **Mirtazapine for fibromyalgia in adults**. Cochrane Database Syst Rev. 2018 Aug 6;8:CD012708.

Wernicke JF, et al. A randomized controlled trial of **duloxetine** in diabetic peripheral **neuropathic** pain. Neurology. 2006 Oct 24;67(8):1411-20.

Westfall E, Brandenburg D. **Probiotics for Symptoms of Depression and Anxiety**. Am Fam Physician. 2018 Mar 15;97(6):Online.

Westley CJ, Amdur RL, Irwig MS. High Rates of Depression and Depressive Symptoms among **Men Referred for Borderline Testosterone Levels**. J Sex Med. 2015 Jun 30.

Wetherell JL, Petkus AJ, White KS, et al. Antidepressant medication augmented with **cognitive-behavioral therapy** for generalized anxiety disorder in older adults. Am J Psychiatry. 2013 Jul 1;170(7):782-9.

Wharton S, Kuk JL, Petrova L, et al. Effectiveness of a **Community-Based Weight Management Program** for Patients Taking Antidepressants and/or Antipsychotics. Obesity (Silver Spring). 2019 Sep;27(9):1539-1544.

White JR, Chang CCH, et al. Depression and **human immunodeficiency virus** infection are risk factors for incident heart failure among veterans: Veterans Aging Cohort Study. Circulation. 2015;132:1630–1638.

Whitley H, Lindsey W. **Sex-based** differences in drug activity. Am Fam Physician. 2009 Dec 1;80(11):1254-8.

Whooley MA. Depression and **cardiovascular disease**: healing the broken-hearted. JAMA. 2006 Jun 28;295(24):2874-81.

Whooley MA. Diagnosis and treatment of **depression in adults with comorbid medical conditions**: a 52-year-old man with depression. JAMA. 2012 May 2;307(17):1848-57.

Wickham ME, Senthilselvan A, Wild TC, et al. **Maternal depressive symptoms** during childhood and risky adolescent health behaviors. Pediatrics. 2015 Jan;135(1):59-67.

Wiles NJ, Mulligan J, Peters TJ, et al. **Severity of depression and response to antidepressants**: **GENPOD** randomised controlled trial. Br J Psychiatry. 2012 Feb;200(2):130-6.

Wiles N, Thomas L, Abel A, et al. **Cognitive behavioural therapy** as an adjunct to pharmacotherapy for primary care based patients with treatment resistant depression: results of the **CoBalT** randomised controlled trial. Lancet 2012; online Dec 7.

Wiles N, Thomas L, Abel A, et al. Clinical effectiveness and cost-effectiveness of **cognitive behavioural** therapy as an adjunct to pharmacotherapy for treatment-resistant depression in primary care: the **CoBalT** randomised controlled trial. Health Technol Assess. 2014 May;18(31):1-168.

Wiles NJ, Thomas L, Turner N, et al. Long-term eff ectiveness and cost-eff ectiveness of **cognitive behavioural therapy** as an **adjunct to pharmacotherapy** for treatment-resistant depression in primary care: follow-up of the **CoBalT** randomized controlled trial. Lancet Psychiatry 2016; online Jan 6.

Wilkinson P, Izmeth Z. **Continuation and maintenance treatments for depression in older people**. Cochrane Database Syst Rev. 2012 Nov 14;11:CD006727. doi: 10.1002/14651858.CD006727.pub2. The long-term benefits of continuing antidepressant medication in the prevention of recurrence of depression in older people are not clear and no firm treatment recommendations can be made on the basis of this review.

Williams K, Wheeler DM, Silove N, Hazell P. Selective serotonin reuptake inhibitors (SSRIs) for **autism spectrum disorders (ASD).** Cochrane Database Syst Rev. 2010 Aug 4;8:CD004677. There is no evidence of effect of SSRIs in children and emerging evidence of harm. There is limited evidence of the effectiveness of SSRIs in adults from small studies in which risk of bias is unclear.

Williams JR, Hirsch ES, Anderson K, et al. A comparison of nine scales to detect **depression in Parkinson disease: Which scale** to use? Neurology. 2012 Mar 27;78(13):998-1006. The GDS-30 may be the most efficient depression screening scale to use in PD because of its brevity, favorable psychometric properties, and lack of copyright protection. However, all scales studied, except for the UPDRS Depression, are valid screening tools when PD-specific cutoff scores are used.

Williams K, Brignell A, Randall M, et al. Selective serotonin reuptake inhibitors **(SSRIs) for autism spectrum disorders** (ASD).Cochrane Database Syst Rev. 2013 Aug 20;8:CD004677. There is no evidence of effect of SSRIs in children and emerging evidence of harm. There is limited evidence of the effectiveness of SSRIs in adults from small studies in which risk of bias is unclear.

Williams NR, Heifets BD, Blasey C, et al. **Attenuation of Antidepressant Effects of Ketamine by Opioid Receptor Antagonism**. Am J Psychiatry. 2018 Aug 29:appiajp201818020138.

Willis BL, Leonard D, Barlow CE, et al. Association of **Midlife Cardiorespiratory Fitness With Incident Depression** and Cardiovascular Death After Depression in Later Life. JAMA Psychiatry. 2018 Jun 27.

Wilson RS, Capuano AW, Boyle PA, et al. Clinical-pathologic study of **depressive symptoms and cognitive decline** in **old age**. Neurology. 2014 Aug 19;83(8):702-9.

Wijkstra J, Lijmer J, Balk F, Geddes J, Nolen W, Wijkstra J. Pharmacological treatment for **psychotic depression**. Cochrane Database Syst Rev. 2005 Oct 19;(4):CD004044.

Wimbiscus M, Kostenko O, Malone D. **MAO inhibitors**: Risks, benefits, and lore *Cleveland Clinic Journal of Medicine* 2010; 77(12):859-882; doi:10.3949/ccjm.77a.09103.

Wisner KL, Sit DK, McShea MC, et al. Onset Timing, Thoughts of Self-harm, and Diagnoses in **Postpartum Women** With Screen-Positive Depression Findings. JAMA Psychiatry. 2013 Mar 13:1-9.

Wong J, Motulsky A, Eguale T, et al. Treatment **Indications for Antidepressants Prescribed in Primary Care in Quebec**, Canada, 2006-2015. JAMA. 2016 May 24 31;315(20):2230-2.

Wong J, Motulsky A, Abrahamowicz M, et al. **Off-label indications for antidepressants in primary care**: descriptive study of prescriptions from an indication based electronic prescribing system. BMJ. 2017 Feb 21;356:j603.

Wong SYS, Sun YY, Chan ATY, et al. **Treating Subthreshold Depression** in Primary Care: A Randomized Controlled Trial of Behavioral Activation With Mindfulness. Ann Fam Med. 2018 Mar;16(2):111-119.

Woolcott John C.; Richardson Kathryn J.; Wiens Matthew O.; et al. Meta-analysis of the Impact of 9 Medication Classes on **Falls** in Elderly Persons. Arch Intern Med. 2009;169(21):1952-1960.

Woolhouse H, Gartland D, Hegarty K, et al. Depressive symptoms and **intimate partner violence** in the 12 months after childbirth: a prospective pregnancy cohort study. BJOG 2012;119:315–23.

Worly BL, Gur TL, Schaffir J. The relationship between **progestin hormonal contraception and depression**: a systematic review. Contraception. 2018 Feb 20.

Worsley R, Bell RJ, Gartoulla P, et al. Moderate-Severe **Vasomotor Symptoms Are Associated** with Moderate-Severe **Depressive** Symptoms. J Womens Health (Larchmt). 2017 Mar 6.

Wu Eric Q, Yu Andrew P, Lauzon Veronique, et al. Economic Impact of Therapeutic Substitution of a **Brand Selective Serotonin Reuptake Inhibitor with an Alternative Generic** Selective Serotonin Reuptake Inhibitor in Patients with Major Depressive Disorder. Articles Ahead of Print published on 1 April 2011, DOI 10.1345/aph.1P482. Ann Pharmacother ;45:441-451.

Wu X, Al-Abedalla K, Rastikerdar E, et al. **Selective Serotonin Reuptake Inhibitors** and the Risk of **Osseointegrated Implant Failure**: A Cohort Study. J Dent Res. 2014 Sep 3.

Xiong GL, et al. Prognosis of patients taking **selective serotonin reuptake** inhibitors before **coronary artery bypass grafting**. Am J Cardiol. 2006 Jul 1;98(1):42-7. Epub 2006 May 5.

Yan T, Goldman RD. **Time-to-effect of fluoxetine** in children with depression. Can Fam Physician. 2019 Aug;65(8):549-551.

Yang A, Ciolino JD, Pinheiro E, et al. **Neonatal Discontinuation Syndrome in Serotonergic Antidepressant-Exposed Neonates**. J Clin Psychiatry. 2017 May;78(5):605-611.

Yang F, Liang H, Chen J, et al. **Prenatal Paternal Selective Serotonin Reuptake Inhibitors Use and Risk of ADHD** in Offspring. Pediatrics. 2017 Dec 11.

Yawn BP et al. TRIPPD: A practice-based network effectiveness study of **postpartum depression** screening and management. Ann Fam Med 2012 Jul/Aug; 10:320.

Yawn BP, Bertram S, Kurland M, et al. Repeated depression **screening during the first postpartum year**. Ann Fam Med. 2015 May;13(3):228-34.

Yesavage JA, Fairchild JK, Mi Z, et al. Effect of Repetitive **Transcranial Magnetic Stimulation on Treatment-Resistant Major Depression** in US Veterans: A Randomized Clinical Trial. JAMA Psychiatry. 2018 Jun 27.

Yohannes AM, Müllerová H, Hanania NA, et al. **Long-term Course of Depression Trajectories** in Patients With **COPD**: A 3-Year Follow-up Analysis of the Evaluation of COPD Longitudinally to Identify Predictive Surrogate Endpoints Cohort. Chest. 2016 Apr;149(4):916-26.

Yonkers KA, Wisner KL, Stewart DE, et al. The management of depression during pregnancy: a report from the American Psychiatric Association (**APA**) and the American College of Obstetricians and Gynecologists (**ACOG**). Gen Hosp Psychiatry. 2009 Sep-Oct;31(5):403-13.

Yonkers KA, Kornstein SG, Gueorguieva R, et al. Symptom-Onset Dosing of **Sertraline** for the Treatment of **Premenstrual Dysphoric Disorder**: A Randomized Clinical Trial. JAMA Psychiatry. 2015 Sep 9:1-8.

Yuet WC, Derasari D, Sivoravong J, et al. **Selective Serotonin Reuptake Inhibitor Use and Risk** of Gastrointestinal and Intracranial Bleeding. J Am Osteopath Assoc. 2019 Feb 1;119(2):102-111.

Zahl T, Steinsbekk S, Wichstrøm L. **Physical Activity, Sedentary Behavior**, and Symptoms of Major Depression in Middle Childhood. Pediatrics. 2017 Jan 9.

Zaman S, Mclaughlin MR. **Levomilnacipran** (**Fetzima**) for Major Depressive Disorder. Am Fam Physician. 2015;92(8):730-731.

Zarate CA Jr, et al. A randomized trial of an N-methyl-D-aspartate antagonist (**ketamine**) in treatment-resistant major depression. Arch Gen Psychiatry. 2006 Aug;63(8):856-64.

Zaremba D, Dohm K, Redlich R, et al. Association of **brain cortical changes with relapse** in patients with major depressive disorder [online Mar 28, 2018].JAMA Psychiatry. 10.1001 /jamapsychiatry.2018.0123.

Zeki Al Hazzouri A, Caunca MR, et al. Greater depressive symptoms, cognition, and markers of brain aging: Northern Manhattan Study. Neurology. 2018 May 9.
Zelefsky JR, Fine HF, Rubinstein VJ, Hsu IS, Finger PT. Escitalopram-induced uveal effusions and bilateral angle closure **glaucoma**. Am J Ophthalmol. 2006 Jun;141(6):1144-7.
Zhang MW, Ho RC. **Ketamine's** potential as a rapid **antidepressant** was overplayed. BMJ. 2015 Aug 19;351:h4467.
Zhao J, Yin H, Zhang G, et al. A meta-analysis of randomized controlled trials of **laughter and humour interventions** on depression, anxiety and sleep quality in adults. J Adv Nurs. 2019 Mar 18.
Zhou H, Polimanti R, Yang B-Z, et al. **Genetic risk variants** associated with **comorbid alcohol dependence and major depression** [online October 25, 2017]. JAMA Psychiatry. 2017. doi:10.1001/jamapsychiatry.2017.3275.
Zhou X, Ravindran AV, et al. Comparative efficacy, acceptability, and tolerability of **augmentation agents in treatment-resistant depression**: systematic review and network meta-analysis. J Clin Psychiatry. 2015;76:e487-98.
Zimmermann P, Brückl T, Nocon A, et al. Interaction of **FKBP5 gene variants** and adverse life events in predicting depression onset: results from a 10-yr prospective community study. Am J Psychiatry 2011; 168:1107–1116.
Zivin K, Pfeiffer PN, Bohnert AS, et al. Evaluation of the **FDA Warning Against Prescribing Citalopram** at Doses Exceeding 40 mg. Am J Psychiatry. 2013 May 3.
Zoellner LA, Roy-Byrne PP, Mavissakalian M, et al. Doubly Randomized Preference Trial of **Prolonged Exposure Versus Sertraline for Treatment of PTSD**. Am J Psychiatry. 2018 Oct 19:appiajp201817090995.
Zuckerbrot RA, Cheung A, Jensen PS, et al. Guidelines for **Adolescent Depression in Primary Care** (**GLAD-PC**): **Part I. Practice Preparation, Identification, Assessment, and Initial Management**.Pediatrics. 2018 Feb 26.

ANTIDEPRESSANT COMPARISON CHART - References

[1]Jefferson J, Greist JH. Mood Disorders in Textbook of Psychiatry, 2nd Ed. Editors: Hales RE, Yudofsky SC, Talbot JA. American Psychiatric Press, Washington, 1994.
[2] Micromedix Drug Information, 2016.
[3] Geddes JR, Carney SM, Davies C, et al. **Relapse prevention** with antidepressant drug treatment in depressive disorders: a systematic review. Lancet. 2003 Feb 22;361(9358):653-61.
[4] Treatment Guidelines: **Drugs for Psychiatric Disorders**. The Medical Letter: July, 2003; p. 69-76, then **June 2006,** & Updated **June 2013.**
Medical Letter. Treatment Guidelines. Drugs for Depression. May 2010. July 2016.
[5] Remick RA. Diagnosis and management of depression in primary care: a clinical update and review. CMAJ. 2002 Nov 26;167(11):1253-60.
[6] Practice guideline for the treatment of patients with major depressive disorder (revision). **American** Psychiatric Association. Am J Psychiatry. **2000** Apr;157(4 Suppl):1-45.
http://www.psych.org/psych_pract/treatg/pg/Practice%20Guidelines8904/MajorDepressiveDisorder_2e.pdf
[7] Trindade E, Menon D, Topfer LA, Coloma C. Adverse effects associated with selective serotonin reuptake inhibitors and tricyclic antidepressants: a meta-analysis. CMAJ. 1998 Nov 17;159(10):1245-52.
[8] Modell JG, Katholi CR, Modell JD, et. al. Comparative sexual side effects of bupropion fluoxetine, paroxetine, and sertraline. Clin Pharmacol Ther 1997;61(4):476-87.
[9] Gonzalez M, Llorca G, Izquierdo JA, et.al. J Sex Marital Ther 1997;23(3):176-94.
[10] Ditto KE. SSRI discontinuation syndrome. Awareness as an approach to prevention. Postgrad Med. 2003 Aug;114(2):79-84.
[11] Glassman AH, O'Connor CM, Califf RM, et al.; Sertraline Antidepressant Heart Attack Randomized Trial (SADHEART) Group. Sertraline treatment of major depression in patients with acute MI or unstable angina. JAMA. 2002 Aug 14;288(6):701-9. (Taylor CB, Youngblood ME, Catellier D, et al.; ENRICHD Investigators. Effects of antidepressant medication on morbidity and mortality in depressed patients after myocardial infarction. Arch Gen Psychiatry. 2005 Jul;62(7):792-8 -Observational secondary analysis)(Lesperance F, et al. CREATE Investigators. Effects of citalopram 20-40mg/d and interpersonal psychotherapy on depression in patients with coronary artery disease: the Canadian Cardiac Randomized Evaluation of Antidepressant and Psychotherapy Efficacy (CREATE) trial. JAMA. 2007 Jan 24;297(4):367-79. (n=284 12weeks)Based on these results and those of previous trials, citalopram or sertraline plus clinical management should be considered as a first-step treatment for patients with CAD and major depression.)
Pizzi C, Rutjes AW, Costa GM, Fontana F, Mezzetti A, Manzoli L. Meta-Analysis of Selective Serotonin Reuptake Inhibitors in Patients With Depression and Coronary Heart Disease. Am J Cardiol. 2011 Jan 20.
[12] Grady-Weliky TA. Clinical practice. Premenstrual dysphoric disorder. N Engl J Med. 2003 Jan 30;348(5):433-8.
[13] Pearlstein T. Selective serotonin reuptake inhibitors for premenstrual dysphoric disorder: the emerging gold standard? Drugs. 2002;62(13):1869-85.
[14] Which SSRI? Med Lett Drugs Ther. 2003 Nov 24;45(1170):93-95.
[15] Glassman AH, O'Connor CM, Califf RM, et al.; Sertraline Antidepressant Heart Attack Randomized Trial (SADHART) Group. Sertraline treatment of major depression in patients with acute MI or unstable angina. JAMA. 2002 Aug 14;288(6):701-9. (Taylor CB, Youngblood ME, Catellier D, et al.; ENRICHD Investigators. Effects of antidepressant medication on morbidity and mortality in **depressed patients after myocardial infarction**. Arch Gen Psychiatry. 2005 Jul;62(7):792-8 -Observational secondary analysis)
Glassman AH, Bigger JT Jr, Gaffney M. Psychiatric characteristics associated with long-term mortality among 361 patients having an acute coronary syndrome and major depression: seven-year follow-up of SADHART participants. Arch Gen Psychiatry. 2009 Sep;66(9):1022-9.
O'Connor CM, Jiang W, Kuchibhatla M, et al. SADHART-CHF Investigators. Safety and efficacy of sertraline for depression in patients with heart failure: results of the SADHART-CHF (Sertraline Against Depression and Heart Disease in Chronic Heart Failure) trial. J Am Coll Cardiol. 2010 Aug 24;56(9):692-9.
[16] Bezchlibnyk-Butler K. Serotonergic antidepressants: Drug response and drug-drug interactions. Pharmacy Practice:National CE Program 1998;Aug:1-8.
[17] Buckley NA, McManus PR. Fatal toxicity of serotoninergic and other antidepressant drugs: analysis of United Kingdom mortality data. BMJ. 2002 Dec 7;325(7376):1332-3.
Hamer Mark, Batty G. David, Seldenrijk Adrie, et al. Antidepressant medication use and future risk of cardiovascular disease: the Scottish Health Survey. Eur Heart J ehq438 first published online November 30, 2010 doi:10.1093/eurheartj/ehq438
[18] Furukawa TA, McGuire H, Barbui C. Meta-analysis of effects and side effects of low dosage tricyclic antidepressants in depression: systematic review. BMJ. 2002 Nov 2;325(7371):991.
[19] Maizels M, McCarberg B. Antidepressants and antiepileptic drugs for chronic non-cancer pain. Am Fam Physician. 2005 Feb 1;71(3):483-90.
[20] Houdenhove BV, Onghena P. Pain and Depression in Depression and Physical Illness. Editors: Robertson MM, Katona CLE. Wiley & Sons, New York, 1997.
[21] Pryse-Phillips WEM, Dodick DW, Edmeads JG. Guidelines for the diagnosis and management of migraine in clinical practice. Can Med Assoc J 1997;156:1273-87.
[22] Wells BG, Mandos LA, Hayes PE. Depressive Disorders in Pharmacotherapy: A Pathophysiologic Approach 3rd Ed., 1996.
[23] Tollefson GD. Antidepressant treatment and side effect considerations. J Clin Psychiatry 1991;52(5-suppl):4-13.
[24] Cole JO, Bodkin JA. Antidepressant side effects. J Clin Psychiatry 1990;51(1):21-26
[25] Nurnberg HG, Hensley PL, Gelenberg AJ, Fava M, Lauriello J, Paine S. Treatment of antidepressant-associated **sexual dysfunction with sildenafil**: a randomized controlled trial. JAMA. 2003 Jan 1;289(1):56-64. (Taylor MJ, Strategies for managing antidepressant-induced sexual dysfunction: systematic review of randomised controlled trials. J Affect Disord. 2005 Nov;88(3):241-54. Epub 2005 Sep 12.)(Basson R. Clinical practice. Sexual desire and arousal disorders in women. N Engl J Med. 2006 Apr 6;354(14):1497-506.) (Fava M, et al. Efficacy and safety of **sildenafil** in men with serotonergic antidepressant-associated erectile dysfunction: results from a randomized, double-blind, placebo-controlled trial.J Clin Psychiatry.2006Feb;67(2):240-6.)
Nurnberg HG, Hensley PL, Heiman JR, Croft HA, Debattista C, Paine S. Sildenafil treatment of women with antidepressant-associated sexual dysfunction: a randomized controlled trial.JAMA. 2008 Jul 23;300(4):395-404.
In this study population, sildenafil treatment of sexual dysfunction in women taking SRIs was associated with a reduction in adverse sexual effects.
[26] Boyer EW, Shannon M. The **serotonin syndrome**. N Engl J Med. 2005 Mar 17;352(11):1112-20. (Pharmacist's Letter: Serotonin Syndrome Sept 2006)
Frank C. Recognition and treatment of **serotonin syndrome**. Can Fam Physician. 2008 Jul;54(7):988-92.
Ables AZ. Prevention, Diagnosis, and Management of **Serotonin Syndrome**. American Family Pysician. May 1, 2010.

FDA has received reports of serious central nervous system (CNS) reactions when the drug methylene blue is given to patients taking psychiatric medications that work through the serotonin system of the brain (serotonergic psychiatric medications).
FDA July/11 has received reports of serious central nervous system (CNS) reactions when the antibacterial drug linezolid (Zyvox) is given to patients taking psychiatric medications that work through the serotonin system of the brain (serotonergic psychiatric medications.

Buckley NA, Dawson AH, Isbister GK. **Serotonin syndrome**. BMJ. 2014 Feb 19;348:g1626.
Sim SS, Sun JT. Ocular Flutter in the Serotonin Syndrome. N Engl J Med. 2016 Nov 3;375(18):e38.
Foong AL, Patel T, Kellar J, Grindrod KA. The **scoop on serotonin syndrome**. Can Pharm J (Ott). 2018 May 30;151(4):233-239.
[27] Bhatia SC, Bhatia SK. Major Depression: Selecting Safe and Effective Treatment. Am Family Physician 1997;55(5):1683-1694.
[28] Watson CPN. Antidepressant Drugs as Adjuvant Analgesics. J Pain Symptom Manage 1994;9:392-405.
[29] The Medical Letter: Drugs that may cause Psychiatric Symptoms. July 8, 2002; (1134) pp. 59-62.
[30] Birrer RB, Vemuri SP. Depression in later life: a diagnostic and therapeutic challenge. Am Fam Physician. 2004 May 15;69(10):2375-82.
[31] Finkel SI. Efficacy and tolerability of antidepressant therapy in the **old-old**. J Clin Psychiatry 1996;57(suppl 5):23-8.
Coupland C, Dhiman P, Morriss R, et al. Antidepressant use and risk of adverse outcomes in **older people**: population based cohort study. BMJ. 2011 Aug 2;343:d4551.
Kok RM, Reynolds CF 3rd. Management of Depression in Older Adults: A Review. JAMA. 2017 May 23;317(20):2114-2122.

[32] Menting JEA, Honig A, Verhey FRJ, et. al. Int Clin Psychophamacology 1996;11:165-175.
[33] Pryse-Phillips WEM, Dodick DW, Edmeads JG. Guidelines for the diagnosis and management of migraine in clinical practice. Can Med Assoc J 1997;156:1273-87.
[34] Reite M, Ruddy J, Nagel K. Evaluation and management of sleep disorders, 2nd Ed. Am Psychiatric Press, Washington, 1997.
[35] Hughes J, Stead L, Lancaster T. Antidepressants for **smoking cessation**. Cochrane Database Syst Rev. 2004 Oct 18;(4):CD000031. Review.
[36] Drugs and Therapy Perspectives 1998;12(7):14-15.
Gafoor R, Booth HP, Gulliford MC. Antidepressant utilisation and incidence of weight gain during 10 years' follow-up: population based cohort study. BMJ 2018;361:k1951.
[37] AHFS (American Hospital Formulary System) Drug Information: Antidepressants. 2005.
[38] Gunnell D, Saperia J, Ashby D. Selective serotonin reuptake inhibitors (SSRIs) and suicide in adults: meta-analysis of drug company data from placebo controlled, randomised controlled trials submitted to the MHRA's safety review. BMJ. 2005 Feb 19;330(7488):385.
[39] Gibbons RD, Hur K, Bhaumik DK, Mann JJ. The relationship between antidepressant medication use and **rate of suicide**. Arch Gen Psychiatry. 2005 Feb;62(2):165-72.
[40] Birmes P, Coppin D, Schmitt L, Lauque D. **Serotonin syndrome**: a brief review. CMAJ. 2003 May 27;168(11):1439-42.
Health Canada May/14 has completed a safety review of the serotonin blocking drugs dolasetron (ANZEMET), granisetron (KYTRIL and generics), ondansetron (ZOFRAN and generics) and palonosetron (ALOXI), which are used for treating nausea and vomiting. This review identified a potential risk of serotonin syndrome.
[41] Hansten, PD and Horn JR. Drug Interactions Analysis and Management. Applied Therapeutics Incorporated. Vancouver, WA. 2008.
[42] Stahl MM, Lindquist M, Pettersson M, et.al. Withdrawal reactions with selective serotonin re-uptake inhibitors as reported to the WHO system. Eur J clin Pharmacol 1997;53(3-4):163-9.
[43] Bleeding: Meijer WE, Heerdink ER, Nolen WA, et al. Association of risk of abnormal bleeding with degree of serotonin reuptake inhibition by antidepressants. Arch Intern Med. 2004 Nov 22;164(21):2367-70. (Benazzi F. Hemorrhages during escitalopram-venlafaxine-mirtazapine combination treatment of depression. Can J Psychiatry. 2005 Mar;50(3):184.) (Ziegelstein RC, Meuchel J, Kim TJ, et al. Selective serotonin reuptake inhibitor use by patients with acute coronary syndromes. Am J Med. 2007 Jun;120(6):525-30. Epub 2007 Apr 30. Selective serotonin reuptake inhibitor use during a hospitalization for an acute coronary syndrome is associated with reduced rates of recurrent ischemia, heart failure, or cardiac enzyme elevation at the expense of increased bleeding in patients receiving maximal conventional antiplatelet medications and heparin.) FRACTURES: Richards JB, Papaioannou A, Adachi JD, et al. Effect of selective serotonin reuptake inhibitors on the **risk of fracture**. Arch Intern Med. 2007 Jan 22;167(2):188-94. Daily SSRI use in adults 50 years and older remained associated with a 2-fold increased risk of clinical fragility fracture after adjustment for potential covariates. Depression and fragility fractures are common in this age group, and the elevated risk attributed to daily SSRI use may have important public health consequences. Diem SJ, Blackwell TL, Stone KL, Yaffe K, Haney EM, Bliziotes MM, Ensrud KE. Use of antidepressants and rates of hip bone loss in older women: the study of osteoporotic fractures. Arch Intern Med. 2007 Jun 25;167(12):1240-5. Use of SSRIs but not TCAs is associated with an increased rate of bone loss at the hip in this cohort of older women. Haney EM, Chan BK, Diem SJ, Ensrud KE, Cauley JA, Barrett-Connor E, Orwoll E, Bliziotes MM; for the Osteoporotic Fractures in Men Study Group. Association of low bone mineral density with selective serotonin reuptake inhibitor use by older men. Arch Intern Med. 2007 Jun 25;167(12):1246-51. In this population of men, BMD was lower among those reporting current SSRI use, but not among users of other antidepressants.
Loke YK, Trivedi AN, Singh S. Meta-analysis: Gastrointestinal bleeding due to interaction between selective serotonin uptake inhibitors and **non-steroidal anti-inflammatory drugs**. Aliment Pharmacol Ther. 2007 Oct 5; [Epub ahead of print]) Upper gastrointestinal (GI) bleeding is associated with the use of selective serotonin reuptake inhibitors (SSRIs); the risk is increased when patients are also taking nonsteroidal anti-inflammatory drugs (NSAIDS). The risk for each individual is still low; but given the number of people taking SSRIs, the impact across a population may be noticeable. (LOE = 3a)
Schalekamp T, Klungel JH, Souverein PC, de Boer A. Increased bleeding risk with concurrent use of selective serotonin reuptake inhibitors and **coumarins**. Arch Intern Med. 2008 Jan 28;168(2):180-5. In users of coumarins, SSRI usage was associated with increased risk of hospitalization because of nongastrointestinal bleeding but not because of gastrointestinal bleeding.
de Abajo FJ, García-Rodríguez LA. Risk of upper gastrointestinal tract bleeding associated with selective serotonin reuptake inhibitors and venlafaxine therapy: interaction with nonsteroidal anti-inflammatory drugs and effect of acid-suppressing agents. Arch Gen Psychiatry. 2008 Jul;65(7):795-803. Antidepressants with a relevant blockade action on the serotonin reuptake mechanism increase the risk of upper gastrointestinal tract bleeding. The increased risk may be of particular relevance when these drugs are associated with nonsteroidal anti-inflammatory drugs. Our study findings also provide evidence that use of acid-suppressing agents limits such increased risk.
Targownik LE, Bolton JM, Metge CJ, et al. Selective serotonin reuptake inhibitors are associated with a modest increase in the risk of upper gastrointestinal bleeding. Am J Gastroenterol. 2009 Jun;104(6):1475-82. Epub 2009 Apr 28. SSRI use is associated with a modestly increased risk of UGIB, which may be significantly reduced with PPI co-therapy. SSRI use is not a major risk factor for NSAID-related UGIB.
Andrade C, Sandarsh S, Chethan KB, Nagesh KS. Serotonin reuptake inhibitor antidepressants and abnormal **bleeding**: a review for clinicians and a reconsideration of mechanisms. J Clin Psychiatry. 2010 Dec;71(12):1565-75.
Labos C, Dasgupta K, Nedjar H, et al. Risk of **bleeding associated with combined use of selective serotonin reuptake inhibitors** and antiplatelet therapy following acute myocardial infarction. CMAJ 2011; DOI:10.1503/cmaj.100912.
Hackam DG, Mrkobrada M. Selective serotonin reuptake inhibitors and brain hemorrhage: A meta-analysis. Neurology. 2012 Oct 17.
Mortensen JK, Larsson H, Johnsen SP, et al. Post stroke use of selective serotonin reuptake inhibitors and clinical outcome among patients with ischemic stroke: a nationwide propensity score-matched follow-up study. Stroke. 2013 Feb;44(2):420-6.
Palmsten K, Hernández-Díaz, Huybrechts KF, et al. Use of antidepressants near delivery and risk of **postpartum hemorrhage**: cohort study of low income women in the United States. BMJ 2013;347:f4877.
Seifert CF, Wiltrout TR. Calcaneal Bone Mineral Density in Young Adults Prescribed Selective Serotonin Reuptake Inhibitors. Clin Ther. 2013 Aug 16.
Diem SJ et al. Rates of bone loss among women initiating antidepressant medication use in midlife. J Clin Endocrinol Metab 2013 Sep 3; [e-pub ahead of print].
Wang YP, Chen YT, Tsai CF, et al. Short-term use of serotonin reuptake inhibitors and risk of upper gastrointestinal bleeding. Am J Psychiatry. 2014 Jan 1;171(1):54-61
Mahdanian AA, Rej S, Bacon SL, et al. **Serotonergic antidepressants and perioperative bleeding risk**: a systematic review. Expert Opin Drug Saf. 2014 Jun;13(6):695-704.
Anglin R, Yuan Y, Moayyedi P, et al. Risk of Upper Gastrointestinal Bleeding With Selective Serotonin Reuptake Inhibitors With or Without Concurrent NonSteroidal Anti-Inflammatory Use: A Systematic Review and Meta-Analysis. Am J Gastroenterol. 2014 Jun;109(6):811-9.
Mortensen JK, Larsson H, Johnsen SP, et al. Impact of Prestroke Selective Serotonin Reuptake Inhibitor Treatment on Stroke Severity and Mortality. Stroke. 2014 Jun 3.
Quinn GR, Singer DE, Chang Y, et al. Effect of selective serotonin reuptake inhibitors on bleeding risk in patients with atrial fibrillation taking **warfarin**. Am J Cardiol. 2014 Aug 15;114(4):583-6.
Jiang HY, Chen HZ, Hu XJ, et al. Use of Selective Serotonin Reuptake Inhibitors and **Risk of Upper Gastrointestinal Bleeding**: A Systematic Review and Meta-analysis. Clin Gastroenterol Hepatol. 2014 Jun 30.
Wu X, Al-Abedalla K, Rastikerdar E, et al. **Selective Serotonin Reuptake Inhibitors** and the Risk of **Osseointegrated Implant Failure**: A Cohort Study. J Dent Res. 2014 Sep 3.
Sheu YH, Lanteigne A, Stürmer T, et al. **SSRI use and risk of fractures** among perimenopausal women without mental disorders. Inj Prev. 2015 Jun 25.
Hanley GE, Smolina K, Mintzes B, et al. **Postpartum Hemorrhage and Use of Serotonin Reuptake Inhibitor Antidepressants in Pregnancy.** Obstet Gynecol. 2016 Mar;127(3):553-61.

Renoux C, Vahey S, Dell'Aniello S, Boivin J-F. Association of selective **serotonin reuptake inhibitors with the risk for spontaneous intracranial hemorrhage** [online Dec 5, 2016]. JAMA Neurol. doi:10.1001/jamaneurol.2016.4529

Bolton JM, Morin SN, Majumdar SR, et al. Association of Mental Disorders and Related Medication Use With Risk for Major **Osteoporotic Fractures**. JAMA Psychiatry. 2017 Apr 19.

Scheitz JF, Turc G, Kujala L, et al. **Intracerebral Hemorrhage and Outcome After Thrombolysis in Stroke Patients Using Selective Serotonin-Reuptake Inhibitors**. Stroke. 2017 Dec;48(12):3239-3244.

Iwagami M, Tomlinson LA, Mansfield KE, et al.**Gastrointestinal bleeding risk of selective serotonin reuptake inhibitors by level of kidney function**: a population-based cohort study. Br J Clin Pharmacol. 2018 Jun 4.

Brännstrom J, Lövheim H, Gustafson Y, Nordström P. Association between **antidepressant drug use and hip fracture** in older people before and after treatment initiation [online Jan 2, 2019]. JAMA Psychiatry. doi:10.1001/jamapsychiatry.2018.3679

Bixby AL, VandenBerg A, Bostwick JR. Clinical Management of **Bleeding Risk With Antidepressants**. Ann Pharmacother. 2018 Aug 6:1060028018794005.

[44] Jureidini JN, Doecke CJ, Mansfield PR, Haby MM, Menkes DB, Tonkin AL. Efficacy and safety of antidepressants for children and adolescents. BMJ. 2004 Apr 10;328(7444):879-83.

[45] Gunnell D, Ashby D. Antidepressants and suicide: what is the balance of benefit and harm. BMJ. 2004 Jul 3;329(7456):34-8.

[46] Whittington CJ, Kendall T, Fonagy P, Cottrell D, et al. Selective serotonin reuptake inhibitors in **childhood** depression: systematic review of **published versus unpublished** data. Lancet. 2004 Apr 24;363(9418):1341-5.
Ryan ND. Treatment of **depression in children** and adolescents. Lancet. **2005** Sep 10-16;366(9489):933-40.

[47] The American Academy of Child and Adolescent Psychiatry: http://www.aacap.org/Announcements/pdfs/physiciansmedguide.pdf .
American College of Neuropsychopharmacology: SSRIs & Suicidal Behavior in youth Jan/04: http://www.acnp.org/exec_summary.pdf **Final Nov/05** http://www.nature.com/npp/journal/vaop/ncurrent/pdf/1300958a.pdf
Sept/05 Nice:Depression in children & young people http://www.nice.org.uk/pdf/CG028NICEguideline.pdf ; (Simon GE, Savarino J, Operskalski B, Wang PS. **Suicide risk during antidepressant treatment**. Am J Psychiatry. 2006 Jan;163(1):41-7. CONCLUSIONS: The risk of suicide during acute-phase antidepressant treatment is approximately one in 3,000 treatment episodes, and risk of serious suicide attempt is approximately one in 1,000. Available data do not indicate a significant increase in risk of suicide or serious suicide attempt after starting treatment with newer antidepressant drugs.)(Cheung AH, et al. The use of antidepressants to treat depression in children and adolescents. CMAJ. 2006 Jan 17;174(2):193-200.) & (Hammad TA, et al. Suicidality in pediatric patients treated with antidepressant drugs. Arch Gen Psychiatry. 2006 Mar;63(3):332-9. CONCLUSION: Use of antidepressant drugs in pediatric patients is associated with a modestly increased risk of suicidality. InfoPOEMs: The use of antidepressant medications in children is associated with an increased risk of suicidal ideation and suicide-related behaviors. It is uncertain what overall effect antidepressant medications have on the morbidity and mortality of treated children. Close monitoring of patients using these medications regarding the risk of suicidality is recommended. (LOE = 1a-)) (Glaxo May/06 Meta analysis: 8958 paroxetine & 5953 placebo pts; suicidal behavior aged 18-24yrs (2.19 vs 0.92%); all ages (0.32 vs 0.05%); all were nonfatal suicide attempts; 8 of 11 attempts were in aged 18-30yrs) Emslie GJ, et al. Paroxetine Treatment in Children and Adolescents With Major Depressive Disorder: A Randomized, Multicenter, Double-Blind, Placebo-Controlled Trial. J Am Acad Child Adolesc Psychiatry. 2006 Jun;45(6):709-719. Paroxetine was not shown to be more efficacious than placebo for treating pediatric major depressive disorder. (Misri S, et al. Internalizing behaviors in 4-year-old children exposed in utero to psychotropic medications. Am J Psychiatry. 2006 Jun;163(6):1026-32.) (Dubicka B, Hadley S, Roberts C. **Suicidal** behaviour in youths with depression treated with new-generation antidepressants: meta-analysis. Br J Psychiatry. 2006 Nov;189:393-8. Self-harm or suicide-related events occurred in 71 of 1487 (4.8%) of depressed youths treated with antidepressants v. 38 of 1254 (3.0%) of those given placebo (fixed effects odds ratio 1.70, 95% CI 1.13-2.54, P=0.01).) (Gibbons RD, Hur K, Bhaumik DK, Mann JJ. The relationship between antidepressant prescription rates and rate of early adolescent **suicide**. Am J Psychiatry. 2006 Nov;163(11):1898-904. The aggregate nature of these observational data precludes a direct causal interpretation of the results. More SSRI prescriptions are associated with lower suicide rates in children and may reflect antidepressant efficacy, treatment compliance, better quality mental health care, and low toxicity in the event of a suicide attempt by overdose.) (Juurlink DN, et al. The risk of **suicide** with selective serotonin reuptake inhibitors in the **elderly**. Am J Psychiatry. 2006 May;163(5):813-21. Initiation of SSRI therapy is associated with an increased risk of suicide during the first month of therapy compared with other antidepressants. The absolute risk is low, suggesting that an idiosyncratic response to these agents may provoke suicide in a vulnerable subgroup of patients.) (Olfson M, Marcus SC, Shaffer D. Antidepressant drug therapy and **suicide** in severely depressed children and adults: A case-control study. Arch Gen Psychiatry. 2006 Aug;63(8):865-72. In these high-risk patients, antidepressant drug treatment does not seem to be related to suicide attempts and death in adults but might be related in children and adolescents. These findings support careful clinical monitoring during antidepressant drug treatment of severely depressed young people.) (Tiihonen J, et al. Antidepressants and the risk of **suicide**, attempted suicide, and overall mortality in a nationwide cohort. Arch Gen Psychiatry. 2006 Dec;63(12):1358-67. Among suicidal subjects who had ever used antidepressants, the current use of any antidepressant was associated with a markedly increased risk of attempted suicide and, at the same time, with a markedly decreased risk of completed suicide and death. Lower mortality was attributable to a decrease in cardiovascular- and cerebrovascular-related deaths during selective serotonin reuptake inhibitor use.) (Simon GE. The antidepressant quandary--considering suicide risk when treating adolescent depression. N Engl J Med. 2006 Dec 28;355(26):2722-3.)
(Bhatia SK, Bhatia SC. Childhood and adolescent depression. Am Fam Physician. 2007 Jan 1;75(1):73-80.) (Bridge JA, et al. Clinical response and risk for reported suicidal ideation and suicide attempts in pediatric antidepressant treatment: a meta-analysis of randomized controlled trials. JAMA. 2007 Apr 18;297(15):1683-96. Relative to placebo, antidepressants are efficacious for pediatric MDD, OCD, and non-OCD anxiety disorders, although the effects are strongest in non-OCD anxiety disorders, intermediate in OCD, and more modest in MDD. Benefits of antidepressants appear to be much greater than risks from suicidal ideation/suicide attempt across indications, although comparison of benefit to risk varies as a function of indication, age, chronicity, and study conditions.) (Gibbons RD, Brown CH, Hur K, Marcus SM, Bhaumik DK, Mann JJ. Relationship between antidepressants and suicide attempts: an analysis of the veterans health administration data sets. Am J Psychiatry. 2007 Jul;164(7):1044-9. These findings suggest that SSRI treatment has a **protective effect** in all adult age groups. They do not support the hypothesis that SSRI treatment places patients at greater risk of suicide.)
Gibbons RD, Brown CH, Hur K, et al. Early Evidence on the Effects of Regulators' Suicidality Warnings on SSRI Prescriptions and Suicide in Children and Adolescents. Am J Psychiatry. 2007 Sep;164(9):1356-63. In both the United States and the Netherlands, SSRI prescriptions for children and adolescents decreased after U.S. and European regulatory agencies issued warnings about a possible suicide risk with antidepressant use in pediatric patients, and these decreases were associated with increases in suicide rates in children and adolescents.
Hetrick S, Merry S, McKenzie J, Sindahl P, Proctor M. Selective serotonin reuptake inhibitors (SSRIs) for depressive disorders in children and adolescents. **Cochrane** Database Syst Rev. 2007 Jul 18;(3):CD004851. There was also evidence of an increased risk of suicidal ideation and behaviour for those prescribed SSRIs (RR 1.80, 95% CI 1.19 to 2.72). Fluoxetine was the only SSRI where there was consistent evidence from three trials that it was effective in reducing depression symptoms in both children and adolescents (CDRS-R treatment effect -5.63, 95% CI -7.38 to -3.88), and 'response' to treatment (RR 1.86, 95% CI 1.49 to 2.32). Where rates of adverse events were reported, this was higher for those prescribed SSRIs. While untreated depression is associated with the risk of completed suicide and impacts on functioning, it is unclear whether SSRIs would modify this risk in a clinically meaningful way. (Cheung AH, Zuckerbrot RA, Jensen PS, Ghalib K, Laraque D, Stein RE; GLAD-PC Steering Group. Guidelines for Adolescent Depression in Primary Care (GLAD-PC): II. Treatment and ongoing management. Pediatrics. 2007 Nov;120(5):e1313-26.)
Brent D, Emslie G, Clarke G, et al. Switching to another SSRI or to venlafaxine with or without cognitive behavioral therapy for adolescents with SSRI-resistant depression: the **TORDIA** randomized controlled trial.JAMA. 2008 Feb 27;299(8):901-13. For adolescents with depression not responding to an adequate initial treatment with an SSRI, the combination of cognitive behavioral therapy and a switch to another antidepressant resulted in a higher rate of clinical response than did a medication switch alone. However, a switch to another SSRI was just as efficacious as a switch to venlafaxine and resulted in fewer adverse effects.
Tsapakis EM, et al. Efficacy of antidepressants in juvenile depression: **meta-analysis**.. Br J Psychiatry. 2008 July:193;10-17. Antidepressants of all types showed limited efficacy in juvenile depression, but fluoxetine might be more effective, especially in adolescents. Studies in children & in severely depressed, hospitalised or suicidal juvenile patients are needed, and effective, safe and readily accessible treatments for juvenile depression are urgently required. This meta-analysis found that selective serotonin reuptake inhibitors (SSRIs) -- fluoxetine, in particular -- are modestly effective for depression in adolescents. Tricyclic antidepressants (TCAs) were not effective. Antidepressants were not effective in younger children. (LOE = 1a)
Wheeler BW, Gunnell D, Metcalfe C, Stephens P, Martin RM. The population impact on incidence of suicide and non-fatal self harm of regulatory action against the use of selective serotonin reuptake inhibitors in under 18s in the United Kingdom: ecological study. BMJ. 2008 Mar 8;336(7643):542-5. Epub 2008 Feb 14. The noticeable reduction in prescribing of antidepressants since regulatory action in 2003 to restrict the use of SSRIs in under 18s does not seem to have been associated with changes in suicidal behaviour in young people. Specifically, these data for England do not indicate that reductions in antidepressant use have led to an increase in suicidal behaviour.
Biddle L, Brock A, Brookes ST, Gunnell D. Suicide rates in young men in England and Wales in the 21st century: time trend study. BMJ. 2008 Mar 8;336(7643):539-42. Epub 2008 Feb 14. Suicide rates in young men have declined markedly in the past 10 years in England and Wales. Reductions in key risk factors for suicide, such as unemployment, might be contributing to lower rates.
Barbui C, Esposito E, Cipriani A. Selective serotonin reuptake inhibitors and risk of suicide: a systematic review of observational studies. CMAJ. 2009 Feb 3;180(3):291-7. Based on data from observational studies, use of SSRIs may be associated with a reduced risk of suicide in adults with depression. Among adolescents, use of SSRIs may increase suicidality.
Stone Marc, Laughren Thomas, Jones M Lisa, et al. Risk of suicidality in clinical trials of antidepressants in adults: analysis of proprietary data submitted to US Food and Drug Administration. BMJ 2009;339:b2880, doi: 10.1136/bmj.b2880 (Published 11 August 2009) Findings showed eight completed suicides, 134 suicide attempts, 10 patients who had made preparations without attempting suicide, and 378 patients who had thoughts about suicide but had not acted on them. These results suggest that, compared with placebo, the risks of suicidality associated with antidepressants are strongly age dependent - the risk is **raised in people under 25**, not affected in those aged 25-64, and reduced in those aged 65 and older, say the authors.
AACAP-Practice parameter on the use of **psychotropic medication in children and adolescents**. J Am Acad Child Adolesc Psychiatry. 2009 Sep;48(9):961-73.
Thapar Anita, Collishaw Stephan, Potter Robert, et al. Managing and preventing depression in **adolescents**. BMJ 2010;340:c209, doi: 10.1136/bmj.c209 (Published 22 January 2010)
Oberlander TF, Papsdorf M, Brain UM, Misri S, Ross C, Grunau RE. **Prenatal effects** of selective serotonin reuptake inhibitor antidepressants, serotonin transporter promoter genotype (SLC6A4), and maternal mood on child behavior at 3 years of age. Arch Pediatr Adolesc Med. 2010 May;164(5):444-51.
Schneeweiss S, Patrick AR, Solomon DH, et al. Variation in the risk of **suicide attempts** and completed suicides by antidepressant agent in **adults**: a propensity score-adjusted analysis of 9 years' data. Arch Gen Psychiatry. 2010 May;67(5):497-506.
Schneeweiss S, Patrick AR, Solomon DH, et al. Comparative Safety of Antidepressant Agents for Children and **Adolescents** Regarding **Suicidal** Acts. Pediatrics. 2010 Apr 12.
Thapar A, Collishaw S, Pine DS, Thapar AK. **Depression in adolescence**. Lancet. 2012 Feb 1.
Stallard P, Sayal K, Phillips R, et al. Classroom based **cognitive behavioural therapy** in reducing symptoms of depression in high risk adolescents: pragmatic cluster randomised controlled trial. BMJ. 2012 Oct 5;345:e6058.

Daphne J Korczak; **Canadian Paediatric Society**, Mental Health and Developmental Disabilities Committee. Use of **selective serotonin reuptake inhibitor** medications for the treatment of child and adolescent mental illness. Paediatr Child Health 2013;18:487-91. www.cps.ca/en/documents/position/use-of-SSRIs-for-child-adolescent-mental-illness (accessed Nov 12, 2013).
Lu CY, Zhang F, Lakoma MD, et al. Changes in **antidepressant use by young people and suicidal behavior after FDA warnings** and media coverage: quasi-experimental study. BMJ. 2014 Jun 18;348:g3596.
Grigoriadis S, Vonderporten EH, Mamisashvili L, et al. **Prenatal exposure to antidepressants and persistent pulmonary hypertension** of the newborn: systematic review and meta-analysis. BMJ. 2014 Jan 14
Grzeskowiak LE, Morrison JL, Henriksen TB, et al. **Prenatal antidepressant exposure and child behavioural outcomes** at 7 years of age: a study within the Danish National Birth Cohort. BJOG. 2016 Nov;123(12):1919-1928.
Yang A, Ciolino JD, Pinheiro E, et al. **Neonatal Discontinuation Syndrome in Serotonergic Antidepressant-Exposed Neonates**. J Clin Psychiatry. 2017 May;78(5):605-611.
Grove K, Lewis AJ, Galbally M. **Prenatal Antidepressant Exposure and Child Motor Development**: A Meta-analysis. Pediatrics. 2018 Jun 21.

[48] Treatment for Adolescents with Depression Study (**TADS**). **Fluoxetine**, Cognitive-Behavioral Therapy, & their Combination for Adolescents with Depression. JAMA. 2004 Aug 18;292(7):807-820. (Kennard B, Silva S, Vitiello B, et al. TADS Team. Remission and residual symptoms after short-term treatment in the Treatment of Adolescents with Depression Study (TADS). J Am Acad Child Adolesc Psychiatry. 2006 Dec;45(12):1404-11. The combination of FLX and CBT was superior to both monotherapy and PBO in terms of remission rates, but overall rates of remission remain low and residual symptoms are common at the end of 12 weeks of treatment.) (March JS, Silva S, Petrycki S, Curry J, Wells K, Fairbank J, Burns B, Domino M, McNulty S, Vitiello B, Severe J. The Treatment for Adolescents With Depression Study (TADS): long-term effectiveness and safety outcomes. Arch Gen Psychiatry. 2007 Oct;64(10):1132-43. In adolescents with moderate to severe depression, treatment with fluoxetine alone or in combination with CBT accelerates the response. Adding CBT to medication enhances the safety of medication. Taking benefits & harms into account, combined treatment appears superior to either monotherapy as a treatment for major depression in adolescents.)
Emslie GJ, Kennard BD, Mayes TL, et al. Fluoxetine Versus Placebo in Preventing Relapse of Major Depression in Children and Adolescents. Am J Psychiatry. 2008 Feb 15; [Epub ahead of print] Continuation treatment with fluoxetine was superior to placebo in preventing relapse and in increasing time to relapse in children and adolescents with major depression.
Goodyer I, Dubicka B, Wilkinson P, et al. Selective serotonin reuptake inhibitors (SSRIs) and routine specialist care with and without cognitive behaviour therapy in **adolescents** with major depression: randomised controlled trial. BMJ. 2007 Jul 21;335(7611):142. (**ADAPT**). For adolescents with moderate to severe major depression there is no evidence that the combination of CBT plus an SSRI in the presence of routine clinical care contributes to an improved outcome by 28 weeks compared with the provision of routine clinical care plus an SSRI alone.
Rohde P, Silva SG, Tonev ST, et al. Achievement and maintenance of sustained response during the Treatment for Adolescents With Depression Study continuation and maintenance therapy.Arch Gen Psychiatry. 2008 Apr;65(4):447-55. Most adolescents with depression who had not achieved sustained response during acute treatment did achieve that level of improvement during continuation and maintenance therapies. The possibility that CBT may help the subset of adolescents with depression who achieve early sustained response maintain their response warrants further investigation.
Hysinger EB, Callahan ST, Caples TL, et al. Suicidal Behavior Differs Among Early and Late Adolescents Treated With Antidepressant Agents. Pediatrics. 2011 Aug 8.
Clark M, Jansen K, and Cloy A. Treatment of Childhood and Adolescent Depression. Am Fam Physician. 2012;85(5):442-448.
Hetrick SE, McKenzie JE, Cox GR, et al. Newer generation antidepressants for depressive disorders in **children and adolescents**. Cochrane Database Syst Rev. 2012 Nov 14;11:CD004851. doi: 10.1002/14651858.CD004851.pub3. Caution is required in interpreting the results given the methodological limitations of the included trials in terms of internal and external validity. Further, the size and clinical meaningfulness of statistically significant results are uncertain. However, given the risks of untreated depression in terms of completed suicide and impacts on functioning, if a decision to use medication is agreed, then fluoxetine might be the medication of first choice given guideline recommendations. Clinicians need to keep in mind that there is evidence of an increased risk of suicide-related outcomes in those treated with antidepressant medications.
Kennard BD, Emslie GJ, Mayes TL, et al. Sequential treatment with **fluoxetine and relapse--prevention CBT to improve outcomes in pediatric depression**. Am J Psychiatry. 2014 Oct;171(10):1083-90.
Cipriani A, Zhou X, Del Giovane C, et al. Comparative effi cacy and tolerability of antidepressants for major depressive disorder in **children and adolescents: a network meta-analysis**. Lancet 2016; online June 8
MacQueen GM, Frey BN, Ismail Z, et al. Canadian Network for Mood and Anxiety Treatments (CANMAT) 2016 clinical guidelines for the management of adults with major depressive disorder: Section 6. **youth**, women, and the elderly. Can J Psychiatry. 2016;61(9):588-603.
Locher C, Koechlin H, Zion SR, et al. Efficacy and safety of selective serotonin reuptake inhibitors, serotonin-norepinephrine reuptake inhibitors, and placebo in common psychiatric disorders among children and adolescents: a systematic review and meta-analysis [online August 30, 2017]. JAMA Psychiatry. doi:10.1001/jamapsychiatry.2017.2432

[49] Pediatric OCD Treatment Study (POTS) Team. Cognitive-behavior therapy, sertraline, and their combination for children and adolescents with obsessive-compulsive disorder: the Pediatric OCD Treatment Study (POTS) randomized controlled trial. JAMA. 2004 Oct 27;292(16):1969-76.
Gibbons RD, Brown CH, Hur K, et al. **Suicidal** Thoughts & Behavior With Antidepressant Treatment: Reanalysis of the Randomized Placebo-Controlled Studies of **Fluoxetine and Venlafaxine**. Arch Gen Psychiatry. 2012 Feb 6
Lu CY, Zhang F, Lakoma MD, et al. Changes in **antidepressant use by young people and suicidal behavior after FDA warnings** and media coverage: quasi-experimental study. BMJ. 2014 Jun 18;348:g3596.
Sharma T, Guski LS, Freund N, et al. **Suicidality and aggression** during antidepressant treatment: systematic review and meta-analyses based on clinical study reports. BMJ 2016;352:i65. (especially in kids & adolescents)

[50] Paxil (Paroxetine) and Birth Defects Pharmacist's Letter October 2005. (First trimester: Paxil any malformations 4% vs ~3% general population; cardiac 2% vs ~1% general population ; most common cardiac malformation was ventricular septal defects) See also: Hallberg P, Sjoblom V. The use of selective serotonin reuptake inhibitors during pregnancy and breast-feeding: a review and clinical aspects. J Clin Psychopharmacol. 2005 Feb;25(1):59-73. & Health Canada warning Oct/05 http://www.hc-sc.gc.ca/dhp-mps/alt_formats/hpfb-dgpsa/pdf/medeff/paxil_3_hpc-cps_e.pdf (Preliminay report of retrospective epidemiological study of 3,581 pregnant women). Dec/05 Health Canada update http://www.hc-sc.gc.ca/dhp-mps/medeff/advisories-avis/prof/paxil_4_hpc-cps_e.html (An independent epidemiological study of delivery outcome following maternal use of SSRI antidepressants in early pregnancy has been conducted utilizing the Swedish national registry data (n=5,123 women). The findings show an approximate 2-fold increased risk of cardiac malformations in infants exposed to paroxetine, compared with the total registry population (approximately 2% incidence vs. 1%, respectively).) (Use of SSRIs During Pregnancy Pharmacist's Letter April 2006) **(ACOG** Publications: Committee Opinion No. 354: Treatment With **Selective Serotonin Reuptake Inhibitors** During **Pregnancy** Obstet Gynecol 2006 108: 1601-1604.) (Djulus J, Koren G, et al. Exposure to **Mirtazapine** During **Pregnancy**: A Prospective, Comparative Study of Birth Outcomes. J Clin Psychiatry. 2006 Aug;67(8):1280-1284. Mirtazapine does not appear to increase the baseline rate of major malformations of 1% to 3%. However, the higher number of spontaneous abortions in the antidepressant groups confirms the higher rates of spontaneous abortions in pregnant women taking antidepressant medications found in previous studies.) (Kristensen JH, et al. Transfer of the antidepressant **mirtazapine** into **breast milk**. Br J Clin Pharmacol. 2006 Sep 13; [Epub ahead of print] Results Mean (95% confidence interval) relative infant doses for mirtazapine and desmethylmirtazapine (n = 8) were 1.5% (0.8, 2.2) and 0.4% (0.2, 0.6) respectively.) (Thormahlen GM. **Paroxetine** Use During **Pregnancy**: Is it Safe? (October). Ann Pharmacother. 2006 Aug 22; [Epub ahead of print]) (Wogelius P, et al. Maternal Use of Selective **Serotonin Reuptake Inhibitors** and Risk of **Congenital Malformations**. Epidemiology. 2006 Nov;17(6):701-704. The 150,780 women with no SSRI prescriptions gave birth to 5112 (3.4%) children with congenital malformations. The 1051 women with SSRI prescriptions any time during early pregnancy gave birth to 51 (4.9%) children with congenital malformations.)
Einarson A, Pistelli A, Desantis M, Malm H, Paulus WD, Panchaud A, Kennedy D, Einarson TR, Koren G. Evaluation of the Risk of Congenital Cardiovascular Defects Associated With Use of Paroxetine During Pregnancy. Am J Psychiatry. 2008 Apr 1; [Epub ahead of print] Paroxetine does not appear to be associated with an increased risk of cardiovascular defects following use in early pregnancy, as the incidence in more than 3,000 infants was well within the population incidence of approximately 1%.
Bakker MK, Kölling P, van den Berg PB, de Walle HE, et al. Increase in use of selective serotonin reuptake inhibitors in pregnancy during the last decade, a population-based cohort study from the Netherlands. Br J Clin Pharmacol. 2008 Apr;65(4):600-6. Epub 2007 Oct 22.
Medical Letter Nov 17, 2008. Safety of SSRIs in Pregnancy.
American College of Obstetricians and Gynecologists (**ACOG**). Use of psychiatric medications during **pregnancy and lactation**. Washington (DC): American College of Obstetricians and Gynecologists (ACOG); 2008 Apr. 20 p. (ACOG practice bulletin; no. 92). [245 references]
Einarson A, Choi J, Einarson TR, Koren G. Incidence of major malformations in infants following antidepressant exposure in pregnancy: results of a large prospective cohort study. Can J Psychiatry. 2009 Apr;54(4):242-6. As a group, antidepressant use in the first trimester of pregnancy is not associated with an increased risk for major malformation above the baseline. In addition, no individual antidepressant was associated with an increased risk of a specific malformation.
Einarson A. **Paroxetine** use in pregnancy and increased risk of heart defects: Evaluating the evidence. Can Fam Physician. 2010 Aug;56(8):767-8.
Hirst KP, Moutier CY. **Postpartum major depression**. Am Fam Physician. 2010 Oct 15;82(8):926-33.
Grote NK, Bridge JA, Gavin AR, et al. A meta-analysis of depression during pregnancy and the risk of **preterm birth, low birth weight**, and intrauterine growth restriction. Arch Gen Psychiatry. 2010 Oct;67(10):1012-24.
Patel BN, Beste J, Blackwell JC. **Antidepressant use during pregnancy**. Am Fam Physician. 2011 May 15;83(10):1211-5.

Malm H, Artama M, Gissler M, Ritvanen A. Selective serotonin reuptake inhibitors and risk for major congenital anomalies. Obstet Gynecol. 2011 Jul;118(1):111-20.
Stewart DE. Clinical practice. **Depression during Pregnancy**. N Engl J Med. 2011 Oct 27;365(17):1605-11.
Croen LA et al. Antidepressant use during pregnancy and childhood **autism spectrum disorders**. Arch Gen Psychiatry 2011 Jul 4.
Jefferies AL; Canadian Paediatric Society, Fetus and Newborn Committee. **Selective serotonin reuptake inhibitors in pregnancy** and infant outcomes. Paediatr Child Health 2011;16(9):562. http://www.cps.ca/english/statements/FN/fn11-02.pdf
De Vera MA, Bérard A. Antidepressant Use During Pregnancy and the Risk of Pregnancy Induced Hypertension. Br J Clin Pharmacol. 2012 Mar 21.
Koren G, Nordeng H. **Antidepressant use during pregnancy**: the benefit-risk ratio. Am J Obstet Gynecol. 2012 Feb 21.
El Marroun H, Jaddoe VW, Hudziak JJ, et al. Maternal Use of Selective Serotonin Reuptake Inhibitors, Fetal Growth, and Risk of Adverse Birth Outcomes. Arch Gen Psychiatry. 2012 Mar 5.
Stephansson O, Kieler H, Haglund B, et al. Selective serotonin reuptake inhibitors during pregnancy and risk of **stillbirth** and infant mortality. JAMA. 2013 Jan 2;309(1):48-54.
Wisner KL, Bogen DL, Sit D, McShea M, et al. Does Fetal Exposure to SSRIs or Maternal Depression Impact Infant Growth? Am J Psychiatry. 2013 Mar 20.
Dennis CL, Dowswell T. Psychosocial and psychological interventions for preventing postpartum depression. Cochrane Database Syst Rev. 2013 Feb 28;2:CD001134. doi: 10.1002/14651858.CD001134.pub3. Overall, psychosocial and psychological interventions significantly reduce the number of women who develop postpartum depression. Promising interventions include the provision of intensive, professionally-based postpartum home visits, telephone-based peer support, and interpersonal psychotherapy.
Rai D, Lee BK, Dalman C, et al. **Parental depression, maternal antidepressant use during pregnancy, and risk of autism** spectrum disorders: population based case-control study. BMJ. 2013 Apr 19;346:f2059.
Grigoriadis S, VonderPorten EH, Mamisashvili L, et al. **Antidepressant exposure** during pregnancy and congenital malformations: is there an association? A systematic review and meta-analysis of the best evidence. J Clin Psychiatry 2013;74:e293–308.
Grigoriadis S, VonderPorten EH, Mamisashvili L, et al. The effect of **prenatal antidepressant exposure** on neonatal adaptation: a systematic review and meta-analysis. J Clin Psychiatry 2013;74:e309–20.
Myles N, Newall H, Ward H, Large M. Systematic meta-analysis of individual **selective serotonin reuptake inhibitor** medications and **congenital malformations**. Aust N Z J Psychiatry. 2013 Nov;47(11):1002-12.
Harrington RA, Lee LC, Crum RM, et al. **Prenatal SSRI** Use and Offspring With **Autism** Spectrum Disorder or Developmental Delay. Pediatrics. 2014 Apr 14.
Barbui C, Ostuzzi G. Beneficial and harmful consequences of prepartum and postpartum antidepressant exposure. Evid Based Ment Health. 2014 Aug;17(3):69-71.
Andersen JT, Andersen NL, Horwitz H, et al. Exposure to **Selective Serotonin Reuptake Inhibitors in Early Pregnancy and the Risk of Miscarriage**. Obstet Gynecol. 2014 Sep 5.
McDonagh MS, Matthews A, Phillipi C, et al. **Depression Drug Treatment Outcomes in Pregnancy and the Postpartum Period**: A Systematic Review and Meta-analysis. Obstet Gynecol. 2014 Sep;124(3):526-34.
Weissman MM et al. Treatment of **maternal depression in a medication** clinical trial and its effect on children. Am J Psychiatry 2015 Jan 23.
Ejaz R, Leibson T, Koren G. **Selective serotonin reuptake inhibitor discontinuation during pregnancy**: at what risk? Can Fam Physician. 2014 Dec;60(12):1105-6.
Furu K, Kieler H, Haglund B, et al. **Selective serotonin reuptake inhibitors and venlafaxine in early pregnancy** and risk of birth defects: population based cohort study and sibling design. BMJ. 2015 Apr 17;350:h1798.
Brandlistuen RE et al. **Behavioural effects of fetal antidepressant exposure** in a Norwegian cohort of discordant siblings. Int J Epidemiol 2015 Apr 14.
Huybrechts KF, Bateman BT, Palmsten K, et al. Antidepressant use late in pregnancy and risk of **persistent pulmonary hypertension** of the newborn. JAMA. 2015 Jun 2;313(21):2142-51.
Molyneaux E, Trevillion K, Howard LM. Antidepressant treatment for **postnatal depression**. JAMA. 2015 May 19;313(19):1965-6.
Reefhuis J, Devine O, Friedman JM, et al; National Birth Defects Prevention Study. Specific **SSRIs and birth defects**: bayesian analysis to interpret new data in the context of previous reports. BMJ. 2015 Jul 8;351:h3190.
Berard A, Zhao JP, Sheehy O. **Sertraline use during pregnancy** and the risk of major malformations. Am J Obstet Gynecol. 2015 Jun;212(6):795.e1-795.e12.
Malm H, Sourander A, Gissler M, et al. **Pregnancy Complications Following Prenatal Exposure to SSRIs** or Maternal Psychiatric Disorders: Results From Population-Based National Register Data. Am J Psychiatry. 2015 Aug 4
Boukhris T, Sheehy O, Mottron L, et al. Antidepressant Use During Pregnancy and the Risk of **Autism Spectrum Disorder** in Children. JAMA Pediatr. 2015 Dec 14:1-8.
Hanley GE, Smolina K, Mintzes B, et al. **Postpartum Hemorrhage and Use of Serotonin Reuptake Inhibitor Antidepressants in Pregnancy.** Obstet Gynecol. 2016 Mar;127(3):553-61.
Brown AS, Gyllenberg D, Malm H, et al. Association of **selective serotonin reuptake inhibitor** exposure during pregnancy with **speech**, scholastic, and motor **disorders** in offspring [online Oct 12, 2016].JAMA Psychiatry. doi:10.1001/jamapsychiatry.2016.2594
Shen ZQ, Gao SY, Li SX, et al. **Sertraline** use in the **first trimester and risk of congenital anomalies**: a systemic review and meta-analysis of cohort studies. Br J Clin Pharmacol. 2016 Oct 22.
Eke AC, Saccone G, Berghella V. **Selective serotonin reuptake inhibitor (SSRI) use during pregnancy** and **risk of preterm birth**: a systematic review and meta-analysis. BJOG. 2016 Nov;123(12):1900-1907.
Jordan S, Morris JK, Davies GI, et al. **Selective Serotonin Reuptake Inhibitor (SSRI)** Antidepressants in Pregnancy and **Congenital Anomalies**: Analysis of Linked Databases in Wales, Norway and Funen, Denmark. PLoS One. 2016 Dec 1;11(12):e0165122.
Bérard A, et al. **Antidepressant use during pregnancy** and the risk of major congenital malformations in a cohort of depressed pregnant women: updated analysis of Quebec Pregnancy Cohort. BMJ Open. 2017Jan 12;7(1):e013372.
Nembhard WN, et al. Maternal and infant genetic variants, **maternal periconceptional use of selective serotonin reuptake inhibitors**, and risk of congenital heart defects in offspring: population based study. BMJ. 2017 Mar 6;356:j832.
Brown HK, Ray JG, Wilton AS, et al. Association between **serotonergic antidepressant use during pregnancy and autism spectrum disorder** in children.JAMA. doi:10.1001 /jama.2017.3415
King BH. Association Between Maternal Use of **SSRI Medications and Autism** in Their Children. JAMA. 2017 Apr 18;317(15):1568-1569
Mezzacappa A, Lasica PA, Gianfagna F, et al. Risk for **Autism Spectrum Disorders According to Period of Prenatal Antidepressant Exposure**: A Systematic Review and Meta-analysis. JAMA Pediatr. 2017 Apr 17.
Sujan AC, Rickert ME, Öberg AS, et al. Associations of **maternal antidepressant use during the first trimester of pregnancy** with preterm birth, small for gestational age, **autism** spectrum disorder, and attention-deficit/hyperactivity disorder in offspring. JAMA. doi:10.1001/jama.2017.3413
Gao SY, Wu QJ, Zhang TN, et al. **Fluoxetine and congenital malformations**: a systematic review and meta-analysis of cohort studies. Br J Clin Pharmacol. 2017 May 17
Man KKC, Chan EW, Ip P, et al. **Prenatal antidepressant use and risk of attention-deficit/hyperactivity disorder** in offspring: population based cohort study. BMJ 2017;357:j2350.
Grigoriadis S, Vonderporten EH, Mamisashvili L, et al. **Prenatal exposure to antidepressants and persistent pulmonary hypertension** of the newborn: systematic review and meta-analysis. BMJ. 2014 Jan 14
Grzeskowiak LE, Morrison JL, Henriksen TB, et al. **Prenatal antidepressant exposure and child behavioural outcomes** at 7 years of age: a study within the Danish National Birth Cohort. BJOG. 2016 Nov;123(12):1919-1928.
Yang A, Ciolino JD, Pinheiro E, et al. **Neonatal Discontinuation Syndrome in Serotonergic Antidepressant-Exposed Neonates**. J Clin Psychiatry. 2017 May;78(5):605-611.
Petersen I, Peltola T, Kaski S, et al. Depression, **depressive symptoms and treatments in women who have recently given birth**: UK cohort study. BMJ Open. 2018 Oct 8(10):e022152
USPSTF: Curry SJ, Krist AH, Owens DK, et al. **Interventions to Prevent Perinatal Depression**: US Preventive Services Task Force Recommendation Statement. JAMA. 2019 Feb 12;321(6):580-587.
USPSTF: O'Connor E, Senger CA, Henninger ML, et al. **Interventions to Prevent Perinatal Depression**: Evidence Report and Systematic Review for the US Preventive Services Task Force. JAMA. 2019 Feb 12;321(6):588-601.
Johansen SL, Robakis TK, Williams KE, Rasgon NL. Management of **perinatal depression with non-drug interventions**. BMJ. 2019 Feb 25;364:l322
Buck K, Zekri S, Nguyen L, Ogar UJ. **Cognitive Behavior Therapy** for Postpartum Depression. Am Fam Physician. 2019 Aug 15;100(4):244-245.
Kirby N, Kilsby A, Walker R. Assessing low mood during pregnancy. BMJ. 2019 Jul 29;366:l4584.
Ngai FW, Wong PC, Chung KF, et al. Effect of couple-based cognitive behavioural intervention on prevention of postnatal depression: multisite randomised controlled trial. BJOG. 2019 Jul 7.

[51] Kulin AK, Pastuszak A, Sage SR, et.al. Pregnancy outcome following maternal use of the new selective serotonin reuptake inhibitors: a prospective controlled multicenter study. JAMA 1998;279:609-610.

Briggs GG, Freeman RK, Yaffe SJ. Drugs in Pregnancy and Lactation 9th Ed. Williams & Wilkins, Media, Pennsilvania, 2011.
Loughhead AM, et al. Antidepressants in **Amniotic Fluid**: Another Route of Fetal Exposure. Am J Psychiatry. 2006 Jan;163(1):145-147.
Simon GE, Cunningham ML, Davis RL. Outcomes of prenatal antidepressant exposure. Am J Psychiatry. 2002 Dec;159(12):2055-61.
Ward RK, Zamorski MA. Benefits and risks of psychiatric medications during pregnancy. Am Fam Physician. 2002 Aug 15;66(4):629-36. (Cohen LS, et al. Relapse of major depression during **pregnancy** in women who maintain or discontinue antidepressant treatment. JAMA. 2006 Feb 1;295(5):499-507. CONCLUSIONS: Pregnancy is not "protective" with respect to risk of relapse of major depression. Women with histories of depression who are euthymic in the context of ongoing

antidepressant therapy should be aware of the association of depressive relapse during pregnancy with antidepressant discontinuation. (InfoPOEMs: Nearly 50% of women currently receiving antidepressant medication will experience a relapse of major depression during pregnancy. The risk is highest for those discontinuing their medication (68% relapse rate). It is likely that this study sample consists of patients with a higher severity of illness than those found in a routine community practice, so the findings may not generalize to other settings. (LOE = 1b))) {Wen SW, et al. Selective serotonin reuptake inhibitors and adverse pregnancy outcomes. Am J Obstet Gynecol. 2006 Apr;194(4):961-6. (InfoPOEMs: The use of selective serotonin reuptake inhibitors (SSRIs) in the year before giving birth is associated with increased risk of prematurity, fetal death, and neonatal seizures. However, these observational data are weakened by the need to make difficult adjustments for other important factors thought to be causally related to the outcomes studied, such as poverty and drug dependence. (LOE = 2b) }

Altshuler LL, Cohen LS, Moline ML, et al. Expert Consensus Panel for Depression in Women. The Expert Consensus Guideline Series. Treatment of depression in women. Postgrad Med. 2001 Mar;(Spec No):1-107.

Nordeng H, Spigset O. Treatment with selective serotonin reuptake inhibitors in the third trimester of pregnancy: effects on the infant. Drug Saf. 2005;28(7):565-81.

Sivojelezova A, Shuhaiber S, Sarkissian L, et al. **Citalopram** use in pregnancy: prospective comparative evaluation of pregnancy and fetal outcome. Am J Obstet Gynecol. 2005 Dec;193(6):2004-9. InfoPOEMs: Citalopram (Celexa) does not appear to be teratogenic. Exposure near the time of birth, however, was associated with increased risk of a diagnosis of fetal distress in labor and neonatal admission to special care nursery. (LOE = 1b))

O'Keane V, Marsh MS. Depression during pregnancy. BMJ. 2007 May 12;334(7601):1003-5.

Alwan S et al. Use of selective serotonin- reuptake inhibitors in pregnancy and the risk of birth defects. N Engl J Med 2007Jun 28; 356:2684-92.)

Louik C et al. First-trimester use of selective serotonin-reuptake inhibitors and the risk of birth defects. N Engl J Med 2007 Jun 28; 356:2675-83.)

Dietz PM, Williams SB, Callaghan WM, Bachman DJ, Whitlock EP, Hornbrook MC. Clinically identified maternal depression before, during, and after pregnancies ending in live births. Am J Psychiatry. 2007 Oct;164(10):1515-20. n=4398. Among 4,398 continuously enrolled women with eligible pregnancies ending in live births, 678 (15.4%) had depression identified during at least one pregnancy phase; 8.7%, 6.9%, and 10.4% had depression identified before, during, and/or after pregnancy, respectively. Approximately one in seven women was identified with and treated for depression during 39 weeks before through 39 weeks after pregnancy, and more than half of these women had recurring indicators for depression.)

Toh S, Mitchell AA, Louik C, Werler MM, Chambers CD, Hernández-Díaz S. Selective Serotonin Reuptake Inhibitor Use and **Risk of Gestational Hypertension**. Am J Psychiatry. 2009 Jan 2. [Epub ahead of print] SSRI exposure during late pregnancy-whether a causal factor or not-might identify women who are at an increased risk for gestational hypertension and preeclampsia. Further investigation is needed in order to separate the effects of treatment with SSRIs from those of underlying mood disorders.

Yonkers KA, Wisner KL, Stewart DE, et al. The management of depression during pregnancy: a report from the American Psychiatric Association (**APA**) and the American College of Obstetricians and Gynecologists (**ACOG**). Gen Hosp Psychiatry. 2009 Sep-Oct;31(5):403-13.

Tuccori M, Testi A, et al.Safety concerns associated with the use of serotonin reuptake inhibitors and other serotonergic/noradrenergic antidepressants during pregnancy: a review. Clin Ther. 2009 Jun;31(Pt 1):1426-53.

Pedersen Lars Henning, Henriksen Tine Brink, Vestergaard Mogens, et al. Selective serotonin reuptake inhibitors in pregnancy and congenital malformations: population based cohort study. BMJ 2009;339:b3569, doi: 10.1136/bmj.b3569 (Published 23 September 2009) There is an increased prevalence of **septal heart defects** among children whose mothers were prescribed an SSRI in early pregnancy, particularly sertraline and citalopram. The largest association was found for children of women who redeemed prescriptions for more than one type of SSRI.

Briggs GG, Ambrose PJ, Ilett KF, Hackett LP, Nageotte MP, Padilla G. Use of Duloxetine in Pregnancy and Lactation (November). Ann Pharmacother. 2009 Oct 6.

Pedersen LH, Henriksen TB, Olsen J. **Fetal Exposure** to Antidepressants and Normal Milestone Development at 6 and 19 Months of Age. Pediatrics. 2010 Feb 22.

Nakhai-Pour HR, Broy P, Bérard A. Use of antidepressants during pregnancy and the risk of **spontaneous abortion**. CMAJ. 2010 May 31.

Croen Lisa A.; Grether Judith K.; Yoshida Cathleen K.; et al. Antidepressant Use During Pregnancy and Childhood **Autism Spectrum Disorders**. Arch Gen Psychiatry. 2011;0(2011):archgenpsychiatry.2011.73.

Patil AS, Kuller JA, Rhee EH. Antidepressants in pregnancy: a review of commonly prescribed medications. Obstet Gynecol Surv. 2011 Dec;66(12):777-87.

Jimenez-Solem E, Andersen JT, Petersen M, et al. SSRI Use During Pregnancy and Risk of **Stillbirth and Neonatal Mortality**. Am J Psychiatry. 2013 Jan 30.

[52] Emilio J Sanz, Carlos et al. Selective serotonin reuptake inhibitors in pregnant women and neonatal withdrawal syndrome: a database analysis Lancet 2005; 365: 482-87 **& ALSO** Moses-Kolko EL, Bogen D, Perel J, et al. Neonatal signs after late in utero exposure to serotonin reuptake inhibitors: literature review and implications for clinical applications. JAMA. 2005 May 18;293(19):2372-83.(InfoPOEMs: Late third trimester exposure to maternal use of SSRIs increases the risk of neonatal behavioral abnormalities. Since the symptoms and signs were relatively benign and short lived, it makes sense to individualize the risks and benefits of continuing SSRI treatment throughout pregnancy. (LOE = 2a-)) (Levinson-Castiel R, Merlob P, Linder N, Sirota L, Klinger G. Neonatal abstinence syndrome after in utero exposure to selective serotonin reuptake inhibitors in term infants. Arch Pediatr Adolesc Med. 2006 Feb;160(2):173-6.) (Oberlander TF, et al. **Neonatal outcomes** after prenatal exposure to selective serotonin reuptake inhibitor antidepressants and maternal depression using population-based linked health data. Arch Gen Psychiatry. 2006 Aug;63(8):898-906. With linked population health data and propensity score matching, prenatal SE-D exposure was associated with an increased risk of low birth weight and respiratory distress, even when maternal illness severity was accounted for.)

Lund N, Pedersen LH, Henriksen TB. Selective serotonin reuptake inhibitor exposure in utero and pregnancy outcomes. Arch Pediatr Adolesc Med. 2009 Oct;163(10):949-54.

Hudak ML, Tan RC et al. **Neonatal Drug Withdrawal**. Pediatrics. 2012 Jan 30.

[53] Chambers CD, et al. Selective serotonin-reuptake inhibitors and risk of persistent **pulmonary hypertension** of the newborn. N Engl J Med. 2006 Feb 9;354(6):579-87. (InfoPOEMs: The use of selective serotonin-reuptake inhibitors (SSRIs) during the second half of pregnancy is associated with an increased risk of persistent pulmonary hypertension of the newborn (PPHN). This type of study cannot establish causation, untreated depression is a serious condition, and 99% of women would give birth to infants unaffected by PPHN, so the potential benefits and harms of continuing SSRIs in these patients should be carefully weighed. (LOE = 3b)) Health Canada Mar/06 warning http://www.hc-sc.gc.ca/ahc-asc/media/advisories-avis/2006/2006_11_e.html

FDA Dec/11 notified healthcare professionals and the public on the use of selective serotonin reuptake inhibitor (SSRI) antidepressants by women during pregnancy and the potential risk of a rare heart and lung condition known as **Persistent Pulmonary Hypertension of the Newborn** (PPHN). FDA has reviewed the additional new study results and has concluded that, given the conflicting results from different studies, it is premature to reach any conclusion about a possible link between SSRI use in pregnancy and PPHN.

Kieler H, Artama M, Engeland A, et al. Selective serotonin reuptake inhibitors during pregnancy and risk of persistent **pulmonary hypertension** in the newborn: population based cohort study from five Nordic countries. BMJ 2012;344:d8012.

Occhiogrosso M, Omran SS, Altemus M: **Persistent pulmonary hypertension** of the newborn and selective serotonin reuptake inhibitors: lessons from clinical and translational studies. Am J Psychiatry 2012;169:134–140

Grigoriadis S, Vonderporten EH, Mamisashvili L, et al. **Prenatal exposure to antidepressants and persistent pulmonary hypertension** of the newborn: systematic review and meta-analysis. BMJ. 2014 Jan 14

Bérard A, Sheehy O, Zhao JP, et al. **SSRI and SNRI** use during pregnancy and the risk of **persistent pulmonary hypertension** of the newborn. Br J Clin Pharmacol. 2016 Nov 22.

Eke AC, Saccone G, Berghella V. **Selective serotonin reuptake inhibitor (SSRI) use during pregnancy** and **risk of preterm birth**: a systematic review and meta-analysis. BJOG. 2016 Nov;123(12):1900-1907.

Yang F, Liang H, Chen J, et al. **Prenatal Paternal Selective Serotonin Reuptake Inhibitors Use and Risk of ADHD** in Offspring. Pediatrics. 2017 Dec 11.

[54] Misri S, Burgmann A, Kostaras D. Are SSRIs safe for pregnant and breastfeeding women? Can Fam Physician. 2000 Mar;46:626-8, 631-3.

Spencer JP, Gonzalez LS 3rd, Barnhart DJ. Medications in the breast-feeding mother. Am Fam Physician. 2001 Jul 1;64(1):119-26.

Wisner KL, Parry BL, Piontek CM. Clinical practice. **Postpartum depression**. N Engl J Med. 2002 Jul 18;347(3):194-9. (Wisner KL, et al. Postpartum depression: a randomized trial of sertraline versus nortriptyline. J Clin Psychopharmacol. 2006 Aug;26(4):353-60. n=95 24week Times to response and remission also did not differ. Breast-fed infant serum levels were near or below the level of quantifiability for both agents.)

Altshuler LL, Cohen LS, Moline ML, Kahn DA, et al; Expert Consensus Panel for Depression in Women. The Expert Consensus Guideline Series. Treatment of depression in women. Postgrad Med. 2001 Mar;(Spec No):1-107.

Fortinguerra, Filomena, Clavenna, Antonio, Bonati, Maurizio. Psychotropic Drug Use During **Breastfeeding**: A Review of the Evidence. Pediatrics 2009 124: e547-e556.

Ng RC, Hirata CK, Yeung W, Haller E, Finley PR. Pharmacologic treatment for postpartum depression: a systematic review. Pharmacotherapy. 2010 Sep;30(9):928-41.

Academy of Breastfeeding Medicine Protocol Committee. ABM clinical protocol #18: use of antidepressants in nursing mothers. [Internet] Breastfeed Med 2008 Mar; [cited 2011 Feb 14] (1):44-52. Summary available from: http://www.guideline.gov/content.aspx?id=13409&search=antidepressants

American College of Obstetricians and Gynecologists (ACOG). Use of psychiatric medications during pregnancy and lactation. [Internet] Washington (DC): American College of Obstetricians and Gynecologiscs (ACOG); 2008 Apr. [cited 2011 Feb 14] (ACOG practice bulletin; no. 92). Summary available from: http://www.guideline.gov/content.aspx?id=12490

CG45 Antenatal and postnatal mental health: full guideline [Internet]. London: National Institute for Clinical Excellence; 2007 Apr 24 [cited 2011 Feb 14]. Available from: http://www.nice.org.uk/nicemedia/live/11004/30431/30431.pdf *See: Management of depression, page 10 and Chapter 7: Pharmacological Treatment of Mental disorders in Pregnant and Breastfeeding Women.*

Neuman G, Colantonio D, Delaney S, et al. **Bupropion and Escitalopram During Lactation**. Ann Pharmacother. 2014 Apr 14;48(7):928-931.

[55] Skowron DM, Stimmel GL. Antidepressants and the risk of seizures. Pharmacotherapy 1992;12(1):18-22.

[56] **Clinical Guidelines** for the Treatment of Depressive Disorders. The Canadian Journal of Psychiatry June 2001.

(Prescribing Antidepressants for Depression in **2005**: Recent Concerns & Recommendations http://www.cpa-apc.org/Publications/Position_Papers/2004-23s-en.pdf)

Patten SB, Kennedy SH, Lam RW, et al. Canadian Network for Mood and Anxiety Treatments (CANMAT) Clinical Guidelines for the Management of Major Depressive Disorder in Adults. I. **Classification, Burden and Principles of Management**. J Affect Disord. 2009 Aug 10. [Epub ahead of print]

Parikh SV, Sega ZV, Grigoriadis S, et al. Canadian Network for Mood and Anxiety Treatments (CANMAT) clinical guidelines for the management of major depressive disorder in adults. II. **Psychotherapy** alone or in combination with antidepressant medication. J Affect Disord. 2009 Aug 12. [Epub ahead of print] CBT and IPT are the only first-line treatment recommendations for acute MDD and remain highly recommended for maintenance. Both computer-based and telephone-delivered psychotherapy-primarily studied with CBT and IPT-are useful second-line recommendations.

Lam RW, Kennedy SH, Grigoriadis S, McIntyre RS, Milev R, Ramasubbu R, Parikh SV, Patten SB, Ravindran AV. **Canadian Network for Mood and Anxiety Treatments** (**CANMAT**) clinical guidelines for the management of major depressive disorder in adults. III. **Pharmacotherapy**. J Affect Disord. 2009 Aug 10. [Epub ahead of print]

Kennedy SH, Milev R, Giacobbe P, et al. Canadian Network for Mood and Anxiety Treatments (CANMAT) clinical guidelines for the management of major depressive disorder in adults. IV. **Neurostimulation** therapies. J Affect Disord. 2009 Aug 4. [Epub ahead of print] There is most evidence to support ECT as a first-line treatment under specific circumstances and rTMS as a second-line treatment. Evidence to support VNS is less robust and DBS remains an investigational treatment.

Ravindran AV, Lam RW, Filteau MJ, et al. Canadian Network for Mood and Anxiety Treatments (CANMAT) clinical guidelines for the management of major depressive disorder in adults. V. **Complementary and alternative** medicine treatments. J Affect Disord. 2009 Aug 8. [Epub ahead of print] There is Level 1 evidence to support light therapy in seasonal MDD and St. John's wort in mild to moderate MDD. There is also some evidence for the use of exercise, yoga and sleep deprivation, as well as for omega-3 fatty acids and SAM-e (but with some potential safety concerns with the latter).

Tess AV, Smetana GW. Medical evaluation of patients undergoing **electroconvulsive** therapy. N Engl J Med. 2009 Apr 2;360(14):1437-44.

APA 2010: Practice Guidelines for Treatment of **Major Depressive Disorder** - American Psychiatric Association http://www.psych.org/guidelines/mdd2010

Kellner CH, Greenberg RM, Murrough JW, et al. ECT in Treatment-Resistant Depression. Am J Psychiatry. 2012 Dec 1;169(12):1238-44.

Lam RW, McIntosh D, Wang J, et al. Canadian Network for Mood and Anxiety Treatments (**CANMAT) 2016** clinical guidelines for the management of adults with major depressive disorder: Section 1. **disease burden** and **principles** of care. Can J Psychiatry. 2016;61(9):510-523.

Parikh SV, Quilty LC, Ravitz P, et al. Canadian Network for Mood and Anxiety Treatments **(CANMAT) 2016** clinical guidelines for the management of adults with major depressive disorder: Section 2. **psychological** treatments. Can J Psychiatry. 2016;61(9):524-539.

Kennedy SH, Lam RW, McIntyre RS, et al. Canadian Network for Mood and Anxiety Treatments (**CANMAT) 2016** clinical guidelines for the management of adults with major depressive disorder: Section 3. **pharmacological** treatments. Can J Psychiatry. 2016;61(9):540-560.

Milev RV, Giacobbe P, Kennedy SH, et al. Canadian Network for Mood and Anxiety Treatments (**CANMAT) 2016** clinical guidelines for the management of adults with major depressive disorder: Section 4. **neurostimulation** treatments. Can J Psychiatry. 2016;61(9):561-575.

Ravindran AV, Balneaves LG, Faulkner G, et al. Canadian Network for Mood and Anxiety Treatments (**CANMAT) 2016** clinical guidelines for the management of adults with major depressive disorder: Section 5. **complementary and alternative medicine** treatments. Can J Psychiatry. 2016;61(9): 576-587.

MacQueen GM, Frey BN, Ismail Z, et al. Canadian Network for Mood and Anxiety Treatments (**CANMAT) 2016** clinical guidelines for the management of adults with major depressive disorder: Section 6. **youth, women, and the elderly**. Can J Psychiatry. 2016;61(9):588-603.

[57] Clinically significant drug interactions with antidepressants in the elderly. Spina E, Scordo MG. Drugs Aging 2002;19(4):299-320.

[59] Bezchlibnyk-Butler KZ. Clinical Handbook of Psychotropic Drugs, 22nd Ed. 22nd Editors: Procyshyn RM, Bezchlibnyk-Butler KZ, Jeffries JJ. Hogrefe Publishing, Massachusetts, 2017.

[60] Duma A, Maleczek M, Panjikaran B, et al. Major Adverse **Cardiac Events and Mortality Associated with Electroconvulsive Therapy**: A Systematic Review and Meta-analysis. Anesthesiology. 2019 Jan;130(1):83-91.

Grindrod K, Kellar J, University of Waterloo School of Pharmacy. Serotonin Syndrome Made Simple. https://www.youtube.com/watch?v=sQ5rwuVP8Kc. Accessed Aug 18, 2017.

Sackeim HA. Modern Electroconvulsive Therapy: Vastly Improved yet Greatly Underused. JAMA Psychiatry. 2017 Aug 1;74(8):779-780.

Slade EP, Jahn DR, Regenold WT, Case BG. Association of Electroconvulsive Therapy With Psychiatric Readmissions in US Hospitals. JAMA Psychiatry. 2017 Aug 1;74(8):798-804.

Ross EL, Zivin K, Maixner DF. Cost-effectiveness of Electroconvulsive Therapy vs Pharmacotherapy/Psychotherapy for Treatment-Resistant Depression in the United States. JAMA Psychiatry. 2018 May 9.

[61] **New Drug: Viibryd (Vilazodone).** Pharmacist's Letter. May 2018.

Choosing and Switching Antidepressants. Pharmacist's Letter. June. 2018.

Kennedy SH, Lam RW, McIntyre RS, et al. **Canadian Network for Mood and Anxiety Treatments (CANMET) 2016 clinical guidelines for the management of adults with major depressive disorder. Section 3. Pharmacological treatments.** Can J Psychiatry 2016;61:540-60.

Hellerstein DJ, Flaxer J. **Vilazodone for the treatment of major depressive disorder: an evidence-based review of its place in therapy.** Core Evid 2015;10:49-62.

Alvarez E, Perez V, Artigas F. Pharmacology and clinical potential of vortioxetine in the treatment of major depressive disorder. Neuropsychiatr Dis Treat 2014;10:1297-307.

Product monograph for *Trintellix*. Lundbeck Canada Inc. Montreal, QC H3B 4W5. October 2014

McIntyre RS, Lophaven S, Olsen CK. **A randomized, double-blind, placebo-controlled study of vortioxetine on cognitive function in depressed adults.** Int J Neuropsychopharmacol 2014;17:1557-67.

[62] Berhan Y, Berhan A**. Is desvenlafaxine effective and safe in the treatment of menopausal vasomotor symptoms? A meta-analysis and meta-regression of randomized double-blind controlled studies.** *Ethiop J Health Sci*. 2014;24(3):209-218.

Sun Z, Hao Y, Zhang M. **Efficacy and safety of desvenlafaxine treatment for hot flashes associated with menopause: a meta-analysis of randomized controlled trials.** *Gynecol Obstet Invest*. 2013;75(4):255-262.

[63] **New Drug: Fetzima (Levomilnacipran).** Pharmacist's Letter. August 2016.

Product monograph for Fetzima. Actavis Specialty Pharmaceuticals/Allergan. Mississauga, ON L5N 6J5. May 2015.

[64] Colucci VJ, Berry BD. **Heart failure worsening and exacerbation after venlafaxine and duloxetine therapy.** Ann Pharmacother 2008;42:882-7.

nefazodone[3A4] SERZONE[FDA only]	carbamazepine⑨⑥ cisapride ⑥②$_{cv}$ lovastatin ⑥$_{rhabdo}$	MAOIs ③	sibutramine ③ simvastatin ⑥$_{rhabdo}$ sumatriptan ③	alprazolam ⑥ atorvastatin ⑥ cyclosporin ⑥	digoxin ⑥, fentanyl ⑧ fluvastatin ⑥ grapefruit juice ⑧	haloperidol ⑥ indinavir/ritonavir ⑧ L-tryptophan ③	midazolam ⑥ paroxetine ③ phenytoin ⑨⑥	**pimozide** ⑥$_{cv}$ pravastatin ⑥ quinidine ⑥②	ritonavir ⑧ **sedatives** ① tacrolimus⑥②	triazolam ⑥

CNS=central nervous system **CV**=cardiovascular **HTN**=hypertension

ANTIDEPRESSANT (AD) DRUG INTERACTIONS

Ref: **1**.Hansten & Horn-Drug Interactions'18. **2**.AHFS'18. **3**.Bezchlibnyk-Butler K. Serotonergic antidepressants:Drug response & drug interactions. Pharmacy Practice, Aug/98. **4**.CPS 2018. **5**.Micromedex 2018. **6**. Guidelines for Depressive Disorders. Cnd J Psyc Jun/01

7. Patsalos PN, Perucca E. Clinically important drug interactions in epilepsy: interactions between antiepileptic drugs and other drugs. Lancet Neurol. 2003 Aug;2(8):473-81.

8. Palylyk-Colwell E. CYP450 genotyping for determining drug metabolizer status. Issues Emerg Health Technol. 2006 Mar;(81):1-4. (Roche AmpliChip does 2D6 & 2C19) **9**. Bezchlibnyk-Butler Clinical Handbook of Psychotropic Drugs, 18th Ed. 2009.

10. Aubert RE, Stanek EJ, Yao J, et al. Increased risk of breast cancer recurrence in women initiating tamoxifen with CYP2D6 inhibitors. Presented at the American Society of Clinical Oncology (ASCO) Annual Meeting, May 30, 2009.

11. Kelly Catherine M, Juurlink David N, Gomes Tara, et al. Selective serotonin reuptake inhibitors and breast cancer mortality in women receiving **tamoxifen**: a population based cohort study BMJ 2010;340:c693, doi: 10.1136/bmj.c693 (Published 8 February 2010).

12. Aung GL, O'Brien JG, Tien PG, et al. Increased Aripiprazole Concentrations in an HIV-Positive Male Concurrently Taking Duloxetine, Darunavir, and Ritonavir. Ahead of Print 1Nov2010, DOI 10.1345/aph.1P139. Ann Pharmacother ;44:1850-1854.

13. Health Canada Feb/11 Methylene blue injectable in combination with serotonin reuptake inhibitors - Association with serotonin toxicity Cases of serotonin toxicity have been reported and published in association with the use of methylene blue injectable in patients exposed to drugs with serotonin reuptake inhibition properties.

14. Desmarais JE, Looper KJ. Interactions between **tamoxifen and antidepressants** via cytochrome P450 2D6. J Clin Psychiatry. 2009 Dec;70(12):1688-97.

15. Donneyong MM, Bykov K, Bosco-Levy P, et al. Risk of mortality with concomitant use of **tamoxifen and selective serotonin reuptake inhibitors**: multi-database cohort study. BMJ. 2016 Sep 30;354:i5014.

16. Bykov K, Schneeweiss S, Donneyong MM, et al. Impact of an **Interaction Between Clopidogrel and Selective Serotonin Reuptake Inhibitors**.Am J Cardio (2016)

17. Jessurun N, van Puijenbroek EP, Otten LS, et al. Inhibition of CYP2D6 with low dose (5 mg) **paroxetine in patients with high 10-hydroxynortriptyline serum levels** - a review of routine practice. Br J Clin Pharmacol. 2017 Jan 29.

18. Bezchlibnyk-Butler KZ. **Clinical Handbook of Psychotropic Drugs, 22nd Ed**. 22nd Editors: Procyshyn RM, Bezchlibnyk-Butler KZ, Jeffries JJ. Hogrefe Publishing, Massachusetts, 2017.

1. Neurology 2000 May 23;54(10):2024 Hypersexuality in patients with dementia: possible response to cimetidine. Wiseman SV, McAuley JW, Freidenberg GR, Freidenberg DL. 2. J Am Geriatr Soc 1999 Feb;47(2):231-4 Pharmacologic treatment of hypersexuality and paraphilias in nursing home residents. Levitsky AM, Owens NJ. ⊗ not covered NIHB
3. Can J Psychiatry 2001 Feb;46(1):26-34 The neurobiology, neuropharmacology, & pharmacological treatment of the paraphilias & compulsive sexual behaviour. Bradford JM. 4. Can J Psyc 2000 Aug;45:559-563. Protocols for the use of cyproterone,medroxyprogeserone & leuprolide in the treatment of paraphilia. ▼ covered by NIHB
5. J Gerontol Nurs1998 Apr;24(4):44-50Addressing hypersexuality in Alzheimer's dx. Kuhn DR, et al. 6. From very limited case reports 7. Clinical Handbook of Psychotropic Drugs,Bezchlibnyk-Butler 23th Ed.
8. Dyer O. Drug treatment is proposed to manage child sex offenders. BMJ. 2007 Jun 30;334(7608):1343. 9. Bardell A, Lau T, Fedoroff JP. Inappropriate sexual behavior in a geriatric population. Int Psychogeriatr. 2011 Apr 19:1-7. 10. Joller P et al. Approach to inappropriate sexual behaviour in people with **dementia**. Canadian Family Physician. Vol 59, March 2013.

Additional references for Treatment of Hypersexuality Patients:

Bardell A, Lau T, Fedoroff JP. Inappropriate sexual behavior in a geriatric population. Int Psychogeriatr 2011;23(7):1182-8. Epub 2011 Apr 19.

Bezchlibnyk-Butler KZ, Procyshyn RM, Jeffries JJ (Eds). Clinical Handbook of Psychotropic Drugs, 22nd Ed. Hogrefe. 2017

Briken P, Hill A, Berner W. Pharmacotherapy of **paraphilias with long-acting agonists of luteinizing hormone-releasing hormone**: a systematic review. J Clin Psychiatry. 2003 Aug;64(8):890-7.

Codispoti VL. **Pharmacology of sexually compulsive behavior**. Psychiatr Clin North Am. 2008 Dec;31(4):671-9. d

Coshway L, Broussard J, Acharya K, et al. Medical Therapy for **Inappropriate Sexual Behaviors in a Teen With Autism Spectrum Disorder**. Pediatrics. 2016 Mar 2.

Coskun M, Karakoc S, Kircelli F, Mukaddes NM. Effectiveness of **mirtazapine** in the treatment of inappropriate sexual behaviors in individuals with autistic disorder. J Child Adolesc Psychopharmacol. 2009 Apr;19(2):203-6.

Cross BS, Deyoung GR, Furmaga KM. High-dose oral **medroxyprogesterone** (100-400mg/d) for inappropriate hypersexuality in elderly men with dementia: a case series. Ann Pharmacother. 2013 Jan;47(1):e1.

Deepmala, Agrawal M. Use of **propranolol for hypersexual behavior** in an adolescent with autism. Ann Pharmacother. 2014 Oct;48(10):1385-8.

Garcia FD, Thibaut F. Current concepts in the pharmacotherapy of **paraphilias**. Drugs. 2011 Apr 16;71(6):771-90.

Guay DR. Drug treatment of **paraphilic and nonparaphilic** sexual disorders. Clin Ther. 2009 Jan;31(1):1-31

Hellemans H, Colson K, Verbraeken C, Vermeiren R, Deboutte D. Sexual behavior in high-functioning male adolescents and young adults with **autism spectrum disorder**. J Autism Dev Disord. 2007 Feb;37(2):260-9.

Johnson C, Knight C, Alderman N. Challenges associated with the definition and assessment of inappropriate sexual behaviour amongst individuals with an acquired neurological impairment. Brain Inj 2006;20(7):687-93.

Joller P, Gupta N, Seitz DP et al. Approach to inappropriate **sexual behaviour in people with dementia.** Canadian Family Physician. Vol 59, March 2013.

Knight C, Alderman N, Johnson C, Green S, Birkett-Swan L, Yorstan G. The **St Andrew's Sexual Behaviour Assessment (SASBA):** development of a standardised recording instrument for the measurement and assessment of challenging Sexual behaviour in people with progressive and acquired neurological impairment. Neuropsychol Rehabil 2008;18(2):129-59.

Lothstein LM, Fogg-Waberski J, Reynolds P. Risk management and treatment of sexual disinhibition in geriatric patients. Conn Med 1997;61(9):609-18.

Rösler A, Witztum E. Pharmacotherapy of **paraphilias** in the next millennium. Behav Sci Law. 2000;18(1):43-56.

Sajith SG, Morgan C, Clarke D. **Pharmacological management** of inappropriate sexual behaviours: a review of its evidence, rationale and scope in relation to **men with intellectual disabilities**. J Intellect Disabil Res. 2008 Dec;52(12):1078-90.

Series H, Dégano P. Hypersexuality in dementia. Adv Psychiatr Treat 2005;11(6):424-31.

St Andrew's Healthcare [website]. St Andrew's Sexual Behaviour Assessment. Northampton, UK: St Andrew's Healthcare; 2008. Available from: www.stah.org/services/brain-injury/sasba.aspx. Accessed 2012 Jun 1.

Tucker I. Management of inappropriate sexual behaviors in dementia: a literature review. Int Psychogeriatr 2010;22(5):683-92. Epub 2010 Mar 15.

ANTIPSYCHOTIC COMPARISON CHART

References

1. Allison DB et al. Antipsychotic Induced Weight Gain: A comprehensive Research Synthesis. Am J Psychiatry 1999;156(11):1686-96.
2. Allison DB, Casey DE. Antipsychotic-induced weight gain: a review of the literature. J Clin Psychiatry. 2001;62 Suppl 7:22-31.
3. Pharmacist Letter. Atypical Antipsychotics in Kids. January 2012.
4. Expert Consensus Guideline Series- Treatment of Schizophrenia 1999. J Clin Psychiatry 1999;60 (Suppl 11)
5. Switching Antipsychotics- Canadian Expert Consensus Panel July 2000
6. Canadian Clinical Practice Guidelines for the Treatment of Schizophrenia, Nov 1998, Vol 43, Supp 2; Can J Psyc Vol 50 Suppl 1 Nov **2005**
https://ww1.cpa-apc.org/Publications/Clinical_Guidelines/schizophrenia/november2005/cjp-cpg-suppl1-05_full_spread.pdf
Remington G, Addington D, Honer W, et al. **Canadian Schizophrenia Guidelines for the Pharmacotherapy of Schizophrenia in Adults**. Can J Psychiatry. **2017** Sep;62(9):604-616.
Addington D, Abidi S, Garcia-Ortega I, et al. **Canadian Guidelines for the Assessment and Diagnosis of Patients with Schizophrenia Spectrum and Other Psychotic Disorders**. Can J Psychiatry. 2017 Sep;62(9):594-603.

NICE: National Collaborating Centre for Mental Health. **Psychosis and schizophrenia in adults**: treatment and management. London (UK): National Institute for Health and Care Excellence (NICE); 2014 Feb.
NICE: National Collaborating Centre for Mental Health. **Psychosis and schizophrenia in children and young people**. London (UK): National Institute for Health and Clinical Excellence; 2013 Jan.
http://www.nice.org.uk/nicemedia/live/14021/62389/62389.pdf
NICE: Clinical Guideline 120. Mar 2011. **Psychosis with coexisting substance misuse**. http://www.nice.org.uk/nicemedia/live/13414/53691/53691.pdf Guick Guide http://www.nice.org.uk/nicemedia/live/13414/53731/53731.pdf
SIGN: Scottish Intercollegiate Guidelines Network. **Management of schizophrenia**. Edinburgh (Scotland): Scottish Intercollegiate Guidelines Network (SIGN); 2013 Mar.
Schultze-Lutter F, Michel C, Schmidt SJ,et al. **EPA (European) guidance on the early detection of clinical high risk states of psychoses**. Eur Psychiatry. 2015 Mar;30(3):405-16.
McClellan J, Stock S, American Academy of Child and Adolescent Psychiatry (**AACAP**) Committee on Quality Issues (CQI). Practice parameter for the **assessment and treatment of children and adolescents with schizophrenia**. J Am Acad Child Adolesc Psychiatry. 2013 Sep;52(9):976-90.
APA Work Group on Psychiatric Evaluation. The **American Psychiatric Association practice guidelines for the psychiatric evaluation of adults**. 3rd ed. Arlington (VA): American Psychiatric Association; 2016.

7. Lehman AF, et al. APA: Practice guideline for the treatment of patients with schizophrenia, 2nd Ed. Am J Psychiatry. 2004 Feb;161(2 Supp):1-56.
http://psychiatryonline.org/data/Books/prac/Schizophrenia2e_Inactivated_04-16-09.pdf
8. Bezchlibnyk-Butler KZ. **Clinical Handbook of Psychotropic Drugs, 22nd Ed**. 22nd Editors: Procyshyn RM, Bezchlibnyk-Butler KZ, Jeffries JJ. Hogrefe Publishing, Massachusetts, 2017.

Additional References

AACAP-Practice parameter on the use of **psychotropic medication in children and adolescents**. J Am Acad Child Adolesc Psychiatry. 2009 Sep;48(9):961-73.
Abbass AA, Kisely SR, Town JM, et al. Short-term **psychodynamic psychotherapies** for common mental disorders. Cochrane Database Syst Rev. 2014 Jul 1;7:CD004687. There has been further study of STPP and it continues to show promise, with modest to large gains for a wide variety of people. However, given the limited data, loss of significance in some measures at long-term follow-up and heterogeneity between studies, these findings should be interpreted with caution. Furthermore, variability in treatment delivery and treatment quality may limit the reliability of estimates of effect for STPP. Larger studies of higher quality and with specific diagnoses are warranted.
Abdullah-Koolmees H, Gardarsdottir H, Yazir D, et al. **Medication Discontinuation** in Patients After Discharge From a Psychiatric Hospital. Ann Pharmacother. 2015 Oct;49(10):1085-95.
Abel KM, Heuvelman HP, Jörgensen L, et al. **Severe bereavement stress during** the prenatal and **childhood** periods and risk of psychosis in later life: population based cohort study. BMJ. 2014 Jan 21;348:f7679
Abi-Jaoude E, Stall NM, Rochon PA**. Psychotropic drugs for the behavioural and psychological symptoms of dementia**: no free ride. CMAJ. 2018 Nov 26;190(47):E1374-E1375.
Aceituno D, Vera N, Prina AM, et al. Cost-effectiveness of **early intervention in psychosis**: systematic review. Br J Psychiatry. 2019 Jan 30:1-7.
Addington DE, Labelle A, Kulkarni J, Johnson G, Loebel A, Mandel FS. A comparison of **ziprasidone and risperidone** in the long-term treatment of schizophrenia: a 44-week, double-blind, continuation study. Can J Psychiatry. 2009 Jan;54(1):46-54. Ziprasidone, 80 to 160 mg/day (n = 62), or risperidone, 6 to 10 mg/day (n = 77). Ziprasidone and risperidone demonstrated similar efficacy during long-term treatment of patients with schizophrenia or schizoaffective disorder. While more subjects on risperidone completed the extension study, ziprasidone was associated with fewer adverse effects on weight, EPS measures, and prolactin than risperidone.
Addington DE, Mohamed S, Rosenheck RA, et al. Impact of **second-generation antipsychotics and perphenazine** on depressive symptoms in a randomized trial of treatment for chronic schizophrenia.J Clin Psychiatry.2010Sep 21.
Agar MR, Lawlor PG, Quinn S, et al. Efficacy of oral **risperidone, haloperidol, or placebo for symptoms of delirium among patients in palliative care**: a randomized clinical trial [online Dec 5, 2016]. JAMA Intern Med. doi:10.1001/jamainternmed.2016.7491
Ahuja TK, Cameron C, Yu C, et al. A systematic review of **combination and high-dose atypical antipsychotic** therapy in patients with schizophrenia Canadian Agency for Drugs and Technologies in Health. 2011 Dec;1:1-207.
Albert N, Melau M, Jensen H, et al. **Five years of specialised early intervention versus two years of specialised early intervention** followed by three years of standard treatment for patients with a first episode psychosis: randomised, superiority, parallel group trial in Denmark (**OPUS II**). BMJ. 2017 Jan 12;356:i6681.
Aleman A, Kahn RS. Effects of the atypical antipsychotic **risperidone on hostility and aggression in schizophrenia**: a metaanalysis of controlled trials. Eur Neuropsychopharmacol. 2001;11(4):289-293.
Alexopoulos GS, Streim J, et al.; Expert Consensus Panel for Using Antipsychotic Drugs in Older Patients. Using antipsychotic agents in older patients. J Clin Psychiatry. 2004;65 Suppl 2:5-99; discussion 100-102; quiz 103-4.
Alnæs D, Kaufmann T, van der Meer D, et al. **Brain Heterogeneity in Schizophrenia** and Its Association With **Polygenic Risk**. JAMA Psychiatry. 2019 Apr 10.
Alphs L, et al. Real-world outcomes of **paliperidone palmitate** compared to daily oral antipsychotic therapy in schizophrenia: a randomized, open-label, review board-blinded 15-month study. J Clin Psychiatry. 2015 May;76(5):554-61.
Alvarez-Jimenez M, et al. Non-pharmacological management of **antipsychotic-induced weight gain**: systematic review and meta-analysis of randomised controlled trials. Br J Psychiatry. 2008 Aug;193(2):101-7. Non-pharmacological weight-management interventions should be a priority, particularly during the early stages of antipsychotic treatment. Preventive approaches have the potential to be more effective, acceptable, cost-efficient and beneficial.
Aman MG, Bukstein OG, et al. What does **risperidone** add to parent training and stimulant for severe aggression in child **attention-deficit/hyperactivity** disorder? J Am Acad Child Adolesc Psychiatry. 2014 Jan;53(1):47-60.e1.
American Psychiatric Association Brochures: http://www.healthyminds.org/Functional-Library/brochures.aspx
Amminger GP, Schafer MR, Papageorgiou K, et al. Long-chain **omega-3 fatty acids** for indicated prevention of psychotic disorders: a randomized, placebo-controlled trial. Arch Gen Psychiatry. 2010 Feb;67(2):146-54.
Anagnostou E, Zwaigenbaum L, Szatmari P, et al. **Autism spectrum disorder**: advances in evidence-based practice. CMAJ. 2014 Jan 13
Anagnostou E, Aman MG, Handen BL, et al. **Metformin for treatment of overweight induced by atypical antipsychotic** medication in young people with autism spectrum disorder: a randomized clinical trial [online August 24, 2016]. JAMA Psychiatry. doi:10.1001/jamapsychiatry.2016 .1232.
Anderson KE, et al. Deutetrabenazine for treatment of involuntary movements in patients with **tardive dyskinesia (AIM-TD):** a double-blind, randomised, placebo-controlled, phase 3 trial. Lancet Psychiatry. 2017 Jun 28.
Anderson KK, Cheng J, Susser E, et al. **Incidence of psychotic disorders** among first-generation **immigrants and refugees** in Ontario. CMAJ. 2015 May 11.

Andrade Susan E, Lo Joan C, Roblin Douglas, et al. Antipsychotic Medication Use Among **Children and Risk of Diabetes Mellitus**. Pediatrics 2011; peds.2011-0855; ahead of print November 21, 2011.
Angstman K, Rasmussen NH. **Personality disorders**: review and clinical application in daily practice. Am Fam Physician. 2011 Dec 1;84(11):1253-60.
Anil Yagcioglu AE, et al. A double-blind controlled study of adjunctive treatment with **risperidone** in schizophrenic patients partially responsive to **clozapine**: efficacy and safety. J Clin Psychiatry. 2005 Jan;66(1):63-72.
Aparasu RR, Chatterjee S, Chen H. **Risk of pneumonia** in elderly nursing home residents using typical versus atypical antipsychotics. Ann Pharmacother. 2013 Apr;47(4):464-74.
Arango C, Rapado-Castro M, Reig S, et al. Progressive **brain changes in children and adolescents** with **first-episode psychosis**. Arch Gen Psychiatry. 2012 Jan;69(1):16-26.
Aripiprazole (Abilify) for schizophrenia. Med Lett Drugs Ther. 2003 Feb 17;45(1150):15-6.
Arora N, Knowles S, Gomes T, et al. **Interprovincial Variation in Antipsychotic and Antidepressant Prescriptions Dispensed** in the **Canadian Pediatric Population**. Can J Psychiatry. 2016 May 12.
Asenapine for **bipolar I disorder**? Drug Ther Bull. 2012 Jun;50(6):69-72.
Asenjo Lobos C, Komossa K, Rummel-Kluge C, et al. **Clozapine versus other atypical antipsychotics** for schizophrenia. Cochrane Database Syst Rev. 2010 Nov 10;11:CD006633. Clozapine may be a little more efficacious than zotepine and risperidone but further trials are required to confirm this finding. Clozapine differs more clearly in adverse effects from other second generation antipsychotics and the side-effect profile could be key in the selection of treatment depending on the clinical situation and a patient's preferences. Data on other important outcomes such as cognitive functioning, quality of life, death or service use are currently largely missing, making further large and well-designed trials necessary. It is also important to take into account that the large number of people leaving the studies early limits the validity and interpretation of our findings.
Asmal L, Flegar SJ, et al. **Quetiapine versus other atypical antipsychotics** for schizophrenia. Cochrane Database Syst Rev. 2013 Nov 18;11:CD006625. Available evidence from trials suggests that most people who start quetiapine stop taking it within a few weeks (around 60%). Comparisons with amisulpride, sertindole and zotepine do not exist. Although efficacy data favour olanzapine and risperidone compared with quetiapine, the clinical meaning of these data remains unclear. Quetiapine may produce fewer parkinsonian effects than paliperidone, aripiprazole, ziprasidone, risperidone and olanzapine. Quetiapine appears to have a similar weight gain profile to risperidone, as well as clozapine and aripiprazole (although data are very limited for the latter two comparators). Quetiapine may produce greater weight gain than ziprasidone and less weight gain than olanzapine and paliperidone.
Athanasiou MC, Dettling M, Cascorbi I, et al. Candidate gene analysis identifies a polymorphism in **HLA-DBQ1** associated with **clozapine-induced agranulocytosis**. J Clin Psychiatry 2011; 72:458–463.
Atlas SJ, Agboola F, Curfman G. Effectiveness and Value of 2 Novel **Treatments for Tardive Dyskinesia**. JAMA Intern Med. 2018 Jun 18.
Bakken MS, Schjott J, Engeland A, et al. **Antipsychotic Drugs and Risk of Hip** Fracture in People Aged 60 and Older in Norway.J Am Geriatr Soc. 2016 Jun;64(6):1203-9.
Ballard C, Waite J. The effectiveness of atypical antipsychotics for the treatment of **aggression and psychosis in Alzheimer's disease**. Cochrane Database Syst Rev. 2006 Jan 25;(1):CD003476.
Ballard C, Hanney ML, Theodoulou M, Douglas S, McShane R, Kossakowski K, Gill R, Juszczak E, Yu LM, Jacoby R; for the DART-AD investigators. The dementia antipsychotic withdrawal trial (**DART-AD**): long-term follow-up of a randomised placebo-controlled trial. Lancet Neurol. 2009 Jan 8. [Epub ahead of print] There is an increased long-term risk of mortality in patients with AD who are prescribed antipsychotic medication; these results further highlight the need to seek less harmful alternatives for the long-term treatment of neuropsychiatric symptoms in these patients.
Ballard C, Gauthier S, Corbett A, et al. **Alzheimer's** disease. Lancet. 2011 Mar 19;377(9770):1019-31.
Ballard C, Corbett A. Management of **neuropsychiatric symptoms** in people with dementia. CNS Drugs. 2010 Sep 1;24(9):729-39. doi:10.2165/11319240-000000000-00000.
Ballard C, Orrell M, YongZhong S, et al. Impact of **Antipsychotic Review and Nonpharmacological Intervention on Antipsychotic Use**, **Neuropsychiatric Symptoms**, **and Mortality in People With Dementia** Living in Nursing Homes: A Factorial Cluster-Randomized Controlled Trial by the Well-Being and Health for People With Dementia (**WHELD**) Program. Am J Psychiatry. 2015 Nov 20
Banerjee S, Hellier J, Dewey M, et al. **Sertraline** (150mg/day) **or mirtazapine** (45mg/day) for depression in dementia (**HTA-SADD**): a randomised, multicentre, double-blind, **placebo**-controlled trial. Lancet 2011; July 18. (absence of benefit)
Baptista T, et al. Metformin for prevention of weight gain and insulin resistance with olanzapine: a double-blind placebo-controlled trial. Can J Psychiatry. 2006 Mar;51(3):192-6.
Baptista T, Kin NM, Beaulieu S, et al. **Obesity and related metabolic abnormalities** during antipsychotic drug administration: mechanisms, management and research perspectives. Pharmacopsychiatry. 2002 Nov;35(6):205-19.
Barak Y, Plopski I, et al. **Escitalopram versus risperidone** for the treatment of behavioral and psychotic symptoms associated with Alzheimer's disease: a randomized double-blind pilot study. Int Psychogeriatr. 2011 Apr 15:1-5.
Barlow J, Bennett C, Midgley N, Larkin SK, Wei Y. **Parent-infant psychotherapy for improving parental and infant mental health**. Cochrane Database Syst Rev. 2015 Jan 8;1:CD010534.
Although the findings of the current review suggest that PIP is a promising model in terms of improving infant attachment security in high-risk families, there were no significant differences compared with no treatment or treatment-as-usual for other parent-based or relationship-based outcomes, and no evidence that PIP is more effective than other methods of working with parents and infants. Further rigorous research is needed to establish the impact of PIP on potentially important mediating factors such as parental mental health, reflective functioning, and parent-infant interaction.
Barnes TR, Paton C. Do **antidepressants improve negative symptoms in schizophrenia**? BMJ. 2011 Jun 10;342:d3371. doi: 10.1136/bmj.d3371.
Barnes TR, Drake MJ, Paton C. **Nocturnal enuresis** with antipsychotic medication. Br J Psychiatry. 2012 Jan;200:7-9. (esp. **clozapine**)
Barrowclough Christine, Haddock Gillian, Wykes Til, et al. **Integrated motivational interviewing and cognitive behavioural therapy** for people with psychosis and comorbid substance misuse: randomised controlled trial. BMJ 341:doi:10.1136/bmj.c6325 (Published 24 Nov 2010).
Bay B, Mortensen EL, Hvidtjorn D, et al. **Fertility treatment** and risk of childhood and adolescent mental disorders: register based cohort study. BMJ. 2013 Jul 5;347:f3978.
Becker SJ, Midoun MM. Effects of **Direct-To-Consumer Advertising** on Patient Prescription Requests and Physician Prescribing: A Systematic Review of Psychiatry-Relevant Studies. J Clin Psychiatry. 2016 Sep 13.
Bennett AC, Vila TM. The role of **ondansetron** in the treatment of schizophrenia. Ann Pharmacother. 2010 Jul-Aug;44(7-8):1301-6.
Benros ME, Waltoft BL, Nordentoft M, et al. **Autoimmune Diseases and Severe Infections** as Risk Factors for Mood Disorders: A Nationwide Study. JAMA Psychiatry. 2013 Jun 12:1-9.
Bergink V et al. Prevention of **postpartum psychosis and mania** in women at high risk. Am J Psychiatry 2012 Mar 8.
Bergink V, Burgerhout KM, Koorengevel KM, et al. Treatment of **psychosis and mania in the postpartum period**. Am J Psychiatry 2015;172:115–23.
Bergman H;Walker DM;Nikolakopoulou A;Soares-Weiser **Systematic review of interventions for treating or preventing antipsychotic-induced tardive dyskinesia.** Health Technol Assess. 2017 Aug;21(43):1-218.
Bergman H, Walker D-M, Nikolakopoulou A, Soares-Weiser K & Adams CE. Systematic review of interventions for treating or preventing **antipsychotic-induced tardive dyskinesia**. Health Technol Assess 2017;21(43)
Bergman H, Bhoopathi PS, Soares-Weiser K. **Benzodiazepines for antipsychotic-induced tardive dyskinesia**. Cochrane Database Syst Rev. 2018 Jan 20;1:CD000205.
There is only evidence of very low quality from a few small and poorly reported trials on the effect of benzodiazepines as an adjunctive treatment for antipsychotic-induced TD. These inconclusive results mean routine clinical use is not indicated and these treatments remain experimental.
Bergman H, Walker DM, Nikolakopoulou A, et al. Systematic review of interventions for **treating or preventing antipsychotic-induced tardive dyskinesia**. Health Technol Assess. 2017 Aug;21(43):1-218.
Berling I, Buckley NA, Isbister GK. The Antipsychotic Story: changes in **prescriptions and overdose** without better safety. Br J Clin Pharmacol. 2016 Mar 6.
Bertelsen M, Jeppesen P, Petersen L, et al. Five-year follow-up of a randomized multicenter trial of intensive early intervention vs standard treatment for patients with a first episode of psychotic illness: the OPUS trial. Arch Gen Psychiatry. 2008 Jul;65(7):762-71. The intensive **early-intervention program** improved clinical outcome after 2 years, but the effects were not sustainable up to 5 years later. Secondary outcome measures showed differences in the proportion of patients living in supported housing and days in hospital at the 5-year follow-up in favor of the intensive early-intervention program.
Berwaerts J, Liu Y, Gopal S, et al. Efficacy and Safety of the **3-Month Formulation of Paliperidone Palmitate** vs Placebo for Relapse Prevention of Schizophrenia: A Randomized Clinical Trial. JAMA Psychiatry. 2015 Mar 29.
Bhattacharjee J, El-Sayeh HG. **Aripiprazole** versus typical antipsychotic drugs for schizophrenia. Cochrane Database Syst Rev. 2008 Jul 16;(3):CD006617.
Bhattacharyya S, Crippa JA, Allen P, et al. Induction of **psychosis by {delta}9-tetrahydrocannabinol** reflects modulation of prefrontal and striatal function during attentional salience processing. Arch Gen Psychiatry. 2012 Jan;69(1):27-36.
Bhidayasiri R, Fahn S, et al. Evidence-based guideline: Treatment of **tardive syndromes**: Report of the Guideline Development Subcommittee of the American Academy of Neurology. Neurology. 2013 Jul 30;81(5):463-469.
Bhui K, Aslam RW, Palinski A, et al. Interventions designed to improve therapeutic **communications between black and minority ethnic people** and professionals working in psychiatric services: a systematic review of the evidence for their effectiveness. Health Technol Assess. 2015 Apr;19(31):1-174.
Biesdorf C, Martins FS, Sy SKB, Diniz A. **Physiologically-based pharmacokinetics of ziprasidone** in **pregnant women**. Br J Clin Pharmacol. 2019 Jan 22.
Bird V, Premkumar P, Kendall T, et al. Early intervention services, **cognitive-behavioural therapy** and family intervention in early psychosis: systematic review. Br J Psychiatry. 2010 Nov;197:350-6.
Bird AM, Smith TL, Walton AE. Current treatment strategies for **clozapine-induced sialorrhea**. Ann Pharmacother. 2011 May;45(5):667-75.
Biscontri RG, Jha S, Collins DM, Bugden S, et al. **Movement Disorders** in Children and Adolescents Receiving Antipsychotic Pharmacotherapy: A Population-Based Study. J Child Adolesc Psychopharmacol. 2017 Nov 1.

Biskin RS, Paris J. Management of **borderline personality disorder**. CMAJ. 2012 Oct 1.

Bjerre LM, Farrell B, et al. **Deprescribing antipsychotics for behavioural and psychological symptoms of dementia and insomnia**: Evidence-based clinical practice guideline. Can Fam Physician. 2018 Jan;64(1):17-27.

Black DW, Zanarini MC, Romine A, et al. Comparison of Low and Moderate Dosages of Extended-Release **Quetiapine in Borderline Personality Disorder**: A Randomized, Double-Blind, Placebo-Controlled Trial. Am J Psychiatry. 2014 Jun 27.

Bliss SA, Warnock JK. Psychiatric medications: **Adverse cutaneous drug reactions**. Clin Dermatol. 2013 Jan;31(1):101-9.

Bobo WV, Cooper WO, Stein CM et al. **Antipsychotics and the Risk of Type 2 Diabetes Mellitus** in Children and Youth. JAMA Psychiatry. 2013 Aug 21.

Bodén R, Lundgren M, Brandt L, et al. **Antipsychotics During Pregnancy**: Relation to Fetal and Maternal Metabolic Effects Antipsychotics During Pregnancy. Arch Gen Psychiatry. 2012 Jul 1;69(7):715-21.

Bobo WV, Cooper WO, Stein CM et al. Antipsychotics and the **Risk of Type 2 Diabetes Mellitus** in Children and Youth. JAMA Psychiatry. 2013 Aug 21.

Borgan F, O'Daly O, Hoang K, et al. Neural **Responsivity to Food Cues in Patients With Unmedicated First-Episode Psychosis**. JAMA Netw Open. 2019;2(1):e186893.

Bourque J, Afzali MH, Conrod PJ. Association of **Cannabis Use With Adolescent Psychotic** Symptoms. JAMA Psychiatry. 2018 Jun 6.

Boyce RD, Collins C, Clayton M, et al. Inhibitory Metabolic **Drug Interactions with Newer Psychotropic Drugs**: Inclusion in Package Inserts and Influences of Concurrencein Drug Interaction Screening Software (October). Ann Pharmacother. 2012 Oct 2.

Boyd A, Van de Velde S, Pivette M et al; EU-WMH investigators. **Gender differences in psychotropic use** across Europe: Results from a large cross-sectional, population-based study. Eur Psychiatry. 2015 Jun 4.

Boyer L, Lancon C, Baumstarck K, et al. Evaluating the **impact of a quality of life** assessment with feedback to clinicians in patients with schizophrenia: randomised controlled trial. Br J Psychiatry. 2013 Jun;202:447-53.

Brandt L, Henssler J, Müller M, et al. **Risk of Psychosis Among Refugees**: A Systematic Review and Meta-analysis. JAMA Psychiatry. 2019 Aug 14.

Brauer R, Douglas I, Smeeth L. The association between **antipsychotic agents** and the risk of myocardial infarction: a systematic review. Br J Clin Pharmacol. 2011 Dec;72(6):871-8. doi: 10.1111/j.1365-2125.2011.04043.x.

Breitbart W, Alici Y. Agitation and **delirium** at the end of life: "We couldn't manage him". JAMA. 2008 Dec 24;300(24):2898-910, E1.

Brett J, Daniels B, Karanges EA, et al. **Psychotropic polypharmacy** in Australia, 2006 to 2015: a descriptive cohort study. Br J Clin Pharmacol. 2017 Jul 9.

Briesacher BA, Limcangco MR, Simoni-Wastila L, Doshi JA, Levens SR, Shea DG, Stuart B. The quality of antipsychotic drug prescribing in nursing homes. Arch Intern Med. 2005 Jun 13;165(11):1280-5.

Briesacher BA et al. **Antipsychotic use among nursing home residents**. JAMA 2013 Feb 6; 309:440.

Brodaty H, Ames D, Snowdon J, et al. **Risperidone** for psychosis of Alzheimer's disease and mixed dementia: results of a double-blind, placebo-controlled trial. Int J Geriatr Psychiatry. 2005 Dec;20(12):1153-7.

Brown HE, Freudenreich O, Fan X, et al. Efficacy and Tolerability of **Adjunctive Intravenous Sodium Nitroprusside Treatment** for Outpatients With Schizophrenia: A Randomized Clinical Trial. JAMA Psychiatry. 2019 Mar 27

Brugger SP, Howes OD. Heterogeneity and homogeneity of **regional brain structure** in schizophrenia: a meta-analysis [published online September 27, 2017].JAMA Psychiatry. doi:10.1001 /jamapsychiatry.2017.2663

Buchanan RW, et al. Schizophrenia Patient Outcomes Research Team (**PORT**): The 2009 Schizophrenia PORT psychopharmacological treatment recommendations and summary statements. Schizophr Bull 2010; 36:71–93.

Brunelin J, Mondino M, Gassab L, et al. Examining **transcranial direct-current stimulation (tDCS)** as a treatment for hallucinations in schizophrenia. Am J Psychiatry. 2012 Jul 1;169(7):719-24.

Burcu M, Zito JM, Ibe A, et al. **Atypical antipsychotic use among medicaid-insured children and adolescents**: duration, safety, and monitoring implications. J Child Adolesc Psychopharmacol. 2014 Apr;24(3):112-9.

Burns T, Rugkåsa J, Molodynski A, et al. **Community treatment orders** (CTOs) for patients with psychosis (**OCTET**): a randomised controlled trial. Lancet 2013; online March 26.

Carrión RE, McLaughlin D, Goldberg TE, et al. Prediction of **Functional Outcome** in Individuals at Clinical High Risk for Psychosis. JAMA Psychiatry. 2013 Sep 4.

Cartwright AL, Wilby KJ, Corrigan S, et al. Pharmacogenetics of **Risperidone**: A Systematic Review of the Clinical Effects of CYP2D6 Polymorphisms. Ann Pharmacother. 2013 Mar;47(3):350-60.

Catone G, Marwaha S, Kuipers E, et al. **Bullying victimisation** and risk of psychotic phenomena: analyses of British national survey data. Lancet Psychiatry 2015;2:618–24.

Cavanna AE, Seri S. **Tourette's syndrome**. BMJ. 2013 Aug 20;347:f4964

Chan SKW, Chan SWY, Pang HH, et al. Association of an **early intervention service for psychosis with suicide rate** among patients with first-episode schizophrenia-spectrum disorders [online Apr 4, 2018].JAMA Psych.

Chandran GJ, Mikler JR, Keegan DL. **Neuroleptic malignant syndrome**: case report and discussion. CMAJ. 2003 Sep 2;169(5):439-42.

Chang A, Krygier DS, Chatur N, Yoshida EM. **Clozapine-induced** fatal fulminant hepatic failure: A case report. Can J Gastroenterol. 2009 May;23(5):376-8.

Chang WC, Kwong VW, Lau ES, et al. Sustainability of treatment effect of a **3-year early intervention programme for first-episode psychosis**. Br J Psychiatry. 2017 Apr 6.

Chang Z, Lichtenstein P, Långström N, Larsson H, Fazel S. Association between prescription of major **psychotropic medications and violent reoffending after prison release**. JAMA. doi:10.1001/jama .2016.15380

Chapel S, Chiu YY, Hsu J, et al. **Lurasidone** Dose Response in **Bipolar Depression**: A Population Dose-Response Analysis. Clin Ther. 2015 Dec 22.

Chatterjee A, Chakos M, Koreen A, et al. **Prevalence and clinical correlates of extrapyramidal signs and spontaneous dyskinesia** in never-medicated schizophrenic patients. Am J Psychiatry. 1995;152(12):1724-1729.

Chatterjee S, Naik S, John S, et al. Effectiveness of a **community-based intervention** for people with schizophrenia and their caregivers in India (COPSI): a randomised controlled trial. Lancet 2014; online March 5.

Chatterjee S, Chen H, Johnson ML, et al. Comparative risk of **cerebrovascular adverse events in community-dwelling older adults using risperidone, olanzapine and quetiapine:** a multiple propensity score-adjusted retrospective cohort study. Drugs Aging. 2012 Oct;29(10):807-17.

Chen Yong; Briesacher Becky A.; Field Terry S.; et al. Unexplained Variation Across US **Nursing Homes** in Antipsychotic Prescribing Rates. Arch Intern Med. 2010;170(1):89-95.

Chen E. Y. H., Hui C. L. M., Lam M. M. L., et al. **Maintenance treatment with quetiapine** versus discontinuation after one year of treatment in patients with remitted first episode psychosis: randomised controlled trial. BMJ 2010;341:c4024, doi: 10.1136/bmj.c4024

Chen JJ, Ondo WG, Dashtipour K, Swope DM. **Tetrabenazine** for the Treatment of Hyperkinetic Movement Disorders: A Review of the Literature. Clin Ther. 2012 Jun 27.

Cheng C, Mithoowani F, et al. **Interaction between Psychotropic Medications and Alcohol**: Perceptions among Patients Attending an Adult Mental Health Day Hospital Program. Can J Hosp Pharm. 2018 Jan-Feb;71(1):7-13.

Chengappa KN, et al. A random-assignment, double-blind, clinical trial of od vs bid administration of quetiapine in patients with schizophrenia or schizoaffective disorder: a pilot study. Can J Psychiatry. 2003 Apr;48(3):187-94.

Chien WT, Yip AL, Liu JY, et al. The effectiveness of manual-guided, problem-solving-based **self-learning programme for family caregivers** of people with recent-onset psychosis: A randomised controlled trial with 6-month follow-up. Int J Nurs Stud. 2016 Jul;59:141-55.

Chirdkiatgumchai V, Xiao H, Fredstrom BK, et al. National Trends in **Psychotropic Medication Use in Young Children**: 1994-2009. Pediatrics. 2013 Oct;132(4):615-623.

Chisolm MS, Payne JL. Management of **psychotropic drugs during pregnancy**. BMJ. 2016 Jan 20;532:h5918.

Choice of an antipsychotic. **Med Lett Drugs Ther. 2003 Dec** 22;45(1172):102-4.

Chrzanowski WK, et al. Effectiveness of long-term **aripiprazole** therapy in patients with acutely relapsing or chronic, stable schizophrenia: a 52-week, open-label comparison with olanzapine. Psychopharmacology (Berl). 2006 Dec;189(2):259-66. Epub 2006 Oct 21. Aripiprazole showed similar efficacy to olanzapine for long-term treatment of acutely psychotic and chronic, stable schizophrenia patients, with a lower liability for weight gain or increased lipid levels.

Cipriani A, Boso M, Barbui C. **Clozapine combined** with different antipsychotic drugs for treatment resistant schizophrenia. Cochrane Database Syst Rev. 2009 Jul 8;(3):CD006324.

Citrome LL, Jaffe AB. Relationship of atypical antipsychotics with development of **diabetes** mellitus. Ann Pharmacother. 2003 Dec;37(12):1849-57.

Citrome L. Comparison of intramuscular **ziprasidone, olanzapine, or aripiprazole for agitation**: a quantitative review of efficacy and safety. J Clin Psychiatry. 2007 Dec;68(12):1876-85. Although the lowest NNT, & hence strongest therapeutic effect, was seen for the studies of ziprasidone and olanzapine as opposed to aripiprazole, head-to-head controlled studies directly comparing these 3 agents are needed.

Citrome L. **Deutetrabenazine for tardive dyskinesia**: A systematic review of the efficacy and safety profile for this newly approved novel medication-What is the number needed to treat, number needed to harm and likelihood to be helped or harmed? Int J Clin Pract. 2017 Oct 12.

Citrome L. **Deutetrabenazine for tardive dyskinesia**: A systematic review of the efficacy and safety profile for this newly approved novel medication-What is the number needed to treat, number needed to harm and likelihood to be helped or harmed? Int J Clin Pract. 2017 Nov;71(11).

Cohen LS, Viguera AC, McInerney KA, et al. **Reproductive Safety of Second-Generation Antipsychotics**: Current Data From the Massachusetts General Hospital National Pregnancy Registry for Atypical Antipsychotics. Am J Psychiatry. 2015 Oct 6:appiajp201515040506.

Cohen LS, Góez-Mogollón L, Sosinsky AZ, et al. **Risk of Major Malformations in Infants Following First-Trimester Exposure to Quetiapine**. Am J Psychiatry. 2018 Aug 16:appiajp201818010098.

Coid JW, Ullrich S, Kallis C, et al. The Relationship Between **Delusions and Violence**: Findings From the East London First Episode Psychosis Study. JAMA Psychiatry. 2013 Mar 6:1-7. (mediated by **anger**)

Colizzi M, Murray R. **Cannabis and psychosis**: what do we know and what should we do? Br J Psychiatry. 2018 Apr;212(4):195-196.

Colodro-Conde L, Couvy-Duchesne B, Whitfield JB, et al. Association Between **Population Density and Genetic Risk for Schizophrenia**. JAMA Psychiatry. 2018 Jun 23.

Comer JS, Mojtabai R, Olfson M: **National trends in the antipsychotic treatment** of psychiatric outpatients with **anxiety** disorders. Am J Psychiatry 2011; 168:1057–1065.

Consensus Development Conference on Antipsychotic Drugs and Obesity and **Diabetes**; Diabetes Care.**2004**; 27: 596-558.

Conti V, Venegoni M, Cocci A, et al. Antipsychotic drug exposure and **risk of pulmonary embolism**: a population-based, nested case-control study. BMC Psychiatry 2015;15:92.

Cooper SJ, Reynolds GP; et al. BAP guidelines on the **management of weight gain, metabolic disturbances and cardiovascular risk associated with psychosis** and antipsychotic drug treatment. J Psychopharmacol. 2016 Aug;30(8):717-48.

Corbett A, Burns A, Ballard C. **Don't use antipsychotics routinely to treat agitation and aggression in people with dementia.** BMJ. 2014 Nov 3;349:g6420.

Correll CU, Leucht S, Kane JM. Lower risk for **tardive dyskinesia** associated with second-generation antipsychotics: a systematic review of 1-year studies. Am J Psychiatry. 2004 Mar;161(3):414-25. CONCLUSIONS: Results from 11 long-term studies support the idea that second-generation antipsychotics have a reduced risk for tardive dyskinesia, compared to first-generation antipsychotics, although the doses of haloperidol used in the comparator studies were relatively high. More carefully designed studies, ideally lasting beyond 1 year and comparing the effects of different second-generation antipsychotics in patients who have never taken first-generation antipsychotics, are needed to estimate the true risk. It would not appear premature for clinicians to consider these findings in making long-term treatment decisions.

Correll CU, Galling B, Pawar A, et al. Comparison of **Early Intervention Services vs Treatment as Usual for Early-Phase Psychosis**: A Systematic Review, Meta-analysis, and Meta-regression. JAMA Psychiatry. 2018 May 2.

Correll Christoph U.; Manu Peter; Olshanskiy Vladimir; et al. **Cardiometabolic Risk of Second-Generation** Antipsychotic Medications During First-Time Use in **Children and Adolescents**. *JAMA*. 2009;302(16):1765-1773.

Correll CU, Schenk EM. **Tardive dyskinesia and new antipsychotics**. Curr Opin Psychiatry. 2008 Mar;21(2):151-6.

Correll CU, Robinson DG, Schooler NR, et al. **Cardiometabolic Risk** in Patients With First-Episode Schizophrenia Spectrum Disorders: Baseline Results From the RAISE-ETP Study. JAMA Psychiatry. 2014 Oct 8.

Coughlin CG, Blackwell KA, Bartley C, Hay M, Yonkers KA, Bloch MH. **Obstetric and neonatal outcomes** after antipsychotic medication exposure in pregnancy. Obstet Gynecol. 2015 May;125(5):1224-35.

Crabtree Brian L., Montgomery John, **Iloperidone** for the Management of Adults with Schizophrenia, Clinical Therapeutics, Volume 33, Issue 3, March 2011, Pages 330-345.

Craig T, Rus-Calafell M, Ward T, et al. **AVATAR therapy for auditory verbal hallucinations** in people with psychosis: a single-blind, randomised controlled trial. Lancet Psychiatry 2017; online Nov 23.

Crawford MJ, Killaspy H, Barnes TRE, Barrett B, Byford S, Clayton K, et al. **Group art therapy** as an adjunctive treatment for people with schizophrenia: multicentre pragmatic randomised trial (**Matisse**). BMJ 2012;344:e846.

Crawford MJ, Jayakumar S, Lemmey SJ, et al. Assessment and treatment of **physical health** problems among people with schizophrenia: national cross-sectional study. Br J Psychiatry. 2014 Oct 16.

Crockford D, Addington D. **Canadian Schizophrenia Guidelines**: **Schizophrenia and Other Psychotic Disorders with Coexisting Substance Use** Disorders. Can J Psychiatry. 2017 Sep;62(9):624-634.

Croft J, Heron J, Teufel C, Cannon M, et al. Association of **Trauma Type, Age of Exposure, and Frequency in Childhood and Adolescence With Psychotic Experiences** in Early Adulthood. JAMA Psychiatry. 2018 Nov 21.

Cross-Disorder Group of the Psychiatrics Genomics Consortium. Identification of risk **loci with shared effects on five major psychiatric disorders**: a genome-wide analysis. Lancet 2013; online Feb 28.

Crossley NA, Constante M, McGuire P, et al. Efficacy of **atypical v. typical antipsychotics in the treatment of early psychosis**: meta-analysis. Br J Psychiatry. 2010;196(6): 434-439.

Crump C, Sundquist K, Winkleby MA, Sundquist J. **Mental disorders and vulnerability** to **homicidal death**: Swedish nationwide cohort study. BMJ 2013;346:f557.

Csernansky JG, Mahmoud R, Brenner R; Risperidone-USA-79 Study Group. A comparison of **risperidone and haloperidol** for the prevention of relapse in patients with schizophrenia. N Engl J Med. 2002 Jan 3;346(1):16-22.

Cullen BA, McGinty EE, Zhang Y, et al. Guideline-Concordant **Antipsychotic Use and Mortality** in Schizophrenia. Schizophr Bull. 2012 Oct 30.

Currie O, Williman J, Mangin D, et al. Comparative **risk of new-onset diabetes following commencement of antipsychotics** in New Zealand: a population-based clustered multiple baseline time series design. BMJ Open. 2019 Feb 21;9(2):e022984.

Damkier P, Christensen LS, Broe A. Patterns and predictors for prescription of **psychotropics and mood-stabilizing antiepileptics during pregnancy** in Denmark 2000-2016. Br J Clin Pharmacol. 2018 Aug 5.

Daniel DG. Antipsychotic treatment of psychosis and agitation in the elderly. J Clin Psychiatry 2000; 61(suppl 14):49-52.

Danielsson B, Collin J, et al. **Antidepressants and antipsychotics classified with Torsades de Pointes** arrhythmia risk and mortality in older adults – a Swedish nationwide study. Br J Clin Pharmacol. 2015 Nov 17.

Davidson M, Galderisi S, et al. **Cognitive Effects** of Antipsychotic Drugs in First-Episode Schizophrenia and Schizophreniform Disorder: A Randomized, Open-Label Clinical Trial (EUFEST). Am J Psychiatry. 2009 Apr 15. Treatment with antipsychotic medication is associated with moderate improvement in the cognitive test performance of patients who have schizophreniform disorder or who are in their first episode of schizophrenia. The magnitude of improvement does not differ between treatment with haloperidol and treatment with second-generation antipsychotics. Moreover, cognitive improvement is weakly related to symptom change.

Davis JM, Chen N, Glick ID. A **meta-analysis** of the efficacy of second-generation antipsychotics. Arch Gen Psychiatry. 2003 Jun;60(6):553-64.

Davis MC, Miller BJ, Kalsi JK, et al. Efficient Trial Design - FDA Approval of **Valbenazine** for Tardive Dyskinesia. N Engl J Med. 2017 May 10.

Deberdt WG, Dysken MW, Rappaport SA, Feldman PD, et al.. Comparison of olanzapine and risperidone in the treatment of psychosis and associated behavioral disturbances in patients with dementia. Am J Geriatr Psychiatry. 2005 Aug;13(8):722-30. CONCLUSIONS: Patients' neuropsychiatric functioning improved with olanzapine, risperidone, and placebo treatment. There was a substantial response in the placebo group, and no significant differences emerged among treatments.

De Deyn PP, Rabheru K, Rasmussen A, et al. A randomized trial of risperidone, placebo, and haloperidol for behavioral symptoms of dementia. Neurology 1999;53:946-55.

De Deyn PP, Drenth AF, Kremer BP, Oude Voshaar RC, Van Dam D. **Aripiprazole** in the treatment of Alzheimer's disease. Expert Opin Pharmacother. 2013 Jan 28.

DeVylder JE, Kelleher I, Lalane M, Oh H, Link BG, Koyanagi A. Association of **urbanicity with psychosis in low- and middle-income countries** [online May 16, 2018]. JAMA Psychiatry. doi:10.1001/jamapsychiatry.2018.0577

Declercq T, Petrovic M, Azermai M, Vander Stichele R, De Sutter AIM, van Driel ML, Christiaens T. **Withdrawal versus continuation of chronic antipsychotic drugs for behavioural and psychological symptoms in older people with dementia**. Cochrane Database of Systematic Reviews 2013, Issue 3. Art. No.: CD007726. DOI: 10.1002/14651858.CD007726.pub2. Our findings suggest that many older people with Alzheimer's dementia and NPS can be withdrawn from chronic antipsychotic medication without detrimental effects on their behaviour. It remains uncertain whether withdrawal is beneficial for cognition or psychomotor status, but the results of this review suggest that discontinuation programmes could be incorporated into routine practice. However, two studies of people whose agitation or psychosis had previously responded well to antipsychotic treatment found an increased risk of relapse or shorter time to relapse after discontinuation. Two other studies suggest that people with more severe NPS at baseline could benefit from continuing their antipsychotic medication. In these people, withdrawal might not be recommended.

Deng H, Xu J. **Wendan decoction (Traditional Chinese medicine)** for schizophrenia. Cochrane Database Syst Rev. 2017 Jun 28;6:CD012217. Limited evidence suggests that WDD may have some positive short-term antipsychotic global effects compared to placebo or no treatment. However when WDD was compared with other antipsychotics there was no effect on global or mental state, but WDD was associated with fewer adverse effects. When WDD was combined with an antipsychotic, positive effects were found for global and mental state and the combination caused fewer adverse effects.

Dent R, Blackmore A, Peterson J, et al. Changes in **body weight and psychotropic drugs**: a systematic synthesis of the literature. PLoS One. 2012;7(6):e36889.

Dent R, Gervais A. **Weight gain induced by psychotropic agents**. CMAJ. 2013 Jul 9;185(10):898.

Deprescribing Guideline and Algorithms (Benzodiazepine receptor agonits, Proton pump inhibitors, Antipsychotics, Antihyperglycemic) http://deprescribing.org/resources/deprescribing-guidelines-algorithms/

Desveaux L, Saragosa M, et al. **Improving the appropriateness of antipsychotic prescribing in nursing homes**: a mixed-methods process evaluation of an academic detailing intervention. Implement Sci. 2017 May 26;12(1):71

Devanand DP, Pelton GH, Cunqueiro K, Sackeim HA, Marder K. A 6-month, randomized, double-blind, placebo-controlled pilot **discontinuation trial following response to haloperidol** treatment of psychosis and agitation In Alzheimer's disease. Int J Geriatr Psychiatry. 2011 Sep;26(9):937-43.

Devlin JW, Roberts RJ, Fong JJ, et al. Efficacy and safety of **quetiapine in critically ill patients with delirium**: a prospective, multicenter, randomized, double-blind, placebo-controlled pilot study. Crit Care Med 2010; 38:419-27.

Dewey RB Jr, O'Suilleabhain PE. Treatment of drug-induced psychosis with quetiapine and clozapine in Parkinson's disease. Neurology 2000;55:1753-4.
Di Forti M, Marconi A, Carra E, et al. Proportion of patients in south London with **first-episode psychosis attributable to use of high potency cannabis**: a case-control study. Lancet Psychiatry. 2015 Mar
Di Pietro N, Illes J; Canadian Working Group on Antipsychotic Medications adn Children. Rising **antipsychotic prescriptions for children and youth**: cross-sectoral solutions for a multimodal problem. CMAJ. 2014 Jun 10;186(9):653-4.
Dold M, Samara MT, Li C, Tardy M, Leucht S. **Haloperidol versus first-generation antipsychotics** for the treatment of schizophrenia and other psychotic disorders. Cochrane Database of Systematic Reviews 2015, Issue 1. Art. No.: CD009831. DOI: 10.1002/14651858.CD009831.pub2. The findings of themeta-analytic calculations support the statements of previous narrative, unsystematic reviews suggesting comparable efficacy of first-generation antipsychotics. In efficacy-related outcomes, There was no clear evidence of a difference between the prototypal drug haloperidol and other, mainly high-potency first-generation antipsychotics. Additionally, we demonstrated that haloperidol is characterised by a similar risk profile compared to the other first- generation antipsychotic compounds. The only statistically significant difference in specific side effects was that haloperidol produced less akathisia in the medium term. The results were limited by the low methodological quality in many of the included original studies. Data for themain results were low or very low quality. Therefore, future clinical trials with high methodological quality are required.
Doody RS, Stevens JC, ET AL. Practice parameter: management of dementia (an evidence-based review). Report of the Quality Standards Subcommittee of the American Academy of Neurology. Neurology 2001;56:1154-66.
Dore DD, Trivedi AN, Mor V, Friedman JH, et al. Atypical antipsychotic use and risk of **fracture in persons with Parkinsonism**. Mov Disord. 2009 Jul 30. [Epub ahead of print] Use of an AA was associated with a higher rate of fracture in persons with parkinsonism.
Dorsey E. Ray; Rabbani Atonu; Gallagher Sarah A.; et al. Impact of **FDA Black Box** Advisory on Antipsychotic Medication Use. Arch Intern Med. 2010;170(1):96-103.
dosReis Susan, Yoon Yesel, Rubin David M., et al. Antipsychotic Treatment **Among Youth in Foster Care**. Pediatrics 2011; peds.2010-2970; published ahead of print November 21, 2011, doi:10.1542/peds.2010-2970.
Dossenbach M, Arango-Davila C, Silva Ibarra H, et al. Response and Relapse in Patients With Schizophrenia Treated With Olanzapine, Risperidone, Quetiapine, or Haloperidol: 12-Month Follow-Up of the Intercontinental Schizophrenia Outpatient Health Outcomes (IC-SOHO) Study. J Clin Psychiatry. 2005 Aug;66(8):1021-1030.
Dossenbach M, et al. Effects of atypical and typical antipsychotic treatments on **sexual function** in patients with schizophrenia: 12-month results from the Intercontinental Schizophrenia Outpatient Health Outcomes (IC-SOHO) study. Eur Psychiatry. 2006 Mar 9; [Epub ahead of print]
Dougall N, Maayan N, Soares-Weiser K, et al. **Transcranial magnetic stimulation (TMS)** for schizophrenia. Cochrane Database Syst Rev. 2015 Aug 20;8:CD006081. Based on this review, there is insufficient evidence to support or refute the use of TMS to treat symptoms of schizophrenia. Although some evidence suggests that TMS, and in particular temporoparietal TMS, may improve certain symptoms (such as auditory hallucinations and positive symptoms of schizophrenia) compared to sham TMS, the results were not robust enough to be unequivocal across the assessment measures used. There was insufficient evidence to suggest any added benefit with TMS used as an adjunctive therapy to antipsychotic medication.The overall quality of evidence was graded as very low due to risk of bias, and this was accompanied by an imprecision in estimates due to the relatively small number of participants in the studies. Thus, consideration is required in improving the quality of trial processes, as well as the quality of reporting of ongoing and future TMS trials, so as to facilitate accurate future judgements in assessing risk of bias. Differences in TMS techniques in relation to stimulation intensity, stimulation length, brain areas stimulated and variations in the design of sham TMS all contributed to the heterogeneity of study findings and limited the interpretation and applicability of the results. In addition, the trials assessed their outcomes with a variety of scales, and usable data were limited. Therefore, to better evaluate the treatment effects of TMS in people with schizophrenia, we favour the use of standardised treatment protocols and outcome measures.
Douglas IJ, Smeeth L. Exposure to antipsychotics and risk of stroke: self controlled case series study. BMJ. 2008 Aug 28;337:a1227. doi: 10.1136/bmj.a1227. **All antipsychotics are associated with an increased risk of stroke**, and the risk might be higher in patients receiving atypical antipsychotics than those receiving typical antipsychotics. People with dementia seem to be at a higher risk of an associated stroke than people without dementia and use of antipsychotics should, when possible, be avoided in these patients.
Dove D, Warren Z, McPheeters ML, et al. Medications for Adolescents and Young Adults With **Autism** Spectrum Disorders: A Systematic Review. Pediatrics. 2012 Sep 24. (risperidone possibly)
Dregan A, Matcham F, Harber-Aschan L, et al. Common **mental disorders within chronic inflammatory disorders**: a primary care database prospective investigation. Ann Rheum Dis. 2019 May;78(5):688-695.
Duggan L, Fenton M, Dardennes RM, El-Dosoky A, Indran S. **Olanzapine** for schizophrenia. Cochrane Database Syst Rev. 2003;(1):CD001359.
Dutta R, Murray RM, Hotopf M, et al. Reassessing the long-term **risk of suicide after a first episode of psychosis**. Arch Gen Psychiatry. 2010 Dec;67(12):1230-7.
Drummond N, McCleary L, Freiheit E, et al. **Antidepressant and antipsychotic prescribing in primary care for people with dementia**. Can Fam Physician. 2018 Nov;64(11):e488-e497.
Einarson A, Boskovic R. Use and safety of antipsychotic drugs during **pregnancy**. J Psychiatr Pract. 2009 May;15(3):183-92.
El Hajj I, Sharara AI, Rockey DC. Subfulminant **liver failure** associated with **quetiapine**. Eur J Gastroenterol Hepatol. 2004 Nov;16(12):1415-8.
El-Sayeh HG, Morganti C. **Aripiprazole** for schizophrenia. Cochrane Database Syst Rev. 2006 Apr 19;(2):CD004578.
El-Sayeh HG, et al. **Aripiprazole** for schizophrenia. Systematic review. Br J Psychiatry. 2006 Aug;189:102-8.
Elley CR, Dawes D, Dawes M, et al. **Screening for lifestyle and mental health risk factors in the waiting room:** feasibility study of the Case-finding Health Assessment Tool. Can Fam Physician. 2014 Nov;60(11):e527-34.
Essali A, Al-Haj Haasan N, Li C, Rathbone J. **Clozapine versus typical neuroleptic** medication for schizophrenia. Cochrane Database Syst Rev. 2009 Jan 21;(1):CD000059. Clozapine may be more effective in reducing symptoms of schizophrenia, producing clinically meaningful improvements and postponing relapse, than typical antipsychotic drugs - but data are weak and prone to bias. Participants were more satisfied with clozapine treatment than with typical neuroleptic treatment. The clinical effect of clozapine, however, is, at least in the short term, not reflected in measures of global functioning such as ability to leave the hospital and maintain an occupation. The short-term benefits of clozapine have to be weighed against the risk of adverse effects. Within the context of trials, the potentially dangerous white blood cell decline seems to be more frequent in children and adolescents and in the elderly than in young adults or people of middle-age.The existing trials have largely neglected to assess the views of participants and their families on clozapine. More community-based long-term randomised trials are needed to evaluate the efficacy of clozapine on global and social functioning as trials in special groups such as people with learning disabilities.
Essali A, Turkmani K, Aboudamaah S, et al. **Haloperidol discontinuation for people with schizophrenia**. Cochrane Database Syst Rev. 2019 Apr 21;4:CD011408. This review provides limited evidence derived from small, short-term studies. The longest study was for one year, making it difficult to generalise the results to a life-long disorder. Very low quality evidence shows that discontinuation of haloperidol is associated with an increased risk of relapse and a reduction in the risk of 'global state improvement'. However, participant satisfaction with haloperidol treatment was not different from participant satisfaction with haloperidol discontinuation as measured by leaving the studies early.
Essock, Susan M., Schooler, Nina R., Stroup, T. Scott, et al. The Schizophrenia Trials Network, Effectiveness of **Switching From Antipsychotic Polypharmacy to Monotherapy**. Am J Psychiatry 2011 168: 702-708.
Fardet L et al. Suicidal behavior and severe **neuropsychiatric disorders following glucocorticoid** therapy in primary care. Am J Psychiatry 2012 May 1; 169:491.
Faulkner G, Cohn TA. Pharmacologic and nonpharmacologic strategies for **weight gain** and metabolic disturbance in patients treated with antipsychotic medications. Can J Psychiatry. 2006 Jul;51(8):502-11. Review. Erratum in: Can J Psychiatry. 2006 Aug;51(9):620. Although difficult, the prevention of weight gain and the promotion of weight loss are possible for individuals treated with antipsychotic medications. Further research, including diabetes prevention studies, is required. We suggest a pathway for the management of weight gain and emerging metabolic disturbance.
Fazel S, Zetterqvist J, Larsson H, et al. Antipsychotics, mood stabilisers, and **risk of violent crime**. Lancet. 2014 May 7.
Fazel S, Gulati G, Linsell L, Geddes JR, Grann M, 2009 Schizophrenia and **Violence**: Systematic Review and Meta-Analysis. PLoS Med 6(8): e1000120. doi:10.1371/journal.pmed.1000120 However, most of the excess risk appears to be mediated by substance abuse comorbidity.
Fazel S, Wolf A, Lichtenstein P, et al. **Violent crime, suicide, and premature mortality** in patients with schizophrenia and related disorders: a 38-year total population study in Sweden. The Lancet Psychiatry 1.1 (2014): 44-54.
FDA Sep/11 notified healthcare professionals and patients that serious allergic reactions have been reported with the use of **Saphris (asenapine maleate).**
FDA Aug/13 Health and Beyond LLC is voluntarily recalling quantity lots of product **Tranquility**. The products have been found to contain a trace of Doxepin which is a pharmaceutical for sleep and Chlorpormazine for psychotic disorders.
FDA Dec/14 is warning that the antipsychotic drug **ziprasidone** (marketed under the brand name, Geodon, and its generics) is associated with a rare but serious skin reaction that can progress to affect other parts of the body. A new warning has been added to the Geodon drug label to describe the serious condition known as Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS).
FDA May/16 is warning that **compulsive or uncontrollable urges to gamble, binge eat, shop, and have sex** have been reported with the use of the antipsychotic drug **aripiprazole** (Abilify, Abilify Maintena, Aristada).
FDA May/16 is warning that the antipsychotic medicine **olanzapine** can cause a rare but serious skin reaction that can progress to affect other parts of the body. FDA is adding a new warning to the drug labels for all olanzapine-containing products that describes this severe condition known as Drug Reaction with Eosinophilia and Systemic Symptoms (**DRESS**).
Fernandez HH, Friedman JH, Jacques C, Rosenfeld M. Quetiapine for the treatment of drug-induced psychosis in Parkinson's disease. Mov Disord 1999; 14:484-7.
Fernandez HH, Trieschmann ME, Burke MA, Jacques C, Friedman JH. Long-term outcome of quetiapine use for psychosis among parkinsonian patients. Mov Disord. 2003 May;18(5):510-4.

Fernandez H, Trieschmann M, Friedman J. Treatment of **psychosis in Parkinson's** disease : safety considerations. Drug Saf. 2003;26(9):643-59.
Findling RL, Robb A, Nyilas M, et al. A multiple-center, randomized, double-blind, placebo-controlled study of oral **aripiprazole** for treatment of adolescents with schizophrenia. Am J Psychiatry. 2008 Nov;165(11):1432-41. Epub 2008 Sep 2. Both 10- and 30-mg/day doses of aripiprazole were superior to placebo in the acute treatment of adolescents with schizophrenia. Aripiprazole was generally well tolerated.
Findling RL, Goldman R, Chiu YY, et al. Pharmacokinetics and Tolerability of **Lurasidone in Children and Adolescents** With Psychiatric Disorders. Clin Ther. 2015 Nov 26.
Fine JD, Moreau AL, Karcher NR, et al. Association of **Prenatal Cannabis Exposure** With Psychosis Proneness Among Children in the Adolescent Brain Cognitive Development (ABCD) Study. JAMA Psychiatry. 2019 Mar 27.
Flaherty JH, Gonzales JP, Dong B. **Antipsychotics in the treatment of delirium** in older hospitalized adults: a systematic review. J Am Geriatr Soc. 2011 Nov;59 Suppl 2:S269-76.
Fleischhacker WW, Sanchez R, Perry PP, et al. **Aripiprazole once-monthly** for treatment of schizophrenia: double-blind, randomised, non-inferiority study. Br J Psychiatry. 2014 Jun 12.
Flint AJ, Meyers BS, Rothschild AJ, et al. Effect of **Continuing Olanzapine vs Placebo on Relapse** Among Patients With Psychotic Depression in Remission: The STOP-PD II Randomized Clinical Trial. JAMA. 2019 Aug 20;322(7):622-631.
Flood C, et al. **Joint crisis plans** for people with psychosis: economic evaluation of a randomised controlled trial. BMJ. 2006 Oct 7;333(7571):729. Epub 2006 Aug 16.
Foley Debra L.; Morley Katherine I.. Systematic Review of Early **Cardiometabolic Outcomes** of the First Treated Episode of Psychosis. *Arch Gen Psychiatry*. 2011;0(2011):archgenpsychiatry.2011.2.
Ford RL, Sallam A, Towler HM. Intraoperative **floppy iris syndrome associated with risperidone** intake. Eur J Ophthalmol. 2010 Sep 7. pii: 5B197916-3344-4098-A76D-04BC44510903.
Fortinguerra, Filomena, Clavenna, Antonio, Bonati, Maurizio. Psychotropic Drug Use During **Breastfeeding**: A Review of the Evidence. Pediatrics 2009 124: e547-e556.
Frampton JE. **Olanzapine Long-Acting Injection**: A Review of its Use in the Treatment of Schizophrenia. Drugs. 2010 Dec 3;70(17):2289-2313.
Fraser LA, Liu K, Naylor KL, et al. **Falls and fractures** with atypical antipsychotic medication use: a population-based cohort study. JAMA Intern Med. 2015 Mar 1;175(3):450-2.
Freedman, R. **Schizophrenia**. N Engl J Med **2003** 349: 1738-1749.
Freudenreich O, Henderson DC, Macklin EA, Evins AE, Fan X, Cather C, Walsh JP, Goff DC. **Modafinil** for clozapine-treated schizophrenia patients: a double-blind, placebo-controlled pilot trial. J Clin Psychiatry. 2009 Aug 11.
Friedman JH. Atypical Antipsychotics in the Treatment of Drug Induced Psychosis in Parkinson's Disease. Movement Disorders 2000;15(2):201-211.
Furukawa TA, Levine SZ, Tanaka S, et al. **Initial Severity of Schizophrenia** and Efficacy of Antipsychotics: Participant-Level Meta-analysis of 6 Placebo-Controlled Studies. JAMA Psychiatry. 2014 Nov 5.
Fusar-Poli P, Bonoldi I, Yung AR, et al. **Predicting Psychosis**: Meta-analysis of Transition Outcomes in Individuals at High Clinical Risk. Arch Gen Psychiatry. 2012 Mar;69(3):220-9.
Fusar-Poli P, Borgwardt S, Bechdolf A, et al. The **Psychosis High-Risk State**: A Comprehensive State-of-the-Art Review. Arch Gen Psychiatry. 2012 Nov 19:1-14.
Fusar-Poli P, Davies C, Bonoldi I. A **Case of a College Student** Presenting With Mild Mental Health Problems. JAMA Psychiatry. 2018 Oct 17.
Fusar-Poli P, et al. Development and validation of a clinically based **risk calculator** for the **transdiagnostic prediction of psychosis** [published online March 29, 2017].JAMA Psychiatry. doi:10.1001/jamapsychiatry.2017.0284.
Gaebel W, Riesbeck M, Wölwer W, Klimke A, et al.; German Study Group on First-Episode Schizophrenia. Maintenance treatment with risperidone or low-dose haloperidol (both target 2-4mg/d) in first-episode schizophrenia: 1-year results of a randomized controlled trial within the German research network on schizophrenia. J Clin Psychiatry. 2007 Nov;68(11):1763-74. Against the background of an overall favorable outcome, the hypothesized difference between risperidone and low-dose haloperidol regarding relapse prevention could not be supported for this sample of patients with first-episode schizophrenia.
Galling B, Roldán A, Hagi K, et al. Antipsychotic **augmentation** vs. **monotherapy** in **schizophrenia**: systematic review, meta-analysis and meta-regression analysis. World Psychiatry. 2017 Feb;16(1):77-89.
Gao K, Muzina D, Gajwani P, et al. Efficacy of **typical and atypical antipsychotics** for primary and comorbid **anxiety** symptoms or disorders: a review. J Clin Psychiatry. 2006 Sep;67(9):1327-40. Except for trifluoperazine, there is no large, well-designed study of antipsychotics in the treatment of primary or comorbid anxiety symptoms or disorders. The efficacy of these agents in various anxiety conditions needs to be further investigated with large, well-designed comparison studies.
Gardner DM, Baldessarini RJ, Waraich P. Modern antipsychotic drugs: a **critical overview**. **CMAJ**. **2005** Jun 21;172(13):1703-11.
Garner B, Phillips LJ, Bendall S, et al. **Antiglucocorticoid and related treatments for psychosis**. Cochrane Database Syst Rev. 2016 Jan 4;1:CD006995. Good evidence is insufficient to conclude whether antiglucocorticoid drugs provide effective treatment for psychosis. Some global state findings suggest a favourable effect for mifepristone, and a few overall adverse effect findings favour placebo. Additional large randomised controlled trials are needed to justify findings.
Gatov E, Rosella L, Chiu M, et al. **Trends in standardized mortality** among individuals with schizophrenia, 1993–2012: a population-based, repeated crosssectional study. CMAJ 2017;189:E1177-87.
Gaynes BN, Brown C, Lux LJ, et al. **Strategies to de-escalate aggressive behavior in psychiatric patients**. Comparative Effectiveness Review No. 180. Rockville (MD): Agency for Healthcare Research and Quality (US); 2016 July. Report No.:16-EHC032-EF
Geddes J, Freemantle N, Harrison P, Bebbington P. Atypical antipsychotics in the treatment of schizophrenia: **systematic overview** and meta-regression analysis. BMJ. 2000 Dec 2;321(7273):1371-6.
Gentile S. Long-term treatment with atypical antipsychotics and the risk of **weight gain** : a literature analysis. Drug Saf. 2006;29(4):303-19.
Gentile S. Infant safety with **antipsychotic therapy in breast-feeding**: a systematic review. J Clin Psychiatry. 2008 Apr;69(4):666-73.
Gerhard T, Huybrechts K, Olfson M, et al. Comparative **mortality risks of antipsychotic** medications in community-dwelling older adults. Br J Psychiatry. 2013 Aug 8.
Gharabawi GM, et al.An assessment of emergent **tardive dyskinesia** and existing dyskinesia in patients receiving long-acting, injectable risperidone: results from a long-term study. Schizophr Res. 2005 Sep 15;77(2-3):129-39. Five of 530 subjects without dyskinesia at baseline (0.94%) over 50week open label trial met the predefined criteria for emergent persistent TD during therapy.
Gill Sudeep S, Rochon Paula A, Herrmann Nathan, et al. Atypical antipsychotic drugs & risk of ischaemic **stroke**: population based retrospective cohort study BMJ, doi:10.1136/bmj.38330.470486.8F (published 24 January 2005)
Gillies D, Sampson S, Beck A, et al. **Benzodiazepines for psychosis-induced aggression or agitation**. Cochrane Database Syst Rev. 2013 Sep 18;9:CD003079. The evidence from trials for the use of benzodiazepines alone is not good. There were relatively little good data and most trials are too small to highlight differences in either positive or negative effects. Adding a benzodiazepine to other drugs does not seem to confer clear advantage and has potential for adding unnecessary adverse effects. Sole use of older antipsychotics unaccompanied by anticholinergic drugs seems difficult to justify.
Girard TD, Exline MC, Carson SS, et al. Haloperidol and ziprasidone for treatment of **delirium in critical illness**. (MIND-USA) N Engl J Med. DOI: 10.1056/NEJMoa1808217.
Gopalakrishnan R, et al. **Sildenafil** in the treatment of antipsychotic-induced erectile dysfunction: a randomized, double-blind, placebo-controlled, flexible-dose, two-way crossover trial. Am J Psychiatry. 2006 Mar;163(3):494-9.
Goetz CG, Blasucci LM, Leurgans S, Pappert EJ. Olanzapine and clozapine: comparative effects on motor function in hallucinating PD patients. Neurology 2000;55:789-94.
Gold JM, Waltz JA, Matveeva TM, et al. Negative symptoms and the failure to represent the **expected reward value of actions**: behavioral and computational modeling evidence. Arch Gen Psychiatry. 2012 Feb;69(2):129-38
Goodwin GM, Consensus Group of the British Association for Psychopharmacology. Evidence-based guidelines for treating **bipolar disorder**: revised second edition—recommendations from the British Association for Psychopharmacology. J Psychopharmacol [Internet]. June 2009 [cited 2011 Feb 18]; 23(4):346-388. Available from: http://www.bap.org.uk/pdfs/Bipolar_guidelines.pdf
Gorczynski P, Faulkner G. **Exercise therapy** for schizophrenia. Cochrane Database Syst Rev. 2010 May 12;5:CD004412. Results of this Cochrane review are similar to existing reviews that have examined the health benefits of exercise in this population.
Gøtzsche PC, Young AH, Crace J. Does long term use of **psychiatric drugs cause more harm than good**? BMJ. 2015 May 12;350:h2435.
Graff-Guerrero A, Rajji TK, Mulsant BH, et al. Evaluation of **antipsychotic dose reduction in late-life schizophrenia**: a prospective dopamine D2/3 receptor occupancy study. JAMA Psychiatry 2015;72:927–34.
Graham KA, Gu H, Lieberman JA, et al. Double-blind, placebo-controlled investigation of **amantadine** for weight loss in subjects who gained weight with **olanzapine**. Am J Psychiatry. 2005 Sep;162(9):1744-6. n=21
Grant PM, Huh GA, Perivoliotis D, et al. Randomized trial to evaluate the efficacy of **cognitive therapy** for low-functioning patients with schizophrenia [online October 3, 2011]. Arch Gen Psychiatry. 2012;69 (2):121-127.
Gray R, et al. **Adherence therapy** for people with schizophrenia: European multicentre randomised controlled trial. Br J Psychiatry. 2006 Dec;189:508-514. This effectiveness trial provides evidence for the lack of effect of adherence therapy in people with schizophrenia with recent clinical instability, treated in ordinary clinical settings.
Green MF, Marder SR, Glynn SM, McGurk SR, Wirshing WC, Wirshing DA, et al. The neurocognitive effects of low-dose haloperidol: a two-year comparison with risperidone. Biol Psychiatry. 2002 Jun 15;51(12):972-8.
Green CA, Yarborough BJ, Leo MC, et al. The **STRIDE** Weight Loss and Lifestyle Intervention for Individuals **Taking Antipsychotic Medications**: A Randomized Trial. Am J Psychiatry. 2014 Sep 15.
Gründer G, Heinze M, Cordes J, et al. Effects of **first-generation antipsychotics versus second-generation** antipsychotics on quality of life in schizophrenia: a double-blind, randomised study. Lancet Psychiatry. 2016 Jun 2.
Gunderson John G., **Borderline Personality Disorder**. N Engl J Med 2011; 364:2037-2042.

Guo JJ, et al. Risk of **diabetes mellitus** associated with **atypical antipsychotic** use among patients with bipolar disorder: A retrospective, population-based, case-control study. J Clin Psychiatry. 2006 Jul;67(7):1055-61. Compared to patients receiving conventional antipsychotics, the risk of diabetes was greatest among patients taking clozapine (hazard ratio [HR] = 7.0, 95% confidence interval [CI] = 1.7 to 28.9), risperidone (HR = 3.4, 95% CI = 2.8 to 4.2), olanzapine (HR = 3.2, 95% CI = 2.7 to 3.8), and quetiapine (HR = 1.8, 95% CI =1.4 to 2.4), with controlling covariates of age; sex; duration of follow-up; use of lithium, anticonvulsants, antidepressants, or concomitant drugs; and psychiatric and medical comorbidities.

Guo X, et al. Effect of Antipsychotic Medication Alone vs Combined With **Psychosocial Intervention** on Outcomes of Early-Stage Schizophrenia: A Randomized, 1-Year Study. Arch Gen Psychiatry. 2010 Sep;67(9):895-904.

Gurvich T, Cunningham JA. Appropriate use of psychotropic drugs in nursing homes. Am Fam Physician 2000;61:1437-46.

Gurwitz JH, Bonner A, Berwick DM. Reducing **Excessive Use of Antipsychotic Agents in Nursing Homes**. JAMA. 2017 Jun 15.

Haddad P. **Weight** change with atypical antipsychotics in the treatment of schizophrenia. J Psychopharmacol. 2005 Nov;19(6 Suppl):16-27.

Hägg S, Bate A, Stahl M, Spigset O. Associations between **venous thromboembolism** and antipsychotics. A study of the WHO database of adverse drug reactions. Drug Saf. 2008;31(8):685-94.

Hallak JE, Maia-de-Oliveira JP, et al. Rapid Improvement of Acute Schizophrenia Symptoms After Intravenous **Sodium Nitroprusside**: A Randomized, Double-blind, Placebo-Controlled Trial. JAMA Psychiatry. 2013 May 8:1-9.

Hampton LM, Daubresse M, Chang HY, et al. **Emergency Department Visits** by Adults for Psychiatric Medication Adverse Events. JAMA Psychiatry. 2014 Jul 9.

Hartling L, Abou-Setta AM, Dursun S, et al. Antipsychotics in Adults With Schizophrenia: Comparative Effectiveness of **First-Generation Versus Second-Generation Medications**: A Systematic Review and Meta-analysis. Ann Intern Med. 2012 Aug 14. Clear benefits of FGAs versus SGAs for treating schizophrenia remain inconclusive because of variation in assessing outcomes and lack of clinically important differences for most comparisons. The strength of evidence on safety for major medical events is low or insufficient.

Haslemo T, et al. The effect of variable **cigarette** consumption on the interaction with **clozapine** and **olanzapine**. Eur J Clin Pharmacol. 2006 Nov 7; [Epub ahead of print] A daily consumption of 7-12 cigarettes is probably sufficient for maximum induction of clozapine and olanzapine metabolism. A 50% lower starting dose of both drugs in non-smokers seems rational to avoid side effects.

Haupt DW, et al. Prevalence and predictors of **lipid and glucose monitoring** in commercially insured patients treated with second-generation antipsychotic agents. Am J Psychiatry. 2009 Mar;166(3):345-53. Epub 2009 Jan 15.

Hauser RA, Factor SA, Marder SR, et al. KINECT 3: A Phase 3 Randomized, Double-Blind, Placebo-Controlled Trial of **Valbenazine** for Tardive Dyskinesia. Am J Psychiatry. 2017 May 1;174(5):476-484

Health Canada Mar/11 **Salvia divinorum** (S. divinorum) is a species of sage belonging to the mint family. Some street names for S. divinorum include: Sally D, Lady Sally, Maria pastora, ska Maria pastora, ska pastora, diviner's sage, magic mint, puff, incense special, and salvia. Canadians are cautioned against the use of products containing S. divinorum and/or salvinorin A because these products are known to cause hallucinations and little is known about the long-term effects of these substances on the brain and body.

Health Canada June/11 Antipsychotic drugs: Labelling update regarding the risk of abnormal **muscle movements and withdrawal symptoms in newborns** exposed during pregnancy.

Health Canada Nov/13 **Risperidone- and paliperidone**-containing products are primarily prescribed for the treatment of schizophrenia; however, the risk of Intraoperative floppy iris syndrome (**IFIS**) applies to all patients undergoing cataract surgery, who have been exposed to these products, irrespective of indication.

Health Canada Feb/15 **Risperidone** - Restriction of the Dementia Indication - Janssen Inc. The indication for risperidone in dementia has been restricted to the **short-term symptomatic management of aggression or psychotic symptoms in patients with severe dementia of the Alzheimer type**. The indication no longer includes the treatment of other types of dementia.

Health Canada Nov/15 Safety information for antipsychotic drug **Abilify and risk of certain impulse-control behaviours**.

Health Canada Sep/16 is recommending that the product labelling for all nine **atypical antipsychotics** be updated to emphasize the risk of **sleep apnea**.

Helfer B, Samara MT, Huhn M, et al. **Efficacy and safety of antidepressants added to antipsychotics for schizophrenia**: a systematic review and meta-analysis. Am J Psychiatry. 2016;173:876-886.

Hemager N, Plessen KJ, Thorup A, et al. Assessment of **Neurocognitive Functions** in 7-Year-Old Children at Familial **High Risk for Schizophrenia or Bipolar Disorder**: The Danish High Risk and Resilience Study VIA 7. JAMA Psychiatry. 2018 Jun 20.

Henderson DC, Copeland PM, Daley TB, et al. A double-blind, placebo-controlled trial of sibutramine for olanzapine-associated weight gain. Am J Psychiatry. 2005 May;162(5):954-62. (n=37 112weeks)

Hennen J, Baldessarini RJ. **Suicidal risk during treatment with clozapine**: a meta-analysis. Schizophr Res. 2005 Mar 1;73(2-3):139-45.

Heres S, Davis J, Maino K, et al. Why olanzapine beats risperidone, risperidone beats quetiapine, and quetiapine beats olanzapine: an exploratory analysis of head-to-head comparison studies of second-generation antipsychotics. Am J Psychiatry. 2006 Feb;163(2):185-94.

Hinds A, Coulter L, Hudson J, et al. **Screening for diabetes** in patients receiving second-generation atypical **antipsychotics**. Am J Health-Syst Pharm 2015;72(suppl 2):S70-3.

Hjorthøj C, Albert N, Nordentoft M. Association of **Substance Use Disorders With Conversion From Schizotypal Disorder to Schizophrenia**. JAMA Psychiatry. 2018 Apr 25.

Ho J, Panagiotopoulos C, McCrindle B, Grisaru S, Pringsheim T; **CAMESA** guideline group. Management recommendations for **metabolic complications** associated with second generation antipsychotic use in **children and youth**. J Can Acad Child Adolesc Psychiatry. 2011 Aug;20(3):234-41.

Hoang U, Stewart R, Goldacre MJ. **Mortality after hospital discharge** for people with schizophrenia or bipolar disorder: retrospective study of linked English hospital episode statistics, 1999-2006. BMJ 2011;343:d5422.

Højlund M, Pottegård A, Johnsen E, et al. Trends in **utilization and dosing of antipsychotic drugs in Scandinavia**: comparison of 2006 and 2016. Br J Clin Pharmacol. 2019 Mar 29.

Holder SD, Wayhs A. **Schizophrenia**. Am Fam Physician. 2014;90(11):775-782.

Hollander AC, Dal H, Lewis G, Magnusson C, Kirkbride JB, Dalman V. **Refugee migration** and risk of schizophrenia and other non-affective psychoses: cohort study of 1.3 million people in Sweden. BMJ 2016;352:i1030.

Holt RI, Hind D, Gossage-Worrall R, et al. Structured **lifestyle education to support weight loss for people with schizophrenia, schizoaffective disorder and first episode** psychosis: the STEPWISE RCT. Health Technol Assess. 2018 Nov;22(65):1-160.

Honer WG, et al. Clozapine and Risperidone Enhancement (CARE) Study Group. Clozapine alone versus **clozapine and risperidone** with refractory schizophrenia. N Engl J Med. 2006 Feb 2;354(5):472-82. CONCLUSIONS: In this short-term study, the addition of risperidone to clozapine did not improve symptoms in patients with severe schizophrenia.

Hong LE, Thaker GK, McMahon RP, et al. Effects of moderate-dose treatment with **varenicline** on neurobiological and cognitive biomarkers in smokers and nonsmokers with schizophrenia or schizoaffective disorder. Arch Gen Psychiatry. 2011;68:1195-206.

Honkaniemi J, et al. **Haloperidol** in the **acute treatment of migraine**: a randomized, double-blind, placebo-controlled study. Headache. 2006 May;46(5):781-7.

Honkola J, Hookana E, Malinen S, et al. Psychotropic medications (antipsychotics & antidepressants) and the **risk of sudden cardiac death** during an acute coronary event. Eur Heart J. 2012 Mar;33(6):745-51.

Hosalli P, Davis JM. **Depot risperidone** for schizophrenia. Cochrane Database Syst Rev. 2003;(4):CD004161.

Hough DW, Natarajan J, Vandebosch A, et al. Evaluation of the effect of **paliperidone** extended release and **quetiapine** on corrected QT intervals: a randomized, double-blind, placebo-controlled study. Int Clin Psychopharmacol. 2010 Sep 28.

Howard R, Costafreda SG, Karcher K, et al. Baseline characteristics and treatment-emergent risk factors associated with **cerebrovascular event and death** with **risperidone** in dementia patients. Br J Psychiatry. 2016 Jul 7.

Howes OD, Kambeitz J, Kim E, et al. The Nature of **Dopamine Dysfunction** in Schizophrenia and What This Means for Treatment: Meta-analysis of Imaging Studies. Arch Gen Psychiatry. 2012 Apr 2.

Howes OD, Murray RM. Schizophrenia: an integrated **sociodevelopmental-cognitive model**. Lancet. 2013 Dec 5

Howes O, Kane J, et al. **Treatment resistant schizophrenia**: Treatment Response and Resistance in Psychosis (**TRIPP**) working group consensus guidelines on diagnosis and terminology Am J Psychiatry. 2017;174(3):216-229.

Hoy SM, Scott LJ, Keating GM. **Intramuscular paliperidone palmitate**. CNS Drugs. 2010 Mar 1;24(3):227-44.

Huf G, Coutinho ES, Adams CE; TREC Collaborative Group. **Rapid tranquillisation** in psychiatric emergency settings in Brazil: pragmatic randomised controlled trial of intramuscular haloperidol versus intramuscular haloperidol plus promethazine. BMJ. 2007 Oct 22; [Epub ahead of print] **Haloperidol plus promethazine** is a better option than haloperidol alone in terms of speed of onset of action & safety. Enough data are now available to change guidelines that continue to recommend treatments that leave people exposed to longer periods of aggression than necessary and patients vulnerable to distressing and unsafe adverse effects.

Huf G, Alexander J, Gandhi P, et al. **Haloperidol plus promethazine for psychosis-induced aggression**. Cochrane Database Syst Rev. 2016 Nov 25;11:CD005146. Haloperidol plus promethazine is effective and safe, and its use is based on good evidence. Benzodiazepines work, with midazolam being particularly swift, but both midazolam and lorazepam cause respiratory depression. Olanzapine intramuscular and ziprasidone intramuscular do seem to be viable options and their action is swift, but resumption of aggression with subsequent

need to re-inject was more likely than with haloperidol plus promethazine. Haloperidol used on its own without something to offset its frequent and serious adverse effects does seem difficult to justify.
Hugenholtz GW, et al. **Haloperidol Dose When Used as Active Comparator** in Randomized Controlled Trials With Atypical Antipsychotics in Schizophrenia: Comparison With Officially Recommended Doses. J Clin Psychiatry. 2006 Jun;67(6):897-903. Compared with recommended doses for severely ill patients in both the United Kingdom and United States (range, 6-15 mg daily), in 17 studies (35%) the mean actual used dose was above the upper dose border for severely ill patients (15 mg daily).
Huhn M, Nikolakopoulou A, Schneider-Thoma J, et al. Comparative **efficacy and tolerability of 32 oral antipsychotics** for the acute treatment of adults with multi-episode schizophrenia: a systematic review and network meta-analysis. Lancet. 2019 Jul 11.
Hui CLM, Honer WG, Lee EHM, et al. Factors Associated With Successful **Medication Discontinuation After a Randomized Clinical Trial of Relapse Prevention in First-Episode Psychosis**: A 10-Year Follow-up. JAMA Psychiatry. 2018 Dec 12.
Huhn M, TardyM, Spineli LM, et al. Efficacy of **pharmacotherapy and psychotherapy** for adult psychiatric disorders: a systematic overview of meta-analyses [online April 30, 2014]. JAMA Psychiatry. doi:10.1001/jamapsychiatry.2014.112.
Hung GC, Liu HC, Yang SY, et al. **Antipsychotic reexposure and recurrent pneumonia** in schizophrenia: a nested case-control study. J Clin Psychiatry. 2015 Nov 24.
Huybrechts KF, Rothman KJ, Silliman RA., et al. **Risk of death and hospital admission** for major medical events after initiation of psychotropic medications in older adults admitted to nursing homes. CMAJ 2011 0: cmaj.101406
Huybrechts KF, Gerhard T, Crystal S, Olfson M, Avorn J, Levin R, et al. Differential risk of **death in older residents in nursing homes prescribed specific antipsychotic drugs**: population based cohort study. BMJ 2012;344:e977.
Huybrechts KF, Hernández-Díaz S, Patorno E, et al. **Antipsychotic Use in Pregnancy** and the Risk for Congenital Malformations. JAMA Psychiatry. 2016 Aug 17.
Huybrechts K, Broms G, Christensen L, et al. Association between **methylphenidate and amphtetamine use in pregnancy and risk of congenital malformations**. JAMA Psychiatry2017;(December).
Hwang YJ, Dixon SN, Reiss JP, et al. **Atypical antipsychotic** drugs and the risk for **acute kidney injury** and other adverse outcomes in older adults: a population-based cohort study. Ann Intern Med. 2014 Aug 19;161(4):242-8.
Ilies D, Huet AS, Lacourse E, et al. Long-Term **Metabolic Effects** in French-Canadian Children and Adolescents Treated with **Second-Generation Antipsychotics** in Monotherapy or Polytherapy: A 24-Month Descriptive Retrospective Study. Can J Psychiatry. 2017 Jan 1:706743717718166.
Ingenhoven T, Lafay P, Rinne T, et al. Effectiveness of pharmacotherapy for **severe personality disorders**: meta-analyses of randomized controlled trials. J Clin Psychiatry 2010; 71:14-25.
Insel TR. **RAISE**-ing our expectations for **first-episode psychosis**. Am J Psychiatry 2015 Oct 20.
Ishoy PL, Knop FK, et al. Effect of **GLP-1 receptor agonist treatment on body weight in obese antipsychotic-treated patients with schizophrenia**: a randomized, placebo-controlled trial. Diabetes Obes Metab. 2016 Sep 26.
Ising HK, Kraan TC, Rietdijk J, et al. Four-year follow-up of **cognitive behavioral therapy** in persons at ultra-high risk for developing psychosis: the Dutch Early Detection and Intervention Evaluation (EDIE-NL) trial. Schizophr Bull 2016;42:1243–52.
Iyer S, Banks N, Roy MA, et al. A qualitative study of experiences with and perceptions regarding **long-acting injectable antipsychotics**: Part I-patient perspectives. Can J Psychiatry. 2013 May;58(5 Suppl 1):14S-22S.
Jarskog LF, Hamer RM, et al; for the **METS** Investigators. **Metformin for Weight Loss** and Metabolic Control in Overweight Outpatients With Schizophrenia and Schizoaffective Disorder. Am J Psychiatry. 2013 Jul 12.
Jauhar S, Nour MM, Veronese M, et al. A test of the **transdiagnostic dopamine hypothesis** of psychosis using positron emission tomographic imaging in bipolar affective disorder and schizophrenia [online Oct 11, 2017]. JAMA Psychiatry. doi:10.1001/jamapsychiatry.2017.2943
Jayaram MB, Hosalli P, Stroup S. **Risperidone versus olanzapine** for schizophrenia. Cochrane Database Syst Rev. 2006 Apr 19;(2):CD005237.
Jeste DV, Rockwell E, Harris MJ, Lohr JB, Lacro J. Conventional vs. newer antipsychotics in elderly patients. Am J Geriatr Psychiatry 1999;7:70-6.
Jin H, Shih PA, Golshan S, et al. Comparison of longer-term safety and effectiveness of **4 atypical antipsychotics** (aripiprazole, olanzapine, quetiapine, and risperidone) in patients over age 40: a trial using equipoise-stratified randomization. J Clin Psychiatry. 2012 Nov 27.
Joffe G, Takala P, Tchoukhine E, et al.. **Orlistat** in Clozapine- or Olanzapine-Treated Patients With Overweight or Obesity: A 16-Week Randomized, Double-Blind, Placebo-Controlled Trial. J Clin Psychiatry. 2008 Mar 11;:e1-e6 [Epub ahead of print] Without a hypocaloric diet, the effect of orlistat in overweight/obese clozapine-or olanzapine-treated patients is modest and may only be seen in men.
Johnson KC, Laprairie JL, Brennan PA, et al. **Prenatal Antipsychotic Exposure and Neuromotor Performance** During Infancy. Arch Gen Psychiatry. 2012 Apr 2.
Jonas BS, Gu Q, Albertorio-Diaz JR. **Psychotropic medication use among adolescents**: United States, 2005-2010. NCHS Data Brief. 2013 Dec;(135):1-8
Jones PB, et al. Randomized controlled trial of the effect on **Quality of Life of second- vs first-generation antipsychotic** drugs in schizophrenia: Cost Utility of the Latest Antipsychotic Drugs in Schizophrenia Study (CUtLASS 1). Arch Gen Psychiatry. 2006 Oct;63(10):1079-87. In people with schizophrenia whose medication is changed for clinical reasons, there is no disadvantage across 1 year in terms of quality of life, symptoms, or associated costs of care in using FGAs rather than nonclozapine SGAs. Neither inadequate power nor patterns of drug discontinuation accounted for the result.
Jones I, Chandra PS, Dazzan P, et al. Bipolar disorder, affective psychosis, and schizophrenia in **pregnancy and the post-partum** period. Lancet. 2014 Nov 15;384(9956):1789-99.
Josephson CB, Engbers JDT, Jette N, et al. Prediction Tools for **Psychiatric Adverse Effects After Levetiracetam** Prescription. JAMA Neurol. 2019 Jan 28
Josiassen RC, et al. **Clozapine augmented with risperidone** in the treatment of schizophrenia: a randomized, double-blind, placebo-controlled trial. Am J Psychiatry. 2005 Jan;162(1):130-6.
Joy CB, Mumby-Croft R, Joy LA. **Polyunsaturated fatty acid supplementation** for schizophrenia. Cochrane Database Syst Rev. 2006 Jul 19;3:CD001257.
Judd LL, Schettler PJ, Brown ES, et al. **Adverse consequences of glucocorticoid** medication: psychological, cognitive, and behavioral effects. Am J Psychiatry. 2014 Oct 1;171(10):1045-51.
Juncos JL. Management of psychotic aspects of Parkinson's Disease. J Clin Psychiatry 1999;60 (suppl 8); 42-53.
Kahn RS, Fleischhacker WW, Boter H, et al. EUFEST study group. Effectiveness of antipsychotic drugs in **first-episode schizophrenia** and schizophreniform disorder: an open randomised clinical trial. Lancet. 2008 Mar 29;371(9618):1085-97. This pragmatic trial suggests that clinically meaningful antipsychotic treatment of first-episode of schizophrenia is achievable, for at least 1 year. However, we cannot conclude that second-generation drugs are more efficacious than is haloperidol, since discontinuation rates are not necessarily consistent with symptomatic improvement.
Kales HC , Kim HM, Zivin K, Valenstein M, Seyfried LS, Chiang C , Cunningham F, Schneider LS, Blow FC: Risk of **mortality among individual antipsychotics** in patients with **dementia**. Am J Psychiatry 2011; 168:71–79.
Kalisvaart KJ, de Jonghe JF, Bogaards MJ, et al. **Haloperidol** prophylaxis for elderly hip-surgery patients at risk for **delirium**: a randomized placebo-controlled study. J Am Geriatr Soc. 2005 Oct;53(10):1658-66. (InfoPOEMs: Low-dose haloperidol was no more effective than placebo in preventing delirium in elderly patients undergoing hip surgery. However, when delirium occurred, it was milder and shorter in patients receiving haloperidol. Furthermore, haloperidol shortened the hospital length of stay among patients who became delirious. (LOE = 1b-))
Kaltsatou A, Kouidi E, Fountoulakis K, et al. Effects of **exercise training with traditional dancing** on functional capacity and quality of life in patients with schizophrenia: randomized controlled study. Clin Rehabil. 2014 Dec 18.
Kamble P, Chen H, Sherer JT, et al. Use of antipsychotics among elderly nursing home residents with dementia in US: an analysis of National Survey Data. Drugs Aging.2009;26(6):483-92.doi:10.2165/00002512-200926060-00005.
Kaminsky BM, Bostwick JR, Guthrie SK. **Alternate Routes of Administration** (intranasal, sublingual, transdermal) of Antidepressant and **Antipsychotic** Medications. Ann Pharmacother. 2015 Jul;49(7):808-17.
Kane JM, Detke HC, Naber D, et al. **Olanzapine Long-Acting Injection**: A 24-Week, Randomized, Double-Blind Trial of Maintenance Treatment in Patients With Schizophrenia. Am J Psychiatry. . [Epub ahead of print]
Kane JM, et al. **Aripiprazole intramuscular depot** as maintenance treatment in patients with schizophrenia: a 52-week, multicenter, randomized, double-blind, placebo-controlled study. J Clin Psychiatry. 2012 May;73(5):617-24.
Kane JM, Robinson DG, Schooler NR, et al. **Comprehensive Versus Usual Community Care for First-Episode Psychosis**: 2-Year Outcomes From the **NIMH RAISE Early Treatment Program**. Am J Psychiatry. 2015 Oct 20.
Kaneriya SH, Robbins-Welty GA, Smagula SF, et al. Predictors and Moderators of Remission With **Aripiprazole Augmentation** in Treatment-Resistant Late-Life **Depression**: An Analysis of the IRL-GRey Randomized Clinical Trial. JAMA Psychiatry. 2016 Apr 1
Kaplan J, Shah P, Faley B, Siegel ME. Case Reports of Aripiprazole Causing False-Positive Urine Amphetamine Drug Screens in Children. Pediatrics. 2015 Nov 2.
Karcher NR, Barch DM, Demers CH, et al. Genetic Predisposition vs Individual-Specific Processes in the Association Between **Psychotic-like Experiences and Cannabis** Use. JAMA Psychiatry. 2018 Oct 17.
Katila H, Mezhebovsky I, Mulroy A, et al. Randomized, Double-Blind Study of the Efficacy and Tolerability of **Extended Release Quetiapine** Fumarate (Quetiapine XR) Monotherapy in Elderly Patients With Major **Depressive**

Disorder. Am J Geriatr Psychiatry. 2012 Jun 7.
Katz IR, Jeste DV, et al.. Comparison of risperidone & placebo for psychosis & behavioral disturbances associated with dementia: a randomized, double-blind trial. Risperidone Study Group. J Clin Psychiatry 1999;60:107-15.
Keefe RS, Seidman LJ, Christensen BK, et al. Comparative effect of atypical and conventional antipsychotic drugs on **neurocognition** in first-episode psychosis: a randomized, double-blind trial of olanzapine versus low doses of haloperidol. Am J Psychiatry. 2004 Jun;161(6):985-95.
Keefe RS, Bilder RM, Davis SM, Harvey PD, et al. **Neurocognitive Effects of Antipsychotic** Medications in Patients With Chronic Schizophrenia in the **CATIE** Trial. Arch Gen Psychiatry. 2007 Jun;64(6):633-47. After 2 months of antipsychotic treatment, all groups had a small but significant improvement in neurocognition. There were no differences between any pair of agents, including the typical drug perphenazine.
Keefe RSE, Davis VG, Harvey PD, et al. **Placebo Response and Practice Effects in Schizophrenia Cognition Trials**. JAMA Psychiatry. 2017 Jun 21.
Kelly DL, Conley RR. A randomized double-blind 12-week study of quetiapine, risperidone or fluphenazine on **sexual functioning** in people with schizophrenia. Psychoneuroendocrinology. 2005 Sep 27; [Epub ahead of print]
Kennedy J, Deberdt W, Siegal A, et al. **Olanzapine does not enhance cognition** in non-agitated and non-psychotic patients with mild to moderate Alzheimer's dementia. Int J Geriatr Psychiatry. 2005 Nov;20(11):1020-7.
Keers R et al. Association of **violence with emergence of persecutory delusions** in untreated schizophrenia. Am J Psychiatry 2013 Nov 13.
Kessing LV, Thomsen AF, Mogensen UB, Andersen PK. Treatment with antipsychotics and the **risk of diabetes** in clinical practice. Br J Psychiatry. 2010 Oct;197(4):266-71.
Khan A, Faucett J, Morrison S, Brown WA. **Comparative Mortality Risk** in Adult Patients With Schizophrenia, Depression, Bipolar Disorder, Anxiety Disorders, and Attention-Deficit/Hyperactivity Disorder Participating in Psychopharmacology Clinical Trials. JAMA Psychiatry. 2013 Aug 28.
Khanna P, Suo T, Komossa Ket al. **Aripiprazole** versus other atypical antipsychotics for schizophrenia. Cochrane Database Syst Rev. 2014 Jan 2;(1):CD006569. Information on all comparisons is of limited quality, is incomplete and problematic to apply clinically. The quality of the evidence is all low or very low. Aripiprazole is an antipsychotic drug with an important adverse effect profile. Long-term data are sparse and there is considerable scope for another update of this review as new data emerge from ongoing larger, independent pragmatic trials.
Kindermann SS, Dolder CR, Bailey A, Katz IR, Jeste DV. Pharmacological treatment of psychosis and agitation in elderly patients with dementia: four decades of experience. Drugs Aging. 2002;19(4):257-76.
Kinon BJ, et al. Randomized, Double-blind 6-Month Comparison of **Olanzapine and Quetiapine** in Patients With Schizophrenia or Schizoaffective Disorder With Prominent Negative Symptoms and Poor Functioning. J Clin Psychopharmacol. 2006 Oct;26(5):453-461.
Kinon BJ, Ahl J, Stauffer VL, Hill AL, Buckley PF. Dose response and atypical antipsychotics in schizophrenia. CNS Drugs. 2004;18(9):597-616.
Kirkham J, Sherman C, Velkers C, et al. **Antipsychotic Use in Dementia**. Can J Psychiatry. 2017 Mar;62(3):170-181.
Kisely S, Smith M, Lawrence D, Maaten S. **Mortality** in individuals who have had psychiatric treatment: Population-based study in Nova Scotia. Br J Psychiatry. 2005 Dec;187:552-558.
Kisely S, Preston N, Xiao J, et al. Reducing all-cause **mortality among patients with psychiatric disorders**: a population-based study. CMAJ. 2013 Jan 8;185(1):E50-6.
Kishi T, Hirota T, Matsunaga S, et al. **Antipsychotic medications for the treatment of delirium**: a systematic review and meta-analysis of randomised controlled trials. J Neurol Neurosurg Psychiatry. 2015 Sep 4.
Kleijer BC, Koek HL, van Marum RJ, et al. Risk of **acute coronary syndrome** in elderly users of antipsychotic drugs: a nested case-control study. Heart. 2012 Jun 11.
Klein LR, Driver BE, Horton G, et al. **Rescue Sedation When Treating Acute Agitation** in the Emergency Department With Intramuscular Antipsychotics. J Emerg Med. 2019 Feb 8.
Klein LR, Driver BE, Miner JR, et al. **Intramuscular Midazolam, Olanzapine, Ziprasidone, or Haloperidol for Treating Acute Agitation in the Emergency Department**. Ann Emerg Med. 2018 Oct;72(4):374-385.
Knapp P, Chait A, Pappadopulos E, et al. Treatment of **Maladaptive Aggression in Youth**: CERT Guidelines I. Engagement, Assessment, and Management. Pediatrics. 2012 May 28.
Knol W, van Marum RJ, Jansen PA, et al. Antipsychotic Drug Use and Risk of **Pneumonia** in Elderly People. J Am Geriatr Soc. 2008 Feb 7; [Epub ahead of print] Use of antipsychotics in elderly people is associated with greater risk of pneumonia. This risk is highest shortly after the initiation of treatment, with the greatest increase in risk found for atypical antipsychotics.
Kochunov P, Coyle TR, Rowland LM, et al. Association of **White Matter** With Core **Cognitive Deficits** in Patients With **Schizophrenia**. JAMA Psychiatry. 2017 Aug 2.
Köhler-Forsberg O, Petersen L, Gasse C, et al. A nationwide study in Denmark of the association between **treated infections and the subsequent risk of treated mental disorders** in children and adolescents [online Dec 5, 2018]. JAMA Psychiatry. doi:10.1001/jamapsychiatry.2018 .3428
Komossa K, Rummel-Kluge C, Hunger H, et al. **Ziprasidone** versus other atypical antipsychotics for schizophrenia. Cochrane Database Syst Rev. 2009 Oct 7;(4):CD006627. Ziprasidone may be a slightly less efficacious antipsychotic drug than amisulpride, olanzapine and risperidone. Its main advantage is the low propensity to induce weight gain and associated adverse effects.
Komossa K, Rummel-Kluge C, Hunger H, Schmid F, Schwarz S, Duggan L, Kissling W, Leucht S. **Olanzapine versus other atypical antipsychotics for schizophrenia**. Cochrane Database Syst Rev. 2010 Mar 17;(3):CD006654.
Komossa K, Rummel-Kluge C, Schmid F, Hunger H, Schwarz S, et al. **Quetiapine** versus other atypical antipsychotics for schizophrenia. Cochrane Database Syst Rev. 2010 Jan 20;(1):CD006625.
Komossa K, Rummel-Kluge C, Schmid F, Hunger H, Schwarz S, El-Sayeh HG, Kissling W, Leucht S. **Aripiprazole** versus other atypical antipsychotics for schizophrenia. Cochrane Database Syst Rev. 2009 Oct 7;(4):CD006569.
Komossa K, Depping AM, Gaudchau A, et al. **Second-generation antipsychotics for major depressive** disorder and dysthymia. Cochrane Database Syst Rev. 2010 Dec 8;12:CD008121
Komossa K, Depping AM, Meyer M, et al. **Second-generation antipsychotics** for **obsessive compulsive disorder**. Cochrane Database Syst Rev. 2010 Dec 8;12:CD008141. The available data of the effects of olanzapine in OCD are too limited to draw any conclusions. There is some evidence that adding quetiapine or risperidone to antidepressants increases efficacy, but this must be weighed against less tolerability and limited data.
Komossa K, Rummel-Kluge C, Schwarz S, et al. **Risperidone** versus other atypical antipsychotics for schizophrenia. Cochrane Database Syst Rev. 2011 Jan 19;1:CD006626. Risperidone seems to produce somewhat more extrapyramidal side effects and clearly more prolactin increase than most other SGAs. It may also differ from other compounds in efficacy and in the occurrence of other adverse effects such as weight gain, metabolic problems, cardiac effects, sedation and seizures. Nevertheless, the large proportion of participants leaving studies early and incomplete reporting of outcomes makes it difficult to draw firm conclusions.
Kontaxakis VP, et al. **Risperidone augmentation** of clozapine : A critical review. Eur Arch Psychiatry Clin Neurosci. 2006 Aug 8; [Epub ahead of print]
Köpke S, Mühlhauser I, Gerlach A, et al. Effect of a guideline-based **multicomponent intervention on use of physical restraints** in nursing homes: a randomized controlled trial. JAMA. 2012 May 23;307(20):2177-84.
Koponen M, Taipale H, et al. Risk of **Mortality Associated** with **Antipsychotic Monotherapy and Polypharmacy** Among Community-Dwelling Persons with Alzheimer's Disease. J Alzheimers Dis. 2017;56(1):107-118.
Krakowski MI, et al. Atypical antipsychotic agents in the treatment of violent patients with schizophrenia and schizoaffective disorder. Arch Gen Psychiatry. 2006 Jun;63(6):622-9. Clozapine shows greater efficacy than olanzapine and olanzapine greater efficacy than haloperidol in reducing aggressive behavior. This antiaggressive effect appears to be separate from the antipsychotic and sedative action of these medications.
Kreinin A, Miodownik C, Mirkin V, et al. Double-blind randomized, placebo-controlled trial of **metoclopramide** for **hypersalivation** associated with **clozapine**. J Clin Psychopharmacol 2016;36:200–5.
Kreider AR, Matone M, Bellonci C, et al. Growth in the concurrent use of antipsychotics with other **psychotropic medications in medicaid-enrolled children**. J Am Acad Child Adolesc Psychiatry. 2014 Sep;53(9):960-970.e2.
Kronenfeld N, Ziv Baran T, Berlin M, et al. **Chronic use of psychotropic medications in breastfeeding women**: Is it safe? PLoS One. 2018 May 21;13(5):e0197196.
Kryzhanovskaya LA, et al. Comparison of Long-Term (At Least 24 Weeks) **Weight Gain** and Metabolic Changes Between **Adolescents and Adults Treated with Olanzapine**. J Child Adolesc Psychopharmacol. 2012 Feb 28.
Kugathasan P, Horsdal HT, Aagaard J, et al. Association of **secondary preventive cardiovascular treatment** after myocardial infarction with mortality among patients with **schizophrenia** [published online October 24, 2018]. JAMA Psychiatry. doi:10.1001/jamapsychiatry.2018.2742
Kunitomi T, Hashiguchi M, Mochizuki M. Indirect comparison analysis of efficacy and safety between **olanzapine and aripiprazole** for schizophrenia. Br J Clin Pharmacol. 2013 Aug 7.
Kurlan R. Clinical practice. **Tourette's Syndrome**. N Engl J Med. 2010 Dec 9;363(24):2332-8.
Krystal JH et al. Adjunctive **risperidone** treatment for antidepressant-resistant symptoms of chronic military service–related PTSD: randomized trial. JAMA 2011 Aug 3. (ineffective)
Kuipers E, Yesufu-Udechuku A, Taylor C, et al. Management of **psychosis and schizophrenia in adults**: summary of updated **NICE** guidance. BMJ. 2014 Feb 12;348:g1173.
Kulkarni J, Worsley R, Gilbert H, et al. A prospective cohort study of **antipsychotic medications in pregnancy**: the first 147 pregnancies and 100 one year old babies. PLoS One. 2014 May 2;9(5):e94788.
Lacey M, Jayaram MB. **Zuclopenthixol versus placebo for schizophrenia**. Cochrane Database of Systematic Reviews 2015, Issue 12. Art. No.: CD010598. DOI: 10.1002/14651858.CD010598.pub2. For people with schizophrenia this review shows that zuclopenthixol dihydrochloride may help with the symptoms of schizophrenia. The review provides some trial evidence that, if taking zuclopenthixol dihydrochloride, people may experience some adverse effects and sedation compared with placebo. However this evidence is of very low quality and with some significant sources of bias. There are no data for zuclopenthixol decanoate or zuclopenthixol acetate. For clinicians, the available trial data on the absolute effectiveness of zuclopenthixol dihydrochloride do support its use but the limited nature of the data and significant sources of bias make conclusions hard to draw. Zuclopenthixol in all three forms is a commonly used antipsychotic and it is disappointing that there are so few data regarding its use.

Lally J, Ajnakina O, Stubbs B, et al. **Remission and recovery from first-episode psychosis in adults:** systematic review and meta-analysis of long-term outcome studies. Br J Psychiatry. 2017 Dec;211(6):350-358.

Lam M, Lee J, Rapisardo A, et al. Longitudinal **cognitive changes in young individuals at ultrahigh risk for psychosis** [online July 25, 2018]. JAMA Psychiatry. doi:10.1001/jamapsychiatry.2018.1668

Lambert BL, et al. **Diabetes risk** associated with use of **olanzapine**, **quetiapine**, and **risperidone** in veterans health administration patients with schizophrenia. Am J Epidemiol. 2006 Oct 1;164(7):672-81. Epub 2006 Aug 30. With patients initiating haloperidol use designated the reference group, diabetes risk was increased equally with new use of olanzapine (hazard ratio (HR) = 1.64, 95% confidence interval (CI): 1.22, 2.19), risperidone (HR = 1.60, 95% CI: 1.19, 2.14), or quetiapine (HR = 1.67, 95% CI: 1.01, 2.76).

Lamberti JS, Olson D, Crilly JF, Olivares T, Williams GC, Tu X, Tang W, Wiener K, Dvorin S, Dietz MB. Prevalence of the metabolic syndrome among patients receiving **clozapine**. Am J Psychiatry. 2006 Jul;163(7):1273-6.

Lambert C, Panagiotopoulos C, Davidson J, et al. **Second-generation antipsychotics in children**: Risks and monitoring needs. Can Fam Physician. 2018 Sep;64(9):660-662.

Larsen JR, Vedtofte L, Jakobsen MSL, et al. Effect of **Liraglutide** Treatment on Prediabetes and Overweight or Obesity in **Clozapine- or Olanzapine-Treated Patients** With Schizophrenia Spectrum Disorder: A Randomized Clinical Trial. JAMA Psychiatry. 2017 Jun 10.

Lawrence D, Hancock KJ, Kisely S. The gap in **life expectancy from preventable physical illness in psychiatric patients** in Western Australia: retrospective analysis of population based registers. BMJ. 2013 May 21;346:f2539.

Lecomte T, Abidi S, Garcia-Ortega I, et al. **Canadian Treatment Guidelines on Psychosocial Treatment of Schizophrenia in Children and Youth**. Can J Psychiatry. 2017 Sep;62(9):648-655.

Lerner V, Miodownik C, Kaptsan A, et al. **Vitamin B6 treatment for tardive dyskinesia**: a randomized, double-blind, placebo-controlled, crossover study. J Clin Psychiatry. 2007 Nov;68(11):1648-54. Vitamin B(6) 1200mg/d appears to be effective in reducing symptoms of TD. The specific mechanisms by which vitamin B(6) attenuates symptoms of TD are not clear.

Lee PE, Sykora K, Gill SS, Mamdani M et al. Antipsychotic medications & drug-induced **movement disorders** other than parkinsonism: a population-based cohort study in older adults. J Am Geriatr Soc. 2005 Aug;53(8):1374-9.

Leong C, Raymond C, Château D, et al. **Psychotropic Drug Use before, during, and after Pregnancy**: A Population-Based Study in a Canadian Cohort (2001-2013). Can J Psychiatry. 2017 Aug;62(8):543-550.

Leopold NA. Risperidone Treatment of Drug Related Psychosis in Patients with Parkinsomism. Movement Disorders 2000;15(1):301-304.

Lepping P, Huber M, Freudenmann RW. How to approach **delusional infestation**. BMJ. 2015 Apr 1;350:h1328.

Leslie DL, Rosenheck RA. Incidence of newly diagnosed diabetes attributable to atypical antipsychotic medications. Am J Psychiatry. 2004 Sep;161(9):1709-11.

Leucht S, Wahlbeck K, Hamann J, Kissling W. New generation antipsychotics versus low-potency conventional antipsychotics: a systematic review and **meta-analysis**. Lancet. 2003 May 10;361(9369):1581-9.

Leucht S, Corves C, Arbter D, Engel RR, Li C, Davis JM. **Second-generation versus first-generation** antipsychotic drugs for schizophrenia: a meta-analysis.Lancet. 2009 Jan 3;373(9657):31-41. Epub 2008 Dec 6. Second-generation antipsychotic drugs differ in many properties and are not a homogeneous class. This meta-analysis provides data for individualised treatment based on efficacy, side-effects, and cost.

Leucht S, Komossa K, Rummel-Kluge C, Corves C, Hunger H, Schmid F, Lobos CA, Schwarz S, Davis JM. A Meta-Analysis of Head-to-Head **Comparisons of Second-Generation** Antipsychotics in the Treatment of Schizophrenia. Am J Psychiatry. 2008 Nov 17. [Epub ahead of print] The findings suggest that some second-generation antipsychotics may be somewhat more efficacious than others, but the limitations of meta-analysis must be considered. In tailoring drug treatment to the individual patient, small efficacy superiorities must be weighed against large differences in side effects and cost.

Leucht S, Hierl S, Kissling W et al. Putting the efficacy of **psychiatric and general medicine medication into perspective**: review of meta-analyses. Br J Psychiatry. 2012 Feb;200:97-106.

Leucht S, Tardy M, Komossa K, et al. **Antipsychotic drugs versus placebo for relapse prevention in schizophrenia**: a systematic review and meta-analysis. Lancet 2012; published online May 3.

Leucht S, Tardy M, Komossa K, et al. **Maintenance treatment** with **antipsychotic drugs** for schizophrenia. Cochrane Database of Systematic Reviews 2012, Issue 5. Art. No.: CD008016. The results clearly demonstrate the superiority of antipsychotic drugs compared to placebo in preventing relapse. This effect must be weighed against the side effects of antipsychotic drugs.

Leucht S, Cipriani A, Spineli L, et al. **Comparative efficacy and tolerability of 15 antipsychotic drugs** in schizophrenia: a multiple-treatments meta-analysis. Lancet 2013; online June 27.

Leucht S, et al. **Sixty Years of Placebo-Controlled Antipsychotic Drug Trials in Acute Schizophrenia**: Systematic Review, Bayesian Meta-Analysis, and Meta-Regression of Efficacy Predictors. Am J Psychiatry. 2017 May 25.

Leung Jonathan G, Breden Ericka L. **Tetrabenazine for the Treatment of Tardive Dyskinesia.** Articles Ahead of Print published on 1 April 2011, DOI 10.1345/aph.1P312. Ann Pharmacother ;45:525-531.

Leung JG, Puri NV, Jacobson MJ. Immediate-release **oxybutynin for the treatment of clozapine-induced sialorrhea**. Ann Pharmacother. 2011 Sep;45(9):e45.

Li C, Xia J, Wang J. **Risperidone** dose for schizophrenia. Cochrane Database Syst Rev. 2009;(4).

Lichtenstein P, Yip BH, Bjork C, et al. **Common genetic determinants of schizophrenia and bipolar disorder in Swedish families: a population-based study.** Lancet. 2009 Jan **17;373(9659):234-239.** Similar to molecular genetic studies, we showed evidence that schizophrenia and bipolar disorder partly share a common genetic cause. These results challenge the current nosological dichotomy between schizophrenia and bipolar disorder, and are consistent with a reappraisal of these disorders as distinct diagnostic entities.

Lieb K, Völlm B, Rücker G, Timmer A, Stoffers JM. Pharmacotherapy for **borderline personality disorder**: Cochrane systematic review of randomised trials. Br J Psychiatry 2010;196:4-12.

Lieberman JA, First MB. **Psychotic Disorders**. N Engl J Med. 2018 Jul 19;379(3):270-280.

Lieberman JA, Stroup TS, McEvoy JP, et al.; Clinical Antipsychotic Trials of Intervention Effectiveness (**CATIE**) Investigators. Effectiveness of **antipsychotic drugs in patients with chronic schizophrenia**. N Engl J Med. 2005 Sep 22;353(12):1209-23. Epub 2005 Sep 19. & see also Pharmacist Letter Nov/05. CONCLUSIONS: The majority of patients in each group discontinued their assigned treatment owing to inefficacy or intolerable side effects or for other reasons. **Olanzapine** was the most effective in terms of the rates of discontinuation, and the efficacy of the conventional antipsychotic agent **perphenazine appeared similar to that of quetiapine, risperidone, and ziprasidone**. **Olanzapine** was associated with greater weight gain and increases in measures of glucose and lipid metabolism. (n=1493 over 18 months; average age 40yrs; not studied was aripiprazole & clozapine) (InfoPOEMs: There are few differences among newer antipsychotics & few differences between newer agents and perphenazine, an older agent. Olanzapine seems to offer somewhat greater effectiveness, but is less well tolerated & can produce adverse changes to physiologic end points. All the newer antipsychotics are also much more expensive, which is a concern for this vulnerable group of patients. Based on its similar efficacy and better-than-expected tolerability, perphenazine at a dose of up to 20 mg per day should remain a treatment option for psychosis. (LOE = 1b))

Lieberman JA, Dixon LB, Goldman HH. **Early detection and intervention in schizophrenia**: a new therapeutic model. JAMA. 2013 Aug 21;310(7):689-90.

Lin ST, Chen CC, Tsang HY, et al. Association between **antipsychotic use and risk of acute myocardial infarction**: a nationwide case-crossover study. Circulation. 2014 Jul 15;130(3):235-43.

Liperoti R, Pedone C, Lapane KL, et al. **Venous Thromboembolism** Among Elderly Patients Treated With **Atypical** and Conventional Antipsychotic Agents. Arch Intern Med. 2005 Dec 12;165(22):2677-2682.

Lipscombe LL, Levesque L, Gruneir A, et al. **Antipsychotic drugs and hyperglycemia** in older patients with diabetes. Arch Intern Med. 2009 Jul 27;169(14):1282-9.

Liu XI, Schuette P, Burckart GJ, et al. A Comparison of **Pediatric and Adult Safety Studies for Antipsychotic and Antidepressant Drugs** Submitted to the United States Food and Drug Administration. J Pediatr. 2019 May;208:236-242.e3.

Lobban F, Glentworth D, Chapman L, et al. Feasibility of a **supported self-management** intervention for relatives of people with recent-onset psychosis: REACT study. Br J Psychiatry. 2013 Nov;203(5):366-72.

Lopez OL, Becker JT, Chang YF, et al. The Long-Term Effects of **Conventional and Atypical Antipsychotics in Patients With Probable Alzheimer`s** Disease. Am J Psychiatry. 2013 Jul 30.

Loy JH, Merry SN, Hetrick SE, et al. Atypical antipsychotics for **disruptive behaviour disorders in children and youths**.Cochrane Database Syst Rev. 2012 Sep 12;9:CD008559. There is some limited evidence of efficacy of risperidone reducing aggression and conduct problems in children aged 5 to 18 with disruptive behaviour disorders in the short term.For aggression, the difference in scores of 6.49 points on the ABC Irritability subscale (range 0 to 45) may be clinically significant. For conduct problems, the difference in scores of 8.61 points on the NCBRF-CP (range 0 to 48) is likely to be clinically significant.

Luft B, Taylor D. A review of **atypical antipsychotic** drugs **versus conventional** medication in schizophrenia. Expert Opin Pharmacother. 2006 Sep;7(13):1739-48.

Luna B, Feinglos MN. Drug-induced hyperglycemia. JAMA 2001;286:1945-8.

Lunsky Y, Khuu W, Tadrous M, et al. **Antipsychotic Use** With and Without Comorbid Psychiatric **Diagnosis** Among Adults with **Intellectual and Developmental Disabilities**. Can J Psychiatry. 2017 Jan 1:706743717727240.

Lutgens D, Gariepy G, Malla A. **Psychological and psychosocial interventions for negative symptoms** in psychosis: systematic review and meta-analysis. Br J Psychiatry. 2017 May;210(5):324-332.

Mackay E, et al Association of **gestational weight gain** and **maternal** body mass index in early **pregnancy** with risk for nonaffective psychosis in offspring [online Feb 22, 2017].JAMA Psyc. doi:10.1001/jamapsychiatry.2016.4257

MacKenzie LE, Abidi S, Fisher HL, et al. **Stimulant Medication** and Psychotic Symptoms in Offspring of Parents With Mental Illness. Pediatrics. 2016 Jan;137(1):1-10.

Mackin P, Thomas SH. **Atypical antipsychotic drugs**. BMJ. 2011 Mar 4;342:d1126. doi: 10.1136/bmj.d1126.

Madsen T, Karstoft KI, Secher RG, et al. **Trajectories of suicidal ideation** in patients with first-episode psychosis: secondary analysis of data from the OPUS trial. Lancet Psychiatry. 2016 Mar 2

Maher AR, Maglione M, Bagley S, et al. Efficacy and comparative effectiveness of **atypical antipsychotic medications for off-label** uses in adults: a systematic review and meta-analysis. JAMA. 2011 Sep 28;306(12):1359-69.

Malla A, Tibbo P, Chue P, et al. **Long-acting injectable antipsychotics**: recommendations for clinicians. Can J Psychiatry. 2013 May;58(5 Suppl 1):30S-5S.

Malhotra AK, Correll CU, Chowdhury NI, et al. Association Between Common Variants Near the **Melanocortin 4 Receptor Gene** and Severe Antipsychotic Drug-Induced Weight Gain. Arch Gen Psychiatry. 2012 May 7.

Man WH, Colen-de Koning JC, Schulte PF, et al. The Effect of **Glycopyrrolate on Nocturnal Sialorrhea in Patients Using Clozapine**: A Randomized, Crossover, Double-Blind, Placebo- Controlled Trial.

J Clin Psychopharmacol. 2017 Apr;37(2):155-161.
Man WH, Pérez-Pitarch A, Wilting I, et al. Development of a **nomogram** for the estimation of **long-term adherence to clozapine** therapy using neutrophil fluorescence. Br J Clin Pharmacol. 2018 Feb 9.
Manchanda R, Chue P, Malla A, et al. **Long-acting injectable antipsychotics**: evidence of effectiveness and use. Can J Psychiatry. 2013 May;58(5 Suppl 1):5S-13S.
Marcantonio Edward R. In the Clinic: **Delirium**. Ann Intern Med June 7, 2011 154:ITC6-1; doi:10.1059/0003-4819-154-11-201106070-01006.
Marcus SC, Olfson M. **National trends in the treatment for depression from 1998 to 2007**. Arch Gen Psychiatry. 2010 Dec;67(12):1265-73.
Margolese HC, Chouinard G, Kolivakis TT, et al. **Tardive dyskinesia** in the era of typical and atypical antipsychotics. Part 1: **pathophysiology and mechanisms** of induction. Can J Psychiatry. 2005 Aug;50(9):541-7. & Margolese HC, et al. Tardive dyskinesia in the era of typical and atypical antipsychotics. Part 2: **Incidence and management** strategies in patients with schizophrenia. Can J Psychiatry. 2005 Oct;50(11):703-14. (Bergman J, Dwolatzky T, Brettholz I, Lerner V. Beneficial effect of **donepezil** in the treatment of elderly patients with tardive movement disorders. J Clin Psychiatry. 2005 Jan;66(1):107-10.)
Marshall M, Rathbone J. **Early intervention for psychosis**. Cochrane Database of Systematic Reviews 2011, Issue 6. Art. No.: CD004718. DOI: 10.1002/14651858.CD004718.pub3. There is emerging, but as yet inconclusive evidence, to suggest that people in the prodrome of psychosis can be helped by some interventions.
Marshall M, Crowther R, Sledge WH, et al. **Day hospital versus admission** for acute psychiatric disorders. Cochrane Database Syst Rev. 2011 Dec 7;12:CD004026. Caring for people in acute day hospitals is as effective as inpatient care in treating acutely ill psychiatric patients. However, further data are still needed on the cost effectiveness of day hospitals.
Mascarenhas Starling F, Medeiros-Souza P, Francisco de Camargos E, et al. **Tablet Splitting of Psychotropic Drugs for Patients With Dementia**: A Pharmacoepidemiologic Study in a Brazilian Sample. Clin Ther. 2015 Sep 14.
Masuda T, Misawa F, Takase M, et al. Association With Hospitalization and All-Cause **Discontinuation Among Patients With Schizophrenia on Clozapine** vs Other Oral Second-Generation Antipsychotics: A Systematic Review and Meta-analysis of Cohort Studies. JAMA Psychiatry. 2019 Jul 31
Matthews PRL, Horder J, Pearce M. **Selective noradrenaline reuptake inhibitors (eg. reboxetine, with atomoxetine and viloxazine) for schizophrenia**. Cochrane Database Syst Rev. 2018 Jan 25;1:CD010219.
Our results provide tentative very low quality evidence that compared to placebo, NRIs (specifically reboxetine) may have a benefit on the negative symptoms of schizophrenia. Limited evidence also suggests that NRIs have no effect on the positive symptoms of schizophrenia or cognitive functioning. NRIs appear generally well tolerated with no real differences in adverse effects such as nausea noted between NRIs and placebo. However, these results are based on short-term follow-up and are poor quality - there is need for more good-quality evidence.
Maust DT, Gerlach LB, Gibson A, et al. **Trends in Central Nervous System-Active Polypharmacy Among Older Adults** Seen in Outpatient Care in the United States. JAMA Intern Med. 2017 Feb 13.
Maust DT, Kim HM, Chiang C, et al. Association of the Centers for Medicare & Medicaid Services' National Partnership to Improve **Dementia Care With the Use of Antipsychotics and Other Psychotropics in Long-term Care** in the United States From 2009 to 2014. JAMA Intern Med. 2018 Mar 17.
Maust DT, Kim HM, Seyfried LS, et al. Antipsychotics, Other Psychotropics, and the Risk of **Death in Patients With Dementia**: Number Needed to Harm. JAMA Psychiatry. 2015 Mar 18.
Mayoral-van Son J, Ortiz-Garcia de la Foz V, Martinez-Garcia O, et al. Clinical outcome after **antipsychotic treatment discontinuation** in functionally recovered first-episode nonaffective psychosis individuals: a 3-year naturalistic follow-up study. J Clin Psychiatry. 2015 Dec 8.
McClellan J, Stock S, American Academy of Child and Adolescent Psychiatry (**AACAP**) Committee on Quality Issues (CQI). Practice parameter for the **assessment and treatment of children and adolescents with schizophrenia**. J Am Acad Child Adolesc Psychiatry. 2013 Sep;52(9):976-90.
McClure MM, Graff F, Triebwasser J, et al. Guanfacine Augmentation of a Combined **Intervention of Computerized Cognitive Remediation Therapy and Social Skills Training** for Schizotypal Personality Disorder. Am J Psychiatry. 2019 Jan 18:appiajp201818030349.
McCrone P, Craig TK, Power P, et al. **Cost-effectiveness of an early intervention** service for people with psychosis. Br J Psychiatry. 2010 May;196(5):377-82.
McCue RE, et al. Comparative effectiveness of **second-generation antipsychotics and haloperidol** in acute schizophrenia. Br J Psychiatry. 2006 Nov;189:433-40. Haloperidol, olanzapine and risperidone are superior to aripiprazole, quetiapine and ziprasidone for the acute treatment of psychosis in hospitalised patients with schizophrenia, schizoaffective disorder or schizophreniform disorder.
McCutcheon R et al. **Antipsychotic plasma levels** in the assessment of poor treatment response in schizophrenia. Acta Psychiatr Scand 2017 Oct 26.
McEvoy JP, Lieberman JA, Stroup TS, Davis SM, Meltzer HY, Rosenheck RA, Swartz MS, Perkins DO, Keefe RS, Davis CE, (Catie trial). Effectiveness of clozapine versus olanzapine, quetiapine, and risperidone in patients with chronic schizophrenia who did **not respond to prior atypical antipsychotic** treatment. Am J Psychiatry. 2006 Apr;163(4):600-10. For these patients with schizophrenia who prospectively failed to improve with an atypical antipsychotic, clozapine was more effective than switching to another newer atypical antipsychotic. Safety monitoring is necessary to detect and manage clozapine's serious side effects.
McEvoy JP, Byerly M, Hamer RM, et al. Effectiveness of **paliperidone palmitate vs haloperidol decanoate for maintenance treatment** of schizophrenia: a randomized clinical trial. JAMA. 2014 May 21;311(19):1978-87.
McGlashan TH, et al. Randomized, double-blind trial of olanzapine versus placebo in patients **prodromally symptomatic for psychosis**. Am J Psychiatry. 2006 May;163(5):790-9.
McKenna K, Koren G, Tetelbaum M, et al. **Pregnancy** Outcome of Women Using **Atypical Antipsychotic Drugs (n=151)**: A Prospective Comparative Study. J Clin Psychiatry. 2005 Apr;66(4):444-449.
McMartin SE, Kingsbury M, Dykxhoorn J, et al. **Time trends in symptoms of mental illness in children and adolescents** in Canada. CMAJ. 2014 Nov 3
McPheeters ML, Warren Z, Sathe N, et al. A systematic review of medical treatments for children with **autism spectrum disorders**. Pediatrics. 2011 May;127(5):e1312-21.
Medical Letter "Treatment Guidelines- Drugs for Psychiatric Disorders August 2010, then June 200, updated June 2013 & updated **Dec 2016.**
Medical Letter. Treatment Guidelines. Drugs for Depression and Bipolar Disorder. May 2010.
Medical Letter. **Iloperidone** –another Second-Generation Antipsychotic. Feb 22, 2010.
Medical Letter. **Asenapine** (Saphris) for Schizophrenia and Bipolar Disorder. Feb 2010.
Medical Letter. **Lurasidone** (Latuda) for Schizophrenia. Feb 21, 2011.
Medicus J. Practice parameter for **psychodynamic psychotherapy** with children. J Am Acad Child Adolesc Psychiatry 2012 May;51(5):541-57.
Mehta D, Tropf FC, Gratten J, et al; Schizophrenia Working Group of the Psychiatric Genomics Consortium, LifeLines Cohort Study, and TwinsUK. Evidence for **Genetic** Overlap Between Schizophrenia and Age at **First Birth** in Women. JAMA Psychiatry. 2016 Mar 23.
Melmed S, Casanueva FF, Hoffman AR, et al. **Diagnosis and treatment of hyperprolactinemia**: an endocrine society clinical practice guideline. J Clin Endocrinol Metab. 2011 Feb;96(2):273-88.
Meltzer HY, Alphs L, Green AI, et al.; International **Suicide** Prevention Trial Study Group. **Clozapine** treatment for suicidality in schizophrenia: International Suicide Prevention Trial (**InterSePT**). Arch Gen Psychiatry. 2003 Jan;60(1):82-91. Erratum in: Arch Gen Psychiatry.2003 Jul;60(7):735.
Meltzer, Herbert Y., Cucchiaro, Josephine, Silva, Robert, et al. **Lurasidone** in the Treatment of Schizophrenia: A Randomized, Double-Blind, Placebo- and Olanzapine-Controlled Study. Am J Psychiatry 2011 168: 957-967
Meltzer HY, Risinger R, Nasrallah HA, et al. A randomized, double-blind, placebo-controlled trial of **aripiprazole lauroxil** in acute exacerbation of schizophrenia. J Clin Psychiatry 2015;76:1085–90.
Merikangas KR, He JP, Rapoport J, et al. **Medication Use in US Youth** With Mental Disorders. JAMA Pediatr. 2013 Feb 1;167(2):141-8.
MHRA Oct/17:**Clozapine**: reminder of potentially fatal risk of **intestinal obstruction**, faecal impaction, and paralytic ileus.
Miller del D, Caroff SN, Davis SM, et a; Clinical Antipsychotic Trials of Intervention Effectiveness (**CATIE**) Investigators. Extrapyramidal side-effects of antipsychotics in a randomised trial. Br J Psychiatry. 2008 Oct;193(4):279-88. The incidence of **treatment-emergent EPS and change in EPS ratings** indicated that there are no significant differences between second-generation antipsychotics and perphenazine or between second-generation antipsychotics in people with schizophrenia.
Minichino A, Senior M, Brondino N, et al. **Measuring Disturbance of the Endocannabinoid System in Psychosis**: A Systematic Review and Meta-analysis. JAMA Psychiatry. 2019 Jun 5.
Molyneaux E, Poston L, Ashurst-Williams S, et al. **Obesity and Mental Disorders During Pregnancy and Postpartum**: A Systematic Review and Meta-analysis. Obstet Gynecol. 2014 Apr;123(4):857-67.
Moncada LV. Management of **falls in older persons**: a prescription for prevention. Am Fam Physician. 2011 Dec 1;84(11):1267-76.
Montastruc F, Nie R, Loo S, et al. Association of **Aripiprazole With the Risk for Psychiatric Hospitalization, Self-harm, or Suicide**. JAMA Psychiatry. 2019 Jan 30.
Moore TJ, Mattison DR. **Adult Utilization of Psychiatric Drugs and Differences by Sex, Age, and Race**. JAMA Intern Med. 2016 Dec 12.

Morgan C, Fearon P, Lappin J, et al. **Ethnicity** and long-term course and **outcome** of **psychotic disorders** in a UK sample: the AESOP-10 study. British Journal of Psychiaty. 2017;211:88-94.
Morriss R, Vinjamuri I, FaizalMA, Bolton CA,McCarthy JP.**Training to recognise the early signs of recurrence in schizophrenia**. Cochrane Database of Systematic Reviews 2013, Issue 2. Art. No.: CD005147. DOI: 10.1002/14651858.CD005147.pub2. This review indicates that early warning signs interventions may have a positive effect on the proportions of people re-hospitalised and on rates of relapse, but not on time to recurrence. However, the overall quality of the evidence was very low, indicating that we do not know if early warning signs interventions will have similar effects outside trials and that it is very likely that further research will alter these estimates.
Morrison AP, French P, Stewart SL, et al. **Early detection and intervention** evaluation for people at risk of psychosis: multisite randomised controlled trial. BMJ. 2012 Apr 5;344:e2233.
Morrison AP, Turkington D, Pyle M, et al. **Cognitive therapy** for people with schizophrenia spectrum disorders not taking antipsychotic drugs: a single-blind randomised controlled trial. Lancet 2014; online Feb 6.
Motsinger CD, Perron GA, Lacy TJ. Use of atypical antipsychotic drugs in patients with **dementia**. Am Fam Physician. 2003 Jun 1;67(11):2335-40.
Muench J, Hamer AM. **Adverse effects of antipsychotic medications**. Am Fam Physician. 2010 Mar 1;81(5):617-22.
Mukundan A, Faulkner G, Cohn T, Remington G. **Antipsychotic switching** for people with schizophrenia who have neuroleptic-induced **weight or metabolic problems**. Cochrane Database of Systematic Reviews 2010, Issue 12. Art. No.: CD006629. DOI: 10.1002/14651858.CD006629.pub2. Evidence from this review suggests that switching antipsychotic medication to one with lesser potential for causing weight gain or metabolic problems could be an effective way to manage these side effects, but the data were weak due to the limited number of trials in this area and small sample sizes. Poor reporting of data also hindered using some trials and outcomes. There was no difference in mental state, global state and other treatment related adverse events between switching to another medication and continuing on the previous one. When the three switching strategies were compared none of them had an advantage over the others in their effects on the primary outcomes considered in this review. Better designed trials with adequate power would provide more convincing evidence for using medication switching as an intervention strategy.
Muller DR, Schmidt SJ, Roder V. One-year randomized controlled trial and follow-up of **Integrated Neurocognitive Therapy** for schizophrenia outpatients. Schizophr Bull 2015;41:604–16.
Munk-Olsen T, Laursen TM, Pedersen CB, Lidegaard O, Mortensen PB. **Induced First-Trimester Abortion** and Risk of Mental Disorder. N Engl J Med. 2011 Jan 27;364(4):332-339.
Munk-Olsen T, Laursen TM, Meltzer-Brody S et al. **Psychiatric disorders with postpartum onset**: possible early manifestations of bipolar affective disorders. Arch Gen Psychiatry. 2012 Apr;69(4):428-34.
Musliner KL, Mortensen PB, McGrath JJ, et al; Bipolar Disorder Working Group of the Psychiatric Genomics Consortium. Association of **Polygenic Liabilities** for Major Depression, Bipolar Disorder, and Schizophrenia With Risk for Depression in the Danish Population. JAMA Psychiatry. 2019 Jan 30.
Musselman ME, Browning LA, Parker D Jr, Saely S. **Neuroleptic malignant syndrome** associated with the use of **prochlorperazine** in a patient with a recent history of antipsychotic-induced neuroleptic malignant syndrome. Ann Pharmacother. 2011 Nov;45(11):e61.
Naharci MI, Karadurmus N, Demir O, et al. **Fatal hepatotoxicity** in an elderly patient receiving low-dose **quetiapine**. Am J Psychiatry. 2011 Feb;168(2):212-3.
Nakagawa S, et al. Antipsychotics and risk of first-time hospitalization for **myocardial infarction**: a population-based case-control study. J Intern Med. 2006 Nov;260(5):451-8.
Navari RM, Qin R, Ruddy KJ, et al. **Olanzapine for the Prevention of Chemotherapy-Induced Nausea and Vomiting**. N Engl J Med. 2016 Jul 14;375(2):134-42.
Nederlof M, Frederix GW, Stoker LJ, et al. **Patient monitoring**: the hidden costs of treatment with antipsychotics. Br J Clin Pharmacol. 2016 May 31.
Nelson JC, Papakostas GI. Atypical **antipsychotic augmentation** in major **depressive** disorder: a meta-analysis of placebo-controlled randomized trials. Am J Psychiatry. 2009 Sep;166(9):980-91. Epub 2009 Aug 17.
Nelson S, Leung JG. **Torsades de pointes** after administration of low-dose **aripiprazole**. Ann Pharmacother. 2013 Feb;47(2):e11.
Németh G, Laszlovszky I, et al. **Cariprazine versus risperidone** monotherapy for treatme nt of predominant negative symptoms in patients with schizophrenia: randomised, double-blind, controlled trial. Lancet 2017; online Feb 6.
Neufeld KJ, Yue J, Robinson TN, Inouye SK, et al. **Antipsychotic Medication for Prevention and Treatment of Delirium** in Hospitalized Adults: A Systematic Review and Meta-Analysis. J Am Geriatr Soc. 2016 Mar 23.
Newcomer JW, Campos JA, Marcus RN, et al. A multicenter, randomized, double-blind study of the effects of **aripiprazole in overweight** subjects with schizophrenia or schizoaffective disorder **switched from olanzapine**. J Clin Psychiatry 2008; 69:1046–1056
Newham JJ, Thomas SH, MacRitchie K, et al. **Birth weight of infants after maternal exposure** to typical and atypical antipsychotics: prospective comparison study. Br J Psychiatry. 2008 May;192(5):333-7.
Newport DJ, Calamaras MR, DeVane CL, et al. Atypical antipsychotic administration during late pregnancy: **placental passage** and obstetrical outcomes. Am J Psychiatry. 2007 Aug;164(8):1214-20.
NICE: National Collaborating Centre for Mental Health. **Antenatal and postnatal mental health**: clinical management and service guidance [Internet]. London: National Institute for Health and Clinical Excellence; 2007 Feb [reissued 2007 Apr; cited 2011 Feb 18]. (NICE clinical guideline 45). Available from: http://www.nice.org.uk/nicemedia/pdf/CG045NICEGuidelineCorrected.pdf *See: Antipsychotics, pp.21-2*
NICE: National Collaborating Centre for Mental Health. Schizophrenia: core interventions in the treatment and management of schizophrenia in adults in primary and secondary care. London (UK): National Institute for Health and Clinical Excellence (**NICE**); 2009 Mar. 41 p. (NICE clinical guideline; no. 82). http://guidance.nice.org.uk/CG82
NICE: Clinical Guideline 120. Mar 2011. **Psychosis with coexisting substance misuse**. http://www.nice.org.uk/nicemedia/live/13414/53691/53691.pdf Guick Guide http://www.nice.org.uk/nicemedia/live/13414/53731/53731.pdf
NICE: Pilling Stephen, Whittington Craig, Taylor Clare, et al. on behalf of the Guideline Development Group. Guidelines: Identification and care pathways for common mental health disorders: summary of NICE guidance. BMJ 2011;342:doi:10.1136/bmj.d2868 (Published 24 May 2011)
NICE: National Institute for Health and Clinical Excellence. Common mental health disorders: identification and pathways to care. (Clinical guideline CG123. 2011. http://guidance.nice.org.uk/CG123 .
NICE: National Collaborating Centre for Mental Health. **Psychosis and schizophrenia in children** and young people. London (UK): National Institute for Health and Clinical Excellence; 2013 Jan. http://www.nice.org.uk/nicemedia/live/14021/62389/62389.pdf
NICE: National Collaborating Centre for Mental Health. **Psychosis and schizophrenia in adults**: treatment and management. London (UK): National Institute for Health and Care Excellence (NICE); 2014 Feb.
Nicol GE, Yingling MD, Flavin KS, et al. Metabolic effects of **antipsychotics on adiposity and insulin sensitivity** in youths: a randomized clinical trial [online June 13, 2018]. JAMA Psychiatry. doi:10.1001/jamapsychiatry.2018.1088
Nielsen MØ, Rostrup E, Wulff S, et al. **Striatal reward activity** and antipsychotic-associated **weight change** in patients with schizophrenia undergoing initial treatment [online Jan 6, 2016].JAMA Psychiatry.
Nielsen RE, Laursen MF, Vernal DL, et al. Risk of **diabetes in children and adolescents exposed to antipsychotics**: a nationwide 12-year case-control study. J Am Acad Child Adolesc Psychiatry. 2014 Sep;53(9):971-979.e6.
Nielsen SF, Hjorthøj CR, Erlangsen A, Nordentoft M. Psychiatric disorders and mortality among people in **homeless shelters** in Denmark: a nationwide register-based cohort study. Lancet 2011; published online June 14.
Niendam TA, Ray KL, Iosif AM, et al. Association of **Age at Onset and Longitudinal Course of Prefrontal Function in Youth With Schizophrenia**. JAMA Psychiatry. 2018 Oct 3.
Nikvarz N;Vahedian M;Khalili N. **Chlorpromazine versus penfluridol** for schizophrenia. Cochrane Database Syst Rev. 2017 Sep 23;9:CD011831. Only three small studies provided data and the quality of reporting and evidence is low. Limited data indicate the efficacy and adverse effects profiles of chlorpromazine and penfluridol are generally similar. Penfluridol, however, may confer advantage by needing to be given only once per week. Firm conclusions are not possible without good-quality trials, and where these treatments are used, such trials are justified.
Nisbet AC. **Intramuscular gluteal injections** in the increasingly obese population: retrospective study. BMJ. 2006 Mar 18;332(7542):637-8. Epub 2006 Mar 8.
Nishikawa T, Araki Y, Hayashi T. Intractable **hiccups** (singultus) **abolished by risperidone**, but not by haloperidol. Ann Gen Psychiatry. 2015 Mar 5;14:13.
Nosarti C, Reichenberg A, Murray RM, et al. **Preterm Birth and Psychiatric Disorders** in Young Adult LifePreterm Birth and Psychiatric Disorders. Arch Gen Psychiatry. 2012 Jun1:610-617.
Nussbaum AM, Stroup TS. Oral **paliperidone** for schizophrenia. Cochrane Database Syst Rev. 2008;(2).
Oderda LH, Young JR, Asche CV, Pepper GA. Psychotropic-related **hip fractures**: meta-analysis of first-generation and second-generation antidepressant and antipsychotic drugs. Ann Pharmacother. 2012 Jul;46(7-8):917-28.
Okpokoro U, Adams CE, Sampson S. **Family intervention** (brief) for schizophrenia. Cochrane Database Syst Rev. 2014 Mar 5;3:CD009802. The findings of this review are not outstanding due to the size and quality of studies providing data; the analysed outcomes were also minimal, with no meta-analysis possible. All outcomes in the `Summary of findings` table were rated low or very low quality evidence. However, the importance of brief family intervention should not be dismissed outright, with the present state of demand and resources available. The designs of such brief interventions could be modified to be more effective with larger studies, which may then have enough power to inform clinical practice.
Oldham JM, Gabbard GO, Goin MK, et al. Practice **guideline for the treatment of patients with borderline personality disorder**. Am J Psychiatry 2001;158:Suppl:1-52.
Olfson M, Blanco C, Liu SM, et al. **National Trends** in the Office-Based Treatment of **Children, Adolescents, and Adults With Antipsychotics**. Arch Gen Psychiatry. 2012 Aug 6:1-10.
Olfson M, Druss BG, Marcus SC. **Trends in mental health care among children and adolescents**. N Engl J Med. 2015 May 21;372(21):2029-38.

Olfson M, King M, Schoenbaum M. **Treatment of Young People With Antipsychotic Medications in the United States**. JAMA Psychiatry. 2015 Jul 1.

Olfson M, Gerhard T, Huang C, et al. **Premature Mortality Among Adults With Schizophrenia** in the United States. JAMA Psychiatry. 2015 Oct 28:1-10.

Orr C, Deshpande S, Sawh S, et al. **Asenapine** for the Treatment of Psychotic Disorders: A Systematic Review and Meta-analysis. Can J Psychiatry. 2016 Aug 1.

Ortiz-Orendain J, Castiello-de Obeso S, Colunga-Lozano LE, et al. **Antipsychotic combinations for schizophrenia**. Cochrane Database of Systematic Reviews 2017, Issue 6. Art. No.: CD009005. Currently, most evidence regarding the use of antipsychotic combinations comes from short-term trials, limiting the assessment of longterm efficacy and safety. We found very low-quality evidence that a combination of antipsychotics may improve the clinical response. We also found low-quality evidence that a combination of antipsychotics is may make no difference at preventing participants from leaving the study early, preventing relapse and/or causing more serious adverse events than monotherapy.

Os Jv. "**Schizophrenia" does not exist**. BMJ. 2016 Feb 2; 352:i375.

Oteri A, Mazzaglia G, Pecchioli S, et al. **Prescribing pattern of antipsychotic** drugs during the years 1996-2010: a population-based database study in **Europe** with a focus on **torsadogenic** drugs. Br J Clin Pharmacol. 2016 Apr 6.

Owen, Randall, Sikich, Linmarie, Marcus, Ronald N., et al. **Aripiprazole** in the Treatment of Irritability in Children and Adolescents With **Autistic** Disorder. Pediatrics 2009 124: 1533-1540.

Owen MJ, Sawa A, Mortensen PB. Schizophrenia. Lancet. 2016 Jan 14.

Owenby RK, Brown LT, Brown JN. Use of **Risperidone** as Augmentation Treatment for Major Depressive Disorder (January). Ann Pharmacother. 2010 Dec 28.

Pagsberg AK, Jeppesen P, Klauber DG, et al. **Quetiapine extended release versus aripiprazole in children and adolescents with first-episode psychosis**: the multicentre, double-blind, randomised tolerability and efficacy of antipsychotics (**TEA**) trial. Lancet Psychiatry. 2017 Jun 6.

Panagiotopoulos C, Ronsley R, Davidson J. Increased Prevalence of **Obesity** and **Glucose Intolerance** in Youths Treated With **Second-Generation** Antipsychotic Medications. Can J Psychiatry. 2009;54(11):743-749

Papakostas GI et al. **Ziprasidone augmentation of escitalopram** for major depressive disorder: Efficacy results from a randomized, double-blind, placebo-controlled study. Am J Psychiatry 2015 Jun 18.

Pariente A, Fourrier-Réglat A, Ducruet T, et al. Antipsychotic use and **myocardial infarction** in older patients with treated **dementia** [published online Mar 26, 2012]. Arch Intern Med doi:10.1001/archinternmed.2012.28.

Park Y, Franklin JM, Schneeweiss S, et al. Antipsychotics and **Mortality**: Adjusting for Mortality Risk Scores to Address Confounding by Terminal Illness. J Am Geriatr Soc. 2015 Mar 6.

Park Y, Bateman BT, Kim DH, et al. Use of **haloperidol versus atypical antipsychotics and risk of in-hospital death in patients with acute myocardial infarction**: cohort study. BMJ. 2018 Mar 28;360:k1218.

Park Y, Hernandez-Diaz S, Bateman BT, et al. Continuation of **Atypical Antipsychotic Medication During Early Pregnancy** and the Risk of **Gestational Diabetes**. Am J Psychiatry. 2018 Jun 1;175(6):564-574.

Parker C et al. **Antipsychotic drugs and risk of venous thromboembolism**: nested case-control study. BMJ 2010; 341: c4245

Patel JJ, Lisi PA, Lathara Z, Lipchik RJ. **Clozapine-Induced Peripheral and Pleural Fluid Eosinophilia** (February). Ann Pharmacother. 2012 Jan 24.

Patel R, Wilson R, Jackson R, et al. Association of **cannabis** use with hospital admission and **antipsychotic treatment failure in first episode psychosis**: an observational study. BMJ Open. 2016 Mar 3;6(3):e009888

Patton SW, Misri S, Corral MR, Perry KF, Kuan AJ. Antipsychotic medication during **pregnancy and lactation** in women with schizophrenia: evaluating the risk. Can J Psychiatry. 2002 Dec;47(10):959-65.

Patton GC, Coffey C, Romaniuk H, Mackinnon et al. The prognosis of **common mental disorders in adolescents**: a 14-year prospective cohort study. Lancet. 2014 Jan 15.

Paulzen M, Haen E, Hiemke C, et al. Cytochrome P450 mediated interaction between **perazine and risperidone**: implications for antipsychotic polypharmacy. Br J Clin Pharmacol.2017 Feb 4.

Peluso MJ, Lewis SW, Barnes TR, Jones PB. **Extrapyramidal motor side-effects of first- and second-generation antipsychotic drugs**. Br J Psychiatry. 2012 May;200:387-92.

Periyasamy S, John S, Padmavati R, et al. Association of Schizophrenia Risk With **Disordered Niacin Metabolism** in an Indian Genome-wide Association Study. JAMA Psychiatry. 2019 Jul 3.

Petersen I, McCrea RL, Sammon CJ, et al. Risks and benefits of psychotropic medication in **pregnancy**: cohort studies based on UK electronic primary care health records. Health Technol Assess. 2016 Mar;20(23):1-176.

Petrides G, Malur C, Braga RJ, et al. **Electroconvulsive Therapy Augmentation in Clozapine**-Resistant Schizophrenia: A Prospective, Randomized Study. Am J Psychiatry. 2014 Aug 26.

Pharmacist's Letter: Drug Treatment for Behavioral Symptoms Associated with **Autism**. Dec/06.

Pharmacist's Letter. **Quetiapine (Seroquel) abuse**. Oct 2007.

Pharoah F, Mari J, Rathbone J, Wong W. **Family intervention** for schizophrenia. Cochrane Database of Systematic Reviews 2006, Issue 4. Art. No.: CD000088. DOI: 10.1002/14651858.CD000088.pub2. Family intervention may reduce the number of relapse events and hospitalisations and would therefore be of interest to people with schizophrenia, clinicians and policy makers.

Picchioni MM, Murray RM. **Schizophrenia**. BMJ. 2007 Jul 14;335(7610):91-5.

Pileggi DJ, Cook AM. **Neuroleptic Malignant Syndrome** Review: Focus on Treatment and Rechallenge. Ann Pharmacother. 2016 Jul 15.

Pillinger T, Beck K, Gobjila C, et al. **Impaired Glucose Homeostasis** in **First-Episode Schizophrenia**: A Systematic Review and Meta-analysis. JAMA Psychiatry. 2017 Jan 11.

Pillay J, Boylan K, Carrey N, et al. **First- and second-generation antipsychotics in children and young adults**: systematic review update. Comparative Effectiveness Review No. 184. AHRQ Comparative Effectiveness Reviews. 2017 Mar. No. 184;1-567.

Pilon D, Tandon N, Lafeuille MH, et al. Treatment Patterns, Health Care Resource **Utilization, and Spending** in Medicaid Beneficiaries **Initiating Second-Generation Long-Acting Injectable Agents Versus Oral Atypical Antipsychotics**. Clin Ther. 2017 Sep 14.

Pollack TM, McCoy C, Stead W. Clinically significant adverse events from a drug interaction between **quetiapine** and **atazanavir-ritonavir** in two patients. Pharmacotherapy. 2009 Nov;29(11):1386-91.

Pottegård A, Lash TL, Cronin-Fenton D, et al. Use of **antipsychotics and risk of breast cancer**: A Danish nationwide case-control study. Br J Clin Pharmacol. 2018 Jun 1.

Powney MJ, Adams CE, Jones H. **Haloperidol for psychosis induced aggression or agitation (rapid tranquillisation).** Cochrane Database Syst Rev. 2012;11:CD009377.

Prasad KM et al. Progressive gray matter loss and changes in cognitive functioning associated with exposure to **herpes simplex virus** 1 in schizophrenia: A longitudinal study. Am J Psychiatry2011 Jun 1

Premkumar TS, Pick J. **Lamotrigine** for schizophrenia. Cochrane Database Syst Rev. 2006 Oct 18;(4):CD005962.

Price C, Dalman C, Zammit S, et al. Association of **Residential Mobility Over the Life Course With Nonaffective Psychosis in 1.4 Million Young People** in Sweden. JAMA Psychiatry. 2018 Aug 22.

Priebe S, Yeeles K, Bremner S, et al. Effectiveness of **financial incentives to improve adherence** to maintenance treatment with antipsychotics: cluster randomised controlled trial. BMJ. 2013 Oct 7;347:f5847.

Pringsheim T, Kelly M, Urness D, et al. Physical health and **drug safety** in individuals with **schizophrenia.** Can J Psychiatry 2017.

Pringsheim T, Lam D, Ching H, Patten S. **Metabolic** and **neurological complications** of second-generation antipsychotic use in **children**: a systematic review and meta-analysis of randomized controlled trials. Drug Saf. 2011 Aug 1;34(8):651-68.

Pringsheim T, Lam D, Patten SB. The **pharmacoepidemiology** of antipsychotic medications for Canadian **children and adolescents**: 2005-2009. J Child Adolesc Psychopharmacol. 2011 Dec;21(6):537-43.

Pringsheim T, Lam D, Tano DS, Patten SB. The **pharmacoepidemiology** of antipsychotics for **adults** with schizophrenia in Canada, 2005 to 2009. Can J Psychiatry. 2011 Oct;56(10):630-4.

Pringsheim T, Panagiotopoulos C, Davidson J, Ho J; **CAMESA** guideline group. Evidence-based recommendations for **monitoring** safety of second generation antipsychotics in **children and youth**. J Can Acad Child Adolesc Psychiatry. 2011 Aug;20(3):218-33.

Pringsheim T, Doja A, Belanger S et al. Treatment recommendations for **extrapyramidal** side effects associated with second-generation antipsychotic use in **children and youth**. Paediatr Child Health 2011;16(9):590-598.

Pringsheim T, Gardner DM. Dispensed prescriptions for **quetiapine and other second-generation antipsychotics in Canada** from 2005 to 2012: a descriptive study. CMAJ Open. 2014 Oct 1;2(4):E225-32.

Pringsheim T, Gardner D, Patten SB. Adjunctive treatment with **quetiapine for major depressive** disorder: are the benefits of treatment worth the risks? BMJ. 2015 Mar 4;350:h569.

Raebel MA, Penfold R, McMahon AW, et al. Adherence to Guidelines for **Glucose Assessment in Starting Second-Generation Antipsychotics**. Pediatrics. 2014 Oct 6.

Rahman T, Clevenger CV, Kaklamani V, et al. **Antipsychotic treatment in breast cancer patients**. Am J Psychiatry. 2014 Jun 1;171(6):616-21.

Raivio MM, Laurila JV, Strandberg TE, et al. **Neither atypical nor conventional antipsychotics increase mortality** or hospital admissions among elderly patients with dementia: a two-year prospective study. Am J Geriatr Psychiatry. 2007 May;15(5):416-24.

Rajkumar AP, et al. Endogenous and Antipsychotic-Related **Risks for Diabetes Mellitus** in Young People With Schizophrenia: A Danish Population-Based Cohort Study. Am J Psychiatry. 2017 Jan 20:appiajp201616040442.

Ramirez R, Stalcup P, Croft B, Darracq MA. **Haloperidol** undermining **gastroparesis symptoms** (**HUGS**) in the emergency department. Am J Emerg Med. 2017 Mar 12.

Rapaport MH, et al. Effects of **Risperidone Augmentation** in Patients with Treatment-Resistant Depression: Results of Open-Label Treatment Followed by Double-Blind Continuation. Neuropsychopharmacology. 2006 Jun 7

Rasmussen MH, et al. **Risk, treatment duration, and recurrence risk of postpartum affective disorder** in women with no prior psychiatric history: A population-based cohort study. PLoS Med. 2017 Sep 26;14(9):e1002392

Rattehalli RD, Jayaram MB, Smith M. **Risperidone** versus placebo for schizophrenia. Cochrane Database Syst Rev. 2010 Jan 20;(1):CD006918.

Raveendran NS, Tharyan P, Alexander J, Adams CE; TREC-India II Collaborative Group. **Rapid tranquillisation** in psychiatric emergency settings in India: pragmatic randomised controlled trial of intramuscular olanzapine versus Intramuscular haloperidol plus promethazine. BMJ. 2007 Oct 22; [Epub ahead of print] Intramuscular olanzapine & intramuscular **haloperidol plus promethazine** were effective at rapidly tranquillising or sedating agitated or violent patients with mental illness but the combination resulted in fewer additional medical interventions within four hours of intervention.

Ray WA, Chung CP, Murray KT et al. Atypical antipsychotic drugs and the risk of **sudden cardiac death**. New Engl J Med 2009; 360: 225-235. Both typical & atypical antipsychotics increase risk of sudden cardiac death. The absolute risk of sudden cardiac death in pts taking these drugs is 1.8 per 100 persons taking the drugs for 10yrs, which is approx. twice as high as for patients in the general population. Newer drugs are not safer than older drugs with respect to cardiovascular outcomes, & thioridazine, clozapine, & risperidone in high doses appear to be slightly more risky. (LOE = 2b)

Ray WA, Stein CM, Murray KT, et al. Association of **antipsychotic treatment with risk of unexpected death among children and youths** [online Dec 12, 2018]. JAMA Psychiatry. doi:10.1001/jamapsychiatry.2018.3421

Remington G, Seeman P, Feingold A, Mann S, Shammi C, Kapur S. "**Extended**" antipsychotic **dosing** in the maintenance treatment of schizophrenia: a double-blind, placebo-controlled trial. J Clin Psychiatry. 2010 Sep 7.

Remington G, Addington D, Honer W, et al. **Canadian Schizophrenia Guidelines for the Pharmacotherapy of Schizophrenia in Adults**. Can J Psychiatry. **2017** Sep;62(9):604-616.

Rettew DC, Greenblatt J, Kamon J, et al. Antipsychotic Medication Prescribing in **Children** Enrolled in Medicaid. Pediatrics. 2015 Mar 2.

Reus VI, et al. The **American Psychiatric Association** (**APA**) Practice Guideline on the Use of **Antipsychotics to Treat Agitation or Psychosis in Patients With Dementia**. Am J Psychiatry. 2016 May 1;173(5):543-6.

Richter C, Berg A, Langner H, et al. Effect of person-centred care on **antipsychotic drug use in nursing homes** (EPCentCare): a cluster-randomised controlled trial. Age Ageing. 2019 Feb 26.

Richter T, Meyer G, Möhler R, Köpke S. **Psychosocial interventions** for reducing antipsychotic medication in **care home residents**. Cochrane Database of Systematic Reviews 2012, Issue 12. Art. No.: CD008634. DOI: 10.1002/14651858.CD008634.pub2. There is evidence to support the effectiveness of psychosocial interventions for reducing antipsychotic medication in care home residents.

Riedel M, et al. **Quetiapine** has equivalent efficacy & **superior tolerability to risperidone** in schizophrenia with predominantly negative symptoms. Eur Arch Psychiatry Clin Neurosci. 2005 Dec;255(6):432-7. Epub 2005 Nov 4.

Risbood V, Lee JR, Roche-Desilets J, Fuller MA. **Lurasidone**: an atypical antipsychotic for schizophrenia. Ann Pharmacother. 2012 Jul;46(7-8):1033-46.

Riesenberg RA, Baldytcheva I, Datto C. Self-Reported Sedation Profile of **Quetiapine** Extended-Release and Quetiapine Immediate-Release During 6-Day Initial Dose Escalation in Bipolar Depression: A Multicenter, Randomized, Double-Blind, Phase IV Study. Clin Ther. 2012 Oct 8.

Robakis T, Williams K. Atypical **Antipsychotics during pregnancy**. Current Psychiatry 2013 July; 12(7).

Robinson DG, Schooler NR, John M, et al. Prescription Practices in the Treatment of **First-Episode Schizophrenia** Spectrum Disorders: Data From the National RAISE-ETP Study. Am J Psychiatry. 2015 Mar 1;172(3):237-48.

Robottom BJ, Factor SA, Weiner WJ. Movement disorders emergencies part 2: **hyperkinetic disorders** (chorea, tics, ballism, myoclonus, dystonia). Arch Neurol. 2011 Jun;68(6):719-24.

Rochon PA, Stukel TA, Sykora K, Gill S, Garfinkel S, et al. **Atypical antipsychotics and parkinsonism**. Arch Intern Med. 2005 Sep 12;165(16):1882-8. CONCLUSIONS: The risk of development of parkinsonism associated with the use of high-dose atypical antipsychotics was **similar** to that associated with the use of typical antipsychotics. Caution should be used when prescribing atypical antipsychotic therapy at high doses.

Rochon PA, Gruneir A, Gill SS, et al. **Older men with dementia** are at greater risk than women of **serious events** after initiating antipsychotic therapy. J Am Geriatr Soc. 2013 Jan;61(1):55-61.

Roffman JL, Lamberti JS, Achtyes E, et al. Randomized Multicenter Investigation of **Folate Plus Vitamin B12** Supplementation in Schizophrenia. JAMA Psychiatry. 2013 Mar 6:1-9.

Romo-Nava F, Alvarez-Icaza González D, et al. **Melatonin** attenuates **antipsychotic metabolic effects**: an eight-week randomized, double-blind, parallel-group, placebo-controlled clinical trial. Bipolar Disord. 2014 Mar 17.

Ronsley R, Scott D, Warburton WP, et al. A population-based study of **antipsychotic prescription trends in children** and adolescents in british columbia, from 1996 to 2011. Can J Psychiatry. 2013 Jun;58(6):361-9.

Rosa RG, Falavigna M, da Silva DB, et al. **Effect of Flexible Family Visitation on Delirium** Among Patients in the Intensive Care Unit: The ICU Visits Randomized Clinical Trial. JAMA. 2019 Jul 16;322(3):216-228.

Rosenbaum L. Swallowing a Spy - The Potential Uses of **Digital Adherence Monitoring**. N Engl J Med. 2017 Dec 27

Rosenberg PB, Mielke MM, Han D, et al. The association of **psychotropic medication use with the cognitive, functional and neuropsychiatric trajectory** of Alzheimer's disease. Int J Geriatr Psychiatry 2012; 27:1248–57.

Rosenheck, Robert; Perlick, Deborah et al. Effectiveness and Cost of **Olanzapine and Haloperidol** in the Treatment of Schizophrenia: A Randomized Controlled Trial. JAMA. 2003;290:2693-2702.

Rosenheck RA., Krystal JH., Lew R, et al. for the CSP555 Research Group. **Long-Acting Risperidone and Oral Antipsychotics** in Unstable Schizophrenia. N Engl J Med 2011; 364:842-851. (No Benefit, More SE With Injectable Risperidone)

Rubin DM, Kreider AR, Matone M, et al. Risk for **Incident Diabetes** Mellitus Following Initiation of Second-Generation Antipsychotics Among Medicaid-Enrolled Youths. JAMA Pediatr. 2015 Apr 6

Rubio G, et al. **Long-acting injectable risperidone** compared with zuclopenthixol in the treatment of schizophrenia with substance abuse comorbidity. Can J Psychiatry. 2006 Jul;51(8):531-9.

Rummel-Kluge C, Komossa K, Schwarz S, et al. **Second-Generation Antipsychotic** Drugs and Extrapyramidal Side Effects: A Systematic Review and Meta-analysis of Head-to-Head Comparisons. Schizophr Bull. 2010 May 31.

Rutherford BR, Pott E, Tandler JM, et al. **Placebo Response in Antipsychotic Clinical Trials**: A Meta-analysis. JAMA Psychiatry. 2014 Oct 8.

Sacarny A, Barnett ML, Le J, et al. Effect of **peer comparison letters** for high-volume primary care prescribers of **quetiapine in older and disabled adults**: a randomized clinical trial [online August 1, 2018]. JAMA Psychiatry.

Sacchetti E, Turrina C, Valsecchi P. **Cerebrovascular accidents in elderly people treated with antipsychotic** drugs: a systematic review. Drug Saf. 2010 Apr 1;33(4):273-88. doi: 10.2165/11319120-000000000-00000.

Sackeim HA. Modern **Electroconvulsive Therapy**: Vastly Improved yet Greatly Underused. JAMA Psychiatry. 2017 Aug 1;74(8):779-780.

Salem H, Andersen EW, Dalton SO, et al. Psychotropic **Medication Use in Parents of Children Diagnosed With Cancer**. Pediatrics. 2019 Apr 3.

Samara MT, Dold M, Gianatsi M, et al. Efficacy, Acceptability, and Tolerability of **Antipsychotics in Treatment-Resistant Schizophrenia**: A Network Meta-analysis. JAMA Psychiatry. 2016 Feb 3.

Samara MT, Leucht C, Leeflang MM, et al. **Early improvement** as a predictor of later response to antipsychotics in schizophrenia: a diagnostic test review. Am J Psychiatry 2015;172:617–29.

Sami MB, Shiers D, Latif S, et al. **How to approach psychotic symptoms in a non-specialist setting**. BMJ. 2017 Nov 8;359:j4752.

Sami MB, Shiers D, Latif S, et al. **Early psychosis for the non-specialist doctor**. BMJ. 2017 Nov 8;357:j4578.

Sampson S,Mansour M,Maayan N, et al. **Intermittent drug techniques for schizophrenia**. Cochrane Database of Systematic Reviews 2013, Issue 7. Art. No.: CD006196. DOI: 10.1002/14651858.CD006196.pub2. Results of this reviewsupport the existing evidence that intermittent antipsychotic treatment is not as effective as continuous,maintained antipsychotic therapy in preventing relapse in people with schizophrenia. More research is needed to assess any potential benefits or harm of intermittent treatment regarding adverse effects typically associated with maintained antipsychotic treatment, as well as any cost-effectiveness of this experimental treatment.

Sanford M, Keating GM. **Quetiapine**: a review of its use in the management of **bipolar depression**. CNS Drugs. 2012 May 1;26(5):435-60.

Schmid I, Burcu M, Zito JM. Medicaid prior authorization policies for **pediatric** use of antipsychotic medications. JAMA. 2015 Mar 3;313(9):966-8.

Schneeweiss S, Setoguchi S, Brookhart A, Dormuth C, Wang PS. Risk of death associated with the use of conventional versus atypical antipsychotic drugs among elderly patients. CMAJ. 2007 Feb 27;176(5):627-32. Among elderly patients, the risk of death associated with conventional antipsychotic medications is comparable to and possibly greater than the risk of death associated with atypical antipsychotic medications. Until further evidence is available, physicians should consider all antipsychotic medications to be equally risky in elderly patients.

Schneider LS, Tariot PN, Dagerman KS, et al. **CATIE-AD** Study Group. Effectiveness of atypical antipsychotic drugs in patients with Alzheimer's disease. N Engl J Med. 2006 Oct 12;355(15):1525-38. (n=421 36weeks risperidone 1mg/d, olanzapine 5.5mg/d, & quetiapine 56.5mg/d) Adverse effects offset advantages in the efficacy of atypical antipsychotic drugs for the treatment of psychosis, aggression, or agitation in patients with Alzheimer's disease. There were no significant differences among treatments with regard to the time to the discontinuation of treatment for any reason: olanzapine (median, 8.1 weeks), quetiapine (median, 5.3 weeks), risperidone (median, 7.4 weeks), and placebo (median, 8.0 weeks) (P=0.52). The median time to the discontinuation of treatment due to a lack of efficacy favored olanzapine (22.1 weeks) and risperidone (26.7 weeks) as compared with quetiapine (9.1 weeks) and placebo (9.0 weeks) (P=0.002). The time to the discontinuation of treatment due to adverse events or intolerability favored placebo. Overall, 24% of patients who received olanzapine, 16% of patients who received quetiapine, 18% of patients who received risperidone, & 5% of patients who received placebo discontinued their assigned treatment owing to intolerability (P=0.009). No significant differences were noted among the groups with regard to improvement on the CGIC scale. Improvement was observed in 32% of patients assigned to olanzapine, 26% of patients assigned to quetiapine, 29% of patients assigned to risperidone, and 21% of patients assigned to placebo (P=0.22). (InfoPOEMs: Atypical antipsychotics are minimally, if at all, effective for patients with Alzheimer's disease (AD), and they have significant adverse effects. They should not be routinely used for the treatment of psychosis, agitation, or aggression in these patients. (LOE = 1b))

Schneider LS, Dagerman K, Insel PS. Efficacy and adverse effects of **atypical antipsychotics for dementia**: meta-analysis of randomized, placebo-controlled trials. Am J Geriatr Psychiatry. 2006 Mar;14(3):191-210.

Schneider-Thoma J, Efthimiou O, Bighelli I, et al. Second-generation **antipsychotic drugs and short-term somatic serious adverse events**: a systematic review and meta-analysis. Lancet Psychiatry 2019; published online July 15.

Schoenbaum M, Sutherland JM, Chappel A, et al. Twelve-Month **Health Care Use and Mortality in Commercially Insured Young People** With Incident Psychosis in the United States. Schizophr Bull. 2017 Apr 7.
Schooler N, Rabinowitz J, et al. **Risperidone and haloperidol in first-episode** psychosis: a long-term randomized trial. Am J Psychiatry. 2005 May;162(5):947-53.
Schreiner A, Bergmans P, Cherubin P, et al. A prospective **flexible-dose study of paliperidone palmitate** in nonacute but symptomatic patients with schizophrenia previously unsuccessfully treated with oral antipsychotic agents. Clin Ther. 2014 Oct 1;36(10):1372-1388.e1.
Schrijver EJM, et al. **Haloperidol versus placebo for delirium prevention** in acutely hospitalised older at risk patients: a multi-centre double-blind randomised controlled clinical trial. Age Ageing. 2017 Jul 15:1-8.
Schultz JL, Killoran A, Nopoulos PC, et al. Evaluating **depression and suicidality in tetrabenazine users with Huntington disease**. Neurology. 2018 Jul 17;91(3):e202-e207.
Scotto Rosato N, Correll CU, Pappadopulos E, et al; on behalf of the Treatment of **Maladaptive Aggressive in Youth** Steering Committee. Treatment of Maladaptive Aggression in Youth: CERT Guidelines II. Treatments and Ongoing Management. Pediatrics. 2012 Jun;129(6):e1577-e1586.
Second generation antipsychotics- **Aripiprazole** revisited. The Medical Letter Oct 10,2005.
Seehusen DA, Bain R. **Antipsychotics** for **Fibromyalgia** in Adults. Am Fam Physician. 2017 Aug 1;96(3):Online.
Seida JC, Schouten JR, Boylan K, et al. **Antipsychotics for children and young adults**: a comparative effectiveness review.Pediatrics. 2012 Mar;129(3):e771-84.
Seidel S, Aigner M, Ossege M, et al. **Antipsychotics for acute and chronic pain in adults**. Cochrane Database Syst Rev. 2013 Aug 29;8:CD004844. doi: 10.1002/14651858.CD004844.pub3. The recent search found five new studies which were all excluded, so the review remains the same as previously.Antipsychotics might be used as an add-on therapy in the treatment of painful conditions.
Seidman LJ, Shapiro DI, et al. Association of **Neurocognition With Transition to Psychosis**: Baseline Functioning in the Second Phase of the North American Prodrome Longitudinal Study. JAMA Psychiatry. 2016 Nov 2.
Sernyak MJ, Leslie DL, Alarcon RD, Losonczy MF, Rosenheck R. Association of **diabetes** mellitus with use of atypical neuroleptics in the treatment of schizophrenia. Am J Psychiatry. 2002 Apr;159(4):561-6.
Shaw P, et al. **Childhood-onset schizophrenia**: a double-blind, randomized clozapine-olanzapine comparison. Arch Gen Psychiatry. 2006 Jul;63(7):721-30.
Sheehan R, Hassiotis A, Walters K, et al. **Mental illness, challenging behaviour, and psychotropic drug prescribing** in people with intellectual disability: UK population based cohort study. BMJ. 2015 Sep 1;351:h4326.
Sheehan R, Hassiotis A. **Reduction or discontinuation of antipsychotics for challenging behaviour in adults with intellectual disability**: a systematic review. Lancet Psychiatry. 2016 Nov 9.
Sheehan R, Horsfall L, et al. **Movement side effects of antipsychotic drugs in adults with and without intellectual disability**: UK population-based cohort study. BMJ Open 2017;358:e017406.
Sheehan R, Hassiotis A. **Reduction or discontinuation of antipsychotics for challenging behaviour in adults with intellectual disability**: a systematic review. Lancet Psychiatry 2017;358:238-56.
Sheehan R, Strydom A, Brown E, et al. Association of focused **medication review with optimization of psychotropic drug prescribing**: a systematic review and meta-analysis. JAMA Netw Open. 2018;1 (6):e183750.
Sheldon Tony. Study of **rivastigmine for delirium** in intensive care is stopped after **deaths.** BMJ 2010;340:c2895, doi: 10.1136/bmj.c2895 (Published 28 May 2010)
Shepshelovich D, Schechter A, Calvarysky B, et al. **Medication-induced SIADH**: distribution and characterization according to medication class. Br J Clin Pharmacol. 2017 Feb 7.
Shtasel DL, Freudenreich O, et al. Case Records of the Massachusetts General Hospital. Case 40-2015. A 40-Year-Old Homeless Woman with Headache, Hypertension, and **Psychosis**. N Engl J Med. 2015 Dec 24;373(26):2563-70.
SIGN: Scottish Intercollegiate Guidelines Network. Management of schizophrenia. Edinburgh (Scotland): Scottish Intercollegiate Guidelines Network (SIGN); 2013 Mar.
Sikich L, Frazier JA, McClellan J, et al. Double-Blind Comparison of First- and Second-Generation Antipsychotics in Early-Onset Schizophrenia and Schizo-affective Disorder: Findings From the Treatment of Early-Onset Schizophrenia Spectrum Disorders (**TEOSS**) Study. Am J Psychiatry. 2008 Sep 15. [Epub ahead of print] n=119. Olanzapine (2.5-20 mg/day), risperidone (0.5-6 mg/day), or molindone (10-140 mg/day, plus 1 mg/day of benztropine) for 8 weeks. Risperidone and olanzapine did not demonstrate superior efficacy over molindone for treating early-onset schizophrenia and schizoaffective disorder. Adverse effects were frequent but differed among medications. The results question the nearly exclusive use of second-generation antipsychotics to treat early-onset schizophrenia and schizoaffective disorder. The safety findings related to weight gain and metabolic problems raise important public health concerns, given the widespread use of second-generation antipsychotics in youth for nonpsychotic disorders.
Simon GE, Stewart C, Yarborough BJ, et al. **Mortality Rates After the First Diagnosis of Psychotic Disorder in Adolescents and Young Adults**. JAMA Psychiatry. 2018 Jan 31.
Simpson HB, Foa EB, Liebowitz MR, et al. **Cognitive-Behavioral Therapy vs Risperidone** for Augmenting Serotonin Reuptake Inhibitors in **Obsessive-Compulsive Disorder**: A Randomized Clinical Trial. JAMA Psychiatry. 2013 Sep 11.
Singh SP, Singh V, Kar N, Chan K. Efficacy of **antidepressants in treating the negative symptoms** of chronic schizophrenia: meta-analysis. Br J Psychiatry. 2010 Sep;197(3):174-9.
Singh J, Kour K, Jayaram MB. **Acetylcholinesterase inhibitors for schizophrenia**. Cochrane Database of Systematic Reviews 2012, Issue 1. Art. No.: CD007967. DOI: 10.1002/14651858.CD007967.pub2.
The results seem to favour the use of acetylcholinesterase inhibitors in combination with antipsychotics on a few domains of mental state and cognition, but because of the various limitations in the studies as mentioned in the main text, the evidence is weak.
Siskind D, Hahn M, Correll CU, et al. **Glucagon-like peptide-1 receptor agonists** for antipsychotic-associated cardio-metabolic risk factors: A systematic review and individual participant data meta-analysis. Diabetes Obes Metab. 2018 Sep 5.
Siskind D, McCartney L, et al. **Clozapine v. first- and second-generation antipsychotics** in **treatment-refractory schizophrenia**: systematic review and meta-analysis. Br J Psychiatry. 2016 Nov;209(5):385-392.
Soares-Weiser K, Maayan N, Bergman H, et al. **First rank symptoms for schizophrenia**. Cochrane Database of Systematic Reviews 2015, Issue 1. Art. No.: CD010653. DOI: 10.1002/14651858.CD010653.pub2.
The synthesis of old studies of limited quality in this review indicates that FRS correctly identifies people with schizophrenia 75% to 95%of the time. The use of FRS to diagnose schizophrenia in triage will incorrectly diagnose around five to 19 people in every 100 who have FRS as having schizophrenia and specialists will not agree with this diagnosis. These people will still merit specialist assessment and help due to the severity of disturbance in their behaviour and mental state. Again, with a sensitivity of FRS of 60%, reliance on FRS to diagnose schizophrenia in triage will not correctly diagnose around 40% of people that specialists will consider to have schizophrenia. Some of these people may experience a delay in getting appropriate treatment. Others, whom specialists will consider to have schizophrenia, could be prematurely discharged from care, if triage relies on the presence of FRS to diagnose schizophrenia. Empathetic, considerate use of FRS as a diagnostic aid - with known limitations - should avoid a good proportion of these errors. We hope that newer tests - to be included in future Cochrane reviews - will show better results. However, symptoms of first rank can still be helpful where newer tests are not available - a situation which applies to the initial screening of most people with suspected schizophrenia. FRS remain a simple, quick and useful clinical indicator for an illness of enormous clinical variability.
Solmi M, Correll CU. Adjunctive **minocycline in schizophrenia**: what one well-conducted study can tell us (and what it can't). Evid Based Ment Health. 2019 Feb;22(1):e3.
Song H, Fang F, Arnberg FK, et al. **Stress related disorders and risk of cardiovascular disease**: population based, sibling controlled cohort study. BMJ. 2019 Apr 10;365:l1255.
Spencer D, Marshall J, Post B, et al. Psychotropic medication use and polypharmacy in children with **autism spectrum disorders**. Pediatrics 2013;132;833-40.
Spielmans GI, Berman MI, E, et al. **Adjunctive atypical antipsychotic treatment for major depressive disorder**: a meta-analysis of depression, quality of life, and safety outcomes. PLoS Med. 2013 Mar;10(3):e1001403.
Stafford MR, Jackson H, Mayo-Wilson E, Morrison AP, Kendall T. Early **interventions to prevent psychosis**: systematic review and meta-analysis. BMJ 2013;346:f185. (Cognitive behavioural therapy-moderate quality evidence)
Stahl SM. Essential psychopharmacology: neuroscientific basis and practical application. 2d ed. New York, N.Y.: Cambridge University Press, 2000.
Starzer MSK, Nordentoft M, Hjorthøj C. Rates and Predictors of **Conversion to Schizophrenia or Bipolar Disorder Following Substance-Induced Psychosis**. Am J Psychiatry. 2017 Nov 28:appiajp201717020223.
Steger M, Schneemann M, Fox M. Systemic review: the pathogenesis and pharmacological **treatment of hiccups**. Aliment Pharmacol Ther. 2015 Nov;42(9):1037-50.
Stip E et al. **Ziprasidone** for psychotic disorders: a meta-analysis and systematic review of the relationship between pharmacokinetics, pharmacodynamics, and clinical profile. Clin Ther. 2011 Dec;33(12):1853-67.
Stoffers J, Vollm BA, Rucker G, et al. Pharmacological interventions for **borderline personality disorder**. Cochrane Database Syst Rev. 2010 Jun 16;6:CD005653.
Straus SM, Bleumink GS, Dieleman JP, et al. Antipsychotics and the **risk of sudden cardiac death**. Arch Intern Med. 2004 Jun 28;164(12):1293-7. Erratum in: Arch Intern Med. 2004 Sep 27;164(17):1839. The risk of sudden cardiac death was highest among those using butyrophenone antipsychotics, those with a defined daily dose equivalent of more than 0.5 and short-term (</=90 days) users.
St Clair D, Xu M, Wang P, Yu Y, Fang Y, Zhang F, Zheng X, Gu N, Feng G, Sham P, He L. Rates of adult schizophrenia following prenatal exposure to the Chinese **famine** of 1959-1961. JAMA. 2005 Aug 3;294(5):557-62.
Street J, Mitan S, Tamura R, et al. Olanzapine in the treatment of psychosis and behavioral disturbances associated with Alzheimer's disease. Eur J Neurology 1998;5:S39.
Steinberg M, Lyketsos CG. **Atypical antipsychotic use in patients with dementia**: managing safety concerns. Am J Psychiatry. 2012 Sep 1;169(9):900-6.
Steiner J, Berger M, Guest PC, et al. Assessment of **Insulin Resistance** Among Drug-Naive Patients With First-Episode Schizophrenia in the Context of Hormonal Stress Axis Activation. JAMA Psychiatry. 2017 Jul 19.
Stepniak B, Papiol S, Hammer C, et al. **Accumulated environmental risk determining age at schizophrenia onset**: a deep phenotyping-based study. Lancet Psychiatry 2014;1:444–53.
Stocks SJ, Kontopantelis E, Webb RT, Avery AJ, Burns A, Ashcroft DM. **Antipsychotic prescribing to patients diagnosed with dementia without a diagnosis of psychosis** in the context of national guidance and

drug safety warnings: longitudinal study in UK general practice. Drug Saf 2017;358:679-92. doi:10.1007/s40264-017-0538-x pmid:28439716.
Stubbs B, Vancampfort D, Hallgren M, et al. **EPA guidance on physical activity as a treatment for severe mental illness**: a meta-review of the evidence and Position Statement from the European Psychiatric Association (EPA), supported by the International Organization of Physical Therapists in Mental Health (IOPTMH). Eur Psychiatry. 2018 Oct;54:124-144.
Strom BL, Eng SM, Faich G, Reynolds RF, et al. Comparative Mortality Associated With **Ziprasidone and Olanzapine** in Real-World Use Among 18,154 Patients With Schizophrenia: The Ziprasidone Observational Study of Cardiac Outcomes (ZODIAC). Am J Psychiatry. 2010 Nov 1.
Stroup TS, Lieberman JA, McEvoy JP, et al. Effectiveness of **olanzapine**, quetiapine, **risperidone**, and ziprasidone in patients with chronic schizophrenia following discontinuation of a previous atypical antipsychotic (from the **Catie** trial). Am J Psychiatry. 2006 Apr;163(4):611-22.
Stroup, T. Scott, McEvoy, Joseph P., Ring, Kimberly D., et al. the Schizophrenia Trials Network, A Randomized Trial Examining the Effectiveness of Switching **From Olanzapine, Quetiapine, or Risperidone to Aripiprazole** to Reduce Metabolic Risk: Comparison of Antipsychotics for Metabolic Problems (**CAMP**). Am J Psychiatry 2011 168: 947-956
Stroup TS, Gerhard T, Crystal S, et al. Comparative effectiveness of **adjunctive psychotropic medications** in patients with schizophrenia [online Feb 20, 2019]. JAMA Psychiatry. doi:10.1001/jamapsychiatry.2018.4489
Subotnik, Kenneth L., Nuechterlein, Keith H., Ventura, Joseph, et al. **Risperidone Nonadherence** and Return of Positive Symptoms in the Early Course of Schizophrenia. Am J Psychiatry 2011 0: appi.ajp.2010.09010087.
Subotnik KL, Casaus LR, Ventura J, et al. **Long-Acting Injectable Risperidone** for Relapse Prevention and Control of Breakthrough Symptoms After a Recent First Episode of Schizophrenia : A Randomized Clinical Trial. JAMA Psychiatry. 2015 Jun 24.
Suh GH, Shah A. Effect of **antipsychotics on mortality** in elderly patients with dementia: a 1-year prospective study in a nursing home. Int Psychogeriatr. 2005 Sep;17(3):429-41.
Sullivan SA, Hamilton W, Tilling K, et al. Association of **primary care consultation patterns with early signs and symptoms of psychosis**. JAMA Netw Open. 2018;1(7):e185174. doi:10.1001/jamanetworkopen.2018.5174
Sultana J, Chang CK, Hayes RD, et al. Associations between risk of **mortality and atypical antipsychotic use in vascular dementia**: a clinical cohort study. Int J Geriatr Psychiatry. 2014 Mar 14. doi: 10.1002/gps.4101.
Sultzer DL, Davis SM, et al. **CATIE-AD**. Clinical **symptom responses** to atypical antipsychotic medications in Alzheimer's disease: phase 1 outcomes CATIE-AD effectiveness trial. Am J Psychiatry. 2008 Jul;165(7):844-54.
Suppes T, Silva R, et al. **Lurasidone** for the Treatment of **Major Depressive Disorder With Mixed Features**: A Randomized, Double-Blind, Placebo-Controlled Study. Am J Psychiatry. 2015 Nov 10:appiajp201515060770.
Suttajit S, Srisurapanont M, Xia J, et al. **Quetiapine versus typical antipsychotic** medications for schizophrenia. Cochrane Database Syst Rev. 2013;5:CD007815. Quetiapine may not differ from typical antipsychotics in the treatment of positive symptoms and general psychopathology. There are no clear differences in terms of the treatment of negative symptoms. However, it causes fewer adverse effects in terms of abnormal ECG, extrapyramidal effects, abnormal prolactin levels and weight gain.
Swanson JW, et al. Facilitated psychiatric **advance directives**: a randomized trial of an intervention to foster advance treatment planning among persons with severe mental illness. Am J Psychiatry. 2006 Nov;163(11):1943-51.
Szarfman A, et al. Atypical antipsychotics and **pituitary tumors**: a pharmacovigilance study. Pharmacotherapy. 2006 Jun;26(6):748-58.
Szczepura A, et al. **Antipsychotic prescribing in care homes before and after launch of a national dementia strategy**: an observational study in English institutions over a 4-year period. BMJ Open 2016;358:e009882.
Szegedi A;Durgam S;Mackle M;et al. Randomized, Double-Blind, Placebo-Controlled Trial of **Asenapine Maintenance Therapy in Adults With an Acute Manic or Mixed Episode** Associated With Bipolar I Disorder. Am J Psychiatry. 2017 Sep 26:appiajp201716040419.
Szmulewicz AG, Angriman F, Pedroso FE, et al. **Long-Term Antipsychotic Use and Major Cardiovascular Events**: A Retrospective Cohort Study. J Clin Psychiatry. 2017 Sep/Oct;78(8):e905-e912.
TardyM,HuhnM, Engel RR, Leucht S. **Perphenazine versus low-potency first-generation antipsychotic** drugs for schizophrenia. Cochrane Database of Systematic Reviews 2014, Issue 10. Art. No.: CD009369. DOI: 10.1002/14651858.CD009369.pub2. The results do not show a superiority in efficacy of high-potency perphenazine compared with low-potency first-generation antipsychotics. There is some evidence that perphenazine is more likely to cause akathisia and less likely to cause severe toxicity, but most adverse effect results were equivocal. The number of studies as well as the quality of studies is low, with quality of evidence for the main outcomes ranging from moderate to very low, so more randomised evidence would be needed for conclusions to be made.
Targum SD, Abbott JL. Efficacy of quetiapine in Parkinson's patients with psychosis. *J Clin Psychopharmacol* 2000; 20(1): 54-60.
Tariot PN, Ryan JM, Porsteinsson AP, Loy R, Schneider LS. Pharmacologic therapy for behavioral symptoms of Alzheimer's disease. Clin Geriatr Med 2001;17:359-76.
Tariot PN, Salzman C, Yeung PP, Pultz J, Rak IW. Long-term use of quetiapine in elderly patients with psychotic disorders. Clin Ther 2000;22:1068-84.
Tchoukhine E, Takala P, et al. **Orlistat** in clozapine- or olanzapine-treated patients with overweight or obesity: a 16-week open-label extension phase and both phases of a randomized controlled trial. J Clin Psychiatry. 2010 Aug 24.
Temmingh HS, Williams T, Siegfried N, Stein DJ. **Risperidone versus other antipsychotics for people with severe mental illness and co-occurring substance misuse**. Cochrane Database of Systematic Reviews 2018, Issue 1. Art. No.: CD011057. There is not sufficient good-quality evidence available to determine the effects of risperidone compared with other antipsychotics in people with a dual diagnosis. Few trials compared risperidone with first-generation agents, leading to limited applicability to settings where access to second-generation agents is limited, such as in low- and middle-income countries. Moreover, heterogeneity in trial design and measurement of outcomes precluded the use of many trials in our analyses.
Tenback DE, van Harten PN, van Os J. Non-therapeutic risk factors for onset of **tardive dyskinesia** in schizophrenia: A meta-analysis. Mov Disord. 2009 Jul 30. [Epub ahead of print] However, the fact that early EPS predicts onset of TD has important clinical and research implications.
Teplin LA, Welty LJ, Abram KM, et al. Prevalence and Persistence of Psychiatric Disorders in **Youth After Detention**: A Prospective Longitudinal Study. Arch Gen Psychiatry. 2012 Oct 1;69(10):1031-1043.
The French Clozapine Parkinson Study Group. Clozapine in drug-induced psychosis in Parkinson's disease. The Lancet 1999;353:2041-2042.
The Parkinson Study Group. Low dose clozapine for the treatment of drug-induced psychosis in Parkinson's disease. *NEJM* 1999;340(10):757-63.
Thornicroft G, et al.; INDIGO Study Group. Global pattern of **experienced and anticipated discrimination** against people with schizophrenia: a cross-sectional survey. Lancet. 2009 Jan 31;373(9661):408-15. Epub 2009 Jan 21.
Thornicroft G, Farrelly S, Szmukler G, et al. Clinical outcomes of Joint Crisis Plans to reduce compulsory treatment for people with psychosis: a randomised controlled trial. (**CRIMSON**) Lancet 2013; online March 26.
Tiihonen J, Halonen P, Wahlbeck K, et a. Topiramate Add-On in Treatment-Resistant Schizophrenia: A Randomized, Double-Blind, Placebo-Controlled, Crossover Trial. J Clin Psychiatry. 2005 Aug;66(8):1012-1015.
Tiihonen J, et al. Effectiveness of antipsychotic treatments in a nationwide cohort of patients in community care after first hospitalisation due to schizophrenia and schizoaffective disorder: observational follow-up study. BMJ. 2006 Jul 6; [Epub ahead of print] The effectiveness of first and second generation antipsychotics varies greatly in the community. Patients treated with perphenazine depot, clozapine, or olanzapine have a substantially lower risk of rehospitalisation or discontinuation (for any reason) of their initial treatment than do patients treated with haloperidol. Excess mortality is seen mostly in patients not using antipsychotic drugs.
Tiihonen J, Lönnqvist J, Wahlbeck K, et al. 11-year follow-up of mortality in patients with schizophrenia: a population-based cohort study (**FIN11 study**). Lancet. 2009 Jul 10. [Epub ahead of print] Long-term treatment with antipsychotic drugs is associated with lower mortality compared with no antipsychotic use. Second-generation drugs are a highly heterogeneous group, and clozapine seems to be associated with a substantially lower mortality than any other antipsychotics. Restrictions on the use of clozapine should be reassessed.
Tiihonen J, Haukka J, Taylor M, et al. A Nationwide Cohort Study of Oral and **Depot Antipsychotics After First Hospitalization** for Schizophrenia. Am J Psychiatry. 2011 Mar 1.
Tiihonen J, Suokas JT, Suvisaari JM, et al. **Polypharmacy with antipsychotics, antidepressants, or benzodiazepines** and mortality in schizophrenia. Arch Gen Psychiatry. 2012 May;69(5):476-83.
Tiihonen J, Mittendorfer-Rutz E, et al. **Mortality and Cumulative Exposure to Antipsychotics, Antidepressants, and Benzodiazepines** in patients with Schizophrenia: An Observational Follow-Up Study. Am J Psyc. 2015 Dec.
Tiihonen J, et al. **Mortality** and cumulative exposure to **antipsychotics, antidepressants, and benzodiazepines** in patients with schizophrenia: an observational follow-up study. Am J Psychiatry 2016;173:600–6.
Tiihonen J, Mittendorfer-Rutz E, Majak M, et al. **Real-World Effectiveness of Antipsychotic Treatments** in a Nationwide Cohort of 29 823 Patients With Schizophrenia. JAMA Psychiatry. 2017 Jun 7.
Tiihonen J, Taipale H, Mehtälä J, et al. Association of **antipsychotic polypharmacy vs monotherapy with psychiatric rehospitalization** among adults with schizophrenia [online Feb 20, 2019]. JAMA Psychiatry. doi:10.1001/jamapsychiatry.2018.4320
Tjia J, Field T, Mazor K, et al. Dissemination of Evidence-Based Antipsychotic Prescribing Guidelines to Nursing Homes: A Cluster Randomized Trial. J Am Geriatr Soc. 2015 Jul;63(7):1289-98.
Tjia J, Hunnicutt JN, Herndon L, et al. Association of a **Communication Training Program** With Use of Antipsychotics in Nursing Homes. JAMA Intern Med. 2017 Apr 17.
Tolppanen AM, Koponen M, Tanskanen A, et al. **Antipsychotic use and risk of hospitalisation or death** due to pneumonia in persons with and without Alzheimer's disease. Chest. 2016 Jun 10.
Tomasik J, Lago SG, Vázquez-Bourgon J, et al. **Association of Insulin Resistance With Schizophrenia** Polygenic Risk Score and Response to Antipsychotic Treatment. JAMA Psychiatry. 2019 Apr 3.
Ton J, Ramji J, Allan GM. Antipsychotics for agitation in dementia. Can Fam Physician. 2018 May;64(5):369.
Torstensson M, Leth-Moller K, et al. Danish register-based study on the association between specific **antipsychotic drugs and fractures** in elderly individuals. Age Ageing. 2016 Dec 7.
Tosh G, Clifton AV, Xia J, et al. **General physical health advice** for people with serious mental illness. Cochrane Database Syst Rev. 2014 Mar 28;3:CD008567.

Treatment Guidelines: Drugs for Psychiatric Disorders. **The Medical Letter**: July, **2003**; p. 69-76. (**Medical Letter "Treatment Guidelines- Drugs for Psychiatric Disorders** Vol 4 (Issue 46) June **2006**.)

Trifirò Gianluca, Gambassi Giovanni, Sen Elif F., et al. Association of **Community-Acquired Pneumonia** With **Antipsychotic** Drug Use in Elderly Patients: A Nested Case–Control Study.*Ann Intern Med* April 6, 2010.

Tritos NA, Klibanski A. **Hyperprolactinemia**. JAMA. 2015 Oct 27;314(16):1742-1743.

Tsai AC, Rosenlicht NZ, Jureidini JN, et al. **Aripiprazole** in the maintenance treatment of bipolar disorder: a **critical review** of the evidence and its dissemination into the scientific literature. PLoS Med 2011;8:e1000434.

Turkington D, et al. Outcomes of an effectiveness trial of **cognitive-behavioural intervention** by mental health nurses in schizophrenia. Br J Psychiatry. 2006 Jul;189:36-40.

Turner EH, Knoepflmacher D, Shapley L. **Publication Bias in Antipsychotic Trials**: An Analysis of Efficacy Comparing the Published Literature to the US Food and Drug Administration Database. PLoS Med. 2012 Mar;9(3):e1001189.

Turner DT, van der Gaag M, Karyotaki E, et al. **Psychological Interventions for Psychosis**: A Meta-Analysis of Comparative Outcome Studies**.** Am J Psychiatry. 2014 Feb 14.

Tyrer P, et al. Risperidone, haloperidol, and placebo in the treatment of aggressive challenging behaviour in patients with **intellectual disability**: a randomised controlled trial. Lancet. 2008 Jan 5;371(9606):57-63. Antipsychotic drugs should no longer be regarded as an acceptable routine treatment for aggressive challenging behaviour in people with intellectual disability.

Udow SJ, Freitas ME, Fox SH, et al. Exacerbation of **psychosis triggered by a synthetic cannabinoid** in a 70-year-old woman with Parkinson disease. CMAJ. 2018 Jan 15;190(2):E50-E52.

Ularntinon S, Tzuang D, Dahl G, Shaw RJ. Concurrent treatment of **steroid-related** mood and psychotic symptoms with risperidone. Pediatrics. 2010 May;125(5):e1241-5. Epub 2010 Apr 12.

Uttley L, Scope A, Stevenson M, et al. Systematic review and economic modelling of the clinical effectiveness and cost-effectiveness of **art therapy** among people with non-psychotic mental health disorders. Health Technol Assess. 2015 Mar;19(18):1-120. : From the limited available evidence, art therapy was associated with positive effects when compared with a control in a number of studies in patients with different clinical profiles, and it was reported to be an acceptable treatment and was associated with a number of benefits. Art therapy appeared to be cost-effective compared with wait-list but further studies are needed to confirm this finding as well as evidence to inform future cost-effective analyses of art therapy versus other treatments.

Van Boekholt AA, Hartong EG, Huntjens-Fleuren H, et al. **Quetiapine concentrations during exclusive breastfeeding and maternal** quetiapine use. Ann Pharmacother. 2015 Jun;49(6):743-4.

Varghese D, et al. Prevalence of **Antidiabetic and Antilipidemic Medications** in **Children and Adolescents** Treated With **Atypical Antipsychotics** in a Virginia Medicaid Population. Ann Pharmacother. 2016 Mar 23.

Various authors. **Long-acting injectable antipsychotics**: recommendations for clinicians. Can J Psychiatry 2013;58(5 Suppl 1):1-36S. http://publications.cpa-apc.org/browse/documents/593 (accessed July 31, 2013).

Veijola J, Guo JY, Moilanen JS, et al. **Longitudinal changes in total brain volume** in schizophrenia: relation to symptom severity, cognition and antipsychotic medication. PLoS One. 2014 Jul 18;9(7):e101689.

Vigen CL, Mack WJ, Keefe RS, et al. **Cognitive Effects of Atypical Antipsychotic** Medications in Patients With Alzheimer's Disease: Outcomes From **CATIE-AD**. Am J Psychiatry. 2011 May 15.

Waade RB, Molden E, Martinsen MI, et al. **Psychotropics and weak opioid analgesics in plasma samples of older hip fracture patients** - detection frequencies and consistency with drug records. Br J Clin Pharmacol. 2017 Mar 7

Walitt B, Klose P, Uceyler N, et al. Antipsychotics **for fibromyalgia** in adults. Cochrane Database Syst Rev. 2016 Jun 2;6:CD011804. Very low quality evidence suggests that quetiapine may be considered for a time-limited trial (4 to 12 weeks) to reduce pain, sleep problems, depression and anxiety in fibromyalgia patients with major depression. Potential side effects such as weight gain should be balanced against the potential benefits in shared decision making with the patient.

Wang CY, Xiang YT, Cai ZJ, et al. For the **Risperidone Maintenance** Treatment in Schizophrenia (**RMTS**) investigators. Risperidone Maintenance Treatment in Schizophrenia: A Randomized, Controlled Trial. Am J Psychiatry. 2010 Mar 15. (initial optimal therapeutic dose continued for 4 weeks ~4.2mg/d, followed by a 50% dose reduction that was maintained until the end of the study), or a 26-week group (initial optimal therapeutic dose continued for 26 weeks, followed by a 50% dose reduction until the end of the study).

Wang MT, Liou JT, Huang YW, et al. Use of antipsychotics and **risk of venous thromboembolism** in postmenopausal women. A population-based nested case-control study. Thromb Haemost. 2016 Mar 3;115(6).

Wang MT, Tsai CL, Lin CW, et al. Association Between **Antipsychotic Agents and Risk of Acute Respiratory Failure** in Patients With Chronic Obstructive Pulmonary Disease. JAMA Psychiatry. 2017 Jan 4.

Wang Q, Wu HM, Yue W, et al; Chinese Antipsychotics Pharmacogenomics Consortium. **Effect of damaging rare mutations in synapse-related gene sets** on response to short-term antipsychotic medication in Chinese patients with schizophrenia: a randomized clinical trial [online Nov 7, 2018]. JAMA Psychiatry.

Wang S et al. Age, Antipsychotics, and the **Risk of Ischemic Stroke** in the Veterans Health Administration. Stroke. 2011 Oct 27.

Wang AM, Pradhan S, Coughlin JM, et al. Assessing **Brain Metabolism With 7-T Proton Magnetic Resonance Spectroscopy in Patients With First-Episode Psychosis**. JAMA Psychiatry. 2019 Jan 9.

Ward RK, Zamorski MA. Benefits and risks of psychiatric medications during **pregnancy**. Am Fam Physician. 2002 Aug 15;66(4):629-36.

Watkins ME, Newport DJ. Psychosis in pregnancy. Obstet Gynecol. 2009 Jun;113(6):1349-53.

Watt JA, Gomes T, Bronskill SE, et al. Comparative risk of **harm associated with trazodone or atypical antipsychotic use in older adults with dementia**: a retrospective cohort study. CMAJ. 2018 Nov 26;190(47):E1376-E1383.

Weiner WJ. **Quetiapine for L-dopa induced psychosis** in PD. Neurology 2000;54: 1538.

Weintraub D, Chiang C, Kim HM, et al. Association of Antipsychotic Use With **Mortality Risk in Patients With Parkinson Disease**. JAMA Neurol. 2016 Mar 21

Weiser M, Levi L, Zamora D, et al. Effect of **Adjunctive Estradiol on Schizophrenia** Among Women of Childbearing Age: A Randomized Clinical Trial. JAMA Psychiatry. 2019 Jul 31.

Weisz JR, Kuppens S, Eckshtain D, et al. Performance of evidence-based **youth psychotherapies** compared with usual clinical care: a multilevel meta-analysis. JAMA Psychiatry. 2013 Jul;70(7):750-61.

Werbeloff N, Drukker M, Dohrenwend BP, et al. **Self-reported Attenuated Psychotic Symptoms as Forerunners** of Severe Mental Disorders Later in Life. Arch Gen Psychiatry. 2012 Jan 2.

Wharton S, Kuk JL, Petrova L, et al. Effectiveness of a Community-Based **Weight Management Program for Patients Taking Antidepressants and/or Antipsychotics**. Obesity (Silver Spring). 2019 Sep;27(9):1539-1544.

Whitehead C, Moss S, Cardno A, et al. **Antidepressants for people with both schizophrenia and depression**. Cochrane Database Syst Rev. 2002;(2):CD002305.

Whitley H, Lindsey W. **Sex-based** differences in drug activity. Am Fam Physician. 2009 Dec 1;80(11):1254-8.

Williams R, Malla A, Roy MA, et al. What Is the **Place of Clozapine** in the Treatment of Early Psychosis **in Canada**? Can J Psychiatry. 2016 May 18.

Wimberley T, Støvring H, Sørensen HJ, et al. **Predictors of treatment resistance** in patients with **schizophrenia**: a population-based cohort study. Lancet Psychiatry. 2016 Apr;3(4):358-66.

Wimberley T, MacCabe JH, Laursen TM, et al. **Mortality and Self-Harm in Association With Clozapine** in Treatment-Resistant Schizophrenia. Am J Psychiatry. 2017 Jul 28:appiajp201716091097.

Winkelbeiner S, Leucht S, Kane JM, Homan P. Evaluation of **Differences in Individual Treatment Response in Schizophrenia Spectrum Disorders**: A Meta-analysis. JAMA Psychiatry. 2019 Jun 3.

Wisniewski CS, Robert S. Strategies for transitioning therapy to **aripiprazole from other antipsychotics** in schizophrenia. Ann Pharmacother. 2012 Jul;46(7-8):1097-104.

Woods A, Jones N, Alderson-Day B, et al. Experiences of **hearing voices**: analysis of a novel phenomenological survey. Lancet Psychiatry. 2015 Apr

Woods SW, Saksa JR, Baker CB, Cohen SJ, Tek C. Effects of levetiracetam (0.5-3g/d) on **tardive dyskinesia**: a randomized, double-blind, placebo-controlled study. J Clin Psychiatry. 2008 Apr;69(4):546-54. (n=50 12+12 weeks) **Levetiracetam appeared effective for TD** in this study. The mechanisms of its therapeutic effect are unclear but may involve reducing neuronal hypersynchrony in basal ganglia.

Woods SW. Chlorpromazine equivalent doses for the newer atypical antipsychotics. J Clin Psychiatry. 2003 Jun;64(6):663-7.

Woods SW, Morgenstern H, Saksa JR, et al. **Incidence of tardive dyskinesia** with atypical versus conventional antipsychotic medications: a prospective cohort study. J Clin Psychiatry. 2010 Apr;71(4):463-74.

Wolters EC. Dopamimetic psychosis in Parkinson's disease patients-diagnosis and treatment. Neurology 1999: 52 (Suppl 3): S10-13.

Wooltorton E. Risperidone (Risperdal): increased rate of cerebrovascular events in dementia trials. CMAJ. 2002 Nov 26;167(11):1269-70.

Wu Chou AI, Wang YC, Lin CL, Kao CH. **Female schizophrenia patients and risk of breast cancer**: A population-based cohort study. Schizophr Res. 2017 Oct;188:165-171.

Wu RR, Zhao JP, Jin H, et al. Lifestyle intervention and **metformin for treatment of antipsychotic-induced** weight gain: a randomized controlled trial. JAMA. 2008 Jan 9;299(2):185-93.Lifestyle intervention and metformin alone and in combination demonstrated efficacy for antipsychotic-induced weight gain. Lifestyle intervention plus metformin showed the best effect on weight loss. Metformin alone was more effective in weight loss and improving insulin sensitivity than lifestyle intervention alone.

Wu RR, Jin H, Gao K, et al. **Metformin** for treatment of **antipsychotic-induced amenorrhea and weight gain** in women with first-episode schizophrenia: a double-blind, randomized, placebo-controlled study. Am J Psychiatry. 2012 Aug 1;169(8):813-21.

Wunderink L, Nieboer RM, Wiersma D, et al. **Recovery in Remitted First-Episode Psychosis** at 7 Years of Follow-up of an Early Dose Reduction/Discontinuation or Maintenance Treatment Strategy: Long-term Follow-up of a 2-Year Randomized Clinical Trial. JAMA Psychiatry. 2013 Jul 3.

Wykes T, Huddy V, Cellard C, et al. A meta-analysis of **cognitive remediation** for schizophrenia: methodology and effect sizes. Am J Psychiatry. 2011 May;168(5):472-85.

Wykes T. **Cognitive-behaviour therapy** and schizophrenia. Evid Based Ment Health. 2014 Aug;17(3):67-8.
Yang T, Liu Q, Lu M, et al. Efficacy of **olanzapine** for the prophylaxis of **chemotherapy-induced nausea and vomiting**: A meta-analysis. Br J Clin Pharmacol. 2017 Jan 23.
Yatham LN et al. Canadian Network for Mood and Anxiety Treatments (**CANMAT**) guidelines for the management of patients with **bipolar** disorder: update **2006**. Bipolar Disorders 2006:8: 1-19
Yatham LN, Mackala S, et al. **Lurasidone** versus treatment as usual for cognitive impairment in **euthymic patients with bipolar I disorder**: a randomised, open-label, pilot study. Lancet Psychiatry 2017; published online Feb 6
Yeh CT, Wu AT, Chang PM, et al. **Trifluoperazine**, an antipsychotic agent, **inhibits cancer stem cell growth** and overcomes drug resistance of lung cancer. Am J Respir Crit Care Med. 2012 Dec 1;186(11):1180-8.
Yohanna D, Cifu AS. **Antipsychotics to Treat Agitation or Psychosis in Patients With Dementia**. JAMA. 2017 Sep 19;318(11):1057-1058.
Yunusa I, Alsumali A, Garba AE, et al. Assessment of Reported Comparative Effectiveness and Safety of **Atypical Antipsychotics** in the Treatment of Behavioral and Psychological Symptoms of Dementia: A Network Meta-analysis. JAMA Netw Open. 2019 Mar 1;2(3):e190828
Zaman H, Sampson SJ, Beck ALS, et al. **Benzodiazepines for psychosis-induced aggression or agitation**. Cochrane Database of Systematic Reviews 2017, Issue 12. Art. No.: CD003079. The evidence from RCTs for the use of benzodiazepines alone is not good. There were relatively few good data. Most trials were too small to highlight differences in either positive or negative effects. Adding a benzodiazepine to other drugs does not seem to confer clear advantage and has potential for adding unnecessary adverse effects. Sole use of older antipsychotics unaccompanied by anticholinergic drugs seems difficult to justify. Much more high-quality research is still needed in this area.
Zehtabchi S. **Aripiprazole vs. Placebo or Haloperidol** for Schizophrenia. Am Fam Physician. 2016 Dec 1;94(11):877-878.
Zhang JP, et al. Efficacy and safety of individual **second-generation vs. first-generation antipsychotics in first-episode psychosis**: a systematic review and meta-analysis. Int J Neuropsychopharmacol. 2013;16(6): 1205-1218.
Zheng W, Xiang YT, Xiang YQ, et al. Efficacy and safety of **adjunctive topiramate for schizophrenia**: a meta-analysis of randomized controlled trials. Acta Psychiatr Scand 2016;134:385–98.
Zheng W, Wang S, Ungvari GS, et al. **Amantadine** for **Antipsychotic-Related Weight Gain**: Meta- Analysis of Randomized Placebo-Controlled Trials. J Clin Psychopharmacol. 2017 Jun;37(3):341-346.
Zhong KX, et al. Comparison of **quetiapine and risperidone** in the treatment of schizophrenia: A randomized, double-blind, flexible-dose, 8-week study. J Clin Psychiatry. 2006 Jul;67(7):1093-103.
Zhong KX, Tariot PN, Mintzer J, Minkwitz MC, Devine NA. **Quetiapine to treat agitation in dementia**: a randomized, double-blind, placebo-controlled study. Curr Alzheimer Res. 2007 Feb;4(1):81-93.(~200mg/day effective)
Zhu Y, Krause M, et al. **Antipsychotic drugs for the acute treatment of patients with a first episode of schizophrenia**: a systematic review with pairwise and network meta-analyses. Lancet Psychiatry. 2017 Sep;4(9):694-705.
Zhuo C, Triplett PT. Association of Schizophrenia With the **Risk of Breast Cancer Incidence**: A Meta-analysis. JAMA Psychiatry. 2018 Mar 7.
Zipursky RB, Gu H, Green AI, et al. Course and predictors of **weight gain in people with first-episode psychosis** treated with olanzapine or haloperidol. Br J Psychiatry. 2005;187(6): 537-543.
Zito JM, Burcu M, McKean S, et al. Pediatric Use of **Antipsychotic Medications Before and After Medicaid Peer Review Implementation**. JAMA Psychiatry. 2017 Nov 15.

June 2005 Health Canada & April 2005 FDA Issues Public Health Advisory for **Antipsychotic Drugs used for Treatment of Behavioral Disorders in Elderly Patients**
http://www.fda.gov/bbs/topics/ANSWERS/2005/ANS01350.html http://www.hc-sc.gc.ca/ahc-asc/media/advisories-avis/2005/2005_63_e.html (Singh S, Wooltorton E. Increased mortality among elderly patients with dementia using atypical antipsychotics. CMAJ. 2005 Aug 2;173(3):252.) (Medical Letter August 1,2005 -Atypical antipsychotics in the Elderly FDA n=5106 17 RCTs mortality rate of 4.5% with atypical antipsychotic therapy vs 2.6% with placebo, most deaths were due to cardiovascular & infectious causes such as pneumonia.) Schneider LS, Dagerman KS, Insel P. Risk of death with atypical antipsychotic drug treatment for dementia: **meta-analysis** of randomized placebo-controlled trials. JAMA. 2005 Oct 19;294(15):1934-43. (InfoPOEMs: The use of atypical antipsychotic drugs for even short periods (less than 8 to 12 weeks) is associated with a significantly increased risk of death. Antipsychotic drugs should be used only in individual situations of an identifiable risk of harm and when alternate therapies have failed. (LOE = 1a)) {15 trials (9 unpublished) of atypical antipsychotics vs placebo for ~10-12weeks n=5110; 3.5 vs 2.3% death rate}(Wang PS et al. **Risk of Death** in Elderly Users of Conventional vs Atypical Antipsychotic Medications. N Engl J Med 2005;353:2335-41. Conclusion: If confirmed, these results suggest that conventional antipsychotic medications are at least as likely as atypical agents to increase the risk of death among elderly persons and that conventional drugs should no be used to replace atypical agents discontinued in response to the FDA warning. (InfoPOEMs: It seems reasonable to conclude that conventional and atypical antipsychotic agents are both associated with an increased risk of death in elderly patients. The limitations of this study do not allow us to confidently conclude that older agents are less safe than newer agents, though. (LOE = 2b)) (Gill SS, Bronskill SE, Normand SL, Anderson GM, Sykora K, Lam K, Bell CM, Lee PE, Fischer HD, Herrmann N, Gurwitz JH, Rochon PA. Antipsychotic drug use and mortality in older adults with dementia. Ann Intern Med. 2007 Jun 5;146(11):775-86. Atypical antipsychotic use is associated with an increased risk for death compared with nonuse among older adults with dementia. The risk for death may be greater with conventional antipsychotics than with atypical antipsychotics.)
Rochon PA, Normand SL, et al. Antipsychotic therapy and short-term **serious events** in older adults with dementia. Arch Intern Med. 2008 May 26;168(10):1090-6. Relative to those who received no antipsychotic therapy, community-dwelling older adults newly dispensed an **atypical antipsychotic therapy were 3.2 times** more likely (95% confidence interval, 2.77-3.68) and those who received **conventional antipsychotic therapy were 3.8 times** more likely (95% confidence interval, 3.31-4.39) to develop any serious event during the 30 days of follow-up. The pattern of serious events was similar but less pronounced among older adults living in a nursing home. Serious events, as indicated by a hospital admission or death, are frequent following the short-term use of antipsychotic drugs in older adults with dementia. Antipsychotic drugs should be used with caution even when short-term therapy is being prescribed.
FDA Conventional Antipsychotic Warning June/08 http://www.fda.gov/cder/drug/InfoSheets/HCP/antipsychotics_conventional.htm
Douglas IJ, Smeeth L. Exposure to antipsychotics and risk of stroke: self controlled case series study. BMJ. 2008 Aug 28;337:a1227. doi: 10.1136/bmj.a1227. **All antipsychotics are associated with an increased risk of stroke**, and the risk might be higher in patients receiving atypical antipsychotics than those receiving typical antipsychotics. People with dementia seem to be at a higher risk of an associated stroke than people without dementia & use of antipsychotics should, when possible, be avoided in these patients.
Ray WA, Chung CP, Murray KT et al. Atypical antipsychotic drugs and the risk of sudden cardiac death. New Engl J Med 2009; 360: 225-235.

Clinical Handbook of Psychotropic Drugs 18th Edition, Bezchlibnyk-Butler K, Jeffries J. 2009
Clinical Handbook of Psychotropic Drugs, 22nd Edition, Procyshyn RM, Bezchlibnyk-Butler KZ, Jeffries JJ. 2017.
Drugs in Pregnancy & Lactation 9th edition 2011
Drug Information Handbook Lexi 17th edition 2008-2009
Therapeutic Choices 5th edition 2007
Geriatric Dosage Handbook 6th Edition
Pharmacotherapy Handbook 2nd edition (Wells,Dipiro et al.)
Micromedex 2016

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Epworth Sleepiness Scale: Score 0-10: Normal Daytime Sleepiness, Score >10: Excessive Daytime Sleepiness http://epworthsleepinessscale.com/about-the-ess/
Resource for Self Help: Silberman, Stephanie. The Insomnia Workbook. A Comprehensive Guide to Getting the Sleep You Need. New Harbinger Publications, Inc. 2009.
Management of Chronic Insomnia – Support Tool (Centre for Effective Practice, Toronto): https://thewellhealth.ca/wp-content/uploads/2017/01/20170116_Insomnia_FINAL.pdf
Online Canadian Resources - https://mysleepwell.ca/, http://sinkintosleep.com/, https://drcolleencarney.com/

SEDATIVE COMPARISON CHART

References:

Adolescent Sleep Working Group; Committee on Adelescence; Council on School Health. **School start times** for adolescents. Pediatrics. 2014 Sep;134(3):642-9.

Aggarwal B, Makarem N, Shah R, et al. Effects of **Inadequate Sleep on Blood Pressure and Endothelial Inflammation** in Women: Findings From the American Heart Association Go Red for Women Strategically Focused Research Network. J Am Heart Assoc. 2018 Jun 9;7(12).

Al Khatib HK, et al. **Sleep extension** is a feasible lifestyle intervention in free-living adults who are habitually short sleepers: a potential strategy for decreasing intake of free sugars? A randomized controlled pilot study. Am J Clin Nutr. 2018 Jan 1;107(1):43-53.

Alessi C, Martin JL, Fiorentino L, et al. **Cognitive Behavioral Therapy** for Insomnia in Older Veterans Using Nonclinician Sleep Coaches: Randomized Controlled Trial. J Am Geriatr Soc. 2016 Aug 22.

Allan GM, Lindblad AJ, Varughese J. Trouble sleeping: spend **less time in bed**? Canadian Family Physician. 2017 August;63:613

Alsaadi SM, McAuley JH, Hush JM, et al. Poor sleep quality is strongly associated with subsequent pain intensity in patients with **acute low back pain**. Arthritis Rheumatol. 2014 May;66(5):1388-94.

Ananthakrishnan AN, Long MD, Martin CF, et al. Sleep disturbance and **risk of active disease in patients with Crohn's disease and ulcerative colitis**. Clin Gastroenterol Hepatol. 2013 Aug;11(8):965-71.

Anderson SE, Andridge R, Whitaker RC. **Bedtime in Preschool**-Aged Children and Risk for Adolescent Obesity. J Pediatr. 2016 Jul 8.

Anthierens, Sibyl, Pasteels, Inge, Habraken, H, et al. Barriers to nonpharmacologic treatments for **stress, anxiety, and insomnia**: Family physicians' attitudes toward benzodiazepine prescribing. Can Fam Physician 2010 56: e398-406.

Appleton RE et al. The use of **MElatonin** in children with Neurodevelopmental Disorders and impaired Sleep: a randomised, double-blind, placebo-controlled, parallel study (MENDS). Health Technol Assess 2012; 16: 1-239.

Araújo J, Severo M, Ramos E. Sleep Duration and **Adiposity** During Adolescence. Pediatrics. 2012 Oct 1.

Archbold KH, Vasquez MM, Goodwin J et al. Effects of **Sleep Patterns** and Obesity on Increases in **Blood Pressure** in a 5-Year Period: Report from the Tucson Children's Assessment of Sleep Apnea Study. J Pediatr. 2012 Jan 25.

Au CT, Ho CK, Wing YK, et al. Acute and Chronic Effects of **Sleep Duration on Blood Pressure**. Pediatrics. 2013 Dec 16

Auld F, Maschauer EL, Morrison I, et al. **Evidence for the efficacy of melatonin** in the treatment of primary adult sleep disorders. Sleep Med Rev. 2017 Aug;34:10-22.

Aurora RN, Zak RS, Auerbach SH, et al. Standards of Practice Committee, American Academy of Sleep Medicine. Best practice guide for the treatment of **nightmare disorder in adults**. J Clin Sleep Med 2010 Aug 15;6(4):389-401. (prazosin, ? clonidine etc)

Aurora RN, Zak RS, et al. Standards of Practice Committee, American Academy of Sleep Medicine. Best practice guide for the treatment of **REM sleep behavior disorder** (RBD). J Clin Sleep Med 2010 Feb15;6(1):85-95.

Aurora RN, Chowdhuri S, Ramar K, et al. The treatment of **central sleep apnea syndromes** in adults: practice parameters with an evidence-based literature review and meta-analyses. Sleep. 2012 Jan 1;35(1):17-40.

Avidan AY, Fries BE, James ML, et al. Insomnia and hypnotic use, recorded in theminimum data set, as predictors of **falls and hip fractures** in Michigan nursing homes. J Am Geriatr Soc. 2005;53(6):955-962.

Baillargeon L, et al. Discontinuation of benzodiazepines among older insomniac adults treated with cognitive-behavioural therapy combined with gradual tapering: a randomized trial. CMAJ. 2003 Nov 11;169(10):1015-1020. (Benzodiazepines: How they work & how to withdraw "aka The Ashton Manual" protocol http://www.benzo.org.uk/manual/index.htm)

Baran RT, Atar M, Pirgon Ö, et al. **Restless Legs Syndrome and Poor Sleep Quality** in Obese Children and Adolescents. J Clin Res Pediatr Endocrinol. 2018 Jun 1;10(2):131-138.

Barbera J, Shaprio C. Benefit-risk assessment of **zaleplon** in the treatment of insomnia. Drug Saf. 2005;28(4):301-18.

Barger LK, Flynn-Evans EE, Kubey A, et al. Prevalence of sleep deficiency and use of **hypnotic drugs in astronauts** before, during, and after spaceflight: an observational study. Lancet Neurol. 2014 Sep;13(9):904-12.

Beck CA, Williams JV, Wang JL, et al. **Psychotropic medication use in Canada**. Can J Psychiatry. 2005 Sep;50(10):605-13. RESULTS: Overall psychotropic drug utilization was 7.2%. Utilization was higher for women and with increasing age. With any lifetime CIDI-diagnosed disorder assessed in the CCHS 1.2, utilization was 19.3%, whereas without such disorders, it was 4.1%. Selective serotonin reuptake inhibitors (SSRIs) were the most commonly used antidepressants for those with a past-year major depressive episode (17.8%), followed by venlafaxine (7.4%). Among people aged 15 to 19 years, antidepressant use was 1.8% overall and 11.7% among those with past-year depression; SSRIs made up the majority of use. **Sedative-hypnotics** were used by 3.1% overall, increasing with age to 11.1% over 75 years.

Bélanger L, **Mortality Hazard** Associated With Anxiolytic and Hypnotic Drug Use in the National Population Health Survey. Can J Psychiatry. 2010;55(9):558–567.

Benedict C et al. **Acute sleep deprivation** enhances the brain's response to hedonic food stimuli: An fMRI study. J Clin Endocrinol Metab 2012 Jan 18.

Benetti-Pinto CL, Menezes C, Yela DA, Cardoso TM. Sleep quality and fatigue in **women with premature ovarian insufficiency receiving hormone therapy**: a comparative study. Menopause. 2019 Jul 8.

Benjamin Neelon SE, Duffey K, Slining MM. Regulations to Promote **Healthy Sleep Practices in Child Care**. Pediatrics. 2014 Nov 10.

Benito-León J, Louis ED, Villarejo-Galende A, et al. Long sleep duration in elders without dementia increases risk of dementia mortality (NEDICES). Neurology. 2014 Oct 21;83(17):1530-7.

Bent S, Padula A, Moore D, Patterson M, Mehling W. **Valerian** for sleep: a systematic review and meta-analysis. Am J Med. 2006 Dec;119(12):1005-12.

Bendz LM, Scates AC. **Melatonin** treatment for insomnia in pediatric patients with attention-deficit/hyperactivity disorder. *Ann Pharmacother*. 2010 Jan;44(1):185-91.

Bernert RA, Turvey CL, Conwell Y, et al. Association of Poor Subjective **Sleep Quality With Risk for Death by Suicide** During a 10-Year Period: Longitudinal, Population-Based Study of Late Life. JAMA Psychiatry. 2014 Aug 13.

Berry SD, Lee Y, Cai S, Dore DD. **Nonbenzodiazepine (zolpidem, eszopiclone, zaleplon) sleep medication use and hip fractures** in nursing home residents [online Mar 4, 2013]. JAMA Intern Med. 2013.

Bjerre LM, Farrell B, Hogel M, et al. **Deprescribing antipsychotics for behavioural and psychological symptoms of dementia and insomnia**. Evidence-based clinical practice guideline. Can Family Physician 2018;64:17-27.

Black DS, O'Reilly GA, Olmstead R, Breen EC, IrwinMR. **Mindfulness meditation** and improvement in sleep quality and daytime impairment among older adults with sleep disturbances: a randomized clinical trial [online February 16, 2015]. JAMA Intern Med. doi:10.1001/jamainternmed.2014.8081.

Blackwell T, Yaffe K, Ancoli-Israel S, et al; Osteoporotic Fractures in Men Study Group. Associations between sleep architecture and sleep-disordered breathing and **cognition** in older community-dwelling men: the Osteoporotic Fractures in Men Sleep Study. J Am Geriatr Soc. 2011 Dec;59(12):2217-25.

Bloom HG, Ahmed I, Alessi CA, et al. **Evidence-based recommendations for the assessment and management of sleep disorders in older persons.** J Am Geriatr Soc. 2009;57:761–89.

Boland EM, Rao H, Dinges DF, et al. Meta-Analysis of the **Antidepressant Effects of Acute Sleep Deprivation**. J Clin Psychiatry. 2017 Sep 19.

Bomalaski MN, Claflin ES, Townsend W, et al. **Zolpidem for the Treatment of Neurologic Disorders**: A Systematic Review. JAMA Neurol. 2017 Jun 26.

Bonuck K, Rao T, Xu L. **Pediatric Sleep Disorders and Special Educational Need** at 8 Years: A Population-Based Cohort Study. Pediatrics. 2012 Sep 3.

Bonuck K, Chervin RD, Howe LD. **Sleep-Disordered Breathing**, **Sleep Duration**, and Childhood **Overweight**: A Longitudinal Cohort Study. J Pediatr. 2014 Nov 6.

Booth JN 3rd, Behring M, Cantor RS, et al. **Zolpidem use and motor vehicle collisions in older drivers**. Sleep Med. 2016 Apr;20:98-102.

Borenstein-Levin L, Synnes A, Grunau RE, et al. **Narcotics and Sedative Use in Preterm Neonates**. J Pediatr. 2016 Sep 7

Brasure M, MacDonald R, et al. **Management of Insomnia Disorder**. Comparative Effectiveness Review No. 159.Rockville (MD): Agency for Healthcare Research and Quality (US); 2015 Dec. Report No.:15(16)-EHC027-EF.

Brasure M, Fuchs E, MacDonald R, Nelson VA, Koffel E, Olson CM, et al. **Psychological and behavioral interventions** for managing insomnia disorder: an evidence report for a clinical practice guideline by the American College of Physicians **(ACP)**. Ann Intern Med. 2016. [Epub ahead of print]. doi:10.7326/M15-1782

Breen DP, Vuono R, Nawarathna U, et al. Sleep and Circadian Rhythm Regulation in **Early Parkinson Disease**. JAMA Neurol.2014 Mar 31.

Bronskill SE, Campitelli MA, Iaboni A, et al. Low-Dose **Trazodone, Benzodiazepines, and Fall-Related Injuries** in Nursing Homes: A Matched-Cohort Study. J Am Geriatr Soc. 2018 Oct;66(10):1963-1971.

Broussard JL, Ehrmann DA, Van Cauter E, Tasali E, Brady MJ. **Impaired insulin signaling** in human adipocytes after experimental sleep restriction. A randomized, crossover study. Ann Intern Med. 2012;157:549-57.

Brumpton B, Xiao-Mei M, Langhammer A, et al. Prospective study of insomnia and **incident asthma** in adults: the HUNT study. Eur Respir J2017;(Feb).

Bruni O, Novelli L. **Sleep disorders in children** [Internet]. BMJ Clinical Evidence. 10; 2009 [cited 2011 Mar 07]. Available from: http://clinicalevidence.bmj.com/ceweb/conditions/chd/2304/2304-get.pdf

Buscemi N, et al. Melatonin for treatment of sleep disorders. Evidence Report/Technology Assessment No. 108. AHRQ Publication No. 05-E002-1. Rockville MD: Agency for Healthcare Research and Quality. November 2004.

Buscemi N, Vandermeer B, Hooton N, et al. Efficacy and safety of exogenous **melatonin** for secondary sleep disorders and sleep disorders accompanying sleep restriction: meta-analysis. BMJ. 2006 Feb 18;332(7538):385-93.
CONCLUSIONS: There is no evidence that melatonin is effective in treating secondary sleep disorders or sleep disorders accompanying sleep restriction, such as jet lag and shiftwork disorder. There is evidence that melatonin is safe with short term use.

Buscemi N, Vandermeer B, Friesen C, et al. The efficacy and safety of drug treatments for **chronic insomnia** in adults: a **meta-analysis of RCTs**. J Gen Intern Med [Internet]. 2007 Sep;22(9):1335-50.

Buxton OM, Ellenbogen JM, Wang W, et al. Sleep Disruption due to **Hospital Noises**: A Prospective Evaluation. Ann Intern Med. 2012 Aug 7;157(3):170-9.

Buysse Daniel J.; Germain Anne; Moul Douglas E.; et al. Efficacy of Brief **Behavioral Treatment** for Chronic Insomnia in Older Adults. Arch Intern Med. 2011;0(2011):archinternmed.2010.535.

Buysse DJ. **Insomnia**. JAMA. 2013 Feb 20;309(7):706-16. doi:10.1001/jama.2013.193.

Buysse DJ, Rush AJ, Reynolds CF 3rd. **Clinical Management of Insomnia Disorder**. JAMA. 2017 Oct 23.

Cadogan CA, Ryan C, Cahir C, et al. **Benzodiazepine and Z-drug prescribing in Ireland**: analysis of national prescribing trends from 2005-2015. Br J Clin Pharmacol. 2018 Feb 28.

CADTH: HTIS – Report Feb08: Safety of Zopiclone or Trazodone for insomnia in adults (upon request from htis@cadth.ca).

Carter PJ, Taylor BJ, Williams SM, Taylor RW. Longitudinal analysis of **sleep in relation to BMI and body fat in children**: the **FLAME** study. BMJ 2011;342:d2712.

CDC: Effect of **Short Sleep Duration on Daily Activities** --- Uni ted States, 2005—2008 Weekly March 4, 2011 / 60(08);239-242 http://www.cdc.gov/mmwr/preview/mmwrhtml/mm6008a3.htm?s_cid=mm6008a3_x

Calhoun DA, Harding SM. **Sleep and hypertension**. Chest. 2010 Aug;138(2):434-43.

Campbell AJ, Robertson MC, Gardner MM, Norton RN, Buchner DM. **Psychotropic medication withdrawal** and a home-based exercise program to **prevent falls**: a randomized, controlled trial. J Am Geriatr Soc. 1999;47(7):850-853.

Campos FL, et al. Melatonin improves sleep in asthma: a randomized, double-blind, placebo-controlled study. (Melatonin improves sleep quality in women with asthma, but not in a clinically meaningful way). (LOE = 2b) Am J Respir Crit Care Med 2004; 170:947-51.

Campos-Rodriguez F, Martinez-Garcia MA, de la Cruz-Moron I et al. Cardiovascular mortality in **women with obstructive sleep apnea** with or without continuous positive airway pressure treatment: a cohort study. Ann Intern Med. 2012 Jan 17;156(2):115-22.

Campos-Rodriguez F, Martinez-Garcia MA, Martinez M, et al; on behalf of the Spanish Sleep Network. Association between Obstructive **Sleep Apnea and Cancer** Incidence in a Large Multicenter Spanish Cohort. Am J Respir Crit Care Med. 2013 Jan 1;187(1):99-105.

Cappuccio FP, Cooper D, D'Elia L, Strazzullo P, Miller MA. **Sleep duration predicts cardiovascular outcomes**: a systematic review and meta-analysis of prospective studies. *Eur Heart J* 2011; online 7 February.

Carlsten A, et al. Are sedatives and hypnotics associated with increased **suicide risk** of suicide in the elderly? BMC Geriatr. 2009 Jun 4;9:20. Sedatives and hypnotics were both associated with increased risk for suicide after adjustment for appropriate indications

Carter B, Rees P, Hale L, et al. Association Between **Portable Screen-Based Media Device Access** or Use and Sleep Outcomes: A Systematic Review and Meta-analysis. JAMA Pediatr. 2016 Oct 31.

Carter KA, Hathaway NE, Lettieri CF. Common **sleep disorders in children.** Am Fam Physician. 2014 Mar 1;89(5):368-77.

Carter MD, Juurlink DN. **Melatonin**. CMAJ. 2012 Apr 16.

Carter SG, Carberry JC, Cho G, et al. Effect of **1 month of zopiclone on obstructive sleep apnoea severity and symptoms**: a randomised controlled trial. Eur Respir J. 2018 Jul 19;52(1).

Carter B, Rees P, Hale L, Bhattacharjee D, et al. Association between **portable screen-based media device access** or use and sleep outcomes: a systematic review and meta-analysis [online Oct 31, 2016].JAMA Pediatr.

Carvalho DZ, St Louis EK, Knopman DS, et al. Association of **Excessive Daytime Sleepiness With Longitudinal β-Amyloid Accumulation in Elderly Persons Without Dementia**. JAMA Neurol. 2018 Mar 12.

Celis-Morales C, Lyall DM, Guo Y, et al. Sleep characteristics modify the association of **genetic predisposition with obesity** and anthropometric measurements in 119,679 UK Biobank participants. Am J Clin Nutr. 2017 Mar 1.

Cespedes EM, Gillman MW, Kleinman K, et al. **Television Viewing, Bedroom Television, and Sleep** Duration From Infancy to Mid-Childhood. Pediatrics. 2014 Apr 14.

Cespedes EM, Bhupathiraju SN, Li Y, et al. Long-term changes in **sleep duration, energy balance and risk of type 2 diabetes**. Diabetologia. 2015 Nov 2.

Cespedes Feliciano EM, Quante M, Rifas-Shiman SL, et al. Objective **Sleep Characteristics and Cardiometabolic Health** in Young Adolescents. Pediatrics. 2018 Jun 15.

Chang CM, Wu EC, Chen CY, et al. Psychotropic Drugs and Risk of **Motor Vehicle Accidents**: a Population-based Case-Control Study. Br J Clin Pharmacol. 2012 Sep 12.

Chang YS, Lin MH, Lee JH, et al. **Melatonin** Supplementation for Children With **Atopic Dermatitis** and **Sleep Disturbance**: A Randomized Clinical Trial. JAMA Pediatr. 2015 Nov 16:1-8.

Chapman JL, Kempler L, et al. **Modafinil** improves daytime sleepiness in patients with mild to moderate **obstructive sleep apnoea** not using standard treatments: a randomised placebo-controlled crossover trial. Thorax. 2013 Nov 28.

Chen X, Broeyer F, de Kam M, et al. **Pharmacodynamic response profiles** of **anxiolytic and sedative drugs**. Br J Clin Pharmacol. 2016 Dec 6.

Cheuk DK, Yeung WF, Chung KF, Wong V. **Acupuncture for insomnia**. Cochrane Database Syst Rev. 2012 Sep 12;9:CD005472.
Due to poor methodological quality, high levels of heterogeneity and publication bias, the current evidence is not sufficiently rigorous to support or refute acupuncture for treating insomnia. Larger high-quality clinical trials are required.

Chinthapalli K. We need to wake up to the **value of sleep medicine**. BMJ. 2014 Oct 15;349:g6099.

Chirinos JA, Gurubhagavatula I, Teff K, et al. **CPAP, weight loss**, or both for obstructive **sleep apnea**. N Engl J Med 2014;370: 2265-75.

Chen YL, Weng SF, Shen YC, et al. **Obstructive Sleep Apnea and Risk of Osteoporosis**: A Population-Based Cohort Study in Taiwan. J Clin Endocrinol Metab. 2014 Apr 15

Cheng HT;Lin FJ;Erickson SR;Hong JL;Wu CH. The Association Between the Use of **Zolpidem and the Risk of Alzheimer`s Disease** Among Older People. J Am Geriatr Soc. 2017 Sep 7.

Chow CK, Koren G. **Sedating drugs and breastfeeding**. Can Fam Physician. 2015 Mar;61(3):241-3.

Christensen H, Batterham PJ, Gosling JA, et al. Effectiveness of an **online insomnia program (SHUTi)** for prevention of depressive episodes (**the GoodNight Study**): a randomised controlled trial. Lancet Psychiatry. 2016 Jan 27.

Christensen MA, Bettencourt L, Kaye L, Moturu et al. Direct Measurements of **Smartphone Screen-Time**: Relationships with Demographics and Sleep. PLoS One. 2016 Nov 9;11(11):e0165331.

Cipolla-Neto J, Amaral FGD. **Melatonin as a Hormone**: New Physiological and Clinical Insights. Endocr Rev. 2018 Dec 1;39(6):990-1028.
Clark A, Lange T, Hallqvist J, et al. Sleep impairment and prognosis of **acute myocardial infarction**: a prospective cohort study. Sleep. 2014 May 1;37(5):851-8.
Clinical Handbook of Psychotropic Drugs 18th edition 2009 (Bezchlibnyk-Butler,Jeffries)
Clinical Handbook of Psychotropic Drugs 22nd edition 2017 (Bezchlibnyk-Butler,Jeffries, Procyshyn)
Coffey SF. Banducci AN, Vinci C. Common Questions About **Cognitive Behavior Therapy** for Psychiatric Disorders. Am Fam Physician. 2015;92(9):807-812.
Cohen S, Doyle WJ, Alper CM, Janicki-Deverts D, Turner RB. Sleep habits and susceptibility to the **common cold**. Arch Intern Med. 2009 Jan 12;169(1):62-7.
Colson ER, Geller NL, Heeren T, Corwin MJ. Factors associated with choice of **infant sleep position**. Pediatrics. 2017;140(3):e20170596
Colvin JD, Collie-Akers V, Schunn C, et al. **Sleep Environment Risks** for Younger and Older Infants. Pediatrics. 2014 Jul 14.
Cordi MJ, Schlarb AA, Rasch B. **Deepening sleep by hypnotic suggestion**. Sleep. 2014 Jun 1;37(6):1143-52.
Costa LR et al. Post-Discharge Adverse Events following Pediatric Sedation with High Doses of Oral Medication. J Pediatr. 2011 Nov 30. (chloral hydrate, midazolam)
Covinsky KE, Pierluissi E, Johnston CB. **Hospitalization-associated disability**: "she was probably able to ambulate, but I'm not sure." JAMA. 2011;306(16):1782-1793.
Crowley SJ, Van Reen E, LeBourgeois MK, et al. A Longitudinal Assessment of **Sleep Timing, Circadian** Phase, and Phase Angle of Entrainment across Human Adolescence. PLoS One. 2014 Nov 7;9(11):e112199.
Cummings C; **Canadian Paediatric Society**, Community Paediatrics Committee. **Melatonin** for the management of sleep disorders in **children and adolescents**. Paediatr Child Health 2012;17:331-3.
http://www.cps.ca/english/statements/CP/Melatonin.htm
Cunnington D, Junge M. **Chronic insomnia**: diagnosis and non-pharmacological management. BMJ. 2016 Nov 16;355:i5819.
Dahiya S, Ahluwalia MS, Walia HK. **Sleep disturbances in cancer patients**: Underrecognized and undertreated. Cleve Clin J Med. 2013 Nov;80(11):722-32.
Davidson JR, Dickson C, Han H **Cognitive behavioural treatment** for insomnia in primary care: a systematic review of sleep outcomes. Br J Gen Pract. 2019 Jul 29.
de Jonghe A, van Munster BC, Goslings JC, et al; on behalf of the Amsterdam Delirium Study Group. Effect of **melatonin on incidence of delirium** among patients with hip fracture: a multicentre, double-blind randomized controlled trial. CMAJ. 2014 Sep 2.
de Oliveira DL, Hirotsu C, Tufik S, et al. The interfaces between **vitamin D, sleep and pain**. J Endocrinol. 2017 May 23.
DePietro RH, Knutson KL, Spampinato L, et al. Association Between **Inpatient Sleep Loss and Hyperglycemia** of Hospitalization. Diabetes Care. 2016 Nov 30.
Domínguez F, Fuster V, Fernández-Alvira JM, et al. Association of **Sleep Duration and Quality With Subclinical Atherosclerosis**. J Am Coll Cardiol. 2019 Jan 22;73(2):134-144.
Dong L, Agnew J, Mojtabai R, et al. **Insomnia as a predictor of job exit** among middle-aged and older adults: results from the Health and Retirement Study. J Epidemiol Community Health. 2017 Mar 15.
Donnelly K, Bracchi R, Hewitt J, et al. **Benzodiazepines, Z-drugs and the risk of hip fracture**: A systematic review and meta-analysis. PLoS One. 2017 Apr 27;12(4):e0174730.
Drug Information Lexi Handbook 17th edition 2008-2009
Drugs in Pregnancy & Lactation 9th edition 2011
Dunster GP, de la Iglesia L, Ben-Hamo M, et al. Sleepmore in Seattle: **Later school start times are associated with more sleep and better performance** in high school students. Sci Adv. 2018 Dec 12;4(12):eaau6200.
Durcan L, Wilson F, Cunnane G. The Effect of **Exercise on Sleep and Fatigue** in **Rheumatoid Arthritis**: A Randomized Controlled Study. J Rheumatol. 2014 Aug 15.
Earley CJ. Clinical practice. Restless legs syndrome. N Engl J Med. 2003 May 22;348(21):2103-9. Review.
Eddy M, Walbroehl GS. Insomnia. Am Fam Physician 1999;59:1911-1916.
Ensrud KE, et al. for the Study of Osteoporotic Fractures Research Group. Use of selective **serotonin reuptake inhibitors** and **sleep** disturbances in community-dwelling older women. J Am Geriatr Soc. 2006 Oct;54(10):1508-15.
Epstein LJ, Kristo D, Strollo PJ Jr, et al. Adult Obstructive Sleep Apnea Task Force of the American Academy of Sleep Medicine. Clinical guideline for the evaluation, management and long-term care of **obstructive sleep apnea** in adults. J Clin Sleep Med 2009 Jun 15;5(3):263-76.
Erland LA, Saxena PK. **Melatonin Natural Health Products and Supplements: Presence of Serotonin and Significant Variability of Melatonin Content**. J Clin Sleep Med. 2017 Feb 15;13(2):275-281.
(Melatonin content did not meet label within a 10% margin of the label claim in more than 71% of supplements and an additional 26% were found to contain serotonin. It is important that clinicians and patients have confidence in the quality of supplements used in the treatment of sleep disorders. To address this, manufacturers require increased controls to ensure melatonin supplements meet both their label claim, and also are free from contaminants, such as serotonin.)
Espie CA, Emsley R, et al. Effect of **Digital Cognitive Behavioral Therapy for Insomnia on Health, Psychological Well-being, and Sleep-Related Quality of Life**: A Randomized Clinical Trial. JAMA Psychiatry. 2018 Sep 25.
Eszopiclone (Lunesta) a New Hypnotic. Med Letter 2005;47:17-19.
Everitt H, Baldwin DS, Stuart B, et al. **Antidepressants for insomnia** in adults. Cochrane Database Syst Rev. 2018 May 14;5:CD010753. We identified relatively few, mostly small studies with short-term follow-up and design limitations. The effects of SSRIs compared with placebo are uncertain with too few studies to draw clear conclusions. There may be a small improvement in sleep quality with short-term use of low-dose doxepin and trazodone compared with placebo. The tolerability and safety of antidepressants for insomnia is uncertain due to limited reporting of adverse events. There was no evidence for amitriptyline (despite common use in clinical practice) or for long-term antidepressant use for insomnia. High-quality trials of antidepressants for insomnia are needed.
Exelmans L, Van den Bulck J. **Binge Viewing**, Sleep, and the Role of Pre-Sleep Arousal. J Clin Sleep Med. 2017 Aug 15;13(8):1001-1008.
Falbe J, Davison KK, Franckle RL, et al. **Sleep Duration, Restfulness, and Screens** in the Sleep Environment. Pediatrics. 2015 Jan 5.
Falloon Karen, Arroll Bruce, Elley C Raina, et al. The **assessment and management of insomnia in primary care**. BMJ 2011;342:doi:10.1136/bmj.d2899 (Published 27 May 2011)
Falloon K, Elley CR, Fernando A III, et al. **Simplified sleep restriction** for insomnia in general practice: a randomised controlled trial. Br J Gen Pract 2015;65:e508–15. Simply decreasing nonsleep time in bed can't possibly improve sleep quality in patients with insomnia, right? It's too simple, cheap, and uses no medications. Oops, I guess I was wrong. My biggest concern with this study is that primary insomnia is not all that common and the authors didn't study whether this could work in patients with secondary sleep disorders.
Farkas RH, Unger EF, Temple R. **Zolpidem and Driving Impairment** – Identifying Persons at Risk. N Engl J Med. 2013 Aug 7.
Faruqui F, Khubchandani J, Price JH, Bolyard D, Reddy R. **Sleep Disorders in Children: A National Assessment of Primary Care Pediatrician Practices and Perceptions**. Pediatrics. 2011 Aug 28.
FDA Sedative warning Mar/07 The U.S. Food and Drug Administration (FDA) has requested that all manufacturers of sedative-hypnotic drug products, a class of drugs used to induce and/or maintain sleep, strengthen their product labeling to include stronger language concerning potential risks. These risks include severe allergic reactions and complex sleep-related behaviors, which may include sleep-driving. Sleep driving is defined as driving while not fully awake after ingestion of a sedative-hypnotic product, with no memory of the event. http://www.fda.gov/bbs/topics/NEWS/2007/NEW01587.html
FDA Jan/13 The recommendation applies to **zolpidem** products approved for bedtime use, marketed as generics and under the brand names *Ambien*, *Ambien CR*, *Edluar*, and *Zolpimist*. Data show the risk for morning impairment is highest with extended-release forms of these drugs, and **women** appear to be more susceptible to this effect because they eliminate zolpidem more slowly than men, a statement from the FDA notes.
FDA May/14 has notified health professionals and their medical care organizations of a new warning that the insomnia drug Lunesta (**eszopiclone**) can cause next-day impairment of driving and other activities that require alertness. FDA recommends a decreased starting dose of Lunesta to 1 mg at bedtime. Women and men are equally susceptible to impairment from **Lunesta**, so the recommended starting dose of 1 mg is the same for both.
FDA Dec/16 is warning that repeated or lengthy use of **general anesthetic and sedation drugs during surgeries or procedures** in **children younger than 3 years or in pregnant women** during their third trimester **may affect the development of children's brains**.
FDA Apr/19: is advising that rare but serious injuries have happened with certain common prescription insomnia medicines because of sleep behaviors, including sleepwalking, sleep driving, and engaging in other activities while not fully awake. These complex sleep behaviors have also resulted in deaths. These behaviors appear to be more common with **Lunesta (eszopiclone), Sonata (zaleplon), Ambien, Ambien CR, Edluar, Intermezzo, Zolpimist**

(zolpidem) than other prescription medicines used for sleep. https://www.fda.gov/drugs/drug-safety-and-availability/fda-adds-boxed-warning-risk-serious-injuries-caused-sleepwalking-certain-prescription-insomnia
Felder JN, Baer RJ, Rand L, et al. **Sleep Disorder** Diagnosis During **Pregnancy** and Risk of Preterm Birth. Obstet Gynecol. 2017 Aug 4.
Ferber SG, Als H, McAnulty G. **Melatonin** and Mental Capacities in Newborn Infants. J Pediatr 2011;159:99-103.
Fernandez-Mendoza J, He F, LaGrotte C, et al. Impact of the **Metabolic Syndrome on Mortality** is Modified by Objective Short Sleep Duration. J Am Heart Assoc. 2017 May 17;6(5).
Fernando Domínguez, Valentín Fuster, Juan Miguel Fernández-Alvira, et al. Association of **Sleep Duration and Quality With Subclinical Atherosclerosis**. Journal of the American College of Cardiology Jan 2019, 73 (2) 134-144
Finan PH, Quartana PJ, Smith MT. The Effects of **Sleep Continuity Disruption** on Positive Mood and Sleep Architecture in Healthy Adults. Sleep. 2015 Jun 11.
Finkle WD, Der JS, Greenland S, et al. **Risk of fractures** requiring hospitalization after an initial prescription for zolpidem, alprazolam, lorazepam, or diazepam in older adults. J Am Geriatr Soc. 2011;59(10):1883-1890.
Fisher HL, Lereya ST, Thompson A, et al. Childhood **parasomnias and psychotic experiences** at age 12 years in a United kingdom birth cohort. Sleep. 2014 Mar 1;37(3):475-82.
Fleetham JA, Fleming JA. **Parasomnias**. CMAJ. 2014 May 13;186(8):E273-80.
Fortinguerra, Filomena, Clavenna, Antonio, Bonati, Maurizio. Psychotropic Drug Use During **Breastfeeding**: A Review of the Evidence. Pediatrics 2009 124: e547-e556.
Frauscher B, Jennum P, Ju YE, et al. Comorbidity and medication in **REM sleep behavior disorder**: A multicenter case-control study. Neurology. 2014 Mar 25;82(12):1076-9.
Freeman D, Sheaves B, Goodwin GM, et al. The effects of **improving sleep on mental health** (**OASIS**): a randomised controlled trial with mediation analysis. Lancet Psychiatry 2017; online Sept 6.
Freeman EW, Sammel MD, Gross SA, Pien GW. **Poor sleep in relation to natural menopause**: a population-based 14-year follow-up of midlife women. Menopause. 2014 Dec 29.
Frey DJ et al. Influence of **zolpidem** and sleep inertia on **balance** and cognition during nighttime awakening: A randomized placebo-controlled trial. J Am Geriatr Soc 2011 Jan; 59:73.
Fung MM, Peters K, Redline S, et al. for the Osteoporotic Fractures in Men Research Group. Decreased Slow Wave Sleep Increases **Risk of Developing Hypertension** in Elderly Men. Hypertension. 2011 Aug 29.
Gangwisch JE. A Review of Evidence for the Link Between **Sleep Duration and Hypertension**. Am J Hypertens. 2014 Apr 28.
Gao C, Chapagain NY, Scullin MK. Sleep Duration and Sleep Quality in **Caregivers of Patients With Dementia**: A Systematic Review and Meta-analysis. JAMA Netw Open. 2019 Aug 2;2(8):e199891.
Garland SN, Carlson LE, Stephens AJ, et al. **Mindfulness-based stress reduction compared** with **cognitive behavioral therapy** for the treatment of insomnia comorbid with cancer: a randomized, partially blinded, noninferiority trial. J Clin Oncol. 2014 Feb 10;32(5):449-57.
Garrison Michelle M., Liekweg Kimberly, Christakis DA. **Media Use** and Child Sleep: The Impact of Content, Timing, and Environment. Pediatrics 2011; peds.2010-3304; published June 27, 2011, doi:10.1542/peds.2010-3304.
Garrison MM, Christakis DA. The impact of a healthy **media use intervention** on sleep in preschool children. Pediatrics. 2012 Sep;130(3):492-9.
Gellis LA et al. **Cognitive refocusing** treatment for insomnia: A randomized controlled trial in university students. Behav Ther2012 Jul 27.
Genuardi MV, Ogilvie RP, Saand AR, et al. Association of **short sleep duration and atrial fibrillation**. Chest. 2019 Feb 27.
Geriatric Dosage Handbook 7th Edition 2002
Giannotti F, Cortesi F. An open-label study of controlled release melatonin in treatment of sleep disorders in children with autism. J Autism Dev Disord 2006;36:741-52
Glass J, Lanctot KL, Herrmann N, et al. Sedative hypnotics in older people with insomnia: **meta-analysis** of risks and benefits. BMJ. 2005 Nov 11; [Epub ahead of print] CONCLUSIONS: Improvements in sleep with sedative use are statistically significant, but the magnitude of effect is small. The increased risk of adverse events is statistically significant and potentially clinically relevant in older people at risk of falls and cognitive impairment. In people over 60, the benefits of these drugs may not justify the increased risk, particularly if the patient has additional risk factors for cognitive or psychomotor adverse events.
Goforth HW, Preud'homme XA, Krystal AD. A randomized, double-blind, placebo-controlled trial of **eszopiclone for the treatment of insomnia in patients with chronic low back pain.** Sleep. 2014 Jun 1;37(6):1053-60.
Goncalves AL, Martini Ferreira A, Ribeiro RT, et al. Randomised clinical trial comparing **melatonin 3 mg, amitriptyline 25 mg and placebo for migraine prevention**. J Neurol Neurosurg Psychiatry. 2016 May 10.
Gordon A, Raynes-Greenow C, Bond D, et al. **Sleep Position**, Fetal Growth Restriction, and Late-**Pregnancy Stillbirth**: The Sydney Stillbirth Study. Obstet Gynecol. 2015 Jan 7.
Gottlieb DJ, Punjabi NM, Mehra R, et al. **CPAP versus oxygen in obstructive sleep apnea**. N Engl J Med 2014;370:2276-85.
Gradisar M, Jackson K, Spurrier NJ, et al. **Behavioral Interventions for Infant Sleep Problems**: A Randomized Controlled Trial. Pediatrics. 2016 May 24.
Grandner MA, Chakravorty S. **Insomnia in Primary Care**: Misreported, Mishandled, and Just Plain Missed. J Clin Sleep Med. 2017 Aug 15;13(8):937-939
Greenblatt DJ, Harmatz JS, Roth T, et al. Comparison of Pharmacokinetic Profiles of **Zolpidem** Buffered Sublingual Tablet and Zolpidem Oral Immediate-Release Tablet: Results from a Single-Center, Single-Dose, Randomized, Open-Label Crossover Study in Healthy Adults. Clin Ther. 2013 Mar 28. (Systemic exposure was higher in females)
Greenstone M, Hack M. **Obstructive sleep apnoea**. BMJ. 2014 Jun 17;348:g3745.
Gregory AM, Van der Ende J, et al. Parent-reported sleep problems during development and self-reported anxiety/depression, attention problems, & aggressive **behavior later in life**. Arch Pediatr Adolesc Med. 2008 Apr;162(4):330-5.
Gringras P, Gamble C, Jones AP, et al; on behalf of the **MENDS** Study Group. **Melatonin** for sleep problems in children with neurodevelopmental disorders: randomised double masked placebo controlled trial. BMJ. 2012 Nov 5;345:e6664. (Children gained little additional sleep on melatonin, though they fell asleep faster, their waking times became earlier.)
Gruber R, Cassoff J, Frenette S, et al. Impact of Sleep Extension and Restriction on Children's Emotional **Lability and Impulsivity**. Pediatrics. 2012 Oct 15.
Guo X, Zheng L, Wang J, et al. Epidemiological evidence for the link between **sleep duration and high blood pressure**: A systematic review and meta-analysis. Sleep Med. 2013 Feb 7.
Hampton LM, Daubresse M, Chang HY, et al. **Emergency Department Visits by Adults for Psychiatric Medication Adverse Events**. JAMA Psychiatry. 2014 Jul 9.
Handbook of Clinical Drug Data 10th edition 2002
Hansen RN, Boudreau DM, Ebel BE, et al. Sedative Hypnotic Medication Use and the **Risk of Motor Vehicle Crash**. Am J Public Health. 2015 Jun 11:e1-e6.
Harris J et al. A randomized controlled trial of **intensive sleep retraining (ISR):** A brief conditioning treatment for chronic insomnia. Sleep 2012 Jan 1; 35:49.
Harsora P, Kessmann J. **Nonpharmacologic management** of chronic insomnia. Am Fam Physician. 2009 Jan 15;79(2):125-30.
Hart CN, Carskadon MA, Considine RV, et al. Changes in Children's **Sleep Duration on Food Intake, Weight, and Leptin**. Pediatrics. 2013 Dec;132(6):e1473-80.
Hatta K, Kishi Y, Wada K, et al; for the DELIRIA-J Group. Preventive Effects of **Ramelteon on Delirium**: A Randomized Placebo-Controlled Trial. JAMA Psychiatry. 2014 Feb 19.
Häusler N, Haba-Rubio J, Heinzer R, Marques-Vidal P. Association of **napping with incident cardiovascular events** in a prospective cohort study. Heart. 2019 Sep 9.
He Q, Zhang P, Li G, et al. The association between insomnia symptoms and **risk of cardio-cerebral vascular events**: A meta-analysis of prospective cohort studies. Eur J Prev Cardiol. 2017 Jan 1:2047487317702043.
Health Canada Aug/06 is advising consumers not to use **Salt Spring Herbals Sleep Well Dietary Supplement** because a sample analyzed by Health Canada has been found to contain **estazolam**,
Health Canada Dec/06 is advising consumers not to use a product called **Eden Herbal Formulations Sleep Ease Dietary Supplement**, because it was found to contain an undeclared drug estazolam http://www.hc-sc.gc.ca/ahc-asc/media/advisories-avis/2006/2006_127_e.html
Health Canada April/07is advising consumers not to use a product called **Eden Herbal Formulations Serenity Pills II** because it contains the undeclared drug **estazolam**.
Health Canada Dec/11 **Sublinox** is the first formulation of **zolpidem** in Canada. Internationally, it has been reported in association with **complex sleep behaviours**.
Health Canada May/12 **[Chung Lien Kulin Brand] Anshen Bunai Pian.** Hong Kong Department of Health warned that this traditional Chinese health product, used for insomnia, contains excessive levels of the heavy metal mercury.
Health Canada Jan/14 **Sublinox (zolpidem** tartrate) - New Dosage Recommendations to Minimize Risk of Next-Day Impairment in Both **Women and Men** - Valeant Canada. The recommended initial dose has been lowered to 5 mg for women and either 5 or 10 mg for men, taken only once per night immediately before bedtime with at least 7-8 hours remaining before awakening.
Health Canada Apr/14: **Dr. Larry's Tranquility**: The U.S. Food and Drug Administration warned consumers not to use this product after it was found to contain undeclared doxepin and chlorpromazine.

Health Canada Nov/14 **IMOVANE (zopiclone)** - New Dosage Recommendations to Minimize the Risk of Next-Day Impairment - sanofi-aventis Canada Inc. Patients who take IMOVANE and other medicines to help them sleep may experience **decreased ability to be alert the day after taking** the medicine, even if they feel fully awake. This can cause next-day impairment of driving or other activities that require full mental alertness.
Health Canada May/17 is advising Canadians that multiple unauthorized products labelled to contain **L-tryptophan** or lithium orotate were being sold on amazon.ca, and may pose serious health risks.
Health Canada Jan/18 is advising Canadians and healthcare professionals that new safety warnings will be added to the product safety information of the following **sedative and anesthetic drugs** when they are used in early childhood and during pregnancy: Diprivan (propofol), Ketalar (ketamine), Sevorane (sevoflurane), Suprane (desflurane), Forane/Isoflurane USP (isoflurane), Ativan (lorazepam), midazolam, phenobarbital and thiopental. The safety review for benzodiazepines (Ativan [lorazepam] and midazolam) and barbiturates (phenobarbital and thiopental) concluded that there is limited evidence linking the use of these drugs by pregnant women and young children to adverse effects on the development of children's brains. However, it is important to note that many of these sedatives may often be used in combination with other intravenous and inhaled anesthetics, which were found to have a risk of adverse effects related to the functioning of the brain.
Hernández-Aceituno A, Guallar-Castillón P, García-Esquinas E, et al. Association between sleep characteristics and **antihypertensive treatment** in older adults. Geriatr Gerontol Int. 2019 Mar 25.
Herring WJ, Snyder E, Budd K, et al. **Orexin receptor antagonism** for treatment of insomnia: A randomized clinical trial of **suvorexant**. Neurology. 2012 Dec 4;79(23):2265-74.
Herxheimer A, Petrie KJ. **Melatonin** for the prevention and treatment of jet lag. Cochrane Database Syst Rev. 2002;(2):CD001520.
Hill CM, Everitt H. **Assessment and initial management of suspected behavioural insomnia in pre-adolescent children**. BMJ. 2018 Oct 16;363:k3797.
Hirshkowitz M, Whiton K, Albert S, et al. National Sleep Foundation's **Sleep Time Duration Recommendations**: Methodology and results summary. Sleep Health. 2015
Hiscock H, Sciberras E, Mensah F, et al. Impact of a **behavioural sleep intervention** on symptoms and sleep in children with attention deficit hyperactivity disorder, and parental mental health: randomised controlled trial. BMJ. 2015 Jan 20;350:h68.
Ho JH, Wood DM, Archer JR, et al. Availability of prescription **zopiclone over the internet**. BMJ. 2015 Nov 4;351:h5710.
Holbrook AM, Crowther R, Lotter A, Cheng C, King D. Meta-analysis of benzodiazepine use in the treatment of insomnia. CMAJ. 2000 Jan 25;162(2):225-33.
Holbrook AM. **Treating insomnia**. BMJ. 2004 Nov 20;329(7476):1198-9.
Holbrook AM, Crowther R, Lotter A, Cheng C, King D. The diagnosis and management of insomnia in clinical practice: a practical evidence-based approach. CMAJ. 2000 Jan 25;162(2):216-20.
Horne Rosemary S. C., Yang Joel S. C., Walter Lisa M., et al. **Elevated Blood Pressure During Sleep** and Wake in Children With Sleep-Disordered Breathing. Pediatrics 2011; 128:1 e85-e92; doi:10.1542/peds.2010-3431
Hsu CY, Chen YT, Chen MH, et al. The association between **insomnia and increased future cardiovascular events**: a nationwide population-based study. Psychosom Med 2015;77:743–51.
Huedo-Medina TB, Kirsch I, Middlemass J, et al. Effectiveness of **non-benzodiazepine hypnotics** in treatment of adult insomnia: meta-analysis of data submitted to the Food and Drug Administration. BMJ. 2012 Dec 17;345:e8343
Huhn M, TardyM, Spineli LM, et al. Efficacy of **pharmacotherapy and psychotherapy** for adult psychiatric disorders: a systematic overview of meta-analyses [online April 30, 2014]. JAMA Psychiatry. doi:10.1001/jamapsychiatry.2014.112.
Hypnotic Drugs, Medical Letter Aug7/2000. (**Durgs for Insomnia**-Medical Letter July **2015**)
Hysing M, Pallesen S, Stormark KM, et al. **Sleep and use of electronic devices in adolescence**: results from a large population-based study. BMJ Open. 2015 Feb 2;5(1):e006748.
Iglayreger HB, Peterson MD, Liu D, et al. **Sleep Duration Predicts Cardiometabolic Risk** in Obese Adolescents. J Pediatr. 2014 Feb 28.
Imbach LL, Büchele F, Valko PO, et al. **Sleep–wake disorders** persist 18 months after **traumatic brain injury** but remain underrecognized. Neurology 2016;86:1945–1949.
Iranzo A, Santamaria J, Tolosa E. **Idiopathic rapid eye movement sleep behaviour disorder**: diagnosis, management, and the need for neuroprotective interventions. Lancet Neurol. 2016 Apr;15(4):405-19.
Irwin MR, Olmstead R, Carrillo C, et al. **Tai Chi** C**hih Compared With Cognitive Behavioral Therapy** for the Treatment of Insomnia in Survivors of Breast Cancer: A Randomized, Partially Blinded, Noninferiority Trial. J Clin Oncol. 2017 May 10:JCO2016710285.
Janjua I, Goldman RD. Sleep-related **melatonin** use in healthy **children**. Can Fam Physician. 2016 Apr;62(4):315-6.
Javaheri S, Redline S. Insomnia and **risk of cardiovascular disease**. Chest. 2017 Jan 30.
Sateia MJ, et al. Clinical practice guideline for the **pharmacologic treatment of chronic insomnia in adults**: an **American Academy of Sleep Medicine** (**AASM**) clinical practice guideline. J Clin Sleep Med. 2017;13(2):307–349.
Johnsa JD, Neville MW. **Tasimelteon**: A **Melatonin Receptor Agonist** for Non-24-Hour Sleep-Wake Disorder. Ann Pharmacother. 2014 Dec;48(12):1636-1641.
Johnson MW, Suess PE, Griffiths RR. **Ramelteon**: a novel hypnotic lacking abuse liability and sedative adverse effects. Arch Gen Psychiatry. 2006 Oct;63(10):1149-57.
Jones GM, Murphy CV, Gerlach AT, et al. High-Dose **Dexmedetomidine** for Sedation in the Intensive Care Unit: An Evaluation of Clinical Efficacy and Safety. 1 June 2011, DOI 10.1345/aph.1P726. Ann Pharmacother ;45:740-747.
Ju YE, McLeland JS, Toedebusch CD, et al. **Sleep Quality** and Preclinical Alzheimer Disease. JAMA Neurol. 2013 Mar 11:1-7.
Jullian-Desayes I, Revol B, Chareyre E, Camus et al. Impact of **concomitant medications on obstructive sleep apnea**.Br J Clin Pharmacol. 2016 Oct 13.
Kahn M, Fridenson S, Lerer R, et al. Effects of **one night of induced night-wakings versus sleep restriction** on sustained attention and mood: a pilot study. Sleep Med. 2014 Jul;15(7):825-32.
Kain ZN, MacLaren JE, Herrmann L, et al. **Preoperative melatonin** and its effects on induction and emergence in children undergoing anesthesia and surgery. Anesthesiology. 2009 Jul;111(1):44-9. Midazolam is more effective than melatonin in reducing children's anxiety at induction of anesthesia. Melatonin showed a direct dose-dependent effect on emergence delirium.
Kandil TS, Mousa AA, El-Gendy AA, Abbas AM. The potential therapeutic effect of **melatonin** in **Gastro-Esophageal Reflux Disease**. BMC Gastroenterol. 2010 Jan 18;10:7.
Kasai T, Floras JS, Bradley TD. **Sleep apnea** and cardiovascular disease: a bidirectional relationship. Circulation. 2012 Sep 18;126(12):1495-510.
Kathol RG, Arnedt JT. **Cognitive Behavioral Therapy for Chronic Insomnia**: Confronting the Challenges to Implementation. Ann Intern Med. 2016 May 3
Kay-Stacey M, Attarian H. Advances in the **management of chronic insomnia**. BMJ. 2016 Jul 6;354:i2123.
Kecklund G, Axelsson J. Health consequences of **shift work and insufficient sleep**. BMJ. 2016 Nov 1;355:i5210.
Kelly Y, Kelly J, Sacker A. Changes in **Bedtime Schedules and Behavioral Difficulties** in 7 Year Old Children. Pediatrics. 2013 Oct 14.
Kent BD, Grote L, Ryan S, et al. **Diabetes Mellitus prevalence** and control in Sleep Disordered Breathing: the European Sleep Apnea Cohort (ESADA) study. Chest. 2014 May 15.
Kennaway DJ. Potential safety issues in the use of the hormone **melatonin** in **paediatrics**. J Paediatr Child Health 2015; online February 3, 2015.http://onlinelibrary.wiley.com/doi/10.1111/jpc.12840/epdf (accessed April 21, 2015).
Keyes KM, Maslowsky J, Hamilton A, Schulenberg J. The Great Sleep Recession: **Changes in Sleep Duration Among US Adolescents**, 1991-2012. Pediatrics. 2015 Mar;135(3):460-8.
Kim J, Cho SJ, Kim WJ, et al. **Insufficient sleep is prevalent among migraineurs**: a population-based study. J Headache Pain. 2017 Dec;18(1):50.
King CR, Knutson KL, Rathouz PJ, Sidney S, Liu K, Lauderdale DS. Short sleep duration and incident **coronary artery** calcification. JAMA. 2008 Dec 24;300(24):2859-66. Longer measured sleep is associated with lower calcification incidence independent of examined potential mediators and confounders.
Kligler B, Teets R, Quick M. **Complementary/Integrative Therapies That Work**: A Review of the Evidence. Am Fam Physician. 2016;94(5):369-374. (acupuncture)
Knutson Kristen L.; Cauter Eve Van; et al. **Association Between Sleep and Blood Pressure in Midlife: The CARDIA Sleep Study.** *Arch Intern Med*. 2009;169(11):1055-1061.
Kolla BP, Auger RR**. Jet lag and shift work** sleep disorders: How to help reset the internal clock. Cleve Clin J Med. 2011 Oct;78(10):675-84.
Kolla BP, Lovely JK, Mansukhani MP, Morgenthaler TI. **Zolpidem** is independently associated with increased risk of inpatient **falls**. J Hosp Med. 2012 Nov 19.
Koo BB, Blackwell T, Ancoli-Israel S, Stone KL, Stefanick ML, Redline S; for the Osteoporotic Fractures in Men (MrOS) Study Group. Association of Incident Cardiovascular Disease With **Periodic Limb Movements During Sleep** in Older Men: Outcomes of Sleep Disorders in Older Men (**MrOS**) Study. Circulation. 2011 Sep 13;124(11):1223-1231.
Koopman-Verhoeff ME, van den Dries MA, van Seters JJ, et al. Association of Sleep Problems and **Melatonin Use in School-aged Children**. JAMA Pediatr. 2019 Jul 22.

Kotagal S, Pianosi P. Sleep disorders in **children and adolescents**. BMJ. 2006 Apr 8;332(7545):828-32.
Kreth M, Shikany T, Lenker C, et al. **Safe Sleep Guideline Adherence** in Nationwide Marketing of Infant Cribs and Products. Pediatrics. 2017; 139(1):e20161729
Kripke DF, Langer RD, Kline LE. Hypnotics' association with **mortality or cancer**: a matched cohort study. BMJ Open. 2012 Feb 27;2(1):e000850.
Krystal AD, Lankford A, Durrence H, et al. Efficacy and safety of **doxepin 3 and 6 mg** in a 35 day sleep laboratory trial in adults with chronic primary insomnia. Sleep 2011;34(10):1433-42.
Kuhnen P, Clement K, Wiegand S, et al. **Proopiomelanocortin deficiency** treated with a melanocortin-4 receptor agonist. N Engl J Med 2016; 375: 240-6.
Kupfer DJ, Reynolds CF. Management of insomnia NEJM 1997;336:341-346.
Lähteenmäki R, Puustinen J, Vahlberg T, et al. **Melatonin** for sedative withdrawal in older patients with primary insomnia: A randomised double-blind placebo-controlled trial. Br J Clin Pharmacol. 2013 Nov 29
Lambrechtse P, Ziesenitz VC, Cohen A, et al. **How reliable are commercially available trackers** in detecting daytime sleep. Br J Clin Pharmacol. 2018 Jan 17.
Lan Y, Wu X, Tan HJ, et al. **Auricular acupuncture with seed or pellet attachments** for primary insomnia: a systematic review and meta-analysis. BMC Complement Altern Med. 2015 Apr 2;15(1):103.
Lan TY, Zeng YF, Tang GJ, et al. The use of **hypnotics and mortality**--a population-based retrospective cohort study. PLoS One. 2015;10:e0145271.
Larson AM, Ryther RC, Jennesson M, et al. Impact of **pediatric epilepsy on sleep** patterns and behaviors in children and parents. Epilepsia. 2012 May 17.
Laugsand LE, Vatten LJ, Platou C, Janszky I. **Insomnia** and the **Risk of Acute Myocardial Infarction**: A Population Study. Circulation. 2011 Oct 24.
Laugsand LE, Strand LB, Platou C, et al. **Insomnia and the risk of incident heart failure**: a population study. Eur Heart J. 2013 Mar 5.
Lederman O, Ward PB, Firth J, et al. **Does exercise improve sleep quality in individuals with mental illness**? A systematic review and meta-analysis. J Psychiatr Res. 2018 Nov 3;109:96-106.
Lee J, Kim Y, Kim YL. **Non-pharmacological therapies for sleep disturbances** in people with **Parkinson's disease**: A systematic review. J Adv Nurs. 2018 Apr 27.
Léger D, Beck F, Richard JB. **Sleep loss in the homeless**—an additional factor of precariousness: survey in a group of homeless people [online Dec 27, 2016].JAMA Intern Med. doi:10.1001/jamainternmed.2016.7827
Lehnich AT, Kowall B, Kuß O, et al. Do patients with intake of **drugs labelled as sleep disturbing really sleep worse?** A population based assessment from the Heinz Nixdorf Recall Study. Br J Clin Pharmacol. 2016 Jun 8.
Leng Y, Cappuccio FP, Wainwright NW, et al. **Sleep duration and risk of fatal and nonfatal stroke**: A prospective study and meta-analysis. Neurology. 2015 Feb 25. pii: 10.1212/WNL.0000000000001371. [Epub ahead of print]
Leng Y, McEvoy CT, Allen IE, et al. Association of **Sleep-Disordered Breathing With Cognitive Function** and Risk of Cognitive Impairment: A Systematic Review Meta-analysis. JAMA Neurol. 2017 Aug 28.
Leproult Rachel, Cauter Eve Van. Effect of 1 Week of **Sleep Restriction on Testosterone Levels** in Young Healthy Men. JAMA. 2011;305(21):2173-2174.doi:10.1001/jama.2011.710.
Lerchl A, Reiter RJ. Treatment of sleep disorders with **melatonin**. BMJ. 2012 Nov 5;345:e6968.
Lettieri CJ, Shah AA, Holley AB, et al. for the CPAP ASAP (**CPAP** Promotion and Prognosis—The Army Sleep Apnea Program) Trial. Effects of a Short Course of Eszopiclone on Continuous Positive Airway Pressure Adherence: A Randomized Trial. Ann Intern Med. 2009 Nov 17;151(10):696-702.
Leufkens TR, Vermeeren A. **Zopiclone's Residual Effects** on Actual **Driving** Performance in a Standardized Test: A Pooled Analysis of Age and Sex Effects in 4 Placebo-Controlled Studies. Clin Ther. 2013 Dec 17
Li Y, Zhang X, Winkelman JW, et al. Association Between **Insomnia Symptoms and Mortality**: A Prospective Study of US Men. Circulation. 2014 Feb 18;129(7):737-46.
Li Y, Vgontzas AN, Fernandez-Mendoza J, et al. Insomnia With **Physiological Hyperarousal Is Associated With Hypertension**. Hypertension. 2015 Jan 26.
Li Y, Gao X, Winkelman JW, et al. Association between **sleeping difficulty and type 2 diabetes** in women. Diabetologia. 2016 Jan 28.
Liira J, Verbeek JH, Costa G, Driscoll TR, Sallinen M, et al. Pharmacological interventions for **sleepiness and sleep disturbances caused by shift work**. Cochrane Database of Systematic Reviews 2014, Issue 8. Art. No.: CD009776.DOI: 10.1002/14651858.CD009776.pub2. There is low quality evidence that melatonin improves sleep length after a night shift but not other sleep quality parameters. Both modafinil and armodafinil increase alertness and reduce sleepiness to some extent in employees who suffer fromshift work sleep disorder but they are associated with adverse events. Caffeine plus naps reduces sleepiness during the night shift, but the quality of evidence is low. Based on one low quality trial, hypnotics did not improve sleep length and quality after a night shift. We need more and better quality trials on the beneficial and adverse effects and costs of all pharmacological agents that induce sleep or promote alertness in shift workers both with and without a diagnosis of shift work sleep disorder. We also need systematic reviews of their adverse effects.
Liira J, Verbeek J, Ruotsalainen J. Pharmacological interventions for sleepiness and sleep disturbances caused by **shift work**. JAMA. 2015 Mar 3;313(9):961-2.
Lim AS, Yu L, Schneider JA, et al. Sleep Fragmentation, **Cerebral Arteriolosclerosis, and Brain Infarct** Pathology in Community-Dwelling Older People. Stroke. 2016 Jan 14.
Littlewood DL, Gooding P, Kyle SD, et al. Understanding the **role of sleep in suicide risk**: qualitative interview study. BMJ Open. 2016 Aug 22;6(8):e012113.
Litton E, Carnegie V, Elliott R, et al. The Efficacy of **Earplugs** as a Sleep Hygiene Strategy for Reducing Delirium in the ICU: A Systematic Review and Meta-Analysis. Crit Care Med. 2016 May;44(5):992-9.
Liu J et al. **Melatonin** increases reactive **aggression** in humans. Psychopharmacology (Berl) 2017 Jul 21.
Lockley SW, Dressman MA, et al. **Tasimelteon** for non-24-hour sleep-wake disorder in totally blind people (SET and RESET): two multicentre, randomised, double-masked, placebo-controlled phase 3 trials. Lancet. 2015 Aug 4.
Louis JM, Mogos MF, Salemi JL, et al. Obstructive **sleep apnea** and severe **maternal-infant morbidity/mortality** in the United States, 1998-2009. Sleep. 2014 May 1;37(5):843-9.
Lupattelli A, Chambers CD, Bandoli G, et al. Association of Maternal Use of **Benzodiazepines and Z-Hypnotics During Pregnancy** With Motor and Communication Skills and Attention-Deficit/Hyperactivity Disorder Symptoms in Preschoolers. JAMA Netw Open. 2019 Apr 5;2(4):e191435.
Luyster FS, Strollo PJ Jr, Holguin F, et al. Association Between Insomnia and **Asthma Burden** in the Severe Asthma Research Program (SARP) III. Chest. 2016 Dec;150(6):1242-1250.
Ma C, Pavlova M, Liu Y, et al. Probable **REM sleep behavior disorder and risk of stroke**: A prospective study. Neurology. 2017 May 9;88(19):1849-1855.
Magee CA, Lee JK, Vella SA. Bidirectional Relationships Between **Sleep Duration and Screen Time** in Early Childhood. JAMA Pediatr. 2014 Mar 3.
Magee CA, Gordon R, Caputi P. Distinct Developmental Trends in **Sleep Duration During Early Childhood.** Pediatrics. 2014 May 19.
Maness DL, Khan M. **Nonpharmacologic Management of Chronic Insomnia**. Am Fam Physician. 2015;92(12):1058-1064.
Marie Trotti L, Saini P, Bliwise DL, et al. **Clarithromycin in GABA-related Hypersomnolence**: A Randomized, Crossover Trial. Ann Neurol. 2015 Jun 10.
Marinelli M, Sunyer J, Alvarez-Pedrerol M, et al. Hours of **Television Viewing and Sleep Duration** in Children: A Multicenter Birth Cohort Study. JAMA Pediatr. 2014 Mar 10.
Masters PA. **In the Clinic: Insomnia**. Ann Intern Med. 2014 Oct 7;161(7). doi: 10.7326/0003-4819-161-7-201410070-01004.
Matheson E, Hainer BL. **Insomnia**: Pharmacologic Therapy. Am Fam Physician. 2017;96(1):29-35.
Matthews KA, Hall M, Dahl RE. **Sleep in Healthy Black and White Adolescents**. Pediatrics. 2014 Apr 21.
Mason M, Welsh EJ, Smith I. Drug therapy for **obstructive sleep apnoea** in adults. Cochrane Database Syst Rev. 2013 May 31;5:CD003002. doi: 10.1002/14651858.CD003002.pub3There is insufficient evidence to recommend the use of drug therapy in the treatment of OSA.
Mason M, Cates CJ, Smith I. Effects of **opioid, hypnotic and sedating medications on sleep-disordered breathing** in adults with obstructive sleep apnoea. Cochrane Database Syst Rev. 2015 Jul 14;7:CD011090. The findings of this review show that currently no evidence suggests that the pharmacological compounds assessed have a deleterious effect on the severity of OSA as measured by change in AHI or ODI. Significant clinical and statistical decreases in minimum overnight SpO2 were observed with remifentanil, zolpidem 20 mg and triazolam 0.25 mg. Eszopiclone 3 mg and sodium oxybate 4.5 g showed a beneficial effect on the severity of OSA with a reduction in AHI and may merit further assessment as a potential therapeutic option for a subgroup of patients with OSA. Only one trial assessed the effect of an opioid (remifentanil); some studies included CPAP treatment, whilst in a significant number of participants, previous treatment with CPAP was not stated and thus a residual treatment effect of CPAP could not be excluded. Most studies were small and of short duration, with indiscernible methodological quality.Caution is therefore required when such agents are prescribed for patients with OSA, especially outside the severity of the OSA cohorts and the corresponding dose of compounds given in the particular studies. Larger, longer trials involving patients across a broader spectrum of OSA severity are needed to clarify these results.
MacFarlane J, Morin CM, Montplaisir J. **Hypnotics in Insomnia**: The Experience of Zolpidem. Clin Ther. 2014 Nov 1;36(11):1676-1701.

Maust DT, Solway E, Clark SJ, et al. Prescription and Nonprescription Sleep Product **Use Among Older Adults** in the United States. Am J Geriatr Psychiatry. 2018 Sep 14.
Mayer G. Efficacy of **sodium oxybate** on REM sleep behavior disorder in a patient with narcolepsy type 1. Neurology. 2016 Dec 13;87(24):2594-2595.
McCleery J, Cohen DA, Sharpley AL. Pharmacotherapies for **sleep disturbances in Alzheimer's disease**. Cochrane Database Syst Rev. 2014 Mar 21;3:CD009178. We discovered a distinct lack of evidence to help guide drug treatment of sleep problems in AD. In particular, we found no RCTs of many drugs that are widely prescribed for sleep problems in AD, including the benzodiazepine and non-benzodiazepine hypnotics, although there is considerable uncertainty about the balance of benefits and risks associated with these common treatments. From the studies we identified for this review, we found no evidence that melatonin is beneficial to AD patients with moderate to severe dementia and sleep problems. There is some evidence to support the use of a low dose (50 mg) of trazodone, although a larger trial is needed to allow a more definitive conclusion to be reached on the balance of risks and benefits. There was no evidence of any effect of ramelteon on sleep in patients with mild to moderate dementia due to AD. This is an area with a high need for pragmatic trials, particularly of those drugs that are in common clinical use for sleep problems in AD. Systematic assessment of adverse effects is essential.
McCleery J, Cohen DA, Sharpley AL. **Pharmacotherapies for sleep disturbances in dementia**. Cochrane Database of Systematic Reviews 2016, Issue 11. Art. No.: CD009178. We discovered a distinct lack of evidence to help guide drug treatment of sleep problems in dementia. In particular, we found no RCTs of many drugs that are widely prescribed for sleep problems in dementia, including the benzodiazepine and non-benzodiazepine hypnotics, although there is considerable uncertainty about the balance of benefits and risks associated with these common treatments. From the studies we identified for this review, we found no evidence that melatonin (up to 10mg) helped sleep problems in patients with moderate to severe dementia due to AD. There was some evidence to support the use of a low dose (50 mg) of trazodone, although a larger trial is needed to allow a more definitive conclusion to be reached on the balance of risks and benefits. There was no evidence of any effect of ramelteon on sleep in patients with mild to moderate dementia due to AD. This is an area with a high need for pragmatic trials, particularly of those drugs that are in common clinical use for sleep problems in dementia. Systematic assessment of adverse effects is essential.
McCrae & Lichstein. **Secondary insomnia: Diagnostic challenges and intervention opportunities**. Sleep Med Rev. 2001;S(1):47-61.
McCurry SM, Guthrie KA, Morin CM, et al. **Telephone-Based Cognitive Behavioral Therapy** for Insomnia in Perimenopausal and Postmenopausal Women With Vasomotor Symptoms: A **MsFLASH** Randomized Clinical Trial. JAMA Intern Med. 2016 May 23.
McKenna H, Wilkes M. **Optimising sleep for night shifts**. BMJ. 2018 Mar 1;360:j5637.
McLarnon ME, Monaghan TL, Stewart SH, Barrett SP. Drug **misuse and diversion** in adults prescribed anxiolytics and sedatives. Pharmacotherapy. 2011;31: 262-272.
McMillan JM, Aitken E, Holroyd-Leduc JM. Management of insomnia and **long-term use of sedative-hypnotic drugs in older patients**. CMAJ. 2013 Sep 23.
Medalie L, Cifu AS. **Management of Chronic Insomnia Disorder in Adults**. JAMA. 2017 Feb 21;317(7):762-763.
Melaku YA, Appleton S, Reynolds AC, et al. Association Between **Childhood Behavioral Problems and Insomnia Symptoms in Adulthood**. JAMA Netw Open. 2019 Sep 4;2(9):e1910861.
Meltzer LJ, Mindell JA, Owens JA, Byars KC. Use of sleep medications in hospitalized **pediatric** patients. Pediatrics. 2007 Jun;119(6):1047-55. Approximately 3% to 6% of children are treated pharmacologically with a broad array of sleep medications in hospital settings. Prescription practices vary by hospital, medical service, child age, and diagnosis. The results from this study indicate that medications are being prescribed for sleep in hospitalized children, especially in children with psychiatric diagnoses.
Michelson D, Snyder E, Paradis E et al. Safety and efficacy of **suvorexant** during 1-year treatment of insomnia with subsequent abrupt treatment discontinuation: a phase 3 randomised, double-blind, placebo-controlled trial. Lancet Neurol 2014; online March 27. (orexin receptor antagonists)
Micromedex 2015.
Mindell JA, et al. Pharmacologic management of insomnia in **children and adolescents**: consensus statement. Pediatrics. 2006 Jun;117(6):e1223-32.
Mindell JA, Moore M. Does Sleep Matter? **Impact on Development and Functioning in Infants**. Pediatrics. 2018 Nov 12.
Mitchell JA, Rodriguez D, Schmitz KH et al. Sleep Duration and **Adolescent Obesity**. Pediatrics. 2013 Apr 8.
Mitka M. **Zolpidem-related surge in emergency department visits**. JAMA. 2013 Jun 5;309(21):2203.
Moncada LV. Management of **falls in older persons**: a prescription for prevention. Am Fam Physician. 2011 Dec 1;84(11):1267-76.
Moon RY, Hauck FR, Colson ER, et al. The Effect of **Nursing Quality Improvement and Mobile Health Interventions on Infant Sleep Practices**: A Randomized Clinical Trial. JAMA. 2017 Jul 25;318(4):351-359
Moore TJ, Mattison DR. Assessment of Patterns of Potentially **Unsafe Use of Zolpidem**. JAMA Intern Med. 2018 Jul 16.
Morgan K, Gregory P, Tomeny M, David BM, Gascoigne C. **Self-help treatment for insomnia** symptoms associated with chronic conditions in older adults: a randomized controlled trial. J Am Geriatr Soc. 2012 Oct;60(10):1803-10.
Morgenthaler TI, Lee-Chiong T, Alessi C, et al. Standards of Practice Committee of the American Academy of Sleep Medicine. Practice parameters for the clinical evaluation and treatment of **circadian rhythm sleep disorders**. An American Academy of Sleep Medicine report. Sleep. 2007 Nov 1;30(11):1445-59.
Morgenthaler T, Kramer M, Alessi C, Friedman L, Boehlecke B, Brown T, et al. Practice parameters for the **psychological and behavioral treatment of insomnia**: an update. An **American academy of sleep medicine** report. Sleep 2006;29:1415-9.
Morin CM, Colecchi C, Stone J, Sood R, Brink D. **Behavioral** and pharmacological therapies for late-life insomnia: a randomized controlled trial. JAMA. 1999 Mar 17;281(11):991-9.
Morin CM, Vallières A, Guay B, et al. **Cognitive behavioral therapy**, singly and combined with medication, for persistent insomnia: a randomized controlled trial. JAMA. 2009 May 20;301(19):2005-15. In patients with persistent insomnia, the addition of medication to CBT produced added benefits during acute therapy, but long-term outcome was optimized when medication is discontinued during maintenance CBT.
Morin CM, Bélanger L, LeBlanc M, Ivers H, Savard J, Espie CA, Mérette C, Baillargeon L, Grégoire JP. The **natural history of insomnia**: a population-based 3-year longitudinal study. Arch Intern Med. 2009 Mar 9;169(5):447-53.
Morin Charles M, Benca Ruth. **Chronic insomnia**. Lancet Online Jan 20, 2012. DOI:10.1016/S0140-6736(11)60750-2.
Narang I, Manlhiot C, Davies-Shaw J. Sleep disturbance and **cardiovascular risk** in adolescents. CMAJ 2012.
Nedeltcheva Arlet V, Kilkus Jennifer M., Imperial J, et al. Insufficient Sleep **Undermines Dietary Efforts to Reduce Adiposity**. Ann Intern Med October 5, 2010 153:435-441; doi:10.1059/0003-4819-153-7-201010050-00006.
Neubauer DN. **Sleep problems in the elderly**. Am Fam Physician. 1999 May 1;59(9):2551-8, 2559-60.
Neubauer DN, Pandi-Perumal SR, Spence DW, Buttoo K, Monti JM. Pharmacotherapy of Insomnia. J Cent Nerv Syst Dis. 2018 Apr 19;10:1179573518770672. doi:10.1177/1179573518770672. eCollection 2018. Review. PubMed PMID: 29881321; PubMed Central PMCID: PMC5987897.
Neutel CI, Patten SB. Sleep medication use in **Canadian seniors**. Can J Clin Pharmacol. 2009 Fall;16(3):e443-52. Epub 2009 Nov 16.
New Zealand Jul/15 The Centre for Adverse Reactions Monitoring (CARM) has received three reports of **hallucinations associated with melatonin** use. Hallucinations generally occurred the same night melatonin was taken. In two of the three reports, no other medicines were reported and in all three reports an improvement in symptoms was reported once the medicine had been stopped.
NICE April 2004: Guidance on the use of zaleplon, zolpidem and zopiclone for the short-term management of insomnia. http://www.nice.org.uk/pdf/TA077fullguidance.pdf
Nieto FJ, Peppard PE, Young T, Finn L, Hla KM, Farre´ R. **Sleep disordered breathing** and **cancer mortality**: results from the Wisconsin Sleep Cohort Study. Am J Respir Crit Care Med 2012;186: 190–194.
Nishtala PS, Chyou TY. **Zopiclone Use and Risk of Fractures** in Older People: Population-Based Study. J Am Med Dir Assoc. 2017 Apr 1;18(4):368.e1-368.e8.
Nixon, Gillian M, Thompson, John M D, Han, et al. **Falling asleep: the determinants of sleep latency.** Arch Dis Child 2009 0: adc.2009.157453
Nurok Michael, Czeisler Charles A., Lehmann Lisa Soleymani. **Sleep Deprivation, Elective Surgical Procedures**, and Informed Consent. N Engl J Med 2010; 363:2577-2579.
Obayashi K, Saeki K, Kurumatani N. **Bedroom Light Exposure** at Night and the Incidence of **Depressive Symptoms**: A Longitudinal Study of the **HEIJO-KYO** Cohort.Am J Epidemiol. 2018 Mar 1;187(3):427-434.
Orriols L, Luxcey A, Contrand B, et al. **Road traffic crash risk** associated with **benzodiazepine and z-hypnotic** use after implementation of a colour-graded pictogram: a responsibility study. Br J Clin Pharmacol. 2016 Aug 21.
Owens J; Adolescent Sleep Working Group, Committee on Adolescence; Adolescent Sleep Working Group. **Insufficient sleep in adolescents and young adults**: an update on causes and consequences. Pediatrics. 2014 Sep;134(3):e921-32.
Owens JA, Dearth-Wesley T, Lewin D, et al. **Self Regulation and Sleep-Duration**, Sleepiness and Chronotype in Adolescents. Pediatrics.2016;138(6):e20151406.
Paruthi S, Brooks LJ, D'Ambrosio C, et al. Recommended **Amount of Sleep for Pediatric Populations**: A Statement of the American Academy of Sleep Medicine. J Clin Sleep Med. 2016 May 25.

Patel D, Goldman-Levine JD. **Doxepin (silenor)** for insomnia. Am Fam Physician. 2011 Aug 15;84(4):453-4.
Paul IM, Savage JS, Anzman-Frasca S, et al. **INSIGHT** Responsive **Parenting Intervention** and Infant Sleep. Pediatrics. 2016 Jun 27.
Pengo M, Won C, Bourjeily G. Sleep in women across the lifespan. Chest. 2018 Apr 18.
Pennestri MH, Laganiere C, Bouvette- Turcot AA, et al. **Uninterrupted infant sleep, development, and maternal mood**. *Pediatrics*. 2018;142(6):e20174330
Petit D, Pennestri MH, Paquet J, et al. Childhood **Sleepwalking and Sleep Terrors**: A Longitudinal Study of Prevalence and Familial Aggregation. JAMA Pediatr. 2015 May 4.
Petrov ME, Goodin BR, Cruz-Almeida Y, et al. Disrupted sleep is associated with altered pain processing by sex and ethnicity in knee osteoarthritis. J Pain. 2015 May;16(5):478-90.
Petrov ME, Howard G, Grandner MA, et al. Sleep duration and **risk of incident stroke** by age, sex, and race: The REGARDS study. Neurology. 2018 Oct 30;91(18):e1702-e1709.
Pharmacotherapy Handbook 2nd edition (Wells,Dipiro et al.)
Pigeon WR, Bishop TM, Marcus JA. Current Pharmacological and Nonpharmacological Options for the Management of Insomnia. Clinical Medicine Insights: Therapeutics. 2013:5 151-162.
Pillai V et al. Effectiveness of **benzodiazepine receptor agonists in the treatment of insomnia**: An examination of response and remission rates. Sleep 2016 Dec 26.
Pollini RA, et al. **Receipt of Warnings Regarding Potentially Impairing Prescription Medications** and Associated Risk Perceptions in a National Sample of U.S. Drivers. J Stud Alcohol Drugs. 2017 Nov;78(6):805-813.
Postuma RB, Montplaisir JY, Pelletier A, et al. **Environmental** risk factors for REM sleep behavior disorder: A multicenter case-control study. Neurology. 2012 Jul 31;79(5):428-34.
Potter GDM, Cade JE, Hardie LJ. **Longer sleep** is associated with lower BMI and **favorable metabolic** profiles in UK adults: Findings from the National Diet and Nutrition Survey. PLoS One. 2017 Jul 27;12(7):e0182195.
Pottie K, Thompson W, Davies S, et al. **Deprescribing benzodiazepine receptor agonists**: Evidence-based clinical practice guideline. Can Fam Physician. 2018 May;64(5):339-351.
Povitz M, Bolo CE, Heitman SJ, et al. Effect of **treatment of obstructive sleep apnea on depressive symptoms**: systematic review and meta-analysis. PLoS Med. 2014 Nov 25;11(11):e1001762.
Powell S, Kubba H, O'Brien C, Tremlett M. **Paediatric obstructive sleep apnoea**. BMJ. 2010 Apr 14;340:c1918. doi: 10.1136/bmj.c1918.
Prather AA, Hall M, Fury JM, et al. Sleep and antibody response to **hepatitis B vaccination**. Sleep. 2012 Aug 1;35(8):1063-9.
Prather AA, Janicki-Deverts D, Hall MH, et al. Behaviorally Assessed Sleep and **Susceptibility to the Common Cold**. Sleep. 2015 Jan 17.
Price AM, Wake M, Ukoumunne OC, Hiscock H. Five-Year Follow-up of Harms and Benefits of **Behavioral Infant Sleep Intervention**: Randomized Trial. Pediatrics. 2012 Sep 10.
Provini LE, Corwin MJ, Geller NL, et al. Differences in **Infant Care Practices** and Smoking among Hispanic Mothers Living in the United States. J Pediatr. 2016 Dec 13.
Punjabi NM, Caffo BS, Goodwin JL, et al. **Sleep-disordered breathing** and **mortality**: a prospective cohort study. PLoS Med 2009; 6:e1000132.
Qaseem A, Dallas P, Owens DK, et al. Clinical Guidelines Committee of the American College of Physicians. **Diagnosis of obstructive sleep apnea in adults**: a clinical practice guideline from the American College of Physicians. Ann Intern Med. 2014 Aug 5;161(3):210-20.
Qaseem A, Kansagara D, Forciea MA, Cooke M, Denberg T; Clinical Guidelines Committee of the **American College of Physicians (ACP)**. Management of **chronic insomnia disorder** in adults: a clinical practice guideline from the American College of Physicians. Ann Intern Med. 2016. [Epub ahead of print]. doi:10.7326/M15-2175
Quach J, Hiscock H, Ukoumunne OC, Wake M. A brief **sleep intervention** improves outcomes in the school entry year: a randomized controlled trial. Pediatrics. 2011 Oct;128(4):692-701.
Rajaratnam SM, Barger LK, Lockley SW, et al. Sleep disorders, health, and **safety in police officers**. JAMA. 2011;306(23):2567-2578.
Ramakrishnan K, Scheid DC. Treatment options for **insomnia**. Am Fam Physician. 2007 Aug 15;76(4):517-26.
Ramar K, Olson EJ. Management of **Common Sleep Disorders**. Am Fam Physician. 2013;88(4):231-238.
Ramelteon (Rozerem) for Insomnia. The Medical Letter. Nov 7,2005. p 89-91. (see also Pharmacist's Letter Nov 2006)
Ramos AR, Gardener H, Rundek T, et al. Sleep disturbances and **cognitive decline** in the Northern Manhattan Study. Neurology. 2016 Oct 4;87(14):1511-1516
Riemann D, Nissen C, Palagini L, et al. The neurobiology, investigation, and treatment of **chronic insomnia**. Lancet Neurol. 2015 May;14(5):547-558.
Riemann D, Baglioni C, Bassetti C, et al. **European guideline for the diagnosis and treatment of insomnia**. J Sleep Res. 2017 Sep 5.
Riesenberg RA, Baldytcheva I, Datto C. Self-Reported Sedation Profile of **Quetiapine** Extended-Release and Quetiapine Immediate-Release During 6-Day Initial Dose Escalation in Bipolar Depression: A Multicenter, Randomized, Double-Blind, Phase IV Study. Clin Ther. 2012 Oct 8.
Ritterband LM, Thorndike FP, Ingersoll KS, et al. Effect of a web-based **cognitive behavior therapy** for insomnia intervention with 1-year follow-up: a randomized clinical trial (**SHUTi**) [online Nov 30, 2016]. JAMA Psychiatry. doi:10.1001 /jamapsychiatry.2016.3249
Ritterband LM, Thorndike FP, Ingersoll KS, et al. Effect of a **Web-Based Cognitive Behavior Therapy for Insomnia** Intervention With 1-Year Follow-up: A Randomized Clinical Trial. JAMA Psychiatry. 2017 Jan 1;74(1):68-75.
Rodriguez CL, Jaimchariyatam N, Budur K. **Rapid Eye Movement Sleep Behavior Disorder**: A Review of the Literature and Update on Current Concepts. Chest. 2017 Sep;152(3):650-662.
Roehrs TA, Harris E, Randall S, Roth T. **Pain sensitivity** and recovery from mild chronic sleep loss. Sleep 2012;35:1667-72.
Romo-Nava F, Alvarez-Icaza González D, et al. **Melatonin** attenuates **antipsychotic metabolic effects**: an eight-week randomized, double-blind, parallel-group, placebo-controlled clinical trial. Bipolar Disord. 2014 Mar 17.
Rondanelli M, Opizzi A, Monteferrario F, et al. The effect of **melatonin, magnesium, and zinc** on primary insomnia in long-term care facility residents in Italy: a double-blind, placebo-controlled clinical trial. J Am Geriatr Soc. 2011 Jan;59(1):82-90. doi: 10.1111/j.1532-5415.2010.03232.x.
Rönnlund H, Elovainio M, Virtanen Iet al. **Poor Parental Sleep** and the Reported Sleep Quality of Their **Children**. Pediatrics. 2016 Mar 24
Rosinger AY, Chang AM, Buxton O, et al. Short sleep duration is associated with **inadequate hydration**: Cross-cultural evidence from US and Chinese adults. Sleep. 2018 Nov 5.
Ross KR et al. Sleep-Disordered Breathing is Associated with **Asthma Severity** in Children. J Pediatr. 2011 Nov 30.
Rudnicka AR, Nightingale CM, Donin AS, et al. Sleep **Duration** and Risk of Type 2 **Diabetes**. Pediatrics. 2017;140(3):e20170338
Russcher M, Koch BC, Nagtegaal JE, et al. Long-term effects of **melatonin on quality of life and sleep in hemodialysis patients (Melody** study): a randomized controlled trial. Br J Clin Pharmacol. 2013 Feb 21.
Sabanayagam C; Shankar A. **Sleep duration** and **cardiovascular disease**: Results from the National Health Interview Survey. Sleep 2010; 33:1037-1042.
Sacarny A, Barnett ML, Le J, et al. Effect of **peer comparison letters for high-volume primary care prescribers of quetiapine** in older and disabled adults: a randomized clinical trial [online August 1, 2018]. JAMA Psychiatry.
Sack, Robert L. **Jet Lag**. N Engl J Med 2010 362: 440-447.
SAMHSA Emergency Department Visits for Adverse Reactions ivolving the Insomnia Medication **Zolpidem**. May 2013. http://www.samhsa.gov/data/2k13/DAWN079/sr079-Zolpidem.htm
Sandlund C, Hetta J, Nilsson GH, et al. Impact of **group treatment for insomnia on daytime symptomatology**: Analyses from a randomized controlled trial in primary care. Int J Nurs Stud. 2018 May 24;85:126-135.
Sangal RB, Blumer JL, Lankford DA, et al. **Eszopiclone for insomnia associated with attention-deficit/hyperactivity disorder**. Pediatrics. 2014 Oct;134(4):e1095-103.
Santamaria J, Iranzo A. **Sleep disorders** matter in neurology. Lancet Neurol. 2014 Jan;13(1):18-20
Sarris J, Byrne GJ. A systematic review of **insomnia and complementary medicine**. Sleep Med Rev. 2011 Apr;15(2):99-106.
Sateia MJ, Buysse DJ, et al Clinical practice guideline for the **pharmacologic treatment of chronic insomnia** in adults: an **American Academy of Sleep Medicine** clinical practice guideline. *J Clin Sleep Med.* 2017;13(2):307–349.
Sauvet F, Erblang M, Gomez-Merino D, et al. Efficacy of **THN102** (a combination of modafinil and flecainide) on vigilance and **cognition during 40-hour total sleep deprivation** in healthy subjects: Glial Connexins as a therapeutic target. Br J Clin Pharmacol. 2019 Aug 16.
Schapira AH. Restless legs syndrome: an update on treatment options. Drugs. 2004;64(2):149-58.

Scheer FA, Morris CJ, Garcia JI, et al. Repeated **melatonin supplementation** improves sleep in **hypertensive** patients treated with Beta-blockers: a randomized controlled trial. Sleep. 2012 Oct 1;35(10):1395-402.
Schmid SM, Hallschmid M, Schultes B. The **metabolic burden of sleep loss**. Lancet Diabetes Endocrinol. 2014 Mar 25.
Schutte-Rodin S, Broch L, Buysse D, Dorsey C, Sateia M. **Clinical guideline** for the evaluation and management of **chronic insomnia** in adults. J Clin Sleep Med 2008 Oct 15;4(5):487-504.
Schroeck JL, Ford J, Conway EL, et al. Review of Safety and Efficacy of **Sleep Medicines in Older Adults**. Clin Ther. 2016 Oct 14
Scoralick FM, Louzada LL, Quintas JL, et al. **Mirtazapine does not improve sleep disorders in Alzheimer's** disease: results from a double-blind, placebo-controlled pilot study. Psychogeriatrics. 2016 Jan 27.
Shadman KA, Wald ER, Smith W, et al. **Improving Safe Sleep Practices** for Hospitalized Infants. Pediatrics. 2016 Sep;138(3).
Shan Z, Ma H, Xie M, et al. Sleep duration and **risk of type 2 diabetes**: a meta-analysis of prospective studies. Diabetes Care. 2015 Mar;38(3):529-37.
Shapiro-Mendoza CK, Colson ER, Willinger M, et al. **Trends in Infant Bedding** Use: National Infant **Sleep Position Study**, 1993-2010. Pediatrics. 2014 Dec 1.
Sharma SK et al. **CPAP** for the metabolic syndrome in patients with **obstructive sleep apnea**. N Engl J Med. 2011 Dec 15;365(24):2277-86.
Sharples L, Glover M, Clutterbuck-James A, et al. Clinical effectiveness and cost-effectiveness results from the randomised controlled Trial of **Oral Mandibular Advancement Devices** for Obstructive sleep apnoea-hypopnoea (TOMADO) and long-term economic analysis of oral devices and continuous positive airway pressure. Health Technol Assess. 2014 Oct;18(67):1-296.
Shayeb ME, Topfer LA, Stafinski T, et al. Diagnostic accuracy of **level 3 portable sleep tests versus level 1 polysomnography** for sleep-disordered breathing: a systematic review and meta-analysis. CMAJ. 2013 Nov 11.
Sheehan DV, Locklear J, Svedsäter H, et al. Long-term functioning and sleep quality in patients with major depressive disorder treated with extended-release **quetiapine** fumarate. Int Clin Psychopharmacol. 2012 Sep;27(5):239-48.
Shiao TH, Liu CJ, Luo JC, et al. **Sleep Apnea and Risk of Peptic Ulcer Bleeding**: A Nationwide Population-based Study. Am J Med. 2013 Mar;126(3):249-255.e1.
Silber M. **Chronic Insomnia.** NEJM **2005**;353:803-10.
Simon SL, Behn CD, Cree-Green M, et al. Too Late and Not Enough: **School Year Sleep** Duration, Timing, and Circadian Misalignment Are **Associated with Reduced Insulin Sensitivity in Adolescents with Overweight/Obesity**. J Pediatr. 2018 Nov 19.
Sivertsen B, et al. **Cognitive behavioral therapy vs zopiclone** for treatment of chronic primary insomnia in older adults: a randomized controlled trial. JAMA. 2006 Jun 28;295(24):2851-8. These results suggest that interventions based on CBT are superior to zopiclone treatment both in short- and long-term management of insomnia in older adults. (InfoPOEMs: Cognitive behavioral therapy (CBT), consisting of one 50-minute session per week for 6 weeks, is significantly more effective than zopiclone (Imovane) in the treatment of chronic insomnia in older adults. It is uncertain whether less intensive counseling offered directly by primary care clinicians is similarly effective. (LOE = 1b))
Sivertsen B, Harvey AG, Reichborn-Kjennerud T, et al. **Later Emotional and Behavioral Problems** Associated With Sleep Problems in Toddlers: A Longitudinal Study. JAMA Pediatr. 2015 Apr 13.
Sletten TL, Magee M, Murray JM, et al. Efficacy of **melatonin with behavioural sleep-wake scheduling** for delayed sleep-wake phase disorder: A double-blind, randomised clinical trial. PLoS Med. 2018 Jun 18;15(6):e1002587.
Smith MT, Perlis ML, Park A, Smith MS, Pennington J, Giles DE, et al. Comparative meta-analysis of **pharmacotherapy and behavior therapy** for persistent insomnia. Am J Psychiatry 2002;159:5-11.
Smith MT, Finan PH, Buenaver LF, et al. **Cognitive-behavior therapy** for insomnia in knee osteoarthritis: A double-blind, randomized, active placebo controlled clinical trial. Arthritis Rheumatol. 2015 Jan 26.
Song GH, Leng PH, et al. **Melatonin** improves abdominal pain in irritable bowel syndrome patients who have sleep disturbances:a randomised, double blind, placebo controlled study. Gut. 2005 Oct;54(10):1402-7. Epub 2005 May 24.
Song A, Severini T, Allada R. How **jet lag** impairs Major League Baseball performance. Proc Natl Acad Sci U S A. 2017 Jan 23.
Spira AP, Gamaldo AA, An Y, et al. Self-reported Sleep and β-Amyloid Deposition in Community-Dwelling Older Adults. JAMA Neurol. 2013 Oct 21.
Sprecher KE, Koscik RL, Carlsson CM, et al. Poor sleep is associated with CSF biomarkers of **amyloid pathology** in cognitively normal adults. Neurology. 2017 Aug 1;89(5):445-453.
Spruyt K, Molfese DL, Gozal D. **Sleep Duration, Sleep Regularity, Body Weight, and Metabolic** Homeostasis in School-aged Children. Pediatrics. 2011 Jan 24.
St-Onge MP, Grandner MA, Brown D, Conroy et al. **Sleep Duration and Quality**: Impact on Lifestyle Behaviors and Cardiometabolic Health: A Scientific Statement From the **American Heart Association**. Circulation. 2016 Sep 19
Stacey T, Thompson JMD, Mitchell EA, Ekeroma AJ, Zuccollo JM, McCowan LME. Association between maternal **sleep position and risk of late stillbirth**: a case-control study. *BMJ* 2011;342:d3403.
Stone KC, LaGasse LL, Lester BM, et al. **Sleep problems in children** with prenatal substance exposure (**nicotine**) : the Maternal Lifestyle study. Arch Pediatr Adolesc Med. 2010 May;164(5):452-6.
Stremler R, Hodnett E, Kenton L, et al. Effect of **behavioural-educational intervention** on sleep for **primiparous women and their infants in early postpartum**: multisite randomised controlled trial. BMJ. 2013 Mar 20;346:f1164.
Strøm T, Martinussen T, Toft P. A protocol of **no sedation for critically ill patients** receiving mechanical ventilation: a randomised trial. Lancet. 2010 Feb 6;375(9713):475-80.
Substance Abuse and Mental Health Services Administration **SAMHSA**, Center for Behavioral Health Quality and Statistics. (Nov 3, 2011). The DAWN Report: **Drug-Related Emergency Department Visits Attributed to Intentional Poisoning**. Rockville, MD. http://oas.samhsa.gov/2k11/DAWN040/WEB_DAWN_040.htm
Suh SW, Han JW, Lee JRet al. **Sleep and Cognitive Decline**: A Prospective Non-demented Elderly Cohort Study. Ann Neurol. 2018 Feb 2.
Taavoni S, Ekbatani N, Kashaniyan M, Haghani H. Effect of **valerian** on sleep quality in postmenopausal women: a randomized placebo-controlled clinical trial. *Menopause*. 2011 Sep;18(9):951-5.
Taibi DM, Landis CA, Petry H, Vitiello MV. A systematic review of **valerian as a sleep aid**: safe but not effective. Sleep Med Rev. 2007 Jun;11(3):209-30.
Tamblyn R, Abrahamowicz M, du Berger R, McLeod P, Bartlett G. A 5-year prospective assessment of the risk associated with individual benzodiazepines and doses in new elderly users. J Am Geriatr Soc. 2005 Feb;53(2):233-41. CONCLUSION: The risk of injury varied by benzodiazepine, independent of half-life, as did the risk associated with increasing dosage for individual products. Higher doses of oxazepam, flurazepam, and chlordiazepoxide are associated with the greatest risk of injury in the elderly.
TASK FORCE ON **SUDDEN INFANT DEATH SYNDROME. SIDS** and Other Sleep-Related Infant Deaths: Expansion of Recommendations for a Safe Infant Sleeping Environment. Pediatrics. 2011 Oct 17.
Taveras EM, Rifas-Shiman SL, Oken E, Gunderson EP, Gillman MW. Short sleep duration in infancy and risk of **childhood overweight**. Arch Pediatr Adolesc Med. 2008 Apr;162(4):305-11. Daily sleep duration of less than 12 hours during infancy appears to be a risk factor for overweight and adiposity in preschool-aged children.
Taveras EM, Gillman MW, Peña MM, et al. Chronic **Sleep Curtailment and Adiposity**. Pediatrics. 2014 May 19.
Thase, ME. Depression, Sleep, and Antidepressants. J Clin Psychiatry 1998;59(suppl 4):55-65.
The Search for Sleep, Pharmacy Practice Oct/2000 p45-51.
Therapeutic Choices 5th edition 2007
Tholfsen LK, Larsen JP, Schulz J, et al. Changes in **insomnia subtypes in early Parkinson disease**. Neurology. 2017 Jan 24;88(4):352-358.
Thorpe K, Staton S, Sawyer E, et al. **Napping**, development and health from 0 to 5 years: a systematic review. Arch Dis Child. 2015 Feb 17. pii: archdischild-2014-307241.
Trauer JM, Qian MY, Doyle JS, Rajaratnam SMW, Cunnington D. **Cognitive behavioral therapy for chronic insomnia**. A systematic review and meta-analysis. Ann Intern Med. 2015;163: doi: 10.7326/M14-2841
Treatments for Insomnia, Pharmacist's Letter. Sept. **2005**.
Treatment of Insomnia. Treatment Guidelines, Med Lett. **2006** Feb;4(42):5-10. Updated Mar 2009. July 2012. July 2015. **Updated Dec 2018.**
Treves N;Perlman A;Kolenberg Geron L;et al. **Z-drugs and risk for falls and fractures** in older adults-a systematic review and meta-analysis. Age Ageing. 2017 Oct 25:1-8.
Touma C, Pannain S. Does lack of sleep **cause diabetes**? Cleve Clin J Med. 2011 Aug;78(8):549-58.
Toward Optimized Practice. Adult Insomnia: Diagnosis to Management, Feb 2006. Revised: Feb 2007; Feb 2008; Feb 2010.
Twenge JM, Krisan Z, Hisler G. **Decreases in self-reported sleep duration among U.S. adolescents** 2009-2015 and links to new media screen time. Sleep Medicine. 2017.
U~Dream Sleep Naturally - https://www.udreamherbal.com/
Vandeleur M, Walter LM, Armstrong DS, et al. **How Well Do Children with Cystic Fibrosis Sleep**? An Actigraphic and Questionnaire-Based Study. J Pediatr. 2016 Dec 28.

Venkateshiah SB, Collop NA. Sleep and **sleep disorders in the hospital**. Chest. 2012 May;141(5):1337-45.
Vinson, Daniel C., Manning, Brian K., Galliher, James M., et al. **Alcohol and Sleep Problems** in Primary Care Patients: A Report from the AAFP National Research Network. Ann Fam Med 2010 8: 484-492.
Wagner J, Wagner ML, Hening. Beyond Benzodiazepines: Alternative Pharmacologic Agents for the Treatment of Insomnia. Ann Pharmacother 1998;32:680-91.
Watson NF, Martin JL, Wise MS, Carden KA, Kirsch DB, Kristo DA, Malhotra RK, Olson EJ, Ramar K, Rosen IM, Rowley JA, Weaver TE, Chervin RD. **Delaying middle school and high school start times** promotes student health and performance: an **American Academy of Sleep Medicine** (**AASM**) position statement. *J Clin Sleep Med*. 2017;13(4):623–625.
Weaver TE, Mancini C, Maislin G, et al. Continuous Positive Airway Pressure Treatment of Sleepy Patients with Milder Obstructive Sleep Apnea: Results of the **CPAP Apnea** Trial North American Program (**CATNAP**) Randomized Clinical Trial. Am J Respir Crit Care Med. 2012 Oct 1;186(7):677-683.
Weaver MD, Barger LK, Malone SK, et al. **Dose-Dependent Associations Between Sleep Duration and Unsafe Behaviors** Among US High School Students. JAMA Pediatr. 2018 Oct 1.
Wei JL, Bond J, Mayo MS, et al. Improved behavior and sleep after **adenotonsillectomy** in children with sleep-disordered breathing: long-term follow-up. Arch Otolaryngol Head Neck Surg. 2009 Jul;135(7):642-6.
Weich S, Pearce HL, Croft P, et al. Effect of **anxiolytic and hypnotic** drug prescriptions on **mortality hazards**: retrospective cohort study. BMJ. 2014 Mar 19;348:g1996.
Wesselius HM, Van den Ende ES, Alsma J, et al. **Quality of sleep in hospitalized patients** [online July 16, 2018]. JAMA Intern Med. doi:10.1001/jamainternmed.2018.2669
Westwood AJ, Beiser A, Jain N, et al. Prolonged sleep duration as a marker of early **neurodegeneration predicting incident dementia**. Neurology. 2017 Mar 21;88(12):1172-1179.
Wiegand MH. **Antidepressants** for the treatment of insomnia : a suitable approach? Drugs. 2008;68(17):2411-7. In general, drugs lacking strong cholinergic activity should be preferred. Drugs blocking serotonin 5-HT(2A) or 5-HT(2C) receptors should be preferred over those whose sedative property is caused by histamine receptor blockade only. The dose should be as low as possible (e.g. as an initial dose: doxepin 25 mg, mirtazapine 15 mg, trazodone 50 mg, trimipramine 25 mg).Regarding the lack of substantial data allowing for evidence-based recommendations, we are facing a clear need for well designed, long-term, comparative studies to further define the role of antidepressants versus other agents in the management of insomnia.
Williams JA, Zimmerman FJ, Bell JF. Norms and Trends of **Sleep Time Among US Children and Adolescents**. JAMA Pediatr. 2013 Jan 1;167(1):55-60.
Wilson SJ, Nutt DJ, Alford C, et al. **British Association for Psychopharmacology consensus statement** on evidence-based treatment of **insomnia, parasomnias and circadian rhythm** disorders. J Psychopharmacol. 2010 Sep 2.
Wilt TJ, MacDonald R, Brasure M, Olson CM, Carlyle M, Fuchs E, et al. **Pharmacologic treatment of insomnia disorder**: an evidence report for a clinical practice guideline by the American College of Physicians **(ACP)**. Ann Intern Med. 2016. [Epub ahead of print]. doi:10 .7326/M15-1781 2.
Wing YK, Chan NY, Man Yu MW, et al. A **School-Based Sleep Education Program for Adolescents**: A Cluster Randomized Trial. Pediatrics. 2015 Feb 16.
Winkelman JW. Clinical Practice. **Insomnia Disorder**. N Engl J Med. 2015 Oct 8;373(15):1437-44.
Wolkove N, Elkholy O, Baltzan M, Palayew M. Sleep and aging: 1. **Sleep disorders** commonly found in older people. CMAJ. 2007 Apr 24;176(9):1299-304.
Wolkove N, Elkholy O, Baltzan M, Palayew M. Sleep and aging: 2. **Management of sleep disorders in older people**. CMAJ. 2007 May 8;176(10):1449-54.
Wolkove N, Baltzan M. A 68-year-old woman with **sleep-onset insomnia**. (Restless leg syndrome) CMAJ.2013 Nov 19;185(17):1517-9.
Wong PM, Hasler BP, Kamarck TW, et al. **Social Jetlag, Chronotype, and Cardiometabolic Risk**. J Clin Endocrinol Metab. 2015 Nov 18:jc20152923.
Woolcott John C.; Richardson Kathryn J.; Wiens Matthew O.; et al. Meta-analysis of the Impact of 9 Medication Classes on **Falls** in Elderly Persons. Arch Intern Med. 2009;169(21):1952-1960.
Wu B, Wang Y, Wu X, Liu D, Xu D, Wang F. On-orbit **sleep problems of astronauts** and countermeasures. Mil Med Res. 2018 May 30;5(1):17.
Wu MP, Lin HJ, Weng SF, et al. Insomnia Subtypes and the Subsequent **Risks of Stroke**: Report From a Nationally Representative Cohort. Stroke. 2014 Apr 3.
Wu JQ, Appleman ER, Salazar RD, Ong JC. **Cognitive Behavioral Therapy** for Insomnia Comorbid With Psychiatric and Medical Conditions: A Meta-analysis. JAMA Intern Med. 2015 Jul 6.
Wu JQ, Appleman ER, Salazar RD, Ong JC. **Cognitive Behavioral Therapy for Insomnia** Comorbid With Psychiatric and Medical Conditions: A Meta-analysis. JAMA Intern Med. 2015 Jul 6.
Yaffe K, Laffan AM, Harrison SL, et al. Sleep-disordered breathing, hypoxia, and risk of mild **cognitive impairment** and dementia in older women. JAMA. 2011; 306(6):613-619.
Yaffe K, Falvey CM, Hoang T. Connections between **sleep and cognition** in older adults. Lancet Neurol. 2014 Oct;13(10):1017-1028.
Zammit G. Comparative tolerability of **newer agents for insomnia**. Drug Saf. 2009;32(9):735-48. doi: 10.2165/11312920-000000000-00000. PubMed PMID: 19670914.
Zhang J, Paksarian D, Lamers F, et al. **Sleep Patterns and Mental Health** Correlates in US Adolescents. J Pediatr. 2016 Dec 7.
Zimmerman KO, Hornik CP, Ku L, et al. **Sedatives and Analgesics Given to Infants** in **Neonatal Intensive Care Units** at the End of Life. J Pediatr. 2015 Aug;167(2):299-304.e3.
Zolpidem (Ambien CR) For Insomnia. Med Letter Dec 2005;47:97-98.

Web Sites:
National Heart Lung and Blood Institute http://www.nhlbi.nih.gov/health/dci/Diseases/inso/inso_whatis.html
American Academy of Sleep Medicine www.sleepeducation.com

---

[1] Kaiser Foundation Health Plan of Washington (Kaiser Permanente). *Insomnia Guideline*. January 2019

[2] Wilt TJ, MacDonald R, Brasure M, Olson CM, Carlyle M, Fuchs E, Khawaja IS, Diem S, Koffel E, Ouellette J, Butler M, Kane RL. Pharmacologic Treatment of Insomnia Disorder: An Evidence Report for a Clinical Practice Guideline by the American College of Physicians. Ann Intern Med. 2016 Jul 19;165(2):103-12. doi:10.7326/M15-1781. Epub 2016 May 3. Review. PubMed PMID: 27136278.

[3] Sateia MJ, Buysse DJ, Krystal AD, Neubauer DN, Heald JL. Clinical Practice Guideline for the Pharmacologic Treatment of Chronic Insomnia in Adults: An American Academy of Sleep Medicine Clinical Practice Guideline. J Clin Sleep Med. 2017 Feb 15;13(2):307-349. doi: 10.5664/jcsm.6470. PubMed PMID: 27998379; PubMed Central PMCID: PMC5263087.

[4] Fleming JA. *Insomnia*. Compendium of Therapeutic Choices. Canadian Pharmacists Association. May 2018.

Asthma: Online Extras

Asthma Clinical Controversies	
In mild asthma, should prn SABA therapy be abandoned in favour of a prn LABA/ICS?	This approach would be supported by some new guidelines (e.g. GINA 2019). The rationale is it prevents patients from becoming accidentally dependent on SABA monotherapy, & LABA/ICS therapy reduces exacerbations compared to SABA prn therapy. Evidence is based on the **SYGMA1** and **Novel START** trials. However, it is important to note that: • Patients in the Novel START trial used a SABA on average 7 times per week. In real-life practice, this level of SABA use would be a signal for stepping up to use of an ICS. In other words, patients with asthma who only use a SABA 2 times per week may still be good candidates to continue SABA monotherapy, and patients using a SABA regularly may be better off stepping up to a scheduled ICS rather than using a prn LABA/ICS. • Since exacerbations in patients with mild asthma are relatively rare, changing exacerbation rates may not be clinically important.
In mild asthma, should scheduled inhaled steroid therapy be abandoned in favour of a prn LABA/ICS?	Similar to the above, this approach is also supported by some new guidelines (e.g. GINA 2019). The rational is it may result in less overall steroid exposure but with a similar or better rate of exacerbations. Evidence is based on the **PRACTICAL**, **SYGMA 1**, and **SYGMA 2** trials. However, it is important to note that: • In the SYGMA 1 and SYGMA 2 trials, prn LABA/ICS resulted in overall less well-controlled asthma versus a scheduled ICS (e.g. about 5 less weeks per year of well-controlled asthma).[21] Thus ICS monotherapy, especially with an added **action plan**, is still a good choice for many patients. • Since exacerbations in patients with mild asthma are relatively rare, changing exacerbation rates may not be clinically important.

REFERENCES FOR ASTHMA PHARMACOTHERAPY AND OVERVIEWS

1. Laugheed MD, Lemiere C, Dell S, Ducharme F, FitzGerald JM, Leigh R, et al. **Canadian Thoracic Society (CTS)** Asthma Management Continuum – **2010 Consensus** Summary for children six years of age and over , and adults. Can Respir J 2010;17:15-24.
Lougheed MD, Lemiere C, Ducharme FM, et al; Canadian Thoracic Society Asthma Clinical Assembly. **Canadian Thoracic Society 2012** guideline update: diagnosis and management of asthma in preschoolers, children and adults. Can Respir J 2012;19(2):127-64.

2. Global Initiative for Asthma (**GINA**). Global strategy for asthma management and prevention. Vancouver (WA): Global Initiative for Asthma (GINA); **2011**. http://www.ginasthma.org/uploads/users/files/GINA_Report2011_May4.pdf

3. Boulet LP et al. Canadian **Asthma Consensus Report 1999**. CMAJ 1999; 161 (11 Suppl) & Boulet LP, et al.. What is new since the last (1999) Canadian Asthma Consensus Guidelines? Can Respir J. **2001** Mar-Apr;8 Suppl A:5A-27A & Lemiere C, Bai T, Balter M, et al. **Adult Asthma Consensus Guidelines Update 2003**. Can Respir J. 2004 May-Jun;11(Suppl A):9A-18A & Becker A, et al.; Asthma Guidelines Working Group of the Canadian Network For Asthma Care. Summary of recommendations from the Canadian Asthma Consensus guidelines, 2003. CMAJ. **2005** Sep 13;173(6 Suppl):S3-11. http://www.pulsus.com/Respir/11_SA/supp_A.pdf (See also: The Global Initiative for Asthma (GINA) **2007 update** http://www.ginasthma.com)

4. **GINA** 2012: Global Strategy for Asthma Management & Prevention. http://www.ginasthma.org/local/uploads/files/GINA_Pocket_Guide_2012_wms.pdf

5. Micromedex 2017; Drugs in Pregnancy and Lactation, 11th ed. Briggs GE, Freeman RK, Yaffe SJ, editors. Williams and Wilkins; Baltimore, MD: 2017.; Hansten & Horn-Drug Interactions 2015.
Respiratory Review Panel. Respiratory (Asthma and COPD) Guidelines for Family Practice. Toronto: MUMS Guidelines Clearinghouse; **2007**.
National Asthma Education & Prevention Program (NAEPP) Expert Panel Report 3 available at www.nhlbi.nih.gov/guidelines/asthma **2007**.

6 Anon. **Drugs for Asthma**. The Medical Letter. March 6, 2000: Vol. 42: issue 1073. & Dec 2008, **Aug 2013** & **Aug 2017**.

7 Walters EH, Walters J. Inhaled **short acting beta2-agonist** use in chronic asthma: regular versus as needed treatment (Cochrane Review). Cochrane Database Syst Rev. 2003;(2):CD001285.

8 Simon RA. Clinical implications of combination therapy on the future of asthma management. Allergy Asthma Proc. 2003 Mar-Apr;24(2):91-3.

[9] Williams SG, Schmidt DK, Redd SC, Storms W; National Asthma Education and Prevention Program. Key clinical activities for quality asthma care. Recommendations of the National Asthma Education and Prevention Program. MMWR Recomm Rep. 2003 Mar 28;52(RR-6):1-8.

[10] **Treatment Guidelines**: **Drugs for Asthma & COPD**. **The Medical Letter**: Oct 2002, May 2005, Dec 2008, Feb 2012. **Aug 2013.**

[11] Sin DD, Man J, Sharpe H, Gan WQ, Man SF. Pharmacological management to reduce exacerbations in adults with asthma: a systematic review and meta-analysis. JAMA. 2004 Jul 21;292(3):367-76.

[12] Wong CA, Walsh LJ, Smith CJ, et al. Inhaled corticosteroid use and bone-mineral density in patients with asthma. Lancet. 2000 Apr 22;355(9213):1399-403. (Hubbard R, Tattersfield A, Smith C, West J, Smeeth L, Fletcher A. Use of inhaled corticosteroids and the risk of fracture. Chest. 2006 Oct;130(4):1082-8.)
Etminan M, Sadatsafavi M, Ganjizadeh Zavareh S, et al. Inhaled corticosteroids and the risk of fractures in older adults: a systematic review and meta-analysis. Drug Saf 2008;5:409-14.
Loke YK et al. **Risk of fractures** with inhaled corticosteroids in COPD: Systematic review and meta-analysis of randomised controlled trials and observational studies. Thorax 2011
Eurich DT, Lee C, Marrie TJ, Majumdar SR. Inhaled corticosteroids and risk of recurrent pneumonia: a population-based, nested case-control study. Clin Infect Dis. 2013 Oct;57(8):1138-44.

[13] Health Canada Endorsed Important Safety Information on FLUTICASONE PROPIONATE (FLONASE/ FLOVENT/ ADVAIR) and RITONAVIR (NORVIR/KALETRA) Jan 22, 2004 & Bolland MJ, Bagg W, Thomas MG, et al. **Cushing's** syndrome due to interaction between inhaled corticosteroids (budesonide) and itraconazole. Ann Pharmacother. 2004 Jan;38(1):46-9.
Foisy MM, Yakiwchuk EM, Chiu I, Singh AE. Adrenal suppression and Cushing's syndrome secondary to an interaction between ritonavir and fluticasone: a review of the literature. HIV Med. 2008 May 3. [Epub ahead of print] The combination of ritonavir and fluticasone should be avoided. Budesonide, beclomethasone, triamcinolone and flunisolide appear to be safer options.
Canalejo E, Pacheco MS. Cushing syndrome due to ritonavir-fluticasone interaction. CMAJ. 2012 May 14.
Kempsford R, Allen A, Bal J, et al. The effect of ketoconazole on the pharmacokinetics and pharmacodynamics of inhaled fluticasone furoate and vilanterol trifenatate in healthy subjects. Br J Clin Pharmacol. 2012 Nov 1.
Mohabeer Hart M, Boffito M, Pozniak A. Unexpected rapid weight gain in a patient with HIV and anorexia. (**Iatrogenic Cushings-fluticasone-ritonavir**) BMJ. 2015 Oct 29;351:h5551.

[14] Sin DD, McAlister FA, Man SF, Anthonisen NR. Contemporary management of chronic obstructive pulmonary disease: scientific review. JAMA. 2003 Nov 5;290(17):2301-12.

[15] Calverley PM, Boonsawat W, Cseke Z, Zhong N, et al. Maintenance therapy with budesonide and formoterol in chronic obstructive pulmonary disease. Eur Respir J. 2003 Dec;22(6):912-9.

[16] Health Canada Sep,2005 http://www.hc-sc.gc.ca/dhp-mps/alt_formats/hpfb-dgpsa/pdf/medeff/serevent_2_hpc-cps_e.pdf , Aug, 2003 http://www.hc-sc.gc.ca/dhp-mps/alt_formats/hpfb-dgpsa/pdf/medeff/serevent_hpc-cps_e.pdf; GlaxoSmithKline Clinical trial registry SLGA5011: http://ctr.gsk.co.uk/Summary/salmeterol/studylist.asp
SMART - the Salmeterol Multi-Center Asthma Research Trial n=26,355; Nelson HS, Weiss ST, Bleecker ER, Yancey SW, Dorinsky PM; SMART Study Group. The Salmeterol Multicenter Asthma Research Trial: a comparison of usual pharmacotherapy for asthma or usual pharmacotherapy plus salmeterol. Chest. 2006 Jan;129(1):15-26. Erratum in: Chest. 2006 May;129(5):1393.
(Salpeter SR, Buckley NS, Ormiston TM, Salpeter EE. Meta-Analysis (19 trials n=33,826): Effect of Long-Acting {beta}-Agonists on Severe Asthma Exacerbations and Asthma-Related Deaths (Smart Trial info: 13 in LABA vs 3 in placebo groups NNH=1300 over 28 weeks). Ann Intern Med. 2006 Jun 5; [Epub ahead of print] Editorial: The Arg/Arg genotype may be reason LABAs less effective in some esp. African Americans. Use good doses of ICS first & if a LABA unresponsive pt the use of anticholinergics may be helpful.)
Rodrigo GJ, Nannini LJ, Rodríguez-Roisin R. Safety of Long-Acting {beta}-Agonists in Stable COPD: A Systematic Review. Chest. 2008 May;133(5):1079-87. This review supports the beneficial effects of the use of LABAs in patients with stable moderate-to-severe COPD, and did not confirm previous data about an increased risk for respiratory deaths. Also, our analysis suggests the superiority of tiotropium over LABAs for the treatment of stable COPD patients.

[17] Calverley PM, Walker P. Chronic obstructive pulmonary disease. Lancet. 2003 Sep 27;362(9389):1053-61.

[18] Kaiser SV, Huynh T, Bacharier LB, et al. Preventing Exacerbations in **Preschoolers With Recurrent Wheeze**: A Meta-analysis. Pediatrics. 2016 May 26.

[19] Paniagua N, Lopez R, Muñoz N, et al. Randomized Trial of **Dexamethasone Versus Prednisone for Children with Acute Asthma Exacerbations**. J Pediatr. 2017 Dec;191:190-196.e1.

[20] Rehrer MW et al. A randomized controlled noninferiority trial of **single dose of oral dexamethasone versus 5 days of oral prednisone** in acute adult **asthma**. Ann Emerg Med 2016 Apr 22.

21. Dugre N, Kolber M. "Less Puffing, More Breathing". Tools for Practice #230. Accessed from gomainpro.ca/wp-content/uploads/tools-for-practice/1550772595_tfp230-intermittenticsfv.pdf on July 25 2019.

22. Beasley R, Harper J, Bird G, Maijers I, Weatherall M, Pavord ID. Inhaled Corticosteroid Therapy in Adult Asthma. Time for a New Therapeutic Dose Terminology. American journal of respiratory and critical care medicine. 2019 Jun 15;199(12):1471-7.

Respiratory Review Panel RRP. Respiratory (Asthma and COPD) Guidelines for Family Practice. Toronto: MUMS Guidelines Clearinghouse; **2007**. (Wilt TJ, Niewoehner D, MacDonald R, Kane RL. Management of stable chronic obstructive pulmonary disease: a systematic review for a clinical practice guideline. Ann Intern Med. 2007 Nov 6;147(9):639-53. Long-acting inhaled therapies, supplemental oxygen, and pulmonary rehabilitation are beneficial in adults who have bothersome respiratory symptoms, especially dyspnea, and FEV1 less than 60% predicted.)

Ducharme FM. Inhaled **glucocorticoids versus leukotriene** receptor antagonists as single agent asthma treatment: systematic review of current evidence. BMJ. 2003 Mar 22;326(7390):621.

Ram F, Cates C, **Long-acting beta2-agonists vs anti-leukotrienes** as add-on therapy to inhaled corticosteroids for chronic asthma. Cochrane Database Syst Rev. 2005 Jan 25;(1):CD003137.

Castro-Rodriguez JA, Rodrigo GJ. The role of **inhaled corticosteroids and montelukast** in children with mild-moderate asthma: results of a systematic review with meta-analysis. Arch Dis Child. 2010 May;95(5):365-70\

Bisgaard H, Zielen S, Garcia-Garcia ML, et al. **Montelukast** reduces asthma exacerbations in 2- to 5-year-old children with intermittent asthma. Am J Respir Crit Care Med 2005; 171:315-22.
(In this manufacturer-sponsored study, montelukast reduced the annual frequency of exacerbations by 0.7 in children with mild intermittent asthma triggered by upper respiratory infections. Hospitalization rates were unaffected. One would need to treat 9 of these children for 1 year to prevent 1 exacerbation. (LOE = 2b-) InfoPOEMs)

Silverman RA, Nowak RM, Korenblat PE, et al. **Zafirlukast** treatment for acute asthma. Chest 2004; 126:1480-89.

Additional references:

Aalbers R et al. **Adjustable** maintenance dosing with budesonide/formoterol vs fixed-dose salmeterol/fluticasone in moderate to severe asthma. Curr Med Res Opin. 2004;20(2):225-40.

Aaron SD, Vandemheen KL, Boulet LP, McIvor RA, Fitzgerald JM, Hernandez P, Lemiere C, Sharma S, Field SK, Alvarez GG, Dales RE, Doucette S, Fergusson D; Canadian Respiratory Clinical Research Consortium. **Overdiagnosis of asthma** in obese and nonobese adults. CMAJ. 2008 Nov 18;179(11):1121-31.

Aaron SD, Vandemheen KL, FitzGerald JM, et al; **Canadian** Respiratory Research Network. **Reevaluation of diagnosis in adults** with physician-diagnosed **asthma**. JAMA. doi:10.1001 /jama.2016.19627

Abrams EM, Szefler SJ, Becker AB. Does inhaled steroid therapy help emerging asthma in early childhood? Lancet Respir Med. 2017 Aug 2.

Abramson MJ, Puy RM, Weiner JM. **Injection allergen immunotherapy** for asthma. *Cochrane Database of Systematic Reviews* 2010, Issue 8. Art. No: CD001186. Immunotherapy reduces asthma symptoms and use of asthma medications and improves bronchial hyper-reactivity. One trial found that the size of the benefit is possibly comparable to inhaled steroids. The possibility of local or systemic adverse effects (such as anaphylaxis) must be considered.

Abramson MJ, Schattner RL, Sulaiman ND, et al. Do **spirometry** and regular follow-up improve health outcomes in general practice patients with asthma or COPD? A cluster randomized controlled trial. Med J Aust. 2010 Jul 19;193(2):104-9.

Adachi M, Taniguchi H, Tohda Y, et al. The Efficacy and Tolerability of **Intravenous Montelukast** in Acute Asthma Exacerbations in Japanese Patients. J Asthma. 2012 Jun 28.

Adams NP, Bestall JC, Jones PW, et al. Inhaled **fluticasone at different doses** for chronic asthma in adults and children. Cochrane Database Syst Rev. 2005 Jul 20;(3):CD003534.

Adams NP, Jones PW. The dose-response characteristics of inhaled corticosteroids when used to treat asthma: An **overview of Cochrane systematic reviews**. Respir Med. 2006 Aug;100(8):1297-306. Epub 2006 Jun 23. The key findings are that all inhaled corticosteroids demonstrate a dose-response relationship for efficacy measures, but most of the benefit in mild-to-moderate severity disease is gained in the low-to-moderate dose range of each drug. In this group, high doses of fluticasone lead to small improvements in measures of control at the expense of a steep increase in the incidence of oral side-effects. In patients with severe disease who are dependent on oral steroids, there may be appreciable benefit in reducing oral steroids from very high compared with high doses of fluticasone.

Adams NP, Bestall JC, Jones P, et al. Fluticasone at different doses for chronic asthma in adults and children. Cochrane Database Syst Rev. 2008 Oct 8;(4):CD003534. We have not found evidence of a pronounced dose response in FEV1 with increasing doses of fluticasone. The number of studies contributing to our primary outcomes was low. At dose ratios of 1:2, there are statistically significant differences in favour of the higher dose in morning peak flow across the low dose range. The clinical impact of these differences is open to interpretation. Patients with moderate disease achieve similar levels of asthma control on medium doses of fluticasone (400 to 500 microg/day) as they do on high doses (800 to 1000 microg/day). More work in severe asthma would help to confirm that doses of FP above 500 microg/day confer greater benefit in this subgroup than doses of around 200 microg/day. In oral corticosteroid-dependent asthmatics, reductions in prednisolone requirement may be gained with FP 2000 microg/day.

Achakulwisut P, Brauer M, Hystad P, Anenberg SC. **Global, national, and urban burdens of paediatric asthma incidence** attributable to ambient NO(2) pollution: estimates from global datasets. Lancet Planet Health. 2019 Apr 10.

Afonso AS, Verhamme KM, Stricker BH, et al. Inhaled anticholinergic drugs and risk of **acute urinary retention**. BJU Int. 2010 Sep 29. doi: 10.1111/j.1464-410X.2010.09600.x.

Agrawal SK, Singh M, Mathew JL, Malhi P. Efficacy of an individualized written **home-management plan** in the control of moderate persistent asthma: A randomized, controlled trial. Acta Paediatr. 2005 Dec;94(12):1742-6.

Aggarwal P, et al. Comparison of nebulised **magnesium** sulphate and salbutamol combined with salbutamol alone in the treatment of acute bronchial asthma: a randomised study. Emerg Med J. 2006 May;23(5):358-62.

Ahmad S, Kew KM, Normansell R. **Stopping long-acting beta-agonists (LABA) for adults with asthma well controlled by LABA and inhaled corticosteroids**. Cochrane Database Syst Rev. 2015 Jun 19;6:CD011306. This review suggests that stopping LABA in adults who have stable asthma while they are taking a combination of LABA and ICS inhalers may increase the likelihood of asthma exacerbations that require treatment with oral corticosteroids, but this is not certain. Stopping LABA may slightly reduce asthma control and quality of life, but evidence was insufficient to show whether this had an effect on important outcomes such as serious adverse events and exacerbations requiring hospital admission, and longer trials are warranted. Trialists should include patient-important outcomes such as asthma control and quality of life and should use validated measurement tools. Definitions of exacerbations should be provided.

Ahmedzai S et al. Managing passengers with stable respiratory disease planning **air travel**: British Thoracic Society recommendations. Thorax 2011; 66: i1ei30

Akuete K, Oh SS, Thyne S, et al. Ethnic Variability in **Persistent Asthma After In Utero Tobacco Exposure**. Pediatrics. 2011 Aug 22.

Alangari AA, Malhis N, Mubasher M, et al. **Budesonide Nebulization** Added to Systemic Prednisolone in The Treatment of Acute Asthma in Children: Double-Blind, Randomized, Controlled Trial. Chest. 2014 Jan 2.

Alair Bronchial Thermoplasty System is a catheter-based device that delivers radiofrequency energy to the airways through the nose or mouth. The energy warms the airway linings and prevents the muscle from contracting. http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm209909.htm

Alansari K, Sakran M, Davidson BL, et al. Oral **Dexamethasone for Bronchiolitis**: A Randomized Trial. Pediatrics. 2013 Sep 16.

Alansari K, Davidson BL, Yousef KI, et al. **Rapid vs Maintenance Vitamin D Supplementation** in Deficient Asthmatic Children to Prevent Exacerbations. Chest. 2017 Jun 23.

Altenburg J, de Graaff CS, Stienstra Y, et al. Effect of **azithromycin maintenance treatment on infectious exacerbations** among patients with non–cystic fibrosis bronchiectasis: the BAT randomized controlled trial. JAMA. 2013;309(12):1251-1259.

Alvaro RE et al. CO(2) Inhalation as a Treatment for **Apnea of Prematurity**: A Randomized Double-Blind Controlled Trial. (**theophylline**) J Pediatr. 2011 Sep 8.

American Lung Association Asthma Clinical Research Centers; Peters SP, Anthonisen N, Castro M, Holbrook JT, Irvin CG, Smith LJ, Wise RA. Randomized comparison of strategies for **reducing treatment in mild persistent** asthma. N Engl J Med. 2007 May 17;356(20):2027-39. We randomly assigned 500 patients that was well controlled by inhaled fluticasone (100 microg twice daily) to receive continued fluticasone (100 microg twice daily) (169 patients), montelukast (5 or 10 mg each night) (166 patients), or fluticasone (100 microg) plus salmeterol (50 microg) each night (165 patients) for 16 weeks. Patients with asthma that is well controlled with the use of twice-daily inhaled fluticasone can be switched to once-daily fluticasone plus salmeterol without increased rates of treatment failure. A switch to montelukast results in an increased rate of treatment failure and decreased asthma control; however, patients taking montelukast remained free of symptoms on 78.7% of treatment days. . InfoPoems (At first glance the results seem to favor fluticasone plus salmeterol over montelukast for step-down therapy in patients with mild persistent asthma. However, a closer look at the benefit of the former (based largely on disease-oriented end points) and its potential harms (more respiratory infections) makes montelukast look like an excellent alternative, particularly given the concerns regarding long-term use of long-acting beta-agonists and corticosteroids. (LOE = 1b))

American Lung Association Asthma Clinical Research Centers. Clinical trial of low-dose theophylline and montelukast in patients with poorly controlled asthma. Am J Respir Crit Care Med. 2007 Feb 1;175(3):235-42. Epub 2006 Sep 22. Neither montelukast nor low-dose theophylline lowered the EPAC rate of poor asthma control in patients with poorly controlled asthma despite improved lung function. For patients not using inhaled corticosteroids, low-dose theophylline improved asthma symptom control more than montelukast or placebo, and provides a safe and low-cost alternative asthma treatment.

Anderson HR, Ayres JG, Sturdy PM, et al. Bronchodilator treatment and **deaths** from asthma: case-control study. BMJ. 2005 Jan 15;330(7483):117. Epub 2004 Dec 23.

Andersson M, Hedman L, Bjerg A, Forsberg B, et al. **Remission and persistence of asthma** followed from 7 to 19 years of age. Pediatrics. 2013 Aug;132(2):e435-42.

Andrew E, Nehme Z, et al. **Stormy weather**: a retrospective analysis of demand for emergency medical services during epidemic thunderstorm asthma. BMJ. 2017 Dec13;359:j5636.

Anthonisen NR, et al.; Lung Health Study Research Group. The effects of a **smoking cessation** intervention on 14.5-year **mortality**: a randomized clinical trial. Ann Intern Med. 2005 Feb 15;142(4):233-9.

Antolín-Amérigo D, Vlaicu PC, De La Hoz Caballer B, Cano MS. **Anaphylaxislike cholinergic urticaria**. Can Fam Physician. 2013 Jul;59(7):745-6. (Montelukast used)

Arrington-Sanders R, et al. **Ritonavir-fluticasone** interaction causing Cushing syndrome in HIV-infected children and adolescents. Pediatr Infect Dis J. 2006 Nov;25(11):1044-8.

Auger KA, Kahn RS, Davis MM, et al. **Pediatric Asthma Readmission**: Asthma Knowledge Is Not Enough? J Pediatr. 2014 Sep 17.

Bacharier LB, et al. Long-term effect of budesonide on **hypothalamic-pituitary-adrenal axis** function in children with mild to moderate asthma. Pediatrics.2004 Jun;113(6):1693-9.

Bacharier LB, Guilbert TW, Mauger DT, et al. **Early administration** of **azithromycin** and prevention of severe lower respiratory tract illnesses in preschool children with a history of such illnesses: a randomized clinical trial. JAMA. doi:10.1001/jama.2015.13896.

Bafadhel M, Clark TW, Reid C, et al. **Procalcitonin and C-reactive protein** in hospitalized adult patients with community-acquired pneumonia or exacerbation of asthma or COPD. Chest. 2011 Jun;139(6):1410-8.

Bain E, Pierides KL, Clifton VL, et al. Interventions for **managing asthma in pregnancy**. Cochrane Database of Systematic Reviews 2014, Issue 10. Art. No.: CD010660. DOI: 10.1002/14651858.CD010660.pub2. Based on eight included trials, of moderate quality overall, no firm conclusions about optimal interventions for managing asthma in pregnancy can be made. Five trials assessing pharmacological interventions did not provide clear evidence of benefits or harms to support or refute current practice. While inhaled magnesium sulphate for acute asthma was shown to reduce exacerbations, this was in one small trial of unclear quality, and thus this finding should be interpreted with caution. Three trials assessing non-pharmacological interventions provided some support for the use of such strategies, however were not powered to detect differences in importantmaternal and infant outcomes. While a FENO-based algorithm reduced exacerbations, the effects on perinatal outcomes were less certain, and thus widespread implementation is not yet appropriate. Similarly, though positive effects on asthma control were shown with PMR and pharmacist-led management, the evidence to date is insufficient to draw definitive conclusions. In view of the limited evidence base, further randomised trials are required to determine the most effective and safe interventions for asthma in pregnancy. Future trials must be sufficiently powered, and well-designed, to allow differences in important outcomes for mothers and babies to be detected. The impact on health services requires evaluation. Any further trials assessing pharmacological interventions should assess novel agents or those used in current practice. Encouragingly, at least five trials have been identified as planned or underway.

Bakel LA, Hamid J, Ewusie J, et al. **International Variation in Asthma and Bronchiolitis Guidelines**. Pediatrics. 2017 Oct 25.

Bakkeheim E, Mowinckel P, Carlsen KH, Håland G, Carlsen KC. Paracetamol (**acetaminophen**) in early infancy: the risk of childhood allergy and asthma. Acta Paediatr. 2011 Jan;100(1):90-6. doi: 10.1111/j.1651-2227.2010.01942.x.

Balter, Meyer S, Bell, Alan D, Kaplan, Alan G, Kim, Harold, McIvor, Andrew. **Management of asthma in adults**. CMAJ 2009 0: cmaj.080007

Barnes PJ. COUNTERPOINT: Will new **anti-eosinophilic drugs** be useful in asthma management? No. Chest. 2016 Oct 6.

Barr, R. Graham, Bluemke, David A., Ahmed, Firas S., et al. Percent Emphysema, Airflow Obstruction, and Impaired **Left Ventricular Filling**. N Engl J Med 2010 362: 217-227.

Bassler D et al. Early inhaled **budesonide for the prevention of bronchopulmonary dysplasia**. (**NEUROSIS**) N Engl J Med 2015 Oct 15; 373:1497.

Bassler D, et al; Neonatal European Study of Inhaled Steroids Trial Group. Long-Term Effects of Inhaled **Budesonide for Bronchopulmonary Dysplasia**. N Engl J Med. 2018 Jan 11;378(2):148-157.

Pdf Stratakis N, Roumeliotaki T, Oken E, et al. Fish and seafood consumption during pregnancy and the risk of asthma and allergic rhinitis in childhood: a pooled analysis of 18 European and US birth cohorts. Int J Epidemiol. 2017 Oct 1;46(5):1465-1477.

Bateman ED, Boushey HA, et al. Can guideline-defined asthma control be achieved? The Gaining Optimal Asthma ControL Study(GOAL salmeterol/fluticasone vs fluticasone).Am J Respir Crit Care Med 2004;170:836-44.

Bateman ED, et al. Asthma control can be maintained when fluticasone propionate/salmeterol in a single inhaler is stepped down. J Allergy Clin Immunol. 2006 Mar;117(3):563-70. CONCLUSION: In pts achieving asthma control with FSC 250/50 microg twice daily, stepping treatment down to a lower dose of **FSC 100/50 microg twice** daily is more effective than switching to an inhaled corticosteroid alone.

Bateman ED, O'Byrne PM, Busse WW, et al. Once-daily fluticasone furoate (FF)/vilanterol reduces risk of severe exacerbations in asthma versus FF alone. Thorax. 2014 Apr;69(4):312-9.

Bateman ED, et al. **Roflumilast** combined **with montelukast versus montelukast** alone as add-on treatment in patients with moderate-to-severe asthma. J Allergy Clin Immun. 2016 Feb 23.

Bateman ED, Reddel HK, O'Byrne PM, et al**. As-needed budesonide–formoterol versus maintenance budesonide in mild asthma**. N Engl J Med 2018; 378: 1877-87.

Bavbek S, et al. Safety of **Meloxicam** in Aspirin-Hypersensitive Patients with Asthma and/or Nasal Polyps. A Challenge-Proven Study. Int Arch Allergy Immunol. 2006 Oct 2;142(1):64-69 [Epub ahead of print]

Beach J, Russell K, Blitz S, Hooton N, Spooner C, Lemiere C, Tarlo SM, Rowe BH. A systematic review of the diagnosis of **occupational asthma**. Chest. 2007 Feb;131(2):569-78.

Beasley R, Holliday M, Reddel HK, et al. Controlled trial of **budesonide–formoterol as needed for mild asthma**. (Novel-START) N Engl J Med. DOI: 10.1056/NEJMoa1901963.

Beasley RW, Clayton TO, Crane J, Lai CK, Montefort SR, von Mutius E, Stewart AW; the ISAAC Phase Three Study Group. **Acetaminophen** Use and Risk of Asthma, Rhinoconjunctivitis and Eczema in Adolescents: ISAAC Phase Three. Am J Respir Crit Care Med. 2010 Aug 13.

Beasley R, Singh S, Loke YK, et al. Call for worldwide **withdrawal of tiotropium Respimat mist inhaler**. BMJ. 2012 Nov 9;345:e7390.

Beasley R, Semprini A, Mitchell EA. **Risk factors for asthma**: is prevention possible? Lancet. 2015 Sep 12;386(9998):1075-85.

Beauchamp MK, Evans R, et al. Systematic Review of Supervised **Exercise Programs** After Pulmonary Rehabilitation in Individuals With COPD. Chest. 2013 Oct;144(4):1124-33.

Beck AF, Bradley CL, Huang B, et al.The **Pharmacy-Level Asthma Medication Ratio** and Population Health. Pediatrics. 2015 May 4.

Becker LA, Hom J, Villasis-Keever M, et al. **Beta2-agonists for acute cough or a clinical diagnosis of acute bronchitis**. Cochrane Database Syst Rev. 2015 Sep 3;9:CD001726. There is no evidence to support the use of beta2-agonists in children with acute cough who do not have evidence of airflow restriction. There is also little evidence that the routine use of beta2-agonists is helpful for adults with acute cough. The se agents may reduce symptoms, including cough, in people with evidence of airflow restriction. However, this potential benefit is not well supported by the available data and must be weighed against the adverse effects associated with their use. There is no evidence to support the use of beta2-agonists in children with acute cough who do not have evidence of airflow restriction. There is also little evidence that the routine use of beta2-agonists is helpful for adults with acute cough. These agents may reduce symptoms, including cough, in people with evidence of airflow restriction. However, this potential benefit is not well supported by the available data and must be weighed against the adverse effects associated with their use.

Beggs S, Foong YC, Le HCT, Noor D, et al. **Swimming training** for asthma in children and adolescents aged 18 years and under. Cochrane Database of Systematic Reviews 2013, Issue 4. Art. No.: CD009607. DOI:10.1002/14651858.CD009607.pub2.

Bel EH. Clinical Practice. **Mild asthma**. N Engl J Med. 2013 Aug 8;369(6):549-57.

Bel EH, Wenzel SE, Thompson PJ, et al. Oral glucocorticoidsparing effect of **mepolizumab** in **eosinophilic asthma**. (**Sirus**) N Engl J Med. DOI: 10.1056/NEJMoa1403291.

Belanger K et al. Effect of **pregnancy on maternal asthma symptoms** and medication use. *Obstet Gynecol* 2010 Mar; 115:559.

Bender BG, Cvietusa PJ, Goodrich GK, et al. Pragmatic Trial of Health Care **Technologies to Improve Adherence** to Pediatric Asthma Treatment: A Randomized Clinical Trial. JAMA Pediatr. 2015 Apr 1;169(4):317-323.

Bergen R, Black S, et al. Safety of cold-adapted live attenuated **influenza vaccine** in a large cohort of children & adolescents. Pediatr Infect Dis J. 2004 Feb;23(2):138-44.

Berry MA, Hargadon B, Shelley M, et al. Evidence of a role of **tumor necrosis factor alpha** in refractory asthma. N Engl J Med. 2006 Feb 16;354(7):697-708.
Beta$_2$-agonists **Drug Class Review Nov/06** Oregon Health & Science University. http://www.ohsu.edu/drugeffectiveness/reports/documents/Beta%20Agonists%20Final%20Report.pdf
Bhogal SK et al. Early administration of systemic **corticosteroids reduces hospital admission rates** for children with asthma exacerbation. Ann Emerg Med 2012 Jul; 60:84.
Biagini Myers JM, Schauberger E, He H, et al. A **Pediatric Asthma Risk Score to better predict asthma developmen**t in young children. J Allergy Clin Immunol. 2018 Dec 7.
Bian J, Cristaldi KK, Summer AP, et al. Association of a School-Based, **Asthma-Focused Telehealth Program With Emergency Department Visits** Among Children Enrolled in South Carolina Medicaid. JAMA Pediatr. 2019 Sep 9.
Birnbaum S. **Pulmonary rehabilitation**: a classic tune with a new beat, but is anyone listening? Chest. 2011 Jun;139(6):1498-502.
Bisgaard H, et al. Twelve-month safety and efficacy of inhaled fluticasone propionate in **children aged 1 to 3** years with recurrent wheezing. Pediatrics. 2004 Feb;113(2):e87-94.
Bisgaard H, et al. **Intermittent** inhaled corticosteroids in **infants** with episodic **wheezing**. N Engl J Med. 2006 May 11;354(19):1998-2005. Intermittent inhaled corticosteroid therapy had no effect on the progression from episodic to persistent wheezing and no short-term benefit during episodes of wheezing in the first three years of life. (budesonide 400ug/d)
Bisgaard H, Stokholm J, Chawes BL, et al. **Fish oil–derived fatty acids in pregnancy** and wheeze and asthma in offspring. N Engl J Med 2016;375:2530-9.
Bjermer L, Lemiere C, et al. **Reslizumab** for Inadequately Controlled Asthma with Elevated Blood Eosinophil Levels: a Randomized Phase 3 Study. Chest. 2016 Apr 4.
Blais L, et al. Use of inhaled corticosteroids during the first trimester of **pregnancy** and the risk of congenital malformations among asthmatic women. Thorax. 2006 Nov 22.
Blais L, Beauchesne MF, Lemière C, Elftouh N. **High doses** of inhaled corticosteroids during the **first trimester of pregnancy** and congenital malformations. J Allergy Clin Immunol. 2009 Dec;124(6):1229-1234.e4.
Bleecker ER, FitzGerald JM, Chanez P, et al. Efficacy and safety of **benralizumab** for patients with severe asthma uncontrolled with high-dosage inhaled corticosteroids and long-acting β2-agonists (**SIROCCO**): a randomised, multicentre, placebo-controlled phase 3 trial. Lancet 2016; online Sept 5.
Bonham CA, Patterson KC, Strek ME. **Asthma Outcomes and Management During Pregnancy**. Chest. 2017 Aug 31.
Bolton CE, Bevan-Smith EF, Blakey JD, et al.British Thoracic Society Pulmonary Rehabilitation Guideline Development Group; British Thoracic Society Standards of Care Committee. British Thoracic Society guideline on **pulmonary rehabilitation in adults**. Thorax. 2013 Sep;68 Suppl 2:ii1-30.
Boluyt N, Rottier BL, de Jongste JC, et al. **Assessment of Controversial** Pediatric Asthma **Management Options** Using GRADE. Pediatrics. 2012 Sep;130(3):e658-68.
Bose S, Diette GB, Woo H, et al. **Vitamin D status modifies the response** to indoor particulate matter in obese urban children with asthma. J Allergy Clin Immunol Pract. 2019 Feb 11.
Boulet LP, Bateman ED, Voves R, Muller T, Wolf S, Engelstatter R. A randomized study comparing **ciclesonide 320ug od and fluticasone** propionate 200ug bid in patients with moderate persistent asthma. Respir Med. 2007 Apr 18; [Epub ahead of print] 12 week n=474. There were no cases of oral candidiasis in patients receiving ciclesonide and nine cases (3.8%) in those receiving fluticasone propionate (p=0.002; one-sided). CONCLUSIONS: Treatment with once-daily ciclesonide and twice-daily fluticasone propionate resulted in similar improvements in lung function in patients with moderate persistent asthma. Ciclesonide showed significant improvements in oral candidiasis and HRQoL over fluticasone.
Boulet LP, O'Byrne PM. Asthma and **exercise-induced bronchoconstriction in athletes**. N Engl J Med. 2015 Feb 12;372(7):641-8.
Bourdin A, Husereau D, Molinari N, et al. **Matching-adjusted indirect comparison of benralizumab versus interleukin-5 inhibitors** for the treatment of severe asthma: a systematic review. Eur Respir J. 2018 Nov 29;52(5).
Bousquet J, Boulet LP, Peters MJ, Magnussen H, Quiralte J, Martinez-Aguilar NE, Carlsheimer A. Budesonide/formoterol for maintenance and relief in uncontrolled asthma vs. high-dose salmeterol/fluticasone. Respir Med. 2007 Sep 28; [Epub ahead of print] In the treatment of uncontrolled asthma, budesonide/formoterol maintenance and reliever therapy reduces the incidence of severe asthma exacerbations and hospitalisation/ER treatment with similar daily symptom control compared with sustained high-dose salmeterol/fluticasone plus SABA. This benefit is achieved with substantially less ICS exposure.
Boushey HA, Sorkness CA, King TS, et al, for the National Heart, Lung, and Blood Institute's Asthma Clinical Research Network. **Daily versus as-needed corticosteroids** for mild persistent asthma. N Engl J Med 2005; 352: 1519-528 & ACP Journal Club. (InfoPOEMs: Intermittent therapy, as measured by the outcomes that matter, is as effective as continuous therapy with oral zafirlukast or inhaled budesonide for patients with very mild but persistent asthma. Note that patients had a clear plan of action for when symptoms flared up: Begin inhaled budesonide in the "yellow zone," when symptoms initially worsen, and add prednisone 0.5 mg/kg if symptoms enter the "red zone," when breathlessness is present at rest or with activities of daily living. (LOE = 1b))
Brandt S, Dickinson B. **Time and Risk Preferences** and the Use of Asthma Controller Medication. Pediatrics. 2013 Mar 11.
Brehm JM, Acosta-Pérez E, Klei L, et al. **Vitamin D Insufficiency** and Severe Asthma Exacerbations in Puerto Rican Children. Am J Respir Crit Care Med. 2012 May 31.
Brittan M, Richardson T, Kenyon C, et al. Association between **Postdischarge Oral Corticosteroid Prescription Fills** and Readmission in Children with Asthma. J Pediatr. 2016 Oct 18
Britto MT, Vockell AL, Munafo JK, et al. **Improving Outcomes for Underserved Adolescents** With Asthma. Pediatrics. 2014 Jan 27
Brode SK, Ling SC, Chapman KR**. Alpha-1 antitrypsin deficiency**: a commonly verlooked cause of lung disease. CMAJ. 2012 Jul 3.
Brode SK, Campitelli MA, Kwong JC, et al. The risk of **mycobacterial infections associated with inhaled corticosteroid use**. Eur Respir J. 2017 Sep 20;50(3).
Brodlie M, Gupta A, Rodriguez-Martinez CE, et al. **Leukotriene receptor antagonists** as maintenance and intermittent therapy for episodic viral wheeze in children. Cochrane Database Syst Rev. 2015 Oct 19;10:CD008202. In pre-school children with EVW, there is no evidence of benefit associated with maintenance or intermittent LTRA treatment, compared to placebo, for reducing the number of children with one or more viral-induced episodes requiring rescue oral corticosteroids, and little evidence of significant clinical benefit for other secondary outcomes. Therefore until further data are available, LTRA should be used with caution in individual children. When used, we suggest a therapeutic trial is undertaken, during which efficacy should be carefully monitored. It is likely that children with an apparent EVW phenotype are not a homogeneous group and that subgroups may respond to LTRA treatment depending on the exact patho-physiological mechanisms involved.
Broekhuizen, Berna D. L., Sachs, Alfred P. E., Moons, Karel G. M., et al. **Diagnostic Value of Oral Prednisolone Test** for Chronic Obstructive Pulmonary Disorders. Ann Fam Med 2011 9: 104-109.
Brozek JL, Bousquet J, Baena-Cagnani CE, et al. Global Allergy and Asthma European Network; Grading of Recommendations Assessment, Development and Evaluation Working Group. **Allergic Rhinitis and its Impact on Asthma (ARIA) guidelines**: 2010 revision. J Allergy Clin Immunol. 2010 Sep;126(3):466-76. ARIA- Allergic Rhinitis and its Impact on Asthma (ARIA) 2010 revision. Geneva: World Health Organization (WHO); 2010 Dec 23. http://whiar.org/docs/ARIAReport_2010.pdf
Brozek JL, Kraft M, et al. **Long-acting B2-agonist step-off** in patients with controlled asthma: systematic review with meta-analysis [published online August 27, 2012]. *Arch Intern Med*. 2012.
Brusselle GG, et al. **Azithromycin for prevention of exacerbations** in severe asthma (**AZISAST**): a multicentre randomised double-blind placebo-controlled trial. Thorax. 2013 Apr;68(4):322-9.
Brustad N, Eliasen AU, Stokholm J, et al. High-Dose **Vitamin D Supplementation During Pregnancy** and Asthma in Offspring at the Age of 6 Years. JAMA. 2019 Mar 12;321(10):1003-1005.

Bruton A, Lee A, Yardley L, et al. **Physiotherapy breathing retraining** for asthma: a randomised controlled trial. Lancet Respir Med 2017; online Dec 13.
Bruzzese JM, Sheares BJ, Vincent EJ, et al. Effects of a **School-based Intervention** for Urban Adolescents with Asthma: A Controlled Trial. Am J Respir Crit Care Med. 2010 Dec 7.
Bryant-Stephens T, Reed-Wells S, Canales M, et al. **Home visits** are needed to address asthma health disparities in adults. J Allergy Clin Immunol. 2016 Dec;138(6):1526-1530.
Bueving HJ, et al. Influenza **vaccination** in children with asthma: randomized double-blind placebo-controlled trial. Am J Respir Crit Care Med. 2004 Feb 15;169(4):488-93. Epub 2003 Dec 04.)
Buhl R, et al. Comparable efficacy of **ciclesonide** once daily versus fluticasone propionate twice daily in asthma. Pulm Pharmacol Ther. 2006;19(6):404-12. Epub 2005 Nov 28.
Brumpton B, Xiao-Mei M, Langhammer A, et al. Prospective study of **insomnia** and incident asthma in adults: the HUNT study. Eur Respir J2017;(Feb).
Burchett DK, Darko W, Zahra J, et al. Mixing and compatibility guide for commonly used aerosolized medications. Am J Health-Syst Pharm. 2010;67:227-30.
Burr JF, Davidson W, Shephard RJ, Eves N. **Physical activity** in chronic respiratory conditions: Assessing risks for physical activity clearance and prescription. Can Fam Physician. 2012 Jul;58(7):761-4.
Bush A, Saglani S. Management of **severe asthma in children**. Lancet. 2010 Sep 4;376(9743):814-25.
Bush A, Fleming L. Diagnosis and management of **asthma in children**. BMJ. 2015 Mar 5;350:h996.
Bush A, Fleming L. **Is asthma overdiagnosed**? Arch Dis Child. 2016 Apr 5.
Bush A, Frey U. **Safety of long-acting beta-agonists in children with asthma**. N Engl J Med 2016 Sep1; 375:889.
Busse, W.W., Managing Asthma During **Pregnancy**: **NAEPP** Recommendations for Pharmacologic Treatment--Update **2004** http://www.nhlbi.nih.gov/health/prof/lung/asthma/astpreg.htm
Busse WW, Bateman ED, Caplan AL, et al. Combined Analysis of **Asthma Safety Trials of Long-Acting β(2)-Agonists**. N Engl J Med. 2018 Jun 28;378(26):2497-2505.
Busse WW, Bleecker ER, FitzGerald JM, et al; BORA study investigators. Long-term safety and efficacy of **benralizumab** in patients with severe, uncontrolled asthma: 1-year results from the **BORA phase 3** extension trial. Lancet Respir Med. 2018 Nov 8.
Busse WW, Lemanske RF Jr, Gern JE. Role of **viral respiratory infections in asthma and asthma exacerbations**. Lancet. 2010 Sep 4;376(9743):826-34.
Busse William W., Morgan Wayne J., Gergen Peter J., et al. Randomized Trial of **Omalizumab (Anti-IgE) for Asthma in Inner-City Children**. (**ICATA**) N Engl J Med 2011; 364:1005-1015.
Butz AM, et al. Effectiveness of nebulizer use-targeted asthma education on underserved children with asthma. Arch Pediatr Adolesc Med. 2006 Jun;160(6):622-8. A nebulizer education intervention had no effect on asthma severity or health care use.
Butz BK, Wen T, Gleich GJ, et al. Efficacy, Dose Reduction, and Resistance to High-dose **Fluticasone** in Patients with **Eosinophilic Esophagitis**. Gastroenterology. 2014 Apr 22.
Cabana MD, McKean M, Caughey AB, et al. Early **Probiotic Supplementation for Eczema and Asthma** Prevention: A Randomized Controlled Trial. Pediatrics. 2017 Sep;140(3). pii: e20163000.
Cahill KN, Katz HR, Cui J, et al. KIT inhibition by **imatinib** in patients with severe refractory asthma. N Engl J Med 2017; 376:1911-20.
Calhoun WJ, Ameredes BT, King TS, et al; Asthma Clinical Research Network of the National Heart, Lung, and Blood Institute. Comparison of **physician-, biomarker-, and symptom**-based strategies for adjustment of inhaled corticosteroid therapy in adults with asthma: the **BASALT** randomized controlled trial. JAMA. 2012;308(10):987- 997.
Caliskan M et al. **Rhinovirus wheezing illness and genetic risk of childhood-onset asthma**. N Engl J Med 2013 Mar 27.
Callaghan-Koru JA, Riekert KA, Ruvalcaba E, et al. Home **Medication Readiness for Preschool Children With Asthma**. Pediatrics. 2018 Aug 7.
Calverley PM, Anderson JA, Celli B, Ferguson GT, Jenkins C, Jones PW, Yates JC, Vestbo J; **TORCH investigators**. Salmeterol and fluticasone propionate and survival in chronic obstructive pulmonary disease. N Engl J Med. 2007 Feb 22;356(8):775-89. n=6112 The reduction in death from all causes among patients with COPD in the combination-therapy group did not reach the predetermined level of statistical significance. There were significant benefits in all other outcomes among these patients. The international, industry-supported TORCH trial, researchers randomized more than 6000 COPD patients to receive either inhaled salmeterol & fluticasone propionate 500/50ug, each drug alone, or placebo. At 3 years, rates of all-cause mortality (the primary outcome) were 12.6% with combination therapy, 13.5% with salmeterol, 16.0% with fluticasone, and 15.2% with placebo. The mortality difference between the combination-therapy and placebo groups fell just short of statistical significance (P=0.052). However, combination therapy was associated with significant improvements in health status, lung function, and the frequency of COPD exacerbations. Patients taking fluticasone, alone or in combination, had an increased rate of pneumonia (Advair 19.6%, Flovent 18.3%, Serevent 13.3%, Placebo 12.3%). (see also Pharmacist's Letter Apr/07) Celli BR, Thomas NE, Anderson JA, Ferguson GT, Jenkins C, Jones PW, Vestbo J, Knobil K, Yates JC, Calverley PM. Effect of Pharmacotherapy on Rate of Decline of Lung Function in COPD: Results from the TORCH Study. Am J Respir Crit Care Med. 2008 May 29. [Epub ahead of print] Pharmacotherapy with salmeterol plus fluticasone propionate, or the components, reduces the rate of decline of FEV1 in patients with moderate-to severe COPD, thus slowing disease progression. Celli BR, Thomas NE, Anderson JA, Ferguson GT, Jenkins CR, Jones PW, Vestbo J, Knobil K, Yates JC, Calverley PM. Effect of pharmacotherapy on rate of decline of lung function in chronic obstructive pulmonary disease: results from the TORCH study. Am J Respir Crit Care Med. 2008 Aug 15;178(4):332-8. Epub 2008 May 29. Rates of decline were similar among the active treatment arms. Pharmacotherapy with salmeterol plus fluticasone propionate, or the components, reduces the rate of decline of FEV(1) in patients with moderate-to-severe COPD, thus slowing disease progression.
Calverley PM, Stockley RA, Seemungal TA, et al; on behalf of the Investigating New Standards for Prophylaxis in Reduction of Exacerbations (**INSPIRE**) Investigators. Reported **Pneumonia** in Patients With COPD: Findings From the INSPIRE Study. Chest. 2011 Mar;139(3):505-512.
Canalejo E, Pacheco MS. **Cushing syndrome due to ritonavir-fluticasone** interaction. CMAJ. 2012 May 14.
Castle W, et al. Serevent nationwide surveillance (**SNS**) study: comparison of **salmeterol** with **salbutamol** in asthmatics who require regular bronchodilator treatment. BMJ. 1993 Apr 17;306(6884):1034-7.
Castro M, Rubin AS, Laviolette M, et al. AIR2 Trial Study Group. Effectiveness and safety of **bronchial thermoplasty** in the treatment of severe asthma: a multicenter, randomized, double-blind, sham-controlled clinical trial. Am J Respir Crit Care Med. 2010 Jan 15;181(2):116-24. Epub 2009 Oct 8. PubMed PMID: 19815809.
Castro M, Corren J, Pavord ID, et al. **Dupilumab** efficacy and safety in moderate-to-severe uncontrolled asthma. N Engl J Med. 2018 May 21. DOI: 10.1056/NEJMoa1804092.
Castro-Rodriguez JA, Rodrigo GJ. Beta-agonists through **metered-dose inhaler with valved holding chamber** versus nebulizer for acute exacerbation of wheezing or asthma in children under 5 years of age: a systematic review with meta-analysis. J Pediatr. 2004 Aug;145(2):172-7.
Castro-Rodriguez JA, Rodrigo GJ. Efficacy of **inhaled corticosteroids in infants and preschoolers** with recurrent wheezing and asthma: a systematic review with meta-analysis. Pediatrics. 2009 Mar;123(3):e519-25. Infants and preschoolers with recurrent wheezing or asthma had less wheezing/asthma exacerbations and improve their symptoms and lung function during treatment with inhaled corticosteroids.
Castro-Rodriguez JA, Rodrigo GJ. The role of inhaled **corticosteroids and montelukast** in children with mild-moderate asthma: results of a systematic review with meta-analysis. Arch Dis Child. 2010 May;95(5):365-70. Epub 2009 Nov 27.
Castro-Rodriguez JA, Rodrigo GJ. A Systematic Review of **Long-Acting β2-Agonists Versus Higher Doses of Inhaled Corticosteroids** in Asthma. Pediatrics. 2012 Sep;130(3):e650-7.
Cates CJ, et al. **Vaccines** for preventing influenza in people with asthma. Cochrane Database Syst Rev. 2004;(2):CD000364. Update of: Cochrane Database Syst Rev. 2000;(4):CD000364.
Cates CJ, Crilly JA, Rowe BH. Holding **chambers (spacers) versus nebulisers** for beta-agonist treatment of acute asthma. Cochrane Database Syst Rev. 2006 Apr 19;(2):CD000052.
Cates CJ, Cates MJ, Lasserson TJ. Regular treatment with **formoterol** for chronic asthma: serious adverse events. Cochrane Database Syst Rev. 2008 Oct 8;(4):CD006923.
Cates CJ, Lasserson TJ. Combination **formoterol and inhaled steroid** versus beta(2)-agonist as relief medication for chronic asthma in adults and children. Cochrane Database Syst Rev. 2009 Jan 21;(1):CD007085. In mild asthma it is not yet known whether patients who use a budesonide/formoterol inhaler for relief of asthma symptoms derive any clinically important benefits. In more severe asthma, one study that enrolled patients who were not controlled on quite high doses of inhaled corticosteroids, and had suffered an exacerbation in the previous year, demonstrated a reduction in the risk of exacerbations that require oral corticosteroids with budesonide/formoterol for maintenance and relief in comparison

with budesonide/formoterol for maintenance and terbutaline or formoterol for relief. The incidence of serious adverse events in children was also less using budesonide/formoterol for maintenance and relief in one study, which similarly enrolled children who were not controlled on medium to high doses of inhaled corticosteroids, and compared to terbutaline relief with an explorative maintenance dose of budesonide/formoterol that is not approved for treatment.

Cates CJ, Lasserson TJ, Jaeschke R. Regular treatment with **formoterol** and inhaled steroids for chronic asthma: serious adverse events. Cochrane Database Syst Rev. 2009 Apr 15;(2):CD006924. It is not possible, from the data in this review, to reassure people with asthma that inhaled corticosteroids with regular formoterol carries no risk of increasing mortality in comparison to inhaled corticosteroids alone as all four deaths occurred among 6,594 people using inhaled corticosteroids with formoterol. On the other hand, we have found no conclusive evidence of harm and there was only one asthma related death registered during over 3,000 patient year observation on formoterol.

Cates CJ, Lasserson TJ, Jaeschke R. Regular treatment with **salmeterol and inhaled steroids** for chronic asthma: serious adverse events. Cochrane Database Syst Rev. 2009 Jul 8;(3):CD006922. No significant differences have been found in fatal or non-fatal serious adverse events in trials in which regular salmeterol has been randomly allocated with inhaled corticosteroids, in comparison to inhaled corticosteroids at the same dose.

Cates CJ, Lasserson TJ. Regular treatment with **formoterol versus** regular treatment with **salmeterol** for chronic asthma: serious adverse events. Cochrane Database Syst Rev. 2009 Oct 7;(4):CD007695.

Cates CJ, Lasserson TJ, Jaeschke R. Regular treatment with **salmeterol and inhaled steroids** for chronic asthma: serious adverse events. Cochrane Database Syst Rev. 2009 Jul 8;(3):CD006922.

Cates CJ, Lasserson TJ. Combination **formoterol and budesonide as maintenance and reliever** therapy versus inhaled steroid maintenance for chronic asthma in adults and children. Cochrane Database Syst Rev. 2009 Apr 15;(2):CD007313.

Cates CJ, Lasserson TJ. Regular treatment with **formoterol** and an inhaled corticosteroid versus regular treatment with **salmeterol** and an inhaled corticosteroid for chronic asthma: serious adverse events. Cochrane Database Syst Rev. 2010 Jan 20;(1):CD007694.

Cates CJ, Rowe BH. Vaccines for preventing **influenza in people with asthma**. Cochrane Database Syst Rev. 2013 Feb 28;2:CD000364. doi: 10.1002/14651858.CD000364.pub4. Uncertainty remains about the degree of protection that vaccination affords against asthma exacerbations that are related to influenza infection. Evidence from more recently published randomised trials of inactivated split-virus influenza vaccination indicates that there is no significant increase in asthma exacerbations immediately after vaccination in adults or children over three years of age.

Cates CJ, Jaeschke R, Schmidt S, et al. Regular treatment with **salmeterol and inhaled steroids for chronic asthma: serious adverse events**. Cochrane Database Syst Rev. 2013 Mar 28;3:CD006922. doi: 10.1002/14651858.CD006922.pub3. We found no statistically significant differences in fatal or non-fatal serious adverse events in trials in which regular salmeterol was randomly allocated with ICS, in comparison to ICS alone at the same dose. Although 13,447 adults and 1862 children have now been included in trials, the frequency of adverse events is too low and the results are too imprecise to confidently rule out a relative increase in all cause mortality or non-fatal adverse events with salmeterol used in conjunction with ICS.

Cates CJ, Karner C. **Combination formoterol and budesonide** as maintenance and reliever therapy versus current best practice (including inhaled steroid maintenance), for chronic asthma in adults and children. Cochrane Database Syst Rev. 2013 Apr 30;4:CD007313. doi: 10.1002/14651858.CD007313.pub3. Single inhaler therapy has now been demonstrated to reduce exacerbations requiring oral corticosteroids against current best practice strategies and against a fixed higher dose of inhaled steroids. The strength of evidence that SiT reduces hospitalisation against these same treatments is weak. There were more discontinuations due to adverse events on SiT compared to current best practice, but no significant differences in serious adverse events.

Cates CJ, Jaeschke R, Schmidt S, et al. Regular treatment with **formoterol and inhaled steroids** for chronic asthma: serious adverse events. Cochrane Database Syst Rev. 2013 Jun 7;6:CD006924. doi: 10.1002/14651858.CD006924.pub3. From the evidence in this review, it is not possible to reassure people with asthma that regular use of inhaled corticosteroids with formoterol carries no risk of increasing mortality in comparison with use of inhaled corticosteroids alone. On the other hand, we have found no conclusive evidence of serious harm, and only one asthma-related death was registered during more than 4200 patient-years of observation with formoterol. In adults, no significant difference in all-cause non-fatal serious adverse events was noted with regular formoterol with inhaled corticosteroids, but a significant reduction in asthma-related serious adverse events was observed in comparison with inhaled corticosteroids alone. In children the number of events was too small, and consequently the results too imprecise, to allow determination of whether the increased risk of all-cause non-fatal serious adverse events found in a previous meta-analysis on regular formoterol alone is abolished by the additional use of inhaled corticosteroids.

Cates CJ, Welsh EJ, Rowe BH. **Holding chambers (spacers) versus nebulisers** for beta-agonist treatment of acute asthma.Cochrane Database Syst Rev. 2013 Sep 13;9:CD000052. Nebuliser delivery produced outcomes that were not significantly better than metered-dose inhalers delivered by spacer in adults or children, in trials where treatments were repeated and titrated to the response of the participant. Spacers may have some advantages compared to nebulisers for children with acute asthma.

Cates CJ, Wieland LS, Oleszczuk M, Kew KM. **Safety of regular formoterol or salmeterol** in adults with asthma: an overview of Cochrane reviews. Cochrane Database of Systematic Reviews 2014, Issue 2. Art. No.: CD010314. DOI: 10.1002/14651858.CD010314.pub2. Available evidence from the reviews of randomised trials cannot definitively rule out an increased risk of fatal serious adverse events when regular formoterol or salmeterol was added to an inhaled corticosteroid (as background or as randomly assigned treatment) in adults or adolescents with asthma.An increase in non-fatal serious adverse events of any cause was found with salmeterol monotherapy, and the same increase cannot be ruled out when formoterol or salmeterol was used in combination with an inhaled corticosteroid, although possible increases are small in absolute terms.However, if the addition of formoterol or salmeterol to an inhaled corticosteroid is found to improve symptomatic control, it is safer to give formoterol or salmeterol in the form of a combination inhaler (recommended by the US Food & Drug Administration (FDA)). This prevents the substitution of LABA for an inhaled corticosteroid if symptom control is improved on LABA.

Cattarelli D, et al. A randomised, double blind, placebo controlled trial of the effect of theophylline in prevention of vasomotor nephropathy in very preterm neonates with respiratory distress syndrome. Arch Dis Child Fetal Neonatal Ed. 2006 Mar;91(2):F80-4. Epub 2005 Oct 4.

Caughey GE, Preiss AK, Vitry AI, et al. Comorbid **Diabetes and COPD: Impact of corticosteroid** use on diabetes complications. Diabetes Care. 2013 Jun 4.

Cazeiro C, Silva C, Mayer S, et al. **Inhaled Corticosteroids and Respiratory Infections in Children** With Asthma: A Meta-analysis. Pediatrics. 2017 Feb 24.

Cazzola M, Matera MG. **Beta-blockers** are safe in patients with chronic obstructive pulmonary disease, but only with caution. Am J Respir Crit Care Med. 2008 Oct 1;178(7):661-2.

Celli B, Decramer M, Leimer I, et al. Cardiovascular Safety of **Tiotropium** in Patients With COPD. Chest. 2009 Jul 10. [Epub ahead of print] Tiotropium was associated with a reduction in the risk of all-cause mortality, cardiovascular mortality and cardiovascular events.

Celli B, Decramer M, Kesten S, et al. **Mortality** in the 4-year trial of tiotropium (**UPLIFT**) in patients with chronic obstructive pulmonary disease. Am J Respir Crit Care Med. 2009 Nov 15;180(10):948-55. Epub 2009 Sep 3.

Cepelis A, Brumpton BM, Malmo V, et al. Associations of **Asthma and Asthma Control With Atrial Fibrillation Risk**: Results From the Nord-Trøndelag Health Study (HUNT). JAMA Cardiol. 2018 Jul 11.

Chan Walter W.; Chiou Eric; Obstein Keith L.; et al. The Efficacy of **Proton Pump Inhibitors** for the **Treatment of Asthma** in Adults: A Meta-analysis. *Arch Intern Med*. 2011;171(7):620-629.

Chandra A, Shim C, Cohen HW, et al. Regular vs **ad-lib albuterol** for patients hospitalized with acute asthma. Chest. 2005 Sep;128(3):1115-20. CONCLUSIONS: In the management of asthma exacerbation, ad-lib administration of albuterol is therapeutically as effective as regular, scheduled administration. This method of drug administration also reduces the total dose of beta-agonists received by the hospitalized patient.

Chandratilleke MG, Carson KV, Picot J,et al. **Physical training for asthma**. Cochrane Database of Systematic Reviews 2012, Issue 5. Art. No.: CD001116. DOI: 10.1002/14651858.CD001116.pub3. This review demonstrated that physical training can improve cardiopulmonary fitness and was well tolerated among people with asthma in the included studies. As such, people with stable asthma should be encouraged to partake in regular exercise training, without fear of symptom exacerbation.

Chang A, Halstead R, Petsky H. **Methylxanthines** for prolonged non-specific cough in children. Cochrane Database Syst Rev. 2005 Jul 20;(3):CD005310.

Chang AB, Clark R, Sloots TP, Stone DG, Petsky HL, Thearle D, Champion AA, Wheeler C, Acworth JP. A **5- versus 3-day course of oral corticosteroids** for children with asthma exacerbations who are not hospitalised: a randomised controlled trial. Med J Aust. 2008 Sep 15;189(6):306-10. A 5-day course of oral prednisolone confers no advantage over a 3-day course for children with asthma exacerbations who are not hospitalised.

Chapman, Kenneth R, McIvor, Andrew. **Asthma that is unresponsive** to usual care. CMAJ 2009 0: cmaj.090089.

Chapman KR, Rennard SI, Dogra A, et al; on behalf of the **INDORSE** Study Investigators. Long-term Safety and Efficacy of **Indacaterol**, a Long-Acting {beta}2-Agonist, in Subjects With COPD: A Randomized, Placebo-Controlled Study. Chest. 2011 Jul;140(1):68-75 (52 weeks)

Chaudhuri R, et al. Effects of smoking cessation on lung function and airway inflammation in smokers with asthma. Am J Respir Crit Care Med. 2006 Jul 15;174(2):127-33. Epub 2006 Apr 27.

Chauhan BF, Ducharme FM. **Anti-leukotriene agents** compared to inhaled corticosteroids in the management of recurrent and/or chronic asthma in adults and children. Cochrane Database Syst Rev. 2012 May 16;5:CD002314. As monotherapy, inhaled corticosteroids display superior efficacy to anti-leukotrienes in adults and children with persistent asthma; the superiority is particularly marked in patients with moderate airway obstruction. On the basis of efficacy, the results support the current guidelines` recommendation that inhaled corticosteroids remain the preferred monotherapy.

Chauhan BF, Chartrand C, Ducharme FM. **Intermittent versus daily inhaled corticosteroids** for persistent asthma in children and adults. Cochrane Database Syst Rev. 2013 Feb 28;2:CD009611. doi: 10.1002/14651858.CD009611.pub3. In children and adults with persistent asthma and in preschool children suspected of persistent asthma, there was low quality evidence that intermittent and daily ICS strategies were similarly effective in the use of rescue oral corticosteroids and the rate of severe adverse health events. The strength of the evidence means that we cannot currently assume equivalence between the two options.. Daily ICS was superior to intermittent ICS in several indicators of lung function, airway inflammation, asthma control and reliever use. Both treatments appeared safe, but a modest growth suppression was associated with daily, compared to intermittent, inhaled budesonide and beclomethasone. Clinicians should carefully weigh the potential benefits and harm of each treatment option, taking into account the unknown long-term (> one year) impact of intermittent therapy on lung growth and lung function decline.

Chauhan BF, Ben Salah R, Ducharme FM. **Addition of anti-leukotriene agents to inhaled corticosteroids** in children with persistent asthma. *Cochrane Database of Systematic Reviews* 2013, Issue 10. Art. No.: CD009585. DOI: 10.1002/14651858.CD009585.pub2. The addition of anti-leukotrienes to ICS is not associatedwith a statistically significant reduction in the need for rescue oral corticosteroids or hospital admission compared to the same or an increased dose of ICS in children and adolescents with mild to moderate asthma.

Chauhan BF, Ducharme FM. Addition to **inhaled corticosteroids of long-acting beta-agonists versus antileukotrienes** for chronic asthma. Cochrane Database Syst Rev 2014;1:CD003137. In adults with asthma that is inadequately controlled by predominantly low-dose ICS with significant bronchodilator reversibility, the addition of LABA to ICS is modestly superior to the addition of LTRA in reducing oral corticosteroid-treated exacerbations, with an absolute reduction of two percentage points. Differences favouring LABA over LTRA as adjunct therapy were observed in lung function and, to a lesser extend, in rescue medication use, symptoms and quality of life. The lower overall withdrawal rate and the higher proportion of participants satisfied with their therapy indirectly favour the combination of LABA + ICS over LTRA + ICS. Evidence showed a slightly increased risk of SAE with LABA compared with LTRA, with an absolute increase of one percentage point. Our findings modestly support the use of a single inhaler for the delivery of both LABA and low- or medium-dose ICS. Because of the paucity of paediatric trials, we are unable to draw firm conclusions about the best adjunct therapy in children.

Chauhan BF, Jeyaraman MM, Singh Mann A, et al. **Addition of antileukotriene agents to inhaled corticosteroids for adults and adolescents with persistent asthma**. Cochrane Database of Systematic Reviews 2017, Issue 3. Art. No.: CD010347. For adolescents and adults with persistent asthma, with suboptimal asthma control with daily use of ICS, the addition of anti-leukotrienes is beneficial for reducing moderate and severe asthma exacerbations and for improving lung function and asthma control compared with the same dose of ICS. We cannot be certain that the addition of anti-leukotrienes is superior, inferior or equivalent to a higher dose of ICS. Scarce available evidence does not support anti-leukotrienes as an ICS sparing agent, and use of LTRAs was not associated with increased risk of withdrawals or adverse effects, with the exception of an increase in serious adverse events when the ICS dose was tapered. Information was insufficient for assessment of mortality.

Checkley, William, West, Keith P., Jr., Wise, Robert A., et al. Maternal **Vitamin A Supplementation and Lung Function** in Offspring. N Engl J Med 2010 362: 1784-1794.

Chen D, Restrepo MI, Fine MJ, et al. Observational study of **inhaled corticosteroids** on outcomes for COPD patients with **pneumonia**. Am J Respir Crit Care Med. 2011 Aug 1;184(3):312-6. For

Chen E, Hayen R, Le V, et al. Neighborhood **Social Conditions, Family Relationships, and Childhood Asthma**. Pediatrics. 2019 Jul 18.

Chen E, Miller GE, Shalowitz MU, et al. **Difficult Family Relationships, Residential Greenspace**, and Childhood Asthma. Pediatrics. 2017 Mar 9.

Chen YZ, et al. Early intervention of recent onset mild persistent asthma in children aged under 11 yrs: the Steroid Treatment As Regular Therapy in early asthma (START) trial. Pediatr Allergy Immunol. 2006 May;17 Suppl 17:7-13.

Chen Z, Salam MT, Alderete TL, et al. Effects of Childhood **Asthma on the Development of Obesity** among School-aged Children. Am J Respir Crit Care Med. 2017 Jan 19.

Cheyne L, Irvin-Sellers MJ, White J. **Tiotropium versus ipratropium** bromide for chronic obstructive pulmonary disease. Cochrane Database Syst Rev. 2013 Sep 16;9:CD009552. This review shows that tiotropium treatment, when compared with ipratropium bromide, was associated with improved lung function, fewer hospital admissions (including those for exacerbations of COPD), fewer exacerbations of COPD and improved quality of life. There were both fewer serious adverse events and disease specific events in the tiotropium group, but no significant difference in deaths with ipratropium bromide when compared to tiotropium. Thus, tiotropium appears to be a reasonable choice (instead of ipratropium bromide) for patients with stable COPD, as proposed in guidelines. We would advise some caution with tiotropium via the Respimat inhaler and suggest waiting for further information from an ongoing head-to-head trial comparing mortality in relation to tiotropium delivery devices and doses.

Cheyne L, Irvin-Sellers MJ, White J. **Tiotropium versus ipratropium bromide for chronic obstructive pulmonary disease**. Cochrane Database Syst Rev. 2015 Sep 22;9:CD009552. This review shows that tiotropium treatment, when compared with ipratropium bromide, was associated with improved lung function, fewer hospital admissions (including those for exacerbations of COPD), fewer exacerbations of COPD and improved quality of life. There were both fewer serious adverse events and disease specific events in the tiotropium group, but no significant difference in deaths with ipratropium bromide when compared to tiotropium. Thus, tiotropium appears to be a reasonable choice (instead of ipratropium bromide) for patients with stable COPD, as proposed in guidelines. A recent large double-blind trial of the two delivery devices found no substantial difference in mortality using 2.5 microg or 5 microg of tiotropium via Respimat in comparison to 18 microg via Handihaler.

Chipps BE, Bacharier LB, Murphy KR, et al. The Asthma Controller Step-down Yardstick. Ann Allergy Asthma Immunol. 2019 Mar;122(3):241-262.e4.

Chipps B, Zeiger RS, Murphy K, et al. Longitudinal validation of the **test for respiratory and asthma control in kids** in pediatric practices (**TRACK**) . Pediatrics. 2011 Mar;127(3):e737-47.

Chiu Y-HM, Coull BA, Cohen S, et al. Prenatal and postnatal **maternal stress** and wheeze in urban children: effect of maternal sensitization. Am J Respir Crit Care Med 2012;186:147–154.

Chong YY, Mak YW, Leung SP, et al. Acceptance and Commitment Therapy for **Parental Management** of Childhood Asthma: An RCT. Pediatrics. 2019 Jan 18.

Chowdhury BA, Seymour SM, Michele TM, Durmowicz AG, Liu D, Rosebraugh CJ. The risks and benefits of **indacaterol**- the FDA's review. N Engl J Med. 2011 Dec 15;365(24):2247-9.

Christiansen SC, Zuraw BL. **Treatment of Hypertension** in Patients with Asthma. N Engl J Med. 2019 Sep 12;381(11):1046-1057.

Chung KF, Wenzel SE, Brozek JL, et al. International **ERS/ATS guidelines** on definition, evaluation and treatment of **severe asthma**. Eur Respir J. 2014 Feb 1;43(2):343-73.

Chung KF. **Dupilumab**: a potential new treatment for severe asthma. Lancet. 2016 Apr 26

Chung KF. Targeting the **interleukin pathway** in the treatment of **asthma**. Lancet. 2015 Sep 12;386(9998):1086-96.

Ciclesonide Alvesco: New drug. Pharmacist's Letter Nov 2006.

Clearie KL, McKinlay L, Williamson PAet al. **Fluticasone/salmeterol** combination confers benefi ts in people with asthma who **smoke**. Chest. 2012;141 (2): 330 -338.

Cohen HA, Blau H, Hoshen M, Batat E, Balicer RD. **Seasonality of Asthma**: A Retrospective Population Study. Pediatrics. 2014 Mar 10.

Comet R, et al. Benefits of low weekly doses of **methotrexate** in steroid-dependent asthmatic patients. A double-blind, randomized, placebo-controlled study. Respir Med. 2005 Aug 12

Connett GJ, Connett LA, Thomas M. Determining the **reasons for poorly controlled asthma in an adolescent**. BMJ. 2019 Jan 21;364:l75.

Corren J, Lemanske RF, Hanania NA, et al. **Lebrikizumab** Treatment in Adults with Asthma. N Engl J Med. 2011 Aug 3.

Corren J, Weinstein S, Janka L, et al. Phase 3 Study of **Reslizumab** in Patients With Poorly Controlled Asthma: Effects Across a Broad Range of Eosinophil Counts. Chest. 2016 Oct;150(4):799-810.

Corren J et al. **Tezepelumab** in adults with uncontrolled asthma. N Engl J Med 2017 Sep 7; 377:936.

Cosio BG, Soriano JB, López-Campos JL, et al; CHAIN Study.. Defining the **Asthma-COPD Overlap Syndrome (ACOS)** in a COPD Cohort. Chest. 2016 Jan;149(1):45-52

Cossette B, Forget A, Beauchesne MF, et al. Impact of **maternal use of asthma-controller therapy on perinatal outcomes**. Thorax. 2013 Apr 13. doi: 10.1136/thoraxjnl-2012-203122.

Covelli H, et al. Absence of electrocardiographic findings and improved function with once-daily **tiotropium** in patients with COPD. Pharmacotherapy. 2005 Winter;25(12):1708-18.
Covvey JR, Johnston BF, Wood F, Boyter AC. Changes to **inhaled corticosteroid dose when initiating combination inhaler** therapy in long-acting β agonist-naïve patients with asthma: a retrospective database analysis. Thorax. 2014 Jan 15.
Cox G, Thomson NC, Rubin AS, et al. AIR Trial Study Group. Asthma control during the year after bronchial **thermoplasty**. N Engl J Med. 2007 Mar 29;356(13):1327-37.
Crider KS, Cordero AM, Qi YP, Mulinare J, Dowling NF, Berry RJ. **Prenatal folic acid and risk of asthma in children**: a systematic review and meta-analysis. Am J Clin Nutr. 2013 Sep 4.
Criner GJ, Bourbeau J, Diekemper RL, et al. **Prevention of Acute Exacerbations of COPD**: American College of Chest Physicians (**ACCP**) and **Canadian Thoracic Society** (**CTS**) Guideline. Chest. 2015 Apr 1;147(4):894-942.
Cronin JJ, McCoy S, Kennedy U, et al. A Randomized Trial of Single-Dose Oral **Dexamethasone Versus Multidose Prednisolone** for Acute Exacerbations of **Asthma** in Children Who Attend the Emergency Department. Ann Emerg Med. 2015 Oct 10.
Cross Keith P, Paul Ronald I, Goldman Ran D.. **Single-dose dexamethasone** for mild-to-moderate asthma exacerbations: Effective, easy, and acceptableCan Fam Physician October 2011 57: 1134-1136
Crossingham I, Evans DJW, Halcovitch NR, Marsden PA. **Stepping down the dose of inhaled corticosteroids for adults with asthma.** Cochrane Database of Systematic Reviews 2017, Issue 2. Art. No.: CD011802. The strength of the evidence is not sufficient to determine whether stepping down the dose of ICS is of net benefit (in terms of fewer adverse effects) or harm (in terms of reduced effectiveness of treatment) for adult patients with well-controlled asthma. A small number of relevant studies and varied outcome measures limited the number of meta-analyses that we could perform. Additional well-designed RCTs of longer duration are needed to inform clinical practice regarding use of a 'stepping down ICS' strategy for patients with wellcontrolled asthma.
Crump, Casey, Winkleby, Marilyn A., Sundquist, Jan, et al. Risk of Asthma in Young Adults Who Were **Born Preterm:** A Swedish National Cohort Study**.** Pediatrics 2011 0: peds.2010-2603
Currie GP, Wedzicha JA. ABC of **chronic obstructive** pulmonary disease. **Acute exacerbations**. BMJ. 2006 Jul 8;333(7558):87-9.
Currie GP, Lee DK, Lipworth BJ. ABC of **chronic obstructive** pulmonary disease. Pharmacological management—**oral** treatment. BMJ. 2006 Jun 24;332(7556):1497-9.
Currie GP, Lipworth BJ. ABC of **chronic obstructive** pulmonary disease Pharmacological management--**inhaled treatment**. BMJ. 2006 Jun 17;332(7555):1439-41.
Currie GP, Douglas JG, Heaney LG. **Difficult to treat asthma** in adults. BMJ. 2009 Feb 24;338:b494. doi: 10.1136/bmj.b494.
Currie GP, Small I, Douglas G. **Long acting β2 agonists** in adult asthma. BMJ. 2013 Aug 6;347:f4662.
D'Urzo AD, Tamari I, Bouchard J, Jhirad R, Jugovic P. A new **spirometry** interpretation **algorithm**. Primary Care Respiratory Alliance of Canada approach. Can Fam Physician 2011;57:1148-52.
D'Urzo AD, Tamari I, Bouchard J, Jhirad R, Jugovic P. Limitations to a **spirometry interpretation algorithm**. Can Fam Physician 2011;57:1153-6.
D'Urzo AD, Wong J. Effectiveness of **omalizumab** in severe persistent asthma under real-life conditions. Can Fam Physician. 2014 Jul;60(7):643-5
Dahl R, et al. EXCEL: A randomised trial comparing **salmeterol/fluticasone** propionate and formoterol/budesonide combinations in adults with persistent asthma. Respir Med. 2006 May 2; [Epub ahead of print] Twice-daily treatment with SFC and FBC over 6 months significantly improved asthma symptoms and lung function in patients with persistent asthma. The rate of exacerbations was significantly reduced over time on both treatments but SFC was found to be significantly superior to FBC in reducing the rate of moderate/severe exacerbations with sustained treatment.
Dahl R, Chung KF, Buhl R, et al. Efficacy of a new once-daily long-acting inhaled beta2- agonist **indacaterol** versus twice-daily formoterol in COPD. Thorax 2010;65:473-9.
Dalhousie Academic Detailing Service Resources: Update on COPD. http://cme.medicine.dal.ca/files/COPD.pdf ; Summary http://cme.medicine.dal.ca/files/COPD%20Summary.pdf
Damgaard AL, Hansen BM, Mathiasen R, et al. **Prematurity and prescription asthma** medication from childhood to young adulthood: a danish national cohort study. PLoS One. 2015 Feb 4;10(2):e0117253.
Daniels JM, Snijders D, de Graaff CS, Vlaspolder F, Jansen HM, Boersma WG. Antibiotics in Addition to Systemic **Corticosteroids for Acute Exacerbations** of COPD. Am J Respir Crit Care Med. 2009 Oct 29.
Davey C, Zoumot Z, Jordan S, et al. **Bronchoscopic lung volume reduction** with endobronchial valves for patients with heterogeneous emphysema and intact interlobar fissures (the BeLieVeR-HIFi study): a randomised controlled trial. Lancet 2015; online June 24.
Dawood Fatimah S., Kamimoto Laurie, D'Mello Tiffany A., et al. and the Emerging Infections Program Network. Children With **Asthma** Hospitalized With Seasonal or Pandemic **Influenza**, 2003–2009. Pediatrics 2011; 128:1 e27-e32; ahead of print June 6, 2011
de Benedictis FM, Bush A. **Corticosteroids in respiratory diseases in children**. Am J Respir Crit Care Med. 2012 Jan 1;185(1):12-23.
de Blic J, Ogorodova L, Klink R, et al. Salmeterol/fluticasone propionate vs. double dose fluticasone propionate on lung function and asthma control in children. Pediatr Allergy Immunol. 2009 Feb 20. [Epub ahead of print] Treatment with SFC 50/100 mug bd compared with twice the steroid dose of FP (200 mug bd), was at least as effective in improving individual clinical outcomes and overall asthma control, in asthmatic children previously uncontrolled on low doses of ICS.
De Boeck K, Vermeulen F, Meyts I, Hutsebaut L, Franckaert D, Proesmans M. Coprescription of **Antibiotics and Asthma** Drugs in Children. Pediatrics 2011;127:1022-6.
De Coster DA, Jones M, Thakrar N. **Beclometasone for chronic obstructive pulmonary disease**. Cochrane Database Syst Rev. 2013 Oct 9;10:CD009769. We found little evidence to suggest that beclometasone is a safer or more effective treatment option for people with COPD when compared with placebo or when used in combination with LABA; when statistically significant differences were found, they mostly were not clinically meaningful or were based on data from only one study. The review was limited by an inability to obtain data from one study and likely publication bias for BDP versus placebo, and by the inclusion of one study only for BDP/LABA versus LABA.
de Jong YP, Uil SM, Grotjohan HP, Postma DS, Kerstjens HA, van den Berg JW. **Oral or IV Prednisolone** in the Treatment of COPD Exacerbations: A Randomized, Controlled, Double-blind Study. Chest. 2007 Dec;132(6):1741-7. Epub 2007 Jul 23. Therapy with oral prednisolone is not inferior to IV treatment in the first 90 days after starting therapy. Oral steroids are as effective as intravenous (IV) steroids for nonsevere exacerbations of chronic obstructive pulmonary disease (COPD). Because they are cheaper and less invasive, oral steroids should be the preferred treatment option. (LOE = 1b)
De Simoni A, Horne R, Fleming L, et al. What do **adolescents with asthma really think about adherence to inhalers**? Insights from a qualitative analysis of a UK online forum. BMJ Open. 2017 Jun 13;7(6):e015245.
de Vries et al. Reported **adverse drug reactions during the use of inhaled steroids** in children with asthma in the Netherlands. Eur J Clin Pharmacol. 2006 May;62(5):343-6. Epub 2006 Apr 1. Alteration of behaviour was the most frequently reported sADR. There are more indications that alterations of behaviour could be a real sADR of ICS. Non-fatal adrenal insufficiency was the only reported possible life threatening sADR. The association of hypertrichosis and teeth abnormalities after ICS in children has not been reported in the literature before.
Decramer M, Celli B, et al. Clinical trial design considerations in assessing long-term functional impacts of tiotropium in COPD: the **UPLIFT trial**.COPD. 2004;1(2):303-12. ?2008

Decramer M, Rutten-van Molken M, et al. Effects of **N-acetylcysteine** on outcomes in COPD (Bronchitis Randomized on NAC Cost-Utility Study, BRONCUS): a randomised placebo-controlled trial. Lancet. 2005 May;365(9470):1552-60. (InfoPOEMs: N-acetylcysteine does not prevent chronic obstructive pulmonary disease lung-function decline or exacerbation. (LOE = 1b))

Decramer M, Celli B, Kesten S, et al. for the **UPLIFT** investigators. Effect of tiotropium on outcomes in patients with **moderate** chronic obstructive pulmonary disease (UPLIFT): a prespecified subgroup analysis of a randomised controlled trial. Lancet. 2009 Aug 27.

Decramer M, Janssens W, Miravitlles M. Chronic obstructive pulmonary disease. Lancet. 2012 Feb 3.

Decramer ML, Chapman KR, Dahl R et al. Once-daily **indacaterol versus tiotropium** for patients with severe chronic obstructive pulmonary disease (**INVIGORATE**): a randomised, blinded, parallel-group study. Lancet Respir Med. 2013 Sep; 1(7): 524-533

Dellon ES, Gonsalves N, Hirano I, Furuta GT, Liacouras CA, Katzka DA. **ACG** clinical guideline: evidenced based approach to the diagnosis and management of **esophageal eosinophilia and eosinophilic esophagitis** (EoE). Am J Gastroenterol. 2013 May;108(5):679-92.

Denlinger LC, King TS, Cardet JC, et al; National Heart Lung and Blood Institute AsthmaNet Investigators. **Vitamin D Supplementation** and the Risk of Colds in Patients with **Asthma**. Am J Respir Crit Care Med. 2015 Nov 5.

Devine RE, McCleary N, et al. **Acid-suppressive medications during pregnancy** and risk of asthma and allergy in children: A systematic review and meta-analysis. J Allergy Clin Immunol. 2016 Dec 20.

Deykin A, et al. Combination Therapy with a **Long-acting {beta}-Agonist and a Leukotriene** Antagonist in Moderate Asthma. Am J Respir Crit Care Med. 2006 Sep 14; [Epub ahead of print] Patients with moderate asthma similar to those we studied should not substitute the combination of an LTRA and a LABA for the combination of ICS and LABA.

Dhuper S, Chandra A, Ahmed A, et al. Efficacy and cost comparisons of bronchodilatator administration between **metered dose inhalers with disposable spacers and nebulizers** for acute asthma treatment. J Emerg Med. 2011 Mar;40(3):247-55.

Dinakar C, Chipps; Section on Allergy & Immunology; Section on Pediatric Pulmonology & Sleep Medicine. **Clinical Tools to Assess Asthma** Control in Children. Pediatrics. 2016 Dec 26.

Divo M, Cote C, de Torres JP, et al.; The **BODE** Collaborative Group. **Comorbidities and risk of mortality** in patients with chronic obstructive pulmonary disease. Am J Respir Crit Care Med 2012;186:155–161.

Doan Q, Shefrin A, Johnson D. **Cost-effectiveness of Metered-Dose Inhalers** for Asthma Exacerbations in the Pediatric Emergency Department. Pediatrics 2011 0: peds.2010-2963

Dodd KE, Mazurek JM. **Pneumococcal Vaccination** Among Adults With Work-related Asthma. Am J Prev Med. 2017 Sep 22.

Dogaru CM, Strippoli MF, et al. **Breastfeeding** and **lung function** at school age: does maternal asthma modify the effect? Am J Respir Crit Care Med 2012;185:874–880.

Doherty S. Prescribe **systemic corticosteroids** in acute asthma. BMJ. 2009 Apr 3;338:b1234. doi: 10.1136/bmj.b1234.

Dolovich MB, Ahrens RC, Hess DR, et al. **Device selection** and outcomes of aerosol therapy: evidence-based guidelines: American College of Chest Physicians/American College of Asthma, Allergy, and Immunology. Chest 2005 Jan;127(1):335-71.

Dombrowski MP, Schatz M; ACOG Committee on Practice Bulletins-Obstetrics. **ACOG practice bulletin**: clinical management guidelines for obstetrician-gynecologists number 90, February 2008: **asthma in pregnancy**. Obstet Gynecol. 2008 Feb;111(2 Pt 1):457-64.

Domingo C, Pomares X, Navarro A, et al. A step down protocol for **omalizumab** treatment in oral corticosteroid-dependent allerci asthma patients. Br J Clin Pharmacol. 2017 Oct 18.

Donaldson GC, Goldring JJ, Wedzicha JA. Influence of **Season on Exacerbation Characteristics in Patients With COPD**. Chest. 2012 Jan;141(1):94-100.

Donaldson GC, Law M, Kowlessar B, et al. **Impact of Prolonged Exacerbation Recovery** in Chronic Obstructive Pulmonary Disease. Am J Respir Crit Care Med. 2015 Jul 7.

Dong Y-H et al. Comparative safety of inhaled medications in patients with chronic obstructive pulmonary disease: systematic review and mixed treatment comparison meta-analysis of randomised controlled trials. Thorax [Epub ahead of print] 6 October 2012; DOI:10.1136/thoraxjnl-2012-201926. Our study provided a comparative safety spectrum for each category of inhaled medications. Tiotropium Soft Mist (Respimat) Inhaler had a higher risk of **mortality** and should be used with caution.

Donohue JF, Fogarty C, Lotvall J, et al; **INHANCE** Study Investigators. Once daily bronchodilators for chronic obstructive pulmonary disease: **indacaterol versus tiotropium**. Am J Respir Crit Care Med 2010;182:155-62.

Dransfield MT, et al.. Use of **beta blockers** & the risk of death in hospitalised patients with acute exacerbations of COPD. Thorax. 2008 Apr;63(4):301-5. Epub 2007 Oct 19. The use of beta blockers by inpatients with exacerbations of COPD is well tolerated and may be associated with reduced mortality. The potential protective effect of beta blockers in this population warrants further study.

Drug & Therapeutics Bulletin: Preventing **exacerbations** in chronic obstructive pulmonary disease. Drug & Therapeutics Bulletin. BMJ 2011;342:doi:10.1136/bmj.c7207 (24 Jan 11)

Drug & Therapeutics Bulletin: Breathing exercises for adults with asthma. Drug Ther Bull. 2015 Nov;53(11):126-9.

Drummond MB, Dasenbrook EC, Pitz MW, et al. Inhaled corticosteroids in patients with stable chronic obstructive pulmonary disease: a systematic review and meta-analysis. JAMA. 2008 Nov 26;300(20):2407-16. Among patients with COPD, ICS therapy does not affect 1-year all-cause mortality. ICS therapy is associated with a higher risk of pneumonia.

Drummond MB, Hansel NN, Connett JE, et al. **Spirometric Predictors** of Lung Function Decline and Mortality in Early COPD. Am J Respir Crit Care Med. 2012 May 3.

Ducharme FM, Lasserson TJ, Cates CJ. Addition to **inhaled corticosteroids of long-acting beta2-agonists versus anti-leukotrienes** for chronic asthma. Cochrane Database Syst Rev. 2011 May 11;5:CD003137. In adults with asthma that is inadequately controlled on low doses of inhaled steroids and showing significant reversibility with beta(2)-agonists, LABA is superior to LTRA in reducing oral steroid treated exacerbations. Differences favouring LABA in lung function, functional status and quality of life scores are generally modest. There is some evidence of increased risk of SAEs with LABA. The findings support the use of a single inhaler for the delivery of LABA and inhaled corticosteroids. We are unable to draw conclusions about which treatment is better as add-on therapy for children.

Ducharme FM, Lemire C, Noya FJ, et al. Preemptive use of **high-dose fluticasone** **750ug bid** **for virus-induced wheezing** in young children. N Engl J Med. 2009 Jan 22;360(4):339-53. In preschool-age children with moderate-to-severe virus-induced wheezing, preemptive treatment with high-dose fluticasone as compared with placebo reduced the use of rescue oral corticosteroids. Treatment with fluticasone was associated with a smaller gain in height and weight. Given the potential for overuse, this preventive approach should not be adopted in clinical practice until long-term adverse effects are clarified.

Ducharme FM, Ni Chroinin M, Greenstone I, et al. **Addition of long-acting beta2-agonists to inhaled corticosteroids** versus same dose inhaled corticosteroids for chronic asthma in adults and children. Cochrane Database Syst Rev. 2010 May 12;5:CD005535.

Ducharme FM. Continuous versus **intermittent inhaled corticosteroids** for mild persistent asthma in children: not too much, not too little. Thorax. 2011 Oct 13.

Ducharme FM, Tse SM, Chauhan B. Diagnosis, management, and prognosis of **preschool wheeze**. Lancet. 2014 May 3;383(9928):1593-604.
Ducharme FM, Dell SD, Radhakrishnan D, et al. Diagnosis and management of asthma in preschoolers: a **Canadian Thoracic Society** and Canadian Paediatric Society position paper. Can Respir J 2015;22:135-43. http://www.respiratoryguidelines.ca/sites/all/files/2015_CTS-CPS_Diagnosis_Management_Asthma_Preschoolers.pdf
Duffy N, Walker P, Diamantea F, et al. Intravenous **aminophylline** in patients admitted to hospital with non-acidotic exacerbations of chronic obstructive pulmonary disease: a prospective randomised controlled trial. Thorax. 2005 Sep;60(9):713-7. Epub 2005 Jun 6.
Dunn RM, Lehman E, Chinchilli VM, et al; NHLBI Asthma Clinical Research Network.. Impact of **Age and Gender on Response** to Asthma Therapy. Am J Respir Crit Care Med. 2015 Jun 11.
Dwan K, Milan SJ, Bax L, et al. **Vilanterol and fluticasone furoate for asthma**. Cochrane Database Syst Rev. 2016 Sep 1;9:CD010758. Some evidence suggests clear advantages for VI/FF, in combination, compared with placebo, particularly for forced expiratory volume in one second (FEV1) and peak expiratory flow; however, the variety of questions addressed in the included studies did not allow review authors to draw firm conclusions. Information was insufficient for assessment of whether once-daily VI/FF was better or worse than twice-daily FP/SAL in terms of efficacy or safety. It is clear that more research is required to reduce the uncertainties that surround interpretation of these studies. It will be necessary for these findings to be replicated in other work before more robust conclusions are revealed. Only five of the 13 included studies provided data on health-related quality of life, and only six recorded asthma exacerbations. Only one study focused on paediatric patients, so no conclusions can be drawn for the paediatric population. More research is needed, particularly in the primary outcome areas selected for this review, so that we can draw firmer conclusions in the next update of this review.
Dwyer-Lindgren L, Bertozzi-Villa A, Stubbs RW, et al. Trends and patterns of differences in **chronic respiratory disease mortality** among US counties, 1980-2014.JAMA. doi:10.1001/jama.2017.11747
Dwyer-Lindgren L, et al. **Trends and Patterns** of Differences in Chronic Respiratory Disease **Mortality** Among US Counties, 1980-2014. JAMA. 2017 Sep 26;318(12):1136-1149.
Dzierba AL, Jelic S. Chronic obstructive pulmonary disease in the **elderly**: an update on pharmacological management. Drugs Aging. 2009;26(6):447-56.
Ebmeier S, Thayabaran D, et al. Trends I international **asthma mortality**: analysis of data from the WHO Mortality Database from 46 countries (1993-2012). Lancet. 2017 Aug 7.
Eder W, Ege MJ, von Mutius E. The **asthma epidemic**. N Engl J Med. 2006 Nov 23;355(21):2226-35.
Effing T, Kerstjens H, van der Valk P, et al. (Cost)-effectiveness of **self-treatment** of exacerbations on the severity of exacerbations in patients with COPD: the COPE II study. Thorax. 2009 Nov;64(11):956-62. Epub 2009 Sep 6.
Ege MJ, Mayer M, Normand AC, et al. GABRIELA Transregio 22 Study Group. **Exposure to environmental microorganisms** and childhood asthma. N Engl J Med. 2011 Feb 24;364(8):701-9.
Ehteshami-Afshar S, FitzGerald JM. **Asthma patient education**, the overlooked aspect of disease management. Can J Respir Crit Care Sleep Med 2017;1(1):43-5.
Eisner MD, Yegin A, Trzaskoma B. Severity of asthma (SOA) score predicts clinical outcomes in patients with moderate to severe persistent asthma. Chest. 2012 Jan;141(1):58-65.
Eltonsy S, Forget A, Beauchesne MF, Blais L. Risk of **congenital m**alformations for asthmatic pregnant women using a long- acting β-agonist and inhaled corticosteroid combination versus higher-dose inhaled corticosteroid monotherapy. J Allergy Clin Immunol. 2015 Jan;135(1):123-30. This study found no difference in the risk of major congenital malformations in infants born to asthmatic pregnant women treated with either a long-acting beta2-agonist (LABA) plus inhaled corticosteroids (ICS) or ICS monotherapy at higher doses. (LOE = 2b)
Enriquez R, et al. Cessation of asthma medication in early **pregnancy**. Am J Obstet Gynecol. 2006 Jul;195(1):149-53. Epub 2006 May 2.
Erin EM, et al. The Effects of Monoclonal Antibody Directed against Tumor Necrosis Factor-{alpha} (**infliximab**)in Asthma. Am J Respir Crit Care Med. 2006 Oct 1;174(7):753-62.
Ermers MJ, Rovers MM, van Woensel JB, Kimpen JL, Bont LJ; RSV Corticosteroid Study Group. The effect of high dose inhaled corticosteroids on wheeze in infants after **respiratory syncytial virus** infection: randomised double blind placebo controlled trial. BMJ. 2009 Mar 31;338:b897. doi: 10.1136/bmj.b897.
Ernst P, et al. Canadian Asthma Guideline Group. Safety and effectiveness of **long-acting inhaled beta**-agonist bronchodilators when taken with inhaled corticosteroids. Ann Intern Med. 2006 Nov 7;145(9):692-4.
Ernst P, Gonzalez AV, Brassard P, Suissa S. Inhaled corticosteroid use in **chronic obstructive pulmonary disease** and the risk of hospitalization for **pneumonia**. Am J Respir Crit Care Med. 2007 Jul 15;176(2):162-6. Epub 2007 Mar 30. The use of inhaled corticosteroids is associated with an excess risk of pneumonia hospitalization and of pneumonia hospitalization followed by death within 30 days, among elderly patients with COPD. (InfoPOEMs: In this well-conducted case-control study, elderly patients with chronic obstructive pulmonary disease (COPD) hospitalized for pneumonia were more likely to have been prescribed inhaled corticosteroids. Even though there was a dose response, we still cannot ascertain if this was cause or effect.)
Erpenbeck VJ, Popov TA, Miller D, et al. The oral **CRTh2 antagonist QAW039 (fevipiprant**): A phase II study in uncontrolled allergic asthma. Pulm Pharmacol Ther. 2016 Aug;39:54-63.
Esposito-Festen J, et al. Aerosol Therapy by Pressured Metered-Dose Inhaler-**Spacer** in Sleeping Young Children: To Do or Not to Do? Chest. 2006 Aug;130(2):487-492.
Esquivel A, Busse WW, et al. Effects of **Omalizumab** on Rhinovirus Infections, Illnesses, and Exacerbations of Asthma. Am J Respir Crit Care Med. 2017 Oct 15;196(8):985-992.
Eurich DT, Lee C, Marrie TJ, Majumdar SR. **Inhaled corticosteroids and risk of recurrent pneumonia**: a population-based, nested case-control study. Clin Infect Dis. 2013 Oct;57(8):1138-44.
Evensen AE. **Management of COPD Exacerbations**. Am Fam Physician. 2010 Mar 1;81(5):607-13.
Fabbri LM, Calverley PM, Izquierdo-Alonso JL, et al.; M2-127 and M2-128 study groups. **Roflumilast** in moderate-to-severe chronic obstructive pulmonary disease treated with longacting bronchodilators: two randomised clinical trials. Lancet. 2009 Aug 29;374(9691):695-703.
Fahy JV, Locksley RM. **Making Asthma Crystal Clear**. N Engl J Med. 2019 Aug 29;381(9):882-884.
Falk NP, Hughes SW, Rodgers B. **Medications for Chronic Asthma**. Am Fam Physician. 2016;94(6):454-462.
Fall T, Lundholm C, Örtqvist AK, et al. Early **Exposure to Dogs and Farm Animals** and the Risk of Childhood Asthma. JAMA Pediatr. 2015 Nov 2;169(11):e153219.
Fan VS, et al. A **comprehensive care management program** (CCMP) to prevent **chronic obstructive pulmonary disease** hospitalizations. A randomized, controlled trial. Ann Intern Med. 2012;156:673-83. (had an unexpected excess mortality in CCMP group)
Fanta CH. **Asthma**.N Engl J Med. 2009 Mar 5;360(10):1002-14.
Farber HJ. Point: Is **escalation of the inhaled corticosteroid dose** appropriate for acute loss of asthma control in an attempt to reduce need for oral corticosteroids in children? Yes. Chest. 2016 Jul 4.
Farber H, Silveira F, Vicere D, et al. **Oral corticosteroid prescribing for children with asthma** in a **Medicaid** managed care program. Pediatrics. 2017;139(5):e20164146.

Farley M, Ryan P, Lynfield R, et al. Emerging Infections Program Network. Children with asthma hospitalized with **seasonal or pandemic influenza**, 2003-2009. Pediatrics. 2011 Jul;128(1):e27-32.

Farne HA;Wilson A;Powell C;Bax L;Milan SJ. **Anti-IL5 therapies for asthma**. Cochrane Database Syst Rev. 2017 Sep 21;9:CD010834. Overall our study supports the use of anti-IL-5 treatments as an adjunct to standard of care in people with severe eosinophilic asthma and poor control. These treatments roughly halve the rate of asthma exacerbations in this population. There is limited evidence for improved HRQoL scores and lung function, which may not meet clinically detectable levels. There were no safety concerns regarding mepolizumab or reslizumab, and no excess serious adverse events with benralizumab, although there remains a question over adverse events significant enough to prompt discontinuation.

FDA Mar/15 is warning consumers **not** to rely on asthma products labeled as **homeopathic** that are sold over-the-counter (OTC). These products have not been evaluated by the FDA for safety and effectiveness.

FDA Dec/17: most prominent warning, the **Boxed Warning**, about asthma-related death has been **removed from the drug labels of medicines that contain both an ICS and LABA**. A FDA review of four large clinical safety trials shows that treating asthma with long-acting beta agonists (LABAs) in combination with inhaled corticosteroids (ICS) does not result in significantly more serious asthma-related side effects than treatment with ICS alone. A description of the four trials is now also included in the Warnings and Precautions section of the drug labels. These trials showed that LABAs, when used with ICS, did not significantly increase the risk of asthma-related hospitalizations, the need to insert a breathing tube known as intubation, or asthma-related deaths, compared to ICS alone.

Feary J, Pinnock H, Cullinan P. **Occupational asthma**. BMJ. 2016 Jun 3;353:i2658.

Federman AD, O'Conor R, Mindlis I, et al. Effect of a **Self-management Support Intervention** on Asthma Outcomes in Older Adults: The SAMBA Study Randomized Clinical Trial. JAMAInternMed. 2019 Jun 10.

Ferguson GT, Calverley PM, Anderson JA, et al. Prevalence and Progression of **Osteoporosis** in Patients With COPD. Results From TORCH. Chest. 2009 Jul 6. [Epub ahead of print] In the **TORCH** study, no significant effect on BMD was detected for inhaled corticosteroid therapy compared with placebo.

Ferreira IM, Brooks D, White J, et al. **Nutritional supplementation** for stable chronic obstructive pulmonary disease. Cochrane Database Syst Rev. 2012 Dec 12;12:CD000998. doi: 10.1002/14651858.CD000998.pub3. We found moderate-quality evidence that nutritional supplementation promotes significant weight gain among patients with COPD, especially if malnourished. Nourished patients may not respond to the same degree to supplemental feeding.

Feuillet-Dassonval C, et al. [Written asthma **action plans**: a useful tool for self-management] Arch Pediatr. 2005 Dec;12(12):1788-96. Epub 2005 Aug 26.

Fiks AG, Mayne SL, Karavite DJ, et al. Parent-Reported Outcomes of a **Shared Decision-Making Portal** in Asthma: A Practice-Based RCT. Pediatrics. 2015 Mar 9.

Fisher AJ, Yadegarfar ME, Collerton J, et al. **Respiratory health** and disease in a UK population-based cohort of 85 year olds: The **Newcastle 85+ Study**. Thorax. 2016 Jan 5.

FitzGerald JM, et al. Asthma control in Canada remains **suboptimal**: the Reality of Asthma Control (**TRAC**) study. Can Respir J. 2006 Jul-Aug;13(5):253-9.

FitzGerald JM, et al. Canadian Asthma Exacerbation Study Group. **Doubling the dose of budesonide** vs maintenance treatment in asthma exacerbations. Thorax. 2004Jul;59(7):550-6.

FitzGerald JM, Boulet LP, Follows RM. The **CONCEPT** trial: a 1-year, multicenter, randomized,double-blind, double-dummy comparison of a stable dosing regimen of Salmeterol/fluticasone propionate with an adjustable maintenance dosing regimen of formoterol/budesonide in adults with persistent asthma. Clin Ther. 2005 Apr;27(4):393-406. CONCLUSIONS: In this adult population with persistent asthma, stable dosing of SAL/FP 50/250 microg BID resulted in significantly greater increases in symptom-free days, days free of rescue medication, and morning PEE, as well as almost halving the exacerbation rate, compared with AMD of FOR/BUD 6/200 microg. The results suggest that there is a minimum daily amount of maintenance therapy necessary to prevent exacerbations in adults with persistent asthma.

FitzGerald JM, Bleecker ER, Nair P, et al. **Benralizumab**, an anti-interleukin-5 receptor monoclonal antibody, as add-on treatment for patients with severe, uncontrolled, eosinophilic asthma (CALIMA): a randomised, double-blind, placebo-controlled phase 3 trial. Lancet 2016; online Sept 5.

FitzGerald JM, Bleecker ER, Menzies-Gow A, et al. Predictors of enhanced response with **benralizumab** for patients with severe asthma: pooled analysis of the **SIROCCO** and **CALIMA** studies. Lancet Respir Med 2017; online Sept 11.

FitzGerald JM, Lemiere C, Lougheed MD, et al. Recog**nition and management of severe asthma: a Canadian Thoracic Society** position statement. Can J Resp Crit Care Sleep Med 2017;1:199-221 (accessed December 15, 2017).

Font-Ribera L et al. **Swimming pool attendance, asthma, allergies, and lung function** in the Avon Longitudinal Study of Parents and Children cohort. Am J Respir Crit Care Med 2011 Mar 1; 183:582.

Ford PA, Durham AL, Russell RE, et al. Treatment effects of **low dose theophylline combined with an inhaled corticosteroid** in COPD. Chest. 2010 Mar 18.

Ford ES, Mannino DM, Zhao G et al. Changes in **Mortality Among US Adults With COPD** in Two National Cohorts Recruited From 1971-1975 and 1988-1994. Chest. 2012 Jan;141(1):101-10.

Foresi A, Morelli MC, Catena E. Low-dose budesonide with the addition of an increased dose during exacerbations is effective in long-term asthma control. On behalf of the Italian Study Group. Chest. 2000 Feb;117(2):440-6. This study demonstrates that when patients with moderate asthma had reached a stable clinical condition with a high dose of budesonide, a low dose of budesonide (200 microg/d) is as effective as the standard dose (800 microg/d) in the control of symptoms and lung function over a period of several months. Furthermore, results showed that the addition of inhaled budesonide (800 microg/d) at onset of an asthmatic exacerbation has a beneficial clinical effect.

França-Pinto A, Mendes FA, de Carvalho-Pinto RM, et al. **Aerobic training** decreases bronchial hyperresponsiveness and systemic inflammation in patients with moderate or severe asthma: a randomised controlled trial. Thorax. 2015 Jun 10.

Franciosi LG, Diamant Z, Banner KH et al. Efficacy and safety of **RPL554**, a dual PDE3 and PDE4 inhibitor, in healthy volunteers and in patients with asthma or chronic obstructive pulmonary disease: findings from four clinical trials. Lancet Respir Med. 2013 Nov;1(9):714-727

Frank PI, Morris JA, Hazell ML, Linehan MF, Frank TL. Long term prognosis in **preschool children with wheeze**: longitudinal postal questionnaire study 1993-2004. BMJ. 2008 Jun 21;336(7658):1423-6. Epub 2008 Jun 16. Using two simple predictive factors (baseline parent reported exercise induced wheeze and a history of atopic disorders), it is possible to estimate the likelihood of future asthma in children presenting with preschool wheeze. The absence of baseline exercise induced wheeze and a history of atopic disorders reduces the likelihood of subsequent asthma by a factor of five.

Frew AJ. **Sublingual immunotherapy**. N Engl J Med. 2008 May 22;358(21):2259-64. (Grass pollen sl tabs -Grazax is available in Europe)

Friedman BC, Goldman RD. **Influenza vaccination for children with asthma**. Can Fam Physician. 2010 Nov;56(11):1137-9.

Fuhr R, Magnussen H, et al. Efficacy of **Aclidinium Bromide** 400 µg Twice Daily Compared With Placebo and Tiotropium in Patients With Moderate to Severe COPD. Chest. 2012 Mar;141(3):745-52.

Fung V, Graetz I, Galbraith A, et al. **Financial Barriers** to Care Among Low-Income Children With **Asthma**: Health Care Reform Implications. JAMA Pediatr. 2014 May 19.

Furuta GT, Katzka DA. **Eosinophilic Esophagitis**. N Engl J Med. 2015 Oct 22;373(17):1640-8.

Gade EJ, Thomsen S, Lindenberg S, et al. **Asthma affects time to pregnancy and fertility**: a register-based twin study. Eur Respir J. 2013 Nov 14.

Gade EJ, Thomsen SF, Lindenberg S, et al. **Fertility** outcomes in **asthma**: a clinical study of 245 women with unexplained infertility. Eur Respir J. 2016 Feb 11.

Gadomski AM, Scribani MB. **Bronchodilators for bronchiolitis**. Cochrane Database of Systematic Reviews 2014, Issue 6. Art. No.: CD001266. DOI: 10.1002/14651858.CD001266.pub4. Bronchodilators such as albuterol or salbutamol do not improve oxygen saturation, do not reduce hospital admission after outpatient treatment, do not shorten the duration of hospitalization and do not reduce the time to resolution of illness at home. Given the adverse side effects and the expense associated with these treatments

bronchodilators are not effective in the routine management of bronchiolitis.
Gaebel K, Blackhouse G, Robertson D, Xie F, Assasi N, McIvor A, Hernandez P, Goeree R. Triple Therapy for Moderate-to-Severe Chronic Obstructive Pulmonary Disease [Internet]. Ottawa: Canadian Agency for Drugs and Technologies in Health; 2010 (CADTH technology report; no. 127). Available:http://www.cadth.ca/index.php/en/hta/reports-publications/search/publication/000
Gagné M, Boulet LP, Pérez N, et al. Patient-reported outcome instruments that evaluate **adherence behaviours in adults with asthma**: a systematic review of measurement properties. Br J Clin Pharmacol. 2018 Apr 30.
Garbe PL, Callahan DB, Lu PJ, Euler GL. First things first: protecting children with asthma from **infection with influenza**. Am J Respir Crit Care Med. 2012 Jun 15;185(12):i-ii.
Garcia E, Berhane KT, Islam T, et al. Association of **changes in air quality with incident asthma** in children in California, 1993-2014 [May 21, 2019]. JAMA. doi:10.1101/jama.2019.5357
Garne E, Vinkel Hansen A, Morris J, et al. Risk of **congenital anomalies after exposure to asthma medication in the first trimester of pregnancy** - a cohort linkage study. BJOG. 2016 May 12.
Gatheral TL, Rushton A, Evans DJ, et al. **Personalised asthma action plans** for adults with asthma. Cochrane Database Syst Rev. 2017 Apr 10;4:CD011859. Analysis of available studies was limited by variable reporting of primary and secondary outcomes; therefore, it is difficult to draw firm conclusions related to the effectiveness of PAAPs in the management of adult asthma. We found no evidence from randomised controlled trials of additional benefit or harm associated with use of PAAP versus no PAAP, or PAAP plus education versus education alone, but we considered the quality of the evidence to be low or very low, meaning that we cannot be confident in the magnitude or direction of reported treatment effects. In the context of this caveat, we found no observable effect on the primary outcomes of hospital attendance with an asthma exacerbation, asthma symptom scores or adverse events. We recommend further research with a particular focus on key patient-relevant outcomes, including exacerbation frequency and quality of life, in a broad spectrum of adults, including those over 60 years of age.
Gauvreau GM, O'Byrne PM, Boulet L-P, et al. Effects of an **anti-TSLP antibody** on allergen-induced asthmatic responses. N Engl J Med. DOI: 10.1056/NEJMoa1402895.
GBD 2015 Chronic Respiratory Disease Collaborators. Global, regional, and national deaths, prevalence, disability-adjusted life years, and years lived with disability for **chronic obstructive pulmonary disease** and **asthma**, 1990–2015: a systematic analysis for the Global Burden of Disease Study 2015. Lancet Respir Med 2017; online August 16.
Geake JB, Dabscheck EJ,Wood-Baker R, Cates CJ. **Indacaterol**, a once-daily beta2-agonist, versus **twice-daily beta2-agonists or placebo for chronic obstructive pulmonary disease**. Cochrane Database of Systematic Reviews 2015, Issue 1. Art. No.: CD010139. DOI: 10.1002/14651858.CD010139.pub2. For patients with stable COPD, use of indacaterol versus placebo results in statistically significant and clinically meaningful improvements in lung function and quality of life. The clinical benefit for lung function is at least as good as that seen with twice-daily long acting beta2-agonists. The comparative effect on quality of life remains uncertain, as important differences cannot be excluded.
Gershon Andrea S.; Wang Chengning; Wilton AS.; et al. **Trends in Chronic Obstructive Pulmonary Disease Prevalence, Incidence, and Mortality** in Ontario, Canada, 1996 to 2007: A Population-Based Study. Arch Intern Med. 2010;170(6):560-565.
Gershon Andrea, Croxford Ruth, To Teresa, et al. Comparison of Inhaled **Long-Acting β-Agonist and Anticholinergic** Effectiveness in Older Patients With Chronic Obstructive Pulmonary Disease: A Cohort Study. *Ann Intern Med* May 3, 2011 154:583-592; doi:10.1059/0003-4819-154-9-201105030-00003.
Gershon AS, Warner L, Cascagnette P, Victor JC, To T. **Lifetime risk of developing chronic obstructive pulmonary disease**: a longitudinal population study. Lancet. 2011 Sep 10;378(9795):991-6.
Gershon A, Croxford R, Calzavara A, et al. **Cardiovascular Safety of Inhaled Long-Acting Bronchodilators** in Individuals With Chronic Obstructive Pulmonary Disease. JAMA Intern Med. 2013 May 20:1-9.
Gershon AS, Campitelli MA, Croxford R, et al. **Combination long-acting β-agonists and inhaled corticosteroids** compared with **long-acting β-agonists alone** in older adults with chronic obstructive pulmonary disease. JAMA. doi:10.1001/jama.2014.11432.
Gibson PG, Powell H, Coughlan J, et al. **Self-management** education and regular practitioner review for adults with asthma. Cochrane Database Syst Rev. 2003;(1):CD001117.
Gibson PG, McDonald VM, Marks GB. **Asthma in older adults.** Lancet. 2010 Sep 4;376(9743):803-13.
Gibson PG, Yang IA, Upham JW, et al. Effect of **azithromycin on asthma exacerbations** and quality of life in adults with persistent uncontrolled asthma (**AMAZES**): a randomised, double-blind, placebo-controlled trial. Lancet 2017; online July 4.
Gildea TR, Khatri SB, Castro M. **Bronchial thermoplasty**: a new treatment for severe refractory asthma. Cleve Clin J Med 2011; 78:477–485.
Gionfriddo MR, Hagan JB, Rank MA. Why and how to **step down chronic asthma drugs**. BMJ. 2017 Oct 16;359:j4438.
Global Initiative for Asthma (**GINA**). Global strategy for asthma management and prevention. Vancouver (WA): Global Initiative for Asthma (GINA); **2011**. http://www.ginasthma.org/uploads/users/files/GINA_Report2011_May4.pdf
Global Initiative for Asthma. (**GINA**). 2016 Pocket Guide for Asthma Management and Prevention. http://ginasthma.org/2016-pocket-guide-for-asthma-management-and-prevention/ Accessed Sept 6, 2016.
Gøtzsche PC, Johansen HK. **Intravenous alpha-1 antitrypsin** augmentation therapy for treating patients with alpha-1 antitrypsin deficiency and lung disease. Cochrane Database of Systematic Reviews 2010, Issue 7. Art. No.: CD007851. DOI: 10.1002/14651858.CD007851.pub2. Augmentation therapy with alpha-1 antitrypsin cannot be recommended, in view of the lack of evidence of clinical benefit and the cost of treatment.
Goldbart AD, Greenberg-Dotan S, Tal A. **Montelukast** for Children With Obstructive **Sleep Apnea**: A Double-blind, Placebo-Controlled Study. Pediatrics. 2012 Aug 6.
Goldbloom EB, Mokashi A, Cummings EA, et al. **Symptomatic adrenal suppression among children** in **Canada**. Arch Dis Child. 2016 Dec 19.
Goldie MH, Brightling CE. **Asthma in pregnancy**. The Obstetrician & Gynaecologist 2013;15:241–5.
Goyal NK, Fiks AG, Lorch SA. Association of **late-preterm birth with asthma** in young children: practice-based study. Pediatrics. 2011 Oct;128(4):e830-8.
Graeme P Currie, Graham S Devereux, Daniel K C Lee, and Jon G Ayres. Recent developments in asthma management. BMJ, Mar 2005; 330: 585 - 589.
Grainge CL, Lau LCK, Ward JA, et al. Effect of **bronchoconstriction on airway remodeling** in asthma. N Engl J Med 2011; 364:2006-15.
Granell R, Henderson AJ, Evans DM, et al. Effects of **BMI, Fat Mass, and Lean Mass on Asthma** in Childhood: A Mendelian Randomization Study. PLoS Med. 2014 Jul 1;11(7):e1001669.
Granger R, et al. Injectable vaccines for preventing **pneumococcal** infection in patients with COPD. Cochrane Database Syst Rev. 2006 Oct 18;(4):CD001390. There is no evidence from randomised controlled trials that injectable pneumococcal vaccination in persons with COPD has a significant impact on morbidity or mortality. Further large randomised controlled trials would be needed to ascertain if the small benefits suggested by individual studies are real.
Gray A, Goodacre S, Cohen J, Braidburn et al. The 3mg trial: a randomised controlled trial of **intravenous or nebulised magnesium** sulphate versus placebo in adults with severe acute asthma. Emerg Med J. 2013 Oct;30(10):866.
Gray MP, Keeney GE, Grahl MJ et al. Improving Guideline-Based Care of **Acute Asthma in a Pediatric Emergency Department**. Pediatrics.2016;138(5):e20153339
Gray N, Howard A, Zhu J, et al. Association Between **Inhaled Corticosteroid Use and Bone Fracture in Children With Asthma**. JAMA Pediatr. 2017 Nov 13.
Green RH, et al. A randomised comparison of the effects of asthma treatment given in addition to inhaled corticosteroids on airway inflammation & airway responsiveness. Eur Respir J. 2006 Feb 2.
Greening NJ, Williams JEA, Hussain SF, Harvey-Dunstan T, Bankart MJ, Chaplin EJ, et al. An **early rehabilitation** intervention to enhance recovery during hospital admission for an **exacerbation of chronic respiratory disease**: randomised controlled trial. BMJ 2014;349:g4315.
Griffiths B, Ducharme FM. **Combined inhaled anticholinergics and short-acting beta-agonists** for initial treatment of acute asthma in children. Cochrane Database Syst Rev. 2013 Aug 21;8:CD000060. Children with an asthma exacerbation experience a lower risk of admission to hospital if they are treated with the combination of inhaled SABAs plus anticholinergic versus SABA alone. They also experience a greater improvement in lung function and less risk of nausea and tremor. Within this group, the findings suggested, but did not prove, the possibility of an effect modification, where intensity of anticholinergic treatment and asthma severity, could be associated with greater benefit.Further research is required to identify the characteristics of children that may benefit from anticholinergic use

Gross NJ, Barnes PJ. **New Therapies** for Asthma and COPD. Am J Respir Crit Care Med. 2016 Dec 6.
Grove A, Lipworth BJ. Bronchodilator subsensitivity to salbutamol after twice daily salmeterol in asthmatic patients. Lancet. 1995 Jul 22;346(8969):201-6.
Guarnieri M, Balmes JR. **Outdoor air pollution** and asthma. Lancet. 2014 May 3;383(9928):1581-92.
Guerrera M. et al. Therapeutic Uses of **Magnesium**. Am Fam Physician. 2009; 80(1):157-162.
Guilbert TW, et al. Long-term inhaled **corticosteroids in preschool children** at high risk for asthma. N Engl J Med. 2006 May 11;354(19):1985-97. In preschool children at high risk for asthma, two years of inhaled-corticosteroid therapy did not change the development of asthma symptoms or lung function during a third, treatment-free year. (fluticasone 88ug bid)
Guilleminault L, Carré P, Beau-Salinas F, et al. Asthma **Unmasked With Tumor Necrosis Factor-{alpha}-Blocking Drugs**. Chest. 2011 Oct;140(4):1068-71.
Guirguis LM. Assessing the knowledge to practice gap: The **asthma practices of community pharmacists**. Can Pharm J (Ott). 2017 Nov 20;151(1):62-70.
Gupta S, Goodridge D, Pakhalé S, et al. **Choosing Wisely**: the Canadian Thoracic Society's list of **six things that physicians and patients should question**. Can J Respir Crit Care Sleep Med 2017;1(2):51-64. www.tandfonline.com/doi/full/10.1080/24745332.2017.1331666 (accessed September 20, 2017).
Haarman MG, van Hunsel F, de Vries TW. **Adverse drug reactions of montelukast** in children and adults. Pharmacol Res Perspect. 2017 Oct;5(5).
Halterman JS, Fagnano M, Tremblay PJ, et al. Prompting Asthma Intervention in Rochester-**Uniting Parents and Providers(PAIR-UP):** A Randomized Trial. JAMA Pediatr. 2014 Oct 6;168(10)
Hardy J, Baggott C, Fingleton J, et al. **Budesonide-formoterol** reliever therapy versus maintenance **budesonide plus terbutaline** reliever therapy in adults with mild to moderate asthma (PRACTICAL): a 52-week, open-label, multicentre, superiority, randomised controlled trial. Lancet. 2019 Aug 23.
Hasegawa K, Tsugawa Y, Brown DF, Camargo CA Jr. **Childhood Asthma Hospitalizations** in the United States, 2000-2009. J Pediatr. 2013 Jun 12.
Hasegawa K, Tsugawa Y, Chang Y, et al. Risk of an **asthma exacerbation after bariatric surgery** in adults. J Allergy Clin Immunol. 2015 Feb 7.
Hahn PY, Morgenthaler TY, Lim KG. Use of **exhaled nitric oxide** in predicting response to **inhaled corticosteroids for chronic cough**. Mayo Clin Proc. 2007 Nov;82(11):1350-5.
Haidl P, Schmidt F, Wiese C, Koehler D. Peak inspiratory flow rate after **methacholine challenge** in asthmatic patients and its impact on the effect of **formoterol** via different inhalers. J Aerosol Med. 2006 Fall;19(3):364-71. If patients fail to generate a PIMF of 30 l/min, 6 microg formoterol via Turbuhaler may provide inadequate relief in a severe asthma attack.
Haland G, et al. ORAACLE. Reduced **lung function** at birth and the risk of asthma at **10 years** of age. N Engl J Med. 2006 Oct 19;355(16):1682-9. Reduced lung function at birth is associated with an increased risk of asthma by 10 years of age. For some measures of lung mechanics, a reading below the median at birth was also associated with severe bronchial hyperresponsiveness (9.1% v 4.9%, P = 0.05) and use of inhaled corticosteroids at 10 years (5.9% v 2.4%, P = 0.02).
Hall SC, Agrawal DK. **Vitamin D** and Bronchial Asthma: An Overview of Data From the Past 5 Years. Clin Ther. 2017 Apr 24.
Halterman JS, et al. Improved preventive care for asthma: a randomized trial of **clinician prompting** in pediatric offices. Arch Pediatr Adolesc Med. 2006 Oct;160(10):1018-25.
Halterman Jill S.; Szilagyi Peter G.; Fisher Susan G.; et al. Randomized Controlled Trial to Improve Care for Urban Children With Asthma: Results of the **School-Based Asthma Therapy Trial**. Arch Pediatr Adolesc Med. 2011;165(3):262-268.
Halterman JS, et al. Effect of the **School-Based Telemedicine** Enhanced Asthma Management (**SB-TEAM**) Program on Asthma Morbidity: A Randomized Clinical Trial. JAMA Pediatr. 2018 Jan 8:e174938.
Hamelmann E, Bateman ED, et al. **Tiotropium** add-on therapy in adolescents with moderate **asthma**: A 1-year randomized controlled trial. J Allergy Clin Immunol. 2016 Mar 5.
Han MK, Tayob N, Murray S, et al. Predictors of chronic obstructive pulmonary disease exacerbation reduction in response to daily **azithromycin** therapy. Am J Respir Crit Care Med. 2014 Jun 15;189(12):1503-8.
Hao Q, Lu Z, Dong BR, Huang CQ, Wu T. **Probiotics for preventing acute upper respiratory tract infections**. Cochrane Database of Systematic Reviews 2011, Issue 9. Art. No.: CD006895. DOI: 10.1002/14651858.CD006895.pub2. Probiotics were better than placebo in reducing the number of participants experiencing episodes of acute URTIs, the rate ratio of episodes of acute URTI and reducing antibiotic use. This indicates that probiotics may be more beneficial than placebo for preventing acute URTIs.
Hall KK, Petsky HL, Chang AB, O'Grady KF. Caseworker-assigned **discharge plans to prevent hospital readmission for acute exacerbations in children with chronic respiratory illness**. Cochrane Database Syst Rev. 2018 Nov 2;11:CD012315.
Hanania NA., Alpan O, Hamilos DL., et al. **Omalizumab in Severe Allergic Asthma** Inadequately Controlled With Standard Therapy: A Randomized Trial. *Ann Intern Med* May 3, 2011 154:573-582.
Harris KM, Kneale D, Lasserson TJ, et al. School-based **self-management interventions for asthma in children and adolescents**: a mixed methods systematic review. Cochrane Database Syst Rev. 2019 Jan 28;1:CD011651. School-based asthma self-management interventions probably reduce hospital admission and may slightly reduce ED attendance, although their impact on school attendance could not be measured reliably. They may also reduce the number of days where children experience asthma symptoms, and probably lead to small improvements in asthma-related quality of life. Many of the studies tested the intervention in younger children from socially disadvantaged populations. Interventions that had a theoretical framework, engaged parents and were run outside of children's free time were associated with successful implementation.
Harrison TW, et al. **Doubling the dose of inhaled corticosteroid** to prevent asthma exacerbations: randomised controlled trial. Lancet. 2004 Jan 24;363(9405):271-5.
Harrison SL, Janaudis-Ferreira T, Brooks D, et al. **Self-Management** Following an Acute **Exacerbation of COPD**: A Systematic Review. Chest. 2015 Mar 1;147(3):646-61.
Hatoun J, Bair-Merritt M, Cabral H, et al. Increasing **Medication Possession at Discharge** for Patients With Asthma: The Meds-in-Hand Project. Pediatrics. 2016 Feb 24.
Hartung DM, Middleton L, Markwardt S, et al. Changes in **Long-acting β-Agonist Utilization After the FDA's 2010 Drug Safety Communication**. Clin Ther. 2014 Nov 25.
Hasegawa K, Tsugawa Y, et al; MARC-37 Investigators. Improving **Quality of Acute Asthma Care** in U.S. Hospitals: Changes between 1999-2000 and 2012-2013. Chest. 2016 Apr 4.
Hatoun J, Davis-Plourde K, Penti B, et al. **Tobacco Control Laws** and Pediatric Asthma. Pediatrics. 2018 Jan;141(Suppl 1):S130-S136.
Hawkins NM, Petrie MC, MacDonald MR, et al. **Heart failure** and chronic obstructive pulmonary disease. The quandary of **beta-blockers** and beta-agonists. J Am Coll Cardiol 2011; 57:2127-2138.
Health Canada June/07 **VENTOLIN** IM injection and VENTOLIN I.V. infusion solution for Pregnant Women & Labour and Delivery. GlaxoSmithKline conducted a review of safety data for salbutamol. There have been 17 occurences worldwide (as of April 2007) of **myocardial ischemia** events in association with salbutamol when used to delay premature labour. There have been no Canadian cases reported to date.
Health Canada Aug/09 is informing health care professionals and Canadians that it is conducting a safety review of the potential association between the asthma drug **Xolair** (the brand name for the drug omalizumab) and an increased risk of cardiovascular problems. http://www.hc-sc.gc.ca/ahc-asc/media/advisories-avis/_2009/2009_129-eng.php
Health Canada May/17: **Placebo tablets** by Australia Therapeutic Goods Administration has undeclared **clenbuterol**.
Health Canada Feb/18: is advising Canadians that GlaxoSmithKline Inc. is voluntarily **recalling** one lot of **Ventolin Diskus inhalers** (lot 786G) because the products may not deliver the intended dose. Individuals who do not receive the intended dose may not be aware that the dose was not delivered.

Heckman EJ, O'Connor GT. **Pulmonary function tests** for diagnosing lung disease. JAMA. 2015 Jun 9;313(22):2278-9.
Helm JS, Nishioka M, Brody JG, et al. Measurement of endocrine disrupting and **asthma-associated chemicals in hair products** used by Black women. Environ Res. 2018 Apr 24.
Henderson-Smart DJ, De Paoli AG. Methylxanthine treatment for apnoea in preterm infants. Cochrane Database Syst Rev 2010; 12: CD000140.
Herath SC, Poole P. **Prophylactic antibiotic therapy** for chronic obstructive pulmonary disease (**COPD**). Cochrane Database of Systematic Reviews 2013, Issue 11. Art. No.: CD009764. DOI: 10.1002/14651858.CD009764.pub2. Use of continuous prophylactic antibiotics results in a clinically significant benefit in reducing exacerbations in COPD patients. All trials of continuous antibiotics used macrolides hence the noted benefit applies only to the use of continuous macrolide antibiotics. The impact of pulsed antibiotics remains uncertain and requires further research. The trials in this review included patients who were frequent exacerbators and needed treatment with antibiotics or systemic steroids, or who were on supplemental oxygen. There were also older individuals with a mean age of 66 years. The results of these trials apply only to the group of patients who were studied in these trials and may not be generalisable to other groups. Because of concerns about antibiotic resistance and specific adverse effects, consideration of prophylactic antibiotic use should be mindful of the balance between benefits to individual patients and the potential harms to society created by antibiotic overuse.
Herath SC, Poole P. **Prophylactic antibiotic** therapy in chronic obstructive pulmonary disease. JAMA. 2014 Jun 4;311(21):2225-6.
Hibbs AM, Ross K, Kerns LA, et al. Effect of **vitamin D supplementation** on recurrent **wheezing in black infants** who were born preterm: the D-Wheeze randomized clinical trial. JAMA.
Hill, Kylie, Hodder, Richard, Blouin, Maria, et al. Identifying adults at risk of COPD who need confirmatory **spirometry** in primary care: Do symptom-based questions help? Can Fam Physician 2011 57: e51-57.
Hodder, Rick, Lougheed, Diane, FitzGerald, J Mark, et al. Management of acute asthma in adults in the **emergency department: assisted ventilation**. CMAJ 2009 0: cmaj.080073
Hodder, Rick, Lougheed, M Diane, et al. Management of acute asthma in adults in the **emergency department: nonventilatory** management. CMAJ 2009 0: cmaj.080072
Hoover Wynton C, Britton LaCrecia J, Gardner Jay, et al. Rapid Onset of Iatrogenic Adrenal Insufficiency in a Patient with Cystic Fibrosis–Related Liver Disease Treated with Inhaled **Corticosteroids and a Moderate CYP3A4 Inhibitor**. Ann Pharmacother July/August 2011 45:e38; June 28
Hoover RM, Erramouspe J, Bell EA, et al. Effect of **inhaled corticosteroids on long-term growth** in pediatric patients with asthma and allergic rhinitis. Ann Pharmacother. 2013 Sep;47(9):1175-81.
Hodyl NA, Stark M, Osei-Kumah A, Bowman M, Gibson P, Clifton VL. **Fetal glucocorticoid** regulated pathways are not affected by inhaled corticosteroid use for asthma during pregnancy. Am J Respir Crit Care Med 2011;183:716–722.
Hodyl NA, Stark MJ, Scheil W, et al. Perinatal outcomes following maternal asthma and cigarette **smoking during pregnancy**. Eur Respir J. 2013 Jul 30.
Holland AE, Hill CJ, Jones AY, et al. **Breathing exercises** for chronic obstructive pulmonary disease. Cochrane Database Syst Rev. 2012 Oct 17;10:CD008250. Breathing exercises over four to 15 weeks improve functional exercise capacity in people with COPD compared to no intervention; however, there are no consistent effects on dyspnoea or health-related quality of life.
Howrylak JA, Spanier AJ, Huang B, et al. **Cotinine** in Children Admitted for Asthma and Readmission. Pediatrics. 2014 Jan 20 (smoking exposure)
Huckvale K, Car M, Morrison C, et al. **Apps for asthma** self-management: a systematic assessment of content and tools. BMC Med 2012;10:144.
Huckvale K, Morrison C, Ouyang J, et al. The evolution of **mobile apps for asthma**: an updated systematic assessment of content and tools. BMC Med. 2015 Mar 23;13:58.
Humbert M, Taillé C, et al. **Omalizumab** effectiveness in patients with severe allergic asthma according to blood eosinophil count: the STELLAIR study. Eur Respir J. 2018 May 10;51(5).
Hurst John R., Vestbo Jørgen, Antonio Anzueto, et al. for the Evaluation of COPD Longitudinally to Identify Predictive Surrogate Endpoints (**ECLIPSE**) Investigators. Susceptibility to **Exacerbation** in Chronic Obstructive Pulmonary Disease. N Engl J Med 2010; 363:1128-1138
Husta BC, Raoof S, Erzurum S, Mehta AC. **Tracheobronchopathy from Inhaled Corticosteroids**. Chest. 2017 Aug 29.
Iftikhar IH, Schimmel M, Bender W, et al. Comparative Efficacy of **Anti IL-4, IL-5 and IL-13 Drugs** for Treatment of Eosinophilic Asthma: A Network Meta-analysis. Lung. 2018 Oct;196(5):517-530.
Irvin CG, et al. Clinical Trial of Low-Dose **Theophylline and Montelukast** in Patients with Poorly Controlled Asthma. Am J Respir Crit Care Med. 2006 Sep 22. Neither montelukast nor low-dose theophylline lowered the event-rate of poor asthma control in patients with poorly-controlled asthma despite improved lung function. For patients not using ICS, low-dose theophylline improved asthma symptom control more than montelukast or placebo and provides a safe and low-cost alternative asthma treatment.
Israel E, Reddel HK. **Severe and Difficult-to-Treat Asthma** in Adults. N Engl J Med. 2017 Sep 7;377(10):965-976
Iyer VN, Schroeder DR, Parker KO, Hyatt RE, Scanlon PD. The **nonspecific pulmonary function test**: longitudinal follow-up and outcomes. Chest. 2011 Apr;139(4):878-86.
Jackson DJ, Evans MD, Gangnon RE, et al. Evidence for a causal relationship between **allergic sensitization and rhinovirus wheezing** in early life. Am J Respir Crit Care Med 2012;185:281–285.
Jackson DJ, Bacharier LB, Mauger DT, et al. **Quintupling inhaled glucocorticoids** to prevent childhood asthma exacerbations. (STICS trial) N Engl J Med. DOI: 10.1056/NEJMoa1710988.
Jaeschke R, O'Byrne PM, Mejza F, et al.. The safety of **long-acting beta-agonists** among patients with asthma using inhaled corticosteroids: systematic review and **metaanalysis**. Am J Respir Crit Care Med. 2008 Nov 15;178(10):1009-16. Epub 2008 Sep 5. Compared with monotherapy, using long-acting beta-agonists (LABAs) plus inhaled corticosteroids in patients with asthma does not appear to increase the risk of hospitalizations. In spite of multiple studies including almost 30,000 patients and more than 8000 patient-years of follow-up, there were too few asthma-related deaths and intubations to draw conclusions about the effect of LABAs on these outcomes. (LOE = 1a)
James AL, Elliot JG, Jones RL, et al. Airway **smooth muscle hypertrophy** and hyperplasia in **asthma**. Am J Respir Crit Care Med 2012;185:1058–1064.
Jang J, Gary Chan KC, Huang H, Sullivan SD. **Trends in cost and outcomes** among adult and pediatric patients with asthma: 2000-2009. Ann Allergy Asthma Immunol. 2013 Dec;111(6):516-22.
Janson C, Larsson K, Lisspers KH, et al. Pneumonia and pneumonia related mortality in patients with COPD treated with fixed combinations of inhaled corticosteroid and long acting β2 agonist: (**Advair vs Symbicort**) observational matched cohort study (PATHOS). BMJ. 2013 May 29;346:f3306.
Jarjour NN, et al. Control of airway inflammation maintained at a lower steroid dose with 100/50 ug of fluticasone propionate/salmeterol. J Allergy Clin Immunol. 2006 Jul;118(1):44-52.Epub 2006 Jun 2.
Jarjour NN, Erzurum SC, Bleecker ER, et al. for the NHLBI Severe Asthma Research Program (SARP). Severe Asthma: Lessons Learned from the National Heart, Lung, and Blood Institute **Severe Asthma** Research Program. Am J Respir Crit Care Med. 2012 Feb 15;185(4):356-362.
Jarvis D, Newson R, Janson C, et al. Prevalence of **asthma-like symptoms with ageing**. Thorax. 2017 Oct 3.
Jat GC, et al. 400 µg of inhaled **budesonide** vs 200 µg of inhaled **budesonide and oral montelukast** in children with moderate persistent asthma: randomized controlled trial . Ann Allergy Asthma Immunol. 2006 Sep;97(3):397-401. The overall control of asthma with 5 mg of oral montelukast and 200 microg of inhaled budesonide is inferior to that with 400 microg of inhaled budesonide in children with moderate persistent asthma.
Jena AB, Ho O, Goldman DP, Karaca-Mandic P. The impact of the US Food and Drug Administration **chlorofluorocarbon ban** on out-of-pocket costs and use of albuterol inhalers among individuals with asthma [online May 11, 2015]. JAMA Intern Med. doi:10.1001/jamainternmed.2015.1665.
Jenkins C. **Eliminating asthma deaths**: have we stalled? Lancet. 2017 Aug 7.
Jenkins C, et al. Efficacy and safety of **high-dose budesonide/formoterol (Symbicort)** compared with budesonide administered either concomitantly with formoterol or alone in patients with

persistent symptomatic asthma. Respirology. 2006 May;11(3):276-86.
Jenkins C, Seccombe L, Tomlins R. **Investigating asthma symptoms in primary care**. BMJ. 2012 Apr 25;344:e2734.
Jeppesen E, Brurberg KG, Vist GE, et al. **Hospital at home for acute exacerbations of chronic obstructive pulmonary disease**. Cochrane Database of Systematic Reviews 2012, Issue 5. Art. No.: CD003573. Selected patients presenting to hospital emergency departments with acute exacerbations of COPD can be safely and successfully treated at home with support from respiratory nurses. We found evidence of moderate quality that hospital at home may be advantageous with respect to readmission rates in these patients. Treatment of acute exacerbation of COPD in hospital at home also show a trend towards reduced mortality rate when compared with conventional inpatient treatment, but these results did not reach statistical significance (moderate quality evidence).
Jeyalingam T, Grover SC. Eosinophilic **esophagitis**. CMAJ. 2018 Apr 30;190(17):E542.
Jin J. Asthma Attacks. JAMA. 2016 Feb 23;315(8):832.
Johannessen A, Nilsen RM, Storebo M, et al. Comparison of 2011 and 2007 **Global Initiative for Chronic Obstructive Lung Disease guidelines** for predicting mortality and hospitalization. Am J Respir Crit Care Med. 2013 Jul 1;188(1):51-9.
Johansson SG, Oman H, Nopp A, Pettersson S. The importance of **IgE antibody** levels in anti-IgE treatment. Allergy. 2006 Oct;61(10):1216-9.
Johnson DP, Arnold DH, Gay JC, et al. **Implementation and Improvement of Pediatric Asthma Guideline** Improves Hospital-Based Care. Pediatrics. 2018 Jan 24.
Johnson JD, Theurer WM. A stepwise approach to the interpretation of **pulmonary function tests**. Am Fam Physician. 2014 Mar 1;89(5):359-66.
Johnston SL, et al. TELICAST Investigators. The effect of **telithromycin** in acute exacerbations of asthma. N Engl J Med. 2006 Apr 13;354(15):1589-600.(InfoPOEMs: Telithromycin may add a small benefit of questionable clinical significance for adult patients with acute asthma. This comes at the price of high drug cost, increased nausea and diarrhea, and a theoretical increased risk of drug resistance in the community. Given this balance of benefits and harms, as well as recent reports of catastrophic liver failure in a small number of patients taking telithromycin, physicians should resist the temptation to prescribe this drug for asthma. (LOE = 1b))
Johnstone KJ, Chang AB, Fong KM, et al. **Inhaled corticosteroids for subacute and chronic cough** in adults. Cochrane Database Syst Rev. 2013 Mar 28;3:CD009305. doi: 10.1002/14651858.CD009305.pub2. The studies were highly heterogeneous and results were inconsistent. Heterogeneity in study design needs to be addressed in future research in order to test the efficacy of this intervention.
Johnston SL, Szigeti M, Cross M, et al; **AZALEA** Trial Team. **Azithromycin** for **acute exacerbations of asthma**: the AZALEA randomized clinical trial [online Sept 19, 2016]. JAMA Intern Med. doi:10.1001/jamainternmed.2016.5664.
Joliffe DA, Greenberg L, et al. **Vitamin D supplementation** to prevent asthma exacerbations: a systematic review and meta-analysis of individual participant data. Lancet Respir Med 2017; online Oct 3.
Jones PW, Chen WH, et al. EXACT-PRO Study Group. Characterizing and quantifying the symptomatic features of **COPD exacerbations**. Chest. 2011 Jun;139(6):1388-94.
Jonkers RE, et al. Onset of relief of dyspnoea with **budesonide/formoterol or salbutamol** following **methacholine-induced** severe bronchoconstriction in adults with asthma: a double-blind, placebo-controlled study. Respir Res. 2006 Dec 4;7(1):141 [Epub ahead of print] Budesonide/formoterol and salbutamol both provided rapid relief of dyspnoea and reversal of airway obstruction in patients with asthma with experimentally induced bronchoconstriction. The perception of relief, as confirmed by objective lung function assessment, provides further evidence that budesonide/formoterol can be used as reliever medication in asthma.
Judd LL, Schettler PJ, Brown ES, et al. **Adverse consequences of glucocorticoid medication**: psychological, cognitive, and behavioral effects. Am J Psychiatry. 2014 Oct 1;171(10):1045-51.
Jung KS et al.Comparison of **tiotropium plus fluticasone propionate/salmeterol** with tiotropium in COPD: A randomized controlled study. Respir Med. 2011 Oct 3.
Jung JW, Kang HR, Kim JY, et al. Are **asthmatic patients prone to bone loss**? Ann Allergy Asthma Immunol. 2014 May;112(5):426-31.
Kalteren WS, Schreurs MWJ, Jorritsma-Smit A, et al. **Ocular myasthenic syndrome**, adverse reaction to **omalizumab**? A case report. Br J Clin Pharmacol. 2017 Jun 19.
Kane Binita, Turkington Peter M, Howard Luke S, et al. Lesson of the Week: Rebound **hypoxaemia after administration of oxygen** in an acute exacerbation of chronic obstructive pulmonary disease. BMJ 2011;342:doi:10.1136/bmj.d1557 (Published 31 March 2011)
Kanemitsu Y, Takakuwa O, Fukumitsu K, et al. **Bronchial Thermoplasty** for Severe Asthmatic Cough. Ann Intern Med. 2018 Mar 13.
Kang EM, Lundsberg LS, Illuzzi JL, Bracken MB. Prenatal exposure to **acetaminophen** and asthma in children. Obstet Gynecol. 2009 Dec;114(6):1295-306.
Kaplan AG, Balter MS, Bell AD, Kim H, McIvor RA. **Diagnosis of asthma** in adults. CMAJ. 2009 Sep 29. [Epub ahead of print]
Kaplan RM, Sun Q, Ries AL. **Quality of Well-being** Outcomes in the National **Emphysema** Treatment Trial. Chest. 2015 Feb 1;147(2):377-87.
Kapur N, Petsky HL, Bell S, Kolbe J, Chang AB. **Inhaled corticosteroids for bronchiectasis**. Cochrane Database of Systematic
Reviews 2018, Issue 5. Art. No.: CD000996. This updated review indicates that there is insufficient evidence to suppor t the routine use of ICS in adults with stable state bronchiectasis.
Further, we cannot draw any conclusion for the use of ICS in adults during an acute exacerbation or in children (for any state), as there were no studies.
Karaca-Mandic P, Jena AB, Joyce GF, Goldman DP. **Out-of-pocket medication costs** and use of medications and health care services among children with asthma. JAMA. 2012;307(12):1284-1291.
Karner C, Cates CJ. The effect of **adding inhaled corticosteroids to tiotropium and long-acting beta(2)-agonists for chronic obstructive pulmonary disease**. Cochrane Database Syst Rev. 2011 Sep 7;9:CD009039. The relative efficacy and safety of adding inhaled corticosteroid to tiotropium and a long-acting beta(2)-agonist for chronic obstructive pulmonary disease patients remains uncertain and additional trials are required to answer this question.
Karner C, Cates CJ. **Long-acting beta(2)-agonist in addition to tiotropium** versus either tiotropium or long-acting beta(2)-agonist alone for chronic obstructive pulmonary disease. Cochrane Database Syst Rev. 2012 Apr 18;4:CD008989. The results from this review indicate a small mean improvement in health-related quality of life for patients on a combination of tiotropium and long-acting beta(2)-agonist compared to tiotropium alone, but it is not clear how clinically important this mean difference may be. Hospital admission and mortality have not been shown to be altered by adding long-acting beta(2)-agonists to tiotropium. There were not enough data to determine the relative efficacy and safety of tiotropium plus long-acting beta(2)-agonist compared to long-acting beta(2)-agonist alone. There were insufficient data to make comparisons between the different long-acting beta(2)-agonists when used in addition to tiotropium.
Karner C, Cates CJ. Combination inhaled steroid and long-acting beta(2)-agonist in addition to **tiotropium versus tiotropium or combination** alone for chronic obstructive pulmonary disease. Cochrane Database Syst Rev. 2011 Mar 16;(3):CD008532.
Karner C, Chong J, Poole P. Tiotropium versus placebo for chronic obstructive pulmonary disease**.** Cochrane Database Syst Rev. 2012 Jul 11;7:CD009285. This review shows that tiotropium treatment was associated with a significant improvement in patients` quality of life and it reduced the risk of exacerbations, with a number needed to treat to benefit (NNTB) of 16 to prevent one exacerbation. Tiotropium also reduced exacerbations leading to hospitalisation but no significant difference was found for hospitalisation of any cause or mortality. Thus, tiotropium appears to be a reasonable choice for the management of patients with stable COPD, as proposed in guidelines. The review however, shows that tiotropium delivered via the Respimat soft mist inhaler was associated with a significantly increased risk of mortality compared with placebo, which calls for caution with this device whilst awaiting the results of an ongoing head-to-head trial comparing tiotropium delivery devices and doses.
Karner C, Chong J, Poole P. **Tiotropium versus placebo** for chronic obstructive pulmonary disease. Cochrane Database Syst Rev. 2014 Jul 21;7:CD009285. This review shows that tiotropium treatment was associated with a significant improvement in patients' quality of life and it reduced the risk of exacerbations, with a number needed to treat to benefit (NNTB) of 16 to prevent one exacerbation. Tiotropium also reduced exacerbations leading to hospitalisation but no significant difference was found for hospitalisation of any cause or mortality. Thus, tiotropium appears to be a reasonable choice for the management of patients with stable COPD, as proposed in guidelines. The trials included in this review showed a difference in the risk of mortality when compared with placebo depending on the type of tiotropium delivery device used. However, these results have not been confirmed in a recent trial when 2.5 mcg or 5 mcg of tiotropium via Respimat was used in a direct comparison to the 18 mcg Handihaler.

Karvonen AM, Hyvärinen A, Korppi M, et. al, **Moisture Damage and Asthma**: A Birth Cohort Study. Pediatrics. 2015 Feb 16. pii: peds.2014-1239. [Epub ahead of print] PubMed PMID: 25687143.

Kawasumi Y, et al. **Comparative Effectiveness of Tiotropium and Ipratropium** in Prevention of Hospital Readmission for COPD: Population-Based Cohort Study. Clin Ther. 2013 Mar 12.

Keeney GE, Gray MP, Morrison AK, et al. **Dexamethasone for Acute Asthma** Exacerbations in Children: A Meta-analysis. Pediatrics. 2014 Feb 10.

Keet CA, McCormack MC, et al. **Neighborhood poverty, urban residence, race/ethnicity, and asthma**: Rethinking inner-city asthma epidemic. J Allergy Clin Immunol. 2015 Jan 7.

Keet CA, Keller JP, Peng RD. **Long-term Coarse PM Exposure** is Associated with Asthma Among Children in Medicaid. Am J Respir Crit Care Med. 2017 Dec 15.

Kelly HW, Van Natta ML, Covar RA, Tonascia J, Green RP, Strunk RC; CAMP Research Group. Effect of long-term corticosteroid use on **bone mineral** density in children: a prospective longitudinal assessment in the childhood Asthma Management Program (CAMP) study. Pediatrics. 2008 Jul;122(1):e53-61. Multiple oral corticosteroid bursts over a period of years can produce a dosage-dependent reduction in bone mineral accretion and increased risk for osteopenia in children with asthma. Inhaled corticosteroid use has the potential for reducing bone mineral accretion in male children progressing through puberty, but this risk is likely to be outweighed by the ability to reduce the amount of oral corticosteroids used in these children.

Kelly HW, Sternberg AL, Lescher R, et al; the **CAMP** Research Group. Effect of Inhaled Glucocorticoids in **Childhood on Adult Height**. N Engl J Med. 2012 Sep 3.

Kempsford R, Allen A, Bal J, et al. The effect of **ketoconazole** on the pharmacokinetics and pharmacodynamics of inhaled **fluticasone** furoate and **vilanterol** trifenatate in healthy subjects. Br J Clin Pharmacol. 2012 Nov 1.

Kennedy S, Bailey R, Jaffee K, et al. **Effectiveness of Evidence-Based Asthma Interventions**. Pediatrics.2017;139(6):e20164221

Kenyon CC, Melvin PR, Chiang VW, et al. **Rehospitalization for Childhood Asthma**: Timing, Variation, and Opportunities for Intervention. J Pediatr. 2013 Nov 14.

Kenyon CC, Rubin DM, Zorc JJ, et al. Childhood Asthma **Hospital Discharge Medication Fills** and Risk of Subsequent **Readmission**. J Pediatr. 2015 Jan 29.

Kenyon CC, Rubin DM, Zorc JJ, et al. Childhood Asthma Hospital **Discharge Medication Fills and Risk of Subsequent Readmission**. J Pediatr. 2015 May;166(5):1121-7.

Kercsmar CM, Beck AF, Sauers-Ford H, et al. Association of an **asthma improvement collaborative** with health care utilization in Medicaid-insured pediatric patients in an urban community [online September 18, 2017]. *JAMA Pediatr*. doi:10.1001/jamapediatrics.2017.2600

Kerstjens HA, Bantje TA, Luursema PB, Sinninghe Damste HE, de Jong JW, Lee A, Wijker SP, Cornelissen PJ. Effects of short-acting bronchodilators added to maintenance tiotropium therapy. Chest. 2007 Nov;132(5):1493-9. Epub 2007 Sep 21. In conclusion, both short-acting bronchodilator classes were effective when added to maintenance treatment with tiotropium. The addition of the beta2-adrenergic fenoterol provided greater additional bronchodilatation than the short-acting anticholinergic ipratropium.

Kerstjens HA, Disse B, Schroder-Babo W, et al. **Tiotropium** improves lung function in patients with severe uncontrolled **asthma**: a randomized controlled trial. J Allergy Clin Immunol. 2011 Aug;128(2):308-14.

Kerstjens HA, Engel M, Dahl R, et al. **Tiotropium in Asthma** Poorly Controlled with Standard Combination Therapy. N Engl J Med. 2012 Sep 2.

Kerstjens HA, Casale TB, Bleecker ER, et al. **Tiotropium or salmeterol** as add-on therapy to inhaled corticosteroids for patients with moderate symptomatic asthma: two replicate, double-blind, placebo-controlled, parallel-group, active-comparator, randomised trials. Lancet Respir Med. 2015 May;3(5):367-76.

Kew KM, Mavergames C, Walters JAE. **Long-acting beta2-agonists for chronic obstructive pulmonary disease**. Cochrane Database of Systematic Reviews 2013, Issue 10. Art. No.: CD010177. Moderate-quality evidence from 26 studies showed that inhaled long-acting beta2-agonists are effective over the medium and long term for patients with moderate to severe COPD. Their use is associated with improved quality of life and reduced exacerbations, including those requiring hospitalisation. Overall, findings showed that inhaled LABAs did not significantly reduce mortality or serious adverse events.

Kew KM, Karner C, Mindus SM, et al. **Combination formoterol and budesonide** as maintenance and reliever therapy versus combination inhaler maintenance for chronic asthma in adults and children. Cochrane Database of Systematic Reviews 2013, Issue 12. Art. No.: CD009019. DOI: 10.1002/14651858.CD009019.pub2. SiT reduces the number of people having asthma exacerbations requiring oral steroids and the number requiring hospitalisation or an ER visit compared with fixed-dose combination inhalers. Evidence for serious adverse events was unclear. The mean daily dose of inhaled corticosteroids (ICS) in SiT, including the total dose administered with reliever use, was always lower than that of the other combination groups. This suggests that the flexibility in steroid administration that is possible with SiT might be more effective than a standard fixed-dose combination by increasing the dose only when needed and keeping it low during stable stages of the disease. Data for hospitalisations alone could not be obtained, and no studies have yet addressed this question in children younger than age 12.

Kew KM, Seniukovich A. **Inhaled steroids and risk of pneumonia** for chronic obstructive pulmonary disease. Cochrane Database of Systematic Reviews 2014, Issue 3. Art. No.: CD010115. DOI: 10.1002/14651858.CD010115.pub2. Budesonide and fluticasone, delivered alone or in combination with a LABA, are associated with increased risk of serious adverse pneumonia events, but neither significantly affected mortality compared with controls. The safety concerns highlighted in this review should be balanced with recent cohort data and established randomised evidence of efficacy regarding exacerbations and quality of life. Comparison of the two drugs revealed no statistically significant difference in serious pneumonias, mortality or serious adverse events. Fluticasone was associated with higher risk of any pneumonia when compared with budesonide (i.e. less serious cases dealt with in the community), but variation in the definitions used by the respectivemanufacturers is a potential confounding factor in their comparison.

Kew KM, Dias S, Cates CJ. **Long-acting inhaled therapy** (beta-agonists, anticholinergics and steroids) for **COPD**: a network meta-analysis.CochraneDatabase of SystematicReviews 2014, Issue 3.Art.No.:CD010844.DOI: 10.1002/14651858.CD010844.pub2. This network meta-analysis compares four different classes of long-acting inhalers for people with COPD who need more than shortacting bronchodilators. Quality of life and lung function were improved most on combination inhalers (LABA and ICS) and least on ICS alone at 6 and at 12 months. Overall LAMA and LABA inhalers had similar effects, particularly at 12 months. The network has demonstrated the benefit of ICS when added to LABA for these outcomes in participants who largely had an FEV1 that was less than 50% predicted, but the additional expense of combination inhalers and any potential for increased adverse events (which has been established by other reviews) require consideration. Our findings are in keeping with current National Institute for Health and Care Excellence (NICE) guidelines.

Kew KM, Kirtchuk L, Michell CI. **Intravenous magnesium** sulfate for treating adults with acute asthma in the emergency department. Cochrane Database of Systematic Reviews 2014, Issue 5. Art. No.: CD010909. DOI: 10.1002/14651858.CD010909.pub2

Kew KM, Beggs S, Ahmad S. **Stopping long-acting beta2-agonists (LABA) for children with asthma well controlled on LABA and inhaled corticosteroids**. Cochrane Database of Systematic Reviews 2015, Issue 5. Art. No.: CD011316. DOI: 10.1002/14651858.CD011316.pub2. There is currently no evidence from randomised trials to inform the discontinuation of LABAs in children once asthma control is achieved with ICS plus LABA. It is disappointing that such an important issue has not been studied, and a randomised double-blind trial recruiting children who are controlled on ICS plus LABA is warranted. The study should be large enough to assess children of different ages, and to measure the important safety and efficacy outcomes suggested in this review over at least six months. The only randomised evidence for stopping LABA has been conducted in adults; it will be summarised in a separate review.

Kew KM, Undela K, Kotortsi I, et al. **Macrolides for chronic asthma**. Cochrane Database Syst Rev. 2015 Sep 15;9:CD002997. Existing evidence does not show macrolides to be better than placebo for the majority of clinical outcomes. However, they may have a benefit on some measures of lung function, and we cannot rule out the possibility of other benefits or harms because the evidence is of very low quality due to heterogeneity among patients and interventions, imprecision and reporting biases.The review highlights the need for researchers to report clinically relevant outcomes accurately and completely using guideline definitions of exacerbations and validated scales. The possible benefit of macrolides in patients with non-eosinophilic asthma based on subgroup analyses in two of the included studies may require further investigation.

Kew KM, Dahri K. Long-acting muscarinic antagonists **(LAMA) added to combination long-acting beta-agonists and inhaled corticosteroids (LABA/ICS) versus LABA/ICS** for adults with asthma. Cochrane Database Syst Rev. 2016 Jan 21;1:CD011721. Tiotropium add-on may have additional benefits over LABA/ICS alone in reducing the need for rescue oral steroids in people with severe asthma. The effect was imprecise, and there was no evidence for other LAMA preparations. Possible benefits on quality of life were negligible, and evidence for the effect on serious adverse events was inconsistent. There are likely to be small added benefits for tiotropium

Respimat 5 µg daily on lung function and asthma control over LABA/ICS alone and fewer non-serious adverse events. The benefit of tiotropium add-on on the frequency of hospital admission is still unknown, despite year-long trials.Ongoing and future trials should clearly describe participants' background medications to help clinicians judge how the findings relate to stepwise care. If studies test LAMAs other than tiotropium Respimat for asthma, they should be at least six months long and use accepted and validated outcomes to allow comparisons of the safety and effectiveness between different preparations.

Kew KM, Cates CJ. **Remote versus face-to-face check-ups** for asthma. Cochrane Database of Systematic Reviews 2016, Issue 4. Art. No.: CD011715. DOI: 10.1002/14651858.CD011715.pub2. Current randomised evidence does not demonstrate any important differences between face-to-face and remote asthma check-ups in terms of exacerbations, asthma control or quality of life. There is insufficient information to rule out differences in efficacy, or to say whether or not remote asthma check-ups are a safe alternative to being seen face-to-face.

Kew KM, Quinn M, Quon BS, et al. **Increased versus stable doses of inhaled corticosteroids for exacerbations of chronic asthma** in adults and children. Cochrane Database Syst Rev. 2016 Jun 7;6:CD007524. Current evidence does not support increasing the dose of ICS as part of a self initiated action plan to treat exacerbations in adults and children with mild to moderate asthma. Increased ICS dose is not associated with a statistically significant reduction in the odds of requiring rescue oral corticosteroids for the exacerbation, or of having adverse events, compared with a stable ICS dose. Wide confidence intervals for several outcomes mean we cannot rule out possible benefits of this approach.

Kew KM, Nashed M, Dulay V, et al. **Cognitive behavioural therapy (CBT) for adults and adolescents with asthma**. Cochrane Database Syst Rev. 2016 Sep 21;9:CD011818. For adults with persistent asthma, CBT may improve quality of life, asthma control, and anxiety levels compared with usual care. Risks of bias, imprecision of effects, and inconsistency between results reduced our confidence in the results to low, and evidence was lacking regarding the effect of CBT on asthma exacerbations, unscheduled contacts, depression, and medication adherence. There was much variation between studies in how CBT was delivered and what constituted usual care, meaning the most optimal method of CBT delivery, format, and target population requires further investigation. There is currently no evidence for the use of CBT in adolescents with asthma.

Kew KM, Carr R, Donovan T, et al. **Asthma education for school staff**. Cochrane Database Syst Rev. 2017 Apr 12;4:CD012255. Asthma education for school staff increases asthma knowledge and preparedness, but studies vary and all available evidence is of low quality. Studies have not yet captured whether this improvement in knowledge has led to appreciable benefits over the short term or the longer term for the safety and health of children with asthma in school. Randomised evidence does not contribute to our knowledge of content or attributes of interventions that lead to the best outcomes, or of resources required for successful implementation.Complete reporting of the content and resources of educational interventions is essential for assessment of their effectiveness and feasibility for implementation. This applies to both randomised and non-randomised studies, although the latter may be better placed to observe important clinical outcomes such as exacerbations and mortality in the longer term.

Kew KM, Malik P, Aniruddhan K, Normansell R. **Shared decision-making** for people with asthma. Cochrane Database Syst Rev. 2017 Oct 3;10:CD012330. Substantial differences between the four included randomised controlled trials (RCTs) indicate that we cannot provide meaningful overall conclusions. Individual studies demonstrated some benefits of SDM over control, in terms of quality of life; patient and parent satisfaction; adherence to prescribed medication; reduction in asthma-related healthcare visits; and improved asthma control. Our confidence in the findings of these individual studies ranges from moderate to very low, and it is important to note that studies did not measure or report adverse events.

Khorfan FM, Smith P, Watt S, Barber KR. Effects of **nebulized bronchodilator** therapy on heart rate and arrhythmias in critically ill adult patients. Chest. 2011 Dec;140(6):1466-72. In critically ill adult patients, nebulized albuterol and ipratropium does not cause significant tachycardia or tachyarrhythmias. Substitution of levalbuterol for albuterol (salbutamol) to avoid tachycardia and tachyarrhythmias is unwarranted.

Khreis H, et al. Full-chain health impact assessment of **traffic-related air pollution and childhood asthma**. Environ Int 2018; online 27 Mar. https://doi.org/10.1016/j.envint.2018.03.008.

Kiljander TO, et al. Effects of **esomeprazole** 40 mg twice daily on asthma: a randomized placebo-controlled trial. Am J Respir Crit Care Med. 2006 May 15;173(10):1091-7. Epub 2005 Dec 15. n=770 16weeks Esomeprazole improved PEF in subjects with asthma who presented with both GERD and NOC. In subjects without both GERD and NOC, no improvement could be detected. (InfoPOEMs: In this study, esomeprazole (Nexium) was no better than placebo in improving peak expiratory flow, asthma symptoms, or quality of life in patients with stable asthma. Furthermore, esomeprazole was no better than placebo in pts with reflux, either. (LOE = 2b-))

Kiljander TO, Junghard O, Beckman O, Lind T. Effect of **Esomeprazole** 40 mg Once or Twice Daily on Asthma: A Randomized, Placebo-controlled Study. Am J Respir Crit Care Med. 2010 Jan 28.

Kim V, Criner GJ. **Chronic bronchitis and chronic obstructive pulmonary disease**. Am J Respir Crit Care Med. 2013 Feb 1;187(3):228-37.

Kim BS, Mehra S, Yawn B, et al. Increased Risk of **Herpes Zoster** in Children with Asthma: A Population-Based Case-Control Study. J Pediatr. 2013 Apr 13.

Kim JM, Lin SY, Suarez-Cuervo C, et al. **Allergen-Specific Immunotherapy** for Pediatric Asthma and Rhinoconjunctivitis: A Systematic Review. Pediatrics. 2013 May 6.

Kirkland SW, Vandenberghe C, Voaklander B, Nikel T, Campbell S, Rowe BH. **Combined inhaled beta-agonist and anticholinergic agents** for **emergency management** in adults with **asthma**. Cochrane Database of Systematic Reviews 2017, Issue 1. Art. No.: CD001284. Overall, combination inhaled therapy with SAAC and SABA reduced hospitalisation and improved pulmonary function in adults presenting to the ED with acute asthma. In particular, combination inhaled therapy was more effective in preventing hospitalisation in adults with severe asthma exacerbations who are at increased risk of hospitalisation, compared to those with mild-moderateexacerbations, who were at a lower risk to be hospitalised. A single dose of combination therapy and multiple doses both showed reductions in the risk of hospitalisation among adults with acute asthma. However, adults receiving combination therapy were more likely to experience adverse events, such as tremor, agitation, and palpitations, compared to patients receiving SABA alone.

Kirkland SW, Cross E, Campbell S, et al. **Intramuscular versus oral corticosteroids to reduce relapses following discharge from the emergency department for acute asthma**. Cochrane Database Syst Rev. 2018 Jun 2;6:CD012629. There is insufficient evidence to identify whether IM corticosteroids are more effective in reducing relapse compared to oral corticosteroids among children or adults discharged from an ED or equivalent acute care setting for acute asthma. While we found no statistical differences, patients receiving IM corticosteroids reported fewer adverse events. Additional studies comparing the effectiveness of IM versus oral corticosteroids could provide further evidence clarity. Furthermore, there is a need for studies comparing different IM corticosteroids (e.g. IM dexamethasone versus IM methylprednisone) and different oral corticosteroids (e.g. oral dexamethasone versus oral prednisone), with consideration for dosing and pharmacokinetic properties, to better identify the optimal IM or oral corticosteroid regimens to improve patient outcomes. Other factors, such as patient preference and potential issues with adherence, may dictate practitioner prescribing.

Kit BK et al. Trends in **Preventive Asthma Medication Use** Among **Children and Adolescents**, 1988-2008. Pediatrics. 2011 Dec 5.

Klijn P, van Keimpema A, Legemaat M, et al. **Nonlinear exercise training** in advanced chronic obstructive pulmonary disease is superior to traditional exercise training. A randomized trial. Am J Respir Crit Care Med. 2013 Jul 15;188(2):193-200.

Kloepfer KM, Olenec JP, Lee WM, et al. Increased **H1N1 Infection Rate** in Children with Asthma. Am J Respir Crit Care Med. 2012 Jun 15;185(12):1275-9.

Klopp A, Vehling L, Becker AB, et al. Modes of **Infant Feeding** and the Risk of Childhood Asthma: A Prospective Birth Cohort Study. JPed. 2017;190:192-9.

Pdf Kneale D, Harris K, McDonald VM, et al. Effectiveness of **school-based self-management interventions** for asthma among children and adolescents: findings from a Cochrane systematic review and meta-analysis. Thorax. 2019 Jan 27.

Konecny, Park, Somers, et al. Relation of Chronic Obstructive Pulmonary Disease to **Atrial and Ventricular Arrhythmias**. The American Journal of Cardiology. 2014.

Konikoff MR, et al. A randomized, double-blind, placebo-controlled trial of fluticasone for pediatric **eosinophilic esophagitis**. Gastroenterology. 2006 Nov;131(5):1381-91. Epub 2006 Aug 16.

Koopmans JG, Lutter R, Jansen HM, van der Zee JS. Adding salmeterol to an ICS: long term effects on bronchial inflammation in asthma. Thorax. 2006 Apr;61(4):306-12. Epub 2006 Jan 31.

Koren G, Sarkar M, Einarson A. Safety of using **montelukast during pregnancy**. Can Fam Physician. 2010 Sep;56(9):881-2.

Kornmann O, Dahl R, Centanni S, Dogra A, Owen R, Lassen C, Kramer B. Once-daily **indacaterol** vs twice-daily salmeterol for COPD: a placebo-controlled comparison. Eur Respir J. 2010 Aug 6.

Kouri A, Boulet LP, Kaplan A, Gupta S. An evidence-based, point-of-care tool to guide completion of asthma **action plans** in practice. Eur Respir J. 2017 May 1;49(5).

Kouri A, Kaplan A, Boulet LP, Gupta S. New evidence-based tool to guide **the creation of asthma action plans for adults**. Can Fam Physician. 2019 Feb;65(2):103-106.

Kovesi, Thomas, Schuh, Suzanne, Spier, Sheldon, et al. Achieving control of asthma in preschoolers. CMAJ 2009 0: cmaj.071638.

Kozer E, Lotem Z, Elgarushe M, et al. RCT of **Montelukast** as Prophylaxis for Upper Respiratory Tract Infections in Children. Pediatrics. 2012 Jan 4. (12 week 4mg oral not effective)

Kravitz J, Dominici P, Ufberg J et al. **Two Days** of Dexamethasone Versus 5 Days of **Prednisone** in the Treatment of Acute Asthma: A Randomized Controlled Trial. Ann Emerg Med. 2011Feb17.

Krieger J, Song L, Philby M. Community Health Worker **Home Visits** for Adults With Uncontrolled Asthma: The **HomeBASE** Trial Randomized Clinical Trial. JAMA Intern Med. 2014 Nov 24.

Krug N, Hohlfeld JM, Kirsten A-M, et al. Allergen-induced asthmatic responses modified by a **GATA3-specific DNAzyme**. N Engl J Med 2015;372:1987-95.

Kruis AL, Smidt N, Assendelft WJ, et al. **Integrated disease management interventions for patients with chronic obstructive pulmonary disease.** Cochrane Database Syst Rev. 2013 Oct 10;10:CD009437. In these COPD participants, IDM not only improved disease-specific QoL and exercise capacity, but also reduced hospital admissions and hospital days per person.

Kruis AL, Smidt N, Assendelft WJ, et al. Cochrane corner: is **integrated disease management** for patients with **COPD** effective?. Thorax. 2014 Jan 14.

Kruis AL, Boland MR, Assendelft WJ, et al. Effectiveness of **integrated disease management for primary care chronic obstructive** pulmonary disease patients: results of cluster randomised trial. BMJ. 2014 Sep 10;349:g5392.

Kwon HJ et al. **Asthma** as a **risk factor for zoster** in adults: A population-based case-control study. J Allergy Clin Immunol 2015 Dec 11.

Kwon YJ, Allen JL, Liu GT, et al. Presumed **Pseudotumor Cerebri Syndrome After Withdrawal of Inhaled Glucocorticoids**. Pediatrics. 2016 May 17.

Irwin RS, et al. American College of Chest Physicians (ACCP). **Diagnosis and management of cough** executive summary: ACCP evidence-based clinical practice guidelines. Chest. 2006 Jan;129(1 Suppl):1S-23S. http://www.chestjournal.org/cgi/content/full/129/1_suppl/1S

Lahousse L, Niemeijer MN, van den Berg ME, et al. **Chronic obstructive pulmonary disease and sudden cardiac death**: the Rotterdam study. Eur Heart J. 2015 Apr 28.

Laidlaw TM, Boyce JA. **Aspirin-Exacerbated Respiratory Disease**--New Prime Suspects. N Engl J Med. 2016 Feb 4;374(5):484-8.

Lang JE, , et al. **Overweight/obesity status in preschool children associates** with worse asthma but robust improvement on inhaled corticosteroids. J Allergy Clin Immunol. 2017 Dec 8.

Lang JE, Mougey EB, Hossain MJ, et al. **Fish Oil Supplementation in Overweight/Obese Patients** with Uncontrolled Asthma: A Randomized Trial. Ann Am Thorac Soc. 2019 Jan 25.

Lange P, et al. Inhaled corticosteroids and decline of **lung function** in community residents with asthma. Thorax. 2006 Feb;61(2):100-4.

Lange P, Celli B, Agustí A, et al. **Lung-function trajectories** leading to chronic obstructive pulmonary disease. N Engl J Med 2015;373:111-22.

Langton D, Ing A, Fielding D, Hersch N, et al. Safety and effectiveness of **bronchial thermoplasty when FEV(1) less than 50**. Chest. 2019 Sep 13.

Lapperre T. S., Snoeck-Stroband J. B., Gosman M. M.E., et al. and the GLUCOLD (Groningen Leiden Universities Corticosteroids in Obstructive Lung Disease) Study Group. Effect of **Fluticasone** With and Without Salmeterol on Pulmonary Outcomes in Chronic Obstructive Pulmonary Disease: A Randomized Trial. Ann Intern Med 2009; 517-527.

Larsson K, Janson C, Lisspers K, et al. Combination of **budesonide/formoterol more effective than fluticasone/salmeterol** in preventing exacerbations in chronic obstructive pulmonary disease. The PATHOS study. J Intern Med. 2013 Mar 15.

Laude EA, et al. The effect of helium and oxygen on exercise performance in COPD: a randomized crossover trial. Am J Respir Crit Care Med. 2006 Apr 15;173(8):865-70. Epub 2006 Jan 26. (InfoPOEMs: Inhaling a combination of 72% helium and 28% oxygen during exertion increases the comfortable walking distance and reduces the perception of exertional difficulty in patients with stable chronic obstructive pulmonary disease (COPD). (LOE = 2b))

Laugheed MD, Lemiere C, Dell S, Ducharme F, FitzGerald JM, Leigh R, et al. **Canadian Thoracic Society** Asthma Management Continuum – **2010 Consensus** Summary for children six years of age and over , and adults. Can Respir J 2010;17:15-24.

Lazarus SC, et al. **Smoking** Affects Response to **Inhaled Corticosteroids** or Leukotriene Receptor Antagonists in Asthma. Am J Respir Crit Care Med. 2007 Jan 4; [Epub ahead of print] In mild asthmatics who smoke, the response to inhaled corticosteroids is attenuated, suggesting that adjustments to standard therapy may be required to attain asthma control. The greater improvement seen in some outcomes in smokers treated with montelukast suggests that leukotrienes may be important in this setting.

Lazarus SC. Clinical practice. **Emergency treatment of asthma**. N Engl J Med. 2010 Aug 19;363(8):755-64.

Lazarus SC, Krishnan JA, King TS, et al. **Mometasone or tiotropium in mild asthma** with a low sputum eosinophil level. (SIENA) N Engl J Med. DOI: 10.1056/NEJMoa1814917.

Lazarinis N, Jorgensen L, Ekstrom T, et al. **Combination of budesonide/formoterol** on demand improves asthma control by reducing **exercise-induced bronchoconstriction (EIB)**. Thorax. 2013Oct 3.

Ledford D, Busse W, Trzaskoma B, et al. A randomized multicenter study evaluating **Xolair** persistence of response after long-term therapy. J Allergy Clin Immunol. 2016 Nov 5.

Lee CM, Heo J, Han SS, et al. **Inhaled corticosteroid-related tuberculosis** in the real world among patients with asthma and COPD: A 10-year nationwide population-based study. J Allergy Clin Immunol Pract. 2018 Oct 16.

Lee HW, Kim HJ, Lee CH. The impact of **olodaterol** on the risk of **mortality** and serious adverse events: a systematic review and meta-analysis. Br J Clin Pharmacol. 2016 Dec 13.

Lee TA, Pickard AS, Au DH, Bartle B, Weiss KB. Risk for death associated with medications for recently diagnosed chronic obstructive pulmonary disease. Ann Intern Med. 2008 Sep 16;149(6):380-90. The possible association between ipratropium and elevated risk for all-cause and cardiovascular death needs further study.

Lee TA, Wilke C, Joo M, Stroupe KT, et al. Outcomes associated with **tiotropium** use in patients with chronic obstructive pulmonary disease. Arch Intern Med. 2009 Aug 10;169(15):1403-10.

Lee YJ, et al. **Health Care Utilization and Direct Costs** in Mild, Moderate, and Severe Adult Asthma: A Descriptive Study Using the 2014 South Korean Health Insurance Database. Clin Ther. 2017 Feb 16.

Leivseth L, Brumpton BM, Nilsen TI, et al. **GOLD classifications and mortality** in chronic obstructive pulmonary disease (**COPD**): the HUNT Study, Norway. Thorax. 2013 Apr 23.

Lemanske, Robert F., Jr., Mauger, David T., Sorkness, Christine A., et al. the Childhood Asthma Research and Education (CARE) Network of the National Heart, Lung, and Blood Institute, Step-up Therapy for Children with Uncontrolled Asthma while Receiving Inhaled Corticosteroids. (**Badger**) N Engl J Med 2010 0: NEJMoa1001278. Nearly all the children had a differential response to each step-up therapy. LABA step-up was significantly more likely to provide the best response than either ICS or LTRA step-up. However, many children had a best response to ICS or LTRA step-up therapy, highlighting the need to regularly monitor and appropriately adjust each child's asthma therapy.

Leung JM, Sin DD. **Asthma-COPD overlap syndrome**: pathogenesis, clinical features, and therapeutic targets. BMJ. 2017 Sep 25;358:j3772.

Leuppi JD, Schuetz P, Bingisser R, et al. **Short-term (5d) vs conventional (14d) glucocorticoid therapy** in acute exacerbations of chronic obstructive pulmonary disease: the REDUCE randomized clinical trial [online May 21, 2013]. JAMA. doi: 10.1001/jama.2013.5023.

Levalbuterol (Xopenex HFA) Medical Letter Mar 13,2006.

Li H, Liu DH, Chen LL, Zhao Q, et al. Meta-analysis of the adverse effects of long-term **azithromycin** use in patients with chronic lung diseases. Antimicrob Agents Chemother. 2014 Jan;58(1):511-7

Li J, Agarwal SK, et al. Airflow Obstruction, Lung Function, and Incidence of **Atrial Fibrillation**: The Atherosclerosis Risk in Communities (ARIC) Study. Circulation. 2014 Mar 4;129(9):971-80.

Lim Angelina, Stewart Kay, König Kai, et al. Systematic Review of the Safety of **Regular Preventive Asthma Medications During Pregnancy**. Ann Pharmacother July/August 2011 45:931-945.

Lin S, Munsie JP, Herdt-Losavio ML et al. Maternal Asthma Medication Use and the Risk of Selected Birth Defects. Pediatrics. 2012 Jan 16.

Lin SY, Erekosima N, Kim JM, et al. **Sublingual immunotherapy** for the treatment of allergic rhinoconjunctivitis and asthma: a systematic review. JAMA. 2013; 309(12):1278-1288.

Lin SY, Azar A, Suarez-Cuervo C, et al. The role of **immunotherapy** in the treatment of asthma. Comparative Effectiveness Review No. 196. AHRQ Publication No. 17(18)-EHC029-EF.

Lindenauer Peter K.; Pekow Penelope S.; Lahti Maureen C.; et al. Association of **Corticosteroid Dose and Route** of Administration With Risk of Treatment Failure in Acute Exacerbation of Chronic Obstructive Pulmonary Disease (**COPD**). JAMA. 2010;303(23):2359-2367.

Lindenauer PK, Stefan MS, Shieh MS, et al. Outcomes Associated With **Invasive and Noninvasive Ventilation** Among Patients Hospitalized With Exacerbations of Chronic Obstructive Pulmonary

Disease. JAMA Intern Med. 2014 Oct 27.
Liptzin DR, Szefler SJ. Evolution of **Asthma Self-Management** Programs in Adolescents: From the Crisis Plan to Facebook. J Pediatr. 2016 Oct 10.
Littner MR, Leung FW, et al. **Lansoprazole Asthma** Study Group. Effects of 24 weeks of lansoprazole therapy on asthma symptoms, exacerbations, quality of life, and pulmonary function in adult asthmatic patients with acid reflux symptoms. Chest. 2005 Sep;128(3):1128-35.
Liu VX, Winthrop KL, Lu Y, et al. Association between **Inhaled Corticosteroid Use and Pulmonary Nontuberculous Mycobacterial Infection**. Ann Am Thorac Soc. 2018 Sep 14.
Liu X, Agerbo E, Schlünssen V, et al. **Maternal asthma severity and control during pregnancy and risk of offspring asthma**. J Allergy Clin Immunol. 2017 Jun 27.
Llor C, Moragas A, Hernández S, et al. Efficacy of **antibiotic therapy for acute exacerbations** of mild to moderate chronic obstructive pulmonary disease. Am J Respir Crit Care Med. 2012 Oct 15;186(8):716-23.
Lodge CJ, Zaloumis S, Lowe AJ, et al. Early-Life Risk Factors for **Childhood Wheeze Phenotypes** in a High-Risk Birth Cohort. J Pediatr. 2013 Nov 14.
Loke YK et al. **Risk of fractures with inhaled corticosteroids** in COPD: Systematic review and meta-analysis of randomised controlled trials and observational studies. Thorax 2011 Aug; 66:699. The use of inhaled corticosteroids as a treatment for chronic obstructive pulmonary disease (COPD) in older adults increases the fracture risk somewhat, with a number needed to treat to harm of 83 over 3 years. This must be balanced against a number needed to treat of 6 per year to prevent exacerbations. (LOE = 1a)
Lokke A, et al. Developing COPD: a **25yr follow up** of the general population. Thorax. 2006 Nov;61(11):935-9. The absolute risk of developing COPD among continuous smokers is at least 25%, which is larger than was previously estimated.
Lossius AK, Magnus MC, Lunde J, Størdal K. Prospective Cohort Study of **Breastfeeding and the Risk of Childhood Asthma**. J Pediatr. 2018 Jan 31.
Lougheed MD, Lemière C, Dell SD, et al. Canadian Thoracic Society Asthma Committee. **Canadian Thoracic Society Asthma Management Continuum--2010 Consensus Summary for children six years of age and over, and adults**. Can Respir J. 2010 Jan-Feb;17(1):15-24. http://www.respiratoryguidelines.ca/guideline/asthma
Lowe AJ, Carlin JB, et al. Paracetamol (**acetaminophen**) use in early life and asthma: prospective birth cohort study. BMJ. 2010 Sep 15;341:c4616. doi: 10.1136/bmj.c4616.
Loymans RJB, Gemperli A, Cohen J, et al. Comparative effectiveness of **long term drug treatment strategies to prevent asthma exacerbations**: network meta-analysis. BMJ 2014;348:g3009.
Loymans RJ, Honkoop PJ, Termeer EH, et al. **Identifying patients at risk for severe exacerbations** of asthma: development and external validation of a multivariable prediction model. Thorax. 2016 Apr 4.
Lu CY, Zhang F, Lakoma MD, et al. Asthma Treatments and Mental Health Visits After a Food and Drug Administration **Label Change for Leukotriene Inhibitors**. Clin Ther. 2015 Apr 25.
Lundback B, Ronmark E, Lindberg A, et al. Control of mild to moderate asthma over 1-year with the **combination** of salmeterol and fluticasone propionate. Respir Med. 2005 Oct 20
Luyster FS, Strollo PJ Jr, Holguin F, et al. Association Between **Insomnia and Asthma** Burden in the Severe Asthma Research Program (SARP) III. Chest. 2016 Dec;150(6):1242-1250.
Lv S, Ye X, Wang Z, et al. A randomized controlled trial of a **mobile application-assisted nurse-led model used to improve treatment** outcomes in children with asthma. J Adv Nurs. 2019 Jun 26.
Ma J, Ward EM, Siegel RL, et al. **Temporal Trends in Mortality** in the United States, 1969-2013. JAMA. 2015 Oct 27;314(16):1731-1739.
Mackay AJ, Donaldson GC, Patel AR, et al. Usefulness of the Chronic Obstructive Pulmonary Disease Assessment **Test to Evaluate Severity of COPD Exacerbations**. (**CAT**) Am J Respir Crit Care Med. 2012 Jun 1;185(11):1218-24.
Macie C, Wooldrage K, Manfreda J, Anthonisen NR. Inhaled **Corticosteroids** and **Mortality** in COPD. Chest. 2006 Sep;130(3):640-6.
Magnus MC, Karlstad Ø, Håberg SE, et al. **Prenatal and infant paracetamol-acetaminophen** exposure and development of **asthma**: the Norwegian Mother and Child Cohort Study. Int J Epidemiol. 2016 Feb 9.
Magnussen H, Disse B, Rodriguez-Roisin R, et al. **Withdrawal of inhaled glucocorticoids** and exacerbations of COPD. (**Wisdom**) N Engl J Med. DOI: 10.1056/NEJMoa1407154.
Mahler DA, D`Urzo A, Bateman ED, et al. Concurrent use of **indacaterol plus tiotropium** in patients with COPD provides superior bronchodilation compared with tiotropium alone: a randomised, double-blind comparison. Thorax. 2012 Apr 27.
Mahler DA, Decramer M, D`Urzo A, et al. Dual bronchodilation with **QVA149** reduces patient-reported dyspnoea in COPD: BLAZE study. Eur Respir J. 2014 Jun;43(6):1599-609.
Mainardi TR, Mellins RB, Miller RL, et al. **Exercise-induced wheeze**, urgent medical visits, and neighborhood asthma prevalence. Pediatrics. 2013 Jan;131(1):e127-35.
Mainguy V, Girard D, Maltais F, et al. Effect of **Bisoprolol** on Respiratory Function and Exercise Capacity in Chronic Obstructive Pulmonary Disease. Am J Cardiol. 2012 Apr 10.
Maltby S, Gibson PG, Powell H, McDonald VM. **Omalizumab** Treatment Response in a Severe Allergic Asthma Population with Overlapping COPD. Chest. 2016 Oct 11.
Man WD, Polkey MI, Donaldson N, Gray BJ, Moxham J. Community **pulmonary rehabilitation** after hospitalisation for acute exacerbations of chronic obstructive pulmonary disease: randomised controlled study. BMJ. 2004 Nov 20;329(7476):1209. Epub 2004 Oct 25.
Mancuso CA, Choi TN, Westerman H, et al. A randomized trial to **increase physical activity** in asthma patients through positive affect and self-affirmation. Arch Intern Med. doi:10.1001/archinternmed.2011.1311.
Manousaki D, Paternoster L, Standl M, et al. **Vitamin D levels** and susceptibility to asthma, elevated immunoglobulin E levels, and atopic dermatitis: A Mendelian randomization study. PLoS Med. 2017 May 9;14(5):e1002294.
Mapel DW, Dalal AA, Johnson P, Becker L, Hunter AG. A Clinical Study of **COPD Severity** Assessment by Primary Care **Physicians and Their Patients Compared with Spirometry**. Am J Med. 2015 Jun;128(6):629-37.
Maricoto T, Monteiro L, Gama JMR, et al. **Inhaler Technique Education and Exacerbation Risk** in Older Adults with Asthma or Chronic Obstructive Pulmonary Disease: A Meta-Analysis. J Am Geriatr Soc. 2019 Jan;67(1):57-66.
Martinez FD, Vercelli D. **Asthma**. Lancet. 2013 Sep 13.
Masoli M, et al. **Moderate** dose inhaled **corticosteroids** plus salmeterol versus **higher** doses of inhaled corticosteroids in symptomatic asthma. Thorax. 2005 Sep;60(9):730-4.
Masoli M, et al. Inhaled fluticasone and **adrenal effects** in adult asthma: systematic review & meta-analysis. Eur Respir J. 2006 May 31; [Epub ahead of print]
Marciniuk DD, Goodridge D, Hernandez P, et al; **Canadian Thoracic Society (CTS)** COPD Committee Dyspnea Expert Working Group. Managing **dyspnea** in patients with advanced chronic obstructive pulmonary disease: A Canadian Thoracic Society clinical practice guide. Can Respir J 2011;18(2). http://www.respiratoryguidelines.ca/sites/all/files/2011_CTS_guideline_COPD_dyspnea.pdf

Maricoto T, Monteiro L, Gama JMR, et al**. Inhaler Technique Education** and Exacerbation Risk in Older Adults with Asthma or Chronic Obstructive Pulmonary Disease: A Meta-Analysis. J Am Geriatr Soc. 2019 Jan;67(1):57-66.

Marks GB, et al. Prevention of asthma during the first 5 years of life: a randomized controlled trial. J Allergy Clin Immunol. 2006 Jul;118(1):53-61. Epub 2006 May 30.
House dust mite avoidance measures and dietary fatty acid modification, as implemented in this trial during infancy and early childhood, did not prevent the onset of asthma, eczema, or atopy in high-risk children.

Marra F, et al. Does **antibiotic exposure** during infancy lead to development of asthma?: a systematic review and metaanalysis. Chest. 2006 Mar;129(3):610-8. Exposure to at least one course of antibiotics in the first year of life appears to be a risk factor for the development of childhood asthma.

Martineau AR, Cates CJ, Urashima M, et al. **Vitamin D** for the management of asthma. Cochrane Database of Systematic Reviews 2016, Issue 9. Art. No.: CD011511. Meta-analysis of a modest number of trials in people with predominantly mild to moderate asthma suggests that vitamin D is likely to reduce both the risk of severe asthma exacerbation and healthcare use. It is as yet unclear whether these effects are confined to people with lower baseline vitamin D status; further research, including individual patient data meta-analysis of existing datasets, is needed to clarify this issue. Children and people with frequent severe asthma exacerbations were under-represented; additional primary trials are needed to establish whether vitamin D can reduce the risk of severe asthma exacerbation in these groups.

Martinez FD, Chinchilli VM, Morgan WJ, et al. Use of **beclomethasone dipropionate as rescue treatment** for children with mild persistent asthma (**TREXA**): a randomised, double-blind, placebo-controlled trial. *Lancet* 2010; published online Feb 15. DOI:10.1016/S0140-6736(10)62145-9.

Martinez FJ, Calverley PM, Goehring UM,et al. Effect of **roflumilast** on exacerbations in patients with severe chronic obstructive pulmonary disease uncontrolled by combination therapy (**REACT**): a multicentre randomised controlled trial. Lancet. 2015 Feb 12. pii: S0140-6736(14)62410-7

Mastronarde JG, Anthonisen NR, Castro M, et al. Efficacy of **esomeprazole** for treatment of poorly controlled asthma**.** (**SARA**) N Engl J Med. 2009 Apr 9;360(15):1487-99.

Matsui EC, Abramson SL, Sandel MT. **Indoor Environment Control Practices** and Asthma Management. Pediatrics. 2016;138(5):e20162589.

Matsui EC, et al. Effect of an **Integrated Pest Management Intervention** on Asthma Symptoms Among Mouse-Sensitized Children & Adolescents With Asthma: Randomized Clinical Trial. JAMA. 2017 Mar 6.

Matthay MA, Brower RG, Carson S, et al. Randomized, Placebo-Controlled Clinical Trial of an Aerosolized Beta-**2 Agonist for Treatment of Acute Lung Injury**. Am J Respir Crit Care Med. 2011 May 11.

Matsuyama W, Mitsuyama H, Watanabe M, et al. Effects of **omega-3 polyunsaturated fatty acids** on inflammatory markers in COPD. Chest. 2005 Dec;128(6):3817-27. (InfoPOEMs: This small study found that a diet rich in omega-3 fatty acids causes small improvements in chronic obstructive pulmonary disease (COPD) symptoms. (LOE = 1b))

Maurer M, Rosén K, Hsieh HJ, et al. **Omalizumab** for the Treatment of Chronic Idiopathic or Spontaneous **Urticaria**. N Engl J Med. 2013 Feb 24.

Mazurek JM, White GE, Moorman JE, Storey E. **Patient-physician communication about work-related asthma**: what we do and do not know. Ann Allergy Asthma Immunol. 2015 Feb;114(2):97-102.e1.

McBride John T. The Association of **Acetaminophen and Asthma** Prevalence and Severity. Pediatrics 2011; peds.2011-1106; ahead of print November 7, 2011.

McCallum GB, Morris PS, Brown N, Chang AB. Culture-specific programs for children and adults from minority groups who have asthma. Cochrane Database Syst Rev. 2017 Aug 2;8:CD006580.

McCarney RW, et al. An overview of two Cochrane reviews of complementary treatments for chronic asthma: **acupuncture** & **homeopathy**. Respir Med. 2004 Aug;98(8):687-96.

McCarthy B, Casey D, Devane D, et al. **Pulmonary rehabilitation for chronic obstructive pulmonary disease**. Cochrane Database Syst Rev. 2015 Feb 23;2:CD003793.
Pulmonary rehabilitation relieves dyspnoea and fatigue, improves emotional function and enhances the sense of control that individuals have over their condition. These improvements are moderately large and clinically significant. Rehabilitation serves as an important component of the management of COPD and is beneficial in improving health-related quality of life and exercise capacity. It is our opinion that additional RCTs comparing pulmonary rehabilitation and conventional care in COPD are not warranted. Future research studies should focus on identifying which components of pulmonary rehabilitation are essential, its ideal length and location, the degree of supervision and intensity of training required and how long treatment effects persist. This endeavour is important in the light of the new subgroup analysis, which showed a difference in treatment effect on the CRQ between hospital-based and community-based programmes but no difference between exercise only and more complex pulmonary rehabilitation programmes.

McCracken JL, Veeranki SP, Ameredes BT, et al. **Diagnosis and Management of Asthma in Adults**: A Review. JAMA. 2017 Jul 18;318(3):279-290.

McDonough JE, Yuan R, Suzuki M, et al. **Small-airway obstruction and emphysema in chronic obstructive pulmonary disease**. N Engl J Med 2011;365:1567-75.

McGeachie MJ, et al; CAMP. **Patterns of Growth and Decline in Lung Function** in Persistent Childhood Asthma. (CAMP) N Engl J Med. 2016 May 12;374(19):1842-52.

McGrath KW, Icitovic N, Boushey HA, et al. for the National Heart, Lung, and Blood Institute's Asthma Clinical Research Network of the National Heart, Lung, and Blood Institute. A Large Subgroup of Mild-to-Moderate Asthma is Persistently **Non-Eosinophilic**. Am J Respir Crit Care Med. 2012 Jan 20. (Approximately half of patients)

McIvor AR, Kaplan A, Koch C, Sampalis JS. **Montelukast** as an alternative to low-dose inhaled corticosteroids in the management of **mild asthma (the SIMPLE trial)**: an open-label effectiveness trial. Can Respir J 2009;16(Suppl A):11A-21A.

McKeever T, Mortimer K, Bradshaw L, et al. TEmporarily **quadrupling the dose of inhaled steroid** to prevent asthma exacerbations: FAST. Health Technol Assess. 2018 Dec;22(70):1-82.

McKeever T, Mortimer K, Wilson A, et al. **Quadrupling inhaled glucocorticoid** dose to abort asthma exacerbations. N Engl J Med. DOI: 10.1056/NEJMoa1714257.

McLean S, Chandler D, Nurmatov U, et al. **Telehealthcare for asthma**. Cochrane Database of Systematic Reviews 2010, Issue 10. Art. No.: CD007717. DOI: 10.1002/14651858. CD007717.pub2. Telehealthcare interventions are unlikely to result in clinically relevant improvements in health outcomes in those with relatively mild asthma, but they may have a role in those with more severe disease who are at high risk of hospital admission.

McMahon Ann W., Levenson Mark S., . McEvoy Bradley W,et al. **Age** and Risks of FDA–Approved **Long-Acting β2-Adrenergic Receptor Agonists**. Pediatrics 2011; peds.2010-1720; published ahead of print October 24, 2011

McNicholl DM, Stevenson M, McGarvey LP, Heaney LG. The utility of fractional **exhaled nitric oxide suppression** in the identification of nonadherence in difficult asthma. Am J Respir Crit Care Med 2012; 186:1102–1108.

Medical Letter. **Arformoterol (Brovana)** for COPD). Jyly 2, 2007.

Medical Letter. Treatment Guidelines: **Drugs for Asthma**. Dec 2008, **Feb 2012.**

Medical Letter- Treatment Guidelines. **Drugs for Allergic Disorders**. Feb 2010, **May 2013**.

Medical Letter. **Bronchial Thermoplasty** for Asthma. Aug 23, 2010.

Medley H, Orozco S, Allen A. Efficacy and Safety Profile of **Fluticasone Furoate** Administered Once Daily in the Morning or Evening: A Randomized, Double-Blind, Double-Dummy, Placebo-Controlled Trial in Adult and Adolescent Patients With Persistent Bronchial Asthma. Clin Ther. 2012 Jul 12.

Mehta AJ, Miedinger D, Keidel D, et al; SAPALDIA-team. **Occupational Exposure to Dusts, Gases and Fumes** and Incidence of COPD in SAPALDIA.

Am J Respir Crit Care Med. 2012 Apr 6.
Mehta R, Hardes K, Kelleher D, et al. Effects of Moderate **Hepatic Impairment** on the Pharmacokinetic Properties and Tolerability of **Umeclidinium and Vilanterol** in Inhalational Umeclidinium Monotherapy and Umeclidinium/Vilanterol Combination Therapy: An Open-Label, Nonrandomized Study. Clin Ther. 2014 Jun 16.
Mendes FA, Gonçalves RC, Nunes MP, et al. Effects of **aerobic training** on psychosocial morbidity and symptoms in patients with asthma: a randomized clinical trial. Chest. 2010 Aug;138(2):331-7.
Mendola P, Wallace M, Hwang BS, et al. **Preterm birth** and **air pollution**: Critical windows of exposure for women with **asthma**. J Allergy Clin Immunol. 2016 Feb 23.
Mendoza L, Horta P, Espinoza J, et al. **Pedometers to enhance physical activity in COPD**: a randomised controlled trial. Eur Respir J. 2014 Sep 26.
Merckx J, Ducharme FM, Martineau C, et al. **Respiratory Viruses and Treatment Failure in Children With Asthma** Exacerbation. Pediatrics. 2018 Jun 4.
Mentz RJ, Wojdyla D, Fiuzat M, et al. Association of **Beta-Blocker Use and Selectivity** With Outcomes in Patients With Heart Failure and Chronic Obstructive Pulmonary Disease (from OPTIMIZE-HF). Am J Cardiol. 2013 Feb 15;111(4):582-7.
Mets OM, Buckens CF, Zanen P, et al. Identification of chronic obstructive pulmonary disease in **lung cancer screening computed tomographic scans**. JAMA. 2011 Oct 26;306(16):1775-81.
Mensah GA, Kiley JP, Gibbons GH. Generating evidence to inform an update of **asthma clinical practice guidelines**: Perspectives from the National Heart, Lung, and Blood Institute. J Allergy Clin Immunol. 2018 Sep;142(3):744-748.
Metz M, Ohanyan T, Church MK, et al. Retreatment With **Omalizumab** Results in Rapid Remission in Chronic Spontaneous and Inducible **Urticaria**. JAMA Dermatol. 2014 Jan 29
Milan SJ, Hart A, Wilkinson M. **Vitamin C for asthma** and exercise-induced bronchoconstriction. Cochrane Database of Systematic Reviews 2013, Issue 10. Art. No.: CD010391. DOI: 10.1002/14651858.CD010391.pub2. Currently, evidence is not available to provide a robust assessment on the use of vitamin C in the management of asthma or exerciseinduced bronchoconstriction.
Milger K, Schroeder I, Behr J, et al. **Omalizumab Rescue Therapy** for Refractory Status Asthmaticus. Ann Intern Med. 2018 Nov 20
Miller MR, Levy ML. **Chronic obstructive pulmonary disease**: **missed diagnosis versus misdiagnosis**. BMJ. 2015 Jul 1;351:h3021.
Millett C, Tayu Lee J, Laverty A, Glantz S, Majeed A. Hospital admissions for childhood asthma after **smoke-free legislation** in England. Pediatrics 21 Jan 2013.
Miravitlles M, Moragas A, Hernández S, Bayona C, Llor C. Is it possible to **identify exacerbations of mild to moderate COPD that do not require antibiotic treatment**? Chest. 2013 Nov;144(5):1571-7.
Miravitlles M. **Diagnosis of asthma-COPD overlap: the five commandments**. Eur Respir J. 2017 May 1;49(5).
Mitchell KE, Johnson-Warrington V, Apps LD, et al. A **self-management programme for COPD**: a randomised controlled trial. Eur Respir J. 2014 Dec;44(6):1538-47.
Moen MD. **Indacaterol**: In Chronic Obstructive Pulmonary Disease. Drugs. 2010 Dec 3;70(17):2269-2280. doi: 10.2165/11203960-000000000-00000.
Moffatt MF, Gut IG, et al. GABRIEL Consortium. A large-scale, consortium-based **genomewide association study of asthma**. N Engl J Med. 2010 Sep 23;363(13):1211-21.
Mohabeer Hart M, Boffito M, et al. Unexpected rapid weight gain in a patient with HIV and anorexia. (**Iatrogenic Cushings-fluticasone-ritonavir**) BMJ. 2015 Oct 29;351:h5551.
Mohammed S, Goodacre S. **Intravenous and nebulised magnesium** sulphate for acute asthma: systematic review and meta-analysis. Emerg Med J. 2007 Dec;24(12):823-30.
Mometasone (Asmanex twisthaler) For Asthma. Med Letter Dec 2005;47:98-99. FDA: age ≥12 220-440ug bid or 440ug od (Fardon TC, Lee DK, Haggart K, et al. Adrenal suppression with dry powder formulations of fluticasone propionate & mometasone furoate. Am J Respir Crit Care Med. 2004 Nov 1;170(9):960-6. Epub 2004 Jun 7; Corren J, Berkowitz R, Murray JJ, Prenner B. Comparison of once-daily mometasone furoate versus once-daily budesonide in patients with moderate persistent asthma. Int J Clin Pract. 2003 Sep;57(7):567-72; Mortimer KJ, Harrison TW, Tattersfield AE. Effects of inhaled corticosteroids on bone. Ann Allergy Asthma Immunol. 2005 Jan;94(1):15-21; quiz 22-3, 79.)
Morales DR, Jackson C, Lipworth BJ, et al. Adverse respiratory effect of acute **beta-blocker exposure in asthma**: a systematic review and meta-analysis of randomized controlled trials. Chest. 2013 Nov 7.
Morales DR, et al. Respiratory effect of **beta-blocker eye drops in asthma**: population based study and meta-analysis of clinical trials. Br J Clin Pharmacol. 2016 May 10.
Morgan WJ, et al. Inner-City Asthma Study Gp. Results of a **home-based environmental intervention** among urban children with asthma. N Engl J Med. 2004 Sep 9;351(11):1068-80.
Morse RB, Hall M, Fieldston ES, et al. Hospital-level compliance with **asthma care quality measures** at children's hospitals and subsequent asthma-related outcomes. JAMA. 2011;306(13):1454-1460.
Mortimer KJ, et al. Oral and inhaled corticosteroids and **adrenal insufficiency**: a case-control study. Thorax. 2006 May;61(5):405-8. Epub 2006 Mar 3.
Mukherjee M, Aleman Paramo F, Kjarsgaard M, et al. **Weight-adjusted Intravenous Reslizumab** in Severe Asthma with Inadequate Response to **Fixed-dose Subcutaneous Mepolizumab**. Am J Respir Crit Care Med. 2017 Sep 15.
Mutius E, Drazen J. A Patient with **Asthma** Seeks Medical Advice in **1828, 1928, and 2012** N Engl J Med 2012; 366:827-834.
Murk W, Risnes KR., Bracken MB. **Prenatal or Early-Life Exposure to Antibiotics** and Risk of Childhood Asthma: A Systematic Review. Pediatrics 2011; 127:6 1125-1138.
Murphy V, Namazy J, Powell H, et al. A meta-analysis of **adverse perinatal outcomes** in women with asthma. BJOG. 2011 Oct;118(11):1314-1323.
Murray C, Dofen P, Lowe, L et al. Diagnosis of asthma in symptomatic children based on measures of lung function: an analysis of data from a population-based birth cohort study. Lancet Child Adolesc Health. 2017.
Murray CS, Foden P, Sumner H, et al. Preventing Severe Asthma Exacerbations in Children: A Randomised Trial of **Mite Impermeable Bedcovers**. Am J Respir Crit Care Med. 2017 Mar 10.
Naar S, Ellis D, Cunningham P, et al. Comprehensive **Community-Based Intervention and Asthma Outcome**s in African American Adolescents. Pediatrics. 2018 Sep 5.
Nair P, Milan SJ, Rowe BH. Addition of **intravenous aminophylline** to inhaled beta(2)-agonists in adults with acute asthma. Cochrane Database Syst Rev. 2012 Dec 12;12:CD002742. doi: 10.1002/14651858.CD002742.pub2. The use of intravenous aminophylline did not result in significant additional bronchodilation compared to standard care with inhaled beta(2)-agonists in patients experiencing an asthma exacerbation in the ED setting, or in a significant reduction in the risk of hospital admission.
Nair P, Wenzel S, Rabe KF, et al. Oral Glucocorticoid-Sparing Effect of **Benralizumab** in Severe Asthma. N Engl J Med. 2017 May 22.
Najafzadeh M, Marra CA, Sadatsafavi M, Aaron SD, Sullivan SD, Vandemheen KL, Jones PW, Fitzgerald JM. Cost effectiveness of therapy with combinations of long acting bronchodilators and inhaled steroids for treatment of COPD. Thorax. 2008 Nov;63(11):962-7. Epub 2008 Jul 11. TFS had significantly better quality of life and fewer hospitalisations than patients treated with

TP but these improvements in health outcomes were associated with increased costs. Neither TFS nor TS are economically attractive alternatives compared with monotherapy with T. (T=tiotropium)

Nannini LJ, Cates CJ, Lasserson TJ, Poole P. Combined **corticosteroid and long-acting** beta-agonist in one inhaler versus long-acting beta-agonists for chronic obstructive pulmonary disease. Cochrane Database Syst Rev. 2007 Oct 17;(4):CD006829. Combination therapy was more effective than long-acting beta-agonists in reducing COPD exacerbation rates, although the evidence for the effects on hospitalisations was mixed, and requires further exploration. No significant impact on mortality was found even with additional information from the TORCH trial. The superiority of combination inhalers should be viewed against the increased risk of side-effects, particularly pneumonia.

Nannini LJ, Lasserson TJ, Poole P. **Combined corticosteroid and long-acting beta(2)-agonist in one inhaler versus long-acting beta(2)-agonists** for chronic obstructive pulmonary disease. Cochrane Database Syst Rev. 2012 Sep 12;9:CD006829. doi: 10.1002/14651858.CD006829.pub2. Concerns over the analysis and availability of data from the studies bring into question the superiority of ICS/LABA over LABA alone in preventing exacerbations. The effects on hospitalisations were inconsistent and require further exploration. There was moderate quality evidence of an increased risk of pneumonia with ICS/LABA. There was moderate quality evidence that treatments had similar effects on mortality. Quality of life, symptoms score, rescue medication use and FEV(1) improved more on ICS/LABA than on LABA, but the average differences were probably not clinically significant for these outcomes. To an individual patient the increased risk of pneumonia needs to be balanced against the possible reduction in exacerbations.

Nannini LJ, Poole P, Milan SJ, et al. **Combined corticosteroid and long-acting beta2-agonist** in one inhaler **versus inhaled corticosteroids** alone for chronic obstructive pulmonary disease. Cochrane Database Syst Rev. 2013 Aug 30;8:CD006826. doi: 10.1002/14651858.CD006826.pub2. Combination ICS and LABA offer some clinical benefits in COPD compared with ICS alone, especially for reduction in exacerbations. This review does not support the use of ICS alone when LABAs are available. Adverse events were not significantly different between treatments.

Nannini LJ, Poole P, Milan SJ, et al. **Combined corticosteroid and long-acting beta-agonist in one inhaler versus placebo** for chronic obstructive pulmonary disease. Cochrane Database Syst Rev. 2013 Nov 10;11:CD003794. Combined inhaler therapy led to around a quarter fewer COPD exacerbations than were seen with placebo. A significant reduction in all-cause mortality was noted, but this outcome was dominated by one trial (TORCH), emphasising the need for further trials of longer duration. Increased risk of pneumonia is a concern; however, this did not translate into increased exacerbations, hospitalisations or deaths.

Navanandan N, Federico M, Mistry RD. **Positive Expiratory Pressure** for the Treatment of Acute Asthma Exacerbations: A Randomized Controlled Trial. J Pediatr. 2017 Mar 8.

Newman NC, Ryan PH, Huang B, et al. **Traffic-Related Air Pollution** and **Asthma** Hospital Readmission in Children: A Longitudinal Cohort Study. J Pediatr. 2014 Mar 25.

Ni CM, Greenstone I, Lasserson TJ, et al. **Addition of inhaled long-acting beta2-agonists to inhaled steroids** as first line therapy for persistent asthma in steroid-naive adults and children. Cochrane Database Syst Rev. 2009 Oct 7;(4):CD005307. In steroid-naive patients with mild to moderate airway obstruction, the combination of ICS and LABA does not significantly reduce the risk of patients with exacerbations requiring rescue oral corticosteroids over that achieved with a similar dose of ICS alone. However, it significantly improves lung function, reduces symptoms and marginally decreases rescue ss2-agonist use. Initiation of a higher dose of ICS is more effective at reducing the risk of exacerbations requiring rescue systemic corticosteroids, and of withdrawals, than combination therapy. Although children appeared to respond similarly to adults, no firm conclusions can be drawn regarding combination therapy in steroid-naive children, given the small number of children contributing data.

Ni CM, Greenstone I, Danish A, et al. Long-acting beta2-agonists versus placebo in addition to inhaled corticosteroids in children and adults with chronic asthma. Cochrane Database Syst Rev. 2005 Oct 19;(4):CD005535.

Ni CM, Lasserson TJ, Greenstone I, et al. Addition of **long-acting beta-agonists** to inhaled corticosteroids for chronic asthma in **children**. Cochrane Database Syst Rev. 2009 Jul 8;(3):CD007949. In children with persistent asthma, the addition of LABA to ICS was not associated with a significant reduction in the rate of exacerbations requiring systemic steroids, but was superior for improving lung function compared to the same dose of ICS. Similarly, compared to a double dose ICS, the combination of LABA and ICS did not significantly increase the risk of exacerbations requiring oral steroids, but was associated with a significantly greater improvement in PEF and growth. The possibility of an increased risk of rescue oral steroids and hospital admission with LABA therapy needs to be further examined.

Ni H, Soe Z, Moe S. **Aclidinium** bromide for stable chronic obstructive pulmonary disease. Cochrane Database Syst Rev. 2014 Sep 19;9:CD010509. Aclidinium is associated with improved quality of life and reduced hospitalisations due to severe exacerbations in patients with moderate to severe stable COPD compared to placebo. Overall, aclidinium did not significantly reduce mortality, serious adverse events or exacerbations requiring oral steroids or antibiotics, or both.Currently, the available data are insufficient and of very low quality in comparisons of the efficacy of aclidinium versus tiotropium. The efficacy of aclidinium versus LABAs cannot be assessed due to inaccurate data. Thus additional trials are recommended to assess the efficacy and safety of aclidinium compared to other LAMAs or LABAs.

NICE Oct/10 Guidance: **Omalizumab** for the treatment of severe persistent allergic asthma in children aged 6-11. http://www.nice.org.uk/nicemedia/live/13256/51345/51345.pdf

NICE: 2010 CG101 **Chronic obstructive pulmonary disease** (update): full guideline. London: National Institute for Health and Clinical Excellence, 2010. (http://guidance.nice.org.uk/CG101/Guidance .)

NICE: National Institute for Health and Care Excellence (NICE). **Omalizumab** for treating severe persistent allergic asthma (review of technology appraisal guidance 133 and 201). London (UK): National Institute for Health and Care Excellence (NICE); 2013 Apr.

Nici L, Donner C, et al., et al. **American Thoracic Society/European Respiratory Society** statement on **pulmonary rehabilitation**. Am J Respir Crit Care Med. 2006 Jun 15;173(12):1390-413.

Nici L, Lareau S, ZuWallack R. **Pulmonary Rehabilitation** in the Treatment of Chronic Obstructive Pulmonary Disease. Am Fam Physician. 2010 Sep 15;82(6):655-660.

Niewoehner DE, et al. Prevention of exacerbations of COPD with **tiotropium**, a once-daily inhaled anticholinergic bronchodilator -an RCT. Ann Intern Med. 2005 Sep 6;143(5):317-26. (InfoPOEMs: Daily treatment with tiotropium for 6 months slightly decreases the number of patients experiencing a chronic obstructive pulmonary disease (COPD) exacerbation, though it doesn't decrease the number of patients who will be hospitalized for an exacerbation. (LOE = 1b-))

Niewoehner, Dennis E. Outpatient Management of **Severe COPD**. N Engl J Med 2010 362: 1407-1416

Nilsson E, Chawes BL, et al. Effect of **delivery device on systemic exposure to inhaled Fluticasone** Propionate in children with asthma. Br J Clin Pharmacol. 2014 Feb 17.

Nkoy FL, Fassl BA, Wilkins VL, et al. **Ambulatory Management of Childhood Asthma** Using a Novel Self-management Application. Pediatrics. 2019 May 16.

Nkoy FL, Stone BL, Fassl BA, et al. Longitudinal Validation of a **Tool for Asthma Self-Monitoring**. Pediatrics. 2013 Nov 11.

Nordin JD, Vazquez-Benitez G, Olsen A, et al. Safety of guidelines recommending live attenuated influenza **vaccine for routine use in children** and adolescents with asthma. Vaccine. 2019 Jul 9;37(30):4055-4060.

Norman G, Faria R, Paton F, et al. **Omalizumab** for the treatment of severe persistent allergic asthma: a systematic review and economic evaluation. Health Technol Assess. 2013 Nov;17(52):1-342.

Normansell R, Walker S, Milan SJ, et al. **Omalizumab for asthma in adults and children**. Cochrane Database Syst Rev. 2014 Jan 13;1:CD003559. Omalizumab was effective in reducing asthma exacerbations and hospitalisations as an adjunctive therapy to inhaled steroids and during steroid tapering phases of clinical trials. Omalizumab was significantly more effective than placebo in increasing the numbers of participants who were able to reduce or withdraw their inhaled steroids. Omalizumab was generally well tolerated, although more injection site reactions were seen with omalizumab. Further assessment in paediatric populations is necessary, as is direct double-dummy comparison with ICS.

Normansell R, Kew KM, Stovold E. Interventions to **improve adherence to inhaled steroids for asthma**. Cochrane Database of Systematic Reviews 2017, Issue 4. Art. No.: CD012226. Pooled results suggest that a variety of interventions can improve adherence. The clinical relevance of this improvement, highlighted by uncertain and inconsistent impact on clinical outcomes such as quality of life and asthma control, is less clear. We have low to moderate confidence in these findings owing to concerns about risk of bias and inconsistency. Future studies would benefit from predefining an evidence-based 'cut-off' for acceptable adherence and using objective adherence measures and validated tools and questionnaires. When possible, covert monitoring and some form of blinding or active control may help disentangle effects of the intervention from effects of inclusion in an adherence trial.

Noyes K, Bajorska A, Fisher S, et al. Cost-Effectiveness of the **School-Based Asthma Therapy (SBAT)** Program. Pediatrics. 2013 Feb 11.

Nyenhuis SM, Krishnan JA, Berry A, et al. **Race** is associated with differences in airway inflammation in patients with asthma. J Allergy Clin Immunol. 2016 Dec 31.

Oba Y, Sarva ST, et al. Efficacy and safety of **long-acting beta-agonist/long-acting muscarinic antagonist combinations in COPD**: a network meta-analysis. Thorax. 2015 Oct 21.

Oborne J, Mortimer K, Hubbard RB, et al. **Quadrupling the Dose of Inhaled Corticosteroid** to Prevent Asthma Exacerbations: A Randomized, Double Blind, Placebo Controlled, Parallel Group, Clinical Trial. Am J Respir Crit Care Med. 2009 Jul 9. [Epub ahead of print] Although our primary outcome did not reach statistical significance, quadrupling the dose of inhaled corticosteroid when asthma control starts to deteriorate appears to

O'byrne PM, et al. Budesonide/Formoterol combination therapy as both **maintenance and reliever** medication in asthma (**STAY** trial). Am J Respir Crit Care Med. 2005 Jan 15;171(2):129-36.
O'Byrne PM, et al. Low dose inhaled budesonide & formoterol in mild persistent asthma: the **OPTIMA** randomized trial. Am J Respir Crit Care Med. 2001 Oct 15;164(8 Pt 1):1392-7.
O'byrne PM, et al. Effects of early intervention with inhaled budesonide on lung function in newly diagnosed asthma. Chest. 2006 Jun;129(6):1478-85. Long-term, once-daily treatment with low-dose budesonide improved both prebronchodilator and postbronchodilator FEV(1) in patients with recent-onset, persistent asthma, and reduced the loss of lung function over time (1 & 3yrs).
O'Byrne PM, Naya IP, Kallen A, et al. Increasing doses of inhaled corticosteroids compared to adding long-acting inhaled beta2-agonists in achieving asthma control. Chest. 2008 Dec;134(6):1192-9. Epub 2008 Aug 8. Time with well-controlled asthma was improved by 19% (95% confidence interval [CI], 3 to 35%; p = 0.017) by adding formoterol, 24 microg/d, to therapy with budesonide, 200 microg/d, compared to 2% (95% CI, -9 to 12%; p=0.76) with therapy with budesonide, 800 microg/d, alone. The addition of formoterol to therapy with low-dose budesonide increases the probability of well-controlled asthma compared to a substantial increase (4X) in the dose of an ICS.
O'Byrne PM, Lamm CJ, Busse WW, Tan WC, Pedersen S; START Investigators Group. The effects of inhaled **budesonide** on lung function in **smokers** and nonsmokers with mild persistent asthma. Chest. 2009 Dec;136(6):1514-20.
O'Byrne PM, Pedersen S, Carlsson LG, et al. **Risks of Pneumonia** in Asthmatic Patients Taking Inhaled Corticosteroids. Am J Respir Crit Care Med. 2010 Oct 1.
O'Byrne PM, FitzGerald JM, Bateman ED, et al. Inhaled combined **budesonide–formoterol as needed** in mild asthma. N Engl J Med 2018; 378: 1865-76.
O'Callaghan C, White JA, Kantar A. **Nebulization of corticosteroids** to asthmatic children: Large variation in dose inhaled. Respirology. 2013 Nov 24
O'Connor GT, Lynch SV, Bloomberg GR, et al. **Early-life home environment** and risk of asthma among inner-city children. J Allergy Clin Immunol. 2017 Sep 12.
O'donnell DE, et al. Effect of **Fluticasone Propionate/Salmeterol** on Lung Hyperinflation and Exercise Endurance in COPD. Chest. 2006 Sep;130(3):647-56.
O'Driscoll BR and Beasley R. Avoidance of high concentration **oxygen in chronic obstructive pulmonary disease**. BMJ 2010 Oct 18; 341:c5549.
Osadnik CR, McDonald CF, Miller BR, et al. The effect of **positive expiratory pressure (PEP) therapy** on symptoms, quality of life and incidence of re-exacerbation in patients with acute exacerbations of chronic obstructive pulmonary disease: a multicentre, randomised controlled trial. Thorax. 2013 Sep 4.
Ogale SS, Lee TA, Au DH, Boudreau DM, et al. **Cardiovascular Events** Associated With **Ipratropium** Bromide in COPD. Chest. 2009 Apr 10. We found an increased risk of CVEs associated with the use of ipratropium within the past 6 months. These findings are consistent with previous concerns raised about the cardiovascular safety of ipratropium bromide.
Okelo SO, Butz AM, Sharma R, et al. **Interventions To Modify Health Care Provider Adherence** to Asthma Guidelines. AHRQ Comparative Effectiveness Review. Rockville (MD): Agency for Healthcare Research and Quality (US); 2013 Mar. Report No.: 13-EHC022-EF
Okelo SO, Butz AM, Sharma R, et al. Interventions to modify **health care provider adherence to asthma guidelines**: a systematic review. Pediatrics. 2013 Sep;132(3):517-34.
Olin JT, Wechsler ME. **Asthma**: pathogenesis and **novel drugs for treatment**. BMJ. 2014 Nov 24;349:g5517.
Oliver A, Vanburen S, et al. Tolerability of **Fluticasone Furoate/Vilanterol** Combination Therapy in **Children** Aged 5 to 11 Years With Persistent **Asthma**. Clin Ther. 2014 Apr 29.
Ortega HG, Liu MC, Pavord ID, et al. **Mepolizumab** treatment in patients with severe eosinophilic asthma. (**Mensa**) N Engl J Med. DOI: 10.1056/NEJMoa1403290.
Ortiz-Alvarez O, Mikrogianakis A; **Canadian Paediatric Society**, Acute Care Committee. Managing the paediatric patient with an **acute asthma** exacerbation. Paediatr Child Health 2012;17:251-5.www.cps.ca/english/statements/AC/AC12-01.htm (accessed May 9, 2012).
Ostrom NK, Decotiis BA, et al. Comparative efficacy & safety of low-dose **fluticasone** propionate & **montelukast** in children with persistent asthma. J Pediatr.2005Aug;147(2):213-20.
Overbeek SE, et al. **Formoterol added** to low-dose budesonide has no additional antiinflammatory effect in asthmatic patients. Chest. 2005 Sep;128(3):1121-7. CONCLUSIONS: Our results demonstrate that BUD administered at a low dose has significant antiinflammatory effects in patients with mild asthma. No significant additional antiinflammatory effects could be demonstrated either by adding formoterol or by increasing the dose of BUD.
Pakhale S, Baron J, Dent R, et al. Effects of **weight loss** on airway responsiveness in obese adults with asthma: does weight loss lead to reversibility of asthma? Chest. 2015 Jun;147(6):1582-90.
Panickar J, Lakhanpaul M, Lambert PC, et al. **Oral prednisolone** 10-20mg od x 5days for preschool children with acute **virus-induced wheezing**. N Engl J Med. 2009 Jan 22;360(4):329-38. In preschool children (n=700) presenting to a hospital with mild-to-moderate wheezing associated with a viral infection, oral prednisolone was not superior to placebo.
Paniagua N, Lopez R, Muñoz Net al. Randomized Trial of **Dexamethasone Versus Prednisone** for Children with Acute Asthma Exacerbations. J Pediatr. 2017 Dec;191:190-196.e1.
Papi A, et al. **Beclomethasone/formoterol vs budesonide/formoterol** combination therapy in asthma. Eur Respir J. 2006 Nov 15; [Epub ahead of print] The new fixed combination of beclomethasone and formoterol 200/12ug in HFA Modulite((R)) pMDI is equivalent to the marketed combination of budesonide and formoterol 400/12ug in terms of efficacy and tolerability profile.
Papi A, Canonica GW, Maestrelli P, et al. BEST Study Group. Rescue use of **beclomethasone and albuterol in a single inhaler** for mild asthma. N Engl J Med. 2007 May 17;356(20):2040-52. In patients with mild asthma, the symptom-driven use of inhaled beclomethasone (250 microg) and albuterol (100 microg) in a single inhaler is as effective as regular use of inhaled beclomethasone (250 microg twice daily) and is associated with a lower 6-month cumulative dose of the inhaled corticosteroid.
Papi A, Corradi M, Pigeon-Francisco C, et al. **Beclometasone–formoterol as maintenance and reliever** treatment in patients with asthma: a double-blind, randomised controlled trial. Lancet Respir Med 2013; 1: 23–31.
Papi A, Brightling C, Pedersen SE, et al. **Asthma**. Lancet. 2017 Dec 19
Pappalardo AA, Gerald LB. Let Them Breathe: A Plea to Pediatricians to **Advocate for Stock Inhaler Policies at School**. Pediatrics. 2019 Jun 4.
Parameswaran K, Belda J, Rowe BH. Addition of **intravenous aminophylline** to beta2-agonists in adults with acute asthma. Cochrane Database Syst Rev. 2000;(4):CD002742.
Parameswaran GI, Sethi S. **Long-term macrolide therapy** in chronic obstructive pulmonary disease. CMAJ. 2014 Oct 21;186(15):1148-1152.
Parikh K, Hall M, Mittal V, et al Comparative Effectiveness of **Dexamethasone versus Prednisone** in Children Hospitalized with **Asthma**. J Pediatr. 2015 Sep;167(3):639-644.e1.
Parikh K, Keller S, Ralston S. **Inpatient Quality Improvement Interventions for Asthma**: A Meta-analysis. Pediatrics. 2018 Apr 5.
Parshall MB, Schwartzstein RM, Adams L, et al. on behalf of the ATS Committee on Dyspnea. An Official American Thoracic Society (**ATS**) Statement: Update on the Mechanisms, Assessment, and Management of **Dyspnea**. Am J Respir Crit Care Med. 2012 Feb 15;185(4):435-452.
Parsons JP, Hallstrand TS, Mastronarde JG, et al; American Thoracic Society Subcommittee on **Exercise-induced Bronchoconstriction**. An Official American Thoracic Society (**ATS**) Clinical Practice Guideline: Exercise-induced Bronchoconstriction. Am J Respir Crit Care Med. 2013 May 1;187(9):1016-27.
Pasqua F, Biscione G, Crigna G, et al. Combining **triple therapy** and pulmonary rehabilitation in patients with advanced **COPD**: A pilot study. Respir Med. 2009 Nov 3.
Patel M, Pilcher J, Pritchard A, et al, for the **SMART** Study Group. Efficacy and safety of **maintenance and reliever** combination **budesonide-formoterol** inhaler in patients with

asthma at risk of severe exacerbations: a randomised controlled trial. Lancet Respir Med 2013; 1: 32–42.
Paton J, et al. **Adrenal** responses to low dose synthetic ACTH (Synacthen) in kids receiving high dose inhaled fluticasone. Arch Dis Child. 2006Oct;91(10):808-13. Epub 2006Mar 23.
Paton J. **Asthma: standards of care**. Arch Dis Child. 2013 Dec;98(12):928-9.
Paul I. M., Maselli J. H., Hersh A. L., et al. **Antibiotic Prescribing** During Pediatric Ambulatory Care Visits for Asthma. *Pediatrics*, 2011; DOI: 10.1542/peds.2011-0218
Pauwels RA, et al. **START** Investigators Group. Early intervention with **budesonide** in mild persistent asthma: a randomised, double-blind trial. Lancet. 2003Mar 29;361(9363):1071-6.
Pauwels RA, et al. Effect of inhaled **formoterol and budesonide** on exacerbations of asthma. Formoterol and Corticosteroids Establishing Therapy (**FACET**) International Study Group. N Engl J Med. 1997 Nov 13;337(20):1405-11. Erratum in: N Engl J Med 1998 Jan 8;338(2):139.
Pauwels RA, et al; **RELIEF** Study investigators. Formoterol as relief medication in asthma: a worldwide safety and effectiveness trial. Eur Respir J. 2003 Nov;22(5):787-94.
Pavord ID, Cox G, Thomson NC, et al Safety and Efficacy of **Bronchial Thermoplasty** in Symptomatic, Severe Asthma. Am J Respir Crit Care Med. 2007 Sep 27; [Epub ahead of print] Bronchial thermoplasty is associated with a short-term increase in asthma-related morbidity. However, there is preliminary evidence of long-lasting improvement in asthma control.
Pavord ID, Korn S, Howarth P, et al. **Mepolizumab** for severe eosinophilic asthma (DREAM): a multicentre, double-blind, placebo-controlled trial. Lancet. 2012 Aug 18;380(9842):651-9.
Pavord ID, Beasley R, Agusti A, et al. **After asthma**: redefining airways diseases. Lancet. 2017 Sep 11.
Pearlman DS, et al. Once-daily **ciclesonide** improves lung function and is well tolerated by patients with mild-to-moderate persistent asthma. J Allergy Clin Immunol. 2005 Dec;116(6):1206-12.
Pearlman DS, Laforce CF, Kaiser K. **Fluticasone/Formoterol combination therapy** compared with monotherapy in adolescent and adult patients with mild to moderate asthma. Clin Ther. 2013 Jul;35(7):950-66.
Pedersen S, et al. A comparative study of inhaled **ciclesonide** 160 microg/day and fluticasone 176 microg/day in children with asthma. Pediatr Pulmonol. 2006 Oct;41(10):954-61.
Peters SP, Kunselman SJ, Icitovic N, et al. **Tiotropium** bromide step-up therapy for adults with uncontrolled **asthma**. (**TALC**) N Engl J Med 2010. DOI: 10.1056/NEJMoa1008770. n=174, 14 wk
Peters SP et al. Predictors of response to **tiotropium versus salmeterol** in asthmatic adults. J Allergy Clin Immunol 2013 Nov; 132:1068.
Peters SP et al. Serious asthma events with **budesonide plus formoterol vs. budesonide** alone. N Engl J Med 2016 Sep 1; 375:850.
Petsky HL, et al. Tailored interventions based on **exhaled nitric oxide** versus clinical symptoms for asthma in children & adults. Cochrane Database Syst Rev. 2009Oct7;(4):CD006340.
Petsky HL, Cates CJ, Lasserson TJ, et al. A systematic review and meta-analysis: tailoring asthma treatment on **eosinophilic markers** (exhaled nitric oxide or sputum eosinophils). Thorax. 2012 Mar;67(3):199-208.
Petsky HL, Cates CJ, Kew KM, et al. Tailoring **asthma treatment on eosinophilic markers (exhaled nitric oxide or sputum eosinophils**): a systematic review and meta-analysis. Thorax. 2018 Jun 1.
Petsky HL, Kew KM, Turner C, Chang AB. **Exhaled nitric oxide levels** to guide treatment for adults with asthma. Cochrane Database of Systematic Reviews 2016, Issue 9. Art. No.: CD011440. With new studies included since the last version of this review, which included adults and children, this updated meta-analysis in adults with asthma showed that tailoring asthma medications based on FeNO levels (compared with primarily on clinical symptoms) decreased the frequency of asthma exacerbations but did not impact on day-to-day clinical symptoms, end-of-study FeNO levels, or inhaled corticosteroid dose. Thus, the universal use of FeNO to help guide therapy in adults with asthma cannot be advocated. As the main benefit shown in the studies in this review was a reduction in asthma exacerbations, the intervention may be most useful in adults who have frequent exacerbations. Further RCTs encompassing different asthma severity, ethnic groups in less affluent settings, and taking into account different FeNO cutoffs are required.
Petsky HL;Li A;Chang AB. Tailored **interventions based on sputum eosinophils** versus clinical symptoms for asthma in children and adults. Cochrane Database Syst Rev. 2017 Aug 24;8:CD005603. In this updated review, tailoring asthma interventions based on sputum eosinophils is beneficial in reducing the frequency of asthma exacerbations in adults with asthma. Adults with frequent exacerbations and severe asthma may derive the greatest benefit from this additional monitoring test, although we were unable to confirm this through subgroup analysis. There is insufficient data available to assess tailoring asthma medications based on sputum eosinophilia in children.Further robust RCTs need to be undertaken and these should include participants with different underlying asthma severities and endotypes.
Peytremann-Bridevaux I, Arditi C, Gex G, Bridevaux PO, Burnand B. **Chronic disease management programmes** for adults with **asthma**. Cochrane Database of Systematic Reviews 2015, Issue 5. Art. No.: CD007988. DOI: 10.1002/14651858.CD007988.pub2. There is moderate to low quality evidence that chronic disease management programmes for adults with asthma can improve asthmaspecific quality of life, asthma severity, and lung function tests. Overall, these results provide encouraging evidence of the potential effectiveness of these programmes in adults with asthma when compared with usual care. However, the optimal composition of asthma chronic disease management programmes and their added value, compared with education or self-management alone that is usually offered to patients with asthma, need further investigation.
Philp JC, Maselli J, Pachter LM, Cabana MD. **Complementary and Alternative** Medicine Use and Adherence With **Pediatric Asthma** Treatment. Pediatrics. 2012 Apr 9.
Pike KC, Akhbari M, Kneale D, Harris KM. **Interventions for autumn exacerbations of asthma in children**. Cochrane Database of Systematic Reviews 2018, Issue 3. Art. No.: CD012393. Seasonal omalizumab treatment from four to six weeks before school return might reduce autumn asthma exacerbations. We found no evidence that this strategy is associated with increased adverse effects other than injection site pain, but it is costly. There were no data upon which to judge the effect of this or other seasonal interventions on asthma control, quality of life, or asthma-related death. In future studies definitions of exacerbations should be provided, and standardised where possible. To investigate possible differential effects according to subgroup, participants in future trials should be well characterised with respect to baseline asthma severity and exacerbation history in addition to age and gender.
Pinnock H, Shah R. Asthma. BMJ. 2007 Apr 21;334(7598):847-50.
Pinnock Hilary, Kendall Marilyn, Murray Scott A, et al. **Living and dying with severe chronic obstructive pulmonary disease**: multi-perspective longitudinal qualitative study. BMJ 2011;342:doi:10.1136/bmj.d142 (Published 24 Jan 2011)
Pinnock H, Hanley J, McCloughan L, et al. Effectiveness of **telemonitoring** integrated into existing clinical services on hospital admission for exacerbation of chronic obstructive pulmonary disease: researcher blind, multicentre, randomised controlled trial. BMJ 2013;347:f6070.
Pinnock H, Taylor SJ. **Self management for a man with asthma**. BMJ. 2015 Jul 24;351:h3970.
Poels PJ, et al. **Spirometry** in chronic obstructive pulmonary disease. BMJ. 2006 Oct 28;333(7574):870-1.
Pollart SM., Compton RM, Elward KS. Management of **Acute Asthma Exacerbations**. Am Fam Physician. 2011;84(1):40-47.
Poole P, Black PN. **Mucolytic agents for chronic bronchitis or chronic obstructive pulmonary disease**. Cochrane Database Syst Rev. 2010 Feb 17;2:CD001287.
Postma DS, O`Byrne PM, Pedersen S. Comparison of the effect of low-dose **ciclesonide and fixed-dose fluticasone propionate and salmeterol** combination on long-term asthma control. Chest. 2011 Feb;139(2):311-8.
Postma DS, Bush A, van den Berge M. **Risk factors** and early origins of **chronic obstructive pulmonary disease**. Lancet. 2014 Aug 11.

Postma DS, Rabe KF. The **Asthma-COPD Overlap Syndrome**. N Engl J Med. 2015 Sep 24;373(13):1241-9.
Powell H, Murphy VE, Taylor DR, et al. Management of asthma in pregnancy guided by measurement of **fraction of exhaled nitric oxide** (**FENO**): a double-blind, randomised controlled trial. Lancet 2011; 378: 983–90.
Powell C, Kolamunnage-Dona R, Lowe J, et al. **MAGNEsium** Trial In Children (**MAGNETIC**): a randomised, placebo-controlled trial and economic evaluation of nebulised magnesium sulphate in acute severe asthma in children. Health Technol Assess. 2013 Oct;17(45):1-216.
Prasad Kerlin M. **In the clinic**. **Asthma**. Ann Intern Med. 2014 Mar 4;160(5). **Updated Oct 2019**.
Price D, Musgrave SD, Shepstone L, et al. **Leukotriene antagonists** as first-line or add-on asthma-controller therapy. N Engl J Med. 2011 May 5;364(18):1695-707.
Pruteanu AI, Chauhan BF, Zhang L, Prietsch SOM, Ducharme FM. **Inhaled corticosteroids in children with persistent asthma: dose-response effects on growth**. Cochrane Database of Systematic Reviews 2014, Issue 7. Art. No.: CD009878. DOI: 10.1002/14651858.CD009878.pub2. In prepubescent school-aged children with mild to moderate persistent asthma, a small but statistically significant group difference in growth velocity was observed between low doses of ICS and low to medium doses of HFA-beclomethasone equivalent, favouring the use of low-dose ICS. No apparent difference in the magnitude of effect was associated with three molecules reporting one-year growth velocity, namely, mometasone, ciclesonide and fluticasone. In view of prevailing parents' and physicians' concerns about the growth suppressive effect of ICS, lack of or incomplete reporting of growth velocity in more than 86% (19/22) of eligible paediatric trials, including those using beclomethasone and budesonide, is a matter of concern. All future paediatric trials comparing different doses of ICS with or without placebo should systematically document growth. Findings support use of the minimal effective ICS dose in children with asthma.
Puhan MA, Garcia-Aymerich J, Frey M, et al. Expansion of the prognostic assessment of patients with chronic obstructive pulmonary disease: the updated **BODE index** and the **ADO** index**.** Lancet. 2009 Aug 29;374(9691):704-11.
Punnoose AR, Burke AE, Golub RM. JAMA **patient page. Childhood asthma**. JAMA. 012 Jan 25;307(4):421.
Qaseem A, Snow V, Shekelle P, et al. Clinical Efficacy Assessment Subcommittee of the American College of Physicians. Diagnosis and management of stable chronic obstructive pulmonary disease: a clinical practice guideline from the American College of Physicians. Ann Intern Med 2007 Nov 6;147(9):633-8.
Qian CJ, Coulombe J, Suissa S, et al. **Pneumonia Risk** in Asthma Patients **using Inhaled Corticosteroids**: A Quasi-Cohort Study. Br J Clin Pharmacol. 2017 Mar 28.
Quint JK, et al. Effect of **β blockers on mortality after myocardial infarction in adults with COPD**: population based cohort study of UK electronic healthcare records. BMJ. 2013 Nov 22;347:f6650.
Quirt J, Hildebrand KJ, Mazza J, et al. Asthma. Allergy Asthma Clin Immunol. 2018 Sep 12;14(Suppl 2):50
Quon BS, FitzGerald JM, Lemière C, Shahidi N, Ducharme FM. **Increased versus stable doses of inhaled corticosteroids** for exacerbations of chronic asthma in adults and children. Cochrane Database of Systematic Reviews 2010, Issue 10. Art. No.: CD007524. DOI: 10.1002/14651858.CD007524.pub2. There is very little evidence from trials in children. In adults with asthma on daily maintenance ICS, a self-initiated ICS increase to 1000 to 2000 mcg/day at the onset of an exacerbation is not associated with a statistically significant reduction in the risk of exacerbations requiring rescue oral corticosteroids. More research is needed to assess the effectiveness of increased ICS doses at the onset of asthma exacerbations (particularly in children).
Qureshi F, et al. Clinical efficacy of racemic **albuterol vs levalbuterol** for the treatment of acute pediatric asthma. Ann Emerg Med. 2005 Jul;46(1):29-36. (InfoPOEMs: Levalbuterol (Xopenex) is no more effective and no safer than albuterol in the treatment of moderate asthma exacerbations in children. These results are similar to the results printed on the product labeling for levalbuterol. In another study of severe asthma, there were fewer hospitalizations with levalbuterol than with albuterol treatment in patients (J Pediatr 2003:143:731-36). Given the 15-fold higher price of levalbuterol, it makes little sense to use it when albuterol is as effective. (LOE = 1b))
Rabe KF, et al. **Budesonide/formoterol** in a **single inhaler** for maintenance and relief in mild-to-moderate asthma: a randomized, double-blind trial. Chest. 2006 Feb;129(2):246-56.
Rabe KF, et al. Effect of **budesonide/formoterol** for **reliever** therapy in asthma exacerbations: a randomised controlled, double-blind study. Lancet. 2006 Aug 26;368(9537):744-53.
Rabe KF, et al. **Roflumilast**--an oral anti-inflammatory treatment for chronic obstructive pulmonary disease: a randomised controlled trial. Lancet. 2005 Aug 13-19;366(9485):563-71.
Rabe KF, Timmer W, Sagkriotis A, Viel K. Comparison of a **combination of tiotropium and formoterol** to salmeterol and fluticasone in moderate COPD. Chest. 2008 Apr 10; [Epub ahead of print] Tiotropium plus formoterol were superior in lung function over the day compared to salmeterol plus fluticasone in patients with moderate COPD. Long-term studies in severe COPD are warranted to assess the relative efficacy of different treatment combinations.
Rabe KF, Nair P, Brusselle G, et al. Efficacy and safety **of dupilumab in glucocorticoid-dependent severe asthma**. N Engl J Med.
Rajagopalan S, Brook RD. **Mortality from myocardial infarction** in chronic obstructive pulmonary disease: minding and mending the 'Gap'. Heart. 2015 Apr 22.
Rajanandh MG, Nageswari AD, Ilango K. Assessment of **Montelukast, Doxofylline, and Tiotropium With Budesonide** for the Treatment of Asthma: Which Is the Best Among the Second-Line Treatment? A Randomized Trial. Clin Ther. 2015 Jan 7.
Ram FS, Picot J, Lightowler J, Wedzicha JA. **Non-invasive positive pressure ventilation** for treatment of respiratory failure due to exacerbations of chronic obstructive pulmonary disease. Cochrane Database Syst Rev. 2004;(3):CD004104.
Ramsay CF, Pearson D, Mildenhall S, Wilson AM. Oral **montelukast in acute asthma exacerbations**: a randomised, double-blind, placebo-controlled trial. Thorax. 2010 Oct 18
Rank MA, Hagan JB, Park MA, et al. The **risk of asthma exacerbation after stopping low-dose inhaled corticosteroids**: a systematic review and meta-analysis of randomized controlled trials. J Allergy Clin Immunol. 2013 Mar;131(3):724-9.
Rasmussen SG, Ogburn EL, et al. Association Between Unconventional **Natural Gas Development** in the Marcellus Shale and Asthma Exacerbations. JAMA Intern Med. 2016 Jul 18.
Reddel H, Busse WW, Pedersen S, et al. Should recommendations about starting **inhaled corticosteroid treatment** for **mild asthma** be based on symptom frequency? A post-hoc effi cacy analysis of the **START** study. Lancet 2016; online Nov 29.
Rees J. **Asthma** control in adults. BMJ. 2006 Apr 1;332(7544):767-71.
Regan EA, Lynch DA, Curran-Everett D, et al; Genetic Epidemiology of COPD (COPDGene) Investigators. Clinical and Radiologic Disease in **Smokers With Normal Spirometry**. JAMA Intern Med. 2015 Jun 22.
Ren CL, Esther CR Jr, Debley JS, et al; ATS Ad Hoc Committee on Infants with Recurrent or Persistent Wheezing. Official American Thoracic Society Clinical Practice Guidelines: Diagnostic Evaluation of **Infants with Recurrent or Persistent Wheezing**. Am J Respir Crit Care Med. 2016 Aug 1;194(3):356-73.
Rennard SI, et al. Chronic obstructive pulmonary disease **exacerbations**: accurate and easy measurement promises much. Am J Respir Crit Care Med. 2012 Jun 1;185(11):1139-41.
Restrepo RD, Wettstein R, Wittnebel L, Tracy M. AARC clinical practice guideline: **incentive spirometry**: 2011. Respir Care 2011 Oct;56(10):1600-4.
Rice JL, Diette GB, Suarez-Cuervo Cet al. **Allergen-Specific Immunotherapy** in the Treatment of Pediatric Asthma: A Systematic Review. Pediatrics. 2018 Mar 23.
Rice KL, Dewan N, Bloomfield HE, et al. **Disease management program** for **chronic obstructive pulmonary disease:** a randomized controlled trial. Am J Respir Crit Care Med. 2010 Oct 1;182(7):890-6.

BMC Fam Pract. 2015 Oct 21;16(1):145.
Ritz T, Rosenfield D, Steptoe A. Physical activity, lung function, and shortness of breath in daily life of individuals with asthma. Chest. 2010 May 14.
Ritz T, Rosenfield D, Steele AM, et al. Controlling Asthma by Training of **Capnometry-Assisted Hypoventilation (CATCH) vs Slow Breathing**: A Randomized Controlled Trial. Chest. 2014 Nov 1;146(5):1237-47.
Rockville, MD: Agency for Healthcare Research and Quality. March 2018.

Rodrigo GJ, Castro-Rodriguez JA. **Anticholinergics** in the treatment of children and adults with acute asthma: a systematic review with meta-analysis. Thorax. 2005 Aug 10. Conclusions: This review strongly suggests that the addition of multiple doses of inhaled ipratropium bromide to beta2-agonists seems indicated as the standard treatment in children, adolescent and adult patients with moderate to severe exacerbations of asthma in the emergency setting.
Rodrigo GJ, Nannini LJ. **Tiotropium** for the treatment of stable chronic obstructive pulmonary disease: A systematic review with meta-analysis. Pulm Pharmacol Ther. 2006 Mar 2
Rodrigo GJ. Rapid effects of **inhaled corticosteroids** in **acute asthma**: an evidence-based evaluation. Chest. 2006 Nov;130(5):1301-11. Data suggests that ICS present early beneficial effects (1 to 2 h) when they were used in multiple doses administered in time intervals </= 30 min over 90 to 120 min.
Rodrigo GJ, Castro-Rodriguez JA, Nannini LJ, et al. **Tiotropium** and risk for fatal and nonfatal cardiovascular events in patients with chronic obstructive pulmonary disease: systematic review with meta-analysis. Respir Med. 2009 Jun 23. [Epub ahead of print] Compared with control (placebo or salmeterol), tiotropium did not significantly increase the risk of adverse major cardiovascular events among COPD patients. Subgroup analysis suggested that smoking history can modify the risk of cardiovascular adverse events.
Rodrigo GJ, Castro-Rodriguez JA, Plaza V. Safety and Efficacy of Combined Long-Acting {beta}-Agonists and Inhaled Corticosteroids vs **Long-Acting {beta}-Agonists** Monotherapy for Stable COPD: A Systematic Review. Chest. 2009 Jul 24. [Epub ahead of print] Compared with LABAs, the magnitude of LABAs/ICS benefits did not reach the criteria for predefined clinical important effects, and were associated with serious adverse effects.
Rodrigo GJ, Neffen H, Castro-Rodriguez JA. Efficacy and safety of subcutaneous **omalizumab** versus placebo as add on therapy to corticosteroids for children and adults with asthma: a systematic review. Chest. 2010 Aug 5. Data indicate that the efficacy of add on omalizumab in patients with moderate to severe allergic asthma is accompanied by an acceptable safety profile.
Rodrigo G, Pollack C, Rodrigo C, Rowe BH. **Heliox** for nonintubated acute asthma patients. Cochrane Database Syst Rev. 2006 Oct 18;(4):CD002884.
Rodrigo GJ, Plaza V. Efficacy and safety of a fixed-dose combination of **indacaterol and Glycopyrronium** for the treatment of COPD: a systematic review. Chest. 2014 Aug;146(2):309-17.
Rodrigo GJ, Castro-Rodriguez JA. What Is the Role of **Tiotropium in Asthma**?: A Systematic Review With Meta- analysis. Chest. 2015 Feb 1;147(2):388-96. doi: 10.1378/chest.14-1698
Rodrigo GJ, Neffen H. A Systematic Review of the Efficacy and Safety of a Fixed-Dose Combination of **Umeclidinium and Vilanterol** for the Treatment of COPD. Chest. 2015 Aug 1;148(2):397-407.
Romieu I, Fabre A, Fournier A, Kauffmann F, Varraso R, Mesrine S, et al. **Postmenopausal hormone therapy** and **asthma onset** in the E3N cohort. Thorax. 2010 Feb 8.
Rossi A, van der Molen T, Olmo RD, et al. **INSTEAD**: a randomised switch trial of **indacaterol versus salmeterol/fluticasone** in moderate **COPD**. Eur Respir J. 2014 Dec;44(6):1548-56.
Rutten FH et al; **Beta-Blocke**rs May Reduce Mortality & Risk of Exacerbations in Patients With **Chronic Obstructive Pulmonary Disease**. Arch Intern Med. 2010;170(10):880-887.
Ryan D, Price D, Musgrave SD, et al. Clinical and cost effectiveness of **mobile phone supported self monitoring** of asthma: multicentre randomised controlled trial. BMJ. 2012 Mar 23;344:e1756.
Sadowski CA, Cor K, Cave A, et al. **Administration Technique and Acceptance of Inhaler Devices** in Patients With Asthma or COPD. Ann Pharmacother. 2015 Jun;49(6):639-48.
Saini S, Rosen KE, Hsieh HJ, et al. A randomized, placebo-controlled, dose-ranging study of single-dose **omalizumab** in patients with H1-antihistamine-refractory **chronic idiopathic urticaria**. J Allergy Clin Immunol. 2011 Sep;128(3):567-73.e1.
Saini SS et al. Efficacy and safety of **omalizumab** in patients with chronic idiopathic/spontaneous urticaria who remain symptomatic on H1 antihistamines: A randomized, placebo-controlled study. J Invest Dermatol 2015 Jan; 135:67.
Sakai-Bizmark R, Chang RR, Mena LA, et al. Asthma **Hospitalizations Among Homeless Children** in New York State. Pediatrics. 2019 Jul 1.
Sakulchit T, Goldman RD. **Acetaminophen use and asthma in children**. Can Fam Physician. 2017 Mar;63(3):211-213
Salciccioli JD, Marshall DC, Shalhoub J, et al. **Respiratory disease mortality in the United Kingdom** compared with EU15+ countries in 1985-2015: observational study. BMJ. 2018 Nov 28;363:k4680.
Salpeter S, Ormiston T, Salpeter E. Cardioselective **beta-blockers** for COPD. Cochrane Database Syst Rev. 2005 Oct 19;4:CD003566. Cardioselective beta- blockers, given to patients with COPD in the identified studies did not produce adverse respiratory effects. Given their demonstrated benefit in conditions such as heart failure, coronary artery disease and hypertension, cardioselective beta-blockers should not be routinely withheld from patients with COPD.
Salpeter SR, et al. Meta-analysis: **anticholinergics**, but not beta-agonists, reduce severe exacerbations and respiratory mortality in COPD. J Gen Intern Med. 2006 Oct;21(10):1011-9. (InfoPOEMs: Anticholinergic treatment in patients with chronic obstructive pulmonary disease (COPD) produces better results than treatment with a beta-2 agonist. Studies comparing anticholinergic treatment with placebo have shown a greater decrease in the number of exacerbations. Studies comparing beta-2 agonist treatment with placebo have shown less benefit. In direct comparison with each other, there were 2.5 more exacerbations for every 100 patients treated with a beta-2 agonist instead of an anticholinergic. (LOE = 1a))
Salpeter SR, Buckley NS. Systematic Review of Clinical Outcomes in COPD: beta-Agonist Use Compared With **Anticholinergics** and Inhaled **Corticosteroids**. Clin Rev Allergy Immunol. 2006 Oct;31(2-3):219-30. In conclusion, inhaled anticholinergic bronchodilators and corticosteroids should be used to improve long-term clinical outcomes in patients with COPD. beta-Agonists increase respiratory deaths in COPD, possibly as a result of poorer disease control.
Salpeter SR, Wall AJ, Buckley NS. **Long-acting beta-agonists** with and without inhaled corticosteroids and **catastrophic asthma events**. Am J Med. 2010 Apr;123(4):322-8.e2.
Salvi SS, Barnes PJ. Chronic obstructive pulmonary disease in **non-smokers**. Lancet. 2009 Aug 29;374(9691):733-43.
Salvi S, Gogtay J, Aggarwal B. Use of **breath-actuated inhalers** in patients with asthma and COPD - an advance in inhalational therapy: a systematic review. Expert Rev Respir Med. 2014 Feb;8(1):89-99.
Sampayo EM, Mazer-Amirshahi M, Camp EA, et al. **Initiation of an Inhaled Corticosteroid During a Pediatric Emergency Visit for Asthma**: A Randomized Clinical Trial. Ann Emerg Med. 2017 Feb 24.
Sanchis J, Gich I, Pedersen S. Systematic Review of **Errors in Inhaler Use**: Has Patient Technique Improved Over Time? Chest. 2016 Apr 6. pii: S0012-3692(16)47571-9.
Sander N, et al. **Dose counting** and the use of pressurized metered-dose inhalers: canisters running on empty. Ann Allergy Asthma Immunol. 2006 Jul;97(1):34-8.
Sandifer JP, Jones AE. **Are Inhaled Steroids Beneficial on Discharge From the Emergency** Department for Acute Asthma? Ann Emerg Med. 2014 Jul 16.

Sano Y, Adachi M, Kiuchi T, Miyamoto T. Effects of nebulized sodium **cromoglycate** on adult patients with severe refractory asthma. Respir Med. 2005 Aug 8

Sauers-Ford HS, Moore JL, Guiot AB, et al. Local **Pharmacy Partnership** to Prevent Pediatric **Asthma Reutilization** in a Satellite Hospital. Pediatrics. 2016 Mar 16

Sauni R, Uitti J, Jauhiainen M, Kreiss K, Sigsgaard T, Verbeek JH. **Remediating buildings damaged by dampness and mould** for preventing or reducing respiratory tract symptoms, infections and asthma. Cochrane Database of Systematic Reviews 2011, Issue 9. Art. No.: CD007897. DOI: 10.1002/14651858.CD007897.pub2. We found moderate to very low-quality evidence that repairing mould-damaged houses and offices decreases asthma-related symptoms and respiratory infections compared to no intervention in adults.

Scarfone RJ, Zorc JJ, Angsuco CJ. Emergency physicians' prescribing of asthma controller medications. Pediatrics. 2006 Mar;117(3):821-7.

Schatz M, Dombrowski MP. Clinical practice. **Asthma in pregnancy**. N Engl J Med. 2009 Apr 30;360(18):1862-9.

Scheltema NM, Nibbelke EE, Pouw J, et al. **Respiratory syncytial virus** prevention and asthma in healthy preterm infants: a randomised controlled trial. Lancet Respir Med. 2018 Feb 27.

Schembri S, Williamson PA, Short PM, et al. **Cardiovascular events after clarithromycin** use in lower respiratory tract infections: analysis of two prospective cohort studies. BMJ. 2013 Mar 20;346:f1235.

Schifano ED, Hollenbach JP, Cloutier MM. **Mismatch between Asthma Symptoms and Spirometry**: Implications for Managing Asthma in Children. J Pediatr. 2014 Aug 28.

Schmidt B. No end to uncertainty about **inhaled glucocorticoids in preterm infants**. N Engl J Med 2015 Oct 15; 373:1566.

Schmiedl S, Fischer R, Ibanez L, et al. **Tiotropium Respimat® vs. HandiHaler®**: real-life usage and TIOSPIR trial generalizability. Br J Clin Pharmacol. 2015 Oct 27.

Schuh S, et al. High-dose inhaled fluticasone does not replace **oral prednisolone** in children with mild to moderate acute asthma. Pediatrics. 2006 Aug;118(2):644-50.

Schuh S, et al. A comparison of inhaled fluticasone and **oral prednisone** for children with severe acute asthma. N Engl J Med. 2000 Sep 7;343(10):689-94.

Schuh S, Willan AR, Stephens D, et al. Can Montelukast Shorten Prednisolone Therapy in Children with Mild to Moderate Acute Asthma? A Randomized Controlled Trial. J Pediatr. 2009 Aug 3. Montelukast does not represent an adequate alternative to corticosteroids after outpatient stabilization in mild to moderate acute asthma.

Schuh S, Zemek R, Plint A, et al. **Magnesium** Use in Asthma Pharmacotherapy: A Pediatric Emergency Research Canada Study. Pediatrics. 2012 Apr 16.

Scicchitano R, et al. Efficacy & safety of **budesonide/formoterol single inhaler** vs a higher dose of budesonide in mod-severe asthma. Curr Med Res Opin. 2004 Sep;20(9):1403-18.

Scottish Intercollegiate Guidelines Network (**SIGN**). **British guideline on the management of asthma**: Quick Reference Guide. September 2016

Seemungal TA, Wilkinson TM, Hurst JR, et al. **Long-term erythromycin** therapy is associated with decreased chronic obstructive pulmonary disease exacerbations. Am J Respir Crit Care Med. 2008 Dec 1;178(11):1139-47.

Serisier DJ, Martin ML, McGuckin MA, et al. Effect of **long-term, low-dose erythromycin on pulmonary exacerbations** among patients with non–cystic fibrosis bronchiectasis: the BLESS randomized controlled trial. JAMA. 2013;309(12):1260-1267.

Sethi S, Jones PW, Theron MS, et al. PULSE Study group. **Pulsed moxifloxacin** for the prevention of exacerbations of chronic obstructive pulmonary disease: a randomized controlled trial. Respir Res. 2010 Jan 28;11:10. Erratum in: Respir Res. 2010;11:88.

Seymour SM, Lim R, Xia C, et al. **Inhaled Corticosteroids and LABAs** - Removal of the FDA's Boxed Warning. N Engl J Med. 2018 Jun 28;378(26):2461-2463.

Sharma Gulshan; Kuo Yong-Fang; Freeman Jean L.; et al. Outpatient Follow-up Visit and 30-Day **Emergency Department Visit and Readmission** in Patients Hospitalized for Chronic Obstructive Pulmonary Disease. Arch Intern Med. 2010;170(18):1664-1670.

Sharma G, Meena R, Goodwin JS, et al. **Burn Injury Associated With Home Oxygen** Use in Patients With Chronic Obstructive Pulmonary Disease. Mayo Clin Proc. 2015 Mar 16.

Sheehan WJ, Mauger DT, Paul IM, et al. **Acetaminophen versus ibuprofen** in young children with mild persistent asthma. (AVICA) N Engl J Med 2016; 375: 619-30.

Sheffer AL, Silverman M, Woolcock AJ, et al. Long-term safety of once-daily **budesonide** in patients with **early onset**, mild persistent asthma: results of the inhaled Steroid Treatment As Regular Therapy in early asthma (START) study. Annals of Allergy, Asthma and Immunology 2005; 94:48-54

Shefrin AE, Goldman RD. Use of **dexamethasone and prednisone** in acute asthma exacerbations in pediatric patients. Can Fam Physician. 2009 Jul;55(7):704-6. Both prednisone (1 to 2 mg/kg daily for 5 days) and dexamethasone (0.3 to 0.6 mg/kg daily for 1 to 5 days) are effective in reducing hospital admissions and unscheduled return to care, with minimal side effects.

Sheehan WJ, Permaul P, et al. Association between **allergen exposure in inner-city schools** and asthma morbidity among students [online Nov 21, 16].JAMA Pediatr. doi:10.1001/jamapediatrics.2016.2543

Shinwell ES, Portnov I, Meerpohl JJ, et al. **Inhaled Corticosteroids for Bronchopulmonary Dysplasia**: A Meta-Analysis. Pediatrics.2016; 138(6):e20162511

Short PM, Lipworth SIW, Elder DHJ, et al. Effect of **β blockers in treatment** of chronic obstructive pulmonary disease: a retrospective cohort study. BMJ 2011;342. (10 May 2011)

Short PM, Williamson PA, Elder DH, et al. The impact of **tiotropium on mortality** and exacerbations when added to inhaled corticosteroids and long-acting β-agonist therapy in COPD. Chest. 2012 Jan;141(1):81-6. The study suggests that the addition of tiotropium to ICSs and LABA therapy may confer benefits in reducing all-cause mortality, hospital admissions, and oral corticosteroid bursts in patients with COPD.

Short PM, Anderson WJ, Williamson PA, et al. Effects of **intravenous and oral β-blockade in persistent asthmatics** controlled on inhaled corticosteroids. Heart. 2013 Nov 7.

Silber JH, Rosenbaum PR, Calhoun SR, et al. **Racial Disparities** in Medicaid Asthma Hospitalizations.Pediatrics. 2016 Dec 26.

Silveira D'Avila R, Piva JP, Jose Cauduro Marostica P, Luis Amantea S. Early administration of two intravenous bolus of aminophylline added to the standard treatment of children with acute asthma. Respir Med. 2007 Sep 13; [Epub ahead of print] In children aged 2-5 years admitted to a PER with asthma, two intravenous doses of 5mg/kg of aminophylline given 6h apart did not change the length of stay in hospital, the number of nebulizations given or the duration of oxygen therapy required. We are unable to tell whether there would be benefit with higher doses of aminophylline designed to give levels in the usual therapeutic range.

Silverman M, et al. Safety and tolerability of inhaled budesonide in children (3yrs) in the Steroid Treatment As Regular Therapy in early asthma (**START**) trial. Pediatr Allergy Immunol. 2006 May;17 Suppl 17:14-20.

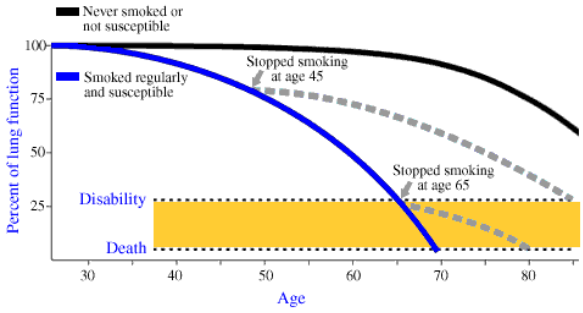
Silverman, Edwin K., Sandhaus, Robert A. **Alpha1-Antitrypsin Deficiency.** N Engl J Med 2009 360: 2749-2757

Silvers KM, Frampton CM, Wickens K, et al. **Breastfeeding** Protects against Current Asthma up to 6 Years of Age. J Pediatr. 2012 Jan 28.

Sin DD, Tashkin D, Zhang X, Radner F, Sjöbring U, Thorén A, Calverley PM, Rennard SI. Budesonide and the risk of **pneumonia**: a meta-analysis of individual patient data. Lancet. 2009 Aug 29;374(9691):712-9.

Singh S, Loke YK, Furberg CD. Inhaled anticholinergics and risk of major adverse cardiovascular events in patients with chronic obstructive pulmonary disease: a systematic review and meta-analysis. JAMA. 2008 Sep 24;300(12):1439-50. **Inhaled anticholinergics** are associated with a significantly increased risk of cardiovascular death, MI, or stroke

among patients with COPD.
Singh S, Amin AV, Loke YK. Long-term Use of Inhaled **Corticosteroids and the Risk of Pneumonia** in Chronic Obstructive Pulmonary Disease: A Meta-analysis. Arch Intern Med. 2009 Feb 9;169(3):219-229. Inhaled corticosteroids were associated with a significantly increased risk of any pneumonia (relative risk [RR], 1.60; 95% confidence interval [CI], 1.33-1.92 [P < .001]; I(2) = 16%) and serious pneumonia (1.71; 1.46-1.99 [P < .001]; I(2) = 0%) but without a significantly increased risk of pneumonia-related mortality (1.27; 0.80-2.03 [P = .31]; I(2) = 0%) or overall mortality (0.96; 0.86-1.08 [P = .51]; I(2) = 0%). Among patients with COPD, inhaled corticosteroid use for at least 24 weeks is associated with a significantly increased risk of serious pneumonia, without a significantly increased risk of death.
Singh D, Brooks J, Hagan G, Cahn A, O'Connor BJ. Superiority of "triple" therapy with **salmeterol/fluticasone propionate and tiotropium** bromide versus individual components in moderate to severe COPD. Thorax. 2008 Jul;63(7):592-8. Epub 2008 Feb 1.
Singh S, Loke YK, Enright PL, Furberg CD. **Mortality associated with tiotropium mist inhaler** not studied: Spriva HandiHaler in patients with chronic obstructive pulmonary disease: Systematic review and meta-analysis of randomised controlled trials. BMJ 2011;342:d3215.
Singh D, van den Berg F, Leaker B, et al. Comparison of the **effect of beclometasone/formoterol in asthma patients after methacholine-induced bronchoconstriction**: a non-inferiority study using metered dose versus dry powder inhaler. Br J Clin Pharmacol. 2018 Dec 26.
Skoner DP, Maspero J, Banerji D; and the Ciclesonide Pediatric Growth Study Group. Assessment of the Long-term Safety of Inhaled **Ciclesonide** on **Growth** in Children With Asthma. Pediatrics. 2007 Dec 10; [Epub ahead of print]n=661 1yr. Ciclesonide demonstrated no detectable effect on childhood growth velocity, even at the highest dosage, which may ease concerns about systemic adverse events.
Skoner DP, Meltzer EO, Milgrom H, et al. Effects of **Inhaled Mometasone Furoate on Growth Velocity** and Adrenal Function: A Placebo-Controlled Trial in Children 4-9 Years Old with Mild Persistent Asthma. J Asthma. 2011 Aug 22. One year of treatment with a total daily dose of 100 µg of MF-DPI in the morning resulted in no significant difference, whereas a total daily dose of 200 µg of MF-DPI was associated with some changes in growth velocity when compared with placebo.
Slatore CG, Bryson CL, Au DH. The association of inhaled corticosteroid use with serum **glucose** concentration in a large cohort. Am J Med. 2009 May;122(5):472-8. Inhaled steroids are not associated with an increase in serum glucose concentrations in patients without diabetes. In patients with diabetes, slightly higher serum glucose levels were associated with higher doses of corticosteroids, increasing an average 1.82 mg/dL (0.101 mmol/L) for every 100 mcg increase in dose of steroid (in triamcinolone equivalents). This increase could be clinically relevant with high doses; fluticasone 1000 mcg per day would increase glucose an average of 72.8 mg/dL (4.04 mmol/L). The increase was higher in patients receiving medication for diabetes, an average 2.65 mg/dL (0.147 mmol/L). (LOE = 1b)
Slats AM, et al. Improvement in bronchodilation following deep inspiration after a course of **high-dose oral prednisone** in asthma. Chest. 2006 Jul;130(1):58-65.
Sleath B, Carpenter DM, Slota C, et al. Communication During Pediatric Asthma Visits and Self-Reported Asthma Medication **Adherence**. Pediatrics. 2012 Sep 3.
Smith AD, Cowan JO, Brassett, KP, et al. Use of exhaled **nitric oxide** measurements to guide treatment in chronic asthma. N Engl J Med 2005;352:2163-72. (InfoPOEMs: Using exhaled nitric oxide measurements to adjust inhaled corticosteroid doses allows patients to use a lower dose than the traditional approach based on symptoms and spirometry. Although there was no statistically significant differences regarding patient-oriented outcomes, all trends were consistent in favor of the fraction of nitric oxide measurement . (LOE = 1b-))
Smith C, Goldman RD. **Nebulizers versus pressurized metered-dose inhalers** in preschool children with wheezing. Can Fam Physician. 2012 May;58(5):528-30.
Smith LJ, Kalhan R, Wise RA, et al; American Lung Association Asthma Clinical Research Centers. Effect of a **soy isoflavone supplement** on lung function and clinical outcomes in patients with poorly controlled asthma: a randomized clinical trial. JAMA. 2015 May 26;313(20):2033-43.
Smith JR, Noble MJ, Musgrave S, et al. The at-risk registers in severe asthma (ARRISA) study: a cluster-randomised controlled trial **examining effectiveness and costs in primary** care. Thorax. 2012 Dec;67(12):1052-60.
Smith, Scott D. **Diagnosis** of asthma in adults. CMAJ 2009 0: cmaj.080006
Smith FG, Perkins GD, Gates S, et al, for the **BALTI-2** study investigators. Effect of intravenous **β-2 agonist** (salbutamol) treatment on clinical outcomes in acute respiratory distress syndrome- ARDS (BALTI-2): a multicentre, randomised controlled trial. Lancet 2011; online Dec 12.
Smoking Cessation benefits: Fletcher C, Peto R. The natural history of chronic airflow obstruction. Br Med J. 1977 Jun 25;1(6077):1645-8.



Smoliga JM, Weiss P, Rundell KW. Exercise induced bronchoconstriction in adults: evidence based diagnosis and management. BMJ. 2016 Jan 13;352:h6951.
Smy L, Chan AC, Bozzo P, et al. Is it safe to use **inhaled corticosteroids in pregnancy**? Can Fam Physician. 2014 Sep;60(9):809-12.
Sobieraj DM, Weeda ER, Nguyen E, et al. Association of **inhaled corticosteroids and long-acting β-agonists** as controller and quick relief therapy with exacerbations and symptom control in persistent asthma: a systematic review and meta-analysis.JAMA. doi:10.1001/jama.2018.2769
Sobieraj DM, Baker WL, Nguyen E, et al. Association of **inhaled corticosteroids and long-acting muscarinic antagonists** with asthma control in patients with uncontrolled, persistent asthma: a systematic review and meta-analysis. JAMA. doi:10.1001/jama.2018.2757

Sobieraj DM, Baker WL. **Medications for Asthma**. (patient information) JAMA. 2018 Apr 10;319(14):1520.
Sobieraj DM, Baker WL, Weeda ER, et al. **Intermittent inhaled corticosteroids and long-acting muscarinic antagonists for asthma**. Comparative Effectiveness Review No. 194. AHRQ Publication No. 17(18)-EHC027-EF. Rockville, MD: Agency for Healthcare Research and Quality; March 2018.
Sokol KC, Sharma G, Lin YL, Goldblum RM. Choosing wisely: adherence by physicians to recommended use of **spirometry** in the diagnosis and management of adult **asthma**. Am J Med. 2015 May;128(5):502-8.
Sonnenschein-van der Voort A, Jaddoe V, Raat H et al. **Fetal and Infant Growth** and Asthma Symptoms in Preschool Children: The Generation R Study. Am. J. Respir. Crit. Care Med. 2012; 185: 731-737.
Sood A, Qualls C, Schuyler M, et al. Low **Serum Adiponectin** Predicts Future Risk for Asthma in Women. Am J Respir Crit Care Med. 2012 Apr 6.
Soria A, Du-Thanh A, Seneschal J, et al. Development or Exacerbation of Head and Neck Dermatitis in Patients **Treated for Atopic Dermatitis With Dupilumab**. JAMA Dermatol. 2019 Sep 4.
Soriano JB, Zielinski J, Price D. **Screening** for and early detection of chronic obstructive pulmonary disease. Lancet. 2009 Aug 29;374(9691):721-32.
Soriano JB, Lamprecht B, Ramírez AS, et al. **Mortality prediction** in chronic obstructive pulmonary disease comparing the **GOLD 2007 and 2011 staging systems**: a pooled analysis of individual patient data. Lancet Respir Med. 2015 May 15.
Sorkness CA, et al. for the Childhood Asthma Research and Education Network of the NHLBI. Long-term comparison of 3 controller regimens (**fluticasone** 100 mug twice daily (fluticasone monotherapy), fluticasone 100 mug/salmeterol 50 mug in the morning and salmeterol 50 mug in the evening (PACT combination), and montelukast 5 mg in the evening) for mild-moderate persistent childhood asthma: The Pediatric Asthma Controller Trial. (**PACT**) J Allergy Clin Immunol. 2006 Nov 29; [Epub ahead of print] Therefore, of the regimens tested, the PACT study findings favor fluticasone monotherapy in treating children with mild-moderate persistent asthma with FEV(1) >/= 80% predicted, confirming current guideline recommendations.
Sovani MP, et al. A benefit-risk assessment of inhaled **long-acting beta2-agonists** in the management of obstructive pulmonary disease. Drug Saf. 2004;27(10):689-715.
Søyseth V, Johnsen HL, et al. The Incidence of **Work-related Asthma-like Symptoms and Dust Exposure in Norwegian Smelters**. Am J Respir Crit Care Med. 2012 Apr 19.
Spanier AJ, Kahn RS, et al. **Bisphenol A Exposure** and the Development of Wheeze and Lung Function in Children Through Age 5 Years. JAMA Pediatr. 2014 Oct 6.
Stallberg B, et al. **Potency ratio** fluticasone (Flixotide Diskus)/budesonide (Pulmicort Turbuhaler). Respir Med. 2006 Aug 2. From these data the potency difference between the present drug inhaler combinations, Flixotide Diskus & Pulmicort Turbuhaler, was calculated to be between 1.50:1 (95% CI 1.10:1-2.05:1) & 1.75:1 (CI 1.26:1-2.43:1) depending on if patients with insufficient steroid-response were excluded from the calculations or not. In these steroid-naive patients, the potency difference was evident only at low daily doses, below 200mcg.
Stefan MS et al. Association between **antibiotic** treatment **&** outcomes in patients hospitalized with **acute exacerbation** of **COPD** treated with systemic steroids. Chest 2013 Jan; 143:82.
Stefan MS, Shieh MS, Spitzer KA, et al. Association of **Antibiotic Treatment** With Outcomes in Patients Hospitalized for an Asthma **Exacerbation Treated With Systemic Corticosteroids**. JAMA Intern Med. 2019 Jan 28.
Stein MM et al. **Innate immunity** and asthma risk in Amish and Hutterite farm children. N Engl J Med2016 Aug 4; 375:411.
Stelmach R, et al. Effect of treating **allergic rhinitis** with corticosteroids in patients with mild-to-moderate persistent asthma. Chest. 2005 Nov;128(5):3140-7.
Stempel DA, Raphiou IH, Kral KM, et al. Serious **asthma** events with **fluticasone plus salmeterol versus fluticasone** alone. (**AUSTRI**) N Engl J Med. DOI: 10.1056/NEJMoa1511049.
Stempel DA, Szefler SJ, Pedersen S, et al. **Safety of adding salmeterol to fluticasone** propionate in children with asthma. (VESTRI) N Engl J Med 2016;375:840-9.
Stephenson Anne; Seitz Dallas; Bell Chaim M.; et al. Inhaled **Anticholinergic Drug Therapy and the Risk of Acute Urinary Retention** in Chronic Obstructive Pulmonary Disease: A Population-Based Study. Arch Intern Med. 2011;171(10):914-920.
Stiell IG, Clement CM, Aaron SD, et al. Clinical characteristics associated with **adverse events in patients with exacerbation of chronic obstructive pulmonary disease**: a prospective cohort study. CMAJ. 2014 Apr 1;186(6):E193-204.
Stockmann C, Fassl B, Gaedigk R, et al. **Fluticasone Propionate** Pharmacogenetics: **CYP3A4***22 Polymorphism and Pediatric Asthma Control. J Pediatr. 2013 Jan 3.
Stojak BJ, Halajian E, Guthmann RA, Nashelsky J. **Intravenous Magnesium Sulfate** for Acute Asthma Exacerbations. Am Fam Physician. 2019 Jan 15;99(2):127-128.
Stoller JK, Aboussouan LS. A Review of **Alpha-1 Antitrypsin Deficiency**. Am J Respir Crit Care Med. 2011 Sep 29.
Stolz D, Kostikas K, Blasi F, et al. **Adrenomedullin** refines mortality prediction by the **BODE index in COPD**: the ``BODE-A`` index. Eur Respir J. 2014 Feb;43(2):397-408.
Stordal K, et al. **Acid suppression** does not change respiratory symptoms in children with asthma and gastro-oesophageal reflux disease. Arch Dis Child. 2005 Sep;90(9):956-60. (InfoPOEMs: Suppressing acid in asthmatic children with minimal symptoms of reflux does not improve asthma. This study does not address whether this holds true for children with clinically significant reflux. (LOE = 2b))
Stout JW, et al. Classification of **asthma severity** in children: the contribution of pulmonary function testing. Arch Pediatr Adolesc Med. 2006 Aug;160(8):844-50.
Strunk RC, et al; for the **CAMP** Research Group. Mild to moderate asthma affects lung growth in children and adolescents. J Allergy Clin Immunol. 2006 Nov;118(5):1040-7. Mild to moderate asthma results in a pattern of airway obstruction that increases in magnitude from age 5 to 18 years.
Strunk RC, Sternberg AL, Szefler SJ, Zeiger RS, Bender B, Tonascia J; on behalf of the Childhood Asthma Management Program (**CAMP**) Research Group. Long-Term Budesonide or Nedocromil Treatment, Once Discontinued, Does Not Alter the Course of Mild to Moderate Asthma in Children and Adolescents. J Pediatr. 2009 Jan 22. [Epub ahead of print] Clinically meaningful improvements in the control of asthma and in airway responsiveness achieved during continuous treatment with inhaled corticosteroids do not persist after continuous treatment is discontinued.
Strunk RC, Bloomberg GR. **Omalizumab** for asthma. N Engl J Med. 2006 Jun 22;354(25):2689-95.
Subbarao P, Mandhane PJ, Sears MR. Asthma: **epidemiology, etiology and risk factors**. CMAJ. 2009 Sep 14. [Epub ahead of print]
Suissa S, Kezouh A, Ernst P. Inhaled Corticosteroids and the Risks of **Diabetes Onset and Progression**. Am J Med. 2010 Sep 24.
Suissa S, Patenaude V, Lapi F, et al. **Inhaled corticosteroids in COPD** and the risk of serious **pneumonia**. Thorax. 2013 Nov;68(11):1029-36.
Suissa S et al. **Discontinuation of inhaled corticosteroids in COPD** and the risk reduction of pneumonia. Chest 2015 Nov; 148:1177.
Suissa S, Israel E, Donohue J, Evans S, Kemp J. **FDA-mandated Trials of LABA Safety in Asthma**: Bang for the Buck? Am J Respir Crit Care Med. 2018 Jan 22.
Sumino K, Bacharier LB, Taylor J, et al. A Pragmatic Trial of **Symptom-Based Inhaled Corticosteroid** Use in African-American Children with Mild Asthma. J Allergy Clin Immunol Pract. 2019 Jul 29.
Suzuki M, Muro S, Ando Y, et al. A randomized, placebo-controlled trial of **acupuncture** in patients with chronic obstructive pulmonary disease (COPD): the COPD-acupuncture trial (CAT). Arch Intern Med. 2012 Jun 11;172(11):878-86.

Sveum R, Bergstrom J, Brottman G, et al. Diagnosis and management of asthma. Bloomington (MN): Institute for Clinical Systems Improvement (ICSI); 2012 Jul.
Sze MA, Dimitriu PA, Hayashi S, et al. The **lung tissue microbiome** in chronic obstructive pulmonary disease. Am J Respir Crit Care Med 2012;185:1073–1080.
Szefler SJ, Murphy K, Harper T 3rd, et al. A phase III randomized controlled trial of **tiotropium add-on therapy in children with severe symptomatic asthma**. J Allergy Clin Immunol. 2017 Feb 9.
Szefler SJ. **Asthma across the lifespan**: Time for a paradigm shift. J Allergy Clin Immunol. 2018 Sep;142(3):773-780.
Tai A, Tran H, Roberts M, et al. The association between **childhood asthma** and **adult chronic obstructive pulmonary disease**. Thorax. 2014 Mar 31.
Tan WC, et al. in **Caucasian versus Asian** patients with asthma: 3-year results of the **START** study.Respirology. 2006 Nov;11(6):767-775.
Tantisira KG, Lasky-Su J, Harada M, et al. **Genomewide association between GLCCI1** and response to **glucocorticoid therapy** in asthma. N Engl J Med 2011.
Tarlo SM, Lemiere C. **Occupational asthma**. N Engl J Med. 2014 Feb 13;370(7):640-9
Tashkin DP, Celli B, Senn S, et al. **UPLIFT** Study Investigators. A 4-Year Trial of Tiotropium in Chronic Obstructive Pulmonary Disease. N Engl J Med. 2008 Oct 5. [Epub ahead of print] In patients with COPD, therapy with tiotropium was associated with improvements in lung function, quality of life, and exacerbations during a 4-year period but did not significantly reduce the rate of decline in FEV(1). (Celli B, Decramer M, Kesten S, Liu D, Mehra S, Tashkin DP. Mortality in the 4 Year Trial of Tiotropium (UPLIFT) in Patients with COPD. Am J Respir Crit Care Med. 2009 Sep 3.)
Tattersfield AE, et al. Comparison of formoterol and terbutaline for as-needed treatment of asthma: a randomised trial. Lancet. 2001 Jan 27;357(9252):257-61.
Tattersfield AE, et al. Exacerbations of **asthma**: a descriptive study of 425 severe exacerbations. The **FACET** International Study Group. Am J Respir Crit Care Med. 1999 Aug;160(2):594-9.
Tattersall MC, Barnet JH, Korcarz CE, et al. **Late-Onset Asthma Predicts Cardiovascular Disease Events**: The Wisconsin Sleep Cohort. J Am Heart Assoc. 2016 Aug 24;5(9).
Teach SJ, et al. Improved asthma outcomes in a high-morbidity pediatric population: results of an emergency **department-based** randomized clinical trial. Arch Pediatr Adolesc Med. 2006 May;160(5):535-41.
Teach SJ, Gill MA, Togias A, et al. Preseasonal treatment with either **omalizumab or an inhaled corticosteroid** boost to prevent fall **asthma** exacerbations. J Allergy Clin Immunol. 2015 Oct 23.
Tegethoff M, Greene N, et al. **Inhaled Glucocorticoids during Pregnancy** and Offspring Pediatric Diseases: A National Cohort Study. Am J Respir Crit Care Med. 2011 Dec 28.
Tegethoff M, Olsen J, Schaffner E, Meinlschmidt G. **Asthma During Pregnancy** and Clinical Outcomes in Offspring: A National Cohort Study. Pediatrics. 2013 Aug 5.
Teodorescu M, Barnet JH, Hagen EW, et al. Association between **asthma and risk of developing obstructive sleep apnea**. JAMA. 2015 Jan 13;313(2):156-64.
Teper AM, Colom AJ, Kofman CD, et al. Effects of inhaled **fluticasone** propionate in **children** less than 2 years old with recurrent wheezing. Pediatr Pulmonol. 2004 Feb;37(2):111-5.
Thakkar K, Boatright RO, Gilger MA, et al. **Gastroesophageal reflux and asthma in children: a systematic review.** Pediatrics. 2010 Apr;125(4):e925-30. Epub 2010 Mar 29.
Tharp MD, Bernstein JA, Kavati A, et al. Benefits and Harms of **Omalizumab Treatment** in Adolescent and Adult Patients **With Chronic Idiopathic (Spontaneous) Urticaria**: A Meta-analysis of "Real-world" Evidence. JAMA Dermatol. 2018 Nov 14.
Thomas M, Bruton A, Little P, et al. A randomised controlled study of the effectiveness of **breathing retraining exercises** taught by a physiotherapist either by instructional DVD or in face-to-face sessions in the management of asthma in adults. Health Technol Assess. 2017 Sep;21(53):1-162.
Thomsen M, Ingebrigtsen TS, et al. **Inflammatory biomarkers** and exacerbations in chronic obstructive pulmonary disease (COPD) . JAMA. 2013 Jun 12;309(22):2353-61.
Thun MJ, Carter BD, Feskanich D, et al. 50-Year trends in **smoking-related mortality** in the United States. N Engl J Med 2013;368:351-64. (increasing **COPD** mortality in men)
To T, Wang C, Guan J, McLimont S, Gershon AS. What is the **Lifetime Risk** of Physician **Diagnosed** Asthma in Ontario, Canada? Am J Respir Crit Care Med. 2009 Nov 19.
To T, Zhu J, Larsen K, et al; Canadian Respiratory Research Network. Progression from **Asthma to Chronic Obstructive Pulmonary Disease** (**COPD**): Is **Air Pollution** a Risk Factor? Am J Respir Crit Care Med. 2016 Mar 7.
To T, Zhu J, Gray N, et al. **Asthma and COPD Overlap in Women**: Incidence and Risk Factors. Ann Am Thorac Soc. 2018 Jul 17.
Tofts RPH, Ferrer G, Oliveira E. How should one investigate a **chronic cough**? *Cleveland Clinic Journal of Medicine* 2011; 78(2):84-85, 89; doi:10.3949/ccjm.77a.10033.
Tomerak A, Vyas H, Lakenpaul M, et al. Inhaled beta2-agonists for treating non-specific **chronic cough** in children. Cochrane Database Syst Rev. 2005 Jul 20;(3):CD005373.
Tommelein E, Mehuys E, et al. Effectiveness Of **PHARMAceutical Care** For Patients with COPD (**PHARMACOP**): a Randomized Controlled Trial. Br J Clin Pharmacol. 2013Oct9.
Tonacci A, Billeci L, Pioggia G, et al. **Omalizumab** for the Treatment of **Chronic Idiopathic Urticaria**: Systematic Review of the Literature. Pharmacotherapy. 2017 Feb 22.
Torrego A, Solà I, Munoz AM, et al. **Bronchial thermoplasty** for moderate or severe persistent **asthma** in adults. Cochrane Database of Systematic Reviews 2014, Issue 3. Art. No.: CD009910. DOI:10.1002/14651858.CD009910.pub2. Bronchial thermoplasty for patients with moderate to severe asthma provides a modest clinical benefit in quality of life and lower rates of asthma exacerbation, but no significant difference in asthma control scores. The quality of life findings are at risk of bias, as the main benefits were seen in the two studies that did not include a sham treatment arm. This procedure increases the risk of adverse events during treatment but has a reasonable safety profile after completion of the bronchoscopies.
Townshend J, Hails S, McKean M. Management of asthma in **children**. BMJ. 2007 Aug 4;335(7613):253-7.
Townshend J, Hails S, McKean M. Diagnosis of asthma in **children**. BMJ. 2007 Jul 28;335(7612):198-202.
Trappenburg JC, Monninkhof EM, Bourbeau J, Trooster T, Schrijvers AJ, Verheij TJ, et al. Effect of an **action plan** with ongoing support by a case manager on exacerbation-related outcome in patients with **COPD**: a multicentre randomised controlled trial. Thorax 2011;66:977-84.
Triebner K, Johannessen A, et al. **Menopause as a predictor of new-onset asthma**: A longitudinal Northern European population study. J Allergy Clin Immunol. 2016 Jan;137(1):50-57.e6.
Trivedi R, Richard N, Mehta R, et al. **Umeclidinium** in patients with COPD: a randomised, placebo-controlled study. Eur Respir J. 2014 Jan;43(1):72-81.
Turpeinen M, Nikander K, Pelkonen AS, et al. **Daily versus as-needed inhaled corticosteroid** for mild persistent asthma (The Helsinki early intervention childhood asthma study). Arch Dis Child. 2008 Aug;93(8):654-9. Epub 2007 Jul 18.
Ungar WJ. **Medication cost sharing** and health outcomes in children with asthma. JAMA. 2012 Mar 28;307(12):1316-8.
Upham BD, Mollen CJ, Scarfone RJ, Seiden J, Chew A, Zorc JJ. **Nebulized budesonide added** to standard pediatric emergency department treatment of acute asthma: a randomized, double-blind trial. Acad Emerg Med. 2011 Jul;18(7):665-73. Nebulized budesonide added to standard therapy in the treatment of acute asthma in children did not significantly improve asthma severity scores or reduce hospital admissions. (LOE = 1b)
Uranic H, McCrory DC, Samsa G, et al. Symptomatic oxygen for non-hypoxaemic chronic obstructive pulmonary disease. Cochrane Database Syst Rev. 2011 Jun 15;6:CD006429.

Oxygen can relieve dyspnoea in mildly and non-hypoxaemic people with COPD who would not otherwise qualify for home oxygen therapy.
Uronis HE, Ekström MP, Currow DC, et al. **Oxygen for relief of dyspnoea** in people with **chronic obstructive pulmonary disease** who would not qualify for home oxygen: a systematic review and meta-analysis. Thorax. 2014 Dec 3. pii: thoraxjnl-2014-205720.
U.S. Preventive Services Task Force. Screening for Chronic Obstructive Pulmonary Disease Using **Spirometry**: U.S. Preventive Services Task Force Recommendation Statement. Ann Intern Med. 2008 Mar 3; [Epub ahead of print] Do not screen adults for COPD using spirometry
Uzun S, Djamin RS, Kluytmans JA, et al. **Azithromycin maintenance** treatment in patients with frequent exacerbations of chronic obstructive pulmonary disease (COLUMBUS): a randomised, double-blind, placebo-controlled trial. Lancet Respir Med. 2014 May;2(5):361-8.
VA/DoD Department of Veterans Affairs and Department of Defense. COPD Guideline 2007 . At www.healthquality.va.gov/Chronic_Obstructive_Pulmonary_Disease_COPD.asp on 27 Nov 2010.
Vaes AW, Annegarn J, Meijer K, et al. The Effects of a "New" **Walking Aid** on Exercise Performance in Patients With COPD: A Randomized Crossover Trial. Chest. 2012 May;141(5):1224-32. (modern draisine vs a rollator)
Vaessen-Verberne AA, van den Berg NJ, van Nierop JC, et al. the **COMBO** study Group. Combination Therapy **Salmeterol/Fluticasone versus Doubling Dose of Fluticasone** in Children with Asthma. Am J Respir Crit Care Med. 2010 Jul 9.
Vaidyanathan S, Williamson P, Clearie K, et al. **Fluticasone Reverses Oxymetazoline Induced Tachyphylaxis** of Response and Rebound Congestion. Am J Respir Crit Care Med. 2010 Mar 4.
Van den Bruel A, Gailly J, Neyt M. Does **tiotropium** lower exacerbation and hospitalization frequency in COPD patients: results of a meta-analysis. BMC Pulm Med. 2010 Sep 21;10(1):50.
van den Wijngaart LS, Roukema J, Boehmer ALM, et al. A **virtual asthma clinic** for children: fewer routine outpatient visits, same asthma control. Eur Respir J. 2017 Oct 5;50(4).
van der Meer V, et al. **Internet-based self-management plus education compared with usual care in asthma: a randomized trial.** Ann Intern Med. 2009 Jul 21;151(2):110-20.
van Gestel YR, Hoeks SE, Sin DD, et al. The Impact of Cardioselective Beta-Blockers on Mortality in Patients with COPD and Atherosclerosis. Am J Respir Crit Care Med. 2008 Jun 19. [Epub ahead of print] Cardioselective beta-blockers were associated with reduced mortality in COPD patients undergoing vascular surgery. In carefully selected patients with COPD, the use of cardioselective beta-blockers appears to be safe and associated with reduced mortality.
van Noord JA, et al. Effects of **tiotropium with and without formoterol** on airflow obstruction and resting hyperinflation in patients with COPD. Chest. 2006 Mar;129(3):509-17.
Varraso R, Chiuve SE, Fung TT, et al. **Alternate Healthy Eating Index 2010** and risk of chronic obstructive pulmonary disease among US women and men: prospective study. BMJ. 2015 Feb 3;350:h286.
Veilleux O, Lee TC, McDonald EG. **Rebound adrenal insufficiency after withdrawal of ritonavir** in a 65-year-old man using inhaled budesonide. CMAJ. 2017Sep 18;189(37):E1188-E1191.
Vennera MD, et al. behalf of the Spanish Registry. **Omalizumab** Therapy in Severe Asthma: Experience from the Spanish Registry-Some New Approaches. J Asthma. 2012 Mar 23.
Vernacchio L, Francis ME, Epstein DM, et al. Effectiveness of an **asthma quality improvement** program designed for maintenance of certification. Pediatrics.2014Jul;134(1):e242-8.
Vestbo J, et al.; TRISTSAN study group. Early onset of effect of salmeterol and fluticasone propionate in chronic obstructive pulmonary disease. Thorax. 2005 Apr;60(4):301-4.
Vestbo J, Anderson W, Coxson HO, et al. ; **ECLIPSE** investigators. Evaluation of COPD Longitudinally to Identify Predictive Surrogate End-points (ECLIPSE). Eur Respir J. 2008 Apr;31(4):869-73. Epub 2008 Jan 23.
Vestbo J, Edwards LD, Scanlon PD, et al. **Changes in forced expiratory volume in 1 second** over time in COPD. N Engl J Med 2011. DOI: 10.1056/NEJMoa1105482
Vestbo J, Hurd SS, Agusti AG, et al. Global Strategy for the Diagnosis, Management and Prevention of **Chronic Obstructive Pulmonary Disease**, **GOLD Executive Summary**. Am J Respir Crit Care Med. 2012 Aug 9.
Vézina K, Chauhan BF, Ducharme FM. **Inhaled anticholinergics and short-acting beta(2)-agonists versus short-acting beta2-agonists alone** for children with acute asthma in hospital. Cochrane Database Syst Rev. 2014 Jul 31;7:CD010283. In children hospitalised for an acute asthma exacerbation, no evidence of benefit for length of hospital stay and othermarkers of response to therapy was noted when nebulised anticholinergics were added to short-acting _2-agonists. No adverse health effects were reported, yet the small number of trials combined with inadequate reporting prevent firm reassurance regarding the safety of anticholinergics. In the absence of trials conducted in ICUs, no conclusion can be drawn regarding children with impending respiratory failure. These findings support current national and international recommendations indicating that healthcare practitioners should refrain fromusing anticholinergics in children hospitalised for acute asthma.
Virchow JC, Backer V, Kuna P, et al. Efficacy of a house **dust mite sublingual allergen immunotherapy** tablet in adults with allergic asthma.JAMA. doi:10.1001/jama.2016.3964.
Vogelmeier C, et al. **Budesonide/formoterol maintenance & reliever**: an effective asthma treatment option? Eur Respir J. 2005 Nov;26(5):819-28. Erratum in: ERJ Dec;26(6):1191.
Vogelmeier C, Kardos P, Harari S, et al. **Formoterol mono and combination therapy with tiotropium** in patients with COPD: a 6-month study. Respir Med 2008;102, 1511-20.
Vogelmeier C, Hederer B, Glaab T, et al. **Tiotropium versus salmeterol** for the prevention of exacerbations of COPD. **POET-COPD**. N Engl J Med 2011;364:1093-103.
Vogelmeier CF, Bateman ED, Pallante J, et al. Efficacy and safety of **once-daily QVA149** compared with twice-daily salmeterol–fluticasone in patients with chronic obstructive pulmonary disease-ILLUMINATE-randomised, double-blind, parallel group study. Lancet Respir Med 2013; 1: 51–60.
Vogt Hartmut, Lindström Karolina, Bråbäck Lennart, et al. **Preterm Birth and Inhaled Corticosteroid Use** in 6- to 19-Year-Olds: A Swedish National Cohort Study. Pediatrics 2011; 127:6 1052-1059; published ahead of print May 9, 2011, doi:10.1542/peds.2010-3083
Volmer T, Effenberger T, Trautner C, Buhl R. Consequences of **long-term OCS therapy and its side effects** in severe asthma in adults - A focused review of the impact data in the literature. Eur Respir J. 2018 Sep 12.
von Leupoldt A, Taube K, Lehmann K, et al. The impact of **anxiety and depression on outcomes of pulmonary rehabilitation** in patients with COPD. Chest. 2011 Mar 31.
Vooijs M, Siemonsma PC, Heus I, et al. Therapeutic validity and effectiveness of supervised **physical exercise training** on exercise capacity in patients with **chronic obstructive pulmonary disease**: A systematic review and meta-analysis. Clin Rehabil. 2015 Oct 8.
Voorend-van Bergen S, Vaessen-Verberne AA, Brackel HJ, et al. **Monitoring strategies in children with asthma**: a randomised controlled trial. Thorax. 2015 Mar 30.
Vozoris NT, Fischer HD, Wang X, et al. Benzodiazepine drug use and **adverse respiratory outcomes among older adults with COPD**. Eur Respir J 2014;online April 17, 2014

Vuillermin PJ, Robertson CF, Carlin JB, Brennan SL, Biscan MI, South M. **Parent initiated prednisolone** (1mg/kg od x 3-5 days)for acute asthma in children of school age: randomised controlled crossover trial. BMJ 2010;340:c843.

Wagena EJ, Knipschild PG, et al. Efficacy of bupropion & nortriptyline for **smoking cessation** among people at risk for or with chronic obstructive pulmonary disease. Arch Intern Med. 2005 Oct 24;165(19):2286-92. CONCLUSIONS: Bupropion SR treatment is an efficacious aid to smoking cessation in patients with COPD. Nortriptyline treatment seems to be a useful alternative.

Wahidi MM, Kraft M. **Bronchial thermoplasty** for severe asthma. Am J Respir Crit Care Med. 2012 Apr 1;185(7):709-14.

Wahn U, et al. Relationship between pretreatment specific IgE and the response to **omalizumab** therapy. Allergy. 2009 Jul 21. [Epub ahead of print]

Walker S, Monteil M, Phelan K, Lasserson TJ, et al. **Anti-IgE omalizumab** for chronic asthma in adults & children. Cochrane Database Syst Rev. 2006 Apr 19;(2):CD003559.

Walters J, Walters E, Wood-Baker R. Oral **corticosteroids** for stable chronic obstructive pulmonary disease. Cochrane Database Syst Rev. 2005 Jul 20;(3):CD005374. CONCLUSIONS: There is no evidence to support the long-term use of oral steroids at doses less than 10-15 mg prednisolone though some evidence that higher doses (>/= 30 mg prednisolone) improve lung function over a short period. Potentially harmful adverse effects e.g.. diabetes, hypertension, osteoporosis would prevent recommending long-term use at these high doses in most patients.

Walters JA, Turnock AC, Walters EH, et al. **Action plans** with limited patient education only for exacerbations of **chronic obstructive pulmonary disease.** Cochrane Database Syst Rev. 2010 May 12;5:CD005074.

Walters JA, Tan DJ, White CJ, et al. **Systemic corticosteroids** for **acute exacerbations of chronic obstructive pulmonary disease**. Cochrane Database Syst Rev. 2014 Sep 1;9: CD001288. There is high-quality evidence to support treatment of exacerbations of COPD with systemic corticosteroid by the oral or parenteral route in reducing the likelihood of treatment failure and relapse by one month, shortening length of stay in hospital inpatients not requiring assisted ventilation in ICU and giving earlier improvement in lung function and symptoms. There is no evidence of benefit for parenteral treatment compared with oral treatment with corticosteroid on treatment failure, relapse or mortality. There is an increase in adverse drug effects with corticosteroid treatment, which is greater with parenteral administration compared with oral treatment.

Walters JA, Tan DJ, White CJ, et al. **Different durations of corticosteroid therapy** for exacerbations of **chronic obstructive pulmonary disease**. Cochrane Database Syst Rev. 2014 Dec 10;12:CD006897. Information from a new large study has increased our confidence that five days of oral corticosteroids is likely to be sufficient for treatment of adults with acute exacerbations of COPD, and this review suggests that the likelihood is low that shorter courses of systemic corticosteroids (of around five days) lead to worse outcomes than are seen with longer (10 to 14 days) courses. We graded most available evidence as moderate in quality because of imprecision; further research may have an important impact on our confidence in the estimates of effect or may change the estimates. The studies in this review did not include people with mild or moderate COPD; further studies comparing short-duration systemic corticosteroid versus conventional longer-duration systemic corticosteroid for treatment of adults with acute exacerbations of COPD are required.

Wang Y, Chen P, Dai A, et al. Intervention Studies of Inhaled Corticosteroids Combined with Long-acting **Theophylline** or **Long-acting β(2-)agonists** in Patients with Moderate to Severe Asthma: A Randomized, Controlled Study. Clin Ther. 2016 Nov 29.

Wang Z, Pianosi P, Keogh K, et al. The clinical utility of **fractional exhaled nitric oxide (FeNO)** in asthma management. Comparative Effectiveness Review No. 197. AHRQ Publication No.17(18)-EHC030-EF. Rockville, MD: Agency for Healthcare Research and Quality. December 2017.

Waschki B, Kirsten A, et al. **Physical Activity** Is the Strongest Predictor of All-Cause Mortality in Patients With COPD: A Prospective Cohort Study. Chest. 2011 Aug;140(2):331-42.

Waschki B, Kirsten AM, Holz O, et al. Disease Progression and Changes in **Physical Activity** in Patients with COPD. Am J Respir Crit Care Med. 2015 May 28.

Watnick CS, Arnold DH, Latuska R, et al. **Successful Chest Radiograph Reduction by Using Quality Improvement Methodology** for Children With Asthma. Pediatrics. 2018 Jul 11.

Watson WT, Gillespie C, et al. Small-group, interactive **education** and the effect on asthma control by children and their families. CMAJ. 2009 Aug 17. [Epub ahead of print]

Weatherall M, Wijesinghe M, et al. Meta-analysis of the risk of **mortality with salmeterol** and the effect of concomitant inhaled corticosteroid therapy. Thorax. 2010 Jan;65(1):39-43.

Wechsler ME, Wong DA, Miller MK, Lawrence-Miyasaki L. **Churg-strauss syndrome** in patients treated with **omalizumab**. Chest. 2009 Aug;136(2):507-18. Epub 2009 May 1.

Wechsler ME, Kunselman SJ, Chinchilli VM, et al. National Heart, Lung and Blood Institute's Asthma Clinical Research Network. Effect of **beta2-adrenergic receptor polymorphism** on response to longacting beta2 agonist in asthma (LARGE trial): a **genotype-stratified**, randomised, placebo-controlled, crossover trial. Lancet. 2009 Nov21;374(9703):1754-64.

Wechsler ME, Kelley JM, Boyd IOE, et al. Active **albuterol (salbutamol)** or placebo, sham acupuncture, or no intervention in asthma. N Engl J Med 2011;365:119-26

Wechsler ME et al. **Bronchial thermoplasty**: Long-term safety and effectiveness in patients with severe persistent asthma. J Allergy Clin Immunol 2013 Aug 30.

Wechsler ME, Yawn BP, Fuhlbrigge AL, et al; **BELT** Investigators. **Anticholinergic vs Long-Acting β-Agonist in Combination With Inhaled Corticosteroids in Black Adults With Asthma**: The BELT Randomized Clinical Trial. JAMA. 2015 Oct 27;314(16):1720-1730.

Wechsler ME, Akuthota P, Jayne D, et al. **Mepolizumab** or placebo for eosinophilic granulomatosis with polyangiitis. N Engl J Med 2017;376:1921-32.

Wedzicha JA, Calverley PM, Seemungal TA, **INSPIRE** Investigators. The prevention of chronic obstructive pulmonary disease exacerbations by salmeterol/fluticasone propionate or tiotropium bromide. Am J Respir Crit Care Med. 2008 Jan 1;177(1):19-26. Epub 2007 Oct 4. n=1,323 patients mean age, 64 yr, post-bronchodilator FEV1, 39% predicted were randomized in this 2-year trial. We found no difference in exacerbation rate between salmeterol/fluticasone propionate and tiotropium. More patients failed to complete the study while receiving tiotropium. A small statistically significant beneficial effect was found on health status, with an unexpected finding of lower deaths in salmeterol/fluticasone propionate-treated patients.

Weinstein CLJ, Ryan N, Shekar T, et al. Serious asthma **events with mometasone furoate plus formoterol compared with mometasone furoate**. J Allergy Clin Immunol. 2018 Dec 8.

Weinstein SM, Pugach O, Rosales G, et al. **Family Chaos and Asthma Control**. Pediatrics. 2019 Jul 9

Wells KE, Peterson EL, Ahmedani BK, et al. The relationship between combination inhaled **corticosteroid and long-acting β-agonist** use and severe asthma exacerbations in a diverse population. J Allergy Clin Immunol. 2012 May;129(5):1274-1279.e2.

Wells JM, Washko GR, et al; the COPDGene and ECLIPSE Study Investigators. **Pulmonary Arterial Enlargement** and Acute Exacerbations of COPD. N Engl J Med. 2012 Sep 3.

Welsh EJ, Bara A, Barley E, Cates CJ. **Caffeine** for asthma. Cochrane Database Syst Rev. 2010 Jan 20;(1):CD001112.

Welsh EJ, Cates CJ. **Formoterol versus short-acting beta-agonists as relief medication for adults and children with asthma.** Cochrane Database Syst Rev. 2010 Sep 8;9:CD008418. In adults, formoterol was similar to short-acting beta(2)-agonists when used as a reliever, and showed a reduction in the number of exacerbations requiring a course of oral corticosteroids. Clinicians should weigh the relatively modest benefits of formoterol as-needed against the benefits of single inhaler therapy and the potential danger of long-term use of long-acting beta(2)-agonists in some patients. We did not find evidence to recommend changes to guidelines that suggest that long-acting beta(2)-agonists should be given only to patients already taking inhaled corticosteroids.There was insufficient information reported from children in the included trials to come to any conclusion on the safety or efficacy of formoterol as relief medication for children with asthma.

Welsh EJ, Cates CJ, Poole P. Combination inhaled **steroid and long-acting beta2-agonist versus tiotropium** for chronic obstructive pulmonary disease. Cochrane Database Syst Rev. 2013 May 31;5:CD007891. doi: 10.1002/14651858.CD007891.pub3. Since the proportion of missing outcome data compared to the observed outcome data is enough to induce a clinically relevant bias in the intervention effect, the relative efficacy and safety of combined inhalers and tiotropium remains uncertain. Further large, long-term randomised controlled trials comparing combination therapy to tiotropium are required, including adequate follow-up of all participants randomised (similar to the procedures undertaken in TORCH and UPLIFT).

Welte T, Miravitlles M, Hernandez P, et al. Efficacy and tolerability of **budesonide/formoterol added to tiotropium** in patients with chronic obstructive pulmonary disease. Am J Respir Crit Care Med. 2009 Oct 15;180(8):741-50. Epub 2009 Jul 30. (n=660 over 12 weeks)

Wen MC, et al. Efficacy and tolerability of anti-asthma **herbal medicine** intervention in adult patients with moderate-severe allergic asthma. J Allergy Clin Immunol. 2005 Sep;116(3):517-24. CONCLUSION: Anti-asthma herbal medicine intervention appears to be a safe and effective alternative medicine for treating asthma. In contrast with prednisone, **ASHMI** had no adverse effect on adrenal function and had a beneficial effect on T(H)1 and T(H)2 balance.

Wenzel RP, Fowler AA 3rd, Edmond MB. Antibiotic prevention (**azithromycin**) of acute exacerbations of COPD. N Engl J Med. 2012 Jul 26;367(4):340-7.

Wenzel S, Ford L, Pearlman D, et al. **Dupilumab** in Persistent Asthma with Elevated Eosinophil Levels. N Engl J Med. 2013 May 21.

Wenzel S, Castro M, Corren J, et al. **Dupilumab** efficacy and safety in adults with uncontrolled persistent asthma despite use of medium-to-high-dose inhaled corticosteroids plus a long-acting beta agonist: a randomised double-blind lacebo-controlled pivotal phase 2b dose-ranging trial. Lancet. 2016 Apr 26.

Williams Kirsten M.; Chien Jason W.; Gladwin Mark T.; et al. **Bronchiolitis Obliterans** After Allogeneic Hematopoietic Stem Cell Transplantation. JAMA. 2009;302(3):306-314.

Wilson AM, Browne P, Olive S, et al.The effects of maintenance schedules following **pulmonary rehabilitation** in patients with chronic obstructive pulmonary disease: a randomised controlled trial. BMJ Open. 2015 Mar 11;5(3)

Wilt TJ, Niewoehner D, Kim C, et al. Use of **spirometry** for case finding, diagnosis, and management of chronic obstructive pulmonary disease (**COPD**). Evid Rep Technol Assess (Summ). 2005 Aug;(121):1-7. http://hiru.mcmaster.ca/PLUS_BATCHES/batch173_110905/8314.pdf

Winter JD, Reetz MR, Kerns JW, et al. **Changes in Asthma Maintenance Therapy** Prescribing Patterns Following the 2006 **Long-Acting β-Agonist FDA Drug Warning**. Clin Ther. 2017 Mar 8

Wise RA, Anzueto A, Cotton D, et al. **Tiotropium Respimat** inhaler and the risk of death in COPD. (**TIOSPIR**) N Engl J Med 2013. DOI:10.1056/NEJMoa1303342.

Wolthers OD, Walters EG. Short-Term Lower Leg Growth in 5- to 11-Year-Old Asthmatic Children Using Beclomethasone Dipropionate Inhalers With Chlorofluorocarbon or Hydrofluoroalkane Propellants: A 9-Week, Open-Label,Randomized, Crossover, Noninferiority Study. Clin Ther. 2011 Jul 22.

Wolthers OD, Stone S, Bareille P, et al. **Knemometry Assessment** of **Short-Term Growth in Children With Asthma Receiving Fluticasone Furoate** for 2 Weeks: A Randomized, Placebo-Controlled, Crossover Trial. Clin Ther. 2017 May 22.

Wong CH, et al. **Gastro-oesophageal reflux** disease in 'difficult-to-control' asthma: prevalence and response to treatment with acid suppressive therapy. Aliment Pharmacol Ther. 2006 May 1;23(9):1321-7.

Wong CX, Carson KV, Smith BJ. **Home care by outreach nursing for chronic obstructive pulmonary disease.** Cochrane Database Syst Rev. 2011 Mar 16;3:CD000994. Outreach nursing programmes for COPD improved disease-specific HRQL.

Wong CX, Carson KV, Smith BJ. **Home care by outreach nursing for chronic obstructive pulmonary disease**. Cochrane Database Syst Rev. 2012 Apr 18;4:CD000994. Outreach nursing programmes for COPD improved disease-specific HRQL. However the effect on hospitalisations was heterogeneous, reducing admissions in one study, but increasing them in others, therefore we could not draw firm conclusions for this outcome.

Wong C, Jayaram L, Karalus N, et al. **Azithromycin** for prevention of exacerbations in non-cystic fibrosis bronchiectasis (EMBRACE): a randomised, double-blind, placebo-controlled trial. Lancet. 2012 Aug 18;380(9842):660-7.

Wong-McGrath K, Denlinger LC, Bleecker ER, et al; National Heart Lung and Blood Institute's Severe Asthma Research Program-3 Investigators. **Internet-based monitoring** in the Severe Asthma Research Program identifies a subgroup of patients with labile asthma control. Chest. 2017 Oct 25.

Woodcock A, Bleecker ER, Lotvall J, et al. Efficacy and safety of **fluticasone furoate/vilanterol** compared with **fluticasone propionate/salmeterol** combination in adult and adolescent patients with persistent asthma: a randomized trial. Chest. 2013 Oct;144(4):1222-9.

Woodcock A, Vestbo J, Bakerly ND, et al, on behalf of the Salford Lung Study Investigators. Effectiveness of **fluticasone furoate plus vilanterol** on asthma control in clinical practice: an open-label, parallel group, randomised controlled trial. (**SaLSA**) Lancet 2017; online Sept 10.

Woods ER, Bhaumik U, Sommer SJ, et al. **Community asthma initiative**: evaluation of a quality improvement program for comprehensive asthma care. Pediatrics. 2012 Mar;129(3):465-72.

Wootton SL, Ng LW, McKeough ZJ, et al. Ground-based **walking training** improves quality of life and exercise capacity in COPD. Eur Respir J. 2014 Oct;44(4):885-94.

Wouters EF, Postma DS, Fokkens B, et al. **COSMIC** (COPD and Seretide: a Multi-Center Intervention and Characterization) Study Group. Withdrawal of fluticasone propionate from combined salmeterol/fluticasone treatment in patients with **COPD** causes immediate and sustained disease deterioration: a randomised controlled trial. Thorax. 2005 Jun;60(6):480-7. CONCLUSIONS: Withdrawal of FP in COPD patients using SFC resulted in acute and persistent deterioration in lung function and dyspnoea and in an increase in mild exacerbations and percentage of disturbed nights. This study clearly indicates a key role for ICS in the management of COPD as their discontinuation leads to disease deterioration, even under treatment with a LABA.

Writing Committee for the American Lung Association Asthma Clinical Research Centers. Holbrook JT, Wise RA, Gold BD, et al. **Lansoprazole** for children with poorly controlled asthma: a randomized controlled trial. JAMA. 2012;307(4):373-381. PPIs does not improve symptom control in children with asthma.

Wu AC, Tantisira K, Li L, et al; for the Childhood Asthma Management Program Research Group. Effect of **Vitamin D and Inhaled Corticosteroid** Treatment on Lung Function in Children. Am J Respir Crit Care Med. 2012 Sep 15;186(6):508-513.

Yancey SW, Keene ON, Albers FC, et al. **Biomarkers for severe eosinophilic asthma**. J Allergy Clin Immunol. 2017 Dec;140(6):1509-1518.

Yang IA, Fong KM, Sim EH, Black PN, Lasserson TJ. Inhaled corticosteroids for stable chronic obstructive pulmonary disease. Cochrane Database Syst Rev. 2007 Apr 18;(2):CD002991. Patients and clinicians should balance the potential benefits of inhaled steroids in COPD (reduced rate of exacerbations, reduced rate of decline in quality of life), against the known increase in local side effects (oropharyngeal candidiasis and hoarseness). The risk of long term adverse effects is unknown.

Yang, Ya-Wen, Chen, Yi-Hua, Wang, Kuo-Hsien, et al. Risk of **herpes zoster** among patients with chronic obstructive pulmonary disease: a population-based study. CMAJ 2011 183: E275-280.

Yang IA, Clarke MS, Sim EH, et al. **Inhaled corticosteroids** for stable chronic obstructive pulmonary disease (COPD). Cochrane Database Syst Rev. 2012 Jul 11;7:CD002991. Patients and clinicians should balance the potential benefits of inhaled steroids in COPD (reduced rate of exacerbations, reduced rate of decline in quality of life and possibly reduced rate of decline in FEV(1)) against the potential side effects (oropharyngeal candidiasis and hoarseness, and risk of pneumonia).

that yoga probably leads to small improvements in quality of life and symptoms in people with asthma. There is more uncertainty about potential adverse effects of yoga and its impact on lung function and medication usage. RCTs with a large sample size and high methodological and reporting quality are needed to confirm the effects of yoga for asthma.

Yin HS, Gupta RS, et al. Readability, suitability, & characteristics of **asthma action plans**: examination of factors that may impair understanding. Pediatrics. 2013 Jan;131(1):e116-26.

Young LD, Berry JG. Shining the Light on **Parity and Disparity** in **Childhood Asthma Care**. Pediatrics. 2016 Dec 26.

Zeiger RS, Szefler SJ, Phillips BR, et al.; for the Childhood Asthma Research and Education Network of the National Heart, Lung, and Blood Institute. Response profiles to **fluticasone** and montelukast in mild-to-moderate persistent childhood asthma. J Allergy Clin Immunol. 2006 Jan;117(1):45-52.

Zeiger RS et al. **Daily or intermittent budesonide** in preschool children with recurrent wheezing. (**MIST**) N Engl J Med 2011 Nov 24; 365:1990.

Zemek RL, et al. Systematic review of randomized controlled trials examining **written action plans** in children: what is the plan? Arch Pediatr Adolesc Med. 2008 Feb;162(2):157-63. Although there are limited data to firmly conclude that provision of an action plan is superior to none, there is clear evidence suggesting that symptom-based plans are superior to peak flow-based plans in children and adolescents.

Zemek R, Plint A, Osmond MH et al. **Triage Nurse Initiation of Corticosteroids** in Pediatric Asthma Is Associated With Improved Emergency Department Efficiency. Pediatrics. 2012 Mar 19

Zervas E, Samitas K, Papaioannou AI, et al. An **algorithmic approach** for the treatment of severe uncontrolled asthma. ERJ Open Res. 2018 Mar 6;4(1).

Zhang L, Axelsson I, Chung M, Lau J. **Dose Response of Inhaled Corticosteroids in Children** With Persistent Asthma: A Systematic Review. Pediatrics. 2010 Dec 6.

Zhang L, Prietsch SOM, Ducharme FM. **Inhaled corticosteroids in children with persistent asthma: effects on growth**. Cochrane Database of Systematic Reviews 2014, Issue 7. Art. No.: CD009471. DOI: 10.1002/14651858.CD009471.pub2. Regular use of ICS at low or medium daily doses is associated with a mean reduction of 0.48 cm/y in linear growth velocity and a 0.61-cm change from baseline in height during a one-year treatment period in children with mild to moderate persistent asthma. The effect size of ICS on linear growth velocity appears to be associated more strongly with the ICS molecule than with the device or dose (low to medium dose range). ICS-induced growth suppression seems to be maximal during the first year of therapy and less pronounced in subsequent years of treatment. However, additional studies are needed to better characterise the molecule dependency of growth suppression, particularly with newer molecules (mometasone, ciclesonide), to specify the respective role of molecule, daily dose, inhalation device and patient age on the effect size of ICS, and to define the growth suppression effect of ICS treatment over a period of several years in children with persistent asthma.

Zhao ZT, Ji CM, Yu WJ, et al. **Omalizumab** for the treatment of chronic spontaneous urticaria: A meta-analysis of randomized clinical trials. J Allergy Clin Immunol. 2016 Mar 31.

Zhou Yumin, Hu Guoping, Wang Dali, et al. **Community based integrated intervention** for prevention and management of chronic obstructive pulmonary disease (COPD) in Guangdong, China: cluster randomised controlled trial. BMJ 341:doi:10.1136/bmj.c6387 (Published 1 Dec 2010).

Zulueta JJ, Wisnivesky JP, Henschke CI, et al. **Emphysema scores** predict death from **COPD and lung cancer**. Chest. 2012 May;141(5):1216-23.

Web sites:

Asthma UK www.asthma.org.uk; Allergy UK www.allergyuk.org; Lung & Asthma Information Agency www.laia.ac.uk.

Canadian Asthma Consensus Guidelines web site http://www.asthmaguidelines.com

Canadian Network For Asthma Care (CNAC) http://www.cnac.net?english/clinics.html

Global Initiative for Asthma (GINA) http://www.ginasthma.com

Additional benefit of pharmacotherapy[24-26,34]

Current therapy	Escalate to …	Change in Exacerbations	Change in Hospitalizations	Change in Quality of Life	Additional $
SAMA	LAMA	Risk of having one or more exacerbation: OR 0.71; 95% CI 0.52-0.95	Risk of being hospitalized (for any cause): OR 0.34; 95% CI 0.15-0.70	Average change in SGRQ of -3.30; 95% CI -5.63 to -0.97	$40-50
LAMA	LAMA + LABA	Risk of having an exacerbation leading to hospitalization: OR 1.02 (0.80-1.28)	Risk of being hospitalized (for any cause): OR 1.01; 95% CI 0.86-1.19	Average change in SGRQ of -1.34; 95% CI -1.87 to -0.8	$10-30
LAMA + LABA	LAMA + LABA + ICS	Decreased rate of exacerbations: 0.78; 95% CI 0.70-0.88 Zheng'18	Risk of being hospitalized (for any cause) over 1 year: OR 0.91; 95% CI 0.53 to 1.58	Average change in SGRQ of -1.81; 95% CI -2.57 to -1.04 Zheng'18	$30-140

SGRQ: St. George's Respiratory Questionnaire. Measures quality of life. A decrease of at least 4 points (on a scale of 0 to 100) is the minimum clinically important difference to indicate an improvement in quality of life.

Increased risk of pneumonia when using an ICS in a COPD patient

Trial	FEV_1	Comparators	Pneumonia rates	↑ risk per year
TORCH [16]	44%	LABA	13.3% over 3 years	2% per year
		LABA/**ICS**	**19.6%** over 3 years	
FLAME [45]	44%	LABA/LAMA	3.2% over 1 year	1.6% per year
		LABA/**ICS**	**4.8%** over 1 year	
IMPACT [46]	45%	LABA/LAMA	2.6% over 1 year	1.8% per year
		LABA/LAMA/**ICS**	**4.4%** over 1 year	

References for COPD Overview Chart. (See below for separate references for COPD Drug Comparison Chart)

1. Global Strategy for the Diagnosis, Management, and Prevention of Chronic Obstructive Pulmonary Disease (GOLD). **2015.** http://www.goldcopd.org/Guidelines/guidelines-resources.html**.** 85% of COPD caused by smoking. 15-20% of smokers will develop COPD.
GOLD: Global Strategy for **Diagnosis, Management and Prevention of COPD**, **Global Initiative for Chronic Obstructive Lung Disease (GOLD) 2017**. http://goldcopd.org/gold-2017-global-strategy-diagnosis-management-prevention-copd/

2. The 10 leading causes of death, 2011. Statistics Canada. Available from http://www.statcan.gc.ca/pub/82-625-x/2014001/article/11896-eng.htm Accessed July 2015. COPD is the fourth leading cause of death in Canada.
3. O'Donnell DE, Aaron S, Bourbeau J, Hernandez P, et al. **Canadian Thoracic Society** recommendations for **management of chronic obstructive pulmonary disease – 2007** update. Can Respir J. 2007 Sep;14 Suppl B:5B-32B.
CTS- Canadian Thoracic Society: Pharmacotherapy in patients with **COPD – 2019 Update** of Evidence. Sept 2019.
4. Criner GJ, Bourbeau J, Diekemper RL,et al. Executive Summary: **Prevention of Acute Exacerbation** of COPD: **American College of Chest Physicians and Canadian Thoracic Society Guideline**. Chest. **2015** Apr 1;147(4):883-93.
5. O'Donnell DE, Hernandez P, et al. **Canadian Thoracic Society** recommendations for management of chronic obstructive pulmonary disease- **2008 update** -highlights for **primary care**. Can Respir J. 2008 Jan-Feb;15 Suppl A:1A-8A
6. **NICE**: National Institute for Health and Clinical Excellence. Chronic obstructive pulmonary disease (update). (Clinical guideline 101.) **2010**. Available from http://guidance.nice.org.uk/CG101. Accessed July 2015.
7. Wedzicha, Jadwiga A., et al. The prevention of chronic obstructive pulmonary disease exacerbations by salmeterol/fluticasone propionate or tiotropium bromide. American journal of respiratory and critical care medicine 2008;177(1):19-26.
8. Chong J, Karner C, Poole P. Tiotropium versus long-acting beta-agonists for stable chronic obstructive pulmonary disease. Cochrane Database Syst Rev 2012; 9:CD009157
9. Bourbeau, J., and S. J. Bartlett. Patient adherence in COPD. *Thorax* 2008;63(9): 831-838.
10. Molimard, Mathieu. How to achieve good compliance and adherence with inhalation therapy. *Current Medical Research and Opinion* 2005;21:S33-S37.
11. Molimard, M., Raherison, C., Lignot, S., Depont, F., Abouelfath, A., & Moore, N. Assessment of handling of inhaler devices in real life: an observational study in 3811 patients in primary care. *Journal of aerosol medicine,* 2003;16(3):249-254.
12. Puhan, Milo A., et al. "Pulmonary rehabilitation following exacerbations of chronic obstructive pulmonary disease." *Cochrane Database Syst Rev* 10.10 (2011).
13. Anthonisen, Nicholas R., et al. The effects of a smoking cessation intervention on 14.5-year mortality: a randomized clinical trial. Annals of internal medicine 2005;142(4):233-239.
14. Godtfredsen, N. S., et al. COPD-related morbidity and mortality after smoking cessation: status of the evidence. European Respiratory Journal 2008;32(4):844-853.
15. Smoking Cessation benefits: Fletcher C, Peto R. The natural history of chronic airflow obstruction. Br Med J. 1977 Jun 25;1(6077):1645-8.
16. Wongsurakiat, Phunsup, et al. Acute respiratory illness in patients with COPD and the effectiveness of influenza vaccination: a randomized controlled study. CHEST Journal 2004 125(6):2011-2020.
17. Walters, J. A., et al. Injectable vaccines for preventing pneumococcal infection in patients with chronic obstructive pulmonary disease. Cochrane Database Syst Rev 11 (2010).
18. Stoller, James K. Acute exacerbations of chronic obstructive pulmonary disease. New England Journal of Medicine 2002;346(13):988-994.
19. Dewar, M. A. R. V. I. N., and R. WHIT Curry Jr. Chronic obstructive pulmonary disease: diagnostic considerations. *American family physician* 2006;73(4):669-676. 20 year pack history indicative of COPD. Expert opinion - sometimes 10 years is enough.
20. Robles, Janie, and Lesley Motheral. Hypersensitivity Reaction After Inhalation of a Lactose-Containing Dry Powder Inhaler. *The Journal of Pediatric Pharmacology and Therapeutics* 2014;19(3):206-211.
21. Lactose-free products: Bricanyl Turbuhaler; Pulmicort Turbuhaler; all MDIs; all Respimats. Vast majority of DPIs contain lactose.
(http://www.aaia.ca/en/milk_proteins_and_allergy_medications.htm)
22. **Milk Proteins and Allergy Medications.** Allergy/Asthma Information Association. Available from http://www.aaia.ca/en/milk_proteins_and_allergy_medications.htm. Accessed July 2015.
23. Silverman, Edwin K., Sandhaus, Robert A. Alpha1-Antitrypsin Deficiency. N Engl J Med 2009 360: 2749-2757
24. Cheyne L, Irvin-Sellers MJ, White J. Tiotropium versus ipratropium bromide for chronic obstructive pulmonary disease. Cochrane Database of Systematic Reviews 2013, Issue 9. Art. No.: CD009552. DOI: 10.1002/14651858.CD009552.pub2.

25. Farne HA, Cates CJ. Long-acting beta2-agonist in addition to tiotropium versus either tiotropium or long-acting beta2-agonist alone for chronic obstructive pulmonary disease. Cochrane Database Syst Rev. 2015 Oct 22;(10):CD008989.
26. Karner C, Cates CJ. Combination inhaled steroid and long-acting beta2-agonist in addition to tiotropium versus tiotropium or combination alone for chronic obstructive pulmonary disease. *Cochrane Database of Systematic Reviews* 2011, (Cazzola 2007, Aaron 2007, Welte 2009). Adding on ICS – one study (Aaron 2007) with good methodology but small sample size.
27. Sestini, Piersante, et al. "Short-acting beta2-agonists for stable chronic obstructive pulmonary disease." *The Cochrane Library* (2002). Beta-agonists shown to be beneficial for improvements in symptoms quality of COPD.
28. Appleton, Sarah, et al. "Ipratropium bromide versus short acting beta-2 agonists for stable chronic obstructive pulmonary disease." *Cochrane Database Syst Rev* 2 (2006). Ipratropium shown to be as good as, and possibly better than, SABAs in COPD for symptoms improvement.
29. Suissa S et al. Discontinuation of inhaled corticosteroids in COPD and the risk reduction of pneumonia. Chest 2015 Nov; 148:1177.
30. Walters, Julia AE, et al. "Pneumococcal vaccines for preventing pneumonia in chronic obstructive pulmonary disease." The Cochrane Library (2017). CD001390
31. Molimard M, Raherison C, Lignot S, Depont F, Abouelfath A, Moore N. Assessment of handling of inhaler devices in real life: an observational study in 3811 patients in primary care. J Aerosol Med. 2003 Fall;16(3):249-54.
32. Nicolas Dugré, William Tenaglia McInnis, G. Michael Allan. Tools for Practice #238: In COPD puffers, does three-of-kind beat a pair? Accessed from https://gomainpro.ca/wp-content/uploads/tools-for-practice/1561388469_copdtfp238.pdf on July 11, 2019.
33. **SUNSET**. Chapman KR, Hurst JR, Frent SM, et al. Long-Term Triple Therapy De-escalation to Indacaterol/Glycopyrronium in Patients with Chronic Obstructive Pulmonary Disease (SUNSET): A Randomized, Double-Blind, Triple-Dummy Clinical Trial. Am J Respir Crit Care Med. 2018 Aug 1;198(3):329-339.
34. Zheng Y, Zhu J, Liu Y, et al. **Triple therapy** in the management of chronic obstructive pulmonary disease: systematic review and meta-analysis. BMJ. 2018 Nov 6;363:k4388.
35. Beltaief K, Msolli MA, Zorgati A, et al. **Nebulized terbutaline & ipratropium bromide vs terbutaline alone** in acute exacerbation of COPD requiring noninvasive ventilation: a randomized double blind controlled trial. Acad Emerg Med. 2018 Aug 29.
36. McDonagh M, Holmes R, Blazina I, et al. Drugs to Treat Asthma and Chronic Obstructive Pulmonary Disease (COPD). Final Update 1 Report prepared by the Pacific Northwest Evidence-based Practice Center for the Drug Effectiveness Review Project. Oregon Health & Science University, Portland, Oregon, June 2016.
37. Murrey Brown, Robert & Spiegel, Rory. (2019). Antibiotic Prophylaxis in Patients with COPD. American family physician. 99. Online. https://www.aafp.org/afp/2019/0601/od1.html
38. Butler CC, Gillespie D, White P, et al. C-Reactive Protein Testing to Guide **Antibiotic Prescribing for COPD Exacerbations**. (**PACE**) N Engl J Med. 2019 Jul 11;381(2):111-120.

References - COPD Drug Comparison Chart

1. Niewoehner, Dennis E., et al. "Prevention of exacerbations of chronic obstructive pulmonary disease with tiotropium, a once-daily inhaled anticholinergic bronchodilator: a randomized trial." *Annals of internal medicine* 143.5 (2005): 317-326. Tiotropium expected to reduce exacerbations by a relative risk reduction of 19% per year vs. placebo (0.85 vs 1.05 exacerbations per year). It also reduced the number of patients experiencing one or more exacerbations during the trial (32.3% vs 27.9%).
2. UPLIFT. Tashkin, Donald P., et al. "A 4-year trial of tiotropium in chronic obstructive pulmonary disease." *New England Journal of Medicine* 359.15 (2008): 1543-1554.
3. Kornmann, O., et al. "**INLIGHT-2** (Indacaterol Efficacy Evaluation Using 150-µg Doses with COPD Patients) Study Investigators: Once-daily indacaterol versus twice-daily salmeterol for COPD: a placebo-controlled comparison." *Eur Respir J* 37.2 (2011): 273-279. Indacaterol noted to have cough immediately after inhalation.
4. Ridolo, Erminia, et al. "Role of indacaterol and the newer very long-acting β2-agonists in patients with stable COPD: a review." *International journal of chronic obstructive pulmonary disease* 8 (2013): 425. Cough for indacterol may go away after 1 week.
5. Chong J, Karner C, Poole P. Tiotropium versus long-acting beta-agonists for stable chronic obstructive pulmonary disease. Cochrane Database Syst Rev 2012; 9:CD009157. Tiotropium superior to salmeterol. In general, LAMAs better tolerated than LABAs.
6. Cazzola, Mario, et al. "Assessing the clinical value of fast onset and sustained duration of action of long-acting bronchodilators for COPD." *Pulmonary pharmacology & therapeutics* 31 (2015): 68-78.
7. Ferguson, Gary T., et al. "Efficacy and safety of olodaterol once daily delivered via Respimat® in patients with GOLD 2–4 COPD: results from two replicate 48-week studies." *International journal of chronic obstructive pulmonary disease* 9 (2014): 629.
8. Centre for Drug Evaluation and Research. Indacaterol Regulatory Action. Available from: http://www.accessdata.fda.gov/drugsatfda_docs/nda/2011/022383Orig1s000SumR.pdf Accessed August 2015.
9. Sears, Malcolm R. "Adverse effects of β-agonists." *Journal of allergy and clinical immunology* 110.6 (2002): S322-S328.
10. DiPiro, J et al. Chapter 16. Chronic Obstructive Pulmonary Disease. Pharmacotherapy: A Pathophysiologic Approach. 9th Edition. 2014. McGraw-Hill Education.
11. Karner C, Cates CJ. Long-acting beta2-agonist in addition to tiotropium versus either tiotropium or long-acting beta2- agonist alone for chronic obstructive pulmonary disease. *Cochrane Database of Systematic Reviews* 2012, Issue 4. CD008989. LABA/TIO vs LABA alone or TIO alone. Statistically, but not clinically, significant differences noted between dual vs mono therapy.
12. Welsh EJ, Cates CJ, Poole P. Combination inhaled steroid and long-acting beta2-agonist versus tiotropium for chronic obstructive pulmonary disease. *Cochrane Database of Systematic Reviews* 2013, Issue 5. CD007891. LABA/ICS - more hospitalizations, less oral steoids, less antibiotics, no difference in rate of exacerbations, better quality of life (not clincally relevant of a change), fewer withdrawals, more pneumonia. Overall: no improvement in exacerbations with more cases of pneumonia. Limitation: lots of withdrawals.

13. Lexi-Drugs Online. Hudson, Ohio: Lexi-Comp, Inc. Accessed August 2015.
14. Pesce, Amadeo J., Mitchell Rashkin, and Uma Kotagal. "Standards of laboratory practice: theophylline and caffeine monitoring." *Clinical chemistry* 44.5 (1998): 1124-1128.
15. Karner C, Cates CJ. The effect of adding inhaled corticosteroids to tiotropium and long-acting beta2-agonists for chronic obstructive pulmonary disease. *Cochrane Database of Systematic Reviews* 2011, Issue 9. CD009039.
16. **TORCH**. Calverley, Peter MA, et al. "Salmeterol and fluticasone propionate and survival in chronic obstructive pulmonary disease." *New England Journal of Medicine* 356.8 (2007): 775-789.
17. **SHINE**. Bateman, Eric D., et al. "Dual bronchodilation with QVA149 versus single bronchodilator therapy: the SHINE study." *European Respiratory Journal* 42.6 (2013): 1484-1494.
18. **SPARK**. Wedzicha, Jadwiga A., et al. "Analysis of chronic obstructive pulmonary disease exacerbations with the dual bronchodilator QVA149 compared with glycopyrronium and tiotropium (SPARK): a randomised, double-blind, parallel-group study." *The Lancet Respiratory Medicine* 1.3 (2013): 199-209.
19. **INVOLVE.** Dahl, Ronald, et al. "Efficacy of a new once-daily long-acting inhaled β2-agonist indacaterol versus twice-daily formoterol in COPD." *Thorax* 65.6 (2010): 473-479.
20. **POET.** Vogelmeier, Claus, et al. "Tiotropium versus salmeterol for the prevention of exacerbations of COPD." *New England Journal of Medicine* 364.12 (2011): 1093-1103.
21. **Oxygen therapy requirements in SK.** Available from: https://www.saskatchewan.ca/~/media/files/health/health%20and%20healthy%20living/manage%20your%20health%20needs/support%20programs%20and%20services/sail/sail-general-policies.pdf Accessed August 2015
22. Doherty, Dennis E., et al. "Effects of mometasone furoate/formoterol fumarate fixed-dose combination formulation on chronic obstructive pulmonary disease (COPD): results from a 52-week Phase III trial in subjects with moderate-to-very severe COPD." *International journal of chronic obstructive pulmonary disease* 7 (2012): 57.
23. Tashkin, Donald P., et al. "Efficacy and safety characteristics of mometasone furoate/formoterol fumarate fixed-dose combination in subjects with moderate to very severe COPD: findings from pooled analysis of two randomized, 52-week placebo-controlled trials." *International journal of chronic obstructive pulmonary disease* 7 (2012): 73.
24. Global Initiative for Chronic Obstructive Lung Disease (**GOLD**). Global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease. Bethesda (MD): Global Initiative for Chronic
Obstructive Lung Disease (GOLD); **2010**. http://www.goldcopd.org/uploads/users/files/GOLDReport_April112011.pdf
Fabbri LM, Hurd SS; GOLD Scientific Committee. Global Strategy for the Diagnosis, Management and Prevention of COPD: **2009 update**. http://www.goldcopd.com
Rabe KF, Hurd S, Anzueto A, Barnes PJ, et al. Global Strategy for the Diagnosis, Management, and Prevention of Chronic Obstructive Pulmonary Disease: **GOLD** Executive Summary. Am J Respir Crit Care Med. 2007 Sep 15;176(6):532-55. Epub **2007** May 16.
Vestbo J, Hurd SS, Agusti AG, et al. Global Strategy for the Diagnosis, Management and Prevention of Chronic Obstructive Pulmonary Disease, **GOLD 2011 Executive Summary**. Am J Respir Crit Care Med. 2012 Aug 9.
Global Initiative for Chronic Obstructive Lung Disease (GOLD). Global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease. Vancouver (WA):
Global Initiative for Chronic Obstructive Lung Disease **(GOLD); 2011.** http://www.goldcopd.org/uploads/users/files/GOLD_Report_2011_Feb21.pdf
Global Initiative for Chronic Obstructive Lung Disease **(GOLD); 2013.** http://www.goldcopd.org/uploads/users/files/GOLD_AtAGlance_2013_Feb20.pdf
Global Initiative for Chronic Obstructive Lung Disease **(GOLD); 2015.** http://www.goldcopd.org/Guidelines/guidelines-resources.html
Global Initiative for Chronic Obstructive Lung Disease **(GOLD); 2017.** http://goldcopd.org/gold-2017-global-strategy-diagnosis-management-prevention-copd/
25. American Thoracic Society Guidelines 2004 http://www.thoracic.org/copd
26. Qaseem A, Wilt TJ, Weinberger SE, et al. American College of Physicians (**ACP**); American College of Chest Physicians (**ACCP**); American Thoracic Society (**ATS**); European Respiratory Society (**ERS**). Diagnosis and management of **stable chronic obstructive pulmonary disease**: a clinical practice guideline update from the American College of Physicians, American College of Chest Physicians, American Thoracic Society, and European Respiratory Society. Ann Intern Med. **2011** Aug 2;155(3):179-91.
27. Nice Guidelines 2004 http://www.nice.org.uk/pdf/CG012_niceguideline.pdf
NICE: National Institute for Health and Clinical Excellence. Chronic obstructive pulmonary disease (update). (Clinical guideline 101.) **2010**. http://guidance.nice.org.uk/CG101.
28. Micromedex 2015; Drugs in Pregnancy and Lactation, 9th ed. Briggs GE, Freeman RK, Yaffe SJ, editors. Williams and Wilkins; Baltimore, MD: 2011.; Hansten & Horn-Drug Interactions 2015.
29. Biggadike, Keith. "Fluticasone furoate/fluticasone propionate–different drugs with different properties." *The clinical respiratory journal* 5.3 (2011): 183-184.
30. Vestbo, Jørgen, et al. "Onset of effect of aclidinium, a novel, long-acting muscarinic antagonist, in patients with COPD." *COPD: Journal of Chronic Obstructive Pulmonary Disease* 7.5 (2010): 331-336. Lists a rapid onset of effect - all patients see onset by 30 minute mark.
31. Sims, Michael W., and Reynold A. Panettieri Jr. "Profile of aclidinium bromide in the treatment of chronic obstructive pulmonary disease." *International journal of chronic obstructive pulmonary disease* 6 (2011): 457. Aclidinium - rapid metabolism by plasma esterase = less systemic side effect potential?
32. Joos, G. F., et al. "Bronchodilatory effects of aclidinium bromide, a long-acting muscarinic antagonist, in COPD patients." *Respiratory medicine* 104.6 (2010): 865-872.
33. **GLOW1** D'Urzo, Anthony, et al. "Efficacy and safety of once-daily NVA237 in patients with moderate-to-severe COPD: the GLOW1 trial." *Respiratory research* 12.1 (2011): 156.

34. **GLOW2** Kerwin, Edward, et al. "Efficacy and safety of NVA237 versus placebo and tiotropium in patients with COPD: the GLOW2 study." *European Respiratory Journal* 40.5 (2012): 1106-1114.
34. **GLOW5** Chapman KR, Beeh KM, Beier J, et al. A blinded evaluation of the efficacy and safety of glycopyrronium, a once-daily long-acting muscarinic antagonist, versus tiotropium, in patients with COPD: the GLOW5 study. BMC Pulm Med. 2014;14(1):4.
35. **INSIST**. Korn, Stephanie, et al. "Indacaterol once-daily provides superior efficacy to salmeterol twice-daily in COPD: a 12-week study." *Respiratory medicine* 105.5 (2011): 719-726.
36. Benzo R, Vickers K, Novotny PJ, et al. **Health Coaching** and Chronic Obstructive Pulmonary Disease Rehospitalization. A Randomized Study. Am J Respir Crit Care Med. 2016 Sep 15;194(6):672-80.
37. Long-Term Oxygen Treatment Trial (**LOTT**) Research Group. A randomized trial of **long-term oxygen** for COPD with moderate desaturation. N Engl J Med 2016;375:1617-27.
38. Polkey MI, Qiu ZH, et al. **Tai Chi and Pulmonary Rehabilitation** Compared for Treatment-Naive Patients With COPD: A Randomized Controlled Trial. Chest. 2018 Mar 28.
39. Gonzalez AV, Coulombe J, Ernst P, et al. **Long-term Use of Inhaled Corticosteroids** in **COPD and the Risk of Fracture**. Chest. 2018 Feb;153(2):321-328.
40. Lee CM, Heo J, Han SS, et al. **Inhaled corticosteroid-related tuberculosis** in the real world among patients with asthma and COPD: A 10-year nationwide population-based study. J Allergy Clin Immunol Pract. 2018 Oct 16.
41. Gordon CS, Waller JW, Cook RM, et al. Effect of **pulmonary rehabilitation on symptoms of anxiety and depression** in chronic obstructive pulmonary disease: a systematic review and meta-analysis. Chest. 2019 Apr 26.
42. Welte T. **Azithromycin, the Holy Grail to Prevent Exacerbations** in Chronic Respiratory Disease. Am J Respir Crit Care Med. 2019 Apr 15.
43. Wise RA, Chapman KR, Scirica BM, et al. Effect of **Aclidinium Bromide on Major Cardiovascular Events and Exacerbations** in High-Risk Patients With Chronic Obstructive Pulmonary Disease: The ASCENT-COPD Randomized Clinical Trial. JAMA. 2019 May 7;321(17):1693-1701.
44. Cramer H, Haller H, Klose P, et al. The **risks and benefits of yoga** for patients with chronic obstructive pulmonary disease: a systematic review and meta-analysis. Clin Rehabil. 2019 Jul 29:269215519860551.
45. **FLAME.** Wedzicha JA, Banerji D, Chapman KR, et al. **Indacaterol–glycopyrronium** versus **salmeterol–fluticasone for COPD**. (**FLAME**) N Engl J Med. DOI: 10.1056/NEJMoa1516385.
46. **IMPACT.** Lipson DA, Barnhart F, Brealey N, et al. **Once-daily singleinhaler triple versus dual therapy** in patients with COPD. (**IMPACT**) N Engl J Med. DOI: 10.1056/NEJMoa1713901
47. Nicolas Dugré, William Tenaglia McInnis, G. Michael Allan. Tools for Practice #238: In COPD puffers, does three-of-kind beat a pair? Accessed from https://gomainpro.ca/wp-content/uploads/tools-for-practice/1561388469_copdtfp238.pdf on July 11, 2019.
Sivapalan P, Lapperre TS, Janner J, et al. Eosinophil-guided corticosteroid therapy in patients admitted to hospital with COPD exacerbation (CORTICO-COP): a multicentre, randomised, controlled, open-label,non-inferiority trial. *Lancet Respir Med* 2019; **7:** 699–709.

COPD – Drug Comparison Chart - Additional references

Aaron SD, Vandemheen KL, Fergusson D, Maltais F, Bourbeau J, Goldstein R, Balter M, O'donnell D, McIvor A, Sharma S, Bishop G, Anthony J, Cowie R, Field S, Hirsch A, Hernandez P, Rivington R, Road J, Hoffstein V, Hodder R, Marciniuk D, McCormack D, Fox G, Cox G, Prins HB, Ford G, Bleskie D, Doucette S, Mayers I, Chapman K, Zamel N, Fitzgerald M. **Tiotropium in Combination** with Placebo, Salmeterol, or Fluticasone-Salmeterol for Treatment of Chronic Obstructive Pulmonary Disease: A Randomized Trial. Ann Intern Med. 2007 Feb 19; [Epub ahead of print] Addition of fluticasone-salmeterol to tiotropium therapy did not statistically influence rates of COPD exacerbation but did improve lung function, quality of life, and hospitalization rates in patients with moderate to severe COPD. The addition of fluticasone-salmeterol (Advair) to a regimen that includes tiotropium (Spiriva) reduces hospitalizations and improves quality of life symptom scores, but does not decrease the frequency of chronic obstructive pulmonary disease (COPD) exacerbations. The addition of salmeterol (Serevent) to tiotropium has no effect on hospitalizations and no clinically significant effect on other quality of life measures. (LOE = 1b)

Aaron SD et al. Diagnostic instability and reversals of chronic obstructive pulmonary disease diagnosis in individuals with mild to moderate **airflow obstruction**. Am J Respir Crit Care Med 2017 Aug 1; 196:306.

Aaron SD. **Management and prevention of exacerbations of COPD**. BMJ. 2014 Sep 22;349:g5237.

Aboumatar H, Naqibuddin M, Chung S, et al. Effect of a **Hospital-Initiated Program Combining Transitional Care and Long-term Self-management** Support on Outcomes of Patients Hospitalized With Chronic Obstructive Pulmonary Disease: A Randomized Clinical Trial. JAMA. 2019 Oct 8;322(14):1371-1380.

Aboumatar H, Naqibuddin M, Chung S, et al. Effect of a program combining **transitional care and long-term self-management support on outcomes of hospitalized patients** with chronic obstructive pulmonary disease: a randomized clinical trial [online Nov 12, 2018]. JAMA.

Abramson MJ, Schattner RL, Sulaiman ND, et al. Do **spirometry** and regular follow-up improve health outcomes in general practice patients with asthma or COPD? A cluster randomized controlled trial. Med J Aust. 2010 Jul 19;193(2):104-9.

Afonso AS, Verhamme KM, Stricker BH, et al. Inhaled anticholinergic drugs and risk of **acute urinary retention**. BJU Int. 2010 Sep 29. doi: 10.1111/j.1464-410X.2010.09600.x.

Agarwal R, Aggarwal AN, Gupta D, Jindal SK. **Inhaled corticosteroids** vs. placebo for preventing COPD exacerbations:a systematic review and meta-regression of randomized controlled trials. Chest. 2009 Sep 25.

Agarwal M, Agrawal S, Garg L, et al. Effect of Chronic Obstructive Pulmonary Disease on In-Hospital Mortality and Clinical Outcomes After ST-Segment Elevation **Myocardial Infarction**. Am J Cardiol. 2017 May 15;119(10):1555-1559.

Agustí A, Celli B, Faner R. What does **endotyping** mean for treatment in chronic obstructive pulmonary disease? Lancet. 2017 Sep 2;390(10098):980-987

Agustí A, Hogg JC. Update on the **Pathogenesis of Chronic Obstructive Pulmonary Disease**. N Engl J Med. 2019 Sep 26;381(13):1248-1256.

Ahmedzai S et al. Managing passengers with stable respiratory disease planning **air travel**: British Thoracic Society recommendations. Thorax 2011; 66: i1ei30

Alair Bronchial Thermoplasty System is a catheter-based device that delivers radiofrequency energy to the airways through the nose or mouth. The energy warms the airway linings and prevents the muscle from contracting. http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm209909.htm

Alansari K, Sakran M, Davidson BL, et al. Oral **Dexamethasone for Bronchiolitis**: A Randomized Trial. Pediatrics. 2013 Sep 16.

Albert RK, Connett J, Bailey WC, et al. **Azithromycin** for prevention of exacerbations of COPD. N Engl J Med 2011;365: 689-98.

Aleva FE, Voets LW, Simons SO, et al. Prevalence and Localization of **Pulmonary Embolism** in Unexplained Acute Exacerbations of COPD: A systematic review and meta-analysis. Chest. 2016 Aug 11. pii: S0012-3692(16)53752-0.

Alfageme I, Vazquez R, Reyes N, et al. Clinical efficacy of **anti-pneumococcal vaccination** in patients with COPD. Thorax. 2005 Oct 14; [Epub ahead of print]

Alía I, de la Cal MA, Esteban A, et al. Efficacy of **corticosteroid therapy** in patients with an acute exacerbation of **chronic obstructive pulmonary disease** receiving **ventilatory support**. Arch Intern Med. 2011;171(21):1939-1946.

Alison JA, McKeough ZJ, Leung RWM, et al. **Oxygen compared to air during exercise training** in COPD with exercise-induced desaturation. Eur Respir J. 2019 May 30;53(5).

Altenburg J, de Graaff CS, Stienstra Y, et al. Effect of **azithromycin maintenance treatment on infectious exacerbations** among patients with non–cystic fibrosis bronchiectasis: the BAT randomized controlled trial. JAMA. 2013;309(12):1251-1259.

Almagro P, Soriano J, Cabrera F, et al; Working Group on COPD, Spanish Society of Internal Medicine.*. Short- and medium-term **prognosis** in patients hospitalized for **COPD** exacerbation: The **CODEX index**. Chest. 2013 Sep 26.

Ameer F, Carson KV, Usmani ZA, et al. **Ambulatory oxygen for people with chronic obstructive pulmonary disease** who are not hypoxaemic at rest. Cochrane Database Syst Rev. 2014 Jun 24;6:CD000238. In patients with COPD with moderate hypoxia, current evidence on ambulatory oxygen therapy reveals improvements in dyspnoea post exercise and in the dyspnoea and fatigue domain of quality of life. However, evidence for the clinical utility and effectiveness of ambulatory oxygen in improving mortality and exercise capacity was not evident in this review. Methodologically rigorous RCTs with sufficient power to detect a difference are required to investigate the role of ambulatory oxygen in the management of COPD.

American Lung Association Asthma Clinical Research Centers. Clinical trial of low-dose theophylline and montelukast in patients with poorly controlled asthma. Am J Respir Crit Care Med. 2007 Feb 1;175(3):235-42. Epub 2006 Sep 22. Neither montelukast nor low-dose theophylline lowered the EPAC rate of poor asthma control in patients with poorly controlled asthma despite improved lung function. For patients not using inhaled corticosteroids, low-dose theophylline improved asthma symptom control more than montelukast or placebo, and provides a safe and low-cost alternative asthma treatment.

Andell P, Erlinge D, Smith JG, et al. **β-blocker use and mortality in COPD** patients **after myocardial infarction**: a Swedish nationwide observational study. J Am Heart Assoc. 2015 Apr 8;4(4).

Anthonisen NR, et al.; Lung Health Study Research Group. The effects of a **smoking cessation** intervention on 14.5-year **mortality**: a randomized clinical trial. Ann Intern Med. 2005 Feb 15;142(4):233-9.

Anthonisen NR, Manfreda J, Warren CP, Hershfield ES, Harding GK, Nelson NA. **Antibiotic therapy in exacerbation** of chronic obstructive pulmonary disease. Ann Intern Med 1987;106(2):196-204.

Antolín-Amérigo D, Vlaicu PC, De La Hoz Caballer B, Cano MS. **Anaphylaxislike cholinergic urticaria**. Can Fam Physician. 2013 Jul;59(7):745-6. (Montelukast used)

Anzueto A, Miravitlles M. Considerations for the **Correct Diagnosis** of Chronic Obstructive Pulmonary Disease and Its Management With Bronchodilators. Chest. 2018 Mar 7.
Appleton S, et al. **Long-acting beta2**-agonists for poorly reversible chronic obstructive pulmonary disease. Cochrane Database Syst Rev. 2006 Jul 19;3:CD001104.
Arrington-Sanders R, et al. **Ritonavir-fluticasone** interaction causing Cushing syndrome in HIV-infected children and adolescents. Pediatr Infect Dis J. 2006 Nov;25(11):1044-8.
Austin MA et al. Effect of high flow **oxygen on mortality in chronic obstructive pulmonary disease** patients in prehospital setting: Randomised controlled trial. BMJ 2010 Oct 18; 341:c5462.
Ayache MB, Boyaji S, Pile JC. Q: Can we reduce the **risk of readmission** for a patient with an exacerbation of **COPD**? Cleve Clin J Med. 2014 Sep;81(9):525-7.
Babu S, Kastelik JA, and Morjaria JB. **Inhaled Corticosteroids in COPD**: A Pro-Con Perspective. British Journal of Clinical Pharmacology. 2014.
Bafadhel M, Clark TW, Reid C, et al. **Procalcitonin and C-reactive protein** in hospitalized adult patients with community-acquired pneumonia or exacerbation of asthma or COPD.
Baker E, Fatoye F. Clinical and cost effectiveness of **nurse-led self-management interventions** for patients with copd in primary care: A systematic review. Int J Nurs Stud. 2017 Jun;71:125-138.
Barr RG, Bourbeau J, Camargo CA, Ram FS. **Tiotropium** for stable chronic obstructive pulmonary disease: A meta-analysis. Thorax. 2006 Oct;61(10):854-62. Epub 2006 Jul 14.
Tiotropium reduced COPD exacerbations and related hospitalisations, improved quality of life and symptoms, and may have slowed the decline in FEV1. Long term trials are warranted to evaluate the effects of tiotropium on decline in FEV1 and to clarify its role compared with LABA.
Barr RG, et al. Inhaled **tiotropium** for stable chronic obstructive pulmonary disease. Cochrane Database Syst Rev. 2005 Apr 18;(2):CD002876 & *ACP* Journal club. AUTHORS' CONCLUSIONS: Tiotropium reduced COPD exacerbations and related hospitalisations compared to placebo and ipratropium. It also improved health-related quality-of-life and symptom scores among patients with moderate and severe disease, and may have slowed decline in FEV1. Additional long-term studies are required to evaluate its effect on mortality and change in FEV1 to clarify its role in comparison to, or in combination with, long-acting ss2-agonists and to assess its effectiveness in mild and very severe COPD. (Barr RG, Bourbeau J, Camargo Jr CA, Ram FS. Tiotropium for stable chronic obstructive pulmonary disease: a meta-analysis. Thorax. 2006 Jul 14; [Epub ahead of print])
Barr, R. Graham, Bluemke, David A., Ahmed, Firas S., et al. Percent Emphysema, Airflow Obstruction, and Impaired **Left Ventricular Filling**. N Engl J Med 2010 362: 217-227.
Barrecheguren M, Miravitlles M. COUNTERPOINT: Should **LAMA/LABA Combination Therapy** Be Used as Initial Maintenance Treatment for COPD? No. Chest. 2018 Oct;154(4):749-751.
Bassler D et al. Early inhaled **budesonide for the prevention of bronchopulmonary dysplasia**. (**NEUROSIS**) N Engl J Med 2015 Oct 15; 373:1497.
Beasley R, Singh S, Loke YK, et al. Call for worldwide **withdrawal of tiotropium Respimat mist inhaler**. BMJ. 2012 Nov 9;345:e7390.
Beauchamp MK, Evans R, et al. Systematic Review of Supervised **Exercise Programs** After Pulmonary Rehabilitation in Individuals With COPD. Chest. 2013 Oct;144(4):1124-33.
Beaumont M, Mialon P, Le Ber C, et al. Effects of inspiratory muscle training on dyspnoea in severe COPD patients during pulmonary rehabilitation: controlled randomised trial. Eur Respir J. 2018 Jan 25;51(1).
Becker LA, Hom J, Villasis-Keever M, et al. **Beta2-agonists for acute cough or a clinical diagnosis of acute bronchitis**. Cochrane Database Syst Rev. 2015 Sep 3;9:CD001726.
There is no evidence to support the use of beta2-agonists in children with acute cough who do not have evidence of airflow restriction. There is also little evidence that the routine use of beta2-agonists is helpful for adults with acute cough. The se agents may reduce symptoms, including cough, in people with evidence of airflow restriction. However, this potential benefit is not well supported by the available data and must be weighed against the adverse effects associated with their use. There is no evidence to support the use of beta2-agonists in children with acute cough who do not have evidence of airflow restriction. There is also little evidence that the routine use of beta2-agonists is helpful for adults with acute cough. These agents may reduce symptoms, including cough, in people with evidence of airflow restriction. However, this potential benefit is not well supported by the available data and must be weighed against the adverse effects associated with their use.
Behrens G, Matthews CE, Moore SC, et al. **Body size and physical activity** in relation to incidence of chronic obstructive pulmonary disease. CMAJ. 2014 Jul 7.
Belgrave DCM, Granell R, Turner SW, et al. **Lung function trajectories** from **pre-school age to adulthood and their associations with early life factors**: a retrospective analysis of three population-based birth cohort studies. Lancet Respir Med 2018; online April 5.
Bellou V, Belbasis L, Konstantinidis AK, et al. Prognostic models for **outcome prediction in patients** with chronic obstructive pulmonary disease: systematic review and critical appraisal. BMJ. 2019 Oct 4;367:l5358.
Bergen R, Black S, et al. Safety of cold-adapted live attenuated **influenza vaccine** in a large cohort of children & adolescents. Pediatr Infect Dis J. 2004 Feb;23(2):138-44.
Bernocchi P; et al. Home-based **telerehabilitation** in older patients with chronic obstructive pulmonary disease & heart failure: randomized trial. Age Ageing. 2017 Aug 30:1-7.
Beta$_2$-agonists **Drug Class Review Nov/06** Oregon Health & Science University. http://www.ohsu.edu/drugeffectiveness/reports/documents/Beta%20Agonists%20Final%20Report.pdf
Bhatt SP, Balte PP, Schwartz JE, et al. Discriminative Accuracy of **FEV1:FVC** Thresholds for COPD-Related Hospitalization and Mortality. JAMA. 2019 Jun 25;321(24):2438-2447.
Bhatt SP, Terry NL, Nath H, et al; Genetic Epidemiology of COPD (COPDGene) Investigators. Association Between Expiratory **Central Airway Collapse** and Respiratory Outcomes Among Smokers. JAMA. 2016 Feb 2;315(5):498-505.
Birnbaum S. **Pulmonary rehabilitation**: a classic tune with a new beat, but is anyone listening? Chest. 2011 Jun;139(6):1498-502.
Bischoff EW, Hamd DH, Sedeno M, Benedetti A, Schermer TR, Bernard S, et al. Effects of written **action plan** adherence on **COPD** exacerbation recovery. Thorax 2011;66:26-31.
Bischoff EW, Akkermans R, Bourbeau J, et al. **Comprehensive self management** and routine monitoring in chronic obstructive pulmonary disease patients in general practice: randomised controlled trial. BMJ. 2012 Nov 28;345:e7642.
Bisgaard H, et al. Twelve-month safety and efficacy of inhaled fluticasone propionate in **children aged 1 to 3** years with recurrent wheezing. Pediatrics. 2004 Feb;113(2):e87-94.
Bisgaard H, et al. **Intermittent** inhaled corticosteroids in **infants** with episodic **wheezing**. N Engl J Med. 2006 May 11;354(19):1998-2005. Intermittent inhaled corticosteroid therapy had no effect on the progression from episodic to persistent wheezing and no short-term benefit during episodes of wheezing in the first three years of life. (budesonide 400ug/d)
Blais L, Beauchesne MF, Lemière C, Elftouh N. **High doses** of inhaled corticosteroids during the **first trimester of pregnancy** and congenital malformations. J Allergy Clin Immunol. 2009 Dec;124(6):1229-1234.e4.
Blanco I, Santos S, Gea J, et al. **Sildenafil** to improve respiratory rehabilitation outcomes in COPD: a controlled trial. Eur Respir J. 2013 Oct;42(4):982-92.
Boeck L, Soriano JB, Brusse-Keizer M, et al. Prognostic assessment in COPD without lung function: the **B-AE-D indices**. Eur Respir J. 2016 Jun;47(6):1635-44.
Bolton CE, Bevan-Smith EF, Blakey JD, et al.British Thoracic Society Pulmonary Rehabilitation Guideline Development Group; British Thoracic Society Standards of Care Committee. British Thoracic Society guideline on **pulmonary rehabilitation in adults**. Thorax. 2013 Sep;68 Suppl 2:ii1-30.
Boucher RC. Muco-Obstructive Lung Diseases. N Engl J Med. 2019 May 16;380(20):1941-1953.

Bourbeau J, Julien M, Maltais F, et al. Reduction of hospital utilization in patients with chronic obstructive pulmonary disease (COPD): a disease-specific self-management intervention. Arch Intern Med 2003;163:585-91

Bourbeau J, Bhutani M, Hernandez P, et al. **CTS (Canadian) position statement: pharmacotherapy in patients with COPD**—an update. Can J Resp Crit Care Sleep Med 2017;1(4):222-41 .

Brode SK, Ling SC, Chapman KR**. Alpha-1 antitrypsin deficiency**: a commonly verlooked cause of lung disease. CMAJ. 2012 Jul 3.

Brode SK, Campitelli MA, Kwong JC, et al. The risk of **mycobacterial infections** associated with inhaled corticosteroid use. Eur Respir J. 2017 Sep 20;50(3).

Broekhuizen, Berna D. L., Sachs, Alfred P. E., Moons, Karel G. M., et al. **Diagnostic Value of Oral Prednisolone Test** for Chronic Obstructive Pulmonary Disorders. Ann Fam Med 2011 9: 104-109.

Brook RD, Anderson JA, et al; **SUMMIT** Investigators.. **Cardiovascular outcomes with an inhaled beta2-agonist/corticosteroid** in patients with COPD at high cardiovascular risk. Heart. 2017 Apr 17.

Bucknall CE, Miller G, Lloyd SM, et al. Glasgow supported **self-management** trial (**GSuST**) for patients with moderate to severe **COPD**: randomised controlled trial. BMJ 2012;344:e1060.

Buhl R, Maltais F, Abrahams R, et al. **Tiotropium and olodaterol** fixed-dose combination versus mono-components in COPD (GOLD 2-4). Eur Respir J. 2015 Apr;45(4):969-79.

Bui DS, Lodge CJ, Burgess JA, et al. **Childhood predictors of lung function trajectories and future COPD risk**: a prospective cohort study from the first to the sixth decade of life. Lancet Respir Med 2018; online April 5.

Burchett DK, Darko W, Zahra J, et al. **Mixing and compatibility guide for commonly used aerosolized medications**. Am J Health-Syst Pharm. 2010;67:227-30.

Burgel PR, Paillasseur JL, Janssens W, et al. A simple **algorithm for the identification of clinical COPD phenotypes**. Eur Respir J. 2017 Nov 2;50(5).

Burr JF, Davidson W, Shephard RJ, Eves N. **Physical activity** in chronic respiratory conditions: Assessing risks for physical activity clearance and prescription. Can Fam Physician. 2012 Jul;58(7):761-4.

Busch R, Han MK, Bowler RP, et al; COPDGene Investigators. Risk factors for **COPD exacerbations** in inhaled medication users: the **COPDGe**ne study biannual longitudinal follow-up prospective cohort. BMC Pulm Med. 2016 Feb 10;16(1):28.

Butz BK, Wen T, Gleich GJ, et al. Efficacy, Dose Reduction, and Resistance to High-dose **Fluticasone** in Patients with **Eosinophilic Esophagitis**. Gastroenterology. 2014 Apr 22.

Calverley PM, Anderson JA, Celli B, Ferguson GT, Jenkins C, Jones PW, Yates JC, Vestbo J; **TORCH investigators**. Salmeterol and fluticasone propionate and survival in chronic obstructive pulmonary disease. N Engl J Med. 2007 Feb 22;356(8):775-89. n=6112 The reduction in death from all causes among patients with COPD in the combination-therapy group did not reach the predetermined level of statistical significance. There were significant benefits in all other outcomes among these patients. The international, industry-supported TORCH trial, researchers randomized more than 6000 COPD patients to receive either inhaled salmeterol & fluticasone propionate 500/50ug, each drug alone, or placebo. At 3 years, rates of all-cause mortality (the primary outcome) were 12.6% with combination therapy, 13.5% with salmeterol, 16.0% with fluticasone, and 15.2% with placebo. The mortality difference between the combination-therapy and placebo groups fell just short of statistical significance (P=0.052). However, combination therapy was associated with significant improvements in health status, lung function, and the frequency of COPD exacerbations. Patients taking fluticasone, alone or in combination, had an increased rate of pneumonia (Advair 19.6%, Flovent 18.3%, Serevent 13.3%, Placebo 12.3%). (see also Pharmacist's Letter Apr/07)

Celli BR, Thomas NE, Anderson JA, Ferguson GT, Jenkins C, Jones PW, Vestbo J, Knobil K, Yates JC, Calverley PM. Effect of Pharmacotherapy on Rate of Decline of Lung Function in COPD: Results from the TORCH Study. Am J Respir Crit Care Med. 2008 May 29. [Epub ahead of print] Pharmacotherapy with salmeterol plus fluticasone propionate, or the components, reduces the rate of decline of FEV1 in patients with moderate-to severe COPD, thus slowing disease progression. Celli BR, Thomas NE, Anderson JA, Ferguson GT, Jenkins CR, Jones PW, Vestbo J, Knobil K, Yates JC, Calverley PM. Effect of pharmacotherapy on rate of decline of lung function in chronic obstructive pulmonary disease: results from the TORCH study. Am J Respir Crit Care Med. 2008 Aug 15;178(4):332-8. Epub 2008 May 29. Rates of decline were similar among the active treatment arms**.** Pharmacotherapy with salmeterol plus fluticasone propionate, or the components, reduces the rate of decline of FEV(1) in patients with moderate-to-severe COPD, thus slowing disease progression.

Calverley PM, Rabe KF, Goehring UM, et al.; M2-124 and M2-125 study groups. **Roflumilast** in symptomatic chronic obstructive pulmonary disease: two randomised clinical trials. Lancet. 2009 Aug 29;374(9691):685-94.

Calverley PM, Stockley RA, Seemungal TA, et al; on behalf of the Investigating New Standards for Prophylaxis in Reduction of Exacerbations (**INSPIRE**) Investigators. Reported **Pneumonia** in Patients With COPD: Findings From the INSPIRE Study. Chest. 2011 Mar;139(3):505-512.

Calverley PMA, Anderson JA, Brook RD, et al. **Fluticasone Furoate, Vilanterol**, **and Lung Function Decline** in Patients with Moderate Chronic Obstructive Pulmonary Disease and Heightened Cardiovascular Risk. Am J Respir Crit Care Med. 2018 Jan 1;197(1):47-55.

Calzetta L, Cazzola M, Matera MG, et al. **Adding a LAMA to ICS/LABA Therapy**: A Meta-analysis of Triple Combination Therapy in COPD. Chest. 2019 Apr;155(4):758-770.

Calzetta L, Rogliani P, Matera MG, Cazzola M. A systematic review with meta-analysis of **dual bronchodilation with LAMA/LABA** for the treatment of stable chronic obstructive pulmonary disease. Chest. 2016 Feb 25.

Canalejo E, Pacheco MS. **Cushing syndrome due to ritonavir-fluticasone** interaction. CMAJ. 2012 May 14.

Casaburi R, ZuWallack R. **Pulmonary rehabilitation** for management of chronic obstructive pulmonary disease. N Engl J Med. 2009 Mar 26;360(13):1329-35.

Caughey GE, Preiss AK, Vitry AI, et al. Comorbid **Diabetes and COPD: Impact of corticosteroid** use on diabetes complications. Diabetes Care. 2013 Jun 4.

Cazzola M, Matera MG. **Beta-blockers** are safe in patients with chronic obstructive pulmonary disease, but only with caution. Am J Respir Crit Care Med. 2008 Oct 1;178(7):661-2.

Cazzola M, Matera MG. POINT: Should **LAMA/LABA Combination Therapy** Be Used as Initial Maintenance Treatment for COPD? Yes. Chest. 2018 Oct;154(4):746-748.

Cazzola M, Rogliani P, Calzetta L, et al. **Triple therapy versus single and dual long-acting bronchodilator therapy** in COPD: a systematic review and meta-analysis. Eur Respir J. 2018 Dec 13;52(6).

Celli B, Decramer M, Leimer I, et al. Cardiovascular Safety of Tiotropium in Patients With COPD. Chest. 2009 Jul 10. [Epub ahead of print] Tiotropium was associated with a reduction in the risk of all-cause mortality, cardiovascular mortality and cardiovascular events.

Celli B, Decramer M, Kesten S, et al. **Mortality** in the 4-year trial of tiotropium (**UPLIFT**) in patients with chronic obstructive pulmonary disease. Am J Respir Crit Care Med. 2009 Nov 15;180(10):948-55. Epub 2009 Sep 3.

Celli B, Tetzlaff K, Criner G, et al; COPD Biomarker Qualification Consortium. The **6-minute Walk Test as a COPD Stratification Tool**: Insights From the COPD Biomarker Qualification Consortium. Am J Respir Crit Care Med. 2016 Jun 22.

Celli BR, Wedzicha JA. **Update on Clinical Aspects** of Chronic Obstructive Pulmonary Disease. N Engl J Med. 2019 Sep 26;381(13):1257-1266.

Chandra D, Stamm JA, Taylor B, et al. Outcomes of **non-invasive ventilation for acute exacerbations of chronic obstructive pulmonary disease** in the United States, 1998–2008. Am J Respir Crit Care Med 2012;185:152–159

Chapman KR, Rennard SI, Dogra A, et al; on behalf of the **INDORSE** Study Investigators. Long-term Safety and Efficacy of **Indacaterol**, a Long-Acting {beta}2-Agonist, in Subjects With COPD: A Randomized, Placebo-Controlled Study. Chest. 2011 Jul;140(1):68-75 (52 weeks)

Chen D, Restrepo MI, Fine MJ, et al. Observational study of **inhaled corticosteroids** on outcomes for COPD patients with **pneumonia**. Am J Respir Crit Care Med. 2011 Aug 1;184(3):312-6. For

Chen W, Sin DD, FitzGerald JM, et al. An individualized **prediction model for long-term lung function trajectory and risk** of COPD in the general population. Chest. 2019 Sep 19.

Cheyne L, Irvin-Sellers MJ, White J. **Tiotropium versus ipratropium** bromide for chronic obstructive pulmonary disease. Cochrane Database Syst Rev. 2013 Sep 16;9:CD009552. This review shows that

tiotropium treatment, when compared with ipratropium bromide, was associated with improved lung function, fewer hospital admissions (including those for exacerbations of COPD), fewer exacerbations of COPD and improved quality of life. There were both fewer serious adverse events and disease specific events in the tiotropium group, but no significant difference in deaths with ipratropium bromide when compared to tiotropium. Thus, tiotropium appears to be a reasonable choice (instead of ipratropium bromide) for patients with stable COPD, as proposed in guidelines. We would advise some caution with tiotropium via the Respimat inhaler and suggest waiting for further information from an ongoing head-to-head trial comparing mortality in relation to tiotropium delivery devices and doses.

Cheyne L, Irvin-Sellers MJ, White J. **Tiotropium versus ipratropium bromide for chronic obstructive pulmonary disease**. Cochrane Database Syst Rev. 2015 Sep 22;9:CD009552. This review shows that tiotropium treatment, when compared with ipratropium bromide, was associated with improved lung function, fewer hospital admissions (including those for exacerbations of COPD), fewer exacerbations of COPD and improved quality of life. There were both fewer serious adverse events and disease specific events in the tiotropium group, but no significant difference in deaths with ipratropium bromide when compared to tiotropium. Thus, tiotropium appears to be a reasonable choice (instead of ipratropium bromide) for patients with stable COPD, as proposed in guidelines. A recent large double-blind trial of the two delivery devices found no substantial difference in mortality using 2.5 microg or 5 microg of tiotropium via Respimat in comparison to 18 microg via Handihaler.

Cho EE, Mecredy GC, Wong HH, et al. **Which physicians are taking care of people with COPD**? Chest. 2019 Jan 18.

Chong J, Poole P, Leung B, Black PN. **Phosphodiesterase 4 inhibitors** for chronic obstructive pulmonary disease. Cochrane Database of Systematic Reviews 2011, Issue 5. Art. No.: CD002309. DOI: 10.1002/14651858.CD002309.pub3. In people with COPD, PDE4 inhibitors offered benefit over placebo in improving lung function and reducing likelihood of exacerbations, however, they had little impact on quality of life or symptoms. Gastrointestinal adverse effects and weight loss were common, and safety data submitted to the US Food and Drug Administration (FDA) have raised concerns over psychiatric adverse events with **roflumilast**.

Chong J, Leung B, Poole P. **Phosphodiesterase 4 inhibitors** for chronic obstructive pulmonary disease. Cochrane Database Syst Rev. 2013 Nov 4;11:CD002309. In people with COPD, PDE4 inhibitors offered benefit over placebo in improving lung function and reducing the likelihood of exacerbations; however, they had little impact on quality of life or symptoms. Gastrointestinal adverse effects and weight loss were common, and safety data submitted to the US Food and Drug Administration (FDA) have raised concerns over psychiatric adverse events with roflumilast.

Chong J, Leung B, Poole P. **Phosphodiesterase 4 inhibitors** for chronic obstructive pulmonary disease. Cochrane Database of Systematic Reviews 2017, Issue 9. Art. No.: CD002309. In people with COPD, PDE4 inhibitors offered benefit over placebo in improving lung function and reducing the likelihood of exacerbations; however, they had little impact on quality of life or symptoms. Gastrointestinal adverse effects and weight loss were common, and safety data submitted to the US Food and Drug Administration (FDA) have raised concerns over psychiatric adverse events with roflumilast. The findings of this review give cautious support to the use of PDE4 inhibitors in COPD. They may be best used as add-on therapy in a subgroup of people with persistent symptoms or exacerbations despite optimal COPD management. This is in accordance with the GOLD 2017 guidelines. Longer-term trials are needed to determine whether or not PDE4 inhibitors modify FEV1 decline, hospitalisation or mortality in COPD.

Chou A, D'Urzo AD. New therapy (**roflumilast**) for managing moderate to severe chronic obstructive pulmonary disease. Can Fam Physician. 2014 Apr;60(4):352-4.

Chowdhury BA, Seymour SM, Michele TM, Durmowicz AG, Liu D, Rosebraugh CJ. The risks and benefits of **indacaterol**- the FDA's review. N Engl J Med. 2011 Dec 15;365(24):2247-9.

Chuang HY, Chang HY, et al. The effects of threshold **inspiratory muscle training** in patients with chronic obstructive pulmonary disease: A randomised experimental study. J Clin Nurs. 2017 Apr 5.

Chuang HY, Chang HY, et al. The effects of **threshold inspiratory muscle training** in patients with chronic obstructive pulmonary disease: A randomised experimental study. J Clin Nurs. 2017 Apr 5.

Clark Z, Maurer DM. Pneumococcal Vaccines in Chronic Obstructive Pulmonary Disease. Am Fam Physician. 2018 Apr 1;97(7):463-464.

Collins BF et al. **Factors predictive of airflow obstruction** among veterans with presumed empirical diagnosis and treatment of **COPD**. Chest 2015 Feb; 147:369.

Conway F, Majeed A, Easton G. **Diagnosing chronic obstructive pulmonary disease**. BMJ. 2015 Nov 24;351:h6171.

Cook R, Thomas V, Martin R; NIHR Dissemination Centre. People with chronic obstructive pulmonary disease exacerbations **prefer early discharge, then treatment at home**. BMJ. 2019 Feb 19;364:k5339.

Cooper CB, Tashkin DP. Recent developments in inhaled therapy in stable chronic obstructive pulmonary disease. BMJ. 2005 Mar 19;330(7492):640-4.

Cosío BG, et al. Oral Low-Dose **Theophylline on Top of Inhaled Fluticasone-Salmeterol** Does Not Reduce Exacerbations in Patients with Severe **COPD**: A Pilot Clinical Trial. Chest. 2016 Apr 20.

Cosio BG, Soriano JB, López-Campos JL, et al; **CHAIN** Study. Defining the **Asthma-COPD Overlap Syndrome (ACOS)** in a COPD Cohort. Chest. 2016 Jan;149(1):45-52

Covelli H, et al. Absence of electrocardiographic findings and improved function with once-daily **tiotropium** in patients with COPD. Pharmacotherapy. 2005 Winter;25(12):1708-18.

Covvey JR, Johnston BF, Wood F, Boyter AC. Changes to **inhaled corticosteroid dose when initiating combination inhaler** therapy in long-acting β agonist-naïve patients with asthma: a retrospective database analysis. Thorax. 2014 Jan 15.

Criner GJ, Connett JE, Aaron SD, et al. **Simvastatin** for the prevention of exacerbations in moderate-to-severe **COPD**. N Engl J Med. DOI: 10.1056/NEJMoa1403086.

Criner GJ, Bourbeau J, Diekemper RL, et al. **Prevention of acute exacerbations of chronic obstructive pulmonary disease: American** College of Chest Physicians (**ACCP**) and **Canadian** Thoracic Society guideline (**CTS**). Chest 2014;online first.http://journal.publications.chestnet.org/data/Journals/CHEST/0/chest.14-1676.pdf (accessed October 22, 2014).

Criner GJ, Bourbeau J, Diekemper RL, et al. Executive summary. Prevention of acute exacerbations of chronic obstructive pulmonary disease: American College of Chest Physicians and Canadian Thoracic Society guideline. Chest 2014;online first.http://journal.publications.chestnet.org/data/Journals/CHEST/0/chest.14-1677.pdf (accessed Oct/14).

Criner GJ, Bourbeau J, Diekemper RL, et al. **Prevention of Acute Exacerbations of COPD**: American College of Chest Physicians (**ACCP**) and **Canadian Thoracic Society** (**CTS**) Guideline. Chest. 2015 Apr 1;147(4):894-942.

Criner GJ, Celli BR, Brightling CE, et al. **Benralizumab** for the Prevention of COPD Exacerbations. N Engl J Med. 2019 May 20.

Croft JB, Wheaton AG, et al. **Urban-Rural County and State Differences** in Chronic Obstructive Pulmonary Disease - United States, 2015. MMWR Morb Mortal Wkly Rep. 2018 Feb 23;67(7):205-211.

Currie GP, Wedzicha JA. ABC of **chronic obstructive** pulmonary disease. **Acute exacerbations**. BMJ. 2006 Jul 8;333(7558):87-9.

Currie GP, Lee DK, Lipworth BJ. ABC of **chronic obstructive** pulmonary disease. Pharmacological management—**oral** treatment. BMJ. 2006 Jun 24;332(7556):1497-9.

Currie GP, Lipworth BJ. ABC of **chronic obstructive** pulmonary disease Pharmacological management--**inhaled treatment**. BMJ. 2006 Jun 17;332(7555):1439-41.

D'Urzo AD, Tamari I, Bouchard J, Jhirad R, Jugovic P. A new **spirometry** interpretation **algorithm**. Primary Care Respiratory Alliance of Canada approach. Can Fam Physician 2011;57:1148-52.

D'Urzo AD, Tamari I, Bouchard J, Jhirad R, Jugovic P. Limitations to a **spirometry interpretation algorithm**. Can Fam Physician 2011;57:1153-6.

Dahl R, Chung KF, Buhl R, et al. Efficacy of a new once-daily long-acting inhaled beta2- agonist **indacaterol** versus twice-daily formoterol in COPD. Thorax 2010;65:473-9.

Dalhousie Academic Detailing Service Resources: Update on COPD. http://cme.medicine.dal.ca/files/COPD.pdf ; Summary http://cme.medicine.dal.ca/files/COPD%20Summary.pdf

Daniels JM, Snijders D, de Graaff CS, Vlaspolder F, Jansen HM, Boersma WG. Antibiotics in Addition to Systemic **Corticosteroids for Acute Exacerbations** of COPD. Am J Respir Crit Care Med. 2009 Oct 29.

Davey C, Zoumot Z, Jordan S, et al. **Bronchoscopic lung volume reduction** with endobronchial valves for patients with heterogeneous emphysema and intact interlobar fissures (the BeLieVeR-HIFi study): a randomised controlled trial. Lancet 2015; online June 24.

de Benedictis FM, Bush A. **Corticosteroids in respiratory diseases in children**. Am J Respir Crit Care Med. 2012 Jan 1;185(1):12-23.

De Coster DA, Jones M, Thakrar N. **Beclometasone for chronic obstructive pulmonary disease**. Cochrane Database Syst Rev. 2013 Oct 9;10:CD009769. We found little evidence to

suggest that beclometasone is a safer or more effective treatment option for people with COPD when compared with placebo or when used in combination with LABA; when statistically significant differences were found, they mostly were not clinically meaningful or were based on data from only one study. The review was limited by an inability to obtain data from one study and likely publication bias for BDP versus placebo, and by the inclusion of one study only for BDP/LABA versus LABA.

de Jong YP, Uil SM, Grotjohan HP, Postma DS, Kerstjens HA, van den Berg JW. **Oral or IV Prednisolone** in the Treatment of COPD Exacerbations: A Randomized, Controlled, Double-blind Study. Chest. 2007 Dec;132(6):1741-7. Epub 2007 Jul 23. Therapy with oral prednisolone is not inferior to IV treatment in the first 90 days after starting therapy. Oral steroids are as effective as intravenous (IV) steroids for nonsevere exacerbations of chronic obstructive pulmonary disease (COPD). Because they are cheaper and less invasive, oral steroids should be the preferred treatment option. (LOE = 1b)

Decramer M, Celli B, et al. Clinical trial design considerations in assessing long-term functional impacts of tiotropium in COPD: the **UPLIFT trial**.COPD. 2004;1(2):303-12. ?2008

Decramer M, Rutten-van Molken M, et al. Effects of **N-acetylcysteine** on outcomes in COPD (Bronchitis Randomized on NAC Cost-Utility Study, BRONCUS): a randomised placebo-controlled trial. Lancet. 2005 May;365(9470):1552-60. (InfoPOEMs: N-acetylcysteine does not prevent chronic obstructive pulmonary disease lung-function decline or exacerbation. (LOE = 1b))

Decramer M, Celli B, Kesten S, et al. for the **UPLIFT** investigators. Effect of tiotropium on outcomes in patients with **moderate** chronic obstructive pulmonary disease (UPLIFT): a prespecified subgroup analysis of a randomised controlled trial. Lancet. 2009 Aug 27.

Decramer M, Janssens W, Miravitlles M. Chronic obstructive pulmonary disease. Lancet. 2012 Feb 3.

Decramer ML, Chapman KR, Dahl R et al. Once-daily **indacaterol versus tiotropium** for patients with severe chronic obstructive pulmonary disease (**INVIGORATE**): a randomised, blinded, parallel-group study. Lancet Respir Med. 2013 Sep; 1(7): 524-533

Dellon ES, Gonsalves N, Hirano I, Furuta GT, Liacouras CA, Katzka DA. **ACG** clinical guideline: evidenced based approach to the diagnosis and management of **esophageal eosinophilia and eosinophilic esophagitis** (EoE). Am J Gastroenterol. 2013 May;108(5):679-92.

Deslée G, Mal H, Dutau H, et al. **Lung volume reduction coil treatment** vs usual care in patients with **severe emphysema**: the **REVOLENS** randomized clinical trial. JAMA. doi: 10.1001/jama .2015.17821.

Devereux G, Cotton S, Fielding S, et al. Effect of **theophylline as adjunct to inhaled corticosteroids** on exacerbations in patients with chronic obstructive pulmonary disease: a randomized clinical trial [Oct 16, 2018]. JAMA.

Dilektasli AG, Porszasz J, Casaburi R, et al. A novel **spirometric measure** identifies mild chronic obstructive pulmonary disease unidentified by standard criteria. Chest. 2016 Jul 21

Divo M, Cote C, de Torres JP, et al.; The **BODE** Collaborative Group. **Comorbidities and risk of mortality** in patients with chronic obstructive pulmonary disease. Am J Respir Crit Care Med 2012;186:155–161.

Dolovich MB, Ahrens RC, Hess DR, et al. **Device selection** and outcomes of aerosol therapy: evidence-based guidelines: American College of Chest Physicians/American College of Asthma, Allergy, and Immunology. Chest 2005 Jan;127(1):335-71.

Donaldson GC, Goldring JJ, Wedzicha JA. Influence of **Season on Exacerbation Characteristics in Patients With COPD**. Chest. 2012 Jan;141(1):94-100.

Donaldson GC, Law M, Kowlessar B, et al. **Impact of Prolonged Exacerbation Recovery** in Chronic Obstructive Pulmonary Disease. Am J Respir Crit Care Med. 2015 Jul 7.

Dong Y-H et al. Comparative safety of inhaled medications in patients with chronic obstructive pulmonary disease: systematic review and mixed treatment comparison meta-analysis of randomised controlled trials. Thorax [Epub ahead of print] 6 October 2012; DOI:10.1136/thoraxjnl-2012-201926. Our study provided a comparative safety spectrum for each category of inhaled medications. Tiotropium Soft Mist (Respimat) Inhaler had a higher risk of **mortality** and should be used with caution.

Donohue JF, Kalberg C, Emmett A, Merchant K, Knobil K. A short-term comparison of **fluticasone propionate/salmeterol** with ipratropium bromide/albuterol for the treatment of COPD. Treat Respir Med. 2004;3(3):173-81.

Donohue JF, Fogarty C, Lotvall J, et al; **INHANCE** Study Investigators. Once daily bronchodilators for chronic obstructive pulmonary disease: **indacaterol versus tiotropium**. Am J Respir Crit Care Med 2010;182:155-62.

Donohue JF, et al. Health Status of Patients with Moderate to Severe COPD after Treatment with Nebulized **Arformoterol** Tartrate or Placebo for 1 Year. Clin Ther. 2016 Dec 20.

Dransfield MT, et al.. Use of **beta blockers** & the risk of death in hospitalised patients with acute exacerbations of COPD. Thorax. 2008 Apr;63(4):301-5. Epub 2007 Oct 19. The use of beta blockers by inpatients with exacerbations of COPD is well tolerated and may be associated with reduced mortality. The potential protective effect of beta blockers in this population warrants further study.

Drug & Therapeutics Bulletin: Preventing **exacerbations** in chronic obstructive pulmonary disease. Drug & Therapeutics Bulletin. BMJ 2011;342:doi:10.1136/bmj.c7207 (24 Jan 11)

Drummond MB, Dasenbrook EC, Pitz MW, et al. Inhaled corticosteroids in patients with stable chronic obstructive pulmonary disease: a systematic review and meta-analysis. JAMA. 2008 Nov 26;300(20):2407-16. Among patients with COPD, ICS therapy does not affect 1-year all-cause mortality. ICS therapy is associated with a higher risk of pneumonia.

Drummond MB, Hansel NN, Connett JE, et al. **Spirometric Predictors** of Lung Function Decline and Mortality in Early COPD. Am J Respir Crit Care Med. 2012 May 3.

Duffy N, Walker P, Diamantea F, et al. Intravenous **aminophylline** in patients admitted to hospital with non-acidotic exacerbations of chronic obstructive pulmonary disease: a prospective randomised controlled trial. Thorax. 2005 Sep;60(9):713-7. Epub 2005 Jun 6.

Dwyer-Lindgren L, et al. **Trends and Patterns** of Differences in Chronic Respiratory Disease **Mortality** Among US Counties, 1980-2014. JAMA. 2017 Sep 26;318(12):1136-1149.

Dzierba AL, Jelic S. Chronic obstructive pulmonary disease in the **elderly**: an update on pharmacological management. Drugs Aging. 2009;26(6):447-56.

Echevarria C, Gray J, Hartley T, et al. **Home treatment of COPD** exacerbation selected by **DECAF score**: a non-inferiority, randomised controlled trial and economic evaluation. Thorax. 2018 Apr 21.

Echevarria C, Steer J, Heslop-Marshall K, et al. Validation of the **DECAF score** to predict hospital mortality in acute exacerbations of COPD. Thorax. 2016 Feb;71(2):133-40.

Echevarria C, Steer J, et al. The **PEARL score** predicts 90-day readmission or death after hospitalisation for acute exacerbation of COPD. Thorax. 2017 Feb 24.

Effing T, Kerstjens H, van der Valk P, et al. (Cost)-effectiveness of **self-treatment** of exacerbations on the severity of exacerbations in patients with COPD: the COPE II study. Thorax. 2009 Nov;64(11):956-62. Epub 2009 Sep 6.

Ekstrom M, Ahmadi Z, Bornefalk-Hermansson A, et al. **Oxygen for breathlessness** in patients with chronic obstructive pulmonary disease who do not qualify for home oxygen

therapy. Cochrane Database Syst Rev. 2016 Nov 25;11:CD006429. We are moderately confident that oxygen can relieve breathlessness when given during exercise to mildly hypoxaemic and non-hypoxaemic people with chronic obstructive pulmonary disease who would not otherwise qualify for home oxygen therapy. Most evidence pertains to acute effects during exercise tests, and no evidence indicates that oxygen decreases breathlessness in the daily life setting. Findings show that oxygen does not affect health-related quality of life.

Ernst P, et al. Canadian Asthma Guideline Group. Safety and effectiveness of **long-acting inhaled beta**-agonist bronchodilators when taken with inhaled corticosteroids. Ann Intern Med. 2006 Nov 7;145(9):692-4.

Ernst P, Gonzalez AV, Brassard P, Suissa S. Inhaled corticosteroid use in **chronic obstructive pulmonary disease** and the risk of hospitalization for **pneumonia**. Am J Respir Crit Care Med. 2007 Jul 15;176(2):162-6. Epub 2007 Mar 30. The use of inhaled corticosteroids is associated with an excess risk of pneumonia hospitalization and of pneumonia hospitalization followed by death within 30 days, among elderly patients with COPD. (InfoPOEMs: In this well-conducted case-control study, elderly patients with chronic obstructive pulmonary disease (COPD) hospitalized for pneumonia were more likely to have been prescribed inhaled corticosteroids. Even though there was a dose response, we still cannot ascertain if this was cause or effect.)

Eurich DT, Lee C, Marrie TJ, Majumdar SR. **Inhaled corticosteroids and risk of recurrent pneumonia**: a population-based, nested case-control study. Clin Infect Dis. 2013 Oct;57(8):1138-44.

Evensen AE. **Management of COPD Exacerbations**. Am Fam Physician. 2010 Mar 1;81(5):607-13.

Fabbri LM, Calverley PM, Izquierdo-Alonso JL, et al.; M2-127 and M2-128 study groups. **Roflumilast** in moderate-to-severe chronic obstructive pulmonary disease treated with longacting bronchodilators: two randomised clinical trials. Lancet. 2009 Aug 29;374(9691):695-703.

Faisy C, Meziani F, Planquette B, et al. DIABOLO Investigators. Effect of **Acetazolamide** vs Placebo on Duration of Invasive Mechanical Ventilation Among Patients With Chronic Obstructive Pulmonary Disease: A Randomized Clinical Trial. JAMA. 2016 Feb 2;315(5):480-488.

Fan VS, et al. A **comprehensive care management program** (CCMP) to prevent **chronic obstructive pulmonary disease** hospitalizations. A randomized, controlled trial. Ann Intern Med. 2012;156:673-83. (had an unexpected excess mortality in CCMP group)

Faner R, Agustí A. **COPD: algorithms and clinical management**. Eur Respir J. 2017 Nov 2;50(5).

Fawzy A, Putcha N, Aaron CP, et al; SPIROMICS Investigators. **Aspirin Use and Respiratory Morbidity** in COPD: a Propensity Score Matched Analysis in SPIROMICS. Chest. 2018 Dec 26.

Feldman G, Maltais F, Khindri S, et al. A randomized, blinded study to evaluate the efficacy and safety of **umeclidinium** 62.5 µg compared with **tiotropium** 18 µg in patients with COPD. Int J Chron Obstruct Pulmon Dis. 2016 Apr 7;11:719-30.

Feldman GJ, Sousa AR, Lipson DA, et al. Comparative Efficacy of Once-Daily **Umeclidinium/Vilanterol and Tiotropium/Olodaterol** Therapy in Symptomatic Chronic Obstructive Pulmonary Disease: A Randomized Study. AdvTher. 2017 Nov 1.

Ferguson GT, Calverley PM, Anderson JA, et al. Prevalence and Progression of **Osteoporosis** in Patients With COPD. Results From TORCH. Chest. 2009 Jul 6. [Epub ahead of print] In the **TORCH** study, no significant effect on BMD was detected for inhaled corticosteroid therapy compared with placebo.

Ferreira IM, Brooks D, White J, et al. **Nutritional supplementation** for stable chronic obstructive pulmonary disease. Cochrane Database Syst Rev. 2012 Dec 12;12:CD000998. doi: 10.1002/14651858.CD000998.pub3. We found moderate-quality evidence that nutritional supplementation promotes significant weight gain among patients with COPD, especially if malnourished. Nourished patients may not respond to the same degree to supplemental feeding.

Fisher AJ, Yadegarfar ME, Collerton J, et al. **Respiratory health** and disease in a UK population-based cohort of 85 year olds: The **Newcastle 85+ Study**. Thorax. 2016 Jan 5.

Ford PA, Durham AL, Russell RE, et al. Treatment effects of **low dose theophylline combined with an inhaled corticosteroid** in COPD. Chest. 2010 Mar 18.

Ford ES, Mannino DM, Zhao G et al. Changes in **Mortality Among US Adults With COPD** in Two National Cohorts Recruited From 1971-1975 and 1988-1994. Chest. 2012 Jan;141(1):101-10.

Franciosi LG, Diamant Z, Banner KH et al. Efficacy and safety of **RPL554**, a dual PDE3 and PDE4 inhibitor, in healthy volunteers and in patients with asthma or chronic obstructive pulmonary disease: findings from four clinical trials. Lancet Respir Med. 2013 Nov;1(9):714-727

Freedman N. **Reducing COPD Readmissions**: Strategies for the Pulmonologist to Improve Outcomes. Chest. 2019 Oct;156(4):802-807.

Frei A, et al. The Inaccuracy of Patient Recall for **COPD Exacerbation Rate Estimation** and its Implications: Results from Central Adjudication. Chest. 2016 Jul 8. pii: S0012-3692(16)52642-7.

Frent SM, Chapman KR, Larbig M, et al. Capturing **Exacerbations of Chronic Obstructive Pulmonary Disease with EXACT**. A Subanalysis of FLAME. Am J Respir Crit Care Med. 2019 Jan 1;199(1):43-51.

Frith PA, Thompson PJ, Ratnavadivel R, et al; Glisten Study Group. **Glycopyrronium** once-daily significantly improves lung function and health status when combined with salmeterol/fluticasone in patients with COPD: the **GLISTEN** study, a randomized controlled trial. Thorax. 2015 Jun;70(6):519-27.

Fuhr R, Magnussen H, et al. Efficacy of **Aclidinium Bromide** 400 µg Twice Daily Compared With Placebo and Tiotropium in Patients With Moderate to Severe COPD. Chest. 2012 Mar;141(3):745-52.

Furian M, Lichtblau M, Aeschbacher SS, et al. Effect of **Dexamethasone on Nocturnal Oxygenation in Lowlanders** With Chronic Obstructive Pulmonary Disease Traveling to 3100 Meters: A Randomized Clinical Trial. JAMA Netw Open. 2019 Feb 1;2(2):e190067.

Gadomski AM, Scribani MB. **Bronchodilators for bronchiolitis**. Cochrane Database of Systematic Reviews 2014, Issue 6. Art. No.: CD001266. DOI: 10.1002/14651858.CD001266.pub4. Bronchodilators such as albuterol or salbutamol do not improve oxygen saturation, do not reduce hospital admission after outpatient treatment, do not shorten the duration of hospitalization and do not reduce the time to resolution of illness at home. Given the adverse side effects and the expense associated with these treatments, bronchodilators are not effective in the routine management of bronchiolitis.

Gaebel K, Blackhouse G, Robertson D, Xie F, Assasi N, McIvor A, Hernandez P, Goeree R. Triple Therapy for Moderate-to-Severe Chronic Obstructive Pulmonary Disease [Internet]. Ottawa: Canadian Agency for Drugs and Technologies in Health; 2010 (CADTH technology report; no. 127). Available:http://www.cadth.ca/index.php/en/hta/reports-publications/search/publication/000

García-Rio F, Soriano JB, Miravitlles M, et al. **Overdiagnosing Subjects With COPD Using the 0.7 Fixed Ratio**: Correlation With a Poor Health-Related Quality of Life. Chest 2011May;139(5):1072-80.

Garne E, Vinkel Hansen A, Morris J, et al. Risk of **congenital anomalies after exposure to asthma medication in the first trimester of pregnancy** - a cohort linkage study. BJOG. 2016 May 12.

Gartlehner G, et al. Efficacy & safety of inhaled **corticosteroids in patients with COPD**: a systematic review and meta-analysis of health outcomes. Ann Fam Med. 2006 May-Jun;4(3):253-62. (InfoPOEMs: Inhaled corticosteroids prevent exacerbations in patients with mod-severe COPD. The benefit is minor, however, and steroids don't prevent exacerbations in patients with mild COPD. The prevention of exacerbations with steroids must be balanced against the higher rate of fractures and glaucoma. (LOE = 1a-))

GBD 2015 Chronic Respiratory Disease Collaborators. Global, regional, and national deaths, prevalence, disability-adjusted life years, and years lived with disability for **chronic obstructive pulmonary disease** and **asthma**, 1990–2015: a systematic analysis for the Global Burden of Disease Study 2015. Lancet Respir Med 2017; online August 16.

Geake JB, Dabscheck EJ,Wood-Baker R, Cates CJ. **Indacaterol**, a once-daily beta2-agonist, versus **twice-daily beta2-agonists or placebo for chronic obstructive pulmonary disease**. Cochrane Database of Systematic Reviews 2015, Issue 1. Art. No.: CD010139. DOI: 10.1002/14651858.CD010139.pub2. For patients with stable COPD, use of indacaterol versus placebo results in statistically significant and clinically meaningful improvements in lung function and quality of life. The clinical benefit for lung function is at least as good as that seen with twice-daily long acting beta2-agonists. The comparative effect on quality of life remains uncertain, as important differences cannot be excluded.

Gentry S, Gentry B. **Chronic Obstructive Pulmonary Disease: Diagnosis and Management**. Am Fam Physician. 2017;95(7):433-441.

Gershon Andrea S.; Wang Chengning; Wilton AS.; et al. **Trends in Chronic Obstructive Pulmonary Disease Prevalence, Incidence, and Mortality** in Ontario, Canada, 1996 to 2007: A Population-Based Study. Arch Intern Med. 2010;170(6):560-565.

Gershon Andrea, Croxford Ruth, To Teresa, et al. Comparison of Inhaled **Long-Acting β-Agonist and Anticholinergic** Effectiveness in Older Patients With Chronic Obstructive Pulmonary Disease: A Cohort Study. *Ann Intern Med* May 3, 2011 154:583-592; doi:10.1059/0003-4819-154-9-201105030-00003.

Gershon AS, Warner L, Cascagnette P, Victor JC, To T. **Lifetime risk of developing chronic obstructive pulmonary disease**: a longitudinal population study. Lancet. 2011 Sep 10;378(9795):991-6.

Gershon A, Croxford R, Calzavara A, et al. **Cardiovascular Safety of Inhaled Long-Acting Bronchodilators** in Individuals With Chronic Obstructive Pulmonary Disease. JAMA Intern Med. 2013 May 20:1-9.

Gershon AS, Campitelli MA, Croxford R, et al. **Combination long-acting β-agonists and inhaled corticosteroids** compared with **long-acting β-agonists alone** in older adults with chronic obstructive pulmonary disease. JAMA. doi:10.1001/jama.2014.11432.

Gershon A, et al. Outcomes of patients with chronic obstructive pulmonary disease **diagnosed with or without pulmonary function testing**. CMAJ. 2017 Apr 10;189(14):E530-E538

Gershon AS, Thiruchelvam D, Chapman KR, et al; Canadian Respiratory Research Network. **Health Services Burden of Undiagnosed and Overdiagnosed COPD**. Chest. 2018 Feb 6.

Gidaya NB, Lee BK, Burstyn I, et al. In utero Exposure to **β-2-Adrenergic Receptor Agonist Drugs and Risk for Autism** Spectrum Disorders. Pediatrics. 2016 Jan 6.

Global Initiative for Chronic Obstructive Lung Disease (GOLD). Global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease. Vancouver (WA): Global Initiative for Chronic Obstructive Lung Disease **(GOLD); 2011.** http://www.goldcopd.org/uploads/users/files/GOLD_Report_2011_Feb21.pdf

Gøtzsche PC, Johansen HK. **Intravenous alpha-1 antitrypsin** augmentation therapy for treating patients with alpha-1 antitrypsin deficiency and lung disease. Cochrane Database of Systematic Reviews 2010, Issue 7. Art. No.: CD007851. DOI: 10.1002/14651858.CD007851.pub2. Augmentation therapy with alpha-1 antitrypsin cannot be recommended, in view of the lack of evidence of clinical benefit and the cost of treatment.

Goldbart AD, Greenberg-Dotan S, Tal A. **Montelukast** for Children With Obstructive **Sleep Apnea**: A Double-blind, Placebo-Controlled Study. Pediatrics. 2012 Aug 6.

Granger R, et al. Injectable vaccines for preventing **pneumococcal** infection in patients with COPD. Cochrane Database Syst Rev. 2006 Oct 18;(4):CD001390. There is no evidence from randomised controlled trials that injectable pneumococcal vaccination in persons with COPD has a significant impact on morbidity or mortality. Further large randomised controlled trials would be needed to ascertain if the small benefits suggested by individual studies are real.

Greening NJ, Williams JEA, Hussain SF, Harvey-Dunstan T, Bankart MJ, Chaplin EJ, et al. An **early rehabilitation** intervention to enhance recovery during hospital admission for an **exacerbation of chronic respiratory disease**: randomised controlled trial. BMJ 2014;349:g4315.

Gross NJ, Barnes PJ. **New Therapies for Asthma and COPD**. Am J Respir Crit Care Med. 2016 Dec 6.

Güell MR, Cejudo P, Ortega F, et al. Benefits of Long-Term **Pulmonary Rehabilitation** Maintenance Program in Severe COPD Patients: 3 Year Follow-Up. Am J Respir Crit Care Med. 2016 Sep 9.

Guerrera M. et al. Therapeutic Uses of **Magnesium**. Am Fam Physician. 2009; 80(1):157-162.

Guirguis-Blake JM, Senger CA, Webber EM, et al. **Screening** for **chronic obstructive pulmonary disease**: evidence report and systematic review for the US Preventive Services Task Force (**USPSTF**). JAMA. doi:10.1001/jama.2016 .2654.

Gupta S, Goodridge D, Pakhalé S, et al. **Choosing Wisely**: the Canadian Thoracic Society's list of **six things that physicians and patients should question**. Can J Respir Crit Care Sleep Med 2017;1(2):51-64. www.tandfonline.com/doi/full/10.1080/24745332.2017.1331666 (accessed September 20, 2017).

Hahn PY, Morgenthaler TY, Lim KG. Use of **exhaled nitric oxide** in predicting response to **inhaled corticosteroids for chronic cough**. Mayo Clin Proc. 2007 Nov;82(11):1350-5.

Han MK, Tayob N, Murray S, et al. Predictors of chronic obstructive pulmonary disease exacerbation reduction in response to daily **azithromycin** therapy. Am J Respir Crit Care Med. 2014 Jun 15;189(12):1503-8.

Hao Q, Lu Z, Dong BR, Huang CQ, Wu T. **Probiotics for preventing acute upper respiratory tract infections**. Cochrane Database of Systematic Reviews 2011, Issue 9. Art. No.: CD006895. DOI: 10.1002/14651858.CD006895.pub2. Probiotics were better than placebo in reducing the number of participants experiencing episodes of acute URTIs, the rate ratio of episodes of acute URTI and reducing antibiotic use. This indicates that probiotics may be more beneficial than placebo for preventing acute URTIs.

Harrison SL, Janaudis-Ferreira T, Brooks D, et al. **Self-Management** Following an Acute **Exacerbation of COPD**: A Systematic Review. Chest. 2015 Mar 1;147(3):646-61.

Hartung DM, Middleton L, Markwardt S, et al. Changes in **Long-acting β-Agonist Utilization After the FDA's 2010 Drug Safety Communication**. Clin Ther. 2014 Nov 25.

Hatipoğlu U, Aboussouan LS. **Chronic obstructive pulmonary disease**: An update for the primary physician. Cleve Clin J Med. 2014 Jun;81(6):373-383.

Hawkins NM, Petrie MC, MacDonald MR, et al. **Heart failure** and chronic obstructive pulmonary disease. The quandary of **beta-blockers** and beta-agonists. J Am Coll Cardiol 2011; 57:2127-2138.

Health Canada June/07 **VENTOLIN** IM injection and VENTOLIN I.V. infusion solution for Pregnant Women & Labour and Delivery. GlaxoSmithKline conducted a review of safety data for salbutamol. There have been 17 occurences worldwide (as of April 2007) of **myocardial ischemia** events in association with salbutamol when used to delay premature labour. There have been no Canadian cases reported to date.

Heckman EJ, O'Connor GT. **Pulmonary function tests** for diagnosing lung disease. JAMA. 2015 Jun 9;313(22):2278-9.

Henderson-Smart DJ, De Paoli AG. **Methylxanthine treatment for apnoea in preterm infants**. *Cochrane Database Syst Rev* 2010*;* **12***:* CD000140.

Herath SC, Poole P. **Prophylactic antibiotic therapy** for chronic obstructive pulmonary disease (**COPD**). Cochrane Database of Systematic Reviews 2013, Issue 11. Art. No.: CD009764. DOI: 10.1002/14651858.CD009764.pub2. Use of continuous prophylactic antibiotics results in a clinically significant benefit in reducing exacerbations in COPD patients. All trials of continuous antibiotics used macrolides hence the noted benefit applies only to the use of continuous macrolide antibiotics. The impact of pulsed antibiotics remains uncertain and requires further research. The trials in this review included patients who were frequent exacerbators and needed treatment with antibiotics or systemic steroids, or who were on supplemental oxygen. There were also older individuals with a mean age of 66 years. The results of these trials apply only to the group of patients who were studied in these trials and may not be generalisable to other groups. Because of concerns about antibiotic resistance and specific adverse effects, consideration of prophylactic antibiotic use should be mindful of the balance between benefits to individual patients and the potential harms to society created by antibiotic overuse.

Herath SC, Normansell R, Maisey S, et al. **Prophylactic antibiotic therapy** for chronic obstructive pulmonary disease (**COPD**). Cochrane Database Syst Rev. 2018 Oct 30;10:CD009764. Use of continuous and intermittent prophylactic antibiotics results in a clinically significant benefit in reducing exacerbations in COPD patients. All studies of continuous and intermittent antibiotics used macrolides, hence the noted benefit applies only to the use of macrolide antibiotics prescribed at least three times per week. The impact of pulsed antibiotics remains uncertain and requires further research.The studies in this review included mostly participants who were frequent exacerbators with at least moderate-severity COPD. There were also older individuals with a mean age over 65 years. The results of these studies apply only to the group of participants who were studied in these studies and may not be generalisable to other groups.Because of concerns about antibiotic resistance and specific adverse effects, consideration of prophylactic antibiotic use should be mindful of the balance between benefits to individual patients and the potential harms to society created by antibiotic overuse. Monitoring of significant side effects including hearing loss, tinnitus, and long QTc in the community in this elderly patient group may require extra health resources.

Herath SC, Poole P. **Prophylactic antibiotic** therapy in chronic obstructive pulmonary disease. JAMA. 2014 Jun 4;311(21):2225-6.

Hew M, Reddel HK. Integrated **Adherence Monitoring for Inhaler Medications**. JAMA. 2019 Mar 1.

Hill K, Cavalheri V, Mathur S, et al. **Neuromuscular electrostimulation for adults with chronic obstructive pulmonary disease.** Cochrane Database Syst Rev. 2018 May 29;5:CD010821. NMES, when applied in isolation, increased quadriceps force and endurance, 6MWD and time to symptom limitation exercising at a submaximal intensity, and reduced the severity of leg fatigue on completion of exercise testing. It may increase VO2peak, but the true effect on this outcome measure could be trivial. However, the quality of evidence was low or very low due to risk of bias within the studies, imprecision of the estimates, small number of studies and inconsistency between the studies.

Hill, Kylie, Hodder, Richard, Blouin, Maria, et al. Identifying adults at risk of COPD who need confirmatory **spirometry** in primary care: Do symptom-based questions help? Can Fam Physician 2011 57: e51-57.

Holland AE, Mahal A, Hill CJ, et al. **Home-based rehabilitation** for COPD using minimal resources: a randomised, controlled equivalence trial. Thorax. 2017 Jan;72(1):57-65.

Hoover Wynton C, Britton LaCrecia J, Gardner Jay, et al. Rapid Onset of Iatrogenic Adrenal Insufficiency in a Patient with Cystic Fibrosis–Related Liver Disease Treated with Inhaled **Corticosteroids and a Moderate CYP3A4 Inhibitor**. Ann Pharmacother July/August 2011 45:e38; June 28

Hodyl NA, Stark MJ, Scheil W, et al. Perinatal outcomes following maternal asthma and cigarette **smoking during pregnancy**. Eur Respir J. 2013 Jul 30.

Holland AE, Hill CJ, Jones AY, et al. **Breathing exercises** for chronic obstructive pulmonary disease. Cochrane Database Syst Rev. 2012 Oct 17;10:CD008250. Breathing exercises over four to 15 weeks improve functional exercise capacity in people with COPD compared to no intervention; however, there are no consistent effects on dyspnoea or health-related quality of life.

Hopkinson NS, Molyneux A, Pink J, et al. Chronic obstructive pulmonary disease: **diagnosis and management**: summary of updated NICE guidance. BMJ. 2019 Jul 29;366:l4486.

Horita N, Goto A, Shibata Y, et al. Long-acting muscarinic antagonist **(LAMA) plus long-acting beta-agonist (LABA)** versus LABA plus inhaled corticosteroid (ICS) for stable chronic obstructive pulmonary disease (COPD). Cochrane Database Syst Rev. 2017 Feb 10;2:CD012066. For the treatment of COPD, LAMA+LABA has fewer exacerbations, a larger improvement of FEV1, a lower risk of pneumonia, and more frequent improvement in quality of life as measured by an increase over 4 units or more of the SGRQ. These data were supported by low or moderate quality evidence generated from mainly participants with moderate to severe COPD in heterogeneous trials with an observation period of less than one year. Our findings support the recently updated GOLD guidance.

Horita N, Nagashima A, Kaneko T. **Long-Acting β-Agonists (LABA) Combined With Long-Acting Muscarinic Antagonists or LABA Combined With Inhaled Corticosteroids** for Patients With Stable COPD. JAMA. 2017 Oct 3;318(13):1274-1275.

Houben CHM, Spruit MA, Luyten H, et al. Cluster-randomised **trial of a nurse-led advance care planning session** in patients with COPD and their loved ones. Thorax. 2019 Jan 19.

Hurst John R., Vestbo Jørgen, Antonio Anzueto, et al. for the Evaluation of COPD Longitudinally to Identify Predictive Surrogate Endpoints (**ECLIPSE**) Investigators. Susceptibility to **Exacerbation** in Chronic Obstructive Pulmonary Disease. N Engl J Med 2010; 363:1128-1138

Janson C, Larsson K, Lisspers KH, et al. Pneumonia and pneumonia related mortality in patients with COPD treated with fixed combinations of inhaled corticosteroid and long acting β2 agonist: (**Advair vs Symbicort**) observational matched cohort study (PATHOS). BMJ. 2013 May 29;346:f3306.

Jarjour NN, et al. Control of airway inflammation maintained at a lower steroid dose with 100/50 ug of fluticasone propionate/salmeterol. J Allergy Clin Immunol. 2006 Jul;118(1):44-52.Epub 2006 Jun 2.

Jarosch I, Gloeckl R, Damm E, et al. Short-term Effects of **Supplemental Oxygen on 6-Min Walk Test** Outcomes in Patients With COPD: A Randomized, Placebo-Controlled, Single-blind, Crossover Trial. Chest. 2017 Apr;151(4):795-803.

Jatene T, Biering-Sørensen T, Nochioka K, et al; **BASKET-PROVE** Investigators.. Frequency of **Cardiac Death and Stent Thrombosis** in Patients With Chronic Obstructive Pulmonary Disease Undergoing Percutaneous Coronary Intervention (from the BASKET-PROVE I and II Trials). Am J Cardiol. 2016 Sep 29.

Jeppesen E, Brurberg KG, Vist GE, et al. **Hospital at home for acute exacerbations of chronic obstructive pulmonary disease**. Cochrane Database of Systematic Reviews 2012, Issue 5. Art. No.: CD003573. Selected patients presenting to hospital emergency departments with acute exacerbations of COPD can be safely and successfully treated at home with support from respiratory nurses. We found evidence of moderate quality that hospital at home may be advantageous with respect to readmission rates in these patients. Treatment of acute exacerbation of COPD in hospital at home also show a trend towards reduced mortality rate when compared with conventional inpatient treatment, but these results did not reach statistical significance (moderate quality evidence).

Jiang X, Xiao H, Segal R, et al. **Trends in Readmission Rates, Hospital Charges, and Mortality** for Patients With Chronic Obstructive Pulmonary Disease (COPD) in Florida From 2009 to 2014. Clin Ther. 2018 Mar 30.

Johannessen A, Nilsen RM, Storebo M, et al. Comparison of 2011 and 2007 **Global Initiative for Chronic Obstructive Lung Disease guidelines** for predicting mortality and hospitalization. Am J Respir Crit Care Med. 2013 Jul 1;188(1):51-9.

Johansson SG, Oman H, Nopp A, Pettersson S. The importance of **IgE antibody** levels in anti-IgE treatment. Allergy. 2006 Oct;61(10):1216-9.

Johnstone KJ, Chang AB, Fong KM, et al. **Inhaled corticosteroids for subacute and chronic cough** in adults. Cochrane Database Syst Rev. 2013 Mar 28;3:CD009305. doi: 10.1002/14651858.CD009305.pub2. The studies were highly heterogeneous and results were inconsistent. Heterogeneity in study design needs to be addressed in future research in order to test the efficacy of this intervention.

Johnson JD, Theurer WM. A stepwise approach to the interpretation of **pulmonary function tests**. Am Fam Physician. 2014 Mar 1;89(5):359-66.

Jolliffe DA, Greenberg L, Hooper RL, et al. **Vitamin D to prevent exacerbations of COPD**: systematic review and meta-analysis of individual participant data from randomised controlled trials. Thorax. 2019 Jan 10.

Jolly K, Sidhu MS, Hewitt CA, et al. **Self management of patients with mild COPD** in primary care: randomised controlled trial. BMJ. 2018 Jun 13;361:k2241.

Jones PW, Chen WH, et al. EXACT-PRO Study Group. Characterizing and quantifying the symptomatic features of **COPD exacerbations**. Chest. 2011 Jun;139(6):1388-94.

Jonkman NH, Westland H, et al. Characteristics of effective **self-management** interventions in patients with **COPD**: individual patient data meta-analysis. Eur Respir J. 2016 Jul;48(1):55-68.

Judd LL, Schettler PJ, Brown ES, et al. **Adverse consequences of glucocorticoid medication**: psychological, cognitive, and behavioral effects. Am J Psychiatry. 2014 Oct 1;171(10):1045-51.

Jung KS et al.Comparison of **tiotropium plus fluticasone propionate/salmeterol** with tiotropium in COPD: A randomized controlled study. Respir Med. 2011 Oct 3.

Kane Binita, Turkington Peter M, Howard Luke S, et al. Lesson of the Week: Rebound **hypoxaemia after administration of oxygen** in an acute exacerbation of chronic obstructive pulmonary disease. BMJ 2011;342:doi:10.1136/bmj.d1557 (Published 31 March 2011)

Kapadia CR, Nebesio TD, Myers SE, et al; Drugs and Therapeutics Committee of the Pediatric Endocrine Society. **Endocrine Effects of Inhaled Corticosteroids in Children**. JAMA Pediatr. 2015 Dec 21:1-9.

Kaplan RM, Sun Q, Ries AL. **Quality of Well-being** Outcomes in the National **Emphysema** Treatment Trial. Chest. 2015 Feb 1;147(2):377-87.

Karner C, Cates CJ. The effect of **adding inhaled corticosteroids to tiotropium and long-acting beta(2)-agonists for chronic obstructive pulmonary disease**. Cochrane Database

Syst Rev. 2011 Sep 7;9:CD009039. The relative efficacy and safety of adding inhaled corticosteroid to tiotropium and a long-acting beta(2)-agonist for chronic obstructive pulmonary disease patients remains uncertain and additional trials are required to answer this question.

Karner C, Cates CJ. **Long-acting beta(2)-agonist in addition to tiotropium** versus either tiotropium or long-acting beta(2)-agonist alone for chronic obstructive pulmonary disease. Cochrane Database Syst Rev. 2012 Apr 18;4:CD008989. The results from this review indicate a small mean improvement in health-related quality of life for patients on a combination of tiotropium and long-acting beta(2)-agonist compared to tiotropium alone, but it is not clear how clinically important this mean difference may be. Hospital admission and mortality have not been shown to be altered by adding long-acting beta(2)-agonists to tiotropium. There were not enough data to determine the relative efficacy and safety of tiotropium plus long-acting beta(2)-agonist compared to long-acting beta(2)-agonist alone. There were insufficient data to make comparisons between the different long-acting beta(2)-agonists when used in addition to tiotropium.

Karner C, Cates CJ. Combination inhaled steroid and long-acting beta(2)-agonist in addition to **tiotropium versus tiotropium or combination** alone for chronic obstructive pulmonary disease. Cochrane Database Syst Rev. 2011 Mar 16;(3):CD008532.

Karner C, Chong J, Poole P. Tiotropium versus placebo for chronic obstructive pulmonary disease**.** Cochrane Database Syst Rev. 2012 Jul 11;7:CD009285. This review shows that tiotropium treatment was associated with a significant improvement in patients` quality of life and it reduced the risk of exacerbations, with a number needed to treat to benefit (NNTB) of 16 to prevent one exacerbation. Tiotropium also reduced exacerbations leading to hospitalisation but no significant difference was found for hospitalisation of any cause or mortality. Thus, tiotropium appears to be a reasonable choice for the management of patients with stable COPD, as proposed in guidelines. The review however, shows that tiotropium delivered via the Respimat soft mist inhaler was associated with a significantly increased risk of mortality compared with placebo, which calls for caution with this device whilst awaiting the results of an ongoing head-to-head trial comparing tiotropium delivery devices and doses.

Karner C, Chong J, Poole P. **Tiotropium versus placebo** for chronic obstructive pulmonary disease. Cochrane Database Syst Rev. 2014 Jul 21;7:CD009285. This review shows that tiotropium treatment was associated with a significant improvement in patients' quality of life and it reduced the risk of exacerbations, with a number needed to treat to benefit (NNTB) of 16 to prevent one exacerbation. Tiotropium also reduced exacerbations leading to hospitalisation but no significant difference was found for hospitalisation of any cause or mortality. Thus, tiotropium appears to be a reasonable choice for the management of patients with stable COPD, as proposed in guidelines. The trials included in this review showed a difference in the risk of mortality when compared with placebo depending on the type of tiotropium delivery device used. However, these results have not been confirmed in a recent trial when 2.5 mcg or 5 mcg of tiotropium via Respimat was used in a direct comparison to the 18 mcg Handihaler.

Kawasumi Y, et al. **Comparative Effectiveness of Tiotropium and Ipratropium** in Prevention of Hospital Readmission for COPD: Population-Based Cohort Study. Clin Ther. 2013 Mar 12.

Kempsford R, Allen A, Bal J, et al. The effect of **ketoconazole** on the pharmacokinetics and pharmacodynamics of inhaled **fluticasone** furoate and **vilanterol** trifenatate in healthy subjects. Br J Clin Pharmacol. 2012 Nov 1.

Kerstjens HA, Bantje TA, Luursema PB, Sinninghe Damste HE, de Jong JW, Lee A, Wijker SP, Cornelissen PJ. Effects of short-acting bronchodilators added to maintenance tiotropium therapy. Chest. 2007 Nov;132(5):1493-9. Epub 2007 Sep 21. In conclusion, both short-acting bronchodilator classes were effective when added to maintenance treatment with tiotropium. The addition of the beta2-adrenergic fenoterol provided greater additional bronchodilatation than the short-acting anticholinergic ipratropium.

Kesimer M, Ford AA, Ceppe A, et al. **Airway mucin concentration** as a marker of chronic bronchitis. N Engl J Med 2017;377: 911-22.

Kessler R, Casan-Clara P, Koehler D, et al. **COMET**: a multicomponent **home-based disease-management programme versus routine care** in severe COPD. Eur Respir J. 2018 Jan 11;51(1).

Kew KM, Mavergames C, Walters JAE. **Long-acting beta2-agonists for chronic obstructive pulmonary disease**. Cochrane Database of Systematic Reviews 2013, Issue 10. Art. No.: CD010177. Moderate-quality evidence from 26 studies showed that inhaled long-acting beta2-agonists are effective over the medium and long term for patients with moderate to severe COPD. Their use is associated with improved quality of life and reduced exacerbations, including those requiring hospitalisation. Overall, findings showed that inhaled LABAs did not significantly reduce mortality or serious adverse events.

Kew KM, Seniukovich A. **Inhaled steroids and risk of pneumonia** for chronic obstructive pulmonary disease. Cochrane Database of Systematic Reviews 2014, Issue 3. Art. No.: CD010115. DOI: 10.1002/14651858.CD010115.pub2. Budesonide and fluticasone, delivered alone or in combination with a LABA, are associated with increased risk of serious adverse pneumonia events, but neither significantly affected mortality compared with controls. The safety concerns highlighted in this review should be balanced with recent cohort data and established randomised evidence of efficacy regarding exacerbations and quality of life. Comparison of the two drugs revealed no statistically significant difference in serious pneumonias, mortality or serious adverse events. Fluticasone was associated with higher risk of any pneumonia when compared with budesonide (i.e. less serious cases dealt with in the community), but variation in the definitions used by the respectivemanufacturers is a potential confounding factor in their comparison.

Kew KM, Dias S, Cates CJ. **Long-acting inhaled therapy** (beta-agonists, anticholinergics and steroids) for **COPD**: a network meta-analysis.CochraneDatabase of SystematicReviews 2014, Issue 3.Art.No.:CD010844.DOI: 10.1002/14651858.CD010844.pub2. This network meta-analysis compares four different classes of long-acting inhalers for people with COPD who need more than shortacting bronchodilators. Quality of life and lung function were improved most on combination inhalers (LABA and ICS) and least on ICS alone at 6 and at 12 months. Overall LAMA and LABA inhalers had similar effects, particularly at 12 months. The network has demonstrated the benefit of ICS when added to LABA for these outcomes in participants who largely had an FEV1 that was less than 50% predicted, but the additional expense of combination inhalers and any potential for increased adverse events (which has been established by other reviews) require consideration. Our findings are in keeping with current National Institute for Health and Care Excellence (NICE) guidelines.

Khorfan FM, Smith P, Watt S, Barber KR. Effects of **nebulized bronchodilator** therapy on heart rate and arrhythmias in critically ill adult patients. Chest. 2011 Dec;140(6):1466-72. In critically ill adult patients, nebulized albuterol and ipratropium does not cause significant tachycardia or tachyarrhythmias. Substitution of levalbuterol for albuterol (salbutamol) to avoid tachycardia and tachyarrhythmias is unwarranted.

Kiljander TO, et al. Effects of **esomeprazole** 40 mg twice daily on asthma: a randomized placebo-controlled trial. Am J Respir Crit Care Med. 2006 May 15;173(10):1091-7. Epub 2005 Dec 15. n=770 16weeks Esomeprazole improved PEF in subjects with asthma who presented with both GERD and NOC. In subjects without both GERD and NOC, no improvement could be detected. (InfoPOEMs: In this study, esomeprazole (Nexium) was no better than placebo in improving peak expiratory flow, asthma symptoms, or quality of life in patients with stable asthma. Furthermore, esomeprazole was no better than placebo in pts with reflux, either. (LOE = 2b-))

Kiljander TO, Junghard O, Beckman O, Lind T. Effect of **Esomeprazole** 40 mg Once or Twice Daily on Asthma: A Randomized, Placebo-controlled Study. Am J Respir Crit Care Med. 2010 Jan 28.

Kim V, Criner GJ. **Chronic bronchitis and chronic obstructive pulmonary disease**. Am J Respir Crit Care Med. 2013 Feb 1;187(3):228-37.

Klijn P, van Keimpema A, Legemaat M, et al. **Nonlinear exercise training** in advanced chronic obstructive pulmonary disease is superior to traditional exercise training. A randomized trial. Am J Respir Crit Care Med. 2013 Jul 15;188(2):193-200.

Ko FW, Cheung NK, Rainer TH, et al. **Comprehensive care programme** for patients with chronic obstructive pulmonary disease: a randomised controlled trial. Thorax. 2016 Jul 28.

Kobylecki CJ, et al. **Plasma urate**, lung function and chronic obstructive pulmonary disease: a Mendelian randomisation study in 114 979 individuals from the general population. Thorax. 2017 Nov 29.

Konecny, Park, Somers, et al. Relation of Chronic Obstructive Pulmonary Disease to **Atrial and Ventricular Arrhythmias**. The American Journal of Cardiology. 2014.

Kornmann O, Dahl R, Centanni S, Dogra A, Owen R, Lassen C, Kramer B. Once-daily **indacaterol** vs twice-daily salmeterol for COPD: a placebo-controlled comparison. Eur Respir J. 2010 Aug 6.

Kruis AL, Smidt N, Assendelft WJ, et al. **Integrated disease management interventions for patients with chronic obstructive pulmonary disease.** Cochrane Database Syst Rev. 2013 Oct 10;10:CD009437. In these COPD participants, IDM not only improved disease-specific QoL and exercise capacity, but also reduced hospital admissions and hospital days per person.

Kruis AL, Smidt N, Assendelft WJ, et al. Cochrane corner: is **integrated disease management** for patients with **COPD** effective?. Thorax. 2014 Jan 14.

Kruis AL, Boland MR, Assendelft WJ, et al. Effectiveness of **integrated disease management for primary care chronic obstructive** pulmonary disease patients: results of cluster randomised trial. BMJ. 2014 Sep 10;349:g5392.

Kwon YJ, Allen JL, Liu GT, et al. Presumed **Pseudotumor Cerebri Syndrome After Withdrawal of Inhaled Glucocorticoids**. Pediatrics. 2016 May 17.

Irwin RS, et al. American College of Chest Physicians (ACCP). **Diagnosis and management of cough** executive summary: ACCP evidence-based clinical practice guidelines. Chest. 2006 Jan;129(1 Suppl):1S-23S. http://www.chestjournal.org/cgi/content/full/129/1_suppl/1S

Labonté LE, Tan WC, Li PZ, et al; Canadian Respiratory Research Network and the CanCOLD Collaborative Research group. **Undiagnosed COPD Contributes to the Burden** of Health Care Utilization: Data from the CanCOLD Study. Am J Respir Crit Care Med. 2016 Feb 2.

Lacasse Y, Bernard S, Sériès F, et al; International Nocturnal **Oxygen (INOX)** Research Group. Multi-center, randomized, placebo-controlled trial of **nocturnal oxygen therapy** in chronic obstructive pulmonary disease: a study protocol for the INOX trial. BMC Pulm Med. 2017;17:8.

Lacasse Y, Tan AM, Maltais F, et al. **Home Oxygen** in Chronic Obstructive Pulmonary Disease. Am J Respir Crit Care Med. 2018 Mar 16.

Lahousse L, Niemeijer MN, van den Berg ME, et al. **Chronic obstructive pulmonary disease and sudden cardiac death**: the Rotterdam study. Eur Heart J. 2015 Apr 28.

Lange P, Celli B, Agustí A, et al. **Lung-function trajectories** leading to chronic obstructive pulmonary disease. N Engl J Med 2015;373:111-22.

Lapperre T. S., Snoeck-Stroband J. B., Gosman M. M.E., et al. and the GLUCOLD (Groningen Leiden Universities Corticosteroids in Obstructive Lung Disease) Study Group. Effect of **Fluticasone** With and Without Salmeterol on Pulmonary Outcomes in Chronic Obstructive Pulmonary Disease: A Randomized Trial. Ann Intern Med 2009; 517-527.

Lareau S, Moseson E, Slatore CG. Exacerbation of COPD. Am J Respir Crit Care Med. 2018 Dec 1;198(11):P21-P22. (patient information)

Lareau SC, Fahy B, Meek P, Wang A. **Chronic Obstructive Pulmonary Disease (COPD)**. Am J Respir Crit Care Med. 2019 Jan 1;199(1):P1-P2. (patient information)

Larsson K, Janson C, Lisspers K, et al. Combination of budesonide/formoterol more effective than fluticasone/salmeterol in preventing exacerbations in chronic obstructive pulmonary disease. The PATHOS study. J Intern Med. 2013 Mar 15.

Laude EA, et al. The effect of helium and oxygen on exercise performance in COPD: a randomized crossover trial. Am J Respir Crit Care Med. 2006 Apr 15;173(8):865-70. Epub 2006 Jan 26. (InfoPOEMs: Inhaling a combination of 72% helium and 28% oxygen during exertion increases the comfortable walking distance and reduces the perception of exertional difficulty in patients with stable chronic obstructive pulmonary disease (COPD). (LOE = 2b))

Lawson CA, Mamas MA, Jones PW, et al. Association of medication intensity and stages of airflow limitation with the risk of hospitalization or death in patients with heart failure and chronic obstructive pulmonary disease. JAMA Netw Open. 2018;1(8):e185489. doi:10.1001/jamanetworkopen.2018.5489

Lee AL, Dolmage TE, Rhim M, et al. The impact of **listening to music** during a high-intensity exercise endurance test in people with chronic obstructive pulmonary disease (COPD). Chest. 2017 Dec 15.

Lee TA, Pickard AS, Au DH, Bartle B, Weiss KB. Risk for death associated with medications for recently diagnosed chronic obstructive pulmonary disease. Ann Intern Med. 2008 Sep 16;149(6):380-90. The possible association between ipratropium and elevated risk for all-cause and cardiovascular death needs further study.

Lee TA, Wilke C, Joo M, Stroupe KT, et al. Outcomes associated with **tiotropium** use in patients with chronic obstructive pulmonary disease. Arch Intern Med. 2009 Aug 10;169(15):1403-10.

Leivseth L, Brumpton BM, Nilsen TI, et al. **GOLD classifications and mortality** in chronic obstructive pulmonary disease (**COPD**): the HUNT Study, Norway. Thorax. 2013 Apr 23.

Lenferink A;Brusse-Keizer M;van der Valk PD;Frith . **Self-management interventions including action plans** for **exacerbations** versus usual care in patients with chronic obstructive pulmonary disease. Cochrane Database Syst Rev. 2017 Aug 4;8:CD011682. Self-management interventions that include a COPD exacerbation action plan are associated with improvements in HRQoL, as measured with the SGRQ, and lower probability of respiratory-related hospital admissions. No excess all-cause mortality risk was observed, but exploratory analysis showed a small, but significantly higher respiratory-related mortality rate for self-management compared to usual care.

Leung JM, Sin DD. **Asthma-COPD overlap syndrome**: pathogenesis, clinical features, and therapeutic targets. BMJ. 2017 Sep 25;358:j3772.

Leuppi JD, Schuetz P, Bingisser R, et al. **Short-term (5d) vs conventional (14d) glucocorticoid therapy** in acute exacerbations of chronic obstructive pulmonary disease: the REDUCE randomized clinical trial [online May 21, 2013]. JAMA. doi: 10.1001/jama.2013.5023.

Levalbuterol (Xopenex HFA) Medical Letter Mar 13,2006.

Li H, Liu DH, Chen LL, Zhao Q, et al. Meta-analysis of the adverse effects of long-term **azithromycin** use in patients with chronic lung diseases. Antimicrob Agents Chemother. 2014 Jan;58(1):511-7

Li J, Agarwal SK, et al. Airflow Obstruction, Lung Function, and Incidence of **Atrial Fibrillation**: The Atherosclerosis Risk in Communities (ARIC) Study. Circulation. 2014 Mar 4;129(9):971-80.

Liistro G, Vanwelde C, Vincken W, et al; COPDAdvisory Board(†). Technical and Functional **Assessment of 10 Office Spirometers**. Chest. 2006 Sep;130(3):657-665.

Lindenauer Peter K.; Pekow Penelope S.; Lahti Maureen C.; et al. Association of **Corticosteroid Dose and Route** of Administration With Risk of Treatment Failure in Acute Exacerbation of Chronic Obstructive Pulmonary Disease (**COPD**). JAMA. 2010;303(23):2359-2367.

Lindenauer PK, Stefan MS, Shieh MS, et al. Outcomes Associated With **Invasive and Noninvasive Ventilation** Among Patients Hospitalized With Exacerbations of Chronic Obstructive Pulmonary Disease. JAMA Intern Med. 2014 Oct 27.

Liou JT, Lin CW, Tsai CL, et al. Risk of Severe **Cardiovascular Events** From Add-On **Tiotropium** in Chronic Obstructive Pulmonary Disease. Mayo Clin Proc. 2018 Oct;93(10):1462-1473.

Lipson DA, Barnacle H, Birk R, et al. **FULFIL** Trial: **Once-Daily Triple Therapy** in Patients with Chronic Obstructive Pulmonary Disease. Am J Respir Crit Care Med. 2017 Apr 4.

Littner Michael R. In the Clinic: **Chronic Obstructive Pulmonary Disease**. *Ann Intern Med* April 5, 2011 154:ITC4-1.

Liu VX, Winthrop KL, Lu Y, et al. **Association between Inhaled Corticosteroid Use and Pulmonary Nontuberculous Mycobacterial Infection**. Ann Am Thorac Soc. 2018 Sep 14.

Llor C, Moragas A, Hernández S, et al. Efficacy of **antibiotic therapy for acute exacerbations** of mild to moderate chronic obstructive pulmonary disease. Am J Respir Crit Care Med. 2012 Oct 15;186(8):716-23.

Lodge CJ, Zaloumis S, Lowe AJ, et al. Early-Life Risk Factors for **Childhood Wheeze Phenotypes** in a High-Risk Birth Cohort. J Pediatr. 2013 Nov 14.

Loke YK et al. **Risk of fractures with inhaled corticosteroids** in COPD: Systematic review and meta-analysis of randomised controlled trials and observational studies. Thorax 2011 Aug; 66:699. The use of inhaled corticosteroids as a treatment for chronic obstructive pulmonary disease (COPD) in older adults increases the fracture risk somewhat, with a number needed to treat to harm of 83 over 3 years. This must be balanced against a number needed to treat of 6 per year to prevent exacerbations. (LOE = 1a)

Lokke A, et al. Developing COPD: a **25yr follow up** of the general population. Thorax. 2006 Nov;61(11):935-9. The absolute risk of developing COPD among continuous smokers is at least 25%, which is larger than was previously estimated.

Ma J, Ward EM, Siegel RL, et al. **Temporal Trends in Mortality** in the United States, 1969-2013. JAMA. 2015 Oct 27;314(16):1731-1739.

MacDonald MI, Osadnik CR, Bulfin L, et al. **Low and high blood eosinophil counts** as biomarkers in hospitalised acute exacerbations of chronic obstructive pulmonary disease. Chest. 2019 Apr 9.

Mackay AJ, Donaldson GC, Patel AR, et al. Usefulness of the Chronic Obstructive Pulmonary Disease Assessment **Test to Evaluate Severity of COPD Exacerbations**. (**CAT**) Am J Respir Crit Care Med. 2012 Jun 1;185(11):1218-24.

Macie C, Wooldrage K, Manfreda J, Anthonisen NR. Inhaled **Corticosteroids** and **Mortality** in COPD. Chest. 2006 Sep;130(3):640-6.

Maddocks M, Kon SS, Canavan JL, et al. **Physical frailty** and pulmonary rehabilitation in COPD: a prospective cohort study. Thorax. 2016 Jun 12.

Maddocks M, et al. **Palliative care** and management of troublesome symptoms for people with chronic obstructive pulmonary disease. Lancet. 2017 Sep 2;390(10098):988-1002.

Magnussen H, Disse B, Rodriguez-Roisin R, et al. **Withdrawal of inhaled glucocorticoids** and exacerbations of COPD. (**Wisdom**) N Engl J Med. DOI: 10.1056/NEJMoa1407154.

Mahler DA, D`Urzo A, Bateman ED, et al. Concurrent use of **indacaterol plus tiotropium** in patients with COPD provides superior bronchodilation compared with tiotropium alone:

a randomised, double-blind comparison. Thorax. 2012 Apr 27.
Mahler DA, Decramer M, D`Urzo A, et al. Dual bronchodilation with **QVA149** reduces patient-reported dyspnoea in COPD: BLAZE study. Eur Respir J. 2014 Jun;43(6):1599-609.
Mahler DA, Kerwin E, Ayers T, et al. FLIGHT1 and FLIGHT2: Efficacy and Safety of QVA149 (**Indacaterol/Glycopyrrolate**) versus Its **Monocomponents** and Placebo in Patients with Chronic Obstructive Pulmonary Disease. Am J Respir Crit Care Med. 2015 Nov 1;192(9):1068-79.
Mainguy V, Girard D, Maltais F, et al. Effect of **Bisoprolol** on Respiratory Function and Exercise Capacity in Chronic Obstructive Pulmonary Disease. Am J Cardiol. 2012 Apr 10.
Man WD, Polkey MI, Donaldson N, Gray BJ, Moxham J. Community **pulmonary rehabilitation** after hospitalisation for acute exacerbations of chronic obstructive pulmonary disease: randomised controlled study. BMJ. 2004 Nov 20;329(7476):1209. Epub 2004 Oct 25.
Mantoani LC, Rubio N, McKinstry B, et al. Interventions to modify **physical activity** in patients with COPD: a systematic review.Eur Respir J. 2016 Jul;48(1):69-81.
Mapel DW, Dalal AA, Johnson P, Becker L, Hunter AG. A Clinical Study of **COPD Severity** Assessment by Primary Care **Physicians and Their Patients Compared with Spirometry**. Am J Med. 2015 Jun;128(6):629-37.
Maqsood U, Ho TN, Palmer K, et al. Once daily **long-acting beta2-agonists and long-acting muscarinic antagonists in a combined inhaler** versus placebo for chronic obstructive pulmonary disease. Cochrane Database Syst Rev. 2019 Mar 6;3:CD012930.
Marciniuk DD, Goodridge D, Hernandez P, et al; **Canadian Thoracic Society (CTS)** COPD Committee Dyspnea Expert Working Group. Managing **dyspnea** in patients with advanced chronic obstructive pulmonary disease: A Canadian Thoracic Society clinical practice guide. Can Respir J 2011;18(2).http://www.respiratoryguidelines.ca/sites/all/files/2011_CTS_guideline_COPD_dyspnea.pdf
Marengoni A, Vetrano DL, et al. The relationship between **chronic obstructive pulmonary disease and frailty**: a systematic review and meta-analysis of observational studies. Chest. 2018 Feb 22.
Maricoto T, Monteiro L, Gama JMR, et al. **Inhaler Technique Education and Exacerbation Risk** in Older Adults with Asthma or Chronic Obstructive Pulmonary Disease: A Meta-Analysis. J Am Geriatr Soc. 2019 Jan;67(1):57-66.
Marth K, Schuller E, Pohl W. Improvements in patient-reported outcomes: A prospective, non-interventional study with **aclidinium bromide** for treatment of COPD. Respir Med. 2015May;109(5):616-24.
Martinez FJ, Calverley PM, Goehring UM,et al. Effect of **roflumilast** on exacerbations in patients with severe chronic obstructive pulmonary disease uncontrolled by combination therapy (**REACT**): a multicentre randomised controlled trial. Lancet. 2015 Feb 12. pii: S0140-6736(14)62410-7
Martinez FD. **Early-Life Origins** of Chronic Obstructive Pulmonary Disease. N Engl J Med. 2016 Sep 1;375(9):871-8.
Martinez FJ, Mannino D, et al. A New Approach for **Identifying Patients with Undiagnosed** Chronic Obstructive Pulmonary Disease. Am J Respir Crit Care Med. 2016 Oct 26.
Martinez FJ, Rabe KF, Ferguson GT, et al. Efficacy and Safety of **Glycopyrrolate/Formoterol** Metered Dose Inhaler Formulated Using **Co-Suspension Delivery** Technology in Patients With COPD. Chest. 2017 Feb;151(2):340-357.
Martinez FJ, Vestbo J, Anderson JA, et al. Effect of **Fluticasone Furoate and Vilanterol** on Exacerbations of Chronic Obstructive Pulmonary Disease in Patients with Moderate Airflow Obstruction. Am J Respir Crit Care Med. 2017 Apr 1;195(7):881-888.
Martinez FJ, Fabbri LM, Ferguson GT, et al. Baseline Symptom Score Impact on Benefits of **Glycopyrrolate/Formoterol** Metered Dose Inhaler in COPD. Chest. 2017 Dec;152(6):1169-1178
Matthay MA, Brower RG, Carson S, et al. Randomized, Placebo-Controlled Clinical Trial of an Aerosolized Beta**-2 Agonist for Treatment of Acute Lung Injury**. Am J Respir Crit Care Med. 2011 May 11.
Matsuyama W, Mitsuyama H, Watanabe M, et al. Effects of **omega-3 polyunsaturated fatty acids** on inflammatory markers in COPD. Chest. 2005 Dec;128(6):3817-27. (InfoPOEMs: This small study found that a diet rich in omega-3 fatty acids causes small improvements in chronic obstructive pulmonary disease (COPD) symptoms. (LOE = 1b))
Maurer M, Rosén K, Hsieh HJ, et al. **Omalizumab** for the Treatment of Chronic Idiopathic or Spontaneous **Urticaria**. N Engl J Med. 2013 Feb 24.
McCarthy B, Casey D, Devane D, et al. **Pulmonary rehabilitation for chronic obstructive pulmonary disease**. Cochrane Database Syst Rev. 2015 Feb 23;2:CD003793.
Pulmonary rehabilitation relieves dyspnoea and fatigue, improves emotional function and enhances the sense of control that individuals have over their condition. These improvements are moderately large and clinically significant. Rehabilitation serves as an important component of the management of COPD and is beneficial in improving health-related quality of life and exercise capacity. It is our opinion that additional RCTs comparing pulmonary rehabilitation and conventional care in COPD are not warranted. Future research studies should focus on identifying which components of pulmonary rehabilitation are essential, its ideal length and location, the degree of supervision and intensity of training required and how long treatment effects persist. This endeavour is important in the light of the new subgroup analysis, which showed a difference in treatment effect on the CRQ between hospital-based and community-based programmes but no difference between exercise only and more complex pulmonary rehabilitation programmes.
McDonough JE, Yuan R, Suzuki M, et al. **Small-airway obstruction and emphysema in chronic obstructive pulmonary disease**. N Engl J Med 2011;365:1567-75.
McKeever TM, Hearson G, et al. Using **venous blood gas analysis** in the assessment of COPD exacerbations: a prospective cohort study. Thorax. 2016 Mar;71(3):210-5.
McMahon Ann W., Levenson Mark S., . McEvoy Bradley W,et al. **Age** and Risks of FDA–Approved **Long-Acting β2-Adrenergic Receptor Agonists**. Pediatrics 2011; peds.2010-1720; published ahead of print October 24, 2011
Medarov B, Chaudhry H, Myint T. Increasing **Hypoxemia and Dyspnea** in Mild Chronic Obstructive Pulmonary Disease. JAMA. 2017 Mar 14;317(10):1072-1073.
Medical Letter. **Arformoterol (Brovana)** for COPD). Jyly 2, 2007.
Medical Letter. Treatment Guidelines: Drugs for **Chronic Obstructive Pulmonary Disease (COPD)**. Nov 2007 & 2010. Revised **Apr 2017.**
Mehta AJ, Miedinger D, Keidel D, et al; SAPALDIA-team. **Occupational Exposure to Dusts, Gases and Fumes** and Incidence of COPD in SAPALDIA. Am J Respir Crit Care Med. 2012 Apr 6.
Mehta R, Hardes K, Kelleher D, et al. Effects of Moderate **Hepatic Impairment** on the Pharmacokinetic Properties and Tolerability of **Umeclidinium and Vilanterol** in Inhalational Umeclidinium Monotherapy and Umeclidinium/Vilanterol Combination Therapy: An Open-Label, Nonrandomized Study. Clin Ther. 2014 Jun 16.
Mendoza L, Horta P, Espinoza J, et al. **Pedometers to enhance physical activity in COPD**: a randomised controlled trial. Eur Respir J. 2014 Sep 26.
Mentz RJ, Wojdyla D, Fiuzat M, et al. Association of **Beta-Blocker Use and Selectivity** With Outcomes in Patients With Heart Failure and Chronic Obstructive Pulmonary Disease (from OPTIMIZE-HF). Am J Cardiol. 2013 Feb 15;111(4):582-7.
Mets OM, Buckens CF, Zanen P, et al. Identification of chronic obstructive pulmonary disease in **lung cancer screening computed tomographic scans**. JAMA. 2011 Oct 26;306(16):1775-81.
Metz M, Ohanyan T, Church MK, et al. Retreatment With **Omalizumab** Results in Rapid Remission in Chronic Spontaneous and Inducible **Urticaria**. JAMA Dermatol. 2014 Jan 29

Miller MR, Levy ML. **Chronic obstructive pulmonary disease**: **missed diagnosis versus misdiagnosis**. BMJ. 2015 Jul 1;351:h3021.

Miravitlles M, Moragas A, Hernández S, Bayona C, Llor C. Is it possible to **identify exacerbations of mild to moderate COPD that do not require antibiotic treatment**? Chest. 2013 Nov;144(5):1571-7.

Miravitlles M. **Diagnosis of asthma-COPD overlap: the five commandments**. Eur Respir J. 2017 May 1;49(5).

Mitchell KE, Johnson-Warrington V, Apps LD, et al. A **self-management programme for COPD**: a randomised controlled trial. Eur Respir J. 2014 Dec;44(6):1538-47.

Moen MD. **Indacaterol**: In Chronic Obstructive Pulmonary Disease. Drugs. 2010 Dec 3;70(17):2269-2280. doi: 10.2165/11203960-000000000-00000.

Moore E, et al. Effects of **pulmonary rehabilitation** on exacerbation number and severity in people with COPD: An historical cohort study using electronic health records. Chest. 2017 May 16.

Mortimer KJ, et al. Oral and inhaled corticosteroids and **adrenal insufficiency**: a case-control study. Thorax. 2006 May;61(5):405-8. Epub 2006 Mar 3.

Mulpuru S, Li L, Ye L, et al. Effectiveness of **Influenza Vaccination on Hospitalizations and Risk Factors for Severe Outcomes in** Hospitalized Patients With COPD. Chest. 2019 Jan;155(1):69-78.

Murphy PB, Rehal S, Arbane G, et al. Effect of **home noninvasive ventilation with oxygen therapy** vs oxygen therapy alone on hospital readmission or death after an acute COPD exacerbation: a randomized clinical trial. JAMA. doi:10.1001/jama .2017.4451

Najafzadeh M, Marra CA, Sadatsafavi M, Aaron SD, Sullivan SD, Vandemheen KL, Jones PW, Fitzgerald JM. Cost effectiveness of therapy with combinations of long acting bronchodilators and inhaled steroids for treatment of COPD. Thorax. 2008 Nov;63(11):962-7. Epub 2008 Jul 11. TFS had significantly better quality of life and fewer hospitalisations than patients treated with TP but these improvements in health outcomes were associated with increased costs. Neither TFS nor TS are economically attractive alternatives compared with monotherapy with T. (T=tiotropium)

Nannini LJ, Cates CJ, Lasserson TJ, Poole P. Combined **corticosteroid and long-acting** beta-agonist in one inhaler versus long-acting beta-agonists for chronic obstructive pulmonary disease. Cochrane Database Syst Rev. 2007 Oct 17;(4):CD006829. Combination therapy was more effective than long-acting beta-agonists in reducing COPD exacerbation rates, although the evidence for the effects on hospitalisations was mixed, and requires further exploration. No significant impact on mortality was found even with additional information from the TORCH trial. The superiority of combination inhalers should be viewed against the increased risk of side-effects, particularly pneumonia.

Nannini LJ, Lasserson TJ, Poole P. **Combined corticosteroid and long-acting beta(2)-agonist in one inhaler versus long-acting beta(2)-agonists** for chronic obstructive pulmonary disease. Cochrane Database Syst Rev. 2012 Sep 12;9:CD006829. doi: 10.1002/14651858.CD006829.pub2. Concerns over the analysis and availability of data from the studies bring into question the superiority of ICS/LABA over LABA alone in preventing exacerbations. The effects on hospitalisations were inconsistent and require further exploration. There was moderate quality evidence of an increased risk of pneumonia with ICS/LABA. There was moderate quality evidence that treatments had similar effects on mortality. Quality of life, symptoms score, rescue medication use and FEV(1) improved more on ICS/LABA than on LABA, but the average differences were probably not clinically significant for these outcomes. To an individual patient the increased risk of pneumonia needs to be balanced against the possible reduction in exacerbations.

Nannini LJ, Poole P, Milan SJ, et al. **Combined corticosteroid and long-acting beta2-agonist** in one inhaler **versus inhaled corticosteroids** alone for chronic obstructive pulmonary disease. Cochrane Database Syst Rev. 2013 Aug 30;8:CD006826. doi: 10.1002/14651858.CD006826.pub2. Combination ICS and LABA offer some clinical benefits in COPD compared with ICS alone, especially for reduction in exacerbations. This review does not support the use of ICS alone when LABAs are available. Adverse events were not significantly different between treatments.

Nannini LJ, Poole P, Milan SJ, et al. **Combined corticosteroid and long-acting beta-agonist in one inhaler versus placebo** for chronic obstructive pulmonary disease. Cochrane Database Syst Rev. 2013 Nov 10;11:CD003794. Combined inhaler therapy led to around a quarter fewer COPD exacerbations than were seen with placebo. A significant reduction in all-cause mortality was noted, but this outcome was dominated by one trial (TORCH), emphasising the need for further trials of longer duration. Increased risk of pneumonia is a concern; however, this did not translate into increased exacerbations, hospitalisations or deaths.

Nguyen HQ, Moy ML, Liu IA, et al. Effect of **Physical Activity Coaching** on Acute Care and Survival Among Patients With Chronic Obstructive Pulmonary Disease: A Pragmatic Randomized Clinical Trial. JAMA Netw Open. 2019 Aug 2;2(8):e199657.

Ni H, Soe Z, Moe S. **Aclidinium** bromide for stable chronic obstructive pulmonary disease. Cochrane Database Syst Rev. 2014 Sep 19;9:CD010509. Aclidinium is associated with improved quality of life and reduced hospitalisations due to severe exacerbations in patients with moderate to severe stable COPD compared to placebo. Overall, aclidinium did not significantly reduce mortality, serious adverse events or exacerbations requiring oral steroids or antibiotics, or both.Currently, the available data are insufficient and of very low quality in comparisons of the efficacy of aclidinium versus tiotropium. The efficacy of aclidinium versus LABAs cannot be assessed due to inaccurate data. Thus additional trials are recommended to assess the efficacy and safety of aclidinium compared to other LAMAs or LABAs.

Ni H, Htet A, Moe S. **Umeclidinium bromide** versus placebo for people with chronic obstructive pulmonary disease (COPD). Cochrane Database Syst Rev. 2017 Jun 20;6:CD011897. Umeclidinium reduced acute exacerbations requiring steroids, antibiotics, or both, although no evidence suggests that it decreased the risk of hospital admission due to exacerbations. Moreover, umeclidinium demonstrated significant improvement in quality of life, lung function, and symptoms, along with lesser use of rescue medications. Studies reported no differences in adverse events, non-fatal serious adverse events, or mortality between umeclidinium and placebo groups; however, larger studies would yield a more precise estimate for these outcomes.

Ni H, Moe S, Soe Z, et al. **Combined aclidinium bromide and long-acting beta2-agonist for chronic obstructive pulmonary disease (COPD**). Cochrane Database Syst Rev. 2018 Dec 11;12:CD011594. FDC improved dyspnoea and lung function compared to aclidinium, formoterol or placebo, and this translated into an increase in the number of responders on combination treatment. Quality of life was better with combination compared to formoterol or placebo. There was no evidence of a difference between FDC and monotherapy or placebo for exacerbations, hospital admissions, mortality, non-fatal SAEs or adverse events. Studies reported a lower risk of moderate exacerbations and adverse events with FDC compared to formoterol; however, larger studies would yield a more precise estimate for these outcomes.

NICE: 2010 CG101 **Chronic obstructive pulmonary disease** (update): full guideline. London: National Institute for Health and Clinical Excellence, 2010. (http://guidance.nice.org.uk/CG101/Guidance .)

NICE: National Institute for Health and Care Excellence. Chronic obstructive pulmonary disease (**acute exacerbation**): **antimicrobial prescribing**. July 2018.www.nice.org.uk/guidance/indevelopment/gid-ng10115.

NICE: National Institute for Health and Care Excellence. Guideline. Chronic obstructive pulmonary disease in over 16s: **diagnosis and management**. Draft for consultation, July 2018. www.nice.org.uk/guidance/indevelopment/gid-ng10026.

Nici L, Donner C, et al., et al. **American Thoracic Society/European Respiratory Society** statement on **pulmonary rehabilitation**. Am J Respir Crit Care Med. 2006 Jun 15;173(12):1390-413.

Nici L, Lareau S, ZuWallack R. **Pulmonary Rehabilitation** in the Treatment of Chronic Obstructive Pulmonary Disease. Am Fam Physician. 2010 Sep 15;82(6):655-660.

Nielsen AO, Pedersen L, Sode BF, Dahl M**. β-Blocker Therapy and Risk** of Chronic Obstructive Pulmonary Disease - A Danish Nationwide Study of 1·3 Million Individuals. EClinicalMedicine. 2019 Jan 29;7:21-26.

Niewoehner DE, et al. Prevention of exacerbations of COPD with **tiotropium**, a once-daily inhaled anticholinergic bronchodilator -an RCT. Ann Intern Med. 2005 Sep 6;143(5):317-26. (InfoPOEMs: Daily treatment with tiotropium for 6 months slightly decreases the number of patients experiencing a chronic obstructive pulmonary disease (COPD) exacerbation, though it doesn't decrease the number of patients who will be hospitalized for an exacerbation. (LOE = 1b-))

Niewoehner, Dennis E. Outpatient Management of **Severe COPD**. N Engl J Med 2010 362: 1407-1416.

Nolan CM, Kon SSC, Patel S, et al. **Gait speed and pedestrian crossings** in COPD. Thorax. 2017 May 5.

Oba Y, Keeney E, Ghatehorde N, et al. **Dual combination therapy versus long-acting bronchodilators alone** for chronic obstructive pulmonary disease (COPD): a systematic review and network meta-analysis. Cochrane Database Syst Rev. 2018 Dec 3;12:CD012620. The LABA/LAMA combination was the highest ranked treatment group to reduce COPD exacerbations although there was some uncertainty in the results. LAMA containing inhalers may have an advantage over those without a LAMA for preventing COPD exacerbations based on the rank statistics. Combination therapies appear more effective than monotherapies for improving symptom and quality-of-life scores. ICS-containing inhalers are associated with an increased risk of pneumonia.Our most comprehensive review including intraclass/group comparisons, free combination therapies, 99 studies, and 20 outcomes for each high- and low-risk population summarises the current literature and could help with updating existing COPD guidelines.

Oba Y, Sarva ST, Dias S. Efficacy and safety of **long-acting beta-agonist/long-acting muscarinic antagonist combinations in COPD**: a network meta-analysis. Thorax. 2015 Oct 21.

O'Byrne PM, Gauvreau G. **Phosphodiesterase-4** inhibition in COPD. Lancet. 2009Aug 29;374(9691):665-7.

O'donnell DE, et al. Effect of **Fluticasone Propionate/Salmeterol** on Lung Hyperinflation and Exercise Endurance in COPD. Chest. 2006 Sep;130(3):647-56.

O'Driscoll BR and Beasley R. Avoidance of high concentration **oxygen in chronic obstructive pulmonary disease**. BMJ 2010 Oct 18; 341:c5549.

Oh EG, Yoo JY. Progression of **erectile function in men with chronic obstructive pulmonary** disease: a cohort study. BMC Pulm Med. 2019 Sep 2;19(1):139.

Osadnik CR, McDonald CF, Miller BR, et al. The effect of **positive expiratory pressure (PEP) therapy** on symptoms, quality of life and incidence of re-exacerbation in patients with acute exacerbations of chronic obstructive pulmonary disease: a multicentre, randomised controlled trial. Thorax. 2013 Sep 4.

Ogale SS, Lee TA, Au DH, Boudreau DM, et al. **Cardiovascular Events** Associated With **Ipratropium** Bromide in COPD. Chest. 2009 Apr 10. We found an increased risk of CVEs associated with the use of ipratropium within the past 6 months. These findings are consistent with previous concerns raised about the cardiovascular safety of ipratropium bromide.

Osadnik CR, Tee VS, Carson-Chahhoud KV, et al. **Non-invasive ventilation** for the management of acute hypercapnic respiratory failure due to exacerbation of chronic obstructive pulmonary disease. Cochrane Database of Systematic Reviews 2017, Issue 7. Art. No.: CD004104. Data from good quality randomised controlled trials show that NIV is beneficial as a first-line intervention in conjunction with usual care for reducing the likelihood of mortality and endotracheal intubation in patients admitted with acute hypercapnic respiratory failure secondary to an acute exacerbation of chronic obstructive pulmonary disease (COPD). The magnitude of benefit for these outcomes appears similar for patients with acidosis of a mild (pH 7.30 to 7.35) versus a more severe nature (pH < 7.30), and when NIV is applied within the intensive care unit (ICU) or ward setting.

Ospina MB, Mrklas K, Deuchar L, et al. A systematic review of the effectiveness of **discharge care bundles** for patients with COPD. Thorax. 2017 Jan;72(1):31-39.

Papi A, Vestbo J, Fabbri L, et al. **Extrafine inhaled triple therapy versus dual bronchodilator therapy** in chronic obstructive pulmonary disease (**TRIBUTE**): a double-blind, parallel group, randomised controlled trial. Lancet. 2018 Feb 8.

Parameswaran GI, Sethi S. **Long-term macrolide therapy** in chronic obstructive pulmonary disease. CMAJ. 2014 Oct 21;186(15):1148-1152.

Park HY, Man SFP, Sin DD. **Inhaled corticosteroids** for chronic obstructive pulmonary disease (**COPD**). BMJ 2012;345:e6843 doi: 10.1136/bmj.e6843 (25 October 2012).

Parshall MB, Schwartzstein RM, Adams L, et al. on behalf of the ATS Committee on Dyspnea. An Official American Thoracic Society (**ATS**) Statement: Update on the Mechanisms, Assessment, and Management of **Dyspnea**. Am J Respir Crit Care Med. 2012 Feb 15;185(4):435-452.

Parsons JP, Hallstrand TS, Mastronarde JG, et al; American Thoracic Society Subcommittee on **Exercise-induced Bronchoconstriction**. An Official American Thoracic Society (**ATS**) Clinical Practice Guideline: Exercise-induced Bronchoconstriction. Am J Respir Crit Care Med. 2013 May 1;187(9):1016-27.

Pasqua F, Biscione G, Crigna G, et al. Combining **triple therapy** and pulmonary rehabilitation in patients with advanced **COPD**: A pilot study. Respir Med. 2009 Nov 3.

Pavord ID, Lettis S, Locantore N, et al. Blood **eosinophils** and inhaled corticosteroid/long-acting β-2 agonist efficacy in **COPD**. Thorax. 2016 Feb;71(2):118-25.

Pavord ID, Chanez P, Criner GJ, et al. **Mepolizumab** for eosinophilic chronic obstructive pulmonary disease. N Engl J Med. DOI: 10.1056/NEJMoa1708208.

Perry J, Trautman B, Takher-Smith J, et al. **Particle Size and Gastrointestinal Absorption Influence Tiotropium Pharmacokinetics**: A Pilot Bioequivalence Study of PUR0200 and Spiriva HandiHaler. Br J Clin Pharmacol. 2018 Dec 6.

Pinnock Hilary, Kendall Marilyn, Murray Scott A, et al. **Living and dying with severe chronic obstructive pulmonary disease**: multi-perspective longitudinal qualitative study. BMJ 2011;342:doi:10.1136/bmj.d142 (Published 24 Jan 2011)

Pinnock H, Hanley J, McCloughan L, et al. Effectiveness of **telemonitoring** integrated into existing clinical services on hospital admission for exacerbation of chronic obstructive pulmonary disease: researcher blind, multicentre, randomised controlled trial. BMJ 2013;347:f6070.

Poels PJ, et al. **Spirometry** in chronic obstructive pulmonary disease. BMJ. 2006 Oct 28;333(7574):870-1.

Pomares X, Montón C, Bullich M, et al. Clinical and safety outcomes of **long-term azithromycin** therapy in severe COPD beyond the first year of treatment. Chest. 2018 Feb 7.

Poole P, Black PN. **Mucolytic agents for chronic bronchitis or chronic obstructive pulmonary disease**. Cochrane Database Syst Rev. 2010 Feb 17;2:CD001287.

Postma DS, Bush A, van den Berge M. **Risk factors** and early origins of **chronic obstructive pulmonary disease**. Lancet. 2014 Aug 11.

Postma DS, Rabe KF. The **Asthma-COPD Overlap Syndrome**. N Engl J Med. 2015 Sep 24;373(13):1241-9.

Press VG, Cifu AS, White SR. **Screening** for Chronic Obstructive Pulmonary Disease. JAMA. 2017 Nov 7;318(17):1702-1703.

Prins HJ, Duijkers R, van der Valk P, et al. **CRP-guided antibiotic treatment in acute exacerbations** of COPD in hospital admissions. Eur Respir J. 2019 May 23;53(5).

Pudi KK, et al. A 28-day randomized, double-blind, placebo-controlled, parallel group study of nebulized **revefenacin** with chronic obstructive pulmonary disease. Respir Res. 2017 Nov 2;18(1):182.

Puhan MA, Garcia-Aymerich J, Frey M, et al. Expansion of the prognostic assessment of patients with chronic obstructive pulmonary disease: the updated **BODE index** and the **ADO** index**.** Lancet. 2009 Aug 29;374(9691):704-11.

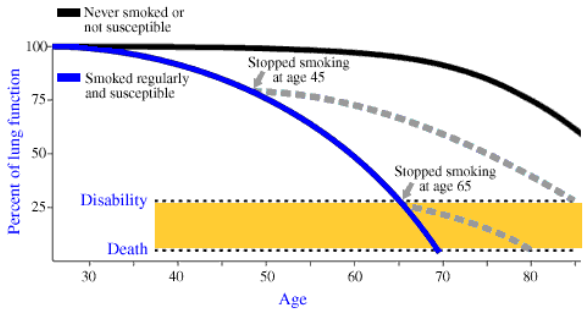
Qaseem A, Snow V, Shekelle P, et al. Clinical Efficacy Assessment Subcommittee of the American College of Physicians. Diagnosis and management of stable chronic obstructive pulmonary disease: a clinical practice guideline from the American College of Physicians. Ann Intern Med 2007 Nov 6;147(9):633-8.

Qaseem A, Wilt TJ, Weinberger SE, et al. for the American College of Physicians, the American College of Chest Physicians, the American Thoracic Society, and the European Respiratory Society. **Diagnosis and Management of Stable Chronic Obstructive Pulmonary Disease**: A Clinical Practice Guideline **Update from the American College of Physicians, American College of Chest Physicians, American Thoracic Society, and European Respiratory Society**. Ann Intern Med. 2011 Aug 2;155(3):179-191.

Quint JK, et al. Effect of **β blockers on mortality after myocardial infarction in adults with COPD**: population based cohort study of UK electronic healthcare records. BMJ. 2013 Nov 22;347:f6650.

Rabe KF, et al. **Roflumilast**--an oral anti-inflammatory treatment for chronic obstructive pulmonary disease: a randomised controlled trial. Lancet. 2005 Aug 13-19;366(9485):563-71.
Rabe KF, Timmer W, Sagkriotis A, Viel K. Comparison of a **combination of tiotropium and formoterol** to salmeterol and fluticasone in moderate COPD. Chest. 2008 Apr 10; [Epub ahead of print] Tiotropium plus formoterol were superior in lung function over the day compared to salmeterol plus fluticasone in patients with moderate COPD. Long-term studies in severe COPD are warranted to assess the relative efficacy of different treatment combinations.
Rabe KF, Watz H. **Chronic obstructive pulmonary disease**. Lancet. 2017 May 13;389(10082):1931-1940.
Rajagopalan S, Brook RD. **Mortality from myocardial infarction** in chronic obstructive pulmonary disease: minding and mending the 'Gap'. Heart. 2015 Apr 22.
Ram FS, Picot J, Lightowler J, Wedzicha JA. **Non-invasive positive pressure ventilation** for treatment of respiratory failure due to exacerbations of chronic obstructive pulmonary disease. Cochrane Database Syst Rev. 2004;(3):CD004104.
Raymakers AJN, Sadatsafavi M, et al. The **Impact of Statin Drug Use on All-Cause Mortality** in Patients With COPD: A Population-Based Cohort Study. Chest. 2017 Sep;152(3):486-493.
Raymakers AJN, Sadatsafavi M, Sin DD, et al. **Inhaled corticosteroids and the risk of lung cancer** in COPD: a population-based cohort study. Eur Respir J. 2019 Jun 5;53(6).Regan EA, Lynch DA, Curran-Everett D, et al; Genetic Epidemiology of COPD (COPDGene) Investigators. Clinical and Radiologic Disease in **Smokers With Normal Spirometry**. JAMA Intern Med. 2015 Jun 22.
Rennard SI, et al. Chronic obstructive pulmonary disease **exacerbations**: accurate and easy measurement promises much. Am J Respir Crit Care Med. 2012 Jun 1;185(11):1139-41.
Restrepo RD, Wettstein R, Wittnebel L, Tracy M. AARC clinical practice guideline: **incentive spirometry**: 2011. Respir Care 2011 Oct;56(10):1600-4.
Rice KL, Dewan N, Bloomfield HE, et al. **Disease management program** for **chronic obstructive pulmonary disease:** a randomized controlled trial. Am J Respir Crit Care Med. 2010 Oct 1;182(7):890-6.
Riley CM, Sciurba FC. **Diagnosis and Outpatient Management** of Chronic Obstructive Pulmonary Disease: A Review. JAMA. 2019 Feb 26;321(8):786-797.
Roche N, Chapman KR, et al. **Blood Eosinophils** and Response to Maintenance **COPD** Treatment: Data from the **FLAME** Trial. Am J Respir Crit Care Med. 2017 Mar 9.
Rocker G. **Harms of overoxygenation** in patients with exacerbation of chronic obstructive pulmonary disease. CMAJ. 2017 Jun 5;189(22):E762-E763
Rodrigo GJ, Nannini LJ. **Tiotropium** for the treatment of stable chronic obstructive pulmonary disease: A systematic review with meta-analysis. Pulm Pharmacol Ther. 2006 Mar 2
Rodrigo GJ, Castro-Rodriguez JA, Nannini LJ, et al. **Tiotropium** and risk for fatal and nonfatal cardiovascular events in patients with chronic obstructive pulmonary disease: systematic review with meta-analysis. Respir Med. 2009 Jun 23. [Epub ahead of print] Compared with control (placebo or salmeterol), tiotropium did not significantly increase the risk of adverse major cardiovascular events among COPD patients. Subgroup analysis suggested that smoking history can modify the risk of cardiovascular adverse events.
Rodrigo GJ, Castro-Rodriguez JA, Plaza V. Safety and Efficacy of Combined Long-Acting {beta}-Agonists and Inhaled Corticosteroids vs **Long-Acting {beta}-Agonists** Monotherapy for Stable COPD: A Systematic Review. Chest. 2009 Jul 24. [Epub ahead of print] Compared with LABAs, the magnitude of LABAs/ICS benefits did not reach the criteria for predefined clinical important effects, and were associated with serious adverse effects.
Rodrigo GJ, Plaza V. Efficacy and safety of a fixed-dose combination of **indacaterol and Glycopyrronium** for the treatment of COPD: a systematic review. Chest. 2014 Aug;146(2):309-17.
Rodrigo GJ, Neffen H. A Systematic Review of the Efficacy and Safety of a Fixed-Dose Combination of **Umeclidinium and Vilanterol** for the Treatment of COPD. Chest. 2015 Aug 1;148(2):397-407.
Rogliani P, et al. The impact of **dual bronchodilation on cardiovascular serious adverse events** and mortality in COPD. Int J Chron Obstruct Pulmon Dis. 2017;12:3469-3485.
Rossi A et al. Acute effects of **indacaterol** on lung hyperinflation in moderate COPD: A comparison with tiotropium. Respir Med. 2012 Jan;106(1):84-90.
Rossi A, van der Molen T, Olmo RD, et al. **INSTEAD**: a randomised switch trial of **indacaterol versus salmeterol/fluticasone** in moderate **COPD**. Eur Respir J. 2014 Dec;44(6):1548-56.
Rutten FH et al; **Beta-Blocke**rs May Reduce Mortality & Risk of Exacerbations in Patients With **Chronic Obstructive Pulmonary Disease**. Arch Intern Med. 2010;170(10):880-887.
Saini S, Rosen KE, Hsieh HJ, et al. A randomized, placebo-controlled, dose-ranging study of single-dose **omalizumab** in patients with H1-antihistamine-refractory **chronic idiopathic urticaria**. J Allergy Clin Immunol. 2011 Sep;128(3):567-73.e1.
Saini SS et al. Efficacy and safety of **omalizumab** in patients with chronic idiopathic/spontaneous urticaria who remain symptomatic on H1 antihistamines: A randomized, placebo-controlled study. J Invest Dermatol 2015 Jan; 135:67.
Salcedo PA, Lindheimer JB, Klein-Adams JC, et al. Effects of **Exercise Training on Pulmonary Function** in Adults With Chronic Lung Disease: A Meta-Analysis of Randomized Controlled Trials. Arch Phys Med Rehabil. 2018 Dec;99(12):2561-2569.e7.
Salciccioli JD, Marshall DC, Shalhoub J, et al. **Respiratory disease mortality** in the United Kingdom compared with EU15+ countries in 1985-2015: observational study. BMJ. 2018 Nov 28;363:k4680.
Salpeter S, Ormiston T, Salpeter E. Cardioselective **beta-blockers** for COPD. Cochrane Database Syst Rev. 2005 Oct 19;4:CD003566. Cardioselective beta- blockers, given to patients with COPD in the identified studies did not produce adverse respiratory effects. Given their demonstrated benefit in conditions such as heart failure, coronary artery disease and hypertension, cardioselective beta-blockers should not be routinely withheld from patients with COPD.
Salpeter SR, et al. Meta-analysis: **anticholinergics**, but not beta-agonists, reduce severe exacerbations and respiratory mortality in COPD. J Gen Intern Med. 2006 Oct;21(10):1011-9. (InfoPOEMs: Anticholinergic treatment in patients with chronic obstructive pulmonary disease (COPD) produces better results than treatment with a beta-2 agonist. Studies comparing anticholinergic treatment with placebo have shown a greater decrease in the number of exacerbations. Studies comparing beta-2 agonist treatment with placebo have shown less benefit. In direct comparison with each other, there were 2.5 more exacerbations for every 100 patients treated with a beta-2 agonist instead of an anticholinergic. (LOE = 1a))
Salpeter SR, Buckley NS. Systematic Review of Clinical Outcomes in COPD: beta-Agonist Use Compared With **Anticholinergics** and Inhaled **Corticosteroids**. Clin Rev Allergy Immunol. 2006 Oct;31(2-3):219-30. In conclusion, inhaled anticholinergic bronchodilators and corticosteroids should be used to improve long-term clinical outcomes in patients with COPD. beta-Agonists increase respiratory deaths in COPD, possibly as a result of poorer disease control.
Salvi SS, Barnes PJ. Chronic obstructive pulmonary disease in **non-smokers**. Lancet. 2009 Aug 29;374(9691):733-43.
Sanchis J, Gich I, Pedersen S. Systematic Review of Errors in Inhaler Use: Has Patient Technique Improved Over Time? Chest. 2016 Apr 6. pii: S0012-3692(16)47571-9.
Sanford M. **Roflumilast**: in chronic obstructive pulmonary disease. Drugs. 2010 Aug 20;70(12):1615-27. doi: 10.2165/11205930-000000000-00000.
Sator L, Horner A, Studnicka M, et al; BOLD Collaborative Research Group. **Overdiagnosis of COPD** in subjects with unobstructed spirometry: a **BOLD** analysis. Chest. 2019;156(2):277-288.
Schembri S, Williamson PA, Short PM, et al. **Cardiovascular events after clarithromycin** use in lower respiratory tract infections: analysis of two prospective cohort studies. BMJ. 2013 Mar 20;346:f1235.

Schmidt B. No end to uncertainty about inhaled glucocorticoids in preterm infants. N Engl J Med 2015 Oct 15; 373:1566.
Schmiedl S, Fischer R, Ibanez L, et al. Tiotropium Respimat® vs. HandiHaler®: real-life usage and TIOSPIR trial generalizability. Br J Clin Pharmacol. 2015 Oct 27.
Schultz K, Jelusic D, Wittmann M, et al. **Inspiratory muscle training does not improve clinical outcomes in 3-week COPD rehabilitation**: results from a randomised controlled trial. Eur Respir J. 2018 Jan 25;51(1).
Sciurba FC, Criner GJ, Strange C, et al; **RENEW** Study Research Group. Effect of **Endobronchial Coils** vs Usual Care on Exercise Tolerance in Patients With Severe Emphysema: The RENEW Randomized Clinical Trial. JAMA. 2016 May 15.
Seemungal TA, Wilkinson TM, Hurst JR, et al. **Long-term erythromycin** therapy is associated with decreased chronic obstructive pulmonary disease exacerbations. Am J Respir Crit Care Med. 2008 Dec 1;178(11):1139-47.
Serisier DJ, Martin ML, McGuckin MA, et al. Effect of **long-term, low-dose erythromycin on pulmonary exacerbations** among patients with non–cystic fibrosis bronchiectasis: the BLESS randomized controlled trial. JAMA. 2013;309(12):1260-1267.
Sethi S, Jones PW, Theron MS, et al. PULSE Study group. **Pulsed moxifloxacin** for the prevention of exacerbations of chronic obstructive pulmonary disease: a randomized controlled trial. Respir Res. 2010 Jan 28;11:10. Erratum in: Respir Res. 2010;11:88.
Seymour JM, Moore L, Jolley CJ, et al. Outpatient **pulmonary rehabilitation** following acute exacerbations of COPD. Thorax. 2010 May;65(5):423-8.
Sharma Gulshan; Kuo Yong-Fang; Freeman Jean L.; et al. Outpatient Follow-up Visit and 30-Day **Emergency Department Visit and Readmission** in Patients Hospitalized for Chronic Obstructive Pulmonary Disease. Arch Intern Med. 2010;170(18):1664-1670.
Sharma G, Meena R, Goodwin JS, et al. **Burn Injury Associated With Home Oxygen** Use in Patients With Chronic Obstructive Pulmonary Disease. Mayo Clin Proc. 2015 Mar 16.
Shorr AF, Sun X, Johannes RS, et al. Validation of a Novel **Risk Score** for Severity of Illness in **Acute Exacerbations of COPD**. (**BAP-65**) Chest. 2011 Nov;140(5):1177-83.
Short PM, Lipworth SIW, Elder DHJ, et al. Effect of **β blockers in treatment** of chronic obstructive pulmonary disease: a retrospective cohort study. BMJ 2011;342. (10 May 2011)
Short PM, Williamson PA, Elder DH, et al. The impact of **tiotropium on mortality** and exacerbations when added to inhaled corticosteroids and long-acting β-agonist therapy in COPD. Chest. 2012 Jan;141(1):81-6. The study suggests that the addition of tiotropium to ICSs and LABA therapy may confer benefits in reducing all-cause mortality, hospital admissions, and oral corticosteroid bursts in patients with COPD.
Silverman, Edwin K., Sandhaus, Robert A. **Alpha1-Antitrypsin Deficiency.** N Engl J Med 2009 360: 2749-2757
Sin DD, Tashkin D, Zhang X, Radner F, Sjöbring U, Thorén A, Calverley PM, Rennard SI. Budesonide and the risk of **pneumonia**: a meta-analysis of individual patient data. Lancet. 2009 Aug 29;374(9691):712-9.
Singh D, Agusti A, Anzueto A, et al. **Global Strategy for the Diagnosis, Management, and Prevention** of Chronic Obstructive Lung Disease: The GOLD Science Committee Report 2019. Eur Respir J. 2019 Mar 7.
Singh D, Brooks J, Hagan G, Cahn A, O'Connor BJ. Superiority of "triple" therapy with **salmeterol/fluticasone propionate and tiotropium** bromide versus individual components in moderate to severe COPD. Thorax. 2008 Jul;63(7):592-8. Epub 2008 Feb 1.
Singh D, Papi A, Corradi M, et al. **Single inhaler triple therapy** versus inhaled **corticosteroid plus long-acting beta2-agonist** therapy for chronic obstructive pulmonary disease (**TRILOGY**): a double-blind, parallel group, randomized controlled trial.Lancet. 2016 Sep 3;388(10048):963-973.
Singh D. **Pharmacological treatment for COPD**; **GOLD 2017** changes direction. Br J Clin Pharmacol. 2017 Mar 9.
Singh S, Loke YK, Furberg CD. Inhaled anticholinergics and risk of major adverse cardiovascular events in patients with chronic obstructive pulmonary disease: a systematic review and meta-analysis. JAMA. 2008 Sep 24;300(12):1439-50. **Inhaled anticholinergics** are associated with a significantly increased risk of cardiovascular death, MI, or stroke among patients with COPD.
Singh S, Amin AV, Loke YK. Long-term Use of Inhaled **Corticosteroids and the Risk of Pneumonia** in Chronic Obstructive Pulmonary Disease: A Meta-analysis. Arch Intern Med. 2009 Feb 9;169(3):219-229. Inhaled corticosteroids were associated with a significantly increased risk of any pneumonia (relative risk [RR], 1.60; 95% confidence interval [CI], 1.33-1.92 [P < .001]; I(2) = 16%) and serious pneumonia (1.71; 1.46-1.99 [P < .001]; I(2) = 0%) but without a significantly increased risk of pneumonia-related mortality (1.27; 0.80-2.03 [P = .31]; I(2) = 0%) or overall mortality (0.96; 0.86-1.08 [P = .51]; I(2) = 0%). Among patients with COPD, inhaled corticosteroid use for at least 24 weeks is associated with a significantly increased risk of serious pneumonia, without a significantly increased risk of death.
Singh S, Loke YK, Enright PL, Furberg CD. **Mortality associated with tiotropium mist inhaler** not studied: Spriva HandiHaler in patients with chronic obstructive pulmonary disease: Systematic review and meta-analysis of randomised controlled trials. BMJ 2011;342:d3215.
Slatore CG, Bryson CL, Au DH. The association of inhaled corticosteroid use with serum **glucose** concentration in a large cohort. Am J Med. 2009 May;122(5):472-8. Inhaled steroids are not associated with an increase in serum glucose concentrations in patients without diabetes. In patients with diabetes, slightly higher serum glucose levels were associated with higher doses of corticosteroids, increasing an average 1.82 mg/dL (0.101 mmol/L) for every 100 mcg increase in dose of steroid (in triamcinolone equivalents). This increase could be clinically relevant with high doses; fluticasone 1000 mcg per day would increase glucose an average of 72.8 mg/dL (4.04 mmol/L). The increase was higher in patients receiving medication for diabetes, an average 2.65 mg/dL (0.147 mmol/L). (LOE = 1b)
Sliwka A, Jankowski M, Gross-Sondej I, et al. Once-daily long-acting beta(2)-agonists/inhaled corticosteroids combined inhalers versus inhaled long-acting muscarinic antagonists for people with chronic obstructive pulmonary disease. Cochrane Database Syst Rev. 2018 Aug 24;8:CD012355. Based on analysis of primary and secondary outcomes, we are uncertain whether once-daily ICS/LABA, combined in one inhaler, has a different efficacy or adverse effect profile compared to LAMA for treatment of people with COPD. However, the current review is based on only two trials with the main focus on primary outcomes other than those considered in this review. The short follow-up period and the very low quality of evidence limit our confidence in the result and increase uncertainty. Further trials of longer duration are needed. Current evidence is not strong enough to demonstrate important differences between inhalers in terms of effects, nor to establish that once-daily fluticasone/vilanterol 100/25 mcg and tiotropium 18 mcg are equivalent.
Smith C, Goldman RD. **Nebulizers versus pressurized metered-dose inhalers** in preschool children with wheezing. Can Fam Physician. 2012 May;58(5):528-30.
Smith FG, Perkins GD, Gates S, et al, for the **BALTI-2** study investigators. Effect of intravenous **β-2 agonist** (salbutamol) treatment on clinical outcomes in acute respiratory distress syndrome- ARDS (BALTI-2): a multicentre, randomised controlled trial. Lancet 2011; online Dec 12.
Smoking Cessation benefits: Fletcher C, Peto R. The natural history of chronic airflow obstruction. Br Med J. 1977 Jun 25;1(6077):1645-8.



Smy L, Chan AC, Bozzo P, et al. Is it safe to use **inhaled corticosteroids in pregnancy**? Can Fam Physician. 2014 Sep;60(9):809-12.

Song S, et al. **Relation of Chronic Obstructive Pulmonary Disease to Cardiovascular Disease** in the General Population. Am J Cardiol. 2017 Oct 15;120(8):1399-1404.

Soriano JB, Zielinski J, Price D. **Screening** for and early detection of chronic obstructive pulmonary disease. Lancet. 2009 Aug 29;374(9691):721-32.

Soriano JB, Lamprecht B, Ramírez AS, et al. **Mortality prediction** in chronic obstructive pulmonary disease comparing the **GOLD 2007 and 2011 staging systems**: a pooled analysis of individual patient data. Lancet Respir Med. 2015 May 15.

Sovani MP, et al. A benefit-risk assessment of inhaled **long-acting beta2-agonists** in the management of obstructive pulmonary disease. Drug Saf. 2004;27(10):689-715.

Spencer S, Evans DJ, Karner C, et al. **Inhaled corticosteroids** versus long-acting beta(2)-agonists for **chronic obstructive pulmonary disease**. Cochrane Database Syst Rev. 2011 Oct 5;10:CD007033. Placebo-controlled trials have established the benefits of both long-acting beta-agonist and inhaled corticosteroid therapy for COPD patients as individual therapies. This review, which included trials allowing comparisons between LABA and ICS, has shown that the two therapies confer similar benefits across the majority of outcomes, including the frequency of exacerbations and mortality. Use of long-acting beta-agonists appears to confer a small additional benefit in terms of improvements in lung function compared to inhaled corticosteroids. On the other hand, inhaled corticosteroid therapy shows a small advantage over long-acting beta-agonist therapy in terms of health-related quality of life, but inhaled corticosteroids also increase the risk of pneumonia.

Spina G, Spruit MA, Alison J, et al. Analysis of **nocturnal** actigraphic **sleep** measures in patients with **COPD** and their association with daytime physical activity. Thorax. 2017 Aug;72(8):694-701

Stallberg B, et al. **Potency ratio** fluticasone (Flixotide Diskus)/budesonide (Pulmicort Turbuhaler). Respir Med. 2006 Aug 2. From these data the potency difference between the present drug inhaler combinations, Flixotide Diskus & Pulmicort Turbuhaler, was calculated to be between 1.50:1 (95% CI 1.10:1-2.05:1) & 1.75:1 (CI 1.26:1-2.43:1) depending on if patients with insufficient steroid-response were excluded from the calculations or not. In these steroid-naive patients, the potency difference was evident only at low daily doses, below 200mcg.

Stefan MS et al. Association between **antibiotic** treatment **&** outcomes in patients hospitalized with **acute exacerbation** of **COPD** treated with systemic steroids. Chest 2013 Jan; 143:82.

Stephenson Anne; Seitz Dallas; Bell Chaim M.; et al. Inhaled **Anticholinergic Drug Therapy and the Risk of Acute Urinary Retention** in Chronic Obstructive Pulmonary Disease: A Population-Based Study. Arch Intern Med. 2011;171(10):914-920.

Stiell IG, Clement CM, Aaron SD, et al. Clinical characteristics associated with **adverse events in patients with exacerbation of chronic obstructive pulmonary disease**: a prospective cohort study. CMAJ. 2014 Apr 1;186(6):E193-204.

Stiell IG, Perry JJ, Clement CM, et al. **Clinical validation of a risk scale** for serious outcomes among patients with chronic obstructive pulmonary disease managed in the emergency department. CMAJ. 2018 Dec 3;190(48):E1406-E1413.

Stockmann C, Fassl B, Gaedigk R, et al. **Fluticasone Propionate** Pharmacogenetics: **CYP3A4***22 Polymorphism and Pediatric Asthma Control. J Pediatr. 2013 Jan 3.

Stoller JK, Aboussouan LS. A Review of **Alpha-1 Antitrypsin Deficiency**. Am J Respir Crit Care Med. 2011 Sep 29.

Stolz D, Hirsch HH, Schilter D, et al. Intensified Therapy with **Inhaled Corticosteroids and Long-Acting beta2-Agonists at the Onset of Upper Respiratory Tract Infection** to Prevent Chronic Obstructive Pulmonary Disease Exacerbations. A Multicenter, Randomized, Double-Blind, Placebo-controlled Trial. Am J Respir Crit Care Med. 2018 May 1;197(9):1136-1146.

Stolz D, Kostikas K, Blasi F, et al. **Adrenomedullin** refines mortality prediction by the **BODE index in COPD**: the ``BODE-A`` index. Eur Respir J. 2014 Feb;43(2):397-408.

Suissa S, Kezouh A, Ernst P. Inhaled Corticosteroids and the Risks of **Diabetes Onset and Progression**. Am J Med. 2010 Sep 24.

Suissa S, Patenaude V, Lapi F, et al. **Inhaled corticosteroids in COPD** and the risk of serious **pneumonia**. Thorax. 2013 Nov;68(11):1029-36.

Suissa S et al. **Discontinuation of inhaled corticosteroids in COPD** and the risk reduction of pneumonia. Chest 2015 Nov; 148:1177.

Suissa S, Dell'Aniello S, Ernst P. Comparative Effectiveness and Safety of Long-Acting **β(2)-Agonist-Long-Acting Muscarinic Antagonists vs Long-Acting β(2)-Agonist-Inhaled** Corticosteroid Treatment of COPD in Real-World Clinical Practice. Chest. 2019 Mar 26.

Suissa S, Dellaniello S, Ernst P. **Long-acting bronchodilator initiation** in COPD and the risk of adverse cardio- pulmonary events: A population-based comparative safety study. Chest. 2016 Aug 20.

Suissa S, Ernst P. Observational studies of inhaled corticosteroid effectiveness in COPD: Lessons learned. Chest. 2018 Apr 18.

Sulaiman I, Cushen B, Greene G, et al. Objective Assessment of **Adherence to Inhalers** by COPD Patients. Am J Respir Crit Care Med. 2016 Jul 13.

Summaries for patients. Chronic obstructive pulmonary disease: a clinical practice guideline. Ann Intern Med. 2011 Aug 2;155(3):I-35.

Suzuki M, Muro S, Ando Y, et al. A randomized, placebo-controlled trial of **acupuncture** in patients with chronic obstructive pulmonary disease (COPD): the COPD-acupuncture trial (CAT). Arch Intern Med. 2012 Jun 11;172(11):878-86.

Sze MA, Dimitriu PA, Hayashi S, et al. The **lung tissue microbiome** in chronic obstructive pulmonary disease. Am J Respir Crit Care Med 2012;185:1073–1080.
Tashkin DP, Celli B, Senn S, et al. **UPLIFT** Study Investigators. A 4-Year Trial of Tiotropium in Chronic Obstructive Pulmonary Disease. N Engl J Med. 2008 Oct 5. [Epub ahead of print] In patients with COPD, therapy with tiotropium was associated with improvements in lung function, quality of life, and exacerbations during a 4-year period but did not significantly reduce the rate of decline in FEV(1). (Celli B, Decramer M, Kesten S, Liu D, Mehra S, Tashkin DP. Mortality in the 4 Year Trial of Tiotropium (UPLIFT) in Patients with COPD. Am J Respir Crit Care Med. 2009 Sep 3.)
Tegethoff M, Greene N, et al. **Inhaled Glucocorticoids during Pregnancy** and Offspring Pediatric Diseases: A National Cohort Study. Am J Respir Crit Care Med. 2011 Dec 28.
Thomsen M, Ingebrigtsen TS, et al. **Inflammatory biomarkers** and exacerbations in chronic obstructive pulmonary disease (COPD) . JAMA. 2013 Jun 12;309(22):2353-61.
Thun MJ, Carter BD, Feskanich D, et al. 50-Year trends in **smoking-related mortality** in the United States. N Engl J Med 2013;368:351-64. (increasing **COPD** mortality in men)
To T, Zhu J, Larsen K, et al; Canadian Respiratory Research Network. Progression from **Asthma to Chronic Obstructive Pulmonary Disease** (**COPD**): Is **Air Pollution** a Risk Factor? Am J Respir Crit Care Med. 2016 Mar 7.
To T, Zhu J, Gray N, et al. **Asthma and COPD Overlap in Women**: Incidence and Risk Factors. Ann Am Thorac Soc. 2018 Jul 17.
Tofts RPH, Ferrer G, Oliveira E. How should one investigate a **chronic cough**? *Cleveland Clinic Journal of Medicine* 2011; 78(2):84-85, 89; doi:10.3949/ccjm.77a.10033.
Tommelein E, Mehuys E, et al. Effectiveness Of **PHARMAceutical Care** For Patients with COPD (**PHARMACOP**): a Randomized Controlled Trial. Br J Clin Pharmacol. 2013Oct9.
Trappenburg JC, Monninkhof EM, Bourbeau J, Trooster T, Schrijvers AJ, Verheij TJ, et al. Effect of an **action plan** with ongoing support by a case manager on exacerbation-related outcome in patients with **COPD**: a multicentre randomised controlled trial. Thorax 2011;66:977-84.
Trivedi R, Richard N, Mehta R, et al. **Umeclidinium** in patients with COPD: a randomised, placebo-controlled study. Eur Respir J. 2014 Jan;43(1):72-81.
Troosters T, Maltais F, Leidy N, et al. Effect of **Bronchodilation, Exercise Training, and Behavior Modification** on Symptoms and Physical Activity in Chronic Obstructive Pulmonary Disease. Am J Respir Crit Care Med. 2018 Oct 15;198(8):1021-1032.
Uronis H, McCrory DC, Samsa G, et al. Symptomatic **oxygen** for non-hypoxaemic chronic obstructive pulmonary disease**.** Cochrane Database Syst Rev. 2011 Jun 15;6:CD006429. Oxygen can relieve dyspnoea in mildly and non-hypoxaemic people with COPD who would not otherwise qualify for home oxygen therapy.
Uronis HE, Ekström MP, Currow DC, et al. **Oxygen for relief of dyspnoea** in people with **chronic obstructive pulmonary disease** who would not qualify for home oxygen: a systematic review and meta-analysis. Thorax. 2014 Dec 3. pii: thoraxjnl-2014-205720.
USPSTF: US Preventive Services Task Force. Screening for Chronic Obstructive Pulmonary Disease Using **Spirometry**: U.S. Preventive Services Task Force Recommendation Statement. Ann Intern Med. 2008 Mar 3; [Epub ahead of print] Do not screen adults for COPD using spirometry
USPSTF: US Preventive Services Task Force. **Screening** for **chronic obstructive pulmonary disease**: US Preventive Services Task Force recommendation statement. JAMA. doi:10.1001/jama.**2016**.2638.
Uzun S, Djamin RS, Kluytmans JA, et al. **Azithromycin maintenance** treatment in patients with frequent exacerbations of chronic obstructive pulmonary disease (COLUMBUS): a randomised, double-blind, placebo-controlled trial. Lancet Respir Med. 2014 May;2(5):361-8.
VA/DoD Department of Veterans Affairs and Department of Defense. COPD Guideline 2007 . At www.healthquality.va.gov/Chronic_Obstructive_Pulmonary_Disease_COPD.asp on 27 Nov 2010.
Vaes AW, Annegarn J, Meijer K, et al. The Effects of a "New" **Walking Aid** on Exercise Performance in Patients With COPD: A Randomized Crossover Trial. Chest. 2012 May;141(5):1224-32. (modern draisine vs a rollator)
Vaidyanathan S, Williamson P, Clearie K, et al. **Fluticasone Reverses Oxymetazoline Induced Tachyphylaxis** of Response and Rebound Congestion. Am J Respir Crit Care Med. 2010 Mar 4.
Van den Bruel A, Gailly J, Neyt M. Does **tiotropium** lower exacerbation and hospitalization frequency in COPD patients: results of a meta-analysis. BMC Pulm Med. 2010 Sep 21;10(1):50.
van der Molen T, van Boven JF, Maguire T,. **Optimizing identification and management** of COPD patients - reviewing the role of the community pharmacist. Br J Clin Pharmacol. 2016 Aug 11.
van Eerd EA, van der Meer RM, van Schayck OC, et al. **Smoking cessation** for people with chronic obstructive pulmonary disease. Cochrane Database Syst Rev. 2016 Aug 20;8:CD010744. We found high-quality evidence in a meta-analysis including four (1,540 participants) of the 16 included studies that a combination of behavioural treatment and pharmacotherapy is effective in helping smokers with COPD to quit smoking. Furthermore, we conclude that there is no convincing evidence for preferring any particular form of behavioural or pharmacological treatment.
van Gestel YR, Hoeks SE, Sin DD, et al. The Impact of Cardioselective Beta-Blockers on Mortality in Patients with COPD and Atherosclerosis. Am J Respir Crit Care Med. 2008 Jun 19. [Epub ahead of print] Cardioselective beta-blockers were associated with reduced mortality in COPD patients undergoing vascular surgery. In carefully selected patients with COPD, the use of cardioselective beta-blockers appears to be safe and associated with reduced mortality.
van Noord JA, et al. Effects of **tiotropium with and without formoterol** on airflow obstruction and resting hyperinflation in patients with COPD. Chest. 2006 Mar;129(3):509-17.
van Velzen P, ter Riet G, Bresser P, et al. **Doxycycline** for outpatient-treated acute **exacerbations of COPD**: a randomised double-blind placebo-controlled trial. Lancet Respir Med 2017; 5: 492–99.
Varraso R, Chiuve SE, Fung TT, et al. **Alternate Healthy Eating Index 2010** and risk of chronic obstructive pulmonary disease among US women and men: prospective study. BMJ. 2015 Feb 3;350:h286.
Vermeersch K, Gabrovska M, Aumann J, et al. **Azithromycin** during Acute Chronic Obstructive Pulmonary Disease Exacerbations Requiring Hospitalization (BACE). A Multicenter, Randomized, Double-Blind, Placebo-controlled Trial. Am J Respir Crit Care Med. 2019 Oct 1;200(7):857-868.
Vestbo J, et al.; TRISTSAN study group. Early onset of effect of salmeterol and fluticasone propionate in chronic obstructive pulmonary disease. Thorax. 2005 Apr;60(4):301-4.
Vestbo J, Anderson JA, Brook RD, et al; **SUMMIT** Investigators. **Fluticasone furoate and vilanterol** and survival in chronic obstructive pulmonary disease with heightened cardiovascular risk (SUMMIT): a double-blind randomised controlled trial. Lancet. 2016 Apr 30;387(10030):1817-26.
Vestbo J, Anderson W, Coxson HO, et al. ; **ECLIPSE** investigators. Evaluation of COPD Longitudinally to Identify Predictive Surrogate End-points (ECLIPSE). Eur Respir J. 2008

Apr;31(4):869-73. Epub 2008 Jan 23.
Vestbo J, Edwards LD, Scanlon PD, et al. **Changes in forced expiratory volume in 1 second** over time in COPD. N Engl J Med 2011. DOI: 10.1056/NEJMoa1105482
Vestbo J, Hurd SS, Agusti AG, et al. Global Strategy for the Diagnosis, Management and Prevention of **Chronic Obstructive Pulmonary Disease**, **GOLD Executive Summary**. Am J Respir Crit Care Med. 2012 Aug 9.
Vestbo J, Lange P. Accuracy of **Airflow Obstruction Thresholds for Predicting COPD**-Related Hospitalization and Mortality: Can Simple Diagnostic Thresholds Be Used for a Complex Disease? JAMA. 2019 Jun 25;321(24):2412-2413
Vestbo J, Leather D, Diar Bakerly N, et al. Effectiveness of **Fluticasone Furoate-Vilanterol** for COPD in Clinical Practice. (Salford) N Engl J Med. 2016 Sep 4.
Vestbo J, Papi A, Corradi M, et al. Single inhaler extrafine triple therapy versus long-acting muscarinic antagonist therapy for chronic obstructive pulmonary disease (**TRINITY**): a double-blind, parallel group, randomised controlled trial. Lancet 2017; online April 3. (beclometasone dipropionate, formoterol fumarate, and glycopyrronium bromide vs tiotropium)
Vogelmeier C, Kardos P, Harari S, et al. **Formoterol mono and combination therapy with tiotropium** in patients with COPD: a 6-month study. Respir Med 2008;102, 1511-20.
Vogelmeier C, Hederer B, Glaab T, et al. **Tiotropium versus salmeterol** for the prevention of exacerbations of COPD. **POET-COPD**. N Engl J Med 2011;364:1093-103.
Vogelmeier CF, Bateman ED, Pallante J, et al. Efficacy and safety of **once-daily QVA149** compared with twice-daily salmeterol–fluticasone in patients with chronic obstructive pulmonary disease-ILLUMINATE-randomised, double-blind, parallel group study. Lancet Respir Med 2013; 1: 51–60.
Vogelmeier C, Paggiaro PL, et al. Efficacy and safety of **aclidinium/formoterol versus salmeterol/fluticasone**: a phase 3 COPD study. Eur Respir J. 2016 Oct;48(4):1030-1039.
Vogelmeier CF, Criner GJ, Martinez FJ, et al. Global Strategy for the **Diagnosis, Management, and Prevention** of Chronic Obstructive Lung Disease 2017 Report: **GOLD Executive** Summary. Am J Respir Crit Care Med. 2017 Jan 27.
Vogt Hartmut, Lindström Karolina, Bråbäck Lennart, et al. **Preterm Birth and Inhaled Corticosteroid Use** in 6- to 19-Year-Olds: A Swedish National Cohort Study. Pediatrics 2011; 127:6 1052-1059; published ahead of print May 9, 2011, doi:10.1542/peds.2010-3083
Vollenweider DJ, Frei A, Steurer-Stey CA, et al. **Antibiotics for exacerbations** of chronic obstructive pulmonary disease. Cochrane Database Syst Rev. 2018 Oct 29;10:CD010257. Researchers have found that antibiotics have some effect on inpatients and outpatients, but these effects are small, and they are inconsistent for some outcomes (treatment failure) and absent for other outcomes (mortality, length of hospital stay). Analyses show a strong beneficial effect of antibiotics among ICU patients. Few data are available on the effects of antibiotics on health-related quality of life or on other patient-reported symptoms, and data show no statistically significant increase in the risk of adverse events with antibiotics compared to placebo.
Vollenweider DJ, Jarrett H, Steurer-Stey CA, et al. **Antibiotics for exacerbations** of chronic obstructive pulmonary disease.Cochrane Database Syst Rev. 2012 Dec 12;12:CD010257. doi: 10.1002/14651858.CD010257. Antibiotics for COPD exacerbations showed large and consistent beneficial effects across outcomes of patients admitted to an ICU.
Vooijs M, Siemonsma PC, Heus I, et al. Therapeutic validity and effectiveness of supervised **physical exercise training** on exercise capacity in patients with **chronic obstructive pulmonary disease**: A systematic review and meta-analysis. Clin Rehabil. 2015 Oct 8.
von Leupoldt A, Taube K, Lehmann K, et al. The impact of **anxiety and depression on outcomes of pulmonary rehabilitation** in patients with COPD. Chest. 2011 Mar 31.
Vozoris NT, Fischer HD, Wang X, et al. **Benzodiazepine drug use** and **adverse respiratory outcomes among older adults with COPD**. Eur Respir J 2014;online April 17, 2014.
Vozoris NT, Wang X, Fischer HD, et al. Incident **opioid drug use and adverse respiratory outcomes among older adults with COPD**. Eur Respir J. 2016;48:683-93.
Vozoris NT, Wang X, Austin PC, et al. Adverse cardiac events associated with **incident opioid drug use among older adults with COPD**. Eur J Clin Pharmacol. 2017 Jun 29.
Vozoris NT, Wang X, Austin PC, et al. Incident **diuretic drug use and adverse respiratory events** among older adults with COPD. Br J Clin Pharmacol. 2017 Nov 15.
Vozoris NT, Wang X, Austin PC, et al. **Serotonergic antidepressant use and morbidity and mortality among older adults with COPD**. Eur Respir J. 2018 Jul 27;52(1).
Vutcovici M, Bitton A, Ernst P, et al. **Inflammatory bowel disease and risk of mortality in COPD**. Eur Respir J. 2016 May;47(5):1357-64.
Wagena EJ, Knipschild PG, et al. Efficacy of bupropion & nortriptyline for **smoking cessation** among people at risk for or with chronic obstructive pulmonary disease. Arch Intern Med. 2005 Oct 24;165(19):2286-92. CONCLUSIONS: Bupropion SR treatment is an efficacious aid to smoking cessation in patients with COPD. Nortriptyline treatment seems to be a useful alternative.
Wahn U, et al. Relationship between pretreatment specific IgE and the response to **omalizumab** therapy. Allergy. 2009 Jul 21. [Epub ahead of print]
Walters J, Walters E, Wood-Baker R. Oral **corticosteroids** for stable chronic obstructive pulmonary disease. Cochrane Database Syst Rev. 2005 Jul 20;(3):CD005374. CONCLUSIONS: There is no evidence to support the long-term use of oral steroids at doses less than 10-15 mg prednisolone though some evidence that higher doses (>/= 30 mg prednisolone) improve lung function over a short period. Potentially harmful adverse effects e.g.. diabetes, hypertension, osteoporosis would prevent recommending long-term use at these high doses in most patients.
Walters JA, Gibson PG, Wood-Baker R, Hannay M, Walters EH. Systemic **corticosteroids for acute exacerbations** of chronic obstructive pulmonary disease. Cochrane Database Syst Rev. 2009 Jan 21;(1):CD001288. Treatment of an exacerbation of COPD with oral or parenteral corticosteroids significantly reduces treatment failure and the need for additional medical treatment and shortens hospital stay. It increases the rate of improvement in lung function and dyspnoea and the improvement continues during treatment, but there is a significantly increase in the risk of an adverse drug event occurring. The optimal dose and length of treatment regime needs to be better defined.
Walters JA, Turnock AC, Walters EH, et al. **Action plans** with limited patient education only for exacerbations of **chronic obstructive pulmonary disease.** Cochrane Database Syst Rev. 2010 May 12;5:CD005074.
Walters JA, Tan DJ, White CJ, et al. **Systemic corticosteroids** for **acute exacerbations of chronic obstructive pulmonary disease**. Cochrane Database Syst Rev. 2014 Sep 1;9: CD001288. There is high-quality evidence to support treatment of exacerbations of COPD with systemic corticosteroid by the oral or parenteral route in reducing the likelihood of treatment failure and relapse by one month, shortening length of stay in hospital inpatients not requiring assisted ventilation in ICU and giving earlier improvement in lung function and symptoms. There is no evidence of benefit for parenteral treatment compared with oral treatment with corticosteroid on treatment failure, relapse or mortality. There is an increase in adverse drug effects with corticosteroid treatment, which is greater with parenteral administration compared with oral treatment.
Walters JA, Tan DJ, White CJ, et al. **Different durations of corticosteroid therapy** for exacerbations of **chronic obstructive pulmonary disease**. Cochrane Database Syst Rev. 2014 Dec 10;12:CD006897. Information from a new large study has increased our confidence that five days of oral corticosteroids is likely to be sufficient for treatment of adults with acute exacerbations of COPD, and this review suggests that the likelihood is low that shorter courses of systemic corticosteroids (of around five days) lead to worse outcomes than are seen with longer (10 to 14 days) courses. We graded most available evidence as moderate in quality because of imprecision; further research may have an important impact on our confidence in the estimates of effect or may change the estimates. The studies in this review did not include people with mild or moderate COPD; further studies comparing short-duration systemic corticosteroid versus conventional longer-duration systemic corticosteroid for treatment of adults with acute exacerbations of COPD are required.
Walters JA, Tang JN, Poole P, et al. **Pneumococcal vaccines** for preventing pneumonia in chronic obstructive pulmonary disease. Cochrane Database Syst Rev. 2017 Jan 24;1:CD001390. Injectable polyvalent pneumococcal vaccination provides significant protection against community-acquired pneumonia, although no evidence indicates that vaccination reduced the risk of confirmed pneumococcal pneumonia, which was a relatively rare event. Vaccination reduced the likelihood of a COPD exacerbation, and moderate-quality evidence suggests the benefits of pneumococcal vaccination in people with COPD. Evidence was insufficient for comparison of different pneumococcal vaccine types.
Walters JA, Tan DJ, White CJ, et al. **Different durations of corticosteroid therapy for exacerbations of chronic obstructive pulmonary disease**. Cochrane Database Syst Rev.

2018 Mar 19;3:CD006897. Information from a new large study has increased our confidence that five days of oral corticosteroids is likely to be sufficient for treatment of adults with acute exacerbations of COPD, and this review suggests that the likelihood is low that shorter courses of systemic corticosteroids (of around five days) lead to worse outcomes than are seen with longer (10 to 14 days) courses. We graded most available evidence as moderate in quality because of imprecision; further research may have an important impact on our confidence in the estimates of effect or may change the estimates. The studies in this review did not include people with mild or moderate COPD; further studies comparing short-duration systemic corticosteroid versus conventional longer-duration systemic corticosteroid for treatment of adults with acute exacerbations of COPD are required.

Wang C, Xu J, Yang L, et al. **Prevalence and risk factors of chronic obstructive pulmonary disease in China** (the China Pulmonary Health [**CPH**] study): a national cross-sectional study. Lancet 2018; online April 9.

Wang M, Aaron CP, Madrigano J, et al. Association Between Long-term Exposure to **Ambient Air Pollution and Change in Quantitatively Assessed Emphysema** and Lung Function. JAMA. 2019 Aug 13;322(6):546-556.

Wang MT, Liou JT, Lin CW, et al. Association of **Cardiovascular Risk With Inhaled Long-Acting Bronchodilators** in Patients With Chronic Obstructive Pulmonary Disease: A Nested Case-Control Study. JAMA Intern Med. 2018 Jan 2.

Waschki B, Kirsten A, et al. **Physical Activity** Is the Strongest Predictor of All-Cause Mortality in Patients With COPD: A Prospective Cohort Study. Chest. 2011 Aug;140(2):331-42.

Waschki B, Kirsten AM, Holz O, et al. Disease Progression and Changes in **Physical Activity** in Patients with COPD. Am J Respir Crit Care Med. 2015 May 28.

Weatherall M, Wijesinghe M, et al. Meta-analysis of the risk of **mortality with salmeterol** and the effect of concomitant inhaled corticosteroid therapy. Thorax. 2010 Jan;65(1):39-43.

Wechsler ME, Wong DA, Miller MK, Lawrence-Miyasaki L. **Churg-strauss syndrome** in patients treated with **omalizumab**. Chest. 2009 Aug;136(2):507-18. Epub 2009 May 1.

Wedzicha JA, Calverley PM, Seemungal TA, **INSPIRE** Investigators. The prevention of chronic obstructive pulmonary disease exacerbations by salmeterol/fluticasone propionate or tiotropium bromide. Am J Respir Crit Care Med. 2008 Jan 1;177(1):19-26. Epub 2007 Oct 4. n=1,323 patients mean age, 64 yr, post-bronchodilator FEV1, 39% predicted were randomized in this 2-year trial. We found no difference in exacerbation rate between salmeterol/fluticasone propionate and tiotropium. More patients failed to complete the study while receiving tiotropium. A small statistically significant beneficial effect was found on health status, with an unexpected finding of lower deaths in salmeterol/fluticasone propionate-treated patients.

Wedzicha JA, Rabe KF, Martinez FJ, et al. Efficacy of **roflumilast** in the COPD frequent exacerbator phenotype. Chest. 2013 May;143(5):1302-11

Wedzicha JA, Banerji D, Vogelmeier CF. **Indacaterol-Glycopyrronium** for COPD. (**FLAME**) N Engl J Med. 2016 Sep 1;375(9):899-900. Correspondence.

Wedzicha JA, et al. **Management of COPD exacerbations**: **European** Respiratory Society/**American** Thoracic Society (**ATS**) guideline. Eur Respir J. 2017 Mar 15;49(3).

Wells JM, Washko GR, et al; the COPDGene and ECLIPSE Study Investigators. **Pulmonary Arterial Enlargement** and Acute Exacerbations of COPD. N Engl J Med. 2012 Sep 3.

Welsh EJ, Cates CJ, Poole P. Combination inhaled **steroid and long-acting beta2-agonist versus tiotropium** for chronic obstructive pulmonary disease. Cochrane Database Syst Rev. 2013 May 31;5:CD007891. doi: 10.1002/14651858.CD007891.pub3. Since the proportion of missing outcome data compared to the observed outcome data is enough to induce a clinically relevant bias in the intervention effect, the relative efficacy and safety of combined inhalers and tiotropium remains uncertain. Further large, long-term randomised controlled trials comparing combination therapy to tiotropium are required, including adequate follow-up of all participants randomised (similar to the procedures undertaken in TORCH and UPLIFT).

Welte T, Miravitlles M, Hernandez P, et al. Efficacy and tolerability of **budesonide/formoterol added to tiotropium** in patients with chronic obstructive pulmonary disease. Am J Respir Crit Care Med. 2009 Oct 15;180(8):741-50. Epub 2009 Jul 30. (n=660 over 12 weeks)

Wenzel RP, Fowler AA 3rd, Edmond MB. Antibiotic prevention (**azithromycin**) of acute exacerbations of COPD. N Engl J Med. 2012 Jul 26;367(4):340-7.

Whittaker H, Connell O, Campbell J, et al. Eligibility for **Lung Volume Reduction Surger**y in Chronic Obstructive Pulmonary Disease patients identified in a UK primary care setting. Chest. 2019 Aug 2.

Wilkie M, Finch S, Schembri S. Inhaled Corticosteroids for Chronic Obstructive Pulmonary Disease--The Shifting Treatment Paradigm. COPD. 2015;12(5):582-90.

Williams Kirsten M.; Chien Jason W.; Gladwin Mark T.; et al. **Bronchiolitis Obliterans** After Allogeneic Hematopoietic Stem Cell Transplantation. JAMA. 2009;302(3):306-314.

Wilson AM, Browne P, Olive S, et al.The effects of maintenance schedules following **pulmonary rehabilitation** in patients with chronic obstructive pulmonary disease: a randomised controlled trial. BMJ Open. 2015 Mar 11;5(3)

Wilt TJ, Niewoehner D, Kim C, et al. Use of **spirometry** for case finding, diagnosis, and management of chronic obstructive pulmonary disease (**COPD**). Evid Rep Technol Assess (Summ). 2005 Aug;(121):1-7. http://hiru.mcmaster.ca/PLUS_BATCHES/batch173_110905/8314.pdf

Wise RA, Anzueto A, Cotton D, et al. **Tiotropium Respimat** inhaler and the risk of death in COPD. (**TIOSPIR**) N Engl J Med 2013. DOI:10.1056/NEJMoa1303342.

Wong CX, Carson KV, Smith BJ. **Home care by outreach nursing for chronic obstructive pulmonary disease.** Cochrane Database Syst Rev. 2011 Mar 16;3:CD000994. Outreach nursing programmes for COPD improved disease-specific HRQL.

Wong CX, Carson KV, Smith BJ. **Home care by outreach nursing for chronic obstructive pulmonary disease**. Cochrane Database Syst Rev. 2012 Apr 18;4:CD000994. Outreach nursing programmes for COPD improved disease-specific HRQL. However the effect on hospitalisations was heterogeneous, reducing admissions in one study, but increasing them in others, therefore we could not draw firm conclusions for this outcome.

Wong C, Jayaram L, Karalus N, et al. **Azithromycin** for prevention of exacerbations in non-cystic fibrosis bronchiectasis (EMBRACE): a randomised, double-blind, placebo-controlled trial. Lancet. 2012 Aug 18;380(9842):660-7.

Wootton SL, Ng LW, McKeough ZJ, et al. Ground-based **walking training** improves quality of life and exercise capacity in COPD. Eur Respir J. 2014 Oct;44(4):885-94.

Wouters EF, Postma DS, Fokkens B, et al. **COSMIC** (COPD and Seretide: a Multi-Center Intervention and Characterization) Study Group. Withdrawal of fluticasone propionate from combined salmeterol/fluticasone treatment in patients with **COPD** causes immediate and sustained disease deterioration: a randomised controlled trial. Thorax. 2005 Jun;60(6):480-7. CONCLUSIONS: Withdrawal of FP in COPD patients using SFC resulted in acute and persistent deterioration in lung function and dyspnoea and in an increase in mild exacerbations and percentage of disturbed nights. This study clearly indicates a key role for ICS in the management of COPD as their discontinuation leads to disease deterioration, even under treatment with a LABA.

Yang IA, Fong KM, Sim EH, Black PN, Lasserson TJ. Inhaled corticosteroids for stable chronic obstructive pulmonary disease. Cochrane Database Syst Rev. 2007 Apr 18;(2):CD002991. Patients and clinicians should balance the potential benefits of inhaled steroids in COPD (reduced rate of exacerbations, reduced rate of decline in quality of life), against the known increase in local side effects (oropharyngeal candidiasis and hoarseness). The risk of long term adverse effects is unknown.

Yang, Ya-Wen, Chen, Yi-Hua, Wang, Kuo-Hsien, et al. Risk of **herpes zoster** among patients with chronic obstructive pulmonary disease: a population-based study. CMAJ 2011 183: E275-280.

Yang IA, Clarke MS, Sim EH, et al. **Inhaled corticosteroids** for stable chronic obstructive pulmonary disease (COPD). Cochrane Database Syst Rev. 2012 Jul 11;7:CD002991. Patients and clinicians should balance the potential benefits of inhaled steroids in COPD (reduced rate of exacerbations, reduced rate of decline in quality of life and possibly reduced rate of decline in FEV(1)) against the potential side effects (oropharyngeal candidiasis and hoarseness, and risk of pneumonia).

Yohannes AM, Müllerová H, Hanania NA, et al. **Long-term Course of Depression Trajectories** in Patients With **COPD**: A 3-Year Follow-up Analysis of the Evaluation of COPD

Longitudinally to Identify Predictive Surrogate Endpoints Cohort. Chest. 2016 Apr;149(4):916-26.
Zafari Z, Sin DD, Postma DS, et al. Individualized prediction of lung-function decline in chronic obstructive pulmonary disease. CMAJ. 2016 Aug 2.
Zhang HL, Tan M, Qiu AM, Tao Z, Wang CH. Antibiotics for treatment of acute exacerbation of chronic obstructive pulmonary disease: a network meta-analysis. BMC Pulm Med. 2017 Dec 12;17(1):196.
Zhang W, Zhang Y, Li CW, et al. Effect of Statins on COPD: A Meta-Analysis of Randomized Controlled Trials. Chest. 2017 Dec;152(6):1159-1168.
Zhou Yumin, Hu Guoping, Wang Dali, et al. **Community based integrated intervention** for prevention and management of chronic obstructive pulmonary disease (COPD) in Guangdong, China: cluster randomised controlled trial. BMJ 341:doi:10.1136/bmj.c6387 (Published 1 Dec 2010).
Zhou Y, Zhong N, Li X, et al. **Tiotropium** in early-stage chronic obstructive pulmonary disease. N Engl J Med 2017;377: 923-35.
Zider AD, Wang X, Buhr RG, et al. **Reduced COPD exacerbation risk correlates with improved FEV(1):** A meta-regression analysis. Chest. 2017 May 5.
Zulueta JJ, Wisnivesky JP, Henschke CI, et al. **Emphysema scores** predict death from **COPD and lung cancer**. Chest. 2012 May;141(5):1216-23.

Online Extras for ASTHMA AND COPD INHALATION DEVICES CHART:

Milk allergies and lactose inhalers Most DPIs contain lactose. This lactose is often derived from milk; trace amounts of residual milk protein has caused allergies in a few case reports. Lactose-free: **BRICANYL** Turbuhaler; **PULMICORT** Turbuhaler; all MDIs; all Respimats. Note: lactose-intolerant patients can still use a lactose-containing inhaler.

▼ covered by NIHB

References:

Burchett DK et al. Mixing and compatibility guide for commonly used aerosolized medications. Am J Health-Syst Pharm 2010; 67:227-30.

Cates CJ, Welsh EJ, Rowe BH. Holding chambers (spacers) versus nebulisers for beta-agonist treatment of acute asthma. Cochrane Database Syst Rev 2013 Sept 13; 9:CD000052.

Choosing a Spacer Device for MDIs. Pharmacist's Letter Sept 2008.

Daman HR. Pulmonary function testing: use of the peak expiratory flow rate in an out-patient or office setting. J Asthma 1984; 21(5):331-7.

Dhuper S et al. Efficacy and cost comparisons of bronchodilatator administration between metered dose inhalers with disposable spacers and nebulizers for acute asthma treatment. J Emerg Med. 2011; 40(3):247-55.

Doan Q, Shefrin A, Johnson D. Cost-effectiveness of Metered-Dose Inhalers for Asthma Exacerbations in the Pediatric Emergency Department. Pediatrics 2011 0: peds.2010-2963

Dolovich MB et al. Device selection & outcomes of aerosol therapy: evidence-based guidelines: American College of Chest Physicians/American College of Asthma, Allergy, and Immunology. Chest 2005 Jan;127(1):335-71.

Dolovich MB, Dhand R. Aerosol drug delivery: developments in device design and clinical use. Lancet. 2011 Mar 19; 377(9770):1032-45.

Haughney J, Price D, Barnes NC, Virchow JC, Roche N, Chrystyn H. Choosing inhaler devices for people with asthma: current knowledge and outstanding research needs. *Respiratory Medicine CME* 2010; 3(3): 125-131.

Lowry J. A Guide to Spirometry for Primary Care Physicians. Available from: http://olapep.ca/wp-content/themes/Total/images/M_images/pdf/spirometry/guide_spirometry.pdf. Accessed online on March 17, 2016.

National Asthma.org Inhaler Technique. Available from: http://www.nationalasthma.org.au/uploads/content/237-Inhaler_technique_in_adults_with_asthma_or_COPD.pdf. Accessed online on March 17, 2016.

Newman, S. P. (2004). Spacer devices for metered dose inhalers. *Clinical pharmacokinetics*, *43*(6), 349-360.

Newman, S. The Pressurized Metered Dose Inhaler – presentation. Available from: www.rddonline.com/education/online_training/MDIs/data/downloads/pressurized%20metered%20dose%20inhalers%20handout.pdf. Accessed online on March 17, 2016.

Pharmacist's Letter. Tips for correct use of Metered-dose Inhalers (MDIs). June 2007.

Sander N et al. Dose counting & the use of pressurized metered-dose inhalers: canisters running on empty. Ann Allergy Asthma Immunol. 2006 Jul;97(1):34-8.

Schultz A et al. Aerosol inhalation from spacers and valved holding chambers requires few tidal breaths for children. Pediatrics 2010 Dec; 126:e1493.

Self TH, Pinner NA, Sowell RS, Headley AS. Does it really matter what volume to exhale before using asthma inhalation devices? J Asthma. 2009 Apr;46(3):212-6.

Sims MW. Aerosol therapy for obstructive lung diseases: device selection and practice management issues. Chest. 2011 Sep;140(3):781-8.

Sleath B, Ayala GX, Gillette C, et al. Provider demonstration and assessment of child device technique during pediatric asthma visits. Pediatrics. 2011;127:642-648.

Sleath B, Carpenter DM, Ayala GX, et al. Communication during pediatric asthma visits and child asthma medication device technique 1 month later. J Asthma. 2012;49:918-925.

Smith C, Goldman RD. Nebulizers versus pressurized metered-dose inhalers in preschool children with wheezing. Can Fam Physician. 2012 May;58(5):528-30.

Svedsater H, Dale P, Garrill K, Walker R, Woepse MW. Qualitative assessment of attributes and ease of use of the ELLIPTA dry powder inhaler for delivery of maintenance therapy for asthma and COPD. *BMC pulmonary medicine*, 2013; 13(1):72.

Svedsater, Henrik, et al. Ease of use of the ELLIPTA dry powder inhaler: data from three randomised controlled trials in patients with asthma. *NPJ primary care respiratory medicine* 24 (2014).

van der Palen J et al. Preference, satisfaction and errors with two dry powder inhalers in patients with COPD. *Expert opinion on drug delivery*, 2013;10(8):1023-1031.

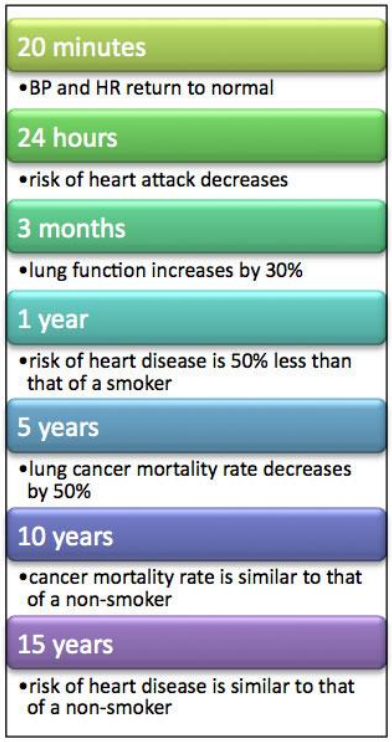
Vella C, Grech V. Assessment of use of spacer devices for inhaled drug delivery to asthmatic children. Pediatr Allergy Immunol. 2005;16:258-261.

Extras: **Rimonabant ACOMPLIA** –(not in Canada) cannabinoid receptor 1 blocker; 36% complete smoking cessation in final 4 wks of a 10 wk trial Dose: 20mg/d SE: nausea, **depression**, anxiety & ↓ weight. [xliii,xliv,xlv] ??Clonidine use
Piper ME, Smith SS, Schlam TR, et al. A **randomized placebo-controlled clinical trial of 5 smoking cessation pharmacotherapies**. Arch Gen Psychiatry. 2009 Nov;66(11):1253-62. {Nicotine lozenge, bupropion, and bupropion plus lozenge produced effects that were comparable with those reported in previous research, the nicotine patch plus lozenge produced the greatest benefit relative to placebo for smoking cessation.}

e-Cigaretes:1) nicotine containing electronic cigarettes (misnomer as aerosolizing delivery device + cartridge). Mostly unregulated in Canada (but illegal to sell technically). Current controversies with regulation in the USA (New York, Massachusetts, Rhode Island, Califonia & Michigan Sep'19: bans sale of Flavored
E-cigarettes). Counsel patients to avoid; alternate products/approaches available for smoking cessation.
2) Concerns: a) risk becoming starter product & skirt smoke free laws, b) potential toxicities, c) lack evidence for benefit as smoking cessation aid & strong potential to ↑ addiction, d) diversion of devices for use in delivering alternate drugs of abuse. e) short term use found to have adverse physiological effects, increased flow resistance and decreased FeNO. f.) toxic and carcinogenic compounds still delivered in e-cigarettes but in lower concentration than traditional cigarettes (Medical Letter Nov 2012.)

Cytisine: Derived from an extract of golden rain acacia seeds; (1.5 mg oral tablets) in 740 adults who smoked ≥ 10 cigarettes/day and were willing to attempt to stop smoking permanently. Patients were randomized to cytisine vs. placebo for 25 days. The dose was 6 tablets for the first 3 days, followed by 5 tablets/day on days 4-12, 4 tablets/day on days 13-16, 3 tablets/day on days 17-20, and finally 2 tablets/day on days 21-25. All patients received minimal counseling during 4 clinical visits and 3 telephone calls over 12 months. Cytisine is currently available in Russia and Poland (at the equivalent of $6 to $15 per course). [West 2011]

Benefits from stopping smoking:



References TOBACCO / SMOKING CESSATION PHARMACOTHERAPY:

[1] MicroMedex 2018; Lexi Drugs 2018
[2] Therapeutic Choices 5th edition 2007
[3] Critchley J, Capewell S. Mortality Risk Reduction Associated with Smoking Cessation in Patients with Coronary Heart Disease. JAMA 2003; 290(1):86-97.
[4] Godtfredsen N, Prescott E, Osler M. Effect of Smoking Reduction on Lung Cancer Risk. JAMA 2005;294:1505-1510(n=19,714; 31 yrs)
[5] Doll R, Peto R, Boneham J. Mortality in relation to smoking:50 years observations on male British doctors.BMJ 2004;328:1519-1529 (n=34,439, 50yrs)

Oberg M, Jaakkola MS, Woodward A, Peruga A, Prüss-Ustün A. Worldwide burden of disease from exposure to **second-hand** smoke: a retrospective analysis of data from 192 countries. Lancet. 2010 Nov 25.
[6] Wilson K, Gibson N, Willan A, Cook D. Effect of Smoking Cessation on Mortality After Myocadial Infarction: Meta-analysis of Cohort Studies. Arch Intern Med 2000; 160; 939-944
[7] Henningfield J, Reginald V, August R, et al. Pharmacotherapy for Nicotine Dependence. CA Cancer J Clin 2005;55:281-299.
[8] Henningfield J, Reginald V, August R, et al. Pharmacotherapy for Nicotine Dependence. CA Cancer J Clin 2005;55:281-299
[9] Silagy C, Lancaster T, Stead L, Mant D, Fowler G. Nicotine replacement therapy for smoking cessation.Cochrane Database Syst Rev. 2004;(3):CD000146
[10] Ludvig J, Miner B, Eisenberg M. Smoking Cessation in patients with coronary artery disease. AHJ 2004;149(4):565-570.
[11] Lam W, Sze PC, Sacks HS, Chalmers TC. Meta-analysis of randomised controlled trials of nicotine chewing-gum. Lancet. 1987 Jul 4;2(8549):27-30.
[12] Cooper S, Lewis S, et al. The **SNAP** trial: a randomised placebo-controlled trial of **nicotine replacement therapy in pregnancy** - clinical effectiveness and safety until 2 years after delivery, with economic evaluation. Health Technol Assess. 2014 Aug;18(54):1-128.
[13] Coleman T, Cooper S, Thornton JG, et al. A randomized trial of **nicotine-replacement therapy patches in pregnancy**. N Engl J Med 2012;366:808-18
[14] Joseph AM, Norman SM, Ferry LH, et al. The safety of transdermal nicotine as an aid to smoking cessation in patients with cardiac disease. N Engl J Med. 1996 Dec 12;335(24):1792-8. (n=584, 14 wks)
[15] Hughes J, Stead L, Lancaster T. Antidepressants for Smoking Cessation. The Cochrane Database of Systemic Reviews 2004;4. Hughes JR, Stead LF, Lancaster T. Antidepressants for smoking cessation. Cochrane Database Syst Rev. 2007 Jan 24;(1):CD000031.
[16] Wagena E, et al. Efficacy of Bupropion & Nortriptyline for Smoking Cessation Among People at Risk for or with Chronic Obstructive Pulmonary Disease. Arch Intern Med 2005;165:2286-2292 (n=225; 12 wks).
[17] Jorenby DE, A controlled trial of sustained-release **bupropion, a nicotine patch, or both** for smoking cessation. N Engl J Med. 1999 Mar 4;340(9):685-91. .
[18] Chatkin JM, Mariante de Abreu C, Haggstram FM, et al.. Abstinence rates and predictors of outcome for smoking cessation: do Brazilian smokers need special strategies? Addiction. 2004 Jun;99(6):778-84.
[19] Simon JA, Duncan C, Carmody TP, Hudes ES. Bupropion for smoking cessation: a randomized trial. Arch Intern Med. 2004 Sep 13;164(16):1797-803.
[20] Haggstram FM, Chatkin JM, et al. A controlled trial of nortriptyline, bupropion SR & placebo for smoking cessation: preliminary results. Pulm Pharmacol Ther. 2006;19(3):205-9. Epub 2006 Mar 6.
[21] Paluck EC, McCormack JP, Ensom MH, Levine M, Soon JA, Fielding DW. Outcomes of bupropion therapy for smoking cessation during routine clinical use. Ann Pharmacother. 2006 Feb;40(2):185-90.
[22] Gonzales D, Rennard SI, Nides M, et al; Varenicline Phase 3 Study Group. Varenicline, an alpha4beta2 nicotinic acetylcholine receptor partial agonist, vs sustained-release bupropion and placebo for smoking cessation: a randomized controlled trial. JAMA. 2006 Jul 5;296(1):47-55. (InfoPOEMs: Varenicline (Chantix) therapy for 12 weeks is significantly more effective than placebo at maintaining smoking abstinence at 52 weeks. Varenicline may also be marginally more effective than bupropion SR. Reported success rates are likely to be higher than real-world settings. (LOE = 1b))
[23] Jorenby DE, Hays JT, Rigotti NA, et al.; Varenicline Phase 3 Study Group. Efficacy of varenicline, an alpha4beta2 nicotinic acetylcholine receptor partial agonist, vs placebo or sustained-release bupropion for smoking cessation: a randomized controlled trial. JAMA. 2006 Jul 5;296(1):56-63.
[24] Tonstad S, Tonnesen P, Hajek P, et al. Varenicline Phase 3 Study Group. Effect of maintenance therapy with varenicline on smoking cessation: a randomized controlled trial. JAMA. 2006 Jul 5;296(1):64-71.
[25] Koegelenberg CFN, Noor F, Bateman ED, et al. Efficacy of **varenicline combined with nicotine replacement therapy** vs varenicline alone for smoking cessation: a randomized clinical trial. JAMA. doi:10.1001/jama.2014.7195.
[26] Evins AE, Cather C, Pratt SA, et al. **Maintenance treatment with varenicline** for smoking cessation in patients with schizophrenia and bipolar disorder: a randomized clinical trial. JAMA. doi:10.1001/jama.2013.285113.
[27] Ebbert JO, Hatsukam DK, Croghan IT, et al. Combination **varenicline and bupropion SR** for tobacco-dependence treatment in cigarette smokers: a randomized trial. JAMA.doi:10.1001/jama.2013.283185.
[28] Critchley J, Capewell S. Mortality Risk Reduction Associated with Smoking Cessation in Patients with Coronary Heart Disease. JAMA 2003; 290(1):86-97.
Weblinks: http://www.healthknowledgecentral.org/onepagers/smoking.pdf; http://www.quitnet.com/Library/Guides/NRT/lozenge_specifics.jtml
Ranney L, Melvin C, Lux L et al. Systematic Review: Smoking cessation Intervention Strategies for adults and adults in special populations. Ann Intern Med. 2006 Sep 5; [Epub ahead of print] Early Release – Accessed online at http://www.annals.org/cgi/content/full/0000605-200612050-00142v1
[29] Lyon ER. A review of the effects of nicotine on schizophrenia and antipsychotic medications. Psychiatr Serv 1999 Oct;50(10):1346-50
[30] Johnson BA, Ait-Daoud N, Akhtar FZ, Javors MA. Use of oral topiramate to promote smoking abstinence among alcohol-dependent smokers: an RCT. Arch Intern Med. 2005 Jul 25;165(14):1600-5.
[31] An LC, et al. Benefits of **telephone** care over primary care for smoking cessation: a randomized trial.Arch Intern Med. 2006 Mar 13;166(5):536-42. (InfoPOEMs: A telephone-based counseling program is effective at helping self-selected older men quit smoking. The men in this study were veterans who had smoked for an average of 40 years, and 1 in 8 was able to quit for at least 6 months. (LOE = 1b))
[32] Chaudhuri R, et al. Effects of Smoking Cessation on Lung Function and Airway Inflammation In Smokers with Asthma. Am J Respir Crit Care Med. 2006 Apr 27; [Epub ahead of print] Six weeks after smoking cessation, smokers with asthma achieved considerable improvement in lung function and a fall in sputum neutrophil count compared to smokers who continued to smoke. These findings highlight the importance of smoking cessation in asthma.
[33] Houston TK, et al. Active and passive smoking and development of **glucose intolerance** among young adults in a prospective cohort: CARDIA study. BMJ. 2006 May 6;332(7549):1064-9. Epub 2006 Apr 7.
[34] Lancaster T, Hajek P, Stead LF, West R, Jarvis MJ. Prevention of relapse after quitting smoking: a systematic review of trials. Arch Intern Med. 2006 Apr 24;166(8):828-35
[35] Zhu SH, et al. Evidence of real-world effectiveness of a telephone quitline for smokers.N Engl J Med. 2002 Oct 3;347(14):1087-93.
[36] Healton CG, et al. Smoking, obesity, & their co-occurrence in the USA: cross sectional analysis. BMJ. 2006 May 12; 23.5% of adults were obese, 22.7% smoked, and **4.7% smoked and were obese**.
[37] Tobacco Use: Prevention, Cessation, and Control. Agency for Healthcare Research and Quality; US Department of Heath and Human Services http://www.ahrq.gov/clinic/tp/tobusetp.htm
[38] Shaw LJ, Raggi P, Callister TQ, Berman DS. Prognostic value of coronary artery calcium screening in asymptomatic smokers and non-smokers. Eur Heart J. 2006 Apr;27(8):968-75. Epub 2006 Jan 27.
[39] Teo KK, et al.; behalf of the INTERHEART Study Investigators. Tobacco use and risk of myocardial infarction in 52 countries in the INTERHEART study: a case-control study. Lancet. 2006 Aug 19;368(9536):647-58.
[40] Wen W, et al. **Environmental tobacco** smoke and mortality in Chinese women who have never smoked: prospective cohort study. BMJ. 2006 Aug 19;333(7564):376. Epub 2006 Jul 12.
[41] Anthonisen NR, et al; **Lung Health Study** Research Group. The effects of a smoking cessation intervention on 14.5-year mortality: a randomized clinical trial. Ann Intern Med. 2005 Feb 15;142(4):233-9. Summary for patients in: Ann Intern Med. 2005 Feb 15;142(4):I12.
[42] Heatherton, TF, Kozlowski LT, Frecker, RC, Fagerstrom KO. The Fagerstrom Test for Nicotine Dependence: A revision of the **Fagerstrom** Tolerance Questionnaire. Brit J Add. 1991; 86:1119-1127. {Fagerstrom KO, Schneider NG. Measuring nicotine dependence: a review of the Fagerstrom tolerance questionnaire. J Behav Med. 1989;12:159-82.} http://www.wfts.org/programs_and_services/images/Fagerstrom_Test.pdf

Modified Fagerström Test for Nicotine Dependence

1. How soon after you wake up do you smoke your first cigarette?
Within 5 minutes (3 points)
5 to 30 minutes (2 points)
31 to 60 minutes (1 point)
After 60 minutes (0 points)

2. Do you find it difficult not to smoke in places where you shouldn't, such as in church or school, in a movie, at the library, on a bus, in court or in a hospital?
Yes (1 point)
No (0 points)

3. Which cigarette would you most hate to give up; which cigarette do you treasure the most?
The first one in the morning (1 point)
Any other one (0 points)

4. How many cigarettes do you smoke each day?
10 or fewer (0 points)
11 to 20 (1 point)
21 to 30 (2 points)
31 or more (3 points)

5. Do you smoke more during the first few hours after waking up than during the rest of the day?
Yes (1 point)
No (0 points)

6. Do you still smoke if you are so sick that you are in bed most of the day, or if you have a cold or the flu and have trouble breathing?
Yes (1 point)
No (0 points)

Scoring: 7 to 10 points = highly dependent; 4 to 6 points = moderately dependent; less than 4 points = minimally dependent.

FIGURE 1. Modified Fagerström test for evaluating intensity of physical dependence on nicotine.
Adapted with permission from Heatherton TF, Kozlowski LT, Frecker RC, Fagerström KO. The Fagerström test for nicotine dependence: a revision of the Fagerström Tolerance Questionnaire. Br J Addict 1991;86:1119-27.

TOBACCO / SMOKING CESSATION PHARMACOTHERAPY Extra articles:

Abascal W, Esteves E, Goja B, et al. Tobacco **control campaign in Uruguay**: a population-based trend analysis. Lancet. 2012 Sep 13.

Abrams DB. Promise and peril of **e-cigarettes**: can disruptive technology make cigarettes obsolete? JAMA. doi:10.1001/jama.2013.285347.

Adriaens K, Van Gucht D, et al. Effectiveness of the **Electronic Cigarette**: An Eight-Week Flemish Study with Six-Month Follow-up on **Smoking Reduction**, Craving and Experienced Benefits and Complaints. Int J Environ Res Public Health. 2014 Oct 29;11(11):11220-48.

Afshin A, Babalola D, Mclean M, et al. **Information Technology and Lifestyle**: A Systematic Evaluation of Internet and Mobile Interventions for Improving Diet, Physical Activity, Obesity, Tobacco, and Alcohol Use. J Am Heart Assoc. 2016 Aug 31;5(9).

Agaku I, Odani S, Armour B, et al. **Social Aspects of Hookah Smoking** Among US Youth. Pediatrics. 2018 Jul 2.

Agaku IT, Vardavas CI, Ayo-Yusuf OA, et al. Temporal trends in **smokeless tobacco** use among US middle and high school students, 2000-2011. JAMA. 2013 May 15;309(19):1992-4.

Agaku IT, Ayo-Yusuf OA, Vardavas CI, et al. Use of **Conventional and Novel Smokeless Tobacco Products** Among US Adolescents. Pediatrics. 2013 Aug 5.

Agaku IT, Singh T, Rolle I, et al. Prevalence and Determinants of **Secondhand Smoke Exposure Among Middle and High School Students**. Pediatrics. 2016 Jan 11.

Agaku I, Odani S, Vardavas C, et al. **Self-Identified Tobacco Use and Harm Perceptions Among US Youth**. Pediatrics. 2018 Mar 15.

Agboola S, McNeill A, Coleman T, Leonardi Bee J. A systematic review of the effectiveness of **smoking relapse prevention** interventions for abstinent smokers. Addiction. 2010 Aug;105(8):1362-80.

Agrawal A, Rogers CE, Lessov-Schlaggar CN, et al. **Alcohol, Cigarette, and Cannabis Use** Between 2002 and 2016 in **Pregnant Women** From a Nationally Representative Sample. JAMA Pediatr. 2018 Nov 5.

Ahn A, Edwards KM, Grijalva CG, et al. **Secondhand Smoke Exposure** and Illness Severity among **Children Hospitalized with Pneumonia**. J Pediatr. 2015 Oct;167(4):869-874.e1.

Akuete K, Oh SS, Thyne S, et al. Ethnic Variability in **Persistent Asthma After In Utero** Tobacco Exposure. Pediatrics. 2011 Aug 22.

Alpert Hillel R, Connolly Gregory N, Biener Lois. A prospective cohort study **challenging the effectiveness (NRT treatment)** of population-based medical intervention for smoking cessation. Tob Control tobaccocontrol-2011-050129. Online First: 10 January 2012.

Al-Delaimy WK, Myers MG, Leas EC, et al. CR**. E-Cigarette Use** in the Past and Quitting Behavior in the Future: A Population-Based Study. Am J Public Health. 2015 Apr 16

Al-Kazwini AT, Said AJ, Sdepanian S. Compartmental analysis of **metals in waterpipe smoking** technique. BMC Public Health. 2015 Dec;15(1):1373.

Aldington S, Williams M, Nowitz M, Weatherall M, Pritchard A, McNaughton A,Robinson G, Beasley R. THE EFFECTS OF **CANNABIS** ON PULMONARY STRUCTURE, FUNCTION AND SYMPTOMS. Thorax. 2007 Jul 31; [Epub ahead of print] Smoking cannabis was associated with a dose-related impairment of large airways function resulting in airflow obstruction and hyperinflation. In contrast, cannabis smoking was seldom associated with macroscopic emphysema. The 1:**2.5 to 5 dose equivalence between cannabis joints and tobacco cigarettes** for adverse effects on lung function is of major public health significance.

Alexakis C, Saxena S, Chhaya V, et al. Smoking **Status** at Diagnosis and Subsequent Smoking Cessation: Associations With **Corticosteroid Use** and **Intestinal Resection** in Crohn's Disease. Am J Gastroenterol. 2018 Oct 15.

Ali FRM, Al-Shawaf M, Wang TW, King BA. U.S. **Adults' Attitudes Toward Lowering Nicotine** Levels in Cigarettes. Am J Prev Med. 2019 Jul 10.

Allen JG, Flanigan SS, LeBlanc M, et al. **Flavoring Chemicals** in E-Cigarettes: Diacetyl, 2,3-Pentanedione, and Acetoin in a Sample of 51 Products, Including Fruit-, Candy-, and Cocktail-Flavored E-Cigarettes. Environ Health Perspect. 2015 Dec 8.

Allem JP, Ayers JW, Althouse BM, et al. When a **ban really is not a ban: internet loopholes and Djarum flavoured cigarettes** in the USA. Tob Control. 2015 Jun 17.

Allen MH, Debanné M, Lazignac C, et al. Effect of Nicotine Replacement Therapy on Agitation in Smokers With **Schizophrenia**: A Double-Blind, Randomized, Placebo-Controlled Study. Am J Psychiatry. 2011 Jan 18.

Almirall J, Serra-Prat M, Bolíbar I, et al; Study Group of Community-Acquired Pneumonia in Catalan Countries (PACAP). **Passive smoking** at home is a risk factor for community-acquired **pneumonia** in older adults: a population-based case-control study. BMJ Open. 2014 Jun 13;4(6):e005133.

Alverson, Clinton J., Strickland, Matthew J., Gilboa, Suzanne M., et al. **Maternal Smoking and Congenital Heart Defects** in the Baltimore-Washington Infant Study. Pediatrics 2011 127: e647-e653

Alwan S, Reefhuis J, Botto LD, Rasmussen SA, Correa A, Friedman JM; National Birth Defects Prevention Study. Maternal use of **bupropion** and risk for **congenital heart defects**. Am J Obstet Gynecol. 2010 Apr 22.

American Lung Association. An emerging deadly trend: **waterpipe tobacco** use. Tobacco policy trend alert. 2007. Available at: http://slati.lungusa.org/reports/Trend%20Alert_Waterpipes.pdf Accessed July 8, 2010.

Amrock SM, Weitzman M. **Adolescents'** Perceptions of **Light and Intermittent Smoking** in the United States. Pediatrics. 2015 Jan 12.

Amrock SM, Weitzman M. **Alternative Tobacco Products** as a Second Front in the War on Tobacco. JAMA. 2015 Oct 13;314(14):1507-8.

Amrock SM, Lee L, Weitzman M. **Perceptions of e-Cigarettes and Noncigarette Tobacco Products Among US** Youth. Pediatrics.2016;138(5):e20154306.

Anderson JC, Calderwood AH, Christensen BC, et al. Smoking and Other Risk Factors in Individuals With **Synchronous Conventional High-Risk Adenomas and Clinically Significant Serrated Polyps**. Am J Gastroenterol. 2018 Nov 1.

Anderson TM, Lavista Ferres JM, Ren SY,et al. Maternal Smoking Before and During **Pregnancy and the Risk of Sudden Unexpected Infant Death**. Pediatrics. 2019 Mar 11.

Andrade Md, Hastings G, Angus K. Promotion of **electronic cigarettes**: tobacco marketing reinvented? BMJ. 2013 Dec 21

Andrews JO, Mueller M, Dooley M, et al. Effect of a smoking cessation intervention for women in **subsidized neighborhoods**: A randomized controlled trial. Prev Med. 2016 Jul 14;90:170-176.

Anthenelli RM et al. Effects of **varenicline** on smoking cessation in adults with stably treated current or past major **depression**: A randomized trial. Ann Intern Med 2013 Sep 16; [e-pub ahead of print].

Anthenelli RM, et al. Neuropsychiatric safety and efficacy of **varenicline, bupropion, and nicotine patch** in smokers **with and without psychiatric disorders** (**EAGLES**): a double-blind, randomised, placebo-controlled clinical trial. Lancet 2016; online April 22.

Apelberg BJ, Feirman SP, Salazar E, et al. Potential **Public Health Effects of Reducing Nicotine Levels** in Cigarettes in the United States. N Engl J Med. 2018 Mar 15.

Apollonio D, Philipps R, Bero L. **Interventions for tobacco use cessation in people in treatment for or recovery from substance use disorders**. Cochrane Database of Systematic Reviews 2016, Issue 11. Art. No.: CD010274. The studies included in this review suggest that providing tobacco cessation interventions targeted to smokers in treatment and recovery for alcohol and other drug dependencies increases tobacco abstinence. There was no evidence that providing interventions for tobacco cessation affected abstinence from alcohol and other drugs. The association between tobacco cessation interventions and tobacco abstinence was consistent for both pharmacotherapy and combined counselling and pharmacotherapy, for participants both in treatment and in recovery, and for people with alcohol dependency or other drug dependency. The evidence for the interventions was low quality due primarily to incomplete reporting of the risks of bias and clinical heterogeneity in the nature of treatment. Certain results were sensitive to the length of follow-up or the type of pharmacotherapy, suggesting that further research is warranted regarding whether tobacco cessation interventions are associated with tobacco abstinence for people in recovery, and the outcomes associated with NRT versus non-NRT or combined pharmacotherapy. Overall, the results suggest that tobacco cessation interventions incorporating pharmacotherapy should be incorporated into clinical practice to reduce tobacco addiction among people in treatment for or recovery from alcohol and other drug dependence.

Arane K, Goldman RD. **Electronic cigarettes and adolescents**. 2016; 62 897-898

Arefalk G, Hambraeus K, Lind L, et al. **Discontinuation of Smokeless Tobacco** and Mortality Risk after Myocardial Infarction. Circulation. 2014 Jun 23.

Armon C. Smoking is a **cause of ALS**. High LDL-cholesterol levels? Unsure. Ann Neurol. 2019 Mar 18.

Arnott D, Wessely S, Fitzpatrick M. **Should psychiatric hospitals completely ban smoking**? BMJ. 2015 Nov 4;351:h5654.

Asch DA, Muller RW, Volpp KG. Conflicts and Compromises in **Not Hiring Smokers**. N Engl J Med. 2013 Mar 27.

Ashraf H, Saghir Z, Dirksen A, et al. Smoking habits in the randomised **Danish Lung Cancer Screening Trial with low-dose CT**: final results after a 5-year screening programme. Thorax. 2014 Jan 17.

Astor RL, Urman R, Barrington-Trimis JL, et al. Tobacco **Retail Licensing and Youth Product Use**. Pediatrics. 2019 Jan 7.

Athanasakis K, Igoumenidis M, Karampli E, et al. Cost-effectiveness of **varenicline versus bupropion, nicotine-replacement therapy, and unaided cessation** in Greece. Clin Ther. 2012 Aug;34(8):1803-14.

Aubin HJ, Bobak A, Britton JR, et a. Varenicline versus transdermal nicotine patch for smoking cessation: Results from a randomised, open-label trial. Thorax. 2008 Feb 8; [Epub ahead of print] The Week 52 CAR (NRT,Weeks 8-52; varenicline,Weeks 9-52) was 26.1% for varenicline and 20.3% for NRT (OR 1.40, 95% CI, 0.99 to 1.99, p=0.056). Varenicline significantly reduced craving (p<0.001), withdrawal symptoms (p<0.001) and smoking satisfaction (p<0.001) versus NRT. The outcomes of this registered clinical trial (NCT00143325) established that abstinence from smoking was greater, and craving, withdrawal symptoms and smoking satisfaction less, at the end of treatment with varenicline than with transdermal nicotine.

Aubin H-J, Farley A, Lycett D, Lahmek P, Aveyard P. **Weight gain in smokers after quitting** cigarettes: meta-analysis. BMJ 2012;345:e4439. (mean gain of4-5kg after 12months of abstinence)

Aubin HJ, Luquiens A, Berlin I. **Pharmacotherapy for smoking cessation**: Pharmacological principles and clinical practice. Br J Clin Pharmacol. 2013 Mar 15.

Audrain-McGovern Janet, Stevens Sarah, Murray Pamela J., et al. The Efficacy of **Motivational Interviewing Versus Brief Advice** for Adolescent Smoking Behavior Change. Pediatrics 2011; 128:1 e101-e111; doi:10.1542/peds.2010-2174.

Audrain-McGovern J, Stone MD, Barrington-Trimis J, et al. **Adolescent E-Cigarette, Hookah, and Conventional Cigarette Use and Subsequent Marijuana Use.** Pediatrics. 2018 Aug 6.

Auer R, Concha-Lozano N, Jacot-Sadowski I, Cornuz J, Berthet A. **Heat-not-burn tobacco cigarettes**: smoke by any other name [published online July 1, 2017].JAMA Intern Med. doi:10.1001/jamainternmed.2017.1419

Avdalovic MV, Murin S. **Electronic cigarettes**: no such thing as a free lunch...Or puff. Chest. 2012 Jun;141(6):1371-2.

Aveyard P, West R. **Managing smoking cessation**. BMJ. 2007 Jul 7;335(7609):37-41.

Aveyard P, Johnson C, Fillingham S, Parsons A, Murphy M. **Nortriptyline** plus nicotine replacement versus placebo plus **nicotine** replacement for smoking cessation: pragmatic randomised controlled trial. BMJ. 2008 Apr 27; [Epub ahead of print] Nortriptyline and nicotine replacement therapy are both effective for smoking cessation but the effect of the combination is less than either alone and evidence is lacking that combination treatment is more effective than either alone.

Aveyard P, Lindson-Hawley N, Hastings G, de Andrade M. Should smokers be advised to **cut down as well as quit**? BMJ. 2014 May 19;348:g2787

Aveyard P, Arnott D, Johnson KC. Should we recommend **e-cigarettes** to help smokers quit? BMJ. 2018 Apr 25;361:k1759.

Ayers JW, Althouse BM, Johnson M, Cohen JE. **Circaseptan (Weekly) Rhythms** in Smoking Cessation Considerations. JAMA Intern Med. 2013 Oct 28.

Ayers JW, Althouse BM, Allem JP, et al. Revisiting the Rise of **Electronic Nicotine Delivery Systems** Using Search Query Surveillance. Am J Prev Med. 2016 Jan 28.

Baardman ME, Kerstjens-Frederikse WS, et al. Combined adverse effects of maternal **smoking and high body mass index** on heart development in offspring: evidence for interaction? Heart. 2012 Jan 30.

Baggett TP, Tobey ML, Rigotti NA. Tobacco use among **homeless people**--addressing the neglected addiction. N Engl J Med. 2013 Jul 18;369(3):201-4.

Baker TB, Piper ME, Stein JH, et al. Effects of **Nicotine Patch vs Varenicline vs Combination Nicotine Replacement Therapy** on Smoking Cessation at 26 Weeks: A Randomized Clinical Trial. JAMA. 2016 Jan 26;315(4):371-9.

Bala MM, Strzeszynski L, Topor-Madry R. **Mass media interventions for smoking cessation in adults**. Cochrane Database of Systematic Reviews 2017, Issue 11. Art. No.: CD004704. There is evidence that comprehensive tobacco control programmes which include mass media campaigns can be effective in changing smoking behaviour in adults, but the evidence comes from a heterogeneous group of studies of variable methodological quality. One state-wide tobacco control programme (Massachusetts) showed positive results up to eight years after the campaign. Another (California) showed positive results during the period of adequate funding and implementation and in final evaluation since the beginning of the programme. Six of nine studies carried out in communities or regions showed some positive effects on smoking behaviour and at least one significant change in smoking prevalence (Sydney). The intensity and duration of mass media campaigns may influence effectiveness, but length of follow-up and concurrent secular trends and events can make this difficult to quantify. No consistent relationship was observed between campaign effectiveness and age, education, ethnicity or gender.

Banks E, Joshy G, Weber MF, et al. Tobacco smoking and all-cause **mortality** in a large Australian cohort study: findings from a mature epidemic with current low smoking prevalence. BMC Med. 2015 Dec;13(1):281.

Barnason S, Zimmerman L, Schulz P, et al. Weight management **telehealth intervention for overweight and obese rural cardiac rehabilitation** participants: A randomised trial. J Clin Nurs. 2019 Jan 22.

Barnes J, McRobbie H, Dong CY, et al. **Hypnotherapy** for smoking cessation. Cochrane Database Syst Rev. 2019 Jun 14;6:CD001008. There is insufficient evidence to determine whether hypnotherapy is more effective for smoking cessation than other forms of behavioural support or unassisted quitting. If a benefit is present, current evidence suggests the benefit is small at most. There is very little evidence on whether hypnotherapy causes adverse effects, but the existing data show no evidence that it does.

Barrientos-Gutierrez I, Kollath-Cattano C, Mejía R, et al. Comparison of **tobacco and alcohol use in films** produced in Europe, Latin America, and the United States. BMC Public Health. 2015 Nov 3;15(1):1096.

Barrington-Trimis JL, Berhane K, Unger JB, et al. **Psychosocial Factors** Associated With **Adolescent Electronic Cigarette** and Cigarette Use. Pediatrics. 2015 Jul 27.

Barrington-Trimis JL, Kong G, Leventhal AM, et al. E-cigarette Use and Subsequent Smoking Frequency **Among Adolescents**. Pediatrics. 2018 Nov 5.

Barrington-Trimis JL, Urman R, Berhane K, et al. **E-Cigarettes and Future Cigarette Use**. Pediatrics. 2016 Jun 13.

Barrington-Trimis JL, Urman R, Leventhal AM, et al. E-cigarettes, Cigarettes, and the Prevalence of **Adolescent Tobacco Use**. Pediatrics. 2016 Jul 11.

Barrington-Trimis JL, Leventhal AM. **Adolescents' Use of "Pod Mod" E-Cigarettes** - Urgent Concerns. N Engl J Med. 2018 Sep 20;379(12):1099-1102.

Bartecchi C, et al. Reduction in the incidence of acute myocardial infarction associated with a **citywide smoking ordinance**. Circulation. 2006 Oct 3;114(14):1490-6. Epub 2006 Sep 25. (InfoPOEMs: This observational study found that a citywide smoking ban was associated with a reduction in the incidence of acute myocardial infarction (AMI) by approximately 70 per 100,000 person-years (that is, approximately 1 fewer AMI for every 1400 persons per year). Share this information with local politicians and other community leaders who are resisting curbs on smoking. Another study by the Centers for Disease Control and Prevention found that a smoking ban in El Paso, Texas, had no negative economic consequences for bars and restaurants.* *http://www.cdc.gov/mmwr/preview/mmwrhtml/mm5307a2.htm (LOE = 4))

Barth J, Jacob T, Daha I, et al. **Psychosocial interventions for smoking cessation in patients with coronary heart disease**. Cochrane Database Syst Rev. 2015 Jul 6;7:CD006886. Psychosocial smoking cessation interventions are effective in promoting abstinence up to 1 year, provided they are of sufficient duration. After one year, the studies showed favourable effects of smoking cessation intervention, but more studies including cost-effectiveness analyses are needed. Further studies should also analyse the additional benefit of a psychosocial intervention strategy to pharmacological therapy (e.g. nicotine replacement therapy) compared with pharmacological treatment alone and investigate economic outcomes.

Bartter T. **Electronic Cigarettes**: Aggregate Harm. Ann Intern Med. 2015 Jul 7;163(1):59-60.

Bass F, Naish B, Buwembo I. **Front-office staff can improve clinical tobacco intervention**: Health coordinator pilot project. Can Fam Physician. 2013 Nov;59(11):e499-506.

Bass F, Naish B. **Advancing preventive care** with clinical tobacco intervention. Can Fam Physician. 2014 Mar;60(3):221-2.

Bassett RA, Osterhoudt K, Brabazon T. **Nicotine Poisoning** in an Infant. N Engl J Med. 2014 May 7.

Basu Sanjay, Stuckler David, Bitton Asaf. Projected effects of **tobacco smoking on worldwide tuberculosis** control: mathematical modelling analysis. BMJ 2011;343:d5506 doi: 10.1136/bmj.d5506

Batty GD, Shipley MJ, Kivimaki M, et al. Impact of smoking cessation advice on **future smoking behavior**, morbidity, and mortality: up to **40 years of follow-up** of the first randomized controlled trial of a general population sample. Arch Intern Med. 2011;171(21):1950-1951.

Beard E, West R, Michie S, Brown J. Association between **electronic cigarette use and changes in quit attempts**, success of quit attempts, use of smoking cessation pharmacotherapy, and use of stop smoking services in England: time series analysis of population trends. BMJ 2016;354:i4645.

Beatty JA, Majumdar SR, Tyrrell GJ, et al. Current Smoking and Reduced Mortality in Bacteremic Pneumococcal Pneumonia: A Population-Based Cohort Study. Chest. 2016 May 2. pii: S0012-3692(16)48803-3.

Benowitz NL. Comprehensive **Nicotine Regulation** to End the **Combustible Tobacco Epidemic**. Ann Intern Med. 2017 Aug 15.

Benowitz NL, Pipe A, West R, et al. **Cardiovascular Safety of Varenicline, Bupropion, and Nicotine Patch** in Smokers: A Randomized Clinical Trial. JAMA Intern Med. 2018 Apr 9.

Britton J, Arnott D, McNeill A, et al. Nicotine without smoke-putting **electronic cigarettes** in context. BMJ. 2016 Apr 27;353:i1745

Been JV, Nurmatov UB, Cox B, Nawrot TS, van Schayck CP, Sheikh A. Effect of **smoke-free legislation** on perinatal and child health: a systematic review and meta-analysis. Lancet 2014; online March 28.

Behbod B, Sharma M, Baxi R, et al. **Family and carer smoking control programmes for reducing children's exposure to environmental tobacco smoke**. Cochrane Database of Systematic Reviews 2018, Issue 1. Art. No.: CD001746. A minority of interventions have been shown to reduce children's exposure to environmental tobacco smoke and improve children's health, but the features that differentiate the effective interventions from those without clear evidence of effectiveness remain unclear. The evidence was judged to be of low or very low quality, as many of the trials are at a high risk of bias, are small and inadequately powered, with heterogeneous interventions and populations.

Bellavia A, Wolk A, Orsini N. Differences in age at **death** according to **smoking and age at menopause**. Menopause. 2015 Jul 31.

Belsky DW, Moffitt TE, Baker TB, et al. **Polygenic Risk and the Developmental Progression to Heavy, Persistent Smoking** and Nicotine Dependence: Evidence From a **4-Decade Longitudinal Study**. JAMA Psychiatry. 2013 Mar 27:1-9.

Benowitz NL, Prochaska JJ. **Smoking cessation after acute myocardial infarction**. J Am Coll Cardiol 2013; 61: 524-32.

Benowitz NL, Goniewicz ML. The Regulatory Challenge of **Electronic Cigarettes**. JAMA. 2013 Jul 15.

Benowitz NL, Nardone N, Dains KM, et al. Effect of **reducing the nicotine content** of cigarettes on cigarette smoking behavior and tobacco smoke toxicant exposure: 2-year follow up. Addiction. 2015 Jul 21.

Benowitz NL, Pipe A, West R, et al. **Cardiovascular Safety of Varenicline, Bupropion, and Nicotine Patch** in Smokers: A Randomized Clinical Trial. (**EAGLES**) JAMA Intern Med. 2018 Apr 9.

Bérard A, Zhao JP, Sheehy O. Success of smoking cessation interventions during **pregnancy**. Am J Obstet Gynecol. 2016 Jul 8.

Bergamini E, Demidenko E, Sargent JD. Trends in **Tobacco and Alcohol Brand Placements in Popular US Movies**, 1996 Through 2009. JAMA Pediatr. 2013 May 27:1-6.

Berlin I, Grange G, Jacob N, Tanguy M-L. Efficacy of **nicotine patches in pregnant smokers**: a randomised, placebo controlled, multicentre trial. BMJ 2014;348:g1622.

Berman ML, Yang YT. **E-Cigarettes**, Youth, and the US Food and Drug Administration's **"Deeming" Regulation**. JAMA Pediatr. 2016 Sep 26.

Bernstein SL, D'Onofrio G, Rosner J, et al. Successful Tobacco **Dependence Treatment in Low-Income Emergency Department Patients**: A Randomized Trial. Ann Emerg Med. 2015 Apr 18.

Berridge V. **Electronic cigarettes** and history. Lancet. 2014 Jun 28;383(9936):2204-5.

Berry KM, Fetterman JL, Benjamin EJ, et al. Association of **Electronic Cigarette Use With Subsequent Initiation of Tobacco Cigarettes** in US Youths. JAMA Netw Open. 2019 Feb 1;2(2):e187794.

Bhatnagar A, Whitsel LP, Ribisl KM, et al; on behalf of the **American Heart Association** –AHA Advocacy Coordinating Committee, Council on Cardiovascular and Stroke Nursing, Council on Clinical Cardiology, and Council on Quality of Care and Outcomes Research. **Electronic cigarettes:** A policy statement from the American Heart Association.*Circulation* 2014.

Bhopal A, Peake MD, Gilligan D, Cosford P. Lun**g cancer in never-smokers**: a hidden disease. J R Soc Med. 2019 Apr 25:141076819843654.

Biedermann L, Zeitz J, Mwinyi J, et al. **Smoking cessation induces** profound changes in the composition of the **intestinal microbiota** in humans. PLoS One. 2013;8(3):e59260.

Binswanger IA, Carson EA, Krueger PM, Mueller SR, Steiner JF, Sabol WJ. **Prison tobacco control** policies and deaths from smoking in United States prisons: population based retrospective analysis. BMJ 2013;349:g4542.

Bjerregaard BK, et al. The effect of **occasional smoking** on smoking-related cancers : In the European Prospective Investigation into Cancer and Nutrition (EPIC). Cancer Causes Control. 2006 Dec;17(10):1305-9.

Bilano V, Gilmour S, Moffiet T, et al. **Global trends and projections for tobacco use**, 1990-2025: an analysis of smoking indicators from the **WHO** Comprehensive Information Systems for Tobacco Control. Lancet. 2015 Mar 14; 385(9972):966-76.

Bock BC, Dunsiger SI, Rosen RK, et al. **Yoga** as a Complementary Therapy for Smoking Cessation:Results from BreathEasy ,a Randomized Clinical trial. Nicotine Tob Res. 2018 Oct 6.

Boffetta Paolo, Straif Kurt. Use of **smokeless tobacco** and risk of myocardial infarction and stroke: systematic review with meta-analysis. BMJ 2009;339:b3060, doi: 10.1136/bmj.b3060 (Published 18 August 2009) An association was detected between use of smokeless tobacco

products and risk of fatal myocardial infarction and stroke, which does not seem to be explained by chance.
Bold KW, Kong G, Cavallo DA, et al. **Reasons for Trying E-cigarettes** and Risk of Continued Use. Pediatrics. 2016 Aug 8.
Bold KW, Kong G, Camenga DR, et al.**Trajectories of E-Cigarette and Conventional Cigarette Use** Among Youth. Pediatrics. 2017 Dec 4.
Klein JD. E-Cigarettes: A 1-Way Street to Traditional Smoking and Nicotine Addiction for Youth. Pediatrics. 2017 Dec 4.
Bolliger CT, Issa JS, Posadas-Valay R, et al. Effects of **varenicline** in adult smokers: a **multinational** (Latin America, Africa & Middle East), 24-week, randomized, double-blind, placebo-controlled study. Clin Ther. 2011 Apr;33(4):465-77.
Bonser RS, Taylor R, Collett D, Thomas HL, Dark JH, Neuberger J, on behalf of members of the Cardiothoracic Advisory Group to NHS Blood and Transplant and the Association of Lung Transplant Physicians (UK). Effect of **donor smoking on survival after lung** transplantation: a cohort study of a prospective registry. Lancet 2012.
Borderud SP, Li Y, Burkhalter JE, et al. **Electronic cigarette use** among patients with **cancer**: Characteristics of electronic cigarette users and their smoking cessation outcomes. Cancer. 2014 Sep 22.
Borland R. Electronic cigarettes as a method of tobacco control. BMJ. 2011 Sep 30;343:d6269.
Borland R, Savvas S. The effects of variant descriptors on the potential effectiveness of **plain packaging**. Tob Control. 2014 Jan;23(1):58-63.
Borzekowski DL, Cohen JE. **International Reach of Tobacco Marketing** Among Young Children. Pediatrics. 2013 Oct;132(4):e825-e831. Epub 2013 Sep 30.
Botteri E, Iodice S, Bagnardi V, Raimondi S, Lowenfels AB, Maisonneuve P. Smoking and **Colorectal Cancer**: A Meta-analysis. JAMA. 2008 Dec 17;300(23):2765-78. Cigarette smoking is significantly associated with colorectal cancer incidence and mortality.
Bottorff JL, Seaton CL, Lamont S. Patients' awareness of the **surgical risks of smoking**: Implications for supporting smoking cessation. Can Fam Physician. 2015 Dec
Boulvain M, Irion O, Dowswell T, Thornton JG. **Induction of labour at or near term for suspected fetal macrosomia**. Cochrane Database of Systematic Reviews 2016, Issue 5. Art. No.: CD000938. DOI: 10.1002/14651858.CD000938.pub2. Induction of labour for suspected fetal macrosomia has not been shown to alter the risk of brachial plexus injury, but the power of the included studies to show a difference for such a rare event is limited. Also antenatal estimates of fetal weight are often inaccurate so many women may be worried unnecessarily, and many inductions may not be needed. Nevertheless, induction of labour for suspected fetal macrosomia results in a lower mean birthweight, and fewer birth fractures and shoulder dystocia. The unexpected observation in the induction group of increased perineal damage, and the plausible, but of uncertain significance, observation of increased use of phototherapy, both in the largest trial, should also be kept in mind.
Boykan R, Messina CR, Chateau G, et al. Self-Reported Use of Tobacco, E-cigarettes, and Marijuana Versus Urinary Biomarkers. Pediatrics. 2019 Apr 22
Brackel CL, Ropers FG, Vermaas-Fricot SF, et al. **Acute eosinophilic pneumonia** after recent start of smoking. Lancet. 2015 Mar 21; 385(9973):1150.
Brain K, Carter B, Lifford KJ, et al. Impact of low-dose CT screening on **smoking cessation** among high-risk participants in the UK **Lung Cancer Screening Trial**. Thorax. 2017 Jul 14.
Brand JS, Chan MF, Dowsett M, et al. Cigarette **Smoking and Endogenous Sex Hormones** in Postmenopausal Women. J Clin Endocrinol Metab. 2011 Aug 10.
Brandon TH, Goniewicz ML, Hanna NH, et al. **Electronic Nicotine Delivery Systems**: A Policy Statement from the **American Association for Cancer Research** and the **American Society of Clinical Oncology**. Clin Cancer Res. 2015 Jan 8.
Brennan TA, Schroeder SA. **Ending Sales of Tobacco** Products in **Pharmacies**. JAMA. 2014 Feb 5.
Brewer NT, Hall MG, Noar SM, et al. Effect of **Pictorial Cigarette Pack Warnings** on Changes in Smoking Behavior: A Randomized Clinical Trial. JAMA Intern Med. 2016 Jun 6.
Britton J. **Taxing tobacco profits** to prevent the smoking epidemic. The Lancet. Published online March 4, 2011 DOI:10.1016/S0140-6736(10)62040-5
Britton J and Bogdanovica I. **Tobacco control efforts in Europe**. Lancet 2013; 381:1588-1595.
Brody AL, Mukhin AG, Mamoun MS, et al. **Brain Nicotinic Acetylcholine Receptor Availability** and Response to Smoking Cessation Treatment: A Randomized Trial. JAMA Psychiatry. 2014 May 21.
Brown JE, Luo W, Isabelle LM, et al. **Candy Flavorings** in Tobacco. N Engl J Med. 2014 May 7.
Brown J, West R, Beard E, et al. Prevalence and characteristics of **e-cigarette users in Great Britain**: Findings from a general population survey of smokers. Addict Behav. 2014 Jun;39(6):1120-5.
Brown-Johnson CG, Burbank A, Daza EJ, et al. Online Patient-Provider **E-Cigarette** Consultations-Perceptions of Safety and Harm. Am J Prev Med. 2016 Aug 24.
Browne HA, Modabbernia A, Buxbaum JD, et al. **Prenatal Maternal Smoking** and Increased Risk for **Tourette Syndrome** and **Chronic Tic Disorders**. J Am Acad Child Adolesc Psychiatry. 2016 Sep;55(9):784-91.
Brownson EG, Thompson CM, Goldsberry S, et al. **Explosion Injuries from E-Cigarettes**. N Engl J Med. 2016 Oct 6;375(14):1400-1402
Buchanan DM, Arnold SV, Gosch KL, et al. Association of **Smoking Status With Angina** and Health-Related Quality of Life After Acute Myocardial Infarction. Circ Cardiovasc Qual Outcomes. 2015 Aug 25.
Bucholz EM, Beckman BS, Kiefe CI, et al. **Life years gained** from **smoking-cessation counselling after myocardial infarction**. *Am J Prev Med* 2016;.
Bullen C, Howe C, Laugesen M, et al. **Electronic cigarettes for smoking cessation**: a randomised controlled trial. Lancet 2013; online Sept 8.
Bunik M, Cavanaugh KL, Herrick D, et al. The **ONE Step Initiative**: Quality Improvement in a Pediatric Clinic for **Secondhand Smoke Reduction**. Pediatrics. 2013 Aug;132(2):e502-11.
Burke GM, Genuardi M, Shappell H, et al. Temporal Associations of **Smoking** and **Cardiovascular Disease**, 1971 to 2006 (From the Framingham Heart Study). Am J Cardio. 2017
Burke H, Leonardi-Bee J, Hashim A et al. **Prenatal and Passive Smoke Exposure** and Incidence of Asthma and Wheeze: Systematic Review and Meta-analysis. Pediatrics. 2012 Mar 19.
Burstein AH, et al. Pharmacokinetics, safety, and tolerability after single and multiple oral doses of **varenicline** in elderly smokers. J Clin Pharmacol. 2006 Nov;46(11):1234-40. Thus, no dose adjustment is necessary based on age alone.
Butt YM, Smith ML, Tazelaar HD, et al. **Pathology of Vaping-Associated Lung Injury**. N Engl J Med. 2019 Oct 2. doi:10.1056/NEJMc1913069.
Cahill K, Stead LF, Lancaster T. **Nicotine receptor partial agonists** for smoking cessation. **Cochrane** Database of Systematic Reviews 2007, Issue 1. Art. No.: CD006103. DOI: 10.1002/14651858.CD006103.pub2. Varenicline increased the odds of successful long-term smoking cessation approximately threefold compared with pharmacologically unassisted quit attempts.In trials reported so far, more participants quit successfully with varenicline than with bupropion. The effectiveness of varenicline as an aid to relapse prevention has not been clearly established. The main adverse effect of varenciline is nausea, but this is mostly at mild to moderate levels and tends to reduce with habituation.There is a need for independent trials of varenicline versus placebo, to test the early findings. There is also a need for direct comparisons with nicotine replacement therapy, and for further trials with bupropion, to establish the relative efficacy of the treatments.Cytisine may also increase the chances of quitting, but the evidence at present is inconclusive.
Cahill K, Moher M, Lancaster T. **Workplace interventions** for smoking cessation. Cochrane Database Syst Rev. 2008 Oct 8;(4):CD003440. We found strong evidence that interventions directed towards individual smokers increase the likelihood of quitting smoking. These include individual and group counselling and pharmacological treatment to overcome nicotine addiction. All these interventions show similar effects whether offered in the workplace or elsewhere. Self-help interventions and social support are less effective. Although people taking up these interventions are more likely to stop, the absolute numbers who quit are low.2. There was limited evidence that participation in programmes can be increased by competitions and incentives organized by the employer.3. We failed to detect an effect of comprehensive programmes in reducing the prevalence of smoking.
Cahill K, Lancaster T, Green N. **Stage-based interventions** for smoking cessation. Cochrane Database of Systematic Reviews 2010, Issue 11. Art. No.: CD004492. DOI: 10.1002/14651858.CD004492.pub4.
Cahill K, Stead LF, Lancaster T. **Nicotine receptor partial agonists** for smoking cessation. **Cochrane** Database Syst Rev. 2010 Dec 8;12:CD006103. **Varenicline** at standard dose increased the chances of successful long-term smoking cessation between two- and threefold compared with pharmacologically unassisted quit attempts. Lower dose regimens also conferred benefits for cessation, while reducing the incidence of adverse events. More participants quit successfully with varenicline than with bupropion. Two open-label trials of varenicline versus NRT suggested a modest benefit of varenicline but confidence intervals did not rule out equivalence. Limited evidence suggests that varenicline may have a role to play in relapse prevention. The main adverse effect of varenicline is nausea, but mostly at mild to moderate levels and tending to subside over time. Possible links with serious adverse events, including depressed mood, agitation and suicidal thoughts, have been reported but are so far not substantiated. There is a need for further independent community-based trials of varenicline, to test its efficacy and safety in smokers with varying co-morbidities and risk patterns. There is a need for further trials of the efficacy of treatment extended beyond 12 weeks. **Cytisine** may also increase the chances of quitting, but the evidence at resent is inconclusive.
Cahill K, Stead LF, Lancaster T. **Nicotine receptor partial agonists for smoking cessation**. Cochrane Database of Systematic Reviews **2012**, Issue 4. Art. No.: CD006103. Cytisine increases the chances of quitting, although absolute quit rates were modest in two recent trials. Varenicline at standard dose increased the chances of successful long-term smoking cessation between two- and threefold compared with pharmacologically unassisted quit attempts. Lower dose regimens also conferred benefits for cessation, while reducing the incidence of adverse events. More participants quit successfully with varenicline than with bupropion. Two open-label trials of varenicline versus NRT suggested a modest benefit of varenicline but confidence intervals did not rule out equivalence. Limited evidence suggests that varenicline may have a role to play in relapse prevention. The main adverse effect of varenicline is nausea, but mostly at mild to moderate levels and tending to subside over time. Possible links with serious adverse events, including serious psychiatric or cardiovascular events, cannot be ruled out.
Cahill K, Stevens S, Perera R, Lancaster T. **Pharmacological interventions for smoking cessation: an overview and network** meta-analysis.CochraneDatabase of SystematicReviews 2013, Issue 5.Art.No.:CD009329.DOI: 10.1002/14651858.CD009329.pub2. NRT, bupropion, varenicline and cytisine have been shown to improve the chances of quitting. Combination NRT and varenicline are equally effective as quitting aids. Nortriptyline also improves the chances of quitting. On current evidence, none of the treatments appear to have an incidence of adverse events that would mitigate their use.
Cahill K, Stevens S, Lancaster T. **Pharmacological treatments for smoking cessation**. JAMA. 2014 Jan 8;311(2):193-4.
Cahill K, Lancaster T. **Workplace interventions** for smoking cessation. Cochrane Database Syst Rev. 2014 Feb 26;2:CD003440. 1. We found strong evidence that some interventions directed towards individual smokers increase the likelihood of quitting smoking. These include individual and group counselling, pharmacological treatment to overcome nicotine addiction, and multiple interventions targeting smoking cessation as the primary or only outcome. All these interventions show similar effects whether offered in the workplace or elsewhere. Self-help interventions and social support are less effective. Although people taking up these interventions are more likely to stop, the absolute numbers who quit are low.
Cahill K, Hartmann-Boyce J, Perera R. **Incentives for smoking cessation**. Cochrane Database Syst Rev. 2015 May 18;5:CD004307. Incentives appear to boost cessation rates while they are in place. The two trials recruiting from work sites that achieved sustained success rates beyond the reward schedule concentrated their resources into substantial cash payments for abstinence. Such an approach may only be feasible where independently-funded smoking cessation programmes are already available, and within a relatively affluent and educated population. Deposit-refund trials can suffer from relatively low rates of uptake, but those who do sign up and contribute their own money may achieve higher quit rates than reward-only participants. Incentive schemes conducted among pregnant smokers improved the cessation rates, both at the end-of-pregnancy and post-partum assessments. Current and future research might continue to explore the scale, loading and longevity of possible cash or voucher reward schedules, within a variety of smoking populations.
Cahill K, Lindson-Hawley N, Thomas KH, Fanshawe TR, Lancaster T. **Nicotine receptor partial agonists** for smoking cessation. Cochrane Database of Systematic Reviews 2016, Issue 5. Art. No.: CD006103. DOI: 10.1002/14651858.CD006103.pub7. Cytisine increases the chances of quitting, although absolute quit rates were modest in two recent trials. Varenicline at standard dose increased the chances of successful long-term smoking cessation between two- and three-fold compared with pharmacologically unassisted quit attempts. Lower dose regimens also conferred benefits for cessation, while reducing the incidence of adverse events. More participants quit successfully with varenicline than with bupropion or with NRT. Limited evidence suggests that varenicline may have a role to play in relapse prevention. The most frequently recorded adverse effect of varenicline is nausea, but mostly at mild to moderate levels and tending to subside over time. Early reports of possible links to suicidal ideation and behaviour have not been confirmed by current research.
Cai HL, Wang C. **Survival with Smog and Smoke**: Precision Intervention? Chest. 2017 Jul 7.
Callaghan, Russell C, Veldhuizen, Scott, Leatherdale, Scott, Murnaghan, Donna, Manske, Steve Use of **contraband cigarettes** among adolescent daily smokers in Canada. CMAJ 2009 0: cmaj.090665.
Callinan JE, Clarke A, Doherty K, Kelleher C. **Legislative smoking bans** for reducing secondhand smoke exposure, smoking prevalence and tobacco consumption. Cochrane Database Syst Rev. 2010 Apr 14;4:CD005992.
Campbell R, Starkey F, Holliday J, et al. An informal **school-based peer-led intervention** for smoking prevention in adolescence (ASSIST): a cluster randomised trial. Lancet. 2008 May 10;371(9624):1595-602. The results suggest that, if implemented on a population basis, the ASSIST intervention could lead to a reduction in adolescent smoking prevalence of public-health importance.
Can A, Castro VM, Ozdemir YH, et al. Association of **intracranial aneurysm rupture** with smoking duration, intensity, and cessation. Neurology 2017;89:1408–1415.
Canadian Task Force on Preventive Health Care. Recommendations on **behavioural interventions** for the prevention and treatment of cigarette smoking among school-aged children and youth. CMAJ. 2017 Feb 27;189(8):E310-E316.

Caporale A, Langham MC, Guo W, et al. Acute Effects of Electronic Cigarette Aerosol **Inhalation on Vascular Function** Detected at Quantitative MRI. Radiology. 2019 Aug 20:190562.

Caputi TL, Leas E, Dredze M, et al. They're heating up: Internet search query trends reveal significant public interest in **heat-not-burn tobacco products**. PLoS One. 2017 Oct 11;12(10):e0185735.

Carandang RA, Barton B, Rordorf GA, et al. Nicotine replacement therapy **after subarachnoid hemorrhage** is not associated with increased vasospasm. Stroke. 2011 Nov;42(11):3080-6.

Carnevale R, Sciarretta S, Violi F, et al. Acute impact of **tobacco versus electronic cigarette smoking** on oxidative stress and vascular function. Chest. 2016 Apr 21.

Carpenter MJ, Hughes JR, Gray KM, et al. **Nicotine therapy sampling** to induce quit attempts among smokers unmotivated to quit: a randomized clinical trial. Arch Intern Med. 2011;171(21): 1901-1907

Carreras-Torres R, Johansson M, Haycock PC, et al. Role of **obesity** in smoking behaviour: Mendelian randomisation study in UK Biobank. BMJ. 2018 May 16;361:k1767.

Carwile JL, Fleisch AF, Young K, Ahrens KA. **Electronic Cigarette Use in US Households With Children**: The "New" Secondhand Smoke. JAMA Pediatr. 2019 May 6.

Cao Yin; Kenfield Stacey; Song Yan; et al. Cigarette Smoking Cessation and Total and Cause-Specific **Mortality: A 22-Year Follow-up** Study Among US Male Physicians (**PHS**). Arch Intern Med. 2011;171(21):1956-1959.

Carlsson S, Andersson T, Araghi M, et al. **Smokeless tobacco (snus)** is associated with an increased risk of type 2 **diabetes**: results from five pooled cohorts. J Intern Med. 2017 Feb 6.

Carson KV, Brinn MP, Labiszewski NA, Esterman AJ, Chang AB, Smith BJ. Community interventions for **preventing smoking in young people**. Cochrane Database Syst Rev. 2011 Jul 6;(7):CD001291. doi: 10.1002/14651858.CD001291.pub2.

Carson KV, Brinn MP, Labiszewski NA, Peters M, Chang AB, Veale A, Esterman AJ, Smith BJ. Interventions for tobacco use **prevention in Indigenous youth**. Cochrane Database Syst Rev. 2012 Aug 15;8:CD009325. doi: 10.1002/14651858.CD009325.pub2.

Carson KV, Verbiest MEA, Crone MR, et al. **Training health professionals** in smoking cessation. Cochrane Database of Systematic Reviews 2012, Issue 5. Art. No.: CD000214. DOI: 10.1002/14651858.CD000214.pub2. Training health professionals to provide smoking cessation interventions had a measurable effect on the point prevalence of smoking, continuous abstinence and professional performance. The one exception was the provision of nicotine gum or replacement therapy, which did not differ between groups.

Carson KV, Brinn MP, Peters M, et al. Interventions for **smoking cessation in Indigenous populations**. Cochrane Database of Systematic Reviews 2012, Issue 1. Art.No.: CD009046. DOI: 10.1002/14651858.CD009046.pub2.

Carter M. Last gasp for **e-cigarette** ads that glamorise the habit? BMJ. 2014 Jan 27;348:g475.

Carter M. The **not so independent tobacco experts**. BMJ. 2014 Apr 25;348:g2908.

Carter BD, Abnet CC, Feskanich D, et al. **Smoking and mortality** — beyond established causes. N Engl J Med 2015;372:631-40.

CDC, Morbidity and Mortality Weekly Report (MMWR). **Cigarette Use Among High School Students** --- United States, 1991—2009. July 9, 2010. For current frequent cigarette use, the prevalence increased from 12.7% in 1991 to 16.8% in 1999, declined to 9.7% in 2003, and then declined more gradually, to 7.3% in 2009. http://www.cdc.gov/mmwr/preview/mmwrhtml/mm5926a1.htm?s_cid=mm5926a1_w

CDC Aug/10 Tobacco Use Among **Middle and High School Students** --- United States, 2000—2009 http://www.cdc.gov/mmwr/pdf/wk/mm5933.pdf

CDC-From the Centers for Disease Control and Prevention **Smoking in Top-Grossing Movies**—United States, 1991-2009 *JAMA*. 2010;304(24):2692-2694.

CDC Sep/11 Vital Signs: Current Cigarette **Smoking Among Adults Aged ≥18 Years** --- United States, 2005—2010 (drop from 20.9% to 19.3%) **http://www.cdc.gov/mmwr/preview/mmwrhtml/mm60e0906a1.htm?s_cid=mm60e0906a1_x**

CDC Centers for Disease Control and Prevention (CDC). **Consumption of cigarettes and combustible tobacco**--United States, 2000-2011. MMWR Morb Mortal Wkly Rep. 2012 Aug 3;61(30):565-9.

CDC – Fact Sheet – **Cigars** – Smoking & Tobacco Use. 2017. Available at: https://www.cdc.gov/tobacco/data_statistics/fact_sheets/tobacco_industry/cigars/. Accessed January 20, 2017.

CDC – Fact Sheet – **Hookahs** – Smoking & Tobacco Use. 2017. Available at: https://www.cdc.gov/tobacco/data_statistics/fact_sheets/tobacco_industry/hookahs/. Accessed January 20, 2017.

Cesaroni G, Forastiere F, Agabiti N, et al. Effect of the **Italian smoking ban on population rates of acute coronary events**. Circulation 2008; DOI: 10.1161/circulationaha.107.729889.

Chadi N, Rodean J, Earlywine JJ, et al. **Treatment for Nicotine Use Disorder** Among Medicaid-Enrolled Adolescents and Young Adults. JAMA Pediatr. 2019 Sep 23.

Chadi N, Schroeder R, Jensen JW, Levy S. Association Between **Electronic Cigarette Use and Marijuana Use** Among Adolescents and Young Adults: A Systematic Review and Meta-analysis. JAMA Pediatr. 2019 Aug 12:e192574.

Chaffee BW, Watkins SL, Glantz SA. **Electronic Cigarette Use** and Progression From Experimentation to Established Smoking. Pediatrics. 2018 Mar 5.

Chaiton M, Diemert L, Cohen JE, et al. Estimating the **number of quit attempts** it takes to quit smoking successfully in a longitudinal cohort of smokers. BMJ Open. 2016 Jun 9;6(6):e011045

Chaiton M, Schwartz R, Cohen JE, et al. Association of **Ontario's ban on menthol cigarettes** with smoking behavior 1 month after implementation [online March 5, 2018].JAMA Intern Med. doi:10.1001/jamainternmed.2017.8650

Chaloupka FJ, Sweanor D, Warner KE. **Differential Taxes** for Differential Risks--Toward Reduced Harm from Nicotine-Yielding Products. N Engl J Med. 2015 Aug 13;373(7):594-7.

Chamberlain C, O'Mara-Eves A, Oliver S, et al. **Psychosocial interventions for supporting women to stop smoking in pregnancy**. Cochrane Database Syst Rev. 2013 Oct 23;10:CD001055.

Chamberlain C, O'Mara-Eves A, Porter J, Coleman T, Perlen SM, Thomas J, McKenzie JE. **Psychosocial interventions** for supporting women to stop smoking in **pregnancy**. Cochrane Database of Systematic Reviews 2017, Issue 2. Art. No.: CD001055. Psychosocial interventions to support women to stop smoking in pregnancy can increase the proportion of women who stop smoking in late pregnancy and the proportion of infants born low birthweight. Counselling, feedback and incentives appear to be effective, however the characteristics and context of the interventions should be carefully considered. The effect of health education and social support is less clear. New trials have been published during the preparation of this review and will be included in the next update.

Chami HA, Isma'eel H, Tamim H, et al. The Association of **Waterpipe Smoking and Coronary Artery Calcium** in a Community-Based Sample. Chest. 2019 Jan 23.

Chan SS, Cheung YT, Fong DY, et al. **Family-Based Smoking Cessation Intervention** for Smoking Fathers and Nonsmoking Mothers with a Child: A Randomized Controlled Trial. J Pediatr. 2016 Dec 15.

Chandler MA, Rennard SI. **Smoking cessation**. Chest. **2010** Feb;137(2):428-35.

Chang AY, Barry M. The **Global Health Implications of e-Cigarettes**. JAMA. 2015 Aug 18;314(7):663-4.

Chang CM, Corey CG, Rostron BL, et al. Systematic review of **cigar smoking** and all cause and smoking related mortality. BMC Public Health. 2015 Apr 24;15(1):390.

Chapman S, Mackenzie R. The global research neglect of **unassisted smoking cessation**: causes and consequences. PLoS Med. 2010 Feb 9;7(2):e1000216.

Chapman S. Should **electronic cigarettes** be as freely available as tobacco cigarettes? No. BMJ. 2013 Jun 14;346:f3840.

Chapman S. When will the tobacco industry **apologise for its monstrous harms**? BMJ. 2014 Jan 29;348:g437.

Chapman S. **E-cigarettes**: the **best and the worst case scenarios** for public health-an essay by Simon Chapman. BMJ. 2014 Sep 9;349:g5512.

Chastang J, Baïz N, Cadwalladder JS, et al. **Postnatal Environmental Tobacco Smoke Exposure** Related to **Behavioral Problems** in Children. PLoS One. 2015 Aug 5;10(8):e0133604.

Chaturvedi P, Singh A, Chien CY, Warnakulasuriya S. **Tobacco related oral cancer**. BMJ. 2019 Jun 5;365:l2142.

Chen LS, Baker TB, Piper ME, et al. Interplay of **genetic risk factors (CHRNA5-CHRNA3-CHRNB4)** and cessation treatments in smoking cessation success. Am J Psychiatry 2012

Chen R, Zhang D, Chen Y, et al. Passive smoking and risk of **cognitive impairment** in women who never smoke. Arch Intern Med. 2012 Feb 13;172(3):271-3.

Chen Z, Peto R, Zhou M, et al, for the China Kadoorie Biobank (CKB) collaborative group. Contrasting **male and female trends in tobacco-attributed mortality in China**: evidence from successive nationwide prospective cohort studies. Lancet 2015; 386: 1447–56

Chinthapalli K. **Exporting disease, disability, and death**. BMJ. 2014 Apr 8;348:g2221.

Cho K, Frijters JC, Zhang H, et al. **Prenatal Exposure to Nicotine** and Impaired **Reading Performance**. J Pediatr. 2012 Nov 1.

Choi A, Le M, Rahim T, et al. **Electronic cigarette exposures reported** to the British Columbia Drug and Poison Information Centre: an observational case series. CMAJ Open. 2019 Jul 18;7(3):E462-E471.

Chung HY, Machado P, van der Heijde D, et al. Smokers in **early axial spondyloarthritis** have earlier disease onset, more disease activity, inflammation and damage, and poorer function and healthrelated quality of life: results from the DESIR cohort. Ann Rheum Dis. Published Online First: 11 Oct 2011.

Christakis NA, Fowler JH. The collective dynamics of smoking in a **large social network**. N Engl J Med. 2008 May 22;358(21):2249-58. Network phenomena appear to be relevant to smoking cessation. Smoking behavior spreads through close and distant social ties, groups of interconnected people stop smoking in concert, and smokers are increasingly marginalized socially

Ciaccio CE, Gurley-Calvez T, Shireman TI. **Indoor tobacco legislation** is associated with fewer emergency department visits for asthma exacerbation in children. Ann Allergy Asthma Immunol. 2016 Dec;117(6):641-645.

Cinciripini PM, Robinson JD, Karam-Hage M, et al. Effects of **Varenicline and Bupropion** Sustained-Release Use Plus Intensive Smoking Cessation Counseling on Prolonged Abstinence From Smoking and on Depression, Negative Affect, and Other Symptoms of Nicotine Withdrawal. JAMA Psychiatry. 2013 Mar 27:1-12.

Ciurea A, Scherer A, et al. behalf of Rheumatologists of Swiss Clinical Quality Management Program for Axial Spondyloarthritis. **Impaired response to treatment with tumour necrosis factor α inhibitors** in smokers with axial spondyloarthritis. Ann Rheum Dis. 2015 Feb 9.

Ciurea A, et al; on behalf of the Rheumatologists of Swiss Clinical Quality Management Program for Axial Spondyloarthritis. **Impaired response to treatment with tumour necrosis factor α inhibitors** in smokers with **axial spondyloarthritis**. Ann Rheum Dis. 2015 Feb 9.

Civljak M, Sheikh A, Stead LF, et al. **Internet-based interventions** for smoking cessation. Cochrane Database Syst Rev. 2010 Sep 8;9:CD007078.

Clair C, Rigotti NA, Porneala B, et al. Association of smoking cessation and **weight change** with **cardiovascular disease** among adults with and without diabetes. JAMA. 2013;309(10):1014-1021.

Clark S, Naka R. Pharmacotherapeutic Management of **Nicotine Dependence in Pregnancy**. Obstet Gynecol Clin N Am 38 (2011) 297–311.

Clarke JG, Stein LA, Martin RA, et al. **Forced Smoking Abstinence**: Not Enough for Smoking Cessation. JAMA Intern Med. 2013 Apr 8:1-6.

Clearie KL, McKinlay L, Williamson PAet al. **Fluticasone/salmeterol** combination confers benefi ts in people with **asthma** who smoke. Chest. 2012;141 (2): 330 -338.

Cobb Nathan K., Abrams David B. **E-Cigarette** or Drug-Delivery Device? Regulating Novel Nicotine Products. N Engl J Med 2011; 365:193-195.

Cobb NK, Abrams DB. The FDA, e-cigarettes, and the demise of combusted tobacco. N Engl J Med. 2014 Oct 16;371(16):1469-71.

Cohen JE. **Saving lives with the US Tobacco Control Act**. Lancet 2013; 381:1513-1514.

Cole HM, Fiore MC. The **war against tobacco: 50 years** and counting. JAMA. doi:10.1001/jama.2013.280767.

Coleman HG, Bhat S, Johnston BT, et al. Tobacco Smoking Increases the Risk of **High-Grade Dysplasia and Cancer Among Patients With Barrett's Esophagus**. Gastroenterology. 2011 Nov 4.

Coleman T, Cooper S, Thornton JG, et al. A randomized trial of **nicotine-replacement therapy patches in pregnancy**. N Engl J Med 2012;366:808-18.

Colivicchi F, Mocini D, Tubaro M, et al. Effect of smoking relapse on outcome **after acute coronary syndromes**. Am J Cardiol. 2011 Sep 15;108(6):804-8.

Collaborative Group on Epidemiological Studies of Ovarian Cancer. **Ovarian cancer** and smoking: individual participant meta-analysis including 28,114 women with ovarian cancer from 51 epidemiological studies. Lancet Oncol. 2012 Aug 2.

Collaco JM, Drummond MB, McGrath-Morrow SA. **Electronic Cigarette** Use and **Exposure** in the **Pediatric** Population. JAMA Pediatr. 2014 Dec 29.

Collaco JM, Aherrera AD, Breysse PN, et al. Hair **Nicotine Levels in Children With Bronchopulmonary Dysplasia**. Pediatrics. 2015 Feb 2.

Collins GB, Jerry JM, Bales R. **Quitting smoking**: Still a challenge, but newer **tools** show promise. Cleve Clin J Med. 2015 Jan;82(1):39-48.

Collins RL and Martino SC. **Noncigarette Tobacco Advertising** May Be Hazardous to a Teen's Health. Peds.2017;139(6):e20170887

Conen David, Everett Brendan M., Kurth Tobias, et al. Smoking, Smoking Status, and Risk for Symptomatic **Peripheral Artery Disease** in Women: A Cohort Study. Ann Intern Med June 7, 2011 154:719-726.

Connolly, Gregory N., Richter, Patricia, Aleguas, Alfred, Jr, et al. **Unintentional Child Poisonings** Through Ingestion of Conventional and Novel Tobacco Products. Pediatrics 2010 0: peds.2009-2835

Cook BL,Wayne GF, Kafali EN, et al. Trends in smoking among adults with **mental illness** and association between mental health treatment and smoking cessation. JAMA. doi:10.1001 /jama.2013.284985.
Cook MB, Shaheen NJ, Anderson LA, et al. Cigarette Smoking Increases **Risk of Barrett's Esophagus**: An Analysis of the Barrett's and Esophageal Adenocarcinoma Consortium. Gastroenterology. 2012 Jan 11.
Cook R, Davidson P, Martin R; NIHR Dissemination Centre. **E-cigarettes helped more smokers quit** than nicotine replacement therapy. BMJ. 2019 May 10;365:l2036.
Cooper S, Taggar J, et al; Smoking, Nicotine and Pregnancy (**SNAP**) Trial Team. Effect of **nicotine patches in pregnancy** on infant and maternal outcomes at 2 years: follow-up from the randomised, double-blind, placebo-controlled SNAP trial. Lancet Respir Med.2014 Aug 8.
Corbett SE, Nitzberg M, Moses E, et al. **Gene Expression Alterations in the Bronchial Epithelium** of Electronic Cigarette Users. Chest. 2019 Jun 21.
Corey C, Wang B, Johnson SE, et al. Notes from the field: **Electronic cigarette use among middle and high school students**—United States, 2011-2012. MMWR Morb Mortal Wkly Rep 2013; 62:729-730.
Cosgrove KP, Esterlis I, McKee SA, et al. Sex Differences in Availability of **β2*-Nicotinic Acetylcholine Receptors** in Recently Abstinent Tobacco Smokers. Arch Gen Psychiatry. 2012 Apr;69(4):418-27.
Cox B, Martens E, Nemery B, et al. Impact of a stepwise introduction of **smoke-free legislation** on the rate of **preterm births**: analysis of routinely collected birth data. BMJ. 2013 Feb 14;346:f441.
Crawford P, Cieslak D. **Varenicline** for Smoking Cessation. Am Fam Physician. 2017 Sep 1;96(5):Online.
Cressman AM, Pupco A, Kim E, et al. **Smoking cessation therapy during pregnancy**. Can Fam Physician. 2012 May;58(5):525-7.
Crippen MM, Patel N, Filimonov A, et al. Association of Smoking Tobacco With **Complications in Head and Neck Microvascular Reconstructive Surgery**. JAMA Facial Plast Surg. 2018 Oct 18.
Cross E, Garrison S, Kolber MR. **Electronic cigarettes**: help, hurt, or hype? Can Fam Physician. 2016 Jan;62(1):51. PubMed PMID: 26796835
Crowley RA; Health Public Policy Committee of the American College of Physicians. Electronic nicotine delivery systems: executive summary of a policy position paper from the american college of physicians. Ann Intern Med. 2015 Apr 21;162(8):583-4.
Croyle RT, Morgan GD, Fiore MC. Addressing a Core Gap in Cancer Care - The NCI **Moonshot Program to Help Oncology Patients Stop Smoking**. N Engl J Med. 2019 Jan 2.
CTFPHC-Canadian Task Force on Preventive Health Care. Recommendations on **behavioural interventions for the prevention and treatment of cigarette smoking among school-aged children and youth**. CMAJ. 2017 Feb 27;189(8):E310-E316.
Cunningham P. **Patient Engagement** During Medical Visits and Smoking Cessation Counseling. JAMA Intern Med. 2014 Jun 9.
Cunningham JA, Kushnir V, Selby P, et al. Effect of **Mailing Nicotine Patches** on Tobacco Cessation Among Adult Smokers : A Randomized Clinical Trial. JAMA Intern Med. 2016 Jan 25.
Dai H. Tobacco Product Use **Among Lesbian, Gay, and Bisexual Adolescents.** Pediatrics. 2017:139(4):e20163276
Dai H. **Attitudes Toward Tobacco 21 Among US Youth**. Peds. 2017'140(1):e20170570
Dai H, Catley D, Richter KP, et al. **Electronic Cigarettes and Future Marijuana Use**: A Longitudinal Study. Pediatrics. 2018 Apr 23.
Dai H, Hao J. **Flavored Electronic Cigarette Use** and Smoking Among **Youth**. Pediatrics. 2016:138(6): e20162513.
Dai H, Leventhal AM. Prevalence of **e-Cigarette Use Among Adults** in the United States, 2014-2018. JAMA. 2019 Sep 16
Daly JB, Mackenzie LJ, Freund M, et al. **Interventions by Health Care Professionals** Who Provide Routine Child Health Care to **Reduce Tobacco Smoke Exposure in Children**: A Review and Meta-analysis. JAMA Pediatr. 2015 Dec 21:1-10.
Darzi A, Keown OP, Chapman S. Is a **smoking ban in UK parks and outdoor spaces** a good idea? BMJ. 2015 Feb 25;350:h958.
Daube M, Moodie R, McKee M. Towards a smoke-free world? **Philip Morris International's new Foundation is not credible**. Lancet. 2017 Oct 14;390(10104):1722-1724.
David SP, Lancaster T, Stead LF, et al. **Opioid antagonists (naltrexone) for smoking cessation**. Cochrane Database Syst Rev. 2013 Jun 6;6:CD003086. doi: 10.1002/14651858.CD003086.pub3. Based on data from eight trials and over 1200 individuals, there was no evidence of an effect of naltrexone alone or as an adjunct to NRT on long-term smoking abstinence, with a point estimate strongly suggesting no effect and confidence intervals that make a clinically important effect of treatment unlikely.
de Boer SP, Serruys PW, Valstar G, et al; interventional cardiologists of the Thoraxcentre 1980 to 1985. **Life-Years Gained by Smoking Cessation After Percutaneous Coronary Intervention**. Am J Cardiol. 2013 Jul 25.
De Pergola G, Ciampolillo A, Alò D, et al. **Free Triiodothyronine** is associated with smoking habit, independently of obesity, body fat distribution, insulin, and metabolic parameters. J Endocrinol Invest. 2010 Jul 13.
de Rooy DP, van Nies JA, Kapetanovic MC, et al. Smoking as a risk factor for the radiological severity of **rheumatoid arthritis**: a study on six cohorts. Ann Rheum Dis. 2014 Jul;73(7):1384-7.
Decramer M; on behalf of the **European Respiratory Roadmap** Initiative. The European Respiratory Roadmap. Lancet. 2011 Jun 22. (for smoking legislation)
Dehghani P, Habib B, Windle SB, et al. **Smokers and Postcessation Weight Gain** After Acute Coronary Syndrome. J Am Heart Assoc. 2017 Apr 18;6(4)
Demissie Z, Everett Jones S, Clayton HB, et al. **Adolescent Risk Behaviors** and Use of **Electronic Vapor Products** and Cigarettes. Pediatrics. 2017 Jan 23.
Desai NR, Mega JL, Jiang S, et al. Interaction between cigarette smoking and clinical benefit of clopidogrel. J Am Coll Cardiol 2009; 53:1273-1278.
Desai RJ, Good MM, San-Juan-Rodriguez A, et al**. Varenicline and Nicotine Replacement Use** Associated With US Food and Drug Administration Drug Safety Communications. JAMA Netw Open. 2019 Sep 4;2(9):e1910626.
Dhalwani NN, Szatkowski L, Coleman T, et al. **Nicotine Replacement Therapy in Pregnancy** and Major Congenital Anomalies in Offspring. Pediatrics. 2015 Apr 6.
Diaz AA, Petersen H, Meek P, et al. Differences in Health-related Quality of Life Between New **Mexican Hispanic and Non-Hispanic White Smokers**. Chest. 2016 Jun 16.
Diaz AA, Strand M, Coxson HO, et al. Disease Severity Dependence Of The Longitudinal Association Between **CT Lung Density And Lung Function In Smokers**. Chest. 2017 Oct 21.
Dinakar C, O'Connor GT. The **Health Effects of Electronic Cigarettes**. N Engl J Med. 2016 Oct 6;375(14):1372-1381.
Ding N, Sang Y, Chen J, et al. Cigarette Smoking, Smoking Cessation, and Long-Term **Risk of 3 Major Atherosclerotic Diseases**. J Am Coll Cardiol. 2019 Jul 30;74(4):498-507.
DiPaula BA, Thomas MD. Worsening **psychosis induced by varenicline** in a hospitalized psychiatric patient. Pharmacotherapy. 2009 Jul;29(7):852-7.
Ditre JW et al. **Nicotine deprivation** increases **pain** intensity, neurogenic **inflammation**, **and mechanical hyperalgesia** among daily tobacco smokers. J Abnorm Psychol 2018 May 21.
Do **electronic cigarettes** help with smoking cessation? Drug Ther Bull. 2014 Nov;52(11):126-9.
Dolk H, Wang H, Loane M, et al. **Lamotrigine use in pregnancy** and risk of orofacial cleft and other congenital anomalies. Neurology. 2016 May 3;86(18):1716-25.
Donny EC, Denlinger RL, Tidey JW, et al. Randomized Trial of **Reduced-Nicotine Standards for Cigarettes**. N Engl J Med. 2015 Oct;373(14):1340-9.
Downard CD, Grant SN, Maki AC, et al. Maternal Cigarette Smoking and the Development of **Necrotizing Enterocolitis**. Pediatrics. 2012 Jun 11.
Drazen JM, Morrissey S, Campion EW. The **Dangerous Flavors of E-Cigarettes**. N Engl J Med. 2019 Feb 14;380(7):679-680
Drehmer JE, Nabi-Burza E, Hipple Walters B, et al. Parental Smoking and E-cigarette **Use in Homes and Cars**. Pediatrics. 2019 Mar 11.
Drug and Therapeutics Bulletin. Republished: **Nicotine and health**. BMJ. 2014 Nov 26;349:2014.
Drugs in Pregnancy and Lactation. 9th ed. Briggs GE, Freeman RK, Yaffe SJ, editors. Williams and Wilkins; Philadelphia, PA: 2011.
Drummond MB. **Electronic Cigarettes**: Perhaps the Devil Unknown Is Better Than the Devil Known. Ann Intern Med. 2015 Jul 7;163(1):61-2.
Duffy EK, Jenssen BP. **Electronic cigarettes**: the new face of nicotine. Pediatrics. 2014 Jul;134(1):1-3.
Dugas E, Tremblay M, Low NC, et al. **Water-pipe smoking** among North American youths. Pediatrics. 2010;125:1184-1189. Abstract
Duijts L, Jaddoe VW, van der Valk RJ, et al. **Fetal exposure to maternal and paternal smoking** and the risks of wheezing in preschool children: the generation R study. Chest. 2012 Apr;141(4):876-85.
Duke JC, Lee YO, Kim AE, et al. Exposure to **Electronic Cigarette Television Advertisements** Among Youth and Young Adults. Pediatrics. 2014 Jun 2.
Duncan MS, Freiberg MS, Greevy RA Jr, et al. Association of Smoking Cessation With **Subsequent Risk of Cardiovascular Disease.** JAMA. 2019 Aug 20;322(7):642-650.
Dutra LM, Glantz SA. **Electronic cigarettes** and conventional cigarette use among **US adolescents**: a cross-sectional study [online March 6, 2014]. JAMA Pediatr. doi:10.1001/jamapediatrics.2013.5488.
Dutra LM, Glantz SA. **E-cigarettes** and National **Adolescent** Cigarette Use: 2004-2014. Pediatrics. 2017 Jan 23.
Duval S, Long KH, Roy SS, et al. The Contribution of Tobacco Use to High Health Care Utilization and Medical Costs in **Peripheral Artery Disease**: A State-Based Cohort Analysis. J Am Coll Cardiol. 2015 Oct 6;66(14):1566-74.
Ebbert JO, Hatsukam DK, Croghan IT, et al. Combination **varenicline and bupropion SR** for tobacco-dependence treatment in cigarette smokers: a randomized trial. JAMA.doi:10.1001/jama.2013.283185.
Ebbert JO, Agunwamba AA, Rutten LJ. Counseling Patients on the Use of **Electronic Cigarettes**. Mayo Clin Proc. 2015 Jan;90(1):128-134.
E-Cigarette- http://en.wikipedia.org/wiki/E-cigarette ; (FDA and Public Health Experts Warn About Electronic Cigarettes July,2009 http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm173222.htm)
Ebbert JO, Burke MV, Hays JT, Hurt RD. **Combination treatment with varenicline and nicotine** replacement therapy. Nicotine Tob Res. 2009;11(5):572-576.
Ebbert J, Montori VM, Erwin PJ, et al. Interventions for **smokeless tobacco** use cessation. Cochrane Database Syst Rev. 2011 Feb 16;2:CD004306. Varenicline and behavioural interventions may help ST users to quit. Behavioural interventions incorporating telephone counselling or an oral examination are likely to increase abstinence rates.
Ebbert JO, Hughes JR, West RJ, et al. Effect of **varenicline** on smoking cessation through **smoking reduction**: a randomized clinical trial. JAMA. 2015 Feb 17; 313(7):687-94.
Ebbert JO, Elrashidi MY, et al. Interventions for **smokeless tobacco use cessation**. Cochrane Database Syst Rev. 2015 Oct 26;10:CD004306. Varenicline, nicotine lozenges and behavioural interventions may help ST users to quit. Confidence in results for nicotine lozenges is limited. Confidence in the size of effect from behavioural interventions is limited because the components of behavioural interventions that contribute to their impact are not clear.
Ebbert JO, Jacobson RM. Reducing **Childhood Tobacco Smoke Exposure**. JAMA. 2016 Jun 21;315(23):2610-1.
Eder L, Shanmugarajah S, Thavaneswaran A et al. The association between smoking and the development of **psoriatic arthritis** among psoriasis patients. Ann Rheum Dis. 2012 Feb;71(2):219-24.
Eisenberg MJ, Filion KB, Yavin D, Bélisle P, Mottillo S, Joseph L, Gervais A, O'Loughlin J, Paradis G, Rinfret S, Pilote L. Pharmacotherapies for smoking cessation: a **meta-analysis** of randomized controlled trials. CMAJ. 2008 Jul 15;179(2):135-44. Varenicline, bupropion and the 5 nicotine replacement therapies were all more efficacious than placebo at promoting smoking abstinence at 6 and 12 mon
Eisenberg MJ, Grandi SM, Gervais A, et al. **Bupropion** for smoking cessation in patients hospitalized with **acute myocardial infarction**. (**ZESCA**) J Am Coll Cardiol 2013.
Eisenberg MJ, Windle SB, Roy N, et al. **Varenicline** for Smoking Cessation in Hospitalized Patients With **Acute Coronary Syndrome**. (**Evita**) Circulation. 2015 Nov 9.
Eisenberg MJ, Windle SB, Roy N, et al; **EVITA** Investigators. **Varenicline** for Smoking Cessation in Hospitalized Patients With **Acute Coronary Syndrome**. Circulation. 2016 Jan 5;133(1):21-30.
Ekblad M, Gissler M, Lehtonen L, Korkeila J. **Prenatal smoking exposure** and the risk of psychiatric morbidity into young adulthood. Arch Gen Psychiatry. 2010 Aug;67(8):841-9.
El-Toukhy S, Sabado M, Choi K. Trends in **Susceptibility** to Smoking by **Race and Ehtnicity**. Pediatrics. 2016.138(5) :e2016254
Ellerbeck EF, Mahnken JD, Cupertino AP, et al. Effect of varying levels of **disease management** on smoking cessation: a randomized trial. Ann Intern Med. 2009 Apr 7;150(7):437-46.
Ellerbeck EF, Nollen N, Hutcheson TD, et al. Effect of **Long-term Nicotine Replacement Therapy vs Standard Smoking Cessation for Smokers With Chronic Lung Disease** A Randomized Clinical Trial. JAMA Netw Open. 2018;1(5):e181843.
Els Charl, Kunyk Diane, Sidhu Harkirat. Smoking cessation and **neuropsychiatric adverse events**: Are family physicians caught between a rock and a hard place? Can Fam Physician June 2011 57: 647-649.
Elton-Marshall, Tara, Leatherdale, Scott T., Burkhalter, Robin. **Tobacco, alcohol and illicit drug use among Aboriginal youth** living off-reserve: results from the Youth Smoking Survey. CMAJ 2011 183: E480-486

Engelhard MM, Oliver JA, Henao R, et al. Identifying **Smoking Environments From Images of Daily Life** With Deep Learning. JAMA Netw Open. 2019 Aug 2;2(8):e197939.
Epstein KA, Viscoli CM, Spence JD, et al. **Smoking cessation and outcome after ischemic stroke or TIA**. Neurology 2017;89:1723–1729.
Eriksson K, Nise L, Alfredsson L, et al. **Seropositivity combined with smoking** is associated with increased prevalence **of periodontitis in patients with rheumatoid arthritis**. Ann Rheum Dis. 2017 Oct 6.
Erwin BL, Slaton RM. **Varenicline** in the Treatment of **Alcohol Use Disorders**. Ann Pharmacother. 2014 Nov;48(11):1445-1455.
Etter JF. **Cytisine** for smoking cessation: a literature review and a meta-analysis. Arch Intern Med. 2006 Aug 14-28;166(15):1553-9.
Etter JF, Huguelet P, et al. **Nicotine gum** treatment before smoking cessation: a randomized trial. Arch Intern Med. 2009 Jun 8;169(11):1028-34. Starting nicotine gum treatment 4 weeks before the target quit date was no more effective than starting treatment on the quit date.
Etter JF. Should **electronic cigarettes** be as freely available as tobacco? Yes. BMJ. 2013 Jun 14;346:f3845.
Etter JF, Schmid F. Effects of Large **Financial Incentives** for Long-Term Smoking Cessation: A Randomized Trial. J Am Coll Cardiol. 2016 Aug 23;68(8):777-85.
Evans AT, Peters E, Strasser AA, Emery LF, et al. **Graphic Warning Labels** Elicit Affective and Thoughtful Responses from Smokers: Results of a Randomized Clinical Trial. PLoS One. 2015 Dec 16;10(12):e0142879.
Evans CM, Dickey BF, Schwartz DA**. E-Cigarettes: Mucus Measurements** Make Marks. Am J Respir Crit Care Med. 2017 Nov 21.
Evlampidou I, Bagkeris M, Vardavas C, et al. M. **Prenatal Second-Hand Smoke Exposure Measured with Urine Cotinine** May Reduce Gross Motor Development at 18 Months of Age. J Pediatr. 2015 Apr 8.
Evins AE, Cather C, Pratt SA, et al. **Maintenance treatment with varenicline** for smoking cessation in patients with schizophrenia and bipolar disorder: a randomized clinical trial. JAMA. doi:10.1001/jama.2013.285113.
Faber T, Kumar A, Mackenbach JP, et al. Effect of **tobacco control policies on perinatal and child health**: a systematic review and meta-analysis. Lancet Public Health 2017; 2: e420–37.
Fagerström Karl, Gilljam Hans, Metcalfe Michael, et al. **Stopping smokeless tobacco with varenicline**: randomised double blind placebo controlled trial. BMJ 341:doi:10.1136/bmj.c6549 (Published 6 Dec 2010).
Fairchild AL, Bayer R, Colgrove J. The Renormalization of Smoking? **E-Cigarettes** and the Tobacco "Endgame". N Engl J Med. 2013 Dec 18
Fairchild AL, Lee JS, Bayer R, et al. **E-Cigarettes and the Harm-Reduction Continuum.** N Engl J Med. 2018 Jan 18;378(3):216-219.
Falkstedt D, Wolff V, Allebeck P, et al. **Cannabis, Tobacco, Alcohol Use**, and the Risk of Early **Stroke**: A Population-Based Cohort Study of 45 000 Swedish Men. Stroke. 2017 Feb;48(2):265-270.
Fang X, Wang X, Bai C. **COPD in China**: The Burden and Importance of Proper Management. Chest. 2011 Apr;139(4):920-9.
Fanshawe TR, Halliwell W, Lindson N, et al. **Tobacco cessation interventions for young people.** Cochrane Database Syst Rev. 2017 Nov 17;11:CD003289. There is limited evidence that either behavioural support or smoking cessation medication increases the proportion of young people that stop smoking in the long-term. Findings are most promising for group-based behavioural interventions, but evidence remains limited for all intervention types. There continues to be a need for well-designed, adequately powered, randomized controlled trials of interventions for this population of smokers.
Farley AC, Hajek P, Lycett D, et al. Interventions for **preventing weight gain** after smoking cessation. Cochrane Database Syst Rev. 2012 Jan 18;1:CD006219. Although some pharmacotherapies tested to limit PCWG show evidence of short-term success, other problems with them and the lack of data on long-term efficacy limits their use. Weight management education only, is not effective and may reduce abstinence. Personalised weight management support may be effective and not reduce abstinence, but there are too few data to be sure.
Faseru B, Richter KP, Scheuermann TS, et al. Enhancing partner support to improve smoking cessation. Cochrane Database Syst Rev. 2018 Aug 13;8:CD002928. Interventions that aim to enhance partner support appear to have no impact on increasing long-term abstinence from smoking. However, most interventions that assessed partner support showed no evidence that the interventions actually achieved their aim and increased support from partners for smoking cessation. Future research should therefore focus on developing behavioural interventions that actually increase partner support, and test this in small-scale studies, before large trials assessing the impact on smoking cessation can be justified.
FDA Chantix/**Champix** Warning Feb/2008: 491 **suicide** reports; **39 completed**. **Canada**: **46 psychiatric** adverse reactions reported from April 1-Nov23/07
FDA and Public Health Experts Warn About **Electronic Cigarettes** July,2009 Laboratory analysis of electronic cigarette samples has found that they contain carcinogens and toxic chemicals such as diethylene glycol, an ingredient used in antifreeze. http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm173222.htm
FDA Aug, 2009 — Announced the launch of a new division, the **Center for Tobacco Products**, "in an historic effort to curb the hundreds of thousands of deaths caused by those products each year." The new center will oversee the Family Smoking Prevention and Tobacco Control Act, signed into law by President Barack Obama in June 2009.
FDA May/11 has decided to oversee **electronic cigarettes** the same way it does tobacco products.
FDA June/11 drug safety communication: **Chantix (varenicline) may increase the risk of certain cardiovascular adverse events** in patients with cardiovascular disease.
FDA Quit Smoking package **images** 2011 http://www.fda.gov/downloads/TobaccoProducts/Labeling/UCM259401.pdf
FDA July/11 has approved an updated drug label for the smoking cessation aid Chantix (**varenicline**) to include information about the efficacy and safety of the drug in two patient populations who may benefit greatly from giving up smoking—those with cardiovascular disease and those with chronic obstructive pulmonary disease (COPD).
FDAOct/11 has reviewed the results from two FDA-sponsored epidemiological studies that evaluated the risk of **neuropsychiatric adverse** events associated with the smoking cessation drug **Chantix (varenicline).** Neither study found a difference in risk of neuropsychiatric hospitalizations between Chantix and nicotine replacement therapy (NRT; e.g., NicoDerm patches). However, both studies had a number of study design limitations, including only assessing neuropsychiatric events that resulted in hospitalization, and not having a large enough sample size to detect rare adverse events (see 10/24/2011 Drug Safety Communication below for more information). Healthcare professionals and patients should continue to follow the recommendations in the physician label and the patient Medication Guide, and to monitor for neuropsychiatric symptoms when prescribing or using Chantix. The drug manufacturer is conducting a large safety clinical trial of Chantix to assess neuropsychiatric adverse events, and results from this study are expected in 2017.
FDA Dec/12 is informing the public about the results of a large, combined analysis (called a meta-analysis) of clinical trials that compared patients who received the smoking cessation drug **Chantix (varenicline)** to patients who received a placebo (an inactive treatment). A higher occurrence of major adverse cardiovascular events (a combined outcome of cardiovascular-related death, nonfatal heart attack, and nonfatal stroke) was observed in patients using Chantix compared to placebo. These events were uncommon in both the Chantix and placebo groups, and the increased risk was not statistically significant, which means it is uncertain whether the excess risk for the Chantix group was due to the drug or due to chance.
FDA Apr/13 is allowing makers of **nicotine-replacement products to change their labeling "to allow some flexibility on how they are used and for how long**," the agency announced. Almost 30 years' experience with the products shows that they "do not appear to have significant potential for abuse or dependence," according to the FDA. Nor are there safety concerns about people using the products even while continuing to smoke or using two products simultaneously. In addition, the agency says if smokers believe they need to use a product longer than the recommended 2 to 3 months in order to quit, "it is safe to do so in most cases."
FDA Mar/15 is warning that the prescription smoking cessation medicine **Chantix (varenicline) can change the way people react to alcohol**. Interactions between alcohol and Chantix have resulted in some patients experiencing increased intoxicating effects of alcohol, sometimes associated with aggressive behavior and/or amnesia. In addition, rare accounts of seizures in patients treated with Chantix have been reported. FDA has approved changes to the Chantix label to warn about these risks.
FDA Dec/16 review of a large clinical trial that FDA required the drug companies to conduct, FDA determined the **risk of serious side effects on mood, behavior, or thinking** with the stop-smoking medicines **Chantix** (varenicline) and Zyban (bupropion) is lower than previously suspected. The risk of these mental health side effects is still present, especially in those currently being treated for mental illnesses such as depression, anxiety disorders, or schizophrenia, or who have been treated for mental illnesses in the past. As a result of the large clinical trial review, **FDA is removing the Boxed Warning**, FDA's most prominent warning, for serious mental health side effects from the Chantix drug label. The language describing the serious mental health side effects seen in patients quitting smoking will also be removed from the Boxed Warning in the **Zyban** label. FDA is also updating the existing warning section in both labels that describes the side effects on mood, behavior, or thinking to include the results from the clinical trial.
FDA Apr/19: E-cigarette: Safety Communication - Related to **Seizures Reported Following E-cigarette Use**, Particularly in Youth and Young Adults.
FDA May/19 has become aware that some people who use e-cigarettes have experienced seizures, with most reports involving youth or young adult users.
FDA Jun/19: Drip More, LP (Drip More) is voluntarily recalling four lots of Candy King – Worms 3mg/100mL that were produced by a contract manufacturer. The product has been found to contain a higher concentration of nicotine than the label indicates.
FDA Sep/19: E-Cigarette Products: Safety Communication - Due to the Incidents of **Severe Respiratory Disease Associated with Use of an E-Cigarette Product**.
FDA Oct/19 is strengthening its warning to consumers to stop using vaping products containing THC amid more than 1,000 reports of lung injuries—including some resulting in deaths—following the use of vaping products. FDA on Friday urged consumers to stop using vaping products that contain tetrahydrocannabinol (THC) or any vaping product obtained off the street, from friends, or otherwise illicitly. The recommendation came a day after the CDC reported 1080 cases of lung injury tied to vaping, with most involving THC. In its warning, the FDA also advised the following: Don't add THC, other oils, or any other substances to vaping products. Children and pregnant women shouldn't vape. Adults who use e-cigarettes as a replacement for traditional cigarettes should not return to traditional cigarettes. Those who vape should be on alert for symptoms like coughing, shortness of breath, and chest pain and should seek medical attention if they're concerned about their health. The agency also noted that it hasn't approved any vaping product for "therapeutic uses."
Feleszko W, Ruszczyn´ ski M, Jaworska J, et al. **Environmental tobacco smoke exposure** and risk of **allergic sensitisation** in **children**: a systematic review and meta-analysis. Arch Dis Child 2014;99:985–92.
Ferguson J, Docherty G, Bauld L, Lewis S, Lorgelly P, Boyd KA, et al. Effect of offering different levels of support and **free nicotine replacement therapy via an English national telephone quitline**: randomised controlled trial. BMJ 2012;344:e1696.
Ferreira GS, Steinberg MB. **Going Slow May Not Be Best** When Quitting Smoking. Ann Intern Med. 2016 May 3;164(9):622-3
Fetterman JL, Weisbrod RM, Feng B, et al. Flavorings in **Tobacco Products Induce Endothelial Cell Dysfunction**. Arterioscler Thromb Vasc Biol. 2018 Jul;38(7):1607-1615.
Filippidis FT, Laverty AA, Hone T, et al. Association of **Cigarette Price Differentials With Infant Mortality** in 23 European Union Countries. JAMA Pediatr. 2017 Sep 18.
Filion KB, Abenhaim HA, Mottillo S, et al. The effect of smoking cessation **counselling in pregnant women**: a meta-analysis of randomised controlled trials. BJOG. 2011 Nov;118(12):1422-8.
Fiore MC, Baker TB. Clinical practice. **Treating smokers in the health care setting**. N Engl J Med. 2011 Sep 29;365(13):1222-31
Fiore MC, Schroeder SA, Baker TB. Smoke, the chief killer--**strategies for targeting combustible tobacco** use. N Engl J Med. 2014 Jan 23;370(4):297-9
Fiore, MC. Tobacco Control in the **Obama Era**-Substantial Progress, Remaining Challenges. N Eng J Med.2016.
Fish JN, Turner B, Phillips G 2nd, Russell ST. Cigarette Smoking **Disparities Between Sexual Minority and Heterosexual Youth**. Pediatrics. 2019 Mar 12.
Foerster B, Pozo C, Abufaraj M, et al. **Association of smoking status** with recurrence, metastasis, and mortality among patients with localized **prostate cancer** undergoing prostatectomy or radiotherapy: a systematic review and meta-analysis [online May 24, 2018]. JAMA Oncol. doi:10.1001 /jamaoncol.2018.1071
Forinash Alicia B, Pitlick Jamie M, Clark Kylie, et al. **Nicotine Replacement Therapy Effect on Pregnancy Outcomes.** Articles Ahead of Print published on 1 November 2010, DOI 10.1345/aph.1P279.
Foulds J, Veldheer S, Yingst J, et al. Development of a questionnaire to assess dependence on **electronic cigarettes** in a large sample of ex-smoking e-cig users. Nicotine Tob Res. 2014 Oct 19.
Franck C, Budlovsky T, Windle SB, et al. **Electronic cigarettes** in north america: history, use, and implications for smoking cessation. Circulation. 2014 May 13;129(19):1945-52.
Franck C, Filion KB, Eisenberg MJ **Smoking Cessation in Patients With Acute Coronary Syndrome.** Am J Cardiol. 2018 Feb 6.
Fraser DL, Fiore MC, Kobinsky K, et al. A Randomized Trial of **Incentives for Smoking Treatment in Medicaid Members**. Am J Prev Med. 2017 Dec;53(6):754-763.
Franssen FM, Soriano JB, Roche N, et al. **Lung Function Abnormalities** in Smokers With Ischemic Heart Disease. Am J Respir Crit Care Med. 2016 Jul 21
Frazer K, Callinan JE, McHugh J, et al. **Legislative smoking bans** for reducing harms from secondhand smoke exposure, smoking prevalence and tobacco consumption. Cochrane Database of Systematic Reviews 2016, Issue 2. Art. No.: CD005992. DOI: 10.1002/14651858.CD005992.pub3. Since the first version of this review was published, the current evidence provides more robust support for the previous conclusions that the introduction of a legislative smoking ban does lead to improved health outcomes through reduction in SHS for

countries and their populations. The clearest evidence is observed in reduced admissions for acute coronary syndrome. There is evidence of reduced mortality from smoking-related illnesses at a national level. There is inconsistent evidence of an impact on respiratory and perinatal health outcomes, and on smoking prevalence and tobacco consumption.
Free C, Knight R, Robertson S, et al. Smoking cessation support delivered via **mobile phone text messaging** (**txt2stop**): a single-blind, randomised trial. Lancet 2011; published online June 30. DOI:10.1016/S0140-6736(11)60701-0.
Freedman R. **Exacerbation of schizophrenia by varenicline**. Am J Psychiatry. 2007 Aug;164(8):1269.
Freedman ND, Silverman DT, Hollenbeck AR, et al. Association between smoking and risk of **bladder cancer** among men and women. JAMA. 2011 Aug 17;306(7):737-45.
Frey P, Waters DD, Demicco DA, et al. Impact of **Smoking on Cardiovascular Events** in Patients With Coronary Disease Receiving Contemporary Medical Therapy (from the Treating to New Targets [TNT] and the Incremental Decrease in End Points Through Aggressive Lipid Lowering [IDEAL] Trials). Am J Cardiol. 2010 Dec 1.
Frieden TR. **Tobacco control progress** and potential. JAMA. doi:10.1001/jama.2013.284534.
Fu SS, van Ryn M, Sherman SE, et al. **Proactive Tobacco Treatment and Population-Level Cessation**: A Pragmatic Randomized Clinical Trial. JAMA Intern Med. 2014 Mar 10.
Fu L, Jacobs MA, Brookover J, et al. An exploration of the **Facebook social networks** of smokers and non-smokers. PLoS One. 2017 Nov 2;12(11):e0187332
Gagne JJ, Bykov K, Choudhry NK, et al. Effect of smoking on **comparative efficacy of antiplatelet agents**: systematic review, meta-analysis, and indirect comparison. BMJ. 2013 Sep 17;347:f5307. (clopidogrel benefit in smokers)
Galandiuk S. **E-cigarettes**: an asset or liability in efforts to lessen tobacco smoking and its consequences. Mayo Clin Proc. 2015 Jan;90(1):1-3.
Gall S, Huynh QL, Magnussen CG, et al. **Exposure to parental smoking in childhood or adolescence** is associated with increased carotid intima-media thickness in young adults: evidence from the Cardiovascular Risk in Young Finns study and the Childhood Determinants of Adult Health Study. Eur Heart J. 2014 Mar 4.
Gallo V, Vineis P, Cancellieri M, et al. Exploring causality of the association **between smoking and Parkinson's disease**. Int J Epidemiol. 2018 Nov 20.
García-Esquinas E, Loeffler LF, Weaver VM, et al. **Kidney Function** and Tobacco Smoke Exposure in US Adolescents. Pediatrics. 2013 Apr 8.
Garza D et al. A double-blind randomized placebo-controlled pilot study of **neuropsychiatric adverse events in abstinent smokers treated with varenicline** or placebo. Biol Psychiatry 2011 Jun 1; 69:1075. (limited efficacy & side effects)
Gaudet MM, Gapstur SM, Sun J, et al. Active Smoking and **Breast Cancer Risk**: Original Cohort Data and Meta-Analysis. J Natl Cancer Inst. 2013 Feb 28.
Gaysina D, Fergusson DM, Leve LD, et al. **Maternal Smoking During Pregnancy and Offspring Conduct Problems**: Evidence From 3 Independent Genetically Sensitive Research Designs. JAMA Psychiatry. 2013 Jul 24.
GBD 2015 Tobacco Collaborators. **Smoking prevalence and attributable disease burden in 195 countries** and territories, 1990–2015: a systematic analysis from the Global Burden of Disease Study 2015. Lancet 2017; online Apr 5.
Geerts CC, Bots ML, van der Ent CK, et al. **Parental Smoking** and Vascular Damage in Their 5-year-old Children. Pediatrics. 2012 Jan;129(1):45-54.
Geller AC, Rees VW, Brooks DR. The Proposal for **Smoke-Free Public Housing**: Benefits, Challenges, and Opportunities for 2 Million Residents. JAMA. 2016 Mar 15;315(11):1105-1106.
Gellert C, Schottker B, Brenner H. **Smoking and all-cause mortality** in older people: systematic review and meta-analysis. Arch Intern Med. 2012; 172(11):837-844.
Gennaro G, Brener SJ, Redfors B, et al. Effect of Smoking on Infarct Size and Major Adverse Cardiac Events in Patients With Large Anterior ST-Elevation **Myocardial Infarction** (from the INFUSE-AMI Trial). Am J Cardiol. 2016 Oct 15;118(8):1097-1104.
Germeroth LJ, Carpenter MJ, Baker NL, et al. Effect of a **Brief Memory Updating Intervention** on Smoking Behavior: A Randomized Clinical Trial. JAMA Psychiatry. 2017 Mar 1;74(3):214-223.
Gerber Y, Rosen LJ, Goldbourt U, et al. Smoking status and long-term survival after first acute **myocardial infarction**. J Am Coll Cardiol 2009; 54:2382-2387.
Gershon AS, Campitelli MA, Hawken S, et al. **Cardiovascular and Neuropsychiatric Events** Following **Varenicline** Use for Smoking Cessation. Am J Respir Crit Care Med. 2017 Dec 20
Ghosh TS, Tolliver R, Reidmohr A, Lynch M. Youth **Vaping and Associated Risk Behaviors** - A Snapshot of Colorado. N Engl J Med. 2019 Jan 30.
Gibbons RD, Mann JJ. **Varenicline, Smoking Cessation, and Neuropsychiatric Adverse Events**. Am J Psychiatry. 2013 Sep 13.
Gibbs K, Collaco JM, McGrath-Morrow SA. Impact of **Tobacco Smoke and Nicotine Exposure on Lung Development**. Chest. 2015 Oct 22.
Gibson L, Porter M. **Drinking or smoking while breastfeeding and later cognition in children**. Pediatrics. 2018;142(2):e20174266.
Gilbert H, Sutton S, Morris R, et al. Effectiveness of **personalised risk information** and taster sessions to increase the uptake of smoking cessation services (Start2quit): a randomised controlled trial. Lancet 2017; online Jan 24.
Giovino GA, Mirza SA, Samet JM, et al. The GATS Collaborative Group. **Tobacco use in 3 billion individuals** from 16 countries: An analysis of nationally representative cross-sectional household surveys. Lancet 2012; 380: 668-679.
Glantz SA, Gibbs E. Changes in **ambulance calls after implementation of a smoke-free law** and its extension to casinos. Circulation. 2013 Aug 20;128(8):811-3.
Glasser AM, Collins L, Pearson JL, et al. Overview of **Electronic Nicotine Delivery Systems**: A Systematic Review. Am J Prev Med. 2016 Nov 30.
Global Tobacco Economics Consortium. The **health, poverty, and financial consequences of a cigarette price** increase among 500 million male smokers in 13 middle income countries: compartmental model study. BMJ 2018;360:k1162.
Godtfredsen NS, Vestbo J, Osler M, Prescott E. Risk of hospital admission for **COPD following smoking cessation** and reduction: a Danish population study. Thorax. 2002 Nov;57(11):967-72.
Goel R, Trushin N, Reilly SM, et al. A survey of **nicotine yields in small cigar smoke**: influence of cigar design and smoking regimens. Nicotine Tob Res. 2017 Sep 27.
Goldenson NI, Leventhal AM, Stone MD, et al. Associations of **Electronic Cigarette Nicotine Concentration** With Subsequent Cigarette Smoking and Vaping Levels in Adolescents. JAMA Pediatr. 2017 Oct 23.
Goldoni M, Bonini S, Urban ML, et al. **Asbestos and smoking** as risk factors for idiopathic retroperitoneal fibrosis: a case-control study. Ann Intern Med. 2014 Aug 5;161(3):181-8.
Gomajee R, El-Khoury F, Goldberg M, et al. Association Between **Electronic Cigarette Use and Smoking Reduction** in France. JAMA Intern Med. 2019 Jul 15.
Goniewicz ML, Zielinska-Danch W. **Electronic Cigarette** Use Among Teenagers and Young Adults in Poland. Pediatrics. 2012 Sep 17.
Goniewicz ML, Knysak J, Gawron M, et al. Levels of selected **carcinogens and toxicants in vapour from electronic cigarettes**. Tob Control. 2013 Mar 6.
Goniewicz M, Gawron M, Smith D, et al. Exposure to **Nicotine and Selected Toxicants** in Cigarette Smokers Who Switched to **Electronic Cigarettes**: A Longitudinal Within-Subjects Observational Study. Nicotine & Tobacco Research.2016;0(0):1-8
Goniewicz ML, Smith DM, Edwards KC, et al. Comparison of **nicotine and toxicant exposure in users of electronic cigarettes** and combustible cigarettes. JAMA Netw Open. 2018;1(8):e185937. doi:10.1001/jamanetworkopen.2018.5937
González G, Ash SY, Vegas Sanchez-Ferrero G, et al. ; **COPDGene** and **ECLIPSE** investigators. Disease Staging and Prognosis in Smokers Using Deep Learning in **Chest Computed Tomography**. Am J Respir Crit Care Med. 2017 Sep 11.
Goodchild M, Nargis N, Tursan d'Espaignet E. **Global economic cost** of smoking-attributable diseases. Tob Control. 2017 Jan 30.
Goodwin RD, Cheslack-Postava K, Nelson DB, et al. **Smoking** during **pregnancy** in the United States, 2005-2014: The role of depression. Drug Alcohol Depend. 2017 Jul 18;179:159-166.
Goodwin RD, Pacek LR, Copeland J, et al. Trends in Daily **Cannabis Use Among Cigarette Smokers**: United States, 2002-2014. Am J Public Health. 2017 Nov 21:e1-e6
Goodwin RD, Cheslack-Postava K, Santoscoy S, et al. **Trends in Cannabis and Cigarette Use Among Parents** With Children at Home: 2002 to 2015. Pediatrics. 2018 May 14.
Goodwin RD, Cheslack-Postava K, Santoscoy S, et al. Trends in **Cannabis and Cigarette Use Among Parents With Children at Home**: 2002 to 2015. Pediatrics. 2018 Jun;141(6).
Gornall J. Slaying the dragon: how the **tobacco industry** refuses to die. BMJ. 2015 Apr 22;350:h2052.
Gornall J. Why **e-cigarettes are dividing the public health** community. BMJ.2015 Jun 24;350:h3317.
Gordon JS, Mahabee-Gittens EM, Andrews JA, et al. A Randomized Clinical Trial of a **Web-Based Tobacco Cessation** Education Program. Pediatrics. 2013 Jan 14.
Gornall J. **Electronic cigarettes**: medical device or consumer product? BMJ. 2012 Sep 25;345:e6417.
Gornall J. Big **tobacco, the new politics, and the threat to public health**. BMJ. 2019 May 15;365:l2164.
Gostin LO, Glasner AY. **E-Cigarettes, Vaping, and Youth**. JAMA. 2014 Jun 30.
Gottlieb S, Zeller M. A Nicotine-Focused Framework for Public Health. N Engl J Med. 2017 Aug 16.
Goto K, Nikolsky E, Lansky AJ, et al. Impact of Smoking on Outcomes of Patients **With ST-Segment Elevation Myocardial Infarction** (from the HORIZONS-AMI Trial). Am J Cardiol. 2011 Aug 23.
Gould GS, Lim LL, Mattes J. The prevention and treatment of **smoking and tobacco use during pregnancy in selected Indigenous communities** in high-income countries of USA, Canada, Australia and New Zealand: an evidence-based review. Chest. 2017 Jul 7.
Govindarajan P, Spiller HA, Casavant MJ, et al. **E-Cigarette and Liquid Nicotine Exposures Among Young Children**. Pediatrics. 2018 Apr 23.
Grana RA, Popova L, Ling PM. A Longitudinal Analysis of **Electronic Cigarette** Use and Smoking Cessation. JAMA Intern Med. 2014 Mar 24.
Grana R, Benowitz N, Glantz SA. **E-cigarettes**: a scientific review. Circulation. 2014 May 13;129(19):1972-86.
Graham Amanda L.; Cobb Nathan K.; Papandonatos George D.; et al. A Randomized Trial of Internet and Telephone Treatment for Smoking Cessation. Arch Intern Med. 2011;171(1):46-53.
Graif Y, German L, Ifrah A, Livne I, Shohat T. Dose-Response Association between Smoking and **Atopic Eczema**: Results from a Large Cross- Sectional Study in Adolescents. Dermatology. 2013 May 24.
Gravely S, Giovino GA, Craig L, et al. Implementation of key **demand-reduction measures of the WHO Framework Convention** on Tobacco Control and change in smoking prevalence in 126 countries: an association study. Lancet Public Health 2017; online March 21.
Gray KM, Upadhyaya HP. Tobacco smoking in individuals with **attention-deficit hyperactivity disorder**: epidemiology and pharmacological approaches to cessation. CNS Drugs. 2009;23(8):661-8. doi: 10.2165/00023210-200923080-00003.
Gray Ron, Bonellie Sandra R, Chalmers James, et al. Contribution of smoking during pregnancy to inequalities in **stillbirth and infant death** in Scotland 1994-2003: retrospective population based study using hospital maternity records.BMJ 2009;339:b3754, doi: 10.1136/bmj.b3754 (Published 1 October 2009)
Green SH, Bayer R, Fairchild AL. Evidence, Policy, and **E-Cigarettes**—Will **England** Reframe the Debate? N Engl J Med. 2016 Apr 7;374(14):1301-3.
Gregson J, Kaptoge S, Bolton T, et al; Emerging Risk Factors Collaboration. **Cardiovascular Risk Factors Associated With Venous Thromboembolism**. JAMA Cardiol. 2019 Jan 16.
Groh CA, Vittinghoff E, Benjamin EJ, et al. **Childhood Tobacco Smoke Exposure and Risk of Atrial Fibrillation** in Adulthood. J Am Coll Cardiol. 2019 Oct 1;74(13):1658-1664.
Groner JA, Huang H, Joshi MS, et al. **Secondhand Smoke Exposure** and Preclinical Markers of **Cardiovascular Risk in Toddlers**. J Pediatr. 2017 Jul 12
Gu D, Kelly TN, Wu X, et al. **Mortality attributable to smoking in China**. N Engl J Med. 2009 Jan 8;360(2):150-9. The leading causes of smoking-related deaths were as follows: cancer, 268,200 (95% CI, 214,500 to 321,900); cardiovascular disease, 146,200 (95% CI, 79,200 to 213,100); and respiratory disease, 66,800 (95% CI, 20,300 to 113,300). Our study documents that smoking is a major risk factor for mortality in China. Continued strengthening of national programs and initiatives for smoking prevention and cessation is needed to reduce smoking-related deaths in China.
Gu F, Wacholder S, Kovalchik S, et al. **Time to smoke first morning cigarette and lung cancer** in a case-control study. J Natl Cancer Inst. 2014 Jun 19;106(6):dju118.
Gubner NR, Kozar-Konieczna A, Szoltysek-Boldys I, et al. **Cessation of alcohol consumption** decreases rate of nicotine metabolism in male alcohol-dependent smokers. Drug Alcohol Depend. 2016 Apr 14.
Guindon GE, Paraje GR, Chaloupka FJ. Association of **Tobacco Control Policies With Youth Smoking Onset** in Chile. JAMA Pediatr. 2019 Jun 10.
Gulland A. **Pension funds: tobacco investment up in smoke**. BMJ. 2016 Mar 11;352:i1491.
Gulland A. Sixty seconds on . . . **marijuana smoke**. BMJ. 2018 Jan 9;360:k72.

Gunnell AS, et al. Synergy between Cigarette Smoking and **Human Papillomavirus** Type 16 in Cervical Cancer In situ Development. Cancer Epidemiol Biomarkers Prev. 2006 Oct 20; [Epub ahead of print]

Gunnell D, Irvine D, Wise L, et al. **Varenicline and suicidal behaviour**: a cohort study based on data from the General Practice Research Database. BMJ 2009;339:b3805, doi: 10.1136/bmj.b3805 (Published 1 October 2009)

Gunnerbeck A, Wikström AK, Bonamy AK, Wickström R, Cnattingius S. Relationship of **Maternal Snuff Use** and Cigarette Smoking With **Neonatal Apnea**. Pediatrics. 2011 Aug 28.

Gupta, Khera, Kolte, et al. Relation of Smoking Status to **Outcomes After Cardiopulmonary Resuscitation** for In-Hospital Cardiac Arrest. The American Journal of Cardiology. 2014.

Gupta S, Gandhi A, Manikonda R. Accidental **nicotine liquid ingestion**: emerging paediatric problem. Arch Dis Child. 2014 Sep 8.

Gurbel PA, Nolin TD, Tantry US. **Clopidogrel efficacy** and cigarette smoking status. JAMA 2012; 307:2495-2496.

Gurillo P, Jauhar S, Murray RM, et al. **Does tobacco use cause psychosis**? Systematic review and meta-analysis. Lancet Psychiatry. 2015 Aug;2(8):718-25.

Gustavson K, Ystrom E, Stoltenberg C, et al. **Smoking in pregnancy** and **child ADHD**. Pediatrics. 2017;139(2):e20162509

Haas JS, Linder JA, Park ER, et al. **Proactive Tobacco Cessation Outreach** to Smokers of Low Socioeconomic Status: A Randomized Clinical Trial. JAMA Intern Med. 2014 Dec 15.

Hackshaw Allan, Rodeck Charles, Boniface Sadie. Maternal smoking in pregnancy and **birth defects**: a systematic review based on 173 687 malformed cases and 11.7 million controls Hum. Reprod. Update (2011) dmr022 online July 11, 2011 doi:10.1093/humupd/dmr022

Hackshaw A, Morris J K, Boniface S et al. **Low cigarette consumption and risk of coronary heart disease and stroke**: meta-analysis of 141 cohort studies in 55 study reports. BMJ 2018;360:j5855.

Hagger-Johnson G, Sabia S, Brunner EJ, et al. Combined impact of **smoking and heavy alcohol use on cognitive decline** in early old age: Whitehall II prospective cohort study. Br J Psychiatry. 2013 Jul 11.

Haghighi A, Schwartz DH, Abrahamowicz M, et al. Prenatal Exposure to Maternal Cigarette Smoking, Amygdala Volume, and **Fat Intake** in Adolescence. Arch Gen Psychiatry. 2012 Sep 3:1-8.

Hagnäs MP, Cederberg H, Jokelainen J, et al. Association of **maternal smoking during pregnancy** with **aerobic fitness of offspring** in young adulthood: a prospective cohort study. BJOG. 2015 Dec 9.

Hahn EJ, Rayens MK, Wiggins AT, et al. **Lung cancer incidence** and the strength of **municipal smoke-free ordinances**. Cancer. 2017 Nov 28.

Hajek P, Smith KM, Dhanji AR, McRobbie H. Is a **combination of varenicline and nicotine patch** more effective in helping smokers quit than varenicline alone? a randomised controlled trial. BMC Med. 2013;11:140.

Hajek P, Stead LF, West R, Jarvis M, Lancaster T. **Relapse prevention** interventions for smoking cessation. Cochrane Database Syst Rev. 2009;(1):CD003999.

Hajek Peter; McRobbie Hayden J.; Myers Katie E.; et al. Use of **Varenicline for 4 Weeks Before** Quitting Smoking: Decrease in Ad Lib Smoking and Increase in Smoking Cessation Rates. Arch Intern Med. 2011;171(8):770-777.

Hajek P, McRobbie H, Myers K. Efficacy of **cytisine** in helping smokers quit: systematic review and meta-analysis. Thorax. 2013 Feb 12.

Hajek P, Stead LF, West R, et al. **Relapse prevention** interventions for smoking cessation. Cochrane Database Syst Rev. 2013 Aug 20;8:CD003999. At the moment, there is insufficient evidence to support the use of any specific behavioural intervention to help smokers who have successfully quit for a short time to avoid relapse. The verdict is strongest for interventions focused on identifying and resolving tempting situations, as most studies were concerned with these. Little research is available regarding other behavioural approaches.Extended treatment with varenicline may prevent relapse. Extended treatment with bupropion is unlikely to have a clinically important effect. Studies of extended treatment with nicotine replacement are needed.

Hajek P, Etter JF, Benowitz N, et al. **Electronic cigarettes**: review of use, content, safety, effects on smokers and potential for harm and benefit. Addiction. 2014 Jul 31.

Hajek P, McRobbie H,Myers Smith K, et al. **Increasing varenicline dose** in smokers who do not respond to the standard dosage: a randomized clinical trial [online Dec 29, 2014]. JAMA Intern Med.

Hajek P, Phillips-Waller A, Przulj D, et al. A randomized trial of **e-cigarettes versus nicotine-replacement therapy**. N Engl J Med. DOI: 10.1056/NEJMoa1808779.

Hall J, Cho HD, Guo Y, et al Association of Rates of Smoking During Pregnancy With **Corporate Tobacco Sales Policies**. JAMA Pediatr. 2019 Jan 14.

Hall SM, Humfleet GL, Reus VI, Muñoz RF, Cullen J. Extended nortriptyline and psychological treatment for cigarette smoking. Am J Psychiatry. 2004 Nov;161(11):2100-7.

Halpern SD, French B, Small DS, et al. Randomized trial of **four financial-incentive programs** for smoking cessation. N Engl J Med. DOI: 10.1056/NEJMoa1414293.

Halpern SD, French B, Small DS, et al. Heterogeneity in the Effects of **Reward- and Deposit-based Financial Incentives on Smoking Cessation**. Am J Respir Crit Care Med. 2016 Apr 11.

Halpern SD, Harhay MO, Saulsgiver K, et al. A Pragmatic Trial of **E-Cigarettes, Incentives, and Drugs for Smoking Cessation**. N Engl J Med. 2018 May 23.

Hammal F, Ezekowitz JA, Norris CM, et al; **APPROACH** Investigators. **Smoking status and survival**: impact on mortality of continuing to smoke one year after the angiographic diagnosis of coronary artery disease, a prospective cohort study. BMC Cardiovasc Disord. 2014 Oct 1;14(1):133.

Hammond, David, Chaiton, Michael, Lee, Alex, Collishaw, Neil. **Destroyed documents**: uncovering the science that Imperial Tobacco Canada sought to conceal. CMAJ 2009 0: cmaj.080566.

Hammond D, Reid JL, Cole AG, Leatherdale ST. **Electronic cigarette use and smoking initiation among youth**: a longitudinal cohort study. CMAJ. 2017 Oct 30;189(43):E1328-E1336.

Hammond D, Reid JL, Rynard VL, et al. **Prevalence of vaping and smoking** among adolescents in Canada, England, and the United States: repeat national cross sectional surveys. BMJ. 2019 Jun 20;365:l2219.

Hanewinkel, Reiner, Isensee, Barbara, Sargent, James D., et al. **Cigarette Advertising** and Teen Smoking Initiation. Pediatrics 2011 127: e271-e278.

Hansson J, Galanti MR, Hergens MP, et al. **Snus** (**Swedish smokeless tobacco**) use and risk of stroke: pooled analyses of incidence and survival. JIntern Med. 2014 Jul;276(1):87-95.

Hartmann-Boyce J, Cahill K, Hatsukami D, Cornuz J. **Nicotine vaccines** for smoking cessation. Cochrane Database of Systematic Reviews 2012, Issue 8. Art. No.: CD007072. DOI: 10.1002/14651858.CD007072.pub2.

Hartmann-Boyce J, Chepkin SC, Ye W, et al. **Nicotine replacement therapy versus control for smoking cessation.** Cochrane Database Syst Rev. 2018 May 31;5:CD000146. : There is high-quality evidence that all of the licensed forms of NRT (gum, transdermal patch, nasal spray, inhalator and sublingual tablets/lozenges) can help people who make a quit attempt to increase their chances of successfully stopping smoking. NRTs increase the rate of quitting by 50% to 60%, regardless of setting, and further research is very unlikely to change our confidence in the estimate of the effect. The relative effectiveness of NRT appears to be largely independent of the intensity of additional support provided to the individual. Provision of more intense levels of support, although beneficial in facilitating the likelihood of quitting, is not essential to the success of NRT. NRT often causes minor irritation of the site through which it is administered, and in rare cases can cause non-ischaemic chest pain and palpitations.

Hartmann-Boyce J, Aveyard P. **Drugs for smoking cessation**. BMJ. 2016 Feb 23;352:i571.

Hartmann-Boyce J,McRobbie H, Bullen C, Begh R, Stead LF,Hajek P. **Electronic cigarettes for smoking cessation**. Cochrane Database of Systematic Reviews 2016, Issue 9. Art. No.: CD010216. There is evidence from two trials that ECs help smokers to stop smoking in the long term compared with placebo ECs. However, the small number of trials, low event rates and wide confidence intervals around the estimates mean that our confidence in the result is rated 'low' by GRADE standards. The lack of difference between the effect of ECs compared with nicotine patches found in one trial is uncertain for similar reasons. None of the included studies (short- to mid-term, up to two years) detected serious adverse events considered possibly related to EC use. The most commonly reported adverse effects were irritation of the mouth and throat. The longterm safety of ECs is unknown. In this update, we found a further 15 ongoing RCTs which appear eligible for this review.

Hartmann-Boyce J, Begh R, Aveyard P. **Electronic cigarettes for smoking cessation**. BMJ. 2018 Jan 17;360:j5543.

Harutyunyan A, Movsisyan N, Petrosyan V, et al. Reducing Children's Exposure to **Secondhand Smoke at Home**: A Randomized Trial. Pediatrics. 2013 Dec;132(6):1071-80

Harrod CS, Reynolds RM, Chasan-Taber L, et al. Quantity and timing of **maternal prenatal smoking** on **neonatal body composition**: the healthy start study. J Pediatr. 2014 Oct;165(4):707 12.

Hartz SM, Short SE, Saccone NL, et al. Increased **Genetic Vulnerability** to Smoking at **CHRNA5** in Early-Onset Smokers. Arch Gen Psychiatry. 2012 Aug 1;69(8):854-60.

Harvard Study Confirms **Rise in Nicotine Delivery of Cigarettes** A reanalysis of data released last summer confirms that the nicotine yield from cigarettes increased about 11% from 1998 to 2005. A Harvard School of Public Health review of the data, which are annually reported to the Massachusetts Department of Public Health by cigarette manufacturers, was released online. It found the nicotine increase across brands from the four major manufacturers and in all categories of cigarettes, such as menthol and ultralight. The report said the nicotine boost was accomplished both by increasing the amount of nicotine in the cigarettes and by redesigning them to burn more slowly, so users take more puffs per cigarette. http://www.hsph.harvard.edu/nicotine/trends.pdf

Haslemo T, et al. The effect of variable cigarette consumption on the interaction with **clozapine** and **olanzapine**. Eur J Clin Pharmacol. 2006 Nov 7; [Epub ahead of print] A daily consumption of 7-12 cigarettes is probably sufficient for maximum induction of clozapine and olanzapine metabolism. A 50% lower starting dose of both drugs in non-smokers seems rational to avoid side effects.

Hastings G, Andrade Md, Moodie C. **Tobacco harm reduction**: the devil is in the deployment. BMJ. 2012 Dec 17;345:e8412.

Hastings G. Tobacco companies are still determined to get **children addicted**. BMJ. 2014 Feb 7;348:g1439.

Hatoun J, Davis-Plourde K, Penti B, et al. **Tobacco Control Laws** and Pediatric Asthma. Pediatrics. 2018 Jan;141(Suppl 1):S130-S136.

Hatsukami DK, Luo X, Jensen JA, et al. Effect of **Immediate vs Gradual Reduction in Nicotine Content of Cigarettes on Biomarkers of Smoke Exposure**: A Randomized Clinical Trial. JAMA. 2018 Sep 4;320(9):880-891.

Hawk LW Jr, Ashare RL, Lohnes SF, et al. The effects of **extended pre-quit varenicline** (4 weeks vs 1 week) treatment on smoking behavior and short-term abstinence: a randomized clinical trial. Clin Pharmacol Ther. 2012 Feb;91(2):172-80.

Hawkes N. Sixty seconds on . . . **snus**. BMJ. 2017 Feb 1;356:j536.

Hawkes N. The mixed messages that led to **an e-cigarette shambles**. BMJ. 2017 Sep 26;358:j4460

Hawkes N. **Big tobacco's new year's resolution to quit smoking.** BMJ. 2018 Jan 5;360:k79.

Hawkins SS, Baum CF, Oken E, et al. Associations of **tobacco control policies with birth outcomes**. JAMA Pediatr. 2014 Nov 3;168(11):e142365.

Hays JT, Ebbert JO. **Varenicline** for tobacco dependence. N Engl J Med. 2008 Nov 6;359(19):2018-24.

Hays JT, Ebbert JO. **Adverse effects and tolerability** of medications for the treatment of tobacco use and dependence. Drugs. 2010 Dec 24;70(18):2357-72.

Health Canada July/07 Unauthorized Smoking Cessation Product **Resolve** May Pose Health Risk - Consumer Information. The product contains an unacceptable amount of an ingredient labelled as "CESTEMENOL-350." Consuming excessive amounts of this ingredient might result in damage to the kidney, liver or red blood cells.

Health Canada June/08 Pfizer Canada in collaboration with Health Canada would like to notify healthcare professionals of important safety information regarding **CHAMPIX**, and post-marketing reports of serious **neuropsychiatric adverse events**, including depressed mood, agitation, hostility, changes in behaviour, suicidal ideation and suicide, as well as worsening of pre-existing psychiatric illness (previously diagnosed or not). Since introduction of CHAMPIX in Canada, in April 2007 through April 30, 2008, a total of **226 Canadian cases** of neuropsychiatric adverse events have been reported. For the same time period, there have been **708 534 prescriptions filled** for CHAMPIX in Canada1. All patients attempting to quit smoking with CHAMPIX, their families & caregivers should be alerted about the need to monitor for symptoms of neuropsychiatric adverse events. Patients should be instructed to stop taking CHAMPIX and contact their healthcare provider immediately if they have or if their families or caregivers observe depressed mood, agitation, hostility or changes in behavior, that are not typical for the patient, or if the patient has suicidal ideation or suicidal behavior. Patients with concomitant psychiatric conditions, even if well controlled, or with a history of psychiatric symptoms, should be diligently monitored.

Health Canada Mar/09 is advising Canadians not to purchase or use **electronic smoking products**, as these products may pose health risks and have not been fully evaluated for safety, quality and efficacy by Health Canada. http://www.hc-sc.gc.ca/ahc-asc/media/advisories-avis/_2009/2009_53-eng.php (FDA and Public Health Experts Warn About Electronic Cigarettes http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm173222.htm)

Health Canada June/10 **CHAMPIX** (varenicline tartrate) - Changes to the Canadian Product Monograph - Pfizer Canada Inc. Changes include: 1- a boxed warning highlighting recommendations about neuropsychiatric adverse events, 2- a warning about rare reports of serious allergic and skin reactions, 3- a guidance for prescribers about information to be shared with their patients prior to and during treatment, and 4- an additional dosing option for CHAMPIX.

Health Canada Jan/12 is informing Canadians that our **review of Champix** is now complete and the label has been updated with new information with respect to cardiovascular safety. Champix (brand name for varenicline tartrate) is a prescription drug used to help patients quit smoking in combination with supportive counselling. Health Canada evaluated data from a quit-smoking clinical trial involving 700 smokers with cardiovascular disease (approximately 350 who received Champix and 350 who received a placebo or "sugar pills"). Cardiovascular disease is a broad term for any condition that affects the heart and/or blood vessels, including heart attack and stroke. Although a slightly increased number of patients experienced serious heart-related events in the group treated with Champix compared to the

group treated with placebo, the study was not adequately designed to be able to test the cardiovascular safety of Champix. The small study size combined with other study design weaknesses make it impossible to draw conclusions based on these data. The possibility of an increased risk of heart attack or stroke in patients with cardiovascular disease can neither be confirmed nor ruled out at this time.
Health Canada May/13 CHAMPIX (**varenicline** tartrate) and ZYBAN (**buproprion** hydrochloride) - Revision to the Consumer Information of Non-Nicotine Smoking Cessation Aids - Pfizer Canada Inc. and Valeant Canada LP. The revised product monographs indicate that thorough consideration should be given to the option of **nicotine replacement therapy**, prior to a decision to prescribe a non-nicotine treatment.
Healton C. The Tobacco Master Settlement Agreement - Strategic Lessons for Addressing Public Health Problems. N Engl J Med. 2018 Sep 13;379(11):997-1000.
Hedman L, Backman H, Stridsman C, et al. **Association of Electronic Cigarette Use With Smoking Habits, Demographic Factors, and Respiratory Symptoms**. *JAMA Network Open.* 2018;1(3):e180789.
Hedström AK, Klareskog L, Alfredsson L. Exposure **to passive smoking and rheumatoid arthritis risk**: results from the Swedish EIRA study. Ann Rheum Dis.2018 Jul;77(7):970-972.
Hegaard HK, Kjaergaard H, Møller LF, Wachmann H, Ottesen B. **Multimodal** intervention raises smoking cessation rate during **pregnancy**. Acta Obstet Gynecol Scand 2003;82:813-9.
Helleberg M et al. Mortality attributable to **smoking among HIV-1**–infected individuals: A nationwide, population-based cohort study. Clin Infect Dis 2012 Dec 18.
Hendlin YH, Elias J, Ling PM. The **Pharmaceuticalization of the Tobacco Industry**. Ann Intern Med. 2017 Jul 18.
Henry TS, Kanne JP, Kligerman SJ. Imaging of **vaping-associated lung disease**. N Engl J Med. DOI: 10.1056/NEJMc1911995.
Herrera KM, Rosenn BM, Foroutan J, et al. Randomized controlled trial of **insulin detemir versus NPH for the treatment of pregnant women with diabetes**. Am J Obstet Gynecol. 2015 Sep;213(3):426.e1-7.
Higgins ST, Heil SH, Sigmon SC, et al. **Addiction Potential of Cigarettes With Reduced Nicotine Content in Populations With Psychiatric Disorders** and Other Vulnerabilities to Tobacco Addiction. JAMA Psychiatry. 2017 Aug 23.
Himes SK, Stroud LR, Scheidweiler KB, et al. Prenatal Tobacco Exposure, Biomarkers for Tobacco in Meconium, and Neonatal Growth Outcomes. J Pediatr. 2012 Dec 1.
Hissaria P, Roberts-Thomson PJ, Lester S, et al. Cigarette smoking in patients with **systemic sclerosis** - reduces overall survival. Arthritis Rheum. 2011 Mar 24. doi: 10.1002/art.30352.
Hitsman B, Baker AL, King A. POINT: Are **advanced practice professionals** more likely to achieve **better tobacco cessation results** than physicians? Yes. Chest. 2017 Apr 12.
Hodyl NA, Stark MJ, Scheil W, et al. Perinatal outcomes following **maternal asthma** and cigarette smoking during pregnancy. Eur Respir J. 2013 Jul 30.
Hoffman SJ, Mammone J, Rogers Van Katwyk S, et al. **Cigarette consumption estimates** for 71 countries from 1970 to 2015: systematic collection of comparable data to facilitate quasi-experimental evaluations of national and global tobacco control interventions. BMJ. 2019 Jun 19;365:l2231.
Hoffman SJ, Poirier MJP, Rogers Van Katwyk S, et al. Impact of the **WHO Framework Convention on Tobacco Control** on global cigarette consumption: quasi-experimental evaluations using interrupted time series analysis and in-sample forecast event modelling. BMJ. 2019 Jun 19;365:l2287.
Højgaard P, Glintborg B, Hetland ML, et al. Association between **tobacco smoking and response to tumour necrosis factor α inhibitor treatment** in psoriatic arthritis: results from the DANBIO registry. Ann Rheum Dis. 2015 Dec;74(12):2130-6.
Holford TR, Meza R,Warner KE, et al. **Tobacco control** and the reduction in smoking-related premature deaths in the United States, 1964-2012. JAMA. doi:10.1001/jama.2013.285112.
Hollands GJ, McDermott MS, Lindson-Hawley N, Vogt F, Farley A, Aveyard P. Interventions to **increase adherence to medications for tobacco dependence**. Cochrane Database of Systematic Reviews 2015, Issue 2. Art. No.: CD009164. DOI:10.1002/14651858.CD009164.pub2. There is some evidence that interventions that devote special attention to improving adherence to smoking cessation medication through providing information and facilitating problem-solving can improve adherence, though the evidence for this is not strong and is limited in both quality and quantity. There is some evidence that such interventions improve the chances of achieving abstinence but again the evidence for this is relatively weak.
Hollands GJ, Naughton F, Farley A, et al. **Interventions to increase adherence to medications** for tobacco dependence. Cochrane Database Syst Rev. 2019 Aug 16;8:CD009164. : In people who are stopping smoking and receiving behavioural support, there is moderate-certainty evidence that enhanced behavioural support focusing on adherence to smoking cessation medications can modestly improve adherence. There is only low-certainty evidence that this may slightly improve the likelihood of cessation in the shorter or longer-term.
Hollams EM, de Klerk NH, Holt PG, Sly PD. Persistent Effects of **Maternal Smoking during Pregnancy on Lung Function and Asthma in Adolescents**. Am J Respir Crit Care Med. 2013 Nov 19.
Holme I, Anderssen SA. Increases in **physical activity** is as important as smoking cessation for reduction in total mortality in elderly men: 12 years of follow-up of the Oslo II study. Br J Sports Med. 2015 Jun;49(11):743-8.
Holme I, Retterstøl K, Norum KR, et al. **Lifelong benefits on myocardial infarction mortality**: 40-year follow-up of the randomized Oslo diet and antismoking study. J Intern Med. 2016 Aug;280(2):221-7.
Holz NE, Boecker R, Baumeister S, et al. Effect of **Prenatal Exposure** to Tobacco Smoke on Inhibitory Control: Neuroimaging Results From a 25-Year Prospective Study. JAMA Psychiatry. 2014 May 14.
Hooper RW 2nd, Garfield JL. An Emerging Crisis: **Vaping-Associated Pulmonary Injury**. Ann Intern Med. 2019 Oct 8. doi: 10.7326/M19-2908.
Hopkinson NS. **Tobacco smoke and environmental injustice**. BMJ. 2018 Oct8;363:k4201.
Hopkinson NS. The prominence of e-cigarettes is a symptom of decades of failure to tackle smoking properly. BMJ. 2019 Feb 14;364:l647
Hopkins M, Hallett C, Babb S, et al. Comprehensive **smoke-free laws—50 largest US cities**, 2000 and 2012. MMWR Morb Mortal Wkly Rep 2012; 61:914-917.
Horn K, Dino G, Branstetter SA, Zhang J, Noerachmanto N, Jarrett T, Taylor M. Effects of **physical activity** on teen smoking cessation. Pediatrics. 2011 Oct;128(4):e801-11.
Hovell MF, Wahlgren DR, Liles S, et al. **Coaching and Cotinine Feedback** to Preteens to Reduce Their Secondhand Smoke Exposure: a Randomized Trial. Chest. 2011 Apr 7.
Howe M, Leidal A, Montgomery D, Jackson E. Role of Cigarette Smoking and **Gender in Acute Coronary Syndrome Events**. Am J Cardiol. 2011 Sep 15. (increased in **female** smokers)
Howrylak JA, Spanier AJ, Huang B, et al. **Cotinine** in Children Admitted for Asthma and Readmission. Pediatrics. 2014 Jan 20
Hswen Y, Brownstein JS. Real-Time **Digital Surveillance of Vaping-Induced Pulmonary Disease**. N Engl J Med. 2019 Sep 20.
Hu Y, Zong G, Liu G, et al. **Smoking cessation, weight change, type 2 diabetes, and mortality**. N Engl J Med 2018; 379: 623-32.
Huang L, Wang Y, Zhang Let al. **Maternal Smoking and Attention-Deficit/Hyperactivity Disorder in Offspring**: A Meta-analysis. Pediatrics. 2017 Dec 29.
Huang X, Wang X, Zou Y, et al. Impact of Cigarette Smoking and Smoking Cessation on **Stent Changes** as Determined by Optical Coherence Tomography After Sirolimus Stent Implantation. Am J Cardiol. 2017 Oct 15;120(8):1279-1284.
Huckvale K, Torous J, Larsen ME. Assessment of the Data Sharing and Privacy Practices of **Smartphone Apps** for Depression and Smoking Cessation. JAMA Netw Open. 2019 Apr 5;2(4):e192542.
Huerta TR, Walker DM, Mullen D, et al. Trends in **E-Cigarette** Awareness and Perceived Harmfulness in the U.S. Am J Prev Med. 2016 Nov 24.
Huf SW, Volpp KG, Asch DA, Bair E, Venkataramani A. Association of Medicaid Healthy Behavior Incentive Programs with smoking cessation, weight loss, and annual preventive health visits. JAMA Netw Open. 2018;1(8): e186185. doi:10.1001/jamanetworkopen.2018.6185
Hughes JR, Stead LF, Hartmann-Boyce J, et al. **Antidepressants for smoking cessation**. Cochrane Database Syst Rev. 2014 Jan 8;1:CD000031. The antidepressants bupropion and nortriptyline aid long-term smoking cessation. Adverse events with either medication appear to rarely be serious or lead to stopping medication. Evidence suggests that the mode of action of bupropion and nortriptyline is independent of their antidepressant effect and that they are of similar efficacy to nicotine replacement. Evidence also suggests that bupropion is less effective than varenicline, but further research is needed to confirm this finding.
Hughes K, Bellis MA, Hardcastle KA, et al. Associations between **e-cigarette** access and smoking and drinking behaviors in **teenagers**. BMC Public Health. 2015 Mar 31;15(1):244.
Hughes SC, Bellettiere J, Nguyen B, et al. Randomized Trial to **Reduce Air Particle Levels in Homes of Smokers and Children**.Am J Prev Med. 2018 Jan 2.
Hui M, Doherty M, Zhang W. Does **smoking protect against osteoarthritis**? Meta-analysis of observational studies. Ann Rheum Dis. 2011 Jul;70(7):1231-7. The protective effect of smoking in OA observed in some epidemiological studies is likely to be **false**.
Hum Ashley M., Robinson Leslie A., Jackson Ashley A., et al. **Physician Communication Regarding Smoking and Adolescent** Tobacco Use. Pediatrics 2011; peds.2010-1195; published ahead of print May 16, 2011, doi:10.1542/peds.2010-1195
Hurt RD, Weston SA, Ebbert JO, et al. Myocardial infarction and sudden cardiac death in Olmsted County, Minnesota, **before and after smoke-free workplace laws** [online October 29, 2012]. Arch Intern Med.
Hurt RD, Sachs DP, Glover ED, et al. A comparison of sustained- release bupropion and placebo for smoking cessation. N Engl J Med 1997;337:1195-202. (**low dose is effective**)
Husten CG, Deyton LR. Understanding the **Tobacco Control Act: efforts by the US Food and Drug Administration** to make tobacco-caused morbidity and mortality part of the USA's past, not its future. Lancet 2013; 381: 1570–80.
Huxley RR, Woodward M. Cigarette smoking as a risk factor for **coronary heart disease in women** compared with men: a systematic review and meta-analysis of prospective cohort studies. Lancet 2011; DOI: DOI:10.1016/S0140-6736(11)60781-2.
Hydes TJ, Burton R, Inskip H, et al. A comparison of **gender-linked population cancer risks** between alcohol and tobacco: how many cigarettes are there in a bottle of wine? BMC Public Health. 2019 Mar 28;19(1):316.
Hyland A, Piazza K, Hovey KM, et al. Associations between **lifetime tobacco exposure** with **infertility** and age at natural **menopause**: the Women's Health Initiative Observational Study. Tob Control. 2015 Dec 14.
Iaccarino JM, Duran C, Slatore CG, et al. Combining smoking **cessation interventions with LDCT lung cancer screening**: A systematic review. Prev Med. 2019 Apr;121:24-32.
Iacobucci G. Stop smoking services: BMJ analysis shows how councils are stubbing them out. BMJ. 2018 Aug 24;362:k3649.
Ikonomidis I, Vlastos D, Kourea K, et al. **Electronic Cigarette Smoking Increases Arterial Stiffness** and Oxidative Stress to a Lesser Extent Than a Single Conventional Cigarette: An Acute and Chronic Study. Circulation. 2018 Jan 16;137(3):303-306.
Inoue-Choi M, Liao LM, Reyes-Guzman C, et al. Association of **Long-term**, **Low-Intensity Smoking** With All-Cause and Cause-Specific Mortality in the National Institutes of Health-**AARP** Diet and Health Study. JAMA Intern Med. 2016 Dec 5.
Itani T, Martin R, Rai D, et al. Use of **varenicline and nicotine replacement therapy** in people with and without general practitioner-recorded dementia: retrospective cohort study of routine electronic medical records. BMJ Open. 2019 Aug 30;9(8):e027569.
Jackson SE, Beard E, Kujawski B, et al. Comparison of **Trends in Self-reported Cigarette Consumption and Sales** in England, 2011 to 2018. JAMA Netw Open. 2019 Aug 2;2(8):e1910161.
Jacobs EJ, Newton CC, Carter BD, et al. What proportion of **cancer deaths** in the contemporary United States is attributable to cigarette smoking? Ann Epidemiol. 2014 Nov 13.
Jamison A, Lockington D. **Ocular Chemical Injury** Secondary to **Electronic Cigarette Liquid Misuse**. JAMA Ophthalmol. 2016 Oct 13
Jang JS, Buchanan DM, Gosch KL, et al. Association of smoking status with health-related **outcomes after percutaneous coronary intervention**. Circ Cardiovasc Interv. 2015 May;8(5).
Japuntich SJ, Eilers MA, Shenhav S, et al. **Secondhand tobacco smoke exposure** among hospitalized nonsmokers with coronary heart disease [online November 10, 2014]. JAMA Intern Med. doi:10.1001 /jamainternmed.2014.5476.
Jarlenski M, Hyon Baik S, Zhang Y. Trends in Use of **Medications for Smoking Cessation in Medicare**, 2007-2012. Am J Prev Med. 2016 Sep;51(3):301-8.
Jaspers NEM, Blaha MJ, Matsushita K, et al. Prediction of individualized lifetime **benefit from cholesterol lowering, blood pressure lowering, antithrombotic therapy, and smoking cessation** in apparently healthy people. Eur Heart J. 2019 May 18.
Jayes L, Haslam PL, Gratziou CG, et al; Tobacco Control Committee of the European Respiratory Society. **SmokeHaz**: Systematic reviews and meta-analyses of the effects of **smoking on respiratory health**. Chest. 2016 Apr 18.
Jenssen BP, Bryant-Stephens T, Leone FT, et al. Clinical Decision Support **Tool for Parental Tobacco Treatment** in Primary Care. Pediatrics. 2016 May;137(5).
Jensen RP, Luo W, Pankow JF, Strongin RM, Peyton DH. Hidden **formaldehyde in e-cigarette** aerosols. N Engl J Med. 2015 Jan 22;372(4):392-4.
Jenssen BP, Walley SC, McGrath-Morrow SA. **Heat-not-Burn Tobacco Products**:Tobacco Industry Claims No Substitute for Science. Pediatrics. 2017 Dec 12.
Jenssen BP, Walley SC; Section on Tobacco Control. **E-Cigarettes and Similar Devices**. Pediatrics. 2019 Feb;143(2).
Jeon J, Holford TR, Levy DT, et al. **Smoking and lung cancer mortality in the United States from 2015 to 2065.** A comparative modeling approach. Ann Intern Med. 2018. [Epub ahead of print]. doi:10.7326/M18-1250
Jetton JA, Ding K, Kim Y, Stone DU. Effects of tobacco smoking on **human corneal wound healing**. Cornea. 2014 May;33(5):453-6.
Jha P, Ramasundarahettige C, Landsman V, et al. **21st-Century hazards of smoking** and benefits of cessation in the United States. N Engl J Med 2013;368:341-50.
Jha P, Peto R. **Global effects of smoking, of quitting, and of taxing tobacco**. N Engl J Med. 2014 Jan 2;370(1):60-8

Jia H, Lubetkin EI. Trends in **quality-adjusted life-years** lost contributed by smoking and obesity. Am J Prev Med 2010; DOI: 10.1016/j.amepre.2009.09.043.

Jiang H, Livingston M, Room R, et al. Temporal Associations of **Alcohol and Tobacco Consumption With Cancer Mortality**. *JAMA Network Open*. 2018;1(3):e180713.

Jiménez-Ruiz C, Berlin I, Hering T. **Varenicline**: a novel pharmacotherapy for smoking cessation. Drugs. 2009;69(10):1319-38. doi: 10.2165/00003495-200969100-00003.

Jin M, Gagnon A, Levine M, et al. Patient-specific **academic detailing for smoking cessation**: Feasibility study. Can Fam Physician. 2014 Jan;60(1):e16-23

Johannessen A, Bakke PS, Hardie JA, et al. Association of exposure to **environmental tobacco smoke in childhood** with chronic obstructive pulmonary disease and respiratory symptoms in adults. Respirology. 2012 Jan 16.

Johnston V, Liberato S, Thomas D. **Incentives for preventing smoking in children and adolescents**. Cochrane Database Syst Rev. 2012 Oct 17;10:CD008645. To date, incentive programmes have not been shown to prevent smoking initiation among youth, although there are relatively few published studies and these are of variable quality. Trials included in this meta-analysis were all studies of the SFC competition, which distributed small to moderately sized prizes to whole classes, usually through a lottery system.

Jones HJ, Gage SH, Heron Jet al. Association of **Combined Patterns of Tobacco and Cannabis Use in Adolescence With Psychotic Experiences**. JAMA Psychiatry. 2018 Jan 17.

Jones LL, Hassanien A, Cook DG, Britton J, Leonardi-Bee J. **Parental Smoking and the Risk of Middle Ear Disease** in Children: A Systematic Review and Meta-analysis. Arch Pediatr Adolesc Med. 2011 Sep 5.

Jones M, Lewis S, Parrott S, et al. **Re-starting smoking in the postpartum period** after receiving a smoking cessation intervention: a systematic review. Addiction. 2016 Mar 16.

Joseph AM, Fu SS, Lindgren B, et al. **Chronic disease management** for tobacco dependence: a randomized, controlled trial. Arch Intern Med. 2011; 171(21):1894-1900.

Joseph RM, Movahedi M, Dixon WG, Symmons DP. Smoking-related mortality in patients with early **rheumatoid arthritis** - a retrospective cohort study using the Clinical Practice Research Datalink. Arthritis Care Res (Hoboken). 2016 Mar 18.

Juvela S, Lehto H. Risk factors for all-cause death after diagnosis of **unruptured intracranial aneurysms**. Neurology 2015;84:456–463.

Kabir Zubair, Connolly Gregory N., Alpert Hillel R. **Secondhand Smoke** Exposure and **Neurobehavioral Disorders** Among Children in the United States. Pediatrics 2011; peds.2011-0023; published ahead of print July 11, 2011, doi:10.1542/peds.2011-0023

Kalkhoran A, Glantz SA. Modeling the health impact of **expanding e-cigarette sales** in the United States and United Kingdom: a Monte Carlo analysis [online August 31, 2015].JAMA Intern Med. doi:10.1001/jamainternmed.2015.4209.

Kalkhoran S, Chang Y, Rigotti NA. **Electronic Cigarette Use and Cigarette Abstinence** Over Two Years among U.S. Smokers in the Population Assessment of Tobacco and Health Study. Nicotine Tob Res. 2019 Jul 11.

Kalkhoran S, Glantz SA. **E-cigarettes and smoking cessation in real-world** and clinical settings: a systematic review and meta-analysis. Lancet Respir Med. 2016 Jan 13.

Källberg H, Ding B, Padyukov L, et al. EIRA Study Group. Smoking is a major preventable risk factor for **rheumatoid arthritis**: estimations of risks after various exposures to cigarette smoke. Ann Rheum Dis. 2010 Dec 13.

Kamboj A, Spiller HA, Casavant MJ, et al. **Pediatric Exposure to E-Cigarettes, Nicotine, and Tobacco** Products in the United States. Pediatrics. 2016 May 9.

Kamerow D. Big Tobacco lights up **e-cigarettes**. BMJ. 2013 May 24;346:f3418.

Kamerow D. The **poisonous "juice" in e-cigarettes**. BMJ. 2014 Apr 1

Kamimura D, Cain LR, Mentz RJ, et al. **Cigarette Smoking and Incident Heart Failure**: Insights From the Jackson Heart Study. Circulation. 2018 Apr 16.

Kandel ER, Kandel DB. Shattuck Lecture. A molecular basis for **nicotine as a gateway drug**. N Engl J Med. 2014 Sep 4;371(10):932-43.

Kang SJ, Mintz GS, Weisz G, et al. Age-related **effects of smoking on coronary artery disease** assessed by gray scale and virtual histology intravascular ultrasound. Am J Cardiol. 2015 Apr 15;115(8):1056-62.

Kantor R, Kim A, Thyssen JP, Silverberg JI. Association of **atopic dermatitis** with smoking: A systematic review and meta-analysis. J Am Acad Dermatol. 2016 Dec;75(6):1119-1125.e1.

Kaplan A. Rebuttal: Can **electronic cigarettes** assist patients with smoking cessation? Yes. Can Fam Physician. 2015 Jun;61(6):e255.

Karagueuzian Hrayr S., White Celia, Sayre James, et al. **Cigarette Smoke Radioactivity [polonium 210 (210Po)]** and Lung Cancer RiskNicotine Tob Res (2011) first published online September 27, 2011 doi:10.1093/ntr/ntr145.

Karnieg T, Wang X. **Cytisine for smoking cessation**. CMAJ. 2018 May14;190(19):E596.

Kassem NO, Kassem NO, Jackson SR, et al. **Benzene Uptake** in Hookah Smokers and Non-smokers Attending Hookah Social Events: Regulatory Implications. Cancer Epidemiol Biomarkers Prev. 2014 Nov 21.

Kasza KA, Ambrose BK, Conway KP, et al. **Tobacco-Product Use by Adults and Youths in the United States in 2013 and 2014**. N Engl J Med. 2017 Jan 26;376(4):342-353.

Katz MG, Russell KW. **Injury from E-Cigarette Explosion**. N Engl J Med. 2019 Jun 20;380(25):2460.

Keating GM, Siddiqui MA. **Varenicline** : A Review of its Use as an Aid to Smoking Cessation Therapy. CNS Drugs. 2006;20(11):945-960.

Kelly SM, Gryczynski J, Mitchell SG, et al. Validity of **Brief Screening Instrument for Adolescent Tobacco, Alcohol, and Drug Use.** Pediatrics. 2014 Apr 21.

Kendzor DE, Businelle MS, Poonawalla IB, et al. **Financial Incentives for Abstinence Among Socioeconomically** Disadvantaged Individuals in Smoking Cessation Treatment. Am J Public Health. 2014 Nov 13:e1-e8.

Kenfield SA, Stampfer MJ, Rosner BA, et al. Smoking and smoking cessation in relation to **mortality in women**. JAMA 2008; 299: 2037-2047.

Kenfield Stacey A., Stampfer Meir J., Chan June M., et al. **Smoking and Prostate Cancer Survival** and Recurrence. JAMA. 2011;305(24):2548-2555.doi:10.1001/jama.2011.879.

Khan A, Scott DL, Batley M. Smoking, rheumatoid factor status and responses to **rituximab**. Ann Rheum Dis. 2012 Sep;71(9):1587-8.

Khariwala SS, Hatsukami DK, Stepanov I, et al. Patterns of **Tobacco Cessation Attempts** and Symptoms Experienced Among Smokers With **Head and Neck Squamous Cell Carcinoma**. JAMA Otolaryngol Head Neck Surg. 2018 Apr 12.

Khoury M, Manlhiot C, Fan CS, et al. Reported **electronic cigarette use** among adolescents in the Niagara region of Ontario. CMAJ. 2016 Jul 18.

Khullar D, Schroeder SA, Maa J. **Helping Smokers Quit Around the Time of Surgery**. JAMA. 2013 Mar 13;309(10):993-994.

Kim AE, Chew R, Wenger M, et al. Estimated **Ages of JUUL Twitter Followers**. JAMA Pediatr. 2019 May 20.

Kim AE, Nonnemaker JM, Loomis BR, et al. Influence of **tobacco displays and ads on youth**: a virtual store experiment. Pediatrics. 2013 Jan;131(1):e88-95.

Kim J, L Gall S, M Dewey H, et al. Baseline Smoking Status and the **Long-Term Risk of Death** or Nonfatal Vascular Event in People with Stroke: A 10-Year Survival Analysis. Stroke. 2012 Oct 25.

King BA, Dube SR, Tynan MA. **Secondhand Smoke Exposure** in Cars Among Middle and High School Students--United States, 2000-2009. Pediatrics. 2012 Feb 6.

King BA, Gammon DG, Marynak KL, Rogers T. **Electronic Cigarette Sales in the United States**, 2013-2017. JAMA. 2018 Oct 2;320(13):1379-1380.

King BA, Tynan MA, Dube SR, Arrazola R. **Flavored-Little-Cigar and Flavored-Cigarette Use** Among U.S. Middle and High School Students. J Adolesc Health. 2013 Sep 17.

King BA, Jama AO, Marynak KL, et al. Attitudes Toward **Raising the Minimum Age of Sale for Tobacco** Among U.S. Adults. Am J Prev Med. 2015 Jun 23.

Kit BK, Simon AE, Brody DJ, Akinbami LJ. US Prevalence and Trends in Tobacco **Smoke Exposure** Among **Children and Adolescents With Asthma**. Pediatrics. 2013 Feb 11.

Klein R, Lee KE, Gangnon RE, et al. Relation of Smoking, Drinking, and Physical Activity to **Changes in Vision** over a 20-Year Period: The Beaver Dam Eye Study. Ophthalmology. 2014 Feb 27.

Klein JD. **Delivering tobacco control interventions in adolescent** health care visits: time for action. Pediatrics. 2014 Sep;134(3):600-1.

Klein MD, Sokol NA, Stroud LR. **Electronic Cigarettes: Common Questions and Answers**. Am Fam Physician. 2019 Aug 15;100(4):227-235.

Kleykamp BA, Heishman SJ. The **older smoker**. JAMA. 2011 Aug 24;306(8):876-7.

Kmietowicz Z. **E-cigarettes** latest: users on the up but rules tighten. BMJ. 2014 Oct 27;349:g6444.

Knutzen KE, Moran MB, Soneji S. Combustible and Electronic Tobacco and Marijuana Products in **Hip-Hop Music** Videos, 2013-2017. JAMA Intern Med. 2018 Oct 15.

Koegelenberg CFN, Noor F, Bateman ED, et al. Efficacy of **varenicline combined with nicotine replacement therapy** vs varenicline alone for smoking cessation: a randomized clinical trial. JAMA. doi:10.1001/jama.2014.7195.

Kohen I, Kremen N. **Varenicline-induced manic episode** in a patient with bipolar disorder. Am J Psychiatry. 2007 Aug;164(8):1269-70.

Kojima G, Iliffe S, Jivraj S, et al. Does current **smoking predict future frailty**? The English longitudinal study of ageing. Age Ageing. 2017 Aug 17:1-6.

Komiyama M, Wada H, Ura S, et al. Analysis of Factors That Determine **Weight Gain during Smoking Cessation** Therapy. PLoS One. 2013 Aug 21;8(8):e72010.

Koplan KE, David SP, Rigotti NA. **Smoking cessation** -10minute Consultation. BMJ. 2008 Jan 26;336(7637):217.

Korja M, Lehto H, Juvela S, Kaprio J. Incidence of **subarachnoid hemorrhage is decreasing** together with decreasing smoking rates. Neurology 2016;87:1118–1123.

Kosmider L, Sobczak A, Prokopowicz A, et al. **Cherry-flavoured electronic cigarettes** expose users to the inhalation irritant, benzaldehyde. Thorax. 2016 Jan 28.

Kostygina G, Glantz SA, Ling PM. **Tobacco industry use of flavours** to recruit new users of little cigars and cigarillos. Tob Control. 2016 Jan;25(1):66-74.

Kotz D, Brown J, West R. Prospective cohort study of the effectiveness of **smoking cessation treatments used in the "real world".** Mayo Clin Proc. 2014 Oct;89(10):1360-7.

Kotz D, Viechtbauer W, Simpson E, et al. **Cardiovascular and neuropsychiatric risks of varenicline**: A retrospective cohort study.*Lancet Respir Med* 2015; DOI:10.1016/S2213-2600(15)00320-3.

Kotz D, Viechtbauer W, Simpson CR, et al. **Cardiovascular and neuropsychiatric risks of varenicline and bupropion** in smokers with chronic obstructive pulmonary disease. Thorax. 2017 May 4.

Koval R, Willett J, Briggs J. Potential **Benefits and Risks of High-Nicotine e-Cigarettes**. JAMA. 2018 Oct 9;320(14):1429-1430.

Kowitt SD, Noar SM, Ranney LM, et al. **Public attitudes toward larger cigarette pack warnings**: Results from a nationally representative U.S. sample. PLoS One. 2017 Mar 2;12(3):e0171496.

Krishnan-Sarin S, Morean M, Kong G, et al. **E-Cigarettes** and "**Dripping**" Among High-School Youth. Pediatrics. 2017 Feb 6.

Kroon LA. **Drug interactions** with smoking. Am J Health Syst Pharm. 2007 Sep 15;64(18):1917-21.

Krumme AA, Choudhry NK, Shrank WH, et al. **Cigarette Purchases at Pharmacies** by Patients at High Risk of Smoking Related Illness. JAMA Intern Med. 2014 Oct 20.

Kufner A, Nolte CH, Galinovic I, et al. **Smoking-thrombolysis paradox**: recanalization and reperfusion rates after intravenous tissue plasminogen activator in smokers with ischemic stroke. Stroke. 2013 Feb;44(2):407-13.

Kulik MC, Glantz SA. **Softening Among U.S. Smokers With Psychological Distress**: More Quit Attempts and Lower Consumption as Smoking Drops. Am J Prev Med. 2017 Sep 27. pii: S0749-3797(17)30439-7.

Kulik MC, Lisha NE, Glantz SA**. E-cigarettes Associated With Depressed Smoking Cessation**: A Cross-sectional Study of 28 European Union Countries. Am J Prev Med. 2018 Apr;54(4):603-609.

Kwok MK, Schooling CM, Ho LM, Leung S, Mak KH, McGhee SM, Lam TH, Leung GM. Early life **second hand smoke** exposure and serious infectious morbidity during the first eight years: evidence from Hong Kong's "Children of 1997" birth cohort. Tob Control. 2008 May 27. [Epub ahead of print]

Labonté R, Lencucha R. **Regulating electronic cigarettes**: finding the balance between precaution and harm reduction. CMAJ. 2015 May 11.

Lacey RE, Zilanawala A, Webb E, et al. **Parental Absence in early Childhood** and onset of smoking and alcohol consumption before adolescence. Arch Dis Child. 2016 ;0 :1-4.

Ladapo Joseph A.; Jaffer Farouc A.; Weinstein Milton C.; et al. Projected Cost-effectiveness of Smoking Cessation Interventions in **Patients Hospitalized With Myocardial Infarction**. *Arch Intern Med*. 2011;171(1):39-45.

Lai, Hak-Kan, Ho, Sai-Yin, Wang, Man-Ping, Lam, Tai-Hing. **Secondhand Smoke** and Respiratory Symptoms Among Adolescent Current Smokers. Pediatrics 2009 124: 1306-1310.

Lai DT, Cahill K, Qin Y, Tang JL. **Motivational interviewing** for smoking cessation. Cochrane Database Syst Rev. 2010 Jan 20;(1):CD006936.

Lamprecht B, McBurnie MA, Vollmer WM, et al. for the BOLD Collaborative Research Group. **COPD in Never Smokers**: Results From the Population-Based Burden of Obstructive Lung Disease Study. Chest. 2011 Apr;139(4):752-763.

Lancaster T, Stead LF. **Individual behavioural counselling** for smoking cessation. Cochrane Database Syst Rev. 2005;(2):CD001292.

Lancaster T, Stead LF**. Individual behavioural counselling** for smoking cessation. Cochrane Database Syst Rev. 2017 Mar 31;3:CD001292. There is high-quality evidence that individually-delivered smoking cessation counselling can assist smokers to quit. There is moderate-quality evidence of a smaller relative benefit when counselling is used in addition to pharmacotherapy, and of more intensive counselling compared to a brief counselling intervention.

Land T, Rigotti N, Levy D, et al. A longitudinal study of **Medicaid coverage for tobacco dependence treatments** in Massachusetts and associated decreases in hospitalizations for cardiovascular disease. PLOS Med 2010; DOI:10.1371/journal.pmed.1000375.

Landry RL, Groom AL, Vu TT, et al. The **role of flavors in vaping initiation and satisfaction** among U.S. adults. Addict Behav. 2019 Aug 2;99:106077.

Larsen GK, Seth M, Gurm HS. The ongoing importance of smoking as a powerful risk factor for **ST-segment elevation myocardial infarction** in young patients. JAMA Intern Med 2013.

Larsson SC, Burgess S, Michaëlsson K. **Smoking and Stroke**: A Mendelian Randomization Study. Ann Neurol. 2019 Jun 25.

Lasser K, Boyd JW, Woolhandler S, Himmelstein DU, McCormick D, Bor DH. **Smoking and mental illness**: a population-based prevalence study. JAMA. 2000; 284(20):2606-2610.

Lasser KE, Quintiliani LM, Truong V, et al. Effect of **Patient Navigation and Financial Incentives on Smoking Cessation** Among Primary Care Patients at an Urban Safety-Net Hospital: A Randomized Clinical Trial. JAMA Intern Med. 2017 Oct 30.

Layden JE, Ghinai I, Pray I, et al. **Pulmonary illness related to e-cigarette use** in Illinois and Wisconsin — preliminary report. N Engl J Med. DOI: 10.1056/NEJMoa1911614.

Lazarus SC, et al. Smoking Affects Response to **Inhaled Corticosteroids** or **Leukotriene Receptor Antagonists** in Asthma. Am J Respir Crit Care Med. 2007 Jan 4; [Epub ahead of print] In mild asthmatics who smoke, the response to inhaled corticosteroids is attenuated, suggesting that adjustments to standard therapy may be required to attain asthma control. The greater improvement seen in some outcomes in smokers treated with montelukast suggests that leukotrienes may be important in this setting.

Larzelere M, Williams D. **Promoting Smoking Cessation** Am Fam Physician. 2012 Mar 15;85(6):591-598.

Leão RM et al. Chronic nicotine activates stress/reward-related brain regions and facilitates the transition to **compulsive alcohol drinking**. J Neurosci 2015 Apr 15; 35:6241.

Le-Ha C, Beilin LJ, Burrows S, et al. Gender Difference in the Relationship between **Passive Smoking Exposure and HDL-Cholesterol** Levels in Late Adolescence. J Clin Endocrinol Metab. 2013 May;98(5):2126-35.

Leas EC, Schleicher NC, Prochaska JJ, Henriksen L. Place-Based Inequity in Smoking Prevalence in the Largest Cities in the United States. JAMA Intern Med. 2019 Jan 7.

Leaviss J, Sullivan W, Ren S, et al. What is the clinical effectiveness and cost-effectiveness of **cytisine compared with varenicline** for smoking cessation? A systematic review and economic evaluation. Health Technol Assess. 2014 May;18(33):1-120. On the basis of the evidence included in this review, varenicline and cytisine are both effective interventions to aid smoking cessation when compared with placebo. Cytisine is estimated to be both more clinically effective and cost-effective than varenicline. However, there is uncertainty in the decision, and a head-to-head trial of cytisine and varenicline would appear to be an effective use of resources.

Lee JGL, Schleicher NC, Leas EC, et al. US Food and Drug Administration Inspection of **Tobacco Sales to Minors at Top Pharmacies**, 2012-2017. JAMA Pediatr. 2018 Sep 4.

Lee PC, Ahmed I, Loroit MA, et al. **Smoking and Parkinson disease**: evidence for gene-by-smoking interactions. Neurology 2018;90:e583–e592.

Lee WH, Ong SG, Zhou Y, et al. Modeling **Cardiovascular Risks of E-Cigarettes With Human-Induced Pluripotent Stem Cell-Derived Endothelial Cells**. J Am Coll Cardiol. 2019 Jun 4;73(21):2722-2737.

Lee YO, Hebert CJ, Nonnemaker JM, Kim AE. **Youth Tobacco** Product Use in the United States. Pediatrics. 2015 Feb 2.

Leistikow BN, Kabir Z, Connolly GN, Clancy L, Alpert HR. Male tobacco smoke load and non-lung **cancer mortality** associations in Massachusetts. BMC Cancer. 2008 Nov 24;8:341. The lung/non-lung cancer death rate associations suggest that all-sites cancer death rate SAFs in year 2003 **were 73%** (Sensitivity Range [SR] 61-82%) for all ages and 74% (SR 61-82%) for ages 30-74 years.

Leonardi-Bee, Jo, Britton, John, Venn, Andrea. **Secondhand Smoke** and Adverse **Fetal Outcomes in Nonsmoking Pregnant Women**: A Meta-analysis. Pediatrics 2011 127: 734-741

Leonardi-Bee J, Ellison T, Bath-Hextall F. Smoking and the Risk of **Nonmelanoma Skin Cancer**: Systematic Review and Meta-analysis. Arch Dermatol. 2012 Aug 1;148(8):939-46.

Leone FT, Evers-Casey S, Toll BA, Vachani A. Treatment of **tobacco use in lung cancer**: diagnosis and management of lung cancer, 3rd ed: American College of Chest Physicians evidence-based clinical practice guidelines. Chest. 2013 May;143(5 Suppl):e61S-77S.

Lerman C, Gu H, Loughead J, et al. Large-Scale Brain **Network Coupling Predicts Acute Nicotine Abstinence** Effects on Craving and Cognitive Function. JAMA Psychiatry. 2014 Mar 12.

Lerman C, Schnoll RA, Hawk LW Jr, et al. **PGRN-PNAT** Research Group. Use of the **nicotine metabolite ratio** as a genetically informed biomarker of response to **nicotine patch or varenicline** for smoking cessation: a randomised, double-blind placebo-controlled trial. Lancet Respir Med. 2015 Jan 9.

Lessov-Schlaggar Christina N., Wahlgren Dennis R., Liles Sandy, et al. Sensitivity to **Secondhand Smoke** Exposure Predicts **Future Smoking Susceptibility**. Pediatrics 2011; peds.2010-3156; published ahead of print July 11, 2011, doi:10.1542/peds.2010-3156

Leung Chi C.; Lam Tai H.; Ho Kin S.; et al. **Passive Smoking and Tuberculosis**. Arch Intern Med. 2010;170(3):287-292.

Leventhal AM, Bello MS, Galstyan E, et al. Association of Cumulative **Socioeconomic and Health-Related Disadvantage** With Disparities in Smoking Prevalence in the United States, 2008 to 2017. JAMA Intern Med. 2019 Apr 22.

Leventhal AM, Strong DR, Kirkpatrick MG, et al. Association of **electronic cigarette** use with **initiation of combustible tobacco product smoking in early adolescence**.JAMA. doi:10.1001/jama .2015.8950.

Leventhal AM, Stone MD, Andrabi N, et al. Association of **e-Cigarette Vaping and Progression to Heavier Patterns of Cigarette Smoking**. JAMA. 2016 Nov 8;316(18):1918-1920.

Levine Michele D.; Perkins Kenneth A.; Kalarchian Melissa A.; et al. **Bupropion and Cognitive Behavioral Therapy** for Weight-Concerned Women Smokers. Arch Intern Med. 2010;170(6):543-550.

Levine MD, Cheng Y, Marcus MD, et al. **Preventing Postpartum Smoking Relapse**: A Randomized Clinical Trial. JAMA Intern Med. 2016 Mar 21.

Levinson AH, Ma M, Jason LA, et al. Assessment of the US Federal Retailer Violation Rate as an Estimate of the **Proportion of Retailers That Illegally Sell Tobacco to Adolescents**. JAMA Pediatr. 2018 Aug 20.

Levy DE, Winickoff JP, Rigotti NA. **School absenteeism** among children living with smokers. Pediatrics. 2011 Oct;128(4):650-6.

Levy D, de Almeida LM, Szklo A. The **Brazil SimSmoke policy** simulation model: the effect of strong tobacco control policies on smoking prevalence and smoking-attributable deaths in a middle income nation. PLoS Med. 2012 Nov;9(11):e1001336.

Levy D, Rodríguez-Buño RL, Hu TW, et al. The potential effects of **tobacco control in China**: projections from the China SimSmoke simulation model. BMJ. 2014 Feb 18;348:g1134.

Levy DT, Yuan Z, Luo Y, Abrams DB. The **Relationship of E-Cigarette Use to Cigarette Quit Attempts** and Cessation: Insights From a Large, Nationally Representative U.S. Survey. Nicotine Tob Res. 2017 Aug 31.

Levy DE, Chang Y, Regan S, et al. Improvements in health-related **quality of life among smokers who quit after hospitalization**. Prev Med. 2018 Feb 7.

Li W, Han J, Qureshi AA. **Smoking and risk of incident psoriatic arthritis** in US women. Ann Rheum Dis Published Online First: 8 Nov 2011. doi:10.1136/ annrheumdis-2011-200416

Li Y et al. **Smoking cessation and the risk of bladder cancer among postmenopausal women**. Cancer Prev Res (Phila) 2019 May; 12:305.

Liberman J, Wann S**. E-Cigarettes-What a Practicing Cardiologist Needs to Know**. American Journal of Cardiology. 2016.

Lightwood JM, Glantz SA. Declines in Acute **Myocardial Infarction** After Smoke-Free Laws and Individual Risk Attributable to Secondhand Smoke. Circulation. 2009 Sep 21. [Epub ahead of print]

Lightwood J, Glantz SA. **Smoking Behavior** and **Healthcare Expenditure** in the United States, 1992-2009: Panel Data Estimates. PLoS Med. 2016 May 10;13(5).

Lin HH, Ezzati M, Chang HY, Murray M. Association between tobacco smoking and **active tuberculosis** in Taiwan: prospective cohort study. Am J Respir Crit Care Med. 2009 Sep 1;180(5):475-80. Epub 2009 Jun 19.

Linakis MW, Rower JE, Roberts JK, et al. Population Pharmacokinetic Model of **Transdermal Nicotine** Delivered from a **Matrix-Type** Patch. Br J Clin Pharmacol. 2017 Aug 3.

Lindblad BE, Håkansson N, Wolk A. Smoking Cessation and the **Risk of Cataract**: A Prospective Cohort Study of Cataract Extraction Among Men. JAMA Ophthalmol. 2014 Jan 2.

Lindson N, Chepkin SC, Ye W, Fanshawe TR, Bullen C, Hartmann-Boyce J. Different doses, durations and **modes of delivery of nicotine replacement therapy** for smoking cessation. Cochrane Database Syst Rev. 2019 Apr 18;4:CD013308. doi:10.1002/14651858.CD013308. There is high-certainty evidence that using combination NRT versus single-form NRT, and 4 mg versus 2 mg nicotine gum, can increase the chances of successfully stopping smoking. For patch dose comparisons, evidence was of moderate certainty, due to imprecision. Twenty-one mg patches resulted In higher quit rates than 14 mg (24-hour) patches, and using 25 mg patches resulted in higher quit rates than using 15 mg (16-hour) patches, although in the latter case the CI included one. There was no clear evidence of superiority for 42/44 mg over 21/22 mg (24-hour) patches. Using a fast-acting form of NRT, such as gum or lozenge, resulted in similar quit rates to nicotine patches. There is moderate-certainty evidence that using NRT prior to quitting may improve quit rates versus using it from quit date only; however, further research is needed to ensure the robustness of this finding. Evidence for the comparative safety and tolerability of different types of NRT use is of low and very low certainty.

Lindson N, Thompson TP, Ferrey A, et al. Motivational interviewing for smoking cessation. Cochrane Database Syst Rev. 2019 Jul 31;7:CD006936. There is insufficient evidence to show whether or not MI helps people to stop smoking compared with no intervention, as an addition to other types of behavioural support for smoking cessation, or compared with other types of behavioural support for smoking cessation. It is also unclear whether more intensive MI is more effective than less intensive MI.

Lindson-Hawley N, Aveyard P, Hughes JR. **Reduction versus abrupt cessation** in smokers who want to quit. Cochrane Database Syst Rev. 2012 Nov 14;11:CD008033. doi: 10.1002/14651858.CD008033.pub3. Reducing cigarettes smoked before quit day and quitting abruptly, with no prior reduction, produced comparable quit rates, therefore patients can be given the choice to quit in either of these ways.

Lindson-Hawley N, Aveyard P, Hughes JR. **Gradual reduction vs abrupt cessation** as a smoking cessation strategy in smokers who want to quit. JAMA. 2013 Jul 3;310(1):91-2.

Lindson-Hawley N, Thompson TP, Begh R. **Motivational interviewing** for smoking cessation. Cochrane Database Syst Rev. 2015 Mar 2;3:CD006936. Motivational interviewing may assist people to quit smoking. However, the results should be interpreted with caution, due to variations in study quality, treatment fidelity, between-study heterogeneity and the possibility of publication or selective reporting bias.

Lindson-Hawley N, Banting M, et al. **Gradual Versus Abrupt Smoking Cessation**: A Randomized, Controlled Noninferiority Trial. Ann Intern Med. 2016 Mar 15.

Lindson-Hawley N, Hartmann-Boyce J, Fanshawe TR, Begh R, Farley A, Lancaster T. **Interventions to reduce harm from continued tobacco use**. Cochrane Database of Systematic Reviews 2016, Issue 10. Art. No.: CD005231. People who do not wish to quit can be helped to cut down the number of cigarettes they smoke and to quit smoking in the long term, using NRT, despite original intentions not to do so. However, we rated the evidence contributing to the cessation outcome for NRT as 'low' by GRADE standards. There is a lack of evidence to support the use of other harm reduction aids to reduce the harm caused by continued tobacco smoking. This could simply be due to the lack of high-quality studies (our confidence in cessation outcomes for these aids is rated 'low' or 'very low' due to imprecision by GRADE standards), meaning that we may have missed a worthwhile effect, or due to a lack of effect on reduction or quit rates. It is therefore important that more high-quality RCTs are conducted, and that these also measure the long-term health effects of treatments.

Linneberg A, Jacobsen RK, Skaaby T, et al. Effect of **smoking on blood pressure and resting heart rate**: A Mendelian randomization meta-analysis in the **CARTA** consortium. Circ Cardiovasc Genet 2015; 8:832-841.

Liu B, Xu G, Rong S, et al. National Estimates of e-Cigarette **Use Among Pregnant and Nonpregnant Women** of Reproductive Age in the United States, 2014-2017. JAMA Pediatr. 2019 Apr 29.

Liu JJ, Wabnitz C, Davidson E, et al. Smoking cessation interventions for **ethnic minority groups**-A systematic review of adapted interventions. Prev Med. 2013 Sep 27. pii: S0091-7435(13)00359-9.

Livingston EH, Lynm C. JAMA **patient page. Smoking cessation**. JAMA. 2012 Oct 17;308(15):1599.

Livingstone-Banks J, Ordonez-Mena JM, Hartmann-Boyce J Print-based self-help interventions for smoking cessation. Cochrane Database Syst Rev. 2019 Jan 9;1:CD001118. Moderate-certainty evidence shows that when no other support is available, written self-help materials help more people to stop smoking than no intervention. No evidence shows that when people receive advice from a health professional or are using nicotine replacement therapy, self-help materials add to the effects of these approaches. However, small benefits cannot be excluded. Moderate-certainty evidence shows that self-help materials that use data from participants to tailor the nature of the advice or support given are more effective than no intervention.

Livingstone-Banks J, Norris E, Hartmann-Boyce J, et al. **Relapse prevention interventions for smoking cessation**. Cochrane Database Syst Rev. 2019 Feb 13;2:CD003999. Behavioural interventions that teach people to recognise situations that are high risk for relapse along with strategies to cope with them provided no worthwhile benefit in preventing relapse in assisted abstainers, although unexplained statistical heterogeneity means we are only moderately certain of this. In people who have successfully quit smoking using pharmacotherapy, there were mixed results regarding extending pharmacotherapy for longer than is standard. Extended treatment with varenicline helped to prevent relapse; evidence for the effect estimate was of moderate certainty, limited by unexplained statistical heterogeneity. Moderate-certainty evidence, limited by imprecision, did not detect a benefit from extended treatment with bupropion, though confidence intervals mean we could not rule out a clinically important benefit at this stage.

Lloyd A, Steele L, Fotheringham J, et al. Pronounced increase in risk of acute ST-segment elevation **myocardial infarction** in younger smokers. Heart Published Online First: doi:10.1136/heartjnl- 2016- 309595

Lochbuehler K, Sargent JD, Scholte RH, et al. Influence of Smoking Cues in **Movies** on Children's Beliefs About Smoking. Pediatrics. 2012 Jul 9.

Lortet-Tieulent J, Goding Sauer A, Siegel RL, et al. **State-Level Cancer Mortality Attributable to Cigarette Smoking** in the **United States**. JAMA Intern Med. 2016 Oct 24.

Loukas A, Paddock EM, Li X, et al. **Electronic Nicotine Delivery Systems Marketing** and Initiation Among Youth and Young Adults. Pediatrics. 2019 Aug 26.

Lovato C, Watts A, Stead LF. Impact of **tobacco advertising and promotion** on increasing adolescent smoking behaviours. Cochrane Database of Systematic Reviews 2011, Issue 10. Art. No.: CD003439. DOI: 10.1002/14651858.CD003439.pub2. Longitudinal studies consistently suggest that exposure to tobacco advertising and promotion is associated with the likelihood that adolescents will start to smoke.

Luo J, Margolis KL, Wactawski-Wende J, et al. Association of active and passive **smoking with risk of breast cancer** among postmenopausal women: a prospective cohort study. BMJ. 2011 Mar 1;342:d1016. doi: 10.1136/bmj.d1016.

Luo J, Rossouw J, Margolis KL. Smoking cessation, **weight change**, and coronary heart disease among postmenopausal women with and without **diabetes**. (**WHI**) JAMA 2013; 310:94-95.

Lycett D, Nichols L, Ryan R, et al. The association between **smoking cessation and glycaemic control** in patients with type 2 diabetes: a THIN database cohort study. Lancet Diabetes Endocrinol. 2015 Jun;3(6):423-30.

Lyngbakken MN, Skranes JB, de Lemos JA, et al. Impact of Smoking on **Circulating Cardiac Troponin I Concentrations** and Cardiovascular Events in the General Population: The HUNT Study. Circulation. 2016 Nov 4.

Maisonneuve P, et al. Impact of smoking on patients with idiopathic chronic **pancreatitis**. Pancreas. 2006 Aug;33(2):163-8.

Mackay D et al. **Smoke-free legislation** and hospitalizations for childhood asthma. N Engl J Med 2010 Sep 16; 363:1139.

Mackay DF, Nelson SM, Haw SJ, et al. Impact of Scotland's Smoke-Free Legislation on **Pregnancy Complications**: Retrospective Cohort Study. PLoS Med 9(3): e1001175.

Mackay DF, Pell JP. Ten-Year Follow-Up of the **Impact of Scottish Smoke-Free Legislation** on Acute Myocardial Infarction. Circ Cardiovasc Qual Outcomes. 2019 Jul;12(7):e005392.

Mackay J, Ritthiphakdee B, Reddy KS. **Tobacco control in Asia**. Lancet. 2013 May 4;381(9877):1581-7.

Maddock SD, Cirulis MM, Callahan SJ, et al. **Pulmonary lipidladen macrophages and vaping**. N Engl J Med. DOI: 10.1056/ NEJMc1912038.

Mahabee-Gittens EM, Merianos AL, Matt GE. Preliminary evidence that high levels of **nicotine on children's** hands may contribute to overall tobacco smoke exposure. Tob Control. 2017 Mar 30.

Mahmoodi BK, Cushman M, et al. Association of traditional cardiovascular risk factors with **venous thromboembolism**: an individual participant data meta-analysis of prospective studies. Circulation. 2017;135:7–16. doi: 10.1161/CIRCULATIONAHA.116.024507. (smoking)

Mahmoudi M, Coleman CI, Sobieraj DM. Systematic review of the **cost-effectiveness of varenicline vs. bupropion** for smoking cessation. Int J Clin Pract. 2012 Feb;66(2):171-82.

Malek AM, Cushman M, Lackland DT, et al. **Secondhand Smoke Exposure and Stroke**: The Reasons for Geographic and Racial Differences in Stroke (REGARDS) Study. Am J Prev Med. 2015 Jun 16.

Malone R, McDaniel P, Smith E. It is time to plan the **tobacco endgame**. BMJ. 2014 Feb 11;348:g1453

Martins-Green M, Adhami N, Frankos M, et al. Cigarette **smoke toxins deposited on surfaces**: implications for human health. PLoS One. 2014 Jan 29;9(1):e86391.

Mays D, Gilman SE, Rende R, et al. **Parental Smoking** Exposure and Adolescent Smoking Trajectories. Pediatrics. 2014 May 12.

Mayne SL, Auchincloss AH, Tabb LP, et al. **Associations of Bar and Restaurant Smoking Bans With Smoking Behavior in the CARDIA Study**: A 25-Year Study. Am J Epidemiol. 2018 Jan 11.

Maziak W, Jawad M, Jawad S, et al. **Interventions for waterpipe smoking cessation**. Cochrane Database Syst Rev. 2015 Jul 31;7:CD005549. Although the literature on waterpipe cessation interventions remains sparse, the reviewed studies provide a basis for developing interventions in this area. The lack of statistically significant effects in one of the three studies is not unexpected, given the small and pilot nature of the studies. The studies highlight important design and content issues that need to be considered for future cessation trials in waterpipe smokers. These include building on the vast experience developed in the study of smoking cessation interventions in cigarette smokers, whilst including components and assessment tools that address the specific aspects of waterpipe smoking, such as its social dimension, unique experiences, and cues.

McAfee T. Encouraging Smokers to **Talk With Their Physicians About Quitting**. JAMA. 2013 May 22:1-2.

McAfee T, Davis KC, Alexander RL Jr, et al. Effect of the first **federally funded US antismoking national media campaign**. Lancet. 2013 Sep 6. doi:pii: S0140-6736(13)61686-4.

McCauley L, Markin C, Hosmer D. An unexpected consequence of **electronic cigarette use**. Chest. 2012 Apr;141(4):1110-3. (lipoid pneumonia)

McConnell R, Barrington-Trimis JL Ph D, Wang K M P H, et al. **Electronic-cigarette** Use and **Respiratory Symptoms in Adolescents**. Am J Respir Crit Care Med. 2016 Nov 2.

McCowan LM, et at.; SCOPE consortium. Spontaneous **preterm birth and small for gestational age infants** in women who stop smoking early in pregnancy: prospective cohort study. BMJ. 2009 Mar 26;338:b1081. doi: 10.1136/bmj.b1081. Erratum in: BMJ. 2009;338. doi: 10.1136/bmj.b1558.

McDermott MS, Marteau TM, Hollands GJ, et al. Change in **anxiety following successful and unsuccessful attempts** at smoking cessation: cohort study. Br J Psychiatry. 2013 Jan;202:62- 7.

McEvoy JW, Blaha M, Rivera JJ, et al. Mortality rates in smokers and nonsmokers in the presence or absence of **coronary artery calcification** (CAC). JACC Cardiovasc Imaging 2012; 5:1037-1045.

McEvoy CT, Schilling D, Clay N, et al. **Vitamin C supplementation** for pregnant smoking women and pulmonary function in their newborn infants: a randomized clinical trial. JAMA. doi:10.1001/jama.2014.5217.

McFall Miles, Saxon Andrew J., Malte Carol A., et al. for the CSP 519 Study Team. Integrating Tobacco Cessation **Into Mental Health Care for Posttraumatic Stress Disorder**: A Randomized Controlled Trial. JAMA. 2010;304(22):2485-2493.doi:10.1001/jama.2010.1769.

McKee M, Capewell S. Evidence about **electronic cigarettes**: a foundation built on rock or sand? BMJ. 2015 Sep 15;351:h4863.

McKee M, Gilmore AB. **European watchdog** is **failing** to hold **tobacco industry** to account over **smuggling**. BMJ. 2015 Dec 29;351:h6973.

McKelvey K, Baiocchi M, Halpern-Felsher B. **Adolescents' and young adults' use** and perceptions of **pod-based** electronic cigarettes. JAMA Netw Open. 2018;1(6): e183535.

McMillen R, Tanski S, Wilson K, et al. **Adolescent Use of Different E-cigarette Products**. Pediatrics. 2018 Sep 10.

McNeill A. **Should Clinicians Recommend E-cigarettes** to Their Patients Who Smoke? **Yes**. Ann Fam Med. 2016 Jul;14(4):300-1.

McNeill A, Gravely S, Hitchman SC, Bauld L, Hammond D, Hartmann-Boyce J. **Tobacco packaging design** for reducing tobacco use. Cochrane Database of Systematic Reviews 2017, Issue 4. Art. No.: CD011244. The available evidence suggests that standardised packaging may reduce smoking prevalence. Only one country had implemented standardised packaging at the time of this review, so evidence comes from one large observational study that provides evidence for this effect. A reduction in smoking behaviour is supported by routinely collected data by the Australian government. Data on the effects of standardised packaging on non-behavioural outcomes (e.g. appeal) are clearer and provide plausible mechanisms of effect consistent with the observed decline in prevalence. As standardised packaging is implemented in different countries, research programmes should be initiated to capture long term effects on tobacco use prevalence, behaviour, and uptake. We did not find any evidence suggesting standardised packaging may increase tobacco use.

McNeish H. **Global watchdog** to counter big tobacco. BMJ. 2018 Mar 14;360:k1172.

McRobbie H, Bullen C, et al.**Electronic cigarettes for smoking cessation and reduction**. Cochrane Database Syst Rev. 2014;12:CD010216. doi: 10.1002/14651858.CD010216.pub2. There is evidence from two trials that ECs help smokers to stop smoking long-term compared with placebo ECs. However, the small number of trials, low event rates and wide confidence intervals around the estimates mean that our confidence in the result is rated 'low' by GRADE standards. The lack of difference between the effect of ECs compared with nicotine patches found in one trial is uncertain for similar reasons. ECs appear to help smokers unable to stop smoking altogether to reduce their cigarette consumption when compared with placebo ECs and nicotine patches, but the above limitations also affect certainty in this finding. In addition, lack of biochemical assessment of the actual reduction in smoke intake further limits this evidence. No evidence emerged that short-term EC use is associated with health risk.

Mdodo R, Frazier EL, Dube SR, et al. **Cigarette Smoking Prevalence Among Adults With HIV** Compared With the General Adult Population in the United States: Cross-sectional Surveys. Ann Intern Med. 2015 Mar 3;162(5):335-44.

Mecredy GC, Diemert LM, Callaghan RC, Cohen JE. Association between use of **contraband tobacco** and smoking cessation outcomes: a population-based cohort study. CMAJ. 2013 Mar 4.

Medical Letter: **Treatment Guidelines- Drugs for Tobacco Dependence/ Drugs for Smoking Cessation**. Sept 2008, Feb 2016 & July **2019**.

Medical Letter. **Safety** of Smoking Cessation Drugs. Aug,2009.

Medical Letter. **Electronic Ciagarettes for Smoking Cessation**. Nov,2012.

Meernik C, Goldstein AO. **Should Clinicians Recommend E-cigarettes** to Their Patients Who Smoke? **No**. Ann Fam Med. 2016 Jul;14(4):302-3.

Mennella JA, Yourshaw LM, Morgan LK. Breastfeeding and smoking: short-term effects on **infant feeding and sleep**.Pediatrics. 2007 Sep;120(3):497-502. An acute episode of smoking by lactating mothers altered infants' sleep/wake patterning.

Menzies D, et al. Respiratory symptoms, pulmonary function, and markers of inflammation among **bar workers** before and after a legislative **ban** on smoking in public places. JAMA. 2006 Oct 11;296(14):1742-8.

Mercincavage M, Lochbuehler K, Wileyto EP, et al. Association of **Reduced Nicotine Content Cigarettes With Smoking Behaviors and Biomarkers of Exposure Among Slow and Fast Nicotine Metabolizers** A Nonrandomized Clinical Trial. JAMA Netw Open. 2018;1(4):e181346.

Merianos AL, Jandarov RA, Mahabee-Gittens EM. **Adolescent Tobacco Smoke Exposure, Respiratory Symptoms, and Emergency Department Use**. Pediatrics. 2018 Aug 6.

Meyers DG, Neuberger JS, He J et al. Cardiovascular effect of bans on **smoking in public places**. A systematic review and meta-analysis. J Am Coll Cardiol 2009; 54: 1249-1255.

Miech R, Johnston L, O'Malley PM, et al. **Adolescent Vaping and Nicotine Use** in 2017-2018 - U.S. National Estimates. N Engl J Med. 2018 Dec 16.

Miech R, Johnston L, O'Malley PM, et al. **Trends in Adolescent Vaping**, 2017-2019. N Engl J Med. 2019 Sep 18.

Miech R, Patrick ME, O'Malley PM, et al. **E-cigarette** use as a **predictor of cigarette smoking**: results from a 1-year follow-up of a national sample of 12th grade students. Tob Control. 2017 Feb 6.

Milidou I, Henriksen TB, Jensen MS, et al. **Nicotine replacement therapy during pregnancy** and **infantile colic** in the offspring. Pediatrics. 2012 Mar;129(3):e652-8.

Miller M, Cho JY, Pham A, et al. **Persistent airway inflammation and emphysema progression** on CT scan in ex-smokers observed for 4 years. Chest. 2011 Jun;139(6):1380-7.

Miller A. **E-cigarette ban** proposed in **Toronto**. CMAJ. 2014 Sep 16;186(13):E481-2.

Millett C, Tayu Lee J, Laverty A, Glantz S, Majeed A. **Hospital admissions for childhood asthma** after smoke-free legislation in England. Pediatrics 21 Jan 2013.

Mills E et al. Smoking cessation **reduces postoperative complications**: A systematic review and meta-analysis. Am J Med 2011 Feb; 124:144.

Mills EJ, Thorlund K, Eapen S, et al. **Cardiovascular events associated with smoking cessation pharmacotherapies**: A network meta-analysis. *Circulation* 2013.

Mirbolouk M, Charkhchi P, Kianoush S, et al. **Prevalence and Distribution of E-Cigarette Use Among U.S. Adults**: Behavioral Risk Factor Surveillance System, 2016. Ann Intern Med. 2018 Aug 28

Mirbolouk M, Charkhchi P, Orimoloye OA, et al. **E-Cigarette Use Without a History of Combustible Cigarette Smoking Among U.S. Adults**: Behavioral Risk Factor Surveillance System, 2016. Ann Intern Med. 2018 Oct 9.

Mirkhel A, et al. Frequency of **aspirin resistance** in a community hospital. Am J Cardiol. 2006 Sep 1;98(5):577-9. Epub 2006 Jun 30. In conclusion, this study estimates aspirin resistance prevalence and shows a strong association of smoking with platelet hyperactivity in a diverse community hospital population. Nonresponders to 81 mg/day frequently responded to 325 mg/day or to the addition of clopidogrel.

MMWR QuickStats: **Percentage of Adults Who Ever Used an E-cigarette** and Percentage Who Currently Use E-cigarettes, by Age Group — National Health Interview Survey, United States, 2016. MMWR Morb Mortal Wkly Rep 2017;66:892.

Moheimani RS, Bhetraratana M, Yin F, et al. Increased **cardiac sympathetic activity and oxidative stres** in **habitual electronic cigarette** users: implications for cardiovascular risk [online Feb 1, 2017].JAMA Cardiol. doi:10.1001 /jamacardio.2016.5303.

Moheimani RS, Bhetraratana M, Peters KM, et al. **Sympathomimetic Effects of Acute E- cigarette Use**: Role of Nicotine and Non-Nicotine Constituents. J Am Heart Assoc. 2017 Sep 20;6(9).

Mohiuddin SM, Mooss AN, Hunter CB, et al. **Intensive smoking cessation** intervention **reduces mortality** in high-risk smokers with cardiovascular disease. Chest. 2007 Feb;131(2):446-52. At 24 month, continuous abstinence smoking cessation rate was 33% in the intensive-treatment group and 9% in the usual-care group ($p < 0.0001$). Over the 2-year follow-up period, 41 patients in the usual-care group were hospitalized compared to 25 patients in the intensive-tx group (relative risk reduction [RRR], 44%; 95% confidence

interval [CI], 16 to 63%; p = 0.007). The all-cause mortality rate was 2.8% in the intensive-tx group and 12.0% in the usual-care group (RRR, 77%; 95% CI, 27 to 93%; p = 0.014). **Absolute risk reduction in mortality was 9.2% with a number needed to treat of 11.**
Molero Y, Lichtenstein P, Zetterqvist J, et al. **Varenicline and risk of psychiatric conditions**, suicidal behaviour, criminal offending, and transport accidents and offences: population based cohort study. BMJ. 2015 Jun 2;350:h2388.
Mons U, Müezzinler A, Gellert C, et al; **CHANCES** consortium. Impact of smoking and smoking cessation on **cardiovascular events and mortality** among older adults: meta-analysis of individual participant data from prospective cohort studies of the CHANCES consortium. BMJ. 2015 Apr 20;350:h1551.
Monuteaux MC, Spencer TJ, Faraone SV, et al. A randomized, placebo-controlled clinical trial of bupropion for the prevention of smoking in children and adolescents with **attention-deficit/hyperactivity disorder**. J Clin Psychiatry. 2007 Jul;68(7):1094-101. While bupropion was not associated with a lower rate of smoking in youth with ADHD, post hoc analyses suggest that stimulant treatment was. Future controlled studies should investigate the role of stimulants in the prevention of smoking in children and adolescents with ADHD.
Moodie C, Gendall P, Hoek J, et al. The response of young adult smokers and non-smokers in the United Kingdom to **dissuasive cigarettes**: An online survey. Nicotine Tob Res. 2017 Nov 28.
Moolgavkar SH, Holford TR, Levy DT et al. Impact of Reduced Tobacco Smoking on **Lung Cancer Mortality** in the United States During 1975-2000. J Natl Cancer Inst. 2012 Mar 14.
Moore D, Aveyard P, Connock M, Wang D, Fry-Smith A, Barton P. Effectiveness and safety of **nicotine replacement therapy assisted reduction** to stop smoking: systematic review and meta-analysis. BMJ. 2009 Apr 2;338:b1024. doi: 10.1136/bmj.b1024.
Moore TJ, Glenmullen J, Furberg CD. **Thoughts and Acts of Aggression/Violence** Toward Others Reported in Association with **Varenicline** (September) (FREE). Ann Pharmacother. 2010 Jul 20.
Moore TJ, Furberg CD, Glenmullen J, Maltsberger JT, Singh S, 2011 **Suicidal Behavior and Depression in Smoking** Cessation Treatments. PLoS ONE 6(11): e27016. doi:10.1371/journal.pone.0027016
Morain SR, Winickoff JP, Mello MM. Have **Tobacco 21 Laws Come of Age**? N Engl J Med. 2016 Mar 23.
Morean ME, Kong G, Camenga DR, et al. High School Students' Use of **Electronic Cigarettes** to **Vaporize Cannabis**. Pediatrics. 2015 Sep 7.
Moreno MA. **Risks of hookah smoking**. JAMA Pediatr. 2015 Feb 1;169(2):196.
Moreno MA. **What Parents Need to Know** About **Electronic Cigarettes**. JAMA Pediatr. 2017 Oct 23.
Morgenstern M, Sargent JD, Isensee B, Hanewinkel R. From never to daily smoking in 30 months: the predictive value of tobacco and non-tobacco **advertising exposure**. BMJ Open. 2013 Jun 20;3(6).
Moshammer H, et al. **Parental smoking** and lung function in children: an international study. Am J Respir Crit Care Med. 2006 Jun 1;173(11):1255-63. Epub 2006 Feb 16.
Moyer VA, MD, MPH, on behalf of the US Preventive Services Task Force-**USPSTF**. Primary care interventions to **prevent tobacco use in children and adolescents**: US Preventive Services Task Force recommendation statement. Ann Intern Med 2013.
Moyer VA; U.S. Preventive Services Task Force. Primary care interventions to **prevent tobacco use in children and adolescents**: US Preventive services task force recommendation statement. Pediatrics. 2013 Sep;132(3):560-5.
Mullane D, Turner SW, Cox D, et al. **Reduced Infant Lung Function, Active Smoking, and Wheeze** in 18-Year-Old Individuals. JAMA Pediatr. 2013 Feb 18:1-6.
Müller KU, Mennigen E, Ripke S, et al; for the IMAGEN Consortium. **Altered Reward Processing in Adolescents** With Prenatal Exposure to Maternal Cigarette Smoking. JAMA Psychiatry. 2013 Jun 19:1-10.
Munro HM, Tarone RE, Wang TJ, Blot WJ. **Menthol and Non-Menthol Cigarette Smoking**: All-Cause, Cardiovascular Disease and Other Causes of Death Among Blacks and Whites. Circulation. 2016 Mar 28.
Muramoto ML, Leischow SJ, Sherrill D, Matthews E, Strayer LJ. Randomized, double-blind, placebo-controlled trial of 2 dosages of sustained-release **bupropion for adolescent** smoking cessation. Arch Pediatr Adolesc Med. 2007 Nov;161(11):1068-74. Sustained-release bupropion hydrochloride, 300 mg/d, plus brief counseling demonstrated short-term efficacy for adolescent smoking cessation. Abstinence rates were lower than those reported for adults, with rapid relapse after medication discontinuation.
Murphy F, Crossley G. Smoking cessation: **state owned tobacco companies in China and Japan are at odds with their countries' commitments**. BMJ. 2019 Jun 19;365:l2328.
Murray RL, Leonardi-Bee J, Marsh J, et al. Systematic identification and treatment of smokers by **hospital based cessation practitioners** in a secondary care setting: cluster randomised controlled trial. BMJ. 2013 Jul 8;347:f4004.
Musallam KM, Rosendaal FR, Zaatari G, et al. Smoking and the Risk of **Mortality** and Vascular and Respiratory Events in Patients **Undergoing Major Surgery**. JAMA Surg. 2013 Jun 19:1-8.
Muscat JE, Ahn K, Richie JP Jr et al. **Nicotine dependence phenotype** and lung cancer risk. Cancer. 2011 Dec 1;117(23):5370-6.
Müssener U, Bendtsen M, Karlsson N, et al. Effectiveness of **Short Message Service Text-Based Smoking Cessation Intervention** Among University Students: A Randomized Clinical Trial. JAMA Intern Med. 2016 Feb 22.
Mutsaerts MAQ et al. Randomized trial of a **lifestyle program in obese infertile women**. N Engl J Med 2016 May 19; 374:1942.
Myers Katie; Hajek Peter; Hinds Charles; et al. **Stopping Smoking Shortly Before Surgery and Postoperative Complications**: A Systematic Review and Meta-analysis. Arch Intern Med. 2011;0(2011):archinternmed.2011.97.
Nabi-Burza E, Drehmer JE, Hipple Walters B, et al. Treating Parents for **Tobacco Use in the Pediatric Setting**: The Clinical Effort Against Secondhand Smoke Exposure Cluster Randomized Clinical Trial. JAMA Pediatr. 2019 Aug 12.
Nabi-Burza E, Regan S, Drehmer J, et al. **Parents Smoking in Their Cars** With Children Present. Pediatrics. 2012 Nov 12.
Nagrebetsky A, Brettell R, Roberts N, et al. **Smoking cessation in adults with diabetes**: a systematic review and meta-analysis of data from randomized controlled trials. BMJ Open. 2014 Mar 6.
Nakamura M, Oshima A, Ohkura M, et al. Predictors of **Lapse and Relapse** to Smoking in Successful Quitters in a **Varenicline** Post Hoc Analysis in Japanese Smokers. Clin Ther. 2014 May 5.
Nakamura M, Abe M, Ohkura M, et al. Efficacy of **Varenicline** for Cigarette Reduction Before Quitting in **Japanese Smokers**: A Subpopulation Analysis of the Reduce to Quit Trial. Clin Ther. 2017 Mar 29.
Nash SH, Liao LM, Harris TB, Freedman ND. Cigarette Smoking and Mortality in Adults **Aged 70 Years and Older**: Results From the **NIH-AARP** Cohort. Am J Prev Med. 2016 Nov 22.
Nathisuwan S, Dilokthornsakul P, Chaiyakunapruk N, et al. Assessing Evidence of **Interaction Between Smoking and Warfarin**: A Systematic Review and Meta-analysis. Chest. 2011 May;139(5):1130-9.
National Institutes of Health State-of-the-Science Conference Statement: **Tobacco Use**: Prevention, Cessation, and Control. Ann Intern Med. 2006 Sep 5; [Epub ahead of print]
Neri AJ, Momin BR, Thompson TD, et al. Use and effectiveness of **quitlines versus Web-based tobacco cessation interventions** among 4 state tobacco control programs. Cancer. 2016 Feb 8.
Ness-Jensen E, Lindam A, Lagergren J, Hveem K. Tobacco Smoking Cessation and **Improved Gastroesophageal Reflux**: A Prospective Population-Based Cohort Study: The HUNT Study. Am J Gastroenterol. 2013 Dec 10.
Ng M, Freeman M, Fleming T, et al. **Smoking prevalence and cigarette consumption in 187 countries**, 1980-2012. JAMA. doi:10.1001/jama.2013.284692.
Nguyen KH, Gomez Y, et al. Tobacco **Use, Secondhand Smoke, and Smoke-Free Home Rules** in **Multiunit Housing**. Am J Prev Med. 2016 Nov;51(5):682-692
Nguyen UDT, Zhang Y, Lu N, et al. Smoking paradox in the development of **psoriatic arthritis** among patients with psoriasis: a population-based study. Ann Rheum Dis. 2018 Jan;77(1):119-123.
Niaura RS, Glynn TJ, Abrams DB. Youth experimentation with **e-cigarettes**: another interpretation of the data. JAMA. 2014 Aug 13;312(6):641-2.
NICE: National Institute for Health and Clinical Excellence. **Smokeless tobacco cessation** - South Asian communities. Sept 2012. www.nice.org.uk/PH39
Nicoll KJ, Rose AM, Khan MA, et al. **Thigh burns from exploding e-cigarette lithium ion batteries**: First case series. Burns. 2016 Apr 22.
Nides M, et al. Smoking cessation with **varenicline**, a selective alpha4beta2 nicotinic receptor partial agonist: results from a 7-week, randomized, placebo- and bupropion-controlled trial with 1-year follow-up. Arch Intern Med. 2006 Aug 14-28;166(15):1561-8. (InfoPOEMs: Approximately 1 in 7 highly motivated patients will not be smoking 1 year after taking varenicline (Chantix) 1 mg twice daily for 6 weeks. Lower doses did not work. Side effects will be common and will not be tolerated by some patients. (LOE = 1b-))
Niemelä S et al. **Prenatal nicotine exposure** and risk of **schizophrenia** among offspring in a national birth cohort. Am J Psychiatry 2016 May 24 .
Noble MJ, Longstreet B, Hendrickson RG, et al. Unintentional **Pediatric Ingestion of Electronic Cigarette Nicotine Refill Liquid** Necessitating Intubation. Ann Emerg Med. 2017 Jan;69(1):94-97.
Nolan MB, Martin DP, et al. Association between **smoking status**, preoperative exhaled carbon monoxide levels, and **postoperative surgical site infection** in patients undergoing elective surgery [online Feb 15, 2017].JAMA Surg. doi:10.1001/jamasurg.2016.5704
Nolan MB, Warner DO. **Perioperative tobacco use treatments**: putting them into practice. BMJ. 2017 Sep 6;358:j3340
Nunes T, Etchevers MJ, García-Sánchez Vet al. Impact of Smoking Cessation on the Clinical Course of **Crohn's Disease** Under Current Therapeutic Algorithms: A Multicenter Prospective Study. Am J Gastroenterol. 2016 Mar;111(3):411-9.
Oberg M, Jaakkola MS, Woodward A, Peruga A, Prüss-Ustün A. Worldwide burden of disease from exposure to **second-hand** smoke: a retrospective analysis of data from 192 countries. Lancet. 2010 Nov 25.
O'Dowd A. What next for **tobacco's legal war against regulation**? BMJ. 2014 Sep 23;349:g5770.
O'Malley SS, Zweben A, Fucito LM, et al. Effect of **varenicline combined with medical management on alcohol use disorder** with comorbid cigarette smoking: a randomized clinical trial [online Dec 20, 2017].JAMA Psychiatry. doi:10.1001/jamapsychiatry.2017.3544
O'Malley SS, et al. A controlled trial of **naltrexone augmentation** of nicotine replacement therapy for smoking cessation. Arch Intern Med. 2006 Mar 27;166(6):667-74.
O'Shea R, Byrne H, Tuckett J, et al. Impact of Current Smoking and **Alcohol Consumption on Gastrostomy Duration** in Patients With Head and Neck Cancer Undergoing Definitive Chemoradiotherapy. JAMA Otolaryngol Head Neck Surg. 2015 Mar 19.
Ockene I and Salmoirago-Blotcher E. **Varenicline** for smoking cessation in patients with **coronary heart disease**. Circulation 2010; 121:188-190.
Oncken C, et al. Efficacy and safety of the novel selective nicotinic acetylcholine receptor partial agonist, **varenicline**, for smoking cessation. Arch Intern Med. 2006 Aug 14-28;166(15):1571-7.
Oncken C, Dornelas E, Greene J, et al. Nicotine **Gum for Pregnant Smokers**: A Randomized Controlled Trial. Obstet Gynecol. 2008 Oct;112(4):859-867. Although nicotine gum did not increase quit rates, use of nicotine gum increased birth weight and gestational age, two key parameters in predicting neonatal wellbeing.
Okuyemi KS, Nollen NL, Ahluwalia JS. **Interventions** to facilitate smoking cessation. Am Fam Physician. 2006 Jul 15;74(2):262-71. Review. Summary for patients in: Am Fam Physician. 2006 Jul 15;74(2):276.
Odani S, Armour BS, Graffunder CM, et al. Prevalence and Disparities in Tobacco Product **Use Among American Indians/Alaska Natives** – United States, 2010-2015. MMWR Morb Mortal Wkly Rep. 2017 Dec 22;66(50):1374-1378.
Orr KK, Asal NJ. Efficacy of **Electronic Cigarettes for Smoking Cessation**. Ann Pharmacother. 2014 Nov;48(11):1502-1506.
Ota E, Hori H, Mori R, et al. **Antenatal dietary education and supplementation to increase energy and protein intake**. Cochrane Database Syst Rev 2015;6:CD000032. This review provides encouraging evidence that antenatal nutritional education with the aim of increasing energy and protein intake in the general obstetric population appears to be effective in reducing the risk of preterm birth, low birthweight, increasing head circumference at birth, increasing birthweight among undernourished women, and increasing protein intake. There was no evidence of benefit or adverse effect for any other outcome reported.
Pack QR, Priya A, Lagu TC, et al. **Smoking Cessation Pharmacotherapy Among Smokers Hospitalized for Coronary Heart Disease**. JAMA Intern Med. 2017 Aug 21.
Padovano HT, Merrill JE, Colby SM, et al. **Affective and Situational Precipitants of Smoking Lapses** among Adolescents. Nicotine Tob Res. 2019 Jan 8.
Pagani LS, Nguyen AK, Fitzpatrick C. Prospective associations between early **long-term household tobacco smoke exposure and subsequent indicators of metabolic risk** at age 10. Nicotine Tob Res. 2015 Jun 11.
Pagidipati NJ, Hellkamp A, Thomas L, et al. Use of **Prescription Smoking Cessation Medications After Myocardial Infarction** Among Older Patients in Community Practice. JAMA Cardiol. 2017 Jul 19.
Palamar JJ, Zhou S, Sherman S, et al. **Hookah** Use Among US High School Seniors. Pediatrics. 2014 Jul 7.
Palmer J, Lloyd A, Steele L, et al. Differential **Risk of ST-Segment Elevation Myocardial Infarction in Male and Female Smokers**. J Am Coll Cardiol. 2019 Jul 2;73(25):3259-3266.
Pan A, Wang Y, Talaei M, et al. Relation of **Smoking with Total Mortality and Cardiovascular Events Among Patients with Diabetes**: A Meta-Analysis and Systematic Review. Circulation. 2015 Aug 26.
Pan A, Wang Y, Talaei M, et al. Relation of **active, passive, and quitting smoking with incident type 2 diabetes**: a systematic review and meta-analysis. Lancet Diabetes Endocrinol. 2015 Sep 17.
Pan A, Wang Y, Talaei M, et al. Relation of active, passive, and quitting **smoking** with incident **type 2 diabetes**: a systematic review and meta-analysis. Lancet Diabetes Endocrinol. 2015 Sep 17.
Papadakis S, Cole AG, Reid RD, et al.Increasing Rates of Tobacco Treatment Delivery in Primary Care Practice: Evaluation of the **Ottawa Model** for Smoking Cessation. Ann Fam Med. 2016 May;14(3):235-43.
Park ER, Gareen IF, Japuntich S, et al. **Primary care provider-delivered smoking cessation interventions** and smoking cessation among participants in the National Lung Screening Trial [online June 15, 2015]. JAMA Intern Med. doi:10.1001/jamainternmed.2015.2391.
Park EW, Tudiver FG, Campbell T. Enhancing **partner support** to improve smoking cessation. Cochrane Database Syst Rev. 2012 Jul 11;7:CD002928. In this review of randomized controlled trials of interventions designed to enhance partner support for smokers in cessation

programmes, we failed to detect an increase in quit rates.
Park SH, Duncan DT, El Shahawy O, et al. Analysis of state-specific prevalence, regional differences, and correlates of **hookah use** in U.S. adults, 2012-2013. Nicotine Tob Res. 2016 Sep 9.
Park SH, Duncan DT, Shahawy OE, et al. Characteristics of Adults Who **Switched From Cigarette Smoking to E-cigarettes**. Am J Prev Med. 2017 Nov;53(5):652-660.
Parker MA, Villanti AC, Quisenberry AJ, et al. Tobacco Product **Harm Perceptions** and New Use. Pediatrics. 2018 Nov 5.
Parkes G, Greenhalgh T, Griffin M, Dent R. Effect on smoking quit rate of telling patients their **lung age**: the Step2quit randomised controlled trial. BMJ. 2008 Mar 6; [Epub ahead of print] Telling smokers their lung age significantly improves the likelihood of them quitting smoking, but the mechanism by which this intervention achieves its effect is unclear.
Parsons A, Daley A, Begh R, Aveyard P. Influence of **smoking cessation after diagnosis** of early stage **lung cancer** on prognosis: systematic review of observational studies with meta-analysis. BMJ 2010;340:b5569, doi: 10.1136/bmj.b5569 (Published 21 January 2010)
Passarelli MN, Newcomb PA, Hampton JM, et al. Cigarette **Smoking Before and After Breast Cancer** Diagnosis: Mortality From Breast Cancer and Smoking-Related Diseases. J Clin Oncol. 2016 Jan 25.
Patel MS, Steinberg MB. **In the Clinic. Smoking Cessation**. Annals of Internal Medicine 1 March 2016.
Patnode CD, O`Connor E, Whitlock EP, et al. **Primary Care-Relevant Interventions for Tobacco Use Prevention and Cessation in Children and Adolescents**: A Systematic Evidence Review for the U.S. Preventive Services Task Force. Ann Intern Med. 2012 Dec 11.
Patnode CD, O'Connor E, Whitlock EP, et al. **Primary Care Relevant Interventions** for Tobacco Use Prevention and Cessation in Children and Adolescents: A Systematic Evidence Review for the U.S. Preventive Services Task Force [Internet]. Rockville (MD): Agency for Healthcare Research and Quality (US); 2012 Dec.
Patnode CD, O'Connor E, Whitlock EP, et al. **Primary care-relevant interventions** for tobacco use prevention and cessation in children and adolescents: a systematic evidence review for the u.s. Preventive services task force. Ann Intern Med. 2013 Feb 19;158(4):253-60.
Patnode CD, Henderson JT, et al. **Behavioral Counseling and Pharmacotherapy Interventions for Tobacco Cessation** in **Adults, Including Pregnant Women**: A **Review** of Reviews for the U.S. Preventive Services Task Force (USPSTF). Ann Intern Med. 2015 Sep 22.
Patrick SW, Warner KE, Pordes E, et al. **Cigarette Tax** Increase and Infant Mortality. Pediatrics. 2015 Dec 1.
Pawson R, Wong G, Owen L. Myths, facts and conditional truths: What is the evidence on the risks associated with **smoking in cars carrying children**? CMAJ. 2011 Jul 12;183(10):E680-4.
Peters SA, Huxley RR, Woodward M. Smoking as a **Risk Factor for Stroke** in Women Compared With Men: A Systematic Review and Meta-Analysis of 81 Cohorts, Including 3 980 359 Individuals and 42 401 Strokes. Stroke. 2013 Aug 22.
Pbert L, Druker S, Difranza JR, et al. Effectiveness of a **School Nurse-Delivered Smoking-Cessation Intervention** for Adolescents. Pediatrics. 2011 Oct 17.
Pbert L, Farber H, Horn K, et al. American Academy of Pediatrics, Julius B. Richmond Center of Excellence Tobacco Consortium. State-of-the-Art Office-Based **Interventions to Eliminate Youth Tobacco Use**: The Past Decade. Pediatrics. 2015 Mar 16.
Pechmann C, Delucchi K, Lakon CM, Prochaska JJ. Randomised controlled trial evaluation of **Tweet2Q**uit: a social network quit-smoking intervention. Tob Control. 2016 Feb 29.
Pell JP, Haw S, Cobbe S, et al. **Smoke-free legislation** and hospitalizations for acute coronary syndrome. N Engl J Med. 2008 Jul 31;359(5):482-91. The number of admissions for acute coronary syndrome decreased after the implementation of smoke-free legislation. A total of 67% of the decrease involved nonsmokers. However, fewer admissions among smokers also contributed to the overall reduction.
Perez MF, Bastian LA, Oncken C. Counterpoint: Are **advanced practice professionals** more likely to **achieve better tobacco cessation** results than physicians? No. Chest. 2017 Apr 12.
Petersen ER, Oturai AB, Koch-Henriksen N, et al. **Smoking affects the interferon beta** treatment response in **multiple sclerosis**. Neurology. 2018 Feb 13;90(7):e593-e600.
Petersson GH, Twetman S. Tobacco use and **caries increment** in young adults: a prospective observational study. BMC Res Notes. 2019 Apr 11;12(1):218.
Petrucci CM, Hyland A. Understanding **the Financial Consequences** of Smoking During Cancer Treatment in the Era of Value-Based Medicine. JAMA Netw Open. 2019 Apr 5;2(4):e191713.
Pharmacist's Letter. **Electronic Cigarettes and Hookah** Pipes. May 2013.
Pharmacists Letter. New Regimen for Nicorette Gum: **Reduce-to-Quit** (RTQ). Aug 2007.
Phung A, Luo L, Breik N, Alessi-Severini S. **Use of smoking cessation products**: A survey of patients in community pharmacies. Can Pharm J (Ott). 2017 Aug 2;150(5):326-333.
Piano Mariann R., Benowitz Neal L., FitzGerald Garret A., et al., and on behalf of the American Heart Association (AHA) Council on Cardiovascular Nursing Impact of **Smokeless Tobacco Products** on Cardiovascular Disease: Implications for Policy, Prevention, and Treatment: A Policy Statement From the American Heart Association. Circulation 122: 1520-1544; published online before print as doi:10.1161/CIR.0b013e3181f432c3
Pierce John P., Messer Karen, White Martha M., et al. **Prevalence of Heavy Smoking** in California and the United States, 1965-2007. *JAMA*. 2011;305(11):1106-1112.doi:10.1001/jama.2011.334
Pierce JP, Sangent JD, White MM, et al. **Receptivity to Tobacco Advertising** and Susceptibility to Tobacco Products. Peds.2017;139(6):e20163353
Pierce JP, Sargent JD, Portnoy DB, et al. Association between **receptivity to tobacco advertising and progression to tobacco use in youth and young adults in the PATH** study [online Mar 26, 2018].JAMA Pediatr. doi:10.1001 /jamapediatrics.2017.5756.
Pinnamaneni K, Sievers RE, Sharma R, et al. Brief exposure to **secondhand smoke** reversibly impairs endothelial vasodilatory function. Nicotine Tob Res. 2014 May;16(5):584-90.
Piper Megan E.; Smith Stevens S.; Schlam Tanya R.; et al. A Randomized Placebo-Controlled Clinical Trial of **5 Smoking Cessation Pharmacotherapies**. Arch Gen Psychiatry. 2009;66(11):1253-1262. While the nicotine lozenge, bupropion, and bupropion plus lozenge produced effects that were comparable with those reported in previous research, the nicotine patch plus lozenge produced the greatest benefit relative to placebo for smoking cessation.
Pirie K, Peto R, Reeves GK, Green J, Beral V, for the **Million Women Study Collaborators**. The 21st century **hazards of smoking and benefits of stopping**: a prospective study of one million women in the UK. Lancet 2012; online Oct 27.
Pisinger C, Døssing M. A systematic review of health effects of **electronic cigarettes**. Prev Med. 2014 Oct 16;69C:248-260.
Planer David; Lev Ishay; Elitzur Yair; et al. **Bupropion** for Smoking Cessation in Patients With **Acute Coronary Syndrome**. Arch Intern Med. 2011;0(2011):archinternmed.2011.72. (Not increase smoking abstinence)
Plank B, Kutyifa V, Moss AJ, et al. Smoking is associated with an increased risk of **first and recurrent ventricular tachyarrhythmias** in mild heart failure patients with ischemic and non-ischemic cardiomyopathy—A MADIT-CRT substudy. *Heart Rhythm* 2014.
Pletcher MJ, et al. Menthol cigarettes, smoking cessation, atherosclerosis, and pulmonary function: the Coronary Artery Risk Development in Young Adults (CARDIA) Study. Arch Intern Med. 2006 Sep 25;166(17):1915-22.
Poddubnyy D, Haibel H, Listing J, et al. Baseline radiographic damage, elevated acute phase reactants and cigarette smoking status predict radiographic progression in the spine in early **axial spondyloarthritis**. Arthritis Rheum. Published Online First: 29 Nov 2011.
Polakowski LL, Akinbami LJ, Mendola P. Prenatal Smoking Cessation and the Risk of Delivering **Preterm and Small-for-Gestational-Age Newborns**. Obstet Gynecol. 2009 Aug;114(2, Part 1):318-325.
Pollak KI, Oncken CA, et al. Nicotine replacement and behavioral therapy for smoking cessation in **pregnancy**. Am J Prev Med. 2007 Oct;33(4):297-305.
Power MC, Deal JA, Sharrett AR, et al. **Smoking and white matter hyperintensity progression**: The ARIC-MRI Study. Neurology. 2015 Feb 24; 84(8):841-8.
Pozuelos GL, Kagda MS, Schick S, et al. Experimental Acute **Exposure to Thirdhand Smoke and Changes in the Human Nasal Epithelial** Transcriptome: A Randomized Clinical Trial. JAMA Netw Open. 2019 Jun 5;2(6):e196362.
Preloading Investigators. Effects on abstinence of **nicotine patch treatment before quitting smoking**: parallel, two arm, pragmatic randomised trial. BMJ. 2018 Jun 13;361:k2164.
Primack BA, Soneji S, Stoolmiller M, et al. Progression to Traditional Cigarette Smoking After **Electronic Cigarette** Use among US Adolescents and Young Adults. JAMA Pediatr. 2015 Sep 8:1-7.
Prochazka AV, Kick S, Steinbrunn C, Miyoshi T, Fryer GE. A randomized trial of **nortriptyline combined with transdermal nicotine** for smoking cessation. Arch Intern Med. 2004 Nov 8;164(20):2229-33.
Prochazka AV, Weaver MJ, Keller RT, Fryer GE, Licari PA, Lofaso D. A randomized trial of **nortriptyline** for smoking cessation. Arch Intern Med. 1998 Oct 12;158(18):2035-9.
Prochaska JJ, Hilton JF. Risk of **cardiovascular serious adverse events associated with varenicline** use for tobacco cessation: systematic review and meta-analysis. BMJ. 2012 May 4;344:e2856.
Prochaska JJ, Das S, Benowitz NL. **Cytisine**, the world's oldest smoking cessation aid. BMJ. 2013 Aug 23;347:f5198.
Prochaska JJ, Michalek AK, Brown-Johnson C, Daza et al. **Likelihood of Unemployed Smokers vs Nonsmokers Attaining Reemployment** in a One-Year Observational Study. JAMA Intern Med. 2016 Apr 11.
Prokhorov Alexander V.; Hudmon Karen Suchanek; Marani Salma; et al. Engaging Physicians and Pharmacists in Providing **Smoking Cessation Counseling**. Arch Intern Med. 2010;170(18):1640-1646.
Provini LE, Corwin MJ, Geller NL, et al. Differences in **Infant Care Practices** and Smoking among Hispanic Mothers Living in the United States. J Pediatr. 2016 Dec 13.
Pulakka A, Halonen JI, Kawachi I, et al. Association Between **Distance From Home to Tobacco Outlet** and Smoking Cessation and Relapse. JAMA Intern Med. 2016 Aug 15.
Quinn PD, Rickert ME, Weibull CE, et al. Association between **maternal smoking during pregnancy** and severe mental illness in offspring [online May 3, 2017].JAMA Psychiatry. doi:10.1001/jamapsychiatry.2017.0456
Raad D, Gaddam S, Schunemann HJ, et al. Effects of **Water-Pipe Smoking** (WPS) on Lung Function: A Systematic Review and Meta-analysis. Chest. 2011 Apr;139(4):764-74.
Raghuveer G, et al. **Cardiovascular Consequences of Childhood Secondhand Tobacco** Smoke Exposure: Prevailing Evidence, Burden, and Racial and Socioeconomic Disparities: A Scientific Statement From the American Heart Association. Circulation. 2016 Sep 12.
Ramanujam R, Hedström AK, Manouchehrinia A, et al. Effect of **Smoking Cessation on Multiple Sclerosis Prognosis**. JAMA. Neurol. 2015 Sep 8:1-7.
Ranney L, Melvin C, Lux L, McClain E, Lohr KN. Systematic Review: Smoking Cessation **Intervention** Strategies for Adults and Adults in Special Populations. Ann Intern Med. 2006 Sep 5; [Epub ahead of print]
Reda AA, Kaper J, Fikrelter H, et al. Healthcare **financing systems** for increasing the use of tobacco dependence treatment. Cochrane Database Syst Rev. 2009 Apr 15;(2):CD004305. Full financial interventions directed at smokers when compared to no financial interventions could increase the proportion quitting, quit attempts and utilization of pharmacotherapy by smokers. Although the absolute differences were small the costs per additional quitter were low.
Reda AA, Kotz D, Evers SM, et al. Healthcare **financing systems** for increasing the use of tobacco dependence treatment. Cochrane Database Syst Rev. 2012 Jun 13;6:CD004305. Full financial interventions directed at smokers when compared to no financial interventions increase the proportion of smokers who attempt to quit, use smoking cessation treatments, and succeed in quitting. The absolute differences are small but the costs per additional quitter are low to moderate. We did not detect an effect on smoking cessation from financial incentives directed at healthcare providers.
Reddy KP, Kong CY, Hyle EP, et al. **Lung cancer mortality** associated with smoking and smoking cessation among people living **with HIV** in the United States [online September 18, 2017].JAMA Intern Med. doi:10.1001 /jamainternmed.2017.4349
Reed JL, Gervais AA, Reid RD. **Electronic cigarettes**. CMAJ. 2013 Nov 5;185(16):1427.
Reid RD, Pritchard G, Walker K, et al. **Managing smoking cessation**. CMAJ. 2016 Dec 6;188(17-18):E484-E492.
Reid RD, Malcolm J, Wooding E, et al. Prospective, Cluster-Randomized Trial to Implement the **Ottawa Model for Smoking Cessation** in Diabetes Education Programs in Ontario, Canada. Diabetes Care. 2017 Dec 21.
Reidel B, Radicioni G, Clapp P, et al. **E-Cigarette** Use Causes a Unique Innate **Immune Response in the Lung** Involving Increased Neutrophilic Activation and Altered Mucin Secretion. Am J Respir Crit Care Med. 2017 Oct 20.
Regan S, Viana JC, Reyen M, Rigotti NA. Prevalence and Predictors of **Smoking by Inpatients During a Hospital Stay**. Arch Intern Med. 2012 Nov 5:1-5.
Retnakaran R, et al. Cigarette smoking and **cardiovascular risk** factors among Aboriginal Canadian youths. CMAJ. 2005 Oct 11;173(8):885-9.
Reynolds K, Liese AD, Anderson AM, et al. Prevalence of Tobacco Use and Association between Cardiometabolic Risk Factors and Cigarette **Smoking in Youth with Type 1 or Type 2 Diabetes Mellitus**. J Pediatr. 2011 Apr;158(4):594-601.e1.
Rezk-Hanna M, Mosenifar Z, Benowitz NL, et al. High Carbon Monoxide Levels from Charcoal Combustion Mask **Acute Endothelial Dysfunction Induced by Hookah (Waterpipe) Smoking** in Young Adults. Circulation. 2019 May 7;139(19):2215-2224.
Rice VH, Hartmann-Boyce J, Stead LF. **Nursing interventions for smoking cessation**. Cochrane Database Syst Rev. 2013 Aug 12;8:CD001188. The results indicate the potential benefits of smoking cessation advice and/or counselling given by nurses, with reasonable evidence that intervention is effective.
Rice VH, Heath L, Livingstone-Banks J, et al. **Nursing interventions for smoking cessation.** Cochrane Database Syst Rev. 2017 Dec 15;12:CD001188. There is moderate quality evidence that behavioural support to motivate and sustain smoking cessation delivered by nurses can lead to a modest increase in the number of people who achieve prolonged abstinence. There is insufficient evidence to assess whether more intensive interventions, those incorporating additional follow-up, or those incorporating pathophysiological feedback are more effective than one-off support. There was no evidence that the effect of support differed by patient group or across healthcare settings.

Richman I, Krumholz HM. **Lessons From the Opioid Epidemic to Reinvigorate Tobacco Control Initiatives**. JAMA. 2018 Jan 23;319(4):339-340.

Riehm KE, Young AS, Feder KA, et al. **Mental Health Problems** and Initiation of E-cigarette and Combustible Cigarette Use. Pediatrics. 2019 Jun 3.

Rigotti NA, et al. Bupropion for smokers hospitalized with acute **cardiovascular disease**. Am J Med. 2006 Dec;119(12):1080-7. Bupropion improved short-term but not long-term smoking cessation rates over intensive counseling and appeared to be safe in hospitalized smokers with acute cardiovascular disease.

Rigotti NA, Munafo MR, and Stead LF. Smoking cessation interventions for **hospitalized smokers**. A systematic review. Arch Intern Med 2008; 168:1950-1960. Offering smoking cessation counseling to all hospitalized smokers is effective as long as supportive contacts continue for more than 1 month after discharge. Adding nicotine replacement therapy to counseling may further increase smoking cessation rates and should be offered when clinically indicated, especially to hospitalized smokers with nicotine withdrawal symptoms.

Rigotti N A, Pipe AL, Benowitz NL, et al. Efficacy and safety of **varenicline** for smoking cessation in patients with cardiovascular disease (**CVD**). Circulation 2010; 121:221-229.

Rigotti NA. **Strategies to help a smoker who is struggling to quit**. JAMA. 2012; 308:1573-1580.

Rigotti NA, Clair C,Munafò MR, Stead LF. Interventions for **smoking cessation in hospitalised patients**. Cochrane Database of Systematic Reviews 2012, Issue 5. Art. No.: CD001837. DOI: 10.1002/14651858.CD001837.pub3.

Rigotti NA, Wakefield M. **Real People, Real Stories**: A New Mass Media Campaign That Could Help Smokers Quit. Ann Intern Med. 2012 Sep 25.

Rigotti NA. Smoking cessation in patients **with respiratory disease**: existing treatments and future directions. Lancet Respir Med. 2013 May;1(3):241-50

Rigotti NA, Regan S, Levy DE, et al. **Sustained care intervention and postdischarge smoking cessation** among hospitalized adults: a randomized clinical trial. JAMA. 2014 Aug 20;312(7):719-28.

Rigotti NA, Park ER, Streck J, et al. An Intervention to Address **Secondhand Tobacco Smoke Exposure** Among Nonsmokers Hospitalized **With Coronary Heart Disease**. Am J Cardiol. 2014 Jul 17.

Rigotti NA. Balancing the **Benefits and Harms of Electronic Cigarettes**: A National Academies of Science, Engineering, and Medicine Report. Ann Intern Med. 2018 Feb 13.

Rigotti NA, Chang Y, Tindle HA, et al. Association of **E-Cigarette Use With Smoking Cessation** Among Smokers **Who Plan to Quit After a Hospitalization**: A Prospective Study. Ann Intern Med. 2018 Mar 27.

Ritz B, Lee PC, Lassen CF, Arah OA. **Parkinson disease and smoking** revisited: ease of quitting is an early sign of the disease. Neurology 2014;83:1396–1402.

Roberts E, Eden Evins A, McNeill A, et al. Efficacy and tolerability of **pharmacotherapy for smoking cessation** in adults with serious **mental illness**: a systematic review and network meta-analysis. Addiction. 2016 Apr;111(4):599-612.

Robson D, Spaducci G, McNeill A, et al. Effect of implementation of a **smoke-free policy on physical violence in a psychiatric inpatient setting**: an interrupted time series analysis. Lancet Psychiatry 2017; online June 14.

Roditis ML, Halpern-Felsher B. **Adolescents' Perceptions** of Risks and Benefits of **Conventional Cigarettes, E-cigarettes, and Marijuana**: A Qualitative Analysis. J Adolesc Health. 2015 Jun 12.

Rodondi N, Collet TH, Nanchen D, et al. Impact of **carotid plaque screening** on smoking cessation and other cardiovascular risk factors: a randomized controlled trial. Arch Intern Med. doi:10.001/archinternmed.2011.1326.

Rodriguez Josanna, Jiang Rui, Johnson W. Craig, Et al. The Association of **Pipe and Cigar** Use With Cotinine Levels, Lung Function, and Airflow Obstruction: A Cross-sectional Study. *Ann Intern Med* February 16, 2010 152:201-210

Roeseler A, Vuong TD, Henriksen L, Zhang X. Assessment of **Underage Sales Violations** in Tobacco Stores and Vape Shops. JAMA Pediatr. 2019 Jun 24.

Rojewski AM, Tanner NT, Dai L, et al. **Tobacco Dependence Predicts Higher Lung Cancer** and Mortality Rates and Lower Rates of Smoking Cessation in the National Lung Screening Trial. Chest. 2018 May 17.

Roosaar A, Johansson AL, Sandborgh-Englund G, Axéll T, Nyrén O. Cancer and mortality among users and nonusers of **snus**. Int J Cancer. 2008 Jul 1;123(1):168-73. A statistically significant increase in the incidence of the combined category of oral and pharyngeal cancer among daily users of snus (incidence rate ratio 3.1, 95% confidence interval 1.5-6.6) was found. Overall mortality was also slightly increased (hazard ratio 1.10, 95% confidence interval 1.01-1.21). Although the combined previous literature on snus and oral cancer weigh toward no association, this population-based prospective study provided suggestive evidence of snus-related risks that cannot be lightly ignored.

Rose JE, Behm FM. **Combination Treatment With Varenicline and Bupropion** in an Adaptive Smoking Cessation Paradigm. Am J Psychiatry. 2014 Jun 17.

Rose-Jacobs R, Richardson MA, Buchanan-Howland K, et al. **Intrauterine exposure to tobacco and executive functioning in high school**. Drug Alcohol Depend. 2017 May 10;176:169-175.

Rosen LJ, Noach MB, Winickoff JP et al. **Parental Smoking Cessation** to Protect Young Children:A Systematic Review and Meta-analysis. Pediatrics. 2012 Jan;129(1):141-52

Rosen LJ, Myers V, Hovell M, et al. Meta-analysis of **Parental Protection of Children** From Tobacco Smoke Exposure. Pediatrics. 2014 Apr;133(4):698-714.

Rosen RL, Steinberg ML. Interest in **Quitting E-Cigarettes among Adults** in the United States. Nicotine Tob Res. 2019 Apr 23.

Rostron B. **Menthol Cigarette** Use and Stroke Risk Among US Smokers: A Critical Reappraisal. JAMA Intern Med. 2014 Mar 10.

Rostron BL, Chang CM, et al. Estimating **cigarette smoking–attributable morbidity** in the United States [online Oct 13, 2014]. JAMA Intern Med. doi: 10.1001/jamainternmed.2014.5219.

Rostron BL, Chang CM, van Bemmel DM, et al. **Nicotine and Toxicant Exposure** among U.S. **Smokeless Tobacco Users**: Results from 1999 to 2012 National Health and Nutrition Examination Survey Data. Cancer Epidemiol Biomarkers Prev. 2015 Nov 18.

Royal College of Physicians. **Nicotine without smoke**: tobacco harm reduction—a report by the Tobacco Advisory Group of the Royal College of Physicians. Apr 2016. www. rcplondon.ac.uk/projects/outputs/nicotine-without-smoke-tobacco-harm-reduction.

Rubinstein ML, Delucchi K, Benowitz NL, et al. Adolescent Exposure to **Toxic Volatile Organic Chemicals From E-Cigarettes**. Pediatrics. 2018 Mar 5.

Rusanen Minna; Kivipelto Miia; Quesenberry Charles P., et al. Heavy Smoking in Midlife and Long-term Risk of **Alzheimer Disease and Vascular Dementia**. Arch Intern Med. 2010;0(2010):archinternmed.2010.393.

Rusanen M, Kivipelto M, et al.,"Heavy Smoking in Midlife and **Long-term Risk of Alzheimer Disease and Vascular Dementia**",Arch Intern Med. Published online October 25, 2010.

Russell C, Dickson T, McKeganey N. Advice From Former-Smoking **E-Cigarette Users to Current Smokers on How to Use E-Cigarettes as Part of an Attempt to Quit Smoking**. Nicotine Tob Res. 2017 Aug 3.

Russell C, Haseen F, McKeganey N. **Factors associated with past 30-day abstinence** from cigarette smoking in a non-probabilistic sample of 15,456 adult established current smokers in the United States who used JUUL vapor products for three months. Harm Reduct J. 2019 Mar 25;16(1):22.

Sabia S, Elbaz A, Dugravot A, et al. Impact of Smoking on **Cognitive Decline** in Early Old Age: The Whitehall II Cohort Study. Arch Gen Psychiatry. 2012 Feb 6.

Saddleson ML, Kozlowski LT, Giovino GA, et al. **Risky behaviors, e-cigarette use** and susceptibility of use among college students. Drug Alcohol Depend. 2015 Apr 1;149:25-30.

Saevarsdottir S, Rezaei H, Geborek P, et al; **SWEFOT** study group. Current **smoking** status is a strong predictor of radiographic **progression in early rheumatoid arthritis**: results from the SWEFOT trial. Ann Rheum Dis. 2015 Aug;74(8):1509-14.

Saffar Soflaei S, Darroudi S, Tayefi M, et al. **Hookah smoking is strongly associated with diabetes mellitus**, metabolic syndrome and obesity: a population-based study. Diabetol Metab Syndr. 2018 Apr 19;10:33.

Sakata R, McGale P, Grant EJ, Ozasa K, Peto R, Darby SC. Impact of **smoking on mortality** and life expectancy in **Japanese smokers**: a prospective cohort study. BMJ. 2012 Oct 25;345:e7093.

Saleheen D, Zhao W, Young R, et al. **Loss of Cardioprotective Effects** at the **ADAMTS7 Locus as a Result of Gene-Smoking Interactions**. Circulation. 2017 Jun 13;135(24):2336-2353.

Samet, JM. Smoking cessation: **Benefits versus risks** of using **pharmacotherapy to quit**. *Circulation* 2013.

Samet JM. Smoking cessation: **benefits versus risks** of using **pharmacotherapy** to quit. Circulation. 2014 Jan 7;129(1):8-10

Sanford NN, Sher DJ, Butler S, et al. **Cancer Screening Patterns** Among Current, Former, and Never Smokers in the United States, 2010-2015. JAMA Netw Open. 2019 May 3;2(5):e193759.

Sanford NN, Sher DJ, Xu X, et al. **Trends in Smoking and e-Cigarette Use Among US Patients With Cancer**, 2014-2017. JAMA Oncol. 2019 Feb 14

Sandhu RK, Jimenez MC, Chiuve SE, et al. Smoking, smoking cessation and risk of **sudden cardiac death in women**. Circ Arrhythm Electrophysiol 2012 .

Sargent JD, Tanski S, Stoolmiller M. Influence of **Motion Picture Rating** on Adolescent Response to Movie Smoking. Pediatrics. 2012 Jul 9.

Sarna L, Bialous SA, Nandy K, et al. Changes in **smoking prevalences among health care professionals** from 2003 to 2010-2011. JAMA. 2014 Jan 8;311(2):197-9.

Saulyte J, Regueira C, Montes-Martínez A, et al. Active or passive exposure to tobacco smoking and **allergic rhinitis, allergic dermatitis, and food allergy** in adults and children: a systematic review and meta-analysis. PLoS Med. 2014 Mar 11;11(3):e1001611.

Schauer GL, Agaku IT, King BA, et al. **Health Care Provider Advice for Adolescent Tobacco Use:** Results From the 2011 National Youth Tobacco Survey. Pediatrics. 2014 Aug 18.

Schipper EM, de Graaff LC, Koch BC, et al. A New Challenge: **Suicide Attempt using Nicotine Fillings** for Electronic Cigarettes. Br J Clin Pharmacol. 2014 Aug 12.

Schmidt H, Voigt K, Emanuel EJ. The **Ethics of Not Hiring Smokers**. N Engl J Med. 2013 Mar 27.

Schnoll Robert A., Patterson Freda, Wileyto E. Paul, Et al. Effectiveness of **Extended-Duration Transdermal Nicotine Therapy**: A Randomized Trial. Ann Intern Med February 2, 2010 152:144-151.

Schnoll RA, Goelz PM, Veluz-Wilkins A, et al. **Long-term Nicotine Replacement Therapy**: A Randomized Clinical Trial. JAMA Intern Med. 2015 Feb 23.

Schoenfelder EN, Faraone SV, Kollins SH. **Stimulant Treatment of ADHD** and Cigarette Smoking: A Meta-Analysis. Pediatrics. 2014 May 12.

Schroeder SA. A 51-year-old woman with **bipolar disorder** who wants to quit smoking. JAMA. 2009 Feb 4;301(5):522-31. Epub 2009 Jan 6.

Schroeder SA. The U.S. Food and Drug Administration's Dilemma**: How Tightly to Regulate Electronic Cigarettes**? Ann Intern Med. 2018 Oct 9.

Schroeder SA, Koh HK. **Tobacco control** 50 years after the 1964 surgeon general's report. JAMA. 2014 Jan 8;311(2):141-3.

Schultz AS et al. A qualitative investigation of **smoke-free policies on hospital property**. CMAJ. 2011 Dec 13;183(18):E1334-44.

Schwartz R, Zhang B. Debunking the taxation-contraband tobacco myth. CMAJ. 2016 Apr 5

SDIS – Guidelines for NRT during pregnancy and lactation. Available at: http://www.usask.ca/pharmacy-nutrition/services/sdis.shtml

Section on Tobacco Control. **Clinical** Practice Policy to **Protect Children From Tobacco**, Nicotine, and Tobacco Smoke. Pediatrics. 2015 Oct 26.

Section on Tobacco Control. **Public** Policy to **Protect Children From Tobacco, Nicotine, and Tobacco Smoke. Pediatrics**. 2015 Oct 26.

Section on Tobacco Control. Electronic **Nicotine Delivery Systems. Pediatrics**. 2015 Oct 26.

Sedgh G, Bearak J, Singh S, et al. **Abortion incidence** between 1990 and 2014: global, regional, and subregional levels and trends. Lancet. 2016 May 11.

Semple S, Apsley A, Azmina Ibrahim T, et al. Fine particulate matter concentrations in smoking households: just how much **secondhand smoke** do you breathe in if you live with a smoker who smokes indoors? Tob Control. 2014 Oct 20.

Seung-Kwon Myung; Diana D. McDonnell; Gene Kazinets; Hong Gwan Seo; Joel M. Moskowitz Effects of **Web- and Computer-Based Smoking Cessation Programs**: Meta-analysis of Randomized Controlled Trials. Arch Intern Med. 2009;169(10):929-937.

Shadel WG, Martino SC, Setodji C, et al. Placing **Antismoking Graphic Warning Posters** at Retail Point-of-Sale Locations Increases Some Adolescents' Susceptibility to Future Smoking. Nicotine Tob Res.2017 Dec 13.

Shahab L, Goniewicz ML, Blount BC, et al. Nicotine, Carcinogen, and **Toxin** Exposure in **Long-Term E-Cigarette** and Nicotine Replacement Therapy Users: A Cross-sectional Study. Ann Intern Med. 2017 Feb 7.

Shang C, Chaloupka FJ, Fong GT, et al. **Weight control belief** and its impact on the effectiveness of tobacco control policies on quit attempts: findings from the ITC 4 Country Project. Tob Control. 2015 Feb 2.

Sharma A, Deeb AP, Iannuzzi JC, et al. Tobacco smoking and **postoperative outcomes after colorectal surgery**. Ann Surg. 2013 Aug;258(2):296-300.

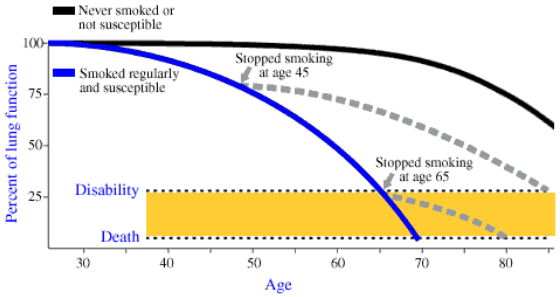
She J, Yang P, Wang Y, et al. **Chinese Water-Pipe Smoking** and the **Risk of COPD**. Chest. 2014 Oct 1;146(4):924-31.

Sheffer MA, Baker TB, Fraser DL, et al. **Fax referrals, academic detailing**, and tobacco quitline use a randomized trial. Am J Prev Med. 2012 Jan;42(1):21-8.

Shen X, Bachyrycz A, Anderson JR, et al. Improving the effectiveness of **pharmacist-assisted tobacco cessation**: a study of participant-and pharmacy-specific differences in quit rates. Ann Pharmacother. 2015 Mar; 49(3):303-10.

Shepshelovich D, Goldvaser H, Edel Y, et al. **High Lung Cancer Incidence** in Heavy Smokers Following Hospitalization due to Pneumonia. Am J Med. 2015 Nov 6.

Shields B, Hill A, Bilous M, Knight B, Hattersley AT, Bilous RW, Vaidya B. Cigarette smoking during pregnancy is associated with alterations in maternal and fetal thyroid function. J Clin Endocrinol Metab. 2008 Nov 18. [Epub ahead of print] Cigarette smoking is associated with changes in maternal thyroid function throughout the pregnancy and in fetal thyroid function as measured in cord blood samples.
Shiffman S, Kurland BF, Scholl SM, et al. Nondaily Smokers' Changes in Cigarette Consumption With **Very Low-Nicotine-Content Cigarettes**: A Randomized Double-blind Clinical Trial. JAMA Psychiatry. 2018 Jun 14.
Sibbald M, Yan AT, Huang W, et al. Association between smoking, outcomes, and early **clopidogrel** use in patients with acute coronary syndrome: Insights from the Global Registry of Acute Coronary Events. *Am Heart J* 2010; 160:855-861. (no effect)
Siddiqi K, Khan A, Ahmad M, et al. Action to **Stop Smoking in Suspected Tuberculosis** (ASSIST) in Pakistan: A Cluster Randomized, Controlled Trial. Ann Intern Med. 2013 May 7;158(9):667-75.
Siddiqi K, Shah S, Abbas SM, et al. Global burden of disease due to **smokeless tobacco consumption** in adults: analysis of data from 113 countries. BMC Med. 2015 Aug 17;13:194.
Siegel M. A Lost Opportunity for Public Health - The FDA Advisory Committee Report on **Menthol**. N Engl J Med. 2011 May 4.
Siegel RL, Jacobs EJ, Newton CC, et al. **Deaths due to cigarette smoking for 12 smoking-related cancers** in the United States [online June 15, 2015]. JAMA Intern Med. doi:10.1001/jamainternmed.2015.2398.
Simón L, Pastor-Barriuso R, Boldo E, et al. **Smoke-free legislation** in Spain and prematurity. Pediatrics. 2017;139(6):e20162068
Sims Michelle, Maxwell Roy, Bauld Linda, Gilmore Anna. Short term impact of smoke-free legislation in England: retrospective analysis of hospital admissions for **myocardial infarction**. BMJ 2010;340:c2161
Sims M, Maxwell R, Gilmore A. Short-term impact of the **smoke free legislation in England on emergency hospital admissions for asthma** among adults: a population-based study. Thorax. 2013 Apr 15.
Singh S, Loke YK, Spangler JG, et al. Risk of serious adverse **cardiovascular events associated with varenicline**: a systematic review and meta-analysis. CMAJ. 2011 Jul 4.
Singh T, Agaku IT, Arrazola RA, et al. **Exposure to Advertisements and Electronic Cigarette Use Among US Middle and High School Students**. Pediatrics. 2016 May;137(5).
Sipilä JO, Gunn JM, Kauko T, et al. Association of **restaurant smoking ban** and the incidence of acute myocardial infarction in Finland. BMJ Open. 2016 Jan 29;6(1):e009320.
Siqueira LM and AAP Committee on Substance Use and Prevention. **Nicotine and Tobacco as Substances of Abuse** in Children and Adolescents. Pediatrics. 2017; 139(1):e20163436
Sitas F, Egger S, Bradshaw D, et al. Differences among the **coloured, white, black, and other South African populations** in **smoking-attributed mortality** at ages 35-74 years: a case-control study of 481,640 deaths. Lancet. 2013 Aug 24;382(9893):685-93.
Siu AL. **Behavioral and Pharmacotherapy Interventions for Tobacco Smoking Cessation in Adults, Including Pregnant Women**: U.S. Preventive Services Task Force **Recommendation** Statement (USPSTF). Ann Intern Med. 2015 Sep 22.
Smith J, Lee K. Protecting the **plain packaging** consultation from tobacco **industry interference**. CMAJ. 2016 Oct 4;188(14):E340-E341.
Smith PH, Kasza KA, Hyland A, et al. **Gender differences** in medication use and cigarette **smoking cessation**: results from the International Tobacco Control Four Country Survey. Nicotine Tob Res. 2015 Apr;17(4):463-72.
Smith PM, Burgess E. Smoking cessation initiated during hospital stay for **patients with coronary artery disease**: a randomized controlled trial. CMAJ 2009; 180:1297-1303.
Smith Stevens S.; McCarthy Danielle E.; Japuntich Sandra J.; et al. Comparative Effectiveness of 5 Smoking Cessation Pharmacotherapies in Primary Care Clinics. *Arch Intern Med*. 2009;169(22):2148-2155. Bupropion SR + lozenge was superior to all of the monotherapies (odds ratio, 0.46-0.56); patch + lozenge was superior to patch and bupropion monotherapies (odds ratio, 0.56 and 0.54, respectively).
Smith AL, Chapman S. **Quitting smoking unassisted**: the 50-year research neglect of a major public health phenomenon. JAMA. doi:10.1001/jama.2013.282618.
Smoking Cessation benefits: Fletcher C, Peto R. The natural history of chronic airflow obstruction. Br Med J. 1977 Jun 25;1(6077):1645-8.



Sobinoff AP, Sutherland JM, Beckett EL, et al. Damaging legacy: **maternal cigarette** smoking has long-term consequences for **male offspring fertility**. Hum Reprod. 2014 Sep 30.
Sochor O, Lennon RJ, Rodriguez-Escudero JP, et al. Trends and Predictors of **Smoking Cessation After Percutaneous Coronary Intervention** (from Olmsted County, Minnesota, 1999 to 2010). Am J Cardiol. 2015 Feb 15;115(4):405-10.
Sommerfeld CG, Weiner DJ, Nowalk A, et al. **Hypersensitivity Pneumonitis and Acute Respiratory Distress Syndrome From E-Cigarette Use**. Pediatrics. 2018 May 17.
Soneji S, Barrington-Trimis JL, Wills TA, et al. Association Between **Initial Use of e-Cigarettes and Subsequent Cigarette Smoking** Among Adolescents and Young Adults: A Systematic Review and Meta-analysis. JAMA Pediatr. 2017 Jun 26.
Soneji S, Beltrán-Sánchez H. Association of **Maternal Cigarette Smoking and Smoking Cessation With Preterm Birth**. JAMA Netw Open. 2019 Apr 5;2(4):e192514.
Soneji S, Sargent J, Tanski S, Primack B. Associations between initial **water pipe tobacco smoking (hookah) and snus** use and subsequent cigarette smoking. Results from a longitudinal study of US adolescents and young adults. JAMA Pediatr Dec 2014.
Soneji S, Yang J, Knutzen KE, et al. **Online 25Tobacco Marketing** and Subsequent Tobacco Use. Pediatrics. 2018 Jan 2.
Song AV, Dutra LM, Neilands TB, et al. Association of **Smoke-Free Laws** With Lower Percentages of New and Current Smokers Among Adolescents and Young Adults: An 11-Year Longitudinal Study. JAMA Pediatr. 2015 Sep 8;169(9):e152285.
Song MA, Benowitz NL, Berman M, et al. **Cigarette Filter Ventilation** and its Relationship to Increasing Rates of **Lung Adenocarcinoma**. J Natl Cancer Inst. 2017 Dec 1;109(12).
Soria R, et al. A randomised controlled trial of **motivational** interviewing for smoking cessation. Br J Gen Pract. 2006 Oct;56(531):768-74. (InfoPOEMs: In this study with several biases favoring the intervention, motivational interviewing appears to be more effective than brief advice in promoting smoking cessation. (LOE = 2b))
Spanier AJ, Beck AF, Huang B, et al. **Family Hardships** and Serum Cotinine in Children With Asthma. Pediatrics. 2015 Jan 12.
Spaniolas K, Yang J, Crowley S, et al. Association of **Long-term Anastomotic Ulceration After Roux-en-Y Gastric Bypass With Tobacco Smoking**. JAMA Surg. 2018 Jun 20.
Sparks JA, Chang SC, Deane KD, et al. Associations of smoking and age with **inflammatory joint signs** among first-degree relatives without rheumatoid arthritis: Results from the Studies of the Etiology of RA. Arthritis Rheumatol. 2016 Feb 11.
Spector LG, Murphy SE, Wickham KM, et al. **Prenatal Tobacco Exposure** and Cotinine in Newborn Dried Blood Spots. Pediatrics. 2014 May 12.
Stanton A, Grimshaw G. Tobacco **cessation interventions for young people**. Cochrane Database Syst Rev. 2013 Aug 23;8:CD003289. doi: 10.1002/14651858.CD003289.pub5. Complex approaches show promise, with some persistence of abstinence (30 days point prevalence abstinence or continuous abstinence at six months), especially those incorporating elements sensitive to stage of change and using motivational enhancement and CBT. Given the episodic nature of adolescent smoking, more data is needed on sustained quitting. There were few trials with evidence about pharmacological interventions (nicotine replacement and bupropion), and none demonstrated effectiveness for adolescent smokers
Stanbrook MB. **Regulate e-cigarettes** as drug-delivery devices. CMAJ. 2013 Nov 5;185(16):1379.
Stanbrook MB. **Electronic cigarettes** and youth: a gateway that must be shut. CMAJ. 2016 Aug 9;188(11):785.
Stapleton JA, Watson L, Spirling LI, et al. **Varenicline** in the routine treatment of tobacco dependence: a pre-post comparison with nicotine replacement therapy and an evaluation in those **with mental illness**. Addiction. 2008 Jan;103(1):146-54. Epub 2007 Nov 19. (n=412 over 6weeks) In this setting and with group support varenicline appears to improve success rates over those achieved with NRT, and is equally effective and safe in those with and without a mental illness.
Stead L, Lancaster T. Interventions to reduce harm from **continued tobacco use**. Cochrane Database Syst Rev. 2007 Jul 18;(3):CD005231.
There is insufficient evidence about long-term benefit to give firm support the use of interventions intended to help smokers reduce but not quit tobacco use.
Stead LF, Perera R, Bullen C, Mant D, et al. **Nicotine replacement therapy** for smoking cessation. **Cochrane** Database Syst Rev. 2008 Jan 23;(1):CD000146. All of the commercially available forms of NRT (gum, transdermal patch, nasal spray, inhaler and sublingual tablets/lozenges) can help people who make a quit attempt to increase their chances of successfully stopping smoking. NRTs increase the rate of quitting by 50-70%, regardless of setting.The effectiveness of NRT appears to be largely independent of the intensity of additional support provided to the individual. Provision of more intense levels of support, although beneficial in facilitating the likelihood of quitting, is not essential to the success of NRT.
Stead LF, et al. **Physician advice** for smoking cessation. Cochrane Database Syst Rev. 2008 Apr 16;(2):CD000165. Simple advice has a small effect on cessation rates. Assuming an unassisted quit rate of 2 to 3%, a brief advice intervention can increase quitting by a further 1 to 3%. Additional components appear to have only a small effect, though there is a small additional benefit of more intensive interventions compared to very brief interventions.
Stead LF, Lancaster T. **Combined pharmacotherapy and behavioural** interventions for smoking cessation. Cochrane Database of Systematic Reviews 2012, Issue 10. Art. No.: CD008286. DOI: 10.1002/14651858.CD008286.pub2. Interventions that combine pharmacotherapy and behavioural support increase smoking cessation success compared to a minimal intervention or usual care. Further trials would be unlikely to change this conclusion. We did not find strong evidence from indirect comparisons that offering more intensive behavioural support was associated with larger treatment effects but this could be because intensive interventions are less likely to be delivered in full.
Stead LF, Lancaster T. **Behavioural interventions** as adjuncts to pharmacotherapy for smoking cessation. Cochrane Database Syst Rev. 2012 Dec 12;12:CD009670. doi: 10.1002/14651858.CD009670.pub2. Providing behavioural support in person or via telephone for people using pharmacotherapy to stop smoking has a small but important effect. Increasing the amount of behavioural support is likely to increase the chance of success by about 10 to 25%, based on a pooled estimate from 38 trials.

Stead LF, Koilpillai P, Fanshawe TR, et al. **Combined pharmacotherapy and behavioural interventions for smoking cessation**. Cochrane Database Syst Rev. 2016 Mar 24;3:CD008286. Interventions that combine pharmacotherapy and behavioural support increase smoking cessation success compared to a minimal intervention or usual care. Updating this review with an additional 12 studies (5,000 participants) did not materially change the effect estimate. Although trials differed in the details of their populations and interventions, we did not detect any factors that modified treatment effects apart from the recruitment setting. We did not find evidence from indirect comparisons that offering more intensive behavioural support was associated with larger treatment effects.

Stead LF, Carroll AJ, Lancaster T. **Group behaviour therapy programmes for smoking cessation**. Cochrane Database Syst Rev. 2017 Mar 31;3:CD001007. Group therapy is better for helping people stop smoking than self-help, and other less intensive interventions. There is not enough evidence to evaluate whether groups are more effective, or cost-effective, than intensive individual counselling. There is not enough evidence to support the use of particular psychological components in a programme beyond the support and skills training normally included.

Stewart ST, Cutler DM, Rosen AB. Forecasting the effects of obesity and smoking on U.S. **life expectancy**. N Engl J Med. 2009 Dec 3;361(23):2252-60. PubMed

Steigerwald S, Wong PO, Cohen BE, et al. **Smoking, Vaping, and Use of Edibles and Other Forms of Marijuana Among U.S. Adults**. Ann Intern Med. 2018 Aug 28.

Steinberg MB, Schmelzer AC, Richardson DL, Foulds J. The case for treating **tobacco dependence as a chronic disease**. Ann Intern Med. 2008 Apr 1;148(7):554-6.

Steinberg MB, Greenhaus S, Schmelzer AC, Bover MT, Foulds J, Hoover DR, et al. **Triple-combination pharmacotherapy** for medically ill smokers: a randomized trial. Ann Intern Med. 2009 Apr 7;150(7):447-54. Flexibly dosed triple-combination pharmacotherapy for up to 6 months was more effective than standard-duration nicotine patch therapy for outpatient smokers with medical illnesses.

Steinberg MB, Delnevo CD. **Increasing the "Smoking Age":** The Right Thing to Do. Ann Intern Med. 2013 Aug 26.

Steinberg MB, Akincigil A, Kim EJ, et al. **Tobacco Smoking** as a Risk Factor for Increased **Antibiotic Prescription**. Am J Prev Med. 2016 Jun;50(6):692-8.

Steinberger E, Kollmeier M, McBride S, et al. **Cigarette smoking during external beam radiation therapy for prostate cancer** is associated with an increased risk of prostate cancer-specific mortality and treatment-related toxicity. BJU Int. 2014 Oct 23.

St Helen G, Eaton DL. Public Health **Consequences of e-Cigarette Use**. JAMA Intern Med. 2018 May 7.

Stone KC, LaGasse LL, Lester BM, et al. **Sleep problems in children** with prenatal substance exposure: the Maternal Lifestyle study. Arch Pediatr Adolesc Med. 2010 May;164(5):452-6.

Strandberg-Larsen K, et al. Use of nicotine replacement therapy during **pregnancy** and stillbirth: a cohort study. BJOG. 2008 Oct;115(11):1405-10. Epub 2008 Aug 20. Our study does not indicate that use of NRT during pregnancy increases the risk of stillbirth.

Strandberg AY, Strandberg TE, Pitkala K, et al. The effect of smoking in midlife on health-related quality of life in old age. A 26-year prospective study. Arch Intern Med 2008; 168:1968-1974. During the 26-year follow-up of this socioeconomically homogeneous male cohort, HRQoL deteriorated with an increase in daily cigarettes smoked in a dose-dependent manner. Never-smokers lived longer than heavy smokers, and their extra years were of better quality.

Stranges S, et al. Lifetime cumulative exposure to **secondhand** smoke and risk of myocardial infarction in never smokers: results from the Western new york health study, 1995-2001. Arch Intern Med. 2006 Oct 9;166(18):1961-7. Exposure to SHS has declined sharply among nonsmokers in recent years. In the absence of high levels of recent exposure to SHS, cumulative lifetime exposure to SHS may not be as important a risk factor for MI as previously thought.

Surgeon General: A Report of "How Tobacco **Smoke Causes Disease**: The Biology and Behavioral Basis for Smoking-Attributable Disease". Executive Summary 2010 http://www.surgeongeneral.gov/library/tobaccosmoke/report/executivesummary.pdf

Sugerman DT. JAMA **patient page. e-Cigarettes**. JAMA. 2014 Jan 8;311(2):212

Suissa K, Larivière J, Eisenberg MJ, et al. Efficacy and Safety of **Smoking Cessation Interventions in Patients With Cardiovascular Disease**: A Network Meta-Analysis of Randomized Controlled Trials. Circ Cardiovasc Qual Outcomes. 2017 Jan;10(1)

Sullivan PM, Dervan LA, Reiger S, et al. Risk of **Congenital Heart Defects** in the **Offspring of Smoking Mothers**: A Population-Based Study. J Pediatr. 2015 Jan 9.

Sussan TE, Gajghate S, Thimmulappa RK, et al. Exposure to **electronic cigarettes impairs pulmonary anti-bacterial and anti-viral defenses** in a mouse model. PLoS One. 2015 Feb 4;10(2):e0116861.

Svanstrom H, Pasternak B, Hviid A. Use of **varenicline for smoking cessation and risk of serious cardiovascular events**: nationwide cohort study. BMJ. 2012 Nov 8;345:e7176.

Swamy GK, Roelands JJ, Peterson BL, et al. Predictors of adverse events among **pregnant** smokers exposed in a nicotine replacement therapy trial. Am J Obstet Gynecol. 2009 Oct;201(4):354.e1-7. Epub 2009 Aug 7.

Sweetland S, Parkin L, Balkwill A, et al; Million Women Study Collaborators. Smoking, surgery, and **venous thromboembolism risk** in women: United kingdom cohort study. Circulation. 2013 Mar 26;127(12):1276-82.

Syamlal G, Mazurek JM, Malarcher AM. Current cigarette smoking **prevalence among working adults**—United States, 2004—2010.MMWR Morb Mortal Wkly Rep 2011; 60:1305-1309.

Sylvestre M-P, Hanusaik N, Berger D, et al. A tool to **identify adolescents at risk of cigarette smoking initiation**. Pediatrics. 2018;142(5):e20183701

Tahiri M, Mottillo S, Joseph L, et al. **Alternative Smoking Cessation Aids**: A Meta-analysis of Randomized Controlled Trials. Am J Med. 2012 Jun;125(6):576-84.

Talati A, Bao Y, Kaufman J, Shen L, Schaefer CA, Brown AS: **Maternal smoking during pregnancy and bipolar disorder** in offspring. Am J Psychiatry 2013; 170:1178–1185

Tammemägi MC, Berg CD, Riley TL, et al. Impact of **lung cancer screening** results on smoking cessation. J Natl Cancer Inst. 2014 May 28;106(6):dju084.

Tan ASL, Bigman CA, Mello S, Sanders-Jackson A. Trends in the **Prevalence of Exposure to e-Cigarette Aerosol in Public Places** Among US Middle and High School Students, 2015 to 2018. JAMA Netw Open. 2019 Aug 2;2(8):e1910184.

Tan CE, Glantz SA. Association between **smoke-free legislation** and hospitalizations for cardiac, cerebrovascular, and respiratory diseases: a meta-analysis. Circulation. 2012 Oct 30;126(18):2177-83.

Tan NS, Goodman SG, Cantor WJ, et al; **TRANSFER-AMI** Investigators. Comparison of the Efficacy of Pharmacoinvasive Management for ST-Segment Elevation Myocardial Infarction in Smokers Versus Non-Smokers (from the Trial of **Routine Angioplasty and Stenting** After Fibrinolysis to Enhance Reperfusion in Acute Myocardial Infarction). Am J Cardiol. 2014 Oct 1;114(7):955-61.

Tanaka S, Shinzawa M, Tokumasu H, et al. **Secondhand smoke and incidence of dental caries** in deciduous teeth among children in Japan: population based retrospective cohort study. BMJ. 2015 Oct 21;351:h5397.

Tanski SE, Wilson KM. Children and **secondhand smoke**: clear evidence for action. Pediatrics. 2012 Jan;129(1):170-1.

Tappin D, Bauld L, Purves D, et al; Cessation in Pregnancy Incentives Trial (**CPIT**) Team. **Financial incentives for smoking cessation in pregnancy**: randomised controlled trial. BMJ. 2015 Jan 27;350:h134.

Tashkin DP, Rennard S, Hays JT, et al. Effects of **Varenicline on Smoking Cessation in Mild-to-Moderate COPD**: A Randomized Controlled Trial. Chest. 2010 Sep 23.

Taylor G, McNeill A, Girling A, et al. Change in **mental health after smoking cessation**: systematic review and meta-analysis. BMJ. 2014 Feb 13;348:g1151.

Teschendorff AE, Yang Z, Wong A, et al. Correlation of Smoking-Associated DNA Methylation Changes in Buccal Cells With DNA Methylation Changes in **Epithelial Cancer**. JAMA Oncol. 2015 Jul 1;1(4):476-85.

Thacher JD, Gruzieva O, Pershagen G, et al. **Pre- and Postnatal Exposure to Parental Smoking** and Allergic Disease Through Adolescence. Pediatrics. 2014 Aug 18.

Thakur GA, Sengupta SM, Grizenko N, et al. Family-based association study of **ADHD and genes increasing the risk for smoking** behaviours. Arch Dis Child. 2012 Oct 29.

Thomas KH, Martin RM, Davies NM, et al. **Smoking cessation treatment and risk of depression, suicide, and self harm** in the Clinical Practice Research Datalink: prospective cohort study. BMJ. 2013 Oct 11;347:f5704.

Thomas RE, McLellan J, Perera R. **School-based programmes for preventing smoking**. Cochrane Database of Systematic Reviews 2013, Issue 4. Art. No.: CD001293. DOI: 10.1002/14651858.CD001293.pub3. Pure Prevention cohorts showed a significant effect at longest follow-up, with an average 12% reduction in starting smoking compared to the control groups. However, no overall effect was detected at one year or less. The combined social competence and social influences interventions showed a significant effect at one year and at longest follow-up.

Thomas KH, Martin RM, Knipe DW, Higgins JP, Gunnell D. Risk of **neuropsychiatric events** associated with **varenicline**: systematic review and meta-analysis. BMJ 2015;350: h1109.

Thomas RE, Baker PR, et al. **Family-based programmes** for preventing smoking by children and adolescents. Cochrane Database Syst Rev. 2015 Feb 27;2:CD004493. There is moderate quality evidence to suggest that family-based interventions can have a positive effect on preventing children and adolescents from starting to smoke. There were more studies of high intensity programmes compared to a control group receiving no intervention, than there were for other compairsons. The evidence is therefore strongest for high intensity programmes used independently of school interventions. Programmes typically addressed family functioning, and were introduced when children were between 11 and 14 years old. Based on this moderate quality evidence a family intervention might reduce uptake or experimentation with smoking by between 16 and 32%. However, these findings should be interpreted cautiously because effect estimates could not include data fromall studies.Our interpretation is that the common feature of the effective high intensity interventions was encouraging authoritative parenting (which is usually defined as showing strong interest in and care for the adolescent, often with rule setting). This is different from authoritarian parenting (do as I say) or neglectful or unsupervised parenting.

Thomsen T, Tønnesen H, Møller AM. Effect of preoperative smoking cessation interventions on postoperative complications and smoking cessation. Br J Surg. 2009 May;96(5):451-61.

Thomsen T, Villebro N, Møller AM. Interventions for **preoperative smoking cessation**. Cochrane Database of Systematic Reviews 2010, Issue 7. Art. No.: CD002294. There is evidence that preoperative smoking interventions including NRT increase short-term smoking cessation and may reduce postoperative morbidity. The optimal preoperative intervention intensity remains unknown. Based on indirect comparisons and evidence from two small trials, interventions that begin four to eight weeks before surgery, include weekly counselling, and use NRT are more likely to have an impact on complications and on long-term smoking cessation.

Thomsen T, Villebro N, Moller AM. Interventions for **preoperative smoking cessation**. Cochrane Database Syst Rev. 2014 Mar 27;3:CD002294. There is evidence that preoperative smoking interventions providing behavioural support and offering NRT increase short-term smoking cessation and may reduce postoperative morbidity. One trial of varenicline begun shortly before surgery has shown a benefit on long-term cessation but did not detect an effect on early abstinence or on postoperative complications. The optimal preoperative intervention intensity remains unknown.

Thorndike AN. **E-Cigarette Use by Young Adult Nonsmokers**: Next-Generation Nicotine Dependence? Ann Intern Med. 2018 Oct 9.

Thun MJ, Carter BD, Feskanich D, et al. **50-Year trends in smoking-related mortality in the United States**. N Engl J Med 2013;368:351-64.

Tidey JW, Miller ME. Smoking cessation and **reduction** in people with **chronic mental illness**. BMJ. 2015 Sep 21;351:h4065.

Tierney PA, Karpinski CD, Brown JE, et al. **Flavour chemicals** in **electronic cigarette** fluids. Tob Control. 2015 Apr 15.

Tischler EH, Matsen Ko L, Chen AF, et al. Smoking **Increases the Rate of Reoperation** for Infection within 90 Days After Primary **Total Joint Arthroplasty**. J Bone Joint Surg Am. 2017 Feb 15;99(4):295-304.

Toh S, Baker MA, Brown JS, et al; for the Mini-Sentinel Investigators. Rapid Assessment of **Cardiovascular Risk Among Users of Smoking Cessation Drugs** Within the US Food and Drug Administration's Mini-Sentinel Program. JAMA Intern Med. 2013 Mar 25:1-3.

Tolstrup JS, Kristiansen L, Becker U, et al. Smoking and risk of acute and chronic **pancreatitis** among women and men: a population-based cohort study. Arch Intern Med. 2009 Mar 23;169(6):603-9. In this population of Danish men and women, smoking was independently associated with increased risk of pancreatitis.

Torjesen I. **E-cigarettes** are to be regulated as medicines from 2016. BMJ. 2013 Jun 14;346:f3859.

Tøttenborg SS, Thomsen RW, Johnsen SP, et al. Determinants of **smoking cessation in COPD patients** treated in the outpatient setting. Chest. 2016 Jun 1. pii: S0012-3692(16)49107-5.

Tran K, Asakawa K, Cimon K, et al. Pharmacologic-based strategies for smoking cessation: **clinical and cost-effectiveness analyses. Canadian Agency for Drugs and Technologies in Health(CADTH)**.2010Sep:1-548.

Trivers KF, Phillips E, Gentzke AS, et al. **Prevalence** of Cannabis Use in Electronic Cigarettes **Among US Youth**. JAMA Pediatr. 2018 Sep 17

Troiano C, Jaleel Z, Spiegel JH. Association of Electronic Cigarette Vaping and Cigarette Smoking With **Decreased Random Flap Viability in Rats**. JAMA Facial Plast Surg. 2018 Oct 18.

Tsoi DT, Porwal M, Webster AC. Efficacy and safety of **bupropion** for smoking cessation and reduction in **schizophrenia**: systematic review and meta-analysis. Br J Psychiatry. 2010 May;196(5):346-53.

Tsoi DT, Porwal M, Webster AC. Interventions for smoking cessation and reduction in individuals with **schizophrenia**. Cochrane Database Syst Rev. 2010 Jun 16;(6):CD007253.

Tsoi DT, Porwal M, Webster AC. Interventions for smoking **cessation and reduction in individuals with schizophrenia**. Cochrane Database Syst Rev. 2013 Feb 28;2:CD007253. doi: 10.1002/14651858.CD007253.pub3. Bupropion increases smoking abstinence rates in smokers with schizophrenia, without jeopardizing their mental state. Varenicline may also improve smoking cessation rates in schizophrenia, but its possible psychiatric adverse effects cannot be ruled out. Contingent reinforcement may help this group of patients to quit and reduce smoking in the short term.

Tulloch HE, Pipe AL, Clyde MJ, et al. The **Quit Experience** and Concerns of Smokers With **Psychiatric Illness**. Am J Prev Med. 2016 Jun;50(6):709-18.

Tverdal A, Bjartveit K. Health consequences of **reduced daily cigarette** consumption. Tob Control. 2006 Dec;15(6):472-80. Long-term follow-up provides no evidence that heavy smokers who cut down their daily cigarette consumption by >50% reduce their risk of premature death significantly. In health education and patient counselling, it may give people false expectations to advise that reduction in consumption is associated with reduction in harm.

Tynan M, Babb S, MacNeil A, Griffin M. **State smoke-free laws** for worksites, restaurants, and bars—United States, 2000-2010. MMWR Morb Mortal Wkly Rep April 22, 2011; 60: 472-475.

Uhl GR, Liu QR, Drgon T, et al. **Molecular genetics** of successful smoking cessation: convergent genome-wide association study results. Arch Gen Psychiatry. 2008 Jun;65(6):683-93.

U.S. Preventive Services Task Force **USPSTF. Counseling and interventions** to prevent tobacco use and tobacco-caused disease in adults and pregnant women: USPSTF reaffirmation recommendation statement. Ann Intern Med. 2009 Apr 21;150(8):551-5.

Ussher MH, Taylor A, Faulkner G. **Exercise interventions** for smoking cessation. Cochrane Database of Systematic Reviews 2008, Issue 4. Art. No.: CD002295. DOI: 10.1002/14651858.CD002295.pub3. Only one of the 15 trials offered evidence for exercise aiding smoking cessation at a 12-month follow up.

Ussher M, Lewis S, Aveyard P, et al. **Physical activity for smoking cessation in pregnancy**: randomised controlled trial. BMJ. 2015 May 14;350

Ussher M, Lewis S, Aveyard P, et al. The London Exercise And Pregnant smokers (**LEAP**) trial: a randomised controlled trial of **physical activity for smoking cessation in pregnancy** with an economic evaluation. Health Technol Assess. 2015 Oct;19(84):1-136.

Valgeirsdottir H, Vanky E, Sundström-Poromaa I, et al. **Prenatal exposures and birth indices**, and subsequent risk of polycystic ovary syndrome: a national registry-based cohort study. BJOG. 2018 Jun 12.

Vallance JK, Gardiner PA, Lynch BM, et al. Evaluating the Evidence on **Sitting, Smoking, and Health**: Is Sitting Really the New Smoking? Am J Public Health. 2018 Nov;108(11):1478-1482

van der Meer RM, Willemsen MC, Smit F, et al. Smoking cessation interventions for smokers with **current or past depression**. Cochrane Database Syst Rev. 2013 Aug 21;8:CD006102. Evidence suggests that adding a psychosocial mood management component to a standard smoking cessation intervention increases long-term cessation rates in smokers with both current and past depression when compared with the standard intervention alone.

van Domburg RT, op Reimer WS, Hoeks SE, Kappetein AP, Bogers AJ. **Three life-years gained** from smoking cessation after coronary artery bypass surgery: a 30-year follow-up study. Am Heart J. 2008 Sep;156(3):473-6. Epub 2008 Jun 26.

van Eerd EA, van der Meer RM, van Schayck OC, et al. **Smoking cessation for people with chronic obstructive pulmonary disease**. Cochrane Database Syst Rev. 2016 Aug 20;8:CD010744. We found high-quality evidence in a meta-analysis including four (1,540 participants) of the 16 included studies that a combination of behavioural treatment and pharmacotherapy is effective in helping smokers with COPD to quit smoking. Furthermore, we conclude that there is no convincing evidence for preferring any particular form of behavioural or pharmacological treatment.

Vardavas CI, Anagnostopoulos N, Kougias M, et al. Short-term Pulmonary Effects of Using an **Electronic Cigarette**: Impact on Respiratory Flow Resistance, Impedance, and Exhaled Nitric Oxide. Chest. 2012 Jun;141(6):1400-6.

Varner MW, Silver RM, Rowland Hogue CJ, et al; Eunice Kennedy Shriver National Institute of Child Health and Human Development Stillbirth Collaborative Research Network. Association between **stillbirth and illicit drug use and smoking during pregnancy**. Obstet Gynecol. 2014 Jan;123(1):113-25.

Veldheer S, Yingst J, Foulds G, et al. Once bitten, twice shy: concern about **gaining weight** after **smoking cessation** and its association with seeking treatment. Int J Clin Pract. 2014 Mar;68(3):388-95.

Verguet S, Gauvreau CL, Mishra S,et al. The consequences of **tobacco tax** on household health and finances in rich and poor smokers in China: an extended cost-effectiveness analysis. Lancet Glob Health. 2015 Mar 12.

Vesperini V, Lukas C, Fautrel B, Le Loet X, Rincheval N, Combe B. Tobacco exposure **reduces radiographic progression in early rheumatoid arthritis**. Results from the ESPOIR cohort. Arthritis Care Res (Hoboken). 2013 Jul 8.

Vidrine JI, Shete S, Cao Y, et al. **Ask-Advise-Connect**: A New Approach to Smoking Treatment Delivery in Health Care Settings. JAMA Intern Med. 2013 Feb 25:1-7.

Vidrine DJ, Frank-Pearce SG, Vidrine JI, et al. Efficacy of **Mobile Phone-Delivered Smoking Cessation** Interventions for Socioeconomically Disadvantaged Individuals: A Randomized Clinical Trial. JAMA Intern Med. 2018 Dec 17.

Volpp KG, Troxel AB, Pauly MV, Glick HA, et al. A randomized, controlled trial of **financial incentives** for smoking cessation.N Engl J Med. 2009 Feb 12;360(7):699-709.

Volpp KG, Galvin R. **Reward-Based Incentives for Smoking Cessation**: How a Carrot Became a Stick. JAMA. 2014 Feb 3.

Vozoris NT. **Mentholated cigarettes** and cardiovascular and pulmonary diseases: a population-based study. Arch Intern Med. 2012 Apr 9;172(7):590-1.

Vuolo M, Staff J. **Parent and Child Cigarette Use**: A Longitudinal, Multigenerational Study. Pediatrics. 2013 Aug 5.

Wahawisan Joy, Kolluru Srikanth, et al. **Methadone Toxicity Due to Smoking Cessation**—A Case Report on the Drug-Drug Interaction Involving Cytochrome P450 Isoenzyme 1A2. Ahead of Print on 1 June 2011, DOI 10.1345/aph.1P759. Ann Pharmacother ;45:e34.

Wailoo K. The FDA's **Proposed Ban on Menthol Cigarettes**. N Engl J Med. 2019 Feb 20.

Wakefield MA, Hayes L, Durkin S, Borland R. Introduction effects of the **Australian plain packaging policy** on adult smokers: a cross-sectional study. BMJ Open. 2013 Jul 22;3(7).

Walker N, Howe C, Glover M, et al. **Cytisine versus nicotine** for smoking cessation. N Engl J Med 2014;371:2353-62.

Walley SC, Mussman GM, Lossius M, et al. Implementing **Parental Tobacco Dependence Treatment Within Bronchiolitis** QI Collaboratives. Pediatrics. 2018 May 16.

Walley SC, Wilson KM, Winickoff JP, Groner J. **A Public Health Crisis**: Electronic Cigarettes, Vape, and JUUL. Pediatrics. 2019 May 23.

Wang AL, Lowen SB, Romer D, et al. Emotional reaction facilitates the brain and behavioural impact of **graphic cigarette warning** labels in smokers. Tob Control. 2015 Jan 6.

Wang CY, Dudzinski J, Nguyen D, et al. Association of **Smoking and Other Factors With the Outcome of Mohs Reconstruction** Using Flaps or Grafts. JAMA Facial Plast Surg. 2019 Jun 13.

Wang H, O'Reilly EJ, Weisskopf MG, et al. Smoking and risk of **amyotrophic lateral sclerosis**: a pooled analysis of 5 prospective cohorts. Arch Neurol. 2011 Feb;68(2):207-13.

Wang MP, Suen YN, Li WH, et al.**Intervention With Brief Cessation Advice Plus Active Referral** for Proactively Recruited Community Smokers: A Pragmatic Cluster Randomized Clinical Trial. JAMA Intern Med. 2017 Oct 23.

Wang TW, Agaku IT, Marynak KL, et al. **Attitudes Toward Prohibiting Tobacco Sales in Pharmacy Stores** Among U.S. Adults. Am J Prev Med. 2016 Aug 23

Wang TW, Asman K, Gentzke AS, et al. Tobacco **Product Use Among Adults** - United States, 2017. MMWR Morb Mortal Wkly Rep. 2018 Nov 9;67(44):1225-1232.

Wang TW, Marynak KL, Agaku IT, et al. **Secondhand Exposure to Electronic Cigarette Aerosol** Among **US Youths**. JAMA Pediatr. 2017 Mar 20.

Wang YY, Liu Z, Wu Y, et al. Efficacy of **Acupuncture** Is Noninferior to Nicotine Replacement Therapy **for Tobacco Cessation**: Results of a Prospective, Randomized, Active-Controlled Open-Label Trial. Chest. 2018 Mar;153(3):680-688.

Warner DO, Borah BJ, Moriarty J, et al. Smoking Status and Health Care **Costs in the Perioperative Period**: A Population-Based Study. JAMA Surg. 2014 Jan 1.

Warner KE. Using **economics** to combat the tobacco disease epidemic. BMJ. 2017 Jan 24;356:j334.

Warren GW, Cartmell KB, Garrett-Mayer E, et al. **Attributable Failure of First-line Cancer Treatment** and Incremental Costs Associated With Smoking by Patients With Cancer. JAMA Netw Open. 2019 Apr 5;2(4):e191703.

Washko George R, Hunninghake Gary M., Fernandez Isis E., et al. for the COPDGene Investigators. **Lung Volumes and Emphysema** in Smokers with Interstitial Lung Abnormalities. N Engl J Med 2011; 364:897-906.

Watkins SL, Glantz SA, Chaffee BW. Association of **Noncigarette Tobacco Product** Use With Future Cigarette Smoking Among Youth in the Population Assessment of Tobacco and Health (PATH) Study, 2013-2015. JAMA Pediatr. 2018 Feb 1;172(2):181-187.

Weeks SG, Glantz SA, De Marco T, Rosen AB, Fleischmann KE. **Secondhand smoke** exposure and quality of life in patients with **heart failure**. Arch Intern Med. 2011;171(21):1887-1893.

Weinberger AH, Gbedemah M, Goodwin RD. **Cigarette smoking quit rates** among adults **with and without alcohol use disorders** and heavy alcohol use, 2002-2015: A representative sample of the United States population. Drug Alcohol Depend. 2017 Aug 5;180:204-207

Weitzman M, Govil N, Liu YH, Lalwani AK. Maternal Prenatal Smoking and **Hearing Loss** Among Adolescents. JAMA Otolaryngol Head Neck Surg. 2013 Jun 20:1-8.

Wellman RJ, Dugas EN, Dutczak H, et al. **Predictors of the Onset of Cigarette Smoking**: A Systematic Review of Longitudinal Population-Based Studies in Youth. Am J Prev Med. 2016 Nov;51(5):767-778.

Weng SF, Redsell SA, Swift JA, et al. Systematic review and meta-analyses of **risk factors for childhood overweight** identifiable during infancy. Arch Dis Child. 2012 Oct 29.

Wertz MS, Kyriss T, Paranjape S, Glantz SA. The **Toxic Effects of Cigarette Additives**. Philip Morris' Project Mix Reconsidered: An Analysis of Documents Released through Litigation. PLoS Med. 2011 Dec;8(12):e1001145.

West R, Sohal T. "Catastrophic" pathways to smoking cessation: findings from national survey. BMJ. 2006 Feb 25;332(7539):458-60. Epub 2006 Jan 27.

West Robert, Zatonski Witold, Cedzynska Magdalena, et al. Placebo-Controlled Trial of **Cytisine** for Smoking Cessation. N Engl J Med 2011;365:1193-20.

West R, May S, West M, et al. Performance of **English stop smoking services** in first 10 years: analysis of service monitoring data. BMJ. 2013 Aug 19;347:f4921.

West HW, Juonala M, Gall SL, et al. Exposure to **Parental Smoking** in Childhood is Associated with Increased Risk of **Carotid Atherosclerotic Plaque** in Adulthood: The Cardiovascular Risk in Young Finns Study. Circulation. 2015 Mar 23.

Westmaas JL, Newton CC, Stevens VL, et al. Does a **Recent Cancer Diagnosis Predict Smoking Cessation**? An Analysis From a Large Prospective US Cohort. J Clin Oncol. 2015 Apr 20.

Westmaas JL, Bontemps-Jones J, Hendricks PS, et al. Randomised controlled trial of stand-alone tailored **emails for smoking cessation**. Tob Control 2017. doi:10.1136/ tobaccocontrol-2016-053056.

Whittaker Brown SA, Liu B, Taioli E. The Relationship between **Tobacco Smoke Exposure and Airflow obstruction** in US Children-Analysis of the National Health and Nutrition Examination Survey (2007-2012). Chest. 2017 Oct 13.

Whittaker R,McRobbie H, Bullen C, Borland R, et al. **Mobile phone-based interventions** for smoking cessation. Cochrane Database of Systematic Reviews 2012, Issue 11. Art. No.: CD006611. DOI: 10.1002/14651858.CD006611.pub3. The current evidence shows a benefit of mobile phone-based smoking cessation interventions on long-termoutcomes, though results were heterogenous with findings from three of five included studies crossing the line of no effect.

Whiteley JA, Williams DM, Dunsiger S, et al. **YMCA commit to quit**: randomized trial outcomes. Am J Prev Med. 2012 Sep;43(3):256-62.

Wille L, Parent MC. Association of No Promotion of Homosexuality Laws and **Electronic Cigarette Use Disparities for Sexual Minority Youth**. JAMA Pediatr. 2019 Aug 26.

Willi C, Bodenmann P, Ghali WA, Faris PD, Cornuz J. Active smoking and the risk of type 2 diabetes: a systematic review and meta-analysis. JAMA. 2007 Dec 12;298(22):2654-64. Active smoking is associated with an increased risk of type 2 diabetes.

Williams KE, Reeves KR, Billing CB Jr, Pennington AM, Gong J. A double-blind study evaluating the long-term (**1yr**) safety of **varenicline** for smoking cessation. Curr Med Res Opin. 2007 Apr;23(4):793-801.

Williams JM, Willett JG,Miller G. **Partnership between tobacco control programs and offices of mental health** needed to reduce smoking rates in the United States. JAMA Psychiatry. 2013;70(12):1261-1262.

Williams RS, Derrick J, Ribisl KM. **Electronic Cigarette Sales to Minors via the Internet**. JAMA Pediatr. 2015 Mar 2; 169(3):e1563.

Wills TA, Knight R, Williams RJ, et al. Risk Factors for Exclusive **E-Cigarette** Use and Dual E-Cigarette Use and Tobacco Use in Adolescents. Pediatrics. 2014 Dec 15.

Wills TA, Knight R, Sargent JD, et al. Longitudinal study of **e-cigarette use and onset of cigarette smoking among high school students** in Hawaii. Tob Control. 2016 Jan 25.

Wills TA. **E-Cigarettes and Adolescents' Risk** Status. Pediatrics. 2017 Jan 23.

Wilson SR, Farber HJ, et al. A Randomized Trial of Parental Behavioral Counseling and Cotinine Feedback for Lowering Environmental Tobacco Smoke Exposure in Children With Asthma: Results of the LET'S Manage Asthma Trial. Chest. 2011 Mar;139(3):581-90.

Wilson KM, Pier JC, Wesgate SC, et al. Second-Hand Tobacco Smoke Exposure and Severity of **Influenza** in Hospitalized Children. J Pediatr. 2012 Aug 3.

Wilson KM, Pier JC, Wesgate SC, et al. **Secondhand Tobacco Smoke** Exposure and Severity of **Influenza** in Hospitalized Children. J Pediatr. 2013 Jan;162(1):16-21.

Wilson KM, Markt SC, Fang F, Net al. **Snus use**, **smoking** and survival among **prostate cancer** patients. Int J Cancer. 2016 Dec 15;139(12):2753-2759.

Wilson KM, Torok MR, Wei B, et al. Marijuana and Tobacco **Coexposure in Hospitalized Children**. Pediatrics. 2018 Nov 19.

Windle SB, Filion KB, Mancini JG, et al. **Combination Therapies** for Smoking Cessation: A Hierarchical Bayesian Meta-Analysis. Am J Prev Med. 2016 Sep 8.

Windle SB, Dehghani P, Roy N, et al. **Smoking abstinence 1 year after acute coronary syndrome**: follow-up from a randomized controlled trial of varenicline in patients admitted to hospital. CMAJ 2018;190:E347-54.

Winkels RM, Botma A, Van Duijnhoven FJ et al. Smoking Increases the Risk for **Colorectal Adenomas** in Patients With Lynch Syndrome. Gastroenterology. 2011 Nov 4.

Winickoff JP, Nabi-Burza E, Chang Y, et al. Implementation of a **Parental Tobacco Control Intervention** in Pediatric Practice. Pediatrics. 2013 Jun 24.

Winickoff JP, Gottlieb M, Mello MM. **Tobacco 21** - An Idea Whose Time Has Come. N Engl J Med. 2014 Jan 8.

Winickoff JP, Nabi-Burza E, Chang Y, et al. Sustainability of a **Parental Tobacco Control Intervention in Pediatric** Practice. Pediatrics. 2014 Oct 20.

Winickoff JP, Winickoff SE. Potential Solutions to **Electronic Cigarette Use** Among Adolescents. Pediatrics. 2016 Jul 11.

Winsløw UC, Rode L, Nordestgaard BG. **High tobacco consumption lowers body weight**: a Mendelian randomization study of the Copenhagen General Population Study. Int J Epidemiol. 2015 Mar 16.

Winterfeld U, Merlob P, Baud D, et al. **Pregnancy outcome following maternal exposure to pregabalin** may call for concern. Neurology. 2016 May 18.
Wisborg K, Henriksen TB, Jespersen LB, Secher NJ. **Nicotine patches for pregnant** smokers: a randomized controlled study. Obstet Gynecol. 2000 Dec;96(6):967-71.
Whittaker R, McRobbie H, Bullen C, Rodgers A, Gu Y. **Mobile phone-based interventions** for smoking cessation. Cochrane Database of Systematic Reviews 2016, Issue 4. Art. No.: CD006611. The current evidence supports a beneficial impact of mobile phone-based smoking cessation interventions on six-month cessation outcomes. While all studies were good quality, the fact that those studies with biochemical verification of quitting status demonstrated an even higher chance of quitting further supports the positive findings. However, it should be noted that most included studies were of text message interventions in high-income countries with good tobacco control policies. Therefore, caution should be taken in generalising these results outside of this type of intervention and context.
Wolfenden L, Goldman S, Stacey FG, et al. **Strategies to improve the implementation of workplace-based policies or practices targeting tobacco, alcohol, diet, physical activity and obesity**. Cochrane Database Syst Rev. 2018 Nov 14;11:CD012439. Available evidence regarding the effectiveness of implementation **strategies for improving implementation of health-promoting policies and practices in the workplace setting is sparse and inconsistent**. Low certainty evidence suggests that such strategies may make little or no difference on measures of implementation fidelity or different employee health behaviour outcomes. It is also unclear if such strategies are cost-effective or have potential unintended adverse consequences. The limited number of trials identified suggests implementation research in the workplace setting is in its infancy, warranting further research to guide evidence translation in this setting.
Woloshin S, Schwartz LM, Welch HG. The risk of **death** by age, sex, and smoking status in the United States: putting health risks in context. J Natl Cancer Inst. 2008 Jun 18;100(12):845-53. Epub 2008 Jun 10. Cigarettes rob 5 to 10 years of life from smokers. Get a copy of this paper because it has several tables that might be useful to help motivate patients to quit smoking. An earlier paper by this team also has useful tables that can be found at http://www.aafp.org/afp/20070315/poc.html. (LOE = 2c)
Woodruff PG, Barr RG, Bleecker E, et al. Clinical significance of **symptoms in smokers with preserved pulmonary function**. N Engl J Med 2016;374:1811-21.
Woolf KJ, Zabad MN, Post JM, et al. Effect of Nicotine Replacement Therapy on Cardiovascular Outcomes After **Acute Coronary Syndromes**. Am J Cardiol. 2012 Jun 20.
Writing Committee, Barua RS, Rigotti NA, et al. 2018 ACC Expert Consensus **Decision Pathway on Tobacco Cessation Treatment**: A Report of the American College of Cardiology Task Force on Clinical Expert Consensus Documents. J Am Coll Cardiol. 2018 Nov 29.
Xi B, Liang Y, Liu Y, et al. **Tobacco use and second-hand smoke exposure in young adolescents** aged 12-15 years: data from 68 low-income and middle-income countries. Lancet Glob Health. 2016 Sep 30
Xu, Xiaohui, Cook, Robert L., Ilacqua, Vito A., et al. Racial Differences in the Effects of Postnatal Environmental Tobacco Smoke on Neurodevelopment (a **ADHD** risk). Pediatrics 2010 0: peds.2009-3589
Xue Fei; Willett Walter C.; Rosner Bernard A.; et al. Cigarette Smoking and the Incidence of **Breast Cancer**. Arch Intern Med. 2011;171(2):125-133.
Yach D. The origins, development, effects, and future of the **WHO Framework Convention on Tobacco Control**: a personal perspective. Lancet. 2014 Jan 21
Yadav Dhiraj; Hawes Robert H.; et al. for the North American Pancreatic Study Group. Alcohol Consumption, Cigarette Smoking, and the Risk of Recurrent Acute and **Chronic Pancreatitis.** Arch Intern Med. 2009;169(11):1035-1045.
Yamin Cyrus K., Bitton Asaf, Bates David W.. **E-Cigarettes**: A Rapidly Growing Internet Phenomenon. *Ann Intern Med* November 2, 2010 153:607-609.
Yang B, Jacobs EJ, Gapstur SM, et al. Active Smoking and **Mortality** Among **Colorectal Cancer Survivors**: The Cancer Prevention Study II Nutrition Cohort. J Clin Oncol. 2015 Mar 10;33(8):885-93.
Yeh Hsin-Chieh, Duncan Bruce B., Schmidt Maria Inês, et al. Smoking, Smoking Cessation, and **Risk for Type 2 Diabetes** Mellitus: A Cohort Study. Ann Intern Med January 5, 2010 152:10-17.
Yeh JS, Bullen C, Glantz SA. Clinical Decisions. **E-Cigarettes and Smoking Cessation**. N Engl J Med. 2016 Jun 2;374(22):2172-4.
Yen AM, et al. Longer Duration and Earlier Age of Onset of **Paternal Betel Chewing** and Smoking Increase Metabolic Syndrome Risk in Human Offspring, Independently, in a Community-Based Screening Program in Taiwan. Circulation. 2016 Aug 2;134(5):392-404.
Yu C, Tang H, Guo Y, et al. **Hot Tea Consumption and Its Interactions With Alcohol and Tobacco** Use on the Risk for Esophageal Cancer: A Population-Based Cohort Study. Ann Intern Med. 2018 Apr 3;168(7):489-497.
Zacher M, Bayly M, Brennan E, et al. Personal tobacco pack display before and after the introduction of **plain packaging** with larger pictorial health warnings in Australia: an observational study of outdoor café strips. Addiction. 2014 Apr;109(4):653-62.
Zacher M, Bayly M, Brennan E, et al. **Personal pack display** and active smoking at outdoor café strips: assessing the impact of plain packaging 1 year postimplementation. BMJ Open Access. Tob Control 2015;24:ii94–ii97
Zammit, Stanley, Thomas, Kate, Thompson, Andrew, et al. Maternal tobacco, cannabis and alcohol use during pregnancy and risk of adolescent **psychotic symptoms** in offspring. The British Journal of Psychiatry 2009 195: 294-300
Zatoński W, Zatoński M. **Cytisine versus nicotine** for smoking cessation. N Engl J Med. 2015 Mar 12;372(11):1072.
Zwar NA, Mendelsohn CP, Richmond RL. **Supporting smoking cessation**. BMJ. 2014 Jan 14
Zesiewicz TA, Greenstein PE, Sullivan KL, et al. A randomized trial of **varenicline** (Chantix) for the treatment of **spinocerebellar ataxia type 3**. Neurology. 2012 Feb 21;78(8):545-50.
Zeliadt SB, Heffner JL, Sayre G, et al. Attitudes and Perceptions About Smoking Cessation in the **Context of Lung Cancer Screening**. JAMA Intern Med. 2015 Jul 27.
Zhan Y, Fang F. **Smoking and Amyotrophic Lateral Sclerosis**: A Mendelian Randomization Study. Ann Neurol. 2019 Feb 20.
Zhang YJ, Iqbal J, van Klaveren D, et al. Smoking is associated with **adverse** clinical outc*omes* in patients undergoing revascularization with **PCI or CABG**. *J Am Coll Cardiol* 2015.
Zheng W, McLerran DF, Rolland BA, et al. Burden of Total and Cause-Specific **Mortality** Related to **Tobacco Smoking** among Adults Aged ≥45 Years in **Asia**: A Pooled Analysis of 21 Cohorts. PLoS Med. 2014 Apr 22;11(4)
Zhou S, Behrooz L, Weitzman M, et al. **Secondhand hookah** smoke: an occupational hazard for hookah bar employees. Tob Control. 2016 Jan 25.
Zhu SH, Sun JY, Bonnevie E, et al. **Four hundred and sixty brands of e-cigarettes** and counting: implications for product regulation. Tob Control. 2014 Jul;23 Suppl 3:iii3-iii9.
Zhu S-H, Zhuang Y-L, Wong S, Cummins SE, Tedeschi GJ. **E-cigarette use and associated changes in population smoking cessation**: evidence from US current population surveys. BMJ 2017;358:j3262.
Zhu JL, Olsen J, Liew Z, Li J, Niclasen J, Obel C. **Parental Smoking** During Pregnancy and **ADHD** in Children: The Danish National Birth Cohort. Pediatrics. 2014 Jul 21.
Zivadinov R, Weinstock-Guttman B, Hashmi K, Abdelrahman N, Stosic M, Dwyer M, Hussein S, Durfee J, Ramanathan M. Smoking is associated with increased lesion volumes and brain atrophy in **multiple sclerosis**. Neurology. 2009 Aug 18;73(7):504-10.

[xliii] Critchley J, Capewell S. Mortality Risk Reduction Associated with Smoking Cessation in Patients with Coronary Heart Disease. JAMA 2003; 290(1):86-97.
[xliv] http://heartdisease.about.com/cs/riskfactors/a/rimonabant_p.htm; http://www.docguide.com/news/content.nsf; http://www.uc.edu/news/NR.asp?id=1417; http://psychiatriymmc.com/displayArticle.cfm?article.cfm?articleID=article105
[xlv] Acomplia (rimonabant) and OTC orlistat for weight loss. Pharmacist's Letter 2006;22(3):220313.

References: Anemia - Hemoglobin Control: Landmark Outcome Trials – Summary (www.RxFiles.ca)

1 Anemia Guidelines for Family Medicine; **Anemia Review Panel**, 2008 Edition.
2 White CT, Barrett BJ, Madore F, Moist LM, Klarenbach SW, Foley RN, Culleton BF, et al. Canadian Society of Nephrology. Clinical practice guidelines for **evaluation of anemia**. Kidney Int Suppl. 2008 Aug;(110):S4-6.
3 Charytan C, Qunibi W, Bailie GR, Venofer Clinical Studies G. Comparison of intravenous **iron sucrose to oral** iron in the treatment of anemic patients with chronic kidney disease not on dialysis. Nephron 2005;100(3):55-62.
4 Van Wyck DB. Roppolo M. Martinez CO. Mazey RM. McMurray S. for the United States **Iron Sucrose** (Venofer) Clinical Trials Group. A randomized, controlled trial comparing IV iron sucrose to oral iron in anemic patients with nondialysis-dependent CKD. Kidney Int. 2005 Dec;68(6):2846-2856.
5 DeVita MV, Frumkin D, Mittal S, Kamran A, Fishbane S, et al. Targeting higher ferritin concentrations with intravenous **iron dextran** lowers erythropoietin requirement in hemodialysis patients. Clin.Nephrol. 2003 Nov;60(5):335-340.
6 Besarab A, Amin N, Ahsan M, Vogel SE, Zazuwa G, Frinak S, et al. Optimization of epoetin therapy with **intravenous iron therapy in hemodialysis** patients. J.Am.Soc.Nephrol. 2000 Mar;11(3):530-538.
7 Macdougall IC, Tucker B, Thompson J, Tomson CR, Baker LR, Raine AE. A randomized controlled study of **iron supplementation** in patients treated **with erythropoietin**. Kidney Int. 1996 Nov;50(5):1694-1699.
8 Fishbane S, Frei GL, Maesaka J. Reduction in recombinant human erythropoietin doses by the use of chronic **intravenous iron** supplementation. Am.J.Kidney Dis. 1995 Jul;26(1):41-46.
9 Coyne DW, Kapoian T, Suki W, Singh AK, Moran JE, Dahl NV, et al. **Ferric gluconate** is highly efficacious in anemic hemodialysis patients with high serum ferritin and low transferrin saturation: results of the Dialysis Patients' Response to IV Iron with Elevated Ferritin (DRIVE) Study. J.Am.Soc.Nephrol. 2007 Mar;18(3):975-984.
10 Kapoian T, O'Mara NB, Singh AK, Moran J, Rizkala AR, Geronemus R, et al. **Ferric gluconate** reduces epoetin requirements in hemodialysis patients with elevated ferritin. J.Am.Soc.Nephrol. 2008 Feb;19(2):372-379.
11 Revicki DA, Brown RE, Feeny DH, Henry D, et al. Health-related **quality of life** associated with recombinant human erythropoietin therapy for predialysis chronic renal disease patients. Am.J.Kidney Dis. 1995 Apr;25(4):548-554.
12 Roth D, Smith RD, Schulman G et al. Effects of recombinant human erythropoietin on **renal function** in chronic renal failure predialysis patients. Am J Kidney Dis 1994; 24: 777–784.
13 Levin A, Djurdjev O, Thompson C, Barrett B, Ethier J, et al. Canadian randomized trial of hemoglobin maintenance to prevent or delay **left ventricular mass** growth in patients with CKD. Am.J.Kidney Dis. 2005 Nov;46(5):799-811.
14 Drueke TB, Locatelli F, Clyne N, Eckardt KU, Macdougall IC, Tsakiris D, et al. **Normalization of hemoglobin level** in patients with chronic kidney disease and anemia. N.Engl.J.Med. 2006 Nov 16;355(20):2071-2084. (**CREATE**)
15 Singh AK, Szczech L, Tang KL, Barnhart H, Sapp S, Wolfson M, et al. Correction of **anemia with epoetin** alfa in chronic kidney disease. N.Engl.J.Med. 2006 Nov 16;355(20):2085-2098. (**CHOIR**)
Inrig JK, Barnhart HX, Reddan D, et al. Effect of hemoglobin target on progression of kidney disease: a secondary analysis of the CHOIR (Correction of Hemoglobin and Outcomes in Renal Insufficiency) trial. Am J Kidney Dis. 2012 Sep;60(3):390-401.
16 Association between recombinant human erythropoietin and **quality of life** and exercise capacity of patients receiving haemodialysis. Canadian Erythropoietin Study Group. BMJ 1990 Mar 3;300(6724):573-578.
Muirhead N, Keown PA, Churchill DN, et al. Dialysis patients treated with Epoetin α show improved exercise tolerance and physical function: A new analysis of the Canadian Erythropoietin Study Group trial. Hemodial Int. 2010 Dec 7. doi: 10.1111/j.1542-4758.2010.00508.x.
17 Parfrey PS, Foley RN, Wittreich BH, et al. Double-blind comparison of **full and partial anemia correction** in incident hemodialysis patients without symptomatic heart disease. J.Am.Soc.Nephrol. 2005 Jul;16(7):2180-2189.
18 Foley RN, Parfrey PS, Morgan J, Barre PE, Campbell P, Cartier P, et al. Effect of hemoglobin levels in hemodialysis patients with asymptomatic **cardiomyopathy**. Kidney Int. 2000 Sep;58(3):1325-1335.
19 Besarab A, Bolton WK, Browne JK, Egrie JC, Nissenson AR, Okamoto DM, et al. The effects of normal as compared with low hematocrit values in patients with cardiac disease who are receiving hemodialysis and epoetin. N.Engl.J.Med. 1998 Aug 27;339(9):584-590. (**Normal Hematocrit Study**)
Coyne DW. The health-related quality of life was not improved by targeting higher hemoglobin in the normal hematocrit trial. Kidney Int , doi:10.1038/ki.2012.76.
20 Tonelli M, Winkelmayer WC, Jindal KK, Owen WF, Manns BJ. The **cost-effectiveness** of maintaining higher hemoglobin targets with erythropoietin in hemodialysis patients. Kidney Int. 2003 Jul;64(1):295-304.
21 Mix TC, et al. Rationale--Trial to Reduce Cardiovascular Events with Aranesp Therapy (**TREAT**): evolving the management of cardiovascular risk in patients with chronic kidney disease. Am.Heart J. 2005 Mar;149(3):408-413.
Pfeffer, Marc A., Burdmann, Emmanuel A., Chen, Chao-Yin, et al. the **TREAT** Investigators, A Trial of Darbepoetin Alfa in Type 2 Diabetes and Chronic Kidney Disease. N Engl J Med 2009 0: NEJMoa0907845.
Solomon Scott D, Lewis Eldrin F., Eckardt Kai-Uwe, et al. for the Trial to Reduce Cardiovascular Events with Aranesp Therapy (TREAT) Investigators. Erythropoietic Response and Outcomes in Kidney Disease and Type 2 Diabetes. N Engl J Med 2010; 363:1146-1155.
Skali H, Parving HH, Parfrey PS, et al. Stroke in patients with type 2 diabetes mellitus, chronic kidney disease, and anemia treated with darboetin alfa: the Trial to Reduce Cardiovascular Events With Aranesp Therapy (TREAT) experience. Circulation. 2011;124:2903–2908.
Mc Causland FR, Claggett B, Burdmann EA, et al. Treatment of Anemia With Darbepoetin Prior to Dialysis Initiation and Clinical Outcomes: Analyses From the Trial to Reduce Cardiovascular Events With Aranesp Therapy (TREAT). Am J Kidney Dis. 2018 Dec 19.
22 Braden J Manns, Colin T White, Francois Madore, et al. **Canadian** Society of Nephrology Clinical Practice Guidelines for the management of **anemia** associated with chronic kidney disease. 2008 Kidney Int 74: S1-S24.
23 KDOQI. **KDOQI** clinical practice guideline and clinical practice recommendations for **anemia** in chronic kidney disease: 2007 update of hemoglobin target. Am J Kidney Dis 2007 Sep;50(3):471-530.
24 Locatelli F. Aljama P. Barany P. et al. **European** Best Practice Guidelines Working Group. Revised European best practice guidelines for the management of **anaemia** in patients with chronic renal failure. Nephrology Dialysis Transplantation. 19 Suppl 2:ii1-47, 2004 May.
25 National Collaborating Centre for Chronic Conditions. **Anaemia** management in chronic kidney disease. National clinical guideline for management in adults and children. London (UK): Royal College of Physicians; 2006. 172 p.
26 **CARI**. The CARI Guidelines Biochemical and Haematological Targets NEPHROLOGY 2008; 13, S44–S56.
27 Tonelli M, Klarenbach S, Wiebe N, et al. Erythropoiesis-Stimulating Agents for Anemia of Chronic Kidney Disease: Systematic Review and Economic Evaluation [Technology report number 106]. Ottawa: Canadian Agency for Drugs and Technologies in Health; 2008. (**CADTH**)
28 Locatelli F, Nissenson AR, Barrett BJ, Walker RG, et al. Clinical Practice Guidelines for Anemia in Chronic Kidney Disease: Problems and Solutions. A Position Statement From **KDIGO**. Kidney Int. 2008;74(10):1237-1240.
Kidney Disease: Improving Global Outcomes (**KDIGO**) Anemia Work Group. KDIGO clinical practice guideline for **anemia in chronic kidney disease**. Kidney Int Suppl 2012 Aug;2(4):279-335.
29. Foley RN, Curtis BM, Parfrey PS. Erythropoietin therapy, hemoglobin targets, & quality of life in healthy **hemodialysis** patients: a randomized trial. Clin J Am Soc Nephrol. 2009 Apr;4(4):726-33. Epub 2009 Apr 1. (n=596 96 weeks)
In relatively healthy hemodialysis pts, normal hemoglobin targets may have beneficial effects on fatigue. Improvement in multiple domains of quality of life is associated with higher body mass index & lower erythropoietin requirements.
30. Uprichard James, Bain Barbara J. **Investigating** suspected anaemia. BMJ 2009;338:b1644, doi: 10.1136/bmj.b1644 (Published 22 May 2009)
31. Moreno Chulilla JA, Romero Colás MS, Gutiérrez Martín M. **Classification of anemia** for gastroenterologists. World J Gastroenterol. 2009 Oct 7;15(37):4627-37.
32. Johansen KL, Finkelstein FO, Revicki DA, Gitlin M, Evans C, Mayne TJ. Systematic Review and Meta-analysis of **Exercise Tolerance and Physical Functioning** in Dialysis Patients Treated With Erythropoiesis-Stimulating Agents. Am J Kidney Dis. 2010 Feb 2.
33. Mehrotra Rajnish; Chiu Yi-Wen; Kalantar-Zadeh Kamyar; et al. Similar Outcomes With **Hemodialysis and Peritoneal Dialysis** in Patients With End-Stage Renal Disease. Arch Intern Med. 2010;0(2010):archinternmed.2010.352.
34. Sood, Manish M., Komenda, Paul, Sood, Amy R., et al. Adverse outcomes among **Aboriginal** patients receiving **peritoneal dialysis**. CMAJ 2010 182: 1433-1439.
35. Bross MH, Soch K, Smith-Knuppel T. **Anemia in older persons**. Am Fam Physician. 2010 Sep 1;82(5):480-7.
36. Himmelfarb J, Ikizler TA. **Hemodialysis**. N Engl J Med. 2010 Nov 4;363(19):1833-45.
37. Fellstrom BC, Jardine AG, Schmeider RE, et al. **Rosuvastatin** and cardiovascular events in patients undergoing hemodialysis. N Engl J Med 2009;360:1395-407.
38. Wanner C, Krane V, M.rz W, et al. **Atorvastatin** in patients with type 2 diabetes mellitus undergoing hemodialysis. N Engl J Med 2005;353:238-48.
39. Jamison RL, Hartigan P, Kaufman JS, et al. Effect of **homocysteine lowering** on mortality and vascular disease in advanced chronic kidney disease and end-stage renal disease: a randomized controlled trial. JAMA 2007;298:1163-70.
40. Suki WN, Zabaneh R, Cangiano JL, et al. Effects of **sevelamer and calciumbased phosphate binders** on mortality in hemodialysis patients. Kidney Int 2007; 72:1130-7.
41. Besarab A, Bolton WK, Browne JK, et al. The effects of **normal as compared with low hematocrit** values in patients with cardiac disease who are receiving hemodialysis and epoetin. N Engl J Med 1998;339:584-90.
42. Rosansky Steven J.; Eggers Paul; Jackson Kirby; et al. **Early Start of Hemodialysis May Be Harmful**. Arch Intern Med. 2010;0(2010):archinternmed.2010.415.
43. **FHN** Trial Group. In-Center **Hemodialysis** Six Times per Week versus Three Times per Week. November 20, 2010 (10.1056/NEJMoa1001593)
44. Cooper BA, Branley P, Bulfone L, et al.; the **IDEAL** Study. A Randomized, Controlled Trial of **Early versus Late Initiation of Dialysis**. N Engl J Med. 2010 Jun 27.
45. Manns B, Hemmelgarn B, Tonelli M, et al; Alberta Kidney Disease Network. **Population based screening** for chronic kidney disease: cost effectiveness study. BMJ. 2010 Nov 8;341:c5869. doi: 10.1136/bmj.c5869.
46. Tonelli Marcello, Muntner Paul, Lloyd Anita, Manns Braden J., et al., for the Alberta Kidney Disease Network. Using **Proteinuria and Estimated Glomerular Filtration Rate** to Classify Risk in Patients With Chronic Kidney Disease: A Cohort Study. Ann Intern Med Jan 4, 2011 154:12-21.
47. Clark, William F., Na, Yingbo, Rosansky, Steven J., et al. Association between **estimated glomerular filtration rate at initiation of dialysis and mortality**. CMAJ 2011 183: 47-53.
48. Mehrotra Rajnish; Chiu Yi-Wen; Kalantar-Zadeh Kamyar; et al. **Similar** Outcomes With **Hemodialysis and Peritoneal Dialysis** in Patients With End-Stage Renal Disease. Arch Intern Med. 2011;171(2):110-118. In the most recent cohorts, patients who began treatment with HD or PD have similar outcomes.
49. Kutner Nancy G.; Zhang Rebecca; Huang Yijian; et al. **Patient Awareness and Initiation of Peritoneal Dialysis**. Arch Intern Med. 2011;171(2):119-124.
50. Hemmelgarn BR, Moist LM, Lok CE, et al. the Prevention of Dialysis Catheter **Lumen Occlusion with rt-PA versus Heparin** (**PreCLOT**) Study Group. Prevention of Dialysis Catheter Malfunction with Recombinant Tissue Plasminogen Activator. N Engl J Med. 2011 Jan 27;364(4):303-312.
51. Tonelli Marcello, Manns Braden. **Supplementing Creatinine-Based Estimates** of Risk in Chronic Kidney Disease: Is It Time? *JAMA*. 2011;Published online April 11, 2011. doi:10.1001/jama.2011.502.
52. Peralta Carmen A., Shlipak Michael G., Judd Suzanne, et al. Detection of Chronic Kidney Disease With **Creatinine, Cystatin C, and Urine Albumin-to-Creatinine** Ratio and Association With Progression to End-Stage Renal Disease and Mortality. *JAMA*. 2011;Published online April 11, 2011.
53. Tangri Navdeep, Stevens Lesley A., Griffith John, et al. A Predictive **Model for Progression of Chronic Kidney Disease** to Kidney Failure. *JAMA*. 2011;Published online April 11, 2011. doi:10.1001/jama.2011.451

54. **FDA** June/11 notified healthcare professionals that new, modified recommendations for more conservative dosing of Erythropoiesis-Stimulating Agents (ESAs) in patients with chronic kidney disease (CKD) have been approved to improve the safe use of these drugs. FDA has made these recommendations because of data showing increased risks of cardiovascular events with ESAs in this patient population. The new dosing recommendations are based on clinical trials showing that using **ESAs to target a hemoglobin level of greater than 11 g/dL in patients with CKD provides no additional benefit** than lower target levels, and increases the risk of experiencing serious adverse cardiovascular events, such as heart attack or stroke. http://www.fda.gov/Safety/MedWatch/SafetyInformation/SafetyAlertsforHumanMedicalProducts/ucm260641.htm
55. Pergola Pablo E., Raskin Philip, Toto Robert D., et al. for the BEAM Study Investigators. **Bardoxolone Methyl** and Kidney Function in CKD with Type 2 Diabetes. June 24, 2011 (10.1056/NEJMoa1105351)
56. Hilton R. **Defining acute renal failure**. CMAJ. 2011 Jul 2;183(10):1167-9.
57. Salisbury AC, Reid KJ, Alexander KP, et al. Diagnostic Blood Loss From **Phlebotomy and Hospital-Acquired Anemia** During Acute Myocardial Infarction. Arch Intern Med. 2011 Aug 8.
58. Vivante A, Afek A, Frenkel-Nir Y, et al. Persistent asymptomatic isolated **microscopic hematuria** in Israeli adolescents and young adults and risk for end-stage renal disease. JAMA. 2011 Aug 17;306(7):729-36.
59. Zhang Y, Thamer M, Kaufman JS et al. **High doses of epoetin** do not lower mortality and cardiovascular risk among elderly **hemodialysis patients with diabetes**. Kidney Int 2011;80:663 – 669.
60. Levey AS, Coresh J. **Chronic kidney disease**. Lancet. 2011 Aug 12.
61. Foley RN, Gilbertson DT, Murray T et al. **Long Interdialytic Interval** and Mortality among Patients Receiving Hemodialysis. N Engl J Med 2011;365:1099-107.
62. Kucirka LM, Grams ME, Lessler J, et al. Association of **race and age** with survival among patients undergoing dialysis. JAMA. 2011 Aug 10;306(6):620-6.
63. Heiwe S, Jacobson SH. **Exercise training for adults** with chronic kidney disease. Cochrane Database of Systematic Reviews 2011, Issue 10. Art. No.: CD003236. DOI: 10.1002/14651858.CD003236.pub2. There is evidence for significant beneficial effects of regular exercise on physical fitness, walking capacity, cardiovascular dimensions (e.g. blood pressure and heart rate), health-related quality of life and some nutritional parameters in adults with CKD.
64. Winkelmayer WC, Liu J, Chertow GM, Tamura MK. **Predialysis nephrology care of older patients** approaching end-stage renal disease. Arch Intern Med. 2011 Aug 8;171(15):1371-8.
65. Kiaii M, Djurdjev O, Farah M, Levin A, Jung B, MacRae J. Use of **electronbeam sterilized hemodialysis** membranes and risk of thrombocytopenia. JAMA. 2011;306(15):1679-1687.
66. O'Hare AM, Choi AI, Boscardin WJ, et al. **Trends in timing of initiation of chronic dialysis** in the United States. Arch Intern Med. 2011 Oct 10;171(18):1663-9.
67. Isakova T, Xie H, Yang W, et al. Chronic Renal Insufficiency Cohort (CRIC) Study Group. Fibroblast growth factor 23 and risks of mortality and end-stage renal disease in patients with chronic kidney disease. JAMA. 2011 Jun 15;305(23):2432-9.
68. Marti-Carvajal AJ, Sola I, Pena-Marti GE, et al. Treatment for anemia in people with **AIDS**. Cochrane Database Syst Rev. 2011 Oct 5;(10):CD004776.
69. Weinhandl ED, Liu J, Gilbertson DT, Arneson TJ, Collins AJ. Survival in **Daily Home Hemodialysis** and Matched Thrice-Weekly In-Center Hemodialysis Patients. J Am Soc Nephrol. 2012 Feb 23.
70. Nesrallah GE, Lindsay RM, Cuerden MS, et al. **Intensive Hemodialysis** Associates with Improved Survival Compared with Conventional Hemodialysis. J Am Soc Nephrol. 2012 Feb 23.
71. Lacson E Jr, Xu J, Suri R, et al. Survival with **Three-Times Weekly In-Center Nocturnal** Versus Conventional Hemodialysis. J Am Soc Nephrol. 2012 Feb 23.
72. Daugirdas JT, Chertow GM, Larive B, et al Effects of **Frequent Hemodialysis** on Measures of CKD Mineral and Bone Disorder. J Am Soc Nephrol. 2012 Feb 23. (control of hyperphosphatemia)
73. Carson JL, Grossman BJ, Kleinman S, et al., for the Clinical Transfusion Medicine Committee of the AABB. **Red Blood Cell Transfusion**: A Clinical Practice Guideline From the AABB. Ann Intern Med ahead of print Mar 26,12.
74. Inker LA, Schmid CH, Tighiouart H, et al. Estimating glomerular filtration rate from serum **creatinine and cystatin C**. N Engl J Med 2012;367:20-9.
75. Bao Y, Dalrymple L, Chertow GM, et al. **Frailty, Dialysis Initiation, and Mortality** in End-Stage Renal Disease Frailty, Dialysis Initiation, & Mortality in ESRD. Arch Intern Med. 2012 Jun 25:1-7.
76. Akbari A, Grimshaw J, Stacey D et al. Change in appropriate referrals to nephrologists after the introduction of automatic reporting of the estimated glomerular filtration rate. CMAJ. 2012 Mar 20;184(5):E269-76.
77. Cladellas M, Farré N, Comín-Colet J, et al. Effects of **Preoperative Intravenous Erythropoietin Plus Iron** on Outcome in Anemic Patients After **Cardiac Valve Replacement**. Am J Cardiol. 2012 Jul 6.
78. Earley A, Miskulin D, Lamb EJ, et al. **Estimating equations for glomerular filtration rate** in the era of creatinine standardization: a systematic review. Ann Intern Med. 2012 Jun 5;156(11):785-95.
79. Morton RL, Snelling P, Webster AC, et al. Factors influencing patient choice of **dialysis versus conservative care** to treat end-stage kidney disease. CMAJ. 2012 Mar 20;184(5):E277-83.
80. Liles AM. **Intravenous versus oral iron** for treatment of iron deficiency in non-hemodialysis-dependent patients with chronic kidney disease. Am J Health Syst Pharm. 2012 Jul 15;69(14):1206-11.
81. Carson JL, Carless PA, Hébert PC. Outcomes using lower vs higher haemoglobin thresholds for red **blood cell transfusion**. JAMA. 2013 Jan 2;309(1):83-4.
82. Villanueva C, Colomo A, Bosch A, et al. **Transfusion strategies for acute upper gastrointestinal bleeding**. N Engl J Med 2013;368:11-21.
83. Chatterjee S, Wetterslev J, Sharma A, et al. Association of **blood transfusion** with increased mortality in **myocardial infarction**: A meta-analysis and diversity-adjusted study sequential analysis. Arch Intern Med. 2012.
84. Macdougall IC, Provenzano R, Sharma A, et al. **Peginesatide** for anemia in patients with chronic kidney disease not receiving dialysis. (**PEARL**) N Engl J Med 2013;368:320-32.
85. Fishbane S, Schiller B, Locatelli F, et al. **Peginesatide** in patients with anemia undergoing hemodialysis. (**EMERALD**) N Engl J Med 2013;368:307-19.
86. Swedberg K et al. Treatment of anemia with **darbepoetin** alfa in systolic heart failure. (**RED-HF**) N Engl J Med 2013 Mar 10. (not an clinical outcome benefit)
87. Carson JL, Carless PA, Hebert PC. **Transfusion thresholds** and other strategies for guiding allogeneic red blood cell transfusion. Cochrane Database Syst Rev. 2012 Apr 18;4:CD002042. The existing evidence supports the use of restrictive transfusion triggers inmost patients, including thosewith pre-existing cardiovascular disease. As there are no trials, the effects of restrictive transfusion triggers in high-risk groups, such as acute coronary syndrome, need to be tested in further large clinical trials. In countries with inadequate screening of donor blood, the data may constitute a stronger basis for avoiding transfusion with allogeneic red cells.
88. Mitsnefes MM, Laskin BL, Dahhou M, et al. Mortality risk among **children initially treated with dialysis** for end-stage kidney disease, 1990-2010. JAMA. 2013 May 8;309(18):1921-9.
89. KDOQI: National Kidney Foundation. **KDOQI** clinical practice guideline for **diabetes and CKD**: 2012 update. Am J Kidney Dis. 2012 Nov;60(5):850-86.
90. Moist LM, Troyanov S, White CT, Wazny LD, Wilson JA, McFarlane P, Harwood L, Sood MM, Soroka SD, Bass A, Manns BJ. **Canadian Society of Nephrology Commentary on the 2012 KDIGO** Clinical Practice Guideline for Anemia in CKD. Am J Kidney Dis. 2013 Sep 17.
91. Harley KT, Streja E, Rhee CM, et al. **Nephrologist Caseload and Hemodialysis Patient Survival** in an Urban Cohort. J Am Soc Nephrol. 2013 Aug 8.
92. Salpeter SR, Buckley JS, Chatterjee S. Impact of more **restrictive blood transfusion** strategies on clinical outcomes: a meta-analysis and systematic review. Am J Med. 2014 Feb;127(2):124-131.e3.
93. Winkelmayer WC, Mitani AA, Goldstein BA, et al. Trends in Anemia Care in Older Patients Approaching **End-Stage Renal Disease** in the United States (1995-2010). JAMA Intern Med. 2014 Mar 3.
94. Coritsidis GN, Maglinte GA, Acharya A, et al. Anemia Management Trends in **Hospital-Based Dialysis** Centers(HBDCs), 2010 to 2013. Clin Ther. 2014 Feb 27.
95. Sherwood MW, Wang Y, Curtis JP, Peterson ED, Rao SV. Patterns and outcomes of red blood cell transfusion in patients undergoing **percutaneous coronary intervention**. *JAMA* 2014; 311: 836-843.
96. DeLoughery TG. **Microcytic anemia**. N Engl J Med. 2014 Oct 2;371(14):1324-31.
97. Carson JL, Sieber F, Cook DR, et al. **Liberal versus restrictive blood transfusion** strategy: 3-year survival and cause of death results from the FOCUS randomised controlled trial. Lancet 2014; online Dec 9.
98. Hecking M, Bieber BA, Ethier J, et al. **Sex Specific Differences in Hemodialysis Prevalence and Practices** and the Male-to Female Mortality Rate: The Dialysis Outcomes and Practice Patterns Study (DOPPS). PLoS Med. 2014 Oct 28;11(10):e1001750.
99. Hesdorffer CS, Longo DL. **Drug-Induced Megaloblastic Anemia**. N Engl J Med. 2015 Oct 22;373(17):1649-58.
100. NICE: National Clinical Guideline Centre. Anaemia management in people with chronic kidney disease. London (UK): National Institute for Health and Care Excellence (NICE); 2015 Jun 3.
101. Slinin Y, Greer N, Ishani A, et al. **Timing of Dialysis Initiation, Duration and Frequency of Hemodialysis Sessions, and Membrane Flux**: A Systematic Review for a KDOQI Clinical Practice Guideline. Am J Kidney Dis. 2015 Nov;66(5):823-36.
102. Li L, Streja E, Rhee CM, et al. **Hypomagnesemia** and mortality in incident hemodialysis patients. Am J Kidney Dis. 2015 Jul 13.
103. Yang L, Xing G, Wang L, et al; ISN AKF 0by25 China Consortiums. **Acute kidney injury in China**: a cross-sectional survey. Lancet. 2015 Oct 10;386(10002):1465-71.
104. Guideline development group. **ERBP**: Clinical Practice Guideline on management of patients with **diabetes and chronic kidney disease stage** 3b or higher (eGFR <45 mL/min). Nephrol Dial Transplant. 2015 May;30 Suppl 2:ii1-142.
105. National Kidney Foundation. **KDOQI** Clinical Practice Guideline for **Hemodialysis Adequacy: 2015 Update**. Am J Kidney Dis. 2015 Nov;66(5):884-930.
106. Dhabangi A, Ainomugisha B, Cserti-Gazdewich C, et al. Effect of **Transfusion of Red Blood Cells With Longer vs Shorter Storage Duration** on Elevated Blood Lactate Levels in Children With Severe Anemia: The TOTAL Randomized Clinical Trial. JAMA. 2015 Dec 15;314(23):2514-2523.
107. Ellam T, Twohig H, Khwaja A. **Chronic kidney disease in elderly people**: disease or disease label? BMJ. 2016 Jan 18;352:h6559.
108. Wong SP, Vig EK, et al. **Timing of Initiation of Maintenance Dialysis**: Qualitative Analysis of the Electronic Medical Records of a National Cohort of Patients From Department of Veterans Affairs. JAMA Intern Med. 2016 Jan 25.
109. Docherty AB, et al. Effect of **restrictive versus liberal transfusion** strategies on outcomes in patients with cardiovascular disease in a non-cardiac surgery setting: systematic review and meta-analysis. BMJ. 2016 Mar 29
110. Rocco MV, Daugirdas JT, et al. FHN Trial Group. Long-term Effects of **Frequent Nocturnal Hemodialysis on Mortality**: The Frequent Hemodialysis Network (**FHN**) Nocturnal Trial. Am J Kidney Dis. 2015 Sep;66(3):459-68.
111. Gaudry S, Hajage D, Schortgen F, et al. **Initiation strategies for renal-replacement therapy** in the intensive care unit. (**AKIKI**) N Engl J Med. DOI: 10.1056/NEJMoa1603017.
112. Kramer A, Pippias M, Stel VS, et al. **Renal replacement therapy in Europe**: a summary of the 2013 ERA-EDTA Registry Annual Report with a focus on diabetes mellitus. Clin Kidney J. 2016 Jun;9(3):457-69.
113. Zarbock A, Kellum JA, et al. Effect of **early vs delayed initiation of renal replacement therapy** on mortality in critically ill patients with acute kidney injury: ELAIN randomized clinical trial.JAMA. doi:10.1001/jama.2016.5828.
114. Carson JL, Guyatt G, Heddle NM, et al. Clinical practice guidelines from the **AABB: red blood cell transfusion thresholds and storage**.JAMA. doi:10 .1001/jama.2016.9185
115. Carson JL, Stanworth SJ, Roubinian N, et al. **Transfusion thresholds and other strategies for guiding allogeneic red blood cell transfusion**. Cochrane Database of Systematic Reviews 2016, Issue 10. Art. No.: CD002042. Transfusing at a restrictive haemoglobin concentration of between 7 g/dL to 8 g/dL decreased the proportion of participants exposed to RBC transfusion by 43% across a broad range of clinical specialities. There was no evidence that a restrictive transfusion strategy impacts 30-day mortality or morbidity (i.e. mortality at other points, cardiac events, myocardial infarction, stroke, pneumonia, thromboembolism, infection) compared with a liberal transfusion strategy. There were insufficient data to inform the safety of transfusion policies in certain clinical subgroups, including acute coronary syndrome, myocardial infarction, neurological injury/traumatic brain injury, acute neurological disorders, stroke, thrombocytopenia, cancer, haematological malignancies, and bone marrow failure. The findings provide good evidence that transfusions with allogeneic RBCs can be avoided in most patients with haemoglobin thresholds above 7 g/dL to 8 g/dL.
116. Cody JD, Hodson EM. **Recombinant human erythropoietin versus placebo or no treatment for the anaemia of chronic kidney disease in people not requiring dialysis**. Cochrane Database Syst Rev 2016;(1):CD003266. Treatment with rHuEPO in predialysis patients corrects anaemia, avoids the requirement for blood transfusions and also improves quality of life and exercise capacity. We were unable to assess the effects of rHuEPO on progression of kidney disease, delay in the onset of dialysis or adverse events. Based on the current evidence, decisions on the putative benefits in terms of quality of life are worth the extra costs of predialysis rHuEPO need careful evaluation.

117. Heddle NM, Cook RJ, Arnold DM, et al. Effect of **short-term vs. long-term blood storage** on mortality after transfusion. N Engl J Med. DOI: 10.1056/NEJMoa1609014.
118. Webster AC, Nagler EV, Morton RL, et al. **Chronic Kidney Disease**. Lancet.2016 Nov 22.

119. Manfredini F, Mallamaci F, D'Arrigo G, et al. **Exercise in Patients on Dialysis**: A Multicenter, Randomized Clinical Trial. J Am Soc Nephrol. 2016 Dec 1.
120. Palmer SC, Gardner S, Tonelli M, et al. **Phosphate-Binding Agents in Adults With CKD**: A Network Meta-analysis of Randomized Trials. Am J Kidney Dis. 2016 Jul 22.
121. Yan H, Fang W, Lin A, et al. **Three Versus 4 Daily Exchanges and Residual Kidney Function Decline in Incident CAPD Patients**: A Randomized Controlled Trial. Am J Kidney Dis. 2016 Oct 14.
122. Webster AC, Nagler EV, Morton RL, et al. **Chronic Kidney Disease**. Lancet.2016 Nov 22.
123. Halmin M, Rostgaard K, Lee BK, et al. **Length of Storage of Red Blood Cells** and Patient Survival After Blood Transfusion: A Binational Cohort Study. Ann Intern Med. 2016 Dec 20.
124. Massicotte-Azarniouch D, Amin SO, Hesketh C, Clark EG. **Recommended Reading** from the University of Ottawa **Nephrology Fellows**. Am J Respir Crit Care Med. 2017 May 2.
125. Pdf Carson JL, Triulzi DJ, Ness PM. **Indications for and Adverse Effects of Red-Cell Transfusion**. N Engl J Med. 2017 Sep 28;377(13):1261-1272
126. Cooper DJ, et al; **TRANSFUSE** Investigators and the Australian and New Zealand Intensive Care Society Clinical Trials Group. **Age of Red Cells for Transfusion** and Outcomes in Critically Ill Adults. N Engl J Med. 2017 Sep 27.
127. Di **Angelantonio** E, Thompson SG, Kaptoge S, et al. Efficiency and safety of varying the **frequency of whole blood donation (INTERVAL):** a randomised trial of 45000 donors. Lancet 2017; online Sept 20.
128. Wick JP, Turin TC, Faris PD, et al. A **Clinical Risk Prediction Tool for 6-Month Mortality After Dialysis Initiation** Among Older Adults. Am J Kidney Dis. 2017 May;69(5):568-575
129. Cervantes L, Tuot D, et al. Association of **Emergency-Only vs Standard Hemodialysis With Mortality** and Health Care Use Among Undocumented Immigrants With End-stage Renal Disease. JAMA Intern Med. 2017 Dec 18.
130. Srivastava T, Jafri S, Truog WE, et al. Successful Reversal of **Furosemide-Induced Secondary Hyperparathyroidism** With **Cinacalcet**. Pediatrics. 2017 Dec;140(6).
131. Tseng J, Halbert RJ, Minissian N, et al.Association of Standardization of **Continuous Renal Replacement Therapy and High-Value Care**: An Evidence-Based Approach. JAMA Intern Med. 2018 Feb 26.
132. Cervantes L, Richardson S, Raghavan R, et al. Clinicians' perspectives on providing **emergency only hemodialysis to undocumented immigrants**. A qualitative study. Ann Intern Med. 2018. [Epub ahead of print].
133. Chan L, Chauhan K, Poojary P, et al. National Estimates of **30-Day Unplanned Readmissions of Patients on Maintenance Hemodialysis**. Clin J Am Soc Nephrol. 2017 Oct 6;12(10):1652-1662.
134. Kurella Tamura M, Thomas I-C, Montez-Rath ME, et al. Dialysis initiation and mortality among older veterans with kidney failure treated in Medicare vs the Department of Veterans Affairs [online April 9, 2018]. JAMA Intern Med.
135. Nigwekar SU, Thadhani R, Brandenburg VM. Calciphylaxis. N Engl J Med. 2018 May 3;378(18):1704-1714.
136. Phillips J, Henderson AC. Hemolytic Anemia: Evaluation and Differential Diagnosis. Am Fam Physician. 2018 Sep 15;98(6):354-361.
137. Mazer CD, Whitlock RP, Fergusson DA, et al; **TRICS**. Six-Month Outcomes after **Restrictive or Liberal Transfusion** for Cardiac Surgery. N Engl J Med. 2018 Aug 26.
138. Pasricha SR, Armitage AE, Prentice AM, et al. **Reducing anaemia in low income countries**: control of infection is essential. BMJ. 2018 Aug 1;362:k3165.
139. Franz D, Zheng Y, Leeper NJ, et al. Trends in Rates of **Lower Extremity Amputation** Among Patients With **End-stage Renal Disease Who Receive Dialysis**. JAMA Intern Med. 2018 Jul 9.
140. Barbar SD, Clere-Jehl R, Bourredjem A, et al. **IDEAL-ICU** Trial Investigators and the **CRICS TRIGGERSEP** Network. Timing of **Renal-Replacement Therapy in Patients with Acute Kidney Injury and Sepsis**. N Engl J Med. 2018 Oct 11;379(15):1431-1442.
141. Gilbert J, Lovibond K, Mooney A, Dudley J; Guideline Committee. **Renal replacement therapy**: summary of **NICE** guidance. BMJ. 2018 Oct 19;363:k4303.
142. NICE:National Institute for Health and Care Excellence. **Renal replacement therapy and conservative management** (**NICE** guideline NG107). 2018. www.nice.org.uk/guidance/ ng107.
143. Swaminathan S, Sommers BD, Thorsness R, et al. Association of **Medicaid expansion with 1-year mortality among patients with end-stage renal disease** [online Oct 25, 2018]. JAMA.
144. Young NS. **Aplastic Anemia**. N Engl J Med. 2018 Oct 25;379(17):1643-1656.
145. Macdougall IC, White C, Anker SD, et al**; PIVOTAL** Investigators and Committees. **Intravenous Iron** in Patients Undergoing Maintenance Hemodialysis. N Engl J Med. 2018 Oct 26
146. Roncarati JS, Baggett TP, O'Connell JJ, et al. **Mortality among unsheltered homeless adults** in Boston, Massachusetts, 2000-2009. (dialysis) JAMA Intern Med. 2018;178(9):1242-1248.
147. Swaminathan S, Sommers BD, Thorsness R,et al. Association of **Medicaid expansion with 1-year mortality among patients with end-stage renal disease** [online Oct 25, 2018]. JAMA.
148. J-DAVID Investigators. Effect of oral **alfacalcidol** on clinical outcomes **in patients without secondary hyperparathyroidism receiving maintenance hemodialysis** [Dec 11,2018]. JAMA. doi:10.1001/jama.2018.17749
149. Nguyen OK, Vazquez MA, Charles L, et al. Association of **Scheduled vs Emergency-Only Dialysis** With Health Outcomes and Costs in Undocumented Immigrants With End-stage Renal Disease. JAMA Intern Med. 2018 Dec 21.
151. Dunlop JL, Vandal AC, Marshall MR. **Low dialysate sodium levels for chronic haemodialysis**. Cochrane Database Syst Rev. 2019 Jan 16;1:CD011204. It is likely that low dialysate [Na+] reduces intradialytic weight gain and BP, which are effects directionally associated with improved outcomes. However, the intervention probably also increases intradialytic hypotension and reduces serum [Na+], effects that are associated with increased mortality risk. The effect of the intervention on overall patient health and well-being is unknown.
152. Eule C, Gupta A, Nagalla S. The Direct **Antiglobulin Test for Evaluating Anemia**. JAMA. 2018 Dec 3.
153. Wong SPY, McFarland LV, Liu C-F, et al. **Care practices for patients** with advanced kidney disease **who forgo dialysis** [online Jan 22, 2019]. JAMA Intern Med. doi:10.1001/jamainternmed.2018.6197
154. Chan CT, Blankestijn PJ, Dember LM, et al; Conference Participants. **Dialysis initiation, modality choice, access, and prescription**: conclusions from a Kidney Disease: Improving Global Outcomes (KDIGO) Controversies Conference. Kidney Int. 2019 Apr 12.
155. Gafni RI, Collins MT. **Hypoparathyroidism**. N Engl J Med. 2019 May 2;380(18):1738-1747.
156. Mueller MM, Van Remoortel H, Meybohm P, et al; ICC PBM Frankfurt 2018 Group. **Patient Blood Management**: Recommendations From the 2018 Frankfurt Consensus Conference. JAMA. 2019 Mar 12;321(10):983-997.
157. Wachterman MW, O'Hare AM, Rahman OK, et al. **One-Year Mortality After Dialysis Initiation** Among Older Adults. JAMA Intern Med. 2019 Apr 22.
158. Maitland K, Kiguli S, Olupot-Olupot P, et al. **Immediate transfusion** in African children with uncomplicated severe anemia. N Engl J Med 2019; 381: 407-19. (TRACT)
159. Maitland K, Olupot-Olupot P, Kiguli S, et al. **Transfusion volume** for children with severe anemia in Africa. N Engl J Med 2019; 381: 420-31. (TRACT)
160. Murugan R, Kerti SJ, Chang CH, et al. Association of **Net Ultrafiltration Rate With Mortality** Among Critically Ill Adults With Acute Kidney Injury Receiving Continuous Venovenous Hemodiafiltration: A Secondary Analysis of the Randomized Evaluation of Normal vs Augmented Level (RENAL) of Renal Replacement Therapy Trial. JAMA Netw Open. 2019 Jun 5;2(6):e195418.
161. Pravoverov LV, Zheng S, Parikh R, et al. Trends Associated With **Large-scale Expansion of Peritoneal Dialysis** Within an Integrated Care Delivery Model. JAMA Intern Med. 2019 Sep 9.
162. Shet AS, Zwarenstein M, Rao A, et al. Effect of a Community Health Worker-Delivered **Parental Education and Counseling Intervention on Anemia Cure Rates** in Rural Indian Children: A Pragmatic Cluster Randomized Clinical Trial. JAMA Pediatr. 2019 Jul 22.

Addional information about Mircera (Web-only)

Methoxy polyethylene glycol-epoetin beta MIRCERA [13] PL Single-dose **vials** (solution): 50, 100, 200, 300, 400, 600, 1000 µg/mL Single-dose **pre-filled syringes:** 50µg/0.3mL, 75µg/0.3mL, 100µg/0.3mL, 150µg/0.3mL, 200µg/0.3mL, 250µg/0.3mL, 400µg/0.6mL, 600µg/0.6mL	✓ **Tx of anemia with CKD** Pre-filled syringes: sterile & do not contain preservatives. Store in fridge at 2-8°. (Do not freeze) Keep in original package to protect from light. Stable at room temperature ≤ 25° C for up to 1 month Allow to reach room temp. before inj.		SC in ND-CKD & PD-CKD; **IV** or SC in HD-CKD Not currently on ESA tx: 0.6 mcg/kg every 2 weeks as a single IV or SQ inj Pts on ESA: can convert to MIRCERA given once a month as a single IV or SQ inj. Monthly Mircera starting IV or SQ dose mcg/monthly: 120 if <40 Aranesp or <8,000 Eprex; 200 if <40-80 Aranesp or 8-16,000 Eprex; 360 if >80 Aranesp or >16,000 Eprex (Aranesp in mcg/week, Eprex in IU/week) Equivalent with IV or SQ. If Hgb target is reached, may give once monthly using a dose equal to twice the previous every two week dose.	✗ ⊗ Not on formulary. Not yet avail. in Canada, but NOC received Mar 2008

Erythropoiesis Stimulating Agents (ESA) in Anemia of Chronic Kidney Disease (CKD): Therapeutic Alternatives

References

1 eCPS Monographs, Lexi-Drugs, Micromedex 2018.
2 Clinical Practice Guidelines for evidence-based use of ESAs (CSN)
3 uptodate.com – EPO for the anemia of CKD among predialysis and peritoneal dialysis pts (accessed nov 19)
4 Continuous Erythropoietin Receptor Activator (Mircera®) for Renal Anemia Issues in Emerging Health Technologies – CADATH Report
5 Fishbane S, Schiller B, Locatelli F, et al. Peginesatide in patients with anemia undergoing hemodialysis. (EMERALD) N Engl J Med 2013;368:307-19.
6 Macdougall IC, Provenzano R, Sharma A, et al. Peginesatide for anemia in patients with chronic kidney disease not receiving dialysis. (PEARL) N Engl J Med 2013;368:320-32.
7 Health Canada - Drugs and Health Products – Public Communication - Black Box Warning 2007
http://www.hc-sc.gc.ca/dhp-mps/medeff/advisories-avis/prof/_2007/aranesp_eprex_hpc-cps-eng.php
8 Bohlius J, Schmidlin K, Brillant C, et al. Recombinant human erythropoiesis-stimulating agents and mortality in patients with cancer: a meta-analysis of randomized trials. Lancet. 2009 May 2;373(9674):1532-42. Treatment with erythropoiesis-stimulating agents in patients with cancer increased mortality during active study periods and worsened overall survival. The increased risk of death associated with treatment with these drugs should be balanced against their benefits.
9 Tonelli M, Hemmelgarn B, Reiman T, et al. Benefits and harms of erythropoiesis-stimulating agents for anemia related to cancer: a meta-analysis. CMAJ. 2009 Apr 30. Use of erythropoiesis-stimulating agents in patients with cancer-related anemia improved some disease-specific measures of quality of life and decreased the use of blood transfusions. However, it increased the risk of death and serious adverse events. Our findings suggest that such therapy not be used routinely as an alternative to blood transfusion in patients with anemia related to cancer.
10 Canadian Society of Nephrology (CSN) 2008
Moist LM, Troyanov S, White CT, Wazny LD, Wilson JA, McFarlane P, Harwood L, Sood MM, Soroka SD, Bass A, Manns BJ. Canadian Society of Nephrology Commentary on the 2012 KDIGO Clinical Practice Guideline for Anemia in CKD. Am J Kidney Dis. 2013 Sep 17.
11 Kidney Disease Outcomes Quality Initiative (National Kidney Foundation) (KDOQI) 2007 NKF KDOQI Guidelines: 2007 Update of Hemoglobin Target.
Kidney Disease: Improving Global Outcomes (**KDIGO**) Anemia Work Group. KDIGO clinical practice guideline for **anemia in chronic kidney disease**. Kidney Int Suppl 2012 Aug;2(4):279-335.
12 Kidney Disease: Improving Global Outcomes (KDIGO) 2008.
Kidney Disease: Improving Global Outcomes (KDIGO) Anemia Work Group. KDIGO clinical practice guideline for anemia in chronic kidney disease. Kidney Int Suppl 2012 Aug;2(4):279-335.
13 Continuous Erythropoietin Receptor Activator (Mircera®) for Renal Anemia Issues in Emerging Health Technologies – CADATH Report
14. Anemia Guidelines for Family Medicine; Anemia Review Panel, 2008 Edition.

Additional references:

Abboud, Hanna, Henrich, William L. **Stage IV** Chronic Kidney Disease.N Engl J Med 2010 362: 56-65.
Aher SM, Ohlsson A. Late **erythropoiesis-stimulating agents to prevent red blood cell transfusion** in preterm or low birth weight infants. Cochrane Database Syst Rev. 2019 Feb 15;2:CD004868.
Aspinall SL, Cunningham FE, Zhao X, et al. ESA Clinic Study Group. Impact of **pharmacist-managed erythropoiesis-stimulating agents clinics** for patients with non-dialysis-dependent CKD. Am J Kidney Dis. 2012 Sep;60(3):371-9.
Benders MJ, van der Aa NE, Roks M, et al. Feasibility and Safety of **Erythropoietin for Neuroprotection** after Perinatal Arterial Ischemic Stroke. J Pediatr. 2013 Dec 7
Bennett CL, Silver SM, Djulbegovic B, et al. Venous **thromboembolism and mortality** associated with recombinant erythropoietin and darbepoetin administration for the treatment of cancer-associated anemia. JAMA. 2008 Feb 27;299(8):914-24.
Bennett CL, Luminari S, Nissenson AR, et al. **Pure red-cell aplasia** and epoetin therapy. N Engl J Med 2004;351:1403-1408.
Berger A, Lord C, Corey-Lisle PK, et al. Utilization and Cost in Clinical Practice of **Darbepoetin Alfa and Epoetin Alfa for Anemia Concomitant With Chemotherapy**. Clin Ther. 2012 May 14.
Besarab A, Frinak S, Yee J. What is so bad about a **hemoglobin level of 12 to 13** g/dL for chronic kidney disease patients anyway? Adv Chronic Kidney Dis 2009;16:131-142.
Besarab A, Bolton WK, Browne JK, Egrie JC, et al. The effects of normal as compared with low **hematocrit** values in patients with cardiac disease who are receiving hemodialysis and epoetin. (**Normal Hematocrit Study**) N Engl J Med. 1998 Aug 27;339(9):584-90.
Blum S, Shapir N, Miari R, et al. **TARGT Gene Therapy** Platform for Correction of Anemia in End-Stage Renal Disease. N Engl J Med. 2017 Jan 12;376(2):189-191.
Bohlius J, Bohlke K, Castelli R, et al. Management of cancer-associated anemia with erythropoiesis-stimulating agents:**ASCO/ASH** clinical practice guideline update. Blood Adv. **2019** Apr 23;3(8):1197-1210.
Bohlius J, Schmidlin K, Brillant C, et al. Erythropoietin or Darbepoetin for **patients with cancer**--meta-analysis based on individual patient data. Cochrane Database Syst Rev. 2009 Jul 8;(3):CD007303. ESA treatment in cancer patients increased on study mortality and worsened overall survival. For patients undergoing chemotherapy the increase was less pronounced, but an adverse effect could not be excluded.
Bohlius J, Wilson J, Seidenfeld J, et al. Recombinant human erythropoietins and **cancer patients**: updated meta-analysis of 57 studies including 9353 patients. J Natl Cancer Inst 2006;98:708-714. Brines M, Cerami A. Erythropoietin-mediated tissue protection: reducing collateral damage from the primary injury response. J Intern Med 2008;264:405-432.
Buckley MS, Kane-Gill SL, Patel SA. **Clinical and Economic Evaluation** of an Evidence-Based Institutional Epoetin-Utilization Management Program. Clin Ther. 2013 Feb 25.
Carson JL, Grossman BJ, Kleinman S, et al., for the Clinical Transfusion Medicine Committee of the AABB. **Red Blood Cell Transfusion**: A Clinical Practice Guideline From the AABB. Ann Intern Med ahead of print Mar 26,12.
Carson JL, Guyatt G, Heddle NM, et al. Clinical practice guidelines from the **AABB: red blood cell transfusion thresholds and storage**.JAMA. doi:10 .1001/jama.2016.9185
Carson JL, Stanworth SJ, Roubinian N, et al. **Transfusion thresholds and other strategies for guiding allogeneic red blood cell transfusion**. Cochrane Database of Systematic Reviews 2016, Issue 10. Art. No.: CD002042. Transfusing at a restrictive haemoglobin concentration of between 7 g/dL to 8 g/dL decreased the proportion of participants exposed to RBC transfusion by 43% across a broad range of clinical specialities. There was no evidence that a restrictive transfusion strategy impacts 30-day mortality or morbidity (i.e. mortality at other points, cardiac events, myocardial infarction, stroke, pneumonia, thromboembolism, infection) compared with a liberal transfusion strategy. There were insufficient data to inform the safety of transfusion policies in certain clinical subgroups, including acute coronary syndrome, myocardial infarction, neurological injury/traumatic brain injury, acute neurological disorders, stroke, thrombocytopenia, cancer, haematological malignancies, and bone marrow failure. The findings provide good evidence that transfusions with allogeneic RBCs can be avoided in most patients with haemoglobin thresholds above 7 g/dL to 8 g/dL.
Chertow GM, Liu J, Monda KL, et al. **Epoetin Alfa** and Outcomes in Dialysis amid Regulatory and Payment Reform. J Am Soc Nephrol. 2016;27:3129-3138.

Choukroun G, Kamar N, Dussol B, et al.; **CAPRIT** study Investigators: Correction of **postkidney transplant** anemia reduces progression of allograft nephropathy. J Am Soc Nephrol 23: 360–368, 2012.
Cladellas M, Farré N, Comín-Colet J, et al. Effects of **Preoperative Intravenous Erythropoietin Plus Iron** on Outcome in Anemic Patients After **Cardiac Valve Replacement**. Am J Cardiol. 2012 Jul 6.

Clement Fiona M.; Klarenbach Scott; Tonelli Marcello; Johnson Jeffrey A.; Manns Braden J. The Impact of Selecting a High Hemoglobin Target Level on Health-Related **Quality of Life** for Patients With Chronic Kidney Disease: A Systematic Review and Meta-analysis. Arch Intern Med. 2009;169(12):1104-1112.
Cody JD, Hodson EM. **Recombinant human erythropoietin versus placebo or no treatment for the anaemia of chronic kidney disease in people not requiring dialysis**. Cochrane Database Syst Rev 2016;(1):CD003266. Treatment with rHuEPO in predialysis patients corrects anaemia, avoids the requirement for blood transfusions and also improves quality of life and exercise capacity.We were unable to assess the effects of rHuEPO on progression of kidney disease, delay in the onset of dialysis or adverse events. Based on the current evidence, decisions on the putative benefits in terms of quality of life are worth the extra costs of predialysis rHuEPO need careful evaluation.
Collister D, Komenda P, Hiebert B, et al. The effect of **erythropoietin-stimulating agents on health-related quality of life** in anemia of chronic kidney disease. Ann Intern Med 2016; doi:10.7326/M15-1839. .
Cooper BA, Branley P, Bulfone L, et al.; the IDEAL Study. A Randomized, Controlled Trial of **Early versus Late Initiation of Dialysis**. N Engl J Med. 2010 Jun 27.
Coritsidis GN, Maglinte GA, Acharya A, et al. Anemia Management Trends in **Hospital-Based Dialysis Centers**(HBDCs), 2010 to 2013. Clin Ther. 2014 Feb 27.
Coyne DW. The health-related **quality of life was not** improved by targeting higher hemoglobin in the **normal hematocrit tria**l. Kidney Int , doi:10.1038/ki.2012.76.
den Elzen, Wendy P.J., Willems, Jorien M., Westendorp, Rudi G.J., et al. Effect of **erythropoietin levels** on mortality in old age: the Leiden 85-plus Study. CMAJ 2010 0: cmaj.100347.
Dharmarajan TS, Widjaja D. Erythropoiesis-stimulating agents in **anemia**. Geriatrics. 2008 Jun;63(6):13-29.
Douros A, Jobski K, Kollhorst B, et al. Risk of **venous thromboembolism in cancer patients treated with epoetins or blood transfusions**(†). Br J Clin Pharmacol. 2016 May 20.
Drüeke TB, Locatelli F, Clyne N, et al. Normalization of haemoglobin level in patients with chronic kidney disease and anemia. N Engl J Med 2006;355:2071-84. (**Choir**)
Drugs in Pregnancy and Lactation. 9th ed. Briggs GE, Freeman RK, Yaffe SJ, editors. Williams and Wilkins; Philadelphia, PA: 2011.
Ehrenreich H, Weissenborn K, Prange H, Schneider D, Weimar C, et al.; for the **EPO Stroke** Trial Group. Recombinant Human Erythropoietin in the Treatment of Acute Ischemic Stroke. Stroke. 2009 Oct 15.
El-Ganzoury MM, Awad HA, El-Farrash RA, et al. Enteral **Granulocyte-Colony Stimulating Factor** and **Erythropoietin** Early in Life Improves **Feeding Tolerance in Preterm Infants**: A Randomized Controlled Trial. J Pediatr. 2014 Aug 22.
Eschbach JW, Egrie JC, Downing MR, Browne JK, Adamson JW. Correction of the anemia of end-stage renal disease with recombinant human erythropoietin: results of a combined phase I and II clinical trial. N Engl J Med **1987**;316:73-78.
Fauchère JC, Koller BM, Tschopp A, et al; Swiss Erythropoietin Neuroprotection Trial Group. Safety of Early High-Dose Recombinant **Erythropoietin for Neuroprotection** in Very Preterm Infants. J Pediatr. 2015 Apr 8.
FDA Feb/10 and Amgen notified healthcare professionals and patients that all ESAs must be used under a REMS risk management program. As part of the risk management program, a Medication Guide explaining the risks and benefits of ESAs must be provided to all patients receiving an ESA. Under the ESA APPRISE Oncology program, Amgen will ensure that only those hospitals and healthcare professionals who have enrolled and completed training in the program will prescribe and dispense ESAs to patients with cancer. Amgen is also required to oversee and monitor the program to ensure that hospitals and healthcare professionals are fully compliant with all aspects of the program. FDA is requiring a REMS because studies show that ESAs can increase the risk of tumor growth and shorten survival in patients with cancer who use these products. Studies also show that ESAs can increase the risk of heart attack, heart failure, stroke or blood clots in patients who use these drugs for other conditions.
FDA June/11 notified healthcare professionals that new, modified recommendations for more conservative dosing of Erythropoiesis-Stimulating Agents (ESAs) in patients with chronic kidney disease (CKD) have been approved to improve the safe use of these drugs. FDA has made these recommendations because of data showing increased risks of cardiovascular events with ESAs in this patient population. The new dosing recommendations are based on clinical trials showing that using **ESAs to target a hemoglobin level of greater than 11 g/dL in patients with CKD provides no additional benefit** than lower target levels, and increases the risk of experiencing serious adverse cardiovascular events, such as heart attack or stroke. http://www.fda.gov/Safety/MedWatch/SafetyInformation/SafetyAlertsforHumanMedicalProducts/ucm260641.htm
FDA: Feb/13 All lots of **peginesatide (Omontys)** — an anemia drug approved less than a year ago for adults on dialysis — are being recalled due to reports of serious and sometimes **fatal adverse hypersensitivity reactions**, including anaphylaxis. Approximately 0.02% of patients had a fatal reaction within 30 minutes of receiving a peginesatide injection, according to postmarketing data. About 0.2% of patients overall had reactions; about a third of these were serious (i.e., requiring immediate medical attention). Some 25,000 patients have received the drug since it was launched, the FDA says.
Ferraris V, Brown J, Despotis G, et al. 2011 Update to The Society of Thoracic Surgeons and the Society of Cardiovascular Anesthesiologists **Blood Conservation Clinical Practice Guidelines**. Ann Thorac Surg 2011; 91:944-82.
Fischer HS, Reibel NJ, Buhrer C, et al. Prophylactic Early **Erythropoietin for Neuroprotection in Preterm Infants**: A Meta-analysis. Pediatrics. 2017;139(5):e20164317
Fontaine C, Cevallos L, Léké A, Krim G, Tourneux P. [Assessment of erythropoietin treatment in **preterm newborns** older than 30 weeks of gestation]. Arch Pediatr. 2009 Apr;16(4):331-6. Epub 2009 Feb 20. This study did not find any benefit using rhEPO in 30 to 32 WG preterm infants in terms of the number of transfusions or hemoglobin levels.
Forbes CA, Worthy G, Harker J, et al. Dose Efficiency of **Erythropoiesis-Stimulating Agents for the Treatment of Patients With Chemotherapy-Induced Anemia**: A Systematic Review. Clin Ther. 2014 Mar 18
Gomollón F, Gisbert JP. Current management of **iron deficiency anemia in inflammatory bowel diseases**: a practical guide. Drugs. 2013 Nov;73(16):1761-70.
Hayden SJ, Albert TJ, Watkins TR, Swenson ER. **Anemia in Critical Illness**: Insights into Etiology, Consequences and Management. Am J Respir Crit Care Med. 2012 Jan 26.
Health Canada May/17: Severe and life-threatening skin reactions including **Stevens-Johnson syndrome and toxic epidermal necrolysis** have been reported in patients treated with **ARANESP** (**darbepoetin alfa**).
Heinze G, Kainz A, Hörl WH, Oberbauer R. **Mortality** in renal transplant recipients given erythropoietins to increase haemoglobin concentration: cohort study. BMJ. 2009 Oct 23;339:b4018. doi: 10.1136/bmj.b4018. Increasing haemoglobin concentrations to above 125 g/l with erythropoietins in renal transplant recipients is associated with an increase in mortality. This increase was significant at concentrations above 140 g/l.
Hershman DL, Buono DL, Malin J, McBride R, Tsai WY, Neugut AI. Patterns of Use and Risks Associated With **Erythropoiesis-Stimulating Agents Among Medicare Patients With Cancer**. J Natl Cancer Inst. 2009 Nov 10. Use of erythropoiesis-stimulating agent increased rapidly after its approval in 1991, but the blood transfusion rate did not change. Use of erythropoiesis-stimulating agents was associated with an increased risk of **venous thromboembolism** but not of mortality.
Heuberger JA, Cohen Tervaert JM, Schepers FM, et ak. Erythropoietin **doping in cycling**: Lack of evidence for efficacy and a negative risk-benefit. Br J Clin Pharmacol. 2012 Dec 6.
Heuberger JA, Cohen AF. **World-class cyclists on EPO**. Br J Clin Pharmacol. 2013 Jun 17.
Himmelfarb J, Ikizler TA. **Hemodialysis**. N Engl J Med. 2010 Nov 4;363(19):1833-45.
Inrig JK, Barnhart HX, Reddan D, et al. Effect of **hemoglobin target on progression of kidney disease**: a secondary analysis of the **CHOIR** (Correction of Hemoglobin and Outcomes in Renal Insufficiency) trial. Am J Kidney Dis. 2012 Sep;60(3):390-401.
Jairath V, Kahan BC, Gray A, et al. **Restrictive versus liberal blood transfusion** for acute upper gastrointestinal bleeding (**TRIGGER**): a pragmatic, open-label, cluster randomised feasibility trial. Lancet 2015; online May 6.
Johansen KL, Finkelstein FO, Revicki DA, Gitlin M, Evans C, Mayne TJ. Systematic Review and Meta-analysis of **Exercise Tolerance and Physical Functioning** in Dialysis Patients Treated With Erythropoiesis-Stimulating Agents. Am J Kidney Dis. 2010 Feb 2.
Jordan J, Breckles J, Leung V, Hopkins M, Battistella M. Conversion from **epoetin alfa to darbepoetin alfa**: effects on patients' hemoglobin and costs to canadian dialysis centres. Can J Hosp Pharm. 2012 Nov;65(6):443-9.
Kansagara D, Dyer E, Englander H, et al. Treatment of **anemia in patients with heart disease**: a systematic review. Ann Intern Med. 2013 Dec 3;159(11):746-57. (ESAs: not seem to benefit pts with mild to mod anemia & heart dx & may be assoc with serous harms)
Katheria AC, Truong G, Cousins L, et al. **Umbilical Cord Milking Versus Delayed Cord Clamping** in Preterm Infants. Pediatrics. 2015 Jun 29.
Kedarisetty CK, Anand L, et al. Combination of **granulocyte colony-stimulating factor and erythropoietin** improves outcomes of patients with decompensated cirrhosis. Gastroenterology. 2015 Jun;148(7):1362-1370.e7.
Kelly AU, McSorley ST, Patel P, et al. Interpreting **iron studies**. BMJ. 2017 Jun 15;357:j2513.
Khuri FR. Weighing the hazards of erythropoiesis stimulation in patients with cancer. N Engl J Med 2007;356:2445-2448.
Kulnigg S, Teischinger L, Dejaco C, Waldhör T, Gasche C. Rapid recurrence of **IBD-associated** anemia and iron deficiency after intravenous iron sucrose and erythropoietin treatment. Am J Gastroenterol. 2009 Jun;104(6):1460-7. Epub 2009 Apr 21.
Lammerich A, Balcke P, Bias P, et al. Cardiovascular Morbidity and **Pure Red Cell Aplasia Associated With Epoetin Theta** Therapy in Patients With Chronic Kidney Disease: A Prospective, Noninterventional, Multicenter Cohort Study. Clin Ther. 2015 Dec 18.
Leuchter RH, Gui L, Poncet A, et al. Association between early administration of high-dose **erythropoietin in preterm infants and brain MRI abnormality** at term-equivalent age. JAMA. 2014 Aug 27;312(8):817-24.
Levey AS, Coresh J. **Chronic kidney disease**. Lancet. 2011 Aug 12.
Levin A, Hemmelgarn B, Culleton B, Tobe S, McFarlane P, Ruzicka M, Burns K, Manns B, White C, Madore F, Moist L, Klarenbach S, Barrett B, Foley R, Jindal K, Senior P, Pannu N, Shurraw S, Akbari A, Cohn A, Reslerova M, Deved V, Mendelssohn D, Nesrallah G, Kappel J, Tonelli M; **Canadian** Society of Nephrology. Guidelines for the management of **chronic kidney disease**. CMAJ. 2008 Nov 18;179(11):1154-62. http://www.cmaj.ca/cgi/data/179/11/1154/DC1/1
Leyland-Jones B, Bondarenko I, Nemsadze G, et al. A Randomized, Open-Label, Multicenter, Phase III Study of **Epoetin Alfa Versus Best Standard of Care** in Anemic Patients With **Metastatic Breast Cancer Receiving Standard Chemotherapy**. J Clin Oncol. 2016 Feb 8.
Lim WH, Chan D, Boudville N, et al. Patients' Perceptions of Subcutaneous Delivery of Darbepoetin Alfa by Autoinjector Prefilled Pen Versus Prefilled Syringe: A Randomized, Crossover Study. Clin Ther. 2012 Aug 15.
Lowe JR, Rieger RE, Moss NC, et al. Impact of Erythropoiesis-Stimulating Agents on **Behavioral Measures in Children Born Preterm**. J Pediatr. 2017 Feb 6.
Macdougall, Iain C., Rossert, Jerome, Casadevall, Nicole, et al. A Peptide-Based Erythropoietin-Receptor Agonist (Hematide) for **Pure Red-Cell Aplasia**. N Engl J Med 2009 361: 1848-1855.
Macdougall IC, White C, Anker SD, et al; **PIVOTAL** Investigators and Committees. **Intravenous Iron sucrose in Patients Undergoing Maintenance Hemodialysis**. N Engl J Med. 2018 Oct 26
McCausland FR, Claggett B, Burdmann EA, et al. Treatment of Anemia With **Darbepoetin Prior to Dialysis Initiation** and Clinical Outcomes: Analyses From the Trial to Reduce Cardiovascular Events With Aranesp Therapy (TREAT). Am J Kidney Dis. 2018 Dec 19.
McFarlane PA, Pisoni RL, Eichleay MA, Wald R, Port FK, Mendelssohn D. **International trends in erythropoietin use** and hemoglobin levels in hemodialysis patients. Kidney Int. 2010 Apr 28.
McMurray JJ, Anand IS, et al.; on behalf of the **RED-HF** Committees and Investigators. Design of the Reduction of Events with Darbepoetin alfa in **Heart Failure** (RED-HF): a Phase III, anaemia correction, morbidity-mortality trial. Eur J Heart Fail. 2009 Aug;11(8):795-801.
Michels WM, Jaar BG, Ephraim PL, et al; **DEcIDE** Network Patient Outcomes in End Stage Renal Disease Study Investigators. **Intravenous iron administration strategies** and anemia management in hemodialysis patients. Nephrol Dial Transplant. 2016 Sep 6.

Miller G, Luo R, Zhang L, et al. Effectiveness of provider incentives for anaemia reduction in rural China: a cluster randomised trial. BMJ. 2012 Jul 27;345:e4809.
Moe SM, Chertow GM, Parfrey PS, et al; Evaluation of **Cinacalcet** HCl Therapy to Lower Cardiovascular Events (**EVOLVE**) Trial Investigators*. Cinacalcet, Fibroblast Growth Factor-23, and Cardiovascular Disease in Hemodialysis: The Evaluation of Cinacalcet HCl Therapy to Lower Cardiovascular Events (EVOLVE) Trial. Circulation. 2015 Jul 7;132(1):27-39.

Moist LM, Foley RN, Barrett BJ, Madore F, White CT, Klarenbach SW, Culleton BF, Tonelli M, Manns BJ; **Canadian** Society of Nephrology. Clinical practice guidelines for evidence-based use of erythropoietic-stimulating agents. Kidney Int Suppl. 2008 Aug;(110):S12-8.
Moist LM, Troyanov S, White CT, Wazny LD, Wilson JA, McFarlane P, Harwood L, Sood MM, Soroka SD, Bass A, Manns BJ. **Canadian Society of Nephrology** Commentary on the **2012 KDIGO** Clinical Practice Guideline for **Anemia in CKD**. Am J Kidney Dis. 2013 Sep 17.
Muirhead N, Keown PA, Churchill DN, et al. Dialysis patients treated with Epoetin α show **improved exercise tolerance and physical function**: A new analysis of the Canadian Erythropoietin Study Group trial. Hemodial Int. 2010 Dec 7. doi: 10.1111/j.1542-4758.2010.00508.x.
Najjar SS, Rao SV, Melloni C, et al. **REVEAL** Investigators. Intravenous **erythropoietin** in patients with **ST-segment elevation myocardial infarction** (STEMI): REVEAL: a randomized controlled trial. JAMA. 2011 May 11;305(18):1863-72.
Natalucci G, Latal B, et al; Swiss EPO Neuroprotection Trial Group. Effect of Early Prophylactic **High-Dose Recombinant Human Erythropoietin in Very Preterm Infants on Neurodevelopmental Outcome** at 2 Years: A Randomized Clinical Trial. JAMA. 2016 May 17;315(19):2079-85.
National Institute for Health and Clinical Excellence (**NICE**). Epoetin alfa, epoetin beta and darbepoetin alfa for cancer treatment-induced anaemia [Internet]. London (UK): NICE; 2008 May. (Technology appraisal guidance; no. 142). [cited 2009 Nov 23]. Available from: http://www.nice.org.uk/nicemedia/pdf/TA142Guidance.pdf
Ngo K, Kotecha D, Walters JA, Manzano L, Palazzuoli A, van Veldhuisen DJ, Flather M. Erythropoiesis-stimulating agents for anaemia in **chronic heart failure** patients. Cochrane Database Syst Rev. 2010 Jan 20;(1):CD007613.
NICE: Clinical Guideline 114- Feb 2011. **Anaemia management** in people with chronic kidney disease. http://www.nice.org.uk/nicemedia/live/13329/52857/52857.pdf
NICE: National Clinical Guideline Centre. **Anaemia management** in people with chronic kidney disease. London (UK): National Institute for Health and Care Excellence (NICE); **2015** Jun 3.
Nichol A, French C, Little L, et al, for the **EPO-TBI** Investigators and the ANZICS Clinical Trials Group. **Erythropoietin in traumatic brain injury** (EPO-TBI): a double-blind randomised controlled trial. Lancet 2015; online Oct 7
Ohls RK, Christensen RD, Kamath-Rayne BD, et al. A Randomized, Masked, Placebo-Controlled Study of **Darbepoetin Alfa in Preterm Infants**. Pediatrics. 2013 Jun 17.
Ohls RK, Kamath-Rayne BD, Christensen RD, et al. **Cognitive Outcomes of Preterm Infants Randomized to Darbepoetin, Erythropoietin**, or Placebo. Pediatrics. 2014 May 12.
Ohls RK, Cannon DC, Phillips J, et al. Preschool Assessment of **Preterm Infants Treated** With **Darbepoetin** and **Erythropoietin**. Pediatrics. 2016 Feb 15.
Palmer Suetonia C., Navaneethan Sankar D., Craig Jonathan C., Et al. Systematic Review: **Erythropoiesis-Stimulating Agents** in Patients With Chronic Kidney Disease. *Ann Intern Med* published ahead of print May 3, 2010, doi:10.1059/0003-4819-153-1-201007060-00252.
Palmer SC, Navaneethan SD, Craig JC, et al. Meta-analysis: **erythropoiesis-stimulating agents** in patients with chronic kidney disease. Ann Intern Med. 2010 Jul 6;153(1):23-33.
Pérez-Ruixo JJ, Cucala-Ramos M, García-Gonzalo E, et al. Between-subjects **hemoglobin variability** is not associated with the erythropoiesis-stimulating agent used to treat anemia in dialysis: a meta-analysis. Br J Clin Pharmacol. 2012 Jul 16.
Pfeffer, Marc A., Burdmann, Emmanuel A., Chen, Chao-Yin, et al. the **TREAT** Investigators, A Trial of Darbepoetin Alfa in Type 2 Diabetes and Chronic Kidney Disease. N Engl J Med 2009 0: NEJMoa0907845.
Phrommintikul A, Haas SJ, Elsik M, Krum H. **Mortality** and target haemoglobin concentrations in anaemic patients with chronic kidney disease treated with erythropoietin: a meta-analysis. Lancet 2007;369:381-388.
Pirker R, Hedenus M, Vansteenkiste J, et al. Effectiveness of **Darbepoetin** Alfa for Chemotherapy-Induced Anemia When Initiated at Hemoglobin ≤10 g/dL. Clin Ther. 2015 Dec 22.
Pirkle JL Jr, Paoli CJ, Russell G, et al. Hemoglobin Stability and Patient Compliance With **Darbepoetin Alfa in Peritoneal Dialysis** Patients After the Implementation of the Prospective Payment System. Clin Ther. 2014 Sep 22.
Qaseem A, Humphrey LL, Fitterman N, et al. Treatment of **anemia in patients with heart disease**: a clinical practice guideline from the american college of physicians. Ann Intern Med. 2013 Dec 3;159(11):770-9.
Rizzo JD, Somerfield MR, Hagerty KL, et al.; **American** Society of Clinical Oncology **(ASCO)**; American Society of Hematology. Use of epoetin and darbepoetin in patients with **cancer**: 2007 American Society of Clinical Oncology/American Society of Hematology clinical practice guideline update. J Clin Oncol. **2008** Jan 1;26(1):132-49. Epub 2007 Oct 22. Erratum in: J Clin Oncol. 2008 Mar 1;26(7):1192.
Rizzo JD, Brouwers M, Hurley P, et al. **American** Society of Clinical Oncology **(ASCO)** / American Society of Hematology Clinical Practice Guideline Update on the Use of **Epoetin and Darbepoetin in Adult Patients With Cancer**. *JCO* JCO.2010.29.2201; online on Oct 25, **2010**. http://jco.ascopubs.org/content/early/2010/10/25/JCO.2010.29.2201.full.pdf+html
Robertson CS, Hannay HJ, Yamal JM, et al. Effect of **erythropoietin and transfusion threshold** on neurological **recovery after traumatic brain injury**: a randomized clinical trial. JAMA. 2014 Jul 2;312(1):36-47.
Saglimbene VM;Palmer SC;Ruospo M;et al. Continuous **erythropoiesis** receptor activator (CERA) for the **anaemia** of chronic kidney disease. Cochrane Database Syst Rev. 2017 Aug 7;8:CD009904. There is low certainty evidence that CERA has little or no effects on patient-centred outcomes compared with placebo, epoetin alfa or beta or darbepoetin alfa for adults with CKD. The effects of CERA among children who have CKD have not studied in RCTs.
Singh AK, Szczech L, Tang KL, et al. Correction of **anemia** with epoetin alfa in chronic kidney disease. N Engl J Med 2006; 355:2085-98.
Singh AK, Himmelfarb J, Szczech LA. Resolved: targeting a **higher hemoglobin** is associated with greater risk in patients with CKD anemia. J Am Soc Nephrol 2009;20:1436-1443.
Skali H, Parving HH, Parfrey PS, et al. **Stroke** in patients with type 2 diabetes mellitus, chronic kidney disease, and anemia treated with **darboetin alfa**: the Trial to Reduce Cardiovascular Events With Aranesp Therapy (**TREAT**) experience. Circulation. 2011;124:2903–2908.
Solomon Scott D, Lewis Eldrin F., Eckardt Kai-Uwe, et al. for the Trial to Reduce Cardiovascular Events with Aranesp Therapy (**TREAT**) Investigators. Erythropoietic Response and Outcomes in Kidney Disease and Type 2 Diabetes. N Engl J Med 2010; 363:1146-1155.
Song J, Sun H, Xu F, et al. **Recombinant human erythropoietin improves neurological outcomes in very preterm infants**. Ann Neurol. 2016 Apr 30
Steensma DP, Sloan JA, Dakhil SR, et al. Phase III, Randomized Study of the Effects of **Parenteral Iron, Oral Iron, or No Iron** Supplementation on the Erythropoietic Response to **Darbepoetin** Alfa for Patients With Chemotherapy-Associated Anemia. J Clin Oncol. 2010 Nov.
Sühs K, Hein K, Sättler M. A randomized, double-blind, phase II study on erythropoietin in **optic neuritis**. Annals of Neurology Accepted manuscript online: 28 FEB 2012.
Swedberg K et al. Treatment of anemia with **darbepoetin** alfa in systolic heart failure. (**RED-HF**) N Engl J Med 2013 Mar 10.
Tehrani F, Dhesi P, Daneshvar D, Phan A, Rafique A, Siegel RJ, Cercek B. Erythropoiesis Stimulating Agents in **Heart Failure** Patients with Anemia: A Meta-Analysis. Cardiovasc Drugs Ther. 2009 Oct 28.
Tseng KC, Chen LH, Chen CY, et al. Low dose erythropoietin-beta improves anemia and maintains ribavirin dose in chronic **hepatitis C** patients receiving combination therapy with ribavirin plus pegylated interferon Alfa-2b.Hepatol Res. 2009 Feb 25. [Epub ahead of print]
Tonelli M, Lloyd A, Lee H, et al. Erythropoiesis-stimulating agents for **anemia of cancer or of chemotherapy**: systematic review and economic evaluation [Technology report number 119]. Ottawa: Canadian Agency for Drugs and Technologies in Health; 2009.
Umanath K, Jalal DI, Greco BA, et al; for the Collaborative Study Group. **Ferric Citrate** Reduces Intravenous Iron and Erythropoiesis-Stimulating Agent Use in ESRD. J Am Soc Nephrol. 2015 Mar 3.
Van der Meer P, Groenveld H, Januzzi JL, Van Veldhuisen DJ. Erythropoietin Treatment in Patients with Chronic **Heart Failure**: a meta-analysis. Heart. 2009 Jan 23. [Epub ahead of print]
van der Putten K, Braam B, Gaillard CA. Epoetin alfa in **critically ill** patients. N Engl J Med. 2007 Dec 13;357(24):2515-6
Vanrenterghem Y. Anemia after **kidney transplantation**. Transplantation. 2009 May 15;87(9):1265-7.
van Veldhuisen DJ, Ponikowski P, van der Meer P, et al; EFFECT-HF Investigators . Effect of **Ferric Carboxymaltose** on Exercise Capacity in Patients with **Chronic Heart Failure** and Iron Deficiency. Circulation. 2017 Jul 12.
Voors AA, Belonje AM, Zijlstra F, et al. A single dose of erythropoietin in **ST-elevation myocardial infarction**. Eur Heart J 2010; DOI:10.1093/eurheartj/ehq304.
Webster AC, Nagler EV, Morton RL, et al. **Chronic Kidney Disease**. Lancet.2016 Nov 22.
Weiner Daniel E. , Miskulin Dana C. Anemia Management in Chronic Kidney Disease: **Bursting the Hemoglobin Bubble**. Ann Intern Med published ahead of print May 3, 2010.
Winearls CG, Oliver DO, Pippard MJ, Reid C, Downing MR, Cotes PM. Effect of human erythropoietin derived from recombinant DNA on the anaemia of patients maintained by chronic haemodialysis. Lancet **1986**;2:1175-1178.
Wang C, Kane R, Levenson M, et al. Association Between Changes in CMS Reimbursement Policy and Drug Labels for **Erythrocyte-Stimulating Agents** With Outcomes for Older Patients Undergoing **Hemodialysis** Covered by Fee-for-Service Medicare. JAMA Intern Med. 2016 Oct 24.
Wu YW, Bauer LA, Ballard RA, et al. **Erythropoietin for Neuroprotection** in Neonatal Encephalopathy: Safety and Pharmacokinetics. Pediatrics. 2012 Sep 24.
Wu YW, Mathur AM, Chang T, et al. **High-Dose Erythropoietin** and Hypothermia for Hypoxic-Ischemic **Encephalopathy**: A Phase II Trial. Pediatrics. 2016 Jun;137(6).
Zhang Y, Thamer M, Kaufman JS et al. **High doses of epoetin** do not lower mortality and cardiovascular risk among elderly **hemodialysis patients with diabetes**. Kidney Int 2011;80:663 – 669.

Extras for Iron Management:

New FDA:

Ferric carboxymaltose Injectafer for IDA if poor response to oral/**ND-CKD**, 750mg/15ml IV x 2 doses 1 week apart;. SE: nausea, dizzy, hypertension hypophosphatemia, anaphylaxis.
Ferric pyrophosphate citrate Triferic for iron replacement with CKD & on dialysis (27.2mg of iron may be added directly to hemodialysis solution in adults); SE: HA, edema, UTI, hypersensitivity rxn.
Ferric citrate **Auryxia** 1g [210mg ferric iron] tabs, 2-4 tabs TID cc, ↓phosphate in pts on dialysis; AE: N/V/D, fecal discoloration, concern iron overload; DI: alenderonate,Cipro,doxycycline,levothyroxine,Vit D. May ↑iron & ↓ESA [in ESRD].
Ferric maltol **Accrufer** oral for iron defiiencey in adutls, 30 mg twice daily, taken 1 hour before or 2 hours after a meal.

Oct/11 The FDA has granted accelerated approval for **deferiprone (Ferriprox)** to treat transfusion-related iron overload in patients with thalassemia who do not respond to prior chelation therapy. The drug, an oral iron chelator, is the first new treatment approved for this disorder since 2005, according to the agency. Agranulocytosis was noted in about 2% of patients in clinical studies. Other adverse effects included nausea, arthralgia, vomiting, neutropenia, and increased alanine aminotransferase levels.

References: Iron Management: Chronic Kidney Disease – Iron Deficiency Anemia (CKD-IDA)

1. Best Practice Guidelines for Management of Renal Anaemia. *Indian J Nephrol* 2005;15(Suppl 1):S32-S41. Available: http://medind.nic.in/iav/t05/s1/iavt05s1p32.pdf (accessed 2009 Feb 18).
2. Comparison of Oral Iron Supplements. Pharmacist's Letter/Prescriber's Letter 2008 ;24(8):240811.
3. Coyne DW, Kapoian T, Suki W, Singh AK, Moran JE, Dahl NV, et al. Ferric Gluconate is Highly Efficacious in Anemic Hemodialysis Patients with High Serum Ferritin and Low Transferrin Saturation: Results of the Dialysis Patients' Response to IV Iron with Elevated Ferritin (DRIVE) Study. *J Am Soc Nephrol* 2007;18:975-984.
4. Coyne DW, Singh AK, Kapoian T, Pizzi LT. A road map for intravenous iron and anemia management: Preparing for the future. *Am J Kidney Dis* 2008;52(6):S1-S33.
5. Drugdex Drug Evaluations - Micromedex 2010, Iron. Dec 2002.
6. e-CPS [database on the Internet]. Ottawa (ON): Canadian Pharmacists Association. c2009 - [cited 2009 Feb 22]. Infufer [product monograph]. Available from: https://www.e-therapeutics.ca/wps/portal/!ut/p/.scr/Login.
7. e-CPS [database on the Internet]. Ottawa (ON): Canadian Pharmacists Association. c2009 - [cited 2009 Feb 22]. Venofer [product monograph]. Available from: https://www.e-therapeutics.ca/wps/portal/!ut/p/.scr/Login.
8. Ferrlecit product monograph. Toronto (ON): Janssen-Ortho Inc. Available from: www.janssen-ortho.com/JOI/pdf_files/FERRLECIT_E.pdf.
9. Hunt J, Roughead Z. Adaptation of iron absorption in men consuming diets with high or low iron bioavailability. *Am J Clin Nutr* 2000;71:94-102.
10. Killip S, Bennett J, Chambers M. Iron deficiency anemia. *Am Fam Physician* 2007;75:671-8.
11. Madore F, White CT, Folet RN, Barrett BJ, Moist LM, Klarenbach SW, et al. **Canadian** Clinical Practice Guidelines for assessment and management of iron deficiency. *Kidney Int* 2008;74(Suppl 110):S7-S11.
    National Kidney Foundation. **KDOQI** clinical practice guidelines and clinical practice recommendations for anemia in chronic kidney disease. *Am J Kidney Dis* 2006;47(5 Suppl 3):S1-S145. Available from: http://www.kidney.org/professionals/KDOQI/guidelines_anemia/pdf/AnemiaInCKD.pdf.
    KDOQI clinical practice guidelines and clinical practice recommendations for anemia in chronic kidney disease: 2007 update of hemoglobin target; 2007 Sep
12. White CT, Barrett BJ, Madore F, Moist LM, Klarenbach SW, Foley RN, et al. Clinical Practice Guidelines for evaluation of anemia. *Kidney Int* 2008;74(Suppl 110):S4-S6.
13. Anemia Guidelines for Family Medicine; Anemia Review Panel, 2008 Edition.
14. Weiss G, Goodnough LT. Anemia of chronic disease. NEJM 2005; 352:1011-23.
16. American College of Obstetricians and Gynecologists (ACOG). Anemia in pregnancy. Washington (DC): American College of Obstetricians and Gynecologists (ACOG); 2008 Jul. 7 p. (ACOG practice bulletin; no. 95).
17. Singh A, Patel T, Hertel J, Bernardo M, Kausz A, Brenner L. Safety of ferumoxytol in patients with anemia and CKD. Am J Kidney Dis. 2008 Nov;52(5):907-15. Epub 2008 Sep 27.
18. Levin A, Hemmelgarn B, Culleton B, Tobe S, McFarlane P, Ruzicka M, Burns K, Manns B, White C, Madore F, Moist L, Klarenbach S, Barrett B, Foley R, Jindal K, Senior P, Pannu N, Shurraw S, Akbari A, Cohn A, Reslerova M, Deved V, Mendelssohn D, Nesrallah G, Kappel J, Tonelli M; Canadian Society of Nephrology. Guidelines for the management of chronic kidney disease. CMAJ. 2008 Nov 18;179(11):1154-62. http://www.cmaj.ca/cgi/data/179/11/1154/DC1/1
19. Crowe E, Halpin D, Stevens P; Guideline Development Group. Early identification and management of chronic kidney disease: summary of NICE guidance. BMJ. 2008 Sep 29;337:a1530. doi: 10.1136/bmj.a1530.
20. Reveiz L, Gyte GM, Cuervo LG. Treatments for iron-deficiency **anaemia in pregnancy**. Cochrane Database Syst Rev. 2007 Apr 18;(2):CD003094.
21. Auerbach M, Rodgers GM. Intravenous iron. N Engl J Med. 2007 Jul 5;357(1):93-4.
22. Killip S, Bennett JM, Chambers MD. Iron deficiency anemia. Am Fam Physician. 2007 Mar 1;75(5):671-8.
23. Uprichard James, Bain Barbara J. Investigating suspected anaemia. BMJ 2009;338:b1644, doi: 10.1136/bmj.b1644 (Published 22 May 2009)
24. Kulnigg S, et al. Rapid recurrence of **IBD-associated** anemia and iron deficiency after intravenous iron sucrose and erythropoietin treatment. Am J Gastroenterol. 2009 Jun;104(6):1460-7. Epub 2009 Apr 21.
25. den Elzen WP, Willems JM, et al. Effect of anemia and comorbidity on functional status and **mortality in old age**: results from the Leiden 85-plus Study. CMAJ. 2009 Aug 4;181(3-4):151-7. Epub 2009 Jul 27.
26. Pfeffer, Marc A., Burdmann, Emmanuel A., Chen, Chao-Yin, et al. the **TREAT** Investigators, A Trial of Darbepoetin Alfa in Type 2 Diabetes and Chronic Kidney Disease. N Engl J Med 2009 0: NEJMoa0907845.
27. Vanrenterghem Y. Anemia after kidney transplantation. Transplantation. 2009 May 15;87(9):1265-7.
28. Anker SD, Comin Colet J, Filippatos G, et al. the **FAIR-HF** Trial Investigators. **Ferric Carboxymaltose** in Patients with **Heart Failure** and Iron Deficiency. N Engl J Med. 2009 Nov 17. Treatment with intravenous ferric carboxymaltose (200mg IV weekly until iron stores repleted then q4wks up to week 24, n=459) in patients with chronic heart failure and iron deficiency, with or without anemia, improves symptoms, functional capacity, and quality of life; the side-effect profile is acceptable.
29. Okonko DO, Grzeslo A, Witkowski T, et al. Effect of intravenous iron sucrose on exercise tolerance in anemic and nonanemic patients with symptomatic chronic heart failure and iron deficiency **FERRIC-HF**: a randomized, controlled, observer-blinded trial. J Am Coll Cardiol. 2008 Jan 15;51(2):103-12. (n=35)
30. Deved V, Poyah P, James MT, Tonelli M, Manns BJ, Walsh M, Hemmelgarn BR; Alberta Kidney Disease Network. Ascorbic Acid for Anemia Management in Hemodialysis Patients: A Systematic Review and Meta-analysis. Am J Kidney Dis. 2009 Sep 22.
31. Chandler G, Harchowal J, Macdougall IC. Intravenous **iron sucrose**: establishing a safe dose. Am J Kidney Dis. 2001 Nov;38(5):988-91.
32. Parker MJ. Iron supplementation for anemia after **hip fracture surgery**: a randomized trial of 300 patients. J Bone Joint Surg Am. 2010 Feb;92(2):265-9.
    Patients treated with iron for anemia after hip fracture surgery have no clinically meaningful differences in hemoglobin response or outcomes compared with patients not treated with iron.
33. Zehetner AA, Orr N, Buckmaster A, Williams K, Wheeler DM. Iron supplementation for **breath-holding attacks** in children. Cochrane Database Syst Rev. 2010 May 12;5:CD008132. Iron supplementation (at 5 mg/kg/day of elemental iron for 16 weeks) appears to be useful in reducing the frequency and severity of breath-holding attacks.
34. Bross MH, Soch K, Smith-Knuppel T. **Anemia in older persons**. Am Fam Physician. 2010 Sep 1;82(5):480-7.
35. Hajjar LA, Vincent JL, Galas FR, et al. **Transfusion requirements** after **cardiac surgery**: the **TRACS** randomized controlled trial. JAMA. 2010 Oct 13;304(14):1559-67.
36. Van Vranken Michele. Evaluation of **Microcytosis**. Am Fam Physician. 2010 Nov 1;82(9):1117-1122.
37. Himmelfarb J, Ikizler TA. **Hemodialysis**. N Engl J Med. 2010 Nov 4;363(19):1833-45.
38. Berglund S, Westrup B, Domellof M. Iron supplements reduce the risk of iron deficiency anemia in **marginally low birth weight infants**. Pediatrics. 2010 Oct;126(4):e874-83.

39. Baker RD, Greer FR, Committee on Nutrition, Clinical Report--Diagnosis and Prevention of Iron Deficiency and **Iron-Deficiency Anemia in Infants and Young Children (0-3 Years of Age)**. Pediatrics 2010 0: peds.2010-2576.
40. Steensma DP, Sloan JA, Dakhil SR, et al. Phase III, Randomized Study of the Effects of **Parenteral Iron, Oral Iron, or No Iron** Supplementation on the Erythropoietic Response to **Darbepoetin** Alfa for Patients With Chemotherapy-Associated Anemia. J Clin Oncol. 2010 Nov.
41. Chi AC, Neville BW, Krayer JW, Gonsalves WC. **Oral manifestations** of systemic disease. Am Fam Physician. 2010 Dec 1;82(11):1381-8.
42. Christian P, Murray-Kolb LE., Khatry SK., et al. **Prenatal Micronutrient Supplementation (iron/folic)** and Intellectual and Motor Function in Early School-aged Children in Nepal. JAMA. 2010;304(24):2716-723.
43. Rimon E, Kagansky N, Kagansky M, et al. Are we giving too much iron? **Low-dose iron therapy is effective in octogenarians**. *Am J Med* 2005;118:1142-7.
    Lindblad AJ, Cotton C, Allan GM. **Iron deficiency anemia in the elderly**. Can Fam Physician. 2015 Feb;61(2):159.
    Lanier JB, Park JJ, Callahan C. **Anemia in Older Adults**. Am Fam Physician. 2018;98(7):437-442.

44. Walsh TS, Wyncoll DL, Stanworth SJ. Managing **anaemia in critically ill** adults. BMJ. 2010 Sep 3;341:c4408. doi: 10.1136/bmj.c4408.
45. Coppol E, Shelly J, Cheng S, et al. A Comparative Look at the Safety Profiles of **Intravenous Iron Products Used in the Hemodialysis** Population. 1 Feb 2011, DOI 10.1345/aph.1P466. Ann Pharmacother ;45:241-247.
46. Daoud E, Nakhla E, Sharma R. Q: Is **iron therapy for anemia harmful in the setting of infection**? Cleveland Clinic Journal of Medicine 2011; 78(3):168-170; doi:10.3949/ccjm.78a.10156
47. Ferraris V, Brown J, Despotis G, et al. 2011 Update to The Society of Thoracic Surgeons and the Society of Cardiovascular Anesthesiologists **Blood Conservation** Clinical Practice Guidelines. Ann Thorac Surg 2011; 91:944-82.
48. **NICE**: Clinical Guideline 114- Feb 2011. Anaemia management in people with chronic kidney disease. http://www.nice.org.uk/nicemedia/live/13329/52857/52857.pdf
49. Lachance K, Savoie M, Bernard M, et al. **Oral Ferrous Sulfate** Does Not Increase Preoperative Hemoglobin in Patients **Scheduled for Hip or Knee Arthroplasty**. 1 June 2011. Ann Pharmacother ;45:764-770.
50. Salisbury AC, Reid KJ, Alexander KP, et al. Diagnostic Blood Loss From **Phlebotomy and Hospital-Acquired Anemia** During Acute Myocardial Infarction. Arch Intern Med. 2011 Aug 8.
51. Levey AS, Coresh J. **Chronic kidney disease**. Lancet. 2011 Aug 12.
52. Musallam KM, Tamim HM, Richards T, et al. **Preoperative anaemia and postoperative outcomes** in non-cardiac surgery: a retrospective cohort study. Lancet 2011; published online Oct 6.
53. Krayenbuehl P-A et al. **Intravenous iron for the treatment of fatigue in nonanemic, premenopausal women** with low serum ferritin concentration. Blood 2011 Sep 22; 118:3222.
54. Andersson O, Hellström-Westas L, Andersson D, Domellöf M. Effect of **delayed versus early umbilical cord clamping** on neonatal outcomes and iron status at 4 months: a randomised controlled trial. BMJ 2011;343:d7156.
55. Drugs in Pregnancy and Lactation. 9th ed. Briggs GE, Freeman RK, Yaffe SJ, editors. Williams and Wilkins; Philadelphia, PA: 2011.
56. Lozoff B et al. Iron-fortified vs low-**iron infant formula: Developmental outcome at 10 years**. Arch Pediatr Adolesc Med2011 Nov 7; [e-pub ahead of print],
57. Carson JL, Terrin ML, Noveck H, et al. **Liberal or restrictive transfusion** in high-risk patients after **hip surgery**. (**Focus**) N Engl J Med 2011. DOI: 10.1056/NEJMoa1012452.
58. De-Regil LM, Jefferds ME, Sylvetsky AC, et al. **Intermittent iron** supplementation for improving nutrition and development in children under 12 years of age. Cochrane Database Syst Rev. 2011 Dec 7;12:CD009085.
    Intermittent iron supplementation is efficacious to improve haemoglobin concentrations and reduce the risk of having anaemia or iron deficiency in children younger than 12 years of age when compared with a placebo or no intervention, but it is less effective than daily supplementation to prevent or control anaemia.
59. Balarajan Y, Ramakrishnan U, Ozaltin E, Shankar AH, Subramanian S. **Anaemia in low-income and middle-income countries**. Lancet. 2011 Aug 1.
60. Carson JL, Grossman BJ, Kleinman S, et al., for the Clinical Transfusion Medicine Committee of the AABB. **Red Blood Cell Transfusion**: A Clinical Practice Guideline From the AABB. Ann Intern Med ahead of print Mar 26,12.
61. Hayden SJ, Albert TJ, Watkins TR, Swenson ER. **Anemia in Critical Illness**: Insights into Etiology, Consequences and Management. Am J Respir Crit Care Med. 2012 Jan 26.
62. Müller KF, Lorenz L, Poets CF, et al **Hepcidin** Concentrations in Serum and Urine Correlate with Iron Homeostasis in Preterm Infants. J Pediatr. 2012 Jan 26.
63. Pattakos G, Koch CG, Brizzio ME, et al. Outcome of patients who **refuse transfusion {Jehovah's Witness** patients (Witnesses)} after cardiac surgery. A natural experiment with severe blood conservation. Arch Intern Med 2012
64. Pena-Rosas JP, De-Regil LM, Dowswell T, et al. **Intermittent oral iron supplementation during pregnancy**. Cochrane Database Syst Rev. 2012 Jul 11;7:CD009997. The present systematic review is the most comprehensive summary of the evidence assessing the benefits and harms of intermittent iron supplementation regimens in pregnant women on haematological and pregnancy outcomes. The findings suggest that intermittent iron+folic acid regimens produce similar maternal and infant outcomes at birth as daily supplementation but are associated with fewer side effects. Women receiving daily supplements had increased risk of developing high levels of Hb in mid and late pregnancy but were less likely to present mild anaemia near term.
    Peña-Rosas JP, De-Regil LM, Dowswell T, Viteri FE. **Daily oral iron supplementation during pregnancy**. Cochrane Database of Systematic Reviews 2012, Issue 12. Art. No.: CD004736. DOI: 10.1002/14651858.CD004736.pub4. Prenatal supplementation with daily iron are effective to reduce the risk of low birthweight, and to prevent maternal anaemia and iron deficiency in pregnancy. Associated maternal side effects and particularly high Hb concentrations during pregnancy at currently used doses suggest the need to update recommendations on doses and regimens for routine iron supplementation.
    Sultan P, Bampoe S, Shah R, et al. Oral vs intravenous iron therapy for postpartum anemia: a systematic review and meta-analysis. Am J Obstet Gynecol. 2019 Jul;221(1):19-29.e3.

65. Liles AM. Intravenous versus oral iron for treatment of iron deficiency in non-hemodialysis-dependent patients with chronic kidney disease. Am J Health Syst Pharm. 2012 Jul 15;69(14):1206-11.
66. Rabe H, Diaz-Rossello JL, Duley L, et al. Effect of timing of **umbilical cord clamping** and other strategies to influence placental transfusion at preterm birth on maternal and infant outcomes. Cochrane Database Syst Rev. 2012 Aug 15;8:CD003248. Providing additional placental blood to the preterm baby by either delaying cord clamping for 30 to 120 seconds, rather than early clamping, seems to be associated with less need for transfusion, better circulatory stability, less intraventricular haemorrhage (all grades) and lower risk for necrotising enterocolitis.
67. Vaucher P, Druais PL, Waldvogel S, Favrat B. Effect of iron supplementation on **fatigue in nonanemic menstruating women** with low ferritin: a randomized controlled trial. CMAJ. 2012 Jul 9.
68. Konrad G, Katz A. Are medication restrictions before **FOBT** necessary?:Practical advice based on a systematic review of the literature. Can Fam Physician. 2012 Sep;58(9):939-48.
69. Ranucci M, Di Dedda U, Castelvecchio S, et al. Impact of **preoperative anemia** on outcome in adult cardiac surgery: A propensity-matched analysis. Ann Thorac Surg 2012; 94:1134-1141.
70. Atsma F, Veldhuizen I, de Kort W, et al. Hemoglobin level is positively associated with **blood pressure** in a large cohort of healthy individuals. Hypertension. 2012 Oct;60(4):936-41.
71. Berglund SK, Westrup B, Hägglöf B, et al. Effects of Iron Supplementation of **LBW Infants on Cognition** and Behavior at 3 Years. Pediatrics. 2013 Jan;131(1):47-55.
72. Short MW, Domagalski JE. **Iron Deficiency Anemia**: Evaluation and Management. Am Fam Physician. 2013;87(2):98-104.
73. Chang S, Zeng L, Brouwer ID, et al. Effect of **Iron Deficiency Anemia in Pregnancy** on Child Mental Development in Rural China. Pediatrics. 2013 Feb 11.
74. Khuong-Quang DA, Schwartzentruber J, Westerman M, et al. **Iron refractory iron deficiency anemia**: presentation with hyperferritinemia and response to oral iron therapy. Pediatrics. 2013 Feb;131(2):e620-5.
75. Taylor T, Kennedy K. Randomized trial comparing **iron supplementation versus routine intake in very low birth weight infants**. Pediatrics. 2013;131(2) .
76. Thompson J, Biggs BA, Pasricha SR. Effects of **Daily Iron Supplementation in 2- to 5-Year-Old Children**: Systematic Review and Meta-analysis. Pediatrics. 2013 Mar 11. In 2 to 5 year olds, daily iron supplementation increases hemoglobin and ferritin. There is a concerning lack of data on the effect of iron supplementation on clinically important outcomes including anemia, ID anemia, ID, and cognitive development.
77. Peña-Rosas JP, De-Regil LM, Dowswell T, Viteri FE. **Daily oral iron supplementation during pregnancy**. Cochrane Database of Systematic Reviews 2012, Issue 12. Art. No.: CD004736. DOI: 10.1002/14651858.CD004736.pub4. Prenatal supplementation with daily iron are effective to reduce the risk of low birthweight, and to prevent maternal anaemia and iron deficiency in pregnancy. Associated maternal side effects and particularly high Hb concentrations during pregnancy at currently used doses suggest the need to update recommendations on doses and regimens for routine iron supplementation.
78. Maguire JL, Salehi L, Birken CS, et al. Association Between Total Duration of **Breastfeeding and Iron Deficiency**. Pediatrics. 2013 Apr 15.
79. Uprichard WO, Uprichard J. **Investigating microcytic anaemia**. BMJ. 2013 Jun 7;346:f3154.
80. Pichler I, Del Greco M F, Gögele M, International Parkinson's Disease Genomics Consortium; et al. Serum **iron levels** and the risk of Parkinson disease: a mendelian randomization study. PLoS Med. 2013 Jun;10(6):e1001462.
81. Haider BA, Olofin I, Wang M, Spiegelman D, Ezzati M, Fawzi WW. Anaemia, **prenatal iron use**, and risk of adverse pregnancy outcomes: systematic review and meta-analysis. BMJ 2013;346:f3443.
82. Brookhart MA, Freburger JK, Ellis AR, et al. A comparison of intravenous **iron supplementation** strategies and **infection risk** in hemodialysis patients. J Am Soc Nephrol. 24: XXX–XXX, 2013.
    Tomer A, Amir B, Alon G, et al. The **Safety of Intravenous Iron Preparations**: Systematic Review and Meta-analysis. Mayo Clin Proc. 2015 Jan;90(1):12-23.
83. Murray MJ, Murray AB, Murray MB, Murray CJ. The adverse effect of iron repletion on the course of certain **infections**. Br Med J. 1978 Oct 21;2(6145):1113-5.
84. McDonald SJ, Middleton P, Dowswell T, et al. Effect of **timing of umbilical cord clamping** of term infants on maternal and neonatal outcomes. Cochrane Database of Systematic Reviews 2013, Issue 7. Art. No.: CD004074.

DOI: 10.1002/14651858.CD004074.pub3. A more liberal approach to delaying clamping of the umbilical cord in healthy term infants appears to be warranted, particularly in light of growing evidence that delayed cord clamping increases early haemoglobin concentrations and iron stores in infants. Delayed cord clamping is likely to be beneficial as long as access to treatment for jaundice requiring phototherapy is available.
85. Hong CH, Falvey C, Harris TB, et al. Anemia and **risk of dementia** in older adults: Findings from the Health ABC study. Neurology. 2013 Aug 6;81(6):528-533.
86. Amin SB, Orlando M, Wang H. Latent Iron Deficiency In Utero Is Associated with **Abnormal Auditory Neural Myelination** in ≥35 Weeks Gestational Age Infants. J Pediatr. 2013 Aug 8.
87. Krebs NF, Sherlock LG, Westcott J, et al. Effects of **different complementary feeding regimens** on iron status and enteric microbiota in breastfed infants. J Pediatr. 2013 Aug;163(2):416-423.e4.
88. Murphy MF, Waters JH, Wood EM, Yazer MH. **Transfusing blood safely** and appropriately. BMJ. 2013 Jul 16;347:f4303.
89. MHRA Aug/13 Previously, an **initial test dose** has been recommended for some IV iron products before administration of the first dose to a new patient. However, there are no clear data that an initial test dose minimises risk: conversely, it may give false reassurance because hypersensitivity reactions have been reported in patients that had a negative initial test dose. Therefore, an **initial test dose on first use of an IV iron product for a patient is no longer** recommended. A Europe-wide review of intravenous iron products for iron deficiency and anaemia has recommended strengthened measures are taken to manage and minimise the risk of hypersensitivity reactions, which may be life-threatening or fatal as outlined in this article.
90. Litton E, Xiao J, Ho KM. Safety and efficacy of **intravenous iron therapy** in reducing requirement for allogeneic blood transfusion: systematic review and meta-analysis of randomised clinical trials. BMJ. 2013 Aug 15;347:f4822.
91. Zlotkin S, Newton S, Aimone AM, et al. Effect of **iron fortification on malaria incidence** in infants and young children in Ghana: a randomized trial. JAMA. 2013;310(9):JOI130053.
92. Vlaar AP, Juffermans NP. **Transfusion-related acute lung injury**: a clinicalreview. Lancet. 2013 Sep 14;382(9896):984-94.
93. Ukachi N, Morrison W, Vanhorn S, et al. A Young Adult **Jehovah's Witness** With Severe Anemia. Pediatrics. 2013 Sep;132(3):547-51.
94. Lozoff B, Smith JB, Kaciroti N, Clark KM, Guevara S, Jimenez E. Functional Significance of Early-Life Iron Deficiency: Outcomes at 25 Years. J Pediatr. 2013 Jul 1.
95. Chang S, Zeng L, Brouwer ID, Kok FJ, Yan H. Effect of **iron deficiency anemia in pregnancy on child mental development** in rural China. Pediatr 2013;131:e755-63.
96. Lozoff, et al. Functional significance of **early-life iron deficiency**: outcomes at 25 years. J Pediatr 2013;163:1260-6.
97. Low M, Farrell A, Biggs BA, Pasricha SR. Effects of daily **iron supplementation in primary-school-aged children**: systematic review and meta-analysis of randomized controlled trials. CMAJ. 2013 Oct 15. (cognitive, anemia…)
98. Parkin PC, Maguire JL. **Iron deficiency in early childhood**. CMAJ. 2013 Oct 1;185(14):1237-1238. Epub 2013 Aug 6.
99. Moschovis PP, Banajeh S, Macleod WB, et al. Childhood **Anemia at High Altitude**: Risk Factors for Poor Outcomes in Severe **Pneumonia**. Pediatrics. 2013 Oct 7.
100. Thomas DW, Hinchliffe RF, Briggs C, Macdougall IC, et al. **British** Committee for Standards in Haematology. Guideline for the laboratory **diagnosis of functional iron deficiency**. Br J Haematol. 2013 Jun;161(5):639-48.
101. Gray-Donald K. **Iron supplementation for children**: Safety in all settings is not clear. CMAJ. 2013 Oct 15.
102. Upadhyay A, Gothwal S, Parihar R, et al. Effect of **umbilical cord milking** in term and near term infants: randomized control trial. Am J Obstet Gynecol 2013;208:120.e1–6.
103. Kansagara D, Dyer E, Englander H, et al. **Treatment of anemia in patients with heart disease: a systematic review.** Ann Intern Med. 2013 Dec 3;159(11):746-57.
104. Qaseem A, Humphrey LL, Fitterman N, et al. Treatment of **anemia in patients with heart disease**: a clinical practice guideline from the american college of physicians. Ann Intern Med. 2013 Dec 3;159(11):770-9.
105. Gomollón F, Gisbert JP. Current management of iron deficiency anemia in **inflammatory bowel diseases**: a practical guide. Drugs. 2013 Nov;73(16):1761-70.
106. Joy R, Krishnamurthy S, Bethou A, et al. Early versus late enteral prophylactic iron supplementation in **preterm very low birth weight infants**: a randomised controlled trial. Arch Dis Child Fetal Neonatal Ed. 2013 Dec 3.
107. Schiller B, Bhat P, Sharma A. Safety and Effectiveness of **Ferumoxytol** in Hemodialysis Patients at 3 Dialysis Chains in the United States Over a 12-Month Period. Clin Ther. 2013 Dec 5.
108. Chang YL, Hung SH, Ling W, et al. Association between **Ischemic Stroke and Iron-Deficiency Anemia**: A Population-Based Study. PLoS One. 2013 Dec 9;8(12):e82952.
109. Gong L, Yuan F, Teng J, et al. Weight Loss, Inflammatory Markers, and Improvements of Iron Status in **Overweight and Obese Children**. J Pediatr. 2014 Feb 8
110. Rhode JM, Dimcheff DE, Blumberg N, et al. **Health care–associated infection after red blood cell transfusion**: a systematic review and meta-analysis. JAMA. doi:10.1001/jama.2014.2726.
Carson JL, Sieber F, Cook DR, et al. **Liberal versus restrictive blood transfusion** strategy: 3-year survival and cause of death results from the FOCUS randomised controlled trial. Lancet 2014; online Dec 9.
Tomer A, Amir B, Alon G, et al. The **Safety of Intravenous Iron Preparations**: Systematic Review and Meta-analysis. Mayo Clin Proc. 2015 Jan;90(1):12-23.
111. Chung SD, Chen PY, Lin HC, et al. **Sudden Sensorineural Hearing Loss** Associated With Iron-Deficiency Anemia: A Population-Based Study. JAMA Otolaryngol Head Neck Surg. 2014 Mar 13.
112. Andersson O, Hellström-Westas L, Andersson D, et al. Effects of **delayed compared with early umbilical cord clamping** on maternal postpartum hemorrhage and cord blood gas sampling: a randomized trial.
Acta Obstet Gynecol Scand. 2013 May;92(5):567-74.
113. Vain NE, Satragno DS, Gorenstein AN, et al. Effect of **gravity on volume of placental transfusion**: a multicentre, randomised, non-inferiority trial. Lancet 2014; online April 17.
114. Smith GA, Fisher SA, Doree C, Di Angelantonio E, Roberts DJ. **Oral or parenteral iron supplementation to reduce deferral, iron deficiency and/or anaemia in blood donors**. Cochrane Database of Systematic Reviews 2014, Issue 7. Art. No.: CD009532. DOI: 10.1002/14651858.CD009532.pub2. There is moderate quality evidence that rates of donor deferral due to low haemoglobin are considerably less in those taking iron supplements compared with
those without iron supplementation, both at the first donation visit and at subsequent donation. Iron supplemented donors also show elevated haemoglobin and iron stores. These beneficial effects are balanced by more frequent adverse events in donors who receive iron supplementation than in those who do not; this is likely to limit acceptability and compliance. The long-term effects of iron supplementation without measurement of iron stores are unknown. These considerations are likely to preclude widespread use of iron supplementation by tablets. Blood services may consider targeted use of supplementation in those at greatest risk of iron deficiency, personalised donation intervals and providing dietary advice.
115. Health Canada July/14 **FERAHEME (ferumoxytol)** – New Restrictions on the Use due to Information on **Serious Allergic Reactions** - Takeda Canada Inc. The Product Monograph (PM) has been revised to reflect new usage restrictions in patients treated with FERAHEME® (ferumoxytol). FERAHEME® is now contraindicated in patients with any allergy to other parenteral iron products or in patients with multiple (two or more) drug allergies. Health care professionals are also reminded that: Serious hypersensitivity reactions including life threatening and fatal anaphylaxis/anaphylactoid reactions have occurred in patients receiving intravenous iron products including FERAHEME®. FERAHEME® should only be administered when personnel and therapies are immediately available for the treatment of anaphylaxis and other hypersensitivity reactions. Patients should be closely monitored for signs and symptoms of hypersensitivity, including clinically significant hypotension, during and for at least 30 minutes after each administration of FERAHEME®. Before each administration patients should be informed of the risk of hypersensitivity. Patients should also be informed of the relevant symptoms and asked to seek urgent medical attention if a reaction occurs.
116. Cippa PE, Boucsein I, Adams H, et al. **Estimating Iron Overload** in Patients with Suspected Liver Disease and Elevated Serum Ferritin. Am J Med. 2014 Mar 22. pii: S0002-9343(14)00270-8.
117. Frosch AE, Ondigo BN, Ayodo GA, et al. Decline in childhood iron deficiency after **interruption of malaria transmission** in highland Kenya. Am J Clin Nutr. 2014 Sep;100(3):968-73.
118. Ponikowski P, van Veldhuisen DJ, Comin-Colet J, et al; for the **CONFIRM-HF** Investigators. Beneficial effects of long-term intravenous iron therapy with **ferric carboxymaltose** in patients with symptomatic **heart failure** and iron deficiency†. Eur Heart J. 2014 Aug 31.
119. Holst LB, Haase N, Wetterslev J, et al. **Lower versus higher hemoglobin threshold for transfusion in septic shock. (TRISS)** N Engl J Med. DOI: 10.1056/NEJMoa1406617.
120. Ponikowski P, van Veldhuisen DJ, Comin-Colet J, et al. Beneficial effects of long-term intravenous iron therapy with **ferric carboxymaltose** in patients with symptomatic **heart failure** and iron deficiency.
Eur Heart J. 2014 Aug 31.
121. DeLoughery TG. **Microcytic anemia**. N Engl J Med. 2014 Oct 2;371(14):1324-31.
122. Helath Canada Nov/14 FERAHEME (ferumoxytol) – Important Changes to the Delivery and New Restrictions on the Use Due to Information on Serious Allergic Reactions - Takeda Canada Inc.
FERAHEME should now only be given by infusion of the diluted product into a vein over a minimum period of 15 minutes. FERAHEME should no longer be used in patients with any known history of drug allergy.
123. Ward RJ, Zucca FA, Duyn JH, et al. The role of **iron in brain ageing** and neurodegenerative disorders. Lancet Neurol. 2014 Oct;13(10):1045-1060.
124. Mbeledogu CN, Cecil EV, Millett C, et al. Hospital admissions for **unintentional poisoning** in preschool children in England; 2000-2011. Arch Dis Child. 2014 Aug 28.
125. Carson JL, Sieber F, Cook DR, et al. **Liberal versus restrictive blood transfusion** strategy: 3-year survival and cause of death results from the FOCUS randomised controlled trial. Lancet 2014; online Dec 9.
126. Caughey MC, Avery CL, Ni H, et al. Outcomes of Patients With Ane**mia and Acute Decompensated Heart Failure** With Preserved Versus Reduced Ejection Fraction (from the ARIC Study Community Surveillance).

Am J Cardiol. 2014 Dec 15;114(12):1850-4.
127. El-Ganzoury MM, Awad HA, El-Farrash RA, et al. **Enteral Granulocyte-Colony Stimulating Factor and Erythropoietin Early** in Life Improves **Feeding** Tolerance in **Preterm Infants**: A Randomized Controlled Trial. J Pediatr. 2014 Dec;165(6):1140-1145.e1.
128. Elimian A, Goodman J, Escobedo M, et al. **Immediate compared with delayed cord clamping** in the preterm neonate: a randomized controlled trial. Obstet Gynecol. 2014 Dec;124(6):1075-9.
129. Goodnough LT, Murphy MF. Do **liberal blood transfusions** cause more harm than good? BMJ. 2014 Dec 5;349:g6897.
130. Kunadian V, Mehran R, Lincoff AM, et al. Effect of **Anemia on Frequency** of Short- and Long-Term Clinical **Events in Acute Coronary Syndromes** (from the Acute Catheterization and Urgent Intervention Triage Strategy Trial). Am J Cardiol. 2014 Dec 15;114(12):1823-9.
131. Avni T, Bieber A, Steinmetz T, et al. Treatment of **anemia in inflammatory bowel disease**--systematic review and meta-analysis. PLoSOne. 2013 Dec 2;8(12)
132. Tomer A, Amir B, Alon G, et al. The **Safety of Intravenous Iron Preparations**: Systematic Review and Meta-analysis. Mayo Clin Proc. 2015 Jan;90(1):12-23.
133. Kiss JE, Brambilla D, Glynn SA, et al.; National Heart, Lung, and Blood Institute (NHLBI) Recipient Epidemiology and Donor Evaluation Study–III (**REDS-III**). **Oral iron supplementation after blood donation**: a randomized clinical trial. JAMA. 2015 Feb 10; 313(6):575-83
134. Lindblad AJ, Cotton C, Allan GM. **Iron deficiency anemia in the elderly**. Can Fam Physician. 2015 Feb;61(2):159.
135. Umanath K, Jalal DI, Greco BA, et al; for the Collaborative Study Group. **Ferric Citrate** Reduces Intravenous Iron and Erythropoiesis-Stimulating Agent Use in ESRD. J Am Soc Nephrol. 2015 Mar 3.
136. FDA Mar/15 is strengthening an existing warning that serious, potentially **fatal allergic reactions** can occur with the anemia drug **Feraheme (ferumoxytol).** FDA changed the prescribing instructions and approved a Boxed Warning, FDA's strongest type of warning, regarding these serious risks. Also added is a new Contraindication, a strong recommendation against use of Feraheme in patients who have had an allergic reaction to any intravenous (IV) iron replacement product.
137. Holst LB, Petersen MW, Haase N, et al. **Restrictive versus liberal transfusion strategy** for red blood cell transfusion: systematic review of randomised trials with meta-analysis and trial sequential analysis. BMJ 2015;350:h1354.
138. Lacroix J, Hébert PC, Fergusson DA, et al. **ABLE** Investigators and the Canadian Critical Care Trials Group. **Age of Transfused Blood in Critically Ill Adults**. N Engl J Med. 2015 Mar 17.
139. MHRA Mar/15 **Ferumoxytol (Rienso) intravenous iron no longer** available for use. The licence-holder of ferumoxytol has voluntarily withdrawn it from the **UK market** for commercial reasons.
140. Murphy GJ, Pike K, Rogers CA, et al. **Liberal or restrictive transfusion** after cardiac surgery. **(TITer-2-)** N Engl J Med 2015;372:997-1008.
141. Ajmera AV, Shastri GS, Gajera MJ, Judge TA. **Suboptimal response to ferrous sulfate** in iron-deficient patients taking **omeprazole**. Am J Ther. 2012 May;19(3):185-9.
142. Al-Wassia H, Shah PS. Efficacy and safety of **umbilical cord milking** at birth: a systematic review and meta-analysis. JAMA Pediatr. 2015 Jan;169(1):18-25.
143. Cantor AG, Bougatsos C, Dana T, et al. **Routine Iron Supplementation and Screening for Iron Deficiency Anemia in Pregnancy**: A Systematic Review for the U.S. Preventive Services Task Force (**USPSTF**) . Ann Intern Med. 2015 Mar 30.
144. Hashimoto R, Matsuda T, Chonan A. **Iron-deficiency anemia** caused by a **proton pump inhibitor**. Intern Med. 2014;53(20):2297-9.
145. Mari G, Norton ME, Stone J, et al. Society for Maternal-Fetal Medicine (**SMFM**) Clinical Guideline #8: the **fetus at risk for anemia-diagnosis and management**. Am J Obstet Gynecol. 2015 Mar 27.
146. McDonagh MS, Blazina I, Dana T, et al. **Screening and Routine Supplementation for Iron Deficiency Anemia**: A Systematic Review. Pediatrics. 2015 Mar 30.
147. Gurusamy KS, Nagendran M, Broadhurst JF, et al. **Iron therapy in anaemic adults without chronic kidney disease**. Cochrane Database Syst Rev. 2014 Dec 31;12:CD010640.
148. Andersson O, Lindquist B, Lindgren M, et al. Effect of **delayed cord clamping** on neurodevelopment at 4 years of age: a randomized clinical trial [onlineMay 26, 2015]. JAMA Pediatr. doi:10.1001/jamapediatrics.2015.0358.
149. Camaschella C. **Iron-deficiency anemia**. N Engl J Med. 2015 May 7;372(19):1832-43.
150. Jobes DR, Sesok-Pizzini D, Friedman D. Reduced Transfusion Requirement With Use of **Fresh Whole Blood** in Pediatric Cardiac Surgical Procedures. Ann Thorac Surg. 2015 Mar 25.
151. Padhi S, Glen J, Pordes BA, et al; Guideline Development Group. Management of **anaemia in chronic kidney disease**: summary of updated **NICE** guidance. BMJ. 2015 Jun 4;350:h2258.
152. Holst LB, Petersen MW, Haase N, et al. **Restrictive versus liberal transfusion strategy** for red blood cell transfusion: systematic review of randomised trials with meta-analysis and trial sequential analysis. BMJ 2015;350:h1354.
153. Whitlock E, Kim H, Auerbach A. Harms associated with **single unit perioperative transfusion**: retrospective population based analysis. BMJ 2015;350:h3037.
154. Jairath V, Kahan BC, Gray A, et al. **Restrictive versus liberal blood transfusion** for acute upper gastrointestinal bleeding (**TRIGGER**): a pragmatic, open-label, cluster randomised feasibility trial. Lancet 2015; online May 6.
155. Katheria AC, Truong G, Cousins L, et al. **Umbilical Cord Milking Versus Delayed Cord Clamping** in Preterm Infants. Pediatrics. 2015 Jun 29.
156. Liu TC, Lin SF, et al. Comparison of a combination **ferrous fumarate product and a polysaccharide iron complex** as oral treatments of iron deficiency anemia: a Taiwanese study. Int J Hematol. 2004 Dec;80(5):416-20.
157. 158. Tinawi M, Martin K, Bastani B. Oral iron absorption test in patients with CAPD: comparison of **ferrous sulfate and a polysaccharide ferric complex**. Nephron. 1996;74:291-294.
159. Zhang YY, Liu JH, et al. Single-dose bioequivalence assessment of two formulations of **polysaccharide iron complex capsules in healthy adult male Chinese volunteers**: A sequence-randomized, double-blind, two-way crossover study. Curr Ther Res Clin Exp. 2009 Apr;70(2):104-15.
160. Etheredge AJ, Premji Z, Gunaratna NS, et al. **Iron Supplementation in Iron-Replete and Nonanemic Pregnant Women** in Tanzania: A Randomized Clinical Trial. JAMA Pediatr. 2015 Aug 17.
161. Pdf Domellöf M, Georgieff MK. **Postdischarge Iron Requirements of the Preterm** Infant. J Pediatr. 2015 Oct;167(4 Suppl):S31-5.
162. Duley L, Dorling J, Gyte G. When should the **umbilical cord be clamped**? BMJ. 2015 Sep 9;351:h4206.
163. Hernell O, Fewtrell MS, et al. Summary of Current Recommendations on **Iron Provision and Monitoring of Iron Status for Breastfed and Formula-Fed Infants** in Resource-Rich and Resource-Constrained Countries. J Pediatr. 2015 Oct;167(4 Suppl):S40-7.
164. Kleinman RE. Expert Recommendations on **Iron Fortification in Infants**. J Pediatr. 2015 Oct;167(4 Suppl):S48-9.
165. Kleinman RE. Introduction: Recommended **Iron Levels for Nutritional Formulas** for Infants. J Pediatr. 2015 Oct;167(4 Suppl):S1-2.
166. Lönnerdal B, Georgieff MK, Hernell O. Developmental Physiology of **Iron Absorption, Homeostasis, and Metabolism** in the Healthy **Term Infant**. J Pediatr. 2015 Oct;167(4 Suppl):S8-S14.
167. Lopez A, Cacoub P, Macdougall IC, et al. **Iron deficiency anaemia**. Lancet. 2015 Aug 24.
168. Mwangi MN, Roth JM, Smit MR, et al. Effect of daily **antenatal iron supplementation on Plasmodium infection in Kenyan women**: a randomized clinical trial.JAMA. doi:10.1001/jama .2015.9496
169. Siu AL. **Screening for Iron Deficiency Anemia and Iron Supplementation in Pregnant** Women to Improve Maternal Health and Birth Outcomes: U.S. Preventive Services Task Force Recommendation Statement (**USPSTF**). Ann Intern Med. 2015 Sep 8.
170. Siu AL; US Preventive Services Task Force. **Screening for Iron Deficiency Anemia in Young Children**: **USPSTF** Recommendation statement. Pediatrics. 2015 Sep 7.
171. Vanderhoof JA, Kleinman RE. **Iron Requirements for Infants with Cow Milk Protein Allergy**. J Pediatr. 2015 Oct;167(4 Suppl):S36-9.
172. Zlotkin SH, Davidsson L, Lozoff B. Balancing the Benefits and Risks of **Iron Fortification** in Resource-Constrained Settings. J Pediatr. 2015 Oct;167(4 Suppl):S26-30.
173. Ducrocq G, Puymirat E, Steg PG, et al. **Blood transfusion, bleeding, anemia, and survival** in patients with acute myocardial infarction: FAST-MI registry. Am Heart J. 2015 Oct;170(4):726-734.e2.
174. Wang C, Graham DJ, Kane RC, et al. Comparative Risk of **Anaphylactic Reactions Associated With Intravenous Iron** Products. JAMA. 2015 Nov 17;314(19):2062-2068.
175. Macdougall IC, Bircher AJ, Eckardt KU, et al; Conference Participants. **Iron management** in chronic kidney disease: conclusions from a "Kidney Disease: Improving Global Outcomes" (**KDIGO**) Controversies Conference. Kidney Int. 2016 Jan;89(1):28-39.
176. Wang M, **Iron Deficiency** and Other Types of Anemia in **Infants** and **Children**. Am Fam Physician. 2016;93(4):270-278.
177. Angulo-Barroso RM, Li M, Santos DC, et al. **Iron Supplementation in Pregnancy** or Infancy and Motor Development: A Randomized Controlled Trial. Pediatrics. 2016 Mar 2.
178. Auerbach M, Adamson JW. How we **diagnose and treat iron deficiency anemia**. Am J Hematol. 2016 Jan;91(1):31-8.
179. Kaminsky BM, Pogue KT, Hanigan S, et al. Effects of **Total Dose Infusion of Iron Intravenously** in Patients With **Acute Heart Failure** and Anemia (Hemoglobin < 13 g/dl). Am J Cardiol. 2016 Jun 15;117(12):1942-6.
180. Arsenault V, Mailloux C, Bonnefoy A, et al. Iron-Refractory Iron Deficiency Anemia May Not Lead to **Neurocognitive Dysfunction**: A Case Report. Pediatrics. 2016 Jul;138(1).

181. Barlas RS, Honney K, et al. Impact of Hemoglobin Levels and Anemia on **Mortality in Acute Stroke**: Analysis of UK Regional Registry Data, Systematic Review, and Meta-Analysis. J Am Heart Assoc. 2016 Aug 17;5(8).
182. Cleland JG, Zhang J, Pellicori P, Dicken et al. Prevalence and Outcomes of **Anemia and Hematinic Deficiencies in Patients With Chronic Heart Failure**. JAMA Cardiol. 2016 Aug1;1(5):539-547
183. World Health Organization (WHO). **WHO guideline: daily iron supplementation in infants and children**. Geneva (Switzerland): World Health Organization (WHO); 2016.
184. Cholette JM, Swartz MF, Rubenstein J, et al. Outcomes Using a **Conservative Versus Liberal Red Blood Cell Transfusion** Strategy in Infants Requiring Cardiac Operation. Ann Thorac Surg. 2016 Aug 2.
185. Michels WM, Jaar BG, Ephraim PL, et al; **DEcIDE** Network Patient Outcomes in End Stage Renal Disease Study Investigators. **Intravenous iron administration strategies** and anemia management in hemodialysis patients. Nephrol Dial Transplant. 2016 Sep 6.
186. Reeves BC, Pike K, Rogers CA, et al. A multicentre randomised controlled trial of **Transfusion Indication Threshold Reduction** on transfusion rates, morbidity and health-care resource use following cardiac surgery (TITRe2). Health Technol Assess. 2016 Aug;20(60):1-260.
187. World Health Organization (WHO). **WHO guideline**: daily iron supplementation in **adult women and adolescent girls**. Geneva (Switzerland): World Health Organization (WHO); 2016.
188. Bager P, Hvas CL, Dahlerup JF. Drug-specific **hypophosphatemia and hypersensitivity reactions** following different **intravenous iron infusions**. Br J Clin Pharmacol. 2016 Nov 17.
189. Mireku MO,Davidson LL, Boivin MJ, et al. **Prenatal Iron Deficiency**. Neonatal Ferritin and Infant Cognitive Function. Pediatrics.2016;138(6):e20161319
190. Rawal S, Hinkle SN, Bao W, et al. A longitudinal study of **iron status during pregnancy** and the risk of gestational diabetes: findings from a prospective, multiracial cohort. Diabetologia. 2016 Nov 10.
191. Webster AC, Nagler EV, Morton RL, et al. **Chronic Kidney Disease**. Lancet.2016 Nov 22.
192. Wienbergen H, Pfister O, Hochadel M, et al.Usefulness of **Iron Deficiency Correction in Management of Patients With Heart Failure** [from the Registry Analysis of Iron Deficiency-Heart Failure (**RAID-HF**)Registry]. Am J Cardiol. 2016 Dec 15;118(12):1875-1880.
193. Anker SD, Colet JC, Filippatos G, et al. Rationale and design of **Ferinject** assessment in patients with iron deficiency and chronic **heart failure** (**FAIR-HF**) study: a randomized, placebo-controlled study of intravenous iron supplementation in patients with and without anaemia. Eur J Heart Fail 2009;11:1084e1091.
194. Anker SD, Comin Colet J, Filippatos G, et al. **Ferric carboxymaltose** in patients with **heart failure** and iron deficiency. N Engl J Med 2009;361: 2436e2448.
195. Avni T, Leibovici L, Gafter-Gvili A. Iron supplementation for the treatment of chronic **heart failure and iron deficiency**: systematic review and meta-analysis. Eur J Heart Fail 2012;14:423e429.
196. Gutzwiller FS, Schwenkglenks M, Blank PR, et al. Health economic assessment of ferric **carboxymaltose** in patients with iron deficiency and chronic heart failure based on the FAIR-HF trial: an analysis for the UK. Eur J Heart Fail 2012;14:782e790.
197. Kapoor M, Schleinitz MD, Gemignani A, Wu WC. Outcomes of patients with chronic **heart failure and iron deficiency** treated with intravenous iron: a meta-analysis. Cardiovasc Hematol Disord Drug Targets 2013;13:35e44.
198. Okonko DO, Grzeslo A, Witkowski T, et al. Effect of intravenous **iron sucrose** on exercise tolerance in anemic and nonanemic patients with symptomatic chronic heart failure and iron deficiency **FERRIC-HF**: a randomized, controlled, observer-blinded trial. J Am Coll Cardiol 2008;51:103e112.
198. Jankowska EA, Tkaczyszyn M, Suchocki T, et al. Effects of intravenous iron therapy in iron-deficient patients with **systolic heart failure**: a meta-analysis of randomized controlled trials. Eur J Heart Fail 2016;18:786e795.
199. Keating GM. **Ferric carboxymaltose**: a review of its use in iron deficiency. Drugs 2015;75:101e127.
200. Ponikowski P, van Veldhuisen DJ, Comin-Colet J, et al. Beneficial effects of long-term intravenous iron therapy with **ferric carboxymaltose** in patients with symptomatic **heart failure** and iron deficiency. Eur Heart J 2015;36:657e668.
201. Powers JM, Shamoun M, McCavit TL, et al. **Intravenous Ferric Carboxymaltose in Children** with Iron Deficiency Anemia Who Respond Poorly to Oral Iron. J Pediatr. 2016 Oct 21.
202. Schieffer KM, Chuang CH, Connor J, et al. Association of **Iron Deficiency Anemia With Hearing Loss** in US Adults. JAMA Otolaryngol Head Neck Surg. 2016 Dec 29.
203. Achebe MM, Gafter-Gvili A. How I treat **anemia in pregnancy**: iron, cobalamin and folate. Blood. 2016 Dec 29.
204. Fishbane S, Block GA, Loram L, Neylan et al. Effects of **Ferric Citrate** in Patients with Nondialysis-Dependent CKD and Iron Deficiency Anemia. J Am Soc Nephrol. 2017 Jan 12.
205. Kc A, Rana N, Målqvist M, et al. Effects of **Umbilical Cord Clamping** vs Early Clamping on Anemia in Infants at 8 and 12 Months: A Randomized Clinical Trial. JAMA Pediatr. 2017 Jan 17.
206. Beck-da-Silva L, Piardi D, Soder S, et al. **IRON-HF** study: a randomized trial to assess the effects of **iron in heart failure** patients with anemia. Int J Cardiol. 2013 Oct 9;168(4):3439-42.
207. Niehaus ED, Malhotra R, Cocca-Spofford D, et al. Repletion of Iron Stores With the Use of **Oral Iron Supplementation in Patients With Systolic Heart Failure**. J Card Fail. 2015 Aug;21(8):694-7.
208. Abdullah K, Birken CS, Maguire JL, et al. Re-Evaluation of **Serum Ferritin** Cut-Off Values for the **Diagnosis of Iron Deficiency in Children** Aged 12-36 Months. J Pediatr. 2017 Apr 18.
209. Zeller MP, Verhovsek M. **Treating iron deficiency**. CMAJ. 2016 Dec 19.
210. Kim YW, Bae JM, Park YK, et al. Effect of Intravenous **Ferric Carboxymaltose** on Hemoglobin Response Among Patients With Acute Isovolemic **Anemia Following Gastrectomy**: The **FAIRY** Randomized Clinical Trial. JAMA. 2017 May 23;317(20):2097-2104
211. Lewis GD, Malhotra R, Hernandez AF, et al. Effect of **Oral Iron Repletion** on Exercise Capacity in Patients With **Heart Failure** With Reduced Ejection Fraction and Iron Deficiency: The **IRONOUT HF** Randomized Clinical Trial. JAMA. 2017 May 16;317(19):1958-1966
212. Powers JM, Buchanan GR, Adix L, et al. Effect of Low-Dose Ferrous Sulfate drops vs Iron Polysaccharide Complex drops on Hemoglobin Concentration in Young Children With Nutritional Iron-Deficiency Anemia: A Randomized Clinical Trial. JAMA. 2017 Jun 13;317(22):2297-2304.
213. van Veldhuisen DJ, Ponikowski P, et al; **EFFECT-HF** Investigators . Effect of **Ferric Carboxymaltose** on Exercise Capacity in Patients with Chronic **Heart Failure** and Iron Deficiency. Circulation. 2017 Jul 12.
214. Kelly AU, McSorley ST, Patel P, et al. **Interpreting iron studies**. BMJ. 2017 Jun 15;357:j2513.
215. Barraclough KA, Brown F, Hawley CM, et al. A randomized controlled trial of **oral heme iron polypeptide versus oral iron supplementation** for the treatment of anaemia in peritoneal dialysis patients: **HEMATOCRIT** trial. Nephrol Dial Transplant. 2012 Nov;27(11):4146-53.
216. Stoffel N, Cercamondi CI, Brittenham G, et al. **Iron absorption from oral iron supplements given on consecutive versus alternate days** and as single morning doses versus twice-daily split dosing in iron-depleted women: two open-label, randomised controlled trials. Lancet Haematology 2017; online Oct 9.
217. van Veldhuisen DJ, Ponikowski P, van der Meer P, et al. Effect of **ferric carboxymaltose** on exercise capacity in patients with chronic **heart failure** and iron deficiency. Circulation. 2017;136:1374–1383.
218. Caram-Deelder C et al. Association of **blood transfusion from female donors with and without a history of pregnancy** with mortality among male and female transfusion recipients. *JAMA* 2017 Oct 17; 318:1471.
219. Shackelford SA, del Junco DJ, Powell-Dunford N, et al. Association of **prehospital blood product transfusion during medical evacuation of combat casualties** in Afghanistan with acute and 30-day survival. JAMA. doi:10.1001/jama.2017.15097
220. Tarnow-Mordi W, Morris J, Kirby A, et al; Australian Placental Transfusion Study Collaborative Group. **Delayed versus Immediate Cord Clamping** in Preterm Infants. N Engl J Med. 2017 Oct 29.
221. Katheria A, Garey D, et al. A Randomized Clinical Trial of **Umbilical Cord Milking vs Delayed Cord Clamping** in Preterm Infants: Neurodevelopmental Outcomes at 22-26 Months of Corrected Age. J Pediatr. 2017 Dec 7.
222. Mazer CD, Whitlock RP, Fergusson DA, et al; **TRICS** Investigators and Perioperative Anesthesia Clinical Trials Group. **Restrictive or Liberal Red-Cell Transfusion for Cardiac Surgery**. N Engl J Med. 2017 Nov 12.
223. MHRA Jan/18: Recombinant human erythropoietins: very rare risk of severe cutaneous adverse reactions (**SCARs**). **Recombinant human erythropoietin (r-HuEPO)** treatment has been associated with very rare cases of life-threatening severe cutaneous adverse reactions (SCARs), including Stevens-Johnson syndrome (**SJS**) and toxic epidermal necrolysis (**TEN**).
224. Papadopoulos M, Patel D, Korologou-Linden R, et al. Safety and efficacy of **parenteral iron in children with inflammatorybowel disease**. Br J Clin Pharmacol. 2017 Dec 20.
225. Sadana D, Pratzer A, Scher LJ, et al. Promoting High-Value Practice by Reducing **Unnecessary Transfusions** With a Patient Blood Management Program. JAMA Intern Med. 2017 Nov 20.
226. Muñoz M, Acheson AG, Auerbach Met al. **International consensus statement on the peri operative management of anaemia and iron deficiency**. Anaesthesia. 2017 Feb;72(2):233-247.
227. Chong MA, Krishnan R, Cheng D, Martin J. **Should Transfusion Trigger Thresholds Differ for Critical Care Versus Perioperative Patients**? A Meta-Analysis of Randomized Trials. Crit Care Med. 2018 Feb;46(2):252-263.
228. Goel R, Chappidi MR, Patel EU, et al. **Trends in Red Blood Cell, Plasma, and Platelet Transfusions in the United States**, 1993-2014. JAMA. 2018 Feb 27;319(8):825-827.
229. Pérez-Pevida B, Kamocka A. **Haemosiderin pigmentation after intravenous iron infusion** BMJ 2018 Jan 25; 360 :k69.
230. Anand IS, Gupta P. Anemia and **Iron Deficiency in Heart Failure**: Current Concepts and Emerging Therapies. Circulation. 2018 Jul 3;138(1):80-98.

231. Böttcher M, Lentini S, Arens ER, et al. First-in-man-proof of concept study with **molidustat**: a novel selective oral **HIF-prolyl hydroxylase inhibitor** for the treatment of renal anaemia. Br J Clin Pharmacol. 2018 Mar 25.
232. Conway M, Marcon P, Meinert P, et al. A Toddler With **Treatment-Resistant Iron Deficiency** Anemia. Pediatrics. 2018 Jun 27.
233. Papadopoulos M, Patel D, Korologou-Linden R, et al. Safety and efficacy of **parenteral iron in children with inflammatory bowel disease**. Br J Clin Pharmacol. 2018 Apr;84(4):694-699.
234. Teng X, Shan Z, Li C, et al. **Iron Deficiency May Predict Greater Risk for Hypothyroxinemia**: A Retrospective Cohort Study of Pregnant Women in China. Thyroid. 2018 Jul 3.
235. Pasricha SR, Armitage AE, Prentice AM, et al. **Reducing anaemia in low income countries**: control of infection is essential. BMJ. 2018 Aug 1;362:k3165.
236. Veenemans J, Milligan P, et al. Effect of supplementation with zinc and other micronutrients on **malaria** in Tanzanian children: a randomised trial. PLoS Med 2011;8:e1001125. 10.1371/journal.pmed.1001125 22131908
237. Esan MO, van Hensbroek MB, Nkhoma E, etal . Iron supplementation in **HIV-infected** Malawian children with anemia: a double-blind, randomized, controlled trial. Clin Infect Dis 2013;57:1626-34. 10.1093/cid/cit528 23956164
238. Pasricha SR, Biggs BA, Prashanth NS, etal . Factors influencing receipt of **iron supplementation by young children and their mothers** in rural India: local and national cross-sectional studies. BMC Public Health 2011;11:617.
239. Tielsch JM, et al . Effect of routine **prophylactic supplementation with iron and folic acid on preschool child mortality in southern Nepal:** community-based, cluster-randomised, placebo-controlled trial. Lancet 2006;367:144-52.
240. Macdougall IC, White C, Anker SD, et al; PIVOTAL Investigators and Committees. **Intravenous Iron in Patients Undergoing Maintenance Hemodialysis**. N Engl J Med. 2018 Oct 26
241. Mulder MB, van den Hoek HL, Birnie E, et al. Comparison of hypersensitivity reactions of intravenous iron: **iron isomaltoside-1000 (Monofer(®)) versus ferric carboxy-maltose (Ferinject(®)**). A single center, cohort study. Br J Clin Pharmacol. 2018 Nov 4.
242. Oatley H, Borkhoff CM, Chen S, et al; TARGet Kids! Collaboration. **Screening for Iron Deficiency in Early Childhood** Using Serum Ferritin in the Primary Care Setting. Pediatrics. 2018 Nov 28.
243. Cohen AR. Looking Behind the Iron Curtain. Pediatrics. 2018 Dec;142(6).
244. Eule C, Gupta A, Nagalla S. The **Direct Antiglobulin Test for Evaluating Anemia**. JAMA. 2018 Dec 3.
245. Roubinian NH, Murphy EL, Mark DG, et al**. Long-term outcomes** among patients discharged from the hospital with **moderate anemia**: a retrospective cohort study. Ann Intern Med. 2018. [Epub ahead of print]. doi:10.7326/M17-3253
246. Fernandez-Gaxiola AC, De-Regil LM. **Intermittent iron supplementation for reducing anaemia** and its associated impairments in adolescent and adult menstruating women. Cochrane Database Syst Rev. 2019 Jan 31;1:CD009218. Intermittent iron supplementation may reduce anaemia and may improve iron stores among menstruating women in populations with different anaemia and malaria backgrounds. In comparison with daily supplementation, the provision of iron supplements intermittently is probably as effective in preventing or controlling anaemia. More information is needed on morbidity (including malaria outcomes), side effects, work performance, economic productivity, depression, and adherence to the intervention.
247. Idris I, Tohid H, Muhammad NA,et al. Anaemia among primary care **patients with type 2 diabetes mellitus (T2DM)and chronic kidney disease (CKD)**: a multicentred cross-sectional study. BMJ Open.2018 Dec 22; 8(12):e025125.
248. Lim W, Afif W, Knowles S, et al. Canadian expert consensus: management of **hypersensitivity reactions to intravenous iron** in adults. Vox Sang. 2019 Apr 2
249. Munting KE, Klein AA. **Optimisation of pre-operative anaemia** in patients before elective major surgery - why, who, when and how? Anaesthesia. 2019 Jan;74 Suppl 1:49-57.
250. Rosen GM, Morrissette S, Larson A, et al. Use of a **Probiotic to Enhance Iron Absorption** in a Randomized Trial of Pediatric Patients Presenting with Iron Deficiency. J Pediatr. 2019 Apr;207:192-197.e1.
251. Schack A, Berkfors AA, Ekeloef S, et al. The Effect of Perioperative Iron Therapy in Acute Major Non-cardiac Surgery on Allogenic Blood Transfusion and Postoperative Haemoglobin Levels: A Systematic Review and Meta-analysis. World J Surg. 2019 Mar 1.
252. Spahn DR, Schoenrath F, Spahn GH, et al. Effect of ultra-short-term treatment of patients with iron deficiency or anaemia undergoing cardiac surgery: a prospective randomised trial. Lancet. 2019 Apr 26.
253. Zhou X, Xu W, Xu Y, et al. Iron Supplementation Improves Cardiovascular Outcomes in Patients with Heart Failure. Am J Med. 2019 Mar 7.

Red Flags for calciphylaxis?

Natural Products Database Search on phosphate-containing products:

Enemol Sodium Phosphate Enema (Dominion Pharmacal): Each 60 ml serving contains: Sodium Phosphate dibasic, heptahydrate 6 g. • Sodium Phosphate monobasic, anhydrous 16 g. Other Ingredients: Benzalkonium Chloride, Edetate Disodium, Purified Water. NPN 02096900.

Enema (HJ Sutton): Each 30 mL serving contains: Dibasic Sodium Phosphate 7 g (118 mL) • Monobasic Sodium Phosphate 19 g (118 mL). Other Ingredients: Benzalkonium Chloride, Disodium EDTA, Purified Water. NPN 02231170.

Kali Phosphoricum 6x (Thompson's Homeopathic Supplies Ltd): For 'stress and tension'. Potassium Phosphate 6X. Other Ingredients: Ground Corn Starch, Lactose. DIN-HM 00190101
Magnesia Phosphorica 6x tabs (Thompson's Homeopathic Supplies Ltd): Oral Laxative. Magnesium Phosphate 6X. Other Ingredients: Ground Corn Starch, Lactose. DIN-HM 00189995.

Natrum Phosphoricum 6x tabs (Thompson's Homeopathic Supplies Ltd.): Oral laxative. Each tablet contains: Sodium Phosphate 6X. Other Ingredients: Corn Starch, Lactose. DIN-HM 00190160

Naturally Sourced Calcium from Milk with Vit D and Magnesium (Immunotec Inc): Oral Laxative. Two tablets contain: Calcium Phosphate 250 mg • Magnesium 15 mg • Vitamin D (D3) 100 IU. Other Ingredients: Acacia Gum, Carnauba Wax, Croscarmellose Sodium, Hypromellose, Magnesium Stearate, Microcrystalline Cellulose, Polyethylene Glycol, Purified Water. NPN 02243453
New Era Biochemic Tissue Salt 10, 2, 6, 8 (Seven Seas Limited): Each tablet contains: Sodium Phosphate 6x 0.07 mcg. Other Ingredients: Acacia Gum, Lactose Monohydrate. DIN-HM 0016935.

New Era Combination F Biochemic Tissue Salts (Seven Seas Limited): Each tablet contains: Magnesium Phosphate 6x 0.0175 mcg • Potassium Phosphate 6x 0.0175 mcg • Silicon Dioxide 6x 0.0175 mcg • Sodium Chloride 6x 0.0175 mcg. Other Ingredients: Acacia Gum, Lactose Monohydrate. DIN-HM 00147028

New Era Combination G Biochemic Tissue Salts (Seven Seas Limited): Each tablet contains: Calcium Fluoride 6x 0.0175 mcg • Calcium Phosphate 6x 0.0175 mcg • Potassium Phosphate 6x 0.0175 mcg • Sodium Chloride 6x 0.0175 mcg. Other Ingredients: Acacia Gum, Lactose Monohydrate. DIN-HM 00147036

New Era Combination N Biochemic Tissue Salts (Seven Seas Limited): Oral Laxative. Each tablet contains: Calcium Phosphate 6x 0.0175 mcg • Magnesium Phosphate 6x 0.0175 mcg • Potassium Chloride 6x 0.0175 mcg • Potassium Phosphate 6x 0.0175 mcg. Other Ingredients: Acacia Gum, Lactose Monohydrate. DIN-HM 00534862
Oral Laxative (HJ Sutton Industries): Each 1 tsp serving contains: Dibasic Sodium Phosphate 0.9 g. Other Ingredients: Glycerin, Sodium Saccharin, Sodium Benzoate, Purified Water. NPN 80003212

Phoslax: Oral Laxative (Odan Laboratories Ltd): Each one tsp serving contains: Dibasic Sodium Phosphate 0.9 g. • Monobasic Sodium Phosphate 2.4 g. Other Ingredients: Glycerin, Natural Ginger Flavour, Natural Lemon Flavour, Sodium Benzoate, Purified Water. NPN 80000689

Schuessler Tissue Salts General Debility Comb B (Martin & Pleasance): Oral Laxative. Each tablet contains: Calcium Phosphate 6.0 X • Ferrum Phosphoricum 6.0 X • Kali Phosphoricum 6.0 X. Other Ingredients: Anhydrous Calcium Hydrogen Phosphate, Lactose, Magnesium Stearate. DIN-HM 80003543

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References: PHOSPHATE BINDERS in HYPERPHOSPHATEMIA of CKD

1 National Kidney Foundation. **K/DOQI** clinical practice guidelines for bone metabolism and disease in chronic kidney disease. Am J Kidney Dis 2003;42:S1-201. Available from http://www.kidney.org/professionals/kdoqi/guidelines_bone/index.htm. Accessed May 1st, 2010.

2 Kidney Disease Improving Global Outcomes. **KDIGO** Clinical Practice Guidelines for the Diagnosis, Evaluation, Prevention and Treatment of Chronic Kidney Disease-Mineral and Bone Disorder (CKD-MBD). Kidney International 2009; 76:(Suppl 113), S1–S130.

3 Guidelines for the Management of Chronic Kidney Disease. Canadian Society of Nephrology (**CSN**). CMAJ. Nov. 2008; 179:(11), 1154-1162.

4 Tonelli M, Pannu N, Manns B. Oral **Phosphate Binders** in Patients with Kidney Failure. N Engl J Med. 2010. 362:1312-24.

5 Tentori F, Blayney MJ, Albert JM et al. Mortality risk for dialysis patients with different levels of serum calcium, phosphorus, and PTH: the Dialysis Outcomes and Practice Patterns Study (**DOPPS**). Am J Kidney Dis 2008; 52: 519–530.

6 Savica V, A. Calo˙, Monardo P et al. Phosphate binders and management of hyperphosphataemia in end-stage renal disease Nephrol Dial Transplant (2006) 21: 2065–2068

7 Burke SK. Phosphate is a uremic toxin. Journal of Renal Nutrition, Vol 18, No 1 (January), 2008: pp 27–32

8 National Collaborating Centre for Chronic Conditions (NHS, NICE- UK). Chronic kidney disease: national clinical guideline for early identification and management in adults in primary and secondary care. London: Royal College of Physicians, September 2008. Available at: http://guidance.nice.org.uk/CG73

9 The Merck Manual Medical Library. Available online at: http://www.merck.com/mmpe/sec12.html?WT.z_section=Endocrine and Metabolic Disorders

10 Selva O'Callaghan A, San Jose A, Simeon CP et al. M. Fatal hypocalcemia from sodium phosphate enemas. J Am Geriatr Soc. 1995 Dec;43(12):1447-8

11 Kirschbaum B. The acidosis of exogenous phosphate intoxication. Review. Arch Intern Med. 1998 Feb 23;158(4):405-8.

12 Blayney M.J., Tentori F. (2009). Trends and consequences of mineral bone disorder in haemodialysis patients: Lessons from the dialysis outcomes and practice patterns study (DOPPS). Journal of Renal Care 35(s1), 7–13.

13 Floege J. 2008 Calcium-containing phosphate binders in dialysis patients with cardiovascular calcifications: should we CARE-2 avoid them? Nephrol Dial Transplant (2008) 23: 3050–3052

14 Plantinga, L. C., Fink, N. E., Melamed, M. L., and others (2008). Serum phosphate levels and risk of infection in incident dialysis patients. Clin Journal of the American Society of Nephrology 3, pp. 1398-1406.

15 Hutchison AJ. Oral Phosphate Binders. Kidney International (2009) 75, 906–914

16 Health Canada. Food and Nutrition. Dietary Reference Intakes. http://www.hc-sc.gc.ca/fn-an/nutrition/reference/table/ref_elements_tbl-eng.php

17 Sullivan C, Sayre S; Leon JB et al. Effect of Food Additives on Hyperphosphatemia Among Patients With End-stage Renal Disease A Randomized Controlled Trial. JAMA. 2009;301(6):629-635

18 Milas NC, Nowalk MP, Akpele L et al. Factors associated with adherence to the dietary protein intervention in the Modification of Diet in Renal Disease Study. J Am Diet Assoc 1995;95:1295- 300

19 Ford JC, Pope JF, Hunt AE et al. The effect of diet education on the laboratory values and knowledge of hemodialysis patients with hyperphosphatemia. J Ren Nutr 2004; 14: 36–44.

20 Silver J. The details bedevil DCOR. Kidney International 2007;72:1041-1043.

21 Salusky IB. A new era in phosphate binding: What are the options? Kidney International (2006) 70, S10–S15.

22 Barna MM, Kapoian T, O'Mara NB. Sevelamer Carbonate. The Annals of Pharmacotherapy. 2010 January, Volume 44. 127 – 134.

23 AlBaaj F, Hutchison AJ. Hyperphosphatemia in Renal Failure. Causes, Consequences and Current Management. Drugs 2003; 63 (6): 577-596

24 European Best Practice Guideline on Nutrition in CKD. 2007. Available at: http://www.ndt-educational.org/guidelines.asp

25 Pierratos A, McFarlane P, Chan CT. Quotidian dialysis–update 2005. Curr Opin Nephrol Hypertens 2005; 14: 119–124.

26 Lindsay RM, Al-Hejaili F, Nesrallah G. Calcium and phosphate balance with quotidian hemodialysis. Am J Kidney Dis 2003; 42 [Suppl 1]: S24–S29

27 Musci I, Hercz G, Uldall R, Ouwendyk M, Francoeur R, Pierratos A. Control of serum phosphate without any phosphate binders in patients treated with nocturnal hemodialysis. Kidney Int 1998; 53: 1399–1404

28 Micromedex® online. 2010. Monographs – Calcium Salts, Amphojel®, Basaljel®, Magnesium Hydroxide, Renagel®, Renvela®, Fosrenol®. Accessed May 2nd, 2010.

29 e-CPS. Ottawa (ON): Canadian Pharmacists Association. c2009. Monographs – Calcium Salts, Amphojel®, Basaljel®, Magnesium Hydroxide, Renagel®, Fosrenol®. Available from: https://www.e-therapeutics.ca/wps/portal/!ut/p/.scr/Login.

30 AHFS-DI online. 2010. Monographs – Calcium Salts, Amphojel®, Basaljel®, Magnesium Hydroxide, Renagel®, Renvela®, Fosrenol®. Accessed May 2nd, 2010.

31 Briggs G, Freeman, Roger, Yaffe, Sumner, ed. Drugs in Pregnancy and Lactation. 9th ed: TechBooks

32 McGuinnes B, Logan JI. Milk alkali syndrome. Ulster Med J. 2002 November; 71(2): 132–135

33 Ross EA, Szabo NJ, Tebbett IR. Lead Content of Calcium Supplements. JAMA. 2000;284:1425-1429.

34 Navaneethan SD, Palmer SC, Craig JC et al. Benefits and Harms of Phosphate Binders in CKD: A **Systematic Review** of Randomized Controlled Trials. Am J Kidney Dis 54:619-637.

35 Schaefer K, Scheer J, Asmus G et al: The treatment of uraemic hyperphosphataemia with calcium acetate and calcium carbonate: A comparative study. Nephrol Dial Transplant.1991. 6:170-175.

36 Cannata-Andia, JB, Fernandez-Martin, JL. The clinical impact of aluminium overload in renal failure. Nephrol Dial Transplant 2002; 17 Suppl 2:9.

37 Llanyee L, Hershman JM.Conditions and Drugs interfering with thyroxine absorption.Best Practice & Research Clinical Endocrinology & Metabolism. 2009. 23;781–792

38 Friedman EA: Calcium-based phosphate binders are appropriate in chronic renal failure. Systematic Review. Clin J Am Soc Nephrol.2006. 1:704-709.

39 Almirall J, Veciana L, Llibre J: Calcium acetate versus calcium carbonate for the control of serum phosphorus in hemodialysis patients. Am J Nephrol 1994. 14:192-196

40 Micromedex 2010. Sucralfate.

41Massey L Magnesium therapy for nephrolithiasis. Magnes Res. 2005 Jun;18(2):123-6.

42 Guillot AP, Hood VL, Runge CF, Gennari FJ: The use of magnesium-containing phosphate binders in patients with endstage renal disease on maintenance hemodialysis. Nephron 30: 114-117, 1982

43 Delmez JA, Kelber J, Norward KY et al. Magnesium carbonate as a phosphorus binder: A prospective, controlled, crossover study. Kidney International 1996 (49): 163-167.

44Spiegel DM, Farmer B, Smits G et al. Magnesium Carbonate is an effective Phosphate binder for Chronic Hemodialysis Patients: A pilot study. J Renal Nutrition. 2007. 17(6); 416-422.

45 Suki WN et al. Effects of sevelamer and calcium-based phosphate binder on mortality in hemodialysis patients (DCOR). Kidney International. 2007;72:1130-1137.

46 Manns B, Klarenbach S, Lee H, Culleton B, Shrive F, Tonelli M. Economic evaluation of sevelamer in patients with end-stage renal disease. Nephrol Dial Transplant 2007;22:2867-78.

47 Sturtevant J, Hawley CM, Reiger K et al. Efficacy and side-effect profile of sevelamer hydrochloride used in combination with conventional phosphate binders. Nephrology. 2004. 9. 406-413.

48 9 studies: CADTH Health Technology Inquire Service. Sevelamer Hydrochloride for the Treatment of Patients with Chronic Kidney Disease : A Review of the Clinical Effectiveness. September 8th 2009. Available at: http://www.cadth.ca/index.php/en/hta/reports-publications/search/publication/665

49 Chertow GM, Dillon M, Burke SK, et al: A randomized trial of sevelamer hydrochloride (RenaGel) with and without supplemental calcium. Strategies for the control of hyperphosphatemia and hyperparathyroidism in hemodialysis patients. Clin Nephrol. 1999. 51:18-26.

50 Koiwa F, Onoda N, Kato H, et al: Prospective randomized multicenter trial of sevelamer hydrochloride and calcium carbonate for the treatment of hyperphosphatemia in hemodialysis patients in Japan. Ther Apher Dial :340-346, 2005

51 Medical Letter. Phosphate Binders. Feb. 13, 2006.

52 Pai AB, Shepler BM. Comparison of Sevelamer hydrochloride and Sevelamer Carbonate: Risk of Metabolic Acidosis and Clinical Implications. Pharmacotherapy. 2009. 29(5):554-561.

53 Namagondlu G, Main N, Yates L et al. Lanthanum associated abnormal liver function tests in two patients on dialysis: a case report. J Med Case Reports. 2009 Dec 9;3:9321.

54 Weitzman S, Ginsburg KC, Carlson HE. Colesevelam hydrochloride and lanthanum carbonate Interfere with the absorption of Levothyroxine. Thyroid. 2009. 19 (1)77-79.

55 E-cps; Product Monograph, Fosrenol®

56 How PP, Mason DL, Lau AH. Current Approaches in the treatment of Chronic Kidney Disease Mineral and Bone Disorder. J Pharmacy Practice. 2008. 21(3)196-213.

57 CADTH-CEDAC final recommendations on reconsideration and reasons for recommendation: Lanthanum carbonate hydrate.2008. (http://wwwcadth.ca/media/cdr/complete/cdr_complete_Fosrenol_February-29-2008.pdf)

58 Davis RL, Abraham JL. Lanthanum deposition in a dialysis patient. Nephrol Dial Transplant. 2009. 24:3247-3250.

59 Fosrenol (lanthanum carbonate). Pharmacist's Letter/Prescriber's Letter 2007;23(4):230419.

60Jaffe, JA, Liftman, C, Glickman, JD. Frequency of elevated serum aluminum levels in adult dialysis patients. Am J Kidney Dis 2005; 46:316

61Goldsmith DR et al. Sevelamer hydrochloride: a review of its use for hyperphosphataemia in pts with end-stage renal disease on haemodialysis. Drugs 2008;68:85-104

62 Poulouse J, Medscape Clinical Meetings 2010, Abstract Poster 180. Presented April 14, 2010

63 Bellasi A, Kooienga L, Block GA. Phosphate Binders: New products and challenges. Hemodialysis International.2006:10-225-234.

64 Savica V, Calò LA, Monardo P et al. (2009) Salivary phosphate-binding chewing gum reduces hyperphosphatemia in dialysis patients. J Am Soc Nephrol.2009. 20:639–644.

Additional References: **PHOSPHATE BINDERS in HYPERPHOSPHATEMIA of CKD**

1. Abboud H, Henrich WL. Stage IV Chronic Kidney Disease. N Engl J Med. 2010. 32; 56-65.
2. Block GA, Spiegel DM, Ehrlich J et al. Effects of sevelamer and calcium on coronary artery calcification in patients new to dialysis. Kidney International. 2005. 68:1815-1824.- New HD pts with no evidence of coronary calcification compared to pts with evidence of at least mild coronary calcification who had SIG progression. Use of Ca-containing binders resulted in more rapid progression than did use of sevelamer in such pts.
3. Brewster UC, Ciampi MA, Abu-Alfa AK et al. Long-term comparison of sevelamer hydrochloride to calcium-containing phoshate binders. Nephrology.2006. 11:142-146. -N=30 HD pts, Pts on sevelamer for >1 yr compared to those on calcium binders had a lower serum bicarb conc, a higher serum phosphorus and a higher CaXP product.
4. Braun J, Asmus HG, Holzer H et al. Long-term comparison of a calcium-free phosphate binder and calcium carbonate- phosphorus metabolism and cardiovascular calcification. Clin Nephrol. 2004; 62(2):104-115.
5. Block GA, Klassen PS, Lazarus JM et al. Mineral metabolism, mortality and morbidity in maintenance hemodialysis. J Am Soc Nephrol. 2004. 15(8):2208-18.
6. Block GA et al. Mortality effect of coronary calcification and phosphate binder choice in incident hemodialysis patients. Kidney International. 2007;71:438-441.
7. CKD-MBD as a systemic disorder. Editorial. Bone. 2009. 45:S1. – describes term CKD-MBD, discusses spectrum of bone disease in CKD (high turnover bone disease (osteitis fibrosa, renal osteodystrophy) to low turnover bone disease (osteomalacia, adynamic bone disease), vascular calcification.
8. Coladonato JA. Control of Hyperphosphatemia among Patients with ESRD. J Am Soc Nephrol. 2005. 16:S107-S114.
9. CSN Hemodialysis Clinical Practice Guidelines. J Am Soc Nephrol 2006. 17: S1-S27.
10. Curran MP, Robinson DM. Lanthanum Carbonate. A review of its use in lowering Serum phosphate in pts with ESRD. Drugs. 2009. 69(16):2329-2349.
11. Geary DF, Hodson EM, Craig JC. Interventions for bone disease in children with CKD. Cochrane Review. Jan. 2010. Issue 1.
12. Ganesh SK, Stack AG, Levin NW et al. Associationof Elevated Serum PO4, Ca x PO4 Product and Parathyroid Hormone with Cardiac Mortality Risk in Chronic Hemodialysis Patients. J Am Soc Nephrol. 2001. 12: 2131-2138. – Study Identifies relationships between elevated serum PO4, CaxPO4 product & PTH and cardiac causes of death in HD pts, especially deaths resulting from CAD & sudden death.
13. Jamal SA, Fitchett D, Lok CE et al. The effects of calcium-based versus non-calcium based phosphate binders on mortality among pts with CKD : a meta-analysis. Nephrol Dial Transplant. 2009. 24:3168-3174. – Did not find a statistically SIG difference in cardiovascular mortality and coronary artery calcification in pts receiving calcium-based phosphate binders compared to non-calcium-based binders. However the data are limited! by the small number of studies and the confidence intervals do not exclude a potentially important beneficial effect. Further RCTs are needed.
14. Kazama JJ. Oral Phosphate binders: History and Prospects. Bone. 2009. 45:S8-S12.
15. Martin KJ, Gonzalez EA. Metabolic Bone disease in CKD. J Am Soc Nephrol. 2007.18:875-885.
16. Mohammed I, Hutchison AJ. Oral Phosphate Binders for the management of serum phosphate levels in dialysis patients. J of Renal Care. 35(21).65-70.
17. Moe SM. Disorders Involving Calcium, Phosphorus and Magnesium. Prim Care. 2008. June; 35(2):215-vi.
18. Persy VP, Behets GJ, Bervoets AR et al. Lanthanum a safe phosphate binder.Seminars in Dialysis. 19(3):195-199.
19. Qunibi W, M Moustafa, Muenz LR et al. A 1 yr Randomized trial of Calcium Acetate vs Sevelamer on Progression of Coronary Artery Calcification in Hemodialysis Patients with Comparable Lipid Control: The Calcium Acetate Renagel Evaluation-2 (CARE-2) Study. Am J Kidney Dis.2008. 51:952-965.
20. Qunibi WY. Consequences of hyperphosphatemia in pts with ESRD. Kidney International. 2004. 66:S8-S12.
21. Rees L, Shroff R. Phosphate binders in CKD: chalking out the differences. Pediatr Nephrol. 2010. 25:385-394.
22. Ring T et al. Calcium acetate versus calcium carbonate as phosphorus binders in patients on chronic haemodialysis: a controlled study. Nephrology Dialysis Transplantation. 1993;8:341-346.
23. Ruffino M, De Bonis E, Martin M et al. Is it possible to control hyperphosphatemia with diet, without inducing protein malnutrition? Nephrol Dial Transplant. 1998. 12 (Supp 3):65-67.- In chronic HD pts, a neutral phosphate balance is hard to achieve despite binder therapy, when protein intake is >50g. Additional protein restriction may impose risk of protein malnutrition.
24. Sprague SM, Abboud H, Qiu P et al. Lanthanum Carbonate Reduces Phosphorus Burden in Patients with CKD Stages 3 and 4: An RCT. Clin J Am Soc Nephrol. 2009. 4:178-185.
25. St Peter W, Liu J, Weinhandl E et al. A Comparison of Sevelamer and Calcium-based Phosphate Binders on Mortality, Hospitalization and Morbidity in Hemodialysis: A Secondary Analysis of the Dialysis Clinical Outcoes Revisited (DCOR) Randomized Trial Using Claims Data. Am J Kidney Dis. 2008. 51:445-454.
26. Add in: O'Donovan R. Lancet 1986. MgCO3 as a binder. 0.5 – 1.5g/d.
27. Matro R, Shnitser A, Spodik M, et al. Efficacy of Morning-Only Compared With Split-Dose Polyethylene Glycol Electrolyte Solution for Afternoon Colonoscopy: A Randomized Controlled Single-Blind Study. Am J Gastroenterol. 2010 Apr 20
28. Prie, Dominique, Friedlander, Gerard. Genetic Disorders of Renal Phosphate Transport. N Engl J Med 2010 362: 2399-2409.
29. Palmer SC, McGregor DO, Craig JC, Elder G, Macaskill P, Strippoli GF. **Vitamin D compounds** for people with chronic kidney disease not requiring dialysis. Cochrane Database Syst Rev. 2009 Oct 7;(4):CD008175.
30. Gutierrez, Orlando M., Anderson, Cheryl, Isakova, Tamara, et al. on behalf of the CRIC Study Group, **Low Socioeconomic Status** Associates with Higher Serum Phosphate Irrespective of Race. J Am Soc Nephrol 2010 0: ASN.2010020221.
31. Mehrotra Rajnish; Chiu Yi-Wen; Kalantar-Zadeh Kamyar; et al. Similar Outcomes With **Hemodialysis and Peritoneal Dialysis** in Patients With End-Stage Renal Disease. Arch Intern Med. 2010;0(2010):archinternmed.2010.352.
32. Block GA, Hulbert-Shearon TE, Levin NW, Port FK. Association of serum phosphorus and calcium x phosphate product with mortality risk in chronic hemodialysis patients: a national study. Am J Kidney Dis. 1998 Apr;31(4):607-17.
33. **FHN** Trial Group. In-Center **Hemodialysis Six Times** per Week versus Three Times per Week. November 20, 2010 (10.1056/NEJMoa1001593)
34. Moe SM, Zidehsarai MP, Chambers MA, et al. **Vegetarian** Compared with Meat Dietary Protein Source and Phosphorus Homeostasis in Chronic Kidney Disease. Clin J Am Soc Nephrol. 2010 Dec 23.
35. Pallan S, Khan A. **Primary hyperparathyroidism**: Update on presentation, diagnosis, and management in primary care. Can Fam Physician. 2011 Feb;57(2):184-9.
36. Palmer Suetonia C., Hayen Andrew, Macaskill Petra, et al. Serum Levels of **Phosphorus, Parathyroid Hormone, and Calcium and Risks of Death and Cardiovascular Disease** in Individuals With Chronic Kidney Disease: A Systematic Review and Meta-analysis. *JAMA*. 2011;305(11):1119-1127.doi:10.1001/jama.2011.308
37. Levey AS, Coresh J. **Chronic kidney disease**. Lancet. 2011 Aug 12.
38. Marcocci C, Cetani F. Clinical practice. **Primary hyperparathyroidism**. N Engl J Med. 2011 Dec 22;365(25):2389-97
39. Thadhani R; Appelbaum E; Pritchett Y, et al. Vitamin D therapy (**paricalcitol**) and **cardiac** structure and function in patients with chronic kidney disease: The PRIMO randomized controlled trial. JAMA 2012; 307:674-684.
40. Daugirdas JT, Chertow GM, Larive B, et al Effects of **Frequent Hemodialysis** on Measures of CKD Mineral and Bone Disorder. J Am Soc Nephrol. 2012 Feb 23. (control of hyperphosphatemia)
41. Vondracek SF, Hoody DW. Combination vitamin D therapy in stage 5 chronic kidney disease. Ann Pharmacother. 2011 Jul;45(7-8):1011-5.
42. Pallan S, Rahman MO, Khan AA. Diagnosis and management of **primary hyperparathyroidism**. BMJ. 2012 Mar 19;344:e1013.
43. Vegter S, Tolley K, Keith MS, et al. Cost-Effectiveness of Lanthanum Carbonate in the Treatment of Hyperphosphatemia in Dialysis Patients: A Canadian Payer Perspective. Clin Ther. 2012 Jun 26.
44. **EVOLVE** Trial Investigators. Effect of **cinacalcet** on cardiovascular disease in patients undergoing dialysis. N Engl J Med 2012. DOI: 10.1056/NEJMoa1205624.
45. van Ballegooijen AJ, Visser M, Kestenbaum B, et al. Relation of Vitamin D and **Parathyroid Hormone** to Cardiac Biomarkers and to Left Ventricular Mass (from the Cardiovascular Health Study). Am J Cardiol. 2012 Nov 17.
46. Health Canada Mar/13 cautions against use of **Sensipar in children**. Following the death of a child enrolled in a clinical trial for the drug Sensipar in the United States, Health Canada is reminding healthcare professionals and consumers that Sensipar is not approved for use in patients under 18 years of age. Sensipar (cinacalcet) is used for treating disorders of the parathyroid gland that result in high blood calcium levels.
47. Shobeiri N, Adams MA, Holden RM. **Phosphate**: an old bone molecule but new **cardiovascular risk factor**. Br J Clin Pharmacol. 2013 Mar 19.
48. Di Iorio B, Bellasi A, Russo D; INDEPENDENT Study Investigators. Mortality in kidney disease patients treated with **phosphate binders**: a randomized study. Clin J Am Soc Nephrol. 2012;7:487-493. (sevelamer)
49. Navaneethan SD, Palmer SC, Vecchio M, Craig JC, Elder GJ, Strippoli GF. Phosphate binders for **preventing and treating bone disease** in chronic kidney disease patients. Cochrane Database Syst Rev. 2011 Feb 16;(2):CD006023. doi: 10.1002/14651858.CD006023.pub2. Available phosphate-binding agents have been shown to reduce phosphorus levels in comparison to placebo. However, there are insufficient data to establish the comparative superiority of novel non-calcium binding agents over
calcium-containing phosphate binders for patient-level outcomes such as all-cause mortality and cardiovascular end-points in CKD.
50. Rao N, Crail S. Images in clinical medicine. **Metastatic calcification** and long-term hemodialysis. N Engl J Med. 2013 Jun 20;368(25):2415. (**Warfarin association with high calcium-phosphorus product**)
51. Jamal SA, Vandermeer B, Raggi P, et al. Effect of **calcium-based versus non-calcium-based phosphate binders** on mortality in patients with chronic kidney disease: an updated systematic review and meta-analysis. Lancet 2013; online July 19.
52. NICE: National Institute for Health and Clinical Excellence. **Hyperphosphataemia** in chronic kidney disease. Management of hyperphosphataemia in patients with stage 4 or 5 chronic kidney disease. London (UK): National Institute for Health and Clinical Excellence (NICE); 2013 Mar. 22 p. (Clinical guideline; no. 157).

53. de Borst MH, Hajhosseiny R, Tamez H, et al. **Active Vitamin D** Treatment for Reduction of Residual **Proteinuria**: A Systematic Review. J Am Soc Nephrol. 2013 Aug 8.
54. KDOQI: National Kidney Foundation. **KDOQI** clinical practice guideline for diabetes and CKD: 2012 update. Am J Kidney Dis. 2012 Nov;60(5):850-86.
55. Health Canada Oct/13 has completed a safety review of the drug Sensipar (**cinacalcet**) that identified a possible link between the drug and abnormal heart rhythm (**QT**) associated with low blood calcium.
56. Sakhuja A, Hyland J, Simon JF. **Managing advanced chronic kidney disease**: A primary care guide. Cleve Clin J Med. 2014 May;81(5):289-99.
57. Lemoine S, Guebre-Egziabher F, Sens F, Nguyen-Tu MS, Juillard L, Dubourg L,Hadj-Aissa A. Accuracy of **GFR Estimation in Obese Patients**. Clin J Am Soc Nephrol. 2014 Feb 20.
58. Nesrallah GE, Mustafa RA, Clark WF, et al. **Canadian Society of Nephrology 2014** clinical practice guideline for timing the **initiation of chronic dialysis**. CMAJ. 2014 Feb 4;186(2):112-7.
59. **Screening, Monitoring, and Treatment of Early Stage Chronic Kidney Disease**: Recommendations from the **American College of Physicians**. Ann Intern Med. 2013 Oct 22
60. Peeters MJ, van Zuilen AD, van den Brand JA, et al. **Nurse Practitioner** Care Improves Renal Outcome in Patients with CKD. J Am Soc Nephrol. 2013 Oct 24. In conclusion, additional support by nurse practitioners attenuated the decline of kidney function and improved renal outcome in patients with CKD.
61. van Walraven C, Manuel DG, Knoll G. **Survival Trends in ESRD** Patients Compared With the General Population in the United States. Am J Kidney Dis. 2013 Nov 6. doi:pii: S0272-6386(13)01227-4.
62. Manns BJ, Hodsman A, Zimmerman DL, Mendelssohn DC, Soroka SD, Chan C, Jindal K, Klarenbach S. Canadian Society of Nephrology commentary on the 2009 KDIGO Clinical Practice Guideline for the Diagnosis, Evaluation, and Treatment of CKD-Mineral and Bone Disorder (CKD-MBD). Am J Kidney Dis. 2010 May;55(5):800-12.
63. **Keith MS, Sibbel S, Copley JB, et al. Real-World Dose-Relativity, Tablet Burden, and Cost Comparison of Conversi**on Between Sevelamer Hydrochloride/Carbonate and Lanthanum Carbonate Monotherapies. Clin Ther. 2014 Aug 19
64. Keith MS, Wilson RJ, Preston P, et al. **Cost-Minimization Analysis of Lanthanum Carbonate Versus Sevelamer** Hydrochloride in US Patients With End-Stage Renal Disease. Clin Ther. 2014 Jul 25.
65. Glendenning P, Bell DA, Clifton-Bligh RJ. Investigating **hypophosphataemia**. BMJ. 2014 May 28;348:g3172.
66. Wiebe N, Klarenbach SW, Allan GM, et al. Alberta Kidney Disease Network. Potentially **Preventable Hospitalizatio**n as a Complication of CKD: A Cohort Study. Am J Kidney Dis. 2014 Apr 12. pii: S0272-6386(14)00696-9.
67. Ortiz A, Covic A, Fliser D, et al; Board of the EURECA-m Working Group of ERA-EDTA. Epidemiology, contributors to, and clinical trials of **mortality risk in chronic kidney failure**. Lancet. 2014 May 24;383(9931):1831-43.
68. Hakim RM, Saha S. **Dialysis frequency versus dialysis time**, that is the question. Kidney Int. 2014 May;85(5):1024-9.
69. Bousher A, Al-Makki A, Sutton J, Shepler B. A Review of **Sucroferric Oxyhydroxide** for the Treatment of Hyperphosphatemia in Patients Receiving Dialysis. Clin Ther. 2014 Dec 1;36(12):2082-2093.
70. Umanath K, Jalal DI, Greco BA, et al; for the Collaborative Study Group. **Ferric Citrate** Reduces Intravenous Iron and Erythropoiesis-Stimulating Agent Use in ESRD. J Am Soc Nephrol. 2015 Mar 3.
71. Ballinger AE, Palmer SC, Nistor I, Craig JC, Strippoli GF. **Calcimimetics for secondary hyperparathyroidism** in chronic kidney disease patients. Cochrane Database Syst Rev. 2014;12:CD006254.
72. Moe SM, Chertow GM, Parfrey PS, et al; Evaluation of Cinacalcet HCl Therapy to Lower Cardiovascular Events (**EVOLVE**) Trial Investigators*. **Cinacalcet**, Fibroblast Growth Factor-23, and Cardiovascular Disease in Hemodialysis: The Evaluation of Cinacalcet HCl Therapy to Lower Cardiovascular Events (EVOLVE) Trial. Circulation. 2015 Jul 7;132(1):27-39.
73. Floege J, Covic AC, Ketteler M, et al. PA21 Study Group. A phase III study of the efficacy and safety of a novel **iron-based phosphate binder** in dialysis patients. Kidney Int. 2014 Sep;86(3):638-47.
74. Patel L, Bernard LM, Elder GJ. **Sevelamer Versus Calcium-Based Binders** for Treatment of Hyperphosphatemia in CKD: A Meta-Analysis of Randomized Controlled Trials. Clin J Am Soc Nephrol. 2015 Dec 14.
75. Lewis JB, Sika M, Koury MJ, et al Collaborative Study Group. **Ferric citrate** controls phosphorus and delivers iron in patients on dialysis. J Am Soc Nephrol. 2015 Feb;26(2):493-503.
76. Palmer SC, Gardner S, Tonelli M, et al. **Phosphate-Binding Agents in Adults With CKD**: A Network Meta-analysis of Randomized Trials. Am J Kidney Dis. 2016 Jul 22.
77. Block GA, Bushinsky DA, Cunningham J, et al. Effect of **etelcalcitide** vs placebo on serum parathyroid hormone in patients receiving hemodialysis with secondary hyperparathyroidism: two randomized clinical trials.JAMA. doi:10.1001 /jama.2016.19456
78. Block GA, Bushinsky DA, Cheng S, et al. Effect of **etelcalcitide vs cinacalcet** on serum parathyroid hormone in patients receiving hemodialysis with secondary hyperparathyroidism: a randomized clinical trial.JAMA. doi:10.1001/jama.2016.19468
79. Cho JH, Jang HM, Jung HY, et al. A Real-world **Cost-effectiveness Analysis of Sevelamer Versus Calcium Acetate** in Korean Dialysis Patients. Clin Ther. 2017 Mar 10.
80. Bilezikian JP, Bandeira L, Khan A, et al. **Hyperparathyroidism**. Lancet.2017 Sep 15.
81. KDIGO : Kidney Disease: Improving Global Outcomes (**KDIGO**) CKD-MBD Update Work Group. KDIGO 2017 clinical practice guideline update for the diagnosis, evaluation, prevention, and treatment of **chronic kidney disease–mineral and bone disorder (CKD-MBD).** Kidney Int Suppl. 2017 Jul;7(1):1-59.
82. Sahbudin I, Peall A, Filer A. **Lanthanum carbonate** in chronic renal failure. BMJ 2016 Jan 19; 352:ij58.
83. Srivastava T, Jafri S, Truog WE, et al. Successful Reversal of **Furosemide-Induced Secondary Hyperparathyroidism With Cinacalcet**. Pediatrics. 2017 Dec;140(6).
84. Insogna KL. Primary Hyperparathyroidism. N Engl J Med. 2018 Sep 13;379(11):1050-1059.
85. Ring Madsen L, Espersen R, Rejnmark L, et al. Effect **of calcium citrate vs calcium carbonate on elevated parathyroid hormone** after Roux-en-Y gastric bypass. A double-blinded, randomized trial. Clin Endocrinol (Oxf). 2018 Aug 14.
86. Ruospo M, Palmer SC, Natale P, et al. **Phosphate binders for preventing and treating chronic kidney disease-mineral and bone disorder (CKD-MBD).** Cochrane Database Syst Rev. 2018 Aug 22;8:CD006023. In studies of adults with CKD G5D treated with dialysis, sevelamer may lower death (all causes) compared to calcium-based binders and incur less treatment-related hypercalcaemia, while we found no clinically important benefits of any phosphate binder on cardiovascular death, myocardial infarction, stroke, fracture or coronary artery calcification. The effects of binders on patient-important outcomes compared to placebo are uncertain. In patients with CKD G2 to G5, the effects of sevelamer, lanthanum, and iron-based phosphate binders on cardiovascular, vascular calcification, and bone outcomes compared to placebo or usual care, are also uncertain and they may incur constipation, while iron-based binders may lead to diarrhoea.

Drug Interactions: References

1. Stockley's Drug Interactions (10th Ed). intro
2. Drug interactions-principles & practice - AustralianPrescriber-12
3. Van Hoover, C. and McCraw, V. D. (2007), The **Top 100 Drug Interactions**. A Guide to Patient Management; By Philip D. Hansten, PharmD and John R. Horn, PharmD. Freeland, WA: H&H Publications, 2006. 226 pages.
4. Lexi-comp Interactions
5. Shapiro LE, Shear NH. Drug-drug interactions: how scared should we be? CMAJ. 1999;161(10):1266-1267.
6. Katz IR, Jeste DV, Mintzer JE, Clyde C, Napolitano J, Brecher M. Comparison of risperidone and placebo for psychosis and behavioral disturbances associated with dementia: a randomized, double-blind trial. **Risperidone** Study Group. J Clin Psychiatry. 1999 Feb;60(2):107-15.
7. Zhanel GG, Siemens S, Slayter K, et al. **Antibiotic and oral contraceptive** drug interactions: Is there a need for concern? The Canadian Journal of Infectious Diseases. 1999;10(6):429-433.
8. Wilkinson GR. Drug metabolism and variability among patients in drug response. N Engl J Med. 2005 May 26;352(21):2211-21.
9. Boyer EW, Shannon M. The **serotonin syndrome**. N Engl J Med. 2005 Mar 17;352(11):1112-20.
10. Lithium DIs: Finley PR, Warner MD, Peabody CA "Clinical relevance of drug interactions with **lithium**." Clin Pharmacokinet 29 (1995): 172-91
11. Juurlink DN, Mamdani MM, Lee DS, Kopp A, et al. Rates of hyperkalemia after publication of the Randomized **Aldactone** Evaluation Study. N Engl J Med. 2004 Aug 5;351(6):543-51.
12. Fralick M, Macdonald EM, Gomes T, Antoniou T, et al; Canadian Drug Safety and Effectiveness Research Network. **Co-trimoxazole** and sudden death in patients receiving **inhibitors** of **renin-angiotensin system**: population based study. BMJ. 2014 Oct 30;349:g6196.
13. Antoniou T, Gomes T, Juurlink DN, Loutfy MR, Glazier RH, Mamdani MM. **Trimethoprim-sulfamethoxazole**-induced hyperkalemia in patients receiving inhibitors of the renin-angiotensin system: a population-based study. Arch Intern Med2010;170:1045-9
14. Sipe BE, Jones RJ, Bokhart GH. Rhabdomyolysis causing AV blockade due to possible **atorvastatin, esomeprazole, and clarithromycin** interaction. Ann Pharmacother.2003;37(6):808-11.
15. Lee AJ, Maddix DS. Rhabdomyolysis secondary to a drug interaction between **simvastatin and clarithromycin**. Ann Pharmacother. 2001 Jan;35(1):26-31.
16. Goldberg RM, Mabee J, Chan L, Wong S. Drug-drug and drug-disease interactions **in the ED**: analysis of a high-risk population. Am J Emerg Med. 1996 Sep;14(5):447-50.
17. 8As – Table - David N Juurlink, Canadian Medical Association Journal 2007;177(4):369-71
18. Indiana University CYP450 Drug Interaction Table: http://medicine.iupui.edu/clinpharm/ddis/clinical-table/
19. PL Detail-Document, **P-glycoprotein** Drug Interactions. Pharmacist's Letter/Prescriber's Letter. October 2013.
20. PL Detail Document, **OATP** Drug Interactions. Pharmacist's Letter/Prescriber's Letter. March 2014.
21. PL Detail Document, **Cytochrome P450** Drug Interactions. Pharmacist's Letter/Prescriber's Letter. October 2013.
22. Kalliokoski A, Niemi M. Review: Impact of **OATP** Transporters on Pharmacokinetics. BJP. 2009; 158: 693-705.
23. Contradictions in Contraindications for Drug-Drug Interactions-AnnPharm-11
24. DI-article-AFP-Mar 2000
25. CYP3A4 – Hansten & Horn – Newsletter 2008
26. Juurlink DN, Mamdani M, Kopp A, et al. Drug-drug interactions **among elderly patients** hospitalized for drug toxicity. JAMA. 2003 Apr 2;289(13):1652-8.
27. Blondeau J, Chan C, Davidson R. Judicious use of antibiotics to minimize emerging resistance: the macrolide **clarithromycin** as a case study. Clinical Practice. May 2013 ,Vol. 10, No. 3, Pages 359-370
28. Tan A, Holmes HM, Kuo Y-F, Raji MA, Goodwin JS. Coadministration of **Co-trimoxazole With Sulfonylureas**: Hypoglycemia Events and Pattern of Use. The Journals of Gerontology Series A: Biological Sciences and Medical Sciences. 2015;70(2):247-254.
29. Lee JW, Morris JK, Wald NJ. **Grapefruit Juice and Statins**. Am J Med. 2016 Jan;129(1):26-9.
30. **ACCORD**: Action to Control Cardiovascular Risk in Diabetes Study Group, Gerstein HC, Miller ME, Byington RP, Goff DC Jr, Bigger JT, Buse JB, et al. Effects of intensive glucose lowering in type 2 diabetes. N Engl J Med. 2008 Jun 12;358(24):2545-59.
31. 2019 American Geriatrics Society Beers Criteria® Update Expert Panel, Fick DM, Semla TP, Steinman M, et al. American Geriatrics Society 2019 updated AGS Beers Criteria® for potentially inappropriate medication use in older adults. Journal of the American Geriatrics Society. 2019 Apr;67(4):674-94.
32. Madadi P, Koren G, Cairns J, Chitayat D, Gaedigk A, Leeder JS, Teitelbaum R,Karaskov T, Aleksa K. Safety of **codeine during breastfeeding**: fatal morphine poisoning in the breastfed neonate of a mother prescribed codeine. Can Fam Physician. 2007 Jan;53(1):33-5.
33. Kotlinska-Lemieszek A, Klepstad P, Haugen DF. Clinically significant drug-drug interactions involving **opioid analgesics** used for pain treatment in patients with cancer: a systematic review. Drug Des Devel Ther. 2015 Sep 16;9:5255-67.
34. Kim MG, Kim Y, Jeon JY, et al. Effect of fermented **Red ginseng** on cytochrome P450 and P-glycoprotein activity in healthy subjects, as evaluated using the cocktail approach. Br J Clin Pharmacol. 2016 Aug 6

35. Miesner AR, Ausman M, Dagraedt B, et al. Probable Drug Interaction Between **Everolimus and Clarithromycin**. Ann Pharmacother. 2016 Aug;50(8):689-90.
36. Ferry SA, Holm SE, Stenlund H, Lundholm R, Monsen TJ. Clinical and bacteriological outcome of different doses and duration of **piv-mecillinam** compared with placebo therapy of uncomplicated lower urinary tract infection in women: the LUTIW project. Scand J Prim Health Care 2007; 25:49–57.
37. Stein GE. Comparison of single-dose **fosfomycin** and a 7-day course of **nitrofurantoin** in female patients with uncomplicated urinary tract infection. Clin Ther 1999; 21:1864–72.
38. Donneyong MM, Bykov K, Bosco-Levy P, et al. Risk of mortality with concomitant use of **tamoxifen and selective serotonin reuptake inhibitors**: multi-database cohort study. BMJ. 2016 Sep 30;354:i5014.
39. Parsad S, Ratain MJ. Drug-Drug Interactions **With Oral Antineoplastic Agents**. JAMA Oncol. 2016 Oct 13.
40. Wiggins BS, Saseen JJ, Page RL 2nd, et al. Recommendations for Management of Clinically Significant **Drug-Drug Interactions With Statins** and Select Agents Used in Patients With Cardiovascular Disease: A Scientific Statement From the American Heart Association. Circulation. 2016 Oct 17.
41. Hammann F, Gotta V, Conen K, et al. Pharmacokinetic interaction between **taxanes and amiodarone** leading to severe toxicity. Br J Clin Pharmacol. 2016 Nov 20.
42. Levy I, Attias S, Ben-Arye E, et al. Adverse Events associated with **Interactions with Dietary and Herbal Supplements** among Inpatients. Br J Clin Pharmacol. 2016 Oct 19.
43. Reeves D, DiDominick S, Finn S, et al. **Methotrexate** Elimination When Coadministered With **Levetiracetam**. Ann Pharmacother. 2016 Dec;50(12):1016-1022.
44. Smolders EJ, Colbers A, de Kanter CTMM, et al. **Metformin and daclatasvir**: absence of a pharmacokinetic-pharmacodynamic drug interaction in healthy volunteers. Br J Clin Pharmacol. 2017 May 5.
45. Nishimoto M, Koh H, Tokuwame A, et al. Drug interactions and safety profiles with concomitant use of **caspofungin and calcineurin inhibitors** in allogeneic hematopoietic cell transplantation. Br J Clin Pharmacol. 2017 Apr 13.
46. Rabinovich-Guilatt L, Steiner L, Hallak H, et al. **Metoprolol-pridopidine** drug-drug interaction and food effect assessments of pridopidine, a new drug for treatment of Huntington Disease. Br J Clin Pharmacol. 2017 Apr 27.
47. Deljehier T, Pariente A, Miremont-Salamé G, et al. **Rhabdomyolysis** after co-administration of a **statin and fusidic acid**: an analysis of the literature and of the WHO database of adverse drug reactions. Br J Clin Pharmacol. 2018 Jan 16.
48. Merel SE, Paauw DS. **Common Drug Side Effects and Drug-Drug Interactions in Elderly** Adults in Primary Care. J Am Geriatr Soc. 2017 Jul;65(7):1578-1585.
49. van Sloten TT, de Klaver PAG, van den Wall Bake AWL. Co-administration of **cyclosporine and ticagrelor** may lead to a higher exposure to cyclosporine: a case report of a 49-year old man. Br J Clin Pharmacol. 2017 Sep 11.

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References

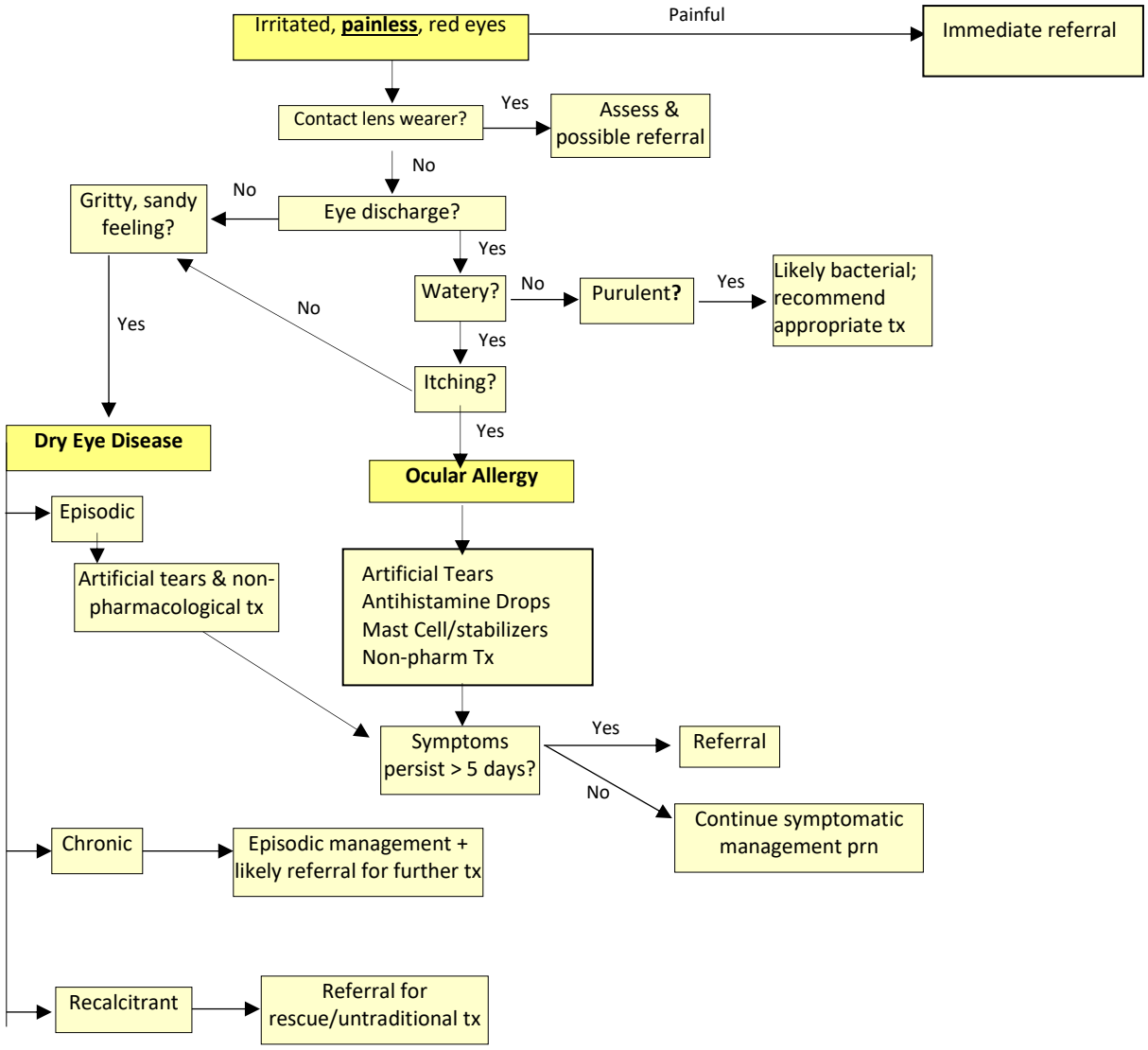
1. Prokopich CL, Bitton E, Caffery B, Michaud L, Cunningham DN, Karpekci PM, et al. Screening, Diagnosis and Management of Dry Eye Disease: Practical Guidelines for Canadian Optometrists. Canadian Journal of Optometry 2014;76:Suppl 1.
2. Donnenfeld E. Deciphering Dry Eye Syndrome and Ocular Allergy: Accurate Diagnosis and Appropriate Treatment (Peer View in Review CME). 2016. Available at: www.peerviewpress.com/NHS900.
3. 2007 Report of the International Dry Eye Workshop (DEWS). The Ocular Surface 2007;5(2).
4. RxTx – Dry Eye, available through the University of Saskatchewan Pharmacy LibGuide. Accessed 2016 Dec 20.
5. Foster CS. Dry Eye Syndrome – Medscape Article. Available at: http://emedicine.medscape.com/article/1210417-overview. Accessed 2016 Dec 20.
6. American Academy of Ophthalmology Corena/External Disease Panel. Preferred Practice Pattern Guidelines. Dry Eye Syndrome. San Francisco, CA: American Academy of Ophthalmology;2013. Available at: www.aao.org/ppp.
7. Eye Allergy Overview– American Academy of Allergy Asthma & Immunology. Available at: https://www.aaaai.org/conditions-and-treatments/allergies/Eye-Allergy. Accessed 2017 Jan 3.
8. UpToDate – Dry Eyes. Available through the University of Toronto Pharmacy LibGuide. Accessed 2017 Jan 3.
9. RxTx – Restasis. Available through the University of Saskatchewan Pharmacy LibGuide. Accessed 2017 Jan 5.
10. RxTx – Alrex. Available through the University of Saskatchewan Pharmacy LibGuide. Accessed 2017 Jan 5
11. Flarex – Product Monograph. Available through Health Canada Drug Product Database. Accessed 2017 Jan 5.
12. FML – Product Monograph. Available through Health Canada Drug Product Database. Accessed 2017 Jan 5.
13. Maxidex – Product Monograph. Available through Health Canada Drug Product Database. Accessed 2017 Jan 5.
14. Allergan Pred Mild Canadian Drug Monograph – Accessed Jan 6 2017 http://allergan-web-cdn-prod.azureedge.net/allergancanadaspecialty/allergancanadaspecialty/media/actavis-canada-specialty/en/products/pms/pred-mild-pi-2015-03-05_e.pdf
15. Zaditor – Product Monograph. Available through Health Canada Drug Product Database. Accessed 2017 Jan 5.
16. Cromolyn – Product Monograph. Available through Health Canada Drug Product Database. Accessed 2017 Jan 5.
17. Proper Use of Eye Drops – Compendium of Therapeutic for Minor Ailments. Available through the University of Saskatchewan Pharmacy LibGuide. Accessed 2017 Jan 9.
18. Friedman NJ. Impact of dry eye disease and treatment on quality of life. Current Opinion in Ophthlamology. 2010;21:310-16.
19. Pflugelder SC, Maskin SL, Anderson B., et al. A Randomized, Double-Masked, Placebo-Controlled, Multicentre Comparison of Loteprednol Etabonate Ophthalmic Suspension, 0.5%, and Placebo for Treatment of Keratoconjunctivitis Sicca in Patients With Delayed Tear Clearance. American Journal of Ophthalmology 2004;138(3):444-457.
20. Ilyas H, Slonim CB, Braswell GR, et al. Long-term Safety of Loteprednol Etabonate 0.2% in the Treatment of Seasonal and Perennial Allergic Conjuntivitis. Eye & Contact Lens 2004;30(1):10-13.
21. UpToDate – Treatment of dry eye in Sjogren's syndrome. Available through the University of Toronto Pharmacy LibGuide. Accessed 2017 Jan 11.
22. Akpek EK, Lindsley KB, Adyanthaya RS, Swamy R, Baer AN, McDonnell PJ. Treatment of Sjögren's Syndrome – Associated Dry Eye. Ophthalmology 2011;118:1242-1252.
23. Zhu W, Wu Y, Li G, Wang J, Li X. Efficacy of polyunsaturated fatty acids for dry eye syndrome: a meta-analysis of randomized controlled trials. Nutrition Reviews 2014;72(10):662-71.
24. RxTx – Red Eye. Available through the University of Saskatchewan Pharmacy LibGuide. Accessed 2017 Jan 12.
25. Bielory BP, Shah SP, O'Brien TP, Perex VL, Bielory L. Emerging therapeutics for ocular surface disease. Current Opinion in Allergy and Clinical Immunology 2016;16:477-86.
26. Pucker AD, Ng SM, Nichols JJ. Over the counter (OTC) artificial tear drops for dry eye syndrome. *Cochrane Database of Systematic Reviews* 2016, Issue 2. Art. No.: CD009729. DOI: 10.1002/14651858.CD009729.pub2.
27. Sacchetti M, Mantelli F, Lambiase A, Mastropasqua A, Merl D, Bonini S. Systematic review of randomized clinical trialson topical ciclosporin A for the treatment of dry eye disease. British Journal of Opthalmology 2014;98:1016-22.
28. Utine CA, Stern M, Akpek E. Clinical Review: Topical Ophthalmic Use of Cyclosporin A. Ocular Immunology and Inflammation 2010;18(5):352-61.
29. van Rensburg EJ, Meyer D. Astute and safe use of topical ocular corticosteroids in general practice: Practical guidelines. AJOL 2013;31(4):127-9.
30. Lacrisert– Product Monograph. Available through Health Canada Drug Product Database. Accessed 2017 Jan 17.
31. HYLO, HYLO DUAL, HYLO GEL, OCUNOX & CALMO Spray. Available at: http://candorvision.com/. Accessed 2017 Jan 17.
32. Natural Medicines Database – Omega-6 supplements. Available through the University of Saskatchewan Pharmacy LibGuide. Accessed 2017 Jan 17.
33. Castillo M, Scott NW, Mustafa MZ, Azuara-Blanco A. Topical antihistamines and mast cell stabilizers for treating seasonal and perennial allergic conjunctivitis (Review). Cochrane Database of Systematic Reviews 2015. Issue 6. Art. No.: CD009566.
34. Partially Covered Services – Government of Saskatchewan. Available at: https://www.saskatchewan.ca/residents/health/prescription-drug-plans-and-health-coverage/health-benefits-coverage/partially-covered-services. Accessed 2017 Jan 17.
35. Ilyas H, Slonim CB, Braswell GR, Favetta JR, Schulman M. Long-term Safety of Loteprednol Etabonate 0.2% in the Treatment of Seasonal and Perennial Allergic Conjunctivitis. Eye & Contact Lens 2004;30(1):10-13.
36. Hom MM, Asbell P, Barry B. Omegas and Dry Eye: More Knowledge, More Questions. Optometry and Vision Science 2015;92(9):948-56.
37. Natural Medicines Database – Fish Oil. Available through the University of Saskatchewan Pharmacy LibGuide. Accessed 2017 Jan 19.
38. Akpek EK, Lindsley KB, Adyanthaya RS, Swamy R, Baer AN, McDonnell PJ. Treatment of Sjögren's Syndrome – Associated Dry Eye – An Evidence-Based Review. Ophthalmology 2011;118(7):1242-52.
39. Gomes J, Azar D, Baudouin C, et al. TFOS DEWS II iatrogenic report. The Ocular Surface. 2017;15:511-538.
40. Jones L, Downie L, Korb D, et al. TFOS DEWS II Management and therapy report. The Ocular Surface. 2017;15:580-634.
41. Canadian Expert Drug Advsory Committee (CEDAC) Final Recommendation. Cyclosporine Ophthalmic Emulsion 0.05% (Restasis – Allergan, Inc). Canadian Agency for Drugs and Technologies in Health. 2011; June 18. https://www.cadth.ca/media/cdr/complete/cdr_complete_Restatis_Final_July-20-2011_e.pdf, accessed June 30, 2019.
42. Schwartz L. A clear-eyed view of Restasis and chronic dry eye disease. JAMA Internal Medicine. 2018;178(2):181-2.
43. Ismail O, Poole Z, Bierly S et al. Association between dry eye disease and migraine headaches in a large population-based study. JAMA Ophthalmol. 2019 Mar 7.
44. Giannaccare G, Pellegrini M, Sebastiani S, et al. Efficacy of Omega-3 Fatty Acid supplementation for treatment of dry eye disease: a meta-analysis of randomized clinical trials. Cornea. 2019;May:38)5):565-73.
45. Chi S, Tuan H, Kang Y. Effects of polyunsaturated fatty acids on nonspecific typical dry eye disease: a systematic review and meta-analysis of randomized clinical trials. Nutrients. 2019; May:11(5):942.
46. The Dry Eye Assessment and Management Study Research Group. n-3 Fatty Acid Supplementation for the treatment of dry eye disease. N Engl J Med. 2018.378;18:1681-90. **DREAM** study.

47. Craig J, Nelson J, Azar D, et al. TFOS DEWS II Report Executive Summary. The Ocular Surface. 2017;15:802-812.
48. Findlay Q, Reid K. **Dry eye disease**: when to treat and when to refer. Aust Prescr. 2018 Oct;41(5):160-163
49. Ismail OM, Poole ZB, Bierly SL, et al. Association Between **Dry Eye Disease and Migraine Headaches** in a Large Population-Based Study. JAMA Ophthalmol. 2019 Mar 7.

Patient Questionnaires for DED

- Ocular Surface Disease Index
- 5-item Dry Eye Questionnaire (DEQ-5)
- Standard Patient Evaluation of Eye Dryness (SPEED)

Treatment Algorithm for the **Painless**, irritated, red eye.



Artificial Tear Products (adapted from CTMA Ophthalmic Products: Ocular Lubricants Chart)
Products organized by ingredient, but may have varying concentrations

Product	Preservative	Contact Lens Compatible
Sodium carboxymethycellulose		
Refresh Celluvisc	None	No
Refresh Contacts	Purite	Yes
Refresh Endura	None	No
Refresh Liquigel	Purite	Yes
Refresh Optive Fusion	Purite	Yes
Refresh Optive Fusion Sensitive	None	Yes
Refresh Plus	None	Yes
Refresh Tears	Purite	Yes
TheraTears Contact Lens Comfort Drops	Patented preservative	Yes
TheraTears Dry Eye Therapy	Sodium perboate	Unknown
TheraTears Dry Eye Therapy Nighttime	None	Unknown
TheraTears Dry Eye Therapy Preservative Free	None	Unknown
Sodium carboxymethylcellulose /Polysorbate 80		
Refresh Optive Advanced	Purite	Yes
Refresh Optive Advanced Sensitive	None	Yes
Dextran 70 0 / Hypromellose		
Bion Tears - Systane	None	No
Tears Naturale II	Polyquad	Yes
Tears Naturale Forte	Polyquad	No
Tears Naturale Free	None	Yes
Hypromellose (hydroxypropyl methylcellulose)		
Genteal	Sodium perborate	No
Isopto Tears	BAK	No
Systane Gel	No	No
Visine for Dry Eye – Tired Eye Relief	BAK	No
Visine for Dry Eye – Environmental Relief	Disodium EDTA	Yes
Visine for Dry Eye – Eye Revival	Disodium EDTA	Yes
Blink-n-clean Lens Drops	Polyhexamethylene biguanide	Yes
Hydroxypropyl-guar (HP-guar)		
Systane Ultra	Polyquaternium-1	Yes
Systane Ultra Hydration	Polyquaternium-1	Yes
Mineral Oil		
Systane Balance	Polyquaternium-1	No
Mineral Oil / White Petrolatum		
Lacri-Lube	Chlorobutanol	No
Duolube	None	Unknown
Systane Ointment (also contains lanolin)	None	No
Polyvinyl alcohol		
Refresh	Sodium chlorite	No
Tears Plus	Chlorobutanol	Unknown
Murine Tears	BAK	No
Propylene Glycol / Polytheylene Glycol 400		
Dry Eyes Soothe (previously Moisture Eyes)	BAK	No
Systane	Polyquaternium-1	No
Systane Ultra High Performance	Polyquaternium-1	Yes

Product	Preservative	Contact Lens Compatible
Systane Ultra High Performance Preservative Free	None	Yes
Systane Balance	Polyquaternium-1	No
Blink Tears (also contains sodium hyaluronate)	Sodium chlorite	Unknown
Blink Tears Preservative Free	None	Unknown
Carbomer / Medium Chain Triglycerides		
Liposic drop/gel	Cetrimide	No
Systane Gel	Sodium perborate	No
Tear-Gel	Unknown	Unknown
Castor oil emulsions		
Refresh Ultra	Purite	Unknown
Refresh Endura	None	Unknown
Sodium hyaluronate		
Systane Ultra Hydration (also contains propylene glycol & polyethylene glycol)	Polyquad	Yes
Blink Contacts	Oxychloro complex	Yes
HYLO	None	Yes
HYLO DUAL	None	Yes
HYLO GEL	None	Yes
Vitamin A		
OCUNOX	None	N/A (HS administration)
Isotonic Solution		
Renu Lubricating Drops (Bausch & Lomb)	EDTA	Yes

DRY EYE & EYE Products References

1. Systane Product Page available at www.systane.ca. Accessed 2017 Jan 18.
2. Refresh Product Page available at http://www.refreshoptive.ca/en?gclid=CMrHmMuaz9ECFQWMaQodL80JlA. Accessed 2017 Jan 18.
3. Murine Tears Product Page available at http://www.murine.com.au/products/eye-drops/murine-tears/. Accessed 2017 Jan 18.
4. Blink Tears Product Page available at http://abbottmedicaloptics.com/products/corneal/dry-eye-lubricating-eye-drops/blink-tears-lubricating-eye-drops. Accessed 2017 Jan 18.
5. HYLO Eye Drops – Candorvision available at http://candorvision.com/professionals/hylo/. Accessed 2017 Jan 18.
6. Personal product research conducted at WalMart Pharmacy – Stonebridge, Saskatoon; 2017 Jan 18.
7. Pucker AD, Ng SM, Nichols JJ, et al. Over the counter (OTC) artificial tear drops for dry eye syndrome. Cochrane Database Syst Rev. 2016;2:CD009729.
8. Schwartz LM, et al. A Clear-eyed View of Restasis and Chronic Dry Eye Disease. JAMA Intern Med. 2018 Feb 1;178(2):181-182.
9. Clayton JA. Dry Eye. N Engl J Med. 2018 Jun 7;378(23):2212-2223.
10. Dry Eye Assessment and Management Study Research Group. n-3 Fatty Acid Supplementation for the Treatment of Dry Eye Disease. **(DREAM**) N Engl J Med. 2018 Apr 13.

REFERENCES FOR PALLIATIVE CARE SYMPTOM MANAGEMENT CONSIDERATIONS:

General References:

1. Fraser Health Hospice Palliative Care Symptom Guidelines. Available at: http://www.fraserhealth.ca/professionals/hospice_palliative_care/
2. Hospital Pharmacists' Special Interest Group in Palliative Care. Care Beyond Cure: Management of Pain and Other Symptoms, 4th ed. APES Quebec, Canada; 2009.
3. Pereia JL, Associates. The Pallium Palliative Pocketbook: a peer-reviewed, referenced resource. 1st Canadian ed. Edmonton, Canada: The Pallium Project; 2008.
4. Downing M, ed. Medical Care of the Dying, 4th ed. Victoria Hospice Society. Victoria, BC; 2006.

Anorexia-Cachexia:

5. Berenstein G, Ortiz Z. Megestrol acetate for treatment of anorexia-cachexia syndrome. Cochrane Database of Systematic Reviews 2005, Issue 2. Art. No.: CD004310. DOI: 10.1002/14651858.CD004310.pub2
6. Loprinzi CL et al. Randomized comparison of megestrol acetate versus dexamethasone versus fluoxymesterone for the treatment of cancer anorexia/cachexia. J Clin Oncol. 1999 Oct;17(10):3299-306.
7. Jatoi A et al. Dronabinol versus megestrol acetate versus combination therapy for cancer-associated anorexia: a North Central Cancer Treatment Group study. J Clin Oncol. 2002 Jan 15;20(2):567-73.
8. Dewey A, Baughan C, Dean TP, Higgins B, Johnson I. Eicosapentaenoic acid (EPA, an omega-3 fatty acid from fish oils) for the treatment of cancer cachexia. Cochrane Database of Systematic Reviews 2007, Issue 1. Art. No.: CD004597. DOI: 10.1002/14651858.CD004597.pub2.

Dyspnea:

9. Jennings AL et al. Opioids for the palliation of breathlessness in advanced disease and terminal illness. Cochrane Database of Systematic Reviews 2001, Issue 3. Art. No.: CD002066. DOI: 10.1002/14651858.CD002066.
10. Polosa R, Simidchiev A, Walters EH. Nebulised morphine for severe interstitial lung disease. Cochrane Database of Systematic Reviews 2002, Issue 3. Art. No.: CD002872. DOI: 10.1002/14651858.CD002872.
11. Penson RT, Joel SP, Roberts M, Gloyne A, Beckwith S, Slevin ML. The bioavailability and pharmacokinetics of subcutaneous, nebulized and oral morphine-6-glucuronide. Br J Clin Pharmacol. 2002 Apr;53(4):347-54.
12. Abernethy AP et al. Randomised,double blind, placebo controlled crossover trial of sustained release morphine for the management of refractory dyspnoea. BMJ. 2003 Sep 6;327(7414):523-8.
13. Currow DC et al. Once-daily opioids for chronic dyspnea: a dose increment and pharmacovigilance study. J Pain Symptom Manage. 2011 Sep;42(3):388-99.
14. Simon ST et al. Benzodiazepines for the relief of breathlessness in advanced malignant and non-malignant diseases in adults. Cochrane Database of Systematic Reviews 2010, Issue 1. Art. No.: CD007354. DOI: 10.1002/14651858.CD007354.pub2.
15. Cranston JM, Crockett A, Currow D. Oxygen therapy for dyspnoea in adults. Cochrane Database of Systematic Reviews 2008, Issue 3. Art. No.: CD004769. DOI: 10.1002/14651858.CD004769.pub2.

Delirium:

16. Jackson KC, Lipman AG. Drug therapy for delirium in terminally ill adult patients. Cochrane Database of Systematic Reviews 2004, Issue 2. Art. No.: CD004770. DOI: 10.1002/14651858.CD004770.

Myoclonus:

17. Stone P, Minton O. European Palliative Care Research collaborative pain guidelines. Central side-effects management: what is the evidence to support best practice in the management of sedation, cognitive impairment and myoclonus? Palliat Med. 2011 Jul;25(5):431-41.

Hypercalcemia:

18. Major P et al. Zoledronic acid is superior to pamidronate in the treatment of hypercalcemia of malignancy: a pooled analysis of two randomized, controlled clinical trials. J Clin Oncol. 2001 Jan 15;19(2):558-67.
19. Wong RKS,Wiffen PJ. Bisphosphonates for the relief of pain secondary to bone metastases. Cochrane Database of Systematic Reviews 2002, Issue 2. Art. No.: CD002068. DOI: 10.1002/14651858.CD002068.

Respiratory Congestion:

20. Wee B, Hillier R. Interventions for noisy breathing in patients near to death. Cochrane Database of Systematic Reviews 2008,Issue 1. Art. No.: CD005177. DOI: 10.1002/14651858.CD005177.pub2.

ADDITIONAL PALLIATIVE CARE REFERENCES

Caregiver Burden/Stress

Bevans M, Sternberg EM. Caregiving burden, stress, and health effects among family caregivers of adult cancer patients. JAMA. 2012 Jan 25;307(4):398-403.

Gallagher R. Compassion fatigue. Can Fam Physician. 2013 Mar;59(3):265-8.

Sleeman KE, Collis E. Caring for a dying patient in hospital. BMJ. 2013 Apr 17;346:f2174.

Delirium

Boettger S, Breitbart W. Atypical antipsychotics in the management of delirium: a review of the empirical literature. Palliat Support Care. 2005 Sep;3(3):227-37.

Early Palliative Care

Greer JA, Pirl WF, Jackson VA, et al. Effect of early palliative care on chemotherapy use and end-of-life care in patients with metastatic non-small-cell lung cancer. J Clin Oncol. 2012 Feb 1;30(4):394-400.

Hypercalcemia

FDA Detailed View: Safety labeling changes approved by FDA Centre for Drug Evaluation and Research: Xgeva (Denosumab). April 2012.

Malignant Wounds

O'Brien. Palliative Care Files: Malignant Wounds – Managing Odour. Canadian Family Physician. March 2012;58:272-4.

Pain

Bennett MI, Graham J, Schmidt-Hansen M, et al; Guideline Development Group. Prescribing strong opioids for pain in adult palliative care: summary of NICE guidance. BMJ. 2012 May 23;344:e2806. doi: 10.1136/bmj.e2806.

National Institute for Health and Clinical Excellence (NICE). Opioids in palliative care: safe and effective prescribing of strong opioids for pain in palliative care of adults. London (UK): National Institute for Health and Clinical Excellence (NICE); 2012 May. http://www.nice.org.uk/nicemedia/live/13745/59285/59285.pdf

Renal Impairment

O'Connor NR, Corcoran AM. End-stage renal disease: symptom management and advance care planning. Am Fam Physician. 2012 Apr 1;85(7):705-10.

Respiratory Congestion

Wildiers H et al; Flemish Federation of Palliative Care. Atropine, hyoscine butylbromide, or scopolamine are equally effective for the treatment of death rattle in terminal care. J Pain Symptom Manage. 2009 Jul;38(1):124-33.

Gray M. The use of anticholinergics for the management of terminal secretions. Hospice Pharmacia, 2007: 1(3).

Nava S, Ferrer M, Esquinas A, et al. Palliative use of non-invasive ventilation in end-of-life patients with solid tumours: a randomised feasibility trial. Lancet Oncol 2013; online Feb 11.

Swallowing Difficulties

Gallagher R. Palliative Care Files: Swallowing difficulties - a prognostic signpost. Canadian Family Physician. December 2011; 57:1407-9.

Other:

Adelman RD, Tmanova LL, Delgado D, Dion S. Lachs MS, **Caregiver burden**: a clinical review. JAMA. 2014;311(10):1052-1059. doi:10.1001/jama.2014.304

Agar M. **Medicinal Cannabinoids** in Palliative Care. Br J Clin Pharmacol. 2018 Jun 20.

Agar MR, Lawlor PG, Quinn S, et al. Efficacy of oral **risperidone, haloperidol, or placebo for symptoms of delirium** among patients in palliative care: a randomized clinical trial [online Dec 5, 2016].JAMA Intern Med. doi:10.1001/jamainternmed.2016.7491 (Placebo better)

Albert RH. End-of-Life Care: **Managing Common Symptoms**. Am Fam Physician. 2017;95(6):356-361.
Aldridge MD, Schlesinger M, Barry CL, et al. **National hospice survey** results: for-profit status, community engagement, and service. JAMA Intern Med. 2014 Apr 1;174(4):500-6.
Ananth P, Melvin P, et al. Hospital Use in the Last Year of Life for **Children With Life-Threatening Complex Chronic Conditions**. Pediatrics. 2015 Nov;136(5):938-46.
Ando M, Sakaguchi Y, Shiihara Y, et al. Universality of Bereavement Life Review for Spirituality and Depression in Bereaved Families. Am J Hosp Palliat Care. 2013 May 14.
Angus DC, Truog RD. **Toward Better ICU Use** at the End of Life. JAMA. 2016 Jan 19;315(3):255-256.
Arcand M. End-of-life issues in **advanced dementia**: **Part 1**: goals of care, decision-making process, and family education. Can Fam Physician. 2015 Apr;61(4):330-334.
Arcand M. End-of-life issues in **advanced dementia**: **Part 2:** management of poor nutritional intake, dehydration, & pneumonia. Can Fam Physician. 2015 Apr;61(4):337-341.
Auriemma CL, Nguyen CA, Bronheim R, et al. **Stability of end-of-life preferences**: a systematic review of the evidence [online May 26, 2014]. JAMA Intern Med.
Bainbridge D, et al. **Common Components** of Efficacious In-Home End-of-Life Care **Programs**: A Review of Systematic Reviews. J Am Geriatr Soc. 2016 Mar;64(3):632-9.
Bajwah S, Ross JR, Wells AU, et al. Palliative care for patients with **advanced fibrotic lung disease**: a randomised controlled phase II and feasibility trial of a community case conference intervention. Thorax. 2015 Jun 23
Barclay JS, Kuchibhatla M, et al. Association of Hospice Patients' Income and Care Level With **Place of Death**. JAMA Intern Med. 2013 Feb 18:1-7.
Bauchner H, Fontanarosa PB. **Death, Dying**, and End of Life. JAMA. 2016 Jan 19;315(3):270-271.
Bekelman JE, Halpern SD, Blankart CR, et al; International Consortium or End-of-Life Research (ICELR). Comparison of **Site of Death**, **Health Care Utilization**, and Hospital Expenditures for Patients Dying With Cancer in 7 Developed Countries. JAMA. 2016 Jan 19;315(3):272-283.
Bergman J, Brook RH, Litwin MS. A call to action: improving value by emphasizing **patient-centered care** at the end of life. JAMA Surg. 2013 Mar 1;148(3):215-6.
Berry M, Brink E, Harris J, et al. **Supporting relatives and carers** at the end of a patient's life. BMJ. 2017 Feb 2;356:j367.
Blanke C, LeBlanc M, Hershman D, et al. Characterizing 18 Years of the **Death With Dignity Act in Oregon**. JAMA Oncol. 2017 Apr 6.
Blecker S, Johnson NJ, Altekruse S, et al. Association of **Occupation as a Physician With Likelihood of Dying in a Hospital**. JAMA. 2016 Jan 19;315(3):301-303.
Blinderman CD, Billings JA. **Comfort Care** for Patients Dying in the Hospital. N Engl J Med. 2015 Dec 24;373(26):2549-61.
Boersma I, Miyasaki J, Kutner J, et al. **Palliative care and neurology**: Time for a paradigm shift. Neurology. 2014 Aug 5;83(6):561-567. Epub 2014 Jul 2. Review.
Boudreau JD, Somerville MA, Biller-Andorno N. Clinical decisions. **Physician-assisted suicide**. N Engl J Med. 2013 Apr 1;368(15):1450-2.
Bowman C, Widera E. **Feeding tube placement** in patients with advanced cancer: a teachable moment. JAMA Intern Med. 2015 Jan 1;175(1):15-6.
Braun LT, Grady KL, et al. Palliative Care and **Cardiovascular Disease and Stroke**: A Policy Statement From the American Heart Association/American Stroke Association. Circulation. 2016 Aug 8.
Braun LT, Grady KL, Kutner JS, et al. **Palliative Care and Cardiovascular Disease and Stroke**: A Policy Statement From the **American Heart Association (AHA)/** American Stroke Association. Circulation. 2016 Sep 13;134(11):e198-225
Brewer C, Irwin M. In support of **assisted dying**. BMJ. 2015 Apr 9;350:h1828.
Briscoe J, Kamal AH, Casarett DJ. Top Ten Tips Palliative Care Clinicians Should Know About **Medical Cannabis**. J Palliat Med. 2019 Jan 14.
Bruce CR, Bibler T, et al. Navigating Ethical **Conflicts between Advance Directives and Surrogate Decision Makers'** Interpretations of Patient Wishes. Chest. 2015 Oct 22.
Bruera E, Hui D, et al. **Parenteral Hydration** in Patients With Advanced Cancer: Multicenter, Double-Blind, Placebo-Controlled Randomized Trial. J Clin Oncol. 2012 Nov 19.
Butler M, Ratner E, McCreedy E, et al. **Decision Aids** for Advance Care Planning [Internet]. Rockville (MD): Agency for Healthcare Research and Quality (US); 2014 Jul.
Carson SS, et al. Effect of Palliative Care-Led **Meetings for Families** of Patients With Chronic Critical Illness: A Randomized Clinical Trial. JAMA. 2016 Jul 5;316(1):51-62.
Caprio AJ. Palliative care: renaming as **supportive care and integration** into comprehensive cancer care. CMAJ. 2016 Jul 12;188(10):711-2.
Chandar M, et al. Perspectives of Health-Care Providers Toward Advance Care Planning in Patients With Advanced Cancer and **Congestive Heart Failure**. Am J Hosp Palliat Care. 2016 Mar 2.
Cheang MH, Rose G, Cheung CC, et al. Current **challenges in palliative care provision for heart failure** in the UK: a survey on the perspectives of palliative care professionals. Open Heart. 2015 Jan 15;2(1):e000188.
Chochinov HM. **Physician-Assisted Death in Canada**. JAMA. 2016 Jan 19;315(3):253-4.
Clodfelter RP, Adashi EY. The **Liberty to Die: California Enacts Physician Aid-in-Dying Law**. JAMA. 2016 Jan 19;315(3):251-252.
Cohen AB, Wright MS, Cooney L Jr, et al. **Guardianship** and End-of-Life Decision Making. JAMA Intern Med. 2015 Oct 1;175(10):1687-91.
Collins A, Leier B. Can **medical assistance in dying harm rural and remote palliative care in Canada**? Can Fam Physician. 2017 Mar;63(3):186-190.
Collis E, Sleeman KE. Do patients need to know they are **terminally ill**? **Yes**. BMJ. 2013 Apr 24;346:f2589.
Collis E, Sleeman KE. Do patients need to know they are **terminally ill**? **No**. BMJ. 2013 Apr 24;346:f2560.
Collis E, Mather H. **Nausea and vomiting** in palliative care. BMJ. 2015 Dec 3;351:h6249.
Cook D, Rocker G, Heyland D. Enhancing the **quality of end-of-life care** in Canada. CMAJ. 2013 Nov 5;185(16):1383-4.

Cook D, Rocker G. **Dying with dignity** in the intensive care unit. N Engl J Med. 2014 Jun 26;370(26):2506-14.
Cook D, Swinton M, et al. **Personalizing death in the intensive care unit**: the 3 Wishes Project: a mixed-methods study. Ann Intern Med. 2015 Aug 18;163(4):271-9.
Cross M. Delivering a **digital death**. BMJ. 2013 Apr 24;346:f2528.
Crow FM. **Final days at home**. Can Fam Physician. 2014 Jun;60(6):543-5.
Cunningham C, Ollendorf D, Travers K. The Effectiveness and Value of Palliative Care in the **Outpatient Setting**. JAMA Intern Med. 2017 Jan 3.
de Boer ME, Depla M, Wojtkowiak J,et al. **Life-and-death decision-making** in the acute phase after a severe **stroke**: Interviews with relatives. Palliat Med. 2015 Jan 29.
de Vos MA, Bos AP, Plötz FB, et al. **Talking With Parents About End-of-Life Decisions for Their Children**. Pediatrics. 2015 Jan 5.
Devlin M, Maida V. The demon in deeming: **Medical paternalism and linguistic issues** in the palliative care setting. Can Fam Physician. 2017 Mar;63(3):191-194.
Dierickx S, Deliens L, Cohen J, Chambaere K. **Euthanasia in Belgium**: trends in reported cases between 2003 and 2013. CMAJ. 2016 Nov 1;188(16):E407-E414.
Downar J, Francescutti LH. **Medical assistance in dying**: time for physicians to step up to protect themselves and patients. CMAJ. 2017 Jun 26;189(25):E849-E850.
Doulton B. Pharmacologic management of **adult breakthrough cancer pain**. Can Fam Physician. 2014 Dec;60(12):1111-4.
Dyer O, White C, et al. **Assisted dying**: law and practice around the world. BMJ. 2015 Aug 19;351:h4481.
Ekström MP, Abernethy AP, Currow DC. The management of **chronic breathlessness** in patients with advanced and terminal illness. BMJ. 2015 Jan 2;349:g7617.
El-Jawahri A, LeBlanc T, VanDusen H, et al. Effect of **inpatient palliative care on quality of life 2 weeks after hematopoietic stem cell transplantation**: a randomized clinical trial.JAMA. doi:10.1001/jama .2016.16786
Epstein AS, Prigerson HG, et al. **Discussions of Life Expectancy** and Changes in Illness Understanding in Patients With Advanced Cancer. J Clin Oncol. 2016 May 23.
Etkind SN, Koffman J. **Approaches to managing uncertainty** in people with life-limiting conditions: role of communication and palliative care. Postgrad Med J. 2016 Apr 29.
Farsides B. Commentary: **Palliative care and assisted dying** are not mutually exclusive. BMJ. 2018 Feb 7;360:k544.
Fernstrom KM, Shippee ND, et al. Development and validation of a **new patient experience tool** in patients with serious illness. BMC Palliat Care. 2016 Dec 30;15(1):99.
Ferrell BR, Temel JS, Temin S, Alesi ER, et al. **Integration of palliative care into standard oncology care**: **American Society of Clinical Oncology** (**ASCO**) clinical practice guideline update. J Clin Oncol. 2017 Jan;35(1):96-112.
Feudtner C, Womer J, Augustin R, et al. **Pediatric Palliative Care** Programs in Children's Hospitals: A Cross-Sectional National Survey. Pediatrics. 2013 Dec;132(6):1063-70.
Fischer SM, Kline DM, Min SJ, et al. Effect of Apoyo con Cariño (**Support With Caring) Trial of a Patient Navigator Intervention** to Improve Palliative Care Outcomes for Latino Adults With Advanced Cancer: A Randomized Clinical Trial. JAMA Oncol. 2018 Sep 20.
Franken LG, et al. **Hypoalbuminemia and decreased midazolam clearance** in terminally ill adult patients, an inflammatory effect? Br J Clin Pharmacol. 2017 Feb 8.
Friedel M, Aujoulat I, Dubois AC, Degryse JM. Instruments to measure **outcomes in pediatric palliative care**: a systematic review. Pediatrics. 2019;143(1):e20182379
Gaertner J, Siemens W, Meerpohl JJ, et al. Effect of specialist palliative care services on quality of life in adults with **advanced incurable illness** in hospital, hospice, or community settings: systematic review and meta-analysis. BMJ. 2017 Jul 4;357:j2925.
Gawande A. Quantity and Quality of Life: **Duties of Care in Life-Limiting Illness**. JAMA. 2016 Jan 19;315(3):267-269.
GBD 2015 Healthcare Access and Quality Collaborators. **Healthcare Access and Quality Index based on mortality** from causes amenable to personal health care in 195 countries and territories, 1990–2015: a novel analysis from the Global Burden of Disease Study 2015. Lancet 2017; 390: 231–66.
Geijteman EC, van Gelder T, van Zuylen L. **Sense and Nonsense of Treatment of Comorbid Diseases** in Terminally Ill Patients. JAMA Intern Med. 2015 Jan 26.
Geurts M, Macleod MR, van Thiel GJ, et al. **End-of-life decisions** in patients with severe acute brain injury. Lancet Neurol. 2014 May;13(5):515-524.
Gill TM, Han L, Leo-Summers L, et al. **Distressing Symptoms, Disability, and Hospice Services** at the End of Life: Prospective Cohort Study. J Am Geriatr Soc. 2017 Sep 12.
Gomes B, Calanzani N, Curiale V, McCrone P, Higginson IJ. Effectiveness and cost-effectiveness of **home palliative care services** for adults with advanced illness and their caregivers. Cochrane Database Syst Rev. 2013 Jun 6;6:CD007760. The results provide clear and reliable evidence that home palliative care increases the chance of dying at home and reduces symptom burden in particular for patients with cancer, without impacting on caregiver grief. This justifies providing home palliative care for patients who wish to die at home.
Gomes B, Calanzani N, Higginson IJ. Benefits and costs of **home palliative care** compared with usual care for patients with advanced illness and their family caregivers. JAMA. 2014 Mar 12;311(10):1060-1.
Gomes B, et al. Is **dying in hospital better than home** in incurable cancer and what factors influence this? A population-based study. BMC Med. 2015 Oct 9;13(1):235.
Good P, Richard R, Syrmis W, et al. **Medically assisted hydration** for adult palliative care patients. Cochrane Database Syst Rev. 2014 Apr 23;4:CD006273.
Gostin LO, Roberts AE. **Physician-Assisted Dying**: A Turning Point? JAMA. 2016 Jan 19;315(3):249-250.
Gray NA, Boucher NA, Kuchibhatla M, et al. Hospice Access for **Undocumented Immigrants**. JAMA Intern Med. 2017 Feb 6.
Griffin S, Cubanski J, Neuman T, et al. **Medicare and End-of-Life Care**. JAMA. 2016 Nov 1;316(17):1754.
Groninger H, Vijayan J. **Pharmacologic management** of pain at the end of life. Am Fam Physician. 2014;90(1):000-000.

Harris JA, Byhoff E, Perumalswami CR, et al. The Relationship of **Obesity to Hospice Use** and Expenditures: A Cohort Study. Ann Intern Med. 2017 Feb 7.
Harrison KL, Adrion ER, et al. Low Completion and **Disparities** in Advance Care Planning Activities Among **Older Medicare Beneficiaries**. JAMA Intern Med. 2016 Oct 31.
Henselmans I, et al. **Shared decision making about palliative chemotherapy**: A qualitative observation of talk about patient's preferences. Palliative Medicine. 2016;1-9
Heyland DK, Ilan R, Jiang X, et al.. The **prevalence of medical error related to end-of-life communication in Canadian** hospitals: results of a multicentre observational study. BMJ Qual Saf. 2015 Nov 9.
Heyland DK, Dodek P, You JJ, et al. **Validation of quality indicators** for end-of-life communication: results of a multicentre survey. CMAJ. 2017 Jul 31;189(30):E980-E989.
Hosker CM, Bennett MI. **Delirium and agitation** at the end of life. BMJ. 2016 Jun 9;353:i3085.
Howard M, Bernard C, Tan A, et al. **Advance care planning**: Let's start sooner. Can Fam Physician. 2015 Aug;61(8):663-5.
Hui D, Dos Santos R, Chisholm G, et al. **Bedside clinical signs associated with impending death** in patients with advanced cancer: Preliminary findings of a prospective, longitudinal cohort study. Cancer. 2015 Feb 9. pii: annrheumdis-2013-205133.
Hui D, Frisbee-Hume S, Wilson A, et al. Effect of **lorazepam with haloperidol vs haloperidol alone** on agitated **delirium** in patients with advanced cancer receiving palliative care: a randomized clinical trial. JAMA. doi:10.1001/jama.2017.11468
Institute for Clinical Systems Improvement (**ICSI**). **Palliative care**. Bloomington (MN): Institute for Clinical Systems Improvement (ICSI); 2011 Nov.
Iyer AS, Bakitas M. **Early Palliative Care in Advanced Illness**: Do Right by Mama. JAMA Intern Med. 2017 Apr 17.
Jena AB, et al. **Physicians' political preferences** and the delivery of end of life care in the United States: retrospective observational study. BMJ. 2018 Apr 11;361:k1161.
Johnston EE, Alvarez E, Saynina O, et al. Disparities in the Intensity of **End-of-Life Care for Children With Cancer**. Pediatrics. 2017 Oct;140(4).
Johnson LM, Frader J, Wolfe J, et al. **Palliative Sedation with Propofol** for an Adolescent With a DNR Order. Peds.2017;140(2):e20170487
Jors K, Tietgen S, et al. **Tidying rooms and tending hearts**: An explorative, mixed-methods study of hospital cleaning staff's experiences with seriously ill and dying patients. Palliat Med. 2016 May 9.
Kamal AH, Maguire JM, Meier DE. Evolving the Palliative Care Workforce to Provide **Responsive, Serious Illness Care**. Ann Intern Med. 2015 Aug 11.
Kavalieratos D, Corbelli J, Zhang D, et al. Association between **palliative care and patient and caregiver outcomes**: a systematic review and meta-analysis. JAMA. doi:10.1001/jama.2016.16840
Kavalieratos D, Gelfman LP, Tycon LE, et al. **Palliative Care in Heart Failure**: Rationale, Evidence, and Future Priorities. J Am Coll Cardiol. 2017 Oct 10;70(15):1919-1930.
Keele L, Keenan HT, Sheetz J, Bratton SL. Differences in Characteristics of **Dying Children** Who Receive and Do Not Receive Palliative Care. Pediatrics. 2013 Jun 10.
Kelley AS, Morrison RS. **Palliative Care for the Seriously Ill**. N Engl J Med. 2015 Aug 20;373(8):747-55.
Kelsall D. **Physicians are not solely responsible for ensuring access** to medical assistance in dying. CMAJ. 2018 Feb 20;190(7):E181.
Kendall M, et al. Outcomes, experiences and palliative care in **major stroke**: a multicentre, mixed-method, longitudinal study. CMAJ. 2018 Mar 5;190(9):E238-E246.
Kirkland KB. Finding Joy in Practice: Cocreation in Palliative Care. JAMA. 2017 May 23;317(20):2065-2066
Kirkpatrick JN, Hauptman PJ, Swetz KM, et al. Palliative Care for Patients With **End-Stage Cardiovascular Disease and Devices**: A Report From the Palliative Care Working Group of the Geriatrics Section of the American College of Cardiology. JAMA Intern Med. 2016 Jul 1;176(7):1017-1019.
Klick JC, Friebert S, Hutton N, et al. American Board of Hospice and Palliative Medicine Competencies Work Group. Developing **competencies for pediatric hospice** and palliative medicine. Pediatrics. 2014 Dec;134(6):e1670-7.
Knaul FM, Farmer PE, Krakauer EL, et al, on behalf of the Lancet Commission on **Global Access to Palliative Care** and Pain Relief Study Group. Alleviating the access abyss in palliative care and pain relief—an imperative of universal health coverage: the Lancet Commission report. Lancet 2017; online Oct 12.
Knoops L, Bastin P. **Escalation of Commitment in Treatment Decisions Near the End of Life**. JAMA Oncol. 2017 Jan 12.
Kwok AO, Yuen SK, Yong DS, et al. The Symptoms Prevalence, Medical Interventions, and Health Care Service Needs for Patients With **End-Stage Renal Disease** in a Renal Palliative Care Program. Am J Hosp Palliat Care. 2015 Aug 9.
Lage DE, Caudry DJ, Ackerly DC, et al. The **Care Continuum for Hospitalized Medicare Beneficiaries Near Death**. Ann Intern Med. 2018 Feb 13.
Largent EA, Terrasse M, Harkins K, et al. Attitudes Toward Physician-Assisted Death From Individuals Who Learn They Have an **Alzheimer Disease Biomarker**. JAMA Neurol. 2019 Apr 29.
Leyenaar JK, Bogetz JF. **Child Mortality** in the United States: Bridging Palliative Care and Public Health Perspectives. Pediatrics. 2018 Sep 19.
Loggers ET, Starks H, Shannon-Dudley M, et al. Implementing a **Death with Dignity program** at a comprehensive cancer center. N Engl J Med. 2013 Apr 11;368(15):1417-24.
Mack JW, Cronin A, Keating NL, Taback N, Huskamp HA, Malin JL, Earle CC, Weeks JC. Associations Between End-of-Life **Discussion Characteristics and Care Received** Near Death: A Prospective Cohort Study. J Clin Oncol. 2012 Nov 13.
Maddocks M, et al. Palliative care & management of troublesome symptoms for people with **chronic obstructive pulmonary disease**. Lancet. 2017 Sep 2;390:988-1002.
Mahtani R, Kurahashi AM, Buchman S, et al. Are **family medicine residents** adequately **trained** to deliver palliative care? Can Fam Physician. 2015 Dec

Matlock DD, Yamashita TE, Min SJ, et al. **How U.S. Doctors Die**: A Cohort Study of Healthcare Use at the End of Life. J Am Geriatr Soc. 2016 May;64(5):1061-7.
McCartney M. Is **discussing futile treatments** really best for dying patients? BMJ. 2014 Jun 24;348:g4180.
McConnell T, Scott D, Porter S. **Music therapy** for end-of-life care: An updated systematic review. Palliat Med. 2016 Mar 4
McCusker M, Ceronsky L, Crone C, et al. **Palliative care for adults**. Bloomington (MN): Institute for Clinical Systems Improvement (**ICSI**); 2013 Nov.
McIlvennan CK, Allen LA. Palliative care in patients with **heart failure**. BMJ. 2016 Apr 14;353:i1010.
Mercadante S, Marinangeli F, Masedu F, et al. **Hyoscine butylbromide** for the management of death rattle: sooner rather than later. J Pain Symptom Manage. 2018 Aug 30.
Mitchell G, Zhang J, Burridge L, et al. Case conferences between general practitioners and specialist teams to plan end of life care of people with **end stage heart failure and lung** disease: an exploratory pilot study. BMC Palliat Care. 2014 May 5;13:24.
Moore KA, Rubin EB, Halpern SD. The Problems With **Physician Orders for Life-Sustaining Treatment**. JAMA. 2016 Jan 19;315(3):259-260.
Morin L, et al. Choosing Wisely? Measuring the **Burden of Medications in Older Adults near the End of Life**: Nationwide, Longitudinal Cohort Study. Am J Med. 2017 Apr 25.
Morita T, Miyashita M, Yamagishi A, et al. Effects of a programme of interventions on **regional comprehensive palliative care** for patients with cancer: a mixed-methods study. Lancet Oncol. 2013 May 8.
Mulder J, Sonneveld JPC. **Organ donation** after medical assistance in dying at home. CMAJ. 2018 Nov 5;190(44):E1305-E1306.
Murakami N, Tanabe K, Morita T, et al. **Going back to home to die**: does it make a difference to patient survival? BMC Palliat Care. 2015 Mar 19;14:7.
Murray SA, Kendall M, Mitchell G, et al. **Palliative care from diagnosis to death**. BMJ. 2017 Feb 27;356:j878.
Myers J. **Measuring quality of end-of-life communication and decision-making**: Do we have this right? CMAJ. 2017 Jul 31;189(30):E978-E979
Narang AK, Wright AA, Nicholas LH. Trends in **Advance Care Planning** in Patients With Cancer: Results From a National Longitudinal Survey. JAMA Oncol. 2015 Jul 9.
Netters S. **How it feels to help a terminally ill patient to die a dignified death**. BMJ. 2018 Feb 7;360:k116.
Nevin M, Smith V, Hynes G. **Non-specialist palliative care**: A principle-based concept analysis. Palliat Med. 2019 Apr 24:269216319840963.
Ng AY, et al. Effects of a transitional palliative care model on patients with end-stage **heart failure**: study protocol for a randomized controlled trial. Trials. 2016 Mar 31
Nosek CL, Kerr CW, Woodworth J, et al. **End-of-Life Dreams** and Visions: A Qualitative Perspective From Hospice Patients. Am J Hosp Palliat Care. 2014 Jan 16.
Nowels D, VandeKieft G, Ballentine JM. **Medical Aid in Dying**. Am Fam Physician. 2018 Mar 1;97(5):339-343.
Nowels D, VandeKieft G, Matlock D. **Palliative Care Through Illness Trajectory**. Am Fam Physician. 2017 Mar 15;95(6):386-388
NICE: National Institute for Health and Care Evidence, 2015. **Care of dying adults in the last days of life** *(NG31)* [online]. Available: http://www.nice.org.uk/guidance/ng31 [Accessed 17 February 2016].
Obermeyer Z, Makar M, Abujaber S, et al. Association between the **Medicare hospice benefit and health care utilization and costs for patients** with poor-prognosis cancer. JAMA. doi:10.1001/jama.2014.14950.
Odejide OO, Cronin AM, et al. **Timeliness of End-of-Life Discussions for Blood Cancers**: A National Survey of Hematologic Oncologists. JAMA Intern Med. 2015 Dec 21:1-3.
Odejide OO. A **Policy Prescription for Hospice Care**. JAMA. 2016 Jan 19;315(3):257-258.
Olié E, Courtet P. The Controversial Issue of **Euthanasia** in Patients With Psychiatric Illness. JAMA. 2016 Aug 9;316(6):656-7.
Onishi E, Biagioli F, Safranek S. **Methylphenidate** for management of **fatigue** in the palliative care setting. Am Fam Physician. 2014 Jan 15;89(2):124-7
Ornstein KA, Aldridge MD, Garrido MM, et al. Association Between **Hospice Use and Depressive Symptoms in Surviving Spouses**. JAMA Intern Med. 2015 May 26.
Paque K, De Schreye R, Elseviers M, et al. **Discontinuation of medications** at the end of life. A population study in Belgium, based on linked administrative databases. Br J Clin Pharmacol. 2019 Jan 22
Payne S, Chan N, Davies A, et al. Supportive, palliative,and end-of-life care for patients with cancer in **Asia**: resource-stratified guidelines from the Asian Oncology Summit 2012. Lancet Oncol. 2012 Nov;13(11):e492-500.
Periyakoil VS, Neri E, Fong A, Kraemer H. Do unto others: **doctors' personal end-of-life resuscitation preferences** and their attitudes toward advance directives. PLoS One. 2014 May 28;9(5):e98246.
Pisani L, Hill NS, Pacilli AMG, et al. **Management of Dyspnea** in the Terminally Ill. Chest. 2018 Apr 18.
Pollock K. **Is home always the best and preferred place of death**? BMJ. 2015 Oct 7;351:h4855.
Prigerson HG, Bao Y, Shah MA, et al. **Chemotherapy Use**, Performance Status, and Quality of Life at the End of Life. JAMA Oncol. 2015 Jul 23.
Quill TE, Back AL, Block SD. Responding to Patients Requesting **Physician-Assisted Death**: Physician Involvement at the Very End of Life. JAMA. 2016 Jan 19;315(3):245-246.
Quill TE, et al. **Voluntarily Stopping Eating and Drinking** Among Patients With Serious Advanced Illness-Clinical, Ethical, and Legal Aspects. JAMA Intern Med. 2017 Nov 6.
Rapoport A, Shaheed J, Newman C, et al. **Parental Perceptions** of Forgoing Artificial Nutrition and Hydration During End-of-Life Care. Pediatrics. 2013 Apr 8.
Razmaria AA. **End-of-Life Care**. JAMA. 2016 Jul 5;316(1):115.
Rivet EB, Ferrada P, Albrecht T, et al. Characteristics of palliative care consultation at an academic level one **trauma center**. Am J Surg. 2017 Oct;214(4):657-660.
Rocker G, Downar J, Morrison RS. **Palliative care for chronic illness**: driving change. CMAJ. 2016 Dec 6;188(17-18):E493-E498. Review.

Roehr B. **Assisted dying in US and Canada**: controversy subsides after legalisation. BMJ. 2018 Feb 7;360:k503.
Rogers JG, Patel CB, Mentz RJ, et al. **Palliative Care in Heart Failure**: The **PAL-HF** Randomized, Controlled Clinical Trial. J Am Coll Cardiol. 2017 Jul 18;70(3):331-341
Rolnick JA, Asch DA, Halpern SD. **Delegalizing Advance Directives** -Facilitating Advance Care Planning. N Engl J Med. 2017 Jun 1;376(22):2105-2107.
Rosenbaum L. Falling Together - **Empathetic Care for the Dying**. N Engl J Med. 2016 Jan 13.
Ruegger J, Hodgkinson S, Field-Smith A, et al; guideline committee. **Care of adults in the last days of life**: summary of **NICE** guidance. BMJ. 2015 Dec 16;351:h6631.
Section on Hospice and Palliative Medicine and Committee on Hospital Care. **Pediatric palliative care** and hospice care commitments, guidelines, and recommendations. Pediatrics. 2013 Nov;132(5):966-72.
Seow H, Brazil K, Sussman J, Pereira J, Marshall D, Austin PC, et al. Impact of **community based, specialist palliative care teams** on hospitalisations and emergency department visits late in life and hospital deaths: a pooled analysis. BMJ 2014;348:g3496.
Shadd JD, Burge F, Stajduhar KI, et al. **Defining and measuring a palliative approach** in primary care. Can Fam Physician. 2013 Nov;59(11):1149-50.
Siden H, Chavoshi N, Harvey B, et al. Characteristics of a **pediatric hospice palliative care program over 15 years**. Pediatrics. 2014 Sep;134(3):e765-72.
Simon J. **Who needs palliative care**? CMAJ. 2018 Mar 5;190(9):E234-E235.
Singer AE, Meeker D, Teno JM, et al. **Symptom trends in the last year of life from 1998 to 2010**: a cohort study. Ann Intern Med. 2015 Feb 3;162(3):175-83.
Sleeman KE, Davies JM, Verne J, et al. The changing **demographics of inpatient hospice death**: Population-based cross-sectional study in England, 1993-2012. Palliat Med. 2015 May 19.
Smith AG, Andrews S, Bratton SL, et al. **Pediatric Palliative Care** and Inpatient Hospital Costs: A Longitudinal Cohort Study. Pediatrics. 2015 Mar 23
Snijdewind MC, Willems DL, et al. A Study of the First Year of the End-of-Life Clinic for **Physician-Assisted Dying** in the Netherlands. JAMA Intern Med. 2015 Aug 10.
Sudore RL, Schillinger D, Katen MT, et al. Engaging Diverse English- and Spanish-Speaking Older Adults in **Advance Care Planning**: The **PREPARE** Randomized Clinical Trial. JAMA Intern Med. 2018 Oct 29.
Swetz KM, Kamal AH. **In the Clinic**: **Palliative Care**. Ann Intern Med. 2018 Mar 6;168(5):ITC33-ITC48.
Temel JS, et al. Effects of Early Integrated **Palliative Care in Patients With Lung and GI Cancer**: A Randomized Clinical Trial. J Clin Oncol. 2016 Dec 28:JCO2016705046.
Teno JM, Plotzke M, Christian T, Gozalo P. Examining variation in **hospice visits by professional staff in the last 2 days of life** [online Feb 8, 2016]. JAMA Intern Med. doi:10.1001/jamainternmed.2015.7479.
Thompson AE. JAMA patient page. **Advance directives**. JAMA. 2015 Feb 24;313(8):868.
Thoonsen B, Gerritzen SH, Vissers KC, et al. **Training general practitioners** contributes to the identification of palliative patients and to multidimensional care provision: secondary outcomes of an RCT. BMJ Support Palliat Care. 2016 Apr 18.
Tjia J, Kutner JS, Ritchie CS, et al. Perceptions of **Statin Discontinuation** among Patients with Life-Limiting Illness. J Palliat Med. 2017 May 18
Todd A, Al-Khafaji J, Akhter N, et al. Missed opportunities: **unnecessary medicine use in patients with lung cancer at the end of life**: an international cohort study. Br J Clin Pharmacol. 2018 Sep 5.
Todorovic A. **Palliative care is not just for those who are dying**. BMJ. 2016 Jun 15;353:i2846.
Tolle SW, Teno JM. Lessons from **Oregon in Embracing Complexity in End-of-Life Care**. N Engl J Med. 2017 Mar 16;376(11):1078-1082.
Tradounsky G. **Seizures** in palliative care. Can Fam Physician. 2013 Sep;59(9):951-5.
van Wijngaarden E, Klink A, Leget C, et al. **Assisted dying** for healthy **older people**: a step too far? BMJ. 2017 May 19;357:j2298.
Villanueva G, Murphy MS, et al. **End of life care for infants, children and young people** with life limiting conditions: summary of **NICE** guidance. BMJ. 2016 Dec 8;355:i6385.
Voeuk A, Oneschuk D. **Continuous palliative sedation** therapy. Can Fam Physician. 2014 Sep;60(9):813-5.
Voltz R, Kamps R, Greinwald R, et al. Silent night: retrospective database study assessing possibility of "**weekend effect" in palliative care.** BMJ. 2014 Dec 16;349:g7370.
Wachterman MW, et al. **Quality of end-of-life care** provided to patients with **different serious illnesses** [June'16].JAMA Intern Med. doi:10.1001/jamainternmed.2016.1200.
Wachterman MW, Hailpern SM, Keating NL, et al. Association Between **Hospice Length of Stay, Health Care Utilization, and Medicare Costs** at the End of Life Among Patients Who Received Maintenance Hemodialysis. JAMA Intern Med. 2018 Apr 30.
Warmenhoven F, van Rijswijk E, van Hoogstraten E, et al. How family physicians address diagnosis and management of **depression** in palliative care patients. Ann Fam Med. 2012 Jul;10(4):330-6.
Warraich HJ, Wolf SP, Mentz RJ, Rogers JG, Samsa G, Kamal AH. **Characteristics and Trends Among Patients With Cardiovascular Disease Referred to Palliative Care**. JAMA Netw Open. 2019 May 3;2(5):e192375.
Weise KL, Okun AL, Carter BS, et al. **Guidance on Forgoing Life-Sustaining Medical Treatment**. Pediatrics. 2017 Sep;140(3).
Weissman JS, Cooper Z, Hyder JA, et al. **End-of-Life Care Intensity for Physicians, Lawyers, and the General Population**. JAMA. 2016 Jan 19;315(3):303-305.
White N, et al. How accurate is the **'Surprise Question'** at identifying patients **at the end of life**? A systematic review and meta-analysis. BMC Med. 2017 Aug 2;15(1):139.
Wilson DG, Harris SK, Peck H, et al. Patterns of Care in Hospitalized **Vascular Surgery Patients** at End of Life. JAMA Surg. 2016 Nov 2.

Wilson E, Caswell G, Turner N, Pollock K. Managing **Medicines for Patients Dying at Home**: A Review of Family Caregivers' Experiences. J Pain Symptom Manage.2018 Dec;56(6):962-974.

Wilson E, Morbey H, Brown J, et al. Administering **anticipatory medications in end-of-life care**: A qualitative study of nursing practice in the community and in nursing homes. Palliat Med. 2014 Jul 28.

Wright AA, Zhang B, Keating NL, et al. Associations between **palliative chemotherapy** and adult cancer patients' end of life care and place of death: prospective cohort study. BMJ. 2014 Mar 4

Wright AA, Keating NL, Ayanian JZ, et al. Family Perspectives on **Aggressive Cancer Care Near the End of Life**. JAMA. 2016 Jan 19;315(3):284-292.

Xander C, Meerpohl JJ, Galandi D, et al. Pharmacological interventions for **pruritus** in adult palliative care patients. Cochrane Database Syst Rev. 2013 Jun 9;6:CD008320.

Yang YT, Curlin FA. Why Physicians Should Oppose **Assisted Suicide**. JAMA. 2016 Jan 19;315(3):247-248.

Yarnell CJ, et al. Association between **immigrant status and end-of-life care** in Ontario, Canada [published online October 2, 2017].JAMA. doi:10.1001/JAMA.2017.14418

Yoong J, Park ER, Greer JA, et al. **Early Palliative Care** in Advanced Lung Cancer: A Qualitative Study. JAMA Intern Med. 2013 Jan 28:1-8.

You JJ, Dodek P, Lamontagne F, et al; for the ACCEPT Study Team and the Canadian Researchers at the End of Life Network (CARENET). What really matters in end-of-life discussions? Perspectives of patients in hospital with serious illness and their families. CMAJ. 2014 Nov 3.

Zahradnik EK, Grossman H. Palliative Care as a **Primary Therapeutic Approach in Advanced Dementia**: A Narrative Review. Clin Ther. 2014 Nov 1;36(11):1512-1517.

Ziegler L, Mulvey M, Blenkinsopp A, et al. **Opioid prescribing** for patients with cancer in the last year of life: a longitudinal population cohort study. Pain. 2016 Jul 16.

Zimmermann C, Swami N, Krzyzanowska M, et al. Early **palliative care for patients with advanced cancer**: a cluster-randomised controlled trial. Lancet. 2014 Feb 18.

Zimmermann C, Swami N, et al. **Perceptions** of palliative care among patients with advanced cancer and their caregivers. CMAJ. 2016 Jul 12;188(10):E217-27.

PATIENT SAFETY – DRUG CONSIDERATIONS

[1] Baker GR, Norton PG, Flintoft V, Blais R, Brown A, Cox J, Etchells E, Ghali WA, Hebert P, Majumdar SR, O'Beirne M, Palacios-Derflingher L, Reid RJ, Sheps S, Tamblyn R. The Canadian Adverse Events Study: the incidence of adverse events among hospital patients in Canada. CMAJ. 2004 May 25;170(11):1678-86.

[2] Finchem JE. An overview of adverse drug reactions. *American Pharmacy*. 1991;NS31 (6):47-52.

[3] Martys CR. Adverse reactions to drugs in general practice. *BMJ*. 1997;2:1194-97.

[4] Gandhi TK, Weingart SN, Borus J, et al. Adverse drug events in ambulatory care. *N Engl J Med*. 2003;348:1556-64.

[5] Budnitz DS, Pollock DA, Weidenbach KN, Mendelsohn AB, Schroeder TJ, Annest JL. National surveillance of emergency department visits for outpatient adverse drug events. JAMA. 2006 Oct 18;296(15):1858-66.

[6] David Flockhart: Important DI cytochrome p450 information http://medicine.iupui.edu/flockhart/

[7] The Institute for Safe Medication Practices – website accessede at www.ismp.org

[8] ISMP Medication Safety Alert – Acute Care, May 31, 2012.

AAP Committee on Medical Liability And Risk Management and AAP Council on Quality Improvement and Patient Safety. **Disclosure of Adverse Events in Pediatrics**. 2016;138(6):e20163215

Agency for Healthcare Research and Quality (**AHRQ**) www.ahrq.gov

Ahuja N, Zhao W, Xiang H. **Medical Errors** in US **Pediatric** Inpatients With Chronic Conditions. Pediatrics. 2012 Sep 10.

Aiken LH, Sermeus W, Van den Heede K, et al. **Patient safety**, satisfaction, and quality of hospital care: cross sectional surveys of nurses and patients in 12 countries in Europe and the United States. BMJ. 2012 Mar 20;344:e1717.

Al Hamid A, Ghaleb M, Aljadhey H et al. A systematic review of **hospitalisation resulting from medicine related problems** in adult patients. Br J Clin Pharmacol. 2013 Nov 28.

Alderman CP. Saving the **Elderly From Drug-Related Harm**. Ann Pharmacother. 2016 Aug;50(8):685-6.

Allegaert K, van den Anker JN. **Adverse drug reactions in neonates and infants**: a population tailored approach is needed. Br J Clin Pharmacol. 2014 May 27.

Allen EN, Chandler CIR, Mandimika N, Leisegang C, Barnes K. **Eliciting adverse effects data from participants in clinical trials**. Cochrane Database of Systematic Reviews 2018, Issue 1. Art. No.: MR000039. This review supports concerns that methods to elicit participant-reported AEs influence the detection of these data. There was a risk for under-detection of AEs in studies using a more general elicitation method compared to those using a comprehensive method. These AEs may be important from a clinical perspective or for patients. This under-detection could compromise ability to pool AE data. However, the impact on the nature of the AE detected by different methods is unclear. The wide variety and low quality of methods to compare elicitation strategies limited this review. Future studies would be improved by using and reporting clear definitions and terminology for AEs (and other important variables), frequency and time period over which they were ascertained, how they were graded, assessed for a relationship to the study drug, coded, and tabulated/reported.

Alingh CW, van Wijngaarden JDH, van de Voorde K, et al. **Speaking up about patient safety concerns**: the influence of safety management approaches and climate on nurses' willingness to speak up. BMJ Qual Saf. 2018 Jun 28.

Almuzaini T, Sammons H, Choonara I. **Quality of medicines in Canada**: a retrospective review of risk communication documents (2005-2013). BMJ Open. 2014 Oct 31;4(10):e006088.

American Academy of Pediatrics, Steering Committee on Quality Improvement and Management and Committee on **Hospital Care**. Principles of **pediatric patient safety**: reducing harm due to medical care. Pediatrics. 2011;127(6):1199 –1210.

American Geriatrics Society (AGS) **2012 Beers Criteria Update** Expert Panel. American Geriatrics Society updated Beers Criteria for potentially inappropriate medication use in older adults. J Am Geriatr Soc 2012 Apr;60(4):616-31.

Andrews LB, Stocking C, Krizek T, Gottlieb L, Krizek C, Vargish T, et al. An **alternative strategy** for studying adverse events in medical care. *Lancet* 1997;349:309-13.

Attenello FJ, Wen T, Cen SY et al. Incidence of "**never events" among weekend admissions versus weekday admissions** to US hospitals: national analysis. BMJ. 2015 Apr 15

Arnott J, Hesselgreaves H, Nunn AJ, et al. Enhancing Communication about Paediatric Medicines: Lessons from a Qualitative Study of Parents' **Experiences of Their Child's Suspected Adverse Drug Reaction**. PLoS One. 2012;7(10):e46022

Arriaga AF, Bader AM, Wong JM, Lipsitz SR, Berry WR, Ziewacz JE, et al. Simulation-based trial of **surgical-crisis checklists**. N Engl J Med 2013;368:246-53.

Avery AJ, Rodgers S, Cantrill JA, et al. A **pharmacist-led information technology intervention** for medication errors (**PINCER**): a multicentre, cluster randomised, controlled trial and cost-effectiveness analysis. Lancet. 2012 Feb 20.

Avorn J. Learning about the **Safety of Drugs** — A Half-Century of Evolution. N Engl J Med 2011; 365:2151-2153.

Avorn J. **Two centuries of assessing drug risks**. N Engl J Med. 2012 Jul 19;367(3):193-7.

Baines R, Langelaan M, de Bruijne M, et al. **How effective are patient safety initiatives**? A retrospective patient record review study of changes to patient safety over time. BMJ Qual Saf. 2015 Jul 6.

Bar-Oz B, Levichek Z, Koren G. Medications that can be **fatal for a toddler** with **one tablet or teaspoonful**: a 2004 update. Pediatr Drugs 2004;6:123-6.

Bardach NS, Vittinghoff E, Asteria-Peñaloza R, et al. Measuring hospital quality using **pediatric readmission** and revisit rates. Pediatrics. 2013 Sep;132(3):429-36.

Bartlett G, Blais R, Tamblyn R, Clermont RJ, MacGibbon B. Impact of **patient communication problems** on the risk of preventable adverse events in acute care settings. CMAJ. 2008 Jun 3;178(12):1555-62. Patients with communication problems appeared to be at highest risk for preventable adverse events.

Basger BJ, Moles RJ, Chen TF. Development of an **aggregated system for classifying causes of drug-related problems**. Ann Pharmacother. 2015 Apr;49(4):405-18.

Bates DW, Spell N, Cullen DJ, Burdick E, Laird N, Petersen LA, et al.; Adverse Drug Events Prevention Study Group. The costs of adverse events in hospitalized patients. JAMA 1997;277(4):307-311.

Bayoumi I, Dolovich L, Hutchison B, Holbrook A. **Medication-related emergency department visits and hospitalizations** among older adults. Can Fam Physician. 2014 Apr;60(4):e217-22.

Beck JB, McGrath C, Toncray K, et al. **Failure Is an Option: Using Errors as Teaching Opportunities**. Pediatrics. 2018 Feb 13.

Bell CM, Brener SS, Gunraj N, et al. Association of ICU or hospital admission with **unintentional discontinuation** of medications for chronic diseases. JAMA. 2011; 306(8):840-847.

Bell SK, Mann KJ, Truog R, et al. Should We **Tell Parents When We've Made an Error**? Pediatrics. 2015 Jan;135(1):159-63.

Bell SK, Martinez W. Every patient should be enabled to **stop the line**. BMJ Qual Saf. 2019 Mar;28(3):172-176.

Bellis JR, Kirkham JJ, Nunn AJ, Pirmohamed M. **Adverse drug reactions and off-label and unlicensed medicines in children**: a prospective cohort study of unplanned admissions to a paediatric hospital. Br J Clin Pharmacol. 2013 Aug 7.

Benjamin L, Frush K, Shaw K, et al. **Pediatric Medication Safety in the Emergency Department**. Ann Emerg Med. 2018 Mar;71(3):e17-e24.

Benning Amirta, Ghaleb M, Suokas A, et al. **Large scale organizational intervention** to improve patient safety in four UK hospitals: mixed method evaluation. BMJ 2011;342:doi:10.1136/bmj.d195 (3 Feb 2011)

Benning Amirta, Dixon-Woods M, Nwulu U, et al. **Multiple component patient safety intervention** in English hospitals: controlled evaluation of second phase. BMJ 2011;342:doi:10.1136/bmj.d199 (3 Feb 2011)

Berger ER, Greenberg CC, Bilimoria KY. Challenges in **Reducing Surgical "Never Events**". JAMA. 2015 Oct 6;314(13):1386-1387.

Berwick DM. Errors today and errors tomorrow. *N Engl J Med* 2003;348:2570-2.

Bhatt M, Johnson DW, Chan J, et al. Risk Factors for Adverse Events in **Emergency Department Procedural Sedation for Children**. JAMA Pediatr. 2017 Aug 21

Bishop TF, Ryan AM, Casalino LP. **Paid malpractice claims** for adverse events in inpatient and outpatient settings. JAMA. 2011;305(23):2427-2431.

Black C, Tagiyeva-Milne N, Helms P, Moir D. **Pharmacovigilance in children**: detecting adverse drug reactions in routine electronic healthcare records. A systematic review. Br J Clin Pharmacol. 2015 Mar 27.

Blais R, Sears NA, Doran D, et al. Assessing **adverse events among home care** clients in three Canadian provinces using chart review. BMJ Qual Saf. 2013 Jul 4.

Blendon RJ, DesRoches CM, Brodie M, Benson JM, Rosen AB, Schneider E, et al. **Views of practicing physicians** and the public on medical errors. *N Engl J Med* 2002;347:1933-40.

Blossom DB, Kallen AJ, Patel PR, Elward A, Robinson L, Gao G, et al. Outbreak of Adverse Reactions Associated with **Contaminated Heparin**. N Engl J Med. 2008 Dec 3. [Epub ahead of print]

Bock M, Fanolla A, Segur-Cabanac I, et al. A Comparative Effectiveness Analysis of the Implementation of **Surgical Safety Checklists** in a Tertiary Care Hospital. JAMA Surg. 2016 Jul 1;151(7):639-46.

Bos JM, van den Bemt PM, Kievit W, et al. A **multifaceted intervention** to reduce drug-related complications in **surgical patients**. Br J Clin Pharmacol. 2016 Sep 27.

Boucher A, Ho C, MacKinnon N, et al. **Quality-related events reported by community pharmacies in Nova Scotia** over a 7-year period: a descriptive analysis. CMAJ Open. 2018 Dec 18;6(4):E651-E656.

Bourgeois, Florence T., Mandl, Kenneth D., Valim, Clarissa, et al. **Pediatric Adverse Drug Events** in the Outpatient Setting: An 11-Year National Analysis. Pediatrics 2009 124: e744-e750.

Brennan TA, Leape LL, Laird NM, Hebert L, et al. Incidence of **adverse events** and negligence in hospitalized patients. Results of the Harvard Medical Practice Study I. *N Engl J Med* 1991;324:370-6.

Brilli RJ, McClead RE Jr, Crandall WV, et al. A **comprehensive patient safety program** can significantly reduce preventable harm, associated costs, and hospital mortality. J Pediatr. 2013 Dec;163(6):1638-45.

Budnitz DS, Shehab N, Kegler SR, Richards CL. Medication use leading to **emergency department visits** for adverse drug events in older adults. Ann Intern Med. 2007;147:755-65.

Budnitz DS et al. **Emergency hospitalizations for adverse drug events** in older Americans. N Engl J Med 2011 Nov 24; 365:2002. A few medications — including **warfarin, insulins, oral antiplatelet agents, and oral hypoglycemic agents** — cause most of the problems that lead to emergency hospitalization in older patients.

Burghardt LC, Ayers JW, Brownstein JS, et al. **Adult Prescription** Drug Use and **Pediatric** Medication **Exposures and Poisonings**. Pediatrics. 2013 Jun 3.

Cahir C, Bennett K, Teljeur C, Fahey T. **Potentially inappropriate prescribing** and adverse health outcomes in community dwelling older patients. Br J Clin Pharmacol. 2013 May 27.

Call RJ, Burlison JD, Robertson JJ, et al. **Adverse Drug Event Detection in Pediatric Oncology and Hematology** Patients: Using Medication Triggers to Identify Patient Harm in a Specialized Pediatric Patient Population. J Pediatr. 2014 Apr 24.

Call RJ, Burlison JD, Robertson JJ, et al. **Adverse drug event detection in pediatric oncology and hematology** patients: using medication triggers to identify patient harm in a specialized pediatric patient population. J Pediatr. 2014 Sep;165(3):447-452.e4.

Camiré E, Moyen E, Stelfox HT. Medication errors in **critical care**: risk factors, prevention and disclosure. CMAJ. 2009 Apr 28;180(9):936-43.

CARN: Canadian Adverse Reaction Newsletter, Volume 22, No. 3 **Adverse reaction and incident reporting — 2011.** http://www.hc-sc.gc.ca/dhp-mps/alt_formats/pdf/medeff/bulletin/carn-bcei_v22n3-eng.pdf

Carnevali L, et al. Performance of the **adverse drug event trigger tool** and the global trigger tool for identifying adverse drug events: experience in a belgian hospital. Ann Pharmacother. 2013 Nov;47(11):1414-9

CDC MMWR Oct/10 QuickStats: Rates of **Drug-Induced Deaths**,* by Race/Ethnicity† --- United States, 1999—2007 Weekly October 29, 2010 / 59(42);1376 http://www.cdc.gov/mmwr/pdf/other/su6001.pdf

Chan PS, Jain R, Nallmothu BK, Berg RA, Sasson C. **Rapid response** teams: a systematic review and meta-analysis. *Arch Intern Med* 2010;170:18-26.

Chan EW, Liu KQ, Chui CS, et al. **Adverse Drug Reactions** - Examples of detection of **rare events using databases**. Br J Clin Pharmacol. 2014 Jul 24.

Chan SL, Ang X, Sani LL, et al. Prevalence and characteristics of **adverse drug reactions at admission to hospital**: a prospective observational study. Br J Clin Pharmacol. 2016 Sep 19.

Chassin MR, Loeb JM, Schmaltz SP, Wachter RM. **Accountability measures** — using measurement to promote quality improvement. N Engl J Med 2010;363:683-8.

Cheng CM, Shin J, Guglielmo BJ. **Trends in Boxed Warnings** and Withdrawals for Novel Therapeutic Drugs, 1996 Through 2012. JAMA Intern Med. 2014 Aug 15.

Classen DC, Griffin FA, Berwick DM. **Measuring Patient Safety in Real Time**: An Essential Method for Effectively Improving the Safety of Care. Ann Intern Med. 2017 Nov 21.

Coloma PM, Trifirò G, Patadia V, Sturkenboom M. **Postmarketing safety surveillance** : where does signal detection using electronic healthcare records fit into the big picture? Drug Saf. 2013 Mar;36(3):183-97.

Committee on Drugs. **Metric Units and the Preferred Dosing of Orally Administered Liquid Medications**. Pediatrics. 2015 Mar 30.

Cooper J, Edwards A, Williams H, et al. **Nature of Blame in Patient Safety Incident Reports**: Mixed Methods Analysis of a National Database. Ann Fam Med. 2017 Sep;15(5):455-461.

Cope JU, Rosenthal GL, Weinel P, Odegaard A, Murphy DM. **FDA Safety Reviews on Drugs, Biologics, and Vaccines: 2007-2013**. Pediatrics. 2015 Nov 23.

Cousins D, Gerrett D, Warner B. A review of medication incidents reported to the **National Reporting and Learning System in England and Wales** over six years (2005 - 2010). Br J Clin Pharmacol. 2011 Dec 22.

CNODES: Feb/13 A national network has been created that promises quicker responses to drug safety issues. The Canadian Network for Observational Drug Effect Studies (CNODES) is part of the national Drug Safety and Effectiveness Network, a body that was created by Health Canada and the Canadian Institutes of Health Research to improve post-marketing surveillance of drugs and help speed up responses to safety concerns. CNODES is a network of researchers and databases from the provinces; right now, seven are involved. It's epidemiology on a large scale, said Dr. David Henry. He is president and CEO of the Institute for Clinical Evaluative Sciences (ICES) and a professor of medicine at the University of Toronto. ICES plays a role in producing and analyzing health services data for Ontario.

Czaja AS, Fiks Ag, Wasserman RC, et al. **Beyond the Label**: Steering the Focus Toward Safe and Effective Prescribing. Pediatrics. 2017;139(5):e20163518 (Off-label)

Daniels JP, Hunc K, Cochrane D, et al. **Identiication by families** of **pediatric adverse events** and near misses overlooked by health care providers CMAJ 2012;184:29-34.

Darnis D, Mahé J, Vrignaud B, et al. **Adverse Drug Reactions in Pediatric Emergency Medicine**. Ann Pharmacother. 2015 Dec;49(12):1298-304.

Dart RC, Paul IM, Bond GR, et al. Pediatric fatalities associated with over the counter (nonprescription) **cough and cold medications**. Ann Emerg Med. 2009 Apr;53(4):411-7. Epub 2008 Dec 19.

Davies EC, Green CF, Taylor S, et al. **Adverse drug reactions in hospital in-patients**: a prospective analysis of 3695 patient-episodes. PLoS One. 2009;4(2):e4439.

Davies EA, O'Mahony MS. **Adverse drug reactions in special populations – the elderly**. Br J Clin Pharmacol. 2015 Jan 24.

De Bruijn, H. Managing professionals. Chapter 3. Routledge, 2010. 15 Wu AW, Folkman S, McPhee SJ, Lo B. Do **house officers learn from their mistakes**? *JAMA* 1991;265:2089-94.

De Vries EN, Prins HA, Crolla RM, den Outer AJ, van Andel G, van Helden SH, et al. Effect of a comprehensive **surgical safety system** on patient outcomes. *N Engl J Med* 2010;363:1928-37.

de Vries ST, Denig P, Ekhart C, et al. **Gender differences in adverse drug reactions** reported to the national pharmacovigilance centre in the Netherlands An explorative observational study. Br J Clin Pharmacol. 2019 Apr 2.

Del Pozzo-Magaña BR, Rieder MJ, Lazo-Langner A. **Quality of life in children with adverse drug reactions**: a narrative and systematic review. Br J Clin Pharmacol. 2014 May 15.

Delaney JAM, Opatrny LMDM, Brophy JMMDP, Suissa SP. **Drug drug interactions between antithrombotic medications and the risk of gastrointestinal bleeding**. Can Med Assoc J 2007;177:347-51.

Denson JL, Jensen A, Saag HS, et al. Association between **end-of-rotation resident transition** in care and mortality among hospitalized patients. JAMA. doi:10.1001/jama.2016.17424

Dyer C. Where should the buck stop? **Doctors taking the blame for system failure**. BMJ. 2016 Nov 23;355:i6274.

Dharmarajan K, Hsieh AF, Lin Z, Bueno H, Ross JS, Horwitz LI, et al. **Hospital readmission performance and patterns of readmission**: retrospective cohort study of Medicare admissions. BMJ 2013;347:f6571.

Dixon-Woods M, Pronovost PJ. **Patient safety and the problem of many hands**. BMJ Qual Saf. 2016 Feb 24.

Doan J, Zakrzewski-Jakubiak H, et al. Prevalence & risk of potential cytochrome p450-mediated **drug-drug interactions** in older hospitalized patients with polypharmacy. Ann Pharmacother. 2013 Mar;47(3):324-32.

Doherty C, Mc Donnell C. **Tenfold Medication Errors**: 5 Years' Experience at a University-Affiliated Pediatric Hospital. Pediatrics. 2012 Apr 2.

Donaldson L et al. **Medication without harm: WHO's third global patient safety challenge**. Lancet 2017; 389: 1680–1.

Donze´ J, Aujesky D, Williams D, Schnipper JL. **Potentially avoidable 30-day hospital readmissions** in medical patients: derivation and validation of a prediction model [online March 25, 2013.

Donzé J, Lipsitz S, Bates DW, et al. **Causes and patterns of readmissions** in patients with common **comorbidities**: retrospective cohort study. BMJ. 2013 Dec 16;347:f7171

Dovey SM, Leitch S. **Triggering safer general practice care**. BMJ Qual Saf. 2016 Aug 2.

Downing NS, Shah ND, et al. **Postmarket Safety Events** Among Novel Therapeutics Approved by the US Food and Drug Administration Between 2001 and 2010. JAMA. 2017 May 9;317(18):1854-1863.

Dudas RA, Bundy DG, Miller MR, Barone M. Can **teaching medical students** to investigate medication errors change their attitudes towards patient safety? Qual Saf Health Care. 2011 Jan 12.
Duke J, Friedlin J, Ryan P. A quantitative analysis of adverse events and **"overwarning" in drug labeling.** Arch Intern Med. 2011 May 23;171(10):944-6.
Dweik RA, Stacey D, Kohen D, et al. **Factors Affecting Patients Reporting** of Adverse Drug Reactions: A Systematic Review. Br J Clin Pharmacol. 2016 Nov 21.
Eggertson Laura. New network (**cNODES**) created to assess drug safety. CMAJ December 13, 2011 183:E1293-E1294; ahead of print Nov 7, 2011, doi:10.1503/cmaj.109-4045.
Epstein AM, Jha AK, Orav JE. The relationship between **hospital readmission rates and rehospitalizations**. N Engl J Med 2011; 365:2287-2295.
Ericsson C, Skagerström J, Schildmeijer K, et al. **Can patients contribute to safer care in meetings** with healthcare professionals? A cross-sectional survey of patient perceptions and beliefs. BMJ Qual Saf. 2019 Apr 24.
Falconer N, Barras M, Cottrell N. Systematic review of **predictive risk models for adverse drug events** in hospitalised patients. Br J Clin Pharmacol. 2018 Jan 16.
Farnan JM, Gaffney S, Poston JT, et al. **Patient safety room of horrors**: a novel method to assess medical students and entering residents' ability to identify hazards of hospitalisation. BMJ Qual Saf. 2015 Nov 30.
FDA November 5, 2009 — The US Food and Drug Administration (FDA) has launched a new program called the **Safe Use Initiative** to reduce drug-related injuries from preventable sources of harm.
FDA Mar/10 In late April, Takeda Pharmaceuticals will begin marketing its proton pump inhibitor **Kapidex** (dexlansoprazole) under the new name **Dexilant**, owing to dispensing errors that have occurred from mix-ups with the prostate cancer drug Casodex (bicalutamide) and the analgesic Kadian (morphine).FDA news release
FDA May/18: Lake Michigan Distilling Company, LLC of La Porte, Indiana, doing business as **Ethanol Extraction, is recalling its 95% Ethyl Alcohol product ("Product") because of possible contamination with methanol**, a highly toxic type of alcohol that can cause serious and sometimes fatal damage if ingested by humans or animals. Recall of the Product was sparked by news that a man in Massachusetts allegedly ingested the Product and later died as a result. There have been no other reports of any ingestion or injury since the Product was first marketed in October 2016.
Feinstein JA, Feudtner C, Kempe A. **Adverse Drug Event-Related Emergency Department Visits** Associated With Complex Chronic Conditions. Pediatrics. 2014 May 19.
Ferner RE, Aronson JK. **Susceptibility to adverse drug reactions**. Br J Clin Pharmacol. 2019 Jun 6.
Ferner RE, McGettigan P. **Adverse drug reactions**. BMJ. 2018 Nov 6;363:k4051.
Fick DM, Cooper JW, Wade WE, Waller JL, Maclean JR, Beers MH. **Updating the Beers criteria for potentially inappropriate medication use in older adults**: results of a US consensus panel of experts. Arch Intern Med. 2003 Dec 8-22;163(22):2716-24. Erratum in: Arch Intern Med. 2004 Feb 9;164(3):298. http://www.hqc.sk.ca/download.jsp?Tnpy1RKzAkMsCVz+LX1gQTBIzBf0QfLQkUwK4QBZaJst2U9rf2NOdQ==
Finn KM, Metlay JP, Chang Y, et al. Effect of **Increased Inpatient Attending Physician Supervision on Medical Errors, Patient Safety, and Resident Education**: A Randomized Clinical Trial. JAMA Intern Med. 2018 Jun 4.
Forster AJ, Clark HD, Menard A, Dupuis N, Chernish R, Chandok N, et al. Adverse events among medical patients after discharge from hospital. CMAJ 2004;170(3):345-349. Erratum in: CMAJ 2004;170(5):771.
Frank C, Himmelstein DU, Woolhandler S, et al. Era of **faster FDA** drug approval has also seen **increased black-box warnings and market withdrawals**. Health Aff (Millwood). 2014 Aug 1;33(8):1453-9.
Franklin BD. **Medication errors**: do they occur in isolation? BMJ Qual Saf. 2014 Feb 27.
Frankovich J, Longhurst CA, Sutherland SM. Evidence-based medicine in the **EMR** era. N Engl J Med 2011;365:1758-9.
Freund Y, Goulet H, Leblanc J, et al. Effect of Systematic **Physician Cross-checking on Reducing Adverse Events in the Emergency Department**: The **CHARMED** Cluster Randomized Trial. JAMA Intern Med. 2018 Apr 23.
Gallagher P, O'Mahony D. **STOPP** (Screening Tool of Older Persons' potentially **inappropriate Prescriptions**): application to acutely ill elderly patients and comparison with Beers' criteria. Age Ageing 2008;37:673-9.
Gallagher PF, O`Connor MN, O`Mahony D. Prevention of Potentially Inappropriate Prescribing for Elderly Patients: A Randomized Controlled Trial Using **STOPP/START** Criteria. Clin Pharmacol Ther. 2011 Jun;89(6):845-54.
Gandhi TK, Lee TH. **Patient safety beyond the hospital**. N Engl J Med. 2010; 363(11):1001-1003.
Gandhi TK, Berwick DM, Shojania KG. **Patient Safety at the Crossroads**. JAMA. 2016 May 3;315(17):1829-30
Gates PJ, Meyerson SA, Baysari MT, et al. **Preventable Adverse Drug Events Among Inpatients**: A Systematic Review. Pediatrics. 2018 Aug 10.
Gay JC, Agrawal R, Auger KA, et al. Rates and Impact of **Potentially Preventable Readmissions** at **Children's Hospitals**. J Pediatr. 2014 Dec 2.
Ghaleb MA, Barber N, Franklin BD, Wong IC. The incidence and nature of **prescribing and medication administration errors in paediatric inpatients**. Arch Dis Child. 2010 Feb;95(2):113-8.
Gislason GH, Rasmussen JN, Abildstrom SZ, et al. Increased mortality and cardiovascular morbidity associated with use of **nonsteroidal anti-inflammatory drugs in chronic heart failure**. Arch Intern Med 2009;169:141-9.
Golder S, Norman G, Loke YK. Systematic review on the prevalence, frequency and comparative value of **adverse events data in social media**. Br J ClinPharmacol. 2015 Aug 14.
Golder S, Loke YK, Wright K, Norman G. Reporting of **Adverse Events in Published and Unpublished** Studies of Health Care Interventions: A Systematic Review. PLoS Med. 2016 Sep 20;13(9):e1002127.
Grant-Orser A, Davies P, Singh SS. The **lost sponge**: patient safety in the operating room. CMAJ. 2012 Aug 7;184(11):1275-8.
Gupta A, Yek C, Hendler RS. **Phenytoin Toxicity-Performance Improvement**. JAMA. 2017 Jun 20;317(23):2445-2446
Guthrie Bruce, McCowan Colin, Davey Peter, et al. **High risk prescribing in primary care** patients particularly vulnerable to adverse drug events: cross sectional population database analysis in Scottish general practice. BMJ 2011
Guthrie B, et al. **Data feedback** and behavioural change intervention to improve primary care prescribing safety (**EFIPPS**): multicentre, three arm, cluster randomized controlled trial. BMJ. 2016 Aug 18;354:i4079.
Guttmann A, Schull MJ, Vermeulen MJ, et al. Association between waiting times and short term mortality and hospital admission **after departure from emergency department**: population based cohort study from Ontario, Canada. BMJ 2011;342:d2983.
Hakala AK, Fergusson D, Kimmelman J. **Nonpublication of Trial Results for New Neurological Drugs**: A Systematic Review. Ann Neurol. 2017 May 9
Hakkarainen KM, Gyllensten H, et al. Prevalence, nature and potential **preventability of adverse drug events** – A population-based medical record study of 4970 adults. Br J Clin Pharmacol. 2013 Dec 25
Hall AJ, Logan JE, Toblin RL, Kaplan JA, Kraner JC, Bixler D, Crosby AE, Paulozzi LJ. Patterns of abuse among unintentional pharmaceutical overdose fatalities. JAMA. 2008 Dec 10;300(22):2613-20. The majority of overdose deaths in West Virginia in 2006 were associated with nonmedical use and diversion of pharmaceuticals, primarily **opioid** analgesics.
Hamilton Hilary; Gallagher Paul; Ryan Cristin; et al. **Potentially Inappropriate Medications** Defined by **STOPP** Criteria and the Risk of Adverse Drug Events in **Older Hospitalized Patients**. Arch Intern Med. 2011;171(11):1013-1019.
Handler SM, Hanlon JT, Perera S, et al. Castle NG, Studenski SA. Consensus list of **signals** to detect potential adverse drug reactions in nursing homes. J Am Geriatr Soc. 2008 May;56(5):808-15. Epub 2008 Mar 21.
Härkänen M, Vehviläinen-Julkunen K, Murrells T, et al. **Medication administration errors and mortality**: Incidents reported in England and Wales between 2007−2016. Res Social Adm Pharm. 2018 Nov 22.
Haynes AB, Weiser TG, et al. Safe Surgery Saves Lives Study. A **surgical safety checklist** to reduce morbidity and mortality in a global population. N Engl J Med. 2009 Jan 29;360(5):491-9. Epub 2009 Jan 14.
Hébert PC, Stanbrook MB, Macdonald N, et al. Can **Health Canada** protect Canadians from unsafe drugs? CMAJ. 2011 Jul 12;183(10):1125-6.
Health Canada: Sound alike, Look alike. http://www.hc-sc.gc.ca/dhp-mps/brgtherap/activit/fs-fi/lasa-pspcs_factsheet-faitsaillant_e.html
Health Canada Mar/17 is advising Canadians that GlaxoSmithKline (GSK) Consumer Healthcare Inc. has initiated a voluntary recall of certain **Buckley's syrup** products from stores. A defect with the plastic seal may cause it to fall into the bottle and present a potential choking hazard if swallowed. This seal is a circular plastic layer that is clear or semi-transparent and approximately 1.7 cm in diameter.

Herder M, Gibson E, Graham J, et al. **Regulating prescription drugs** for patient safety: Does Bill C-17 go far enough? CMAJ. 2014 May 13;186(8):E287-92.
Heyland DK, Ilan R, Jiang X, et al.. The prevalence of **medical error related to end-of-life communication** in Canadian hospitals: results of a multicentre observational study. BMJ Qual Saf. 2015 Nov 9.
Hodges NL, Spiller HA, Casavant MJ, et al. **Non-health care facility medication errors** resulting in serious medical outcomes. Clin Toxicol (Phila). 2017 Jul 10:1-8.
Hoekman J, Klamer TT, Mantel-Teeuwisse AK, et al. Characteristics and follow-up of **post-marketing studies** of conditionally authorised medicines in the **EU**. Br J Clin Pharmacol. 2016 Mar 18
Hohl C, Lexchin JR, Balka E. Can **reporting of adverse drug reactions** create safer systems while improving health data? CMAJ. 2015 Aug 11;187(11):789-90.
Hohl CM, Woo SA, Cragg A, et al. Repeat **adverse drug events associated with outpatient medications**: a descriptive analysis of 3 observational studies in British Columbia, Canada. CMAJ Open. 2019 Jul 18;7(3):E446-E453.
Holbrook AM, Pereira JA, Labiris R, et al. Systematic overview of **warfarin and its drug and food interactions**. Arch Intern Med. 2005;165: 1095-106.
Howard R, Avery A, Slavenburg S, Royal S, Pipe G, Lucassen P, et al. Which **drugs cause preventable admissions** to hospital? A systematic review. Br J Clin Pharmacol 2007;63:136-47.
Hwang TJ, Bourgeois FT, Seeger JD. **Drug safety in the digital age**. N Engl J Med. 2014 Jun 26;370(26):2460-2.
Hwang TJ, Carpenter D, Lauffenburger JC, et al. **Failure of Investigational Drugs in Late-Stage Clinical Development and Publication** of Trial Results. JAMA Intern Med. 2016 Oct 10.
Institute of Medicine. **Health IT** and patient safety: building safer systems for better care. 2011. www.iom.edu/Reports/2011/Health-IT-and-Patient-Safety-Building-Safer-Systemsfor-Better-Care.aspx.
ISMP: **Anticoagulants the Leading Reported Drug Risk** in 2011. QuarterWatch 2012. http://www.ismp.org/quarterwatch/pdfs/2011Q4.pdf (suspect drugs list: 1) dabigatran, 2) Warfarin)
James JT. A New, Evidence-based Estimate of **Patient Harms Associated with Hospital Care**. J Patient Saf. 2013 Sep;9(3):122-8.
Jefferson T, Doshi P, Thompson M, et al. **Ensuring safe and effective drugs**: who can do what it takes? BMJ. 2011 Jan 11;342:c7258. doi:10.1136/bmj.c7258.
Jha A, Pronovost P. Toward a Safer Health Care System: The Critical **Need to Improve Measurement**. JAMA. 2016 Apr 14.
Johnson KB, Lehmann CU; the Council on Clinical Information Technology. **Electronic Prescribing** in Pediatrics: Toward Safer and More Effective Medication Management. Pediatrics. 2013 Mar 25.
Joint Commission on Accreditation of Healthcare Organizations (JCAHO) www.jointcommission.org
Kachalia Allen, Kaufman Samuel R., Boothman Richard, Et al. Liability Claims and Costs Before and After Implementation of a **Medical Error Disclosure Program**. *Ann Intern Med* August 17, 2010 153:213-221.
Kachalia A, Mello MM, Nallamothu BK, Studdert DM. **Legal and Policy Interventions** to Improve Patient Safety. Circulation. 2016 Feb 16;133(7):661-71.
Kaguelidou F, Beau-Salinas F, Jonville-Bera AP, et al. **Neonatal Adverse Drug Reactions**: An analysis of reports to the **French** pharmacovigilance Database. Br J Clin Pharmacol. 2016 Jun 8.
Kaldjian LC, Jones EW, Wu BJ, Forman-Hoffman VL, et al. **Reporting medical errors** to improve patient safety: a survey of physicians in teaching hospitals.Arch Intern Med. 2008 Jan 14;168(1):40-6.
Kanaan AO, Donovan JL, Duchin NP, et al. **Adverse drug events** after hospital discharge in older adults: types, severity, and involvement of **Beers** Criteria Medications. J Am Geriatr Soc. 2013 Nov;61(11):1894-9.
Kang AM, Brooks DE. US Poison Control Center Calls for Infants 6 Months of Age and Younger. Pediatrics. 2016 Jan 13.
Kapoor A, Field T, Handler S, et al. **Adverse Events in Long-term Care Residents** Transitioning From Hospital Back to Nursing Home. JAMA Intern Med. 2019 Jul 22.
Kaur S, Roberts JA, Roberts MS. Evaluation of **medication-related problems in medication reviews**: a comparative perspective. Ann Pharmacother. 2012 Jul;46(7-8):972-82.
Kellogg KM, Hettinger Z, Shah M, et al. Our current approach to **root cause analysis**: is it contributing to our failure to improve patient safety? BMJ Qual Saf. 2016 Dec 9.
Khalil H;Bell B;Chambers H;Sheikh A;Avery AJ **Professional, structural and organisational interventions in primary care for reducing medication errors.** Cochrane Database Syst Rev. 2017 Oct 4;10:CD003942. Based on moderate- and low-certainty evidence, interventions in primary care for reducing preventable medication errors probably make little or no difference to the number of people admitted to hospital or the number of hospitalisations, emergency department visits, or mortality. The variation in heterogeneity in the pooled estimates means that our results should be treated cautiously as the interventions may not have worked consistently across all studies due to differences in how the interventions were provided, background practice, and culture or delivery of the interventions.
Khan A, Furtak SL, Melvin P, et al. **Parent-Reported Errors** and Adverse Events in Hospitalized Children. JAMA Pediatr. 2016 Feb 29.
Khan A, Coffey M, Litterer KP, et al. **Families as Partners in Hospital Error** and Adverse Event Surveillance. JAMA Pediatr. 2017 Feb 27.
Khan A, Spector ND, Baird JD, et al. Patient safety after implementation of a coproduced **family centered communication programme**: multicenter before and after intervention study. BMJ. 2018 Dec 5;363:k4764.
Kiekkas P, Karga M, Lemonidou C, Aretha D, Karanikolas M. Medication **errors in critically ill adults**: a review of direct observation evidence. Am J Crit Care. 2011 Jan;20(1):36-44.
Kirkendall ES, Kloppenborg E, Papp J, et al. Measuring **Adverse Events and Levels of Harm in Pediatric Inpatients** With the Global Trigger Tool. Pediatrics. 2012 Oct 8.
Klein J, Delany C, Fischer MD, et al. A **growth mindset approach** to preparing trainees for medical error. BMJ Qual Saf. 2017 Apr 11
Kohn LT, Corrigan JM, Donaldson MS, eds. **To Err Is Human: Building a Safer Health System**. Washington, DC: Institute of Medicine; 2000.
Kripalani S, Roumie CL, Dalal AK, et al; for the **PILL-CVD** (Pharmacist Intervention for Low Literacy in Cardiovascular Disease)Study Group. Effect of a **Pharmacist Intervention** on Clinically Important Medication Errors After **Hospital Discharge**: A Randomized Trial. Ann Intern Med. 2012 Jul 3;157(1):1-10.
Krumholz HM, Lin Z, et al. Relationship between **hospital readmission and mortality** rates for patients hospitalized with acute myocardial infarction, heart failure, or pneumonia. JAMA 2013;309:587-93.
Kuehn BM. Group Urges **Going Metric** to Head Off Dosing Mistakes. JAMA. 2014 May 21.
Kwa M, Welty LJ, Xu S. **Adverse events** reported to the **US** Food and Drug Administration for **cosmetics & personal care products** [online June 26, 17].JAMA Intern Med. doi:10 .1001/jamainternmed.2017.2762
Kwan JL, Lo L, Sampson M, Shojania KG. **Medication reconciliation** during transitions of care as a patient safety strategy. A systematic review. Ann Intern Med. 2013;158:397-403.
Lamont T, Beaumont C, Fayaz A, et al. Checking placement of **nasogastric feeding tubes** in adults (interpretation of x ray images): summary of a safety report from the National Patient Safety Agency. BMJ. 2011 May 5;342:d2586. doi:10.1136/bmj.d2586
Landrigan CP, Parry GJ, Bones CB, Hackbarth AD, Goldmann DA, Sharek PJ. **Temporal trends** in rates of patient harm resulting from medical care. *N Engl J Med* 2010;363:2124-34.
Landrigan CP, Stockwell D, Toomey SL, et al. Performance of the **Global Assessment of Pediatric Patient Safety (GAPPS) Tool**. Pediatrics. 2016 May 24.
Larose G, Levy A, Bailey B, et al. **Decreasing Prescribing Errors During Pediatric Emergencies**: A Randomized Simulation Trial. Pediatrics. 2017 Mar;139(3).
Lasser KE, Allen PD et al. JAMA 2002;287:2215. (New drugs – SAEs – black box or withdrawal from market)
Lavonas EJ, Banner W, Bradt P, et al. **Root Causes, Clinical Effects, and Outcomes of Unintentional Exposures to Buprenorphine** by Young Children. J Pediatr. 2013 Aug 22.
Lazarou J, Pomeranz BH, Corey PN. Incidence of adverse drug reactions in hospitalized patients: a meta-analysis of prospective studies. JAMA. 1998 Apr 15;279(15):1200-5. The overall incidence of serious ADRs was **6.7%** (95% confidence interval [CI], 5.2%-8.2%) and of fatal ADRs was 0.32% (95% CI, 0.23%-0.41%) of hospitalized patients. We estimated that in 1994 overall **2,216,000** (1721000-2711000) hospitalized patients had serious ADRs and **106,000** (76000-137000) had **fatal** ADRs, making these reactions between the fourth and sixth leading cause of death.
Leape LL, Berwick DM. **Five years after To Err Is Human**: what have we learned? *JAMA* 2005;293:2384-90.
Leppin AL, Gionfriddo MR, Kessler M, et al. **Preventing 30-Day Hospital Readmissions**: A Systematic Review and Meta-analysis of Randomized Trials. JAMA Intern Med. 2014 May 12.
Lexchin J. Arch Intern Med. 2012;172:1680. (New drugs – SAEs – black box or withdrawal from market)
Lexchin J. **New drugs and safety**: what happened to new active substances approved in Canada between 1995 and 2010? Arch Intern Med. 2012 Nov 26;172(21):1680-1.
Lexchin J. How safe are **new drugs**? Market withdrawal of drugs approved in Canada between 1990 and 2009. Open Med. 2014 Jan 28;8(1):e14-9.
Lexchin J. **Postmarket safety warnings** for drugs approved in **Canada** under the Notice of Compliance with **conditions policy**. Br J Clin Pharmacol. 2014 Nov 12.
Lineberry N, Berlin JA, et al. Recommendations to **improve adverse event reporting in clinical trial publications**: a joint pharmaceutical industry/journal editor perspective. BMJ. 2016 Oct 3;355:i5078.
Lipitz-Snyderman Allison, Steinwachs Donald, Needham Dale M, et al. Impact of a **statewide intensive care unit quality improvement initiative** on hospital mortality and length of stay: retrospective comparative

analysis. BMJ 2011;342:doi:10.1136/bmj.d219 (Published 31 January 2011)
Loboz K, Shenfield G. **Drug combinations and impaired renal function—the "triple whammy**". Br J Clin Pharmacol 2005;59:239-43.
Longhurst CA, Parast L, Sandborg CI, Widen E, Sullivan J, Hahn JS, Dawes CG, Sharek PJ. Decrease in Hospital-wide Mortality Rate After Implementation of a Commercially Sold **Computerized Physician Order Entry System**. Pediatrics. 2010 May 3.
Longhurst CA, Landa HM. **Health information technology** and patient safety. BMJ. 2012 Feb 20;344:e1096.
Lopez Lenny; Weissman Joel S.; Schneider Eric C.; et al. **Disclosure of Hospital Adverse Events** and Its Association With Patients' Ratings of the Quality of Care. Arch Intern Med. 2009;169(20):1888-1894.
Lovegrove MC, Mathew J, Hampp C, et al. **Emergency Hospitalizations** for Unsupervised Prescription Medication Ingestions by Young **Children**. Pediatrics. 2014 Sep 15.
Lovegrove MC, Geller AI, Fleming-Dutra KE, et al. US **Emergency Department Visits for Adverse Drug Events From Antibiotics in Children**, 2011-2015. J Pediatric Infect Dis Soc. 2018 Aug 23.
Lyons M. Do classical origins of **medical terms** endanger patients? Lancet. 2008 Apr 19;371(9621):1321-2.
Ma P, Marinovic I, Karaca-Mandic P. Drug **Manufacturers' Delayed Disclosure of Serious and Unexpected Adverse Events** to the US Food and Drug Administration. JAMA Intern Med. 2015 Jul 27.
Madlon-Kay DJ,Mosch FS. Liquid medication dosing errors. J Fam Pract. 2000; 49(8):741-744.
Makary MA, Daniel M. **Medical error-the third leading cause of death** in the US. BMJ. 2016 May 3;353:i2139
Manias E, Kinney S, Cranswick N, et al. Interventions to Reduce **Medication Errors in Pediatric Intensive Care**. Ann Pharmacother. 2014 Oct;48(10):1313-1331. Epub 2014 Jul 24.
Marshall M, de Silva D, Cruickshank L, et al. What we know about **designing an effective improvement intervention** (but too often fail to put into practice). BMJ Qual Saf. 2016 Dec 16.
Matlow AG, Baker GR, Flintoft V, et al. **Adverse events among children** in Canadian hospitals: the Canadian Paediatric Adverse Events Study. CMAJ. 2012 Aug 7.
Mattison MLP; Afonso KA; Ngo LH. et al. Preventing Potentially Inappropriate Medication Use in Hospitalized Older Patients With a **Computerized Provider Order Entry** Warning System. Arch Intern Med. 2010;170(15):1331-1336.
Mazer-Amirshahi M, Rasooly I, Brooks G, et al. The Impact of **Pediatric Labeling Changes on Prescribing Patterns of Cough and Cold Medications**. J Pediatr. 2014 Sep 3.
Mbeledogu CN, Cecil EV, Millett C, et al. **Hospital admissions for unintentional poisoning in preschool children** in England; 2000-2011. Arch Dis Child. 2014 Aug 28.
McBride WG. **Thalidomide** and congenital abnormalities. Lancet 1961;2:1358.
McCannon J, Berwick DM. A **new frontier in patient safety**. JAMA. 2011 Jun 1;305(21):2221-2.
McClead RE Jr, Catt C, Davis JT, et al; Adverse Drug Event Quality Collaborative. An **Internal Quality Improvement Collaborative Significantly Reduces Hospital-Wide Medication Error** Related Adverse Drug Events. J Pediatr. 2014 Oct 8.
McCulloch P, Kreckler S, New S, et al. Effect of a **"Lean" intervention** to improve safety processes and outcomes on a surgical emergency unit. BMJ. 2010 Nov 2;341:c5469. doi: 10.1136/bmj.c5469.
McDonald KM, Matesic B, Contopoulos-Ioannidis DG, Lonhart J, Schmidt E, Pineda N, et al. Patient safety strategies targeted at **diagnostic errors**. A systematic review. Ann Intern Med. 2013;158:381-9.
Mello MM, Kachalia A, Roche S, et al. Outcomes in two Massachusetts hospital systems give reason for optimism about **communication-and-resolution programs**. Health Aff 2017.
Merrick MT, Ford DC, Ports KA, et al. Prevalence of **Adverse Childhood Experiences** From the 2011-2014 Behavioral Risk Factor Surveillance System in 23 States. JAMA Pediatr. 2018 Nov 1;172(11):1038-1044.
Merry AF, Webster CS, et al. Multimodal system designed to **reduce errors** in recording and administration of drugs in **anaesthesia**: prospective randomised clinical evaluation. BMJ. 2011 Sep 22;343:d5543.
Miake-Lye IM, Hempel S, Ganz DA, Shekelle PG. **Inpatient fall prevention programs** as a patient safety strategy. A systematic review. Ann Intern Med. 2013;158:390-6.
Mixon AS et al. Characteristics associated with **postdischarge medication errors**. Mayo Clin Proc 2014 Aug; 89:1042.
Montané E, Arellano AL, Sanz Yet al. **Drug-related deaths in hospital inpatients**: A retrospective cohort study. Br J Clin Pharmacol. 2017 Nov 17.
Moore TJ, Glenmullen J, Furberg CD (2010) Prescription **Drugs Associated with Reports of Violence** Towards Others. PLoS ONE 5(12): e15337. doi:10.1371/journal.pone.0015337
Morgan DJ, Wright SM, Dhruva S. Update on **Medical Overuse**. JAMA Intern Med. 2014 Nov 3.
Mostaghim SR, Gagne JJ, Kesselheim AS. **Safety related label changes** for new **drugs after approval in the US through expedited regulatory pathways**: retrospective cohort study. BMJ. 2017 Sep 7;358:j3837.
Mouton JP, Mehta U, Parrish AG, et al. **Mortality from adverse drug reactions** in adult medical inpatients at four hospitals in South Africa: a cross-sectional survey. Br J Clin Pharmacol. 2014 Dec 5.
Mueller BU, Neuspiel DR, Fisher ERS; Council on Quality Improvement and Patient Safety. Principles of **Pediatric Patient Safety**: Reducing Harm Due to Medical Care. Pediatrics. 2019 Jan 22.
Murray MD, Ritchey ME, Wu J, Tu W. Effect of a pharmacist on adverse drug events and medication errors in outpatients with cardiovascular disease. Arch Intern Med. 2009 Apr 27;169(8):757-63
MyMedRec: Jun/12 launched to include a free new iPhone and iPad app, **MyMedRec,** and website www.knowledgeisthebestmedicine.org which have been developed by the Institute for Safe Medication Practices Canada with input from Canadian patient groups and health care provider organizations.
National Patient Safety Agency Alerts (**NHS**) http://www.nrls.npsa.nhs.uk/resources/type/alerts/
Nebeker JR, Barach P, Samore MH. Clarifying adverse drug events: a clinician's guide to terminology, documentation, and reporting. Ann Intern Med. 2004 May 18;140(10):795-801.
Nellis G, Metsvaht T, Varendi H, et al; ESNEE consortium. Potentially **harmful excipients in neonatal** medicines: a pan-European observational study. Arch Dis Child. 2015 Apr 8
Nieuwlaat R, Wilczynski N, Navarro T, et al. Interventions for **enhancing medication adherence**. Cochrane Database Syst Rev. 2014 Nov 20;11:CD000011. Across the body of evidence, effects were inconsistent from study to study, and only a minority of lowest risk of bias RCTs improved both adherence and clinical outcomes. Current methods of improving medication adherence for chronic health problems are mostly complex and not very effective, so that the full benefits of treatment cannot be realized. The research in this field needs advances, including improved design of feasible long-term interventions, objective adherence measures, and sufficient study power to detect improvements in patient-important clinical outcomes. By making our comprehensive database available for sharing we hope to contribute to achieving these advances.
Nguyen HT, Pham HT, Vo DK, et al. The effect of a clinical **pharmacist-led training programme on intravenous medication errors**: a controlled before and after study. BMJ Qual Saf. 2013 Nov 6
O'Connor NR. **FDA boxed warnings**: how to prescribe drugs safely. Am Fam Physician. 2010 Feb 1;81(3):298-303.
O'Hara JK, Armitage G, Reynolds C, et al. How might health services **capture patient-reported safety concerns** in a hospital setting? An exploratory pilot study of three mechanisms. BMJ Qual Saf. 2016 Feb 4.
O'Hara JK, Reynolds C, Moore S, et al. What can **patients tell us about the quality and safety of hospital care**? Findings from a UK multicentre survey study. BMJ Qual Saf. 2018 Mar 15.
O'Leary Kevin J.; Buck Ryan; Fligiel Helene M.; et al. **Structured Interdisciplinary Rounds** in a Medical Teaching Unit: Improving Patient Safety.*Arch Intern Med*. 2011;171(7):678-684.
O'Leary JD, Wijeysundera DN, Crawford MW. Effect of **surgical safety checklists** on pediatric surgical complications in Ontario. CMAJ. 2016 Mar 14
Oduyebo I, Lehmann CU, Pollack CE, et al. Association of **self-reported hospital discharge handoffs** with 30-day readmissions [online March 25, 2013.
Onakpoya IJ, Heneghan CJ, Aronson JK. **Delays in the post-marketing withdrawal of drugs to which deaths** have been attributed: a systematic investigation and analysis. BMC Med. 2015 Feb 5;13:26.
Onakpoya IJ, Heneghan CJ, Aronson JK. **Post-marketing withdrawal of 462 medicinal products** because of adverse drug reactions: a systematic review of the world literature. BMC Med. 2016 Feb 4;14(1):10.
Onakpoya IJ. **Rare adverse events in clinical trials: understanding the rule of three**. Evid Based Med. 2018 Feb;23(1):6.
Onder Graziano; Petrovic Mirko; Tangiisuran Balamurugan; et al. Development and Validation of a Score to Assess Risk of Adverse Drug Reactions Among In-Hospital Patients 65 Years or Older: The **GerontoNet ADR Risk Score**. Arch Intern Med. 2010;170(13):1142-1148.
Panagioti M, Khan K, Keers R N, etal . Prevalence, severity, and nature of **preventable patient harm across medical care settings**: systematic review and meta-analysis. BMJ 2019;366:l4185.
Parshuram CS, Amaral AC, Ferguson ND, et al. Canadian Critical Care Trials Group. Patient safety, resident well-being and continuity of care with **different resident duty schedules** in the intensive care unit: a randomized trial. CMAJ. 2015 Mar 17;187(5):321-9.

Perla RJ, Hohmann SF, Annis K. **Whole-patient measure of safety**: using administrative data to assess the probability of highly undesirable events during hospitalization. J Healthc Qual. 2013 Sep;35(5):20-31.

Perras C, Jacobs P, Boucher M, Murphy G, et al. **Technologies to Reduce Errors** in Dispensing and Administration of Medication in Hospitals: Clinical and Economic Analyses [Technology report number 121]. In particular, the use of barcoding for medication dispensing and administration systems, and the simultaneous use of technologies and ward-based automatic dispensing devices could reduce the risk of medication errors in hospitals.

Perry LT, Bhasale A, Fabbri A, et al. Comparative analysis of medicines safety advisories released by Australia, Canada, the United States, and the United Kingdom [online April 29, 2019]. JAMA Intern Med. doi:10.1001/jamainternmed.2019.0294

Pettker CM, Thung SF, Lipkind HS, et al. A comprehensive **obstetric patient safety program** reduces liability claims and payments. Am J Obstet Gynecol. 2014 Jun 9.

Pretorius RW, Gataric G, Swedlund SK. **Reducing the Risk of Adverse Drug Events in Older Adults**. Am Fam Physician. 2013;87(5):331-336.

Pharmacist's Letter. May 2007. Medication Errors and Patient Safety Resources.

Pharmacist's Letter. June 2008. Preventing Pediatric Medication Errors. See also Joint Commission: http://www.jointcommission.org/SentinelEvents/SentinelEventAlert/sea_39.htm

Phillips EJ. **Classifying ADRs - Does dose matter**? Br J Clin Pharmacol. 2015 Aug 18.

Pierluissi E, Fischer MA, Campbell AR, Landefeld CS. **Discussion of medical errors** in morbidity and mortality conferences. *JAMA* 2003;290:2838-42.

Pirmohamed M, James S, Meakin S, et al. **Adverse drug reactions as cause of admission to hospital**: prospective analysis of 18 820 patients. BMJ. 2004 Jul 3;329(7456):15-9.

Pitrou Isabelle; Boutron Isabelle; Ahmad Nizar; et al. **Reporting of Safety** Results in Published Reports of Randomized Controlled Trials. *Arch Intern Med*. 2009;169(19):1756-1761.

Poon EG et al. Effect of **bar-code technology** on the safety of medication administration. N Engl J Med 2010 May 6; 362:1698.

Powers A, Cook GE. Potential **safety signals** and their significance [published online November 14, 2011]. Arch Intern Med. doi:10.1001/archinternmed .2011.525.

Price J. **Pharmacovigilance in Crisis**: Drug Safety at a Crossroads. Clin Ther. 2018 Mar 28.

Pronovost Peter J.; Faden Ruth R. **Setting Priorities** for Patient Safety: Ethics, Accountability, and Public Engagement. JAMA. 2009;302(8):890-891.

Qato DM, Alexander GC, Conti RM, et al. Use of prescription and over-the-counter medications and dietary supplements among older adults in the United States. JAMA. 2008 Dec 24;300(24):2867-78. In this sample of community-dwelling older adults, prescription and nonprescription medications were commonly used together, with nearly **1 in 25 individuals potentially at risk for a major drug-drug interaction**.

Qato DM, Wilder J, Schumm LP, et al. Changes in **prescription and over-the-counter medication and dietary supplement use** among older adults in the United States, 2005 vs 2011 [online March 21, 2016].JAMA Intern Med. doi:10.1001 /jamainternmed.2015.8581.

Quach C, McArthur M, McGeer A, et al. Risk of **infection following a visit to the emergency department**: a cohort study. CMAJ. 2012 Mar 6;184(4):E232-9.

Raban MZ, Westbrook JI. Are interventions to **reduce interruptions and errors during medication administration** effective?: a systematic review. BMJ Qual Saf. 2013 Aug 26.

Raine JM. **Drug safety**: reporting systems for the general public. BMJ. 2012 Aug 7;345:e4916.

Ratanawongsa N, Barton JL, et al. Association between **clinician computer use** and communication with patients in safety-net clinics [online Nov 30, 15].JAMA Intern Med. doi:10.1001/jamainternmed.2015 .6186.

Rees P, Edwards A, Panesar S, et al. A. **Safety Incidents in the Primary Care** Office Setting. Pediatrics. 2015 May 4.

Renaudin P, Boyer L, Esteve MA, et al. Do **pharmacist-led medication reviews** in hospitals help reduce hospital readmissions? A systematic review and meta-analysis. Br J Clin Pharmacol. 2016 Aug 11.

Rennke S, Nguyen OK, Shoeb MH, Magan Y, Wachter RM, Ranji SR. **Hospital-initiated transitional care interventions** as a patient safety strategy. A systematic review. Ann Intern Med. 2013;158:432-40.

Reston JT, Schoelles KM. **In-facility delirium programs** as a patient safety strategy. A systematic review. Ann Intern Med. 2013;158:375-80.

Rinke ML, Bundy DG, Velasquez CA, et al. Interventions to Reduce **Pediatric Medication Errors**: A Systematic Review. Pediatrics. 2014 Aug;134(2):338-360.

Rohrhoff NJ, McNeill DB, Boggan JC. An **adverse reaction to a medication given to treat an adverse reaction**: a teachable moment. JAMA Intern Med. 2014 Jul 1;174(7):1035-6.

Rojas-Velandia C, Ruiz-Garzón J, Moscoso-Alcina JC, et al. Characterization of **Adverse Drug Reactions Causing Admission to an Intensive Care Unit**. Br J Clin Pharmacol. 2016 Dec 1.

Rolfes L, van Hunsel F, Caster Oet al. Does **Patient Reporting lead to Earlier Detection of Drug Safety Signals**? A Retrospective Comparison of Time to Reporting Between Patients and Healthcare Professionals in a Global Database. Br J Clin Pharmacol. 2018 Mar 9.

Roter DL, Wolff J, Wu A, et al. **Patient and family empowerment** as agents of ambulatory care safety and quality. BMJ Qual Saf. 2017 Jun;26(6):508-512.

Rothschild JM et al. Risks of complications by attending physicians after performing **nighttime procedures**. JAMA 2009 Oct 14; 302:1565.

Routledge PA. **Safe prescribing**: a titanic challenge. Br J Clin Pharmacol. 2012 Oct;74(4):676-84.

Ryan R, Santesso N, Lowe D, et al. Interventions to **improve safe and effective medicines use by consumers**: an overview of systematic reviews. Cochrane Database Syst Rev. 2014 Apr 29;4:CD007768. This overview presents evidence from 75 reviews that have synthesised trials and other studies evaluating the effects of interventions to improve consumers' medicines use.Systematically assembling the evidence across reviews allows identification of effective or promising interventions to improve consumers' medicines use, as well as those for which the evidence indicates ineffectiveness or uncertainty.

Saber Tehrani AS, Lee H, Mathews SC, et al. 25-Year summary of US **malpractice claims** for diagnostic errors 1986-2010: an analysis from the National Practitioner Data Bank. BMJ Qual Saf. 2013 Apr 22.

Saedder EA, Brock B, Nielsen LP, Bonnerup DK, Lisby M. **Identifying high-risk medication**: a systematic literature review. Eur J Clin Pharmacol. 2014 Jun;70(6):637-45.

Saedder EA, Lisby M, Nielsen LP, et. al. **Number of drugs most frequently found to be independent risk factor for serious adverse reactions**: a systematic literature review. Br J Clin Pharmacol. 2015 Feb 10.

Saluja S, Woolhandler S, Himmelstein DU, et al. **Unsafe Drugs Were Prescribed More Than One Hundred Million Times** in the United States Before Being Recalled. Int J Health Serv. 2016 Jul;46(3):523-30.

Samoy LJ, Zed PJ, Wilbur K, et al. Drug-related hospitalizations in a tertiary care internal medicine service of a Canadian hospital: a prospective study. Pharmacotherapy 2006;26(11): 1578-1586.

Schneider EL, Campese VM. Adverse drug responses: an increasing threat to the well-being of older patients: Comment on "Development and **validation of a score to assess risk of adverse drug reactions** among in-hospital patients 65 years or older." Arch Intern Med. 2010;170:1148-9.

Schiff Gordon D.; Hasan Omar; Kim Seijeoung; et al. **Diagnostic Error** in Medicine: Analysis of 583 Physician-Reported Errors. Arch Intern Med. 2009;169(20):1881-1887.

Schiff Gordon D.; Galanter William L.; Duhig Jay; et al. **Principles of Conservative Prescribing**. Arch Intern Med. 2011;0(2011):archinternmed.2011.256.

Schmidt E, Goldhaber-Fiebert SN, Ho LA, McDonald KM. **Simulation exercises** as a patient safety strategy. A systematic review. Ann Intern Med. 2013; 158:425-31.

Schmidtke KA, Poots AJ, Carpio J, et al. **Considering chance in quality and safety performance measures**: an analysis of performance reports by boards in English NHS trusts. BMJ Qual Saf. 2016 Mar 31.

Schwartz LM, Woloshin S. Communicating **uncertainties about prescription drugs to the public**: a national randomized trial. Arch Intern Med. 2011;171 (16):1463-1468.

Shah R, Blustein L, Kuffner E, et al. Communicating **doses of pediatric liquid medicines** to parents/caregivers: a comparison of written dosing directions on prescriptions with labels applied by dispensed pharmacy. J Pediatr. 2014 Mar;164(3):596-601.

Sharek PJ, McClead RE Jr, Taketomo C, Luria JW, Takata GS, Walti B, Tanski M, Nelson C, Logsdon TR, Thurm C, Federico F. An intervention to decrease **narcotic**-related adverse drug events in children's hospitals. Pediatrics. 2008 Oct;122(4):e861-6.

Sharfstein JM, Kesselheim AS. The **Safety of Prescription Drugs. (pioglitazone, rosiglitazone)** JAMA. 2015 Jul 21;314(3):233-4.

Shehab N, Patel PR, Srinivasan A, Budnitz DS. Emergency department visits for antibiotic-associated adverse events. Clin Infect Dis. 2008 Sep 15;47(6):735-43. On the basis of 6614 cases, an estimated 142,505 visits (95% confidence interval [CI], 116,506-168,504 visits) annually were made to US EDs for drug-related adverse events attributable to systemic antibiotics. Antibiotics were implicated in 19.3% of all ED visits for drug-related adverse events. Most ED visits for antibiotic-associated adverse events were for allergic reactions (78.7% of visits; 95% CI, 75.3%-82.1% of visits). One-half of the estimated ED visits were attributable to penicillins (36.9% of visits; 95% CI, 34.7%-39.2% of visits) and cephalosporins (12.2%; 95% CI, 10.9%-13.5%). Among commonly prescribed antibiotics, sulfonamides and clindamycin were associated with the highest rate of ED visits (18.9 ED visits per 10,000 outpatient prescription visits [95% CI, 13.1-24.7 ED visits per 10,000 outpatient prescription visits] and 18.5 ED visits per 10,000 outpatient prescription visits [95% CI, 12.1-25.0 ED visits per 10,000 outpatient prescription visits], respectively). Compared with all other antibiotic classes, sulfonamides were associated with a significantly higher rate of moderate-to-severe allergic reactions (4.3% [95% CI, 2.9%-5.8%] vs. 1.9 % [95% CI, 1.5%-2.3%]), and sulfonamides and fluoroquinolones were associated with a significantly higher rate of neurologic or psychiatric disturbances (1.4% [95% CI, 1.0%-1.7%] vs. 0.5% [95% CI, 0.4%-0.6%]). CONCLUSIONS: Antibiotic-associated adverse events lead to many ED visits, and allergic reactions are the most common events. Minimizing unnecessary antibiotic use by even a small percentage could significantly reduce the immediate and direct risks of drug-related adverse events in individual patients.

Shehab N, Lovegrove MC, Geller AI, et al. **US emergency department visits** for outpatient adverse drug events, 2013-2014.JAMA. doi:10.1001/jama.2016.16201
Shekelle Paul G., Pronovost Peter J., Wachter Robert M., et al. Advancing the **Science of Patient Safety**. Ann Intern Med May 17, 2011 154:693-696.
Shekelle PG. **Nurse–patient ratios** as a patient safety strategy. A systematic review. Ann Intern Med. 2013;158:404-9.
Shekelle PG, Pronovost PJ, Wachter RM, McDonald KM, Schoelles K, Dy SM, et al. The top **patient safety strategies that can be encouraged for adoption now**. Ann Intern Med. 2013;158:365-8.
Shekelle PG, Wachter RM, Pronovost PJ, et al. Making Health Care Safer II: An **Updated Critical Analysis** of the **Evidence for Patient Safety** Practices. (Prepared by the Southern California-RAND Evidence-based Practice Center under contract HHSA290200710062I.) Rockville, MD: Agency for Healthcare Research and Quality; 2013. [Forthcoming].
Shepherd G, Mohorn P, Yacoub K, Williams May D. **Adverse Drug Reaction Deaths** Reported in United States Vital Statistics, 1999-2006 (February). Ann Pharmacother. 2012 Jan 17.
Sheth S, McCarthy E, Kipps AK, et al. Changes in Efficiency and Safety Culture After Integration of an **I-PASS-Supported Handoff Process**. Pediatrics. 2016 Jan 7.
Shojania KG, Duncan BW, McDonald KM, Wachter RM, et al. **Making health care safer**: a critical analysis of patient safety practices. Evid Rep Technol Assess (Summ). 2001:i-x, 1-668. [PMID: 11510252]
Shojania KG, Thomas EJ. Trends in **adverse events** over time: **why are we not improving**? BMJ Qual Saf. 2013 Apr;22(4):273-7.
Shojania KG, Dixon-Woods M. **Estimating deaths due to medical error**: the ongoing controversy and why it matters. BMJ Qual Saf. 2016 Oct 12.
Sikdar KC, Alaghehbandan R, MacDonald D, Barrett B, Collins KD, Donnan J, Gadag V. Adverse drug events in adult patients leading to **emergency department visits**. Ann Pharmacother. 2010 Apr;44(4):641-9.
Sikdar KC, Dowden J, Alaghehbandan R, et al. **Adverse drug reactions** in **elderly hospitalized patients**: a 12-year population-based retrospective cohort study. Ann Pharmacother. 2012 Jul;46(7-8):960-71.
Silber JH, Bellini LM, Shea JA, et al; iCOMPARE Research Group. Patient Safety Outcomes under Flexible and **Standard Resident Duty-Hour Rules**. N Engl J Med. 2019 Mar 7; 380(10):905-914.
Singh H, Graber M. **Reducing diagnostic error** through medical home-based primary care reform. JAMA. 2010;304(4):463-464.
Singh H, Meyer AN, Thomas EJ. The frequency of **diagnostic errors** in outpatient care: estimations from three large observational studies involving US adult populations. BMJ Qual Saf. 2014 Apr 17.
Smith MD, Spiller HA, Casavant MJ, et al. **Out-of-Hospital Medication Errors** Among Young Children in the United States, 2002-2012. Pediatrics. 2014 Oct 20.
Smolina K, Persaud N, Morgan SG. **Toward better prescription drug surveillance** in Canada. CMAJ. 2016 Aug 9;188(11):E252-3.
Smyth RMD et al. Adverse drug reactions in children—a systematic review. PLoS ONE 2012; 7: e24061.
Soar J, Peyton J, Leonard M, Pullyblank AM. **Surgical safety checklists**. BMJ. 2009 Jan 21;338:b220. doi: 10.1136/bmj.b220.
Spelsberg A, Prugger C, Doshi P, et al. Contribution of **industry funded post-marketing studies** to drug safety: survey of notifications submitted to regulatory agencies. BMJ 2017;356:j337.
Starmer AJ, Sectish TC, Simon DW, et al. Rates of medical errors and preventable adverse events among hospitalized children following implementation of a **resident handoff bundle**. JAMA. doi:10.1001/jama.2013.281961.
Starmer AJ, Spector ND, Srivastava R, et al; I-PASS Study Group. Changes in **medical errors after implementation of a handoff program**. N Engl J Med. 2014 Nov 6;371(19):1803-12.
Stefanacci RG, Cavallaro E, Beers MH, Fick DM. Developing explicit positive **beers criteria** for preferred central nervous system medications in older adults. Consult Pharm. 2009 Aug;24(8):601-10.
Steinman MA**. Reducing hospital admissions for adverse drug events** through coordinated pharmacist care: learning from Hawai'i without a field trip. BMJ Qual Saf. 2018 Nov 24.
Subramanyam R, Mahmoud M, Buck D, et al. **Infusion** Medication Error Reduction by **Two-Person Verification**: A Quality Improvement Initiative. Pediatrics.2016;138(6):e20154413
Sullivan N, Schoelles KM. **Preventing in-facility pressure ulcers** as a patient safety strategy. A systematic review. Ann Intern Med. 2013;158:410-6.
Sunshine JE, Meo N, Kassebaum NJ, et al. Association of **Adverse Effects of Medical Treatment With Mortality** in the United States: A Secondary Analysis of the Global Burden of Diseases, Injuries, and Risk Factors Study. JAMA Netw Open. 2019 Jan 4;2(1):e187041.
Sutcliffe KM, Paine L, Pronovost PJ. **Re-examining high reliability**: actively organising for safety. BMJ Qual Saf. 2017 Mar;26(3):248-251.
Taché SV, Sönnichsen A, Ashcroft DM. Prevalence of adverse drug events in **ambulatory care**: a systematic review. Ann Pharmacother 2011;45(7-8): 977-989.
Takata GS, Mason W, Taketomo C, et al. Development, testing, and findings of a **pediatric-focused trigger tool** to identify medication-related harm in US children's hospitals. Pediatrics. 2008 Apr;121(4):e927-35.
Tan K, Petrie KJ, Faasse K, et al. **Unhelpful information about adverse drug reactions**. BMJ. 2014 Aug 12;349:g5019.
Tawfik DS, Profit J, Morgenthaler TI, et al. **Physician Burnout, Well-being, and Work Unit Safety Grades in Relationship to Reported Medical Errors**. Mayo Clin Proc. 2018 Jul 4.
Thomas EJ, Classen DC. Patient Safety: **Let's Measure What Matters**. Ann Intern Med. 2014 May 6;160(9):642-3.
Thorpe JM, Thorpe CT, Schleiden L, et al. Association Between **Dual Use of Department of Veterans Affairs and Medicare** Part D Drug Benefits and Potentially Unsafe Prescribing. JAMA Intern Med. 2019Jul22
Urbach DR, Govindarajan A, Saskin R, Wilton AS, Baxter NN. Introduction of **surgical safety checklists** in Ontario, Canada. N Engl J Med 2014;370:1029-38.
Valentin A, Capuzzo M, Guidet B, et al. Research Group on Quality Improvement of the European Society of Intensive Care Medicine (ESICM); Sentinel Events Evaluation (SEE) Study Investigators. Errors in administration of **parenteral drugs in intensive care units**: multinational prospective study. BMJ. 2009 Mar 12;338:b814. doi: 10.1136/bmj.b814.
van Walraven, Carl, Bennett, Carol, Jennings, Alison, Austin, Peter C., Forster, Alan J. Proportion of **hospital readmissions deemed avoidable**: a systematic review CMAJ 2011 183: E391-402
Vincent C, Aylin P, Franklin BD, Holmes A, Iskander S, Jacklin A, Moorthy K. Is health care getting safer? BMJ. 2008 Nov 13;337:a2426. doi: 10.1136/bmj.a2426.
Volpp KG, Grande D. Residents' suggestions for **reducing errors** in teaching hospitals. *N Engl J Med* 2003;348:851-5.
Wallace E, Lowry J, Smith SM, Fahey T. The epidemiology of **malpractice claims in primary care**: a systematic review. BMJ Open. 2013 Jul 18;3(7).
Walsh KE, Roblin DW, Weingart SN, et al. **Medication Errors** in the Home: A Multisite Study of Children With Cancer. Pediatrics. 2013 Apr 29.
Wang Y, Eldridge N, et al. National trends in **patient safety for four common conditions**, 2005-2011. N Engl J Med. 2014 Jan 23;370(4):341-51. (Heart failue, myocardial infarction, pneumonia, & surgery)
Weaver SJ, Lubomski LH, Wilson RF, Pfoh ER, Martinez KA, Dy SM. Promoting a **culture of safety** as a patient safety strategy. A systematic review. Ann Intern Med. 2013;158:369-74.
Weingart Saul N.; Simchowitz Brett; Padolsky Harper; et al. An Empirical Model to Estimate the Potential Impact of **Medication Safety Alerts** on Patient Safety, Health Care Utilization, and Cost in Ambulatory Care. Arch Intern Med. 2009;169(16):1465-1473.
Wells S, Tamir O, Gray J, et al. Are **quality improvement collaboratives effective**? A systematic review. BMJ Qual Saf. 2017 Oct 21. pii: bmjqs-2017-006926.
West Colin P.; Tan Angelina D.; Habermann Thomas M.; et al. Association of **Resident Fatigue** and Distress With Perceived Medical Errors. JAMA. 2009;302(12):1294-1300.
Westbrook Johanna I.; Woods Amanda; Rob Marilyn I.; et al. Association of **Interruptions** With an Increased Risk and Severity of Medication Administration Errors. Arch Intern Med. 2010;170(8):683-690.
Weiss-Smith S, Deshpande G, Chung S, et al. The **FDA drug safety surveillance program**: adverse event reporting trends. Arch Intern Med 2011;171:591-3. In the FDA database, when an outcome was reported, patients were hospitalized in 42% and the patient died in 15% of cases. Overall, women were represented in 55% of reports. One-third of reports were among adults aged 30–64 years of age. The drugs most frequently cited were biologic agents etanercept, adalimumab and infliximab (the first, third and fourth most frequently reported suspect drugs). Others in the top 10 suspect list were rofecoxib, quetiapine, exenatide (Byetta, to be marketed in Canada in June), teriparatide, interferon beta-1a (Avonex), norelgestromin–ethinyl estradiol transdermal system (Ortho Evra) and levonorgestrel-releasing intrauterine system (Mirena).
WHO Collaborating Centre for Patient Safety Releases **Nine Life-Saving Patient Safety Solutions** http://www.jointcommissioninternational.org/24839/
Wilson RM, Michel P, Olsen S, et al; for the WHO Patient Safety EMRO/AFRO Working group. **Patient safety in developing countries**: retrospective estimation of scale and nature of harm to patients in hospital. BMJ. 2012 Mar 13;344:e832.
Willson MN, Greer CL, Weeks DL. **Medication regimen complexity** and hospital readmission for an adverse drug event. Ann Pharmacother. 2014 Jan;48(1):26-32
Winters BD, Weaver SJ, Pfoh ER, Yang T, Pham JC, Dy SM. **Rapid response systems** as a patient safety strategy. A systematic review. Ann Intern Med. 2013;158:417-25.

Wolf MS, Curtis LM, Waite K, et al. Helping patients simplify and **safely use complex prescription regimens**. Arch Intern Med. 2011 Feb 28;171(4):300-5.
Wong BM, Ginsburg S. **Speaking up against unsafe unprofessional behaviours**: the difficulty in knowing when and how. BMJ Qual Saf. 2017 Jul 22.
Writing Group for the **CHECKLIST-ICU** Investigators and the Brazilian Research in Intensive Care Network (BRICNet), Cavalcanti AB, Bozza FA, et al. Effect of a Quality Improvement Intervention With Daily **Round Checklists**, Goal Setting, and Clinician Prompting on Mortality of Critically Ill Patients: A Randomized Clinical Trial. JAMA. 2016 Apr 12;315(14):1480-90
Wu J, Juhaeri J. The **US Food and Drug Administration's Risk Evaluation and Mitigation Strategy** (**REMS**) Program - Current Status and Future Direction. Clin Ther. 2016 Nov 30.
Wysowski DK, Swartz L. **Adverse drug event surveillance and drug withdrawals** in the United States, 1969-2002: the importance of reporting suspected reactions. Arch Intern Med. 2005;165(12):1363-1369.
Yin H. Shonna; Wolf Michael S.; Dreyer Benard P.; et al. Evaluation of Consistency in **Dosing Directions and Measuring Devices** for Pediatric Nonprescription Liquid Medications. JAMA. 2010;0(2010):jama.2010.1797.
Yin HS, Dreyer BP, Ugboaja DC, et al. **Unit of Measurement** Used and Parent Medication **Dosing Errors**.Pediatrics. 2014 Jul 14.
Yin HS, Parker RM, Sanders LM, et al. **Liquid Medication Errors and Dosing Tools**: A Randomized Controlled Experiment. Pediatrics. 2016 Sep 12.
Yin HS, Parker RM, Sanders LM, et al**. Pictograms, Units and Dosing Tools, and Parent Medication Errors**: A randomized Study. Pediatrics. 2017;140(1):e20163237
Zandieh SO, Goldmann DA, Keohane CA, Yoon C, Bates DW, Kaushal R. Risk factors in preventable adverse drug events in pediatric outpatients. J Pediatr. 2008 Feb;152(2):225-31. Epub 2007 Nov 19.
Zapata JA, Lai AR, Moriates C. Is **excessive resource utilization** an adverse event? JAMA. doi:10.1001/jama.2017.0698
Zed PJ, Abu-Laban RB, Balen RM, Loewen PS, et al. Incidence, severity and preventability of medication-related visits to the emergency department: a prospective study. CMAJ. 2008 Jun 3;178(12):1563-9. More than **1 in 9 emergency department visits** are due to drug-related adverse events, a potentially preventable problem in our health care system.
Zhang M, Holman CD, Price SD, et al. **Comorbidity** and repeat admission to hospital for adverse drug reactions in older adults: retrospective cohort study. BMJ. 2009 Jan 7;338:a2752. doi: 10.1136/bmj.a2752.
Comorbidity, but not advancing age, predicts repeat admission for ADRs in older adults, especially those with comorbidities often managed in the community. Awareness of these predictors can help clinicians to identify which older adults are at greater risk of admission for ADRs and, therefore, who might benefit from closer monitoring.
Zed PJ, Haughn C, Black KJ, et al. **Medication-related emergency department visits and hospital admissions in pediatric patients**: a qualitative systematic review. J Pediatr. 2013 Aug;163(2):477-83.
Zed PJ, Black KJ, Fitzpatrick EA, et al. **Medication-Related Emergency Department Visits in Pediatrics**: a Prospective Observational Study. Pediatrics. 2015 Feb 2.
Zeitoun JD, Lefèvre JH, Downing NS, et al. **Regulatory review time and post-market safety** events for novel medicines approved by the EMA between 2001 and 2010: a cross-sectional study. Br J Clin Pharmacol. 2015 Mar 25.
Zorzela L, Golder S, Liu Y, Pilkington K, Hartling L, Joffe A, Loke Y, Vohra S. Quality of reporting in systematic reviews of **adverse events**: systematic review. BMJ. 2014 Jan 8

Academic Detailing:

Canada

- BC CDUP: http://www.cdup.org/
- Dalhousie: http://cme.medicine.dal.ca/ADS.htm
- Saskatchewan: www.rxfiles.ca
- Ontario: https://cep.health/academic-detailing/
- Alberta: https://acfp.ca/advocacy/partnerships-collaborations/peer/

Non-Canadian

- Academic Detailing – National Resource Centre for Academic Detailing (USA): http://www.narcad.org/
- Pennsylvania (RxFacts.org): http://www.rxfacts.org/detailing.php
- Vermont Academic Detailing Program: https://www.med.uvm.edu/ahec/vermontacademicdetailing
- Australia – National Prescribing Service (NPS): https://www.nps.org.au/

References

[i] Groves KE, Sketris I, Tett SE. Prescription drug samples--does this marketing strategy counteract policies for quality use of medicines? J Clin Pharm Ther. 2003 Aug;28(4):259-71.
[ii] Gourlay DL, Heit HA. Universal precautions revisited: managing the inherited pain patient. Pain Med. 2009 Jul;10 Suppl 2:S115-23.
Margaret Jin (*2012*) A brief overview of academic detailing in Canada: Another role for pharmacists. Canadian Pharmacists Journal: May 2012, Vol. 145, No. 3, pp. 142-146.e2.
http://www.cpjournal.ca/doi/abs/10.3821/145.3.cpj142

Buprenorphine/Naloxone for Opioid Dependence: Clinical Practice Guideline CAMH: http://www.cpso.on.ca/uploadedFiles/policies/guidelines/office/buprenorphine_naloxone_gdlns2011.pdf

Other Links of Interest: **See RxFiles Alcohol Use Disorder Chart: http://www.rxfiles.ca/rxfiles/uploads/documents/members/CHT-Alcohol-Use-Disorder.pdf v**

http://addictionlibrary.org/

SK Helath Links:

www.saskatchewan.ca/addictions; the target audience is the public.

Here are the direct links re Crystal Meth:

- Infographic: http://publications.gov.sk.ca/documents/13/106826-Crystal-Meth-Infographic-2018.pdf
- FaQ : http://publications.gov.sk.ca/documents/13/106827-CM-FAQ-2018.pdf
- Fact Sheet : http://publications.gov.sk.ca/documents/13/99220-CrystalMeth%20Factsheet%20Sept%202016.pdf

Additional refs for SUBSTANCE ABUSE/ADDICTION: Overview & Treatment Considerations:

A voice from the streets about **Spice**. BMJ. 2016 Jun 7;353:i2708.
AAP Committee on Substance Use and Prevention. **Medication-Assisted Treatment of Adolescents with Opioid Use Disorders**. Pediatrics.2016:138(3):e20161893
AAP: Committee on Substance Use and Prevention. Medication-Assisted Treatment of **Adolescents With Opioid Use Disorders**. Pediatrics. 2016 Sep;138(3).
Abouk R et al. Association between **state laws facilitating pharmacy distribution of naloxone and risk of fatal overdose**. JAMA Intern Med 2019 May 6.
Achar S, Rostamian A, Narayan SM. Cardiac and metabolic effects of **anabolic-androgenic steroid abuse** on lipids, blood pressure, left ventricular dimensions, and rhythm. Am J Cardiol. 2010 Sep 15;106(6):893-901.
Ackerman AL, O'Connor PG, Doyle DL, et al. Association of an **Opioid Standard of Practice Intervention With Intravenous Opioid Exposure** in Hospitalized Patients. JAMA Intern Med. 2018 May 14.
ACOG: Committee on Obstetric Practice. Committee Opinion No. 711: **Opioid Use and Opioid Use Disorder in Pregnancy**. Obstet Gynecol. 2017 Aug;130(2):e81-e94.
Adams AJ, Banister SD, Irizarry L, et al. "**Zombie**" **Outbreak** Caused by the **Synthetic Cannabinoid AMB-FUBINACA in** New York. N Engl JMed. 2016 Dec 14.
Adams JM. Increasing **Naloxone Awareness and Use:** The Role of Health Care Practitioners. JAMA. 2018 Apr 5.
Admon LK, Bart G, Kozhimannil KB, et al. **Amphetamine- and Opioid-Affected Births**: Incidence, Outcomes, and Costs, United States, 2004-2015. Am J Public Health. 2018 Nov 29:e1-e7.
Agabio R. Non-specialist health workers to treat **excessive alcohol consumption** and depression. Lancet. 2016 Dec 14.
Afshar M, Poole JA, Cao G, Durazo et al. Exhaled **Nitric Oxide** Levels Among Adults With Excessive **Alcohol Consumption**. Chest. 2016 Jul;150(1):196-209.
Akiyama MJ, Norton BL, Arnsten JH, et al. Intensive Models of **Hepatitis C Care for People Who Inject Drugs Receiving Opioid Agonist Therapy**: A Randomized Controlled Trial. Ann Intern Med. 2019 Apr 9.
Alati R, Betts KS, Williams GM, et al. **Generational Increase in Young Women's Drinking**: A Prospective Analysis of Mother-Daughter Dyads. JAMA Psychiatry. 2014 Jun 25.
Alambyan V, Pace J, Miller B, et al. The Emerging Role of **Inhaled Heroin in the Opioid Epidemic**: A Review. JAMA Neurol. 2018 Jul 9.
Albadareen R, Thornton S, Heshmati A, et al. Unusually Prolonged Presentation of Designer Drug (**methylenedioxybenzylpiperazine**) Encephalopathy Responsive to Steroids. Pediatrics. 2015 Jun 8.
Alcohol Use and Pregnancy Consensus Clinical Guidelines. SOGC 2010. http://www.sogc.org/guidelines/documents/gui245cpg1008e.pdf
Alford Daniel P.; LaBelle Colleen T.; Kretsch Natalie; et al. Collaborative Care of **Opioid-Addicted Patients in Primary Care Using Buprenorphine**: Five-Year Experience. Arch Intern Med. 2011;171(5):425-431.
Alford DP. **Opioid Prescribing for Chronic Pain**--Achieving the Right Balance through Education. N Engl J Med. 2016 Jan 28;374(4):301-3.
Alford DP, Cohen ML, Reynolds EE. How Would You **Manage Opioid Use** in These Three Patients?: Grand Rounds Discussion From Beth Israel Deaconess Medical Center. Ann Intern Med. 2017 Apr 4;166(7):506-513
Ali WM, Al Habib KF, Al-Motarreh A, et al. Acute coronary syndrome use and **khat herbal amphetamine use (Catha edulis)**. An observational report.Circulation 2011
Allen B, Nolan ML, Kunins HV, Paone D. **Racial differences in opioid overdose deaths** in New York City, 2017 [online Feb 11, 2019]. JAMA Intern Med.
Allsop DJ, Copeland J, Lintzeris N, et al. **Nabiximols** as an Agonist Replacement Therapy During Cannabis Withdrawal: A Randomized Clinical Trial. JAMA Psychiatry. 2014 Jan 15
Almeida OP, Hankey GJ, Yeap BB, et al. **Alcohol consumption** and cognitive impairment in older men: A mendelian randomization study. Neurology. 2014 Mar 25;82(12):1038-44.
Altice FL, Kamarulzaman A, Soriano VV, et al. Treatment of **medical, psychiatric, and substance-use comorbidities in people infected with HIV** who use drugs. Lancet. 2010 Jul 31;376(9738):367-87.
Amato L, Minozzi S, Vecchi S, Davoli M. **Benzodiazepines** for **alcohol withdrawal**. Cochrane Database Syst Rev. 2010 Mar 17;3:CD005063. Benzodiazepines showed a protective benefit against alcohol withdrawal symptoms, in particular seizures, when compared to placebo and a potentially protective benefit for many outcomes when compared with other drugs. Nevertheless, no definite conclusions about the effectiveness and safety of benzodiazepines was possible, because of the heterogeneity of the trials both in interventions and the assessment of outcomes.
Amato L, Minozzi S, Pani PP, et al. **Dopamine agonists** for the treatment of **cocaine dependence**. Cochrane Database Syst Rev. 2011 Dec 7;12:CD003352. Current evidence from randomised controlled trials does not support the use of dopamine agonists for treating cocaine dependence.
Amato L, Davoli M, Minozzi S, et al. **Methadone at tapered doses for the management of opioid withdrawal**. Cochrane Database Syst Rev. 2013 Feb 28;2:CD003409. doi: 10.1002/14651858.CD003409.pub4. Data from literature are hardly comparable; programs vary widely with regard to the assessment of outcome measures, impairing the application of meta-analysis. The studies included in this review confirm that slow tapering with temporary substitution of long- acting opioids, can reduce withdrawal severity. Nevertheless, the majority of patients relapsed to heroin use.
Ambasta A, Malebranche M. **Opioid use disorder in pregnancy**. CMAJ. 2019 Sep 23;191(38):E1057.Pdf Dai H, Richter KP. A National Survey of Marijuana Use Among US Adults With Medical Conditions, 2016-2017. JAMA Netw Open. 2019 Sep 4;2(9):e1911936.
American Psychiatric Association Brochures: http://www.healthyminds.org/Functional-Library/brochures.aspx
Anderson DM, Hansen B, Rees DI, Sabia JJ. Association of Marijuana **Laws With Teen Marijuana Use**: New Estimates From the Youth Risk Behavior Surveys. JAMA Pediatr. 2019 Jul 8.
Anton RF, Myrick H, Wright TM, et al. **Gabapentin Combined With Naltrexone** for the Treatment of Alcohol Dependence. Am J Psychiatry. 2011 Mar 31.
Antoniou T, Juurlink DN. "**Bath salts**". CMAJ. 2012 Oct 16;184(15):1713.
Antoniou T, Juurlink DN. **Synthetic cannabinoids**. CMAJ. 2014 Feb 18;186(3):210.
Antoniou T, Juurlink DN. **Dextromethorphan abuse**. CMAJ. 2014 Nov 4;186(16):E631.
Antoniou T, Juurlink DN. **Loperamide abuse**. CMAJ. 2017 Jun 12;189(23):E803.
Aquaro GD, Gabutti A, Meini M, Prontera C, Pasanisi E, Passino C, Emdin M, Lombardi M. **Silent myocardial damage in cocaine** addicts. Heart. 2011 Jun 20.
Armenian P, Olson A, Anaya A, Kurtz Aet al. **Fentanyl** and a Novel **Synthetic Opioid U-47700** Masquerading as Street "Norco" in Central California: A Case Report. Ann Emerg Med. 2016 Jul 20.
Arnold C. The new danger of **synthetic drugs**. Lancet. 2013 Jul 6;382(9886):15-6.
Arora NP, Berk WA, Aaron CK, Williams KA. Usefulness of Intravenous **Lipid Emulsion for Cardiac Toxicity from Cocaine** Overdose. Am J Cardiol. 2012 Nov 24.
Artenie AA, Minoyan N, Jacka B, et al. **Opioid agonist treatment** dosage and patient-perceived dosage adequacy, and risk of hepatitis C infection among people who inject drugs. CMAJ 2019;191:E462-8.
Arterberry BJ, Treloar Padovano H, Foster KT, et al. Higher average potency across the United States is associated with progression to **first cannabis use disorder symptom**. Drug Alcohol Depend. 2018 Dec 6.
Askgaard G, Grønbæk M, Kjær MS, et al. **Alcohol drinking** pattern and risk of alcoholic liver cirrhosis: A prospective cohort study. J Hepatol. 2015 Jan 20.
Auger N, Low N, Carrier FM, et al. Maternal **prepregnancy surgery and risk of neonatal abstinence syndrome** in future newborns: a longitudinal cohort study. CMAJ. 2019 Jul 15;191(28):E779-E786.
Aulet RM, Trieu V, Landrigan GP, Millay DJ. Changes in Opioid **Prescribing Habits for Patients Undergoing Rhinoplasty and Septoplasty**. JAMA Facial Plast Surg. 2019 Oct 10. doi: 10.1001/jamafacial.2019.0937
Axelsson A, et al. "Echocardiographic Findings Suggestive of **Infective Endocarditis** in Asymptomatic Danish Injection Drug Users Attending Urban Injection Facilities." The American Journal of Cardiology (2014).
Aydelotte JD, Brown LH, Luftman KM, et al. **Crash Fatality Rates After Recreational Marijuana Legalization** in Washington and Colorado. Am J Public Health. 2017 Jun 22:e1-e3.
Ayers JW, Nobles AL, Dredze M. **Media Trends** for the Substance Abuse and Mental Health Services Administration 800-662-HELP Addiction Treatment Referral Services **After a Celebrity Overdose**. JAMA Intern Med. 2019 Jan 14.
Azuine RE, Ji Y, Chang HY, et al. **Prenatal Risk Factors and Perinatal and Postnatal Outcomes** Associated With Maternal Opioid Exposure in an Urban, Low-Income, Multiethnic US Population. JAMA Netw Open. 2019 Jun 5;2(6):e196405.
Babu KM, Brent J, Juurlink DN. **Prevention of Opioid Overdose**. N Engl J Med. 2019 Jun 6;380(23):2246-2255.
Bachhuber MA, Saloner B, Cunningham CO, Barry CL. Medical **cannabis laws and opioid analgesic overdose** mortality in the United States, 1999-2010 [online August 25, 2014]. JAMA Intern Med.
Bachhuber MA, Hennessy S, Cunningham CO, Starrels JL. Increasing **Benzodiazepine Prescriptions** and Overdose Mortality in the United States, 1996-2013. Am J Public Health. 2016 Feb 18:e1-e3.
Bada HS, Bann CM, Whitaker TM, et al. Protective Factors Can Mitigate Behavior Problems After Prenatal **Cocaine** and Other Drug Exposures. Pediatrics. 2012 Nov 26.

Additonal References:

Banerji D, Alvi RM, Afshar M, et al. Carvedilol Among Patients With Heart Failure With a Cocaine-Use Disorder. JACC Heart Fail. 2019 Sep;7(9):771-778.

Chan B, Freeman M, Kondo K, et al. Pharmacotherapy for Methamphetamine/Amphetamine Use Disorder – A Systematic Review and Meta-analysis. Addiction. 2019 Jul 22.

Center for Substance Abuse Treatment. Treatment for Stimulant Use Disorders. Rockville (MD): Substance Abuse and Mental Health Services Administration (US); 1999. (Treatment Improvement Protocol (TIP) Series, No. 33.) Chapter 5—Medical Aspects of Stimulant Use Disorders. Available from: https://www.ncbi.nlm.nih.gov/books/NBK64323/ Accessed online at: https://www.ncbi.nlm.nih.gov/books/NBK64323/

References for Stimulant Use Disorder Chart – www.RxFiles.ca

[1] Glasner-Edwards S, Mooney LJ. Methamphetamine psychosis: epidemiology and management. *CNS Drugs*. 2014;28(12):1115–1126. doi:10.1007/s40263-014-0209-8

[2] Wodarz N, Krampe-Scheidler A, Christ M, Fleischmann H, Looser W, Schoett K, Vilsmeier F, Bothe L, Schaefer C, Gouzoulis-Mayfrank E. Evidence-Based Guidelines for the Pharmacological Management of Acute Methamphetamine-Related Disorders and Toxicity. Pharmacopsychiatry. 2017 May;50(3):87-95.

[3] Minozzi S, Saulle R, De Crescenzo F, Amato L. Psychosocial interventions for psychostimulant misuse. Cochrane Database of Systematic Reviews 2016, Issue 9. Art. No.: CD011866. DOI: 10.1002/14651858.CD011866.pub2. https://www.cochranelibrary.com/cdsr/doi/10.1002/14651858.CD011866.pub2/full?highlightAbstract=withdrawn%7Ccocaine%7Ccocain

[4] Winslow BT, Voorhees KI, Pehl KA. Methamphetamine abuse. Am Fam Physician. 2007 Oct 15;76(8):1169-74.

[5] NIH: National Institute on Drug Abuse. Methamphetamine. Accessed 28 June 2019 online at https://www.drugabuse.gov/publications/methamphetamine/what-treatments-are-effective-people-who-misuse-methamphetamine .

[6] Hill, R. (2015). Evidence-based practices for treatment of methamphetamine dependency: A review. Guelph, ON: Community Engaged Scholarship Institute. https://atrium.lib.uoguelph.ca/xmlui/handle/10214/8902

[7] Meader N, Li R, Des Jarlais DC, Pilling S. Psychosocial interventions for reducing injection and sexual risk behaviour for preventing HIV in drug users. Cochrane Database of Systematic Reviews 2010, Issue 1. Art. No.: CD007192. DOI: 10.1002/14651858.CD007192.pub2.

[8] Petry NM, Alessi SM, Olmstead TA, Rash CJ, Zajac K. Contingency management treatment for substance use disorders: How far has it come, and where does it need to go?. *Psychol Addict Behav*. 2017;31(8):897–906. doi:10.1037/adb0000287

[9] Klega AE, Keehbauch JT. Stimulant and Designer Drug Use: Primary Care Management. Am Fam Physician. 2018 Jul 15;98(2):85-92.

[10] Chan B, Kondo K, Ayers C, Freeman M, et al. Pharmacotherapy for Stimulant Use Disorders: A Systematic Review of the Evidence. VA ESP Project #05-225; 2018. Accessed online 09 Sep 2019 at https://www.hsrd.research.va.gov/publications/esp/pharmacotherapy-sud-exec.pdf ; Detailed report https://www.hsrd.research.va.gov/publications/esp/pharmacotherapy-sud.pdf

[11] Castells X, Cunill R, Pérez-Mañá C, Vidal X, Capellà D. Psychostimulant drugs for cocaine dependence. Cochrane Database of Systematic Reviews 2016, Issue 9. Art. No.: CD007380. DOI: 10.1002/14651858.CD007380.pub4. https://www.cochranelibrary.com/cdsr/doi/10.1002/14651858.CD007380.pub4/full

[12] Cook J, Lloyd-Jones M, Arunogiri S, Ogden E, Bonomo Y. Managing attention deficit hyperactivity disorder in adults using illicit psychostimulants: A systematic review. Aust N Z J Psychiatry. 2017 Sep;51(9):876-885. doi: 10.1177/0004867417714878.

[13] Indave BI, Minozzi S, Pani PP, Amato L. Antipsychotic medications for cocaine dependence. Cochrane Database of Systematic Reviews 2016, Issue 3. Art. No.: CD006306. DOI: 10.1002/14651858.CD006306.pub3.

[14] Pani PP, Trogu E, Vecchi S, Amato L. Antidepressants for cocaine dependence and problematic cocaine use. Cochrane Database of Systematic Reviews 2011, Issue 12. Art. No.: CD002950. DOI: 10.1002/14651858.CD002950.pub3.

[15] Johnson BA, Ait-Daoud N, Wang XQ, Penberthy JK, Javors MA, Seneviratne C, Liu L. Topiramate for the treatment of cocaine addiction: a randomized clinicaltrial. JAMA Psychiatry. 2013 Dec;70(12):1338-46.

[16] Minozzi S, Cinquini M, Amato L, Davoli M, Farrell MF, Pani PP, Vecchi S. Anticonvulsants for cocaine dependence. Cochrane Database of Systematic Reviews 2015, Issue 4. Art. No.: CD006754. DOI: 10.1002/14651858.CD006754.pub4.

[17] Blevins D, Wang XQ, Sharma S, Ait-Daoud N. Impulsiveness as a predictor of topiramate response for cocaine use disorder. Am J Addict. 2019 Feb;28(2):71-76.

[18] Klega AE, Keehbauch JT. Stimulant and Designer Drug Use: Primary Care Management. Am Fam Physician. 2018 Jul 15;98(2):85-92.

[19] Harris DS, Boxenbaum H, Everhart ET, Sequeira G, Mendelson JE, Jones RT. The bioavailability of intranasal and smoked methamphetamine. Clin Pharmacol Ther. 2003 Nov;74(5):475-86.

[20] Jufer RA, Wstadik A, Walsh SL, Levine BS, Cone EJ. Elimination of cocaine and metabolites in plasma, saliva, and urine following repeated oral administration to human volunteers. J Anal Toxicol. 2000 Oct;24(7):467-77.

[21] Jenner L and Lee N (2008). Treatment Approaches for Users of Methamphetamine: A Practical Guide for Frontline Workers. Australian Government Department of Health and Ageing, Canberra. Accessed online, 16 July at http://www.nationaldrugstrategy.gov.au/internet/drugstrategy/Publishing.nsf/content/8D2E281FAC2346BBCA25764D007D2D3A/$File/tremeth.pdf

[22] Management of Acute Withdrawal and Detoxification for Adults who Misuse Methamphetamine: A Review of the Clinical Evidence and Guidelines. Ottawa: CADTH; 2019 Feb.(CADTH rapid response report: summary with critical appraisal).

[23] http://www.nationaldrugstrategy.gov.au/internet/drugstrategy/Publishing.nsf/content/8D2E281FAC2346BBCA25764D007D2D3A/$File/tremeth.pdf

[24] Management of Acute Withdrawal and Detoxification for Adults who Misuse Methamphetamine: A Review of the Clinical Evidence and Guidelines. Ottawa: CADTH; 2019 Feb.(CADTH rapid response report: summary with critical appraisal).

[25] Winslow BT, Voorhees KI, Pehl KA. Methamphetamine abuse. Am Fam Physician.2007 Oct 15;76(8):1169-74.

[26] NIH: National Institute on Drug Abuse. Methamphetamine. Accessed 28 June 2019 online at https://www.drugabuse.gov/publications/methamphetamine/what-treatments-are-effective-people-who-misuse-methamphetamine .

[27] Colfax GN, Santos GM, Das M, et al. Mirtazapine to reduce methamphetamine use: a randomized controlled trial. *Arch Gen Psychiatry*. 2011;68(11):1168–1175. doi:10.1001/archgenpsychiatry.2011.124

[28] Tennant FS Jr, Rawson RA. Cocaine and amphetamine dependence treated with desipramine. NIDA Res Monogr. 1983 Apr;43:351-5.

[29] Wodarz N, Krampe-Scheidler A, Christ M, et al. Evidence-Based Guidelines for the Pharmacological Management of Acute Methamphetamine-Related Disorders and Toxicity. Pharmacopsychiatry. 2017 May;50(3):87-95. doi: 10.1055/s-0042-123752.

[30] Chan B, Freeman M, Kondo K, Ayers C, Montgomery J, Paynter R, Kansagara D. Pharmacotherapy for Methamphetamine/Amphetamine Use Disorder - A Systematic Review and Meta-analysis. Addiction. 2019 Jul 22.

[31] Humphreys KL, Eng T, Lee SS. Stimulant medication and substance use outcomes: a meta-analysis. JAMA Psychiatry. 2013 Jul;70(7):740-9.

[32] Newton TF, Reid MS, De La Garza R, Mahoney JJ, Abad A, Condos R, Palamar J, Halkitis PN, Mojisak J, Anderson A, Li SH, Elkashef A. Evaluation of subjective effects of aripiprazole and methamphetamine in methamphetamine-dependent volunteers. Int J Neuropsychopharmacol. 2008;11:1037–1045.

[33] Galloway GP, Buscemi R, Coyle JR, Flower K, Siegrist JD, Fiske LA, Baggott MJ, Li L, Polcin D, Chen CY, Mendelson J. A randomized, placebo-controlled trial of sustained-release dextroamphetamine for treatment of methamphetamine addiction. Clin Pharmacol Ther. 2011;89:276–282.

[34] Hill, R. (2015). Evidence-based practices for treatment of methamphetamine dependency: A review. Guelph, ON: Community Engaged Scholarship Institute. https://atrium.lib.uoguelph.ca/xmlui/handle/10214/8902

[35] Voce A, Calabria B, Burns R, Castle D, McKetin R. A Systematic Review of the Symptom Profile and Course of Methamphetamine-Associated Psychosis(Substance Use and Misuse). Subst Use Misuse. 2019;54(4):549-559.

[36] Chiang M, Lombardi D, Du J, Makrum U, Sitthichai R, Harrington A, Shukair N, Zhao M, Fan X. Methamphetamine-associated psychosis: Clinical presentation, biological basis, and treatment options. Hum Psychopharmacol. 2019 Aug 22:e2710. Accessed online Sept 15, 2019 at https://onlinelibrary.wiley.com/doi/full/10.1002/hup.2710#hup2710-bib-0015

[37] Wodarz N, Krampe-Scheidler A, Christ M, Fleischmann H, Looser W, Schoett K, Vilsmeier F, Bothe L, Schaefer C, Gouzoulis-Mayfrank E. Evidence-Based Guidelines for the Pharmacological Management of Acute Methamphetamine-Related Disorders and Toxicity. Pharmacopsychiatry. 2017 May;50(3):87-95.

[38] Gillies D, Sampson S, Beck A, Rathbone J. Benzodiazepines for psychosis-induced aggression or agitation. Cochrane Database of Systematic Reviews 2013, Issue 4. Art. No.: CD003079. DOI: 10.1002/14651858.CD003079.pub3..

[39] Rossi J, Swan MC, Isaacs ED. The violent or agitated patient. Emerg Med Clin North Am. 2010 Feb;28(1):235-56, x. doi: 10.1016/j.emc.2009.10.006.

[40] Management of Acute Withdrawal and Detoxification for Adults who Misuse Methamphetamine: A Review of the Clinical Evidence and Guidelines. Ottawa: CADTH; 2019 Feb.(CADTH rapid response report: summary with critical appraisal).

[41] Shoptaw SJ, Kao U, Ling W. Treatment for amphetamine psychosis. Cochrane Database of Systematic Reviews 2009, Issue 1. Art. No.: CD003026. DOI: 10.1002/14651858.CD003026.pub3.

[42] Rossi J, Swan MC, Isaacs ED. The violent or agitated patient. Emerg Med ClinNorth Am. 2010 Feb;28(1):235-56, x. doi: 10.1016/j.emc.2009.10.006. Accessed online Sept 15, 2019 at https://www.sciencedirect.com/science/article/pii/S0733862709001242?via%3Dihub

[43] Leelahanaj T, Kongsakon R, Netrakom P. A 4-week, double-blind comparison of olanzapine with haloperidol in the treatment of amphetamine psychosis. J Med Assoc Thai. 2005 Nov;88 Suppl 3:S43-52.

[44] Wang G, Zhang Y, Zhang S, Chen H, Xu Z, Schottenfeld RS, Hao W, Chawarski MC. Aripiprazole and Risperidone for Treatment of Methamphetamine-Associated Psychosis in Chinese Patients. J Subst Abuse Treat. 2016 Mar;62:84-8.

[45] Farnia V, Shakeri J, Tatari F, Juibari TA, Yazdchi K, Bajoghli H, Brand S, Abdoli N, Aghaei A. Randomized controlled trial of aripiprazole versus risperidone for the treatment of amphetamine-induced psychosis. Am J Drug Alcohol Abuse. 2014 Jan;40(1):10-5.

[46] Verachai V, Rukngan W, Chawanakrasaesin K, Nilaban S, Suwanmajo S, et al.. Treatment of methamphetamine-induced psychosis: a double-blind randomized controlled trial comparing haloperidol and quetiapine. Psychopharmacology (Berl). 2014; 231(16):3099–108.

[47] http://www.nationaldrugstrategy.gov.au/internet/drugstrategy/Publishing.nsf/content/8D2E281FAC2346BBCA25764D007D2D3A/$File/tremeth.pdf

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References

1. Zoorob R, Kowalchuk A, Mejia de Grubb M. **Buprenorphine Therapy** for Opioid Use Disorder. Am Fam Physician. 2018 Mar 1;97(5):313-320
2. **Buprenorphine formulations** for the treatment of opioid use disorders: a review of comparative clinical effectiveness, cost-effectiveness and guidelines. Ottawa: CADTH; 2017 Jul. (CADTH rapid response report: summary with critical appraisal).
3. **Buprenorphine Implants** *(Probuphine)* for Opioid Dependence - Medical Letter; July 2016; 58(1499).
4. Mattick RP,Breen C,Kimber J, et al. **Buprenorphine maintenance versus placebo or methadone** maintenance for opioid dependence. *Cochrane Database of Systematic Reviews* 2014, Issue 2. Art. No.: CD002207
5. Noormohammadi A, Forinash A, Yancey A, Crannage E, Campbell K, Shyken J. **Buprenorphine Versus Methadone** for Opioid Dependence in Pregnancy. Ann Pharmacother. 2016 Aug;50(8):666-72
6. New drug: **Suboxone** (buprenorphine / naloxone). Pharmacist's Letter/Prescriber's Letter 2007;23(12):231218.
7. DynaMed Plus [Internet]. Ipswich (MA): EBSCO Information Services. 1995 - . Record No. 219069, **Opioid abuse and dependence**; [updated 2018 May 02, cited July 2, 2018]; [about 55 screens]. Available from http://www.dynamed.com.cyber.usask.ca/login.aspx?
8. **Alpha2-adrenergic Agonists** for the Reduction or Discontinuation of Opioids or Opioid Substitution Therapy: A Review of Clinical Efficacy and Guidelines. Ottawa: CADTH; 2018 Feb. (CADTH rapid response report)
9. British Columbia Centre on Substance Use and B.C. Ministry of Health. A Guideline for the **Clinical Management of Opioid Use Disorder**. Published June 5, 2017.
10. LUCEMYRA Drug Monograph https://www.multivu.com/players/English/8314851-us-world-meds-lucemyra-fda-approval/docs/PrescribingInformat_1526505076265-1171755477.pdf. Accessed July 8, 2018
11. Schuckit MA. Treatment of Opioid-Use Disorders. N Engl J Med. 2016 Oct 20;375(16):1596-1597.
12. Dooley J, Gerber-Finn L, Antone I, et al. **Buprenorphine-naloxone use in pregnancy** for treatment of opioid dependence-*Retrospective cohort study of 30 patients.* Can Fam Physician 2016;62:e194-200
13. Bruneau J, Ahamad K, Goyer ME, et al. Management of opioid use disorders: a national clinical practice guideline. *CMAJ* 2018 March 5;190:E247-57.
14. **OPIOID SUBSTITUTION THERAPY GUIDELINES** AND STANDARDS for the Treatment of Opioid Addiction/Dependence. Saskatchewan Methadone Program. Mar 2018.
15. Clinical Resource, *FAQs About Buprenorphine for Chronic Pain. Pharmacist's Letter/Prescriber's Letter.* April 2018.
16. Clinical Resource, *Management of Opioid Dependence. Pharmacist's Letter/Prescriber's Letter.* January 2018.
17. Lee JD, Nunes EV Jr, Novo P, et al. Comparative effectiveness of **extended-release naltrexone versus buprenorphine-naloxone** for opioid relapse prevention (X:BOT): a multicentre, open-label, randomised controlled trial. Lancet. 2018 Jan 27;391(10118):309-318
18. Michael Soyka, Henry R. Kranzler, Wim van den Brink, et al. **Guidelines for Substance Use Disorders (2011**) The World Federation of Societies of Biological Psychiatry (WFSBP) Guidelines for the Biological Treatment of Substance Use and Related Disorders. Part 2: Opioid dependence, The World Journal of Biological Psychiatry, 12:3, 160-187.
19. Gowing L, Farrell M, Ali R, et al. **Alpha$_2$-adrenergic agonists** for the management of opioid withdrawal. *Cochrane Database of Systematic Reviews* 2016, Issue 5. Art. No.: CD002024.
20. Miller R, BC Centre on Substance Use. **Buprenorphine/naloxone** in opioid use disorder. BC Provincial Academic Detailing Service.
21. Kahan, M. META:PHI in Primary Care: Implementing Best Practices for Addictions: **Managing Opioid Use Disorders in Chronic Pain Patients**. http://www.metaphi.ca/provider-tools.html
22. Kahan, M. META:PHI in Primary Care: Implementing Best Practices for Addictions: **Long-Term Management of Patients with Substance Use Disorders**. http://www.metaphi.ca/provider-tools.html
23. Kahan, M. **Emergency department protocols** for alcohol- and opioid- related presentations. META:PHI. http://www.metaphi.ca/provider-tools.html
24. Kahan M, Srivastava A, Ordean A, Cirone S. **Buprenorphine**: new treatment of opioid addiction in primary care. Can Fam Physician. 2011 Mar;57(3):281-9. Review
25. Summary Safety Review- **Methadose, Metadol-D** (methadone hydrochloride)- Health Canada. Issued 2018-08-02. Accessed 2018-08-14. https://hpr-rps.hres.ca/reg-content/summary-safety-review-detail.php?lang=en&linkID=SSR00207
27. Verbal communication - Dr Carmen Johnson.
28. Jonan AB, Kaye AD, Urman RD. **Buprenorphine Formulations**: Clinical BestPractice Strategies Recommendations for Perioperative Management of Patients Undergoing Surgical or Interventional Pain Procedures. Pain Physician. 2018 Jan;21(1):E1-E12.
29. Ton J, Korownyk C, Allan GM. Does this patient taking prescription opioids have **opioid use disorder?** In ACFP Tools for Practice (POMI). Oct 22, 2018. Accessed online June 26, 2019 at https://www.acfp.ca/wp-content/uploads/tools-for-practice/1539789463_tfp222opioidscreeningfv.pdf
30. Korownyk C, Perry D, Ton J, Kolber MR, Garrison S, Thomas B, Allan GM, Dugré N, Finley CR, Ting R, Yang PR, Vandermeer B, Lindblad AJ. **Opioid use disorder in primary care**: PEER umbrella systematic review of systematic reviews. Can Fam Physician. 2019 May;65(5):e194-e206.
31. **UBC – CPD E-learning module**.
32. Hämmig R, Kemter A, Strasser J, et al. Use of **microdoses for induction of buprenorphine** treatment with overlapping full opioid agonist use: the Bernese method. Subst Abuse Rehabil. 2016 Jul 20;7:99-105.
33. Welsh C, Valadez-Meltzer A. **Buprenorphine**: a (relatively) new treatment for opioid dependence. Psychiatry (Edgmont). 2005;2(12):29–39.
34. Carroll KM, DeVito EE, Yip SW, et al. Double-Blind Placebo-Controlled Trial of **Galantamine for Methadone-Maintained Individuals With Cocaine Use Disorder**: Secondary Analysis of Effects on Illicit Opioid Use. Am J Addict. 2019 Jul;28(4):238-245.
35. Chou R, Ballantyne J, Lembke A. **Rethinking Opioid Dose Tapering,** Prescription Opioid Dependence, and Indications for Buprenorphine. Ann Intern Med. 2019 Aug 27.
36. Dakwar E, Nunes EV, Hart CL, et al. A Single **Ketamine Infusion** Combined With Mindfulness-Based Behavioral Modification **to Treat Cocaine Dependence**: A Randomized Clinical Trial. Am J Psychiatry. 2019 Jun 24:appiajp201918101123.
37. Jones CM, Compton W, Vythilingam M, Giroir B. **Naloxone Co-prescribing** to Patients Receiving Prescription Opioids in the Medicare Part D Program, United States, 2016-2017. JAMA. 2019 Aug 6;322(5):462-464.
38. Meisel ZF, Lupulescu-Mann N, Charlesworth CJ, et al. Conversion to Persistent or **High-Risk Opioid Use After a New Prescription** From the Emergency Department: Evidence From Washington Medicaid Beneficiaries. Ann Emerg Med. 2019 Jun 20.
39. Phillips RH, Salzman M, Haroz R, et al. Elective **Naloxone-Induced Opioid Withdrawal** for Rapid Initiation of Medication-Assisted Treatment of Opioid Use Disorder. Ann Emerg Med. 2019 Feb 14.
40. Segura LE, Mauro CM, Levy NS, et al. Association of US **Medical Marijuana Laws With Nonmedical Prescription Opioid Use** and Prescription Opioid Use Disorder. JAMA Netw Open. 2019 Jul 3;2(7):e197216.
41. **Microdosing** of Buprenorphine for Induction (The Bernese Method). Cho E, Lu S. - BC Pharmacy Association. 26 Nov 2018. Accessed online 01 Sept 2019 at https://www.bcpharmacy.ca/news/microdosing-buprenorphine-induction-bernese-method
42. Nadia Fairbairn, Josey Ross, Michael Trew, et al. **Injectable opioid agonist treatment** for opioid use disorder: a national clinical **guideline**. CMAJ September 23, **2019** 191 (38) E1049-E1056; DOI: https://doi.org/10.1503/cmaj.190344
43. Trujols J, Campins J, Ribalta E. Opioid agonist dosage adequacy from clinical and patient perspectives: further considerations. CMAJ 2019;191:E1084. Accessed online 01Oct at http://www.cmaj.ca/content/191/39/E1084 .
44. Coffa D, Snhyder H. Opioid Use Disorder: Medical Treatment Options. AFP 2019:100(7):416-425.
45. Canadian Research Initiative in Substance Misuse (**CRISM**). **National Injectable Opioid Agonist Treatment** for Opioid Use Disorder Clinical Guideline. Published September 23, **2019**. Available at: https://crism.ca/projects/ioat-guideline
46. ACOG: Committee on Obstetric Practice. Committee Opinion No. 711: **Opioid Use and Opioid Use Disorder in Pregnancy**. Obstet Gynecol. 2017 Aug;130(2):e81-e94.
47. Coffa D, Snyder H. Opioid Use Disorder: **Medical Treatment Options**. Am Fam Physician. 2019 Oct 1;100(7):416-425.
48. Fairbairn N, Ross J, Trew M, et al. **Injectable opioid agonist treatment for opioid use disorder**: a national clinical guideline. CMAJ. 2019 Sep 23;191(38):E1049-E1056.

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References – RxFiles - Alcohol Use Disorder (AUD) Tx Chart

1. Kahan, M., Hardy, K (Ed), Clarke, S(Ed). Management of alcohol use disorders, opioid prescribing, and opioid use disorders in primary care: A pocket reference for family physicians. 2015 Toronto: Women's College Hospital.
2. Litten RZ, Wilford BB, Falk DE, Ryan ML, Fertig JB. Potential medications for the treatment of alcohol use disorder: An evaluation of clinical efficacy and safety. Subst Abus. 2016 Apr-Jun;37(2):286-98
3. McClay,E. How pharmacists can help patients reduce their alcohol intake: A guide to new and existing treatments. Pharmacy Management. 2016 Jan;32(1):18-23
4. Johnson,BA. Pharmacotherapy for alcohol use disorder. In: UpToDate, Saitz,R., Hermann,R. (Eds). UpToDate, Waltham MA. (Accessed June15, 2016)
5. Erwin BL, Slaton RM. Varenicline in the treatment of alcohol use disorders. Ann Pharmacother. 2014 Nov;48(11):1445-55.
6. Kahan M, Watts K. 2015. *CAMH*. [ONLINE] Available at:https://www.porticonetwork.ca/web/alcohol-toolkit/treatment/medications-for-alcohol-use-disorders. [Accessed 10 August 2016].
7. Flannery AH, Adkins DA, Cook AM. Unpeeling the Evidence for the Banana Bag: Evidence-Based Recommendations for the Management of Alcohol-Associated Vitamin and Electrolyte Deficiencies in the ICU. Crit Care Med. 2016 Aug;44(8):1545-52.
8. Crowley,P. Long-term drug treatment of patients with alcohol dependence. Aust Presc. 2015;38:41-3
9. Leung JG, Hall-Flavin D, Nelson S, Schmidt KA, Schak KM. The role ofgabapentin in the management of alcohol withdrawal and dependence. Ann Pharmacother. 2015 Aug;49(8):897-906.
10. van Amsterdam J, van den Brink W. Reduced-risk drinking as a viable treatment goal in problematic alcohol use and alcohol dependence. J Psychopharmacol. 2013 Nov;27(11):987-97.
11. Guglielmo R, Martinotti G, Quatrale M, Ioime L, Kadilli I, Di Nicola M, JaniriL. Topiramate in Alcohol Use Disorders: Review and Update. CNS Drugs. 2015 May;29(5):383-95.
12. Cutcliffe JR, Travale R, Richmond MM, Green T. Considering the Contemporary Issues and Unresolved Challenges Facing Therapeutic Communities for Clients with Alcohol and Substance Abuse. Issues Ment Health Nurs. 2016 Apr 29:1-9.
13. Rolland B, Paille F, Gillet C, Rigaud A, Moirand R, Dano C, Dematteis M, Mann K, Aubin HJ. Pharmacotherapy for Alcohol Dependence: The 2015 Recommendations of the French Alcohol Society, Issued in Partnership with the European Federation of Addiction Societies. CNS Neurosci Ther. 2016 Jan;22(1):25-37.
14. Martinotti G, Orsolini L, Fornaro M, Vecchiotti R, De Berardis D, Iasevoli F, Torrens M, Di Giannantonio M. Aripiprazole for relapse prevention and craving in alcohol use disorder: current evidence and future perspectives. Expert Opin Investig Drugs. 2016 Jun;25(6):719-28.
15. Concurrent Disorders and withdrawal management protocols/guidelines and services. Saskatoon (SK): Addictions Medical Advisory Committee, July 2016 08. Available from https://www.saskatoonhealthregion.ca/locations_services/Services/mhas/Documents/Resources%20for%20Professionals/COMPLETE.pdf
16. Jonas DE, Amick HR, Feltner C, Bobashev G, Thomas K, Wines R, Kim MM, Shanahan E, Gass CE, Rowe CJ, Garbutt JC. Pharmacotherapy for Adults With Alcohol-Use Disorders in Outpatient Settings [Internet]. Rockville (MD): Agency for Healthcare Research and Quality (US); 2014 May
17. Long-term Use of Acamprosate Calcium for Alcoholism: A Review of the Clinical Effectiveness, Safety, and Guidelines [Internet]. Ottawa (ON): Canadian Agency for Drugs and Technologies in Health; 2015 May 29. Available from http://www.ncbi.nlm.nih.gov/books/NBK304665/
18. Winslow BT, Onysko M, Hebert M. Medications for Alcohol Use Disorder. Am Fam Physician. 2016 Mar 15;93(6):457-65.
19. Harrison,P. High-Dose Baclofen Supports Abstinence in Alcoholism. Medscape. June 30,2015
20. Sechi G, Serra A. Wernicke's encephalopathy: new clinical settings and recent advances in diagnosis and management. Lancet Neurol. 2007 May;6(5):442-55.Review.
21. Day GS, del Campo CM. Wernicke encephalopathy: a medical emergency. CMAJ. 2014 May 13;186(8):E295. PMID: 24016788;
22. Donnino MW, Vega J, Miller J, Walsh M. Myths and misconceptions of Wernicke's encephalopathy: what every emergency physician should know. Ann Emerg Med. 2007 Dec;50(6):715-21.
23. DeVido JJ, Weiss RD. Treatment of the depressed alcoholic patient. Curr Psychiatry Rep. 2012 Dec;14(6):610-8.
24. Benson G, McPherson A, Reid S. An alcohol withdrawal tool for use in hospitals. Nurs Times. 2012 Jun 26-Jul 2;108(26):15-7.
25. Cresce ND, McManus KA, Sifri CD, Wilson BB. Encephalopathy despite thiamine repletion during alcohol withdrawal. Cleve Clin J Med. 2014 Jun;81(6):350-2.
26. Salisbury-Afshar E. Pharmacotherapy for Adults with Alcohol Use Disorder. AmFam Physician. 2016 Jul 15;94(2):155-7.
27. Whalen K.L., Borja-Hart N (2015). Interpretation of Clinical Laboratory Data. InNemire R.E., Kier K.L., Assa-Eley M (Eds), *Pharmacy Student Survival Guide, 3e.* Retrieved August 11, 2016 fromhttp://accesspharmacy.mhmedical.com.cyber.usask.ca/content.aspx?bookid=1593&Sectionid=99824844
28. Connor J. Alcohol consumption as a cause of cancer. Addiction. 2016 Jul 21
29. Butt, P., Beirness, D., Cesa, F., Gliksman, L., Paradis, C., & Stockwell, T. (2011). Alcohol and health in Canada: A summary of evidence and guidelines for low-risk drinking. Ottawa, ON: Canadian Centre on Substance Abuse
30. Alcohol poisoning. Mayo Clinic Staff. Retrieved August 11, 2016, from http://www.mayoclinic.org/
31. Anton RF, O'Malley SS, Ciraulo DA, et al. Combined pharmacotherapies and behavioral interventions for alcohol dependence: the COMBINE study: a randomized controlled trial. JAMA. 2006 May 3;295(17):2003-17.
32. Anton RF, Myrick H, Wright TM, et al. Gabapentin combined with naltrexone for the treatment of alcohol dependence. Am JPsychiatry. 2011 Jul;168(7):709-17.
33. DSM-5, Available at: http://dsm.psychiatryonline.org/ (Accessed: 19th August 2016).
34. Heinälä P, Alho H, Kiianmaa K, Lönnqvist J, Kuoppasalmi K, Sinclair JD. Targeted use of naltrexone without prior detoxification in the treatment of alcohol dependence: a factorial double-blind, placebo-controlled trial. J Clin Psychopharmacol. 2001 Jun;21(3):287-92
35. Gianni E, Forte P, Galli V, Razzolini et al. Prospective Evaluation of Liver Stiffness Using Transient Elastography in Alcoholic Patients Following Abstinence. Alcohol Alcohol. 2016 Aug 19.
36. Vogrig A, Zanoni T, Moretto G. Nystagmus and Lower Extremity Hyperalgesia After Colectomy. (Wernicke encephalopathy: Thiamine) JAMA. 2016 Oct 11;316(14):1488-1489.
37. Johnson BA, Rosenthal N, Capece JA et al. Topiramate for Alcoholism Study Group. Topiramate for treating alcohol dependence: a randomized controlled trial. JAMA. 2007 Oct 10;298(14):1641-51.
38. Smith PC, Schmidt SM, Allensworth-Davies D, et al. Primary care validation of a single-question alcohol screening test. J Gen Intern Med. 2009Jul;24(7):783-8.
39. McCambridge J, Saitz R. Rethinking brief interventions for alcohol in general practice. BMJ. 2017 Jan 20;356:j116.
40. Popova S, et al. Estimation of national, regional, and global prevalence of alcohol use during pregnancy and fetal alcohol syndrome: a systematic review and meta-analysis. Lancet Glob Health 2017; online Jan 12.
41. Spirito A, Bromberg JR, Casper TC, et al. Reliability and Validity of a Two-Question Alcohol Screen in the Pediatric Emergency Department. Pediatrics.2016;138(6):e20160691

42. Kaplan LM, Nayak MB, Greenfield TK, et al. Alcohol's Harm to Children: Findings from the 2015 United States National Alcohol's Harm to Others Survey. J Pediatr. 2017 Feb 10.
43. O'Neill D, Britton A, Brunner EJ, et al. Twenty-five-year alcohol consumption trajectories and their association with arterial aging: a prospective cohort study. *J Am Heart Assoc* 2017.
44. Roerecke M, Kaczorowski J, Tobe SW, et al. The effect of a reduction in alcohol consumption on blood pressure: a systematic review and meta-analysis. *Lancet Public Health* 2017.
45. Samokhvalov AV, Le Foll B. A 35-year-old woman with low mood and concerns about her alcohol use. CMAJ. 2017 Feb 27;189(8):E317-E318.
46. Sedhai YR, Patel D. Calcific Pancreatitis Associated with Alcohol Use. N Engl J Med. 2017 Feb 2;376(5):e6.
47. Hadland SE, Xuan Z, Sarda V, et al. Alcohol Policies and Alcohol-Related Motor Vehicle Crash Fatalities Among Young People in the US. Pediatrics. 2017 Feb 13.
48. Bell S, Daskalopoulou M, Rapsomaniki E, et al. Association between clinically recorded alcohol consumption and initial presentation of 12 cardiovascular diseases: population based cohort study using linked health records. BMJ 2017;356:j909.
49. Meda SA, Gueorguieva RV, Pittman B, et al. Longitudinal influence of alcohol and marijuana use on academic performance in college students. PLoS One. 2017 Mar 8;12(3):e0172213.
50. Pryor J, Patrick SW, Sundermann AC, et al. Pregnancy Intention and Maternal Alcohol Consumption. Obstet Gynecol. 2017 Mar 6.
51. Roemer A, Stockwell T. Alcohol Mixed With Energy Drinks and Risk of Injury: A Systematic Review. J Stud Alcohol Drugs. 2017 Mar;78(2):175-183
52. Stickel F, Datz C, Hampe J, Bataller R. Pathophysiology and Management of Alcoholic Liver Disease: Update 2016. Gut Liver. 2017 Mar 15;11(2):173-188.
53. Buzzetti E, Kalafateli M, Thorburn D, et al. Pharmacological interventions for alcoholic liver disease (alcohol-related liver disease). Cochrane Database of Systematic Reviews 2017, Issue 3. Art. No.: CD011646. Because of very low-quality evidence, there is uncertainty in the effectiveness of any pharmacological intervention versus no intervention in people with alcoholic hepatitis or severe alcoholic hepatitis. Based on low-quality evidence, propylthiouracil may decrease mortality in people with other alcohol-related liver diseases. However, these results must be confirmed by adequately powered trials with low risk of bias before propylthiouracil can be considered effective.
54. Hasin DS, Wall M, Witkiewitz K, et al. Change in non-abstinent WHO drinking risk levels and alcohol dependence: a 3 year follow-up study in the US general population. Lancet Psychiatry 2017; online April 26.
55. Li S, Cho E, Drucker AM, et al. Alcohol intake and risk of rosacea in US women. J Am Acad Dermatol. 2017 Apr 1.
56. Brunner S, Herbel R, Drobesch C, et al. Alcohol consumption, sinus tachycardia, and cardiac arrhythmias at the Munich Octoberfest: results from the Munich Beer Related Electrocardiogram Workup Study (MunichBREW). Eur Heart J. 2017 Apr 25.
57. Williams LA, Olshan AF, Hong CC, et al. Alcohol Intake and Breast Cancer Risk in African American Women from the AMBER Consortium. Cancer Epidemiol Biomarkers Prev. 2017 Apr 18.
58. Spithoff S, Turner S, Gomes T, et al. First-line medications for alcohol use disorders among public drug plan beneficiaries in Ontario. Can Fam Physician. 2017 May;63(5):e277-e283
59. Vergis N, Atkinson SR, Knapp S, et al. In Patients With Severe Alcoholic Hepatitis, Prednisolone Increases Susceptibility to Infection and Infection-Related Mortality, and Is Associated With High Circulating Levels of Bacterial DNA. Gastroenterology. 2017 Apr;152(5):1068-1077.e4.
60. Pdf Chen CJ, Brown WM, Moomaw CJ, et al. Alcohol use and risk of intracerebral hemorrhage. Neurology. 2017 May 23;88(21):2043-2051
61. Hirst JA, et al. Short- & medium-term effects of light to moderate alcohol intake on glycaemic control in diabetes mellitus: a systematic review & meta-analysis of randomized trials. Diabet Med. 2017 May;34(5):604-611.
62. Jang JB, Patrick ME, Keyes KM et al. Frequent Binge Drinking Among US Adolescents, 1991 to 2015. Peds.2017;139(6):e20164023
63. Welsh JW, Knight JR, Hadland SE. Adolescent Frequent Heavy Drinking From 1991-2015. Peds. 2017;139(6):e20170932
64. Lefebvre, L. Alcohol-related disorders. Compendium of Therapeutic Choices-Canadian Pharmacists Association. May 2017. (Accessed May 2017).
65. Pettinati HM, Oslin DW, Kampman KM, Dundon WD, Xie H, Gallis TL, Dackis CA, O'Brien CP. A double-blind, placebo-controlled trial combining sertraline and naltrexone for treating co-occurring depression and alcohol dependence. Am J Psychiatry. 2010 Jun;167(6):668-75.
66. Herbert A, Gilbert R, Cottrell D, et al. Causes of death up to 10 years after admissions to hospitals for self-inflicted, drug-related or alcohol-related, or violent injury during adolescence: a retrospective, nationwide, cohort study. Lancet. 2017 May 25.
67. QuickStats: Age-Adjusted Death Rates* Attributable to Alcohol-Induced Causes,(†) by Race/Ethnicity - United States, 1999-2015. MMWR Morb Mortal Wkly Rep. 2017 May 12;66(18):491.
68. Topiwala A, Allan C, Valkanova V, et al. Moderate alcohol consumption as risk factor for adverse brain outcomes and cognitive decline: longitudinal cohort study. BMJ 2017;357:j2353.
69. Bower C, Baynam G. New Opportunities for Evidence in Fetal Alcohol Spectrum Disorder. JAMA Pediatr. 2017 Jun 5.
70. Dunne PDJ, Forrest EH. Review article: recent insights into clinical decision-making in severe alcoholic hepatitis. Aliment Pharmacol Ther. 2017 May 21.
71. Kwon YJ, Lim HJ, Lee YJ, et al. Associations between high-risk alcohol consumption and sarcopenia among postmenopausal women. Menopause. 2017 Jun 5.
72. Nygren K, Hammarström A, Rolandsson O. Binge drinking and total alcohol consumption from 16 to 43 years of age are associated with elevated fasting plasma glucose in women: results from the northern Swedish cohort study. BMC Public Health. 2017 Jun 8;17(1):509
73. Procyshyn RM, Bezchlubnyk-Butler K, Jeffries JJ (Eds). Clinical Handbook of Psychotropic Drugs, 22nd Edition. Hogrefe. 2017.
74. Grant BF, Chou SP, Saha TD, et al. Prevalence of 12-Month Alcohol Use, High-Risk Drinking, and DSM-IV Alcohol Use Disorder in the United States, 2001-2002 to 2012-2013: Results From the National Epidemiologic Survey on Alcohol and Related Conditions. JAMA Psychiatry. 2017 Aug 9
75. Holst C, Becker U, Jørgensen ME, et al. Alcohol drinking patterns and risk of diabetes: a cohort study of 70,551 men and women from the general Danish population. Diabetologia. 2017 Jul 27.
76. Humphreys JH, Warner A, Costello R, et al. Quantifying the hepatotoxic risk of alcohol consumption in patients with rheumatoid arthritis taking methotrexate. Ann Rheum Dis. 2017 Mar 23.
77. Mayor S. Sixty seconds on…drinking and diabetes. BMJ. 2017 Aug 2;358:j3672
78. Richard EL, Kritz-Silverstein D, Laughlin GA, et al. Alcohol Intake and Cognitively Healthy Longevity in Community-Dwelling Adults: The Rancho Bernardo Study. J Alzheimers Dis. 2017;59(3):803-814.
79. Schuckit MA. Remarkable Increases in Alcohol Use Disorders. JAMA Psychiatry. 2017 Aug 9
80. VanWagner LB et al. Alcohol use and cardiovascular disease risk in patients with nonalcoholic fatty liver disease. Gastroenterology 2017 Aug 9.
81. Xi B, Veeranki SP, Zhao M, et al. Relationship of alcohol consumption to all-cause, cardiovascular, and cancer-related mortality in U.S. adults. J Am Coll Cardiol 2017;70:913–22.
82. Abernethy C, McCall KE, Cooper G, et al. Determining the pattern and prevalence of alcohol consumption in pregnancy by measuring biomarkers in meconium. Arch Dis Child Fetal Neonatal Ed. 2017 Jul 4.
83. Andersen AM, Pietrzak RH, Kranzler HR, et al. Polygenic Scores for Major Depressive Disorder and Risk of Alcohol Dependence. JAMA Psychiatry. 2017 Aug 16.
84. Kamboj SK, Irez D, Serfaty S, et al. Ultra-Bried Mindfulness Training Reduces Alcohol Consumption in At-Risk Drinkers: A Randomized Double-Blind Active-Controlled Experiment. International Journal of Neuropsychopharmacology.2017.00(00):1-12.
85. Lange S, Probst C, Gmel G,et al. Global prevalence of fetal alcohol spectrum disorder among children and youth: a systematic review and meta-analysis [online August 21, 2017]. JAMA Pediatr. doi:10.1001/jamapediatrics.2017.1919
86. Richard EL, Kritz-Silverstein D, Laughlin GA, et al. Alcohol Intake and Cognitively Healthy Longevity in Community-Dwelling Adults: The Rancho Bernardo Study. J Alzheimers Dis. 2017;59(3):803-814.
87. VanWagner LB, Ning H, Allen NB, et al. Alcohol Use and Cardiovascular Disease Risk in Patients with Nonalcoholic Fatty Liver Disease. Gastroenterology. 2017 Aug 9.
88. Verbeek J et al. Hair ethyl glucuronide is a highly accurate biomarker of chronic excessive alcohol use in patients with alcoholic cirrhosis. Clin Gastroenterol Hepatol 2017 Aug 19;
89. Knight E, Lappalainen L. Clinical Institute Withdrawal Assessment for Alcohol-Revised might be an unreliable tool in the management of alcohol withdrawal. Can Fam Physician. 2017 Sep;63(9):691-695.

90. Kojima G, Liljas A, Iliffe S, et al. A systematic review and meta-analysis of prospective associations between alcohol consumption and incident frailty. Age Ageing. 2017 May 25:1-9.
91. Mamluk L, Edwards HB, Savović J, et al. Low alcohol consumption and pregnancy and childhood outcomes: time to change guidelines indicating apparently 'safe' levels of alcohol during pregnancy? A systematic review and meta-analyses. BMJ Open. 2017 Aug 3;7(7):e015410
92. Parisi R, Webb RT, Carr MJ, et al. Alcohol-Related Mortality in Patients With Psoriasis: A Population-Based Cohort Study. JAMA Dermatol. 2017 Sep 15.
93. Weinberger AH, Gbedemah M, Goodwin RD. Cigarette smoking quit rates among adults with and without alcohol use disorders and heavy alcohol use, 2002-2015: A representative sample of the United States population. Drug Alcohol Depend. 2017 Aug 5;180:204-207
94. Kaner EFS, Beyer FR, Garnett C, et al. Personalised digital interventions for reducing hazardous and harmful alcohol consumption in community-dwelling populations. Cochrane Database of Systematic Reviews 2017, Issue 9. Art. No.: CD011479. There is moderate-quality evidence that digital interventions may lower alcohol consumption, with an average reduction of up to three (UK) standard drinks per week compared to control participants. Substantial heterogeneity and risk of performance and publication bias may mean the reduction was lower. Low-quality evidence from fewer studies suggested there may be little or no difference in impact on alcohol consumption between digital and face-to-face interventions.
95. Palpacuer C, Duprez R, Huneau A, et al. Pharmacologically controlled drinking in the treatment of alcohol dependence or alcohol use disorders: a systematic review with direct and network meta-analyses on nalmefene, naltrexone, acamprosate, baclofen, and topiramate. Addiction 2017.
96. Naimi TS, Xuan Z, Coleman SM, et al. Alcohol Policies and Alcohol-Involved Homicide Victimization in the United States. J Stud Alcohol Drugs. 2017 Sep;78(5):781-788.
97. Palmer BF, Clegg DJ. Electrolyte Disturbances in Patients with Chronic Alcohol-Use Disorder. N Engl J Med. 2017 Oct 5;377(14):1368-1377.
98. Primack BA, Colditz JB, Rosen EB, et al. Portrayal of Alcohol Brands Popular Among Underage Youth on YouTube: A Content Analysis. J Stud Alcohol Drugs. 2017 Sep;78(5):654-664.
99. Denny L, Coles S, Blitz R. Fetal Alcohol Syndrome and Fetal Alcohol Spectrum Disorders. Am Fam Physician. 2017;96(8):515-522.
100. Ladouceur R. What if alcohol were harmful, even in moderation? Can Fam Physician. 2017 Oct;63(10):742.
101. Pfefferbaum A et al. Altered brain developmental trajectories in adolescents after initiating drinking. Am J Psych 2017 Oct 31.
102. Zhou H, Polimanti R, Yang B-Z, et al. Genetic risk variants associated with comorbid alcohol dependence and major depression [online October 25, 2017]. *JAMA Psychiatry*. 2017. doi:10.1001/jamapsychiatry.2017.3275.
103. Ashton K, Bellis MA, Davies AR, et al. Do emotions related to alcohol consumption differ by alcohol type? An international cross-sectional survey of emotions associated with alcohol consumption and influence on drink choice in different settings. BMJ Open. 2017 Nov 20;7(10):e016089.
104. Gill J, Black H, Rush R, et al. Heavy Drinkers and the Potential Impact of Minimum Unit Pricing-No Single or Simple Effect? Alcohol Alcohol. 2017 Nov 1;52(6):722-729.
105. Spadola CE, Wagner EF, Varga LM, et al. A Qualitative Examination of Increased Alcohol Use after Bariatric Surgery among Racially/Ethnically Diverse Young Adults. Obes Surg. 2017 Nov 19.
106. Valentine M, Bihm DCJ, Wolf L, et al. Computer-Aided Recognition of Facial Attributes for Fetal Alcohol Spectrum Disorders. Pediatrics. 2017 Dec;140(6).
107. Cheng HG, Kaakarli H, Breslau J, et al. Assessing Changes in Alcohol Use and Alcohol Use Disorder Prevalence in the United States: Evidence From National Surveys From 2002 Through 2014. JAMA Psychiatry. 2017 Dec 27.
108. Cholankeril G and Ahmed A. Alcoholic liver disease replaces hepatitis C virus infection as the leading indication for liver transplantation in the United States. Clin Gastroenterol Hepatol 2017 Nov 30.
109. O'Malley SS, Zweben A, Fucito LM, et al. Effect of varenicline combined with medical management on alcohol use disorder with comorbid cigarette smoking: a randomized clinical trial [online Dec 20, 2017]. JAMA Psychiatry. doi:10.1001/jamapsychiatry.2017.3544
110. Subbaraman MS, Metrik J, Patterson D, et al. Cannabis use during treatment for alcohol use disorders predicts alcohol treatment outcomes. Addiction. 2017 Apr;112(4):685-694.
111. Zupan Z, Evans A, Couturier DL, et al. Wine glass size in England from 1700 to 2017: a measure of our time. BMJ. 2017 Dec 13;359:j5623.
112. Degerud E, et al. Life course socioeconomic position, alcohol drinking patterns in midlife, and cardiovascular mortality: Analysis of Norwegian population-based health surveys. PLoS Med. 2018 Jan 2;15(1):e1002476.
113. Mattick RP, et al. Association of parental supply of alcohol with adolescent drinking, alcohol-related harms, and alcohol use disorder symptoms: a prospective cohort study. Lancet Public Health 2018; online Jan 22.
114. Reus VI, Fochtmann LJ, et al. The **American Psychiatric Association (APA) Practice Guideline for the Pharmacological Treatment of Patients With Alcohol Use Disorder**. Am J Psychiatry. 2018 Jan 1;175(1):86-90.
115. Topiwala A, Ebmeier KP. Effects of drinking on late-life brain and cognition. Evid Based Ment Health. 2018 Feb;21(1):12-15.
116. Teutsch SM, Naimi TS. Eliminating Alcohol-Impaired Driving Fatalities: What Can Be Done? Ann Intern Med. 2018 Jan 17.
117. Dakhoul L, et al. Heavy Consumption of Alcohol is Not Associated With Worse Outcomes in Patients With Idiosyncratic Drug-induced Liver Injury Compared to Non-Drinkers. Clin Gastroenterol Hepatol. 2018 Jan 3.
118. May PA, Chambers CD, Kalberg WO, et al. Prevalence of fetal alcohol spectrum disorders in 4 US communities [online Feb 6, 2018].JAMA. doi:10.1001/jama.2017.21896
119. Yu C, Tang H, Guo Y, et al. Effect of hot tea consumption and its interactions with alcohol and tobacco use on the risk for esophageal cancer. A populationbased cohort study. Ann Intern Med. 2018. [Epub ahead of print].
120. Bryan AD, Magnan RE, Gillman AS, et al. Effect of Including Alcohol and Cannabis Content in a Sexual Risk-Reduction Intervention on the Incidence of Sexually Transmitted Infections in Adolescents: A Cluster Randomized Clinical Trial. JAMA Pediatr. 2018 Feb 12:e175621.
121. Kaner EF, Beyer FR, Muirhead C, et al. Effectiveness of brief alcohol interventions in primary care populations. Cochrane Database Syst Rev. 2018 Feb 24;2:CD004148. We found moderate-quality evidence that brief interventions can reduce alcohol consumption in hazardous and harmful drinkers compared to minimal or no intervention. Longer counselling duration probably has little additional effect. Future studies should focus on identifying the components of interventions which are most closely associated with effectiveness.
122. Kendler KS, Lönn SL, Salvatore J, et al. The Origin of Spousal Resemblance for Alcohol Use Disorder. JAMA Psychiatry. 2018 Feb 7.
123. Khouri C, Arbib F, Revol B, et al. Severe central sleep apnoea associated with nalmefene: a case report. Br J Clin Pharmacol. 2018 Feb 26.
124. Rose AK, Jones A. Baclofen: its effectiveness in reducing harmful drinking, craving, and negative mood: a meta-analysis.Addiction2018. doi:10.1111/add.14191
125. Schwarzinger M, Pollock B, Hasan O, etal Contribution of alcohol use disorders to the burden of dementia in France 2008-13: a nationwide retrospective cohort study. Lancet Public Health10.1016/S2468-2667(18)30022-7.
126. Singal AK, Bataller R, Ahn J, et al. **ACG Clinical Guideline**: Alcoholic Liver Disease. Am J Gastroenterol. 2018 Jan 16.
127. Cheng C, et al. Interaction between **Psychotropic Medications and Alcohol**: Perceptions among Patients Attending an Adult Mental Health Day Hospital Program. Can J Hosp Pharm. 2018 Jan-Feb;71(1):7-13.
128. Kanny D, Naimi TS, Liu Y, et al. **Annual Total Binge Drinks Consumed by U.S. Adults**, 2015. Am J Prev Med. 2018 Apr;54(4):486-496.
129. Sullivan EV, et al. The role of **aging, drug dependence, and hepatitis C comorbidity in alcoholism** cortical compromise [online Mar 14, 2018].JAMA Psychiatry. doi:10.1001/jamapsychiatry.2018.0021
130. Bradley KA, Bobb JF, Ludman EJ, et al. **Alcohol-Related Nurse Care Management** in Primary Care: A Randomized Clinical Trial. JAMA Intern Med. 2018 Mar 26.
131. Gonzales NA, et al. Effect of **Middle School Interventions on Alcohol Misuse and Abuse in Mexican American High School Adolescents**: Five-Year Follow-up of a Randomized Clinical Trial. JAMA Psychiatry. 2018 Mar 21.
132. Pauly BB, Vallance K, Wettlaufer A, et al. **Community managed alcohol programs in Canada**: Overview of key dimensions and implementation. Drug Alcohol Rev. 2018 Mar 24.
133. Wood AM, Kaptoge S, Butterworth AS, et al. **Risk thresholds for alcohol consumption**: combined analysis of individual-participant data for 599 912 current drinkers in 83 prospective studies. Lancet 2018; 391: 1513–23.
134. Yan J, Thomson JK, Zhao W, et al. Role of **Stress Kinase JNK** in **Binge Alcohol**-Evoked Atrial **Arrhythmia**. J Am Coll Cardiol. 2018 Apr 3;71(13):1459-1470.
135. Yu C, Tang H, Guo Y, et al. **Hot Tea Consumption** and Its Interactions With **Alcohol and Tobacco Use on the Risk for Esophageal Cancer**: A Population-Based Cohort Study. Ann Intern Med. 2018 Apr 3;168(7):489-497.
136. **EASL**: **European** Association for the Study of the Liver. EASL Clinical Practice **Guidelines**: **Management of alcohol-related liver disease**. J Hepatol. 2018 Apr 5.
137. Fan X, Peters BA, Jacobs EJ, et al. **Drinking alcohol is associated with variation in the human oral microbiome** in a large study of American adults. Microbiome. 2018 Apr 24;6(1):59.
138. Newton AS, Mushquash C, Krank M, et al. **When and How Do Brief Alcohol Interventions** in Primary Care Reduce Alcohol Use and Alcohol-Related Consequences among Adolescents? J Pediatr. 2018 Apr 12.

139. Thiele M, Madsen BS, Hansen JF, et al. Accuracy of the **Enhanced Liver Fibrosis Test vs FibroTest, Elastography, and Indirect Markers** in Detection of **Advanced Fibrosis** in Patients With Alcoholic Liver Disease. Gastroenterology. 2018 Apr;154(5):1369-1379.
140. Bowden B et al. Risk of **suicide following an alcohol-related emergency hospital admission**: An electronic cohort study of 2.8 million people. PLoS One 2018 Apr 27;
141. Fernández MDM, Saulyte J, Inskip HM, et al. **Premenstrual syndrome and alcohol consumption**: a systematic review and meta-analysis. BMJ Open. 2018 Apr 16;8(3):e019490.
142. Naimi TS, Xuan Z, Sarda V, et al. Association of state alcohol policies with **alcohol-related motor vehicle crash fatalities** among US adults [online May 29, 2018]. JAMA Intern Med. doi:10.1001/jamainternmed.2018.1406
143. Ricci C, Wood A, Muller D, et al. **Alcohol intake** in relation to non-fatal and fatal **coronary heart disease and stroke**: EPIC-CVD case-cohort study. BMJ. 2018 May 29;361:k934.
144. Gupte A, Goede D, Tuite R, et al. **Chronic pancreatitis**. BMJ. 2018 Jun 7;361:k2126.
145. Mitchell T, Jeffrey GP, de Boer B, et al. Type and Pattern of **Alcohol Consumption is Associated With Liver Fibrosis** in Patients With Non-alcoholic Fatty Liver Disease. Am J Gastroenterol. 2018 Jun 14.
146. Ngo QM, Eisman AB, Walton MA, et al. **Emergency Department Alcohol Intervention**: Effects on Dating Violence and Depression. Pediatrics. 2018 Jun 5.
147. Piano MR, Burke L, Kang M, Phillips SA. Effects of **repeated binge drinking on blood pressure levels and other cardiovascular health** metrics in young adults: National Health Nutrition Examination Survey, 2011–2014. J Am Heart Assoc. 2018;7:e008733.
148. Roerecke M, Tobe SW, Kaczorowski J, et al. **Sex-specific associations between alcohol consumption and incidence of hypertension**: a systematic review and meta-analysis of cohort studies. J Am Heart Assoc. 2018;7:e008202.
149. De Santis S, Bach P, Pérez-Cervera L, et al. **Microstructural White Matter Alterations** in Men With Alcohol Use Disorder and Rats With Excessive Alcohol Consumption During Early Abstinence. JAMA Psychiatry. 2019 Apr 3.
150. Falk DE, O'Malley SS, Witkiewitz K, et al; for the Alcohol Clinical Trials Initiative (ACTIVE) Workgroup. Evaluation of **drinking risk levels as outcomes in alcohol pharmacotherapy trials**: a secondary analysis of 3 randomized clinical trials [online Mar 13, 2019]. JAMA Psychiatry.
151. Hydes TJ, Burton R, Inskip H, et al. A comparison of **gender-linked population cancer risks between alcohol and tobacco**: how many cigarettes are there in a bottle of wine? BMC Public Health. 2019 Mar 28;19(1):316.
152. Millwood IY, Walters RG, Mei XW, et al. Conventional and genetic evidence on alcohol and vascular disease aetiology: a prospective study of 500 000 men and women in China. Lancet. 2019 Apr 4.
153. Denny CH, Acero CS, Naimi TS, Kim SY. **Consumption of Alcohol Beverages and Binge Drinking Among Pregnant Women Aged 18-44 Years** - United States, 2015-2017. MMWR Morb Mortal Wkly Rep. 2019 Apr 26;68(16):365-368.
154. Holleck JL, Merchant N, Gunderson CG. **Symptom-Triggered Therapy for Alcohol Withdrawal Syndrome**: a Systematic Review and Meta-analysis of Randomized Controlled Trials. J Gen Intern Med. 2019 Apr 1.
155. Norman SB, Trim R, Haller M, et al. Efficacy of **Integrated Exposure Therapy vs Integrated Coping Skills Therapy for Comorbid Posttraumatic Stress Disorder and Alcohol Use Disorder**: A Randomized Clinical Trial. JAMA Psychiatry. 2019 Apr 24.
156. Onderwater GLJ, van Oosterhout WPJ, Schoonman GG, et al. **Alcoholic beverages as trigger factor and the effect on alcohol consumption behavior in patients with migraine.** Eur J Neurol. 2019 Apr;26(4):588-595.
157. Esser MB, Guy GP Jr, Zhang K, Brewer RD. **Binge Drinking and Prescription Opioid Misuse** in the U.S., 2012-2014. Am J Prev Med. 2019 Jun 7.
158. Gupta NM, Lindenauer PK, Yu P-C, et al. Association between alcohol use disorders and **outcomes of patients hospitalized with community-acquired pneumonia**. JAMA Netw Open. 2019;2(6):e195172.
159. Kranzler HR et al. A meta-analysis of the efficacy of **gabapentin for treating alcohol use disorder**. Addiction 2019 May 11; [e-pub].
160. Kulak JA, Griswold KS. **Adolescent Substance Use and Misuse**: Recognition and Management Am Fam Physician 2019;99(11): 689-696.
161. Rosoff DB, Charlet K, Jung J, et al. Association of High-Intensity **Binge Drinking With Lipid and Liver Function Enzyme Levels**. JAMA Netw Open. 2019 Jun 5;2(6):e195844.
162. Sinclair J, McCann M, Sheldon E, et al. The acceptability of **addressing alcohol consumption as a modifiable risk factor for breast cancer**: a mixed method study within breast screening services and symptomatic breast clinics. BMJ Open. 2019 Jun 17;9(6):e027371.
163. West MA, Smith A, Helm T, et al. Use of a Statewide Public Health **Tool to Estimate Miles Driven by Intoxicated Drivers**. JAMA Surg. 2019 Jun 19.
164. Quigley J; COMMITTEE ON SUBSTANCE USE AND PREVENTION. **Alcohol Use by Youth**. Pediatrics. 2019 Jun 24
165. Ryan SA, Kokotailo P; COMMITTEE ON SUBSTANCE USE AND PREVENTION. **Alcohol Use by Youth**. Pediatrics. 2019 Jun 24.
166. Yao XI, Ni MY, Cheung F, et al. **Change in moderate alcohol consumption and quality of life**: evidence from 2 population-based cohorts. CMAJ. 2019 Jul 8;191(27):E753-E760.
167. Crabb DW, Im GY, Szabo G, et al. Diagnosis and Treatment of Alcohol-Related **Liver Diseases**: 2019 Practice Guidance from the American Association for the Study of Liver Diseases. Hepatology. 2019 Jul 17
168. Han BH, Moore AA, Ferris R, Palamar JJ. **Binge Drinking** Among Older Adults in the United States, 2015 to 2017. J Am Geriatr Soc. 2019 Jul 31.
169. Myran DT, Hsu AT, Smith G, Tanuseputro P. Rates of **emergency department visits** attributable to alcohol use in Ontario from 2003 to 2016: a retrospective population-level study. CMAJ. 2019 Jul 22;191(29):E804-E810.

Additional articles for solid organ Transplantation (sot): Drug Management Chart:

Abd Rahman AN, Tett SE, Abdul Gafor HA, et al. Exposure-effect relationship of **mycophenolic acid and prednisolone** in adult lupus nephritis patients. Br J Clin Pharmacol. 2015 May 9.
Abdel Jalil MH, Hawwa AF, McKiernan PJ, et al. Population pharmacokinetic and pharmacogenetic analysis of **tacrolimus** in paediatric liver transplant patients. Br J Clin Pharmacol. 2013 Jun 6.
Acuna SA, Huang JW, Daly C, et al. Outcomes of Solid Organ Transplant Recipients With **Preexisting Malignancies in Remission**: A Systematic Review and Meta-Analysis. Transplantation. 2016 Apr 20
Adams DM, Trenor CC 3rd, Hammill AM, et al. Efficacy and Safety of **Sirolimus** in the Treatment of Complicated Vascular Anomalies. Pediatrics. 2016 Jan 18.
Ahmad S, Shlobin OA, Nathan SD. **Pulmonary complications of lung transplantation**. Chest. 2011 Feb;139(2):402-11.
Ahya VN. Counterpoint: Should United States Centers Transplant Solid Organs Into International Recipients? No. Chest. 2017 Feb 13.
Alemtuzumab-based induction treatment versus **basiliximab**-based induction treatment in kidney transplantation (the 3C Study): a randomised trial. Lancet 2014; online July 28.
Andreoni KA, Forbes R, Andreoni RM, Phillips G, Stewart H, Ferris M. **Age-Related Kidney Transplant Outcomes**: Health Disparities Amplified in Adolescence. JAMA Intern Med. 2013 Jul 29.
Andrews LM, Hesselink DA, van Schaik RHN, et al. A population **pharmacokinetic model to predict the individual starting dose of tacrolimus** in adult renal transplant recipients. Br J Clin Pharmacol. 2018 Dec 14.
Anutrakulchai S, Pongskul C, Kritmetapak K, et al. **Therapeutic concentration achievement and allograft survival comparing usage of conventional tacrolimus** doses and CYP3A5 genotype-guided doses in renal transplantation patients. Br J Clin Pharmacol. 2019 May 11.
Armenian SH, Sun CL, Vase T, Ness KK, et al. **Cardiovascular risk factors in hematopoietic cell transplantation** (HCT) survivors: Role in development of subsequent cardiovascular disease. Blood 2012
Ardehali A, Esmailian F, Deng M, et al; PROCEED II trial investigators. **Ex-vivo perfusion of donor hearts** for human heart transplantation (PROCEED II): a prospective, open-label, multicentre, randomised non-inferiority trial. Lancet. 2015 Jun 27;385(9987):2577-84.
Asberg A, Humar A, Jardine AG, et al. VICTOR Study Group. Long-term outcomes of CMV disease treatment with **valganciclovir** versus IV **ganciclovir** in solid organ transplant recipients. Am J Transplant. 2009 May;9(5):1205-13.
Asberg A, Jardine AG, Bignamini AA, et al. on behalf of the VICTOR Study Group. Effects of the Intensity of **Immunosuppressive** Therapy on Outcome of Treatment for **CMV** Disease in Organ Transplant Recipients. Am J Transplant. 2010 May 10.
Ascha M, Ascha MS, Tanenbaum J, et al. **Risk** Factors for **Melanoma** in **Renal** Transplant Recipients. JAMA Dermatol. 2017 Jul 26.
Asleh R, Clavell AL, Pereira NL, et al. Incidence of **Malignancies in Patients Treated With Sirolimus** Following Heart Transplantation. J Am Coll Cardiol. 2019 Jun 4;73(21):2676-2688.
Aubert O, Reese PP, Audry B, et al. **Disparities in Acceptance of Deceased Donor Kidneys** Between the United States and France and Estimated Effects of Increased US Acceptance. JAMA Intern Med. 2019 Aug 26.
Bailey P, Edwards A, Courtney AE. **Living kidney donation**. BMJ. 2016 Sep 14;354:i4746
Baker WL, Jennings DL. Pre-Cardiac **Transplant Amiodarone Use** Increases Postoperative Mortality: A Meta-analysis. Ann Pharmacother. 2016 Apr 15.
Baran DA, Zucker MJ, Arroyo LH, et al. A prospective, randomized trial of single-drug versus dual-drug immunosuppression in heart transplantation: the **tacrolimus** in combination (mycophenolate), tacrolimus alone compared (TICTAC) trial. Circ Heart Fail. 2011 Mar;4(2):129-37.
Barnett R, Barta VS, Jhaveri KD. **Preserved Renal-Allograft Function** and the PD-1 Pathway Inhibitor **Nivolumab**. N Engl J Med. 2017 Jan 12;376(2):191-192.
Baughman RP, Meyer KC, Nathanson I, et al. **Monitoring of nonsteroidal immunosuppressive** drugs in patients with lung disease and **lung transplant** recipients: American College of Chest Physicians evidence-based clinical practice guidelines. Chest. 2012 Nov;142(5):e1S-e111S.
Bax K, Tijssen J, Rieder MJ, et al. Rapid Resolution of **Tacrolimus Intoxication-Induced AKI With a Corticosteroid and Phenytoin.** Ann Pharmacother. 2014 Nov;48(11):1525-8.
Benck U, Hoeger S, Brinkkoetter PT, et al. Effects of donor **pretreatment with dopamine on survival after heart transplantation**: a cohort study of heart transplant recipients nested in a randomized controlled multicenter trial. J Am Coll Cardiol 2011;58:1768 –77.
Berger FA, Mulder MB, Ten Bosch-Dijksman W, et al. **Differences in CYP3A genotypes** of a liver transplant recipient and the donor liver graft and adjustment of tacrolimus dose. Br J Clin Pharmacol. 2019 Jun 12.
Bergeron A, Chevret S, Granata A, et al. Effect of **Azithromycin** on Airflow Decline-Free Survival After Allogeneic Hematopoietic **Stem Cell** Transplant: The ALLOZITHRO Randomized Clinical Trial. JAMA. 2017 Aug 8;318(6):557-566.
Bernard E, Goutelle S, et al. Pharmacokinetic **drug-drug interaction of calcium channel blockers with cyclosporine** in hematopoietic stem cell transplant children. Ann Pharmacother. 2014 Dec;48(12):1580-4.
Bernat JL. Life or Death for the **Dead-Donor Rule**? N Engl J Med. 2013 Oct 3;369(14):1289-1291.
Bertsias GK, Tektonidou M, Amoura Z, et al. Joint European League Against Rheumatism and European Renal Association-European Dialysis and Transplant Association (EULAR/ERA-EDTA) recommendations for the management of adult and paediatric **lupus nephritis**. Ann Rheum Dis. 2012 Nov;71(11):1771-82.
Birdwell KA, Decker B, Barbarino JM, et al. Clinical Pharmacogenetics Implementation Consortium (CPIC) guidelines for **CYP3A5 genotype and tacrolimus dosing**. Clin Pharmacol Ther. 2015 Jul;98(1):19-24.
Bloom, RD & Reese, PP. **Chronic Kidney Disease** after Nonrenal Solid-Organ Transplantation. J Am Soc Nephrol 2007:18:3031-3041.
Boeckh M, et al. **Valganciclovir** for the prevention of complications of late **cytomegalovirus** infection after allogeneic hematopoietic cell transplantation: a randomized trial. Ann Intern Med. 2015 Jan 6;162(1):1-10.
Bollen J, van Smaalen T, Ten Hoopen R, et al. Potential Number of **Organ Donors After Euthanasia** in Belgium. JAMA. 2017 Apr 11;317(14):1476-1477.
Bonser RS, Taylor R, Collett D, Thomas HL, Dark JH, Neuberger J, on behalf of members of the Cardiothoracic Advisory Group to NHS Blood and Transplant and the Association of Lung Transplant Physicians (UK). Effect of **donor smoking on survival after lung transplantation**: a cohort study of a prospective registry. Lancet 2012.
Bostom AG, Carpenter MA, Kusek JW, et al. **Homocysteine-lowering** and cardiovascular disease outcomes in kidney transplant recipients: primary results from the folic Acid for vascular outcome reduction in transplantation trial. Circulation. 2011 Apr 26;123(16):1763-70. (no reduction in CV disease)
Boughton O, Borgulya G, Cecconi M, et al. A published pharmacogenetic algorithm was poorly predictive of **tacrolimus clearance** in an independent cohort of renal transplant recipients. Br J Clin Pharmacol. 2013 Jan 11.
Boyarsky BJ, Massie AB, Alejo JL, et al. Experiences Obtaining **Insurance After Live Kidney Donation**. Am J Transplant. 2014 Jul 16.
Braun M, Young J, Reiner CS, et al. **Ovarian toxicity from sirolimus**. N Engl J Med. 2012 Mar 15;366(11):1062-4.
Bravo, C. Prevalence and management of **gastrointestinal complications** in lung transplant patients: MIOS study group. Trans Proceed 2007;39:2409-2412.
Brewer J, Colegio OR, Phillips PK, et al. Incidence of and risk factors for **skin cancer** after heart transplant. *Arch Dermatol* 2009; 145:1391-1396.
British Transplantation Society. United Kingdom guidelines for **living donor kidney transplantation**. 2011. www.bts.org.uk/transplantation/standards-and-guidelines/.
Budde K, Becker T, Arns W, et al. on behalf of the **ZEUS** Study Investigators. **Everolimus-based, calcineurin-inhibitor-free** regimen in recipients of de-novo kidney transplants: an open-label, randomised, controlled trial. Lancet. 2011 Feb 18.
Bugeja A, Clark EG. Five things to know about: **Living Kidney Donation**. CMAJ. 2017 August 14;189:E1041.
Bureau C, et al. **Transjugular Intrahepatic Portosystemic Shunts** With Covered Stents Increase Transplant-Free Survival of Patients **With Cirrhosis and Recurrent Ascites**. Gastroenterology. 2017 Jan;152(1):157-163.
Burt RK, Shah SJ, Dill K, Grant T, et al. Autologous non-myeloablative haemopoietic **stem-cell transplantation** compared with pulse cyclophosphamide once per month for systemic sclerosis (ASSIST): an open-label, randomised phase 2 trial. Lancet. 2011 Aug 6;378(9790):498-506.
Burton JR, Burton I, Pearson GJ. **Clopidogrel**-precipitated rhabdomyolysis in a stable heart transplant patient. Ann Pharmacother. 2007 Jan;41(1):133-7. Epub 2007 Jan 2.

Calne RY, Rolles K, White DJ, et al. **Cyclosporin A initially** as the only immunosuppressant in 34 recipients of cadaveric organs: 32 kidneys, 2 pancreases, and 2 livers. Lancet 1979;2:1033-6.

Calvo PL, Serpe L, Brunati A, et al. Donor **CYP3A5 genotype** influences **tacrolimus** disposition on the first day after paediatric liver transplantation. Br J Clin Pharmacol. 2017 Jan 3.

Cameron AM, Massie AB, Alexander CE, et al. **Social Media and Organ Donor Registration**: The Facebook Effect. Am J Transplant. 2013 Jun 18.

Campagne O, Mager DE, Brazeau D, et al. The Impact of **Tacrolimus Exposure on Extrarenal Adverse Effects** in Adult Renal Transplant Recipients. Br J Clin Pharmacol. 2018 Nov 10.

Castleberry C, Ryan TD, Chin C. Transplantation in the highly sensitized **pediatric patient**. Circulation. 2014 Jun 3;129(22):2313-9.

Caulfield T, Zarzeczny A. **Curbing transplant tourism**: Canadian physicians and the law. CMAJ. 2016 Sep 20;188(13):935-936.

Chamberlain K, Baker MR, Kandaswamy P, et al. On behalf of the Guideline Development Group. **Donor identification and consent** for deceased organ donation: summary of NICE guidance. BMJ. 2011 Sep 1;343:d5249.

Chang CH, Bryce CL, Shneider BL, et al. Accuracy of the **Pediatric End-stage Liver Disease Score in Estimating Pretransplant Mortality** Among Pediatric Liver Transplant Candidates. JAMA Pediatr. 2018 Nov 1;172(11):1070-1077.

Charlton M et al. **Sofosbuvir and ribavirin** for **treatment of compensated recurrent hepatitis C virus infection after liver transplantation**. **Gastroenterology** 2015 Jan; 148:108.

Chatterjee P, Venkataramani AS, Vijayan A, et al. The Effect of **State Policies on Organ Donation** and Transplantation in the United States. JAMA Intern Med. 2015 Jun 1.

Chemaly RF, Ullmann AJ, Stoelben S, et al. **Letermovir** for cytomegalovirus prophylaxis in hematopoietic-cell transplantation. N Engl J Med 2014;370:1781-9.

Chen J, Bhattacharya S, Sirota M, et al. Assessment of **Postdonation Outcomes in US Living Kidney Donors** Using Publicly Available Data Sets. JAMA Netw Open. 2019 Apr 5;2(4):e191851.

Chinnakotla S, Verghese P, Chavers B, et al. Outcomes and **Risk Factors for Graft Loss**: Lessons Learned from 1,056 **Pediatric Kidney Transplants** at the University of Minnesota. J Am Coll Surg. 2017 Jan 11.

Choi SW, Braun T, Chang L, et al. **Vorinostat plus tacrolimus and mycophenolate to prevent graft-versus-host disease** after related-donor, reduced-intensity, conditioning allogeneic haemopoietic stem-cell transplantation: a phase 1/2 trial. Lancet Oncol 2013; online Nov 30.

Chow EJ, Mueller BA, Baker KS, et al. **Cardiovascular hospitalizations and mortality** among recipients of hematopoietic stem cell transplantation. Ann Intern Med. 2011 Jul 5;155(1):21-32.

Christenson ES, Ahmed HM, Durand CM. **Pasteurella multocida infection** in solid organ transplantation. Lancet Infect Dis. 2014 Nov 21. pii: S1473-3099(14)70895-3.

Christie JD, Edwards LB, Aurora P, et al. Registry of the International Society for Heart and Lung Transplantation: Twenty-sixth Official **Adult Lung and Heart-Lung** Transplantation Report-2009. J Heart Lung Transplant. 2009 Oct;28(10):1031-49.

Ciarka A, Lund LH, Van Cleemput J, et al. Effect of **Heart Rate and Use of Beta Blockers** on Mortality After Heart Transplantation. Am J Cardiol. 2016 Dec 15;118(12):1916-1921.

Ciancio G, Gaynor JJ, Zarak A, et al. Randomized Trial of Mycophenolate Mofetil Versus Enteric-Coated Mycophenolate Sodium in Primary Renal Transplantation With Tacrolimus and Steroid Avoidance: Four-Year Analysis. Transplantation. 2010 Nov 23.

Ciavarella, D et al. Update on **gingival overgrowth** by **cyclosporine** A in renal transplants. Med Oral Patol Oral Cir Bucal 2007;12E19-25.

Cimino FM, Snyder KAM, **Primary Care of the Solid Organ Transplant Recipient**. Am Fam Physician. 2016;93(3):203-210.

Cocchi E, Chiale F, Gianoglio B, et al. **Colchicine**: An Impressive Effect on Posttransplant Capillary Leak Syndrome and Renal Failure. Pediatrics. 2019 Apr 18.

Collins MG, Teo E, Cole SR, et al. **Screening for colorectal cancer** and advanced colorectal neoplasia in kidney transplant recipients: cross sectional prevalence and diagnostic accuracy study of faecal immunochemical testing for haemoglobin and colonoscopy. BMJ. 2012 Jul 25;345:e4657.

Colman R, Singer LG, Barua R, et. al, Outcomes of **lung transplant candidates referred for co-management by palliative care**: A retrospective case series. Palliat Med. 2015 Jan 29. [Epub ahead of print]

Committee on Bioethics. **Ethical Controversies in Organ Donation** After Circulatory Death. Pediatrics. 2013 Apr 29.

Cooper AJ, Dholakia S, Holland CV, et al. **Helminths** in organ transplantation. Lancet Infect Dis. 2017 Feb 20.

Cooper WO, Cheetham TC, Li DK et al. Brief report: Risk of adverse fetal outcomes associated with immunosuppressive medications for chronic immune-mediated diseases in pregnancy. Arthritis Rheumatol. 2014 Feb;66(2):444-50.

Cornu C, Dufays C, Gaillard S, et al. Impact of the Reduction of **Calcineurin Inhibitors on Renal Function in Heart Transplant** Patients: A Systematic Review and Meta-Analysis. Br J Clin Pharmacol. 2013 Nov 20.

Costanzo Maria Rosa, Costanzo Maria Rosa, Dipchand Anne. The International Society of Heart and Lung Transplantation **Guidelines for the care of heart transplant recipients.** The Journal of Heart and Lung Transplantation - August 2010 (Vol. 29, Issue 8, Pages 914-956, DOI: 10.1016/j.healun.2010.05.034). http://www.jhltonline.org/article/S1053-2498(10)00358-X/fulltext

Cowley NJ, Owen A, et al. Safety and Efficacy of Antiviral Therapy for **Prevention of Cytomegalovirus Reactivation** in Immunocompetent Critically Ill Patients: A Randomized Clinical Trial. JAMA Intern Med. 2017 Apr 24.

Croome KP, Lee DD, Burns JM, et al. The Use of **Donation After Cardiac Death** Allografts Does Not Increase Recurrence of Hepatocellular Carcinoma. Am J Transplant. 2015 May 12.

Curry MP et al. **Sofosbuvir and ribavirin prevent recurrence of HCV infection after liver transplantation**: An open-label study. **Gastroenterology** 2015 Jan; 148:100.

Cypel Marcelo, Yeung Jonathan C., Liu Mingyao, et al. **Normothermic Ex Vivo Lung Perfusion** in Clinical Lung Transplantation. N Engl J Med 2011; 364:1431-1440.

Dall CH, Snoer M, Christensen S, et al. Effect of **High-Intensity Training Versus Moderate Training** on Peak Oxygen Uptake and Chronotropic Response in Heart Transplant Recipients: A Randomized Crossover Trial. Am J Transplant. 2014 Aug 18.

Dardas T, Mokadam N, Pagani F, et al. Transplant registrants with implanted **left-ventricular assist devices** have insufficient risk to justify elective organ procurement and transplantation network status 1A time. J Am Coll Cardiol 2012 ;60:36-43.

Das S, Cherian SV, Das N, et al. Persistent dyspnea in a 59-year-old woman receiving immunosuppressants (**sirolimus induced diffuse alveolar hemorrhage**). Chest. 2011 Sep;140(3):818-22.

Davids MS, Kim HT, Bachireddy P, et al. **Ipilimumab** for Patients with Relapse after Allogeneic Transplantation. N Engl J Med. 2016 Jul 14;375(2):143-53.

De Rosa N, Paddon VL, Liu Z, et al**. Nonmelanoma Skin Cancer Frequency** and Risk Factors in Australian Heart and Lung Transplant Recipients. JAMA Dermatol. 2019 Mar 13.

De Simone P, et al. H2304 Study Group. **Everolimus with reduced tacrolimus** improves renal function in de novo liver transplant recipients: a randomized controlled trial. Am J Transplant. 2012 Nov;12(11):3008-20.

Dean PG, Kukla A, Stegall MD, et al. **Pancreas transplantation**. BMJ. 2017 Apr 3;357:j1321

Delmonico FL, Domínguez-Gil B, Matesanz R, Noel L. A call for government accountability to achieve national **self-sufficiency in organ donation** and transplantation. Lancet 2011; 378: 1414–18.

Dew MA, DiMartini AF, De Vito Dabbs A, et al. Rates and risk factors for **nonadherence** to the medical regimen after adult solid organ transplantation. Transplantation. 2007 Apr 15;83(7):858-73.

Dharnidharka VR, Fiorina P, Harmon WE. **Kidney transplantation in children**. N Engl J Med. 2014 Aug 7;371(6):549-58.

Dhital KK, Iyer A, Connellan M, et al. **Adult heart transplantation with distant procurement and ex-vivo preservation** of donor hearts after circulatory death: a case series. Lancet. 2015 Jun 27;385(9987):2585-91.

Diamond JM, Lee JC, Kawut SM, et al. Clinical risk factors for **primary graft dysfunction after lung transplantation**. Am J Respir Crit Care Med 2013;187:527–534.

Dienstag JL, Cosimi AB. **Liver Transplantation** - A Vision Realized. N Engl J Med. 2012 Sep 19.

Dierickx D, Habermann TM. **Post-Transplantation Lymphoproliferative Disorders** in Adults. N Engl J Med. 2018 Feb 8;378(6):549-562.

Dignan FL, Clark A, Amrolia P, et al. behalf of the Haemato-oncology Task Force of the British Committee [trunc]. Diagnosis and management of **acute graft-versus-host disease**. Br J Haematol 2012 Jul;158(1):30-45.

Dignan FL, Amrolia P, Clark A, et al. behalf of the Haemato-oncology Task Force of the British Committee [trunc]. Diagnosis and management of **chronic graft-versus-host disease**. Br J Haematol 2012 Jul;158(1):46-61.

Dodds-Ashley E. Management of **drug and food interactions with azole antifungal agents** in transplant recipients. Pharmacotherapy. 2010 Aug;30(8):842-54.

Domingo-Chiva E, Ruíz-Ramos J, Marqués-Miñana MR, et al. Drug Interaction Between Oral **Cyclosporine** Modified and **Iron**. Ann Pharmacother. 2014 Apr 15;48(7):932-935.

Durand CM, , et al. **Direct-Acting Antiviral Prophylaxis in Kidney Transplantation From Hepatitis C Virus-Infected Donors** to Noninfected Recipients: An Open-Label Nonrandomized Trial. Ann Intern Med. 2018 Mar 6.

Durand CM, et al. The **drug overdose epidemic and deceased donor transplantation** in the United States. A national registry study. Ann Intern Med. 2018. [Epub ahead of print]. doi:10.7326/M17-2451

Durrbach A, Pestana JM, Pearson T, et al. A phase III study of **belatacept** versus cyclosporine in kidney transplants from extended criteria donors (BENEFIT-EXT study). Am J Transplant. 2010 Mar;10(3):547-57.

Eapen M, Klein JP, Sanz GF, et al. Effect of donor–recipient **HLA matching** at HLA A, B, C, and DRB1 on outcomes after umbilical-cord blood transplantation for leukaemia and myelodysplastic syndrome: a retrospective analysis. Lancet Oncol 2011; published online Oct 7. DOI:10.1016/S1470-2045(11)70260-1.

Ebeling PR. Approach to the patient with transplantation-related **bone loss**. J Clin Endocrinol Metab. 2009 May;94(5):1483-90.

Eberlein M, Reed RM, Bolukbas S, Parekh KR, Arnaoutakis GJ, et al. **Lung size mismatch and survival** after single and bilateral lung transplantation. Ann Thorac Surg. 2013 Aug;96(2):457-63.
Eid AJ, Arthurs SK, Deziel PJ, et al. Clinical predictors of relapse after treatment of primary gastrointestinal **cytomegalovirus** disease in solid organ transplant recipients. Am J Transplant. 2010 Jan;10(1):157-61.
Eid AJ, Razonable RR. New developments in the management of **cytomegalovirus** infection after solid organ transplantation. Drugs. 2010 May 28;70(8):965-81. doi: 10.2165/10898540-000000000-00000.
Ekberg H, Tedesco-Silva H, Demirbas A, et al. **ELITE**-Symphony Study. Reduced exposure to **calcineurin inhibitors** in renal transplantation. N Engl J Med. 2007 Dec 20;357(25):2562-75.
Ekberg H, Bernasconi C, Nöldeke J, et al. **Cyclosporine, tacrolimus and sirolimus** retain their distinct toxicity profiles despite low doses in the Symphony study. Nephrol Dial Transplant. 2010 Jan 26.
Ekser Burcin, Ezzelarab Mohamed, Hara Hidetaka, et al, Clinical **xenotransplantation**: the next medical revolution?, The Lancet, Available online 20 October 2011.
Elbarbry FA, Marfleet T, Shoker AS. **Drug-drug interactions** with immunosuppressive agents: Review of the in vitro functional assays and role of cytochrome P450 enzymes. *Transplantation* 2008;85(9):1222-1229.
Elens L, Bouamar R, Shuker N, et al. Clinical implementation of **pharmacogenetics in kidney transplantation: CNIs** in the starting blocks. Br J Clin Pharmacol. 2013 Oct 10.
Elman A, Wright L, Zaltzman JS. **Public solicitation for organ donors**: a time for direction in Canada. CMAJ. 2016 Apr 19;188(7):487-8.
Emery V, Zuckerman M, Jackson G, et al. British Committee for Standards in Haematology, British Society of Blood and Marrow Transplantation, UK Virology Network. Management of **cytomegalovirus** infection in haemopoietic stem cell transplantation. Br J Haematol. 2013 Jul;162(1):25-39.
Engels EA, Pfeiffer RM, Fraumeni JF Jr, et al. Spectrum of **cancer risk among US solid organ transplant recipients**. JAMA. 2011 Nov 2;306(17):1891-901.
English V, Johnson E, Sadler BL, Sadler AM Jr. **Is an opt-out system likely to increase organ donation**? BMJ. 2019 Mar 6;364:l967.
European Medicines Agency (EMA) Dec/17: issued updated recommendations for **contraception in men and women taking mycophenolate** medicines to prevent rejection of transplanted organs. The immunosuppressant mycophenolate is known to increase the risk for malformations and miscarriages during pregnancy if the fetus is exposed in utero. However, the EMA has concluded that current available evidence does not indicate a risk for malformations or miscarriages during pregnancy when the father has taken mycophenolate medicines, although the risk for genotoxicity cannot be completely ruled out. For a male patient, the EMA now recommends that either he or his female partner use reliable contraception during mycophenolate treatment and for at least 90 days after stopping treatment. It is no longer required that they both use contraception. "The previous recommendation that male patients should use condoms in addition to their female partners using a highly effective method of contraception has now been removed as this does not reflect the level of risk," the EMA said in a statement. For female patients, the risk is unchanged. "These medicines must not be used in pregnant women unless there are no suitable alternatives to prevent transplant rejection. In addition, female patients who can become pregnant must use at least one reliable form of contraception before, during and for 6 weeks after stopping treatment. Two forms of contraception are preferred but no longer mandatory," the EMA advised.
Euvrard S, Morelon E, Rostaing L, et al; **TUMORAPA** Study Group. **Sirolimus and secondary skin-cancer** prevention in kidney transplantation. N Engl J Med. 2012 Jul 26;367(4):329-39.
Evangelisti C, Cenni V, Lattanzi G. Potential therapeutic effects of the **mtor inhibitors for preventing ageing** and progeria-related disorders. Br J Clin Pharmacol. 2016 Mar 8.
Evans JD, Morris PJ, Knight SR. **Antifungal prophylaxis in liver transplantation**: a systematic review and network meta-analysis. Am J Transplant. 2014 Dec;14(12):2765-76.
Farge D, Gluckman E. **Autologous HSCT in systemic sclerosis**: a step forward. Lancet. 2011 Aug 6;378(9790):460-2.
FDA July/11 Bristol-Myers Squibb informed healthcare professionals about the REMS that is required for Nulojix (**belatacept**) to ensure that the benefits of Nulojix outweigh the risks of PTLD and PML, both of which can be fatal. Patients treated with Nulojix are at an increased risk for developing **PTLD**, predominantly involving the CNS. PML reported in patients receiving Nulojix at higher than recommended doses.
FDA Aug/18: Zithromax, Zmax (azithromycin): FDA Warning - Increased Risk of Cancer Relapse With Long-Term Use After Donor Stem Cell Transplant.
Feldman D, Pamboukian SV, Teuteberg JJ, et al. The 2013 International Society for Heart and Lung Transplantation Guidelines for **Mechanical Circulatory Support**: Executive Summary. J Heart Lung Transplant 2013; 32:157-187.
Feldman AG, Feudtner C, Kempe A. **Reducing the Underimmunization of Transplant Recipients**. JAMA Pediatr. 2017 Dec 4.
Feldman AG, Feudtner C, Kempe A. **Reducing the Underimmunization of Transplant Recipients**. JAMA Pediatr. 2018 Feb 1;172(2):111-112.
Feldman AG, Beaty BL, Curtis D, et al. Incidence of **Hospitalization for Vaccine-Preventable Infections** in Children Following Solid Organ Transplant and Associated Morbidity, Mortality, and Costs. JAMA Pediatr. 2019 Jan 14.
Feng S, Ekong UD, Lobritto SJ et al. Complete immunosuppression withdrawal and subsequent allograft function among pediatric recipients of **parental living donor liver transplants**. JAMA. 2012 Jan 18;307(3):283-93.
Ferguson R, Grinyó J, Vincenti F, et al. Immunosuppression with **Belatacept**-Based, Corticosteroid-Avoiding Regimens in De Novo Kidney Transplant Recipients. Am J Transplant. 2010 Nov 29. doi: 10.1111/j.1600-6143.2010.03338.x.
Fishbein, Thomas M. **Intestinal** Transplantation. N Engl J Med 2009 361: 998-1008
Fleischhlauer K, Shaw BE, Gooley T, for the International Histocompatibility Working Group in Hematopoietic Cell Transplantation. Effect of **T-cell-epitope matching at HLA-DPB1** in recipients of unrelated-donor haemopoietic cell transplantation: a retrospective study. Lancet Oncol 2012
Foroutan F, Alba AC, Guyatt G, et al. Predictors of 1-year **mortality in heart transplant recipients**: a systematic review and meta-analysis. Heart. 2017 Aug 30.
Francis GS, Greenberg BH, Hsu DT, et al. **ACCF/AHA/ACP/HFSA/ISHLT 2010** clinical competence statement on management of patients with **advanced heart failure and cardiac transplant**: a report of the ACCF/AHA/ACP Task Force on Clinical Competence and Training. Circulation. 2010 Aug 10;122(6):644-72.
Fraser CD Jr, Jaquiss RD, Rosenthal DN et al; Berlin Heart Study Investigators. Prospective trial of a **pediatric ventricular assist device**. N Engl J Med. 2012 Aug 9;367(6):532-41.
Fröhlich GM, Rufibach K, Enseleit F, et al. **Statins and the risk of cancer** after heart transplantation. Circulation. 2012 Jul 24;126(4):440-7.
Fuehner T, Kuehn C, Hadem J, et al. **Extracorporeal membrane oxygenation** in awake patients as bridge to **lung transplantation**. Am J Respir Crit Care Med 2012;185:763–768.
Gabardi S, Catella J, Martin ST, et al. Maintenance Immunosuppression with Intermittent Intravenous **IL-2 Receptor Antibody** (**basiliximab**) Therapy in Renal Transplant Recipients. Ann Pharmacother. 2011 Sep;45(9):e48.
Gabardi S, Olyaei A. Evaluation of potential interactions between **mycophenolic Acid derivatives and proton pump inhibitors**. Ann Pharmacother. 2012 Jul;46(7-8):1054-64.
Gallagher MP, Kelly PJ, Jardine M, Perkovic V, Cass A, Craig JC, Eris J, Webster AC. Long-term **cancer risk of immunosuppressive regimens** after kidney transplantation. J Am Soc Nephrol. 2010 May;21(5):852-8.
Gallegos-Orozco JF, Vargas, HE. **Liver Transplantation**: From Child to MELD. Med Clin N Am 93 (2009)931-950.
Gander JC, Zhang X, Ross K, et al. Association Between **Dialysis Facility Ownership and Access to Kidney Transplantation**. JAMA. 2019 Sep 10;322(10):957-973.
Gao Y, Twigg AR, Hirose R, et al. Association of **HLA Antigen Mismatch With Risk of Developing Skin Cancer** After Solid-Organ Transplant. JAMA Dermatol. 2019 Jan 23.
Garcia GG, Harden P, Chapman J; The global role of **kidney transplantation**. Lancet. 2012 Mar 7.
Garg A, Meirambayeva A, Huang A, Kim S, Prasad GVR, Knoll G, et al. **Cardiovascular disease in kidney donors**: matched cohort study. BMJ 2012;344:e1113.
Garg AX, Nevis IF, McArthur E, et al. the DONOR Network. **Gestational Hypertension and Preeclampsia in Living Kidney Donors**. N Engl J Med. 2014 Nov 14.
Garrett GL, Blanc PD, Boscardin J, et al. Incidence of and Risk Factors for **Skin Cancer in Organ Transplant Recipients** in the United States. JAMA Dermatol. 2017 Jan 11.
Gathogo EN, Hamzah L, Hilton R, et al; for the UK HIV/Kidney Transplantation Study Group (see appendix). **Kidney transplantation in HIV-positive adults**: The UK experience. Int J STD AIDS. 2013 Jul 25.
George Timothy J., Arnaoutakis George J., Merlo Christian A., et al. Association of **Operative Time of Day** With Outcomes After Thoracic Organ Transplant. JAMA. 2011;305(21):2193-2199.doi:10.1001/jama.2011.726
Gilbo N, Jochmans I, Jacobs-Tulleneers-Thevissen D, et al. **Survival of Patients With Liver Transplants** Donated After Euthanasia, Circulatory Death, or Brain Death at a Single Center in Belgium. JAMA. 2019 Jul 2;322(1):78-80.
Gill John S., Tonelli Marcello. Penny Wise, Pound Foolish? **Coverage Limits on Immunosuppression after Kidney Transplantation**. N Engl J Med 2012 February 1, 2012 (10.1056/NEJMp1114394)
Gill JS, Lan J, Dong J, et al. The **Survival Benefit** of Kidney Transplantation in **Obese Patients**. Am J Transplant. 2013 Jul 25.
Gill J, Dong J, Gill J. Population **Income and Longitudinal Trends in Living Kidney Donation** in the United States. J Am Soc Nephrol. 2014 Jul 17.
Gill J, Rose C, Lesage J, et al. Use and Outcomes of **Kidneys from Donation after Circulatory Death** Donors in the United States. J Am Soc Nephrol. 2017 Oct 5.
Goldaracena N, Spetzler VN, Marquez M, et al. **Live Donor Liver Transplantation**: A Valid Alternative for Critically Ill Patients Suffering From Acute Liver Failure. Am J Transplant. 2015 Mar 19.

Goldberg DS, French B, et al. Association of **distance from a transplant center** with access to waitlist placement, receipt of liver transplantation, and survival among US veterans. JAMA. 2014 Mar 26;311(12):1234-43.
Goldberg DS, Abt PL, Blumberg EA, et al. Trial of **Transplantation of HCV-Infected Kidneys into Uninfected Recipients**. N Engl J Med. 2017 Apr 30.
Golshayan D, Pascual M, Vogt B. **Mycophenolic** acid formulations in adult renal transplantation - update on efficacy and tolerability. Ther Clin Risk Manag. 2009 Aug;5(4):341-51. Epub 2009 May 4.
Gondos A, Döhler B, Brenner H, Opelz G. **Kidney Graft Survival in Europe and the United States**: Strikingly Different Long-term Outcomes. Transplantation. 2012 Oct 10.
Grabowsky JA. **Drug interactions** and the pharmacist: focus on **everolimus**. Ann Pharmacother. 2013 Jul;47(7-8):1055-63.
Gragert L, Eapen M, Williams E, et al. **HLA match likelihoods** for **hematopoietic stem-cell** grafts in the U.S. registry. N Engl J Med. 2014 Jul 24;371(4):339-48.
Grams ME, Sang Y, Levey AS, et al. **Kidney-failure risk projection** for the **living kidney-donor candidate**. N Engl J Med. DOI: 10.1056/NEJMoa1510491.
Grgic Tatjana, Mis Lydia, Hammond Julia M. **Everolimus**: A New Mammalian Target of Rapamycin Inhibitor for the Treatment of Advanced Renal Cell Carcinoma. Articles Ahead of Print published on 1 January 2011, DOI 10.1345/aph.1M288. Ann Pharmacother ;45:78-83.
Griffiths PD. Burden of disease associated with human **cytomegalovirus** and prospects for elimination by universal immunisation. Lancet Infect Dis. 2012 Oct;12(10):790-8.
Grupper A, Grupper A, Daly RC, et al. Renal Allograft Outcome After **Simultaneous Heart** and **Kidney** Transplantation. Am J Cardiol. 2017 Aug 1;120(3):494-499.
Guerra G, Ciancio G, Gaynor JJ, et al. Randomized trial of **immunosuppressive regimens in renal transplantation**. J Am Soc Nephrol. 2011 Sep;22(9):1758-68. (**Tacrolimus/mycophenolate** more favourable).
Gulmez SE, Larrey D, Pageaux GP, et al. **Liver transplant associated with paracetamol (acetaminophen) overdose**: results from the seven-country SALT study. Br J Clin Pharmacol. 2015 May 27.
Hackman KL, Bailey MJ, Snell GI, Bach LA. **Diabetes** is a major risk factor for mortality after lung transplantation. Am J Transplant. 2014 Feb;14(2):438-45.
Haddad EM, McAlister VC, Renouf E, Malthaner R, Kjaer MS, Gluud LL. **Cyclosporin versus tacrolimus** for liver transplanted patients. Cochrane Database Syst Rev. 2006 Oct 18;(4):CD005161.
Haddad H, Isaac D, Legare JF, et al. Canadian Cardiovascular Society Consensus Conference update on **cardiac transplantation** 2008: Executive Summary. Can J Cardiol. 2009 Apr;25(4):197-205.
Hall IE, Schröppel B, Doshi MD, et al. Associations of **Deceased Donor Kidney Injury** With Kidney Discard and Function After Transplantation. Am J Transplant. 2015 Mar 11.
Hall SR, Mecham JC, Lott DG. **Airway Obstruction in a Patient After Kidney Transplant.** JAMA Otolaryngol Head Neck Surg. 2019 May 9.
Haller MC, Royuela A, Nagler EV, Pascual J,Webster AC. **Steroid avoidance or withdrawal** for kidney transplant recipients. Cochrane Database of Systematic Reviews 2016, Issue 8. Art. No.: CD005632. This updated review increases the evidence that steroid avoidance and withdrawal after kidney transplantation significantly increase the risk of acute rejection. There was no evidence to suggest a difference in patient mortality or graft loss up to five year after transplantation, but long-term consequences of steroid avoidance and withdrawal remain unclear until today, because prospective long-term studies have not been conducted.
Halpern SD, Barnes B, Hasz RD, Abt PL. Estimated supply of organ donors after **circulatory determination of death**: a population-based cohort study. JAMA. 2010;304(23):2592-2594.
Halpern SD, Goldberg D. **Allocating Organs to Cognitively Impaired Patients**. N Engl J Med. 2017 Jan 26;376(4):299-301.
Hammerstrom AE. Possible **amlodipine-induced hepatotoxicity** after stem cell transplant. Ann Pharmacother. 2015 Jan;49(1):135-9.
Hanaway Michael J., Woodle E. Steve, Mulgaonkar Shamkant, et al. and John Holman, M.D. for the INTAC Study Group. **Alemtuzumab Induction in Renal** Transplantation. N Engl J Med 2011; 364:1909-1919.
Hanley H, Kim S, Willey E, et al. Identifying Potential **Kidney Donors** Among Newborns Undergoing **Circulatory Determination of Death**. Pediatrics. 2013 Dec 2
Hartman RI, Green AC, Gordon LG; Skin Tumours and Allograft Recipients (STAR) Study. **Sun Protection Among Organ Transplant Recipients** After Participation in a Skin Cancer Research Study. JAMA Dermatol. 2018 Jun 6.
Health Canada Jan/16: CellCept (**mycophenolate mofetil**) and MYFORTIC (mycophenolate sodium) - Serious Risk of Teratogenicity in Mycophenolate-Containing Products - Hoffmann-La Roche Limited and Novartis Pharmaceuticals Canada Inc
Health Canada July/19: Tacrolimus and the Risk of Graft Rejection due to Medication Errors: Inadvertent Switching between Different Oral Formulations
Heilman RL, Mazur MJ, Reddy KS. Immunosuppression in simultaneous **pancreas-kidney transplantation**: progress to date. Drugs. 2010 May 7;70(7):793-804.
Heinze G, Kainz A, Hörl WH, Oberbauer R. Mortality in renal transplant recipients given **erythropoietins** to increase haemoglobin concentration: cohort study. BMJ. 2009 Oct 23;339:b4018. doi: 10.1136/bmj.b4018.
Heisel, O et al. **New Onset Diabetes Mellitus** in Patients Receiving Calcinuerin Inhibitors: A Systematic Review and Meta-Analysis. Am J Transplant 2004:4:583-595.
Hingorani S. **Renal Complications of Hematopoietic-Cell Transplantation**. N Engl J Med. 2016 Jun 9;374(23):2256-67.
Hirschfield G M, Gibbs P, Griffiths W J H. **Adult liver transplantation**: what **non-specialists need to know** BMJ 2009;338:b1670, doi: 10.1136/bmj.b1670 (Published 22 May 2009)
Hodson EM, Craig JC, Strippoli GF, Webster AC. Antiviral medications for preventing **cytomegalovirus** disease in solid organ transplant recipients. Cochrane Database Syst Rev. 2008 Apr 16;(2):CD003774.
Hol JA, Wolfs TF, Bierings MB, et al. Predictors of **invasive fungal** infection in **pediatric allogeneic hematopoietic SCT recipients**. Bone Marrow Transplant. 2013 Oct 14.
Holdaas H, Fellström B, Jardine AG, et al. Assessment of LEscol in Renal Transplantation (**ALERT**) Study Investigators. Effect of **fluvastatin** on cardiac outcomes in renal transplant recipients: a multicentre, randomised, placebo-controlled trial. Lancet. 2003 Jun 14;361(9374):2024-31.
Holtick U, Albrecht M, Chemnitz JM, Theurich S, Skoetz N, Scheid C, von Bergwelt-Baildon M. **Bone marrow versus peripheral blood allogeneic haematopoietic stem cell transplantation** for haematological malignancies in adults. Cochrane Database of Systematic Reviews 2014, Issue 4. Art. No.: CD010189. DOI: 10.1002/14651858.CD010189.pub2.
Hong JC, Venick R, et al. **Liver Transplantation in Children Using Organ Donation After Circulatory Death**: A Case-Control Outcomes Analysis of a 20-Year Experience in a Single Center. JAMA Surg. 2013 Nov 20.
Hooper DK, Kirby CL, Margolis PA, Goebel J. Reliable individualized monitoring improves **cholesterol control in kidney transplant** recipients. Pediatrics. 2013 Apr;131(4):e1271-9.
Horvat Lucy D., Cuerden Meaghan S., Kim S. Joseph, et al. Informing the Debate: Rates of Kidney Transplantation in Nations With **Presumed Consent**. Ann Intern Med Nov 16, 2010 153:641-649.
Hsieh MM, Fitzhugh CD, Weitzel RP, et al. Nonmyeloablative **HLA-Matched Sibling** Allogeneic Hematopoietic Stem Cell Transplantation for Severe **Sickle Cell** Phenotype. JAMA. 2014 Jul 2;312(1):48-56.
Hsu DT, Lamour JM. **Changing indications** for **pediatric heart transplantation**: complex congenital heart disease. Circulation. 2015 Jan 6;131(1):91-9.
Hua C, Zehou O, Ducassou S, et al. **Sirolimus** Improves Pain in NF1 Patients With Severe Plexiform Neurofibromas. Pediatrics. 2014 May 26.
Hunt SA, Haddad F. The changing face of **heart transplantation**. J Am Coll Cardiol. 2008 Aug 19;52(8):587-98.
Hunt S, Burch M, Bhat G, et al. Task Force 3: **long-term care of heart transplant recipients**. In: the International Society of Heart and Lung Transplantation guidelines for the care of heart transplant recipients. J Heart Lung Transplant. 2010 Aug;29(8):933-44.
Husain SA, Chiles MC, Lee S, et al. Characteristics and Performance of **Unilateral Kidney Transplants from Deceased Donors**. Clin J Am Soc Nephrol. 2018 Jan 6;13(1):118-127.
Husain SA, King KL, Pastan S, et al. Association Between **Declined Offers of Deceased Donor Kidney Allograft and Outcomes** in Kidney Transplant Candidates. JAMA Netw Open. 2019 Aug 2;2(8):e1910312.
Ibrahim HN, Foley R, Tan L-P, Rogers T, Bailey R, Guo H, et al. Long-term consequences of **kidney donation**. N Engl J Med 2009;360:459-69.
Ibrahim HN, Jackson S, Connaire J, et al M. **Angiotensin II Blockade (losartan)** in Kidney Transplant Recipients. J Am Soc Nephrol. 2013 Jan 10.
Jacquet, A et al. Prevention of **calcineurin** inhibitor **nephrotoxicity** in renal transplantation. Transplant Immunology 2008; 20:29-31.
Jamil A, et al. Comparison of Clinical Characteristics,Complications, and Outcomes in **Recipients Having Heart Transplants** <65 Years of Age Versus ≥65 Years of Age. Am J Cardiol. 2017 Dec 15;120(12):2207-2212.
Jansman FG, Reyners AK, van Roon EN, et al; Scientific Institute for Dutch Pharmacists (WINAp), the Dutch Society for Medical Oncology (NVMO); Dutch Society of Clinical Pharmacology and Biopharmacy (NVKF&B). Consensus-Based Evaluation of Clinical Significance and Management of **Anticancer Drug Interactions**. Clin Ther. 2011 Apr 1.
Jardine AG, Gaton RS, Fellstrom B, Holdaas H. **Prevention of cardiovascular disease** in adult recipients of kidney transplants. Lancet 2011; 378: 1419–27.
Jeong R, Quinn RR, Lentine KL, et al. Outcomes Following **Macrolide Use in Kidney Transplant Recipients**. Can J Kidney Health Dis. 2019 Feb 21;6:2054358119830706.
Jesse MT, Abouljoud M, Eshelman A. Determinants of **burnout among transplant surgeons**: a national survey in the United States. Am J Transplant. 2015 Mar;15(3):772-8.
Jorge A, Wallace ZS, Lu N, Zhang Y, Choi HK. **Renal transplantation and survival among patients with lupus nephritis**. A cohort study. Ann Intern Med. 2019. [Epub ahead of print]. doi:10.7326/M18-1570
Kainz Alexander, Wilflingseder J, Mitterbauer C, Et al. **Steroid Pretreatment** of Organ Donors to Prevent Postischemic Renal Allograft Failure: A Randomized, Controlled Trial. *Ann Intern Med* August 17, 2010 153:222-230.
Kajstura J, Rota M, Hall SR, et al. **Evidence for human lung stem cells**. N Engl J Med 2011;364:1795-806.
Kalnins D, Pencharz PB, Grasemann H, Solomon M. **Energy Expenditure and Nutritional Status** in Pediatric Patients before and after Lung Transplantation. J Pediatr. 2013 Jul 16.

Kapoor A. **Malignancy** in kidney transplant recipients. Drugs. 2008;68 Suppl 1:11-9.
Karabsheh S et al. Clinical and hemodynamic effects of **Renin-Angiotensin system blockade in cardiac transplant** recipients. Am J Cardiol. 2011 Dec 15;108(12):1836-9.
Karia PS, Azzi JR, Heher EC, et al. Association of **Sirolimus Use With Risk for Skin Cancer** in a Mixed-Organ Cohort of Solid-Organ Transplant Recipients With a History of Cancer. JAMA Dermatol. 2016 Jan 20.
Karpe KM, Talaulikar GS, Walters GD. **Calcineurin inhibitor** withdrawal or tapering for **kidney transplant recipients**. Cochrane Database Syst Rev. 2017 Jul 21;7:CD006750.
Kasiske BL, Israni AK, Snyder JJ, Skeans MA, Peng Y, Weinhandl ED. A **simple tool to predict outcomes after kidney transplant**. Am J Kidney Dis. 2010 Nov;56(5):947-60.
KDIGO clinical practice guideline for the management of **blood pressure in chronic kidney disease**. Kidney Int Suppl. 2012 Dec;2(5):337-414.
KDIGO Kidney Disease: Improving Global Outcomes (KDIGO) Lipid Work Group. **KDIGO** clinical practice guideline for **lipid management in chronic kidney disease**. Kidney Int Suppl. 2013;3(3):259-305.
KDIGO Kidney Disease: Improving Global Outcomes (KDIGO) CKD-MBD Work Group. KDIGO clinical practice guideline for the diagnosis, evaluation, prevention, and treatment of **chronic kidney disease-mineral and bone disorder (CKD-MBD).** Kidney Int Suppl. 2009;(113):S1-S130.
Keddis MT, El Ters M, Rodrigo E, et al. Enhanced posttransplant management of patients with **diabetes** improves patient outcomes. Kidney Int. 2014 Apr 2.
Kelly DA, Bucuvalas JC, Alonso EM, et al. Long-term medical management of the **pediatric patient after liver transplantation**: 2013 practice guideline by the American Association for the Study of Liver Diseases and the American Society of Transplantation. Liver Transpl. 2013 Aug;19(8):798-825.
Keough-Ryan TM, Prasad GV, Hewlett T, Shapiro RJ; Canadian Community Nephrology Study Group. Similar outcomes for Canadian **renal transplant recipients followed up in transplant centers and satellite clinics**. Transplantation. 2010 Sep 27;90(6):591-6.
Kesari NK, Sivakumar S, Kapadia AM, et al. Mystery Case: **CNS posttransplant lymphoproliferative** disorder. Neurology. 2017 Jul 25;89(4):e32-e37.
Kidney Disease: Improving Global Outcomes (**KDIGO**) Transplant Work Group. KDIGO clinical practice guideline for the **care of kidney transplant recipients**. Am J Transplant 2009 Nov;9(Suppl 3):S1-155.
Kilic A, Weiss ES, Allen JG, et al. Simple **score to assess the risk of rejection after orthotopic heart transplantation**. Circulation. 2012 Jun 19;125(24):3013-21.
Kilic A, Higgins RSD, Whitson BA, Kilic A. **Racial disparities** in outcomes of adult heart transplant. Circulation. 2015;131:882–889.
Kim HB, Lillehei CW. **Organ Donation for Children**: The Road Ahead. Pediatrics. 2013 May 20.
Kim MG, Kim IW, Choi B, et al. Population pharmacokinetics of **cyclosporine** in hematopoietic stem cell transplant patients: consideration of genetic polymorphisms. Ann Pharmacother. 2015 Jun;49(6):622-30.
Kimberlin DW, Jester PM, Sánchez PJ, et al; the National Institute of Allergy and Infectious Diseases Collaborative Antiviral Study Group. **Valganciclovir** for Symptomatic Congenital **Cytomegalovirus** Disease. N Engl J Med. 2015 Mar 5;372(10):933-943.
Kittleson Michelle M., Kobashigawa Jon A.. Management of **Advanced Heart Failure**: The Role of Heart **Transplantation**. Circulation 123: 1569-1574, doi:10.1161/CIRCULATIONAHA.110.972810
Knoll GA, Kokolo MB, Mallick R, et al. Effect of **sirolimus on malignancy** and survival in kidney transplantation: systematic review and meta-analysis of individual patient data. BMJ 2014;34:10.1136/bmj.g6679.
Knoll GA, Humar A, Fergusson D, et al. **Levofloxacin for BK virus** prophylaxis following kidney transplantation: a randomized clinical trial. JAMA. 2014 Nov 26;312(20):2106-14.
Knoll GA, Fergusson D, Chassé M, et al. **Ramipril versus placebo** in kidney **transplant patients with proteinuria**: a multicentre, double-blind, randomised controlled trial. Lancet Diabetes Endocrinol. 2015 Oct 21.
Knoll GA, Fergusson D, Chassé M, et al. **Ramipril** versus placebo in **kidney transplant patients** with **proteinuria**: a multicentre, double-blind, randomised controlled trial. Lancet Diabetes Endocrinol. 2015 Oct 21.
Kopolovic I, Turner R. **Donation and transplantation of allogeneic hematopoietic stem cells**. CMAJ. 2011 Jul 4.
Kotloff RM. Risk stratification of **lung** transplant candidates: implications for organ **allocation**. Ann Intern Med. 2013 May 7;158(9):699-700.
Krämer BK, Charpentier B, Bäckman L, et al. for the Tacrolimus Prolonged Release Renal Study Group. Tacrolimus Once Daily (**ADVAGRAF**) Versus Twice Daily (**PROGRAF**) in De Novo Renal Transplantation: A Randomized Phase III Study. Am J Transplant. 2010 Sep 14.
Kröger N, Solano C, Wolschke C, et al. **Antilymphocyte Globulin** for Prevention of Chronic Graft-versus-Host Disease. N Engl J Med. 2016 Jan 7;374(1):43-53.
Kumar D, Michaels MG, Morris MI, et al. American Society of Transplantation H1N1 Collaborative Study Group. Outcomes from **pandemic influenza A H1N1 infection** in recipients of solid-organ transplants: a multicentre cohort study. Lancet Infect Dis. 2010 Aug;10(8):521-6.
Khush KK, Zaroff JG, Nguyen J, Menza R, Goldstein BA. **National decline in donor heart utilization** with regional variability: 1995-2010. Am J Transplant. 2015 Mar;15(3):642-9.
Ladin K, Hanto DW. Rationing Lung Transplants - Procedural **Fairness in Allocation and Appeals**. N Engl J Med. 2013 Jul 24.
Lai JC, Feng S, Roberts JP. An Examination of **Liver Offers to Candidates on the Liver Transplant** Wait-List. Gastroenterology. 2012 Jul 27. pii:S0016-5085(12)01130-4.
Langer D, Burtin C, Schepers L, et al. **Exercise training** after lung transplantation improves participation in daily activity: a randomized controlled trial. Am J Transplant. 2012 Jun;12(6):1584-92.
Lanz J, Bouwes Bavinck JN, Westhuis M, et al. **Aggressive Squamous Cell Carcinoma** in Organ Transplant Recipients. JAMA Dermatol. 2018 Dec 5.
Larsen CP, Grinyó J, Medina-Pestana J, et al. **Belatacept**-Based Regimens Versus a Cyclosporine A-Based Regimen in Kidney Transplant Recipients: 2-Year Results From the BENEFIT and BENEFIT-EXT Studies. Transplantation. 2010 Nov 11.
Larsen HK, Thomsen LT, Haedersdal M, et al. **Risk of genital warts in renal transplant recipients** - a registry-based, prospective cohort study. Am J Transplant. 2018 Aug 6.
LaRosa, Christopher, Glah, Caryle, Baluarte, H. Jorge, et al. **Solid-Organ Transplantation in Childhood**: Transitioning to Adult Health Care. Pediatrics 2011 127: 742-753
Lebranchu Y, Thierry A, Toupance O, et al. Effi cacy on renal function of early conversion from **cyclosporin to sirolimus** 3 months after renal transplantation: Concept Study. Am J Transplant 2009; 9: 1115–23.
Lee BP, Vittinghoff E, Dodge JL, Cullaro G, Terrault NA. National trends and long-term outcomes of liver **transplant for alcohol-associated liver disease** in the United States [online Jan 22, 2019]. JAMA Intern Med. doi:10.1001/jamainternmed.2018.6536
Lee WM, Larson AM, Stravitz T. AASLD position paper: the management of **acute liver failure**: update 2011. Baltimore (MD): American Association for the Study of Liver Diseases; 2011 Sep. 26
Lefaucheur C, Loupy A, Vernerey D, et al. **Antibody-mediated vascular rejection** of kidney allografts: a population-based study. Lancet. 2012 Nov 22.
Lehrnbecher T, et al. Guideline for Management of **Fever & Neutropenia in Children With Cancer and Hematopoietic Stem-Cell Transplantation Recipients**: 2017 Update. J Clin Oncol. 2017 Jun 20;35(18):2082-2094.
Leichtman Alan B., McCullough Keith P., Wolfe Robert A., Improving the **Allocation System for Deceased-Donor Kidneys**. NEJM March 16, 2011.
Lentine KL, Costa SP, Weir MR, et al; on behalf of the American Heart Association (**AHA**) Council on the Kidney in Cardiovascular Disease and Council on Peripheral Vascular Disease. **Cardiac Disease Evaluation** and Management Among **Kidney and Liver Transplantation Candidates**: A Scientific Statement From the American Heart Association and the American College of Cardiology Foundation. Circulation. 2012 Jul 2.
Lim AK, Manley KJ, Roberts MA, Fraenkel MB. **Fish oil** for kidney transplant recipients. Cochrane Database Syst Rev. 2007 Apr 18;(2):CD005282.
Limaye AP, Stapleton RD, Peng L. Effect of **ganciclovir** on IL-6 levels among **cytomegalovirus seropositive** adults with critical illness: a randomized clinical trial.JAMA. doi:10.1001/jama .2017.10569
Liu W, Guan X, Yu Z, et al. A **Drug-drug Interaction** Between **Cyclosporine and Nystatin**. Clin Ther. 2018 Mar 15.
Locke JE, Mehta S, Reed RD, et al. A National Study of Outcomes among **HIV-Infected Kidney Transplant** Recipients. J Am Soc Nephrol. 2015 Mar 19.
Loupy A, Aubert O, Orandi BJ, et al. **Prediction system for risk of allograft loss** in patients receiving kidney transplants: international derivation and validation study. BMJ. 2019 Sep 17;366:l4923.
Loupy A, Duong Van Huyen JP, Hidalgo L, et al. **Gene expression profiling** for the identification and classification of **antibody-mediated heart rejection**. Circulation. 2017;135:917– 935.
Loupy A, Lefaucheur C, Vernerey D, et al. **Complement-binding anti-HLA antibodies** and kidney-allograft survival. N Engl J Med 2013;369:1215-26.
Loupy A, Lefaucheur C. **Antibody-Mediated Rejection of Solid-Organ Allografts**. N Engl J Med. 2018 Sep 20;379(12):1150-1160.
Lu Z, Bonate P, Keirns J. Population pharmacokinetics of immediate- and prolonged-release **tacrolimus** formulations in liver, kidney and heart transplant recipients. Br J Clin Pharmacol. 2019 Apr 4.
Lucey MR, Terrault N, Ojo L, et al. **Long-term management of the successful adult liver transplant**: 2012 practice guideline by the American Association for the Study of Liver Diseases (AASLD) and the American Society of Transplantation. Liver Transpl. 2013 Jan;19(1):3-26.
Luskin R, Nathan H. **Eligible Death Statistic**: Not a True Measure of OPO Performance nor the Potential to Increase Transplantation. Am J Transplant. 2015 May 28.
Maalouf NM, Shane E. **Osteoporosis** after solid organ transplantation. J Clin Endocrinol Metab. 2005 Apr;90(4):2456-65. Epub 2004 Dec 28. Review. Erratum in: J Clin Endocrinol Metab. 2005 Jul;90(7):4118.
Macera F, Occhi L, Masciocco G, et al. A new life:. A single center experience and review of literature. Transplantation. 2018 May 14.

Madan S, Saeed O, Shin J, Sims et al. **Donor Troponin** and Survival After Cardiac Transplantation: An Analysis of the United Network of Organ Sharing Registry. Circ Heart Fail. 2016 Jun;9(6).
Maertens J, Cordonnier C, Jaksch P, et al. **Maribavir for Preemptive Treatment of Cytomegalovirus Reactivation**. N Engl J Med. 2019 Sep 19;381(12):1136-1147
Mahler C, Unterrainer M, Muth C,et al. **Imaging microglial activation in tacrolimus-associated CNS vasculitis** with translocator protein PET. Neurology. 2018 Nov 13; 91(20):936-937.
Makkar KM, Sanoski CA, Goldberg LR, et al. An observational study of **ezetimibe** in cardiac transplant recipients receiving calcineurin inhibitors. Ann Pharmacother. 2013 Nov;47(11):1457-62.
Manitpisitkul W, Drachenberg C, Ramos E, et al. Maintenance immunosuppressive agents as risk factors for **BK virus** nephropathy: a case-control study. Transplantation. 2009 Jul 15;88(1):83-8.
Mañalich R, Paez G, Valero R, Manyalich M. IRODaT: the **International Online Registry for Organ Donation** and Transplantation 2007. Transplant Proc 2009; 41: 2030–34.
Manook M, Koeser L, Ahemed Z, et al. **Post-listing survival** for highly sensitised patients on the **UK kidney transplant waiting list**: a matched cohort analysis. Lancet 2016; online Jan 5.
Marshall CD, Richmond ME, Singh RK, et al. A Comparison of **Traditional versus Contemporary Immunosuppressive** Regimens in Pediatric **Heart** Recipients. J Pediatr. 2013 Feb 4.
Martin ST, Torabi MJ, Gabardi S. **Influenza** in Solid Organ Transplant Recipients (February). Ann Pharmacother. 2012 Jan 10.
Marty FM, Winston DJ, Rowley SD, et al; **CMX001-201** Clinical Study Group. CMX001 to prevent **cytomegalovirus** disease in hematopoietic-cell transplantation. N Engl J Med. 2013 Sep 26;369(13):1227-36.
Marty FM, Ljungman P, Chemaly RF, et al. **Letermovir Prophylaxis for Cytomegalovirus in Hematopoietic-Cell Transplantation**. N Engl J Med. 2017 Dec 6.
Mateen FJ, Muralidharan R, Carone M, et al. **Progressive Multifocal Leukoencephalopathy** (PML) in Transplant Recipients. Ann Neurol. 2011 March 7; Accepted manuscript online: 1-87.
Mathurin P, Moreno C, Samuel D, et al. **Early liver transplantation** for severe **alcoholic hepatitis**. N Engl J Med 2011;365:1790-800.
McAdams-DeMarco MA, Law A, King E, et al. **Frailty and Mortality** in Kidney Transplant Recipients. Am J Transplant. 2014 Oct 30.
McAdams-DeMarco MA, Bae S, Chu N, et al. **Dementia and Alzheimer's Disease** among Older **Kidney Transplant Recipients**. J Am Soc Nephrol. 2016 Dec 15.
McKay DB, Josephson MA. **Pregnancy in recipients of solid organs**--effects on mother and child. N Engl J Med. 2006 Mar 23;354(12):1281-93.
McKellar S. Clinical **Firsts - Christiaan Barnard's Heart Transplantations**. N Engl J Med. 2017 Dec 7;377(23):2211-2213.
Md Dom ZI, Coller JK, Carroll RP, et al. **Mycophenolic Acid Concentrations in Peripheral Blood Mononuclear Cells** are Associated with the Incidence of **Rejection in Renal Transplant Recipients**. Br J Clin Pharmacol. 2018 Jul 2.
Méder Ü, Bokodi G, Balogh L, et al. **Severe Hyperinsulinemic Hypoglycemia** in a Neonate: Response to **Sirolimus** Therapy. Pediatrics. 2015 Nov;136(5):e1369-72.
Mehra MR, Kobashigawa J, Starling R, et al. **Listing criteria for heart transplantation**: International Society for Heart and Lung Transplantation guidelines for the care of cardiac transplant candidates–2006. J Heart Lung Transplant 2006; 25:1024–1042.
Mehra MR, Canter CE, Hannan MM, et al. The 2016 International Society for Heart Lung Transplantation **listing criteria for heart transplantation**: A 10-year update. **J Heart Lung Transplant** 2016.
Mehra MR, Jarcho JA, Cherikh W, et al. The **Drug-Intoxication Epidemic and Solid-Organ Transplantation**. N Engl J Med. 2018 May 17;378(20):1943-1945.
Mendoza N, Prasad P. **Pulmonary nodules** in a man with a history of **bone marrow transplantation**. BMJ. 2016 Apr 28;353:i1805
Miesner AR, Ausman M, Dagraedt B, et al. Probable Drug **Interaction** Between **Everolimus and Clarithromycin**. Ann Pharmacother. 2016 Aug;50(8):689-90.
Millan O, Budde K, et al. **Urinary miR- 155-5p and CXCL-10** as prognostic and predictive biomarkers of rejection, graft outcome and treatment response in kidney transplantation. BJCP 2017; xxxxx.
Mjoen G, Hallan S, Hartmann A, et al. **Long-term risks for kidney donors**. Kidney Int. 2013 Nov 27.
Minute M, Patti G, Tornese G, et al. **Sirolimus** Therapy in **Congenital Hyperinsulinism**: A Successful Experience Beyond Infancy.Pediatrics. 2015 Nov;136(5):e1373-6.
Mogul DB, Luo X, Bowring MG, et al. **Fifteen-Year Trends in Pediatric Liver Transplants**: Split, Whole Deceased, and Living Donor Grafts. J Pediatr. 2018 Jan 4.
Mohammad S, Grimberg A, Rand E, et al. Studies of Pediatric Liver Transplantation (SPLIT) Research Consortium. Long-Term Linear **Growth and Puberty in Pediatric Live**r Transplant Recipients. J Pediatr. 2013 Aug 2.
Molnar A, Fergusson D, Tsampalieros A, et al. **Generic immunosuppression** in solid organ transplantation:systenmtica review and meta-analysis. BMJ 2015;350:h3163
Momper JD, Ridenour TA, Schonder KS, et al. The Impact of Conversion From **Prograf to Generic Tacrolimus** in Liver and Kidney Transplant Recipients With Stable Graft Function. Am J Transplant. 2011 Jun 30.
Monostory K, Tóth K, Kiss Á, et al. **Personalizing initial calcineurin inhibitor dosing by adjusting to donor CYP3A-status** in liver transplant patients. Br J Clin Pharmacol. 2015 Aug 14.
Montgomery RA, Lonze BE, King KE, et al. **Desensitization in HLA-incompatible kidney recipients** and survival. N Engl J Med. 2011 Jul 28;365(4):318-26.
Montgomery RA, Loupy A, Segev DL. **Antibody-mediated rejection**: New approaches in prevention and management. Am J Transplant. 2018 Jan;18 Suppl 3:3-17.
Moulik M, Breinholt JP, Dreyer WJ, et al. Viral **Endomyocardial Infection** Is an Independent Predictor and Potentially Treatable Risk Factor for Graft Loss and Coronary Vasculopathy in Pediatric Cardiac Transplant
Moody WE, Ferro CJ, Edwards NC, et al; CRIB-Donor Study Investigators. **Cardiovascular Effects of Unilateral Nephrectomy** in Living Kidney Donors. Hypertension. 2016 Feb;67(2):368-77.
Moore Jason; McKnight Amy Jayne; Simmonds Matthew J.; et al. Association of **Caveolin-1 Gene Polymorphism With Kidney Transplant Fibrosis** and Allograft Failure. JAMA. 2010;303(13):1282-1287. Recipients. J Am Coll Cardiol. 2010 Aug 10;56(7):582-592.
Muhetaer G, Takeuchi H, Unezaki S, et al. Clinical Significance of **Peripheral Blood Lymphocyte Sensitivity to Glucocorticoids** for the Differentiation of High-Risk Patients With Decreased Allograft Function After Glucocorticoid Withdrawal in Renal Transplantation. Clin Ther. 2014 Jul 15.
Muller E, Barday Z, Mendelson M, Kahn D. **HIV-positive to HIV-positive kidney transplantation** — results at 3 to 5 years. N Engl J Med 2015;372:613-20.
Mulvihill MS, Cox ML, Bishawi M, et al**. Decline of Increased Risk Donor Offers on Waitlist Survival in Heart Transplantation**. J Am Coll Cardiol. 2018 Nov 6;72(19):2408-2409.
Murukesan V, Mukherjee S. Managing **post-transplant lymphoproliferative disorders** (PTLD) in solid-organ transplant recipients: a review of immunosuppressant regimens. Drugs. 2012 Aug 20;72(12):1631-43.
Muzaale AD, Dagher NN, Montgomery RA, et al. Estimates of early death, acute liver failure, and long-term mortality among **live liver donors**. Gastroenterology 2012;142:273–280
Muzaale AD, Massie AB, Wang MC, et al. Risk of end-stage **renal disease following live kidney donation**. JAMA. 2014 Feb 12;311(6):579-86
Na R, Laaksonen MA, Grulich AE, et al. High **azathioprine dose and lip cancer risk** in liver, heart, and lung transplant recipients: A population-based cohort study. J Am Acad Dermatol. 2016 Jun;74(6):1144-1152.e6.
Naesens M, Heylen L, Lerut E, et al. **Intrarenal resistive index after renal transplantation**. N Engl J Med. 2013 Nov 7;369(19):1797-806.
Nanga TM, Doan TTP, Marquet P, Musuamba FT. Toward a robust tool for pharmacokinetic-based **personalization of treatment with tacrolimus** in solid organ transplantation: a model-based meta-analysis approach. Br J Clin Pharmacol. 2019 Aug 31.
Nankivell BJ, Borrows RJ, Fung CL, O'Connell PJ, Allen RD, Chapman JR. The natural history of **chronic allograft nephropathy**. N Engl J Med 2003; 349: 2326–33.
Nankivell Brian J., Alexander Stephen I., **Rejection of the Kidney Allograft**. N Engl J Med 2010; 363:1451-1462.
Nankivell BJ, Kuypers DRJ. **Diagnosis and prevention of chronic kidney allograft loss**. Lancet 2011; 378: 1228–37.
National Institute for Health and Clinical Excellence. **Organ donation**: improving donor identification and consent rates for cadaveric organ donation. (Clinical guideline 135.) 2011. http://guidance.nice.org.uk/CG135
Nelson JS, Jackson AL, Darling JM, Gerber DA. **Chest pain and progressive shortness of breath** in a 60-year-old woman following **liver transplantation**. Chest. 2011 Feb;139(2):464-8.
Nevers W, Pupco A, Koren G, et al. Safety of **tacrolimus in pregnancy**. Can Fam Physician. 2014 Oct;60(10):905-6.
NICE: National Institute for Health and Care Excellence. **Immunosuppressive therapy for kidney transplant in children and young people**. NICE. 2017 Oct 11.
Nieto T, Inston N, Cockwell P. **Renal transplantation in adults**. BMJ. 2016 Nov 30;355:i6158.
Nishimoto M, Koh H, et al. **Drug interactions** and safety profiles with concomitant use of **caspofungin and calcineurin inhibitors** in allogeneic hematopoietic cell transplantation. Br J Clin Pharmacol. 2017 Apr 13.
Ng VL, Alonso EM, Bucuvalas JC, et al; Studies of Pediatric Liver Transplantation (SPLIT) Research Group. Health Status of **Children Alive 10 Years after Pediatric Liver Transplantation** Performed in the US and Canada: Report of the Studies of Pediatric Liver Transplantation Experience. J Pediatr. 2012 May;160(5):820-826.e3.
Ng V, Nicholas D, Dhawan A, et al; PeLTQL study group. **Development and validation of the pediatric liver transplantation quality of life**: a disease-specific quality of life measure for pediatric liver transplant recipients. J Pediatr. 2014 Sep;165(3):547-555.e7.
Niemann CU, Feiner J, Swain S, et al. **Therapeutic hypothermia** in deceased organ donors and kidney-graft function. N Engl J Med 2015;373:405-14.
Nighoghossian N, Berthezène Y, Mechtouff L, et al. **Cyclosporine** in acute ischemic **stroke**. Neurology. 2015 Jun 2;84(22):2216-23.

Nykänen AI, Holmström EJ, Tuuminen R, et al. **Donor Simvastatin Treatment in Heart Transplantation**: A Randomized and Blinded Clinical Trial. Circulation. 2019 Jul 29.
O'Keeffe LM, Ramond A, Oliver-Williams C, et al. Mid- and long-term health risks in **living kidney donors**. A systematic review and meta-analysis. Ann Intern Med. 2018. [Epub eahead of print]. doi:10.7326/M17-1235
O'Keeffe LM, Ramond A, Oliver-Williams C, et al. Mid- and long-term health **risks in living kidney donors**. A systematic review and meta-analysis. Ann Intern Med. 2018; 168:276-84.
Other herpesviruses: HHV-6,HHV-7,HHV-8,HSV-1and -2, VZVAm J Transplant 2004; 4 (Suppl. 10): 66–71 Blackwell MunksgaardBlackwell Munksgaard 2004
Ohler, L & Cupples, S. **Core Curriculum** for Transplant Nurses. Mosby, Inc. 2008
Olivier A, Kamar N, Vernerey D, et al. Long term outcomes of transplantation using **kidneys from expanded criteria donors**: prospective, population based cohort study. BMJ 2015;351:h3557.
Omland SH, et al. Skin Cancer Risk in **Hematopoietic Stem-Cell Transplant** Recipients Compared With Background Population & **Renal Transplant Recipients**: Population-Based Cohort Study. JAMA Derm. 2015 Oct 10:1-7.
Orandi BJ, Luo X, Massie AB, et al. Survival benefit with **kidney transplants from HLA-incompatible** live donors. N Engl J Med 2016;374:940-50.
Oskarsson B, Rocke DM, Dengel K, Richman DP. **Myasthenia gravis** exacerbation after discontinuing **mycophenolate**: A single-center cohort study. Neurology. 2016 Mar 22;86(12):1159-63.
Pai SY, Logan BR, Griffith LM, et al. **Transplantation outcomes for severe combined immunodeficiency**, 2000-2009. N Engl J Med. 2014 Jul 31;371(5):434-46.
Palmer SC, McGregor DO, Strippoli GF. Interventions for preventing **bone disease** in kidney transplant recipients. Cochrane Database Syst Rev. 2007 Jul 18;(3):CD005015.
Palmer Scott M., Limaye AP., Banks M, et al; Extended **Valganciclovir Prophylaxis to Prevent Cytomegalovirus** After Lung Transplantation: A Randomized, Controlled Trial. Ann Intern Med June 15, 2010 152:761-769.
Palmer SC, Navaneethan SD, Craig JC, et al. HMG CoA reductase inhibitors **(statins) for kidney transplant recipients**. Cochrane Database Syst Rev. 2014 Jan 28;1:CD005019. Statins may reduce cardiovascular events in kidney transplant recipients, although treatment effects are imprecise. Statin treatment has uncertain effects on overall mortality, stroke, kidney function, and toxicity outcomes in kidney transplant recipients. Additional studies would improve our confidence in the treatment benefits and harms of statins on cardiovascular events in this clinical setting.
Paoletti E, Bellino D, Marsano L, et al. Effects of **ACE inhibitors on long-term** outcome of **renal transplant recipients**: a randomized controlled trial. Transplantation. 2013 Mar 27;95(6):889-95.
Park KT, Bensen R, Lu B, et al. **Geographical Rural Status** and Health Outcomes in Pediatric Liver Transplantation: An Analysis of 6 Years of National United Network of Organ Sharing Data. J Pediatr. 2012 Aug 20.
Parker WF, Anderson AS, Hedeker D, et al. **Geographic Variation in the Treatment of U.S. Adult Heart Transplant Candidates**. J Am Coll Cardiol. 2018 Mar 20.
Patel Jignesh K, Kobashigawa Jon A. Cardiology Patient Page: **Heart Transplantation**. Circulation. 2011;124:e132-e134, doi:10.1161/CIRCULATIONAHA.110.017319
Patel UD. **Outcomes after pediatric kidney transplantation** improving: how can we do even better? Pediatrics. 2014 Apr;133(4):734-5.
Patlolla, V. et al. Efficacy of **Anti-IL-2 Receptor Antibodies** Compared to no Induction and to **Antilymphocyte Antibodies** in Renal Transplantation. Am J Transplant. 2007;7:1832-1841.
Patzer RE, Plantinga LC, Paul S, et al. Variation in **Dialysis Facility Referral for Kidney Transplantation** Among Patients With End-Stage Renal Disease in Georgia. JAMA. 2015 Aug 11;314(6):582-94.
Paya, C et al. Efficacy and Safety of **Valganciclovir vs. Oral Ganciclovir** for Prevention of **Cytomegalovirus** Disease in Solid Organ Transplant Recipients. Am J Transplant. 2004 Apr;4(4):611-20.
Peng DM, Zhang Y, Rosenthal DN, et al. Impact of **Heart Transplantation on the Functional Status of US Children** With End-Stage Heart Failure. Circulation. 2017 Mar 7;135(10):939-950.
Penninga L, Møller CH, Gustafsson F, et al. **Tacrolimus versus cyclosporine** as primary immunosuppression after heart transplantation: systematic review with meta-analyses and trial sequential analyses of randomised trials. Eur J Clin Pharmacol. 2010 Sep 30.
Pentz RD, Alderfer MA, Pelletier W, et al. Unmet Needs of **Siblings of Pediatric Stem Cell Transplant Recipients**. Pediatrics. 2014 Apr 28.
Perito ER, Rhee S, Glidden D, et al. Impact of the donor **body mass index** on the survival of pediatric liver transplant recipients and Post-transplant obesity. Liver Transpl. 2012 Aug;18(8):930-9.
Peters TG, Fisher JS, Gish RG, Howard RJ. Views of US Voters on **Compensating Living Kidney Donors**. JAMA Surg. 2016 Mar 23.
Peveling-Oberhag J, Zeuzem S, Yong WP, et al. Effects of **Hepatic Impairment** on the Pharmacokinetics of **Everolimus**: A Single-Dose, Open-Label, Parallel-Group Study. Clin Ther. 2013 Feb 28.
Pham MX, Teuteberg JJ, Kfoury AG, et al. **Gene-expression profiling** for rejection surveillance after cardiac transplantation. N Engl J Med 2010.
Pharm PT et al. **Cardiovascular disease** posttransplant. Seminars in Nephrology 2007;27(4):430-440.
Pinsky BW, Takemoto SK, Lentine KL, et al. Transplant outcomes and economic costs associated with **patient noncompliance** to immunosuppression. Am J Transplant. 2009 Nov;9(11):2597-606.
Phipps S, Peasant C, Barrera M, et al. Resilience in **Children Undergoing Stem Cell Transplantation**: Results of a Complementary Intervention Trial. Pediatrics. 2012 Feb 6.
Pierce Dwayne A, Reeves-Daniel Amber M. **Ranolazine-Tacrolimus Interaction**. Articles Ahead of Print published on 1 November 2010, DOI 10.1345/aph.1P297. Ann Pharmacother ;44:1844-1849.
Pietra BA, Kantor PF, Bartlett HL, et al. Early Predictors of Survival to and After **Heart Transplantation** in Children with Dilated Cardiomyopathy. Circulation. 2012 Jul 16.
Potluri V, Harhay MN, Wilson FP, et al. Kidney Transplant Outcomes for **Prior Living Organ Donors**. J Am Soc Nephrol. 2014 Nov 20.
Prasad GV, Ruzicka M, Burns KD, Tobe SW, Lebel M. **Hypertension** in dialysis and kidney transplant patients. Can J Cardiol. 2009 May;25(5):309-14.
Pundole XN, Barbo AG, Lin H, et al. Increased Incidence of **Fractures in Recipients of Hematopoietic Stem-Cell Transplantation**. J Clin Oncol. 2015 Mar 16.
Purnell TS, Luo X, Kucirka LM, et al. Reduced **Racial Disparity** in Kidney Transplant Outcomes in the United States from 1990 to 2012. J Am Soc Nephrol. 2016 Feb 4.
Purnell TS, Luo X, Cooper LA, et al. Association of **race and ethnicity with live donor kidney transplantation** in the United States from 1995 to 2014.JAMA. doi:10.1001/jama.2017.19152
Puza CJ, Cardones AR, Mosca PJ. Examining the Incidence and Presentation of **Melanoma in the Cardiothoracic Transplant Population**. JAMA Dermatol. 2018 Feb 16.
Rabinstein AA, Yee AH, Mandrekar J, et al. Prediction of potential for **organ donation after cardiac death** in patients in neurocritical state: a prospective observational study. Lancet Neurol 2012
Ramalho, V & Ramalho, H. Comparison of **azithromycin** and oral hygiene program in the treatment of **cyclosporine**-induced **gingival hyperplasia**. Renal Failure 2007;29:265-270.
Rana A, Gruessner A, Agopian VG, et al. **Survival Benefit of Solid-Organ Transplant** in the United States. JAMA Surg. 2015 Jan 28.
Rana A, Pallister Z, Halazun K, et al. **Pediatric Liver Transplant Center Volume and the Likelihood of Transplantation**. Pediatrics. 2015 Jun 15.
Rao V, Dhanani S, et al. Effect of **organ donation after circulatory determination of death** on number of organ transplants from donors with neurologic determination of death. CMAJ. 2017 Sep 25;189(38):E1206-E1211.
Ravanan R, Udayaraj U, Ansell D, et al. Variation between centres in **access to renal transplantation** in UK: longitudinal cohort study. BMJ 2010;341:c3451
Redelmeier DA, Markel F, Scales DC. **Organ donation after death** in Ontario: a population-based cohort study. CMAJ. 2013 Apr 2.
Reese PP, Bloom RD, Feldman HI, et al. **Mortality** and cardiovascular disease among **older live kidney donors**. Am J Transplant. 2014 Aug;14(8):1853-61.
Reese PP, Boudville N, Garg AX. **Living kidney donation**: outcomes, ethics, and uncertainty. Lancet. 2015 May 16;385(9981):2003-13.
Reese PP, Abt PL, Blumberg EA, Goldberg DS. **Transplanting Hepatitis C-Positive Kidneys**. N Engl J Med. 2015 Jul 23;373(4):303-5.
Repp KL, Hayes C 3rd, Woods TM, et al. **Drug-Related Problems** and Hospital Admissions in CardiacTransplant Recipients (October). Ann Pharmacother. 2012 Oct 2.
Reshef R, Luger SM, Hexner EO, et al. Blockade of lymphocyte chemotaxis (**maraviroc**) in visceral **graft-versus-host disease**. N Engl J Med. 2012 Jul 12;367(2):135-45.
Richterman A, Sawinski D, Reese PP, et al. An Assessment of **HIV-Infected Patients Dying in Care for Deceased Organ Donation** in a United States Urban Center. Am J Transplant. 2015 May 14.
Riff C, Debord J, Monchaud C, et al. Population pharmacokinetic model and Bayesian estimator for two **tacrolimus formulations** in adult liver transplant patients. Br J Clin Pharmacol. 2019 Apr 11.
Rissling O, Glander P, Hambach P, et al. No relevant pharmacokinetic interaction between **pantoprazole and mycophenolate** in renal transplant patients: a randomized crossover study. Br J Clin Pharmacol. 2015 Apr 24.
Rizvi SMH, Aagnes B, Holdaas H, et al. Long-term Change in the Risk of **Skin Cancer After Organ Transplantation**: A Population-Based Nationwide Cohort Study. JAMA Dermatol. 2017 Oct 18.
Robert N, Wong GW, Wright JM. Effect of **cyclosporine** on blood pressure. Cochrane Database Syst Rev. 2010 Jan 20;(1):CD007893. There appears to be a dose-related effect with lower doses (1-4 mg/kg/d) increasing mean BP by an average of 5 mmHg and higher doses (>10 mg/kg/d) increasing mean BP by 11 mmHg on average.
Roedder S, Sigdel T, Salomonis N, et al. The **kSORT Assay** to Detect **Renal** Transplant Patients at High Risk for Acute **Rejection**: Results of the Multicenter AART Study. PLoS Med. 2014 Nov 11;11(11):e1001759.
Rose C, Schaeffner E, Frei U, et al. A Lifetime of **Allograft Function with Kidneys from Older Donors**. J Am Soc Nephrol. 2015 Mar 26.
Ruebner RL, Reese PP, Denburg MR, et al. **End-Stage Kidney Disease After Pediatric Nonrenal** Solid Organ Transplantation. Pediatrics. 2013 Oct 14.
Ruggenenti P, Gentile G, Perico N, et al; SIRENA 2 Study Group. Effect of **Sirolimus** on Disease Progression in Patients with **Autosomal Dominant Polycystic Kidney Disease** and CKD Stages 3b-4. Clin J Am Soc Nephrol. 2016 Feb 22.
Sallustio BC, Noll BD, Coller JKet al. Relationship between **allograft cyclosporin concentrations and P-glycoprotein expression** in the first month following renal transplantation. Br J Clin

Pharmacol. 2019 Jan 28.
SM, Foster BJ, Tonelli MA, et al; the Pediatric Renal Outcomes Canada Group. **Dialysis and transplantation among Aboriginal** children with kidney failure. CMAJ. 2011 Jul 12;183(10):E665-E672.
Scalea JR, Menaker J, Meeks AK, et al. **Trauma patients with a previous organ transplant**: Outcomes are better than expected-A retrospective analysis. J Trauma Acute Care Surg. 2013 Jun;74(6):1498-503.
Scandling John D., Busque Stephan, Shizuru Judith A. **Induced Immune Tolerance for Kidney Transplantation**. N Engl J Med 365;14 nejm.org october 6, 2011.
Scandling JD, Busque S, Shizuru JA, et al. **Induced immune tolerance for kidney transplantation**. N Engl J Med. 2011 Oct 6;365(14):1359-60.
Schaffer JM, Singh SK, Reitz BA, et al. **Single- vs double-lung transplantation** in patients with **chronic obstructive pulmonary disease and idiopathic pulmonary fibrosis** since the implementation of lung allocation based on medical need. JAMA. 2015 Mar 3;313(9):936-48.
Schena FP, Pascoe MD, Alberu J, et al. **Sirolimus** CONVERT Trial Study Group. Conversion from calcineurin inhibitors to sirolimus maintenance therapy in renal allograft recipients: 24-month efficacy and safety results from the CONVERT trial. Transplantation. 2009 Jan 27;87(2):233-42.
Schumacher KR, Almond C, Singh TP, et al; on behalf of the PHTS Study Group Investigators. Predicting **Graft Loss by 1-Year in Pediatric Heart Transplant** Candidates: An Analysis of the PHTS Database. Circulation. 2015 Jan 13.
Segev Dorry L.; Muzaale Abimereki D.; Caffo Brian S.; et al. Perioperative Mortality and Long-term Survival Following **Live Kidney Donation**. JAMA. 2010;303(10):959-966.
Sharif A. Should Metformin be Our Antiglycemic Agent of Choice Post-transplantation? American Journal of Transplantation 2011;11(7):1376-1381. Accessed online 03 Aug 2011 at: http://www.medscape.com/viewarticle/745820
Sheil AG. **Cancer in renal allograft recipients** in Australia and New Zealand. *Transplant Proc* 1977; 9: 1133–36.
Shemie SD, Macdonald S; et al. Improving the process of **deceased organ and tissue donation**: a role for donation physicians as specialists. CMAJ. 2014 Feb 4;186(2):95-6.
Shemie SD. **Trends in deceased organ donation in Canada**. CMAJ. 2017 Sep 25;189(38):E1204-E1205.
Shilliday IR, Sherif M. **Calcium channel blockers** for preventing acute tubular necrosis in kidney transplant recipients. Cochrane Database Syst Rev. 2007 Oct 17;(4):CD003421.
Shivaswamy V, Boerner B, Larsen J. **Post-transplant diabetes mellitus**: Causes, treatment, and impact on outcomes. Endocr Rev. 2015 Dec 9:er20151084.
Shore PM, Huang R, Roy L, Darnell C, Grein H, Robertson T, Thompson L. Potential for **Liver and Kidney Donation After Circulatory Death** in Infants and Children. Pediatrics. 2011 Aug 22.
Shpigel AA, Saeed MJ, Novak E, et al. **Center-Related Variation in Cardiac Stress Testing** in the 18 Months Prior to Renal Transplantation. JAMA Intern Med. 2019 May 13.
Shullo MA, Schonder K, Teuteberg JJ. Elevated **tacrolimus** levels associated with intravenous **azithromycin and ceftriaxone**: a case report. Transplant Proc. 2010 Jun;42(5):1870-2.
Silva HT Jr, Yang HC, Abouljoud M, et al. One-year results with extended-release **tacrolimus/MMF**, **tacrolimus/MMF** & **cyclosporine/MMF** in de novo kidney transplant recipients. Am J Transplant. 2007 Mar;7(3):595-608.
Siminoff LA, Molisani AJ, Traino HM. A Comparison of the **Request Process and Outcomes** in Adult and Pediatric Organ Donation. Pediatrics. 2015 Jun 1.
Singh TP, Almond CS, Taylor DO, et al. **Racial and Ethnic Differences in Wait-List Outcomes** in Patients Listed for Heart Transplantation in the United States. Circulation. 2012 May 15.
Slaughter MS, Pagani FD, et al; HeartMate II Clinical Investigators. Clinical management of **continuous flow left ventricular assist devices** in advanced heart failure. J Heart Lung Transplant 2010; 29(4 suppl):S1–S39.
Snell GI, Westall GP, Paraskeva MA. **Immunosuppression and allograft rejection following lung transplantation**: evidence to date. Drugs. 2013 Nov;73(16):1793-813.
Song Y, Qiao J, Giovanni G, et al. **Mucormycosis in renal transplant recipients**: review of 174 reported cases. BMC Infect Dis. 2017 Apr 18;17(1):283
Sorror ML, Sandmaier BM, Storer BE, et al. Long-term outcomes among older patients following nonmyeloablative conditioning and **allogeneic hematopoietic cell transplantation** for advanced hematologic malignancies. *JAMA*. 2011;306 (17):1874-1883.
Spence-Shishido A, Streicher JL, George RP, et al.**Folliculotropic Mycosis** Fungoides as a **Posttransplant Lymphoproliferative Disorder**. Pediatrics. 2015 Aug 17.
Srinivasan S. Has Tamil Nadu turned the tide on the **transplant trade**? BMJ. 2013 Apr 12;346:f2155.
Stamp L, Searle M, O'Donnell J, Chapman P. **Gout** in solid organ transplantation: a challenging clinical problem. Drugs. 2005;65(18):2593-611.
Starzl TE, Demetris AJ, Van Thiel D. **Liver transplantation**. N Engl J Med 1989;321:1014-22, 1092-9.
Steers NJ, Li Y, Drace Z, et al. **Genomic Mismatch at LIMS1 Locus and Kidney Allograft Rejection**. N Engl J Med. 2019 May 16;380(20):1918-1928.
Stifft F, Vanmolkot F, Scheffers I, et al. Rectal and Sublingual Administration of **Tacrolimus**: a Single Dose Pharmacokinetic Study in Healthy Volunteers. Br J Clin Pharmacol. 2014 May 9.
Stock Peter G., Barin Burc, Murphy Barbara, et al. Outcomes of Kidney Transplantation in **HIV-Infected Recipients**. N Engl J Med 2010; 363:2004-2014
Størset E, Hole K, Midtvedt K, et al. Bodyweight-adjustments introduce significant correlations between **CYP3A** metrics and tacrolimus clearance. Br J Clin Pharmacol. 2016 Dec 22.
Strachnan et al. Is oral **azithromycin** effective for the treatment of **cyclosporine**-induced **gingival hyperplasia** in cardiac transplant recipients? J Clin PharmTher 2003;28:329-338.
Strippoli GF, Hodson EM, Jones CJ, et al. Pre-emptive treatment for **cytomegalovirus** viraemia to prevent cytomegalovirus disease in solid organ transplant recipients. Cochrane Database Syst Rev. 2006 Jan 25;(1):CD005133.
Summers DM, Johnson RJ, Allen J, et al. Analysis of factors that affect outcome after transplantation of **kidneys donated after cardiac death** in the UK: a cohort study. Lancet. 2010 Aug 18.
Summers DM, Johnson RJ, Hudson A, et al. Effect of **donor age and cold storage time** on outcome in recipients of **kidneys** donated after circulatory death in the UK: a cohort study. Lancet. 2012 Dec 19.
Summers DM, Watson CJE, Pettigrew G, et al. **Kidney donation after circulatory death (DCD):** state of the art. Kidney Int 2015; online March 18.
Suzuki Y, Fujioka T, Sato F, et al. **CYP3A5 polymorphism** affects the increase in CYP3A activity after living kidney transplantation in patients with end stage renal disease. Br J Clin Pharmacol. 2015 Dec;80(6):1421-8.
Tan J, Wu W, Xu X,et al. Induction therapy with **autologous mesenchymal stem cells in living-related kidney transplants**: a randomized controlled trial. JAMA. 2012 Mar 21;307(11):1169-77.
Tancredi DJ, Butani L. **Pretransplant serum albumin** is an independent predictor of graft failure in pediatric renal transplant recipients. J Pediatr. 2014 Mar;164(3):602-6.
Taylor D, Meiser B, Webber S, et al. Task Force 2: **immunosuppression and rejection**. In: the International Society of Heart and Lung Transplantation guidelines for the care of **heart transplant** recipients. J Heart Lung Transplant. 2010 Aug;29(8):926-33.
Tedla, F et al. **Hypertension** after Renal Transplant. The Journal of Clinical Hypertension 2007; 9(7):538-545.
Tennankore KK, Kim SJ, Baer HJ, et al. Survival and Hospitalization for Intensive **Home Hemodialysis** Compared with Kidney Transplantation. J Am Soc Nephrol. 2014 May 22.
Ter Heine R, van Erp NP, Guchelaar HJ, et al. A pharmacological rationale for improved **everolimus dosing in oncology and transplant patients**. Br J Clin Pharmacol. 2018 Mar 25.
Terasaki PI, Cecka JM, Gjertson DW, Takemoto S. High survival rates of **kidney transplants** from **spousal and living unrelated donors**. N Engl J Med 1995;333:333-6.
Teschner S, Gerke P, Geyer M, et al. **Leflunomide** therapy for polyomavirus-induced allograft nephropathy: efficient BK virus elimination without increased risk of rejection. Transplant Proc. 2009 Jul-Aug;41(6):2533-8.
Thabut Gabriel; Christie Jason D.; Kremers Walter K.; et al. **Survival Differences Following Lung Transplantation** Among US Transplant Centers. JAMA. 2010;304(1):53-60.
Thao V, Kozhimannil KB, Thomas W, et al. Variation in Inpatient **Costs of Hematopoietic Cell Transplantation** Among Transplant Centers in the United States. JAMA Intern Med. 2014 Jun 16.
Thiruchelvam Paul T R, Willicombe Michelle, Taube David et al.. **Renal transplantation**. BMJ 2011; 343 doi: 10.1136/bmj.d7300 (Published 14 Nov 2011)
Thomusch O, Wiesener M, et al. **Rabbit-ATG or basiliximab induction** for rapid steroid withdrawal after **renal transplantation** (**Harmony**): open-label, multicentre, randomised controlled trial. Lancet 2016; online Nov 18.
Thornton JD, Alejandro-Rodriguez M, León JB, et al. Effect of an **iPod Video Intervention on Consent to Donate Organs**: A Randomized Trial. Ann Intern Med. 2012 Apr 3;156(7):483-90.
Tichelli A, Beohou E, Labopin M, et al; Transplant Complications Working Party of the EBMT. Evaluation of **Second Solid Cancers After Hematopoietic Stem Cell Transplantation** in European Patients. JAMA Oncol. 2018 Nov 21.
Todd JL, Palmer SM. **Bronchiolitis obliterans syndrome**: the final frontier for lung transplantation. Chest. 2011 Aug;140(2):502-8.
Tong A, Tjaden L, Howard K, Wong G, Morton R, Craig JC. **Quality of life of adolescent kidney transplant** recipients. J Pediatr. 2011 Oct;159(4):670-675.e2.
Topilsky Y, et al. **Sirolimus** as primary immunosuppression attenuates allograft vasculopathy with improved late survival and decreased cardiac events after **cardiac transplantation**. Circulation. 2012 Feb 7;125(5):708-20.
Torpy JM, Lynm C, Golub RM. JAMA patient page. **Liver transplantation**. JAMA. 2012 Jan 18;307(3):320.
Truog RD, Miller FG, Halpern SD. The **Dead-Donor Rule** and the Future of Organ Donation. N Engl J Med. 2013 Oct 3;369(14):1287-1289.
Tsuang WM, Vock DM, Finlen Copeland CA, Lederer DJ, Palmer SM. An acute change in lung **allocation score** and survival after lung transplantation. A cohort study. Ann Intern Med. 2013;158:650-7.

Uno T, Wada K, Matsuda S, et al. **Clotrimazole troches can alter everolimus** pharmacokinetics in post-transplant patients: A case report. Br J Clin Pharmacol. 2019 Jun 26.
Ushijima K, Mizuta K, Otomo S, et al. **Increased tacrolimus blood concentration by Beni-Madonna** -a new hybrid citrus cultivar categorized as 'Tangor', in a liver transplant patient: likely furanocoumarin-mediated inhibition of CYP3A4 or P-glycoprotein.Br J Clin Pharmacol. 2018 Sep 14.
Vaduganathan M, Machado SR, DeFilippis EM, et al. Organ Donation and **Drug Intoxication-Related Deaths** in the United States. N Engl J Med. 2019 Feb 7;380(6):597-599.
Vaidya OU, House JA, Coggins TR, et al. Effect of **Renal Transplantation** for Chronic Renal Disease on **Left Ventricular Mass**. Am J Cardiol. 2012 Apr 5.
Vajdic CM, McDonald SP, McCredie MR, et al. **Cancer incidence before and after kidney transplantation**. JAMA 2006; 296: 2823–31.
Van Arendonk KJ, Boyarsky BJ, Orandi BJ, et al. National Trends Over **25 Years in Pediatric Kidney Transplant Outcomes**. Pediatrics. 2014 Mar 10.
van der Beek MT, Berger SP, Vossen AC, et al. Preemptive versus sequential prophylactic-preemptive treatment regimens for **cytomegalovirus** in renal transplantation: comparison of treatment failure and antiviral resistance. Transplantation. 2010 Feb 15;89(3):320-6.
Van Driest SL, Webber SA. **Pharmacogenomics**: **personalizing pediatric heart transplantation**. Circulation. 2015 Feb 3;131(5):503-12.
van Gelder T. **Mycophenolate** Blood Level **Monitoring**: Recent Progress. Am J Transplant. 2009 Jun 10.
van Laar JM, Farge D, Sont JK, et al; EBMT/EULAR Scleroderma Study Group. Autologous **hematopoietic stem cell transplantation** vs intravenous pulse cyclophosphamide in diffuse cutaneous systemic sclerosis: a randomized clinical trial. JAMA. doi:10.1001/jama.2014.6368.
Van Laecke S, Van Biesen W, Verbeke F, et al. Posttransplantation **Hypomagnesemia** and Its Relation with Immunosuppression as Predictors of New-Onset Diabetes after Transplantation. Am J Transplant. 2009 Jul 16.
van Leeuwen MT, Webster AC, McCredie MR, et al. Effect of reduced immunosuppression after kidney transplant failure on **risk of cancer**: population based retrospective cohort study. BMJ. 2010 Feb 11.
van Sloten TT, de Klaver PAG, et al. Co-administration of **cyclosporine and ticagrelor** may lead to a higher exposure to cyclosporine: a case report of a 49-year old man. Br J Clin Pharmacol. 2017 Sep 11.
van Walraven, Carl, Austin, Peter C, Knoll, Greg. **Predicting** potential **survival benefit of renal transplantation** in patients with chronic kidney disease. CMAJ 2010 0: cmaj.091661.
Vanlemmens C, Di Martino V, Milan C, et al. TRANSCIAL Study Group. **Immediate listing** for **liver** transplantation versus **standard care** for Child-Pugh stage B alcoholic cirrhosis: a randomized trial. Ann Intern Med. 2009 Feb 3;150(3):153-61.
Vannaprasaht S, Reungjui S, Supanya D, et al. Personalized **Tacrolimus Doses Determined by CYP3A5 Genotype** for Induction and Maintenance Phases of Kidney Transplantation. Clin Ther. 2013 Oct 10.
Vanrenterghem Y, Bresnahan B, Campistol J, et al. **Belatacept**-based regimens are associated with improved cardiovascular and metabolic risk factors compared with cyclosporine in kidney transplant recipients (**BENEFIT** and **BENEFIT-EXT** studies). Transplantation. 2011 May 15;91(9):976-83.
Vargo PR, Schiltz NK, Johnston DR, et al. **Outcomes of Cardiac Surgery** in Patients With Previous Solid Organ Transplantation (Kidney, Liver, and Pancreas). Am J Cardiol. 2015 Oct 9.
Ven Gelder, T & Shaw, L. The Rationale foe and limitations of Therapeutic drug **monitoring for MMF** in transplantation 2005;80(2S)oct 14
Verhave JC, Tagalakis V, Suissa S, et al. The risk of **thromboembolic events in kidney transplant** patients**.** Kidney Int. 2014 Jan 15.
Vincenti F, Rostaing L, Grinyo J, et al. **Belatacept** and longterm outcomes (7 years) in kidney transplantation. N Engl J Med 2016; 374:333-43.
Volk ML, Biggins SW, Huang MA, et al. **Decision making in liver transplant selection** committees: a multicenter study. Ann Intern Med. 2011 Oct 18;155(8):503-8.
Voora S, Adey DB. Management of **Kidney Transplant Recipients by General Nephrologists:** Core Curriculum 2019. Am J Kidney Dis. 2019 Apr 10.
Vora NM, Basavaraju SV, et al; Transplant-Associated Rabies Virus Transmission Investigation Team. **Raccoon rabies virus** variant transmission through solid organ transplantation. JAMA. 2013 Jul 24;310(4):398-407.
Vos R, Vanaudenaerde BM, Verleden SE, et al. A randomized placebo-controlled trial of **azithromycin** to **prevent bronchiolitis obliterans** syndrome after lung transplantation. Eur Respir J. 2010 Jun 18.
Vos R, Vanaudenaerde BM, Ottevaere A, et al. Long-term **azithromycin** therapy for **bronchiolitis obliterans** syndrome: Divide and conquer? J Heart Lung Transplant. 2010 Jul 7.
Waits SA, Kim EK, Terjimanian MN, et al. **Morphometric Age and Mortality After Liver** Transplant. JAMA Surg. 2014 Feb 5.
Waldner M, Fantus D, Solari M, et al. New perspectives on mTOR inhibitors (Rapamycin, Rapalogs and TORKinibs) in transplantation. Br J Clin Pharmacol. 2016 Jan 26.
Walker E. **My three livers**: how transplants gave me my life back. BMJ. 2019 Mar 6;364:l1004.
Walker I, Panzarella T, Couban S, et al; Canadian Blood and Marrow Transplant Group. **Pretreatment with anti-thymocyte globulin** versus no anti-thymocyte globulin in patients with haematological malignancies undergoing haemopoietic cell transplantation from unrelated donors: a randomised, controlled, open-label, phase 3, multicentre trial. Lancet Oncol. 2015 Dec 23.
Watt KD, Dierkhising R, Heimbach JK, Charlton MR. Impact of **sirolimus and tacrolimus** on mortality and graft loss in **liver transplant** recipients with or without hepatitis C virus: An analysis of the Scientific Registry of Transplant Recipients Database. Liver Transpl. 2012 Sep;18(9):1029-36.
Warnecke G, et al. **Normothermic perfusion** of donor **lungs** for preservation and assessment with the Organ Care System Lung before bilateral transplantation: a pilot study of 12 patients. Lancet 2012; online Oct 10.
Weber M, Dindo D, Demartines N, Ambühl PM, Clavien PA. **Kidney transplantation from donors without a heartbeat**. N Engl J Med. 2002;347(4):248-255.
Webster A, Woodroffe RC, Taylor RS, Chapman JR, Craig JC. **Tacrolimus versus cyclosporin** as primary immunosuppression for kidney transplant recipients. Cochrane Database Syst Rev. 2005 Oct 19;(4):CD003961.
Weir MR, Mulgaonkar S, Chan L, et al. **Mycophenolate mofetil-based immunosuppression with sirolimus** in renal transplantation: a randomized, controlled Spare-the-Nephron trial. Kidney Int 2010; online Dec 29.
Wekerle T, Segev D, Lechler R, et al. Strategies for long-term **preservation** of **kidney graft function**. Lancet. 2017 May 27;389(10084):2152-2162
Wetmore JB, Calvet JP, Yu AS, et al. **Polycystic Kidney Disease and Cancer after Renal Transplantation**. J Am Soc Nephrol. 2014 May 22.
Wever-Pinzon O, Drakos SG, Kfoury AG, et al. Morbidity and mortality in **heart transplant candidates supported with mechanical circulatory support**: is reappraisal of the current United network for organ sharing thoracic organ allocation policy justified? Circulation. 2013 Jan 29;127(4):452-62.
White TE, Hendershot KA, Dixon MD, et al. **Family Strategies** to Support **Siblings of Pediatric Hematopoietic Stem Cell Transplant Patients**. Pediatrics. 2017 Jan 24.
Wilkinson et al. Guidelines for the treatment & management of **new-onset diabetes** after transplant. Clin Transplant 2005:19:291-298.
Wolf MF, George RP, Warshaw B, et al. **Physical Activity** and Kidney Injury in Pediatric and Young Adult **Kidney Transplant Recipients**. J Pediatr. 2016 Oct 11
Wolfe RA, Ashby VB, Milford EL, et al. Comparison of **mortality** in all patients on **dialysis, patients on dialysis awaiting transplantation, and** recipients of a **first cadaveric transplant**. N Engl J Med 1999; 341: 1725–30.
Workman JK, Myrick CW, Meyers RL, et al. **Pediatric Organ Donation and Transplantation**. Pediatrics. 2013 May 20.
Wyld ML, Clayton PA, Kennedy SE, et al. **Pregnancy outcomes for kidney transplant** recipients with transplantation as a child. JAMA Pediatr. 2015 Feb 2;169(2):e143626.
Yamashita T, Ando Y, Okamoto S, et al. Long-term survival after **liver transplantation** in patients with **familial amyloid polyneuropathy**. Neurology. 2012 Feb 28;78(9):637-43.
Yamashiki N, Sugawara Y, Tamura S, et al. Outcomes after **living donor liver transplantation** for acute liver failure in Japan: Results of a nationwide survey. Liver Transpl. 2012 Sep;18(9):1069-77.
Yang HM, Khush K, Luikart H, et al. Invasive Assessment of **Coronary Physiology Predicts Late Mortality** After Heart Transplantation. Circulation. 2016 May 17;133(20):1945-50.
Yanik E, Smith J, Shiels M, et al. **Cancer risk** among pediatric solid organ transplant recipients in the United States. Pediatrics. 2017;139(5):e20163893
Yoshizawa S, Kato TS, Mancini D, Marboe CC. Outcome of Patients Having **Heart Transplantation for Lymphocytic Myocarditis**. Am J Cardiol. 2013 Apr 25.
Zeiser R, Blazar BR. **Acute Graft-versus-Host Disease** - Biologic Process,Prevention, and Therapy. N Engl J Med. 2017 Nov 30;377(22):2167-2179.
Zeiser R, Blazar BR. Pathophysiology of **Chronic Graft-versus-Host Disease and Therapeutic Targets**. N Engl J Med. 2017 Dec 28;377(26):2565-2579.
Zhang HX, Sheng CC, Liu LS, et al. Systematic external evaluation of published population pharmacokinetic models of **mycophenolate mofetil in adult kidney transplant recipients co-administered with tacrolimus**. Br J Clin Pharmacol. 2018 Dec 29.
Zheng S, Easterling TR, Hays K, et al. **Tacrolimus** Placental Transfer at Delivery and Neonatal Exposure through Breast Milk. Br J Clin Pharmacol. 2013 Mar 26.
Zwart TC, Gokoel SRM, van der Boog PJM, etal. **Therapeutic drug monitoring of tacrolimus and mycophenolic acid** in outpatient renal transplant recipients using a **volumetric dried blood spot sampling device**. Br J Clin Pharmacol. 2018 Sep 3.

Organ Transplant Facts:

Canada: There were 2,083 solid organ transplants in Canada, as compared with 2,188 in 2007, according to Canadian Organ Replacement Register statistics (http://cihi.ca /cihiweb/dispPage.jsp?cw_page=AR3230_E&cw_topic=3230). The total number of organ donors also decreased, to 1038 from 1046 in 2007.
Roughly 4380 Canadians were on waiting lists for transplants as of Dec. 31, 2008. — Sabrina Doyle, Ottawa, Ont. http://secure.cihi.ca/cihiweb/dispPage.jsp?cw_page=media_20091222_e

Organ Donor Activity in Canada, 1999 to 2008 http://secure.cihi.ca/cihiweb/products/CORR_AiB_EN_20091222_rev20100106.pdf

During the past decade, the number of organ donors in Canada increased from 812 to 1,038 per year; living donors accounted for 69% of this increase. While there were increases in organ donation during the past decade, the demand for organs also grew. For example, in the case of kidneys, the incidence rate of end-stage renal disease increased from 149 to 168 per million population. The availability of donated organs in Canada rose by more than one-quarter (28%) over the past decade, but this increase is not keeping pace with demand. More than 1,000 Canadians donated organs in 2008, up from 812 in 1999, according to a new study released today by the Canadian Institute for Health Information (CIHI). With an increase in the number of Canadians with organ failure, combined with medical advancements that are keeping these patients alive longer, the results show an increase in the demand for organs. Last year, about 215 Canadians died while waiting for an organ transplant. A **national** paired exchange program has been launched for donor and recipient pairs who do not match as an initiatives to maximize the number of live-donor organs available at http://www.ccdt.ca/english/ldpe/index.htm called the **Living Donor Paired Exchange Registry (LDPE).**

According to the Canadian Organ Replacement Registry's 2008 annual report, there were an estimated 33,832 people with end-stage renal disease in Canada at the end of 2006, an increase of 69.7% since 1997. Of these, 20,465 were on dialysis and 13,367 were living with a functioning kidney transplant.

US Dept of Health and Human Services: Organ Procurement and Transplantation Network (OPTN) Data reports: http://optn.transplant.hrsa.gov/latestData/viewDataReports.asp

References – Transplantation Drug Treatment – www.RxFiles.ca

[1] Micromedex. 2018

2 Briggs G, Freeman, Roger, Yaffe, Sumner, ed. Drugs in Pregnancy and Lactation. 11th ed: TechBooks 2017

3 e-CPS [Internet]. Ottawa (ON): Canadian Pharmacists Association; c2017 [cited 2017 Jul 30]. Available from: http://www.e-cps.ca. Also available in paper copy from the publisher.

4 Schonder Kristine S, Johnson Heather J, "Chapter 92. Solid-Organ Transplantation" (Chapter). Joseph T. DiPiro, Robert L. Talbert, Gary C. Yee, Gary R. Matzke, Barbara G. Wells, L. Michael Posey: Pharmacotherapy: A Pathophysiologic Approach, 7e: http://www.accesspharmacy.com/content.aspx?aID=3210287.
Gao Y, Twigg AR, Hirose R, et al. Association of HLA Antigen Mismatch With Risk of Developing Skin Cancer After Solid-Organ Transplant. JAMA Dermatol. 2019 Jan 23.
De Rosa N, Paddon VL, Liu Z, et al. Nonmelanoma Skin Cancer Frequency and Risk Factors in Australian Heart and Lung Transplant Recipients. JAMA Dermatol. 2019 Mar 13.

5 Ross, H & Hendry, P et al. 2001 Canadian Cardiovascular society consensus conference on cardiac transplantation. Can J Cardiol 2003:19(6)

6 Kasiske B et al. (2004) National Kidney Foundation: clinical practice guidelines for managing dyslipidemias in kidney transplant patients: a report from the Managing Dyslipidemias in Chronic Kidney Disease Work Group of the National Kidney Foundation Kidney Disease Outcomes Quality Initiative. Am J Transplant 4 (Suppl 7): S13–S53

7 Rigatto, C& Parfrey, P. Therapy Insight: management of cardiovascular disease in the renal transplant recipient. Nature Clinical Practice Nephrology 2006;2:514-526.

8 De Vitto, D & Song, M. Risk profile for cardiovascular morbidity and mortality after lung transplantation. Nurs Clin N Am 2008;43:37-53.

9 Estes CM, Westhoff C. Contraception for the transplant patient. Semin Perinatol. 2007 Dec;31(6):372-7. Review.
McKay DB, Josephson MA. Pregnancy in recipients of solid organs--effects on mother and child. N Engl J Med. 2006 Mar 23;354(12):1281-93.

10 Helderman, JH & Goral, S. Gastrointestinal complications of transplant immunosuppresion. Review. Am J Nephrol 2002;13:277.

11 Clive, DM. Renal transplant-associated hyperuricemia and gout. J Am Soc Nephrol 2000; 11:974.

12Guidelines for vaccination of solid organ transplant candidates and recipients. Am J Transplant. 2004; 4 (Suppl. 10): 160–163

13 Avery RK, Michaels M. Update on immunizations in solid organ transplant recipients: what clinicians need to know. Am J Transplant. 2008 Jan;8(1):9-14. Epub 2007 Dec 18.

14 Stein, E. et al. Post-transplant osteoporosis. Endocrinol Metab Clin N Am 36 (2007) 937-963

15 Epstein–Barr virus and lymphoproliferative disorders after transplantation. Am J Transplant 2004; 4 (Suppl. 10): 59–65

16 Preiksaitis JK. New developments in the diagnosis and management of posttransplant lymphoproliferative disorders in solid organ transplant recipients. CID 2004;34:1016-23
Trappe R, Oertel S, Leblond V, et al, for the German PTLD Study Group and the European **PTLD** Network. Sequential treatment with rituximab followed by CHOP chemotherapy in adult B-cell post-transplant lymphoproliferative disorder (PTLD): the prospective international multicentre phase 2 PTLD-1 trial. Lancet Oncol 2011; online Dec 13.
Murukesan V, Mukherjee S. Managing **post-transplant lymphoproliferative disorders** (PTLD) in solid-organ transplant recipients: a review of immunosuppressant regimens. Drugs. 2012 Aug 20;72(12):1631-43.
Dierickx D, Habermann TM. **Post-Transplantation Lymphoproliferative Disorders** in Adults. N Engl J Med. 2018 Feb 8;378(6):549-562.

17 Cytomegalovirus. American Journal of Transplantation 2004; 4 (Suppl. 10): 51–58

18 Preiksaitis, J et al. Canadian society of transplant consensus workshop on cytomegalovirus management in solid organ transplantation final report. American Journal of Tranplantation 2005;5:218-227.
Kalil Andre C., Mindru Cezarina, Florescu Diana F. Effectiveness of Valganciclovir 900 mg versus 450 mg for Cytomegalovirus Prophylaxis in Transplantation: Direct and Indirect Treatment Comparison Meta-analysis Clin Infect Dis. ciq143 first published online Dec 28, 2010 doi:10.1093/cid/ciq143

19 Davidson et al. New onset diabetes after transplantation: 2003 International Consensus Guidelines. Transplantation 2003:75;10

20 Marchetti, P. New-Onset Diabetes after transplantation. J Heart Lung Transplantation 2004;23:S104-201

21 Ponticelli, C & Passerini, P. Gastrointestinal complications in renal transplant recipients. Transplant International 2005;18:643-650.

22 Ojo, A.O. **Renal disease** in recipients of **nonrenal** solid organ transplantation. Semin Nephrol. 2007; 27(4): 498-507

23 Park, JM & Luan FL. Management of hypertension in solid-organ transplantation. Progress in Transplantation 2005;15(1):17-23.
Dunn BL, Teusink AC, Taber DJ, et al; Management of hypertension in renal transplant patients: a comprehensive review of nonpharmacologic and pharmacologic treatment strategies. Ann Pharmacother. 2010 Jul-Aug;44(7-8):1259-70.

24 Orens, JB & Garrity, ER. Lung Transplantation and Organ Allocation. Proc Am Thorac Soc. 2009;6:13-19
Thabut Gabriel; Christie Jason D.; Kremers Walter K.; et al. **Survival Differences Following Lung Transplantation** Among US Transplant Centers. JAMA. 2010;304(1):53-60.
Mascia Luciana, Pasero Daniela, Slutsky Arthur S., et al. Preliminary Communication Effect of a **Lung Protective Strategy** for Organ Donors on Eligibility and Availability of Lungs for Transplantation: A Randomized Controlled Trial. *JAMA*. 2010;304(23):2620-2627.doi:10.1001/jama.2010.1796.

25 Simonson SG et al. Rosuvastatin pharmacokinetics in heart transplant recipients administered an antirejection regimen including cyclosporine. Clin Pharmacol Ther. 2004 Aug;76(2):167-77.

26. Lichtenstein GR, Abreu MT, Cohen R, Tremaine W; American Gastroenterological Association. American Gastroenterological Association Institute technical review on corticosteroids, immunomodulators, and infliximab in inflammatory bowel disease. Gastroenterology. 2006 Mar;130(3):940-87.

27. Stamp L, Searle M, O'Donnell J, Chapman P. Gout in solid organ transplantation: a challenging clinical problem. Drugs. 2005;65(18):2593-611.

28. Navaneethan SD, Perkovic V, Johnson DW, Nigwekar SU, Craig JC, Strippoli GF. HMG CoA reductase inhibitors (statins) for kidney transplant recipients. Cochrane Database Syst Rev. 2009 Apr 15;(2):CD005019.
Riella LV, Gabardi S, Chandraker A. Dyslipidemia and Its Therapeutic Challenges in Renal Transplantation. Am J Transplant. 2012 May 11.

29. Burton JR, Burton I, Pearson GJ. Clopidogrel-precipitated rhabdomyolysis in a stable heart transplant patient. Ann Pharmacother. 2007 Jan;41(1):133-7. Epub 2007 Jan 2.

30. Mascia Luciana, Pasero Daniela, Slutsky Arthur S., et al. Preliminary Communication Effect of a **Lung Protective Strategy** for Organ Donors on Eligibility and Availability of Lungs for Transplantation: A Randomized Controlled Trial. *JAMA*. 2010;304(23):2620-2627.doi:10.1001/jama.2010.1796.

31. Torpy Janet M., Lynm Cassio, Golub Robert M.. JAMA **Patient Page : Kidney Transplantation**. *JAMA*. 2011;305(6):634.doi:10.1001/jama.305.6.634.

32. Pavlakis Martha. **Live Kidney Donation**: A 36-Year-Old Woman Hoping to Donate a Kidney **to Her Mother**. *JAMA*. 2011;305(6):592-599.Published online January 18, 2011. doi:10.1001/jama.2011.56.

33. Vitale A, Ramirez MR, Zanus G, et al, on behalf of the Italian Liver Cancer group. Barcelona Clinic Liver Cancer staging and transplant survival benefi t for patients with **hepatocellular carcinoma**: a multicentre, cohort study. Lancet Oncol 2011.

34. Trappe R, Oertel S, Leblond V, et al, for the German PTLD Study Group and the European **PTLD** Network. Sequential treatment with rituximab followed by CHOP chemotherapy in adult B-cell post-transplant lymphoproliferative disorder (PTLD): the prospective international multicentre phase 2 PTLD-1 trial. Lancet Oncol 2011; online Dec 13.
35. Kharfan-Dabaja MA, et al. A novel therapeutic **cytomegalovirus DNA vaccine (TransVax)** in allogeneic haemopoietic stem-cell transplantation: randomised, double-blind, placebo-controlled, phase 2 trial. Lancet Infect Dis 2012; online Jan 10.
36. Deshpande NA, James NT, Kucirka LM, et al. **Pregnancy outcomes in liver transplant** recipients: a systematic review and meta-analysis. Liver Transpl 2012;18:621–629.
37. Vos R, Vanaudenaerde BM, Verleden SE, et al. Antiinflammatory and Immunomodulatory Properties of **Azithromycin** Involved in Treatment and Prevention of Chronic Lung Allograft Rejection.Transplantation. 2012 Mar 28.
38. Vos R, Vanaudenaerde BM, Ottevaere A, Verleden SE, et al. Long-term azithromycin therapy for bronchiolitis obliterans syndrome: divide and conquer?J Heart Lung Transplant. 2010 Dec;29(12):1358-68.
Vos R, Vanaudenaerde BM, Verleden SE, et al. A randomised controlled trial of azithromycin to prevent chronic rejection after lung transplantation. Eur Respir J. 2011 Jan;37(1):164-72.
Bergeron A, Chevret S, Granata A, et al. Effect of Azithromycin on Airflow Decline-Free Survival After Allogeneic Hematopoietic Stem Cell Transplant: The ALLOZITHRO Randomized Clinical Trial. JAMA. 2017 Aug 8;318(6):557-566.
39. Lentine KL, Costa SP, Weir MR, et al; on behalf of the American Heart Association (**AHA**) Council on the Kidney in Cardiovascular Disease and Council on Peripheral Vascular Disease. **Cardiac Disease Evaluation** and Management Among **Kidney and Liver Transplantation Candidates**: A Scientific Statement From the American Heart Association and the American College of Cardiology Foundation. Circulation. 2012 Jul 2.
40. FDA has approved a test to help gauge the progress of cytomegalovirus (CMV) antiviral therapy in solid-organ transplant recipients. The **COBAS AmpliPrep/COBAS TaqMan CMV test** measures the patient's viral load by determining the amount of CMV nucleic acid present in the plasma. The test is intended to monitor treatment efficacy, and is not approved for CMV screening or diagnosis.
41. Lentine KL, Costa SP, Weir MR et al; American Heart Association Council on the Kidney in Cardiovascular Disease and Council on Peripheral Vascular Disease. **Cardiac disease evaluation and management among kidney and liver transplantation** candidates: a scientific statement from the american heart association and the american college of cardiology foundation. J Am Coll Cardiol. 2012 Jul 31;60(5):434-80.
42. Kilic A, Merlo CA, Conte JV, Shah AS. **Lung transplantation in patients 70 years** old or older: Have outcomes changed after implementation of the lung allocation score? J Thorac Cardiovasc Surg. 2012 Nov;144(5):1133-8.
43. Starling RC. Advanced heart failure: **Transplantation, LVADs**, and beyond. Cleve Clin J Med. 2013 Jan;80(1):33-40.
44. Halpern SD. Turning wrong into right: the 2013 **lung allocation** controversy. Ann Intern Med. 2013 Sep 3;159(5):358-9.
45. Sorensen LG, et al; Studies of Pediatric Liver Transplantation (SPLIT) Research Group and the Functional Outcomes Group (FOG). Longitudinal Study of **Cognitive and Academic Outcomes** after Pediatric Liver Transplantation. J Pediatr. 2014May3.
46. Woillard J, Lebreton V, Neely M, et al. Pharmacokinetic tools for the dose adjustment of **cyclosporine in Hematopoietic Stem Cell transplant** patients. Br J Clin Pharmacol. 2014 Apr 2.